Joint range of motion findings among female patients with hemophilia A from the ATHNdataset

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CONCLUSIONS

- **Females are likely underdiagnosed with hemophilia, as evidenced by the limited data for this population from the ATHNdataset**
- **These data show that females with hemophilia A have reduced range of motion (ROM) similar to males, despite having near normal Factor VIII levels and mild disease, with joint ROM limitations likely beginning prior to adolescence**
  - **Data also suggest that female patients with hemophilia A may have less joint damage in the upper extremities compared with the lower extremities**
- **Females with one abnormal Factor VIII gene should be closely monitored for life at hemophilia treatment centers, and should be classified as having hemophilia if complications arise**
  - **Females should not be diagnosed based on criteria for males, but by phenotype**
- **Additional research, including systematic data on the evolution of joint ROM in females with hemophilia A, is needed**

OBJECTIVES

- **To explore the ROM in females with hemophilia A treated with either BAY 94-9027 (damoctocog alfa pegol, Jivi®, Bayer) or BAY 81-8973 (octocog alfa, Kovaltry®, Bayer) using data from the ATHNdataset**

INTRODUCTION

- Joint bleeding is a major clinical manifestation of hemophilia A[1]
- Repeat bleeding into the joint eventually leads to limited joint mobility, reduced ROM, and arthropathy[2,3]
  - There is also evidence that joint damage can result from even a single joint bleed[3–5]
- Although it is known that joint bleeding is common in males with hemophilia,[2] less is known about the prevalence of joint bleeding and the subsequent morbidity in females with hemophilia A
- A previous study demonstrated that females with Factor VIII deficiency had reduced ROM compared with controls, and that subclinical joint bleeding may be occurring before adolescence[2]
- There is currently a lack of randomized clinical trials in females with hemophilia; thus, real-world databases are important to provide data
- The ATHNdataset is a Health Insurance Portability and Accountability Act-compliant, de-identified database sponsored by the American Thrombosis and Hemostasis Network, including 17,109 patients with hemophilia A

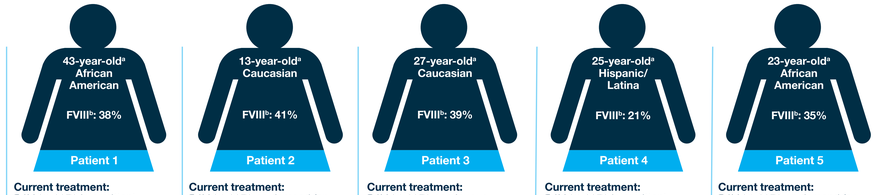
METHODS

- The ATHNdataset was used to identify female patients who received BAY 94-9027 or BAY 81-8973 between January 1, 2010 and April 30, 2022
- Baseline demographics, medical history, and ROM were extracted for female patients with ROM assessment included in their medical record
- ROM data were compared with normative Centers for Disease Control and Prevention (CDC) values for age-matched females[6]

RESULTS

- Data for 354 patients receiving BAY 81-8973 were available for this analysis; no data were available for patients receiving BAY 94-9027
- ROM data were available for five of the 13 female patients enrolled in the database who were receiving BAY 81-8973 at the time of analysis (**Table 1**)
  - Baseline Factor VIII levels ranged from 21% to 41%, and all patients had mild disease
- All five female patients had decreased ROM values over multiple joints when compared with normative CDC values (**Table 1**)
- The reduction in joint ROM was more pronounced in the lower-extremity joints compared with the upper-extremity joints, particularly at the ankles, hips, and knees
  - Index joints (ankles, knees, and elbows) are also the most frequently affected joints in males[1]

Table 1: CHARACTERISTICS, MEDICAL HISTORY, AND ROM DATA AVAILABLE IN FEMALES WITH HEMOPHILIA



			Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
			Current treatment: BAY 81-8973 intermittent prophylaxis[c] for 0.38 years **Bleeds on current treatment:** 0 **Previous treatment:** SHL recombinant FVIII concentrate on demand for 14.65 years **Bleeds on previous treatment:** 2 trauma and 1 joint	**Current treatment:** BAY 81-8973 on demand for 2.55 years **Bleeds on current treatment:** 0 **Previous treatment:** Aminocaproic acid on demand for 0.01 years **Bleeds on previous treatment:** 0	**Current treatment:** BAY 81-8973 continuous prophylaxis for 5.04 years **Bleeds on current treatment:** 0 **Previous treatment:** No data **Bleeds on previous treatment:** No data	**Current treatment:** BAY 81-8973 intermittent prophylaxis[c] for 5.02 years **Bleeds on current treatment:** 0 **Previous treatment:** SHL recombinant FVIII concentrate on demand for 9.11 years **Bleeds on previous treatment:** 0	**Current treatment:** BAY 81-8973 on demand for 5.08 years **Bleeds on current treatment:** 0 **Previous treatment:** Recombinant FVIII concentrate intermittent prophylaxis[c] for 1.09 years **Bleeds on previous treatment:** 0
Location	**Motion**	**Normative range (age 20–44/age 9–19)**	**(2008; 44 years)[d] (left/right ROM)**	**(2010; 16 years)[d] (left/right ROM)**	**(2010; 28 years)[d] (left/right ROM)**	**(2017; 27 years)[d] (left/right ROM)**	**(2020; 27 years)[d] (left/right ROM)**
Shoulder	Flexion	180.0/169.8–173.8	180/180	180/180	180/180	170/166	156/165
Elbow	Flexion	149.1–150.9/ 148.5–150.9	103/145	140/145	130/120	152/152	155/156
Elbow	Supination	80.0–104.0/ 88.0–92.0	80/80	88/90	80/80	75/70	80/80
Elbow	Pronation	81.0–83.0/79.6–82.8	80/80	72/70	80/80	75/75	80/80
Knee	Flexion	140.9–142.9/140.8–143.8	135/135	145/147	124/135	112/118	124/124
Hip	Extension	17.0–19.2/18.6–22.4	27/24	27/28	N/A	10/15	16/21
Hip	Flexion	132.5–135.1/133.0–136.8	120/120	124/123	120/120	122/NA	142/140
Ankle	Dorsiflexion	12.9–14.7/15.6–19.0	20/18	10/10	N/A	8/10	5/10
Ankle	Plantarflexion	60.6–63.6/54.8–59.8	50/50	75/74	35/40	46/50	49/50

[a]Age at first ROM evaluation; [b]Lowest ever FVIII level; [c]Defined as event-based, short-term, or intermittent prophylaxis; [d]Year of and age at most recent ROM evaluation.
Orange boxes indicate abnormal ROM values. FVIII, Factor VIII; NA, not available; ROM, range of motion; SHL, standard half-life

Limitations

- The real-world data in the ATHNdataset were captured during ATHN-affiliated hemophilia treatment center reviews and patients sharing bleeding events at those reviews
- Due to the potentially incomplete nature of such datasets, results from real-world studies could be subject to recall bias
- These limitations should be taken into consideration while interpreting the data presented here

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Disclosures
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