Multicenter, Retrospective Real-World Experience of Voxelotor-Treated Patients With SCD

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Disclosures

Biree Andemariam: Consultant, advisory board: Agios, Aruvant, Bluebird Bio, CRISPR, Emmaus, Forma Therapeutics, Global Blood Therapeutics, Hemanext, Novartis, Novo Nordisk, Sanofi Genzyme, Shenox, Terumo BCT, Vertex; research funding: Forma Therapeutics, Global Blood Therapeutics, Hemanext, Imara, Novartis

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Archana Sharma: Nothing to disclose

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Maureen Achebe: Advisory board: Fulcrum Therapeutics, Pharmacosmos

Alecia Nero: Consultant: Global Blood Therapeutics, Editas Medicine, Bluebird Bio, Novartis

Susanna Curtis: Consultant: Global Blood Therapeutics

Caterina Minniti: Consultant, advisory board: Global Blood Therapeutics, Novartis, Novo Nordisk, Roche, Forma Therapeutics, Agios, Chiesi, Emmaus Life Sciences, Sanguine Bio, Sangamo, CSL Behring, Bluebird Bio

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Background

- Sickle cell disease (SCD) is characterized by the polymerization of sickle hemoglobin (HbS) in the deoxygenated state.[1,2]
  - HbS polymerization causes sickling of red blood cells that leads to hemolysis, anemia, and vaso-occlusion.[1,2]
- Voxelotor is a first-in-class HbS polymerization inhibitor that reversibly binds to hemoglobin (Hb) and stabilizes Hb in the oxygenated state.[3,4]
  - Approved by the US Food and Drug Administration for the treatment of SCD in patients aged ≥4 years and in the European Union and United Arab Emirates for patients aged ≥12 years.[5,6]
- Initial approval of voxelotor was based on results from the phase 3 HOPE trial, in which voxelotor-treated adolescents and adults with SCD achieved a significantly increased level of Hb and decreased markers of hemolysis compared with placebo-treated patients.[4]
- This real-world study expands upon our understanding of the safety and efficacy of voxelotor in clinical practice, complementing results observed in the pivotal HOPE trial.

1. Kato GJ, et al. *Nat Rev Dis Primer*. 2018;4:18010. 2. Ware RE, et al. *Lancet*. 2017;390(10091):311-323 3. Estepp JH, et al. *Am J Hematol*. 2018;93:326-329. 4. Vichinsky E, et al. *N Engl J Med*. 2019;381(6):509-519. 5. Oxbryta Prescribing Information. Global Blood Therapeutics; December 2021. 6. Global Blood Therapeutics. Accessed February 16, 2022. https://www.globenewswire.com/en/news-release/2022/02/16/2386014/37049/en/European-Commission-Approves-Oxbryta-voxelotor-for-the-Treatment-of-Hemolytic-Anemia-in-Patients-with-Sickle-Cell-Disease-Age-12-Years-and-Older.html#:~:text=In%20November%202019%2C%20the%20U.S.,of%20age%20and%20older%20.

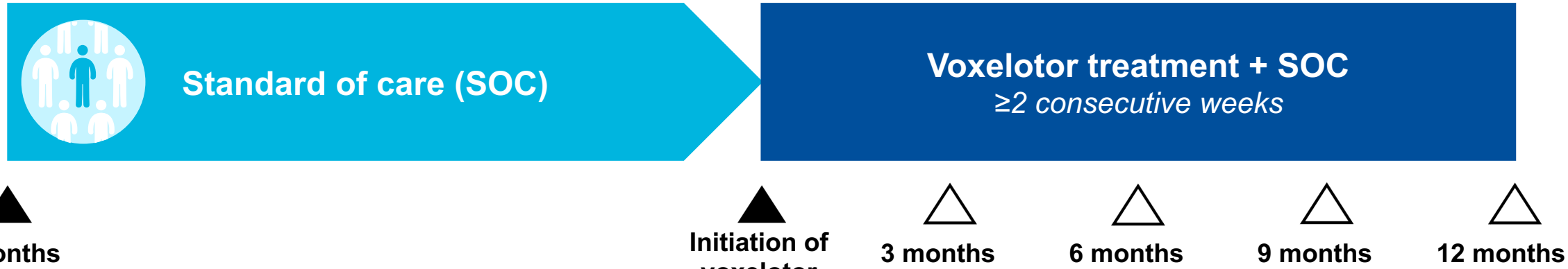
Objective

- The Retrospective Study to Evaluate Outcomes in Patients With Sickle Cell Disease Treated With Oxbryta (RETRO) aims to characterize real-world safety and effectiveness of voxelotor in adults and adolescents with SCD treated with voxelotor as part of their usual care.

SCD, sickle cell disease.

Methods

- RETRO is a post-marketing study (NCT04930328) that included voxelotor-treated patients from 9 clinical sites in the United States.[1]
- Patients with SCD aged ≥12 years who received voxelotor for ≥2 consecutive weeks were included.
- Laboratory and clinical data were collected retrospectively from patients' medical records from 1 year before and up to 1 year after the first voxelotor dose.



Patients were ineligible if they had participated in a prior investigation (within 1 year), clinical trial, or expanded access program with voxelotor

Assessments: hematological outcomes, clinically significant events, healthcare resource utilization, health-related quality of life, and safety

SCD, sickle cell disease.

ClinicalTrials.gov identifier: NCT04930328. Accessed April 15, 2022. https://clinicaltrials.gov/ct2/show/NCT04930328.

Results: Patient Demographics

	Patients (N=216)[a]
Age, years	
Mean (SD)	33.5 (14.2)
Range	12, 71
Patients per age group, n (%)	
<18 years	31 (14.4)
18 to <45 years	136 (63.0)
45 to <65 years	43 (19.9)
≥65 years	6 (2.8)
Sex, n (%)	
Male	96 (44.4)
Female	120 (55.6)
HbS genotype, n (%)	
HbSS	199 (92.1)
HbSβ^0	10 (4.6)
HbSβ$^+$	3 (1.4)
HbSC	2 (0.9)
Other	1 (0.5)

	Patients (N=216)[a]
Patient insurance, n (%)	
Private	94 (43.5)
Medicaid	75 (34.7)
Medicare	36 (16.7)
Medicaid & Medicare	7 (3.2)
Self-insured	2 (0.9)
Baseline Hb, g/dL	
Mean (SD)	7.8 (1.5)
Range	4.3, 13.5
Patient baseline Hb, n (%)	
< 7 g/dL	60 (27.8)
7 to 10.5 g/dL	140 (64.8)
>10.5 g/dL	9 (4.2)
Concomitant HU, n (%)	
Yes	147 (68.1)
No	68 (31.5)

[a]Missing data: HbS genotype (n=1); patient insurance (n=2); patient baseline Hb (n=7); concomitant HU (n=1).
Hb, hemoglobin; HbS, sickle hemoglobin; HbSC, hemoglobin SC disease; HbSβ$^+$, sickle beta plus thalassemia; HbSβ^0, sickle beta zero thalassemia; HbSS, homozygous for sickle hemoglobin gene; HU, hydroxyurea; SD, standard deviation.

Results: Voxelotor Administration

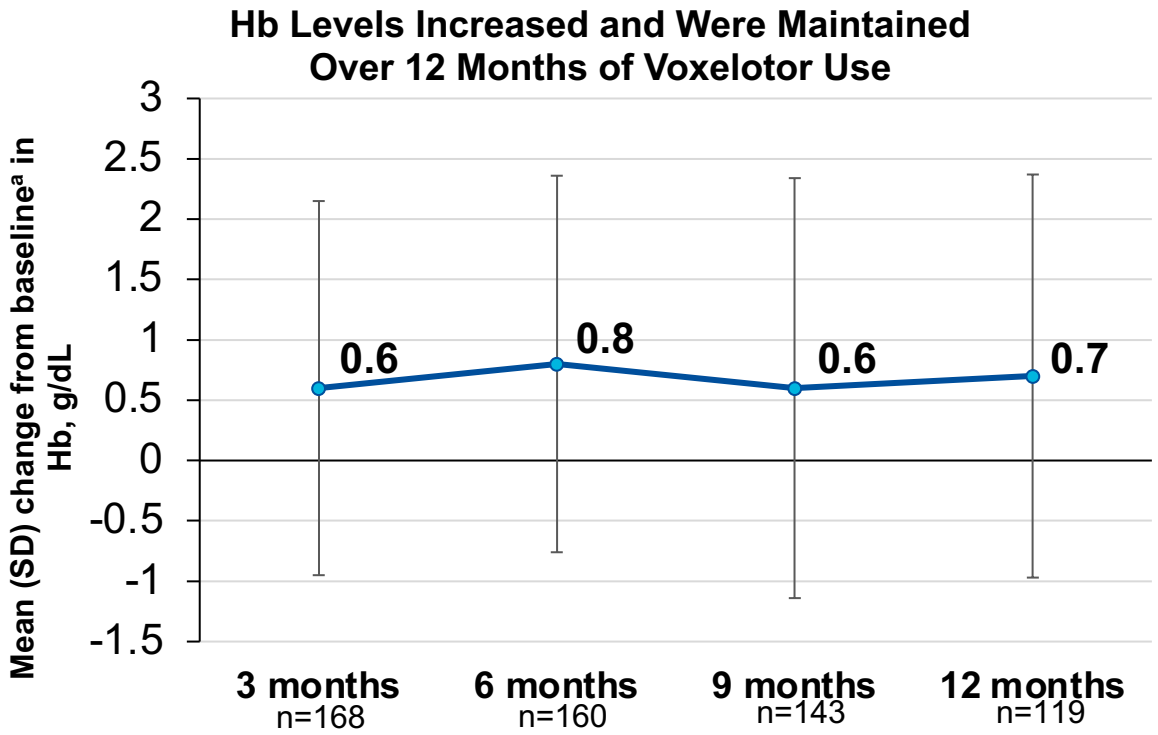
	Patients (N=216)
Mean (SD) duration of therapy, weeks	51.1 (25.5)
Initial prescription strength, n (%)	
500 mg	13 (6.0)
1000 mg	16 (7.4)
1500 mg	187 (86.6)
Dosage change, n (%)	
Yes[a]	54 (25.0)
Adjustment	46 (21.3)
Interruption	8 (3.7)
No[a]	161 (74.5)
Reasons for voxelotor use, n (%)	
Reducing anemia	151 (69.9)
Reducing pain	51 (23.6)
Reducing frequency of VOCs	45 (20.8)
Reducing need for blood transfusion	17 (7.9)
Other	44 (20.4)

- Mean duration of voxelotor treatment was 51 weeks; 86.6% initiated treatment with 1500 mg.
  - Treatment duration was variable:
    - <3 months, 10.2%
    - 3 to <6 months, 7.9%
    - 6 to <9 months, 10.6%
    - 9 to <12 months, 13.0%
    - ≥12 months, 58.3%
- A total of 25% of patients (n=54) had a dose change initiated by their physician.
  - Reasons for dose change were:
    - Adverse event (n=37)
    - Pill burden (n=2)
    - Lack of efficacy (n=1)
    - Other (n=22)

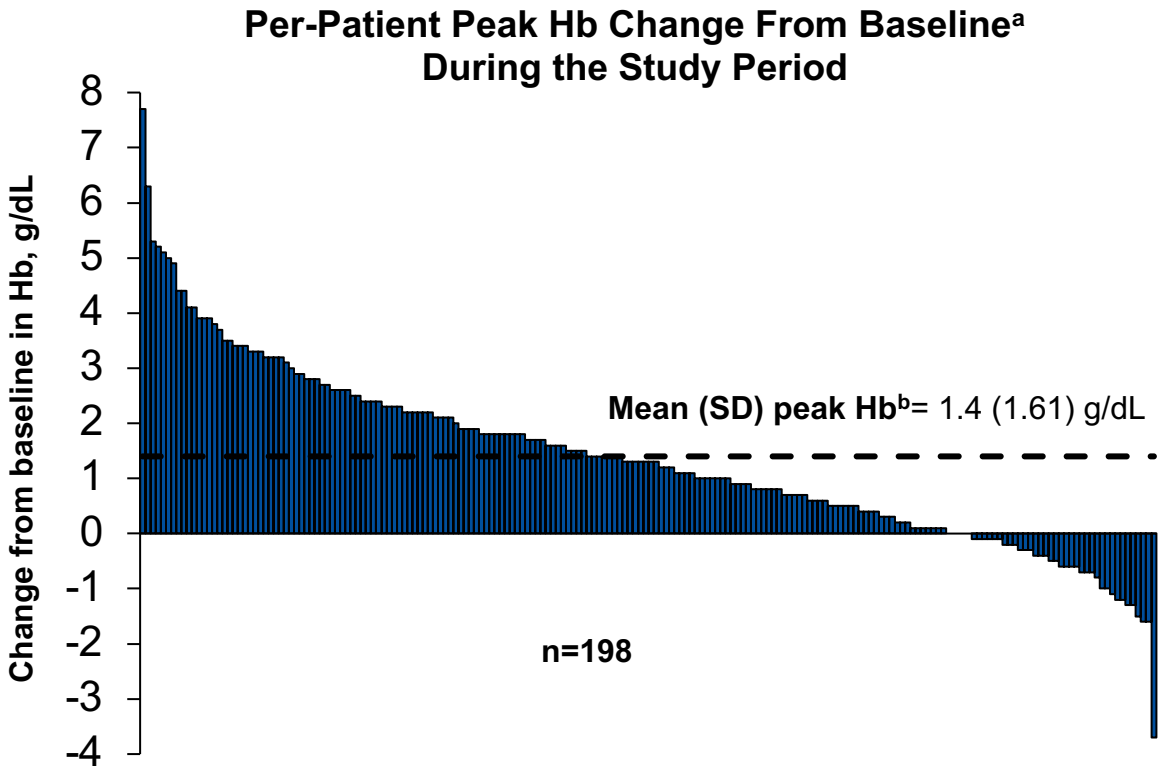
[a]Missing data for n=1 patient.
SD, standard deviation; VOC, vaso-occlusive crisis.

Results: Improvements in Hb Levels With Voxelotor

- Mean Hb levels remained elevated over the 12-month treatment period.



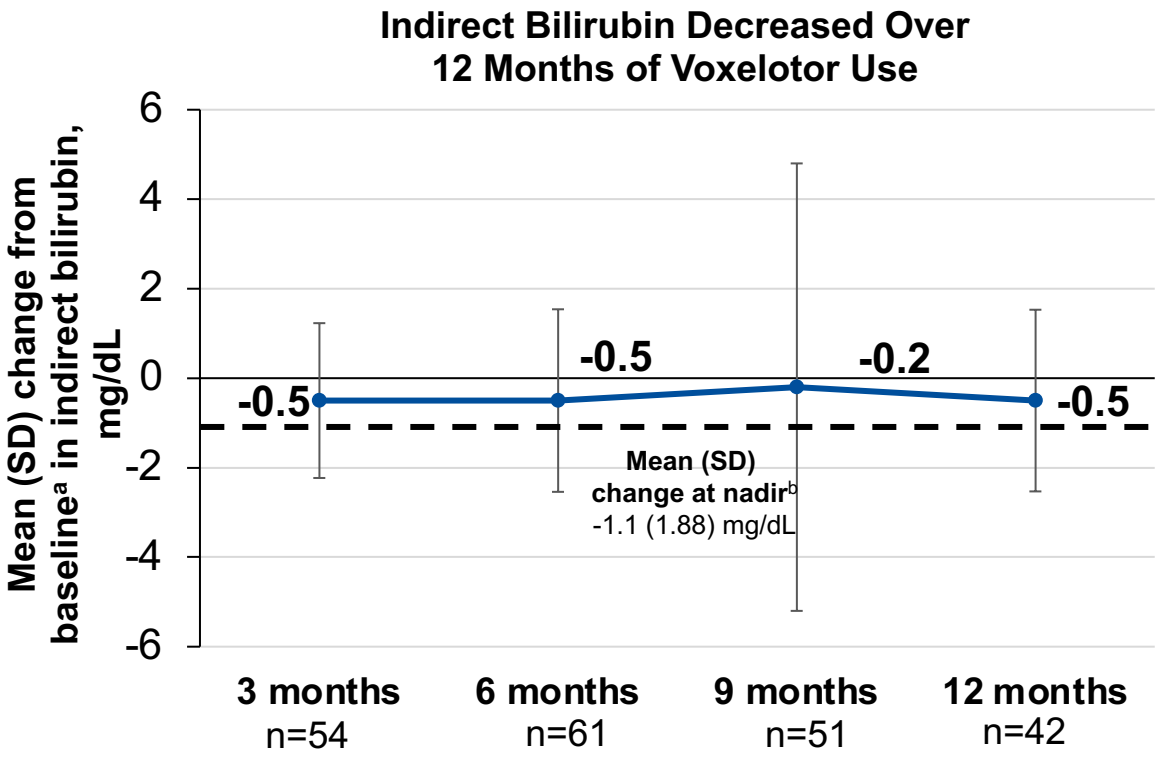
- Mean (SD) peak Hb increased from baseline by 1.4 (1.61) g/dL with voxelotor treatment.

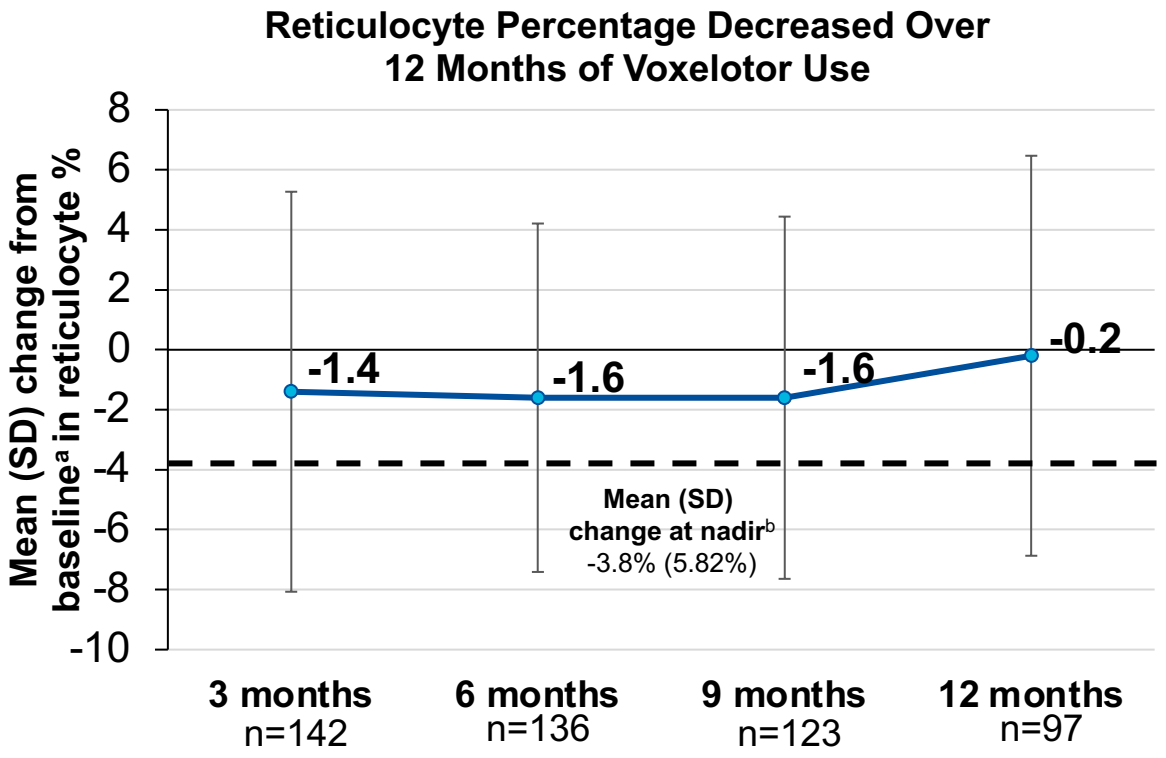


[a]Baseline was defined as the mean of available measurements up to 1 year prior to initiation of voxelotor treatment.
[b]Peak Hb was defined as the highest post-baseline Hb value while on voxelotor treatment.
[c]With recorded Hb 12 months post-treatment.
Hb, hemoglobin; HU, hydroxyurea; SD, standard deviation.

Results: Reductions in Hemolytic Markers With Voxelotor

- Mean indirect bilirubin and mean reticulocyte percentage remained decreased over the 12 months after voxelotor initiation.





[a]Baseline was defined as the mean of available measurements up to 1 year prior to initiation of voxelotor treatment.
[b]Nadir indirect bilirubin and reticulocyte percentage were defined as the lowest post-baseline values while on voxelotor treatment.
SD, standard deviation.

Results: Safety and Tolerability of Voxelotor

TEAEs related to voxelotor treatment, n (%)	Patients (N=216)
Total	55 (25.5)
TEAEs related to treatment with ≥3% incidence	
Diarrhea	28 (13.0)
Headache	16 (7.4)
Abdominal pain	7 (3.2)
Rash	12 (5.6)

TEAEs not related to SCD, n (%)	
Total	80 (37.0)
Severity of TEAEs, n (%)[a]	
Mild	32 (14.8)
Moderate	22 (10.2)
Severe	25 (11.6)

TEAEs of interest or leading to voxelotor dose modification or discontinuation, n (%)	
Total	67 (31.0)
TEAEs with ≥3% incidence	
Diarrhea	37 (17.1)
Headache	27 (12.5)
Abdominal Pain	7 (3.2)
Rash	14 (6.5)

[a]Missing data on TEAE severity in 1 (0.5%) patient.
SCD, sickle cell disease; TEAE, treatment-emergent adverse event.

RETRO Limitations

- As with all retrospective studies, data were limited to those captured in medical records.
- Data in this study were limited to 9 clinical sites in the United States.
- The incidences of non-SCD-related adverse events in RETRO were lower from those observed in the phase 3 HOPE trial, which was likely due to the retrospective nature of this study in which AEs were not solicited.

SCD, sickle cell disease.

Conclusions

RETRO is the largest multicenter study to collect and analyze retrospective data from patients with SCD treated with voxelotor in a real-world setting, providing essential information on the clinical use of voxelotor in patients aged ≥12 years.

Results were consistent with those of the pivotal HOPE trial, demonstrating that voxelotor increases Hb levels and decreases hemolytic markers in clinical practice.

Fewer than 40% of participants reported a TEAE unrelated to SCD, and most TEAEs were mild to moderate in severity; no new safety signals were identified.

Hb, hemoglobin; SCD, sickle cell disease; TEAEs, treatment-emergent adverse events.

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