Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Patient-Reported Outcome (PRO) Weekly Survey Items and Alert Notification Criteria

PRO-TECT weekly patient-reported outcome (PRO) survey: PRO survey items, sent weekly to participating PRO intervention arm patients via web or automated telephone interactive voice response (IVR) system, with associated verbiage for <u>reports</u> generated at clinic visits, and criteria for triggering real-time <u>alerts</u> to the care team. Alert thresholds are based on prior research and study advisory board consensus. Items 1, 2, and 4-10 are derived from the National Cancer Institute PRO-CTCAE item library. Item 3 is the patient version of ECOG performance status. Item 12 is from the COST-FACIT questionnaire. Items 11, 13, and 14 were developed for this trial.

Question	Response Options	Survey Skip Pattern Rules	Language for Inclusion in Report at Clinic Visits	Criteria for Inclusion in Real-Time Alert Notifications to Care Team
1. In the last 7 days, has your EATING and DRINKING DECREASED?	• Not at all • A little bit • Somewhat • Quite a bit • Very much		Food/fluid Intake: Not at all, A little bit, Somewhat, Quite a bit, Very much	Absolute score of Quite a bit or Very much; or change since prior questionnaire from Not at all to Somewhat or higher
2a. In the last 7 days, how OFTEN did you have PAIN?	• Never • Rarely • Occasionally • Frequently • Almost constantly	If answered "Rarely", "Occasionally", "Frequently", or "Almost constantly", then answer questions 2b and 2c. If answered "Never", then skip to question 3	Pain Frequency: Never, Rarely, Occasionally, Frequently, Almost constantly	Absolute score of Frequently or Almost constantly; or change since prior questionnaire from Never to Occasionally or higher
2b. In the last 7 days, what was the SEVERITY of your PAIN at its WORST?	• None • Mild • Moderate • Severe • Very severe		Pain Severity: None, Mild, Moderate, Severe, Very severe	Absolute score of Severe or Very severe; or change since prior questionnaire from None to Moderate or higher
2c. In the last 7 days, how much did your PAIN INTERFERE with your usual or daily activities?	• Not at all • A little bit • Somewhat • Quite a bit • Very much		Pain Interference: Not at all, A little bit, Somewhat, Quite a bit, Very much	Absolute score of Quite a bit or Very much; or change since prior questionnaire from Not at all to Somewhat or higher
3. In the last 7 days, how would you generally rate your ACTIVITY:	• Normal with no limitations (0) • Not your normal self, but able to be up and about with		Patient ECOG Performance Status: ECOG 0 (Fully Active), ECOG 1 (Cannot do strenuous activities but up and about most of the day and can do light house	Absolute score of ECOG 3 or ECOG 4; or worsened by 2 grade levels from prior questionnaire*

Question	Response Options	Survey Skip Pattern Rules	Language for Inclusion in Report at Clinic Visits	Criteria for Inclusion in Real-Time Alert Notifications to Care Team
	fairly normal activities (1) • Not feeling up to most things, but in bed or chair less than half the day (2) • Able to do little activity & spend most of the day in bed or chair (3) • Pretty much bedridden, rarely out of bed (4)		work), ECOG 2 (Moderate impairment), ECOG 3 (Cannot do most house work, but able to take care of myself and am up and about more than half the day), ECOG 4 (Rarely or never out of bed)	
4. In the last 7 days, how often have you been bothered by FEELING DOWN, DEPRESSED, OR HOPELESS?	• Not at all • Several days • More than half the days • Nearly every day		Depression: Not at all, Several days, More than half the days, Nearly every day	Absolute score of More than half the days or Nearly every day
5a. In the last 7 days, how OFTEN did you have NAUSEA?	• Never • Rarely • Occasionally • Frequently • Almost constantly	If answered "Rarely", "Occasionally", "Frequently", or "Almost constantly" then answer question 5b. If answered "Never" then skip to question 6	Nausea Frequency: Never, Rarely, Occasionally, Frequently, Almost constantly	Absolute score of Frequently or Almost constantly; or change since prior questionnaire from Never to Occasionally or higher
5b. In the last 7 days, what was the SEVERITY of your NAUSEA at its WORST?	• None • Mild • Moderate • Severe • Very severe		Nausea Severity: None, Mild, Moderate, Severe, Very severe	Absolute score of Severe or Very severe; or change since prior questionnaire from None to Moderate or higher
6. In the last 7 days, how OFTEN did you have VOMITING?	• Never • Rarely • Occasionally • Frequently • Almost constantly		Vomiting: Never, Rarely, Occasionally, Frequently, Almost constantly	Absolute score of Frequently or Almost constantly; or change since prior questionnaire from Never to Occasionally or higher

Question	Response Options	Survey Skip Pattern Rules	Language for Inclusion in Report at Clinic Visits	Criteria for Inclusion in Real-Time Alert Notifications to Care Team
7. In the last 7 days, how OFTEN did you have LOOSE OR WATERY STOOLS (DIARRHEA)?	• Never • Rarely • Occasionally • Frequently • Almost constantly		Diarrhea: Never, Rarely, Occasionally, Frequently, Almost constantly	Absolute score of Frequently or Almost constantly; or change since prior questionnaire from Never to Occasionally or higher
8. In the last 7 days, what was the SEVERITY of your CONSTIPATION at its WORST?	• None • Mild • Moderate • Severe • Very severe		Constipation: None, Mild, Moderate, Severe, Very severe	Absolute score of Severe or Very severe; or change since prior questionnaire from None to Moderate or higher
9a. In the last 7 days, what was the SEVERITY of your SHORTNESS OF BREATH at its WORST?	• None • Mild • Moderate • Severe • Very severe	If answered "Mild", "Moderate", "Severe", or "Very Severe" then answer question 9b. If answered "None" then skip to question 10	Dyspnea Severity: None, Mild, Moderate, Severe, Very severe	Absolute score of Severe or Very severe; or change since prior questionnaire from None to Moderate or higher
9b. In the last 7 days, how much did your SHORTNESS OF BREATH INTERFERE with your usual or daily activities?	• Not at all • A little bit • Somewhat • Quite a bit • Very much		Dyspnea Interference: Not at All, A little bit, Somewhat, Quite a bit, Very much	Absolute score of Quite a bit or Very much; or change since prior questionnaire from Not at all to Somewhat or higher
10. In the last 7 days, what was the SEVERITY of your INSOMNIA (including difficulty falling asleep, staying asleep, or waking up too early) at its WORST?	• None • Mild • Moderate • Severe • Very severe		Insomnia: None, Mild, Moderate, Severe, Very severe	Absolute score of Severe or Very severe; or change since prior questionnaire from None to Moderate or higher
11. In the last 7 days, have you fallen?	• No • Yes		Falls: No, Yes	Yes
12. In the last month, my illness has been a financial hardship to my family and me.	• Not at all • A little bit • Somewhat • Quite a bit • Very much	Note: Question was added to survey in March 2019. Question appeared every 4 weeks.	Not listed on report	Absolute score of Quite a bit or Very much

Question	Response Options	Survey Skip Pattern Rules	Language for Inclusion in Report at Clinic Visits	Criteria for Inclusion in Real-Time Alert Notifications to Care Team
	• Prefer not to answer			
13. Do you have any other symptoms that are interfering with your daily activities that you would like to discuss with your cancer care team?	• No • Yes (please list below)		Other Symptoms: if patient reports by web, text from free text box; if patient reports by IVR, simply report patient responded "Yes"	If response is "Yes" for IVR or "Yes" and/or text in the text box for web, then response triggers alert to cancer care team. If patient reports by web, then text from text box is forwarded; if IVR, alert indicates the patient responded "Yes" (no text-to-speech capacity)
14. Who completed this survey?	• Myself (the patient) • Caregiver (family member, friend, or professional helper) • Research staff • Other, please specify		Not listed on report (question is for research purposes)	Not applicable

* Alerts were initially triggered by an ECOG score worsening by 1-point, but due to a large number of resulting alerts, as well as feedback from practice nurses of limited perceived usefulness of these alerts, plus data showing that nurses did not act on these 1-point worsening alerts, and deliberation by the trial's multidisciplinary Advisory Board and patient representatives, the threshold was changed on March 21, 2018 to triggering by a 2-point worsening.

eTable 2. Subgroup Analysis Variables

Age
- Age <60
- Age ≥60

Sex
- Male
- Female

Race
- White
- Non-white

Ethnicity
- Hispanic
- Non-Hispanic

Education
- ≤High school
- ≥Some college

Employment status
- Working
- Not currently working

Marital status
- Married/partnered
- Other

Device use
- Inexperienced
- Experienced

Internet use
- Inexperienced
- Experienced

Email use
- Inexperienced
- Experienced

Site location
- Urban/Suburban
- Rural

Cancer type
- Thoracic
- Breast
- Colorectal
- GU
- Gynecologic
- Other

eTable 3. Roster of Participating Practices, Locations, Allocations, and Patient Accrual
Roster of participating community oncology practice (cluster) locations, and respective study arm
allocations, patient enrollment, rurality, geographic region, and proportion of enrolled patients who
are Black/African American. Rurality is based on 2010 US Census data, confirmed with practice self-
designation. Geographic region of practices is based on the Geographic Management of Cancer
Health Disparities Program (GMaP) designations (https://www.cancer.gov/about-
nci/organization/crchd/inp/gmap).

Community Oncology Practice # (Cluster)	Site Location	# of Sites of Service	Study Arm	# of Patients enrolled	Practice Rurality (Census)*	GMaP Region	Black/ African American ≥ 20%**
101	Iowa	1	PROs	10	Urban	4	No
102	Pennsylvania	4	PROs	48	Urban	4	No
103	New Hampshire	2	PROs	31	Rural	1N	No
104	Illinois	3	Control	32	Urban	4	No
105	Illinois	3	PROs	31	Rural	4	No
106	Missouri	1	PROs	19	Urban	2	No
107	Iowa	1	PROs	19	Urban	4	No
108	Montana	1	Control	11	Urban	6	No
109	Montana	1	Control	3	Urban	6	No
110	Michigan	2	Control	34	Urban	4	No
111	Michigan	5	PROs	23	Urban	4	Yes
112	Massachusetts	1	Control	12	Urban	4	No
113	Wisconsin	2	Control	26	Urban	4	No
114	New York	1	PROs	30	Urban	4	No
115	Missouri	1	Control	22	Rural	2	No
116	Michigan	1	PROs	10	Urban	4	Yes
117	Ohio	3	Control	31	Rural	4	No
118	Missouri	1	PROs	12	Rural	2	No
119	Minnesota	3	Control	25	Urban	4	No
120	Minnesota	4	PROs	25	Urban	4	No
121	Minnesota	3	Control	25	Urban	4	No
122	Minnesota	3	PROs	21	Urban	4	No
123	North Carolina	2	Control	25	Rural	1S	Yes
124	Indiana	2	Control	27	Urban	4	No
125	Indiana	1	PROs	2	Rural	4	No
126	Maryland	1	Control	24	Urban	1N	No
127	Nevada	4	PROs	35	Urban	6	No
128	Virginia	1	PROs	50	Urban	1N	No
129	West Virginia	1	Control	13	Rural	1N	No
130	Illinois	2	PROs	39	Rural	4	No
131	Illinois	2	Control	19	Urban	4	No
132	Indiana	1	PROs	20	Urban	4	No
133	Maine	1	Control	32	Rural	1N	No
134	South Dakota	1	PROs	19	Rural	6	No
135	Rhode Island	1	Control	20	Urban	4	No
136	North Carolina	1	Control	24	Urban	1S	Yes
137	Illinois	1	PROs	19	Urban	4	Yes
138	Maryland	1	Control	35	Urban	1N	No

139	Nebraska	1	PROs	30	Urban	3	No
140	Colorado	1	Control	20	Rural	3	No
141	North Carolina	1	PROs	20	Rural	1S	Yes
142	Illinois	1	Control	20	Rural	4	No
143	Georgia	4	Control	42	Urban	2	Yes
144	North Carolina	5	PROs	35	Urban	1S	Yes
145	Wisconsin	2	Control	13	Urban	4	No
146	Pennsylvania	2	PROs	14	Urban	4	Yes
147	Maryland	1	PROs	5	Urban	1N	Yes
148	Iowa	1	Control	25	Urban	4	No
149	Nebraska	1	Control	20	Urban	3	No
150	Wisconsin	4	PROs	22	Urban	4	No
151	Texas	2	PROs	4	Urban	3	Yes
152	New York	1	Control	18	Urban	4	Yes

GMaP, Geographic Management of Cancer Health Disparities Program designations (https://www.cancer.gov/about-nci/organization/crchd/inp/gmap)

* Based on 2010 US Census data (County Rurality Census Table), confirmed with practice self-designation.

** Based on practice self-report.

eTable 4. Intracluster Correlation Coefficient for Each Patient-Reported Outcome Endpoint

The intracluster correlation coefficient was estimated at month 3 using a general linear mixed model of each patient-reported outcome endpoint which included a fixed effect for arm and a random effect for cluster. The original statistical design conservatively assumed an intracluster correlation coefficient of 0.055 for physical function, which was identified as a co-primary endpoint with overall survival.

Patient-reported outcome endpoint	Intracluster correlation coefficient
Physical functioning	0.020
Role functioning	0.002
Emotional functioning	0.039
Cognitive functioning	0.021
Social functioning	0.028
Global health status/quality of life	0.031
Fatigue	0.016
Nausea/vomiting	<0.001
Pain	<0.001
Dyspnea	0.016
Insomnia	0.002
Appetite loss	<0.001
Constipation	<0.001
Diarrhea	0.024
Financial concerns	0.015
Health-related quality of life	0.021
Symptom control	0.014

eTable 5. Physical Function, Symptom Control, and Health-Related Quality of Life Mean Score Estimates and Differences in Mean Changes From Baseline Between Arms at Each Visit

Physical function is tabulated from 5 dedicated items in the EORTC QLQ-C30 questionnaire. Symptom control is tabulated from symptom scales of the QLQ-C30. Health-related quality of life is tabulated from functioning and symptom scales of the QLQ-C30. All tabulations are based on published scoring procedures.

Outcome Scale	Timepoint	PRO Arm Mean Estimate	Control Arm Mean Estimate	Difference in Mean Change from Baseline between Groups (95% CI)	P-value of Difference between Groups
Physical Function	Baseline	74.27	73.54	-	N/A
	Month 1	76.63	74.62	1.28 (-0.73, 3.29)	0.21
	Month 3	75.81	72.61	2.47 (0.41, 4.53)	0.02
	Month 6	75.21	71.15	3.33 (1.16, 5.51)	0.003
	Month 9	73.15	69.69	2.74 (0.41, 5.07)	0.02
	Month 12	71.26	70.01	0.52 (-1.94, 2.98)	0.68
Symptom Control	Baseline	77.67	76.75	-	N/A
	Month 1	79.91	76.63	2.36 (0.79, 3.93)	0.003
	Month 3	80.03	76.55	2.56 (0.95, 4.17)	0.002
	Month 6	79.28	76.30	2.06 (0.37, 3.76)	0.02
	Month 9	78.59	75.81	1.86 (0.04, 3.67)	0.045
	Month 12	77.33	75.43	0.98 (-0.94, 2.90)	0.32
Health-Related Quality of Life	Baseline	78.11	77.00	-	N/A
	Month 1	80.52	77.18	2.24 (0.75, 3.74)	0.003
	Month 3	80.03	76.50	2.43 (0.90, 3.96)	0.002
	Month 6	79.48	76.13	2.25 (0.63, 3.86)	0.006
	Month 9	78.42	75.37	1.94 (0.21, 3.67)	0.03
	Month 12	77.47	75.26	1.10 (-0.72, 2.93)	0.24

eTable 6. Proportion of Patients in the Patient-Reported Outcome (PRO) Intervention Arm and Control Arm With 5-Point and 10-Point Changes in Physical Function, Symptom Control, and Health-Related Quality of Life

eTable 6A. Proportion of patients in the patient-reported outcome (PRO) intervention arm and control arm with 5-point improvement or worsening in physical function compared to baseline, as measured by the EORTC QLQ-C30, at each assessment timepoint.

	PRO Intervention (N=593)	Control (N=598)	Total (N=1191)	P-Value
Physical Function, Month 1				0.10
Missing	20	13	33	
N/A: Off-Study	7 (0.0%)	13 (0.0%)	20 (0.0%)	
Responder Improving (+5)	247 (43.6%)	215 (37.6%)	462 (40.6%)	
Non-Responder	148 (26.1%)	169 (29.5%)	317 (27.9%)	
Responder Worsening (-5)	171 (30.2%)	188 (32.9%)	359 (31.5%)	
Physical Function, Month 3				0.009
Missing	20	12	32	
N/A: Off-Study	51 (0.0%)	42 (0.0%)	93 (0.0%)	
Responder Improving (+5)	227 (43.5%)	195 (35.8%)	422 (39.6%)	
Non-Responder	133 (25.5%)	147 (27.0%)	280 (26.3%)	
Responder Worsening (-5)	162 (31.0%)	202 (37.1%)	364 (34.1%)	
Physical Function, Month 6				0.004
Missing	23	22	45	
N/A: Off-Study	126 (0.0%)	112 (0.0%)	238 (0.0%)	
Responder Improving (+5)	180 (40.5%)	152 (32.8%)	332 (36.6%)	
Non-Responder	120 (27.0%)	119 (25.6%)	239 (26.3%)	
Responder Worsening (-5)	144 (32.4%)	193 (41.6%)	337 (37.1%)	
Physical Function, Month 9				0.11
Missing	24	21	45	
N/A: Off-Study	220 (0.0%)	179 (0.0%)	399 (0.0%)	
Responder Improving (+5)	129 (37.0%)	133 (33.4%)	262 (35.1%)	
Non-Responder	92 (26.4%)	92 (23.1%)	184 (24.6%)	
Responder Worsening (-5)	128 (36.7%)	173 (43.5%)	301 (40.3%)	
Physical Function, Month 12				0.22
Missing	20	26	46	
N/A: Off-Study	278 (0.0%)	230 (0.0%)	508 (0.0%)	

	PRO Intervention (N=593)	Control (N=598)	Total (N=1191)	P-Value
Responder Improving (+5)	120 (40.7%)	120 (35.1%)	240 (37.7%)	
Non-Responder	67 (22.7%)	76 (22.2%)	143 (22.4%)	
Responder Worsening (-5)	108 (36.6%)	146 (42.7%)	254 (39.9%)	

eTable 6B. Proportion of patients in the patient-reported outcome (PRO) intervention arm and control arm with <u>10-point</u> improvement or worsening in <u>physical function</u> compared to baseline, as measured by the EORTC QLQ-C30, at each assessment timepoint.

	PRO Intervention (N=593)	Control (N=598)	Total (N=1191)	P-Value
Physical Function, Month 1				0.48
Missing	20	13	33	
N/A: Off-Study	7 (0.0%)	13 (0.0%)	20 (0.0%)	
Responder Improving (+10)	138 (24.4%)	134 (23.4%)	272 (23.9%)	
Non-Responder	349 (61.7%)	347 (60.7%)	696 (61.2%)	
Responder Worsening (-10)	79 (14.0%)	91 (15.9%)	170 (14.9%)	
Physical Function, Month 3				0.007
Missing	20	12	32	
N/A: Off-Study	51 (0.0%)	42 (0.0%)	93 (0.0%)	
Responder Improving (+10)	135 (25.9%)	109 (20.0%)	244 (22.9%)	
Non-Responder	294 (56.3%)	304 (55.9%)	598 (56.1%)	
Responder Worsening (-10)	93 (17.8%)	131 (24.1%)	224 (21.0%)	
Physical Function, Month 6				<0.001
Missing	23	22	45	
N/A: Off-Study	126 (0.0%)	112 (0.0%)	238 (0.0%)	
Responder Improving (+10)	113 (25.5%)	82 (17.7%)	195 (21.5%)	
Non-Responder	246 (55.4%)	260 (56.0%)	506 (55.7%)	
Responder Worsening (-10)	85 (19.1%)	122 (26.3%)	207 (22.8%)	
Physical Function, Month 9				0.05
Missing	24	21	45	
N/A: Off-Study	220 (0.0%)	179 (0.0%)	399 (0.0%)	
Responder Improving (+10)	81 (23.2%)	76 (19.1%)	157 (21.0%)	
Non-Responder	193 (55.3%)	215 (54.0%)	408 (54.6%)	
Responder Worsening (-10)	75 (21.5%)	107 (26.9%)	182 (24.4%)	
Physical Function, Month 12				0.59
Missing	20	26	46	
N/A: Off-Study	278 (0.0%)	230 (0.0%)	508 (0.0%)	
Responder Improving (+10)	65 (22.0%)	65 (19.0%)	130 (20.4%)	
Non-Responder	159 (53.9%)	188 (55.0%)	347 (54.5%)	
Responder Worsening (-10)	71 (24.1%)	89 (26.0%)	160 (25.1%)	

eTable 6C. Proportion of patients in the patient-reported outcome (PRO) intervention arm and control arm with <u>5-point</u> improvement or worsening in <u>symptom control</u> compared to baseline, as measured by the EORTC QLQ-C30, at each assessment timepoint.

	PRO Intervention (N=593)	Control (N=598)	Total (N=1191)	P-Value
Symptom control, Month 1				0.002
Missing	20	16	36	
N/A: Off-Study	7 (0.0%)	13 (0.0%)	20 (0.0%)	
Responder Improving (+5)	208 (36.7%)	149 (26.2%)	357 (31.5%)	
Non-Responder	227 (40.1%)	266 (46.7%)	493 (43.4%)	
Responder Worsening (-5)	131 (23.1%)	154 (27.1%)	285 (25.1%)	
Symptom control, Month 3				0.003
Missing	25	13	38	
N/A: Off-Study	51 (0.0%)	42 (0.0%)	93 (0.0%)	
Responder Improving (+5)	195 (37.7%)	158 (29.1%)	353 (33.3%)	
Non-Responder	199 (38.5%)	215 (39.6%)	414 (39.1%)	
Responder Worsening (-5)	123 (23.8%)	170 (31.3%)	293 (27.6%)	
Symptom control, Month 6				0.006
Missing	25	23	48	
N/A: Off-Study	126 (0.0%)	112 (0.0%)	238 (0.0%)	
Responder Improving (+5)	160 (36.2%)	139 (30.0%)	299 (33.0%)	
Non-Responder	168 (38.0%)	169 (36.5%)	337 (37.2%)	
Responder Worsening (-5)	114 (25.8%)	155 (33.5%)	269 (29.7%)	
Symptom control, Month 9				0.03
Missing	25	23	48	
N/A: Off-Study	220 (0.0%)	179 (0.0%)	399 (0.0%)	
Responder Improving (+5)	124 (35.6%)	123 (31.1%)	247 (33.2%)	
Non-Responder	128 (36.8%)	132 (33.3%)	260 (34.9%)	
Responder Worsening (-5)	96 (27.6%)	141 (35.6%)	237 (31.9%)	
Symptom control, Month 12				0.59
Missing	21	27	48	
N/A: Off-Study	278 (0.0%)	230 (0.0%)	508 (0.0%)	
Responder Improving (+5)	94 (32.0%)	117 (34.3%)	211 (33.2%)	
Non-Responder	123 (41.8%)	111 (32.6%)	234 (36.9%)	
Responder Worsening (-5)	77 (26.2%)	113 (33.1%)	190 (29.9%)	

eTable 6D. Proportion of patients in the patient-reported outcome (PRO) intervention arm and control arm with 10-point improvement or worsening in symptom control compared to baseline, as measured by the EORTC QLQ-C30, at each assessment timepoint.

	PRO Intervention (N=593)	Control (N=598)	Total (N=1191)	P-Value
Symptom control, Month 1				0.003
Missing	20	16	36	
N/A: Off-Study	7 (0.0%)	13 (0.0%)	20 (0.0%)	
Responder Improving (+10)	119 (21.0%)	84 (14.8%)	203 (17.9%)	
Non-Responder	378 (66.8%)	394 (69.2%)	772 (68.0%)	
Responder Worsening (-10)	69 (12.2%)	91 (16.0%)	160 (14.1%)	
Symptom control, Month 3				0.004
Missing	25	13	38	
N/A: Off-Study	51 (0.0%)	42 (0.0%)	93 (0.0%)	
Responder Improving (+10)	118 (22.8%)	101 (18.6%)	219 (20.7%)	
Non-Responder	331 (64.0%)	331 (61.0%)	662 (62.5%)	
Responder Worsening (-10)	68 (13.2%)	111 (20.4%)	179 (16.9%)	
Symptom control, Month 6				0.02
Missing	25	23	48	
N/A: Off-Study	126 (0.0%)	112 (0.0%)	238 (0.0%)	
Responder Improving (+10)	91 (20.6%)	87 (18.8%)	178 (19.7%)	
Non-Responder	286 (64.7%)	273 (59.0%)	559 (61.8%)	
Responder Worsening (-10)	65 (14.7%)	103 (22.2%)	168 (18.6%)	
Symptom control, Month 9				0.19
Missing	25	23	48	
N/A: Off-Study	220 (0.0%)	179 (0.0%)	399 (0.0%)	
Responder Improving (+10)	67 (19.3%)	72 (18.2%)	139 (18.7%)	
Non-Responder	222 (63.8%)	238 (60.1%)	460 (61.8%)	
Responder Worsening (-10)	59 (17.0%)	86 (21.7%)	145 (19.5%)	
Symptom control, Month 12				0.63
Missing	21	27	48	
N/A: Off-Study	278 (0.0%)	230 (0.0%)	508 (0.0%)	
Responder Improving (+10)	56 (19.0%)	67 (19.6%)	123 (19.4%)	
Non-Responder	183 (62.2%)	200 (58.7%)	383 (60.3%)	
Responder Worsening (-10)	55 (18.7%)	74 (21.7%)	129 (20.3%)	

eTable 6E. Proportion of patients in the patient-reported outcome (PRO) intervention arm and control arm with <u>5-point</u> improvement or worsening in <u>health-related quality of life</u> compared to baseline, as measured by the EORTC QLQ-C30, at each assessment timepoint.

	PRO Intervention (N=593)	Control (N=598)	Total (N=1191)	P-Value
Health-related quality of life, Month 1				<0.001
Missing	22	16	38	
N/A: Off-Study	7 (0.0%)	13 (0.0%)	20 (0.0%)	
Responder Improving (+5)	196 (34.8%)	144 (25.3%)	340 (30.0%)	
Non-Responder	256 (45.4%)	278 (48.9%)	534 (47.1%)	
Responder Worsening (-5)	112 (19.9%)	147 (25.8%)	259 (22.9%)	
Health-related quality of life, Month 3				0.006
Missing	25	13	38	
N/A: Off-Study	51 (0.0%)	42 (0.0%)	93 (0.0%)	
Responder Improving (+5)	191 (36.9%)	154 (28.4%)	345 (32.5%)	
Non-Responder	199 (38.5%)	229 (42.2%)	428 (40.4%)	
Responder Worsening (-5)	127 (24.6%)	160 (29.5%)	287 (27.1%)	
Health-related quality of life, Month 6				0.003
Missing	25	23	48	
N/A: Off-Study	126 (0.0%)	112 (0.0%)	238 (0.0%)	
Responder Improving (+5)	146 (33.0%)	128 (27.6%)	274 (30.3%)	
Non-Responder	188 (42.5%)	178 (38.4%)	366 (40.4%)	
Responder Worsening (-5)	108 (24.4%)	157 (33.9%)	265 (29.3%)	
Health-related quality of life, Month 9				0.04
Missing	25	23	48	
N/A: Off-Study	220 (0.0%)	179 (0.0%)	399 (0.0%)	
Responder Improving (+5)	111 (31.9%)	115 (29.0%)	226 (30.4%)	
Non-Responder	148 (42.5%)	143 (36.1%)	291 (39.1%)	
Responder Worsening (-5)	89 (25.6%)	138 (34.8%)	227 (30.5%)	
Health-related quality of life, Month 12				0.52
Missing	22	27	49	
N/A: Off-Study	278 (0.0%)	230 (0.0%)	508 (0.0%)	
Responder Improving (+5)	88 (30.0%)	103 (30.2%)	191 (30.1%)	
Non-Responder	130 (44.4%)	127 (37.2%)	257 (40.5%)	
Responder Worsening (-5)	75 (25.6%)	111 (32.6%)	186 (29.3%)	

eTable 6F. Proportion of patients in the patient-reported outcome (PRO) intervention arm and control arm with <u>10-point</u> improvement or worsening in <u>health-related quality of life</u> compared to baseline, as measured by the EORTC QLQ-C30, at each assessment timepoint.

	PRO Intervention (N=593)	Control (N=598)	Total (N=1191)	P-Value
Health-related quality of life, Month 1				0.01
Missing	22	16	38	
N/A: Off-Study	7 (0.0%)	13 (0.0%)	20 (0.0%)	
Responder Improving (+10)	108 (19.1%)	72 (12.7%)	180 (15.9%)	
Non-Responder	397 (70.4%)	430 (75.6%)	827 (73.0%)	
Responder Worsening (-10)	59 (10.5%)	67 (11.8%)	126 (11.1%)	
Health-related quality of life, Month 3				<0.001
Missing	25	13	38	
N/A: Off-Study	51 (0.0%)	42 (0.0%)	93 (0.0%)	
Responder Improving (+10)	103 (19.9%)	79 (14.5%)	182 (17.2%)	
Non-Responder	352 (68.1%)	357 (65.7%)	709 (66.9%)	
Responder Worsening (-10)	62 (12.0%)	107 (19.7%)	169 (15.9%)	
Health-related quality of life, Month 6				0.006
Missing	25	23	48	
N/A: Off-Study	126 (0.0%)	112 (0.0%)	238 (0.0%)	
Responder Improving (+10)	83 (18.8%)	73 (15.8%)	156 (17.2%)	
Non-Responder	302 (68.3%)	295 (63.7%)	597 (66.0%)	
Responder Worsening (-10)	57 (12.9%)	95 (20.5%)	152 (16.8%)	
Health-related quality of life, Month 9				0.04
Missing	25	23	48	
N/A: Off-Study	220 (0.0%)	179 (0.0%)	399 (0.0%)	
Responder Improving (+10)	60 (17.2%)	59 (14.9%)	119 (16.0%)	
Non-Responder	236 (67.8%)	254 (64.1%)	490 (65.9%)	
Responder Worsening (-10)	52 (14.9%)	83 (21.0%)	135 (18.1%)	
Health-related quality of life, Month 12				0.23
Missing	22	27	49	
N/A: Off-Study	278 (0.0%)	230 (0.0%)	508 (0.0%)	
Responder Improving (+10)	53 (18.1%)	59 (17.3%)	112 (17.7%)	
Non-Responder	189 (64.5%)	199 (58.4%)	388 (61.2%)	
Responder Worsening (-10)	51 (17.4%)	83 (24.3%)	134 (21.1%)	

eTable 7. Preplanned Subgroup Analysis of Physical Function, as Measured by the EORTC QLQ-C30

A general linear mixed model was fit within each level of the subgroup variable, and effect of the PRO intervention at month 3 was tested similar to the primary analysis. Next, a general linear mixed model of physical function was fit including all patients and included fixed effects for arm, timepoint, and the given subgrouping variable, as well as pairwise interactions between arm and visit, arm and subgroup variable, and visit and subgroup variable. Higher order interactions were explored but found to be statistically insignificant so were removed from the model. A random practice intercept term was included to account for clustering by practice. Repeated observations by patient were modeled using compound symmetric correlation structure over time. The interaction test p-value is based on the Type 3 test of the interaction effect between arm and the given subgroup variable.

Subgroup	Time point	PRO Mean Change from Baseline (95% CI)	P-value of PRO Change from Baseline	Control Mean Change from Baseline (95% CI)	P-value of Control Change from Baseline	Difference in Mean Change from Baseline between Arms (95% CI)	P-value of Difference between Arms	Subgroup Interaction Test P-value
Age								0.09
Age <60	Month 3	3.40 (1.25, 5.56)	0.002	-0.44 (-2.52, 1.65)	0.68	3.84 (0.84, 6.84)	0.01	
Age ≥60	Month 3	0.41 (-1.55, 2.37)	0.68	-1.21 (-3.16, 0.74)	0.22	1.62 (-1.14, 4.38)	0.25	
Sex								0.72
Male	Month 3	-0.91 (-3.21, 1.40)	0.44	-1.45 (-3.60, 0.71)	0.19	0.54 (-2.62, 3.69)	0.74	
Female	Month 3	3.13 (1.23, 5.03)	0.001	-0.49 (-2.43, 1.45)	0.62	3.62 (0.91, 6.34)	0.009	
Race								0.19
White	Month 3	0.75 (-0.88, 2.38)	0.37	-1.63 (-3.28, 0.02)	0.05	2.38 (0.06, 4.70)	0.04	
Non-white	Month 3	4.68 (1.30, 8.05)	0.007	1.30 (-1.70, 4.30)	0.39	3.37 (-1.14, 7.89)	0.14	
Ethnicity								0.97
Hispanic	Month 3	4.34 (-5.88, 14.56)	0.40	3.19 (-2.63, 9.01)	0.28	1.15 (-10.61, 12.91)	0.85	
Non-Hispanic	Month 3	1.47 (-0.01, 2.95)	0.05	-1.23 (-2.72, 0.26)	0.11	2.70 (0.60, 4.80)	0.01	
Education								0.30
≤High school	Month 3	2.43 (-0.04, 4.90)	0.05	-3.24 (-5.52, -0.95)	0.006	5.67 (2.30, 9.03)	<0.001	
≥Some college	Month 3	1.02 (-0.80, 2.85)	0.27	0.66 (-1.21, 2.54)	0.49	0.36 (-2.25, 2.98)	0.79	
Employment status								0.51
Working	Month 3	-0.32 (-2.76, 2.12)	0.80	-1.11 (-3.76, 1.53)	0.41	0.79 (-2.80, 4.39)	0.67	

Subgroup	Time point	PRO Mean Change from Baseline (95% CI)	P-value of PRO Change from Baseline	Control Mean Change from Baseline (95% CI)	P-value of Control Change from Baseline	Difference in Mean Change from Baseline between Arms (95% CI)	P-value of Difference between Arms	Subgroup Interaction Test P-value
Not currently working	Month 3	2.29 (0.49, 4.10)	0.01	-0.90 (-2.62, 0.82)	0.30	3.19 (0.70, 5.69)	0.01	
Marital status								0.64
Married/partnered	Month 3	2.19 (0.39, 4.00)	0.02	-1.31 (-3.19, 0.57)	0.17	3.51 (0.90, 6.11)	0.008	
Other	Month 3	0.25 (-2.28, 2.77)	0.85	-0.37 (-2.63, 1.90)	0.75	0.61 (-2.78, 4.00)	0.72	
Device use								0.86
Inexperienced	Month 3	3.07 (-1.02, 7.16)	0.14	-0.42 (-3.96, 3.13)	0.82	3.49 (-1.93, 8.90)	0.21	
Experienced	Month 3	1.22 (-0.34, 2.77)	0.12	-1.04 (-2.62, 0.54)	0.20	2.26 (0.04, 4.47)	0.046	
Internet use								0.48
Inexperienced	Month 3	1.38 (-2.09, 4.85)	0.43	0.20 (-2.91, 3.30)	0.90	1.18 (-3.47, 5.84)	0.62	
Experienced	Month 3	1.59 (-0.00, 3.18)	0.05	-1.34 (-2.95, 0.28)	0.11	2.92 (0.65, 5.19)	0.01	
Email use								0.20
Inexperienced	Month 3	2.35 (-0.35, 5.05)	0.09	-1.20 (-3.56, 1.15)	0.32	3.55 (-0.03, 7.14)	0.05	
Experienced	Month 3	1.08 (-0.63, 2.79)	0.21	-0.66 (-2.49, 1.16)	0.48	1.75 (-0.75, 4.25)	0.17	
Site location								0.17
Urban/Suburban	Month 3	0.98 (-0.72, 2.69)	0.26	-0.51 (-2.22, 1.21)	0.56	1.49 (-0.92, 3.90)	0.23	
Rural	Month 3	3.15 (0.24, 6.05)	0.03	-1.95 (-4.64, 0.74)	0.16	5.10 (1.14, 9.05)	0.01	
Cancer type								0.12
Thoracic	Month 3	2.55 (-1.06, 6.16)	0.17	-0.48 (-4.27, 3.31)	0.80	3.03 (-2.21, 8.26)	0.26	
Breast	Month 3	2.22 (-1.24, 5.69)	0.21	1.02 (-2.68, 4.72)	0.59	1.20 (-3.86, 6.27)	0.64	
Colorectal	Month 3	2.78 (-0.44, 6.00)	0.09	-0.93 (-3.67, 1.82)	0.51	3.71 (-0.52, 7.94)	0.09	
GU	Month 3	-1.35 (-5.52, 2.82)	0.52	-3.85 (-8.92, 1.23)	0.14	2.49 (-4.07, 9.06)	0.46	
Gynecologic	Month 3	5.79 (1.15, 10.43)	0.01	-3.59 (-8.67, 1.49)	0.17	9.38 (2.50, 16.27)	0.008	
Other	Month 3	-1.10 (-4.14, 1.93)	0.48	-0.43 (-3.13, 2.28)	0.76	-0.68 (-4.75, 3.39)	0.74	

eTable 8. Individual Symptom Scale Mean Score Estimates and Differences Between Groups in Mean Change From Baseline at Each Measured Timepoint, From the EORTC QLQ-C30 Questionnaire

Individual Symptom Scale	Timepoint	PRO Arm Mean Estimate	Control Arm Mean Estimate	Difference in Mean Change from Baseline between Groups (95% CI)	P-value of Difference between Groups
Fatigue	Baseline	40.07	40.48	-	N/A
	Month 1	36.70	41.10	-3.99 (-6.62, -1.35)	0.003
	Month 3	36.44	42.29	-5.44 (-8.14, -2.74)	<0.001
	Month 6	36.72	41.98	-4.85 (-7.69, -2.00)	<0.001
	Month 9	37.67	44.24	-6.15 (-9.20, -3.11)	<0.001
	Month 12	38.82	44.13	-4.90 (-8.12, -1.68)	0.003
Nausea / Vomiting	Baseline	9.92	10.47	-	N/A
	Month 1	8.81	11.98	-2.62 (-4.61, -0.62)	0.01
	Month 3	7.73	10.50	-2.22 (-4.26, -0.17)	0.03
	Month 6	8.90	10.60	-1.15 (-3.30, 1.00)	0.29
	Month 9	9.66	10.47	-0.25 (-2.56, 2.05)	0.83
	Month 12	11.08	11.54	0.10 (-2.34, 2.53)	0.94
Pain	Baseline	25.92	28.19	-	N/A
	Month 1	23.93	26.89	-0.69 (-3.67, 2.28)	0.65
	Month 3	25.34	29.98	-2.37 (-5.41, 0.67)	0.13
	Month 6	26.87	31.53	-2.39 (-5.60, 0.82)	0.14
	Month 9	28.29	32.23	-1.67 (-5.10, 1.77)	0.34
	Month 12	30.08	32.74	-0.39 (-4.03, 3.24)	0.83
Dyspnea	Baseline	20.22	20.54	-	N/A
	Month 1	20.63	23.30	-2.33 (-5.21, 0.54)	0.11
	Month 3	22.60	24.32	-1.39 (-4.34, 1.55)	0.35
	Month 6	22.61	25.37	-2.43 (-5.53, 0.68)	0.13
	Month 9	24.16	27.04	-2.54 (-5.86, 0.77)	0.13
	Month 12	25.02	24.36	0.98 (-2.53, 4.49)	0.58
Insomnia	Baseline	28.00	31.67	-	N/A
	Month 1	22.50	30.56	-4.39 (-7.86, -0.93)	0.01
	Month 3	20.81	29.46	-4.99 (-8.53, -1.45)	0.006
	Month 6	22.62	29.13	-2.85 (-6.58, 0.89)	0.13

Individual Symptom Scale	Timepoint	PRO Arm Mean Estimate	Control Arm Mean Estimate	Difference in Mean Change from Baseline between Groups (95% CI)	P-value of Difference between Groups
	Month 9	21.43	29.19	-4.10 (-8.08, -0.11)	0.04
	Month 12	23.28	30.41	-3.47 (-7.68, 0.75)	0.11
	Baseline	22.66	22.75	-	N/A
	Month 1	18.77	21.40	-2.55 (-5.98, 0.88)	0.15
	Month 3	18.21	21.34	-3.04 (-6.55, 0.47)	0.09
Appetite loss	Month 6	18.46	21.87	-3.32 (-7.01, 0.37)	0.08
	Month 9	18.24	23.06	-4.74 (-8.69, -0.79)	0.02
	Month 12	21.41	23.15	-1.65 (-5.83, 2.52)	0.44
	Baseline	18.03	16.55	-	N/A
	Month 1	15.47	15.37	-1.38 (-4.38, 1.62)	0.37
	Month 3	15.60	15.30	-1.18 (-4.25, 1.89)	0.45
Constipation	Month 6	14.78	14.23	-0.93 (-4.16, 2.31)	0.57
	Month 9	16.91	14.59	0.84 (-2.62, 4.30)	0.63
	Month 12	14.50	15.86	-2.84 (-6.49, 0.82)	0.13
	Baseline	13.46	15.58	-	N/A
	Month 1	13.22	16.30	-0.97 (-3.96, 2.02)	0.52
	Month 3	12.40	14.86	-0.34 (-3.40, 2.71)	0.83
Diarrhea	Month 6	13.05	14.08	1.09 (-2.13, 4.30)	0.51
	Month 9	13.32	12.83	2.60 (-0.84, 6.04)	0.14
	Month 12	15.41	13.37	4.16 (0.53, 7.80)	0.02

eTable 9. Completion Rates by Study Week

Week	N	Completed	Rate
0	592	497	84.0%
1	591	505	85.4%
2	590	522	88.5%
3	586	535	91.3%
4	578	540	93.4%
5	571	534	93.5%
6	568	523	92.1%
7	555	507	91.4%
8	551	507	92.0%
9	544	500	91.9%
10	542	496	91.5%
11	534	486	91.0%
12	526	491	93.3%
13	514	464	90.3%
14	510	464	91.0%
15	500	463	92.6%
16	493	444	90.1%
17	481	440	91.5%
18	471	437	92.8%
19	467	437	93.6%
20	458	421	91.9%
21	452	424	93.8%
22	443	411	92.8%
23	439	404	92.0%
24	431	397	92.1%
25	422	395	93.6%
26	418	382	91.4%
27	414	375	90.6%
28	410	380	92.7%
29	404	366	90.6%
30	399	362	90.7%
31	389	360	92.5%
32	383	360	94.0%
33	378	344	91.0%
34	370	345	93.2%
35	360	335	93.1%

Week	N	Completed	Rate
36	356	323	90.7%
37	347	323	93.1%
38	345	320	92.8%
39	342	316	92.4%
40	336	309	92.0%
41	334	307	91.9%
42	330	304	92.1%
43	326	295	90.5%
44	320	290	90.6%
45	312	285	91.3%
46	310	283	91.3%
47	306	282	92.2%
48	303	275	90.8%
49	301	277	92.0%
50	295	265	89.8%
51	289	258	89.3%
Total	22486	20565	91.5%

eTable 10. Alerts Triggered by the Weekly Survey System to the Care Team, by Symptom

Individual symptom alerts contained in the alert notification messages triggered by the weekly survey system to the care team. Each notification could include one or more individual symptom alerts (for example, if both nausea and pain surpassed the triggering threshold, both would be included in that week's alert notification). Among a total of 6,979 alert notifications triggered during the trial, how often each specific symptom item was included as an alert is shown.

