



Clinical trial results:

A Phase 1b/2 Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of GS-5829 as a Single Agent and In Combination with Enzalutamide in Subjects with Metastatic Castrate-Resistant Prostate Cancer

Summary

EudraCT number	2015-003741-26
Trial protocol	BE
Global end of trial date	03 September 2019

Results information

Result version number	v1
This version publication date	19 September 2020
First version publication date	19 September 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-350-1604
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02607228
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	03 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2017
Global end of trial reached?	Yes
Global end of trial date	03 September 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase 1b Dose Escalation: To characterize safety & tolerability of alobresib alone and in combination with enzalutamide in participants with metastatic castrate-resistant prostate cancer (mCRPC); determine the maximum tolerated dose (MTD) of alobresib alone and in combination with enzalutamide.

Phase 2 Dose Expansion: Group 1: Evaluate the efficacy of alobresib alone in participants with mCRPC who have progressed while receiving enzalutamide (may have also received abiraterone); Group 2: Evaluate the efficacy of alobresib combined with enzalutamide in participants with mCRPC who have progressed while receiving treatment with abiraterone; Group 3: Evaluate the efficacy of alobresib combined with enzalutamide in participants with mCRPC who had prostate-specific antigen, but not radiographic progression, while receiving treatment with enzalutamide.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance

with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	31
EEA total number of subjects	0

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)	11
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 4 study sites in the United States. The first participant was screened on 08 December 2015. The last study visit occurred on 03 September 2019. Phase 2 Dose Expansion of the study was not conducted. Results are reported for only Dose Escalation Monotherapy and Combination Therapy.

Pre-assignment

Screening details:

43 participants were screened.

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	Monotherapy: Alobresib 2 mg

Arm description:

Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 2 mg tablets administered orally once daily to determine the maximum tolerated dose (MTD).

Arm type	Experimental
Investigational medicinal product name	Alobresib
Investigational medicinal product code	
Other name	GS-5829
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 mg administered once daily.

Arm title	Monotherapy: Alobresib 3 mg
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Arm description:

Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 3 mg tablets administered orally once daily to determine the MTD.

Arm type	Experimental
Investigational medicinal product name	Alobresib
Investigational medicinal product code	
Other name	GS-5829
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3 mg administered once daily.

Arm title	Monotherapy: Alobresib 4 mg
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Arm description:

Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 4 mg tablets administered orally once daily to determine the MTD.

Arm type	Experimental
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Investigational medicinal product name	Alobresib
Investigational medicinal product code	
Other name	GS-5829
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 4 mg administered once daily.	
Arm title	Monotherapy: Alobresib 6 mg
Arm description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 6 mg tablets administered orally once daily to determine the MTD.	
Arm type	Experimental
Investigational medicinal product name	Alobresib
Investigational medicinal product code	
Other name	GS-5829
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 6 mg administered once daily.	
Arm title	Monotherapy: Alobresib 9 mg
Arm description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 9 mg tablets administered orally once daily to determine the MTD.	
Arm type	Experimental
Investigational medicinal product name	Alobresib
Investigational medicinal product code	
Other name	GS-5829
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 9 mg administered once daily.	
Arm title	Combination Therapy: Alobresib 3 mg + Enzalutamide
Arm description: Participants who had progressed on abiraterone, received alobresib 3 mg tablets administered orally once daily in combination with enzalutamide 160 mg capsules administered orally once daily.	
Arm type	Experimental
Investigational medicinal product name	Alobresib
Investigational medicinal product code	
Other name	GS-5829
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 3 mg administered once daily.	
Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	XTANDI®
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 160 mg administered once daily.	
Arm title	Combination Therapy: Alobresib 6 mg + Enzalutamide

Arm description:

Participants who had progressed on abiraterone, received alobresib 6 mg tablets administered orally once daily in combination with enzalutamide 160 mg capsules administered orally once daily.

Arm type	Experimental
Investigational medicinal product name	Alobresib
Investigational medicinal product code	
Other name	GS-5829
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

6 mg administered once daily.

