Clinical trial results:
A Phase II, Open-label Study to Assess the Efficacy, Safety, and Tolerability of AZD4635 in Combination with Durvalumab and in Combination with Cabazitaxel and Durvalumab in Patients Who Have Progressive Metastatic Castrate-Resistant Prostate Cancer (AARDVARC)

Summary

EudraCT number	2020-000209-10
Trial protocol	BE DE FR DK NL
Global end of trial date	08 August 2022

Results information

Result version number	v1 (current)
This version publication date	23 August 2023
First version publication date	23 August 2023

Trial information

Trial identification

Sponsor protocol code	D8731C00002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04495179
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	NA, NA, United States, NA
Public contact	Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, information.center@astrazeneca.com
Scientific contact	Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, information.center@astrazeneca.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	29 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy (as assessed by radiographic progression free survival [rPFS]) of AZD4635 plus durvalumab and separately of AZD4635 plus durvalumab plus cabazitaxel in participants with metastatic castrate-resistant prostate cancer (mCRPC).

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organisations of Medical Sciences (CIOMS) International Ethical Guidelines, applicable International Council for Harmonisation Good Clinical Practice (ICH GCP) Guidelines, and the applicable laws and regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 August 2020
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	Belgium: 4
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	30
EEA total number of subjects	15

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)	8
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled in this study from 04-August-2020 to 08-August-2022.

Pre-assignment

Screening details:

Participants who met the inclusion and none of the exclusion criteria were enrolled to the study. All study assessments were performed as per the schedule of assessment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: AZD4635 + durvalumab

Arm description:

Participants received AZD4635 Dose A orally daily, and durvalumab Dose B intravenously every 4 weeks.

Arm type	Experimental
Investigational medicinal product name	AZD4635
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants were administered AZD4635 75 mg tablets orally daily.

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Concentrate for solution for injection
Routes of administration	Oral use, Intravenous use

Dosage and administration details:

Participants were administered durvalumab 1500 mg intravenously (IV) every 4 weeks (Q4W).

Arm title	Arm B: AZD4635 + durvalumab + cabazitaxel

Arm description:

Participants received AZD4635 Dose A orally daily, durvalumab Dose B intravenously (IV) every 3 weeks (Q3W), and cabazitaxel Dose C IV Q3W

Arm type	Experimental
Investigational medicinal product name	AZD4635
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants were administered AZD4635 75 mg tablets orally daily.

Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Concentrate for solution for injection
Routes of administration	Oral use, Intravenous use

Dosage and administration details:

Participants were administered cabazitaxel 20 or 25 mg/m2 intravenously every 3 weeks (Q3W).

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants were administered durvalumab 1500 mg intravenously every 4 weeks.

Number of subjects in period 1	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel
Started	2	28
Completed	0	0
Not completed	2	28
Adverse event, serious fatal	-	4
Consent withdrawn by subject	2	4
Adverse event, non-fatal	-	1
Study terminated by sponsor	-	18
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: AZD4635 + durvalumab
Reporting group description:	
Participants received AZD4635 Dose A orally daily, and durvalumab Dose B intravenously every 4 weeks.	
Reporting group title	Arm B: AZD4635 + durvalumab + cabazitaxel
Reporting group description:	
Participants received AZD4635 Dose A orally daily, durvalumab Dose B intravenously (IV) every 3 weeks (Q3W), and cabazitaxel Dose C IV Q3W	

Reporting group values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel	Total
Number of subjects	2	28	30
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	7	8
From 65-84 years	1	21	22
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	0	68.0	
standard deviation	± 0	± 8.18	-
Sex/Gender, Customized Units: Participants			
Male	2	28	30
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	5	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	19	19
More than one race	0	0	0
Unknown or Not Reported	2	4	6
Ethnicity (NIH/OMB)			
The data for Arm A was not calculated because of only two participants in this arm due to which there will be a patient identification risk.			
Units: Subjects			
Hispanic or Latino	0	4	4
Not Hispanic or Latino	0	21	21

Unknown or Not Reported	2	3	5

End points

End points reporting groups

Reporting group title	Arm A: AZD4635 + durvalumab
Reporting group description:	
Participants received AZD4635 Dose A orally daily, and durvalumab Dose B intravenously every 4 weeks.	
Reporting group title	Arm B: AZD4635 + durvalumab + cabazitaxel
Reporting group description:	
Participants received AZD4635 Dose A orally daily, durvalumab Dose B intravenously (IV) every 3 weeks (Q3W), and cabazitaxel Dose C IV Q3W	

Primary: Radiographic Progression Free Survival (rPFS) in each arm separately to determine the efficacy of AZD4635 plus durvalumab and of AZD4635 plus durvalumab plus cabazitaxel in patients with metastatic castrate-resistant prostate cancer (mCRPC)

End point title	Radiographic Progression Free Survival (rPFS) in each arm separately to determine the efficacy of AZD4635 plus durvalumab and of AZD4635 plus durvalumab plus cabazitaxel in patients with metastatic castrate-resistant prostate cancer (mCRPC)[1]
End point description:	
rPFS was defined as the time from first dose to radiographic progression, assessed by the Investigator per RECIST 1.1 (soft tissue) and PCWG3 (Prostate Cancer Working Group 3) criteria [bone] or death from any cause, whichever occurred first.	
End point type	Primary
End point timeframe:	
From first dose to first documented progression or death from any cause (whichever comes first) (approximately 1 year)	

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: Statistical Analyses were not performed for these Outcome Measures as this study is non-comparative.

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	28[3]		
Units: months				
median (confidence interval 95%)	(to)	5.8 (4.2 to 9999.9999)		

Notes:

[2] - The data for Arm A was not calculated because of a patient identification risk.

[3] - "9999.9999" indicates that a upper limit was not calculated due to not enough events at later times.

Statistical analyses

No statistical analyses for this end point

Secondary: rPFS by adenosine (ADO) signalling gene expression in high and low

subgroups to determine the efficacy of AZD4635 plus durvalumab plus cabazitaxel in participants with mCRPC

End point title	rPFS by adenosine (ADO) signalling gene expression in high and low subgroups to determine the efficacy of AZD4635 plus durvalumab plus cabazitaxel in participants with mCRPC

End point description:

rPFS was defined as the time from first dose to radiographic progression, assessed by the Investigator per RECIST 1.1 (soft tissue) and PCWG3 criteria (bone) or death from any cause, whichever occurred first.

End point type	Secondary

End point timeframe:

From first dose to first documented progression or death from any cause (whichever comes first), up to two years

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	27		
Units: Participants				
High ADO		14		
Low ADO		13		

Notes:

[4] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS) in each arm separately to determine the efficacy of AZD4635 plus durvalumab and of AZD4635 plus durvalumab plus cabazitaxel in participants with mCRPC

End point title	Overall survival (OS) in each arm separately to determine the efficacy of AZD4635 plus durvalumab and of AZD4635 plus durvalumab plus cabazitaxel in participants with mCRPC

End point description:

OS was defined as the time from first dose until death due to any cause regardless of whether the participant withdrew from study treatment or received another anti-cancer therapy.

End point type	Secondary

End point timeframe:

Arm A and B: Every 90 days from the last dose of study drug up to 2 years

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	28[6]		
Units: months				
median (confidence interval 95%)	(to)	9999.9999 (7.9 to 9999.9999)		

Notes:

[5] - The data for Arm A was not calculated because of a patient identification risk.

[6] - "9999.9999" indicates that these values were not calculated as less than 50% patients died.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Objective Response in Subjects with MCRPC who received AZD4635 Plus Durvalumab Plus Cabazitaxel

End point title	Number of Subjects with Objective Response in Subjects with MCRPC who received AZD4635 Plus Durvalumab Plus Cabazitaxel

End point description:

Confirmed ORR was defined as the proportion of participants with a confirmed complete response (CR) or partial response (PR) using overall radiographic response assessed by RECIST v1.1 and PCWG-3 criteria (bone), and was based on a subset of all treated participants with measurable disease at baseline per the site Investigator.

End point type	Secondary

End point timeframe:

From first dose to first documented progression or death from any cause (whichever comes first), up to two years

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[7]	28		
Units: Participants		2		

Notes:

[7] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Prostate-specifin Antigen (PSA50) Response in Subjects with MCRPC who Received AZD4635 Plus Durvalumab Plus Cabazitaxel

End point title	Number of Subjects with Prostate-specifin Antigen (PSA50) Response in Subjects with MCRPC who Received AZD4635 Plus Durvalumab Plus Cabazitaxel

End point description:

Confirmed PSA50 response is defined as the proportion of participants who achieved a ≥50% decrease

in PSA from baseline to the lowest post-baseline PSA, confirmed by a consecutive PSA at least 3 weeks later and was based on PSA evaluable participants (dosed participants with an abnormal baseline PSA [≥1 ng/mL]).

End point type	Secondary

End point timeframe:

Arm A: Screening, Day 1 of each cycle up to 11 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 11 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	28		
Units: Participants		5		

Notes:

[8] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in worst pain in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF)

End point title	Change from baseline in worst pain in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF)

End point description:

"Worst pain" and "Average pain" are 'single question' scores from the BPI short form and may take any value from 0 to 10 (worst outcome). "Interference Pain" is the total score of 7 sub-scores, where each value may take any value from 0 to 10 (worst outcome). The range of the "Interference Score" can be from 0 to 70.

Note: None of the 14 participants at Baseline answered the questionnaire at Cycle 1 Day 1. Therefore, related statistics were not derived for this timepoint.

n = Number of participants included in analysis

End point type	Secondary

End point timeframe:

Arm A: Screening, Day 1 of each cycle up to 9 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 9 months (Each cycle was 21 days in length)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[9]	28[10]		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Baseline (n = 14)	()	3.4 (± 2.44)		

Cycle 1 Day 1 (n = 0)	()	9999.9999 (± 9999.9999)		
Cycle 2 Day 1 (n = 11)	()	-1.6 (± 2.94)		
Cycle 3 Day 1 (n = 13)	()	-0.3 (± 4.40)		
Cycle 4 Day 1 (n = 9)	()	-1.6 (± 2.88)		
Cycle 5 Day 1 (n = 7)	()	-2.1 (± 3.58)		
Cycle 6 Day 1 (n = 8)	()	-1.9 (± 3.00)		
Cycle 7 Day 1 (n = 8)	()	1.0 (± 1.85)		
Cycle 8 Day 1 (n = 6)	()	-1.7 (± 2.66)		
Cycle 9 Day 1 (n = 5)	()	-0.2 (± 2.17)		

Notes:

[9] - The data for Arm A was not calculated because of a patient identification risk.

[10] - Here, arbitrary value 9999.9999 indicates that the values are not available.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in average pain in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF)

End point title	Change from baseline in average pain in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF)

End point description:

"Worst pain" and "Average pain" are 'single question' scores from the BPI short form and may take any value from 0 to 10 (worst outcome). "Interference Pain" is the total score of 7 sub-scores, where each value may take any value from 0 to 10 (worst outcome). The range of the "Interference Score" can be from 0 to 70.

Note: None of the 14 participants at Baseline answered the questionnaire at Cycle 1 Day 1. Therefore, related statistics were not derived for this timepoint.

n = Number of participants included in analysis

End point type	Secondary

End point timeframe:

Arm A: Screening, Day 1 of each cycle up to 9 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 9 months (Each cycle was 21 days in length)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[11]	28[12]		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Baseline (n = 14)	()	2.3 (± 2.09)		
Cycle 1 Day 1 (n = 0)	()	9999.9999 (± 9999.9999)		
Cycle 2 Day 1 (n = 11)	()	-1.3 (± 1.19)		
Cycle 3 Day 1 (n = 13)	()	0.6 (± 3.15)		
Cycle 4 Day 1 (n = 9)	()	-0.9 (± 1.27)		
Cycle 5 Day 1 (n = 7)	()	-1.6 (± 2.15)		
Cycle 6 Day 1 (n = 8)	()	-1.4 (± 1.51)		
Cycle 7 Day 1 (n =8)	()	0.0 (± 1.41)		

Cycle 8 Day 1 (n = 6)	()	-0.8 (± 1.47)		
Cycle 9 Day 1 (n = 5)	()	-1.2 (± 0.84)		

Notes:

[11] - The data for Arm A was not calculated because of a patient identification risk.

[12] - Here, arbitrary value 9999.9999 indicates that the values are not available.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in pain interference in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF)

End point title	Change from baseline in pain interference in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF)

End point description:

"Worst pain" and "Average pain" are 'single question' scores from the BPI short form and may take any value from 0 to 10 (worst outcome). "Interference Pain" is the total score of 7 sub-scores, where each value may take any value from 0 to 10 (worst outcome). The range of the "Interference Score" can be from 0 to 70.

Note: None of the 14 participants at Baseline answered the questionnaire at Cycle 1 Day 1. Therefore, related statistics were not derived for this timepoint.

n = Number of participants included in analysis

End point type	Secondary

End point timeframe:

Arm A: Screening, Day 1 of each cycle up to 9 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 9 months (Each cycle was 21 days in length)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[13]	28[14]		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Baseline (n = 14)	()	8.0 (± 8.47)		
Cycle 1 Day 1 (n = 0)	()	9999.9999 (± 9999.9999)		
Cycle 2 Day 1 (n = 11)	()	2.5 (± 13.90)		
Cycle 3 Day 1 (n = 13)	()	12.3 (± 18.96)		
Cycle 4 Day 1 (n = 9)	()	4.9 (± 12.73)		
Cycle 5 Day 1 (n = 7)	()	1.3 (± 5.19)		
Cycle 6 Day 1 (n = 8)	()	2.0 (± 8.40)		
Cycle 7 Day 1 (n = 8)	()	8.1 (± 9.93)		
Cycle 8 Day 1 (n = 6)	()	7.2 (± 13.98)		
Cycle 9 Day 1 (n =5)	()	5.4 (± 15.16)		

Notes:

[13] - The data for Arm A was not calculated because of a patient identification risk.

[14] - Here, arbitrary value 9999.9999 indicates that the values are not available.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in the FACT Advanced Prostate Symptom Indext-6 (FAPSI-6), as derived from 6 items, the FAPSI-8 from 8 items within the FACT-P and the Prostate Cancer Symptoms (PCS), from the 12 items in the prostrate-specific module of the FACT-P

End point title	Change from baseline in the FACT Advanced Prostate Symptom Indext-6 (FAPSI-6), as derived from 6 items, the FAPSI-8 from 8 items within the FACT-P and the Prostate Cancer Symptoms (PCS), from the 12 items in the prostrate-specific module of the FACT-P

End point description:

The Functional Assessment of Cancer Therapy-Prostate (FACT-P) will be used to measure health related quality of life (HRQL) in men with prostate cancer. It consists of 4 subscales (physical, emotional, functional and social/family well-being) plus a 12-item prostate-specific module, the PCS subscale, which highlights concerns specific to participants with prostate cancer. Each question in the FACT-P questionnaires has a choice of 5 responses, "Not at all", "A little bit", "Somewhat", "Quite a bit" and "Very much". The scores range from 0 ("Not at all") to 4 ("Very much") for positively phrased questions. Negatively phrased questions have a reverse scoring, from 0 ("Very much") to 4 ("Not at all").
n = Number of participants included in analysis
Note: None of the 10 participants at Baseline answered the questionnaire at Cycle 1 Day 1. Therefore, related statistics were not derived for this timepoint.

End point type	Secondary

End point timeframe:

Arm A: Screening, Day 1 of each cycle up to 9 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 9 months (Each cycle was 21 days in length)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[15]	28[16]		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Baseline (n = 10)	()	16.6 (± 2.88)		
Cycle 1 Day 1 (n = 0)	()	9999.9999 (± 9999.9999)		
Cycle 2 Day 1 (n = 7)	()	1.9 (± 1.68)		
Cycle 3 Day 1 (n = 9)	()	-0.7 (± 5.52)		
Cycle 4 Day 1 (n = 7)	()	-0.1 (± 3.34)		
Cycle 5 Day 1 (n = 5)	()	0.6 (± 3.36)		
Cycle 6 Day 1 (n = 6)	()	1.5 (± 1.38)		
Cycle 7 Day 1 (n = 7)	()	0.0 (± 3.92)		
Cycle 8 Day 1 (n = 5)	()	-1.8 (± 4.15)		
Cycle 9 Day 1 (n = 4)	()	-3.0 (± 4.55)		

Notes:

[15] - The data for Arm A was not calculated because of a patient identification risk.

[16] - Here, arbitrary value 9999.9999 indicates that the values are not available.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Progressed Based on BPI-SF Item 3

End point title	Number of Subjects Who Progressed Based on BPI-SF Item 3

End point description:

Pain progression was assessed using BPI-SF.

End point type	Secondary

End point timeframe:

Arm A: Screening, Day 1 of each cycle up to 12 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 12 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[17]	28		
Units: Participants		1		

Notes:

[17] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed plasma concentration (Cmax)

End point title	Maximum observed plasma concentration (Cmax)

End point description:

Investigate the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.

End point type	Secondary

End point timeframe:

Arm A:Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length];Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	15		
Units: ng/mL				
arithmetic mean (standard deviation)	()	483.0 (± 231.1)		

Notes:

[18] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal half-life (t1/2λz)

End point title	Terminal half-life (t1/2λz)

End point description:

Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.

End point type	Secondary

End point timeframe:

Arm A:Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length];Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[19]	13		
Units: hour (h)				
arithmetic mean (standard deviation)	()	8.87 (± 4.82)		

Notes:

[19] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration time curve from zero to the time of the last measurable concentration (AUClast)

End point title	Area under the plasma concentration time curve from zero to the time of the last measurable concentration (AUClast)

End point description:

Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.

End point type	Secondary

End point timeframe:

Arm A:Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length];Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	15		
Units: h*ng/mL				
arithmetic mean (standard deviation)	()	2787 (± 1056)		

Notes:

[20] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration time curve from zero to 24 hours [AUC(0-24)]

End point title	Area under the plasma concentration time curve from zero to 24 hours [AUC(0-24)]

End point description:

Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.

End point type	Secondary

End point timeframe:

Arm A:Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length];Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[21]	14		
Units: h*ng/mL				
arithmetic mean (standard deviation)	()	2874 (± 1084)		

Notes:

[21] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration time curve from zero extrapolated to infinity (AUCinf)

End point title	Area under the plasma concentration time curve from zero extrapolated to infinity (AUCinf)

End point description:

Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.

End point type	Secondary

End point timeframe:

Arm A:Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length];Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[22]	13		
Units: h*ng/mL				
arithmetic mean (standard deviation)	()	3311 (± 1272)		

Notes:

[22] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent volume of distribution during the terminal phase (Vz/F)

End point title	Apparent volume of distribution during the terminal phase (Vz/F)

End point description:

Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.

End point type	Secondary

End point timeframe:

Arm A:Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length];Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[23]	13		
Units: Litre (L)				
arithmetic mean (standard deviation)	()	334.6 (± 254.4)		

Notes:

[23] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious and non-serious adverse events

End point title	Number of subjects with serious and non-serious adverse events

End point description:

Safety and tolerability of each treatment regimen were assessed in participants with mCRPC.

End point type	Secondary

End point timeframe:

Arm A: From Screening up to 14 months (Each cycle was 28 days in length); Arm B: From Screening up to 14 months (Cycle 1 to Cycle 10 was 21 days in length, and Cycle 11 onwards was 28 days in length)

End point values	Arm A: AZD4635 + durvalumab	Arm B: AZD4635 + durvalumab + cabazitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	28		
Units: Participants				
Any Adverse Event (AE)		28		
Any AE possibly related to treatment		28		
Any AE possibly related to AZD4635		23		
Any AE possibly related to Durvalumab		20		
Any AE possibly related to Cabazitaxel		28		
Any AE of CTCAE grade 3 or higher		24		
Any AE of CTCAE grade 3/higher treatment-related		20		
Any AE of CTCAE grade 3 or higher AZD4635-related		9		
Any AE of CTCAE grade 3/higher Durvalumab-related		9		
Any AE of CTCAE grade 3/higher Cabazitaxel-related		19		
Any Adverse Event of Special Interest - Durvalumab		17		
Any possibly related AESI for Durvalumab		10		
Any AE with outcome = death		2		
Any AE with death possibly related to treatment		1		
Any Serious Adverse Event (SAE) (including death)		19		
Any SAE (including death) treatment-related		12		
Any SAE leading to discontinuation of AZD4635		4		
Any SAE leading to stopping of AZD4635 related		1		
Any AE leading to discontinuation of AZD4635		5		
Any AE leading to dose reduction of AZD4635		4		
Any AE leading to dose interruption of AZD4635		15		

Any AE leading to discontinuation of Durvalumab		4		
Any AE leading to dose interruption of Durvalumab		5		
Any AE leading to discontinuation of Cabazitaxel		7		
Any AE leading to dose reduction of Cabazitaxel		4		
Any AE leading to dose interruption of Cabazitaxel		8		
Any other significant AEs		0		

Notes:

[24] - The data for Arm A was not calculated because of a patient identification risk.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: Up to 2 years;
Serious and/or other adverse events: From Screening up to 14 months

(Each cycle was 28 days in length) for Arm A (Cycle 1 to Cycle 10 was 21 days in length, and Cycle 11 onwards was 28 days in length) for Arm B.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Arm B: AZD4635 + durvalumab + cabazitaxel

Reporting group description:

Participants received AZD4635 Dose A orally daily, durvalumab Dose B intravenously (IV) every 3 weeks (Q3W), and cabazitaxel Dose C IV Q3W

Reporting group title	Arm A: AZD4635 + durvalumab

Reporting group description:

Participants received AZD4635 Dose A orally daily, and durvalumab Dose B intravenously every 4 weeks.

Serious adverse events	Arm B: AZD4635 + durvalumab + cabazitaxel	Arm A: AZD4635 + durvalumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 28 (67.86%)	2 / 2 (100.00%)	
number of deaths (all causes)	7	2	
number of deaths resulting from adverse events			
Investigations			
Neutrophil Count Decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Neutropenia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Post Hemorrhagic Anemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nausea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Haemorrhage			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis Acute			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Cystitis Haemorrhagic			

subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 28 (3.57%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Retention			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary tract infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteritis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 28 (3.57%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm B: AZD4635 + durvalumab + cabazitaxel	Arm A: AZD4635 + durvalumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 28 (100.00%)	2 / 2 (100.00%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Hypertension			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 28 (35.71%)	1 / 2 (50.00%)	
occurrences (all)	15	1	
Chills			
subjects affected / exposed	0 / 28 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Fatigue			

subjects affected / exposed	5 / 28 (17.86%)	2 / 2 (100.00%)	
occurrences (all)	7	2	
Pyrexia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Reproductive system and breast disorders			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 28 (10.71%)	1 / 2 (50.00%)	
occurrences (all)	3	3	
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Insomnia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Amylase increased			

subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 28 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 28 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Lipase increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Neutrophil count decreased			
subjects affected / exposed	4 / 28 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	8	0	
Weight decreased			
subjects affected / exposed	4 / 28 (14.29%)	2 / 2 (100.00%)	
occurrences (all)	7	2	
White blood cell count decreased			
subjects affected / exposed	4 / 28 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	7	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 28 (17.86%)	1 / 2 (50.00%)	
occurrences (all)	5	2	
Headache			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Dysgeusia			

subjects affected / exposed	6 / 28 (21.43%)	0 / 2 (0.00%)	
occurrences (all)	7	0	
Neuropathy peripheral			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 28 (50.00%)	1 / 2 (50.00%)	
occurrences (all)	19	4	
Neutropenia			
subjects affected / exposed	6 / 28 (21.43%)	0 / 2 (0.00%)	
occurrences (all)	12	0	
Thrombocytopenia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 28 (14.29%)	1 / 2 (50.00%)	
occurrences (all)	5	1	
Constipation			
subjects affected / exposed	8 / 28 (28.57%)	1 / 2 (50.00%)	
occurrences (all)	8	1	
Diarrhoea			
subjects affected / exposed	14 / 28 (50.00%)	2 / 2 (100.00%)	
occurrences (all)	21	4	
Dyspepsia			
subjects affected / exposed	4 / 28 (14.29%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
Dry mouth			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Gastrooesophageal reflux disease			

subjects affected / exposed	2 / 28 (7.14%)	1 / 2 (50.00%)	
occurrences (all)	2	1	
Oral pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	17 / 28 (60.71%)	1 / 2 (50.00%)	
occurrences (all)	20	1	
Vomiting			
subjects affected / exposed	9 / 28 (32.14%)	0 / 2 (0.00%)	
occurrences (all)	12	0	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	0 / 28 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	3	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	5 / 28 (17.86%)	0 / 2 (0.00%)	
occurrences (all)	7	0	
Urinary retention			
subjects affected / exposed	0 / 28 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 28 (32.14%)	0 / 2 (0.00%)	
occurrences (all)	11	0	
Back pain			
subjects affected / exposed	5 / 28 (17.86%)	1 / 2 (50.00%)	
occurrences (all)	5	1	
Flank pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Muscle spasms			

subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Muscular weakness			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	6	0	
Myalgia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	6 / 28 (21.43%)	1 / 2 (50.00%)	
occurrences (all)	7	2	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Decreased appetite			
subjects affected / exposed	7 / 28 (25.00%)	2 / 2 (100.00%)	
occurrences (all)	8	2	
Hyperkalaemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Hyperuricaemia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Hypocalcaemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Hypokalaemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Hypophosphataemia			

subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 4	0 / 2 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 September 2020	The global protocol was amended to address comments received from various health authorities in the EU.
24 November 2020	The global protocol was amended due to the Sponsor’s decision to close enrolment in Arm A.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The arbitrary value 9999.9999 indicates that the parameter was not measured.

Notes: