Clinical trial results:
A Phase 1/2 Study Exploring the Safety, Tolerability, Effect on the Tumor Microenvironment, and Efficacy of Azacitidine in Combination With Pembrolizumab and Epacadostat in Subjects With Advanced Solid Tumors and Previously Treated Stage IIIB or Stage IV Non–Small Cell Lung Cancer and Stage IV Microsatellite-Stable Colorectal Cancer

Summary

EudraCT number	2016-004289-25
Trial protocol	GB ES
Global end of trial date	02 March 2020

Results information

Result version number	v1 (current)
This version publication date	18 March 2021
First version publication date	18 March 2021

Trial information

Trial identification

Sponsor protocol code	INCB 24360-206

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cut-Off, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation Call Centre, +800 00027423, globalmedinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation Call Centre, +800 00027423, 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	02 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 March 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety, tolerability, and efficacy of Azacitidine in combination with Pembrolizumab and Epacadostat in subjects With Advanced Solid Tumors and Previously Treated Stage IIIB or Stage IV Non–Small Cell Lung Cancer and Stage IV Microsatellite-Stable Colorectal Cancer.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 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	United States: 63
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Spain: 1
Worldwide total number of subjects	70
EEA total number of subjects	1

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)	51
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 8 study sites in United States, 2 sites in UK and 1 site in Spain.

Pre-assignment

Screening details:

A total of 70 participants were enrolled in the study. Study enrollment was permanently discontinued on 15-Feb-2019 as a strategic decision. No patients were enrolled in Treatment Group B and Treatment Group C.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Group A :100mg of INCB24360

Arm description:

In Treatment Group A, subjects will receive the DNMT inhibitor azacitidine in combination with the PD-1 inhibitor pembrolizumab and the IDO1 inhibitor epacadostat at 100mg. Due to early termination of study subjects from dose escalation and dose expansion are combined.

Arm type	Experimental
Investigational medicinal product name	azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion, Infusion
Routes of administration	Subcutaneous use, Intravenous use

Dosage and administration details:

Intravenous Injection

Investigational medicinal product name	Epacadostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orally twice daily

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous Injection

Arm title	Treatment Group A :300mg of INCB24360

Arm description:

In Treatment Group A, subjects will receive the DNMT inhibitor azacitidine in combination with the PD-1 inhibitor pembrolizumab and the IDO1 inhibitor epacadostat at 300mg.

Arm type	Experimental

Investigational medicinal product name	azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion, Infusion
Routes of administration	Subcutaneous use, Intravenous use
Dosage and administration details: Intravenous Injection	
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: Intravenous Injection	
Investigational medicinal product name	Epacadostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Orally twice daily	

Number of subjects in period 1	Treatment Group A :100mg of INCB24360	Treatment Group A :300mg of INCB24360
Started	62	8
Completed	0	0
Not completed	62	8
Adverse event, serious fatal	33	3
Consent withdrawn by subject	11	3
Progressive Disease	9	1
Study Terminated by Sponsor	2	-
Lost to follow-up	3	1
Other Unspecified	4	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Group A :100mg of INCB24360
Reporting group description:	
In Treatment Group A, subjects will receive the DNMT inhibitor azacitidine in combination with the PD-1 inhibitor pembrolizumab and the IDO1 inhibitor epacadostat at 100mg. Due to early termination of study subjects from dose escalation and dose expansion are combined.	
Reporting group title	Treatment Group A :300mg of INCB24360
Reporting group description:	
In Treatment Group A, subjects will receive the DNMT inhibitor azacitidine in combination with the PD-1 inhibitor pembrolizumab and the IDO1 inhibitor epacadostat at 300mg.	

Reporting group values	Treatment Group A :100mg of INCB24360	Treatment Group A :300mg of INCB24360	Total
Number of subjects	62	8	70
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	45	6	51
From 65-84 years	17	2	19
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	57.0	53.0	
standard deviation	± 11.92	± 11.31	-
Sex: Female, Male Units:			
Female	19	4	23
Male	43	4	47
Race/Ethnicity, Customized Units: Subjects			
White/Caucasian	56	5	61
Black/African-American	3	0	3
Asian	2	0	2
American-Indian/Alaska Native	0	0	0
Native Hawaiian/Pacific Islander	0	0	0
Other	1	3	4
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	4	2	6
Not Hispanic or Latino	54	6	60
Unknown	4	0	4

End points

End points reporting groups

Reporting group title	Treatment Group A :100mg of INCB24360

Reporting group description:

In Treatment Group A, subjects will receive the DNMT inhibitor azacitidine in combination with the PD-1 inhibitor pembrolizumab and the IDO1 inhibitor epacadostat at 100mg. Due to early termination of study subjects from dose escalation and dose expansion are combined.

Reporting group title	Treatment Group A :300mg of INCB24360

Reporting group description:

In Treatment Group A, subjects will receive the DNMT inhibitor azacitidine in combination with the PD-1 inhibitor pembrolizumab and the IDO1 inhibitor epacadostat at 300mg.

Subject analysis set title	Treatment Group A :100 or 300mg of INCB24360
Subject analysis set type	Full analysis

Subject analysis set description:

Treatment Group A :100mg of INCB24360
In Treatment Group A, subjects will receive the DNMT inhibitor azacitidine in combination with the PD-1 inhibitor pembrolizumab and the IDO1 inhibitor epacadostat at 100mg or 300mg. Due to early termination of study subjects from dose escalation and dose expansion are combined.

Primary: Part 1 and 2 : Frequency, duration, and severity of adverse events

End point title	Part 1 and 2 : Frequency, duration, and severity of adverse events[1]

End point description:

A treatment-emergent AE was defined as an event occurring after exposure to at least 1 dose of study drug. A treatment-related AE was defined as an event with a definite, probable, or possible causality to study medication. A serious AE is an event resulting in death, hospitalization, persistent or significant disability/incapacity, or is life threatening, a congenital anomaly/birth defect or requires medical or surgical intervention to prevent 1 of the outcomes above. The intensity of an AE was graded according to the National Cancer Institute common terminology criteria for adverse events (NCI-CTCAE) version 4.03: Grade 1 (Mild); Grade 2 (Moderate); Grade 3 (Severe); Grade 4 (life-threatening).

End point type	Primary

End point timeframe:

Baseline through 42-49 days after end of treatment, estimated up to 27 months (24 months with 100 day FU period).

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 for this end point

End point values	Treatment Group A :100mg of INCB24360	Treatment Group A :300mg of INCB24360		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	8		
Units: participants	62	8		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1 and 2: Objective response rate based on Response Evaluation

Criteria in Solid Tumors version 1.1 (RECIST v1.1)

End point title	Part 1 and 2: Objective response rate based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)[2]

End point description:

ORR was defined as the percentage of participants having a complete response (CR) or partial response (PR) as determined by investigator assessment of radiographic disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. CR is disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. A participant was considered as an objective responder if the participant had a best overall response of CR or PR.

End point type	Primary

End point timeframe:

Every 9 weeks for the duration of study participation; estimated minimum of 6 months.

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: No statistical analyses for this end point

End point values	Treatment Group A :100mg of INCB24360	Treatment Group A :300mg of INCB24360		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	8		
Units: participants	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of responders determined by immunohistochemistry

End point title	Parts 1 and 2: Percentage of responders determined by immunohistochemistry

End point description:

Responder is defined as an increase in the number of tumor-infiltrating lymphocytes or the ratio of CD8+ lymphocytes to T regulatory cells infiltrating tumor post-treatment versus pretreatment with pembrolizumab and epacadostat in combination with azacitidine.

End point type	Secondary

End point timeframe:

Baseline to Week 5/6 or week 8/9

End point values	Treatment Group A :100 or 300mg of INCB24360			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: participants				
Intratumoral CD8+ T cells	14			

CD8+:FoxP3+ ratios	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Progression-free survival based on RECIST v1.1.

End point title	Parts 1 and 2: Progression-free survival based on RECIST v1.1.

End point description:

Defined as the time from date of first dose of study drug until the earliest date of disease progression per RECIST v1.1, or death due to any cause, if occurring sooner than progression.

End point type	Secondary

End point timeframe:

Every 9 weeks for the duration of study participation; estimated minimum of 6 months.

End point values	Treatment Group A :100mg of INCB24360	Treatment Group A :300mg of INCB24360		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	8		
Units: Months				
median (confidence interval 95%)	2.07 (1.97 to 2.17)	2.64 (1.31 to 6.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Duration of response based on RECIST v1.1

End point title	Parts 1 and 2: Duration of response based on RECIST v1.1

End point description:

Defined as the time from earliest date of disease response until the earliest date of disease progression per RECIST v1.1, or death due to any cause, if occurring sooner than progression.

End point type	Secondary

End point timeframe:

Every 9 weeks for the duration of study participation; estimated minimum of 6 months.

End point values	Treatment Group A :100mg of INCB24360	Treatment Group A :300mg of INCB24360		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	1[3]		
Units: Months				
median (confidence interval 95%)	2.63 (2.20 to 21.85)	1.22 (-99.99 to 99.99)		

Notes:

[3] - Upper and lower limits are not estimablle

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From study start up to clinical data cut-off date of 15 Feb 2019 (approximately 21 months)

Adverse event reporting additional description:

The safety population included all participants enrolled in the study who received at least 1 dose of study drug. Data is presented for Group A only, no participants enrolled in Treatment Groups Band C.

Assessment type	Systematic

Dictionary used

Dictionary name	19.1
Dictionary version	19.1

Reporting groups

Reporting group title	Treatment Group A :300mg of INCB24360

Reporting group description:

In Treatment Group A, subjects will receive the DNMT inhibitor azacitidine in combination with the PD-1 inhibitor pembrolizumab and the IDO1 inhibitor epacadostat at 300mg.

Reporting group title	Treatment Group A :100mg of INCB24360

Reporting group description:

In Treatment Group A, subjects will receive the DNMT inhibitor azacitidine in combination with the PD-1 inhibitor pembrolizumab and the IDO1 inhibitor epacadostat at 100mg. Due to early termination of study subjects from dose escalation and dose expansion are combined.

Serious adverse events	Treatment Group A :300mg of INCB24360	Treatment Group A :100mg of INCB24360	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 8 (37.50%)	28 / 62 (45.16%)	
number of deaths (all causes)	4	41	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Neoplasm Progression			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rectal Cancer Metastatic			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lymphangiosis Carcinomatosa			

subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Disease Progression			
subjects affected / exposed	0 / 8 (0.00%)	8 / 62 (12.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 7	
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac Chest Pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cough			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional State			
subjects affected / exposed	1 / 8 (12.50%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental Status Changes			

subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head Injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinua tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain Injury			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain Oedema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dizziness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dysmetria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of Consciousness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal Nerve Palsy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			

subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 8 (12.50%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 8 (12.50%)	4 / 62 (6.45%)	
occurrences causally related to treatment / all	1 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Obstruction			
subjects affected / exposed	0 / 8 (0.00%)	3 / 62 (4.84%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 8 (12.50%)	2 / 62 (3.23%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary Retention			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 8 (0.00%)	3 / 62 (4.84%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone Pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular Weakness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in Extremity			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection			

subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract Infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 8 (0.00%)	1 / 62 (1.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Treatment Group A :300mg of INCB24360	Treatment Group A :100mg of INCB24360	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	59 / 62 (95.16%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	2 / 62 (3.23%)	
occurrences (all)	2	2	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 8 (12.50%)	4 / 62 (6.45%)	
occurrences (all)	1	4	
Fatigue			
subjects affected / exposed	6 / 8 (75.00%)	28 / 62 (45.16%)	
occurrences (all)	7	28	
Injection site erythema			

subjects affected / exposed	0 / 8 (0.00%)	5 / 62 (8.06%)	
occurrences (all)	0	5	
Injection site pain			
subjects affected / exposed	0 / 8 (0.00%)	4 / 62 (6.45%)	
occurrences (all)	0	4	
Injection site reaction			
subjects affected / exposed	0 / 8 (0.00%)	13 / 62 (20.97%)	
occurrences (all)	0	13	
Local swelling			
subjects affected / exposed	1 / 8 (12.50%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	6 / 62 (9.68%)	
occurrences (all)	0	7	
Oedema peripheral			
subjects affected / exposed	1 / 8 (12.50%)	6 / 62 (9.68%)	
occurrences (all)	1	6	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 8 (25.00%)	9 / 62 (14.52%)	
occurrences (all)	2	9	
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	8 / 62 (12.90%)	
occurrences (all)	1	8	
Dyspnoea exertional			
subjects affected / exposed	0 / 8 (0.00%)	4 / 62 (6.45%)	
occurrences (all)	0	4	
Productive cough			
subjects affected / exposed	2 / 8 (25.00%)	2 / 62 (3.23%)	
occurrences (all)	2	2	
Wheezing			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			

Insomnia			
subjects affected / exposed	1 / 8 (12.50%)	5 / 62 (8.06%)	
occurrences (all)	1	5	
Anxiety			
subjects affected / exposed	1 / 8 (12.50%)	3 / 62 (4.84%)	
occurrences (all)	1	3	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 8 (25.00%)	4 / 62 (6.45%)	
occurrences (all)	2	4	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 8 (37.50%)	5 / 62 (8.06%)	
occurrences (all)	3	7	
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 8 (25.00%)	7 / 62 (11.29%)	
occurrences (all)	2	7	
Blood creatinine increased			
subjects affected / exposed	0 / 8 (0.00%)	4 / 62 (6.45%)	
occurrences (all)	0	4	
Blood phosphorus decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	1 / 8 (12.50%)	2 / 62 (3.23%)	
occurrences (all)	1	2	
White blood cell count decreased			
subjects affected / exposed	1 / 8 (12.50%)	3 / 62 (4.84%)	
occurrences (all)	1	3	
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Sinus Tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 8 (50.00%)	4 / 62 (6.45%)	
occurrences (all)	4	4	
Neuropathy peripheral			
subjects affected / exposed	1 / 8 (12.50%)	2 / 62 (3.23%)	
occurrences (all)	1	2	
Peroneal nerve palsy			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 8 (25.00%)	11 / 62 (17.74%)	
occurrences (all)	2	15	
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	2 / 8 (25.00%)	2 / 62 (3.23%)	
occurrences (all)	2	2	
Abdominal pain			
subjects affected / exposed	1 / 8 (12.50%)	12 / 62 (19.35%)	
occurrences (all)	1	15	
Constipation			
subjects affected / exposed	3 / 8 (37.50%)	16 / 62 (25.81%)	
occurrences (all)	3	18	
Abdominal pain lower			
subjects affected / exposed	1 / 8 (12.50%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	1 / 8 (12.50%)	3 / 62 (4.84%)	
occurrences (all)	1	3	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 8 (12.50%)	4 / 62 (6.45%)	
occurrences (all)	1	4	
Nausea			

subjects affected / exposed	3 / 8 (37.50%)	34 / 62 (54.84%)	
occurrences (all)	3	38	
Vomiting			
subjects affected / exposed	2 / 8 (25.00%)	21 / 62 (33.87%)	
occurrences (all)	3	26	
Diarrhoea			
subjects affected / exposed	3 / 8 (37.50%)	12 / 62 (19.35%)	
occurrences (all)	3	14	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Dermatitis acneiform			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 8 (12.50%)	6 / 62 (9.68%)	
occurrences (all)	1	6	
Rash			
subjects affected / exposed	2 / 8 (25.00%)	9 / 62 (14.52%)	
occurrences (all)	2	10	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Pneumaturia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Terminal dribbling			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 8 (12.50%)	7 / 62 (11.29%)	
occurrences (all)	1	7	
Back pain			

subjects affected / exposed	2 / 8 (25.00%)	6 / 62 (9.68%)	
occurrences (all)	2	7	
Flank pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
Musculoskeletal discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 8 (12.50%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 8 (12.50%)	2 / 62 (3.23%)	
occurrences (all)	1	2	
Musculoskeletal pain			
subjects affected / exposed	2 / 8 (25.00%)	0 / 62 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	2 / 8 (25.00%)	4 / 62 (6.45%)	
occurrences (all)	2	4	
Neck pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 62 (1.61%)	
occurrences (all)	1	1	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Mastoiditis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	3 / 62 (4.84%)	
occurrences (all)	1	3	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	5 / 8 (62.50%)	12 / 62 (19.35%)	
occurrences (all)	5	12	
Hypercalcaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	0 / 8 (0.00%)	4 / 62 (6.45%)	
occurrences (all)	0	4	
Hypomagnesaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 62 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	4 / 62 (6.45%)	
occurrences (all)	0	4	
Hypoalbuminaemia			
subjects affected / exposed	1 / 8 (12.50%)	4 / 62 (6.45%)	
occurrences (all)	1	4	
Hyponatraemia			
subjects affected / exposed	1 / 8 (12.50%)	3 / 62 (4.84%)	
occurrences (all)	2	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2016	The primary purpose of this amendment is to address FDA's October 20, 2016, clinical information request.
02 June 2017	The primary purpose of this amendment is to extend the length of azacitidine treatment and add new expansion cohorts to evaluate different sequences of treatment for the 3 study drugs.
20 October 2017	The primary purpose of this amendment is to add 2 additional treatment groups, which include regimens with INCB057643 and INCB059872.
30 August 2018	specify that scans to confirm disease progression should be conducted at least 4 weeks and no later than 8 weeks from the initial scans showing PD

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported