WFH COMPREHENSIVE CARE SUMMIT

New Developments in Bleeding Disorders and MSK

PP-046

Plain language summary: Efanesoctocog alfa treatment outcomes over 3 years in adults & adolescents with severe haemophilia A in the long-term XTEND-ed study

Robert Klamroth,[1] Stephanie P'ng,[2] Sophie Susen,[3] Davide Matino,[4] Angela Weyand,[5] Toshko Lissitchkov,[6] Young-Shil Park,[7] Maria Teresa Alvarez-Román,[8] Liqi Feng,[9] Helena Palmborg,[10] Jennifer Dumont,[11] **Elena Santagostino**,[12*] Lara Mamikonian,[11] Keiji Nogami[13]

[1]Vivantes Klinikum, Friedrichshain, Berlin, Germany; [2]The Haemophilia and Haemostasis Centre, Fiona Stanley Hospital, Murdoch, WA, Australia; [3]Centre Hospitalier Universitaire de Lille, Université de Lille, Lille, France; [4]Division of Hematology & Thromboembolism, Department of Medicine, McMaster University, Ontario, Canada; [5]Division of Hematology/Oncology, Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI, USA; [6]Specialized Hospital for Active Treatment of Hematological Diseases, Department of Chemotherapy, Hemotherapy and Hereditary Blood Diseases at Clinical Hematology Clinic, Sofia, Bulgaria; [7]Department of Pediatrics, Kyung Hee University Hospital at Gangdong, School of Medicine, Kyung Hee University, Seoul, Korea; [8]Department of Hematology, University Hospital La Paz, Autonoma University of Madrid, Madrid, Spain; [9]Sanofi, Shanghai, China; [10]Sobi, Stockholm, Sweden; [11]Sanofi, Cambridge, MA, USA; [12]Sobi, Basel, Switzerland; [13]Nara Medical University, Nara, Japan

*presenting author

INTRODUCTION

- People with haemophilia A receive therapy with factor VIII (FVIII) replacement products which provides the missing FVIII protein to prevent or stop bleeding
- The interaction of FVIII with von Willebrand factor (VWF) limits how long the infused FVIII stays in the body[1]. As a result, frequent injections with FVIII products are given to prevent bleeding
- **Efanesoctocog alfa is a first-in-class high-sustained FVIII replacement therapy** that is distinct from standard half-life and extended half-life FVIII replacement products. It is designed to avoid interaction with VWF thereby sustaining higher FVIII levels in the blood for approximately 3–4 times longer compared to other FVIII replacement therapies[2]
- In the pivotal Phase 3 study, XTEND-1 (NCT04161495), once-weekly injections of efanesoctocog alfa provided better bleed protection than previous FVIII prophylaxis treatments in adults and adolescents with severe haemophilia A. It was well tolerated and maintained normal to near-normal (>40%) FVIII activity for most of the week and 15% at the end of the week[3]

AIM

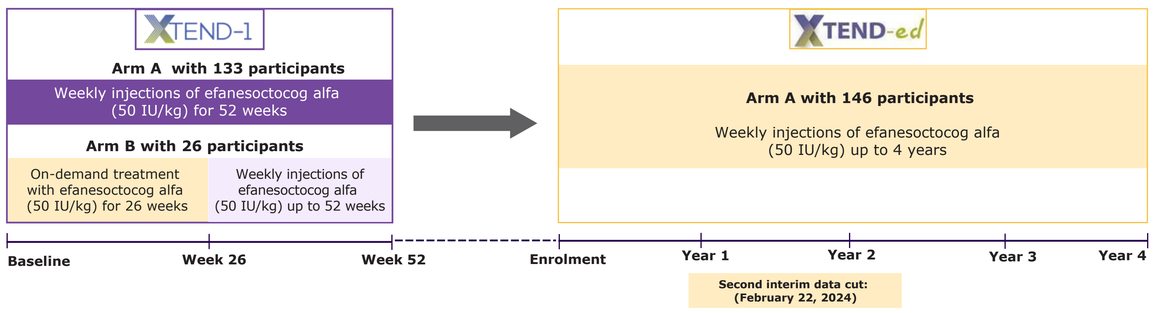
- To report the safety and efficacy outcomes from adults and adolescents with severe haemophilia A enrolled in the ongoing, Phase 3, global, long-term extension study XTEND-ed (NCT04644575; second interim analysis)

METHODS

Who could take part in the study?

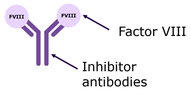
- People with severe haemophilia A (less than 1% of normal FVIII activity in the blood) or having a known gene mutation for severe haemophilia A, 12 years of age or older who completed the XTEND-1 study
- Participants who had previous treatment with FVIII medicine

How was efanesoctocog alfa treatment given to patients in XTEND-ed Arm A who rolled over from XTEND-1?



As of the second interim data cut, 85.6% of participants remain in XTEND-ed study; 11 completed and 10 discontinued from the study. Reasons for discontinuation were adverse event (1 participant), consent withdrawn (4 participants), prohibited concomitant medication (4 participants), and other (1 participant).

What was the primary goal of XTEND-ed study?



To test if participants developed FVIII inhibitors which are antibodies produced against the infused FVIII that reduce its therapeutic activity, causing difficulties in bleed management[4]

What were the secondary goals of this study?

- To determine the number of bleeds that occurred while receiving efanesoctocog alfa prophylaxis
- To evaluate if efanesoctocog alfa prophylaxis helped to improve quality of life (QoL)
- To evaluate how effective efanesoctocog alfa was in stopping bleeds
- To evaluate if efanesoctocog alfa prophylaxis was well-tolerated by the participants

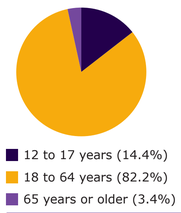
CONCLUSIONS

In adults and adolescents with severe haemophilia A, once-weekly injections of efanesoctocog alfa for over 3 years were well-tolerated and remained highly effective for bleed protection

- No FVIII inhibitors developed
- Annual bleeding rates remained low
- Number of participants with no bleeds at all remained high
- Health-related quality of life was maintained

RESULTS

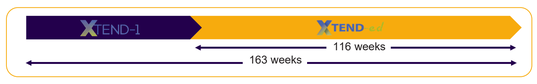
1 What were the characteristics of participants in XTEND-ed (Arm A)?



- Overall, **146 participants** including one female with severe haemophilia A rolled over from XTEND-1 to XTEND-ed Arm A
- The average age was 37 years and ranged between 13 and 74 years

2 How long were the participants treated with efanesoctocog alfa?

- At the second interim data cut of the XTEND-ed study, participants had on average **more than 3 years of efanesoctocog alfa treatment** from parent study, XTEND-1 baseline

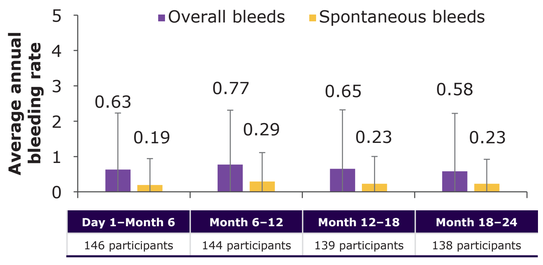


3 Did participants receiving efanesoctocog alfa in XTEND-ed Arm A develop FVIII inhibitors?

- **No FVIII inhibitor** antibodies were detected in any participant receiving more than 3 years of efanesoctocog alfa treatment

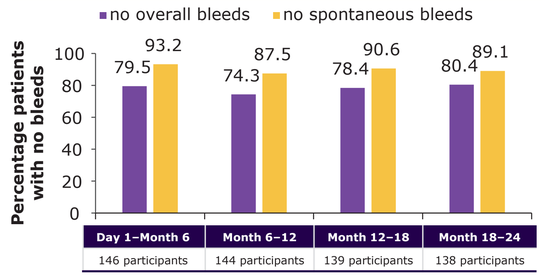
4 How effective was efanesoctocog alfa in preventing bleeds during the XTEND-ed study?

Average annual bleeding rate remained low



Day 1–Month 6	Month 6–12	Month 12–18	Month 18–24
146 participants	144 participants	139 participants	138 participants

The majority of participants had no bleeds

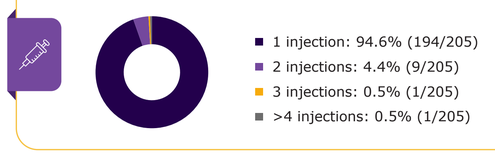


Day 1–Month 6	Month 6–12	Month 12–18	Month 18–24
146 participants	144 participants	139 participants	138 participants

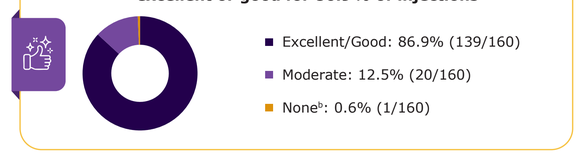
- The average annual bleed rates evaluated at **6-month intervals** remained below 1 per patient, and the number of patients with no bleeds at all remained high (approximately 80%–90%) during 2 years in XTEND-ed
- The annual bleed rate evaluated at **12-month intervals** were approximately 0.7 for overall bleeds; 0.25 for spontaneous bleeds; 0.3 for traumatic bleeds and 0.5 for joint bleeds with the corresponding percentage of patients with no bleeds at approximately 67% for overall bleeds; 84% for spontaneous bleeds; 80% for traumatic bleeds and 75% for joint bleeds, each year during 2 years in XTEND-ed

5 How effective was efanesoctocog alfa in stopping bleeds during the XTEND-ed study?

One injection was sufficient to stop 94.6% of bleeds



Haemostatic response[a] was rated by participants as excellent or good for 86.9% of injections



[a]Based on the International Society on Thrombosis and Hemostasis 4-point response scale, a way for doctors to measure how well a treatment stops bleeding. The clotting response may be rated as follows:
Excellent: The bleeding stops completely and does not need extra FVIII treatment; **Good**: The bleeding stops to a significant extent but requires extra FVIII treatment; **Moderate**: Modest improvement in bleeding that requires additional FVIII treatment to control it; **None**: No improvement in bleeding, not that the participant did not provide a response.
[b]The participant with response "None" had no reduction in elbow pain after receiving an injection to treat it, assuming it was an elbow bleed. Subsequent clinical evaluation revealed that the participant was experiencing a gout flare (pain and swelling) in the elbow.

- The average dose per injection and the average total dose for treatment of a bleed were 44.9 IU/kg and 48.7 IU/kg, respectively

6 How effective was efanesoctocog alfa in improving health-related QoL and pain during the XTEND-ed study?

- **Improvement in QoL, physical health**[c] and **pain**[d] observed with efanesoctocog alfa treatment in the parent study, XTEND-1 was maintained over an additional 2 years of prophylaxis in XTEND-ed

[c]The Haemophilia Quality of Life Questionnaire for Adults (Haem-A-QoL) questionnaire was used to assess QoL in participants aged 17 years or older. A reduction in the Haem-A-QoL total score and physical health score is indicative of improvement in health-related QoL and physical health.
[d]The Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Intensity–Short Form 3a was used to assess the degree of pain experienced by the participants. A reduction in the score indicates improvement in pain.

7 Were any adverse events reported in participants during the XTEND-ed study?

- **The treatment was well-tolerated**; common minor adverse events unrelated to treatment included COVID-19, joint pain, and cold
- Two events were reported in two participants that were considered related to efanesoctocog alfa treatment; facial paralysis and an isolated incidence of decreased FVIII trough level (measured at a local laboratory). Both events resolved
- There were two reported thrombotic events in two participants with other associated risk factors; both events were considered unrelated to efanesoctocog alfa treatment

REFERENCES

1. Chhabra ES, et al. *Blood*. 2020;135(17):1484-1496.
2. Konkle BA, et al. *N Engl J Med*. 2020;383(11):1018-1027.
3. Von Drygalski A, et al. *N Engl J Med*. 2023;388(4):310-318.
4. Jardim LL, et al. *Res Pract Thromb Haemost*. 2020 May 26;4(5):752-760.

FUNDING

This study was funded by Sanofi and Sobi.

ACKNOWLEDGEMENTS

- Publication coordination was provided by Alicia Mack, PharmD, CMPP (Sanofi) and Nick Fulcher, PhD, CMPP (Sobi). Sanofi and Sobi reviewed and provided feedback on the abstract.
- The authors had full editorial control of the abstract and provided their final approval of all content.
- The authors acknowledge Marc Pangilinan, Shellye Horowitz, and Clive Smith for their inputs during the initial review of this poster.
- Editorial assistance for the development of this poster was provided by Subhasri Ghosh, PhD, of Sanofi.

DISCLOSURES

Originally presented at the American Society of Hematology Annual Meeting 2024, December 7-10, San Diego, USA.
RK received honoraria and/or been a member of advisory committees for Bayer, Biomarin, Biotest, CSL Behring, Grifols, Novo Nordisk, Octapharma, Pfizer, Roche/Chugai, Sanofi, Sobi, and Shire/Takeda. **SP** received honoraria for Ad Board from Sanofi, Novo Nordisk, Roche, CSL and Pfizer. **SS** received research support from CSL Behring, Roche/Chugai, Stago, Siemens Healthiners, and honoraria for lectures or consultancy from Biomarin, Bioverativ, CSL Behring, Hemosonics, LFB, Novo Nordisk, Roche/Chugai, Sanofi, Siemens Healthiners, Shire/Takeda, and Sobi. **DM** received research grants paid directly to the Institution (McMaster University) from Bayer, Pfizer, Novo Nordisk, Sanofi, Spark, Octapharma, Roche and personal fees/honoraria from Sanofi, Sobi, Novo Nordisk, Bayer, Pfizer, Octapharma for participation in advisory boards, lectures, and preparation of educational material. **AW** received consulting fees/honoraria from Genentech, Sanofi, Sobi, Takeda, Bayer, BioMarin, Novo Nordisk and research support from Pfizer, Takeda, Novo Nordisk, Sanofi. **TL** is a principal investigator of clinical trials for Sanofi and Sobi. **Y-SP** received research support from or participated as a principal investigator for BioMarin Pharmaceutical Inc., CSL Behring, Novo Nordisk, Sanofi, Takeda, Pfizer, and Chugai.
MTA-R received honoraria for speaking and/or honoraria for consulting, and/or funds for research from Takeda, Bayer, CSL-Behring, Grifols, Novo Nordisk, Sobi, Octapharma, LFB, Roche, Amgen, Novartis and Pfizer. **KN** received research funding from Chugai, Bioverativ/Sanofi, Bayer, Novo Nordisk, CSL Behring, Shire/Takeda, KM Biologics, Fujimoto Pharm., SEKISUI MEDICAL, Sysmex and consultant fee from Chugai and was a principal investigator for Chugai, Bioverativ/Sanofi, Novo Nordisk, CSL Behring, Shire/Takeda, KM Biologics, Pfizer. **LF, JD, LM** are employees of Sanofi and may hold shares and/or stock options in the company. **HP** and **ES** are employees of Sobi and may hold shares and/or stock options in the company.

Access poster via the Sanofi Library of Congress

Access poster via the Sobi Science Library