[1300] Evaluation of AMG 531 Safety in Splenectomized (S) and Nonsplenectomized (NS) Patients with Chronic Immune Thrombocytopenic Purpura (ITP) in Two Randomized Placebo-Controlled Phase 3 Studies. Session Type: Poster Session, Board #454-I

Roger Lyons, James N. George, Francois Lefrere, Alan E. Lichtin, Michael D. Tarantino, Howard R. Terebelo, Jean-Francois Viallard, Reggie Kelly, Matthew Guo, Janet Nichol Cancer Care, Hem-Onc Assoc So Tex, San Antonio, TX, USA; Health Sci Ctr, Univ of Oklahoma, Oklahoma City, OK, USA; Hematologie, Hopital Necker, Paris, France; Hem-Onc Cleveland Clin Found, Cleveland, OH, USA; Comp Bleeding Disorder Ctr, Peoria, IL, USA; Providence Hospital, Southfield, MI, USA; Hopital Haut-Leveque, Pessac Cedex, France; Amgen Inc., Thousand Oaks, CA, USA

AMG 531 is a novel platelet-stimulating peptibody that stimulates the thrombopoietin (TPO) receptor, and is being studied for its ability to increase production of platelets. We report safety data in both S and NS patients (pts) from 2 randomized, double blind, placebo-controlled Phase 3 studies designed to evaluate the efficacy and safety of AMG 531 in adult pts with chronic ITP. All pts that received at least 1 dose of AMG 531 were counted as AMG 531-treated pts in this safety analysis. Of the 125 pts enrolled, 63 were S (placebo, 21; AMG 531, 42), and 62 were NS (placebo, 21; AMG 531, 41) with a median age of 52 years (range 21 to 88) and a mean baseline platelet count of $16.5x10^9$/L. Subcutaneous AMG 531 or placebo was administered weekly for 24 weeks at a starting dose of 1 μg/kg, and adjusted to maintain a target platelet count of $50\text{-}200x10^9$/L. Among AMG 531 pts, the mean weekly dose was 3.3 ± 2.7 μg/kg, with most pts (54/84, 64%) receiving a dose between 1 and 4 μg/kg. There was no difference in the safety profile between S and NS pts treated with AMG 531; therefore safety data were pooled. Adverse events were reported in 39/41 (95%) placebo and in all (100%) AMG 531 pts. The most frequently reported adverse events (AEs) were: headache (placebo vs AMG 531; 32% vs 35%), fatigue (29% vs 33%), epistaxis (24% vs 32%), arthralgia (20% vs 26%), and contusion (24% vs 25%). There were 2 AMG 531-related serious AEs, both in S pts; 1 pt with elevated bone marrow reticulin after 4 weeks of receiving AMG 531 that returned to baseline 3 months after drug withdrawal, and 1 pt experienced thrombosis (right transfemoral popliteal embolectomy) that was successfully treated allowing study continuation. One (2.4%) placebo and 3 (3.6%) AMG 531 pts withdrew from the study due to AEs. Three placebo pts died of cerebral hemorrhage, atypical pneumonia, and pulmonary embolism. One AMG 531 pt died of intracranial hemorrhage 2 weeks after discontinuation of AMG 531. The total number of bleeding events in the 42 placebo pts and 83 AMG 531 pts were 76 and 152, respectively, corresponding to an exposure-adjusted incidence of 7.9 and 7.8 per 100 Patient-Weeks, reduced to 5.2 per 100 Patient-Weeks in AMG 531-treated pts when their platelet counts were $\geq 50x10^9$/L (platelet response). Clinically significant bleeding events (MedDRA 9.0 defined severity grade ≥ 3) did not occur in responding pts, and were reported only when platelet counts were $<20x10^9$/L. Among non-responders, there were 5 significant bleeding events in placebo pts and 10 in AMG 531 pts, corresponding to an exposure-adjusted incidence of 0.5 per 100 Patient-Weeks in each group. Blood chemistry and complete blood counts remained stable, with no clinically significant changes occurring except for platelet counts. No pts tested positive for neutralizing antibodies against either AMG 531 or endogenous TPO. In summary, AMG 531 appeared to be well-tolerated in ITP pts and reduced the incidence of bleeding events among pts exhibiting a platelet response.

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