

**[250] Phase 1/2 Study of AMG 531 in Thrombocytopenic Patients (pts) with Low-Risk Myelodysplastic Syndrome (MDS): Update Including Extended Treatment. Session Type: Oral Session**

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**Background:** AMG 531 is a novel thrombopoiesis-stimulating peptibody that is being studied for its ability to increase platelet production by stimulating the thrombopoietin receptor. This report updates outcomes in Part A of the study as of May 2007 on pts who continued into the extension phase of this ongoing phase 1/2, open-label, sequential-cohort, dose-escalation study to evaluate the safety and efficacy of AMG 531 in low risk MDS pts with severe thrombocytopenia (Kantarjian et al., ASCO, 2007). **Methods:** Pts with low-risk MDS (IPSS Low or Intermediate-1, excluding CMML), a mean baseline platelet count  $\leq 50 \times 10^9/L$ , and only receiving supportive care were eligible to enter this study. Pts were enrolled into sequential cohorts of 300, 700, 1000, and 1500 $\mu$ g, receiving 3 weekly subcutaneous injections of AMG 531. After evaluation of platelet response at week 4, pts could continue AMG 531 in an optional treatment extension at their assigned dose or dose adjust to achieve or maintain a response. **Results:** The mean duration of exposure to AMG 531 was  $23 \pm 15.5$  (SD) weeks. Of 44 pts enrolled, 40 continued into the extension phase; 16 pts remain on treatment. Eighteen pts (41%) achieved a durable platelet response (per IWG 2006 criteria for at least 8 consecutive weeks). Evaluation of durable responses based on baseline platelet count showed that responses occurred in 12/29 (41%) pts with a baseline count of  $\geq 20 \times 10^9/L$ , and in 6/15 (40%) pts with a baseline count of  $< 20 \times 10^9/L$ . The mean duration of the platelet response was  $22.8 \pm 13.3$  (SD) weeks. A total of 104 platelet transfusions were given to 17/44 (39%) pts during this study; of these transfusions, 7 were given in 3/18 (17%) pts who achieved a durable response. Treatment-related AEs were reported in 17 pts. There were 3 deaths unrelated to treatment. Two confirmed cases of transformation to AML were reported. These two pts received maximum doses of 300 and 1000 $\mu$ g. Six pts were confirmed to have temporary blast cell increases, three of whom had increases above 20%. Of the 6, 4 were receiving 1500 $\mu$ g and 2 were receiving 1000 $\mu$ g. In all 6 pts, blast cell counts were observed to have fallen upon follow-up assessments within 7 weeks after treatment discontinuation. In one case, treatment was reinitiated at 700 $\mu$ g. **Conclusions:** In this study, AMG 531 appeared to be well-tolerated in severely thrombocytopenic low-risk MDS pts, and resulted in increased and sustained platelet counts in the responding pts. AMG 531 may have a role in the treatment of low-risk MDS pts who are thrombocytopenic or have a history of bleeding. These data suggest that further exploration is merited in this pt population. Pt recruitment is ongoing until reaching the planned 84 pts.

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