NON-INTERVENTIONAL (NI)/LOW-INTERVENTIONAL STUDY TYPE 1 (LIS1) STUDY REPORT

Study Information

Title	Machine learning prediction of anemia events before and after talazoparib dose modification using TALAPRO-2 phase 3 trial data
Protocol number	C3441068
Version identifier of the study report	1.0
Date	21 August 2026
EU Post Authorization Study (PAS) register number	EUPAS1000000344
Active substance	talazoparib tosylate
Medicinal product	Talzenna
Research question and objectives	Research question: How well can machine learning models predict anemia events before and after talazoparib dose modification? Primary objectives: 1. Describe patient characteristics, dosing patterns and hemoglobin trajectories with respect to anemia events in talazoparib-treated metastatic castrate-resistant prostate cancer (mCRPC) patients from the TALAPRO-2 trial data. 2. Develop and evaluate machine learning prediction models of anemia risk after treatment initiation and preceding dose modification. 3. Develop and evaluate machine learning prediction models of anemia recovery after dose modification.
Country(-ies) of study	United States

Author	[redacted]

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Appendix 1. SIGNATURES

Appendix 2.1 Protocol

Appendix 3. INVESTIGATORS AND CORRESPONDING INDEPENDENT ETHICS COMMITTEES (IECs) OR INSTITUTIONAL REVIEW BOARDS (IRBs)

Not applicable

Appendix 3.1. List of Investigators by Country

Not applicable

Appendix 3.2. List of Independent Ethics Committee (IEC) or Institutional Review Board (IRB) and Corresponding Protocol Approval Dates

Not applicable

Appendix 4. STATISTICAL ANALYSIS PLAN

Appendix 5. SAMPLE CASE REPORT FORM (CRF)/DATA COLLECTION TOOL (DCT)

Not applicable

Appendix 6. SAMPLE STANDARD SUBJECT INFORMATION SHEET AND INFORMED CONSENT DOCUMENT (ICD)

Not applicable

Appendix 7. LIST OF SUBJECT DATA LISTINGS

Not applicable

Appendix 7.1 Withdrawn Subjects

Not applicable

Appendix 7.2 Protocol Deviations

Not applicable

Appendix 7.3 Subjects Excluded from the Analysis

Not applicable

Appendix 7.4 Demographic Data

Not applicable

Appendix 7.5 Medication/Treatment Data

Not applicable

Appendix 7.6 Endpoint Data

Not applicable

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Not applicable

Appendix 7.8 Laboratory listings

Not applicable

Appendix 8. ADDITIONAL DOCUMENTS

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1. ABSTRACT (STAND-ALONE DOCUMENT)

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ADT	Androgen Deprivation Therapy
AE	Adverse Event
AJCC	American Joint Committee on Cancer
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
ARPI	Androgen Receptor Pathway Inhibitors
AST	Aspartate Aminotransferase
ATM	Ataxia Telangiectasia Mutated
ATR	Ataxia Telangiectasia and Rad3-related
AUC	Area Under the Curve
BMI	Body Mass Index
BRCA	BReast CAncer gene
BUN	Blood Urea Nitrogen
Ca	Calcium
Cavg,t	Blood Concentration of Talazoparib
Cl	Chloride
CCI	Charlson Comorbidity Index
CDK12	Cyclin-Dependent Kinase 12
CHEK2	Checkpoint Kinase 2
CK	Creatine Kinase
CSR	Clinical Study Report

CTCAE	Common Terminology Criteria for Adverse Events
CV	Cross Validation
DNA	Deoxyribonucleic Acid
DDR	DNA Damage Response
IEC	Ethics Committee
ECOG	Eastern Cooperative Oncology Group
eGFR	Estimated Glomerular Filtration Rate
EMBRACA	Elucidating the Efficacy and Safety of Talazoparib in Advanced Breast Cancer
EMA	European Medicines Agency
ENCePP	European Network of Centers for Pharmacoepidemiology and Pharmacovigilance
EPO	Erythropoietin
EU	European Union
FANCA	Fanconi Anemia Complementation Group A
FDA	Food and Drug Administration
GBR	United Kingdom
GPP	Good Pharmacoepidemiology Practices
HCO3	Bicarbonate
HCT	Hematocrit
Hgb	Hemoglobin
HRR	Homologous Recombination Repair
HRRm	HRR Mutated
IRB	Institutional Review Board
IRCCS IRST	Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori"

LASSO	Least Absolute Shrinkage and Selection Operator
LDH	Lactate Dehydrogenase
mCRPC	Metastatic Castrate-Resistant Prostate Cancer; Metastatic Castration-Resistant Prostate Cancer (terms used interchangeably in this document)
Mg	Magnesium
ML	Machine Learning
MLH1	MutL Homolog 1
MCV	Mean Corpuscular Volume
MRE11A	MRE11 Homolog A
NA	Not Applicable
Na	Sodium
NBN	Nibrin
NI	Non-Interventional
PALB2	Partner and Localizer of BRCA2
PARP	Poly (ADP-ribose) polymerase
PLTS	Platelets
PAS	Post-Authorization Studies
PASS	Post-Authorization Safety Study
PSA	Prostate-Specific Antigen
PCWG3	Prostate Cancer Working Group 3
Q1	First Quartile (25th percentile)
Q3	Third Quartile (75th percentile)
QC	Quality Control
RAD51C	RAD51 Paralog C
RBC	Red Blood Cell

RBCT	Red Blood Cell Transfusion
RECIST	Response Evaluation Criteria In Solid Tumors
SAP	Statistical Analysis Plan
SD	Standard Deviation
SVM	Support Vector Machine
TALAPRO-2	Talazoparib plus enzalutamide in men with first-line metastatic castration-resistant prostate cancer: a randomized, placebo-controlled, phase 3 trial
US	United States
WBC	White Blood Cell
XGB	Extreme Gradient Boosting

3. INVESTIGATORS

Principal Investigator(s) of the Protocol

Name, degree(s)	Title	Affiliation
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

4. OTHER RESPONSIBLE PARTIES

Not applicable

5. MILESTONES

Milestone	Planned date	Actual date	Comments
Start of data collection	11 November 2024	20 November 2024	
End of data collection	31 July 2025	30 August 2025	
Registration in the HMA-EMA Catalogues of RWD Studies	08 November 2024	19 November 2024	
Final report of study results	30 June 2026	21 August 2026	

6. RATIONALE AND BACKGROUND

TALZENNA (talazoparib), a poly (ADP-ribose) polymerase (PARP) inhibitor, in combination with enzalutamide, was approved by the US Food and Drug Administration (FDA) in June 2023 for the treatment of homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC), and by the European Medicines Agency (EMA) in January 2024 for the treatment of any mCRPC regardless of HRR mutation status. Along with clinically meaningful and statistically significant improvement in radiographic progression-free survival, anemia, a hematologic disorder characterized by insufficient hemoglobin (Hgb) in the blood, was reported as a common adverse event (AE) in the talazoparib group. Grade 3-4 anemia (Hgb < 8.0 g/dL) was observed in 46% of treated patients, with median time to anemia onset of 3.3 months[1]. Although many patients resumed talazoparib after treatment-emergent anemia, ultimately 8% of patients permanently discontinued talazoparib. Given the potential barrier in talazoparib utilization and/or premature treatment discontinuation due to anemia risk, successful prediction of this adverse event via an individualized patient-centered approach may be a potential strategy for early detection and prevention measures among at-risk patients.

Based on a review of prespecified target safety events and pharmacokinetics data, a starting dose of 0.5 mg/day talazoparib (in combination with 160 mg daily enzalutamide) was specified for the study, with a reduced 0.35 mg/day given to patients with moderate renal impairment (estimated glomerular filtration rate 30–59 ml/min/1.73 m^2) to account for lower clearance in this subpopulation[2]. Per protocol mandate, patients experiencing grade 3-4 anemia underwent dose interruption, followed by dose reduction of talazoparib upon hemoglobin recovery, while patients experiencing Grade 1-2 anemia were managed by the investigator as warranted on an individual basis (interruption and/or reduction). Patients at baseline were allowed to have up to Grade 2 baseline anemia and still be included in the study. Therefore, a variety of patient characteristics and treatment strategies are represented in the existing data from the clinical trial before and after treatment initiation and modification which allows for the opportunity to characterize and model the dose patterns and trajectories of anemia risk among patients treated with talazoparib.

Anemia risk has previously been described more generally among men with prostate cancer, including due to the cancer itself (replacement of normal marrow with cancer cells); due to treatments including bilateral orchiectomy, androgen deprivation therapy, radiation therapy, chemotherapy, and targeted therapy; as well as being associated with patient characteristics such as advanced age, bone metastasis, low baseline hemoglobin levels[3–13]. Prior findings from the EMBRACA trial of talazoparib in patients with germline BRCA-mutated advanced breast cancer also showed that higher talazoparib exposure (calculated using average daily dose intensity divided by the product of talazoparib oral clearance) is associated with higher risk of anemia[14], although this value is typically only measured in the trial setting during pharmacokinetic analyses and not readily available during routine clinical practice. Given the large number of potential predictors of anemia risk for prostate cancer in general and additional less well-understood risk factors among talazoparib-treated mCRPC patients, an integrated prediction approach may improve the ability to anticipate treatment-related toxicity and in the future, aid early dose management to prevent severe anemia-related discontinuation of talazoparib in the clinical setting.

Machine learning (ML) modeling is increasingly being used to predict outcomes in oncology [15], and drug-related adverse events[16–18], proposed because of its ability to integrate complex, multifaceted data in a customizable and scalable manner, often without assumptions about underlying data distributions. Therefore, ML is a promising tool for prediction, prevention, and ultimately, clinical decision support in the effort to reduce treatment-related toxicity. This study serves as an exploratory effort to assess the ability of machine learning models to predict anemia risk and recovery, with future directions to validate the models in the real-world setting, and eventually, to develop diagnostic tools for predicting and preventing anemia in real time in the clinical setting.

This non-interventional study was designated as a Post-Authorization Safety Study (PASS) and was conducted voluntarily by Pfizer.

7. RESEARCH QUESTION AND OBJECTIVES

Research question:

How well can machine learning models predict anemia events before and after talazoparib dose modification?

Primary objectives:

1. Describe patient characteristics, dosing patterns and hemoglobin trajectories with respect to anemia events in talazoparib-treated metastatic castrate-resistant prostate cancer (mCRPC) patients from the TALAPRO-2 trial data.
2. Develop and evaluate machine learning prediction models of anemia risk after treatment initiation and preceding dose modification.
3. Develop and evaluate machine learning prediction models of anemia recovery after dose modification.

Exploratory objective:

1. Describe patient characteristics and hemoglobin trajectories with respect to anemia events in control-arm mCRPC patients from the TALAPRO-2 trial data

8. AMENDMENTS AND UPDATES

Table 1. Amendments to the Protocol

Amendment number	Date	Substantial or administrative amendment	Protocol section(s) changed	Summary of amendment	Reason
1.0	12 June 2025	Substantial	6. Milestones	1. End of data collection changed from 14 March 2025 to 31 July 2025 2. Final study report changed from 14 February 2026 to 30 June 2026	Later end of data collection date than originally anticipated due to contracting finalization, data analysis, and quality control requirements for the PASS study

9. RESEARCH METHODS

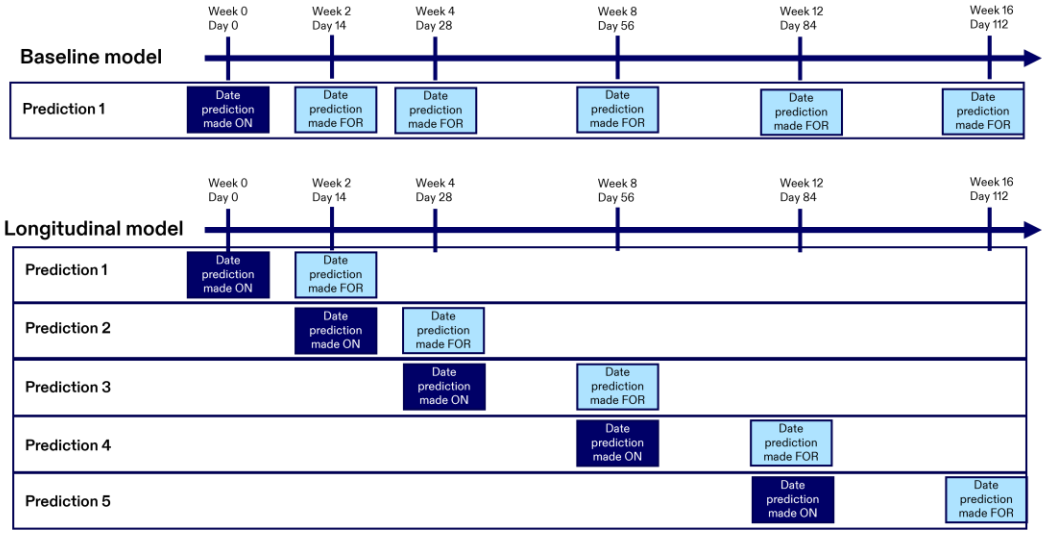
The research methods based on the final protocol are described below and presented in full in Appendix 2.

9.1. Study design

This is a NI, observational, retrospective cohort study of mCRPC patients who received talazoparib in the treatment arm, utilizing descriptive statistics and machine learning prediction modeling with secondary data analysis of existing trial data from TALAPRO-2. A non-interventional observational design was selected because the objective of the study was not to evaluate the effects of assigned treatments, but rather to characterize the occurrence of anemia and assess associations between candidate predictors and subsequent anemia outcomes within a well-defined patient population. Because the required data had already been collected during TALAPRO-2, no additional subject contact or data collection was needed. A retrospective approach was selected because all data had been collected and recorded before initiation of the present analysis. A cohort design was chosen because a defined population of patients treated with talazoparib plus enzalutamide was followed longitudinally in TALAPRO-2, allowing the assessment of the occurrence and timing of anemia events and evaluation of baseline and longitudinal factors that preceded the development of anemia. The primary endpoint in this study is anemia, categorized as overall (all grades), mild-to-moderate (Grade 1 or 2), and severe (Grade 3, 4 or 5), defined based on hemoglobin levels according to Common Terminology Criteria for Adverse Events (CTCAE) classification[19]. Patient characteristics are described with respect to talazoparib dose patterns and subsequent anemia. Machine learning models are generated to predict anemia risk/recovery and assessed with respect to prediction performance. While the eventual application of this work includes enabling diagnostic and predictive tools for preventing anemia at the point of care, this initial exploratory study aims to assess the performance of a machine learning model in a controlled setting, ie, in the clinical trial setting. Trial data is less prone to issues of missing data and loss to follow-up that real-world data is susceptible to and serves as an ideal data source for developing model parameters as a preliminary step before assessing real-world data directly. Furthermore, given the recent approval of talazoparib, real-world cohorts are still limited in sample size for talazoparib-treated patients, which may result in the study being underpowered for performing machine learning predictive modeling. The machine learning model approach is selected because of its ability to integrate complex, multifaceted data in a customizable and scalable manner, often without assumptions about underlying data distributions.

Baseline and longitudinal models are assessed using the timing framework depicted in Figure 1. For the baseline models, all predictions are made on Week/Day 0 of talazoparib initiation for the end of weeks 2, 4, 8, 12 and 16 (corresponding to days 14, 28, 56, 84, and 112 days, respectively) after talazoparib initiation. Note that weeks are referenced to allow for intuitive interpretation, and corresponding days are also provided to remove ambiguity regarding the timing within each week. For the longitudinal models, predictions were modeled in a serial manner for end of Week 2 from Week 0; then modeled for end of Week 4 among those who did not have anemia by Week 2; then modeled for end of Week 8 among those who did not have anemia by Week 4; and so on.

Figure 1. Baseline and longitudinal modeling timing



Note: data used for predictive modeling to be truncated at the first of any of the following: red blood cell transfusion (RBCT), dose modification, initiation of subsequent antineoplastic therapy, or date of last contact, death, or data cutoff

Baseline model		Prediction 1a	Prediction 1b	Prediction 1c	Prediction 1d	Prediction 1e
	Baseline	Week 0 Day 0	Week 0 Day 0	Week 0 Day 0	Week 0 Day 0	Week 0 Day 0
	Follow-up	Week 2 Day 14	Week 4 Day 28	Week 8 Day 56	Week 12 Day 84	Week 16 Day 112
Longitudinal model		Prediction 1	Prediction 2	Prediction 3	Prediction 4	Prediction 5
	Baseline	Week 0 Day 0	Week 2 Day 14	Week 4 Day 28	Week 8 Day 56	Week 12 Day 84
	Follow-up	Week 2 Day 14	Week 4 Day 28	Week 8 Day 56	Week 12 Day 84	Week 16 Day 112

9.2. Setting

This study uses the existing TALAPRO-2 trial data of metastatic castrate-resistant prostate cancer (mCRPC) patients allocated to the talazoparib + enzalutamide treatment arm and included in the safety analysis. Details of the clinical trial are published elsewhere[2]. Patients with mCRPC were enrolled between 07 January 2019, and 17 September 2020 from hospitals, cancer centers and medical centers from 26 countries in North America, Europe, Israel, South America, South Africa, and the Asia-Pacific region and received talazoparib plus enzalutamide versus placebo plus enzalutamide as a first-line treatment. The trial included two cohorts: Cohort 1, ie, “all-comers” regardless of homologous recombination repair (HRR) gene alteration status, and Cohort 2, ie, “HRR-deficient” patients who were enrolled for Cohort 2 plus patients already enrolled in Cohort 1 who were HRR-deficient. Non-overlapping patient data from both cohorts are included in this study. Data cutoff was 16 August 2022 for Cohort 1 and 03 October 2022 for Cohort 2.

9.3. Subjects

The source population for this study comprised patients enrolled in the TALAPRO-2 Phase 3 clinical trial. Subjects included in the present study were selected from the talazoparib plus enzalutamide treatment arm of TALAPRO-2 and were required to satisfy all protocol-defined eligibility criteria for enrollment in the parent trial. Eligibility for TALAPRO-2 was based on predefined inclusion and exclusion criteria, including a diagnosis of mCRPC and satisfaction of protocol-specified clinical, laboratory, and disease-related requirements. No additional sampling, matching, or subject selection procedures were applied for the current study beyond restriction to the relevant TALAPRO-2 analysis population. Because this study represents a secondary analysis of clinical trial data, all subjects had been followed prospectively during TALAPRO-2 according to protocol-defined assessment schedules, and all data were derived from records collected during the conduct of the parent trial. In the context of this secondary analysis, admission criteria to the database corresponded to the eligibility criteria for enrollment in TALAPRO-2; data were collected prospectively throughout study participation with data cutoff on 16 August 2022 for Cohort 1 and 03 October 2022 for Cohort 2.

9.3.1. Inclusion Criteria

Patients met all of the following:

1. Male
2. Aged ≥18 years (≥20 years in Japan)
3. Histologically/cytologically confirmed adenocarcinoma of the prostate
4. Asymptomatic or mildly symptomatic mCRPC
5. Underwent bilateral orchiectomy or receiving ongoing ADT with a gonadotropin-releasing hormone agonist/antagonist, with serum testosterone ≤50 ng/dl (≤1.73 nmol/l) at screening
6. Progressive disease at study entry defined by at least one of the following: PSA progression, defined as ≥2 rising PSA values from three consecutive assessments with ≥7 days between assessments; and/or soft tissue disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1; and/or bone disease progression per Prostate Cancer Working Group 3 (PCWG3) guidelines, with ≥2 new metastatic bone lesions on whole body radionuclide bone scan.

Note that only key inclusion criteria are listed above, with the full list reported previously[2]

9.3.2. Exclusion Criteria

Patients meeting any of the following criteria were not included in the study:

1. Receipt of any prior systemic cancer treatment initiated in the nonmetastatic CRPC or mCRPC disease state, with the exception of prior treatment with ADT and first-generation antiandrogens. Docetaxel and abiraterone received in the castrate sensitive prostate cancer setting are not exclusionary.
2. Has known or suspected brain metastases, or active leptomeningeal disease; any history of myelodysplastic syndrome, acute myeloid leukemia, or prior malignancy (except for carcinoma *in situ* or nonmelanoma skin cancer, any prior malignancies ≥3 years before randomization with no subsequent evidence of recurrence or

progression regardless of the stage, or American Joint Committee on Cancer Stage 0/1 cancer <3 years before randomization that has a remote probability of recurrence or progression as per investigator opinion); clinically significant cardiovascular disease; or significant renal, hepatic or bone marrow organ dysfunction

Note that only key exclusion criteria are listed above, with the full list reported previously[2]:

9.4. Variables

Exposure variables in this study are defined as potential predictors for anemia risk, including demographic characteristics, clinical characteristics, treatment history, talazoparib and enzalutamide starting dosages, medical comorbidities, baseline anemia, and baseline and longitudinal laboratory values. Baseline characteristics are captured up to the index date, which is defined as the time of talazoparib treatment initiation, while longitudinal lab values are captured any time after treatment initiation throughout the study. The outcome is anemia, categorized as overall (all grades), mild-to-moderate (Grade 1-2), and severe (Grade ≥3), defined based on hemoglobin levels according to Common Terminology Criteria for Adverse Events (CTCAE) classification. While Objective 1 aims to characterize anemia events both before and after (or in the absence of) a dose modification event, Objective 2 aims to model only anemia events preceding dose modification, and Objective 3 aims to model only anemia events after dose modification. This is to allow optimal parameterization of the machine learning model without potential unmeasured confounding associated with patient receiving non-randomized dose modification during the trial. Covariates are defined as potential predictors of anemia risk that are considered interventions intended to manage anemia such as dose modification (ie, interruption or reduction) and standard supportive care (e.g. transfusions, erythropoiesis-stimulating agents, iron supplementation) received either at baseline or due to anemia events, which may be received in a non-random way during the trial, such that it is associated with both patient baseline characteristics (whether measured or unmeasured), as well as anemia events. However, these treatment-related intervention variables may also be considered as exposure or outcome variables depending on the objective.

Of note, “dose modification” refers to any subsequent receipt of talazoparib dose that was different from the initiating dose. A related narrower definition, “dose deviation”, refers to the receipt of a subsequent dose different from the initiating dose that was sustained for 7 days or longer (or if <7 days, explicitly documented as due to an AE). This enabled the exclusion of one-off dose interruptions or errors that immediately reverted to baseline dose, which are unlikely to influence hemoglobin trajectory or anemia risk. This narrow definition was described in the SAP update on 15 Dec 2025. Both the broader dose modification and the narrower dose deviation definitions were assessed, with dose deviation used as the primary analysis definition in the Results and Discussion sections.

The main study variables of interest, including demographics, diagnostic, therapeutic and laboratory/examinations and outcomes, along with associated roles, and operational definitions are listed in Table 2 and were assessed as available from the trial data. Further details on operational definitions and any additional variables are provided in the SAP.

Table 2. Study Variables

Variable	Role	Operational Definition
Demographics		
Age at treatment initiation	Baseline, Exposure	Continuous (years)
Race	Baseline, Exposure	White; Black or African American; Asian; Other; Unknown/missing
Ethnicity	Baseline, Exposure	Hispanic; Non-Hispanic; Unknown/missing
Geographic region	Baseline, Exposure	North America; Europe; Israel; South America; South Africa; Asia-Pacific; Unknown/Missing
Study cohort	Baseline, Exposure	Cohort 1; Cohort 2
Trial site	Baseline, Exposure	Trial site 1; Trial site 2; …, Trial site n
Clinical characteristics		
Body weight	Baseline, Exposure	Continuous (kg)
BMI	Baseline, Exposure	Continuous (kg/m^2)
Charlson Comorbidity Index (CCI)	Baseline, Exposure	Continuous
Baseline anemia	Baseline, Exposure	No anemia; Grade 1; Grade 2; Unknown/missing
Prior medical history of anemia	Baseline, Exposure	Yes; No; Unknown/missing
Prior medical history of kidney disease	Baseline, Exposure	Yes; No; Unknown/missing
Date of prostate cancer diagnosis	Baseline, Exposure	Year/Month/Day
AJCC Stage at prostate cancer diagnosis	Baseline, Exposure	I, II, III, IV, Unknown/missing
Gleason score	Baseline, Exposure	<8; ≥8; Unknown/missing
Date of mCRPC diagnosis	Baseline, Exposure	Year/Month/Day
Bone Metastases at Baseline	Baseline, Exposure	Yes; No
Number of bone metastases at screening	Baseline, Exposure	Continuous
Germline HRR mutation status	Baseline, Exposure	Deficient; Non-deficient; Unknown/missing
Somatic HRR mutation status	Baseline, Exposure	Deficient; Non-deficient; Unknown/missing
ECOG	Baseline, Exposure	0; 1; Other; Unknown/missing
Pre-index treatments		
Androgen deprivation therapy at baseline type	Baseline, Exposure	Chemical castration; Bilateral orchiectomy; Unknown/missing
Prior radiotherapy	Baseline, Exposure	Yes; No; Unknown/missing

Table 2. Study Variables

Variable	Role	Operational Definition
Prior radiotherapy dose (Gy)	Baseline, Exposure	Continuous
Prior radiotherapy start date	Baseline, Exposure	Year/Month/Day
Prior radiotherapy end date	Baseline, Exposure	Year/Month/Day
Prior ADT	Baseline, Exposure	Yes; No; Unknown/missing
Prior ADT start date	Baseline, Exposure	Year/Month/Day
Prior ADT stop date	Baseline, Exposure	Year/Month/Day
Prior second generation ARPI	Baseline, Exposure	Yes; No; Unknown/missing
Prior second generation ARPI start date	Baseline, Exposure	Year/Month/Day
Prior second generation ARPI end date	Baseline, Exposure	Year/Month/Day
Prior chemotherapy	Baseline, Exposure	Yes; No; Unknown/missing
Prior chemotherapy Start date	Baseline, Exposure	Year/Month/Day
Prior chemotherapy Stop date	Baseline, Exposure	Year/Month/Day
Index treatments		
Talazoparib dose 1	Baseline, Exposure	0.5 mg; 0.35 mg; Other
Talazoparib dose 1 initiation date	Baseline, Exposure	Year/Month/Day
Time between initial prostate diagnosis and talazoparib initiation	Baseline, Exposure	Continuous (days)
Concomitant antineoplastic treatment received	Baseline, Exposure	<drug name>
Concomitant antineoplastic treatment start date	Baseline, Exposure	Year/Month/Day
Concomitant treatment stop date	Baseline, Exposure	Year/Month/Day
Post-index treatments		
Talazoparib dose 2 quantitative	Exposure, Covariate, Outcome	0.35 mg; 0.25mg; 0.1 mg; 0 mg; Other
Talazoparib dose 2 descriptive narrow	Exposure, Covariate, Outcome	Interruption; Reduction; No change
Talazoparib dose 2 descriptive broad	Exposure, Covariate, Outcome	Dose modification; No change
Talazoparib dose 2 initiation date	Exposure, Covariate, Outcome	Year/Month/Day
Talazoparib dose 2 modification reason	Exposure, Covariate, Outcome	Toxicity; Not toxicity; Unknown/missing
Anemia management		
Oral iron supplementation start date	Baseline, Exposure, Covariate	Year/Month/Day

Table 2. Study Variables

Variable	Role	Operational Definition
Oral iron supplementation stop date	Baseline, Exposure, Covariate	Year/Month/Day
Intravenous iron supplementation date	Baseline, Exposure, Covariate	Year/Month/Day
RBC transfusion date	Baseline, Exposure, Covariate	Year/Month/Day
Erythropoiesis-stimulating agent administration date	Baseline, Exposure, Covariate	Year/Month/Day
Lab values (at visit 0, 1, 2, …n)		
eGFR	Baseline, Exposure	Continuous
eGFR date	Baseline, Exposure	Year/Month/Day
ALT	Baseline, Exposure	Continuous
ALT date	Baseline, Exposure	Year/Month/Day
Albumin	Baseline, Exposure	Continuous
Albumin date	Baseline, Exposure	Year/Month/Day
ALP	Baseline, Exposure	Continuous
ALP date	Baseline, Exposure	Year/Month/Day
AST	Baseline, Exposure	Continuous
AST date	Baseline, Exposure	Year/Month/Day
HCO3	Baseline, Exposure	Continuous
HCO3 date	Baseline, Exposure	Year/Month/Day
Total bilirubin	Baseline, Exposure	Continuous
Total bilirubin date	Baseline, Exposure	Year/Month/Day
BUN	Baseline, Exposure	Continuous
BUN date	Baseline, Exposure	Year/Month/Day
Ca	Baseline, Exposure	Continuous
Ca date	Baseline, Exposure	Year/Month/Day
Cl	Baseline, Exposure	Continuous
Cl date	Baseline, Exposure	Year/Month/Day
CK	Baseline, Exposure	Continuous
CK date	Baseline, Exposure	Year/Month/Day
Random glucose	Baseline, Exposure	Continuous
Random glucose date	Baseline, Exposure	Year/Month/Day
LDH	Baseline, Exposure	Continuous
LDH date	Baseline, Exposure	Year/Month/Day
Mg	Baseline, Exposure	Continuous
Mg date	Baseline, Exposure	Year/Month/Day
K	Baseline, Exposure	Continuous
K date	Baseline, Exposure	Year/Month/Day
Total protein	Baseline, Exposure	Continuous
Total protein date	Baseline, Exposure	Year/Month/Day
Na	Baseline, Exposure	Continuous
Na date	Baseline, Exposure	Year/Month/Day
Creatinine	Baseline, Exposure	Continuous
Creatinine date	Baseline, Exposure	Year/Month/Day

Table 2. Study Variables

Variable	Role	Operational Definition
Phosphate	Baseline, Exposure	Continuous
Phosphate date	Baseline, Exposure	Year/Month/Day
Testosterone	Baseline, Exposure	Continuous
Testosterone date	Baseline, Exposure	Year/Month/Day
Folic acid	Baseline, Exposure	Continuous
Folic acid date	Baseline, Exposure	Year/Month/Day
Vitamin B12	Baseline, Exposure	Continuous
Vitamin B12 date	Baseline, Exposure	Year/Month/Day
Urea	Baseline, Exposure	Continuous
Urea date	Baseline, Exposure	Year/Month/Day
PSA	Baseline, Exposure	Continuous
PSA date	Baseline, Exposure	Year/Month/Day
MCV	Baseline, Exposure	Continuous
MCV date	Baseline, Exposure	Year/Month/Day
RBC	Baseline, Exposure	Continuous
RBC date	Baseline, Exposure	Year/Month/Day
HCT	Baseline, Exposure	Continuous
HCT date	Baseline, Exposure	Year/Month/Day
WBC	Baseline, Exposure	Continuous
WBC date	Baseline, Exposure	Year/Month/Day
Differential	Baseline, Exposure	Continuous
Differential date	Baseline, Exposure	Year/Month/Day
PLTS	Baseline, Exposure	Continuous
PLTS date	Baseline, Exposure	Year/Month/Day
Retics	Baseline, Exposure	Continuous
Retics date	Baseline, Exposure	Year/Month/Day
EPO	Baseline, Exposure	Continuous
EPO date	Baseline, Exposure	Year/Month/Day
Lab values principal components	Baseline, Exposure	Continuous
Hemoglobin	Baseline, Exposure, Outcome	Continuous
Hemoglobin date	Baseline, Exposure, Outcome	Year/Month/Day
Hemoglobin change from baseline (g/dL)	Baseline, Exposure, Outcome	Continuous
Symptoms (at visit 0, 1, 2, …n)		
Fatigue	Baseline, Exposure	Yes; No; Unknown/missing
Fatigue visit date	Baseline, Exposure	Year/Month/Day
Shortness of breath	Baseline, Exposure	Yes; No; Unknown/missing
Shortness of breath visit date	Baseline, Exposure	Year/Month/Day
Decreased appetite	Baseline, Exposure	Yes; No; Unknown/missing
Decreased appetite visit date	Baseline, Exposure	Year/Month/Day

Table 2. Study Variables

Variable	Role	Operational Definition
Asthenia	Baseline, Exposure	Yes; No; Unknown/missing
Asthenia visit date	Baseline, Exposure	Year/Month/Day
Dyspnea	Baseline, Exposure	Yes; No; Unknown/missing
Dyspnea visit date	Baseline, Exposure	Year/Month/Day
Dizziness	Baseline, Exposure	Yes; No; Unknown/missing
Dizziness visit date	Baseline, Exposure	Year/Month/Day
Outcomes (at visit 1, 2, …n)		
Anemia status during visit – clinician-documented	Exposure, Outcome	No anemia; Grade 1; Grade 2; Grade 3; Grade 4; Grade 5; Unknown/missing
Anemia status visit date – clinician-documented	Exposure, Outcome	Year/Month/Day
Anemia status during visit – lab-based	Exposure, Outcome	No anemia; Grade 1; Grade 2; Grade 3; Grade 4; Grade 5; Unknown/missing
Anemia status visit date – lab-based	Exposure, Outcome	Year/Month/Day
Outcomes		
Highest-grade anemia narrow	Outcome	No anemia; Grade 1; Grade 2; Grade 3; Grade 4; Grade 5; Unknown/missing The highest-grade anemia observed during the study. Inclusion of variable in analysis depends on its availability in trial data
Highest-grade anemia broad	Outcome	No anemia; Grade 1-2 anemia; Grade ≥3 anemia; Unknown/missing Roll-up of the highest-grade anemia observed during the study.
Highest-grade anemia date	Outcome	Year/Month/Day Date that the highest-grade anemia was observed during the study
Any-grade anemia	Outcome	No anemia; any-grade anemia; Unknown/missing Any anemia observed during the study

Table 2. Study Variables

Variable	Role	Operational Definition
1st worse-grade anemia date	Outcome	Year/Month/Day Earliest date that the anemia status during the study is worse (by any increase in grade) than baseline anemia status
1st Grade ≥3 anemia date	Outcome	Year/Month/Day Earliest date that the anemia status during the study is Grade 3 or worse

Table 2. Study Variables

Variable	Role	Operational Definition
Post-index pre-dose modification anemia shift summary	Outcome	None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3 Variable used to derive early dose pattern. Shift is defined as moving between the broad anemia categories: No anemia; Grade 1/2; Grade ≥3. If no dose modification observed during study, take 1st shift in anemia status after index. If no anemia shift occurred during study, value is “None to none” or “Grade 1-2 to Grade 1-2" depending on the starting dose. If dose modification is observed, take the anemia shift between baseline and the dose modification date. If no shift occurred on dose modification date, value is “None to none” or “Grade 1-2 to Grade 1-2" depending on the starting dose. *Note that the operational definition for this variable may be updated upon reviewing trial data and determining whether dose modification typically occurs at the same visit or a subsequent visit of a triggering anemia event.*

Table 2. Study Variables

Variable	Role	Operational Definition
Talazoparib first dose modification descriptive narrow (This variable was labeled "Talazoparib dose 2 descriptive narrow" in the protocol but renamed in the SAP for clarity)	Exposure, Covariate, Outcome	Interruption; Reduction; No change Variable used to derive early dose pattern. Earliest observed difference in talazoparib dose compared to baseline. If dose becomes 0 mg, value is "Interruption". If dose is lower than baseline but not 0 mg, value is "Reduction". If no dose change is observed during the study, value is "No change".
Talazoparib first dose modification descriptive broad (This variable was labeled "Talazoparib dose 2 descriptive broad" in the protocol but renamed in the SAP for clarity)	Exposure, Covariate, Outcome	Dose modification; No change Rolled up version of previous variable. "Interruption" and "Reduction" roll up as "Dose modification"
Talazoparib first dose modification date (This variable was labeled "Talazoparib dose 2 initiation date" in the protocol but renamed in the SAP for clarity)	Exposure, Covariate, Outcome	Year/Month/Day Date of the earliest observed difference in talazoparib dose during the study compared to baseline.
Talazoparib first dose modification date – prolonged, also referred to as "dose deviation" (This is an alternate definition for "Talazoparib first dose modification date")	Exposure, Covariate, Outcome	Year/Month/Day Date of receipt of first dose that was different from the initiating dose and that was sustained for 7 days or longer, or if dose deviation period was <7 days, was explicitly stated as a dose modification due to AE.

Table 2. Study Variables

Variable	Role	Operational Definition
Early dose pattern narrow	Outcome	1; 2a; 2b; 3; 4a; 4b; 5; 6a; 6b; 7; 8a; 8b; 9; 10a; 10b This is a derived variable describing initial post-index anemia status up to 1st dose modification or study end, whichever is first. The variable is derived based on the algorithm described in Table 3 which includes the variables "Post-index pre-dose modification anemia shift summary" and "Talazoparib first dose modification descriptive narrow".
Early dose pattern broad	Outcome	1; 2; 3; 4; 5; 6; 7; 8; 9; 10 This is a derived variable describing initial post-index anemia status up to 1st dose modification or study end, whichever is first. The variable is derived based on the algorithm described in Table 3 which includes the variables "Post-index pre-dose modification anemia shift summary" and "Talazoparib first dose modification descriptive broad".
Anemia status at first dose modification	Outcome	No anemia; Grade 1; Grade 2; Grade 3; Grade 4; Grade 5; Unknown/missing The anemia status observed at the date of the first dose modification. Inclusion of variable in analysis depends on its availability in trial data

Table 2. Study Variables

Variable	Role	Operational Definition
Talazoparib first dose modification due to Grade 1-2 anemia (This variable was labeled "Talazoparib 1st dose after Grade 1-2 anemia" in the protocol but renamed in the SAP for clarity)	Exposure, Covariate, Outcome	Yes; No; NA Among patients with "Talazoparib first dose modification descriptive broad" = "Dose modification", "Yes" if "Anemia status at first dose modification" was Grade 1 or 2. "No" if "Anemia status at first dose modification" was not Grade 1 or 2. "NA" if "Talazoparib first dose modification descriptive broad" = "No change" *Note that the operational definition for this variable may be updated upon reviewing trial data and determining whether dose modification typically occurs at the same visit or a subsequent visit of a triggering anemia event.*

Table 2. Study Variables

Variable	Role	Operational Definition
Talazoparib first dose modification due to Grade ≥3 anemia (This variable was labeled "Talazoparib 1st dose after Grade 3/4 anemia" in the protocol but renamed in the SAP for clarity)	Exposure, Covariate, Outcome	Yes; No; NA Among patients with "Talazoparib first dose modification descriptive broad" = "Dose modification", "Yes" if "Anemia status at first dose modification" was Grade 3 or 4. "No" if "Anemia status at first dose modification" was not Grade 3 or 4. "NA" if "Talazoparib first dose modification descriptive broad" = "No change" *Note that the operational definition for this variable may be updated upon reviewing trial data and determining whether dose modification typically occurs at the same visit or a subsequent visit of a triggering anemia event.*
Early hemoglobin change	Outcome	Continuous Difference in hemoglobin (g/dL) between baseline and first follow-up visit divided by difference in days.
Pre-dose modification hemoglobin change	Outcome	Continuous (NA if no dose modification) Among patients with "Talazoparib first dose modification descriptive broad" = "Dose modification", difference in hemoglobin (g/dL) between baseline and dose modification date divided by difference in days.

Table 2. Study Variables

Variable	Role	Operational Definition
Post-dose modification hemoglobin change 1 (Hemoglobin from dose modification date to following visit. g/dL per day)	Outcome	Continuous (NA if no dose modification) Among patients with "Talazoparib first dose modification descriptive broad" = "Dose modification", difference in hemoglobin (g/dL) between dose modification date and 1st visit after dose modification, divided by difference in days. Note that specifics on window defining status 1 and status 2 (e.g. number of weeks post dose-modification) to be determined upon access to data.
Post-dose modification hemoglobin change 2 (Hemoglobin from dose modification date to 2 visits later. g/dL per day)	Outcome	Continuous (NA if no dose modification) Among patients with "Talazoparib first dose modification descriptive broad" = "Dose modification", difference in hemoglobin (g/dL) between dose modification date and 2nd visit after dose modification, divided by difference in days. Note that specifics on window defining status 1 and status 2 (e.g. number of weeks post dose-modification) to be determined upon access to data.

Table 2. Study Variables

Variable	Role	Operational Definition
Post-dose modification anemia status 1	Outcome	Improved; Unchanged; Worsened; NA Anemia status at the 1st visit after dose modification among patients with "Talazoparib first dose modification descriptive broad" = "Dose modification". If anemia status is any grade better than at the time of dose modification, value is "Improved". If anemia status is unchanged from the time of dose modification, value is "Unchanged". If anemia status is any grade worse than at the time of dose modification, value is "Worsened". If patient did not have any dose modification, value is "NA". Note that specifics on availability of granular anemia grade and window defining status 1 and status 2 (e.g. number of weeks post dose-modification) to be determined upon access to data.

