Clinical trial results:
Induction therapy with gefitinib followed by taxane platinum chemotherapy and intercalated gefitinib in NSCLC stages II-IIIB with activating EGFR mutation – A single arm Phase II trial.

Summary

EudraCT number	2014-005595-28
Trial protocol	DE
Global end of trial date	16 March 2017

Results information

Result version number	v1 (current)
This version publication date	30 April 2022
First version publication date	30 April 2022

Trial information

Trial identification

Sponsor protocol code	AIO-TRK-0214

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02326285
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AIO-Studien-gGmbH
Sponsor organisation address	Kuno-Fischer-Str. 8, Berlin, Germany, 14057
Public contact	AIO-Studien-gGmbH, AIO-Studien-gGmbH, +49 30814534431, info@aio-studien-ggmbh.de
Scientific contact	AIO-Studien-gGmbH, AIO-Studien-gGmbH, +49 30814534431, info@aio-studien-ggmbh.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 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 March 2017
Global end of trial reached?	Yes
Global end of trial date	16 March 2017
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 assess the pathologic complete remission rate (according to the Junker criteria regression IIB and III) after induction therapy with gefitinib D-12 to D -1 followed by docetaxel 75 mg/m² and cisplatin 50 mg/m2 D1+2 q21d (or paclitaxel 200 mg/m² D1 and carboplatin AUC 6.0 D1) and intercalated gefitinib 250 mg D4 to D20 (cycles 1 + 2) and D4-D17 (cycle 3) in mediastinal/hilar lymph nodes as well as primary tumor.

Protection of trial subjects:

This study was planned, analyzed and conducted according to the study protocol and in accordance with the International Conference on Harmonization (ICH) ‚Guideline for Good Clinical Practice E6(R1)‘, CPMP/ICH/135/95, based on the principles of the Declaration of Helsinki (1964) and its October 1996 amendment (Somerset West, South Africa). The study was duly conducted in compliance with the German Arzneimittelgesetz (AMG; German Drug Law), and the corresponding Directive 2001/20/EC. Subjects were fully informed regarding all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 2015
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	Germany: 1
Worldwide total number of subjects	1
EEA total number of subjects	1

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)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Of 39 patients pre-screened between November 2015 and March 2017, 37 were assessed for EGFR mutation status. Only one of the these was tested positive for an EGFR mutation.

Pre-assignment

Screening details:

Of 39 patients pre-screened between November 2015 and March 2017, 37 were assessed for EGFR mutation status. Only one of the these was tested positive for an EGFR mutation.

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	Overall trial

Arm description:

Per protocol, treatment was to be administered in three cycles of a duration of three weeks each. Per protocol treatment started with 12 days of gefitinib at 250 mg/day p.o. (D-12 to -1) and subsequent induction with doublet chemotherapy of docetaxel 75 mg/m2 i.v. on D1 and cisplatin 50 mg/m2 i.v. on D1 and 2. Gefitinib was to be given daily on D4 to D20 of the first two cycles. In the third cycle, gefitinib was administered on D4 to D17. Surgery was planned to take place within the 4th week after D1 of the last cycle.

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

Dosage and administration details:

Three cycles at 75 mg/m2 on Day 1

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Three cycles at 50 mg/m2 on Day 1+2

Investigational medicinal product name	Gefitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

12 days of induction treatment, followed by three cycles of intercalated gefitinib at 250 mg/day on Days 4-20 (cycles 1 and 2) or Days 4-17 (cycle 3).

Number of subjects in period 1	Overall trial
Started	1
Completed	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	1	1	
Age categorical Units: Subjects			
Adults (18-64 years)	1	1	
Gender categorical Units: Subjects			
Female	1	1	
Male	0	0	

End points

End points reporting groups

Reporting group title	Overall trial

Reporting group description:

Per protocol, treatment was to be administered in three cycles of a duration of three weeks each. Per protocol treatment started with 12 days of gefitinib at 250 mg/day p.o. (D-12 to -1) and subsequent induction with doublet chemotherapy of docetaxel 75 mg/m2 i.v. on D1 and cisplatin 50 mg/m2 i.v. on D1 and 2. Gefitinib was to be given daily on D4 to D20 of the first two cycles. In the third cycle, gefitinib was administered on D4 to D17. Surgery was planned to take place within the 4th week after D1 of the last cycle.

Primary: Rate of pathologic complete remissions (pCR) of hilar and mediastinal lymph nodes after induction CTx + surgery

End point title	Rate of pathologic complete remissions (pCR) of hilar and mediastinal lymph nodes after induction CTx + surgery[1]

End point description:

Primary endpoint was the regression grading by Junker of hilar and mediastinal lymph nodes. For both lymph nodes, regression was rated with grade III, i.e. pathologic complete remission (pCR) was achieved.

End point type	Primary

End point timeframe:

From baseline until surgery

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 analyses were carried out. The data set generated by a single patient is too small for meaningful analysis.

End point values	Overall trial			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: pCR rate				
Pathologic complete remission (pCR)	1			
No pCR	0			

Statistical analyses

No statistical analyses for this end point

Secondary: R0 resection rate

End point title	R0 resection rate

End point description:

End point type	Secondary

End point timeframe:

At surgery

End point values	Overall trial			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: R0 resection rate				
R0 resection	1			
Other	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Regression grading of the primary tumor according to the Junker criteria

End point title	Regression grading of the primary tumor according to the Junker criteria

End point description:

End point type	Secondary

End point timeframe:

From baseline until surgery

End point values	Overall trial			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Regression grading				
Grade IIa	1			
Other	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of informed consent until study termination by sponsor: September 2016 - March 2017

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Paraesthesia			

subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1 1 / 1 (100.00%) 1		
General disorders and administration site conditions Chronic fatigue syndrome subjects affected / exposed occurrences (all)	 1 / 1 (100.00%) 1		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	 1 / 1 (100.00%) 1		
Gastrointestinal disorders Aphthous ulcer subjects affected / exposed occurrences (all)	 1 / 1 (100.00%) 1		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	 1 / 1 (100.00%) 1		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 1 / 1 (100.00%) 1 1 / 1 (100.00%) 1 1 / 1 (100.00%) 1		
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all)	 1 / 1 (100.00%) 1		
Infections and infestations			

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2016	Several smaller improvements to the study protocol were made: - Inclusion criteria slightly extended (e.g., added eligibility for cytologically confirmed disease, not only histologic confirmation) - Edits to schedule of assessments (time points changed for some assessments, and some assessments added, e.g. full blood count, ALT, bilirubin, GFR) - Some clarifications added (e.g., that tumor surgery is not a study procedure)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported