



Clinical trial results:

A randomized phase II trial of standard carboplatin-based chemotherapy with or without panitumumab in platinum-sensitive recurrent ovarian cancer

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2010-018849-59 |
| Trial protocol | DE |
| Global end of trial date | 28 November 2016 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 01 September 2021 |
| First version publication date | 01 September 2021 |

Trial information

Trial identification

| | |
|-----------------------|---------------------|
| Sponsor protocol code | GMIHO-008/2009_AG56 |
|-----------------------|---------------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | GMIHO Gesellschaft für Medizinische Innovation - Hämatologie und Onkologie mbH, |
| Sponsor organisation address | Almstadtstraße 7, Berlin, Germany, 10119 |
| Public contact | CRO, ClinAssess GmbH, 49 2171363360, info@clinassess.de |
| Scientific contact | CRO, ClinAssess GmbH, 49 2171363360, info@clinassess.de |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 23 February 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 28 November 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 November 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of panitumumab plus either the carboplatin/PLD or the carboplatin/gemcitabine combination chemotherapy in k-ras wildtype ovarian cancer patients with platinum-sensitive recurrence, compared to the historical data for the same chemotherapies, which are verified by a randomised control group without the antibody.

Protection of trial subjects:

The conduct of this study was in compliance with the Good Clinical Practice Guidelines and under the guiding principles detailed in the Declaration of Helsinki. The study was also be carried out in keeping with applicable local law(s) and regulation(s).

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 15 March 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 96 |
| Worldwide total number of subjects | 96 |
| EEA total number of subjects | 96 |

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) | 62 |
| From 65 to 84 years | 34 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The clinical trial was conducted at 22 sites in Germany. From March 15, 2012 a total of 102 were randomized in one of two arms (experimental arm A and standard arm B) and two chemotherapy backbone cohorts.

Pre-assignment

Screening details:

In total, 102 patients were randomised whereof 6 patients were not treated due to withdrawal of consent or other reason. Thus, 96 Patients were treated in 13 study sites. The enrolment period was from April 17, 2012 until May 19, 2015.

Period 1

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

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | A1: Gem/Carb + Pan |

Arm description:

Patients are scheduled to receive a maximum of six cycles, if they do not experience prior progression of disease. In case of no progression, but CR, PR or SD in the experimental arm, patients may receive maintenance therapy with Panitumumab for up to six months. Only patients of arm A are eligible for maintenance therapy.

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | Gemzar® |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1000 mg/m² on day 1 and 8 of each three-week cycle until progressive disease or for a max. of 6 cycles

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Carboplatin AUC 4 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Carboplatin AUC 4 (according to the formula by Calvert) on day 1 of each three-week cycle until progressive disease or for a max. of 6 cycles

| | |
|--|---------------------------------------|
| 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:

9 mg/kg/KG on day 1 of each three-week cycle until progressive disease or for a max. of 6 cycles

| | |
|------------------|--------------------|
| Arm title | A2: PLD/Carb + Pan |
|------------------|--------------------|

Arm description:

Patients are scheduled to receive a maximum of six cycles, if they do not experience prior progression of disease. In case of no progression, but CR, PR or SD in the experimental arm, patients may receive maintenance therapy with Panitumumab for up to six months. Only patients of arm A are eligible for maintenance therapy.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pegylated liposomal doxorubicin |
| Investigational medicinal product code | |
| Other name | Caelyx® |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

30 mg/m² on day 1 of each four-week cycle until progressive disease or for a max. of 6 cycles

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Carboplatin AUC 5 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Carboplatin AUC 5 (according to the formula by Calvert) on day 1 of each four-week cycle until progressive disease or for a max. of 6 cycles

| | |
|--|---------------------------------------|
| 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:

6 mg/kg/KG on day 1 and day 15 of each four-week cycle until progressive disease or for a max. of 6 cycles

| | |
|------------------|--------------|
| Arm title | B1: Gem/Carb |
|------------------|--------------|

Arm description: -

| | |
|--|----------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | Gemzar® |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1000 mg/m² on day 1 and day 8 of each three-week cycle until progressive disease or for a max. of 6 cycles

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Carboplatin AUC 4 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Carboplatin AUC 4 (according to the formula by Calvert) on day 1 of each three-week cycle until progressive disease or for a max. of 6 cycles

| | |
|------------------|--------------|
| Arm title | B2: PLD/Carb |
|------------------|--------------|

Arm description: -

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Pegylated liposomal doxorubicin |
| Investigational medicinal product code | |
| Other name | Caelyx® |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

30 mg/m² on day 1 of each four-week cycle until progressive disease or for a max. of 6 cycles

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Carboplatin AUC 5 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Carboplatin AUC 5 (according to the formula by Calvert) on day 1 of each four-week cycle until progressive disease or for a max. of 6 cycles

| Number of subjects in period 1 | A1: Gem/Carb + Pan | A2: PLD/Carb + Pan | B1: Gem/Carb |
|-----------------------------------|--------------------|--------------------|--------------|
| Started | 23 | 26 | 19 |
| Completed | 6 | 6 | 9 |
| Not completed | 17 | 20 | 10 |
| Adverse event, serious fatal | 1 | 1 | 2 |
| Consent withdrawn by subject | - | 1 | 1 |
| Adverse event, non-fatal | 4 | 6 | - |
| Not known | 1 | 1 | 1 |
| Patient refuses further treatment | 4 | 5 | 1 |
| Lost to follow-up | - | - | 1 |
| Lack of efficacy | 7 | 6 | 4 |
| Protocol deviation | - | - | - |

| Number of subjects in period 1 | B2: PLD/Carb |
|-----------------------------------|--------------|
| Started | 28 |
| Completed | 14 |
| Not completed | 14 |
| Adverse event, serious fatal | - |
| Consent withdrawn by subject | - |
| Adverse event, non-fatal | 2 |
| Not known | 2 |
| Patient refuses further treatment | 5 |
| Lost to follow-up | 1 |
| Lack of efficacy | 3 |
| Protocol deviation | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values | overall trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 96 | 96 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 62 | 62 | |
| From 65-84 years | 34 | 34 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: days | | | |
| median | 59.7 | | |
| full range (min-max) | 31 to 77 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 96 | 96 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | A1: Gem/Carb + Pan |
| Reporting group description: Patients are scheduled to receive a maximum of six cycles, if they do not experience prior progression of disease. In case of no progression, but CR, PR or SD in the experimental arm, patients may receive maintenance therapy with Panitumumab for up to six months. Only patients of arm A are eligible for maintenance therapy. | |
| Reporting group title | A2: PLD/Carb + Pan |
| Reporting group description: Patients are scheduled to receive a maximum of six cycles, if they do not experience prior progression of disease. In case of no progression, but CR, PR or SD in the experimental arm, patients may receive maintenance therapy with Panitumumab for up to six months. Only patients of arm A are eligible for maintenance therapy. | |
| Reporting group title | B1: Gem/Carb |
| Reporting group description: - | |
| Reporting group title | B2: PLD/Carb |
| Reporting group description: - | |

Primary: Progression-free survival (PFS) rate after 12 months

| | |
|---|--|
| End point title | Progression-free survival (PFS) rate after 12 months |
| End point description: PFS is defined as the duration from the date of randomisation to the date of progressive disease (acc. to RECIST 1.1) or death, whichever occurs first. | |
| End point type | Primary |
| End point timeframe: 12 months | |

| End point values | A1: Gem/Carb + Pan | A2: PLD/Carb + Pan | B1: Gem/Carb | B2: PLD/Carb |
|----------------------------------|---------------------|---------------------|---------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 26 | 19 | 28 |
| Units: percent | | | | |
| number (confidence interval 95%) | 26.1 (10.2 to 48.4) | 30.8 (14.3 to 51.8) | 31.6 (12.6 to 56.6) | 28.6 (13.2 to 48.7) |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Full Analysis |
| Comparison groups | A1: Gem/Carb + Pan v A2: PLD/Carb + Pan v B2: PLD/Carb v B1: Gem/Carb |

| | |
|---|---------------|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.9999 |
| Method | Fisher exact |

Secondary: Overall response rate

| | |
|--|-----------------------|
| End point title | Overall response rate |
| End point description: | |
| Overall response is defined as best response from start of cycle one until the end of last cycle with background chemotherapy and/ or Panitumumab plus 28 days. Patients experiencing CR or PR are considered to be responders. | |
| Overall response was assessed during combination chemotherapy in cycle 3 and cycle 6 as well as at the end of combination chemotherapy. In case of maintenance therapy, overall response was scheduled after every 12 weeks. During follow-up response was assessed every third month. | |
| End point type | Secondary |
| End point timeframe: | |
| cycle 3, cycle 6, end of combination chemotherapy, every 12 weeks (maintenance therapy), every third month (follow-up) | |

| End point values | A1: Gem/Carb + Pan | A2: PLD/Carb + Pan | B1: Gem/Carb | B2: PLD/Carb |
|----------------------------------|---------------------|---------------------|---------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 22 | 19 | 27 |
| Units: percent | | | | |
| number (confidence interval 95%) | 69.6 (47.1 to 86.8) | 50.0 (28.2 to 71.8) | 36.8 (16.3 to 61.6) | 29.6 (13.8 to 50.2) |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

| | |
|--------------------------------------|----------------------|
| End point title | Duration of response |
| End point description: | |
| | |
| End point type | Secondary |
| End point timeframe: | |
| time of disease progression or death | |

| End point values | A1: Gem/Carb + Pan | A2: PLD/Carb + Pan | B1: Gem/Carb | B2: PLD/Carb |
|-----------------------------|--------------------|--------------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 5 | 4 | 3 |
| Units: percent | | | | |
| number (not applicable) | 81.8 | 100.0 | 80.0 | 50.0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

| | |
|--------------------------------------|---------------------------|
| End point title | Progression-free survival |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| date of progressive disease or death | |

| End point values | A1: Gem/Carb + Pan | A2: PLD/Carb + Pan | B1: Gem/Carb | B2: PLD/Carb |
|----------------------------------|--------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 | 20 | 14 | 17 |
| Units: month | | | | |
| median (confidence interval 95%) | 8.9 (7.9 to 12.4) | 10.5 (8.5 to 12.2) | 10.6 (7.1 to 13.1) | 10.9 (8.5 to 15.4) |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

| | |
|------------------------|------------------|
| End point title | Overall survival |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| date of death | |

| End point values | A1: Gem/Carb + Pan | A2: PLD/Carb + Pan | B1: Gem/Carb | B2: PLD/Carb |
|-----------------------------|-----------------------|-----------------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 12 | 4 | 5 |
| Units: percent | | | | |
| number (not applicable) | 34.8 | 46.2 | 21.1 | 17.9 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from first intake of study medication until 28 days after last intake of any study medication

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Most frequent events |
|-----------------------|----------------------|

Reporting group description: -

| Serious adverse events | Most frequent events | | |
|--|----------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 47 / 96 (48.96%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 47 / 96 (48.96%) | | |
| occurrences causally related to treatment / all | 6 / 13 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 47 / 96 (48.96%) | | |
| occurrences causally related to treatment / all | 11 / 18 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 47 / 96 (48.96%) | | |
| occurrences causally related to treatment / all | 5 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Most frequent events | | |
|---|----------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 95 / 96 (98.96%) | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 46 / 96 (47.92%) | | |
| occurrences (all) | 186 | | |
| Leukopenia | | | |
| subjects affected / exposed | 47 / 96 (48.96%) | | |
| occurrences (all) | 197 | | |
| Neutropenia | | | |
| subjects affected / exposed | 49 / 96 (51.04%) | | |
| occurrences (all) | 204 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 52 / 96 (54.17%) | | |
| occurrences (all) | 221 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 57 / 96 (59.38%) | | |
| occurrences (all) | 107 | | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 33 / 96 (34.38%) | | |
| occurrences (all) | 48 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 35 / 96 (36.46%) | | |
| occurrences (all) | 59 | | |
| Nausea | | | |
| subjects affected / exposed | 65 / 96 (67.71%) | | |
| occurrences (all) | 102 | | |
| Vomiting | | | |
| subjects affected / exposed | 33 / 96 (34.38%) | | |
| occurrences (all) | 49 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |

| | | | |
|--|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 30 / 96 (31.25%) 52 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 32 / 96 (33.33%) 35 | | |
| Dry skin subjects affected / exposed occurrences (all) | 31 / 96 (32.29%) 52 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 16 April 2012 | Amendment1: Addition of an alternative chemotherapy backbone consisting of Gemcitabin and Carboplatin as possible replacement for the PLD/Carboplatin chemotherapy with the option to switch back (for new patients) to the PLD/Carboplatin-regime, if PLD becomes available during the course of the trial. |
| 17 October 2012 | Amendment 2: CRO change |
| 16 July 2013 | Amendment 3: IB update Panitumumba (version 12.0); amended Protocol (Version 3.0) - modification of chemotherapy dose levels and deletion of translational research program |
| 24 November 2014 | Amendment 4: amended Protocol (version 4.0) - reduction of the number of patients and adjustment if the sample size, extension of study duration |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported