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Oral Session

Disorders of Platelet Number or Function: Clinical Studies of ITP

Long-Term Efficacy and Safety of Romiplostim Treatment of Adult Patients with Chronic Immune Thrombocytopenia (ITP): Final Report from an Open-Label Extension Study

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Chronic ITP is characterized by increased platelet destruction and suboptimal platelet production. Romiplostim is a peptibody that increases platelet production by a mechanism similar to thrombopoietin (TPO). We report final cumulative data from adult patients with ITP who after completing a romiplostim study subsequently received romiplostim in an open-label extension study from as early as August 2004 through January 2010 for as long as 277 weeks. Romiplostim was administered once weekly sc, with dose adjustments to maintain platelet counts in the target range of 50–200x10^9/L. Patients who achieved a stable dose for 3 consecutive weeks were eligible to administer romiplostim at home (self or caregiver), returning to clinic every 4 weeks for evaluation. A total of 292 adult patients, mostly female (63%), received romiplostim. The median time since ITP diagnosis was 4.9 years (range, 0.6–46.4 years) and 32.5% had undergone a splenectomy. Patients received romiplostim for a median of 78 weeks (range, 1–277); taking the average weekly dose of all patients, the median was 4 mcg/kg (interquartile range, 2.2–7.3 mcg/kg). After week 12, romiplostim doses remained relatively constant, with 78% of patients administered a dose within 2 mcg/kg of their most frequent dose at least 90% of the time. Home administration was started by 82% of patients; 28/239 patients (12%) discontinued home administration and resumed weekly study-site injection. Almost all patients (94.5%) achieved a platelet count ≥50x10^9/L during the study. More than 50% had platelet counts ≥50x10^9/L on ≥90% of all visits. After the first week, median platelet counts remained within the target range of 50–200x10^9/L. Of patients receiving concurrent ITP medication at baseline, 81% (30/37) were able to discontinue or reduce their dose by >25%. Patients were divided into 4 cohorts corresponding to protocol changes; cohorts differed regarding baseline platelet count, duration of disease,

and splenectomy status. Median weekly platelet counts on study were similar for the cohorts and for the overall population. Adverse events were reported in 98% of patients; the most common were mild and included headache (38%), nasopharyngitis (34%), and fatigue (32%). The frequency of adverse events, including bleeding events of moderate or greater severity (≥Grade 2) and of clinical significance (≥Grade 3) and thrombotic events did not increase with time on study (Table). The types of adverse events did not differ in the four cohorts. Bone marrow biopsies were performed at the investigators' discretion on a small proportion of patients; bone marrow reticulin was present or increased in 11 patients. In general, patients with reticulin had a longer duration of disease, were splenectomized, and received higher doses of romiplostim. Two patients developed neutralizing antibodies to romiplostim that did not cross-react with thrombopoietin; these were absent on retesting after drug withdrawal. Sixteen patients died; 2 deaths were considered by the investigator as possibly related to treatment (unstable angina, myocardial infarction). In conclusion, in this study, the largest and longest interventional ITP study of TPO-mimetic exposure to date, almost 300 romiplostim-treated adults were able to maintain platelet counts within the target range, with modest dose adjustments for up to 277 weeks. In adults with ITP, the most common and serious adverse events associated with romiplostim were consistent with those reported in past studies and adverse events did not increase with longer duration of treatment. Most patients could successfully administer romiplostim at home.

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