# Clinical trial results:
# A SINGLE-ARM, MULTICENTER, PHASE II STUDY OF PANITUMUMAB IN COMBINATION WITH CAPECITABINE / OXALIPLATIN IN FIRST-LINE, WILD-TYPE K-RAS METASTATIC COLORECTAL CANCER PATIENTS

## Summary

| | |
|---|---|
| EudraCT number | 2009-012655-26 |
| Trial protocol | GR |
| Global end of trial date | 26 August 2014 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 14 November 2018 |
| First version publication date | 14 November 2018 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | HE 6A/09 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01215539 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Hellenic Cooperative Oncology Group |
| Sponsor organisation address | Hatzikonstandi 18, Athens, Greece, 11524 |
| Public contact | Hellenic Cooperative Oncology Group, Hellenic Cooperative Oncology Group, hecogoff@otenet.gr |
| Scientific contact | Hellenic Cooperative Oncology Group, Hellenic Cooperative Oncology Group, hecogoff@otenet.gr |

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 | 26 August 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 26 August 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To estimate the objective response rate in wild-type k-ras, metastatic colorectal cancer patients treated with panitumumab in combination with capecitabine/oxaliplatin as first-line therapy.

Protection of trial subjects:

This study was conducted in conformance with ICH GCP, all applicable laws and regulations. All participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 13 October 2010 |
| 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 | Greece: 78 |
| Worldwide total number of subjects | 78 |
| EEA total number of subjects | 78 |

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) | 37 |
| From 65 to 84 years | 41 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled in the study from 13 October 2010 until 10 September 2013 from 12 sites in Greece.

### Pre-assignment

Screening details:

All potentially eligible subjects underwent screening in order to confirm that all eligibility criteria were met prior to the first administration of the study treatment.

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | Panitumumab+capecitabine+oxaliplatin |

Arm description:

Panitumumab was administered by IV infusion on day 1 of each 3-week cycle prior to the administration of chemotherapy. The starting panitumumab dose was 9 mg/kg. Oxaliplatin 130 mg/m2 IV infusion over 2 hours on Day 1 of each cycle after the administration of panitumumab, capecitabine 2000 mg/m2 divided in two doses, orally, on Days 1 - 14.

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

Dosage and administration details:

The starting panitumumab dose was 9 mg/kg iv administration on day 1 of each 3-week cycle.

| **Number of subjects in period 1** | Panitumumab+capecitabine+oxaliplatin |
|---|---|
| Started | 78 |
| Completed | 45 |
| Not completed | 33 |
| Physician decision | 5 |
| Consent withdrawn by subject | 6 |
| Adverse event, non-fatal | 3 |
| Death | 4 |
| Other | 3 |
| Progression | 10 |
| Moved to other hospital | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Overall trial |

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---|---|---|---|
| Number of subjects | 78 | 78 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 37 | 37 | |
| From 65-84 years | 41 | 41 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 63.4 | | |
| full range (min-max) | 30.1 to 80.9 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 33 | 33 | |
| Male | 45 | 45 | |

## End points

### End points reporting groups

| Reporting group title | Panitumumab+capecitabine+oxaliplatin |
|---|---|

Reporting group description:

Panitumumab was administered by IV infusion on day 1 of each 3-week cycle prior to the administration of chemotherapy. The starting panitumumab dose was 9 mg/kg. Oxaliplatin 130 mg/m2 IV infusion over 2 hours on Day 1 of each cycle after the administration of panitumumab, capecitabine 2000 mg/m2 divided in two doses, orally, on Days 1 - 14.

### Primary: Objective Response Rate

| End point title | Objective Response Rate[1] |
|---|---|

End point description:

Response was centrally assessed using RECIST criteria.An objective response was defined as either a complete or a partial response.

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

End point timeframe:

Tumor response was assessed every 6 weeks through week 18 and every 3 months thereafter, until disease progression

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: The percentage of patients that achieved a complete or partial response out of the total number of enrolled patients is provided. No comparisons were performed since this was a single-arm study.

| End point values | Panitumumab+capecitabine+oxaliplatin | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: percentage of patients | | | | |
| number (not applicable) | 44.9 | | | |

### 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 was defined as the time from the date of enrollment to the date of documented disease progression, death or last contact. Deaths without a documented progression were treated as events at the time of death for the PFS analysis.

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

End point timeframe:

Tumor response was assessed every 6 weeks through week 18 and every 3 months thereafter, until disease progression.

| End point values | Panitumumab+ capecitabine+oxaliplatin | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 8.1 (6.5 to 9.9) | | | |

| Attachments (see zip file) | Kaplan-meier with respect to PFS/PFS_HE6A09.png |
|---|---|

### Statistical analyses

No statistical analyses for this end point

### Secondary: Safety profile

| End point title | Safety profile |
|---|---|

End point description:

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

End point timeframe:

Adverse Events of all participants were recorded and assessed upon signature of the Informed Consent Form, until 30 days after the last administration of study treatment.

| End point values | Panitumumab+ capecitabine+oxaliplatin | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: number of patients | | | | |
| Any adverse event | 76 | | | |
| Adverse event grade≥3 | 54 | | | |
| Adverse event grade≥4 | 12 | | | |
| Fatal adverse events | 6 | | | |
| Serious adverse events | 27 | | | |

### 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 enrollment to the date of death or last contact. Alive patients were censored at the date of their last contact.

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

End point timeframe:

The median follow-up time was 12.8 months (range 0-39).

| **End point values** | Panitumumab+ capecitabine+oxaliplatin | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 78 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 23.2 (18.0 to 28.8) | | | |

| **Attachments (see zip file)** | Kaplan-meier curve with respect to OS/OS_HE6A09.png |
|---|---|

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events of all participants were recorded and assessed upon signature of the Informed Consent Form, until 30 days after the last administration of study treatment.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 12.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Panitumumab+capecitabine+oxaliplatin |

Reporting group description:

Panitumumab was administered by IV infusion on day 1 of each 3-week cycle prior to the administration of chemotherapy. The starting panitumumab dose was 9 mg/kg. Oxaliplatin 130 mg/m2 IV infusion over 2 hours on Day 1 of each cycle after the administration of panitumumab, capecitabine 2000 mg/m2 divided in two doses, orally, on Days 1 - 14.

| Serious adverse events | Panitumumab+capecitabine+oxaliplatin | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 27 / 78 (34.62%) | | |
| number of deaths (all causes) | 26 | | |
| number of deaths resulting from adverse events | 6 | | |
| Investigations | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 2 / 78 (2.56%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Phlebitis superficial | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ischaemic stroke | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Cardiac disorders | | | | |
| Cardiac arrest | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Nervous system disorders | | | | |
| Depressed level of consciousness | Additional description: Somnolence | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Neuropathy | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neuropathy sensory | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood and lymphatic system disorders | | | | |
| Anaemia | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| Catheter site thrombosis | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sudden death | Additional description: Cause unknown | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Immune system disorders | | | |
| Allergic reaction | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 6 / 78 (7.69%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ileus | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 3 / 78 (3.85%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 78 (3.85%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal perforation | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rectal haemorrhage | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| Pulmonary embolism | | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspnoea | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Chronic obstructive pulmonary disease | Additional description: Exacerbation of Chronic Obstructive Pulmonary Disease | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Infections and infestations | | | | |
| Infection | | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung infection | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|---|---|---|---|
| Infectious colitis | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | Panitumumab+capecitabine+oxaliplatin | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 76 / 78 (97.44%) | | |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 26 / 78 (33.33%) | | |
| occurrences (all) | 36 | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Fever | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 78 (3.85%) | | |
| occurrences (all) | 4 | | |
| Edema head and neck | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Edema limbs | | | |
| subjects affected / exposed | 4 / 78 (5.13%) | | |
| occurrences (all) | 4 | | |
| Flu like symptomes | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Pain | | | |
| subjects affected / exposed | 10 / 78 (12.82%) | | |
| occurrences (all) | 11 | | |
| Immune system disorders | | | |
| Allergic reaction | | | |
| subjects affected / exposed | 5 / 78 (6.41%) | | |
| occurrences (all) | 9 | | |
| Immune system disorder | Additional description: Allergy-Dermatology-Skin | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hemorrhage pulmonary | | | |
| subjects affected / exposed | 3 / 78 (3.85%) | | |
| occurrences (all) | 4 | | |
| Bronchospasm | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Cough | | | |
| subjects affected / exposed | 4 / 78 (5.13%) | | |
| occurrences (all) | 4 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 4 / 78 (5.13%) | | |
| occurrences (all) | 5 | | |
| Voice alteration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Personality change | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 8 / 78 (10.26%) | | |
| occurrences (all) | 8 | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 19 / 78 (24.36%) | | |
| occurrences (all) | 33 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 36 / 78 (46.15%) | | |
| occurrences (all) | 67 | | |
| Alkaline phosphatase increased | | | |
| subjects affected / exposed | 29 / 78 (37.18%) | | |
| occurrences (all) | 38 | | |
| Amylase increased | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | |
| occurrences (all) | 3 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 20 / 78 (25.64%) | | |
| occurrences (all) | 31 | | |
| Hypercholesterolaemia | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 4 / 78 (5.13%) | | | |
| occurrences (all) | 4 | | | |
| Creatinine increased | | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | | |
| occurrences (all) | 2 | | | |
| Gamma-glutamyltransferase increased | | | | |
| subjects affected / exposed | 28 / 78 (35.90%) | | | |
| occurrences (all) | 33 | | | |
| Hyperkalaemia | | | | |
| subjects affected / exposed | 7 / 78 (8.97%) | | | |
| occurrences (all) | 8 | | | |
| Hypermagnesaemia | | | | |
| subjects affected / exposed | 9 / 78 (11.54%) | | | |
| occurrences (all) | 11 | | | |
| Hypernatraemia | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences (all) | 1 | | | |
| Hypertriglyceridaemia | | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | | |
| occurrences (all) | 2 | | | |
| Hyperuricaemia | | | | |
| subjects affected / exposed | 3 / 78 (3.85%) | | | |
| occurrences (all) | 4 | | | |
| Hypoalbuminaemia | | | | |
| subjects affected / exposed | 24 / 78 (30.77%) | | | |
| occurrences (all) | 29 | | | |
| Hypocalcaemia | | | | |
| subjects affected / exposed | 12 / 78 (15.38%) | | | |
| occurrences (all) | 14 | | | |
| Hypokalaemia | | | | |
| subjects affected / exposed | 22 / 78 (28.21%) | | | |
| occurrences (all) | 37 | | | |
| Hypomagnesaemia | | | | |
| subjects affected / exposed | 24 / 78 (30.77%) | | | |
| occurrences (all) | 33 | | | |

| | | | |
|---|---|---|---|
| Hyponatraemia | | | |
| subjects affected / exposed | 10 / 78 (12.82%) | | |
| occurrences (all) | 15 | | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 4 / 78 (5.13%) | | |
| occurrences (all) | 6 | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 20 / 78 (25.64%) | | |
| occurrences (all) | 35 | | |
| Blood urea increased | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | |
| occurrences (all) | 2 | | |
| Injury, poisoning and procedural complications | | | |
| Vascular access complication | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Dysgeusia | | | |
| subjects affected / exposed | 5 / 78 (6.41%) | | |
| occurrences (all) | 6 | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | |
| occurrences (all) | 2 | | |
| Mood altered | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | |
| occurrences (all) | 2 | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Peripheral motor neuropathy | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | |
| occurrences (all) | 2 | | |

| | | | |
|---|---|---|---|
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 35 / 78 (44.87%) | | |
| occurrences (all) | 53 | | |
| Neuropathy cranial | | | |
| alternative dictionary used: CTCAE 3 | | | |
| subjects affected / exposed | 3 / 78 (3.85%) | | |
| occurrences (all) | 4 | | |
| Speech disorder | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 28 / 78 (35.90%) | | |
| occurrences (all) | 45 | | |
| Leukopenia | | | |
| subjects affected / exposed | 26 / 78 (33.33%) | | |
| occurrences (all) | 46 | | |
| Neutropenia | | | |
| subjects affected / exposed | 24 / 78 (30.77%) | | |
| occurrences (all) | 44 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 26 / 78 (33.33%) | | |
| occurrences (all) | 51 | | |
| Ear and labyrinth disorders | | | |
| Ear and labyrinth disorder- other | Additional description: Partial temporary hearing loss | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Ocular surface disease | | | |
| subjects affected / exposed | 4 / 78 (5.13%) | | |
| occurrences (all) | 4 | | |
| Gastrointestinal disorders | | | |

| | | | | |
|---|---|---|---|---|
| Constipation | | | | |
| subjects affected / exposed | 11 / 78 (14.10%) | | | |
| occurrences (all) | 13 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 34 / 78 (43.59%) | | | |
| occurrences (all) | 60 | | | |
| Flatulence | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences (all) | 1 | | | |
| Dry mouth | | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | | |
| occurrences (all) | 2 | | | |
| Dysphagia | | | | |
| subjects affected / exposed | 4 / 78 (5.13%) | | | |
| occurrences (all) | 4 | | | |
| Stomatitis | | | | |
| subjects affected / exposed | 10 / 78 (12.82%) | | | |
| occurrences (all) | 13 | | | |
| Nausea | | | | |
| subjects affected / exposed | 17 / 78 (21.79%) | | | |
| occurrences (all) | 26 | | | |
| Vomiting | | | | |
| subjects affected / exposed | 16 / 78 (20.51%) | | | |
| occurrences (all) | 26 | | | |
| Gastrointestinal pain | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences (all) | 1 | | | |
| Abdominal distension | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences (all) | 1 | | | |
| Esophagitis | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences (all) | 1 | | | |
| Hemorrhage gastrointestinal | | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | | |
| occurrences (all) | 1 | | | |

| | | | |
|---|---|---|---|
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 13 / 78 (16.67%) | | |
| occurrences (all) | 13 | | |
| Cheilitis | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Skin disorder | | | |
| subjects affected / exposed | 6 / 78 (7.69%) | | |
| occurrences (all) | 6 | | |
| Dry skin | | | |
| subjects affected / exposed | 6 / 78 (7.69%) | | |
| occurrences (all) | 6 | | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 20 / 78 (25.64%) | | |
| occurrences (all) | 23 | | |
| Nail disorder | | | |
| subjects affected / exposed | 4 / 78 (5.13%) | | |
| occurrences (all) | 4 | | |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Pruritus | | | |
| subjects affected / exposed | 4 / 78 (5.13%) | | |
| occurrences (all) | 4 | | |
| Rash | | | |
| subjects affected / exposed | 56 / 78 (71.79%) | | |
| occurrences (all) | 63 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Hair growth rate abnormal | | | |
| subjects affected / exposed | 2 / 78 (2.56%) | | |
| occurrences (all) | 2 | | |
| Subcutaneous abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Renal and urinary disorders | | | |
| Hematuria | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Hemorrhage GU | | | |
| alternative dictionary used: CTCAE 3 | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Infections and infestations- Other specify | | | |
| subjects affected / exposed | 4 / 78 (5.13%) | | |
| occurrences (all) | 5 | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Nail infection | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Herpes virus infection | | | |
| subjects affected / exposed | 1 / 78 (1.28%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 19 / 78 (24.36%) | | |
| occurrences (all) | 24 | | |

| | | | |
|---|---|---|---|
| Hyperglycemia<br>subjects affected / exposed<br>occurrences (all) | 32 / 78 (41.03%)<br>65 | | |
| Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 78 (1.28%)<br>1 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported