
**Profound clinical benefit in a patient with
severe, transfusion-refractory anemia treated
with GBT440 through Compassionate Use**

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Disclosures

None

Presentation Overview

- Investigation of treatment options for patients with sickle cell is expanding after years of stagnation
- Unfortunately, options remain limited for patients with severe disease, including those with extreme anemia refractory to transfusion
- We report the experience of a patient treated for over 66 weeks with GBT440*, obtained for compassionate use from Global Blood Therapeutics, Inc., (GBT) the longest exposure to GBT440 of any patient to date

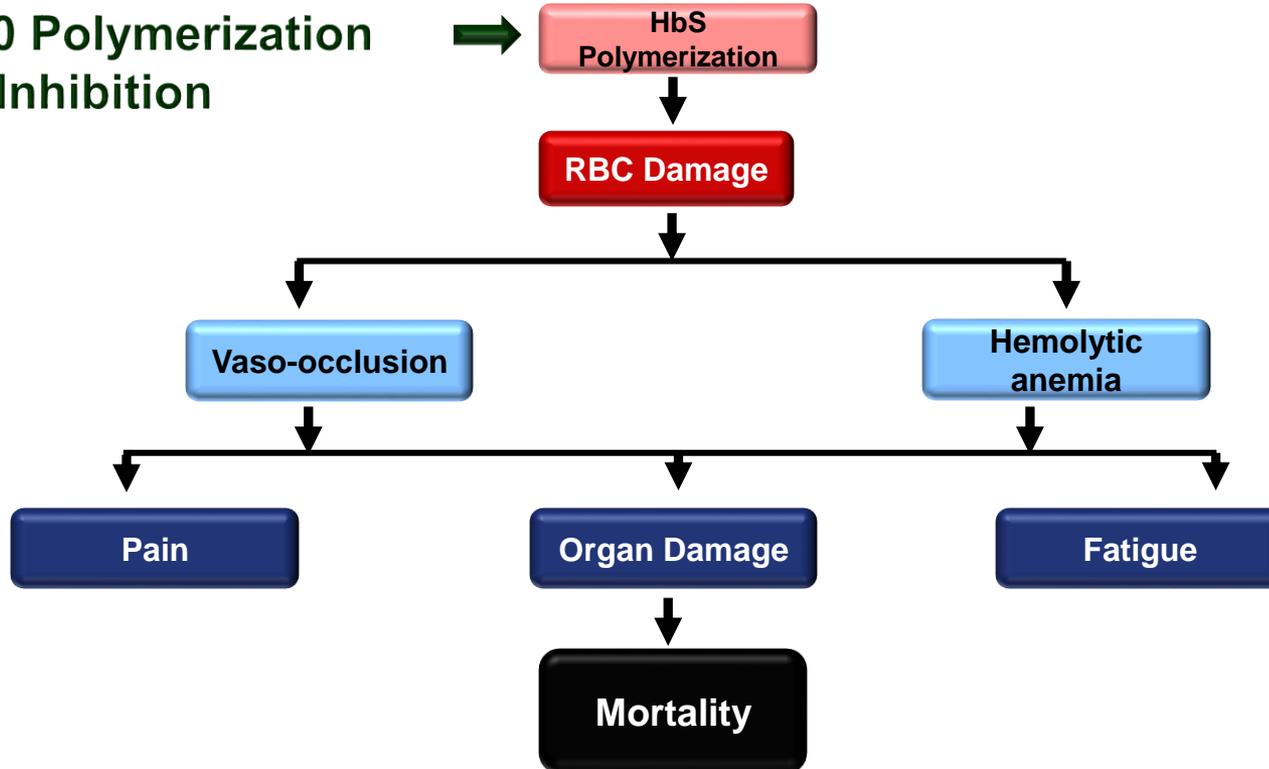
** GBT is an investigational drug for treatment of sickle cell disease and is not approved for patient use by the FDA or any other Regulatory Authority*

GBT440- Background

- **GBT440 is an oral, once-daily therapy that modulates hemoglobin's affinity for oxygen, thereby inhibiting hemoglobin polymerization in sickle cell disease**
 - **HbS polymerization is the trigger that initiates the cascade of events leading to all clinical problems in sickle cell disease including vaso-occlusive pain and anemia**
 - **By inhibiting HbS polymerization, GBT440 is expected to reduce or prevent the clinical manifestations of sickle cell disease**
 - **This hypothesis is being tested in the HOPE Phase 3 trial of GBT440 safety and efficacy**
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GBT440 Inhibits HbS polymerization, the fundamental cause of clinical injury in sickle cell disease

GBT440 Polymerization
Inhibition

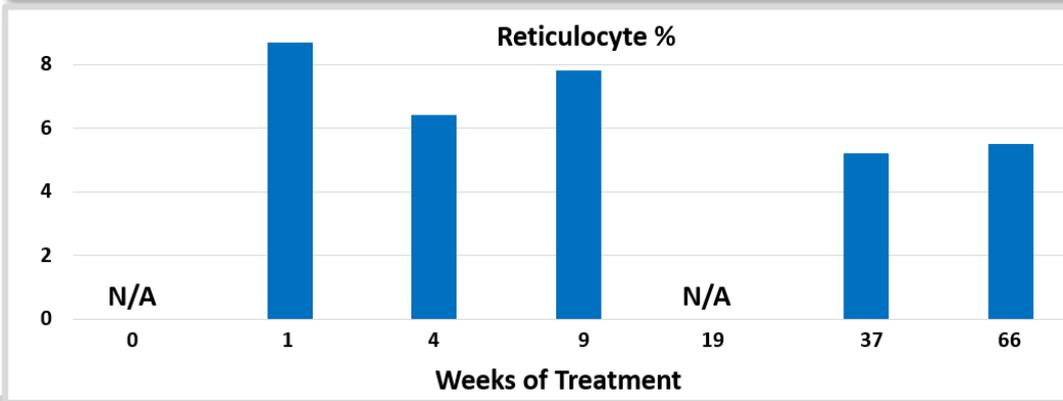
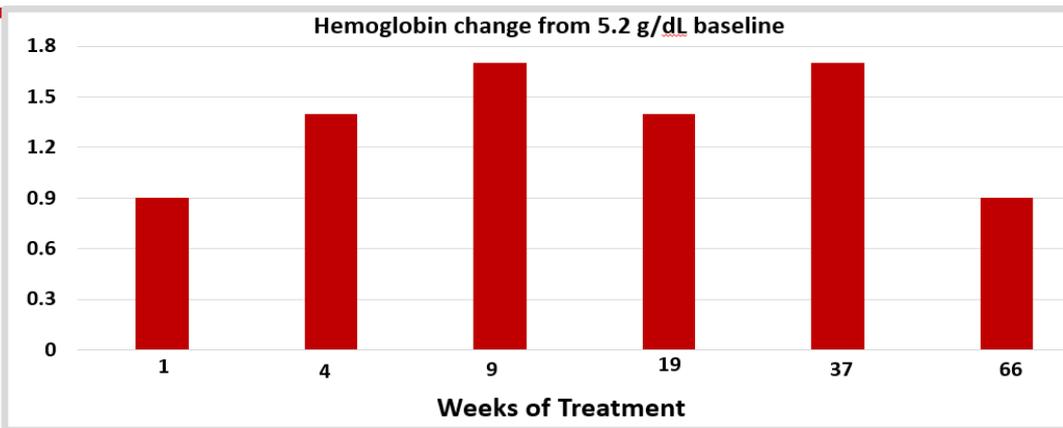


Patient History

- 67 y.o. man with HbSS disease and multiple RBC alloantibodies that prevent transfusion
- Clinical characteristics include:
 - Hb decline to the range of ~4.5 to 6 g/dL over recent years
 - eGFR stable in the 70 to 75 cc/mm/1.73 m² range
 - Chronic supplemental oxygen therapy for moderate COPD. Room air resting blood O₂ saturations in the range of 90 to 91 mmHg
 - Recurrent, frequent pain exacerbations
 - Extreme fatigue and lethargy
- Ineligible for HOPE trial due to clinical severity including extreme anemia
- GBT440 was provided through single-patient compassionate access by the Sponsor (GBT)

Patient Response to GBT440

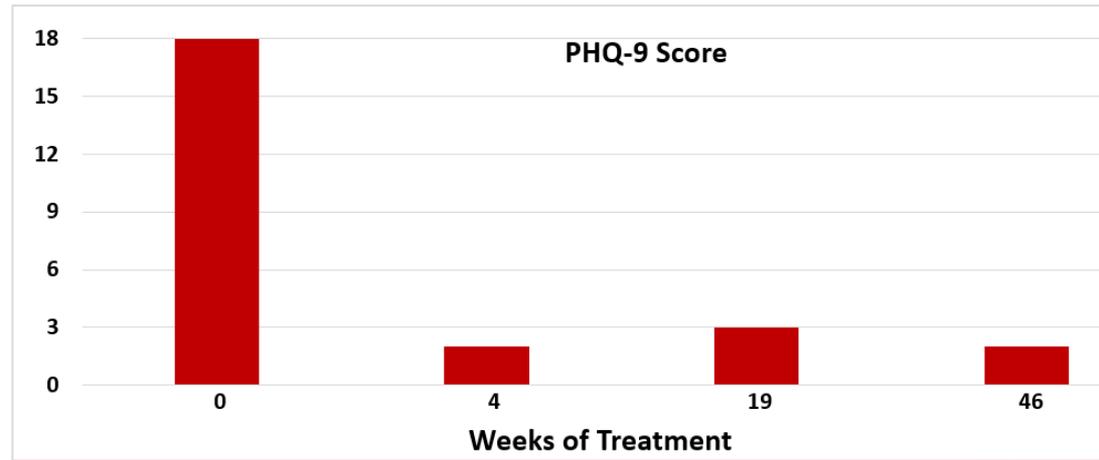
- Symptom improvement in 1 to 2 weeks
- Sustained hemoglobin rise ~ 1 to 1.5 g/dL over baseline
- Reticulocytes reduced consistently from baseline
- Indirect bilirubin:
Baseline 2.4 mg/dL
66 weeks 1.6 mg/dL



Patient Response to GBT440 (cont.)

- Sustained improved RA resting O₂ saturations (91 mmHg baseline; 96 mmHg week 65)
- Sustained improved RA O₂ saturation after six-minute walk test
- Oxygen independent during the day
- Only hospitalization for pain came after motor vehicle accident
- Improved Patient Health Quality-9 (PHQ-9) score consistent with improved mental status
- Quality of life substantially improved
 - Back to driving on his own and able to travel
 - Friends described him as “back to his old self”
 - Self-description of life quality: “excellent,” “great”

Room Air O ₂ sat after 6-minute walk test			
	Baseline	Week 20	Week 65
O ₂ Sat	86	93	96
Pulse	102	96	93



Adverse Events

- No serious adverse events occurred with GBT440 treatment
 - August 2016: Patient clinically stable.
 - GBT440 dose was increased from 900 mg to 1500 mg to boost the percent HbS modification
 - Grade 2 diarrhea developed after several days at 1500mg. The diarrhea resolved with return to the 900 mg dose
 - No other grade 1/2 adverse events have been observed through month 17
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Conclusions

- **GBT440 administered through the compassionate use program produced substantial clinical benefits in this single patient who did not qualify for the HOPE trial due to disease severity**
 - **Clinical benefits were both objective (e.g., sustained rise in hemoglobin) and subjective (less depression as assessed by PHQ-9)**
 - **GBT440 has now been well-tolerated for more than 66 weeks**
 - **These data provide encouraging evidence of the potential benefit of GBT440 in a broad range of patients**
 - **Controlled clinical trials will be needed to assess possible GBT440 benefit in other patients with severe anemia**
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Questions?
