Efficacy and safety of avatrombopag for the treatment of pediatric immune thrombocytopenia in the open-label extension of a phase 3, randomized, double-blind, placebo-controlled trial

Rachael F. Grace, MD, MMSc,[1] Göksel Leblebisatan, MD,[2] Yesim Aydinok, MD,[3] Şule Ünal, MD,[4] John Grainger, MBChB, MRCP, FRCPath, MD,[5] Jessica Zhang, MS,[6] Liza Alkhori Franzén, PhD,[7] Nina Skuban, MD[6]

[1]Dana-Farber Cancer Institute/Boston Children's Cancer and Blood Disorders Center, Harvard Medical School, Boston, MA, USA; [2]Division of Pediatric Hematology and Oncology, Department of Pediatrics, Faculty of Medicine, Çukurova University, Adana, Turkey; [3]Department of Pediatric Hematology, Faculty of Medicine, Ege University Hospital, Izmir, Turkey; [4]Department of Pediatric Hematology, Hacettepe University Medical School, Ankara, Turkey; [5]Department of Hematology, Royal Manchester Children's Hospital, Manchester, UK; [6]Sobi, Waltham, MA, USA; [7]Sobi, Stockholm, Sweden

PS2234

CONCLUSIONS

- Avatrombopag demonstrated sustained efficacy during this open-label extension, with a cumulative safety profile consistent with that of the double-blind, placebo-controlled core phase
- No new or unexpected safety concerns were identified
- These findings support the long-term efficacy and safety of avatrombopag for treating children with ITP

BACKGROUND

- There is an unmet need for new treatment options for pediatric patients with chronic immune thrombocytopenia (ITP), as many currently approved options have challenges related to tolerability, long-term effectiveness, route of administration, and/or dietary restrictions[1,2]
- Avatrombopag, an oral thrombopoietin receptor agonist (TPO-RA) approved for the treatment of ITP in adults,[3] was shown to be efficacious and well tolerated in children and adolescents with ITP in the core phase of a 12-week, double-blind, placebo-controlled study[4]
  - Median platelet counts for avatrombopag-treated patients remained ≥50×10^9/L throughout the last 8 weeks of treatment

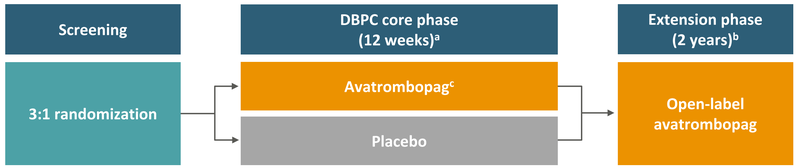
AIMS

- To assess the long-term efficacy and safety of avatrombopag for treating pediatric patients with ITP

METHODS

- **Study design:** Open-label extension (OLE) of a phase 3b, multicenter, randomized, double-blind, placebo-controlled, parallel group study (NCT04516967)
- **Setting:** 62 clinical study sites worldwide (France, Germany, Hungary, Poland, Russia, Turkey, Ukraine, United Kingdom, United States)
- **Patients:** Children aged ≥1 to <18 years who had been diagnosed with primary ITP ≥6 months earlier and had experienced insufficient increases in platelet count (PC) with previous treatments
- **Statistical analysis:** Patient characteristics and efficacy endpoints during the OLE were summarized descriptively

Study schematic



DBPC, double-blind placebo-controlled; PC, platelet count.
[a]Study drug dosage was titrated to target a PC range of ≥50×10^9/L to ≤150×10^9/L. [b]Patients who completed the core phase or discontinued early because of lack of treatment effect entered the extension phase. [c]Avatrombopag starting dose was 10 mg once daily for patients aged ≥1 to <6 years and 20 mg once daily for patients aged ≥6 to <12 years or ≥12 to 18 years.

Study endpoints

Efficacy

- PC in the absence of rescue therapy (target range: ≥50×10^9/L to ≤150×10^9/L)

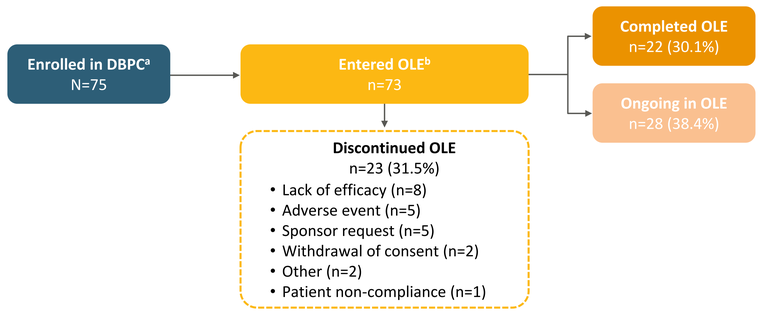
Safety

- Treatment-emergent adverse events (TEAEs)
- Serious TEAEs
- Adverse events of special interest (AESIs; thromboembolic events, bleeding events of Common Terminology Criteria for Adverse Events [CTCAE] grade ≥3)

RESULTS

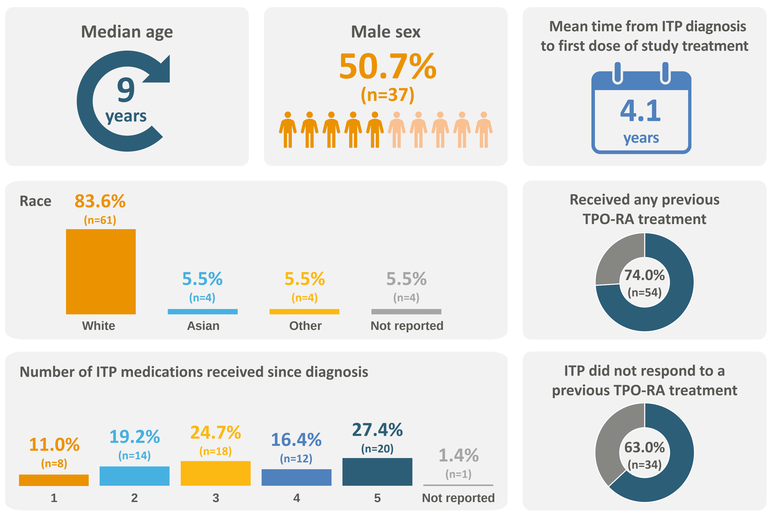
- Of the 75 patients enrolled in the core phase, 73 entered the OLE (**Figure 1**)
- As of the data cutoff date (September 30, 2024), 30.1% of patients had completed the OLE, 38.4% were ongoing, and 31.5% had discontinued; the most common reason for discontinuation was lack of efficacy (**Figure 1**)
- The mean time from ITP diagnosis to first dose of study medication was 4.1 years; 74.0% of patients had previous TPO-RA treatment and 63.0% had lack of ITP response to a previous TPO-RA (**Figure 2**)
- Median PCs in the absence of rescue therapy among patients receiving avatrombopag in the OLE remained within the target range throughout months 2–24 (**Figure 3**)
- Serious TEAEs were reported in 20 (27.4%) patients, with the most common being thrombocytopenia and epistaxis (5.5% each) and mucosal hemorrhage and gastroenteritis (2.7% each) (**Table 1**)
- AESIs were reported by 5 (6.8%) patients, with no new AESIs reported since the previous data cutoff date (December 18, 2023) (**Table 1**)
- There was 1 report each of avatrombopag-related thrombocytosis and deep vein thrombosis and 4 non–avatrombopag-related CTCAE grade ≥3 bleeding events; no deaths occurred (**Table 1**)

Figure 1: Patient disposition as of September 30, 2024



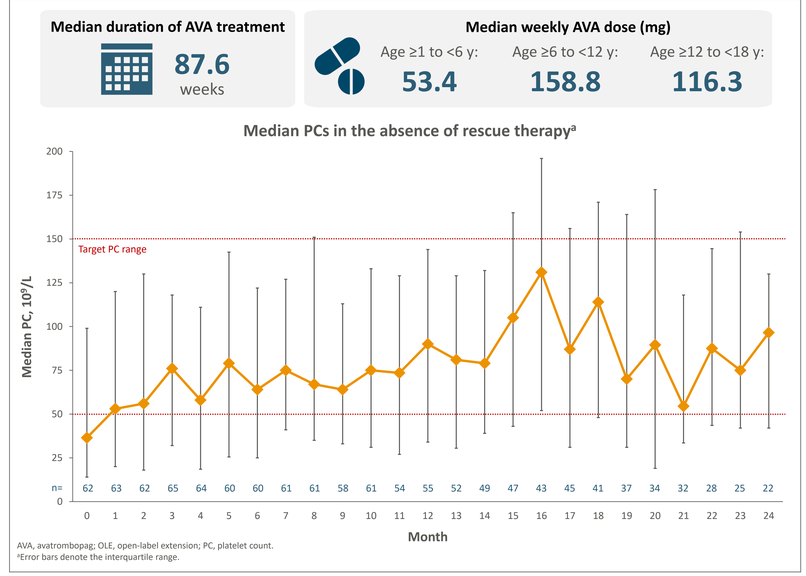
DBPC, double-blind placebo-controlled phase; OLE, open-label extension.
[a]Avatrombopag, n=54; placebo, n=21. [b]Patients who completed the core phase or discontinued early because of lack of treatment effect entered the extension phase.

Figure 2: Patient demographic and clinical characteristics (N=73)



ITP, immune thrombocytopenia; TPO-RA, thrombopoietin receptor agonist.

Figure 3: Avatrombopag exposure and PCs during the OLE



AVA, avatrombopag; OLE, open-label extension; PC, platelet count.
[a]Error bars denote the interquartile range.

Table 1: Safety outcomes during the extension phase

	Total (N=73)
Patients with TEAEs, n (%)	72 (98.6)
Treatment-related TEAEs	10 (13.7)
TEAEs resulting in study discontinuation	6 (8.2)
Serious TEAEs[a]	20 (27.4)
Epistaxis	4 (5.5)
Thrombocytopenia	4 (5.5)
Gastroenteritis	2 (2.7)
Mucosal hemorrhage	2 (2.7)
Patients with AESIs, n (%)	5 (6.8)
Thromboembolic events	1 (1.4)[b]
CTCAE grade ≥3 bleeding events	4 (5.5)[c]
Deaths, n (%)	0

AE, adverse event; AESI, AE of special interest (thromboembolic events, bleeding events of CTCAE grade ≥3); CTCAE, Common Terminology Criteria for Adverse Events; TEAE, treatment-emergent AE. [a]Serious TEAEs reported in >1 patient are shown. One patient reported a grade 4 TEAE (aplastic anemia, not avatrombopag related). There was 1 report each of avatrombopag-related thrombocytosis and deep vein thrombosis. [b]Avatrombopag-related deep vein thrombosis. [c]No CTCAE grade ≥3 bleeding events were determined to be avatrombopag related.

References

1. Neunert C, et al. *Blood Adv*. 2019;3:3829-3866.
2. Provan D, et al. *Blood Adv*. 2019;3:3780-3817.
3. Doptelet [package insert]. Morrisville, NC: AkaRx, Inc; 2024.
4. Grace RF, et al. Abstract presented at: European Hematology Association 2024 Hybrid Congress; June 13-16, 2024; Madrid, Spain. Abstract S318.

Acknowledgments

This study was funded by Sobi. The authors would like to thank the patients, caregivers, investigators, and staff for their participation in this study. Medical writing and editorial assistance, under the guidance of the authors, were provided by Yvette Edmonds, PhD, and Jane Moore of Peloton Advantage, LLC, an OPEN Health company, funded by Sobi, in accordance with Good Publication Practice (GPP 2022) guidelines.

Disclosures

RFG: Research funding: Agios Pharmaceuticals, Novartis, and Sobi; consultancy fees: Agios Pharmaceuticals, Sanofi, and Sobi. **GL:** Nothing to declare. **YA:** Research funding: Bristol Myers Squibb (Celgene), Cerus, Novartis, and Sobi; honoraria and advisory board fees: Chiesi; consultancy fees: Bristol Myers Squibb (Celgene), Cerus, Silence Therapeutics, and Vertex Pharmaceuticals/CRISPR Therapeutics. **ŞÜ:** Nothing to declare. **JG:** Research funding: Amgen, GSK, and Novartis; honoraria and advisory board fees: Alexion, Amgen, Biotest, and Ono Pharmaceutical; consultancy fees: Sobi. **JZ:** Current employment: Sobi. **LAF:** Current employment: Sobi. **NS:** Current employment: Sobi.

Presented at: the European Hematology Association 2025 Congress; June 12–15, 2025; Milan, Italy