Clinical trial results:
A PHASE 1B/2 OPEN-LABEL STUDY EVALUATING TAZEMETOSTAT IN COMBINATION WITH ENZALUTAMIDE OR ABIRATERONE/PREDNISONE IN CHEMOTHERAPY NAIVE SUBJECTS WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER

Summary

EudraCT number	2019-003649-14
Trial protocol	BE
Global end of trial date	04 November 2024

Results information

Result version number	v1
This version publication date	19 November 2025
First version publication date	19 November 2025

Trial information

Trial identification

Sponsor protocol code	EZH-1101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04179864
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 143032

Notes:

Sponsors

Sponsor organisation name	Epizyme, Inc.
Sponsor organisation address	400 Technology Square, 4th Floor, Cambridge, MA, United States, 02139
Public contact	Medical Director, Ipsen, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen, clinical.trials@ipsen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 November 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 November 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase Ib: To determine the safety and tolerability of each of the combinations (tazemetostat with enzalutamide or tazemetostat with abiraterone/prednisone); To select the recommended phase 2 doses (RP2Ds) of tazemetostat for each combination treatment based on pharmacokinetic (PK) and pharmacodynamic (PD) parameters as well as efficacy and the overall tolerability of each of the combinations (tazemetostat with enzalutamide or tazemetostat with abiraterone/prednisone).
Phase II: To determine the benefit of combining tazemetostat with enzalutamide when compared to enzalutamide monotherapy, as assessed by radiographic progression-free survival (rPFS) according to Prostate Cancer Clinical Trials Working Group 3 (PCWG3) criteria for progression in bone or in soft tissue (the latter by Response Evaluation Criteria in Solid Tumours 1.1 [RECIST 1.1]).

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, following the International Conference on Harmonisation (ICH) Consolidated Guideline on Good Clinical Practice (GCP) and in compliance with IECs/IRBs, informed consent regulations and the sponsor's policy on bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	United States: 84
Worldwide total number of subjects	102
EEA total number of subjects	18

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	29
From 65 to 84 years	69
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

This Phase 1b/2, 2-part, open-label study was conducted at 21 sites in asymptomatic or mildly symptomatic participants with progressive, metastatic castration resistant prostate cancer (mCRPC).

Pre-assignment

Screening details:

The study consisted of 2 parts: Phase 1b (dose-escalation) and Phase 2 (randomized). The study was terminated early as Sponsor decided to discontinue the development of tazemetostat in mCRPC and the primary endpoint was not met for this study. There were no safety concerns.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1b: Tazemetostat 400 mg + Enzalutamide

Arm description:

Participants received tazemetostat 400 milligrams (mg) tablet orally twice daily (BID) from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally once daily (OD) from Cycle 1 Day 1 until death, disease progression (PD), development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received tazemetostat 400 mg tablet orally BID in continuous 28-day cycles.

Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received enzalutamide 160 mg capsule orally OD in continuous 28-day cycles.

Arm title	Phase 1b: Tazemetostat 600 mg + Enzalutamide

Arm description:

Participants received tazemetostat 600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received tazemetostat 600 mg tablet orally BID in continuous 28-day cycles.

Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received enzalutamide 160 mg capsule orally OD in continuous 28-day cycles.

Arm title	Phase 1b: Tazemetostat 800 mg + Enzalutamide

Arm description:

Participants received tazemetostat 800 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received tazemetostat 800 mg tablet orally BID in continuous 28-day cycles.

Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received enzalutamide 160 mg capsule orally OD in continuous 28-day cycles.

Arm title	Phase 1b: Tazemetostat 1200 mg + Enzalutamide

Arm description:

Participants received tazemetostat 1200 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received tazemetostat 1200 mg tablet orally BID in continuous 28-day cycles.

Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received enzalutamide 160 mg capsule orally OD in continuous 28-day cycles.

Arm title	Phase 1b: Tazemetostat 1600 mg + Enzalutamide

Arm description:

Participants received tazemetostat 1600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160

mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received tazemetostat 1600 mg tablet orally BID in continuous 28-day cycles.

Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received enzalutamide 160 mg capsule orally OD in continuous 28-day cycles.

Arm title	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone

Arm description:

Participants received tazemetostat 400 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received tazemetostat 400 mg tablet orally BID in continuous 28-day cycles.

Investigational medicinal product name	Abiraterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received abiraterone 1000 mg tablet orally OD in continuous 28-day cycles.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received prednisone 5 mg tablet orally BID in continuous 28-day cycles.

Arm title	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone

Arm description:

Participants received tazemetostat 600 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental

Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received tazemetostat 600 mg tablet orally BID in continuous 28-day cycles.

Investigational medicinal product name	Abiraterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received abiraterone 1000 mg tablet orally OD in continuous 28-day cycles.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received prednisone 5 mg tablet orally BID in continuous 28-day cycles.

Arm title	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone

Arm description:

Participants received tazemetostat 800 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received tazemetostat 800 mg tablet orally BID in continuous 28-day cycles.

Investigational medicinal product name	Abiraterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received abiraterone 1000 mg tablet orally OD in continuous 28-day cycles.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received prednisone 5 mg tablet orally BID in continuous 28-day cycles.

Arm title	Phase 2: Tazemetostat 1200 mg + Enzalutamide

Arm description:

Participants received tazemetostat 1200 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160

mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental
Investigational medicinal product name	Tazemetostat
Investigational medicinal product code	EPZ-6438
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received tazemetostat 1200 mg tablet orally BID in continuous 28-day cycles.

Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received enzalutamide 160 mg capsule orally OD in continuous 28-day cycles.

Arm title	Phase 2: Enzalutamide

Arm description:

Participants received enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Arm type	Experimental
Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received enzalutamide 160 mg capsule orally OD in continuous 28-day cycles.

Number of subjects in period 1	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide
Started	2	3	3
Completed	0	0	0
Not completed	2	3	3
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	1	-	-
Non- Compliance With Study Drug	-	-	-
Death	-	-	-
Progressive Disease	1	3	3
Study Terminated by Sponsor	-	-	-
Sponsor Request	-	-	-

Number of subjects in period 1	Phase 1b:	Phase 1b:	Phase 1b:

	Tazemetostat 1200 mg + Enzalutamide	Tazemetostat 1600 mg + Enzalutamide	Tazemetostat 400 mg + Abiraterone/prednisone
Started	3	3	1
Completed	0	0	0
Not completed	3	3	1
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	-	-	-
Non- Compliance With Study Drug	-	-	-
Death	-	-	-
Progressive Disease	3	2	1
Study Terminated by Sponsor	-	-	-
Sponsor Request	-	1	-

Number of subjects in period 1	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide
Started	3	3	41
Completed	0	0	0
Not completed	3	3	41
Consent withdrawn by subject	-	-	5
Physician decision	-	-	1
Adverse event, non-fatal	-	-	3
Non- Compliance With Study Drug	-	-	1
Death	-	-	-
Progressive Disease	3	3	28
Study Terminated by Sponsor	-	-	3
Sponsor Request	-	-	-

Number of subjects in period 1	Phase 2: Enzalutamide
Started	40
Completed	0
Not completed	40
Consent withdrawn by subject	5
Physician decision	2
Adverse event, non-fatal	1
Non- Compliance With Study Drug	-
Death	2
Progressive Disease	28
Study Terminated by Sponsor	2
Sponsor Request	-

Reporting groups

Reporting group title	Phase 1b: Tazemetostat 400 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 400 milligrams (mg) tablet orally twice daily (BID) from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally once daily (OD) from Cycle 1 Day 1 until death, disease progression (PD), development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 600 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 800 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 800 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 1200 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 1200 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 1600 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 1600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone

Reporting group description:

Participants received tazemetostat 400 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone

Reporting group description:

Participants received tazemetostat 600 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone

Reporting group description:

Participants received tazemetostat 800 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 2: Tazemetostat 1200 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 1200 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 2: Enzalutamide

Reporting group description:

Participants received enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group values	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide
Number of subjects	2	3	3
Age categorical Units: Subjects			
<65 years	0	1	2
>=65 years	2	2	1
Gender categorical Units: Subjects			
Female	0	0	0
Male	2	3	3
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	2	2	3
Unknown or Not Reported	0	0	0
Race Units: Subjects			
Black or African American	0	0	1
White	2	3	2
Unknown or Not Reported	0	0	0

Reporting group values	Phase 1b: Tazemetostat 1200 mg + Enzalutamide	Phase 1b: Tazemetostat 1600 mg + Enzalutamide	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone
Number of subjects	3	3	1
Age categorical Units: Subjects			
<65 years	0	2	0
>=65 years	3	1	1
Gender categorical Units: Subjects			
Female	0	0	0
Male	3	3	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	2	2	0
Unknown or Not Reported	1	0	0
Race Units: Subjects			
Black or African American	0	0	0
White	3	3	1
Unknown or Not Reported	0	0	0

Reporting group values	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednis	Phase 1b: Tazemetostat 800 mg + Abiraterone/predniso	Phase 2: Tazemetostat 1200 mg + Enzalutamide

	one	ne	
Number of subjects	3	3	41
Age categorical Units: Subjects			
<65 years	1	0	12
>=65 years	2	3	29
Gender categorical Units: Subjects			
Female	0	0	0
Male	3	3	41
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	5
Not Hispanic or Latino	3	2	35
Unknown or Not Reported	0	0	1
Race Units: Subjects			
Black or African American	0	0	0
White	3	3	35
Unknown or Not Reported	0	0	6

Reporting group values	Phase 2: Enzalutamide	Total	
Number of subjects	40	102	
Age categorical Units: Subjects			
<65 years	11	29	
>=65 years	29	73	
Gender categorical Units: Subjects			
Female	0	0	
Male	40	102	
Ethnicity Units: Subjects			
Hispanic or Latino	3	12	
Not Hispanic or Latino	33	84	
Unknown or Not Reported	4	6	
Race Units: Subjects			
Black or African American	6	7	
White	31	86	
Unknown or Not Reported	3	9	

End points reporting groups

Reporting group title	Phase 1b: Tazemetostat 400 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 400 milligrams (mg) tablet orally twice daily (BID) from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally once daily (OD) from Cycle 1 Day 1 until death, disease progression (PD), development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 600 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 800 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 800 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 1200 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 1200 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 1600 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 1600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone

Reporting group description:

Participants received tazemetostat 400 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone

Reporting group description:

Participants received tazemetostat 600 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone

Reporting group description:

Participants received tazemetostat 800 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 2: Tazemetostat 1200 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 1200 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 2: Enzalutamide

Reporting group description:

Participants received enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Subject analysis set title	Phase 1b: Tazemetostat Dose-escalation
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received tazemetostat 400 mg, 600 mg, 800 mg, 1200 mg and 1600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1; Participants received tazemetostat 400 mg, 600 mg and 800 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Subject analysis set title	Phase 1b: Tazemetostat + Enzalutamide
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received tazemetostat 400 mg, 600 mg, 800 mg, 1200 mg and 1600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Subject analysis set title	Phase 1b: Tazemetostat + Abiraterone/prednisone
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received tazemetostat 400 mg, 600 mg and 800 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Subject analysis set title	Phase 2: Tazemetostat 1200 mg + Enzalutamide
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received tazemetostat 1200 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Subject analysis set title	Phase 2: Enzalutamide
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Primary: Phase 1b: Number of Participants With Treatment-Emergent non-Serious Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Phase 1b: Number of Participants With Treatment-Emergent non-Serious Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)[1][2]

End point description:

AE:untoward medical occurrence in a participant or clinical investigation participant administered a medicinal product and which did not necessarily had a causal relationship with this study drug. SAE: AE which occurred during any study phase and at any dose of study drug, that fulfilled 1 or more of following:resulted in death,was life-threatening,required hospitalization or prolongation of existing hospitalization,resulted in disability or incapacity,was a congenital abnormality or birth defect,or was an important medical event that might jeopardize participant or might require medical intervention to prevent one of outcomes listed above.TEAEs:AEs that started or worsened in severity on or after date of first dose of study drug through 30 after end of study drug, or prior to initiation of another investigational agent or cytotoxic chemotherapy. Safety population:all participants who received any dose of study drugs. TE non-serious AEs are presented with a frequency threshold of 5%.

End point type	Primary

End point timeframe:

From first dose of study drug (Day 1) up to either 30 days after last dose of study drug or until the initiation of subsequent anticancer therapy or end of treatment visit. Assessed up to 149 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was reported.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 1b arms.

End point values	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide	Phase 1b: Tazemetostat 1200 mg + Enzalutamide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	3	3
Units: participants				
Treatment-emergent non-serious AEs	2	3	3	3
TESAEs	0	1	0	0

End point values	Phase 1b: Tazemetostat 1600 mg + Enzalutamide	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	1	3	3
Units: participants				
Treatment-emergent non-serious AEs	3	1	3	3
TESAEs	2	0	1	1

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1b: Recommended Phase 2 Dose of Tazemetostat

End point title	Phase 1b: Recommended Phase 2 Dose of Tazemetostat[3]

End point description:

RP2D was based on PK parameters, PD parameters as well as efficacy and the overall tolerability of each combination (tazemetost with enzalutamide or tazemetostat with abiraterone/prednisone). The safety population included all participants who received any dose of the study drugs.

End point type	Primary

End point timeframe:

From Day 1 up to Day 28 of Cycle 1 (each cycle was 28 days)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Phase 1b: Tazemetostat Dose-escalation			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: mg				
number (not applicable)	1200			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Radiographic Progression-Free Survival

End point title	Phase 2: Radiographic Progression-Free Survival[4][5]

End point description:

rPFS was defined as the time from date of randomization (phase 2)/date of first dose of study drug (phase 1b) to the first objective evidence of radiographic progression using RECIST 1.1 (soft tissue) and PCWG3 (bone), or death from any cause, whichever occurred first. The radiographic PD for soft tissue lesion was determined based on computed tomography (CT) or magnetic resonance imaging (MRI) per RECIST 1.1 criteria and no confirmatory scan was required for soft tissue PD; for bone lesion was determined by 2 or more new bone lesions on bone scan per PCWG3 criteria (i.e., the appearance of 2 or more new bone lesions on bone scan) and the 2 scans (i.e., the confirmatory scan is required for bone disease progression) should be at least 6 weeks apart from each other. The intent-to-treat (ITT) population included all participants who were randomized into the study.

End point type	Primary

End point timeframe:

Assessments performed at screening (within 4 weeks of randomization) and every 8 weeks for first 6 months and then every 12 weeks thereafter, until death, PD, unacceptable toxicity, consent withdrawal, or termination of study. Approximately 200 weeks

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was reported.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 2 arms.

