Clinical trial results:
A Phase II, randomized (1:1) open label study to assess the efficacy and safety of eltrombopag in combination with dexamethasone compared to dexamethasone, as first-line treatment in adult patients with newly diagnosed immune thrombocytopenia (XPAG-ITP)

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

Summary

EudraCT number	2019-002658-21
Trial protocol	DE
Global end of trial date	22 September 2023

Results information

Result version number	v1 (current)
This version publication date	25 September 2024
First version publication date	25 September 2024

Trial information

Trial identification

Sponsor protocol code	CETB115JDE01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04346654
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric	No

investigation plan (PIP)	
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	22 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the ability of eltrombopag in combination with a short course of dexamethasone to induce a sustained response off treatment at 52 weeks versus a defined course of dexamethasone

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 October 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 26
Worldwide total number of subjects	26
EEA total number of subjects	26

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	26
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 25 centers in Germany.

Pre-assignment

Screening details:

Participants had to abstain from using investigational/marketed drugs and taking herbal supplements prior to taking the first dose of study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Eltrombopag + Dexamethasone

Arm description:

Patients were treated with eltrombopag in combination with a standard high-dose dexamethasone (1 cycle: 40 mg once daily (QD) from day 1-4) to induce sustained response off treatment.

Arm type	Experimental
Investigational medicinal product name	Eltrombopag
Investigational medicinal product code	ETB115
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Eltrombopag 25 mg, 50 mg taken daily

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	ETB115
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dexamethasone 40 mg taken daily

Arm title	Dexamethasone

Arm description:

Patients were treated with a standard high-dose dexamethasone (1-3 cycles: 40 mg QD day 1-4 at 4 weeks intervals (or at 14-28 days intervals if needed) to induce sustained response off treatment.

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	ETB115
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dexamethasone 40 mg taken daily

Number of subjects in period 1	Eltrombopag + Dexamethasone	Dexamethasone
Started	13	13
Randomized, not treated	1 [1]	0 [2]
Completed	8	10
Not completed	5	3
Consent withdrawn by subject	2	-
Adverse event, non-fatal	2	-
Pregnancy	-	1
Lost to follow-up	-	1
Non-response	1	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of subjects is consistent. Just added this milestone for clarification to the reader.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of subjects is consistent. Just added this milestone for clarification to the reader.

Baseline characteristics

Reporting groups	
Reporting group title	Eltrombopag + Dexamethasone
Reporting group description:	
Patients were treated with eltrombopag in combination with a standard high-dose dexamethasone (1 cycle: 40 mg once daily (QD) from day 1-4) to induce sustained response off treatment.	
Reporting group title	Dexamethasone
Reporting group description:	
Patients were treated with a standard high-dose dexamethasone (1-3 cycles: 40 mg QD day 1-4 at 4 weeks intervals (or at 14-28 days intervals if needed) to induce sustained response off treatment.	

Reporting group values	Eltrombopag + Dexamethasone	Dexamethasone	Total
Number of subjects	13	13	26
Age categorical Units: Subjects			
Adults (18-64 years)	13	13	26
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	60.6	45.3	
standard deviation	± 14.5	± 14.3	-
Sex: Female, Male Units: Participants			
Female	6	6	12
Male	7	7	14
Race/Ethnicity, Customized Units: Subjects			
Caucasian	12	12	24
Other	1	1	2

End points

End points reporting groups

Reporting group title	Eltrombopag + Dexamethasone
Reporting group description:	
Patients were treated with eltrombopag in combination with a standard high-dose dexamethasone (1 cycle: 40 mg once daily (QD) from day 1-4) to induce sustained response off treatment.	
Reporting group title	Dexamethasone
Reporting group description:	
Patients were treated with a standard high-dose dexamethasone (1-3 cycles: 40 mg QD day 1-4 at 4 weeks intervals (or at 14-28 days intervals if needed) to induce sustained response off treatment.	

Primary: Percentage of patients with sustained response off treatment at 52 weeks

End point title	Percentage of patients with sustained response off treatment at 52 weeks
End point description:	
Sustained response off treatment at 52 weeks is defined as maintenance of platelet count ≥ 30 × 10^9/L after treatment discontinuation until Week 52 in the absence of bleeding events ≥ Grade II or use of any rescue medication at all visits until Week 52	
End point type	Primary
End point timeframe:	
Study treatment discontinuation until week 52	

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Participants	2	2		

Statistical analyses

Statistical analysis title	Sustained Response of treatment - Primary endpoint
Comparison groups	Eltrombopag + Dexamethasone v Dexamethasone
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5133
Method	Regression, Logistic

Secondary: Percentage of patients with overall response at Week 52

End point title	Percentage of patients with overall response at Week 52

End point description:

Overall response after treatment at week 52 was defined as maintenance of platelet count ≥ 30 x 109/L and ≥ 2-fold increase of screening platelet count after treatment discontinuation in the absence of bleeding event ≥ Grade II and no rescue therapy at all visits until Week 52.

End point type	Secondary

End point timeframe:

Study treatment discontinuation until week 52

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Participants	2	2		

Statistical analyses

Statistical analysis title	ORR at week 52
Comparison groups	Eltrombopag + Dexamethasone v Dexamethasone
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5133
Method	Regression, Logistic

Secondary: Duration of sustained response off treatment

End point title	Duration of sustained response off treatment

End point description:

Duration of sustained response off treatment is defined as time of treatment discontinuation until platelet count < 30 × 109/L or bleeding events ≥ Grade II or use of any rescue therapy. If a patient did not loose sustained response the interval was censored with the date of the last platelet assessment.

End point type	Secondary

End point timeframe:

from last dose of study treatment until loss of response, approx. 52 weeks

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: Weeks				
arithmetic mean (standard deviation)	49.1 (± 0.0)	45.7 (± 2.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete response by Week 4

End point title	Complete response by Week 4

End point description:

Complete Response by week 4 is defined as platelet count ≥ 100 × 109/L and absence of bleeding and no rescue therapy until week 4.

End point type	Secondary

End point timeframe:

By Week 4

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Participants	8	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response by Week 4

End point title	Overall response by Week 4

End point description:

Overall response by week 4 is defined as platelet count ≥ 30 × 109/L and ≥ 2 fold increase of screening platelet count and absence of bleeding and no rescue therapy within the first 4 weeks

End point type	Secondary

End point timeframe:

By Week 4

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Participants	10	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in platelet count from pre-treatment/screening to baseline and to various time points

End point title	Absolute change in platelet count from pre-treatment/screening to baseline and to various time points

End point description:

Absolute change in platelet count from pre-treatment or screening to baseline and to 1, 2, 4, 13, 27 and 53 weeks. If pre-treatment was necessary before inclusion, platelet count data performed directly before pre-treatment were used for study inclusion (screening value to be used for inclusion/exclusion check and for analysis as a covariate).

End point type	Secondary

End point timeframe:

Pre-treatment/screening, Week 1 (baseline), 2, 4, 13, 27, and 53

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: G/L				
arithmetic mean (standard deviation)				
Week 1 (Baseline) (n = 11, 11)	32.0 (± 44.3)	23.2 (± 48.0)		
Week 2 (n = 11, 12)	145.2 (± 151.9)	80.7 (± 68.8)		
Week 4 (n = 11, 12)	192.5 (± 165.8)	92.0 (± 68.7)		
Week 13 (n = 10, 11)	119.4 (± 115.9)	143.0 (± 88.5)		
Week 27 (n = 9, 11)	217.8 (± 126.5)	141.2 (± 94.7)		
Week 53 (n = 8, 10)	139.0 (± 88.0)	141.7 (± 61.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in platelet count from pre-treatment/screening to baseline and to various time points

End point title	Relative change in platelet count from pre-treatment/screening to baseline and to various time points

End point description:

Relative change in platelet count from pre-treatment or screening to baseline and to 1, 2, 4, 13, 27, and 53 weeks. If pre-treatment was necessary before inclusion, platelet count data performed directly before pre-treatment were used for study inclusion (screening value to be used for inclusion/exclusion check and for analysis as a covariate).

End point type	Secondary

End point timeframe:

Pre-treatment/screening, Week 1 (baseline), 2, 4, 13, 27, and 53

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Percentage change in platelet counts				
arithmetic mean (standard deviation)				
Week 1 (Baseline) (n = 10, 11)	347.9 (± 486.8)	293.4 (± 418.4)		
Week 2 (n = 10, 12)	5795.5 (± 9672.4)	2028.2 (± 4382.0)		
Week 4 (n = 10, 12)	11400.9 (± 16875.2)	2865.4 (± 3805.4)		
Week 13 (n = 9, 11)	8050.6 (± 12277.8)	4725.7 (± 8418.2)		
Week 27 (n = 8, 11)	13667.9 (± 15717.1)	4381.1 (± 8195.2)		
Week 53 (n = 7, 10)	9392.3 (± 11476.0)	5612.1 (± 8300.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to overall response (TOR)

End point title	Time to overall response (TOR)

End point description:

Time to overall response is defined as time from starting study treatment to time of achievement of overall response. Overall response is defined as a platelet count ≥ 30 × 10^9/L and ≥ 2 fold increase of baseline platelet count and absence of bleeding and no rescue therapy censored with the last visit date for patients not achieving overall response. Results of TOR are reported per Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Time from starting study treatment to achievement of complete response (up to 52 weeks)

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Weeks				
median (confidence interval 95%)	1.1 (0.0 to 4.1)	1.0 (0.1 to 1.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to complete response

End point title	Time to complete response

End point description:

Time to complete response is defined as time from starting study treatment to time of achievement of complete response. Complete response is defined as a platelet count ≥ 100 × 109/L and absence of bleeding and no rescue therapy. Results of time to complete response are reported per Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Time from starting study treatment to achievement of complete response (up to 52 weeks)

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Weeks				
median (confidence interval 95%)	1.1 (0.1 to 999)	2.1 (0.6 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of overall response (OR) and complete response (CR)

End point title	Duration of overall response (OR) and complete response (CR)

End point description:

Duration of overall or complete response is defined as time of achievement of overall or complete response (as defined above) until loss of overall or complete response. The duration of CR was calculated from the date of onset of CR until platelet count < 100 x 109/L, or bleeding events ≥ Grade II, or use of any rescue therapy, whatever was earlier. Results of duration of overall and complete response are reported per Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Achievement of overall or complete response until loss of response (up to 52 weeks)

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Weeks				
median (confidence interval 95%)				
Median duration of overall response	8.3 (0.3 to 999)	3.6 (1.1 to 999)		
Median duration of complete response	9.7 (1.3 to 999)	1.3 (0.9 to 6.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) questionaire

End point title	Change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) questionaire

End point description:

The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) instrument is a 13-item validated tool used to measure an individual's level of fatigue during usual daily activities over the past 7 days. Items are scored on a 0-4 response scale (4=not at all to 0=very much) where the total possible score ranges from 0-52 (all items are summed up to create the total score); A score of less than 30 indicates severe fatigue. The higher scores represent better HRQoL.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Week 2, 3, 5, 13, 27 and 53

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: scores on a scale				
median (standard deviation)				
Change from Baseline (BL) to Week 2 (n = 10, 11)	-4.2 (± 9.6)	-4.5 (± 6.9)		
Change from BL to Week 3 (n = 9, 10)	1.0 (± 4.4)	-2.9 (± 5.1)		
Change from BL to Week 5 (n = 10, 10)	1.2 (± 5.0)	-5.1 (± 6.9)		
Change from BL to Week 13 (n = 8, 9)	0.3 (± 8.3)	0.3 (± 2.8)		
Change from BL to Week 27 (n = 8, 10)	-3.6 (± 11.0)	-3.1 (± 7.7)		
Change from BL to Week 53 (n = 6, 9)	2.7 (± 5.6)	-3.4 (± 5.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire

End point title	Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire

End point description:

SF36 questionnaire is a tool to measure health-related QoL. SF36 questionnaires (physical and mental score) were answered throughout the study and is a validated instrument with 36 questions to measure general physical and mental health status via assessment of 8 domains—Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, and Mental Health—over the past 4 weeks. The SF36 is scored using norm-based scoring procedures and scores ranging from 0-100; higher values indicate less impairment, a higher QoL. In addition to this SAP-planned scoring score, an alternative scoring for both the physical SF36 score and the mental SF36 were performed by QualityMetric (QM) Incorporated, an IQVIA business.

End point type	Secondary

End point timeframe:

Baseline (Week 1), Week 2, 3, 5, 13, 27 and 53

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: scores on a scale				
arithmetic mean (standard deviation)				
CBL to Wk 2: Physical Score (PS) (n = 10, 11)	1.9 (± 4.6)	-3.3 (± 6.6)		
CBL to Week 3: PS (n = 8, 10)	2.5 (± 5.8)	-1.4 (± 8.8)		
CBL to Week 5: PS (n = 8, 9)	1.5 (± 6.2)	-2.7 (± 10.5)		
CBL to Week 13: PS (n = 7, 10)	3.5 (± 9.9)	0.3 (± 8.0)		
CBL to Week 27: PS (n = 7, 10)	2.6 (± 14.7)	-0.9 (± 10.8)		
CBL to Week 53: PS (n = 6, 10)	8.1 (± 11.8)	0.3 (± 10.0)		
CBL to Week 2: Mental Score (MS) (n = 10, 11)	-0.8 (± 6.1)	-1.2 (± 7.6)		
CBL to Week 3: MS (n = 8, 10)	-2.0 (± 11.0)	-1.6 (± 9.7)		
CBL to Week 5: MS (n = 8, 9)	0.1 (± 7.3)	-1.7 (± 11.5)		
CBL to Week 13: MS (n = 7, 10)	3.3 (± 7.5)	4.1 (± 7.4)		
CBL to Week 27: MS (n = 7, 10)	-1.4 (± 4.9)	-2.7 (± 7.4)		
CBL to Week 53: MS (n = 6, 10)	2.1 (± 8.8)	0.6 (± 5.7)		
CBL to Week 2: PS-QM (n = 11, 12)	2.0 (± 4.1)	-3.3 (± 6.0)		
CBL to Week 3: PS-QM (n = 11, 11)	3.4 (± 6.4)	-1.4 (± 7.8)		
CBL to Week 5: PS-QM (n = 9, 12)	2.4 (± 6.0)	-2.7 (± 8.5)		
CBL to Week 13: PS-QM (n = 10, 10)	4.1 (± 8.5)	0.3 (± 7.6)		

CBL to Week 27: PS-QM (n = 9, 11)	3.6 (± 12.4)	-1.0 (± 9.7)		
CBL to Week 53: PS-QM (n = 7, 10)	6.2 (± 10.7)	0.2 (± 9.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and severity of bleeding events

End point title	Incidence and severity of bleeding events

End point description:

Incidence and severity of bleeding assessed by the modified World Health Organization (WHO) Bleeding Scale; Bleeding is graded based on a 1-4 scale (1=minor bleeding to 4=severe bleeding).
Incidence of bleeding: participants had at least one bleeding event.
Severity of bleeding: bleeding event is from grade 2 and higher

End point type	Secondary

End point timeframe:

Baseline up to 52 weeks

End point values	Eltrombopag + Dexamethasone	Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Participants				
Incidence of Bleeding events	10	12		
Severity of Bleeding events: ≥ grade 2	6	2		
Severity of Bleeding events: ≥ grade 3	2	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) are collected from first dose of study treatment until end of study treatment plus 30 days post treatment. AEs reported in this record are from first dose of study treatment until 30 days after end of treatment, approx. 3 years.

Adverse event reporting additional description:

Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Dexamethasone

Reporting group description:

Patients were treated with a standard high-dose dexamethasone (1-3 cycles: 40 mg QD day 1-4 at 4 weeks intervals (or at 14-28 days intervals if needed) to induce sustained response off treatment.

Reporting group title	Eltrombopag + Dexamethasone

Reporting group description:

Patients were treated with eltrombopag in combination with a standard high-dose dexamethasone (1 cycle: 40 mg once daily (QD) from day 1-4) to induce sustained response off treatment.

Serious adverse events	Dexamethasone	Eltrombopag + Dexamethasone	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 13 (38.46%)	5 / 12 (41.67%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
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 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Aplastic anaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Vascular stent occlusion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Oesophageal stenosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dexamethasone	Eltrombopag + Dexamethasone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	11 / 12 (91.67%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
General physical health deterioration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	3 / 13 (23.08%)	2 / 12 (16.67%)	
occurrences (all)	4	2	
Non-cardiac chest pain			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	4 / 13 (30.77%)	1 / 12 (8.33%)	
occurrences (all)	4	1	
Performance status decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Hiccups			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Dyspnoea			
subjects affected / exposed	2 / 13 (15.38%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Cough			
subjects affected / exposed	2 / 13 (15.38%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Psychiatric disorders			
Initial insomnia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	2 / 13 (15.38%)	2 / 12 (16.67%)	
occurrences (all)	2	3	
Nervousness			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Nocturnal fear			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Lipase increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Weight increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Infusion related reaction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Ligament sprain			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Rib fracture			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Transfusion reaction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Cardiovascular disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Coronary artery disease			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Restless legs syndrome			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Polyneuropathy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Headache			

subjects affected / exposed	4 / 13 (30.77%)	2 / 12 (16.67%)	
occurrences (all)	8	6	
Dizziness postural			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	5	
Ageusia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Taste disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Anaemia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Thrombocytosis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Leukopenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

Eye disorders			
Hypermetropia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Conjunctival oedema			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Photopsia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Loose tooth			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Irritable bowel syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hiatus hernia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Haemorrhoids			

subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	3 / 13 (23.08%)	3 / 12 (25.00%)	
occurrences (all)	3	3	
Nausea			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 13 (15.38%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Skin exfoliation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	3 / 13 (23.08%)	1 / 12 (8.33%)	
occurrences (all)	3	1	
Pruritus			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Dry skin			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dermatitis atopic			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Joint swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Coccydynia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Bone pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	1	7	
Myalgia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Neck pain			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Plantar fascial fibromatosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Infection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Helicobacter infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastroenteritis viral			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
COVID-19			
subjects affected / exposed	4 / 13 (30.77%)	3 / 12 (25.00%)	
occurrences (all)	4	3	
Bronchitis			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Rhinitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	2 / 13 (15.38%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Pneumonia fungal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	4	2	
Keratitis viral			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	2 / 13 (15.38%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dyslipidaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Steroid diabetes			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Iron deficiency			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 July 2020	To address the requirement of the Ethics committee to include a more detailed information on the recruitment procedure in the protocol. Version 00 of this protocol was approved by end of March 2020 by the German health authority (Bundesamt für Arzneimittel und Medizinprodukte, BfArM) and by the Ethics Committee Halle-Wittenberg. As feedback, inclusion of recruitment procedures was requested by the Ethics Committee, which was covered by this amendment. In addition, other clarifications and administrative changes were included as needed.
27 November 2020	Due to slow enrollment, it was decided to relax inclusion criteria to one single assessment of thrombocyte count at the time of screening and omitting the second threshold check at baseline. This was due to the fact that for some patients the thrombocyte count was below the pre-specified threshold at screening, but above at baseline and after pretreatment. It was decided to also include the screening instead of baseline thrombocyte count as a cofactor into the statistical model for the primary outcome analysis, as this was regarded as the more adequate way of taking into account the initial value at the time of diagnosis and before pre-treatment for all patients. Additional sensitivity analyses were included to assess the impact of pre-treatment and baseline thrombocyte count.
28 July 2022	Due to slow enrollment the feasibility of this trial has been considered and led to the following changes: Premature termination of recruitment due to feasibility reasons, resulting in an expected sample size of ca. 24 patients at the time of approval by the EC/HA. A scenario based on 12 patients per group, assuming the above rates of 30 versus 65%, would allow for a power of 24% to analyze the primary endpoint. Consequently, all analyses were to be interpreted in a purely descriptive manner; Reduction of the follow-up for responders after Week 52 (secondary endpoint). Assuming that 65% of the patients in the combination arm were in sustained response off treatment at Week 52 and in respect to slow enrollment, the sample size for this secondary endpoint would be insufficient to detect a meaningful result; Based on the proposed changes to reduce the follow-up of the responders it was possible to share the study data 6 months earlier to increase the benefits of future patients and support recent updates in ITP guidelines to prevent an extended and recurrent use of corticosteroids that is associated with substantial toxicity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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

Notes: