Clinical trial results:
An extension study of eltrombopag in pediatric patients with chronic immune (idiopathic) thrombocytopenia purpura (ITP)

Summary

EudraCT number	2017-004082-27
Trial protocol	Outside EU/EEA
Global end of trial date	04 July 2017

Results information

Result version number	v1 (current)
This version publication date	24 February 2018
First version publication date	24 February 2018

Trial information

Trial identification

Sponsor protocol code	117366

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02201290
WHO universal trial number (UTN)	-
Other trial identifiers	CETB115BRU01: 2017-004082-27

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 July 2017
Global end of trial reached?	Yes
Global end of trial date	04 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to provide continued treatment to patients who have completed the TRA115450 study and to describe the safety and tolerability of Eltrombopag when administered to pediatric subjects with previously treated chronic ITP.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2013
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	Russian Federation: 9
Worldwide total number of subjects	9
EEA total number of subjects	0

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)	6
Adolescents (12-17 years)	3
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study included pediatric patients with chronic ITP.

Pre-assignment

Screening details:

Study screening period was followed by a single arm treatment period and a follow-up period

Period 1

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

Blinding implementation details:

This was an open-label study.

Arms

Arm title	Treated participants

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Eltrombopag (CETB115B)
Investigational medicinal product code	Eltrombopag tablets
Other name	CETB115B
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

40mg

Number of subjects in period 1	Treated participants
Started	9
Completed	4
Not completed	5
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Lack of efficacy	2

Baseline characteristics

Reporting groups

Reporting group title	Treated participants

Reporting group description: -

Reporting group values	Treated participants	Total	
Number of subjects	9	9	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	5	5	
Adolescents (12-17 years)	4	4	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	9.7		
standard deviation	± 3.81	-	
Gender, Male/Female Units: Subjects			
Female	4	4	
Male	5	5	

Subject analysis sets

Subject analysis set title	ATS
Subject analysis set type	Safety analysis

Subject analysis set description:

The all treated subjects (ATS) analysis set included all patients who received at least one dose of Eltrombopag.

Reporting group values	ATS		
Number of subjects	9		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	5		
Adolescents (12-17 years)	4		

Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean	9.7		
standard deviation	± 3.81		
Gender, Male/Female Units: Subjects			
Female	4		
Male	5		

End points

End points reporting groups

Reporting group title	Treated participants
Reporting group description: -	
Subject analysis set title	ATS
Subject analysis set type	Safety analysis

Subject analysis set description:

The all treated subjects (ATS) analysis set included all patients who received at least one dose of Eltrombopag.

Primary: Adverse Events

End point title	Adverse Events[1]

End point description:

Frequency of all adverse events (including Ophthalmic events) categorized using CTCAE toxicity grades and clinical laboratory test [Time Frame: Up to Week 4 Follow-up period] Clinical laboratory assessments and frequency of all adverse events, categorized using Common Terminology Criteria for Adverse Events (CTCAE) toxicity grades will present safety and tolerability endpoints

End point type	Primary

End point timeframe:

Up to week 4 follow up period

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: Stats analysis does not apply to this endpoint

End point values	Treated participants	ATS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9	9		
Units: participants				
Number of subjects with at least one event	3	6		
Infections and infestations	0	3		
Nervous system disorders	0	2		
Respiratory, thoracic and mediastinal disorders	1	0		
Eye disorders	1	0		
Hepatobiliary disorders	1	0		
Investigations	0	0		
Metabolism and nutrition disorders	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Eltrombopag

Reporting group description:

Eltrombopag

Serious adverse events	Eltrombopag		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Eye disorders			
Scleral haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Eltrombopag		
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 9 (66.67%)		
Investigations Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 10		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) Tonsillitis subjects affected / exposed occurrences (all)	3 / 9 (33.33%) 4 1 / 9 (11.11%) 1 1 / 9 (11.11%) 2		
Metabolism and nutrition disorders Iron deficiency subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2013	Protocol was amended 1 time. Previous sections of this report describe the study conduct as amended. The key features of amendment are given below: Amendment 01 (08-Jul-2013) introduced the following changes: Sponsor Medical Monitor was updated. The rationale of the study was clarified and the study assessments simplified Clarification of the term 'study treatment'. Clarification of dosing by age rather than cohort. Additional guidance was included for those subjects who switched formulation during the study. Clarification around the time period to record prior medications. Correction of study number within table as well as clarification of assessments. Clarification of endpoints. Clarification consistent with revised assessments and match Time and Events Table. Clarification physical examination and the removal of vital signs. Renal assessments were removed. Title was changed to reflect more streamlined assessment and focus on cataract assessment. Subsections 7.2.1.5.1. Baseline, Ocular History and Risk Factors, 7.2.1.5.2, Ophthalmic Examinations and 7.2.1.5.4 Additional Ocular Follow-up were removed. Laboratory assessments were streamlined. Table 4 was amended to reflect this change. Clarification around administration of Eltrombopag. Clarification to data process and removal of repeated text. The Reporting and Analysis Plan was removed. This section and each sub-section within were changed for the modification of analysis and data collection. These amendments were not considered to have affected the interpretation of study results.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported