Clinical trial results:
A Phase 1/2, Open-Label, Multi-Arm Trial to Investigate the Safety, Tolerability, Pharmacokinetics, Biological, and Clinical Activity of AGEN1884 in Combination with AGEN2034 in Subjects with Metastatic or Locally Advanced Solid Tumors, and Expansion into Select Solid Tumors

Summary

EudraCT number	2018-000120-33
Trial protocol	HU PL ES
Global end of trial date	15 July 2022

Results information

Result version number	v2 (current)
This version publication date	10 May 2024
First version publication date	29 July 2023
Version creation reason	• New data added to full data set Addition of Phase 1 data.

Trial information

Trial identification

Sponsor protocol code	C-550-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03495882
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Agenus, Inc.
Sponsor organisation address	3 Forbes Road, Lexington, MA, United States, 02421
Public contact	Agenus, Inc. Clinical Trial Information, Agenus, Inc., 1 781-674-4265, clinicaltrialinfo@agenusbio.com
Scientific contact	Agenus, Inc. Clinical Trial Information, Agenus, Inc., 1 781-674-4265, clinicaltrialinfo@agenusbio.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	15 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of Phase 1 of this study was to assess safety and tolerability of zalifrelimab (AGEN1884) in combination with balstilimab (AGEN2034) in participants with locally advanced, recurrent and/or metastatic solid tumors. The main objective of Phase 2 was to assess ORR (objective response rate) according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) as determined by the Independent Endpoint Review Committee (IERC).

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	United States: 19
Country: Number of subjects enrolled	Ukraine: 48
Country: Number of subjects enrolled	Australia: 40
Country: Number of subjects enrolled	Georgia: 11
Country: Number of subjects enrolled	Moldova, Republic of: 9
Country: Number of subjects enrolled	Brazil: 5
Worldwide total number of subjects	175
EEA total number of subjects	43

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)	155
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The trial was conducted at 46 trial centres.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1 – Dose 1: Zalifrelimab + Balstilimab

Arm description:

Participants received zalifrelimab in combination with balstilimab.

Arm type	Experimental
Investigational medicinal product name	Zalifrelimab
Investigational medicinal product code	
Other name	AGEN1884
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Zalifrelimab was administered over 30 minutes and following the infusion of balstilimab.

Investigational medicinal product name	Balstilimab
Investigational medicinal product code	
Other name	AGEN2034, Anti-PD-1
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Balstilimab infusion was administered over 30 minutes.

Arm title	Phase 1 – Dose 2: Zalifrelimab + Balstilimab

Arm description:

Participants received zalifrelimab in combination with balstilimab.

Arm type	Experimental
Investigational medicinal product name	Zalifrelimab
Investigational medicinal product code	
Other name	AGEN1884
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Zalifrelimab was administered over 30 minutes and following the infusion of balstilimab.

Investigational medicinal product name	Balstilimab
Investigational medicinal product code	
Other name	AGEN2034, Anti-PD-1
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Balstilimab infusion was administered over 30 minutes.

Arm title	Phase 2: Zalifrelimab + Balstilimab
Arm description: Participants received zalifrelimab in combination with balstilimab.	
Arm type	Experimental
Investigational medicinal product name	Zalifrelimab
Investigational medicinal product code	
Other name	AGEN1884
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Zalifrelimab was administered over 30 minutes and following the infusion of balstilimab.	
Investigational medicinal product name	Balstilimab
Investigational medicinal product code	
Other name	AGEN2034, Anti-PD-1
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Balstilimab infusion was administered over 30 minutes.	

Number of subjects in period 1	Phase 1 – Dose 1: Zalifrelimab + Balstilimab	Phase 1 – Dose 2: Zalifrelimab + Balstilimab	Phase 2: Zalifrelimab + Balstilimab
Started	10	10	155
Received at Least 1 Dose of Study Drug	10	10	155
Completed	2	0	36
Not completed	8	10	119
Consent withdrawn by subject	-	-	15
Adverse event, non-fatal	2	-	2
Death	-	-	88
Progressive Disease	6	10	2
Study Terminated by Sponsor	-	-	5
Lost to follow-up	-	-	7

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
Safety Analysis Set: all participants who received ≥1 dose of any study treatment.	

Reporting group values	Overall Study	Total	
Number of subjects	175	175	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	155	155	
From 65-84 years	20	20	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	170	170	
Male	5	5	
Race Units: Subjects			
American Indian or Alaska Native	1	1	
Asian (Chinese)	1	1	
Black or African American	1	1	
White	168	168	
South African	1	1	
Indigenous And Torres Strait Islander	1	1	
Australian Aboriginal	1	1	
Unknown	1	1	
Ethnicity Units: Subjects			
Hispanic or Latino	9	9	
Not Hispanic or Latino	163	163	
Unknown	3	3	

End points

End points reporting groups

Reporting group title	Phase 1 – Dose 1: Zalifrelimab + Balstilimab
Reporting group description:	
Participants received zalifrelimab in combination with balstilimab.	
Reporting group title	Phase 1 – Dose 2: Zalifrelimab + Balstilimab
Reporting group description:	
Participants received zalifrelimab in combination with balstilimab.	
Reporting group title	Phase 2: Zalifrelimab + Balstilimab
Reporting group description:	
Participants received zalifrelimab in combination with balstilimab.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All participants who received ≥1 dose of any study treatment.	
Subject analysis set title	Intent-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All participants who received ≥1 dose of any study treatment, with measurable disease at baseline (per IERC).	
Subject analysis set title	Pharmacokinetics (PK) Set
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants who received ≥1 dose of any study drug and who had sufficient evaluable drug concentrations measurements prior to and after treatment.	
Subject analysis set title	Dose-limiting Toxicity (DLT) Analysis Set
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants who were enrolled for DLT evaluation (excluding participants enrolled to backfill cohorts) and either received all study treatment administrations or stopped treatment due to a DLT during the DLT evaluation period.	
Subject analysis set title	Receptor Occupancy (RO) Analysis Set
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants who completed ≥ 1 infusion of study drug, with adequate measurements of PD-1 receptor occupancy on circulating T cells.	

Primary: Phase 2: Objective Response Rate (ORR): IERC

End point title	Phase 2: Objective Response Rate (ORR): IERC[1][2]
End point description:	
The ORR was defined as the proportion of participants with a confirmed best overall response (BOR) of partial response (PR) or complete response (CR), as determined by an IERC per RECIST 1.1.	
End point type	Primary
End point timeframe:	
Up to 2 years	

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: Only percentage of participants is reported for this end point.

[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 applies only to Phase 2 of the study.

End point values	Phase 2: Zalifrelimab + Balstilimab			
Subject group type	Reporting group			
Number of subjects analysed	145[3]			
Units: Percentage of participants				
number (confidence interval 95%)	26.2 (19.7 to 33.9)			

Notes:

[3] - Intent-to-treat

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants Experiencing DLTs

End point title	Phase 1: Number of Participants Experiencing DLTs[4][5]

End point description:

The number of participants with an occurrence of a DLT during dose escalation during the first 21 days of treatment in Phase 1 are reported. Any DLT immediately led to permanent withdrawal of zalifrelimab and balstilimab.

End point type	Primary

End point timeframe:

Up to Day 21

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only number of participants is reported for this end point.

[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 applies only to Phase 1 of the study.

End point values	Phase 1 – Dose 1: Zalifrelimab + Balstilimab	Phase 1 – Dose 2: Zalifrelimab + Balstilimab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[6]	10[7]		
Units: Participants	0	0		

Notes:

[6] - DLT Analysis Set

[7] - DLT Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1/2: Maximum Drug Concentration Observed Postdose at Steady-state (Cmax-ss)

End point title	Phase 1/2: Maximum Drug Concentration Observed Postdose at Steady-state (Cmax-ss)

End point description:

Blood samples were collected for serum balstilimab and zalifrelimab concentration analyses. Each cycle was 6 weeks (42 days) long. Results are reported as micrograms/millilitre (ug/mL).

End point type	Secondary

End point timeframe:

Pre-dose, up to 4 hours post-dose (Phase 1: Cycle 2 and Cycle 3; Phase 2: Cycle 4)

End point values	Phase 1 – Dose 1: Zalifrelimab + Balstilimab	Phase 1 – Dose 2: Zalifrelimab + Balstilimab	Phase 2: Zalifrelimab + Balstilimab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[8]	10[9]	145[10]	
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Zalifrelimab	28.7 (± 26.6)	27.3 (± 16.4)	16.45 (± 120.2)	
Balstilimab	23.1 (± 28.7)	71.4 (± 26.5)	62.40 (± 26.7)	

Notes:

[8] - Zalifrelimab PK Set: N=6; Balstilimab PK Set: N=9

[9] - Zalifrelimab PK Set: N=5; Balstilimab PK Set: N=10

[10] - Zalifrelimab PK Set: N=42; Balstilimab PK Set: N=7

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1/2: Area Under the Drug Concentration-time Curve From Day 0 to Day 14 at Steady-state (AUC0-14d-ss)

End point title	Phase 1/2: Area Under the Drug Concentration-time Curve From Day 0 to Day 14 at Steady-state (AUC0-14d-ss)

End point description:

Blood samples were collected for serum balstilimab and zalifrelimab concentration analyses. Each cycle was 6 weeks (42 days) long. Results are reported as day times ug/mL (day*ug/mL).

End point type	Secondary

End point timeframe:

Pre-dose, up to 4 hours post-dose (Phase 1: Cycle 2 and Cycle 3; Phase 2: Cycle 4)

End point values	Phase 1 – Dose 1: Zalifrelimab + Balstilimab	Phase 1 – Dose 2: Zalifrelimab + Balstilimab	Phase 2: Zalifrelimab + Balstilimab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[11]	10[12]	145[13]	
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
Zalifrelimab	213 (± 29.4)	185 (± 13.2)	131.1 (± 119.5)	
Balstilimab	74.8 (± 37.4)	245 (± 28.9)	250.9 (± 119.5)	

Notes:

[11] - Zalifrelimab PK Set: N=6; Balstilimab PK Set: N=8

[12] - Zalifrelimab PK Set: N=5; Balstilimab PK Set: N=9

[13] - Zalifrelimab PK Set: N=41; Balstilimab PK Set: N=6

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1/2: Number of Participants with Serum Anti-drug Antibodies (ADAs) for Balstilimab and Zalifrelimab

End point title	Phase 1/2: Number of Participants with Serum Anti-drug Antibodies (ADAs) for Balstilimab and Zalifrelimab

End point description:

Blood samples were collected for serum balstilimab and zalifrelimab ADA determination.

End point type	Secondary

End point timeframe:

Pre-dose through Month 27

End point values	Phase 1 – Dose 1: Zalifrelimab + Balstilimab	Phase 1 – Dose 2: Zalifrelimab + Balstilimab	Phase 2: Zalifrelimab + Balstilimab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[14]	10[15]	155[16]	
Units: Participant				
Zalifrelimab	0	0	3	
Balstilimab	0	0	6	

Notes:

[14] - Safety Analysis Set

[15] - Safety Analysis Set

[16] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: ORR: Investigator

End point title	Phase 2: ORR: Investigator[17]

End point description:

The ORR was defined as the proportion of participants with a confirmed BOR of PR or CR, as determined by the investigator per RECIST 1.1.

End point type	Secondary

End point timeframe:

Up to 2 years

Notes:

[17] - 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 applies only to Phase 2 of the study.

End point values	Phase 2: Zalifrelimab + Balstilimab			
Subject group type	Reporting group			
Number of subjects analysed	145[18]			
Units: Percentage of participants				
number (confidence interval 95%)	23.4 (17.3 to 31.0)			

Notes:

[18] - Intent-to-treat

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Response (DOR)

End point title	Phase 2: Duration of Response (DOR)[19]

End point description:

DOR was defined as time from first observation of response to first observation of documented disease progression (or death within 12 weeks after last tumor assessment), as determined by an IERC and investigator, per RECIST 1.1. Participants without an event at the analysis cutoff date were censored on date of last tumor assessment.

End point type	Secondary

End point timeframe:

Up to 3 years

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 applies only to Phase 2 of the study.

End point values	Phase 2: Zalifrelimab + Balstilimab			
Subject group type	Reporting group			
Number of subjects analysed	145[20]			
Units: month				
number (confidence interval 95%)				
IERC	9.7 (5.6 to 9999)			
Investigator	8.5 (6.9 to 18.1)			

Notes:

[20] - IERC Intent-to-treat: N=38; 9999=Not available;
Investigator Intent-to-treat: N=34

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Disease Control Rate (DCR)

End point title	Phase 2: Disease Control Rate (DCR)[21]

End point description:

DCR was defined as proportion of participants with CR, PR, or stable disease (SD) without progressive disease (PD) within 81 days of study start, or durable SD following PD, as determined by the investigator per RECIST 1.1.

End point type	Secondary

End point timeframe:

Up to 3 years

Notes:

[21] - 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 applies only to Phase 2 of the study.

