



Clinical trial results:

Phase 1/2a dose-escalation and expansion study to evaluate the safety, tolerability, and pharmacokinetics of CORT125281 with enzalutamide in patients with metastatic castration-resistant prostate cancer.

Summary

EudraCT number	2017-003287-12
Trial protocol	GB
Global end of trial date	12 January 2023

Results information

Result version number	v1 (current)
This version publication date	17 October 2026
First version publication date	17 October 2026

Trial information

Trial identification

Sponsor protocol code	CORT125281-601
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03437941
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Corcept Therapeutics
Sponsor organisation address	149 Commonwealth Drive, Menlo Park, United States,
Public contact	Clinical Operations, Corcept Therapeutics, +1 650 3273270, clinicalstudies@corcept.com
Scientific contact	Clinical Operations, Corcept Therapeutics, +1 650 3273270, clinicalstudies@corcept.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	12 January 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 January 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine the maximum tolerated dose (MTD) and/or biologically active doses of exicorilant in combination with enzalutamide to identify the recommended dose (RD) for Phase 2 studies.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 February 2018
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 Kingdom: 12
Country: Number of subjects enrolled	United States: 27
Worldwide total number of subjects	39
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)	15
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

By Sponsor decision, no patients were enrolled in the study after the Dose Determination Segment 2; thus, no patients were enrolled in the Dose Expansion arms.

Pre-assignment

Screening details:

Patients were screened 28 days before the first dose of study treatment. A total of 58 patients were screened and 39 were enrolled.

Pre-assignment period milestones

Number of subjects started	39
Number of subjects completed	37

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Death: 1
Reason: Number of subjects	Consent withdrawn by subject: 1

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant

Arm description:

Patients in this dose determination cohort received lead-in enzalutamide monotherapy once daily for 28 days. Patients then received combination treatment with twice-daily exicorilant 180 mg (total daily dose 360 mg) and enzalutamide once daily in 28-day dosing cycles.

Arm type	Experimental
Investigational medicinal product name	Exicorilant
Investigational medicinal product code	
Other name	CORT125281
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Exicorilant was supplied as capsules for oral dosing.

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

Dosage and administration details:

Enzalutamide was taken orally.

Arm title	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant
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Arm description:

Patients in this dose determination cohort received lead-in enzalutamide monotherapy once daily for 28 days. Patients then received combination treatment with twice-daily exicorilant 140 mg (total daily dose 280 mg) and enzalutamide once daily in 28-day dosing cycles.

Arm type	Experimental
Investigational medicinal product name	Exicorilant
Investigational medicinal product code	
Other name	CORT125281
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Exicorilant was supplied as capsules for oral dosing.

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

Dosage and administration details:

Enzalutamide was taken orally.

Arm title	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant
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Arm description:

Patients in this dose determination cohort did not receive lead-in enzalutamide monotherapy. Patients received combination treatment with twice-daily exicorilant 140 mg (total daily dose 280 mg) and enzalutamide once daily in 28-day dosing cycles.

Arm type	Experimental
Investigational medicinal product name	Exicorilant
Investigational medicinal product code	
Other name	CORT125281
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Exicorilant was supplied as capsules for oral dosing.

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

Dosage and administration details:

Enzalutamide was taken orally.

Arm title	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
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Arm description:

Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 240 mg exicorilant.

Arm type	Experimental
Investigational medicinal product name	Exicorilant
Investigational medicinal product code	
Other name	CORT125281
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Exicorilant was supplied as capsules for oral dosing.

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

Dosage and administration details:

Enzalutamide was taken orally.

Arm title	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant
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Arm description:

Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 280 mg exicorilant.

Arm type	Experimental
Investigational medicinal product name	Exicorilant
Investigational medicinal product code	
Other name	CORT125281
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Exicorilant was supplied as capsules for oral dosing.

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

Dosage and administration details:

Enzalutamide was taken orally.

Arm title	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant
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Arm description:

Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 320 mg exicorilant.

Arm type	Experimental
Investigational medicinal product name	Exicorilant
Investigational medicinal product code	
Other name	CORT125281
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Exicorilant was supplied as capsules for oral dosing.

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

Dosage and administration details:

Enzalutamide was taken orally.

Arm title	Segment 2: Arm B - 240 mg Exicorilant
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Arm description:

Patients in this dose determination arm received combination treatment with once-daily exicorilant 240 mg, enzalutamide once daily, and placebo in 28-day dosing cycles.

Arm type	Experimental
Investigational medicinal product name	Exicorilant
Investigational medicinal product code	
Other name	CORT125281
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Exicorilant was supplied as capsules for oral dosing.

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

Dosage and administration details:

Enzalutamide was taken orally.

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

Dosage and administration details:

Placebo capsules matched the appearance of the exicorilant capsules.

Number of subjects in period 1^[1]	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant
Started	2	3	7
Completed	0	0	0
Not completed	2	3	7
Physician decision	1	-	-
Consent withdrawn by subject	-	-	-
Study terminated by Sponsor	-	2	2
Death	1	1	5

Number of subjects in period 1^[1]	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant
Started	8	1	10
Completed	0	0	0
Not completed	8	1	10
Physician decision	-	-	-
Consent withdrawn by subject	-	-	2
Study terminated by Sponsor	7	1	3
Death	1	-	5

Number of subjects in period 1^[1]	Segment 2: Arm B - 240 mg Exicorilant
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Started	6
Completed	0
Not completed	6
Physician decision	-
Consent withdrawn by subject	-
Study terminated by Sponsor	2
Death	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Two patients were enrolled in the study but discontinued before being allocated into a treatment group.

Baseline characteristics

Reporting groups

Reporting group title	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant
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Reporting group description:

Patients in this dose determination cohort received lead-in enzalutamide monotherapy once daily for 28 days. Patients then received combination treatment with twice-daily exicorilant 180 mg (total daily dose 360 mg) and enzalutamide once daily in 28-day dosing cycles.

Reporting group title	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant
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Reporting group description:

Patients in this dose determination cohort received lead-in enzalutamide monotherapy once daily for 28 days. Patients then received combination treatment with twice-daily exicorilant 140 mg (total daily dose 280 mg) and enzalutamide once daily in 28-day dosing cycles.

Reporting group title	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant
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Reporting group description:

Patients in this dose determination cohort did not receive lead-in enzalutamide monotherapy. Patients received combination treatment with twice-daily exicorilant 140 mg (total daily dose 280 mg) and enzalutamide once daily in 28-day dosing cycles.

Reporting group title	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
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Reporting group description:

Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 240 mg exicorilant.

Reporting group title	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant
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Reporting group description:

Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 280 mg exicorilant.

Reporting group title	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant
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Reporting group description:

Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 320 mg exicorilant.

Reporting group title	Segment 2: Arm B - 240 mg Exicorilant
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Reporting group description:

Patients in this dose determination arm received combination treatment with once-daily exicorilant 240 mg, enzalutamide once daily, and placebo in 28-day dosing cycles.

