



Clinical trial results:

NEO -ADJUVANT CHEMO/IMMUNOTHERAPY FOR THE TREATMENT OF RESECTABLE STAGE IIIA NON SMALL CELL LUNG CANCER (NSCLC): A PHASE II MULTICENTER EXPLORATORY STUD

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2016-003732-20 |
| Trial protocol | ES |
| Global end of trial date | 18 October 2023 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 30 October 2024 |
| First version publication date | 30 October 2024 |
| Summary attachment (see zip file) | Lancet Oncol article_NADIM (NADIM I_Provencio _ The Lancet Onco 2020.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | GECP16/03 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03081689 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Fundación GECP |
| Sponsor organisation address | Avda. Meridiana 358, Barcelona, Spain, 08027 |
| Public contact | Eva Pereira, Fundación GECP, +34 934302006, epereira@gecp.org |
| Scientific contact | Eva Pereira, Fundación GECP, +34 934302006, epereira@gecp.org |

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 | 19 March 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 October 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 October 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Estimate progression-free survival (PFS) at 24 months from diagnosis

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 February 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 | Spain: 46 |
| Worldwide total number of subjects | 46 |
| EEA total number of subjects | 46 |

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) | 44 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Between April 26, 2017, and Aug 25, 2018, we screened 51 patients for eligibility, of whom 46 patients were enrolled from 25 different sites and received neoadjuvant treatment.

Pre-assignment

Screening details:

Screening details: Patients eligible for the trial are those with a histological diagnosis or cytologically proven operable and resectable non-small-cell lung cancer, stage IIIA.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|--------------|
| Arm title | Experimental |
|-----------|--------------|

Arm description:

Patients received the following drugs intravenously, as neoadjuvant treatment: nivolumab (360 mg), paclitaxel (200 mg/m²), and carboplatin (area under the curve 6; 6 mg/mL per min), on day 1 of each 21-day cycle, for three cycles before surgical resection. After completion of neoadjuvant chemoimmunotherapy, surgery was planned

42–49 days after the first day of the third treatment cycle.

Resection of the primary tumour and lymph nodes was done according to standard institutional procedures. Once

the patients were deemed fully recovered from surgery, adjuvant treatment with nivolumab was scheduled to commence 3–8 weeks after surgery. Patients received intravenous nivolumab as adjuvant treatment at a fixed dose of 240 mg every 2 weeks for 4 months, followed by a fixed dose of 480 mg every 4 weeks, until month 12.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | BMS-936558 or MDX1106 |
| Other name | Opdivo |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

- Neoadjuvant treatment: Nivolumab 360 mg IV Q3W + Paclitaxel 200mg/m² + Carboplatin AUC 6 IV Q3W, 3 cycles
- Surgery
- Adjuvant treatment: Nivolumab 240 mg Q2W for 4 months and Nivolumab 480 mg Q4W for 8 months (1 year) after surgical resection

Dose reductions were not permitted for nivolumab; however, nivolumab treatment could be interrupted, delayed, or discontinued depending on tolerability

| Number of subjects in period 1 | Experimental |
|---------------------------------------|--------------|
| Started | 46 |
| Completed | 46 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Overall study (overall period) |
|-----------------------|--------------------------------|

Reporting group description: -

| Reporting group values | Overall study (overall period) | Total | |
|---|--------------------------------|-------|--|
| Number of subjects | 46 | 46 | |
| 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 | 63.1 | | |
| standard deviation | ± 8.9 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 34 | 34 | |
| Male | 12 | 12 | |
| ECOG performance status | | | |
| Units: Subjects | | | |
| ECOG 0 | 25 | 25 | |
| ECOG 1 | 21 | 21 | |
| Smoking status | | | |
| Units: Subjects | | | |
| Former smoker (≥ 1 year) | 25 | 25 | |
| Current smoker | 21 | 21 | |
| Never smoker | 0 | 0 | |
| Histology | | | |
| Units: Subjects | | | |
| Adenocarcinoma | 26 | 26 | |
| Squamous cell carcinoma | 16 | 16 | |
| Not specified or undifferentiated | 4 | 4 | |
| Tumor node, metastasis staging classification | | | |
| 8th ed. TNM for Lung Cancer Primary tumor (T) T1-T4 describe the size & location of the tumor, on a scale of 1 to 4. A larger tumor or a tumor that has grown deeper into nearby tissue will get a higher number. Distant metastasis (M) M1: Cancer has spread to other parts of the body or not (M0) | | | |

| | | | |
|---|----------|----|--|
| Regional lymph nodes (N) N0: No regional lymph node metastases N1: Metastasis in ipsilateral peribronchial or ipsilateral hilar lymph nodes & intrapulmonary N2: Metastasis in ipsilateral mediastinal or subcarinal lymph node N3:Metastasis in contralateral hilar, scalene or supraclavicular lymph node | | | |
| Units: Subjects | | | |
| T1N2M0 | 15 | 15 | |
| T2N1M0 | 1 | 1 | |
| T2N2M0 | 6 | 6 | |
| T3N1M0 | 1 | 1 | |
| T3N2M0 | 13 | 13 | |
| T4N0M0 | 9 | 9 | |
| T4N1M0 | 1 | 1 | |
| Tumour lesion size | | | |
| Units: millilitre(s)/millilitre | | | |
| median | 35 | | |
| full range (min-max) | 23 to 60 | - | |

End points

End points reporting groups

| | |
|--|--------------|
| Reporting group title | Experimental |
| Reporting group description: | |
| Patients received the following drugs intravenously, as neoadjuvant treatment: nivolumab (360 mg), paclitaxel (200 mg/m ²), and carboplatin (area under the curve 6; 6 mg/mL per min), on day 1 of each 21-day cycle, for three cycles before surgical resection. After completion of neoadjuvant chemoimmunotherapy, surgery was planned 42–49 days after the first day of the third treatment cycle. Resection of the primary tumour and lymph nodes was done according to standard institutional procedures. Once the patients were deemed fully recovered from surgery, adjuvant treatment with nivolumab was scheduled to commence 3–8 weeks after surgery. Patients received intravenous nivolumab as adjuvant treatment at a fixed dose of 240 mg every 2 weeks for 4 months, followed by a fixed dose of 480 mg every 4 weeks, until month 12. | |

Primary: Progression Free Survival at 24 months

| | |
|---|---|
| End point title | Progression Free Survival at 24 months ^[1] |
| End point description: | |
| Rate of PFS at 24 months from diagnosis defined as the rate of patients free of disease progression or death from any cause whichever occurs first as determined by the investigator according to RECIST v1.1. criteria for systemic disease. | |
| End point type | Primary |
| End point timeframe: | |
| At 24 months from diagnosis | |

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: Progression-free survival, compared with that reported for these patients in previous studies (ranging from 40% in patients receiving standard therapy, considered here as the null hypothesis, to 55% in patients receiving the analysed treatment), 15–17 with a one-sided type I error of 5%. We used the Kaplan-Meier method to estimate progression-free survival and overall survival and corresponding 95% CIs.

| End point values | Experimental | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 46 | | | |
| Units: Subject | | | | |
| number (confidence interval 95%) | 77.1 (59.9 to 87.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

| | |
|-----------------|------------------|
| End point title | Overall Survival |
|-----------------|------------------|

End point description:

Percentage of patients are still alive

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 3 years from the first dose of neoadjuvant treatment

| | | | | |
|----------------------------------|---------------------|--|--|--|
| End point values | Experimental | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 46 | | | |
| Units: Subjects | | | | |
| number (confidence interval 95%) | 89.9 (74.5 to 96.2) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Any adverse event or breakdown occurring during the course of the study.

The investigator will have to collect all adverse events once they have signed informed consent, during treatment and 30 days after the last dose study treatment administration.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 12.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | As-treated population |
|-----------------------|-----------------------|

Reporting group description: -

| Serious adverse events | As-treated population | | |
|---|-----------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 0 | | |
| Blood and lymphatic system disorders | | | |
| Increased lipase | | | |
| subjects affected / exposed | 2 / 46 (4.35%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 46 (2.17%) | | |
| 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 | As-treated population | | |
|---|-----------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 43 / 46 (93.48%) | | |
| Nervous system disorders | | | |
| Neurotoxicity | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 13 / 46 (28.26%) | | |
| occurrences (all) | 13 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 8 / 46 (17.39%) | | |
| occurrences (all) | 8 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 7 / 46 (15.22%) | | |
| occurrences (all) | 7 | | |
| Increased aminotransferases | | | |
| subjects affected / exposed | 5 / 46 (10.87%) | | |
| occurrences (all) | 5 | | |
| Increased creatinine level | | | |
| subjects affected / exposed | 3 / 46 (6.52%) | | |
| occurrences (all) | 3 | | |
| Increased lipase | | | |
| subjects affected / exposed | 4 / 46 (8.70%) | | |
| occurrences (all) | 4 | | |
| General disorders and administration site conditions | | | |
| Asthenia or fatigue | | | |
| subjects affected / exposed | 23 / 46 (50.00%) | | |
| occurrences (all) | 23 | | |
| Constipation | | | |
| subjects affected / exposed | 8 / 46 (17.39%) | | |
| occurrences (all) | 8 | | |
| Decreased appetite or anorexia | | | |
| subjects affected / exposed | 9 / 46 (19.57%) | | |
| occurrences (all) | 9 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 11 / 46 (23.91%) | | |
| occurrences (all) | 11 | | |
| Nausea | | | |
| subjects affected / exposed | 11 / 46 (23.91%) | | |
| occurrences (all) | 11 | | |
| Vomiting | | | |

| | | | |
|--|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 8 / 46 (17.39%) 8 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 8 / 46 (17.39%) | | |
| occurrences (all) | 8 | | |
| Pruritus | | | |
| subjects affected / exposed | 13 / 46 (28.26%) | | |
| occurrences (all) | 13 | | |
| Skin disorders (rash) | | | |
| subjects affected / exposed | 19 / 46 (41.30%) | | |
| occurrences (all) | 19 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 12 / 46 (26.09%) | | |
| occurrences (all) | 12 | | |
| Myalgia | | | |
| subjects affected / exposed | 9 / 46 (19.57%) | | |
| occurrences (all) | 9 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 22 June 2017 | New protocol version: Modify the version of TNM required for staging patients from TNM 7th edition to TNM 8th editing and clarify schedule of study procedures |
| 09 May 2018 | New version of protocol: Add the option to replace invalid patients to complete the patient sample initially calculated in order to meet the initially set statistical objectives and clarify an inclusion criterion in relation to the version of the TNM accepted by protocol |
| 15 January 2019 | Change of Sponsor of study |
| 20 June 2019 | Changes in the protocol: The information contained in the protocol is reviewed regarding the pharmacogenetic analyzes to be performed on the samples extracted from the patients included in the study. A more detailed description of said analyzes and the objectives that are intended to be met with said analyzes is made. |
| 16 November 2020 | Changes in the protocol: The information contained in the protocol is reviewed regarding the analyzes to be performed on the computed tomography (CT) scans of the patients included in the study. A new analysis is added that can contribute to better understanding the clinical evolution of patients with lung cancer by obtaining predictions of the results of possible treatments. |
| 22 September 2022 | Changes in the protocol: The follow-up period of the NADIM study was planned to last 3 years and will be extended to 5 years. The analysis of these 2 additional years may contribute to better understanding the clinical evolution of patients with lung cancer. |

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/35576508>

<http://www.ncbi.nlm.nih.gov/pubmed/32979984>