End point values	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	40		
Units: months				
median (confidence interval 95%)	22.1 (16.6 to 27.6)	11.1 (5.7 to 16.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and 2: Percentage of Participants With Confirmed Prostate-Specific Antigen >=50% (PSA50) Response

End point title	Phase 1b and 2: Percentage of Participants With Confirmed Prostate-Specific Antigen >=50% (PSA50) Response

End point description:

Blood samples were collected for evaluation of PSA. Confirmed PSA50 response was defined as >=50% decline of PSA from baseline at any time on study for participants with a baseline PSA >=1.0 microgram per liter (mcg/L) (nanogram/milliliter [ng/mL]) per PCWG3 criteria. Baseline was defined as: Phase 1b: last value recorded for a variable prior to or on the date the participant received the first dose of study drug; Phase 2: last value recorded for a variable prior to or on the date of randomization. Phase 1b: The safety population included all participants who received any dose of the study drugs. Phase 2: The ITT population included all participants who were randomized into the study.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 (Baseline) up to either 30 days after last dose of study drug or until initiation of subsequent anticancer therapy or end of treatment visit. Assessed up to 149 weeks and 191 weeks for Phase 1b and Phase 2 respectively

End point values	Phase 1b: Tazemetostat + Enzalutamide	Phase 1b: Tazemetostat + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	7	41	40
Units: percentage of participants				
number (confidence interval 95%)	28.6 (8.39 to 58.10)	14.3 (0.36 to 57.87)	19.5 (8.82 to 34.87)	15.0 (5.71 to 29.84)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and 2: Objective Response Rate (ORR)

End point title	Phase 1b and 2: Objective Response Rate (ORR)

End point description:

ORR was defined as the percentage of participants with complete response (CR) or partial response (PR). CR was defined as disappearance of all target lesions, any pathological lymph nodes (LN) must be <10 millimeter (mm) in the short axis. PR was defined as at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference, the baseline sum of the diameters. Phase 1b: The safety population included all participants who received any dose of the study drugs. Phase 2: The ITT population included all participants who were randomized into the study. Only those participants with response are reported.

End point type	Secondary

End point timeframe:

Tumor assessments performed at screening (within 4 weeks of randomization) and every 8 weeks for first 6 months and then every 12 weeks thereafter, until death, PD, unacceptable toxicity, consent withdrawal, or termination of study.Approximately 259 weeks

End point values	Phase 1b: Tazemetostat + Enzalutamide	Phase 1b: Tazemetostat + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	1	10	14
Units: percentage of participants				
number (confidence interval 95%)	16.7 (0.42 to 64.12)	0.0 (0 to 97.50)	10.0 (0.25 to 44.50)	0.0 (0 to 23.16)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and 2: Best Overall Response (BOR)

End point title	Phase 1b and 2: Best Overall Response (BOR)

End point description:

BOR was defined as percentage of participants with CR, PR, stable disease (SD), PD, or not evaluable (NE). CR was defined as disappearance of all target lesions, any pathological LN must be <10 mm in the short axis. PR: at least a 30% decrease in the sum of diameters of target lesions, taking as a reference, baseline sum of diameters. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. PD: at least a 20% increase in the sum of diameters of target lesions, taking as a reference, smallest sum of diameters recorded since the drug started. In addition, sum had an absolute increase from nadir of 5 mm. NE: which cannot be classified by 1 of above preceding definitions. Phase 1b: safety population: all participants who received any dose of the study drugs. Phase 2: ITT population: all participants who were randomized into study. Only those participants with response are reported. Percentages are rounded off to the tenth decimal place.

End point type	Secondary

End point timeframe:

Tumor assessments performed at screening (within 4 weeks of randomization) and every 8 weeks for first 6 months and then every 12 weeks thereafter, until death, PD, unacceptable toxicity, consent withdrawal, or termination of study.Approximately 259 weeks

End point values	Phase 1b: Tazemetostat + Enzalutamide	Phase 1b: Tazemetostat + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	1	10	14
Units: percentage of participants				
number (not applicable)				
Complete response	0.0	0.0	0.0	0.0
Partial response	16.7	0.0	10.0	0.0
Stable disease	66.7	100.0	70.0	57.1
Progressive disease	16.7	0.0	20.0	35.7
Not evaluable	0.0	0.0	0.0	7.1

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and 2: Disease Control Rate (DCR) at 6 Months

End point title	Phase 1b and 2: Disease Control Rate (DCR) at 6 Months

End point description:

DCR at 6 months (24 weeks) was defined as percentage of participants with measurable soft tissue disease at baseline who had BOR of CR or PR and remaining on study without progression at 23 weeks or with a duration of SD for at least 23 weeks after of randomization (phase 2)/first dose (phase 1b) using overall imaging-based response assessed by RECIST 1.1 (soft tissue) and PCWG-3 criteria (bone). BOR:percentage of participants with CR, PR, SD, PD, or NE.CR: disappearance of all target lesions,any pathological LN must be <10 mm in the short axis.PR:at least a 30% decrease in sum of diameters of target lesions, taking as a reference, baseline sum of diameters.SD:neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.PD:at least a 20% increase in sum of diameters of target lesions,taking as a reference, smallest sum of diameters recorded since the drug started.In addition, sum had an absolute increase from nadir of 5 mm. Phase 1b: safety, Phase 2: ITT.

End point type	Secondary

End point timeframe:

Baseline and at 6 months (24 weeks)

End point values	Phase 1b: Tazemetostat + Enzalutamide	Phase 1b: Tazemetostat + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	1	10	14
Units: percentage of participants				
number (confidence interval 95%)	50.0 (11.81 to 88.19)	100.0 (2.50 to 100)	40.0 (40.0 to 73.76)	21.4 (4.66 to 50.80)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and 2: Time to First Skeletal-Related Event (SRE) Per Prostate Cancer Clinical Trials Working Group 3 Criteria

End point title	Phase 1b and 2: Time to First Skeletal-Related Event (SRE) Per Prostate Cancer Clinical Trials Working Group 3 Criteria

End point description:

Time to first SRE per PCWG3 criteria was defined as the time from the date of randomization (phase II)/date of the first dose of study drug (phase Ib) to the date of first SRE. An SRE was defined as radiation therapy or surgery to bone, pathologic bone fracture, or spinal cord compression. Phase 1b: The safety population included all participants who received any dose of the study drugs. Phase 2: The ITT population included all participants who were randomized into the study. Only those participants with confirmed SRE event are reported. "9999": indicates that the values were not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of study drug (Phase 1b) and randomization (Phase 2) (Day 1) up to approximately 259 weeks

End point values	Phase 1b: Tazemetostat + Enzalutamide	Phase 1b: Tazemetostat + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	3	7	9
Units: months				
median (confidence interval 95%)	16.2 (4.4 to 9999)	26.3 (4.0 to 9999)	9999 (16.9 to 9999)	9999 (9.0 to 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and 2: Time to Initiation of the Next Systemic Treatment (TTNT) for Prostate Cancer

End point title	Phase 1b and 2: Time to Initiation of the Next Systemic Treatment (TTNT) for Prostate Cancer

End point description:

TTNT was defined as the time from the date of randomization (phase II)/date of the first dose of the study drug (phase Ib) to the date of the first documented administration of systemic treatment for prostate cancer. Phase 1b: The safety population included all participants who received any dose of the study drugs. Phase 2: The ITT population included all participants who were randomized into the study. Only those participants who initiated the next systemic treatment are reported. "9999": indicates that the values were not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of study drug (Phase 1b) and randomization (Phase 2) (Day 1) up to approximately 259 weeks

End point values	Phase 1b: Tazemetostat + Enzalutamide	Phase 1b: Tazemetostat + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	5	27	21
Units: months				
median (confidence interval 95%)	8.2 (2.6 to 13.9)	13.4 (5.4 to 9999)	9.0 (6.5 to 17.0)	10.6 (5.0 to 15.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and 2: Time to Prostate-Specific Antigen Progression (TTPP)

End point title	Phase 1b and 2: Time to Prostate-Specific Antigen Progression (TTPP)

End point description:

TTPP was defined as the duration from the date of randomization (phase II)/date of first dose of study drug (phase Ib) to the date of first PSA progression per PCWG3 criteria. PSA progression was defined as a >=25% increase and an absolute increase of >=2 mcg/L (2 ng/mL) above the nadir (or baseline value for participants who did not have a decline in PSA value beyond 12 weeks). Baseline was defined as: Phase 1b: last value recorded for a variable prior to or on the date the participant received the first dose of study drug; Phase 2: last value recorded for a variable prior to or on the date of randomization. Phase 1b: The safety population included all participants who received any dose of the study drugs. Phase 2: The ITT population included all participants who were randomized into the study. Only those participants with confirmed PSA progression are reported.

