**Quality of Life and Treatment Satisfaction in People with Haemophilia on Fitusiran Prophylaxis: Evidence from a Subset of ATLAS-OLE Trial Participants Mainly from India**

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Dear Editor,

The traditional treatment strategy for haemophilia involves clotting factor concentrates administered ‘on-demand’ (episodic) to treat bleeds or as a prophylaxis to prevent bleeds. The World Federation of Haemophilia recommends prophylaxis for people with moderate or severe haemophilia who experience frequent bleeding [1]. However, people with haemophilia (PwH) find prophylactic treatments burdensome because of the limited access to treatments, venous access issues, the duration and pain associated with infusions, treatment frequency, inadequate bleed control, the risk of developing an inhibitor and the associated costs [2-4]. Hence, there is an unmet need to reduce the treatment burden and improve outcomes in PwH.

Fitusiran is a subcutaneous, antithrombin (AT)-lowering therapeutic that leads to increased thrombin generation to restore haemostasis in PwH [5]. Fitusiran AT-based dose regimen (AT-DR) aims at achieving AT levels between 15% and 35% in PwH. It got approved by United States Food and Drug administration in March 2025 for the prophylaxis to prevent or reduce the frequency of bleeding in patients aged ≥12 years with haemophilia A or B, with or without inhibitors [6].

This qualitative study involved a subset of the ATLAS-OLE trial (NCT03754790) participants (or their caregivers) who were on fitusiran AT-DR prophylaxis and received on-demand haemophilia treatments prior to study participation. Participants who provided informed consent were recruited between September 2021 and August 2022 from the ATLAS-OLE clinical sites. Adult participants and caregivers (for adolescents [aged 12 to <18 years] or patients with cognitive impairment) were eligible if they could speak, read and comprehend English and participants had received two or more doses of the fitusiran AT-DR at least 1 month ago. The study protocol was approved by the Institutional Review Boards of the participating clinical sites.

Experienced interviewers skilled in eliciting meaningful data conducted in-depth telephone interviews with participants by following semi-structured interview guides. All interviews were conducted in English, lasted approximately 60 min and were audio recorded and transcribed for data analysis. The interviews included both open-ended and closed-ended questions. The interviewers reviewed all transcripts meticulously before their anonymisation and finalisation for analysis. RTI Health Solutions (NC, United States) analysed the qualitative data, identified dominant trends in each interview and generated themes based on the manner participants shared their experiences. **Table 1** provides examples of quotes to support the themes. The analysis was descriptive.

A total of 24 participants (mean age [SD]: 27 [8.9] years), including 21 PwH and three caregivers, were interviewed. All participants, except for one from the United States, were from India. Fourteen participants were from the ATLAS-A/B trial ([NCT03417245](https://clinicaltrials.gov/study/NCT03417245); without inhibitors) and 10 (41.7%) were from the ATLAS-INH trial ([NCT03417102](https://clinicaltrials.gov/study/NCT03417102); with inhibitors). Eighteen participants (75%) had haemophilia A, whereas 25% (n = 6) had haemophilia B.

All 24 participants spontaneously reported improvement in at least one aspect of their haemophilia symptoms since participating in the ATLAS-OLE trial. None reported ‘no change’ or ‘worsening’ in their haemophilia symptoms. Nine participants (37.5%) reported improvements within the first month of initiating fitusiran, whereas 12 participants (50.0%) reported improvements within 2 to 4 months. Each participant reported an improvement in bleeding events, with more than half reporting no bleeds and others reporting a decrease in the number of bleeds (**Table 1**). All participants who were asked about specific aspects of quality of life (QoL) reported improvements in their (or their child’s) daily physical activities (24/24), family life (22/22), social activities (20/20), overall QoL (18/18), feeling of safety (23/23) and mood (15/15) since their participation in the ATLAS-OLE trial.

Participants were asked for a hypothetical treatment for haemophilia: how important it would be to address a pre-specified list of 10 concepts using a 5-point rating scale, where 1 was ‘not at all important’ and 5 was ‘extremely important’. Participants rated ‘decreased bleeds’ and ‘improved joint health’ as the most important desired attributes of a treatment, each with the mean (SD) rating of 4.9 (0.34) on a 5-point scale. Participants were subsequently asked to rate the improvement they noticed in each attribute with the fitusiran AT-DR using a 3-point scale, where 1 was ‘a little improvement’ and 3 was ‘a lot of improvement’. All participants experienced improvements in all important treatment outcomes with the fitusiran AT-DR. Participants mostly reported ‘a lot of improvement’ for the most important desired treatment attributes, that are bleeding events and joint health (3.0 [0.21] and 2.8 [0.39], respectively). Participants also rated several other aspects. These aspects included ‘provide protection from bleeds for an entire month’ (importance: 4.8 [0.41]; improvement: 2.8 [0.39]), ‘improve joint mobility/ability to move around easily’ (importance: 4.8 [0.38]; improvement: 2.9 [0.29]), ‘minimise anxiety or stress related to managing haemophilia’ (importance: 4.8 [0.44]; improvement: 2.8 [0.39]), ‘prevent the fear and anxiety of bleeds’ (importance: 4.7 [0.48]; improvement: 2.9 [0.29]) and ‘be a subcutaneous versus intravenous treatment’ (importance: 4.1 [0.88]; improvement: 3.0 [0.21]). Participants’ statements (verbatim) on their experiences are provided in **Table 1**.

Of the 24 participants, 22 (91.7%) were ‘very satisfied’ with the fitusiran treatment, whereas two (8.3%) were ‘satisfied’. Participants described improvements in symptoms (e.g. decreased bleeds, pain and swelling) and physical function as key factors in their satisfaction ratings (**Table 1**).

Twenty-three (95.8%) of the 24 participants preferred the fitusiran AT-DR prophylaxis over previous on-demand haemophilia treatments. Most of the participants (21; 87.5%) showed confidence in fitusiran protecting them from bleeds for a longer time. Three participants (12.5%) conveyed a lack of confidence in fitusiran, which was driven by the fear of losing access to the treatment for unexpected external reasons (i.e. relocation or a pause in the trial) rather than the duration of protection from bleeds.

This qualitative study confirms treatment attributes of utmost importance to PwH, that is fewer bleeds, less pain, improved joint mobility and health and reduced treatment burden. Collectively, these findings highlight the need for more effective and consistent bleed protection and reduced treatment burden for PwH. PwH face significant challenges with haemophilia and its treatments, which adversely affect their QoL [7,8]. Consistent with the previous observations [9,10], participants highlighted decreased bleeds, stable haemostatic protection without fear of inhibitors and progressive improvement of musculoskeletal health and reduced anxiety as the most important treatment attributes.

Furthermore, participants in the present study noted that the effect of the subcutaneous administration of fitusiran alleviates venous access challenges, and the pharmacodynamic effect of stable reduced AT levels at the selected dose with much lower treatment burden improved treatment adherence. A subcutaneous treatment option with infrequent dosing could be especially valuable when home-based prophylactic clotting-factor therapies are not readily accessible. With the fitusiran regimen, nearly all participants observed ‘a lot of improvement’ across the desired treatment attributes, resulting in an improved QoL.

Of the 24 participants, only one participant did not prefer the fitusiran AT-DR prophylaxis over previous treatments. This participant discontinued fitusiran prior to knee surgery as per the study protocol at the time. However, discontinuing fitusiran during surgical procedures is not necessary. These findings, consistent with the previous reports, indicate that effectiveness, dosing frequency and the route of administration are pivotal factors influencing a treatment choice for PwH [9,10].

This study had a few limitations. Firstly, participants were receiving episodic treatment prior to enrolling in the ATLAS trials. Their perspectives may not entirely represent those of PwH on prophylaxis, which is the standard of care for people with moderate or severe haemophilia who experience frequent bleeding. Nonetheless, a large number of PwH are still receiving episodic treatments globally. These data are generally reflective of them, particularly regarding the high haemostatic efficacy and reduced treatment burden. Secondly, as 23 of the 24 participants were from India, therefore, these findings might not be generalisable to more diverse populations and healthcare settings. Finally, because of time constraints, not all participants were asked every question contained in the interview guide.

This qualitative study demonstrates that the fitusiran AT-DR prophylaxis reduces bleeds and improves joint health and mobility with a markedly lowered treatment and disease burden for PwH. Nearly all participants were very satisfied (91.7%) with fitusiran and preferred it (95.8%) over their previous treatments. These findings indicate the potential of fitusiran to enhance outcomes and QoL in PwH.

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**DATA AVAILABILITY STATEMENT**

Qualified researchers may request access to patient-level data and related study documents, including the study protocol with any amendments, statistical analysis plan and dataset specifications. Further details on Sanofi’s data sharing criteria, eligible studies and process for requesting access can be found at <https://www.vivli.org/>.

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**CONFLICTS OF INTEREST**

Alok Srivastava has received research funding from Roche, Novo Nordisk, Sanofi, Pfizer and Octapharma and has been part of advisory committees/grant review committees of Sanofi, Takeda, Novo Nordisk, Roche, Pfizer and Bayer Healthcare.

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Shariq Ali, Laurel A. Menapace and Marion Afonso are employees of Sanofi and may hold shares or stock options in the company. Shauna Andersson and Marja Puurunen were employees of Sanofi at the time of the study conduct.

**AUTHORS’ CONTRIBUTIONS**

Conception or design of the study: All authors

Data acquisition, analysis and interpretation: All authors

Drafting the work: All authors

Final approval of the version to be published: All authors

**ETHICS STATEMENT**

The study protocol was approved by the Institutional Review Boards of the participating clinical sites. All participants provided informed consent to participate in the interviews.

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**Table 1. Selected quotes from participants.**

| **Aspects** | **Selected quotes** |
| --- | --- |
| Pre-study impact of haemophilia | *‘He used to live life at a reduced scale in the sense that all his activities used to be curtailed or torn down…where with the bleeding he would be immobile for a few days…his left elbow was quite distorted and swollen’.* (IDI 1, Caregiver)*‘It was difficult to move around for my everyday activities…haemophilia restrained me…’* (IDI 9, Patient)*‘Haemophilia sometimes affected [me] in exam time. When bleedings come, I can’t attend the exams and [have] continuous bleeding in my knees…’* (IDI 6, Patient) |
| Pre-study impact of haemophilia treatments | *‘For treatment, we have to go to the hospital because [the] government used to provide all those things…the process used to take a lot of time…it was unbearable. You have to run over here and there…the time consumption… we have to give much more time, so half of the day used to go behind all that’.* (IDI 2, Patient)*‘He had a port, so multiple port infections, changing the port multiple times, also at times he had PICC lines so managing those lines…basically life was miserable for us and him. So, I cannot go anywhere. If we are traveling, we have to carry so much supplies…I would say international travel, we never did that’.* (IDI 1, Caregiver)*‘Traveling and the time taking for treatment was much more complicated before. I had to travel a lot. I could not compensate the delay for my college or school’.* (IDI 9, Patient) |
| Expectations from the treatment in ATLAS-OLE | *‘First thing, the bleeding should stop and stop swelling, stop painand I wanted to become normal…[and have] joint relief, like knee jointand ankle joint’.* (IDI 5, Patient)*‘The first thing I wanted…I do not bleed in between; that was first outcome I wanted’.**‘The second outcome was that stopping the bleeds then I would like to work on my physical fitness’.* (IDI 18, Patient) |
| Improvements with fitusiran and important attributes of a haemophilia treatment | *‘I got relief from joint pain first thing and stopped swelling in the muscles and joints. Mentally I feel good…relief from the pain, swelling, and bleeding…’* (IDI 5, Patient)*‘No bleeding, nothing. Very normal life. [Fitusiran] it will make you a normal person’.* (IDI 6, Patient)*‘Please don’t stop this [study]. I have forgotten my pain. I don’t remember that pain after taking fitusiran’.* (IDI 12, Patient) |
| ATLAS-OLEtrial experience – the impact of improvements on the quality of life | *‘I used to stand for a maximum 10 to 15 minutes, and now I can stand for 1 hour to 1.5 hours. I can walk for 1 hour to 1.5 hours without a bleed being developed’.* (IDI 17, Patient)*‘Quality of life improved, I can take part in other activities like family functions and all and some social impact is there, so that has changed, people’s perspective about thinking about me that has changed’.* (IDI 13, Patient)*‘There is a lot of improvement, like I could take my family out for a holiday, and I did not have a single bleed in my holiday…’* (IDI 18, Patient) |
| Confidence in fitusiran | *‘As time progresses, we could see he’s doing good. Over 2 months, nothing [no bleeds] happened. Then I said, well, that is no miracle’.* (IDI 1, Caregiver)*‘I am confident about fitusiran because in the last 1 and a half years it has changed my life drastically…I feel confident [managing my haemophilia]’.* (IDI 14, Patient)*‘I would say that I feel very confident about myself [managing haemophilia]…if it is available at the right cost I would stick to this therapy’.* (IDI 18, Patient) |
| Satisfaction with fitusiran | *‘Very satisfied. The fact that I do not have to go to the hospital that much and it [fitusiran] gives me strength to go out and do what I want’.* (IDI 2, Patient)*‘Very satisfied because I can do my job very comfortably…no bleeds’.* (IDI 4, patient)*‘Very satisfied. I can walk normal…now no one notices [my walk], now they treat me like normal. I am progressing in my work’.* (IDI 13, Patient) |
| Preference for fitusiran | *‘Fitusiran definitely [prefer]. The half-life of it that it lasts longer unlike other Factors, would be one reason’.* (IDI 8, Patient)*‘It is long lasting. It is safe, easily administered’.* (IDI 10, Caregiver)*‘I prefer fitusiran…the reason behind this is in my case I had very fewer bleeds even in the second dosing’.* (IDI 18, Patient) |

IDI, in-depth interview.