Clinical trial results:
A Phase 3 Multicenter, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of Rozanolixizumab in Adult Study Participants With Persistent or Chronic Primary Immune Thrombocytopenia (ITP)

Summary

EudraCT number	2019-000884-26
Trial protocol	PL BG HU BE CZ AT ES NL GB FR GR IT HR RO
Global end of trial date	27 April 2022

Results information

Result version number	v2 (current)
This version publication date	21 September 2023
First version publication date	05 May 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	TP0003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04200456
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, 1070
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 March 2022
Global end of trial reached?	Yes
Global end of trial date	27 April 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Demonstrate the clinical efficacy of rozanolixizumab in maintenance treatment in study participants with primary immune thrombocytopenia

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable

Actual start date of recruitment	31 January 2020
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	France: 1
Country: Number of subjects enrolled	Georgia: 4
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Moldova, Republic of: 2
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Ukraine: 5
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	33
EEA total number of subjects	15

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)	29
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll study participants in Jan 2020 and terminated in April 2022.

Pre-assignment

Screening details:

Participant Flow refers to the Randomized Set.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received a fixed-unit starting dose of placebo subcutaneous (sc) infusion matched to rozanolixizumab Dose A on Day 1. Following the initial dose, participants received a fixed-unit dose of placebo sc infusion matched to rozanolixizumab Dose B every 2 weeks until Week 23. Participants were followed up to a maximum of Week 31.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received placebo at prespecified time points.

Arm title	Rozanolixizumab

Arm description:

Participants received a fixed-unit starting dose of rozanolixizumab sc infusion equivalent to Dose A on Day 1. Following the initial dose, participants received a fixed-unit dose of rozanolixizumab sc infusion equivalent to Dose B every 2 weeks until Week 23. After protocol amendment 3, the starting dose was removed and the frequency of administration of the Dose B was changed to weekly. Participants were followed up to a maximum of Week 31.

Arm type	Experimental
Investigational medicinal product name	Rozanolixizumab
Investigational medicinal product code	UCB7665
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received rozanolixizumab at prespecified time points.

Number of subjects in period 1	Placebo	Rozanolixizumab
Started	12	21
Completed	9	15
Not completed	3	6
Consent withdrawn by subject	2	2
Physician decision	-	1
Administration of Rescue and concern about IMP	-	1
Adverse event, non-fatal	-	1
Lack of efficacy	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received a fixed-unit starting dose of placebo subcutaneous (sc) infusion matched to rozanolixizumab Dose A on Day 1. Following the initial dose, participants received a fixed-unit dose of placebo sc infusion matched to rozanolixizumab Dose B every 2 weeks until Week 23. Participants were followed up to a maximum of Week 31.	
Reporting group title	Rozanolixizumab
Reporting group description:	
Participants received a fixed-unit starting dose of rozanolixizumab sc infusion equivalent to Dose A on Day 1. Following the initial dose, participants received a fixed-unit dose of rozanolixizumab sc infusion equivalent to Dose B every 2 weeks until Week 23. After protocol amendment 3, the starting dose was removed and the frequency of administration of the Dose B was changed to weekly. Participants were followed up to a maximum of Week 31.	

Reporting group values	Placebo	Rozanolixizumab	Total
Number of subjects	12	21	33
Age Categorical Units: participants			
<=18 years	0	1	1
Between 18 and 65 years	10	18	28
>=65 years	2	2	4
Age Continuous Units: years			
arithmetic mean	51.4	41.4	
standard deviation	± 15.9	± 12.8	-
Sex: Female, Male Units: participants			
Female	11	12	23
Male	1	9	10
Platelet count Units: *10^9/L			
arithmetic mean	17.2	17.0	
standard deviation	± 11.3	± 9.4	-

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received a fixed-unit starting dose of placebo subcutaneous (sc) infusion matched to rozanolixizumab Dose A on Day 1. Following the initial dose, participants received a fixed-unit dose of placebo sc infusion matched to rozanolixizumab Dose B every 2 weeks until Week 23. Participants were followed up to a maximum of Week 31.

Reporting group title	Rozanolixizumab

Reporting group description:

Participants received a fixed-unit starting dose of rozanolixizumab sc infusion equivalent to Dose A on Day 1. Following the initial dose, participants received a fixed-unit dose of rozanolixizumab sc infusion equivalent to Dose B every 2 weeks until Week 23. After protocol amendment 3, the starting dose was removed and the frequency of administration of the Dose B was changed to weekly. Participants were followed up to a maximum of Week 31.

Primary: Percentage of Participants With Durable Clinically Meaningful Platelet Response of ≥50x10^9/L, for at least 8 out of 12 weeks during the last 12 weeks

End point title	Percentage of Participants With Durable Clinically Meaningful Platelet Response of ≥50x10^9/L, for at least 8 out of 12 weeks during the last 12 weeks[1]

End point description:

Percentage of Participants With Durable Clinically Meaningful Platelet Response of ≥50×10^9/L, for at least 8 out of 12 weeks during the last 12 weeks were reported. Randomized Set consisted of all enrolled study participants who were randomized. No formal analysis was carried out as the program was terminated.

End point type	Primary

End point timeframe:

During the last 12 weeks (Week 13 to Week 25)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Placebo	Rozanolixizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	21		
Units: Percentage of participants				
number (not applicable)	0	19.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of weeks with Clinically Meaningful Platelet Response of ≥50×10^9/L over the 24-week Treatment Period

End point title	Cumulative number of weeks with Clinically Meaningful Platelet Response of ≥50×10^9/L over the 24-week Treatment Period

End point description:

Total number of weeks with platelet counts ≥50×10^9/L over the 24-week Treatment Period of the study (Week 1 to Week 25) were reported. Randomized Set consisted of all enrolled study participants who were randomized. No formal analysis was carried out as the program was terminated.

End point type	Secondary

End point timeframe:

Week 1 up to Week 25

End point values	Placebo	Rozanolixizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	21		
Units: Weeks				
median (full range (min-max))	0.0 (0 to 7)	3.0 (0 to 24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first Clinically Meaningful Platelet Response (CMPR) of ≥50×10^9/L: time from starting treatment to achievement of first response of ≥50×10^9/L

End point title	Time to first Clinically Meaningful Platelet Response (CMPR) of ≥50×10^9/L: time from starting treatment to achievement of first response of ≥50×10^9/L

End point description:

Time from starting treatment to achievement of first Clinically Meaningful Platelet Response of ≥50×10^9/L was defined as date of first clinically meaningful response - date of first treatment + 1. Median was calculated based upon the Kaplan-Meier estimate. Randomized Set consisted of all enrolled study participants who were randomized. 999 for placebo arm signifies that upper confidence limit for placebo is not provided for the 95% CI of the median time to first CMPR as there is no time at which the upper bound of the CI for the Kaplan-Meier estimator is less than or equal to 0.5 and 999 for rozanolixizumab arm signifies that upper confidence limit for rozanolixizumab is not provided for the 95% CI of the median time to first CMPR as there is no time at which the upper bound of the CI for the Kaplan-Meier estimator is less than or equal to 0.5.

End point type	Secondary

End point timeframe:

Time from starting treatment to achievement of first response of ≥50×10^9/L (up to Week 25)

End point values	Placebo	Rozanolixizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	21		
Units: days				
median (confidence interval 95%)	44.0 (6.0 to 999)	8.0 (6.0 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Response defined as platelet count ≥30*10^9/L and at least doubling of baseline, at least 2 separate occasions at two adjacent nominal visits at least 7 days apart, and absence of bleeding

End point title	Percentage of Participants with Response defined as platelet count ≥30*10^9/L and at least doubling of baseline, at least 2 separate occasions at two adjacent nominal visits at least 7 days apart, and absence of bleeding

End point description:

Response was defined as platelet count ≥30×10^9/L and at least doubling of baseline, at least 2 separate occasions at two adjacent nominal visits at least 7 days apart, and absence of bleeding. Randomized Set consisted of all enrolled study participants who were randomized. No formal analysis was carried out as the program was terminated.

End point type	Secondary

End point timeframe:

From Baseline during Treatment Period (up to Week 25)

End point values	Placebo	Rozanolixizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	21		
Units: Percentage of participants				
number (not applicable)	8.3	33.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Clinically Meaningful Platelet Response of ≥50×10^9/L by Day 8

End point title	Percentage of Participants with Clinically Meaningful Platelet Response of ≥50×10^9/L by Day 8

End point description:

Clinically meaningful platelet response was defined as platelet count of ≥50×10^9/L. Randomized Set consisted of all enrolled study participants who were randomized. No formal analysis was carried out as the program was terminated.

End point type	Secondary

End point timeframe:

Baseline to Day 8

End point values	Placebo	Rozanolixizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	21		
Units: Percentage of participants				
number (not applicable)	16.7	52.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 25 in Primary Immune Thrombocytopenia Patient Assessment Questionnaire (ITP-PAQ) Symptoms Score

End point title	Change from Baseline to Week 25 in Primary Immune Thrombocytopenia Patient Assessment Questionnaire (ITP-PAQ) Symptoms Score

End point description:

ITP-PAQ version 1 is a 44 item disease-specific Health-Related Quality of Life questionnaire developed for use in adults with chronic ITP. It includes 10 scales as physical health: Symptoms (6 items), Bother (3 items), Fatigue (4 items), Activity (2 items); emotional health: Fear (5 items) and Psychological (5 items); quality of life (QOL): Work QOL (4 items), Social QOL (4 items), Women's Reproductive QOL (6 items) and Overall QOL (5 items). Each item is rated on a Likert-type scale containing 4 to 7 responses. All item scores are transformed to a 0 to 100 continuum and are weighted equally to derive individual scale scores and total score (0-100) is calculated as per formula: Sum of item scores within the scale/raw sum range*100. Higher scores indicate better health status. Randomized Set: enrolled study participants who were randomized. Number of Participants analyzed signifies participants evaluable for this endpoint. No formal analysis was carried out as program was terminated.

End point type	Secondary

End point timeframe:

From Baseline during Treatment Period (up to Week 25)

End point values	Placebo	Rozanolixizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	16		
Units: units on a scale				
arithmetic mean (standard deviation)	6.9 (± 13.8)	5.5 (± 9.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first rescue therapy

End point title	Time to first rescue therapy

End point description:

Time to first rescue therapy was defined as date of first rescue therapy use - date of first treatment + 1. Median was calculated based upon Kaplan-Meier estimate. The probability of requiring rescue medication did not reach 0.5 so KM median in the rozanolixizumab arm could not be estimated. Randomized Set consisted of all enrolled study participants who were randomized. 999 for placebo arm signifies that upper confidence limit for placebo is not provided for 95% CI of median time to rescue therapy as there is no time at which upper bound of CI for Kaplan-Meier estimator is less than or equal to 0.5. 999 for median signifies that probability of participants requiring rescue medication did not reach 0.5 so the Kaplan-Meier median could not be estimated. 999 signifies that upper confidence limit for rozanolixizumab is not provided for the 95% CI of median time to rescue therapy as there is no time at which upper bound of CI for the Kaplan-Meier estimator is less than or equal to 0.5.

End point type	Secondary

End point timeframe:

From Baseline to first rescue therapy (up to Week 25)

End point values	Placebo	Rozanolixizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	21		
Units: Days				
median (confidence interval 95%)	34.5 (4.0 to 999)	999 (23.0 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With treatment-emergent adverse events (TEAEs)

End point title	Percentage of Participants With treatment-emergent adverse events (TEAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of investigational medicinal product (IMP), whether or not considered related to the IMP. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of IMP. TEAEs are defined as AEs starting after the time of first IMP administration up to and including 8 weeks (56 days) after the final dose. Safety set included all randomized study participants who received at least one dose of IMP.

End point type	Secondary

End point timeframe:

From Baseline to end of Safety Follow-Up Period (up to Week 31)

End point values	Placebo	Rozanolixizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	21		
Units: Percentage of participants				
number (not applicable)	75.0	85.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With TEAEs leading to withdrawal of investigational medicinal product (ie, study discontinuation)

End point title	Percentage of Participants With TEAEs leading to withdrawal of investigational medicinal product (ie, study discontinuation)

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of IMP, whether or not considered related to the IMP. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of IMP. TEAEs are defined as AEs starting after the time of first IMP administration up to and including 8 weeks (56 days) after the final dose. Safety set included all randomized study participants who received at least one dose of IMP.

End point type	Secondary

End point timeframe:

From Baseline to end of Safety Follow-Up Period (up to Week 31)

End point values	Placebo	Rozanolixizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	21		
Units: Percentage of participants				
number (not applicable)	0	4.8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline to end of Safety Follow-Up Period (up to Week 31)

Adverse event reporting additional description:

TEAEs are defined as AEs starting after the time of first IMP administration up to and including 8 weeks (56 days) after the final dose. TEAEs were analyzed for Safety Set.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Rozanolixizumab

Reporting group description:

Participants received a fixed-unit starting dose of rozanolixizumab sc infusion equivalent to Dose A on Day 1. Following the initial dose, participants received a fixed-unit dose of rozanolixizumab sc infusion equivalent to Dose B every 2 weeks until Week 23. After protocol amendment 3, the starting dose was removed and the frequency of administration of the Dose B was changed to weekly. Participants were followed up to a maximum of Week 31.

Reporting group title	Placebo

Reporting group description:

Participants received a fixed-unit starting dose of placebo sc infusion matched to rozanolixizumab Dose A on Day 1. Following the initial dose, participants received a fixed-unit dose of placebo sc infusion matched to rozanolixizumab Dose B every 2 weeks until Week 23. Participants were followed up to a maximum of Week 31.

Serious adverse events	Rozanolixizumab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 21 (9.52%)	1 / 12 (8.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Haemorrhage			
subjects affected / exposed	0 / 21 (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	
Blood and lymphatic system disorders			
Immune thrombocytopenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Urethritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 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	Rozanolixizumab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 21 (76.19%)	9 / 12 (75.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	9 / 21 (42.86%)	0 / 12 (0.00%)	
occurrences (all)	34	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 21 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Investigations			
Body temperature increased			
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Alanine aminotransferase increased			

subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 21 (66.67%)	5 / 12 (41.67%)	
occurrences (all)	48	8	
Dizziness			
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 21 (14.29%)	2 / 12 (16.67%)	
occurrences (all)	12	2	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 21 (23.81%)	1 / 12 (8.33%)	
occurrences (all)	6	1	
Vomiting			
subjects affected / exposed	4 / 21 (19.05%)	0 / 12 (0.00%)	
occurrences (all)	5	0	
Constipation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	2 / 21 (9.52%)	2 / 12 (16.67%)	
occurrences (all)	9	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)	
occurrences (all)	2	0	

Rash macular			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Infections and infestations			
Rhinitis			
subjects affected / exposed	2 / 21 (9.52%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
COVID-19			
subjects affected / exposed	1 / 21 (4.76%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Cystitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Enterocolitis infectious			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory tract infection viral			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 21 (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
21 November 2019	The primary purpose of this substantial amendment (21 Nov 2019) was to incorporate the feedback from the United States Food and Drug Administration (FDA) received on 23 October 2019. In addition to updates to provide clarity and consistency within the protocol and administrative revisions, the following modifications were made: • Added details on study stopping rules • Added ADA postdose samples to facilitate clinical validation of drug tolerance in the ADA assay • Eligibility criteria were modified to exclude participants with undiagnosed IgA deficiency and to include patients with moderate renal impairment. • Updated rescue therapy to include any systemic increase in corticosteroids dose above the Baseline dose • Included new wording specific to the predefined order of formal hypotheses testing and the sequence in which testing would be performed • Added an additional estimand for a secondary endpoint • Provided timing for obtaining IgG samples due to interference of other tests • Country-specific requirements: − Information specific to Moldova was no longer applicable to the study. − Updates to Poland were made to align with Polish Health Authority's and Clinical Trial Facilitation Group recommendations regarding pregnancy testing. • Added new wording that local guidelines should be followed regarding antibiotic prophylaxis in asplenic participants to remind investigators about the importance of antibiotic therapy in management of infections in splenectomized participants.
29 September 2020	The primary reason for this substantial amendment (29 Sep 2020) was to incorporate changes in the endpoints and the statistical analysis section, and to incorporate agency-required local protocol amendments into 1 global protocol. The country-specific changes were incorporated in Protocol Amendment 2 Appendix. In addition to updates to provide clarity and consistency within the protocol and administrative revisions, the following modifications were made: • Changed the number of additional participants that could be recruited into the study from 75 to 60 (maximum total sample size was changed from 105 to 90) based on revised sample size calculation method and assumptions • Primary analysis (previously incorporated by local Protocol Amendments 1.1, 1.2, and 1.3) − Removed all reference to the Fisher's Exact test and included as a separate supplemental estimand − Added more details regarding the Cochran-Mantel-Haenszel test • Added details to explain that the interim analysis was to have been conducted on combined data from TP0003 and TP0006, including amendment of the futility stopping rule • Modified study criteria to include study participants who had failed or were intolerant to 2 or more prior ITP therapies per global implementation of an ANSM request and implement feedback received from the FD • Deleted or moved to "other efficacy endpoints" endpoints that did not measure different manifestation of the disease and provided redundant information • Included additional "other" efficacy endpoints • Provided additional wording for clarification on the action taken for study participants on the lowest dose level with a platelet count between >200x109/L and <400x109/L (previously incorporated by local Protocol Amendments 1.2 and 1.3).

29 September 2020	This includes the continued information from Protocol Amendment 2 • Added that an independent Quantitative Clinical Pharmacologist/Modeling and Simulation Scientist may have access to the randomization code to review unblinded PK, platelet and serum IgG data to allow modelling activities to be started by an independent scientist • Explained that contingency measures during a pandemic and other exceptional circumstances had been included • Increased the number of sites from 50 to 70 • Country-specific requirements: − United States and Canada only: Updated and clarified study stopping rule per FDA request to change the study stopping rule − Japan only (previously incorporated by local Protocol Amendment 1.2): ▪ Added instructions for SAE reporting (investigational device) and device deficiency reporting specific for Japan, in accordance with local regulations in Japan ▪ Added chest X-ray assessment to early withdrawal (EW) visit and EOS visit to confirm safety at study termination ▪ Added the T-SPOT test as a recommended IGRA test in addition to the QuantiFERON test ▪ Included details on the consent requirements for participants aged <20 years of age ▪ Added exclusion criterion relative to partial splenic artery embolization as this procedure might have been used for treatment of ITP in Japan ▪ Removed wording on use of cannabinoids and medicinal marijuana because these drugs are prohibited by law in Japan.
03 December 2021	The primary reason for this substantial amendment (03 Dec 2021) was to modify the dosing regimen of the study on the recommendation of the IDMC. Only 1 study participant was enrolled under Protocol Amendment 3, and this participant was not treated prior to study termination. Thus, this aCSR, including analysis of the data for this study, was based on the protocol under Amendment 2.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 March 2020	From 24 March 2020 through 04 June 2020, enrollment into the study was temporarily on hold due to the coronavirus disease 2019 (COVID-19) pandemic outbreak.	05 June 2020
19 November 2021	From 19 Nov 2021, enrollment into the study was temporarily suspended to allow for the development of a protocol amendment (#3) to change the dosing frequency from biweekly to weekly. Reactivation commenced on 19 March 2022 with first screening after the re-start occuring 06 April 2022.	06 April 2022

Notes:

Limitations and caveats

None reported