



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

904. OUTCOMES RESEARCH-NON-MALIGNANT CONDITIONS

Identifying Ideal Individuals for PK-Guided Dosing; Recreational Risks and Elevated Breakthrough Bleeding

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Introduction

PK-guided dosing is a useful tool for personalized FVIII prophylaxis for people living with Hemophilia A (PwHA). While many individuals can benefit from this intervention, certain subsets of the population of PwHA may see increased benefit and be considered ideal candidates for PK-guided dosing. We aim to identify sub-populations of interest who may have increased benefit of PK-guided dosing, namely those with high levels of bleeding risk from recreational activity, and PwHA with elevated levels of bleeding. Clinical and FVIII utilization outcomes are analyzed in these cohorts to determine if these populations have increased benefit from PK-guided dosing.

Methods

Based on a retrospective study of 132 PwHA with moderate to severe Hemophilia A (FVIII < 5%) to determine effects of PK-guided dosing on clinical and utilization outcomes (Young, 2022), 58 matched criteria for undergoing a PK for optimization of therapy with a given product. Individuals were stratified by recreational activity risk using a modification of the National Hemophilia Foundation's activity risk scale (Anderson, 2017, p. 22), grouping individuals into mild, moderate, and high recreational activity risk for bleeding. Bleeding rates prior to PK assessment were calculated, and individuals were classified into groups based on pre-index annualized bleed rate (ABR) ≥ 3 and pre-index ABR < 3, due to bimodal distribution. Index date was defined as date of the PK-guided prescription.

Results

Recreational activity risk was available for 56/58 individuals, and after PK-guided dosing 53/56 had no change in activity level. Analyses were limited to these 53, 28 with mild risk, 19 with moderate risk, and 6 with high risk. Individuals with high activity risk had severe Hemophilia A (FVIII < 1%), and had median age of 12 years (IQR: 12-17) at PK-guidance. Overall mean pre-index ABR was 3.6 (sd: 4.2), with majority of bleeds associated with joint or traumatic bleeds. High activity risk individuals had higher traumatic ABR prior to index date compared to those with low or moderate activity risk. Soccer was the most common high risk activity reported by 4/6 individuals (66.7%), with tackle football and martial arts reported in the remaining individuals. Individuals with mild/moderate risk did not differ from those with high activity risk by age, hemophilia severity, number of target joints, or pre-index ABR.

Within these groups, we found significant decreases in ABR after PK-guidance among those with mild risk (-2.6 [95% CI: -4.4, -1.0]), driven by decrease in joint (-1.7 [-3.2, -0.4]) and traumatic (-1.2 [-2.2, -0.3]) bleeds. Similar trends were observed in high activity risk group for overall ABR (-2.2 [-4.8, 0.4]), joint bleeds (-1.6 [-4.0, 0.2]) and traumatic bleeds (-1.1, [-2.4, 0.4]) but limited sample increased uncertainty of estimates. No change in ABR was identified for those with moderate activity risk. No major difference in mean weekly consumption (MWC) after PK guidance was observed in those with mild risk (+3.6 IU/kg [-6.2, 13.3]), but those with high risk trended towards increase in MWC (+11.0 IU/kg [-4.8, 26.7]) of FVIII for prophylaxis. Annualized cost of FVIII prophylaxis similarly trended towards increase in those with high activity risk (+\$49270 [-\$24698, \$123237]).

High levels of pre-index ABR was identified in 25/58 individuals with mean pre-index ABR of 8.2 (sd: 5.6). Individuals with high reported bleeding prior to PK-guidance were median 13 years (IQR: 8-20) of age at PK-guidance, with 88% having severe Hemophilia A. Significant decreases in ABR were observed after PK-guidance (-5.3 [95% CI: -7.2, -3.2]), driven by decrease in joint and traumatic bleeds. Significant increases in MWC (+18.11 IU/kg [7.0, 29.2]) and annualized cost (+\$45783 [\$17943,

\$73624)) of prophylaxis were observed in these individuals. Although quantity of FVIII used to treat breakthrough bleeds was not captured in this study, use of on-demand FVIII likely decreased with lower observed ABR.

Conclusion

Individuals with elevated bleeding levels are prime candidates for PK-guided dosing, with significantly lower bleeding rates observed after PK-guided dosing, leading to improved quality of life and decreased risks of joint degeneration. While sample was limited, individuals with high activity risk appear to benefit from PK-assessment as well, to attain increased bleed protection during recreational activities in spite of inherent risks.

Disclosures Young: *Hema Biologics:* Speakers Bureau; *Hema Biologics/LFB:* Consultancy; *CSL Behring:* Consultancy, Speakers Bureau; *Spark:* Consultancy, Speakers Bureau; *Genentech/Roche:* Consultancy; *Sanofi Genzyme:* Consultancy, Speakers Bureau; *Novo Nordisk:* Consultancy; *Genentech, Inc.:* Research Funding; *Takeda:* Consultancy, Research Funding; *Viatrix:* Patents & Royalties. **Balasa:** *CSL Behring:* Speakers Bureau; *Sanofi:* Speakers Bureau; *Takeda:* Speakers Bureau. **Roberts:** *Genentech:* Membership on an entity's Board of Directors or advisory committees; *Novo Nordisk:* Honoraria; *Takeda:* Honoraria, Other: Consulting; *Sanofi:* Honoraria, Other: Consulting; *HEMA Biologics:* Other: Consulting; *Novartis:* Other: Consulting; *Pfizer:* Honoraria; *F. Hoffmann-La Roche AG:* Other: Consulting; *CSL Behring:* Membership on an entity's Board of Directors or advisory committees, Other: Consulting. **Frick:** *Trio Health Inc:* Current Employment; *Takeda:* Research Funding; *Sanofi:* Research Funding; *Janssen:* Research Funding; *Gilead Sciences:* Research Funding; *Horizon Therapeutics:* Research Funding; *GSK ViiV:* Research Funding; *AbbVie:* Research Funding; *Scipher Medicine:* Research Funding; *AstraZeneca:* Research Funding. **Mokdad:** *Takeda:* Current Employment, Current equity holder in publicly-traded company. **Caicedo:** *Takeda:* Current Employment, Current equity holder in publicly-traded company.

Table 1: Baseline Characteristics of Study Population at Index Date

Category	Characteristic	Pre-PK ABR Cohort		Recreational Risk Cohort		
		Pre-PK ABR < 3	Pre-PK ABR ≥ 3	Low Activity Risk	Moderate Activity Risk	High Activity Risk
Sample	N	33	25	28	19	6
Age	Med (IQR); years	12 (9,16)	13 (8,20)	12 (9,18)	11 (5,17)	12 (12,17)
Race/Ethnicity	White non-Hispanic	14 (42.4%)	8 (32.0%)	13 (46.4%)	7 (36.8%)	1 (16.7%)
	Black non-Hispanic	4 (12.1%)	6 (24.0%)	2 (7.1%)	6 (31.6%)	0 (0%)
	Asian	2 (6.1%)	2 (8.0%)	1 (3.6%)	1 (5.3%)	2 (33.3%)
	Hispanic/Latino	11 (33.3%)	8 (32.0%)	11 (39.3%)	5 (26.3%)	2 (33.3%)
	Other Race	1 (3.0%)	1 (4.0%)	0 (0%)	0 (0%)	1 (16.7%)
	Unknown Race	1 (3.0%)	0 (0%)	1 (3.6%)	0 (0%)	0 (0%)
Hemophilia Severity	Moderate (1-5% FVIII)	2 (6.1%)	3 (12.0%)	1 (3.6%)	3 (15.8%)	0 (0%)
	Severe (<1% FVIII)	31 (93.9%)	22 (88.0%)	27 (96.4%)	16 (84.2%)	6 (100.0%)
Target Joints	Med (IQR)	0 (0,4)	1 (0,8)	0 (0,7)	0 (0,8)	0 (0,2)
Pre-Index ABR	Mean (SD)	0.5 (0.8)	8.2 (5.6)	4.4 (6.8)	2.7 (3.7)	3.6 (4.2)

Figure 1: Change in ABR After PK-Guidance

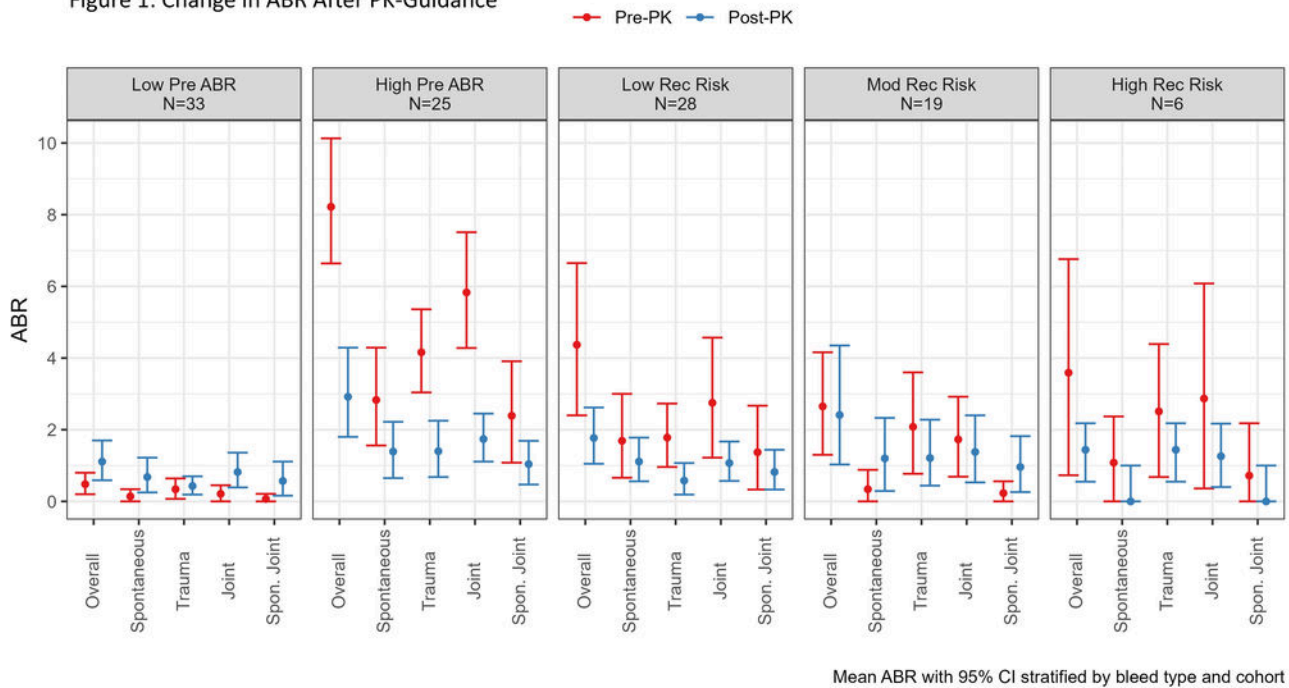


Figure 1

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