Real-World Experience of Patients with Sickle Cell Disease Treated with Voxelotor: A Multicenter, Retrospective Study

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VOXELOTOR IS AN ORAL, ONCE-DAILY SICKLE HEMOGLOBIN POLYMERIZATION INHIBITOR

Sickle cell disease (SCD) is an inherited systemic disorder in which sickle hemoglobin (HbS) polymerization triggers red blood cell sickling, chronic hemolytic anemia, and recurrent episodes of vaso-occlusion.[1]

SCD-related complications lead to acute and chronic life-threatening events, cumulative organ damage, disability, and early mortality.[2]

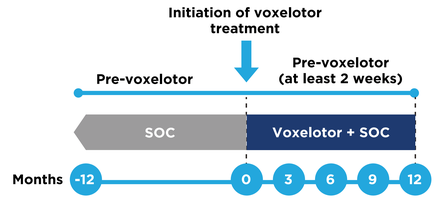
Voxelotor has been shown to increase hemoglobin (Hb) levels and reduce markers of hemolysis.[3,4]

Voxelotor, a first-in-class HbS polymerization inhibitor, is approved in the United States for treatment of SCD in adults and adolescents aged ≥12 years, based on the efficacy and safety data from the randomized, placebo-controlled, multicenter HOPE trial.[3,5]

RETRO: STUDY DESIGN

- RETRO is a post-marketing study designed to collect, aggregate, and characterize real-world, retrospective laboratory and clinical data on adults and adolescents (aged ≥12 years) with SCD treated with voxelotor as part of their usual care at multiple clinical centers in the United States.
  - The study will include approximately 200 patients with SCD from 10 study sites.
- Data available from patients' medical records (and other secondary data sources) 1 year before and up to 1 year after the first voxelotor dose were documented in de-identified case report forms via an electronic data capture system.
- A steering committee provided independent SCD expertise to inform the design and conduct of the voxelotor registry.

KEY ELIGIBILITY CRITERIA
- Patients with documented SCD (all genotypes)
- Treatment with voxelotor for ≥2 consecutive weeks
- No current or prior participation (within 1 year before enrollment) in an investigation, clinical trial, or expanded access program with voxelotor in which the patient received voxelotor treatment



SOC, standard of care.

DEMOGRAPHICS AND BASELINE CHARACTERISTICS[a]

	Patients (N=140)
Age, years	
Mean (SD)	32.7 (13.36)
Minimum, maximum	12, 71
Age groups, n (%)	
<18 years	22 (15.7)
18 to <35 years	63 (45.0)
35 to <45 years	25 (17.9)
45 to <65 years	27 (19.3)
≥65 years	2 (1.4)
Missing	1 (0.7)
Sex, n (%)	
Male	62 (44.3)
Female	78 (55.7)
Race, n (%)	
Black or African American	123 (87.9)
Other	12 (8.6)
White	3 (2.1)
American Indian or Alaska Native	1 (0.7)
Multiracial[b]	1 (0.7)

	Patients (N=140)
HbS genotype, n (%)	
HbSS	122 (87.1)
HbSβ[0]	8 (5.7)
HbSC	1 (0.7)
HbSβ[+]	2 (1.4)
Other	1 (0.7)
Missing	6 (4.3)
Baseline Hb	
n (%)	
<7 g/dL	35 (25.0)
7 to 10.5 g/dL	83 (59.3)
>10.5 g/dL	7 (5.0)
Missing	15 (10.7)
Mean (SD), g/dL	7.9 (1.67)
Range, g/dL	4.3-13.5
Current HU use, n (%)	
Yes	91 (65.0)
No	44 (31.4)
Missing	5 (3.6)

[a]Data cutoff: October 7, 2021. [b]Patients checking more than 1 race are classified as multiracial.

Hb, hemoglobin; HbS, sickle hemoglobin; HbSβ[0], sickle beta zero thalassemia; HbSβ[+], sickle beta plus thalassemia; HbSC, hemoglobin SC disease; HbSS, homozygous for SCD; SCD, sickle cell disease; HU, hydroxyurea.

STUDY DRUG ADMINISTRATION

	Patients (N=140)
Duration of therapy, weeks	
Mean (SD)	53.2 (23.05)
Minimum, maximum	5, 124
Duration of therapy category	
<3 months	7 (5.0)
3 to <6 months	15 (10.7)
6 to <9 months	16 (11.4)
9 to <12 months	21 (15.0)
≥12 months	81 (57.9)
Initial prescribed dose strength, n (%)	
500 mg	10 (7.1)
1000 mg	8 (5.7)
1500 mg	122 (87.1)
Reasons for prescribing voxelotor,[a] n (%)	
Reduces anemia	90 (64.3)
Reduces pain	44 (31.4)
Reduces the frequency of vaso-occlusive crises	34 (24.3)
Reduces the need for blood transfusion	12 (8.6)
Other	27 (19.3)

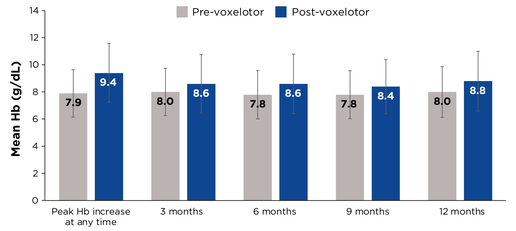
	Patients (N=140)
Dosage change initiated by physician, n (%)	
Yes[b]	31 (22.1)
Interrupted[c]	6 (4.3)
Dose adjustment[c]	26 (18.6)
No	73 (52.1)
Missing	36 (25.7)
Reason(s) for physician-initiated dose change,[a,c] n (%)	
Adverse event	23 (16.4)
Lack of efficacy	1 (0.7)
Pill burden	1 (0.7)
Other	12 (8.6)

[a]Physicians can enter multiple reasons. [b]Patients may have multiple selected during the administration. [c]Percentages based on total number of patients (N=140).

RESULTS

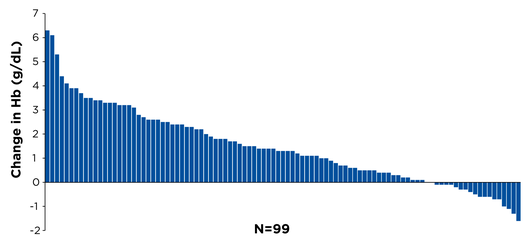
Mean Change in Hb in Response to Voxelotor Treatment through Month 12

Compared to baseline, mean (SD) post-treatment Hb level increased by:
- 0.7 (1.59) g/dL at 3 months
- 0.8 (1.57) g/dL at 6 months
- 0.6 (1.53) g/dL at 9 months
- 0.8 (1.59) g/dL at 12 months



Timeline of x-axis represents the number of months after initiation of voxelotor treatment. Error bars represent SD values.
Hb, hemoglobin.

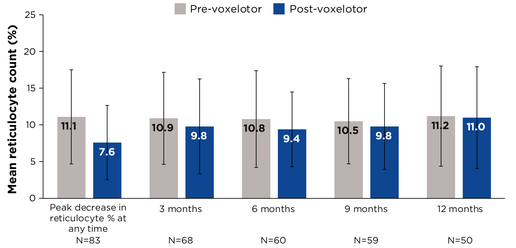
Per-Patient Peak Hb Change from Baseline during the Study Period



Hb, hemoglobin.

Mean Change in Reticulocyte Percentage in Response to Voxelotor Treatment through Month 12

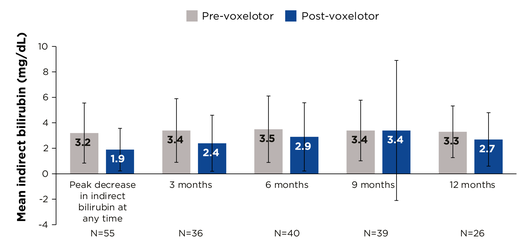
Compared to baseline, mean (SD) post-treatment reticulocyte percentage decreased by:
- 1.1% (6.56%) at 3 months
- 1.4% (6.13%) at 6 months
- 0.6% (5.64%) at 9 months
- 0.3% (7.46%) at 12 months



Timeline of x-axis represents the number of months after initiation of voxelotor treatment. Error bars represent SD values.

Mean Change in Indirect Bilirubin in Response to Voxelotor Treatment through Month 12

Compared to baseline, mean (SD) post-treatment indirect bilirubin decreased by:
- 1.0 (1.68) mg/dL at 3 months
- 0.6 (2.16) mg/dL at 6 months
- 0.0 (5.54) mg/dL at 9 months
- 0.6 (2.30) mg/dL at 12 months



Timeline of x-axis represents the number of months after initiation of voxelotor treatment. Error bars represent SD values.

Safety and Tolerability of Voxelotor

	Patients (N=140)
Treatment-emergent adverse events not related to SCD, n (%)	
Patients with any adverse event	43 (30.7)
Adverse events with ≥5% incidence	
Diarrhea	19 (13.6)
Headache	11 (7.9)
Rash	8 (5.7)
Uncoded	17 (12.1)
Voxelotor dose discontinuations and modifications due to adverse events, n (%)	
Discontinuation	8 (5.7)
Dose interruption	17 (12.1)
Dose reduction	22 (15.7)

SCD, sickle cell disease.

CONCLUSIONS

RETRO is the first multicenter, retrospective study to examine the real-world effectiveness of voxelotor and describe the observed changes in laboratory and clinical outcomes after ≥2 weeks of therapy in patients with SCD.

This study shows that voxelotor treatment was associated with increased Hb levels and decreased hemolytic markers.

The safety data are consistent with those from the HOPE trial.

Further evaluation is needed, with additional data from all 10 sites; findings will be presented later.

DISCLOSURES

Biree Andemariam
- Consultant, advisory board: CRISPR/Vertex, Pfizer, Cyclerion, Sanofi Genzyme
- Consultant: Global Blood Therapeutics, Community Health Network of Connecticut, Inc.
- Consultant, research funding: Novartis Pharmaceuticals

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- Consultant, advisory board: Forma Therapeutics
- Consultant: Terumo, Acceleron, Pfizer, Chiesi, Cyclerion, Emmaus
- Advisory board: Micella Biopharma

Modupe Idowu
- Research funding: Pfizer, Ironwood, Forma Therapeutics
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Nirmish Shah
- Speaker, research funding, consultant: Global Blood Therapeutics
- Speaker, research funding: Novartis Pharmaceuticals
- Consultant: bluebird bio, CSL Behring
- Speaker: Alexion Pharmaceuticals

Richard Drachtman
- Nothing to disclose

Archana Sharma
- Nothing to disclose

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Susanna Curtis
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Caterina Minniti
- Consultant: Global Blood Therapeutics, Novartis Pharmaceuticals, NovoNordisk, Roche, Forma, Agios, Chiesi

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ACKNOWLEDGMENTS

- The authors wish to thank all the patients with SCD, families, caregivers, RETRO investigators, research nurses, study coordinators, and support staff who contributed to this study.
- The authors thank site staff who assisted with data entry:
  - Franklin Ude, MPH, New England Sickle Cell Institute
  - Alicia Patrick, MA, and Megan Lattanze, Levine Cancer Institute
  - Arthi Sridhar, MD, University of Texas Health
  - Stephanie Padrick, Duke University School of Medicine
  - Ben Richlin, MD, Rutgers Robert Wood Johnson Medical School
  - Charmaine Williams-Farr, Central Michigan University
  - Katherine Jolley and Hae Soo Park, Brigham and Women's Hospital
  - Ishaan Sangwan, University of Texas Southwestern Medical Center
  - Julissa Morales, Montefiore Medical Center
- This study was supported by Global Blood Therapeutics.

The authors thank Arpita Biswas, PhD (Healthcare Consultancy Group, with funding from Global Blood Therapeutics) for editorial assistance in the preparation of this report.

Presented at: American Society of Hematology Annual Meeting & Exposition 2021; December 11-14, 2021