Clinical trial results:
A randomized, double blind, placebo-controlled, multicenter, Phase III study investigating the efficacy and safety of ruxolitinib in early myelofibrosis patients with high molecular risk mutations (ReTHINK)
Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results

Summary

EudraCT number	2014-004928-21
Trial protocol	ES SE GB AT BE HU GR FR PT FI DK PL IT
Global end of trial date	23 October 2017

Results information

Result version number	v1 (current)
This version publication date	08 November 2018
First version publication date	08 November 2018

Trial information

Trial identification

Sponsor protocol code	CINC424A2353

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02598297
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.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	23 October 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 October 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of ruxolitinib in delaying progression of MF from early disease to advanced disease.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Japan: 4
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Turkey: 4

Worldwide total number of subjects	49
EEA total number of subjects	31

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)	24
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately 320 male or female adults (age 18 or over) with a confirmed diagnosis of MF were planned to be enrolled. The target population was not met due to early study termination. A total of 49 subjects were enrolled in the study, 25 in the ruxolitinib arm and 24 in the placebo arm.

Pre-assignment

Screening details:

Approximately 320 male or female adults (age 18 or over) with a confirmed diagnosis of MF were planned to be enrolled. The target population was not met due to early study termination. A total of 49 subjects were enrolled in the study, 25 in the ruxolitinib arm and 24 in the placebo arm.

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	Investigator, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Ruxolitinib (INC424)

Arm description:

Two tablets of ruxolitinib 5 mg were administered orally twice per day

Arm type	Experimental
Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	INC424
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment period 1: Two tablets of ruxolitinib 5 mg were administered orally twice per day.
Treatment period 2: tablets of either 5, 15, 20 mg twice orally per day based on platelet counts

Arm title	Ruxolitinib Placebo

Arm description:

Two tablets of 5mg placebo were administered orally twice per day

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

Dosage and administration details:

Treatment period 1: Two tablets of placebo 5 mg were administered orally twice per day.
Treatment period 2: tablets of either 5, 15, 20 mg twice orally per day based on platelet counts

Number of subjects in period 1	Ruxolitinib (INC424)	Ruxolitinib Placebo
Started	25	24
Not treted withstudy drug	1	0
Subjects followed for survival	1	0
Completed	0	0
Not completed	25	24
Physician decision	1	-
Study terminated by Sponsor	21	23
Adverse event, non-fatal	1	1
Followed for survival	1	-
Subject/guardian decision	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Ruxolitinib (INC424)
Reporting group description:	
Two tablets of ruxolitinib 5 mg were administered orally twice per day	
Reporting group title	Ruxolitinib Placebo
Reporting group description:	
Two tablets of 5mg placebo were administered orally twice per day	

Reporting group values	Ruxolitinib (INC424)	Ruxolitinib Placebo	Total
Number of subjects	25	24	49
Age categorical Units: Subjects			
Adults (18-64 years)	14	10	24
From 65-84 years	11	14	25
Age Continuous Units: Years			
arithmetic mean	59.0	67.4	
standard deviation	± 14.23	± 7.72	-
Sex: Female, Male Units: Subjects			
Female	12	7	19
Male	13	17	30
Race/Ethnicity, Customized Units: Subjects			
Caucasian|	19	23	42
Asian|	4	1	5
Other|	1	0	1
Missing|	1	0	1

End points

End points reporting groups

Reporting group title	Ruxolitinib (INC424)
Reporting group description:	
Two tablets of ruxolitinib 5 mg were administered orally twice per day	
Reporting group title	Ruxolitinib Placebo
Reporting group description:	
Two tablets of 5mg placebo were administered orally twice per day	

Primary: Progression free survival (PFS-1)

End point title	Progression free survival (PFS-1)[1]
End point description:	
Progression free survival (PFS-1) from date of randomization until the occurrence of any of the criteria for disease progression: ● Progressive splenomegaly ● Circulating peripheral blast counts > 10% ● Leukemic transformation ● Hb < 10g/dl with absolute decrease of at least 3 g/dl from baseline ● White blood cell (WBC) counts > 25 x 103/ µL ● MF-7 score ≥ 30 ● Death from any cause	
End point type	Primary
End point timeframe:	
From randomization till disease progression (estimated to be assessed up 48 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 analysis was performed for this endpoint as the study terminated early.

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to primary progression (TTP)

End point title	Time to primary progression (TTP)
End point description:	
TTP is defined as time from randomization until disease progression as defined for PFS-1 excluding death as an event.	
End point type	Secondary
End point timeframe:	
From randomization till progression (estimated to be assessed up to 48 months)	

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Months	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change in spleen volume from baseline

End point title	Percentage Change in spleen volume from baseline

End point description:

Change in spleen volume (by MRI/CT) from baseline

End point type	Secondary

End point timeframe:

From baseline and assessed on 12 week intervals until end of treatment (EOT)

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Percentage change from baseline				
arithmetic mean (standard deviation)				
Week 12 (N = 19, 19)|	-10.8 (± 24.45)	9.1 (± 12.34)		
Week 24 (N = 13, 8)|	-17.8 (± 18.83)	17.6 (± 17.78)		
Week 36 (N = 7, 2)|	-18.4 (± 31.62)	32.5 (± 18.81)		
Week 48 (N = 2, 0)|	-23.5 (± 10.57)	999 (± 999)		
End of Treatment (EOT) (N = 10, 9)|	-11.6 (± 8.08)	18.1 (± 18.58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change in symptoms from baseline using MF-7

End point title	Percentage change in symptoms from baseline using MF-7

End point description:

Percentage change from Baseline in MF-7 total symptom score and 7 individual symptoms at each visit was summarized with descriptive statistics. For this scale, symptoms range from 0 to 10 for the severity experienced within the past 24 hours, with 0 being for absence of symptoms and 10 for worst imaginable symptoms.

End point type	Secondary

End point timeframe:
From Baseline and assessed every 4 weeks until end of treatment

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25[2]	24[3]		
Units: Percentage change in scores				
arithmetic mean (standard deviation)				
TSD change from baseline @ W12|	-0.3 (± 4.45)	0.5 (± 6.08)		
TSD change from baseline @ W24|	0.5 (± 3.71)	-0.8 (± 6.44)		
TSD change from baseline @ W48|	-0.3 (± 3.06)	999 (± 999)		
TSD change from BL @ EOT|	1.1 (± 4.40)	3.3 (± 9.53)		
Tiredness: Baseline (BL)|	1.8 (± 1.45)	1.5 (± 1.53)		
Tiredness: change from baseline @ W12|	0.1 (± 1.47)	0.4 (± 1.27)		
Tiredness: change from baseline @ W24|	-0.1 (± 0.76)	1.1 (± 2.52)		
Tiredness: change from baseline @ W48|	-0.3 (± 0.58)	999 (± 999)		
Tiredness change from BL @ EOT|	0.8 (± 1.32)	1.1 (± 2.28)		
Filling up quickly when you eat (FUQWYE):BL|	1.0 (± 1.41)	0.8 (± 1.27)		
FUQWYE: change from BL @W12|	0.1 (± 1.49)	-0.1 (± 2.09)		
FUQWYE: change from BL @W24|	-0.2 (± 0.99)	0.1 (± 1.17)		
FUQWYE: change from BL @W48|	0.7 (± 1.15)	999 (± 999)		
FUQWYE: change from BL @ EOT|	0.2 (± 1.08)	0.3 (± 2.29)		
Abdominal discomfort (AD): BL|	0.7 (± 1.43)	0.6 (± 1.10)		
Abdominal discomfort change from BL @W12|	-0.1 (± 1.66)	-0.1 (± 0.85)		
Abdominal discomfort change from BL @W24|	0.0 (± 1.15)	-0.3 (± 0.71)		
Abdominal discomfort change from BL @W48|	0.0 (± 0.00)	999 (± 999)		
AD: change from BL @ EOT|	0.1 (± 0.92)	0.3 (± 1.40)		
Night sweat (NS): Baseline (BL)|	0.7 (± 1.07)	1.1 (± 1.45)		
Night sweat change from BL @W12|	-0.1 (± 0.71)	-0.3 (± 1.29)		
Night sweat change from BL @W24|	0.5 (± 1.45)	-0.7 (± 1.41)		
Night sweat change from BL @W48|	-0.3 (± 0.58)	999 (± 999)		
Night Sweat: change from BL @ EOT|	0.0 (± 0.85)	0.3 (± 2.12)		
Itching (Pruritus):BL|	0.9 (± 1.42)	0.6 (± 0.93)		
Itching (Pruritus): change from BL @W12|	-0.3 (± 0.67)	0.1 (± 1.45)		
Itching (Pruritus): change from BL @W24|	0.4 (± 0.77)	-0.3 (± 1.22)		
Itching (Pruritus): change from BL @W48|	-1.0 (± 1.73)	999 (± 999)		
Itching: change from BL @ EOT|	0.1 (± 1.03)	0.4 (± 1.75)		
Bone Pain: BL|	0.9 (± 1.35)	0.9 (± 1.33)		
Bone Pain: change from BL @W12|	-0.4 (± 1.01)	0.3 (± 1.56)		
Bone Pain: change from BL @W24|	-0.2 (± 1.17)	-0.8 (± 1.79)		
Bone Pain: change from BL @W48|	0.7 (± 1.15)	999 (± 999)		
Bone Pain: change from BL @ EOT|	0.1 (± 0.96)	0.6 (± 1.50)		

Pain under ribs on left side (PUROLS): BL|	0.7 (± 1.18)	0.4 (± 0.82)		
PUROLS: change from BL @W12|	0.4 (± 1.01)	0.1 (± 0.76)		
PUROLS: change from BL @W24|	0.0 (± 0.41)	0.1 (± 1.17)		
PUROLS: change from BL @W48|	0.0 (± 0.00)	999 (± 999)		
PUROLS: change from BL @ EOT|	-0.2 (± 0.68)	0.3 (± 1.00)		

Notes:

[2] - Baseline n = 25
Week 12 (n= 19)
Week 24 (n = 13)
Week 48 (n = 3)
EOT (n = 15)

[3] - Baseline n = 24
Week 12 (n= 20)
Week 24 (n = 9)
Week 48 (n = 0)
EOT (n = 16)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change in symptoms from baseline using EQ-5D

End point title	Percentage change in symptoms from baseline using EQ-5D

End point description:

EQ-5D profiles were tabulated at baseline and each scheduled assessment. EQ visual analogue scale values were summarized descriptively by arm for each scheduled visit. The 5 scores for mobility, self-care, usual activities, pain/discomfort and anxiety/depression are all self-explanatory (eg "I have no problems walking" to "I am unable to walk"), except for the following overall health check, where 100 is the best of health, and 0 is the worst health, Only the categories with non-zero counts are presented with these results.

End point type	Secondary

End point timeframe:

From Baseline and assessed every 4 weeks until end of treatment

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Participants				
Mobility- Baseline: No problem|	17	18		
Mobility- Baseline: Slight problems|	4	5		
Mobility- Baseline: Moderate problems|	1	1		
Mobility- Baseline: Extreme problems|	1	0		
Mobility - Week 4:No prob.|	17	14		
Mobility - Week 4: Slight problems|	4	7		
Mobility - Week 4: Moderate problems|	1	2		
Mobility - Week 8: No problem|	17	15		
Mobility - Week 8: Slight problems|	3	6		
Mobility - Week 8: Moderate problems|	0	1		
Mobility - Week 12: No problem|	15	12		
Mobility - Week 12: Slight problems|	4	6		
Mobility - Week 12: Moderate problems|	0	2		
Mobility - Week 16: No problem|	12	10		

Mobility - Week 16: Slight problems|	2	7		
Mobility - Week 16: Moderate problems|	1	0		
Mobility - Week 20: No problem|	12	5		
Mobility - Week 20: Slight problems|	2	6		
Mobility - Week 24: No problem|	12	5		
Mobility - Week 24: Slight problems|	1	3		
Mobility - Week 24: Moderate problems|	0	1		
Mobility - Week 32: No problem|	8	1		
Mobility - Week 32: Slight problems|	0	1		
Mobility - Week 32: Moderate problems|	1	0		
Mobility - Week 40: No problem|	5	0		
Mobility - Week 40: Slight problems|	1	0		
Mobility - Week 48: No problem|	2	0		
Mobility - Week 48: Slight problems|	1	0		
Mobility - EOT: No problem|	11	12		
Mobility - EOT: Slight problems|	4	3		
Mobility - EOT: Moderate problems|	0	1		
Mobility- 30 day safety FU: No problem|	2	3		
Mobility- 30 day safety FU: Slight problems|	1	0		
Self-care - Baseline: No problem|	23	22		
Self-care - Baseline: Slight problems|	0	2		
Self-care - Week 4: No problem|	21	20		
Self-care - Week 4: Slight problems|	0	3		
Self-care - Week 4: Moderate problems|	1	0		
Self-care - Week 8: No problem|	19	21		
Self-care - Week 8: Slight problems|	1	1		
Self-care - Week 12: No problem|	17	19		
Self-care - Week 12: Slight problems|	1	1		
Self-care - Week 12: Moderate problems|	1	0		
Self-care - Week 16: No problem|	15	16		
Self-care - Week 16: Slight problems|	0	1		
Self-care - Week 20: No problem|	14	11		
Self-care - Week 24: No problem|	12	9		
Self-care - Week 24: Slight problems|	1	0		
Self-care - Week 32: No problem|	8	2		
Self-care - Week 32: Slight problems|	1	0		
Self-care - Week 40: No problem|	5	0		
Self-care - Week 40: Slight problems|	1	0		
Self-care - Week 48: No problem|	3	0		
Self-care - EOT: No problem|	14	15		
Self-care - EOT: Slight problems|	1	1		
Self-care - 30 day Safety FU: No problem|	3	3		
Usual activities -Baseline: No problem|	18	21		
Usual activities -Baseline: Slight problems|	4	3		
Usual activities - Baseline: Moderate problems|	1	0		
Usual activities - Week 4: No problem|	20	18		
Usual activities - Week 4: Slight problems|	1	4		

Usual activities - Week 4: Moderate problems|	1	0		
Usual activities - Week 4: Severe problems|	0	1		
Usual activities - Week 8: No problem|	20	18		
Usual activities - Week 8: Slight problems|	0	3		
Usual activities - Week 8: Moderate problems|	0	1		
Usual activities - Week 12: No problem|	16	16		
Usual activities - Week 12: Slight problems|	3	3		
Usual activities - Week 12: Moderate problems|	0	1		
Usual activities - Week 16: No problem|	13	14		
Usual activities - Week 16: Slight problems|	2	3		
Usual activities - Week 20: No problem|	13	9		
Usual activities - Week 20: Slight problems|	1	2		
Usual activities - Week 24: No problem|	12	9		
Usual activities - Week 24: Slight problems|	1	0		
Usual activities - Week 32: No problem|	8	2		
Usual activities - Week 32: Slight problems|	1	0		
Usual activities - Week 40: No problem|	5	0		
Usual activities - Week 40: Slight problems|	1	0		
Usual activities - Week 48: No problem|	3	0		
Usual activities - EOT: No problem|	12	13		
Usual activities -EOT: Slight problems|	3	3		
Usual activities - 30 day Safety FU: No problem|	2	3		
Usual activities - 30 say Safety FU: Slight probs|	1	0		
Pain/Discomfort - Baseline: No problem|	13	11		
Pain/Discomfort - Baseline: Slight problems|	8	12		
Pain/Discomfort - Baseline: Moderate problems|	2	1		
Pain/Discomfort - Week 4: No problem|	11	15		
Pain/Discomfort - Week 4: Slight problems|	10	6		
Pain/Discomfort - Week 4: Moderate problems|	1	2		
Pain/Discomfort - Week 8: No problem|	14	13		
Pain/Discomfort - Week 8: Slight problems|	5	7		
Pain/Discomfort - Week 8: Moderate problems|	1	2		
Pain/Discomfort - Week 12: No problem|	12	10		
Pain/Discomfort - Week 12: Slight problems|	7	6		
Pain/Discomfort - Week 12: Moderate problems|	0	4		
Pain/Discomfort - Week 16: No problem|	9	11		

Pain/Discomfort - WK16: Slight problems|	6	3		
Pain/Discomfort - WK16: Moderate problems|	0	3		
Pain/Discomfort - WK20: No problem|	8	8		
Pain/Discomfort - WK20: Slight problems|	6	3		
Pain/Discomfort - WK24: No problem|	9	7		
Pain/Discomfort - WK24: Slight problems|	4	2		
Pain/Discomfort - WK32: No problem|	7	2		
Pain/Discomfort - WK32: Slight problems|	2	0		
Pain/Discomfort - WK40: No problem|	4	0		
Pain/Discomfort - WK40: Slight problems|	2	0		
Pain/Discomfort - WK48: No problem|	3	0		
Pain/Discomfort - EOT: No problem|	8	10		
Pain/Discomfort - EOT: Slight problems|	7	3		
Pain/Discomfort - EOT: Moderate problems|	0	3		
Pain/Discomfort - 30 day Safety FU: No problem|	1	2		
Pain/Discomfort - 30 day safety FU: Slight probs|	2	0		
Pain/Discomfort - 30 day Safety FU: Moderate probs	0	1		
Anxiety/Depression - Baseline: No problem	14	18		
Anxiety/Depression - Baseline: Slight problems	6	3		
Anxiety/Depression - Baseline: Moderate problems	3	3		
Anxiety/Depression - WK4: No problem	13	15		
Anxiety/Depression - WK4: Slight problems|	7	6		
Anxiety/Depression - WK4: Moderate problems|	2	2		
Anxiety/Depression - WK8: No problem|	11	16		
Anxiety/Depression - WK8: Slight problems|	8	2		
Anxiety/Depression - WK8: Moderate problems|	1	4		
Anxiety/Depression - WK12: No problem|	8	13		
Anxiety/Depression - WK12: Slight problems|	10	3		
Anxiety/Depression -WK12: Moderate problems|	1	4		
Anxiety/Depression - WK16: No problem|	10	10		
Anxiety/Depression - WK16: Slight problems|	5	5		
Anxiety/Depression - WK16: Moderate problems|	0	2		
Anxiety/Depression -WK20: No problem|	10	8		
Anxiety/Depression - WK20: Slight problems|	4	3		

Anxiety/Depression - WK24: No problem|	11	7		
Anxiety/Depression - WK24: Slight problems|	2	2		
Anxiety/Depression - WK32: No problem|	7	2		
Anxiety/Depression - WK32: Slight problems|	2	0		
Anxiety/Depression - WK40: No problem|	5	0		
Anxiety/Depression - WK40: Slight problems	1	0		
Anxiety/Depression - WK48: No problem	3	0		
Anxiety/Depression - EOT: No problem	11	12		
Anxiety/Depression - EOT: Slight probs	4	3		
Anxiety/Depression - EOT: Moderate probs	0	1		
Anxiety/Depression - 30 day Safety FU: No probs	2	2		
Anxiety/Depression-30 day Safety FU: Slight probs	1	0		
Anxiety/Depression-30 day Safety FU: Severe probs|	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

To evaluate the effect of ruxolitinib on overall survival

End point type	Secondary

End point timeframe:

Time from randomization to date of death due to any cause (estimated to be assessed up to 48 months).

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma ruxolitinib concentrations

End point title	Plasma ruxolitinib concentrations

End point description:

Characterize pharmacokinetics (PK)by utilizing a population PK approach.

End point type	Secondary

End point timeframe:

Week 12, Wk 48

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS-2)

End point title	Progression free survival (PFS-2)

End point description:

PFS-2 assessed by 25% increase over new baseline of PFS-1 in any of the following: ● Progressive splenomegaly ● 25 % increase in MF-7 score with absolute score ≥ 30

End point type	Secondary

End point timeframe:

From date of randomization until second disease progression or death, whichever comes first (estimated to be assessed up to 72 months)

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality-adjusted life years from baseline

End point title	Quality-adjusted life years from baseline

End point description:

EQ-5D-5L (EuroQol-5D-5L, is a standardized instrument for measuring health outcomes, is consists of a descriptive system and a visual analogue scale - scores can be summarized into a single index score that provides a simple measure of health for clinical and economic appraisal) The EQ-5D-5L health

states will be converted into index values (utilities) from which the QALY (Quality - adjusted life years) will be calculated. QALY will be summarized descriptively by treatment arm.

End point type	Secondary

End point timeframe:

Change from Baseline compared with schduled study visits at the following intervals every 4 weeks up to week 24, every 8 weeks up to Week 48, every 12 weeks past Wk 48 until End of treatment and 30 day follow up visit

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first progressive splenomegaly (TTPS)

End point title	Time to first progressive splenomegaly (TTPS)

End point description:

Time to first progressive splenomegaly as determined by spleen volume (by Magnetic Resonance Imaging (MRI)/Computed Tomography (CT).

End point type	Secondary

End point timeframe:

From randomization until earliest time to progressive splenomegaly (estimated to be assesed up to 48 months)

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Months	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first symptomatic progression (TTSP)

End point title	Time to first symptomatic progression (TTSP)

End point description:

Time to first symptomatic progression as determined by Myelofibrosis 7 Item Symptom Scale (MF-7)

End point type	Secondary

End point timeframe:

From randomization until symptomatic progression (MF-7)(estimated to be assesed up to 48 months)

End point values	Ruxolitinib (INC424)	Ruxolitinib Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Months	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse Events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit, up to about 48 months.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	PLACEBO

Reporting group description:

PLACEBO

Reporting group title	INC424

Reporting group description:

INC424

Serious adverse events	PLACEBO	INC424	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	2 / 24 (8.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric cancer			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			

subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (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	INC424	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 24 (45.83%)	17 / 24 (70.83%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 24 (12.50%)	3 / 24 (12.50%)	
occurrences (all)	3	0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 24 (8.33%)	0 / 24 (0.00%)	
occurrences (all)	2	0	
Anaemia			
subjects affected / exposed	6 / 24 (25.00%)	7 / 24 (29.17%)	
occurrences (all)	6	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 24 (16.67%)	3 / 24 (12.50%)	
occurrences (all)	4	0	
Pyrexia			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 24 (0.00%)	3 / 24 (12.50%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	
occurrences (all)	2	0	
Pruritus			

subjects affected / exposed	3 / 24 (12.50%)	0 / 24 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 24 (0.00%)	4 / 24 (16.67%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 24 (0.00%)	3 / 24 (12.50%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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 EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results

Notes: