Which Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) Should Be Treated with Eculizumab?

ASH Evidence-based Review 2008

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A 45-year-old woman presents for evaluation as a result of persistent anemia. Ultimately, she is diagnosed with hemolytic anemia ascribed to paroxysmal nocturnal hemoglobinuria. She is otherwise well and has an otherwise normal complete blood cell count. She requires transfusion about once every 6 weeks for symptomatic anemia. She wonders whether she would benefit from eculizumab.

A Medline search for "eculizumab" (keyword, 49 hits) combined with "paroxysmal nocturnal hemoglobinuria" (keyword, 2628 hits) yielded 29 articles. Twenty-four articles were excluded as they were reviews or case reports. The remaining papers included a Phase III randomized controlled trial, a pilot study with extended follow-up, a Phase III non-randomized study and a combined analysis of the aforementioned studies assessing thromboembolic risk.[1-5] As the pilot study included only 11 patients, we will focus on the Phase III trials for this review. All articles cited in this review were co-authored by Dr. Hillmen and were carried out in the development program of eculizumab for Alexion Pharmaceuticals.

A double-blind randomized trial included 87 patients with a transfusion requirement of at least 4 red cell units in the previous 12 months and a platelet count of at least 100,000.[3] Forty-four patients received placebo and 43 received eculizumab for 26 weeks. Eculizumab-treated patients had reduced need for transfusion (0 versus 10 units in patients not treated with eculizumab). Quality of life (QOL) scores improved with eculizumab treatment but not with placebo, although baseline QOL scores were not reported. Adverse events were similar in both groups.

A Phase III non-randomized trial included 97 patients with less pronounced transfusion requirements (at least 1 red cell transfusion in the last 2 years) and lower average platelet counts (at least 30,000).[5] Patients were followed for 52 weeks and compared before and after treatment—both transfusion requirements and QOL improved with the greatest effects on dyspnea and fatigue. Of 44 serious adverse events, only 7 were considered possibly related to eculizumab and there were no severe bacterial infections.

These findings confirm that eculizumab decreases hemolysis and the resultant symptoms and transfusion requirements. Extended patient follow-up will further define adverse effects associated with long-term treatment and whether eculizumab reduces the incidence of other complications of PNH (e.g., thromboembolism).[4] Based on this analysis, eculizumab should be considered in patients with significant symptoms from hemolysis that are not adequately managed with transfusion (Grade 1A recommendation). The cost and therefore a potential lack of access to this medication in some healthcare communities may influence decisions about its use.

Disclosures

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