MPE-066

Improved joint health after gene therapy with dirloctocogene samoparvovec (SPK-8011) in people with hemophilia A

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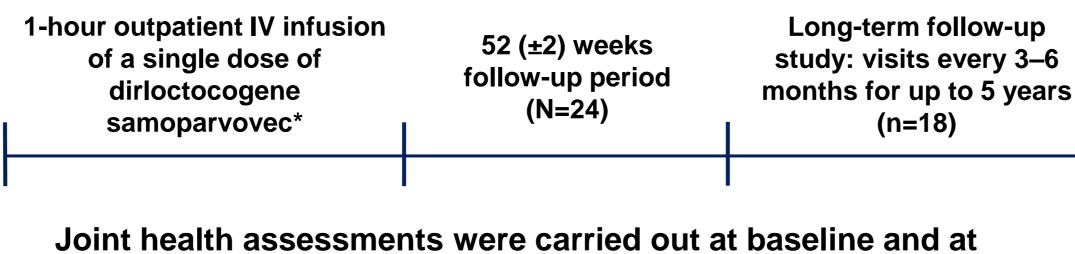
Background

- Hemophilia A (HA) is a bleeding disorder associated with frequent bleeding into the joints. This can cause hemophilic arthropathy, a common complication of hemophilia.¹
- Dirloctocogene samoparvovec (SPK-8011) is an investigational gene therapy for HA that uses a modified adeno-associated vector to deliver factor (F)VIII to liver cells.
- The phase I/II trial (NCT03003533/NCT03432520) investigating dirloctocogene samoparvovec reported reductions in annualized bleeding rate (ABR) of 99% and 82% for people with HA previously receiving on-demand and prophylactic FVIII treatment, respectively.²
- The aim of this analysis is to report the clinical impact of dirloctocogene samoparvovec on the joints of people with HA who participated in the phase I/II trial.

Methods

Figure 1. Phase I/II dirloctocogene samoparvovec clinical trial design

Trial design (NCT03003533/NCT03432520)

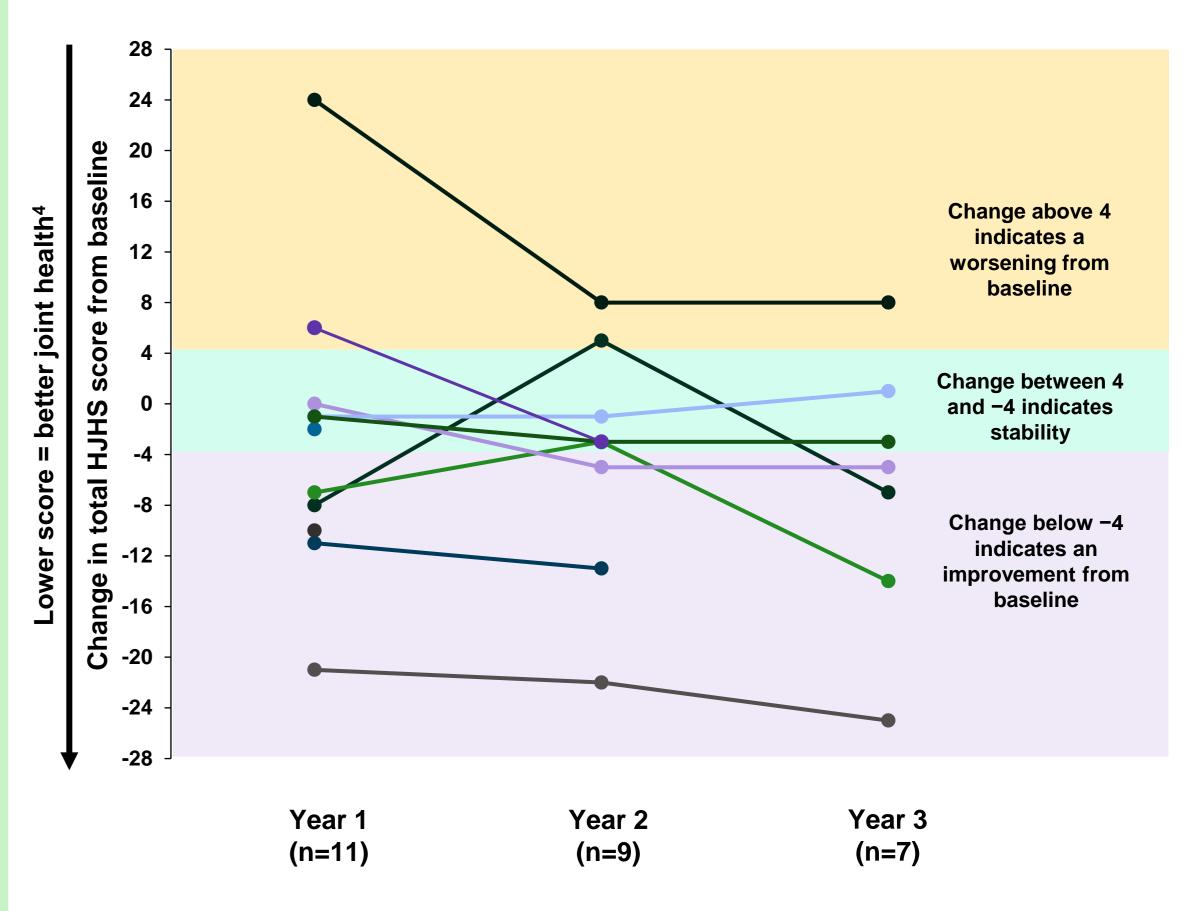


regular intervals during the trial

Presence and resolution Joint pain Self-reported

Clinically meaningful changes in total HJHS score were observed between baseline and Years 2–3 for almost all individual participants

Figure 5: Yearly change in total HJHS score from baseline following dirloctocogene samoparvovec infusion (each line represents one participant)



Summary and Conclusions

This exploratory analysis investigates the clinical impact on joints for a subset of participants who received the investigational gene therapy dirloctocogene samoparvovec in a Phase I/II trial (NCT03003533/NCT03432520)



Clinically meaningful improvement in total Hemophilia Joint Health Score was observed following dirloctocogene samoparvovec infusion, alongside improvements in self-reported function and target joint resolution



of target joints^{3†} (HJHS) joint function (HAL) Lower score = better Higher score = better Higher score = better ioint health4 function reported by the

joint health⁴ (A change of ≥4 is considered clinically meaningful)⁴ Higher score = better function reported by the participant⁵

health⁴

ioint

better

Lower

Full study design details have been published previously.6

The closest assessments after each time point are used for this analysis.

In most participants, baseline target joint involvement was identified by retrospective medical record review. *Participants received one of four doses: 5x10¹¹ vg/kg (n=2), 1x10¹² vg/kg (n=3), 2x10¹² vg/kg (n=9), 1.5x10¹² vg/kg (n=10). A maximum dose was based on a BMI of 30 kg/m.²

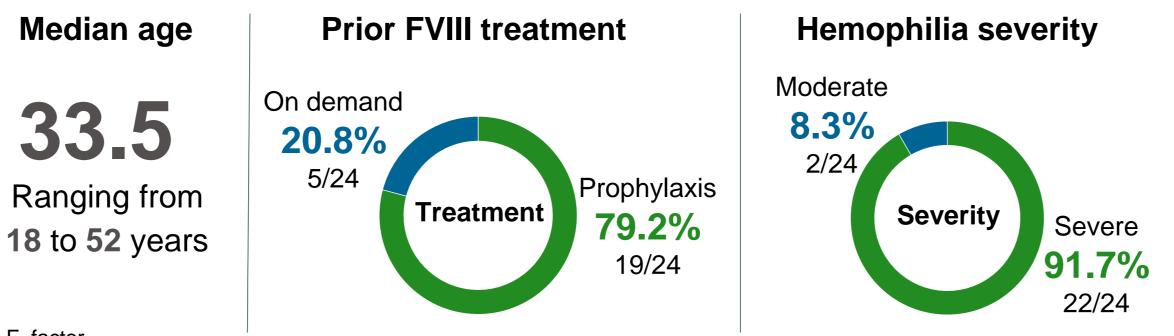
[†]According to ISTH definitions: a target joint is defined as a single major joint (i.e., hip, elbow, wrist, shoulder, knee or ankle) into which \geq 3 spontaneous bleeds occur within a consecutive 6-month period. The joint is no longer considered a target joint when there has been \leq 2 bleeds into the joint within a consecutive 12-month period.³ BMI, body mass index; HAL, Hemophilia Activities List; HJHS, Hemophilia Joint Health Score; IV, intravenous; vg, vector genome.

Results

Study population

- At data cut-off (October 4, 2022), 24 participants were included across the four dosing cohorts (Figure 2).
- The median observation time was 191 weeks (range: 2–285 weeks).

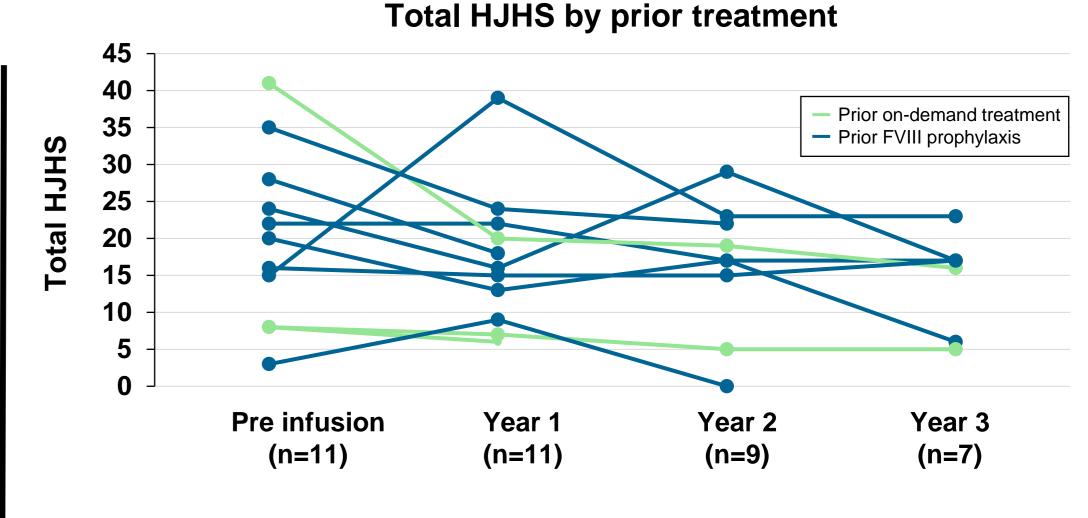
Figure 2. Baseline demographics and characteristics of participants who had received dirloctocogene samoparvovec at data cut-off (N=24)

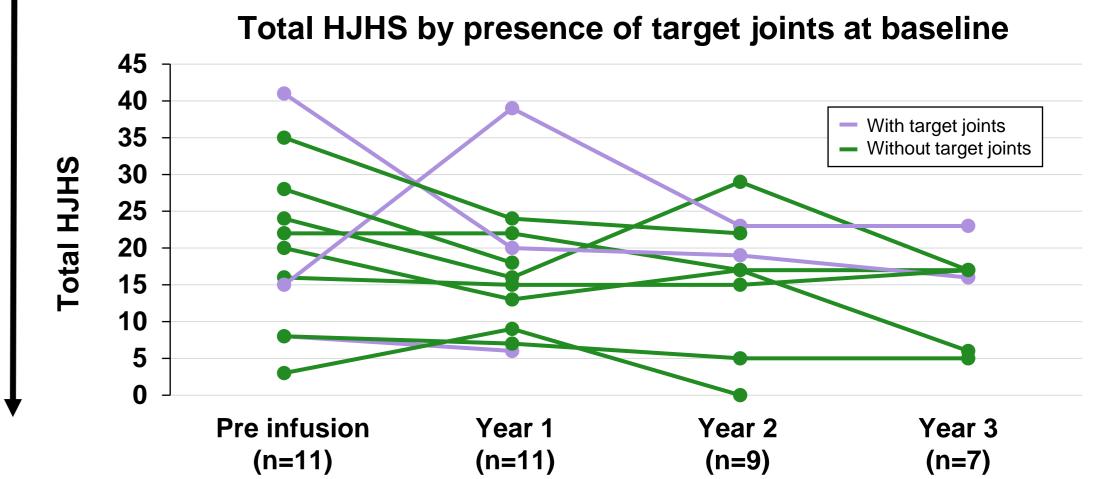


Participants with data at baseline and Year 1 for each measure were included for each analysis. HJHS, Hemophilia Joint Health Score.

Trends towards improvement in total HJHS were observed regardless of previous on-demand or prophylactic FVIII treatment, or whether target joints were present at baseline

Figure 6: Total HJHS following dirloctocogene samoparvovec infusion by prior treatment and baseline target joints (each line represents one participant)





Improvements in joint health were observed in all groups: prior on-demand or prophylactic factor VIII treatment, and presence or absence of target joints at baseline

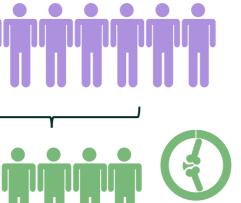


Although interpretation of these results is limited by the small sample size, exploratory observations support improvement of joint health following treatment with dirloctocogene samoparvovec. Additional investigation is warranted



All target joints present at baseline had resolved by Year 1 in participants with sufficient follow-up time (n=5), with no new target joints being identified following treatment with dirloctocogene samoparvovec

Figure 3: Impact of dirloctocogene samoparvovec infusion on target joints

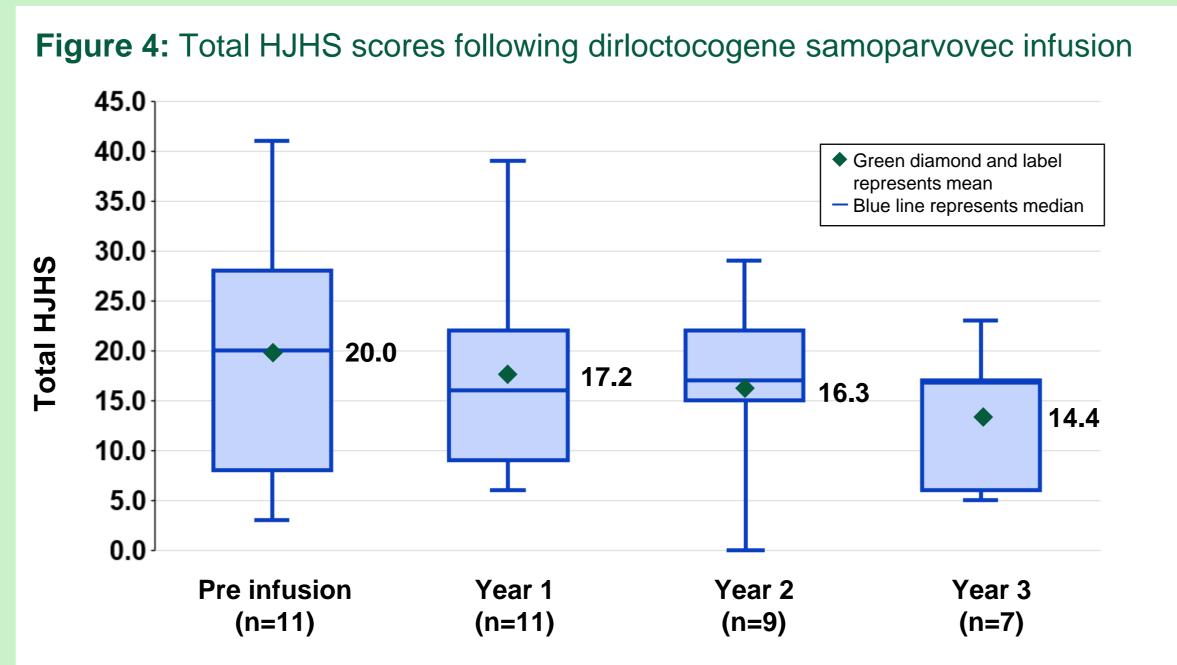


In the 52 weeks prior to dirloctocogene samoparvovec infusion, 7/24 participants had a total of 13 target joints

At 1 year following dirloctocogene samoparvovec treatment, **100%** of **evaluable target joints*** resolved

*Evaluable target joints are those in patients who had a minimum of 12 months of follow up (n=5)

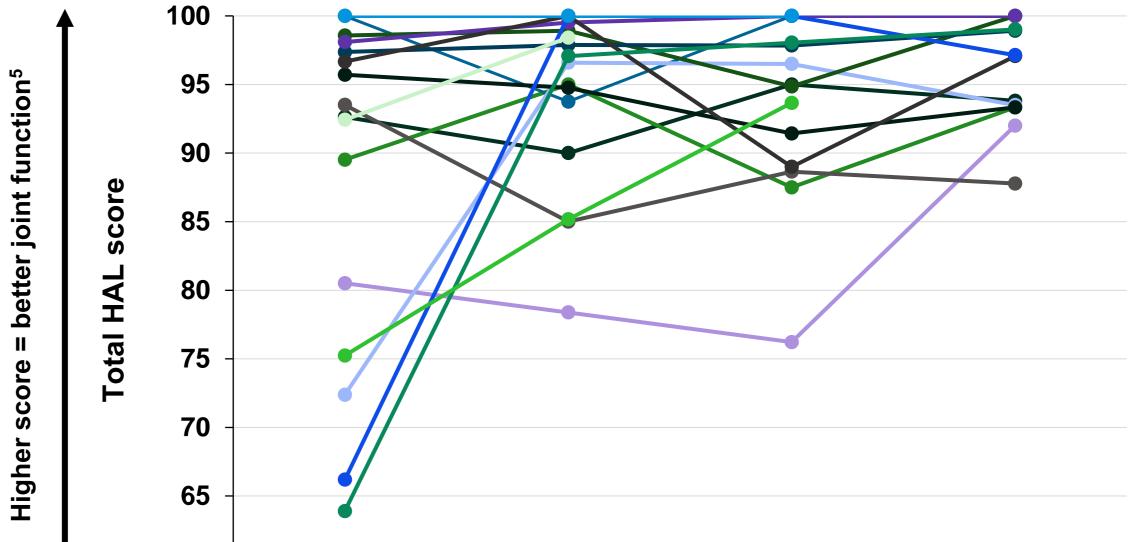
Clinically meaningful improvements in total HJHS score were observed at Years 2 and 3, indicating improved joint health



Participants with data at baseline and Year 1 for each measure were included for each analysis. F, factor; HJHS, Hemophilia Joint Health Score.

Trends towards improvement in total HAL score were observed at Year 1 and maintained over Years 2 and 3, indicating an improvement in the participants' self-reported joint function

Figure 7: Total HAL scores following dirloctocogene samoparvovec infusion (each line represents one participant)



F, factor.



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The box represents the interquartile range. The whiskers represent the range. HJHS, Hemophilia Joint Health Score.

60			
Pre infusion	Year 1	Year 2	Year 3
(n=16)	(n=16)	(n=15)	(n=13)

Participants with data at baseline and Year 1 for each measure were included for each analysis. A metric for clinically meaningful change in HAL has not been determined. F, factor; HAL, Hemophilia Activities List.

Trends towards improvement in self-perceived function were also observed through to Year 3, regardless
of prior FVIII treatment type and the presence of target joints.

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Disclosures

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