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REFINE study protocol: Real-world outcomes of EFanesoctocog alfa IN Central and Eastern Europe Study Design

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INTRODUCTION

Hemophilia A (HA) is a rare, lifelong bleeding disorder caused by factor VIII (FVIII) deficiency, leading to recurrent joint bleeds, progressive arthropathy, and reduced health-related quality of life.[1]

Despite advances in prophylactic therapies, subclinical bleeds remain an important concern, as joint deterioration may still occur even in the absence of symptomatic bleeds, contributing to cumulative joint damage, pain, and functional limitations despite standard prophylaxis.[1,2]

Efanesoctocog alfa is a new class of high-sustained activity / ultra long (HSA/UL) FVIII, designed to maintain FVIII activity in the non-hemophilic range (>40 IU/dL) for most of the week, enabling once-weekly dosing.[3,4]

While Efanesoctocog alfa was introduced in Europe in 2024 and became available in Central and Eastern Europe (CEE) in 2025,[3] region-specific real-world data on its effectiveness, safety, and routine use remain limited.

AIMS

- To describe the use and effectiveness of Efanesoctocog alfa in the CEE region.
- To assess the long-term real-world effectiveness, safety, and usage patterns of Efanesoctocog alfa prophylaxis over 24 months in people with HA (PwHA), while evaluating its intra-individual effectiveness and safety compared to previous prophylaxis regimens.

ENDPOINTS

Primary Endpoint:

- Change in annualized bleeding rate (ABR) from the 12-month pre-index period to the 24-month post-index period.

Secondary Endpoints:

- Change in annualized joint bleeding rate (AjBR) from the 12-month pre-index period to the 24-month post-index period.
- Target joint development, resolution, and recurrence over 24 months.
- Changes in HEAD-US and HJHS scores over 24 months compared to baseline.
- Proportion of patients with zero bleeds or joint bleeds in 6-month intervals.
- Timing of bleeds relative to the last prophylactic injection.
- Annualized consumption (IU, IU/kg), injection frequency, and dose metrics.
- Details of bleeding episode treatments.
- Efanesoctocog alfa consumption, injections, and hemostasis maintenance during surgeries.
- Hospitalizations, outpatient consultations, and physiotherapy sessions.
- Occurrence of SAEs and AESIs.
- Percentage of Florio™ HAEMO and other application users.
- Trough/peak levels, timing, and assay details.
- Frequency and days missed from work/school due to hemophilia.
- Changes in PROMIS/Hemo-QoL scores and physical activity patterns over 24 months.

STUDY DESIGN

- This is a phase IV, non-interventional, multicenter, ambispective chart review, divided into three key periods:
  - **Pre-index period:** A 12-month period prior to switching to Efanesoctocog alfa prophylaxis.
  - **Index date:** The date when patients switch to Efanesoctocog alfa prophylaxis.
  - **Post-index period:** A 24-month follow-up period after the switch to Efanesoctocog alfa.
  - Data will be collected retrospectively at five predefined time points throughout the study duration, ensuring comprehensive insights into patient outcomes (**Figure 1**).

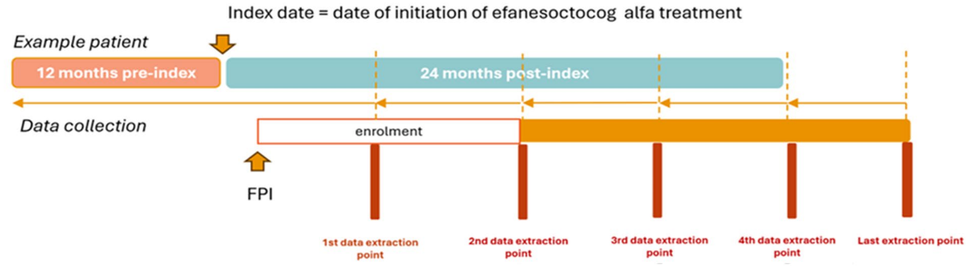

Figure 1. Overview of the REFINE study design.

The pre-index (enrollment) period will continue for up to 12 months or until the target sample size of approximately 100 patients is achieved.

STUDY POPULATION AND PARTICIPATING SITES

- The study aims to enroll 100 patients across 10 hemophilia treatment centers in CEE (**Figure 2**).
- It includes male and female patients of all ages diagnosed with any severity HA.
- Eligible participants must have been on prophylaxis for at least 12 months prior to switching to Efanesoctocog alfa and must have received at least one dose of Efanesoctocog alfa prophylaxis at enrollment.
- Participants must have complete pre-index clinical data, including bleeding episodes, factor use, and surgical history.
- Informed consent is required, with agreement obtained for pediatric patients in accordance with local regulations.
- Patients with active or past FVIII inhibitors without successful immune tolerance, other bleeding disorders, or those in interventional trials are excluded.

Figure 2. REFINE study sites.

The study will be conducted across 10 hemophilia centers in 4 countries: Bulgaria (n=1), Croatia (n=1), Czechia (n=6), and Slovenia (n=1).

References: 1. Mannucci et al. Haemophilia. 2023;29(4):954–62; 2. Mahlangu et al. Haemophilia. 2018;24(3):348–58; 3. European Medicines Agency (EMA). Altuvoct product information; 4. Hermans et al. Blood Adv. 2026;10(10):3409-3417.

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Abbreviations: ABR, annualized bleed rate; AjBR, annualized joint bleeding rate; CEE, Central and Eastern Europe; CMPP, Certified Medical Publication Professional; FPI, first participant in; FVIII, Factor VIII; Florio™ HAEMO, digital hemophilia monitoring application; HA, hemophilia A; Hemo-QoL: Haemophilia Quality of Life Questionnaire; HEAD-US: Hemophilia Early Arthropathy Detection with Ultrasound; HJHS: Hemophilia Joint Health Score; IU, international units; SAEs, serious adverse events; AESIs, adverse events of special interest; PROMIS, Patient-Reported Outcomes Measurement Information System.