Abstract: S318

Title: A PHASE 3, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF AVATROMBOPAG FOR THE TREATMENT OF CHILDREN WITH CHRONIC IMMUNE THROMBOCYTOPENIA (AVA-PED-301)

Abstract Type: Oral Presentation

Session Title: Platelet disorders in the spotlight: Clinical and translational

Background:

Avatrombopag (AVA) is approved for the treatment of chronic immune thrombocytopenia (ITP) in adults (≥18 years). AVA, an oral thrombopoietin receptor agonist (TPO-RA) without food restrictions, would be especially desirable for children and adolescents with ITP if found to be effective and safe.

Aims:

To assess the efficacy, safety, and pharmacokinetics of AVA in children and adolescents with ITP of ≥6 months.

Methods:

In this Phase 3b double-blind study (NCT04516967), eligible subjects were children >1 to <18 years with ITP of ≥6 months duration and mean platelet counts (PC) <30×109/L (from two PC during screening) with no PC >35×109/L. Subjects were recruited from 34 sites in France, Germany, Hungary, Poland, Russia, Turkey, UK, Ukraine, and US. Subjects were randomly assigned (3:1) to receive AVA or placebo (PBO) for 12 weeks stratified by age group (1 to <6 years, 6 to <12 years, 12 to <18 years); the dose of study drug was adjusted to target PC of 50 to 150×109/L. Subjects and investigators were blinded during the 12-week core phase. Subjects completing the core phase, or without any platelet response at the maximum dose of blinded study drug, could enroll into the open-label extension (OLE) phase for up to 2 years.

The primary analysis included all randomized subjects; the safety analysis included all subjects who received ≥1 dose of study drug. The primary endpoint was durable platelet response, defined as a PC ≥50×109/L in the absence of rescue therapy in ≥6 of the last 8 weeks of the core phase. The main secondary endpoint was ≥2 consecutive PC ≥50×109/L in the absence of rescue therapy in the 12-week core phase. Other secondary endpoints included platelet response at Day 8 and use of rescue therapy.

Results:

Between 5 March 2021 and 30 August 2023, 75 subjects aged 1 to 17 years were enrolled; 54 randomized to AVA and 21 to PBO. The median (min, max) time from ITP diagnosis to enrollment was 3.1 years (0.5, 12.3) for AVA subjects and 3.4 years (0.5, 11.8) for PBO subjects. Approximately 80% of subjects had PC ≤15×109/L, 68% had received ≥3 prior ITP medications, and 73% had received prior TPO-RAs. Median age at enrolment was 8.5 years for AVA subjects and 10.0 years for PBO subjects; overall, 52% of subjects were males and 84% reported White race.

Forty-four (81.5%) AVA subjects and 1 (4.8%) PBO subject completed the 12-week Core Phase. Durable platelet response (weeks 5-12) was observed in 15 (28%) AVA subjects and 0 PBO subjects (p=0.0077, 95% CI 15.8-39.7). Two consecutive PC ≥50×109/L were observed in 44 (81.5%) AVA subjects and 0 PBO subjects (p=<0.0001, 95% CI 71.1-91.8). Day 8 platelet response ≥50×109/L was observed in 30 (56%) AVA subjects and 0 PBO subjects (p=<0.0001), and rescue therapy use occurred in 4 (7%) AVA subjects and 9 (43%) PBO subjects (p=0.0008).

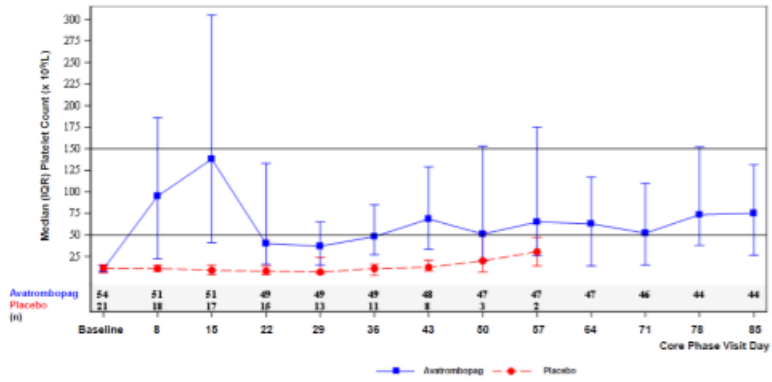
Severe adverse events occurred in 5 (9%) AVA subjects and 1 (5%) PBO subjects. Two SAEs (headache; thrombocytosis) occurring in 1 (2%) AVA subject were considered treatment-related by the investigator. Two (4%) AVA subjects withdrew due to adverse events (leukocytosis on day 12; vomiting on day 63) compared to

1 (5%) PBO subject (contusion on day 43). WHO Grade ≥2 bleeding events occurred in 10 (19%) AVA subjects and 8 (38%) PBO subjects. No thromboembolic events or deaths occurred in the core phase. Seventy-three subjects (97%) entered the ongoing OLE phase of the study.

Summary/Conclusion:

Avatrombopag is an effective and well-tolerated oral TPO-RA for patients ≥1 and <18 years with persistent and chronic ITP who have had an insufficient response to prior therapy.

Figure 1: Median (IQR) Platelet Counts in the Absence of Rescue Therapy in the Core Phase – Full Analysis Set



Keywords: Clinical trial, Phase III, Pediatric, Immune thrombocytopenia (ITP)