Clinical trial results:
An open-label, randomised, multicentre, phase II clinical study of panitumumab plus pemetrexed and cisplatin (PemCisP) versus PemCis in the first-line treatment of patients with stage IIIB or IV primary nonsquamous non-small cell lung cancer, with particular regard to the KRAS status

Summary

EudraCT number	2009-014677-41
Trial protocol	DE
Global end of trial date	30 August 2013

Results information

Result version number	v1 (current)
This version publication date	16 July 2022
First version publication date	16 July 2022

Trial information

Trial identification

Sponsor protocol code	AG47/GMIHO-006/2008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01088620
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	Medical Consulting, GWT-TUD GmbH, +49 35125933100, info@gmiho.de
Scientific contact	Medical Consulting, GWT-TUD GmbH, +49 35125933100, info@gmiho.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	16 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 August 2013
Global end of trial reached?	Yes
Global end of trial date	30 August 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to estimate the efficacy of the combination consisting of cisplatin/pemetrexed and panitumumab in patients with wild-type KRAS (non-mutated status). The progression-free survival rate at 6 months was compared to expectations derived from historical data, which were verified by a randomized 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 carried out in keeping with applicable local law(s) and regulation(s).
Participants were monitored losely for toxicity, especially myelosuppression, renal, and gastrointestinal toxicity. An interim analysis of safety was presented to the Data Safety and Monitoring Board (DSMB) after documentation of the first 10 randomized patients in each arm. The DSMB received regular information on safety results of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 April 2010
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)	61
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From the 26th Apr 2010 through 11th Jan 2013, a total of 98 patients were randomised at 13 participating centers in Germany. The assumption of 67 patients with KRAS wild type per arm (in total 134 patients) was not achieved.

Pre-assignment

Screening details:

Out of 98 randomized patients, 96 patients were included in the full analysis set. One patient had to be excluded because of the violation of inclusion criteria. Another patient withdrew his consent after randomisation but before the first cycle of combination therapy. Randomization was stratified by participating center.

Period 1

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

Blinding implementation details:

The study was performed in a non-blinded design because this was considered adequate to meet the study objectives.

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Pemetrexed plus Cisplatin plus Panitumumab (PemCisP)

Arm type	Experimental
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	Alimta®
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed was administered at a dose of 500 mg/m² as a 10 minute infusion, before the application of cisplatin on day 1 of each three-week cycle for up to 4 cycles or until diagnosis of disease progression if occurring earlier.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 75 mg/m² was applied i.v. on day 1 of each three-week cycle, after the administration of pemetrexed, according to routine procedures for up to 4 cycles or until diagnosis of disease progression if occurring earlier.

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:

Panitumumab 9 mg/kg b.w. qw3 as infusion was administered on Day 1 of each three-week cycle for up to 4 cycles or until diagnosis of disease progression if occurring earlier.

Arm title	Arm B

Arm description:

Pemetrexed plus Cisplatin (PemCis)

Arm type	Active comparator
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	Alimta®
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed was administered at a dose of 500 mg/m² as a 10 minute infusion, before the application of cisplatin on day 1 of each three-week cycle for up to 4 cycles or until diagnosis of disease progression if occurring earlier.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 75 mg/m² was applied i.v. on day 1 of each three-week cycle, after the administration of pemetrexed, according to routine procedures for up to 4 cycles or until diagnosis of disease progression if occurring earlier.

Number of subjects in period 1	Arm A	Arm B
Started	49	47
Completed	23	33
Not completed	26	14
Adverse event, non-fatal	5	-
Refusal by patient (not associated with toxicity)	2	-
Lack of efficacy	15	12
Protocol deviation	1	-
not specified	3	2

Baseline characteristics

End points

End points reporting groups	
Reporting group title	Arm A
Reporting group description: Pemetrexed plus Cisplatin plus Panitumumab (PemCisP)	
Reporting group title	Arm B
Reporting group description: Pemetrexed plus Cisplatin (PemCis)	

Primary: Progression Free Survival (PFS) Rate	
End point title	Progression Free Survival (PFS) Rate
End point description:	
End point type	Primary
End point timeframe: after 6 months	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	46		
Units: patients				
number (not applicable)	14	24		

Statistical analyses

Statistical analysis title	Efficacy analysis
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Logrank
Parameter estimate	Mean difference (final values)
Point estimate	173.915
Confidence interval	
level	95 %
sides	2-sided
lower limit	133.43
upper limit	214.399
Variability estimate	Standard error of the mean
Dispersion value	20.656

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

at the time when the subject is enrolled into the study (date of signature of the informed consent) until the End of Treatment Visit has been performed or 30 days after the last dose of study treatment

Adverse event reporting additional description:

The investigator was responsible for ensuring that all AEs observed by the investigator or reported by subjects were properly captured in the subjects' medical records.

Assessment type	Systematic

Dictionary used

Dictionary name	WHO-ART
Dictionary version	2013AA

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: In total, 40 patients experienced one or more SAE, 24 patients of Arm A and 16 patients of Arm B. Among them, 14 patients of Arm A and 8 patients of Arm B reported SAEs that were assessed as being drug related. With 24 versus 16 the number of patients with one or more SAEs was higher within the panitumumab arm as compared to the control arm. Furthermore, the total number of SAEs was also higher in the panitumumab arm as compared to the control arm (33 in Arm A versus 22 in Arm B).

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 October 2012	Protocol Version 1.9-2 dated 13.08.2012: CRO change
12 July 2013	Protocol Version 2.1 dated 08.04.2013: in consequence of the premature stop of the patient recruitment only the data sets of 98 patients were evaluable

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

A futility analysis was performed to support the safety assessment of the DSMB. On the basis of interim toxicity data and the futility analysis of PFS the DSMB recommended to immediately stop patient recruitment.

Notes: