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	1 / 2 (50.00%)		
occurrences (all)	1		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	2 / 2 (100.00%)		
occurrences (all)	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