2nd Interim Analysis Results of the Global AHEAD Study in Hemophilia A Patients

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INTRODUCTION

- Hemophilic arthropathy is a major cause of disability for patients with hemophilia A .[1] Multiple studies have confirmed the clinical benefits of prophylaxis compared with on-demand treatment for hemophilic arthropathy.[2] However, given the limitations of most post-approval safety surveillance studies with the objective to monitor safety and effectiveness for only 6 to 12 months, there is a gap in our understanding of long-term joint health outcomes and health-related quality of life (HRQoL).
- The AHEAD (ADVATE Hemophilia A Outcome Database) study is designed to assess long-term outcome data in patients with hemophilia A receiving ADVATE treatment in routine clinical practice.
- This prospective cohort study collects data from hemophilia A patients on ADVATE on-demand (OD), standard or pharmacokinetic (PK)-guided prophylaxis, or immune tolerance induction (ITI).
- We report data from two years of observation from the International study arm.

OBJECTIVE

The AHEAD study aims to evaluate effectiveness of a prophylactic treatment regimen of ADVATE in severe and moderate (FVIII < 5%) hemophilia A patients in a real world setting.

METHODS

Study design:

- Post-authorization, prospective, non-interventional, multicenter study
- Recruitment target: globally the study will enroll a total of > 1000 severe to moderate hemophilia A patients receiving ADVATE
- Observation period: 4- up to 8 years per subject
- Main inclusion criteria: Moderate to severe hemophilia A (factor VIII activity [FVIII:C] ≤ 5%); ADVATE is the routinely prescribed treatment
- Study endpoints include long-term joint health outcomes, annualized (joint) bleeding rates (ABR/AJBR), factor consumption, and safety
- We evaluate overall annual bleeding rate in patients prospectively followed up in the frame of the AHEAD study.
- We present here the preliminary results from an interim analysis.

ENROLLMENT STATUS

Enrollment Update

- Study start: June 2011
- Status as of 30 June 2016:
  - 555 patients enrolled
  - 94 study sites initiated in: Australia, Austria, Belgium, Brazil, Canada, Colombia, Czech Republic, Denmark, France, Greece, Hungary, Italy, Norway, Poland, Portugal, Russia, Slovenia, Spain, Sweden, Switzerland and United Kingdom

Interim Analysis International Study Arm

- The second interim analysis of September 2015 includes 376 patients from 18 countries, of whom 243 completed the year 1 and 154 completed the year 2 visits.
- Median age at screening was 15 years (min-max: 0–72) and 68% of patients had severe HA (FVIII:C < 1%).
- 293 (78.1%) were on prophylaxis, 77 (20.5%) were on OD and 5 (1.3%) on ITI treatment.

RESULTS

Table 1: Demographic Data at Screening

	International Study Arm
Median Age, years (range)	15.0 (0–72)
Baseline FVIII activity, n (%)	
Severe (< 1%)	253 (68.4)
Moderate (1–≤ 5%)	117(31.6)
Missing	5
Target joint at Screening, n (%)	
≥ 1 target joint	124 (33.7)
Treatment Screening, n (%)	
Prophylaxis	293 (78.1)
On-demand	77 (20.5)
ITI	5 (1.3)

Figure 1: Treatment by Age Group at Screening

Effectiveness

- Median ABRs/AJBRs were 1.4/1.0 in the prophylaxis group and 11.1/6.5 in the OD one for annual visit 1, and 1.1/1.0 and 10.4/5.6, respectively, in the second year.
- 48% of patients on prophylaxis and 23% of patients OD had an AJBR < 1 in the first year and 49% and 32% in the second year.
- In the OD group, 60% and 47% had an AJBR ≥ 6 after the first and second year respectively, while only 9% and 7% in the prophylaxis group.
- Median annualized total dose in the prophylaxis group was 200,343 IU and 237,968 IU and 35,346 IU and 26,245 IU in the OD group during year one and two, respectively.
- Effectiveness of prophylaxis assessed by investigators was excellent/good in 95% of cases during the first and 97% during the second year of observation.
- Effectiveness for treating an acute bleeding event assessed by patient/caregiver was excellent/good in 91% of bleeding in prophylaxis patients and 79% in OD patients during year 1 and 93% and 94% during year 2, respectively.

Safety

- There were 8 treatment-related adverse events (AEs): one mild allergic cutaneous reaction with rhinitis and 7 low-titre inhibitors (4 already positive at screening). All patients continued to receive ADVATE.

Figure 2: Patients (%) per AJBR Category at Annual Visit 1

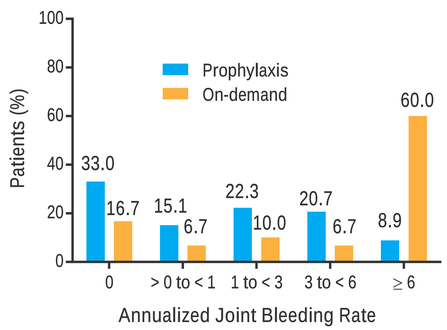


Figure 3: Patients (%) per AJBR Category at Annual Visit 2

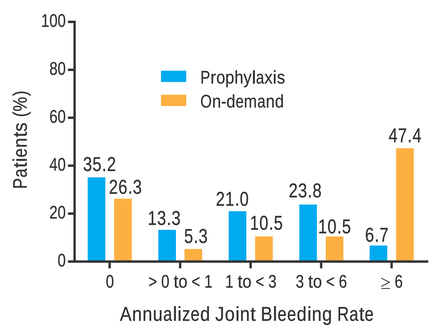
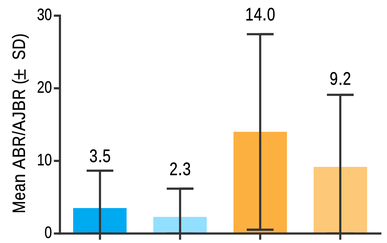
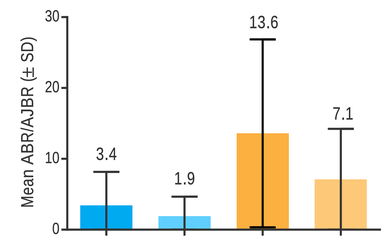


Figure 4: ABR and AJBR at Annual Visit 1



	Prophylaxis (n = 206)		On-demand (n = 40)	
Median	1.4	1	11.1	6.5
Min-Max	0-29	0-27	0-51	0-36

Figure 5: ABR and AJBR at Annual Visit 2



	Prophylaxis (n = 123)		On-demand (n = 32)	
Median	1.1	1	10.4	5.6
Min-Max	0-29	0-13	0-47	0-26

ACKNOWLEDGEMENTS

To the AHEAD study group members: To the International AHEAD study group members: Dr. Hermans (BE), Dr. Dolnicar (SI), Dr. Schwarz (AT), Dr. Pabinger (AT), Dr. Claeyssens (FR), Dr. Komrska (CZ), Dr. Zapletal (CZ), Dr. Blazek (CZ), Dr. Cermakova (CZ), Dr. Chamouni (FR), Dr. Leinoe (DK), Dr. Liesner/Khair (UK), Dr. Perry (UK), Dr. Rangarajan (UK), Dr. Evans (UK), Dr. Borel-Derlon (FR), Dr. Luciani (IT), Dr. Katsarou (GR), Dr. Platokouki (GR), Dr. Oikonomou (GR), Dr. Theodosiadis (GR), Dr. Klukowska (PL), Dr. Wlazlowski (PL), Dr. Koltan (PL), Dr. Dobaczewski (PL), Dr. Pan-Petesch, Dr. Bardi (HU), Dr. Kardos (HU), Dr. Erzébet (HU), Dr. Marian (HU), Dr. Kiss (HU), Dr. Zombori (HU), Dr. Siragusa (IT), Dr. Zanon (IT), Dr. Gervasi (IT), Dr. Di Minno (IT), Dr. Coluccia (IT), Dr. Ettorre (IT), Dr. Mazzucconi (IT), Dr. Santoro (IT), Dr. Giuffrida (IT), Dr. Borchiellini (IT), Dr. Cantori (IT), Dr. Valdre (IT), Dr. Holme (NO), Dr. Klaassen (CA), Dr. Samad (CA), Dr. Sinha (CA), Dr. Belletrutti (CA), Dr. Sholzberg (CA), Dr. de Raucourt (CA), Dr. Santagostino (IT), Dr. Tavares (PT), Dr. Sevivas (PT), Dr. Carvalho (PT), Dr. Fraga (PT), Dr. Guillet (FR), Dr. Roussel-Robert (FR), Dr. Volot (FR), Dr. Tardy (FR), Dr. Parra (ES), Dr. Lopez (ES), Dr. Canaro (ES), Dr. Berrueco (ES), Dr. Linari (IT), Dr. Baghaei (SE), Dr. Holmstrom (SE), Dr. Berntorp/Astermark (SE), Dr. Sossa (CO), Dr. Gay (FR), Dr. Pignon (FR), Dr. Trossaert (FR), Dr. Castet (FR), Dr. Lehmann (CH), Dr. Kremer (CH), Dr. Albisetti (CH), Dr. Kobelt (CH), Dr. Brand (CH), Dr. Hegemann (CH), Dr. Tsakiris (CH), Dr. Beck-Popovic (CH), Dr. Rischewski (CH), Dr. Ozelo (BR), Dr. Pinto (BR), Dr. Ferreira (BR), Dr. Oliveira (BR), Dr. Ribeiro (BR), Dr. Lorenzato (BR), Dr. Hermida (BR), Dr. Prezotti (BR), Dr. Khoo (AU), Dr. P'ng (AU), Dr. Blanchette (CA), Dr. Oudot (FR), Dr. De Cristofaro (IT), Dr. Zozulya (RU), Dr. Andreeva (RU).

To the AHEAD study project team lead: Manfred Pirck

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2. Manco-Johnson MJ, et al. *N Engl J Med.* 2007;357(6):535-544.

DISCLOSURES

Author is an employee of Baxalta ([6]Baxalta Healthcare SA; [7*]Baxalta Innovations GmbH), now part of Shire.

The study was sponsored by Baxalta, now part of Shire.

DISCUSSION & CONCLUSION

- Presented interim results of the AHEAD study show a distinct reduction in ABR/AJBR for patients on prophylaxis vs OD.
- Treatment efficacy was rated excellent/good in the majority of cases. ADVATE was very well tolerated with very few treatment-related AEs.
- Since recruitment started in 2011, 956 patients (555 in the International study arm and 401 in the German study arm) have been enrolled.
- The AHEAD study continues to enroll patients and will accrue significant long-term outcomes data in patients on ADVATE in routine clinical practice.