Long-Term Efficacy and Safety of Voxelotor in Adolescents and Adults with Sickle Cell Disease: HOPE Trial 72-Week Analysis

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Disclosures

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• Membership on entity’s advisory committees: Global Blood Therapeutics, Agios Pharmaceuticals, Novartis, Forma Therapeutics, Imara
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Voxelotor Is an Oral, Once-Daily HbS Polymerization Inhibitor

SCD is a lifelong, inherited disorder characterized by HbS polymerization and associated with chronic hemolytic anemia, episodic VOCs, and progressive organ dysfunction.¹

Voxelotor is indicated for the treatment of SCD in adults and adolescent patients ≥12 years of age.²

In the phase 3 HOPE trial, significantly greater proportion of patients achieved a >1 g/dL Hb increase with voxelotor 1500 mg compared with placebo at week 24 (51.1% vs 6.5%, P<0.001).³

Here we report the long-term efficacy and safety of voxelotor 1500 mg at 72 weeks, the conclusion of the placebo-controlled HOPE trial
HOPE Trial: Study Design

Phase 3, randomized, double-blind, placebo-controlled, multicenter trial evaluating voxelotor

Eligibility criteria
- Aged 12 to 65 years with confirmed SCD
- Hb 5.5 to 10.5 g/dL
- Between 1 and 10 VOCs in prior 12 months
- Concomitant HU, if stable for ≥3 months

Week 72 Analyses
- Hb level: post-baseline levels achieved and change from baseline
- Hemolysis markers: change from baseline
- Annualized incidence of VOCs
- Safety: AEs during the treatment period

Baseline characteristics were generally well balanced

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Voxelotor 1500 mg Resulted in Rapid and Durable Improvements in Hb Maintained Through Week 72

Adjusted Mean Change in Hb Levels From Baseline to Week 72

*Adjusted Mean Change in Hb Levels From Baseline to Week 72

*P<0.001 versus placebo at week 72.
Analysis of change from baseline in Hb level over time was based on a regression model for repeated measures. Hb values within 8 weeks after any red blood cell transfusion were imputed as the last value before the transfusion. Hb values obtained after HU treatment had been initiated post-randomization were excluded for the patients who had not been receiving HU at baseline. Hb, hemoglobin; HU, hydroxyurea.
Patients Receiving Voxelotor Achieved Substantially Larger Improvements in Hb Throughout the 72-Week Treatment Period

Proportion of Patients Achieving Hb Increases >1 g/dL, >2 g/dL, and >3 g/dL at Any Point During the 72-Week Treatment Period

Baseline and Average Post-baseline Hb Level Achieved

For each patient, the average post-baseline Hb value is the mean of all Hb values for each post-baseline summary visit (based on window average) up to week 72.

Hb, hemoglobin.

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*For each patient, the average post-baseline Hb value is the mean of all Hb values for each post-baseline summary visit (based on window average) up to week 72. Hb, hemoglobin.*
Improvements in Markers of Hemolysis Were Observed at Week 72

<table>
<thead>
<tr>
<th>Hemolysis Marker</th>
<th>Difference in Adjusted Mean Percent Change from Baseline to Week 72, Voxelotor vs Placebo (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indirect bilirubin*</td>
<td>−26.6% (−40.2%, −13.0%)</td>
</tr>
<tr>
<td>Reticulocytes percentage*</td>
<td>−18.6% (−33.9%, −3.3%)</td>
</tr>
<tr>
<td>Absolute reticulocytes</td>
<td>−5.8% (−23.4%, 11.9%)</td>
</tr>
<tr>
<td>Lactate dehydrogenase</td>
<td>−4.8% (−13.8%, 4.1%)</td>
</tr>
</tbody>
</table>

*P<0.05 versus placebo.
Analysis of change from baseline in markers of hemolysis were based on a regression model for repeated measures.
Hb, hemoglobin.
## TEAEs and Rates of Treatment Discontinuation Were Similar Between Treatment Groups During the 72-Week Treatment Period

<table>
<thead>
<tr>
<th></th>
<th>Voxelotor 1500 mg n=88</th>
<th>Placebo n=91</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with TEAEs not-related to SCD(^a), n (%)</td>
<td>85 (96.6)</td>
<td>82 (90.1)</td>
</tr>
<tr>
<td>Grade ≥3</td>
<td>29 (33.0)</td>
<td>34 (37.4)</td>
</tr>
<tr>
<td>TEAEs leading to treatment discontinuation</td>
<td>9 (10.2)</td>
<td>6 (6.6)</td>
</tr>
<tr>
<td>Patients with serious TEAEs(^b) not-related to SCD(^a), n (%)</td>
<td>25 (28.4)</td>
<td>23 (25.3)</td>
</tr>
<tr>
<td>Serious TEAE leading to treatment discontinuation</td>
<td>4 (4.5)</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td>Patients with SCD-related TEAE(^a), n (%)</td>
<td>69 (78.4)</td>
<td>73 (80.2)</td>
</tr>
<tr>
<td>Grade ≥3</td>
<td>50 (56.8)</td>
<td>52 (57.1)</td>
</tr>
<tr>
<td>TEAEs leading to treatment discontinuation</td>
<td>4 (4.5)</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td>Patients with SCD-related serious TEAE(^a,b), n (%)</td>
<td>46 (52.3)</td>
<td>48 (52.7)</td>
</tr>
<tr>
<td>Serious TEAE leading to treatment discontinuation</td>
<td>3 (3.4)</td>
<td>2 (2.2)</td>
</tr>
</tbody>
</table>

\(^a\)SCD-related adverse events includes sickle cell anemia with crisis, acute chest syndrome, pneumonia (all terms), priapism, and osteonecrosis.

\(^b\)Serious TEAEs were defined as any untoward medical occurrence that resulted in death, life-threatening event, unexpected or prolonged hospitalizations, significant disability or incapacity, congenital anomaly or birth defect, other events that places the patient at jeopardy of a serious adverse event.

SCD, sickle cell disease; TEAE, treatment-emergent adverse events.
Conclusions

Voxelotor 1500 mg resulted in durable improvements in Hb levels and markers of hemolysis out to 72 weeks of treatment.

The majority of patients (approximately 90%) achieved a Hb improvement of >1 g/dL from baseline at one or more time points during the study.

Treatment with voxelotor remained well tolerated, with no new safety signals detected with longer-term follow-up.

These results support the sustained and chronic use of voxelotor to reduce anemia and hemolysis, thereby potentially mitigating the associated morbidity and mortality of SCD.

Hb, hemoglobin; SCD, sickle cell disease.
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