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rFVIIIFc for first-time immune tolerance induction therapy: interim results from the global, prospective verITI-8 study

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Abstract

OBJECTIVE: Immune tolerance induction (ITI) is the standard of care for inhibitor eradication and restoration of factor VIII (FVIII) responsiveness in subjects with severe hemophilia who develop high-titer inhibitors. Retrospective data support the use of recombinant FVIII Fc fusion protein (rFVIIIFc) in ITI (Carcao et al. Haemophilia. 2018) but this has yet to be confirmed in prospective studies. This study presents preplanned interim results of verITI-8 (NCT03093480). METHODS: VerITI-8 is a single-arm, nonrandomized, open-label, ethics-approved study of rFVIIIFc (200 IU/kg/day) for first-time ITI. Eligible subjects had a history of high-titer inhibitors (historical peak ≥5 Bethesda units [BU]/mL) and provided informed consent. The primary endpoint is time to tolerization, defined by negative inhibitor titer (<0.6 BU/mL) at two consecutive visits; incremental recovery ≥66% of expected at two consecutive visits; and rFVIIIFc half-life ≥7 hours. ITI failure is defined as not meeting the above criteria by Week 48. This interim analysis was planned when ≥10 subjects had received ≥6 months of rFVIIIFc ITI.SUMMARY: Fifteen subjects were screened as of the December 5, 2018 cutoff, while 14 subjects enrolled and had received ≥1 dose of rFVIIIFc for ITI. The median (range) age at start of ITI was 2.6 (0.8–16.0) years and historical peak inhibitor titer was 29.6 (6.2–256.0) BU/mL. Six subjects have been successfully tolerized, with a median (range) time to first negative titer, normal incremental recovery, and tolerization of 2.3 (1.7–15.6), 6.0 (4.3–28.1), and 11.7 (8.1–32.0) weeks, respectively. Seven subjects continue to receive rFVIIIFc ITI (median [range] time on ITI: 16.0 [0.1–35.6] weeks) and 1 subject has failed. No adverse events related to rFVIIIFc have been reported. CONCLUSIONS: Early results from this prospective/ongoing study of first-time ITI indicate that rFVIIIFc may offer rapid time to tolerization in some subjects with severe hemophilia A and high-titer inhibitors. Achieving tolerance faster can improve quality of life and reduce costs.