Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of Efgartigimod (ARGX-113) 10 mg/kg Intravenous in Adult Patients With Primary Immune Thrombocytopenia

Summary

EudraCT number	2019-002100-41
Trial protocol	NL FR HU CZ ES PL BE DE AT GB IT
Global end of trial date	03 February 2022

Results information

Result version number	v1 (current)
This version publication date	22 February 2023
First version publication date	22 February 2023

Trial information

Trial identification

Sponsor protocol code	ARGX-113-1801

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04188379
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	argenx BV
Sponsor organisation address	Industriepark Zwijnaarde 7, Zwijnaarde (Ghent), Belgium, 9052
Public contact	Regulatory Manager, argenx BV, +32 9 310 3400, regulatory@argenx.com
Scientific contact	Regulatory Manager, argenx BV, +32 9 310 3400, regulatory@argenx.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	16 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of efgartigimod compared to placebo in achieving a sustained platelet count response in subjects with primary chronic immune thrombocytopenia (ITP), with a sustained platelet count response defined as platelet counts of at least 50×10^9/L for at least 4 of the 6 visits between weeks 19 and 24 of the trial.

Protection of trial subjects:

This study was conducted according to the ICH GCP, the principles of the Declaration of Helsinki, and other applicable local ethical and legal requirements.

Background therapy:

Subjects receiving at least 1 permitted concurrent ITP therapy were eligible for the trial (if the dose and schedule have remained unchanged in the last 4 weeks before randomisation).

Evidence for comparator: -

Actual start date of recruitment	09 December 2019
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	Netherlands: 2
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Georgia: 20
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Turkey: 20
Country: Number of subjects enrolled	Ukraine: 3

Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	131
EEA total number of subjects	57

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)	107
From 65 to 84 years	23
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 71 active sites that enrolled patient in 18 countries. Recruitment started on 09 December 2019.

Pre-assignment

Screening details:

During the screening period (up to 2 weeks) the subject's eligibility for trial participation was evaluated. A total of 205 subjects were screened, of which 74 subjects were screen failures. 131 of 205 were enrolled and randomised at a ratio of 2:1 to receive efgartigimod or placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Efgartigimod

Arm description:

The subjects entered a 24-week treatment period and were randomised to receive efgartigimod 10 mg/kg intravenous (IV). The investigational medicinal product (IMP) infusion (efgartigimod) was administered weekly from visits 1 to 4, either weekly or every other week (q2w) from visits 5 to 16, and fixed on the dosing schedule of visit 16 (or the last visit at which IMP was administered) from visits 17 to 24 (ie, either weekly or q2w).

Arm type	Experimental
Investigational medicinal product name	Efgartigimod
Investigational medicinal product code	ARGX-113
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The subjects received IV efgartigimod infusion 10 mg/kg (fixed dose) either weekly or q2W. The IV infusion was administered over the period of approximately 1 hour. The maximum total dose per efgartigimod infusion was 1200 mg for subjects with a body weight ≥120 kg measured at infusion visits.

Arm title	Placebo

Arm description:

The subjects entered a 24-week treatment period and were randomized to receive placebo intravenous (IV).The placebo infusion was administered weekly from visits 1 to 4, either weekly or q2w from visits 5 to 16, and fixed on the dosing schedule of visit 16 (or the last visit at which placebo was administered) from visits 17 to 24 (ie, either weekly or q2w).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The subjects received The subjects received IV placebo infusion either weekly or q2w. The IV infusion was administered over the period of approximately 1 hour.

Number of subjects in period 1	Efgartigimod	Placebo
Started	86	45
Completed	64	32
Not completed	22	13
Consent withdrawn by subject	10	3
Physician decision	-	1
Adverse event, non-fatal	3	1
Not specified	-	3
Pregnancy	1	-
Lack of efficacy	8	5

Baseline characteristics

Reporting groups

Reporting group title	Efgartigimod

Reporting group description:

The subjects entered a 24-week treatment period and were randomised to receive efgartigimod 10 mg/kg intravenous (IV). The investigational medicinal product (IMP) infusion (efgartigimod) was administered weekly from visits 1 to 4, either weekly or every other week (q2w) from visits 5 to 16, and fixed on the dosing schedule of visit 16 (or the last visit at which IMP was administered) from visits 17 to 24 (ie, either weekly or q2w).

Reporting group title	Placebo

Reporting group description:

The subjects entered a 24-week treatment period and were randomized to receive placebo intravenous (IV).The placebo infusion was administered weekly from visits 1 to 4, either weekly or q2w from visits 5 to 16, and fixed on the dosing schedule of visit 16 (or the last visit at which placebo was administered) from visits 17 to 24 (ie, either weekly or q2w).

Reporting group values	Efgartigimod	Placebo	Total
Number of subjects	86	45	131
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	75	32	107
From 65-84 years	10	13	23
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	46.9	51.7	
standard deviation	± 16.55	± 17.93	-
Gender categorical Units: Subjects			
Female	47	24	71
Male	39	21	60
Race Units: Subjects			
Asian	5	3	8
White	80	41	121
Not reported	0	1	1
Other-unspecified	1	0	1
Ethnicity Units: Subjects			
Japanese	5	3	8
Hispanic or Latino	4	1	5
Not Hispanic or Latino	77	40	117

Not reported	0	1	1

End points

End points reporting groups

Reporting group title	Efgartigimod

Reporting group description:

The subjects entered a 24-week treatment period and were randomised to receive efgartigimod 10 mg/kg intravenous (IV). The investigational medicinal product (IMP) infusion (efgartigimod) was administered weekly from visits 1 to 4, either weekly or every other week (q2w) from visits 5 to 16, and fixed on the dosing schedule of visit 16 (or the last visit at which IMP was administered) from visits 17 to 24 (ie, either weekly or q2w).

Reporting group title	Placebo

Reporting group description:

The subjects entered a 24-week treatment period and were randomized to receive placebo intravenous (IV).The placebo infusion was administered weekly from visits 1 to 4, either weekly or q2w from visits 5 to 16, and fixed on the dosing schedule of visit 16 (or the last visit at which placebo was administered) from visits 17 to 24 (ie, either weekly or q2w).

Primary: Proportion of Subjects with Chronic ITP with a Sustained Platelet Count Response for at Least 4 of the 6 Visits Between Weeks 19 and 24 of the Study

End point title	Proportion of Subjects with Chronic ITP with a Sustained Platelet Count Response for at Least 4 of the 6 Visits Between Weeks 19 and 24 of the Study

End point description:

Proportion of subjects with chronic ITP with a sustained platelet count response was defined as achieving platelet counts of at least 50 × 10^9 per litre for at least 4 of the 6 visits between weeks 19 and 24 of the study.
Analysis was performed on Full analysis Set-Chronic population that included all randomised subjects with chronic ITP.

End point type	Primary

End point timeframe:

From Week 19 up to Week 24

End point values	Efgartigimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	40		
Units: Percentage of subjects				
number (not applicable)	21.8	5.0		

Statistical analyses

Statistical analysis title	Comparison of Efgartigimod Versus Placebo
Comparison groups	Placebo v Efgartigimod

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0316
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.884
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.007
upper limit	43.591

Secondary: Extent of Disease Control over the Planned 24-Week Treatment Period in the Chronic ITP Population

End point title	Extent of Disease Control over the Planned 24-Week Treatment Period in the Chronic ITP Population

End point description:

Extent of disease control, defined as the cumulative number of weeks over the planned 24-week treatment period with platelet counts of ≥50 × 10^9/L in the chronic ITP population.
Analysis was performed on Full Analysis Set-Chronic population that included all randomized subjects with chronic ITP.

End point type	Secondary

End point timeframe:

From Week 1 up to Week 24

End point values	Efgartigimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	40		
Units: Weeks				
median (inter-quartile range (Q1-Q3))	2.00 (0.00 to 11.00)	0.00 (0.00 to 1.00)		

Statistical analyses

Statistical analysis title	Comparison of Efgartigimod Versus Placebo
Comparison groups	Efgartigimod v Placebo
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0009
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (net)
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	4

Secondary: Proportion of Subjects with a Sustained Platelet Count Response for at least 4 of the 6 visits between weeks 19 and 24 of the study

End point title	Proportion of Subjects with a Sustained Platelet Count Response for at least 4 of the 6 visits between weeks 19 and 24 of the study

End point description:

Proportion of subjects in the overall population (chronic and persistent ITP) with a sustained platelet count response, defined as achieving platelet counts of at least 50 × 10^9/L for at least 4 of the 6 visits between weeks 19 and 24 of the study.
The analysis was performed on Full Analysis set population that included all randomized subjects in the study.

End point type	Secondary

End point timeframe:

From Week 19 up to Week 24

End point values	Efgartigimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	45		
Units: Percentage of subjects				
number (not applicable)	25.6	6.7		

Statistical analyses

Statistical analysis title	Comparison of Efgartigimod Versus Placebo
Comparison groups	Efgartigimod v Placebo
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0108
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	5.224
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.268
upper limit	26.268

Secondary: Incidence of WHO-Classified Bleeding Events (WHO Bleeding Scale ≥ 1) in the Overall Population

End point title	Incidence of WHO-Classified Bleeding Events (WHO Bleeding Scale ≥ 1) in the Overall Population

End point description:

Incidence of the World Health Organization (WHO)-classified bleeding events in the overall population. Analysis was performed on Full Analysis Set population that included all randomised subjects.
This secondary endpoint used the WHO-classified bleeding scale. Bleeding was the predominant clinical manifestation of ITP and was typically related to platelet count. Accordingly, measuring bleeding was important for monitoring this subject population. The WHO bleeding scale was neither specific to nor validated for ITP, but had been implemented in ITP clinical studies; no specific and validated tools for assessing bleeding in ITP were available.

End point type	Secondary

End point timeframe:

From Week 1 to Week 24

End point values	Efgartigimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	45		
Units: Number				
median (inter-quartile range (Q1-Q3))	4.0 (1.0 to 10.0)	5.0 (2.0 to 14.0)		

Statistical analyses

Statistical analysis title	Comparison of Efgartigimod Versus Placebo
Comparison groups	Efgartigimod v Placebo
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8287
Method	Wald test
Parameter estimate	Rate Ratio
Point estimate	0.958
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.651
upper limit	1.41

Secondary: Proportion of Participants in the Overall Population Achieving Platelet Counts of at Least 50 × 10^9/L for at Least 6 of the 8 Visits Between Week 17 and 24

End point title	Proportion of Participants in the Overall Population Achieving Platelet Counts of at Least 50 × 10^9/L for at Least 6 of the 8 Visits Between Week 17 and 24

End point description:

Proportion of subjects in the overall population achieving platelet counts of at least 50 × 10^9/L for at least 6 of the 8 visits between weeks 17 and 24 of the study.
Analysis was performed on Full Analysis Set population that included all randomised subjects.

End point type	Secondary

End point timeframe:

From Week 17 up to Week 24

End point values	Efgartigimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	45		
Units: Percentage of subjects				
number (not applicable)	22.1	6.7		

Statistical analyses

Statistical analysis title	Comparison of Efgartigimod versus Placebo
Comparison groups	Placebo v Efgartigimod
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0265
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.354
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.048
upper limit	22.865

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Full study duration (31 Weeks)

Adverse event reporting additional description:

Treatment emergent adverse events are defined as adverse events starting on or after first administration of any study drug. Safety analyses were performed on the safety analysis set which included all subjects in the randomized population who received at least 1 dose or part of a dose of IMP. No deaths occurred during the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Efgartigimod

Reporting group description:

The subjects entered a 24-week treatment period and were randomised to receive efgartigimod 10 mg/kg IV , weekly from visits 1 to 4 and then from visits 5 to 16 either weekly or q2w, adjusted according to their platelet counts. From visits 17 to 24, subjects were fixed on the dosing schedule at visit 16 or at the last visit at which IMP was administered (ie, either weekly or q2w).

Reporting group title	Placebo

Reporting group description:

The subjects entered a 24-week treatment period and were randomized to receive placebo IV, weekly from visits 1 to 4 and then from visits 5 to 16 either weekly or q2w, adjusted according to their platelet counts. From visits 17 to 24, subjects were fixed on the dosing schedule at visit 16 or at the last visit at which IMP was administered (ie, either weekly or q2w).

Serious adverse events	Efgartigimod	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 86 (8.14%)	7 / 45 (15.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic myelomonocytic leukaemia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 86 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Headache			
subjects affected / exposed	1 / 86 (1.16%)	0 / 45 (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			
Anaemia			
subjects affected / exposed	0 / 86 (0.00%)	1 / 45 (2.22%)	
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 / 86 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 86 (2.33%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 86 (1.16%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	0 / 86 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			

subjects affected / exposed	1 / 86 (1.16%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 86 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 86 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 86 (1.16%)	0 / 45 (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			
Appendicitis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 86 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	1 / 86 (1.16%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 86 (1.16%)	0 / 45 (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	Efgartigimod	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 86 (93.02%)	43 / 45 (95.56%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	8 / 86 (9.30%)	11 / 45 (24.44%)	
occurrences (all)	17	34	
Hypertension			
subjects affected / exposed	5 / 86 (5.81%)	0 / 45 (0.00%)	
occurrences (all)	6	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 86 (6.98%)	0 / 45 (0.00%)	
occurrences (all)	8	0	
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	5 / 86 (5.81%)	3 / 45 (6.67%)	
occurrences (all)	9	4	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	8 / 86 (9.30%)	8 / 45 (17.78%)	
occurrences (all)	24	12	
Investigations			
Blood urine present			
subjects affected / exposed	31 / 86 (36.05%)	17 / 45 (37.78%)	
occurrences (all)	66	32	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	17 / 86 (19.77%)	6 / 45 (13.33%)	
occurrences (all)	52	42	

Nervous system disorders			
Headache			
subjects affected / exposed	14 / 86 (16.28%)	6 / 45 (13.33%)	
occurrences (all)	20	22	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 86 (6.98%)	3 / 45 (6.67%)	
occurrences (all)	8	4	
Neutropenia			
subjects affected / exposed	2 / 86 (2.33%)	3 / 45 (6.67%)	
occurrences (all)	7	4	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 86 (3.49%)	4 / 45 (8.89%)	
occurrences (all)	4	6	
Gingival bleeding			
subjects affected / exposed	4 / 86 (4.65%)	6 / 45 (13.33%)	
occurrences (all)	6	12	
Mouth haemorrhage			
subjects affected / exposed	7 / 86 (8.14%)	7 / 45 (15.56%)	
occurrences (all)	13	10	
Oral blood blister			
subjects affected / exposed	2 / 86 (2.33%)	3 / 45 (6.67%)	
occurrences (all)	3	7	
Nausea			
subjects affected / exposed	5 / 86 (5.81%)	2 / 45 (4.44%)	
occurrences (all)	9	2	
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	5 / 86 (5.81%)	6 / 45 (13.33%)	
occurrences (all)	10	13	
Petechiae			
subjects affected / exposed	13 / 86 (15.12%)	12 / 45 (26.67%)	
occurrences (all)	21	20	
Purpura			
subjects affected / exposed	7 / 86 (8.14%)	4 / 45 (8.89%)	
occurrences (all)	12	12	

Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	 14 / 86 (16.28%) 30	 6 / 45 (13.33%) 11	
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	 1 / 86 (1.16%) 1	 5 / 45 (11.11%) 5	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	 7 / 86 (8.14%) 7	 2 / 45 (4.44%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2019	Amendment 1: The eligibility criteria were changed from 1 prior therapy to 2 prior therapies. The eligibility criteria were updated to specify highly effective methods of contraception per Clinical Trials Facilitation and Coordination Group recommendations (part of the Heads of Medicines Agencies). The conditions for (temporarily) withholding treatment, early discontinuation from the study, and early discontinuation from treatment were updated. The determination of the sample size, the primary endpoint analysis, and the key secondary endpoint analysis subject to alpha control were updated. A key secondary efficacy endpoint subject to alpha control was added. Japan-specific eligibility criteria were removed in lieu of a separate Japan-specific protocol.
18 September 2019	Amendment 2: The protocol was aligned with ICH E2A guideline and the categories of seriousness on the sponsor's SAE report form.
27 May 2020	Amendment 3: The postbaseline platelet count measurement was permitted within 1 day of the next procedure, for more flexibility. Fostamatinib was added as a permitted concurrent ITP medication upon its regulatory approval as ITP therapy. Eltrombopag was replaced with "oral thrombopoietin receptor agonist (TPO-RA)" to consider all TPO-RAs. An eligibility criterion was added regarding live/live-attenuated vaccines, as a preventive protection measure for participants. The key secondary endpoint analysis subject to alpha control and the determinations of sample size were updated to allow data from participants who met the definition of disease control during the study but who subsequently did not meet the criteria for disease control before the end of the treatment period, to contribute more data to the final estimate of the length of disease control. Derivation of pharmacokinetic parameters by noncompartmental methods became less appropriate with the limited pharmacokinetic sampling. Therefore, only efgartigimod serum concentration data were summarized. It was added to specify that IgG testing could not be performed locally to avoid unintentional unblinding. COVID-19 mitigation measures were added.
16 November 2020	Amendment 4: The eligibility criterion regarding the number of platelet counts at study entry was updated to allow more flexibility. Acceptable methods of contraception were added to the eligibility criteria per the results of the reproductive toxicity studies. The visit duration after the end of IMP infusions was shortened based on supporting safety data. The definition of AEs was updated and clarified. The definition of rescue therapy was updated to consist of an "occurrence," which was defined as a ≤5-day period in which 1 or more rescue treatments were administered to a participant.
15 July 2021	Amendment 5: The primary endpoint analysis was updated. The key secondary endpoint analysis subject to alpha control was updated for consistency with the primary endpoint analysis.
19 July 2021	Country-Specific Amendment France version 5.1: The description of the 24-week treatment period (ie, "trial period") was updated to "treatment period" to clarify the duration of the period, per central IEC request. Clarifications in the protocol summary were added to state the number of visits and the time duration of each visit. Reference to the Summary of Product Characteristics was added to the Concurrent ITP Therapy section. The participant demographic assessment was modified to provide that source data verification of race and ethnicity should not be performed per French regulations.

20 July 2021	Country-Specific Amendment Japan version 5.1: The sample size for Japanese participants was added. The stratification and randomization strategy was updated for Japanese participants. Specific safety measures were added. The eligibility criteria were aligned with Japanese regulations: the minimum age of enrollment was changed to 20 years of age to align with Japanese age of majority, a definition of a Japanese participant was added, and a Helicobacter pylori test was added per current management of ITP in Japan.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported