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322.DISORDERS OF COAGULATION OR FIBRINOLYSIS: CLINICAL AND EPIDEMIOLOGICAL

Matching-Adjusted Indirect Comparison of Personalized Prophylaxis with Simoctocog Alfa Versus Standard Prophylaxis with Efanesoctocog Alfa in Adults with Severe Hemophilia a

Craig Kessler, MD[1], Fernando F Corrales-Medina, MD[2,3], Pier Mannuccio Mannucci[4], Michael D. Tarantino, MD[5]

[1] Lombardi Comprehensive Cancer Center, MedStar Georgetown University Hospital, Washington, DC
[2] Division of Pediatric Hematology-Oncology, University of Miami-Miller School of Medicine-Sylvester Cancer Center, Miami, FL
[3] University of Miami-Hemophilia Treatment Center, Miami, FL
[4] Ospedale Maggiore Policlinico, Angelo Bianchi Bonomi, Hemophilia and Thrombosis Center, IRCCS Ca' Granda Foundation, Milano, Italy
[5] The Bleeding and Clotting Disorders Institute, University of Illinois College of Medicine-Peoria, Peoria, IL

Background:
Personalized factor VIII (FVIII) prophylaxis is currently the gold standard approach for the treatment of patients with severe hemophilia A. Although several FVIII concentrates are available, head-to-head comparative studies of their relative efficacy are not feasible in rare diseases such as hemophilia A. In such situation, the use of validated indirect comparison methods such as matching-adjusted indirect comparison (MAIC) methodology can be used to indirectly compare outcomes from separate clinical studies. MAIC can be used to adjust for differences in patient characteristics between studies, with the goal to reduce bias in the treatment effect estimates which can occur with comparison of efficacy data across clinical trials.
Aims:
To indirectly compare the efficacy of a pharmacokinetic (PK)-guided personalized prophylaxis regimen with simoctocog alfa (Nuwiq ®; a 4 th-generation recombinant FVIII [rFVIII] concentrate with no chemical modifications of fusion proteins) against a standard prophylaxis regimen with efanesoctocog alfa (Altuviiio ®; an Fc-fusion rFVIII concentrate with chemical modifications including Von Willebrand factor independent-XTEN fusion protein), in previously-treated patients (PTPs) with severe hemophilia A.
Methods:
After matching study populations by accounting for clinically important baseline characteristics,individual patient-level data (IPD) from 65 patients treated with simoctocog alfa from the NuPreviq study were compared against aggregate data from the once-weekly efanesoctocog alfa arm of the XTEND-1 study (n=133). All patients enrolled in both studies were male, with the exception of one female in XTEND-1. Baseline age and body weight were used to re-weight the simoctocog alfa IPD to match the aggregate data reported for efanesoctocog alfa from the XTEND-1 study. Unanchored indirect treatment comparisons were performed for various clinical outcomes using the re-weighted data for simoctocog alfa and the published comparator study data. The endpoints analysed were annualized bleeding rates (ABRs), percentage of patients with zero bleeds, and weekly consumption of FVIII. All efficacy endpoints reported here consider treated and untreated bleeds.
Results:
After matching populations, the effective sample size for simoctocog alfa was 35.3. Although, the percentage of patients with zero bleeds was higher with simoctocog alfa versus efanesoctocog alfa (64.1% vs 55.5%), this difference was not statistically significant (Table 1). The mean total ABRs were similar between the two products: 1.5 for simoctocog alfa and 1.1 for efanesoctocog alfa (Table 1). The mean weekly dose was significantly higher in patients treated with simoctocog alfa versus efanesoctocog alfa (98.3 IU/kg vs 52.2 IU/kg, respectively; $p<0.0001$).
Conclusion:
An indirect comparison analysis demonstrated that a PK-guided, personalized prophylaxis with simoctocog alfa in adult PTPs resulted in zero bleed rates and ABRs that are not statistically different from those with efanesoctocog alfa. The higher total weekly dose observed with simoctocog alfa is to be expected based on the dosing recommendations for each respective FVIII replacement product. This MAIC analysis provides important comparative efficacy and utilization data, which can help guide patients and physicians in making decisions regarding product choice for prophylaxis regimens.

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Table 1. Results of a matching-adjusted indirect comparison of simoctocog alfa vs efanesoctocog alfa

Outcome	Simoctocog alfa (IPD)* N=65 (ESS=35.3)	Efanesoctocog alfa (aggregate data) N=133	Ratio or difference† (95% CI)	p value
Patients with zero bleeds (%)	64.1	55.5	8.7 (-7.4, 24.8)	0.291
Mean total ABR	1.5	1.1	1.38 (0.71, 2.70)	0.342
Mean weekly FVIII dose (IU/kg)	98.3	52.2	46.1 (41.1, 51.0)	<0.0001

*Weighted outcomes based on IPD.

†Risk difference for % patients with zero bleeds, rate ratio for total ABR, and mean difference for weekly dose.

ABR: annualized bleeding rate; CI: confidence interval; ESS: effective sample size; IPD: individual patient-level data; N: number of patients; IU: international unit.

Figure 1

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