# Real-World Experience of Voxelotor for the Treatment of Patients With Sickle Cell Disease: A Single-Center Study

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## Introduction

- Sickle cell disease (SCD) is an inherited disorder of the red blood cells in which sickle hemoglobin (Hb) polymerizes and leads to a detrimental change of shape in the red blood cell.
- This change, known as sickling, can trigger serious consequences, including chronic hemolysis, anemia, and episodic vaso-occlusion, and often leads to complications such as cumulative organ damage, disability, and accelerated mortality.
- Voxelotor is a first-in-class therapy that interferes with sickle Hb polymerization, increases Hb levels, and reduces hemolysis. It is FDA approved for the treatment of SCD in patients aged 12 years and older.
- The objective of this ongoing study is to quantify the clinical response to voxelotor treatment in a single-center study of 77 patients with baseline data from 12 to 70 years of age.

**Methods:**

- We collected real-world clinical data from 77 SCD patients with baseline data (aged 12-70 years) at the Prisma Health – Upstate Comprehensive SCD Program, Greenville, South Carolina, USA, under a data collection protocol for standard-of-care clinical data.
- All patients included in this analysis had been receiving voxelotor for a minimum of 1.9 months.
- Hematologic outcome data for 11 patients were not included in the analysis for the following reasons: n=2 each for adverse events (hypersensitivity reaction [n=1], diarrhea [n=1]), noncompliance, medicine not received, and unknown; n=1 each for insurance issues, inability to swallow, and loss to follow-up.
- Hb and bilirubin levels and reticulocyte percentages were compared before and during voxelotor therapy.

## Results

- Baseline demographics for the 77 patients included a mean (SD) age of 30.4 years (14.2 years), 63% female, and 86% with the HbSS (sickle cell anemia) genotype.
- The mean (range) duration of voxelotor treatment was 9.7 months (1.9-17 months). Three patients received between 1.9 and 3 months of therapy. All other patients had more than 5 months of therapy.
- Signs of clinical improvement included increased Hb. Decreased reticulocyte percentage and total bilirubin levels were observed after voxelotor therapy.
- Regardless of baseline Hb levels, patients responded favorably to voxelotor therapy. In patients treated with hydroxyurea at baseline, a more robust improvement with voxelotor was observed, suggesting a complementary effect with combination hydroxyurea and voxelotor therapy.
- Adverse effects of voxelotor therapy were mostly mild and self-limited. Four patients had adverse events (2 diarrhea, 1 rash, 1 fever) that led to temporary dose modification.

## Demographics and Baseline Characteristics

| | Hydroxyurea use | No hydroxyurea use | Total[a] |
|---|---|---|---|
| N | 62 | 14 | 76 |
| **Age**, years | | | |
| Mean (SD) | 28.2 (12.2) | 41.7 (16.5) | 30.4 (14.2) |
| Minimum, maximum | 12, 70 | 18, 66 | 12, 70 |
| **Sex**, n (%) | | | |
| Male | 27 (44) | 1 (7) | 28 (37) |
| Female | 35 (56) | 13 (93) | 48 (63) |
| **HbS genotypes**, n (%) | | | |
| HbSS | 56 (90) | 9 (64) | 65 (86) |
| HbSC | 1 (2) | 5 (36) | 6 (8) |
| HBSβ⁺ | 1 (2) | 0 | 1 (1) |
| HbSβ⁰ | 4 (6) | 0 | 4 (5) |
| **Mean baseline Hb**, n (%) | | | |
| <7 g/dL | 9 (15) | 3 (21) | 12 (16) |
| 7-10 g/dL | 43 (72) | 8 (57) | 51 (69) |
| >10 g/dL | 8 (13) | 3 (21) | 11 (15) |

[a]Note: Missing hydroxyurea data (n=1) and missing baseline Hb (n=3).
Hb, hemoglobin; HbS, sickle hemoglobin; HbSβ⁰, sickle beta zero thalassemia; HbSβ⁺, sickle beta plus thalassemia; HbSC, hemoglobin SC disease; HbSS, sickle cell anemia.

## Duration of Voxelotor Therapy

| | Total[a] |
|---|---|
| N | 77 |
| **Months** | |
| Mean (SD) | 9.7 (3.8) |
| Minimum, maximum | 1.9, 17.0 |
| N | 75 |

[a]Missing data, n=2 (3%) because patients lacked a start date for voxelotor.
All but 3 treated patients had at least 5 months of voxelotor therapy.
Note: Data cutoff date of May 13, 2021.

## Clinical Response to Voxelotor Treatment

| | Pre-voxelotor | Post-voxelotor | Absolute change from baseline | Relative change from baseline |
|---|---|---|---|---|
| **Hb**, g/dL | | | | |
| N | 74 | 66 | 66 | 66 |
| Mean (SD/ confidence interval) | 8.3 (1.4) | 10.3 (1.5) | 2.0 (1.0) | 25.6 (22.1, 29.0) |
| **Reticulocytes**, % | | | | |
| N | 73 | 66 | 66 | 66 |
| Mean (SD/ confidence interval) | 11.5 (5.9) | 6.5 (4.1) | −4.6 (3.9) | −37.6 (−44.2, −31.0) |
| **Total bilirubin**, mg/dL | | | | |
| N | 72 | 65 | 65 | 65 |
| Mean (SD/ confidence interval) | 3.5 (2.7) | 2.0 (1.4) | −1.4 (2.1) | −31.9 (−41.6, −22.1) |

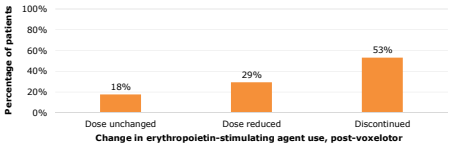
Hb, hemoglobin.

## Adverse Events Leading to Temporary Dose Modification

| Reported adverse event | Action taken | Event resolved |
|---|---|---|
| Diarrhea | Reduced dose to 1000 mg for 1 month; resumption to 1500 mg | Yes |
| Diarrhea | Reduced dose to 1000 mg; resumption to 1500 mg | Yes |
| Rash | Reduced dose to 1000 mg; resumption to 1500 mg with loratadine | Yes |
| Fever | Reduced dose to 500 mg; resumption to 1500 mg | Yes |

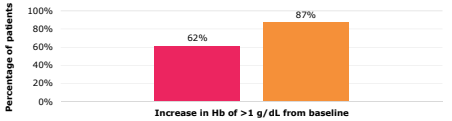
## Change in Concomitant Medication Use After Voxelotor Therapy

**82% of patients who received erythropoietin-stimulating agents reduced or discontinued use after voxelotor therapy.**



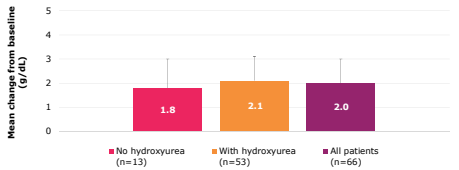

- Hydroxyurea use was prevalent in most patients at baseline (62/76) and remained unchanged after therapy.
- One patient who received regular transfusions before treatment no longer needed them after voxelotor therapy.

## Clinical Response to Voxelotor Treatment by Hydroxyurea Use

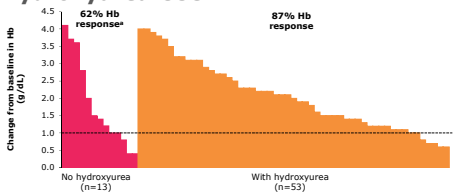



Hb, hemoglobin.

## Clinical Response to Voxelotor Treatment
### Hemoglobin by Hydroxyurea Use




## Per-Patient Hb Change by Hydroxyurea Use

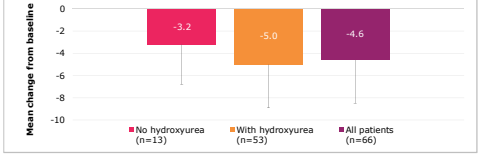



[a]Defined as an increase in Hb >1 g/dL.
Hb, hemoglobin.

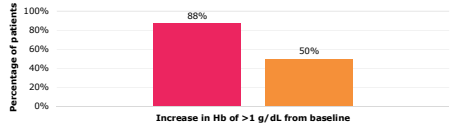
## Clinical Improvement as Measured by PGI-C and CGI-C


CGI-C, Clinical Global Impression of Change; PGI-C, Patient Global Impression of Change.

## Clinical Response to Voxelotor Treatment
### Reticulocytes (%) by Hydroxyurea Use

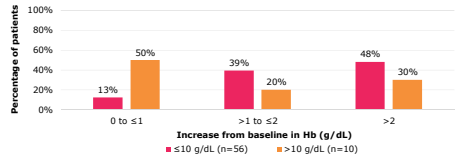



## Responder Analysis to Voxelotor Treatment by Baseline Hb Concentration (≤10 g/dL vs >10 g/dL)



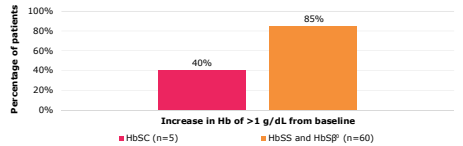

Hb, hemoglobin.

## Magnitude of Hb Change by Baseline Hb Concentration (≤10 g/dL vs >10 g/dL)



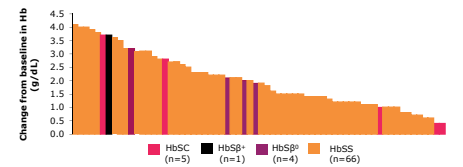

Hb, hemoglobin.

## Clinical Response to Voxelotor Treatment by Genotype




Note: One patient with the HbSβ⁺ genotype is not included in the subgroup analysis.
Hb, hemoglobin; HbSβ⁰, sickle beta zero thalassemia; HbSβ⁺, sickle beta plus thalassemia; HbSC, hemoglobin SC disease; HbSS, sickle cell anemia.

## Per-Patient Hb Change by Genotype

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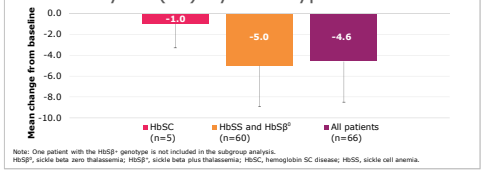
## Clinical Response to Voxelotor Treatment
### Reticulocytes (%) by Genotype

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## Conclusions

- This ongoing study examines the real-world impact of voxelotor in an SCD population aged between 12 and 70 years.
- This study was conducted in a lifespan model setting that allows more active monitoring of patients.
- Greater responses to voxelotor therapy in Hb, total bilirubin levels, and reticulocyte percentage were observed compared with those in the HOPE trial.
- A clinically significant Hb response was observed in patients who were not treated with hydroxyurea; an even greater response was observed in patients who were treated with hydroxyurea, suggesting a possible complementary effect between voxelotor and hydroxyurea therapy.
- The greatest Hb response was observed in patients with baseline Hb ≤10 g/dL; patients with baseline Hb >10 g/dL also showed increases in Hb.
- Recorded adverse events were infrequent, and all resolved after temporary dose modification.
- Further evaluation with a larger population of patients with SCD and longer follow-up period will help confirm these findings.

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