Clinical trial results:
Ruxolitinib versus allogeneic stem cell transplantation for patients with myelofibrosis according to donor availability: A prospective phase II trial (MMM 02 study)

Summary

EudraCT number	2014-005210-28
Trial protocol	DE
Global end of trial date	07 October 2024

Results information

Result version number	v1 (current)
This version publication date	18 October 2026
First version publication date	18 October 2026
Summary attachment (see zip file)	Summary results (MMM 02 Study Synopsis CSR 2025_10_08_.pdf)

Trial information

Trial identification

Sponsor protocol code	MMM02Study

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03333187
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center Hamburg-Eppendorf
Sponsor organisation address	Martinistr. 52, Hamburg, Germany, 20246
Public contact	Study Investigator, University Medical Center Hamburg-Eppendorf , bmt@uke.de
Scientific contact	Study Investigator, University Medical Center Hamburg-Eppendorf , bmt@uke.de

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	07 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 October 2024
Global end of trial reached?	Yes
Global end of trial date	07 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare efficacy in terms of event free survival of allogeneic SCT for patients with myelofibrosis who have a suitable stem cell donor after a 3 months Ruxolitinib induction therapy with patients who lack a suitable stem cell donor and will continue to receive Ruxolitinib.

Protection of trial subjects:

The responsible Investigator ensured that this study was conducted in conformity with the declaration of Helsinki (latest version) and the national laws and regulations. The protocol had been written and the study was conducted according to the ICH Harmonized Tripartite Guideline for Good Clinical Practice, issued by the European Union. The responsible Ethics Committee and the Competent Authority approvals were obtained before starting the trial.
Among other documents the study protocol, the patient information and the informed consent form were initially submitted to the responsible Ethics Committees to request for approval (favorable opinion). In parallel the necessary documents were initially submitted to the Competent Authority (Paul Ehrlich Institute, PEI) for approval.
If any amendments had been necessary during study conduct, they were submitted in the same way.
The beginning (initiation visit) and the end (last patient's last visit) of this trial and all amendments were announced to the appropriated local authority for each study site in accordance with § 67 (1) AMG.
The approval of both, the Ethics Committee and the PEI for each study site was obtained prior to the start of the study. Copies of the original approval documents were immediately sent to the Sponsor and were included in the study report. A list of members of the independent Ethics Committee had also been provided with the final report.

Background therapy:

Ruxolitinib was prescribed and used as directed in the current Summary of Product Characteristics (SmPC).
After enrollment the patient started with Ruxolitinib 2 x 15 mg daily if platelet count was between 100 and 200 x 10E9/L and with 2 x 20 mg daily if platelet count was more than 200 x 10E9/L. If platelet count was between 50 and 100 x 10E9/L the starting dose should be 2 x 5 mg daily. If platelet count dropped to less than 50 x 10E9/L or neutrophil count to less than 0.5 x 10E9/L Ruxolitinib medication should be discontinued until cytopenia was resolved. If after 3 months of treatment no compatible stem cell donor had been found, Ruxolitinib was continued until disease progression or unacceptable side effects as toxicities defined per NCI CTCAE.

Evidence for comparator:

Ruxolitinib continuous therapy: standard treatment for patients with myelofibrosis. The comparator is the current standard therapy, which is well established and supported by clinical guidelines and evidence from multiple studies.

Actual start date of recruitment	21 December 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	Germany: 83
Worldwide total number of subjects	83
EEA total number of subjects	83

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)	60
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

21.12.2016: first study site active; first patient consented: 09.01.2017; end of recruitment phase 31.05.2021. This study was conducted in Germany. 14 study sites were involved.

Pre-assignment

Screening details:

All patients with myelofibrosis (intermediate 2- or high-risk or intermediate 1- with high-risk cytogenetics, or transfusion-dependency, or thrombocytopenia) from each participating center, who are 18 to 70 years of age, were enrolled.

Period 1

Period 1 title	Entered Population
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Entered population (EP)/ Pre-assignment

Arm description:

Entered population (EP) includes all enrolled patients who were eligible to enter the study, whether treated or not. It is used for disposition displays, demographics and baseline characteristics.

Arm type	Entered population before randomisation
Investigational medicinal product name	human allogeneic hematopoietic stem cells (allo-HSC)
Investigational medicinal product code	NA
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

in accordance with routine care

Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	SUB32897
Other name	Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 - 40 mg milligram(s)

Number of subjects in period 1	Entered population (EP)/ Pre-assignment
Started	83
Completed	71
Not completed	12
Donor is from antother EU Member State	5
Terminated during induction therapy	7

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment A: Allogeneic SCT

Arm description:

Allogeneic SCT after 3 months of Ruxolitinib induction therapy

Arm type	Experimental
Investigational medicinal product name	human allogeneic hematopoietic stem cells (allo-HSC)
Investigational medicinal product code	NA
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

in accordance with routine care

Arm title	Treatment B: Ruxolitinib continuous therapy

Arm description:

Treatment B: Ruxolitinib induction therapy followed by Ruxolitinib continuous therapy

Arm type	Active comparator
Investigational medicinal product name	human allogeneic hematopoietic stem cells (allo-HSC)
Investigational medicinal product code	NA
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

in accordance with routine care

Investigational medicinal product name	Ruxolitinib
Investigational medicinal product code	SUB32897
Other name	Jakavi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 - 40 mg milligram(s)

Number of subjects in period 2	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy
Started	57	14
Completed	39	4
Not completed	18	10
Patient´s decision	1	-
Toxicity	-	1
Other	8	4
Disease Progression	9	5

Baseline characteristics

Reporting groups

Reporting group title	Entered Population

Reporting group description: -

Reporting group values	Entered Population	Total	
Number of subjects	83	83	
Age categorical Units: Subjects			
24 - 70 years	83	83	
Age continuous Units: years			
arithmetic mean	58		
standard deviation	± 9.7	-	
Gender categorical Units: Subjects			
Female	26	26	
Male	57	57	
Disease classification IPSS Units: Subjects			
High-risk	5	5	
Intermediate 1	6	6	
Intermediate 2	17	17	
Missing	55	55	
Disease classification DIPSS Units: Subjects			
High (5-6)	9	9	
Intermediate 1 - risk (1-2)	14	14	
Intermediate 2 - risk (3-4)	51	51	
Missing	9	9	
Disease History - Type of Myelofibrosis Units: Subjects			
Primary Myelofibrosis (PMF)	59	59	
Post Essential Thrombocythemia Myelofibrosis (Post	14	14	
Post Polycythemia Vera Myelofibrosis (Post PV MF)	10	10	

End points

End points reporting groups

Reporting group title	Entered population (EP)/ Pre-assignment
Reporting group description:	
Entered population (EP) includes all enrolled patients who were eligible to enter the study, whether treated or not. It is used for disposition displays, demographics and baseline characteristics.	
Reporting group title	Treatment A: Allogeneic SCT
Reporting group description:	
Allogeneic SCT after 3 months of Ruxolitinib induction therapy	
Reporting group title	Treatment B: Ruxolitinib continuous therapy
Reporting group description:	
Treatment B: Ruxolitinib induction therapy followed by Ruxolitinib continuous therapy	

Primary: Event free survival (EFS) at 3 years after allogeneic SCT compared to Ruxolitinib continuous therapy in patients without a suitable donor.

End point title	Event free survival (EFS) at 3 years after allogeneic SCT compared to Ruxolitinib continuous therapy in patients without a suitable donor.[1]

End point description:

Event-free survival (EFS) was defined as the probability of being alive with no sign of relapse or progression and without changing therapy. The associated time span was defined as the interval from Day 0 (inclusion into the study, that is, assessment date of eligibility) to relapse or progression or death due to any cause or change of therapy whatever comes first. A progress, a relapse, death from any cause and a change of therapy will be considered as an event. Patients without an event are censored at the last time without indication of an event.

The primary efficacy analysis was performed in the Full Analysis Set. The asymptotic Z-test will be used to test for differences in the 3 year EFS rates measured by Kaplan-Meier method. Cox model, log-rank test and Kaplan-Meier survival analysis was used to determine the hazard ratio, p-values, risk estimates and related measures for time-to-event endpoints (event-free survival, overall survival).

End point type	Primary

End point timeframe:

3 years

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: Please refer to: End point description

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	14		
Units: Survival probability				
number (not applicable)	0.744	0.144		

Attachments (see zip file)	Event free survival/MMM 02 Study Primary Endpoint.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival at 3 years after allogeneic SCT compared to Ruxolitinib continuous therapy in patients without a suitable donor

End point title	Overall survival at 3 years after allogeneic SCT compared to Ruxolitinib continuous therapy in patients without a suitable donor

End point description:

Overall survival at 3 years
will was compared between the two treatment groups "SCT" and "ContRuxo" in the same way as primary analysis of the primary endpoint.
Overall survival (OS) was defined as the probability of surviving a specific time. Survival time was defined as the time span from Day 0 to death due to any cause. Patients alive are censored at their last follow-up.
Population: FAP

End point type	Secondary

End point timeframe:

3 years

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	14		
Units: days				
median (full range (min-max))	1231 (173 to 1439)	1176 (169 to 1253)		

Attachments (see zip file)	Overall survival/MMM 02 Study Secondary Endpoint 1.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Spleen reduction after 3 months Ruxolitinib induction therapy (the effect on spleen size will be analyzed according to the pretreatment versus no pretreatment of Ruxolitinib prior to study inclusion)

End point title	Spleen reduction after 3 months Ruxolitinib induction therapy (the effect on spleen size will be analyzed according to the pretreatment versus no pretreatment of Ruxolitinib prior to study inclusion)

End point description:

Change in percentage of patients with spleen response (spleen volume reduction) from before Ruxolitinib induction therapy to after 3 months from start of Ruxolitinib induction therapy
was tested by McNemar's test.
Population: SP
Analysis not conducted since spleen response not determined at before Ruxolitinib induction therapy

End point type	Secondary

End point timeframe:
3 month

End point values	Entered population (EP)/ Pre-assignment			
Subject group type	Reporting group			
Number of subjects analysed	83[2]			
Units: Number of patients	0			

Notes:

[2] - Analysis not conducted since spleen response not determined at before Ruxolitinib induction therapy.

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement of constitutional symptoms (Loose of weight and night sweat) after 3 months Ruxolitinib induction therapy (the effect on constitutional symptoms will be analyzed according to the pretreatment versus no pretreatment of Ruxolitinib prior to stud

End point title	Improvement of constitutional symptoms (Loose of weight and night sweat) after 3 months Ruxolitinib induction therapy (the effect on constitutional symptoms will be analyzed according to the pretreatment versus no pretreatment of Ruxolitinib prior to stud

End point description:

Change in constitutional symptoms
from before Ruxolitinib induction therapy to after 3 months from start of Ruxolitinib induction therapy, in particular
a) Change in weight
was tested by a paired t-test and
b) Change in number of sweats per night
was tested by Wilcoxon signed-rank test (number of night sweats is defined as a score (0=absent, 1, 2, …, 10, 11=worst imaginable)
Population: SP

End point type	Secondary

End point timeframe:
3 month

End point values	Entered population (EP)/ Pre-assignment			
Subject group type	Reporting group			
Number of subjects analysed	74[3]			
Units: Kg				
arithmetic mean (confidence interval 95%)				
Change in weigh	2.443 (1.605 to 3.281)			

Notes:
[3] - Safety Population

Attachments (see zip file)	Change in constitutional symptoms/MMM 02 Study Secondary

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement of bone marrow fibrosis after 3 months of Ruxolitinib induction therapy

End point title	Improvement of bone marrow fibrosis after 3 months of Ruxolitinib induction therapy

End point description:

Change in grading of bone marrow fibrosis
from before Ruxolitinib induction therapy to after 3 months from start of Ruxolitinib induction therapy was tested by Wilcoxon signed-rank test (there are 4 gradings of bone marrow fibrosis: MF-0, MF-1, MF-2, MF-3, MF-4)
Population: SP

End point type	Secondary

End point timeframe:

3 month

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[4]	8[5]		
Units: Number of patients				
Baseline MF-1	1	1		
Baseline MF-2	13	4		
Baseline MF-3	23	3		
After 3 month of induction MF-1	3	1		
After 3 month of induction MF-2	13	3		
After 3 month of induction MF-3	21	4		

Notes:
[4] - Safety Population
[5] - Safety Population

Attachments (see zip file)	Change in grading of bone marrow/MMM 02 Study Secondary

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of acute graft-versus-host disease on Day +100 after

allogeneic SCT according to the Glucksberg scale revised by Przepiorka et al.

End point title	Incidence of acute graft-versus-host disease on Day +100 after allogeneic SCT according to the Glucksberg scale revised by Przepiorka et al.

End point description:

Incidence of acute graft-versus-host disease on Day +100 after allogeneic SCT according to the Glucksberg scale revised by Przepiorka et al. was evaluated by means of estimating cumulative incidence functions.

Cumulative incidence functions was estimated for the competing events
• any acute GvHD and
• death before any acute GvHD
and if possible
cumulative incidence functions was estimated for the competing events
• acute GvHD of grade 0-II and
• death before acute GvHD of grade 0-II
and if possible
cumulative incidence functions was estimated for the competing events
• acute GvHD of grade III-IV and
• death before acute GvHD of grade III-IV.
Population: FAP_SCT

End point type	Secondary

End point timeframe:

day + 100

End point values	Treatment A: Allogeneic SCT			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Proportion				
number (confidence interval 95%)				
Any acute GvHD	0.411 (0.280 to 0.536)			
Death before any acute GcHD	0 (0 to 0)			

Attachments (see zip file)	actute GVHD/MMM 02 Study Secondary Endpoint 5.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of chronic graft-versus-host disease according to the NIH consensus criteria of Filipovich et al. at 1, 2 and 3 years after allogeneic SCT

End point title	Incidence of chronic graft-versus-host disease according to the NIH consensus criteria of Filipovich et al. at 1, 2 and 3 years after allogeneic SCT

End point description:

Incidence of chronic graft-versus-host disease according to the NIH consensus criteria of Filipovich et al. at 1, 2 and 3 years after allogeneic SCT.
For chronic GvHD relapse and death are competing events.
Cumulative incidence functions will be estimated for the competing events
• any chronic GvHD
• relapse before any chronic GvHD

• death before any chronic GvHD
Population: FAP_SCT

End point type	Secondary

End point timeframe:

1, 2 and 3 years after allogeneic SCT

End point values	Treatment A: Allogeneic SCT			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Proportion				
number (confidence interval 95%)				
1 year: any chronic GvHD	0.499 (0.358 to 0.625)			
1 year: relapse before any chronic GvHD	0.091 (0.033 to 0.186)			
1 year: death before any chronic GvHD	0.037 (0.007 to 0.115)			
2 years: Any chronic GvHD	0.575 (0.429 to 0.696)			
2 years: relapse before any chronic GvHD	0.091 (0.033 to 0.186)			
2 years: death before any chronic gvHD	0.037 (0.007 to 0.115)			
3 years: any chronic GvHD	0.634 (0.486 to 0.750)			
3 years: relapse before any chronic GvHD	0.151 (0.069 to 0.262)			
3 years: death before any chronic GvHD	0.037 (0.007 to 0.115)			

Attachments (see zip file)	Incidence of chronic graft-versus-host disease/MMM 02 Study

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity of Ruxolitinib scored according to NCI CTCAE, Version 4.0

End point title	Toxicity of Ruxolitinib scored according to NCI CTCAE, Version 4.0

End point description:

Toxicity of Ruxolitinib scored according to NCI CTCAE, Version 4.0 will be evaluated as a safety endpoint in section 10.8.3 on the SP population.

End point type	Secondary

End point timeframe:

study period

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[6]	14[7]		
Units: patients				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Notes:

[6] - Not provided. Please refer to SAE section.

[7] - Not provided. Please refer to SAE section.

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity of conditioning therapy scored according to NCI CTCAE, Version 4.0

End point title	Toxicity of conditioning therapy scored according to NCI CTCAE, Version 4.0

End point description:

Toxicity of conditioning therapy scored according to NCI CTCAE, Version 4.0 will be evaluated as a safety endpoint in section 10.8.3 on the SP population.

End point type	Secondary

End point timeframe:

study period

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[8]	14[9]		
Units: patients				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Notes:

[8] - Not provided. Please refer to SAE section.

[9] - Not provided. Please refer to SAE section.

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative incidence of relapse at 3 years after allogeneic SCT

End point title	Cumulative incidence of relapse at 3 years after allogeneic SCT

End point description:

Cumulative incidence of relapse at 3 years after allogeneic SCT
Cumulative incidence of relapse was defined as the probability of having had a relapse before or at time t.

End point type	Secondary

End point timeframe:

3 years

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	14		
Units: Proportion				
number (not applicable)	0.183	0.563		

Attachments (see zip file)	Cumulative incidence of relapse/MMM 02 Study Secondary

Statistical analyses

No statistical analyses for this end point

Secondary: Disease-related mortality at 3 years after allogeneic SCT and Ruxolitinib continuous therapies

End point title	Disease-related mortality at 3 years after allogeneic SCT and Ruxolitinib continuous therapies

End point description:

Disease-related mortality
at 3 years
was compared between the two treatment groups “SCT” and “ContRuxo” in the same way as the primary endpoint.
A CRF field (with the following two checkboxes: disease related and non-disease related) will ask for the reason of death. Depending on this the cumulative distribution functions for the two competing events will be calculated. Patients alive was censored at last contact similar to all other analyses.
Population: FAP

End point type	Secondary

End point timeframe:

3 years after allogeneic SCT

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	14		
Units: Proportion				
number (not applicable)				
Disease-related mortality	0.093	0.171		
Relapse	0.099	0.400		

Attachments (see zip file)	Incidence of Disease-related mortality/MMM 02 Study

Statistical analyses

No statistical analyses for this end point

Secondary: Non-relapsed mortality at 1 and 3 years after allogeneic SCT and Ruxolitinib continuous therapy

End point title	Non-relapsed mortality at 1 and 3 years after allogeneic SCT and Ruxolitinib continuous therapy

End point description:

Non-relapse mortality
Non-relapse mortality (NRM) was defined as the probability of dying without previous occurrence of a relapse. The associated time span was defined as the interval from Day 0 to death without previous relapse. Patients alive without relapse are censored at last contact. Relapse was considered a competing event. A relapse (first relapse) was experienced for a patient
• in the "SCT"-arm if = Relapse or Progressive disease
• in the "ContRuxo"-arm if change of therapy is documented as a valid date in CRF-form called "Ruxo-Discontinuation".

End point type	Secondary

End point timeframe:

1 year and 3 years after allogeneic SCT and Ruxolitinib continuous therapy

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	14		
Units: Proportion				
number (not applicable)				
100 days non-relapse mortatlity	0.000	0.000		
100 days Relapse	0.018	0.214		
1 year non-relapse mortality	0.055	0.000		
1 year relapse	0.107	0.476		

Attachments (see zip file)	Incidence of non-relapse mortality/MMM 02 Study Secondary

Statistical analyses

No statistical analyses for this end point

Secondary: Discontinuation rate at 3 years after Ruxolitinib continuous therapy (End of study)

End point title	Discontinuation rate at 3 years after Ruxolitinib continuous therapy (End of study)

End point description:

Discontinuation rate
at 3 years after Ruxolitinib continuous therapy (End of study)
were compared between the two treatment groups "SCT" and "ContRuxo" descriptively by means of

Kaplan Meier curves. The associated time span was defined as the interval from Day 0 (inclusion into the study, that is, assessment date of eligibility) to study discontinuation (documented in the End-of-study form). Patients not having discontinued the study were censored at their last follow-up.
Population: FAP

End point type	Secondary

End point timeframe:

3 years after start of continuous Ruxolitinib therapy (End of study)

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	14		
Units: Proportion				
number (not applicable)	0.789	0.714		

Attachments (see zip file)	Discontinuation rate/MMM 02 Study Secondary Endpoint 12.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of Sorror Risk Score on outcome after allogeneic SCT

End point title	Evaluation of Sorror Risk Score on outcome after allogeneic SCT

End point description:

The impact of the comorbidity-index (HCT-CI) according to Sorror on event-free survival were be assessed by a Cox model with comorbidity-index HCT-CI as continuous covariate and treatment as categorical covariate.
Population: FAP

End point type	Secondary

End point timeframe:

after allogeneic SCT

End point values	Entered population (EP)/ Pre-assignment			
Subject group type	Reporting group			
Number of subjects analysed	71[10]			
Units: Hazard Ratio				
number (confidence interval 95%)				
SCT	0.289 (0.115 to 0.726)			
HCT-CI	1.391 (1.119 to 1.729)			

Notes:
[10] - Full Analysis Population

Attachments (see zip file)	Evaluation of Sorror Score/MMM 02 Study Secondary Endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of chimerism on relapse incidence after allogeneic SCT

End point title	Impact of chimerism on relapse incidence after allogeneic SCT

End point description:

To assess the impact of chimerism on incidence of relapse after allogeneic SCT.
Complete donor chimerism was defined as more than 95% of haematopoietic cells derived from the donor, that is, if for a patient i_chim-bone-res >= 95% in the form f_chimerism then this patient is considered to be a patient with "complete chimerism".
Else if i_chim-bone-res < 95% then this patient is considered to be a patient with "mixed chimerism".
The frequency of SCT-patients with complete and mixed chimerism were shown in a table. Additionally, the frequency of SCT-patients with complete chimerism and relapse as well as patients with mixed chimerism and relapse were summarised in a table.

End point type	Secondary

End point timeframe:

Follow-up after SCT

End point values	Treatment A: Allogeneic SCT			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Number of patients				
Patient chimerism status: Complete chimerism	30			
Patient chimerism status: Mixed chimerism	3			
Patient chimerism status: Missing	24			
Patient with complete chimerism and relapse: yes	4			
Patient with complete chimerism and relapse: no	35			
Patient with complete chimerism and relapse: miss.	18			
Patient with mixed chimerism and relapse: no	39			
Patient with mixed chimerism and relapse: missing	18			

Attachments (see zip file)	Impact of chimerism/MMM 02 Study Secondary Endpoint 14.

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of bone marrow fibrosis regression after allogeneic SCT at 30 days, 100 days, 1 year, and 3 years

End point title	Evaluation of bone marrow fibrosis regression after allogeneic SCT at 30 days, 100 days, 1 year, and 3 years

End point description:

Evaluation of grading of bone marrow fibrosis
from baseline to

after allogeneic SCT + 30d
after allogeneic SCT + 100d
after allogeneic SCT + 1 year
after allogeneic SCT + 3 years
were shown by frequency tables and descriptive statistics (n Mean standard deviation (SD) coefficient of variation (CV) Min Median Max) by treatment group and visit. (There are 4 gradings of bone marrow fibrosis: MF-0, MF-1, MF-2, MF-3, MF-4).
Population: FAP

End point type	Secondary

End point timeframe:

after allogeneic SCT at 30 days, 100 days, 1 year, and 3 years

End point values	Treatment A: Allogeneic SCT			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Number of patients				
Allogeneic SCT day +30 days: MF-0	5			
Allogeneic SCT day +30 days: MF-1	9			
Allogeneic SCT day +30 days: MF-2	10			
Allogeneic SCT day +30 days: MF-3	9			
Allogeneic SCT day +30 days: Missing	24			
Allogeneic SCT day +100 days: MF-0	6			
Allogeneic SCT day +100 days: MF-1	11			
Allogeneic SCT day +100 days: MF-2	7			
Allogeneic SCT day +100 days: MF-3	8			
Allogeneic SCT day +100 days: Missing	25			
Allogeneic SCT day +1 year: MF-0	18			
Allogeneic SCT day +1 year: MF-1	4			
Allogeneic SCT day +1 year: MF-2	3			
Allogeneic SCT day +1 year: MF-3	3			
Allogeneic SCT day +1 year: Missing	29			
Allogeneic SCT day +3 years: MF-0	8			
Allogeneic SCT day +3 years: MF-1	2			
Allogeneic SCT day +3 years: Missing	46			

Attachments (see zip file)	Evaluation of bone marrow fibrosis regression/MMM 02 Study

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of bone marrow fibrosis regression after Ruxolitinib continuous therapy at 30 days, 100 days, 1 year and 3 years

End point title	Evaluation of bone marrow fibrosis regression after Ruxolitinib continuous therapy at 30 days, 100 days, 1 year and 3 years

End point description:

Evaluation of grading of bone marrow fibrosis
from baseline to
after 2 months of Ruxolitinib continuous therapy
after 4 months of Ruxolitinib continuous therapy
after 1 year of Ruxolitinib continuous therapy
after 3 years of Ruxolitinib continuous therapy
were shown by frequency tables and descriptive statistics (n Mean standard deviation (SD) coefficient of variation (CV) Min Median Max) by treatment group and visit. (There are 4 gradings of bone marrow fibrosis: MF-0, MF-1, MF-2, MF-3, MF-4).
Population: FAP

End point type	Secondary

End point timeframe:

after Ruxolitinib continuous therapy at 30 days, 100 days, 1 year and 3 years

End point values	Treatment B: Ruxolitinib continuous therapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Number of patients				
After 2 months of Ruxo. con. therapy: MF-1	1			
After 2 months of Ruxo. con. therapy: MF-2	1			
After 2 months of Ruxo. con. therapy: MF-3	2			
After 2 months of Ruxo. con. therapy: Missing	10			
After 4 months of Ruxo. con. therapy: MF-3	3			
After 4 months of Ruxo. con. therapy: missing	11			
After 1 year of Ruxo. con. therapy: MF-1	1			
After 1 year of Ruxo. con. therapy: missing	13			

After 3 year of Ruxo. con. therapy: missing	14			

Attachments (see zip file)	Evaluation of bone marrow fibrosis regression/MMM 02 Study

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of QoL (FACT-BMT) and QoL Myeloproliferated neoplasm (MPN) before Ruxolitinib induction therapy (= baseline), at transplantation, and after transplantation at 6 months, 1 year, 2 years and 3 years

End point title	Evaluation of QoL (FACT-BMT) and QoL Myeloproliferated neoplasm (MPN) before Ruxolitinib induction therapy (= baseline), at transplantation, and after transplantation at 6 months, 1 year, 2 years and 3 years

End point description:

The Quality of Life Score Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS)
before Ruxolitinib induction therapy (= baseline),
after 3 months of Ruxolitinib induction therapy
at transplantation (for "SCT" arm)
at 6 months
1 year
2 years and
3 years
were evaluated with frequency tables by study arms ("ContRuxo", "SCT", "Not Assigned") and visit.
Population: FAP

End point type	Secondary

End point timeframe:

before Ruxolitinib induction therapy (= baseline), at transplantation, and after transplantation at 6 months, 1 year, 2 years and 3 years

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	14		
Units: Number of patients				
Before induction therapy: Score 0	3	0		
Before induction therapy: Score 1	5	2		
Before induction therapy: Score 2	11	2		
Before induction therapy: Score 3	8	0		
Before induction therapy: Score 4	10	2		
Before induction therapy: Score 5	10	4		
Before induction therapy: Score 6	5	1		
Before induction therapy: Score 7	1	2		
Before induction therapy: Score 8	1	0		
Before induction therapy: Score NA	1	1		

Before induction therapy: missing	2	0		
After 3 Month induction therapy: Score 0	1	1		
After 3 Month induction therapy: Score 1	8	4		
After 3 Month induction therapy: Score 2	11	0		
After 3 Month induction therapy: Score 3	8	2		
After 3 Month induction therapy: Score 4	7	2		
After 3 Month induction therapy: Score 5	4	2		
After 3 Month induction therapy: Score 6	3	1		
After 3 Month induction therapy: Score 7	2	1		
After 3 Month induction therapy: Score 8	1	0		
After 3 Month induction therapy: Score 9	1	0		
After 3 Month induction therapy: missing	11	1		
After 1 year SCT or Cont. Ruxo.: Score 0	7	0		
After 1 year SCT or Cont. Ruxo.: Score 1	9	2		
After 1 year SCT or Cont. Ruxo.: Score 2	6	2		
After 1 year SCT or Cont. Ruxo.: Score 3	6	1		
After 1 year SCT or Cont. Ruxo.: Score 4	4	0		
After 1 year SCT or Cont. Ruxo.: Score 5	1	0		
After 1 year SCT or Cont. Ruxo.: Score 6	1	0		
After 1 year SCT or Cont. Ruxo.: Score 7	0	1		
After 1 year SCT or Cont. Ruxo.: Score 8	2	0		
After 1 year SCT or Cont. Ruxo.: Score 9	1	0		
After 1 year SCT or Cont. Ruxo.: missing	20	8		
After 3 years SCT or Cont. Ruxo.: Score 0	6	0		
After 3 years SCT or Cont. Ruxo.: Score 1	11	0		
After 3 years SCT or Cont. Ruxo.: Score 2	2	1		
After 3 years SCT or Cont. Ruxo.: Score 3	2	1		
After 3 years SCT or Cont. Ruxo.: missing	36	12		

Attachments (see zip file)	Evaluation of QoL /MMM 02 Study Secondary Endpoint 17.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of QoL (FACT-BMT) and QOL (MPN-SAF-TSS) before Ruxolitinib induction therapy (= baseline), at confinement to Ruxolitinib continuous therapy and after confinement at 6 months, 1 year, 2 years and 3 years

End point title	Evaluation of QoL (FACT-BMT) and QOL (MPN-SAF-TSS) before Ruxolitinib induction therapy (= baseline), at confinement to Ruxolitinib continuous therapy and after confinement at 6 months, 1 year, 2 years and 3 years

End point description:

The Quality of Life Score Functional Assessment of Cancer Therapy - Bone Marrow Transplant (FACT-BMT) Score
before Ruxolitinib induction therapy (= baseline),
after 3 months of Ruxolitinib induction therapy
at transplantation
at 6 months
1 year
2 years and
3 years
were evaluated with frequency tables for the study arm "SCT by visit.
Population: FAP_SCT

End point type	Secondary

End point timeframe:

after confinement at 6 months, 1 year, 2 years and 3 years

End point values	Treatment A: Allogeneic SCT	Treatment B: Ruxolitinib continuous therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[11]	14[12]		
Units: patients				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Notes:

[11] - Analysis not conducted

[12] - Analysis not conducted

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Beside the defined expections of AEs all AE within the study period will be recorded in the eCRF. SAE reporting timeframe for this study begins after consenting to study participation until 28 days after SCT or 3 cycles of Ruxolitinib continuous therapy.

Adverse event reporting additional description:

After SCT the following events are not considered as AE and are therefore not recorded in the eCRF, but a detailed documentation in the patient's record (source data) is mandatory:
• Cytopenia until day +100 post transplantation
• Nausea, alopecia, vomiting, or constipation until day +100 post transplantation
• CTCAE grade 1 and 2
[...]

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Continuous Ruxolitinib

Reporting group description:

Comparator arm. Safety Population (SP)

Reporting group title	Allogeneic SCT Arm

Reporting group description:

Test arm. Safety Population (SP)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Only SAE are presented.

Serious adverse events	Continuous Ruxolitinib	Allogeneic SCT Arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 16 (31.25%)	32 / 64 (50.00%)	
number of deaths (all causes)	2	9	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myelofibrosis			
subjects affected / exposed	2 / 16 (12.50%)	4 / 64 (6.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma			

subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Orthostatic hypertension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Disease progression			
subjects affected / exposed	3 / 16 (18.75%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Chronic graft versus host disease			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Organising pneumonia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
General physical condition abnormal			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Graft complication			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Spinal fracture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
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			
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 16 (0.00%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis cytomegalovirus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye infection			

subjects affected / exposed	1 / 16 (6.25%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Staphylococcal infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxoplasmosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tuberculosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 64 (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			
Hyperglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Continuous Ruxolitinib	Allogeneic SCT Arm	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 16 (0.00%)	0 / 64 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 August 2017	Due to official instructions the protocol version 3.0 was revised: - Restriction due to the origination of the allo-HSC donor. - In the course of the above mentioned changes inconsistencies have been removed and editorial changes have been made.
25 March 2020	Due to Amendment the protocol version 4.0 was revised: - Recruitment period was prolonged - Inclusion Criteria No. 5 was changed - Insurance company change was adapted

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported