A Single Center’s Experience With Voxelotor (GBT440) Treatment in Patients With Severe Sickle Cell Disease

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BACKGROUND
• Sickle cell disease (SCD) is an autosomal recessive inherited disorder in which a mutation in the chain of hemoglobin (Hb) produces sickle-like hemoglobin (HbS), which polymerizes in the presence of low oxygen levels to form an insoluble fibrous protein that deforms red blood cells (RBCs) into a sickle shape and damage microangiopathy.
• Infrequent, sickled RBCs include the body’s microvasculature and hemolyze.
• This causes downstream effects that include tissue ischemia, pain, organ damage, and, early death.
• Current treatments for SCD inadequately control these complications and do not address the primary pathogenesis of SCD, leaving a high unmet need for additional therapies.

Voxelotor (previously called GBT440) is a first-in-class, once-daily drug for the treatment of SCD. The drug stabilizes the protein in the R-sickle shape, which is known to interrupt HbS polymerization.2

In a phase 3 study of voxelotor in over 1000 patients with severe SCD, Hb levels increased by 1.1 g/dL over 24 weeks of treatment with voxelotor.5

METHODS

GBT CMOSÁ PATENT TOXICITY USE
• Beginning in 2016, GBT granted voxelotor access to a limited number of patients with severe SCD through a compassionate use program.
• Inflexible, sickled RBCs occlude the body’s microvasculature and hemolyze with a consequent increase in Hb concentration.5

OBJECTIVE
• To contribute to the emerging clinical profile of voxelotor, we present the outcomes of 7 patients with severe SCD who received voxelotor for up to 17 months under Global Blood Therapeutics’ compassionate use program.

RESULTS

PATIENT DISPOSITION AND CHARACTERISTICS
• All patients had a diagnosis of SCD with a documented history of severe complications and severe clinical symptoms.
• Seven patients included in the compassionate use activity (i.e., Patients A–G). Voxelotor treatment was initiated between May 2016 and June 2017 with treatment durations ranging from 6 to 17 months.

PATIENT CHARACTERISTICS

Table 3. Patient Characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Race</th>
<th>SCD Phenotype</th>
<th>Hospitalizations for VOC</th>
<th>Transfusions</th>
<th>Iron Overload</th>
<th>Hemoglobin A2 (%)</th>
<th>Phlebotomy Count</th>
<th>Pain</th>
<th>Fatigue</th>
<th>Hospitalization for Severe Sickle Cell Crisis</th>
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<tr>
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<td>14</td>
<td>M</td>
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<td>SS S/B</td>
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<td>150</td>
<td>X</td>
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<td>7</td>
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<td>1</td>
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<td>M</td>
<td>B</td>
<td>SS S/B</td>
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</table>

PHQ-9 score was observed in Patients A and D 24 weeks before treatment initiation (13 vs 33, respectively) (Figure 6). Transfusions fell by 60% in Patient A, who was initially on continuous supplemental oxygen, had a RA SpO2 (% ) improved to 98%–99% with voxelotor treatment, and Patients A and E no longer required continuous supplemental oxygen therapy.

In 7 patients with severe SCD who were not eligible for the HOPE study, transfusion requirements, and hospitalizations for VOC. The 1500 mg dose was well tolerated and improved oxygen delivery with voxelotor.

—In 7 patients with severe SCA who were not eligible for the HOPE study, voxelotor was very well tolerated for a treatment duration up to 17 months. Patients received voxelotor for up to 17 months under Global Blood Therapeutics’ compassionate use program.

CONCLUSIONS
—In patients with severe SCA who were not eligible for the HOPE study, voxelotor administered by compassionate use substantially increased the quality of clinical, laboratory, and functional parameters, including Hb levels, hospital admissions related to VOC, frequency of transfusion, pain, overall well-being, and long-term survival.

—Compassionate clinical trials are needed to confirm the benefits of voxelotor in severe SCD.

REFERENCES:

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DISCLOSURES
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