Weekly PRO Survey Symptom Item	# (%) of Alert Notifications Containing the Symptom Item
Activity Level (Diminished Performance Status)	1438 (20.6%)
Appetite Loss	694 (9.9%)
Constipation	579 (8.3%)
Depression	771 (11.1%)
Diarrhea	1268 (18.2%)
Dyspnea (overall)	959 (13.7%)
Dyspnea Severity	*625 (9.0%)*
Dyspnea Interference	*760 (10.9%)*
Fall	475 (6.8%)
Insomnia	749 (10.7%)
Nausea (overall)	941 (13.5%)
Nausea Frequency	*883 (12.7%)*
Nausea Severity	*214 (3.1%)*
Pain (overall)	3513 (50.3%)
Pain Severity	*1523 (21.8%)*
Pain Frequency	*3096 (44.4%)*
Pain Interference	*1565 (22.4%)*
Vomiting	275 (3.9%)

What can I do to manage my sleep problems?

Tips to help you sleep:

- **Tell your cancer care team about problems that are getting in the way of your sleep.** Getting treatment to lower side effects such as pain or bladder or bowel problems may help you sleep better.

- **Set good bedtime habits.**
  - Go to bed only when sleepy, in a quiet and dark room, and in a comfortable bed.
  - Go to bed and wake up at the same time.
  - Avoid napping if possible.
  - Make sure your bedroom is not overly hot or cold.
  - Stop watching television or using devices with screens a couple of hours before going to bed.
    - Devices like: iPads, laptops, and smart phones.
  - Don't drink or eat a lot starting about 2-3 hours before bedtime.
  - Exercising too close to bedtime may make sleep more difficult.
    - Exercise before 2:00pm promotes sleep.
  - Don't watch the clock at night.
  - Keep out pets who wake you up.

- **Don't stay awake in bed** for more than 5-10 minutes. If you do not fall asleep, get out of bed, sit in a chair in the dark until you are sleepy. It's okay if this happens several times a night.

- **Avoid caffeine after midday.** Also cigarettes, alcohol and some 'over-the-counter' medications may interfere with sleep.

- **Sleep medicine may be prescribed** by your cancer care team for a short period if other strategies don't work.

- **Cognitive behavioral therapy (CBT) and/or relaxation therapy may help.** For example, a CBT therapist can help you learn to change negative thoughts and beliefs about sleep into positive ones.
  - Muscle relaxation, guided imagery, and self-hypnosis may help.

eFigure 2.Example Clinician-Level Educational Materials for Symptom Management

2017 version for trial

PAIN

Pain is common in patients with cancer and impacts patients' functional status and quality of life.
- Cancer patients often have multiple sites of pain.
- Cancer pain is associated with increased emotional distress and risk of developing depression.

Sources of pain in cancer patients include:
- Direct effects of cancer (bone pain, pressure on internal organs, ascites).
- Surgery pain.
- Radiation therapy (mucositis, dermatologic changes, brachytherapy pain, mucosal inflammation).
- Chemotherapy or targeted therapy (arthralgia, myalgia, neuropathy, bowel function changes, mucositis, rash).
- Diagnostic procedures.
- Other health conditions (arthritis, osteoporosis)

Assessment

- Assess pain medication history.
  - What is prescribed, what is the patient actually taking, how it is working?
  - Is the patient taking opioids, and are they long acting, short acting, or both?
  - How long has the patient been on their pain regimen?
- Conduct comprehensive pain assessment:
  - Location of pain (Where does pain originate? Does it radiate to another area of the body?).
  - Intensity of pain (use pain scale of 0-10 with 10 being the worst pain imaginable).
  - Quality of pain (sharp, stabbing, burning, aching).
  - Using scale of 1-10 with 10 being the worst pain imaginable: What is your pain at its best? What is it at its peak? What is your pain after taking your pain medications?
  - Assess for breakthrough pain (Does the pain return or increase in intensity before the next dose?).
  - Onset, duration and aggravating/alleviating factors (When does it start? What makes it worse/better? How often does it occur? How long does it last?)
- Assess for changes in activity level, sleep, general activities of daily living, depression.
- If taking opioids, assess for constipation.

Severity			
Grade 1 *Mild*	Grade 2 *Moderate*	Grade 3 *Severe*	Grade 4 *Life Threatening*
Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self-care, ADL	

Interventions Based on Severity

Management of Pain:
1. Non-opioids (acetaminophen, COX-2 inhibitor, NSAID). Note that COX-2 inhibitor (celecoxib, meloxicam) does not inhibit platelet aggregation; NSAID toxic effects can include acute renal failure, gastrointestinal toxicity, cardiovascular toxicity, and CNS toxicity such as memory loss and confusion. NSAIDs should be avoided or used with caution if patient has: stomach or intestinal ulcers; cardiovascular disease and/or hypertension; kidney disease; bleeding disorders; pregnancy; taking other prescription anti-coagulants such as warfarin (Coumadin) or heparin, phenytoin (Dilantin), and/or cyclosporine; use of acetaminophen may cause hepatic injury; use caution with liver disease.
2. Opioids such as morphine when pain persists or increases and cannot be controlled by non-opioids.
3. Non-medication treatments should be offered for all patients with pain. These include emotional support, distraction (music, social engagement), appropriate physical activity (positioning, cushioning, supportive devices, exercise. Physical therapy), and topical application of heat or cold.

Considerations:
- Pain medication scheduled "around the clock" when pain is constant. Consider long-acting agent.
- Use the simplest route of administration possible.
- Consider additional supportive drugs to address anxiety, depression, or neuropathic pain symptoms.
- Provide patient/family/caregiver education about treatment approaches and safe medication use.
- Consider suggesting a pain diary to monitor characteristics of pain, medication regimen, and response to medication.
- No driving when using opioids.

This form and its content are for use by health care providers, not patients, is provided as general health information and is a tool to assist clinicians in the assessment of patients, and is not intended to: invite or establish a health care provider-patient relationship, constitute furnishing professional services, constitute, or substitute for, the advice or judgment of a medical professional; or serve as the sole basis for medical treatment.

eFigure 3. Example Actual Clinician Report Showing Longitudinal Trajectory of Patient-Reported Outcomes (for Visualizing/Printing at Clinic Visit)
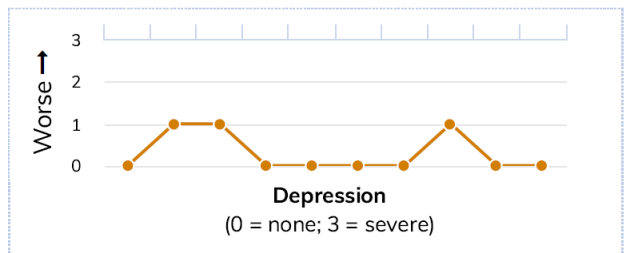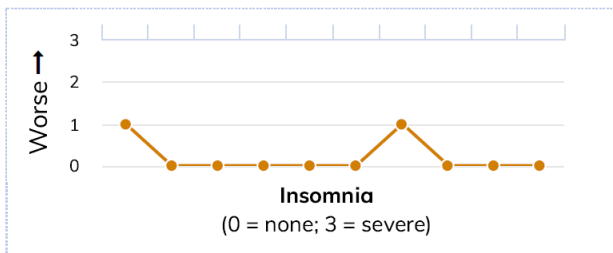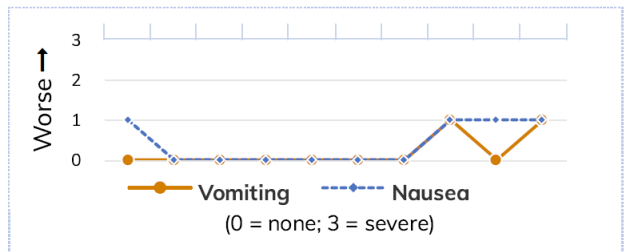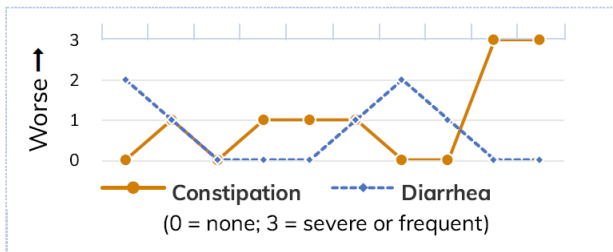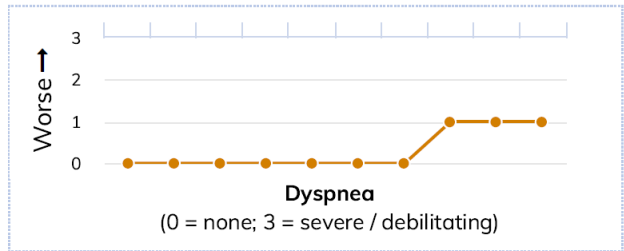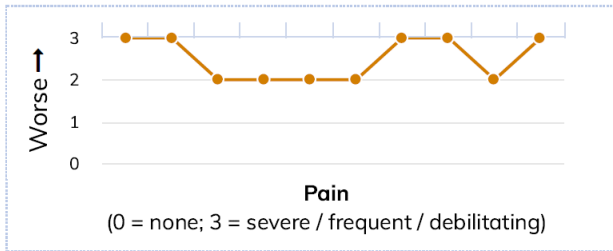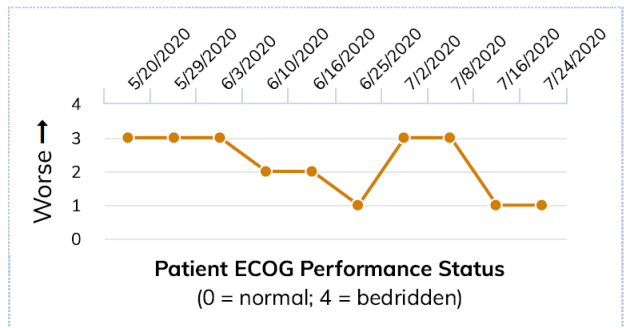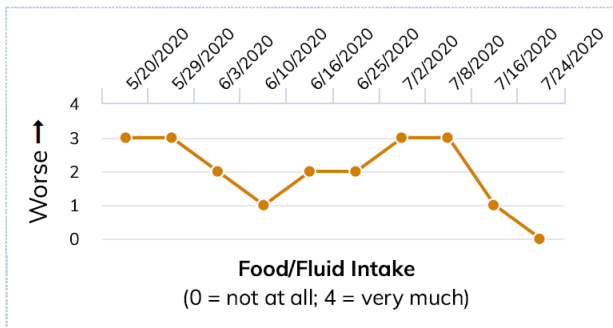
Patient name and identifiers have been removed. For symptoms based on the PRO-CTCAE, composite grades are generated in reports based on a published algorithm (*Clin Trials. 2021 Feb;18(1):104-114*).

Patient Symptom Report

This is a symptom report based on answers your patient self-reported weekly for the <u>past 10 weeks</u> in the PRO-TECT trial.

███████ ████████   Date Range: 5/20/2020 - 7/24/2020   MRN:_____

❶ **Severe symptoms on 7/24/2020:** Pain, Constipation

❶ **Worsened symptoms between 7/16/2020 and 7/24/2020:** Pain, Vomiting

❶ **Falls:** None

✔ **Improved symptoms between 7/16/2020 and 7/24/2020:** Food/Fluid Intake

Food/Fluid Intake
(0 = not at all; 4 = very much)

Patient ECOG Performance Status
(0 = normal; 4 = bedridden)

Pain
(0 = none; 3 = severe / frequent / debilitating)

Dyspnea
(0 = none; 3 = severe / debilitating)

Constipation ••• Diarrhea
(0 = none; 3 = severe or frequent)

Vomiting ••• Nausea
(0 = none; 3 = severe)

Insomnia
(0 = none; 3 = severe)
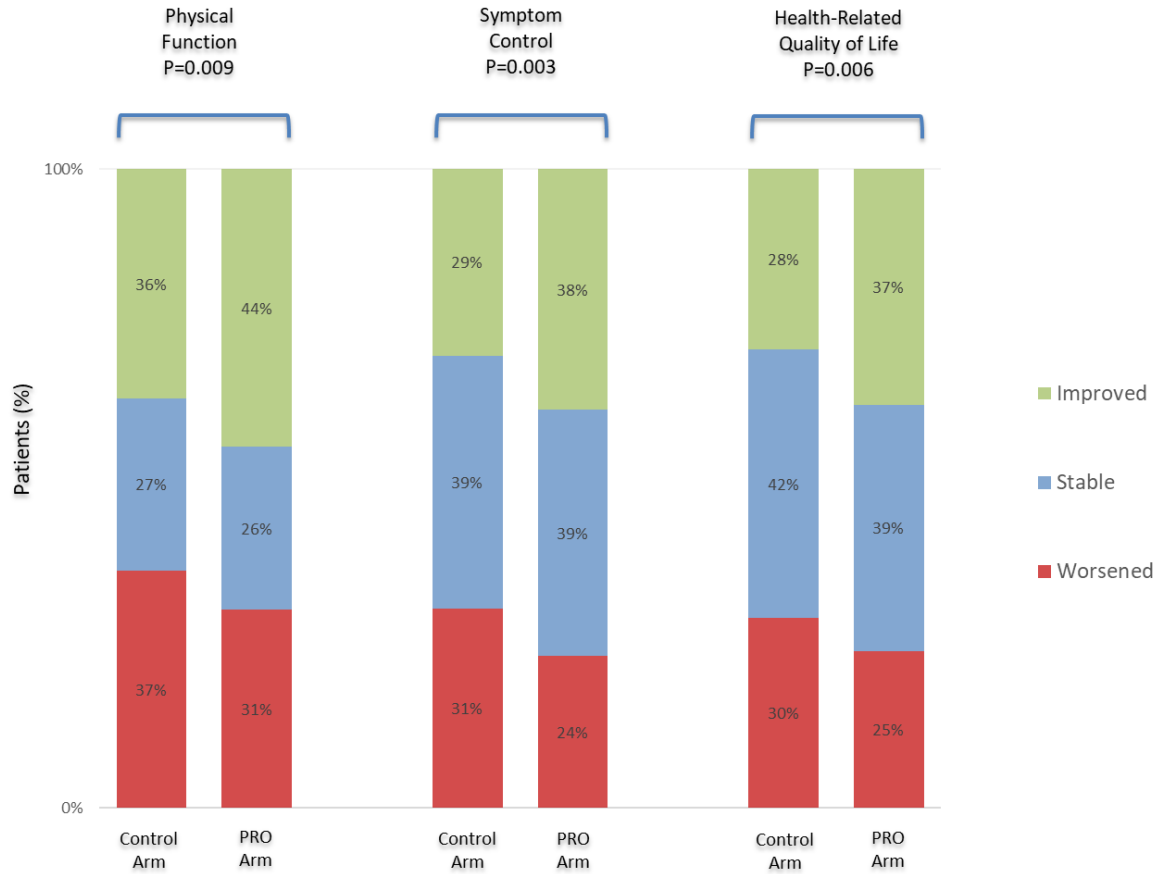
Depression
(0 = none; 3 = severe)

Patient write-ins of other symptoms:
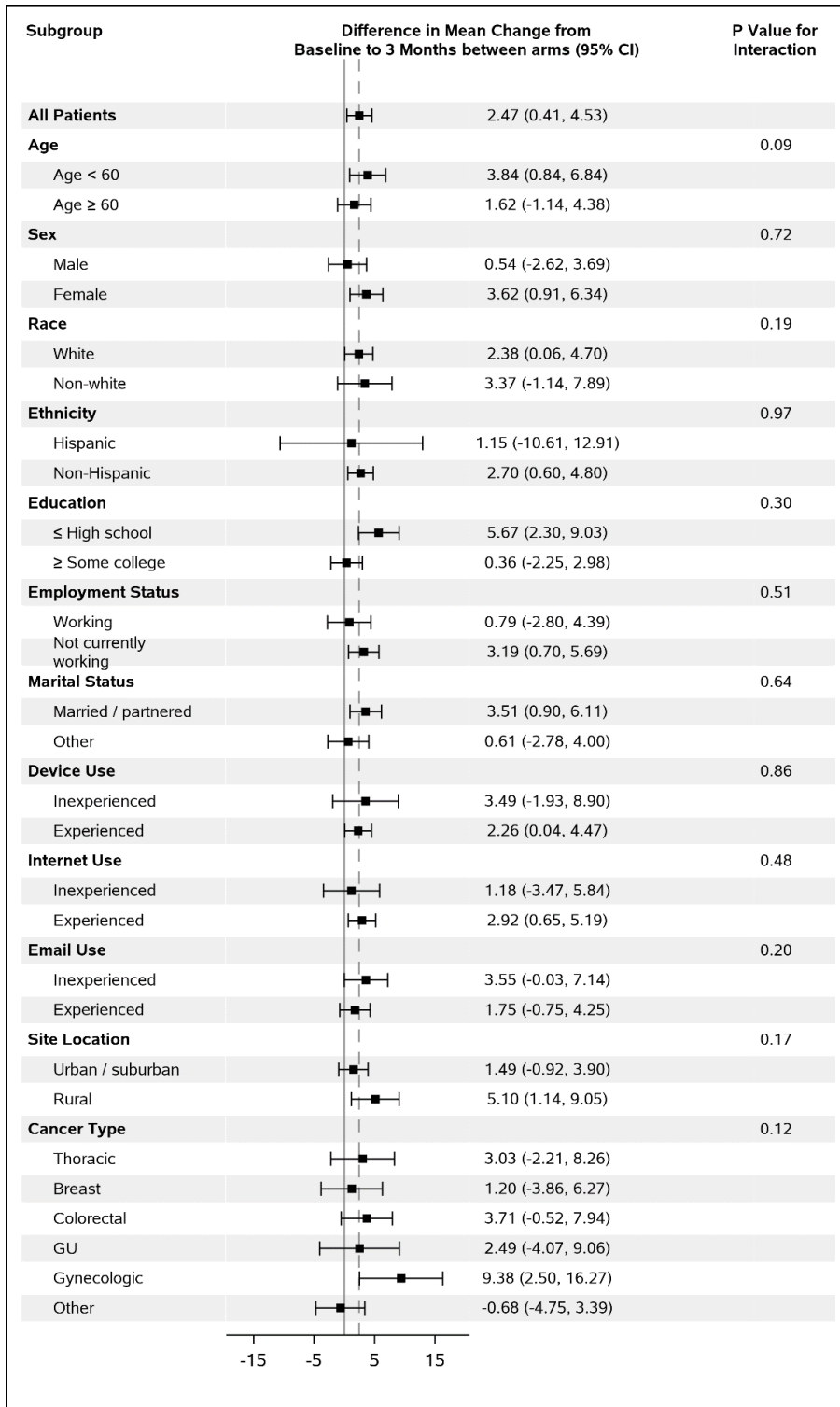- None reported

eFigure 4. Responder Analysis

Proportion of patients experiencing improved, stable, or worsened outcomes at 3 months compared to baseline based on a 5-point change from baseline in the 100-point physical function scale of the EORTC QLQ-C30 questionnaire.
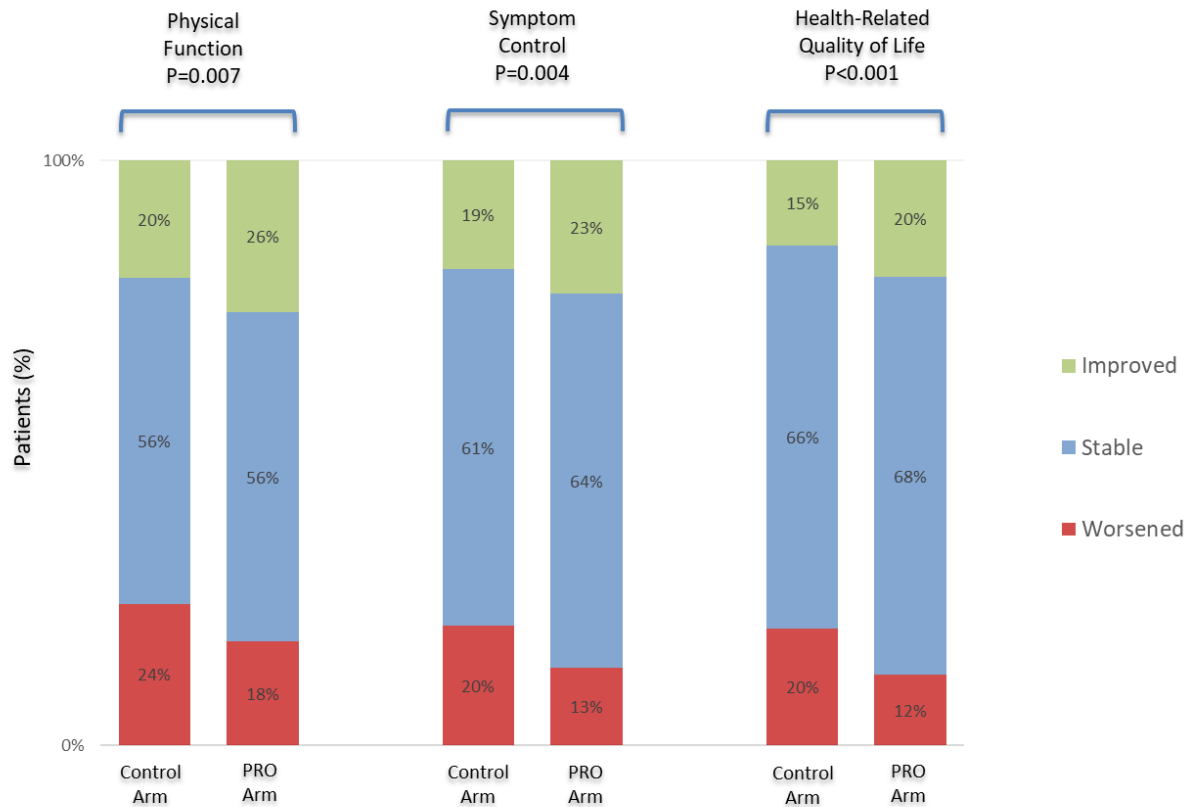

PRO, patient-reported outcome

eFigure 5. Preplanned Subgroup Analysis of Physical Function, as Measured by the EORTC QLQ-C30

This graphic uses general linear mixed models of physical function including all patients with fixed effects for arm, timepoint, and the given subgrouping variable, as well as pairwise interactions between arm and visit, arm and subgroup variable, and visit and subgroup variable. Higher order interactions were explored but found to be statistically insignificant so were removed from the model. A random practice intercept term was included to account for clustering by practice. Repeated observations by patient were modeled using compound symmetric correlation structure over time. The interaction test p-value is based on the Type 3 test of the interaction effect between arm and the given subgroup variable. Difference in confidence intervals were computed from a contrast statement within each mixed model. Data are also shown in eTable 8.

Subgroup	Difference in Mean Change from Baseline to 3 Months between arms (95% CI)	P Value for Interaction
All Patients	2.47 (0.41, 4.53)	
Age		0.09
Age < 60	3.84 (0.84, 6.84)	
Age ≥ 60	1.62 (-1.14, 4.38)	
Sex		0.72
Male	0.54 (-2.62, 3.69)	
Female	3.62 (0.91, 6.34)	
Race		0.19
White	2.38 (0.06, 4.70)	
Non-white	3.37 (-1.14, 7.89)	
Ethnicity		0.97
Hispanic	1.15 (-10.61, 12.91)	
Non-Hispanic	2.70 (0.60, 4.80)	
Education		0.30
≤ High school	5.67 (2.30, 9.03)	
≥ Some college	0.36 (-2.25, 2.98)	
Employment Status		0.51
Working	0.79 (-2.80, 4.39)	
Not currently working	3.19 (0.70, 5.69)	
Marital Status		0.64
Married / partnered	3.51 (0.90, 6.11)	
Other	0.61 (-2.78, 4.00)	
Device Use		0.86
Inexperienced	3.49 (-1.93, 8.90)	
Experienced	2.26 (0.04, 4.47)	
Internet Use		0.48
Inexperienced	1.18 (-3.47, 5.84)	
Experienced	2.92 (0.65, 5.19)	
Email Use		0.20
Inexperienced	3.55 (-0.03, 7.14)	
Experienced	1.75 (-0.75, 4.25)	
Site Location		0.17
Urban / suburban	1.49 (-0.92, 3.90)	
Rural	5.10 (1.14, 9.05)	
Cancer Type		0.12
Thoracic	3.03 (-2.21, 8.26)	
Breast	1.20 (-3.86, 6.27)	
Colorectal	3.71 (-0.52, 7.94)	
GU	2.49 (-4.07, 9.06)	
Gynecologic	9.38 (2.50, 16.27)	
Other	-0.68 (-4.75, 3.39)	

-15   -5   5   15

eFigure 6. Responder Sensitivity Analysis

Proportion of patients experiencing clinically meaningful improved, stable, or worsened outcomes at 3 months compared to baseline, at control arm practices versus patient-reported outcome (PRO) intervention arm practices, based on a <u>10-point change</u> from baseline in the 100-point scales of the EORTC QLQ-C30 questionnaire. Data are also shown in **eTable 7**. A primary analysis reported in the manuscript text and in **Figure 2** employing a 5-point change threshold shows similar results.

PRO, patient-reported outcome

eFigure 7. Mean Changes From Baseline at Each Visit for Symptom Scales

Mean changes from baseline at each visit for symptom scales for patients at oncology practices allocated to patient-reported outcomes (PRO) vs control, as measured by the EORTC QLQ-C30. Negative values represent improvements. + denotes between-arm difference p-value <0.05, and ++ denotes between-arm difference p-value <0.01.

+ between-arm difference p-value<0.05; ++ between-arm difference p-value<0.01