



Clinical trial results:

An Open-Label Phase 1b Study of the Safety, Tolerability, and Preliminary Antitumor Activity of INCB059872 in Participants With Relapsed or Refractory Ewing Sarcoma

Summary

EudraCT number	2018-000062-11
Trial protocol	GB ES IT
Global end of trial date	06 July 2020

Results information

Result version number	v1 (current)
This version publication date	08 January 2021
First version publication date	08 January 2021

Trial information

Trial identification

Sponsor protocol code	INCB 59872-103
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03514407
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	Clinical Trials Information, Incyte Corporation, RA@incyte.com
Scientific contact	Clinical Trials Information, Incyte Corporation, RA@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	06 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 July 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study to evaluate the safety and tolerability of INCB059872 in subjects with relapsed/refractory Ewing sarcoma.

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 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	24
EEA total number of subjects	12

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)	5
Adults (18-64 years)	19
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 9 investigative sites in Spain, United Kingdom, Italy, and the United States from 27 June 2018 to 06 Jul 2020.

Pre-assignment

Screening details:

Subjects with histologically or cytologically confirmed diagnosis of Ewing sarcoma and have progressed on or after standard therapies were enrolled.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	INCB059872 2 mg QOD

Arm description:

Subjects received INCB059872 2 mg, tablets, orally, once every other day (QOD) in consecutive 28-day cycles as long as participants are receiving benefit and have not met any criteria for study withdrawal. Subjects had an option to continue Part 2 (expansion phase) of the study based on the investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	INCB059872
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

INCB059872 1 mg tablets self-administered in the morning either once every other day.

Arm title	INCB059872 3 mg QOD
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Arm description:

Subjects received INCB059872 3 mg, tablets, orally, once every other day (QOD) in consecutive 28-day cycles as long as participants are receiving benefit and have not met any criteria for study withdrawal. Subjects had an option to continue Part 2 (expansion phase) of the study based on the investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	INCB059872
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

INCB059872 1 mg tablets self-administered in the morning either once every other day.

Number of subjects in period 1	INCB059872 2 mg QOD	INCB059872 3 mg QOD
Started	5	19
Completed	0	0
Not completed	5	19
Physician decision	-	1
Consent withdrawn by subject	-	2
Death	3	9
Study Terminated by Sponsor	1	5
Global Pandemic	-	1
Reason not Specified	1	1

Baseline characteristics

Reporting groups

Reporting group title	INCB059872 2 mg QOD
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Reporting group description:

Subjects received INCB059872 2 mg, tablets, orally, once every other day (QOD) in consecutive 28-day cycles as long as participants are receiving benefit and have not met any criteria for study withdrawal. Subjects had an option to continue Part 2 (expansion phase) of the study based on the investigator's discretion.

Reporting group title	INCB059872 3 mg QOD
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Reporting group description:

Subjects received INCB059872 3 mg, tablets, orally, once every other day (QOD) in consecutive 28-day cycles as long as participants are receiving benefit and have not met any criteria for study withdrawal. Subjects had an option to continue Part 2 (expansion phase) of the study based on the investigator's discretion.

Reporting group values	INCB059872 2 mg QOD	INCB059872 3 mg QOD	Total
Number of subjects	5	19	24
Age categorical			
Units: Subjects			
Adolescents (12-17 years)	0	5	5
Adults (18-64 years)	5	14	19
Age continuous			
Units: years			
arithmetic mean	32.6	24.5	
standard deviation	± 9.79	± 9.44	-
Gender categorical			
Units: Subjects			
Female	2	8	10
Male	3	11	14

End points

End points reporting groups

Reporting group title	INCB059872 2 mg QOD
Reporting group description: Subjects received INCB059872 2 mg, tablets, orally, once every other day (QOD) in consecutive 28-day cycles as long as participants are receiving benefit and have not met any criteria for study withdrawal. Subjects had an option to continue Part 2 (expansion phase) of the study based on the investigator's discretion.	
Reporting group title	INCB059872 3 mg QOD
Reporting group description: Subjects received INCB059872 3 mg, tablets, orally, once every other day (QOD) in consecutive 28-day cycles as long as participants are receiving benefit and have not met any criteria for study withdrawal. Subjects had an option to continue Part 2 (expansion phase) of the study based on the investigator's discretion.	

Primary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs) ^[1]
End point description: A TEAE is any untoward medical occurrence in a clinical investigation administered a drug; it does not necessarily have a causal relationship with the treatment. A serious TEAE is defined as any untoward medical occurrence that resulted in death, was life-threatening, required or prolonged inpatient hospitalization, resulted in persistent or significant disability or incapacity, led to a birth defect, or was an important medical event that may have required intervention to prevent any of items above. Data for severity was presented as Grade 3 or higher. Grade 3 AEs are defined as any severe or medically significant but not immediately life-threatening events; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living, and Grade 4 AEs are considered events with life-threatening consequences; urgent intervention indicated. Safety set included all subjects enrolled in the study who received at least 1 dose of the study drug.	
End point type	Primary
End point timeframe: From signing the informed consent form up to 30 days after the last dose of study treatment or until the start of new anticancer therapy (approximately up to 6 months)	

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	INCB059872 2 mg QOD	INCB059872 3 mg QOD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	19		
Units: subjects				
Subject With TEAEs	4	17		
Subjects with Serious TEAEs	2	3		
Subjects with Grade 3 or 4 TEAEs	3	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
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End point description:

ORR is defined as the percentage of subjects who have a Complete Response (CR) or Partial Response (PR) as determined by investigator assessment of response in accordance with Response Evaluation Criteria in Solid Tumors (RECIST version 1.1). CR is the disappearance of all target lesions. PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. Full analysis set all included all subjects enrolled in the study who received at least 1 dose of the study drug.

End point type	Secondary
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End point timeframe:

Every 8 weeks from Cycle 1 Day 1 (each cycle of 28 days) up to follow up (approximately up to 6 months)

End point values	INCB059872 2 mg QOD	INCB059872 3 mg QOD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	19		
Units: percentage of subjects				
number (confidence interval 95%)	20 (0.51 to 71.64)	0 (0.00 to 17.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (C_{max}) in INCB059872 2 mg Treatment Arm

End point title	Maximum Observed Plasma Concentration (C _{max}) in INCB059872 2 mg Treatment Arm ^[2]
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End point description:

Pharmacokinetic/Pharmacodynamic (PK/PD) evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s).

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical analyses for this end point.

End point values	INCB059872 2 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: nanomoles (nM)				
arithmetic mean (standard deviation)				
Day 1 (n=5)	46.9 (± 18.4)			
Day 15 (n=3)	40.6 (± 6.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax in INCB059872 3 mg Treatment Arm

End point title	Cmax in INCB059872 3 mg Treatment Arm ^[3]
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s). Here, 99999 indicates that standard deviation was not calculated as only 1 subject was evaluated.

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point.

End point values	INCB059872 3 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: nM				
arithmetic mean (standard deviation)				
Day 1 Adolescent (n=4)	174.0 (± 89.8)			
Day 1 Adult (n=10)	81.7 (± 35.9)			
Day 15 Adolescent (n=1)	61.5 (± 99999)			
Day 15 Adult (n=8)	96.3 (± 66.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Concentration (Tmax) in INCB059872 2 mg Treatment Arm

End point title	Time to Maximum Concentration (Tmax) in INCB059872 2 mg Treatment Arm ^[4]
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s).

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point.

End point values	INCB059872 2 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: hour (hr)				
median (full range (min-max))				
Day 1 (n=5)	1.0 (0.5 to 2.0)			
Day 15 (n=3)	1.0 (0.5 to 2.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax in INCB059872 3 mg Treatment Arm

End point title	Tmax in INCB059872 3 mg Treatment Arm ^[5]
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s). Here, 99999 indicates that the lower and upper limit for median was not calculated as only 1 subject was evaluated.

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point.

End point values	INCB059872 3 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: hr				
median (full range (min-max))				
Day 1 Adolescent (n=4)	1.0 (0.5 to 1.0)			
Day 1 Adult (n=10)	1.0 (0.5 to 2.0)			
Day 15 Adolescent (n=1)	1.0 (-99999 to 99999)			
Day 15 Adult (n=8)	1.0 (0.5 to 2.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination Half-life ($t_{1/2}$) in INCB059872 2 mg Treatment Arm

End point title	Elimination Half-life ($t_{1/2}$) in INCB059872 2 mg Treatment
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s).

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point.

End point values	INCB059872 2 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: hr				
arithmetic mean (standard deviation)				
Day 1 (n=5)	3.65 (\pm 0.0388)			
Day 15 (n=3)	4.21 (\pm 0.901)			

Statistical analyses

No statistical analyses for this end point

Secondary: $t_{1/2}$ in INCB059872 3 mg Treatment Arm

End point title	$t_{1/2}$ in INCB059872 3 mg Treatment Arm ^[7]
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s). Here, 99999 indicates that the values were not estimable.

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point.

End point values	INCB059872 3 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: hr				
arithmetic mean (standard deviation)				
Day 1 Adolescent (n=4)	2.29 (\pm 0.509)			
Day 1 Adult (n=10)	2.79 (\pm 0.816)			

Day 15 Adolescent (n=1)	99999 (\pm 99999)			
Day 15 Adult (n=8)	4.03 (\pm 0.903)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Concentration (Cmin) in INCB059872 2 mg Treatment Arm

End point title	Minimum Observed Plasma Concentration (Cmin) in INCB059872 2 mg Treatment Arm ^[8]
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s). Here, 99999 indicates that data was not estimable for this endpoint because of the short half-life and use of QOD dose regimes.

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point.

End point values	INCB059872 2 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: nM				
arithmetic mean (standard deviation)				
Day 1 (n=5)	99999 (\pm 99999)			
Day 15 (n=3)	99999 (\pm 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmin in INCB059872 3 mg Treatment Arm

End point title	Cmin in INCB059872 3 mg Treatment Arm ^[9]
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s). Here, 99999 indicates that data was not estimable for this endpoint because of the short half-life and use of QOD dose regimes.

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point.

End point values	INCB059872 3 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: nM				
arithmetic mean (standard deviation)				
Day 1 Adolescent (n=4)	99999 (± 99999)			
Day 1 Adult (n=10)	99999 (± 99999)			
Day 15 Adolescent (n=1)	99999 (± 99999)			
Day 15 Adult (n=8)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma or Serum Concentration From Time Zero to Time of Last Measurable Concentration (AUClast) of INCB059872 2 mg Treatment Arm

End point title	Area Under the Plasma or Serum Concentration From Time Zero to Time of Last Measurable Concentration (AUClast) of INCB059872 2 mg Treatment Arm ^[10]
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s).

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point.

End point values	INCB059872 2 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: nanomoles*hour (nM*hr)				
arithmetic mean (standard deviation)				
Day 1 (n=5)	166.0 (± 71.4)			
Day 15 (n=3)	261.0 (± 137.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUClast of INCB059872 3 mg Treatment Arm

End point title	AUClast of INCB059872 3 mg Treatment Arm ^[11]
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s). Here, 99999 indicates that standard deviation was not calculated as only 1 subject was evaluated.

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point.

End point values	INCB059872 3 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: nM*hr				
arithmetic mean (standard deviation)				
Day 1 Adolescent (n=4)	468.0 (± 199.0)			
Day 1 Adult (n=10)	290.0 (± 81.8)			
Day 15 Adolescent (n=1)	253 (± 99999)			
Day 15 Adult (n=8)	368.0 (± 168.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (Cl/F) in INCB059872 2 mg Treatment Arm

End point title	Apparent Clearance (Cl/F) in INCB059872 2 mg Treatment
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End point description:

PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s).

End point type	Secondary
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End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point.

End point values	INCB059872 2 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: liters per hour (L/hr)				
arithmetic mean (standard deviation)				
Day 1 (n=5)	10.0 (± 3.92)			
Day 15 (n=3)	9.66 (± 2.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cl/F in INCB059872 3 mg Treatment Arm

End point title	Cl/F in INCB059872 3 mg Treatment Arm ^[13]
End point description:	
PK/PD evaluable set included all subjects who received at least 1 dose of study drug and provided at least 1 postdose blood sample for PK/PD assessment(s). Here, 99999 indicates that the values were not estimable.	
End point type	Secondary

End point timeframe:

Pre-dose, and post-dose 0.5, 1, 2, 4, 6, and 24 hours on Days 1 and 15, and pre-dose on Day 8 of Cycle 1

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point.

End point values	INCB059872 3 mg QOD			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: L/h				
arithmetic mean (standard deviation)				
Day 1 Adolescent (n=4)	8.51 (± 4.35)			
Day 1 Adult (n=10)	12.2 (± 3.20)			
Day 15 Adolescent (n=1)	99999 (± 99999)			
Day 15 Adult (n=8)	7.97 (± 2.03)			

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing the informed consent form up to 30 days after the last dose of study treatment or until the start of new anticancer therapy (approximately up to 6 months)

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21
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Reporting groups

Reporting group title	INCB059872 2 mg
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Reporting group description:

Subjects received INCB059872 2 mg, tablets, orally, once every other day (QOD) for Cycle 1 (each cycle of 28 days) for a maximum of up to 6 months. Subjects had an option to continue Part 2 (expansion phase) of the study based on the investigator's discretion.

Reporting group title	INCB059872 3 mg
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Reporting group description:

Subjects received INCB059872 3 mg, tablets, orally, QOD for Cycle 1 (each cycle of 28 days) for a maximum of up to 6 months. Subjects had an option to continue Part 2 (expansion phase) of the study based on the investigator's discretion.

Reporting group title	Total
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Reporting group description:

Total

Serious adverse events	INCB059872 2 mg	INCB059872 3 mg	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	3 / 19 (15.79%)	5 / 24 (20.83%)
number of deaths (all causes)	3	10	13
number of deaths resulting from adverse events	0	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 19 (5.26%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Kidney infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	INCB059872 2 mg	INCB059872 3 mg	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	17 / 19 (89.47%)	20 / 24 (83.33%)
Vascular disorders			
Hypertension			

subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 4	1 / 19 (5.26%) 2	2 / 24 (8.33%) 6
Pallor subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 19 (0.00%) 0	1 / 24 (4.17%) 1
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Fatigue subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	5 / 19 (26.32%) 7	5 / 24 (20.83%) 7
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	3 / 19 (15.79%) 3	4 / 24 (16.67%) 4
Pyrexia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	5 / 19 (26.32%) 7	5 / 24 (20.83%) 7
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	1 / 19 (5.26%) 2	3 / 24 (12.50%) 4
Dyspnoea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Epistaxis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 2	1 / 24 (4.17%) 2
Hypocapnia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 2	1 / 24 (4.17%) 2
Oropharyngeal pain			

subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Sinus congestion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Throat irritation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 5 (20.00%)	2 / 19 (10.53%)	3 / 24 (12.50%)
occurrences (all)	1	2	3
Alanine aminotransferase decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Alanine aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	2 / 19 (10.53%)	3 / 24 (12.50%)
occurrences (all)	1	2	3
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	4 / 19 (21.05%)	5 / 24 (20.83%)
occurrences (all)	1	5	6
Blood bicarbonate increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Blood creatinine increased			

subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Haematocrit decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	4	4
International normalised ratio increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	3	0	3
Lymphocyte count increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	5 / 19 (26.32%)	5 / 24 (20.83%)
occurrences (all)	0	5	5
Prothrombin level increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Red blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Weight decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
White blood cell count decreased			
subjects affected / exposed	1 / 5 (20.00%)	2 / 19 (10.53%)	3 / 24 (12.50%)
occurrences (all)	2	3	5
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	4 / 19 (21.05%)	4 / 24 (16.67%)
occurrences (all)	0	4	4
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Headache subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 19 (5.26%) 1	2 / 24 (8.33%) 2
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 19 (0.00%) 0	1 / 24 (4.17%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	8 / 19 (42.11%) 8	8 / 24 (33.33%) 8
Leukopenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Lymphopenia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	2 / 19 (10.53%) 3	3 / 24 (12.50%) 4
Neutropenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	2 / 19 (10.53%) 2	2 / 24 (8.33%) 2
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 2	5 / 19 (26.32%) 9	6 / 24 (25.00%) 11
Eye disorders			
Vision blurred subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Abdominal pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 19 (5.26%) 1	2 / 24 (8.33%) 2
Constipation			

subjects affected / exposed	1 / 5 (20.00%)	3 / 19 (15.79%)	4 / 24 (16.67%)
occurrences (all)	1	3	4
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	1 / 19 (5.26%)	2 / 24 (8.33%)
occurrences (all)	1	1	2
Dry mouth			
subjects affected / exposed	1 / 5 (20.00%)	1 / 19 (5.26%)	2 / 24 (8.33%)
occurrences (all)	1	1	2
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	5 / 19 (26.32%)	5 / 24 (20.83%)
occurrences (all)	0	5	5
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)	3 / 19 (15.79%)	4 / 24 (16.67%)
occurrences (all)	1	3	4
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Hyperhidrosis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Night sweats			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1

Skin exfoliation subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 19 (0.00%) 0	1 / 24 (4.17%) 1
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Haematuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Myalgia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Infections and infestations Lung infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Systemic infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 19 (5.26%) 1	1 / 24 (4.17%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 19 (5.26%) 1	2 / 24 (8.33%) 2
Metabolism and nutrition disorders Decreased appetite			

subjects affected / exposed	2 / 5 (40.00%)	3 / 19 (15.79%)	5 / 24 (20.83%)
occurrences (all)	2	3	5
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 19 (5.26%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 19 (10.53%)	2 / 24 (8.33%)
occurrences (all)	0	3	3
Hypochloraemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 19 (0.00%)	1 / 24 (4.17%)
occurrences (all)	3	0	3
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 19 (10.53%)	2 / 24 (8.33%)
occurrences (all)	0	3	3
Hyponatraemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 19 (5.26%)	2 / 24 (8.33%)
occurrences (all)	1	1	2
Hypophosphataemia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 19 (5.26%)	2 / 24 (8.33%)
occurrences (all)	5	1	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 February 2018	The primary purpose of this amendment was to revise and/or clarify treatment group assignments, the definition of dose-limiting toxicities, and the criteria for intraparticipant dose escalation in addition to providing a conversion table to ECOG performance status for Karnofsky and Lansky performance measures.
20 May 2018	The primary purpose of this amendment was to remove the INCB057643 treatment group, add a PK timepoint, and add a pharmacodynamic sample collection.
22 July 2018	The primary purpose of this amendment was to include additional safety monitoring.
24 June 2019	The primary purpose of this amendment was to include additional safety monitoring.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 June 2020	This study was terminated due to strategic business decision.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The last patient was not able to finish the study due to the Covid-19 pandemic.

Notes: