



Clinical trial results:

Efficacy and Safety of Eltrombopag in Patients with Acquired Moderate Aplastic Anemia (EMAA) who are treated with Ciclosporin A

Prospective Randomized Multicenter Study comparing Thrombopoietin-Receptor agonist Eltrombopag with Placebo in Patients with Acquired Moderate Aplastic Anemia who are treated with Ciclosporin A

Summary

EudraCT number	2014-000174-19
Trial protocol	DE FR
Global end of trial date	23 December 2024

Results information

Result version number	v1 (current)
This version publication date	14 February 2026
First version publication date	14 February 2026
Summary attachment (see zip file)	CSR_EMAA-trial (EMAA CSR V1.0_20250727.pdf) Patient characteristics EMAA-trial (Demographic and Baseline characteristics.pdf) SAE_listing_EMAA-trial (SAE classified by organ system.pdf) AE_listing_EMAAtrial (TEAEs with organ system classification.pdf)

Trial information

Trial identification

Sponsor protocol code	EMAA study / 9345
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02773225
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Ulm
Sponsor organisation address	Albert-Einstein-Allee 29, Ulm, Germany, 89081
Public contact	Britta Höchsmann, Universitätsklinikum Ulm, 0049 731150560, b.hoechsmann@blutspende.de
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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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	08 January 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 December 2024
Global end of trial reached?	Yes
Global end of trial date	23 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this trial is to improve treatment of Moderate Aplastic Anemia (MAA) by evaluating the safety and efficiency of Eltrombopag as a new treatment option in patients with MAA requiring therapy.

The primary objective of this trial is the evaluation of the superiority of Eltrombopag on top of background treatment with Ciclosporin (CSA) regarding hematologic response (PR +CR) at 6 months in comparison with treatment with CSA alone in untreated MAA patient.

Protection of trial subjects:

In general examinations (especially bone marrow punctures) was reduced to as few as possible to minimize pain and distress of the patients. For early detection of patient complaints patient diary and quality of life questionnaires was used in a regular manner.

Safety assessment before start and during therapy were:

- collection of demographic data and medical history
- complete physical examination
- Full blood count with WBC differential and microscopic peripheral blood count
- Reticulocyte count
- blood samples for blood chemistry and coagulation profile: creatinine, urea, uric acid, glucose, LDH, AST, ALT, γ-GT, AP, protein, bilirubin (direct and total), INR, PTT, CSA trough level
- blood samples for GPI-deficiency
- bone marrow histology and cytology, cytogenetics
- Quality of Life instruments
- ophthalmologic examination (cataract)
- electrocardiogram, QT-time
- in female patients of childbearing potential, a pregnancy test has to be performed with a negative result before inclusion in the study
- pregnancy test may be repeated at each visit within the discretion of the investigator

These investigations were conducted because they enable the early detection of possible adverse events caused by the study or background therapy or the disease itself.

Suspected adverse events of Eltrombopag are hepatotoxicity, thrombotic/thromboembolic complications, cataract, bleeding after discontinuation of Eltrombopag, bone marrow reticuline formation, risk of bone marrow fibrosis, malignancies. Suspected adverse events due to aplastic anemia are cytopenias with clinical symptoms like bleedings, infections, anemia and clonal evolution. Suspected adverse events due to CSA are renal dysfunction, hypertension, hepatotoxicity, neurotoxicity, skin abnormalities, hirsutism, gum hyperplasia, malignancies, infections, hypomagnesemia and hyperkalemia, increases in uric acid, dose related hyperbilirubinemia, modest increase of serum triglycerides or cholesterol.

Background therapy:

Cyclosporin A

Evidence for comparator:

Eltrombopag is an oral thrombopoietin mimetic that binds to c-MPL, promoting mega-karyopoiesis and release of platelets from mature megakaryocytes and has been approved for SAA refractory to immunosuppressive therapy by the Food and Drug Administration (FDA) in 2014 and the European Medicines Agency (EMA) in 2015. This decision was based on long-term data regarding to safety and efficacy of a phase II study in SAA patients. This data raises also the hope for thrombopoietin as an effective new therapeutic option in patients with MAA.

We hypothesize that there might be a higher rate of patients responding to Eltrombopag in a group of therapy naïve AA patients, especially in MAA. Furthermore, we assume that the addition of Eltrombopag to the routinely used immunosuppression CSA might lead to a further increase of the remission rates.

Thus, we see a strong need for more data regarding efficacy and tolerability of Eltrombopag in Aplastic Anemia in order to clarify the role of Eltrombopag within standard treatment of Aplastic Anemia, especially in Moderate Aplastic Anemia.

Therefore, we considered a blinded comparison between immunosuppressive therapy (CSA + placebo) and the addition of eltrombopag to immunosuppressive therapy (CSA + eltrombopag) to be logical for improving the treatment of MAA patients.

In the meantime data of a combination therapy with intensified immunosuppressive therapy (hATG + CSA) and eltrombopag in first line therapy of SAA and VSAA without the option of SCT show a significant benefit for the addition of Eltrombopag to the immunosuppressive therapy without an increase of adverse events. Based on this data Eltrombopag was approved in 2018 by the FDA for the first line treatment of SAA/VSAA in combination with intensified immunosuppressive therapy, which supported our approach

Actual start date of recruitment	01 May 2015
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	Switzerland: 6
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 78
Worldwide total number of subjects	85
EEA total number of subjects	79

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)	59
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 27 May 2015 (First patient first visit (FPFV)) and 09 May 2023 (Last patient first visit (LPFV)) ninety-three (93) patients were enrolled and screened at nine study centers in three countries (France, Germany, Switzerland). 85 patients successfully completed screening and were randomized to one of the two treatment arms.

Pre-assignment

Screening details:

93 patients were screened, 8 were not eligible, 7 because of violation of the inclusion/exclusion criteria, in one case the cause is missing

Pre-assignment period milestones

Number of subjects started	85
Number of subjects completed	85

Period 1

Period 1 title	Blinded Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Subject

Blinding implementation details:

On receipt of the patient registration and randomization form, the patient data were entered in the Electronic Trial Data Base (eCRF). The assignment to either the standard (placebo) or the investigational treatment (eltrombopag) was done by an independent data manager to guarantee that the randomization was separated from the clinical investigators. The ratio of patients included in each arm for placebo versus eltrombopag treatment was 1:1.

Arms

Are arms mutually exclusive?	Yes
Arm title	Verum

Arm description:

Eltrombopag (150 mg) treatment + background therapy with CSA

Arm type	Experimental
Investigational medicinal product name	Eltrombopag 75 mg Tabletten
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg (2 x 75 mg) once daily

Arm title	Placebo
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Arm description:

placebo treatment

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

Dosage and administration details:

2 tablets once daily

Number of subjects in period 1	Verum	Placebo
Started	41	44
Primary endpoint reached, unblinding	35	40
Completed	35	40
Not completed	6	4
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	-
reason unknoww	2	-
completion per protocol	1	-
Unknown reason	-	1
Progressive disease	-	3
disease progression	1	-

Period 2

Period 2 title	Unblinded period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	A: Placebo, no CR

Arm description:

Patient received background therapy with CSA and Placebo in the blinded period and had no CR (complete remission) at the primary endpoint.

Arm type	Active comparator
Investigational medicinal product name	Eltrombopag 75 mg Tabletten
Investigational medicinal product code	Verum, Eltrombopag
Other name	EU/1/10/612/013 Revolade® 75 mg
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg (2 x 75 mg) once daily

Arm title	Arm B: Placebo and CR
Arm description: Arm B: Placebo + Background Therapy (CSA) during blinded period with CR at primary endpoint. No further study treatment after unblinding.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Arm C: Eltrombopag and PR/CR
Arm description: Arm C Patients with Eltrombopag and background therapy in the blinded period and responde with complete or partial remission (PR/CR) at the primary endpoint. Further eltrombopag treatment according the protocoll.	
Arm type	Active comparator
Investigational medicinal product name	Eltrombopag 75 mg Tabletten
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 150 mg (2 x 75 mg) once daily	
Arm title	Arm D: Eltrombopag and non response (NR)
Arm description: Arm D: patients received Eltrombopag and background therapy during the blinded period. At primary endpoint no response. Stop of study treatment and further therapy according to the decision of the treating phycisian	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	A: Placebo, no CR	Arm B: Placebo and CR	Arm C: Eltrombopag and PR/CR
Started	38	2	26
Completed	20	1	20
Not completed	18	1	6
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	2	-	-
Physician decision	3	-	1
per protocol	-	-	-
completion per protocol	7	-	3
Unknown reason	4	-	1
Lost to follow-up	2	1	1

Number of subjects in period 2	Arm D: Eltrombopag and non response (NR)
Started	9
Completed	5
Not completed	4
Adverse event, serious fatal	1

Consent withdrawn by subject	1
Physician decision	-
per protocol	1
completion per protocol	-
Unknown reason	1
Lost to follow-up	-

Baseline characteristics

Reporting groups

Reporting group title	Verum
Reporting group description: Eltrombopag (150 mg) treatment + background therapy with CSA	
Reporting group title	Placebo
Reporting group description: placebo treatment	

Reporting group values	Verum	Placebo	Total
Number of subjects	41	44	85
Age categorical			
The median age of patients was 53 years (range 19-84 years) with 37.6% of them being older than 60 years. Since age plays an important role in the response to therapy for aplastic anemia, it was important for us to ensure a balanced age distribution between the verum and placebo groups during randomization.			
Units: Subjects			
Adults (18-64 years)	29	30	59
From 65-84 years	12	14	26
85 years and over	0	0	0
Gender categorical			
40 patients were female			
Units: Subjects			
Female	18	22	40
Male	23	22	45

End points

End points reporting groups

Reporting group title	Verum
Reporting group description: Eltrombopag (150 mg) treatment + background therapy with CSA	
Reporting group title	Placebo
Reporting group description: placebo treatment	
Reporting group title	A: Placebo, no CR
Reporting group description: Patient received background therapy with CSA and Placebo in the blinded period and had no CR (complete remission) at the primary endpoint.	
Reporting group title	Arm B: Placebo and CR
Reporting group description: Arm B: Placebo + Background Therapy (CSA) during blinded period with CR at primary endpoint. No further study treatment after unblinding.	
Reporting group title	Arm C: Eltrombopag and PR/CR
Reporting group description: Arm C Patients with Eltrombopag and background therapy in the blinded period and responde with complete or partial remission (PR/CR) at the primary endpoint. Further eltrombopag treatment according the protocoll.	
Reporting group title	Arm D: Eltrombopag and non response (NR)
Reporting group description: Arm D: patients received Eltrombopag and background therapy during the blinded period. At primary endpoint no response. Stop of study treatment and further therapy according to the decision of the treating phycisian	

Primary: change in measure response between time point Baseline and time point 6 months'

End point title	change in measure response between time point Baseline and time point 6 months'
End point description: Assessment of hematologic response after 6 months prior to unblinding. The primary objective of this trial is the evaluation of the superiority of Eltrombopag on top of background treatment with Ciclosporin (CSA) regarding hematologic response (PR + CR) at 6 months in comparison with treatment with CSA alone in untreated MAA patient. The primary endpoint of the study is the hematologic response rate (CR + PR) at 6 months.	
End point type	Primary
End point timeframe: Response-rate after 6 months after start of study treatment	

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	40		
Units: percent				
arithmetic mean (confidence interval 95%)	71.4 (54.8 to 83.8)	42.5 (28.5 to 57.8)		

Attachments (see zip file)	Response Rate 6 months/Statistical analysis Primary endpoint
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Statistical analyses

Statistical analysis title	Response rate at 6 months
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Statistical analysis description:

Chi-square test was used to compare categorical variables and the Mann-Whitney U test (nonparametric) or student t-test (parametric) to compare continuous variables. The probability of survival was analyzed using the method of Kaplan and Meier and log rank test. Cumulative incidences were estimated by the multi-stage method by Aalen-Johansen and compared between treatment arms by cox regression. A logistic regression of binary outcomes provided results with respect to the relevant covariate

Comparison groups	Verum v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.05 ^[2]
Method	Fisher exact
Parameter estimate	Cox regression
Point estimate	95
Confidence interval	
level	95 %
sides	1-sided
lower limit	95
Variability estimate	Standard deviation
Dispersion value	5

Notes:

[1] - analysis of primary endpoint based on PPS. Absolute and relative frequency of patients with response (CR or PR) will be derived by treatment arm. Let the counts in the true population denote (Treatment Response: Yes - No; Eltrombopag: n11 - n12; Placebo: n21-n22.

If the hematological response is independent of the treatment arm the odds ratio ($OR = n11 \cdot n22 / (n12 \cdot n21)$.) will be 1. Thus, Fisher's exact test may be interpreted as a test of the OR and is suitable for comparing the frequenc

[2] - P-values ≥ 0.001 reported to 3 decimal places; p-values < 0.001 reported as "< 0.001". Mean, standard deviation and any quantiles other than minimum and maximum, reported to one decimal place greater than the original data.

Secondary: change in measure response between time point Baseline and time point 3 months'

End point title	change in measure response between time point Baseline and time point 3 months'
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End point description:

The secondary objective of this trial is to investigate the impact of Eltrombopag added to background therapy with CSA.

Secondary endpoints are:

- Response rate at 3 months

End point type	Secondary
End point timeframe:	
Change in response rate between start of study treatment and 3 months	

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	44		
Units: percent				
arithmetic mean (confidence interval 95%)	48.8 (34.3 to 63.5)	25.0 (14.4 to 39.6)		

Attachments (see zip file)	Response 3 months/Statistical analysis Secondary endpoint 3
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Statistical analyses

Statistical analysis title	Response rate
Comparison groups	Verum v Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.05
Method	Chi-squared
Parameter estimate	Cox proportional hazard
Point estimate	95
Confidence interval	
level	95 %
sides	1-sided
lower limit	95
Variability estimate	Standard deviation
Dispersion value	5

Secondary: change in measure response between time point Baseline and time point 12 months'

End point title	change in measure response between time point Baseline and time point 12 months'
End point description:	
change in measure response between time point Baseline and time point 12 months	
End point type	Secondary
End point timeframe:	
12 months	

End point values	A: Placebo, no CR	Arm B: Placebo and CR	Arm C: Eltrombopag and PR/CR	Arm D: Eltrombopag and non response (NR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	2	26	9
Units: percent				
number (not applicable)	65.8	50.0	88.5	22.2

Attachments (see zip file)	Response rate after 12 months/Statistical analysis Secondary
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Statistical analyses

Statistical analysis title	Response Rate at 12 months
Statistical analysis description: change in measure response between time point Baseline and time point 12 months'	
Comparison groups	A: Placebo, no CR v Arm B: Placebo and CR v Arm C: Eltrombopag and PR/CR v Arm D: Eltrombopag and non response (NR)
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Cox regression
Point estimate	95
Confidence interval	
level	95 %
sides	1-sided
lower limit	95
Variability estimate	Standard deviation
Dispersion value	5

Secondary: change in measure response between time point Baseline and time point 18 months'

End point title	change in measure response between time point Baseline and time point 18 months'
End point description: The response assessment will be calculated as defined by the response criteria according to the protocol. Additionally, the investigator will classify hematologic response. Both assessments will be evaluated descriptively, but the calculated assessment will be prevailing for hypothesis testing. Proportions of hematological response (CR +PR) will be estimated 18 months after therapy start for each group and study arm. Withdrawals and dropouts in the preceding period since last response assessment will be listed in the descriptive table as "missing response". A comparison between treatment arms (Placebo and Eltrombopag) will be performed after 3, 12 and 18 months after therapy start.	
End point type	Secondary
End point timeframe:	
18 months	

End point values	A: Placebo, no CR	Arm B: Placebo and CR	Arm C: Eltrombopag and PR/CR	Arm D: Eltrombopag and non response (NR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	2	22	5
Units: percent				
number (not applicable)	62.1	50.0	65.4	11.1

Attachments (see zip file)	Response Rate 18 months/Statistical analysis Secondary
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Statistical analyses

Statistical analysis title	Response rate after 18 months
Comparison groups	A: Placebo, no CR v Arm B: Placebo and CR v Arm C: Eltrombopag and PR/CR v Arm D: Eltrombopag and non response (NR)
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Cox regression
Point estimate	95
Confidence interval	
level	95 %
sides	1-sided
lower limit	95
Variability estimate	Standard deviation
Dispersion value	5

Secondary: change in measure relapse between time point Baseline and time point 6 months

End point title	change in measure relapse between time point Baseline and time point 6 months
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End point description:

Clinical relapse is considered as the occurrence of any of the following events in a patient who had shown a hematological response (CR or PR or single lineage response):

- meeting again the criteria for MAA
- renewed transfusion requirement
- decrease in any of the responded peripheral blood counts to the pre-study baseline

Patients who withdrew consent or dropped out after hematological response before the respective visit will be counted as "missing" in descriptive tables. Proportions of relapse will be estimated at 6, 12 and 18 months per treatment arm / group. 95% confidence limits according to Agresti and Coull for the proportions of relapse will be computed.

Only after 6 months from therapy start, the null hypothesis that the OR is 1 will be assessed by Fisher's exact test. The hypothesis will be tested against two-sided alternative at the 5% level of significance

End point type	Secondary
End point timeframe:	
from baseline to 6 months evaluation	

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	40		
Units: percent				
arithmetic mean (confidence interval 95%)	16.7 (6.9 to 34.0)	0 (0 to 0)		

Attachments (see zip file)	Relapse Rate 6 months/Relapse rate at 6.pdf
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Statistical analyses

No statistical analyses for this end point

Secondary: change in measure relapse between time point Baseline and time point 12 months

End point title	change in measure relapse between time point Baseline and time point 12 months
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End point description:

Clinical relapse is considered as the occurrence of any of the following events in a patient who had shown a hematological response (CR or PR or single lineage response):

- meeting again the criteria for MAA
- renewed transfusion requirement
- decrease in any of the responded peripheral blood counts to the pre-study baseline.

Proportions of relapse will be estimated at 6, 12 and 18 months per treatment arm / group. 95% confidence limits according to Agresti and Coull for the proportions of relapse will be computed.

Only after 6 months from therapy start, the null hypothesis that the OR is 1 will be assessed by Fisher's exact test. The hypothesis will be tested against two-sided alternative at the 5% level of significance. A 95% confidence interval for the OR will be provided.

A cox regression will be performed to quantify the relationship between relapse and total dose of Eltrombopag administered. "Age" and "disease severity" will be included in the regression model.

End point type	Secondary
End point timeframe:	
12 months	

End point values	A: Placebo, no CR	Arm B: Placebo and CR	Arm C: Eltrombopag and PR/CR	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	2	26	
Units: percent				
arithmetic mean (confidence interval 95%)	10.7 (2.9 to 28.0)	50.0 (9.5 to 90.5)	38.5 (22.4 to 57.5)	

Attachments (see zip file)	Relapse Rate/Relapse rate at 6.pdf
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Statistical analyses

No statistical analyses for this end point

Secondary: change in measure relapse between time point Baseline and time point 18 months

End point title	change in measure relapse between time point Baseline and time point 18 months
End point description: Clinical relapse is considered as the occurrence of any of the following events in a patient who had shown a hematological response (CR or PR or single lineage response): <ul style="list-style-type: none"> • meeting again the criteria for MAA • renewed transfusion requirement • decrease in any of the responded peripheral blood counts to the pre-study baseline Patients who withdrew consent or dropped out after hematological response before the respective visit will be counted as "missing" in descriptive tables. Proportions of relapse will be estimated at 6, 12 and 18 months per treatment arm / group. 95% confidence limits according to Agresti and Coull for the proportions of relapse will be computed. Only after 6 months from therapy start, the null hypothesis that the OR is 1 will be assessed by Fisher's exact test. The hypothesis will be tested against two-sided alternative at the 5% level of significance	
End point type	Secondary
End point timeframe: 18 months	

End point values	A: Placebo, no CR	Arm B: Placebo and CR	Arm C: Eltrombopag and PR/CR	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	2	22	
Units: percent				
arithmetic mean (confidence interval 95%)	34.6 (19.3 to 53.9)	50.0 (9.5 to 90.5)	38.5 (22.4 to 57.5)	

Attachments (see zip file)	Relapse/Relapse rate at 6.pdf
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Statistical analyses

No statistical analyses for this end point

Secondary: Time to best Single lineage response neutrophils

End point title	Time to best Single lineage response neutrophils
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End point description:

The median time to best trilineage response for patients with response in the FAS population was 8.31 months. The median time to reach single lineage response was 7.08 months (erythroid), 5.52 months (platelet) and 2.91 months (neutrophil). A significant difference between the Placebo and Eltrombopag Arm was observed only for neutrophil response ($p=0.025$),

End point type	Secondary
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End point timeframe:

not special time point, will be measured in this analysis

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	34		
Units: months				
arithmetic mean (standard deviation)	4.13 (\pm 3.62)	6.51 (\pm 4.74)		

Attachments (see zip file)	Secondary endpoint Time to best neutrophil respons/Secondary
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Statistical analyses

No statistical analyses for this end point

Secondary: Time to best hematological response

End point title	Time to best hematological response
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End point description:

The median time to best trilineage response for patients with response in the FAS population was 8.31 months. The median time to reach single lineage response was 7.08 months (erythroid), 5.52 months (platelet) and 2.91 months (neutrophil). A significant difference between the Placebo and Eltrombopag Arm was observed only for neutrophil response ($p=0.025$), see Table

End point type	Secondary
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End point timeframe:

depends on results, time of best response

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	31		
Units: month				
arithmetic mean (standard deviation)	9.35 (\pm 8.21)	10.26 (\pm 6.88)		

Attachments (see zip file)	Secondary endpoint Time to best response/Secondary endpoint
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Statistical analyses

No statistical analyses for this end point

Secondary: Time to best Single lineage response erythrocytes

End point title	Time to best Single lineage response erythrocytes
End point description: The median time to best trilineage response for patients with response in the FAS population was 8.31 months. The median time to reach single lineage response was 7.08 months (erythroid), 5.52 months (platelet) and 2.91 months (neutrophil). A significant difference between the Placebo and Eltrombopag Arm was observed only for neutrophil response (p=0.025),	
End point type	Secondary
End point timeframe: depending on result	

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: months				
arithmetic mean (standard deviation)	8.47 (\pm 7.99)	8.58 (\pm 7.39)		

Attachments (see zip file)	Secondary endpoint Time to best response.pdf
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Statistical analyses

No statistical analyses for this end point

Secondary: Time to best Single lineage response platelets

End point title	Time to best Single lineage response platelets
End point description: Time to best Single lineage response platelets. The median time to best trilineage response for patients with response in the FAS population was 8.31 months. The median time to reach single lineage response was 7.08 months (erythroid), 5.52 months (platelet) and 2.91 months (neutrophil). A significant difference between the Placebo and Eltrombopag Arm was observed only for neutrophil response (p=0.025),	
End point type	Secondary
End point timeframe: depend on results	

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	33		
Units: month				
arithmetic mean (standard deviation)	5.32 (\pm 4.29)	6.89 (\pm 4.17)		

Attachments (see zip file)	Secondary endpoint Single lineage response erythro/Secondary
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of pc units transfused within the first 6 months

End point title	Number of pc units transfused within the first 6 months
End point description: There was no significant difference between the treatment arms in the proportion of patients requiring transfusions (Table 14.2.6.1) and in the number of transfused units. In the FAS population, a median number of 6 units of PC and 7 units of pRBC were transfused within the first 6 months,	
End point type	Secondary
End point timeframe: 6 months	

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	20		
Units: PC				
arithmetic mean (standard deviation)	9.2 (\pm 11.0)	14.0 (\pm 12.6)		

Attachments (see zip file)	transfusions at 6 months/Proportion of patients with need for
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of pRBC units transfused within the first 6 months Status: Ready for collecting values

End point title	Number of pRBC units transfused within the first 6 months Status: Ready for collecting values
End point description: There was no significant difference between the treatment arms in the proportion of patients requiring transfusions (Table 14.2.6.1) and in the number of transfused units (Table 14.2.6.2). In the FAS population, a median number of 6 units of PC and 7 units of pRBC were transfused within the first 6 months,	
End point type	Secondary
End point timeframe: 6 months	

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: pRBC				
arithmetic mean (standard deviation)	8.5 (± 8.6)	10.2 (± 6.9)		

Attachments (see zip file)	Transfusion pRBC at 6 months/Proportion of patients with need
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Statistical analyses

No statistical analyses for this end point

Secondary: FFS by study group

End point title	FFS by study group
End point description:	
No significant difference was found between treatment arms (p=0.872). The median FFS was 24.86 weeks (95% CI 24.00; 87.29) in the Eltrombopag Arm and 24.29 weeks (95% CI 24.00; 36.00) in the Placebo Arm.	
The median FFS was longest in Group C with 99.00 weeks	
End point type	Secondary
End point timeframe:	
dependend on result	
bei group B and C no upper value is available, therefore the results could not be entered without error warning. The available results are:Group Median (weeks) 95% CI	
B 36.00 [36.00; NA]	
C 99.00 [36.14; NA]	

End point values	A: Placebo, no CR	Arm D: Eltrombopag and non response (NR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	9		
Units: weeks				
median (confidence interval 95%)	24.50 (24.00 to 56.14)	24.00 (24.00 to 24.00)		

Attachments (see zip file)	Secondary endpoint FFS/FFS by study arm and study group.pdf
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Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

between the first study-related procedure (i.e. screening) and 30 days post the last study treatment

Adverse event reporting additional description:

All adverse events that occur between the first study-related procedure (i.e. screening) and 30 days post the last study treatment (or after this date if the investigator feels the event is related to the IMP) must be recorded.

All Adverse Events will be graded according to Common Terminology Criteria for Adverse Events v4.0 (CTCAE), available

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	28.0

Reporting groups

Reporting group title	Verum (Eltrombopag) (TEAEs within 10 wks after therapy start)
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Reporting group description:

TEAEs in patients with Eltrombopag added to the background therapy (CSA) within 10 weeks after therapy start.

Reporting group title	Placebo (TEAEs reported within 10 weeks after therapy start)
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Reporting group description:

Overall summary of number of patients with TEAEs reported within 10 weeks after therapy start (SAF) treated with background therapy (CSA) + Placebo

Reporting group title	TEAEs reported after 6 months after therapy start
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Reporting group description:

TEAEs reported after 6 months after therapy start.

Die Gesamtzahl der von schwerwiegenden unerwünschten Ereignissen betroffenen Probanden ist geringer als die Gesamtzahl der von schwerwiegenden unerwünschten Ereignissen betroffenen Probanden in der Berichtsgruppe. Berücksichtigen Sie alle betroffenen Probanden oder korrigieren Sie die Gesamtzahl der von schwerwiegenden unerwünschten Ereignissen betroffenen Probanden in der Berichtsgruppe.

Reporting group title	Verum (Eltrombopag) (TEAEs 10 wks -6 months)
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Reporting group description:

Verum (Eltrombopag) (TEAEs between 10 wks and 6 months after therapy start)

Reporting group title	Placebo (Eltrombopag) (TEAEs between 10 wks and 6 mo)
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Reporting group description:

Placebo (TEAEs between 10 wks and 6 months after therapy start)

Serious adverse events	Verum (Eltrombopag) (TEAEs within 10 wks after therapy start)	Placebo (TEAEs reported within 10 weeks after therapy start)	TEAEs reported after 6 months after therapy start
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 36 (8.33%)	5 / 41 (12.20%)	17 / 77 (22.08%)
number of deaths (all causes)	0	1	2
number of deaths resulting from adverse events	0	0	0

Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Condition aggravated			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General physical health deterioration subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Serum sickness subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Heavy menstrual bleeding subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Subcutaneous haematoma subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Myocardial infarction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral venous thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache	Additional description: Headache,		
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolysis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 36 (2.78%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			

subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubo-ovarian abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Verum	Placebo	
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	(Eltrombopag) (TEAEs 10 wks -6 months)	(Eltrombopag) (TEAEs between 10 wks and 6 mo)	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 36 (11.11%)	4 / 41 (9.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Condition aggravated			
subjects affected / exposed	1 / 36 (2.78%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			

subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Serum sickness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
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			
Pulmonary embolism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			

subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
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			
Subcutaneous haematoma			
subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 36 (2.78%)	0 / 41 (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			
Syncope			
subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache	Additional description: Headache,		
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubo-ovarian abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	Verum (Eltrombopag) (TEAEs within 10 wks after therapy start)	Placebo (TEAEs reported within 10 weeks after therapy start)	TEAEs reported after 6 months after therapy start
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 36 (86.11%)	39 / 41 (95.12%)	58 / 77 (75.32%)
Vascular disorders			
Haematoma			
subjects affected / exposed	5 / 36 (13.89%)	6 / 41 (14.63%)	2 / 77 (2.60%)
occurrences (all)	5	6	3
Hypertension			
subjects affected / exposed	4 / 36 (11.11%)	3 / 41 (7.32%)	3 / 77 (3.90%)
occurrences (all)	4	3	3
General disorders and administration site conditions			
Nausea			
subjects affected / exposed	6 / 36 (16.67%)	9 / 41 (21.95%)	4 / 77 (5.19%)
occurrences (all)	6	9	8
Fatigue			
subjects affected / exposed	8 / 36 (22.22%)	11 / 41 (26.83%)	9 / 77 (11.69%)
occurrences (all)	8	11	9
Oedema peripheral			
subjects affected / exposed	3 / 36 (8.33%)	6 / 41 (14.63%)	4 / 77 (5.19%)
occurrences (all)	3	6	1
Pyrexia			

subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4	0 / 41 (0.00%) 0	1 / 77 (1.30%) 1
Reproductive system and breast disorders Dyspnoea subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 5	8 / 41 (19.51%) 8	5 / 77 (6.49%) 5
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 5 3 / 36 (8.33%) 3	8 / 41 (19.51%) 8 1 / 41 (2.44%) 1	5 / 77 (6.49%) 5 1 / 77 (1.30%) 1
Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	3 / 41 (7.32%) 3	2 / 77 (2.60%) 2
Product issues Headache subjects affected / exposed occurrences (all)	10 / 36 (27.78%) 14	15 / 41 (36.59%) 17	8 / 77 (10.39%) 10
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	3 / 41 (7.32%) 3	3 / 77 (3.90%) 3
Nervous system disorders Paraesthesia subjects affected / exposed occurrences (all) Dysaesthesia subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Tremor	8 / 36 (22.22%) 8 1 / 36 (2.78%) 1 2 / 36 (5.56%) 2	6 / 41 (14.63%) 6 5 / 41 (12.20%) 5 3 / 41 (7.32%) 3	5 / 77 (6.49%) 5 0 / 77 (0.00%) 0 3 / 77 (3.90%) 3

subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	2 / 41 (4.88%) 2	0 / 77 (0.00%) 0
Blood and lymphatic system disorders Petechia subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4	0 / 41 (0.00%) 0	0 / 77 (0.00%) 0
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	3 / 41 (7.32%) 3	2 / 77 (2.60%) 2
Eye disorders Ocular icterus subjects affected / exposed occurrences (all)	7 / 36 (19.44%) 7	1 / 41 (2.44%) 1	0 / 77 (0.00%) 0
Gastrointestinal disorders Gingival hypertrophy subjects affected / exposed occurrences (all)	7 / 36 (19.44%) 7	9 / 41 (21.95%) 10	4 / 77 (5.19%) 4
Abdominal pain subjects affected / exposed occurrences (all)	Additional description: Abdominal pain and Abdominal pain upper		
	10 / 36 (27.78%) 12	10 / 41 (24.39%) 10	5 / 77 (6.49%) 7
Gingival bleeding subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 4	3 / 41 (7.32%) 3	1 / 77 (1.30%) 1
Vomiting subjects affected / exposed occurrences (all)	Additional description: Vomiting		
	2 / 36 (5.56%) 2	2 / 41 (4.88%) 2	2 / 77 (2.60%) 2
Abdominal pain upper subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 5	5 / 41 (12.20%) 5	1 / 77 (1.30%) 2
Hepatobiliary disorders Diarrhoea subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	3 / 41 (7.32%) 3	4 / 77 (5.19%) 4
Skin and subcutaneous tissue disorders Hair growth abnormal	Additional description: Hair growth abnormal including Hirsutism and Hypertrichiosis		

subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	7 / 41 (17.07%) 7	3 / 77 (3.90%) 3
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	9 / 36 (25.00%)	14 / 41 (34.15%)	7 / 77 (9.09%)
occurrences (all)	9	12	5
Arthralgia			
subjects affected / exposed	1 / 36 (2.78%)	3 / 41 (7.32%)	1 / 77 (1.30%)
occurrences (all)	1	3	0
Back pain			
subjects affected / exposed	1 / 36 (2.78%)	2 / 41 (4.88%)	4 / 77 (5.19%)
occurrences (all)	1	2	5
Infections and infestations			
Rhinitis			
subjects affected / exposed	2 / 36 (5.56%)	4 / 41 (9.76%)	1 / 77 (1.30%)
occurrences (all)	2	4	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	3 / 41 (7.32%)	15 / 77 (19.48%)
occurrences (all)	2	3	12
Nasopharyngitis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 41 (2.44%)	2 / 77 (2.60%)
occurrences (all)	1	1	2
COVID-19	Additional description: including Coronavirus infection		
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	10 / 77 (12.99%)
occurrences (all)	0	0	10

Non-serious adverse events	Verum (Eltrombopag) (TEAEs 10 wks -6 months)	Placebo (Eltrombopag) (TEAEs between 10 wks and 6 mo)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 36 (83.33%)	28 / 41 (68.29%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Hypertension			

subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	2 / 41 (4.88%) 2	
General disorders and administration site conditions Nausea subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4	2 / 41 (4.88%) 2	
Fatigue subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	2 / 41 (4.88%) 2	
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 41 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 41 (0.00%) 0	
Reproductive system and breast disorders Dyspnoea subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	1 / 41 (2.44%) 1	
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	1 / 41 (2.44%) 1	
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 41 (0.00%) 0	
Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 41 (0.00%) 0	
Product issues Headache subjects affected / exposed occurrences (all)	6 / 36 (16.67%) 7	3 / 41 (7.32%) 3	
Investigations			

Blood creatinine increased subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	1 / 41 (2.44%) 1	
Nervous system disorders			
Paraesthesia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 41 (2.44%) 1	
Dysaesthesia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 41 (2.44%) 1	
Dizziness subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 41 (0.00%) 0	
Tremor subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	1 / 41 (2.44%) 1	
Blood and lymphatic system disorders			
Petechia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 41 (0.00%) 0	
Ear and labyrinth disorders			
Vertigo subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 41 (2.44%) 1	
Eye disorders			
Ocular icterus subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 41 (0.00%) 0	
Gastrointestinal disorders			
Gingival hypertrophy subjects affected / exposed occurrences (all)	6 / 36 (16.67%) 6	3 / 41 (7.32%) 3	
Abdominal pain subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 41 (2.44%) 1	
Gingival bleeding			

Additional description: Abdominal pain and Abdominal pain upper

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	2 / 41 (4.88%) 2	
Vomiting	Additional description: Vomiting		
subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	2 / 41 (4.88%) 2	
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	2 / 41 (4.88%) 2	
Hepatobiliary disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	2 / 41 (4.88%) 2	
Skin and subcutaneous tissue disorders Hair growth abnormal	Additional description: Hair growth abnormal including Hirsutism and Hypertrichiosis		
subjects affected / exposed occurrences (all)	8 / 36 (22.22%) 8	10 / 41 (24.39%) 10	
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	2 / 41 (4.88%) 2	
Arthralgia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 41 (0.00%) 0	
Back pain subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 41 (0.00%) 0	
Infections and infestations Rhinitis subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	1 / 41 (2.44%) 1	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	2 / 41 (4.88%) 3	
Nasopharyngitis			

subjects affected / exposed	2 / 36 (5.56%)	2 / 41 (4.88%)	
occurrences (all)	2	3	
COVID-19	Additional description: including Coronavirus infection		
subjects affected / exposed	2 / 36 (5.56%)	0 / 41 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 May 2017	Substantial protocol changes The study was conducted according to the Clinical Study Protocol (CSP) version 1.15 dated 08 Jan 2015 and the following amendments: <ul style="list-style-type: none">Version 2.0 dated 08 May 2017: change of financial support and marketing authorization holder of Investigational Medicinal Product (IMP)
31 May 2017	Substantial protocol changes The study was conducted according to the Clinical Study Protocol (CSP) version 1.15 dated 08 Jan 2015 and the following amendments: <ul style="list-style-type: none">Version 3.0 dated 31 May 2017: corrections of terms and clarifications approved by the ethics committee
03 March 2020	Substantial protocol changes The study was conducted according to the Clinical Study Protocol (CSP) version 1.15 dated 08 Jan 2015 and the following amendments: <ul style="list-style-type: none">Version 4.0 dated 03 Mar 2020: reduction of sample size and follow-up period, modification of the pharmacokinetic section, adjustment of eltrombopag treatment period
22 July 2021	Substantial protocol changes The study was conducted according to the Clinical Study Protocol (CSP) version 1.15 dated 08 Jan 2015 and the following amendments: <ul style="list-style-type: none">Version 4.1 dated 22 Jul 2021: initial protocol for France
28 April 2022	Substantial protocol changes The study was conducted according to the Clinical Study Protocol (CSP) version 1.15 dated 08 Jan 2015 and the following amendments: <ul style="list-style-type: none">Version 5.0 dated 28 Apr 2022: extension of recruitment period and adjustment of study timelines, addition of telomeric analysis and flow cytometry for Group A2 visit XIII
09 October 2024	Version 6.0 dated 09 Oct 2024: administrative changes at the Sponsor, addition of an exploratory endpoint, change of the end of trial definition

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported