Analysis of Baseline Influences on the Durable Response to Avatrombopag (AVA) from a Phase 3b Multicenter, Randomized, Double-Blind, Placebo (PBO)-controlled, Parallel-group Trial to Evaluate the Efficacy and Safety of AVA for the Treatment of Pediatric Patients with Immune Thrombocytopenia (ITP)

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CONCLUSIONS

Despite a high proportion of prior TPO-RA failure, durable platelet response to AVA was noted across a variety of clinical and demographic characteristics. Given the small sub-groups numbers, some characteristics may yield higher response rates and should be further studied.

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).
- The oral TPO-RA AVA could be a desirable option for pediatric patients as AVA does not require an injection in a physician's office, is taken with meals, and does not carry food-type or timing restrictions.
- 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 were recently reported[1].
- The primary efficacy endpoint of this study was the durable platelet response as measured by the proportion of patients achieving at least 6 out of 8 weekly platelet counts ≥50 × 10^9/L during the last 8 weeks of the 12-week core-phase treatment period in the absence of rescue therapy.
  - 27.8% for AVA versus 0% for PBO (p=0.0077) in a population where 35/55 (63.6%) had failed to respond to a previous TPO-RA.
- The aim of this analysis was to evaluate the correlation of baseline characteristics with durable platelet response to AVA in pediatric ITP.

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**).
- These post-hoc analyses evaluate the proportion of patients randomized to AVA with a durable platelet response based on baseline characteristics [sex, presence of WHO-defined bleeding (Grades ≥1), ITP duration, number of prior ITP treatments, prior treatment with TPO-RA, type of prior TPO-RA treatment, response to prior TPO-RA, low weight for age (Low Weight: <55kg in Cohort 1, <33kg in Cohort 2, <18kg in Cohort 3)].

RESULTS

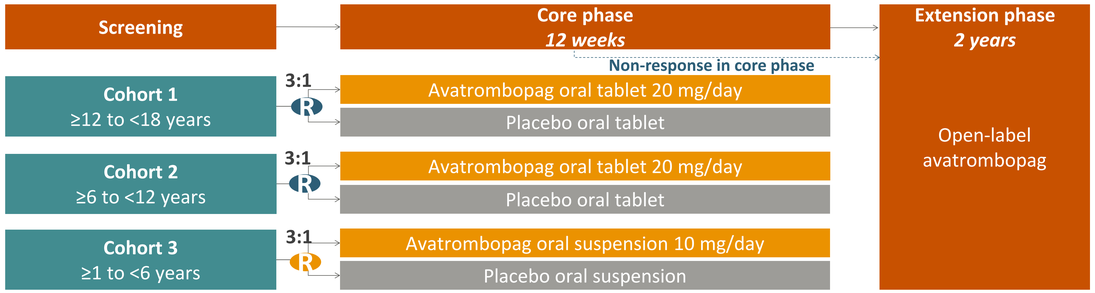
- Overall, 75 patients aged 1 to 17 years were enrolled; 54 were randomized to AVA and 21 to PBO (**Table 1**).

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)
Previous platelet transfusion, n (%)	11 (20.4)	1 (4.8)
Splenectomy, n (%)	2 (3.7)	2 (9.5)

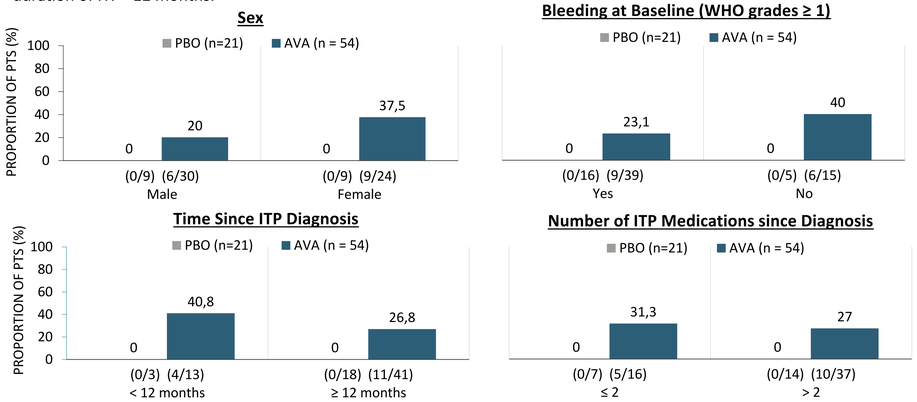
Figure 1: Phase 3b Study Design

Participants
- Children and adolescents aged ≥1 and <18 years with a diagnosis of primary ITP for ≥6 months
- Average of 2 platelet counts <30 × 10^9/L with no single count >35 × 10^9/L
- Previous therapy with immunoglobulins (IVIg and anti-D) or corticosteroid rescue therapy completed ≥14 days prior to Day 1; with cyclophosphamide and vinca alkaloid completed ≥30 days prior to Day 1; with rituximab or splenectomy completed ≥90 days prior to Day 1

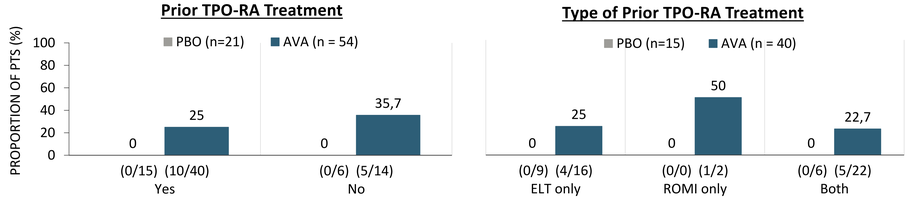


Figures: Baseline Characteristic Influences on Durable Platelet Response to AVA (achieving at least 6 out of 8 weekly platelet counts ≥50 × 10^9/L)

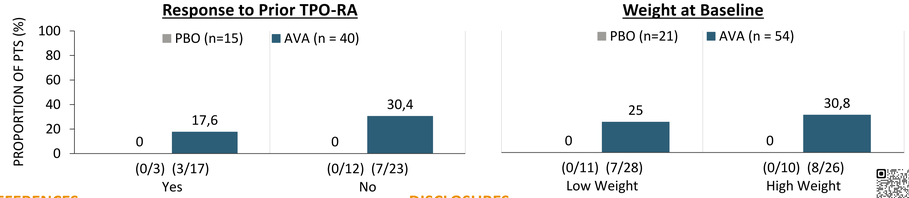
- The baseline characteristics correlating with durable platelet response to AVA include female sex, no bleeding at baseline, and duration of ITP <12 months.



- Patients without prior treatment with a TPO-RA had a higher rate of durable platelet response to AVA: 35.7% (5/14) vs those with prior TPO-RA treatment at 25% (10/40).



- Patients without a response to a prior TPO-RA had a higher rate of durable platelet response to AVA: 30.4% (7/23) vs 17.6% (3/17). Differences based on specific prior TPO-RA could not be determined based on small sample size. Nominal differences were seen based on number of prior ITP treatments and weight.



REFERENCES

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

DISCLOSURES

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