



Clinical trial results:

A Phase 3, Randomized, Global Trial of Nivolumab and Epacadostat with Platinum Doublet Chemotherapy versus Platinum Doublet Chemotherapy in First-line Treatment of Stage IV or Recurrent Non-Small Cell Lung Cancer (NSCLC)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-003304-43 |
| Trial protocol | ES |
| Global end of trial date | 22 May 2018 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 29 December 2018 |
| First version publication date | 29 December 2018 |

Trial information

Trial identification

| | |
|-----------------------|---------------------------|
| Sponsor protocol code | INCB 24360-309 (CA2099NC) |
|-----------------------|---------------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03348904 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Incyte Corporation |
| Sponsor organisation address | 1801 Augustine Cut-Off, Wilmington, DE, United States, 19803 |
| Public contact | Incyte Corporation, Incyte Corporation Call Center, +44 (0)330 100 3677, globalmedinfo@incyte.com |
| Scientific contact | Incyte Corporation, Incyte Corporation Call Center, +44 (0)330 100 3677, globalmedinfo@incyte.com |

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 | 22 May 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 May 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To compare overall survival (OS) and progression-free survival (PFS) per blinded independent central review (BICR) of nivolumab plus epacadostat in combination with chemotherapy (Arm A) to chemotherapy (Arm B) in NSCLC participants whose tumors express programmed death-ligand 1 (PD-L1) at 0 to 49%.

Protection of trial subjects:

The study was conducted in compliance with the ethical principles derived from the Declaration of Helsinki and the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of study participants were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 27 December 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 | United States: 2 |
| Worldwide total number of subjects | 2 |
| EEA total number of subjects | 0 |

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) | 2 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In this study, 2 participants were randomized to the chemotherapy only (Arm B) treatment.

Period 1

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

Blinding implementation details:

Double-blind for arms A and C (no participants enrolled); open-label for Arm B.

Arms

| | |
|-----------|-------|
| Arm title | Arm B |
|-----------|-------|

Arm description:

Platinum doublet chemotherapy

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Carboplatin administered intravenously at the protocol-defined dose every 3 weeks for up to 4 cycles.

| | |
|--|---------------------------------------|
| 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 administered intravenously at the protocol-defined dose every 3 weeks for up to 4 cycles.

| | |
|--|----------------------------------|
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Gemcitabine administered intravenously at the protocol-defined dose on days 1 and 8 of a 3 week cycle.

| | |
|--|------------------------|
| Investigational medicinal product name | Paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Paclitaxel administered intravenously at the protocol-defined dose every 3 weeks for up to 4 cycles.

| | |
|--|--|
| Investigational medicinal product name | Pemetrexed |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Pemetrexed administered intravenously at the protocol-defined dose every 3 weeks for up to 4 cycles.
Optional continuation maintenance every 3 weeks, if eligible.

| Number of subjects in period 1 | Arm B |
|---------------------------------------|-------|
| Started | 2 |
| Completed | 1 |
| Not completed | 1 |
| Administrative reason | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Overall Period |
|-----------------------|----------------|

Reporting group description:

All randomized participants.

| Reporting group values | Overall Period | Total | |
|------------------------|----------------|-------|--|
| Number of subjects | 2 | 2 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 2 | 2 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 2 | 2 | |

End points

End points reporting groups

| | |
|---|-------|
| Reporting group title | Arm B |
| Reporting group description: Platinum doublet chemotherapy | |

Primary: Overall survival (OS) of nivolumab plus epacadostat in combination with chemotherapy (Arm A) compared to chemotherapy (Arm B)

| | |
|-----------------|--|
| End point title | Overall survival (OS) of nivolumab plus epacadostat in combination with chemotherapy (Arm A) compared to chemotherapy (Arm B) ^[1] |
|-----------------|--|

End point description:

Defined as the time from randomization to the date of death from any cause.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Month 38

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 have been provided as analysis was not completed for early termination.

| End point values | Arm B | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[2] | | | |
| Units: months | | | | |
| number (not applicable) | | | | |

Notes:

[2] - Study was terminated; there were no participants enrolled in Arms A and C - no analysis completed.

Statistical analyses

No statistical analyses for this end point

Primary: Progression-free survival (PFS) of nivolumab plus epacadostat in combination with chemotherapy (Arm A) compared to chemotherapy (Arm B)

| | |
|-----------------|--|
| End point title | Progression-free survival (PFS) of nivolumab plus epacadostat in combination with chemotherapy (Arm A) compared to chemotherapy (Arm B) ^[3] |
|-----------------|--|

End point description:

Defined as the time between the date of randomization and the first date of documented progression assessed by blinded independent central review, or death due to any cause, whichever occurs first.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Approximately 25 months

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: No statistical analyses have been provided as analysis was not completed for early termination.

| End point values | Arm B | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[4] | | | |
| Units: days | | | | |
| number (not applicable) | | | | |

Notes:

[4] - Study was terminated; there were no participants enrolled in Arms A and C - no analysis completed.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR) of nivolumab plus epacadostat in combination with chemotherapy (Arm A) compared to chemotherapy (Arm B)

| | |
|-----------------|---|
| End point title | Objective response rate (ORR) of nivolumab plus epacadostat in combination with chemotherapy (Arm A) compared to chemotherapy (Arm B) |
|-----------------|---|

End point description:

Defined as the proportion of participants who achieve a confirmed best response of complete response (CR) or partial response (PR) per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) criteria.

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

End point timeframe:

Approximately 25 months

| End point values | Arm B | | | |
|-----------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[5] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[5] - Study was terminated; there were no participants enrolled in Arms A and C - no analysis completed.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR) of nivolumab plus epacadostat in combination with chemotherapy (Arm A) compared to chemotherapy (Arm B)

| | |
|-----------------|--|
| End point title | Duration of response (DOR) of nivolumab plus epacadostat in combination with chemotherapy (Arm A) compared to chemotherapy (Arm B) |
|-----------------|--|

End point description:

Defined as the time between the date of first confirmed response and the date of the first documented

tumor progression (per RECIST v1.1) assessed by blinded independent central review or death due to any cause, whichever occurs first.

| | |
|-------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Approximately 25 months | |

| End point values | Arm B | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[6] | | | |
| Units: months | | | | |
| number (not applicable) | | | | |

Notes:

[6] - Study was terminated; there were no participants enrolled in Arms A and C - no analysis completed.

Statistical analyses

No statistical analyses for this end point

Secondary: Estimate of overall survival (OS) of nivolumab and placebo in combination with chemotherapy (Arm C)

| | |
|-----------------|---|
| End point title | Estimate of overall survival (OS) of nivolumab and placebo in combination with chemotherapy (Arm C) |
|-----------------|---|

End point description:

Defined as the time from randomization to the date of death from any cause.

| | |
|-------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Approximately 38 months | |

| End point values | Arm B | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[7] | | | |
| Units: days | | | | |
| number (not applicable) | | | | |

Notes:

[7] - Study was terminated; there were no participants enrolled in Arms A and C - no analysis completed.

Statistical analyses

No statistical analyses for this end point

Secondary: Estimate of PFS of nivolumab and placebo in combination with chemotherapy (Arm C)

| | |
|-----------------|---|
| End point title | Estimate of PFS of nivolumab and placebo in combination with chemotherapy (Arm C) |
|-----------------|---|

End point description:

Defined as the time between the date of randomization and the first date of documented progression assessed by blinded independent central review or death due to any cause, whichever occurs first.

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

End point timeframe:

Approximately 25 months

| End point values | Arm B | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[8] | | | |
| Units: days | | | | |
| number (not applicable) | | | | |

Notes:

[8] - Study was terminated; there were no participants enrolled in Arms A and C - no analysis completed.

Statistical analyses

No statistical analyses for this end point

Secondary: Estimate of ORR of nivolumab and placebo in combination with chemotherapy (Arm C)

| | |
|-----------------|---|
| End point title | Estimate of ORR of nivolumab and placebo in combination with chemotherapy (Arm C) |
|-----------------|---|

End point description:

Defined as the proportion of participants who achieve a confirmed best response of CR or PR per RECIST v1.1 criteria as assessed by blinded independent central review.

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

End point timeframe:

Approximately 25 months

| End point values | Arm B | | | |
|-----------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[9] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[9] - Study was terminated; there were no participants enrolled in Arms A and C - no analysis completed.

Statistical analyses

No statistical analyses for this end point

Secondary: Estimate of DOR of nivolumab and placebo in combination with chemotherapy (Arm C)

| | |
|---|---|
| End point title | Estimate of DOR of nivolumab and placebo in combination with chemotherapy (Arm C) |
| End point description: Defined as the time between the date of first confirmed response and the date of the first documented tumor progression (per RECIST v1.1) assessed by blinded independent central review or death due to any cause, whichever occurs first. | |
| End point type | Secondary |
| End point timeframe: Approximately 25 months | |

| | | | | |
|-----------------------------|-------------------|--|--|--|
| End point values | Arm B | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[10] | | | |
| Units: months | | | | |
| number (not applicable) | | | | |

Notes:

[10] - Study was terminated; there were no participants enrolled in Arms A and C - no analysis completed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the initiation of study treatment until 30 days after last dose of study treatment.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Arm B |
|-----------------------|-------|

Reporting group description:

Platinum doublet chemotherapy.

| Serious adverse events | Arm B | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Osteomyelitis | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| 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 | Arm B | | |
|--|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 2 / 2 (100.00%) | | |
| Investigations Weight decreased subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Nervous system disorders Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 1 / 2 (50.00%) 1 | | |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 1 / 2 (50.00%) 1 2 / 2 (100.00%) 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|--|--|--|
| Dyspnoea subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | | |
| Musculoskeletal and connective tissue disorders Flank pain subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 1 / 2 (50.00%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 23 October 2017 | *ALK and ROS1 testing are mandatory for participants with nonsquamous histology. *Table for expected toxicities from study drugs added. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|-------------|---|--------------|
| 22 May 2018 | Following an interim analysis of a pivotal Phase 3 study with epacadostat and an PD-1 inhibitor that concluded the pre-specified co-primary endpoints would not be met, the strategic decision was made to discontinue, stop enrollment and close the Checkmate 9NC/ECHO-309 study. | - |

Notes:

Limitations and caveats

None reported