



Talazoparib plus enzalutamide in metastatic castration-resistant prostate cancer: Safety analyses from the randomized, placebo-controlled, phase III TALAPRO-2 study

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ABSTRACT

Background: This detailed analysis further characterizes the safety profile of talazoparib plus enzalutamide in the ongoing randomized, phase III TALAPRO-2 study in patients with metastatic castration-resistant prostate cancer (mCRPC). In both the all-comers and homologous recombination repair (HRR)-deficient populations, talazoparib plus enzalutamide significantly improved radiographic progression-free survival compared with placebo plus enzalutamide.

Methods: The talazoparib plus enzalutamide safety populations in TALAPRO-2 included 398 patients from cohort 1 (all-comers, unselected for HRR gene alterations) and 198 patients from the combined HRR-deficient population (patients from the all-comers population with HRR gene alterations plus subsequently enrolled patients with HRR gene alterations; cohort 2). Patients received talazoparib 0.5 mg (0.35 mg, moderate renal impairment) and enzalutamide 160 mg once daily. Safety analyses evaluated common treatment-emergent adverse events (TEAE), their type, severity, timing, seriousness, and relationship to study treatment.

Results: In the all-comers (n = 398) and HRR-deficient populations (n = 198), all-cause grade 3/4 (G3/4) TEAEs with talazoparib plus enzalutamide were reported in 71.9 % and 66.2 % of patients, respectively. Most common G3/4 hematologic TEAEs were anemia (46.7 % and 40.9 %, respectively), neutropenia (18.3 % and 18.7 %), and thrombocytopenia (7.3 % and 7.1 %). Median time to event was 3.3 and 3.3 months for G3/4 anemia, 2.3 and 2.3 months for G3/4 neutropenia, and 2.3 and 1.5 months for G3/4 thrombocytopenia. Maximum hemoglobin reduction occurred after 13 and 15 weeks of treatment. 18.8 % and 10.1 % of patients discontinued talazoparib.

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TEAEs were managed with dose interruption (62.1 % and 57.6 %), reduction (52.8 % and 52.0 %), hematologic supportive care (13.1 % and 10.6 %), and packed red blood cell transfusions (39.2 % and 35.9 %).

Conclusion: Talazoparib plus enzalutamide had a generally manageable safety profile in patients with mCRPC within the all-comers and the HRR-deficient populations.

ClinicalTrials.gov Identifier: NCT03395197

1. Introduction

Despite the lethality of metastatic castration-resistant prostate cancer (mCRPC), novel therapeutic strategies such as poly(ADP-ribose) polymerase (PARP) inhibitors are improving outcomes for patients [1, 2]. However, treatment of mCRPC with PARP inhibitors can cause hematologic toxicity when administered alone or in combination with a novel hormonal therapy [3–10].

TALAPRO-2 (NCT03395197) is an ongoing, randomized, double-blind phase III study investigating first-line treatment with talazoparib plus enzalutamide in adult patients with asymptomatic or mildly symptomatic mCRPC [11–13]. Results from TALAPRO-2 demonstrated an improvement in radiographic progression-free survival (rPFS) versus placebo plus enzalutamide in both an all-comers population unselected for homologous recombination repair (HRR) gene alterations (hazard ratio [HR], 0.63; 95 % CI, 0.51–0.78; $p < 0.0001$) and a combined HRR-deficient population (HR, 0.45; 95 % CI, 0.33–0.61; $p < 0.0001$) [11,12].

Here, we present a detailed safety analysis of talazoparib plus enzalutamide in patients with mCRPC from both the all-comers and the HRR-deficient population in TALAPRO-2, to inform healthcare providers on the safety profile of the combination therapy, irrespective of patient HRR gene alteration status.

2. Patients and methods

2.1. Study design

In TALAPRO-2, patients were recruited in two populations [11–13]. The all-comers population (cohort 1) included 805 patients (HRR-deficient, $N = 169$) [11,12]. The 169 patients with HRR gene alterations from cohort 1 were grouped with 230 subsequently enrolled patients with HRR gene alterations, and comprised the HRR-deficient population (cohort 2; $N = 399$; Fig 1) [12,13]. There were 1035 unique patients combined across both intent-to-treat (ITT) populations. Results are

reported for the talazoparib plus enzalutamide treatment arm for these populations, unless otherwise stated.

Eligibility criteria included: Eastern Cooperative Oncology Group performance status score of 0 or 1, ongoing androgen deprivation therapy or surgical orchiectomy, and progressive disease at study entry (prostate-specific antigen [PSA] or imaging-based) [13]. Prior docetaxel, abiraterone, or orteronel in the castration-sensitive setting were allowed [11,13]. Reflective of a real-world patient population, study patients were eligible to enter with lowered (≥ 9 g/dL) hemoglobin levels [11,14]. A dose modification of talazoparib was not required until anemia was grade 3 or worse [11].

Patients in TALAPRO-2 received talazoparib 0.5 mg once daily (QD; moderate renal impairment, 0.35 mg QD) or placebo plus enzalutamide 160 mg QD [13]. Study treatment continued until radiographic progression by blinded independent central review (BICR), an adverse event leading to permanent discontinuation, patient decision to discontinue treatment, or death [11].

TALAPRO-2 followed ICH Guideline for Good Clinical Practice, the Declaration of Helsinki, the International Ethical Guidelines for Biomedical Research Involving Human Subjects, and local laws [11,13]. The institutional review board and independent ethics committee at each study site approved the protocol [11]. All patients provided written informed consent [13].

Full details of the study design and inclusion/exclusion criteria have been previously published [13].

2.2. Outcomes

Outcomes and assessments have been previously reported [11,12]. Briefly, the primary endpoint was rPFS, assessed by BICR per Response Evaluation Criteria in Solid Tumors (RECIST version 1.1; soft tissue disease) and Prostate Cancer Clinical Trials Working Group 3 (bone disease) [11,13]. Safety was a secondary endpoint.

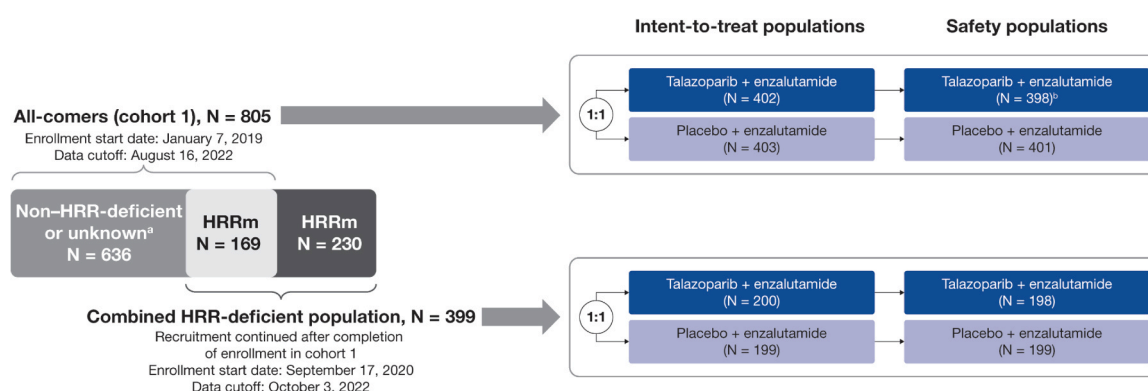


Fig. 1. TALAPRO-2 study design. This figure is modified from Fizazi K et al., 04 December 2023. First-line talazoparib with enzalutamide in HRR-deficient metastatic castration-resistant prostate cancer: the phase 3 TALAPRO-2 trial. *Nature Medicine* 2024;30:257–264. This figure is licensed under a Creative Commons Attribution 4.0 International License. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>. HRR, homologous recombination repair; HRRm, positive for alterations in homologous recombination repair genes. ^aIn the all-comers population, 27 % of patients in the talazoparib plus enzalutamide arm and 25 % in the placebo plus enzalutamide arm were of unknown HRR gene alteration status. In the combined HRR-deficient population, 3 patients (1, talazoparib plus enzalutamide; 2, placebo plus enzalutamide) did not have HRR gene alterations and 1 patient in the talazoparib arm was of unknown HRR gene alteration status. ^bIncludes one patient who was randomized to talazoparib plus enzalutamide, but received only enzalutamide. Per the study protocol, this patient was retained in the talazoparib plus enzalutamide safety population.

2.3. Safety assessments

The safety population included patients who received at least one dose of study drug. Safety analyses evaluated the most common treatment-emergent adverse events (TEAEs), type, severity, timing, seriousness, and relationship to study treatment.

Adverse events were graded by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 4.03 [14]. Adverse events of special interest (AESI) were acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), pneumonitis, venous thromboembolism, and second primary nonhematologic malignancies.

Preferred terms were clustered to better assess hematologic TEAEs where indicated. Anemia: anemia, hematocrit decreased, hemoglobin decreased, red blood cell count decreased. Neutropenia: neutropenia, neutrophil count decreased. Thrombocytopenia: thrombocytopenia, platelet count decreased. Leukopenia: leukopenia, white blood cell count decreased. Lymphopenia: lymphopenia, lymphocyte count decreased.

2.4. Statistical analysis

The full statistical methodology has been reported previously [11–13]. Adverse events were coded to preferred term and system organ class using Medical Dictionary for Regulatory Activities (MedDRA) and classified by severity using NCI-CTCAE version 4.03. The sponsor, Pfizer, commissioned an independent external data monitoring committee for ongoing monitoring of efficacy and safety.

3. Results

3.1. Patients

3.1.1. Safety population and treatment duration

In the talazoparib plus enzalutamide arm of the all-comers and the combined HRR-deficient safety populations, 398 and 198 patients were included, respectively (Fig 1). One patient in the all-comers safety population was randomized to talazoparib plus enzalutamide but received enzalutamide only; per the study protocol, this patient was retained in the safety population. A summary of baseline characteristics of the ITT all-comers and HRR-deficient populations is included in Appendix Table A1. Data cutoff was August 16, 2022, for the all-comers safety population and October 3, 2022, for the HRR-deficient safety population. Median follow-up for safety was 23.2 months (95 % confidence interval, 19.3–21.3) in the all-comers population and 15.4 months (95 % confidence interval, 15.7–18.2) in the HRR-deficient population.

At baseline, in the all-comers safety population, 49.0 % of patients had grade 1 or 2 anemia (grade 1, 44.7 %; grade 2, 4.3 %) in the talazoparib plus enzalutamide arm compared with 54.6 % of patients in the placebo plus enzalutamide arm (grade 1, 51.1 %; grade 2, 3.5 %). In the HRR-deficient population, 55.6 % of patients had grade 1 or 2 anemia at baseline (grade 1, 51.5 %; grade 2, 4.0 %) in the talazoparib plus enzalutamide arm compared with 57.3 % of patients in the placebo plus enzalutamide arm (grade 1, 55.3 %; grade 2, 2.0 %). The median treatment duration of talazoparib was longer for the all-comers population (19.8 months; range, 0.7–42.8) than the HRR-deficient population (14.6 months; range, 0.3–39.1).

3.2. Incidence and timing of TEAEs

In the all-comers safety population, all-cause any-grade TEAEs were observed in 98.5 % of patients (grade 1, 5.3 %; grade 2, 18.1 %; grade 3, 61.1 %; grade 4, 10.8 %; grade 5, 3.3 %). A similar incidence of all-cause TEAEs (any-grade, 99.0 %; grade 1, 6.6 %; grade 2, 24.7 %; grade 3, 59.1 %; grade 4, 7.1 %; grade 5, 1.5 %) was observed in the HRR-deficient population.

The incidence of all-cause hematologic TEAEs in both the all-comers

and the HRR-deficient populations is shown in Fig 2A. Anemia was the most common grade 3/4 TEAE in both the all-comers population (grade 3, 43.2 %; grade 4, 3.3 %) and the HRR-deficient population (grade 3, 39.4 %; grade 4, 1.5 %).

The incidence of the most common hematologic grade 3/4 TEAEs (anemia, neutropenia, and thrombocytopenia) by week in the all-comers and the HRR-deficient safety populations is shown in Fig 3A and B. Hematologic TEAEs typically occurred within the first 4 months of treatment and declined thereafter. In the all-comers population, the median time from the first dose of talazoparib to onset of the first grade 3/4 episode and duration of episode were 3.3 months and 16 days, respectively, for anemia, 2.3 months and 12 days for neutropenia, and 2.3 months and 19 days for thrombocytopenia. In the HRR-deficient population, the median time from the first dose of talazoparib to onset of the first grade 3/4 episode and duration of episode were 3.3 months and 17 days, respectively, for anemia, 2.3 months and 14 days for neutropenia, and 1.5 months and 15 days for thrombocytopenia.

The most common (≥ 20 %) all-cause nonhematologic TEAEs by grade in both the all-comers and the HRR-deficient populations are shown in Fig 2B. Fatigue was the most common nonhematologic TEAE in both the all-comers (33.7 %) and the HRR-deficient (33.3 %) populations. In the all-comers population, gastrointestinal toxicities were primarily low grade: decreased appetite (all-grades, 21.6 %; grade 1, 13.8 %; grade 2, 6.5 %; grade 3, 1.3 %), nausea (all-grades, 20.6 %; grade 1, 12.1 %; grade 2, 8.0 %; grade 3, 0.5 %), and vomiting (all-grades, 7.3 %; grade 1, 4.8 %; grade 2, 2.5 %).

In the all-comers population, the median time to onset and duration of first any-grade episode for nausea was 1.7 months and 2.7 months, respectively, for decreased appetite was 2.4 months and 6.2 months, respectively, and for vomiting was 3.1 months and 2 days, respectively.

In the all-comers and the HRR-deficient populations, 19.6 % and 13.6 % of patients experienced serious treatment-related TEAEs, respectively. There were no treatment-related deaths in the talazoparib plus enzalutamide group for either population. Serious TEAEs and deaths are summarized in Appendix Table A2.

One instance of MDS occurred in the all-comers population during the safety reporting period and one instance of AML was reported during the follow-up period; there were no instances of MDS or AML in the HRR-deficient population. In the all-comers population, venous embolic and thrombotic events were reported in 4.0 % (16/398) of patients, including 2.5 % (10/398) of patients with pulmonary embolism. In the HRR-deficient population, venous embolic and thrombotic events were reported in 3.5 % (7/198) of patients, including 2.0 % (4/198) of patients with pulmonary embolism. In both the all-comers and the HRR-deficient populations, there was one instance of pneumonitis. In the all-comers population, second primary malignancies were infrequent and similar between the talazoparib plus enzalutamide (3.0 %; 12/398) and placebo plus enzalutamide (5.0 %; 20/401) arms. In the HRR-deficient population, second primary malignancies were also infrequent and similar between the treatment arms (talazoparib plus enzalutamide, 2.0 % [4/198]; placebo plus enzalutamide, 3.5 % [7/199]).

3.3. Dose modification and discontinuations

In TALAPRO-2, the recommended first, second, and third dose reduction levels for adverse events were 0.35 mg, 0.25 mg, and 0.1 mg, QD, respectively. The current prescribing information for talazoparib in the United States follows the same recommended dose reduction levels for treatment of patients with mCRPC harboring HRR gene alterations [15].

The incidence of talazoparib dose interruptions and reductions due to TEAEs was similar between the all-comers and the HRR-deficient populations; however, the rate of talazoparib discontinuation due to TEAEs was lower in the HRR-deficient population than in the all-comers population (Table 1). Overall, in the all-comers population, 18.8 % of patients discontinued talazoparib due to TEAEs (compared with 12.2 %

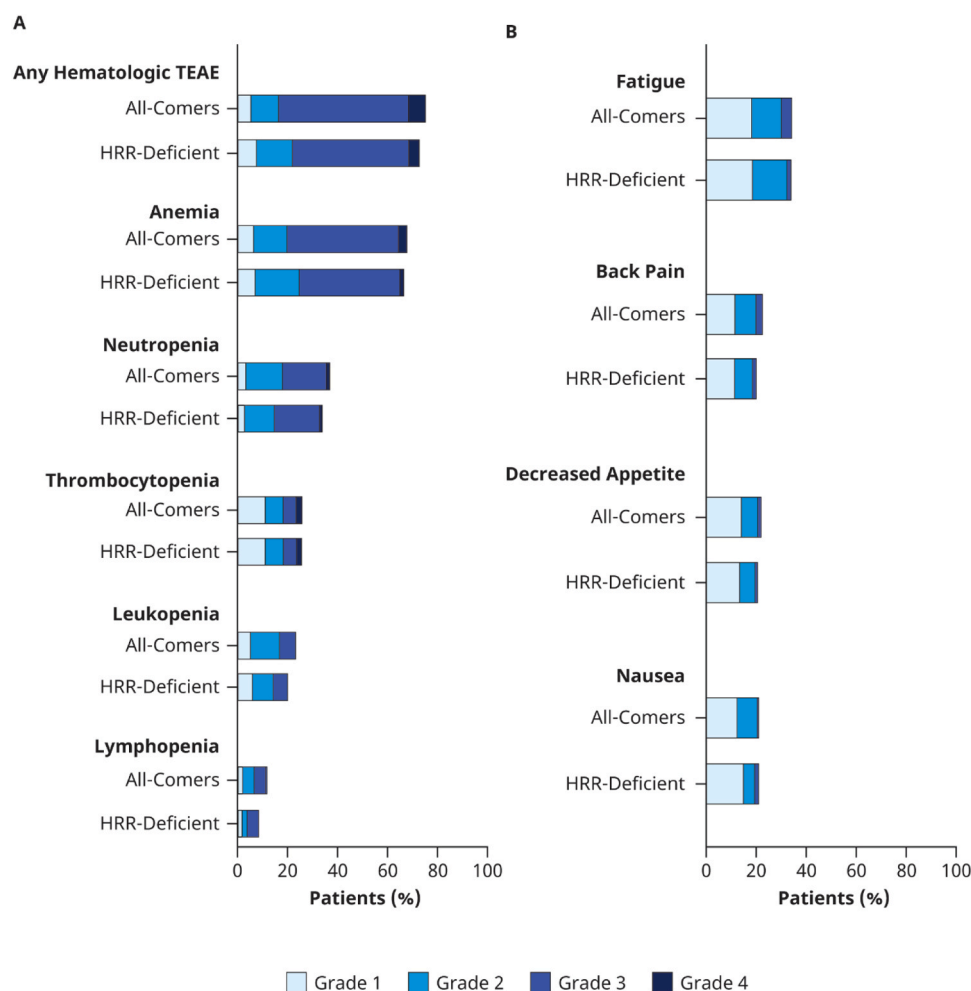


Fig. 2. All-cause (A) hematologic TEAEs and (B) most common ($\geq 20\%$) nonhematologic TEAEs for the all-comers and the HRR-deficient populations. $N = 398$ (all-comers safety population) and $N = 198$ (HRR-deficient safety population). The treatment-emergent period is from first dose through 28 days after the last dose of study treatment, or before new systemic (ie, not including surgery or radiotherapy) antineoplastic therapy, whichever occurs first. MedDRA v25.0 coding dictionary applied. Preferred terms clustered for anemia (anemia, hematocrit decreased, hemoglobin decreased, red blood cell count decreased), leukopenia (leukopenia, white blood cell count decreased), lymphopenia (lymphopenia, lymphocyte count decreased), neutropenia (neutropenia, neutrophil count decreased), and thrombocytopenia (thrombocytopenia, platelet count decreased). HRR, homologous recombination repair; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

who discontinued placebo in the control arm, $N = 401$). Of the three most common hematologic TEAEs, anemia was the most common cause of dose interruption (44.2 %), reduction (43.2 %), and discontinuation (8.3 %) (Table 1). To ensure optimal dosing of talazoparib at the individual level, the protocol did not require dose modification of talazoparib until anemia was grade ≥ 3 for either population. Further dose modification recommendations are described in Appendix Table A3. Despite dose reduction, the relative median dose intensity of talazoparib was 83.5 %.

Overall, in the HRR-deficient population, 10.1 % of patients discontinued talazoparib because of TEAEs (Table 1; compared with 7.0 % who discontinued placebo, $N = 199$). Anemia was also the most common cause of dose interruption (41.4 %), reduction (42.9 %), and discontinuation (4.0 %) in the HRR-deficient population (Table 1). Similar to the all-comers population, despite dose reduction, the relative median dose intensity of talazoparib was 81.0 %.

3.4. Management of anemia

Anemia was not a cumulative drug-related toxicity. The mean change in hemoglobin from baseline was < 2 g/dL for patients in the talazoparib plus enzalutamide arm for both the all-comers and the HRR-

deficient populations (Fig 4). In the all-comers population, maximum reduction from baseline in hemoglobin levels occurred after 13 weeks of treatment with talazoparib plus enzalutamide compared with 15 weeks in the HRR-deficient population. Accordingly, the median time to dose interruption and reduction of talazoparib was 14 weeks and 15 weeks, respectively, in the all-comers population, and 12 weeks and 13 weeks, respectively, in the HRR-deficient population. Hemoglobin levels increased after weeks 13 and 15 in the all-comers and HRR-deficient population, respectively, and roughly plateaued around weeks 25 and 29, respectively.

Hematologic supportive care measures are shown in Table 2. 39.2 % and 35.9 % of patients in the all-comers and HRR-deficient population, respectively, required packed red blood cell transfusions. Of the 398 patients in the all-comers population who received talazoparib plus enzalutamide, 21.1 % had more than one episode of grade 3/4 anemia. Of the patients who experienced an episode of grade 3/4 anemia ($n = 186$), 45.2 % had a recurrent episode; recurrent grade 3/4 anemia occurred in 19.9 % of patients after dose reduction.

Of the 198 patients in the HRR-deficient population who received talazoparib plus enzalutamide, 19.2 % had more than one episode of grade 3/4 anemia. Of the patients who experienced an episode of grade 3/4 anemia ($n = 81$), 46.9 % had a recurrent episode; recurrent grade

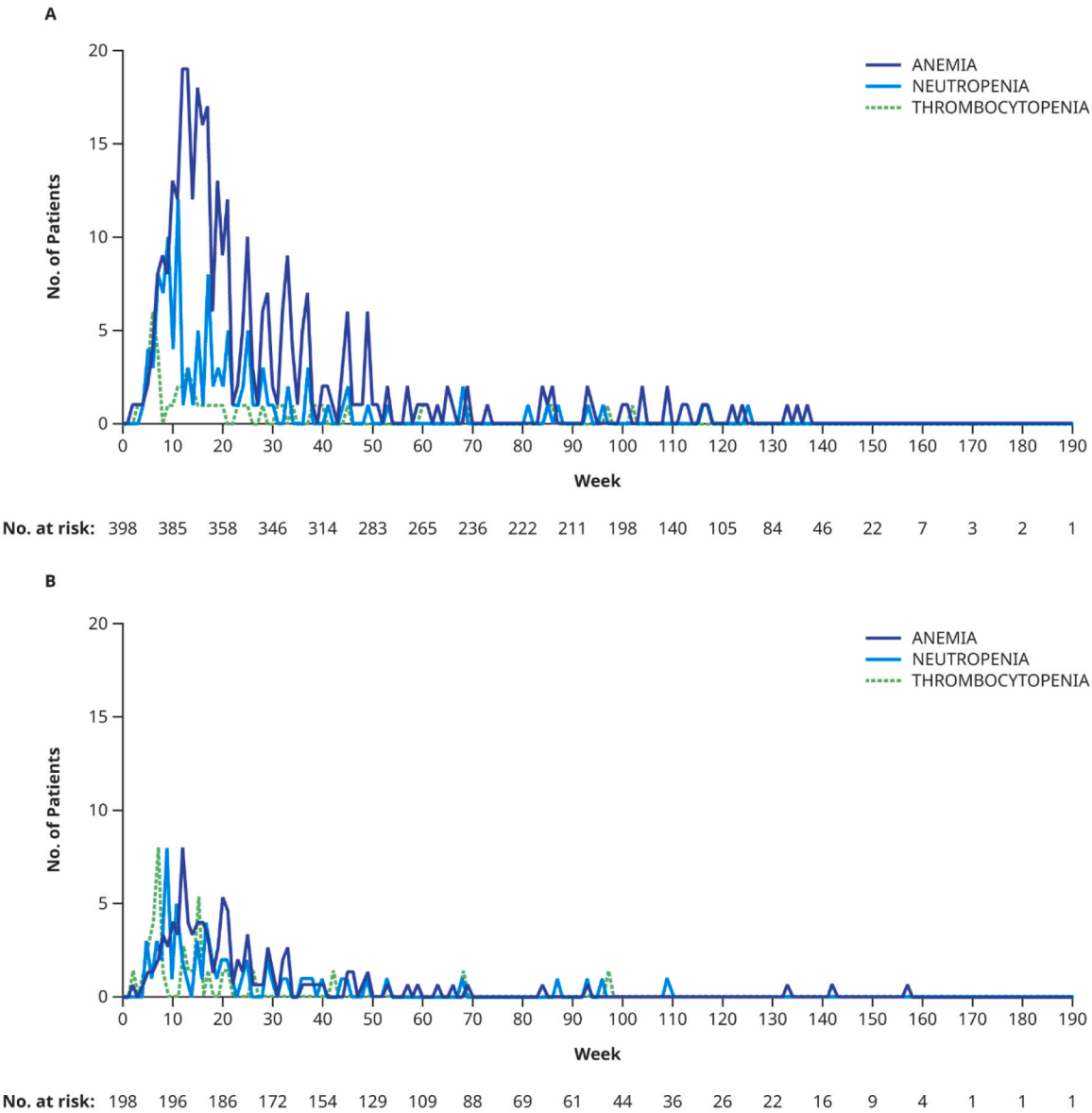


Fig. 3. Incidence of anemia, neutropenia, and thrombocytopenia by week in the talazoparib plus enzalutamide arm for (A) the all-comers population and (B) the HRR-deficient population. N = 398 (All-comers safety population) and N = 198 (HRR-deficient safety population). The treatment-emergent period is from first dose through 28 days after the last dose of study treatment, or before new systemic (ie, not including surgery or radiotherapy) antineoplastic therapy, whichever occurs first. Within each week, patients with new reports of TEAEs within the clustered preferred term are counted. MedDRA v25.0 coding dictionary applied. Preferred terms clustered for anemia (anemia, hematocrit decreased, hemoglobin decreased, red blood cell count decreased), neutropenia (neutropenia, neutrophil count decreased), and thrombocytopenia (thrombocytopenia, platelet count decreased). HRR, homologous recombination repair; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

Table 1
Summary of dose modifications and discontinuations of talazoparib due to all-causalities, anemia, neutropenia, and thrombocytopenia (safety populations).

	All-comers population (N = 398)			HRR-deficient population (N = 198)		
	Interruption n (%)	Reduction n (%)	Discontinuation n (%)	Interruption n (%)	Reduction n (%)	Discontinuation n (%)
All-causalities	247 (62.1)	210 (52.8)	75 (18.8)	114 (57.6)	103 (52.0)	20 (10.1)
Anemia	176 (44.2)	172 (43.2)	33 (8.3)	82 (41.4)	85 (42.9)	8 (4.0)
Neutropenia	54 (13.6)	60 (15.1)	13 (3.3)	29 (14.6)	30 (15.2)	1 (0.5)
Thrombocytopenia	31 (7.8)	22 (5.5)	2 (0.5)	17 (8.6)	11 (5.6)	0 (0.0)

NOTE. Preferred terms clustered for anemia (anemia, hematocrit decreased, hemoglobin decreased, red blood cell count decreased), neutropenia (neutropenia, neutrophil count decreased), and thrombocytopenia (thrombocytopenia, platelet count decreased).
Abbreviation: HRR, homologous recombination repair.

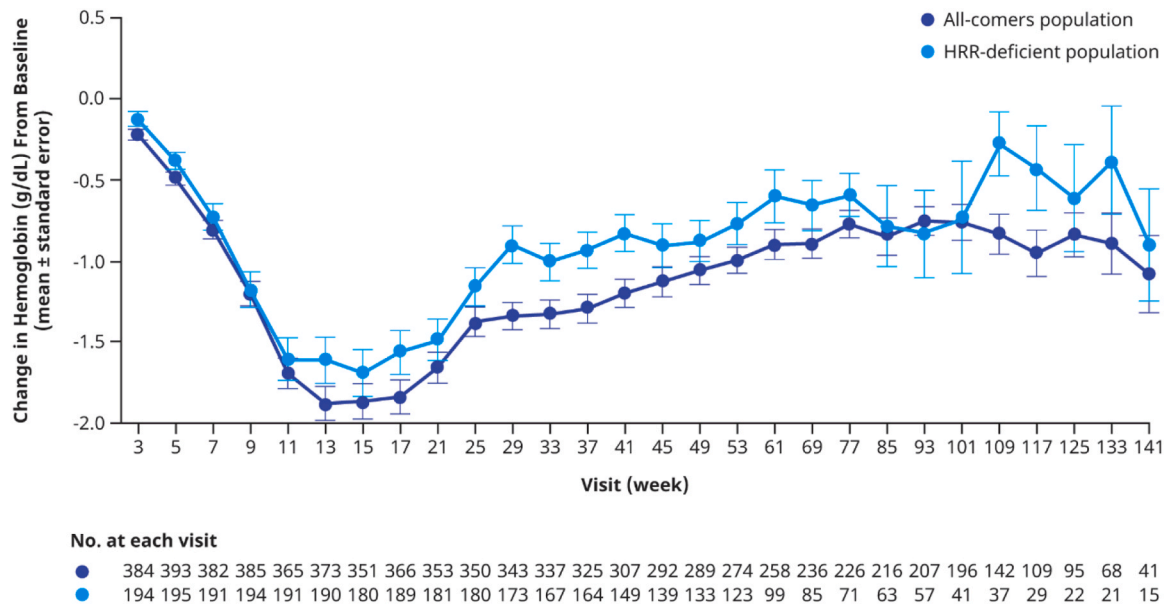


Fig. 4. Change in hemoglobin from baseline by week in the talazoparib plus enzalutamide arm (safety population). HRR, homologous recombination repair.

Table 2
Summary of hematologic supportive care measures and blood transfusions in the talazoparib + enzalutamide arm (safety populations).

	All-comers population (N = 398)	HRR-deficient population (N = 198)
Patients receiving ≥ 1 hematologic supportive treatment	52 (13.1)	21 (10.6)
Erythropoietin-stimulating agents ^a	33 (8.3)	15 (7.6)
Granulocyte-stimulating factors ^b	30 (7.5)	12 (6.1)
Platelet-stimulating factors ^c	6 (1.5)	2 (1.0)
Patients with ≥ 1 blood transfusion	169 (42.5)	80 (40.4)
Packed red blood cells	156 (39.2)	71 (35.9)
Platelets	13 (3.3)	5 (2.5)
Whole blood	13 (3.3)	5 (2.5)
Plasma	3 (0.8)	3 (1.5)
Other	6 (1.5)	7 (3.5)

NOTE. All values are shown as n (%).
Abbreviation: HRR, homologous recombination repair.
The following medications are considered as hematologic supportive treatments and included in the table:
^aEpoetin alfa, darbepoetin alfa, epoetin theta, erythropoietin, erythropoietin human, epoetin zeta.
^bFilgrastim, lenograstim, lipegfilgrastim, granulocyte colony-stimulating factor, pegylated granulocyte colony-stimulating factor, granulocyte-macrophage colony-stimulating factor, filgrastim-sndz, pegfilgrastim.
^cOprelvekin, recombinant human thrombopoietin.

3/4 anemia occurred in 18.5 % of patients after dose reduction.

4. Discussion

Based on results from the TALAPRO-2 study, talazoparib 0.5 mg QD in combination with enzalutamide 160 mg QD significantly improved rPFS compared with placebo plus enzalutamide in patients with mCRPC in both an all-comers and an HRR-deficient population [11,12]. Importantly, the safety profile of talazoparib plus enzalutamide in TALAPRO-2 was qualitatively similar between the all-comers and the HRR-deficient population and consistent with the established individual

safety profiles of talazoparib monotherapy and enzalutamide [7,15,16]. As anticipated, anemia was the most common TEAE, and was manageable via dose modifications and/or standard supportive care, including blood transfusions [3–7,17]. On this basis, regular blood counts are recommended to monitor for hematologic AEs in patients receiving talazoparib [15]. Close monitoring of blood counts is especially important during the first 3 months of treatment with talazoparib, when anemia is most likely to occur.

Although in the all-comers population anemia led to dose interruption and dose reductions in 44.2 % and 43.2 % of patients, respectively, only 8.3 % discontinued talazoparib due to anemia. This indicates that anemia was generally manageable with supportive measures in a majority of patients, although 45.2 % of patients with grade 3/4 anemia had at least one recurrent episode. Nevertheless, hemoglobin levels reached a nadir at week 13 and thereafter improved, reflecting the benefit of dose modifications. In the TALAPRO-1 study of heavily pre-treated patients with mCRPC who received talazoparib 1 mg QD, patients with lower hemoglobin levels at baseline were more likely to develop grade 3/4 anemia [6,18]. In TALAPRO-2, approximately half of the patients in both the all-comers and the HRR-deficient populations started talazoparib with grade 1 or 2 anemia, which is likely to have contributed to a higher risk of developing grade 3 or 4 anemia. Monitoring these patients particularly during the first 3 months of treatment is paramount.

Of note, incidence of gastrointestinal toxicity was lower than expected based on prior studies of PARP inhibitors either without or in combination with an androgen receptor signaling inhibitor [3,7,19–21]. In the TALAPRO-1 study, 31 %, 25 %, and 12 % of patients had grade 1 or 2 nausea, decreased appetite, and vomiting, respectively, compared with 20.1 %, 20.4 %, and 7.3 % of all-comers patients who received talazoparib plus enzalutamide in TALAPRO-2 [7]. Decreased appetite, nausea, and vomiting were primarily low grade in both the all-comers and the HRR-deficient populations.

The incidence of AESIs in TALAPRO-2 for patients receiving talazoparib plus enzalutamide was lower than, or similar to, that observed in the TALAPRO-1 study of talazoparib monotherapy in patients with mCRPC and the ARCHES study of enzalutamide monotherapy (160 mg QD) for patients with metastatic hormone-sensitive prostate cancer [7, 22]. In the TALAPRO-1 study, 6 % of patients who received talazoparib 1 mg QD had pulmonary embolism, including one who died [7]; in TALAPRO-2, 2.5 % and 2.0 % of patients in the all-comers and the

HRR-deficient populations experienced pulmonary embolism. The incidence of second primary malignancies in the talazoparib plus enzalutamide arm of both the all-comers and the HRR-deficient populations was similar compared with the respective placebo plus enzalutamide arms, and also similar to the rate reported with enzalutamide monotherapy in the ARCHES study [22]. In TALAPRO-2, the incidence of MDS/AML (2/398 patients in the all-comers population) was similar to the incidence in previous studies of patients with solid tumors who received talazoparib monotherapy (3/788) [15].

5. Conclusions

In conclusion, TALAPRO-2 shows that toxicities associated with talazoparib plus enzalutamide, most commonly anemia, are manageable in most patients with mCRPC through supportive measures, including dose modification. These data provide reassurance for physicians treating patients with mCRPC that talazoparib plus enzalutamide has a generally manageable safety profile.

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CRediT authorship contribution statement

Liza DeAnnuntis: Writing – review & editing, Investigation. **Ugo De Giorgi:** Writing – review & editing. **Jae Young Joung:** Writing – review & editing. **Andre P. Fay:** Writing – review & editing. **Nobuaki Matsubara:** Writing – review & editing. **Xun Lin:** Writing – review & editing, Investigation, Formal analysis. **Fred Saad:** Writing – review & editing. **Curtis Dunshee:** Writing – review & editing. **Arun A. Azad:** Writing – review & editing, Investigation. **Joan Carles:** Writing – review & editing. **Karim Fizazi:** Writing – review & editing. **Jan Oldenburg:** Writing – review & editing. **Neal D. Shore:** Writing – review & editing. **Neeraj Agarwal:** Writing – review & editing. **Robert J. Jones:** Writing – review & editing, Investigation. **Stefanie Zschäbitz:** Writing – review & editing. **Nicola Di Santo:** Writing – review & editing. **Michael A. Zielinski:** Writing – review & editing. **Peter C. C. Fong:** Writing – review & editing.

Declaration of Competing Interest

Arun A. Azad reports honoraria from Aculeus Therapeutics, Amgen, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Daiichi Sankyo, Ipsen, Janssen, Merck Serono, Merck Sharp & Dohme, Novartis, Noxopharm, Pfizer, Sanofi, Telix Pharmaceuticals, and Tolmar; consulting fees from Aculeus Therapeutics, Astellas Pharma, Janssen, and Novartis; participation on advisory boards for Amgen, Arvinas, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Daiichi Sankyo, Ipsen, Janssen, Merck Serono, Merck Sharp & Dohme, Novartis, Noxopharm, Pfizer, Sanofi, Telix, and Tolmar; participation on a data safety monitoring board for OncoSec; research funding (institution unless stated otherwise) from Aptevo Therapeutics, Astellas Pharma (investigator), AstraZeneca (investigator), Bionomics, Bristol Myers Squibb, Exelixis, Gilead Sciences, GlaxoSmithKline, Hirona Pharmaceuticals, Ipsen, Janssen, Lilly, MedImmune, Merck Serono (investigator), Merck Serono (institutional), MSD, Novartis, Pfizer, Sanofi, and Synthon; and travel, accommodations, and/or expenses from Amgen, Astellas Pharma, Bayer, Hirona Pharmaceuticals, Janssen, Merck Serono, Novartis, Pfizer, and Tolmar; and support for medical writing services from Astellas Pharma, Exelixis, and Pfizer; he is Chair of the Urologic Oncology Group for the Clinical Oncology Society of Australia, and Chair of the Translational Research Subcommittee and on the Scientific Advisory Committee for the ANZUP Cancer Trials Group. Karim Fizazi reports honoraria (institution) for participation in advisory boards and

talks from Advanced Accelerator Applications/Novartis, Amgen, Astellas Pharma, AstraZeneca, Bayer, Clovis Oncology, Daiichi Sankyo, Janssen, MSD, Novartis, Pfizer, and Sanofi; and honoraria (personal) for participation in advisory boards from Arvinas, CureVac, MacroGenics, and Orion. Nobuaki Matsubara reports honoraria (personal) from Sanofi; research funding (institution) from Amgen, Astellas Pharma, AstraZeneca, Bayer, Chugai Pharma, Eisai, Janssen, Lilly, MSD, Pfizer, PRA Health Science, Roche, Seagen, Taiho, and Takeda; and travel, accommodations, and/or expenses (personal) from Pfizer. Fred Saad reports a consulting or advisory role for AbbVie, Advanced Accelerator Applications, Astellas Pharma, AstraZeneca/MedImmune, Bayer, Janssen Oncology, Knight Therapeutics, Myovant Sciences, Novartis, Pfizer, and Sanofi; honoraria from AbbVie, Advanced Accelerator Applications, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Janssen Oncology, Knight Therapeutics, Merck, Myovant Sciences, Novartis, Pfizer, and Sanofi; and research funding to their institution from Advanced Accelerator Applications, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Janssen Oncology, Merck, Novartis, Pfizer, and Sanofi. Ugo De Giorgi reports a consulting or advisory role for Amgen, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Dompé Farmaceutici, Eisai, Ipsen, Janssen, Merck KGaA, MSD, Novartis, and Pfizer; research funding (institution) from AstraZeneca, Roche, and Sanofi; and travel, accommodations, and/or expenses from Ipsen and Pfizer. Jae Young Joung declares no competing interests. Peter C. C. Fong reports a consulting or advisory role for MSD and travel, accommodations, and/or expenses from Pfizer. Robert J. Jones reports honoraria from Astellas Pharma, Bayer, Bristol Myers Squibb, Gilead Sciences, Ipsen, Janssen, Merck Serono, MSD, Pfizer, and Roche; a consulting or advisory role for Astellas Pharma, Bayer, Bristol Myers Squibb, Ipsen, Janssen, Merck Serono, MSD, Novartis, Pfizer, and Roche; research funding from Astellas Pharma, Bayer, Clovis Oncology, Exelixis, and Roche; and travel, accommodations, and/or expenses from Bayer and Janssen. Stefanie Zschäbitz reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing, or educational events from Amgen (personal and institution), Astellas Pharma (personal and institution), Bayer (personal and institution), Bristol Myers Squibb (personal and institution), Eisai (personal), Gilead Sciences (personal), Janssen (personal), Merck Serono (personal and institution), MSD (institution), Novartis (personal), and Pfizer (personal and institution); participation on a data safety monitoring board or advisory board for Amgen (personal and institution), Bayer (personal and institution), Bristol Myers Squibb (institution), Eisai (personal), Gilead Sciences (personal), Ipsen (personal), Janssen (personal), Merck Serono (personal and institution), MSD (institution), Novartis (personal), and Pfizer (institution); research funding (institution) from Eisai; and travel, accommodations, and/or expenses from Amgen, Astellas Pharma, AstraZeneca, Bayer, Ipsen, Janssen, Merck Serono, MSD, and Pfizer. Jan Oldenburg reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing, or educational events from Astellas Pharma, AstraZeneca, Bayer, BMS Norway, Eisai, Ipsen, Janssen-Cilag, Merck, and Roche; participation on a data safety monitoring board or advisory board for Astellas Pharma, AstraZeneca, Bayer, BMS, Eisai, Ipsen, Janssen-Cilag, Merck, and Roche; and travel, accommodations, and/or expenses from Astellas Pharma. Neal D. Shore reports a consulting or advisory role for AbbVie, Alestra Therapeutics, Akido, Amgen, Arquar, Asieris, Astellas Pharma, AstraZeneca, Bayer, Boston Scientific, Bristol Myers Squibb, CG Oncology, Clarity Pharmaceuticals, Clovis Oncology, Dendreon, Exact Imaging, Exact Sciences, FerGene, Ferring, FIZE Medical, Foundation Medicine, GenesisCare, Genentech, Guardant Health, ImmunityBio, Incyte, Invitae, Janssen, Lantheus, Lilly, Mdxhealth, Merck, Minomic, Myovant Sciences, Myriad Genetics, Nymox, Pacific Edge Biotechnology, Pfizer, Photocure, PlatformQ, ProFound, Promaxo, Propella Therapeutics, Protara, Sanofi, Sesen Bio, Specialty Networks, Telix Pharmaceuticals, Tolmar, UroGen Pharma, Vaxiion, and Vessi; providing expert testimony for Ferring; and leadership or other fiduciary role in other board, society, committee, or

advocacy group with Photocure. Curtis Dunshee reports participation on advisory boards for Astellas Pharma, Bayer, Janssen, and Pfizer; and research funding from AstraZeneca, Bayer, Dendreon, Hengrui Pharmaceuticals, Janssen, Laekna Therapeutics, Myovant Sciences, and Pfizer. Joan Carles reports a consulting or advisory role for Advanced Accelerator Applications/Novartis, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Ipsen, Johnson & Johnson, MSD Oncology, Pfizer, Roche, and Sanofi; participation in speakers' bureaus for Astellas Pharma, Bayer, and Johnson & Johnson; research funding (institution) from AB Science, Aragon Pharmaceuticals, AROG Pharmaceuticals, Astellas Pharma, AstraZeneca AB, AVEO Pharmaceuticals, Bayer AG, Blueprint Medicines, BN ImmunoTherapeutics, Boehringer Ingelheim España SA, Bristol Myers Squibb International Corporation, Clovis Oncology, Cougar Biotechnology, Deciphera, Exelixis, Genentech, GlaxoSmithKline, Incyte, Janssen-Cilag International NV, Karyopharm Therapeutics, Laboratoires Leurquin Mediolanum, Lilly, MedImmune, Millennium Pharmaceuticals, Nanobiotix, Novartis Farmacéutica SA, Pfizer, Puma Biotechnology, Roche, Sanofi Aventis GmbH, SFJ Pharmaceuticals Group, and Teva; and travel, accommodations, and/or expenses from AstraZeneca, BMS, Ipsen, and Roche. Andre P. Fay reports honoraria from Astellas Pharma, AstraZeneca, Bristol Myers Squibb, Ipsen, Janssen, MSD, Novartis, Pfizer, and Roche; a consulting or advisory role for Bayer, Ipsen, Janssen, MSD, Novartis, Pfizer, and Roche; stock or stock options in Brazilian Information Oncology; and research funding from AstraZeneca, Bristol Myers Squibb, CAPES – CNPq, Foundation Medicine, Ipsen, MSD, and Roche; and travel, accommodations and/or expenses from Astellas Pharma, AstraZeneca, BMS, Ipsen, Janssen, MSD, Novartis, Pfizer, and Roche. Xun Lin, Liza DeAnnuntis, and Michael A. Zielinski are employees of Pfizer and may hold Pfizer stock/stock options. Nicola Di Santo is a former employee of Pfizer and may hold Pfizer stock/stock options. Neeraj Agarwal (lifetime disclosures): No personal COIs since April 15, 2021. Consultancy to Astellas Pharma, AstraZeneca, AVEO Pharmaceuticals, Bayer, Bristol Myers Squibb, Calithera, Clovis, Eisai, Eli Lilly, EMD Serono, Exelixis, Foundation Medicine, Genentech, Gilead Sciences, Janssen, Merck, MEI Pharma, Nektar, Novartis, Pfizer, Pharmacyclics, and Seattle Genetics. Research funding to institution (lifetime): Arvinas, Astellas Pharma, AstraZeneca, Bavarian Nordic, Bayer, Bristol Myers Squibb, Calithera, Celldex, Clovis, CRISPR, Eisai, Eli Lilly, EMD Serono, Exelixis, Genentech, Gilead Sciences, GlaxoSmithKline, Immunomedics, Janssen, Lava, Medivation, Merck, Nektar, Neoleukin, NewLink Genetics, Novartis, ORIC, Pfizer, Prometheus, Rexahn, Roche, Sanofi, Seattle Genetics, Takeda, Telix, and TRACON.

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Data Sharing Statement

Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions and exceptions, Pfizer may also provide access to the related individual de-identified participant data. See <https://www.pfizer.com/science/clinical-trials/trial-data-and-results> for more information.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.ejca.2024.115078](https://doi.org/10.1016/j.ejca.2024.115078).

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