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ORAL ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Primary Analysis of Spartan: A Phase 2 Trial to Assess the Efficacy and Safety of Crizanlizumab in Patients with Sickle Cell Disease Related Priapism

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Introduction: Priapism is a painful, sustained penile erection that occurs in 35% of adult men with sickle cell disease (SCD) and may result from the underlying mechanism of vaso-occlusion. To date, there is no effective disease-modifying drug proven to treat priapism. Crizanlizumab is a monoclonal antibody that binds and blocks P-selectin, a key mechanistic component of vascular endothelial adhesion. Based on the results of the SUSTAIN trial, crizanlizumab was approved by the FDA to reduce the frequency of vaso-occlusive crises in patients with SCD aged ≥16 years. In this primary analysis of the Phase 2 SPARTAN trial (NCT03938454), we evaluated the efficacy and safety of crizanlizumab after 26 weeks of treatment in patients with SCD-related priapism.

Methods: The SPARTAN trial included male patients aged ≥12 years with all SCD genotypes who experienced ≥4 priapic episodes lasting ≥60 min over the 14-week period preceding screening. Eligible patients also experienced ≥3 priapic episodes during the subsequent 12-week screening period with ≥1 event occurring within 4 weeks prior to the first treatment. After enrollment priapic events were documented through electronic self-reporting tools and validated patient-reported outcomes surveys for 26 weeks and included start/end date, sleep status, duration, non-pharmacological treatment, triggers, emergency department visit, and pain intensity during the screening period. Baseline priapic events were collected for each patient during the 12-week screening period. Patients received crizanlizumab 5.0 mg/kg IV infusion on week 1, week 3, and every 4 weeks thereafter. The primary endpoint was percent reduction from adjusted baseline period in priapic events by 26

weeks. Percent reduction from baseline in priapic events was tested using a one-sided Wilcoxon's Sign Rank test. Hodges-Lehmann estimate of median percent reduction in priapic events (with 95% CIs) was also reported.

Results: Data cutoff was March 28, 2023. Of the 36 patients enrolled, 26 (72.2%) were between 18 and 40 years, and the median (range) age was 29 (14-58) years. Most patients were HbSS genotype (n=29, [80.6%]) and more than half were on hydroxyurea (n=21, [58.3%]). Patient-reported history prior to crizanlizumab treatment revealed that more than half of patients experienced priapism daily or every other day (n=21, [58.3%]) and most reported a duration of 1 to 5 h (n=33, [91.7%]). The most common patient-reported emotions at the start of the study were frustration and exhaustion, reported by ≈50% of patients. The median (IQR) baseline number of priapic events adjusted for 26 weeks per patient was 42 (13-73) events (**Table**). All patients experienced events lasting 1 to ≤4 h, although some also experienced severe events lasting >4 to 6 h (n=19, [52.8%]) and >6 to ≤12 h (n=11, [30.6%]). In one case, 38 days of screening period baseline data was not reported, resulting in a strong outlier that affected the results (**Patient 1, Figure**). Thirty-six patients received ≥1 dose of crizanlizumab, with a median cumulative dose of 35.0 mg/kg over 26 weeks; 5 patients each missed 1 infusion and 1 patient missed 2 infusions. The Hodges-Lehmann estimate of median percent reduction from baseline in priapic events per patient was 46.0% (95% CI: 23.5%-65.4%; *P*=.068). Twenty-eight patients (77.8%) reported a reduction from baseline in priapic events (**Figure**). A subgroup analysis revealed a trend towards a larger percent reduction in events for patients with ≥22 baseline events, possibly indicating that patients with severe disease benefitted more from treatment. The most frequent treatment-emergent adverse event (TEAE) was headache (16.7%). No patients discontinued crizanlizumab prematurely and only one patient withdrew consent by week 26.

Conclusions: Primary analyses from the SPARTAN trial showed that patients with SCD-related priapism treated with crizanlizumab over 26 weeks experienced approximately half as many priapic events compared with baseline. There was a trend towards a more significant reduction in frequency of episodes in patients with severe disease. Crizanlizumab was safe and well tolerated, with observed TEAEs consistent with the safety profile seen in other clinical trials. Final analyses of the SPARTAN trial will provide data over 52 weeks and may provide further support for the role of crizanlizumab in reducing frequency of priapic events.

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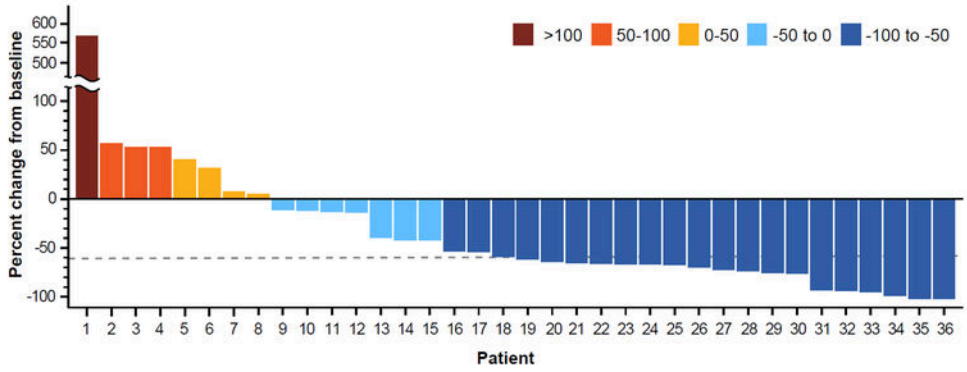
Table. Summary of Reduction of Priapic Events ≥60 Minutes in the Study Population

	Crizanlizumab 5.0 mg/kg, N=36
Primary reduction in no. of priapic events	
Baseline no. of events (adjusted for 26 weeks), median (IQR)[a]	42.0 (13 to 73)
No. of events by week 26, median (IQR)	15.5 (5 to 50)
Percent change from baseline, median (IQR)[b]	−61.3 (−80.1 to −17.3)
Statistical analysis for primary endpoint	
Percent reduction from baseline (adjusted for 26 weeks) by week 26, median (95% CI)[c]	46.0 (23.5-65.4)
P value[d]	.068
Percent change by no. of baseline events (adjusted for 26 weeks), median (IQR)	
7-13 Adjusted baseline events (n=10)	−54.2 (−69.2 to 22.2)
14-21 Adjusted baseline events (n=4)	−45.3 (−77.8 to 7.6)
≥22 Adjusted baseline events (n=22)	−65.8 (−83.6 to −20.3)

[a] Baseline (adjusted for 26 weeks) = number of priapic events in 12-week screening period × (26/12).
[b] Percent change from baseline = (by week 26 value – baseline [adjusted to 26 weeks] value) × 100/baseline (adjusted to 26 weeks) value. Percent change from baseline is calculated based on individual patient values for respective visits, for which both baseline and by week 26 values are available.
[c] Median percent change and 95% CI are Hodges-Lehmann estimates of median percent reduction from baseline (adjusted for 26 weeks).
[d] *P* value is from one-sided Wilcoxon Sign Rank Test with at least 25% percent reduction from baseline (adjusted for 26 weeks) as outcome variable.

Figure. Percent Change from Baseline in Cumulative Number of Priapic Events by Week 26[a,b]



[a] Baseline (adjusted for 26 weeks) = number of priapic events in 12 weeks screening period × (26/12).
[b] Percent change from baseline = (by 26 weeks value – baseline [adjusted to 26 weeks] value) × 100/baseline (adjusted to 26 weeks) value.
The horizontal line in the interior of the plot represents the median.

Figure 1

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