**BACKGROUND**

- Sickle cell disease (SCD) is an autoimmune disorder caused by a mutation in the β-globin gene that leads to the production of sickle hemoglobin (HbS).
- Deoxygenated HbS polymerizes and deforms red blood cells (RBCs), which decreases RBC damage.
- When deoxygenated, HbS polymerizes and deforms red blood cells (RBCs) into a sickle shape and damages cell membranes. These damaged RBCs block blood flow and cause organ damage, leading to a shortened quality of life.
- GBT440-007 is an ongoing phase 2a study in children aged 6 to 17 years with SCD.
- The TSS is the sum of 9 questions (ranging from 0 [no symptoms] to 3 [severe symptoms]) for any given day, ranked on a 5-point Likert scale.
- 42% of patients (5 of 12) had a mean TSS of 0 (no symptoms) at week 16.
- 58% of patients (7 of 12) had a numerical decrease in TCD velocity at week 12.
- 83% of patients (10 of 12) showed reduction in TSS from baseline to week 16.
- There was a 94% median reduction in TSS from baseline to week 16.

**OBJECTIVES AND STUDY DESIGN**

- OBJECTIVES
  - The TSS is the sum of 9 questions (ranging from 0 [no symptoms] to 3 [severe symptoms]) for any given day, ranked on a 5-point Likert scale.
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- 58% of patients (7 of 12) had a numerical decrease in TCD velocity at week 12.
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- STUDY DESIGN
  - This ongoing study is being conducted in 2 parts (Figure 2).
  - Part A: a single dose of voxelotor 600 mg in pediatric and adolescent patients (12 to 17 years) with sickle cell disease (HbSS genotype).
  - Part B: voxelotor 900 mg daily to date.

**RESULTS**

- Baseline Characteristics
  - Age, median (range), y 13 (12-17) 14 (12-17)
  - Current HU use, n (%) 11 (92) 21 (88)
  - Baseline Hb, g/dL 10.5 ≤ 11.0
  - Reticulocytes, % –10.5 ≤ –6.7
  - Baseline TSS at week 0, n (%) 12 (100) 12 (100)

- **Change From Baseline to Week 16**
  - Change in Hb, g/dL: 1.7 (0.1, 3.5)
  - Change in HbF, %: –0.5 (–2.4, 1.6)
  - Change in TSS: –67.9 (–10.0, –73.9)

- **42% of patients (5 of 12) had a mean TSS of 0 (no symptoms) at week 16.**

**DISCUSSION**

- The results demonstrate voxelotor's potential to improve quality of life in adolescents with SCD.
- Future studies to assess the effect of voxelotor on TCD velocity are planned to include patients with conditional/normal TCD at baseline.