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

Dosage and administration details:

160 mg administered once daily.

Number of subjects in period 1	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg
Started	5	4	3
Completed	0	0	0
Not completed	5	4	3
Withdrew Consent	-	1	-
Adverse Event	1	-	1
Progressive Disease	4	3	1
Investigator's Discretion	-	-	1
Study Terminated by Sponsor	-	-	-

Number of subjects in period 1	Monotherapy: Alobresib 6 mg	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide
Started	6	5	6
Completed	0	0	0
Not completed	6	5	6
Withdrew Consent	-	-	1
Adverse Event	-	1	1
Progressive Disease	5	4	3
Investigator's Discretion	-	-	1
Study Terminated by Sponsor	1	-	-

Number of subjects in period 1	Combination Therapy: Alobresib 6 mg + Enzalutamide
Started	2

Completed	0
Not completed	2
Withdrew Consent	-
Adverse Event	1
Progressive Disease	1
Investigator's Discretion	-
Study Terminated by Sponsor	-

Baseline characteristics

Reporting groups

Reporting group title	Monotherapy: Alobresib 2 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 2 mg tablets administered orally once daily to determine the maximum tolerated dose (MTD).	
Reporting group title	Monotherapy: Alobresib 3 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 3 mg tablets administered orally once daily to determine the MTD.	
Reporting group title	Monotherapy: Alobresib 4 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 4 mg tablets administered orally once daily to determine the MTD.	
Reporting group title	Monotherapy: Alobresib 6 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 6 mg tablets administered orally once daily to determine the MTD.	
Reporting group title	Monotherapy: Alobresib 9 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 9 mg tablets administered orally once daily to determine the MTD.	
Reporting group title	Combination Therapy: Alobresib 3 mg + Enzalutamide
Reporting group description: Participants who had progressed on abiraterone, received alobresib 3 mg tablets administered orally once daily in combination with enzalutamide 160 mg capsules administered orally once daily.	
Reporting group title	Combination Therapy: Alobresib 6 mg + Enzalutamide
Reporting group description: Participants who had progressed on abiraterone, received alobresib 6 mg tablets administered orally once daily in combination with enzalutamide 160 mg capsules administered orally once daily.	

Reporting group values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg
Number of subjects	5	4	3
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	68.2 ± 9.28	67.3 ± 10.69	67.7 ± 5.69
Gender categorical Units: Subjects			
Female	0	0	0
Male	5	4	3
Race Units: Subjects			
Black or African American	1	0	1
White	4	4	2
Other	0	0	0
Ethnicity			

Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	5	4	3
Unknown or Not Reported	0	0	0

Reporting group values	Monotherapy: Alobresib 6 mg	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide
Number of subjects	6	5	6
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	66.8 ± 9.39	69.2 ± 6.61	62.5 ± 10.23
Gender categorical Units: Subjects			
Female	0	0	0
Male	6	5	6
Race Units: Subjects			
Black or African American	0	0	1
White	6	4	5
Other	0	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	6	3	5
Unknown or Not Reported	0	1	0

Reporting group values	Combination Therapy: Alobresib 6 mg + Enzalutamide	Total	
Number of subjects	2	31	
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	67.0 ± 0.00	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	2	31	
Race Units: Subjects			
Black or African American	0	3	
White	2	27	
Other	0	1	
Ethnicity Units: Subjects			

Hispanic or Latino	0	2	
Not Hispanic or Latino	2	28	
Unknown or Not Reported	0	1	

End points

End points reporting groups

Reporting group title	Monotherapy: Alobresib 2 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 2 mg tablets administered orally once daily to determine the maximum tolerated dose (MTD).	
Reporting group title	Monotherapy: Alobresib 3 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 3 mg tablets administered orally once daily to determine the MTD.	
Reporting group title	Monotherapy: Alobresib 4 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 4 mg tablets administered orally once daily to determine the MTD.	
Reporting group title	Monotherapy: Alobresib 6 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 6 mg tablets administered orally once daily to determine the MTD.	
Reporting group title	Monotherapy: Alobresib 9 mg
Reporting group description: Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 9 mg tablets administered orally once daily to determine the MTD.	
Reporting group title	Combination Therapy: Alobresib 3 mg + Enzalutamide
Reporting group description: Participants who had progressed on abiraterone, received alobresib 3 mg tablets administered orally once daily in combination with enzalutamide 160 mg capsules administered orally once daily.	
Reporting group title	Combination Therapy: Alobresib 6 mg + Enzalutamide
Reporting group description: Participants who had progressed on abiraterone, received alobresib 6 mg tablets administered orally once daily in combination with enzalutamide 160 mg capsules administered orally once daily.	

Primary: Phase 1b Dose Escalation: Number of Participants Experienced Dose Limiting Toxicities (DLTs)

End point title	Phase 1b Dose Escalation: Number of Participants Experienced Dose Limiting Toxicities (DLTs) ^[1]
End point description: A DLT was a toxicity, considered possibly related to alobresib, and which occurred during the DLT assessment window (Days 1 through 28) in each cohort: Grade ≥ 4 neutropenia (absolute neutrophil count (ANC) $< 500/\text{mm}^3$), Grade ≥ 3 neutropenia (ANC $< 1000/\text{mm}^3$) with fever (a single temperature $> 38.3^\circ\text{C}$ or a sustained temperature of $\geq 38^\circ\text{C}$ for more than 1 hour (h)), Grade ≥ 3 thrombocytopenia, Grade ≥ 2 bleeding (eg, gastrointestinal, respiratory, epistaxis, purpura), Grade ≥ 3 non hematologic toxicity, except- Grade 3 nausea or emesis with maximum duration of 48 h on adequate medical therapy and Grade 3 diarrhea which persists for < 72 h in the absence of maximal medical therapy, Grade ≥ 2 non hematologic treatment emergent adverse event (TEAE) that in the opinion of the investigator was of potential clinical significance such that further dose escalation would expose participants to unacceptable risk, treatment interruption ≥ 7 days due to unresolved toxicity. The DLT Analysis Set.	
End point type	Primary
End point timeframe: Day 1 through Day 28	

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: No statistical comparison was planned or performed.

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	3	6
Units: percentage of participants				
number (not applicable)	0	0	0	0

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide	Combination Therapy: Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	2	
Units: percentage of participants				
number (not applicable)	0	1	0	

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2 Dose Expansion: Non-progression Rate at Week 24 According to Prostate Cancer Working Group (PCWG2) Criteria

End point title	Phase 2 Dose Expansion: Non-progression Rate at Week 24 According to Prostate Cancer Working Group (PCWG2) Criteria ^[2]
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End point description:

The non-progression rate at Week 24, was defined as the percentage of participants who did not progress by Week 24 and was estimated by Kaplan-Meier method. Responses were determined by the investigators based on PCWG2 Criteria. PCWG2 criteria for progression was determined as 'Decline from baseline' when record start of therapy to first prostate-specific antigen (PSA) increase that is $\geq 25\%$ and ≥ 2 ng/mL above the nadir and confirmed by a second value 3 or more weeks later; 'No decline from baseline' when PSA progression $\geq 25\%$ and ≥ 2 ng/mL after 12 weeks. The Full Analysis Set (FAS) included participants who received ≥ 1 dose of study drug (Alobresib or Enzalutamide), with treatment group designated according to the planned treatment. Here, 999 = Upper and lower limit of 95% Confidence Interval was not estimable.

End point type	Primary
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End point timeframe:

Week 24

Notes:

[2] - 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: No statistical comparison was planned or performed.

