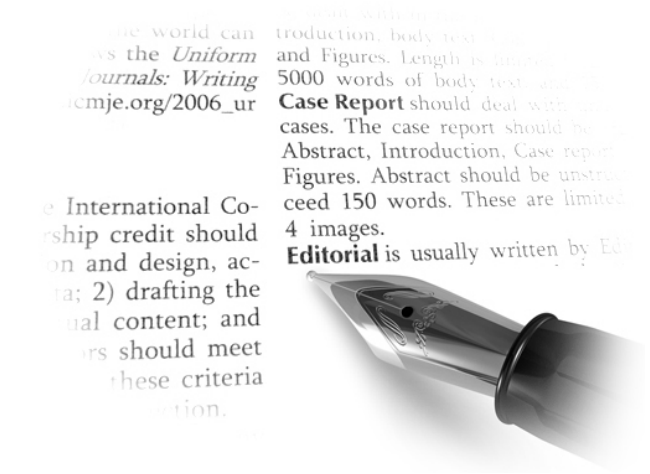

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Editorial

Eltrombopag: a new treatment option for chronic refractory adult immune thrombocytopenia

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Chronic immune thrombocytopenia (ITP) is an autoimmune disease characterized by immune-mediated platelet destruction and reduced platelet production caused by antiplatelet autoantibodies, leading to a marked decrease in platelet count and rarely life-threatening bleeding [1]. The main treatment purpose for chronic ITP is to maintain platelet counts sufficient to minimize bleeding risk [2]. First-line treatments for chronic ITP include corticosteroids, intravenous immunoglobulins, anti-D, and various immunosuppressive or cytotoxic drugs (e.g., vincristine, cyclophosphamide, cyclosporine A, and rituximab), with the main emphasis on preventing platelet destruction. However, first-line therapy is often ineffective and can be limited by side effects [3].

Based on the evidence that ITP might be attributed to decreased platelet production due to inhibition of megakaryopoiesis by antiplatelet antibodies [4], megakaryopoietic stimulation therapy aimed at increasing platelet production by thrombopoietin or thrombopoietin mimetics was considered as an alternative in management of ITP. Recombinant thrombopoietin was not efficient because it produced autoantibodies that cross-react with and neutralize endogenous thrombopoietin, leading to severe thrombocytopenia [5], although it had a positive effect on platelet counts in patients with ITP. The novel thrombopoietin receptor agonists romiplostim and eltrombopag were developed in 2004. Subsequently, they were approved by the U.S. Food and Drug Administration for the second-line treatment of chronic ITP owing to their excellent therapeutic efficacy in treating ITP. Romiplostim is a peptibody (Fc-peptide fusion protein) that is administered by subcutaneous injection, whereas eltrombopag is an oral, nonpeptide agent that has an effect similar to romiplostim [2, 6]. These thrombopoietin mimetics bind to and activate the thrombopoietin receptor, c-Mpl, and cause proliferation and differentiation of megakaryocyte progenitor cells [7]. In particular, they have no sequence homology with human thrombopoietin and should not stimulate production of antithrombopoietin antibodies.

Clinical studies proved the safety and efficacy of eltrombopag in the management of chronic ITP [2, 4]. A safe platelet count was recovered in 70–80% of cases with chronic ITP resistant to one or more treatments, including splenectomy. No clinically relevant side effects such as bone marrow fibrosis, bleeding by rebound thrombocytopenia on eltrombopag withdrawal, or serious liver damage were observed with the eltrombopag treatments [3]. Since the dose-response study [8], many trials reached an agreement that the starting dose of eltrombopag should be 50 mg/day and the dosage could be increased up to 75 mg/day. For patients of East Asian descent, eltrombopag 25 mg/day is recommended as the initiation dose [3].

In the current issue of **Blood Research**, Kim and colleagues [9] report the results of a retrospective study of eltrombopag treatment for adults with chronic ITP in Korea. The authors concluded that eltrombopag was generally well tolerated

in adult refractory ITP patients. Eighteen adult refractory ITP patients were treated with eltrombopag until reaching a safe platelet count (50,000/μL). The drug dose was adjusted according to the platelet count during treatment. The response rate of a platelet count >50,000/μL during the study period was 72.3% (13 patients), which is compatible with result of the Eltrombopag eXTENded Dosing (EXTEND) study [2]. The effective dose of eltrombopag for chronic ITP was 25 mg/day, indicating a racial difference in eltrombopag pharmacokinetics [10]. Splenectomy status did not affect the platelet response in most randomized studies for thrombopoietin receptor agonists including eltrombopag. On the contrary, in this study, nonsplenectomized patients had a higher platelet response rate than splenectomized patients. Further study is warranted in a larger number of patients to clarify the influence of splenectomy on the platelet response during eltrombopag treatment. This report contributes valuable information for the management of chronic ITP patients in Korea. It is hoped that more extensive information regarding the safety and efficacy of eltrombopag should be provided through a randomized and prospective study of thrombopoietin receptor agonist treatment with chronic ITP in the near future.

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