PO111

Safety and Efficacy of Damoctocog Alfa Pegol Prophylaxis in Patients With Severe Haemophilia A: Final Results of an Interventional Post-Marketing Study Confirm Pivotal Study Results

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CONCLUSIONS

- **In this interventional post-marketing study, individualised prophylaxis regimens of damoctocog alfa pegol were well tolerated with no observed immunogenicity concerns**
- **Annualised bleeding rates (ABRs) improved during the study compared with pre-study, with many patients achieving zero bleeds**
- **These findings are consistent with PROTECT VIII[1] and further support the favourable safety and efficacy profile of damoctocog alfa pegol prophylaxis for patients in routine clinical practice**

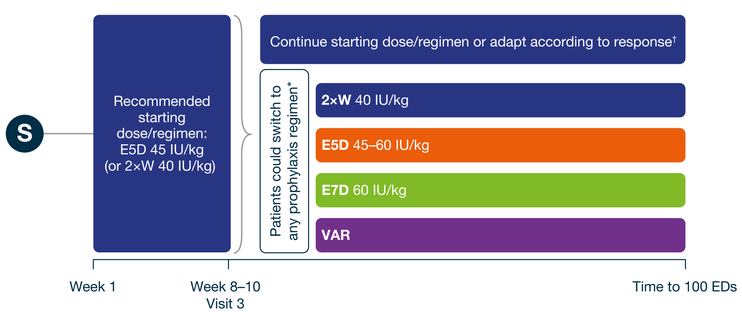
INTRODUCTION

- Damoctocog alfa pegol (BAY 94-9027, Jivi®, Bayer) is a B-domain deleted, site-specifically PEGylated, recombinant factor VIII (FVIII) product, indicated for prophylaxis and treatment of bleeds in previously treated patients with haemophilia A, aged ≥12 years[2]
- The efficacy and safety of damoctocog alfa pegol for prophylaxis of bleeding episodes was demonstrated in the phase 2/3 PROTECT VIII trial (NCT01580293)[1]
  - At PROTECT VIII extension completion, median ABR was 1.5 for prophylaxis treated patients, and 50% and 58% were bleed-free and joint bleed-free in their last 6 months of treatment[1]
- A multicentre, uncontrolled, open-label, interventional, post-marketing phase 4 study (NCT04085458) explored the real-world safety and effectiveness of damoctocog alfa pegol
- Here we report the final results of this post-marketing, open-label study of damoctocog alfa pegol prophylaxis in previously treated adults with haemophilia A

METHODS

- Eligible patients were male, aged ≥18 years with severe haemophilia A (FVIII:C <1%) and ≥150 exposure days (EDs) prior to enrolment
  - Exclusion criteria included participation in PROTECT VIII or PROTECT VIII Kids studies, presence or history of a FVIII inhibitor (≥0.6 Bethesda units [BU]/mL) and diagnosis of any bleeding disorder other than haemophilia A
- Participants received damoctocog alfa pegol for 100 EDs at the recommended starting dose of 45 IU/kg every 5 days (E5D) until Visit 3 (**Figure 1**) after 10–15 EDs
  - A starting dose of 40 IU/kg twice weekly was also permitted based on the investigator's judgement

Figure 1: STUDY DESIGN



*Change in dose frequency was permitted at any time; patients who changed dose frequency after Visit 3 were included in the VAR group.

†Based on investigator's judgement and the number of bleeds in the first 8–10 weeks; dosing recommendations were provided as guidance but were not mandatory.

2×W, twice weekly; E5D, every 5 days; E7D, every 7 days; ED, exposure day; S, screening; VAR, variable frequency.

- At Visit 3, patients continued the same regimen, increased the dose, or switched to twice weekly, E5D, or every 7 days (E7D), based on investigator's judgement and the number of bleeds in the first 8–10 weeks
- Primary endpoint was FVIII inhibitor development (titre ≥0.6 BU/mL)
- Secondary endpoints included treatment-emergent adverse events (TEAEs), anti-polyethylene glycol (PEG) antibody (Ab) development and ABR
- All analyses were exploratory

RESULTS

Safety

- Of the 36 patients enrolled, 32 received ≥1 infusion of study drug and were eligible for safety analysis
  - Mean age was 42.8 years and median (range) time in study was 16.0 (0.3–24.3) months
- TEAEs are summarised in **Table 1**
  - TEAEs were observed in 65.6% (n = 21) of patients, and most (43.8% [n = 14]) were mild in severity
  - Three (9.4%) patients had TEAEs (mild or moderate in severity) that were considered related to study drug
  - Serious AEs were reported in 2 (6.3%) patients; no SAE was considered to be related to the study drug
- No patients developed FVIII inhibitors during the study
- Three patients (9.4%) had a transient positive anti-PEG Ab result without clinical impact
  - Anti-PEG Ab titres were very low and negative at study end

Table 1: TREATMENT-EMERGENT ADVERSE EVENTS (SAFETY ANALYSIS SET)

	Patients (N = 32) n (%)
Any AE Mild Moderate Severe	21 (65.6) 14 (43.8) 5 (15.6) 2 (6.3)
Any study-drug-related AE Mild Moderate Severe	3 (9.4)* 2 (6.3) 1 (3.1) 0
Any SAE Any study-drug-related SAE	2 (6.3)† 0
Discontinuation of study drug due to AE	2 (6.3)
Discontinuation of study drug due to SAE	0
Presence of FVIII inhibitor (titre ≥0.6 Bethesda units)	0
Presence of anti-PEG antibody in plasma	3 (9.4)

*Study-drug-related AEs were observed in three patients: injection site erythema, skin wound (leading to discontinuation), hypersensitivity (leading to discontinuation), dysgeusia, cough, pruritus, and rash maculo-papular.

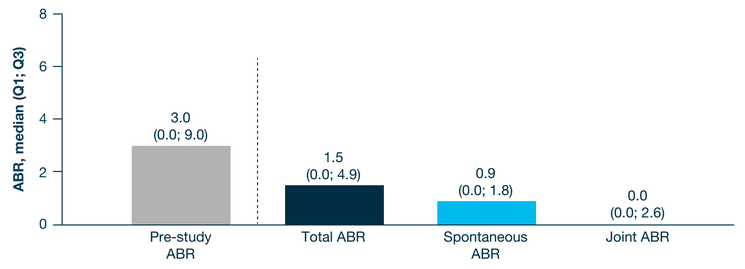
†SAEs were fall (n = 1) and osteoarthritis (n = 1).

AE, adverse event; FVIII, factor VIII; PEG, polyethylene glycol; SAE, serious adverse event.

Bleeding outcomes

- Thirty patients received ≥1 infusion of damoctocog alfa pegol and had electronic patient diary data for ≥3 months, and were eligible for efficacy analysis (modified intent-to-treat [mITT] population)
  - Most patients (70%, n = 21) were on E5D (n = 11) or E7D (n = 10) prophylaxis at the end of the study, similar to observations in PROTECT VIII[1]
- Median (Q1; Q3) total, spontaneous and joint ABRs from Visit 3 to end of study were 1.5 (0.0; 4.9), 0.9 (0.0; 1.8) and 0.0 (0.0; 2.6), respectively, as shown in **Figure 2**
  - Median total ABR (Q1; Q3) pre-study was 3.0 (0.0; 9.0)
- Median (Q1; Q3) total, spontaneous and joint ABRs were 1.8 (0.7; 3.8), 1.4 (0.0; 3.0) and 0.3 (0.0; 2.7), respectively, from baseline to end of study

Figure 2: MEDIAN TOTAL, SPONTANEOUS AND JOINT ABR* (mITT POPULATION, N = 30) FROM VISIT 3 TO END OF STUDY



*On-study evaluation period covers time from Visit 3 to end of study. These data consider all bleeds, including untreated bleeds.

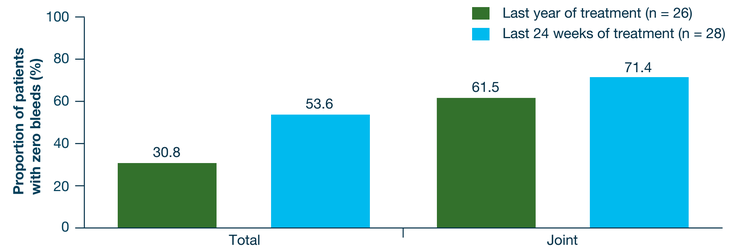
ABR, annualised bleeding rate; mITT, modified intent-to-treat; Q, quartile

- Proportions of patients with zero bleeds during study treatment are shown in **Figure 3**
  - During their last year of treatment (n = 26 with available data), 30.8% (n = 8) of patients had zero total bleeds and 61.5% (n = 16) had zero joint bleeds
  - In their last 24 weeks of treatment (n = 28 with available data), 53.6% (n = 15) of patients had zero total bleeds and 71.4% (n = 20) had zero joint bleeds

FVIII utilisation

- Median (range) FVIII dose per kg per prophylaxis infusion was 50.6 (40–63) IU/kg with a median (range) of 73.6 (54–99) infusions per year (mITT population)
  - Median (range) total annual FVIII utilisation for prophylaxis was 3603 (3160–4460) IU/kg/year
  - Median (range) total annual FVIII utilisation was 3736 (3200–5481) IU/kg/year

Figure 3: PROPORTIONS OF PATIENTS WITH ZERO BLEEDS DURING TREATMENT (mITT POPULATION*)



*Patients who received ≥1 infusion of damoctocog alfa pegol and had EPD data for ≥3 months were included in the mITT population.

EPD, electronic patient diary; mITT, modified intent-to-treat.

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References: **1.** Reding MT, et al. *Haemophilia* 2021;27:e347–e356. **2.** US Food and Drug Administration. JIVI® Prescribing Information. Available from: https://www.fda.gov/files/vaccines,%20blood%20%26%20biologics/published/Package-Insert-JIVI.pdf. Accessed December 2022.

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