# Clinical trial results:
# A Phase 3, Multicenter, Randomized, Open-label Trial to Evaluate the Survival Benefit of Panitumumab and Best Supportive Care, Compared to Best Supportive Care Alone, in Subjects With Chemorefractory Wild-type KRAS Metastatic Colorectal Cancer

## Summary

| | |
|---|---|
| EudraCT number | 2010-022951-49 |
| Trial protocol | GR EE LV LT |
| Global end of trial date | 11 November 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 23 November 2017 |
| First version publication date | 23 November 2017 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 20100007 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01412957 |
| 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 | 24 July 2015 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 11 November 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the benefit of panitumumab in addition to best supportive care compared to best supportive care alone in patients with chemorefractory wild-type KRAS (Kirsten rat sarcoma viral oncogene homolog) metastatic colorectal cancer.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines. Essential documents will be retained in accordance with ICH GCP. 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 | 08 November 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 2 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | China: 34 |
| Country: Number of subjects enrolled | India: 23 |
| Country: Number of subjects enrolled | Korea, Republic of: 79 |
| Country: Number of subjects enrolled | Malaysia: 16 |
| Country: Number of subjects enrolled | Philippines: 10 |
| Country: Number of subjects enrolled | Croatia: 59 |
| Country: Number of subjects enrolled | Estonia: 27 |
| Country: Number of subjects enrolled | Greece: 2 |
| Country: Number of subjects enrolled | Latvia: 11 |
| Country: Number of subjects enrolled | Lithuania: 14 |
| Country: Number of subjects enrolled | Romania: 48 |
| Country: Number of subjects enrolled | Serbia: 10 |
| Country: Number of subjects enrolled | Brazil: 14 |
| Country: Number of subjects enrolled | Canada: 7 |

| | |
|---|---|
| Country: Number of subjects enrolled | Chile: 7 |
| Country: Number of subjects enrolled | Mexico: 16 |
| Worldwide total number of subjects | 377 |
| EEA total number of subjects | 161 |

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) | 241 |
| From 65 to 84 years | 136 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

A total of 377 participants were randomized at 66 centers in Europe, Asia, North and South America from 8 November 2011 until 30 July 2013. Results are reported as of the final analysis data cut-off date of 24 July 2015.

### Pre-assignment

Screening details:

Participants were stratified according to geographic region (Europe vs Asia vs rest of the world) and Eastern Cooperative Oncology Group (ECOG) performance status (0 or 1 vs 2) and randomized (1:1 ratio) to 1 of 2 treatment groups.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Panitumumab + BSC |

Arm description:

Participants received panitumumab administered intravenously 6 mg/kg every 14 days plus best supportive care (BSC) until disease progression, withdrawal of consent, death, or intolerance of study drug.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Panitumumab |
| Investigational medicinal product code | |
| Other name | Vectibix |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

The starting panitumumab dose was 6 mg/kg; panitumumab was administered by intravenous infusion on day 1 of every 14-day cycle.

| | |
|---|---|
| **Arm title** | BSC Alone |

Arm description:

Participants received best supportive care until disease progression, withdrawal of consent, or death.

| | |
|---|---|
| Arm type | Best Supportive Care |

No investigational medicinal product assigned in this arm

| **Number of subjects in period 1** | Panitumumab + BSC | BSC Alone |
|---|---|---|
| Started | 189 | 188 |
| Completed | 189 | 188 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Panitumumab + BSC |
| Reporting group description: | |
| Participants received panitumumab administered intravenously 6 mg/kg every 14 days plus best supportive care (BSC) until disease progression, withdrawal of consent, death, or intolerance of study drug. | |
| Reporting group title | BSC Alone |
| Reporting group description: | |
| Participants received best supportive care until disease progression, withdrawal of consent, or death. | |

| Reporting group values | Panitumumab + BSC | BSC Alone | Total |
|---|---|---|---|
| Number of subjects | 189 | 188 | 377 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 114 | 127 | 241 |
| From 65-84 years | 75 | 61 | 136 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 60.2 | 58.7 | |
| standard deviation | ± 10.7 | ± 11.1 | - |
| Gender, Male/Female<br>Units: Subjects | | | |
| Female | 82 | 79 | 161 |
| Male | 107 | 109 | 216 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| Hispanic or Latino | 23 | 22 | 45 |
| Not Hispanic or Latino | 166 | 166 | 332 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 3 | 3 |
| Asian | 79 | 82 | 161 |
| White | 107 | 102 | 209 |
| Other | 3 | 1 | 4 |
| Geographic Region<br>Units: Subjects | | | |
| Europe | 86 | 85 | 171 |
| Asia | 80 | 82 | 162 |
| Rest of world | 23 | 21 | 44 |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| A scale to assess a patient's disease status. 0 = Fully active, able to carry out all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity, ambulatory and able to carry out work of a light nature; 2 = Ambulatory and capable of all self care, unable to carry out any work activities. Up and about > 50% of waking hours; 3 = Capable of only limited self-care, confined to bed or chair > 50% of waking hours; 4 = Completely disabled, confined to bed or chair; 5 = Dead. | | | |
| Units: Subjects | | | |
| Grade 0 | 71 | 65 | 136 |

| | | | |
|---|---|---|---|
| Grade 1 | 100 | 107 | 207 |
| Grade 2 | 18 | 16 | 34 |
| Location of Primary Tumor<br>Units: Subjects | | | |
| Colon | 108 | 106 | 214 |
| Rectum | 81 | 81 | 162 |
| Missing | 0 | 1 | 1 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Panitumumab + BSC |

Reporting group description:

Participants received panitumumab administered intravenously 6 mg/kg every 14 days plus best supportive care (BSC) until disease progression, withdrawal of consent, death, or intolerance of study drug.

| | |
|---|---|
| Reporting group title | BSC Alone |

Reporting group description:

Participants received best supportive care until disease progression, withdrawal of consent, or death.

### Primary: Overall Survival

| | |
|---|---|
| End point title | Overall Survival |

End point description:

Overall survival was defined as the time from the randomization date to the date of death. Participants who had not died by the analysis data cut-off date were censored at their last contact date and participants with survival data obtained after the planned analysis data cut-off date had survival censored at the cut-off date. The Intent to Treat (ITT) Analysis Set included all randomized participants; participants in the ITT Analysis Set were required to have wild-type KRAS exon 2 (codons 12 and 13, alleles G12A, G12D, G12R, G12C, G12S, G12V, or G13D) per protocol.

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

End point timeframe:

From randomization to the last on-study or long-term follow-up visit, as of the data cut-off date of 24 July 2015. The median follow-up time was 34.4 weeks (panitumumab plus BSC: 40.3 weeks; BSC alone: 25.3 weeks).

| End point values | Panitumumab + BSC | BSC Alone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 189 | 188 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 10.0 (8.7 to 11.3) | 7.4 (5.8 to 9.3) | | |

### Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|

Statistical analysis description:

The primary hypothesis was that panitumumab plus BSC would improve overall survival compared to BSC alone. A comparison between treatments was performed using the log-rank test stratified by the randomization factors at a 5% significance level.

| | |
|---|---|
| Comparison groups | Panitumumab + BSC v BSC Alone |

| | |
|---|---|
| Number of subjects included in analysis | 377 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0086 [1] |
| Method | Logrank |

Notes:

[1] - Log-rank test stratified by randomization factors: geographic region (Europe vs Asia vs rest of world) and ECOG performance status (0 or 1 vs 2).

## Secondary: Progression-free Survival

| | |
|---|---|
| End point title | Progression-free Survival |

End point description:

Progression-free survival (PFS) was defined as the time from the randomization date to the date of disease progression per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1 or death. Progressive disease (PD): At least a 20% increase in the size of target lesions compared with the smallest size since treatment started and an absolute increase of at least 5 mm, any new lesions or an increase in size of non-target lesions thought be ≥ 20% and an absolute increase of at least 5 mm, or significant increase in pleural effusions, ascites or other fluid collections with cytologic proof of malignancy. Participants who were alive and did not meet the criteria for progression by the analysis data cut-off date were censored at their last evaluable disease assessment date.

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

End point timeframe:

From randomization to the last on-study or long-term follow-up visit, as of the data cut-off date of 24 July 2015. The median follow-up time was 34.4 weeks (panitumumab plus BSC: 40.3 weeks; BSC alone: 25.3 weeks).

| End point values | Panitumumab + BSC | BSC Alone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 189 | 188 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 3.6 (3.4 to 5.3) | 1.7 (1.6 to 1.9) | | |

### Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|

Statistical analysis description:

PFS in the ITT Analysis Set was tested at a significance level of 5% conditional on a significant treatment effect on overall survival in the ITT Analysis Set.

| | |
|---|---|
| Comparison groups | Panitumumab + BSC v BSC Alone |
| Number of subjects included in analysis | 377 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [2] |
| Method | Logrank |

Notes:

[2] - Log-rank test stratified by randomization factors: geographic region (Europe vs Asia vs rest of world) and ECOG performance status (0 or 1 vs 2).

## Secondary: Overall Survival in Participants with Wild-type RAS

| End point title | Overall Survival in Participants with Wild-type RAS |
|---|---|

End point description:

A secondary efficacy endpoint was overall survival in participants with wild-type rat sarcoma viral oncogene homolog (RAS) (without mutation in exons 2 [codons 12 and 13], 3 [codons 59 and 61], and 4 [codons 117 and 146] of KRAS and neuroblastoma RAS viral oncogene (NRAS)). In participants with wild-type RAS, RAS mutation status was defined by KRAS exon 2 mutation status per clinical trial assay testing and mutation status of KRAS exon 3 and 4 and NRAS exons 2, 3 and 4 per Sanger bi-directional sequencing. Overall survival was defined as the time from the randomization date to the date of death. Participants who had not died by the analysis data cut-off date were censored at their last contact date and participants with survival data obtained after the planned analysis data cut-off date had survival censored at the cut-off date.

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

End point timeframe:

From randomization to the last on-study or long-term follow-up visit, as of the data cut-off date of 24 July 2015. The median follow-up time was 36.1 weeks (panitumumab plus BSC: 43.7 weeks; BSC alone: 23.6 weeks).

| **End point values** | Panitumumab + BSC | BSC Alone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 128 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 10.0 (8.7 to 11.6) | 6.9 (5.2 to 7.9) | | |

**Statistical analyses**

| **Statistical analysis title** | Primary Analysis |
|---|---|

Statistical analysis description:

Overall survival in the Wild-type RAS Efficacy Analysis Set was compared at a significance level of 5% conditional on a significant treatment effect for progression-free survival in the ITT Analysis Set.

| Comparison groups | Panitumumab + BSC v BSC Alone |
|---|---|
| Number of subjects included in analysis | 270 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0152 [3] |
| Method | Logrank |

Notes:

[3] - Log-rank test stratified by randomization factors: geographic region (Europe vs Asia vs rest of world) and ECOG performance status (0 or 1 vs 2).

**Secondary: Progression Free Survival (PFS) in Participants with Wild-type RAS**

| End point title | Progression Free Survival (PFS) in Participants with Wild-type RAS |
|---|---|

End point description:

PFS was defined as the time from the randomization date to the date of disease progression per RECIST version 1.1 or death. Progressive disease (PD): At least a 20% increase in the size of target lesions compared with the smallest size since treatment started and an absolute increase of at least 5 mm, any new lesions, or an increase in size of non-target lesions thought be ≥ 20% with an absolute increase of at least 5 mm, or significant increase in pleural effusions, ascites or other fluid collections with cytologic proof of malignancy. Participants who were alive and did not meet the criteria for progression by the analysis data cut-off date were censored at their last evaluable disease assessment date. The Wild-type RAS Efficacy Analysis Set consists of a subset of participants in the ITT Analysis Set without mutation in

exon 2, 3, and 4 of KRAS or NRAS).

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

End point timeframe:

From randomization to the last on-study or long-term follow-up visit, as of the data cut-off date of 24 July 2015. The median follow-up time was 36.1 weeks (panitumumab plus BSC: 43.7 weeks; BSC alone: 23.6 weeks).

| **End point values** | Panitumumab + BSC | BSC Alone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 128 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 5.2 (3.5 to 5.3) | 1.7 (1.6 to 2.2) | | |

### Statistical analyses

| **Statistical analysis title** | Primary Analysis |
|---|---|

Statistical analysis description:

PFS in the Wild-type RAS Efficacy Analysis Set was to be compared at a significance level of 5% if overall survival in the wild-type RAS Efficacy Anaysis Set demonstrated a significant treatment effect.

| Comparison groups | Panitumumab + BSC v BSC Alone |
|---|---|
| Number of subjects included in analysis | 270 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [4] |
| Method | Logrank |

Notes:

[4] - Log-rank test stratified by randomization factors: geographic region (Europe vs Asia vs rest of world) and ECOG performance status (0 or 1 vs 2).

### Secondary: Objective Response Rate

| End point title | Objective Response Rate |
|---|---|

End point description:

Objective response rate (ORR) is defined as the percentage of participants with either a complete response (CR) or partial response (PR) per RECIST version 1.1. Radiographic tumor assessments and investigator's assessment of response were performed at Week 4, Week 8, and then every 8 weeks until disease progression (radiographic or clinical progression). CR: Disappearance of all target and non-target lesions and no new lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR: At least a 30% decrease in the size of target lesions with no progression of non-target lesions and no new lesions, or, the disappearance of all target lesions with persistence of one or more non-target lesions not qualifying for either CR or PD and no new lesions.

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

End point timeframe:

Response was assessed at Week 4, Week 8, and then every 8 weeks until the data cut-off date of 24 July 2015. The median follow-up time was 34.4 weeks (panitumumab plus BSC: 40.3 weeks; BSC alone: 25.3 weeks).

| End point values | Panitumumab + BSC | BSC Alone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 189 | 188 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 26.98 (20.80 to 33.91) | 1.60 (0.33 to 4.59) | | |

### Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|

Statistical analysis description:

ORR was not formally tested and the p-values are descriptive only. An exact test was used to test the hypothesis that the common odds ratio for panitumumab plus BSC relative to BSC alone for the objective response is equal to 1.0 stratified by the randomization factors.

| | |
|---|---|
| Comparison groups | Panitumumab + BSC v BSC Alone |
| Number of subjects included in analysis | 377 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [5] |
| Method | Stratified exact test |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 24.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7.47 |
| upper limit | 123.77 |

Notes:

[5] - Stratified by randomization factors: geographic region (Europe vs Asia vs rest of world) and ECOG performance status (0 or 1 vs 2).

### Secondary: Objective Response Rate in Participants with Wild-type RAS

| End point title | Objective Response Rate in Participants with Wild-type RAS |
|---|---|

End point description:

Objective response rate is defined as the percentage of participants with either a complete response (CR) or partial response (PR) per RECIST version 1.1. Radiographic tumor assessments and investigator's assessment of response were performed at Week 4, Week 8, and then every 8 weeks until disease progression (radiographic or clinical progression). CR: Disappearance of all target and non-target lesions and no new lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR: At least a 30% decrease in the size of target lesions with no progression of non-target lesions and no new lesions, or, the disappearance of all target lesions with persistence of one or more non-target lesions not qualifying for either CR or PD and no new lesions. The Wild-type RAS Efficacy Analysis Set was used for the analysis.

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

End point timeframe:

Response was assessed at Week 4, Week 8, and then every 8 weeks until the data cut-off date of 24 July 2015. The median follow-up time was 36.1 weeks (panitumumab plus BSC: 43.7 weeks; BSC alone: 23.6 weeks).

| End point values | Panitumumab + BSC | BSC Alone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 128 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 30.99 (23.50 to 39.28) | 2.34 (0.49 to 6.70) | | |

### Statistical analyses

| Statistical analysis title | Primary Analysis |
|---|---|

Statistical analysis description:

ORR was not formally tested and the p-values are descriptive only. An exact test was used to test the hypothesis that the common odds ratio for panitumumab plus BSC relative to BSC alone for the objective response is equal to 1.0 stratified by the randomization factors.

| | |
|---|---|
| Comparison groups | Panitumumab + BSC v BSC Alone |
| Number of subjects included in analysis | 270 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [6] |
| Method | Stratified exact test |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 20 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.89 |
| upper limit | 101.62 |

Notes:

[6] - Stratified by randomization factors: geographic region (Europe vs Asia vs rest of world) and ECOG performance status (0 or 1 vs 2).

### Secondary: Number of Participants with Adverse Events (AEs)

| End point title | Number of Participants with Adverse Events (AEs) |
|---|---|

End point description:

The severity of each AE was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 (Grade 1 = Mild; 2 = Moderate (discomfort enough to cause interference with usual activity); 3 = Severe (incapacitating with inability to work or do usual activity); 4 = Life-threatening and 5 = Fatal), with the exception of the skin-or nail-related AEs which were graded using a CTCAE version 3.0 with modifications. A serious AE was defined as an AE that met at least 1 of the following criteria:
• fatal,
• life-threatening,
• required in-patient hospitalization or prolongation of existing hospitalization, • resulted in persistent or significant disability/incapacity,
• congenital anomaly/birth defect, and/or
• other medically important serious event.
Treatment-related AEs (TRAEs) are those the investigator considered there was reasonable possibility that the event might have been caused by study drug.

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

End point timeframe:

From first dose until 30 days after last dose; median safety reporting periods were 4.2 months and 2.2 months for panitumumab plus BSC arm and BSC alone arm, respectively.

| End point values | Panitumumab + BSC | BSC Alone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 189 | 188 | | |
| Units: participants | | | | |
| Any adverse event (AE)\| | 184 | 115 | | |
| AE with worst grade of 3\| | 71 | 30 | | |
| AE with worst grade of 4\| | 17 | 5 | | |
| AE with worst grade of 5\| | 8 | 15 | | |
| Serious adverse event (SAE)\| | 48 | 37 | | |
| AE leading to discontinuation of panitumumab\| | 19 | 0 | | |
| Treatment-related adverse event (TRAE)\| | 166 | 7 | | |
| Treatment-related AE with worst grade of 3\| | 42 | 1 | | |
| Treatment-related AE with worst grade of 4\| | 4 | 1 | | |
| Treatment-related AE with worst grade of 5\| | 0 | 1 | | |
| Serious treatment-related AE\| | 2 | 3 | | |
| TRAE leading to discontinuation of panitumumab\| | 1 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Post-baseline Change from Baseline in Corrected QT (QTc) Interval

| End point title | Maximum Post-baseline Change from Baseline in Corrected QT (QTc) Interval |
|---|---|

End point description:

QT interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle as measured by electrocardiogram (ECG). QTc is the QT interval corrected for heart rate. ECGs were collected at the following time points from participants randomized to panitumumab arm at a limited number of sites: Week 1 prior to first panitumumab infusion (Baseline) and within 30 minutes following the end of the first infusion of panitumumab (Cmax), Week 7 after 3 doses of panitumumab (steady state), and the safety follow-up visit. ECGs were submitted for independent central review to calculate the reported QTc interval using both the Bazett correction (QTcB) and the Fridericia correction (QTcF). The QTc Analysis Set consists of a subset of participants in the Safety Analysis Set who received at least one panitumumab dose and were enrolled at one of the sites participating in QTc evaluation and had baseline and at least 1 post-baseline QTc assessment.

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

End point timeframe:

Baseline (pre-dose), Week 1 and Week 7 (post-dose) and 4 weeks after the last dose (Safety Follow-up visit)

| End point values | Panitumumab + BSC | BSC Alone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 53 | 0[7] | | |
| Units: msec | | | | |
| arithmetic mean (standard deviation) | | | | |
| QTcF | 14.58 (± 13.60) | () | | |
| QTcB | 12.57 (± 12.15) | () | | |

Notes:

[7] - QTC was only analyzed in participants who received panitumumab

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose until 30 days after last dose; median safety reporting periods were 4.2 months and 2.2 months for panitumumab plus BSC arm and BSC alone arm, respectively.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Panitumumab + BSC |

Reporting group description:

Participants received panitumumab administered intravenously 6 mg/kg every 14 days plus best supportive care (BSC) until disease progression, withdrawal of consent, death, or intolerance of study drug.

| | |
|---|---|
| Reporting group title | BSC Alone |

Reporting group description:

Participants received best supportive care until disease progression, withdrawal of consent, or death.

| Serious adverse events | Panitumumab + BSC | BSC Alone | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 48 / 189 (25.40%) | 37 / 188 (19.68%) | |
| number of deaths (all causes) | 8 | 15 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 3 / 189 (1.59%) | 3 / 188 (1.60%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 3 | |
| Colorectal cancer | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 3 / 188 (1.60%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 1 / 3 | |
| Colorectal cancer metastatic | | | |
| subjects affected / exposed | 2 / 189 (1.06%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Colorectal cancer recurrent | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 2 / 189 (1.06%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to ovary | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal cancer | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chills | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 2 / 188 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 189 (0.00%) | 3 / 188 (1.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 2 / 188 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Reproductive system and breast disorders** | | | |
| Pelvic pain | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Injury, poisoning and procedural complications | | | |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Pyloric stenosis | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Myocardial ischaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 2 / 188 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lateral medullary syndrome | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensory neuropathy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 2 / 189 (1.06%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Speech disorder | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord compression | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Blood and lymphatic system disorders** | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 2 / 188 (1.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone marrow toxicity | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| **Ear and labyrinth disorders** | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Eye disorders** | | | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 189 (1.59%) | 3 / 188 (1.60%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fistula | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Gastrointestinal obstruction | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 3 / 189 (1.59%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 189 (1.59%) | 3 / 188 (1.60%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stenosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 189 (0.53%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstructive uropathy | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract inflammation | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Musculoskeletal and connective tissue disorders** | | | |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Infections and infestations** | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal abscess | | | |
| subjects affected / exposed | 2 / 189 (1.06%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung abscess | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Pneumonia | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 189 (0.00%) | 1 / 188 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 189 (0.53%) | 0 / 188 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Panitumumab + BSC | BSC Alone | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 174 / 189 (92.06%) | 75 / 188 (39.89%) | |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 13 / 189 (6.88%) | 5 / 188 (2.66%) | |
| occurrences (all) | 19 | 6 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 14 / 189 (7.41%) | 16 / 188 (8.51%) | |
| occurrences (all) | 28 | 21 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 28 / 189 (14.81%) | 14 / 188 (7.45%) | |
| occurrences (all) | 42 | 20 | |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 16 / 189 (8.47%) | 9 / 188 (4.79%) | |
| occurrences (all) | 21 | 12 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 29 / 189 (15.34%) | 18 / 188 (9.57%) | |
| occurrences (all) | 38 | 24 | |
| Constipation | | | |
| subjects affected / exposed | 16 / 189 (8.47%) | 12 / 188 (6.38%) | |
| occurrences (all) | 17 | 13 | |
| Diarrhoea | | | |
| subjects affected / exposed | 25 / 189 (13.23%) | 7 / 188 (3.72%) | |
| occurrences (all) | 44 | 7 | |
| Dyspepsia | | | |
| subjects affected / exposed | 10 / 189 (5.29%) | 2 / 188 (1.06%) | |
| occurrences (all) | 10 | 2 | |
| Nausea | | | |
| subjects affected / exposed | 11 / 189 (5.82%) | 10 / 188 (5.32%) | |
| occurrences (all) | 18 | 13 | |
| Stomatitis | | | |
| subjects affected / exposed | 12 / 189 (6.35%) | 0 / 188 (0.00%) | |
| occurrences (all) | 15 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 12 / 189 (6.35%) | 7 / 188 (3.72%) | |
| occurrences (all) | 12 | 8 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 54 / 189 (28.57%) | 0 / 188 (0.00%) | |
| occurrences (all) | 105 | 0 | |
| Acne | | | |
| subjects affected / exposed | 26 / 189 (13.76%) | 0 / 188 (0.00%) | |
| occurrences (all) | 49 | 0 | |
| Dry skin | | | |
| subjects affected / exposed | 29 / 189 (15.34%) | 1 / 188 (0.53%) | |
| occurrences (all) | 40 | 1 | |
| Erythema | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 23 / 189 (12.17%) | 0 / 188 (0.00%) | |
| occurrences (all) | 35 | 0 | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 20 / 189 (10.58%) | 0 / 188 (0.00%) | |
| occurrences (all) | 25 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 47 / 189 (24.87%) | 0 / 188 (0.00%) | |
| occurrences (all) | 80 | 0 | |
| Rash | | | |
| subjects affected / exposed | 73 / 189 (38.62%) | 2 / 188 (1.06%) | |
| occurrences (all) | 142 | 2 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 10 / 189 (5.29%) | 0 / 188 (0.00%) | |
| occurrences (all) | 35 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 14 / 189 (7.41%) | 10 / 188 (5.32%) | |
| occurrences (all) | 20 | 11 | |
| Infections and infestations | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 12 / 189 (6.35%) | 0 / 188 (0.00%) | |
| occurrences (all) | 28 | 0 | |
| Paronychia | | | |
| subjects affected / exposed | 27 / 189 (14.29%) | 0 / 188 (0.00%) | |
| occurrences (all) | 56 | 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 18 / 189 (9.52%) | 16 / 188 (8.51%) | |
| occurrences (all) | 25 | 16 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 10 / 189 (5.29%) | 3 / 188 (1.60%) | |
| occurrences (all) | 16 | 3 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 14 / 189 (7.41%) | 1 / 188 (0.53%) | |
| occurrences (all) | 23 | 1 | |
| Hypokalaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 11 / 189 (5.82%) | 1 / 188 (0.53%) | |
| occurrences (all) | 17 | 1 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 53 / 189 (28.04%) | 2 / 188 (1.06%) | |
| occurrences (all) | 112 | 2 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 25 October 2012 | • Clarified that the investigator's assessment of response will be used to determine tumor response and progression for the purposes of management of a subject and for the analysis of PFS and ORR endpoints. Tumor imaging studies will be submitted to a central repository location.<br>• Specified that tumor radiographic imaging scans performed according to the Schedule of Assessments must be submitted to the central imaging vendor.<br>• Specified additional collection of blood for biomarker development: blood collection for exploratory biomarker development (at study day 1 [prior to the panitumumab administration for subjects randomized to panitumumab plus BSC arm]), at time of each scheduled radiographic tumor imaging assessment (ie, at week 4 [+ 1 week], week 8 [± 1 week] and then every 8 weeks [± 1 week]) until disease progression, and at the safety follow-up visit.<br>• Clarified that in case Amgen elects to have scans reviewed by an independent centralized radiology vendor, additional available imaging data may be requested from subjects who discontinue the treatment phase due to assessment of disease progression by the investigator that is not subsequently confirmed by the central radiology review.<br>• Clarified that for the purposes of the PFS and ORR analyses, the determination of objective disease progression will be based on investigator's assessments. In the case Amgen elects to have scans reviewed by an independent centralized radiology vendor, additional analyses of PFS and ORR will be provided based on the central review of the scans. |
| 25 July 2013 | • Expanded the codons examined in subjects with wild-type RAS to include exons 2 [codons 12 and 13], 3 [codons 59 and 61], and 4 [codons 117 and 146] of KRAS; specify that the NRAS gene will be examined; and specify that exon 2 (codons 12 and 13) will be examined in subjects with wild-type KRAS tumors.<br>• Updated the background and rationale sections to provide the justification for incorporating additional RAS mutations into the study objectives<br>• Corrected Section 7 and Schedule of Assessment to ensure biomarker blood samples are collected from both arms<br>• Updated the planned method of statistical analyses to include an alternative definition for progression-free survival by excluding deaths occurring more than 60 days after the last evaluable tumor assessment or randomization date (whichever is later) as events which will also be considered as part of planned PFS analyses.<br>• Added language to inform the investigator to report a serious adverse event that occurs outside the protocol-specified reporting period per EU CT-3 Guidance<br>• Added pregnancy and lactation reporting procedures |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported