MÆDICA - a Journal of Clinical Medicine

JOURNAL CLUB

Is romiplostim an alternative treatment for Immune thrombocytopenic purpura (ITP)?

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Immune thrombocytopenic purpura (ITP), a chronic autoimmune disorder, is a disease of autoantibody-mediated platelet destruction and of impaired platelet pro duction, characterized by mucocutaneous bleeding and low platelet counts. Administration of steroids, intravenous immunoglobulin (IVIG), and intravenous anti-D, or on long-term maintenance of platelet counts through splenectomy or other treatments such as rituximab, danazol, azathioprine, or even prolonged steroid treatment have tried to stabilize the disease.

A new class of drugs which stimulates the platelet production is now available for ITP. Romiplostim (AMG 531, Nplate) has recently been shown to induce increases in platelet counts for patients with ITP. This drug is an unique thrombopoiesis-stimulating protein, referred to as a peptibody, which is composed of 2 IgG Fc domains coupled with 4 copies of a TPO mimetic peptide.

An ongoing, long-term open-label, single-arm study investigated safety and efficacy of romiplostim in patients who have platelet counts less than 5 x 10^9/L. 142 patients were treated with romiplostim, for up to 156 weeks (mean, 69 weeks). The dose of romiplostim was adjusted on the basis of the patient's platelet count using prespeci?ed rules for adjustment. The target platelet count range was 50 to 250 x 10^9/L. Initially 30 µg/kg was the maximum allowed dose of romiplostim, reduced later in 2 stages to the current maximum dose of 10 µg/kg after it was determined that few patients derived additional clinical bene?t from increasing doses above this level. Before the maximum dose was reduced, patients whose weekly dose was greater than 10 µg/kg, either because they entered the study at a dose greater than 10 µg/kg or whose dose was increased to greater than 10 µg/kg, could remain on that dose. After the maximum allowed dose was reduced, these patients could not increase their doses, and those whose dose was reduced could not subsequently increase it until their dose was less than 10 µg/kg.

In 87% of patients the platelet responses (platelet count > 50 x 10^9/L and double baseline) and occurred on average 67% of the time in responding patients. The 2 µg/kg romiplostim dose was the most frequent dose at least 90% of the time, for 77% of patients. 90 patients (63%) were treated by self administration. The serious adverse events related to romiplostim were found in 13 patients (9%). 8 patients had bone marrow reticulin, but the true

incidence of this event cannot be determined because the marrows were not routinely performed in this study. 12 patients (9%) had severe bleeding and 7 patients (5%) thrombotic events.

In conclusion, this study, the longest to date by far of a thrombopoietic agent in the treatment of ITP, shows romiplostim to be an effective and well-tolerated maintenance treatment in patients with chronic ITP for up to 3 years, even in those with severe, refractory disease who had undergone splenectomy.

Even the results of this open-label study are limited by the lack of control group, the romiplostim increased platelet counts in most patients for up to 156 weeks without tachyphylaxis and had an acceptable safety profile. ❑

Comment on the paper:
Bussel JB, Kuter DJ, Pullarkat V, et al – Safety and efficacy of long-term treatment with romiplostim in thrombocytopenic patients with chronic ITP; *Blood* 2009; 113:2161-2171