Table 2. Study Variables

Variable	Role	Operational Definition
Post-dose modification anemia status 2	Outcome	Improved; Unchanged; Worsened; NA Anemia status at the 2nd visit after dose modification among patients with "Talazoparib first dose modification descriptive broad" = "Dose modification". If anemia status is any grade better than at the time of dose modification, value is "Improved". If anemia status is unchanged from the time of dose modification, value is "Unchanged". If anemia status is any grade worse than at the time of dose modification, value is "Worsened". If patient did not have any dose modification, value is "NA". Note that specifics on availability of granular anemia grade and window defining status 1 and status 2 (e.g. number of weeks post dose-modification) to be determined upon access to data.
1st post-dose modification anemia improvement date	Outcome	Year/Month/Day Earliest date that the anemia status is better (by any increase in grade) than anemia status at first dose modification among patients with "Talazoparib first dose modification descriptive broad" = "Dose modification".
Date of death	Outcome	Year/Month/Day
Date of loss to follow-up	Outcome	Year/Month/Day

Table 2. Study Variables

Variable	Role	Operational Definition
Time to dose modification	Outcome	Followed from the date of talazoparib initiation until the date of talazoparib treatment modification, or censored at the first of: (1) death; (2) date of last contact; or (3) study end date
Time to Grade ≥3 anemia	Outcome	Followed from the date of talazoparib initiation until the date of Grade ≥3 anemia, or censored at the first of: (1) dose modification; (2) death, (3) date of last contact; or (4) study end date (In instances where RBC transfusion occurs without evidence of anemia, RBC transfusion will be treated as a censoring event.)
Time to worse-grade anemia	Outcome	Followed from the date of talazoparib initiation until the date of worse-grade anemia compared to baseline, or censored at the first of: (1) dose modification; (2) death, (3) date of last contact; or (4) study end date (In instances where RBC transfusion occurs without evidence of anemia, RBC transfusion will be treated as a censoring event.)

Table 2. Study Variables

Variable	Role	Operational Definition
Time to anemia improvement	Outcome	Followed from the date of 1st dose modification until the date of anemia improvement, or censored at the first of: (1) subsequent dose modification; (2) death; (3) date of last contact; or (4) study end date (In instances where RBC transfusion occurs without evidence of change in anemia status, RBC transfusion will be treated as a censoring event.)

Table 3 further defines “early dose pattern narrow” and “early dose pattern broad” as derived variables based on the values of variables “post-index pre-dose modification anemia shift” and “Talazoparib dose 2 descriptive” variables. Two versions of early dose patterns are generated, one based on the broad dose modification definition and another based on the narrow dose deviation definition (as described in 9.4 Variables) and used accordingly for subsequent descriptive analyses.

Table 3. Early dose patterns for patients initiating talazoparib.

Post-index pre-dose modification/deviation anemia shift	Talazoparib dose 2 descriptive narrow	Talazoparib dose 2 descriptive broad	Early dose pattern narrow	Early dose pattern broad
None to none	No change	No change	1	1
None to none	Interruption	Dose modification/deviation	2a	2
None to none	Reduction	Dose modification/deviation	2b	2
None to Grade 1-2 anemia	No change	No change	3	3
None to Grade 1-2 anemia	Interruption	Dose modification/deviation	4a	4
None to Grade 1-2 anemia	Reduction	Dose modification/deviation	4b	4

Table 3. Early dose patterns for patients initiating talazoparib.

Post-index pre-dose modification/deviation anemia shift	Talazoparib dose 2 descriptive narrow	Talazoparib dose 2 descriptive broad	Early dose pattern narrow	Early dose pattern broad
None to Grade ≥3 anemia	No change	No change	5[a]	5
None to Grade ≥3 anemia	Interruption	Dose modification/deviation	6a	6
None to Grade ≥3 anemia	Reduction	Dose modification/deviation	6b[a]	6
Grade 1-2 to Grade 1-2 anemia	No change	No change	7	7
Grade 1-2 to Grade 1-2 anemia	Interruption	Dose modification/deviation	8a	8
Grade 1-2 to Grade 1-2 anemia	Reduction	Dose modification/deviation	8b	8
Grade 1-2 to Grade ≥3 anemia	No change	No change	9[a]	9
Grade 1-2 to Grade ≥3 anemia	Interruption	Dose modification/deviation	10a	10
Grade 1-2 to Grade ≥3 anemia	Reduction	Dose modification/deviation	10b[a]	10

[a]*Note that certain patterns are expected to have zero counts in the data due to trial protocol mandating dose interruption upon observing Grade ≥3 anemia*

9.5. Data sources and measurement

This study uses the existing TALAPRO-2 trial data of mCRPC patients allocated to the talazoparib + enzalutamide treatment arm and included in the safety analysis. Data for all study variables were originally collected prospectively using protocol-specified case report forms and study procedures. Definitions, collection methods, schedules of assessment, and grading criteria for study variables were consistent with the TALAPRO-2 protocol and associated study documentation. Because this study represents a secondary analysis of an existing clinical trial dataset, no additional outcome adjudication, data review or abstraction were conducted. The TALAPRO-2 database was generated through GCP-compliant clinical trial conduct with protocol-defined data collection, monitoring, and quality control procedures. Additional details regarding collection and measurement of study variables are provided in the TALAPRO-2 protocol (Appendix 8.2).

9.6. Bias

Several biases relating to the clinical trial data source and the application of machine learning (ML) methods are relevant to this study.

First, although ML approaches are often described as being less reliant on parametric assumptions compared with traditional regression-based models, ML models may be more prone to overfitting due to their flexibility. As a result, models may capture noise or data-specific patterns, leading to optimistic performance estimates even when internal validation such as cross-validation is applied[20,21].

Second, ML models may reflect and potentially amplify biases present in the underlying data[22]. For example, if certain patient subgroups are underrepresented or differ systematically in data completeness or measurement frequency, model performance may vary across these groups. This may result in differential predictive accuracy and reduced reliability for specific subpopulations.

Third, inherent features of the clinical trial design may introduce biases that influence both descriptive analyses and model development[21]. Clinical trial populations are selected based on protocol-defined inclusion and exclusion criteria and may not represent the full spectrum of patients encountered in routine practice. Additionally, standardized treatment protocols, including predefined dose modification rules and adverse event assessment using CTCAE criteria, may result in more homogeneous data patterns than those observed in real-world settings. These structured patterns may be learned by the model and may not fully generalize outside of the trial context.

These sources of bias are addressed through study design and analysis strategies to the extent possible, including the evaluation of multiple ML methods and internal validation via cross-validation.

9.7. Study Size

This is a NI study with no *a priori* hypotheses specified; therefore, sample size calculations are not applicable. TALAPRO-2 included two cohorts: Cohort 1, ie, “all-comers” regardless of homologous recombination repair (HRR) gene alteration status, and Cohort 2, ie, “HRR-deficient” patients who were enrolled for Cohort 2 plus patients already enrolled in Cohort 1 who were HRR-deficient. Data from the non-overlapping set of patients among the two cohorts are used for this study, including approximately 398 patients from Cohort 1 and 115 patients from Cohort 2.

9.8. Data transformation

Detailed methodology for data transformations, particularly complex transformations (eg, many raw variables used to derive an analytic variable), are documented in the statistical analysis plan (SAP), which is dated, filed and maintained by the sponsor (Appendix 4).

9.9. Statistical methods

9.9.1. Main summary measures

To address Primary Objective 1 description of patient characteristics, baseline patient characteristics (demographic, clinical, treatment history, baseline anemia) are summarized across the overall study cohort and by strata defined as the highest-grade anemia category (any, Grade 1-2, Grade ≥3) experienced during the study. Total numbers in each stratum are shown. Variables specified under “Demographics”, “Clinical characteristics”, “Pre-index treatments”, and “Index treatments” sections of Table 2 defined as continuous variables (e.g. age at treatment initiation, body weight, number of bone metastases at screening) are summarized with mean, standard deviation (SD), median (Q1 – Q3), min and max. Variables defined as categorical variables (e.g. race, ethnicity, geographic region, Gleason score) are summarized as number (n) and percent (%).

To address Primary Objective 1 description of dosing patterns, patients belonging to each dosing pattern category (Table 3) are counted, and baseline patient characteristics are summarized by strata defined as the dosing pattern categories. Variables are summarized as continuous or categorical as described above. In addition, the proportion of patients experiencing anemia during the study (none, any, Grade 1-2, Grade ≥3) are summarized by dose pattern categories. Finally, time to dose modification are summarized for the overall study cohort and stratified by initial anemia status and highest-grade anemia status during the study using Kaplan-Meier survival analyses.

To address Primary Objective 1 description of hemoglobin trajectories, the proportion of patients who improved, remained the same, or worsened in anemia severity in the following visit among patients who experienced dose modification due to an anemia event are summarized as number (n) and percent (%). This summary is performed for the overall study cohort and stratified by initial dose, and dose modification is defined as dose interruption or reduction after any anemia in general and stratified by Grade 1-2 and Grade ≥3 anemia-related modification. In addition, the rate of hemoglobin change before and after dose modification is summarized, with stratification by initial dose for the former and stratification by anemia severity triggering dose modification for the latter. Time to anemia events (time to Grade ≥3 anemia, time to worse-grade anemia) are assessed using Kaplan-Meier survival analyses. Finally, time to anemia improvement after dose modification among patients who experienced dose modification is summarized using Kaplan-Meier survival analyses.

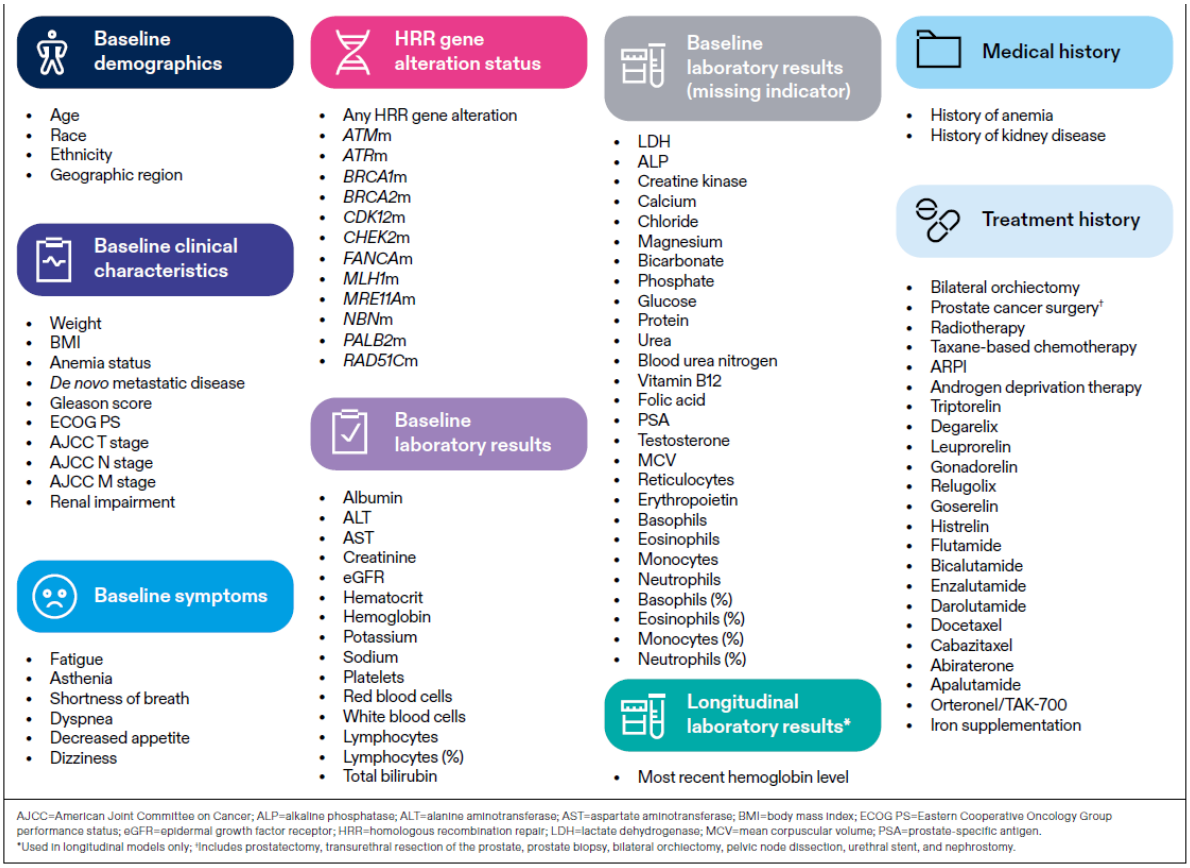
Exploratory Objective 1 is assessed similarly as Objective 1, with descriptive statistics used to summarize baseline patient characteristics (demographic, clinical, treatment history, lab values) overall and stratified by subsequent anemia status; and to summarize the rate of hemoglobin change after study initiation. Time to anemia is assessed using Kaplan-Meier survival analyses. No dose modification-related concepts are assessed for Exploratory Objective 1 since dosing is not applicable for the control arm.

9.9.2. Main statistical methods

For Objectives 2 and 3, a variety of machine learning (ML) models including LASSO Cox regression, extreme gradient boosting, and survival support vector machine, were evaluated to compare the predictive performance of candidate models. Model discrimination was assessed using dynamic area under the curve (AUC) as the primary performance metric.

Because the objective of the study was to descriptively compare candidate approaches, no single model or minimum AUC threshold was specified a priori. Results are presented for all evaluated models; however, models with the highest observed AUC values were considered the best-performing models and are emphasized in the interpretation of study findings. Three-fold cross-validation was performed for internal validation and hyperparameter tuning. Specifically, the dataset was randomly split into three equal-sized folds (stratified by anemia outcomes). In each iteration, two folds were used as training data to optimize hyperparameters for each ML model, while the remaining fold served as validation data to compute AUCs. To ensure robust statistical power, categories within categorical variables with counts below five were combined with other categories until all counts reached a minimum of five. All variables labeled as “Exposure” and “Covariate” in the “Role” column of Table 2 and summarized in Figure 2 are considered as features for building the models.

Figure 2. Variables included as candidate predictors during machine learning model development



AJCC=American Joint Committee on Cancer; ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BMI=body mass index; ECOG PS=Eastern Cooperative Oncology Group performance status; eGFR=epidermal growth factor receptor; HRR=homologous recombination repair; LDH=lactate dehydrogenase; MCV=mean corpuscular volume; PSA=prostate-specific antigen.
*Used in longitudinal models only; †Includes prostatectomy, transurethral resection of the prostate, prostate biopsy, bilateral orchiectomy, pelvic node dissection, urethral stent, and nephrostomy.

9.9.3. Missing values

When missing data occurs, no imputation is made, and all statistics are calculated with non-missing values. Counts and percentages of missing values are presented in the tables where applicable. For purposes of predictive modeling, baseline labs without missing values were treated as continuous predictor variables whereas baseline labs with missing values were treated as binary predictor variables (available, not available) to allow the greatest retention of granularity for the former and cohort size for the latter. The complete-case approach only including baseline labs with <5% missing data was also assessed but not performed as the primary analysis due to the reduced sample size of 440 patients.

9.9.4. Sensitivity analyses

To address Primary Objectives 2 and 3, the primary modeling approach does not include blood concentration of talazoparib (Cavg,t) as a feature because this variable is only measured in the trial setting during pharmacokinetic analyses and not readily available during routine clinical practice. However, as sensitivity analyses, additional models do include Cavg,t as a feature to provide additional knowledge on its importance when predicting anemia (Objective 2) in the trial setting, as prespecified in the SAP.

9.9.5. Amendments to the statistical analysis plan

An amendment was made to the SAP on 15 December 2025 with additional clarifications and definitions that were not specified in the protocol or original version of the SAP. The updates and rationale are described in Table 4.

Table 4. SAP amendment changes and rationale

Change	Rationale
Clarified existing variable definition: RBC transfusion as a censoring event	To account for rare instances where RBC transfusion occurs without evidence of anemia
Clarified existing variable definition: "anemia status during visit"	To document additional details made available in the trial data dictionary upon “start of data collection” window
Clarified existing variable definition: "dose modification"	Dose modification was not defined in detail previously. This provided further granularity
Defined additional variables that fall under the broad categories of potential predictors to include in the model (medical comorbidities, treatment history) in the original SAP Section “4.3 Variables” but were not explicitly listed in the original SAP “Table 1 Study Variables”	All variables that are considered within the categories of medical comorbidities and treatment history as available in the trial study were to be included. Therefore, "Moderate renal impairment" and "Prior hormonal therapy" were included in the assessment.
Added the qualifier “as available” in the updated SAP Table 1 description to account for any variables not assessed due to data unavailability	Some candidate predictors were included in the original protocol and SAP “Table 1 Study Variables” but were not available in the subsequently provided trial dataset and were therefore not assessed.
Updated title of Table Shell Table 1 to reflect the corresponding analyses stated in Section 4.7.2 Primary Analyses which were omitted in the original SAP. SAP “Table 1 Study Variables”: corrected BMI units from “kg/m3” to “kg/m2”	Administrative minor edits/typo in SAP

Note: The abovementioned changes were not influenced by any analyses performed after start of the analysis period

9.10. Quality control

Data used in this study were obtained from the TALAPRO-2 Phase 3 clinical trial database and were originally collected prospectively according to protocol-defined procedures. Data quality and integrity were maintained through the quality assurance, monitoring, and data management processes implemented for the parent clinical trial, including source data verification, query resolution, review of CRF data against source documents, and audit and inspection activities, as described in the TALAPRO-2 protocol. The parent study was conducted in accordance with Good Clinical Practice (GCP) requirements, and data coding, recording, and management followed trial-specific standards and procedures. Prior to the current secondary analysis, study data underwent cleaning, review, and validation as part of the TALAPRO-2 database management process. No additional data collection, transcription, abstraction, or validation activities were performed for the present study. Further details regarding trial conduct, monitoring, data management, and quality assurance procedures are provided in the TALAPRO-2 protocol. Laboratory assessments were performed as part of the TALAPRO-2 clinical trial using protocol-specified procedures at qualified study laboratories; additional details are provided in the parent trial documentation.

Quality control (QC) checks are performed on all programming, data tables, and reports generated in the course of this research. QC review and documentation of reports were conducted by the Global Medical Epidemiology Technical Review Committee to assure that the deliverable met defined expectations for the six dimensions of quality: Best Practice, Timeliness, Accuracy, Completeness, Clarity and Relevance. QC findings and documentation of remedial action are maintained. Storage of programming, data, and reports are carried out per standard procedures, including being uploaded to the Global Document Management System (GDMS).

A second programmer independently checked the SAS program and outputs and make sure that they were consistent with the protocol and tables in the study report. The quality control (QC) form was signed and documented.

9.11. Protection of human subjects

Subject information and consent

Not Applicable

Independent Ethics Committee (IEC)/Institutional Review Board (IRB)

The original TALAPRO-2 trial was governed by an IEC/IRB-approved protocol. The current study utilized existing data from the TALAPRO-2 clinical trial and did not involve additional subject contact, intervention, or collection of identifiable personal data. Because the study used deidentified data, it did not constitute human subjects research under the Common Rule and thus did not require Independent Ethics Committee (IEC)/ Institutional Review Board (IRB) review, nor required a waiver.

Ethical conduct of the study

The study was conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and followed generally accepted research practices

described in Guidelines for Good Pharmacoepidemiology Practices (GPP) [23], European Medicines Agency (EMA) European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Guide on Methodological Standards in Pharmacoepidemiology [24], and Good practices for real-world data studies of treatment and/or comparative effectiveness: Recommendations from the joint International Society for Pharmacoeconomics and Outcomes Research (ISPOR)–International Society for Pharmacoepidemiology (ISPE) Special Task Force on real-world evidence in health care decision making [25].

10. RESULTS

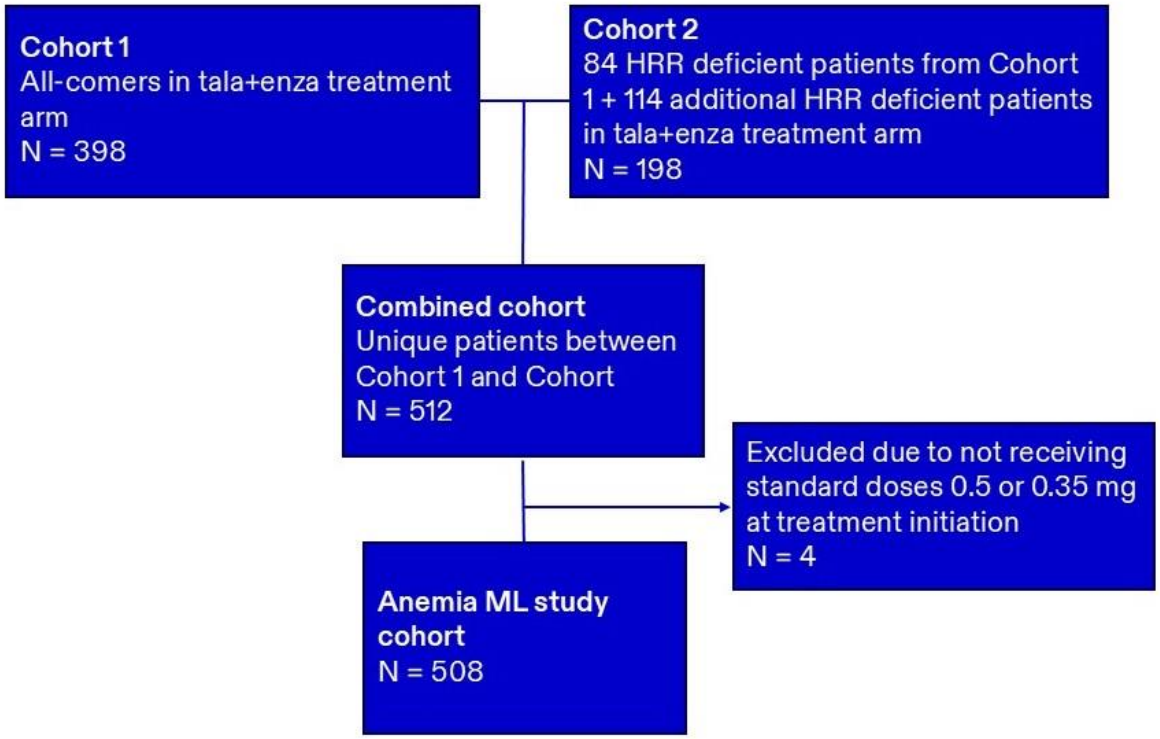
10.1. Participants

The TALAPRO-2 trial consisted of two partially overlapping cohorts of patients treated with talazoparib plus enzalutamide (Figure 3).

Cohort 1, i.e. “all-comers”, comprised 398 patients of any homologous recombination repair (HRR) mutation status who were randomized to the talazoparib treatment arm, as previously described in the primary TALAPRO-2 trial publications[1]. Cohort 2, i.e. “HRR-deficient” patients, comprised 198 patients with HRR-deficient tumors, including 84 HRR-deficient patients already enrolled in Cohort 1, plus an additional 114 HRR-deficient patients separately enrolled for Cohort 2.

There were 512 unique, non-overlapping patients treated with talazoparib across Cohorts 1 and 2. Of these, four patients did not receive a standard talazoparib starting dose of 0.5 mg or 0.35 mg at treatment initiation and were therefore excluded, resulting in a final analytic cohort of 508 patients. All 508 patients met the inclusion criteria for the present non-interventional study and were included in the descriptive analyses for Objective 1 and predictive modeling for anemia risk in Objective 2. A total of 257 patients were subsequently identified (as reported in section 10.3) as those who experienced dose deviation and included in predictive modeling for anemia recovery in Objective 3. No additional subject exclusions, withdrawals, or losses to follow-up were applied for the three respective objectives. Because this was a secondary analysis of an existing clinical trial database, all available follow-up data through the applicable TALAPRO-2 data cutoffs were included.

Figure 3. Study Cohort



10.2. Descriptive data

Study Objective 1 - Describe patient characteristics, dosing patterns and hemoglobin trajectories with respect to anemia events

Baseline demographic, clinical, treatment history, and laboratory characteristics of talazoparib-treated patients in TALAPRO-2 are shown for patients stratified by the highest grade treatment-emergent anemia experienced during the study (no anemia; Grade 1-2; Grade ≥3) in Table 5A; and stratified by any anemia shift experienced prior to dose deviation (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3) in Table 5B. Baseline characteristics stratified by any treatment-emergent anemia (no anemia; any-grade anemia) are shown in Appendix 8.1 **Error! Reference source not found.**. Variables assessed as potential predictors, including baseline anemia status, renal function, ECOG performance status, treatment history, and laboratory measures, are presented within the corresponding tables. Missing data for each variable of interest are reported in the respective tables.

Among the 508 talazoparib-treated patients included in the study, 231 patients (45.5%) experienced Grade 3 or higher anemia at any time during follow-up (regardless of whether anemia was preceded by dose deviation) while 168 patients (33.1%) experienced no treatment-emergent anemia. Baseline characteristics differed between patients who

experienced Grade ≥3 anemia and those who did not experience treatment-emergent anemia (Table 5A).

Patients who developed Grade ≥3 anemia were older at treatment initiation (median age 73.0 years; Q1–Q3: 67.0–77.0) than patients who experienced no treatment-emergent anemia (median age 68.0 years; Q1–Q3: 63.0–74.0). Patients with Grade ≥3 anemia were also more frequently of Asian race (n=80, 34.6% vs n=27, 16.1%) and enrolled from Asian countries (N=78, 33.8% vs N=26, 15.5%) compared with patients who experienced no treatment-emergent anemia.

In addition, patients who experienced Grade ≥3 anemia had lower baseline body weight (median 76.6 kg [Q1–Q3: 67.0–87.2]) compared with patients who experienced no treatment-emergent anemia (median 85.0 kg [Q1–Q3: 76.3–97.9]). A prior medical history of anemia was more common among patients with Grade ≥3 anemia (n=36, 15.6%) than among those with no anemia (n=10, 6.0%). Baseline anemia was also more common among patients who later developed Grade ≥3 anemia (52.8% and 7.8% had baseline Grade 1 and Grade 2 anemia, respectively), compared to patients who experienced no treatment-emergent anemia (36.3% and 1.8% had baseline Grade 1 and Grade 2 anemia, respectively). Relatedly, median baseline hemoglobin was lower in patients who developed Grade ≥3 anemia (127 g/L [Q1–Q3: 116–136]) compared with those who experienced no treatment-emergent anemia (135 g/L [Q1–Q3: 126–141]). Other baseline hematology parameters also observed to be lower in patients who developed Grade ≥3 anemia compared to those with no treatment-emergent anemia include HCT (median 34.8% vs 37.7%) and RBC (4.15 vs 4.47 × 10^{12}/L).

Patients who experienced Grade ≥3 anemia were less likely to have been treated with taxane-based chemotherapy than those who experienced no treatment-emergent anemia (20.8% vs 32.1%, respectively). Other baseline treatment history was broadly comparable between patients with Grade ≥3 anemia and those with no treatment-emergent anemia, with no consistent or clinically meaningful differences observed (Table 5A).

Table 5B summarizes baseline patient characteristics with respect to anemia patterns observed prior to dose deviation or the end of the study, whichever occurs first. Among the 508 talazoparib-treated patients included in the study, 104 patients (20.5%) had no baseline anemia and experienced no anemia shift (i.e. none to none), and 168 patients (33.1%) had baseline anemia and experienced no change in anemia status (Grade 1-2 to Grade 1-2), for a total of 272 patients (53.5%) that experienced no worsening anemia prior to dose change (or the end of the study in the absence of dose change). Patients with no baseline anemia that later experienced Grade 1-2, and Grade ≥3 anemia composed of 87 (17.1%) and 59 (11.6%) patients, respectively, out of the total study cohort. Finally, 90 patients (17.7%) had baseline anemia and subsequently experienced Grade ≥3 anemia.

Patients with no baseline anemia and no subsequent anemia (“none to none”; n=104, 20.5%) consistently had the youngest median age (68.0 years [Q1–Q3: 63.0–74.0]), the lowest proportion of patients of Asian race (14/104, 13.5%) and enrollment from Asian countries (13/104, 12.5%), the highest baseline body weight (median 87.8 kg [Q1–Q3: 77.8–98.0]), the lowest prevalence of prior anemia history (1/104, 1.0%), and among the highest median baseline hemoglobin (139 g/L [Q1–Q3: 135–143]) compared with all other groups (Table 5B). Patients from the other “non-worsening” group (“Grade 1-2 to Grade 1-2”)

similarly demonstrated higher baseline body weight (79.0 kg [Q1–Q3: 69.2–89.8]) when compared with the "worsening" groups "none to Grade ≥3," and "Grade 1-2 to Grade ≥3"; however, this group did not consistently demonstrate younger age, lower representation of Asian race or Asian enrollment, lower prevalence of prior anemia history, or higher baseline hemoglobin relative to the worsening groups.

Table 5A. Baseline characteristics of talazoparib-treated patients in TALAPRO-2, stratified by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3) experienced during the study

	No treatment-emergent anemia	Grade 1-2 anemia	Grade ≥3 anemia	Overall
	(N=168)	(N=109)	(N=231)	(N=508)
Demographics				
Age, Median [Q1,Q3]	68.0 [63.0,74.0]	73.0 [68.0,78.0]	73.0 [67.0,77.0]	71.0 [66.0,76.0]
Race, n (%)				
White	121 (72.0%)	69 (63.3%)	133 (57.6%)	323 (63.6%)
Black or African American	7 (4.2%)	2 (1.8%)	6 (2.6%)	15 (3.0%)
Asian	27 (16.1%)	32 (29.4%)	80 (34.6%)	139 (27.4%)
Native Hawaiian or other Pacific Islander	2 (1.2%)	0 (0%)	1 (0.4%)	3 (0.6%)
Not Reported	11 (6.5%)	6 (5.5%)	11 (4.8%)	28 (5.5%)
Ethnicity, n (%)				
Hispanic or Latino	21 (12.5%)	10 (9.2%)	26 (11.3%)	57 (11.2%)
Not Hispanic or Latino	137 (81.5%)	90 (82.6%)	194 (84.0%)	421 (82.9%)
Not reported	10 (6.0%)	9 (8.3%)	11 (4.8%)	30 (5.9%)
Region, n (%)				
1) North America	27 (16.1%)	14 (12.8%)	29 (12.6%)	70 (13.8%)
2) European Union/GBR	78 (46.4%)	48 (44.0%)	76 (32.9%)	202 (39.8%)
3) Asia	26 (15.5%)	32 (29.4%)	78 (33.8%)	136 (26.8%)
4) Rest of the world	37 (22.0%)	15 (13.8%)	48 (20.8%)	100 (19.7%)
Cohort, n (%)				
1	100 (59.5%)	62 (56.9%)	150 (64.9%)	312 (61.4%)
2	68 (40.5%)	47 (43.1%)	81 (35.1%)	196 (38.6%)
Clinical characteristics				
Weight, Median [Q1,Q3]	85.0 [76.3,97.9]	79.0 [71.0,93.0]	76.6 [67.0,87.2]	80.0 [70.6,92.9]
BMI, Median [Q1,Q3]	28.1 [25.8,31.0]	27.2 [24.2,30.7]	26.1 [23.8,28.9]	27.1 [24.2,30.2]
Missing	0 (0%)	0 (0%)	2 (0.9%)	2 (0.4%)
Anemia Status, n (%)				
0	104 (61.9%)	55 (50.5%)	91 (39.4%)	250 (49.2%)
1	61 (36.3%)	53 (48.6%)	122 (52.8%)	236 (46.5%)
2	3 (1.8%)	1 (0.9%)	18 (7.8%)	22 (4.3%)

Table 5A. Baseline characteristics of talazoparib-treated patients in TALAPRO-2, stratified by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3) experienced during the study

	No treatment-emergent anemia	Grade 1-2 anemia	Grade ≥3 anemia	Overall
	(N=168)	(N=109)	(N=231)	(N=508)
Prior History Anemia	10 (6.0%)	15 (13.8%)	36 (15.6%)	61 (12.0%)
Prior History Kidney Disease	5 (3.0%)	3 (2.8%)	5 (2.2%)	13 (2.6%)
Renal Impairment, n (%)				
Mild/Normal (>=60)	144 (85.7%)	98 (89.9%)	198 (85.7%)	440 (86.6%)
Moderate (30-59)	18 (10.7%)	9 (8.3%)	25 (10.8%)	52 (10.2%)
Not reported	6 (3.6%)	2 (1.8%)	8 (3.5%)	16 (3.1%)
Gleason score category, n (%)				
High [8-10]	124 (73.8%)	71 (65.1%)	164 (71.0%)	359 (70.7%)
Low [2-7]	41 (24.4%)	37 (33.9%)	61 (26.4%)	139 (27.4%)
Not reported	3 (1.8%)	1 (0.9%)	6 (2.6%)	10 (2.0%)
Bone metastases at baseline, n (%)	137 (81.5%)	95 (87.2%)	200 (86.6%)	432 (85.0%)
Prostate cancer diagnosis year, Median [Q1,Q3]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]
Baseline bone metastases number, Median [Q1,Q3]	4.00 [3.00,5.00]	3.00 [2.00,5.00]	4.00 [3.00,5.00]	4.00 [3.00,5.00]
De novo metastatic disease, n (%)	90 (53.6%)	45 (41.3%)	114 (49.4%)	249 (49.0%)
Somatic HRR mutation, n (%)				
1) DDR Deficient	69 (41.1%)	47 (43.1%)	81 (35.1%)	197 (38.8%)
2) Non-DDR Deficient	69 (41.1%)	39 (35.8%)	95 (41.1%)	203 (40.0%)
3) Unknown	30 (17.9%)	23 (21.1%)	55 (23.8%)	108 (21.3%)
Deficient ATM	13 (7.7%)	10 (9.2%)	24 (10.4%)	47 (9.3%)
Deficient ATR	1 (0.6%)	1 (0.9%)	1 (0.4%)	3 (0.6%)
Deficient BRCA1	2 (1.2%)	3 (2.8%)	5 (2.2%)	10 (2.0%)
Deficient BRCA2	21 (12.5%)	16 (14.7%)	23 (10.0%)	60 (11.8%)
Deficient CDK12	13 (7.7%)	7 (6.4%)	17 (7.4%)	37 (7.3%)
Deficient CHEK2	14 (8.3%)	7 (6.4%)	14 (6.1%)	35 (6.9%)
Deficient FANCA	2 (1.2%)	1 (0.9%)	1 (0.4%)	4 (0.8%)
Deficient MLH1	2 (1.2%)	3 (2.8%)	4 (1.7%)	9 (1.8%)
Deficient NBN	6 (3.6%)	1 (0.9%)	1 (0.4%)	8 (1.6%)
Deficient PALB2	2 (1.2%)	4 (3.7%)	3 (1.3%)	9 (1.8%)
Deficient RAD51C	1 (0.6%)	1 (0.9%)	0 (0%)	2 (0.4%)
ECOG, n (%)				
0	113 (67.3%)	69 (63.3%)	143 (61.9%)	325 (64.0%)
1	55 (32.7%)	40 (36.7%)	88 (38.1%)	183 (36.0%)
Treatment history				

Table 5A. Baseline characteristics of talazoparib-treated patients in TALAPRO-2, stratified by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3) experienced during the study

	No treatment-emergent anemia	Grade 1-2 anemia	Grade ≥3 anemia	Overall
	(N=168)	(N=109)	(N=231)	(N=508)
Bilateral orchiectomy	7 (4.2%)	6 (5.5%)	13 (5.6%)	26 (5.1%)
Prior prostate cancer surgery[a]	126 (75.0%)	83 (76.1%)	188 (81.4%)	397 (78.1%)
Prior radiation therapy	36 (21.4%)	25 (22.9%)	52 (22.5%)	113 (22.2%)
Prior hormonal therapy	8 (4.8%)	3 (2.8%)	20 (8.7%)	31 (6.1%)
Androgen deprivation therapy at baseline	162 (96.4%)	105 (96.3%)	220 (95.2%)	487 (95.9%)
Triptorelin	32 (19.0%)	15 (13.8%)	40 (17.3%)	87 (17.1%)
Degarelix	21 (12.5%)	14 (12.8%)	50 (21.6%)	85 (16.7%)
Leuprorelin	94 (56.0%)	67 (61.5%)	120 (51.9%)	281 (55.3%)
Gonadorelin	1 (0.6%)	2 (1.8%)	0 (0%)	3 (0.6%)
Relugolix	2 (1.2%)	3 (2.8%)	1 (0.4%)	6 (1.2%)
Goserelin	11 (6.5%)	12 (11.0%)	21 (9.1%)	44 (8.7%)
Histrelin	1 (0.6%)	0 (0%)	0 (0%)	1 (0.2%)
Flutamide	8 (4.8%)	4 (3.7%)	12 (5.2%)	24 (4.7%)
Bicalutamide	84 (50.0%)	69 (63.3%)	131 (56.7%)	284 (55.9%)
Taxane Based Chemotherapy	54 (32.1%)	22 (20.2%)	48 (20.8%)	124 (24.4%)
Docetaxel	54 (32.1%)	22 (20.2%)	48 (20.8%)	124 (24.4%)
Abiraterone	7 (4.2%)	2 (1.8%)	20 (8.7%)	29 (5.7%)
Orteronel	1 (0.6%)	1 (0.9%)	0 (0%)	2 (0.4%)
Baseline labs				
Hemoglobin	135 [126,141]	131 [124,138]	127 [116,136]	131 [121,139]
eGFR	90.0 [76.8,107]	84.0 [66.8,95.0]	85.0 [70.0,95.0]	86.9 [71.0,97.6]
ALT	0.330 [0.270,0.470]	0.320 [0.250,0.450]	0.300 [0.230,0.400]	0.320 [0.250,0.423]
Albumin	41.5 [39.0,44.0]	42.0 [40.0,44.0]	42.0 [39.0,44.9]	42.0 [39.0,44.0]
ALP	1.77 [1.22,2.91]	1.62 [1.27,3.26]	2.22 [1.42,4.45]	1.93 [1.27,3.70]
Missing	0 (0%)	1 (0.9%)	2 (0.9%)	3 (0.6%)
AST	0.370 [0.300,0.450]	0.380 [0.320,0.500]	0.370 [0.300,0.470]	0.370 [0.300,0.463]
HCO3	25.2 [23.7,27.0]	25.8 [23.5,27.3]	25.5 [23.7,27.2]	25.5 [23.6,27.0]
Missing	25 (14.9%)	13 (11.9%)	48 (20.8%)	86 (16.9%)
Total bilirubin	8.60 [6.58,12.0]	10.0 [7.00,12.0]	8.60 [6.80,12.0]	8.60 [6.80,12.0]
BUN	5.85 [5.00,7.18]	6.80 [5.70,7.85]	6.40 [5.38,8.20]	6.40 [5.40,7.90]
Missing	106 (63.1%)	66 (60.6%)	119 (51.5%)	291 (57.3%)
Ca	2.33 [2.26,2.40]	2.32 [2.24,2.41]	2.34 [2.26,2.39]	2.33 [2.26,2.40]
Missing	2 (1.2%)	0 (0%)	0 (0%)	2 (0.4%)
Cl	104 [102,106]	105 [102,106]	104 [102,106]	104 [102,106]
Missing	1 (0.6%)	0 (0%)	2 (0.9%)	3 (0.6%)
CK	1.79 [1.16,2.41]	1.58 [1.11,2.28]	1.42 [0.925,2.12]	1.50 [1.04,2.20]
Missing	134 (79.8%)	82 (75.2%)	180 (77.9%)	396 (78.0%)
Glucose	5.70 [5.30,6.53]	5.72 [5.30,6.21]	5.92 [5.30,6.77]	5.80 [5.30,6.60]
Missing	1 (0.6%)	0 (0%)	1 (0.4%)	2 (0.4%)
LDH	205 [179,243]	214 [188,242]	211 [183,285]	209 [182,254]

Table 5A. Baseline characteristics of talazoparib-treated patients in TALAPRO-2, stratified by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3) experienced during the study

	No treatment-emergent anemia	Grade 1-2 anemia	Grade ≥3 anemia	Overall
	(N=168)	(N=109)	(N=231)	(N=508)
Missing	2 (1.2%)	0 (0%)	4 (1.7%)	6 (1.2%)
Mg	0.850 [0.800,0.910]	0.860 [0.800,0.910]	0.860 [0.798,0.910]	0.860 [0.800,0.910]
Missing	1 (0.6%)	0 (0%)	3 (1.3%)	4 (0.8%)
K	4.30 [4.00,4.50]	4.24 [4.00,4.60]	4.30 [4.04,4.57]	4.30 [4.00,4.54]
Protein	71.0 [67.6,74.0]	70.0 [67.0,73.0]	71.0 [68.0,74.0]	71.0 [67.6,74.0]
Missing	1 (0.6%)	0 (0%)	4 (1.7%)	5 (1.0%)
Na	140 [139,142]	141 [138,142]	141 [139,142]	141 [139,142]
Creatinine	76.0 [64.5,89.3]	78.0 [69.8,92.0]	79.6 [70.7,93.4]	78.0 [68.0,92.0]
Phosphate	1.10 [1.00,1.30]	1.15 [1.00,1.30]	1.10 [1.00,1.20]	1.10 [1.00,1.30]
Missing	1 (0.6%)	1 (0.9%)	4 (1.7%)	6 (1.2%)
Testosterone	12.0 [7.15,18.5]	11.5 [7.00,20.1]	11.5 [6.00,17.0]	11.5 [7.00,18.0]
Missing	5 (3.0%)	2 (1.8%)	3 (1.3%)	10 (2.0%)
Urea	6.20 [5.01,7.18]	6.01 [4.75,7.77]	6.51 [5.10,8.10]	6.40 [5.00,7.58]
Missing	53 (31.5%)	39 (35.8%)	102 (44.2%)	194 (38.2%)
Folic Acid	8.60 [6.50,13.7]	8.84 [6.63,15.1]	8.50 [5.56,13.2]	8.56 [6.01,13.7]
Missing	11 (6.5%)	8 (7.3%)	16 (6.9%)	35 (6.9%)
Vitamin B12	383 [299,524]	392 [252,505]	398 [282,553]	388 [285,535]
Missing	7 (4.2%)	4 (3.7%)	11 (4.8%)	22 (4.3%)
PSA	21.4 [7.65,49.9]	12.6 [4.25,59.9]	19.6 [6.18,64.6]	18.1 [6.40,61.7]
Missing	1 (0.6%)	1 (0.9%)	0 (0%)	2 (0.4%)
MCV	90.0 [87.0,93.0]	92.0 [89.0,95.0]	92.0 [88.0,95.0]	91.0 [88.0,95.0]
Missing	0 (0%)	0 (0%)	2 (0.9%)	2 (0.4%)
RBC	4.47 [4.16,4.74]	4.30 [3.98,4.55]	4.15 [3.81,4.47]	4.29 [3.96,4.56]
HCT	37.7 [0.420,40.7]	37.7 [0.430,39.9]	34.8 [0.430,39.0]	36.4 [0.420,40.0]
WBC	6.20 [4.90,7.65]	5.70 [5.00,6.70]	5.99 [4.86,7.09]	5.94 [4.90,7.25]
Basophils	0.0300 [0,0.0500]	0.0300 [0.0100,0.0500]	0.0300 [0.0200,0.0500]	0.0300 [0.0100,0.0500]
Missing	19 (11.3%)	18 (16.5%)	47 (20.3%)	84 (16.5%)
Basophils/Leukocytes	0.527 [0,0.845]	0.531 [0.229,0.770]	0.564 [0.290,0.862]	0.542 [0.222,0.839]
Missing	19 (11.3%)	18 (16.5%)	47 (20.3%)	84 (16.5%)
Eosinophils	0.170 [0.100,0.238]	0.160 [0.0900,0.245]	0.140 [0.100,0.208]	0.150 [0.100,0.220]
Missing	18 (10.7%)	18 (16.5%)	45 (19.5%)	81 (15.9%)
Eosinophils/Leukocytes	2.57 [1.72,3.99]	2.54 [1.63,4.05]	2.30 [1.57,3.86]	2.39 [1.61,3.95]
Missing	18 (10.7%)	18 (16.5%)	45 (19.5%)	81 (15.9%)
Lymphocytes	1.50 [1.10,1.94]	1.45 [1.11,2.01]	1.45 [1.11,1.81]	1.48 [1.10,1.90]
Lymphocytes/Leukocytes	25.0 [20.0,30.8]	25.8 [20.0,32.7]	24.6 [20.0,30.0]	24.8 [20.0,30.9]
Monocytes	0.530 [0.400,0.620]	0.490 [0.390,0.600]	0.485 [0.378,0.600]	0.500 [0.390,0.605]
Missing	20 (11.9%)	18 (16.5%)	47 (20.3%)	85 (16.7%)
Monocytes/Leukocytes	8.33 [6.74,9.79]	8.06 [6.76,10.2]	8.02 [6.43,9.52]	8.11 [6.61,9.81]
Missing	20 (11.9%)	18 (16.5%)	47 (20.3%)	85 (16.7%)
Neutrophils	3.92 [2.81,4.69]	3.38 [2.77,4.50]	3.71 [2.92,4.62]	3.63 [2.85,4.63]
Missing	0 (0%)	0 (0%)	1 (0.4%)	1 (0.2%)

Table 5A. Baseline characteristics of talazoparib-treated patients in TALAPRO-2, stratified by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3) experienced during the study

	No treatment-emergent anemia	Grade 1-2 anemia	Grade ≥3 anemia	Overall
	(N=168)	(N=109)	(N=231)	(N=508)
Neutrophils/Leukocytes	62.5 [56.5,68.6]	61.2 [54.6,67.4]	63.3 [56.9,68.1]	62.7 [56.2,68.2]
Missing	0 (0%)	0 (0%)	1 (0.4%)	1 (0.2%)
Platelets	231 [194,275]	214 [175,251]	223 [187,264]	223 [187,267]
Retics	64.4 [51.5,79.1]	67.7 [50.5,81.5]	59.3 [47.9,74.6]	62.0 [49.8,78.1]
Missing	54 (32.1%)	46 (42.2%)	100 (43.3%)	200 (39.4%)
EPO	11.8 [8.75,16.9]	13.1 [9.70,18.2]	13.7 [10.2,20.3]	12.9 [9.45,19.0]
Missing	33 (19.6%)	20 (18.3%)	44 (19.0%)	97 (19.1%)
Baseline anemia symptoms				
Fatigue	48 (28.6%)	37 (33.9%)	83 (35.9%)	168 (33.1%)
Shortness Breath	2 (1.2%)	5 (4.6%)	6 (2.6%)	13 (2.6%)
Decreased Appetite	1 (0.6%)	0 (0%)	4 (1.7%)	5 (1.0%)
Asthenia	18 (10.7%)	15 (13.8%)	16 (6.9%)	49 (9.6%)
Dyspnea	10 (6.0%)	13 (11.9%)	14 (6.1%)	37 (7.3%)
Dizziness	15 (8.9%)	11 (10.1%)	28 (12.1%)	54 (10.6%)
Baseline anemia management				
Iron treatment up to and prior to baseline	1 (0.6%)	2 (1.8%)	0 (0%)	3 (0.6%)
Index treatment details				
Baseline Talazoparib Dose, n (%)				
0.35	20 (11.9%)	9 (8.3%)	26 (11.3%)	55 (10.8%)
0.5	148 (88.1%)	100 (91.7%)	205 (88.7%)	453 (89.2%)
Years between prostate cancer diagnosis and Talazoparib initiation, Median [Q1,Q3]	2.50 [1.00,6.00]	4.00 [1.00,7.00]	3.00 [1.00,6.00]	3.00 [1.00,6.00]

[a]Includes prostatectomy, transurethral resection of the prostate, prostate biopsy, bilateral orchiectomy, pelvic node dissection, urethral stent, and nephrostomy
Units: Hemoglobin (g/L); eGFR (mL/min/1.73 m²); ALT (µkat/L); Albumin (g/L); ALP (µkat/L); AST (µkat/L); Bicarbonate (mmol/L); Total Bilirubin (µmol/L); BUN (mmol/L); Calcium (mmol/L); Chloride (mmol/L); Creatine Kinase (µkat/L); Glucose (mmol/L); LDH (U/L); Magnesium (mmol/L); Potassium (mmol/L); Protein (g/L); Sodium (mmol/L); Creatinine (µmol/L); Phosphate (mmol/L); Testosterone (ng/dL); Urea (mmol/L); Vitamin B9 (µg/L); Vitamin B12 (ng/L); PSA (µg/L); MCV (fL); RBC (10^{12}/L); Hematocrit (L/L); WBC (10^9/L); Basophils (10^9/L); Basophils/Leukocytes (%); Eosinophils (10^9/L); Eosinophils/Leukocytes (%); Lymphocytes (10^9/L); Lymphocytes/Leukocytes (%); Monocytes (10^9/L); Monocytes/Leukocytes (%); Neutrophils (10^9/L); Neutrophils/Leukocytes (%); Platelets (10^9/L).

Table 5B. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3)

	None to None	None to Grade 1-2	None to Grade ≥3	Grade 1-2 to Grade 1-2	Grade 1-2 to Grade ≥3	Overall
	(N=104)	(N=87)	(N=59)	(N=168)	(N=90)	(N=508)
Demographics						
Age, Median [Q1,Q3]	68.0 [63.0,74.0]	73.0 [67.0,77.5]	71.0 [67.0,76.0]	71.0 [66.0,76.0]	72.5 [67.3,76.8]	71.0 [66.0,76.0]
Race, n (%)						
White	81 (77.9%)	54 (62.1%)	35 (59.3%)	99 (58.9%)	54 (60.0%)	323 (63.6%)
Black or African American	2 (1.9%)	2 (2.3%)	0 (0%)	8 (4.8%)	3 (3.3%)	15 (3.0%)
Asian	14 (13.5%)	28 (32.2%)	19 (32.2%)	51 (30.4%)	27 (30.0%)	139 (27.4%)
Native Hawaiian or other Pacific Islander	0 (0%)	0 (0%)	1 (1.7%)	2 (1.2%)	0 (0%)	3 (0.6%)
Not Reported	7 (6.7%)	3 (3.4%)	4 (6.8%)	8 (4.8%)	6 (6.7%)	28 (5.5%)
Ethnicity, n (%)						
Hispanic or Latino	12 (11.5%)	7 (8.0%)	7 (11.9%)	21 (12.5%)	10 (11.1%)	57 (11.2%)
Not Hispanic or Latino	87 (83.7%)	77 (88.5%)	48 (81.4%)	135 (80.4%)	74 (82.2%)	421 (82.9%)
Not reported	5 (4.8%)	3 (3.4%)	4 (6.8%)	12 (7.1%)	6 (6.7%)	30 (5.9%)
Region, n (%)						
1) North America	11 (10.6%)	12 (13.8%)	3 (5.1%)	29 (17.3%)	15 (16.7%)	70 (13.8%)
2) European Union/GBR	53 (51.0%)	33 (37.9%)	27 (45.8%)	63 (37.5%)	26 (28.9%)	202 (39.8%)
3) Asia	13 (12.5%)	28 (32.2%)	17 (28.8%)	51 (30.4%)	27 (30.0%)	136 (26.8%)
4) Rest of the world	27 (26.0%)	14 (16.1%)	12 (20.3%)	25 (14.9%)	22 (24.4%)	100 (19.7%)
Cohort, n (%)						
1	64 (61.5%)	53 (60.9%)	45 (76.3%)	93 (55.4%)	57 (63.3%)	312 (61.4%)
2	40 (38.5%)	34 (39.1%)	14 (23.7%)	75 (44.6%)	33 (36.7%)	196 (38.6%)
Clinical characteristics						
Weight, Median [Q1,Q3]	87.8 [77.8,98.0]	79.3 [70.6,96.0]	78.0 [66.8,88.5]	79.0 [69.2,89.8]	76.6 [68.7,85.8]	80.0 [70.6,92.9]
BMI, Median [Q1,Q3]	28.3 [26.1,31.0]	27.2 [24.2,31.0]	25.9 [23.8,29.2]	26.7 [24.0,29.8]	26.5 [24.2,29.0]	27.1 [24.2,30.2]
Missing	0 (0%)	1 (1.1%)	1 (1.7%)	0 (0%)	0 (0%)	2 (0.4%)
Anemia Status, n (%)						
0	104 (100%)	87 (100%)	59 (100%)	0 (0%)	0 (0%)	250 (49.2%)

Table 5B. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3)

	None to None	None to Grade 1-2	None to Grade ≥3	Grade 1-2 to Grade 1-2	Grade 1-2 to Grade ≥3	Overall
	(N=104)	(N=87)	(N=59)	(N=168)	(N=90)	(N=508)
1	0 (0%)	0 (0%)	0 (0%)	164 (97.6%)	72 (80.0%)	236 (46.5%)
2	0 (0%)	0 (0%)	0 (0%)	4 (2.4%)	18 (20.0%)	22 (4.3%)
Prior History Anemia	1 (1.0%)	3 (3.4%)	1 (1.7%)	31 (18.5%)	25 (27.8%)	61 (12.0%)
Prior History Kidney Disease	1 (1.0%)	4 (4.6%)	0 (0%)	6 (3.6%)	2 (2.2%)	13 (2.6%)
Renal Impairment, n (%)						
Mild/Normal (>=60)	88 (84.6%)	78 (89.7%)	55 (93.2%)	150 (89.3%)	69 (76.7%)	440 (86.6%)
Moderate (30-59)	11 (10.6%)	5 (5.7%)	2 (3.4%)	16 (9.5%)	18 (20.0%)	52 (10.2%)
Not reported	5 (4.8%)	4 (4.6%)	2 (3.4%)	2 (1.2%)	3 (3.3%)	16 (3.1%)
Gleason score category, n (%)						
High [8-10]	78 (75.0%)	62 (71.3%)	38 (64.4%)	114 (67.9%)	67 (74.4%)	359 (70.7%)
Low [2-7]	25 (24.0%)	25 (28.7%)	20 (33.9%)	49 (29.2%)	20 (22.2%)	139 (27.4%)
Not reported	1 (1.0%)	0 (0%)	1 (1.7%)	5 (3.0%)	3 (3.3%)	10 (2.0%)
Bone metastases at baseline, n (%)	82 (78.8%)	75 (86.2%)	51 (86.4%)	147 (87.5%)	77 (85.6%)	432 (85.0%)
Prostate cancer diagnosis year, Median [Q1,Q3]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]
Baseline bone metastases number, Median [Q1,Q3]	3.00 [2.00,5.00]	3.00 [2.50,5.00]	4.00 [2.50,5.00]	4.00 [3.00,5.00]	4.00 [3.00,5.00]	4.00 [3.00,5.00]
De novo metastatic disease, n (%)	51 (49.0%)	39 (44.8%)	26 (44.1%)	84 (50.0%)	49 (54.4%)	249 (49.0%)
Somatic HRR mutation, n (%)						
1) DDR Deficient	41 (39.4%)	34 (39.1%)	15 (25.4%)	75 (44.6%)	32 (35.6%)	197 (38.8%)

Table 5B. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3)

	None to None	None to Grade 1-2	None to Grade ≥3	Grade 1-2 to Grade 1-2	Grade 1-2 to Grade ≥3	Overall
	(N=104)	(N=87)	(N=59)	(N=168)	(N=90)	(N=508)
2) Non-DDR Deficient	44 (42.3%)	37 (42.5%)	29 (49.2%)	54 (32.1%)	39 (43.3%)	203 (40.0%)
3) Unknown	19 (18.3%)	16 (18.4%)	15 (25.4%)	39 (23.2%)	19 (21.1%)	108 (21.3%)
Deficient ATM	10 (9.6%)	9 (10.3%)	6 (10.2%)	15 (8.9%)	7 (7.8%)	47 (9.3%)
Deficient ATR	1 (1.0%)	1 (1.1%)	0 (0%)	1 (0.6%)	0 (0%)	3 (0.6%)
Deficient BRCA1	2 (1.9%)	3 (3.4%)	1 (1.7%)	2 (1.2%)	2 (2.2%)	10 (2.0%)
Deficient BRCA2	10 (9.6%)	9 (10.3%)	5 (8.5%)	28 (16.7%)	8 (8.9%)	60 (11.8%)
Deficient CDK12	9 (8.7%)	6 (6.9%)	3 (5.1%)	11 (6.5%)	8 (8.9%)	37 (7.3%)
Deficient CHEK2	8 (7.7%)	7 (8.0%)	0 (0%)	14 (8.3%)	6 (6.7%)	35 (6.9%)
Deficient FANCA	1 (1.0%)	1 (1.1%)	0 (0%)	2 (1.2%)	0 (0%)	4 (0.8%)
Deficient MLH1	1 (1.0%)	1 (1.1%)	1 (1.7%)	3 (1.8%)	3 (3.3%)	9 (1.8%)
Deficient NBN	4 (3.8%)	1 (1.1%)	1 (1.7%)	2 (1.2%)	0 (0%)	8 (1.6%)
Deficient PALB2	0 (0%)	1 (1.1%)	0 (0%)	5 (3.0%)	3 (3.3%)	9 (1.8%)
Deficient RAD51C	1 (1.0%)	1 (1.1%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)
ECOG, n (%)						
0	77 (74.0%)	56 (64.4%)	39 (66.1%)	108 (64.3%)	45 (50.0%)	325 (64.0%)
1	27 (26.0%)	31 (35.6%)	20 (33.9%)	60 (35.7%)	45 (50.0%)	183 (36.0%)
Treatment history						
Bilateral orchiectomy	5 (4.8%)	4 (4.6%)	4 (6.8%)	8 (4.8%)	5 (5.6%)	26 (5.1%)
Prior prostate cancer surgery[a]	78 (75.0%)	69 (79.3%)	47 (79.7%)	129 (76.8%)	74 (82.2%)	397 (78.1%)
Prior radiation therapy	21 (20.2%)	11 (12.6%)	12 (20.3%)	46 (27.4%)	23 (25.6%)	113 (22.2%)
Prior hormonal therapy	4 (3.8%)	3 (3.4%)	4 (6.8%)	12 (7.1%)	8 (8.9%)	31 (6.1%)
Androgen deprivation therapy at baseline	101 (97.1%)	83 (95.4%)	54 (91.5%)	164 (97.6%)	85 (94.4%)	487 (95.9%)
Triptorelin	20 (19.2%)	14 (16.1%)	14 (23.7%)	27 (16.1%)	12 (13.3%)	87 (17.1%)
Degarelix	13 (12.5%)	8 (9.2%)	10 (16.9%)	31 (18.5%)	23 (25.6%)	85 (16.7%)

Table 5B. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3)

	None to None	None to Grade 1-2	None to Grade ≥3	Grade 1-2 to Grade 1-2	Grade 1-2 to Grade ≥3	Overall
	(N=104)	(N=87)	(N=59)	(N=168)	(N=90)	(N=508)
Leuprorelin	56 (53.8%)	48 (55.2%)	27 (45.8%)	103 (61.3%)	47 (52.2%)	281 (55.3%)
Gonadorelin	1 (1.0%)	1 (1.1%)	0 (0%)	1 (0.6%)	0 (0%)	3 (0.6%)
Relugolix	2 (1.9%)	4 (4.6%)	0 (0%)	0 (0%)	0 (0%)	6 (1.2%)
Goserelin	9 (8.7%)	9 (10.3%)	8 (13.6%)	11 (6.5%)	7 (7.8%)	44 (8.7%)
Histrelin	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	1 (0.2%)
Flutamide	4 (3.8%)	3 (3.4%)	3 (5.1%)	10 (6.0%)	4 (4.4%)	24 (4.7%)
Bicalutamide	54 (51.9%)	51 (58.6%)	30 (50.8%)	104 (61.9%)	45 (50.0%)	284 (55.9%)
Taxane Based Chemotherapy	35 (33.7%)	15 (17.2%)	17 (28.8%)	36 (21.4%)	21 (23.3%)	124 (24.4%)
Docetaxel	35 (33.7%)	15 (17.2%)	17 (28.8%)	36 (21.4%)	21 (23.3%)	124 (24.4%)
Abiraterone	4 (3.8%)	3 (3.4%)	4 (6.8%)	10 (6.0%)	8 (8.9%)	29 (5.7%)
Orteronel	0 (0%)	0 (0%)	0 (0%)	2 (1.2%)	0 (0%)	2 (0.4%)
Baseline labs						
Hemoglobin	139 [135,143]	139 [133,145]	138 [132,143]	125 [116,128]	118 [106,126]	131 [121,139]
eGFR	89.0 [74.5,101]	86.3 [73.5,94.0]	91.0 [77.5,106]	86.5 [69.0,104]	78.2 [62.7,91.0]	86.9 [71.0,97.6]
ALT	0.370 [0.278,0.520]	0.350 [0.270,0.470]	0.370 [0.270,0.500]	0.280 [0.230,0.385]	0.275 [0.200,0.350]	0.320 [0.250,0.423]
Albumin	42.0 [40.0,45.0]	43.0 [40.9,44.4]	43.0 [40.0,45.0]	41.0 [38.1,43.2]	41.0 [38.0,43.0]	42.0 [39.0,44.0]
ALP	1.63 [1.17,2.30]	1.73 [1.27,3.00]	1.93 [1.29,3.40]	2.19 [1.38,3.99]	2.45 [1.42,5.29]	1.93 [1.27,3.70]
Missing	0 (0%)	1 (1.1%)	0 (0%)	0 (0%)	2 (2.2%)	3 (0.6%)
AST	0.380 [0.320,0.450]	0.400 [0.320,0.500]	0.380 [0.330,0.475]	0.350 [0.280,0.450]	0.370 [0.300,0.445]	0.370 [0.300,0.463]
HCO3	25.1 [23.9,27.9]	26.2 [24.0,27.9]	25.7 [23.5,27.4]	25.0 [23.0,26.9]	26.0 [23.6,27.4]	25.5 [23.6,27.0]
Missing	14 (13.5%)	11 (12.6%)	13 (22.0%)	29 (17.3%)	19 (21.1%)	86 (16.9%)
Total bilirubin	8.95 [7.00,12.0]	10.3 [8.60,12.6]	10.3 [7.00,13.0]	8.60 [6.30,12.0]	7.70 [6.23,10.3]	8.60 [6.80,12.0]
BUN	5.70 [5.00,6.70]	6.20 [5.40,7.45]	5.55 [4.63,6.40]	6.70 [5.35,8.20]	6.90 [6.10,8.60]	6.40 [5.40,7.90]
Missing	77 (74.0%)	52 (59.8%)	37 (62.7%)	84 (50.0%)	41 (45.6%)	291 (57.3%)
Ca	2.33 [2.27,2.40]	2.34 [2.25,2.38]	2.32 [2.27,2.40]	2.32 [2.25,2.40]	2.35 [2.26,2.41]	2.33 [2.26,2.40]
Missing	1 (1.0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	2 (0.4%)
Cl	104 [102,106]	104 [102,106]	104 [102,107]	105 [103,107]	104 [102,106]	104 [102,106]
Missing	1 (1.0%)	1 (1.1%)	0 (0%)	0 (0%)	1 (1.1%)	3 (0.6%)
CK	1.67 [1.14,2.53]	1.28 [0.830,2.15]	1.45 [1.26,1.96]	1.85 [1.40,2.55]	1.23 [0.750,1.99]	1.50 [1.04,2.20]
Missing	81 (77.9%)	66 (75.9%)	43 (72.9%)	135 (80.4%)	71 (78.9%)	396 (78.0%)

Table 5B. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3)

	None to None	None to Grade 1-2	None to Grade ≥3	Grade 1-2 to Grade 1-2	Grade 1-2 to Grade ≥3	Overall
	(N=104)	(N=87)	(N=59)	(N=168)	(N=90)	(N=508)
Glucose	5.60 [5.22,6.73]	5.75 [5.30,6.85]	5.88 [5.30,6.77]	5.77 [5.26,6.42]	6.10 [5.55,6.87]	5.80 [5.30,6.60]
Missing	0 (0%)	1 (1.1%)	0 (0%)	1 (0.6%)	0 (0%)	2 (0.4%)
LDH	198 [179,227]	219 [193,246]	205 [183,233]	210 [180,266]	223 [181,318]	209 [182,254]
Missing	2 (1.9%)	1 (1.1%)	2 (3.4%)	0 (0%)	1 (1.1%)	6 (1.2%)
Mg	0.860 [0.810,0.920]	0.840 [0.785,0.895]	0.860 [0.813,0.918]	0.860 [0.800,0.910]	0.860 [0.770,0.900]	0.860 [0.800,0.910]
Missing	1 (1.0%)	0 (0%)	1 (1.7%)	1 (0.6%)	1 (1.1%)	4 (0.8%)
K	4.30 [4.00,4.51]	4.20 [4.10,4.50]	4.20 [4.00,4.60]	4.28 [4.00,4.60]	4.34 [4.02,4.55]	4.30 [4.00,4.54]
Protein	71.0 [68.0,74.0]	71.0 [68.0,74.0]	71.0 [69.1,75.1]	70.0 [67.0,73.0]	70.3 [68.0,74.0]	71.0 [67.6,74.0]
Missing	1 (1.0%)	2 (2.3%)	0 (0%)	1 (0.6%)	1 (1.1%)	5 (1.0%)
Na	141 [139,142]	140 [139,142]	141 [140,142]	141 [139,142]	140 [138,142]	141 [139,142]
Creatinine	76.5 [65.4,88.6]	76.0 [70.7,86.6]	76.9 [66.5,85.7]	78.7 [67.0,94.0]	85.9 [74.7,104]	78.0 [68.0,92.0]
Phosphate	1.10 [1.00,1.30]	1.10 [1.00,1.20]	1.10 [1.05,1.25]	1.10 [1.00,1.30]	1.10 [1.00,1.25]	1.10 [1.00,1.30]
Missing	1 (1.0%)	0 (0%)	0 (0%)	2 (1.2%)	3 (3.3%)	6 (1.2%)
Testosterone	11.5 [7.05,17.3]	11.6 [7.00,18.0]	11.4 [8.44,17.2]	11.5 [5.76,18.6]	11.8 [6.75,18.0]	11.5 [7.00,18.0]
Missing	4 (3.8%)	1 (1.1%)	0 (0%)	3 (1.8%)	2 (2.2%)	10 (2.0%)
Urea	6.01 [5.01,7.18]	6.25 [4.68,7.30]	5.65 [4.93,7.34]	6.51 [5.01,7.88]	6.80 [5.65,8.35]	6.40 [5.00,7.58]
Missing	20 (19.2%)	33 (37.9%)	21 (35.6%)	77 (45.8%)	43 (47.8%)	194 (38.2%)
FolicAcid	8.60 [6.63,13.7]	8.67 [6.10,13.8]	8.40 [6.10,13.3]	8.82 [6.01,13.8]	8.20 [5.13,12.8]	8.56 [6.01,13.7]
Missing	8 (7.7%)	3 (3.4%)	6 (10.2%)	12 (7.1%)	6 (6.7%)	35 (6.9%)
VitaminB12	383 [301,523]	392 [268,514]	417 [282,546]	397 [294,564]	381 [266,540]	388 [285,535]
Missing	6 (5.8%)	2 (2.3%)	4 (6.8%)	6 (3.6%)	4 (4.4%)	22 (4.3%)
PSA	19.6 [6.45,47.7]	13.5 [4.18,58.7]	17.4 [6.05,42.8]	16.6 [7.82,69.3]	27.9 [7.56,93.4]	18.1 [6.40,61.7]
Missing	1 (1.0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	2 (0.4%)
MCV	90.0 [88.0,94.0]	93.0 [90.0,96.0]	94.0 [90.0,95.0]	90.0 [87.0,94.0]	91.0 [87.0,94.0]	91.0 [88.0,95.0]
Missing	0 (0%)	0 (0%)	1 (1.7%)	0 (0%)	1 (1.1%)	2 (0.4%)
RBC	4.60 [4.40,4.83]	4.52 [4.22,4.71]	4.47 [4.26,4.61]	4.12 [3.83,4.35]	3.90 [3.59,4.15]	4.29 [3.96,4.56]
HCT	39.9 [0.420,41.8]	39.7 [0.430,42.3]	36.3 [0.415,41.2]	36.0 [30.2,38.3]	33.9 [27.3,36.9]	36.4 [0.420,40.0]
WBC	6.30 [5.10,7.70]	5.80 [5.16,6.50]	6.00 [5.10,7.29]	5.60 [4.60,7.08]	6.18 [4.92,7.42]	5.94 [4.90,7.25]
Basophils	0.0300 [0.00500,0.0600]	0.0300 [0.0100,0.0400]	0.0400 [0.0300,0.0600]	0.0300 [0.0150,0.0500]	0.0300 [0.0100,0.0500]	0.0300 [0.0100,0.0500]

Table 5B. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3)

	None to None	None to Grade 1-2	None to Grade ≥3	Grade 1-2 to Grade 1-2	Grade 1-2 to Grade ≥3	Overall
	(N=104)	(N=87)	(N=59)	(N=168)	(N=90)	(N=508)
Missing	9 (8.7%)	14 (16.1%)	7 (11.9%)	33 (19.6%)	21 (23.3%)	84 (16.5%)
Basophils/Leukocytes	0.551 [0.0543,1.01]	0.477 [0.208,0.762]	0.660 [0.427,0.971]	0.550 [0.275,0.762]	0.476 [0.152,0.762]	0.542 [0.222,0.839]
Missing	9 (8.7%)	14 (16.1%)	7 (11.9%)	33 (19.6%)	21 (23.3%)	84 (16.5%)
Eosinophils	0.170 [0.100,0.243]	0.130 [0.0900,0.210]	0.160 [0.100,0.270]	0.150 [0.0900,0.210]	0.140 [0.100,0.235]	0.150 [0.100,0.220]
Missing	8 (7.7%)	14 (16.1%)	6 (10.2%)	33 (19.6%)	20 (22.2%)	81 (15.9%)
Eosinophils/Leukocytes	2.38 [1.60,4.04]	2.30 [1.33,3.94]	2.68 [1.75,4.04]	2.59 [1.69,3.66]	2.24 [1.55,3.97]	2.39 [1.61,3.95]
Missing	8 (7.7%)	14 (16.1%)	6 (10.2%)	33 (19.6%)	20 (22.2%)	81 (15.9%)
Lymphocytes	1.60 [1.20,2.14]	1.52 [1.15,2.02]	1.69 [1.31,1.99]	1.35 [1.05,1.75]	1.39 [1.05,1.74]	1.48 [1.10,1.90]
Lymphocytes/Leukocytes	25.4 [20.6,32.5]	27.5 [20.3,33.3]	25.4 [22.3,34.4]	24.3 [19.9,29.7]	24.2 [18.1,28.2]	24.8 [20.0,30.9]
Monocytes	0.530 [0.400,0.638]	0.470 [0.400,0.530]	0.500 [0.398,0.600]	0.500 [0.370,0.610]	0.490 [0.350,0.640]	0.500 [0.390,0.605]
Missing	10 (9.6%)	14 (16.1%)	7 (11.9%)	33 (19.6%)	21 (23.3%)	85 (16.7%)
Monocytes/Leukocytes	8.31 [6.71,9.75]	8.06 [6.74,9.71]	7.87 [6.73,9.27]	8.33 [6.78,10.1]	8.00 [6.25,9.52]	8.11 [6.61,9.81]
Missing	10 (9.6%)	14 (16.1%)	7 (11.9%)	33 (19.6%)	21 (23.3%)	85 (16.7%)
Neutrophils	3.93 [3.07,4.80]	3.56 [2.68,4.12]	3.50 [2.97,4.62]	3.41 [2.71,4.58]	4.07 [3.09,4.94]	3.63 [2.85,4.63]
Missing	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	1 (0.2%)
Neutrophils/Leukocytes	62.5 [56.2,67.9]	60.3 [54.4,67.1]	61.9 [55.0,67.6]	62.7 [56.8,68.5]	65.1 [59.5,71.2]	62.7 [56.2,68.2]
Missing	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	1 (0.2%)
Platelets	233 [194,269]	214 [185,244]	222 [186,262]	221 [179,263]	234 [199,285]	223 [187,267]
Retics	63.5 [54.7,78.4]	62.9 [49.4,80.6]	65.0 [58.1,79.5]	63.5 [46.8,79.5]	56.5 [42.7,70.0]	62.0 [49.8,78.1]
Missing	28 (26.9%)	37 (42.5%)	17 (28.8%)	74 (44.0%)	44 (48.9%)	200 (39.4%)
EPO	9.95 [7.85,13.7]	11.1 [8.10,14.8]	11.9 [9.10,18.0]	15.0 [10.9,20.5]	15.0 [11.2,25.0]	12.9 [9.45,19.0]
Missing	26 (25.0%)	16 (18.4%)	10 (16.9%)	26 (15.5%)	19 (21.1%)	97 (19.1%)
Baseline anemia symptoms						
Fatigue	36 (34.6%)	30 (34.5%)	20 (33.9%)	50 (29.8%)	32 (35.6%)	168 (33.1%)
Shortness Breath	0 (0%)	3 (3.4%)	3 (5.1%)	6 (3.6%)	1 (1.1%)	13 (2.6%)
Decreased Appetite	0 (0%)	0 (0%)	1 (1.7%)	1 (0.6%)	3 (3.3%)	5 (1.0%)
Asthenia	12 (11.5%)	10 (11.5%)	8 (13.6%)	14 (8.3%)	5 (5.6%)	49 (9.6%)
Dyspnea	9 (8.7%)	10 (11.5%)	2 (3.4%)	10 (6.0%)	6 (6.7%)	37 (7.3%)
Dizziness	9 (8.7%)	9 (10.3%)	12 (20.3%)	18 (10.7%)	6 (6.7%)	54 (10.6%)

Table 5B. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by A) highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3); and B) pre-dose deviation anemia shift (None to none; None to Grade 1-2; None to Grade ≥3; Grade 1-2 to Grade 1-2; Grade 1-2 to Grade ≥3)

	None to None	None to Grade 1-2	None to Grade ≥3	Grade 1-2 to Grade 1-2	Grade 1-2 to Grade ≥3	Overall
	(N=104)	(N=87)	(N=59)	(N=168)	(N=90)	(N=508)
Baseline anemia management						
Iron treatment up to and prior to baseline	0 (0%)	1 (1.1%)	0 (0%)	2 (1.2%)	0 (0%)	3 (0.6%)
Index treatment details						
Baseline Talazoparib Dose, n (%)						
0.35	12 (11.5%)	6 (6.9%)	1 (1.7%)	17 (10.1%)	19 (21.1%)	55 (10.8%)
0.5	92 (88.5%)	81 (93.1%)	58 (98.3%)	151 (89.9%)	71 (78.9%)	453 (89.2%)
Year between prostate cancer diagnosis and Talazoparib initiation, Median [Q1,Q3]	3.00 [2.00,6.00]	3.00 [1.00,7.00]	3.00 [2.00,6.50]	3.00 [1.00,6.00]	2.50 [1.00,6.00]	3.00 [1.00,6.00]

[a]Includes prostatectomy, transurethral resection of the prostate, prostate biopsy, bilateral orchiectomy, pelvic node dissection, urethral stent, and nephrostomy
Units: Hemoglobin (g/L); eGFR (mL/min/1.73 m²); ALT (µkat/L); Albumin (g/L); ALP (µkat/L); AST (µkat/L); Bicarbonate (mmol/L); Total Bilirubin (µmol/L); BUN (mmol/L); Calcium (mmol/L); Chloride (mmol/L); Creatine Kinase (µkat/L); Glucose (mmol/L); LDH (U/L); Magnesium (mmol/L); Potassium (mmol/L); Protein (g/L); Sodium (mmol/L); Creatinine (µmol/L); Phosphate (mmol/L); Testosterone (ng/dL); Urea (mmol/L); Vitamin B9 (µg/L); Vitamin B12 (ng/L); PSA (µg/L); MCV (fL); RBC (10^{12}/L); Hematocrit (L/L); WBC (10^9/L); Basophils (10^9/L); Basophils/Leukocytes (%); Eosinophils (10^9/L); Eosinophils/Leukocytes (%); Lymphocytes (10^9/L); Lymphocytes/Leukocytes (%); Monocytes (10^9/L); Monocytes/Leukocytes (%); Neutrophils (10^9/L); Neutrophils/Leukocytes (%); Platelets (10^9/L).

Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; and C) anemia symptoms are characterized in Table 6. Talazoparib dose is recorded at least once per patient at treatment initiation (Table 6A). There was a median of 3.00 [2.00,6.00] unique dose records per patient, with a median duration of 60.1 days [37.7,98.0] between unique dose observations.

For longitudinal laboratory variables summarized in Table 6B, core hematology and serum chemistry variables for routinely collected analytes (e.g. ALT, AST, albumin, alkaline phosphatase, total bilirubin, electrolytes, creatinine, hemoglobin) were measured at least

once for nearly all patients and were generally collected longitudinally with medians ranging 20–25 unique observations per patient and median duration ranging 23-26 days for successive laboratory observations between records. Select laboratory variables (e.g. creatine kinase, blood urea nitrogen/urea, reticulocytes, erythropoietin, differential white blood cell components) were measured less frequently (37-89% of patients), with medians ranging 10–24 unique observations per patient and median duration ranging 24-30 days for successive laboratory observations between records. Estimated glomerular filtration rate (eGFR) and testosterone were primarily only assessed at baseline (median number of observations = 1) and had limited or no repeated measurements over follow-up, consistent with their role in eligibility determination and dose assignment rather than ongoing safety monitoring.

For Table 6C, the original intent was to capture the frequency with which patients were assessed for symptoms during follow-up. However, it was determined during analysis that the available data on symptoms from TALAPRO2 only reflects observed symptoms rather systematic assessments at scheduled visits, as symptom records were sparse, irregularly collected after baseline, and never documented the absence of symptoms. Therefore, the current Table 6C reflects anemia symptoms observed over the course of the study for which study assessment visits were planned for every 2 weeks up to week 17, every 4 weeks up to week 53, every 8 weeks thereafter while on study drug[1].

Table 6A. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

Talazoparib dose	Number of unique observations	Median [Q1,Q3]	3.00 [2.00,6.00]
		[Min, Max]	[1.00, 53.0]
		Missing	0 (0%)
	Duration between unique observations*	Median [Q1,Q3]	60.1 [37.7,98.0]
		[Min, Max]	[4.30, 675]
		Missing	119 (23.4%)

*Number of days between baseline measure and last repeated measure, divided by the number of repeated measures. E.g. 4 total measures with 30 days in between = 30/3=10 days between measures

Table 6B. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

Hemoglobin	Number of unique observations	Median [Q1,Q3]	25.0 [19.0,29.0]
		[Min, Max]	[1.00, 68.0]
		Missing	0 (0%)
	Duration between unique observations	Median [Q1,Q3]	23.2 [17.8,29.6]
		[Min, Max]	[4.60, 39.9]
		Missing	1 (0.2%)
eGFR	Number of unique observations	Median [Q1,Q3]	1.00 [1.00,1.00]
		[Min, Max]	[1.00, 2.00]

Table 6B. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

		Missing	0 (0%)
eGFR	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	20.0 [20.0,20.0] [20.0, 20.0] 507 (99.8%)
ALT	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.0,27.0] [1.00, 45.0] 0 (0%)
ALT	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.5 [19.9,30.8] [7.80, 84.3] 1 (0.2%)
Albumin	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.8,27.0] [1.00, 44.0] 0 (0%)
Albumin	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.7 [19.9,30.8] [10.3, 40.5] 1 (0.2%)
ALP	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.0,26.0] [1.00, 44.0] 0 (0%)
ALP	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.5 [19.9,30.9] [10.3, 365] 1 (0.2%)
AST	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [17.0,27.0] [1.00, 45.0] 0 (0%)
AST	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.5 [20.0,31.0] [7.80, 84.3] 1 (0.2%)
HCO3	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	20.0 [15.0,26.0] [1.00, 44.0] 72 (14.2%)
HCO3	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.8 [20.5,32.0] [7.00, 133] 79 (15.6%)

Table 6B. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

Total_bilirubin	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.8,27.0] [1.00, 45.0] 0 (0%)
Total_bilirubin	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.5 [19.9,30.9] [10.3, 84.3] 1 (0.2%)
BUN	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [14.0,27.0] [1.00, 45.0] 280 (55.1%)
BUN	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.8 [19.6,31.1] [11.4, 55.5] 288 (56.7%)
Ca	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.0,26.0] [2.00, 44.0] 1 (0.2%)
Ca	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.0 [19.9,31.0] [11.0, 40.5] 1 (0.2%)
Cl	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.0,26.0] [1.00, 45.0] 0 (0%)
Cl	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.0 [20.1,31.0] [3.40, 84.3] 1 (0.2%)
CK	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	9.50 [2.00,20.0] [1.00, 32.0] 320 (63.0%)
CK	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	29.9 [20.5,42.0] [4.50, 537] 358 (70.5%)
Glucose	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.0,26.0] [1.00, 44.0] 0 (0%)

Table 6B. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

Glucose	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.8 [20.0,31.0] [8.00, 175] 1 (0.2%)
LDH	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.0,26.0] [1.00, 45.0] 0 (0%)
LDH	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.1 [20.1,31.3] [10.3, 84.3] 1 (0.2%)
Mg	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.0,26.0] [1.00, 37.0] 0 (0%)
Mg	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.0 [20.0,31.3] [11.0, 94.9] 1 (0.2%)
K	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [17.0,27.0] [1.00, 45.0] 0 (0%)
K	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.5 [19.9,31.0] [2.80, 84.3] 1 (0.2%)
Protein	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.0,26.0] [1.00, 44.0] 0 (0%)
Protein	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.1 [20.1,31.0] [11.0, 84.3] 1 (0.2%)
Na	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.8,27.0] [1.00, 45.0] 0 (0%)
Na	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.7 [20.0,30.9] [3.40, 84.3] 1 (0.2%)

Table 6B. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

Creatinine	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [17.0,27.0] [1.00, 45.0] 0 (0%)
Creatinine	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.5 [19.8,31.0] [7.80, 108] 1 (0.2%)
Phosphate	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.0,26.0] [1.00, 38.0] 0 (0%)
Phosphate	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.4 [20.2,31.6] [11.0, 126] 1 (0.2%)
Testosterone	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	1.00 [1.00,1.00] [1.00, 7.00] 10 (2.0%)
Testosterone	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	19.9 [18.0,41.5] [11.0, 108] 494 (97.2%)
Urea	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	22.0 [16.5,26.0] [1.00, 35.0] 193 (38.0%)
Urea	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	25.8 [20.1,31.4] [8.50, 124] 194 (38.2%)
FolicAcid	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	20.0 [13.5,25.0] [1.00, 37.0] 13 (2.6%)
FolicAcid	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	27.3 [20.5,33.4] [11.0, 308] 20 (3.9%)
VitaminB12	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	21.0 [14.5,25.0] [1.00, 37.0] 9 (1.8%)

Table 6B. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

VitaminB12	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.7 [20.3,32.5] [6.00, 308] 16 (3.1%)
PSA	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	14.0 [9.00,18.0] [2.00, 33.0] 0 (0%)
PSA	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	49.9 [46.2,55.0] [16.0, 152] 0 (0%)
MCV	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.0,28.0] [1.00, 68.0] 1 (0.2%)
MCV	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.3,29.8] [6.70, 124] 2 (0.4%)
RBC	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.0,28.0] [1.00, 68.0] 0 (0%)
RBC	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	23.8 [18.1,29.8] [6.70, 39.9] 1 (0.2%)
HCT	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.0,28.0] [1.00, 68.0] 0 (0%)
HCT	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.2,29.8] [6.70, 86.7] 1 (0.2%)
WBC	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	25.0 [18.0,29.0] [1.00, 68.0] 0 (0%)
WBC	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	23.7 [18.1,29.8] [5.60, 39.9] 1 (0.2%)

Table 6B. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

Basophils	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.0,28.0] [1.00, 46.0] 84 (16.5%)
Basophils	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.3,30.0] [6.40, 55.5] 85 (16.7%)
Eosinophils	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.0,28.0] [1.00, 46.0] 80 (15.7%)
Eosinophils	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.3,30.0] [6.40, 61.3] 81 (15.9%)
Lymphocytes	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.0,28.3] [1.00, 66.0] 0 (0%)
Lymphocytes	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.2,29.8] [6.40, 39.9] 1 (0.2%)
Monocytes	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.0,28.0] [1.00, 46.0] 83 (16.3%)
Monocytes	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.3,29.9] [6.40, 61.3] 84 (16.5%)
Neutrophils	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	24.0 [18.0,28.3] [1.00, 66.0] 0 (0%)
Neutrophils	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	24.1 [18.3,29.8] [6.40, 103] 1 (0.2%)
Platelets	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	25.0 [18.0,29.0] [1.00, 67.0] 0 (0%)

Table 6B. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

Platelets	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	23.7 [18.1,29.8] [5.80, 39.9] 1 (0.2%)
Reticulocytes	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	20.0 [13.0,25.0] [1.00, 38.0] 166 (32.7%)
Reticulocytes	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.8 [19.9,32.5] [7.50, 210] 176 (34.6%)
EPO	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	18.0 [11.0,24.0] [1.00, 37.0] 54 (10.6%)
EPO	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	28.3 [20.4,33.9] [10.5, 323] 67 (13.2%)

Table 6C. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

Fatigue	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	1.00 [1.00,2.00] [1.00, 7.00] 340 (66.9%)
Fatigue	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	87.0 [35.3,168] [3.00, 955] 444 (87.4%)
Shortness Breath	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	1.00 [1.00,1.00] [1.00, 2.00] 495 (97.4%)
Shortness Breath	Duration between unique observations	Median [Q1,Q3] [Min, Max] Missing	26.0 [22.0,30.0] [18.0, 34.0] 506 (99.6%)
Decreased Appetite	Number of unique observations	Median [Q1,Q3] [Min, Max] Missing	1.00 [1.00,1.00] [1.00, 1.00] 503 (99.0%)

Table 6C. Repeated measures of longitudinal variables per patient for A) talazoparib doses; B) laboratory values; C) anemia symptoms

Decreased Appetite	Duration between unique observations	Yes	0 (0%)
		No	0 (0%)
		Missing	508 (100%)
Asthenia	Number of unique observations	Median [Q1,Q3]	1.00 [1.00,2.00]
		[Min, Max]	[1.00, 6.00]
		Missing	459 (90.4%)
Asthenia	Duration between unique observations	Median [Q1,Q3]	86.6 [39.7,151]
		[Min, Max]	[12.0, 462]
		Missing	491 (96.7%)
Dyspnea	Number of unique observations	Median [Q1,Q3]	1.00 [1.00,1.00]
		[Min, Max]	[1.00, 4.00]
		Missing	471 (92.7%)
Dyspnea	Duration between unique observations	Median [Q1,Q3]	120 [65.0,192]
		[Min, Max]	[10.0, 252]
		Missing	499 (98.2%)
Dizziness	Number of unique observations	Median [Q1,Q3]	1.00 [1.00,1.00]
		[Min, Max]	[1.00, 4.00]
		Missing	454 (89.4%)
Dizziness	Duration between unique observations	Median [Q1,Q3]	46.0 [9.50,108]
		[Min, Max]	[1.00, 220]
		Missing	500 (98.4%)

10.3. Outcome data

The primary outcome was treatment-emergent anemia categorized as no anemia, Grade 1-2 anemia, and Grade ≥3 anemia. Additional related outcomes such as dose deviation, anemia improvement following dose deviation, and hemoglobin trajectory outcomes are also characterized in this section. The number of subjects contributing to each outcome analysis is reported in the corresponding tables and figures, with outcome frequencies summarized below.

In the overall cohort of 508 patients, n=319 (62.8%) experienced at least one dose deviation during follow-up. Time to first dose deviation was evaluated among patients receiving talazoparib, with analyses conducted in the overall cohort (Figure 4A), and stratified by patients with baseline Grade 1 anemia (Figure 4B), and baseline Grade 2 anemia (Figure 4C). Dose deviation was defined as receipt of dose that was different from the initiating dose and that was sustained for 7 days or longer, or if dose deviation period was <7 days, was

explicitly stated as a dose modification due to an adverse event. Time to dose deviation was censored at the first of: i) death; ii) date of last contact; or iii) study end date.

Median time to first dose deviation was at 24 weeks (95% CI: 20–29). When stratified by initial talazoparib dose, patients who initiated therapy at 0.5 mg experienced dose deviations earlier, with a median time to first deviation of 21 weeks (95% CI: 19–29), compared with 29 weeks (95% CI: 15–68) among those who started at 0.35 mg, although confidence intervals overlap. At 2 and 4 weeks, approximately 95% or more of patients in both dose groups remained free of dose deviation. By 16 weeks, the event-free rate declined to 57.2% (95% CI, 52.5%–61.6%) among patients initiating the 0.5-mg dose and to 61.6% (95% CI, 47.4%–73.0%) among those initiating the 0.35-mg dose. Kaplan–Meier curves showed broadly similar time to first dose deviation between the 0.35 mg and 0.5 mg starting dose groups. Although the curve for the 0.35 mg group lay above that of the 0.5 mg group around the median event time, the difference was not consistent over time.

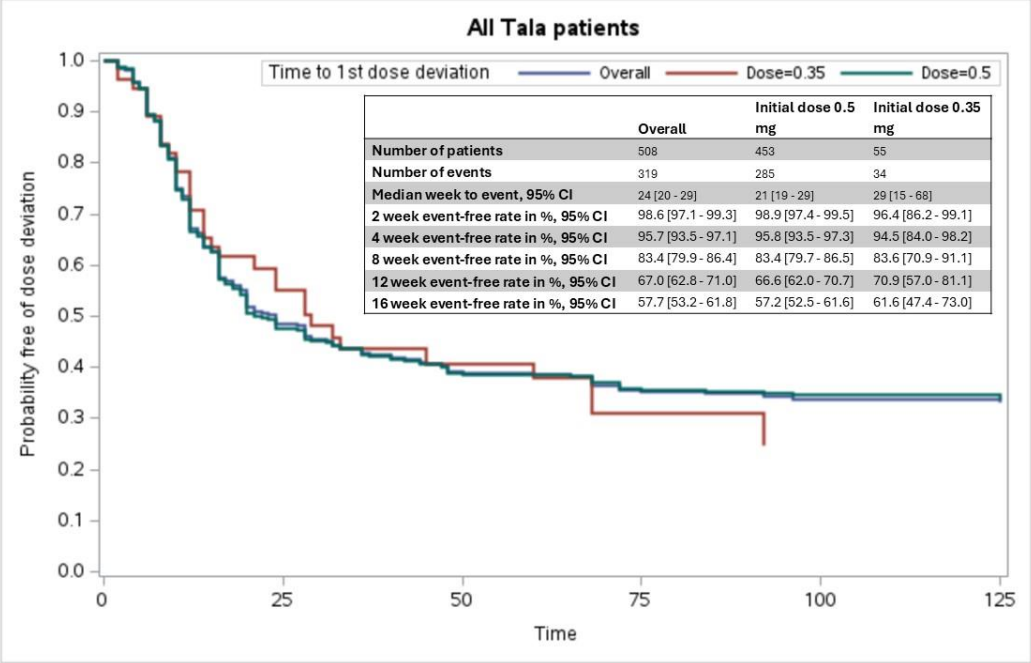
Among patients with Grade 1 anemia (n=236) and Grade 2 anemia (n=22) at baseline, dose deviations occurred in 66.5% and 86.4% of patients, with median time to first dose deviation of 19 weeks (95% CI: 16–24) and 7 weeks (95% CI: 4–21), respectively. Among patients with baseline anemia, the Kaplan–Meier curves followed a pattern similar to that of the overall population, with a transiently higher event-free rate for the lower dose group around the median event time and no sustained difference between dose groups thereafter.

Additional Kaplan-Meier estimates and curves for the broad definition of time to dose modification (defined as the receipt of talazoparib dose that was different from the initiating dose) are shown in Appendix 8.1 **Error! Reference source not found.**.

Figure 4. Time to dose deviation, followed from the date of talazoparib initiation until the date of first talazoparib treatment deviation, or censored at the first of: i) death; ii) date of last contact; or iii) study end date, for A) all patients; B)

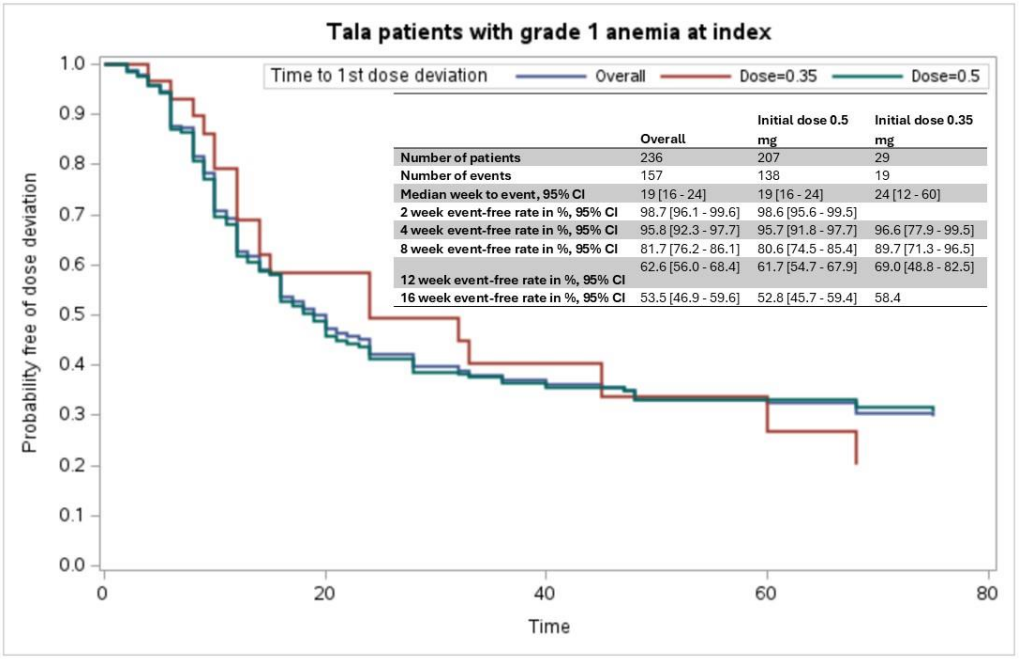
patients with Grade 1 anemia at index; C) patients with Grade 2 anemia at index

4A



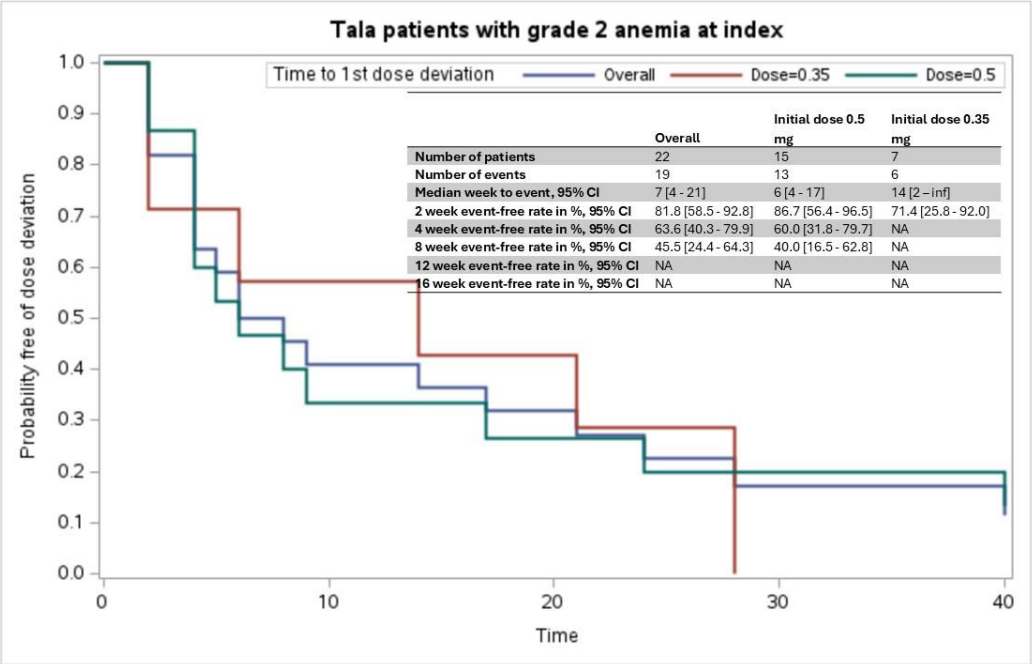
	Overall	Initial dose 0.5 mg	Initial dose 0.35 mg
Number of patients	508	453	55
Number of events	319	285	34
Median week to event, 95% CI	24 [20 - 29]	21 [19 - 29]	29 [15 - 68]
2 week event-free rate in %, 95% CI	98.6 [97.1 - 99.3]	98.9 [97.4 - 99.5]	96.4 [86.2 - 99.1]
4 week event-free rate in %, 95% CI	95.7 [93.5 - 97.1]	95.8 [93.5 - 97.3]	94.5 [84.0 - 98.2]
8 week event-free rate in %, 95% CI	83.4 [79.9 - 86.4]	83.4 [79.7 - 86.5]	83.6 [70.9 - 91.1]
12 week event-free rate in %, 95% CI	67.0 [62.8 - 71.0]	66.6 [62.0 - 70.7]	70.9 [57.0 - 81.1]
16 week event-free rate in %, 95% CI	57.7 [53.2 - 61.8]	57.2 [52.5 - 61.6]	61.6 [47.4 - 73.0]

4B



	Overall	Initial dose 0.5 mg	Initial dose 0.35 mg
Number of patients	236	207	29
Number of events	157	138	19
Median week to event, 95% CI	19 [16 - 24]	19 [16 - 24]	24 [12 - 60]
2 week event-free rate in %, 95% CI	98.7 [96.1 - 99.6]	98.6 [95.6 - 99.5]	
4 week event-free rate in %, 95% CI	95.8 [92.3 - 97.7]	95.7 [91.8 - 97.7]	96.6 [77.9 - 99.5]
8 week event-free rate in %, 95% CI	81.7 [76.2 - 86.1]	80.6 [74.5 - 85.4]	89.7 [71.3 - 96.5]
12 week event-free rate in %, 95% CI	62.6 [56.0 - 68.4]	61.7 [54.7 - 67.9]	69.0 [48.8 - 82.5]
16 week event-free rate in %, 95% CI	53.5 [46.9 - 59.6]	52.8 [45.7 - 59.4]	58.4

4C



	Overall	Initial dose 0.5 mg	Initial dose 0.35 mg
Number of patients	22	15	7
Number of events	19	13	6
Median week to event, 95% CI	7 [4 - 21]	6 [4 - 17]	14 [2 – inf]
2 week event-free rate in %, 95% CI	81.8 [58.5 - 92.8]	86.7 [56.4 - 96.5]	71.4 [25.8 - 92.0]
4 week event-free rate in %, 95% CI	63.6 [40.3 - 79.9]	60.0 [31.8 - 79.7]	NA
8 week event-free rate in %, 95% CI	45.5 [24.4 - 64.3]	40.0 [16.5 - 62.8]	NA
12 week event-free rate in %, 95% CI	NA	NA	NA
16 week event-free rate in %, 95% CI	NA	NA	NA

Table 7 summarizes the initial changes in anemia status preceding any dose deviation, as well as initial dose deviation characteristics. For the overall cohort, initial changes in anemia status, i.e. “Anemia Change” are as previously summarized for the stratified groups in Table 5B. Among the 508 patients, 189 (37.2%) had no dose deviation during the study; 299 (58.9%) experienced a dose interruption, defined as a decrease in talazoparib dose to 0 mg sustained for ⩾7 days or, if <7 days, explicitly documented as an interruption due to an adverse event; and a smaller number, 20 (3.9%) experienced a dose reduction, defined as a sustained decrease to a non-zero dose for ⩾7 days or, if <7 days, explicitly documented as due to an adverse event. Among the total cohort of patients, 106 (20.9%) had a Grade 1 or 2 anemia and 130 (25.6%) had a Grade ≥3 anemia event within 7 days prior to the dose deviation event, whereas 83 (16.3%) had no record of anemia prior to the dose deviation event. A diverse range of early dose patterns were observed across all categories for both the “narrow” and “broad” definitions as defined in Table 3, with smaller counts observed for patterns that were expected to occur infrequently in the data due to trial protocol mandated dose interruption for Grade ≥3 anemia (patterns 5, 6b, 9, and 10b each represent less than 0.5% of the cohort). Dose patterns corresponding to initial dose reduction rather than dose interruption were also less common (patterns 2b, 4b, 6b, 8b, and 10b each represent less than 2.5% of the cohort), consistent with the overall smaller number of patients who experienced a dose reduction rather than a dose interruption.

Initial changes in anemia status and initial dose deviation characteristics are stratified by the highest-grade anemia category experienced during the study irrespective of dose deviation in Table 7, and stratified by any anemia status (no anemia; any-grade anemia) experienced during the study in Appendix 8.1 **Error! Reference source not found.**. The same tables are repeated using the broad definition of time to dose modification (defined as the receipt of talazoparib dose that was different from the initiating dose) in Appendix 8.1 **Error! Reference source not found.**.

Table 7. Post-index dose patterns of talazoparib-treated patients in TALAPRO-2, stratified by the highest-grade anemia category (Grade 1-2; Grade ≥3) experienced during the study

		No treatment-emergent anemia (N=168)	Grade 1-2 anemia (N=109)	Grade ≥3 anemia (N=231)	Overall (N=508)
Anemia Change	None to None	104 (61.9%)	0 (0%)	0 (0%)	104 (20.5%)
	None to Grade 1-2	0 (0%)	55 (50.5%)	32 (13.9%)	87 (17.1%)
	None to Grade ≥3	0 (0%)	0 (0%)	59 (25.5%)	59 (11.6%)
	Grade 1-2 to Grade 1-2	64 (38.1%)	54 (49.5%)	50 (21.6%)	168 (33.1%)
	Grade 1-2 to Grade ≥3	0 (0%)	0 (0%)	90 (39.0%)	90 (17.7%)
Talazoparib dose 2 descriptive narrow	No change	119 (70.8%)	38 (34.9%)	32 (13.9%)	189 (37.2%)
	Interruption	44 (26.2%)	67 (61.5%)	188 (81.4%)	299 (58.9%)
	Reduction	5 (3.0%)	4 (3.7%)	11 (4.8%)	20 (3.9%)
Talazoparib dose 2 descriptive broad	No change	119 (70.8%)	38 (34.9%)	32 (13.9%)	189 (37.2%)
	Dose deviation	49 (29.2%)	71 (65.1%)	199 (86.1%)	319 (62.8%)
Reason Talazoparib dose 2 descriptive broad	No dose change	119 (70.8%)	38 (34.9%)	32 (13.9%)	189 (37.2%)
	Dose change not due to anemia	49 (29.2%)	11 (10.1%)	23 (10.0%)	83 (16.3%)
	Dose change due to grade 1 or 2 anemia	0 (0%)	60 (55.0%)	46 (19.9%)	106 (20.9%)
	Dose change due to grade 3 or higher anemia	0 (0%)	0 (0%)	130 (56.3%)	130 (25.6%)
Early dose pattern narrow	1	60 (35.7%)	0 (0%)	0 (0%)	60 (11.8%)
	2a	42 (25.0%)	0 (0%)	0 (0%)	42 (8.3%)
	2b	2 (1.2%)	0 (0%)	0 (0%)	2 (0.4%)
	3	0 (0%)	14 (12.8%)	3 (1.3%)	17 (3.3%)
	4a	0 (0%)	38 (34.9%)	25 (10.8%)	63 (12.4%)
	4b	0 (0%)	3 (2.8%)	4 (1.7%)	7 (1.4%)
	5	0 (0%)	0 (0%)	1 (0.4%)	1 (0.2%)
	6a	0 (0%)	0 (0%)	58 (25.1%)	58 (11.4%)
	6b	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	7	32 (19.0%)	11 (10.1%)	3 (1.3%)	46 (9.1%)

Table 7. Post-index dose patterns of talazoparib-treated patients in TALAPRO-2, stratified by the highest-grade anemia category (Grade 1-2; Grade ≥3) experienced during the study

		No treatment-emergent anemia (N=168)	Grade 1-2 anemia (N=109)	Grade ≥3 anemia (N=231)	Overall (N=508)
	8a	29 (17.3%)	40 (36.7%)	41 (17.7%)	110 (21.7%)
	8b	3 (1.8%)	3 (2.8%)	6 (2.6%)	12 (2.4%)
	9	0 (0%)	0 (0%)	2 (0.9%)	2 (0.4%)
	10a	0 (0%)	0 (0%)	86 (37.2%)	86 (16.9%)
	10b	0 (0%)	0 (0%)	2 (0.9%)	2 (0.4%)
Early dose pattern broad	1	60 (35.7%)	0 (0%)	0 (0%)	60 (11.8%)
	2	44 (26.2%)	0 (0%)	0 (0%)	44 (8.7%)
	3	0 (0%)	14 (12.8%)	3 (1.3%)	17 (3.3%)
	4	0 (0%)	41 (37.6%)	29 (12.6%)	70 (13.8%)
	5	0 (0%)	0 (0%)	1 (0.4%)	1 (0.2%)
	6	0 (0%)	0 (0%)	58 (25.1%)	58 (11.4%)
	7	32 (19.0%)	11 (10.1%)	3 (1.3%)	46 (9.1%)
	8	32 (19.0%)	43 (39.4%)	47 (20.3%)	122 (24.0%)
	9	0 (0%)	0 (0%)	2 (0.9%)	2 (0.4%)
	10	0 (0%)	0 (0%)	88 (38.1%)	88 (17.3%)

Early dose pattern definitions based on anemia and dose deviation patterns as specified in Table 3.

Table 8 summarizes baseline characteristics of patients in the study, stratified by early dose pattern strata experienced during the study. Baseline variables showing variability across dose deviation categories include younger age at baseline for patterns 1 (median 66.0 years) and 7 (median 69.0 years) compared to overall (median 71.0 years). Patterns 1 and 7 correspond to no worsening anemia. More patients of Asian race (30.7%–37.1%) and lower baseline body weight (median 76.4–78.3 kg) were observed for patterns 4, 6, 8 and 10 compared to overall (27.4% Asian; median 80.0 kg). Patterns 4, 6, 8 and 10 correspond to worsening anemia from baseline anemia-free and low-grade anemia statuses. No other consistent differences were noted by pattern category, although sample sizes are limited upon stratification.

The same tables are repeated using the broad definition of dose modification for differentiating early dose pattern strata in Appendix 8.1 **Error! Reference source not found.**.

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
Demographics											
Age, Median [Q1,Q3]	66.0 [62.0,72.0]	73.0 [66.3,76.0]	73.0 [66.0,75.0]	74.0 [67.0,78.0]	79.0 [77.5,81.5]	71.0 [67.0,75.3]	69.0 [64.5,73.0]	74.0 [68.0,78.0]	78.0 [74.0,83.5]	72.0 [67.0,75.3]	71.0 [66.0,76.0]
Race, n (%)											
White	60 (81.1%)	21 (70.0%)	18 (60.0%)	36 (63.2%)	1 (33.3%)	34 (60.7%)	44 (58.7%)	55 (59.8%)	4 (57.1%)	50 (59.5%)	323 (63.6%)
Black or African American	2 (2.7%)	0 (0%)	1 (3.3%)	1 (1.8%)	0 (0%)	0 (0%)	4 (5.3%)	3 (3.3%)	0 (0%)	4 (4.8%)	15 (3.0%)
Asian	9 (12.2%)	5 (16.7%)	11 (36.7%)	17 (29.8%)	1 (33.3%)	18 (32.1%)	21 (28.0%)	30 (32.6%)	3 (42.9%)	24 (28.6%)	139 (27.4%)
Native Hawaiian or other Pacific Islander	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.8%)	2 (2.7%)	0 (0%)	0 (0%)	0 (0%)	3 (0.6%)
Not Reported	3 (4.1%)	4 (13.3%)	0 (0%)	3 (5.3%)	1 (33.3%)	3 (5.4%)	4 (5.3%)	4 (4.3%)	0 (0%)	6 (7.1%)	28 (5.5%)
Ethnicity, n (%)											
Hispanic or Latino	9 (12.2%)	3 (10.0%)	3 (10.0%)	4 (7.0%)	0 (0%)	7 (12.5%)	9 (12.0%)	12 (13.0%)	0 (0%)	10 (11.9%)	57 (11.2%)
Not Hispanic or Latino	62 (83.8%)	25 (83.3%)	26 (86.7%)	51 (89.5%)	3 (100%)	45 (80.4%)	60 (80.0%)	74 (80.4%)	6 (85.7%)	69 (82.1%)	421 (82.9%)
Not reported	3 (4.1%)	2 (6.7%)	1 (3.3%)	2 (3.5%)	0 (0%)	4 (7.1%)	6 (8.0%)	6 (6.5%)	1 (14.3%)	5 (6.0%)	30 (5.9%)
Region, n (%)											
1) North America	9 (12.2%)	2 (6.7%)	4 (13.3%)	8 (14.0%)	0 (0%)	3 (5.4%)	16 (21.3%)	13 (14.1%)	0 (0%)	15 (17.9%)	70 (13.8%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
2) European Union/GBR	37 (50.0%)	16 (53.3%)	10 (33.3%)	23 (40.4%)	1 (33.3%)	26 (46.4%)	27 (36.0%)	36 (39.1%)	3 (42.9%)	23 (27.4%)	202 (39.8%)
3) Asia	8 (10.8%)	5 (16.7%)	11 (36.7%)	17 (29.8%)	1 (33.3%)	16 (28.6%)	21 (28.0%)	30 (32.6%)	3 (42.9%)	24 (28.6%)	136 (26.8%)
4) Rest of the world	20 (27.0%)	7 (23.3%)	5 (16.7%)	9 (15.8%)	1 (33.3%)	11 (19.6%)	11 (14.7%)	13 (14.1%)	1 (14.3%)	22 (26.2%)	100 (19.7%)
Cohort, n (%)											
1	44 (59.5%)	20 (66.7%)	18 (60.0%)	35 (61.4%)	3 (100%)	42 (75.0%)	40 (53.3%)	53 (57.6%)	6 (85.7%)	51 (60.7%)	312 (61.4%)
2	30 (40.5%)	10 (33.3%)	12 (40.0%)	22 (38.6%)	0 (0%)	14 (25.0%)	35 (46.7%)	39 (42.4%)	1 (14.3%)	33 (39.3%)	196 (38.6%)
Clinical characteristics											
Weight, Median [Q1,Q3]	89.4 [79.9,103]	80.6 [72.4,88.2]	84.0 [72.8,98.1]	76.9 [68.0,93.0]	66.2 [66.1,75.5]	78.3 [67.8,89.0]	81.0 [74.0,97.4]	77.0 [66.0,88.1]	68.8 [61.9,87.2]	76.8 [69.0,85.5]	80.0 [70.6,92.9]
BMI, Median [Q1,Q3]	29.0 [26.2,31.2]	27.7 [25.4,29.6]	28.5 [25.4,31.7]	26.5 [23.3,29.7]	23.9 [23.4,26.0]	26.0 [23.9,29.4]	27.2 [24.7,30.7]	25.9 [23.5,29.2]	25.6 [24.5,29.7]	26.6 [24.2,28.9]	27.1 [24.2,30.2]
Missing	0 (0%)	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)	1 (1.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)
Anemia Status, n (%)											
0	74 (100%)	30 (100%)	30 (100%)	57 (100%)	3 (100%)	56 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	250 (49.2%)
1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	75 (100%)	88 (95.7%)	4 (57.1%)	69 (82.1%)	236 (46.5%)
2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (4.3%)	3 (42.9%)	15 (17.9%)	22 (4.3%)
Prior History Anemia	1 (1.4%)	0 (0.0%)	2 (6.7%)	1 (1.8%)	0 (0.0%)	1 (1.8%)	11 (14.7%)	20 (21.7%)	2 (28.6%)	23 (27.4%)	61 (12.0%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
Prior History Kidney Disease	0 (0.0%)	1 (3.3%)	2 (6.7%)	2 (3.5%)	0 (0.0%)	0 (0.0%)	2 (2.7%)	4 (4.3%)	0 (0.0%)	2 (2.4%)	13 (2.6%)
Renal Impairment, n (%)											
Mild/Normal (>=60)	61 (82.4%)	27 (90.0%)	26 (86.7%)	52 (91.2%)	3 (100%)	52 (92.9%)	68 (90.7%)	81 (88.0%)	3 (42.9%)	67 (79.8%)	440 (86.6%)
Moderate (30-59)	8 (10.8%)	3 (10.0%)	2 (6.7%)	3 (5.3%)	0 (0%)	2 (3.6%)	7 (9.3%)	9 (9.8%)	3 (42.9%)	15 (17.9%)	52 (10.2%)
Not reported	5 (6.8%)	0 (0%)	2 (6.7%)	2 (3.5%)	0 (0%)	2 (3.6%)	0 (0%)	2 (2.2%)	1 (14.3%)	2 (2.4%)	16 (3.1%)
Gleason score category, n (%)											
High [8-10]	56 (75.7%)	22 (73.3%)	21 (70.0%)	41 (71.9%)	0 (0%)	38 (67.9%)	51 (68.0%)	62 (67.4%)	5 (71.4%)	63 (75.0%)	359 (70.7%)
Low [2-7]	17 (23.0%)	8 (26.7%)	9 (30.0%)	16 (28.1%)	3 (100%)	17 (30.4%)	22 (29.3%)	27 (29.3%)	2 (28.6%)	18 (21.4%)	139 (27.4%)
Not reported	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.8%)	2 (2.7%)	3 (3.3%)	0 (0%)	3 (3.6%)	10 (2.0%)
Bone metastases at baseline, n (%)	57 (77.0%)	25 (83.3%)	26 (86.7%)	49 (86.0%)	3 (100.0%)	48 (85.7%)	65 (86.7%)	81 (88.0%)	7 (100.0%)	71 (84.5%)	432 (85.0%)
Prostate cancer diagnosis year, Median [Q1,Q3]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2010 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2010,2020]

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
Baseline bone metastases number, Median [Q1,Q3]	3.00 [2.00,4.00]	4.00 [2.25,5.00]	4.00 [3.00,5.00]	3.00 [2.00,5.00]	4.00 [3.50,4.00]	4.00 [2.00,5.00]	4.00 [3.00,5.00]	4.00 [3.00,5.00]	5.00 [4.00,5.50]	4.00 [2.75,5.00]	4.00 [3.00,5.00]
De novo metastatic disease, n (%)	38 (51.4%)	13 (43.3%)	15 (50.0%)	24 (42.1%)	0 (0.0%)	26 (46.4%)	39 (52.0%)	45 (48.9%)	5 (71.4%)	44 (52.4%)	249 (49.0%)
Somatic HRR mutation, n (%)											
1) DDR Deficient	30 (40.5%)	11 (36.7%)	12 (40.0%)	22 (38.6%)	0 (0%)	15 (26.8%)	35 (46.7%)	39 (42.4%)	1 (14.3%)	32 (38.1%)	197 (38.8%)
2) Non-DDR Deficient	33 (44.6%)	11 (36.7%)	11 (36.7%)	26 (45.6%)	2 (66.7%)	27 (48.2%)	23 (30.7%)	31 (33.7%)	3 (42.9%)	36 (42.9%)	203 (40.0%)
3) Unknown Deficient	11 (14.9%)	8 (26.7%)	7 (23.3%)	9 (15.8%)	1 (33.3%)	14 (25.0%)	17 (22.7%)	22 (23.9%)	3 (42.9%)	16 (19.0%)	108 (21.3%)
ATM Deficient	7 (9.5%)	3 (10.0%)	4 (13.3%)	5 (8.8%)	0 (0.0%)	6 (10.7%)	6 (8.0%)	8 (8.7%)	0 (0.0%)	8 (9.5%)	47 (9.3%)
ATR Deficient	1 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	3 (0.6%)
BRCA1 Deficient	1 (1.4%)	1 (3.3%)	2 (6.7%)	1 (1.8%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	2 (2.2%)	0 (0.0%)	2 (2.4%)	10 (2.0%)
BRCA2 Deficient	7 (9.5%)	3 (10.0%)	2 (6.7%)	7 (12.3%)	0 (0.0%)	5 (8.9%)	14 (18.7%)	14 (15.2%)	1 (14.3%)	7 (8.3%)	60 (11.8%)
CDK12 Deficient	5 (6.8%)	4 (13.3%)	1 (3.3%)	5 (8.8%)	0 (0.0%)	3 (5.4%)	5 (6.7%)	6 (6.5%)	0 (0.0%)	8 (9.5%)	37 (7.3%)
CHEK2 Deficient	6 (8.1%)	2 (6.7%)	4 (13.3%)	3 (5.3%)	0 (0.0%)	0 (0.0%)	7 (9.3%)	7 (7.6%)	0 (0.0%)	6 (7.1%)	35 (6.9%)
FANCA Deficient	1 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	4 (0.8%)
MLH1	1 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	1 (1.8%)	1 (1.3%)	2 (2.2%)	0 (0.0%)	3 (3.6%)	9 (1.8%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
Deficient NBN	4 (5.4%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	1 (1.8%)	1 (1.3%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	8 (1.6%)
Deficient PALB2	0 (0.0%)	0 (0.0%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.7%)	3 (3.3%)	0 (0.0%)	3 (3.6%)	9 (1.8%)
Deficient RAD51C	1 (1.4%)	0 (0.0%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.4%)
ECOG, n (%)											
0	53 (71.6%)	24 (80.0%)	23 (76.7%)	33 (57.9%)	1 (33.3%)	38 (67.9%)	48 (64.0%)	59 (64.1%)	1 (14.3%)	45 (53.6%)	325 (64.0%)
1	21 (28.4%)	6 (20.0%)	7 (23.3%)	24 (42.1%)	2 (66.7%)	18 (32.1%)	27 (36.0%)	33 (35.9%)	6 (85.7%)	39 (46.4%)	183 (36.0%)
Treatment history											
Bilateral orchiectomy	3 (4.1%)	2 (6.7%)	2 (6.7%)	2 (3.5%)	1 (33.3%)	3 (5.4%)	4 (5.3%)	4 (4.3%)	0 (0.0%)	5 (6.0%)	26 (5.1%)
Prior prostate cancer surgery[a]	56 (75.7%)	22 (73.3%)	24 (80.0%)	45 (78.9%)	2 (66.7%)	45 (80.4%)	54 (72.0%)	74 (80.4%)	7 (100.0%)	68 (81.0%)	397 (78.1%)
Prior radiation therapy	14 (18.9%)	7 (23.3%)	2 (6.7%)	9 (15.8%)	2 (66.7%)	10 (17.9%)	19 (25.3%)	27 (29.3%)	3 (42.9%)	20 (23.8%)	113 (22.2%)
Prior hormonal therapy	3 (4.1%)	1 (3.3%)	1 (3.3%)	2 (3.5%)	0 (0.0%)	4 (7.1%)	6 (8.0%)	6 (6.5%)	0 (0.0%)	8 (9.5%)	31 (6.1%)
Androgen deprivation therapy at baseline	73 (98.6%)	28 (93.3%)	28 (93.3%)	55 (96.5%)	2 (66.7%)	52 (92.9%)	73 (97.3%)	90 (97.8%)	7 (100.0%)	79 (94.0%)	487 (95.9%)
Triptorelin	15 (20.3%)	5 (16.7%)	4 (13.3%)	10 (17.5%)	2 (66.7%)	12 (21.4%)	12 (16.0%)	15 (16.3%)	2 (28.6%)	10 (11.9%)	87 (17.1%)
Degarelix	10 (13.5%)	3 (10.0%)	3 (10.0%)	5 (8.8%)	0 (0.0%)	10 (17.9%)	14 (18.7%)	17 (18.5%)	3 (42.9%)	20 (23.8%)	85 (16.7%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
Leuprorelin	36 (48.6%)	20 (66.7%)	18 (60.0%)	30 (52.6%)	1 (33.3%)	26 (46.4%)	51 (68.0%)	52 (56.5%)	2 (28.6%)	45 (53.6%)	281 (55.3%)
Gonadorelin	1 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	3 (0.6%)
Relugolix	2 (2.7%)	0 (0.0%)	2 (6.7%)	2 (3.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (1.2%)
Goserelin	8 (10.8%)	1 (3.3%)	3 (10.0%)	6 (10.5%)	0 (0.0%)	8 (14.3%)	5 (6.7%)	5 (5.4%)	0 (0.0%)	8 (9.5%)	44 (8.7%)
Histrelin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)
Flutamide	2 (2.7%)	2 (6.7%)	2 (6.7%)	1 (1.8%)	1 (33.3%)	2 (3.6%)	7 (9.3%)	3 (3.3%)	1 (14.3%)	3 (3.6%)	24 (4.7%)
Bicalutamide	37 (50.0%)	17 (56.7%)	19 (63.3%)	32 (56.1%)	2 (66.7%)	28 (50.0%)	36 (48.0%)	67 (72.8%)	4 (57.1%)	42 (50.0%)	284 (55.9%)
Enzalutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Darolutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Taxane Based Chemotherapy	29 (39.2%)	6 (20.0%)	4 (13.3%)	11 (19.3%)	0 (0.0%)	17 (30.4%)	18 (24.0%)	18 (19.6%)	3 (42.9%)	18 (21.4%)	124 (24.4%)
Carbazitaxel	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Docetaxel	29 (39.2%)	6 (20.0%)	4 (13.3%)	11 (19.3%)	0 (0.0%)	17 (30.4%)	18 (24.0%)	18 (19.6%)	3 (42.9%)	18 (21.4%)	124 (24.4%)
Abiraterone	3 (4.1%)	1 (3.3%)	1 (3.3%)	2 (3.5%)	0 (0.0%)	4 (7.1%)	4 (5.3%)	6 (6.5%)	0 (0.0%)	8 (9.5%)	29 (5.7%)
Daralutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Apalutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Orteronel/TAK700	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.4%)
Baseline labs											
Hemoglobin, Median [Q1,Q3]	138 [135,143]	141 [136,143]	141 [134,147]	139 [132,143]	126 [123,129]	138 [133,143]	125 [118,129]	124 [116,128]	117 [97.0,124]	118 [107,126]	131 [121,139]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
eGFR, Median [Q1,Q3]	90.5 [77.0,106]	86.5 [68.8,94.8]	87.5 [82.3,96.5]	85.5 [73.0,93.0]	101 [90.3,117]	91.0 [77.0,105]	90.0 [74.0,109]	83.9 [66.9,94.8]	66.2 [59.0,75.5]	79.5 [66.5,91.3]	86.9 [71.0,97.6]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ALT, Median [Q1,Q3]	0.370 [0.280,0.495]	0.355 [0.270,0.528]	0.370 [0.285,0.465]	0.320 [0.270,0.470]	0.300 [0.275,0.340]	0.370 [0.270,0.528]	0.300 [0.230,0.400]	0.270 [0.220,0.385]	0.280 [0.225,0.325]	0.275 [0.200,0.355]	0.320 [0.250,0.423]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Albumin, Median [Q1,Q3]	42.0 [39.3,44.9]	43.0 [40.0,44.8]	42.7 [40.3,44.0]	43.0 [41.0,44.5]	42.0 [40.5,45.7]	43.0 [40.0,45.0]	41.0 [38.0,43.8]	41.0 [39.0,43.0]	36.0 [35.5,42.0]	41.0 [38.0,43.3]	42.0 [39.0,44.0]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ALP, Median [Q1,Q3]	1.60 [1.19,2.38]	1.70 [1.14,2.25]	1.68 [1.19,2.37]	1.75 [1.38,3.58]	2.00 [1.39,2.20]	1.92 [1.31,3.47]	2.15 [1.28,3.69]	2.25 [1.43,4.67]	7.35 [5.83,11.7]	2.24 [1.28,4.56]	1.93 [1.27,3.70]
Missing	0 (0%)	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (2.4%)	3 (0.6%)
AST, Median [Q1,Q3]	0.380 [0.323,0.450]	0.380 [0.320,0.430]	0.400 [0.355,0.495]	0.400 [0.300,0.500]	0.400 [0.340,0.425]	0.380 [0.330,0.485]	0.370 [0.280,0.460]	0.350 [0.280,0.435]	0.430 [0.350,0.610]	0.350 [0.300,0.430]	0.370 [0.300,0.463]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HCO3, Median [Q1,Q3]	25.1 [24.0,27.9]	25.0 [23.6,28.0]	25.0 [24.0,27.0]	27.0 [25.0,27.9]	27.8 [27.6,27.9]	25.4 [23.2,27.0]	25.3 [23.1,26.5]	25.0 [23.0,27.0]	29.0 [28.0,29.0]	25.5 [23.0,27.1]	25.5 [23.6,27.0]
Missing	9 (12.2%)	5 (16.7%)	5 (16.7%)	6 (10.5%)	1 (33.3%)	12 (21.4%)	13 (17.3%)	16 (17.4%)	4 (57.1%)	15 (17.9%)	86 (16.9%)
Total_bilirubin, Median [Q1,Q3]	9.00 [7.00,12.0]	8.65 [7.00,13.3]	9.45 [8.00,12.0]	10.3 [8.60,12.7]	9.40 [7.70,460]	10.3 [7.00,13.0]	8.00 [6.00,10.3]	8.60 [6.80,12.0]	8.00 [5.05,9.30]	7.35 [6.28,10.3]	8.60 [6.80,12.0]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
BUN, Median [Q1,Q3]	5.70 [5.00,6.80]	5.80 [4.70,6.25]	5.90 [5.25,8.10]	6.35 [5.55,7.18]	4.50 [4.50,4.50]	5.60 [4.70,6.40]	6.60 [5.45,8.15]	6.80 [5.40,8.20]	9.90 [8.15,10.7]	6.85 [6.03,8.50]	6.40 [5.40,7.90]
Missing	57 (77.0%)	20 (66.7%)	19 (63.3%)	33 (57.9%)	2 (66.7%)	35 (62.5%)	36 (48.0%)	47 (51.1%)	4 (57.1%)	38 (45.2%)	291 (57.3%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
Ca, Median [Q1,Q3]	2.33 [2.26,2.40]	2.32 [2.28,2.38]	2.35 [2.29,2.40]	2.30 [2.24,2.37]	2.39 [2.30,2.43]	2.32 [2.27,2.39]	2.31 [2.26,2.43]	2.34 [2.24,2.40]	2.30 [2.26,2.35]	2.35 [2.27,2.41]	2.33 [2.26,2.40]
Missing	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)	0 (0%)	2 (0.4%)
Cl, Median [Q1,Q3]	104 [102,106]	104 [101,106]	104 [101,106]	104 [102,105]	102 [102,103]	105 [102,107]	105 [103,106]	105 [103,107]	105 [104,107]	104 [102,105]	104 [102,106]
Missing	1 (1.4%)	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.2%)	3 (0.6%)
CK, Median [Q1,Q3]	1.94 [1.22,2.87]	1.37 [1.08,1.83]	1.24 [0.858,2.17]	1.28 [0.830,1.90]	0.630 [0.630,0.630]	1.47 [1.29,2.00]	1.91 [1.50,3.48]	1.86 [1.34,2.15]	0.950 [0.490,1.14]	1.45 [0.850,2.20]	1.50 [1.04,2.20]
Missing	58 (78.4%)	23 (76.7%)	22 (73.3%)	44 (77.2%)	2 (66.7%)	41 (73.2%)	65 (86.7%)	70 (76.1%)	4 (57.1%)	67 (79.8%)	396 (78.0%)
Glucose, Median [Q1,Q3]	5.58 [5.22,6.56]	5.69 [5.12,7.27]	5.83 [5.32,7.16]	5.66 [5.30,6.48]	5.16 [5.08,5.58]	5.89 [5.38,6.77]	5.92 [5.32,6.43]	5.58 [5.24,6.41]	6.20 [5.83,7.58]	6.08 [5.55,6.84]	5.80 [5.30,6.60]
Missing	0 (0%)	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)	0 (0%)	1 (1.3%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)
LDH, Median [Q1,Q3]	198 [178,236]	197 [179,218]	220 [194,242]	215 [194,252]	216 [166,223]	204 [183,235]	214 [182,277]	207 [177,266]	249 [210,322]	216 [180,313]	209 [182,254]
Missing	2 (2.7%)	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)	2 (3.6%)	0 (0%)	0 (0%)	0 (0%)	1 (1.2%)	6 (1.2%)
Mg, Median [Q1,Q3]	0.860 [0.810,0.920]	0.860 [0.813,0.900]	0.820 [0.780,0.860]	0.860 [0.800,0.900]	0.870 [0.815,0.930]	0.860 [0.815,0.915]	0.860 [0.810,0.900]	0.860 [0.800,0.920]	0.870 [0.840,0.900]	0.850 [0.770,0.905]	0.860 [0.800,0.910]
Missing	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)	1 (1.1%)	0 (0%)	1 (1.2%)	4 (0.8%)
K, Median [Q1,Q3]	4.30 [4.03,4.60]	4.30 [4.03,4.48]	4.20 [4.10,4.58]	4.20 [4.00,4.50]	4.30 [4.15,4.60]	4.20 [4.00,4.60]	4.30 [4.00,4.59]	4.24 [4.00,4.60]	4.40 [3.95,4.60]	4.30 [4.05,4.52]	4.30 [4.00,4.54]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Protein, Median [Q1,Q3]	71.0 [68.0,74.0]	71.0 [68.3,74.0]	71.2 [69.0,73.9]	71.0 [68.0,74.5]	73.1 [73.1,74.6]	70.6 [69.0,75.1]	70.4 [67.0,74.0]	70.0 [66.0,73.0]	73.0 [69.0,75.0]	70.0 [68.0,73.5]	71.0 [67.6,74.0]
Missing	1 (1.4%)	0 (0%)	0 (0%)	2 (3.5%)	0 (0%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)	1 (1.2%)	5 (1.0%)
Na, Median [Q1,Q3]	141 [139,142]	140 [138,142]	141 [139,142]	140 [138,142]	138 [137,139]	141 [140,142]	140 [138,142]	141 [139,142]	140 [140,142]	140 [138,142]	141 [139,142]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
Creatinine, Median [Q1,Q3]	76.0 [65.6,86.7]	78.8 [65.6,93.1]	76.0 [71.8,80.1]	77.0 [70.7,88.4]	72.0 [67.0,75.8]	77.5 [66.8,85.8]	76.9 [66.8,94.5]	82.1 [68.7,93.8]	102 [79.6,123]	85.0 [75.6,102]	78.0 [68.0,92.0]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Phosphate, Median [Q1,Q3]	1.20 [1.10,1.30]	1.10 [1.00,1.20]	1.20 [1.03,1.30]	1.10 [1.00,1.20]	1.30 [1.15,1.35]	1.10 [1.08,1.20]	1.10 [1.10,1.30]	1.10 [1.00,1.30]	1.10 [1.05,1.15]	1.10 [1.00,1.30]	1.10 [1.00,1.30]
Missing	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (2.7%)	0 (0%)	0 (0%)	3 (3.6%)	6 (1.2%)
Testosterone, Median [Q1,Q3]	11.5 [7.18,17.0]	13.0 [6.62,20.0]	11.5 [9.00,17.1]	12.5 [4.89,18.3]	8.53 [6.27,9.16]	11.5 [8.57,17.7]	12.0 [8.00,19.6]	11.0 [5.76,17.0]	13.5 [11.9,17.0]	11.5 [6.50,18.0]	11.5 [7.00,18.0]
Missing	2 (2.7%)	2 (6.7%)	0 (0%)	1 (1.8%)	0 (0%)	0 (0%)	2 (2.7%)	1 (1.1%)	1 (14.3%)	1 (1.2%)	10 (2.0%)
Urea, Median [Q1,Q3]	6.11 [5.01,7.08]	5.90 [4.90,7.20]	5.20 [4.47,7.20]	6.40 [5.43,7.78]	7.91 [7.61,8.22]	5.50 [4.82,7.12]	6.90 [5.34,7.68]	6.30 [4.84,7.90]	7.25 [5.50,10.5]	6.75 [5.80,8.35]	6.40 [5.00,7.58]
Missing	12 (16.2%)	8 (26.7%)	11 (36.7%)	22 (38.6%)	1 (33.3%)	20 (35.7%)	38 (50.7%)	39 (42.4%)	3 (42.9%)	40 (47.6%)	194 (38.2%)
FolicAcid, Median [Q1,Q3]	8.81 [6.88,13.9]	8.35 [6.50,13.3]	9.00 [6.30,11.3]	8.20 [5.88,14.5]	7.47 [6.41,8.54]	8.40 [6.14,13.4]	9.00 [6.47,13.3]	8.71 [5.75,14.9]	7.60 [4.16,10.8]	8.20 [5.31,13.0]	8.56 [6.01,13.7]
Missing	3 (4.1%)	5 (16.7%)	1 (3.3%)	2 (3.5%)	1 (33.3%)	5 (8.9%)	8 (10.7%)	4 (4.3%)	0 (0%)	6 (7.1%)	35 (6.9%)
VitaminB12, Median [Q1,Q3]	380 [304,472]	428 [271,612]	458 [321,571]	371 [246,478]	451 [372,715]	414 [269,545]	402 [298,581]	384 [293,534]	389 [366,635]	366 [264,540]	388 [285,535]
Missing	2 (2.7%)	4 (13.3%)	0 (0%)	2 (3.5%)	0 (0%)	4 (7.1%)	4 (5.3%)	2 (2.2%)	0 (0%)	4 (4.8%)	22 (4.3%)
PSA, Median [Q1,Q3]	16.3 [5.15,46.9]	27.0 [11.9,48.1]	12.7 [4.88,59.0]	14.5 [3.90,48.5]	25.4 [18.1,117]	17.0 [5.93,40.5]	24.7 [8.60,78.6]	13.6 [6.08,53.1]	35.6 [14.4,212]	25.4 [7.47,74.4]	18.1 [6.40,61.7]
Missing	0 (0%)	1 (3.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.3%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)
MCV, Median [Q1,Q3]	91.0 [88.0,94.0]	90.0 [89.0,93.8]	93.0 [91.0,95.8]	93.0 [90.0,96.0]	89.0 [88.5,95.0]	94.0 [90.0,95.0]	90.0 [86.0,93.5]	91.0 [88.0,95.0]	92.0 [87.5,93.5]	91.0 [87.0,94.0]	91.0 [88.0,95.0]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)	0 (0%)	0 (0%)	1 (1.2%)	2 (0.4%)
RBC, Median [Q1,Q3]	4.56 [4.41,4.84]	4.61 [4.42,4.82]	4.56 [4.36,4.75]	4.50 [4.10,4.70]	4.13 [3.86,4.32]	4.47 [4.28,4.64]	4.20 [4.02,4.37]	4.00 [3.69,4.31]	3.49 [3.44,3.80]	3.92 [3.63,4.19]	4.29 [3.96,4.56]

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HCT, Median [Q1,Q3]	39.7 [0.420,41.9]	40.4 [0.443,41.8]	40.6 [0.430,43.0]	39.6 [0.430,42.2]	0.400 [0.385,18.4]	39.0 [0.420,41.5]	36.4 [32.0,38.4]	35.8 [30.2,38.3]	0.380 [0.325,32.5]	33.9 [29.1,37.0]	36.4 [0.420,40.0]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
WBC, Median [Q1,Q3]	6.43 [5.15,7.85]	5.90 [5.11,7.60]	5.98 [5.65,7.39]	5.63 [4.80,6.38]	4.90 [4.35,5.25]	6.06 [5.18,7.38]	5.79 [4.82,7.36]	5.36 [4.25,6.63]	6.10 [5.25,6.76]	6.20 [4.87,7.52]	5.94 [4.90,7.25]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Basophils, Median [Q1,Q3]	0.0400 [0.0200,0.0800]	0.0200 [0,0.0500]	0.0300 [0.0200,0.0600]	0.0300 [0.00500,0.0400]	0.0300 [0.0300,0.0500]	0.0400 [0.0300,0.0600]	0.0300 [0.0200,0.0500]	0.0300 [0.0100,0.0500]	0.0500 [0.0400,0.0500]	0.0300 [0.0100,0.0500]	0.0300 [0.0100,0.0500]
Missing	7 (9.5%)	2 (6.7%)	4 (13.3%)	10 (17.5%)	0 (0%)	7 (12.5%)	15 (20.0%)	18 (19.6%)	2 (28.6%)	19 (22.6%)	84 (16.5%)
Basophils/ Leukocytes, Median [Q1,Q3]	0.602 [0.244,1.02]	0.333 [0,0.707]	0.511 [0.360,0.754]	0.468 [0.104,0.810]	0.789 [0.701,1.02]	0.654 [0.385,0.962]	0.596 [0.342,0.740]	0.548 [0.228,0.767]	0.746 [0.532,0.980]	0.457 [0.152,0.755]	0.542 [0.222,0.839]
Missing	7 (9.5%)	2 (6.7%)	4 (13.3%)	10 (17.5%)	0 (0%)	7 (12.5%)	15 (20.0%)	18 (19.6%)	2 (28.6%)	19 (22.6%)	84 (16.5%)
Eosinophils, Median [Q1,Q3]	0.150 [0.100,0.230]	0.190 [0.100,0.260]	0.195 [0.103,0.240]	0.110 [0.0700,0.200]	0.0900 [0.0650,0.125]	0.175 [0.100,0.270]	0.165 [0.100,0.243]	0.120 [0.0900,0.200]	0.100 [0.100,0.100]	0.150 [0.0925,0.240]	0.150 [0.100,0.220]
Missing	5 (6.8%)	3 (10.0%)	4 (13.3%)	10 (17.5%)	0 (0%)	6 (10.7%)	15 (20.0%)	18 (19.6%)	2 (28.6%)	18 (21.4%)	81 (15.9%)
Eosinophils/Leukocytes , Median [Q1,Q3]	2.37 [1.57,4.00]	2.75 [1.76,4.37]	3.23 [1.86,4.06]	2.11 [1.14,3.78]	1.84 [1.44,2.35]	2.74 [1.76,4.12]	2.66 [1.72,3.82]	2.52 [1.68,3.55]	1.73 [1.64,1.96]	2.31 [1.52,4.19]	2.39 [1.61,3.95]
Missing	5 (6.8%)	3 (10.0%)	4 (13.3%)	10 (17.5%)	0 (0%)	6 (10.7%)	15 (20.0%)	18 (19.6%)	2 (28.6%)	18 (21.4%)	81 (15.9%)
Lymphocytes, Median [Q1,Q3]	1.62 [1.20,2.18]	1.60 [1.13,2.05]	1.63 [1.22,2.20]	1.50 [1.11,1.98]	1.71 [1.52,1.82]	1.65 [1.30,2.02]	1.40 [1.13,1.85]	1.27 [1.00,1.56]	1.40 [1.28,1.77]	1.38 [1.05,1.73]	1.48 [1.10,1.90]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
Lymphocytes/Leukocytes , Median [Q1,Q3]	25.5 [20.6,30.7]	25.4 [21.0,33.9]	27.5 [18.6,32.7]	26.4 [21.3,33.3]	39.4 [31.5,42.2]	25.3 [21.9,33.2]	24.6 [19.8,30.4]	24.0 [20.8,29.4]	25.1 [20.8,28.1]	24.1 [17.6,28.1]	24.8 [20.0,30.9]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Monocytes, Median [Q1,Q3]	0.560 [0.405,0.640]	0.460 [0.315,0.600]	0.470 [0.400,0.530]	0.460 [0.400,0.530]	0.380 [0.355,0.480]	0.500 [0.400,0.600]	0.540 [0.400,0.623]	0.455 [0.320,0.600]	0.510 [0.350,0.700]	0.490 [0.350,0.620]	0.500 [0.390,0.605]
Missing	7 (9.5%)	3 (10.0%)	4 (13.3%)	10 (17.5%)	0 (0%)	7 (12.5%)	15 (20.0%)	18 (19.6%)	2 (28.6%)	19 (22.6%)	85 (16.7%)
Monocytes/Leukocytes , Median [Q1,Q3]	8.33 [6.98,9.87]	7.84 [6.08,9.30]	7.65 [6.15,9.44]	8.29 [7.04,10.0]	8.68 [8.22,9.53]	7.84 [6.67,9.23]	8.71 [6.99,10.4]	8.17 [6.49,9.93]	10.0 [4.65,11.5]	7.83 [6.25,9.38]	8.11 [6.61,9.81]
Missing	7 (9.5%)	3 (10.0%)	4 (13.3%)	10 (17.5%)	0 (0%)	7 (12.5%)	15 (20.0%)	18 (19.6%)	2 (28.6%)	19 (22.6%)	85 (16.7%)
Neutrophils, Median [Q1,Q3]	4.02 [3.19,4.91]	3.60 [2.51,4.64]	3.81 [3.12,4.79]	3.29 [2.55,4.00]	2.46 [2.08,2.96]	3.62 [3.00,4.66]	3.50 [2.81,4.63]	3.40 [2.68,4.46]	3.45 [3.30,3.87]	4.15 [3.08,4.99]	3.63 [2.85,4.63]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)	0 (0%)	1 (0.2%)
Neutrophils/Leukocytes, Median [Q1,Q3]	62.6 [56.3,68.2]	62.3 [54.9,67.0]	60.2 [55.6,69.4]	60.6 [54.2,66.1]	50.2 [47.3,56.1]	62.1 [55.1,68.0]	62.3 [55.1,68.6]	63.8 [58.1,68.0]	63.1 [59.7,65.1]	65.3 [59.6,71.6]	62.7 [56.2,68.2]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)	0 (0%)	1 (0.2%)
Platelets, Median [Q1,Q3]	232 [198,270]	251 [189,269]	219 [192,301]	211 [176,235]	227 [219,258]	222 [185,261]	223 [191,264]	219 [175,264]	279 [245,319]	230 [197,283]	223 [187,267]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Retics, Median [Q1,Q3]	60.0 [54.5,75.0]	75.5 [56.5,87.9]	68.0 [49.2,78.3]	59.3 [50.0,81.0]	48.2 [41.3,55.1]	66.5 [58.3,81.0]	63.0 [48.3,69.8]	64.8 [49.2,82.0]	46.5 [43.5,51.0]	56.5 [42.6,72.0]	62.0 [49.8,78.1]
Missing	21 (28.4%)	7 (23.3%)	13 (43.3%)	24 (42.1%)	1 (33.3%)	16 (28.6%)	35 (46.7%)	39 (42.4%)	3 (42.9%)	41 (48.8%)	200 (39.4%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
EPO, Median [Q1,Q3]	9.90 [7.70,13.1]	10.0 [8.16,16.7]	11.2 [8.60,12.8]	11.1 [7.20,16.4]	23.7 [19.8,28.5]	11.7 [9.03,17.7]	14.4 [10.6,19.7]	15.7 [11.8,22.6]	10.0 [8.80,22.9]	15.2 [11.5,25.0]	12.9 [9.45,19.0]
Missing	17 (23.0%)	9 (30.0%)	6 (20.0%)	10 (17.5%)	0 (0%)	10 (17.9%)	12 (16.0%)	14 (15.2%)	2 (28.6%)	17 (20.2%)	97 (19.1%)
Baseline anemia symptoms											
Fatigue	26 (35.1%)	10 (33.3%)	10 (33.3%)	20 (35.1%)	1 (33.3%)	19 (33.9%)	19 (25.3%)	30 (32.6%)	1 (14.3%)	32 (38.1%)	168 (33.1%)
Shortness Breath	0 (0.0%)	0 (0.0%)	2 (6.7%)	1 (1.8%)	0 (0.0%)	3 (5.4%)	1 (1.3%)	5 (5.4%)	0 (0.0%)	1 (1.2%)	13 (2.6%)
Decreased Appetite	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	3 (3.6%)	5 (1.0%)
Asthenia	8 (10.8%)	4 (13.3%)	3 (10.0%)	7 (12.3%)	0 (0.0%)	8 (14.3%)	4 (5.3%)	10 (10.9%)	0 (0.0%)	5 (6.0%)	49 (9.6%)
Dyspnea	7 (9.5%)	2 (6.7%)	2 (6.7%)	8 (14.0%)	0 (0.0%)	2 (3.6%)	4 (5.3%)	6 (6.5%)	0 (0.0%)	6 (7.1%)	37 (7.3%)
Dizziness	7 (9.5%)	2 (6.7%)	2 (6.7%)	7 (12.3%)	1 (33.3%)	11 (19.6%)	6 (8.0%)	11 (12.0%)	1 (14.3%)	6 (7.1%)	54 (10.6%)
Baseline anemia management											
Iron treatment up to and prior to baseline	0 (0.0%)	0 (0.0%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.2%)	0 (0.0%)	0 (0.0%)	3 (0.6%)
Index treatment details											
Baseline Talazoparib Dose											
0.35	8 (10.8%)	4 (13.3%)	2 (6.7%)	4 (7.0%)	0 (0%)	1 (1.8%)	8 (10.7%)	9 (9.8%)	3 (42.9%)	16 (19.0%)	55 (10.8%)

Table 8. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 by early dose pattern strata experienced during the study

	1 (N=74)	2 (N=30)	3 (N=30)	4 (N=57)	5 (N=3)	6 (N=56)	7 (N=75)	8 (N=92)	9 (N=7)	10 (N=84)	Overall (N=508)
0.5	66 (89.2%)	26 (86.7%)	28 (93.3%)	53 (93.0%)	3 (100%)	55 (98.2%)	67 (89.3%)	83 (90.2%)	4 (57.1%)	68 (81.0%)	453 (89.2%)
Years between prostate cancer diagnosis and Talazoparib initiation, Median [Q1,Q3]	3.00 [2.00,6.00]	3.50 [2.00,7.00]	3.00 [2.00,5.75]	3.00 [1.00,7.00]	7.00 [4.50,8.00]	3.00 [2.00,6.00]	3.00 [1.00,6.00]	3.00 [1.00,6.25]	2.00 [2.00,7.00]	3.00 [1.00,6.00]	3.00 [1.00,6.00]

[a]Includes prostatectomy, transurethral resection of the prostate, prostate biopsy, bilateral orchiectomy, pelvic node dissection, urethral stent, and nephrostomy

Units: Hemoglobin (g/L); eGFR (mL/min/1.73 m²); ALT (µkat/L); Albumin (g/L); ALP (µkat/L); AST (µkat/L); Bicarbonate (mmol/L); Total Bilirubin (µmol/L); BUN (mmol/L); Calcium (mmol/L); Chloride (mmol/L); Creatine Kinase (µkat/L); Glucose (mmol/L); LDH (U/L); Magnesium (mmol/L); Potassium (mmol/L); Protein (g/L); Sodium (mmol/L); Creatinine (µmol/L); Phosphate (mmol/L); Testosterone (ng/dL); Urea (mmol/L); Vitamin B9 (µg/L); Vitamin B12 (ng/L); PSA (µg/L); MCV (fL); RBC (10^{12}/L); Hematocrit (L/L); WBC (10^9/L); Basophils (10^9/L); Basophils/Leukocytes (%); Eosinophils (10^9/L); Eosinophils/Leukocytes (%); Lymphocytes (10^9/L); Lymphocytes/Leukocytes (%); Monocytes (10^9/L); Monocytes/Leukocytes (%); Neutrophils (10^9/L); Neutrophils/Leukocytes (%); Platelets (10^9/L).

Early dose pattern categories based on anemia and dose deviation patterns as specified in Table 3.

Post-dose deviation anemia outcomes were summarized in Table 9 with the proportions of patients who improved, remained the same, or worsened in anemia severity during the 1st and 2nd visits after dose deviation. The table shows the summaries overall and stratified by anemia severity at dose deviation and initial talazoparib dose. Among the overall cohort of n=319 patients that had a dose deviation, n=34 (10.7%) did not have an anemia event recorded at time of dose deviation, and n=102 (32.0%) patients received a RBC transfusion on or after the dose deviation date and before the 1st follow-up lab visit measuring hemoglobin. At the 1st follow-up lab visit, 22 (6.9%) had an improved anemia status; 146 (45.8%) had an unchanged anemia status; and 15 (4.7%) had a worse anemia status than at dose deviation. No additional patients received RBC transfusion during the intervening period between the 1st and 2nd follow-up lab visits. At the 2nd follow-up lab visit, the proportion of patients classified as improved remained the same as the 1st visit, i.e. 22 (6.9%). At this visit, 154 (48.3%) had an unchanged anemia status and 7 (2.2%) had a worse anemia status than at dose deviation. When stratified by the severity of the anemia grade at dose deviation, a larger proportion of patients with Grade ≥3 anemia showed improvement than those with Grade 1 or 2 at dose deviation (13.5% vs 3.5%) at the 1st visit after dose deviation, and similarly at the 2nd visit after dose deviation (11.9% vs 4.9%). When stratified by the initial talazoparib dose, only patients that initiated at the higher dose of 0.5 mg showed improvement after the 1st and 2nd weeks post dose deviation whereas no improvement was observed among patients who initiated at 0.35 mg. Also of note, patients who initiated at the lower dose of 0.35 mg had a larger proportion of patients who did not have an anemia event recorded at time of dose deviation compared to patients who initiated at the higher dose of 0.5 mg (23.5% vs 9.1%).

Table 9 is repeated using the broad definition of time to dose modification (defined as the receipt of talazoparib dose that was different from the initiating dose) in Appendix 8.1 **Error! Reference source not found.**.

Table 9. Anemia status at 1st and 2nd visits after dose deviation, stratified by anemia severity and initial talazoparib dose

	Overall			Post Grade 1-2 anemia			Post Grade ≥3 anemia		
	0.35 (N=34)	0.5 (N=285)	Overall (N=319)	0.35 (N=9)	0.5 (N=133)	Overall (N=142)	0.35 (N=14)	0.5 (N=112)	Overall (N=126)
Post dose deviation anemia status 1									
Improved	0 (0%)	22 (7.7%)	22 (6.9%)	0 (0%)	5 (3.8%)	5 (3.5%)	0 (0%)	17 (15.2%)	17 (13.5%)
Unchanged	15 (44.1%)	131 (46.0%)	146 (45.8%)	5 (55.6%)	67 (50.4%)	72 (50.7%)	8 (57.1%)	53 (47.3%)	61 (48.4%)
Worsened	1 (2.9%)	14 (4.9%)	15 (4.7%)	1 (11.1%)	13 (9.8%)	14 (9.9%)	0 (0%)	0 (0%)	0 (0%)
Transfusion	10 (29.4%)	92 (32.3%)	102 (32.0%)	3 (33.3%)	48 (36.1%)	51 (35.9%)	6 (42.9%)	42 (37.5%)	48 (38.1%)
N/A	8 (23.5%)	26 (9.1%)	34 (10.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 9. Anemia status at 1st and 2nd visits after dose deviation, stratified by anemia severity and initial talazoparib dose

	Overall			Post Grade 1-2 anemia			Post Grade ≥3 anemia		
	0.35 (N=34)	0.5 (N=285)	Overall (N=319)	0.35 (N=9)	0.5 (N=133)	Overall (N=142)	0.35 (N=14)	0.5 (N=112)	Overall (N=126)
Post dose deviation anemia status 2									
Improved	0 (0%)	22 (7.7%)	22 (6.9%)	0 (0%)	7 (5.3%)	7 (4.9%)	0 (0%)	15 (13.4%)	15 (11.9%)
Unchanged	16 (47.1%)	138 (48.4%)	154 (48.3%)	6 (66.7%)	71 (53.4%)	77 (54.2%)	8 (57.1%)	55 (49.1%)	63 (50.0%)
Worsened	0 (0%)	7 (2.5%)	7 (2.2%)	0 (0%)	7 (5.3%)	7 (4.9%)	0 (0%)	0 (0%)	0 (0%)
Transfusion	10 (29.4%)	92 (32.3%)	102 (32.0%)	3 (33.3%)	48 (36.1%)	51 (35.9%)	6 (42.9%)	42 (37.5%)	48 (38.1%)
N/A	8 (23.5%)	26 (9.1%)	34 (10.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

i. Dose deviation is defined as receipt of dose that was different from the initiating dose and that was sustained for 7 days or longer, or if dose deviation period was <7 days, was explicitly stated as a dose modification due to an adverse event.
ii. Counts not expected to add up between Post Grade 1-2 anemia and Post Grade ≥3 anemia because anemia events did not precede all dose deviations
iii. If a post-index RBC transfusion date occurs on or after 1st dose deviation and before the next visit capturing hemoglobin-inferred anemia status, the “Post Dose Deviation Anemia Status” value is "Transfusion". Otherwise: If the hemoglobin-inferred anemia status is any grade lower than "Anemia status at first dose deviation", value is “Improved”. If the hemoglobin-inferred anemia status is unchanged from "Anemia status at first dose deviation", value is “Unchanged”. If the hemoglobin-inferred anemia status is any grade worse than "Anemia status at first dose deviation", value is “Worsened”. If patient did not have any anemia at time of dose deviation, value is “N/A”.

Table 10 summarizes patient characteristics corresponding to change in anemia status at 1 and 2 visits after dose deviation. At the first follow-up visit after dose deviation, a greater proportion of patients with improvement were White (16/22, 72.7%) and a smaller proportion were Asian (5/22, 22.7%), relative to patients with unchanged (White: 90/146, 61.6%; Asian: 44/146, 30.1%) and worse anemia status (White: 7/15, 46.7%; Asian: 7/15, 46.7%). Patients with improvement also had higher baseline body size measures, with a higher median baseline weight (84.0 [72.2, 91.9] kg) and higher median BMI (27.1 [24.9, 28.9] kg/m²) compared with those with unchanged (median weight 77.7 [68.1, 87.6] kg; median BMI 26.6 [23.9, 29.3] kg/m²) or worse anemia status (median weight 70.2 [61.0, 78.5] kg; median BMI 23.9 [22.2, 26.7] kg/m²). A large proportion of patients with improvement had normal renal function (21/22, 95.5%) than among those with unchanged (125/146, 85.6%) or worse (13/15, 86.7%) anemia status. Per trial protocol guidance, reduced 0.35 mg/day dose was given to patients with moderate renal impairment. Accordingly, receiving 0.5 mg/day (i.e. had normal renal function) was more common among patients with improvement (22/22, 100.0%) than among those with unchanged (131/146, 89.7%) or worse (14/15, 90.2%) anemia status. Being HRR-deficient was less common in the improved group (4/22, 18.2%) compared with those with unchanged (58/146, 39.7%) or worse (8/15, 53.3%) anemia status. Per study design, Cohort 1 consisted of all-comers regardless of HRR gene alteration status, and Cohort 2 consisted of only HRR-deficient patients. Accordingly, being part of Cohort 1 was more common among patients with improvement (18/22, 81.8%) than among those with unchanged (89/146, 61.0%) or worse (7/15, 46.7%) anemia status.

Similar broad patterns were observed at the second follow-up visit, with improvement corresponding to a higher proportion of White patients, higher baseline weight and BMI, a greater prevalence of normal renal function, and fewer patients with HRR mutations.

Table 10 is repeated using the broad definition of time to dose modification (defined as the receipt of talazoparib dose that was different from the initiating dose) in Appendix 8.1 **Error! Reference source not found.**.

Table 10. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 for the overall study cohort and by post-dose deviation anemia status at 1 visit and 2 visits after dose deviation

	Post-dose deviation anemia status 1: Improved (N=22)	Post-dose deviation anemia status 1: Unchanged (N=146)	Post-dose deviation anemia status 1: Worsened (N=15)	Post-dose deviation anemia status 2: Improved (N=22)	Post-dose deviation anemia status 2: Unchanged (N=154)	Post-dose deviation anemia status 2: Worsened (N=7)	Overall (N=319)
Demographics							
Age, Median [Q1,Q3]	74.5 [68.5,80.8]	73.0 [67.0,77.8]	73.0 [69.0,77.5]	72.0 [69.3,75.8]	74.0 [67.0,78.0]	71.0 [65.0,74.0]	71.0 [66.0,76.0]
Race, n (%)							
White	16 (72.7%)	90 (61.6%)	7 (46.7%)	14 (63.6%)	96 (62.3%)	3 (42.9%)	323 (63.6%)
Black or African American	1 (4.5%)	2 (1.4%)	0 (0%)	0 (0%)	3 (1.9%)	0 (0%)	15 (3.0%)
Asian	5 (22.7%)	44 (30.1%)	7 (46.7%)	7 (31.8%)	45 (29.2%)	4 (57.1%)	139 (27.4%)
Native Hawaiian or other Pacific Islander	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (0.6%)
Not Reported	0 (0%)	10 (6.8%)	1 (6.7%)	1 (4.5%)	10 (6.5%)	0 (0%)	28 (5.5%)
Ethnicity, n (%)							
Hispanic or Latino	4 (18.2%)	15 (10.3%)	1 (6.7%)	2 (9.1%)	17 (11.0%)	1 (14.3%)	57 (11.2%)
Not Hispanic or Latino	18 (81.8%)	120 (82.2%)	13 (86.7%)	19 (86.4%)	126 (81.8%)	6 (85.7%)	421 (82.9%)
Not reported	0 (0%)	11 (7.5%)	1 (6.7%)	1 (4.5%)	11 (7.1%)	0 (0%)	30 (5.9%)
Region, n (%)							
1) North America	5 (22.7%)	15 (10.3%)	1 (6.7%)	2 (9.1%)	18 (11.7%)	1 (14.3%)	70 (13.8%)
2) European Union/GBR	8 (36.4%)	61 (41.8%)	4 (26.7%)	10 (45.5%)	63 (40.9%)	0 (0%)	202 (39.8%)
3) Asia	5 (22.7%)	43 (29.5%)	7 (46.7%)	7 (31.8%)	44 (28.6%)	4 (57.1%)	136 (26.8%)
4) Rest of the world	4 (18.2%)	27 (18.5%)	3 (20.0%)	3 (13.6%)	29 (18.8%)	2 (28.6%)	100 (19.7%)
Cohort, n (%)							
1	18 (81.8%)	89 (61.0%)	7 (46.7%)	15 (68.2%)	96 (62.3%)	3 (42.9%)	312 (61.4%)
2	4 (18.2%)	57 (39.0%)	8 (53.3%)	7 (31.8%)	58 (37.7%)	4 (57.1%)	196 (38.6%)

Table 10. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 for the overall study cohort and by post-dose deviation anemia status at 1 visit and 2 visits after dose deviation

	Post-dose deviation anemia status 1: Improved (N=22)	Post-dose deviation anemia status 1: Unchanged (N=146)	Post-dose deviation anemia status 1: Worsened (N=15)	Post-dose deviation anemia status 2: Improved (N=22)	Post-dose deviation anemia status 2: Unchanged (N=154)	Post-dose deviation anemia status 2: Worsened (N=7)	Overall (N=319)
Clinical characteristics							
Weight, Median [Q1,Q3]	84.0 [72.2,91.9]	77.7 [68.1,87.6]	70.2 [61.0,78.5]	83.4 [68.0,90.9]	77.2 [68.1,87.6]	70.5 [56.4,82.4]	80.0 [70.6,92.9]
BMI, Median [Q1,Q3]	27.1 [24.9,28.9]	26.6 [23.9,29.3]	23.9 [22.2,26.7]	26.5 [24.7,28.3]	26.5 [23.7,29.3]	25.5 [22.1,27.5]	27.1 [24.2,30.2]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)
Anemia Status, n (%)							
0	10 (45.5%)	67 (45.9%)	5 (33.3%)	9 (40.9%)	71 (46.1%)	2 (28.6%)	250 (49.2%)
1	11 (50.0%)	70 (47.9%)	10 (66.7%)	12 (54.5%)	74 (48.1%)	5 (71.4%)	236 (46.5%)
2	1 (4.5%)	9 (6.2%)	0 (0%)	1 (4.5%)	9 (5.8%)	0 (0%)	22 (4.3%)
Prior History Anemia	4 (18.2%)	19 (13.0%)	3 (20.0%)	3 (13.6%)	22 (14.3%)	1 (14.3%)	61 (12.0%)
Prior History Kidney Disease	0 (0.0%)	4 (2.7%)	0 (0.0%)	0 (0.0%)	4 (2.6%)	0 (0.0%)	13 (2.6%)
Renal Impairment, n (%)							
Mild/Normal (>=60)	21 (95.5%)	125 (85.6%)	13 (86.7%)	21 (95.5%)	131 (85.1%)	7 (100%)	440 (86.6%)
Moderate (30-59)	0 (0%)	15 (10.3%)	1 (6.7%)	0 (0%)	16 (10.4%)	0 (0%)	52 (10.2%)
Not reported	1 (4.5%)	6 (4.1%)	1 (6.7%)	1 (4.5%)	7 (4.5%)	0 (0%)	16 (3.1%)
Gleason score category, n (%)							
High [8-10]	15 (68.2%)	98 (67.1%)	12 (80.0%)	16 (72.7%)	103 (66.9%)	6 (85.7%)	359 (70.7%)
Low [2-7]	7 (31.8%)	44 (30.1%)	3 (20.0%)	6 (27.3%)	47 (30.5%)	1 (14.3%)	139 (27.4%)
Not reported	0 (0%)	4 (2.7%)	0 (0%)	0 (0%)	4 (2.6%)	0 (0%)	10 (2.0%)
Bone metastases at baseline, n (%)	20 (90.9%)	126 (86.3%)	12 (80.0%)	21 (95.5%)	131 (85.1%)	6 (85.7%)	432 (85.0%)
Prostate cancer diagnosis year, Median [Q1,Q3]	2020 [2010,2020]	2020 [2010,2020]	2020 [2020,2020]	2020 [2010,2020]	2020 [2010,2020]	2020 [2020,2020]	2020 [2010,2020]

Table 10. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 for the overall study cohort and by post-dose deviation anemia status at 1 visit and 2 visits after dose deviation

	Post-dose deviation anemia status 1: Improved (N=22)	Post-dose deviation anemia status 1: Unchanged (N=146)	Post-dose deviation anemia status 1: Worsened (N=15)	Post-dose deviation anemia status 2: Improved (N=22)	Post-dose deviation anemia status 2: Unchanged (N=154)	Post-dose deviation anemia status 2: Worsened (N=7)	Overall (N=319)
Baseline bone metastases number, Median [Q1,Q3]	3.50 [3.00,4.00]	4.00 [2.25,5.00]	3.00 [2.00,5.50]	4.00 [3.00,5.00]	4.00 [2.00,5.00]	4.00 [2.00,5.00]	4.00 [3.00,5.00]
De novo metastatic disease, n (%)	13 (59.1%)	66 (45.2%)	9 (60.0%)	14 (63.6%)	69 (44.8%)	5 (71.4%)	249 (49.0%)
Somatic HRR mutation, n (%)							
1) DDR Deficient	4 (18.2%)	58 (39.7%)	8 (53.3%)	7 (31.8%)	59 (38.3%)	4 (57.1%)	197 (38.8%)
2) Non-DDR Deficient	11 (50.0%)	64 (43.8%)	3 (20.0%)	9 (40.9%)	67 (43.5%)	2 (28.6%)	203 (40.0%)
3) Unknown Deficient	7 (31.8%)	24 (16.4%)	4 (26.7%)	6 (27.3%)	28 (18.2%)	1 (14.3%)	108 (21.3%)
ATM Deficient	0 (0.0%)	11 (7.5%)	2 (13.3%)	0 (0.0%)	13 (8.4%)	0 (0.0%)	47 (9.3%)
ATR Deficient	0 (0.0%)	1 (0.7%)	1 (6.7%)	0 (0.0%)	2 (1.3%)	0 (0.0%)	3 (0.6%)
BRCA1 Deficient	0 (0.0%)	4 (2.7%)	0 (0.0%)	0 (0.0%)	4 (2.6%)	0 (0.0%)	10 (2.0%)
BRCA2 Deficient	1 (4.5%)	17 (11.6%)	1 (6.7%)	2 (9.1%)	16 (10.4%)	1 (14.3%)	60 (11.8%)
CDK12 Deficient	1 (4.5%)	13 (8.9%)	3 (20.0%)	2 (9.1%)	14 (9.1%)	1 (14.3%)	37 (7.3%)
CHEK2 Deficient	1 (4.5%)	9 (6.2%)	1 (6.7%)	1 (4.5%)	9 (5.8%)	1 (14.3%)	35 (6.9%)
FANCA Deficient	0 (0.0%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.3%)	0 (0.0%)	4 (0.8%)
MLH1 Deficient	1 (4.5%)	3 (2.1%)	0 (0.0%)	1 (4.5%)	3 (1.9%)	0 (0.0%)	9 (1.8%)
NBN Deficient	1 (4.5%)	2 (1.4%)	0 (0.0%)	1 (4.5%)	2 (1.3%)	0 (0.0%)	8 (1.6%)
PALB2 Deficient	0 (0.0%)	3 (2.1%)	1 (6.7%)	1 (4.5%)	2 (1.3%)	1 (14.3%)	9 (1.8%)
RAD51C	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.4%)
ECOG, n (%)							
0	9 (40.9%)	90 (61.6%)	8 (53.3%)	9 (40.9%)	95 (61.7%)	3 (42.9%)	325 (64.0%)
1	13 (59.1%)	56 (38.4%)	7 (46.7%)	13 (59.1%)	59 (38.3%)	4 (57.1%)	183 (36.0%)
Treatment history							
Bilateral orchiectomy	0 (0.0%)	7 (4.8%)	2 (13.3%)	1 (4.5%)	7 (4.5%)	1 (14.3%)	26 (5.1%)

Table 10. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 for the overall study cohort and by post-dose deviation anemia status at 1 visit and 2 visits after dose deviation

	Post-dose deviation anemia status 1: Improved (N=22)	Post-dose deviation anemia status 1: Unchanged (N=146)	Post-dose deviation anemia status 1: Worsened (N=15)	Post-dose deviation anemia status 2: Improved (N=22)	Post-dose deviation anemia status 2: Unchanged (N=154)	Post-dose deviation anemia status 2: Worsened (N=7)	Overall (N=319)
Prior prostate cancer surgery[a]	16 (72.7%)	119 (81.5%)	15 (100.0%)	15 (68.2%)	130 (84.4%)	5 (71.4%)	397 (78.1%)
Prior radiation therapy	5 (22.7%)	33 (22.6%)	4 (26.7%)	6 (27.3%)	35 (22.7%)	1 (14.3%)	113 (22.2%)
Prior hormonal therapy	2 (9.1%)	10 (6.8%)	2 (13.3%)	1 (4.5%)	13 (8.4%)	0 (0.0%)	31 (6.1%)
Androgen deprivation therapy at baseline	22 (100.0%)	142 (97.3%)	13 (86.7%)	22 (100.0%)	148 (96.1%)	7 (100.0%)	487 (95.9%)
Triptorelin	5 (22.7%)	28 (19.2%)	0 (0.0%)	5 (22.7%)	28 (18.2%)	0 (0.0%)	87 (17.1%)
Degarelix	3 (13.6%)	26 (17.8%)	3 (20.0%)	3 (13.6%)	26 (16.9%)	3 (42.9%)	85 (16.7%)
Leuprorelin	12 (54.5%)	80 (54.8%)	6 (40.0%)	12 (54.5%)	84 (54.5%)	2 (28.6%)	281 (55.3%)
Gonadorelin	1 (4.5%)	1 (0.7%)	0 (0.0%)	1 (4.5%)	1 (0.6%)	0 (0.0%)	3 (0.6%)
Relugolix	1 (4.5%)	1 (0.7%)	0 (0.0%)	1 (4.5%)	1 (0.6%)	0 (0.0%)	6 (1.2%)
Goserelin	3 (13.6%)	17 (11.6%)	2 (13.3%)	3 (13.6%)	18 (11.7%)	1 (14.3%)	44 (8.7%)
Histrelin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)
Flutamide	0 (0.0%)	5 (3.4%)	1 (6.7%)	1 (4.5%)	5 (3.2%)	0 (0.0%)	24 (4.7%)
Bicalutamide	11 (50.0%)	88 (60.3%)	9 (60.0%)	11 (50.0%)	93 (60.4%)	4 (57.1%)	284 (55.9%)
Enzalutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Darolutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Taxane Based Chemotherapy	5 (22.7%)	33 (22.6%)	2 (13.3%)	7 (31.8%)	30 (19.5%)	3 (42.9%)	124 (24.4%)
Carbazitaxel	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Docetaxel	5 (22.7%)	33 (22.6%)	2 (13.3%)	7 (31.8%)	30 (19.5%)	3 (42.9%)	124 (24.4%)
Abiraterone	2 (9.1%)	10 (6.8%)	2 (13.3%)	1 (4.5%)	13 (8.4%)	0 (0.0%)	29 (5.7%)
Daralutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Apalutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Orteronel/TAK700	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.4%)
Baseline labs							
Hemoglobin, Median [Q1,Q3]	130 [122,135]	130 [120,141]	126 [120,132]	130 [120,135]	130 [120,141]	121 [120,138]	131 [121,139]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
eGFR, Median [Q1,Q3]	85.0 [76.0,91.6]	85.3 [69.0,94.5]	89.0 [78.0,91.0]	81.5 [71.5,87.8]	85.8 [69.0,93.0]	91.0 [87.0,108]	86.9 [71.0,97.6]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 10. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 for the overall study cohort and by post-dose deviation anemia status at 1 visit and 2 visits after dose deviation

	Post-dose deviation anemia status 1: Improved (N=22)	Post-dose deviation anemia status 1: Unchanged (N=146)	Post-dose deviation anemia status 1: Worsened (N=15)	Post-dose deviation anemia status 2: Improved (N=22)	Post-dose deviation anemia status 2: Unchanged (N=154)	Post-dose deviation anemia status 2: Worsened (N=7)	Overall (N=319)
ALT, Median [Q1,Q3]	0.280 [0.200,0.328]	0.315 [0.250,0.445]	0.280 [0.225,0.320]	0.325 [0.273,0.365]	0.300 [0.230,0.420]	0.300 [0.290,0.590]	0.320 [0.250,0.423]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Albumin, Median	44.1	42.0	43.0	44.9	42.0	42.0	42.0
[Q1,Q3]	[40.3,45.7]	[39.0,44.0]	[40.6,44.0]	[40.5,46.5]	[39.0,44.0]	[40.6,43.0]	[39.0,44.0]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ALP, Median	1.94	1.84	3.50	2.05	1.82	5.80	1.93
[Q1,Q3]	[1.55,3.63]	[1.27,3.95]	[1.54,5.40]	[1.37,3.14]	[1.27,4.03]	[3.21,6.74]	[1.27,3.70]
Missing	0 (0%)	2 (1.4%)	0 (0%)	0 (0%)	2 (1.3%)	0 (0%)	3 (0.6%)
AST, Median	0.340	0.380	0.300	0.380	0.370	0.400	0.370
[Q1,Q3]	[0.285,0.380]	[0.320,0.480]	[0.275,0.425]	[0.323,0.445]	[0.305,0.450]	[0.360,0.690]	[0.300,0.463]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HCO3, Median	25.5	25.3	27.3	24.0	25.7	25.6	25.5
[Q1,Q3]	[24.0,27.4]	[23.0,27.0]	[26.0,28.0]	[23.0,27.0]	[23.2,27.2]	[24.8,26.5]	[23.6,27.0]
Missing	4 (18.2%)	22 (15.1%)	6 (40.0%)	5 (22.7%)	24 (15.6%)	3 (42.9%)	86 (16.9%)
Total_bilirubin, Median	8.65	8.85	12.0	10.5	8.65	10.3	8.60
[Q1,Q3]	[5.90,12.0]	[6.80,12.0]	[7.20,12.5]	[6.35,12.0]	[6.80,12.0]	[6.80,12.4]	[6.80,12.0]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
BUN, Median	6.65	6.20	5.95	6.80	6.20	5.90	6.40
[Q1,Q3]	[6.08,8.00]	[4.93,7.65]	[5.63,7.55]	[6.10,7.50]	[5.00,7.85]	[5.28,6.80]	[5.40,7.90]
Missing	10 (45.5%)	84 (57.5%)	9 (60.0%)	13 (59.1%)	87 (56.5%)	3 (42.9%)	291 (57.3%)
Ca, Median	2.36	2.34	2.30	2.32	2.35	2.31	2.33
[Q1,Q3]	[2.29,2.41]	[2.26,2.41]	[2.24,2.37]	[2.26,2.41]	[2.26,2.41]	[2.28,2.38]	[2.26,2.40]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)
Cl, Median	105	105	106	106	104	105	104
[Q1,Q3]	[102,105]	[102,106]	[104,108]	[105,106]	[102,106]	[104,106]	[102,106]
Missing	0 (0%)	1 (0.7%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	3 (0.6%)
CK, Median	1.19	1.56	1.63	1.30	1.53	1.42	1.50
[Q1,Q3]	[0.963,1.28]	[0.993,2.08]	[1.42,1.90]	[1.23,1.58]	[1.00,2.02]	[1.42,1.42]	[1.04,2.20]
Missing	16 (72.7%)	110 (75.3%)	10 (66.7%)	17 (77.3%)	113 (73.4%)	6 (85.7%)	396 (78.0%)
Glucose, Median	5.77	5.88	5.49	5.77	5.86	5.49	5.80
[Q1,Q3]	[5.41,6.33]	[5.40,6.71]	[5.10,6.16]	[5.55,6.31]	[5.40,6.68]	[5.19,6.58]	[5.30,6.60]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)
LDH, Median	214	207	218	209	208	196	209
[Q1,Q3]	[198,295]	[182,244]	[188,339]	[195,239]	[182,267]	[175,213]	[182,254]
Missing	1 (4.5%)	1 (0.7%)	0 (0%)	0 (0%)	2 (1.3%)	0 (0%)	6 (1.2%)
Mg, Median	0.890	0.860	0.920	0.900	0.860	0.860	0.860
[Q1,Q3]	[0.780,0.940]	[0.800,0.908]	[0.860,0.975]	[0.860,0.945]	[0.800,0.920]	[0.860,0.940]	[0.800,0.910]
Missing	1 (4.5%)	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	4 (0.8%)

Table 10. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 for the overall study cohort and by post-dose deviation anemia status at 1 visit and 2 visits after dose deviation

	Post-dose deviation anemia status 1: Improved (N=22)	Post-dose deviation anemia status 1: Unchanged (N=146)	Post-dose deviation anemia status 1: Worsened (N=15)	Post-dose deviation anemia status 2: Improved (N=22)	Post-dose deviation anemia status 2: Unchanged (N=154)	Post-dose deviation anemia status 2: Worsened (N=7)	Overall (N=319)
K, Median	4.23	4.30	4.10	4.10	4.30	4.10	4.30
[Q1,Q3]	[4.03,4.55]	[4.00,4.50]	[3.93,4.61]	[3.97,4.45]	[4.00,4.60]	[3.90,4.25]	[4.00,4.54]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Protein,							
Median	71.0	71.0	71.8	71.0	71.0	72.0	71.0
[Q1,Q3]	[66.5,74.5]	[68.0,74.0]	[65.5,74.4]	[66.5,73.0]	[67.6,74.0]	[70.5,75.5]	[67.6,74.0]
Missing	0 (0%)	1 (0.7%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	5 (1.0%)
Na, Median	140	141	141	141	140	141	141
[Q1,Q3]	[138,142]	[139,142]	[139,141]	[140,142]	[139,142]	[139,142]	[139,142]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Creatinine,							
Median	79.3	79.6	81.0	79.6	79.8	70.7	78.0
[Q1,Q3]	[72.5,87.1]	[67.7,93.7]	[72.1,91.1]	[75.2,88.0]	[69.2,93.5]	[70.4,74.4]	[68.0,92.0]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Phosphate,							
Median	1.10	1.15	1.20	1.20	1.10	1.20	1.10
[Q1,Q3]	[1.00,1.20]	[1.00,1.30]	[1.10,1.25]	[1.03,1.30]	[1.00,1.30]	[1.10,1.25]	[1.00,1.30]
Missing	1 (4.5%)	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	6 (1.2%)
Testosteron							
e, Median	11.1	11.5	9.00	10.5	11.5	28.0	11.5
[Q1,Q3]	[8.83,16.9]	[6.96,18.3]	[4.00,18.3]	[5.82,14.0]	[6.96,18.1]	[14.5,30.1]	[7.00,18.0]
Missing	0 (0%)	3 (2.1%)	0 (0%)	0 (0%)	3 (1.9%)	0 (0%)	10 (2.0%)
Urea,							
Median	6.28	6.01	4.54	5.93	6.18	4.54	6.40
[Q1,Q3]	[5.38,7.98]	[5.14,7.10]	[4.30,7.90]	[5.26,7.96]	[5.05,7.28]	[4.17,4.94]	[5.00,7.58]
Missing	10 (45.5%)	55 (37.7%)	6 (40.0%)	8 (36.4%)	59 (38.3%)	4 (57.1%)	194 (38.2%)
FolicAcid,							
Median	10.1	7.55	9.00	7.66	7.62	9.00	8.56
[Q1,Q3]	[5.48,14.3]	[5.61,13.4]	[6.37,10.9]	[5.18,12.8]	[5.61,13.4]	[7.66,10.0]	[6.01,13.7]
Missing	4 (18.2%)	11 (7.5%)	0 (0%)	4 (18.2%)	11 (7.1%)	0 (0%)	35 (6.9%)
VitaminB12,							
Median	323	389	281	358	379	341	388
[Q1,Q3]	[244,441]	[271,540]	[234,428]	[259,492]	[255,527]	[272,678]	[285,535]
Missing	2 (9.1%)	8 (5.5%)	0 (0%)	1 (4.5%)	9 (5.8%)	0 (0%)	22 (4.3%)
PSA,							
Median	12.6	18.7	20.7	13.1	19.8	5.68	18.1
[Q1,Q3]	[4.63,51.6]	[7.91,61.5]	[5.72,37.3]	[4.08,44.0]	[8.13,65.2]	[2.34,20.9]	[6.40,61.7]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)
MCV,							
Median	93.0	91.0	92.0	94.0	91.0	90.0	91.0
[Q1,Q3]	[88.0,94.0]	[88.0,94.0]	[89.0,95.0]	[88.3,95.0]	[88.0,94.3]	[89.0,92.0]	[88.0,95.0]
Missing	1 (4.5%)	1 (0.7%)	0 (0%)	0 (0%)	2 (1.3%)	0 (0%)	2 (0.4%)
RBC,							
Median	4.20	4.35	4.10	4.18	4.28	4.37	4.29
[Q1,Q3]	[3.98,4.45]	[3.91,4.60]	[3.92,4.28]	[3.93,4.45]	[3.92,4.57]	[4.01,4.70]	[3.96,4.56]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HCT,							
Median	36.7	36.6	32.2	35.0	36.5	37.9	36.4
[Q1,Q3]	[33.1,39.7]	[0.430,40.4]	[0.385,37.2]	[0.415,39.1]	[0.430,40.0]	[34.2,40.9]	[0.420,40.0]

Table 10. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 for the overall study cohort and by post-dose deviation anemia status at 1 visit and 2 visits after dose deviation

	Post-dose deviation anemia status 1: Improved (N=22)	Post-dose deviation anemia status 1: Unchanged (N=146)	Post-dose deviation anemia status 1: Worsened (N=15)	Post-dose deviation anemia status 2: Improved (N=22)	Post-dose deviation anemia status 2: Unchanged (N=154)	Post-dose deviation anemia status 2: Worsened (N=7)	Overall (N=319)
Missing WBC,	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Median [Q1,Q3]	5.95 [5.13,6.75]	5.92 [4.72,7.40]	5.30 [4.59,5.67]	5.76 [5.13,6.21]	5.89 [4.66,7.41]	5.70 [5.16,6.37]	5.94 [4.90,7.25]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Basophils, Median [Q1,Q3]	0.0200 [0.00500,0.0350]	0.0300 [0.0100,0.0500]	0.0400 [0.0200,0.0500]	0.0200 [0.00500,0.0300]	0.0300 [0.0100,0.0500]	0.0600 [0.0550,0.0700]	0.0300 [0.0100,0.0500]
Missing	3 (13.6%)	28 (19.2%)	4 (26.7%)	3 (13.6%)	29 (18.8%)	3 (42.9%)	84 (16.5%)
Basophils/Leukocytes, Median [Q1,Q3]	0.363 [0.0847,0.578]	0.477 [0.186,0.776]	0.571 [0.406,1.07]	0.363 [0.0800,0.604]	0.476 [0.189,0.771]	1.05 [0.800,1.35]	0.542 [0.222,0.839]
Missing	3 (13.6%)	28 (19.2%)	4 (26.7%)	3 (13.6%)	29 (18.8%)	3 (42.9%)	84 (16.5%)
Eosinophils, Median [Q1,Q3]	0.120 [0.0750,0.200]	0.130 [0.0900,0.220]	0.150 [0.105,0.185]	0.120 [0.0800,0.190]	0.135 [0.0900,0.213]	0.135 [0.0750,0.190]	0.150 [0.100,0.220]
Missing	3 (13.6%)	29 (19.9%)	4 (26.7%)	3 (13.6%)	30 (19.5%)	3 (42.9%)	81 (15.9%)
Eosinophils/ Leukocytes, Median [Q1,Q3]	1.93 [1.16,3.17]	2.08 [1.39,3.85]	2.71 [1.80,3.60]	2.04 [1.24,3.57]	2.08 [1.43,3.79]	2.52 [1.32,3.33]	2.39 [1.61,3.95]
Missing	3 (13.6%)	29 (19.9%)	4 (26.7%)	3 (13.6%)	30 (19.5%)	3 (42.9%)	81 (15.9%)
Lymphocytes, Median [Q1,Q3]	1.40 [1.04,1.70]	1.50 [1.10,1.90]	1.34 [1.20,1.68]	1.44 [1.04,1.70]	1.50 [1.10,1.91]	1.40 [1.29,1.66]	1.48 [1.10,1.90]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lymphocytes/Leukocytes, Median [Q1,Q3]	22.7 [19.9,29.6]	24.8 [20.5,31.6]	24.6 [21.7,33.6]	24.4 [21.5,30.0]	24.5 [20.4,31.8]	24.2 [22.2,25.8]	24.8 [20.0,30.9]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Monocytes, Median [Q1,Q3]	0.490 [0.410,0.655]	0.460 [0.370,0.620]	0.500 [0.435,0.525]	0.460 [0.340,0.565]	0.475 [0.390,0.623]	0.500 [0.493,0.525]	0.500 [0.390,0.605]
Missing	3 (13.6%)	29 (19.9%)	4 (26.7%)	3 (13.6%)	30 (19.5%)	3 (42.9%)	85 (16.7%)
Monocytes/Leukocytes, Median [Q1,Q3]	8.82 [7.73,9.68]	7.81 [6.42,9.52]	8.77 [8.09,9.91]	8.51 [6.42,9.41]	8.02 [6.55,9.64]	8.33 [7.67,9.10]	8.11 [6.61,9.81]
Missing	3 (13.6%)	29 (19.9%)	4 (26.7%)	3 (13.6%)	30 (19.5%)	3 (42.9%)	85 (16.7%)
Neutrophils, Median [Q1,Q3]	3.72 [3.10,4.59]	3.53 [2.90,4.68]	3.08 [2.54,3.73]	3.38 [3.01,4.02]	3.65 [2.81,4.68]	3.70 [3.19,4.10]	3.63 [2.85,4.63]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)
Neutrophils/ Leukocytes, Median [Q1,Q3]	66.1 [60.4,68.4]	63.4 [56.4,67.6]	60.6 [55.9,66.7]	62.5 [57.3,67.6]	63.5 [56.1,68.0]	64.9 [61.8,66.1]	62.7 [56.2,68.2]

Table 10. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 for the overall study cohort and by post-dose deviation anemia status at 1 visit and 2 visits after dose deviation

	Post-dose deviation anemia status 1: Improved (N=22)	Post-dose deviation anemia status 1: Unchanged (N=146)	Post-dose deviation anemia status 1: Worsened (N=15)	Post-dose deviation anemia status 2: Improved (N=22)	Post-dose deviation anemia status 2: Unchanged (N=154)	Post-dose deviation anemia status 2: Worsened (N=7)	Overall (N=319)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)
Platelets,							
Median	224	219	222	206	223	193	223
[Q1,Q3]	[196,280]	[181,266]	[175,250]	[173,248]	[183,267]	[163,248]	[187,267]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Retics,							
Median	71.8	67.3	58.4	75.3	64.0	82.0	62.0
[Q1,Q3]	[57.6,89.2]	[50.8,84.3]	[56.7,64.0]	[58.2,85.0]	[50.0,83.9]	[58.4,94.0]	[49.8,78.1]
Missing	10 (45.5%)	54 (37.0%)	6 (40.0%)	7 (31.8%)	61 (39.6%)	2 (28.6%)	200 (39.4%)
EPO,							
Median	13.7	14.3	16.6	13.7	14.5	11.9	12.9
[Q1,Q3]	[11.6,18.2]	[10.1,20.4]	[10.4,19.7]	[11.6,20.5]	[10.3,20.4]	[9.28,15.5]	[9.45,19.0]
Missing	2 (9.1%)	26 (17.8%)	3 (20.0%)	4 (18.2%)	26 (16.9%)	1 (14.3%)	97 (19.1%)
Baseline anemia symptoms							
Fatigue	10 (45.5%)	48 (32.9%)	5 (33.3%)	9 (40.9%)	53 (34.4%)	1 (14.3%)	168 (33.1%)
Shortness Breath	0 (0.0%)	4 (2.7%)	1 (6.7%)	0 (0.0%)	4 (2.6%)	1 (14.3%)	13 (2.6%)
Decreased Appetite	1 (4.5%)	1 (0.7%)	0 (0.0%)	1 (4.5%)	1 (0.6%)	0 (0.0%)	5 (1.0%)
Asthenia	3 (13.6%)	12 (8.2%)	1 (6.7%)	2 (9.1%)	14 (9.1%)	0 (0.0%)	49 (9.6%)
Dyspnea	0 (0.0%)	12 (8.2%)	0 (0.0%)	1 (4.5%)	11 (7.1%)	0 (0.0%)	37 (7.3%)
Dizziness	2 (9.1%)	18 (12.3%)	2 (13.3%)	2 (9.1%)	20 (13.0%)	0 (0.0%)	54 (10.6%)
Baseline anemia management							
Iron treatment up to and prior to baseline	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	3 (0.6%)
Index treatment details							
Baseline Talazoparib Dose							
0.35	0 (0%)	15 (10.3%)	1 (6.7%)	0 (0%)	16 (10.4%)	0 (0%)	55 (10.8%)
0.5	22 (100%)	131 (89.7%)	14 (93.3%)	22 (100%)	138 (89.6%)	7 (100%)	453 (89.2%

Table 10. Baseline characteristics of talazoparib-treated patients in TALAPRO-2 for the overall study cohort and by post-dose deviation anemia status at 1 visit and 2 visits after dose deviation

	Post-dose deviation anemia status 1: Improved (N=22)	Post-dose deviation anemia status 1: Unchanged (N=146)	Post-dose deviation anemia status 1: Worsened (N=15)	Post-dose deviation anemia status 2: Improved (N=22)	Post-dose deviation anemia status 2: Unchanged (N=154)	Post-dose deviation anemia status 2: Worsened (N=7)	Overall (N=319)
Years between prostate cancer diagnosis and Talazoparib initiation,							
Median [Q1,Q3]	2.00 [1.00,6.75]	3.00 [1.00,6.75]	3.00 [2.00,3.50]	2.00 [1.00,6.75]	3.00 [1.00,6.75]	1.00 [1.00,2.50]	3.00 [1.00,6.00]

[a]Includes prostatectomy, transurethral resection of the prostate, prostate biopsy, bilateral orchiectomy, pelvic node dissection, urethral stent, and nephrostomy
Units: Hemoglobin (g/L); eGFR (mL/min/1.73 m²); ALT (µkat/L); Albumin (g/L); ALP (µkat/L); AST (µkat/L); Bicarbonate (mmol/L); Total Bilirubin (µmol/L); BUN (mmol/L); Calcium (mmol/L); Chloride (mmol/L); Creatine Kinase (µkat/L); Glucose (mmol/L); LDH (U/L); Magnesium (mmol/L); Potassium (mmol/L); Protein (g/L); Sodium (mmol/L); Creatinine (µmol/L); Phosphate (mmol/L); Testosterone (ng/dL); Urea (mmol/L); Vitamin B9 (µg/L); Vitamin B12 (ng/L); PSA (µg/L); MCV (fL); RBC (10^{12}/L); Hematocrit (L/L); WBC (10^9/L); Basophils (10^9/L); Basophils/Leukocytes (%); Eosinophils (10^9/L); Eosinophils/Leukocytes (%); Lymphocytes (10^9/L); Lymphocytes/Leukocytes (%); Monocytes (10^9/L); Monocytes/Leukocytes (%); Neutrophils (10^9/L); Neutrophils/Leukocytes (%); Platelets (10^9/L).

Among patients diagnosed with anemia at the time of dose deviation and did not receive a RBC transfusion on or after 1st dose deviation and before the next visit capturing hemoglobin-inferred anemia status: If the hemoglobin-inferred anemia status is any grade lower than "Anemia status at first dose deviation", value is “Improved”. If the hemoglobin-inferred anemia status is unchanged from "Anemia status at first dose deviation", value is “Unchanged”

Table 11 summarizes hemoglobin change (g/dL per day) before dose deviation, calculated as the difference in hemoglobin measured at baseline and on or closest date prior to first dose deviation (or RBC transfusion date, whichever occurred first), divided by the number of intervening days between those two measures. The median hemoglobin change overall was -0.366 [-0.554, -0.169] g/dL per day, with a steeper decrease among patients initiating 0.5 mg talazoparib dose (-0.391 [-0.571, -0.174] g/dL per day) than patients initiating 0.35 mg (-0.209 [-0.367, -0.0246] g/dL per day).

Table 11 is repeated using the broad definition of time to dose modification (defined as the receipt of talazoparib dose that was different from the initiating dose) in Appendix 8.1 **Error! Reference source not found.**.

Table 11. Hemoglobin change (g/dL per day) before dose deviation

	0.35 (N=34)	0.5 (N=285)	Overall (N=319)
Mean (SD)	-0.229 (0.231)	-0.397 (0.302)	-0.380 (0.300)
Median [Q1,Q3]	-0.209 [-0.367, -0.0246]	-0.391 [-0.571, -0.174]	-0.366 [-0.554, -0.169]
[Min, Max]	[-0.857, 0.204]	[-1.95, 0.929]	[-1.95, 0.929]
Missing	2 (5.9%)	5 (1.8%)	7 (2.2%)

Table 11. Hemoglobin change (g/dL per day) before dose deviation

	0.35 (N=34)	0.5 (N=285)	Overall (N=319)

Dose deviation is defined as receipt of dose that was different from the initiating dose and that was sustained for 7 days or longer, or if dose deviation period was <7 days, was explicitly stated as a dose modification due to an adverse event

Table 12 summarizes hemoglobin change (g/dL per day) at the first and second visits following dose deviation. Hemoglobin change was calculated as the difference between the hemoglobin value at dose deviation and the value at the corresponding follow-up visit, divided by the number of days between measurements. Important to note, hemoglobin change was only calculated among patients who did not experience a subsequent dose deviation or receive a RBC transfusion during the intervening period in order to assess trajectory in the absence of additional intervention. At the first visit after dose deviation, the median hemoglobin change overall for all doses was -0.586 [-1.01, -0.0300] g/dL per day, with a smaller decline in hemoglobin patients initiating talazoparib dose 0.35 mg compared to 0.5 mg (-0.560 [-0.952, -0.184] versus -0.586 [-1.00,0] g/dL per day). When stratified by the severity of the anemia event preceding the dose deviation, the median hemoglobin change was -0.667 [-1.18, -0.0667] g/dL per day among those with Grade 1-2 anemia and -0.547 [-1.00, -0.0300] g/dL per day among those with Grade ≥3 anemia. The smaller decline in hemoglobin among patients initiating talazoparib dose 0.35 mg compared to 0.5 mg was more pronounced in the anemia severity-stratified groups: -0.619 [-0.905, -0.468] versus -0.690 [-1.18, -0.0167] g/dL per day among patients with Grade 1-2 anemia; -0.500 [-0.583,0.750] versus -0.571 [-1.00, -0.0400] g/dL per day among patients with Grade ≥3 anemia. At visit 2 after dose deviation, hemoglobin levels are still generally lower than at dose deviation but improved compared to visit 1. The exception was among the strata of patients with Grade ≥3 anemia at dose deviation and 0.5 mg initial dose, who had higher median change in hemoglobin levels compared to date of dose deviation (0.0952 [-0.174,0.529] g/DL per day). However, this stratum only consisted of 17 patients (112 total − 95 missing), and should therefore be interpreted with caution, particularly given that patients with declining hemoglobin trajectories are more likely to be among those who subsequently received additional dose deviation or RBC transfusion and were excluded from this summary statistic, resulting in an enrichment of patients who have better hemoglobin improvement in the absence of RBC transfusion.

Table 12 is repeated using the broad definition of time to dose modification (defined as the receipt of talazoparib dose that was different from the initiating dose) in Appendix 8.1 **Error! Reference source not found.**.

Table 12. Hemoglobin change (g/dL per day) at 1 visit and 2 visits after dose deviation, stratified by anemia severity and initial talazoparib dose

	Overall			Grade 1-2			Grade ≥3		
	0.35 (N=34)	0.5 (N=285)	All (N=319)	0.35 (N=9)	0.5 (N=133)	All (N=142)	0.35 (N=14)	0.5 (N=112)	All (N=126)
Hgb change 1st visit post dose deviation									

Table 12. Hemoglobin change (g/dL per day) at 1 visit and 2 visits after dose deviation, stratified by anemia severity and initial talazoparib dose

	Overall			Grade 1-2			Grade ≥3		
	0.35 (N=34)	0.5 (N=285)	All (N=319)	0.35 (N=9)	0.5 (N=133)	All (N=142)	0.35 (N=14)	0.5 (N=112)	All (N=126)
Mean (SD)	-1.04 (2.56)	-0.462 (1.24)	-0.512 (1.39)	-0.709 (0.443)	-0.625 (0.866)	-0.629 (0.850)	0.278 (1.49)	-0.159 (1.94)	-0.118 (1.88)
Median [Q1,Q3]	-0.560 [-0.952,-0.184]	-0.586 [-1.00,0]	-0.586 [-1.01,-0.0300]	-0.619 [-0.905,-0.468]	-0.690 [-1.18,-0.0167]	-0.667 [-1.18,-0.0667]	-0.500 [-0.583,0.750]	-0.571 [-1.00,-0.0400]	-0.547 [-1.00,-0.0300]
[Min, Max]	[-7.89, 2.00]	[-4.07, 7.29]	[-7.89, 7.29]	[-1.19, -0.317]	[-3.00, 1.13]	[-3.00, 1.13]	[-0.667, 2.00]	[-4.07, 7.29]	[-4.07, 7.29]
Missing	24 (70.6%)	179 (62.8%)	203 (63.6%)	6 (66.7%)	67 (50.4%)	73 (51.4%)	11 (78.6%)	83 (74.1%)	94 (74.6%)
Hgb change 2nd visit post dose deviation									
Mean (SD)	-0.463 (0.713)	-0.264 (1.14)	-0.282 (1.11)	-0.571 (0.303)	-0.589 (1.00)	-0.588 (0.978)	-0.414 (1.10)	0.440 (1.24)	0.312 (1.23)
Median [Q1,Q3]	-0.375 [-0.688,-0.304]	-0.174 [-0.955,0.357]	-0.179 [-0.924,0.304]	-0.571 [-0.679,-0.464]	-0.591 [-1.09,0.214]	-0.591 [-1.08,0.143]	-0.286 [-0.929,0.165]	0.0952 [-0.174,0.529]	0.0182 [-0.179,0.551]
[Min, Max]	[-1.57, 0.615]	[-5.00, 4.43]	[-5.00, 4.43]	[-0.786, -0.357]	[-5.00, 0.909]	[-5.00, 0.909]	[-1.57, 0.615]	[-1.30, 4.43]	[-1.57, 4.43]
Missing	28 (82.4%)	224 (78.6%)	252 (79.0%)	7 (77.8%)	92 (69.2%)	99 (69.7%)	11 (78.6%)	95 (84.8%)	106 (84.1%)

Dose deviation is defined as receipt of dose that was different from the initiating dose and that was sustained for 7 days or longer, or if dose deviation period was <7 days, was explicitly stated as a dose modification due to an adverse event

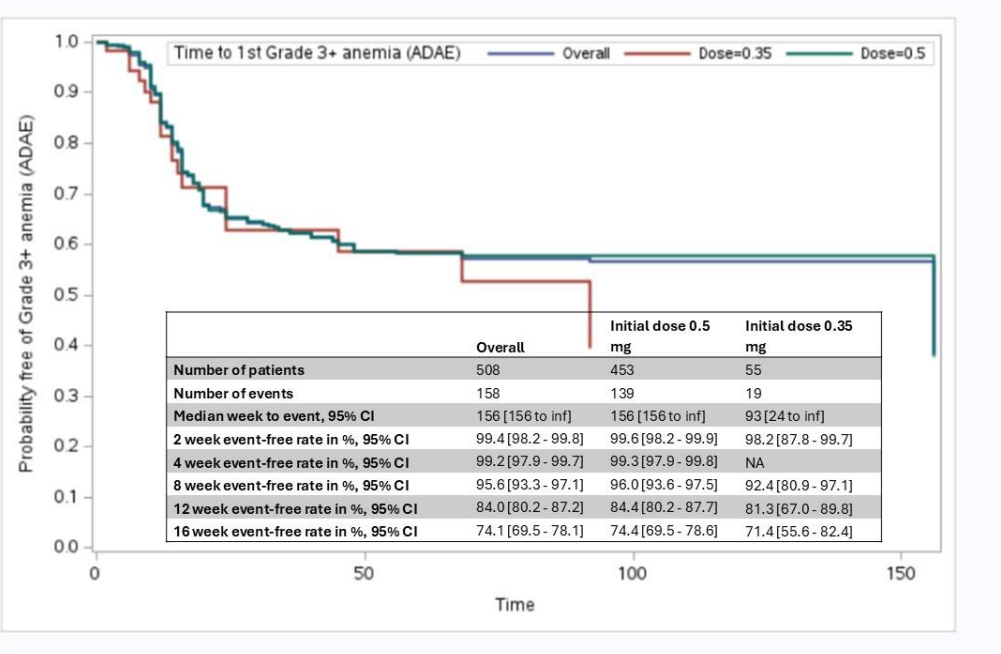
In the overall cohort of 508 patients, n=158 experienced at least one Grade ≥3 anemia during follow-up and prior to censoring, of whom 104 (65.8%) experienced the Grade ≥3 anemia by 16 weeks of treatment. Time to first Grade ≥3 anemia was evaluated among patients receiving talazoparib, with analyses conducted in the overall cohort and stratified by initial dose. Time to anemia was censored at the first of: i) RBC transfusion; ii) dose deviation; iii) death, iv) date of last contact; or v) study end date. The Kaplan-Meier curves and corresponding summary statistics are shown in Figure 5.

Median time to first Grade ≥3 anemia was at 156 weeks (95% CI: 156 to inf). When stratified by initial talazoparib dose, patients who initiated therapy at 0.35 mg experienced anemia earlier, with a median time to event of 156 weeks (95% CI: 156–inf), compared with 93 weeks (95% CI: 24–inf) among those who started at 0.5 mg, although not enough events occurred to estimate the upper limits of the medians for any strata. By week 8, more than 90% of patients in both dose groups remained free of Grade ≥3 anemia. By 16 weeks, the event-free rate declined to 74.4% (95% CI, 69.5%–78.6%) among patients initiating the 0.5-mg dose and to 71.4% (95% CI, 55.6%–82.4%) among those initiating the 0.35-mg

dose. Kaplan–Meier curves showed broadly similar time to anemia between the 0.35 mg and 0.5 mg starting dose groups.

Additional Kaplan-Meier estimates and curves for the alternate outcome of any treatment-emergent anemia (no anemia; any-grade anemia), and with the alternate censoring event at time to dose modification (defined as the receipt of talazoparib dose that was different from the initiating dose) are shown in Appendix 8.1 **Error! Reference source not found.** and **Error! Reference source not found.**, respectively.

Figure 5. Time to Grade ≥3 anemia, followed from the date of talazoparib initiation until the date of anemia or censored at the first of: i) RBC transfusion; ii) dose deviation; iii) death, iv) date of last contact; or v) study end date



	Overall	Initial dose 0.5 mg	Initial dose 0.35 mg
Number of patients	508	453	55
Number of events	158	139	19
Median week to event, 95% CI	156 [156 to inf]	156 [156 to inf]	93 [24 to inf]
2 week event-free rate in %, 95% CI	99.4 [98.2 - 99.8]	99.6 [98.2 - 99.9]	98.2 [87.8 - 99.7]
4 week event-free rate in %, 95% CI	99.2 [97.9 - 99.7]	99.3 [97.9 - 99.8]	NA
8 week event-free rate in %, 95% CI	95.6 [93.3 - 97.1]	96.0 [93.6 - 97.5]	92.4 [80.9 - 97.1]
12 week event-free rate in %, 95% CI	84.0 [80.2 - 87.2]	84.4 [80.2 - 87.7]	81.3 [67.0 - 89.8]
16 week event-free rate in %, 95% CI	74.1 [69.5 - 78.1]	74.4 [69.5 - 78.6]	71.4 [55.6 - 82.4]

In the overall cohort of 257 patients who experienced dose deviation, n=46 (17.9%) had an observed anemia improvement. Figure 6 summarizes time to anemia improvement after dose deviation among patients who experienced A) any dose deviation; B) dose deviation after Grade 1 or 2 anemia; and C) dose deviation after Grade ≥3 anemia. Patients were followed from the date of dose deviation until the date of anemia improvement or censored at the first of: i) RBC transfusion; ii) any subsequent dose deviation; iii) death; iv) date of last contact; or v) study end date. Date of anemia improvement was defined as date of first measured hemoglobin level corresponding to a lower grade than that observed at first dose deviation

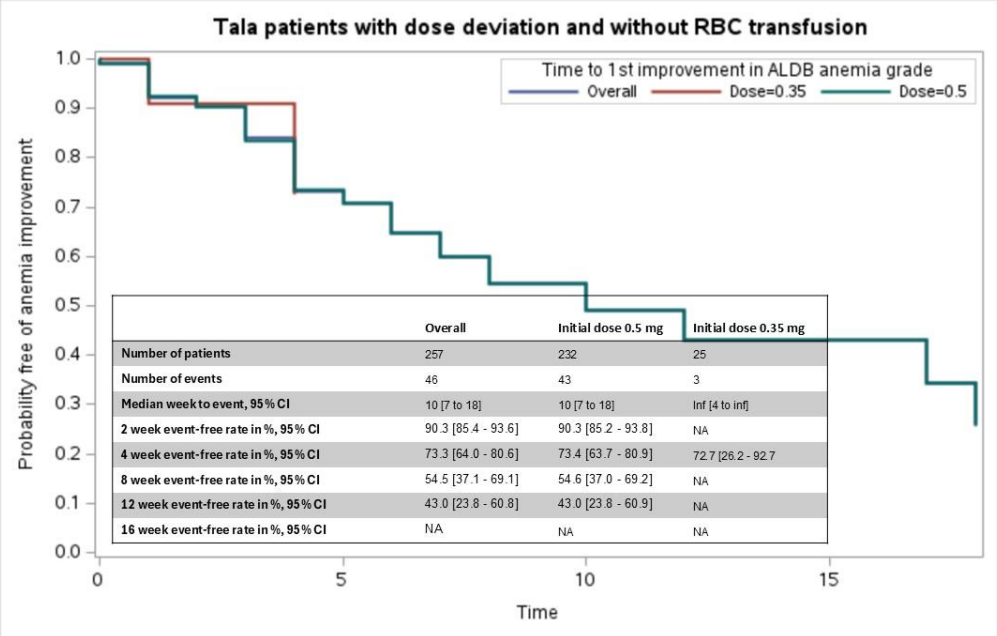
Median time to improvement was 10 weeks (95% CI: 7–18). When stratified by initial talazoparib dose, patients who initiated therapy at 0.5 mg experienced improvement at a similar time, also with a median time to improvement of 10 weeks (95% CI: 7–18), while not enough events occurred among those who started at 0.35 mg to generate a stratified estimate. By 8 weeks, about half of patients experienced improvement in anemia grade, i.e.

event-free event rate was 54.5% (95% CI, 37.1%–69.1%) among the overall starting cohort of patients.

Additional Kaplan-Meier estimates and curves for the expanded definition of anemia improvement (defined as the date of first dose increase or date of first measured hemoglobin level corresponding to a lower grade than that observed at first dose deviation, whichever is observed first) are shown in Appendix 8.1 **Error! Reference source not found.**.

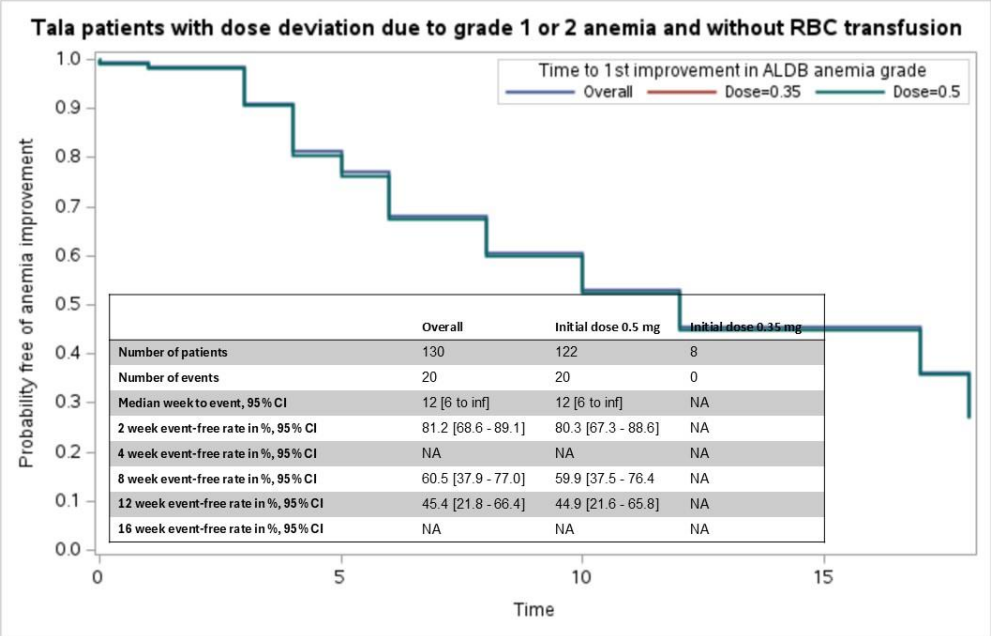
Figure 6. Time to anemia improvement after dose deviation among patients who experienced A) any dose deviation; B) dose deviation after Grade 1 or 2 anemia; C) dose deviation after Grade ≥3 anemia. Followed from the date of dose deviation until the date of anemia improvement, or censored at the first of: i) RBC transfusion; ii) any subsequent dose deviation; iii) death; iv) date of last contact; or v) study end date. Date of anemia improvement is defined as date of first measured hemoglobin level corresponding to a lower grade than that observed at first dose deviation

A



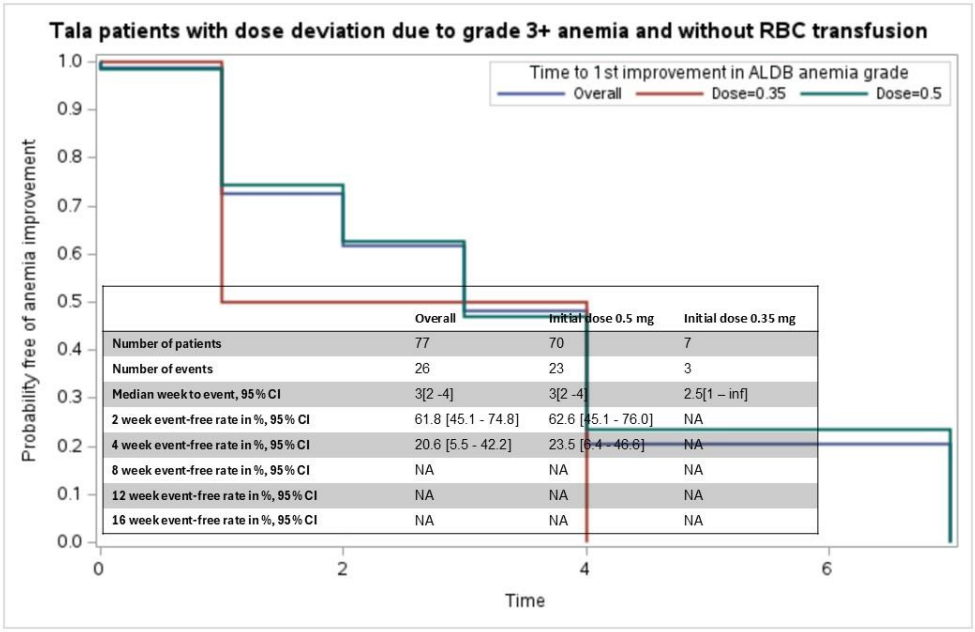
	Overall	Initial dose 0.5 mg	Initial dose 0.35 mg
Number of patients	257	232	25
Number of events	46	43	3
Median week to event, 95% CI	10 [7 to 18]	10 [7 to 18]	Inf [4 to inf]
2 week event-free rate in %, 95% CI	90.3 [85.4 - 93.6]	90.3 [85.2 - 93.8]	NA
4 week event-free rate in %, 95% CI	73.3 [64.0 - 80.6]	73.4 [63.7 - 80.9]	72.7 [26.2 - 92.7
8 week event-free rate in %, 95% CI	54.5 [37.1 - 69.1]	54.6 [37.0 - 69.2]	NA
12 week event-free rate in %, 95% CI	43.0 [23.8 - 60.8]	43.0 [23.8 - 60.9]	NA
16 week event-free rate in %, 95% CI	NA	NA	NA

B



	Overall	Initial dose 0.5 mg	Initial dose 0.35 mg
Number of patients	130	122	8
Number of events	20	20	0
Median week to event, 95% CI	12 [6 to inf]	12 [6 to inf]	NA
2 week event-free rate in %, 95% CI	81.2 [68.6 - 89.1]	80.3 [67.3 - 88.6]	NA
4 week event-free rate in %, 95% CI	NA	NA	NA
8 week event-free rate in %, 95% CI	60.5 [37.9 - 77.0]	59.9 [37.5 - 76.4	NA
12 week event-free rate in %, 95% CI	45.4 [21.8 - 66.4]	44.9 [21.6 - 65.8]	NA
16 week event-free rate in %, 95% CI	NA	NA	NA

C



	Overall	Initial dose 0.5 mg	Initial dose 0.35 mg
Number of patients	77	70	7
Number of events	26	23	3
Median week to event, 95% CI	3[2 -4]	3[2 -4]	2.5[1 – inf]
2 week event-free rate in %, 95% CI	61.8 [45.1 - 74.8]	62.6 [45.1 - 76.0]	NA
4 week event-free rate in %, 95% CI	20.6 [5.5 - 42.2]	23.5 [6.4 - 46.6]	NA
8 week event-free rate in %, 95% CI	NA	NA	NA
12 week event-free rate in %, 95% CI	NA	NA	NA
16 week event-free rate in %, 95% CI	NA	NA	NA

10.4. Main results

Results for machine learning model development and evaluation are summarized below according to the corresponding study objectives. Because the objectives of this study were

prediction-oriented, results are presented as predictive performance measures (AUC with 95% confidence intervals) and top predictors based on the absolute values of the coefficient of the associations. Analyses are presented separately for each study objective, with exploratory and sensitivity analyses described in Section 10.5.

Study Objective 2 - Develop and evaluate machine learning prediction models of anemia risk

Table 13 summarizes the predictive performance of the three modeling approaches LASSO, XGB, and SVM for Grade ≥3 anemia in baseline and longitudinal settings. Among baseline models, LASSO demonstrated the highest predictive accuracies across all evaluation periods, including as high as 0.99 [95% CI: 0.98 - 1.00] at the end of Week 2 compared to 0.85 [0.72 - 0.98] and 0.69 [0.20 - 1.00] respectively for XGB and SVM approaches for the baseline models. Prediction accuracies decreased to 0.62 [0.52 - 0.73], 0.59 [0.48 - 0.69] and 0.54 [0.44 - 0.65] for LASSO, XGB and SVM approaches respectively when predicting 16 weeks after talazoparib initiation. The longitudinal models also performed the most accurately using the LASSO approach, with AUC of 0.95 [0.90 - 1.00], 0.81 [0.67 - 0.96] and 0.76 [0.56 - 0.95] using the LASSO, XGB and SVM approaches respectively when predicting anemia status at end of Week 4 for Week 8. While longitudinal model prediction accuracies also decreased after week 8, AUC remained higher at 16 weeks after talazoparib initiation, with AUCs of 0.79 [0.66 - 0.93], 0.78 [0.67 - 0.90] and 0.62 [0.45 - 0.80], using the LASSO, XGB and SVM approaches respectively, with LASSO demonstrating the best predictive accuracy. Overall, the longitudinal models had improved accuracies compared to baseline models when predicting anemia at longer windows after talazoparib initiation.

Table 13 is repeated for the alternate outcome of any treatment-emergent anemia (no anemia; any-grade anemia) in Appendix 8.1 **Error! Reference source not found.**, and with the alternate truncation rule at dose modification instead of dose deviation during model training in Appendix 8.1 **Error! Reference source not found.**. Results using the broader dose modification truncation rules were consistent with those observed using dose deviation, with similar AUC estimates across prediction timepoints for the LASSO approach.

Table 13. Prediction accuracy with AUC based on 3-fold CV for Grade ≥3 anemia

Baseline Model						Longitudinal Time-Varying Model					
Prediction Date	Evaluation Date	Events*/N	LASSO (AUC)	XGB (AUC)	SVM (AUC)	Prediction Date	Evaluation Date	Events/N	LASSO (AUC)	XGB (AUC)	SVM (AUC)
Day 0	Week 2	3/508	0.99 [0.98 - 1.00]	0.85 [0.72 - 0.98]	0.69 [0.20 - 1.00]	Day 0	Week 2	3/508 †	0.99 [0.98 - 1.00]†	0.84 [0.71 - 0.97]†	0.69 [0.20 - 1.00]†
Day 0	Week 4	4/508	1.00 [0.99 - 1.00]	0.57 [0.01 - 1.00]	0.38 [0.07 - 0.69]	Week 2	Week 4	1/502	0.50‡	0.50‡	0.50‡
Day 0	Week 8	21/508	0.90 [0.82 - 0.97]	0.80 [0.65 - 0.95]	0.68 [0.52 - 0.85]	Week 4	Week 8	17/487	0.95 [0.90 - 1.00]	0.81 [0.67 - 0.96]	0.76 [0.56 - 0.95]
Day 0	Week 12	65/508	0.65 [0.52 - 0.78]	0.61 [0.48 - 0.74]	0.58 [0.46 - 0.70]	Week 8	Week 12	44/425	0.71 [0.56 - 0.86]	0.72 [0.57 - 0.87]	0.62 [0.47 - 0.78]

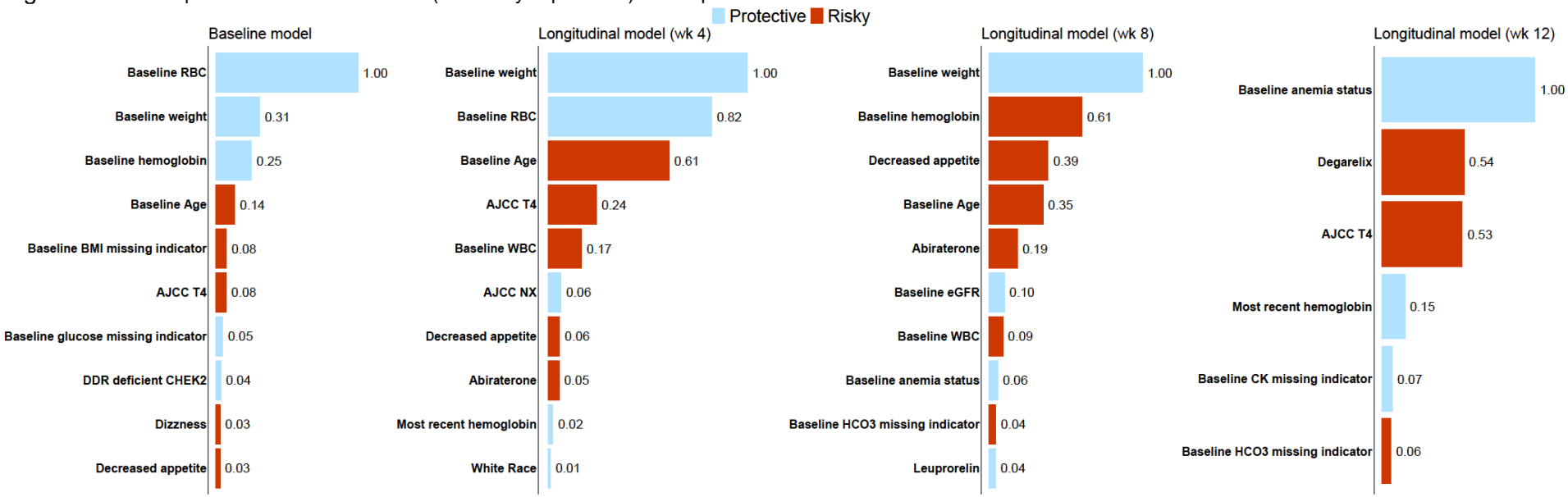
Table 13. Prediction accuracy with AUC based on 3-fold CV for Grade ≥3 anemia

Baseline Model						Longitudinal Time-Varying Model					
Prediction Date	Evaluation Date	Events*/N	LASSO (AUC)	XGB (AUC)	SVM (AUC)	Prediction Date	Evaluation Date	Events/N	LASSO (AUC)	XGB (AUC)	SVM (AUC)
Day 0	Week 16	104/508	0.62 [0.52 - 0.73]	0.59 [0.48 - 0.69]	0.54 [0.44 - 0.65]	Week 12	Week 16	39/329	0.79 [0.66 - 0.93]	0.78 [0.67 - 0.90]	0.62 [0.45 - 0.80]

Model trained on data truncated at the first of any of the following: red blood cell transfusion (RBCT), dose deviation, initiation of subsequent antineoplastic therapy, or date of last contact, death, or data cutoff
Day 0 corresponds to baseline before talazoparib initiation. Weeks 2, 4, 8, 12, and 16 correspond to days 14, 28, 56, 84, and 112 after initiation, respectively.
AUC=area under receiver operating characteristic curve; CV=cross-validation; LASSO=least absolute shrinkage and selection operator; SVM=survival support vector machine; XGB=extreme gradient boosting.
*Cumulative; †Equivalent to the respective baseline model with prediction on Day 0 and evaluation on Day 14; ‡Not enough events observed.

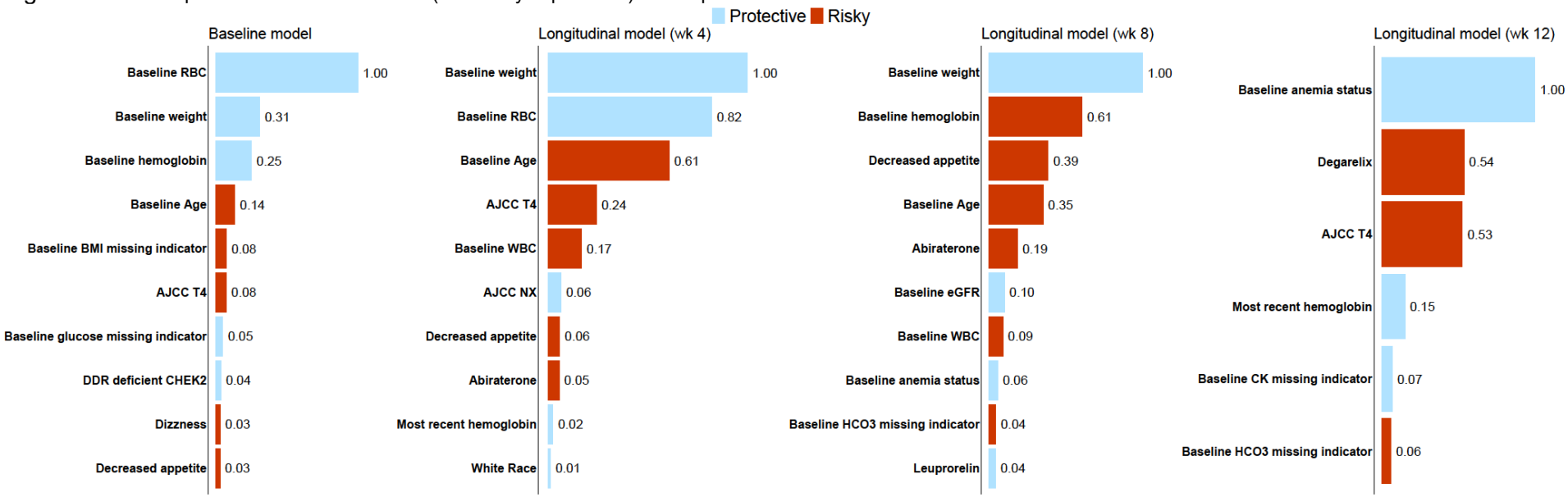
As LASSO consistently demonstrated the highest predictive performance across evaluation periods, variable importance results are presented for the LASSO models.

Figure 7. Top LASSO model risk factors (ranked by importance) for the prediction of Grade ≥3 anemia



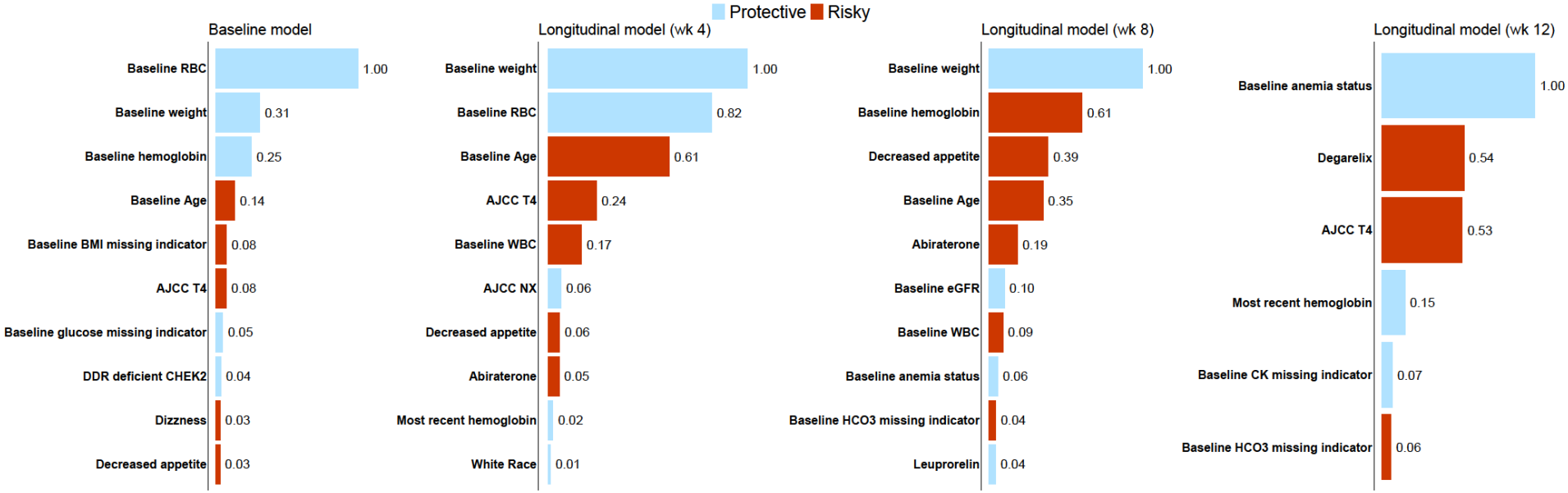
shows the top LASSO model risk factors (ranked by importance) for the prediction of Grade ≥3 anemia, with bar lengths corresponding to the absolute value of the coefficient of the association, standardized relative to the strongest predictor which is normalized as 1. For the baseline model, top protective predictors of anemia included higher baseline RBC, weight, and hemoglobin, while top risk predictors of anemia included older age, missing BMI at baseline, and AJCC T4 tumor staging at diagnosis. Top predictors for the longitudinal LASSO models varied over time, including some of the protective predictors seen from the baseline model such as higher baseline weight and RBC, and some risk predictors such as older age and T4 staging at diagnosis. Additionally, lower recent hemoglobin level, defined as the hemoglobin level captured at the most recent lab visit prior to the prediction date, was a top predictor in the longitudinal models at weeks 4 and 12. Directionality was not always consistent between baseline and longitudinal models, or across prediction windows. While higher baseline hemoglobin was a protective predictor for anemia in the baseline model, it was a risk predictor in the longitudinal model for predicting anemia at week 8 based on data up to week 4. Also of note, baseline anemia status was among the top predictors for anemia in the longitudinal models at weeks 8 and 12.

Figure 7. Top LASSO model risk factors (ranked by importance) for the prediction of Grade ≥3 anemia



is repeated for the alternate outcome of any treatment-emergent anemia (no anemia; any-grade anemia) in Appendix 8.1 **Error! Reference source not found.**, and with the alternate truncation rule at dose modification instead of dose deviation during model training in Appendix 8.1 **Error! Reference source not found.**.

Figure 7. Top LASSO model risk factors (ranked by importance) for the prediction of Grade ≥3 anemia



Study Objective 3 - Develop and evaluate machine learning prediction models of anemia recovery after dose modification

Table 14 shows the accuracies of the 3 modeling approaches LASSO, XGB, and SVM for predicting anemia improvement after dose deviation in baseline and longitudinal settings. Prediction accuracies were low for all three approaches across all time periods, with no AUC exceeding 0.6. Longitudinal models could not be generated for predicting anemia improvement because the available sample size decreased substantially after application of truncation rules, resulting in insufficient observations for stable model development and evaluation.

Table 14. Prediction accuracy with AUC based on 3-fold CV for anemia improvement among patients who experienced dose deviation

Prediction Date	Evaluation Date	Events*/N	Baseline Model LASSO (AUC)	XGB (AUC)	SVM (AUC)
Day 0	Week 2	20/257	0.54 [0.28 - 0.80]	0.47 [0.24 - 0.70]	0.55 [0.30 - 0.81]
Day 0	Week 4	37/257	0.58 [0.39 - 0.76]	0.54 [0.36 - 0.72]	0.49 [0.30 - 0.68]
Day 0	Week 8	42/257	0.60 [0.42 - 0.77]	0.57 [0.41 - 0.73]	0.54 [0.37 - 0.71]

Model trained on data truncated at the first of any of the following: red blood cell transfusion (RBCT), dose deviation, initiation of subsequent antineoplastic therapy, or date of last contact, death, or data cutoff. Among the 319 patients with dose deviation, 62 patients had RBC on or before the date of dose deviation, resulting in 257 patients evaluated for anemia improvement prediction accuracy.
*Cumulative
Day 0 corresponds to baseline before talazoparib initiation. Weeks 2, 4, and 8 correspond to days 14, 28, and 56 after initiation, respectively.

10.5. Other analyses

Additional sensitivity and exploratory analyses (as prespecified in the SAP and protocol, respectively) were conducted to evaluate the robustness of the primary findings and to provide contextual information beyond the primary study objectives. No post-hoc analyses were performed.

Table 15 summarizes a prespecified sensitivity analysis evaluating the impact of including Cavg,t as an additional candidate predictor variable in the machine learning models for prediction of Grade ≥3 anemia. It repeats the 3 modeling approaches LASSO, XGB, and SVM for predicting Grade ≥3 anemia, this time in the absence and presence of Cavg,t as a candidate predictor variable. This sensitivity analysis was limited to 390 patients with Cavg,t data available. No prediction was made at baseline on Day 0 because Cavg,t was calculated based on blood concentration of talazoparib after treatment initiation. Since Cavg,t was calculated based on post-baseline values, only longitudinal models were evaluated.

Similar to the main longitudinal assessment, too few events occurred to allow any prediction during the week 2-4 period in the n=390 subset. The LASSO approach showed the highest predictive accuracies across all subsequent evaluation periods, including as high as 0.94

during the week 4-8 period compared to 0.78 and 0.60 respectively for XGB and SVM approaches for the models without Cavg,t. Prediction accuracies decreased to 0.77, 0.67 and 0.62 for LASSO, XGB and SVM approaches respectively when predicting anemia status at 16 weeks after talazoparib initiation. The models including Cavg,t also performed the most accurately using the LASSO approach, with AUC of 0.84, 0.75 and 0.62 using the LASSO, XGB and SVM approaches respectively when predicting anemia status during the week 4-8 period. Models that included Cavg,t as a candidate predictor also demonstrated decreases in accuracy when predicting anemia status 16 weeks after talazoparib initiation, with AUCs of 0.77, 0.72 and 0.62, using the LASSO, XGB and SVM approaches respectively. Overall, including Cavg,t as a candidate predictor did not demonstrate substantial improved accuracies compared to models that did not include Cavg,t, supporting the robustness of the primary modeling results.

Table 15. Longitudinal model prediction accuracy with AUC based on 3-fold CV for Grade ≥3 anemia in the absence and in the presence of Cavg,t as a candidate predictor variable

			Cavg,t not included as candidate predictor			Cavg,t included as candidate predictor		
Prediction Date	Evaluation Date	Events*/ N	LASSO (AUC)	XGB (AUC)	SVM (AUC)	LASSO (AUC)	XGB (AUC)	SVM (AUC)
Week 2	Week 4	0/386	No events	No events	No events	No events	No events	No events
Week 4	Week 8	15/374	0.94 [0.89 - 0.99]	0.78 [0.60 - 0.96]	0.60 [0.33 - 0.87]	0.84 [0.69 - 0.99]	0.75 [0.55 - 0.94]	0.62 [0.38 - 0.87]
Week 8	Week 12	33/326	0.69 [0.51 - 0.86]	0.70 [0.52 - 0.88]	0.58 [0.38 - 0.78]	0.76 [0.62 - 0.90]	0.69 [0.54 - 0.84]	0.58 [0.37 - 0.79]
Week 12	Week 16	36/255	0.77 [0.62 - 0.93]	0.67 [0.51 - 0.83]	0.62 [0.45 - 0.79]	0.77 [0.62 - 0.92]	0.72 [0.58 - 0.87]	0.62 [0.46 - 0.79]

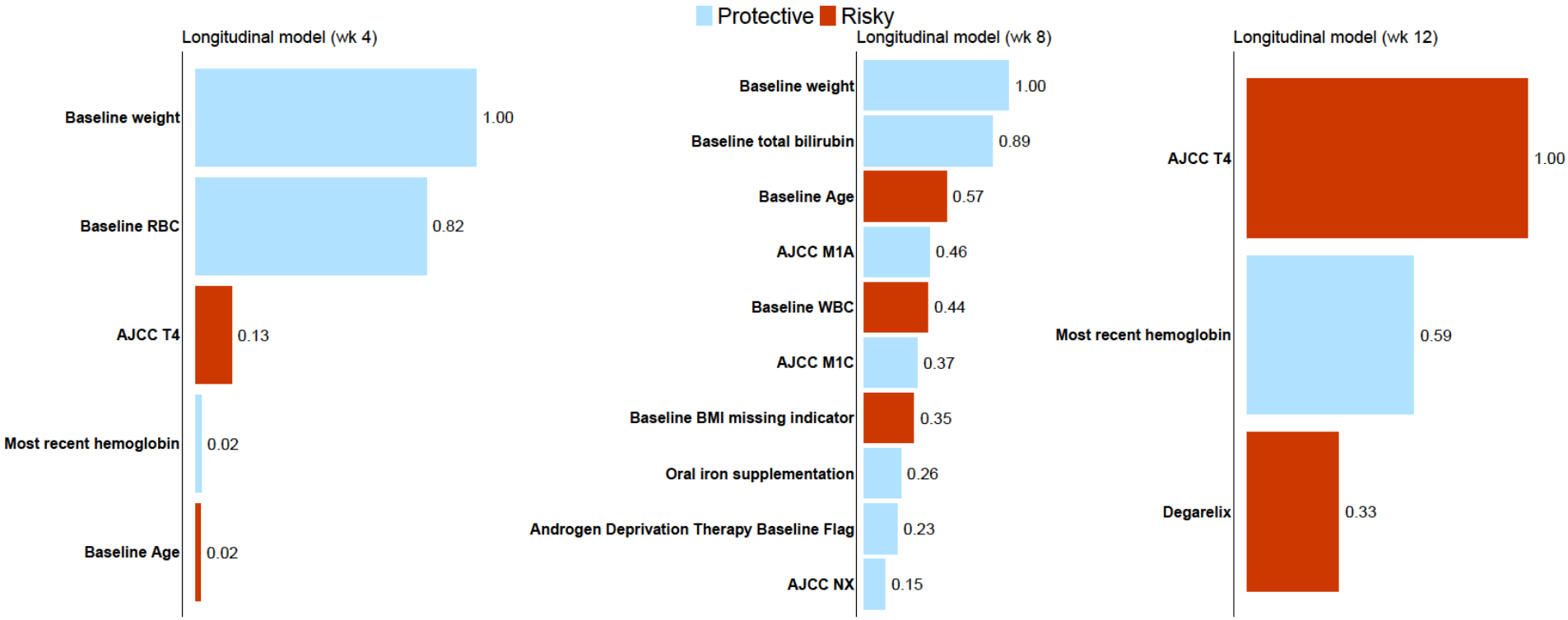
Model trained on data truncated at the first of any of the following: red blood cell transfusion (RBCT), dose deviation, initiation of subsequent antineoplastic therapy, or date of last contact, death, or data cutoff
Weeks 2, 4, 8, 12, and 16 correspond to days 14, 28, 56, and 84 after initiation, respectively.
AUC=area under receiver operating characteristic curve; Cavg,t=blood concentration of talazoparib; CV=cross-validation; LASSO=least absolute shrinkage and selection operator; SVM=survival support vector machine; XGB=extreme gradient boosting.
Analysis limited to 390 patients with Cavg,t data available
No prediction made on Day 0 because Cavg,t was calculated based on blood concentration of talazoparib after treatment initiation

To support interpretation of the sensitivity analysis results, **Error! Reference source not found.** shows the top LASSO model risk factors for the prediction of Grade ≥3 anemia, in the absence and presence of Cavg,t as a candidate predictor variable. During the week 4-8 period, both models consisted of four common top predictors, including baseline weight, baseline RBC, AJCC stage T4 at diagnosis, and recent hemoglobin. The non-Cavg,t model included age as the fifth top predictor while the Cavg,t model included the most recent Cavg,t as a top risk predictor. During the week 8-12 period, the non-Cavg,t model had at least 10 predictors, including baseline weight, baseline total bilirubin, age, AJCC stage M, baseline WBC, among others. The Cavg,t model was more parsimonious, including only four top predictors: Cavg,t, baseline weight, AJCC stage M1C, and recent hemoglobin. During the week 12-16 period, both models were parsimonious, composing of three predictors for

the non-Cavg,t model: AJCC stage T4 at diagnosis, recent hemoglobin, and past degarelix treatment; and two predictors for the Cavg,t model: Cavg,t and recent hemoglobin.

Figure 8. Top LASSO model risk factors (ranked by importance) for the prediction of Grade ⩾3 anemia in A) the absence and B) the presence of Cavg,t as a candidate predictor variable

A)



B)

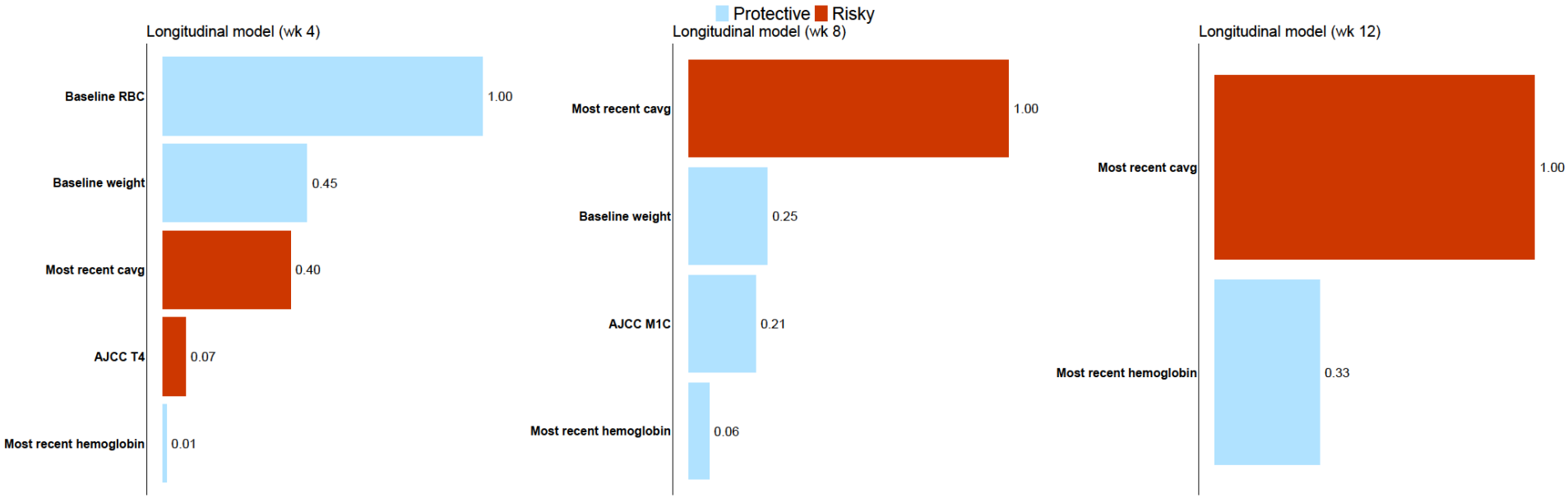

Protective
Risky
Longitudinal model (wk 4)
Baseline RBC
1.00
Baseline weight
0.45
Most recent cavg
0.40
AJCC T4
0.07
Most recent hemoglobin
0.01
Longitudinal model (wk 8)
Most recent cavg
1.00
Baseline weight
0.25
AJCC M1C
0.21
Most recent hemoglobin
0.06
Longitudinal model (wk 12)
Most recent cavg
1.00
Most recent hemoglobin
0.33

Table 16 summarizes the protocol-specified exploratory analyses of describing baseline characteristics of patients in the control arm of TALAPRO-2, stratified by the highest grade treatment-emergent anemia experienced during follow-up (no anemia; Grade 1-2; Grade ≥3). Patients who developed Grade ≥3 anemia were older than those with no treatment-emergent anemia (median age: 77.0 vs 71.0 years), consistent with the direction of the association observed in the treatment arm. A higher proportion of patients with Grade ≥3 anemia were Asian (39.1% vs 23.9%) and were enrolled from Asia (39.1% vs 22.8%) compared with patients with no treatment-emergent anemia; similar directional patterns were also observed in the treatment arm. The distribution of study cohort also differed by anemia severity, with patients with Grade ≥3 anemia comprising a smaller proportion from Cohort 1 (52.2% vs 61.3%) and a correspondingly larger proportion from Cohort 2 (47.8% vs 38.7%) relative to patients with no treatment-emergent anemia; this trend was not observed in the treatment arm.

Among clinical characteristics, baseline renal impairment and ECOG performance status appeared broadly similar across anemia strata, consistent with the treatment arm. Baseline PSA was lower among patients who developed Grade ≥3 anemia compared with patients with no treatment-emergent anemia (median [Q1, Q3]: 6.40 [4.94, 87.8] vs 16.2 [6.42, 51.6]); this pattern was less apparent in the treatment arm. Patients who developed Grade ≥3 anemia also had lower baseline body weight (median [Q1, Q3]: 78.4 [69.3,84.9] vs 82.2 [72.3, 93.4] kg); this was a similar but weaker trend than that observed in the treatment arm. This similar weaker trend was also observed for BMI. Baseline anemia and prior medical history of anemia were more common among those who later developed Grade ≥3 anemia, including fewer patients with baseline no anemia (4.3% vs 48.4%) and more patients with baseline Grade 2 anemia (26.1% vs 0.9%) in the Grade ≥3 group compared with the no treatment-emergent anemia group. Prior history of anemia was also more frequent (39.1% vs 8.7%). These baseline anemia patterns were directionally similar to those observed in the treatment arm. A higher proportion of patients with any HRRm was observed among those who developed Grade ≥3 anemia versus no treatment-emergent anemia (47.8% vs 38.5%); this trend was not observed in the treatment arm.

Baseline treatment history was broadly comparable between patients with Grade ≥3 anemia and those with no treatment-emergent anemia in the control arm, similar to what was observed in the treatment arm. One exception was that patients with Grade ≥3 anemia in the control arm did not differ from those with no treatment-emergent anemia with respect to past treatment with taxane-based chemotherapy.

In baseline laboratory assessments, patients who developed Grade ≥3 anemia had lower hemoglobin (median 113 vs 131 g/dL), HCT (30.1% vs 37.2%) and RBC (3.82vs 4.31 $x10^{12}$/L) than patients who had no treatment-emergent anemia, consistent with patterns observed in the treatment arm.

Baseline characteristics stratified by any treatment-emergent anemia (no anemia; any-grade anemia) are shown in Appendix 8.1 **Error! Reference source not found.**

Table 16. Baseline characteristics of patients in the control arm of TALAPRO-2, stratified by highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3)

	No treatment-emergent anemia (N=426)	Grade 1-2 anemia (N=63)	Grade ≥3 anemia (N=23)	Overall (N=512)
Demographics				
Age, Median [Q1,Q3]	71.0 [65.0,76.0]	72.0 [66.5,77.0]	77.0 [71.0,79.5]	71.0 [65.0,76.0]
Race, n (%)				
White	288 (67.6%)	39 (61.9%)	13 (56.5%)	340 (66.4%)
Black or African American	8 (1.9%)	0 (0%)	0 (0%)	8 (1.6%)
Asian	102 (23.9%)	20 (31.7%)	9 (39.1%)	131 (25.6%)
Native Hawaiian or other Pacific Islander	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)
Not Reported	26 (6.1%)	4 (6.3%)	1 (4.3%)	31 (6.1%)
	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)
Ethnicity, n (%)				
Hispanic or Latino	55 (12.9%)	7 (11.1%)	1 (4.3%)	63 (12.3%)
Not Hispanic or Latino	341 (80.0%)	49 (77.8%)	19 (82.6%)	409 (79.9%)
Not reported	30 (7.0%)	7 (11.1%)	3 (13.0%)	40 (7.8%)
Region, n (%)				
1) North America	61 (14.3%)	12 (19.0%)	2 (8.7%)	75 (14.6%)
2) European Union/GBR	192 (45.1%)	24 (38.1%)	9 (39.1%)	225 (43.9%)
3) Asia	97 (22.8%)	20 (31.7%)	9 (39.1%)	126 (24.6%)
4) Rest of the world	76 (17.8%)	7 (11.1%)	3 (13.0%)	86 (16.8%)
Cohort, n (%)				
1	261 (61.3%)	39 (61.9%)	12 (52.2%)	312 (60.9%)
2	165 (38.7%)	24 (38.1%)	11 (47.8%)	200 (39.1%)
Clinical characteristics				
Weight, Median [Q1,Q3]	82.2 [72.3,93.4]	77.0 [68.9,91.5]	78.4 [69.3,84.9]	82.0 [71.3,93.0]
Missing	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)
BMI, Median [Q1,Q3]	27.7 [24.9,30.8]	27.3 [24.6,30.4]	25.6 [24.1,28.7]	27.7 [24.6,30.8]
Missing	8 (1.9%)	1 (1.6%)	0 (0%)	9 (1.8%)
Anemia Status, n (%)				
0	206 (48.4%)	25 (39.7%)	1 (4.3%)	232 (45.3%)
1	216 (50.7%)	33 (52.4%)	16 (69.6%)	265 (51.8%)
2	4 (0.9%)	5 (7.9%)	6 (26.1%)	15 (2.9%)
Prior History Anemia	37 (8.7%)	7 (11.1%)	9 (39.1%)	53 (10.4%)
Prior History Kidney Disease	8 (1.9%)	4 (6.3%)	1 (4.3%)	13 (2.5%)
Renal Impairment, n (%)				
Mild/Normal (>=60)	369 (86.6%)	57 (90.5%)	19 (82.6%)	445 (86.9%)
Moderate (30-59)	43 (10.1%)	6 (9.5%)	4 (17.4%)	53 (10.4%)
Not reported	14 (3.3%)	0 (0%)	0 (0%)	14 (2.7%)

Table 16. Baseline characteristics of patients in the control arm of TALAPRO-2, stratified by highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3)

	No treatment-emergent anemia (N=426)	Grade 1-2 anemia (N=63)	Grade ≥3 anemia (N=23)	Overall (N=512)
Gleason score category, n (%)				
High [8-10]	292 (68.5%)	44 (69.8%)	20 (87.0%)	356 (69.5%)
Low [2-7]	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not reported	134 (31.5%)	19 (30.2%)	3 (13.0%)	156 (30.5%)
Bone metastases at baseline, n (%)	343 (80.5%)	54 (85.7%)	18 (78.3%)	415 (81.1%)
Prostate cancer diagnosis year,				
Median [Q1,Q3]	2020 [2010,2020]	2020 [2010,2020]	2020 [2020,2020]	2020 [2010,2020]
Missing	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)
Baseline bone metastases number, Median [Q1,Q3]	3.00 [2.00,5.00]	3.00 [2.00,5.00]	4.00 [2.50,6.00]	3.00 [2.00,5.00]
De novo metastatic disease, n (%)	191 (44.8%)	37 (58.7%)	13 (56.5%)	241 (47.1%)
Somatic HRR mutation, n (%)				
1) DDR Deficient	164 (38.5%)	23 (36.5%)	11 (47.8%)	198 (38.7%)
2) Non-DDR Deficient	182 (42.7%)	23 (36.5%)	8 (34.8%)	213 (41.6%)
3) Unknown	80 (18.8%)	17 (27.0%)	4 (17.4%)	101 (19.7%)
Deficient ATM	33 (7.7%)	6 (9.5%)	0 (0.0%)	39 (7.6%)
Deficient ATR	9 (2.1%)	1 (1.6%)	3 (13.0%)	13 (2.5%)
Deficient BRCA1	12 (2.8%)	0 (0.0%)	0 (0.0%)	12 (2.3%)
Deficient BRCA2	60 (14.1%)	11 (17.5%)	2 (8.7%)	73 (14.3%)
Deficient CDK12	33 (7.7%)	2 (3.2%)	4 (17.4%)	39 (7.6%)
Deficient CHEK2	31 (7.3%)	5 (7.9%)	1 (4.3%)	37 (7.2%)
Deficient FANCA	4 (0.9%)	1 (1.6%)	0 (0.0%)	5 (1.0%)
Deficient MLH1	0 (0.0%)	1 (1.6%)	0 (0.0%)	1 (0.2%)
Deficient NBN	2 (0.5%)	1 (1.6%)	0 (0.0%)	3 (0.6%)
Deficient PALB2	7 (1.6%)	0 (0.0%)	1 (4.3%)	8 (1.6%)
Deficient RAD51C	2 (0.5%)	0 (0.0%)	0 (0.0%)	2 (0.4%)
ECOG, n (%)				
0	285 (66.9%)	36 (57.1%)	16 (69.6%)	337 (65.8%)
1	141 (33.1%)	27 (42.9%)	7 (30.4%)	175 (34.2%)
Treatment history				
Bilateral orchiectomy	27 (6.3%)	5 (7.9%)	3 (13.0%)	35 (6.8%)
Prior prostate cancer surgery[a]	319 (74.9%)	52 (82.5%)	20 (87.0%)	391 (76.4%)
Prior radiation therapy	101 (23.7%)	12 (19.0%)	5 (21.7%)	118 (23.0%)
Prior hormonal therapy	25 (5.9%)	7 (11.1%)	3 (13.0%)	35 (6.8%)
Androgen deprivation therapy at baseline	403 (94.6%)	60 (95.2%)	22 (95.7%)	485 (94.7%)
Triptorelin	72 (16.9%)	10 (15.9%)	5 (21.7%)	87 (17.0%)
Degarelix	82 (19.2%)	4 (6.3%)	3 (13.0%)	89 (17.4%)

Table 16. Baseline characteristics of patients in the control arm of TALAPRO-2, stratified by highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3)

	No treatment-emergent anemia (N=426)	Grade 1-2 anemia (N=63)	Grade ≥3 anemia (N=23)	Overall (N=512)
Leuprorelin	236 (55.4%)	41 (65.1%)	12 (52.2%)	289 (56.4%)
Gonadorelin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Relugolix	6 (1.4%)	0 (0.0%)	0 (0.0%)	6 (1.2%)
Goserelin	46 (10.8%)	4 (6.3%)	2 (8.7%)	52 (10.2%)
Histrelin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Flutamide	21 (4.9%)	6 (9.5%)	2 (8.7%)	29 (5.7%)
Bicalutamide	227 (53.3%)	42 (66.7%)	15 (65.2%)	284 (55.5%)
Enzalutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Darolutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Taxane Based Chemotherapy	114 (26.8%)	12 (19.0%)	6 (26.1%)	132 (25.8%)
Carbazitaxel	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Docetaxel	114 (26.8%)	12 (19.0%)	6 (26.1%)	132 (25.8%)
Abiraterone	23 (5.4%)	7 (11.1%)	3 (13.0%)	33 (6.4%)
Daralutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Apalutamide	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Orteronel/TAK700	2 (0.5%)	0 (0.0%)	0 (0.0%)	2 (0.4%)
Baseline labs				
Hemoglobin, Median [Q1,Q3]	131 [123,139]	128 [116,136]	113 [99.0,117]	130 [120,138]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
eGFR, Median [Q1,Q3]	87.0 [73.0,100]	88.0 [77.5,102]	82.0 [72.0,99.1]	87.0 [74.0,100]
Missing	4 (0.9%)	0 (0%)	0 (0%)	4 (0.8%)
ALT, Median [Q1,Q3]	0.320 [0.250,0.458]	0.280 [0.215,0.390]	0.270 [0.200,0.325]	0.320 [0.250,0.450]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Albumin, Median [Q1,Q3]	42.0 [39.0,45.0]	42.2 [38.6,45.0]	43.0 [39.5,44.0]	42.0 [39.0,44.9]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ALP, Median [Q1,Q3]	1.78 [1.29,3.18]	1.47 [1.16,2.57]	2.09 [1.55,4.31]	1.75 [1.28,3.18]
Missing	3 (0.7%)	0 (0%)	0 (0%)	3 (0.6%)
AST, Median [Q1,Q3]	0.370 [0.320,0.480]	0.370 [0.315,0.450]	0.420 [0.370,0.540]	0.370 [0.320,0.480]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HCO3, Median [Q1,Q3]	25.0 [23.8,27.4]	25.3 [23.0,27.0]	25.3 [23.1,26.0]	25.0 [23.6,27.2]
Missing	66 (15.5%)	8 (12.7%)	4 (17.4%)	78 (15.2%)
Total_bilirubin, Median [Q1,Q3]	8.60 [6.05,12.0]	8.60 [6.40,10.8]	8.60 [7.00,10.3]	8.60 [6.20,11.3]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
BUN, Median [Q1,Q3]	6.40 [5.40,7.90]	6.40 [4.53,7.50]	6.80 [5.98,7.25]	6.40 [5.40,7.55]
Missing	261 (61.3%)	43 (68.3%)	13 (56.5%)	317 (61.9%)
Ca, Median [Q1,Q3]	2.34 [2.27,2.41]	2.28 [2.23,2.39]	2.27 [2.21,2.41]	2.33 [2.26,2.41]
Missing	0 (0%)	1 (1.6%)	0 (0%)	1 (0.2%)
Cl, Median [Q1,Q3]	104 [102,106]	104 [102,106]	105 [104,106]	104 [102,106]
Missing	3 (0.7%)	0 (0%)	0 (0%)	3 (0.6%)

Table 16. Baseline characteristics of patients in the control arm of TALAPRO-2, stratified by highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3)

	No treatment-emergent anemia (N=426)	Grade 1-2 anemia (N=63)	Grade ≥3 anemia (N=23)	Overall (N=512)
CK, Median [Q1,Q3]	1.37 [0.940,1.94]	1.48 [0.835,1.81]	1.45 [0.950,1.87]	1.37 [0.923,1.91]
Missing	327 (76.8%)	49 (77.8%)	18 (78.3%)	394 (77.0%)
Glucose, Median [Q1,Q3]	5.90 [5.30,6.79]	5.80 [5.38,6.78]	5.80 [5.09,7.44]	5.90 [5.30,6.80]
Missing	3 (0.7%)	0 (0%)	0 (0%)	3 (0.6%)
LDH, Median [Q1,Q3]	210 [177,251]	207 [186,254]	236 [209,297]	211 [178,255]
Missing	6 (1.4%)	0 (0%)	0 (0%)	6 (1.2%)
Mg, Median [Q1,Q3]	0.860 [0.803,0.900]	0.850 [0.795,0.905]	0.870 [0.845,0.940]	0.860 [0.800,0.900]
Missing	4 (0.9%)	0 (0%)	0 (0%)	4 (0.8%)
K, Median [Q1,Q3]	4.30 [4.10,4.60]	4.30 [4.10,4.49]	4.40 [4.20,4.65]	4.30 [4.10,4.56]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Protein, Median [Q1,Q3]	70.2 [67.0,74.0]	70.0 [67.4,73.3]	69.0 [66.3,73.0]	70.0 [67.0,74.0]
Missing	7 (1.6%)	0 (0%)	1 (4.3%)	8 (1.6%)
Na, Median [Q1,Q3]	140 [139,142]	140 [138,142]	142 [138,143]	140 [138,142]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Creatinine, Median [Q1,Q3]	78.0 [68.0,91.1]	75.0 [68.2,87.5]	78.7 [68.1,95.6]	77.8 [68.0,91.1]
Missing	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)
Phosphate, Median [Q1,Q3]	1.10 [1.00,1.30]	1.10 [1.00,1.30]	1.20 [1.05,1.30]	1.10 [1.00,1.30]
Missing	9 (2.1%)	2 (3.2%)	0 (0%)	11 (2.1%)
Testosterone, Median [Q1,Q3]	11.5 [5.20,18.0]	10.1 [2.88,14.4]	7.17 [2.59,11.8]	11.5 [4.61,17.3]
Missing	5 (1.2%)	2 (3.2%)	0 (0%)	7 (1.4%)
Urea, Median [Q1,Q3]	6.01 [5.18,7.34]	6.20 [5.10,7.90]	6.68 [5.93,7.87]	6.10 [5.18,7.35]
Missing	152 (35.7%)	18 (28.6%)	9 (39.1%)	179 (35.0%)
FolicAcid, Median [Q1,Q3]	8.20 [5.70,13.1]	9.26 [6.59,13.2]	9.43 [7.07,12.9]	8.40 [5.88,13.1]
Missing	41 (9.6%)	6 (9.5%)	1 (4.3%)	48 (9.4%)
VitaminB12, Median [Q1,Q3]	408 [298,565]	378 [267,497]	412 [297,630]	406 [290,565]
Missing	31 (7.3%)	4 (6.3%)	0 (0%)	35 (6.8%)
PSA, Median [Q1,Q3]	16.2 [6.42,51.6]	23.4 [7.75,63.3]	6.40 [4.94,87.8]	16.3 [6.34,54.1]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
MCV, Median [Q1,Q3]	91.0 [87.0,95.0]	92.0 [87.5,94.5]	93.0 [87.0,94.0]	91.0 [87.0,94.0]
Missing	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)
RBC, Median [Q1,Q3]	4.31 [4.07,4.60]	4.24 [3.78,4.50]	3.82 [3.38,3.92]	4.30 [4.00,4.58]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HCT, Median [Q1,Q3]	37.2 [0.430,40.5]	33.9 [0.390,40.1]	30.1 [0.335,35.1]	36.7 [0.420,40.4]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
WBC, Median [Q1,Q3]	6.00 [5.00,7.29]	5.70 [4.51,6.75]	5.40 [4.65,7.63]	6.00 [4.90,7.26]

Table 16. Baseline characteristics of patients in the control arm of TALAPRO-2, stratified by highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3)

	No treatment-emergent anemia (N=426)	Grade 1-2 anemia (N=63)	Grade ≥3 anemia (N=23)	Overall (N=512)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Basophils, Median [Q1,Q3]	0.0300 [0,0.0500]	0.0300 [0.00500,0.0550]	0.0300 [0.0125,0.0375]	0.0300 [0,0.0500]
Missing	67 (15.7%)	4 (6.3%)	5 (21.7%)	76 (14.8%)
Basophils/Leukocytes, Median [Q1,Q3]	0.512 [0,0.841]	0.482 [0.100,0.898]	0.449 [0.203,0.636]	0.501 [0,0.834]
Missing	67 (15.7%)	4 (6.3%)	5 (21.7%)	76 (14.8%)
Eosinophils, Median [Q1,Q3]	0.150 [0.100,0.230]	0.110 [0.0850,0.200]	0.115 [0.0800,0.210]	0.150 [0.100,0.220]
Missing	64 (15.0%)	4 (6.3%)	5 (21.7%)	73 (14.3%)
Eosinophils/Leukocytes , Median [Q1,Q3]	2.32 [1.54,3.85]	2.25 [1.58,3.08]	2.09 [1.19,2.72]	2.28 [1.52,3.68]
Missing	64 (15.0%)	4 (6.3%)	5 (21.7%)	73 (14.3%)
Lymphocytes, Median [Q1,Q3]	1.50 [1.09,1.87]	1.30 [0.980,1.80]	1.40 [1.15,1.79]	1.45 [1.08,1.85]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lymphocytes/Leukocytes , Median [Q1,Q3]	24.5 [18.9,30.5]	23.8 [18.0,31.6]	27.4 [20.0,33.0]	24.5 [18.9,30.6]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Monocytes, Median [Q1,Q3]	0.500 [0.400,0.630]	0.450 [0.375,0.600]	0.495 [0.330,0.555]	0.500 [0.400,0.623]
Missing	67 (15.7%)	4 (6.3%)	5 (21.7%)	76 (14.8%)
Monocytes/Leukocytes , Median [Q1,Q3]	8.30 [6.84,9.79]	8.04 [6.92,9.74]	8.23 [6.54,9.98]	8.25 [6.82,9.80]
Missing	67 (15.7%)	4 (6.3%)	5 (21.7%)	76 (14.8%)
Neutrophils, Median [Q1,Q3]	3.71 [3.00,4.76]	3.61 [2.94,4.34]	3.10 [2.88,4.41]	3.68 [3.00,4.71]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Neutrophils/Leukocytes , Median [Q1,Q3]	63.1 [57.1,70.0]	65.4 [57.2,70.4]	60.4 [55.4,67.0]	63.2 [57.1,69.9]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Platelets, Median [Q1,Q3]	227 [188,266]	215 [182,260]	239 [175,309]	225 [187,267]
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Retics, Median [Q1,Q3]	60.9 [50.2,78.0]	65.0 [54.4,77.0]	67.1 [36.6,77.3]	61.3 [50.6,78.0]
Missing	158 (37.1%)	20 (31.7%)	9 (39.1%)	187 (36.5%)
EPO, Median [Q1,Q3]	12.1 [9.00,17.1]	15.8 [11.0,19.4]	21.7 [14.5,31.2]	12.7 [9.13,18.6]
Missing	82 (19.2%)	19 (30.2%)	5 (21.7%)	106 (20.7%)
Baseline anemia symptoms				
Fatigue	125 (29.3%)	15 (23.8%)	4 (17.4%)	144 (28.1%)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Shortness Breath	4 (0.9%)	0 (0.0%)	0 (0.0%)	4 (0.8%)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 16. Baseline characteristics of patients in the control arm of TALAPRO-2, stratified by highest grade treatment-emergent anemia (no anemia; Grade 1-2; Grade ≥3)

	No treatment-emergent anemia (N=426)	Grade 1-2 anemia (N=63)	Grade ≥3 anemia (N=23)	Overall (N=512)
Decreased Appetite	8 (1.9%)	1 (1.6%)	0 (0.0%)	9 (1.8%)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Asthenia	37 (8.7%)	5 (7.9%)	1 (4.3%)	43 (8.4%)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dyspnea	23 (5.4%)	4 (6.3%)	1 (4.3%)	28 (5.5%)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dizziness	22 (5.2%)	4 (6.3%)	3 (13.0%)	29 (5.7%)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Baseline anemia management				
Iron treatment up to and prior to baseline	3 (0.7%)	0 (0.0%)	0 (0.0%)	3 (0.6%)
Index treatment details				
Baseline Talazoparib Dose				
0.35	43 (10.1%)	6 (9.5%)	4 (17.4%)	53 (10.4%)
0.5	383 (89.9%)	57 (90.5%)	19 (82.6%)	459 (89.6%)
Years between prostate cancer diagnosis and control treatment initiation, Median [Q1,Q3]	3.00 [2.00,6.00]	3.00 [1.50,6.00]	2.00 [1.00,4.50]	3.00 [2.00,6.00]
Missing	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)

[a]Includes prostatectomy, transurethral resection of the prostate, prostate biopsy, bilateral orchiectomy, pelvic node dissection, urethral stent, and nephrostomy

Units: Hemoglobin (g/L); eGFR (mL/min/1.73 m²); ALT (µkat/L); Albumin (g/L); ALP (µkat/L); AST (µkat/L); Bicarbonate (mmol/L); Total Bilirubin (µmol/L); BUN (mmol/L); Calcium (mmol/L); Chloride (mmol/L); Creatine Kinase (µkat/L); Glucose (mmol/L); LDH (U/L); Magnesium (mmol/L); Potassium (mmol/L); Protein (g/L); Sodium (mmol/L); Creatinine (µmol/L); Phosphate (mmol/L); Testosterone (ng/dL); Urea (mmol/L); Vitamin B9 (µg/L); Vitamin B12 (ng/L); PSA (µg/L); MCV (fL); RBC (10^{12}/L); Hematocrit (L/L); WBC (10^9/L); Basophils (10^9/L); Basophils/Leukocytes (%); Eosinophils (10^9/L); Eosinophils/Leukocytes (%); Lymphocytes (10^9/L); Lymphocytes/Leukocytes (%); Monocytes (10^9/L); Monocytes/Leukocytes (%); Neutrophils (10^9/L); Neutrophils/Leukocytes (%); Platelets (10^9/L).

Table 17 summarizes the protocol-specified exploratory analyses of hemoglobin change (g/dL per day) during the first months after treatment initiation in the control arm. No notable changes in hemoglobin was observed over time, as the median deviation from baseline to weeks 2, 4, 8, 12 and 16 remained at or close to 0 median g/dL.

Table 17. Hemoglobin change (g/dL per day) at 2, 4, 8, 12, and 16 weeks after treatment initiation

Hgb change week 2	
Median [Q1,Q3]	0 [-0.286,0.286]
Missing	1 (0.2%)

Table 17. Hemoglobin change (g/dL per day) at 2, 4, 8, 12, and 16 weeks after treatment initiation

Hgb change week 4	
Median [Q1,Q3]	0 [-0.143,0.179]
[Min, Max]	2 (0.4%)
Hgb change week 8	
Median [Q1,Q3]	0.0182 [-0.0684,0.0943]
Missing	13 (2.5%)
Hgb change week 12	
Median [Q1,Q3]	0.0119 [-0.0468,0.0741]
Missing	41 (8.0%)
Hgb change week 16	
Median [Q1,Q3]	0.00901 [-0.0399,0.0535]
Missing	58 (11.3%)

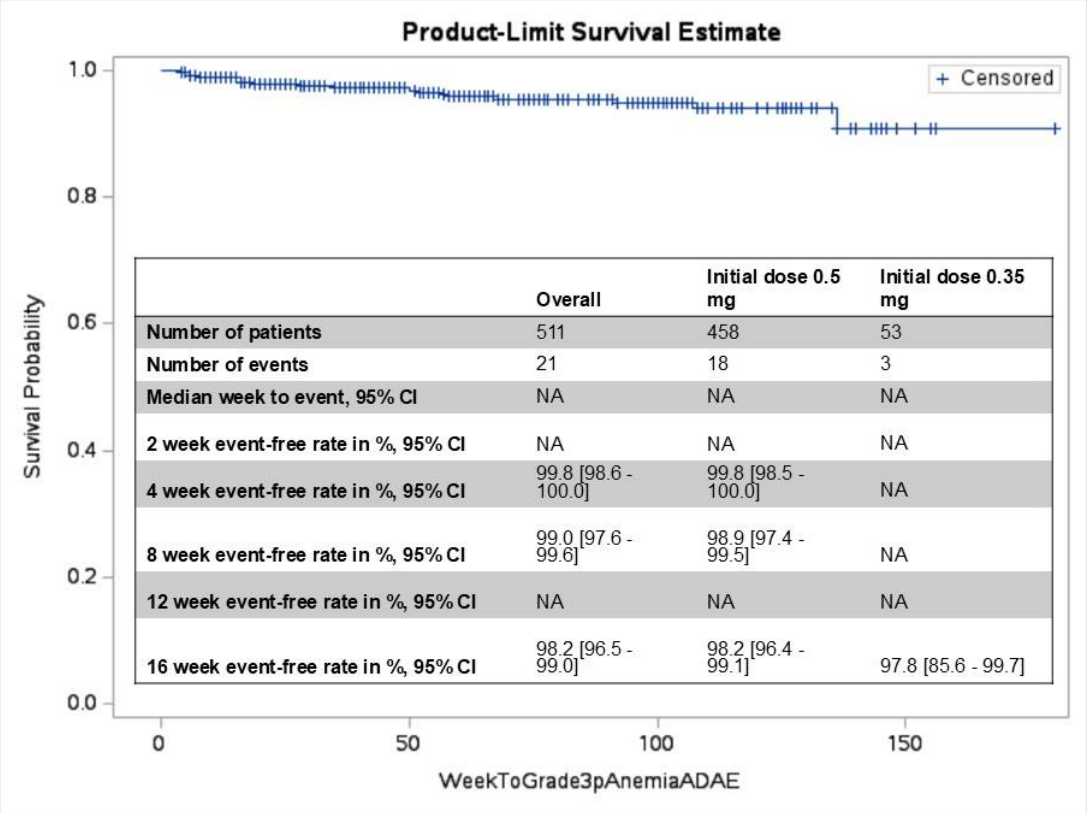
Weeks 2, 4, 8, 12 and 16 correspond to Visits 1, 2, 4, 6 and 8 after treatment initiation

As a protocol-specified exploratory analysis, time to first Grade ≥3 anemia was evaluated among patients on the control arm receiving enzalutamide. Time to anemia was censored at the first of: i) RBC transfusion; ii) death, iii) date of last contact; or iv) study end date. The Kaplan-Meier curves and corresponding summary statistics are shown in Figure 9.

In the cohort of 511 patients, n=21 (4.1%) experienced at least one Grade ≥3 anemia during follow-up and prior to censoring, with median time to first Grade ≥3 anemia not reached during the study period. By 16 weeks, the event-free rate was still high, at 98.2% (95% CI, 96.5%–99.0%). The Kaplan–Meier curve showed a steady decline over time with a slight drop around 135 weeks after treatment initiation.

Figure 9. Time to Grade ≥3 anemia, followed from the date of talazoparib initiation until the date of the anemia or censored at the first of: i) RBC transfusion;

ii) death, iii) date of last contact; or iv) study end date, among patients in the control arm of TALAPRO-2.



	Overall	Initial dose 0.5 mg	Initial dose 0.35 mg
Number of patients	511	458	53
Number of events	21	18	3
Median week to event, 95% CI	NA	NA	NA
2 week event-free rate in %, 95% CI	NA	NA	NA
4 week event-free rate in %, 95% CI	99.8 [98.6 - 100.0]	99.8 [98.5 - 100.0]	NA
8 week event-free rate in %, 95% CI	99.0 [97.6 - 99.6]	98.9 [97.4 - 99.5]	NA
12 week event-free rate in %, 95% CI	NA	NA	NA
16 week event-free rate in %, 95% CI	98.2 [96.5 - 99.0]	98.2 [96.4 - 99.1]	97.8 [85.6 - 99.7]

10.6. Adverse events/adverse reactions

This study was a secondary analysis of existing de-identified TALAPRO-2 trial data and was not designed to collect, assess, or report additional adverse events or to perform individual case causality assessments. Adverse events occurring during TALAPRO-2 were collected, assessed, and reported according to the safety reporting requirements applicable to the parent trial at the time of study conduct. No aggregate safety risks beyond the predefined study outcomes and sensitivity analyses were identified during the analyses conducted for this study.

11. DISCUSSION

11.1. Key results

There are three main groups of key results based on the three study objectives.

Study objective 1 descriptive analyses showed that patients who developed Grade ≥3 anemia were older at treatment initiation (median age 73.0 years vs 68.0 years); more

frequently of Asian race (n=80, 34.6% vs n=27, 16.1%) and had lower baseline body weight (median 76.6 vs 85.0 kg) compared with patients who experienced no treatment-emergent anemia. Almost half of patients (45.5%) experienced a Grade ≥3 anemia anytime during study follow-up, while 31.1% experienced a Grade ≥3 anemia prior to a censoring event such as a dose deviation event or a RBC transfusion, with nearly two-thirds of these events occurring within the first 16 weeks of treatment. Therefore, patients may be at the most risk and stand to benefit most from personalized monitoring and accurate assessment of potential anemia risk during the early months of talazoparib treatment.

Study objective 2 machine learning predictive modeling of Grade ≥3 anemia showed predictive accuracy AUCs 0.90 to 0.99 during the initial 8 weeks of talazoparib treatment for both baseline and longitudinal models using the LASSO approach. Predictive performance declined for both approaches when predicting events occurring 8-16 weeks after treatment initiation, although longitudinal models (AUCs 0.79-0.99) consistently outperformed baseline-only models (AUCs <0.70). AUC estimates were also similar when an alternative dose modification truncation rule was applied, suggesting that model performance is robust to the choice of dose-change definition in this study. Top predictors in both baseline and longitudinal models included baseline weight, hemoglobin levels, RBC, and older age based on LASSO modeling approaches. In sensitivity analyses further including Cavg,t (blood concentration of talazoparib) as a predictor, it was observed that despite models being overall more parsimonious compared to those not including Cavg,t, prediction accuracies did not substantially improve. Given that this variable is only measured in the trial setting during pharmacokinetic analyses and not readily available during routine clinical practice, this suggests that future studies in the real-world setting would not be substantially disadvantaged by the absence of this variable.

Study objective 3 machine learning predictive modeling of anemia improvement following dose modification showed limited predictive performance, with no AUC exceeding 0.6. These findings were in part due to too few events occurring prior to censoring: only patients who experienced dose modification could be assessed, and censoring events such as RBC transfusion and subsequent dose modification occurred frequently during follow-up, resulting in a limited dataset on which to train the machine learning models.

This is the first study to use machine-learning models to predict adverse events in talazoparib-treated mCRPC patients. Prior studies in talazoparib-treated patients, including those with metastatic castration-resistant prostate cancer and advanced breast cancer, have evaluated risk factors for hematologic adverse events using descriptive summaries and regression-based characterization of patient characteristics associated with treatment-emergent anemia[26–30]. Similarly, association analyses have been conducted to identify risk factors for severe anemia in advanced ovarian or breast cancer patients receiving olaparib[30], but no study to date for PARP inhibitors have evaluated individual-level anemia risk using prediction models in general, nor ML prediction models specifically. Among other cancer therapy classes across solid tumors in general, chemotherapy-related anemia risk prediction models are the most commonly described[31–33], with AUCs ranging from 0.74 to 0.88. ML prediction models of anemia risk have also been reported for non-cancer indications including linezolid treatment of bacterial infections in elderly patients [34,35], with AUCs ranging from 0.74 to 0.83. However, prior studies on prediction of anemia have been for the overall follow-up period without specifying a specific window. In contrast, the present study is more granular and temporally explicit, evaluating time-specific predictive

performance at clinically relevant landmarks (i.e. 2, 4, 8, 12 and 16 weeks), enabling assessment of how discrimination evolves over the treatment course and supporting dynamic risk stratification.

11.2. Strengths and limitations of the research methods

This study has several strengths. First, clinical trial datasets are generated under protocol-defined assessments and monitoring intended to support consistent, high-quality data collection[36]., Therefore, the TALAPRO-2 trial data serves as an ideal data source for developing model parameters as a preliminary step before assessing more heterogeneous real-world data in which relevant variables may not have been extracted or were not routinely collected. Second, the TALAPRO2 trial is still among the largest available datasets with talazoparib exposure and safety data given the recent approval of talazoparib for mCRPC at the time of study development. Real-world cohorts are still limited in sample size for talazoparib-treated patients at this time. Finally, the machine learning model approach is a strong methodologic approach selected for its ability to integrate complex, high-dimensional data and model nonlinear relationships and interactions with fewer prespecified assumptions than many traditional regression-based approaches[21,37].

Despite these strengths, several limitations should be considered. First, the study was conducted using data from a randomized clinical trial population and therefore may not be fully representative of broader patients with mCRPC treated in routine clinical practice. Trial participants were enrolled according to protocol-defined eligibility criteria and underwent protocol-specified monitoring, supportive care, and dose modification procedures. As a result, patient characteristics, frequency of laboratory assessments, and clinical management may differ from real-world settings, potentially affecting the transportability of the findings and prediction models beyond the trial setting. These differences may result in more complete ascertainment of predictor variables and anemia events than would occur in routine clinical practice. The direction and magnitude of any resulting bias on model performance or variable important in external populations cannot be quantified from the current study.

Second, although trial data are collected under procedures designed to promote completeness, it is still possible for some amount of missingness to occur due to skipped visits or labs[38]. Because the longitudinal model incorporates the most recently measured hemoglobin value, deviations from the protocol-specified laboratory assessment schedule may result in less current predictor information which could affect model performance. The availability and longitudinal measurement frequency of all laboratory variables used for the machine learning model were assessed. Although core hematology labs were measured at least once for nearly all patients and were generally collected longitudinally, other select laboratory variables (e.g. creatine kinase, blood urea nitrogen/urea, reticulocytes, erythropoietin, differential white blood cell components) were measured less frequently at baseline (37-89% of patients) and longitudinally. In this study, baseline labs with missingness <5% were treated as continuous predictor variables whereas baseline labs with missingness ≥5% were treated as binary predictor variables (available, not available) to allow the greatest retention of granularity for the former and cohort size for the latter. For the assessment of longitudinal predictors of anemia, it was necessary to develop a more flexible framework allowing for the assessment of hemoglobin values measured over time without dictating the specific dates that hemoglobin must have been measured. This resulted in an approach in which hemoglobin was treated as a time-updated longitudinal predictor, defined

as the most recent measurement available prior to each prediction. Although these approaches were implemented to mitigate the impact of missing data, residual bias or loss of precision related to incomplete laboratory measurements cannot be excluded. The direction and magnitude of any such impact are expected to vary by predictor and could not be directly quantified.

Third, while the assessment of a common condition in a sample size of the total study cohort of ~500 patients is “reasonably powered”[39], some subgroup/stratified analyses were expected to be limited in power for precise estimates. Notably, study objective 3 machine learning predictive modeling of anemia improvement following dose modification showed limited predictive performance, likely in part driven by small sample sizes resulting from subsetting the cohort to patients who experienced dose modification. Consequently, performance estimates for some subgroup analyses may be subject to greater variability and lower precision than estimates derived from the overall study population.

Fourth, the study focuses on predictive modeling using trial data, and as such, identified associations between predictors and outcomes should not be interpreted as causal relationships. The modeling approach is designed to optimize prediction accuracy rather than to estimate causal effects. Multiple analyses were performed to address distinct study objectives; however, these analyses were undertaken for predictive model development and evaluation rather than formal hypothesis testing, and therefore concerns regarding multiplicity were limited.

Finally, although internal validation techniques such as cross-validation were used to assess model performance within the study dataset, these approaches do not replace evaluation in independent datasets. Consequently, the generalizability and transportability of the prediction models remain uncertain until external validation is conducted in datasets that more closely reflect routine clinical practice. The direction and magnitude of any differences in model performance between the trial setting and external populations cannot be determined from the current study.

11.3. Interpretation

This analysis of TALAPRO-2 suggests that ML models can support individualized prediction of Grade ≥3 anemia during the early months of talazoparib treatment. Across the evaluated algorithms and feature sets, discrimination ranged from 0.62 to 0.99 by AUC using 3-fold cross-validation, indicating that severe anemia risk is, at least in part, predictable from routinely collected baseline characteristics and laboratory data. The most influential predictors in baseline models included older age, Asian race, and lower body weight, while longitudinal models additionally identified recent hemoglobin level as a key predictor.

From a clinical and risk-management perspective, these results support the feasibility of using predictive modeling to identify patients who may benefit from closer monitoring and earlier proactive anemia management (e.g., more frequent hemoglobin assessment, earlier supportive care consideration, including temporary dose modification), with the goal of reducing downstream consequences such as RBC transfusion requirement and permanent dose discontinuation resulting from poorly managed anemia. Importantly, the observation that the additional inclusion of recent hemoglobin measure as a longitudinal predictor further improved prediction accuracy indicates that dynamic, updated risk estimation may be more informative than baseline-only prediction.

While ML models can provide accurate prediction, the identified predictors reflect associations and should not be interpreted as causal. Because models were trained to maximize discrimination, they do not provide estimates of independent effects in the presence of correlated covariates. For instance, lower body weight and Asian race were both more frequent among patients with treatment-emergent Grade ≥3 anemia, but this study was not designed to quantify their independent contributions. However, the fact that both variables ranked among the most influential predictors in the final model suggests that each may contribute unique information for risk stratification, even if partially correlated.

This work is, to our knowledge, among the first to evaluate individual-level prediction models for severe anemia risk in the talazoparib setting and therefore direct comparison of predictive performance to prior talazoparib anemia prediction studies is not available. However, the directionality of several predictors is broadly concordant with not only prior clinical trial descriptive safety studies of talazoparib-treated mCRPC patients [29], but also more generally among PARP inhibitor-treated breast and ovarian cancer patients [28,30]. While this suggests that shared predictors may reflect biologically plausible correlates of hematologic vulnerability and PARP inhibitor tolerability, the relative importance of predictors and model performance should be confirmed through external validation in each disease setting and treatment context.

11.4. Generalizability

The generalizability of the prediction models developed in this study beyond the TALAPRO-2 population remains uncertain because external validation was not conducted. Assessment through internal cross-validation provides evidence of performance within the trial dataset but does not establish performance in independent populations. Several characteristics of the study setting may affect transportability to other populations and healthcare settings.

This analysis was conducted in a randomized clinical trial population with protocol-specified monitoring schedules, supportive care practices, and mandated dose modification rules for anemia, which differ from routine clinical practice. In real-world settings, visit frequency, laboratory monitoring, and clinical decision thresholds may vary substantially, resulting in differences in the availability and timing of predictor variables as well as the detection of anemia events. As a result, models developed using trial data may capture patterns partially driven by the structured nature of trial assessments and may perform differently when applied to real-world populations, where data are often more sparse, irregularly measured, and heterogeneous.

In addition, the trial population is defined by eligibility criteria related to performance status, organ function, and prior treatments, which may limit representativeness relative to broader mCRPC populations. Differences in patient characteristics, geographic distribution, and care delivery between trial and real-world settings may further affect the transportability of model predictions.

While internal validation approaches such as cross-validation provide an assessment of model performance within the trial dataset, such approaches do not evaluate generalizability to independent populations. Therefore, external validation in real-world datasets is necessary to provide an unbiased assessment of model performance, including discrimination and calibration, in settings that more closely reflect routine clinical practice. Evaluation across datasets with differing structures, patient populations, and care patterns

will be critical to establishing the robustness and transportability of the prediction models developed in this study.

12. OTHER INFORMATION

Not applicable

13. CONCLUSIONS

This secondary analysis of TALAPRO-2 data suggests that machine learning models can support individualized prediction of Grade ≥3 anemia during the early months of talazoparib treatment. Although performance varied across candidate algorithms, several models demonstrated strong discrimination, with LASSO achieving the highest AUCs across all evaluations in 3-fold cross-validation. For the first 8 weeks of talazoparib treatment, both baseline and longitudinal prediction models demonstrated excellent discrimination (AUCs 0.90–0.99). The preferred model depends on data availability, with longitudinal models favored when serial hemoglobin measurements are available. For weeks 8–16, longitudinal models demonstrated the strongest performance, achieving AUCs of 0.71–0.79. Lower AUC values (AUC < 0.70) reflect predictions over longer time horizons from baseline. The most influential predictors in baseline models included older age, lower body weight, RBC, and hemoglobin, while longitudinal models additionally identified recent hemoglobin level as a key predictor. Overall, these findings indicate that severe anemia risk is, at least in part, predictable from routinely collected baseline characteristics and laboratory data, and may complement existing label-recommended monitoring by identifying higher-risk patients earlier and supporting more individualized anemia management strategies.

There is no direct impact of the results on the risk-benefit balance of the product. Rather, the results provide additional evidence on the feasibility of individualized, time-specific anemia risk stratification in talazoparib-treated mCRPC patients, which may help inform future clinical monitoring and proactive supportive care strategies such as more frequent laboratory surveillance and earlier anemia management to mitigate severe anemia risk and treatment interruptions.

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15. LIST OF SOURCE TABLES AND FIGURES

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