

Long-term dosing of AMG 531 in thrombocytopenic patients with immune thrombocytopenic purpura: 48-week update

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Origin of Study	USA, France, the Netherlands
Type of Study	ONGOING, OPEN-LABEL EXTENSION TRIAL
Objectives	Assess the safety and efficacy of long-term, weekly, subcutaneous administration of AMG 531 in immune thrombocytopenic purpura (ITP) patients who completed a previous AMG 531 study (<i>Bussel et al. N Engl J Med</i> 2006;355:1672–1681; <i>Newland et al. Br J Haematol</i> 2006;135:547–553).
Study Design	Patients previously treated with the drug received the same starting dose as the final dose received in the previous study; placebo-treated patients began the extension with a 1- $\mu\text{g}/\text{kg}$ dose. The doses could be skipped, decreased, maintained, or increased based on platelet response. Patients achieving a stable dose for at least 3 weeks (later amended to 4 weeks) could self-administer the drug.
Patients	In all, 104 patients were enrolled; the planned interim analysis included 36 patients (safety subset) whose previous study was a phase II trial. Data for patients previously enrolled in a phase III trial are still blinded. In all, 83% of the 25 women and 11 men (mean age, 50 \pm 13 years) underwent a splenectomy.
Observations	Overall, 31 patients (86%) achieved a platelet response, with a median time to response of 3.1 weeks and a mean dose at first response of 3.4 $\mu\text{g}/\text{kg}$. Twenty-nine patients (81%) achieved a platelet count of $\geq 150 \times 10^9/\text{L}$ at any time and 15 (42%) achieved a count of at least $400 \times 10^9/\text{L}$ at any time. Most patients receiving concurrent corticosteroids were able to discontinue them or reduce the dose. Adverse-event profiles were similar for weeks 1–24 and 25–48 and beyond. The most frequent reactions were headache, upper respiratory infection, and fatigue. Four patients had serious treatment-related reactions (vaginal hemorrhage/anemia, diffuse reticulin formation in the bone marrow, bone pain, and transverse sinus thrombosis with papilledema and temporary decrease in visual acuity). No neutralizing antibodies have yet been identified.
Conclusions	Individualized weekly doses of AMG 531 provide a therapeutic option for ITP.
Discussion	AMG 531 is a novel thrombopoiesis-stimulating peptibody that targets the thrombopoietin receptor and is being investigated for ITP. Describing the drug, Dr. Kuter said, “Unlike most other ITP treatments, which interfere with platelet destruction, AMG 531 is designed to increase the production of platelets at a rate that outpaces their destruction of the immune system.” Investigators reported the results from a 48-week extension study that has been under way for more than 2 years and is open to patients who have completed a previous AMG 531 study. A total of 104 patients were enrolled in the extension study; the longest duration of treatment was 96 weeks. The planned interim analysis included 36 patients who had rolled over from a phase I study; 29 were treated for at least 40 weeks and most had undergone a splenectomy. Data for patients previously enrolled in two phase III trials are still blinded.

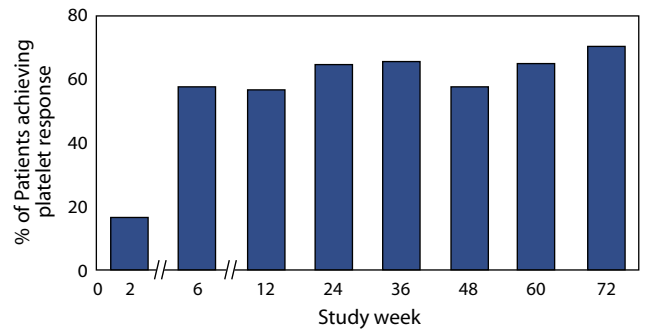
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The efficacy subset consists of 27 patients completing week 48 and beyond. Both the mean platelet count and the mean AMG 531 dose remained stable from weeks 24–48 (Figure). In addition, 11 patients had at least 1 platelet count $> 450 \times 10^9/L$, excluding counts associated with ITP rescue medication. Also, 6 of 12 patients were able to discontinue concurrent corticosteroids, and 2 had a $> 25\%$ reduction in steroid dose.

The most common adverse event was headache, which occurred in about 50% of patients and was probably a true effect of the medication. Four serious treatment-related events occurred, and three adverse events led to discontinuation of AMG 531. There was no development of neutralizing antibodies, he reported.

“This study now includes 2 years of follow-up data, and the interim results at 48 weeks are encouraging,” Dr. Kuter said. “Individualized dosing of AMG 531 may provide a new option for patients with ITP, potentially allowing them to taper off steroid therapy.”

Platelet Response by Week



Patient response is defined as achieving platelet count $\geq 50 \times 10^9/L$ and double the baseline amount; excludes patients who discontinued the study or were within 8 weeks of rescue medication.

Key Points

- The majority of patients treated with AMG 531 have been able to maintain a safe platelet count.
- Most patients were able to decrease or discontinue concurrent steroid therapy.
- AMG 531 was generally well tolerated in this long-term extension study.

Reference

Kuter D, Bussel JB, George J, et al. Long-term dosing of AMG 531 in thrombocytopenic patients with immune thrombocytopenic purpura: 48-week update. Presented at the 48th Annual Meeting of the American Society of Hematology; December 9–12, 2006; Orlando, Florida. Abstract 476.