End point type	Secondary

End point timeframe:

From first dose of study drug (Phase 1b) and randomization (Phase 2) (Day 1) up to approximately 259 weeks

End point values	Phase 1b: Tazemetostat + Enzalutamide	Phase 1b: Tazemetostat + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	7	26	25
Units: months				
median (confidence interval 95%)	4.6 (2.1 to 8.3)	2.8 (2.8 to 4.6)	4.6 (3.3 to 11.1)	3.0 (2.8 to 5.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and 2: Percentage of Participants With Reduction in Circulating Tumor Cells (CTC)

End point title	Phase 1b and 2: Percentage of Participants With Reduction in Circulating Tumor Cells (CTC)

End point description:

Blood samples were collected for evaluation of CTC. Reduction in CTC was defined as participants from a state of having a detectable number of CTCs to having an undetectable number of CTCs. Percentage of participants with detectable CTC at baseline and non-detectable CTC are presented. Baseline was defined as: Phase 1b: last value recorded for a variable prior to or on the date the participant received the first dose of study drug; Phase 2: last value recorded for a variable prior to or on the date of randomization. Phase 1b: The safety population included all participants who received any dose of the study drugs. Phase 2: The ITT population included all participants who were randomized into the study.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 (Baseline) up to either 30 days after last dose of study drug or until initiation of subsequent anticancer therapy or end of treatment visit. Assessed up to 149 weeks and 191 weeks for Phase 1b and Phase 2 respectively

End point values	Phase 1b: Tazemetostat + Enzalutamide	Phase 1b: Tazemetostat + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	7	41	40
Units: percentage of participants				
number (not applicable)				
Detectable CTC at baseline	64.3	100.0	36.6	52.5
Non-detectable CTC	35.7	0.0	63.4	47.5

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and 2: Percentage of Participants With Circulating Tumor Cells Response

End point title	Phase 1b and 2: Percentage of Participants With Circulating Tumor Cells Response

End point description:

Blood samples were collected for evaluation of CTC. CTC response was defined as a >=30% reduction in CTC number from baseline in participants who entered the study. Baseline was defined as: Phase 1b: last value recorded for a variable prior to or on the date the participant received the first dose of study drug; Phase 2: last value recorded for a variable prior to or on the date of randomization. Phase 1b: The safety population included all participants who received any dose of the study drugs. Phase 2: The ITT population included all participants who were randomized into the study.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 (Baseline) up to either 30 days after last dose of study drug or until initiation of subsequent anticancer therapy or end of treatment visit. Assessed up to 149 weeks and 191 weeks for Phase 1b and Phase 2 respectively

End point values	Phase 1b: Tazemetostat + Enzalutamide	Phase 1b: Tazemetostat + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	7	41	40
Units: percentage of participants				
number (confidence interval 95%)	88.9 (51.75 to 99.72)	100.0 (59.04 to 100.00)	80.0 (51.91 to 95.67)	42.9 (21.82 to 65.98)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Participants With Treatment-Emergent non-Serious Adverse Events and Treatment-Emergent Serious Adverse Events

End point title	Phase 2: Number of Participants With Treatment-Emergent non-Serious Adverse Events and Treatment-Emergent Serious Adverse Events[6]

End point description:

AE:any untoward medical occurrence in a participant or clinical investigation participant administered a medicinal product and which did not necessarily had a causal relationship with this study drug. SAE:AE which occurred during any study phase and at any dose of the study drug,that fulfilled 1 or more of following:resulted in death,was life-threatening,required hospitalization or prolongation of existing hospitalization,resulted in disability or incapacity,was a congenital abnormality or birth defect,or was an important medical event that might jeopardize participant or might require medical intervention to prevent one of outcomes listed above.TEAEs:AEs that started or worsened in severity on or after date of first dose of study drug through 30 after end of study drug,or prior to initiation of another investigational agent or cytotoxic chemotherapy.Safety population:all participants who received any dose of study drugs.TE non-serious AEs are presented with frequency threshold of 5%.

End point type	Secondary

End point timeframe:

From first dose of study drug (Day 1) up to either 30 days after last dose of study drug or until the initiation of subsequent anticancer therapy or end of treatment visit. Assessed up to 191 weeks

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The endpoint was evaluated for only Phase 2 arms.

End point values	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	40		
Units: participants				
Treatment-emergent non-serious AEs	41	39		
TESAEs	13	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Tazemetostat

End point title	Phase 1b: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Tazemetostat[7]

End point description:

Blood samples were collected at specified timepoints for the assessment of AUC0-last of tazemetostat. The PK population included all participants in the safety population who had at least 1 post-dose sample collected to allow estimation of the PK parameters. Only those participants with data collected at specified timepoints are reported. Here, n= number of participants analyzed for specified category. "9999": indicates that the values were not estimable as they were below the lower limit of quantification (LLOQ) of 1.00 ng/mL.

End point type	Secondary

End point timeframe:

Cycle 1 Days 2 and 21 (each cycle was 28 days)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 1b arms.

End point values	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide	Phase 1b: Tazemetostat 1200 mg + Enzalutamide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	3	3
Units: hour*nanograms per milliliter (ng/ mL)				
arithmetic mean (standard deviation)				
Cycle 1 Day 2 (n=2, 3, 3, 3, 3, 1, 3, 3)	1640 (± 150)	3350 (± 2020)	2860 (± 866)	7060 (± 1580)
Cycle 1 Day 21 (n=1, 3, 3, 3, 3, 1, 3, 3)	9999 (± 9999)	1230 (± 168)	1490 (± 606)	2800 (± 2020)

End point values	Phase 1b: Tazemetostat 1600 mg + Enzalutamide	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	1	3	3
Units: hour*nanograms per milliliter (ng/ mL)				
arithmetic mean (standard deviation)				
Cycle 1 Day 2 (n=2, 3, 3, 3, 3, 1, 3, 3)	6830 (± 5880)	9999 (± 9999)	3480 (± 2990)	4380 (± 4680)
Cycle 1 Day 21 (n=1, 3, 3, 3, 3, 1, 3, 3)	1120 (± 620)	9999 (± 9999)	2290 (± 1100)	3500 (± 1570)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Maximum Plasma Concentration (Cmax) of Tazemetostat

End point title	Phase 1b: Maximum Plasma Concentration (Cmax) of Tazemetostat[8]

End point description:

Blood samples were collected at specified timepoints for the assessment of Cmax of tazemetostat. The PK population included all participants in the safety population who had at least 1 post-dose sample collected to allow estimation of the PK parameters. Only those participants with data collected at specified timepoints are reported. Here, n= number of participants analyzed for specified category. "9999": indicates that the values were not estimable as they were below the LLOQ of 1.00 ng/mL.

End point type	Secondary

End point timeframe:

Cycle 1 Days 2 and 21 (each cycle was 28 days)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 1b arms.

End point values	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide	Phase 1b: Tazemetostat 1200 mg + Enzalutamide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	3	3
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 2 (n=2, 3, 3, 3, 3, 1, 3, 3)	341 (± 69.3)	911 (± 609)	888 (± 97.8)	1470 (± 217)
Cycle 1 Day 21 (n=1, 3, 3, 3, 3, 1, 3, 3)	9999 (± 9999)	364 (± 36.8)	530 (± 436)	568 (± 341)

End point values	Phase 1b: Tazemetostat 1600 mg + Enzalutamide	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	1	3	3
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 2 (n=2, 3, 3, 3, 3, 1, 3, 3)	1730 (± 1100)	9999 (± 9999)	851 (± 348)	1060 (± 916)
Cycle 1 Day 21 (n=1, 3, 3, 3, 3, 1, 3, 3)	254 (± 118)	9999 (± 9999)	810 (± 327)	1140 (± 646)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of 8 Hours Post-Dose (AUC0-8) of Tazemetostat

End point title	Phase 1b: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of 8 Hours Post-Dose (AUC0-8) of Tazemetostat[9]

End point description:

Blood samples were collected at specified timepoints for the assessment of AUC0-8 of tazemetostat. The PK population included all participants in the safety population who had at least 1 post-dose sample collected to allow estimation of the PK parameters. Only those participants with data collected at specified timepoints are reported. Here, n= number of participants analyzed for specified category. "9999": indicates that the values were not estimable as they were below the LLOQ of 1.00 ng/mL.

End point type	Secondary

End point timeframe:

8 hours post-dose on Cycle 1 Days 2 and 21 (each cycle was 28 days)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 1b arms.

End point values	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide	Phase 1b: Tazemetostat 1200 mg + Enzalutamide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	3	3
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 2 (n=2, 3, 3, 3, 3, 1, 3, 3)	1240 (± 705)	3350 (± 2020)	2860 (± 866)	7060 (± 1580)
Cycle 1 Day 21 (n=1, 3, 3, 2, 2, 1, 2, 3)	9999 (± 9999)	1230 (± 168)	1490 (± 606)	3770 (± 1590)

End point values	Phase 1b: Tazemetostat 1600 mg + Enzalutamide	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	1	3	3
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 2 (n=2, 3, 3, 3, 3, 1, 3, 3)	6830 (± 5880)	9999 (± 9999)	3130 (± 2390)	4380 (± 4680)
Cycle 1 Day 21 (n=1, 3, 3, 2, 2, 1, 2, 3)	1440 (± 310)	9999 (± 9999)	2280 (± 1560)	3500 (± 1570)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of 12 Hours Post-Dose (AUC0-12) of Tazemetostat

End point title	Phase 1b: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of 12 Hours Post-Dose (AUC0-12) of Tazemetostat[10]

End point description:

Blood samples were collected at specified timepoints for the assessment of AUC0-12 of tazemetostat. The PK population included all participants in the safety population who had at least 1 post-dose sample collected to allow estimation of the PK parameters. Only those participants with data collected at specified timepoints are reported. Here, n= number of participants analyzed for specified category. "9999": indicates that the values were not estimable as they were below the LLOQ of 1.00 ng/mL. "99999": indicates that no participants were analyzed for that category.

End point type	Secondary

End point timeframe:

12 hours post-dose on Cycle 1 Days 2 and 21 (each cycle was 28 days)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 1b arms.

End point values	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide	Phase 1b: Tazemetostat 1200 mg + Enzalutamide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	2	1
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 2 (n=1, 0, 1, 1, 1, 1, 2, 1)	9999 (± 9999)	99999 (± 99999)	9999 (± 9999)	9999 (± 9999)
Cycle 1 Day 21 (n=0, 2, 2, 0, 0, 1, 1, 0)	99999 (± 99999)	1300 (± 121)	1800 (± 863)	99999 (± 99999)

End point values	Phase 1b: Tazemetostat 1600 mg + Enzalutamide	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	2	1
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 2 (n=1, 0, 1, 1, 1, 1, 2, 1)	9999 (± 9999)	9999 (± 9999)	4480 (± 3460)	9999 (± 9999)
Cycle 1 Day 21 (n=0, 2, 2, 0, 0, 1, 1, 0)	99999 (± 99999)	9999 (± 9999)	9999 (± 9999)	99999 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of 24 Hours Post-Dose (AUC0-24) of Enzalutamide

End point title	Phase 1b: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of 24 Hours Post-Dose (AUC0-24) of Enzalutamide[11]

End point description:

Blood samples were collected at specified timepoints for the assessment of AUC0-24 of enzalutamide. The PK population included all participants in the safety population who had at least 1 post-dose sample collected to allow estimation of the PK parameters. Only those participants with data collected at specified timepoints are reported. Here, n= number of participants analyzed for specified category. "9999": indicates that the values were not estimable as they were below the LLOQ of 1.00 ng/mL.

End point type	Secondary

End point timeframe:

24 hours post-dose on Cycle 1 Days 1, 2 and 21 (each cycle was 28 days)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 1b arms.

End point values	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide	Phase 1b: Tazemetostat 1200 mg + Enzalutamide
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	3	3
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=1, 3, 3, 3, 3)	9999 (± 9999)	33000 (± 15600)	28800 (± 5780)	36800 (± 6440)
Cycle 1 Day 2 (n=2, 3, 3, 3, 3)	56700 (± 7900)	57700 (± 30100)	57400 (± 18400)	66800 (± 10500)
Cycle 1 Day 21 (n=1, 3, 3, 3, 3)	9999 (± 9999)	272000 (± 106000)	263000 (± 50400)	251000 (± 47400)

End point values	Phase 1b: Tazemetostat 1600 mg + Enzalutamide			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=1, 3, 3, 3, 3)	27500 (± 5270)			
Cycle 1 Day 2 (n=2, 3, 3, 3, 3)	60300 (± 19900)			
Cycle 1 Day 21 (n=1, 3, 3, 3, 3)	199000 (± 30800)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Maximum Plasma Concentration of Enzalutamide

End point title	Phase 2: Maximum Plasma Concentration of Enzalutamide[12]

End point description:

Blood samples were collected at specified timepoints for the assessment of Cmax of enzalutamide. The PK population included all participants in the safety population who had at least 1 post-dose sample collected to allow estimation of the PK parameters. Only those participants with data collected at specified timepoints are reported. Here, n= number of participants analyzed for specified category. "99999": indicates that no participants were analyzed for that category.

End point type	Secondary

End point timeframe:

Cycle 1 Days 1, 2 and 21 (each cycle was 28 days)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 2 arms.

End point values	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=0, 14)	99999 (± 99999)	3000 (± 577)		
Cycle 1 Day 2 (n=14, 0)	3960 (± 773)	99999 (± 99999)		
Cycle 1 Day 21 (n=13, 0)	12100 (± 3080)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of the Last Quantifiable Concentration of Enzalutamide

End point title	Phase 2: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of the Last Quantifiable Concentration of Enzalutamide[13]

End point description:

Blood samples were collected at specified timepoints for the assessment of AUC0-last of enzalutamide. The PK population included all participants in the safety population who had at least 1 post-dose sample collected to allow estimation of the PK parameters. Only those participants with data collected at specified timepoints are reported. Here, n= number of participants analyzed for specified category. "99999": indicates that no participants were analyzed for that category.

End point type	Secondary

End point timeframe:

Cycle 1 Days 1, 2 and 21 (each cycle was 28 days)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 2 arms.

End point values	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=0, 14)	99999 (± 99999)	30100 (± 9540)		
Cycle 1 Day 2 (n=14, 0)	60400 (± 17200)	99999 (± 99999)		
Cycle 1 Day 21 (n=13, 0)	259000 (± 67300)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of 24 Hours Post-Dose of Enzalutamide

End point title	Phase 2: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of 24 Hours Post-Dose of Enzalutamide[14]

End point description:

Blood samples were collected at specified timepoints for the assessment of AUC0-24 of enzalutamide. The PK population included all participants in the safety population who had at least 1 post-dose sample collected to allow estimation of the PK parameters. Only those participants with data collected at specified timepoints are reported. Here, n= number of participants analyzed for specified category. "99999": indicates that no participants were analyzed for that category.

End point type	Secondary

End point timeframe:

24 hours post-dose on Cycle 1 Days 1, 2 and 21 (each cycle was 28 days)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 2 arms.

End point values	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=0, 13)	99999 (± 99999)	31400 (± 8430)		
Cycle 1 Day 2 (n=14, 0)	60000 (± 17000)	99999 (± 99999)		
Cycle 1 Day 21 (n=13, 0)	253000 (± 64500)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Change From Baseline in Functional Assessment of Cancer Therapy-Prostrate (FACT-P): Functional Wellbeing Subscale (FWB) and Prostate Cancer Subscale (PCS) Scores

End point title	Phase 2: Change From Baseline in Functional Assessment of Cancer Therapy-Prostrate (FACT-P): Functional Wellbeing

	Subscale (FWB) and Prostate Cancer Subscale (PCS) Scores[15]

End point description:

FACT-P questionnaire included subscales:physical well-being(PWB)(Questions [Q]GP1 to GP7),social/family wellbeing subscale(SWB)(Q GS1 to GS7),emotional well-being subscale(EWB)(Q GE1 to GE6),functional well-being subscale(FWB) (Q GF1 to GF7) and prostate cancer subscale(PCS)(Q C2, C6, P1 to P8, BL2 and BL5).Each question had 5 responses,0:"not at all", 1:"a little bit", 2:"somewhat", 3:"quite a bit" and 4:"very much". Scores ranged: 0 ("not at all") to 4("very much") for positively phrased questions.Negatively phrased questions had a reverse scoring,from 0("very much") to 4("not at all"). Q that were reversed (via subtraction of the response from 4)were: GP1-7, GE1, GE3-6, C2, P1-3, P6-P8 and BL2.Total FACT-P score:sum of scores of all sub-scales(PWB, SWB, EWB, FWB and PCS).Higher scores:better quality of life.Baseline:last value recorded for a variable prior to or on date of randomization."9999": standard deviation not estimable for 1 participant. "99999": no participants analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Cycle (C) 3 Day 57, C 5 Day 113, C 7 Day 169, C 10 Day 253, C 13 Day 337, C 14 Day 421, C 15 Day 505, C 16 Day 589, C 17 Day 673, C 18 Day 757, C 19 Day 841, C 20 Day 925, C 21 Day 1009, C 22 Day 1093, C 23 Day 1177 and C 24 Day 1261

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 2 arms.

End point values	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	36		
Units: score on a scale				
arithmetic mean (standard deviation)				
FWB: Cycle 3 Day 57 (n=33, 36)	-0.8 (± 4.73)	-1.2 (± 6.22)		
FWB: Cycle 5 Day 113 (n=31, 23)	-0.8 (± 4.61)	-0.6 (± 4.14)		
FWB: Cycle 7 Day 169 (n=22, 14)	-0.1 (± 5.68)	1.4 (± 5.72)		
FWB: Cycle 10 Day 253 (n=17, 13)	-0.6 (± 4.82)	-0.6 (± 5.11)		
FWB: Cycle 13 Day 337 (n=15, 10)	0.4 (± 3.58)	1.1 (± 4.61)		
FWB: Cycle 14 Day 421 (n=12, 9)	2.1 (± 4.32)	1.0 (± 6.44)		
FWB: Cycle 15 Day 505 (n=12, 6)	0.3 (± 2.70)	1.7 (± 5.09)		
FWB: Cycle 16 Day 589 (n=8, 4)	0.4 (± 3.46)	5.0 (± 6.06)		
FWB: Cycle 17 Day 673 (n=8, 5)	1.4 (± 3.50)	2.0 (± 4.64)		
FWB: Cycle 18 Day 757 (n=6, 3)	1.7 (± 1.51)	5.0 (± 4.36)		
FWB: Cycle 19 Day 841 (n=5, 2)	2.6 (± 3.51)	7.5 (± 3.54)		
FWB: Cycle 20 Day 925 (n=3, 2)	2.0 (± 4.00)	4.0 (± 4.24)		
FWB: Cycle 21 Day 1009 (n=3, 0)	1.7 (± 2.31)	99999 (± 99999)		
FWB: Cycle 22 Day 1093 (n=3, 0)	2.7 (± 4.73)	99999 (± 99999)		
FWB: Cycle 23 Day 1177 (n=2, 0)	4.5 (± 6.36)	99999 (± 99999)		
FWB: Cycle 24 Day 1261 (n=1, 0)	7.0 (± 9999)	99999 (± 99999)		
PCS: Cycle 3 Day 57 (n=33, 36)	-0.8 (± 5.69)	-1.3 (± 5.85)		
PCS: Cycle 5 Day 113 (n=31, 23)	-0.9 (± 5.12)	-0.7 (± 4.60)		
PCS: Cycle 7 Day 169 (n=23, 14)	-1.2 (± 6.07)	-0.8 (± 5.08)		
PCS: Cycle 10 Day 253 (n=17, 13)	0.0 (± 7.62)	-0.4 (± 7.89)		
PCS: Cycle 13 Day 337 (n=15, 10)	0.8 (± 5.63)	-1.8 (± 7.73)		
PCS: Cycle 14 Day 421 (n=12, 8)	0.8 (± 6.82)	-0.8 (± 5.19)		

PCS: Cycle 15 Day 505 (n=12, 6)	2.0 (± 5.02)	4.1 (± 2.65)		
PCS: Cycle 16 Day 589 (n=8, 4)	2.3 (± 3.49)	2.6 (± 6.26)		
PCS: Cycle 17 Day 673 (n=8, 5)	1.6 (± 5.50)	3.6 (± 3.07)		
PCS: Cycle 18 Day 757 (n=6, 3)	1.3 (± 3.72)	0.2 (± 6.81)		
PCS: Cycle 19 Day 841 (n=4, 2)	1.8 (± 3.50)	7.3 (± 1.80)		
PCS: Cycle 20 Day 925 (n=3, 2)	3.3 (± 4.73)	-1.0 (± 7.07)		
PCS: Cycle 21 Day 1009 (n=3, 0)	5.0 (± 1.73)	99999 (± 99999)		
PCS: Cycle 22 Day 1093 (n=3, 0)	6.0 (± 2.65)	99999 (± 99999)		
PCS: Cycle 23 Day 1177 (n=2, 0)	6.5 (± 0.71)	99999 (± 99999)		
PCS: Cycle 24 Day 1261 (n=1, 0)	3.0 (± 9999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Time to Definitive Deterioration (TDD) in Prostate Symptoms as Assessed by the Functional Assessment of Cancer Therapy-Prostrate: Prostate Cancer Subscale Score

End point title	Phase 2: Time to Definitive Deterioration (TDD) in Prostate Symptoms as Assessed by the Functional Assessment of Cancer Therapy-Prostrate: Prostate Cancer Subscale Score[16]

End point description:

TTD:interval from date of randomization until date of first clinically meaningful deterioration(3 points or more decline for subscale score,10 points or more decline for total score)that was confirmed at subsequent visit at least 3 weeks apart with no improvement in between visits or death(by any cause) in absence of a clinically meaningful deterioration,regardless of whether participant discontinued study drug(s) prior to deterioration.PCS included Q C2, C6, P1 to P8, BL2 and BL5.Each question had 5 responses,0:"not at all",1:"a little bit",2:"somewhat",3:"quite a bit" and 4:"very much". Scores ranged:0("not at all") to 4("very much") for positively phrased Q.Negatively phrased Q: reverse scoring,from 0("very much") to 4("not at all").Total FACT-P: sum of scores of all subscales(PWB, SWB, EWB, FWB and PCS). Higher scores:better quality of life.TDD in prostate symptoms as assessed by FACT-P: PCS score is presented. "9999": not estimable due to insufficient participants with events.

End point type	Secondary

End point timeframe:

Baseline (Day 1) up to Cycle 24 Day 1261

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was evaluated for only Phase 2 arms.

End point values	Phase 2: Tazemetostat 1200 mg + Enzalutamide	Phase 2: Enzalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	21		
Units: months				
median (confidence interval 95%)	11.2 (3.9 to 9999)	3.7 (2.5 to 11.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

TEAEs:first dose of study drug (Day 1) up to either 30 days after last dose or until initiation of subsequent anticancer therapy or end of treatment.Up to 149 and 191 weeks for Phases 1b and 2 respectively. Deaths:From Day 1 up to approximately 259 weeks.

Adverse event reporting additional description:

The safety population included all participants who received any dose of the study drugs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Phase 1b: Tazemetostat 400 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 400 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 600 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 800 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 800 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 1200 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 1200 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 1600 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 1600 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone

Reporting group description:

Participants received tazemetostat 400 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone

Reporting group description:

Participants received tazemetostat 600 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone

Reporting group description:

Participants received tazemetostat 800 mg tablet orally BID from Cycle 1 Day 2 and abiraterone 1000 mg tablet orally OD/prednisone 5 mg tablet orally BID from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28

days.

Reporting group title	Phase 2: Tazemetostat 1200 mg + Enzalutamide

Reporting group description:

Participants received tazemetostat 1200 mg tablet orally BID from Cycle 1 Day 2 and enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Reporting group title	Phase 2: Enzalutamide

Reporting group description:

Participants received enzalutamide 160 mg capsule orally OD from Cycle 1 Day 1 until death, PD, development of unacceptable toxicity, withdrawal of consent, or termination of the study. Each cycle duration was 28 days.

Serious adverse events	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
number of deaths (all causes)	2	2	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Acquired haemophilia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Gastritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1b: Tazemetostat 1200 mg + Enzalutamide	Phase 1b: Tazemetostat 1600 mg + Enzalutamide	Phase 1b: Tazemetostat 400 mg + Abiraterone/prednisone
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 1 (0.00%)
number of deaths (all causes)	3	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal			

disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Acquired haemophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	13 / 41 (31.71%)
number of deaths (all causes)	2	3	7
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Acquired haemophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 2: Enzalutamide		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 40 (25.00%)		
number of deaths (all causes)	18		

number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular access complication			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Atrioventricular block			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Acquired haemophilia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Phase 1b: Tazemetostat 400 mg + Enzalutamide	Phase 1b: Tazemetostat 600 mg + Enzalutamide	Phase 1b: Tazemetostat 800 mg + Enzalutamide
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin cancer			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	2
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	3 / 3 (100.00%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Influenza like illness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pyrexia			

subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Thirst			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pelvic pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Penile pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dyspnoea at rest			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			

subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pulmonary congestion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Disorientation			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Heart rate irregular			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
White blood cell count decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin abrasion			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nodal rhythm			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sinus bradycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Neuralgia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Anaemia macrocytic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Vision blurred			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diverticulum			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	1 / 2 (50.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	3	1
Oral pruritus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blister			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ecchymosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			

subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Skin ulcer			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pollakiuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine odour abnormal			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	0	3	2
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Flank pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Osteoporosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Tendonitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Conjunctivitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Otitis media			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection fungal			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 2 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Dehydration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Phase 1b: Tazemetostat 1200 mg + Enzalutamide	Phase 1b: Tazemetostat 1600 mg + Enzalutamide	Phase 1b: Tazemetostat 400 mg +

			Abiraterone/prednisone
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin cancer subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vascular disorders Hot flush subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	1	0	1
Hypertension subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypotension subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions Asthenia subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Chills subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Fatigue subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 1 (100.00%)
occurrences (all)	2	5	1
Influenza like illness subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Injection site bruising subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Thirst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Penile pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyspnoea at rest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1

Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Pulmonary congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Upper-airway cough syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Disorientation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Investigations			

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Heart rate irregular			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Fall			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nodal rhythm			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Neuralgia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Anaemia macrocytic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Eye disorders			
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	1	0	1
Diarrhoea			

subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	1 / 1 (100.00%)
occurrences (all)	2	2	1
Diverticulum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Oral pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Night sweats			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urine odour abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 1 (100.00%)
occurrences (all)	0	1	1
Flank pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Joint range of motion decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Osteoporosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Onychomycosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection fungal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Increased appetite			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 1b: Tazemetostat 600 mg + Abiraterone/prednisone	Phase 1b: Tazemetostat 800 mg + Abiraterone/prednisone	Phase 2: Tazemetostat 1200 mg + Enzalutamide
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	41 / 41 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin cancer			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 41 (4.88%)
occurrences (all)	0	1	5
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	3
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	26 / 41 (63.41%)
occurrences (all)	3	0	36
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 41 (9.76%)
occurrences (all)	0	0	5
Injection site bruising			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 41 (2.44%)
occurrences (all)	1	1	2
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	7 / 41 (17.07%)
occurrences (all)	1	3	7
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 41 (7.32%)
occurrences (all)	5	0	3
Thirst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Penile pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 41 (9.76%)
occurrences (all)	0	0	4
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	2
Dyspnoea at rest			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Tachypnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Disorientation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	5 / 41 (12.20%)
occurrences (all)	0	0	5
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Heart rate irregular			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	2	0	0
Urine output decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	8 / 41 (19.51%)
occurrences (all)	0	0	9
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 3 (33.33%)	3 / 3 (100.00%)	4 / 41 (9.76%)
occurrences (all)	1	6	5
Skin abrasion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Nodal rhythm			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	6 / 41 (14.63%)
occurrences (all)	1	0	8
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	10 / 41 (24.39%)
occurrences (all)	0	0	14
Headache			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 41 (4.88%)
occurrences (all)	0	0	2
Neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	5
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	9 / 41 (21.95%)
occurrences (all)	0	0	12
Anaemia macrocytic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 41 (9.76%)
occurrences (all)	0	0	6
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Constipation			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	7 / 41 (17.07%)
occurrences (all)	2	0	7
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	15 / 41 (36.59%)
occurrences (all)	0	0	20
Diverticulum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 41 (9.76%)
occurrences (all)	0	0	5
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	19 / 41 (46.34%)
occurrences (all)	2	0	23
Oral pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	5 / 41 (12.20%)
occurrences (all)	0	0	9
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Pollakiuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Urine odour abnormal			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	11 / 41 (26.83%)
occurrences (all)	1	5	17
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	3 / 41 (7.32%)
occurrences (all)	0	2	3
Flank pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 41 (4.88%)
occurrences (all)	0	1	2
Musculoskeletal chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 41 (7.32%)
occurrences (all)	1	0	3
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 41 (4.88%)
occurrences (all)	1	0	2
Neck pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Osteoporosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	3 / 41 (7.32%)
occurrences (all)	0	1	4
Tendonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 41 (9.76%)
occurrences (all)	0	0	4
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Herpes zoster			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Onychomycosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	3 / 41 (7.32%)
occurrences (all)	3	0	3
Urinary tract infection fungal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	12 / 41 (29.27%)
occurrences (all)	0	0	16
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 41 (7.32%)
occurrences (all)	1	0	3
Hypokalaemia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	4 / 41 (9.76%)
occurrences (all)	0	1	4
Increased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2: Enzalutamide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 40 (97.50%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin cancer			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	9		
Hypotension			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	5		
Chills			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	12 / 40 (30.00%)		
occurrences (all)	12		
Influenza like illness			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		

Injection site bruising subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3		
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Pyrexia subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Thirst subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Reproductive system and breast disorders Balanoposthitis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Pelvic pain subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Penile pain subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Dyspnoea subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3		

Dyspnoea at rest			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Productive cough			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Pulmonary congestion			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Upper-airway cough syndrome			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	5		
Disorientation			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Heart rate irregular			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Urine output decreased			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
White blood cell count decreased			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Bradycardia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Nodal rhythm			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Sinus bradycardia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Dysgeusia			

subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Neuralgia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Tremor			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Anaemia macrocytic			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	7		
Diarrhoea			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	9		
Diverticulum			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	9		
Oral pruritus			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Blister			

subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Ecchymosis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Night sweats subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Skin ulcer subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Renal and urinary disorders Chronic kidney disease subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Haematuria subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4		
Pollakiuria subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Proteinuria subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Urine odour abnormal subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	9 / 40 (22.50%) 10		
Back pain			

subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	10		
Flank pain			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Joint range of motion decreased			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Muscular weakness			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	6		
Musculoskeletal chest pain			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Neck pain			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Osteoporosis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Tendonitis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		

Conjunctivitis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Herpes zoster subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Onychomycosis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Otitis media subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Pneumonia subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Sinusitis subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Tooth abscess subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Urinary tract infection fungal subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	9 / 40 (22.50%) 9		
Dehydration subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Hyperglycaemia			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Increased appetite			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 July 2019	The potential dose level of tazemetostat was increased up to 1600 mg BID when given in combination with enzalutamide. Addition of death of any cause as an event in the definition of the rPFS endpoint and an assessment of the PK of enzalutamide and abiraterone/prednisone when administered in combination with tazemetostat. Participants with human immunodeficiency virus (HIV) or hepatitis who met specific criteria for immune function and HIV or hepatitis treatment were included. Criteria for dose-limiting toxicities (DLTs) was adjusted. The tazemetostat dose modification levels for combination treatment-related toxicities when administered with abiraterone/prednisone was corrected.
10 January 2020	The abiraterone/prednisone arm in the phase 2 portion of the study was removed. Clarifications provided regarding participants treated in phase Ib and AEs collection procedures. The location for the phase Ib portion of the study was expanded from the United States to global. Clinical experience information and the anticipated tazemetostat safety profile updated. Secondary objectives pertaining to CTCs, inclusion and exclusion criteria refined and exploratory objectives were expanded. Dose reduction amounts were modified for abiraterone-related toxicity to align with the package insert and clarified dose reduction procedures for tazemetostat. Instructions and guidance added for dosing in case of vomiting investigational drug and for the treatment of overdose and clarified permitted concomitant medications. Mandatory paired pre- and post-treatment biopsies were added for the additional participants to be enrolled at the RP2D in the phase 1 portion and allowed baseline biopsies from archival tumour sample if the sample was obtained less than 1 year before enrolment. PK sampling removed at 10 and 12 hours post-dose and deleted the CTC sample collection at Cycle 6. An optional chest ultrasound at screening and every 8 weeks at the investigator’s discretion and an annual blood sample for PK assessment for tazemetostat-treated participants added. Corrections made in the errors in the schedule of assessments, names and roles of safety committees and removed erroneously stated plans for an independent data monitoring committee. Analysis procedure and wording of record retention requirements revised.
05 June 2020	Since the original protocol was written, the sponsor had completed aggregate analysis of cumulative safety data for two New Drug Application submissions in the US and their subsequent safety updates. These analyses were supplemented by data from participants enrolled in 5 different dose-escalation cohort levels in the EZH-1101 trial with no observed DLTs. A review of cumulative safety data demonstrates a stable AE profile of tazemetostat managed by dose interruption and, uncommonly, by dose reduction or discontinuation. Based on this data, the sponsor reassessed the need for the additional number of participants considered for this study. Accordingly, the modified 3 + 3 dose-escalation design had been adjusted such that the RP2D could be determined based on the first three participants treated at any dose level if no DLTs occurred among them, without an additional three participants for added safety and PK information. Cohort expansion occurred only if a DLT was observed at any given cohort level. The availability of PK data in this study was adequate to characterize the PK of tazemetostat in the combination setting without additional participants (to a total of 12 at the RP2D) in the phase Ib portion of the study; the addition of these participants, therefore, was removed. The annual PK assessment that had been required for participants receiving tazemetostat was removed. The current information was updated on the medications to be used with caution and prohibited medications. A whole blood sample was added for potential genotype analysis at the 30-day follow-up visit to correct an oversight. Simplified, updated and applied consistency with other Epizyme documents and industry standards in safety reporting definitions, management and instructions.

27 December 2020	Declared the RP2D of tazemetostat when given in combination with enzalutamide. The total number of participants planned in the phase II randomized component of the study was increased from 32 per arm to 40 per arm (a total increase of 16 participants) in order to achieve 80% power and account for a 10% dropout rate; a critical boundary was also added. Reflection of the prevalence of measurable disease in the population (approximately 60%) was achieved by capping the enrolment of participants without measurable disease at 15 participants per treatment arm, as necessary. Updated to require tumour biopsies, when safe and feasible, from 12-20 participants randomized to receive tazemetostat plus enzalutamide in the phase II portion of the study. Included additional health-related quality of life measures. PK sample collection time points adjusted in phase 2 to coincide with efficacy assessments. Language to clarify safety/adverse event of special interest definitions adjusted. An exploratory objective was added.
14 April 2022	The name of the responsible medical officer and contact information in case of emergency was updated. The cap of 15 participants per treatment group without measurable disease in phase 2 was removed. Adjusted the phase 2 study duration from approximately 30 months to approximately 38 months and the estimated date of last participant completion from August 2023 to February 2024 and the timeframe for participants who discontinued treatment for reasons other than confirmed radiographic progression from up to 2 years post last dose to up to 18 months post last dose. Follow-up procedures and pregnancy prevention wording for participants' partners who were females of childbearing potential revised. PK sample collection was specified in phase 2. Added that Epizyme would request available archival tumour samples from all participants who did not provide matched biopsies at screening, to allow randomization of phase 2 participants to occur before Cycle 1 Day 1. Any second-generation androgen targeted agents as a class in phase 2 was excluded. Herbal remedies from the list of prohibited concomitant medications and the 400 mg formulation of tazemetostat from the list of available formulations was removed. The order of presentation was adjusted and additional details clarification was provided concerning secondary and exploratory endpoint definitions and planned statistical analyses. Clarification provided for the detection of myeloid malignancies in study participants. Safety information was updated to align with the current Investigator's Brochure (IB). Serum chromogranin A assessment at screening and to include a section on the future use of biosamples was removed.
31 August 2022	Background and clinical information regarding tazemetostat was updated to align with the updated tazemetostat IB (IB v12.0). The requirement of scans for confirmation of progression in soft tissue at Week 9 based on RECIST 1.1 criteria was removed. The list of responsible personnel and emergency contact information was updated. Internal conflict errors introduced in Protocol Amendment #5 was corrected and concomitant medication and supplement advice was clarified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early as Sponsor decided to discontinue the development of tazemetostat in mCRPC and the primary endpoint was not met for this study. There were no safety concerns.

Notes: