

**Clinical trial results:****A Multicenter, Phase 2, Single Arm, Two Cohort Study Evaluating the Efficacy, Safety, and Pharmacokinetics of AMG 337 in Subjects with MET Amplified Gastric/Gastroesophageal Junction/Esophageal Adenocarcinoma or Other MET Amplified Solid Tumors****Summary**

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2013-001277-24 |
| Trial protocol | CZ GR DE BE GB IT AT HU PL ES |
| Global end of trial date | 10 October 2016 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 22 October 2017 |
| First version publication date | 22 October 2017 |

Trial information**Trial identification**

| | |
|-----------------------|----------|
| Sponsor protocol code | 20130111 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02016534 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Amgen Inc. |
| Sponsor organisation address | One Amgen Center Drive, Thousand Oaks, CA, United States, 91320 |
| Public contact | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com |
| Scientific contact | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, 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 | 16 May 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 October 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine antitumor activity of AMG 337 in subjects with mesenchymal epithelial transition factor (MET)-amplified gastric (G), gastroesophageal junction (GEJ), or esophageal (E) adenocarcinoma.

Protection of trial subjects:

This study was conducted in accordance with the principles of the applicable country, Food and Drug Administration and International Conference on Harmonization (ICH) Good Clinical Practice (GCP) regulations/guidelines.

All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.

The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 14 February 2014 |
| 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 | Australia: 6 |
| Country: Number of subjects enrolled | Belgium: 3 |
| Country: Number of subjects enrolled | France: 4 |
| Country: Number of subjects enrolled | Germany: 2 |
| Country: Number of subjects enrolled | Greece: 1 |
| Country: Number of subjects enrolled | Hungary: 1 |
| Country: Number of subjects enrolled | Italy: 5 |
| Country: Number of subjects enrolled | Korea, Republic of: 20 |
| Country: Number of subjects enrolled | Poland: 7 |
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | United States: 5 |
| Worldwide total number of subjects | 60 |
| EEA total number of subjects | 29 |

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) | 38 |
| From 65 to 84 years | 21 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 34 centers across 12 countries in Asia, Australia, Europe, and North America. Adults with mesenchymal epithelial transition factor (MET)-amplified gastric (G), gastroesophageal junction (GEJ), or esophageal (E) adenocarcinoma or other MET-amplified solid tumors were enrolled.

Pre-assignment

Screening details:

Participants were enrolled in the following 2 cohorts:

- Cohort 1: MET-amplified G/GEJ/E adenocarcinoma with measurable tumor per RECIST version 1.1
- Cohort 2: Non-measurable G/GEJ/E adenocarcinoma (2A), measurable G/GEJ/E adenocarcinoma with prior MET antibody therapy (2B), or MET-amplified mixed solid tumors with measurable tumor (2C).

Period 1

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

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Measurable G/GEJ/E |

Arm description:

Participants with measurable G/GEJ/E adenocarcinoma were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | AMG 337 |
| Investigational medicinal product code | AMG 337 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects self-administered AMG 337 300 mg orally daily on an empty stomach.

| | |
|------------------|------------------------|
| Arm title | Non-measurable G/GEJ/E |
|------------------|------------------------|

Arm description:

Participants with non-measurable G/GEJ/E adenocarcinoma were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | AMG 337 |
| Investigational medicinal product code | AMG 337 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects self-administered AMG 337 300 mg orally daily on an empty stomach.

| | |
|------------------|---|
| Arm title | Measurable G/GEJ/E + Prior MET Antibody Therapy |
|------------------|---|

Arm description:

Participants with measurable G/GEJ/E adenocarcinoma who received prior MET antibody therapy were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|----------|
| Investigational medicinal product name | AMG 337 |
| Investigational medicinal product code | AMG 337 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects self-administered AMG 337 300 mg orally daily on an empty stomach.

| | |
|------------------|-------|
| Arm title | NSCLC |
|------------------|-------|

Arm description:

Participants with non-small cell lung cancer (NSCLC) were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | AMG 337 |
| Investigational medicinal product code | AMG 337 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects self-administered AMG 337 300 mg orally daily on an empty stomach.

| Number of subjects in period 1 | Measurable G/GEJ/E | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy |
|--------------------------------|--------------------|------------------------|---|
| | Started | 45 | 10 |
| Received AMG 337 | 45 | 9 | 1 |
| Completed | 1 | 0 | 0 |
| Not completed | 44 | 10 | 1 |
| Consent withdrawn by subject | 4 | 2 | - |
| Death | 29 | 7 | 1 |
| Lost to follow-up | 2 | - | - |
| Decision by sponsor | 9 | 1 | - |

| Number of subjects in period 1 | NSCLC |
|--------------------------------|-------|
| Started | 4 |
| Received AMG 337 | 3 |
| Completed | 0 |
| Not completed | 4 |
| Consent withdrawn by subject | - |
| Death | 4 |
| Lost to follow-up | - |
| Decision by sponsor | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Measurable G/GEJ/E |
|-----------------------|--------------------|

Reporting group description:

Participants with measurable G/GEJ/E adenocarcinoma were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|-----------------------|------------------------|
| Reporting group title | Non-measurable G/GEJ/E |
|-----------------------|------------------------|

Reporting group description:

Participants with non-measurable G/GEJ/E adenocarcinoma were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|-----------------------|---|
| Reporting group title | Measurable G/GEJ/E + Prior MET Antibody Therapy |
|-----------------------|---|

Reporting group description:

Participants with measurable G/GEJ/E adenocarcinoma who received prior MET antibody therapy were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|-----------------------|-------|
| Reporting group title | NSCLC |
|-----------------------|-------|

Reporting group description:

Participants with non-small cell lung cancer (NSCLC) were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| Reporting group values | Measurable G/GEJ/E | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy |
|---|--------------------|------------------------|---|
| Number of subjects | 45 | 10 | 1 |
| Age Categorical Units: Subjects | | | |
| 18 - 64 years | 28 | 6 | 1 |
| 65 - 84 years | 16 | 4 | 0 |
| 85 years and over | 1 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 60 | 59.6 | 59 |
| standard deviation | ± 13.4 | ± 17.3 | ± 99999 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 11 | 4 | 1 |
| Male | 34 | 6 | 0 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Asian | 17 | 4 | 0 |
| Other | 1 | 0 | 0 |
| White | 27 | 6 | 1 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 0 | 1 | 0 |
| Not Hispanic or Latino | 45 | 9 | 1 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Region Units: Subjects | | | |
| Asia | 17 | 3 | 0 |
| Australia | 3 | 0 | 1 |

| | | | |
|--|----|----|---|
| Europe | 23 | 4 | 0 |
| North America | 2 | 3 | 0 |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| Eastern Cooperative Oncology Group (ECOG) Performance Status is used by doctors and researchers to assess how a participants disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. 0 = Fully Active; 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self- Care; 4 = Completely Disabled, no self-care, confined to bed or chair; 5 = Dead. | | | |
| Units: Subjects | | | |
| 0 (Fully active) | 15 | 3 | 1 |
| 1 (Restrictive but ambulatory) | 30 | 7 | 0 |
| Disease Stage at Screening | | | |
| Units: Subjects | | | |
| Locally advanced | 2 | 0 | 0 |
| Metastatic | 43 | 10 | 1 |

| Reporting group values | NSCLC | Total | |
|---|--------|-------|--|
| Number of subjects | 4 | 60 | |
| Age Categorical | | | |
| Units: Subjects | | | |
| 18 - 64 years | 3 | 38 | |
| 65 - 84 years | 1 | 21 | |
| 85 years and over | 0 | 1 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 62.5 | | |
| standard deviation | ± 3.87 | - | |
| Gender, Male/Female | | | |
| Units: Subjects | | | |
| Female | 2 | 18 | |
| Male | 2 | 42 | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Asian | 1 | 22 | |
| Other | 0 | 1 | |
| White | 3 | 37 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 1 | |
| Not Hispanic or Latino | 4 | 59 | |
| Unknown or Not Reported | 0 | 0 | |
| Region | | | |
| Units: Subjects | | | |
| Asia | 0 | 20 | |
| Australia | 2 | 6 | |
| Europe | 2 | 29 | |
| North America | 0 | 5 | |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| Eastern Cooperative Oncology Group (ECOG) Performance Status is used by doctors and researchers to assess how a participants disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. 0 = Fully Active; 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self- Care; | | | |

| 4 = Completely Disabled, no self-care, confined to bed or chair; 5 = Dead. | | | |
|--|---|----|--|
| Units: Subjects | | | |
| 0 (Fully active) | 0 | 19 | |
| 1 (Restrictive but ambulatory) | 4 | 41 | |
| Disease Stage at Screening | | | |
| Units: Subjects | | | |
| Locally advanced | 0 | 2 | |
| Metastatic | 4 | 58 | |

End points

End points reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Measurable G/GEJ/E |
|-----------------------|--------------------|

Reporting group description:

Participants with measurable G/GEJ/E adenocarcinoma were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|-----------------------|------------------------|
| Reporting group title | Non-measurable G/GEJ/E |
|-----------------------|------------------------|

Reporting group description:

Participants with non-measurable G/GEJ/E adenocarcinoma were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|-----------------------|---|
| Reporting group title | Measurable G/GEJ/E + Prior MET Antibody Therapy |
|-----------------------|---|

Reporting group description:

Participants with measurable G/GEJ/E adenocarcinoma who received prior MET antibody therapy were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|-----------------------|-------|
| Reporting group title | NSCLC |
|-----------------------|-------|

Reporting group description:

Participants with non-small cell lung cancer (NSCLC) were assigned to receive 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|----------------------------|----------|
| Subject analysis set title | Cohort 1 |
|----------------------------|----------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Subjects with MET-amplified gastric/gastroesophageal junction/esophageal adenocarcinoma

| | |
|----------------------------|----------------------|
| Subject analysis set title | Cohort 2A, 2B and 2C |
|----------------------------|----------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Subjects with non-measurable G/GEJ/E, measurable G/GEJ/E with prior MET antibody therapy.

Primary: Objective Response Rate in Participants with MET-amplified Measurable G/GEJ/E Adenocarcinoma (Cohort 1)

| | |
|-----------------|---|
| End point title | Objective Response Rate in Participants with MET-amplified Measurable G/GEJ/E Adenocarcinoma (Cohort 1) ^{[1][2]} |
|-----------------|---|

End point description:

Tumor assessments were based on Investigator assessment of disease progression as per Response Evaluation Criteria In Solid Tumors (RECIST) 1.1. Objective response rate was defined as the percentage of subjects who achieved either a complete response (CR) or a partial response (PR) per RECIST v1.1. Subjects who did not meet the criteria for response by the data cutoff date were considered non-responders.

The Response Analysis Set was defined as all enrolled subjects with measurable tumor per RECIST v1.1 at baseline who received at least one dose of AMG 337.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Tumor assessment scans were performed every 8 weeks during study treatment until week 32, thereafter tumor assessment scans were taken every 12 weeks during study treatment. Median follow-up time was 5.5 months.

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: A formal hypothesis was not tested in this study.

[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: The primary endpoint was analyzed in cohort 1 subjects only

| | | | | |
|-----------------------------------|--------------------|--|--|--|
| End point values | Measurable G/GEJ/E | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 45 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 17.8 (8 to 32.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate in Participants in Cohort 2

| | |
|-----------------|--|
| End point title | Objective Response Rate in Participants in Cohort 2 ^[3] |
|-----------------|--|

End point description:

Tumor assessments were based on Investigator assessment of disease progression as per Response Evaluation Criteria In Solid Tumors (RECIST) 1.1. Objective response rate was defined as the percentage of subjects who achieved either a complete response (CR) or a partial response (PR) per RECIST v1.1. Subjects who did not meet the criteria for response by the data cutoff date were considered non-responders.

The Response Analysis Set was defined as all enrolled subjects with measurable tumor per RECIST v1.1 at baseline who received at least one dose of AMG 337.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Tumor assessment scans were performed every 8 weeks during study treatment until week 32, and thereafter every 12 weeks during study treatment. Median follow-up time was 11.4, 20.3, and 2.2 months in each group respectively.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was analyzed in cohort 2 subjects only

| End point values | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC | |
|-----------------------------------|------------------------|---|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[4] | 0 ^[5] | 0 ^[6] | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[4] - Response analysis set (only includes subjects with measurable tumor at baseline)

[5] - Not analyzed due to small number of subjects

[6] - Not analyzed due to small number of subjects

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

| | |
|-----------------|----------------------|
| End point title | Duration of Response |
|-----------------|----------------------|

End point description:

Duration of response was calculated for responders only and defined as the time from the first

observation of a response to the first observation of a disease progression per RECIST v1.1 or death due to any cause. If a responding subject had not progressed or died by the data cutoff date, duration of response was censored at the time of the last evaluable tumor assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Tumor assessment scans were performed every 8 weeks during study treatment until week 32, and thereafter every 12 weeks during study treatment. Median follow-up time was 5.5, 11.4, 20.3, and 2.2 months in each group respectively.

| End point values | Measurable G/GEJ/E | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC |
|----------------------------------|--------------------|------------------------|---|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 ^[7] | 0 ^[8] | 0 ^[9] | 0 ^[10] |
| Units: months | | | | |
| median (confidence interval 95%) | 6 (3.7 to 16.7) | (to) | (to) | (to) |

Notes:

[7] - Response analysis set with an objective response

[8] - Not analyzed due to small number of subjects

[9] - Not analyzed due to small number of subjects

[10] - Not analyzed due to small number of subjects

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

| | |
|-----------------|------------------|
| End point title | Time to Response |
|-----------------|------------------|

End point description:

Time to response was calculated for those subjects with an objective response and defined as the time from the first dose date to the first observation of a response (CR or PR) per RECIST v1.1.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Tumor assessment scans were performed every 8 weeks during study treatment until week 32, and thereafter every 12 weeks during study treatment. Median follow-up time was 5.5, 11.4, 20.3, and 2.2 months in each group respectively.

| End point values | Measurable G/GEJ/E | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC |
|---------------------------------------|----------------------|------------------------|---|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 ^[11] | 0 ^[12] | 0 ^[13] | 0 ^[14] |
| Units: weeks | | | | |
| median (inter-quartile range (Q1-Q3)) | 7.64 (7.14 to 11.86) | (to) | (to) | (to) |

Notes:

[11] - Response analysis set with an objective response

[12] - Not analyzed due to small number of subjects

[13] - Not analyzed due to small number of subjects

[14] - Not analyzed due to small number of subjects

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival

End point title | Progression-free Survival

End point description:

Progression-free survival (PFS) was defined as the time from the first dose date to the first observation of a disease progression per RECIST v1.1 or death due to any cause. If a subject had not progressed or died by the data cutoff date, progression-free survival was censored at the time of the last evaluable tumor assessment.

The analysis of PFS was conducted on the Full Analysis Set.

End point type | Secondary

End point timeframe:

Tumor assessment scans were performed every 8 weeks during study treatment until week 32, and thereafter every 12 weeks during study treatment. Median follow-up time was 5.5, 11.4, 20.3, and 2.2 months in each group respectively.

| End point values | Measurable G/GEJ/E | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC |
|----------------------------------|--------------------|------------------------|---|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 45 | 9 | 0 ^[15] | 0 ^[16] |
| Units: months | | | | |
| median (confidence interval 95%) | 3.4 (2.1 to 5) | 3.6 (2.2 to 10.3) | (to) | (to) |

Notes:

[15] - Measurable G/GEJ/E subjects with prior MET therapy were excluded

[16] - NSCLC subjects were excluded

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title | Overall Survival

End point description:

Overall survival was defined as the time from the first dose date to the date of death due to any cause. If a subject was lost to follow-up before the data cutoff date or still alive at the data cutoff date, overall survival was censored at the last contact date.

This analysis was conducted in the full analysis set.

End point type | Secondary

End point timeframe:

Median follow-up time was 5.5, 11.4, 20.3, and 2.2 months in each group respectively.

| End point values | Measurable G/GEJ/E | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC |
|----------------------------------|--------------------|------------------------|---|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 45 | 9 | 0 ^[17] | 0 ^[18] |
| Units: months | | | | |
| median (confidence interval 95%) | 7 (4.4 to 10.9) | 11.4 (4.9 to 18.5) | (to) | (to) |

Notes:

[17] - Measurable G/GEJ/E subjects with prior MET therapy were excluded

[18] - NSCLC subjects were excluded

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events

| | |
|-----------------|--|
| End point title | Number of Participants with Adverse Events |
|-----------------|--|

End point description:

The adverse event grading scale used was the Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0.

A serious adverse event was defined as an adverse event that meets at least 1 of the following serious criteria:

- fatal
- life threatening (places the subject at immediate risk of death)
- requires in-patient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- congenital anomaly/birth defect
- other medically important serious event

The Safety Analysis Set included all enrolled subjects who received at least one dose of AMG 337.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the first dose of study drug up to 30 days after the last dose; median duration of treatment was 2.3, 2.4, 2.1, and 1.6 months in each group respectively.

| End point values | Measurable G/GEJ/E | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC |
|-----------------------------|--------------------|------------------------|---|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 45 ^[19] | 9 ^[20] | 1 ^[21] | 3 ^[22] |
| Units: participants | | | | |
| All adverse events | 44 | 9 | 1 | 3 |
| Adverse events ≥ grade 2 | 41 | 9 | 1 | 2 |
| Adverse events ≥ grade 3 | 34 | 4 | 1 | 2 |
| Adverse events ≥ grade 4 | 9 | 1 | 0 | 2 |
| Serious adverse events | 26 | 5 | 1 | 2 |

| | | | | |
|--|---|---|---|---|
| Leading to discontinuation of study drug | 7 | 1 | 1 | 1 |
| Fatal adverse events | 7 | 0 | 0 | 2 |

Notes:

[19] - Safety analysis set

[20] - Safety analysis set

[21] - Safety analysis set

[22] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Treatment

| | |
|-----------------|-----------------------|
| End point title | Duration of Treatment |
|-----------------|-----------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose until last dose

| End point values | Measurable G/GEJ/E | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC |
|---------------------------------------|--------------------|------------------------|---|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 45 ^[23] | 9 ^[24] | 1 ^[25] | 3 ^[26] |
| Units: months | | | | |
| median (inter-quartile range (Q1-Q3)) | 2.3 (0.9 to 5.4) | 2.4 (1.2 to 5.7) | 2.1 (2.1 to 2.1) | 1.6 (1 to 3.9) |

Notes:

[23] - Safety analysis set

[24] - Safety analysis set

[25] - Safety analysis set

[26] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Actual Dose Intensity

| | |
|-----------------|-----------------------|
| End point title | Actual Dose Intensity |
|-----------------|-----------------------|

End point description:

Actual dose intensity is defined as the average amount of drug delivered per day.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to last dose of study drug

| End point values | Measurable G/GEJ/E | Non-measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC |
|---------------------------------------|----------------------|------------------------|---|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 45 | 9 | 1 | 3 |
| Units: mg/day | | | | |
| median (inter-quartile range (Q1-Q3)) | 288.5 (208.2 to 300) | 300 (300 to 301.9) | 300 (300 to 300) | 265 (104.1 to 300) |

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Drug Concentration of AMG 337

| | |
|-----------------|--|
| End point title | Maximum Observed Drug Concentration of AMG 337 |
|-----------------|--|

End point description:

Intensive pharmacokinetic sampling was conducted at selected sites. Plasma concentrations below the lower limit of quantification (5.0 ng/mL) were set to 0 before the analysis.

The PK Analysis Set includes all subjects in the Safety Analysis Set who underwent blood sampling during the study and had measurable concentrations above the assay's limit of quantification. In addition, the non-compartmental analyses excluded subjects for whom non-compartmental parameters could not be derived.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 and day 28, predose up to 24 hours post-dose

| End point values | Cohort 1 | Cohort 2A, 2B and 2C | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 12 ^[27] | 4 ^[28] | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (N = 12, 4) | 4110 (± 1850) | 3080 (± 535) | | |
| Day 28 (N = 8, 3) | 3260 (± 832) | 3100 (± 448) | | |

Notes:

[27] - PK analysis set exclude subjects for whom non-compartmental parameters could be derived

[28] - PK analysis set exclude subjects for whom non-compartmental parameters could be derived

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Observed Concentration of AMG 337

| | |
|-----------------|---|
| End point title | Time to Maximum Observed Concentration of AMG 337 |
|-----------------|---|

End point description:

Intensive pharmacokinetic sampling was conducted at selected sites. Plasma concentrations below the lower limit of quantification (5.0 ng/mL) were set to 0 before the analysis.

The PK Analysis Set includes all subjects in the Safety Analysis Set who underwent blood sampling

during the study and had measurable concentrations above the assay's limit of quantification. In addition, the non-compartmental analyses excluded subjects for whom non-compartmental parameters could not be derived.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 and day 28, predose up to 24 hours post-dose | |

| End point values | Cohort 1 | Cohort 2A, 2B and 2C | | |
|-------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 12 ^[29] | 4 ^[30] | | |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Day 1 (N = 12, 4) | 3 (1.5 to 6.1) | 2.3 (1.5 to 6) | | |
| Day 28 (N = 8, 3) | 3 (1.5 to 6) | 1.9 (0.48 to 3) | | |

Notes:

[29] - PK analysis set exclude subjects for whom non-compartmental parameters could be derived

[30] - PK analysis set exclude subjects for whom non-compartmental parameters could be derived

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve From time 0 to 24 hours

| | |
|-----------------|--|
| End point title | Area Under the Plasma Concentration-time Curve From time 0 to 24 hours |
|-----------------|--|

End point description:

Intensive pharmacokinetic sampling was conducted at selected sites. Plasma concentrations below the lower limit of quantification (5.0 ng/mL) were set to 0 before the analysis.

The PK Analysis Set includes all subjects in the Safety Analysis Set who underwent blood sampling during the study and had measurable concentrations above the assay's limit of quantification. In addition, the non-compartmental analyses excluded subjects for whom non-compartmental parameters could not be derived.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 and day 28, predose up to 24 hours post-dose | |

| End point values | Cohort 1 | Cohort 2A, 2B and 2C | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 12 ^[31] | 3 ^[32] | | |
| Units: hr*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (N = 12, 3) | 48200 (± 22900) | 36000 (± 7530) | | |
| Day 28 (N = 7, 3) | 36800 (± 11800) | 32800 (± 9020) | | |

Notes:

[31] - PK analysis set exclude subjects for whom non-compartmental parameters could be derived

[32] - PK analysis set exclude subjects for whom non-compartmental parameters could be derived

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug up to 30 days after the last dose; median duration of treatment was 2.3, 2.4, 2.1, and 1.6 months in each group respectively.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 19.0 |

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Measurable G/GEJ/E |
|-----------------------|--------------------|

Reporting group description:

Participants with measurable G/GEJ/E adenocarcinoma received 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|-----------------------|---|
| Reporting group title | Measurable G/GEJ/E + Prior MET Antibody Therapy |
|-----------------------|---|

Reporting group description:

Participants with measurable G/GEJ/E adenocarcinoma who received prior MET antibody therapy received 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|-----------------------|-------|
| Reporting group title | NSCLC |
|-----------------------|-------|

Reporting group description:

Participants with NSCLC received 300 mg AMG 337 orally once a day for up to 12 months.

| | |
|-----------------------|------------------------|
| Reporting group title | Non-measurable G/GEJ/E |
|-----------------------|------------------------|

Reporting group description:

Participants with non-measurable G/GEJ/E adenocarcinoma received 300 mg AMG 337 orally once a day for up to 12 months.

| Serious adverse events | Measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC |
|---|--------------------|---|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 26 / 45 (57.78%) | 1 / 1 (100.00%) | 2 / 3 (66.67%) |
| number of deaths (all causes) | 7 | 0 | 2 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Gastric cancer | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |

| | | | |
|--|----------------|---------------|----------------|
| Non-small cell lung cancer subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Tumour pain subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders Deep vein thrombosis subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (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 |
| General disorders and administration site conditions Asthenia subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (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 |
| Multiple organ dysfunction syndrome subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|---------------|----------------|
| Pyrexia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (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 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (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 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Blood creatinine increased | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 1 (100.00%) | 0 / 3 (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 |
| Congenital, familial and genetic disorders | | | |
| Pyloric stenosis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (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 |
| Headache | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|---------------|----------------|
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstruction gastric | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (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 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|----------------|---------------|---------------|
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Flank pain | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Soft tissue infection | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Non-measurable G/GEJ/E | | |
|---|---------------------------------|--|--|
| Total subjects affected by serious adverse events subjects affected / exposed number of deaths (all causes) number of deaths resulting from adverse events | 5 / 9 (55.56%) 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Gastric cancer subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 9 (0.00%) 0 / 0 0 / 0 | | |
| Lung neoplasm malignant subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 9 (0.00%) 0 / 0 0 / 0 | | |
| Non-small cell lung cancer subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 9 (0.00%) 0 / 0 0 / 0 | | |
| Tumour pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 9 (0.00%) 0 / 0 0 / 0 | | |
| Vascular disorders Deep vein thrombosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 9 (0.00%) 0 / 0 0 / 0 | | |
| Hypotension subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 9 (0.00%) 0 / 0 0 / 0 | | |
| General disorders and administration site conditions Asthenia | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---------------|--|--|
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Pyloric stenosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ascites | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dysphagia | | | |

| | | | |
|---|---------------|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ileus | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Obstruction gastric | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal obstruction | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Flank pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Clostridium difficile colitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Soft tissue infection | | | |
| subjects affected / exposed | 0 / 9 (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 | Measurable G/GEJ/E | Measurable G/GEJ/E + Prior MET Antibody Therapy | NSCLC |
|--|--------------------|---|-----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 44 / 45 (97.78%) | 1 / 1 (100.00%) | 3 / 3 (100.00%) |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphoedema | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 6 | 0 | 2 |
| Orthostatic hypotension | | | |

| | | | |
|--|------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 1 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 10 / 45 (22.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 18 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Face oedema | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 8 / 45 (17.78%) | 1 / 1 (100.00%) | 2 / 3 (66.67%) |
| occurrences (all) | 10 | 2 | 2 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema | | | |
| subjects affected / exposed | 24 / 45 (53.33%) | 0 / 1 (0.00%) | 2 / 3 (66.67%) |
| occurrences (all) | 81 | 0 | 6 |
| Oedema peripheral | | | |
| subjects affected / exposed | 14 / 45 (31.11%) | 0 / 1 (0.00%) | 3 / 3 (100.00%) |
| occurrences (all) | 22 | 0 | 3 |
| Pain | | | |

| | | | |
|---|----------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 3 / 45 (6.67%) 3 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 7 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Reproductive system and breast disorders Testicular pain subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 3 / 45 (6.67%) 4 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Dyspnoea subjects affected / exposed occurrences (all) | 2 / 45 (4.44%) 3 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 2 / 45 (4.44%) 2 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 4 / 45 (8.89%) 4 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 4 / 45 (8.89%) 7 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 3 / 45 (6.67%) 6 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 2 / 45 (4.44%) 2 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Neutrophil count decreased | | | |

| | | | |
|---|------------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 3 / 45 (6.67%) 6 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Transaminases increased subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Tachycardia subjects affected / exposed occurrences (all) | 2 / 45 (4.44%) 2 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 6 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 24 / 45 (53.33%) 41 | 1 / 1 (100.00%) 1 | 2 / 3 (66.67%) 3 |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Presyncope subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Syncope subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Tremor subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---------------------------------|------------------|---------------|----------------|
| Anaemia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 15 / 45 (33.33%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 18 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 5 | 0 | 1 |
| Ascites | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 8 / 45 (17.78%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 8 | 0 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 8 / 45 (17.78%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 1 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 7 / 45 (15.56%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |

| | | | |
|--|------------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 15 / 45 (33.33%) 17 | 1 / 1 (100.00%) 1 | 1 / 3 (33.33%) 1 |
| Oesophagitis subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Proctalgia subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 1 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 16 / 45 (35.56%) 21 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Hepatobiliary disorders Hepatotoxicity subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 6 | 1 / 1 (100.00%) 1 | 0 / 3 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 6 / 45 (13.33%) 6 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 7 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 7 / 45 (15.56%) 8 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Flank pain subjects affected / exposed occurrences (all) | 4 / 45 (8.89%) 6 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |

| | | | |
|--|------------------------|--------------------|---------------------|
| Muscle spasms subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 2 / 45 (4.44%) 2 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Myalgia subjects affected / exposed occurrences (all) | 4 / 45 (8.89%) 6 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 45 (4.44%) 2 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 16 / 45 (35.56%) 21 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Dehydration subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 1 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 3 / 45 (6.67%) 4 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 9 / 45 (20.00%) 10 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 3 / 45 (6.67%) 4 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Hyponatraemia subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 3 (33.33%) 1 |

| | | | |
|-----------------------------------|---------------------------|--|--|
| Non-serious adverse events | Non-measurable G/GEJ/E | | |
|-----------------------------------|---------------------------|--|--|

| | | | |
|--|-----------------|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 9 / 9 (100.00%) | | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 5 / 9 (55.56%) | | |
| occurrences (all) | 5 | | |
| Lymphoedema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 2 | | |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Chills | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| Face oedema | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Localised oedema | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| Non-cardiac chest pain | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed occurrences (all)</p> <p>Oedema</p> <p>subjects affected / exposed occurrences (all)</p> <p>Oedema peripheral</p> <p>subjects affected / exposed occurrences (all)</p> <p>Pain</p> <p>subjects affected / exposed occurrences (all)</p> <p>Pyrexia</p> <p>subjects affected / exposed occurrences (all)</p> | <p>0 / 9 (0.00%) 0</p> <p>4 / 9 (44.44%) 31</p> <p>2 / 9 (22.22%) 5</p> <p>0 / 9 (0.00%) 0</p> <p>2 / 9 (22.22%) 2</p> | | |
| <p>Reproductive system and breast disorders</p> <p>Testicular pain</p> <p>subjects affected / exposed occurrences (all)</p> | <p>1 / 9 (11.11%) 1</p> | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed occurrences (all)</p> <p>Dyspnoea</p> <p>subjects affected / exposed occurrences (all)</p> | <p>0 / 9 (0.00%) 0</p> <p>1 / 9 (11.11%) 1</p> | | |
| <p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed occurrences (all)</p> <p>Insomnia</p> <p>subjects affected / exposed occurrences (all)</p> | <p>1 / 9 (11.11%) 1</p> <p>1 / 9 (11.11%) 1</p> | | |
| <p>Investigations</p> <p>Alanine aminotransferase increased</p> <p>subjects affected / exposed occurrences (all)</p> | <p>2 / 9 (22.22%) 2</p> | | |

| | | | |
|--|---|--|--|
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 2 | | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Transaminases increased subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 1 / 9 (11.11%) 1 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 7 / 9 (77.78%) 10 2 / 9 (22.22%) 2 1 / 9 (11.11%) 1 | | |

| | | | |
|--|---------------------|--|--|
| Syncope subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Tremor subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 3 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Neutropenia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 3 / 9 (33.33%) 4 | | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Ascites subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | | |
| Constipation subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 9 (33.33%) 3 | | |
| Dry mouth subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Dyspepsia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Gastrooesophageal reflux disease | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Melaena subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Nausea subjects affected / exposed occurrences (all) | 4 / 9 (44.44%) 5 | | |
| Oesophagitis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Proctalgia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Vomiting subjects affected / exposed occurrences (all) | 4 / 9 (44.44%) 6 | | |
| Hepatobiliary disorders Hepatotoxicity subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) | 3 / 9 (33.33%) 5 | | |
| Pruritus subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | | |
| Rash subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 4 | | |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|------------------------------------|----------------|--|--|
| Back pain | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| Flank pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 3 | | |
| Hypokalaemia | | | |

| | | | |
|-----------------------------|---------------|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------|--|
| 30 May 2014 | The protocol was amended for the following reasons: 1. Allow ECOG Performance Status 2 subjects to participate in the study 2. Reduce the time interval when no food or liquids can be consumed relative to administration of AMG 337 3. Add dose modifications for when subjects experience \geq grade 3 headache for which AMG 337 is considered as a cause 4. Add information about management of headaches 5. Add collection of lymphocyte results 6. Add an collection of cell pellet, circulating tumor cells, and optional tumor biopsy at the time of disease progression 7. Include details and clarification of planned efficacy and safety reviews 8. Clarification of minor inconsistencies and correction of minor errors |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported