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LETTER TO THE EDITOR
Response of Refractory Immune Thrombocytopenia After Bone Marrow Transplantation to Romiplostim

To the Editor: Immune thrombocytopenia (ITP) is an immune-mediated process characterized by increased destruction of and decreased production of platelets. Despite normal or increased megakaryocytes in the bone marrow, thrombocytopenia persists, presumably because of enhanced platelet clearance stimulated by anti-platelet antibodies [1,2]. Although the majority of children with ITP respond to conventional therapies, refractory patients are at risk for life-threatening bleeding. We report the use of the thrombopoietin (TPO)-agonist romiplostim in a patient with X-linked adrenoleukodystrophy (ALD) who developed refractory ITP after allogeneic bone marrow transplantation (allo-BMT).

A 4-year-old male with ALD received an 8/8 HLA-matched unrelated allo-BMT and engrafted platelets by day +30 after transplant. On day +42, elevation of adenoviral genomes were detected in blood and stool, and he was effectively treated with three doses of intravenous cidofovir. On day +55 he presented with mucocutaneous bleeding and a platelet count of 2×10^9/L. Despite receiving multiple platelet transfusions, his platelet count remained below 10×10^9/L. Peripheral blood smear revealed thrombocytopenia with large platelets. Other laboratory findings revealed a white blood count of 3.1×10^9/L, hemoglobin 8.3 g/dl, and negative direct antiglobulin and platelet antibody tests. He was treated with intravenous immunoglobulin (1 gm/kg/day for 2 days) without any platelet response. On day +57, elevation of Epstein-Barr viral genomes was detected in his blood, and he was treated effectively with four weekly doses of rituximab (375 mg/m^2). He continued to be profoundly thrombocytopenic throughout this time period. On day +73 he developed a severe headache, and a head CT revealed a posterior interhemispheric subdural hemorrhage. He was treated with methylprednisolone (2 mg/kg/day for 4 days) and later received one dose of Rho(D) immune globulin (35 mcg/kg), one dose of vincristine (1.5 mg/m^2), and four doses of dexamethasone (40 mg/m^2 daily). A bone marrow biopsy on day +83 showed trilineage hematopoietic maturation with adequate megakaryopoiesis in the setting of profound thrombocytopenia consistent with ITP. Due to his complete refractoriness to conventional therapies, he was treated with romiplostim at 1 mcg/kg and escalated to 3 mcg/kg for a total of four weekly subcutaneous doses. During the second week of romiplostim treatment his platelet count increased from $<10 \times 10^9$ to 30×10^9/L. Romiplostim was discontinued after the fourth dose, when his platelet count was 49×10^9/L. Two weeks after completing romiplostim, his platelet count had risen to 150×10^9/L and currently remains above 100×10^9/L.

Given the capacity of romiplostim to amplify thrombopoietin activity, we used it to treat a patient with life-threatening, treatment-resistant, immune thrombocytopenia after bone marrow

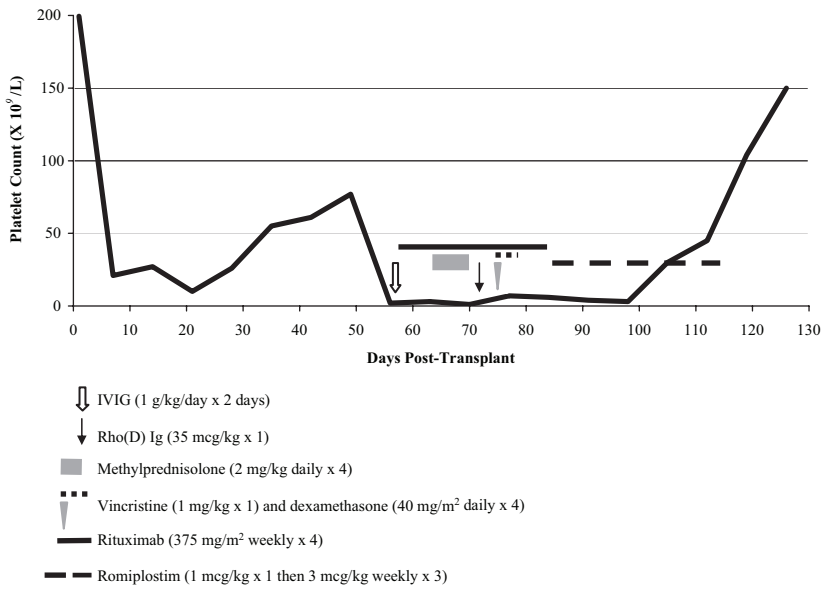

Fig. 1. Romiplostim can accelerate platelet production and overcome immune thrombocytopenia after bone marrow transplantation. ⇩, IVIG (1 g/kg/day × 2 days); ↓, Rho(D)Ig (35 mcg/kg × 1); ▬, Methylprednisolone (2 mg/kg daily × 4); ⋮, Vincristine (1 mg/kg × 1) and dexamethasone (40 mg/m^2 daily × 4); —, Rituximab (375 mg/m^2 weekly × 4); – –, Romiplostim (1 mcg/kg × 1 then 3 mcg/kg weekly × 3).

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transplantation. The patient was refractory to all immune-modulatory treatments focused towards diminishing platelet clearance. Two weeks after initiating treatment with romiplostim, a complete response to therapy was achieved with platelet counts $>100 \times 10^9$/L, which have been sustained for greater than 2 months. Although rapid platelet clearance is thought to contribute to thrombocytopenia in ITP, studies have found the rate of thrombopoiesis also impacts platelet levels [3]. The effectiveness of romiplostim in this patient supports the use of TPO-agonists in patients after allo-BMT who develop life-threatening ITP refractory to standard therapies (Fig. 1).

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