



## Clinical trial results:

### A Phase 3b, Multi-center, Randomized, Double-blind, Placebo-controlled, Parallel-group Trial with an Open-label Extension Phase to Evaluate the Efficacy and Safety of Avatrombopag for the Treatment of Thrombocytopenia in Pediatric Subjects with Immune Thrombocytopenia for 6 Months

#### Summary

EudraCT number	2020-003232-24
Trial protocol	FR HU DE PL
Global end of trial date	

#### Results information

Result version number	v1
This version publication date	22 May 2024
First version publication date	22 May 2024

#### Trial information

##### Trial identification

Sponsor protocol code	AVA-PED-301
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04516967
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Sobi Inc.
Sponsor organisation address	890 Winter Street, Suite 200, Waltham, United States, 02451
Public contact	Medical Information, Sobi, Inc., +1 781 786 7370, medinfo.us@sobi.com
Scientific contact	Medical Information, Sobi, Inc., +1 781 786 7370, medinfo.us@sobi.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001136-PIP01-11
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	Interim
Date of interim/final analysis	18 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 November 2023
Global end of trial reached?	No

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that the efficacy of avatrombopag is superior to placebo for the treatment of pediatric subjects with ITP of  $\geq 6$  months duration who have had an insufficient response to a previous treatment

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) and 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	02 March 2021
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	Poland: 4
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	United States: 13
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Ukraine: 2
Country: Number of subjects enrolled	Türkiye: 29
Worldwide total number of subjects	75
EEA total number of subjects	13

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)	1

Children (2-11 years)	45
Adolescents (12-17 years)	29
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

To be eligible for the study, the subject must have had a confirmed diagnosis of primary ITP for  $\geq 6$  months duration and had an insufficient response to a previous treatment with an average of 2 platelet counts  $< 30 \times 10^9/L$  with no single count  $> 35 \times 10^9/L$ .

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Avatrombopag
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Avatrombopag
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received avatrombopag or matching placebo as either the film-coated oral tablet or the powder for oral suspension. The powder for oral suspension was contained in a capsule that was to be opened to sprinkle the contents into an appropriate vehicle to prepare the suspension. No partial dosing from the capsule was allowed; the entire contents were to be used to prepare the suspension. On Day 1, Cohort 1 ( $\geq 12$  to  $< 18$  years old) and Cohort 2 ( $\geq 6$  to  $< 12$  years old) had a starting dose of avatrombopag of 20 mg once daily, administered as an oral tablet, consistent with the approved adult dosing. The starting dose for Cohort 3 ( $\geq 1$  to  $< 6$  years old) was 10 mg once daily administered as an oral suspension. The dose of study drug was to be titrated up or down based on the subject's platelet count to maintain a platelet count between  $\geq 50$  and  $\leq 150 \times 10^9/L$ .

<b>Arm title</b>	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo to match avatrombopag
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received avatrombopag or matching placebo as either the film-coated oral tablet or the powder for oral suspension. The powder for oral suspension was contained in a capsule that was to be opened to sprinkle the contents into an appropriate vehicle to prepare the suspension. No partial dosing from the capsule was allowed; the entire contents were to be used to prepare the

suspension. On Day 1, Cohort 1 ( $\geq 12$  to  $< 18$  years old) and Cohort 2 ( $\geq 6$  to  $< 12$  years old) had a starting dose of avatrombopag of 20 mg once daily, administered as an oral tablet, consistent with the approved adult dosing. The starting dose for Cohort 3 ( $\geq 1$  to  $< 6$  years old) was 10 mg once daily administered as an oral suspension. The dose of study drug was to be titrated up or down based on the subject's platelet count to maintain a platelet count between  $\geq 50$  and  $\leq 150 \times 10^9/L$ .

<b>Number of subjects in period 1</b>	Avatrombopag	Placebo
Started	54	21
Completed	44	1
Not completed	10	20
Physician decision	1	1
Adverse event, non-fatal	2	1
Lack of efficacy	7	18

## Baseline characteristics

### Reporting groups

Reporting group title	Avatrombopag
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Avatrombopag	Placebo	Total
Number of subjects	54	21	75
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	1	0	1
Children (2-11 years)	32	13	45
Adolescents (12-17 years)	21	8	29
Age continuous			
Units: years			
arithmetic mean	8.9	9.9	
standard deviation	± 4.36	± 4.13	-
Gender categorical			
Units: Subjects			
Female	24	12	36
Male	30	9	39

### Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomized subjects.	

Reporting group values	Full Analysis Set		
Number of subjects	75		
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	1		
Children (2-11 years)	45		
Adolescents (12-17 years)	29		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±		
Gender categorical			
Units: Subjects			
Female			
Male			



## End points

### End points reporting groups

Reporting group title	Avatrombopag
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomized subjects.	

### Primary: Durable Platelet Response

End point title	Durable Platelet Response
End point description:	The primary efficacy endpoint was durable platelet response as defined by the proportion of subjects achieving at least 6 out of 8 weekly platelet counts $\geq 50 \times 10^9/L$ during the last 8 weeks of the 12-week Treatment Period in the Core Phase in the absence of rescue medication.
End point type	Primary
End point timeframe:	
12 Weeks	

End point values	Avatrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	21		
Units: Percentage				
Yes	15	0		
No	39	21		

### Statistical analyses

Statistical analysis title	Durable Platelet Response
Comparison groups	Avatrombopag v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0077
Method	Fisher exact

### Primary: Platelet Response

End point title	Platelet Response
End point description:	
Platelet response was defined as having at least 2 consecutive platelet assessments $\geq 50 \times 10^9/L$ over	



the 12 weeks of treatment in the Core Phase in the absence of rescue medication.

End point type	Primary
End point timeframe:	
12 Weeks	

<b>End point values</b>	Avatrombopag	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	21		
Units: Percentage				
Yes	44	0		
No	10	21		

### Statistical analyses

<b>Statistical analysis title</b>	Platelet Response - FAS
Comparison groups	Avatrombopag v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0067
Method	Fisher exact

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

12 weeks

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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### Reporting groups

Reporting group title	Avatrombopag
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Avatrombopag	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 54 (9.26%)	1 / 21 (4.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 54 (1.85%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Immune thrombocytopenia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytosis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Mouth haemorrhage			

subjects affected / exposed	1 / 54 (1.85%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral purpura			
subjects affected / exposed	1 / 54 (1.85%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 54 (1.85%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Avatrombopag	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 54 (92.59%)	16 / 21 (76.19%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 54 (5.56%)	1 / 21 (4.76%)	
occurrences (all)	7	1	
Vascular disorders			
Haematoma			

subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 3	3 / 21 (14.29%) 6	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	10 / 54 (18.52%) 22	4 / 21 (19.05%) 4	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	9 / 54 (16.67%) 9	0 / 21 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)  Vomiting subjects affected / exposed occurrences (all)  Abdominal Pain subjects affected / exposed occurrences (all)  Gingival bleeding subjects affected / exposed occurrences (all)  Rectal haemorrhage subjects affected / exposed occurrences (all)	4 / 54 (7.41%) 5  4 / 54 (7.41%) 6  3 / 54 (5.56%) 3  2 / 54 (3.70%) 2  0 / 54 (0.00%) 0	0 / 21 (0.00%) 0  0 / 21 (0.00%) 0  0 / 21 (0.00%) 0  2 / 21 (9.52%) 3  2 / 21 (9.52%) 2	
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)  Cough subjects affected / exposed occurrences (all)  Oropharyngeal pain subjects affected / exposed occurrences (all)	12 / 54 (22.22%) 30  9 / 54 (16.67%) 11  7 / 54 (12.96%) 7	4 / 21 (19.05%) 9  0 / 21 (0.00%) 0  0 / 21 (0.00%) 0	

Rhinorrhoea subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 3	0 / 21 (0.00%) 0	
Skin and subcutaneous tissue disorders Petechiae subjects affected / exposed occurrences (all)	14 / 54 (25.93%) 20	6 / 21 (28.57%) 6	
Ecchymosis subjects affected / exposed occurrences (all)	10 / 54 (18.52%) 19	1 / 21 (4.76%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 54 (7.41%) 6	0 / 21 (0.00%) 0	
Pain in extremity subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 4	0 / 21 (0.00%) 0	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 54 (11.11%) 6	2 / 21 (9.52%) 2	
COVID-19 subjects affected / exposed occurrences (all)	4 / 54 (7.41%) 4	1 / 21 (4.76%) 1	
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 54 (7.41%) 5	0 / 21 (0.00%) 0	
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 5	0 / 21 (0.00%) 0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 December 2020	Amendment 1 refined several inclusion and exclusion criteria, clarified the allowable contraception methods, aligned the definition of a lack of treatment effect in the Extension Phase with the Core Phase definition, and confirmed that a protocol amendment would be implemented if two subjects in Cohort 3 require medical monitor approved dose escalations above 20 mg daily.
02 November 2021	Amendment 2 updated the sponsor name, and clarified corticosteroid use prior to Baseline, the minimum subject age at Baseline, and the timing of serial PK sampling.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported