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 unitl 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 occurrences (all)	46 / 96 (47.92%) 186		
Leukopenia subjects affected / exposed occurrences (all)	47 / 96 (48.96%) 197		
Neutropenia subjects affected / exposed occurrences (all)	49 / 96 (51.04%) 204		
Thrombocytopenia subjects affected / exposed occurrences (all)	52 / 96 (54.17%) 221		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	57 / 96 (59.38%) 107		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	33 / 96 (34.38%) 48		
Diarrhoea subjects affected / exposed occurrences (all)	35 / 96 (36.46%) 59		
Nausea subjects affected / exposed occurrences (all)	65 / 96 (67.71%) 102		
Vomiting subjects affected / exposed occurrences (all)	33 / 96 (34.38%) 49		
Respiratory, thoracic and mediastinal disorders Dyspnoea			

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