Clinical trial results:
Neoadjuvant anti PD-1 immunotherapy in resectable non-small cell lung cancer

Summary

EudraCT number	2017-000105-20
Trial protocol	DE
Global end of trial date	05 May 2023

Results information

Result version number	v1 (current)
This version publication date	04 April 2025
First version publication date	04 April 2025

Trial information

Trial identification

Sponsor protocol code	0316-ASG

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	Help desk, AIO-Studien-gGmbH, 0049 30814534431, info@aio-studien-ggmbh.de
Scientific contact	Help desk, AIO-Studien-gGmbH, 0049 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	05 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 May 2023
Global end of trial reached?	Yes
Global end of trial date	05 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- feasibility and safety of a neoadjuvant application of pembrolizumab
- antitumor activity of pembrolizumab with regard to clinical and pathologic tumor response

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	03 July 2017
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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	23
From 65 to 84 years	7

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Between 18-Jun-2018 and 03-Feb-2020, 30 patients were recruited into the study. One patient withdrew informed consent prior to treatment start.

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	Pembrolizumab
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Study treatment consisted of neoadjuvant pembrolizumab at a dose of 200 mg q3w i.v. for 2 cycles.

Number of subjects in period 1[1]	Pembrolizumab
Started	29
Completed	29

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One patient was screened and found eligible for study participation, but withdrew consent before treatment start. This patient was removed from all analyses.

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	29	29	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	60.0		
full range (min-max)	40 to 83	-	
Gender categorical Units: Subjects			
Female	16	16	
Male	13	13	
ECOG status Units: Subjects			
ECOG 0	14	14	
ECOG 1	15	15	

End points

End points reporting groups

Reporting group title	Pembrolizumab

Reporting group description: -

Primary: Number of Patients Treated in Compliance With Protocol

End point title	Number of Patients Treated in Compliance With Protocol[1]

End point description:

The definition for this endpoint was neoadjuvant pembrolizumab treatment followed by successful curative intent tumor resection.

End point type	Primary

End point timeframe:

From screening until surgery, ca. 6-8 weeks

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: This was a single-arm exploratory study with a small sample size. No statistical tests were specified.

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Patients	29			

Statistical analyses

No statistical analyses for this end point

Primary: Tumor Response According to RECIST 1.1 Criteria

End point title	Tumor Response According to RECIST 1.1 Criteria[2]

End point description:

Radiologic tumor assessments for this endpoint were performed at screening and pre-surgery.

End point type	Primary

End point timeframe:

From screening until pre-surgery radiologic assessment, ca. 6-8 weeks

Notes:

[2] - 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: This was a single-arm exploratory study with a small sample size. No statistical tests were specified.

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Patients				
Complete response (CR)	0			
Partial response (PR)	6			
Stable disease (SD)	19			
Progressive disease (PD)	3			

Statistical analyses

No statistical analyses for this end point

Primary: Tumor Response Evaluation - Pathologic Response

End point title	Tumor Response Evaluation - Pathologic Response[3]

End point description:

Pathologic regression grading according to Junker criteria (Junker K, Langner K, Klinke F, Bosse U, Thomas M. Grading of tumor regression in non-small cell lung cancer : morphology and prognosis. Chest 2001; 120:1584-91).

End point type	Primary

End point timeframe:

From screening until surgery, ca. 6-8 weeks

Notes:

[3] - 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: This was a single-arm exploratory study with a small sample size. No statistical tests were specified.

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Patients				
Grade I	4			
Grade IIa	18			
Grade IIb	3			
Grade III	4			

Statistical analyses

No statistical analyses for this end point

Primary: Tumor Response Evaluation - Δ Tumor Size

End point title	Tumor Response Evaluation - Δ Tumor Size[4]

End point description:

Δ tumor size was defined as the difference [mm] between longest diameter at baseline and pre-surgery.

End point type	Primary

End point timeframe:

From screening until pre-surgery radiologic assessment, ca. 6-8 weeks

Notes:

[4] - 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: This was a single-arm exploratory study with a small sample size. No statistical tests were specified.

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: mm				
median (inter-quartile range (Q1-Q3))	-4 (-13.5 to 0.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Tumor Response - Δ PET Activity

End point title	Tumor Response - Δ PET Activity[5]

End point description:

End point type	Primary

End point timeframe:

From screening until pre-surgery radiologic assessment, ca. 6-8 weeks

Notes:

[5] - 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: This was a single-arm exploratory study with a small sample size. No statistical tests were specified.

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Standardized uptake value (SUV)				
median (inter-quartile range (Q1-Q3))	-1 (-7 to 2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease-free Survival (DFS) at 6 Months

End point title	Disease-free Survival (DFS) at 6 Months

End point description:

Probability DFS was calculated using Kaplan-Meier statistics from date of surgery to the date until tumor recurrence or death. Follow-up was until 24 months after last-patient-out.

End point type	Secondary

End point timeframe:

6 months after surgery, i.e. circa 8 months after treatment start

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Probability of DFS in %				
number (confidence interval 95%)	86.2 (67.3 to 94.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease-free Survival (DFS) at 12 Months

End point title	Disease-free Survival (DFS) at 12 Months

End point description:

Probability of disease-free survival (DFS) were calculated from date of surgery until tumor recurrence or death using Kaplan-Meier statistics. Follow-up was until 24 months after last-patient-out.

End point type	Secondary

End point timeframe:

12 months after surgery, i.e. circa 14 months after treatment start

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Probability of DFS in %				
number (confidence interval 95%)	86.2 (67.3 to 94.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) at 12 Months

End point title	Overall Survival (OS) at 12 Months

End point description:

Probability of overall survival (OS) was calculated from date of surgery until tumor recurrence or death using Kaplan-Meier statistics. Follow-up was until 24 months after last-patient-out.

End point type	Secondary

End point timeframe:

12 months after surgery, i.e. circa 14 months after treatment start

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Probability of OS in %				
number (confidence interval 95%)	93.1 (75.1 to 98.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival at 18 Months

End point title	Overall Survival at 18 Months

End point description:

Probability of overall survival (OS) was calculate from date of surgery until tumor recurrence or death using Kaplan-Meier statistics. Follow-up was until 24 months after last-patient-out.

End point type	Secondary

End point timeframe:

18 months after surgery, i.e. circa 20 months after treatment start

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Probability of OS in %				
number (confidence interval 95%)	89.7 (71.3 to 96.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival at 24 Months

End point title	Overall Survival at 24 Months

End point description:

Probability of overall survival (OS) was calculated from date of surgery until death using Kaplan-Meier statistics. Follow-up was until 24 months after last-patient-out.

End point type	Secondary

End point timeframe:

24 months after surgery, i.e. circa 26 months after treatment start

End point values	Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Probability of OS in %				
number (confidence interval 95%)	86.2 (67.3 to 94.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the signing of informed consent until the EoT visit, which was scheduled to take place approx. six weeks after surgery.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

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	8 / 29 (27.59%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	1		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

Skin and subcutaneous tissue disorders			
Lichen planus			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 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	21 / 29 (72.41%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	3		
Paraesthesia			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 29 (13.79%)		
occurrences (all)	4		

Pain subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Decreased appetite subjects affected / exposed occurrences (all)	 3 / 29 (10.34%) 3 3 / 29 (10.34%) 3 2 / 29 (6.90%) 2 2 / 29 (6.90%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 5 / 29 (17.24%) 5		
Endocrine disorders Autoimmune thyreoditis subjects affected / exposed occurrences (all) Hyperthyroidism subjects affected / exposed occurrences (all)	 2 / 29 (6.90%) 2 2 / 29 (6.90%) 3		
Infections and infestations Pneumonia subjects affected / exposed occurrences (all)	 3 / 29 (10.34%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 January 2019	In the inclusion criteria, allowed thresholds for INR and PTT values were reduced to improve suitability of patients regarding surgery.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33529989