# CRA 79

## Five-year safety and efficacy of N9-GP (REBINYN®) in previously treated children with hemophilia B in the ongoing paradigm 5 trial

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Clinical Research/Clinical Trials

**Abstract**

Objective: The ongoing pediatric phase 3 paradigm 5 trial is assessing N9-GP (nonacog beta pegol, REBINYN®) use for routine prophylaxis and treatment of breakthrough bleeds in previously treated children with hemophilia B (FIX ≤2%). This analysis presents 5-year safety and efficacy data in a group of children treated with weekly prophylaxis to a higher mean FIX trough (≥15%). Methods: paradigm 5 is a multinational, single-arm study evaluating safety, efficacy, and pharmacokinetics. Children (aged ≤12 years at enrollment) were administered weekly prophylaxis (N9-GP 40 IU/kg) through a 52-week main phase followed by an ongoing extension study. Mild/moderate bleeds were treated with 40 IU/kg. Prophylaxis, bleed treatments, and hemostatic efficacy were captured in electronic diaries. Current analysis extends from May 2012 through October 2018. Summary: Of the 25 children enrolled in the main phase (12 ages 0-6, 13 ages 7-12), 24 completed the main phase and 22 entered the extension (11 per age group). At the time of this analysis, 17 remain in the trial. No patients withdrew due to adverse events. Ten participants remaining in the trial have become adolescents (mean 2.6 adolescent-years of exposure). The cumulative exposure in the study was 116 patient-years (6,194 exposure days). The median (range) time in study was 5.2 (0.2-6.1) years representing 290 (10-325) N9-GP doses per patient. The median/mean prophylactic dose was 43.1 IU/kg/wk. A total of 573 adverse events were reported, including 4 serious adverse events, all of which were considered unlikely related by the investigator. No patients developed anti-FIX inhibitory antibodies (primary endpoint). There were 7 medical events of interest, including 6 allergic reactions (no anaphylaxis). Age-related increase in trough FIX levels was seen; the mean FIX trough levels were 0.179 IU/mL (overall), 0.166 IU/mL (younger), and 0.192 IU/mL (older). Mean PEG plasma concentration reached steady state after ~6 months. Overall, 20 patients (80.0%) experienced 115 bleeds, the majority of which were traumatic (64%) or spontaneous (33%) and in joints (43%). Most (93%) were treated with 1-2 doses with 89% rated as excellent/good. Median individual ABRs are shown in the TABLE ; 64% of patients were spontaneous-bleed-free throughout the study. Median ABR Age 0-6 Age 7-12 Total Overall 0.41 0.99 0.66 Spontaneous 0.00 0.00 0.00 Traumatic 0.41 0.50 0.47 Ten minor surgeries and 1 major surgery were performed successfully. Conclusion: These data support the safety and efficacy of N9-GP 40 IU/kg weekly over a median of 5 years in a controlled phase 3 trial setting in children. N9-GP prophylaxis with a trough of ~18% was effective in preventing bleeds with low reported ABR and with 64% of patients reporting no spontaneous bleeds during the entire study period. No unexpected safety issues were identified.