Effectiveness and Safety of Damoctocog Alfa Pegol in Patients With Hemophilia A With a History of Factor VIII Inhibitors: Interim Analysis From the Real-World HEM-POWR Study

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CONCLUSIONS

- **Damoctocog alfa pegol demonstrates real-world effectiveness and a favorable safety profile in previously treated patients (PTPs) with hemophilia A who have a history of factor VIII (FVIII) inhibitors.**

AIMS

- **To assess the real-world effectiveness and safety of damoctocog alfa pegol in PTPs with hemophilia A receiving prophylactic treatment and with a history of FVIII inhibitors.**

INTRODUCTION

- FVIII inhibitors present a complex challenge for the treatment of patients with hemophilia A and develop in approximately 30% of patients with severe disease.[1]
- Immune tolerance induction is effective in eradicating inhibitors in 70% of patients with hemophilia A, leaving a significant proportion with resistant inhibitors.[2]
- Patients with FVIII inhibitors have been excluded from registrational clinical trial programs of FVIII replacement therapies, including the PROTECT VIII (NCT01580293) and PROTECT VIII Kids (NCT01775618)[3,4] trials for damoctocog alfa pegol, an extended half-life recombinant FVIII product approved for treatment of hemophilia A in PTPs aged ≥12 years.
- Real-world evidence includes the analysis of a broader patient population with a more complex medical history, allowing for real-world study of patients often excluded from clinical trials.

METHODS

- HEM-POWR (NCT03932201) is an ongoing, prospective, observational, multicenter Phase IV study of damoctocog alfa pegol in PTPs with non-severe and severe hemophilia A.[5]
- This interim subgroup analysis included patients with hemophilia A with a history of FVIII inhibitors, who received a FVIII prophylaxis therapy for ≥1 year prior to enrollment, and with no current evidence of FVIII inhibitors.
- The primary endpoint was annualized bleeding rate (ABR). Secondary endpoints included joint health and safety, and treatment-emergent adverse events (TEAEs).
- Baseline characteristics and endpoints were reported as descriptive statistics. Data were collated from patient diaries and physician records and described in a safety analysis set (SAF) and full analysis set (FAS). Ethical approval was obtained at all sites.
- Patients included in the SAF had ≥1 study dose in the observation period and provided informed consent; the FAS was defined as patients who fulfilled all inclusion criteria with a documented first study drug dose and ≥1 infusion during the observation period.

RESULTS

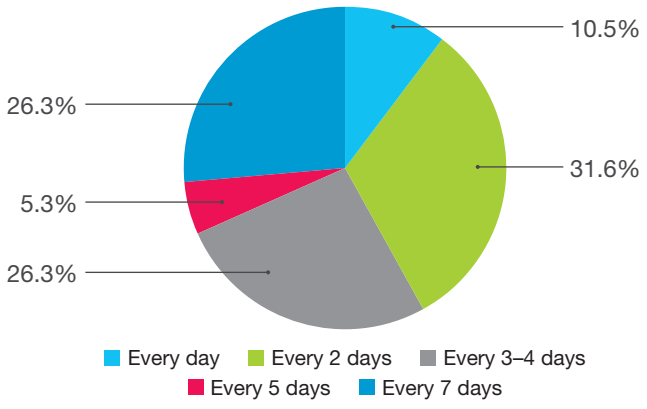
- At the data cut-off (August 17, 2022), of 270 patients enrolled in the HEM-POWR study, 35 patients (1 non-severe [2.9%], 34 severe disease [97.1%]) in the SAF had a previous history of inhibitors. In the FAS, a total of 20 patients (20 severe disease [100.0%]) were included in the effectiveness analysis.
- Baseline characteristics are reported in **Table 1**.

Table 1: BASELINE DEMOGRAPHICS AND CHARACTERISTICS

Characteristic	Safety Analysis Set (n=35)	Full Analysis Set (n=20)
Observation period, days, mean (SD), range	198.3 (195.2), 1–596	249.7 (185.6), 2–596
Male, n (%)	35 (100.0)	20 (100.0)
Age at enrollment, years, median (Q1, Q3)	26.0 (19.0, 37.0)	29.0 (19.5, 40.0)
Race, n (%)*		
White	20 (57.1)	8 (40.0)
Asian	11 (31.4)	9 (45.0)
Not reported	1 (2.9)	0
Country of recruitment, n (%)		
Germany	14 (40.0)	8 (40.0)
Japan	8 (22.9)	7 (35.0)
Taiwan	3 (8.6)	2 (10.0)
Colombia	2 (5.7)	0
Sweden	2 (5.7)	2 (10.0)
Greece	2 (5.7)	0
United States of America	2 (5.7)	0
Denmark	1 (2.9)	1 (5.0)
Spain	1 (2.9)	0
Disease severity at diagnosis, n (%)		
Non-severe	1 (2.9)	0
Severe	34 (97.1)	20 (100.0)
Family history of hemophilia, yes, n (%)	19 (54.3)	11 (55.0)
Prophylactic treatment before enrollment, yes, n (%)	35 (100.0)	20 (100.0)
Family history of inhibitors, yes, n (%)	3 (8.6)†	3 (15.0)‡
Immune tolerance induction history, yes, n (%)	16 (45.7)	11 (55.0)

Q1, 1st quartile; Q3, 3rd quartile; SD, standard deviation. *Missing data for 3 patients; †Unknown for 15 patients; ‡Unknown for 7 patients.

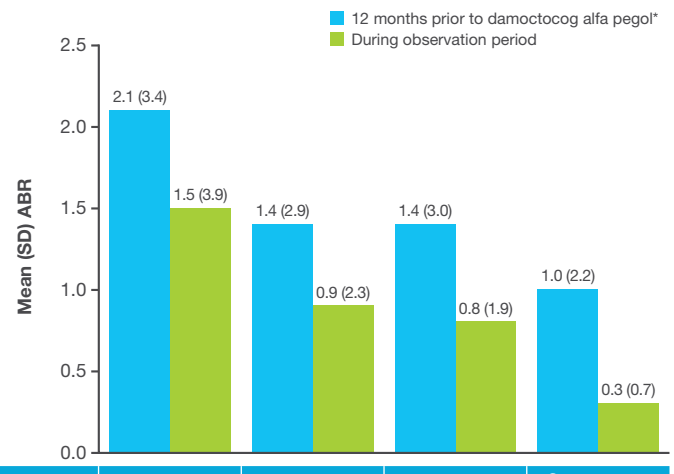
Figure 1: DAMOCTOCOG ALFA PEGOL PROPHYLAXIS DOSING REGIMEN FOR PATIENTS IN THE FAS DURING THE OBSERVATION PERIOD (N=19)



FAS, full analysis set.

- During the observation period, the most common prophylaxis regimen was every 2 days (6/19; 31.6%), followed by every 3–4 days (5/19; 26.3%) and every 7 days (5/19; 26.3%) (**Figure 1**).
- In the FAS, the total median (mean, SD) number of bleeds within the 12 months prior to damoctocog alfa pegol initiation was 0.0 (2.1, 3.4) and during the observation period was 0.0 (1.5, 3.9) (**Table 2**, **Figure 2**).
- Prior to damoctocog alfa pegol initiation, 10/20 (50.0%) patients had no joints affected. At the first follow-up window, 7/9 (77.8%) had no joints affected (**Figure 3**).
- In the SAF, TEAEs were reported for 6/35 (17.1%) of patients; 4/35 (11.4%) patients experienced TEAEs that led to a change in treatment regimen and 1 (2.9%) patient had a serious TEAE. There were no study-drug related TEAEs and no patients developed FVIII inhibitors.

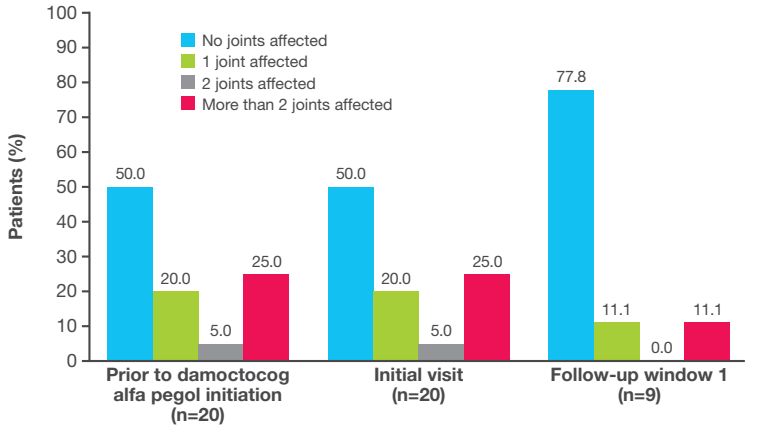
Figure 2: MEAN (SD) ABR WITHIN 12 MONTHS PRIOR TO DAMOCTOCOG ALFA PEGOL INITIATION AND DURING OBSERVATION PERIOD FOR PATIENTS IN THE FAS WITH A HISTORY OF FVIII INHIBITORS (N=20)



	Total	Spontaneous	Joint	Spontaneous joint
Difference in ABR, median (Q1, Q3); mean (SD)*	0.0 (–2.1, 0.0); –0.5 (3.7)	0.0 (0.0, 0.0); –0.5 (2.4)	0.0 (–1.2, 0.0); –0.6 (2.9)	0.0 (–1.0, 0.0); –0.7 (1.6)

ABR, annualized bleeding rate; FAS, full analysis set; FVIII, factor VIII; Q1, 1st quartile; Q3, 3rd quartile; SD, standard deviation.
*Data missing for 1 patient prior to damoctocog initiation. Data during the observation period were calculated based on an annualized rate, data from 12 months prior to initiation were the average number of bleeds over 12 months.

Figure 3: PERCENTAGE OF PATIENTS IN THE FAS WITH AFFECTED JOINTS (N=20)



FAS, full analysis set.

Table 2: MEDIAN ABR DURING AND PRIOR TO OBSERVATION PERIOD FOR PATIENTS WITH A HISTORY OF FVIII INHIBITORS IN THE FAS (N=20)

Characteristic	ABR by bleed type			
	Total	Spontaneous	Joint	Spontaneous joint
Number of bleeds within 12 months prior to initiation of damoctocog alfa pegol, median (Q1, Q3)*	0.0 (0.0, 3.0)	0.0 (0.0, 1.0)	0.0 (0.0, 3.0)	0.0 (0.0, 1.0)
Annualized number of bleeds, median (Q1, Q3)	0.0 (0.0, 0.9)	0.0 (0.0, 0.4)	0.0 (0.0, 0.4)	0.0 (0.0, 0.0)

ABR, annualized bleeding rate; FAS, full analysis set; Q1, 1st quartile; Q3, 3rd quartile; SD, standard deviation. *Data missing for 1 patient prior to damoctocog initiation. Data during the observation period were calculated based on an annualized rate, data from 12 months prior to initiation were the average number of bleeds over 12 months.

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