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POSTER ABSTRACTS

801.GENE THERAPIES

Health-Related Quality of Life in Adults with Hemophilia B after Receiving Gene Therapy with Fidanacogene Elaparvovec

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Introduction : The burden of the management and clinical sequelae of hemophilia B (HB) negatively impacts health-related quality of life (HRQoL), including chronic pain and mental health. Fidanacogene elaparvovec (PF-06838435, formerly SPK-9001) is an adeno-associated virus-based gene therapy vector transferring the high activity variant of human factor IX (FIX), FIX-R338L, aimed at enabling endogenous FIX expression in individuals with hemophilia B. We present descriptive data on the impact on HRQoL for participants in the fidanacogene elaparvovec phase 1/2a study.

Methods: Fifteen participants with moderately severe to severe hemophilia B (FIX activity ≤2%) received a single infusion of fidanacogene elaparvovec 5e11 vg/kg as part of a phase 1/2a study (NCT02484092). The study was 52 weeks in duration, after which participants were eligible to enroll in a long-term follow-up (LTFU) study for up to 5 years (NCT03307980). All 15 participants completed the phase 1/2a study and 14 subsequently enrolled in the LTFU study (1 participant declined participation). Participants in both studies completed patient-reported outcome (PRO) HRQoL assessments, including the Haemophilia Quality of Life Questionnaire for Adults (Haem-A-QoL), the visual analog scale of the EQ-5D (EQ-VAS), and the Change in Level of Activity questionnaire, every 6 months through Week 156 post infusion and then once annually during the LTFU study. The Haem-A-QoL questionnaire consists of 46 items pertaining to 10 domains to assess HRQoL, and domains scores and the Total Score ranging from 0-100 based on the individual items (high scores indicate high impairment in HRQoL). In the EQ-VAS, participants rate their current health state for endpoints of 100 (best imaginable health) to 0 (worst imaginable health). In the Change in Level of Activity questionnaire, participants assess whether they have been doing more/fewer/the same amount or intensity of physical activities in the past month. The data cutoff date was August 2, 2022.

Results: For 14 participants (aged 20 to 63 years), the mean (SD) age at entry to the LTFU study was 42 (13.7) years, body mass index was 26.4 (4.4) kg/m ^{2}, and 85.7% were White. Of the 14 participants, 13 had HRQoL data available through Week 156; beyond this time point, there were 10 or fewer participants with both post- and pre-vector infusion (baseline) values. For the Haem-A-QoL assessment, the mean (SD) Total Score at Week 156 (n=12) decreased by 15.2 (10.3) from pre-vector infusion, indicating an improvement in HRQoL (**Fig. 1**). A 7-point reduction in the total score has been shown to be clinically meaningful in previous studies (Von Mackensen S et al, Haemophilia 2020;26:1019-30; Wyrwich KW et al, Haemophilia 2015;21:578-84). Of the 12 participants with data at Week 156, 8 had Total Score decreases of 7 or more at each visit through Week 156. Similarly, participant scores for each individual domain decreased over time (implying an improvement in HRQoL) from pre-vector infusion in all instances except for the Dealing with Hemophilia domain (**Fig. 1**). Mean EQ-VAS scores were above mean

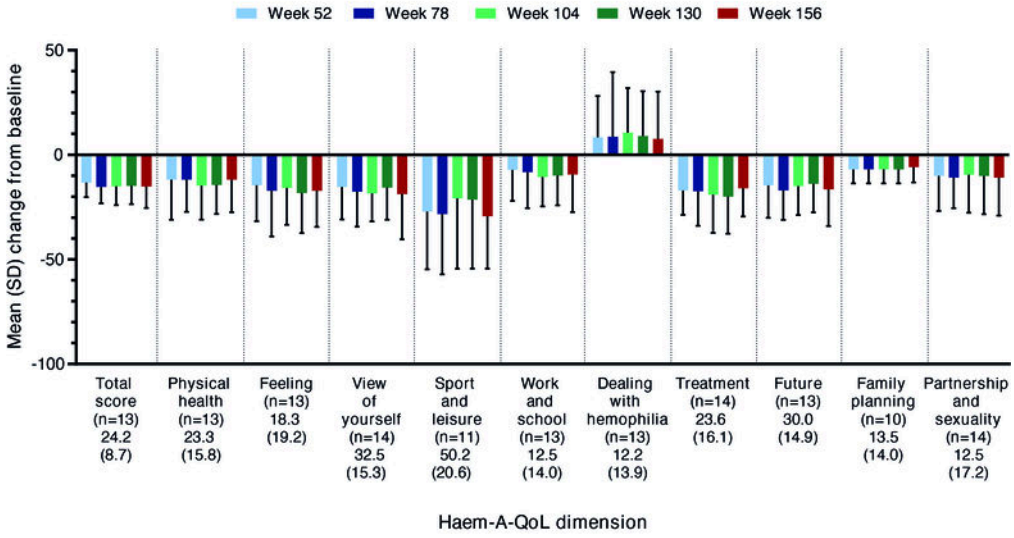
baseline score and were consistently greater than baseline by 7 to 8 points during Year 2 onward, suggesting an improvement in overall health status. At Week 156, the EQ-VAS score increased from baseline by mean (SD) 7.2 (6.2): baseline 83.7 (7.3), n=13; Week 156 91.5 (5.4), n=12. An EQ-VAS score change of 7 points has been shown to be clinically meaningful (Pickard AS et al. Health Qual Life Outcomes 2007;21:5:70). Responses in the Change in Level of Activity questionnaire showed that a greater proportion of participants at each visit (n=12-14) reported doing the same or more intensive physical activities up to Week 156 than reported at baseline (**Fig. 2**). No participant reported a reduction in the amount or intensity of physical activities at Week 156 (n=13) (**Fig. 2**).

Conclusion **:** HRQoL improvements after gene therapy are an indicator that fidanacogene elaparvovec can reduce the burden associated with hemophilia. PRO assessments will be a part of BENEGENE-2, an ongoing pivotal phase 3 study to demonstrate the efficacy of fidanacogene elaparvovec and will provide additional insights via the analyses of secondary endpoints into HRQoL benefits for participants with HB following gene therapy with fidanacogene elaparvovec.

Disclosures von Mackensen: *Sobi:* Research Funding; *Takeda:* Research Funding, Speakers Bureau; *Chugai:* Speakers Bureau; *Kedrion:* Speakers Bureau; *Biomarin:* Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Roche:* Consultancy; *Spark:* Consultancy; *Pfizer:* Consultancy; *Chugai/Roche:* Membership on an entity's Board of Directors or advisory committees. **Ducore:** *Bayer:* Consultancy. **George:** *STRM.BIO:* Other: has a leadership/fiduciary role ; *Spark Therapeutics:* Consultancy; *Regeneron:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *AskBio:* Patents & Royalties, Research Funding. **Giermasz:** *Bayer:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *BioMarin Pharmaceutical Inc.:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel grants; *uniQure:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Genentech:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Novo Nordisk:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Sanofi Genzyme:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bioverativ, Genentech/Roche, Biomarin, uniQure, American Thrombosis and Hemostasis Network:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees. **McGuinn:** *Roche/Genetech:* Other: Clinical Trial Investigator; *Sanofi:* Other: Clinical Trial Investigator; *Takeda:* Other: Clinical Trial Investigator; *Bayer:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *BPL:* Consultancy, Other: has received support for attending meetings/travel; *CSL Behring:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Genentech:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Octapharma:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *HEMA Biologics:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Rasko:** *BeiGene:* Honoraria; *Rarecyte:* Current holder of *stock options* in a privately-held company, Honoraria; *Novartis:* Honoraria; *Bluebird Bio:* Honoraria; *Spark Therapeutics:* Honoraria; *Cynata:* Honoraria; *Pfizer:* Consultancy, Honoraria; *Woke:* Current holder of *stock options* in a privately-held company. **Samelson-Jones:** *Amarna:* Current holder of *stock options* in a privately-held company; *GeneVentiv:* Current holder of *stock options* in a privately-held company; *Biomarin:* Consultancy; *Genentech:* Consultancy; *Pfizer:* Consultancy, Honoraria. **Sullivan:** *Pfizer:* Membership on an entity's Board of Directors or advisory committees, Other: Clinical Trial Investigator; *Spark Therapeutics:* Other: Clinical Trial Investigator; *Biomarin:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Octapharma:* Consultancy; *Genentech:* Membership on an entity's Board of Directors or advisory committees. **Teitel:** *Biomarin:* Other: participated on a Data Safety Monitoring Board/Advisory Board; *Sanofi:* Consultancy; *Octapharma:* Consultancy; *Bayer:* Consultancy; *Spark:* Other: Clinical Trial Investigator; *Pfizer:* Other: Clinical Trial Investigator; *Vega Therapeutics:* Other: participated on a Data Safety Monitoring Board/Advisory Board. **Chhabra:** *Pfizer:* Current Employment, Current equity holder in publicly-traded company. **Fang:** *Pfizer Inc:* Current Employment, Current equity holder in publicly-traded company. **O'Brien:** *Pfizer:* Current Employment, Current equity holder in publicly-traded company. **Plonski:** *Pfizer:* Consultancy, Current equity holder in publicly-traded company. **Rupon:** *Pfizer:* Current Employment, Current equity holder in publicly-traded company. **Smith:** *Pfizer:* Current Employment, Current equity holder in publicly-traded company. **Winburn:** *Pfizer:* Current Employment, Current equity holder in publicly-traded company.

OffLabel Disclosure: Fidanacogene elaparvovec incorporates a hepatotropic AAV capsid and a high-activity FIX transgene encoding FIX-R338L and is currently in development for patients with severe and moderately severe hemophilia B

Fig. 1: Change from baseline in Haem-A-QoL over time



Week 52 assessment was from the End of Study visit in the phase 1 dosing study or Visit 1 of the LTFU study. Scores range from 0 to 100, with lower scores indicating better HRQoL.
Change from baseline: post-baseline value – baseline value.
Numbers shown on x-axis represent the number of participants with responses for each individual domain at baseline and mean (SD) score at baseline; numbers of participants may be lower at subsequent timepoints. For the change from baseline, only participants with a value at both baseline visit and the specified post-baseline visit were included.

Fig. 2: Change in Level of Activity questionnaire responses over time

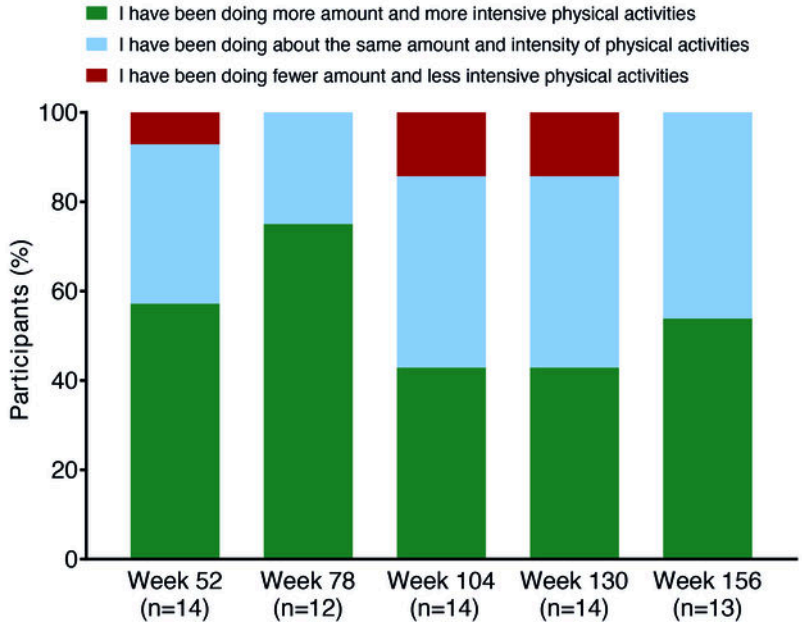


Figure 1

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