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Baseline patient characteristics in ReITIrate: A prospective study of rescue ITI with recombinant factor VIII Fc fusion protein (rFVIIIFc) in patients who have failed previous ITI attempts

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Abstract

Objective: Inhibitor development is the most serious complication of hemophilia A therapy. Immune tolerance induction (ITI) is the gold standard for inhibitor eradication, restoring factor VIII (FVIII) responsiveness. Retrospective data on ITI therapy using rFVIIIFc have been reported (Carcao et al. Haemophilia. 2018). The ReITIrate study (NCT03103542) was designed to prospectively evaluate success of rescue ITI with rFVIIIFc. Methods: ReITIrate, a prospective, interventional, multicenter, open-label study, enrolled patients with severe hemophilia A and inhibitors, who failed previous ITI attempts. The primary purpose is to describe the outcome of ITI performed with rFVIIIFc (200 IU/kg/day) within a maximum of 60 weeks. Here, patient baseline characteristics are reported using descriptive statistics and listings. Summary: Sixteen subjects were included in the study between November 2017 and December 2018. The median (range) age at study enrollment was 7.5 (2–46) years. Seven subjects had a known family history of inhibitors. The median (range) number of prior ITI attempts was 1 (1–3) and the median (range) total ITI duration was 51.5 (12–155) months. All subjects had previously received high-dose ITI, with 3 subjects receiving plasma products, 6 subjects receiving recombinant products, and 7 subjects receiving both recombinant and plasma products for previous courses of ITI. Four subjects received prior immunomodulatory therapy. The median (range) inhibitor titer at screening and historical peak were 11 (0.9–635) BU/mL and 127 (8–3000) BU/mL, respectively. During the 12 months prior to enrollment, the median (range) number of bleeds was 5 (0–24); 11 subjects used activated prothrombin complex concentrate (aPCC) for treatment of bleeds, 5 subjects received recombinant factor VIIa (rFVIIa), and 1 subject each received FVIII/von Willebrand factor, recombinant FVIII, and tranexamic acid. Twelve subjects received prophylaxis with bypassing agents during this period (10 aPCC, 1 rFVIIa, and 1 both products). Conclusions: This is the first prospective study describing rescue ITI with an extended half-life recombinant FVIII product. Enrolled subjects had multiple risk factors for poor ITI outcomes and a long duration of previous ITI. There is an unmet need for successful tolerization in such patients, allowing regular FVIII prophylaxis and potentially leading to improved clinical outcomes and quality of life.