

CRA 75

Five-year safety and efficacy of N8-GP (ESPEROCT®) in previously treated children with hemophilia A in the completed pathfinder 5 trial

Raffini, Leslie; Staber, Janice M; Yee, Donald L; Acharya, Suchitra; Clausen, Wan Hui Ong; Cooper, David L; Kearney, Susan

Submission Group

Clinical Research/Clinical Trials

Abstract

Objective: The completed pediatric phase 3 pathfinder 5 trial assessed the safety and efficacy of N8-GP (turoctocog alfa pegol, ESPEROCT®) use for routine prophylaxis and treatment of breakthrough bleeds in previously treated children. Methods pathfinder 5 was a multicenter, multinational, single-arm study evaluating safety, efficacy, and pharmacokinetics. Children (aged <12) with severe hemophilia A were administered prophylaxis (target 60 [50-75] IU/kg twice weekly) in the main phase (26 weeks) followed by an extension phase. Current analysis covers study initiation (February 2013) through completion (September 2018). Summary Of the 68 children (34 aged 0-5, 34 aged 6-11) enrolled, 63 completed the main phase and 62 completed the extension. Most (95%) were previously on prophylaxis. The total study period amounted to 306 patient-years (32,138 exposure days); median (mean) patient exposure was 4.9 (4.5) years. Overall, 838 adverse events (AEs) were reported; 18 serious AEs included 2 possibly/probably related to N8-GP (severe allergic reaction [1] and increasing bleeding symptoms [1]). No inhibitor development was observed in the trial. Two AEs resulted in withdrawal; a third patient with severe allergic reactions (after 4 doses) that resolved after 2 hours without any treatment met preestablished withdrawal criteria. There were no anti-PEG antibodies of clinical significance; however, 21 (31%) patients had anti-PEG antibodies at baseline (prior to exposure), and 1 patient had a single positive measurement after exposure at a titer <1. Overall, 55 patients (81%) reported 330 bleeds during the study; most were traumatic (67%). The success rate for hemostasis was 84% (excellent/good); 71% were treated with 1 injection, and 88% of patients were successfully treated with 1-2 injections. Median (mean) utilization for bleeds was 68 (95) IU/kg. Median ABRs are shown below; estimated mean ABR was 1.1. Forty-seven percent of children had no spontaneous bleeds throughout the trial. Of 13 children with 17 target joints at baseline, 77% (main phase) and 46% (complete trial) reported no bleeds in their target joints. For those previously on prophylaxis, the mean observed ABR was 2.3 compared with the historical ABR of 6.4. The mean prophylaxis dose was 64.7 IU/kg with an interval of 3.5 days. Median ABR Age 0-5 y Age 6-11 y Total Overall 0.6 0.9 0.8 Spontaneous 0.1 0.2 0.2 Traumatic 0.3 0.8 0.5 N8-GP prolonged single dose half-life by 1.9x compared with the child's prior FVIII product. The mean trough levels on twice-weekly dosing were 0.019 IU/mL (0.016 ages 0-5, 0.024 ages 6-11). **Conclusion** These data support the safety and efficacy of N8-GP in a controlled phase 3 trial setting in children. Prophylaxis with N8-GP using a consistent dose/interval (65 IU/kg twice weekly) was effective in preventing bleeds. No unexpected safety issues were identified.