Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of the Combination of PI3K Inhibitor Parsaclisib and Ruxolitinib in Participants With Myelofibrosis

Summary

EudraCT number	2020-003130-21
Trial protocol	AT DE NO FR DK FI IT
Global end of trial date	25 November 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	INCB 50465-313/LIMBER-313

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 Cutoff, Wilmington, United States, 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	25 November 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 November 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study was conducted to evaluate and compare the efficacy of parsaclisib plus ruxolitinib versus placebo plus ruxolitinib on spleen volume at Week 24.

Protection of trial subjects:

This study was 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 conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 May 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	China: 27
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Italy: 38
Country: Number of subjects enrolled	Japan: 31
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Norway: 9
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	Türkiye: 8
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 58

Worldwide total number of subjects	252
EEA total number of subjects	115

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)	129
From 65 to 84 years	122
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted at 93 study sites in Austria, Belgium, China, Denmark, Finland, France, Germany, Israel, Italy, Japan, Norway, Poland, South Korea, Spain, Turkey, the United Kingdom, and the United States.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Parsaclisib plus ruxolitinib

Arm description:

Participants were randomized to receive parsaclisib plus ruxolitinib beginning on Day 1 and continued on this regimen as long as it was tolerated and the participants did not meet any discontinuation criteria. Participants with a Baseline platelet count ≥100 × 10^9/Liter received ruxolitinib 15 milligrams (mg) twice daily (BID). Participants with a Baseline platelet count of 50 to < 100 × 10^9/Liters inclusive received ruxolitinib 5 mg BID. Participants were also stratified according to the Dynamic International Prognostic Scoring System (DIPSS) risk category (high versus intermediate-2 versus intermediate-1). Participants received parsaclisib at a dose of 5 mg once daily (QD).

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

Dosage and administration details:

Unit dose strength(s)/dosage level(s): 5 mg tablets, 2.5 mg tablets, 1.0 mg tablets

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

Dosage and administration details:

Unit dose strength(s)/dosage level(s): 5 mg tablets, 2.5 mg tablets, 1.0 mg tablets

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

Dosage and administration details:

Unit dose strength(s)/dosage level(s): 5 mg tablets; 15 mg tablets (in some countries)

Arm title	Placebo plus ruxolitinib

Arm description:

Participants were randomized to receive placebo plus ruxolitinib beginning on Day 1 and continued on

this regimen until they left the study. Participants with a Baseline platelet count ≥100 × 10^9/Liter received ruxolitinib 15 mg BID. Participants with a Baseline platelet count of 50 to < 100 × 10^9/Liters inclusive received ruxolitinib 5 mg BID. Participants were also stratified according to the DIPSS risk category (high versus intermediate-2 versus intermediate-1). Participants received matching placebo at a dose of 5 mg QD. After 24 weeks, participants randomized to receive placebo plus ruxolitinib could have switched to treatment with parsaclisib plus ruxolitinib per the regimen received during the first 24 weeks of the study. Treatment continued for as long as the regimen was tolerated and the participant did not meet any discontinuation criteria.

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

Dosage and administration details:

Unit dose strength(s)/dosage level(s): 5 mg tablets; 15 mg tablets (in some countries)

Number of subjects in period 1	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib
Started	125	127
Completed	0	0
Not completed	125	127
Adverse event, serious fatal	5	3
Consent withdrawn by subject	8	2
Physician decision	2	-
Adverse event, non-fatal	2	-
Sponsor Decision	104	117
Lost to follow-up	1	-
Mature Plasmacytoid Dendritic Cell Proliferation	-	1
Transitioned to Rollover Study with Ruxolitinib	2	3
Protocol deviation	1	-
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Parsaclisib plus ruxolitinib

Reporting group description:

Participants were randomized to receive parsaclisib plus ruxolitinib beginning on Day 1 and continued on this regimen as long as it was tolerated and the participants did not meet any discontinuation criteria. Participants with a Baseline platelet count ≥100 × 10^9/Liter received ruxolitinib 15 milligrams (mg) twice daily (BID). Participants with a Baseline platelet count of 50 to < 100 × 10^9/Liters inclusive received ruxolitinib 5 mg BID. Participants were also stratified according to the Dynamic International Prognostic Scoring System (DIPSS) risk category (high versus intermediate-2 versus intermediate-1). Participants received parsaclisib at a dose of 5 mg once daily (QD).

Reporting group title	Placebo plus ruxolitinib

Reporting group description:

Participants were randomized to receive placebo plus ruxolitinib beginning on Day 1 and continued on this regimen until they left the study. Participants with a Baseline platelet count ≥100 × 10^9/Liter received ruxolitinib 15 mg BID. Participants with a Baseline platelet count of 50 to < 100 × 10^9/Liters inclusive received ruxolitinib 5 mg BID. Participants were also stratified according to the DIPSS risk category (high versus intermediate-2 versus intermediate-1). Participants received matching placebo at a dose of 5 mg QD. After 24 weeks, participants randomized to receive placebo plus ruxolitinib could have switched to treatment with parsaclisib plus ruxolitinib per the regimen received during the first 24 weeks of the study. Treatment continued for as long as the regimen was tolerated and the participant did not meet any discontinuation criteria.

Reporting group values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib	Total
Number of subjects	125	127	252
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)	67	62	129
From 65-84 years	58	64	122
85 years and over	0	1	1
Age Continuous Units: years			
arithmetic mean	63.2	63.3	
standard deviation	± 10.34	± 10.90	-
Sex: Female, Male Units: participants			
Female	49	49	98
Male	76	78	154
Race/Ethnicity, Customized Units: Subjects			
White or Caucasian	80	84	164
Black or African American	1	1	2
Asian	33	31	64
Not Reported	10	10	20

"Not Hispanic, Latino or Spanish" in Database	1	0	1
Turkish	0	1	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	7	7	14
Not Hispanic or Latino	103	110	213
Unknown or Not Reported	15	10	25

End points

End points reporting groups

Reporting group title	Parsaclisib plus ruxolitinib

Reporting group description:

Participants were randomized to receive parsaclisib plus ruxolitinib beginning on Day 1 and continued on this regimen as long as it was tolerated and the participants did not meet any discontinuation criteria. Participants with a Baseline platelet count ≥100 × 10^9/Liter received ruxolitinib 15 milligrams (mg) twice daily (BID). Participants with a Baseline platelet count of 50 to < 100 × 10^9/Liters inclusive received ruxolitinib 5 mg BID. Participants were also stratified according to the Dynamic International Prognostic Scoring System (DIPSS) risk category (high versus intermediate-2 versus intermediate-1). Participants received parsaclisib at a dose of 5 mg once daily (QD).

Reporting group title	Placebo plus ruxolitinib

Reporting group description:

Participants were randomized to receive placebo plus ruxolitinib beginning on Day 1 and continued on this regimen until they left the study. Participants with a Baseline platelet count ≥100 × 10^9/Liter received ruxolitinib 15 mg BID. Participants with a Baseline platelet count of 50 to < 100 × 10^9/Liters inclusive received ruxolitinib 5 mg BID. Participants were also stratified according to the DIPSS risk category (high versus intermediate-2 versus intermediate-1). Participants received matching placebo at a dose of 5 mg QD. After 24 weeks, participants randomized to receive placebo plus ruxolitinib could have switched to treatment with parsaclisib plus ruxolitinib per the regimen received during the first 24 weeks of the study. Treatment continued for as long as the regimen was tolerated and the participant did not meet any discontinuation criteria.

Primary: Percentage of participants achieving ≥35% reduction in spleen volume from Baseline to Week 24 as measured by magnetic resonance imaging [MRI] (or computed tomography [CT] scan in applicable participants)

End point title	Percentage of participants achieving ≥35% reduction in spleen volume from Baseline to Week 24 as measured by magnetic resonance imaging [MRI] (or computed tomography [CT] scan in applicable participants)

End point description:

Participants had an MRI of the upper and lower abdomen and pelvis to determine the spleen volume. A CT scan was substituted for participants who were not candidates for MRI or when MRI was not readily available. Determination of spleen length below the left costal margin was measured by palpation, using a flexible ruler provided by the sponsor. Intent-to-Treat (ITT) Population: all randomized participants. Treatment groups were defined according to the treatment assignment at randomization regardless of the actual study drug the participant took during their participation. Participants who had both Baseline and Week 24 measurements, or discontinued treatment before 27APR2023, or reached Week 24 before 27APR2023 but were missing Week 24 assessments were analyzed.

End point type	Primary

End point timeframe:

Baseline; Week 24

End point values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89[1]	92[2]		
Units: percentage of participants				
number (not applicable)	52.8	46.7		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	≥35% reduction in spleen volume
Comparison groups	Parsaclisib plus ruxolitinib v Placebo plus ruxolitinib
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4224 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	2.26

Notes:

[3] - calculated from Cochran Mantel-Haenszel test stratified by Baseline platelet count ≥100 x 10^9/Liters versus 50 to <100 x 10^9/Liters inclusive

Secondary: Percentage of participants who had a ≥50% reduction in Total Symptom Score (TSS) from Baseline to Week 24 as measured by the Myelofibrosis (MF) Symptom Assessment Form v4.0 (MFSAF v4.0) diary

End point title	Percentage of participants who had a ≥50% reduction in Total Symptom Score (TSS) from Baseline to Week 24 as measured by the Myelofibrosis (MF) Symptom Assessment Form v4.0 (MFSAF v4.0) diary

End point description:

Symptoms of MF were assessed using the MFSAF v4.0 diary, composed of 7 individual symptom scores (SSs) (fatigue, night sweats, itchiness, abdominal discomfort, pain under left ribs, early satiety, bone pain), collected daily using a 0- (no symptoms) to 10-point (worst imaginable symptoms) scale. The daily TSS (0-70)=sum of the 7 individual symptom scores (SSs) collected on the same day. Higher TSS indicate more severe symptoms. The TSS was missing if there were any missing individual scores. Observations with missing dates were excluded from the analysis. The Baseline (BL)/Week (W) 24 total score (TS)=the average of the daily TSs from the last 7 days before the first dose of parsaclisib, placebo, or ruxolitinib/the Week 24 visit. The Baseline/W24 TS was missing if there were ≥4 missing out of the 7 daily TSs. Participants who had both BL and W24 measurements, or discontinued treatment before 27APR2023, or reached W24 before 27APR2023 but were missing W24 assessments were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89[4]	98[5]		
Units: percentage of participants				
number (not applicable)	34.8	38.8		

Notes:

[4] - ITT Population

[5] - ITT Population

Statistical analyses

Statistical analysis title	≥50% reduction in Total Symptom Score (TSS)
Comparison groups	Parsaclisib plus ruxolitinib v Placebo plus ruxolitinib
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5728 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	1.53

Notes:

[6] - calculated from Cochran Mantel-Haenszel test stratified by Baseline platelet count ≥100 x 10^9/Liters versus 50 to <100 x 10^9/Liters inclusive

Secondary: Change in TSS from Baseline to Week 24 as measured by the MFSAF v4.0 diary

End point title	Change in TSS from Baseline to Week 24 as measured by the MFSAF v4.0 diary

End point description:

Symptoms of myelofibrosis were assessed using the MFSAF v4.0 diary. The MFSAF v4.0 is composed of 7 individual symptom scores (fatigue, night sweats, itchiness, abdominal discomfort, pain under left ribs, early satiety, bone pain), each collected daily using a 0- (no symptoms) to 10-point (worst imaginable symptoms) scale. The daily TSS (0 to 70) is the sum of the 7 individual symptom scores collected on the same day. Higher TSS indicate more severe symptoms. The TSS was missing if there were any missing individual scores. Observations with missing dates were excluded from the analysis. The Baseline/Week 24 total score was defined as the average of the daily total scores from the last 7 days before the first dose of parsaclisib, placebo, or ruxolitinib/the Week 24 visit. The Baseline/Week 24 total scores was missing if there were ≥4 missing out of the 7 daily total scores. Change from Baseline was calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline; Week 24

End point values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119[7]	125[8]		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline, n=119, 125	19.8 (± 14.29)	19.6 (± 13.07)		
Change from Baseline at Week 24, n=75, 89	-6.6 (± 12.36)	-6.8 (± 10.74)		

Notes:

[7] - ITT Population. Only participants with available data were analyzed.

[8] - ITT Population. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to the first ≥50% reduction in TSS as measured by the MFSAF v4.0 diary

End point title	Time to the first ≥50% reduction in TSS as measured by the MFSAF v4.0 diary

End point description:

Symptoms of MF were assessed using the MFSAF v4.0 diary, composed of 7 individual SSs, collected daily using a 0- (no symptoms) to 10-point (worst imaginable symptoms) scale. The daily TSS (0-70) is the sum of the 7 individual SSs collected on the same day. Higher TSS indicate more severe symptoms. The TSS was missing if there were any missing individual scores. Observations with missing dates were excluded from the analysis. The BL/W24 TS was defined as the average of the daily TSs from the last 7 days before the first dose of parsaclisib, placebo, or ruxolitinib/the W24 visit. The BL/W24 TS was missing if there were ≥4 missing out of the 7 daily TSs. Censored participants didn't have a response at any time up to the last assessment date. Participants who didn't have a >=50% reduction in TSS was censored at the time of the last assessment. Participants with a DIPSS risk level of Low Risk Level (0 prognostic points) were excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline; up to Week 24

End point values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[9]	127[10]		
Units: days				
median (confidence interval 95%)	67.0 (27.0 to 131.0)	69.0 (35.0 to 143.0)		

Notes:

[9] - ITT Population, including censored participants

[10] - ITT Population, including censored participants

Statistical analyses

Statistical analysis title	Time to the first ≥50% reduction in TSS
Comparison groups	Parsaclisib plus ruxolitinib v Placebo plus ruxolitinib

Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.949 [11]
Method	Logrank

Notes:

[11] - calculated from log-rank test stratified by Baseline platelet count ≥100 × 10^9/Liters versus 50 to <100 × 10^9/Liters inclusive

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival was defined as the interval between the randomization date and the date of death due to any cause. Due to participants rolling over to another study (NCT02955940), the follow-up time was not long enough to estimate the median and the upper and lower limits of the confidence interval.

End point type	Secondary

End point timeframe:

up to 749 days

End point values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: days				
median (confidence interval 95%)	(to)	(to)		

Notes:

[12] - ITT Population

[13] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any treatment-emergent adverse event (TEAE)

End point title	Number of participants with any treatment-emergent adverse event (TEAE)

End point description:

An adverse event (AE) is defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not it is considered drug related. An AE could therefore be 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 is defined as any AE either reported for the first time or the worsening of a pre-existing event after the first dose of study drug until 30 to 35 days after the last dose of parsaclisib/matching placebo or ruxolitinib. Safety Population: all participants who received at least 1 dose of parsaclisib, placebo, or ruxolitinib. Treatment groups for this population were determined according to the actual treatment the participant received regardless of assigned study drug treatment.

End point type	Secondary

End point timeframe:

up to 960 days

End point values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[14]	127[15]		
Units: participants	117	119		

Notes:

[14] - Safety Population

[15] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any Grade 3 or Higher TEAE

End point title	Number of participants with any Grade 3 or Higher TEAE

End point description:

An AE is defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not it is considered drug related. A TEAE is defined as any AE either reported for the first time or the worsening of a pre-existing event after the first dose of study drug until 30 to 35 days after the last dose of parsaclisib/matching placebo or ruxolitinib. The severity of AEs was assessed using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 Grades 1 through 5. Grade 1: mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2: moderate; minimal, local or noninvasive intervention indicated; limiting instrumental activities of daily living (ADL). Grade 3: severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL. Grade 4: life-threatening urgent intervention indicated. Grade 5: death related to AE.

End point type	Secondary

End point timeframe:

up to 960 days

End point values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[16]	127[17]		
Units: participants	75	75		

Notes:

[16] - Safety Population

[17] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time of onset of a ≥35% reduction in spleen volume

End point title	Time of onset of a ≥35% reduction in spleen volume

End point description:

The time to the first ≥35% reduction in spleen volume is defined as the time from randomization to the first time participants had ≥35% reduction in spleen volume. Censored participants didn’t have a response at any time up to the last assessment date. Participants who didn’t have a >=35% reduction

in spleen volume were censored at the time of the last assessment. Participants with a DIPSS risk level of Low Risk Level (0 prognostic points) were excluded from the analysis. The 95% confidence interval was calculated using the Brookmeyer and Crowley's method with log-log transformation.

End point type	Secondary

End point timeframe:

up to 925 days

End point values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[18]	127[19]		
Units: days				
median (confidence interval 95%)	88.0 (86.0 to 99.0)	92.0 (87.0 to 253.0)		

Notes:

[18] - ITT Population, including censored participants

[19] - ITT Population, including censored participants

Statistical analyses

Statistical analysis title	Time of onset of a ≥35% reduction in spleen volume
Comparison groups	Placebo plus ruxolitinib v Parsaclisib plus ruxolitinib
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1085 [20]
Method	Logrank

Notes:

[20] - calculated from log-rank test stratified by Baseline platelet count ≥100 × 10^9/Liters versus 50 to <100 × 10^9/Liters inclusive

Secondary: Duration of maintenance (DoM) of a ≥35% reduction in spleen volume

End point title	Duration of maintenance (DoM) of a ≥35% reduction in spleen volume

End point description:

The duration of ≥35% reduction from Baseline in spleen volume was defined as the interval between the first spleen volume measurement that was a ≥35% reduction from Baseline and the date of the first measurement that was no longer a ≥35% reduction from Baseline. Participants with DIPSS risk level being low risk level (0 prognostic points) have been excluded from the analysis. Only those participants with a ≥35% reduction in spleen volume who then had a loss of ≥35% reduction in spleen volume with a 25% increase from NADIR were analyzed. If the maintenance end date was not observed before the database cutoff, the duration was censored at the last assessment. 9999=The upper limit of the confidence interval was not estimable because too few participants lost a >=35% reduction in spleen volume at the time of rollover to another study (NCT02955940).

End point type	Secondary

End point timeframe:

up to 925 days

End point values	Parsaclisib plus ruxolitinib	Placebo plus ruxolitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73[21]	61[22]		
Units: days				
median (confidence interval 95%)	505.0 (339.0 to 9999)	9999 (337.0 to 9999)		

Notes:

[21] - ITT Population

[22] - ITT Population

Statistical analyses

Statistical analysis title	DoM of a ≥35% reduction in spleen volume
Comparison groups	Parsaclisib plus ruxolitinib v Placebo plus ruxolitinib
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6127 [23]
Method	Logrank

Notes:

[23] - calculated from log-rank test stratified by Baseline platelet count ≥100 × 10^9/Liters versus 50 to <100 × 10^9/Liters inclusive

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 960 days

Adverse event reporting additional description:

Treatment-emergent adverse events, defined as AEs either reported for the first time or the worsening of pre-existing events after the first dose of study drug until 30 to 35 days after the last dose of parsaclisib/matching placebo or ruxolitinib, have been reported for the Safety Population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Placebo plus ruxolitinib

Reporting group description:

Participants were randomized to receive placebo plus ruxolitinib beginning on Day 1 and continued on this regimen until they left the study. Participants with a Baseline platelet count ≥100 × 10^9/Liter received ruxolitinib 15 mg BID. Participants with a Baseline platelet count of 50 to < 100 × 10^9/Liters inclusive received ruxolitinib 5 mg BID. Participants were also stratified according to the DIPSS risk category (high versus intermediate-2 versus intermediate-1). Participants received matching placebo at a dose of 5 mg QD. After 24 weeks, participants randomized to receive placebo plus ruxolitinib could have switched to treatment with parsaclisib plus ruxolitinib per the regimen received during the first 24 weeks of the study. Treatment continued for as long as the regimen was tolerated and the participant did not meet any discontinuation criteria.

Reporting group title	Parsaclisib plus ruxolitinib

Reporting group description:

Participants were randomized to receive parsaclisib plus ruxolitinib beginning on Day 1 and continued on this regimen as long as it was tolerated and the participants did not meet any discontinuation criteria. Participants with a Baseline platelet count ≥100 × 10^9/Liter received ruxolitinib 15 milligrams (mg) twice daily (BID). Participants with a Baseline platelet count of 50 to < 100 × 10^9/Liters inclusive received ruxolitinib 5 mg BID. Participants were also stratified according to the Dynamic International Prognostic Scoring System (DIPSS) risk category (high versus intermediate-2 versus intermediate-1). Participants received parsaclisib at a dose of 5 mg once daily (QD).

Serious adverse events	Placebo plus ruxolitinib	Parsaclisib plus ruxolitinib	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 127 (14.17%)	26 / 125 (20.80%)	
number of deaths (all causes)	3	6	
number of deaths resulting from adverse events	1	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myxofibrosarcoma			

subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 127 (0.00%)	2 / 125 (1.60%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory failure			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Blood creatinine increased			

subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood fibrinogen decreased			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Extradural haematoma			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 127 (1.57%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac arrest			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Supraventricular tachycardia			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Intracranial mass			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelitis transverse			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 127 (0.79%)	4 / 125 (3.20%)	
occurrences causally related to treatment / all	1 / 1	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			

subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular hole			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
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 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 127 (0.00%)	3 / 125 (2.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			

subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypoparathyroidism			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 127 (0.79%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			

subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster meningomyelitis			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	2 / 127 (1.57%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 127 (1.57%)	4 / 125 (3.20%)	
occurrences causally related to treatment / all	1 / 2	2 / 4	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 127 (0.00%)	2 / 125 (1.60%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			

subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 127 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 127 (0.79%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo plus ruxolitinib	Parsaclisib plus ruxolitinib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	109 / 127 (85.83%)	109 / 125 (87.20%)	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 127 (1.57%)	11 / 125 (8.80%)	
occurrences (all)	2	12	
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 127 (7.87%)	22 / 125 (17.60%)	
occurrences (all)	12	38	
Alanine aminotransferase increased			
subjects affected / exposed	11 / 127 (8.66%)	18 / 125 (14.40%)	
occurrences (all)	14	29	
Blood creatinine increased			

subjects affected / exposed	6 / 127 (4.72%)	11 / 125 (8.80%)	
occurrences (all)	6	13	
Neutrophil count decreased			
subjects affected / exposed	7 / 127 (5.51%)	7 / 125 (5.60%)	
occurrences (all)	11	14	
Weight increased			
subjects affected / exposed	5 / 127 (3.94%)	7 / 125 (5.60%)	
occurrences (all)	7	7	
White blood cell count decreased			
subjects affected / exposed	5 / 127 (3.94%)	8 / 125 (6.40%)	
occurrences (all)	5	16	
Platelet count decreased			
subjects affected / exposed	19 / 127 (14.96%)	29 / 125 (23.20%)	
occurrences (all)	38	48	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	4 / 127 (3.15%)	8 / 125 (6.40%)	
occurrences (all)	4	9	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 127 (3.94%)	8 / 125 (6.40%)	
occurrences (all)	8	8	
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 127 (5.51%)	6 / 125 (4.80%)	
occurrences (all)	7	6	
Headache			
subjects affected / exposed	11 / 127 (8.66%)	7 / 125 (5.60%)	
occurrences (all)	14	7	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	11 / 127 (8.66%)	11 / 125 (8.80%)	
occurrences (all)	14	13	
Fatigue			
subjects affected / exposed	12 / 127 (9.45%)	11 / 125 (8.80%)	
occurrences (all)	14	13	

Pyrexia			
subjects affected / exposed	8 / 127 (6.30%)	9 / 125 (7.20%)	
occurrences (all)	8	11	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	68 / 127 (53.54%)	57 / 125 (45.60%)	
occurrences (all)	94	70	
Neutropenia			
subjects affected / exposed	5 / 127 (3.94%)	11 / 125 (8.80%)	
occurrences (all)	6	15	
Thrombocytopenia			
subjects affected / exposed	21 / 127 (16.54%)	26 / 125 (20.80%)	
occurrences (all)	33	31	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 127 (6.30%)	8 / 125 (6.40%)	
occurrences (all)	9	10	
Abdominal distension			
subjects affected / exposed	7 / 127 (5.51%)	0 / 125 (0.00%)	
occurrences (all)	9	0	
Constipation			
subjects affected / exposed	11 / 127 (8.66%)	8 / 125 (6.40%)	
occurrences (all)	11	8	
Diarrhoea			
subjects affected / exposed	21 / 127 (16.54%)	21 / 125 (16.80%)	
occurrences (all)	30	28	
Nausea			
subjects affected / exposed	10 / 127 (7.87%)	6 / 125 (4.80%)	
occurrences (all)	13	7	
Vomiting			
subjects affected / exposed	8 / 127 (6.30%)	8 / 125 (6.40%)	
occurrences (all)	10	8	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 127 (7.87%)	8 / 125 (6.40%)	
occurrences (all)	11	10	

Dyspnoea			
subjects affected / exposed	7 / 127 (5.51%)	7 / 125 (5.60%)	
occurrences (all)	9	8	
Epistaxis			
subjects affected / exposed	5 / 127 (3.94%)	10 / 125 (8.00%)	
occurrences (all)	6	11	
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	5 / 127 (3.94%)	7 / 125 (5.60%)	
occurrences (all)	5	8	
Pruritus			
subjects affected / exposed	9 / 127 (7.09%)	7 / 125 (5.60%)	
occurrences (all)	10	8	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	7 / 127 (5.51%)	3 / 125 (2.40%)	
occurrences (all)	9	3	
Pain in extremity			
subjects affected / exposed	8 / 127 (6.30%)	3 / 125 (2.40%)	
occurrences (all)	9	4	
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	1 / 127 (0.79%)	9 / 125 (7.20%)	
occurrences (all)	1	9	
COVID-19			
subjects affected / exposed	15 / 127 (11.81%)	26 / 125 (20.80%)	
occurrences (all)	16	27	
Urinary tract infection			
subjects affected / exposed	7 / 127 (5.51%)	5 / 125 (4.00%)	
occurrences (all)	7	5	
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	7 / 127 (5.51%)	5 / 125 (4.00%)	
occurrences (all)	8	5	
Hyperuricaemia			

subjects affected / exposed occurrences (all)	7 / 127 (5.51%) 9	5 / 125 (4.00%) 5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 October 2021	The primary purpose of this amendment was to address changes requested by different national regulatory agencies and ethics committees.
14 October 2022	The primary purpose of this amendment was to update safety information for parsaclisib, including information regarding COVID-19, and the potential impact of parsaclisib therapy on infection risk, vaccine effectiveness, and severity of disease.

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.

Due to participants rolling over to another study (NCT02955940), no participants randomized to receive placebo plus ruxolitinib switched to treatment with parsaclisib plus ruxolitinib.

Notes: