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AN INTERVENTIONAL, PHASE 2, SINGLE-ARM STUDY TO ASSESS THE EFFICACY AND SAFETY OF ELTROMBOPAG COMBINED WITH CYCLOSPORINE AS FIRST-LINE THERAPY IN ADULTS WITH SEVERE ACQUIRED APLASTIC ANEMIA (SOAR)

Topic: 12. Bone marrow failure syndromes incl. PNH - Clinical

Keywords: Aplastic anemia | Immunosuppressive therapy | Thrombopoietin (TPO)

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Background:

Severe aplastic anemia (SAA) is a life-threatening bone marrow failure disorder characterized by pancytopenia and a hypocellular bone marrow. The standard of care for patients that are ineligible for hemopoietic stem cell transplant is immunosuppressive therapy (IST), comprising antithymocyte globulin (ATG) and cyclosporine A (CsA). Horse (h-) ATG is considered more effective than rabbit ATG; however, lack of response, relapse, and clonal evolution remain significant limitations. Expense, individual intolerance, and a lack of global availability of h-ATG also leave many patients (pts) with more limited treatment options and poorer outcomes. Eltrombopag (ETB) is indicated for use in patients with SAA who have had an insufficient response to IST (FDA PI, 2014) or are refractory to IST (EMA SmPC, 2015). More recently in the USA, ETB may also be used in combination with IST as first-line treatment (FDA PI, 2018).

Aims: To assess the efficacy and safety of an ATG-free regimen (ETB + CsA) in treatment-naïve pts with SAA.

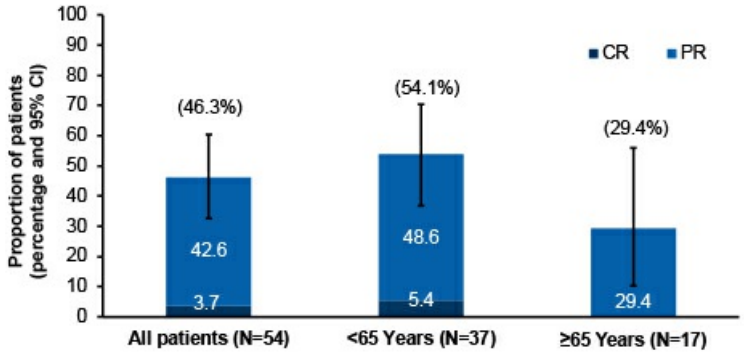
Methods: SOAR (NCT02998645) is a Ph2, single-arm, multicenter, open-label study. Adult pts with SAA received ETB + CsA as first-line therapy for 6 months; responders continued CsA therapy for an additional 24 months (subsequently reduced to 18 months). The primary efficacy endpoint was overall response rate (ORR) by 6 months. ORR was defined as the proportion of pts with complete response ([CR] = absolute neutrophil count [ANC] ≥1000/μL AND platelet count ≥100,000/μL AND hemoglobin ≥10 g/dL) plus the proportion of pts with partial response ([PR] = any 2 of the following counts: ANC ≥500/μL; platelet count ≥20,000/μL; automated reticulocyte count ≥60,000/μL, but not sufficient for a CR). CR and PR were confirmed by 2 assessments ≥7 days apart; transfusion restrictions were applied. Based on historical data, an ORR of ≥30% was considered clinically meaningful.

Results: A total of 54 pts were enrolled. The median (interquartile range [IQR]) age was 55.0 (40.0-67.0) years, 63.0% were male, and the majority of pts were White (40.7%) or Asian (40.7%). The median (IQR) duration of exposure to ETB and CsA were 5.7 (2.5-5.8) months and 5.7 (2.4-8.1) months, respectively, and the median (IQR) daily ETB dose was 150.0 (100.0-150.0) mg/day. In the full analysis set, the primary endpoint was met with an ORR by 6 months of 46.3% (25/54); 95% CI, 32.6-60.4% (Fig. 1). Of the 25 responders, 2 (3.7%) achieved CR by 6 months. ORR by 6 months is also shown by age group (<65 and ≥65 years) (Fig. 1). Secondary endpoints included ORR by 3 months (40.7% [22/54]; 95% CI, 27.6-55.0%), and ORR at 6 months (ie, patients with confirmed response at 6-month visit: 37.0% [20/54]; 95% CI, 24.3-51.3%). Adverse events (AEs) occurred in 52/54 pts; 45 (83.3%) pts experienced treatment-related AEs (TAEs), 23 (42.6%) of whom had a grade ≥3 TAE. The most common all-grade AEs were increased blood bilirubin (40.7%), nausea (29.6%), increased alanine aminotransferase (22.2%), and diarrhea (22.2%). Seven (13.0%) pts discontinued study due to AEs. There were 8 on-treatment deaths (aplastic anemia [n=3]; COVID-19, hemorrhage, multi-organ dysfunction syndrome, pyrexia, and thrombosis [all n=1]); no

deaths were considered treatment-related.

Image:

Figure 1: ORR by 6 months (full analysis set)



CI, confidence interval; CR, complete response; ORR, overall response rate; PR, partial response

Summary/Conclusion: Data from the SOAR study indicate that ETB + CsA therapy may be beneficial as first-line treatment for SAA pts who cannot use ATG. The ORR is particularly notable, given the median age of this pt cohort (55.0 years). No new safety signals were identified.

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