ELSEVIER

Blood 142 (2023) 4999–5000

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

801.GENE THERAPIES

Improvements in Health-Related Quality of Life after Exagamglogene Autotemcel in Patients with Severe Sickle Cell Disease

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Background: Severe sickle cell disease (SCD), which is characterized by recurrent vaso-occlusive crises (VOCs), has a substantial negative impact on health-related quality of life (HRQoL). Exagamglogene autotemcel (exa-cel) is a one-time, non-viral, ex vivo CRISPR/Cas9 gene-edited autologous cell therapy in phase 3 clinical trials that has been shown to eliminate VOCs. Here, we report HRQoL data from a pre-specified interim analysis of the exa-cel CLIMB SCD-121 study.
Methods: CLIMB SCD-121 is an ongoing phase 3 trial of a single dose of exa-cel in patients ages 12-35 years with SCD and a history of ≥2 VOCs/year in each of the 2 years prior to screening. Changes in patient reported outcomes measures EuroQol Quality of Life Scale 5 dimensions 5 levels of severity (EQ-5D-5L, including descriptive system and visual analog scale [VAS]), Functional Assessment of Cancer Therapy Bone Marrow Transplant (FACT-BMT, including FACT-General [FACT-G] and bone marrow transplant subscale [BMTS]), Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me), and the 11-point pain Numerical Rating Scale (NRS) were assessed from baseline through month 24 as a secondary endpoint in the trial. Data is presented as of 10 Feb 2023 for the 17 adult patients (aged ≥18-35 years) who had been followed for ≥16 months after exa-cel infusion.
Results: Substantial and clinically meaningful improvements exceeding minimal clinically important difference (MCID) thresholds were observed in all assessed patient reported outcomes measures. At baseline, the EQ-5D-5L health utility US index (n=17; mean [SD]: 0.71 [0.23]) and EQ VAS (63.5 [22.5]) scores were lower than the US general population norm and similar to baseline scores reported for adult SCD patients with recurrent VOCs. By month 6, both EQ-5D-5L health utility US index score and EQ VAS score showed substantial improvements, which were maintained through month 24 (mean changes [SD] at month 24 [n=8]: 0.23 [0.20]; MCID 0.078 and 28.3 [16.2]; MCID 7 to 10, respectively). FACT-G Total Score improved from baseline at month 24 (mean [SD] change at month 24 [n=8]: 29.8 [17.2]; MCID 3 to 7), with improvements observed in all 4 subscales (physical, social/family, emotional, and functional well-being). BMTS score improved by month 6 and was sustained through month 24 (mean [SD] change at month 24 [n=8]: 3.9 [5.7]; MCID 2 to 3). All subscales of the ASCQ-Me, including emotional (mean [SD] change [n=7] 17.7 [9.8]), social (23.8 [6.7]), stiffness (7.9 [12.9]), and sleep impact (8.4 [8.3]), demonstrated clinically meaningful improvements from baseline through month 24. For the ASCQ-Me pain-related subscales evaluating pain impact, pain episode frequency and pain severity, the largest numerical improvement was observed in pain episode frequency (mean [SD] change at month 24 [n=8]: -22.8 [8.2]; MCID -5). Improvements in the pain NRS were observed by month 12 and sustained through Month 24 (mean [SD] change at month 24 [n=8]: -1.8 [3.1]; MCID -1).
Conclusion: Adults infused with exa-cel reported sustained and clinically meaningful improvements in their HRQoL, with improvements observed across different instruments and domains, including physical, emotional, social/family, and functional well-being, pain experience, and overall health status. These results demonstrate the broad clinical benefits of exa-cel in patients with SCD.

Disclosures Sharma: *Sangamo Therapeutics:* Consultancy; *Vertex Pharmaceuticals:* Consultancy, Other: Clinical Trial Site PI; *Medexus Inc:* Consultancy; *Editas Medicine:* Consultancy; *CRISPR Therapeutics:* Other: Clinical Trial Site PI, Research Funding; *RCI BMT/NMDP:* Honoraria, Other: Clinical Trial Medical Monitor. **Frangoul:** *Rocket Pharmaceuticals:* Consultancy, Other: Member of DSMB for a study; *Jazz Pharmaceuticals:* Speakers Bureau; *Editas Medicine:* Consultancy; *Vertex Pharmaceuticals:*

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https://doi.org/10.1182/blood-2023-190203