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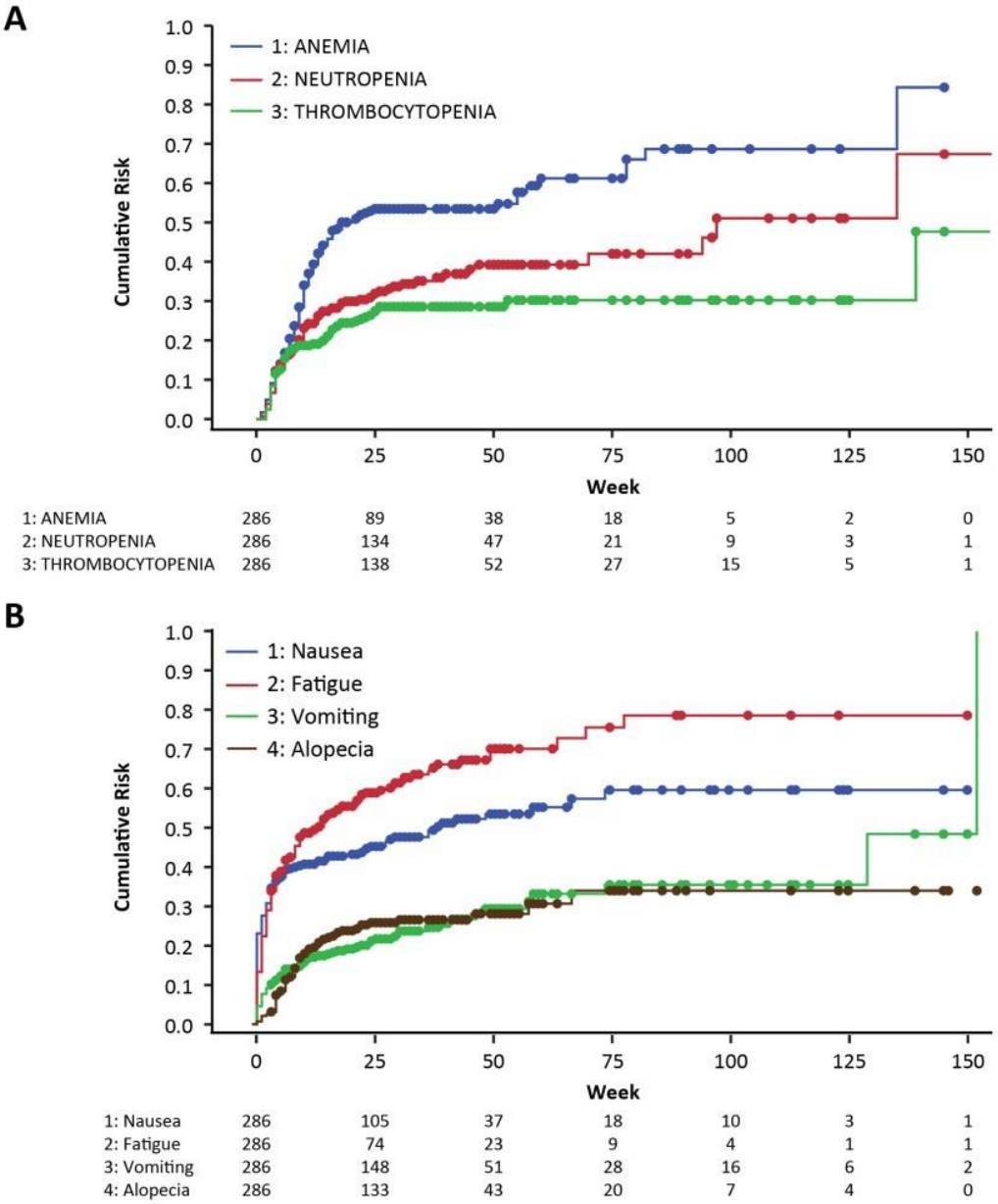
Supplemental Figures for:
Talazoparib in Patients with a Germline BRCA-mutated Advanced Breast Cancer: Detailed Safety Analyses from the Phase 3 EMBRACA Trial Sara Hurvitz et al.

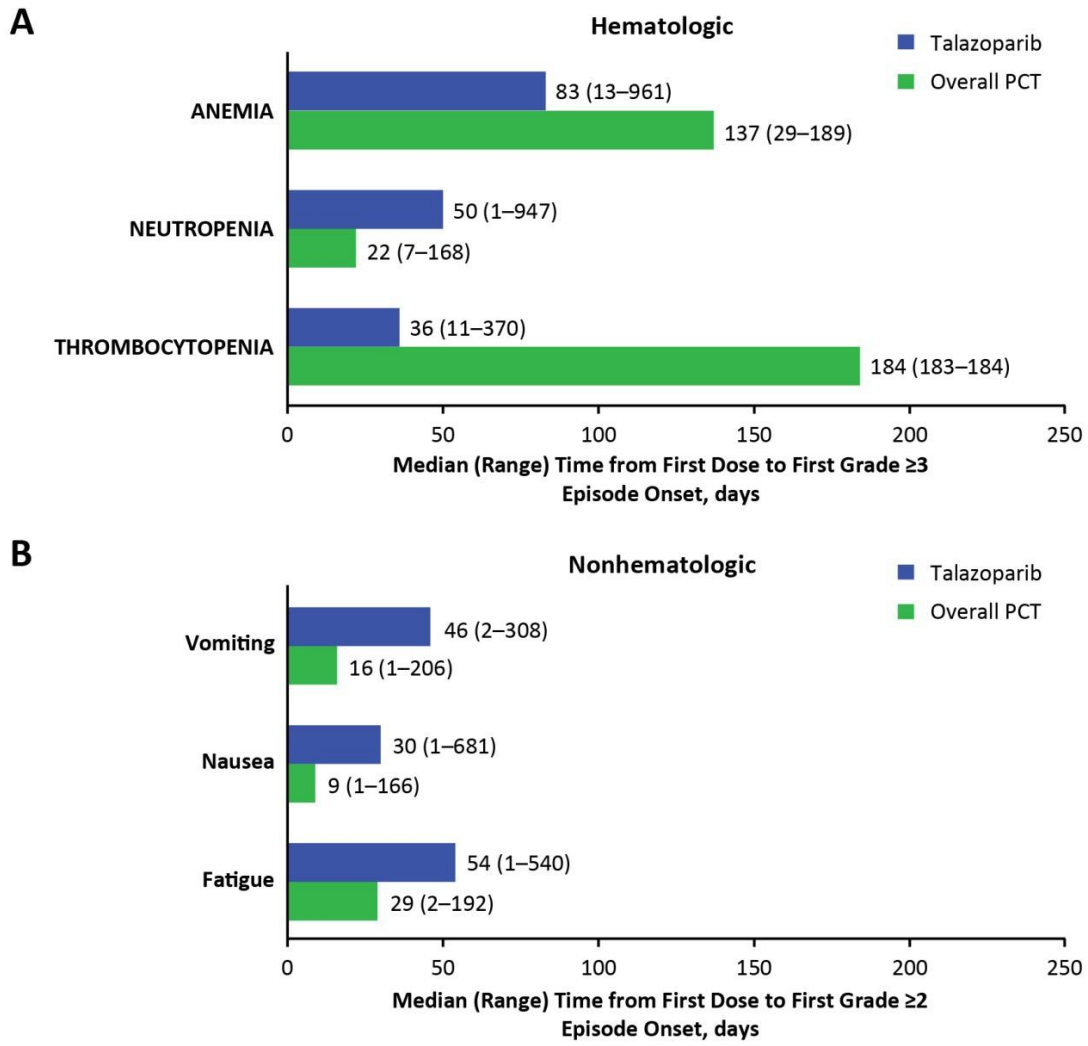
Figure S1. Cumulative risk plot for time to first TEAE: (A) anemia, neutropenia, thrombocytopenia[a]; (B) nausea, fatigue, vomiting, alopecia[b] (safety population – talazoparib)



[a]ANEMIA includes preferred terms: anemia, decreased hemoglobin, decreased hematocrit. NEUTROPENIA includes preferred terms: neutropenia, decreased neutrophil count. THROMBOCYTOPENIA includes preferred terms: thrombocytopenia, platelet count decreased. [b]Nonhematologic AEs (fatigue, nausea, alopecia, vomiting) are based on a single preferred term.

Abbreviation: TEAE, treatment-emergent adverse event.

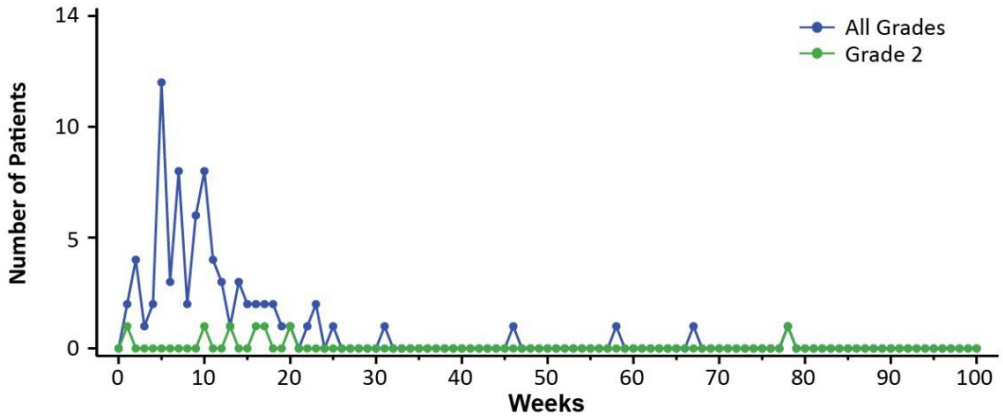
Figure S2. Time to onset of (A) first treatment-emergent hematologic grade ≥3 AEs and (B) selected first treatment-emergent nonhematologic[a] grade ≥2 AEs.



[a]Nonhematologic adverse events (nausea, vomiting) are based on a single preferred term, whereas fatigue was inclusive of fatigue/asthenia. ANEMIA includes preferred terms: anemia, decreased hemoglobin, decreased hematocrit. NEUTROPENIA includes preferred terms: neutropenia, decreased neutrophil count. THROMBOCYTOPENIA includes preferred terms: thrombocytopenia, platelet count decreased.
Abbreviation: PCT, physician's choice of chemotherapy.

Figure S3. Nonhematologic treatment-emergent adverse events (all grades) by week, preferred term (safety population – talazoparib arm)

A. Alopecia

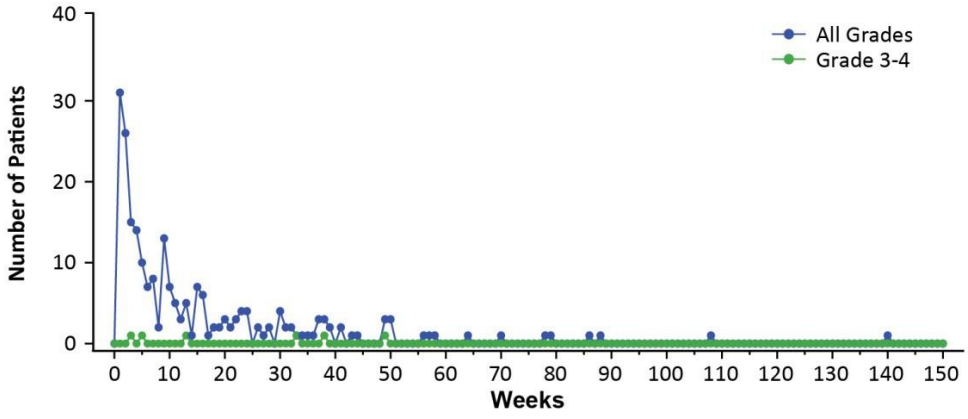


Patients at risk:	286	258	201	138	91	64	43	38	30	22	18
Patients with TEAEs:											
All Grades *n* =	0	8	1	0	0	0	0	0	0	0	0
Grade 2 *n* =	0	1	1	0	0	0	0	0	0	0	0

Talazoparib: Alopecia grade 1 (65 patients); grade 2 (7 patients).

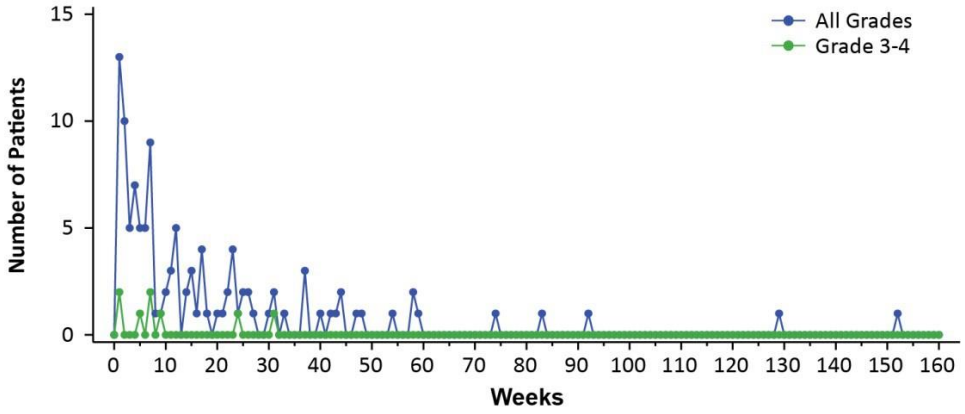
PCT: Alopecia grade 1 (25 patients); grade 2 (10 patients)

B. Fatigue



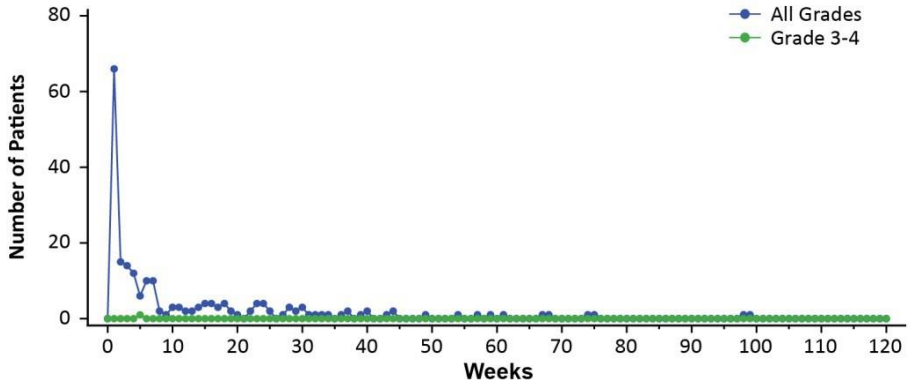
Patients at risk:	286	258	201	138	91	64	43	38	30	22	18	14	12	7	6	3
Patients with TEAEs:																
All Grades *n* =	0	7	3	4	0	3	0	1	0	0	0	0	0	0	1	0
Grade 3-4 *n* =	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

C. Vomiting



Patients at risk:	286	258	201	138	91	64	43	38	30	22	18	14	12	7	6	3	3
Patients with TEAEs:																	
All Grades *n* =	0	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Grade 3-4 *n* =	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

D. Nausea



Patients at risk:	286	258	201	138	91	64	43	38	30	22	18	14	12
Patients with TEAEs:													
All Grades *n* =	0	3	1	3	2	0	0	0	0	0	0	0	0
Grade 3-4 *n* =	0	0	0	0	0	0	0	0	0	0	0	0	0

Abbreviations: PCT, physician's choice of chemotherapy; TEAE, treatment-emergent adverse event.

Figure S4. Incidence of grade 3-4 TEAEs (hematologic) after the first dose reduction due to TEAEs by decreasing frequency of preferred term

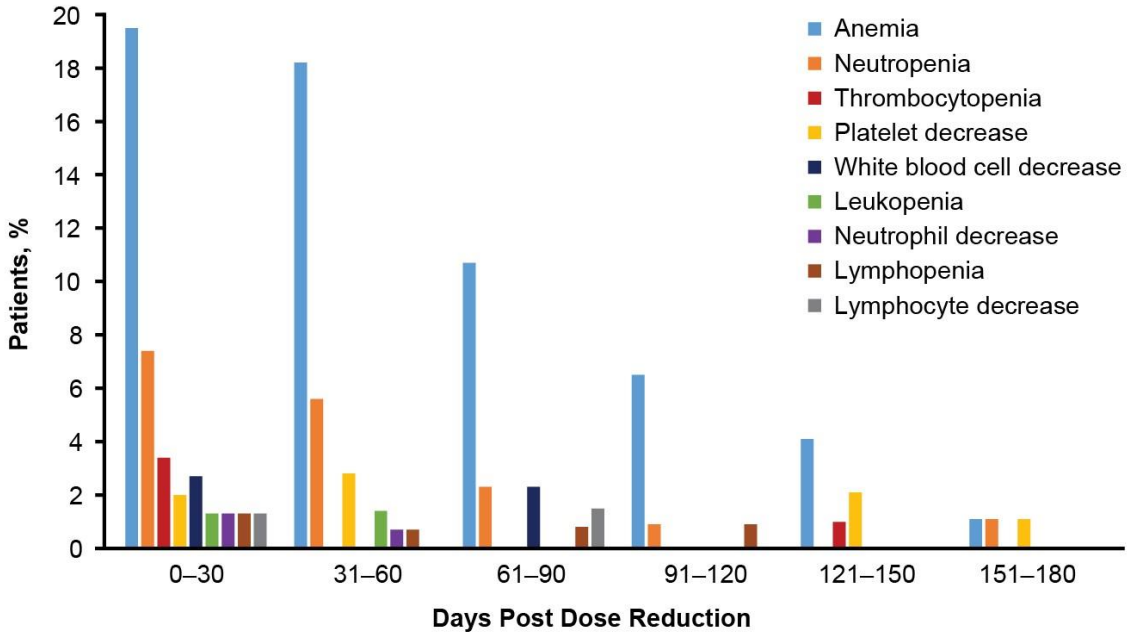
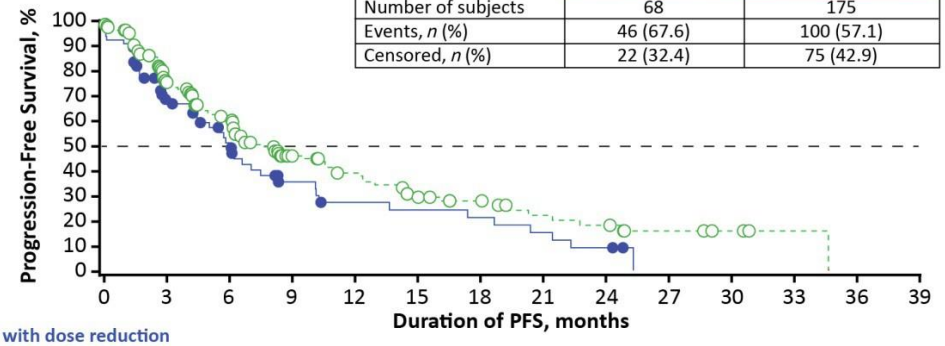


Figure S5. Landmark analysis of PFS based on independent radiology facility assessment at (A) 12 weeks, (B) 18 weeks, and (C) 24 weeks (intent-to-treat population)

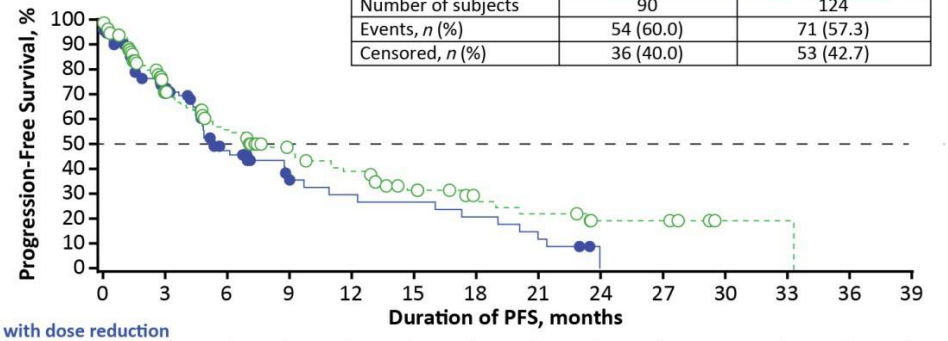
A. Landmark 12 weeks



	Talazoparib with dose reduction	Talazoparib without dose reduction
Number of subjects	68	175
Events, *n* (%)	46 (67.6)	100 (57.1)
Censored, *n* (%)	22 (32.4)	75 (42.9)

Talazoparib with dose reduction														
Events/cumulative:	0/0	21/21	8/29	7/36	3/39	1/40	1/41	2/43	2/45	1/46	0/46	0/46	0/46	0/46
Patients at risk:	68	37	25	13	9	8	7	5	3	0	0	0	0	0
Talazoparib without dose reduction														
Events/cumulative:	0/0	40/40	21/61	17/78	6/84	8/92	1/93	3/96	2/98	1/99	0/99	0/99	1/100	0/100
Patients at risk:	175	113	78	43	33	22	17	11	9	5	3	1	0	0

B. Landmark 18 weeks



	Talazoparib with dose reduction	Talazoparib without dose reduction
Number of subjects	90	124
Events, *n* (%)	54 (60.0)	71 (57.3)
Censored, *n* (%)	36 (40.0)	53 (42.7)

Talazoparib with dose reduction														
Events/cumulative:	0/0	22/22	17/39	5/44	2/46	1/47	2/49	3/52	2/54	0/54	0/54	0/54	0/54	0/54
Patients at risk:	90	53	27	13	10	9	7	4	0	0	0	0	0	0
Talazoparib without dose reduction														
Events/cumulative:	0/0	33/33	14/47	6/53	7/60	5/65	1/66	3/69	1/70	0/70	0/70	0/70	1/71	0/71
Patients at risk:	124	69	49	36	28	18	12	9	5	5	1	1	0	0

C. Landmark 24 weeks

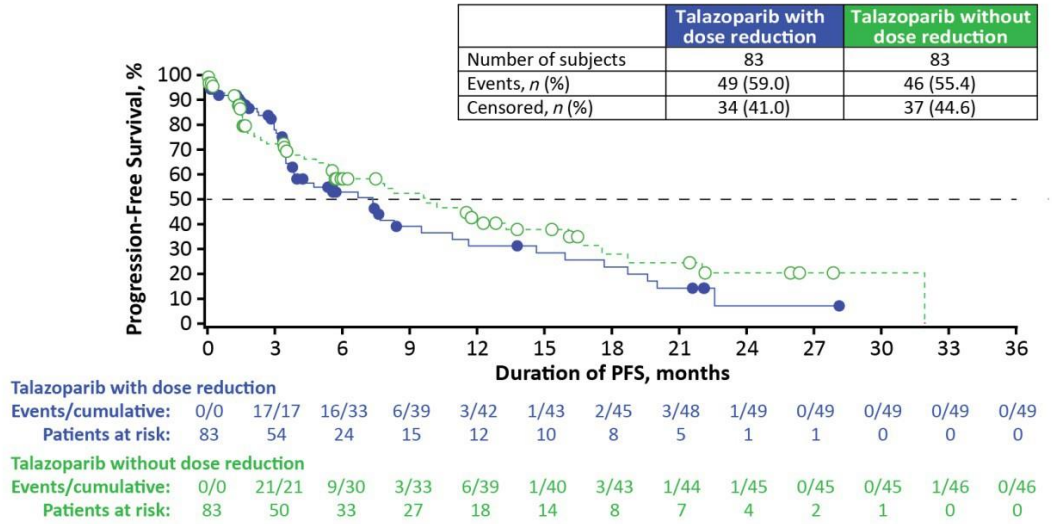


Figure S6. Histogram of last hemoglobin before (A) 1st, (B) 2nd, and (C) 3rd PRBC transfusion in the talazoparib arm (safety population)

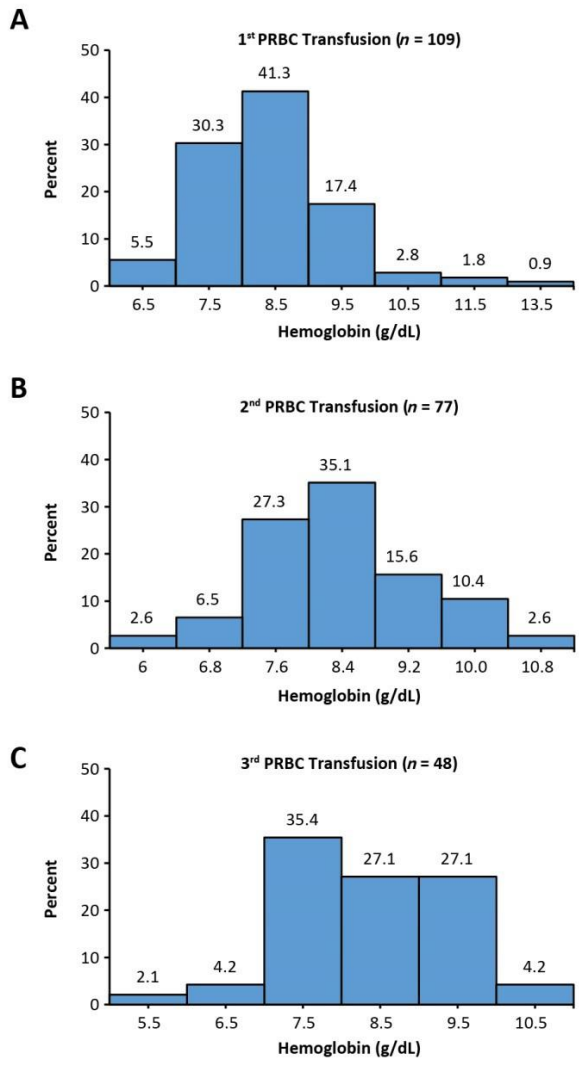
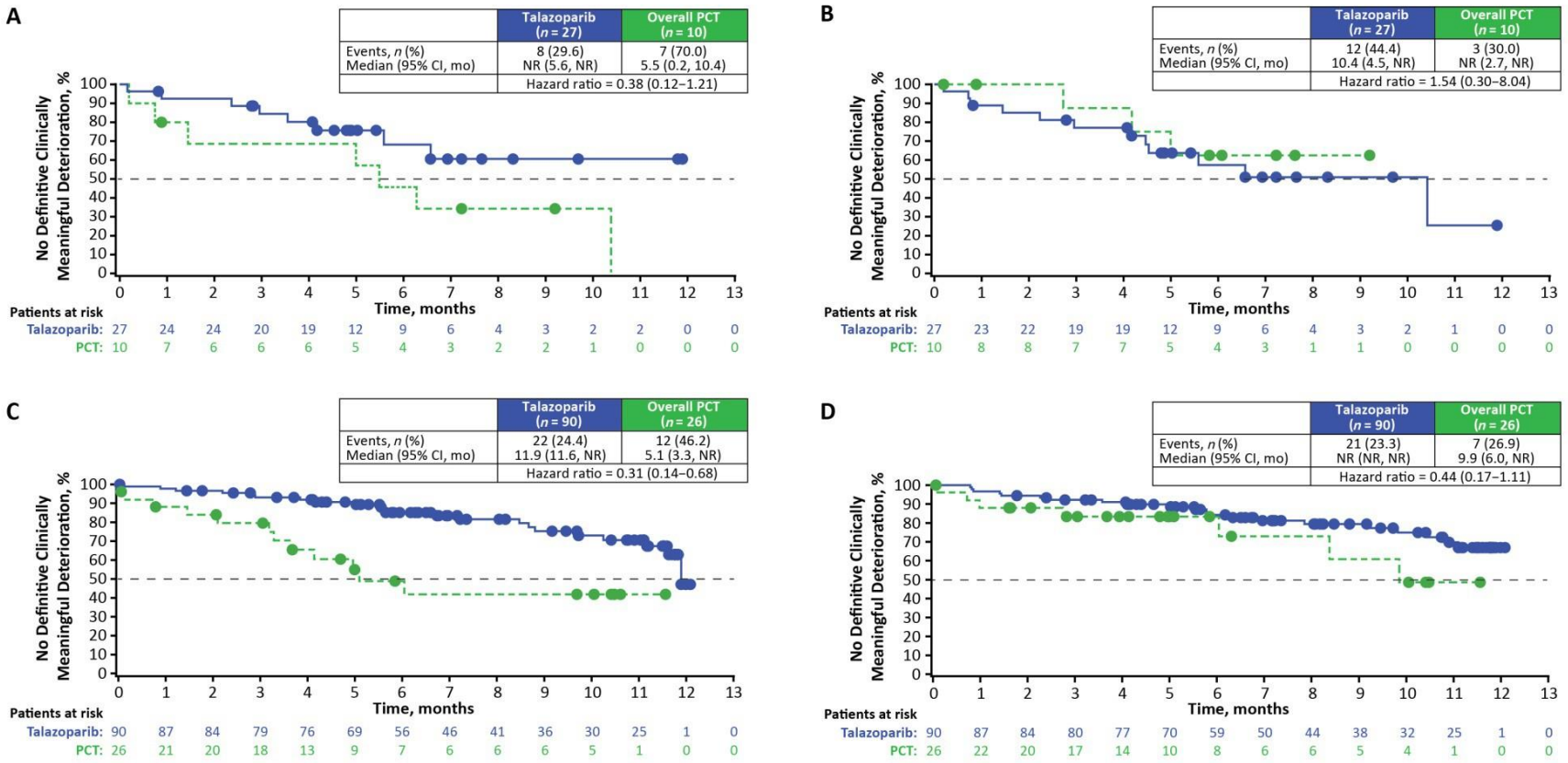


Figure S7. Patient-reported outcomes in patients with anemia AEs who did not receive PRBC transfusion and/or antianemic medication (A[a] and B[a]) or patients with nausea/vomiting AEs who did not receive antiemetic and/or antinauseant (C[a] and D[a])



A, C = GHS/QoL; B = patient-reported fatigue; D = patient-reported nausea and vomiting. TTD (PRO evaluable subpopulation). Time to definitive clinically meaningful deterioration for 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 scales was defined as the time from randomization to the first observation with a ≥10-point increase and no subsequent observations with a <10-point increase from baseline.

Due to the small sample size of patients post week 52 in EMBRACA (as observed in Figure 3A and Figure S3C and SCD, 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.

Abbreviations: CI, confidence interval; EORTC, European Organisation for Research and Treatment of Cancer; GHS, global health status; HR+, hormone receptor positive; NR, not reported; PCT, physician's choice of chemotherapy treatment; PRO, patient-reported outcomes; QLQ-BR23, Quality of Life Questionnaire breast cancer module; QLQ-C30, Quality of Life Questionnaire Core 30; QoL, quality of life; TTD, time to definitive clinically meaningful deterioration.