Reporting group values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant
Number of subjects	2	3	7
Age categorical Units: Subjects			
Age continuous Units: years median full range (min-max)	67.5 59 to 76	60.0 53 to 71	70.0 58 to 80

Gender categorical Units: Subjects			
Female	0	0	0
Male	2	3	7
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	1	3	7
Unknown or Not Reported	1	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	0
White	2	2	7
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant
Number of subjects	8	1	10
Age categorical Units: Subjects			

Age continuous Units: years			
median	72.0	75.0	64.0
full range (min-max)	60 to 82	75 to 75	53 to 76
Gender categorical Units: Subjects			
Female	0	0	0
Male	8	1	10
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	7	1	8
Unknown or Not Reported	1	0	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	2
White	4	1	5
More than one race	0	0	0
Unknown or Not Reported	3	0	2

Reporting group values	Segment 2: Arm B - 240 mg Exicorilant	Total	
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Number of subjects	6	37	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
median	66.0		
full range (min-max)	55 to 74	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	6	37	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	5	32	
Unknown or Not Reported	1	5	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	4	
White	5	26	
More than one race	0	0	
Unknown or Not Reported	0	5	

End points

End points reporting groups

Reporting group title	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant
Reporting group description: Patients in this dose determination cohort received lead-in enzalutamide monotherapy once daily for 28 days. Patients then received combination treatment with twice-daily exicorilant 180 mg (total daily dose 360 mg) and enzalutamide once daily in 28-day dosing cycles.	
Reporting group title	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant
Reporting group description: Patients in this dose determination cohort received lead-in enzalutamide monotherapy once daily for 28 days. Patients then received combination treatment with twice-daily exicorilant 140 mg (total daily dose 280 mg) and enzalutamide once daily in 28-day dosing cycles.	
Reporting group title	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant
Reporting group description: Patients in this dose determination cohort did not receive lead-in enzalutamide monotherapy. Patients received combination treatment with twice-daily exicorilant 140 mg (total daily dose 280 mg) and enzalutamide once daily in 28-day dosing cycles.	
Reporting group title	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Reporting group description: Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 240 mg exicorilant.	
Reporting group title	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant
Reporting group description: Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 280 mg exicorilant.	
Reporting group title	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant
Reporting group description: Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 320 mg exicorilant.	
Reporting group title	Segment 2: Arm B - 240 mg Exicorilant
Reporting group description: Patients in this dose determination arm received combination treatment with once-daily exicorilant 240 mg, enzalutamide once daily, and placebo in 28-day dosing cycles.	

Primary: Number of Patients With One or More Dose-Limiting Toxicity (DLT)

End point title	Number of Patients With One or More Dose-Limiting Toxicity (DLT) ^[1]
End point description: Assess the maximum tolerated dose (MTD) and/or biologically active doses of exicorilant in combination with enzalutamide to identify the recommended dose (RD) for Phase 2 studies based on the number of patients who experienced a DLT while receiving exicorilant in combination with enzalutamide. DLTs were defined as any of the protocol-specified toxicities that the Investigator considered possibly or probably related to study drug that occurred during the DLT-evaluation period. The MTD was defined as the highest dose at which the DLT rate was <33%. The DLT-Evaluable Population included all patients in the Dose-Determination cohorts who received at least 1 dose of exicorilant and fulfilled at least 1 of the following: 1) received at least 75% of the study regimen; 2) experienced a DLT within the DLT-evaluation period.	
End point type	Primary

End point timeframe:

From first dose of exicorilant through completion of Cycle 1 (up to 28 days) for Segment 1 and from first dose of exicorilant through completion of Cycle 3 (up to 84 days) for Segment 2.

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 between-group statistical analyses were planned for this endpoint.

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	6	4
Units: Patients	2	1	0	4

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	5	6	
Units: Patients	1	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With 1 or More Treatment-Emergent Adverse Events

End point title	Number of Patients With 1 or More Treatment-Emergent Adverse Events
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End point description:

The safety of each treatment group was assessed by evaluating the incidence of treatment-emergent adverse events. The Safety Population included all patients who received ≥ 1 dose of exicorilant.

End point type	Secondary
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End point timeframe:

Up to 27 months for Segment 1 and up to 19 months for Segment 2

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	7	8
Units: Patients	2	3	7	8

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	10	6	
Units: Patients	1	10	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Versus Time Curve (AUC) of Plasma Exicorilant: Segment 1

End point title	Area Under the Concentration Versus Time Curve (AUC) of Plasma Exicorilant: Segment 1 ^[2]
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End point description:

AUC from time zero to 12 hours postdose (AUC₀₋₁₂) calculated using linear up and log down method. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 12 hours postdose on Cycle 1 Day 1 and Cycle 2 Day 1

Notes:

[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: This end point reports results for Segment 1 only.

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3 ^[3]	7 ^[4]	
Units: ng-hr/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	387 (± 11.3)	275 (± 64.2)	477 (± 82.4)	
Cycle 2 Day 1	433 (± 14.8)	431 (± 29.0)	747 (± 82.2)	

Notes:

[3] - Patients analyzed in each category: N=3, N=2

[4] - Patients analyzed in each category: N=5, N=5

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (C_{max}) of Plasma Exicorilant: Segment 1

End point title	Maximum Observed Concentration (Cmax) of Plasma Exicorilant: Segment 1 ^[5]
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End point description:

Maximum observed concentration over the dosing interval. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 12 hours postdose on Cycle 1 Day 1 and Cycle 2 Day 1

Notes:

[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: This end point reports results for Segment 1 only.

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3 ^[6]	7 ^[7]	
Units: ng/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	84.2 (± 24.5)	91.6 (± 34.5)	186.1 (± 70.5)	
Cycle 2 Day 1	108 (± 59.2)	125 (± 15.4)	174 (± 68.7)	

Notes:

[6] - Patients analyzed in each category: N=3, N=2

[7] - Patients analyzed in each category: N=5, N=5

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Plasma Enzalutamide: Segment 1

End point title	AUC of Plasma Enzalutamide: Segment 1 ^[8]
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End point description:

AUC from time zero to 24 hours postdose (AUC₀₋₂₄) calculated using linear up and log down method. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 24 hours postdose on Cycle 1 Day -1, Cycle 1 Day 1, and Cycle 2 Day 1

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: This end point reports results for Segment 1 only.

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2 ^[9]	3 ^[10]	7 ^[11]	
Units: ng-hr/ml				
geometric mean (geometric coefficient of variation)				

Cycle 1 Day -1 lead-in	281499 (± 2.7)	255623 (± 20.0)	9999 (± 9999)	
Cycle 1 Day 1	307849 (± 9999)	278573 (± 25.6)	36979 (± 21.4)	
Cycle 2 Day 1	334761 (± 3.8)	410557 (± 16.3)	386651 (± 15.3)	

Notes:

[9] - Patients analyzed in each category: N=2, N=1, N=1. Missing values are indicated by "9999".

[10] - Patients analyzed in each category: N=3, N=2, N=2

[11] - Patients analyzed in each category: N=0, N=6, N=5. Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Plasma Enzalutamide: Segment 1

End point title	Cmax of Plasma Enzalutamide: Segment 1 ^[12]
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End point description:

Maximum observed concentration over the dosing interval. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 24 hours postdose on Cycle 1 Day -1, Cycle 1 Day 1, and Cycle 2 Day 1

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: This end point reports results for Segment 1 only.

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3 ^[13]	7 ^[14]	
Units: ng/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 Lead-in	15112 (± 15.5)	12759 (± 27.5)	9999 (± 9999)	
Cycle 1 Day 1	15500 (± 0.9)	14186 (± 13.0)	4260 (± 36.5)	
Cycle 2 Day 1	16497 (± 2.6)	19669 (± 7.9)	19338 (± 11.6)	

Notes:

[13] - Patients analyzed in each category: N=3, N=3, N=2

[14] - Patients analyzed in each category: N=0, N=6, N=5. Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Plasma N-Desmethyl Enzalutamide: Segment 1

End point title	AUC of Plasma N-Desmethyl Enzalutamide: Segment 1 ^[15]
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End point description:

AUC0-24 calculated using linear up and log down method. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study

treatment at any time point.

End point type	Secondary
End point timeframe:	
Predose and at time intervals up to 24 hours postdose on Cycle 1 Day -1, Cycle 1 Day 1, and Cycle 2 Day 1	
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: This end point reports results for Segment 1 only.	

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2 ^[16]	3 ^[17]	7 ^[18]	
Units: ng-hr/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day -1 lead-in	143300 (± 9999)	121320 (± 26.1)	9999 (± 9999)	
Cycle 1 Day 1	9999 (± 9999)	146225 (± 21.0)	717 (± 9999)	
Cycle 2 Day 1	180628 (± 21.5)	181855 (± 7.8)	146580 (± 42.7)	

Notes:

[16] - Patients analyzed in each category: N=1, N=0, N=2. Missing values are indicated by "9999".

[17] - Patients analyzed in each category: N=2, N=2, N=2

[18] - Patients analyzed in each category: N=0, N=1, N=5. Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Plasma N-Desmethyl Enzalutamide: Segment 1

End point title	Cmax of Plasma N-Desmethyl Enzalutamide: Segment 1 ^[19]
End point description:	
Maximum observed concentration over the dosing interval. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.	
End point type	Secondary
End point timeframe:	
Predose and at time intervals up to 24 hours postdose on Cycle 1 Day -1, Cycle 1 Day 1, and Cycle 2 Day 1.	
Notes:	
[19] - 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: This end point reports results for Segment 1 only.	

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3 ^[20]	7 ^[21]	
Units: ng/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 Lead-in	7835 (± 14.3)	5812 (± 12.6)	9999 (± 9999)	
Cycle 1 Day 1	8570 (± 18.3)	7074 (± 20.4)	112 (± 1152.2)	
Cycle 2 Day 1	7760 (± 21.2)	7996 (± 6.8)	6742 (± 46.1)	

Notes:

[20] - Patients analyzed in each category: N=3, N=3, N=2

[21] - Patients analyzed in each category: N=0, N=6, N=5. Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Plasma Enzalutamide Carboxylic Acid: Segment 1

End point title	AUC of Plasma Enzalutamide Carboxylic Acid: Segment 1 ^[22]
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End point description:

AUC0-24 calculated using linear up and log down method. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 24 hours postdose on Cycle 1 Day -1, Cycle 1 Day 1, and Cycle 2 Day 1

Notes:

[22] - 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: This end point reports results for Segment 1 only.

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2 ^[23]	3 ^[24]	7 ^[25]	
Units: ng-hr/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day -1 lead-in	19108 (± 9999)	34493 (± 9999)	9999 (± 9999)	
Cycle 1 Day 1	125786 (± 9999)	52471 (± 26.3)	1287 (± 9999)	
Cycle 2 Day 1	80970 (± 219.0)	52579 (± 23.1)	63388 (± 93.3)	

Notes:

[23] - Patients analyzed in each category: N=1, N=1, N=2. Missing values are indicated by "9999".

[24] - Patients analyzed in each category: N=1, N=3, N=2. Missing values are indicated by "9999".

[25] - Patients analyzed in each category: N=0, N=1, N=5. Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Plasma Enzalutamide Carboxylic Acid: Segment 1

End point title	Cmax of Plasma Enzalutamide Carboxylic Acid: Segment 1 ^[26]
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End point description:

Maximum observed concentration over the dosing interval. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 24 hours postdose on Cycle 1 Day -1, Cycle 1 Day 1, and Cycle 2 Day 1

Notes:

[26] - 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: This end point reports results for Segment 1 only.

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3 ^[27]	7 ^[28]	
Units: ng/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day -1 lead-in	2286 (± 121.4)	1930 (± 39.5)	9999 (± 9999)	
Cycle 1 Day 1	3181 (± 113.8)	2554 (± 26.6)	127 (± 180.0)	
Cycle 2 Day 1	3719 (± 235.9)	2862 (± 31.6)	3088 (± 88.0)	

Notes:

[27] - Patients analyzed in each category: N=3, N=3, N=2

[28] - Patients analyzed in each category: N=0, N=6, N=5. Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Plasma Exicorilant: Segment 2

End point title	AUC of Plasma Exicorilant: Segment 2 ^[29]
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End point description:

AUC from time zero to 6 hours postdose (AUC0-6) calculated using linear up and log down method. Patients in Arm B did not receive dose escalations, but they were sampled for pharmacokinetic analysis on the same time frame as the Arm A patients: Cycle 1 Day 15, Week 4, and Week 6. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 6 hours on Cycle 1 Day 15 (before dose escalation) and at 2 weeks after each dose escalation (Week 4 for escalation from 240 mg to 280 mg exicorilant and Week 6 for escalation from 280 mg to 320 mg exicorilant)

Notes:

[29] - 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: This end point reports results for Segment 2 only.

End point values	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[30]	1 ^[31]	9 ^[32]	5 ^[33]
Units: ng-hr/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15 before dose escalation	1086 (± 43.4)	511 (± 9999)	1125 (± 56.1)	1201 (± 77.0)
After 240 to 280 mg dose escalation	974 (± 9999)	9999 (± 9999)	1424 (± 53.3)	990 (± 33.2)
After 280 to 320 mg dose escalation	9999 (± 9999)	9999 (± 9999)	1589 (± 38.8)	1012 (± 48.3)

Notes:

[30] - Patients analyzed in each category: N=4, N=1, N=0. Missing values are indicated by "9999".

[31] - Patients analyzed in each category: N=1, N=0, N=0. Missing values are indicated by "9999".

[32] - Patients analyzed in each category: N=9, N=7, N=6

[33] - Patients analyzed in each category: N=5, N=4, N=4

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Plasma Exicorilant: Segment 2

End point title	Cmax of Plasma Exicorilant: Segment 2 ^[34]
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End point description:

Maximum observed concentration over the dosing interval. Patients in Arm B did not receive dose escalations, but they were sampled for pharmacokinetic analysis on the same time frame as the Arm A patients: Cycle 1 Day 15, Week 4, and Week 6. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 6 hours on Cycle 1 Day 15 (before dose escalation) and at 2 weeks after each dose escalation (Week 4 for escalation from 240 mg to 280 mg exicorilant and Week 6 for escalation from 280 mg to 320 mg exicorilant)

Notes:

[34] - 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: This end point reports results for Segment 2 only.

End point values	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[35]	1 ^[36]	9 ^[37]	5 ^[38]
Units: ng/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15 before dose escalation	402 (± 34.7)	157 (± 9999)	418 (± 61.7)	495 (± 80.7)

After 240 to 280 mg dose escalation	247 (± 9999)	9999 (± 9999)	528 (± 58.6)	398 (± 63.8)
After 280 to 320 mg dose escalation	9999 (± 9999)	9999 (± 9999)	534 (± 56.8)	374 (± 65.9)

Notes:

[35] - Patients analyzed in each category: N=4, N=1, N=0. Missing values are indicated by "9999".

[36] - Patients analyzed in each category: N=1, N=0, N=0. Missing values are indicated by "9999".

[37] - Patients analyzed in each category: N=9, N=9, N=6

[38] - Patients analyzed in each category: N=5, N=4, N=4

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Plasma Enzalutamide: Segment 2

End point title	AUC of Plasma Enzalutamide: Segment 2 ^[39]
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End point description:

AUC from time zero to 6 hours postdose (AUC₀₋₆) calculated using linear up and log down method. Patients in Arm B did not receive dose escalations, but they were sampled for pharmacokinetic analysis on the same time frame as the Arm A patients: Cycle 1 Day 15, Week 4, and Week 6. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 6 hours on Cycle 1 Day 15 (before dose escalation) and at 2 weeks after each dose escalation (Week 4 for escalation from 240 mg to 280 mg exicorilant and Week 6 for escalation from 280 mg to 320 mg exicorilant)

Notes:

[39] - 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: This end point reports results for Segment 2 only.

End point values	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[40]	1 ^[41]	9 ^[42]	5 ^[43]
Units: ng-hr/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15 before dose escalation	93894 (± 27.5)	90563 (± 9999)	98157 (± 26.1)	95735 (± 8.5)
After 240 to 280 mg dose escalation	150022 (± 9999)	9999 (± 9999)	102373 (± 20.3)	96684 (± 17.6)
After 280 to 320 mg dose escalation	9999 (± 9999)	9999 (± 9999)	111632 (± 12.4)	95653 (± 11.8)

Notes:

[40] - Patients analyzed in each category: N=4, N=1, N=0. Missing values are indicated by "9999".

[41] - Patients analyzed in each category: N=1, N=0, N=0. Missing values are indicated by "9999".

[42] - Patients analyzed in each category: N=9, N=6, N=6

[43] - Patients analyzed in each category: N=4, N=3, N=3

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Plasma Enzalutamide: Segment 2

End point title	Cmax of Plasma Enzalutamide: Segment 2 ^[44]
End point description: Maximum observed concentration over the dosing interval. Patients in Arm B did not receive dose escalations, but they were sampled for pharmacokinetic analysis on the same time frame as the Arm A patients: Cycle 1 Day 15, Week 4, and Week 6. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.	
End point type	Secondary
End point timeframe: Predose and at time intervals up to 6 hours on Cycle 1 Day 15 (before dose escalation) and at 2 weeks after each dose escalation (Week 4 for escalation from 240 mg to 280 mg exicorilant and Week 6 for escalation from 280 mg to 320 mg exicorilant)	
Notes: [44] - 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: This end point reports results for Segment 2 only.	

End point values	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[45]	1 ^[46]	9 ^[47]	5 ^[48]
Units: ng/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15 before dose escalation	17609 (± 28.3)	16800 (± 9999)	18004 (± 25.6)	18440 (± 15.2)
After 240 to 280 mg dose escalation	27000 (± 9999)	9999 (± 9999)	18899 (± 17.9)	18408 (± 22.8)
After 280 to 320 mg dose escalation	9999 (± 9999)	9999 (± 9999)	20235 (± 13.2)	18157 (± 17.0)

Notes:

[45] - Patients analyzed in each category: N=4, N=1, N=0. Missing values are indicated by "9999".

[46] - Patients analyzed in each category: N=1, N=0, N=0. Missing values are indicated by "9999".

[47] - Patients analyzed in each category: N=9, N=6, N=6

[48] - Patients analyzed in each category: N=4, N=3, N=3

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Plasma N-Desmethyl Enzalutamide: Segment 2

End point title	AUC of Plasma N-Desmethyl Enzalutamide: Segment 2 ^[49]
End point description: AUC from time zero to 6 hours postdose (AUC0-6) calculated using linear up and log down method. Patients in Arm B did not receive dose escalations, but they were sampled for pharmacokinetic analysis on the same time frame as the Arm A patients: Cycle 1 Day 15, Week 4, and Week 6. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.	
End point type	Secondary
End point timeframe: Predose and at time intervals up to 6 hours on Cycle 1 Day 15 (before dose escalation) and at 2 weeks after each dose escalation (Week 4 for escalation from 240 mg to 280 mg exicorilant and Week 6 for escalation from 280 mg to 320 mg exicorilant)	

Notes:

[49] - 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: This end point reports results for Segment 2 only.

End point values	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[50]	1 ^[51]	9 ^[52]	5 ^[53]
Units: ng-hr/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15 before dose escalation	67872 (± 7.0)	34131 (± 9999)	50752 (± 20.6)	49744 (± 21.0)
After 240 to 280 mg dose escalation	49995 (± 9999)	9999 (± 9999)	51977 (± 22.0)	50353 (± 28.2)
After 280 to 320 mg dose escalation	9999 (± 9999)	9999 (± 9999)	48255 (± 11.2)	48411 (± 20.6)

Notes:

[50] - Patients analyzed in each category: N=4, N=1, N=0. Missing values are indicated by "9999".

[51] - Patients analyzed in each category: N=1, N=0, N=0. Missing values are indicated by "9999".

[52] - Patients analyzed in each category: N=9, N=6, N=6

[53] - Patients analyzed in each category: N=4, N=3, N=3

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Plasma N-Desmethyl Enzalutamide: Segment 2

End point title	Cmax of Plasma N-Desmethyl Enzalutamide: Segment 2 ^[54]
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End point description:

Maximum observed concentration over the dosing interval. Patients in Arm B did not receive dose escalations, but they were sampled for pharmacokinetic analysis on the same time frame as the Arm A patients: Cycle 1 Day 15, Week 4, and Week 6. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 6 hours on Cycle 1 Day 15 (before dose escalation) and at 2 weeks after each dose escalation (Week 4 for escalation from 240 mg to 280 mg exicorilant and Week 6 for escalation from 280 mg to 320 mg exicorilant)

Notes:

[54] - 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: This end point reports results for Segment 2 only.

End point values	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[55]	1 ^[56]	9 ^[57]	5 ^[58]
Units: ng/ml				

geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15 before dose escalation	12448 ($\pm$ 7.7)	6520 ($\pm$ 9999)	9350 ($\pm$ 22.8)	10116 ($\pm$ 24.3)
After 240 to 280 mg dose escalation	8600 ($\pm$ 9999)	9999 ($\pm$ 9999)	9682 ($\pm$ 20.4)	9873 ($\pm$ 28.4)
After 280 to 320 mg dose escalation	9999 ($\pm$ 9999)	9999 ($\pm$ 9999)	8870 ($\pm$ 13.4)	9185 ($\pm$ 23.8)

Notes:

[55] - Patients analyzed in each category: N=4, N=1, N=0. Missing values are indicated by "9999".

[56] - Patients analyzed in each category: N=1, N=0, N=0. Missing values are indicated by "9999".

[57] - Patients analyzed in each category: N=9, N=6, N=6

[58] - Patients analyzed in each category: N=4, N=3, N=3

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Plasma Enzalutamide Carboxylic Acid: Segment 2

End point title	AUC of Plasma Enzalutamide Carboxylic Acid: Segment 2 ^[59]
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End point description:

AUC from time zero to 6 hours postdose (AUC0-6) calculated using linear up and log down method. Patients in Arm B did not receive dose escalations, but they were sampled for pharmacokinetic analysis on the same time frame as the Arm A patients: Cycle 1 Day 15, Week 4, and Week 6. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 6 hours on Cycle 1 Day 15 (before dose escalation) and at 2 weeks after each dose escalation (Week 4 for escalation from 240 mg to 280 mg exicorilant and Week 6 for escalation from 280 mg to 320 mg exicorilant)

Notes:

[59] - 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: This end point reports results for Segment 2 only.

End point values	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[60]	1 ^[61]	9 ^[62]	5 ^[63]
Units: ng-hr/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15 before dose escalation	25662 ($\pm$ 55.7)	14108 ($\pm$ 9999)	24863 ($\pm$ 41.6)	19310 ($\pm$ 56.9)
After 240 to 280 mg dose escalation	86613 ($\pm$ 9999)	9999 ($\pm$ 9999)	25995 ($\pm$ 42.6)	23393 ($\pm$ 21.1)
After 280 to 320 mg dose escalation	9999 ($\pm$ 9999)	9999 ($\pm$ 9999)	31814 ($\pm$ 20.8)	18047 ($\pm$ 43.6)

Notes:

[60] - Patients analyzed in each category: N=4, N=1, N=0. Missing values are indicated by "9999".

[61] - Patients analyzed in each category: N=1, N=0, N=0. Missing values are indicated by "9999".

[62] - Patients analyzed in each category: N=9, N=6, N=6

[63] - Patients analyzed in each category: N=4, N=3, N=3

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Plasma Enzalutamide Carboxylic Acid: Segment 2

End point title	Cmax of Plasma Enzalutamide Carboxylic Acid: Segment 2 ^[64]
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End point description:

Maximum observed concentration over the dosing interval. Patients in Arm B did not receive dose escalations, but they were sampled for pharmacokinetic analysis on the same time frame as the Arm A patients: Cycle 1 Day 15, Week 4, and Week 6. The PK-Evaluable Population included all patients who received active study treatment and had measurable plasma concentration of study treatment at any time point.

End point type	Secondary
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End point timeframe:

Predose and at time intervals up to 6 hours on Cycle 1 Day 15 (before dose escalation) and at 2 weeks after each dose escalation (Week 4 for escalation from 240 mg to 280 mg exicorilant and Week 6 for escalation from 280 mg to 320 mg exicorilant)

Notes:

[64] - 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: This end point reports results for Segment 2 only.

End point values	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 ^[65]	1 ^[66]	9 ^[67]	5 ^[68]
Units: ng/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15 before dose escalation	4693 (± 50.8)	2480 (± 9999)	4572 (± 40.8)	3713 (± 58.3)
After 240 to 280 mg dose escalation	15400 (± 9999)	9999 (± 9999)	4821 (± 43.1)	4745 (± 15.1)
After 280 to 320 mg dose escalation	9999 (± 9999)	9999 (± 9999)	6032 (± 24.8)	3524 (± 44.1)

Notes:

[65] - Patients analyzed in each category: N=4, N=1, N=0. Missing values are indicated by "9999".

[66] - Patients analyzed in each category: N=1, N=0, N=0. Missing values are indicated by "9999".

[67] - Patients analyzed in each category: N=9, N=6, N=6

[68] - Patients analyzed in each category: N=4, N=3, N=3

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
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End point description:

Confirmed ORR is defined as the proportion of patients with measurable disease at Baseline who achieved a complete regression (CR) or partial regression (PR) by Prostate Cancer Clinical Trials Working Group 3 (PCWG3) / Modified Response Evaluation Criteria in Solid Tumors v1.1 (mRECIST) criteria, after confirmation. The Response-Evaluable (RE) Population included all patients who received ≥1 dose of the combination (exicorilant + enzalutamide) study treatment and had measurable disease at Baseline.

End point type	Secondary
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End point timeframe:

Up to 22 months

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	0 ^[69]	5	3
Units: Patients	1		1	0

Notes:

[69] - No patients with measurable disease at Baseline

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[70]	6	1	
Units: Patients		0	0	

Notes:

[70] - No patients with measurable disease at Baseline

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With ≥50% Reduction in Prostate-Specific Antigen (PSA)

End point title	Number of Patients With ≥50% Reduction in Prostate-Specific Antigen (PSA)
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End point description:

The Intent-to-treat (ITT) Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.

End point type	Secondary
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End point timeframe:

Up to 39 months

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	7	8
Units: Patients	2	0	3	0

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	10	6	
Units: Patients	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PSA Progression

End point title	Time to PSA Progression
End point description:	
Assess the time to PSA progression defined as the first occurrence of 50% or greater increase in PSA levels. Kaplan-Meier estimates of time to PSA progression were calculated as (earliest date of PSA progression or censoring - date of first study treatment + 1)/30.4375. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.	
End point type	Secondary
End point timeframe:	
Up to 39 months	

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[71]	3 ^[72]	7 ^[73]	8 ^[74]
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (0.99 to 9999)	38.90 (0.99 to 9999)	1.43 (0.49 to 9999)

Notes:

[71] - Missing values are indicated by "9999".

[72] - Missing values are indicated by "9999".

[73] - Missing values are indicated by "9999".

[74] - Missing values are indicated by "9999".

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[75]	10 ^[76]	6 ^[77]	
Units: months				
median (confidence interval 95%)	1.41 (-9999 to 9999)	1.41 (0.49 to 9999)	3.25 (0.95 to 9999)	

Notes:

[75] - Missing values are indicated by "9999".

[76] - Missing values are indicated by "9999".

[77] - Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients Who Are Progression-Free by PSA Criteria at 4, 6, and 12 Months

End point title	Percentage of Patients Who Are Progression-Free by PSA Criteria at 4, 6, and 12 Months
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End point description:

Assess the percentage of patients who are progression-free by PSA criteria, or death. PSA progression was defined as the first occurrence of 50% or greater increase in PSA levels. Values are Kaplan-Meier estimates of the patients progression free at the time points specified. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.

End point type	Secondary
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End point timeframe:

4, 6, and 12 months

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[78]	3 ^[79]	7	8 ^[80]
Units: Percentage of patients				
number (confidence interval 95%)				
4 months	0 (-9999 to 9999)	9999 (9999 to 9999)	85.71 (33.41 to 97.86)	0 (-9999 to 9999)
6 months	0 (-9999 to 9999)	9999 (9999 to 9999)	85.71 (33.41 to 97.86)	0 (-9999 to 9999)
12 months	0 (-9999 to 9999)	9999 (9999 to 9999)	85.71 (33.41 to 97.86)	0 (-9999 to 9999)

Notes:

[78] - Missing values are indicated by "9999".

[79] - Missing values are indicated by "9999".

[80] - Missing values are indicated by "9999".

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[81]	10	6	
Units: Percentage of patients				
number (confidence interval 95%)				

4 months	0 (-9999 to 9999)	40.00 (12.27 to 67.02)	50.00 (11.09 to 80.37)	
6 months	0 (-9999 to 9999)	40.00 (12.27 to 67.02)	33.33 (4.61 to 67.56)	
12 months	0 (-9999 to 9999)	26.67 (4.76 to 56.34)	16.67 (0.77 to 51.68)	

Notes:

[81] - Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Symptomatic Skeletal Event (SSE)

End point title	Time to First Symptomatic Skeletal Event (SSE)
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End point description:

Assess the time to first SSE defined as symptomatic fracture, radiation or surgery to bone, or spinal cord compression. Kaplan-Meier estimates of time to first SSE were calculated as (earliest date of SSE or censoring - date of first study treatment + 1)/30.4375. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.

End point type	Secondary
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End point timeframe:

Up to 39 months

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[82]	3 ^[83]	7 ^[84]	8 ^[85]
Units: months				
median (confidence interval 95%)	0 (-9999 to 9999)	9999 (2.83 to 9999)	9999 (25.79 to 9999)	9999 (9999 to 9999)

Notes:

[82] - Missing values are indicated by "9999".

[83] - Missing values are indicated by "9999".

[84] - Missing values are indicated by "9999".

[85] - Missing values are indicated by "9999".

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[86]	10 ^[87]	6 ^[88]	
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	

Notes:

[86] - Missing values are indicated by "9999".

[87] - Missing values are indicated by "9999".

[88] - Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression by Radiographic Criteria

End point title	Time to Progression by Radiographic Criteria
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End point description:

Assess radiographic progression free survival (PFS) defined as the time interval from first dose of study drug (exicorilant and/or enzalutamide) to the date when the first site of disease progression was found on computerized tomography (CT), magnetic resonance imaging (MRI), or radionuclide bone scan per PCWG3/mRECIST v1.1, or death whichever occurred first. The data values are Kaplan-Meier estimates. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.

End point type	Secondary
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End point timeframe:

Up to 22 months

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[89]	3 ^[90]	7 ^[91]	8 ^[92]
Units: months				
median (confidence interval 95%)	18.46 (-9999 to 9999)	1.81 (0.82 to 9999)	6.21 (0.49 to 9999)	5.55 (1.02 to 9999)

Notes:

[89] - Missing values are indicated by "9999".

[90] - Missing values are indicated by "9999".

[91] - Missing values are indicated by "9999".

[92] - Missing values are indicated by "9999".

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[93]	10 ^[94]	6 ^[95]	
Units: months				
median (confidence interval 95%)	0 (-9999 to 9999)	5.08 (1.02 to 9999)	9999 (3.91 to 9999)	

Notes:

[93] - Missing values are indicated by "9999".

[94] - Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients Who Are Progression-Free by Radiographic Criteria at 4, 6, and 12 Months

End point title	Percentage of Patients Who Are Progression-Free by Radiographic Criteria at 4, 6, and 12 Months
End point description: Assess the percentage of patients who were progression-free by radiographic criteria per PCWG3/RECIST v1.1, or death whichever occurred first. Values are Kaplan-Meier estimates of the patients progression free at the time points specified. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.	
End point type	Secondary
End point timeframe: 4, 6, and 12 months	

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[96]	3 ^[97]	7	8 ^[98]
Units: Percentage of patients				
number (confidence interval 95%)				
4 months	100.0 (100.0 to 100.0)	0 (-9999 to 9999)	83.33 (27.31 to 97.47)	62.50 (14.19 to 89.31)
6 months	100.0 (100.0 to 100.0)	0 (-9999 to 9999)	62.50 (14.19 to 89.31)	0 (-9999 to 9999)
12 months	100.0 (100.0 to 100.0)	0 (-9999 to 9999)	41.67 (5.60 to 76.65)	0 (-9999 to 9999)

Notes:

[96] - Missing values are indicated by "9999".

[97] - Missing values are indicated by "9999".

[98] - Missing values are indicated by "9999".

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[99]	10	6	
Units: Percentage of patients				
number (confidence interval 95%)				

4 months	0 (-9999 to 9999)	66.67 (28.17 to 87.83)	83.33 (27.31 to 97.47)	
6 months	0 (-9999 to 9999)	33.33 (5.26 to 66.38)	62.50 (14.19 to 89.31)	
12 months	0 (-9999 to 9999)	33.33 (5.26 to 66.38)	62.50 (14.19 to 89.31)	

Notes:

[99] - Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression by Clinical or Radiographic Criteria

End point title	Time to Progression by Clinical or Radiographic Criteria
End point description:	
Determine PFS by clinical or radiographic criteria, or death, whichever occurred first. Clinical progression was defined as treatment discontinuation due to disease progression by investigator assessment per PCWG3/mRECIST v1.1, or by PSA criteria. The data values are Kaplan-Meier estimates. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.	
End point type	Secondary
End point timeframe:	
Up to 22 months	

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[100]	3 ^[101]	7 ^[102]	8 ^[103]
Units: months				
median (confidence interval 95%)	18.46 (-9999 to 9999)	1.81 (0.82 to 9999)	6.21 (0.49 to 9999)	1.84 (0.99 to 9999)

Notes:

[100] - Missing values are indicated by "9999".

[101] - Missing values are indicated by "9999".

[102] - Missing values are indicated by "9999".

[103] - Missing values are indicated by "9999".

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[104]	10 ^[105]	6 ^[106]	
Units: months				
median (confidence interval 95%)	0 (-9999 to 9999)	3.68 (1.02 to 9999)	9999 (3.91 to 9999)	

Notes:

[104] - Missing values are indicated by "9999".

[105] - Missing values are indicated by "9999".

[106] - Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients Who Are Progression-Free by Clinical or Radiographic Criteria at 4, 6, and 12 Months

End point title	Percentage of Patients Who Are Progression-Free by Clinical or Radiographic Criteria at 4, 6, and 12 Months
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End point description:

Assess the percentage of patients who were progression-free by clinical or radiographic measures at 4, 6, and 12 months. Values are Kaplan-Meier estimates of the patients progression free at the time points specified. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.

End point type	Secondary
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End point timeframe:

4, 6, and 12 months

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3 ^[107]	7	8 ^[108]
Units: Percentage of patients				
number (confidence interval 95%)				
4 months	100.0 (100.0 to 100.0)	0 (-9999 to 9999)	83.33 (27.31 to 97.47)	44.44 (6.62 to 78.49)
6 months	100.0 (100.0 to 100.0)	0 (-9999 to 9999)	62.50 (14.19 to 89.31)	0 (-9999 to 9999)
12 months	100.0 (100.0 to 100.0)	0 (-9999 to 9999)	41.67 (5.60 to 76.65)	0 (-9999 to 9999)

Notes:

[107] - Missing values are indicated by "9999".

[108] - Missing values are indicated by "9999".

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[109]	10	6	
Units: Percentage of patients				
number (confidence interval 95%)				
4 months	0 (-9999 to 9999)	50.00 (18.36 to 75.32)	83.33 (27.31 to 97.47)	

6 months	0 (-9999 to 9999)	33.33 (6.33 to 64.58)	62.50 (14.19 to 89.31)	
12 months	0 (-9999 to 9999)	33.33 (6.33 to 64.58)	62.50 (14.19 to 89.31)	

Notes:

[109] - Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression by Clinical or Biochemical Criteria

End point title	Time to Progression by Clinical or Biochemical Criteria
End point description:	
Determine PFS by clinical criteria or biochemical criteria (defined as treatment discontinuation due to clinical progression by investigator assessment, or by PSA criteria) PCWG3/mRECIST v1.1, or death whichever occurred first. The data values are Kaplan-Meier estimates. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.	
End point type	Secondary
End point timeframe:	
Up to 33 months	

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[110]	3 ^[111]	7 ^[112]	8 ^[113]
Units: months				
median (confidence interval 95%)	32.72 (-9999 to 9999)	5.85 (-9999 to 9999)	11.96 (3.68 to 9999)	3.55 (0.99 to 9999)

Notes:

[110] - Missing values are indicated by "9999."

[111] - Missing values are indicated by "9999."

[112] - Missing values are indicated by "9999."

[113] - Missing values are indicated by "9999."

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[114]	10	6 ^[115]	
Units: months				
median (confidence interval 95%)	0 (-9999 to 9999)	6.77 (1.41 to 16.53)	9999 (4.86 to 9999)	

Notes:

[114] - Missing values are indicated by "9999."

[115] - Missing values are indicated by "9999."

Statistical analyses

Secondary: Percentage of Patients Who Are Progression-Free by Clinical or Biochemical Criteria at 4, 6, and 12 Months

End point title	Percentage of Patients Who Are Progression-Free by Clinical or Biochemical Criteria at 4, 6, and 12 Months
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End point description:

Assess the percentage of patients who are progression-free by clinical or biochemical criteria (defined as treatment discontinuation due to clinical progression by investigator assessment or by PSA criteria) PCWG3/mRECIST v1.1, or death whichever occurred first at 4, 6, and 12 months. Values are Kaplan-Meier estimates of the patients progression free at the time points specified. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.

End point type	Secondary
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End point timeframe:

4, 6, and 12 months

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3 ^[116]	7	8 ^[117]
Units: Percentage of patients				
number (confidence interval 95%)				
4 months	100.0 (100.0 to 100.0)	100.0 (100.0 to 100.0)	80.00 (20.38 to 96.92)	41.67 (1.12 to 84.31)
6 months	100.0 (100.0 to 100.0)	0 (-9999 to 9999)	60.00 (12.57 to 88.18)	9999 (9999 to 9999)
12 months	100.0 (100.0 to 100.0)	0 (-9999 to 9999)	40.00 (5.20 to 75.28)	9999 (9999 to 9999)

Notes:

[116] - Missing values are indicated by "9999".

[117] - Missing values are indicated by "9999".

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[118]	10	6	
Units: Percentage of patients				
number (confidence interval 95%)				
4 months	0 (-9999 to 9999)	70.00 (32.87 to 89.19)	100.0 (100.0 to 100.0)	
6 months	0 (-9999 to 9999)	58.33 (22.98 to 82.07)	75.00 (12.79 to 96.05)	
12 months	0 (-9999 to 9999)	35.00 (8.48 to 63.98)	75.00 (12.79 to 96.05)	

Notes:

[118] - Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)
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End point description:

Determine the DOR as defined as the time from the first occurrence of a documented objective tumor response to the time of radiographic progression (per investigator using PCWG3/mRECIST v1.1 criteria) or death from any cause on study, whichever occurred first. DOR was calculated as (earliest date of progression, death, or censoring - date of first documented objective response +1)/30.4375. The data values are Kaplan-Meier estimates. The population analyzed included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment (ITT Population) and had an uncensored response (CR or PR).

End point type	Secondary
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End point timeframe:

Up to 11 months

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[119]	0 ^[120]	1 ^[121]	0 ^[122]
Units: months				
median (confidence interval 95%)	(to)	(to)	10.97 (-9999 to 9999)	(to)

Notes:

[119] - No patients had an uncensored response.

[120] - No patients had an uncensored response.

[121] - Missing values are indicated by "9999".

[122] - No patients had an uncensored response.

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[123]	0 ^[124]	0 ^[125]	
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[123] - No patients had an uncensored response.

[124] - No patients had an uncensored response.

[125] - No patients had an uncensored response.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

Determine OS assessed as the time from the first dose of study drug (exicorilant and/or enzalutamide) to the date of death from any cause. The data values are Kaplan-Meier estimates. The ITT Population included all patients who received at least 1 dose of the combination (exicorilant + enzalutamide) study treatment.

End point type	Secondary
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End point timeframe:

Up to 52 months

End point values	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[126]	3 ^[127]	7 ^[128]	8 ^[129]
Units: months				
median (confidence interval 95%)	32.72 (-9999 to 9999)	9999 (5.85 to 9999)	13.73 (4.63 to 9999)	9999 (3.55 to 9999)

Notes:

[126] - Missing values are indicated by "9999".

[127] - Missing values are indicated by "9999".

[128] - Missing values are indicated by "9999".

[129] - Missing values are indicated by "9999".

End point values	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant	Segment 2: Arm B - 240 mg Exicorilant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1 ^[130]	10 ^[131]	6 ^[132]	
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	13.96 (4.47 to 9999)	17.23 (10.02 to 9999)	

Notes:

[130] - Missing values are indicated by "9999".

[131] - Missing values are indicated by "9999".

[132] - Missing values are indicated by "9999".

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were reported from randomization up to 27 months for Segment 1 and up to 19 months for Segment 2. All-cause mortality was reported from enrollment up to 52 months.

Adverse event reporting additional description:

The population analyzed was the Safety Population, including all patients who received ≥ 1 dose of exicorilant.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	≥ 20.1
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Reporting groups

Reporting group title	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant
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Reporting group description:

Patients in this dose determination cohort received lead-in enzalutamide monotherapy once daily for 28 days. Patients then received combination treatment with twice-daily exicorilant 180 mg (total daily dose 360 mg) and enzalutamide once daily in 28-day dosing cycles.

Reporting group title	Segment 1 (Open label) Cohort 2 - 280 mg Exicorilant
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Reporting group description:

Patients in this dose determination cohort received lead-in enzalutamide monotherapy once daily for 28 days. Patients then received combination treatment with twice-daily exicorilant 140 mg (total daily dose 280 mg) and enzalutamide once daily in 28-day dosing cycles.

Reporting group title	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant
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Reporting group description:

Patients in this dose determination cohort did not receive lead-in enzalutamide monotherapy. Patients received combination treatment with twice-daily exicorilant 140 mg (total daily dose 280 mg) and enzalutamide once daily in 28-day dosing cycles.

Reporting group title	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant
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Reporting group description:

Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 240 mg exicorilant.

Reporting group title	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant
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Reporting group description:

Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 280 mg exicorilant.

Reporting group title	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant
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Reporting group description:

Patients in this dose determination arm received treatment with once-daily exicorilant starting at 240 mg and titrating to 280 mg and then to 320 mg at 2-week intervals, as tolerated, in combination with enzalutamide once daily in 28-day dosing cycles. Patients in this arm are reported at the highest titrated dose of exicorilant achieved: 320 mg exicorilant.

Reporting group title	Segment 2: Arm B - 240 mg Exicorilant
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Reporting group description:

Patients in this dose determination arm received combination treatment with once-daily exicorilant 240 mg, enzalutamide once daily, and placebo in 28-day dosing cycles.

Serious adverse events	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	2 / 7 (28.57%)
number of deaths (all causes)	1	1	5
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
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			
Fatigue			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 7 (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
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (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			
Urinary retention			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (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 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (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 / 7 (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 pain			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (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	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	2 / 10 (20.00%)
number of deaths (all causes)	1	0	5
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (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			

Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (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			
Pancreatitis acute			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (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			
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (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			
Urinary retention			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (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 pain			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (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			
Sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Segment 2: Arm B - 240 mg Exicorilant		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 6 (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 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 6 (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	Segment 1 (Open-label) Cohort 1 - 360 mg Exicorilant	Segment 1 (Open-label) Cohort 2 - 280 mg Exicorilant	Segment 1 (Open-label) Cohort 3 - 280 mg Exicorilant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	3 / 3 (100.00%)	7 / 7 (100.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps) Cancer pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 3 (33.33%) 1	1 / 7 (14.29%) 4
Deep vein thrombosis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Hot flush subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Hypotension subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Lymphoedema subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	2 / 2 (100.00%) 6	0 / 3 (0.00%) 0	4 / 7 (57.14%) 6
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 2	1 / 3 (33.33%) 1	0 / 7 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1

Peripheral swelling subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Chills subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Gait disturbance subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Dyspnoea subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0	1 / 7 (14.29%) 3
Wheezing subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 2
Bronchospasm subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 2
Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 2	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Dysphonia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract congestion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pulmonary fibrosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Lipase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	2	0	2
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	3
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Lymphocyte count decreased			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Troponin increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Incision site pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Procedural pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Fall subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Meniscus injury subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Radiation skin injury subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Spinal fracture subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 2
Tachycardia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Palpitations subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0	2 / 7 (28.57%) 2
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Dizziness			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	3
Dysgeusia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Neuralgia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Restless legs syndrome			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dysarthria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dysmetria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Visual field defect			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Aphasia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Memory impairment			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Transient ischaemic attack			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dry eye			

subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Ocular hyperaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	3 / 7 (42.86%)
occurrences (all)	0	1	3
Abdominal pain			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	2	1	1
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Abdominal discomfort			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Dental caries subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Dental necrosis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Dysphagia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 2
Flatulence subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 3 (33.33%) 1	1 / 7 (14.29%) 1
Dry skin subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1
Skin lesion subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Milia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Nail disorder			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Nail ridging subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Renal and urinary disorders			
Haematuria subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Proteinuria subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Nocturia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Micturition frequency decreased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Urinary hesitation subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	2 / 2 (100.00%) 2	1 / 3 (33.33%) 1	4 / 7 (57.14%) 7
Pain in extremity subjects affected / exposed occurrences (all)	2 / 2 (100.00%) 8	1 / 3 (33.33%) 1	0 / 7 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 3 (33.33%) 1	1 / 7 (14.29%) 2
Musculoskeletal chest pain			

subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Musculoskeletal pain			
subjects affected / exposed	2 / 2 (100.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	4	0	0
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pain in jaw			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Arthritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Synovitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 2 (50.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Furuncle			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
COVID-19			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 2 (50.00%)	2 / 3 (66.67%)	1 / 7 (14.29%)
occurrences (all)	2	2	1
Hyperglycaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypermagnesaemia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Segment 2: Arm A - Maximum Dose 240 mg Exicorilant	Segment 2: Arm A - Maximum Dose 280 mg Exicorilant	Segment 2: Arm A - Maximum Dose 320 mg Exicorilant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	1 / 1 (100.00%)	10 / 10 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 8 (62.50%)	0 / 1 (0.00%)	6 / 10 (60.00%)
occurrences (all)	6	0	7
Non-cardiac chest pain			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Asthenia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Gait disturbance subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	2 / 10 (20.00%) 3
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	2 / 10 (20.00%) 3
Dyspnoea			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Bronchospasm			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lower respiratory tract congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pulmonary fibrosis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Irritability			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Lipase increased			

subjects affected / exposed	3 / 8 (37.50%)	1 / 1 (100.00%)	0 / 10 (0.00%)
occurrences (all)	5	1	0
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	3
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Alanine aminotransferase increased			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Amylase increased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Troponin increased			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Injury, poisoning and procedural complications			
Incision site pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Procedural pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Meniscus injury subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Radiation skin injury subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Spinal fracture subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Cardiac disorders			
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Tachycardia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
Dysgeusia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Restless legs syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysmetria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Tremor			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Visual field defect			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Memory impairment			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Transient ischaemic attack			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 8 (25.00%)	1 / 1 (100.00%)	3 / 10 (30.00%)
occurrences (all)	3	1	3
Ear and labyrinth disorders			

Ear congestion subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Ear discomfort subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 2
Ear pain subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Eye disorders			
Vision blurred subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Dry eye subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Periorbital oedema subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Ocular hyperaemia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Visual acuity reduced subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	0 / 1 (0.00%) 0	4 / 10 (40.00%) 6
Abdominal pain subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	1 / 1 (100.00%) 2	0 / 10 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	1 / 1 (100.00%) 2	2 / 10 (20.00%) 3
Diarrhoea			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dental necrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Dry skin			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Milia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nail disorder			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nail ridging			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Pollakiuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Proteinuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Nocturia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Micturition frequency decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 8 (50.00%)	1 / 1 (100.00%)	5 / 10 (50.00%)
occurrences (all)	7	3	7
Pain in extremity			
subjects affected / exposed	4 / 8 (50.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	7	0	4
Arthralgia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Musculoskeletal pain			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Muscular weakness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Flank pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Pain in jaw			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Arthritis			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Groin pain subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Synovitis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Furuncle subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	0 / 10 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Laryngitis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Sinusitis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 1 (0.00%) 0	1 / 10 (10.00%) 1
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 1 (0.00%) 0	3 / 10 (30.00%) 3
Hyperglycaemia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypermagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Segment 2: Arm B - 240 mg Exicorilant		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hot flush			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Lymphoedema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 6 (83.33%)		
occurrences (all)	13		
Non-cardiac chest pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gait disturbance			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Influenza like illness			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bronchospasm			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lower respiratory tract congestion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pulmonary fibrosis			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Investigations			
Lipase increased			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	4		
Weight decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	4		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood phosphorus decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Troponin increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Incision site pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Meniscus injury			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Radiation skin injury			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Spinal fracture			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Lethargy			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Restless legs syndrome			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dysarthria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysmetria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Visual field defect			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Aphasia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Memory impairment			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Sensory disturbance			

subjects affected / exposed occurrences (all) 0 / 6 (0.00%) 0			
Syncope subjects affected / exposed occurrences (all) 0 / 6 (0.00%) 0			
Transient ischaemic attack subjects affected / exposed occurrences (all) 0 / 6 (0.00%) 0			
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) 2 / 6 (33.33%) 2			
Ear and labyrinth disorders Ear congestion subjects affected / exposed occurrences (all) 1 / 6 (16.67%) 1 Ear discomfort subjects affected / exposed occurrences (all) 0 / 6 (0.00%) 0 Ear pain subjects affected / exposed occurrences (all) 0 / 6 (0.00%) 0			
Eye disorders Vision blurred subjects affected / exposed occurrences (all) 1 / 6 (16.67%) 1 Dry eye subjects affected / exposed occurrences (all) 0 / 6 (0.00%) 0 Periorbital oedema subjects affected / exposed occurrences (all) 0 / 6 (0.00%) 0 Ocular hyperaemia subjects affected / exposed occurrences (all) 0 / 6 (0.00%) 0 Visual acuity reduced			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	6		
Abdominal pain			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dental caries			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dental necrosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Milia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nail disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nail ridging			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pollakiuria			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nocturia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Micturition frequency decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Urinary hesitation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 6 (83.33%)		
occurrences (all)	8		
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	3		
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Myalgia			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Arthritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Synovitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Furuncle			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Laryngitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hypercalcaemia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	4		
Hypoalbuminaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypermagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 September 2017	- Modified the duration of enzalutamide lead-in for patients in the Dose Escalation Phase from 21 days to 28 days to ensure enzalutamide and its metabolites reach steady state on Cycle 1 Day -1 (Section 3.1) - Clarified that patients who have received prior 2nd generation anti-androgen and require urgent disease stabilization will be excluded from Dose Escalation and Cohort A and patients who require urgent disease stabilization will be excluded from Cohort B (Exclusion Criterion 3) - Revised the dose escalation rules (Table 6) to allow no more than a 50% dose increase after observing a related Grade 2 toxicity or DLT (Section 5.4) - Provided additional rationale to support the selection of the starting dose (Section 1.5.2) - Modified the definition of DLTs to include additional DLT criteria and to include only those toxicities that the investigator believes are possibly or probably related to the study drug (Section 5.5) - Revisions to Dose Modifications or Delays (Section 5.7) - As patients with CRPC may have received glucocorticoids previously, Inclusion Criterion 12 has been added to specify that patients receiving glucocorticoids greater than 2-weeks in duration within 6 months of study entry must have evidence of adequate adrenal function.
19 December 2017	- Section 5.6 has been amended to clarify that the recommended Phase 2 dose (RD) will always be less than or equal to the MTD. Thus, the recommended phase 2 dose will have a DLT rate of <33%, in keeping with the European definition of MTD. - Sections 8.1.2 and 8.2.2 have been amended to provide more detail for adverse event reporting for the following: 1) events due to progression, 2) documentation of death, including death due to progression of the cancer under study, and 3) reporting of serious adverse reactions deemed related to study drug. - Section 8.4 has been deleted to remove the statement that progression of the malignancy under study is not an AE, and therefore, not a serious adverse event (SAE) per se. Individual cases of progression deemed related to study drug will be recorded as adverse drug reactions; as consistent with the management of all AEs/SAEs that occur during the study.
09 January 2018	- Added clarification that initial dosing for the first 3 patients within a dose level (in Dose Escalation) will have a minimum of one day between Cycle 1 Day 1 for each patient. - Updated protocol and title to Phase 1/2a, and clarified the focus of the statistical methods on estimation of safety, tolerability and preliminary efficacy - Clarified that the number of patients in the Dose Escalation phase will depend on the number of dose levels assessed and the DLTs observed. Updated the study sample size section to state the statistical power of the study and the level of evidence in the data that will support further evaluation of the regimen in the clinical program. - Modified starting dose of CORT125281 to 180mg twice daily (360mg total daily dose) based upon the latest data from the ongoing Phase 1 study in healthy subjects. - Added 12 hour PK collection timepoints in the Dose Escalation and Dose Expansion cohorts to align with the latest data from the ongoing Phase 1 study in healthy subjects and the change to twice daily dosing of CORT125281. - Clarified the following: 1) Survival follow up period to continue every 4 months until 2 years from the date that the last patient enrolls in the study or until all patients have completed follow-up for radiographic disease progression (whichever is later). 2) Added dosing timing and windows along with instructions for missed doses. 3) Clarified procedures for collecting vital signs blood samples, and quality of life (FACT-P questionnaire). 4) Corrected collection of on-study radiographic tumor assessments to occur every 8 weeks from the first dose of CORT125281 or enzalutamide, whichever is earlier.

25 July 2018	- Refine criteria within Section 4: Study Population, specifically Inclusion Criteria 7, 8, and 9 and Exclusion Criterion 13, to select patients for whom protocol treatment is considered appropriate and avoid excluding patients appropriate for the study - Modify Section 4: Study Population to specify windows for restricted medications relative to the first dose of CORT125281, and not enzalutamide (Exclusion Criteria 1, 4, 5, 11) - Clarify eligibility for patients in the Dose Escalation Phase (Exclusion Criterion 3) such that patients who have received enzalutamide, but who did not experience disease progression during treatment, may be considered eligible - Modify collection of Pharmacogenomics sample from optional to mandatory, due to data indicative of a possible relevant genetic polymorphism in a drug metabolizing pathway in the ongoing Phase 1 study in healthy volunteers. Inclusion Criterion 10 has been added to align with this change. - Modify the excluded period (washout) for restricted concomitant medications, to allow patients time to transition to alternative therapies during the screening period, with consideration for concomitant medication half-life and the timing of pharmacokinetic assessments (Exclusion Criteria 1, 10, 11) - Modify Inclusion Criterion 13 such that patients with clinical evidence of adrenal insufficiency will require demonstration of adequate adrenal function to be eligible. For patients receiving systemic corticosteroids prior to enrolling in CORT125281-601, the window for which demonstration of adequate adrenal function is required has been decreased from within 6 months to within 3 months, to better capture patients most likely to have adrenal suppression from treatment with corticosteroids.
21 February 2020	- Added a double-blind portion (Segment 2) to the Dose-Determination Phase to determine the recommended dose (RD) for CORT125281 administered once daily (QD) under fed conditions - Revised the wording for the other portions of the study for clarity, upon addition of Dose-Determination Phase Segment 2: 1) Changed the name for the "Dose-Escalation Phase" to "Dose-Determination Phase" to better capture the intent for this part of the study and renamed the first portion of the Dose-Determination Phase (the open-label portion) as "Segment 1" now that there are 2 segments in the Dose-Determination Phase. 2) Changed the name for the Expansion Phase cohorts to avoid confusion with Arms A and B in Dose-Determination Phase Segment 2 and renamed "Cohort A" as the Abiraterone (Abi)-Resistant Cohort and renamed "Cohort B" as the Androgen-Receptor (AR)-Resistant Cohort. - Updated eligibility criteria to allow patients with metastatic castration-resistant prostate cancer (mCRPC) with rising prostate-specific antigen (PSA) - Added the 40-mg softgel capsule formulation of CORT125281 and the placebo capsule - Revised the text related to the interim safety analyses to reflect that the Data Review Committee (DRC) will evaluate data from Dose-Determination Phase Segment 2 after all patients have completed 3 cycles of treatment in this part of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported