The Oncologist
The official journal of the Society for Translational Oncology

Supplemental Tables for:
Talazoparib in Patients with a Germline BRCA-mutated Advanced Breast Cancer: Detailed Safety Analyses from the Phase 3 EMBRACA Trial
Sara Hurvitz et al.

SUPPLEMENTAL MATERIALS

Table S1. Original and amended dose modifications guidelines for talazoparib* based on toxicity

Original guidance	Amended guidance
Grade 1 or 2 toxicity: No requirement for dose interruption or dose reduction. If the toxicity persists at grade 2, a dose reduction to the next lower dose level (e.g., from 1.0 mg/day to 0.75 mg/day) may be implemented at the discretion of the Investigator.	**Grade 1 or 2 toxicity** (other than abnormal liver tests): No requirement for dose interruption or dose reduction. If the toxicity persists at grade 2 (for ≥ 7 days), a dose reduction to the next lower dose level (e.g., from 1.0 mg/day to 0.75 mg/day) may be implemented at the discretion of the Investigator.
Grade 3 toxicity: Daily dosing should be stopped. Talazoparib dosing may resume at the next lower dose level (e.g., from 1.0 mg/day to 0.75 mg/day, 0.75 mg/day to 0.5 mg/day) when toxicity resolves to grade 1 or returns to *baseline.*[a]	**Grade 3 nonhematologic toxicity** (other than abnormal liver tests): Daily dosing must be held for grade 3 AEs considered related to talazoparib. Supportive care should be implemented as appropriate (e.g., antiemetics, antidiarrheal agents). Talazoparib dosing may resume at the next lower dose level (e.g., from 1.0 mg/day to 0.75 mg/day, 0.75 mg/day to 0.5 mg/day to 0.25 mg/day) when toxicity resolves to grade 1 or returns to *baseline*. **Grade 3 hematologic toxicity:** Daily dosing must be held for grade 3 laboratory abnormalities known to be associated with talazoparib. Supportive care should be implemented as appropriate (e.g., growth factor support, blood products). Talazoparib dosing may resume at the next lower dose level when toxicity resolves to grade 1 or would meet *the eligibility criteria.*[a,b]
Grade 4 toxicity: Daily dosing should be stopped. Talazoparib may resume at a lower dose level (1–2 lower dose level decrease) with the approval of the medical monitor when toxicity resolves to grade 1 or returns to *baseline.*[a]	**Grade 4 nonhematologic toxicity** (other than abnormal liver tests): Daily dosing must be held for grade 4 AEs (regardless of relationship to talazoparib). Supportive care should be implemented as appropriate (e.g., antiemetics, antidiarrheal agents). Talazoparib may resume at a lower dose level (1–2 dose level decrease) when toxicity resolves to grade 1 or returns to *baseline*. **Grade 4 hematologic toxicity:** Daily dosing must be held for grade 4 abnormal laboratory values (regardless of relationship to talazoparib). Supportive care should be implemented as appropriate (e.g., growth factor support, blood products). Talazoparib may resume but must be at a lower dose level when toxicity resolves to grade 1 or would meet

	the eligibility criteria[a,b]; this should be a 1–2 dose level decrease per Investigator discretion.

*PCT dosing and dose modifications followed local practice/prescribing guidelines.
[a]For the most common hematologic AE (anemia), initial EMBRACA protocol requirements after a grade ≥3 anemia AE (hemoglobin <8 g/dL) required that the talazoparib dose be interrupted until hemoglobin levels recovered to grade 1 (≥10 g/dL) or *baseline* before resuming talazoparib at the next lower dose level, whereas EMBRACA eligibility criteria were permitted with a hemoglobin value ≥9 g/dL. EMBRACA protocol was later amended as follows: in the case of a grade ≥3 anemia (<8 g/dL), hemoglobin levels must return to grade 1 or meet study inclusion criteria (≥ 9 g/dL) before talazoparib could resume at the next lower dose level. This requirement potentially facilitated investigators to provide PRBC transfusions and/or anti-anemic use at a higher hemoglobin level than recommended by current clinical practice/international clinical guidelines (1, 2).
[b]In the talazoparib arm, before the protocol amendment, 43.3% of patients had PRBC transfusions and after the amendment, 32.4% of patients had PRBC transfusions to manage anemia.
Abbreviations: AE, adverse event; NCCN, National Comprehensive Cancer Network; PCT, physician's choice of chemotherapy; PRBC, packed red blood cells.
1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Management of Cancer- and Chemotherapy-Induced Anemia 2019. https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf. Accessed June 7, 2019.
2. Aapro M, Beguin Y, Bokemeyer C et al. Management of anaemia and iron deficiency in patients with cancer: ESMO Clinical Practice Guidelines. Ann Oncol 2018;29(Supplement_4):iv271.

Table S2. Dose modification and management from US prescribing information

Adverse reactions	Withhold talazoparib until levels resolve	Resume talazoparib
Hemoglobin <8 g/dL	≥9 g/dL	Resume talazoparib at a reduced dose
Platelet count <50 × 10^9/L	≥75 × 10^9/L	
Neutrophil count <1000 × 10^6/L	≥1500 × 10^6/L	
Nonhematologic grade 3 or 4	Grade ≤1	Consider resuming talazoparib at a reduced dose or discontinue

1.0 Supportive Medications

Supportive medications could be provided prophylactically or therapeutically at the discretion of the investigator. Granulocyte colony-stimulating factor was allowed only in the rescue setting. Allowed medications included, but were not limited to, antiemetics (e.g., dexamethasone, metoclopramide, ondansetron, aprepitant), antidiarrheals (e.g., loperamide hydrochloride), and appetite stimulants (e.g., megestrol acetate). Bisphosphonates and denosumab were allowed for the treatment or prophylaxis of bone metastases per local standards of care.

Gonadotropin-releasing hormones were permitted to maintain ovarian suppression in patients with hormone receptor-positive breast cancer.

2.0 Patient-Reported Outcomes (PRO) Analyses

Patient-reported outcome analyses were performed in 2 subgroups of patients with (A) anemia reported as an adverse event (AE) and (B) nausea and/or vomiting reported as an AE. To account for the potential confounding effects of supportive care medications that may have led to improvements in PROs, we removed patients (A) if they received any packed red blood cells (PRBC) transfusion and/or antianemic medication at any point during EMBRACA. We also removed patients (B) if they received any antiemetic and/or antinauseant medication at any point during EMBRACA. The PRO analyses specifically focused on the global health status/quality of life (GHS/QoL) and fatigue scales (per European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-30 [EORTC QLQ-C30]) for (A) and GHS/QoL and nausea/vomiting scales (per EORTC QLQ-C30) for (B). Due to the small sample sizes of patients in (A) and (B) post week 52 of EMBRACA (as observed in **Figure 3A** and **Figure S3 C** and **D** respectively), the PRO analyses focused on the PRO-evaluable population during the first 52 weeks of EMBRACA. The PRO-evaluable population was defined as patients who completed ≥1 question at baseline and ≥1 time point post baseline.

The statistical analyses conducted included (i) overall change from baseline, estimated using the longitudinal mixed effects model, and (ii) time to definitive clinically meaningful deterioration (TTD), analyzed using a stratified log-rank test, summarized using Kaplan-Meier methods. Time to definitive clinically meaningful deterioration in GHS/QoL was defined as the time from randomization to the first observation with a ≥10-point decrease and no subsequent observations with a <10-

point decrease from baseline. Time to definitive clinically meaningful deterioration on the fatigue and nausea/vomiting symptoms scales was defined as the time from randomization to the first observation with a ≥10-point increase and no subsequent observations with <10-point increase from baseline [1].

Reference
1. Osoba D, Rodrigues G, Myles J et al. Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol 1998;16:139–144.

3.0 Health Resource Utilization (HRU) Analyses

Serious Adverse Event-Associated Hospitalization

Only serious adverse event (SAE)-associated hospitalization was recorded in EMBRACA and assessed a priori. An SAE was defined as any AE that resulted in death, was considered to be life-threatening or medically important, resulted in hospitalization or prolongation of existing hospitalization, or resulted in persistent or clinically significant disability or incapacity or a congenital anomaly or birth defect.

SAE-associated hospitalization rate was calculated using the following equation:

$$\text{SAE-associated hospitalization rate (per 100 patient-years)} = \frac{\text{Number of patients with occurrence of ≥1 SAE-associated hospitalization}}{\text{Total treatment-emergent period (years)}^{a}} \times 100$$

[a]Total time from the start date of treatment-emergent (TE) period to the start date of first SAE-associated hospitalization or the end date of TE period, whichever is earlier.

Due to data limitations, the SAE-associated hospitalization rates do not account for the length of hospitalization for each patient. Other types of hospitalizations are also not captured in EMBRACA.

Supportive Care Medication Utilization

The following categories of supportive care medication (SCM) were selected a priori and assessed in this study:

Platelet transfusion

PRBC transfusion

Antianemic

Antidiarrheal

Antiemetic/antinauseant

Appetite stimulant

Bone disease treatment

Immunostimulant (filgrastim, pegfilgrastim, granulocyte colony-stimulating factor, sargramostim, lenograstim)

Opiate

SCM (for each category of SCM) was assessed and calculated using the following equation:

$$\text{Mean SCM utilization ratio} = \frac{\text{Total duration of patients treated on each SCM category}^{a,b}}{\text{Total treatment-emergent period}}$$

[a]SCM category includes opiates, antiemetics/antinauseants, antidiarrheals, immunostimulants, appetite stimulants, bone disease medications, antianemics, PRBC transfusions, platelet transfusions.
[b]When deriving the total duration of SCM treatment, if a patient has >1 concomitant medication (of the same SCM category) on the same calendar day, the patient would be attributed the corresponding >1 day.

4.0 Methods for Landmark Analysis

Landmark analyses using the Kaplan-Meier method were conducted to assess the impact of talazoparib dose reduction, regardless of cause, on progression-free survival (PFS) in patients. Three landmarks (12, 18 and 24 weeks) were used. Patients whose PFS time was shorter than the landmarks were excluded. Patients whose talazoparib dose was reduced before a landmark were assigned to the dose reduction group. Those without dose reduction or those with a dose reduction after the landmark were assigned to the group without a dose reduction. PFS time was calculated from landmark.

Table S3. Summary of selected TEAEs of all grades by 6-month treatment intervals (safety population)

	Treatment Duration (Months)				
Treatment and TEAE, *n* (%)	**≥0**	**≥6**	**≥12**	**≥18**	**≥24**
Talazoparib (*n* = 286)	286 (100.0)	146 (51.0)	53 (18.5)	30 (10.5)	14 (4.9)
Number of patients with at least 1 TEAE	265 (92.7)	139 (95.2)	53 (100)	30 (100)	14 (100)
Hematologic[a]					
ANEMIA	151 (52.8)	85 (58.2)	31 (58.5)	19 (63.3)	11 (78.6)
NEUTROPENIA	99 (34.6)	53 (36.3)	23 (43.4)	17 (56.7)	7 (50.0)
THROMBOCYTOPENIA	77 (26.9)	38 (26.0)	16 (30.2)	7 (23.3)	4 (28.6)
Nonhematologic[b]					
Alopecia	72 (25.2)	47 (32.2)	22 (41.5)	16 (53.3)	7 (50.0)
Fatigue	178 (62.2)	99 (67.8)	42 (79.2)	23 (76.7)	11 (78.6)
Nausea	139 (48.6)	71 (48.6)	27 (50.9)	14 (46.7)	6 (42.9)
Vomiting	71 (24.8)	41 (28.1)	16 (30.2)	9 (30.0)	4 (28.6)
Overall PCT (*n* = 126)	126 (100.0)	29 (23.0)	6 (4.8)	0 (0.0)	0 (0.0)
Number of patients with at least 1 TEAE	107 (84.9)	26 (89.7)	4 (66.7)	0 (0.0)	0 (0.0)
Hematologic[a]					
ANEMIA	23 (18.3)	7 (24.1)	0 (0.0)	0 (0.0)	0 (0.0)
NEUTROPENIA	54 (42.9)	14 (48.3)	1 (16.7)	0 (0.0)	0 (0.0)
THROMBOCYTOPENIA	9 (7.1)	2 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)
Nonhematologic[b]					
Alopecia	35 (27.8)	12 (41.4)	2 (33.3)	0 (0.0)	0 (0.0)
Fatigue	63 (50.0)	14 (48.3)	4 (66.7)	0 (0.0)	0 (0.0)
Nausea	59 (46.8)	16 (55.2)	3 (50.0)	0 (0.0)	0 (0.0)
Vomiting	29 (23.0)	7 (24.1)	1 (16.7)	0 (0.0)	0 (0.0)

[a]ANEMIA includes preferred terms: anemia, decreased hemoglobin, decreased hematocrit. NEUTROPENIA includes preferred terms: neutropenia, decreased neutrophil count. THROMOBOCYTOPENIA includes preferred terms: thrombocytopenia, platelet count decreased.
[b]Nonhematologic adverse events (nausea, alopecia, vomiting) are based on a single preferred term, whereas fatigue was inclusive of fatigue/asthenia.
Patients are counted only once within each preferred term, and treatment intervals.
The analysis data cutoff date is September 15, 2017.
MedDRA Version: 20.0
Abbreviations: *N*, number of patients with ongoing treatment on lower bound of the treatment duration interval. Percentages are calculated in reference to *N* in each column; *n*, number of patients in the treatment group; TEAE, treatment-emergent adverse event

5.0 AEs of Special Interest

An analysis of potential Hy's Law cases was performed. At baseline, 9 (3.1%) patients in the talazoparib arm and 5 (4.0%) patients in the PCT arm had alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels ≥3 × upper limit of normal (ULN). Post baseline, 17 (6.0%) patients in the talazoparib arm and 13 (11.0%) patients in the PCT arm had ALT or AST levels ≥3 × ULN; 6 (2.1%) patients in the talazoparib arm and 5 (4.2%) patients in the PCT arm had post-baseline ALT or AST levels >5 × ULN. Increases in AST/ALT ≥3 × ULN and bilirubin >2 × ULN within 14 days were reported in 5 (1.8%) patients in the talazoparib arm and 1 (0.8%) patient in the PCT arm.

As of the data cutoff date (September 15, 2017), none of the patients in the talazoparib arm had developed acute myeloid leukemia (AML); 1 (0.8%) patient in the PCT arm developed AML. This patient was taking capecitabine. Two (0.7%) patients in the talazoparib arm reported pancytopenia; none of the patients in the PCT arm had an AE with a preferred term identified by the broad search of the Standardised MedDRA Query (SMQ) "myelodysplastic syndrome" for MDS. No cases of MDS were identified in a search of the narrow SMQ.

With talazoparib, 9.1% of patients had ≥1 hepatotoxicity-related AE versus 19.8% of patients in the PCT arm. Hepatotoxicity-related AEs were reported in 12.7% of patients taking capecitabine, 20.0% eribulin, 41.7% gemcitabine, and 33.3% of patients taking vinorelbine. None of the patients in the study met the criteria for Hy's Law. Additionally, 22.2% of patients presented with palmar-plantar erythrodysesthesia in the PCT arm versus 1.4% of patients in the talazoparib arm,

and 8.7% of patients in the PCT arm had pleural effusion versus 2.1% in the talazoparib arm.

6.0 AEs in Patients ≥65 Years of Age

The proportion of elderly patients aged ≥65 years was small in both treatment arms, with 27 patients (9.4%) receiving talazoparib and 8 patients (6.3%) receiving PCT. The overall incidence of AEs was generally similar across treatment arms and age subgroups (98.8% and 96.3% for talazoparib and 97.5% and 100% for PCT in patients age >65 and ≥65 respectively). The incidence of Grade 3 or 4 AEs was similar across the treatment arms for patients age <65 years (66.8% in the talazoparib arm and 65.3% in the PCT arm). The incidence of Grade 3 or 4 AEs in patients ≥65 years was 74.1% in the talazoparib arm (20/27 patients) and 37.5% in the PCT arm (3/8 patients). Given the small groups, any conclusions should be made with caution. In the talazoparib arm, the incidence of SAEs was higher in patients age ≥65 years (48.1%) than in patients age <65 years (30.1%). The incidence of SAEs in the PCT arm was 25.0% in patients age ≥65 years and 29.7% in patients age <65 years.

7.0 Incidence of Serious AEs

Study drug-related SAEs were reported in 26 (9.1%) patients in the talazoparib arm and 11 (8.7%) patients in the PCT arm (Table S4). Other SAEs ≤1% in the talazoparib arm included neutrophil count decreased, febrile neutropenia, abdominal pain, atrial flutter, constipation, cytomegalovirus infection, and furuncle.

Table S4. SAEs in ≥2% of patients in either treatment arm by decreasing frequency of preferred term (safety population)

Preferred Term	Talazoparib (*n* = 286) *n* (%)	Overall PCT (*n* = 126) *n* (%)
Patients with ≥1 SAE	91 (31.8)	37 (29.4)
Patients with ≥1 study drug-related SAE	26 (9.1)	11 (8.7)
Anemia	15 (5.2)	0 (0.0)
Neutropenia	3 (1.0)	4 (3.2)

Abbreviation: SAE, serious adverse event.

8.0 Deaths

As of the data cutoff date (September 15, 2017), 163 (39.6%) patients had died, 108 (37.8%) patients in the talazoparib arm and 55 (43.7%) patients in the PCT arm. The majority of deaths in both arms were attributed to disease progression, 88.9% in the talazoparib arm and 96.2% in the PCT arm. AEs associated with death were reported in 6 (2.1%) patients in the talazoparib arm and 4 (3.2%) patients in the PCT arm. Of these fatal AEs, 2 events were considered by the investigator to be related to the study drug: veno-occlusive liver disease in the talazoparib arm and sepsis (1 patient in the PCT arm who received capecitabine). For the patient with veno-occlusive liver disease, standard diagnostic criteria for veno-occlusive liver disease (such as hepatomegaly and right upper quadrant pain) were not observed; the presenting laboratory data included only elevated liver transaminases.

9.0 Dosing Interruptions

Among patients receiving talazoparib, the following number of patients required a dosing interruption due to these selected AEs: 105 (36.7%) anemia, 62 (21.7%) neutropenia, 47 (16.4%) thrombocytopenia, 12 (4.2%) fatigue, 9 (3.1%) vomiting, and 5 (1.7%) nausea (Supplemental Materials, Table S5).

Table S5. Summary of key adverse-drug reactions that led to study drug dosing interruption (safety population)

TEAE[a,b]	**Talazoparib (*n* = 286)** ***n* (%)**	**Overall PCT (*n* = 126)** ***n* (%)**
Hematologic		
ANEMIA	105 (36.7)	2 (1.6)
NEUTROPENIA	62 (21.7)	26 (20.6)
THROMBOCYTOPENIA	47 (16.4)	1 (0.8)
Nonhematologic		
Nausea	5 (1.7)	8 (6.3)
Fatigue	12 (4.2)	7 (5.6)
Vomiting	9 (3.1)	3 (2.4)

[a]ANEMIA includes preferred terms: anemia, decreased hemoglobin, decreased hematocrit. NEUTROPENIA includes preferred terms: neutropenia, decreased neutrophil count. THROMOBOCYTOPENIA includes preferred terms: thrombocytopenia, platelet count decreased.
[b]Nonhematologic adverse events (nausea, vomiting) are based on a single preferred term, whereas fatigue is inclusive of fatigue/asthenia. Abbreviation: TEAE, treatment-emergent adverse event.

10.0 Dose Reductions

AEs associated with dose reduction in ≥2% of patients are presented by decreasing frequency (Table S6). In those receiving talazoparib, the most frequently reported (≥5%) AEs associated with dose reductions were anemia (90 [31.5%] patients), neutropenia (42 [14.7%] patients), and thrombocytopenia (18 [6.3%] patients). The most frequently reported AEs associated with dose reductions with PCT included palmar-plantar erythrodysesthesia syndrome (13 [10.3%] patients) and diarrhea (7 [5.6%] patients), all among patients receiving capecitabine, and neutropenia (8 [6.3%] patients) and decreased neutrophil count (7 [5.6%] patients). Other AEs associated with dose reduction were generally similar across the different PCTs. After dose reduction, frequency and grades of AEs decreased (Figure S4).

Table S6. TEAEs associated with dose reduction based on medical review* in ≥2% of patients in either treatment arm by decreasing frequency of preferred term (safety population)

Preferred Term	Talazoparib (*n* = 286) *n* (%)	Overall PCT (*n* = 126) *n* (%)
Number of patients with at least 1 TEAE associated with dose reduction	150 (52.4)	45 (35.7)
Anemia	90 (31.5)	1 (0.8)
Neutropenia	42 (14.7)	8 (6.3)
Thrombocytopenia	18 (6.3)	0 (0.0)
Platelet count decreased	12 (4.2)	0 (0.0)
Neutrophil count decreased	11 (3.8)	7 (5.6)
Leukopenia	6 (2.1)	3 (2.4)
Nausea	2 (0.7)	5 (4.0)
Vomiting	2 (0.7)	3 (2.4)
Palmar-plantar erythrodysesthesia syndrome	0 (0.0)	13 (10.3)
Diarrhea	0 (0.0)	7 (5.6)
Abdominal pain	0 (0.0)	3 (2.4)

*To provide a more accurate assessment of AEs associated with dose reduction, AEs leading to dose interruption or dose reduction were cross-referenced by the medical reviewer with the study drug dosing records. If a dose interruption was followed by a dose reduction, the most likely preceding AE was identified as the cause of the dose reduction.
Abbreviations: AE, adverse event; TEAE, treatment-emergent AE.

11.0 Dose Modifications Associated With AEs

Dose modifications associated with AEs based on dosing record for talazoparib are presented in Table S7. A total of 52.1% of patients had ≥1 dose reduction associated with AEs. The median time to the first talazoparib dose reduction was 19.3 weeks (95% CI: 17.1, 30.9). Dosing interruptions associated with AEs were reported for 172 of 286 patients (60.1%) in the talazoparib arm (Table S7). The median duration of each talazoparib dosing interruption was 8.0 days (range, 1–50) and the median total duration of dosing interruptions was 18.5 days (range, 1–96).

Table S7. Dose reductions and dosing interruptions

	Talazoparib *n* = 286
Patients with at least 1 dose reduction due to AE, *n* (%)	149 (52.1)
Patients experiencing ≥1 dose reduction due to AE, *n* (%)[a]	
1	70 (24.5)
2	58 (20.3)
3	20 (7.0)
Time to first dose reduction due to AE, weeks	
Median	19.3
95% CI	(17.1–30.9)
Patients with at least 1 dosing interruption due to AE, *n* (%)	172 (60.1)
Patients experiencing ≥1 dosing interruption due to AE, *n* (%)	
1	79 (27.6)
2	42 (14.7)
3	31 (10.8)
>3	20 (7.0)
Duration of each dosing interruption due to AE, days	
Mean (SD)	10.7 (8.35)
Median	8.0
Minimum, maximum	1.0–50.0
Total duration of dosing interruptions due to AE for each patient, days	
Mean (SD)	21.7 (17.58)
Median	18.5
Minimum, maximum	1.0–96.0

[a]One patient had >3 dose reductions due to the availability of 0.1 mg talazoparib formulation on trial.

Abbreviation: AE, adverse event.

12.0 Landmark Analysis of Talazoparib Dose Reductions

Landmark analyses showed a trend towards a slightly less favorable PFS for patients that had a dose reduction versus those who did not (Figure S5A, B, and C, respectively). Landmark analyses have lower efficiency to evaluate the effect of dose reductions on PFS than the Cox Models (Table 3) because a landmark analysis excludes patients and events that occur before the landmark, as well as not reflecting patients who may switch groups after the landmark. Nonetheless, both analyses cannot adjust for the lack of randomization, and therefore we do not know if dose reduction itself leads to worse PFS or if it is just a marker for patients with worse prognosis and hence shorter PFS.

Table S8. Supportive care medications and PRBC transfusions

	Talazoparib (*n* = 286)	**PCT (*n* = 126)**
Safety population		
Number of patients with ANEMIA,[a] *n* (%)[b]	151 (52.8)	23 (18.3)
Number of patients with ≥1 PRBC Transfusion, *n* (%)[b,c]	109 (38.1)	7 (5.6)
Safety population with ANEMIA		
Number of patients with ≥1 supportive medication for ANEMIA,[a] *n* (%)[d]	59 (39.1)	9 (39.1)
Iron preparations, n (%)[d]	25 (16.6)	6 (26.1)
Other antianemic preparations, *n* (%)[d]	25 (16.6)	3 (13.0)
Darbepoetin alfa	9 (6.0)	2 (8.7)
Epoetin alfa	9 (6.0)	1 (4.3)
Epoetin beta	4 (2.6)	0 (0)
Epoetin theta	1 (0.7)	0 (0)
Epoetin zeta	1 (0.7)	0 (0)
Erythropoietin	1 (0.7)	0 (0)
Erythropoietin human	1 (0.7)	0 (0)
Peginesatide	1 (0.7)	0 (0)
Vitamin B12 and folic acid, *n* (%)[d]	22 (14.6)	4 (17.4)
Folic acid	15 (9.9)	2 (8.7)
Vitamin B12 Nos	7 (4.6)	2 (8.7)
Hydroxocobalamin	2 (1.3)	0 (0)
Juice Plus	1 (0.7)	0 (0)

[a]ANEMIA includes preferred terms: anemia, decreased hemoglobin, decreased hematocrit.
[b]Percentages based on safety population (*n* = 286 for talazoparib; *n* = 126 for PCT).
[c]Median of 2.0 PRBC transfusions per patient receiving talazoparib (in 109 patients) and median of 1.0 PRBC transfusion per patient with PCT (in 7 patients).
[d]Percentages based on safety population with ANEMIA (cluster of preferred terms[a] [*n* = 151 for talazoparib; *n* = 23 for PCT]).
Abbreviations: PCT, physician's choice of chemotherapy; PRBC, packed red blood cells.

Table S9. Mean supportive care medication utilization ratio among EMBRACA safety population

	Utilization ratio[a] Talazoparib (*n* = 286) Mean (SD)	**Utilization ratio[a] Overall PCT (*n* = 126) Mean (SD)**
Platelet transfusion[b]	0.01 (0.01)	0 (NA)
PRBC transfusion[c]	0.02 (0.07)	0.04 (0.07)
Antianemic[c]	0.57 (0.47)	0.93 (0.73)
Antidiarrheal	0.53 (0.52)	0.57 (0.49)
Antiemetic/antinauseant	0.85 (0.71)	0.88 (0.68)
Appetite stimulant	0.43 (0.41)	0.58 (0.46)
Bone disease treatment	0.88 (0.27)	0.89 (0.20)
Immunostimulant[d]	0.08 (0.15)	0.32 (0.40)
Opiate	0.98 (0.76)	1.17 (0.77)

[a]Total duration of patients treated on each SCM category divided by the TE period; when deriving the total duration of SCM treatment, if a patient has >1 concomitant medication (of the same SCM category) on the same calendar day, the patient would be attributed to the corresponding >1 day, the utilisation ratio may be >1 (see Supplemental Materials, section 3.0)

[b]None of the PCT-treated patients had platelet transfusion during EMBRACA.

[c]Of note, initial study protocol requirements for hemoglobin levels to recover to grade 1 (≥ 10 g/dL) or baseline following dose interruption due to an anaemia event before resuming talazoparib/PCT were amended during the trial, whereas study entry was permitted with a hemoglobin value ≥ 9 g/dL.3 Prior to the protocol amendment, these requirements may have encouraged RBC transfusion and/or antianaemic use in order to resume talazoparib/PCT, more than would be expected in routine clinical practice.

[d]Filgrastim, pegfilgrastim, granulocyte colony-stimulating factor, sargramostim, lenograstim.

Abbreviations: PCT, physician's choice chemotherapy; PRBC, packed red blood cells; SD, standard deviation.