Clinical trial results:
A Master Protocol Evaluating the Safety and Efficacy of Therapies for Metastatic Castration-resistant Prostate Cancer (mCRPC)

Summary

EudraCT number	2020-001305-23
Trial protocol	DE NL SE DK IT
Global end of trial date	23 October 2023

Results information

Result version number	v1 (current)
This version publication date	07 November 2024
First version publication date	07 November 2024

Trial information

Trial identification

Sponsor protocol code	20190505

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04631601
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, United States,
Public contact	Amgen (EUROPE) GmbH, Amgen Inc., MedInfoInternational@amgen.com
Scientific contact	Study Director, Amgen Inc., MedInfoInternational@amgen.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	23 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective was to evaluate the safety, tolerability and maximum tolerated dose or recommended phase 2 dose (RP2D) of acapatamab in combination with enzalutamide (Subprotocol A), acapatamab in combination with abiraterone (Subprotocol B), or acapatamab in combination with AMG 404 (Subprotocol C, Parts 1 and 2), evaluate preliminary antitumor activity of AMG monotherapy (Subprotocol C, Part 3) and to evaluate the safety and tolerability of acapatamab (Subprotocol D) in participants with mCRPC.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 24
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	United Kingdom: 4
Worldwide total number of subjects	54
EEA total number of subjects	26

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)	16
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

54 participants were enrolled at 11 centers in Denmark, Spain, Sweden, the United Kingdom, and the United States between 15 January 2021 and 23 October 2023.

One additional participant was enrolled in Subprotocol D. To protect participant privacy, the results of this participant are not included in this summary.

Pre-assignment

Screening details:

A total of 54 participants were enrolled and 53 received study treatment.

Period 1

Period 1 title	Main 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	Subprotocol A: Acapatamab and Enzalutamide

Arm description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) extended intravenous (eIV) infusion, followed by the target dose (60-minute intravenous [IV] infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received enzalutamide as oral tablets or oral capsules.

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

Dosage and administration details:

Enzalutamide was taken as either oral capsules or oral tablets.

Investigational medicinal product name	Acapatamab
Investigational medicinal product code	
Other name	AMG 160
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Acapatamab was administered as a short-term or extended IV infusion.

Arm title	Subprotocol B: Acapatamab and Abiraterone

Arm description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions).

Arm type	Experimental

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

Dosage and administration details:

Abiraterone was taken as oral tablets.

Investigational medicinal product name	Acapatamab
Investigational medicinal product code	
Other name	AMG 160
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Acapatamab was administered as a short-term or extended IV infusion.

Arm title	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404

Arm description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles (≥ 2), participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions). Participants also received AMG 404 as a short-term 30 minute IV infusion once per cycle.

Arm type	Experimental
Investigational medicinal product name	AMG 404
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

AMG 404 was administered as a short-term IV infusion.

Investigational medicinal product name	Acapatamab
Investigational medicinal product code	
Other name	AMG 160
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Acapatamab was administered as a short-term or extended IV infusion.

Arm title	Subprotocol C, Part 3: AMG 404 Monotherapy

Arm description:

Participants received AMG 404 as a short-term 30-minute IV infusion once during each cycle.

Arm type	Experimental
Investigational medicinal product name	AMG 404
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

AMG 404 was administered as a short-term IV infusion.

Number of subjects in period 1	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404
Started	14	15	15
Received study treatment	14	14	15
Completed	1	0	2
Not completed	13	15	13
Adverse event, serious fatal	4	5	8
Consent withdrawn by subject	2	-	-
Lost to follow-up	-	1	-
Decision by sponsor	7	9	5

Number of subjects in period 1	Subprotocol C, Part 3: AMG 404 Monotherapy
Started	10
Received study treatment	10
Completed	5
Not completed	5
Adverse event, serious fatal	2
Consent withdrawn by subject	1
Lost to follow-up	-
Decision by sponsor	2

Baseline characteristics

Reporting groups	
Reporting group title	Subprotocol A: Acapatamab and Enzalutamide
Reporting group description:	
In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) extended intravenous (eIV) infusion, followed by the target dose (60-minute intravenous [IV] infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received enzalutamide as oral tablets or oral capsules.	
Reporting group title	Subprotocol B: Acapatamab and Abiraterone
Reporting group description:	
In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions).	
Reporting group title	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404
Reporting group description:	
In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles (≥ 2), participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions). Participants also received AMG 404 as a short-term 30 minute IV infusion once per cycle.	
Reporting group title	Subprotocol C, Part 3: AMG 404 Monotherapy
Reporting group description:	
Participants received AMG 404 as a short-term 30-minute IV infusion once during each cycle.	

Reporting group values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404
Number of subjects	14	15	15
Age Categorical Units: Subjects			
Adults (18-64 years)	3	7	4
From 65-84 years	11	8	11
Age Continuous Units: years			
arithmetic mean	68.43	64.5	68.47
standard deviation	± 4.83	± 8.6	± 9.33
Gender Categorical Units: Subjects			
Female	0	0	0
Male	14	15	15
Ethnicity Units: Subjects			
Hispanic/Latino	0	2	0
Not Hispanic/Latino	14	13	15
Race Units: Subjects			
Asian	0	0	1
Black or African American	0	0	0
White	14	14	14
Other	0	1	0

Reporting group values	Subprotocol C, Part 3: AMG 404 Monotherapy	Total	
Number of subjects	10	54	
Age Categorical Units: Subjects			
Adults (18-64 years)	2	16	
From 65-84 years	8	38	
Age Continuous Units: years			
arithmetic mean	64.40		
standard deviation	± 9.94	-	
Gender Categorical Units: Subjects			
Female	0	0	
Male	10	54	
Ethnicity Units: Subjects			
Hispanic/Latino	0	2	
Not Hispanic/Latino	10	52	
Race Units: Subjects			
Asian	0	1	
Black or African American	1	1	
White	9	51	
Other	0	1	

End points

End points reporting groups

Reporting group title	Subprotocol A: Acapatamab and Enzalutamide

Reporting group description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) extended intravenous (eIV) infusion, followed by the target dose (60-minute intravenous [IV] infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received enzalutamide as oral tablets or oral capsules.

Reporting group title	Subprotocol B: Acapatamab and Abiraterone

Reporting group description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions).

Reporting group title	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404

Reporting group description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles (≥ 2), participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions). Participants also received AMG 404 as a short-term 30 minute IV infusion once per cycle.

Reporting group title	Subprotocol C, Part 3: AMG 404 Monotherapy

Reporting group description:

Participants received AMG 404 as a short-term 30-minute IV infusion once during each cycle.

Subject analysis set title	Subprotocol A (Cohort 1a): Acapatamab and Enzalutamide
Subject analysis set type	Full analysis

Subject analysis set description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received enzalutamide as oral tablets or oral capsules.

Subject analysis set title	Subprotocol A (Cohort 1b): Acapatamab and Enzalutamide
Subject analysis set type	Full analysis

Subject analysis set description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received enzalutamide as oral tablets or oral capsules.

Subject analysis set title	Subprotocol A (Cohort 2a): Acapatamab and Enzalutamide
Subject analysis set type	Full analysis

Subject analysis set description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received enzalutamide as oral tablets or oral capsules.

Subject analysis set title	Subprotocol A (Cohort 2b): Acapatamab and Enzalutamide
Subject analysis set type	Full analysis

Subject analysis set description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received enzalutamide as oral tablets or oral capsules.

Subject analysis set title	Subprotocol B (Cohort 1): Acapatamab and Abiraterone
Subject analysis set type	Full analysis

Subject analysis set description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by

the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions).

Subject analysis set title	Subprotocol B (Cohort 2): Acapatamab and Abiraterone
Subject analysis set type	Full analysis

Subject analysis set description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions).

Subject analysis set title	Subprotocol B (Cohort 2, Expansion): Acapatamab & Abiraterone
Subject analysis set type	Full analysis

Subject analysis set description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions).

Subject analysis set title	Subprotocol C, Parts 1 & 2 (Exploration): Acapatamab & AMG 404
Subject analysis set type	Full analysis

Subject analysis set description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles (≥ 2), participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions). Participants also received AMG 404 as a short-term 30 minute IV infusion once per cycle.

Subject analysis set title	Subprotocol C, Parts 1 & 2 (Expansion): Acapatamab & AMG 404
Subject analysis set type	Full analysis

Subject analysis set description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles (≥ 2), participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions). Participants also received AMG 404 as a short-term 30 minute IV infusion once per cycle.

Primary: Subprotocols A, B and C (Parts 1 and 2): Number of Participants Who Experienced a Dose-limiting Toxicity (DLT)

End point title	Subprotocols A, B and C (Parts 1 and 2): Number of Participants Who Experienced a Dose-limiting Toxicity (DLT)[1][2]

End point description:

DLTs were defined as any adverse event (per Common Terminology Criteria for Adverse Events (CTCAE) v5: Grade 5=Death, Grade 4=Life-threatening, Grade 3=Moderate) occurring within 28 days of the first AMG 160 dose, possibly related to the treatment, including:
- Grade 5 toxicity
- Grade 4 thrombocytopenia
- Grade 3 thrombocytopenia with significant hemorrhage
- Grade 4 neutropenia > 5 days
- Febrile neutropenia
- Grade 3 anemia requiring transfusion
- Grade ≥3 non-hematologic toxicity (with exceptions per protocol)
- Aspartate transaminase/alanine transaminase >3x upper limit of normal (ULN) with serum total bilirubin >2x ULN without cholestasis or another clear cause
- Grade ≥3 non-hematological toxicity delaying treatment > 2 weeks or resulting in <75% dose administration

DLT Analysis Set: Included all participants who received at least one AMG 160 dose and had an evaluable DLT endpoint (had a DLT or completed all planned doses without a DLT within 28-day DLT window in Cycle 1).

End point type	Primary

End point timeframe:

Day 1 to Day 28

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were pre-planned for this endpoint.

[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: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	13	15	
Units: participants	3	1	6	

Statistical analyses

No statistical analyses for this end point

Primary: Subprotocol C, Part 3: Percentage of Participants Who Experienced a Circulating Tumor Cell 0 (CTC0) Response

End point title	Subprotocol C, Part 3: Percentage of Participants Who Experienced a Circulating Tumor Cell 0 (CTC0) Response[3][4]

End point description:

CTC0 response was defined as CTC0 (reduction of CTCs > 0 to 0 at any post-baseline measurement). The baseline was defined as the last non-missing value on or prior to the pre-dose of AMG 404 assessments on Cycle 1 Day 1.

CTC0 Evaluable Analysis Set: Included all participants that were enrolled, received at least 1 dose of AMG 404 and had baseline CTC > 0.

End point type	Primary

End point timeframe:

Cycle 1 Day 1 to 14 days post-last dose of AMG 404 (each cycle was 28 days, maximum duration of AMG 404 treatment was 105.1 weeks).

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were pre-planned for this endpoint.

[4] - 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: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol C, Part 3: AMG 404 Monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: percentage of participants				
number (confidence interval 95%)	20.0 (0.51 to 71.64)			

Statistical analyses

No statistical analyses for this end point

Primary: Subprotocol C, Part 3: Percentage of Participants Who Experienced a CTC Conversion Response

End point title	Subprotocol C, Part 3: Percentage of Participants Who Experienced a CTC Conversion Response[5][6]

End point description:

CTC conversion response was defined as ≥ 5 CTCs/7.5 mL blood at baseline that converted to ≤ 4 CTCs/7.5 mL blood at any post-baseline measurement. The baseline was defined as the last non-missing value on or prior to the pre-dose assessments of AMG 404 on Cycle 1 Day 1.

CTC Conversion Evaluable Analysis Set: Included all participants that were enrolled, received at least 1 dose of AMG 404 and had baseline CTC ≥ 5.

End point type	Primary

End point timeframe:

Cycle 1 Day 1 to 14 days post-last dose of AMG 404 (each cycle was 28 days, maximum duration of AMG 404 treatment was 105.1 weeks).

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were pre-planned for this endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol C, Part 3: AMG 404 Monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.00 to 70.76)			

Statistical analyses

No statistical analyses for this end point

Primary: Subprotocol C, Part 3: Percentage of Participants Who Experienced a Prostate Specific Antigen (PSA) Response

End point title	Subprotocol C, Part 3: Percentage of Participants Who Experienced a Prostate Specific Antigen (PSA) Response[7][8]

End point description:

A PSA response was defined as the below and must have been confirmed by a second consecutive value 3 weeks later:

- PSA 30 response: ≥ 30% reduction from the baseline PSA.
- PSA 50 response: ≥ 50% reduction from the baseline PSA.
- PSA 70 response: ≥ 70% reduction from the baseline PSA.
- PSA 90 response: ≥ 90% reduction from the baseline PSA.

The baseline was defined as the last non-missing value on or prior to the pre-dose of AMG 404 assessments on Cycle 1 Day 1.

PSA Response Evaluable Set: Included all participants that were enrolled, received at least 1 dose of AMG 404, had measurable (i.e., > 0) baseline PSA and had the opportunity to be followed for at least 9 weeks starting from study Day 1.

End point type	Primary

End point timeframe:

Cycle 1 Day 1 to 5 months post-last dose of AMG 404 (each cycle was 28 days, maximum duration of AMG 404 treatment was 105.1 weeks).

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were pre-planned for this endpoint.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol C, Part 3: AMG 404 Monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)				
PSA 30 Response	20.0 (2.52 to 55.61)			
PSA 50 Response	20.0 (2.52 to 55.61)			
PSA 70 Response	10.0 (0.25 to 44.50)			
PSA 90 Response	10.0 (0.25 to 44.50)			

Statistical analyses

No statistical analyses for this end point

Primary: Subprotocols A, B and C (Parts 1 and 2): Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)

End point title	Subprotocols A, B and C (Parts 1 and 2): Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)[9][10]

End point description:

A TEAE was defined as any untoward medical occurrence in a clinical study participant irrespective of a causal relationship with the study treatment that started after the first dose of acapatamab, or AMG 404 (subprotocol C, parts 1 and 2), whichever was earlier.

A treatment-related TEAE was defined as a TEAE that had a reasonable possibility of being caused by acapatamab, or AMG 404 (subprotocol C, parts 1 and 2 only).

Clinically significant changes from baseline in vital signs and clinical laboratory tests were also recorded

as TEAEs.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab, or AMG 404 (subprotocol C, parts 1 and 2 only).

End point type	Primary

End point timeframe:

From first dose of acapatamab/AMG 404 to the first of 30 days after last dose of acapatamab/AMG404, end of study date or the initiation of a new anticancer therapy (up to a maximum of 3 years).

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were pre-planned for this endpoint.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	15	
Units: participants				
At least 1 TEAE	14	14	15	
At least 1 treatment-related TEAE	14	14	15	

Statistical analyses

No statistical analyses for this end point

Primary: Subprotocol C, Part 3: Objective Response Rate (ORR)

End point title	Subprotocol C, Part 3: Objective Response Rate (ORR)[11][12]

End point description:

ORR was defined as the percentage of participants who experienced a complete response (CR) or partial response (PR), per response evaluation criteria in solid tumors (RECIST) 1.1 with Prostate Cancer Working Group 3 (PCWG3) modifications. Responses were required to be confirmed at least 4 weeks later.

RECIST Evaluable Analysis Set: Included all participants that were enrolled and received at least 1 dose of AMG 404 and had measurable baseline disease per RECIST 1.1 and had the opportunity to be followed for at least 9 weeks starting from study Day 1.

End point type	Primary

End point timeframe:

From Cycle 1 Day 1 until progression, start of new anticancer therapy, or up to 3 years after the first dose of AMG 404 (each cycle was 28 days, maximum duration of AMG 404 treatment was 105.1 weeks).

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were pre-planned for this endpoint.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol C, Part 3: AMG 404 Monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percentage of participants				
number (confidence interval 95%)	0 (0.00 to 45.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A. B and C (Parts 1 and 2): ORR

End point title	Subprotocols A. B and C (Parts 1 and 2): ORR[13]

End point description:

ORR was defined as the percentage of participants who experienced a CR or PR, per RECIST 1.1 with PCWG3 modifications. Responses were required to be confirmed at least 4 weeks later.

RECIST 1.1 Evaluable Analysis Set: Included all participants that were enrolled, received at least 1 dose of AMG 160 and had measurable baseline disease per RECIST 1.1 per protocol and had the opportunity to be followed for at least 9 weeks starting from study Day 1.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 until progression, start of new anticancer therapy, or up to 3 years after the first dose of acapatamab/AMG 404 (each cycle was 28 days, maximum duration of acapatamab treatment was 98.4 weeks/AMG 404 treatment was 95.3 weeks).

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	5	7	
Units: percentage of participants				
number (confidence interval 95%)	50.0 (1.26 to 98.74)	40.0 (5.27 to 85.34)	14.3 (0.36 to 57.87)	

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1 and 2): Percentage of Participants Who Experienced a CTC Conversion Response

End point title	Subprotocols A, B and C (Parts 1 and 2): Percentage of Participants Who Experienced a CTC Conversion Response[14]

End point description:

CTC conversion response was defined as ≥ 5 CTCs/7.5 mL blood at baseline that converted to ≤ 4 CTCs/7.5 mL blood at any post-baseline measurement. The baseline was defined as the last non-missing value on or prior to the pre-dose of acapatamab assessments on Cycle 1 Day 1.

CTC Conversion Evaluable Analysis Set: Included all participants that were enrolled, received at least 1 dose of acapatamab/AMG 404 and had baseline CTC ≥ 5.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 to 14 days post-last dose of acapatamab/AMG 404 (each cycle was 28 days, maximum duration of acapatamab treatment was 98.4 weeks/AMG 404 treatment was 95.3 weeks).

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	5	3	
Units: percentage of participants				
number (confidence interval 95%)	75.0 (34.91 to 96.81)	100.0 (47.82 to 100.00)	66.7 (9.43 to 99.16)	

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1 and 2): Percentage of Participants Who Experienced a CTC0 Response

End point title	Subprotocols A, B and C (Parts 1 and 2): Percentage of Participants Who Experienced a CTC0 Response[15]

End point description:

CTC0 response was defined as CTC0 (reduction of CTCs > 0 to 0 at any post-baseline measurement). The baseline was defined as the last non-missing value on or prior to the pre-dose of acapatamab assessments on Cycle 1 Day 1.

CTC0 Evaluable Analysis Set: Included all participants that were enrolled, received at least 1 dose of acapatamab/AMG 404 and had baseline CTC > 0.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 to 14 days post-last dose of acapatamab/AMG 404 (each cycle was 28 days, maximum duration of acapatamab treatment was 98.4 weeks/AMG 404 treatment was 95.3 weeks).

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	6	5	
Units: percentage of participants				
number (confidence interval 95%)	63.6 (30.79 to 89.07)	16.7 (0.42 to 64.12)	60.0 (14.66 to 94.73)	

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Duration of CTC0 Response

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Duration of CTC0 Response

End point description:

Duration of CTC0 response was defined as the time from the date of initial CTC0 response to the earlier of CTC0 progression or death. Participants who had not ended their response at the time of analysis had duration of CTC0 response censored on the date of their last CTC0 or CTC conversion assessment.

Duration of CTC0 was not calculable due to too few responders. Calculation required > 10 responders to be accurate and meaningful.

End point type	Secondary

End point timeframe:

From date of initial CTC0 response to the earlier of CTC0 progression or death (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[16]	0[17]	0[18]	0[19]
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[16] - Duration of CTC0 response was not calculable.

[17] - Duration of CTC0 response was not calculable.

[18] - Duration of CTC0 response was not calculable.

[19] - Duration of CTC0 response was not calculable.

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1 and 2): Percentage of Participants Who Experienced a PSA Response

End point title	Subprotocols A, B and C (Parts 1 and 2): Percentage of Participants Who Experienced a PSA Response[20]

End point description:

A PSA response was defined as the below and must have been confirmed by a second consecutive value 3 weeks later:
- PSA 30 response: ≥ 30% reduction from the baseline PSA.
- PSA 50 response: ≥ 50% reduction from the baseline PSA.
- PSA 70 response: ≥ 70% reduction from the baseline PSA.
- PSA 90 response: ≥ 90% reduction from the baseline PSA.

The baseline was defined as the last non-missing value on or prior to the pre-dose of acapatamab assessments on Cycle 1 Day 1.

PSA Response Evaluable Set: Included all participants that were enrolled, received at least 1 dose of acapatamab/AMG 404, had measurable (i.e., > 0) baseline PSA and had the opportunity to be followed for at least 9 weeks starting from study Day 1.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 to 5 months post-last dose of acapatamab/AMG 404 (each cycle was 28 days, maximum duration of acapatamab treatment was 98.4 weeks/AMG 404 treatment was 95.3 weeks).

Notes:

[20] - 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: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	15	
Units: percentage of participants				
number (confidence interval 95%)				
PSA 30 Response	71.4 (41.90 to 91.61)	50.0 (23.04 to 76.96)	33.3 (11.82 to 61.62)	
PSA 50 Response	71.4 (41.90 to 91.61)	42.9 (17.66 to 71.14)	26.7 (7.79 to 55.10)	
PSA 70 Response	64.3 (35.14 to 87.24)	35.7 (12.76 to 64.86)	20.0 (4.33 to 48.09)	
PSA 90 Response	64.3 (35.14 to 87.24)	21.4 (4.66 to 50.80)	13.3 (1.66 to 40.46)	

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Duration of Response per RECIST 1.1

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Duration of Response per RECIST 1.1

End point description:

Duration of response per RECIST 1.1 was defined as the time from the date of an initial objective response (CR/PR) per RECIST 1.1 to the earlier of soft-tissue progression per RECIST 1.1 or death. CR/PR must have been confirmed at least 4 weeks later. Participants who had not ended their response at the time of analysis had duration of response censored at their last evaluable tumor assessment by computed tomography (CT)/magnetic resonance imaging (MRI) scan.

Duration of response was not calculable due to too few responders. Calculation required > 10 responders to be accurate and meaningful.

End point type	Secondary

End point timeframe:

From date of an initial objective response per RECIST 1.1 to the earlier of soft-tissue progression per RECIST 1.1 or death (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[21]	0[22]	0[23]	0[24]
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[21] - Duration of response was not calculable.

[22] - Duration of response was not calculable.

[23] - Duration of response was not calculable.

[24] - Duration of response was not calculable.

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Duration of CTC Conversion Response

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Duration of CTC Conversion Response

End point description:

Duration of CTC conversion response was defined as the time from the date of an initial CTC conversion response to the earlier of CTC conversion progression or death. Participants who had not ended their response at the time of analysis had duration of CTC response censored on the date of their last CTC0 or CTC conversion assessment.

Duration of CTC conversion response was not calculable due to too few responders. Calculation required > 10 responders to be accurate and meaningful.

End point type	Secondary

End point timeframe:

From the date of an initial CTC conversion response to the earlier of CTC conversion progression or death (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[25]	0[26]	0[27]	0[28]
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[25] - Duration of CTC conversion response was not calculable.

[26] - Duration of CTC conversion response was not calculable.

[27] - Duration of CTC conversion response was not calculable.

[28] - Duration of CTC conversion response was not calculable.

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Duration of PSA Response

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Duration of PSA Response

End point description:

Duration of PSA response was defined as the time of an initial PSA response (PSA 50) to the earlier of PSA progression or death. Participants who had not ended their response at the time of analysis had duration of PSA response censored on the date of their last PSA measurement.

Duration of PSA response was not calculable due to too few responders. Calculation required > 10 responders to be accurate and meaningful.

End point type	Secondary

End point timeframe:

From date of an initial PSA response (PSA 50) to the earlier of PSA progression or death (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[29]	0[30]	0[31]	0[32]
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[29] - Duration of PSA response was not calculable.

[30] - Duration of PSA response was not calculable.

[31] - Duration of PSA response was not calculable.

[32] - Duration of PSA response was not calculable.

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C: PSA Progression Free Survival (PFS)

End point title	Subprotocols A, B and C: PSA Progression Free Survival (PFS)

End point description:

PSA PFS was defined as the interval from study Day 1 to the earlier of a PSA progression or death from any cause; otherwise, PSA PFS was censored on the date of the last PSA measurement. If a participant had no baseline or post-baseline PSA measurement and a vital status of alive or known, PSA PFS was censored at study Day 1. The median was estimated using the Kaplan-Meier method and the 95% confidence interval was estimated using the method by Brookmeyer and Crowley.

99999 = upper limit was not calculable due to low number of events.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

From study Day 1 to the earlier of a PSA progression or death from any cause (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	15	10
Units: months				
median (confidence interval 95%)	20.30 (3.35 to 99999)	6.31 (3.94 to 99999)	3.94 (2.37 to 10.64)	4.30 (2.76 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Overall Survival (OS)

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Overall Survival (OS)

End point description:

OS was defined as the time from the date of study Day 1 until death due to any cause. OS time (months) = (date of death - study Day 1 + 1) x 12/365.25. Any participant known to have died at the time of analysis was censored based on the last recorded date on which the participant was alive. The median was estimated using the Kaplan-Meier method and the 95% confidence interval was estimated using the method by Kalbfleisch and Prentice.

9999 = median and upper limit not calculable due to fewer than 50% events. Lower bound was calculated from observed data that was available (25% percentile).
99999 = upper limit was not calculable due to low number of events.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

From the date of study Day 1 until death due to any cause (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	15	10
Units: months				
median (confidence interval 95%)	9999 (10.97 to	21.75 (13.17	16.82 (12.06	9999 (0.33 to

9999)	to 99999)	to 99999)	9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Radiographic Progression Free Survival (rPFS)

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Radiographic Progression Free Survival (rPFS)

End point description:

rPFS was defined as the interval from study Day 1 to the earlier of a radiographic progression or death from any cause; otherwise, rPFS was censored at the last evaluable tumor assessment date. If a participant had no post-baseline radiographic tumor assessment and a vital status of alive or known, rPFS was censored at study Day 1. The median was estimated using the Kaplan-Meier method and the 95% confidence interval was estimated using the method by Brookmeyer and Crowley.

9999 = median and upper limit not calculable due to fewer than 50% events. Lower bound was calculated from observed data that was available (25% percentile).
99999 = upper limit was not calculable due to low number of events.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

From study Day 1 to the earlier of a radiographic progression or death from any cause (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	15	10
Units: months				
median (confidence interval 95%)	18.20 (10.97 to 99999)	8.51 (3.71 to 99999)	9999 (2.00 to 9999)	3.48 (1.61 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Clinical PFS

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Clinical PFS

End point description:

Clinical PFS was defined as the time from the first dose of acapatamab or AMG 404 (subprotocol C only) to clinical disease progression or death from any cause; otherwise, clinical PFS was censored on the date

of last disease assessment. If a participant had no post-baseline disease assessment and a vital status of alive or known, clinical PFS was censored at study Day 1. The median was estimated using the Kaplan-Meier method and the 95% confidence interval was estimated using the method by Brookmeyer and Crowley.

9999 = median and upper limit not calculable due to fewer than 50% events. Lower bound was calculated from observed data that was available (25% percentile).
99999 = upper limit was not calculable due to low number of events.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

From first dose of acapatamab or AMG 404 (subprotocol C only) to clinical disease progression or death from any cause (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	15	10
Units: months				
median (confidence interval 95%)	20.30 (10.97 to 99999)	15.93 (6.31 to 99999)	15.67 (7.20 to 99999)	9999 (3.71 to 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Time to Radiographic Progression

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Time to Radiographic Progression

End point description:

Time to radiographic progression was defined as the interval from study Day 1 to radiographic progression in the absence of subsequent anticancer therapy. Time to radiographic progression was censored at the last evaluable post-baseline tumor assessment prior to subsequent anti-cancer therapy; otherwise at study Day 1. The median was estimated using the Kaplan-Meier method and the 95% confidence interval was estimated using the method by Brookmeyer and Crowley.

9999 = median and upper limit not calculable due to fewer than 50% events. Lower bound was calculated from observed data that was available (25% percentile).
99999 = upper limit was not calculable due to low number of events.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

From study Day 1 to radiographic progression in the absence of subsequent anticancer therapy (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	15	10
Units: months				
median (confidence interval 95%)	9999 (11.27 to 9999)	8.51 (3.71 to 99999)	9999 (2.00 to 9999)	3.48 (1.61 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Percentage of Participants Who Experienced a Gallium Prostate-specific Membrane Antigen-11 (PSMA-11) Response

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Percentage of Participants Who Experienced a Gallium Prostate-specific Membrane Antigen-11 (PSMA-11) Response

End point description:

A Gallium PSMA-11 response was defined as a ≥ 50% reduction from baseline in the maximum standardized update value (SUV) using 68Gallium (68Ga)-PSMA-11 positron emission tomography (PET)/CT. PSMA-11 response percentages were based on the number of participants with a baseline PSMA assessment (defined as the last non-missing value on or prior to the pre-dose of AMG 160/AMG 404 assessments) on Cycle 1 Day 1. The 95% confidence interval was calculated based on the Clopper-Pearson method.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 to 14 days post-last dose of AMG 404 (each cycle was 28 days).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	13	9
Units: percentage of participants				
number (confidence interval 95%)	66.7 (29.93 to 92.51)	20.0 (2.52 to 55.61)	23.1 (5.04 to 53.81)	0.0 (0.00 to 33.63)

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Time to Subsequent Therapy

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Time to Subsequent Therapy

End point description:

Time to subsequent therapy was defined as the interval from study Day 1 to the time a participant starts/receives the subsequent cancer therapy/subsequent therapy; otherwise, time to subsequent therapy was censored at the last known date of any of the study assessments prior to initiating the subsequent cancer therapy/subsequent therapy. The median was estimated using the Kaplan-Meier method and the 95% confidence interval was estimated using the method by Brookmeyer and Crowley.

9999 = median and upper limit not calculable due to fewer than 50% events. Lower bound was calculated from observed data that was available (25% percentile).
99999 = upper limit was not calculable due to low number of events.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

From study Day 1 to the time a participant starts/receives the subsequent cancer therapy/subsequent therapy (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	15	10
Units: months				
median (confidence interval 95%)	16.39 (8.84 to 20.07)	23.52 (5.98 to 99999)	9999 (4.40 to 9999)	9999 (0.89 to 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Time to PSA Progression

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Time to PSA Progression

End point description:

Time to PSA progression was defined as the interval from study Day 1 to PSA progression, otherwise time to PSA progression was censored at the last PSA assessment. The median was estimated using the Kaplan-Meier method and the 95% confidence interval was estimated using the method by Brookmeyer and Crowley.

9999 = median and upper limit not calculable due to fewer than 50% events. Lower bound was calculated from observed data that was available (25% percentile).
99999 = upper limit was not calculable due to low number of events.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

From study Day 1 to PSA progression (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	15	10
Units: months				
median (confidence interval 95%)	9999 (5.09 to 9999)	4.83 (2.99 to 99999)	3.94 (2.37 to 99999)	4.30 (2.76 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Time to Symptomatic Skeletal Events

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Time to Symptomatic Skeletal Events

End point description:

Time to symptomatic skeletal events was defined as time from study Day 1 to the first symptomatic skeletal event, otherwise time to symptomatic skeletal event was censored at the last dose of acapatamab/AMG 404 or end of safety follow-up date, whichever was later. Symptomatic skeletal events included fracture, spinal cord compression and radiation or surgery to bone. The median was estimated using the Kaplan-Meier method and the 95% confidence interval was estimated using the method by Brookmeyer and Crowley.

9999 = median and upper limit not calculable due to fewer than 50% events. Lower bound was calculated from observed data that was available (25% percentile).
999999 = median, lower and upper limits were not calculable due to very low number of events.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

From study Day 1 to the first symptomatic skeletal event (up to a maximum of 3 years).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	15	10
Units: months				
median (confidence interval 95%)	9999 (13.50 to 9999)	999999 (999999 to 999999)	999999 (999999 to 999999)	999999 (999999 to 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Total Alkaline Phosphatase Levels

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Total Alkaline Phosphatase Levels

End point description:

Alkaline phosphatase levels were collected centrally.

Safety Analysis Set: Included all participants with data available at each time point who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

Baseline and end of treatment visit (up to 14 days post-last dose of acapatamab/AMG 404. Each cycle was 28 days, maximum duration of acapatamab treatment was 98.4 weeks/AMG 404 treatment was 105.1 weeks).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14[33]	13[34]	15[35]	10[36]
Units: U/L				
arithmetic mean (standard deviation)				
Baseline	198.21 (± 264.79)	305.85 (± 356.76)	179.00 (± 221.12)	167.70 (± 219.41)
End of Treatment Visit	180.00 (± 198.27)	329.11 (± 425.58)	133.70 (± 106.41)	398.50 (± 627.04)

Notes:

[33] - End of treatment visit N = 12

[34] - End of treatment visit N = 9

[35] - End of treatment visit N = 10

[36] - End of treatment visit N = 6

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Lactate Dehydrogenase Levels

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Lactate Dehydrogenase Levels

End point description:

Lactate dehydrogenase levels were collected centrally.

Safety Analysis Set: Included all participants with data available at each time point who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

Baseline and end of treatment visit (up to 14 days post-last dose of acapatamab/AMG 404. Each cycle was 28 days, maximum duration of acapatamab treatment was 98.4 weeks/AMG 404 treatment was 105.1 weeks).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13[37]	13[38]	14[39]	9[40]
Units: U/L				
arithmetic mean (standard deviation)				
Baseline	209.54 (± 62.41)	268.54 (± 117.29)	241.50 (± 149.98)	267.89 (± 263.29)
End of Treatment Visit	261.18 (± 134.21)	210.11 (± 24.15)	177.00 (± 40.70)	238.50 (± 77.06)

Notes:

[37] - End of treatment visit N = 11

[38] - End of treatment visit N = 9

[39] - End of treatment visit N = 10

[40] - End of treatment visit N = 6

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Bone Specific Alkaline Phosphatase Levels

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Bone Specific Alkaline Phosphatase Levels

End point description:

Bone specific alkaline phosphatase levels were collected centrally.

Safety Analysis Set: Included all participants with data available at each time point who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

Baseline and end of treatment visit (up to 14 days post-last dose of acapatamab/AMG 404. Each cycle was 28 days, maximum duration of acapatamab treatment was 98.4 weeks/AMG 404 treatment was 105.1 weeks).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13[41]	12[42]	15[43]	10[44]
Units: ug/L				
arithmetic mean (standard deviation)				
Baseline	56.85 (± 109.65)	96.29 (± 129.56)	44.37 (± 68.69)	27.89 (± 30.24)
End of Treatment Visit	35.31 (± 55.21)	103.42 (± 165.94)	29.44 (± 34.98)	145.76 (± 238.81)

Notes:

[41] - End of treatment visit N = 11

[42] - End of treatment visit N = 9

[43] - End of treatment visit N = 9

[44] - End of treatment visit N = 5

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Hemoglobin Levels

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Hemoglobin Levels

End point description:

Hemoglobin levels were collected locally.

9999 = Data not available as data was only collected for safety-follow up visit 2 for subprotocol C.

Safety Analysis Set: Included all participants with data available at each time point who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

Baseline, safety follow-up visit (up to 30 days post-last dose of acapatamab/AMG 404), safety follow-up 2 (subprotocol C only, up to 5 months post-dose). Each cycle = 28 days, max acapatamab duration = 98.4 weeks, max AMG 404 duration = 105.1 weeks.

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14[45]	14[46]	15[47]	10[48]
Units: g/L				
arithmetic mean (standard deviation)				
Baseline	123.70 (± 18.98)	125.01 (± 12.45)	116.51 (± 11.23)	122.77 (± 12.96)
Safety Follow-up Visit	123.15 (± 22.45)	115.21 (± 13.71)	102.34 (± 13.82)	121.50 (± 12.81)
Safety Follow-up Visit 2	9999 (± 9999)	9999 (± 9999)	106.86 (± 21.41)	112.00 (± 12.12)

Notes:

[45] - Safety follow-up visit N = 7
Safety follow-up visit 2 N = 0

[46] - Safety follow-up visit N = 7
Safety follow-up visit 2 N = 0
[47] - Safety follow-up visit N = 8
Safety follow-up visit 2 N = 6
[48] - Safety follow-up visit N = 5
Safety follow-up visit 2 N = 3

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Neutrophil-to-lymphocyte Ratio

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Neutrophil-to-lymphocyte Ratio

End point description:

Data for the neutrophil-to-lymphocyte ratio were collected locally. Neutrophil-to-lymphocyte ratio was calculated by dividing the number of absolute neutrophils by the number of lymphocytes.

9999 = Data not available as data was only collected for safety-follow up visit 2 for subprotocol C.

Safety Analysis Set: Included all participants with data available at each time point who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

Baseline, safety follow-up visit (up to 30 days post-last dose of acapatamab/AMG 404), safety follow-up 2 (subprotocol C only, up to 5 months post-dose). Each cycle = 28 days, max acapatamab duration = 98.4 weeks, max AMG 404 duration = 105.1 weeks.

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14[49]	14[50]	15[51]	10[52]
Units: ratio				
arithmetic mean (standard deviation)				
Baseline	4.74 (± 3.03)	4.93 (± 4.94)	4.04 (± 2.90)	4.40 (± 2.93)
Safety Follow-up Visit	2.41 (± 1.66)	2.44 (± 1.14)	2.72 (± 1.94)	2.69 (± 0.82)
Safety Follow-up Visit 2	9999 (± 9999)	9999 (± 9999)	4.16 (± 4.10)	4.73 (± 2.36)

Notes:

[49] - Safety follow-up visit N = 6
Safety follow-up visit 2 N = 0
[50] - Safety follow-up visit N = 7
Safety follow-up visit 2 N = 0
[51] - Safety follow-up visit N = 8
Safety follow-up visit 2 N = 5
[52] - Safety follow-up visit N = 5
Safety follow-up visit 2 N = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1, 2 and 3): Urine N-telopeptide Levels

End point title	Subprotocols A, B and C (Parts 1, 2 and 3): Urine N-telopeptide Levels

End point description:

Urine N-telopeptide levels were collected centrally.

Safety Analysis Set: Included all participants with data available at each time point who were enrolled and received at least 1 dose of acapatamab or AMG 404 (Subprotocol C only).

End point type	Secondary

End point timeframe:

Baseline and end of treatment visit (up to 14 days post-last dose of acapatamab/AMG 404. Each cycle was 28 days, maximum duration of acapatamab treatment was 98.4 weeks/AMG 404 treatment was 105.1 weeks).

End point values	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404	Subprotocol C, Part 3: AMG 404 Monotherapy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[53]	9[54]	11[55]	0[56]
Units: nmol/mmol				
arithmetic mean (standard deviation)				
Baseline	155.99 (± 303.45)	88.67 (± 43.52)	61.06 (± 111.99)	()
End of Treatment Visit	109.52 (± 100.17)	160.10 (± 150.76)	60.57 (± 70.62)	()

Notes:

[53] - End of treatment visit N = 10

[54] - End of treatment visit N = 4

[55] - End of treatment visit N = 7

[56] - No data was collected for participants in subprotocol C, part 3.

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocol A, B and C (Parts 1 and 2): Maximum Serum Concentration (Cmax) of Acapatamab

End point title	Subprotocol A, B and C (Parts 1 and 2): Maximum Serum Concentration (Cmax) of Acapatamab

End point description:

Serum concentrations of acapatamab were determined using a validated assay.

9999 = Data was not available due to low number of participants with available samples.

Pharmacokinetic (PK) Concentration Analysis Set: Included all participants who received acapatamab and had at least 1 PK concentration available for analysis.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 to 7 and Cycle 2: Days 1 to 14 (each cycle was 28 days).

End point values	Subprotocol A (Cohort 1a): Acapatamab and Enzalutamide	Subprotocol A (Cohort 1b): Acapatamab and Enzalutamide	Subprotocol A (Cohort 2a): Acapatamab and Enzalutamide	Subprotocol A (Cohort 2b): Acapatamab and Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3[57]	3[58]	3[59]	3[60]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	10.5 (± 7)	7.24 (± 19)	8.20 (± 29)	7.83 (± 9999)
Cycle 2	51.4 (± 9999)	21.4 (± 729)	30.7 (± 9999)	31.1 (± 32)

Notes:

[57] - Cycle 2 N = 2

[58] - Cycle 2 N = 3

[59] - Cycle 2 N = 2

[60] - Cycle 1 N = 2

End point values	Subprotocol B (Cohort 1): Acapatamab and Abiraterone	Subprotocol B (Cohort 2): Acapatamab and Abiraterone	Subprotocol B (Cohort 2, Expansion): Acapatamab & Abiraterone	Subprotocol C, Parts 1 & 2 (Exploration): Acapatamab & AMG 404
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4[61]	5[62]	4[63]	8[64]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	9.30 (± 33)	10.4 (± 55)	8.74 (± 23)	11.6 (± 49)
Cycle 2	19.5 (± 402)	66.7 (± 35)	38.2 (± 73)	21.3 (± 167)

Notes:

[61] - Cycle 2 N = 4

[62] - Cycle 2 N = 3

[63] - Cycle 2 N = 4

[64] - Cycle 2 N = 6

End point values	Subprotocol C, Parts 1 & 2 (Expansion): Acapatamab & AMG 404			
Subject group type	Subject analysis set			
Number of subjects analysed	4[65]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	16.4 (± 35)			
Cycle 2	27.8 (± 43)			

Notes:

[65] - Cycle 2 N = 3

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocol A. B and C (Parts 1 and 2): Area Under the Curve During a

Dosing Interval (AUCtau)

End point title	Subprotocol A. B and C (Parts 1 and 2): Area Under the Curve During a Dosing Interval (AUCtau)

End point description:

Serum concentrations of acapatamab were determined using a validated assay.

9999 = Data was not available due to low number of participants with available samples.

PK Concentration Analysis Set: Included all participants who received acapatamab and had at least 1 PK concentration available for analysis.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 to 7 and Cycle 2: Days 1 to 14 (each cycle was 28 days).

End point values	Subprotocol A (Cohort 1a): Acapatamab and Enzalutamide	Subprotocol A (Cohort 1b): Acapatamab and Enzalutamide	Subprotocol A (Cohort 2a): Acapatamab and Enzalutamide	Subprotocol A (Cohort 2b): Acapatamab and Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[66]	2[67]	3[68]	3[69]
Units: hr•ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	()	867 (± 9999)	906 (± 22)	883 (± 9999)
Cycle 2	()	5510 (± 9999)	4400 (± 9999)	2700 (± 39)

Notes:

[66] - No participants had available samples.

[67] - Cycle 1 N = 1

[68] - Cycle 2 N = 1

[69] - Cycle 1 N = 2

End point values	Subprotocol B (Cohort 1): Acapatamab and Abiraterone	Subprotocol B (Cohort 2): Acapatamab and Abiraterone	Subprotocol B (Cohort 2, Expansion): Acapatamab & Abiraterone	Subprotocol C, Parts 1 & 2 (Exploration): Acapatamab & AMG 404
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[70]	2[71]	4[72]	4[73]
Units: hr•ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	9999 (± 9999)	1330 (± 9999)	962 (± 27)	1270 (± 72)
Cycle 2	291 (± 9999)	4510 (± 9999)	2900 (± 66)	2490 (± 145)

Notes:

[70] - Cycle 1 N = 0

[71] - Cycle 2 N = 2

[72] - Cycle 2 N = 4

[73] - Cycle 2 N = 4

End point values	Subprotocol C, Parts 1 & 2 (Expansion): Acapatamab &			

	AMG 404			
Subject group type	Subject analysis set			
Number of subjects analysed	3[74]			
Units: hr•ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	1960 (± 19)			
Cycle 2	2310 (± 69)			

Notes:

[74] - Cycle 2 N = 3

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1 and 2): Accumulation Ratio of Acapatamab

End point title	Subprotocols A, B and C (Parts 1 and 2): Accumulation Ratio of Acapatamab

End point description:

Serum concentrations of acapatamab were determined using a validated assay.

Accumulation ratio was not calculated due to the differences in dosing length and dosage between the lead in dose and the target dose administrations.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 to 7 and Cycle 2: Days 1 to 14 (each cycle was 28 days).

End point values	Subprotocol A (Cohort 1a): Acapatamab and Enzalutamide	Subprotocol A (Cohort 1b): Acapatamab and Enzalutamide	Subprotocol A (Cohort 2a): Acapatamab and Enzalutamide	Subprotocol A (Cohort 2b): Acapatamab and Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[75]	0[76]	0[77]	0[78]
Units: ratio				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[75] - Accumulation ratio was not calculated.

[76] - Accumulation ratio was not calculated.

[77] - Accumulation ratio was not calculated.

[78] - Accumulation ratio was not calculated.

End point values	Subprotocol B (Cohort 1): Acapatamab and Abiraterone	Subprotocol B (Cohort 2): Acapatamab and Abiraterone	Subprotocol B (Cohort 2, Expansion): Acapatamab & Abiraterone	Subprotocol C, Parts 1 & 2 (Exploration): Acapatamab & AMG 404
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[79]	0[80]	0[81]	0[82]
Units: ratio				

geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[79] - Accumulation ratio was not calculated.

[80] - Accumulation ratio was not calculated.

[81] - Accumulation ratio was not calculated.

[82] - Accumulation ratio was not calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocols A, B and C (Parts 1 and 2): Terminal half-life (t1/2z) of Acapatamab

End point title	Subprotocols A, B and C (Parts 1 and 2): Terminal half-life (t1/2z) of Acapatamab

End point description:

Serum concentrations of acapatamab were determined using a validated assay.

9999 = Data was not available due to low number of participants with available samples.

PK Concentration Analysis Set: Included all participants who received acapatamab and had at least 1 PK concentration available for analysis.

End point type	Secondary

End point timeframe:

Cycle 2: Days 1 to 14 (each cycle was 28 days).

End point values	Subprotocol A (Cohort 1a): Acapatamab and Enzalutamide	Subprotocol A (Cohort 1b): Acapatamab and Enzalutamide	Subprotocol A (Cohort 2a): Acapatamab and Enzalutamide	Subprotocol A (Cohort 2b): Acapatamab and Enzalutamide
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	1	3
Units: hours				
geometric mean (geometric coefficient of variation)	64.2 (± 9999)	83.1 (± 9999)	111 (± 9999)	113 (± 3)

End point values	Subprotocol B (Cohort 1): Acapatamab and Abiraterone	Subprotocol B (Cohort 2): Acapatamab and Abiraterone	Subprotocol B (Cohort 2, Expansion): Acapatamab & Abiraterone	Subprotocol C, Parts 1 & 2 (Exploration): Acapatamab & AMG 404
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	2	4	3
Units: hours				
geometric mean (geometric coefficient of variation)	74.4 (± 9999)	107 (± 9999)	98.3 (± 17)	84.4 (± 37)

End point values	Subprotocol C, Parts 1 & 2 (Expansion): Acapatamab & AMG 404			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: hours				
geometric mean (geometric coefficient of variation)	107 (± 25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subprotocol C, Part 3: Number of Participants Who Experienced a TEAE

End point title	Subprotocol C, Part 3: Number of Participants Who Experienced a TEAE[83]

End point description:

A TEAE was defined as any untoward medical occurrence in a clinical study participant irrespective of a causal relationship with the study treatment that started after the first dose of AMG 404, whichever was earlier.

A treatment-related TEAE was defined as a TEAE that had a reasonable possibility of being caused by AMG 404.

Clinically significant changes from baseline in vital signs and clinical laboratory tests were also recorded as TEAEs.

Safety Analysis Set: Included all participants who were enrolled and received at least 1 dose of AMG 404.

End point type	Secondary

End point timeframe:

From first dose of AMG 404 to the first of 30 days after last dose of AMG 404, end of study date or the initiation of a new anticancer therapy (up to a maximum of 3 years).

Notes:

[83] - 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: No statistical analyses were pre-planned for this endpoint.

End point values	Subprotocol C, Part 3: AMG 404 Monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: participants				
At least 1 TEAE	10			
At least 1 treatment-related TEAE	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Death: 1st dose of acapatamab/AMG 404 to end of study (up to a maximum of 3 years). TEAE: 1st dose of acapatamab/AMG 404 to min end of treatment + 30 days, end of study, 1st new anti-cancer therapy) (up to a maximum of 3 years)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Subprotocol A: Acapatamab and Enzalutamide

Reporting group description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received enzalutamide as oral tablets or oral capsules.

Reporting group title	Subprotocol B: Acapatamab and Abiraterone

Reporting group description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles, participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions).

Reporting group title	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404

Reporting group description:

In Cycle 1, participants initially received acapatamab as a 3-day (ie, 72-hour) eIV infusion, followed by the target dose (60-minute IV infusion) for the following doses throughout the first cycle. In subsequent cycles (≥ 2), participants received acapatamab at the target dose in 28-day cycles. Participants also received abiraterone as oral tablets and prednisone (or prednisolone in some regions). Participants also received AMG 404 as a short-term 30 minute IV infusion once per cycle.

Reporting group title	Subprotocol C, Part 3: AMG 404 Monotherapy

Reporting group description:

Participants received AMG 404 as a short-term 30-minute IV infusion once during each cycle.

Serious adverse events	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 14 (71.43%)	9 / 14 (64.29%)	11 / 15 (73.33%)
number of deaths (all causes)	4	5	8
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (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

Prostate cancer			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Asthenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (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 system disorders			
Cytokine release syndrome			
subjects affected / exposed	6 / 14 (42.86%)	4 / 14 (28.57%)	3 / 15 (20.00%)
occurrences causally related to treatment / all	14 / 14	5 / 5	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (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
Lumbar vertebral fracture			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Post procedural haematoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (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 prescribing error			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (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
Atrial flutter			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Atrial fibrillation			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Immune effector cell-associated neurotoxicity syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Myasthenia gravis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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			
Thrombocytopenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (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
Lymphopenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Anaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Uveitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (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
Rash			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Rash maculo-papular			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (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
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (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 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (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

Serious adverse events	Subprotocol C, Part 3: AMG 404 Monotherapy		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Cytokine release syndrome			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haematoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product prescribing error			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Immune effector cell-associated neurotoxicity syndrome				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myasthenia gravis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Thrombocytopenia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphopenia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Anaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Uveitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glaucoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Subprotocol A: Acapatamab and Enzalutamide	Subprotocol B: Acapatamab and Abiraterone	Subprotocol C, Parts 1 and 2: Acapatamab and AMG 404
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	14 / 14 (100.00%)	15 / 15 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Vascular disorders			
Embolism venous			

subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Hot flush			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Hypertension			
subjects affected / exposed	1 / 14 (7.14%)	2 / 14 (14.29%)	3 / 15 (20.00%)
occurrences (all)	1	3	3
Thrombophlebitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pallor			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Peripheral artery thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Phlebitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	3 / 14 (21.43%)	1 / 14 (7.14%)	5 / 15 (33.33%)
occurrences (all)	6	1	7
Surgical and medical procedures			
Functional endoscopic sinus surgery			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Facial pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Chills			

subjects affected / exposed	4 / 14 (28.57%)	2 / 14 (14.29%)	8 / 15 (53.33%)
occurrences (all)	9	4	21
Chest pain			
subjects affected / exposed	0 / 14 (0.00%)	3 / 14 (21.43%)	0 / 15 (0.00%)
occurrences (all)	0	3	0
Axillary pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	5 / 14 (35.71%)	3 / 14 (21.43%)	2 / 15 (13.33%)
occurrences (all)	13	3	4
Fatigue			
subjects affected / exposed	5 / 14 (35.71%)	5 / 14 (35.71%)	11 / 15 (73.33%)
occurrences (all)	5	8	20
Pyrexia			
subjects affected / exposed	4 / 14 (28.57%)	4 / 14 (28.57%)	10 / 15 (66.67%)
occurrences (all)	10	4	25
Peripheral swelling			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	2 / 14 (14.29%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	3	1	5
Oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Localised oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Influenza like illness			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	4 / 15 (26.67%)
occurrences (all)	0	0	8
Generalised oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Feeling hot			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Swelling			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Temperature regulation disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	13 / 14 (92.86%)	14 / 14 (100.00%)	13 / 15 (86.67%)
occurrences (all)	90	90	58
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pelvic discomfort			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pelvic pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Testicular pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Catarrh			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	2 / 14 (14.29%)	2 / 14 (14.29%)	4 / 15 (26.67%)
occurrences (all)	2	8	7
Dysphonia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	3 / 15 (20.00%)
occurrences (all)	2	0	3
Hiccups			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypoxia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Nasal congestion			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Nasal polyps			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	0	3	2
Rales			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rhinitis allergic			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Tachypnoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pneumonitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Confusional state			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Delirium			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	2	1	3
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 14 (7.14%)	7 / 14 (50.00%)	2 / 15 (13.33%)
occurrences (all)	1	15	5
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 14 (14.29%)	4 / 14 (28.57%)	2 / 15 (13.33%)
occurrences (all)	2	10	7
Blood bilirubin increased			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Coagulation time prolonged			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Inflammatory marker increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
International normalised ratio increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Platelet count decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
SARS-CoV-2 antibody test positive			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 14 (7.14%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Transaminases increased			

subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	2 / 15 (13.33%)
occurrences (all)	1	1	4
Weight decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	3 / 15 (20.00%)
occurrences (all)	0	3	3
Injury, poisoning and procedural complications			
Radiation associated pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Eye contusion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Gilbert's syndrome			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	4 / 15 (26.67%)
occurrences (all)	0	0	4
Sinus bradycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cardiac failure			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Cardiac disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Bradycardia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Atrial flutter			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Nervous system disorders			
Lethargy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Anosmia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	3	0
Balance disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Brain fog			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Dysgeusia			
subjects affected / exposed	3 / 14 (21.43%)	2 / 14 (14.29%)	2 / 15 (13.33%)
occurrences (all)	4	3	3
Headache			
subjects affected / exposed	4 / 14 (28.57%)	4 / 14 (28.57%)	5 / 15 (33.33%)
occurrences (all)	7	6	9
Immune effector cell-associated neurotoxicity syndrome			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	4 / 15 (26.67%)
occurrences (all)	1	0	5
Nervous system disorder			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Sciatica			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Sensory disturbance			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Taste disorder			
subjects affected / exposed	3 / 14 (21.43%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	3	0	1
Tremor			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	4 / 14 (28.57%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	4	1	0
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Disseminated intravascular coagulation			

subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Anaemia			
subjects affected / exposed	6 / 14 (42.86%)	1 / 14 (7.14%)	9 / 15 (60.00%)
occurrences (all)	27	1	20
Thrombocytopenia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	7	1	0
Leukocytosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	2 / 14 (14.29%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Presbyacusis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Ototoxicity			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hypoacusis			
subjects affected / exposed	3 / 14 (21.43%)	3 / 14 (21.43%)	4 / 15 (26.67%)
occurrences (all)	4	3	4
Deafness neurosensory			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Deafness			
subjects affected / exposed	3 / 14 (21.43%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	4	0	0
Ear pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Eye disorders			
Choroidal neovascularisation			

subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Conjunctival haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	3 / 14 (21.43%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	3	2	0
Exfoliation syndrome			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Chorioretinopathy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Central serous chorioretinopathy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cataract nuclear			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cataract			
subjects affected / exposed	3 / 14 (21.43%)	3 / 14 (21.43%)	1 / 15 (6.67%)
occurrences (all)	5	3	3
Blepharitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Astigmatism			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Angle closure glaucoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Age-related macular degeneration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eye pain			

subjects affected / exposed	1 / 14 (7.14%)	2 / 14 (14.29%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Vision blurred			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Retinal exudates			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Retinal degeneration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pseudophakia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Presbyopia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Myopia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Keratitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eyelid ptosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Visual acuity reduced			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Visual impairment			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Vitreous detachment			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Uveitis			

subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	2	1	1
Gastrointestinal disorders			
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	4
Constipation			
subjects affected / exposed	3 / 14 (21.43%)	3 / 14 (21.43%)	6 / 15 (40.00%)
occurrences (all)	10	3	7
Diarrhoea			
subjects affected / exposed	3 / 14 (21.43%)	8 / 14 (57.14%)	10 / 15 (66.67%)
occurrences (all)	5	14	23
Dry mouth			
subjects affected / exposed	2 / 14 (14.29%)	3 / 14 (21.43%)	7 / 15 (46.67%)
occurrences (all)	3	4	10
Dyspepsia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	4	0	1
Eructation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	3 / 14 (21.43%)	5 / 14 (35.71%)	9 / 15 (60.00%)
occurrences (all)	3	8	18
Proctalgia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 14 (28.57%)	3 / 14 (21.43%)	8 / 15 (53.33%)
occurrences (all)	5	14	15

Haemorrhoids			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypertransaminasaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dermal cyst			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Eczema			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Miliaria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pruritus			

subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	2 / 15 (13.33%)
occurrences (all)	0	3	2
Rash			
subjects affected / exposed	3 / 14 (21.43%)	3 / 14 (21.43%)	1 / 15 (6.67%)
occurrences (all)	4	3	1
Rash maculo-papular			
subjects affected / exposed	2 / 14 (14.29%)	2 / 14 (14.29%)	4 / 15 (26.67%)
occurrences (all)	5	3	7
Urticaria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Acute kidney injury			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Bladder spasm			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Calculus urethral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Nephrolithiasis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Renal colic			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	2	0

Urinary incontinence			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	4	0	0
Urinary retention			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	3
Hydronephrosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	3 / 14 (21.43%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	3	3	0
Arthritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	2 / 14 (14.29%)	4 / 14 (28.57%)	5 / 15 (33.33%)
occurrences (all)	3	7	7
Bone pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Fracture pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Immune-mediated arthritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			

subjects affected / exposed	3 / 14 (21.43%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	4	1	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	2
Neck pain			
subjects affected / exposed	1 / 14 (7.14%)	2 / 14 (14.29%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Osteonecrosis of jaw			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Pain in jaw			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 14 (0.00%)	3 / 14 (21.43%)	1 / 15 (6.67%)
occurrences (all)	0	3	1
Infections and infestations			
Urinary tract infection bacterial			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Abscess			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Bacteraemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

COVID-19			
subjects affected / exposed	4 / 14 (28.57%)	1 / 14 (7.14%)	1 / 15 (6.67%)
occurrences (all)	4	1	1
Herpes simplex reactivation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	3 / 14 (21.43%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	3	1	0
Sinusitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Parotitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	2	0	2
Nasopharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Mucosal infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	1	1	0

Vascular device infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 14 (35.71%)	3 / 14 (21.43%)	5 / 15 (33.33%)
occurrences (all)	5	3	6
Hypercalcaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	2	0	4
Hyperkalaemia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 14 (7.14%)	0 / 15 (0.00%)
occurrences (all)	3	2	0
Hyperphosphataemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	2 / 15 (13.33%)
occurrences (all)	3	0	6
Hypocalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	0	5	0
Hypokalaemia			
subjects affected / exposed	2 / 14 (14.29%)	2 / 14 (14.29%)	5 / 15 (33.33%)
occurrences (all)	2	2	7
Hypomagnesaemia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	2 / 15 (13.33%)
occurrences (all)	0	2	3
Hyponatraemia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 14 (14.29%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Hypophosphataemia			

subjects affected / exposed	2 / 14 (14.29%)	2 / 14 (14.29%)	4 / 15 (26.67%)
occurrences (all)	2	5	5
Malnutrition			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Subprotocol C, Part 3: AMG 404 Monotherapy		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Embolism venous			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Thrombophlebitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pallor			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Peripheral artery thrombosis			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Phlebitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Functional endoscopic sinus surgery			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Facial pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	4		
Axillary pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Peripheral swelling			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Localised oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Generalised oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Feeling hot			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Swelling			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Temperature regulation disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pelvic discomfort			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pelvic pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Testicular pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Catarrh			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hiccups			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nasal congestion			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nasal polyps			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pulmonary embolism			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rales			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tachypnoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Confusional state			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Delirium			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Depressed mood			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Coagulation time prolonged			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Inflammatory marker increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
International normalised ratio increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Neutrophil count decreased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
SARS-CoV-2 antibody test positive subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
SARS-CoV-2 test positive subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Transaminases increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Weight decreased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Injury, poisoning and procedural complications			
Radiation associated pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Eye contusion subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 3		
Congenital, familial and genetic disorders			
Gilbert's syndrome subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Cardiac disorders			

Tachycardia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Sinus bradycardia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Cardiac failure subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Cardiac disorder subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Bradycardia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Atrial flutter subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Nervous system disorders Lethargy subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Anosmia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Balance disorder subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Brain fog				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Dizziness				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Dysgeusia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Headache				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	3			
Immune effector cell-associated neurotoxicity syndrome				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Nervous system disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Peripheral sensory neuropathy				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Presyncope				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Sciatica				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Sensory disturbance				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Syncope				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Taste disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Tremor			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Leukocytosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Presbyacusis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ototoxicity			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoacusis			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Deafness neurosensory subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Deafness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Ear pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Eye disorders Choroidal neovascularisation subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Dry eye subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Exfoliation syndrome subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Chorioretinopathy subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Central serous chorioretinopathy subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Cataract nuclear subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Cataract subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		

Blepharitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Astigmatism				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Angle closure glaucoma				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Age-related macular degeneration				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Eye pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Vision blurred				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Retinal exudates				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Retinal degeneration				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pseudophakia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Presbyopia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Myopia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Keratitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

Eyelid ptosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Visual acuity reduced			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Visual impairment			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vitreous detachment			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Uveitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspepsia			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eructation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Proctalgia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Haemorrhoids			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypertransaminasaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dermal cyst			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dry skin			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Miliaria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Acute kidney injury			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bladder spasm			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Calculus urethral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nephrolithiasis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal colic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hydronephrosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Arthritis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Back pain			

subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Bone pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Flank pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Fracture pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Immune-mediated arthritis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Muscular weakness				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	2			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Musculoskeletal pain				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Myalgia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Neck pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Osteonecrosis of jaw				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Pain in extremity				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Pain in jaw				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Urinary tract infection bacterial			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abscess			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Herpes simplex reactivation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rash pustular			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Parotitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Mucosal infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Influenza subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Hordeolum subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Vascular device infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1			
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0			
Hyperphosphataemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1			
Hypoalbuminaemia				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Malnutrition			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2020	The following updates were made to the master protocol: - Removed Appendix 3 (Safety Events: Definitions and Procedures for Recording, Evaluating, Follow-up and Reporting) as this appendix was added to all subprotocols. - Additional changes were made to align with subprotocol amendments (removal of electrocardiograms from endpoint and "subject's legally acceptable representative").
30 March 2021	The following updates were made to the master protocol: - Clarified that participant randomization into subprotocols depended on upon slot availability . - Approximate total participant enrollment was updated to align with changes made in subprotocols A, B, and C (addition of Asia cohort). - Administrative changes and minor changes to align with protocol template were made.
13 May 2021	The following updates were made to the master protocol: - Included a new subprotocol ((Subprotocol D: A Phase 1b Study Evaluating the Safety and Efficacy of AMG 160 Monotherapy in Subjects With Metastatic Castration Resistant Prostate Cancer [mCRPC]). The study schema, number of participants and measures to minimize bias were updated. - The primary endpoint was clarified to indicate that dose-limiting toxicities are only an endpoint for the dose exploration phase of associated subprotocols. - Reference included to the master informed consent form.
16 July 2021	The following updates were made to the master protocol: - Clarified the definition of screen failures. - Aligned with updated protocol template. - Minor clarifications to language. - Administrative and editorial changes throughout protocol.

21 February 2022	The following updates were made: - Study Governance Considerations were updated to include that Amgen or its designee reserved the right to stop one or multiple subprotocols in addition to the study or study site participation. - In case tocilizumab is not available, siltuximab language was added to include instructions for administration and conduction of a subgroup analysis of safety with cytokine release syndrome outcome and pharmacokinetics for participants who received siltuximab treatment. - Since an analysis based on RECIST 1.1 without PCWG3 modifications was performed, secondary endpoint was updated to remove PCWG3 modifications for RECIST assessment. PCWG3 recommended endpoints were also, albeit separately, evaluated. - Anemia was added as a new hematology-related sign and symptom of cytokine release syndrome. - The approximate number of participants to be enrolled in subprotocols A-D was updated to 136 participants to reflect a change made in the number of participants to be enrolled for subprotocol C (reduced to 30). - A clarification was provided to specify that countries in Asia did not participate in subprotocol D. - A clarification was provided to align naming of the investigational product AMG 160 in study protocol with the name used in Investigator's Brochure, Acapatamab. - Reference section was updated to add two citations supporting the newly added siltuximab language. - Administrative and editorial changes (including grammatical, typographical, and formatting) were made throughout the protocol.

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.

Study 20190505 (including all subprotocols) was discontinued early after a strategic decision by Amgen. This study was not stopped for safety reasons or lack of efficacy.

Notes: