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The use of turoctocog alfa for the prevention and treatment of bleeds in patients with hemophilia A: efficacy data from European countries included in the guardian™2 clinical trial

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Objective

- To investigate whether annualized bleeding rate (ABR) variation among European countries may be related to differences in patient age between countries.

Conclusions

- Although adult, adolescent, and pediatric patients treated with long-term standard prophylaxis with turoctocog alfa had low ABRs, variation was observed across European countries.
- Variability in ABR across countries does not appear to be explained by the differences between countries in patient age. An alternative explanation, that the variability may be due to unequal access to hemophilia services, warrants further analyses.

Introduction

- Prophylaxis with coagulation factor VIII (FVIII) is the gold standard for preventing bleeds in hemophilia A.
- However, treatment practices regarding primary and secondary prophylaxis vary by country, which may have a profound impact on patients' long-term outcomes and quality of life.
- Novo Nordisk has developed turoctocog alfa, a B-domain truncated recombinant FVIII product for the prevention and treatment of bleeds in patients with hemophilia A.
- Two phase 3 clinical trials have demonstrated that turoctocog alfa is safe and effective for prophylaxis and treatment of bleeds in adults and adolescents aged ≥12 years (guardian™1)[1] and in children aged <12 years (guardian™3)[2] with hemophilia A. Patients who completed guardian™1 or guardian™3 could choose to continue treatment with turoctocog alfa by enrolling in the guardian™2 extension trial.
- Variability in annualized bleeding rate (ABR) between countries has previously been noted in this trial; however, an analysis to explore whether prior treatment may underpin this finding was inconclusive.

Methods

Patients and trial design

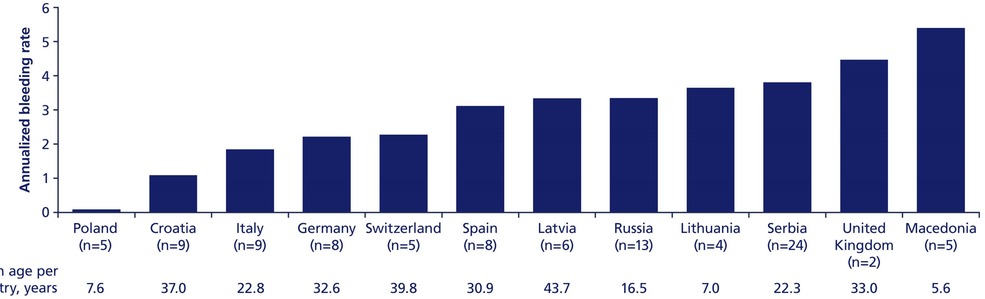
- guardian™2 was a multicenter, multinational, open-label, non-randomized, safety and efficacy extension trial that was conducted at 52 sites in 19 countries.
- Previously treated male patients aged 1–61 years, with severe hemophilia A (FVIII activity ≤1%) and no history of inhibitors, were eligible for inclusion in guardian™2 if they had completed guardian™1, guardian™3, or preceding pharmacokinetics trials.
- Data were analyzed from patients from 12 European countries participating in guardian™2 as of the interim cutoff (December 31, 2013).
- Patients received turoctocog alfa for prophylaxis (20–50 IU/kg once every second day, or 20–60 IU/kg three times weekly), and on-demand (20–200 IU/kg/day [dose levels totaling up to 200 IU/kg/day depending on severity/location of the bleed]) for the treatment of bleeds.
- ABRs were determined per European country and age. Analyses were descriptive.

Results

Patients

- Of the 200 patients in guardian™2, 98 were from Europe (Croatia, Germany, Italy, Latvia, Lithuania, Macedonia, Poland, Russian Federation, Serbia, Spain, Switzerland, and the UK).

Figure 1 Annualized bleeding rate and mean age per country in the guardian™2 trial



- Mean patient age at baseline by country ranged from 5.6 to 43.7 years (Figure 1).
- The majority of patients were adults (n=60); six countries included pediatric patients (n=29), while four recruited adolescent patients (n=9).

Annualized bleeding rate by country

- ABR following prophylaxis with turoctocog alfa ranged from 0.09 (Poland) to 5.40 (Macedonia) (Figure 1). For adult patients only, ABR ranged from 1.09 (Croatia) to 7.17 (Russia).
- Data from Macedonia and Poland were from pediatric patients (lowest age group) but their respective ABR varies from highest to lowest in the total group.
- The difference in ABR between countries remained significant after adjusting for patient age.
- As of the cutoff date (December 31, 2013), no FVIII inhibitors were detected and no safety issues were identified.

References

1. Lentz SR, *et al. Haemophilia* 2013;19:691–697.
2. Kulkarni R, *et al. Haemophilia* 2013;19:698–705.

Conflict of interest disclosure

BB has received grant/research support from Bayer HealthCare, Baxalta, CSL, and Novo Nordisk, and is a consultant for a Bayer study; BB is also active in advisory boards and as a speaker for Alnylam, Baxalta, Biotest, Novo Nordisk, and Pfizer. **DJ** has received speaker fees from Baxter, Bayer, Novo Nordisk, Octapharma, and Pfizer. **AR** and **NT** are full-time employees of Novo Nordisk. **PL** and **AS** have no conflicts of interest to declare.

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