Crizanlizumab Shows Efficacy in Sickle Cell Pain Crisis Prevention

The novel antibody crizanlizumab provided significant benefit in preventing pain crises caused by sickle cell disease in a Phase II trial.

Ilana Goldowitz Jimenez, PhD

February 22, 2017 – Patients with sickle cell disease had 45.3% fewer pain crises when treated with the monoclonal, humanized antibody crizanlizumab as compared to placebo in a Phase II trial.

Kenneth Ataga, MBBS, of the University of North Carolina at Chapel Hill and colleagues reported the results of the SUSTAIN study in the *New England Journal of Medicine* on February 2, 2017.

This international, double-blind study was designed to investigate the efficacy and safety of crizanlizumab in preventing pain crises, a major cause of reduced quality of life and mortality in patients with sickle cell disease. The authors noted that "the prevention of crises could minimize or prevent tissue and organ damage and decrease the subsequent risk of death among patients with sickle cell disease."

Crizanlizumab is a novel antibody against the cell adhesion molecule P-selectin. P-selectin has been shown to contribute to the vaso-occlusion characteristic of sickle cell pain crises by promoting the adhesion of leukocytes and sickled erythrocytes to the endothelium and the aggregation of platelets with neutrophils. Therefore, the researchers hypothesized that crizanlizumab could prevent vaso-occlusion and reduce sickle cell pain crises by blocking P-selectin binding.

For the SUSTAIN study, 198 patients with sickle cell disease and 2 to 10 sickle cell pain crises per year were recruited. The patients were stratified based on whether they used hydroxyurea and the number of pain crises in the previous year. Patients were randomized to receive high-dose crizanlizumab, low-dose crizanlizumab, or placebo at a 1:1:1 ratio.

During the 52 weeks of treatment, the primary outcome was the rate of pain crises. High-dose intravenous crizanlizumab (5.0 mg/kg, every 4 weeks) significantly reduced the rate of pain crises as compared with placebo (45.3% lower rate, $p=0.01$) in the intention-to-treat population. Low-dose crizanlizumab (2.5 mg/kg, every 4 weeks) showed a benefit compared with placebo (32.6% lower rate, $p=0.18$), but this did not reach significance. Each of the patient subgroups based on hydroxyurea use, number of annual crises, and genotype showed a clinically meaningful benefit from high-dose crizanlizumab.

Crizanlizumab also showed a benefit in several secondary outcomes, including time to first and second on-study pain crises, number of days hospitalized, and number of patients who experienced zero pain crises, although some of these were not statistically significant.

The rate of adverse events was similar between high-dose and placebo groups.

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