



Clinical trial results:

Phase II trial to evaluate the efficacy and safety of chemoradiotherapy with 5-fluorouracil, mitomycin C and panitumumab as a treatment for squamous cell carcinoma of the anal canal

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-018430-48 |
| Trial protocol | ES |
| Global end of trial date | 16 April 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 31 July 2019 |
| First version publication date | 31 July 2019 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | GEMCAD-09-02 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01285778 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Grupo Español Multidisciplinar en Cáncer Digestivo (GEMCAD) |
| Sponsor organisation address | Pau Alsina, 64-68, esc. B, entlo. 5ª, Barcelona, Spain, 08024 |
| Public contact | Dr. Carlos Fernández Martos , Grupo Español Multidisciplinar en Cáncer Digestivo (GEMCAD), 0034 934344412, secretaria@gemcad.org |
| Scientific contact | Dr. Carlos Fernández Martos , Grupo Español Multidisciplinar en Cáncer Digestivo (GEMCAD), 0034 934344412, secretaria@gemcad.org |

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 April 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 January 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 April 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To estimate the three-year disease-free survival rate in patients treated with 5-FU, mytomicin C and panitumumab concurrently with radiation therapy as treatment for squamous cell carcinoma of the anal canal (SCCAC).

Protection of trial subjects:

For subjects who experienced unacceptable toxicity while in the study, one or more doses of panitumumab were suspended, reduced or delayed. Once the toxicity was solved, a limited number of attempts were made to re-increase the reduced doses of panitumumab. Escalations of doses higher than the initial dose of 6.0 mg / kg were not allowed.

Background therapy:

None.

Evidence for comparator:

Chemoradiotherapy with 5-FU and mitomycin C is the standard of care in Europe and U.S for the SCCAC. Panitumumab has been effective in other tumors and anti-EGFR treatment has demonstrated clinical activity in a single report of a refractory patient with SCCAC.

| | |
|---|------------------|
| Actual start date of recruitment | 24 January 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 3 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Spain: 58 |
| Worldwide total number of subjects | 58 |
| EEA total number of subjects | 58 |

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) | 41 |
| From 65 to 84 years | 17 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

58 patients were included in this study. All of them were included in the ITT, PP and safety populations. This national study included patients from 25 Spanish centers.

Pre-assignment

Screening details:

Key inclusion criteria: Male or female ≥ 18 years with histologically or cytologically confirmed SCACC; T2-T4 stage and any N stage (pelvic or inguinal) determined radiologically by MRI; ECOG performance status 0 to 2. All patients met the inclusion criteria.

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Baseline (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

Not applicable.

Arms

| Arm title | Treatment |
|-----------|-----------|
|-----------|-----------|

Arm description:

Patients received treatment with panitumumab (Vectibix®, Amgen) 6 mg/kg intravenously (IV) on day 1 and every 2 weeks for 8 weeks. Panitumumab treatment was followed by 5-FU 1 000 mg/day by continuous IV infusion on days 1-4 and 29-32, and mitomycin C 10 mg/m² IV on days 1 and 29. Radiotherapy was given on day 1-37 to a total dose of 45 Gy (1.8 Gy/fraction, 5 fractions per week) to the primary tumour and mesorectal, iliac and inguinal lymph nodes, plus a boost dose of 10-15 Gy to the primary tumour and affected lymph nodes.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Panitumumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Panitumumab was administered by i.v. infusion. on day 1 and every 2 weeks for 8 weeks. The dose of panitumumab was 6 mg / kg. The total dose could be rounded up or down by no more than 10 mg. The dose of panitumumab was calculated from the subject's actual body weight at baseline (ie, cycle 1) and was not recalculated unless the changes in actual body weight were at least 10% from baseline. Panitumumab was diluted in a minimum of 100 mL of 0.9% sodium chloride apyrogenic solution, according to the USP / PhEur / JP (normal saline, provided by the center). The maximum concentration of the diluted solution that was administered by infusion should not exceed 10 mg / mL; if necessary, the volume of normal saline should be increased to 150 mL.

| | |
|--|-----------------|
| Investigational medicinal product name | Mitomycin C |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients received treatment with panitumumab (Vectibix®, Amgen) 6 mg/kg intravenously (IV) on day 1 and every 2 weeks for 8 weeks. Panitumumab treatment was followed by 5-FU 1 000 mg/day by continuous IV infusion on days 1-4 and 29-32, and mitomycin C 10 mg/m² IV on days 1 and 29.

| | |
|--|-----------------------|
| Investigational medicinal product name | 5-fluorouracil (5-FU) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients received treatment with panitumumab (Vectibix®, Amgen) 6 mg/kg intravenously (IV) on day 1 and every 2 weeks for 8 weeks. Panitumumab treatment was followed by 5-FU 1 000 mg/day by continuous IV infusion on days 1-4 and 29-32, and mitomycin C 10 mg/m² IV on days 1 and 29.

| | |
|--|-----------------|
| Investigational medicinal product name | Radiotherapy |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Radiotherapy was administered on day 1-37 to a total dose of 45 Gy (1.8 Gy/fraction, 5 fractions per week) to the primary tumour and mesorectal, iliac and inguinal lymph nodes, plus a boost dose of 10-15 Gy to the primary tumour and affected lymph nodes.

| Number of subjects in period 1 | Treatment |
|--------------------------------|-----------|
| Started | 58 |
| Completed | 58 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Baseline |
|-----------------------|----------|

Reporting group description: -

| Reporting group values | Baseline | Total | |
|---|--------------|-------|--|
| Number of subjects | 58 | 58 | |
| Age categorical | | | |
| Adults aged between 33 and 83 years. | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 41 | 41 | |
| From 65-84 years | 17 | 17 | |
| Age continuous | | | |
| Units: years | | | |
| median | 59.2 | | |
| inter-quartile range (Q1-Q3) | 49.9 to 66.0 | - | |
| Gender categorical | | | |
| Adult men and women | | | |
| Units: Subjects | | | |
| Female | 31 | 31 | |
| Male | 27 | 27 | |
| ECOG performance status | | | |
| Units: Subjects | | | |
| ECOG 0 | 24 | 24 | |
| ECOG 1 | 33 | 33 | |
| ECOG 2 | 1 | 1 | |
| TNM stage | | | |
| Units: Subjects | | | |
| TNM stage I | 0 | 0 | |
| TNM stage II | 17 | 17 | |
| TNM stage IIIA | 12 | 12 | |
| TNM stage IIIB | 27 | 27 | |
| TNM stage NE | 2 | 2 | |
| HIV positive | | | |
| 13 patients for the HIV results were not evaluated. | | | |
| Units: Subjects | | | |
| HIV positive | 4 | 4 | |
| HIV negative | 41 | 41 | |
| Not recorded | 13 | 13 | |
| HPV positive | | | |
| 12 patients for the HPV results were not evaluated. | | | |
| Units: Subjects | | | |
| HPV positive | 39 | 39 | |
| HPV negative | 7 | 7 | |
| Not recorded | 12 | 12 | |
| Ethnicity | | | |
| Units: Subjects | | | |

| | | | |
|-----------|----|----|--|
| Caucasian | 57 | 57 | |
| Other | 1 | 1 | |

End points

End points reporting groups

| Reporting group title | Treatment |
|---|-----------|
| Reporting group description: | |
| Patients received treatment with panitumumab (Vectibix®, Amgen) 6 mg/kg intravenously (IV) on day 1 and every 2 weeks for 8 weeks. Panitumumab treatment was followed by 5-FU 1 000 mg/day by continuous IV infusion on days 1-4 and 29-32, and mitomycin C 10 mg/m ² IV on days 1 and 29. Radiotherapy was given on day 1-37 to a total dose of 45 Gy (1.8 Gy/fraction, 5 fractions per week) to the primary tumour and mesorectal, iliac and inguinal lymph nodes, plus a boost dose of 10-15 Gy to the primary tumour and affected lymph nodes. | |

Primary: 3-year disease-free survival (DFS %)

| End point title | 3-year disease-free survival (DFS %) ^[1] |
|---|---|
| End point description: | |
| Disease free survival was defined as number of months between the first treatment dose until the first treatment failure (defined as disease progression by MRI or CT, persistence of disease confirmed by biopsy performed at least 6 months after end of treatment, rescue surgery/colostomy by progression or death by progression). | |
| End point type | Primary |
| End point timeframe: | |
| Percentage of subjects who are still alive and without disease after 3 years of follow-up. | |

Notes:

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

Justification: No statistical analysis was performed. There was only one arm treatment.

| End point values | Treatment | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 36 months | 61.09 (47.13 to 72.40) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS %)

| End point title | Progression Free Survival (PFS %) |
|---|-----------------------------------|
| End point description: | |
| Progression free survival was defined as the number of months between the first treatment dose until progression, rescue surgery/colostomy due to progression or death. | |
| End point type | Secondary |
| End point timeframe: | |
| Time from the 1st dose of treatment to 3 years of progression. | |

| End point values | Treatment | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 36 months | 57.54 (43.64 to 69.19) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS %)

| | |
|---|-------------------------|
| End point title | Overall survival (OS %) |
| End point description: Overall survival was defined as number of months between first treatment dose and death for any reason. | |
| End point type | Secondary |
| End point timeframe: Overall survival at 3 years. | |

| End point values | Treatment | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 36 months | 78.4 (65.1 to 87.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Colostomy free survival (CFS %)

| | |
|---|---------------------------------|
| End point title | Colostomy free survival (CFS %) |
| End point description: Colostomy free survival rate was defined as the number of patients alive and without a colostomy. | |
| End point type | Secondary |
| End point timeframe: Percentage of subjects who are still alive and without colostomy after 2 years of follow-up. | |

| End point values | Treatment | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 24 months | 68.11 (54.24 to 78.58) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Locoregional failure (LRF %) free rate

| | |
|---|--|
| End point title | Locoregional failure (LRF %) free rate |
| End point description: LRF was defined as relapse of disease in the anal canal and/or regional organs and/or regional lymph nodes. | |
| End point type | Secondary |
| End point timeframe: Percentage of subjects who continue without local-regional relapses after 3 years of follow-up. | |

| End point values | Treatment | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 36 months | 64.77 (50.87 to 75.65) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Distant failure free rate (%)

| | |
|--|-------------------------------|
| End point title | Distant failure free rate (%) |
| End point description: LRF was defined as relapse of disease in the anal canal and/or regional organs and/or regional lymph nodes. All other relapses were considered distant failures. | |
| End point type | Secondary |
| End point timeframe: Percentage of subjects who continue without relapses at distance after 3 years of follow-up. | |

| End point values | Treatment | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 36 months | 92.98 (82.37 to 97.31) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Complete response (CR) rate

| | |
|---|-----------------------------|
| End point title | Complete response (CR) rate |
| End point description: Percentage of subjects who have reached a clinical and radiological CR. Response was evaluated clinically or radiologically according to Response Evaluation Criteria in Solid Tumours (RECIST) criteria (version 1.1). | |
| End point type | Secondary |
| End point timeframe: Patients who have reached at some point a clinical and/or radiological CR during the study. | |

| End point values | Treatment | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 81.0 (69.8 to 92.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Recurrence free survival (CFS %)

| | |
|--|----------------------------------|
| End point title | Recurrence free survival (CFS %) |
| End point description: Recurrence free survival was defined as number of months between the first CR to the treatment until the first treatment failure (disease progression analysed by MRI or TC, rescue surgery/colostomy due to progression or death due to progression). | |
| End point type | Secondary |

End point timeframe:

CFS at 2 years.

| End point values | Treatment | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 24 months | 72.75 (56.20 to 83.89) | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Analysis of duplication

| | |
|-----------------|-------------------------|
| End point title | Analysis of duplication |
|-----------------|-------------------------|

End point description:

Evaluation of the predictive molecular markers of response: the presence of duplications in 23 different genes in 27 patients with available samples.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

During the study

| End point values | Treatment | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 27 | | | |
| Units: frequency | | | | |
| number (not applicable) | | | | |
| EGFR | 26 | | | |
| KRAS | 37 | | | |
| BRAF | 0 | | | |
| PIK3CA | 85 | | | |
| PTEN | 26 | | | |
| BRCA1 | 4 | | | |
| BRCA2 | 22 | | | |
| ERCC1 | 48 | | | |
| ERCC6 | 4 | | | |
| ERCC3 | 4 | | | |
| ERCC4 | 26 | | | |
| ERCC2 | 37 | | | |
| ERCC8 | 33 | | | |
| ERCC5 | 19 | | | |

| | | | | |
|------------------|----|--|--|--|
| XRCC1 | 30 | | | |
| XRCC2 | 59 | | | |
| XRCC3 | 4 | | | |
| XRCC5 | 4 | | | |
| XRCC6 | 26 | | | |
| XRCC4 | 30 | | | |
| CCNA2 (cyclin a) | 19 | | | |
| TP53 | 15 | | | |
| MDM2 | 30 | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Analysis of deletions

| | |
|-----------------|-----------------------|
| End point title | Analysis of deletions |
|-----------------|-----------------------|

End point description:

Evaluation of the predictive molecular markers of response: the presence of deletions in 23 different genes in 27 patients with available samples.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

During the study

| End point values | Treatment | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 27 | | | |
| Units: frequency | | | | |
| number (not applicable) | | | | |
| EGFR | 7 | | | |
| KRAS | 0 | | | |
| BRAF | 15 | | | |
| PIK3CA | 0 | | | |
| PTEN | 15 | | | |
| BRCA1 | 59 | | | |
| BRCA2 | 33 | | | |
| ERCC1 | 4 | | | |
| ERCC6 | 74 | | | |
| ERCC3 | 30 | | | |
| ERCC4 | 7 | | | |
| ERCC2 | 7 | | | |
| ERCC8 | 15 | | | |
| ERCC5 | 22 | | | |
| XRCC1 | 0 | | | |
| XRCC2 | 7 | | | |
| XRCC3 | 33 | | | |
| XRCC5 | 37 | | | |

| | | | | |
|------------------|----|--|--|--|
| XRCC6 | 7 | | | |
| XRCC4 | 15 | | | |
| CCNA2 (cyclin a) | 19 | | | |
| TP53 | 48 | | | |
| MDM2 | 7 | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Analysis of single nucleotide polymorphisms (SNP)

| | |
|-----------------|---|
| End point title | Analysis of single nucleotide polymorphisms (SNP) |
|-----------------|---|

End point description:

Evaluation of the predictive molecular markers of response: the presence of SNP in 23 different genes in 27 patients with available samples.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

During the study

| End point values | Treatment | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: frequency | | | | |
| number (not applicable) | | | | |
| EGFR | 0 | | | |
| KRAS | 0 | | | |
| BRAF | 4 | | | |
| PIK3CA | 33 | | | |
| PTEN | 4 | | | |
| BRCA1 | 15 | | | |
| BRCA2 | 7 | | | |
| ERCC1 | 0 | | | |
| ERCC6 | 7 | | | |
| ERCC3 | 7 | | | |
| ERCC4 | 4 | | | |
| ERCC2 | 4 | | | |
| ERCC8 | 0 | | | |
| ERCC5 | 4 | | | |
| XRCC1 | 0 | | | |
| XRCC2 | 0 | | | |
| XRCC3 | 0 | | | |
| XRCC5 | 0 | | | |
| XRCC6 | 4 | | | |
| XRCC4 | 7 | | | |
| CCNA2 (cyclin a) | 0 | | | |
| TP53 | 4 | | | |

| | | | | |
|------|---|--|--|--|
| MDM2 | 0 | | | |
|------|---|--|--|--|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The medically significant AEs that the investigator or the promoter considered related to the product under investigation were monitored until their resolution or until stabilization.

Adverse event reporting additional description:

SAEs were collected and reported within 1 working day of the discovery or notification of the event if it appeared > 30 days after the last dose of the investigational product or after the end of the study and if it was believed that it was possibly related to the product under investigation.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Treatment |
|-----------------------|-----------|

Reporting group description:

Patients received treatment with: 1,000 mg² of 5-FU on days 1-4 and 29-32; 10 mg / m² of mitomycin C on days 1 and 29; 6 mg / m² of panitumumab on day 1 and every 2 weeks for 8 weeks; Radiotherapy: 45 Gy (1.8 Gy per fraction) in the regional and inguinal lymph nodes and the primary tumor, and then a 10-15 Gy boost in the primary tumor and affected lymph nodes.

| Serious adverse events | Treatment | | |
|--|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 24 / 58 (41.38%) | | |
| number of deaths (all causes) | 13 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Radiation skin injury | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | | |
| occurrences causally related to treatment / all | 2 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Weight decreased | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 58 (1.72%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 2 / 58 (3.45%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 3 / 58 (5.17%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | | |
| occurrences causally related to treatment / all | 3 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancytopenia | | | |
| subjects affected / exposed | 2 / 58 (3.45%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Colitis | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 4 / 58 (6.90%) | | |
| occurrences causally related to treatment / all | 2 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enteritis | | | |
| subjects affected / exposed | 2 / 58 (3.45%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Proctalgia | | | |
| subjects affected / exposed | 3 / 58 (5.17%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subileus | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 2 / 58 (3.45%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Pneumonia | | | |
| subjects affected / exposed | 2 / 58 (3.45%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Treatment | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 58 / 58 (100.00%) | | |
| Injury, poisoning and procedural complications | | | |
| Radiation skin injury | | | |
| subjects affected / exposed | 38 / 58 (65.52%) | | |
| occurrences (all) | 110 | | |
| Nervous system disorders | | | |
| Dysgeusia | | | |
| subjects affected / exposed | 6 / 58 (10.34%) | | |
| occurrences (all) | 7 | | |
| Blood and lymphatic system disorders | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 7 / 58 (12.07%) | | |
| occurrences (all) | 12 | | |
| Anaemia | | | |
| subjects affected / exposed | 16 / 58 (27.59%) | | |
| occurrences (all) | 35 | | |
| Leukopenia | | | |
| subjects affected / exposed | 11 / 58 (18.97%) | | |
| occurrences (all) | 13 | | |
| Lymphopenia | | | |
| subjects affected / exposed | 12 / 58 (20.69%) | | |
| occurrences (all) | 26 | | |
| Neutropenia | | | |
| subjects affected / exposed | 25 / 58 (43.10%) | | |
| occurrences (all) | 46 | | |
| Febrile neutropenia | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Thrombocytopenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 58 (8.62%)</p> <p>9</p> <p>14 / 58 (24.14%)</p> <p>19</p> | | |
| <p>General disorders and administration site conditions</p> <p>Asthenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Mucosal inflammation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Xerosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oedema peripheral</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>33 / 58 (56.90%)</p> <p>54</p> <p>5 / 58 (8.62%)</p> <p>6</p> <p>25 / 58 (43.10%)</p> <p>38</p> <p>10 / 58 (17.24%)</p> <p>13</p> <p>4 / 58 (6.90%)</p> <p>6</p> <p>4 / 58 (6.90%)</p> <p>5</p> | | |
| <p>Eye disorders</p> <p>Conjunctivitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 58 (5.17%)</p> <p>3</p> | | |
| <p>Reproductive system and breast disorders</p> <p>Perineal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 58 (5.17%)</p> <p>4</p> | | |
| <p>Gastrointestinal disorders</p> <p>Diarrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>44 / 58 (75.86%)</p> <p>90</p> | | |

| | | | |
|-----------------------------|------------------|--|--|
| Abdominal pain | | | |
| subjects affected / exposed | 14 / 58 (24.14%) | | |
| occurrences (all) | 18 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 5 / 58 (8.62%) | | |
| occurrences (all) | 5 | | |
| Enteritis | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | | |
| occurrences (all) | 5 | | |
| Perianal erythema | | | |
| subjects affected / exposed | 3 / 58 (5.17%) | | |
| occurrences (all) | 8 | | |
| Stomatitis | | | |
| subjects affected / exposed | 10 / 58 (17.24%) | | |
| occurrences (all) | 18 | | |
| Constipation | | | |
| subjects affected / exposed | 12 / 58 (20.69%) | | |
| occurrences (all) | 14 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | | |
| occurrences (all) | 4 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 3 / 58 (5.17%) | | |
| occurrences (all) | 5 | | |
| Anal incontinence | | | |
| subjects affected / exposed | 3 / 58 (5.17%) | | |
| occurrences (all) | 3 | | |
| Anal inflammation | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | | |
| occurrences (all) | 9 | | |
| Anorectal discomfort | | | |
| subjects affected / exposed | 3 / 58 (5.17%) | | |
| occurrences (all) | 4 | | |
| Nausea | | | |
| subjects affected / exposed | 18 / 58 (31.03%) | | |
| occurrences (all) | 22 | | |

| | | | |
|--|------------------|--|--|
| Odynophagia | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | | |
| occurrences (all) | 4 | | |
| Proctalgia | | | |
| subjects affected / exposed | 20 / 58 (34.48%) | | |
| occurrences (all) | 26 | | |
| Proctitis | | | |
| subjects affected / exposed | 5 / 58 (8.62%) | | |
| occurrences (all) | 8 | | |
| Rectal tenesmus | | | |
| subjects affected / exposed | 6 / 58 (10.34%) | | |
| occurrences (all) | 6 | | |
| Vomiting | | | |
| subjects affected / exposed | 13 / 58 (22.41%) | | |
| occurrences (all) | 17 | | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 6 / 58 (10.34%) | | |
| occurrences (all) | 14 | | |
| Alopecia | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | | |
| occurrences (all) | 4 | | |
| Dermatitis | | | |
| subjects affected / exposed | 9 / 58 (15.52%) | | |
| occurrences (all) | 18 | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 13 / 58 (22.41%) | | |
| occurrences (all) | 20 | | |
| Erythema | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | | |
| occurrences (all) | 7 | | |
| Rash | | | |
| subjects affected / exposed | 31 / 58 (53.45%) | | |
| occurrences (all) | 52 | | |
| Skin fissures | | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dry skin</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 58 (5.17%)</p> <p>5</p> <p>5 / 58 (8.62%)</p> <p>10</p> <p>3 / 58 (5.17%)</p> <p>4</p> | | |
| <p>Psychiatric disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 58 (6.90%)</p> <p>4</p> | | |
| <p>Renal and urinary disorders</p> <p>Dysuria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>11 / 58 (18.97%)</p> <p>14</p> | | |
| <p>Infections and infestations</p> <p>Oral candidiasis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pneumonia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 58 (6.90%)</p> <p>4</p> <p>3 / 58 (5.17%)</p> <p>3</p> <p>4 / 58 (6.90%)</p> <p>4</p> | | |
| <p>Metabolism and nutrition disorders</p> <p>Decreased appetite</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypokalaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypomagnesaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>16 / 58 (27.59%)</p> <p>23</p> <p>7 / 58 (12.07%)</p> <p>7</p> <p>15 / 58 (25.86%)</p> <p>17</p> | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 16 March 2010 | Through this amendment, the changes suggested by the Clinical Research Ethics Committees in the protocol were: the Subject Information Sheet, the Informed Consent Form, the Subject Information Sheet and the Informed Consent form of the optional study of molecular predictors. The changes to the protocol were as follows: the amount of panitumumab per vial was specified; and appendix E (panitumumab pharmaceutical guide) was modified in order to facilitate its comprehension. |
| 25 January 2011 | Through this amendment several typographical errors were amended in the protocol in order to facilitate its comprehension. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported