

**Clinical trial results:****A 2-Part, Phase 2, Open-Label Study of the Safety, Tolerability, and Efficacy of Itacitinib Immediate Release in Participants With Primary Myelofibrosis or Secondary Myelofibrosis (Post–Polycythemia Vera Myelofibrosis or Post–Essential Thrombocythemia Myelofibrosis) Who Have Received Prior Ruxolitinib and/or Fedratinib Monotherapy****Summary**

EudraCT number	2020-003123-42
Trial protocol	AT FR DE ES BE PL IT
Global end of trial date	24 August 2023

Results information

Result version number	v1 (current)
This version publication date	05 September 2024
First version publication date	05 September 2024

Trial information**Trial identification**

Sponsor protocol code	INCB 39110-213/LIMBER-213
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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, DE 19803
Public contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@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	24 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 August 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Part 1 was conducted to evaluate the safety and tolerability of itacitinib immediate release (IR) and to select the recommended phase 2 dose (RP2D) for Part 2 of the study. Part 2 was to be conducted to evaluate the efficacy of itacitinib IR at the RP2D with respect to spleen volume reduction at Week 24.

Protection of trial subjects:

This study was to be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, applicable Good Clinical Practices, and applicable laws and country-specific regulations in which the study was being conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 July 2021
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
Country: Number of subjects enrolled	Italy: 2
Worldwide total number of subjects	4
EEA total number of subjects	2

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)	1
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted at 3 study centers in the United States and Italy.

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

Arm title	Itacitinib 300 mg
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Arm description:

Participants received itacitinib immediate release 300 milligrams (mg) twice a day (BID) orally (PO) for at least 24 weeks. Participants could remain on treatment as long as they were receiving clinical benefit and had not met any criteria for treatment discontinuation.

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

Dosage and administration details:

100 and 300 mg immediate release tablets

Number of subjects in period 1	Itacitinib 300 mg
Started	4
Completed	0
Not completed	4
Adverse event, serious fatal	2
Adverse event, non-fatal	1
Protocol-specified withdrawal criterion met	1

Baseline characteristics

Reporting groups

Reporting group title	Itacitinib 300 mg
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Reporting group description:

Participants received itacitinib immediate release 300 milligrams (mg) twice a day (BID) orally (PO) for at least 24 weeks. Participants could remain on treatment as long as they were receiving clinical benefit and had not met any criteria for treatment discontinuation.

Reporting group values	Itacitinib 300 mg	Total	
Number of subjects	4	4	
Age Categorical Units: participants			
<=18 years	0	0	
Between 18 and 65 years	1	1	
>=65 years	3	3	
Sex: Female, Male Units: participants			
Female	2	2	
Male	2	2	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	3	3	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	3	3	
Unknown or Not Reported	1	1	

End points

End points reporting groups

Reporting group title	Itacitinib 300 mg
Reporting group description: Participants received itacitinib immediate release 300 milligrams (mg) twice a day (BID) orally (PO) for at least 24 weeks. Participants could remain on treatment as long as they were receiving clinical benefit and had not met any criteria for treatment discontinuation.	

Primary: Part 1: Number of participants with any treatment-emergent adverse event (TEAE)

End point title	Part 1: Number of participants with any treatment-emergent adverse event (TEAE) ^[1]
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End point description:

An adverse event was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not it was considered drug-related. An AE could therefore have been any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study treatment. A TEAE was defined as an AE that was reported for the first time or the worsening of a pre-existing event after the first dose of study treatment.

End point type	Primary
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End point timeframe:

up to 724 days

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: Statistical analysis was not conducted for this endpoint.

End point values	Itacitinib 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: participants	4			

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of participants with any Grade 3 or higher TEAE

End point title	Part 1: Number of participants with any Grade 3 or higher
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End point description:

A TEAE was defined as an AE that was reported for the first time or the worsening of a pre-existing event after the first dose of study treatment. The severity of AEs was assessed using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 Grades 1 through 5. The investigator made an assessment of intensity for each AE and SAE reported during the study and assigned it to 1 of the following categories: Grade 1: mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; treatment not indicated. Grade 2: moderate; minimal, local, or noninvasive treatment indicated; limiting age-appropriate activities of daily living. Grade 3: severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living. Grade 4: life-threatening consequences; urgent treatment indicated. Grade 5: fatal.

End point type	Primary
End point timeframe: up to 724 days	
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: Statistical analysis was not conducted for this endpoint.	

End point values	Itacitinib 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: participants	4			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Splenic response rate (SRR) at Week 24

End point title	Part 2: Splenic response rate (SRR) at Week 24 ^[3]
End point description: SRR was defined as the percentage of participants who had a reduction in spleen volume (by imaging) of at least 35% when compared with Baseline.	
End point type	Primary
End point timeframe: Baseline; Week 24	
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: Analysis was not conducted because Part 2 never opened for enrollment.	

End point values	Itacitinib 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[4]			
Units: percentage of participants				

Notes:
[4] - Analysis was not conducted because Part 2 never opened for enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of participants with any Grade 3 or higher TEAE

End point title	Part 2: Number of participants with any Grade 3 or higher TEAE
End point description: A TEAE was defined as an AE that was reported for the first time or the worsening of a pre-existing event after the first dose of study treatment. The severity of AEs was assessed using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 Grades 1 through 5. The investigator made an assessment of intensity for each AE and SAE reported during the study and assigned it to 1 of the following categories: Grade 1: mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; treatment not indicated. Grade 2: moderate; minimal, local, or noninvasive treatment indicated;	

limiting age-appropriate activities of daily living. Grade 3: severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living. Grade 4: life-threatening consequences; urgent treatment indicated. Grade 5: fatal.

End point type	Secondary
End point timeframe:	
up to at least 24 weeks	

End point values	Itacitinib 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[5]			
Units: participants				

Notes:

[5] - Analysis was not conducted because Part 2 never opened for enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Total symptom score (TSS) response rate at Week 24

End point title	Part 2: Total symptom score (TSS) response rate at Week 24
End point description:	
TSS response was defined as the percentage of participants who achieved at least 50% reduction in TSS over the 28 days immediately before the end of Week 24 compared with the 7 days immediately before the initiation of itacitinib immediate release (aseline).B	
End point type	Secondary
End point timeframe:	
Baseline; Week 24	

End point values	Itacitinib 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[6]			
Units: percentage of participants				

Notes:

[6] - Analysis was not conducted because Part 2 never opened for enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Mean change (from Day 1 versus Week 12 and Week 24) in the 5 multi-item functional scale scores and the multi-item global health status scale score (EORTC QLQ-C30)

End point title	Part 2: Mean change (from Day 1 versus Week 12 and Week 24) in the 5 multi-item functional scale scores and the multi-item global health status scale score (EORTC QLQ-C30)
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End point description:

The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) was to be used to assess the improvement in quality of life.

End point type	Secondary
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End point timeframe:

Baseline; Weeks 12 and 24

End point values	Itacitinib 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[7]			
Units: score on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[7] - Analysis was not conducted because Part 2 never opened for enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of participants categorized as improved on the Week 24 Patient Global Impression of Change (PGIC)

End point title	Part 2: Percentage of participants categorized as improved on the Week 24 Patient Global Impression of Change (PGIC)
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End point description:

The PGIC consists of a single question pertaining to a participant's overall status since the start of the study. The questionnaire gives participants 7 options to describe their overall status including: very much improved, much improved, minimally improved, no change, minimally worse, much worse, and very much worse.

End point type	Secondary
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End point timeframe:

Baseline; Week 24

End point values	Itacitinib 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[8]			
Units: percentage of participants				

Notes:

[8] - Analysis was not conducted because Part 2 never opened for enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of participants with any TEAE

End point title	Part 2: Number of participants with any TEAE
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End point description:

An adverse event was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not it was considered drug-related. An AE could therefore have been any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study treatment. A TEAE was defined as an AE that was reported for the first time or the worsening of a pre-existing event after the first dose of study treatment.

End point type	Secondary
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End point timeframe:

up to at least 24 weeks

End point values	Itacitinib 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[9]			
Units: participants				

Notes:

[9] - Analysis was not conducted because Part 2 never opened for enrollment.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 724 days

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs), defined as AEs that were reported for the first time or the worsening of pre-existing events after the first dose of study treatment, were reported for the Safety Evaluable Population.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22
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Reporting groups

Reporting group title	Total
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Reporting group description:

Total

Reporting group title	itacitinib 300 mg
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Reporting group description:

itacitinib 300 mg

Serious adverse events	Total	itacitinib 300 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	3 / 4 (75.00%)	
number of deaths (all causes)	2	2	
number of deaths resulting from adverse events	2	2	
Vascular disorders			
Shock haemorrhagic			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine storm			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haematoma			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			

subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Enterocolitis infectious			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Total	itacitinib 300 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Blood bilirubin increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Cardiac disorders			

Cardiac failure subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Sinus bradycardia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Nervous system disorders Syncope subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2	1 / 4 (25.00%) 2	
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Asthenia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Gastrointestinal disorders Mouth haemorrhage subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Vomiting subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Hepatobiliary disorders Hepatotoxicity subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2	2 / 4 (50.00%) 2	
Renal and urinary disorders			

Nephropathy toxic subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 4	2 / 4 (50.00%) 4	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Infections and infestations Candida infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1 1 / 4 (25.00%) 1	1 / 4 (25.00%) 1 1 / 4 (25.00%) 1	
Metabolism and nutrition disorders Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 January 2022	The study sponsor decided not to proceed with the study any further; the primary purpose of this amendment was to update the Schedule of Activities for study participants ongoing as of the date of this decision to simplify and minimize the required assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The sponsor terminated study enrollment following an assessment regarding the expected duration of recruitment for the Phase 2 portion of the study combined with the availability of other study options for this patient population.

Notes: