Clinical trial results:
Safety and Efficacy of Itacitinib in Combination With Corticosteroids for Treatment of Graft-Versus-Host Disease in Pediatric Subjects

Summary

EudraCT number	2018-002253-30
Trial protocol	GB FR DE ES IT
Global end of trial date	20 February 2020

Results information

Result version number	v1 (current)
This version publication date	28 August 2020
First version publication date	28 August 2020

Trial information

Trial identification

Sponsor protocol code	INCB 39110-120

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03721965
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	Incyte Corporation Call Center, Incyte Corporation, +44 (0)330 100 3677, globalmedinfo@incyte.com
Scientific contact	Incyte Corporation Call Center, Incyte Corporation, +44 (0)330 100 3677, globalmedinfo@incyte.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002178-PIP01-17
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 February 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate itacitinib in combination with corticosteroids for the treatment of Grades II to IV acute graft-versus-host disease (aGVHD) in steroid-naive pediatric participants.

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	31 December 2019
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	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)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study is conducted at 1 site in USA

Pre-assignment

Screening details:

2 participants were screened and enrolled in the study

Period 1

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

Arms

Arm title	Itacitinib + Corticosteroids
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	itacitinib
Investigational medicinal product code	
Other name	INCB039110
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

itacitinib was administered orally at 200 mg once daily

Number of subjects in period 1	Itacitinib + Corticosteroids
Started	2
Completed	0
Not completed	2
Death	1
Study terminated by sponsor	1

Baseline characteristics

Reporting groups	
Reporting group title	Itacitinib + Corticosteroids

Reporting group description: -

Reporting group values	Itacitinib + Corticosteroids	Total	
Number of subjects	2	2	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	2	2	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	13.5		
standard deviation	± 2.12	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	1	1	
Race Units: Subjects			
White	2	2	
Ethnicity Units: Subjects			
Not Hispanic or Latino	2	2	

End points

End points reporting groups

Reporting group title	Itacitinib + Corticosteroids

Reporting group description: -

Primary: Phase 1: Participants with treatment-emergent adverse events (TEAEs)

End point title	Phase 1: Participants with treatment-emergent adverse events (TEAEs)[1]

End point description:

End point type	Primary

End point timeframe:

Up to 12 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: There is no hypothesis testing for this endpoint , descriptive analysis is provided.

End point values	Itacitinib + Corticosteroids			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Participants				
Participants	2			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Cmax of itacitinib when administered with corticosteroids

End point title	Phase 1: Cmax of itacitinib when administered with corticosteroids[2]

End point description:

Maximum observed plasma concentration.

End point type	Primary

End point timeframe:

Day 7

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: Due to small sample size (n=2), PK data was not summarized.

End point values	Itacitinib + Corticosteroids			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: nM				
arithmetic mean (standard deviation)	()			

Notes:

[3] - Due to small sample size (n=2), PK data was not summarized

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Cmin of itacitinib when administered with corticosteroids

End point title	Phase 1: Cmin of itacitinib when administered with corticosteroids[4]

End point description:

Minimum observed plasma concentration.

End point type	Primary

End point timeframe:

Up to 28 days

Notes:

[4] - 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: Due to small sample size (n=2), PK data was not summarized.

End point values	Itacitinib + Corticosteroids			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: nM				
arithmetic mean (standard deviation)	()			

Notes:

[5] - Due to small sample size (n=2), PK data was not summarized

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Tmax of itacitinib when administered with corticosteroids

End point title	Phase 1: Tmax of itacitinib when administered with corticosteroids[6]

End point description:

Time to maximum concentration.

End point type	Primary

End point timeframe:

Up to 28 days

Notes:

[6] - 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: Due to small sample size (n=2), PK data was not summarized.

End point values	Itacitinib + Corticosteroids			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: hours				
arithmetic mean (standard deviation)	()			

Notes:

[7] - Due to small sample size (n=2), PK data was not summarized

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: AUC of itacitinib when administered with corticosteroids

End point title	Phase 1: AUC of itacitinib when administered with corticosteroids[8]

End point description:

Area under the plasma concentration-time curve.

End point type	Primary

End point timeframe:

Up to 28 days

Notes:

[8] - 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: Due to small sample size (n=2), PK data was not summarized.

End point values	Itacitinib + Corticosteroids			
Subject group type	Reporting group			
Number of subjects analysed	0[9]			
Units: nM/h				
arithmetic mean (standard deviation)	()			

Notes:

[9] - Due to small sample size (n=2), PK data was not summarized

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Cl/F of itacitinib when administered with corticosteroids

End point title	Phase 1: Cl/F of itacitinib when administered with corticosteroids[10]

End point description:

Apparent oral dose clearance.

End point type	Primary

End point timeframe:

Up to 28 days

Notes:

[10] - 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: Due to small sample size (n=2), PK data was not summarized.

End point values	Itacitinib + Corticosteroids			
Subject group type	Reporting group			
Number of subjects analysed	0[11]			
Units: Liter/hour				
arithmetic mean (standard deviation)	()			

Notes:

[11] - Due to small sample size (n=2), PK data was not summarized

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Overall response rate

End point title	Phase 1: Overall response rate

End point description:

Defined as the proportion of participants demonstrating a CR, VGPR, or PR.

End point type	Secondary

End point timeframe:

Day 28

End point values	Itacitinib + Corticosteroids			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: Percentage of Participants				

Notes:

[12] - The study was terminated before participants reached Day 28, time point for analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 months

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Itacitinib + Corticosteroids

Reporting group description: -

Serious adverse events	Itacitinib + Corticosteroids		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Idiopathic pneumonia syndrome			

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			
Parvovirus infection			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Itacitinib + Corticosteroids		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)		
Investigations			
Ejection fraction decreased			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
White blood cell count decreased			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		

Neutropenia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 2		
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Respiratory, thoracic and mediastinal disorders Pulmonary haemorrhage subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Skin and subcutaneous tissue disorders Skin exfoliation subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Psychiatric disorders Agitation subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) Micturition urgency subjects affected / exposed occurrences (all) Pollakiuria subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1 1 / 2 (50.00%) 1 1 / 2 (50.00%) 1		
Musculoskeletal and connective tissue disorders Arthralgia			

subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2019	The primary purpose of this amendment (Protocol Amendment 2) was to add recommendations for concomitant administration of potent CYP3A4 inhibitors based on emergent data from the INCB 39110-108 study. Additional clarification on study procedures and other updates have also been included.
02 July 2019	The primary purpose of this amendment (Protocol Amendment 3) was to revise the toxicity monitoring and stopping boundaries. Eligibility criteria referring to renal and liver function have been modified to address comments the Health Authorities. Itacitinib clinical background has also been updated to align with the most recent data available.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported