

On-line Only Supplemental Material for:

**Validity and Reliability of the U.S. National Cancer Institute's Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)**

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**eFigure 1.** Participant Flow Diagram (N=1,100)

**eFigure 2.** Distribution of PRO-CTCAE Item Scores at Visit 1

**eFigure 3.** Mean PRO-CTCAE Item Scores by Eastern Cooperative Oncology Group (ECOG) Performance Status Score, for PRO-CTCAE Frequency, Severity, and Interference Items at Visit 1

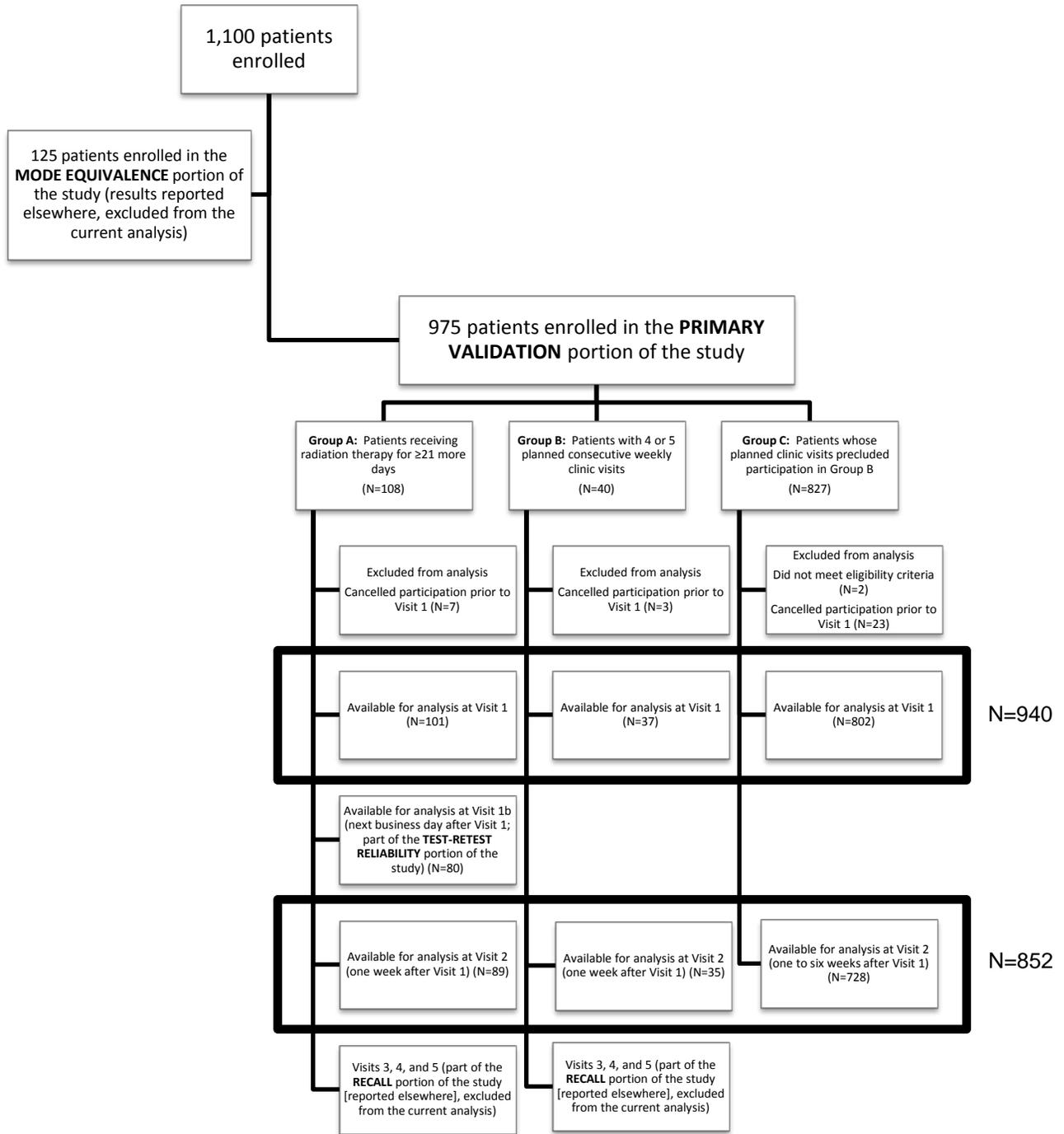
**eTable 1.** PRO-CTCAE Symptomatic AEs by Electronic Survey

**eTable 2.** PRO-CTCAE Symptomatic AEs by Analysis

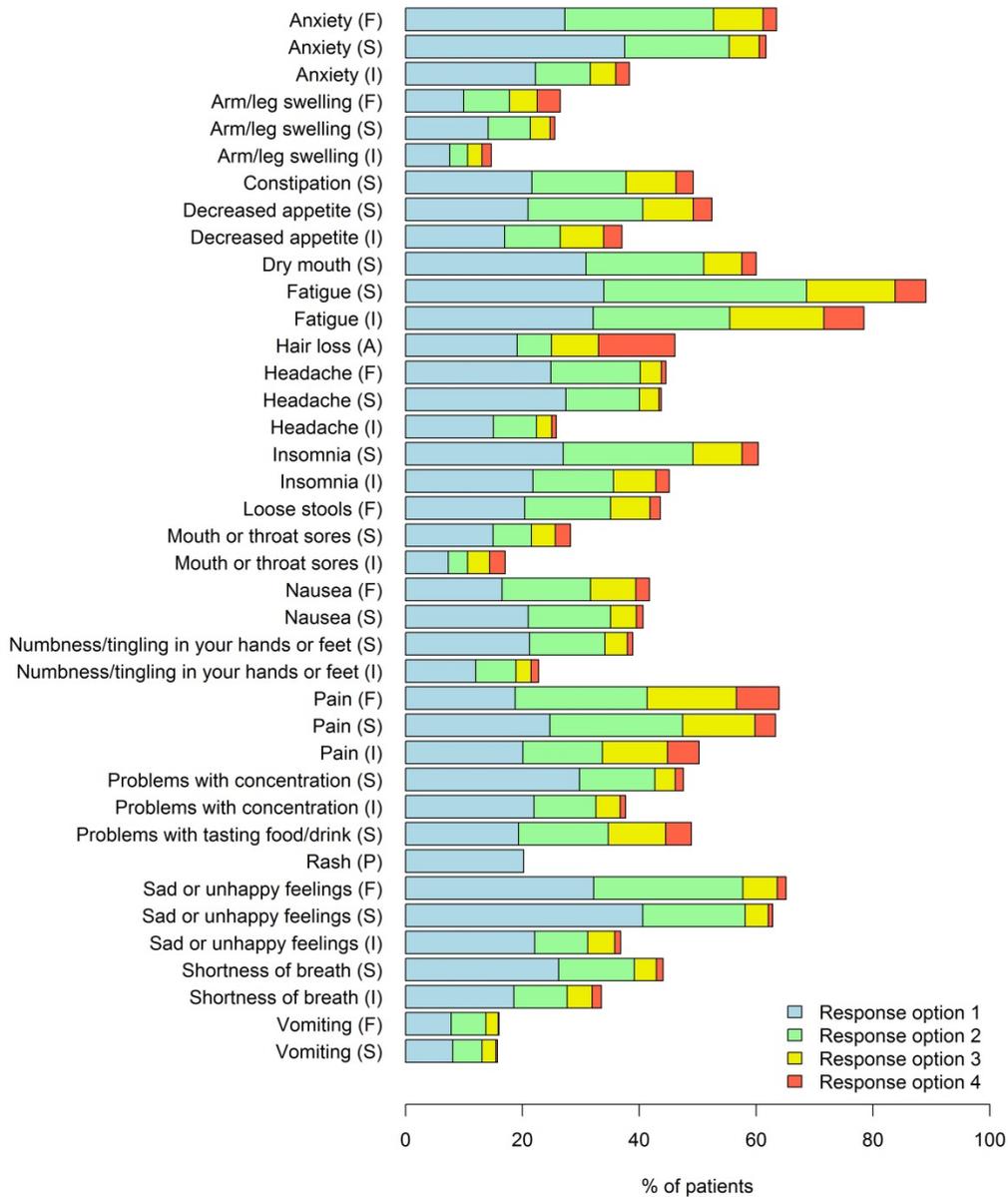
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**eFigure 1.** Participant Flow Diagram (N=1,100)



**eFigure 2.** Distribution of PRO-CTCAE Item Scores at Visit 1†



**Abbreviations:** PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; F, Frequency; S, Severity; I, Interference with usual or daily activities; A, Amount; P, Presence

†eFigure 2 includes items for the 20 “core” symptomatic AEs selected a priori based on high prevalence in prior National Cancer Institute sponsored clinical trials.

**Response options:**

Frequency: 0=“Never”, 1=“Rarely”, 2=“Occasionally”, 3=“Frequently”, 4=“Almost constantly”

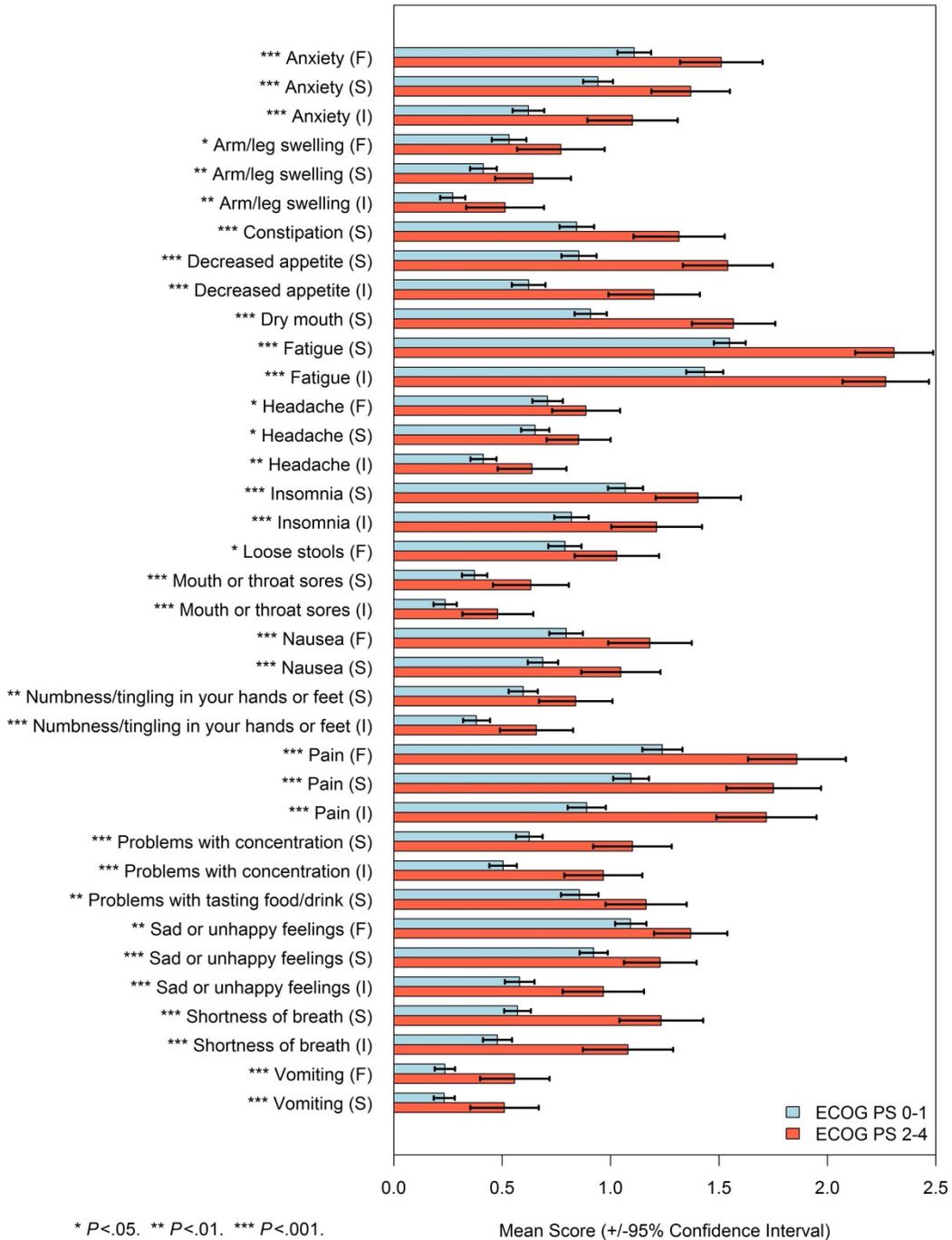
Severity: 0=“None”, 1=“Mild”, 2=“Moderate”, 3=“Severe”, 4=“Very severe”

Interference: 0=“Not at all”, 1=“A little bit”, 2=“Somewhat”, 3=“Quite a bit”, 4=“Very much”

Presence: 0=“No”, 1=“Yes”

Amount: 0=“Not at all”, 1=“A little bit”, 2=“Somewhat”, 3=“Quite a bit”, 4=“Very much”

**eFigure 3.** Mean PRO-CTCAE Item Scores by Eastern Cooperative Oncology Group (ECOG) Performance Status Score, for PRO-CTCAE Frequency, Severity, and Interference Items at Visit 1†



**Abbreviations:** PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; PS, Performance status; F, Frequency; S, Severity; I, Interference with usual or daily activities

†eFigure 3 includes frequency, severity, and interference items for the 20 “core” symptomatic AEs selected a priori based on high prevalence in prior National Cancer Institute sponsored clinical trials. Numerical data for ECOG PS comparisons appear in eTable 3 for all PRO-CTCAE items at both visits.

**eTable 1.** PRO-CTCAE Symptomatic AEs by Electronic Survey

| PRO-CTCAE Symptomatic AE Term               | Surveys Based on Cancer Type |                          |                          |             |                   |                                 |                           | Survey for all patients after 80% were accrued |
|---|------------------------------|--------------------------|--------------------------|-------------|-------------------|---------------------------------|---------------------------|--|
|   | Breast Survey                | Lymphoma/ Myeloma Survey | Prostate/ Bladder Survey | Lung Survey | Colorectal Survey | Head/Neck and Esophageal Survey | Other Disease Site Survey |  |
| Anxiety                                     | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Arm/leg swelling                            | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Constipation                                | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Decreased appetite                          | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Dry mouth                                   | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Fatigue                                     | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Hair loss                                   | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Headache                                    | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Insomnia                                    | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Loose stools                                | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Mouth or throat sores                       | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Nausea                                      | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Numbness/tingling in your hands or feet     | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Pain  | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Problems with concentration                 | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Problems with tasting food/drink            | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Rash  | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Sad or unhappy feelings                     | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Shortness of breath                         | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Vomiting                                    | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |
| Aching joints                               | X                            | X                        | X                        |             |                   |                                 |                           | X  |
| Aching muscles                              |                              | X                        | X                        |             |                   |                                 |                           | X  |
| Acne  | X                            |                          |                          | X           |                   |                                 |                           | X  |
| Bed sores                                   |                              |                          |                          | X           | X                 |                                 |                           | X  |
| Bloating                                    |                              |                          |                          | X           | X                 |                                 |                           | X  |
| Blurry vision                               |                              |                          |                          |             | X                 | X                               |                           | X  |
| Body odor                                   |                              | X                        |                          |             | X                 |                                 |                           | X  |
| Breast area enlargement or tenderness       |                              |                          | X                        |             | X                 |                                 |                           | X  |
| Bruise easily                               |                              | X                        |                          | X           |                   |                                 |                           | X  |
| Change in the color of fingernails/toenails | X                            |                          | X                        | X           |                   |                                 |                           | X  |
| Cough                                       |                              |                          | X                        | X           |                   | X                               |                           | X  |
| Decreased sexual interest                   | X                            |                          | X                        |             |                   |                                 |                           | X  |
| Difficulty getting or keeping an erection   |                              | X                        | X                        |             |                   |                                 |                           | X  |
| Difficulty swallowing                       |                              | X                        |                          |             |                   | X                               |                           | X  |
| Dizziness                                   | X                            |                          |                          | X           |                   |                                 |                           | X  |
| Dry skin                                    | X                            |                          |                          | X           |                   |                                 |                           | X  |
| Ejaculation problems                        |                              | X                        | X                        |             |                   |                                 |                           | X  |
| Feelings that nothing could cheer you up    | X                            | X                        | X                        | X           | X                 | X                               | X                         |  |

| PRO-CTCAE<br>Symptomatic AE Term              | Surveys Based on Cancer Type |                                |                                |                |                      |  |                                    | Survey<br>for all<br>patients<br>after<br>80%<br>were<br>accrued |
|---|------------------------------|--------------------------------|--------------------------------|----------------|----------------------|--|------------------------------------|--|
|   | Breast<br>Survey             | Lymphoma/<br>Myeloma<br>Survey | Prostate/<br>Bladder<br>Survey | Lung<br>Survey | Colorectal<br>Survey | Head/Neck<br>and<br>Esophageal<br>Survey | Other<br>Disease<br>Site<br>Survey |  |
| Flashing lights in eyes                       |                              |                                |                                |                | X                    | X  |                                    | X  |
| Frequent urination                            |                              | X                              | X                              |                |                      |  |                                    | X  |
| Hand-foot syndrome                            | X                            |                                |                                | X              | X                    |  |                                    | X  |
| Heartburn                                     |                              | X                              |                                |                |                      | X  |                                    | X  |
| Hiccups                                       |                              |                                |                                | X              | X                    | X  |                                    | X  |
| Hives   | X                            |                                |                                | X              |                      |  |                                    | X  |
| Hoarse voice                                  |                              | X                              |                                |                |                      | X  |                                    | X  |
| Hot flashes                                   | X                            |                                | X                              |                | X                    |  |                                    | X  |
| Increased passing of gas                      |                              |                                |                                | X              | X                    |  |                                    | X  |
| Increased skin sensitivity to<br>sunlight     | X                            |                                |                                | X              |                      |  |                                    | X  |
| Irregular menstrual periods                   | X                            | X                              |                                |                |                      |  |                                    | X  |
| Itchy skin                                    | X                            |                                |                                | X              |                      |  |                                    | X  |
| Lose any fingernails/toenails                 | X                            |                                | X                              | X              |                      |  |                                    | X  |
| Loss of control of bowel<br>movements         |                              |                                | X                              | X              |                      |  |                                    | X  |
| Loss of control of urine                      |                              | X                              | X                              |                |                      |  |                                    | X  |
| Miss an expected menstrual<br>period          | X                            | X                              |                                |                |                      |  |                                    | X  |
| Nosebleeds                                    |                              | X                              |                                | X              |                      |  |                                    | X  |
| Pain during vaginal sex                       | X                            | X                              |                                |                |                      |  |                                    | X  |
| Pain in the abdomen                           |                              |                                |                                | X              | X                    |  |                                    | X  |
| Pain or burning with<br>urination             |                              | X                              | X                              |                |                      |  |                                    | X  |
| Pain/swelling/redness at IV                   | X                            |                                |                                |                | X                    |  |                                    | X  |
| Pounding/racing heartbeat                     | X                            |                                |                                | X              |                      |  |                                    | X  |
| Problems with memory                          | X                            |                                | X                              |                | X                    |  |                                    | X  |
| Ridges/bumps on<br>fingernails/toenails       | X                            |                                | X                              | X              |                      |  |                                    | X  |
| Ringing in ears                               |                              |                                | X                              |                |                      | X  |                                    | X  |
| Shivering or shaking chills                   |                              | X                              |                                |                | X                    |  |                                    | X  |
| Skin burns from radiation                     | X                            | X                              |                                | X              |                      | X  |                                    | X  |
| Skin cracking at the corners<br>of your mouth |                              | X                              |                                |                |                      | X  |                                    | X  |
| Spots/lines/floaters) in eyes                 |                              |                                |                                |                | X                    | X  |                                    | X  |
| Stretch marks                                 |                              | X                              |                                |                | X                    |  |                                    | X  |
| Sudden urges to urinate                       |                              | X                              | X                              |                |                      |  |                                    | X  |
| Took too long to have an<br>orgasm or climax  | X                            | X                              | X                              |                |                      |  |                                    | X  |
| Unable to have an orgasm<br>or climax         | X                            | X                              | X                              |                |                      |  |                                    | X  |
| Unexpected decrease in<br>sweating            | X                            |                                |                                | X              |                      |  |                                    | X  |
| Unexpected or excessive<br>sweating           | X                            |                                | X                              |                | X                    |  |                                    | X  |
| Unusual darkening of the<br>skin              | X                            |                                |                                | X              |                      | X  |                                    | X  |
| Unusual vaginal discharge                     | X                            | X                              |                                |                |                      |  |                                    | X  |

| PRO-CTCAE<br>Symptomatic AE Term | Surveys Based on Cancer Type |                                |                                |                |                      |  |                                    | Survey<br>for all<br>patients<br>after<br>80%<br>were<br>accrued |
|----------------------------------|------------------------------|--------------------------------|--------------------------------|----------------|----------------------|--|------------------------------------|--|
|                                  | Breast<br>Survey             | Lymphoma/<br>Myeloma<br>Survey | Prostate/<br>Bladder<br>Survey | Lung<br>Survey | Colorectal<br>Survey | Head/Neck<br>and<br>Esophageal<br>Survey | Other<br>Disease<br>Site<br>Survey |  |
| Urine color change               |                              | X                              | X                              |                |                      |  |                                    | X  |
| Vaginal dryness                  | X                            | X                              |                                |                |                      |  |                                    | X  |
| Voice changes                    |                              | X                              |                                |                |                      | X  |                                    | X  |
| Watery eyes                      |                              |                                |                                |                | X                    | X  |                                    | X  |
| Wheezing                         |                              |                                | X                              | X              |                      | X  |                                    | X  |

**Abbreviations:** PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; AE, adverse event

**eTable 2.** PRO-CTCAE Symptomatic AEs by Analysis

| PRO-CTCAE Symptomatic AE Term               | Construct validity analyses  |   |  |  | Test-retest reliability | Responsive-ness |
|---|--|---|--|--|-------------------------|-----------------|
|   | Convergent validity analyses   |   | Known-groups validity analyses               |  |                         |                 |
|   | Pearson correlation with QLQ-C30 HRQOL summary and functioning/global scales | Pearson correlation with QLQ-C30 symptom scales | Comparison between ECOG PS 0-1 vs 2-4 groups | Comparison between groups based on cancer type, treatment, or other characteristic |                         |                 |
| Anxiety                                     | X  |   | X  | X  | X                       | X               |
| Arm/leg swelling                            | X  |   | X  |  | X                       |                 |
| Constipation                                | X  | X   | X  | X  | X                       | X               |
| Decreased appetite                          | X  | X   | X  | X  | X                       | X               |
| Dry mouth                                   | X  |   | X  | X  | X                       |                 |
| Fatigue                                     | X  | X   | X  | X  | X                       | X               |
| Hair loss                                   | X  |   | X  | X  | X                       |                 |
| Headache                                    | X  |   | X  |  | X                       |                 |
| Insomnia                                    | X  | X   | X  | X  | X                       | X               |
| Loose stools                                | X  | X   | X  | X  | X                       | X               |
| Mouth or throat sores                       | X  |   | X  | X  | X                       | X               |
| Nausea                                      | X  | X   | X  | X  | X                       | X               |
| Numbness/tingling in your hands or feet     | X  |   | X  | X  | X                       | X               |
| Pain  | X  | X   | X  | X  | X                       | X               |
| Problems with concentration                 | X  |   | X  | X  | X                       |                 |
| Problems with tasting food/drink            | X  |   | X  |  | X                       |                 |
| Rash  | X  |   | X  | X  | X                       |                 |
| Sad or unhappy feelings                     | X  |   | X  | X  | X                       | X               |
| Shortness of breath                         | X  | X   | X  | X  | X                       | X               |
| Vomiting                                    | X  | X   | X  | X  | X                       | X               |
| Aching joints                               | X  |   | X  | X  |                         |                 |
| Aching muscles                              | X  |   | X  |  |                         |                 |
| Acne  | X  |   | X  | X  |                         |                 |
| Bed sores                                   | X  |   | X  |  |                         |                 |
| Bloating                                    | X  |   | X  | X  |                         |                 |
| Blurry vision                               | X  |   | X  |  |                         |                 |
| Body odor                                   | X  |   | X  |  |                         |                 |
| Breast area enlargement or tenderness       | X  |   | X  | X  |                         |                 |
| Bruise easily                               | X  |   | X  |  |                         |                 |
| Change in the color of fingernails/toenails | X  |   | X  |  |                         |                 |
| Cough                                       | X  |   | X  | X  | X                       |                 |
| Decreased sexual interest                   | X  |   | X  |  |                         |                 |
| Difficulty getting or keeping an erection   | X  |   | X  |  |                         |                 |
| Difficulty swallowing                       | X  |   | X  | X  |                         |                 |
| Dizziness                                   | X  |   | X  |  |                         |                 |

| PRO-CTCAE<br>Symptomatic AE Term           | Construct validity analyses  |   |  |  | Test-retest reliability | Responsive-ness |
|--|--|---|--|--|-------------------------|-----------------|
|  | Convergent validity analyses   |   | Known-groups validity analyses               |  |                         |                 |
|  | Pearson correlation with QLQ-C30 HRQOL summary and functioning/global scales | Pearson correlation with QLQ-C30 symptom scales | Comparison between ECOG PS 0-1 vs 2-4 groups | Comparison between groups based on cancer type, treatment, or other characteristic |                         |                 |
| Dry skin                                   | X  |   | X  |  |                         |                 |
| Ejaculation problems                       | X  |   | X  |  |                         |                 |
| Feelings that nothing could cheer you up   | X  |   | X  | X  | X                       |                 |
| Flashing lights in eyes                    | X  |   | X  |  |                         |                 |
| Frequent urination                         | X  |   | X  | X  |                         |                 |
| Hand-foot syndrome                         | X  |   | X  | X  |                         |                 |
| Heartburn                                  | X  |   | X  | X  |                         |                 |
| Hiccups                                    | X  |   | X  | X  | X                       |                 |
| Hives                                      | X  |   | X  | X  |                         |                 |
| Hoarse voice                               | X  |   | X  | X  |                         |                 |
| Hot flashes                                | X  |   | X  | X  |                         |                 |
| Increased passing of gas                   | X  |   | X  | X  |                         |                 |
| Increased skin sensitivity to sunlight     | X  |   | X  |  |                         |                 |
| Irregular menstrual periods                | X  |   | X  | X  |                         |                 |
| Itchy skin                                 | X  |   | X  |  |                         |                 |
| Lose any fingernails/toenails              | X  |   | X  |  |                         |                 |
| Loss of control of bowel movements         | X  |   | X  | X  |                         |                 |
| Loss of control of urine                   | X  |   | X  | X  |                         |                 |
| Miss an expected menstrual period          | X  |   | X  | X  |                         |                 |
| Nosebleeds                                 | X  |   | X  | X  |                         |                 |
| Pain during vaginal sex                    | X  |   | X  | X  |                         |                 |
| Pain in the abdomen                        | X  |   | X  | X  |                         |                 |
| Pain or burning with urination             | X  |   | X  | X  |                         |                 |
| Pain/swelling/redness at IV                | X  |   | X  | X  |                         |                 |
| Pounding/racing heartbeat                  | X  |   | X  |  |                         |                 |
| Problems with memory                       | X  |   | X  | X  |                         |                 |
| Ridges/bumps on fingernails/toenails       | X  |   | X  |  |                         |                 |
| Ringing in ears                            | X  |   | X  | X  |                         |                 |
| Shivering or shaking chills                | X  |   | X  |  |                         |                 |
| Skin burns from radiation                  | X  |   | X  | X  | X                       |                 |
| Skin cracking at the corners of your mouth | X  |   | X  | X  |                         |                 |
| Spots/lines/floaters) in eyes              | X  |   | X  |  |                         |                 |
| Stretch marks                              | X  |   | X  | X  |                         |                 |
| Sudden urges to urinate                    | X  |   | X  | X  |                         |                 |
| Took too long to have an orgasm or climax  | X  |   | X  |  |                         |                 |

| PRO-CTCAE<br>Symptomatic AE Term   | Construct validity analyses  |   |  |  | Test-retest reliability | Responsive-ness |
|------------------------------------|--|---|--|--|-------------------------|-----------------|
|                                    | Convergent validity analyses   |   | Known-groups validity analyses               |  |                         |                 |
|                                    | Pearson correlation with QLQ-C30 HRQOL summary and functioning/global scales | Pearson correlation with QLQ-C30 symptom scales | Comparison between ECOG PS 0-1 vs 2-4 groups | Comparison between groups based on cancer type, treatment, or other characteristic |                         |                 |
| Unable to have an orgasm or climax | X  |   | X  |  |                         |                 |
| Unexpected decrease in sweating    | X  |   | X  |  |                         |                 |
| Unexpected or excessive sweating   | X  |   | X  | X  |                         |                 |
| Unusual darkening of the skin      | X  |   | X  | X  | X                       |                 |
| Unusual vaginal discharge          | X  |   | X  | X  |                         |                 |
| Urine color change                 | X  |   | X  | X  |                         |                 |
| Vaginal dryness                    | X  |   | X  | X  |                         |                 |
| Voice changes                      | X  |   | X  | X  |                         |                 |
| Watery eyes                        | X  |   | X  |  |                         |                 |
| Wheezing                           | X  |   | X  | X  | X                       |                 |

**Abbreviations:** PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire; HRQOL, Health-related quality of life; ECOG, Eastern Cooperative Oncology Group; PS, Performance status



| PRO-CTCAE Item     | Visit | N   | Worse Symptom Level Group                                   | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size*             | EORTC QLQ-C30         | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--------------------|-------|-----|---|----------------------------|----------------------------|------|--------------------------|-----------------------|---------------------|--------------------|------------------|
| Aching muscles (S) | 1     | 227 | ECOG PS 2-4   | ECOG PS 0-1                | 0.48                       | 1.01 | 0.48                     | Physical Functioning  | 0.32                | <0.001             | <0.001           |
| Aching muscles (S) | 1     | 226 |   |                            |                            |      | Role Functioning         | 0.28                  | <0.001              | <0.001             |                  |
| Aching muscles (S) | 1     | 226 |   |                            |                            |      | Emotional Functioning    | 0.21                  | 0.001               | 0.005              |                  |
| Aching muscles (S) | 1     | 226 |   |                            |                            |      | Cognitive Functioning    | 0.25                  | <0.001              | <0.001             |                  |
| Aching muscles (S) | 1     | 226 |   |                            |                            |      | Social Functioning       | 0.25                  | <0.001              | <0.001             |                  |
| Aching muscles (S) | 1     | 226 |   |                            |                            |      | Global Health Status/QoL | 0.27                  | <0.001              | <0.001             |                  |
| Aching muscles (S) | 1     | 224 |   |                            |                            |      | HRQL Summary Score       | 0.40                  | <0.001              | <0.001             |                  |
| Aching muscles (S) | 2     | 201 | ECOG PS 2-4   | ECOG PS 0-1                | 0.19                       | 0.98 | 0.19                     | Physical Functioning  | 0.40                | <0.001             | <0.001           |
| Aching muscles (S) | 2     | 199 |   |                            |                            |      | Role Functioning         | 0.39                  | <0.001              | <0.001             |                  |
| Aching muscles (S) | 2     | 198 |   |                            |                            |      | Emotional Functioning    | 0.20                  | 0.004               | 0.01               |                  |
| Aching muscles (S) | 2     | 198 |   |                            |                            |      | Cognitive Functioning    | 0.27                  | <0.001              | <0.001             |                  |
| Aching muscles (S) | 2     | 197 |   |                            |                            |      | Social Functioning       | 0.30                  | <0.001              | <0.001             |                  |
| Aching muscles (S) | 2     | 198 |   |                            |                            |      | Global Health Status/QoL | 0.31                  | <0.001              | <0.001             |                  |
| Aching muscles (S) | 2     | 195 |   |                            |                            |      | HRQL Summary Score       | 0.47                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 1     | 227 | ECOG PS 2-4   | ECOG PS 0-1                | 0.71                       | 1.09 | 0.65                     | Physical Functioning  | 0.39                | <0.001             | <0.001           |
| Aching muscles (I) | 1     | 226 |   |                            |                            |      | Role Functioning         | 0.38                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 1     | 226 |   |                            |                            |      | Emotional Functioning    | 0.32                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 1     | 226 |   |                            |                            |      | Cognitive Functioning    | 0.28                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 1     | 226 |   |                            |                            |      | Social Functioning       | 0.40                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 1     | 226 |   |                            |                            |      | Global Health Status/QoL | 0.32                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 1     | 224 |   |                            |                            |      | HRQL Summary Score       | 0.49                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 2     | 201 | ECOG PS 2-4   | ECOG PS 0-1                | 0.32                       | 1.05 | 0.31                     | Physical Functioning  | 0.42                | <0.001             | <0.001           |
| Aching muscles (I) | 2     | 199 |   |                            |                            |      | Role Functioning         | 0.42                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 2     | 198 |   |                            |                            |      | Emotional Functioning    | 0.25                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 2     | 198 |   |                            |                            |      | Cognitive Functioning    | 0.32                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 2     | 197 |   |                            |                            |      | Social Functioning       | 0.37                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 2     | 198 |   |                            |                            |      | Global Health Status/QoL | 0.28                  | <0.001              | <0.001             |                  |
| Aching muscles (I) | 2     | 195 |   |                            |                            |      | HRQL Summary Score       | 0.50                  | <0.001              | <0.001             |                  |
| Acne (S)           | 1     | 409 | ECOG PS 2-4   | ECOG PS 0-1                | -0.04                      | 0.66 | -0.06                    | Physical Functioning  | 0.03                | 0.66               | 0.82             |
| Acne (S)           | 1     | 394 | Epidermal growth factor receptor inhibitor in prior 2 weeks | Other                      | 0.41                       | 0.65 | 0.63                     | Role Functioning      | -0.03               | 0.005              | 0.09             |
| Acne (S)           | 1     | 394 |   |                            |                            |      | Emotional Functioning    | 0.06                  | 0.26                | 0.82               |                  |
| Acne (S)           | 1     | 394 |   |                            |                            |      | Cognitive Functioning    | 0.02                  | 0.69                | 0.82               |                  |
| Acne (S)           | 1     | 394 |   |                            |                            |      | Social Functioning       | -0.01                 | 0.79                | 0.82               |                  |
| Acne (S)           | 1     | 394 |   |                            |                            |      | Global Health Status/QoL | 0.07                  | 0.14                | 0.82               |                  |
| Acne (S)           | 1     | 394 |   |                            |                            |      | HRQL Summary Score       | 0.04                  | 0.47                | 0.82               |                  |
| Acne (S)           | 1     | 391 |   |                            |                            |      | Physical Functioning     | 0.02                  | 0.7                 | 0.82               |                  |
| Acne (S)           | 2     | 372 | ECOG PS 2-4   | ECOG PS 0-1                | -0.14                      | 0.68 | -0.20                    | Role Functioning      | 0.03                | 0.22               | 0.82             |
| Acne (S)           | 2     | 372 | Epidermal growth factor receptor inhibitor in prior 2 weeks | Other                      | 0.45                       | 0.67 | 0.67                     | Emotional Functioning | 0.10                | 0.05               | 0.81             |
| Acne (S)           | 2     | 356 |   |                            |                            |      | Cognitive Functioning    | -0.04                 | 0.5                 | 0.82               |                  |
| Acne (S)           | 2     | 356 |   |                            |                            |      | Social Functioning       | 0.03                  | 0.56                | 0.82               |                  |
| Acne (S)           | 2     | 356 |   |                            |                            |      | Global Health Status/QoL | 0.08                  | 0.13                | 0.82               |                  |
| Acne (S)           | 2     | 356 |   |                            |                            |      | HRQL Summary Score       | -0.01                 | 0.82                | 0.82               |                  |
| Anxiety (F)        | 1     | 837 | ECOG PS 2-4   | ECOG PS 0-1                | 0.40                       | 1.07 | 0.38                     | Physical Functioning  | 0.04                | 0.49               | 0.82             |
| Anxiety (F)        | 1     | 837 | Currently taking anxiety med                                | Other                      | 0.79                       | 1.02 | 0.77                     | Role Functioning      | 0.28                | <0.001             | <0.001           |
| Anxiety (F)        | 1     | 821 |   |                            |                            |      | Emotional Functioning    | 0.36                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 1     | 818 |   |                            |                            |      | Cognitive Functioning    | 0.70                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 1     | 818 |   |                            |                            |      | Social Functioning       | 0.42                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 1     | 818 |   |                            |                            |      | Global Health Status/QoL | 0.41                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 1     | 816 |   |                            |                            |      | HRQL Summary Score       | 0.30                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 2     | 778 | ECOG PS 2-4   | ECOG PS 0-1                | 0.36                       | 1.07 | 0.34                     | Physical Functioning  | 0.50                | <0.001             | <0.001           |
| Anxiety (F)        | 2     | 778 | Currently taking anxiety med                                | Other                      | 0.78                       | 1.02 | 0.77                     | Role Functioning      | 0.32                | <0.001             | <0.001           |
| Anxiety (F)        | 2     | 756 |   |                            |                            |      | Emotional Functioning    | 0.32                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 2     | 754 |   |                            |                            |      | Cognitive Functioning    | 0.72                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 2     | 754 |   |                            |                            |      | Social Functioning       | 0.43                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 2     | 753 |   |                            |                            |      | Global Health Status/QoL | 0.35                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 2     | 754 |   |                            |                            |      | HRQL Summary Score       | 0.35                  | <0.001              | <0.001             |                  |
| Anxiety (F)        | 2     | 747 |   |                            |                            |      | Physical Functioning     | 0.49                  | <0.001              | <0.001             |                  |
| Anxiety (S)        | 1     | 837 | ECOG PS 2-4   | ECOG PS 0-1                | 0.43                       | 0.96 | 0.45                     | Role Functioning      | 0.30                | <0.001             | <0.001           |
| Anxiety (S)        | 1     | 837 | Currently taking anxiety med                                | Other                      | 0.65                       | 0.93 | 0.70                     | Emotional Functioning | 0.36                | <0.001             | <0.001           |
| Anxiety (S)        | 1     | 821 |   |                            |                            |      | Physical Functioning     | 0.30                  | <0.001              | <0.001             |                  |
| Anxiety (S)        | 1     | 821 |   |                            |                            |      | Emotional Functioning    | 0.36                  | <0.001              | <0.001             |                  |
| Anxiety (S)        | 1     | 818 |   |                            |                            |      | Role Functioning         | 0.70                  | <0.001              | <0.001             |                  |

| PROCTCAE Item        | Visit | N   | Worse Symptom Level Group    | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|----------------------|-------|-----|------------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Anxiety (S)          | 1     | 818 |                              |                            |                            |      |              |                          | 0.44                | <0.001             | <0.001           |
| Anxiety (S)          | 1     | 818 |                              |                            |                            |      |              | Cognitive Functioning    | 0.42                | <0.001             | <0.001           |
| Anxiety (S)          | 1     | 818 |                              |                            |                            |      |              | Social Functioning       | 0.32                | <0.001             | <0.001           |
| Anxiety (S)          | 1     | 816 |                              |                            |                            |      |              | Global Health Status/QoL | 0.51                | <0.001             | <0.001           |
| Anxiety (S)          | 2     | 778 | ECOG PS 2-4                  | ECOG PS 0-1                | 0.35                       | 0.92 | 0.38         | HRQOL Summary Score      |                     | <0.001             | <0.001           |
| Anxiety (S)          | 2     | 778 | Currently taking anxiety med | Other                      | 0.66                       | 0.89 | 0.75         |                          |                     | <0.001             | <0.001           |
| Anxiety (S)          | 2     | 756 |                              |                            |                            |      |              | Physical Functioning     | 0.34                | <0.001             | <0.001           |
| Anxiety (S)          | 2     | 756 |                              |                            |                            |      |              | Role Functioning         | 0.33                | <0.001             | <0.001           |
| Anxiety (S)          | 2     | 754 |                              |                            |                            |      |              | Emotional Functioning    | 0.70                | <0.001             | <0.001           |
| Anxiety (S)          | 2     | 754 |                              |                            |                            |      |              | Cognitive Functioning    | 0.43                | <0.001             | <0.001           |
| Anxiety (S)          | 2     | 753 |                              |                            |                            |      |              | Social Functioning       | 0.37                | <0.001             | <0.001           |
| Anxiety (S)          | 2     | 754 |                              |                            |                            |      |              | Global Health Status/QoL | 0.38                | <0.001             | <0.001           |
| Anxiety (S)          | 2     | 747 |                              |                            |                            |      |              | HRQOL Summary Score      | 0.52                | <0.001             | <0.001           |
| Anxiety (S)          | 1     | 837 | ECOG PS 2-4                  | ECOG PS 0-1                | 0.48                       | 1.03 | 0.46         |                          |                     | <0.001             | <0.001           |
| Anxiety (I)          | 1     | 837 | Currently taking anxiety med | Other                      | 0.63                       | 1.01 | 0.63         |                          |                     | <0.001             | <0.001           |
| Anxiety (I)          | 1     | 821 |                              |                            |                            |      |              | Physical Functioning     | 0.33                | <0.001             | <0.001           |
| Anxiety (I)          | 1     | 821 |                              |                            |                            |      |              | Role Functioning         | 0.39                | <0.001             | <0.001           |
| Anxiety (I)          | 1     | 818 |                              |                            |                            |      |              | Emotional Functioning    | 0.64                | <0.001             | <0.001           |
| Anxiety (I)          | 1     | 818 |                              |                            |                            |      |              | Cognitive Functioning    | 0.42                | <0.001             | <0.001           |
| Anxiety (I)          | 1     | 818 |                              |                            |                            |      |              | Social Functioning       | 0.49                | <0.001             | <0.001           |
| Anxiety (I)          | 1     | 818 |                              |                            |                            |      |              | Global Health Status/QoL | 0.33                | <0.001             | <0.001           |
| Anxiety (I)          | 1     | 816 |                              |                            |                            |      |              | HRQOL Summary Score      | 0.51                | <0.001             | <0.001           |
| Anxiety (I)          | 2     | 778 | ECOG PS 2-4                  | ECOG PS 0-1                | 0.46                       | 0.97 | 0.47         |                          |                     | <0.001             | <0.001           |
| Anxiety (I)          | 2     | 778 | Currently taking anxiety med | Other                      | 0.59                       | 0.95 | 0.62         |                          |                     | <0.001             | <0.001           |
| Anxiety (I)          | 2     | 756 |                              |                            |                            |      |              | Physical Functioning     | 0.39                | <0.001             | <0.001           |
| Anxiety (I)          | 2     | 756 |                              |                            |                            |      |              | Role Functioning         | 0.39                | <0.001             | <0.001           |
| Anxiety (I)          | 2     | 754 |                              |                            |                            |      |              | Emotional Functioning    | 0.65                | <0.001             | <0.001           |
| Anxiety (I)          | 2     | 754 |                              |                            |                            |      |              | Cognitive Functioning    | 0.43                | <0.001             | <0.001           |
| Anxiety (I)          | 2     | 753 |                              |                            |                            |      |              | Social Functioning       | 0.41                | <0.001             | <0.001           |
| Anxiety (I)          | 2     | 754 |                              |                            |                            |      |              | Global Health Status/QoL | 0.36                | <0.001             | <0.001           |
| Anxiety (I)          | 2     | 747 |                              |                            |                            |      |              | HRQOL Summary Score      | 0.51                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 1     | 827 | ECOG PS 2-4                  | ECOG PS 0-1                | 0.24                       | 1.10 | 0.22         |                          |                     | 0.02               | 0.02             |
| Arm/leg swelling (F) | 1     | 811 |                              |                            |                            |      |              | Physical Functioning     | 0.23                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 1     | 811 |                              |                            |                            |      |              | Role Functioning         | 0.19                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 1     | 808 |                              |                            |                            |      |              | Emotional Functioning    | 0.16                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 1     | 808 |                              |                            |                            |      |              | Cognitive Functioning    | 0.20                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 1     | 808 |                              |                            |                            |      |              | Social Functioning       | 0.13                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 1     | 808 |                              |                            |                            |      |              | Global Health Status/QoL | 0.19                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 1     | 807 |                              |                            |                            |      |              | HRQOL Summary Score      | 0.24                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 2     | 763 | ECOG PS 2-4                  | ECOG PS 0-1                | 0.28                       | 1.07 | 0.26         |                          |                     | 0.01               | 0.02             |
| Arm/leg swelling (F) | 2     | 741 |                              |                            |                            |      |              | Physical Functioning     | 0.22                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 2     | 741 |                              |                            |                            |      |              | Role Functioning         | 0.17                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 2     | 741 |                              |                            |                            |      |              | Emotional Functioning    | 0.19                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 2     | 739 |                              |                            |                            |      |              | Cognitive Functioning    | 0.14                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 2     | 738 |                              |                            |                            |      |              | Social Functioning       | 0.11                | 0.003              | 0.01             |
| Arm/leg swelling (F) | 2     | 739 |                              |                            |                            |      |              | Global Health Status/QoL | 0.17                | <0.001             | <0.001           |
| Arm/leg swelling (F) | 2     | 732 |                              |                            |                            |      |              | HRQOL Summary Score      | 0.20                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 1     | 828 | ECOG PS 2-4                  | ECOG PS 0-1                | 0.23                       | 0.87 | 0.26         |                          |                     | 0.004              | 0.006            |
| Arm/leg swelling (S) | 1     | 812 |                              |                            |                            |      |              | Physical Functioning     | 0.24                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 1     | 812 |                              |                            |                            |      |              | Role Functioning         | 0.18                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 1     | 809 |                              |                            |                            |      |              | Emotional Functioning    | 0.19                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 1     | 809 |                              |                            |                            |      |              | Cognitive Functioning    | 0.20                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 1     | 809 |                              |                            |                            |      |              | Social Functioning       | 0.13                | <0.001             | 0.001            |
| Arm/leg swelling (S) | 1     | 809 |                              |                            |                            |      |              | Global Health Status/QoL | 0.21                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 1     | 807 |                              |                            |                            |      |              | HRQOL Summary Score      | 0.26                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 2     | 763 | ECOG PS 2-4                  | ECOG PS 0-1                | 0.27                       | 0.82 | 0.33         |                          |                     | <0.001             | 0.003            |
| Arm/leg swelling (S) | 2     | 741 |                              |                            |                            |      |              | Physical Functioning     | 0.23                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 2     | 741 |                              |                            |                            |      |              | Role Functioning         | 0.17                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 2     | 739 |                              |                            |                            |      |              | Emotional Functioning    | 0.21                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 2     | 739 |                              |                            |                            |      |              | Cognitive Functioning    | 0.13                | <0.001             | 0.001            |
| Arm/leg swelling (S) | 2     | 738 |                              |                            |                            |      |              | Social Functioning       | 0.10                | 0.006              | 0.006            |
| Arm/leg swelling (S) | 2     | 739 |                              |                            |                            |      |              | Global Health Status/QoL | 0.17                | <0.001             | <0.001           |
| Arm/leg swelling (S) | 2     | 732 |                              |                            |                            |      |              | HRQOL Summary Score      | 0.20                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 1     | 828 | ECOG PS 2-4                  | ECOG PS 0-1                | 0.24                       | 0.84 | 0.29         |                          |                     | 0.002              | 0.003            |
| Arm/leg swelling (I) | 1     | 812 |                              |                            |                            |      |              | Physical Functioning     | 0.25                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 1     | 812 |                              |                            |                            |      |              | Role Functioning         | 0.21                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 1     | 809 |                              |                            |                            |      |              | Emotional Functioning    | 0.23                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 1     | 809 |                              |                            |                            |      |              | Cognitive Functioning    | 0.21                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 1     | 809 |                              |                            |                            |      |              | Social Functioning       | 0.19                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 1     | 809 |                              |                            |                            |      |              | Global Health Status/QoL | 0.22                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 1     | 807 |                              |                            |                            |      |              | HRQOL Summary Score      | 0.29                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 2     | 763 | ECOG PS 2-4                  | ECOG PS 0-1                | 0.18                       | 0.77 | 0.24         |                          |                     | 0.02               | 0.02             |
| Arm/leg swelling (I) | 2     | 741 |                              |                            |                            |      |              | Physical Functioning     | 0.25                | <0.001             | <0.001           |

| PROCTCAE Item        | Visit | N   | Worse Symptom Level Group | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|----------------------|-------|-----|---------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Arm/leg swelling (I) | 2     | 741 |                           |                            |                            |      |              | Role Functioning         | 0.24                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 2     | 739 |                           |                            |                            |      |              | Emotional Functioning    | 0.22                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 2     | 739 |                           |                            |                            |      |              | Cognitive Functioning    | 0.16                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 2     | 739 |                           |                            |                            |      |              | Social Functioning       | 0.17                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 2     | 732 |                           |                            |                            |      |              | Global Health Status/QoL | 0.15                | <0.001             | <0.001           |
| Arm/leg swelling (I) | 2     | 732 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.26                | <0.001             | <0.001           |
| Bed sores (P)        | 1     | 329 | ECOG PS 2-4               | ECOG PS 0-1                | 0.11%                      |      | 0.01         | Physical Functioning     | 0.12                | 0.95               | 0.98             |
| Bed sores (P)        | 1     | 321 |                           |                            |                            |      |              | Role Functioning         | 0.14                | 0.04               | 0.54             |
| Bed sores (P)        | 1     | 321 |                           |                            |                            |      |              | Emotional Functioning    | 0.10                | 0.01               | 0.17             |
| Bed sores (P)        | 1     | 321 |                           |                            |                            |      |              | Cognitive Functioning    | 0.02                | 0.07               | 0.79             |
| Bed sores (P)        | 1     | 321 |                           |                            |                            |      |              | Social Functioning       | 0.09                | 0.77               | 0.98             |
| Bed sores (P)        | 1     | 321 |                           |                            |                            |      |              | Global Health Status/QoL | 0.09                | 0.12               | 0.98             |
| Bed sores (P)        | 1     | 318 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.14                | 0.01               | 0.2              |
| Bed sores (P)        | 2     | 292 | ECOG PS 2-4               | ECOG PS 0-1                | -0.21%                     |      | -0.01        | Physical Functioning     | 0.05                | 0.93               | 0.98             |
| Bed sores (P)        | 2     | 287 |                           |                            |                            |      |              | Role Functioning         | 0.00                | 0.45               | 0.98             |
| Bed sores (P)        | 2     | 287 |                           |                            |                            |      |              | Emotional Functioning    | 0.00                | 0.98               | 0.98             |
| Bed sores (P)        | 2     | 285 |                           |                            |                            |      |              | Cognitive Functioning    | -0.01               | 0.92               | 0.98             |
| Bed sores (P)        | 2     | 285 |                           |                            |                            |      |              | Social Functioning       | -0.01               | 0.83               | 0.98             |
| Bed sores (P)        | 2     | 285 |                           |                            |                            |      |              | Global Health Status/QoL | -0.11               | 0.06               | 0.75             |
| Bed sores (P)        | 2     | 285 |                           |                            |                            |      |              | HRQOL Summary Score      | -0.09               | 0.12               | 0.98             |
| Bed sores (P)        | 2     | 284 |                           |                            |                            |      |              | HRQOL Summary Score      | -0.02               | 0.68               | 0.98             |
| Bloating (F)         | 1     | 332 | ECOG PS 2-4               | ECOG PS 0-1                | 0.10                       | 1.07 | 0.09         | Physical Functioning     | 0.23                | 0.51               | 0.91             |
| Bloating (F)         | 1     | 240 | Gastrointestinal          | Lung/Head/Neck             | 0.43                       | 0.99 | 0.44         | Role Functioning         | 0.26                | 0.005              | 0.02             |
| Bloating (F)         | 1     | 324 |                           |                            |                            |      |              | Emotional Functioning    | 0.20                | <0.001             | <0.001           |
| Bloating (F)         | 1     | 323 |                           |                            |                            |      |              | Cognitive Functioning    | 0.23                | <0.001             | 0.002            |
| Bloating (F)         | 1     | 323 |                           |                            |                            |      |              | Social Functioning       | 0.21                | <0.001             | <0.001           |
| Bloating (F)         | 1     | 323 |                           |                            |                            |      |              | Global Health Status/QoL | 0.14                | 0.01               | 0.06             |
| Bloating (F)         | 1     | 320 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.31                | <0.001             | <0.001           |
| Bloating (F)         | 2     | 292 | ECOG PS 2-4               | ECOG PS 0-1                | -0.02                      | 1.01 | -0.02        | Physical Functioning     | 0.27                | 0.91               | 0.91             |
| Bloating (F)         | 2     | 287 | Gastrointestinal          | Lung/Head/Neck             | 0.24                       | 0.98 | 0.25         | Role Functioning         | 0.31                | 0.13               | 0.39             |
| Bloating (F)         | 2     | 287 |                           |                            |                            |      |              | Emotional Functioning    | 0.28                | <0.001             | <0.001           |
| Bloating (F)         | 2     | 285 |                           |                            |                            |      |              | Cognitive Functioning    | 0.19                | <0.001             | <0.001           |
| Bloating (F)         | 2     | 285 |                           |                            |                            |      |              | Social Functioning       | 0.25                | <0.001             | 0.006            |
| Bloating (F)         | 2     | 285 |                           |                            |                            |      |              | Global Health Status/QoL | 0.20                | <0.001             | <0.001           |
| Bloating (F)         | 2     | 285 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.35                | <0.001             | 0.006            |
| Bloating (F)         | 2     | 284 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.35                | <0.001             | <0.001           |
| Bloating (F)         | 1     | 332 | ECOG PS 2-4               | ECOG PS 0-1                | 0.12                       | 0.89 | 0.14         | Physical Functioning     | 0.22                | 0.32               | 0.62             |
| Bloating (S)         | 1     | 240 | Gastrointestinal          | Lung/Head/Neck             | 0.39                       | 0.84 | 0.46         | Role Functioning         | 0.26                | 0.003              | 0.01             |
| Bloating (S)         | 1     | 324 |                           |                            |                            |      |              | Emotional Functioning    | 0.21                | <0.001             | <0.001           |
| Bloating (S)         | 1     | 323 |                           |                            |                            |      |              | Cognitive Functioning    | 0.22                | <0.001             | <0.001           |
| Bloating (S)         | 1     | 323 |                           |                            |                            |      |              | Social Functioning       | 0.24                | <0.001             | <0.001           |
| Bloating (S)         | 1     | 323 |                           |                            |                            |      |              | Global Health Status/QoL | 0.17                | 0.002              | 0.01             |
| Bloating (S)         | 1     | 320 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.33                | <0.001             | <0.001           |
| Bloating (S)         | 2     | 292 | ECOG PS 2-4               | ECOG PS 0-1                | 0.07                       | 0.84 | 0.08         | Physical Functioning     | 0.21                | 0.62               | 0.62             |
| Bloating (S)         | 2     | 212 | Gastrointestinal          | Lung/Head/Neck             | 0.20                       | 0.84 | 0.24         | Role Functioning         | 0.28                | 0.14               | 0.42             |
| Bloating (S)         | 2     | 287 |                           |                            |                            |      |              | Emotional Functioning    | 0.23                | <0.001             | 0.003            |
| Bloating (S)         | 2     | 287 |                           |                            |                            |      |              | Cognitive Functioning    | 0.17                | <0.001             | <0.001           |
| Bloating (S)         | 2     | 285 |                           |                            |                            |      |              | Social Functioning       | 0.23                | 0.004              | 0.02             |
| Bloating (S)         | 2     | 285 |                           |                            |                            |      |              | Global Health Status/QoL | 0.23                | <0.001             | <0.001           |
| Bloating (S)         | 2     | 285 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.20                | <0.001             | 0.004            |
| Bloating (S)         | 2     | 284 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.29                | <0.001             | <0.001           |
| Blurry vision (S)    | 1     | 270 | ECOG PS 2-4               | ECOG PS 0-1                | 0.21                       | 0.84 | 0.25         | Physical Functioning     | 0.30                | 0.16               | 0.27             |
| Blurry vision (S)    | 1     | 267 |                           |                            |                            |      |              | Role Functioning         | 0.20                | <0.001             | <0.001           |
| Blurry vision (S)    | 1     | 263 |                           |                            |                            |      |              | Emotional Functioning    | 0.26                | <0.001             | 0.005            |
| Blurry vision (S)    | 1     | 263 |                           |                            |                            |      |              | Cognitive Functioning    | 0.45                | <0.001             | <0.001           |
| Blurry vision (S)    | 1     | 263 |                           |                            |                            |      |              | Social Functioning       | 0.26                | <0.001             | <0.001           |
| Blurry vision (S)    | 1     | 263 |                           |                            |                            |      |              | Global Health Status/QoL | 0.25                | <0.001             | <0.001           |
| Blurry vision (S)    | 1     | 261 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.39                | <0.001             | <0.001           |
| Blurry vision (S)    | 2     | 239 | ECOG PS 2-4               | ECOG PS 0-1                | 0.16                       | 0.74 | 0.22         | Physical Functioning     | 0.24                | 0.27               | 0.27             |
| Blurry vision (S)    | 2     | 237 |                           |                            |                            |      |              | Role Functioning         | 0.19                | <0.001             | 0.002            |
| Blurry vision (S)    | 2     | 237 |                           |                            |                            |      |              | Emotional Functioning    | 0.23                | 0.004              | 0.02             |
| Blurry vision (S)    | 2     | 237 |                           |                            |                            |      |              | Cognitive Functioning    | 0.39                | <0.001             | 0.003            |
| Blurry vision (S)    | 2     | 237 |                           |                            |                            |      |              | Social Functioning       | 0.14                | 0.03               | <0.001           |
| Blurry vision (S)    | 2     | 237 |                           |                            |                            |      |              | Global Health Status/QoL | 0.13                | 0.046              | 0.14             |

| PRO-CTCAE Item                                  | Visit | N   | Worse Symptom Level Group | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30 HRQL Summary Score | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|---|-------|-----|---------------------------|----------------------------|----------------------------|------|--------------|----------------------------------|---------------------|--------------------|------------------|
| Blurry vision (S)                               | 2     | 237 | ECOG PS 2-4               | ECOG PS 0-1                | 0.29                       | 0.83 | 0.36         | HRQL Summary Score               | 0.32                | <0.001             | <0.001           |
| Blurry vision (I)                               | 1     | 270 |                           |                            |                            |      |              | Physical Functioning             | 0.26                | 0.048              | 0.14             |
| Blurry vision (I)                               | 1     | 267 |                           |                            |                            |      |              | Role Functioning                 | 0.18                | <0.001             | <0.001           |
| Blurry vision (I)                               | 1     | 267 |                           |                            |                            |      |              | Emotional Functioning            | 0.23                | 0.003              | 0.02             |
| Blurry vision (I)                               | 1     | 263 |                           |                            |                            |      |              | Cognitive Functioning            | 0.41                | <0.001             | 0.002            |
| Blurry vision (I)                               | 1     | 263 |                           |                            |                            |      |              | Social Functioning               | 0.29                | <0.001             | <0.001           |
| Blurry vision (I)                               | 1     | 263 |                           |                            |                            |      |              | Global Health Status/QoL         | 0.19                | <0.001             | <0.001           |
| Blurry vision (I)                               | 1     | 261 |                           |                            |                            |      |              | HRQL Summary Score               | 0.35                | <0.001             | <0.001           |
| Blurry vision (I)                               | 2     | 239 | ECOG PS 2-4               | ECOG PS 0-1                | 0.09                       | 0.69 | 0.13         | Physical Functioning             | 0.19                | 0.51               | 0.51             |
| Blurry vision (I)                               | 2     | 237 |                           |                            |                            |      |              | Role Functioning                 | 0.16                | 0.003              | 0.02             |
| Blurry vision (I)                               | 2     | 237 |                           |                            |                            |      |              | Emotional Functioning            | 0.25                | 0.01               | 0.046            |
| Blurry vision (I)                               | 2     | 237 |                           |                            |                            |      |              | Cognitive Functioning            | 0.30                | <0.001             | <0.001           |
| Blurry vision (I)                               | 2     | 237 |                           |                            |                            |      |              | Social Functioning               | 0.17                | 0.01               | 0.046            |
| Blurry vision (I)                               | 2     | 237 |                           |                            |                            |      |              | Global Health Status/QoL         | 0.11                | 0.09               | 0.19             |
| Blurry vision (I)                               | 2     | 237 |                           |                            |                            |      |              | HRQL Summary Score               | 0.30                | <0.001             | <0.001           |
| Body odor (S)                                   | 1     | 200 | ECOG PS 2-4               | ECOG PS 0-1                | 0.16                       | 0.45 | 0.35         | Physical Functioning             | 0.20                | 0.005              | 0.62             |
| Body odor (S)                                   | 1     | 199 |                           |                            |                            |      |              | Role Functioning                 | 0.13                | 0.005              | 0.07             |
| Body odor (S)                                   | 1     | 199 |                           |                            |                            |      |              | Emotional Functioning            | 0.09                | 0.08               | 0.83             |
| Body odor (S)                                   | 1     | 199 |                           |                            |                            |      |              | Cognitive Functioning            | 0.21                | 0.21               | 0.91             |
| Body odor (S)                                   | 1     | 199 |                           |                            |                            |      |              | Social Functioning               | 0.09                | 0.23               | 0.91             |
| Body odor (S)                                   | 1     | 199 |                           |                            |                            |      |              | Global Health Status/QoL         | 0.16                | 0.02               | 0.34             |
| Body odor (S)                                   | 1     | 199 |                           |                            |                            |      |              | HRQL Summary Score               | 0.23                | 0.046              | 0.59             |
| Body odor (S)                                   | 2     | 176 | ECOG PS 2-4               | ECOG PS 0-1                | -0.01                      | 0.30 | -0.02        | Physical Functioning             | 0.09                | <0.001             | 0.02             |
| Body odor (S)                                   | 2     | 175 |                           |                            |                            |      |              | Role Functioning                 | 0.23                | 0.91               | 0.91             |
| Body odor (S)                                   | 2     | 175 |                           |                            |                            |      |              | Emotional Functioning            | 0.09                | 0.23               | 0.91             |
| Body odor (S)                                   | 2     | 175 |                           |                            |                            |      |              | Cognitive Functioning            | 0.03                | 0.65               | 0.91             |
| Body odor (S)                                   | 2     | 175 |                           |                            |                            |      |              | Social Functioning               | -0.01               | 0.9                | 0.91             |
| Body odor (S)                                   | 2     | 175 |                           |                            |                            |      |              | Global Health Status/QoL         | 0.09                | 0.25               | 0.91             |
| Body odor (S)                                   | 2     | 175 |                           |                            |                            |      |              | HRQL Summary Score               | 0.09                | 0.25               | 0.91             |
| Body odor (S)                                   | 2     | 175 |                           |                            |                            |      |              | HRQL Summary Score               | 0.10                | 0.18               | 0.91             |
| Breast area enlargement or tenderness (S)       | 1     | 241 | ECOG PS 2-4               | ECOG PS 0-1                | -0.22                      | 0.64 | -0.34        | Physical Functioning             | 0.08                | 0.08               | 0.92             |
| Breast area enlargement or tenderness (S)       | 1     | 127 | Prostate                  | Gastrointestinal           | 0.30                       | 0.58 | 0.51         | Role Functioning                 | -0.01               | 0.005              | 0.09             |
| Breast area enlargement or tenderness (S)       | 1     | 240 |                           |                            |                            |      |              | Emotional Functioning            | -0.08               | 0.82               | 0.92             |
| Breast area enlargement or tenderness (S)       | 1     | 240 |                           |                            |                            |      |              | Cognitive Functioning            | 0.05                | 0.22               | 0.92             |
| Breast area enlargement or tenderness (S)       | 1     | 240 |                           |                            |                            |      |              | Social Functioning               | 0.07                | 0.45               | 0.92             |
| Breast area enlargement or tenderness (S)       | 1     | 240 |                           |                            |                            |      |              | Global Health Status/QoL         | -0.03               | 0.3                | 0.92             |
| Breast area enlargement or tenderness (S)       | 1     | 240 |                           |                            |                            |      |              | HRQL Summary Score               | -0.05               | 0.6                | 0.92             |
| Breast area enlargement or tenderness (S)       | 1     | 240 |                           |                            |                            |      |              | HRQL Summary Score               | -0.04               | 0.47               | 0.92             |
| Breast area enlargement or tenderness (S)       | 2     | 213 | ECOG PS 2-4               | ECOG PS 0-1                | -0.18                      | 0.60 | -0.29        | Physical Functioning             | 0.08                | 0.53               | 0.92             |
| Breast area enlargement or tenderness (S)       | 2     | 115 | Prostate                  | Gastrointestinal           | 0.11                       | 0.40 | 0.27         | Role Functioning                 | 0.08                | 0.2                | 0.92             |
| Breast area enlargement or tenderness (S)       | 2     | 211 |                           |                            |                            |      |              | Emotional Functioning            | -0.03               | 0.15               | 0.92             |
| Breast area enlargement or tenderness (S)       | 2     | 211 |                           |                            |                            |      |              | Cognitive Functioning            | -0.12               | 0.62               | 0.92             |
| Breast area enlargement or tenderness (S)       | 2     | 210 |                           |                            |                            |      |              | Social Functioning               | 0.14                | 0.07               | 0.92             |
| Breast area enlargement or tenderness (S)       | 2     | 210 |                           |                            |                            |      |              | Global Health Status/QoL         | 0.18                | 0.04               | 0.63             |
| Breast area enlargement or tenderness (S)       | 2     | 209 |                           |                            |                            |      |              | HRQL Summary Score               | -0.03               | 0.08               | 0.92             |
| Breast area enlargement or tenderness (S)       | 2     | 210 |                           |                            |                            |      |              | HRQL Summary Score               | -0.01               | 0.66               | 0.92             |
| Breast area enlargement or tenderness (S)       | 2     | 207 |                           |                            |                            |      |              | HRQL Summary Score               | -0.01               | 0.92               | 0.92             |
| Bruise easily (P)                               | 1     | 316 | ECOG PS 2-4               | ECOG PS 0-1                | 17.51%                     |      | 0.36         | Physical Functioning             | 0.04                | 0.008              | 0.12             |
| Bruise easily (P)                               | 1     | 308 |                           |                            |                            |      |              | Role Functioning                 | 0.07                | 0.48               | 0.57             |
| Bruise easily (P)                               | 1     | 308 |                           |                            |                            |      |              | Emotional Functioning            | 0.12                | 0.21               | 0.57             |
| Bruise easily (P)                               | 1     | 308 |                           |                            |                            |      |              | Cognitive Functioning            | 0.17                | 0.04               | 0.57             |
| Bruise easily (P)                               | 1     | 308 |                           |                            |                            |      |              | Social Functioning               | 0.03                | 0.003              | 0.06             |
| Bruise easily (P)                               | 1     | 308 |                           |                            |                            |      |              | Global Health Status/QoL         | 0.05                | 0.55               | 0.57             |
| Bruise easily (P)                               | 1     | 305 |                           |                            |                            |      |              | HRQL Summary Score               | 0.09                | 0.41               | 0.57             |
| Bruise easily (P)                               | 2     | 278 | ECOG PS 2-4               | ECOG PS 0-1                | 9.08%                      |      | 0.19         | Physical Functioning             | 0.08                | 0.12               | 0.57             |
| Bruise easily (P)                               | 2     | 273 |                           |                            |                            |      |              | Role Functioning                 | 0.19                | 0.21               | 0.57             |
| Bruise easily (P)                               | 2     | 271 |                           |                            |                            |      |              | Emotional Functioning            | 0.08                | 0.19               | 0.57             |
| Bruise easily (P)                               | 2     | 271 |                           |                            |                            |      |              | Cognitive Functioning            | 0.11                | 0.06               | 0.57             |
| Bruise easily (P)                               | 2     | 271 |                           |                            |                            |      |              | Social Functioning               | 0.09                | 0.15               | 0.57             |
| Bruise easily (P)                               | 2     | 271 |                           |                            |                            |      |              | Global Health Status/QoL         | 0.03                | 0.57               | 0.57             |
| Bruise easily (P)                               | 2     | 271 |                           |                            |                            |      |              | HRQL Summary Score               | 0.06                | 0.31               | 0.57             |
| Bruise easily (P)                               | 2     | 271 |                           |                            |                            |      |              | HRQL Summary Score               | 0.10                | 0.09               | 0.57             |
| Change in the color of fingernails/toenails (P) | 1     | 483 | ECOG PS 2-4               | ECOG PS 0-1                | -6.81%                     |      | -0.19        | Physical Functioning             | 0.07                | 0.2                | 0.71             |
| Change in the color of fingernails/toenails (P) | 1     | 468 |                           |                            |                            |      |              | Role Functioning                 | 0.05                | 0.13               | 0.71             |
| Change in the color of fingernails/toenails (P) | 1     | 468 |                           |                            |                            |      |              | Emotional Functioning            | 0.02                | 0.28               | 0.71             |
| Change in the color of fingernails/toenails (P) | 1     | 468 |                           |                            |                            |      |              | Cognitive Functioning            | 0.12                | 0.71               | 0.71             |
| Change in the color of fingernails/toenails (P) | 1     | 468 |                           |                            |                            |      |              | Social Functioning               | 0.11                | 0.08               | 0.14             |
| Change in the color of fingernails/toenails (P) | 1     | 468 |                           |                            |                            |      |              | Global Health Status/QoL         | 0.12                | 0.02               | 0.34             |

| PRO-CTCAE Item                                  | Visit | N   | Worse Symptom Level Group                | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|---|-------|-----|--|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Change in the color of fingernails/toenails (P) | 1     | 468 |  |                            |                            |      |              | Global Health Status/QoL | 0.08                | 0.09               | 0.71             |
| Change in the color of fingernails/toenails (P) | 1     | 465 |  |                            |                            |      |              | HRQoL Summary Score      | 0.10                | 0.04               | 0.51             |
| Change in the color of fingernails/toenails (P) | 2     | 441 | ECOG PS 2-4                              | ECOG PS 0-1                | -6.96%                     |      | -0.19        | Physical Functioning     | 0.09                | 0.26               | 0.71             |
| Change in the color of fingernails/toenails (P) | 2     | 424 |  |                            |                            |      |              | Role Functioning         | 0.03                | 0.51               | 0.71             |
| Change in the color of fingernails/toenails (P) | 2     | 423 |  |                            |                            |      |              | Emotional Functioning    | 0.02                | 0.66               | 0.71             |
| Change in the color of fingernails/toenails (P) | 2     | 423 |  |                            |                            |      |              | Cognitive Functioning    | 0.09                | 0.07               | 0.71             |
| Change in the color of fingernails/toenails (P) | 2     | 422 |  |                            |                            |      |              | Social Functioning       | 0.07                | 0.15               | 0.71             |
| Change in the color of fingernails/toenails (P) | 2     | 423 |  |                            |                            |      |              | Global Health Status/QoL | 0.10                | 0.04               | 0.51             |
| Change in the color of fingernails/toenails (P) | 2     | 416 |  |                            |                            |      |              | HRQoL Summary Score      | 0.07                | 0.14               | 0.71             |
| Constipation (S)                                | 1     | 847 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.47                       | 1.11 | 0.42         | Global Health Status/QoL | 0.08                | <0.001             | <0.001           |
| Constipation (S)                                | 1     | 847 | Laxative in prior week                   | Other                      | 1.03                       | 1.02 | 1.01         | HRQoL Summary Score      | 0.10                | <0.001             | <0.001           |
| Constipation (S)                                | 1     | 847 | Opioid [narcotic] pain med in prior week | Other                      | 0.57                       | 1.09 | 0.52         |                          | 0.25                | 0.005              | 0.01             |
| Constipation (S)                                | 1     | 831 | Surgery in prior 2 weeks                 | Other                      | 0.56                       | 1.12 | 0.50         | Physical Functioning     | 0.25                | <0.001             | <0.001           |
| Constipation (S)                                | 1     | 827 |  |                            |                            |      |              | Role Functioning         | 0.23                | <0.001             | <0.001           |
| Constipation (S)                                | 1     | 827 |  |                            |                            |      |              | Emotional Functioning    | 0.23                | <0.001             | <0.001           |
| Constipation (S)                                | 1     | 827 |  |                            |                            |      |              | Cognitive Functioning    | 0.29                | <0.001             | <0.001           |
| Constipation (S)                                | 1     | 827 |  |                            |                            |      |              | Social Functioning       | 0.25                | <0.001             | <0.001           |
| Constipation (S)                                | 1     | 825 |  |                            |                            |      |              | Global Health Status/QoL | 0.25                | <0.001             | <0.001           |
| Constipation (S)                                | 1     | 830 |  |                            |                            |      |              | HRQoL Summary Score      | 0.42                | <0.001             | <0.001           |
| Constipation (S)                                | 2     | 782 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.31                       | 1.12 | 0.28         | Constipation             | 0.76                | <0.001             | <0.001           |
| Constipation (S)                                | 2     | 782 | Laxative in prior week                   | Other                      | 1.02                       | 1.02 | 0.99         |                          | 0.29                | 0.004              | 0.01             |
| Constipation (S)                                | 2     | 782 | Opioid [narcotic] pain med in prior week | Other                      | 0.51                       | 1.10 | 0.46         | Physical Functioning     | 0.28                | <0.001             | <0.001           |
| Constipation (S)                                | 2     | 760 | Surgery in prior 2 weeks                 | Other                      | 0.36                       | 1.13 | 0.32         | Role Functioning         | 0.28                | <0.001             | <0.001           |
| Constipation (S)                                | 2     | 760 |  |                            |                            |      |              | Emotional Functioning    | 0.27                | <0.001             | <0.001           |
| Constipation (S)                                | 2     | 758 |  |                            |                            |      |              | Cognitive Functioning    | 0.24                | <0.001             | <0.001           |
| Constipation (S)                                | 2     | 757 |  |                            |                            |      |              | Social Functioning       | 0.27                | <0.001             | <0.001           |
| Constipation (S)                                | 2     | 758 |  |                            |                            |      |              | Global Health Status/QoL | 0.30                | <0.001             | <0.001           |
| Constipation (S)                                | 2     | 751 |  |                            |                            |      |              | HRQoL Summary Score      | 0.46                | <0.001             | <0.001           |
| Constipation (S)                                | 2     | 760 |  |                            |                            |      |              | Constipation             | 0.80                | <0.001             | <0.001           |
| Cough (S)                                       | 1     | 455 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.36                       | 0.90 | 0.40         | Physical Functioning     | 0.32                | 0.003              | 0.01             |
| Cough (S)                                       | 1     | 455 | Currently using an inhaler               | Other                      | 0.65                       | 0.88 | 0.74         | Role Functioning         | 0.24                | <0.001             | <0.001           |
| Cough (S)                                       | 1     | 364 | Lung/Head/Neck                           | Prostate/Bladder           | 0.40                       | 0.91 | 0.44         | Emotional Functioning    | 0.25                | <0.001             | <0.001           |
| Cough (S)                                       | 1     | 445 |  |                            |                            |      |              | Cognitive Functioning    | 0.21                | <0.001             | <0.001           |
| Cough (S)                                       | 1     | 442 |  |                            |                            |      |              | Social Functioning       | 0.25                | <0.001             | <0.001           |
| Cough (S)                                       | 1     | 442 |  |                            |                            |      |              | Global Health Status/QoL | 0.25                | <0.001             | <0.001           |
| Cough (S)                                       | 1     | 439 |  |                            |                            |      |              | HRQoL Summary Score      | 0.36                | <0.001             | <0.001           |
| Cough (S)                                       | 2     | 408 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.19                       | 0.87 | 0.22         | Physical Functioning     | 0.27                | 0.15               | 0.15             |
| Cough (S)                                       | 2     | 408 | Currently using an inhaler               | Other                      | 0.45                       | 0.85 | 0.53         | Role Functioning         | 0.12                | <0.001             | 0.03             |
| Cough (S)                                       | 2     | 327 | Lung/Head/Neck                           | Prostate/Bladder           | 0.29                       | 0.86 | 0.34         | Emotional Functioning    | 0.15                | 0.008              | 0.03             |
| Cough (S)                                       | 2     | 401 |  |                            |                            |      |              | Cognitive Functioning    | 0.26                | <0.001             | <0.001           |
| Cough (S)                                       | 2     | 398 |  |                            |                            |      |              | Social Functioning       | 0.21                | 0.01               | 0.03             |
| Cough (S)                                       | 2     | 398 |  |                            |                            |      |              | Global Health Status/QoL | 0.19                | <0.001             | <0.001           |
| Cough (S)                                       | 2     | 398 |  |                            |                            |      |              | HRQoL Summary Score      | 0.33                | <0.001             | <0.001           |
| Cough (S)                                       | 2     | 394 |  |                            |                            |      |              |                          | 0.33                | <0.001             | <0.001           |
| Cough (I)                                       | 1     | 455 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.31                       | 0.86 | 0.36         | Physical Functioning     | 0.31                | 0.007              | 0.007            |
| Cough (I)                                       | 1     | 455 | Currently using an inhaler               | Other                      | 0.38                       | 0.86 | 0.44         | Role Functioning         | 0.29                | <0.001             | 0.006            |
| Cough (I)                                       | 1     | 364 | Lung/Head/Neck                           | Prostate/Bladder           | 0.33                       | 0.87 | 0.38         | Emotional Functioning    | 0.26                | <0.001             | <0.001           |
| Cough (I)                                       | 1     | 445 |  |                            |                            |      |              | Cognitive Functioning    | 0.16                | <0.001             | <0.001           |
| Cough (I)                                       | 1     | 442 |  |                            |                            |      |              | Social Functioning       | 0.25                | <0.001             | <0.001           |
| Cough (I)                                       | 1     | 442 |  |                            |                            |      |              | Global Health Status/QoL | 0.15                | 0.001              | 0.007            |
| Cough (I)                                       | 1     | 439 |  |                            |                            |      |              | HRQoL Summary Score      | 0.30                | <0.001             | <0.001           |
| Cough (I)                                       | 2     | 408 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.43                       | 0.86 | 0.50         | Physical Functioning     | 0.31                | <0.001             | <0.001           |
| Cough (I)                                       | 2     | 408 | Currently using an inhaler               | Other                      | 0.33                       | 0.86 | 0.38         | Role Functioning         | 0.31                | <0.001             | <0.001           |
| Cough (I)                                       | 2     | 327 | Lung/Head/Neck                           | Prostate/Bladder           | 0.38                       | 0.85 | 0.44         | Emotional Functioning    | 0.18                | <0.001             | 0.003            |
| Cough (I)                                       | 2     | 401 |  |                            |                            |      |              | Cognitive Functioning    | 0.14                | 0.007              | 0.007            |
| Cough (I)                                       | 2     | 398 |  |                            |                            |      |              | Social Functioning       | 0.31                | <0.001             | <0.001           |
| Cough (I)                                       | 2     | 397 |  |                            |                            |      |              | Global Health Status/QoL | 0.17                | <0.001             | <0.001           |
| Cough (I)                                       | 2     | 398 |  |                            |                            |      |              | HRQoL Summary Score      | 0.31                | <0.001             | 0.006            |

| PRO-CTCAE Item                                | Visit | N   | Worse Symptom Level Group     | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30 HRQL Summary Score | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|---|-------|-----|-------------------------------|----------------------------|----------------------------|------|--------------|----------------------------------|---------------------|--------------------|------------------|
| Cough (I)                                     | 2     | 394 |                               |                            |                            |      |              |                                  | 0.36                | <0.001             | <0.001           |
| Decreased appetite (S)                        | 1     | 841 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.69                       | 1.12 | 0.61         |                                  |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 1     | 841 | Chemotherapy in prior 2 weeks | Other                      | 0.42                       | 1.13 | 0.37         | Physical Functioning             |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 1     | 825 |                               |                            |                            |      |              | Role Functioning                 |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 1     | 825 |                               |                            |                            |      |              | Emotional Functioning            |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 1     | 822 |                               |                            |                            |      |              | Cognitive Functioning            |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 1     | 822 |                               |                            |                            |      |              | Social Functioning               |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 1     | 822 |                               |                            |                            |      |              | Global Health Status/QoL         |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 1     | 820 |                               |                            |                            |      |              | HRQL Summary Score               |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 1     | 825 |                               |                            |                            |      |              | Appetite Loss                    |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 2     | 778 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.61                       | 1.12 | 0.54         |                                  |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 2     | 778 | Chemotherapy in prior 2 weeks | Other                      | 0.21                       | 1.14 | 0.18         | Physical Functioning             |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 2     | 756 |                               |                            |                            |      |              | Role Functioning                 |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 2     | 756 |                               |                            |                            |      |              | Emotional Functioning            |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 2     | 754 |                               |                            |                            |      |              | Cognitive Functioning            |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 2     | 754 |                               |                            |                            |      |              | Social Functioning               |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 2     | 753 |                               |                            |                            |      |              | Global Health Status/QoL         |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 2     | 747 |                               |                            |                            |      |              | HRQL Summary Score               |                     | <0.001             | <0.001           |
| Decreased appetite (S)                        | 2     | 755 |                               |                            |                            |      |              | Appetite Loss                    |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 840 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.58                       | 1.09 | 0.53         |                                  |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 824 | Chemotherapy in prior 2 weeks | Other                      | 0.42                       | 1.09 | 0.38         | Physical Functioning             |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 824 |                               |                            |                            |      |              | Role Functioning                 |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 821 |                               |                            |                            |      |              | Emotional Functioning            |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 821 |                               |                            |                            |      |              | Cognitive Functioning            |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 821 |                               |                            |                            |      |              | Social Functioning               |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 821 |                               |                            |                            |      |              | Global Health Status/QoL         |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 821 |                               |                            |                            |      |              | HRQL Summary Score               |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 819 |                               |                            |                            |      |              | Appetite Loss                    |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 1     | 824 |                               |                            |                            |      |              |                                  |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 778 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.57                       | 1.08 | 0.52         |                                  |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 778 | Chemotherapy in prior 2 weeks | Other                      | 0.08                       | 1.10 | 0.07         | Physical Functioning             |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 756 |                               |                            |                            |      |              | Role Functioning                 |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 756 |                               |                            |                            |      |              | Emotional Functioning            |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 754 |                               |                            |                            |      |              | Cognitive Functioning            |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 754 |                               |                            |                            |      |              | Social Functioning               |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 753 |                               |                            |                            |      |              | Global Health Status/QoL         |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 754 |                               |                            |                            |      |              | HRQL Summary Score               |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 747 |                               |                            |                            |      |              | Appetite Loss                    |                     | <0.001             | <0.001           |
| Decreased appetite (I)                        | 2     | 755 |                               |                            |                            |      |              |                                  |                     | <0.001             | <0.001           |
| Decreased sexual interest (S)                 | 1     | 321 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.10                       | 1.46 | 0.07         |                                  |                     | 0.74               | 0.95             |
| Decreased sexual interest (S)                 | 1     | 313 |                               |                            |                            |      |              | Physical Functioning             |                     | 0.005              | 0.04             |
| Decreased sexual interest (S)                 | 1     | 313 |                               |                            |                            |      |              | Role Functioning                 |                     | <0.001             | <0.001           |
| Decreased sexual interest (S)                 | 1     | 313 |                               |                            |                            |      |              | Emotional Functioning            |                     | <0.001             | <0.001           |
| Decreased sexual interest (S)                 | 1     | 313 |                               |                            |                            |      |              | Cognitive Functioning            |                     | <0.001             | <0.001           |
| Decreased sexual interest (S)                 | 1     | 313 |                               |                            |                            |      |              | Social Functioning               |                     | <0.001             | <0.001           |
| Decreased sexual interest (S)                 | 1     | 313 |                               |                            |                            |      |              | Global Health Status/QoL         |                     | <0.001             | <0.001           |
| Decreased sexual interest (S)                 | 1     | 311 |                               |                            |                            |      |              | HRQL Summary Score               |                     | <0.001             | <0.001           |
| Decreased sexual interest (S)                 | 2     | 295 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.02                       | 1.40 | 0.01         |                                  |                     | 0.95               | 0.95             |
| Decreased sexual interest (S)                 | 2     | 282 |                               |                            |                            |      |              | Physical Functioning             |                     | 0.02               | 0.11             |
| Decreased sexual interest (S)                 | 2     | 282 |                               |                            |                            |      |              | Role Functioning                 |                     | 0.03               | 0.13             |
| Decreased sexual interest (S)                 | 2     | 283 |                               |                            |                            |      |              | Emotional Functioning            |                     | 0.42               | 0.95             |
| Decreased sexual interest (S)                 | 2     | 283 |                               |                            |                            |      |              | Cognitive Functioning            |                     | 0.11               | 0.26             |
| Decreased sexual interest (S)                 | 2     | 282 |                               |                            |                            |      |              | Social Functioning               |                     | 0.06               | 0.01             |
| Decreased sexual interest (S)                 | 2     | 283 |                               |                            |                            |      |              | Global Health Status/QoL         |                     | 0.002              | 0.01             |
| Decreased sexual interest (S)                 | 2     | 277 |                               |                            |                            |      |              | HRQL Summary Score               |                     | <0.001             | 0.006            |
| Difficulty getting or keeping an erection (S) | 1     | 45  | ECOG PS 2-4                   | ECOG PS 0-1                | 0.15                       | 1.54 | 0.10         |                                  |                     | 0.84               | 0.88             |
| Difficulty getting or keeping an erection (S) | 1     | 45  |                               |                            |                            |      |              | Physical Functioning             |                     | 0.36               | 0.88             |
| Difficulty getting or keeping an erection (S) | 1     | 45  |                               |                            |                            |      |              | Role Functioning                 |                     | 0.19               | 0.88             |
| Difficulty getting or keeping an erection (S) | 1     | 45  |                               |                            |                            |      |              | Emotional Functioning            |                     | 0.19               | 0.88             |
| Difficulty getting or keeping an erection (S) | 1     | 45  |                               |                            |                            |      |              | Cognitive Functioning            |                     | 0.21               | 0.88             |
| Difficulty getting or keeping an erection (S) | 1     | 45  |                               |                            |                            |      |              | Social Functioning               |                     | 0.04               | 0.7              |
| Difficulty getting or keeping an erection (S) | 1     | 45  |                               |                            |                            |      |              | Global Health Status/QoL         |                     | 0.26               | 0.88             |
| Difficulty getting or keeping an erection (S) | 1     | 45  |                               |                            |                            |      |              | HRQL Summary Score               |                     | 0.14               | 0.88             |
| Difficulty getting or keeping an erection (S) | 2     | 40  | ECOG PS 2-4                   | ECOG PS 0-1                | -0.27                      | 1.44 | -0.19        |                                  |                     | 0.76               | 0.88             |
| Difficulty getting or keeping an erection (S) | 2     | 40  |                               |                            |                            |      |              | Physical Functioning             |                     | 0.17               | 0.88             |
| Difficulty getting or keeping an erection (S) | 2     | 40  |                               |                            |                            |      |              | Role Functioning                 |                     | 0.07               | 0.88             |
| Difficulty getting or keeping an erection (S) | 2     | 39  |                               |                            |                            |      |              | Emotional Functioning            |                     | -0.04              | 0.88             |
| Difficulty getting or keeping an erection (S) | 2     | 39  |                               |                            |                            |      |              | Cognitive Functioning            |                     | 0.79               | 0.88             |
| Difficulty getting or keeping an erection (S) | 2     | 39  |                               |                            |                            |      |              | Social Functioning               |                     | 0.27               | 0.88             |
| Difficulty getting or keeping an erection (S) | 2     | 39  |                               |                            |                            |      |              | Global Health Status/QoL         |                     | 0.13               | 0.88             |
| Difficulty getting or keeping an erection (S) | 2     | 39  |                               |                            |                            |      |              | HRQL Summary Score               |                     | 0.24               | 0.88             |

| PRO-CTCAE Item            | Visit | N   | Worse Symptom Level Group                         | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|---------------------------|-------|-----|---|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Difficulty swallowing (S) | 1     | 254 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.19                       | 1.01 | 0.19         |                          |                     | 0.28               | 0.95             |
| Difficulty swallowing (S) | 1     | 254 | Head/Neck with radiation therapy in prior 2 weeks | Other                      | 0.61                       | 0.97 | 0.63         | Physical Functioning     |                     | <0.001             | <0.001           |
| Difficulty swallowing (S) | 1     | 250 |   |                            |                            |      |              | Role Functioning         | 0.14                | 0.03               | 0.13             |
| Difficulty swallowing (S) | 1     | 247 |   |                            |                            |      |              | Emotional Functioning    | 0.25                | <0.001             | <0.001           |
| Difficulty swallowing (S) | 1     | 247 |   |                            |                            |      |              | Cognitive Functioning    | 0.28                | <0.001             | <0.001           |
| Difficulty swallowing (S) | 1     | 247 |   |                            |                            |      |              | Social Functioning       | 0.18                | 0.005              | 0.03             |
| Difficulty swallowing (S) | 1     | 247 |   |                            |                            |      |              | Global Health Status/QoL | 0.24                | <0.001             | 0.001            |
| Difficulty swallowing (S) | 1     | 245 |   |                            |                            |      |              | HRQOL Summary Score      | 0.32                | <0.001             | <0.001           |
| Difficulty swallowing (S) | 2     | 223 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.01                       | 1.02 | 0.01         |                          |                     | 0.95               | 0.95             |
| Difficulty swallowing (S) | 2     | 223 | Head/Neck with radiation therapy in prior 2 weeks | Other                      | 0.86                       | 0.93 | 0.93         | Physical Functioning     |                     | <0.001             | <0.001           |
| Difficulty swallowing (S) | 2     | 221 |   |                            |                            |      |              | Role Functioning         | 0.16                | 0.02               | 0.08             |
| Difficulty swallowing (S) | 2     | 221 |   |                            |                            |      |              | Emotional Functioning    | 0.30                | <0.001             | <0.001           |
| Difficulty swallowing (S) | 2     | 221 |   |                            |                            |      |              | Cognitive Functioning    | 0.23                | <0.001             | 0.004            |
| Difficulty swallowing (S) | 2     | 221 |   |                            |                            |      |              | Social Functioning       | 0.13                | 0.06               | 0.17             |
| Difficulty swallowing (S) | 2     | 221 |   |                            |                            |      |              | Global Health Status/QoL | 0.29                | <0.001             | <0.001           |
| Difficulty swallowing (S) | 2     | 221 |   |                            |                            |      |              | HRQOL Summary Score      | 0.32                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 411 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.40                       | 0.71 | 0.56         | Physical Functioning     |                     | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 396 |   |                            |                            |      |              | Role Functioning         | 0.36                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 396 |   |                            |                            |      |              | Emotional Functioning    | 0.37                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 396 |   |                            |                            |      |              | Cognitive Functioning    | 0.33                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 396 |   |                            |                            |      |              | Social Functioning       | 0.33                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 396 |   |                            |                            |      |              | Global Health Status/QoL | 0.35                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 393 |   |                            |                            |      |              | HRQOL Summary Score      | 0.34                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 373 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0                          | 0.69 | 0            | Physical Functioning     |                     | 0.98               | 0.98             |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Role Functioning         | 0.28                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Emotional Functioning    | 0.35                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Cognitive Functioning    | 0.37                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Social Functioning       | 0.33                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Global Health Status/QoL | 0.35                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | HRQOL Summary Score      | 0.27                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 353 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.41                       | 0.73 | 0.55         | Physical Functioning     |                     | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 411 |   |                            |                            |      |              | Role Functioning         | 0.38                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 396 |   |                            |                            |      |              | Emotional Functioning    | 0.38                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 396 |   |                            |                            |      |              | Cognitive Functioning    | 0.39                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 396 |   |                            |                            |      |              | Social Functioning       | 0.30                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 396 |   |                            |                            |      |              | Global Health Status/QoL | 0.38                | <0.001             | <0.001           |
| Dizziness (S)             | 1     | 393 |   |                            |                            |      |              | HRQOL Summary Score      | 0.31                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 373 | ECOG PS 2-4                                       | ECOG PS 0-1                | -0.02                      | 0.73 | -0.03        | Physical Functioning     |                     | 0.85               | 0.85             |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Role Functioning         | 0.31                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Emotional Functioning    | 0.37                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Cognitive Functioning    | 0.39                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Social Functioning       | 0.32                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | Global Health Status/QoL | 0.35                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 357 |   |                            |                            |      |              | HRQOL Summary Score      | 0.26                | <0.001             | <0.001           |
| Dizziness (S)             | 2     | 353 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.66                       | 1.03 | 0.64         | Physical Functioning     |                     | <0.001             | <0.001           |
| Dry mouth (S)             | 1     | 842 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.46                       | 1.05 | 0.44         | Role Functioning         |                     | <0.001             | <0.001           |
| Dry mouth (S)             | 1     | 826 | Head/Neck with radiation therapy in prior 2 weeks | Other                      |                            |      |              | Emotional Functioning    | 0.36                | <0.001             | <0.001           |
| Dry mouth (S)             | 1     | 826 |   |                            |                            |      |              | Cognitive Functioning    | 0.35                | <0.001             | <0.001           |
| Dry mouth (S)             | 1     | 823 |   |                            |                            |      |              | Social Functioning       | 0.31                | <0.001             | <0.001           |
| Dry mouth (S)             | 1     | 823 |   |                            |                            |      |              | Global Health Status/QoL | 0.30                | <0.001             | <0.001           |
| Dry mouth (S)             | 1     | 823 |   |                            |                            |      |              | HRQOL Summary Score      | 0.32                | <0.001             | <0.001           |
| Dry mouth (S)             | 1     | 821 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.49                       | 1.03 | 0.47         | Physical Functioning     |                     | <0.001             | <0.001           |
| Dry mouth (S)             | 2     | 780 | Head/Neck with radiation therapy in prior 2 weeks | Other                      | 0.69                       | 1.01 | 0.68         | Role Functioning         |                     | <0.001             | <0.001           |
| Dry mouth (S)             | 2     | 758 |   |                            |                            |      |              | Emotional Functioning    | 0.31                | <0.001             | <0.001           |
| Dry mouth (S)             | 2     | 758 |   |                            |                            |      |              | Cognitive Functioning    | 0.34                | <0.001             | <0.001           |
| Dry mouth (S)             | 2     | 756 |   |                            |                            |      |              | Social Functioning       | 0.26                | <0.001             | <0.001           |
| Dry mouth (S)             | 2     | 755 |   |                            |                            |      |              | Global Health Status/QoL | 0.27                | <0.001             | <0.001           |
| Dry mouth (S)             | 2     | 756 |   |                            |                            |      |              | HRQOL Summary Score      | 0.35                | <0.001             | <0.001           |
| Dry mouth (S)             | 2     | 749 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.01                       | 0.91 | 0.01         | Physical Functioning     |                     | <0.001             | <0.001           |
| Dry skin (S)              | 1     | 411 |   |                            |                            |      |              | Role Functioning         | 0.22                | <0.001             | <0.001           |
| Dry skin (S)              | 1     | 396 |   |                            |                            |      |              | Emotional Functioning    | 0.18                | 0.002              | 0.002            |
| Dry skin (S)              | 1     | 396 |   |                            |                            |      |              | Cognitive Functioning    | 0.15                | 0.002              | 0.006            |
| Dry skin (S)              | 1     | 396 |   |                            |                            |      |              | Global Health Status/QoL | 0.18                | <0.001             | 0.001            |

| PRO-CTCAE Item           | Visit | N   | Worse Symptom Level Group          | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--------------------------|-------|-----|------------------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Dry skin (S)             | 1     | 396 |                                    |                            |                            |      |              | Social Functioning       | 0.21                | <0.001             | <0.001           |
| Dry skin (S)             | 1     | 396 |                                    |                            |                            |      |              | Global Health Status/QoL | 0.22                | <0.001             | <0.001           |
| Dry skin (S)             | 1     | 393 |                                    |                            |                            |      |              | HRQL Summary Score       | 0.25                | <0.001             | <0.001           |
| Dry skin (S)             | 2     | 374 | ECOG PS 2-4                        | ECOG PS 0-1                | 0.13                       | 0.91 | 0.14         |                          |                     | 0.38               | 0.77             |
| Dry skin (S)             | 2     | 368 |                                    |                            |                            |      |              | Physical Functioning     | 0.29                | <0.001             | <0.001           |
| Dry skin (S)             | 2     | 358 |                                    |                            |                            |      |              | Role Functioning         | 0.28                | <0.001             | <0.001           |
| Dry skin (S)             | 2     | 358 |                                    |                            |                            |      |              | Emotional Functioning    | 0.31                | <0.001             | <0.001           |
| Dry skin (S)             | 2     | 358 |                                    |                            |                            |      |              | Cognitive Functioning    | 0.26                | <0.001             | <0.001           |
| Dry skin (S)             | 2     | 358 |                                    |                            |                            |      |              | Social Functioning       | 0.31                | <0.001             | <0.001           |
| Dry skin (S)             | 2     | 358 |                                    |                            |                            |      |              | Global Health Status/QoL | 0.26                | <0.001             | <0.001           |
| Dry skin (S)             | 2     | 354 |                                    |                            |                            |      |              | HRQL Summary Score       | 0.37                | <0.001             | <0.001           |
| Ejaculation problems (F) | 1     | 75  | ECOG PS 2-4                        | ECOG PS 0-1                | -0.77                      | 1.68 | -0.46        |                          |                     | 0.29               | 0.96             |
| Ejaculation problems (F) | 1     | 75  |                                    |                            |                            |      |              | Physical Functioning     | 0.20                | 0.08               | 0.96             |
| Ejaculation problems (F) | 1     | 75  |                                    |                            |                            |      |              | Role Functioning         | 0.26                | 0.02               | 0.35             |
| Ejaculation problems (F) | 1     | 75  |                                    |                            |                            |      |              | Emotional Functioning    | 0.09                | 0.45               | 0.96             |
| Ejaculation problems (F) | 1     | 75  |                                    |                            |                            |      |              | Cognitive Functioning    | -0.01               | 0.96               | 0.96             |
| Ejaculation problems (F) | 1     | 75  |                                    |                            |                            |      |              | Social Functioning       | 0.18                | 0.13               | 0.96             |
| Ejaculation problems (F) | 1     | 75  |                                    |                            |                            |      |              | Global Health Status/QoL | 0.11                | 0.34               | 0.96             |
| Ejaculation problems (F) | 1     | 75  |                                    |                            |                            |      |              | HRQL Summary Score       | 0.14                | 0.24               | 0.96             |
| Ejaculation problems (F) | 2     | 61  | ECOG PS 2-4                        | ECOG PS 0-1                | -0.98                      | 1.59 | -0.62        |                          |                     | 0.19               | 0.96             |
| Ejaculation problems (F) | 2     | 61  |                                    |                            |                            |      |              | Physical Functioning     | 0.27                | 0.04               | 0.54             |
| Ejaculation problems (F) | 2     | 60  |                                    |                            |                            |      |              | Role Functioning         | 0.26                | 0.046              | 0.64             |
| Ejaculation problems (F) | 2     | 60  |                                    |                            |                            |      |              | Emotional Functioning    | 0.11                | 0.42               | 0.96             |
| Ejaculation problems (F) | 2     | 60  |                                    |                            |                            |      |              | Cognitive Functioning    | 0.10                | 0.44               | 0.96             |
| Ejaculation problems (F) | 2     | 60  |                                    |                            |                            |      |              | Social Functioning       | 0.16                | 0.22               | 0.96             |
| Ejaculation problems (F) | 2     | 60  |                                    |                            |                            |      |              | Global Health Status/QoL | 0.08                | 0.53               | 0.96             |
| Ejaculation problems (F) | 2     | 59  |                                    |                            |                            |      |              | HRQL Summary Score       | 0.22                | 0.1                | 0.96             |
| Fatigue (S)              | 1     | 878 | ECOG PS 2-4                        | ECOG PS 0-1                | 0.76                       | 1.03 | 0.74         |                          |                     | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 878 | Chemotherapy in prior 2 weeks      | Other                      | 0.17                       | 1.06 | 0.16         |                          |                     | 0.02               | 0.1              |
| Fatigue (S)              | 1     | 878 | Currently taking anxiety med       | Other                      | 0.38                       | 1.05 | 0.36         |                          |                     | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 878 | Radiation therapy in prior 2 weeks | Other                      | 0.02                       | 1.07 | 0.02         |                          |                     | 0.81               | 0.89             |
| Fatigue (S)              | 1     | 878 | Sleep aid in prior week            | Other                      | 0.39                       | 1.05 | 0.37         |                          |                     | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 878 | Surgery in prior 2 weeks           | Other                      | -0.03                      | 1.07 | -0.02        |                          |                     | 0.89               | 0.89             |
| Fatigue (S)              | 1     | 861 |                                    |                            |                            |      |              | Physical Functioning     | 0.59                | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 861 |                                    |                            |                            |      |              | Role Functioning         | 0.60                | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 858 |                                    |                            |                            |      |              | Emotional Functioning    | 0.46                | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 858 |                                    |                            |                            |      |              | Cognitive Functioning    | 0.46                | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 858 |                                    |                            |                            |      |              | Social Functioning       | 0.53                | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 858 |                                    |                            |                            |      |              | Global Health Status/QoL | 0.56                | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 855 |                                    |                            |                            |      |              | HRQL Summary Score       | 0.72                | <0.001             | <0.001           |
| Fatigue (S)              | 1     | 861 |                                    |                            |                            |      |              | Fatigue                  | 0.76                | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 813 | ECOG PS 2-4                        | ECOG PS 0-1                | 0.63                       | 1.00 | 0.63         |                          |                     | 0.28               | 0.89             |
| Fatigue (S)              | 2     | 813 | Chemotherapy in prior 2 weeks      | Other                      | 0.08                       | 1.02 | 0.08         |                          |                     | 0.03               | 0.02             |
| Fatigue (S)              | 2     | 813 | Currently taking anxiety med       | Other                      | 0.25                       | 1.02 | 0.24         |                          |                     | 0.81               | 0.89             |
| Fatigue (S)              | 2     | 813 | Radiation therapy in prior 2 weeks | Other                      | 0.02                       | 1.03 | 0.02         |                          |                     | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 813 | Sleep aid in prior week            | Other                      | 0.48                       | 1.01 | 0.47         |                          |                     | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 813 | Surgery in prior 2 weeks           | Other                      | 0.31                       | 1.02 | 0.30         |                          |                     | 0.15               | 0.76             |
| Fatigue (S)              | 2     | 790 |                                    |                            |                            |      |              | Physical Functioning     | 0.60                | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 788 |                                    |                            |                            |      |              | Role Functioning         | 0.59                | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 788 |                                    |                            |                            |      |              | Emotional Functioning    | 0.43                | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 788 |                                    |                            |                            |      |              | Cognitive Functioning    | 0.44                | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 787 |                                    |                            |                            |      |              | Social Functioning       | 0.53                | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 788 |                                    |                            |                            |      |              | Global Health Status/QoL | 0.55                | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 781 |                                    |                            |                            |      |              | HRQL Summary Score       | 0.69                | <0.001             | <0.001           |
| Fatigue (S)              | 2     | 790 |                                    |                            |                            |      |              | Fatigue                  | 0.73                | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 875 | ECOG PS 2-4                        | ECOG PS 0-1                | 0.83                       | 1.18 | 0.71         |                          |                     | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 875 | Chemotherapy in prior 2 weeks      | Other                      | 0.20                       | 1.22 | 0.17         |                          |                     | 0.01               | 0.09             |
| Fatigue (I)              | 1     | 875 | Currently taking anxiety med       | Other                      | 0.50                       | 1.20 | 0.42         |                          |                     | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 875 | Radiation therapy in prior 2 weeks | Other                      | 0.10                       | 1.22 | 0.08         |                          |                     | 0.24               | 0.73             |
| Fatigue (I)              | 1     | 875 | Sleep aid in prior week            | Other                      | 0.47                       | 1.21 | 0.39         |                          |                     | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 875 | Surgery in prior 2 weeks           | Other                      | -0.05                      | 1.22 | -0.04        |                          |                     | 0.82               | 0.82             |
| Fatigue (I)              | 1     | 858 |                                    |                            |                            |      |              | Physical Functioning     | 0.61                | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 858 |                                    |                            |                            |      |              | Role Functioning         | 0.65                | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 855 |                                    |                            |                            |      |              | Emotional Functioning    | 0.46                | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 855 |                                    |                            |                            |      |              | Cognitive Functioning    | 0.44                | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 855 |                                    |                            |                            |      |              | Social Functioning       | 0.61                | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 855 |                                    |                            |                            |      |              | Global Health Status/QoL | 0.55                | <0.001             | <0.001           |
| Fatigue (I)              | 1     | 852 |                                    |                            |                            |      |              | HRQL Summary Score       | 0.74                | <0.001             | <0.001           |
| Fatigue (I)              | 2     | 813 | ECOG PS 2-4                        | ECOG PS 0-1                | 0.69                       | 1.16 | 0.60         |                          |                     | <0.001             | <0.001           |
| Fatigue (I)              | 2     | 813 | Chemotherapy in prior 2 weeks      | Other                      | 0.04                       | 1.19 | 0.03         |                          |                     | 0.66               | 0.82             |
| Fatigue (I)              | 2     | 813 | Currently taking anxiety med       | Other                      | 0.42                       | 1.18 | 0.36         |                          |                     | <0.001             | <0.001           |
| Fatigue (I)              | 2     | 813 | Radiation therapy in prior 2 weeks | Other                      | 0.16                       | 1.19 | 0.14         |                          |                     | 0.049              | 0.24             |

| PRO-CTCAE Item                               | Visit | N   | Worse Symptom Level Group       | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--|-------|-----|---------------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Fatigue (I)                                  | 2     | 813 | Sleep aid in prior week         | Other                      | 0.65                       | 1.16 | 0.56         |                          |                     | <0.001             | <0.001           |
| Fatigue (I)                                  | 2     | 813 | Surgery in prior 2 weeks        | Other                      | 0.38                       | 1.19 | 0.32         |                          |                     | 0.13               | 0.54             |
| Fatigue (I)                                  | 2     | 790 |                                 |                            |                            |      |              | Physical Functioning     | 0.59                | <0.001             | <0.001           |
| Fatigue (I)                                  | 2     | 790 |                                 |                            |                            |      |              | Role Functioning         | 0.63                | <0.001             | <0.001           |
| Fatigue (I)                                  | 2     | 788 |                                 |                            |                            |      |              | Emotional Functioning    | 0.43                | <0.001             | <0.001           |
| Fatigue (I)                                  | 2     | 788 |                                 |                            |                            |      |              | Cognitive Functioning    | 0.44                | <0.001             | <0.001           |
| Fatigue (I)                                  | 2     | 788 |                                 |                            |                            |      |              | Social Functioning       | 0.59                | <0.001             | <0.001           |
| Fatigue (I)                                  | 2     | 781 |                                 |                            |                            |      |              | Global Health Status/QoL | 0.52                | <0.001             | <0.001           |
| Fatigue (I)                                  | 2     | 790 |                                 |                            |                            |      |              | HRQOL Summary Score      | 0.70                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 1     | 815 | ECOG PS 2-4                     | ECOG PS 0-1                | 0.52                       | 0.94 | 0.55         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 1     | 815 | Currently taking depression med | Other                      | 0.49                       | 0.95 | 0.52         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 1     | 799 |                                 |                            |                            |      |              | Physical Functioning     | 0.30                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 1     | 799 |                                 |                            |                            |      |              | Role Functioning         | 0.36                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 1     | 796 |                                 |                            |                            |      |              | Emotional Functioning    | 0.57                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 1     | 796 |                                 |                            |                            |      |              | Cognitive Functioning    | 0.38                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 1     | 796 |                                 |                            |                            |      |              | Social Functioning       | 0.38                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 1     | 794 |                                 |                            |                            |      |              | Global Health Status/QoL | 0.38                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 2     | 748 | ECOG PS 2-4                     | ECOG PS 0-1                | 0.51                       | 0.94 | 0.54         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 2     | 748 | Currently taking depression med | Other                      | 0.58                       | 0.94 | 0.61         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 2     | 726 |                                 |                            |                            |      |              | Physical Functioning     | 0.35                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 2     | 724 |                                 |                            |                            |      |              | Role Functioning         | 0.36                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 2     | 724 |                                 |                            |                            |      |              | Emotional Functioning    | 0.61                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 2     | 723 |                                 |                            |                            |      |              | Cognitive Functioning    | 0.43                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 2     | 724 |                                 |                            |                            |      |              | Social Functioning       | 0.39                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 2     | 717 |                                 |                            |                            |      |              | Global Health Status/QoL | 0.43                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (F) | 2     | 717 |                                 |                            |                            |      |              | HRQOL Summary Score      | 0.50                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 1     | 815 | ECOG PS 2-4                     | ECOG PS 0-1                | 0.44                       | 0.86 | 0.52         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 1     | 815 | Currently taking depression med | Other                      | 0.45                       | 0.86 | 0.52         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 1     | 799 |                                 |                            |                            |      |              | Physical Functioning     | 0.29                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 1     | 799 |                                 |                            |                            |      |              | Role Functioning         | 0.35                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 1     | 796 |                                 |                            |                            |      |              | Emotional Functioning    | 0.57                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 1     | 796 |                                 |                            |                            |      |              | Cognitive Functioning    | 0.36                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 1     | 796 |                                 |                            |                            |      |              | Social Functioning       | 0.37                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 1     | 794 |                                 |                            |                            |      |              | Global Health Status/QoL | 0.35                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 2     | 748 | ECOG PS 2-4                     | ECOG PS 0-1                | 0.47                       | 0.80 | 0.59         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 2     | 748 | Currently taking depression med | Other                      | 0.51                       | 0.79 | 0.65         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 2     | 726 |                                 |                            |                            |      |              | Physical Functioning     | 0.37                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 2     | 726 |                                 |                            |                            |      |              | Role Functioning         | 0.35                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 2     | 724 |                                 |                            |                            |      |              | Emotional Functioning    | 0.59                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 2     | 724 |                                 |                            |                            |      |              | Cognitive Functioning    | 0.41                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 2     | 723 |                                 |                            |                            |      |              | Social Functioning       | 0.37                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 2     | 724 |                                 |                            |                            |      |              | Global Health Status/QoL | 0.40                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (S) | 2     | 717 |                                 |                            |                            |      |              | HRQOL Summary Score      | 0.50                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 1     | 815 | ECOG PS 2-4                     | ECOG PS 0-1                | 0.37                       | 0.86 | 0.43         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 1     | 815 | Currently taking depression med | Other                      | 0.42                       | 0.86 | 0.49         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 1     | 799 |                                 |                            |                            |      |              | Physical Functioning     | 0.30                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 1     | 799 |                                 |                            |                            |      |              | Role Functioning         | 0.33                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 1     | 796 |                                 |                            |                            |      |              | Emotional Functioning    | 0.54                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 1     | 796 |                                 |                            |                            |      |              | Cognitive Functioning    | 0.32                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 1     | 796 |                                 |                            |                            |      |              | Social Functioning       | 0.39                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 1     | 794 |                                 |                            |                            |      |              | Global Health Status/QoL | 0.35                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 2     | 748 | ECOG PS 2-4                     | ECOG PS 0-1                | 0.50                       | 0.82 | 0.61         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 2     | 748 | Currently taking depression med | Other                      | 0.52                       | 0.82 | 0.64         |                          |                     | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 2     | 726 |                                 |                            |                            |      |              | Physical Functioning     | 0.39                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 2     | 726 |                                 |                            |                            |      |              | Role Functioning         | 0.40                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 2     | 724 |                                 |                            |                            |      |              | Emotional Functioning    | 0.59                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 2     | 724 |                                 |                            |                            |      |              | Cognitive Functioning    | 0.41                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 2     | 723 |                                 |                            |                            |      |              | Social Functioning       | 0.38                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 2     | 724 |                                 |                            |                            |      |              | Global Health Status/QoL | 0.37                | <0.001             | <0.001           |
| Feelings that nothing could cheer you up (I) | 2     | 717 |                                 |                            |                            |      |              | HRQOL Summary Score      | 0.51                | <0.001             | <0.001           |
| Flashing lights in eyes (P)                  | 1     | 269 | ECOG PS 2-4                     | ECOG PS 0-1                | -1.11%                     |      | -0.04        |                          |                     | 0.83               | 0.91             |
| Flashing lights in eyes (P)                  | 1     | 266 |                                 |                            |                            |      |              | Physical Functioning     | 0.05                | 0.41               | 0.91             |
| Flashing lights in eyes (P)                  | 1     | 266 |                                 |                            |                            |      |              | Role Functioning         | 0.03                | 0.6                | 0.91             |
| Flashing lights in eyes (P)                  | 1     | 262 |                                 |                            |                            |      |              | Emotional Functioning    | 0.08                | 0.21               | 0.91             |
| Flashing lights in eyes (P)                  | 1     | 262 |                                 |                            |                            |      |              | Cognitive Functioning    | 0.14                | 0.03               | 0.35             |
| Flashing lights in eyes (P)                  | 1     | 262 |                                 |                            |                            |      |              | Social Functioning       | -0.04               | 0.48               | 0.91             |
| Flashing lights in eyes (P)                  | 1     | 262 |                                 |                            |                            |      |              | Global Health Status/QoL | 0.01                | 0.91               | 0.91             |
| Flashing lights in eyes (P)                  | 2     | 236 | ECOG PS 2-4                     | ECOG PS 0-1                | 19.86%                     |      | 0.54         |                          |                     | 0.39               | 0.91             |
| Flashing lights in eyes (P)                  | 2     | 236 |                                 |                            |                            |      |              | HRQOL Summary Score      | 0.05                | <0.001             | 0.01             |

| PRO-CTCAE Item              | Visit | N   | Worse Symptom Level Group  | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size*             | EORTC QLQ-C30         | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|-----------------------------|-------|-----|--|----------------------------|----------------------------|------|--------------------------|-----------------------|---------------------|--------------------|------------------|
| Flashing lights in eyes (P) | 2     | 234 | ECOG PS 2-4  | ECOG PS 0-1                | 0.13                       | 1.26 | 0.10                     | Physical Functioning  | 0.11                | 0.09               | 0.91             |
| Flashing lights in eyes (P) | 2     | 234 | Prostate/Bladder with radiation therapy in prior 2 weeks               | Hematologic                | 1.08                       | 1.17 | 0.92                     | Role Functioning      | 0.05                | 0.41               | 0.91             |
| Flashing lights in eyes (P) | 2     | 234 |  |                            |                            |      | Emotional Functioning    | 0.15                  | 0.02                | 0.3                |                  |
| Flashing lights in eyes (P) | 2     | 234 |  |                            |                            |      | Cognitive Functioning    | 0.18                  | 0.007               | 0.1                |                  |
| Flashing lights in eyes (P) | 2     | 234 |  |                            |                            |      | Social Functioning       | 0.13                  | 0.06                | 0.67               |                  |
| Flashing lights in eyes (P) | 2     | 234 |  |                            |                            |      | Global Health Status/QoL | 0.01                  | 0.87                | 0.91               |                  |
| Flashing lights in eyes (P) | 2     | 234 |  |                            |                            |      | HRQOL Summary Score      | 0.08                  | 0.23                | 0.6                |                  |
| Frequent urination (F)      | 1     | 223 | ECOG PS 2-4  | ECOG PS 0-1                | 0.23                       | 1.21 | 0.19                     | Physical Functioning  | 0.07                | 0.002              | 0.03             |
| Frequent urination (F)      | 1     | 56  | Prostate/Bladder with radiation therapy in prior 2 weeks               | Hematologic                | 1.20                       | 1.16 | 1.03                     | Role Functioning      | 0.09                | 0.27               | 0.6              |
| Frequent urination (F)      | 1     | 222 |  |                            |                            |      | Emotional Functioning    | 0.14                  | 0.16                | 0.6                |                  |
| Frequent urination (F)      | 1     | 222 |  |                            |                            |      | Cognitive Functioning    | 0.16                  | 0.03                | 0.31               |                  |
| Frequent urination (F)      | 1     | 222 |  |                            |                            |      | Social Functioning       | 0.16                  | 0.07                | 0.6                |                  |
| Frequent urination (F)      | 1     | 222 |  |                            |                            |      | Global Health Status/QoL | 0.16                  | 0.02                | 0.16               |                  |
| Frequent urination (F)      | 1     | 220 |  |                            |                            |      | HRQOL Summary Score      | 0.17                  | 0.01                | 0.13               |                  |
| Frequent urination (F)      | 2     | 194 | ECOG PS 2-4  | ECOG PS 0-1                | 0.23                       | 1.21 | 0.19                     | Physical Functioning  | 0.13                | 0.37               | 0.6              |
| Frequent urination (F)      | 2     | 49  | Prostate/Bladder with radiation therapy in prior 2 weeks               | Hematologic                | 1.20                       | 1.16 | 1.03                     | Role Functioning      | 0.13                | 0.001              | 0.02             |
| Frequent urination (F)      | 2     | 192 |  |                            |                            |      | Emotional Functioning    | 0.12                  | 0.07                | 0.56               |                  |
| Frequent urination (F)      | 2     | 192 |  |                            |                            |      | Cognitive Functioning    | 0.21                  | 0.09                | 0.6                |                  |
| Frequent urination (F)      | 2     | 191 |  |                            |                            |      | Social Functioning       | 0.21                  | 0.004               | 0.06               |                  |
| Frequent urination (F)      | 2     | 191 |  |                            |                            |      | Global Health Status/QoL | 0.18                  | 0.01                | 0.16               |                  |
| Frequent urination (F)      | 2     | 190 |  |                            |                            |      | HRQOL Summary Score      | 0.11                  | 0.14                | 0.6                |                  |
| Frequent urination (F)      | 2     | 191 |  |                            |                            |      | Physical Functioning     | 0.19                  | 0.009               | 0.13               |                  |
| Frequent urination (F)      | 2     | 188 |  |                            |                            |      | HRQOL Summary Score      | 0.22                  | 0.03                | 0.04               |                  |
| Frequent urination (I)      | 1     | 222 | ECOG PS 2-4  | ECOG PS 0-1                | 0.18                       | 1.16 | 0.15                     | Physical Functioning  | 0.22                | 0.43               | 0.43             |
| Frequent urination (I)      | 1     | 55  | Prostate/Bladder with radiation therapy in prior 2 weeks               | Hematologic                | 0.62                       | 1.21 | 0.51                     | Role Functioning      | 0.18                | 0.07               | 0.22             |
| Frequent urination (I)      | 1     | 221 |  |                            |                            |      | Emotional Functioning    | 0.20                  | 0.001               | 0.02               |                  |
| Frequent urination (I)      | 1     | 221 |  |                            |                            |      | Cognitive Functioning    | 0.20                  | 0.008               | 0.08               |                  |
| Frequent urination (I)      | 1     | 221 |  |                            |                            |      | Social Functioning       | 0.12                  | 0.003               | 0.03               |                  |
| Frequent urination (I)      | 1     | 221 |  |                            |                            |      | Global Health Status/QoL | 0.28                  | 0.07                | 0.22               |                  |
| Frequent urination (I)      | 1     | 221 |  |                            |                            |      | HRQOL Summary Score      | 0.15                  | <0.001              | <0.001             |                  |
| Frequent urination (I)      | 1     | 219 |  |                            |                            |      | Physical Functioning     | 0.16                  | 0.02                | 0.15               |                  |
| Frequent urination (I)      | 2     | 194 | ECOG PS 2-4  | ECOG PS 0-1                | 0.24                       | 1.05 | 0.23                     | Role Functioning      | 0.31                | <0.001             | <0.001           |
| Frequent urination (I)      | 2     | 49  | Prostate/Bladder with radiation therapy in prior 2 weeks               | Hematologic                | 0.86                       | 0.92 | 0.94                     | Emotional Functioning | 0.28                | 0.28               | 0.43             |
| Frequent urination (I)      | 2     | 192 |  |                            |                            |      | Cognitive Functioning    | 0.14                  | 0.03                | 0.03               |                  |
| Frequent urination (I)      | 2     | 192 |  |                            |                            |      | Social Functioning       | 0.16                  | 0.047               | 0.22               |                  |
| Frequent urination (I)      | 2     | 191 |  |                            |                            |      | Global Health Status/QoL | 0.26                  | 0.02                | 0.15               |                  |
| Frequent urination (I)      | 2     | 191 |  |                            |                            |      | HRQOL Summary Score      | 0.26                  | <0.001              | 0.004              |                  |
| Frequent urination (I)      | 2     | 191 |  |                            |                            |      | Physical Functioning     | 0.16                  | 0.03                | 0.15               |                  |
| Frequent urination (I)      | 2     | 190 |  |                            |                            |      | Emotional Functioning    | 0.20                  | 0.006               | 0.07               |                  |
| Frequent urination (I)      | 2     | 191 |  |                            |                            |      | Cognitive Functioning    | 0.19                  | 0.01                | 0.09               |                  |
| Frequent urination (I)      | 2     | 188 |  |                            |                            |      | HRQOL Summary Score      | 0.23                  | 0.001               | 0.02               |                  |
| Hair loss (A)               | 1     | 815 | ECOG PS 2-4  | ECOG PS 0-1                | 0.07                       | 1.50 | 0.05                     | Physical Functioning  | 0.11                | 0.58               | 0.84             |
| Hair loss (A)               | 1     | 815 | Chemotherapy in prior 2 weeks  | Other                      | 0.45                       | 1.48 | 0.31                     | Role Functioning      | 0.14                | <0.001             | <0.001           |
| Hair loss (A)               | 1     | 799 |  |                            |                            |      | Emotional Functioning    | 0.10                  | 0.001               | 0.01               |                  |
| Hair loss (A)               | 1     | 796 |  |                            |                            |      | Cognitive Functioning    | 0.10                  | <0.001              | <0.001             |                  |
| Hair loss (A)               | 1     | 796 |  |                            |                            |      | Social Functioning       | 0.18                  | 0.003               | 0.03               |                  |
| Hair loss (A)               | 1     | 796 |  |                            |                            |      | Global Health Status/QoL | 0.17                  | <0.001              | <0.001             |                  |
| Hair loss (A)               | 1     | 796 |  |                            |                            |      | HRQOL Summary Score      | 0.10                  | <0.001              | <0.001             |                  |
| Hair loss (A)               | 1     | 794 |  |                            |                            |      | Physical Functioning     | 0.10                  | 0.005               | 0.04               |                  |
| Hair loss (A)               | 1     | 748 | ECOG PS 2-4  | ECOG PS 0-1                | -0.03                      | 1.45 | -0.02                    | Role Functioning      | 0.11                | 0.003              | 0.03             |
| Hair loss (A)               | 1     | 748 | Chemotherapy in prior 2 weeks  | Other                      | 0.41                       | 1.43 | 0.29                     | Emotional Functioning | 0.08                | 0.03               | 0.09             |
| Hair loss (A)               | 2     | 726 |  |                            |                            |      | Cognitive Functioning    | 0.08                  | 0.03                | 0.09               |                  |
| Hair loss (A)               | 2     | 724 |  |                            |                            |      | Social Functioning       | 0.09                  | 0.01                | 0.07               |                  |
| Hair loss (A)               | 2     | 724 |  |                            |                            |      | Global Health Status/QoL | 0.09                  | 0.02                | 0.09               |                  |
| Hair loss (A)               | 2     | 723 |  |                            |                            |      | HRQOL Summary Score      | 0.15                  | <0.001              | 0.001              |                  |
| Hair loss (A)               | 2     | 717 |  |                            |                            |      | Physical Functioning     | 0.10                  | 0.001               | 0.04               |                  |
| Hand-foot syndrome (S)      | 1     | 456 | ECOG PS 2-4  | ECOG PS 0-1                | -0.02                      | 0.62 | -0.03                    | Role Functioning      | 0.11                | 0.003              | 0.03             |
| Hand-foot syndrome (S)      | 1     | 456 | Hand-foot syndrome-inducing chemotherapy [footnote 1] in prior 2 weeks | Other                      | 0.24                       | 0.62 | 0.39                     | Emotional Functioning | 0.08                | 0.02               | 0.26             |
| Hand-foot syndrome (S)      | 1     | 441 |  |                            |                            |      | Cognitive Functioning    | 0.06                  | 0.09                | 0.95               |                  |
| Hand-foot syndrome (S)      | 1     | 441 |  |                            |                            |      | Social Functioning       | 0.06                  | 0.25                | 0.95               |                  |
| Hand-foot syndrome (S)      | 1     | 441 |  |                            |                            |      | Global Health Status/QoL | 0.00                  | 0.95                | 0.95               |                  |
| Hand-foot syndrome (S)      | 1     | 441 |  |                            |                            |      | HRQOL Summary Score      | 0.04                  | 0.4                 | 0.95               |                  |
| Hand-foot syndrome (S)      | 1     | 441 |  |                            |                            |      | Physical Functioning     | 0.05                  | 0.32                | 0.95               |                  |
| Hand-foot syndrome (S)      | 1     | 441 |  |                            |                            |      | Emotional Functioning    | 0.08                  | 0.11                | 0.95               |                  |
| Hand-foot syndrome (S)      | 1     | 438 |  |                            |                            |      | Cognitive Functioning    | 0.09                  | 0.07                | 0.8                |                  |
| Hand-foot syndrome (S)      | 2     | 416 | ECOG PS 2-4  | ECOG PS 0-1                | 0.02                       | 0.67 | 0.03                     | Role Functioning      | 0.09                | 0.82               | 0.95             |
| Hand-foot syndrome (S)      | 2     | 416 | Hand-foot syndrome-inducing chemotherapy [footnote 1] in prior 2 weeks | Other                      | 0.25                       | 0.66 | 0.37                     | Emotional Functioning | 0.09                | 0.03               | 0.47             |
| Hand-foot syndrome (S)      | 2     | 400 |  |                            |                            |      | HRQOL Summary Score      | 0.13                  | 0.01                | 0.18               |                  |

| PRO-CTCAE Item         | Visit | N   | Worse Symptom Level Group | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|------------------------|-------|-----|---------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Hand-foot syndrome (S) | 2     | 400 |                           |                            |                            |      |              | Role Functioning         | 0.06                | 0.26               | 0.95             |
| Hand-foot syndrome (S) | 2     | 400 |                           |                            |                            |      |              | Emotional Functioning    | 0.12                | 0.02               | 0.26             |
| Hand-foot syndrome (S) | 2     | 400 |                           |                            |                            |      |              | Cognitive Functioning    | 0.10                | 0.04               | 0.47             |
| Hand-foot syndrome (S) | 2     | 400 |                           |                            |                            |      |              | Social Functioning       | 0.04                | 0.44               | 0.95             |
| Hand-foot syndrome (S) | 2     | 396 |                           |                            |                            |      |              | Global Health Status/QoL | 0.08                | 0.1                | 0.95             |
| Hand-foot syndrome (S) | 2     | 396 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.13                | 0.01               | 0.2              |
| Headache (F)           | 1     | 837 | ECOG PS 2-4               | ECOG PS 0-1                | 0.18                       | 0.94 | 0.19         | Physical Functioning     | 0.13                | 0.04               | 0.07             |
| Headache (F)           | 1     | 821 |                           |                            |                            |      |              | Role Functioning         | 0.18                | <0.001             | <0.001           |
| Headache (F)           | 1     | 821 |                           |                            |                            |      |              | Emotional Functioning    | 0.23                | <0.001             | <0.001           |
| Headache (F)           | 1     | 818 |                           |                            |                            |      |              | Cognitive Functioning    | 0.23                | <0.001             | <0.001           |
| Headache (F)           | 1     | 818 |                           |                            |                            |      |              | Social Functioning       | 0.17                | <0.001             | <0.001           |
| Headache (F)           | 1     | 818 |                           |                            |                            |      |              | Global Health Status/QoL | 0.18                | <0.001             | <0.001           |
| Headache (F)           | 1     | 816 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.29                | <0.001             | <0.001           |
| Headache (F)           | 2     | 772 | ECOG PS 2-4               | ECOG PS 0-1                | 0.14                       | 0.91 | 0.15         | Physical Functioning     | 0.11                | 0.03               | 0.13             |
| Headache (F)           | 2     | 750 |                           |                            |                            |      |              | Role Functioning         | 0.16                | 0.003              | 0.01             |
| Headache (F)           | 2     | 750 |                           |                            |                            |      |              | Emotional Functioning    | 0.18                | <0.001             | <0.001           |
| Headache (F)           | 2     | 748 |                           |                            |                            |      |              | Cognitive Functioning    | 0.19                | <0.001             | <0.001           |
| Headache (F)           | 2     | 748 |                           |                            |                            |      |              | Social Functioning       | 0.13                | <0.001             | <0.001           |
| Headache (F)           | 2     | 747 |                           |                            |                            |      |              | Global Health Status/QoL | 0.17                | <0.001             | <0.001           |
| Headache (F)           | 2     | 748 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.26                | <0.001             | <0.001           |
| Headache (F)           | 2     | 741 |                           |                            |                            |      |              | Physical Functioning     | 0.15                | 0.01               | 0.02             |
| Headache (S)           | 1     | 836 | ECOG PS 2-4               | ECOG PS 0-1                | 0.20                       | 0.87 | 0.23         | Physical Functioning     | 0.21                | <0.001             | <0.001           |
| Headache (S)           | 1     | 820 |                           |                            |                            |      |              | Emotional Functioning    | 0.22                | <0.001             | <0.001           |
| Headache (S)           | 1     | 820 |                           |                            |                            |      |              | Cognitive Functioning    | 0.22                | <0.001             | <0.001           |
| Headache (S)           | 1     | 817 |                           |                            |                            |      |              | Social Functioning       | 0.20                | <0.001             | <0.001           |
| Headache (S)           | 1     | 817 |                           |                            |                            |      |              | Global Health Status/QoL | 0.20                | <0.001             | <0.001           |
| Headache (S)           | 1     | 817 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.31                | <0.001             | <0.001           |
| Headache (S)           | 1     | 817 |                           |                            |                            |      |              | Physical Functioning     | 0.11                | 0.03               | 0.03             |
| Headache (S)           | 2     | 772 | ECOG PS 2-4               | ECOG PS 0-1                | 0.18                       | 0.85 | 0.21         | Physical Functioning     | 0.18                | 0.002              | 0.007            |
| Headache (S)           | 2     | 750 |                           |                            |                            |      |              | Role Functioning         | 0.20                | <0.001             | <0.001           |
| Headache (S)           | 2     | 750 |                           |                            |                            |      |              | Emotional Functioning    | 0.19                | <0.001             | <0.001           |
| Headache (S)           | 2     | 748 |                           |                            |                            |      |              | Cognitive Functioning    | 0.17                | <0.001             | <0.001           |
| Headache (S)           | 2     | 747 |                           |                            |                            |      |              | Social Functioning       | 0.18                | <0.001             | <0.001           |
| Headache (S)           | 2     | 748 |                           |                            |                            |      |              | Global Health Status/QoL | 0.18                | <0.001             | <0.001           |
| Headache (S)           | 2     | 741 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.29                | <0.001             | <0.001           |
| Headache (I)           | 1     | 836 | ECOG PS 2-4               | ECOG PS 0-1                | 0.22                       | 0.83 | 0.27         | Physical Functioning     | 0.21                | 0.003              | 0.006            |
| Headache (I)           | 1     | 820 |                           |                            |                            |      |              | Role Functioning         | 0.27                | <0.001             | <0.001           |
| Headache (I)           | 1     | 820 |                           |                            |                            |      |              | Emotional Functioning    | 0.28                | <0.001             | <0.001           |
| Headache (I)           | 1     | 817 |                           |                            |                            |      |              | Cognitive Functioning    | 0.27                | <0.001             | <0.001           |
| Headache (I)           | 1     | 817 |                           |                            |                            |      |              | Social Functioning       | 0.31                | <0.001             | <0.001           |
| Headache (I)           | 1     | 817 |                           |                            |                            |      |              | Global Health Status/QoL | 0.25                | <0.001             | <0.001           |
| Headache (I)           | 1     | 817 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.39                | <0.001             | <0.001           |
| Headache (I)           | 1     | 815 |                           |                            |                            |      |              | Physical Functioning     | 0.17                | 0.11               | 0.11             |
| Headache (I)           | 2     | 771 | ECOG PS 2-4               | ECOG PS 0-1                | 0.13                       | 0.80 | 0.16         | Physical Functioning     | 0.24                | <0.001             | <0.001           |
| Headache (I)           | 2     | 749 |                           |                            |                            |      |              | Role Functioning         | 0.24                | <0.001             | <0.001           |
| Headache (I)           | 2     | 749 |                           |                            |                            |      |              | Emotional Functioning    | 0.24                | <0.001             | <0.001           |
| Headache (I)           | 2     | 747 |                           |                            |                            |      |              | Cognitive Functioning    | 0.22                | <0.001             | <0.001           |
| Headache (I)           | 2     | 746 |                           |                            |                            |      |              | Social Functioning       | 0.22                | <0.001             | <0.001           |
| Headache (I)           | 2     | 747 |                           |                            |                            |      |              | Global Health Status/QoL | 0.20                | <0.001             | <0.001           |
| Headache (I)           | 2     | 747 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.32                | <0.001             | <0.001           |
| Headache (I)           | 2     | 740 |                           |                            |                            |      |              | Physical Functioning     | 0.17                | 0.03               | 0.33             |
| Heartburn (F)          | 1     | 252 | ECOG PS 2-4               | ECOG PS 0-1                | 0.19                       | 1.10 | 0.17         | Physical Functioning     | 0.17                | <0.001             | <0.001           |
| Heartburn (F)          | 1     | 252 | Antacid in prior week     | Other                      | 0.65                       | 1.05 | 0.62         | Role Functioning         | 0.17                | 0.008              | 0.04             |
| Heartburn (F)          | 1     | 249 |                           |                            |                            |      |              | Emotional Functioning    | 0.15                | 0.02               | 0.08             |
| Heartburn (F)          | 1     | 246 |                           |                            |                            |      |              | Cognitive Functioning    | 0.28                | <0.001             | <0.001           |
| Heartburn (F)          | 1     | 246 |                           |                            |                            |      |              | Social Functioning       | 0.22                | <0.001             | 0.005            |
| Heartburn (F)          | 1     | 246 |                           |                            |                            |      |              | Global Health Status/QoL | 0.18                | 0.006              | 0.04             |
| Heartburn (F)          | 1     | 246 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.26                | <0.001             | <0.001           |
| Heartburn (F)          | 1     | 244 |                           |                            |                            |      |              | Physical Functioning     | 0.20                | 0.06               | 0.17             |
| Heartburn (F)          | 2     | 222 | ECOG PS 2-4               | ECOG PS 0-1                | 0.37                       | 1.04 | 0.35         | Physical Functioning     | 0.20                | <0.001             | <0.001           |
| Heartburn (F)          | 2     | 222 | Antacid in prior week     | Other                      | 0.75                       | 0.98 | 0.76         | Role Functioning         | 0.20                | 0.003              | 0.02             |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | Emotional Functioning    | 0.22                | 0.001              | 0.01             |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | Cognitive Functioning    | 0.12                | 0.08               | 0.17             |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | Social Functioning       | 0.18                | 0.008              | 0.04             |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | Global Health Status/QoL | 0.26                | <0.001             | <0.001           |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.35                | <0.001             | <0.001           |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | Physical Functioning     | 0.20                | 0.001              | 0.01             |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | Emotional Functioning    | 0.22                | 0.001              | 0.01             |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | Cognitive Functioning    | 0.12                | 0.08               | 0.17             |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | Social Functioning       | 0.18                | 0.008              | 0.04             |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | Global Health Status/QoL | 0.26                | <0.001             | <0.001           |
| Heartburn (F)          | 2     | 220 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.35                | <0.001             | <0.001           |
| Heartburn (S)          | 1     | 252 | ECOG PS 2-4               | ECOG PS 0-1                | 0.28                       | 1.00 | 0.28         | Physical Functioning     | 0.20                | 0.001              | 0.01             |
| Heartburn (S)          | 1     | 252 |                           |                            |                            |      |              | Role Functioning         | 0.20                | <0.001             | <0.001           |
| Heartburn (S)          | 1     | 252 |                           |                            |                            |      |              | Emotional Functioning    | 0.22                | 0.001              | 0.01             |
| Heartburn (S)          | 1     | 252 |                           |                            |                            |      |              | Cognitive Functioning    | 0.12                | 0.08               | 0.17             |
| Heartburn (S)          | 1     | 252 |                           |                            |                            |      |              | Social Functioning       | 0.18                | 0.008              | 0.04             |
| Heartburn (S)          | 1     | 252 |                           |                            |                            |      |              | Global Health Status/QoL | 0.26                | <0.001             | <0.001           |
| Heartburn (S)          | 1     | 252 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.35                | <0.001             | <0.001           |

| PRO-CTCAE Item | Visit | N   | Worse Symptom Level Group                                | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size*             | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|----------------|-------|-----|--|----------------------------|----------------------------|------|--------------------------|--------------------------|---------------------|--------------------|------------------|
| Heartburn (S)  | 1     | 252 | Antacid in prior week                                    | Other                      | 0.67                       | 0.95 | 0.70                     | Physical Functioning     | 0.20                | <0.001             | <0.001           |
| Heartburn (S)  | 1     | 249 |  |                            |                            |      | Role Functioning         | 0.18                     | 0.004               | 0.02               | 0.02             |
| Heartburn (S)  | 1     | 249 |  |                            |                            |      | Emotional Functioning    | 0.29                     | <0.001              | 0.03               | 0.03             |
| Heartburn (S)  | 1     | 246 |  |                            |                            |      | Cognitive Functioning    | 0.27                     | <0.001              | <0.001             | <0.001           |
| Heartburn (S)  | 1     | 246 |  |                            |                            |      | Social Functioning       | 0.19                     | 0.003               | 0.03               | 0.03             |
| Heartburn (S)  | 1     | 246 |  |                            |                            |      | Global Health Status/QoL | 0.29                     | <0.001              | <0.001             | <0.001           |
| Heartburn (S)  | 1     | 244 |  |                            |                            |      | HRQL Summary Score       | 0.36                     | 0.11                | 0.13               | 0.13             |
| Heartburn (S)  | 2     | 222 | ECOG PS 2-4  | ECOG PS 0-1                | 0.28                       | 0.93 | 0.30                     | Physical Functioning     | 0.16                | <0.001             | <0.001           |
| Heartburn (S)  | 2     | 222 | Antacid in prior week                                    | Other                      | 0.66                       | 0.87 | 0.75                     | Role Functioning         | 0.16                | 0.02               | 0.06             |
| Heartburn (S)  | 2     | 220 |  |                            |                            |      | Emotional Functioning    | 0.19                     | 0.005               | 0.04               | 0.04             |
| Heartburn (S)  | 2     | 220 |  |                            |                            |      | Cognitive Functioning    | 0.17                     | 0.01                | 0.06               | 0.06             |
| Heartburn (S)  | 2     | 220 |  |                            |                            |      | Social Functioning       | 0.10                     | 0.13                | 0.13               | 0.13             |
| Heartburn (S)  | 2     | 220 |  |                            |                            |      | Global Health Status/QoL | 0.18                     | 0.007               | 0.04               | 0.04             |
| Heartburn (S)  | 2     | 220 |  |                            |                            |      | HRQL Summary Score       | 0.24                     | <0.001              | 0.05               | 0.05             |
| Hiccups (F)    | 1     | 428 | ECOG PS 2-4  | ECOG PS 0-1                | 0.27                       | 0.85 | 0.32                     | Physical Functioning     | 0.16                | 0.01               | 0.1              |
| Hiccups (F)    | 1     | 428 | Currently taking nausea med                              | Other                      | 0.29                       | 0.85 | 0.34                     | Role Functioning         | 0.16                | <0.001             | <0.001           |
| Hiccups (F)    | 1     | 428 | Lung/Head/Neck/Gastrointestinal                          | Other                      | 0.22                       | 0.85 | 0.26                     | Emotional Functioning    | 0.17                | <0.001             | 0.07             |
| Hiccups (F)    | 1     | 418 |  |                            |                            |      | Cognitive Functioning    | 0.19                     | <0.001              | <0.001             |                  |
| Hiccups (F)    | 1     | 415 |  |                            |                            |      | Social Functioning       | 0.20                     | <0.001              | <0.001             |                  |
| Hiccups (F)    | 1     | 415 |  |                            |                            |      | Global Health Status/QoL | 0.18                     | <0.001              | 0.004              |                  |
| Hiccups (F)    | 1     | 415 |  |                            |                            |      | HRQL Summary Score       | 0.27                     | <0.001              | <0.001             |                  |
| Hiccups (F)    | 2     | 381 | ECOG PS 2-4  | ECOG PS 0-1                | 0.08                       | 0.77 | 0.11                     | Physical Functioning     | 0.12                | 0.46               | 0.46             |
| Hiccups (F)    | 2     | 381 | Currently taking nausea med                              | Other                      | 0.24                       | 0.77 | 0.31                     | Role Functioning         | 0.05                | 0.004              | 0.03             |
| Hiccups (F)    | 2     | 375 | Lung/Head/Neck/Gastrointestinal                          | Other                      | 0.11                       | 0.77 | 0.14                     | Emotional Functioning    | 0.15                | 0.26               | 0.46             |
| Hiccups (F)    | 2     | 375 |  |                            |                            |      | Cognitive Functioning    | 0.12                     | 0.003               | 0.03               |                  |
| Hiccups (F)    | 2     | 373 |  |                            |                            |      | Social Functioning       | 0.11                     | 0.02                | 0.1                |                  |
| Hiccups (F)    | 2     | 373 |  |                            |                            |      | Global Health Status/QoL | 0.17                     | 0.001               | 0.01               |                  |
| Hiccups (F)    | 2     | 373 |  |                            |                            |      | HRQL Summary Score       | 0.17                     | <0.001              | 0.009              |                  |
| Hiccups (F)    | 2     | 372 |  |                            |                            |      | HRQL Summary Score       | 0.19                     | <0.001              | 0.004              |                  |
| Hiccups (S)    | 1     | 428 | ECOG PS 2-4  | ECOG PS 0-1                | 0.14                       | 0.73 | 0.20                     | Physical Functioning     | 0.13                | 0.13               | 0.51             |
| Hiccups (S)    | 1     | 428 | Currently taking nausea med                              | Other                      | 0.24                       | 0.72 | 0.34                     | Role Functioning         | 0.13                | <0.001             | 0.01             |
| Hiccups (S)    | 1     | 418 | Lung/Head/Neck/Gastrointestinal                          | Other                      | 0.19                       | 0.73 | 0.26                     | Emotional Functioning    | 0.16                | 0.007              | 0.16             |
| Hiccups (S)    | 1     | 415 |  |                            |                            |      | Cognitive Functioning    | 0.18                     | 0.001               | 0.01               |                  |
| Hiccups (S)    | 1     | 415 |  |                            |                            |      | Social Functioning       | 0.21                     | <0.001              | 0.002              |                  |
| Hiccups (S)    | 1     | 415 |  |                            |                            |      | Global Health Status/QoL | 0.21                     | <0.001              | <0.001             |                  |
| Hiccups (S)    | 1     | 415 |  |                            |                            |      | HRQL Summary Score       | 0.26                     | <0.001              | <0.001             |                  |
| Hiccups (S)    | 2     | 381 | ECOG PS 2-4  | ECOG PS 0-1                | 0.06                       | 0.72 | 0.09                     | Physical Functioning     | 0.06                | 0.55               | 0.55             |
| Hiccups (S)    | 2     | 381 | Currently taking nausea med                              | Other                      | 0.25                       | 0.71 | 0.35                     | Role Functioning         | 0.18                | 0.001              | 0.01             |
| Hiccups (S)    | 2     | 375 | Lung/Head/Neck/Gastrointestinal                          | Other                      | 0.12                       | 0.71 | 0.17                     | Emotional Functioning    | 0.14                | 0.19               | 0.53             |
| Hiccups (S)    | 2     | 375 |  |                            |                            |      | Cognitive Functioning    | 0.14                     | 0.26                | 0.53               |                  |
| Hiccups (S)    | 2     | 373 |  |                            |                            |      | Social Functioning       | 0.11                     | <0.001              | 0.006              |                  |
| Hiccups (S)    | 2     | 373 |  |                            |                            |      | Global Health Status/QoL | 0.21                     | 0.03                | 0.17               |                  |
| Hiccups (S)    | 2     | 373 |  |                            |                            |      | HRQL Summary Score       | 0.21                     | <0.001              | <0.001             |                  |
| Hives (P)      | 1     | 409 | ECOG PS 2-4  | ECOG PS 0-1                | -1.35%                     |      | -0.05                    | Physical Functioning     | 0.22                | 0.75               | 0.92             |
| Hives (P)      | 1     | 409 | Chemotherapy in prior 2 weeks                            | Other                      | 2.17%                      |      | 0.07                     | Role Functioning         | 0.03                | 0.47               | 0.92             |
| Hives (P)      | 1     | 394 | Skin-reaction chemotherapy [footnote 2] in prior 2 weeks | Other                      | 6.07%                      |      | 0.20                     | Emotional Functioning    | 0.00                | 0.045              | 0.9              |
| Hives (P)      | 1     | 394 |  |                            |                            |      | Cognitive Functioning    | 0.03                     | 0.54                | 0.92               |                  |
| Hives (P)      | 1     | 394 |  |                            |                            |      | Social Functioning       | 0.03                     | 0.92                | 0.92               |                  |
| Hives (P)      | 1     | 394 |  |                            |                            |      | Global Health Status/QoL | 0.09                     | 0.58                | 0.92               |                  |
| Hives (P)      | 1     | 394 |  |                            |                            |      | HRQL Summary Score       | 0.03                     | 0.08                | 0.92               |                  |
| Hives (P)      | 1     | 394 |  |                            |                            |      | Physical Functioning     | 0.01                     | 0.61                | 0.92               |                  |
| Hives (P)      | 1     | 391 |  |                            |                            |      | Role Functioning         | 0.03                     | 0.77                | 0.92               |                  |
| Hives (P)      | 2     | 372 | ECOG PS 2-4  | ECOG PS 0-1                | -2.45%                     |      | -0.09                    | Emotional Functioning    | 0.03                | 0.55               | 0.92             |
| Hives (P)      | 2     | 372 | Chemotherapy in prior 2 weeks                            | Other                      | -0.53%                     |      | -0.02                    | Cognitive Functioning    | 0.17                | 0.6                | 0.92             |
| Hives (P)      | 2     | 372 | Skin-reaction chemotherapy [footnote 2] in prior 2 weeks | Other                      | 1.90%                      |      | 0.06                     | Global Health Status/QoL | 0.01                | 0.86               | 0.92             |
| Hives (P)      | 2     | 356 |  |                            |                            |      | HRQL Summary Score       | -0.01                    | 0.55                | 0.92               |                  |
| Hives (P)      | 2     | 356 |  |                            |                            |      | Physical Functioning     | -0.01                    | 0.6                 | 0.92               |                  |
| Hives (P)      | 2     | 356 |  |                            |                            |      | Role Functioning         | -0.01                    | 0.87                | 0.92               |                  |
| Hives (P)      | 2     | 356 |  |                            |                            |      | Emotional Functioning    | -0.01                    | 0.91                | 0.92               |                  |

| PRO-CTCAE Item               | Visit | N   | Worse Symptom Level Group                         | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|------------------------------|-------|-----|---|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Hives (P)                    | 2     | 356 |   |                            |                            |      |              | Cognitive Functioning    | 0.03                | 0.54               | 0.92             |
| Hives (P)                    | 2     | 356 |   |                            |                            |      |              | Social Functioning       | 0.08                | 0.15               | 0.92             |
| Hives (P)                    | 2     | 356 |   |                            |                            |      |              | Global Health Status/QoL | -0.03               | 0.59               | 0.92             |
| Hives (P)                    | 2     | 352 |   |                            |                            |      |              | HRQOL Summary Score      | -0.02               | 0.73               | 0.92             |
| Hoarse voice (S)             | 1     | 253 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.04                       | 0.97 | 0.04         |                          |                     | 0.82               | 0.82             |
| Hoarse voice (S)             | 1     | 253 | Head/Neck with radiation therapy in prior 2 weeks | Other                      | 0.28                       | 0.96 | 0.29         |                          |                     | 0.01               | 0.1              |
| Hoarse voice (S)             | 1     | 250 |   |                            |                            |      |              | Physical Functioning     | 0.16                | 0.02               | 0.08             |
| Hoarse voice (S)             | 1     | 250 |   |                            |                            |      |              | Role Functioning         | 0.21                | <0.001             | 0.007            |
| Hoarse voice (S)             | 1     | 247 |   |                            |                            |      |              | Emotional Functioning    | 0.27                | <0.001             | <0.001           |
| Hoarse voice (S)             | 1     | 247 |   |                            |                            |      |              | Cognitive Functioning    | 0.23                | <0.001             | 0.003            |
| Hoarse voice (S)             | 1     | 247 |   |                            |                            |      |              | Social Functioning       | 0.20                | 0.002              | 0.02             |
| Hoarse voice (S)             | 1     | 247 |   |                            |                            |      |              | Global Health Status/QoL | 0.24                | <0.001             | 0.002            |
| Hoarse voice (S)             | 1     | 245 |   |                            |                            |      |              | HRQOL Summary Score      | 0.34                | <0.001             | <0.001           |
| Hoarse voice (S)             | 1     | 245 |   |                            |                            |      |              |                          | 0.75                | 0.02               | 0.82             |
| Hoarse voice (S)             | 2     | 222 | ECOG PS 2-4                                       | ECOG PS 0-1                | 0.06                       | 1.02 | 0.06         |                          |                     | 0.002              | 0.02             |
| Hoarse voice (S)             | 2     | 222 | Head/Neck with radiation therapy in prior 2 weeks | Other                      | 0.42                       | 1.00 | 0.42         |                          |                     | 0.005              | 0.04             |
| Hoarse voice (S)             | 2     | 220 |   |                            |                            |      |              | Physical Functioning     | 0.19                | 0.005              | 0.04             |
| Hoarse voice (S)             | 2     | 220 |   |                            |                            |      |              | Role Functioning         | 0.27                | <0.001             | <0.001           |
| Hoarse voice (S)             | 2     | 220 |   |                            |                            |      |              | Emotional Functioning    | 0.16                | 0.02               | 0.09             |
| Hoarse voice (S)             | 2     | 220 |   |                            |                            |      |              | Cognitive Functioning    | 0.03                | 0.62               | 0.82             |
| Hoarse voice (S)             | 2     | 220 |   |                            |                            |      |              | Social Functioning       | 0.25                | <0.001             | 0.003            |
| Hoarse voice (S)             | 2     | 220 |   |                            |                            |      |              | Global Health Status/QoL | 0.18                | 0.007              | 0.05             |
| Hoarse voice (S)             | 2     | 220 |   |                            |                            |      |              | HRQOL Summary Score      | 0.34                | <0.001             | <0.001           |
| Hot flashes (F)              | 1     | 369 | ECOG PS 2-4                                       | ECOG PS 0-1                | -0.14                      | 1.11 | -0.13        |                          |                     | 0.46               | 0.46             |
| Hot flashes (F)              | 1     | 292 | Breast/Prostate                                   | Gastrointestinal           | 0.49                       | 1.14 | 0.43         |                          |                     | 0.004              | 0.06             |
| Hot flashes (F)              | 1     | 369 | Currently receiving hormone therapy               | Other                      | 0.62                       | 1.08 | 0.58         |                          |                     | <0.001             | <0.001           |
| Hot flashes (F)              | 1     | 361 |   |                            |                            |      |              | Physical Functioning     | 0.07                | 0.16               | 0.46             |
| Hot flashes (F)              | 1     | 361 |   |                            |                            |      |              | Role Functioning         | 0.07                | 0.2                | 0.46             |
| Hot flashes (F)              | 1     | 361 |   |                            |                            |      |              | Emotional Functioning    | 0.15                | 0.006              | 0.07             |
| Hot flashes (F)              | 1     | 361 |   |                            |                            |      |              | Cognitive Functioning    | 0.12                | 0.03               | 0.25             |
| Hot flashes (F)              | 1     | 361 |   |                            |                            |      |              | Social Functioning       | 0.15                | 0.004              | 0.06             |
| Hot flashes (F)              | 1     | 361 |   |                            |                            |      |              | Global Health Status/QoL | 0.14                | 0.04               | 0.46             |
| Hot flashes (F)              | 1     | 359 |   |                            |                            |      |              | HRQOL Summary Score      | 0.14                | 0.007              | 0.08             |
| Hot flashes (F)              | 2     | 339 | ECOG PS 2-4                                       | ECOG PS 0-1                | -0.23                      | 1.11 | -0.20        |                          |                     | 0.3                | 0.46             |
| Hot flashes (F)              | 2     | 273 | Breast/Prostate                                   | Gastrointestinal           | 0.71                       | 1.10 | 0.65         |                          |                     | <0.001             | <0.001           |
| Hot flashes (F)              | 2     | 339 | Currently receiving hormone therapy               | Other                      | 0.57                       | 1.08 | 0.53         |                          |                     | <0.001             | 0.002            |
| Hot flashes (F)              | 2     | 326 |   |                            |                            |      |              | Physical Functioning     | 0.15                | 0.008              | 0.08             |
| Hot flashes (F)              | 2     | 326 |   |                            |                            |      |              | Role Functioning         | 0.04                | 0.43               | 0.46             |
| Hot flashes (F)              | 2     | 326 |   |                            |                            |      |              | Emotional Functioning    | 0.22                | <0.001             | <0.001           |
| Hot flashes (F)              | 2     | 327 |   |                            |                            |      |              | Cognitive Functioning    | 0.27                | <0.001             | <0.001           |
| Hot flashes (F)              | 2     | 327 |   |                            |                            |      |              | Social Functioning       | 0.11                | 0.048              | 0.39             |
| Hot flashes (F)              | 2     | 326 |   |                            |                            |      |              | Global Health Status/QoL | 0.10                | 0.07               | 0.46             |
| Hot flashes (F)              | 2     | 327 |   |                            |                            |      |              | HRQOL Summary Score      | 0.22                | <0.001             | 0.001            |
| Hot flashes (F)              | 2     | 321 | ECOG PS 2-4                                       | ECOG PS 0-1                | -0.08                      | 1.02 | -0.08        |                          |                     | 0.64               | 0.64             |
| Hot flashes (F)              | 2     | 292 | Breast/Prostate                                   | Gastrointestinal           | 0.45                       | 1.05 | 0.42         |                          |                     | 0.005              | 0.049            |
| Hot flashes (F)              | 2     | 369 | Currently receiving hormone therapy               | Other                      | 0.43                       | 1.01 | 0.43         |                          |                     | 0.001              | 0.02             |
| Hot flashes (F)              | 2     | 361 |   |                            |                            |      |              | Physical Functioning     | 0.10                | 0.06               | 0.29             |
| Hot flashes (F)              | 2     | 361 |   |                            |                            |      |              | Role Functioning         | 0.07                | 0.2                | 0.59             |
| Hot flashes (F)              | 2     | 361 |   |                            |                            |      |              | Emotional Functioning    | 0.18                | <0.001             | 0.01             |
| Hot flashes (F)              | 2     | 361 |   |                            |                            |      |              | Cognitive Functioning    | 0.14                | 0.007              | 0.06             |
| Hot flashes (F)              | 2     | 361 |   |                            |                            |      |              | Social Functioning       | 0.19                | <0.001             | 0.006            |
| Hot flashes (F)              | 2     | 361 |   |                            |                            |      |              | Global Health Status/QoL | 0.12                | 0.03               | 0.15             |
| Hot flashes (F)              | 2     | 359 |   |                            |                            |      |              | HRQOL Summary Score      | 0.18                | <0.001             | 0.01             |
| Hot flashes (F)              | 2     | 339 | ECOG PS 2-4                                       | ECOG PS 0-1                | -0.15                      | 0.99 | -0.15        |                          |                     | 0.44               | 0.64             |
| Hot flashes (F)              | 2     | 273 | Breast/Prostate                                   | Gastrointestinal           | 0.61                       | 0.98 | 0.62         |                          |                     | <0.001             | 0.002            |
| Hot flashes (F)              | 2     | 339 | Currently receiving hormone therapy               | Other                      | 0.42                       | 0.97 | 0.43         |                          |                     | 0.002              | 0.02             |
| Hot flashes (F)              | 2     | 326 |   |                            |                            |      |              | Physical Functioning     | 0.18                | 0.001              | 0.02             |
| Hot flashes (F)              | 2     | 326 |   |                            |                            |      |              | Role Functioning         | 0.08                | 0.16               | 0.59             |
| Hot flashes (F)              | 2     | 327 |   |                            |                            |      |              | Emotional Functioning    | 0.27                | <0.001             | <0.001           |
| Hot flashes (F)              | 2     | 327 |   |                            |                            |      |              | Cognitive Functioning    | 0.29                | <0.001             | <0.001           |
| Hot flashes (F)              | 2     | 326 |   |                            |                            |      |              | Social Functioning       | 0.14                | 0.01               | 0.09             |
| Hot flashes (F)              | 2     | 327 |   |                            |                            |      |              | Global Health Status/QoL | 0.13                | 0.02               | 0.11             |
| Hot flashes (F)              | 2     | 321 | ECOG PS 2-4                                       | ECOG PS 0-1                | -5.78%                     |      | -0.12        |                          |                     | 0.4                | 0.52             |
| Hot flashes (F)              | 2     | 331 | Gastrointestinal                                  | Lung                       | 17.44%                     |      | 0.36         |                          |                     | 0.02               | 0.21             |
| Increased passing of gas (P) | 1     | 226 |   |                            |                            |      |              | Physical Functioning     | 0.12                | 0.03               | 0.23             |
| Increased passing of gas (P) | 1     | 323 |   |                            |                            |      |              | Role Functioning         | 0.10                | 0.06               | 0.44             |
| Increased passing of gas (P) | 1     | 323 |   |                            |                            |      |              | Emotional Functioning    | 0.13                | 0.02               | 0.21             |
| Increased passing of gas (P) | 1     | 323 |   |                            |                            |      |              | Cognitive Functioning    | 0.16                | 0.004              | 0.07             |
| Increased passing of gas (P) | 1     | 323 |   |                            |                            |      |              | Social Functioning       | 0.13                | 0.02               | 0.21             |
| Increased passing of gas (P) | 1     | 323 |   |                            |                            |      |              | Global Health Status/QoL | 0.09                | 0.12               | 0.52             |
| Increased passing of gas (P) | 1     | 320 |   |                            |                            |      |              | HRQOL Summary Score      | 0.19                | <0.001             | 0.009            |
| Increased passing of gas (P) | 2     | 293 | ECOG PS 2-4                                       | ECOG PS 0-1                | 5.94%                      |      | 0.12         |                          |                     | 0.46               | 0.52             |
| Increased passing of gas (P) | 2     | 200 | Gastrointestinal                                  | Lung                       | 5.22%                      |      | 0.11         |                          |                     | 0.52               | 0.52             |

| PRO-CTCAE Item                             | Visit | N   | Worse Symptom Level Group     | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--|-------|-----|-------------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Increased passing of gas (P)               | 2     | 288 |                               |                            |                            |      |              | Physical Functioning     | 0.16                | 0.007              | 0.09             |
| Increased passing of gas (P)               | 2     | 288 |                               |                            |                            |      |              | Role Functioning         | 0.16                | 0.006              | 0.08             |
| Increased passing of gas (P)               | 2     | 286 |                               |                            |                            |      |              | Emotional Functioning    | 0.06                | 0.34               | 0.52             |
| Increased passing of gas (P)               | 2     | 286 |                               |                            |                            |      |              | Cognitive Functioning    | 0.10                | 0.08               | 0.51             |
| Increased passing of gas (P)               | 2     | 286 |                               |                            |                            |      |              | Social Functioning       | 0.16                | 0.007              | 0.09             |
| Increased passing of gas (P)               | 2     | 286 |                               |                            |                            |      |              | Global Health Status/QoL | 0.14                | 0.02               | 0.21             |
| Increased passing of gas (P)               | 2     | 285 |                               |                            |                            |      |              | HRQOL Summary Score      | 0.16                | 0.006              | 0.08             |
| Increased skin sensitivity to sunlight (P) | 1     | 409 | ECOG PS 2-4                   | ECOG PS 0-1                | 1.27%                      |      | 0.04         | Physical Functioning     | 0.14                | 0.007              | 0.8              |
| Increased skin sensitivity to sunlight (P) | 1     | 394 |                               |                            |                            |      |              | Role Functioning         | 0.13                | 0.009              | 0.046            |
| Increased skin sensitivity to sunlight (P) | 1     | 394 |                               |                            |                            |      |              | Emotional Functioning    | 0.13                | 0.008              | 0.046            |
| Increased skin sensitivity to sunlight (P) | 1     | 394 |                               |                            |                            |      |              | Cognitive Functioning    | 0.17                | <0.001             | 0.007            |
| Increased skin sensitivity to sunlight (P) | 1     | 394 |                               |                            |                            |      |              | Social Functioning       | 0.22                | <0.001             | <0.001           |
| Increased skin sensitivity to sunlight (P) | 1     | 394 |                               |                            |                            |      |              | Global Health Status/QoL | 0.06                | 0.19               | 0.19             |
| Increased skin sensitivity to sunlight (P) | 1     | 391 |                               |                            |                            |      |              | HRQOL Summary Score      | 0.14                | 0.006              | 0.046            |
| Increased skin sensitivity to sunlight (P) | 2     | 372 | ECOG PS 2-4                   | ECOG PS 0-1                | -2.16%                     |      | -0.06        | Physical Functioning     | 0.15                | 0.006              | 0.046            |
| Increased skin sensitivity to sunlight (P) | 2     | 356 |                               |                            |                            |      |              | Role Functioning         | 0.17                | 0.002              | 0.02             |
| Increased skin sensitivity to sunlight (P) | 2     | 356 |                               |                            |                            |      |              | Emotional Functioning    | 0.26                | <0.001             | <0.001           |
| Increased skin sensitivity to sunlight (P) | 2     | 356 |                               |                            |                            |      |              | Cognitive Functioning    | 0.14                | 0.008              | 0.046            |
| Increased skin sensitivity to sunlight (P) | 2     | 356 |                               |                            |                            |      |              | Social Functioning       | 0.28                | <0.001             | <0.001           |
| Increased skin sensitivity to sunlight (P) | 2     | 356 |                               |                            |                            |      |              | Global Health Status/QoL | 0.13                | 0.01               | 0.049            |
| Increased skin sensitivity to sunlight (P) | 2     | 352 |                               |                            |                            |      |              | HRQOL Summary Score      | 0.20                | <0.001             | 0.005            |
| Insomnia (S)                               | 1     | 855 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.34                       | 1.12 | 0.30         | Physical Functioning     | 0.26                | <0.001             | <0.001           |
| Insomnia (S)                               | 1     | 855 | Chemotherapy in prior 2 weeks | Other                      | 0.07                       | 1.12 | 0.06         | Role Functioning         | 0.28                | <0.001             | 0.62             |
| Insomnia (S)                               | 1     | 855 | Sleep aid in prior week       | Other                      | 0.81                       | 1.08 | 0.75         | Emotional Functioning    | 0.39                | <0.001             | <0.001           |
| Insomnia (S)                               | 1     | 855 | Surgery in prior 2 weeks      | Other                      | -0.10                      | 1.12 | -0.09        | Cognitive Functioning    | 0.32                | <0.001             | <0.001           |
| Insomnia (S)                               | 1     | 839 |                               |                            |                            |      |              | Social Functioning       | 0.32                | <0.001             | <0.001           |
| Insomnia (S)                               | 1     | 839 |                               |                            |                            |      |              | Global Health Status/QoL | 0.26                | <0.001             | <0.001           |
| Insomnia (S)                               | 1     | 836 |                               |                            |                            |      |              | HRQOL Summary Score      | 0.48                | <0.001             | <0.001           |
| Insomnia (S)                               | 1     | 836 |                               |                            |                            |      |              | Insomnia                 | 0.78                | <0.001             | <0.001           |
| Insomnia (S)                               | 1     | 834 |                               |                            |                            |      |              | Physical Functioning     | 0.29                | 0.001              | 0.006            |
| Insomnia (S)                               | 1     | 839 |                               |                            |                            |      |              | Role Functioning         | 0.27                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 785 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.35                       | 1.09 | 0.32         | Emotional Functioning    | 0.37                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 785 | Chemotherapy in prior 2 weeks | Other                      | -0.07                      | 1.10 | -0.06        | Cognitive Functioning    | 0.33                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 785 | Sleep aid in prior week       | Other                      | 0.69                       | 1.07 | 0.65         | Social Functioning       | 0.29                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 785 | Surgery in prior 2 weeks      | Other                      | 0.20                       | 1.10 | 0.18         | Global Health Status/QoL | 0.27                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 763 |                               |                            |                            |      |              | HRQOL Summary Score      | 0.50                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 763 |                               |                            |                            |      |              | Insomnia                 | 0.79                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 761 |                               |                            |                            |      |              | Physical Functioning     | 0.29                | 0.4                | 0.62             |
| Insomnia (S)                               | 2     | 761 |                               |                            |                            |      |              | Role Functioning         | 0.27                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 761 |                               |                            |                            |      |              | Emotional Functioning    | 0.37                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 761 |                               |                            |                            |      |              | Cognitive Functioning    | 0.33                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 760 |                               |                            |                            |      |              | Social Functioning       | 0.29                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 761 |                               |                            |                            |      |              | Global Health Status/QoL | 0.27                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 754 |                               |                            |                            |      |              | HRQOL Summary Score      | 0.50                | <0.001             | <0.001           |
| Insomnia (S)                               | 2     | 753 |                               |                            |                            |      |              | Insomnia                 | 0.79                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 853 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.39                       | 1.12 | 0.35         | Physical Functioning     | 0.30                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 853 | Chemotherapy in prior 2 weeks | Other                      | 0.04                       | 1.13 | 0.03         | Role Functioning         | 0.33                | 0.63               | 0.82             |
| Insomnia (I)                               | 1     | 853 | Sleep aid in prior week       | Other                      | 0.77                       | 1.09 | 0.71         | Emotional Functioning    | 0.30                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 853 | Surgery in prior 2 weeks      | Other                      | -0.05                      | 1.13 | -0.04        | Cognitive Functioning    | 0.43                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 837 |                               |                            |                            |      |              | Social Functioning       | 0.33                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 834 |                               |                            |                            |      |              | Global Health Status/QoL | 0.42                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 834 |                               |                            |                            |      |              | HRQOL Summary Score      | 0.29                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 834 |                               |                            |                            |      |              | Insomnia                 | 0.70                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 834 |                               |                            |                            |      |              | Physical Functioning     | 0.29                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 832 |                               |                            |                            |      |              | Role Functioning         | 0.52                | <0.001             | <0.001           |
| Insomnia (I)                               | 1     | 837 |                               |                            |                            |      |              | Emotional Functioning    | 0.29                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 784 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.46                       | 1.06 | 0.44         | Cognitive Functioning    | 0.36                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 784 | Chemotherapy in prior 2 weeks | Other                      | -0.11                      | 1.07 | -0.10        | Global Health Status/QoL | 0.29                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 784 | Sleep aid in prior week       | Other                      | 0.68                       | 1.04 | 0.66         | HRQOL Summary Score      | 0.70                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 784 | Surgery in prior 2 weeks      | Other                      | 0.39                       | 1.07 | 0.36         | Insomnia                 | 0.42                | 0.15               | 0.46             |
| Insomnia (I)                               | 2     | 762 |                               |                            |                            |      |              | Physical Functioning     | 0.35                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 760 |                               |                            |                            |      |              | Role Functioning         | 0.36                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 760 |                               |                            |                            |      |              | Emotional Functioning    | 0.43                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 759 |                               |                            |                            |      |              | Cognitive Functioning    | 0.34                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 760 |                               |                            |                            |      |              | Social Functioning       | 0.41                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 753 |                               |                            |                            |      |              | Global Health Status/QoL | 0.52                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 753 |                               |                            |                            |      |              | HRQOL Summary Score      | 0.66                | <0.001             | <0.001           |
| Insomnia (I)                               | 2     | 762 |                               |                            |                            |      |              | Insomnia                 | 0.68                | <0.001             | <0.001           |
| Irregular menstrual periods (P)            | 1     | 77  | ECOG PS 2-4                   | ECOG PS 0-1                | 0.00%                      |      | 0.00         | Physical Functioning     | 0.35                | 1                  | 1                |
| Irregular menstrual periods (P)            | 1     | 29  | Age <40                       | Age >60                    | 35.51%                     |      | 0.77         | Role Functioning         | 0.36                | 0.12               | 1                |

| PRO-CTCAE Item                         | Visit | N   | Worse Symptom Level Group     | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--|-------|-----|-------------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Irregular menstrual periods (P)        | 1     | 75  |                               |                            |                            |      |              | Physical Functioning     | 0.21                | 0.08               | 1                |
| Irregular menstrual periods (P)        | 1     | 75  |                               |                            |                            |      |              | Role Functioning         | 0.25                | 0.03               | 0.54             |
| Irregular menstrual periods (P)        | 1     | 75  |                               |                            |                            |      |              | Emotional Functioning    | 0.09                | 0.46               | 1                |
| Irregular menstrual periods (P)        | 1     | 75  |                               |                            |                            |      |              | Cognitive Functioning    | 0.24                | 0.04               | 0.64             |
| Irregular menstrual periods (P)        | 1     | 75  |                               |                            |                            |      |              | Social Functioning       | 0.19                | 0.1                | 1                |
| Irregular menstrual periods (P)        | 1     | 75  |                               |                            |                            |      |              | Global Health Status/QoL | -0.07               | 0.58               | 1                |
| Irregular menstrual periods (P)        | 2     | 61  | ECOG PS 2-4                   | ECOG PS 0-1                | 7.63%                      |      | 0.15         | HRQL Summary Score       | 0.22                | 0.05               | 0.79             |
| Irregular menstrual periods (P)        | 2     | 21  | Age <40                       | Age >60                    | 47.37%                     |      | 1.52         |                          |                     | 0.83               | 1                |
| Irregular menstrual periods (P)        | 2     | 59  |                               |                            |                            |      |              | Physical Functioning     | -0.22               | 0.09               | 1                |
| Irregular menstrual periods (P)        | 2     | 59  |                               |                            |                            |      |              | Role Functioning         | -0.12               | 0.35               | 1                |
| Irregular menstrual periods (P)        | 2     | 59  |                               |                            |                            |      |              | Emotional Functioning    | 0.14                | 0.29               | 1                |
| Irregular menstrual periods (P)        | 2     | 59  |                               |                            |                            |      |              | Cognitive Functioning    | 0.09                | 0.48               | 1                |
| Irregular menstrual periods (P)        | 2     | 59  |                               |                            |                            |      |              | Social Functioning       | -0.18               | 0.17               | 1                |
| Irregular menstrual periods (P)        | 2     | 59  |                               |                            |                            |      |              | Global Health Status/QoL | -0.33               | 0.01**             | 0.19             |
| Irregular menstrual periods (P)        | 2     | 59  |                               |                            |                            |      |              | HRQL Summary Score       | -0.19               | 0.15               | 1                |
| Itchy skin (S)                         | 1     | 411 | ECOG PS 2-4                   | ECOG PS 0-1                | -0.05                      | 0.79 | -0.07        | Physical Functioning     | 0.11                | 0.63               | 0.81             |
| Itchy skin (S)                         | 1     | 396 |                               |                            |                            |      |              | Role Functioning         | 0.09                | 0.03               | 0.25             |
| Itchy skin (S)                         | 1     | 396 |                               |                            |                            |      |              | Emotional Functioning    | 0.08                | 0.1                | 0.4              |
| Itchy skin (S)                         | 1     | 396 |                               |                            |                            |      |              | Cognitive Functioning    | 0.07                | 0.18               | 0.55             |
| Itchy skin (S)                         | 1     | 396 |                               |                            |                            |      |              | Social Functioning       | 0.13                | 0.01               | 0.11             |
| Itchy skin (S)                         | 1     | 396 |                               |                            |                            |      |              | Global Health Status/QoL | 0.08                | 0.09               | 0.4              |
| Itchy skin (S)                         | 1     | 393 |                               |                            |                            |      |              | HRQL Summary Score       | 0.13                | 0.008              | 0.08             |
| Itchy skin (S)                         | 2     | 374 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.03                       | 0.80 | 0.04         | Physical Functioning     | 0.15                | 0.81               | 0.81             |
| Itchy skin (S)                         | 2     | 359 |                               |                            |                            |      |              | Role Functioning         | 0.15                | 0.004              | 0.049            |
| Itchy skin (S)                         | 2     | 359 |                               |                            |                            |      |              | Emotional Functioning    | 0.14                | 0.004              | 0.049            |
| Itchy skin (S)                         | 2     | 359 |                               |                            |                            |      |              | Cognitive Functioning    | 0.21                | <0.001             | 0.08             |
| Itchy skin (S)                         | 2     | 359 |                               |                            |                            |      |              | Social Functioning       | 0.19                | <0.001             | 0.005            |
| Itchy skin (S)                         | 2     | 359 |                               |                            |                            |      |              | Global Health Status/QoL | 0.10                | 0.07               | 0.4              |
| Itchy skin (S)                         | 2     | 355 |                               |                            |                            |      |              | HRQL Summary Score       | 0.22                | <0.001             | <0.001           |
| Loose stools (F)                       | 1     | 817 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.24                       | 1.04 | 0.23         | Physical Functioning     | 0.17                | 0.01               | 0.02             |
| Loose stools (F)                       | 1     | 817 | Chemotherapy in prior 2 weeks | Other                      | 0.24                       | 1.04 | 0.23         | Role Functioning         | 0.18                | <0.001             | <0.001           |
| Loose stools (F)                       | 1     | 801 | Diarrhea med in prior week    | Other                      | 1.51                       | 0.97 | 1.56         | Emotional Functioning    | 0.17                | <0.001             | <0.001           |
| Loose stools (F)                       | 1     | 801 |                               |                            |                            |      |              | Cognitive Functioning    | 0.17                | <0.001             | <0.001           |
| Loose stools (F)                       | 1     | 798 |                               |                            |                            |      |              | Social Functioning       | 0.16                | <0.001             | <0.001           |
| Loose stools (F)                       | 1     | 798 |                               |                            |                            |      |              | Global Health Status/QoL | 0.14                | <0.001             | <0.001           |
| Loose stools (F)                       | 1     | 798 |                               |                            |                            |      |              | HRQL Summary Score       | 0.28                | <0.001             | <0.001           |
| Loose stools (F)                       | 1     | 796 |                               |                            |                            |      |              | Diarrhea                 | 0.71                | <0.001             | <0.001           |
| Loose stools (F)                       | 1     | 801 |                               |                            |                            |      |              |                          | 0.02                | 0.02               | 0.02             |
| Loose stools (F)                       | 2     | 755 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.24                       | 1.04 | 0.23         | Physical Functioning     | 0.17                | <0.001             | <0.001           |
| Loose stools (F)                       | 2     | 755 | Chemotherapy in prior 2 weeks | Other                      | 0.18                       | 1.04 | 1.71         | Role Functioning         | 0.14                | <0.001             | <0.001           |
| Loose stools (F)                       | 2     | 755 | Diarrhea med in prior week    | Other                      | 1.59                       | 0.93 |              | Emotional Functioning    | 0.12                | 0.001              | 0.006            |
| Loose stools (F)                       | 2     | 733 |                               |                            |                            |      |              | Cognitive Functioning    | 0.14                | <0.001             | <0.001           |
| Loose stools (F)                       | 2     | 731 |                               |                            |                            |      |              | Social Functioning       | 0.18                | <0.001             | <0.001           |
| Loose stools (F)                       | 2     | 730 |                               |                            |                            |      |              | Global Health Status/QoL | 0.13                | <0.001             | 0.002            |
| Loose stools (F)                       | 2     | 731 |                               |                            |                            |      |              | HRQL Summary Score       | 0.27                | <0.001             | <0.001           |
| Loose stools (F)                       | 2     | 724 |                               |                            |                            |      |              | Diarrhea                 | 0.78                | <0.001             | <0.001           |
| Loose any fingernails/toenails (P)     | 1     | 483 | ECOG PS 2-4                   | ECOG PS 0-1                | -2.19%                     |      | -0.14        | Physical Functioning     | 0.00                | 0.38               | 0.99             |
| Loose any fingernails/toenails (P)     | 1     | 468 |                               |                            |                            |      |              | Role Functioning         | -0.03               | 0.99               | 0.99             |
| Loose any fingernails/toenails (P)     | 1     | 468 |                               |                            |                            |      |              | Emotional Functioning    | -0.01               | 0.85               | 0.99             |
| Loose any fingernails/toenails (P)     | 1     | 468 |                               |                            |                            |      |              | Cognitive Functioning    | 0.10                | 0.03               | 0.4              |
| Loose any fingernails/toenails (P)     | 1     | 468 |                               |                            |                            |      |              | Social Functioning       | 0.06                | 0.2                | 0.99             |
| Loose any fingernails/toenails (P)     | 1     | 468 |                               |                            |                            |      |              | Global Health Status/QoL | -0.01               | 0.81               | 0.99             |
| Loose any fingernails/toenails (P)     | 1     | 465 |                               |                            |                            |      |              | HRQL Summary Score       | 0.00                | 0.99               | 0.99             |
| Loose any fingernails/toenails (P)     | 2     | 439 | ECOG PS 2-4                   | ECOG PS 0-1                | -1.90%                     |      | -0.11        | Physical Functioning     | 0.06                | 0.53               | 0.99             |
| Loose any fingernails/toenails (P)     | 2     | 423 |                               |                            |                            |      |              | Role Functioning         | 0.04                | 0.25               | 0.99             |
| Loose any fingernails/toenails (P)     | 2     | 423 |                               |                            |                            |      |              | Emotional Functioning    | 0.10                | 0.36               | 0.99             |
| Loose any fingernails/toenails (P)     | 2     | 422 |                               |                            |                            |      |              | Cognitive Functioning    | 0.06                | 0.048              | 0.72             |
| Loose any fingernails/toenails (P)     | 2     | 422 |                               |                            |                            |      |              | Social Functioning       | 0.08                | 0.23               | 0.99             |
| Loose any fingernails/toenails (P)     | 2     | 421 |                               |                            |                            |      |              | Global Health Status/QoL | 0.06                | 0.1                | 0.99             |
| Loose any fingernails/toenails (P)     | 2     | 422 |                               |                            |                            |      |              | HRQL Summary Score       | 0.06                | 0.25               | 0.99             |
| Loose any fingernails/toenails (P)     | 2     | 415 |                               |                            |                            |      |              |                          | 0.09                | 0.08               | 0.99             |
| Loss of control of bowel movements (F) | 1     | 347 | ECOG PS 2-4                   | ECOG PS 0-1                | 0.12                       | 0.64 | 0.18         | Physical Functioning     | 0.18                | 0.21               | 0.63             |
| Loss of control of bowel movements (F) | 1     | 240 | Colorectal/Prostate           | Lung                       | 0.19                       | 0.60 | 0.31         |                          |                     | 0.03               | 0.15             |
| Loss of control of bowel movements (F) | 1     | 339 |                               |                            |                            |      |              |                          | 0.18                | 0.001              | 0.01             |

| PROCTCAE Item                          | Visit | N   | Worse Symptom Level Group | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--|-------|-----|---------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Loss of control of bowel movements (F) | 1     | 339 |                           |                            |                            |      |              | Role Functioning         | 0.18                | <0.001             | 0.01             |
| Loss of control of bowel movements (F) | 1     | 339 |                           |                            |                            |      |              | Emotional Functioning    | 0.14                | 0.01               | 0.08             |
| Loss of control of bowel movements (F) | 1     | 339 |                           |                            |                            |      |              | Cognitive Functioning    | 0.14                | 0.01               | 0.08             |
| Loss of control of bowel movements (F) | 1     | 339 |                           |                            |                            |      |              | Social Functioning       | 0.14                | 0.008              | 0.08             |
| Loss of control of bowel movements (F) | 1     | 339 |                           |                            |                            |      |              | Global Health Status/QoL | 0.17                | 0.002              | 0.02             |
| Loss of control of bowel movements (F) | 1     | 336 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.27                | <0.001             | <0.001           |
| Loss of control of bowel movements (F) | 2     | 304 | ECOG PS 2-4               | ECOG PS 0-1                | -0.04                      | 0.56 | -0.07        |                          |                     |                    |                  |
| Loss of control of bowel movements (F) | 2     | 208 | Colorectal/Prostate       | Lung                       | 0.05                       | 0.57 | 0.09         |                          |                     |                    |                  |
| Loss of control of bowel movements (F) | 2     | 298 |                           |                            |                            |      |              | Physical Functioning     | 0.21                | <0.001             | 0.003            |
| Loss of control of bowel movements (F) | 2     | 298 |                           |                            |                            |      |              | Role Functioning         | 0.21                | <0.001             | 0.005            |
| Loss of control of bowel movements (F) | 2     | 295 |                           |                            |                            |      |              | Emotional Functioning    | 0.12                | 0.046              | 0.23             |
| Loss of control of bowel movements (F) | 2     | 295 |                           |                            |                            |      |              | Cognitive Functioning    | 0.08                | 0.15               | 0.61             |
| Loss of control of bowel movements (F) | 2     | 294 |                           |                            |                            |      |              | Social Functioning       | 0.15                | 0.01               | 0.08             |
| Loss of control of bowel movements (F) | 2     | 295 |                           |                            |                            |      |              | Global Health Status/QoL | 0.15                | 0.01               | 0.08             |
| Loss of control of bowel movements (F) | 2     | 291 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.26                | <0.001             | <0.001           |
| Loss of control of bowel movements (I) | 1     | 348 |                           |                            |                            |      |              |                          |                     |                    |                  |
| Loss of control of bowel movements (I) | 1     | 241 | ECOG PS 2-4               | ECOG PS 0-1                | 0.09                       | 0.63 | 0.15         |                          |                     |                    |                  |
| Loss of control of bowel movements (I) | 1     | 340 | Colorectal/Prostate       | Lung                       | 0.07                       | 0.67 | 0.10         |                          |                     |                    |                  |
| Loss of control of bowel movements (I) | 1     | 340 |                           |                            |                            |      |              | Physical Functioning     | 0.20                | 0.45               | 0.72             |
| Loss of control of bowel movements (I) | 1     | 340 |                           |                            |                            |      |              | Role Functioning         | 0.21                | <0.001             | 0.003            |
| Loss of control of bowel movements (I) | 1     | 340 |                           |                            |                            |      |              | Emotional Functioning    | 0.13                | 0.02               | 0.002            |
| Loss of control of bowel movements (I) | 1     | 340 |                           |                            |                            |      |              | Cognitive Functioning    | 0.18                | 0.001              | 0.01             |
| Loss of control of bowel movements (I) | 1     | 340 |                           |                            |                            |      |              | Social Functioning       | 0.19                | <0.001             | 0.006            |
| Loss of control of bowel movements (I) | 1     | 340 |                           |                            |                            |      |              | Global Health Status/QoL | 0.11                | 0.04               | 0.28             |
| Loss of control of bowel movements (I) | 1     | 337 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.28                | <0.001             | <0.001           |
| Loss of control of bowel movements (I) | 2     | 304 | ECOG PS 2-4               | ECOG PS 0-1                | -0.03                      | 0.53 | -0.06        |                          |                     |                    |                  |
| Loss of control of bowel movements (I) | 2     | 208 | Colorectal/Prostate       | Lung                       | 0.11                       | 0.55 | 0.19         |                          |                     |                    |                  |
| Loss of control of bowel movements (I) | 2     | 298 |                           |                            |                            |      |              | Physical Functioning     | 0.20                | 0.19               | 0.72             |
| Loss of control of bowel movements (I) | 2     | 298 |                           |                            |                            |      |              | Role Functioning         | 0.22                | <0.001             | 0.007            |
| Loss of control of bowel movements (I) | 2     | 295 |                           |                            |                            |      |              | Emotional Functioning    | 0.10                | 0.09               | 0.44             |
| Loss of control of bowel movements (I) | 2     | 295 |                           |                            |                            |      |              | Cognitive Functioning    | 0.10                | 0.08               | 0.44             |
| Loss of control of bowel movements (I) | 2     | 294 |                           |                            |                            |      |              | Social Functioning       | 0.15                | 0.008              | 0.07             |
| Loss of control of bowel movements (I) | 2     | 295 |                           |                            |                            |      |              | Global Health Status/QoL | 0.19                | <0.001             | 0.009            |
| Loss of control of bowel movements (I) | 2     | 291 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.27                | <0.001             | <0.001           |
| Loss of control of urine (F)           | 1     | 222 |                           |                            |                            |      |              |                          |                     |                    |                  |
| Loss of control of urine (F)           | 1     | 112 | ECOG PS 2-4               | ECOG PS 0-1                | -0.02                      | 0.90 | -0.02        |                          |                     |                    |                  |
| Loss of control of urine (F)           | 1     | 221 | Colorectal/Prostate       | Hematologic                | 0.54                       | 0.93 | 0.58         |                          |                     |                    |                  |
| Loss of control of urine (F)           | 1     | 221 |                           |                            |                            |      |              | Physical Functioning     | 0.05                | 0.005              | 0.09             |
| Loss of control of urine (F)           | 1     | 221 |                           |                            |                            |      |              | Role Functioning         | 0.00                | 0.47               | 0.98             |
| Loss of control of urine (F)           | 1     | 221 |                           |                            |                            |      |              | Emotional Functioning    | -0.01               | 0.98               | 0.98             |
| Loss of control of urine (F)           | 1     | 221 |                           |                            |                            |      |              | Cognitive Functioning    | 0.00                | 0.97               | 0.98             |
| Loss of control of urine (F)           | 1     | 221 |                           |                            |                            |      |              | Social Functioning       | 0.05                | 0.49               | 0.98             |
| Loss of control of urine (F)           | 1     | 221 |                           |                            |                            |      |              | Global Health Status/QoL | 0.07                | 0.3                | 0.98             |
| Loss of control of urine (F)           | 1     | 219 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.07                | 0.31               | 0.98             |
| Loss of control of urine (F)           | 2     | 192 | ECOG PS 2-4               | ECOG PS 0-1                | -0.04                      | 0.89 | -0.04        |                          |                     |                    |                  |
| Loss of control of urine (F)           | 2     | 96  | Colorectal/Prostate       | Hematologic                | 0.33                       | 0.97 | 0.34         |                          |                     |                    |                  |
| Loss of control of urine (F)           | 2     | 190 |                           |                            |                            |      |              | Physical Functioning     | 0.08                | 0.13               | 0.98             |
| Loss of control of urine (F)           | 2     | 190 |                           |                            |                            |      |              | Role Functioning         | 0.03                | 0.25               | 0.98             |
| Loss of control of urine (F)           | 2     | 189 |                           |                            |                            |      |              | Emotional Functioning    | 0.02                | 0.66               | 0.98             |
| Loss of control of urine (F)           | 2     | 189 |                           |                            |                            |      |              | Cognitive Functioning    | 0.09                | 0.81               | 0.98             |
| Loss of control of urine (F)           | 2     | 188 |                           |                            |                            |      |              | Social Functioning       | 0.09                | 0.23               | 0.98             |
| Loss of control of urine (F)           | 2     | 188 |                           |                            |                            |      |              | Global Health Status/QoL | 0.06                | 0.38               | 0.98             |
| Loss of control of urine (F)           | 2     | 186 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.09                | 0.23               | 0.98             |
| Loss of control of urine (I)           | 1     | 222 |                           |                            |                            |      |              |                          |                     |                    |                  |
| Loss of control of urine (I)           | 1     | 112 | ECOG PS 2-4               | ECOG PS 0-1                | 0                          | 0.78 | 0            |                          |                     |                    |                  |
| Loss of control of urine (I)           | 1     | 221 | Colorectal/Prostate       | Hematologic                | 0.32                       | 0.76 | 0.42         |                          |                     |                    |                  |
| Loss of control of urine (I)           | 1     | 221 |                           |                            |                            |      |              | Physical Functioning     | 0.10                | 0.04               | 0.7              |
| Loss of control of urine (I)           | 1     | 221 |                           |                            |                            |      |              | Role Functioning         | 0.06                | 0.12               | 0.99             |
| Loss of control of urine (I)           | 1     | 221 |                           |                            |                            |      |              | Emotional Functioning    | 0.10                | 0.36               | 0.99             |
| Loss of control of urine (I)           | 1     | 221 |                           |                            |                            |      |              | Cognitive Functioning    | 0.04                | 0.15               | 0.99             |
| Loss of control of urine (I)           | 1     | 221 |                           |                            |                            |      |              | Social Functioning       | 0.12                | 0.07               | 0.99             |
| Loss of control of urine (I)           | 1     | 219 |                           |                            |                            |      |              | Global Health Status/QoL | 0.05                | 0.42               | 0.99             |
| Loss of control of urine (I)           | 1     | 219 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.14                | 0.04               | 0.7              |
| Loss of control of urine (I)           | 2     | 192 | ECOG PS 2-4               | ECOG PS 0-1                | -0.17                      | 0.62 | -0.27        |                          |                     |                    |                  |
| Loss of control of urine (I)           | 2     | 96  | Colorectal/Prostate       | Hematologic                | 0.18                       | 0.62 | 0.29         |                          |                     |                    |                  |
| Loss of control of urine (I)           | 2     | 190 |                           |                            |                            |      |              | Physical Functioning     | 0.10                | 0.18               | 0.99             |
| Loss of control of urine (I)           | 2     | 190 |                           |                            |                            |      |              | Role Functioning         | 0.00                | 0.98               | 0.99             |
| Loss of control of urine (I)           | 2     | 189 |                           |                            |                            |      |              | Emotional Functioning    | 0.06                | 0.42               | 0.99             |
| Loss of control of urine (I)           | 2     | 188 |                           |                            |                            |      |              | Cognitive Functioning    | 0.04                | 0.6                | 0.99             |
| Loss of control of urine (I)           | 2     | 188 |                           |                            |                            |      |              | Social Functioning       | 0.03                | 0.66               | 0.99             |
| Loss of control of urine (I)           | 2     | 189 |                           |                            |                            |      |              | Global Health Status/QoL | 0.04                | 0.56               | 0.99             |
| Loss of control of urine (I)           | 2     | 186 |                           |                            |                            |      |              | HRQOL Summary Score      | 0.04                | 0.59               | 0.96             |
| Miss an expected menstrual period (F)  | 1     | 69  | ECOG PS 2-4               | ECOG PS 0-1                | -12.81%                    |      | -0.29        |                          |                     |                    |                  |
| Miss an expected menstrual period (F)  | 1     | 27  | Age <40                   | Age >60                    | 5.43%                      |      | 0.12         |                          |                     |                    |                  |
| Miss an expected menstrual period (F)  | 1     | 67  |                           |                            |                            |      |              | Physical Functioning     | 0.29                | 0.83               | 0.96             |
| Miss an expected menstrual period (F)  | 1     | 67  |                           |                            |                            |      |              | Role Functioning         | 0.26                | 0.02               | 0.29             |

| PROCTCAE Item                         | Visit | N   | Worse Symptom Level Group  | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|---------------------------------------|-------|-----|--|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Miss an expected menstrual period (P) | 1     | 67  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     | -39.66%                    |      | -1.36        | Emotional Functioning    | -0.01               | 0.96               | 0.96             |
| Miss an expected menstrual period (P) | 1     | 67  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     | 42.11%                     |      | 1.41         | Cognitive Functioning    | 0.31                | 0.01               | 0.15             |
| Miss an expected menstrual period (P) | 1     | 67  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | Social Functioning       | 0.32                | 0.009              | 0.15             |
| Miss an expected menstrual period (P) | 1     | 67  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | Global Health Status/QoL | -0.09               | 0.48               | 0.96             |
| Miss an expected menstrual period (P) | 1     | 67  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | HRQOL Summary Score      | 0.22                | 0.07               | 0.9              |
| Miss an expected menstrual period (P) | 2     | 60  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              |                          |                     | 0.26               | 0.96             |
| Miss an expected menstrual period (P) | 2     | 20  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | Physical Functioning     | -0.08               | 0.4                | 0.96             |
| Miss an expected menstrual period (P) | 2     | 58  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | Role Functioning         | -0.10               | 0.53               | 0.96             |
| Miss an expected menstrual period (P) | 2     | 58  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | Emotional Functioning    | -0.05               | 0.71               | 0.96             |
| Miss an expected menstrual period (P) | 2     | 58  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | Cognitive Functioning    | -0.10               | 0.46               | 0.96             |
| Miss an expected menstrual period (P) | 2     | 58  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | Social Functioning       | -0.13               | 0.33               | 0.96             |
| Miss an expected menstrual period (P) | 2     | 58  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | Global Health Status/QoL | -0.34               | 0.009**            | 0.15             |
| Miss an expected menstrual period (P) | 2     | 58  | ECOG PS 2-4<br>Age <40   | ECOG PS 0-1<br>Age >60     |                            |      |              | HRQOL Summary Score      | -0.22               | 0.1                | 0.96             |
| Mouth or throat sores (S)             | 1     | 824 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.26                       | 0.84 | 0.31         |                          |                     | <0.001             | 0.003            |
| Mouth or throat sores (S)             | 1     | 824 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.19                       | 0.84 | 0.22         |                          |                     | 0.001              | 0.004            |
| Mouth or throat sores (S)             | 1     | 808 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       | 0.52                       | 0.82 | 0.64         |                          |                     | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 808 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Physical Functioning     | 0.17                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 805 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Role Functioning         | 0.19                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 805 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Emotional Functioning    | 0.24                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 805 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Cognitive Functioning    | 0.16                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 805 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Social Functioning       | 0.22                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 805 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Global Health Status/QoL | 0.18                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 803 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       | 0.21                       | 0.97 | 0.22         |                          |                     | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 761 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       | 0.19                       | 0.97 | 0.20         |                          |                     | 0.007              | 0.01             |
| Mouth or throat sores (S)             | 2     | 761 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       | 0.64                       | 0.94 | 0.68         |                          |                     | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 739 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Physical Functioning     | 0.22                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 739 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Role Functioning         | 0.23                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 737 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Emotional Functioning    | 0.19                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 737 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Cognitive Functioning    | 0.16                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 736 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Social Functioning       | 0.30                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 737 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | Global Health Status/QoL | 0.26                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 737 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       |                            |      |              | HRQOL Summary Score      | 0.34                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 730 | ECOG PS 2-4<br>Head/Neck with radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other       | 0.24                       | 0.76 | 0.32         |                          |                     | <0.001             | 0.002            |
| Mouth or throat sores (S)             | 1     | 822 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.14                       | 0.77 | 0.19         |                          |                     | 0.007              | 0.01             |
| Mouth or throat sores (S)             | 1     | 822 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.46                       | 0.75 | 0.61         |                          |                     | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 806 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Physical Functioning     | 0.18                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 806 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Role Functioning         | 0.24                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 803 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Emotional Functioning    | 0.25                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 803 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Cognitive Functioning    | 0.12                | <0.001             | 0.002            |
| Mouth or throat sores (S)             | 1     | 803 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Social Functioning       | 0.24                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 803 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Global Health Status/QoL | 0.18                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 1     | 801 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.26                       | 0.91 | 0.28         |                          |                     | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 762 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.12                       | 0.92 | 0.13         |                          |                     | 0.005              | 0.01             |
| Mouth or throat sores (S)             | 2     | 762 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.61                       | 0.89 | 0.68         |                          |                     | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 740 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Physical Functioning     | 0.21                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 738 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Role Functioning         | 0.24                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 738 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Emotional Functioning    | 0.20                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 737 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Cognitive Functioning    | 0.17                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 738 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Social Functioning       | 0.31                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 737 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Global Health Status/QoL | 0.23                | <0.001             | <0.001           |
| Mouth or throat sores (S)             | 2     | 731 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | HRQOL Summary Score      | 0.33                | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 835 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.39                       | 1.06 | 0.36         |                          |                     | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 835 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.46                       | 1.05 | 0.44         |                          |                     | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 835 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.98                       | 0.96 | 1.02         |                          |                     | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 819 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.56                       | 1.04 | 0.54         |                          |                     | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 819 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Physical Functioning     | 0.24                | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 816 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Role Functioning         | 0.31                | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 816 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Emotional Functioning    | 0.31                | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 816 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Cognitive Functioning    | 0.28                | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 816 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Social Functioning       | 0.33                | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 814 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Global Health Status/QoL | 0.28                | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 814 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | HRQOL Summary Score      | 0.49                | <0.001             | <0.001           |
| Nausea (F)                            | 1     | 819 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.36                       | 1.09 | 0.33         |                          |                     | <0.001             | <0.001           |
| Nausea (F)                            | 2     | 774 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.30                       | 1.09 | 0.28         |                          |                     | <0.001             | <0.001           |
| Nausea (F)                            | 2     | 774 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.96                       | 1.00 | 0.95         |                          |                     | <0.001             | <0.001           |
| Nausea (F)                            | 2     | 774 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       | 0.65                       | 1.06 | 0.61         |                          |                     | <0.001             | <0.001           |
| Nausea (F)                            | 2     | 752 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Physical Functioning     | 0.29                | <0.001             | <0.001           |
| Nausea (F)                            | 2     | 752 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Role Functioning         | 0.30                | <0.001             | <0.001           |
| Nausea (F)                            | 2     | 750 | ECOG PS 2-4<br>Chemotherapy in prior 2 weeks                     | ECOG PS 0-1<br>Other       |                            |      |              | Emotional Functioning    | 0.26                | <0.001             | <0.001           |

| PRO-CTCAE Item                             | Visit | N   | Worse Symptom Level Group  | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--|-------|-----|--|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Nausea (F)                                 | 2     | 750 |  |                            |                            |      |              | Cognitive Functioning    | 0.33                | <0.001             | <0.001           |
| Nausea (F)                                 | 2     | 749 |  |                            |                            |      |              | Social Functioning       | 0.35                | <0.001             | <0.001           |
| Nausea (F)                                 | 2     | 750 |  |                            |                            |      |              | Global Health Status/QoL | 0.31                | <0.001             | <0.001           |
| Nausea (F)                                 | 2     | 743 |  |                            |                            |      |              | HRQOL Summary Score      | 0.50                | <0.001             | <0.001           |
| Nausea (F)                                 | 2     | 752 |  |                            |                            |      |              | Nausea and Vomiting      | 0.75                | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 834 | ECOG PS 2-4  | ECOG PS 0-1                | 0.36                       | 0.97 | 0.37         |                          |                     | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 834 | Chemotherapy in prior 2 weeks                                    | Other                      | 0.34                       | 0.97 | 0.35         |                          |                     | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 834 | Currently taking nausea med                                      | Other                      | 0.88                       | 0.88 | 1.00         |                          |                     | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 834 | Opioid [narcotic] pain med in prior week                         | Other                      | 0.58                       | 0.94 | 0.61         |                          |                     | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 818 |  |                            |                            |      |              | Physical Functioning     | 0.26                | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 818 |  |                            |                            |      |              | Role Functioning         | 0.33                | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 815 |  |                            |                            |      |              | Emotional Functioning    | 0.33                | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 815 |  |                            |                            |      |              | Cognitive Functioning    | 0.30                | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 815 |  |                            |                            |      |              | Social Functioning       | 0.35                | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 815 |  |                            |                            |      |              | Global Health Status/QoL | 0.30                | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 813 |  |                            |                            |      |              | HRQOL Summary Score      | 0.51                | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 818 |  |                            |                            |      |              | Nausea and Vomiting      | 0.73                | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 775 | ECOG PS 2-4  | ECOG PS 0-1                | 0.34                       | 0.94 | 0.36         |                          |                     | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 775 | Chemotherapy in prior 2 weeks                                    | Other                      | 0.28                       | 0.94 | 0.30         |                          |                     | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 775 | Currently taking nausea med                                      | Other                      | 0.79                       | 0.88 | 0.90         |                          |                     | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 775 | Opioid [narcotic] pain med in prior week                         | Other                      | 0.56                       | 0.91 | 0.61         |                          |                     | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 753 |  |                            |                            |      |              | Physical Functioning     | 0.31                | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 751 |  |                            |                            |      |              | Role Functioning         | 0.31                | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 751 |  |                            |                            |      |              | Emotional Functioning    | 0.29                | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 750 |  |                            |                            |      |              | Cognitive Functioning    | 0.33                | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 751 |  |                            |                            |      |              | Social Functioning       | 0.37                | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 744 |  |                            |                            |      |              | Global Health Status/QoL | 0.35                | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 753 |  |                            |                            |      |              | HRQOL Summary Score      | 0.53                | <0.001             | <0.001           |
| Nausea (S)                                 | 2     | 753 |  |                            |                            |      |              | Nausea and Vomiting      | 0.76                | <0.001             | <0.001           |
| Nausea (S)                                 | 1     | 315 | ECOG PS 2-4  | ECOG PS 0-1                | 0.00                       | 0.62 | -0.01        |                          |                     | 0.96               | 0.99             |
| Nausea (S)                                 | 1     | 315 | Bevacizumab in prior 2 weeks                                     | Other                      | 0.06                       | 0.61 | 0.10         |                          |                     | 0.62               | 0.99             |
| Nausea (S)                                 | 1     | 307 |  |                            |                            |      |              | Physical Functioning     | -0.01               | 0.83               | 0.99             |
| Nausea (S)                                 | 1     | 307 |  |                            |                            |      |              | Role Functioning         | 0.00                | 0.99               | 0.99             |
| Nausea (S)                                 | 1     | 307 |  |                            |                            |      |              | Emotional Functioning    | -0.09               | 0.12               | 0.99             |
| Nausea (S)                                 | 1     | 307 |  |                            |                            |      |              | Cognitive Functioning    | 0.07                | 0.25               | 0.99             |
| Nausea (S)                                 | 1     | 307 |  |                            |                            |      |              | Social Functioning       | -0.01               | 0.81               | 0.99             |
| Nausea (S)                                 | 1     | 307 |  |                            |                            |      |              | Global Health Status/QoL | -0.02               | 0.73               | 0.99             |
| Nausea (S)                                 | 1     | 304 |  |                            |                            |      |              | HRQOL Summary Score      | 0.03                | 0.65               | 0.99             |
| Nausea (S)                                 | 2     | 278 | ECOG PS 2-4  | ECOG PS 0-1                | 0.04                       | 0.50 | 0.08         |                          |                     | 0.63               | 0.99             |
| Nausea (S)                                 | 2     | 278 | Bevacizumab in prior 2 weeks                                     | Other                      | 0.07                       | 0.50 | 0.15         |                          |                     | 0.48               | 0.99             |
| Nausea (S)                                 | 2     | 273 |  |                            |                            |      |              | Physical Functioning     | 0.00                | 0.96               | 0.99             |
| Nausea (S)                                 | 2     | 273 |  |                            |                            |      |              | Role Functioning         | -0.02               | 0.68               | 0.99             |
| Nausea (S)                                 | 2     | 271 |  |                            |                            |      |              | Emotional Functioning    | 0.04                | 0.53               | 0.99             |
| Nausea (S)                                 | 2     | 271 |  |                            |                            |      |              | Cognitive Functioning    | 0.01                | 0.93               | 0.99             |
| Nausea (S)                                 | 2     | 271 |  |                            |                            |      |              | Social Functioning       | 0.08                | 0.17               | 0.99             |
| Nausea (S)                                 | 2     | 271 |  |                            |                            |      |              | Global Health Status/QoL | 0.02                | 0.74               | 0.99             |
| Nausea (S)                                 | 2     | 270 |  |                            |                            |      |              | HRQOL Summary Score      | 0.02                | 0.62               | 0.97             |
| Nausea (S)                                 | 1     | 314 | ECOG PS 2-4  | ECOG PS 0-1                | -0.04                      | 0.51 | -0.07        |                          |                     | 0.81               | 0.97             |
| Nausea (S)                                 | 1     | 314 | Bevacizumab in prior 2 weeks                                     | Other                      | 0.02                       | 0.51 | 0.05         |                          |                     | 0.97               | 0.97             |
| Nausea (S)                                 | 1     | 306 |  |                            |                            |      |              | Physical Functioning     | 0.00                | 0.76               | 0.97             |
| Nausea (S)                                 | 1     | 306 |  |                            |                            |      |              | Role Functioning         | 0.02                | 0.76               | 0.97             |
| Nausea (S)                                 | 1     | 306 |  |                            |                            |      |              | Emotional Functioning    | -0.06               | 0.3                | 0.97             |
| Nausea (S)                                 | 1     | 306 |  |                            |                            |      |              | Cognitive Functioning    | 0.06                | 0.27               | 0.97             |
| Nausea (S)                                 | 1     | 306 |  |                            |                            |      |              | Social Functioning       | 0.02                | 0.74               | 0.97             |
| Nausea (S)                                 | 1     | 306 |  |                            |                            |      |              | Global Health Status/QoL | 0.01                | 0.91               | 0.97             |
| Nausea (S)                                 | 1     | 303 |  |                            |                            |      |              | HRQOL Summary Score      | 0.04                | 0.46               | 0.97             |
| Nausea (S)                                 | 2     | 277 | ECOG PS 2-4  | ECOG PS 0-1                | -0.01                      | 0.47 | -0.01        |                          |                     | 0.93               | 0.97             |
| Nausea (S)                                 | 2     | 277 | Bevacizumab in prior 2 weeks                                     | Other                      | 0.10                       | 0.47 | 0.22         |                          |                     | 0.31               | 0.97             |
| Nausea (S)                                 | 2     | 272 |  |                            |                            |      |              | Physical Functioning     | 0.05                | 0.41               | 0.97             |
| Nausea (S)                                 | 2     | 270 |  |                            |                            |      |              | Role Functioning         | 0.05                | 0.45               | 0.97             |
| Nausea (S)                                 | 2     | 270 |  |                            |                            |      |              | Emotional Functioning    | 0.08                | 0.21               | 0.97             |
| Nausea (S)                                 | 2     | 270 |  |                            |                            |      |              | Cognitive Functioning    | 0.02                | 0.76               | 0.97             |
| Nausea (S)                                 | 2     | 270 |  |                            |                            |      |              | Social Functioning       | 0.11                | 0.08               | 0.97             |
| Nausea (S)                                 | 2     | 269 |  |                            |                            |      |              | Global Health Status/QoL | 0.02                | 0.7                | 0.97             |
| Nausea (S)                                 | 2     | 269 |  |                            |                            |      |              | HRQOL Summary Score      | 0.07                | 0.26               | 0.97             |
| Numness/tingling in your hands or feet (S) | 1     | 846 | ECOG PS 2-4  | ECOG PS 0-1                | 0.24                       | 0.93 | 0.26         |                          |                     | 0.004              | 0.02             |
| Numness/tingling in your hands or feet (S) | 1     | 846 | Taxane/vinorelbine/alkaloid/platin chemotherapy in prior 2 weeks | Other                      | 0                          | 0.94 | 0            |                          |                     | 0.97               | 0.97             |
| Numness/tingling in your hands or feet (S) | 1     | 829 |  |                            |                            |      |              | Physical Functioning     | 0.28                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 829 |  |                            |                            |      |              | Role Functioning         | 0.21                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 826 |  |                            |                            |      |              | Emotional Functioning    | 0.20                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 826 |  |                            |                            |      |              | Cognitive Functioning    | 0.26                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 826 |  |                            |                            |      |              | Social Functioning       | 0.19                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 826 |  |                            |                            |      |              | Global Health Status/QoL | 0.19                | <0.001             | <0.001           |

| PRO-CTCAE Item                             | Visit | N   | Worse Symptom Level Group                                  | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--|-------|-----|--|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Numness/tingling in your hands or feet (S) | 1     | 824 | ECOG PS 2-4  | ECOG PS 0-1                | 0.10                       | 0.91 | 0.11         | HRQL Summary Score       | 0.32                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 782 | Taxane/vinca alkaloid/platin chemotherapy in prior 2 weeks | Other                      | 0                          | 0.91 | 0            | Physical Functioning     | 0.29                | 0.26               | 0.77             |
| Numness/tingling in your hands or feet (S) | 2     | 759 |  |                            |                            |      |              | Role Functioning         | 0.17                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 757 |  |                            |                            |      |              | Emotional Functioning    | 0.21                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 756 |  |                            |                            |      |              | Cognitive Functioning    | 0.18                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 757 |  |                            |                            |      |              | Social Functioning       | 0.11                | 0.002              | 0.01             |
| Numness/tingling in your hands or feet (S) | 2     | 750 |  |                            |                            |      |              | Global Health Status/QoL | 0.20                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 750 |  |                            |                            |      |              | HRQL Summary Score       | 0.26                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 846 | ECOG PS 2-4  | ECOG PS 0-1                | 0.28                       | 0.88 | 0.32         | Physical Functioning     | 0.29                | 0.5                | 0.002            |
| Numness/tingling in your hands or feet (S) | 1     | 846 | Taxane/vinca alkaloid/platin chemotherapy in prior 2 weeks | Other                      | 0.04                       | 0.88 | 0.05         | Role Functioning         | 0.20                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 829 |  |                            |                            |      |              | Emotional Functioning    | 0.25                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 826 |  |                            |                            |      |              | Cognitive Functioning    | 0.28                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 826 |  |                            |                            |      |              | Social Functioning       | 0.23                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 826 |  |                            |                            |      |              | Global Health Status/QoL | 0.20                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 1     | 824 |  |                            |                            |      |              | HRQL Summary Score       | 0.34                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 782 | ECOG PS 2-4  | ECOG PS 0-1                | 0.13                       | 0.83 | 0.16         | Physical Functioning     | 0.31                | 0.43               | 0.5              |
| Numness/tingling in your hands or feet (S) | 2     | 759 | Taxane/vinca alkaloid/platin chemotherapy in prior 2 weeks | Other                      | -0.05                      | 0.83 | -0.06        | Role Functioning         | 0.23                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 759 |  |                            |                            |      |              | Emotional Functioning    | 0.30                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 757 |  |                            |                            |      |              | Cognitive Functioning    | 0.22                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 756 |  |                            |                            |      |              | Social Functioning       | 0.20                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 757 |  |                            |                            |      |              | Global Health Status/QoL | 0.21                | <0.001             | <0.001           |
| Numness/tingling in your hands or feet (S) | 2     | 750 |  |                            |                            |      |              | HRQL Summary Score       | 0.33                | <0.001             | <0.001           |
| Pain (F)                                   | 1     | 848 | ECOG PS 2-4  | ECOG PS 0-1                | 0.62                       | 1.27 | 0.49         | Physical Functioning     | 0.39                | <0.001             | <0.001           |
| Pain (F)                                   | 1     | 848 | Chemotherapy in prior 2 weeks                              | Other                      | -0.07                      | 1.29 | -0.06        | Role Functioning         | 0.41                | 0.4                | 0.4              |
| Pain (F)                                   | 1     | 848 | Opioid [narcotic] pain med in prior week                   | Other                      | 1.41                       | 1.11 | 1.27         | Emotional Functioning    | 0.38                | <0.001             | <0.001           |
| Pain (F)                                   | 1     | 848 | Surgery in prior 2 weeks                                   | Other                      | 0.35                       | 1.29 | 0.27         | Cognitive Functioning    | 0.36                | 0.13               | 0.26             |
| Pain (F)                                   | 1     | 832 |  |                            |                            |      |              | Social Functioning       | 0.41                | <0.001             | <0.001           |
| Pain (F)                                   | 1     | 829 |  |                            |                            |      |              | Global Health Status/QoL | 0.41                | <0.001             | <0.001           |
| Pain (F)                                   | 1     | 829 |  |                            |                            |      |              | HRQL Summary Score       | 0.59                | <0.001             | <0.001           |
| Pain (F)                                   | 1     | 827 |  |                            |                            |      |              | Pain                     | 0.77                | <0.001             | <0.001           |
| Pain (F)                                   | 1     | 833 |  |                            |                            |      |              | Physical Functioning     | 0.41                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 793 | ECOG PS 2-4  | ECOG PS 0-1                | 0.62                       | 1.29 | 0.48         | Role Functioning         | 0.38                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 793 | Chemotherapy in prior 2 weeks                              | Other                      | -0.21                      | 1.30 | -0.16        | Emotional Functioning    | 0.38                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 793 | Opioid [narcotic] pain med in prior week                   | Other                      | 1.31                       | 1.15 | 1.14         | Cognitive Functioning    | 0.33                | 0.02**             | 0.07             |
| Pain (F)                                   | 2     | 793 | Surgery in prior 2 weeks                                   | Other                      | 0.63                       | 1.30 | 0.48         | Social Functioning       | 0.37                | 0.02               | 0.07             |
| Pain (F)                                   | 2     | 771 |  |                            |                            |      |              | Global Health Status/QoL | 0.41                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 769 |  |                            |                            |      |              | HRQL Summary Score       | 0.55                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 769 |  |                            |                            |      |              | Pain                     | 0.78                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 768 |  |                            |                            |      |              | Physical Functioning     | 0.41                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 768 |  |                            |                            |      |              | Role Functioning         | 0.38                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 768 |  |                            |                            |      |              | Emotional Functioning    | 0.38                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 768 |  |                            |                            |      |              | Cognitive Functioning    | 0.33                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 768 |  |                            |                            |      |              | Social Functioning       | 0.37                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 762 |  |                            |                            |      |              | Global Health Status/QoL | 0.41                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 776 |  |                            |                            |      |              | HRQL Summary Score       | 0.55                | <0.001             | <0.001           |
| Pain (F)                                   | 2     | 776 |  |                            |                            |      |              | Pain                     | 0.78                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 848 | ECOG PS 2-4  | ECOG PS 0-1                | 0.66                       | 1.16 | 0.57         | Physical Functioning     | 0.42                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 848 | Chemotherapy in prior 2 weeks                              | Other                      | -0.03                      | 1.18 | -0.02        | Role Functioning         | 0.43                | 0.73               | 0.73             |
| Pain (S)                                   | 1     | 848 | Opioid [narcotic] pain med in prior week                   | Other                      | 1.31                       | 1.01 | 1.31         | Emotional Functioning    | 0.40                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 848 | Surgery in prior 2 weeks                                   | Other                      | 0.40                       | 1.18 | 0.34         | Cognitive Functioning    | 0.40                | 0.06               | 0.18             |
| Pain (S)                                   | 1     | 832 |  |                            |                            |      |              | Social Functioning       | 0.37                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 829 |  |                            |                            |      |              | Global Health Status/QoL | 0.42                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 829 |  |                            |                            |      |              | Pain                     | 0.76                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 829 |  |                            |                            |      |              | Physical Functioning     | 0.42                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 829 |  |                            |                            |      |              | Role Functioning         | 0.43                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 829 |  |                            |                            |      |              | Emotional Functioning    | 0.38                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 829 |  |                            |                            |      |              | Cognitive Functioning    | 0.40                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 829 |  |                            |                            |      |              | Social Functioning       | 0.37                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 827 |  |                            |                            |      |              | Global Health Status/QoL | 0.42                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 827 |  |                            |                            |      |              | HRQL Summary Score       | 0.61                | <0.001             | <0.001           |
| Pain (S)                                   | 1     | 833 |  |                            |                            |      |              | Pain                     | 0.76                | <0.001             | <0.001           |
| Pain (S)                                   | 2     | 793 | ECOG PS 2-4  | ECOG PS 0-1                | 0.52                       | 1.15 | 0.46         | Physical Functioning     | 0.44                | 0.16               | 0.31             |
| Pain (S)                                   | 2     | 793 | Chemotherapy in prior 2 weeks                              | Other                      | -0.12                      | 1.17 | -0.10        | Role Functioning         | 0.38                | <0.001             | <0.001           |
| Pain (S)                                   | 2     | 793 | Opioid [narcotic] pain med in prior week                   | Other                      | 1.19                       | 1.02 | 1.16         | Emotional Functioning    | 0.36                | <0.001             | <0.001           |
| Pain (S)                                   | 2     | 771 | Surgery in prior 2 weeks                                   | Other                      | 0.50                       | 1.16 | 0.43         | Cognitive Functioning    | 0.32                | <0.001             | <0.001           |
| Pain (S)                                   | 2     | 769 |  |                            |                            |      |              | Social Functioning       | 0.38                | <0.001             | <0.001           |
| Pain (S)                                   | 2     | 769 |  |                            |                            |      |              | Global Health Status/QoL | 0.44                | <0.001             | <0.001           |
| Pain (S)                                   | 2     | 768 |  |                            |                            |      |              | HRQL Summary Score       | 0.32                | <0.001             | <0.001           |
| Pain (S)                                   | 2     | 768 |  |                            |                            |      |              | Pain                     | 0.38                | <0.001             | <0.001           |

| PROCTCAE Item               | Visit | N   | Worse Symptom Level Group                | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|-----------------------------|-------|-----|--|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Pain (S)                    | 2     | 769 |  |                            |                            |      |              | Global Health Status/QoL | 0.41                | <0.001             | <0.001           |
| Pain (S)                    | 2     | 762 |  |                            |                            |      |              | HRQOL Summary Score      | 0.57                | <0.001             | <0.001           |
| Pain (S)                    | 2     | 776 |  |                            |                            |      |              | Pain                     | 0.78                | <0.001             | <0.001           |
| Pain (I)                    | 1     | 848 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.83                       | 1.23 | 0.67         |                          |                     |                    | 0.9              |
| Pain (I)                    | 1     | 848 | Chemotherapy in prior 2 weeks            | Other                      | -0.01                      | 1.27 | -0.01        | Physical Functioning     | 0.47                | <0.001             | <0.001           |
| Pain (I)                    | 1     | 848 | Opioid [narcotic] pain med in prior week | Other                      | 1.31                       | 1.11 | 1.19         | Role Functioning         | 0.48                | <0.001             | <0.001           |
| Pain (I)                    | 1     | 832 | Surgery in prior 2 weeks                 | Other                      | 0.32                       | 1.27 | 0.25         | Emotional Functioning    | 0.42                | <0.001             | <0.001           |
| Pain (I)                    | 1     | 829 |  |                            |                            |      |              | Cognitive Functioning    | 0.43                | <0.001             | <0.001           |
| Pain (I)                    | 1     | 829 |  |                            |                            |      |              | Social Functioning       | 0.46                | <0.001             | <0.001           |
| Pain (I)                    | 1     | 829 |  |                            |                            |      |              | Global Health Status/QoL | 0.42                | <0.001             | <0.001           |
| Pain (I)                    | 1     | 827 |  |                            |                            |      |              | HRQOL Summary Score      | 0.65                | <0.001             | <0.001           |
| Pain (I)                    | 1     | 833 |  |                            |                            |      |              | Pain                     | 0.76                | <0.001             | <0.001           |
| Pain (I)                    | 2     | 792 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.65                       | 1.23 | 0.53         |                          |                     |                    | <0.001           |
| Pain (I)                    | 2     | 792 | Chemotherapy in prior 2 weeks            | Other                      | -0.11                      | 1.25 | -0.08        | Physical Functioning     | 0.49                | <0.001             | <0.001           |
| Pain (I)                    | 2     | 792 | Opioid [narcotic] pain med in prior week | Other                      | 1.28                       | 1.09 | 1.17         | Role Functioning         | 0.48                | <0.001             | <0.001           |
| Pain (I)                    | 2     | 792 | Surgery in prior 2 weeks                 | Other                      | 0.74                       | 1.25 | 0.59         | Emotional Functioning    | 0.40                | <0.001             | <0.001           |
| Pain (I)                    | 2     | 770 |  |                            |                            |      |              | Cognitive Functioning    | 0.36                | <0.001             | <0.001           |
| Pain (I)                    | 2     | 768 |  |                            |                            |      |              | Social Functioning       | 0.46                | <0.001             | <0.001           |
| Pain (I)                    | 2     | 767 |  |                            |                            |      |              | Global Health Status/QoL | 0.44                | <0.001             | <0.001           |
| Pain (I)                    | 2     | 768 |  |                            |                            |      |              | HRQOL Summary Score      | 0.62                | <0.001             | <0.001           |
| Pain (I)                    | 2     | 761 |  |                            |                            |      |              | Pain                     | 0.78                | <0.001             | <0.001           |
| Pain (I)                    | 2     | 775 |  |                            |                            |      |              |                          |                     |                    | <0.001           |
| Pain during vaginal sex (S) | 1     | 86  | ECOG PS 2-4                              | ECOG PS 0-1                | -0.37                      | 0.78 | -0.48        |                          |                     | 0.3                | 1                |
| Pain during vaginal sex (S) | 1     | 34  | Age <40                                  | Age >60                    | 0                          | 0.69 | 0            | Physical Functioning     | -0.13               | 0.25               | 1                |
| Pain during vaginal sex (S) | 1     | 82  |  |                            |                            |      |              | Role Functioning         | 0.15                | 0.17               | 1                |
| Pain during vaginal sex (S) | 1     | 82  |  |                            |                            |      |              | Emotional Functioning    | 0.19                | 0.1                | 1                |
| Pain during vaginal sex (S) | 1     | 82  |  |                            |                            |      |              | Cognitive Functioning    | 0.06                | 0.61               | 1                |
| Pain during vaginal sex (S) | 1     | 82  |  |                            |                            |      |              | Social Functioning       | 0.18                | 0.11               | 1                |
| Pain during vaginal sex (S) | 1     | 82  |  |                            |                            |      |              | Global Health Status/QoL | 0.10                | 0.38               | 1                |
| Pain during vaginal sex (S) | 1     | 82  |  |                            |                            |      |              | HRQOL Summary Score      | 0.39                | 0.31               | 1                |
| Pain during vaginal sex (S) | 2     | 74  | ECOG PS 2-4                              | ECOG PS 0-1                | -0.47                      | 0.88 | -0.54        |                          |                     | 0.3                | 1                |
| Pain during vaginal sex (S) | 2     | 30  | Age <40                                  | Age >60                    | -0.66                      | 0.93 | -0.71        | Physical Functioning     | -0.01               | 0.06               | 1                |
| Pain during vaginal sex (S) | 2     | 70  |  |                            |                            |      |              | Role Functioning         | 0.10                | 0.91               | 1                |
| Pain during vaginal sex (S) | 2     | 70  |  |                            |                            |      |              | Emotional Functioning    | 0.11                | 0.39               | 1                |
| Pain during vaginal sex (S) | 2     | 70  |  |                            |                            |      |              | Cognitive Functioning    | -0.01               | 0.34               | 1                |
| Pain during vaginal sex (S) | 2     | 70  |  |                            |                            |      |              | Social Functioning       | -0.01               | 0.94               | 1                |
| Pain during vaginal sex (S) | 2     | 70  |  |                            |                            |      |              | Global Health Status/QoL | -0.07               | 0.55               | 1                |
| Pain during vaginal sex (S) | 2     | 70  |  |                            |                            |      |              | HRQOL Summary Score      | 0.02                | 0.85               | 1                |
| Pain during vaginal sex (S) | 2     | 69  |  |                            |                            |      |              |                          | 0.04                | 0.77               | 1                |
| Pain in the abdomen (F)     | 1     | 331 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.2                        | 0.84 | 0.24         |                          |                     | 0.09               | 0.17             |
| Pain in the abdomen (F)     | 1     | 226 | Gastrointestinal                         | Lung                       | 0.6                        | 0.80 | 0.76         | Physical Functioning     | 0.27                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 1     | 323 |  |                            |                            |      |              | Role Functioning         | 0.36                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 1     | 323 |  |                            |                            |      |              | Emotional Functioning    | 0.28                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 1     | 323 |  |                            |                            |      |              | Cognitive Functioning    | 0.21                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 1     | 323 |  |                            |                            |      |              | Social Functioning       | 0.33                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 1     | 323 |  |                            |                            |      |              | Global Health Status/QoL | 0.28                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 1     | 320 |  |                            |                            |      |              | HRQOL Summary Score      | 0.46                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 2     | 293 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.23                       | 0.88 | 0.26         |                          |                     | 0.11               | 0.17             |
| Pain in the abdomen (F)     | 2     | 200 | Gastrointestinal                         | Lung                       | 0.31                       | 0.89 | 0.35         | Physical Functioning     | 0.25                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 2     | 288 |  |                            |                            |      |              | Role Functioning         | 0.26                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 2     | 288 |  |                            |                            |      |              | Emotional Functioning    | 0.23                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 2     | 286 |  |                            |                            |      |              | Cognitive Functioning    | 0.08                | 0.17               | 0.17             |
| Pain in the abdomen (F)     | 2     | 286 |  |                            |                            |      |              | Social Functioning       | 0.23                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 2     | 286 |  |                            |                            |      |              | Global Health Status/QoL | 0.24                | <0.001             | <0.001           |
| Pain in the abdomen (F)     | 2     | 285 |  |                            |                            |      |              | HRQOL Summary Score      | 0.36                | <0.001             | <0.001           |
| Pain in the abdomen (S)     | 1     | 331 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.13                       | 0.81 | 0.16         |                          |                     | 0.26               | 0.26             |
| Pain in the abdomen (S)     | 1     | 226 | Gastrointestinal                         | Lung                       | 0.50                       | 0.77 | 0.65         | Physical Functioning     | 0.25                | <0.001             | <0.001           |
| Pain in the abdomen (S)     | 1     | 323 |  |                            |                            |      |              | Role Functioning         | 0.32                | <0.001             | <0.001           |
| Pain in the abdomen (S)     | 1     | 323 |  |                            |                            |      |              | Emotional Functioning    | 0.27                | <0.001             | <0.001           |
| Pain in the abdomen (S)     | 1     | 323 |  |                            |                            |      |              | Cognitive Functioning    | 0.24                | <0.001             | <0.001           |
| Pain in the abdomen (S)     | 1     | 323 |  |                            |                            |      |              | Social Functioning       | 0.30                | <0.001             | <0.001           |
| Pain in the abdomen (S)     | 1     | 323 |  |                            |                            |      |              | Global Health Status/QoL | 0.26                | <0.001             | <0.001           |
| Pain in the abdomen (S)     | 1     | 320 |  |                            |                            |      |              | HRQOL Summary Score      | 0.43                | <0.001             | <0.001           |
| Pain in the abdomen (S)     | 2     | 293 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.27                       | 0.90 | 0.29         |                          |                     | 0.07               | 0.14             |

| PROCTCAE Item                      | Visit | N   | Worse Symptom Level Group                                | Better Symptom Level Group | Mean Or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|------------------------------------|-------|-----|--|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Pain in the abdomen (S)            | 2     | 200 | Gastrointestinal   | Lung                       | 0.31                       | 0.92 | 0.34         | Physical Functioning     | 0.31                | 0.04               | 0.12             |
| Pain in the abdomen (S)            | 2     | 288 |  |                            |                            |      |              | Role Functioning         | 0.29                | <0.001             | <0.001           |
| Pain in the abdomen (S)            | 2     | 288 |  |                            |                            |      |              | Emotional Functioning    | 0.25                | <0.001             | <0.001           |
| Pain in the abdomen (S)            | 2     | 286 |  |                            |                            |      |              | Cognitive Functioning    | 0.14                | 0.02               | 0.08             |
| Pain in the abdomen (S)            | 2     | 286 |  |                            |                            |      |              | Social Functioning       | 0.26                | <0.001             | <0.001           |
| Pain in the abdomen (S)            | 2     | 286 |  |                            |                            |      |              | Global Health Status/QoL | 0.29                | <0.001             | <0.001           |
| Pain in the abdomen (S)            | 2     | 285 |  |                            |                            |      |              | HRQL Summary Score       | 0.42                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 1     | 331 | ECOG PS 2-4  | ECOG PS 0-1                | 0.14                       | 0.71 | 0.20         |                          |                     | 0.17               | 0.17             |
| Pain in the abdomen (I)            | 1     | 226 | Gastrointestinal   | Lung                       | 0.48                       | 0.68 | 0.70         | Physical Functioning     | 0.26                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 1     | 323 |  |                            |                            |      |              | Role Functioning         | 0.32                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 1     | 323 |  |                            |                            |      |              | Emotional Functioning    | 0.27                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 1     | 323 |  |                            |                            |      |              | Cognitive Functioning    | 0.21                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 1     | 323 |  |                            |                            |      |              | Social Functioning       | 0.33                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 1     | 323 |  |                            |                            |      |              | Global Health Status/QoL | 0.23                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 1     | 320 |  |                            |                            |      |              | HRQL Summary Score       | 0.43                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 2     | 293 | ECOG PS 2-4  | ECOG PS 0-1                | 0.30                       | 0.83 | 0.36         | Physical Functioning     | 0.30                | 0.03               | 0.06             |
| Pain in the abdomen (I)            | 2     | 200 | Gastrointestinal   | Lung                       | 0.30                       | 0.83 | 0.36         | Role Functioning         | 0.30                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 2     | 288 |  |                            |                            |      |              | Emotional Functioning    | 0.25                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 2     | 286 |  |                            |                            |      |              | Cognitive Functioning    | 0.20                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 2     | 286 |  |                            |                            |      |              | Social Functioning       | 0.28                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 2     | 286 |  |                            |                            |      |              | Global Health Status/QoL | 0.29                | <0.001             | <0.001           |
| Pain in the abdomen (I)            | 2     | 285 |  |                            |                            |      |              | HRQL Summary Score       | 0.41                | <0.001             | <0.001           |
| Pain or burning with urination (S) | 1     | 215 | ECOG PS 2-4  | ECOG PS 0-1                | -0.15                      | 0.58 | -0.26        | Physical Functioning     | 0.12                | 0.17               | 0.23             |
| Pain or burning with urination (S) | 1     | 53  | Prostate/Bladder with radiation therapy in prior 2 weeks | Hematologic                | 0.79                       | 0.66 | 1.19         | Role Functioning         | 0.08                | <0.001             | 0.02             |
| Pain or burning with urination (S) | 1     | 214 |  |                            |                            |      |              | Emotional Functioning    | 0.17                | 0.01               | 0.16             |
| Pain or burning with urination (S) | 1     | 214 |  |                            |                            |      |              | Cognitive Functioning    | 0.09                | 0.21               | 0.23             |
| Pain or burning with urination (S) | 1     | 214 |  |                            |                            |      |              | Social Functioning       | 0.15                | 0.03               | 0.23             |
| Pain or burning with urination (S) | 1     | 214 |  |                            |                            |      |              | Global Health Status/QoL | 0.11                | 0.1                | 0.23             |
| Pain or burning with urination (S) | 1     | 212 |  |                            |                            |      |              | HRQL Summary Score       | 0.20                | 0.004              | 0.06             |
| Pain or burning with urination (S) | 2     | 190 | ECOG PS 2-4  | ECOG PS 0-1                | -0.15                      | 0.52 | -0.28        | Physical Functioning     | 0.09                | 0.23               | 0.23             |
| Pain or burning with urination (S) | 2     | 48  | Prostate/Bladder with radiation therapy in prior 2 weeks | Hematologic                | 0.71                       | 0.64 | 1.11         | Role Functioning         | 0.18                | 0.01               | 0.16             |
| Pain or burning with urination (S) | 2     | 188 |  |                            |                            |      |              | Emotional Functioning    | 0.19                | 0.009              | 0.13             |
| Pain or burning with urination (S) | 2     | 187 |  |                            |                            |      |              | Cognitive Functioning    | 0.21                | 0.003              | 0.05             |
| Pain or burning with urination (S) | 2     | 186 |  |                            |                            |      |              | Social Functioning       | 0.16                | 0.03               | 0.23             |
| Pain or burning with urination (S) | 2     | 187 |  |                            |                            |      |              | Global Health Status/QoL | 0.18                | 0.02               | 0.17             |
| Pain or burning with urination (S) | 2     | 184 |  |                            |                            |      |              | HRQL Summary Score       | 0.17                | 0.02               | 0.19             |
| Pain/swelling/redness at IV (P)    | 1     | 208 | ECOG PS 2-4  | ECOG PS 0-1                | -4.28%                     |      | -0.14        | Physical Functioning     | 0.09                | 0.56               | 0.99             |
| Pain/swelling/redness at IV (P)    | 1     | 208 | Irritant chemotherapy [footnote 3] in prior 2 weeks      | Other                      | 2.52%                      |      | 0.08         | Role Functioning         | -0.05               | 0.59               | 0.99             |
| Pain/swelling/redness at IV (P)    | 1     | 203 |  |                            |                            |      |              | Emotional Functioning    | -0.05               | 0.48               | 0.99             |
| Pain/swelling/redness at IV (P)    | 1     | 203 |  |                            |                            |      |              | Cognitive Functioning    | -0.01               | 0.88               | 0.99             |
| Pain/swelling/redness at IV (P)    | 1     | 203 |  |                            |                            |      |              | Social Functioning       | -0.01               | 0.85               | 0.99             |
| Pain/swelling/redness at IV (P)    | 1     | 203 |  |                            |                            |      |              | Global Health Status/QoL | 0.08                | 0.25               | 0.99             |
| Pain/swelling/redness at IV (P)    | 1     | 203 |  |                            |                            |      |              | HRQL Summary Score       | 0.00                | 0.99               | 0.99             |
| Pain/swelling/redness at IV (P)    | 1     | 201 | ECOG PS 2-4  | ECOG PS 0-1                | -5.90%                     |      | -0.21        | Physical Functioning     | 0.02                | 0.73               | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 210 | Irritant chemotherapy [footnote 3] in prior 2 weeks      | Other                      | 2.17%                      |      | 0.07         | Role Functioning         | -0.07               | 0.44               | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 201 |  |                            |                            |      |              | Emotional Functioning    | 0.00                | 0.62               | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 201 |  |                            |                            |      |              | Cognitive Functioning    | 0.00                | 0.3                | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 202 |  |                            |                            |      |              | Social Functioning       | -0.05               | 0.94               | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 202 |  |                            |                            |      |              | Global Health Status/QoL | -0.03               | 0.49               | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 202 |  |                            |                            |      |              | HRQL Summary Score       | -0.05               | 0.66               | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 202 |  |                            |                            |      |              | Physical Functioning     | -0.05               | 0.45               | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 202 |  |                            |                            |      |              | Role Functioning         | -0.13               | 0.07               | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 200 |  |                            |                            |      |              | Emotional Functioning    | -0.08               | 0.24               | 0.99             |
| Pain/swelling/redness at IV (P)    | 2     | 200 |  |                            |                            |      |              | Cognitive Functioning    | 0.11                | 0.11               | 0.2              |
| Pain/swelling/redness at IV (P)    | 1     | 412 | ECOG PS 2-4  | ECOG PS 0-1                | 0.19                       | 0.85 | 0.23         | Physical Functioning     | 0.30                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)      | 1     | 397 |  |                            |                            |      |              | Role Functioning         | 0.27                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)      | 1     | 397 |  |                            |                            |      |              | Emotional Functioning    | 0.21                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)      | 1     | 397 |  |                            |                            |      |              | Cognitive Functioning    | 0.23                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)      | 1     | 397 |  |                            |                            |      |              | Social Functioning       | 0.29                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)      | 1     | 397 |  |                            |                            |      |              | Global Health Status/QoL | 0.27                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)      | 1     | 394 |  |                            |                            |      |              | HRQL Summary Score       | 0.31                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)      | 2     | 372 | ECOG PS 2-4  | ECOG PS 0-1                | 0.17                       | 0.83 | 0.21         | Physical Functioning     | 0.29                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)      | 2     | 356 |  |                            |                            |      |              | Role Functioning         | 0.26                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)      | 2     | 356 |  |                            |                            |      |              | Emotional Functioning    | 0.26                | <0.001             | <0.001           |

| PROCTCAE Item                   | Visit | N   | Worse Symptom Level Group                | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|---------------------------------|-------|-----|--|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Pounding/racing heartbeat (F)   | 2     | 356 |  |                            |                            |      |              | Emotional Functioning    | 0.24                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)   | 2     | 356 |  |                            |                            |      |              | Cognitive Functioning    | 0.20                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)   | 2     | 356 |  |                            |                            |      |              | Social Functioning       | 0.28                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)   | 2     | 356 |  |                            |                            |      |              | Global Health Status/QoL | 0.24                | <0.001             | <0.001           |
| Pounding/racing heartbeat (F)   | 2     | 352 |  |                            |                            |      |              | HRQOL Summary Score      | 0.34                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 1     | 412 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.15                       | 0.74 | 0.20         | Physical Functioning     | . .                 | 0.17               | 0.17             |
| Pounding/racing heartbeat (S)   | 1     | 397 |  |                            |                            |      |              | Role Functioning         | 0.31                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 1     | 397 |  |                            |                            |      |              | Emotional Functioning    | 0.29                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 1     | 397 |  |                            |                            |      |              | Cognitive Functioning    | 0.23                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 1     | 397 |  |                            |                            |      |              | Social Functioning       | 0.24                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 1     | 397 |  |                            |                            |      |              | Global Health Status/QoL | 0.35                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 1     | 397 |  |                            |                            |      |              | HRQOL Summary Score      | 0.31                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 1     | 394 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.16                       | 0.71 | 0.22         | Physical Functioning     | 0.25                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 2     | 356 |  |                            |                            |      |              | Role Functioning         | 0.26                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 2     | 356 |  |                            |                            |      |              | Emotional Functioning    | 0.22                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 2     | 356 |  |                            |                            |      |              | Cognitive Functioning    | 0.15                | 0.004              | 0.01             |
| Pounding/racing heartbeat (S)   | 2     | 356 |  |                            |                            |      |              | Social Functioning       | 0.26                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 2     | 356 |  |                            |                            |      |              | Global Health Status/QoL | 0.21                | <0.001             | <0.001           |
| Pounding/racing heartbeat (S)   | 2     | 352 |  |                            |                            |      |              | HRQOL Summary Score      | 0.31                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 837 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.48                       | 0.88 | 0.54         | Physical Functioning     | . .                 | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 837 | Opioid [narcotic] pain med in prior week | Other                      | 0.37                       | 0.88 | 0.41         | Role Functioning         | . .                 | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 837 | Sleep aid in prior week                  | Other                      | 0.22                       | 0.90 | 0.24         | Emotional Functioning    | . .                 | 0.006              | 0.006            |
| Problems with concentration (S) | 1     | 821 |  |                            |                            |      |              | Cognitive Functioning    | 0.39                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | Social Functioning       | 0.40                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | Global Health Status/QoL | 0.47                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | HRQOL Summary Score      | 0.71                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | Physical Functioning     | 0.43                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | Role Functioning         | 0.34                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | Emotional Functioning    | 0.56                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 776 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.45                       | 0.90 | 0.50         | Cognitive Functioning    | . .                 | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 776 | Opioid [narcotic] pain med in prior week | Other                      | 0.41                       | 0.90 | 0.46         | Role Functioning         | . .                 | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 776 | Sleep aid in prior week                  | Other                      | 0.33                       | 0.91 | 0.37         | Emotional Functioning    | . .                 | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 754 |  |                            |                            |      |              | Cognitive Functioning    | 0.39                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 752 |  |                            |                            |      |              | Social Functioning       | 0.37                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 752 |  |                            |                            |      |              | Global Health Status/QoL | 0.47                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 751 |  |                            |                            |      |              | HRQOL Summary Score      | 0.76                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 752 |  |                            |                            |      |              | Physical Functioning     | 0.35                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 752 |  |                            |                            |      |              | Role Functioning         | 0.35                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 745 |  |                            |                            |      |              | Emotional Functioning    | 0.54                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 837 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.46                       | 0.90 | 0.51         | Cognitive Functioning    | . .                 | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 837 | Opioid [narcotic] pain med in prior week | Other                      | 0.32                       | 0.90 | 0.36         | Role Functioning         | . .                 | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 837 | Sleep aid in prior week                  | Other                      | 0.19                       | 0.91 | 0.21         | Emotional Functioning    | . .                 | 0.02               | 0.02             |
| Problems with concentration (S) | 1     | 821 |  |                            |                            |      |              | Cognitive Functioning    | 0.38                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 821 |  |                            |                            |      |              | Social Functioning       | 0.40                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | Global Health Status/QoL | 0.49                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | HRQOL Summary Score      | 0.70                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | Physical Functioning     | 0.49                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 818 |  |                            |                            |      |              | Role Functioning         | 0.34                | <0.001             | <0.001           |
| Problems with concentration (S) | 1     | 816 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.46                       | 0.89 | 0.52         | Cognitive Functioning    | 0.55                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 773 | Opioid [narcotic] pain med in prior week | Other                      | 0.34                       | 0.89 | 0.38         | Role Functioning         | . .                 | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 773 | Sleep aid in prior week                  | Other                      | 0.21                       | 0.90 | 0.23         | Emotional Functioning    | . .                 | 0.01               | 0.02             |
| Problems with concentration (S) | 2     | 751 |  |                            |                            |      |              | Cognitive Functioning    | 0.39                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 751 |  |                            |                            |      |              | Social Functioning       | 0.39                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 749 |  |                            |                            |      |              | Global Health Status/QoL | 0.46                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 749 |  |                            |                            |      |              | HRQOL Summary Score      | 0.70                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 748 |  |                            |                            |      |              | Physical Functioning     | 0.37                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 748 |  |                            |                            |      |              | Role Functioning         | 0.34                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 742 |  |                            |                            |      |              | Emotional Functioning    | 0.52                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 742 |  |                            |                            |      |              | Cognitive Functioning    | 0.34                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 742 |  |                            |                            |      |              | Global Health Status/QoL | 0.34                | <0.001             | <0.001           |
| Problems with concentration (S) | 2     | 742 |  |                            |                            |      |              | HRQOL Summary Score      | 0.52                | <0.001             | <0.001           |
| Problems with memory (S)        | 1     | 291 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.32                       | 0.79 | 0.40         | Physical Functioning     | . .                 | 0.18               | 0.09             |
| Problems with memory (S)        | 1     | 291 | Breast/Prostate                          | Gastrointestinal           | -0.17                      | 0.82 | -0.20        | Role Functioning         | . .                 | 0.02               | 0.08             |
| Problems with memory (S)        | 1     | 360 |  |                            |                            |      |              | Emotional Functioning    | 0.31                | <0.001             | <0.001           |
| Problems with memory (S)        | 1     | 360 |  |                            |                            |      |              | Cognitive Functioning    | 0.30                | <0.001             | <0.001           |
| Problems with memory (S)        | 1     | 360 |  |                            |                            |      |              | Social Functioning       | 0.32                | <0.001             | <0.001           |
| Problems with memory (S)        | 1     | 360 |  |                            |                            |      |              | Global Health Status/QoL | 0.69                | <0.001             | <0.001           |
| Problems with memory (S)        | 1     | 360 |  |                            |                            |      |              | HRQOL Summary Score      | 0.39                | <0.001             | <0.001           |
| Problems with memory (S)        | 1     | 360 |  |                            |                            |      |              | Physical Functioning     | 0.22                | <0.001             | <0.001           |
| Problems with memory (S)        | 1     | 358 |  |                            |                            |      |              | Role Functioning         | 0.45                | <0.001             | <0.001           |
| Problems with memory (S)        | 2     | 338 | ECOG PS 2-4                              | ECOG PS 0-1                | 0.21                       | 0.79 | 0.26         | Cognitive Functioning    | . .                 | 0.19               | 0.38             |
| Problems with memory (S)        | 2     | 272 | Breast/Prostate                          | Gastrointestinal           | 0.09                       | 0.84 | 0.11         | Role Functioning         | . .                 | 0.49               | 0.49             |
| Problems with memory (S)        | 2     | 325 |  |                            |                            |      |              | Emotional Functioning    | 0.26                | <0.001             | <0.001           |

| PRO-CTCAE Item                           | Visit | N   | Worse Symptom Level Group                         | Better Symptom Level Group      | Mean or Percent Difference | SD           | Effect Size*  | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--|-------|-----|---|---------------------------------|----------------------------|--------------|---------------|--------------------------|---------------------|--------------------|------------------|
| Problems with memory (S)                 | 2     | 325 |   |                                 |                            |              |               | Role Functioning         | 0.21                | <0.001             | <0.001           |
| Problems with memory (S)                 | 2     | 326 |   |                                 |                            |              |               | Emotional Functioning    | 0.30                | <0.001             | <0.001           |
| Problems with memory (S)                 | 2     | 326 |   |                                 |                            |              |               | Cognitive Functioning    | 0.75                | <0.001             | <0.001           |
| Problems with memory (S)                 | 2     | 326 |   |                                 |                            |              |               | Social Functioning       | 0.28                | <0.001             | <0.001           |
| Problems with memory (S)                 | 2     | 326 |   |                                 |                            |              |               | Global Health Status/QoL | 0.13                | 0.02               | 0.08             |
| Problems with memory (S)                 | 2     | 320 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.38                | <0.001             | <0.001           |
| Problems with memory (I)                 | 1     | 368 | ECOG PS 2-4<br>Breast/Prostate                    | ECOG PS 0-1<br>Gastrointestinal | 0.37<br>-0.08              | 0.85<br>0.89 | 0.43<br>-0.09 |                          |                     | 0.01               | 0.05             |
| Problems with memory (I)                 | 1     | 291 |   |                                 |                            |              |               | Physical Functioning     | 0.31                | <0.001             | <0.001           |
| Problems with memory (I)                 | 1     | 360 |   |                                 |                            |              |               | Role Functioning         | 0.29                | <0.001             | <0.001           |
| Problems with memory (I)                 | 1     | 360 |   |                                 |                            |              |               | Emotional Functioning    | 0.39                | <0.001             | <0.001           |
| Problems with memory (I)                 | 1     | 360 |   |                                 |                            |              |               | Cognitive Functioning    | 0.60                | <0.001             | <0.001           |
| Problems with memory (I)                 | 1     | 360 |   |                                 |                            |              |               | Social Functioning       | 0.48                | <0.001             | <0.001           |
| Problems with memory (I)                 | 1     | 360 |   |                                 |                            |              |               | Global Health Status/QoL | 0.25                | <0.001             | <0.001           |
| Problems with memory (I)                 | 1     | 358 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.45                | <0.001             | <0.001           |
| Problems with memory (I)                 | 2     | 338 | ECOG PS 2-4<br>Breast/Prostate                    | ECOG PS 0-1<br>Gastrointestinal | 0.25<br>0.17               | 0.78<br>0.82 | 0.32<br>0.20  |                          |                     | 0.1<br>0.19        | 0.31<br>0.39     |
| Problems with memory (I)                 | 2     | 272 |   |                                 |                            |              |               | Physical Functioning     | 0.25                | <0.001             | <0.001           |
| Problems with memory (I)                 | 2     | 325 |   |                                 |                            |              |               | Role Functioning         | 0.24                | <0.001             | <0.001           |
| Problems with memory (I)                 | 2     | 325 |   |                                 |                            |              |               | Emotional Functioning    | 0.34                | <0.001             | <0.001           |
| Problems with memory (I)                 | 2     | 326 |   |                                 |                            |              |               | Cognitive Functioning    | 0.62                | <0.001             | <0.001           |
| Problems with memory (I)                 | 2     | 325 |   |                                 |                            |              |               | Social Functioning       | 0.29                | <0.001             | <0.001           |
| Problems with memory (I)                 | 2     | 326 |   |                                 |                            |              |               | Global Health Status/QoL | 0.16                | 0.003              | 0.01             |
| Problems with memory (I)                 | 2     | 320 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.37                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 1     | 839 | ECOG PS 2-4                                       | ECOG PS 0-1                     | 0.31                       | 1.16         | 0.27          | Physical Functioning     | 0.25                | 0.003              | 0.003            |
| Problems with tasting food/drink (S)     | 1     | 823 |   |                                 |                            |              |               | Role Functioning         | 0.30                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 1     | 823 |   |                                 |                            |              |               | Emotional Functioning    | 0.24                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 1     | 820 |   |                                 |                            |              |               | Cognitive Functioning    | 0.27                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 1     | 820 |   |                                 |                            |              |               | Social Functioning       | 0.32                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 1     | 820 |   |                                 |                            |              |               | Global Health Status/QoL | 0.22                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 1     | 818 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.44                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 2     | 775 | ECOG PS 2-4                                       | ECOG PS 0-1                     | 0.36                       | 1.20         | 0.30          | Physical Functioning     | 0.25                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 2     | 753 |   |                                 |                            |              |               | Role Functioning         | 0.29                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 2     | 751 |   |                                 |                            |              |               | Emotional Functioning    | 0.18                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 2     | 751 |   |                                 |                            |              |               | Cognitive Functioning    | 0.22                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 2     | 750 |   |                                 |                            |              |               | Social Functioning       | 0.34                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 2     | 751 |   |                                 |                            |              |               | Global Health Status/QoL | 0.29                | <0.001             | <0.001           |
| Problems with tasting food/drink (S)     | 2     | 744 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.43                | <0.001             | <0.001           |
| Rash (P)                                 | 1     | 821 | ECOG PS 2-4<br>Radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other            | -2.31%<br>2.73%            |              | -0.06<br>0.07 | Physical Functioning     | 0.03                | 0.51               | 0.93             |
| Rash (P)                                 | 1     | 805 |   |                                 |                            |              |               | Role Functioning         | 0.42                | 0.42               | 0.93             |
| Rash (P)                                 | 1     | 805 |   |                                 |                            |              |               | Emotional Functioning    | 0.03                | 0.42               | 0.93             |
| Rash (P)                                 | 1     | 802 |   |                                 |                            |              |               | Cognitive Functioning    | 0.01                | 0.7                | 0.93             |
| Rash (P)                                 | 1     | 802 |   |                                 |                            |              |               | Social Functioning       | 0.04                | 0.26               | 0.93             |
| Rash (P)                                 | 1     | 802 |   |                                 |                            |              |               | Global Health Status/QoL | 0.23                | 0.93               | 0.93             |
| Rash (P)                                 | 1     | 800 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.02                | 0.51               | 0.93             |
| Rash (P)                                 | 2     | 756 | ECOG PS 2-4<br>Radiation therapy in prior 2 weeks | ECOG PS 0-1<br>Other            | -0.67%<br>7.39%            |              | -0.02<br>0.18 | Physical Functioning     | 0.04                | 0.24               | 0.93             |
| Rash (P)                                 | 2     | 735 |   |                                 |                            |              |               | Role Functioning         | 0.05                | 0.87               | 0.93             |
| Rash (P)                                 | 2     | 735 |   |                                 |                            |              |               | Emotional Functioning    | 0.01                | 0.01               | 0.21             |
| Rash (P)                                 | 2     | 733 |   |                                 |                            |              |               | Social Functioning       | 0.04                | 0.21               | 0.93             |
| Rash (P)                                 | 2     | 733 |   |                                 |                            |              |               | Cognitive Functioning    | -0.02               | 0.31               | 0.93             |
| Rash (P)                                 | 2     | 732 |   |                                 |                            |              |               | Global Health Status/QoL | 0.03                | 0.47               | 0.93             |
| Rash (P)                                 | 2     | 733 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.04                | 0.31               | 0.93             |
| Rash (P)                                 | 2     | 726 |   |                                 |                            |              |               | Global Health Status/QoL | 0.03                | 0.43               | 0.93             |
| Rash (P)                                 | 2     | 726 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.00                | 0.93               | 0.93             |
| Ridges/bumps on fingernails/toenails (P) | 1     | 483 | ECOG PS 2-4                                       | ECOG PS 0-1                     | -1.40%                     |              | -0.04         | Physical Functioning     | 0.06                | 0.78               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 1     | 468 |   |                                 |                            |              |               | Role Functioning         | 0.17                | 0.17               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 1     | 468 |   |                                 |                            |              |               | Emotional Functioning    | -0.01               | 0.89               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 1     | 468 |   |                                 |                            |              |               | Cognitive Functioning    | -0.03               | 0.58               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 1     | 468 |   |                                 |                            |              |               | Social Functioning       | 0.11                | 0.01               | 0.22             |
| Ridges/bumps on fingernails/toenails (P) | 1     | 468 |   |                                 |                            |              |               | Global Health Status/QoL | -0.01               | 0.89               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 1     | 465 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.01                | 0.86               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 1     | 465 |   |                                 |                            |              |               | Physical Functioning     | 0.03                | 0.49               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 2     | 439 | ECOG PS 2-4                                       | ECOG PS 0-1                     | -5.90%                     |              | -0.15         | Role Functioning         | 0.06                | 0.35               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 2     | 423 |   |                                 |                            |              |               | Emotional Functioning    | 0.03                | 0.2                | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 2     | 423 |   |                                 |                            |              |               | Cognitive Functioning    | 0.04                | 0.49               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 2     | 422 |   |                                 |                            |              |               | Social Functioning       | 0.04                | 0.41               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 2     | 422 |   |                                 |                            |              |               | Global Health Status/QoL | 0.06                | 0.23               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 2     | 421 |   |                                 |                            |              |               | HRQOL Summary Score      | 0.02                | 0.66               | 0.89             |
| Ridges/bumps on fingernails/toenails (P) | 2     | 422 |   |                                 |                            |              |               | Physical Functioning     | 0.08                | 0.08               | 0.89             |

| PRO-CTCAE Item                           | Visit | N   | Worse Symptom Level Group                      | Better Symptom Level Group      | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30 HRQL Summary Score | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--|-------|-----|--|---------------------------------|----------------------------|------|--------------|----------------------------------|---------------------|--------------------|------------------|
| Ridges/bumps on fingernails/hoenails (P) | 2     | 415 |  |                                 |                            |      |              |                                  | 0.06                | 0.21               | 0.89             |
| Ringing in ears (S)                      | 1     | 294 | ECOG PS 2-4<br>Head/Neck                       | ECOG PS 0-1<br>Prostate/Bladder | 0.19                       | 0.79 | 0.25         |                                  |                     | 0.21               | 0.67             |
| Ringing in ears (S)                      | 1     | 191 |  |                                 | 0.29                       | 0.78 | 0.38         | Physical Functioning             | 0.06                | 0.01               | 0.12             |
| Ringing in ears (S)                      | 1     | 291 |  |                                 |                            |      |              | Role Functioning                 | 0.18                | 0.33               | 0.67             |
| Ringing in ears (S)                      | 1     | 288 |  |                                 |                            |      |              | Emotional Functioning            | 0.19                | 0.002              | 0.03             |
| Ringing in ears (S)                      | 1     | 288 |  |                                 |                            |      |              | Cognitive Functioning            | 0.13                | <0.001             | 0.01             |
| Ringing in ears (S)                      | 1     | 288 |  |                                 |                            |      |              | Social Functioning               | 0.20                | <0.001             | 0.15             |
| Ringing in ears (S)                      | 1     | 288 |  |                                 |                            |      |              | Global Health Status/QoL         | 0.13                | 0.02               | 0.15             |
| Ringing in ears (S)                      | 1     | 286 |  |                                 |                            |      |              | HRQL Summary Score               | 0.25                | <0.001             | <0.001           |
| Ringing in ears (S)                      | 2     | 262 | ECOG PS 2-4<br>Head/Neck                       | ECOG PS 0-1<br>Prostate/Bladder | -0.01                      | 0.74 | -0.02        |                                  |                     | 0.94               | 0.94             |
| Ringing in ears (S)                      | 2     | 175 |  |                                 | 0.27                       | 0.72 | 0.37         | Physical Functioning             | 0.06                | 0.01               | 0.15             |
| Ringing in ears (S)                      | 2     | 259 |  |                                 |                            |      |              | Role Functioning                 | 0.15                | 0.31               | 0.67             |
| Ringing in ears (S)                      | 2     | 259 |  |                                 |                            |      |              | Emotional Functioning            | 0.19                | 0.003              | 0.03             |
| Ringing in ears (S)                      | 2     | 258 |  |                                 |                            |      |              | Cognitive Functioning            | 0.13                | 0.04               | 0.2              |
| Ringing in ears (S)                      | 2     | 257 |  |                                 |                            |      |              | Social Functioning               | 0.14                | 0.03               | 0.15             |
| Ringing in ears (S)                      | 2     | 258 |  |                                 |                            |      |              | Global Health Status/QoL         | 0.14                | 0.02               | 0.15             |
| Ringing in ears (S)                      | 2     | 255 |  |                                 |                            |      |              | HRQL Summary Score               | 0.23                | <0.001             | 0.003            |
| Sad or unhappy feelings (F)              | 1     | 840 | ECOG PS 2-4<br>Currently taking depression med | ECOG PS 0-1<br>Other            | 0.28                       | 0.98 | 0.28         |                                  |                     | 0.002              | 0.002            |
| Sad or unhappy feelings (F)              | 1     | 840 |  |                                 | 0.53                       | 0.97 | 0.55         | Physical Functioning             | 0.32                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 1     | 824 |  |                                 |                            |      |              | Role Functioning                 | 0.38                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 1     | 824 |  |                                 |                            |      |              | Emotional Functioning            | 0.66                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 1     | 821 |  |                                 |                            |      |              | Cognitive Functioning            | 0.38                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 1     | 821 |  |                                 |                            |      |              | Social Functioning               | 0.41                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 1     | 821 |  |                                 |                            |      |              | Global Health Status/QoL         | 0.37                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 1     | 819 |  |                                 |                            |      |              | HRQL Summary Score               | 0.49                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 2     | 783 | ECOG PS 2-4<br>Currently taking depression med | ECOG PS 0-1<br>Other            | 0.30                       | 0.98 | 0.30         |                                  |                     | 0.002              | 0.002            |
| Sad or unhappy feelings (F)              | 2     | 783 |  |                                 | 0.67                       | 0.96 | 0.70         | Physical Functioning             | 0.31                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 2     | 761 |  |                                 |                            |      |              | Role Functioning                 | 0.29                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 2     | 759 |  |                                 |                            |      |              | Emotional Functioning            | 0.69                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 2     | 759 |  |                                 |                            |      |              | Cognitive Functioning            | 0.40                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 2     | 758 |  |                                 |                            |      |              | Social Functioning               | 0.35                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 2     | 759 |  |                                 |                            |      |              | Global Health Status/QoL         | 0.37                | <0.001             | <0.001           |
| Sad or unhappy feelings (F)              | 2     | 752 |  |                                 |                            |      |              | HRQL Summary Score               | 0.47                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 1     | 840 | ECOG PS 2-4<br>Currently taking depression med | ECOG PS 0-1<br>Other            | 0.31                       | 0.90 | 0.34         |                                  |                     | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 1     | 840 |  |                                 | 0.52                       | 0.89 | 0.58         | Physical Functioning             | 0.32                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 1     | 824 |  |                                 |                            |      |              | Role Functioning                 | 0.37                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 1     | 824 |  |                                 |                            |      |              | Emotional Functioning            | 0.64                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 1     | 821 |  |                                 |                            |      |              | Cognitive Functioning            | 0.39                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 1     | 821 |  |                                 |                            |      |              | Social Functioning               | 0.40                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 1     | 821 |  |                                 |                            |      |              | Global Health Status/QoL         | 0.37                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 1     | 819 |  |                                 |                            |      |              | HRQL Summary Score               | 0.50                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 2     | 783 | ECOG PS 2-4<br>Currently taking depression med | ECOG PS 0-1<br>Other            | 0.29                       | 0.87 | 0.34         |                                  |                     | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 2     | 783 |  |                                 | 0.68                       | 0.84 | 0.81         | Physical Functioning             | 0.33                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 2     | 761 |  |                                 |                            |      |              | Role Functioning                 | 0.32                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 2     | 759 |  |                                 |                            |      |              | Emotional Functioning            | 0.66                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 2     | 758 |  |                                 |                            |      |              | Cognitive Functioning            | 0.40                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 2     | 759 |  |                                 |                            |      |              | Social Functioning               | 0.37                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 2     | 752 |  |                                 |                            |      |              | Global Health Status/QoL         | 0.38                | <0.001             | <0.001           |
| Sad or unhappy feelings (S)              | 2     | 752 |  |                                 |                            |      |              | HRQL Summary Score               | 0.49                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 1     | 840 | ECOG PS 2-4<br>Currently taking depression med | ECOG PS 0-1<br>Other            | 0.39                       | 0.96 | 0.40         |                                  |                     | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 1     | 840 |  |                                 | 0.57                       | 0.95 | 0.60         | Physical Functioning             | 0.34                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 1     | 824 |  |                                 |                            |      |              | Role Functioning                 | 0.40                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 1     | 824 |  |                                 |                            |      |              | Emotional Functioning            | 0.63                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 1     | 821 |  |                                 |                            |      |              | Cognitive Functioning            | 0.38                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 1     | 821 |  |                                 |                            |      |              | Social Functioning               | 0.49                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 1     | 821 |  |                                 |                            |      |              | Global Health Status/QoL         | 0.37                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 1     | 819 |  |                                 |                            |      |              | HRQL Summary Score               | 0.50                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 2     | 782 | ECOG PS 2-4<br>Currently taking depression med | ECOG PS 0-1<br>Other            | 0.35                       | 0.90 | 0.39         |                                  |                     | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 2     | 782 |  |                                 | 0.64                       | 0.88 | 0.73         | Physical Functioning             | 0.38                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 2     | 760 |  |                                 |                            |      |              | Role Functioning                 | 0.38                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 2     | 758 |  |                                 |                            |      |              | Emotional Functioning            | 0.63                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 2     | 758 |  |                                 |                            |      |              | Cognitive Functioning            | 0.41                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 2     | 757 |  |                                 |                            |      |              | Social Functioning               | 0.43                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 2     | 758 |  |                                 |                            |      |              | Global Health Status/QoL         | 0.36                | <0.001             | <0.001           |
| Sad or unhappy feelings (I)              | 2     | 751 |  |                                 |                            |      |              | HRQL Summary Score               | 0.52                | <0.001             | <0.001           |

| PRO-CTCAE Item                  | Visit | N   | Worse Symptom Level Group  | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size*             | EORTC QLQ-C30        | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|---------------------------------|-------|-----|----------------------------|----------------------------|----------------------------|------|--------------------------|----------------------|---------------------|--------------------|------------------|
| Shivering or shaking chills (F) | 1     | 200 | ECOG PS 2-4                | ECOG PS 0-1                | 0.37                       | 0.91 | 0.41                     | Physical Functioning | 0.28                | 0.02               | 0.07             |
| Shivering or shaking chills (F) | 1     | 199 |                            |                            |                            |      | Role Functioning         | 0.28                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (F) | 1     | 199 |                            |                            |                            |      | Emotional Functioning    | 0.22                 | 0.002               | 0.02               |                  |
| Shivering or shaking chills (F) | 1     | 199 |                            |                            |                            |      | Cognitive Functioning    | 0.17                 | 0.02                | 0.07               |                  |
| Shivering or shaking chills (F) | 1     | 199 |                            |                            |                            |      | Social Functioning       | 0.30                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (F) | 1     | 199 |                            |                            |                            |      | Global Health Status/QoL | 0.30                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (F) | 1     | 197 |                            |                            |                            |      | HRQL Summary Score       | 0.37                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (F) | 2     | 176 | ECOG PS 2-4                | ECOG PS 0-1                | 0.29                       | 0.84 | 0.34                     | Physical Functioning | 0.20                | 0.007              | 0.04             |
| Shivering or shaking chills (F) | 2     | 175 |                            |                            |                            |      | Role Functioning         | 0.31                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (F) | 2     | 175 |                            |                            |                            |      | Emotional Functioning    | 0.23                 | 0.002               | 0.02               |                  |
| Shivering or shaking chills (F) | 2     | 175 |                            |                            |                            |      | Cognitive Functioning    | 0.22                 | 0.004               | 0.02               |                  |
| Shivering or shaking chills (F) | 2     | 175 |                            |                            |                            |      | Social Functioning       | 0.15                 | 0.049               | 0.09               |                  |
| Shivering or shaking chills (F) | 2     | 175 |                            |                            |                            |      | Global Health Status/QoL | 0.18                 | 0.02                | 0.07               |                  |
| Shivering or shaking chills (F) | 2     | 175 |                            |                            |                            |      | HRQL Summary Score       | 0.36                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (S) | 1     | 200 | ECOG PS 2-4                | ECOG PS 0-1                | 0.31                       | 0.82 | 0.38                     | Physical Functioning | 0.28                | 0.03               | 0.1              |
| Shivering or shaking chills (S) | 1     | 199 |                            |                            |                            |      | Role Functioning         | 0.25                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (S) | 1     | 199 |                            |                            |                            |      | Emotional Functioning    | 0.23                 | 0.001               | 0.01               |                  |
| Shivering or shaking chills (S) | 1     | 199 |                            |                            |                            |      | Cognitive Functioning    | 0.16                 | 0.02                | 0.09               |                  |
| Shivering or shaking chills (S) | 1     | 199 |                            |                            |                            |      | Social Functioning       | 0.28                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (S) | 1     | 199 |                            |                            |                            |      | Global Health Status/QoL | 0.34                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (S) | 1     | 197 |                            |                            |                            |      | HRQL Summary Score       | 0.37                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (S) | 2     | 176 | ECOG PS 2-4                | ECOG PS 0-1                | 0.25                       | 0.78 | 0.32                     | Physical Functioning | 0.19                | 0.01               | 0.07             |
| Shivering or shaking chills (S) | 2     | 175 |                            |                            |                            |      | Role Functioning         | 0.31                 | <0.001              | <0.001             |                  |
| Shivering or shaking chills (S) | 2     | 175 |                            |                            |                            |      | Emotional Functioning    | 0.21                 | 0.004               | 0.04               |                  |
| Shivering or shaking chills (S) | 2     | 175 |                            |                            |                            |      | Cognitive Functioning    | 0.18                 | 0.02                | 0.08               |                  |
| Shivering or shaking chills (S) | 2     | 175 |                            |                            |                            |      | Social Functioning       | 0.14                 | 0.07                | 0.11               |                  |
| Shivering or shaking chills (S) | 2     | 175 |                            |                            |                            |      | Global Health Status/QoL | 0.18                 | 0.02                | 0.08               |                  |
| Shivering or shaking chills (S) | 2     | 175 |                            |                            |                            |      | HRQL Summary Score       | 0.36                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 1     | 832 | ECOG PS 2-4                | ECOG PS 0-1                | 0.66                       | 0.90 | 0.74                     | Physical Functioning | 0.47                | <0.001             | <0.001           |
| Shortness of breath (S)         | 1     | 832 | Currently using an inhaler | Other                      | 0.91                       | 0.89 | 1.03                     | Role Functioning     | 0.36                | <0.001             | <0.001           |
| Shortness of breath (S)         | 1     | 816 |                            |                            |                            |      | Emotional Functioning    | 0.26                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 1     | 813 |                            |                            |                            |      | Cognitive Functioning    | 0.25                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 1     | 813 |                            |                            |                            |      | Social Functioning       | 0.30                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 1     | 813 |                            |                            |                            |      | Global Health Status/QoL | 0.33                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 1     | 811 |                            |                            |                            |      | HRQL Summary Score       | 0.48                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 1     | 816 |                            |                            |                            |      | Dyspnea                  | 0.79                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 2     | 771 | ECOG PS 2-4                | ECOG PS 0-1                | 0.46                       | 0.90 | 0.51                     | Physical Functioning | 0.45                | <0.001             | <0.001           |
| Shortness of breath (S)         | 2     | 749 | Currently using an inhaler | Other                      | 0.90                       | 0.88 | 1.03                     | Role Functioning     | 0.34                | <0.001             | <0.001           |
| Shortness of breath (S)         | 2     | 749 |                            |                            |                            |      | Emotional Functioning    | 0.26                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 2     | 747 |                            |                            |                            |      | Cognitive Functioning    | 0.28                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 2     | 746 |                            |                            |                            |      | Social Functioning       | 0.26                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 2     | 747 |                            |                            |                            |      | Global Health Status/QoL | 0.33                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 2     | 740 |                            |                            |                            |      | HRQL Summary Score       | 0.46                 | <0.001              | <0.001             |                  |
| Shortness of breath (S)         | 2     | 749 |                            |                            |                            |      | Dyspnea                  | 0.81                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 1     | 832 | ECOG PS 2-4                | ECOG PS 0-1                | 0.60                       | 0.97 | 0.62                     | Physical Functioning | 0.46                | <0.001             | <0.001           |
| Shortness of breath (I)         | 1     | 832 | Currently using an inhaler | Other                      | 0.73                       | 0.97 | 0.76                     | Role Functioning     | 0.38                | <0.001             | <0.001           |
| Shortness of breath (I)         | 1     | 816 |                            |                            |                            |      | Emotional Functioning    | 0.26                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 1     | 813 |                            |                            |                            |      | Cognitive Functioning    | 0.23                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 1     | 813 |                            |                            |                            |      | Social Functioning       | 0.34                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 1     | 813 |                            |                            |                            |      | Global Health Status/QoL | 0.31                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 1     | 811 |                            |                            |                            |      | HRQL Summary Score       | 0.47                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 1     | 816 |                            |                            |                            |      | Dyspnea                  | 0.69                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 2     | 770 | ECOG PS 2-4                | ECOG PS 0-1                | 0.48                       | 0.92 | 0.52                     | Physical Functioning | 0.46                | <0.001             | <0.001           |
| Shortness of breath (I)         | 2     | 748 | Currently using an inhaler | Other                      | 0.74                       | 0.91 | 0.81                     | Role Functioning     | 0.38                | <0.001             | <0.001           |
| Shortness of breath (I)         | 2     | 746 |                            |                            |                            |      | Emotional Functioning    | 0.29                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 2     | 745 |                            |                            |                            |      | Cognitive Functioning    | 0.29                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 2     | 746 |                            |                            |                            |      | Social Functioning       | 0.32                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 2     | 739 |                            |                            |                            |      | Global Health Status/QoL | 0.36                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 2     | 748 |                            |                            |                            |      | HRQL Summary Score       | 0.48                 | <0.001              | <0.001             |                  |
| Shortness of breath (I)         | 2     | 748 |                            |                            |                            |      | Dyspnea                  | 0.73                 | <0.001              | <0.001             |                  |
| Skin burns from radiation (S)   | 1     | 351 | ECOG PS 2-4                | ECOG PS 0-1                | -0.09                      | 0.71 | -0.12                    |                      |                     | 0.39               | 0.71             |

| PRO-CTCAE Item              | Visit | N   | Worse Symptom Level Group                                | Better Symptom Level Group | Mean or Percent Difference | SD                   | Effect Size*          | EORTC QLQ-C30                                     | Pearson Correlation | Unadjusted P-value | Hochberg P-value |               |                       |       |        |        |
|-----------------------------|-------|-----|--|----------------------------|----------------------------|----------------------|-----------------------|---|---------------------|--------------------|------------------|---------------|-----------------------|-------|--------|--------|
| ECOG PS 2-4                 | 1     | 351 | Radiation therapy in prior 2 weeks                       | Other                      | 0.09                       | 0.70                 | 0.12                  | Physical Functioning                              | 0.05                | 0.27               | 0.71             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 334 | Radiation therapy in prior 2 weeks                       | Other                      | -0.25<br>0.53              | 0.94<br>0.92         | -0.26<br>0.58         | Role Functioning                                  | 0.08                | 0.39               | 0.71             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 334 |  |                            |                            |                      |                       | Emotional Functioning                             | 0.11                | 0.14               | 0.71             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 332 |  |                            |                            |                      |                       | Cognitive Functioning                             | 0.19                | 0.047              | 0.52             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 332 |  |                            |                            |                      |                       | Social Functioning                                | 0.13                | <0.001             | 0.008            |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 332 |  |                            |                            |                      |                       | Global Health Status/QoL                          | 0.14                | 0.02               | 0.21             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 330 |  |                            |                            |                      |                       | HRQOL Summary Score                               | 0.16                | 0.009              | 0.13             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 314 |  |                            |                            |                      |                       | Radiation therapy in prior 2 weeks                | Other               | -0.25<br>0.53      | 0.94<br>0.92     | -0.26<br>0.58 | Physical Functioning  | 0.02  | <0.001 | <0.001 |
| ECOG PS 2-4                 | 2     | 299 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Role Functioning      | 0.09  | 0.11   | 0.71   |
| ECOG PS 2-4                 | 2     | 299 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Emotional Functioning | 0.09  | 0.11   | 0.69   |
| ECOG PS 2-4                 | 2     | 298 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Cognitive Functioning | 0.20  | <0.001 | 0.007  |
| ECOG PS 2-4                 | 2     | 298 | Social Functioning                                       | 0.09                       | 0.11                       | 0.69                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 298 | Global Health Status/QoL                                 | 0.10                       | 0.09                       | 0.69                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 298 | HRQOL Summary Score                                      | 0.09                       | 0.11                       | 0.69                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 296 | Physical Functioning                                     | 0.15                       | 0.01                       | 0.16                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 296 | Role Functioning   | 0.15                       | 0.01                       | 0.16                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 296 | Emotional Functioning                                    | 0.15                       | 0.01                       | 0.16                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 296 | Cognitive Functioning                                    | 0.15                       | 0.01                       | 0.16                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 296 | Social Functioning                                       | 0.15                       | 0.01                       | 0.16                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 296 | Global Health Status/QoL                                 | 0.15                       | 0.01                       | 0.16                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 296 | HRQOL Summary Score                                      | 0.15                       | 0.01                       | 0.16                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 252 | ECOG PS 2-4  | ECOG PS 0-1                | 0.15                       | 0.74                 | 0.20                  | Physical Functioning                              | 0.25                | 0.26               | 0.79             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 139 | Head/Neck  | Hematologic                | -0.04                      | 0.84                 | -0.04                 | Role Functioning                                  | 0.25                | 0.82               | 0.95             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 252 | Head/Neck with radiation therapy in prior 2 weeks        | Other                      | 0.13                       | 0.74                 | 0.18                  | Emotional Functioning                             | 0.23                | 0.17               | 0.79             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 249 | Head/Neck with radiation therapy in prior 2 weeks        | Other                      | 0.18<br>-0.01<br>0.16      | 0.79<br>0.87<br>0.79 | 0.22<br>-0.01<br>0.20 | Physical Functioning                              | 0.25                | <0.001             | <0.001           |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 249 |  |                            |                            |                      |                       | Role Functioning                                  | 0.23                | <0.001             | 0.004            |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 246 |  |                            |                            |                      |                       | Emotional Functioning                             | 0.14                | 0.03               | 0.18             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 246 |  |                            |                            |                      |                       | Cognitive Functioning                             | 0.20                | 0.002              | 0.02             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 246 |  |                            |                            |                      |                       | Social Functioning                                | 0.16                | 0.01               | 0.1              |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 246 |  |                            |                            |                      |                       | Global Health Status/QoL                          | 0.29                | <0.001             | <0.001           |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 244 |  |                            |                            |                      |                       | HRQOL Summary Score                               | 0.28                | <0.001             | <0.001           |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 220 |  |                            |                            |                      |                       | ECOG PS 2-4                                       | ECOG PS 0-1         | 0.18               | 0.79             | 0.22          | Physical Functioning  | 0.24  | 0.24   | 0.79   |
| ECOG PS 2-4                 | 2     | 124 |  |                            |                            |                      |                       | Head/Neck   | Hematologic         | -0.01              | 0.87             | -0.01         | Role Functioning      | 0.24  | 0.95   | 0.95   |
| ECOG PS 2-4                 | 2     | 220 |  |                            |                            |                      |                       | Head/Neck with radiation therapy in prior 2 weeks | Other               | 0.16               | 0.79             | 0.20          | Emotional Functioning | 0.25  | 0.15   | 0.79   |
| ECOG PS 2-4                 | 2     | 218 | Head/Neck with radiation therapy in prior 2 weeks        | Other                      | 0.18<br>-0.01<br>0.16      | 0.79<br>0.87<br>0.79 | 0.22<br>-0.01<br>0.20 | Physical Functioning                              | 0.30                | <0.001             | <0.001           |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 218 |  |                            |                            |                      |                       | Role Functioning                                  | 0.24                | <0.001             | 0.004            |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 218 |  |                            |                            |                      |                       | Emotional Functioning                             | 0.22                | 0.001              | 0.01             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 218 |  |                            |                            |                      |                       | Social Functioning                                | 0.33                | <0.001             | <0.001           |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 218 |  |                            |                            |                      |                       | Global Health Status/QoL                          | 0.22                | 0.01               | 0.01             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 218 |  |                            |                            |                      |                       | HRQOL Summary Score                               | 0.38                | <0.001             | <0.001           |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 218 |  |                            |                            |                      |                       | Physical Functioning                              | 0.09                | 0.34               | 0.95             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 266 |  |                            |                            |                      |                       | ECOG PS 2-4                                       | ECOG PS 0-1         | 7.09%              |                  | 0.17          | Role Functioning      | 0.16  | 0.16   | 0.95   |
| ECOG PS 2-4                 | 1     | 265 |  |                            |                            |                      |                       | ECOG PS 2-4                                       | Other               | 7.09%              |                  | 0.17          | Emotional Functioning | 0.05  | 0.41   | 0.95   |
| ECOG PS 2-4                 | 1     | 265 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Cognitive Functioning | 0.20  | 0.001  | 0.02   |
| ECOG PS 2-4                 | 1     | 261 | Social Functioning                                       | 0.15                       | 0.02                       | 0.22                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 261 | Global Health Status/QoL                                 | 0.05                       | 0.45                       | 0.95                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 261 | HRQOL Summary Score                                      | 0.11                       | 0.09                       | 0.95                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 236 | ECOG PS 2-4  | ECOG PS 0-1                | 8.81%                      |                      | 0.20                  |   |                     |                    |                  |               | Physical Functioning  | 0.16  | 0.008  | 0.95   |
| ECOG PS 2-4                 | 2     | 234 | ECOG PS 2-4  | Other                      | 8.81%                      |                      | 0.20                  |   |                     |                    |                  |               | Role Functioning      | 0.08  | 0.22   | 0.95   |
| ECOG PS 2-4                 | 2     | 234 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Emotional Functioning | 0.01  | 0.89   | 0.95   |
| ECOG PS 2-4                 | 2     | 234 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Cognitive Functioning | 0.05  | 0.45   | 0.95   |
| ECOG PS 2-4                 | 2     | 234 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Social Functioning    | 0.04  | 0.57   | 0.95   |
| ECOG PS 2-4                 | 2     | 234 |  |                            |                            |                      |                       | Global Health Status/QoL                          | -0.04               | 0.54               | 0.95             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 234 |  |                            |                            |                      |                       | HRQOL Summary Score                               | 0.01                | 0.88               | 0.95             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 234 |  |                            |                            |                      |                       | Physical Functioning                              | 0.00                | 0.95               | 0.95             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 200 |  |                            |                            |                      |                       | ECOG PS 2-4                                       | ECOG PS 0-1         | -2.17%             |                  | -0.07         | Role Functioning      | 0.01  | 0.71   | 0.99   |
| ECOG PS 2-4                 | 1     | 200 |  |                            |                            |                      |                       | ECOG PS 2-4                                       | Male                | -2.17%             |                  | -0.07         | Emotional Functioning | -0.03 | 0.01   | 0.21   |
| ECOG PS 2-4                 | 1     | 199 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Cognitive Functioning | -0.07 | 0.35   | 0.99   |
| ECOG PS 2-4                 | 1     | 199 | Social Functioning                                       | -0.02                      | 0.74                       | 0.99                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 199 | Global Health Status/QoL                                 | 0.04                       | 0.54                       | 0.99                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 199 | HRQOL Summary Score                                      | -0.01                      | 0.85                       | 0.99                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 176 | ECOG PS 2-4  | ECOG PS 0-1                | 6.94%                      |                      | 0.19                  |   |                     |                    |                  |               | Physical Functioning  | 0.01  | 0.85   | 0.99   |
| ECOG PS 2-4                 | 2     | 176 | ECOG PS 2-4  | Male                       | 6.94%                      | 13.15%               | 0.19<br>0.42          |   |                     |                    |                  |               | Role Functioning      | 0.00  | 0.31   | 0.99   |
| ECOG PS 2-4                 | 2     | 175 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Emotional Functioning | 0.01  | 0.01   | 0.21   |
| ECOG PS 2-4                 | 2     | 175 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Cognitive Functioning | 0.14  | 0.06   | 0.88   |
| ECOG PS 2-4                 | 2     | 175 |  |                            |                            |                      |                       |   |                     |                    |                  |               | Social Functioning    | 0.11  | 0.13   | 0.99   |
| ECOG PS 2-4                 | 2     | 175 |  |                            |                            |                      |                       | Global Health Status/QoL                          | 0.11                | 0.15               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 175 |  |                            |                            |                      |                       | HRQOL Summary Score                               | 0.01                | 0.87               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 175 |  |                            |                            |                      |                       | Physical Functioning                              | 0.05                | 0.52               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 175 |  |                            |                            |                      |                       | Role Functioning                                  | 0.05                | 0.52               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 175 |  |                            |                            |                      |                       | Emotional Functioning                             | 0.05                | 0.52               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 175 |  |                            |                            |                      |                       | Social Functioning                                | 0.05                | 0.52               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 175 | Global Health Status/QoL                                 | 0.20                       | 0.08                       | 0.15                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 2     | 175 | HRQOL Summary Score                                      | 0.20                       | 0.02                       | 0.38                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 | ECOG PS 2-4  | ECOG PS 0-1                | 0.26                       | 1.03                 | 0.25                  | Physical Functioning                              | 0.20                | 0.2                | 0.38             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 55  | Prostate/Bladder with radiation therapy in prior 2 weeks | Hematologic                | 0.93                       | 1.03                 | 0.90                  | Role Functioning                                  | 0.02                | 0.002              | 0.03             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 | ECOG PS 2-4  | Hematologic                | 0.26<br>0.93               | 1.03<br>1.03         | 0.25<br>0.90          | Emotional Functioning                             | 0.11                | 0.15               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 |  |                            |                            |                      |                       | Cognitive Functioning                             | 0.11                | 0.15               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 |  |                            |                            |                      |                       | Social Functioning                                | 0.01                | 0.87               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 |  |                            |                            |                      |                       | Global Health Status/QoL                          | 0.05                | 0.52               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 |  |                            |                            |                      |                       | HRQOL Summary Score                               | 0.05                | 0.52               | 0.99             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 |  |                            |                            |                      |                       | Physical Functioning                              | 0.20                | 0.08               | 0.15             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 |  |                            |                            |                      |                       | Role Functioning                                  | 0.20                | 0.08               | 0.15             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 |  |                            |                            |                      |                       | Emotional Functioning                             | 0.20                | 0.08               | 0.15             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 |  |                            |                            |                      |                       | Cognitive Functioning                             | 0.20                | 0.08               | 0.15             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 |  |                            |                            |                      |                       | Social Functioning                                | 0.20                | 0.08               | 0.15             |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 | Global Health Status/QoL                                 | 0.20                       | 0.08                       | 0.15                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| ECOG PS 2-4                 | 1     | 219 | HRQOL Summary Score                                      | 0.20                       | 0.08                       | 0.15                 |                       |   |                     |                    |                  |               |                       |       |        |        |
| Sudden urges to urinate (F) | 1     | 219 | ECOG PS 2-4  | ECOG PS 0-1                | 0.26                       | 1.03                 | 0.25                  | Physical Functioning                              | 0.20                | 0.2                | 0.38             |               |                       |       |        |        |
| Sudden urges to urinate (F) | 1     | 55  | Prostate/Bladder with radiation therapy in prior 2 weeks | Hematologic                | 0.93                       | 1.03                 | 0.90                  | Role Functioning                                  | 0.02                | 0.002              | 0.03             |               |                       |       |        |        |

| PROCTCAE Item                            | Visit | N   | Worse Symptom Level Group                                | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--|-------|-----|--|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Sudden urges to urinate (F)              | 1     | 218 |  |                            |                            |      |              | Physical Functioning     | 0.16                | 0.02               | 0.15             |
| Sudden urges to urinate (F)              | 1     | 218 |  |                            |                            |      |              | Role Functioning         | 0.14                | 0.04               | 0.16             |
| Sudden urges to urinate (F)              | 1     | 218 |  |                            |                            |      |              | Emotional Functioning    | 0.20                | 0.003              | 0.03             |
| Sudden urges to urinate (F)              | 1     | 218 |  |                            |                            |      |              | Cognitive Functioning    | 0.12                | 0.07               | 0.22             |
| Sudden urges to urinate (F)              | 1     | 218 |  |                            |                            |      |              | Social Functioning       | 0.16                | 0.02               | 0.15             |
| Sudden urges to urinate (F)              | 1     | 218 |  |                            |                            |      |              | Global Health Status/QoL | 0.23                | <0.001             | 0.009            |
| Sudden urges to urinate (F)              | 1     | 216 | ECOG PS 2-4  | ECOG PS 0-1                | 0.21                       | 1.08 | 0.19         | HRQL Summary Score       | 0.25                | <0.001             | 0.003            |
| Sudden urges to urinate (F)              | 2     | 193 | Prostate/Bladder with radiation therapy in prior 2 weeks | Hematologic                | 1.68                       | 1.06 | 1.58         | Physical Functioning     |                     | 0.38               | 0.38             |
| Sudden urges to urinate (F)              | 2     | 48  |  |                            |                            |      |              | Role Functioning         | 0.16                | <0.001             | <0.001           |
| Sudden urges to urinate (F)              | 2     | 191 |  |                            |                            |      |              | Emotional Functioning    | 0.19                | 0.03               | 0.16             |
| Sudden urges to urinate (F)              | 2     | 190 |  |                            |                            |      |              | Cognitive Functioning    | 0.15                | 0.009              | 0.09             |
| Sudden urges to urinate (F)              | 2     | 189 |  |                            |                            |      |              | Social Functioning       | 0.19                | 0.008              | 0.09             |
| Sudden urges to urinate (F)              | 2     | 190 |  |                            |                            |      |              | Global Health Status/QoL | 0.16                | 0.03               | 0.16             |
| Sudden urges to urinate (F)              | 2     | 187 |  |                            |                            |      |              | HRQL Summary Score       | 0.27                | <0.001             | 0.003            |
| Sudden urges to urinate (F)              | 2     | 187 |  |                            |                            |      |              | HRQL Summary Score       | 0.24                | <0.001             | 0.01             |
| Sudden urges to urinate (I)              | 1     | 219 | ECOG PS 2-4  | ECOG PS 0-1                | 0.20                       | 0.99 | 0.20         | Physical Functioning     |                     | 0.32               | 0.63             |
| Sudden urges to urinate (I)              | 1     | 55  | Prostate/Bladder with radiation therapy in prior 2 weeks | Hematologic                | 0.90                       | 1.13 | 0.80         | Role Functioning         | 0.25                | <0.001             | 0.04             |
| Sudden urges to urinate (I)              | 1     | 218 |  |                            |                            |      |              | Emotional Functioning    | 0.16                | 0.02               | 0.18             |
| Sudden urges to urinate (I)              | 1     | 218 |  |                            |                            |      |              | Cognitive Functioning    | 0.23                | <0.001             | 0.01             |
| Sudden urges to urinate (I)              | 1     | 218 |  |                            |                            |      |              | Social Functioning       | 0.07                | 0.27               | 0.63             |
| Sudden urges to urinate (I)              | 1     | 218 |  |                            |                            |      |              | Global Health Status/QoL | 0.21                | 0.001              | 0.02             |
| Sudden urges to urinate (I)              | 1     | 218 |  |                            |                            |      |              | HRQL Summary Score       | 0.29                | <0.001             | 0.03             |
| Sudden urges to urinate (I)              | 1     | 216 | ECOG PS 2-4  | ECOG PS 0-1                | 0.05                       | 0.86 | 0.06         | Physical Functioning     |                     | 0.79               | <0.001           |
| Sudden urges to urinate (I)              | 2     | 193 | Prostate/Bladder with radiation therapy in prior 2 weeks | Hematologic                | 1.14                       | 0.88 | 1.30         | Role Functioning         | 0.12                | <0.001             | 0.001            |
| Sudden urges to urinate (I)              | 2     | 48  |  |                            |                            |      |              | Emotional Functioning    | 0.16                | 0.11               | 0.57             |
| Sudden urges to urinate (I)              | 2     | 191 |  |                            |                            |      |              | Cognitive Functioning    | 0.17                | 0.03               | 0.19             |
| Sudden urges to urinate (I)              | 2     | 190 |  |                            |                            |      |              | Social Functioning       | 0.17                | 0.02               | 0.18             |
| Sudden urges to urinate (I)              | 2     | 190 |  |                            |                            |      |              | Global Health Status/QoL | 0.10                | 0.15               | 0.61             |
| Sudden urges to urinate (I)              | 2     | 189 |  |                            |                            |      |              | HRQL Summary Score       | 0.16                | 0.03               | 0.18             |
| Sudden urges to urinate (I)              | 2     | 190 |  |                            |                            |      |              | HRQL Summary Score       | 0.17                | 0.02               | 0.18             |
| Sudden urges to urinate (I)              | 2     | 187 |  |                            |                            |      |              | HRQL Summary Score       | 0.16                | 0.02               | 0.18             |
| Too long to have an orgasm or climax (P) | 1     | 101 | ECOG PS 2-4  | ECOG PS 0-1                | -8.05%                     |      | -0.21        | Physical Functioning     | 0.18                | 0.62               | 0.62             |
| Too long to have an orgasm or climax (P) | 1     | 97  |  |                            |                            |      |              | Role Functioning         | 0.07                | 0.08               | 0.47             |
| Too long to have an orgasm or climax (P) | 1     | 97  |  |                            |                            |      |              | Emotional Functioning    | 0.16                | 0.51               | 0.62             |
| Too long to have an orgasm or climax (P) | 1     | 97  |  |                            |                            |      |              | Cognitive Functioning    | 0.23                | 0.12               | 0.47             |
| Too long to have an orgasm or climax (P) | 1     | 97  |  |                            |                            |      |              | Social Functioning       | 0.19                | 0.02               | 0.31             |
| Too long to have an orgasm or climax (P) | 1     | 97  |  |                            |                            |      |              | Global Health Status/QoL | 0.18                | 0.07               | 0.47             |
| Too long to have an orgasm or climax (P) | 1     | 92  | ECOG PS 2-4  | ECOG PS 0-1                | -25.58%                    |      | -1.06        | HRQL Summary Score       | 0.24                | 0.02               | 0.24             |
| Too long to have an orgasm or climax (P) | 2     | 86  |  |                            |                            |      |              | Physical Functioning     | 0.20                | 0.16               | 0.47             |
| Too long to have an orgasm or climax (P) | 2     | 88  |  |                            |                            |      |              | Role Functioning         | 0.28                | 0.07               | 0.47             |
| Too long to have an orgasm or climax (P) | 2     | 88  |  |                            |                            |      |              | Emotional Functioning    | 0.16                | 0.14               | 0.11             |
| Too long to have an orgasm or climax (P) | 2     | 87  |  |                            |                            |      |              | Cognitive Functioning    | 0.24                | 0.03               | 0.32             |
| Too long to have an orgasm or climax (P) | 2     | 87  |  |                            |                            |      |              | Social Functioning       | 0.35                | <0.001             | 0.01             |
| Too long to have an orgasm or climax (P) | 2     | 87  |  |                            |                            |      |              | Global Health Status/QoL | 0.18                | 0.1                | 0.47             |
| Too long to have an orgasm or climax (P) | 2     | 86  |  |                            |                            |      |              | HRQL Summary Score       | 0.23                | 0.03               | 0.38             |
| Unable to have an orgasm or climax (P)   | 1     | 113 | ECOG PS 2-4  | ECOG PS 0-1                | -2.62%                     |      | -0.06        | Physical Functioning     | 0.19                | 0.87               | 0.87             |
| Unable to have an orgasm or climax (P)   | 1     | 110 |  |                            |                            |      |              | Role Functioning         | 0.06                | 0.53               | 0.62             |
| Unable to have an orgasm or climax (P)   | 1     | 110 |  |                            |                            |      |              | Emotional Functioning    | 0.06                | 0.51               | 0.87             |
| Unable to have an orgasm or climax (P)   | 1     | 110 |  |                            |                            |      |              | Cognitive Functioning    | 0.10                | 0.28               | 0.87             |
| Unable to have an orgasm or climax (P)   | 1     | 110 |  |                            |                            |      |              | Social Functioning       | 0.11                | 0.27               | 0.87             |
| Unable to have an orgasm or climax (P)   | 1     | 110 |  |                            |                            |      |              | Global Health Status/QoL | 0.16                | 0.09               | 0.8              |
| Unable to have an orgasm or climax (P)   | 2     | 92  | ECOG PS 2-4  | ECOG PS 0-1                | -12.77%                    |      | -0.32        | HRQL Summary Score       | 0.17                | 0.08               | 0.8              |
| Unable to have an orgasm or climax (P)   | 2     | 89  |  |                            |                            |      |              | Physical Functioning     | 0.23                | 0.46               | 0.87             |
| Unable to have an orgasm or climax (P)   | 2     | 89  |  |                            |                            |      |              | Role Functioning         | 0.28                | 0.03               | 0.4              |
| Unable to have an orgasm or climax (P)   | 2     | 88  |  |                            |                            |      |              | Emotional Functioning    | 0.07                | 0.007              | 0.12             |
| Unable to have an orgasm or climax (P)   | 2     | 88  |  |                            |                            |      |              | Cognitive Functioning    | 0.19                | 0.54               | 0.87             |
| Unable to have an orgasm or climax (P)   | 2     | 88  |  |                            |                            |      |              | Social Functioning       | 0.27                | 0.07               | 0.79             |
| Unable to have an orgasm or climax (P)   | 2     | 88  |  |                            |                            |      |              | Global Health Status/QoL | 0.15                | 0.16               | 0.15             |
| Unable to have an orgasm or climax (P)   | 2     | 87  |  |                            |                            |      |              | HRQL Summary Score       | 0.23                | 0.16               | 0.87             |
| Unexpected decrease in sweating (P)      | 1     | 409 | ECOG PS 2-4  | ECOG PS 0-1                | -1.96%                     |      | -0.10        | Physical Functioning     | 0.00                | 0.53               | 0.98             |
| Unexpected decrease in sweating (P)      | 1     | 394 |  |                            |                            |      |              | Role Functioning         | 0.07                | 0.98               | 0.98             |
| Unexpected decrease in sweating (P)      | 1     | 394 |  |                            |                            |      |              | Emotional Functioning    | 0.11                | 0.17               | 0.84             |
| Unexpected decrease in sweating (P)      | 1     | 394 |  |                            |                            |      |              | Cognitive Functioning    | 0.05                | 0.03               | 0.27             |
| Unexpected decrease in sweating (P)      | 1     | 394 |  |                            |                            |      |              | Social Functioning       | 0.10                | 0.34               | 0.98             |
| Unexpected decrease in sweating (P)      | 1     | 394 |  |                            |                            |      |              | Global Health Status/QoL | 0.12                | 0.04               | 0.32             |
| Unexpected decrease in sweating (P)      | 1     | 394 |  |                            |                            |      |              | HRQL Summary Score       | 0.10                | 0.02               | 0.18             |

| PRO-CTCAE Item                       | Visit | N   | Worse Symptom Level Group          | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|--------------------------------------|-------|-----|------------------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Unexpected decrease in sweating (P)  | 1     | 391 | ECOG PS 2-4                        | ECOG PS 0-1                | -0.84%                     |      | -0.04        | HRQOL Summary Score      | 0.08                | 0.12               | 0.89             |
| Unexpected decrease in sweating (P)  | 2     | 371 | ECOG PS 2-4                        | ECOG PS 0-1                | -0.84%                     |      | -0.04        | Physical Functioning     | 0.09                | 0.82               | 0.98             |
| Unexpected decrease in sweating (P)  | 2     | 356 | ECOG PS 2-4                        | ECOG PS 0-1                | -0.84%                     |      | -0.04        | Role Functioning         | 0.18                | 0.08               | 0.59             |
| Unexpected decrease in sweating (P)  | 2     | 356 | ECOG PS 2-4                        | ECOG PS 0-1                | -0.84%                     |      | -0.04        | Emotional Functioning    | 0.23                | <0.001             | 0.006            |
| Unexpected decrease in sweating (P)  | 2     | 356 | ECOG PS 2-4                        | ECOG PS 0-1                | -0.84%                     |      | -0.04        | Cognitive Functioning    | 0.22                | <0.001             | <0.001           |
| Unexpected decrease in sweating (P)  | 2     | 356 | ECOG PS 2-4                        | ECOG PS 0-1                | -0.84%                     |      | -0.04        | Social Functioning       | 0.23                | <0.001             | <0.001           |
| Unexpected decrease in sweating (P)  | 2     | 352 | ECOG PS 2-4                        | ECOG PS 0-1                | -0.84%                     |      | -0.04        | Global Health Status/QoL | 0.11                | 0.03               | 0.3              |
| Unexpected decrease in sweating (P)  | 2     | 352 | ECOG PS 2-4                        | ECOG PS 0-1                | -0.84%                     |      | -0.04        | HRQOL Summary Score      | 0.21                | <0.001             | <0.001           |
| Unexpected or excessive sweating (F) | 1     | 368 | Breast/Prostate                    | Gastrointestinal           | 0.21                       | 1.00 | 0.21         | Physical Functioning     | 0.12                | 0.22               | 0.35             |
| Unexpected or excessive sweating (F) | 1     | 291 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Role Functioning         | 0.14                | 0.02               | 0.35             |
| Unexpected or excessive sweating (F) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Emotional Functioning    | 0.19                | 0.007              | 0.06             |
| Unexpected or excessive sweating (F) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Cognitive Functioning    | 0.20                | <0.001             | 0.003            |
| Unexpected or excessive sweating (F) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Social Functioning       | 0.20                | 0.03               | 0.12             |
| Unexpected or excessive sweating (F) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Global Health Status/QoL | 0.15                | <0.001             | 0.002            |
| Unexpected or excessive sweating (F) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | HRQOL Summary Score      | 0.22                | 0.04               | 0.04             |
| Unexpected or excessive sweating (F) | 1     | 358 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Physical Functioning     | 0.19                | 0.001              | <0.001           |
| Unexpected or excessive sweating (F) | 1     | 358 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Role Functioning         | 0.13                | 0.02               | 0.12             |
| Unexpected or excessive sweating (F) | 2     | 326 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Emotional Functioning    | 0.28                | <0.001             | <0.001           |
| Unexpected or excessive sweating (F) | 2     | 326 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Cognitive Functioning    | 0.22                | <0.001             | <0.001           |
| Unexpected or excessive sweating (F) | 2     | 325 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Social Functioning       | 0.18                | <0.001             | 0.009            |
| Unexpected or excessive sweating (F) | 2     | 325 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | Global Health Status/QoL | 0.16                | 0.003              | 0.03             |
| Unexpected or excessive sweating (F) | 2     | 320 | Breast/Prostate                    | Gastrointestinal           | 0.14                       | 1.03 | 0.14         | HRQOL Summary Score      | 0.26                | <0.001             | <0.001           |
| Unexpected or excessive sweating (S) | 1     | 368 | ECOG PS 2-4                        | ECOG PS 0-1                | 0.22                       | 0.88 | 0.25         | Physical Functioning     | 0.10                | 0.14               | 0.23             |
| Unexpected or excessive sweating (S) | 1     | 291 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Role Functioning         | 0.13                | 0.17               | 0.23             |
| Unexpected or excessive sweating (S) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Emotional Functioning    | 0.13                | 0.049              | 0.19             |
| Unexpected or excessive sweating (S) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Cognitive Functioning    | 0.19                | 0.02               | 0.09             |
| Unexpected or excessive sweating (S) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Social Functioning       | 0.13                | <0.001             | 0.004            |
| Unexpected or excessive sweating (S) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Global Health Status/QoL | 0.18                | 0.02               | 0.09             |
| Unexpected or excessive sweating (S) | 1     | 360 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | HRQOL Summary Score      | 0.22                | <0.001             | <0.001           |
| Unexpected or excessive sweating (S) | 1     | 358 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Physical Functioning     | 0.19                | 0.01               | 0.09             |
| Unexpected or excessive sweating (S) | 1     | 358 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Role Functioning         | 0.13                | <0.001             | 0.006            |
| Unexpected or excessive sweating (S) | 2     | 326 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Emotional Functioning    | 0.28                | 0.02               | 0.09             |
| Unexpected or excessive sweating (S) | 2     | 326 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Cognitive Functioning    | 0.23                | <0.001             | <0.001           |
| Unexpected or excessive sweating (S) | 2     | 325 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Social Functioning       | 0.20                | <0.001             | 0.004            |
| Unexpected or excessive sweating (S) | 2     | 326 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | Global Health Status/QoL | 0.18                | 0.001              | 0.01             |
| Unexpected or excessive sweating (S) | 2     | 320 | Breast/Prostate                    | Gastrointestinal           | 0.19                       | 0.90 | 0.21         | HRQOL Summary Score      | 0.28                | <0.001             | <0.001           |
| Unusual darkening of the skin (P)    | 1     | 508 | ECOG PS 2-4                        | ECOG PS 0-1                | -7.42%                     |      | -0.24        | Physical Functioning     | 0.07                | 0.1                | 0.2              |
| Unusual darkening of the skin (P)    | 1     | 508 | Radiation therapy in prior 2 weeks | Other                      | 4.90%                      |      | 0.14         | Role Functioning         | 0.12                | 0.11               | 0.2              |
| Unusual darkening of the skin (P)    | 1     | 491 | Radiation therapy in prior 2 weeks | Other                      | 4.90%                      |      | 0.14         | Emotional Functioning    | 0.12                | 0.01               | 0.14             |
| Unusual darkening of the skin (P)    | 1     | 491 | Radiation therapy in prior 2 weeks | Other                      | 4.90%                      |      | 0.14         | Cognitive Functioning    | 0.19                | 0.01               | 0.14             |
| Unusual darkening of the skin (P)    | 1     | 488 | Radiation therapy in prior 2 weeks | Other                      | 4.90%                      |      | 0.14         | Social Functioning       | 0.06                | <0.001             | <0.001           |
| Unusual darkening of the skin (P)    | 1     | 488 | Radiation therapy in prior 2 weeks | Other                      | 4.90%                      |      | 0.14         | Global Health Status/QoL | 0.16                | 0.2                | 0.2              |
| Unusual darkening of the skin (P)    | 1     | 488 | Radiation therapy in prior 2 weeks | Other                      | 4.90%                      |      | 0.14         | HRQOL Summary Score      | 0.16                | <0.001             | 0.004            |
| Unusual darkening of the skin (P)    | 2     | 459 | ECOG PS 2-4                        | ECOG PS 0-1                | -9.53%                     |      | -0.28        | Physical Functioning     | 0.06                | 0.09               | 0.2              |
| Unusual darkening of the skin (P)    | 2     | 459 | Radiation therapy in prior 2 weeks | Other                      | 12.55%                     |      | 0.33         | Role Functioning         | 0.06                | <0.001             | 0.007            |
| Unusual darkening of the skin (P)    | 2     | 443 | ECOG PS 2-4                        | ECOG PS 0-1                | -9.53%                     |      | -0.28        | Emotional Functioning    | 0.07                | 0.19               | 0.2              |
| Unusual darkening of the skin (P)    | 2     | 443 | Radiation therapy in prior 2 weeks | Other                      | 12.55%                     |      | 0.33         | Cognitive Functioning    | 0.06                | 0.16               | 0.2              |
| Unusual darkening of the skin (P)    | 2     | 443 | Radiation therapy in prior 2 weeks | Other                      | 12.55%                     |      | 0.33         | Social Functioning       | 0.07                | 0.17               | 0.2              |
| Unusual darkening of the skin (P)    | 2     | 443 | Radiation therapy in prior 2 weeks | Other                      | 12.55%                     |      | 0.33         | Global Health Status/QoL | 0.09                | 0.14               | 0.2              |
| Unusual darkening of the skin (P)    | 2     | 443 | Radiation therapy in prior 2 weeks | Other                      | 12.55%                     |      | 0.33         | HRQOL Summary Score      | 0.09                | 0.05               | 0.2              |
| Unusual vaginal discharge (A)        | 1     | 224 | ECOG PS 2-4                        | ECOG PS 0-1                | 0.04                       | 0.48 | 0.08         | Physical Functioning     | 0.06                | 0.73               | 0.95             |
| Unusual vaginal discharge (A)        | 1     | 100 | Age >60                            | Age >60                    | 0.47                       | 0.57 | 0.83         | Role Functioning         | 0.04                | <0.001             | 0.005            |
| Unusual vaginal discharge (A)        | 1     | 180 | Breast                             | Hematologic                | -0.09                      | 0.43 | -0.20        | Emotional Functioning    | 0.06                | 0.39               | 0.95             |
| Unusual vaginal discharge (A)        | 1     | 216 | Breast                             | Hematologic                | -0.09                      | 0.43 | -0.20        | Cognitive Functioning    | 0.06                | 0.52               | 0.95             |
| Unusual vaginal discharge (A)        | 1     | 216 | Breast                             | Hematologic                | -0.09                      | 0.43 | -0.20        | Social Functioning       | 0.11                | 0.39               | 0.95             |
| Unusual vaginal discharge (A)        | 1     | 216 | Breast                             | Hematologic                | -0.09                      | 0.43 | -0.20        | Global Health Status/QoL | 0.09                | 0.008              | 0.15             |
| Unusual vaginal discharge (A)        | 1     | 216 | Breast                             | Hematologic                | -0.09                      | 0.43 | -0.20        | HRQOL Summary Score      | 0.18                | 0.09               | 0.95             |
| Unusual vaginal discharge (A)        | 1     | 216 | Breast                             | Hematologic                | -0.09                      | 0.43 | -0.20        | Physical Functioning     | 0.09                | 0.2                | 0.95             |
| Unusual vaginal discharge (A)        | 1     | 216 | Breast                             | Hematologic                | -0.09                      | 0.43 | -0.20        | Role Functioning         | 0.08                | 0.24               | 0.95             |
| Unusual vaginal discharge (A)        | 1     | 215 | Breast                             | Hematologic                | -0.09                      | 0.43 | -0.20        | Emotional Functioning    | 0.16                | 0.02               | 0.31             |



| PRO-CTCAE Item  | Visit | N   | Worse Symptom Level Group   | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|-----------------|-------|-----|-----------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Vomiting (F)    | 1     | 807 |                             |                            |                            |      |              | Cognitive Functioning    | 0.18                | <0.001             | <0.001           |
| Vomiting (F)    | 1     | 807 |                             |                            |                            |      |              | Social Functioning       | 0.24                | <0.001             | <0.001           |
| Vomiting (F)    | 1     | 805 |                             |                            |                            |      |              | Global Health Status/QoL | 0.21                | <0.001             | <0.001           |
| Vomiting (F)    | 1     | 810 |                             |                            |                            |      |              | HRQOL Summary Score      | 0.40                | <0.001             | <0.001           |
| Vomiting (F)    | 1     | 810 |                             |                            |                            |      |              | Nausea and Vomiting      | 0.74                | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 756 | ECOG PS 2-4                 | ECOG PS 0-1                | 0.34                       | 0.67 | 0.51         |                          |                     | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 756 | Currently taking nausea med | Other                      | 0.38                       | 0.65 | 0.58         |                          |                     | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 734 |                             |                            |                            |      |              | Physical Functioning     | 0.29                | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 734 |                             |                            |                            |      |              | Role Functioning         | 0.27                | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 732 |                             |                            |                            |      |              | Emotional Functioning    | 0.25                | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 732 |                             |                            |                            |      |              | Cognitive Functioning    | 0.29                | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 731 |                             |                            |                            |      |              | Social Functioning       | 0.34                | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 732 |                             |                            |                            |      |              | Global Health Status/QoL | 0.30                | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 725 |                             |                            |                            |      |              | HRQOL Summary Score      | 0.44                | <0.001             | <0.001           |
| Vomiting (F)    | 2     | 734 |                             |                            |                            |      |              | Nausea and Vomiting      | 0.70                | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 826 | ECOG PS 2-4                 | ECOG PS 0-1                | 0.28                       | 0.71 | 0.39         |                          |                     | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 810 | Currently taking nausea med | Other                      | 0.47                       | 0.68 | 0.70         |                          |                     | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 810 |                             |                            |                            |      |              | Physical Functioning     | 0.19                | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 807 |                             |                            |                            |      |              | Role Functioning         | 0.24                | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 807 |                             |                            |                            |      |              | Emotional Functioning    | 0.21                | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 807 |                             |                            |                            |      |              | Cognitive Functioning    | 0.20                | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 807 |                             |                            |                            |      |              | Social Functioning       | 0.25                | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 807 |                             |                            |                            |      |              | Global Health Status/QoL | 0.19                | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 805 |                             |                            |                            |      |              | HRQOL Summary Score      | 0.39                | <0.001             | <0.001           |
| Vomiting (S)    | 1     | 810 |                             |                            |                            |      |              | Nausea and Vomiting      | 0.70                | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 756 | ECOG PS 2-4                 | ECOG PS 0-1                | 0.36                       | 0.67 | 0.54         |                          |                     | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 756 | Currently taking nausea med | Other                      | 0.39                       | 0.66 | 0.59         |                          |                     | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 734 |                             |                            |                            |      |              | Physical Functioning     | 0.29                | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 734 |                             |                            |                            |      |              | Role Functioning         | 0.25                | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 732 |                             |                            |                            |      |              | Emotional Functioning    | 0.27                | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 732 |                             |                            |                            |      |              | Cognitive Functioning    | 0.28                | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 731 |                             |                            |                            |      |              | Social Functioning       | 0.34                | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 732 |                             |                            |                            |      |              | Global Health Status/QoL | 0.28                | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 725 |                             |                            |                            |      |              | HRQOL Summary Score      | 0.44                | <0.001             | <0.001           |
| Vomiting (S)    | 2     | 734 |                             |                            |                            |      |              | Nausea and Vomiting      | 0.68                | <0.001             | <0.001           |
| Watery eyes (S) | 1     | 268 | ECOG PS 2-4                 | ECOG PS 0-1                | 0.04                       | 0.84 | 0.05         |                          |                     | 0.77               | 0.77             |
| Watery eyes (S) | 1     | 265 |                             |                            |                            |      |              | Physical Functioning     | 0.20                | <0.001             | 0.01             |
| Watery eyes (S) | 1     | 265 |                             |                            |                            |      |              | Role Functioning         | 0.16                | 0.16               | 0.47             |
| Watery eyes (S) | 1     | 261 |                             |                            |                            |      |              | Emotional Functioning    | 0.13                | 0.03               | 0.21             |
| Watery eyes (S) | 1     | 261 |                             |                            |                            |      |              | Cognitive Functioning    | 0.19                | 0.003              | 0.03             |
| Watery eyes (S) | 1     | 261 |                             |                            |                            |      |              | Social Functioning       | 0.10                | 0.1                | 0.41             |
| Watery eyes (S) | 1     | 261 |                             |                            |                            |      |              | Global Health Status/QoL | 0.04                | 0.24               | 0.24             |
| Watery eyes (S) | 1     | 259 |                             |                            |                            |      |              | HRQOL Summary Score      | 0.17                | 0.006              | 0.06             |
| Watery eyes (S) | 2     | 236 | ECOG PS 2-4                 | ECOG PS 0-1                | 0.07                       | 0.75 | 0.10         |                          |                     | 0.62               | 0.77             |
| Watery eyes (S) | 2     | 234 |                             |                            |                            |      |              | Physical Functioning     | 0.24                | <0.001             | 0.004            |
| Watery eyes (S) | 2     | 234 |                             |                            |                            |      |              | Role Functioning         | 0.13                | 0.049              | 0.24             |
| Watery eyes (S) | 2     | 234 |                             |                            |                            |      |              | Emotional Functioning    | 0.17                | 0.009              | 0.08             |
| Watery eyes (S) | 2     | 234 |                             |                            |                            |      |              | Cognitive Functioning    | 0.20                | 0.002              | 0.03             |
| Watery eyes (S) | 2     | 234 |                             |                            |                            |      |              | Social Functioning       | 0.16                | 0.02               | 0.13             |
| Watery eyes (S) | 2     | 234 |                             |                            |                            |      |              | Global Health Status/QoL | 0.21                | 0.001              | 0.02             |
| Watery eyes (S) | 2     | 234 |                             |                            |                            |      |              | HRQOL Summary Score      | 0.20                | 0.002              | 0.02             |
| Watery eyes (I) | 1     | 268 | ECOG PS 2-4                 | ECOG PS 0-1                | 0.13                       | 0.65 | 0.20         |                          |                     | 0.26               | 0.61             |
| Watery eyes (I) | 1     | 265 |                             |                            |                            |      |              | Physical Functioning     | 0.14                | 0.02               | 0.18             |
| Watery eyes (I) | 1     | 265 |                             |                            |                            |      |              | Role Functioning         | 0.04                | 0.48               | 0.61             |
| Watery eyes (I) | 1     | 261 |                             |                            |                            |      |              | Emotional Functioning    | 0.19                | 0.002              | 0.03             |
| Watery eyes (I) | 1     | 261 |                             |                            |                            |      |              | Cognitive Functioning    | 0.10                | 0.1                | 0.61             |
| Watery eyes (I) | 1     | 261 |                             |                            |                            |      |              | Social Functioning       | 0.14                | 0.02               | 0.18             |
| Watery eyes (I) | 1     | 261 |                             |                            |                            |      |              | Global Health Status/QoL | 0.09                | 0.16               | 0.61             |
| Watery eyes (I) | 1     | 259 |                             |                            |                            |      |              | HRQOL Summary Score      | 0.16                | 0.009              | 0.1              |
| Watery eyes (I) | 2     | 236 | ECOG PS 2-4                 | ECOG PS 0-1                | 0.07                       | 0.69 | 0.10         |                          |                     | 0.61               | 0.61             |
| Watery eyes (I) | 2     | 234 |                             |                            |                            |      |              | Physical Functioning     | 0.12                | 0.06               | 0.4              |
| Watery eyes (I) | 2     | 234 |                             |                            |                            |      |              | Role Functioning         | 0.08                | 0.22               | 0.61             |
| Watery eyes (I) | 2     | 234 |                             |                            |                            |      |              | Emotional Functioning    | 0.19                | 0.003              | 0.047            |
| Watery eyes (I) | 2     | 234 |                             |                            |                            |      |              | Cognitive Functioning    | 0.23                | <0.001             | 0.006            |
| Watery eyes (I) | 2     | 234 |                             |                            |                            |      |              | Social Functioning       | 0.18                | 0.006              | 0.08             |
| Watery eyes (I) | 2     | 234 |                             |                            |                            |      |              | Global Health Status/QoL | 0.15                | 0.02               | 0.18             |
| Watery eyes (I) | 2     | 234 |                             |                            |                            |      |              | HRQOL Summary Score      | 0.17                | 0.007              | 0.09             |
| Wheezing (S)    | 1     | 455 | ECOG PS 2-4                 | ECOG PS 0-1                | 0.33                       | 0.69 | 0.48         |                          |                     | <0.001             | <0.001           |
| Wheezing (S)    | 1     | 365 | Lung/Head/Neck              | Prostate/Bladder           | 0.17                       | 0.71 | 0.24         |                          |                     | 0.05               | 0.1              |
| Wheezing (S)    | 1     | 445 |                             |                            |                            |      |              | Physical Functioning     | 0.24                | <0.001             | <0.001           |
| Wheezing (S)    | 1     | 445 |                             |                            |                            |      |              | Role Functioning         | 0.18                | <0.001             | 0.001            |
| Wheezing (S)    | 1     | 442 |                             |                            |                            |      |              | Emotional Functioning    | 0.27                | <0.001             | <0.001           |
| Wheezing (S)    | 1     | 442 |                             |                            |                            |      |              | Cognitive Functioning    | 0.19                | <0.001             | <0.001           |

| PRO-CTCAE Item | Visit | N   | Worse Symptom Level Group | Better Symptom Level Group | Mean or Percent Difference | SD   | Effect Size* | EORTC QLQ-C30            | Pearson Correlation | Unadjusted P-value | Hochberg P-value |
|----------------|-------|-----|---------------------------|----------------------------|----------------------------|------|--------------|--------------------------|---------------------|--------------------|------------------|
| Wheezing (S)   | 1     | 442 |                           |                            |                            |      |              | Social Functioning       | 0.15                | 0.001              | 0.005            |
| Wheezing (S)   | 1     | 442 |                           |                            |                            |      |              | Global Health Status/QoL | 0.24                | <0.001             | <0.001           |
| Wheezing (S)   | 1     | 439 |                           |                            |                            |      |              | HRQoL Summary Score      | 0.32                | <0.001             | <0.001           |
| Wheezing (S)   | 2     | 405 | ECOG PS 2-4               | ECOG PS 0-1                | 0.27                       | 0.63 | 0.44         |                          | .                   | 0.004              | 0.01             |
| Wheezing (S)   | 2     | 327 | Lung/Head/Neck            | Prostate/Bladder           | 0.03                       | 0.68 | 0.05         |                          | .                   | 0.71               | 0.71             |
| Wheezing (S)   | 2     | 398 |                           |                            |                            |      |              | Physical Functioning     | 0.29                | <0.001             | <0.001           |
| Wheezing (S)   | 2     | 398 |                           |                            |                            |      |              | Role Functioning         | 0.28                | <0.001             | <0.001           |
| Wheezing (S)   | 2     | 395 |                           |                            |                            |      |              | Emotional Functioning    | 0.27                | <0.001             | <0.001           |
| Wheezing (S)   | 2     | 395 |                           |                            |                            |      |              | Cognitive Functioning    | 0.33                | <0.001             | <0.001           |
| Wheezing (S)   | 2     | 394 |                           |                            |                            |      |              | Social Functioning       | 0.17                | <0.001             | 0.004            |
| Wheezing (S)   | 2     | 395 |                           |                            |                            |      |              | Global Health Status/QoL | 0.21                | <0.001             | <0.001           |
| Wheezing (S)   | 2     | 391 |                           |                            |                            |      |              | HRQoL Summary Score      | 0.37                | <0.001             | <0.001           |

**Abbreviations:** PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; SD, Standard deviation; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire; F, Frequency; S, Severity; I, Interference with usual or daily activities; P, Presence/absence; A, Amount; ECOG PS, Eastern Cooperative Oncology Group Performance Status; QoL, Quality of Life; HRQoL, Health-related quality of life

\* Cohen's *d* for group differences; Cohen's *h* for differences in proportions

\*\* Not considered as evidence of validity because direction of effect is the opposite of that hypothesized

1 - Hand-foot syndrome-inducing chemotherapies include capecitabine, fluorouracil, sunitinib, and sorafenib

2 - Skin-reaction chemotherapies include epidermal growth factor receptor inhibitors, docetaxel, gemcitabine, paclitaxel, and pemetrexed

3 - Irritant chemotherapies include bleomycin, bortezomib, carboplatin, cyclophosphamide, cytarabine, dacarbazine, daunorubicin, docetaxel, doxorubicin, etoposide, fluorouracil, gemcitabine, ifosfamide, irinotecan, nab-paclitaxel, oxaliplatin, paclitaxel, topotecan, and trastuzumab

**eTable 4.** Test-retest Reliability for 49 Preselected PRO-CTCAE Items (N=80)

| PRO-CTCAE Symptomatic AE Term            | Intra-class Correlation Coefficient |          |              |          |        |
|--|-------------------------------------|----------|--------------|----------|--------|
|  | Frequency                           | Severity | Interference | Presence | Amount |
| Anxiety                                  | 0.78                                | 0.69     | 0.83         | -        | -      |
| Arm/leg swelling                         | 0.86                                | 0.68     | 0.64         | -        | -      |
| Constipation                             | -                                   | 0.83     | -            | -        | -      |
| Cough                                    | -                                   | 0.74     | 0.53         | -        | -      |
| Decreased appetite                       | -                                   | 0.80     | 0.80         | -        | -      |
| Dry mouth                                | -                                   | 0.74     | -            | -        | -      |
| Fatigue                                  | -                                   | 0.77     | 0.79         | -        | -      |
| Feelings that nothing could cheer you up | 0.70                                | 0.75     | 0.72         | -        | -      |
| Hair loss                                | -                                   | -        | -            | -        | 0.96   |
| Headache                                 | 0.80                                | 0.78     | 0.78         | -        | -      |
| Hiccups                                  | 0.69                                | 0.71     | -            | -        | -      |
| Insomnia                                 | -                                   | 0.64     | 0.72         | -        | -      |
| Loose stools                             | 0.54                                | -        | -            | -        | -      |
| Mouth or throat sores                    | -                                   | 0.82     | 0.81         | -        | -      |
| Nausea                                   | 0.80                                | 0.84     | -            | -        | -      |
| Numbness/tingling in your hands or feet  | -                                   | 0.80     | 0.55         | -        | -      |
| Pain                                     | 0.83                                | 0.82     | 0.84         | -        | -      |
| Problems with concentration              | -                                   | 0.74     | 0.70         | -        | -      |
| Problems with tasting food/drink         | -                                   | 0.84     | -            | -        | -      |
| Rash                                     | -                                   | -        | -            | 0.86     | -      |
| Sad or unhappy feelings                  | 0.72                                | 0.61     | 0.76         | -        | -      |
| Shortness of breath                      | -                                   | 0.70     | 0.66         | -        | -      |
| Skin burns from radiation                | -                                   | 0.65     | -            | -        | -      |
| Unusual darkening of the skin            | -                                   | -        | -            | 0.73     | -      |
| Vomiting                                 | 0.81                                | 0.79     | -            | -        | -      |
| Wheezing                                 |                                     | 0.65     |              |          |        |

**Abbreviations:** PRO-CTCAE, Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; AE, adverse event