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

Jo Howard (presenting author)
- Membership on entity's advisory committees: Global Blood Therapeutics, Agios Pharmaceuticals, Novartis, Forma Therapeutics, Imara
- Honoraria: Novartis, Imara, Resonance Health

Kenneth I. Ataga
- Consultancy: Forma Therapeutics, Novartis
- Honoraria: Bioverativ, Editas Medicine, Global Blood Therapeutics, Modus Therapeutics, Novartis, Novo Nordisk
- Membership on entity's advisory committees: Bioverativ, Global Blood Therapeutics, Novo Nordisk
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R. Clark Brown
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- Nothing to disclose

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- Research funding: Global Blood Therapeutics, Novartis, ApoPharma

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- Research funding: Global Blood Therapeutics

Irene Agodoa
- Current employment and current equity holder in a publicly traded company: Global Blood Therapeutics

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Elliott Vichinsky
- Consultancy: Global Blood Therapeutics
- Research funding: Agios, Pfizer

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

Hb, hemoglobin; HbS, sickle hemoglobin; HOPE, Hemoglobin Oxygen Affinity Modulation to Inhibit HbS Polymerization; SCD, sickle cell disease; VOC, vaso-occlusive crisis.

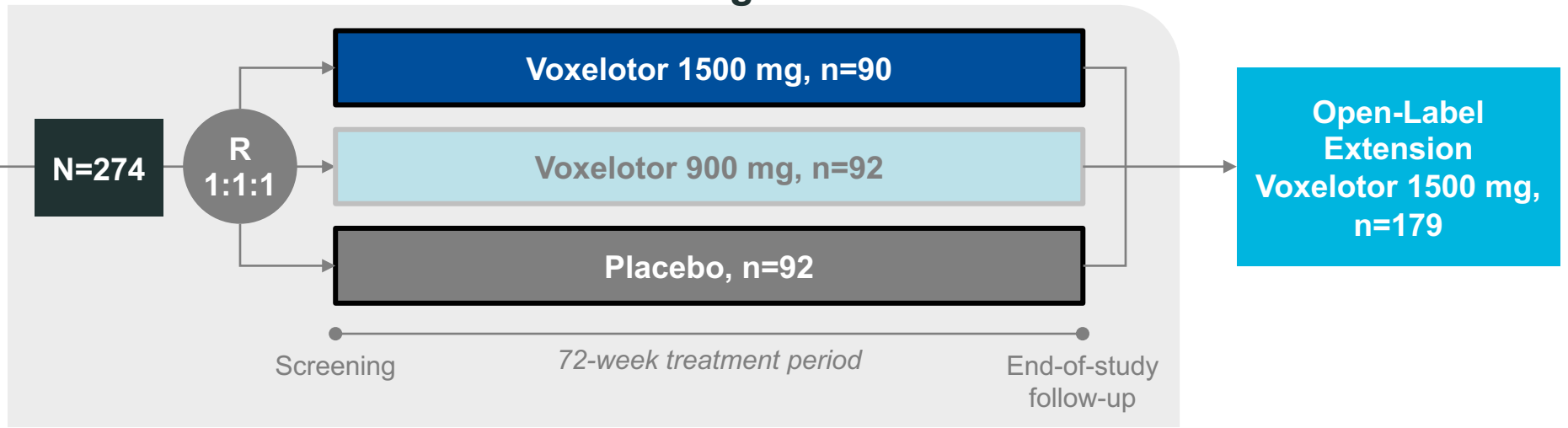
1. Kato GJ, et al. *Nat Rev Dis Primers.* 2018;4:18010. 2. Oxbryta (voxelotor). Prescribing information. Global Blood Therapeutics, Inc; 2019. 3. Vichinsky E, et al. *N Engl J Med*. 2019;381(6):509-519.

HOPE Trial: Study Design[1-3]

Eligibility criteria

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

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



Week 72 Analyses[b]

