# 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<br>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<br>Units: years | | | |
| median | 60.0 | | |
| full range (min-max) | 40 to 83 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 16 | 16 | |
| Male | 13 | 13 | |
| ECOG status<br>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<br>subjects affected / exposed<br>occurrences (all) | 2 / 29 (6.90%)<br>2 | | |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all)<br><br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | <br><br>3 / 29 (10.34%)<br>3<br><br><br>3 / 29 (10.34%)<br>3<br><br><br>2 / 29 (6.90%)<br>2<br><br><br>2 / 29 (6.90%)<br>2 | | |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | <br><br>5 / 29 (17.24%)<br>5 | | |
| Endocrine disorders<br>Autoimmune thyreoditis<br>subjects affected / exposed<br>occurrences (all)<br><br>Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all) | <br><br>2 / 29 (6.90%)<br>2<br><br><br>2 / 29 (6.90%)<br>3 | | |
| Infections and infestations<br>Pneumonia<br>subjects affected / exposed<br>occurrences (all) | <br><br>3 / 29 (10.34%)<br>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