Efficacy and Safety of Avatrombopag in Children with Immune Thrombocytopenia Based on Disease Duration: Results from the Phase 3b Multicenter, Randomized, Double-Blind, Placebo (PBO)-controlled, Parallel-group Trial

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Poster #PS2250

CONCLUSION

Avatrombopag (AVA) is an effective, durable, and safe therapy in children with immune thrombocytopenia (ITP), regardless of disease duration.

BACKGROUND

- After failure of first-line therapies (e.g. corticosteroids or immunoglobulin) in pediatric immune thrombocytopenia (ITP), treatment options for children include immunosuppressants and thrombopoietin receptor agonists (TPO-RAs).
- AVA, a TPO-RA approved for the treatment of adult patients with ITP, could be a desirable option for pediatric patients as it is an oral agent taken with meals, without dietary food-type or timing restrictions, and is not associated with risk of hepatotoxicity
- Top-line results of the phase 3b, multicenter, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the efficacy and safety of AVA for the treatment of pediatric patients with immune thrombocytopenia have been previously reported[1].
  - The primary endpoint of platelet response (≥2 consecutive platelet counts (PC) ≥50×10^9/L without rescue therapy) was met by 81.5% for AVA versus 0% for placebo (p<0.0001).
  - The primary durable platelet response endpoint (achieving PC ≥ 50×10^9/L without rescue therapy in 6 of final 8 weeks of the 12-week core phase) was met by 27.8% for AVA versus 0% for placebo (p=0.0077).
- The aim of this analysis was to evaluate the efficacy and safety of AVA in children with ITP based on disease duration at enrollment.

METHODS

- The phase 3b, multicenter, randomized, double-blind, placebo-controlled, parallel-group trial evaluated the efficacy and safety of AVA for the treatment of pediatric patients with ITP for ≥6 months (NCT04516967) (**Figure 1**).
- This post-hoc analysis evaluates the proportion of patients achieving platelet response and durable response as well as treatment-emergent adverse events (TEAEs) and TEAEs of interest based on length of disease duration at enrollment (<12 months versus ≥12 months).

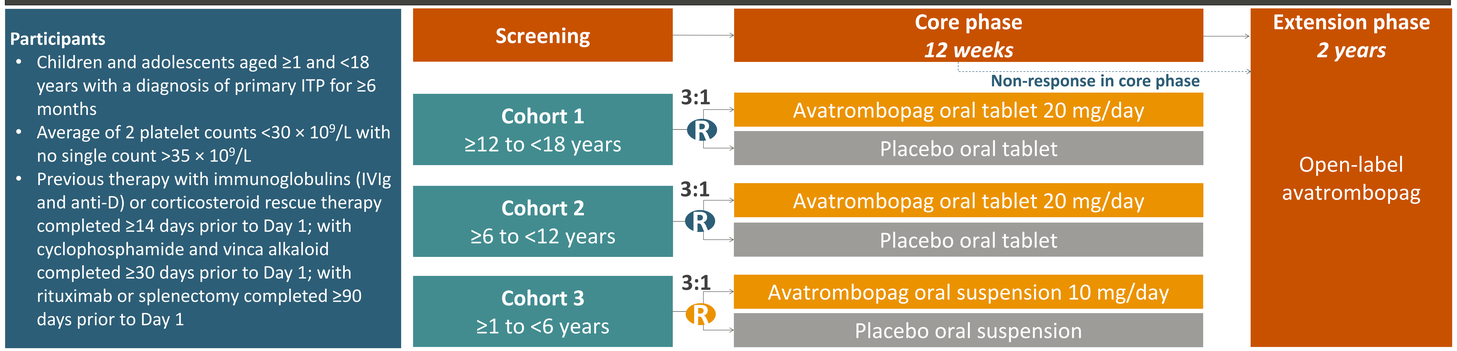
RESULTS

- Overall, 75 patients aged 1 to 17 years were enrolled; 54 were randomized to AVA and 21 to PBO (**Table 1**). 41 AVA and 18 PBO patients had a disease duration ≥12 months, and 13 AVA and 3 PBO patients had a disease duration <12 months.

Table 1: Patient Baseline Characteristics

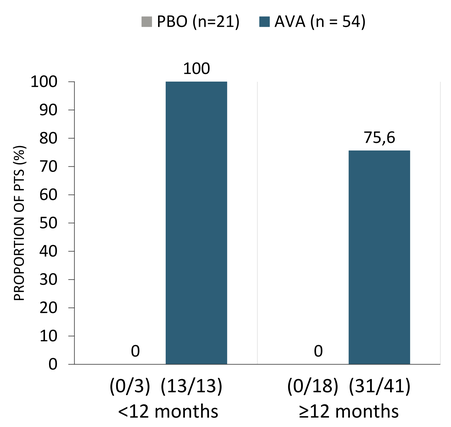
	AVA (N=54)	PBO (N=21)
Female, n (%)	24 (44.4)	12 (57.1)
Age, years (mean ± SD)	8.9 ± 4.4	9.9 ± 4.1
Race, n (%) White Asian	 48 (88.9) 3 (5.6)	 15 (71.4) 1 (4.8)
Platelet count ≤15 × 10^9/L, n (%)	45 (83.3)	17 (81.0)
Platelet count (mean ± SD)	12.0 ± 6.8	11.2 ± 6.6
Bruising or bleeding, n (%)	39 (72.2)	16 (76.2)
WHO bleeding scale for the 7 days prior to baseline, n (%) Grade 1 Grade 2	 36 (66.7) 3 (5.6)	 14 (66.7) 2 (9.5)
Time from primary ITP diagnosis to first dose, weeks (mean ± SD)	202 ± 164	225 ± 181
≥3 previous ITP medications received since diagnosis, n (%)	37 (68.5)	14 (66.7)
Prior TPO-RA use, n (%)	40 (74.1)	15 (71.4)
Prior TPO-RA response, n (%)	17 (42.5)	3 (20.0)
Splenectomy, n (%)	2 (3.7)	2 (9.5)

Figure 1: Phase 3b Study Design



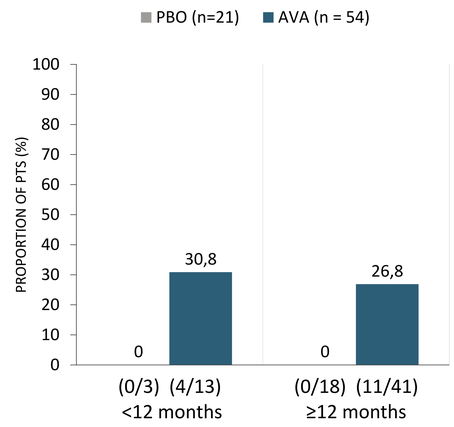
- The proportion of patients achieving a platelet response (**Figure 2**) and a durable response (**Figure 3**) was moderately higher in the disease duration <12 months group and in line with the overall population although the numbers are small.

Figure 2: Platelet Response* to AVA Based on Disease Duration



*achieving at least 2 consecutive PC ≥ 50×10^9/L without rescue therapy during the 12-week core phase

Figure 3: Durable Response to AVA Based on Disease Duration**



**achieving PC ≥ 50×10^9/L without rescue therapy in 6 of final 8 weeks of the 12-week core phase

- Exposure-adjusted TEAEs and TEAEs of interest were similar to placebo and between disease duration sub-groups (**Table 2**). There were no thromboembolic events, CTCAE grade ≥ 3 bleeding events, or deaths in either the AVA or PBO arms for either disease duration.

Table 2: Exposure-adjusted Treatment Emergent Adverse Events and Treatment Emergent Adverse Events of Interest based on Disease Duration at Baseline

	Disease Duration <12 Months		Disease Duration ≥12 Months	
	AVA (N=13)	Placebo (N=2)	AVA (N=41)	Placebo (N=18)
Treatment-related TEAE: event rate*, [n, (%)]	8.6 [13/13,100%]	20.8 [2/2,100%]	8.2 [37/41, 90.2%]	11.2 [13/18, 72.2%]
TEAE leading to study drug being withdrawn: event rate*, [n, (%)]	0.7 [1/13, 7.7%]	0	0.2 [1/41, 2.4%]	0
Treatment-related Serious TEAEs: event rate*, [n, (%)]	0	0	0.2 [1/41, 2.4%]	0
Thromboembolic events, n	0	0	0	0
CTCAE grade ≥3 bleeding event, n	0	0	0	0
Deaths, n	0	0	0	0

*Event rate is calculated as 100 * (number of subjects with events/total exposure in subject-weeks); CTCAE= CTCAE, Common Terminology Criteria for Adverse Events; TEAE= Treatment-emergent adverse event; n= number; %= percentage

REFERENCES

1. Grace R, et al. European Hematological Association 2024 Hybrid Congress; Madrid, Spain; June 13–16, 2024

DISCLOSURES

Study was funded by Sobi, Inc.