End point values	Phase 2: Zalifrelimab + Balstilimab			
Subject group type	Reporting group			
Number of subjects analysed	145[22]			
Units: Percentage of participants				
number (confidence interval 95%)	58.6 (50.5 to 66.3)			

Notes:

[22] - Intent-to-treat

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Time to Response (TTR)

End point title	Phase 2: Time to Response (TTR)[23]

End point description:

TTR was defined as the time interval between the date of treatment initiation and the earliest date of first documented confirmed complete response or partial response based on independent radiologic review, as determined by an IERC and investigator, per RECIST 1.1.

End point type	Secondary

End point timeframe:

Up to 2 years

Notes:

[23] - 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 applies only to Phase 2 of the study.

End point values	Phase 2: Zalifrelimab + Balstilimab			
Subject group type	Reporting group			
Number of subjects analysed	145[24]			
Units: day				
median (confidence interval 95%)	79.5 (66.5 to 123.5)			

Notes:

[24] - Intent-to-treat: N=38

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Progression-free Survival (PFS)

End point title	Phase 2: Progression-free Survival (PFS)[25]

End point description:

PFS was defined as the interval from the date of first dose of investigational agent until the earliest date of PD, as determined by IERC and investigator assessment of objective radiographic disease assessments per RECIST 1.1, or death due to any cause if occurring sooner than progression.

End point type	Secondary

End point timeframe:

Up to 2 years

Notes:

[25] - 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 applies only to Phase 2 of the study.

End point values	Phase 2: Zalifrelimab + Balstilimab			
Subject group type	Reporting group			
Number of subjects analysed	145[26]			
Units: month				
median (confidence interval 95%)				
IERC	2.7 (1.5 to 3.7)			
Investigator	3.0 (2.7 to 5.4)			

Notes:

[26] - IERC Intent-to-treat: N=110;
Investigator Intent-to-treat: N=118

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Survival (OS)

End point title	Phase 2: Overall Survival (OS)[27]

End point description:

OS was defined as the interval from the date of first dose of investigational agent until the date of death.

End point type	Secondary

End point timeframe:

Up to 2 years

Notes:

[27] - 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 applies only to Phase 2 of the study.

End point values	Phase 2: Zalifrelimab + Balstilimab			
Subject group type	Reporting group			
Number of subjects analysed	145[28]			
Units: month				
median (confidence interval 95%)	13.0 (9.7 to 18.5)			

Notes:

[28] - Intent-to-treat

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: RO of Balstilimab on Circulating T Cells

End point title	Phase 1: RO of Balstilimab on Circulating T Cells[29]

End point description:

A validated flow cytometry-based assay was used to evaluate programmed cell death protein 1 (PD-1) RO on circulating T cells as an indication of target engagement of balstilimab. Blood samples were collected for the assay. Results are reported as a percentage of available drug receptors occupied (%RO) by balstilimab; the higher the percentage, the greater the engagement of balstilimab with the target receptor. Initial testing revealed technical limitations of the sample isolation procedure prior to the PD-1 RO assessment, causing the PD-1 RO assay to inaccurately reflect the actual PD-1 RO status in response to balstilimab/zalifrelimab combination treatment. As a result, further sample collection and subsequent testing was not conducted. Only initial test results are reported.

End point type	Secondary

End point timeframe:

Day 8 through Day 50

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 applies only to Phase 1 of the study.

End point values	Phase 1 – Dose 1: Zalifrelimab + Balstilimab			
Subject group type	Reporting group			
Number of subjects analysed	3[30]			
Units: Percent				
number (not applicable)	30.9			

Notes:

[30] - RO Analysis Set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 36 months	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1
Reporting groups	
Reporting group title	Phase 2: Zalifrelimab + Balstilimab
Reporting group description: Participants received zalifrelimab in combination with balstilimab.	
Reporting group title	Phase 1 – Dose 1: Zalifrelimab + Balstilimab
Reporting group description: Participants received zalifrelimab in combination with balstilimab.	
Reporting group title	Phase 1 – Dose 2: Zalifrelimab + Balstilimab
Reporting group description: Participants received zalifrelimab in combination with balstilimab.	

Serious adverse events	Phase 2: Zalifrelimab + Balstilimab	Phase 1 – Dose 1: Zalifrelimab + Balstilimab	Phase 1 – Dose 2: Zalifrelimab + Balstilimab
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 155 (43.87%)	6 / 10 (60.00%)	2 / 10 (20.00%)
number of deaths (all causes)	88	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	2 / 155 (1.29%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Metastases to the respiratory system			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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

Tumour associated fever			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Tumour pain			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Cancer pain			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Shock haemorrhagic			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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 / 1	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Hypotension			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Nephrostomy			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	2 / 155 (1.29%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Disease progression			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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 / 1	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Sudden death			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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 / 1	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervix haemorrhage uterine			
subjects affected / exposed[1]	1 / 155 (0.65%)	0 / 8 (0.00%)	0 / 7 (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
Female genital tract fistula			
subjects affected / exposed[2]	1 / 155 (0.65%)	0 / 8 (0.00%)	0 / 7 (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
Vaginal discharge			
subjects affected / exposed[3]	1 / 155 (0.65%)	0 / 8 (0.00%)	0 / 7 (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
Vaginal haemorrhage			

subjects affected / exposed[4]	1 / 155 (0.65%)	0 / 8 (0.00%)	0 / 7 (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
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	3 / 155 (1.94%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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 / 1	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Dyspnoea			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Pleural effusion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Respiratory arrest			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (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
Psychiatric disorders			

Confusional state			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Product issues			
Device occlusion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Cardiac disorders			
Immune-mediated myocarditis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Pericardial effusion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Nervous system disorders			
Thrombotic cerebral infarction			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Headache			

subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Hemiparesis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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 / 1	0 / 0	0 / 0
Neurological decompensation			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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 / 1	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 155 (3.87%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 155 (1.94%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	3 / 155 (1.94%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			

subjects affected / exposed	2 / 155 (1.29%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Colonic fistula			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Dysphagia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Ileus			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Large intestinal haemorrhage			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Nausea			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Small intestinal obstruction			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Colitis			

subjects affected / exposed	0 / 155 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Immune-mediated hepatitis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 155 (1.29%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	2 / 155 (1.29%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postrenal failure			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Immune-mediated nephritis			

subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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 impairment			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Hypercalcaemia of malignancy			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Hypophysitis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Hypopituitarism			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Immune-mediated hypothyroidism			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	2 / 155 (1.29%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 155 (2.58%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	4 / 155 (2.58%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 155 (1.94%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	2 / 155 (1.29%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Device related infection			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Enterocolitis infectious			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Escherichia urinary tract infection			

subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Kidney infection			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Lower respiratory tract infection			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Pelvic infection			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Urosepsis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Gastroenteritis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (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
Diabetes mellitus			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This adverse event was only experienced by female participants.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This adverse event was only experienced by female participants.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This adverse event was only experienced by female participants.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This adverse event was only experienced by female participants.

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

Non-serious adverse events	Phase 2: Zalifrelimab + Balstilimab	Phase 1 – Dose 1: Zalifrelimab + Balstilimab	Phase 1 – Dose 2: Zalifrelimab + Balstilimab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	145 / 155 (93.55%)	10 / 10 (100.00%)	9 / 10 (90.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	2	1
Flushing			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	30 / 155 (19.35%)	6 / 10 (60.00%)	5 / 10 (50.00%)
occurrences (all)	43	6	8
Pyrexia			
subjects affected / exposed	25 / 155 (16.13%)	2 / 10 (20.00%)	2 / 10 (20.00%)
occurrences (all)	36	4	3
Asthenia			

subjects affected / exposed	18 / 155 (11.61%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	23	0	0
Oedema peripheral			
subjects affected / exposed	10 / 155 (6.45%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	11	0	0
Chills			
subjects affected / exposed	2 / 155 (1.29%)	3 / 10 (30.00%)	2 / 10 (20.00%)
occurrences (all)	2	4	2
Influenza like illness			
subjects affected / exposed	2 / 155 (1.29%)	3 / 10 (30.00%)	0 / 10 (0.00%)
occurrences (all)	2	5	0
Chest discomfort			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Chest pain			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Injection site pain			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tenderness			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Application site rash			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			

Vaginal haemorrhage			
subjects affected / exposed[5]	8 / 155 (5.16%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	10	1	0
Breast pain			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 155 (9.68%)	2 / 10 (20.00%)	3 / 10 (30.00%)
occurrences (all)	20	3	3
Dyspnoea			
subjects affected / exposed	5 / 155 (3.23%)	1 / 10 (10.00%)	2 / 10 (20.00%)
occurrences (all)	5	1	2
Haemoptysis			
subjects affected / exposed	2 / 155 (1.29%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	2	5	1
Oropharyngeal pain			
subjects affected / exposed	2 / 155 (1.29%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	2	0	2
Productive cough			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Pneumonitis			
subjects affected / exposed	3 / 155 (1.94%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Nasal congestion			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Wheezing			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Asthma			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Orthopnoea			

subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pleuritic pain			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 155 (1.94%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Depression			
subjects affected / exposed	3 / 155 (1.94%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Sleep disorder			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	19 / 155 (12.26%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	31	0	1
Blood creatinine increased			
subjects affected / exposed	18 / 155 (11.61%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	42	0	1
Alanine aminotransferase increased			
subjects affected / exposed	16 / 155 (10.32%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	35	0	3
Blood alkaline phosphatase increased			
subjects affected / exposed	8 / 155 (5.16%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	16	0	0
Transaminases increased			
subjects affected / exposed	2 / 155 (1.29%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	7	3	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Blood urea increased			

subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
International normalised ratio increased			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	0 / 155 (0.00%)	3 / 10 (30.00%)	0 / 10 (0.00%)
occurrences (all)	0	6	0
Nail injury			
subjects affected / exposed	0 / 155 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Foot fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Muscle injury			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Radiation injury			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			

Sinus tachycardia			
subjects affected / exposed	8 / 155 (5.16%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	8	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	11 / 155 (7.10%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	12	2	1
Headache			
subjects affected / exposed	14 / 155 (9.03%)	3 / 10 (30.00%)	1 / 10 (10.00%)
occurrences (all)	19	3	1
Lethargy			
subjects affected / exposed	2 / 155 (1.29%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Neuropathy peripheral			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Somnolence			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Dysarthria			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Intention tremor			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	43 / 155 (27.74%)	1 / 10 (10.00%)	5 / 10 (50.00%)
occurrences (all)	122	1	11
Thrombocytopenia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Iron deficiency anaemia			
subjects affected / exposed	2 / 155 (1.29%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Eosinophilia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Coagulopathy			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 155 (1.29%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	3	2	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	38 / 155 (24.52%)	4 / 10 (40.00%)	3 / 10 (30.00%)
occurrences (all)	66	7	3
Nausea			
subjects affected / exposed	32 / 155 (20.65%)	5 / 10 (50.00%)	6 / 10 (60.00%)
occurrences (all)	45	6	7
Vomiting			
subjects affected / exposed	30 / 155 (19.35%)	3 / 10 (30.00%)	3 / 10 (30.00%)
occurrences (all)	36	4	7
Constipation			
subjects affected / exposed	19 / 155 (12.26%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	25	1	1
Abdominal pain			
subjects affected / exposed	19 / 155 (12.26%)	4 / 10 (40.00%)	0 / 10 (0.00%)
occurrences (all)	20	4	0
Abdominal pain upper			

subjects affected / exposed	3 / 155 (1.94%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	3	1	1
Dry mouth			
subjects affected / exposed	5 / 155 (3.23%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	5	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 155 (3.23%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	6	1	1
Toothache			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Abdominal pain lower			
subjects affected / exposed	5 / 155 (3.23%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	7	1	0
Dysphagia			
subjects affected / exposed	4 / 155 (2.58%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	4	0	1
Abdominal discomfort			
subjects affected / exposed	2 / 155 (1.29%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Haemorrhoids			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	12 / 155 (7.74%)	2 / 10 (20.00%)	4 / 10 (40.00%)
occurrences (all)	15	4	8
Rash			
subjects affected / exposed	11 / 155 (7.10%)	3 / 10 (30.00%)	3 / 10 (30.00%)
occurrences (all)	14	4	4
Rash maculo-papular			
subjects affected / exposed	10 / 155 (6.45%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	10	0	1
Dry skin			
subjects affected / exposed	3 / 155 (1.94%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1

Hyperhidrosis			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Alopecia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blister			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Psoriasis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blister rupture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	23 / 155 (14.84%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	28	1	1
Hyperthyroidism			
subjects affected / exposed	17 / 155 (10.97%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	19	1	0
Adrenal insufficiency			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	16 / 155 (10.32%)	5 / 10 (50.00%)	1 / 10 (10.00%)
occurrences (all)	24	11	1

Arthralgia			
subjects affected / exposed	11 / 155 (7.10%)	2 / 10 (20.00%)	2 / 10 (20.00%)
occurrences (all)	16	2	2
Muscle spasms			
subjects affected / exposed	6 / 155 (3.87%)	3 / 10 (30.00%)	0 / 10 (0.00%)
occurrences (all)	7	3	0
Groin pain			
subjects affected / exposed	4 / 155 (2.58%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	6	2	0
Musculoskeletal chest pain			
subjects affected / exposed	3 / 155 (1.94%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	3	1	1
Musculoskeletal pain			
subjects affected / exposed	3 / 155 (1.94%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	3	3	0
Myalgia			
subjects affected / exposed	7 / 155 (4.52%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	10	1	2
Pain in extremity			
subjects affected / exposed	3 / 155 (1.94%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Bone pain			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	2
Musculoskeletal discomfort			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Bursitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Muscle twitching			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Infections and infestations			
Urinary tract infection			
subjects affected / exposed	26 / 155 (16.77%)	1 / 10 (10.00%)	3 / 10 (30.00%)
occurrences (all)	40	1	4
Upper respiratory tract infection			
subjects affected / exposed	9 / 155 (5.81%)	1 / 10 (10.00%)	2 / 10 (20.00%)
occurrences (all)	11	1	3
Sinusitis			
subjects affected / exposed	4 / 155 (2.58%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	4	5	1
Pneumonia			
subjects affected / exposed	5 / 155 (3.23%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	5	0	1
Cystitis			
subjects affected / exposed	4 / 155 (2.58%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	5	1	0
Fungal skin infection			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Lower respiratory tract infection			
subjects affected / exposed	1 / 155 (0.65%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Nail bed infection			
subjects affected / exposed	0 / 155 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lymphangitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			

subjects affected / exposed	0 / 155 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	14 / 155 (9.03%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	22	2	0
Decreased appetite			
subjects affected / exposed	11 / 155 (7.10%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	13	2	0
Hyponatraemia			
subjects affected / exposed	8 / 155 (5.16%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	12	0	0
Hypercalcaemia			
subjects affected / exposed	2 / 155 (1.29%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	3	2	1
Hypoalbuminaemia			
subjects affected / exposed	4 / 155 (2.58%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	7	1	0
Iron deficiency			
subjects affected / exposed	2 / 155 (1.29%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	2	1	0

Notes:

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This adverse event was only experienced by female participants.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 November 2017	- Added the following language in the 5.4 Dosage and Administration "Relevant clinical laboratory results essential for subject management decisions (hematology, biochemistry, liver function tests) must be available and reviewed before administration of AGEN1884 and/or AGEN2034."
09 March 2018	- Addition of best overall response, duration of response, and progression-free survival per immune-RECIST as secondary end points, including the requirement for a repeat scan to be performed 4-8 weeks after initial diagnosis of progressive disease - Screening period shortened from 42 days to 28 days
22 August 2018	- A 2-week washout was permitted for palliative radiation to non-central nervous system disease with sponsor approval - Infusion times and waiting period were shortened in dosage and administration of zalifrelimab and balstilimab
15 April 2019	- Reorganized and refined the trial objectives and endpoints for Phase 1 versus Phase 2 - Added information from Phase 1 part of the trial that was not available at the time of the previous amendment to support Phase 2 part - Increased sample size to 100 participants in Phase 2 - Changed tumor assessments to continue at 6-week intervals rather than 9-week intervals after Week 18 in order to collect more comprehensive data and consistent tumor response data - Modified the schedule of assessments to align with Study C-700-01 and to increase and enhance data collected to support registration - Updated the planned trial duration from 60 months to 73 months - Updated that administration of balstilimab and zalifrelimab was over 30 minutes - Updated duration of the Follow-up Phase and overall trial duration - Added that response assessment was to be done according to RECIST 1.1 in both phases - The primary end point changed from BOR to ORR to align with change in objectives
29 September 2019	- The Phase 2 sample size was increased from approximately 100 to 150 participants to allow for a more robust analysis of safety and PK data - Eligible participants required to have measurable disease per RECIST 1.1 confirmed by an independent central review prior to trial entry; the prior version of the protocol did not specify central review of measurable disease - Statistical assumptions were updated to accommodate the change in sample size - The planned interim analyses were updated, with a second interim analysis added for 3 months after 100 participants have been treated - New information (per RECIST 1.1) on what constitutes clinical disease progression in the absence of radiologic progression was added

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported