

## **Fostamatinib, an Oral Spleen Tyrosine Kinase (SYK) Inhibitor, as Second-Line Therapy for Immune Thrombocytopenia (ITP)**

Rigel Pharmaceuticals conducted a post-hoc analysis of data from its Phase 3 clinical program of fostamatinib, an oral spleen tyrosine kinase (SYK) inhibitor, in adult patients with immune thrombocytopenia (ITP). The Phase 3 clinical program served as the foundation for FDA approval of fostamatinib for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment. We explored the possibility that fostamatinib may produce better response rates when used early in the treatment paradigm.

ITP is characterized by autoantibody-mediated phagocytosis of platelets via Fc $\gamma$  receptors on macrophages in a SYK-dependent signaling pathway. Fostamatinib addresses a critical mechanism of disease pathophysiology in ITP through the inhibition of SYK signaling, which prevents destruction of platelets in ITP.

In the Phase 3 trial, 145 adults with ITP were given fostamatinib 100mg BID (increased to 150mg BID after 4 weeks if platelets were  $<50,000/\mu\text{L}$ ). A platelet response was  $\geq 1$  platelet count  $\geq 50,000/\mu\text{L}$  at any visit without rescue therapy. Second-line patients had previously received only steroids +/- immunoglobulins.

Of 145 patients in the Phase 3 studies, 32 patients received fostamatinib as a second-line therapy. This analysis showed that 78% (25/32) of second-line patients achieved a response, which was defined as  $\geq 1$  platelet count of  $\geq 50,000/\mu\text{L}$  (without rescue therapy). This compares to a response rate of 48% in third-or-later-line patients, and 54% of the total study population. Adverse events were manageable and consistent with those previously reported with fostamatinib.