Clinical trial results:
The ReTreatment Trial: A Phase II, open-label, single-arm study of re-treating myelofibrosis patients with ruxolitinib/Jakavi after treatment interruption due to loss of response and/or adverse event.

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2013-004816-22
Trial protocol	ES AT DE IT
Global end of trial date	29 January 2015

Results information

Result version number	v2 (current)
This version publication date	17 August 2016
First version publication date	15 May 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CINC424A2407

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02091752
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,
Scientific contact	Clincal Disclosure Office, Novartis Pharma AG, 41 613241111,

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	29 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 January 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the effect of re-treatment with ruxolitinib on reduction in spleen volume of at least 20% from Baseline, by Week 24.

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	16 September 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Italy: 1
Worldwide total number of subjects	3
EEA total number of subjects	3

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	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients who previously discontinued ruxolitinib due to loss of response and/or AE. Patients were required to have received at least 12 consecutive weeks of treatment with ruxolitinib prior to discontinuation due to AE and/or loss of response were screened to assess their eligibility and enrolled to enter the treatment phase of the trial.

Period 1

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

Arms

Arm title	Ruxolitinib

Arm description:

All participants received ruxolitinib.

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:

Starting dose was based on reason for previous discontinuation of ruxolitinib (i.e. loss of response or AE) and baseline platelet count. For participants who previously discontinued ruxolitinib due to loss of

Number of subjects in period 1	Ruxolitinib
Started	3
Completed	0
Not completed	3
Study terminated by Sponsor	2
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Ruxolitinib
Reporting group description:	
All participants received ruxolitinib.	

Reporting group values	Ruxolitinib	Total	
Number of subjects	3	3	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	1	1	
From 65-84 years	2	2	
85 years and over	0	0	
Age Continuous | Units: Years			
arithmetic mean	68		
standard deviation	± 9.165	-	
Gender, Male/Female Units: Participants			
Female	2	2	
Male	1	1	

End points

End points reporting groups

Reporting group title	Ruxolitinib
Reporting group description:	
All participants received ruxolitinib.	

Primary: Percentage of patients achieving ≥20% reduction from baseline in spleen volume

End point title	Percentage of patients achieving ≥20% reduction from baseline in spleen volume[1]
End point description:	
End point type	Primary
End point timeframe:	
Week 24	

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: Analysis was not done due to a low number of enrolled participants

End point values	Ruxolitinib			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: percentage of participants				

Notes:

[2] - Analysis was not done due to a low number of enrolled participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients achieving ≥35% reduction from baseline in spleen volume

End point title	Percentage of patients achieving ≥35% reduction from baseline in spleen volume
End point description:	
End point type	Secondary
End point timeframe:	
Week 24	

End point values	Ruxolitinib			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: percentage of participants				

Notes:

[3] - Analysis was not done due to a low number of enrolled participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients achieving ≥25% and ≥50% reduction, respectively from baseline, in spleen length

End point title	Percentage of patients achieving ≥25% and ≥50% reduction, respectively from baseline, in spleen length

End point description:

End point type	Secondary

End point timeframe:

Week 24

End point values	Ruxolitinib			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: percentage of participants				

Notes:

[4] - Analysis was not done due to a low number of enrolled participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients achieving ≥25% and ≥50% reduction, respectively, from baseline in total symptom score (MPN-SAF TSS)

End point title	Percentage of patients achieving ≥25% and ≥50% reduction, respectively, from baseline in total symptom score (MPN-SAF TSS)

End point description:

End point type	Secondary

End point timeframe:

Week 24

End point values	Ruxolitinib			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: percentage of participants				

Notes:

[5] - Analysis was not done due to a low number of enrolled participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in spleen length and spleen volume

End point title	Change from baseline in spleen length and spleen volume

End point description:

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ruxolitinib			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: CM				
least squares mean (standard error)	()			

Notes:

[6] - Analysis was not done due to a low number of enrolled participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in MPN-SAF TSS score

End point title	Change from baseline in MPN-SAF TSS score

End point description:

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ruxolitinib			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: units on a scale				

Notes:

[7] - Analysis was not done due to a low number of enrolled participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIC) score

End point title	Patient Global Impression of Change (PGIC) score

End point description:

End point type	Secondary

End point timeframe:

Week 1, Week 24

End point values	Ruxolitinib			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: units on a scale				

Notes:

[8] - Analysis was not done due to a low number of enrolled participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 and EuroQol (EQ)-5D-5L scores

End point title	Change from baseline in European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 and EuroQol (EQ)-5D-5L scores

End point description:

End point type	Secondary

End point timeframe:

Baseline, Day 1, Week 8, Week 12, Week 16, Week 24

End point values	Ruxolitinib			
Subject group type	Reporting group			
Number of subjects analysed	0[9]			
Units: units on a scale				

Notes:

[9] - Analysis was not done due to a low number of enrolled participants.

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 are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Ruxolitinib

Reporting group description:

All participants received ruxolitinib.

Serious adverse events	Ruxolitinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Immune system disorders			
CYTOKINE RELEASE SYNDROME			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
RENAL FAILURE			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
LISTERIOSIS			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Ruxolitinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	7		
Gastrointestinal disorders			
ANAL HAEMORRHAGE			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
ASCITES			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
CONSTIPATION			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
DIARRHOEA			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
VARICES OESOPHAGEAL			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Hepatobiliary disorders PORTAL VEIN THROMBOSIS subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		
Infections and infestations CYSTITIS subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		

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.

The study was terminated due to low enrollment. No analysis was done due to low enrollment.

Notes: