

American Society of Hematology 47th Annual Meeting and Exposition
December 10-13, 2005
Atlanta, Georgia

Presented by Roger M. Lyons, MD, FACP
Cancer Care Centers of South Texas
4411 Medical Drive, Suite 100
San Antonio, Texas 78229

[220] Long-Term Dosing of AMG 531 Is Effective and Well Tolerated in Thrombocytopenic Patients with Immune Thrombocytopenic Purpura. Session Type: Oral Session

James B. Bussel, David J. Kuter, James N. George, Louis M. Aledort, Alan E. Lichtin, Roger M. Lyons, Jorge Nieva, Jeffrey S. Wasser, Emanuelle Bourgeois, Mies Kappers-Klunne, Francois LeFrere, Martin R. Schipperus, Reggie Kelly, Jenny Christal, Chien-Feng Chen, Janet L. Nichol Weill, Cornell Med Ctr, NY, NY, USA; Hematology, Mass Gen Hosp, Boston, MA, USA; Health Sci Ctr, Univ of OK, Oklahoma City, OK, USA; Hematology, Mt Sinai Hosp, New York, NY, USA; Hematology/Oncology, Cleveland Clin Found, Cleveland, OH, USA; Cancer Care, Hematology-Oncology Assoc So Tex, San Antonio, TX, USA; Hematology & Oncology, Scripps Clin, La Jolla, CA, USA; DeQuattro, Community Cancer Ctr, Manchester, CT, USA; CHRU, Claude Huriet, Lille, France; Erasmus, MC, Rotterdam, Netherlands; Hematologie, Hopital Necker, Paris, France; Haematology, HagaZiekenhuis, Den Haag, Netherlands; Global Development, Amgen Inc., Thousand Oaks, CA, USA

AMG 531 is a novel platelet-stimulating peptibody that targets the TPO receptor, resulting in increased production of platelets. This ongoing, open-label study assessed the safety and efficacy of long-term AMG 531 dosing in ITP patients. Eligible patients have completed a previous AMG 531 study in ITP, are ≥ 18 years of age, have a baseline platelet count $\leq 50 \times 10^9/L$, with no recent significant change in medical history. The AMG 531 starting dose is $1 \mu g/kg$ by SC injection with dose adjustment to an original maximum of $30 \mu g/kg$, since reduced to $15 \mu g/kg$. Patients are treated weekly unless the platelet count is $>400 \times 10^9/L$. Concurrent corticosteroids can be tapered when the platelet count is $\geq 50 \times 10^9/L$. Preliminary data are available for 26 patients treated for up to 24 weeks: 17 women and 9 men; mean age, 48.4 ± 11.6 (SD) years; mean baseline platelet count, 18.5 ± 12.3 (SD) $\times 10^9/L$. Twenty-one patients (80.8%) had undergone a splenectomy before study entry; 6 (23.1%) were receiving concurrent corticosteroids for ITP. Twenty-one of 26 patients (80.8%) had a protocol-defined platelet response to AMG 531 (doubling of the baseline platelet count and $\geq 50 \times 10^9/L$). The mean AMG 531 dose at the first response was 3.7 ± 2.7 (SD) $\mu g/kg$ (at median 5 weeks); the mean dose at week 24 was 7.2 ± 4.2 (SD) $\mu g/kg$. Twelve of 26 patients (46.2%) had a durable platelet response (doubling of the baseline count and $\geq 50 \times 10^9/L$ at 6 or more of weeks 17-24). Twenty patients (76.9%) had a platelet count $\geq 100 \times 10^9/L$ at least once; 7 (26.9%) had a platelet count $\geq 400 \times 10^9/L$. Of 6 patients on concurrent corticosteroids, 3 discontinued treatment and 2 had a $\geq 25\%$ dose reduction. At least 1 serious adverse event was reported in 4 patients: anal fistula (unrelated to treatment), adverse drug reaction (unrelated), multiple sclerosis relapse (unrelated), bone pain (related), and diffuse reticulin formation in the bone marrow reported as myelofibrosis (related). Reticulin formation is hypothesized as due to excessive accumulation of megakaryocytes in the bone marrow. AMG 531 was discontinued, and a bone marrow 3 months later showed improvement. One patient experienced adverse events (musculoskeletal pain and headache) resulting in withdrawal from the study. No neutralizing antibodies have been detected to date. In summary, repeated exposure to AMG 531 has been generally well tolerated in this ongoing study. A total 80.8% of patients achieved a platelet response, defined as doubling of the baseline count and $\geq 50 \times 10^9/L$. Individualized weekly doses of AMG 531 may provide a therapeutic option in ITP, potentially enabling patients to taper off long-term corticosteroid therapy.

Abstract #220 appears in Blood, Volume 106, issue 11, November 16, 2005

Keywords: Platelet count|Thrombopoiesis|Thrombopoietin (TPO)

Monday, December 12, 2005 8:15 AM

Simultaneous Session: Immune Thrombocytopenic Purpura (7:30 AM-9:00 AM)