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POSTER ABSTRACTS

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

Real-World Experience of Individuals with Sickle Cell Disease Treated with Voxelotor: Initial Report from the Multicenter, Prospective Prospect Study

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Introduction: Sickle cell disease (SCD) is an inherited blood disorder in which sickle hemoglobin (HbS) polymerization results in red blood cell sickling, which in turn leads to chronic hemolytic anemia, unpredictable pain episodes, and recurrent vaso-occlusive crises (VOCs). Hemolysis and low hemoglobin (Hb) are associated with organ damage, increased morbidity, and early mortality. Voxelotor, a first-in-class HbS polymerization inhibitor, is approved in the US for the treatment of patients with SCD aged ≥4 years and in Europe for the treatment of hemolytic anemia due to SCD in patients aged ≥12 years. In the phase 3, randomized, controlled HOPE (NCT03036813) and the phase 2, open-label HOPE-KIDS 1 (NCT02850406) trials, patients treated with once daily oral voxelotor experienced increased Hb levels and reductions in markers of hemolysis at Week 24 compared with baseline. Here we report the first efficacy and safety data from patients with SCD enrolled in the prospective PROSPECT registry who received voxelotor in a real-world setting.
Methods: PROSPECT (NCT04930445) is a post-marketing, open-label, observational, prospective patient registry of patients with SCD (aged ≥4 years) in the US. Eligible participants are being treated with voxelotor as prescribed by their physician as part of their usual care. Participants are treated and evaluated per standard of care and at the physician's discretion. Treatment, including interruptions and restarting treatment, continue at the discretion of the treating physician. Patients receive any additional medications or transfusions as determined and prescribed by their physician. Follow-up duration is 5 years after the first dose of voxelotor therapy. Study data are collected from patient medical records and secondary data sources and entered in case report forms via an electronic data capture system.
Results: At data cutoff (May 30, 2023), 85 patients were enrolled at 5 sites. The mean (SD) age was 33.2 (15.3) years, 51.8% of patients were female, and most (92.9%) were Black or African American. Overall, 72.9% of patients were genotype HbSS, 62.4% were taking concurrent hydroxyurea, and mean (SD) Hb at baseline was 7.7 (1.53) g/dL. The mean (SD) duration of treatment, excluding gaps, was 47.0 (12.35) weeks. At the data cutoff, 76 patients (89.4%) continued voxelotor treatment; 7 patients (8.2%) never started voxelotor, and 2 patients (2.4%) discontinued treatment because of adverse events (AEs).The initial prescribed daily doses of voxelotor were 1500 mg (84.7%), 1000 mg (8.2%), 900 mg (4.7%), or 500 mg (2.4%). The most common reasons for prescribing voxelotor were to reduce either anemia (74.1%), frequency of VOCs (15.3%), pain (14.1%), or the frequency of blood transfusion (9.4%); multiple reasons could be selected. In 66 patients with recorded baseline and posttreatment Hb values, the observed mean (SD) peak posttreatment Hb value was 9.0 (1.75) g/dL, representing a mean (SD)

increase from baseline of 1.3 (1.25) g/dL. The range of peak Hb change from baseline was −1.4 to 4.6 g/dL and 52/66 patients (78.8%) had a positive Hb response (Figure). Reductions in markers of hemolysis were also observed following voxelotor treatment, with nadir mean (SD) decreases from baseline of −23.9% (55.92%) in reticulocyte percentage (n=54), −1.8 (2.36) mg/dL in total bilirubin (n=61), and −1.6 (1.95) mg/dL in indirect bilirubin (n=38). AEs of special interest reported in >3% of patients included diarrhea, headache, nausea, abdominal pain, and rash (Table); most of these AEs were mild or moderate in severity.

Conclusions: PROSPECT is the first prospective patient registry of voxelotor, with the potential to follow up to 1000 participants for up to 5 years and enable long-term, robust data collection of real-world care patterns that could inform how best to incorporate voxelotor into the treatment paradigm of patients with SCD. In this initial cohort of participants enrolled to date, following voxelotor treatment for a mean duration of 47.0 weeks, the mean peak increase from baseline in Hb was 1.3 g/dL, and associated reductions in markers of hemolysis were observed. Safety data were consistent with the phase 3 HOPE and HOPE-KIDS 1 trials. Overall, these initial findings provide support for the real-world safety, tolerability, and effectiveness of voxelotor treatment in individuals with SCD. While enrollment is ongoing, updated data will be regularly reported.

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Figure. Per Patient Peak Hemoglobin Change from Baseline (n=66)

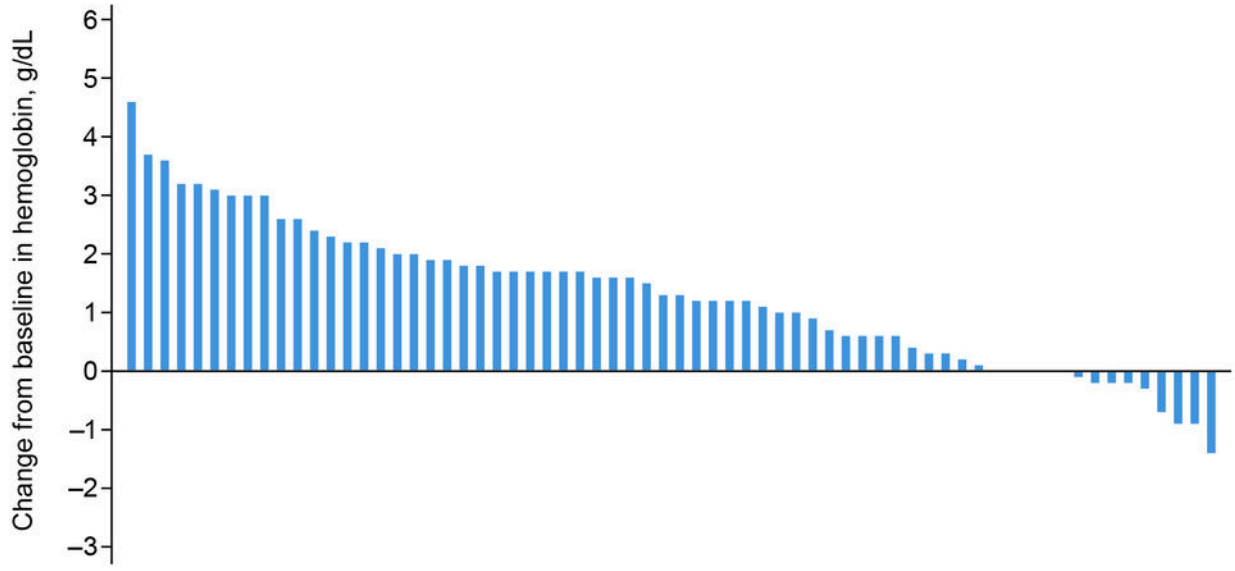

Table. AEs of Special Interest

	Patients (N=85)
Patients with any AE of special interest, n (%)	24 (28.2)
Patients with AEs of special interest (>3% incidence), n (%)	
Diarrhea	17 (20.0)
Headache	13 (15.3)
Nausea	10 (11.8)
Abdominal pain	6 (7.1)
Rash	3 (3.5)

AE=adverse event

Figure 1

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