Real-world data on patients with hemophilia A with previous inhibitors switching to either BAY 94-9027 or BAY 81-8973 in the ATHNdataset

Martin Chandler,[1] Jessica Charlet,[2] Thomas Moulton,[2] Michael Recht[1,3]
[1]American Thrombosis & Hemostasis Network, Rochester, NY, USA; [2]Bayer, Whippany, NJ, USA; [3]Yale University School of Medicine, New Haven, CT, USA

CONCLUSIONS

- **In this real-world study, patients with hemophilia A with previous inhibitors who switched to BAY 94-9027 (damoctocog alfa pegol, Jivi®, Bayer) or BAY 81-8973 (octocog alfa, Kovaltry®, Bayer) in routine clinical practice did not have an increase in inhibitor titer or bleeding events in the real world**
  - **For BAY 94-9027 and BAY 81-8973, most patients had a lower annualized bleed rate (ABR) compared with previous treatment**
- **Therefore, BAY 94-9027 and BAY 81-8973 may represent alternative treatment options in patients requiring switching, including in those with previous inhibitors**
- **These data should be interpreted with caution owing to the limitations of real-world studies, and further studies are needed to confirm the impact of switching to BAY 94-9027 and BAY 81-8973 in real-world settings**

OBJECTIVES

- **To generate real-world evidence on patients with hemophilia A with inhibitors from prior treatments who switched to either BAY 94-9027 (damoctocog alfa pegol, Jivi®, Bayer) or BAY 81-8973 (octocog alfa, Kovaltry®, Bayer)**

INTRODUCTION

- Development of inhibitors to Factor VIII (FVIII) is a major complication when treating hemophilia A with FVIII replacement products, occurring in ~30% of previously treated patients with severe disease and ~5% of those with mild or moderate disease[1,2]
- For patients with hemophilia A and low-responding or low-titer inhibitors, FVIII concentrates are the standard of care for managing bleeding events[3]
- Patients may be concerned about recurrence. As patients with previous and current inhibitors are excluded from clinical trials of FVIII products, data are limited with regard to the propensity for the recurrence of inhibitors and outcomes when switching FVIII treatment
- BAY 94-9027 is a B-domain deleted recombinant FVIII (rFVIII), site-specifically PEGylated with a 60 kDa (dual-branched) polyethylene glycol to extend its half-life, first approved in the USA in August 2018 for use in previously treated patients aged ≥12 years with congenital hemophilia A[4]
- BAY 81-8973 is an unmodified, full-length, standard half-life rFVIII product approved in March 2016, indicated for prophylaxis and on-demand treatment of bleeding events in adults and children with congenital hemophilia A[5]
- The ATHNdataset is a Health Insurance Portability and Accountability Act-compliant, de-identified database, sponsored by the American Thrombosis and Hemostasis Network[6]
  - The dataset contains patient data gathered from hemophilia treatment centers across the USA, including patients with hemophilia A

METHODS

- The ATHNdataset was used to identify patients who received BAY 94-9027 or BAY 81-8973 as prophylaxis or on-demand treatment between January 1, 2010 and April 30, 2022
- Baseline demographic data, treatment history, inhibitor status/history, and bleed rates were collected from patient electronic medical records
- Patients with an inhibitor titer ≥0.6 BU/mL with any FVIII product were included in the current analysis

RESULTS

- At data cut-off (April 30, 2022), of 17,109 people with hemophilia A in the ATHNdataset, 205 were receiving BAY 94 9027 and 354 were receiving BAY 81-8973

Patients receiving BAY 94-9027

- Fifteen patients (7.3%) had an inhibitor titer ≥0.6 BU/mL with a previous FVIII product before switching to BAY 94-9027 (range: 0.6–56 BU/mL) (**Table 1**)
  - Fourteen patients had severe disease, of whom 10 were treated prophylactically, one underwent immune tolerance induction, and three were treated on demand
  - One patient had moderate disease and was treated on demand
  - None of these 15 patients had a recorded inhibitor titer ≥0.6 BU/mL during treatment with BAY 94-9027
- After switching to BAY 94-9027: 8 patients had a lower ABR, 4 patients had an equal ABR, and 1 patient had a higher ABR than on their previous treatment
  - Data was not available for 2 patients
- Only three patients experienced an ABR >0 after switching to BAY 94-9027 (**Table 2**). Of these, one patient had a lower ABR after switching to BAY 94-9027 than on their previous treatment, and there were no previous data for comparison for one patient

Table 1: DEMOGRAPHICS AND DISEASE HISTORY AT BASELINE FOR PATIENTS SWITCHING TO BAY 94-9027 WITH PREVIOUS TITER

		Patients switching to BAY 94-9027 with previous titer (n=15)
Age, years	Mean (SD)	28.5 (11.8)
	Median (range)	24.9 (13.2–57.0)
Sex, n (%)	Male	15 (100)
Disease severity, n (%)	Severe	14 (93.3)
	Moderate	1 (6.7)
Previous treatment modality[a]	Prophylaxis	11 (73.3)
	On demand	7 (46.7)
	Immune tolerance induction	3 (20.0)
	Unknown	1 (6.7)
	Missing	2 (13.3)
Treatment modality while receiving BAY 94-9027, n (%)	Prophylaxis	10 (66.7)
	On demand	4 (26.7)
	Immune tolerance induction	1 (6.7)
Duration of treatment with BAY 94-9027, years	Mean (SD)	1.9 (0.9)
	Median (range)	2.2 (0.1–3.3)

[a]Patients may have received more than one type of prior treatment
SD, standard deviation

Table 2: INDIVIDUAL DATA FOR PATIENTS WITH INHIBITORS DURING PREVIOUS TREATMENT WHO HAD AN ABR >0 AFTER SWITCHING TO BAY 94-9027

Patient	Disease severity	Treatment modality	Previous treatments	Titer on previous product (BU/mL)	Mean ABR on previous treatment	Titer on BAY 94-9027 (BU/mL)	Mean ABR on BAY 94-9027	Time on BAY 94-9027 (years)
A	Severe	Prophylaxis	Octocog alfa, BAY 81-8973	0.60	4.10	0.50	3.35	2.09
B	Severe	Prophylaxis	No data	0.65	No data	0	3.15	2.22
C	Severe	Prophylaxis	Aminocaproic acid, SHL rFVIII concentrate	0.95	0	0	0.61	3.27

ABR, annualized bleed rate; rFVIII, recombinant Factor VIII; SHL, standard half-life

Patients receiving BAY 81-8973

- Of the 354 patients who received BAY 81-8973, 52 (15%) had an inhibitor titer ≥0.6 BU/mL (range: 0.6–2150 BU/mL) at some point during their therapies
  - After switching to BAY 81-8973: 26 patients had a lower ABR, 10 patients had a higher ABR, and 9 had a similar ABR than on their previous treatment. Data were not available for 7 patients
- All but six patients had a history of inhibitor titers prior to switching to BAY 81-8973
  - Of the six patients who had inhibitor titers ≥0.6 BU/mL during BAY 81-8973 treatment, four had severe disease (prophylaxis, n=2; episodic treatment, n=2) and two had mild disease, both of whom were treated on demand (**Table 3**)
  - Three of the six patients also had a recorded antibody titer during their prior therapy (<1 BU/mL on both prior treatment and during BAY 81-8973 treatment), the other three patients did not

Table 3: DEMOGRAPHICS AND DISEASE HISTORY AT BASELINE FOR PATIENTS SWITCHING TO BAY 81-8973 WITH TITER

		Patients switching to BAY 81-8973 with remaining titer (n=6)
Age, years	Mean (SD)	34.2 (19.5)
	Median (range)	35.5 (9.2–55.4)
Sex, n (%)	Male	6 (100)
Disease severity, n (%)	Mild	2 (33.3)
	Severe	4 (66.7)
Prior treatment type[a]	Prophylaxis	5 (83.3)
	On demand	5 (83.3)
Treatment type while receiving BAY 81-8973, n (%)	Prophylaxis	2 (33.3)
	On demand	4 (66.7)
Duration of BAY 81-8973 treatment, years	Mean (SD)	3.4 (2.0)
	Median (range)	3.9 (0.6–5.3)

[a]Patients may have received more than one type of prior treatment
SD, standard deviation

  - Four patients experienced an ABR >0 after switching to BAY 81-8973 (**Table 4**). Of these, three patients had recorded antibody titers during prior therapy and two had a lower ABR following a switch to BAY 81-8973
  - The remaining 2 patients had an ABR of 0 after switching to BAY 81-8973

Table 4: INDIVIDUAL DATA FOR PATIENTS WITH INHIBITOR TITER AND ABR >0 WITH BAY 81-8973

Patient	Disease severity	Treatment modality	Previous products	Titer on previous product (BU/mL)	Mean ABR on previous product	Titer on BAY 81-8973 (BU/mL)	Mean ABR on BAY 81-8973	Time on BAY 81-8973 (years)
A	Severe	Prophylaxis	SHL rFVIII concentrate	No data	0	0.60	0.38	5.30
B	Mild	On demand	SHL rFVIII concentrate, octocog alfa	<1	0	<1	0.62	3.20
C	Severe	Episodic	Aminocaproic acid, SHL rFVIII concentrate, EHL rFVIII concentrate, plasma-derived FVIII, tranexamic acid, blood bank product	<1	2.00	<1	0.40	5.00
D	Mild	Episodic	SHL rFVIII concentrate, desmopressin, aminocaproic acid	<1	0.80	<1	0.65	4.60

ABR, annualized bleed rate; EHL, extended half-life; FVIII, Factor VIII; rFVIII, recombinant Factor VIII; SHL, standard half-life

Limitations

- The real-world data in the ATHNdataset were captured during ATHN-affiliated hemophilia treatment center reviews and patients sharing bleed events at those reviews
- Due to the potentially incomplete nature of such datasets, results from real-world studies could be subject to recall bias and hence might have an influence on the observed low ABRs in this study
- These limitations should be taken into consideration while interpreting the effectiveness data presented here

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