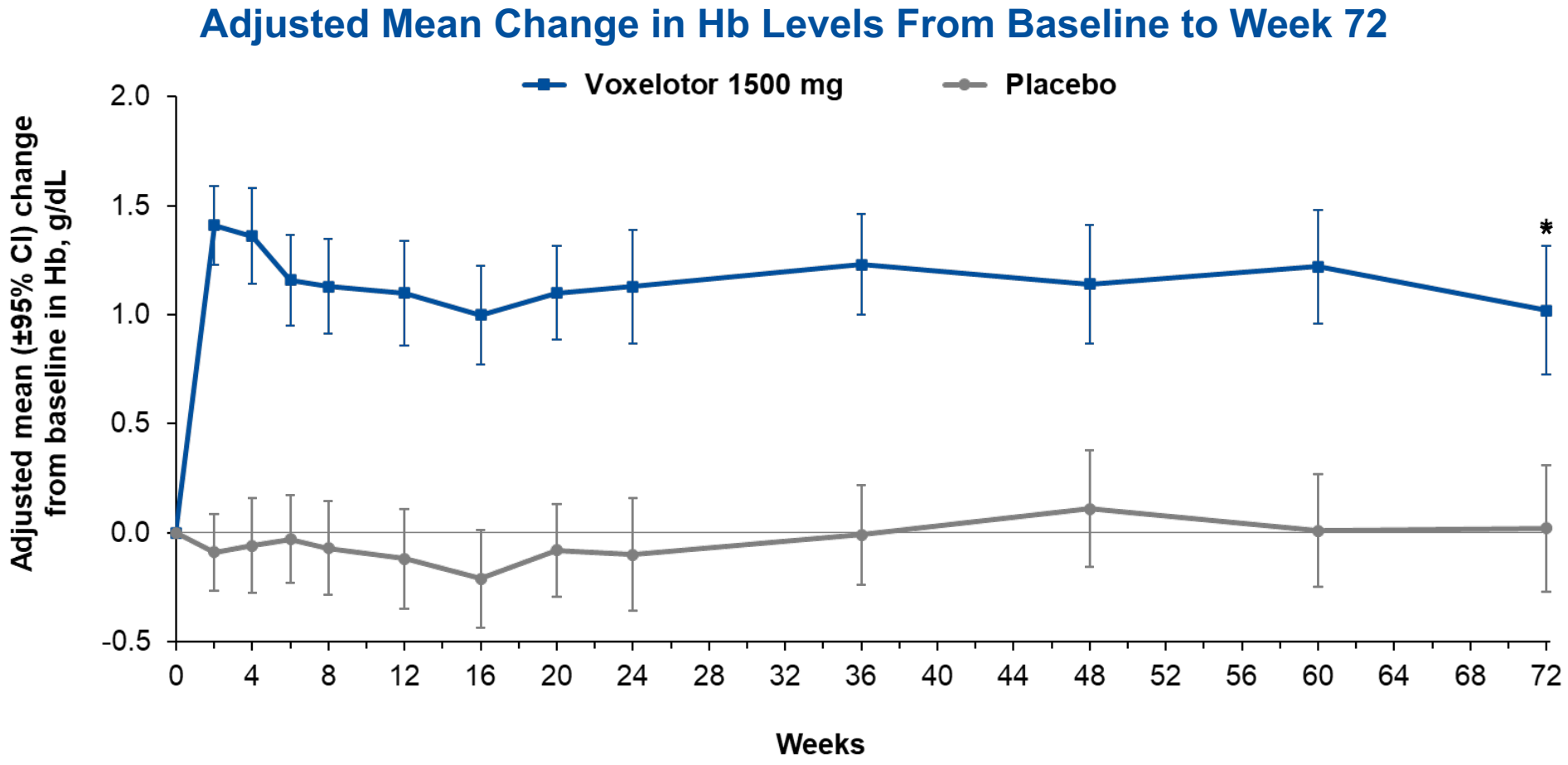
- **Hb level:** post-baseline levels achieved and change from baseline
- **Hemolysis markers:** change from baseline
- **Annualized incidence of VOCs**
- **Safety:** AEs during the treatment period

Baseline characteristics were generally well balanced

[a]Eligible genotypes: HbSS, HbSβ^0, HBSβ$^+$, HbSC, and other documented variants. [b]Efficacy and safety analyses reported for voxelotor 1500 mg, the approved dose in the US.
Hb, hemoglobin; HbS, sickle hemoglobin; HbSβ^0, sickle beta zero thalassemia; HbSβ$^+$, sickle beta plus thalassemia; HbSC, hemoglobin SC disease; HbSS, homozygous for SCD; HU, hydroxyurea; R, randomization; SCD, sickle cell disease; VOC, vaso-occlusive crisis.

1. Vichinsky E, et al. *N Engl J Med*. 2019;381(6):509-519. 2. Data on file. GBT, South San Francisco, CA. 3. NCT03573882. Accessed October 27, 2020. https://clinicaltrials.gov/ct2/show/NCT03573882.

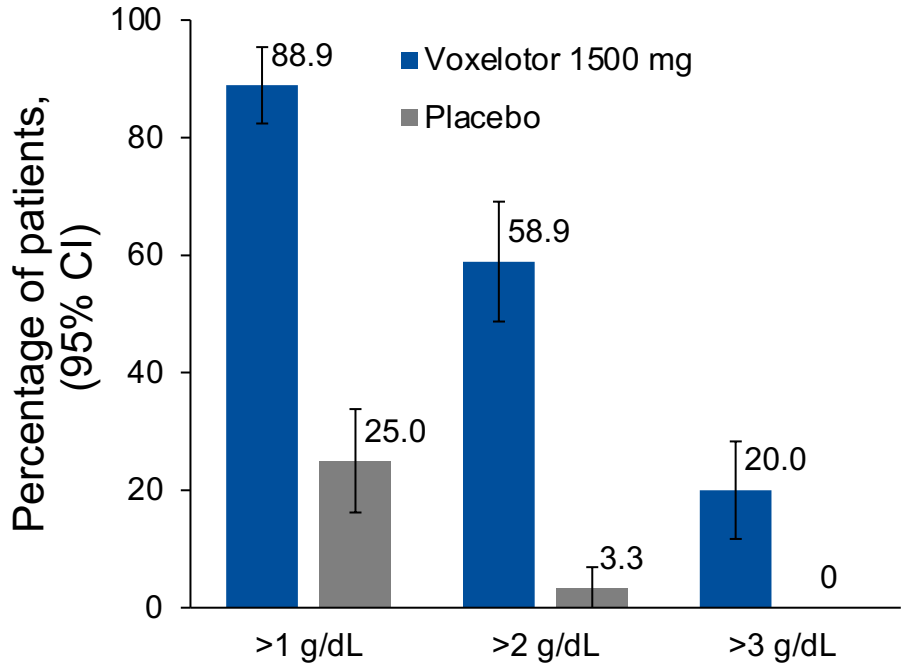
Voxelotor 1500 mg Resulted in Rapid and Durable Improvements in Hb Maintained Through Week 72



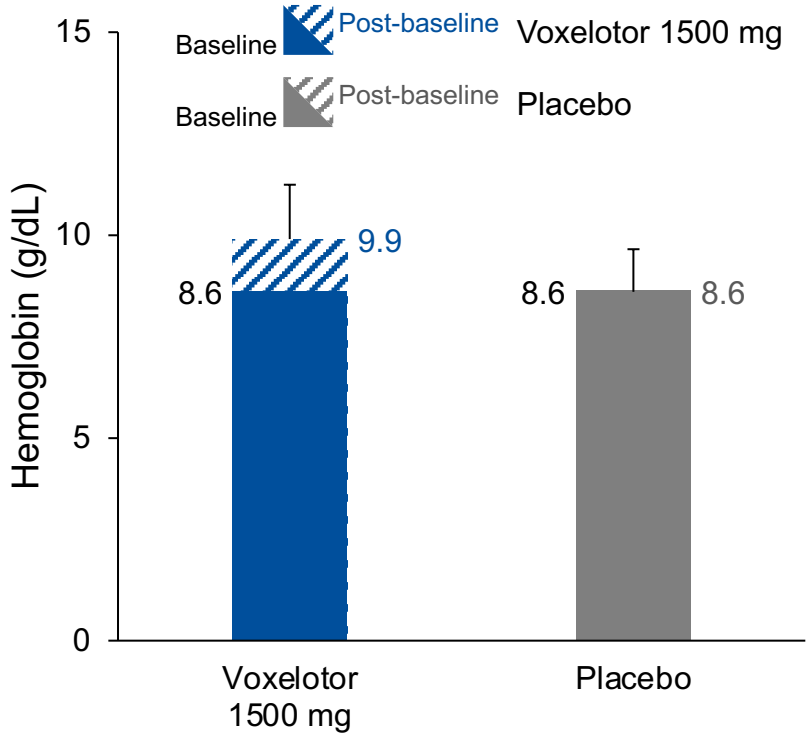
**P*<0.001 versus placebo at week 72.
Analysis of change from baseline in Hb level over time was based on a regression model for repeated measures. Hb values within 8 weeks after any red blood cell transfusion were imputed as the last value before the transfusion. Hb values obtained after HU treatment 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[a]



[a]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

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

**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

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

[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-threating 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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