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	3	6
Units: months				
median (confidence interval 95%)	0.25 (0.01 to 0.67)	0.0 (0.0 to 0.0)	0.50 (0.01 to 0.91)	0.17 (0.01 to 0.52)

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide	Combination Therapy: Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	2	
Units: months				
median (confidence interval 95%)	0.25 (0.01 to 0.67)	0.17 (0.01 to 0.52)	1.00 (.999 to 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b Dose Escalation: Cmax: Maximum Observed Plasma Concentration of Alobresib

End point title	Phase 1b Dose Escalation: Cmax: Maximum Observed Plasma Concentration of Alobresib
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End point description:

Cmax is the maximum observed concentration of drug in plasma. The PK Analysis Set included participants who took at least 1 dose of study drug and have at least 1 non-missing postdose concentration value. Participants with available data were analyzed. Here, 99999 = Samples were not collected at this timepoint. 9999 = Standard Deviation (SD) was not estimable for 1 participant.

End point type	Secondary
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End point timeframe:

Monotherapy: Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 hours (h) postdose on Cycle 1 Day 8; Predose and 1-4 h postdose on Cycle 1 Days 15. Combination therapy: Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 h postdose on Cycle 1 Day 1; Anytime Day 1 of Cycles 2-6

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	3	6
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=5,4,3,6,4,6,2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1 Day 8 (n=5,4,3,6,4,6,2)	263.00 (± 141.875)	263.75 (± 132.011)	367.33 (± 49.359)	293.33 (± 123.362)

Cycle 1 Day 15 (n=5,4,3,6,5,6,2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 2 Day 1 (n=5,2,3,2,1,6,2)	99999 (± 99999)	220.50 (± 95.459)	99999 (± 99999)	203.50 (± 143.543)

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide	Combination Therapy: Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	2	
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=5,4,3,6,4,6,2)	99999 (± 99999)	111.07 (± 37.957)	199.00 (± 9.899)	
Cycle 1 Day 8 (n=5,4,3,6,4,6,2)	526.00 (± 280.391)	99999 (± 99999)	99999 (± 99999)	
Cycle 1 Day 15 (n=5,4,3,6,5,6,2)	99999 (± 99999)	84.4 (± 48.58)	173.5 (± 28.99)	
Cycle 2 Day 1 (n=5,2,3,2,1,6,2)	641.00 (± 9999)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b Dose Escalation: Ctau: Observed Drug Concentration at the End of the Dosing Interval of Alobresib

End point title	Phase 1b Dose Escalation: Ctau: Observed Drug Concentration at the End of the Dosing Interval of Alobresib
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End point description:

Ctau is the observed concentration of drug in plasma at the end of dosing. Participants in the PK Analysis Set with available data were analyzed. Here, 99999 = Samples were not collected at this timepoint. 9999 = SD was not estimable for 1 participant.

End point type	Secondary
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End point timeframe:

Monotherapy: Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 h postdose on Cycle 1 Day 8; Predose and 1-4 h postdose on Cycle 1 Days 15. Combination therapy: Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 h postdose on Cycle 1 Day 1; Anytime Day 1 of Cycles 2-6

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	3	6
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 8 (n=5,4,3,6,2,6,2)	180.00 (± 77.679)	156.78 (± 100.307)	141.67 (± 22.811)	70.93 (± 32.905)

Cycle 1 Day 15 (n=5,4,3,6,5,5,2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 2 Day 1 (n=5,2,3,1,1,6,2)	99999 (± 99999)	127.60 (± 59.963)	99999 (± 99999)	33.80 (± 9999)

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide	Combination Therapy: Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	2	
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 8 (n=5,4,3,6,2,6,2)	157.20 (± 126.996)	99999 (± 99999)	99999 (± 99999)	
Cycle 1 Day 15 (n=5,4,3,6,5,5,2)	99999 (± 99999)	8.8 (± 7.77)	3.9 (± 3.21)	
Cycle 2 Day 1 (n=5,2,3,1,1,6,2)	268.00 (± 9999)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b Dose Escalation: AUClast: Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Quantifiable Concentration of Alobresib

End point title	Phase 1b Dose Escalation: AUClast: Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Last Quantifiable Concentration of Alobresib
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End point description:

AUClast is the concentration of drug over time zero to last concentration (area under the plasma concentration versus time curve). Participants in the PK Analysis Set with available data were analyzed. Here, 99999 = Samples were not collected at this timepoint. 9999 = SD was not estimable for 1 participant.

End point type	Secondary
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End point timeframe:

Monotherapy: Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 h postdose on Cycle 1 Day 8; Predose and 1-4 h postdose on Cycle 1 Days 15. Combination therapy: Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 h postdose on Cycle 1 Day 1; Anytime Day 1 of Cycles 2-6

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	3	6
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=5,4,3,6,5,6,2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Cycle 1 Day 8 (n=5,4,3,6,4,6,2)	4207.55 (± 2319.854)	3742.30 (± 2106.308)	4646.08 (± 890.441)	3105.70 (± 1008.730)
Cycle 1 Day 15 (n=5,4,3,6,5,6,2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 2 Day 1 (n=5,2,3,2,1,6,2)	99999 (± 99999)	3264.79 (± 2024.141)	99999 (± 99999)	1709.71 (± 264.402)

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide	Combination Therapy: Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	2	
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=5,4,3,6,5,6,2)	99999 (± 99999)	1026.99 (± 359.220)	1741.42 (± 737.521)	
Cycle 1 Day 8 (n=5,4,3,6,4,6,2)	4494.79 (± 4124.948)	99999 (± 99999)	99999 (± 99999)	
Cycle 1 Day 15 (n=5,4,3,6,5,6,2)	99999 (± 99999)	652.7 (± 395.52)	701.3 (± 353.25)	
Cycle 2 Day 1 (n=5,2,3,2,1,6,2)	10264.74 (± 9999)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b Dose Escalation: AUCtau: Area Under the Plasma Concentration Versus Time Curve Over the Dosing Interval of Alobresib

End point title	Phase 1b Dose Escalation: AUCtau: Area Under the Plasma Concentration Versus Time Curve Over the Dosing Interval of Alobresib
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End point description:

AUCtau is defined as the concentration of drug over time (the area under the concentration versus time curve over the dosing interval). Participants in the PK Analysis Set with available data were analyzed. Here, 99999 = Samples were not collected at this timepoint. 9999 = SD was not estimable for 1 participant.

End point type	Secondary
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End point timeframe:

Monotherapy: Pre-dose, 0.5, 1, 2, 3, 4, 6, 8, and 24 hours post-dose at Cycle 1 Day 8; Pre-dose and 1-4 hours after alobresib administration on Cycle 1 Days 1 and 15. Combination therapy: Anytime at Day 1 of Cycles 2 through 6. Cycle = 28 days

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	3	6
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 8 (n=5,4,3,6,5,6,2)	4264.51 (± 2384.628)	3758.92 (± 2076.013)	4655.48 (± 949.099)	3128.58 (± 998.059)
Cycle 1 Day 15 (n=5,4,3,6,5,4,2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 2 Day 1 (n=5,2,3,1,1,6,2)	99999 (± 99999)	3243.01 (± 2110.324)	99999 (± 99999)	1522.75 (± 9999)

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide	Combination Therapy: Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	2	
Units: hour*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 8 (n=5,4,3,6,5,6,2)	7217.02 (± 4559.957)	99999 (± 99999)	99999 (± 99999)	
Cycle 1 Day 15 (n=5,4,3,6,5,4,2)	99999 (± 99999)	765.3 (± 373.39)	701.3 (± 353.25)	
Cycle 2 Day 1 (n=5,2,3,1,1,6,2)	10264.74 (± 9999)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b Dose Escalation: Tmax: Time (Observed Time Point) of Cmax of Alobresib

End point title	Phase 1b Dose Escalation: Tmax: Time (Observed Time Point) of Cmax of Alobresib
End point description: Tmax is the time observed for the Cmax of alobresib. Participants in the PK Analysis Set with available data were analyzed. Here, 99999 = Samples were not collected at this timepoint.	
End point type	Secondary
End point timeframe: Monotherapy: Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 h postdose on Cycle 1 Day 8; Predose and 1-4 h postdose on Cycle 1 Days 15. Combination therapy: Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 h postdose on Cycle 1 Day 1; Anytime Day 1 of Cycles 2-6	

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	3	6
Units: hour				
median (full range (min-max))				
Cycle 1 Day 1 (n=5,4,3,6,5,6,2)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Cycle 1 Day 8 (n=5,4,3,6,4,6,2)	0.50 (0.48 to 23.85)	0.66 (0.50 to 1.05)	0.58 (0.50 to 2.00)	1.42 (0.50 to 3.97)
Cycle 1 Day 15 (n=5,4,3,6,5,6,2)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Cycle 2 Day 1 (n=5,2,3,2,1,6,2)	99999 (99999 to 99999)	1.76 (0.50 to 3.02)	99999 (99999 to 99999)	4.93 (3.87 to 6.00)

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide	Combination Therapy: Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	2	
Units: hour				
median (full range (min-max))				
Cycle 1 Day 1 (n=5,4,3,6,5,6,2)	99999 (99999 to 99999)	1.07 (0.50 to 2.92)	0.46 (0.42 to 0.50)	
Cycle 1 Day 8 (n=5,4,3,6,4,6,2)	0.72 (0.50 to 2.08)	99999 (99999 to 99999)	99999 (99999 to 99999)	
Cycle 1 Day 15 (n=5,4,3,6,5,6,2)	99999 (99999 to 99999)	0.5 (0.5 to 7.9)	0.5 (0.5 to 0.5)	
Cycle 2 Day 1 (n=5,2,3,2,1,6,2)	4.08 (4.08 to 4.08)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Had $\geq 30\%$ Reduction in Prostate Specific Antigen (PSA) From Baseline at Week 12

End point title	Percentage of Participants Who Had $\geq 30\%$ Reduction in Prostate Specific Antigen (PSA) From Baseline at Week 12
End point description:	
PSA response was defined as percentage of participants with $\geq 30\%$ decline in PSA from baseline by 12 weeks. Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline; Week 12	

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	3	6
Units: percentage of participants				
number (not applicable)	0.0	0.0	33.3	0.0

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide	Combination Therapy: Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	2	
Units: percentage of participants				
number (not applicable)	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description:	
PFS was defined as the interval from first dose date of study drug to the earlier of the first documentation of definitive disease progression (assessed per PCWG2) or death from any cause. PCWG2 criteria for progression was determined as 'Decline from baseline' when record start of therapy to first prostate-specific antigen (PSA) increase that is $\geq 25\%$ and ≥ 2 ng/mL above the nadir and confirmed by a second value 3 or more weeks later; 'No decline from baseline' when PSA progression $\geq 25\%$ and ≥ 2 ng/mL after 12 weeks. Participants in the Full Analysis Set with available data were analyzed. Here, 999999 = Upper and lower limit of 95% confidence interval are not estimable for 1 participant.	
End point type	Secondary
End point timeframe:	
Up to approximately 4 years	

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	2	6
Units: months				
median (confidence interval 95%)	2.61 (1.58 to 8.61)	2.10 (1.97 to 2.60)	4.17 (2.79 to 5.55)	2.78 (2.69 to 11.07)

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy:	Combination Therapy:	
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		Alobresib 3 mg + Enzalutamide	Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	5	1	
Units: months				
median (confidence interval 95%)	2.69 (0.53 to 14.00)	3.25 (1.15 to 21.59)	5.98 (.999999 to 999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS is defined as the interval from first dose date of study drug to death from any cause. Participants in the Full Analysis Set were analyzed. Here, 999999 = Data were not evaluable because participants discontinued the study without death.	
End point type	Secondary
End point timeframe:	
Up to approximately 4 years	

End point values	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg	Monotherapy: Alobresib 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	3	6
Units: years				
median (full range (min-max))	999999 (999999 to 999999)	999999 (3.12 to 999999)	999999 (999999 to 999999)	999999 (999999 to 999999)

End point values	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide	Combination Therapy: Alobresib 6 mg + Enzalutamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	2	
Units: years				
median (full range (min-max))	999999 (999999 to 999999)	999999 (1.15 to 999999)	999999 (999999 to 999999)	

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: From first dose through last dose of the study drug (maximum: 131 weeks) plus 30 days; All-Cause Mortality: First dose date up to approximately 4 years

Adverse event reporting additional description:

The Safety Analysis Set included all participants who received ≥ 1 dose of study treatment with treatment group designated according to actual treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	Monotherapy: Alobresib 2 mg
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Reporting group description:

Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 2 mg tablets administered orally once daily to determine the MTD.

Reporting group title	Monotherapy: Alobresib 3 mg
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Reporting group description:

Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 3 mg tablets administered orally once daily to determine the MTD.

Reporting group title	Monotherapy: Alobresib 4 mg
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Reporting group description:

Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 4 mg tablets administered orally once daily to determine the MTD.

Reporting group title	Monotherapy: Alobresib 6 mg
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Reporting group description:

Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 6 mg tablets administered orally once daily to determine the MTD.

Reporting group title	Monotherapy: Alobresib 9 mg
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Reporting group description:

Participants who had progressed on either abiraterone and/or enzalutamide, received alobresib 9 mg tablets administered orally once daily to determine the MTD.

Reporting group title	Combination Therapy: Alobresib 3 mg + Enzalutamide
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Reporting group description:

Participants who had progressed on abiraterone, received alobresib 3 mg tablets administered orally once daily in combination with enzalutamide 160 mg capsules administered orally once daily.

Reporting group title	Combination Therapy: Alobresib 6 mg + Enzalutamide
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Reporting group description:

Participants who had progressed on abiraterone, received alobresib 6 mg tablets administered orally once daily in combination with enzalutamide 160 mg capsules administered orally once daily.

Serious adverse events	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (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			
Central nervous system lesion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (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
Embolic stroke			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (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 / 5 (0.00%)	0 / 4 (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 / 5 (0.00%)	0 / 4 (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
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (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
Eye disorders			
Retinal detachment			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (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			
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (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
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
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			
Pneumothorax			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (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			
Acute kidney injury			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (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	Monotherapy: Alobresib 6 mg	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	2 / 5 (40.00%)	2 / 6 (33.33%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
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			
Central nervous system lesion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (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
Embolic stroke			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (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
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (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
Diverticular perforation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (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
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (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			
Pneumothorax			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (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			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (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			
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (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	Combination Therapy: Alobresib 6 mg + Enzalutamide		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Central nervous system lesion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Embolitic stroke			

subjects affected / exposed	0 / 2 (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	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticular perforation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Pelvic pain			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Monotherapy: Alobresib 2 mg	Monotherapy: Alobresib 3 mg	Monotherapy: Alobresib 4 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	3 / 4 (75.00%)	3 / 3 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hot flush			

subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	3 / 3 (100.00%)
occurrences (all)	2	0	3
Pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Influenza like illness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site extravasation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Device related thrombosis			

subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Early satiety			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Feeling cold			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pelvic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			

subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Iliotibial band syndrome			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper limb fracture	Additional description: 1		
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Wound haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Burning sensation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cognitive disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hemiparesis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Memory impairment subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Paraesthesia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Ear and labyrinth disorders Ear pruritus subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 4 (25.00%) 1	1 / 3 (33.33%) 1
Nausea subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	0 / 4 (0.00%) 0	1 / 3 (33.33%) 1
Abdominal pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0
Vomiting			

subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pain of skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			

subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Renal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Urinary tract disorder			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Urinary tract obstruction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Arthralgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Joint swelling			

subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pathological fracture			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Kidney infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Tooth infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0	1 / 3 (33.33%) 1
Viral infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Dehydration subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0

Non-serious adverse events	Monotherapy: Alobresib 6 mg	Monotherapy: Alobresib 9 mg	Combination Therapy: Alobresib 3 mg + Enzalutamide
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 6 (100.00%)	5 / 5 (100.00%)	5 / 6 (83.33%)
Vascular disorders			
Deep vein thrombosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Hot flush subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Hypertension subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0

Hypotension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	4 / 5 (80.00%) 5	2 / 6 (33.33%) 2
Pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 2	1 / 6 (16.67%) 1
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
Catheter site extravasation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Device related thrombosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Early satiety subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Feeling cold			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Gait disturbance subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Pelvic pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
Dyspnoea subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
Pulmonary embolism subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 2	0 / 6 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Psychiatric disorders Abnormal dreams subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
Anxiety			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	9	0
Blood bilirubin increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	2	7	0
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Iliotibial band syndrome			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Joint injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle strain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture	Additional description: 1		
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wound haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Neuropathy peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Burning sensation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Memory impairment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1	1 / 6 (16.67%) 1
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 4	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Ear and labyrinth disorders			
Ear pruritus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	2 / 5 (40.00%) 3	1 / 6 (16.67%) 1
Nausea subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	3 / 5 (60.00%) 3	0 / 6 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1	1 / 6 (16.67%) 1
Abdominal pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
Abdominal pain upper			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eructation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haematuria			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract obstruction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	2
Muscle spasms			
subjects affected / exposed	3 / 6 (50.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Joint swelling			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Flank pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pathological fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Kidney infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	4 / 5 (80.00%)	1 / 6 (16.67%)
occurrences (all)	1	5	1
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Combination Therapy: Alobresib 6 mg + Enzalutamide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Catheter site extravasation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Device related thrombosis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Early satiety			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Feeling cold			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Oedema peripheral			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all) Pelvic pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea exertional subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Pulmonary embolism subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Psychiatric disorders Abnormal dreams subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Confusional state subjects affected / exposed occurrences (all) Depression	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Investigations			
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Weight decreased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Iliotibial band syndrome subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Joint injury subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Muscle strain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Skin abrasion subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Upper limb fracture	Additional description: 1		

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Wound haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Burning sensation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cognitive disorder			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hemiparesis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Memory impairment			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pruritus			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dry mouth			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Eructation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pain of skin			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pollakiuria			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Renal pain			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Urinary tract disorder			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Urinary tract obstruction			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pathological fracture			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Kidney infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 September 2015	Amendment 1 included the following major changes: • Updated study design including objective and endpoints, number of participants, the introduction of a Study Day 1 visit to allow for an enzalutamide lead in for participants in the Phase 1b combination therapy and Phase 2 groups. • Modified the starting dose to a dose that was deemed safe and tolerable in Study GS-US-350-1599. • Added a risk:benefit assessment section • Updated planned number of study centers and regions. • Introduced new formulations of alobresib available for use. • Clarified the SRT members that would assess dose level reviews. • Included a study schema for additional clarification of study design. • Updated reasons for discontinuing treatment or discontinuation from the study. • Added minor clarifications to the study procedures table.
30 June 2016	Amendment 2 included the following major changes: • Updated the background, risk/benefit, study design, objectives, endpoints and number of participants to allow a third group of participants in the Phase 2 portion of this study (participants who were currently on enzalutamide and showing the early signs of progressive disease). • Updated the change in Gilead medical oversight of the study. • Modified the study design to allow enrollment in the Phase 1b combination therapy dose escalation cohorts prior to determination of the MTD in the monotherapy cohorts. • Updated inclusion/exclusion criteria for participants participating in Group 3. • Updated PK/PD collections for Group 3 participants. • Updated the statistical analysis sections and the study schema based on the new study design. • Updated current clinical experience with alobresib. • Removed the 0.2 mg formulation of alobresib and updated the minimum dose reduction level allowed. • Clarified food effect sub study procedures. • Included additional laboratory analytes for safety monitoring.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported