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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Eltrombopag

Trial Indication(s)

Immune thrombocytopenia (ITP)

Protocol Number

CETB115JDE01

Protocol Title

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

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase II

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Study Start/End Dates

Study Start Date: October 09, 2020 (Actual)
Primary Completion Date: September 22, 2023 (Actual)
Study Completion Date: September 22, 2023 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was a phase II, multicenter, randomized (1:1), open-label study to compare the efficacy and safety of eltrombopag in combination with a short course of high dose dexamethasone to 1-3 cycles of high dose dexamethasone monotherapy, as first-line treatment in adult patients with newly diagnosed ITP.

- Arm A: Eltrombopag + a short course of high-dose dexamethasone (dexamethasone therapy was limited to 1 cycle)
- Arm B: 1-3 cycles of high-dose dexamethasone

The study was designed to include 106 adult patients with newly diagnosed primary ITP with screening platelet count < 30 × 10^9/L and assessed as requiring treatment (per physician's discretion). According to Amendment 3 (dated 28-Jul-2022) for premature discontinuation of recruitment, the planned sample size was not expected to be reached and a total of ca. 24 patients was expected. 33 patients were enrolled, 7 patients were screening failures and not randomized, 26 patients were randomized (13 per treatment arm) and 1 of these patients (ETB+DEX group) was randomized but not treated.

Centers

Germany(10)

Objectives:

Primary Objective:

- 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

Secondary Objectives:

- To compare the ability of eltrombopag in combination with a short course of dexamethasone to induce overall response (OR) after treatment discontinuation at Week 52 versus a defined course of dexamethasone
- To assess the ability of eltrombopag to induce overall response (OR) byWeek 4
- To assess the ability of eltrombopag to induce complete response (CR) by Week 4
- To quantify the increase in platelet count from screening to baseline, and to 1, 2, 4, 12, 26, and 52 weeks
- To assess the time to overall and complete response
- To assess the duration of overall and complete response
- To evaluate patient-oriented outcomes for health-related quality of life
- To evaluate the safety and tolerability of eltrombopag + dexamethasone
- To evaluate the incidence and severity of bleeding events
- To evaluate the safety and tolerability of eltrombopag + dexamethasone
- To evaluate the incidence and severity of bleeding events

Test Product (s), Dose(s), and Mode(s) of Administration

Eltrombopag study drug as provided as film-coated tablets in 25 mg and 50 mg doses for oral use and taken daily. Dexamethasone was the Standard of Care treatment and was supplied as 40 mg tablets for oral use and taken daily.

Statistical Methods

The statistical analysis was based on all patient data at the time the trial ends. This analysis was performed once all patients completed their final visits or terminated the study prematurely.

The primary endpoint was the proportion of patients with sustained response off treatment at 52 weeks (i.e. until study visit Week 53, W53D1) (according to SAP).

Sustained response off treatment was defined as:

- achieved platelet count ≥ 30 $\times 10^9$/L and then maintained platelet counts ≥ 30 × 10^9/L after discontinuation of study treatment AND

- maintained platelet count ≥ 30 × 10^9/L in the absence of bleeding events ≥ Grade II AND
- without the use of any rescue therapy until week 52

The analysis of the primary endpoint was based on the following estimand:

The population will be the FAS.

Variable of interest: the primary endpoint is the response rate in terms of sustained response off treatment at 52 weeks (i.e. until study Visit Week 53), in absence of bleeding or use of rescue therapy as defined above, i.e. a composite estimand.

Intervention effect: effect of eltrombopag in combination with a short course of high-dose dexamethasone versus 1-3 cycles of high-dose dexamethasone alone at 52 weeks, regardless of adherence to randomized treatment.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Signed informed consent must be obtained prior to participation in the study.
- Men and women ≥ 18 years of age
- Newly diagnosed with primary ITP (time from diagnosis within 3 months)
- Platelet count < 30 × 109/L at screening and a need for treatment (per physician's discretion)

Note: If pre-treatment is necessary, platelet count data performed directly before pre-treatment (can be used for study inclusion (screening value). Treatment-naïve patients will be included based on their platelet counts performed at screening

Exclusion Criteria:

- Previous history of treatment for ITP, except any ITP-directed therapy for a maximum of 3 days within 7 days before randomization

- Patients with diagnosis of secondary thrombocytopenia
- Patients who have life threatening bleeding complications per physician´s discretion
- Patients with a history of thromboembolic events in the 6 months preceding enrollment or known risk factors for thromboembolism
- Serum creatinine > 1.5 mg/dL
- Total bilirubin (TBIL) > 1.5 × upper limit of normal (ULN)
- Aspartate transaminase (AST) > 3.0 × ULN
- Alanine transaminase (ALT) > 3.0 × ULN
- Patients who are human immune deficiency virus (HIV),hepatitis C virus (HCV) or hepatitis B surface antigen (HBsAg) positive
- Patients with hepatic impairment (Child-Pugh score > 5)
- Patients with known active or uncontrolled infections not responding to appropriate therapy
- History of current diagnosis of cardiac disease or impaired cardiac function denoted
- Patients who have active malignancy
- Patients with evidence of current alcohol/drug abuse
- Any serious and/or unstable pre-existing medical, psychiatric disorder, or other conditions that could interfere with subject’s safety, obtaining informed consent or compliance with the study procedures
- Female subjects who are nursing or pregnant (positive serum or urine B-human chorionic gonadotrophin (B-hCG) pregnancy test) at screening or pre-dose on Day 1
- Women of child-bearing potential and males unwilling to use adequate contraception during the study

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Participant Flow Table

Overall Study

	Eltrombopag + Dexamethasone	Dexamethasone	Total
Arm/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.	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.	
Started	13	13	26
Randomized, not treated	1	0	1
Completed	8	10	18
Not Completed	5	3	8
Adverse Event	2	0	2
Non-response	1	1	2
Withdrawal by Subject	2	0	2
Lost to Follow-up	0	1	1
Pregnancy	0	1	1

Baseline Characteristics

	Eltrombopag + Dexamethasone	Dexamethasone	Total
Arm/Group Description	Patients were treated with eltrombopag in combination with a standard high-dose dexamethasone (1 cycle: 40 mg once daily (QD) from day	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	

	1-4) to induce sustained response off treatment.	induce sustained response off treatment.	
Number of Participants [units: participants]	13	13	26
Baseline Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.		
Age Continuous (units: Years) Analysis Population Type: Participants Mean ± Standard Deviation			
	60.6±14.5	45.3±14.3	53.0±16.1
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	6	6	12
Male	7	7	14
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants			
Caucasian	12	12	24
Other	1	1	2

Primary Outcome Result(s)

Percentage of patients with sustained response off treatment at 52 weeks

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
Time Frame	Study treatment discontinuation until week 52

Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	Dexamethasone
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Percentage of patients with sustained response off treatment at 52 weeks (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	2 (15.38%)	2 (15.38%)

Statistical Analysis

Groups	Eltrombopag + Dexamethasone, Dexamethasone
Type of Statistical Test	Superiority
P Value	0.5133
Method	Regression, Logistic

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Secondary Outcome Result(s)

Percentage of patients with overall response at Week 52

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.
Time Frame	Study treatment discontinuation until week 52
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	Dexamethasone
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Percentage of patients with overall response at Week 52 (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	2 (15.38%)	2 (15.38%)

Statistical Analysis

Groups	Eltrombopag + Dexamethasone, Dexamethasone
Type of Statistical Test	Superiority
P Value	0.5133
Method	Regression, Logistic

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Duration of sustained response off treatment

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.
Time Frame	from last dose of study treatment until loss of response, approx. 52 weeks
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization and who had a response.

	Eltrombopag + Dexamethasone	**Dexamethasone**
Arm/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.	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.
Number of Participants Analyzed [units: participants]	2	2
Duration of sustained response off treatment (units: Weeks)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	49.1 ± 0.0	45.7 ± 2.8

Overall response by Week 4

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
Time Frame	By Week 4
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	Dexamethasone
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Overall response by Week 4 (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	10 (76.92%)	11 (84.62%)

Complete response by Week 4

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.
Time Frame	By Week 4
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	Dexamethasone
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Complete response by Week 4 (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	8 (61.54%)	9 (69.23%)

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

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).
Time Frame	Pre-treatment/screening, Week 1 (baseline), 2, 4, 13, 27, and 53
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	**Dexamethasone**
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Absolute change in platelet count from pre-treatment/screening to baseline and to various time points (units: G/L)	**Mean ± Standard Deviation**	**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

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

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).
Time Frame	Pre-treatment/screening, Week 1 (baseline), 2, 4, 13, 27, and 53
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	**Dexamethasone**
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Relative change in platelet count from pre-treatment/screening to baseline and to various time points (units: Percentage change in platelet counts)	**Mean ± Standard Deviation**	**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

Time to overall response (TOR)

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.
Time Frame	Time from starting study treatment to achievement of complete response (up to 52 weeks)
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	**Dexamethasone**
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Time to overall response (TOR) (units: Weeks)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	1.1 (0.0 to 4.1)	1.0 (0.1 to 1.3)

Time to complete response

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.
Time Frame	Time from starting study treatment to achievement of complete response (up to 52 weeks)
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	Dexamethasone
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Time to complete response (units: Weeks)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	1.1 (0.1 to NA)[1]	2.1 (0.6 to NA)[1]

[1] NA = upper limit of CI is inestimable because there were not enough events to calculate

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

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.
Time Frame	Achievement of overall or complete response until loss of response (up to 52 weeks)
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	Dexamethasone
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13

Duration of overall response (OR) and complete response (CR) (units: Weeks)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
Median duration of overall response	8.3 (0.3 to NA)[1]	3.6 (1.1 to NA)[1]
Median duration of complete response	9.7 (1.3 to NA)[1]	1.3 (0.9 to 6.1)

[1] NA = upper limit of CI is inestimable because there were not enough events to calculate

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

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.
Time Frame	Baseline (Week 1), Week 2, 3, 5, 13, 27 and 53
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	**Dexamethasone**
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) questionaire (units: scores on a scale)	**Median ± Standard Deviation**	**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

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

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.
Time Frame	Baseline (Week 1), Week 2, 3, 5, 13, 27 and 53
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	**Dexamethasone**
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Change from baseline in Short Form 36 Health Survey (SF-36v2) questionnaire (units: scores on a scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Change from Baseline (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

Incidence and severity of bleeding events

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
Time Frame	Baseline up to 52 weeks
Analysis Population Description	The Full Analysis Set (FAS) consists of all patients to whom study treatment has been assigned by randomization.

	Eltrombopag + Dexamethasone	Dexamethasone
Arm/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.	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.
Number of Participants Analyzed [units: participants]	13	13
Incidence and severity of bleeding events (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Incidence of Bleeding events	10 (76.92%)	12 (92.31%)
Severity of Bleeding events: ≥ grade 2	6 (46.15%)	2 (15.38%)
Severity of Bleeding events: ≥ grade 3	2 (15.38%)	1 (7.69%)

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

No data identified.

Safety Results

Time Frame	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.

Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (26.1)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Eltrombopag + Dexamethasone N = 12	**Dexamethasone N = 13**
Arm/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.	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.
Total Number Affected	0	1
Total Number At Risk	12	13

Serious Adverse Events

Time Frame	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.
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (26.1)

Collection Approach for Table Default Systematic Assessment

	Eltrombopag + Dexamethasone N = 12	Dexamethasone N = 13
Arm/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.	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.
Total # Affected by any Serious Adverse Event	5	5
Total # at Risk by any Serious Adverse Event	12	13
Blood and lymphatic system disorders		
Aplastic anaemia	1 (8.33%)	0 (0.00%)
Immune thrombocytopenia	2 (16.67%)	0 (0.00%)
Iron deficiency anaemia	1 (8.33%)	0 (0.00%)
Thrombocytopenia	0 (0.00%)	1 (7.69%)
Cardiac disorders		
Myocardial infarction	0 (0.00%)	1 (7.69%)
Gastrointestinal disorders		
Oesophageal stenosis	1 (8.33%)	0 (0.00%)
Pancreatitis	0 (0.00%)	1 (7.69%)
General disorders and administration site conditions		
Vascular stent occlusion	0 (0.00%)	1 (7.69%)

Infections and infestations		
Herpes zoster	1 (8.33%)	0 (0.00%)
Pneumonia	1 (8.33%)	0 (0.00%)
Metabolism and nutrition disorders		
Hyperglycaemia	0 (0.00%)	1 (7.69%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
B-cell lymphoma	1 (8.33%)	0 (0.00%)
Breast cancer	1 (8.33%)	0 (0.00%)
Myelodysplastic syndrome	0 (0.00%)	1 (7.69%)
Prostate cancer	0 (0.00%)	1 (7.69%)
Renal and urinary disorders		
Renal colic	1 (8.33%)	0 (0.00%)
Ureterolithiasis	1 (8.33%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Pulmonary embolism	0 (0.00%)	2 (15.38%)
Vascular disorders		
Haematoma	1 (8.33%)	0 (0.00%)

Other (Not Including Serious) Adverse Events

Time Frame	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.
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (26.1)
Collection Approach for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 5%

	Eltrombopag + Dexamethasone N = 12	**Dexamethasone N = 13**
Arm/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.	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.
Total # Affected by any Other Adverse Event	11	13
Total # at Risk by any Other Adverse Event	12	13
Blood and lymphatic system disorders		
Anaemia	1 (8.33%)	1 (7.69%)
Febrile neutropenia	1 (8.33%)	0 (0.00%)
Iron deficiency anaemia	1 (8.33%)	0 (0.00%)
Leukocytosis	0 (0.00%)	1 (7.69%)

Leukopenia	1 (8.33%)	0 (0.00%)
Thrombocytosis	1 (8.33%)	1 (7.69%)
Cardiac disorders		
Arteriosclerosis coronary artery	0 (0.00%)	1 (7.69%)
Cardiovascular disorder	1 (8.33%)	0 (0.00%)
Coronary artery disease	0 (0.00%)	1 (7.69%)
Tachycardia	0 (0.00%)	1 (7.69%)
Endocrine disorders		
Hyperthyroidism	1 (8.33%)	0 (0.00%)
Eye disorders		
Conjunctival oedema	0 (0.00%)	1 (7.69%)
Dry eye	1 (8.33%)	0 (0.00%)
Hypermetropia	0 (0.00%)	1 (7.69%)
Photopsia	1 (8.33%)	0 (0.00%)
Vision blurred	1 (8.33%)	0 (0.00%)
Gastrointestinal disorders		
Abdominal pain	3 (25.00%)	0 (0.00%)
Abdominal pain upper	0 (0.00%)	1 (7.69%)
Constipation	3 (25.00%)	0 (0.00%)
Diarrhoea	3 (25.00%)	3 (23.08%)
Gastrooesophageal reflux disease	0 (0.00%)	2 (15.38%)
Haemorrhoids	1 (8.33%)	1 (7.69%)
Hiatus hernia	1 (8.33%)	0 (0.00%)
Irritable bowel syndrome	1 (8.33%)	0 (0.00%)

Loose tooth	0 (0.00%)	1 (7.69%)
Nausea	2 (16.67%)	1 (7.69%)
Vomiting	1 (8.33%)	0 (0.00%)
General disorders and administration site conditions		
Fatigue	2 (16.67%)	3 (23.08%)
General physical health deterioration	1 (8.33%)	0 (0.00%)
Generalised oedema	0 (0.00%)	1 (7.69%)
Non-cardiac chest pain	0 (0.00%)	1 (7.69%)
Oedema peripheral	1 (8.33%)	1 (7.69%)
Pain	0 (0.00%)	1 (7.69%)
Performance status decreased	0 (0.00%)	1 (7.69%)
Pyrexia	1 (8.33%)	4 (30.77%)
Hepatobiliary disorders		
Hepatotoxicity	0 (0.00%)	1 (7.69%)
Infections and infestations		
Bronchitis	0 (0.00%)	2 (15.38%)
COVID-19	3 (25.00%)	4 (30.77%)
Gastroenteritis viral	0 (0.00%)	1 (7.69%)
Helicobacter infection	1 (8.33%)	0 (0.00%)
Infection	1 (8.33%)	1 (7.69%)
Influenza	1 (8.33%)	2 (15.38%)
Keratitis viral	0 (0.00%)	1 (7.69%)
Nasopharyngitis	2 (16.67%)	1 (7.69%)
Pneumonia fungal	0 (0.00%)	1 (7.69%)

Respiratory tract infection	0 (0.00%)	1 (7.69%)
Rhinitis	0 (0.00%)	1 (7.69%)
Sinusitis	1 (8.33%)	2 (15.38%)
Upper respiratory tract infection	1 (8.33%)	1 (7.69%)
Injury, poisoning and procedural complications		
Fall	2 (16.67%)	1 (7.69%)
Infusion related reaction	1 (8.33%)	0 (0.00%)
Ligament sprain	1 (8.33%)	0 (0.00%)
Rib fracture	0 (0.00%)	1 (7.69%)
Transfusion reaction	1 (8.33%)	0 (0.00%)
Investigations		
Alanine aminotransferase increased	0 (0.00%)	1 (7.69%)
Aspartate aminotransferase increased	0 (0.00%)	1 (7.69%)
Gamma-glutamyltransferase increased	0 (0.00%)	1 (7.69%)
Lipase increased	1 (8.33%)	1 (7.69%)
Weight increased	1 (8.33%)	0 (0.00%)
Metabolism and nutrition disorders		
Diabetes mellitus	1 (8.33%)	0 (0.00%)
Dyslipidaemia	0 (0.00%)	1 (7.69%)
Hypokalaemia	2 (16.67%)	0 (0.00%)
Iron deficiency	1 (8.33%)	0 (0.00%)
Steroid diabetes	0 (0.00%)	1 (7.69%)
Musculoskeletal and connective tissue disorders		
Arthralgia	2 (16.67%)	1 (7.69%)

Back pain	1 (8.33%)	0 (0.00%)
Bone pain	0 (0.00%)	1 (7.69%)
Coccydynia	0 (0.00%)	1 (7.69%)
Joint swelling	1 (8.33%)	0 (0.00%)
Muscle spasms	0 (0.00%)	1 (7.69%)
Musculoskeletal pain	1 (8.33%)	0 (0.00%)
Myalgia	1 (8.33%)	1 (7.69%)
Neck pain	1 (8.33%)	0 (0.00%)
Pain in extremity	0 (0.00%)	1 (7.69%)
Plantar fascial fibromatosis	0 (0.00%)	1 (7.69%)
Nervous system disorders		
Ageusia	0 (0.00%)	1 (7.69%)
Dizziness	2 (16.67%)	0 (0.00%)
Dizziness postural	1 (8.33%)	0 (0.00%)
Headache	2 (16.67%)	4 (30.77%)
Paraesthesia	1 (8.33%)	1 (7.69%)
Polyneuropathy	1 (8.33%)	0 (0.00%)
Restless legs syndrome	0 (0.00%)	1 (7.69%)
Sciatica	0 (0.00%)	1 (7.69%)
Taste disorder	0 (0.00%)	1 (7.69%)
Tremor	1 (8.33%)	0 (0.00%)
Psychiatric disorders		
Initial insomnia	0 (0.00%)	1 (7.69%)
Insomnia	2 (16.67%)	2 (15.38%)
Nervousness	1 (8.33%)	0 (0.00%)

Nocturnal fear	1 (8.33%)	0 (0.00%)
Restlessness	1 (8.33%)	0 (0.00%)
Sleep disorder	0 (0.00%)	1 (7.69%)
Renal and urinary disorders		
Pollakiuria	1 (8.33%)	0 (0.00%)
Reproductive system and breast disorders		
Erectile dysfunction	0 (0.00%)	1 (7.69%)
Respiratory, thoracic and mediastinal disorders		
Cough	2 (16.67%)	2 (15.38%)
Dyspnoea	1 (8.33%)	2 (15.38%)
Hiccups	1 (8.33%)	1 (7.69%)
Skin and subcutaneous tissue disorders		
Alopecia	2 (16.67%)	2 (15.38%)
Dermatitis atopic	0 (0.00%)	1 (7.69%)
Dry skin	1 (8.33%)	0 (0.00%)
Pruritus	1 (8.33%)	1 (7.69%)
Rash	1 (8.33%)	3 (23.08%)
Skin exfoliation	0 (0.00%)	1 (7.69%)
Vascular disorders		
Hot flush	0 (0.00%)	1 (7.69%)
Hypertension	0 (0.00%)	1 (7.69%)
Hypotension	1 (8.33%)	0 (0.00%)

Other Relevant Findings

Not Applicable

Conclusion:

In this study, no differences between treatment with eltrombopag in combination with dexamethasone treatment and treatment with dexamethasone alone could be observed. The limitation of this study was the small number of patients included, based on premature recruitment discontinuation due to feasibility reasons, resulting in a much lower patient number than intended. The safety profile in this study aligns with the established safety profile of eltrombopag.

Date of Clinical Trial Report

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