Improvement in the Clinical Global Impression of Change with Voxelotor in Patients with Sickle Cell Disease in the Phase 3 HOPE Trial

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Disclosures

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- Research funding: Global Blood Therapeutics, NHLBI, The Links Incorporated, Novartis
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- Membership: Global Blood Therapeutics, Pfizer, ApoPharma

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- Honoraria: Global Blood Therapeutics, Terumo, Bluebird Bio
- Membership: Global Blood Therapeutics, Pfizer, ApoPharma

Tools Capturing the Broad Symptomatology of SCD Are Needed to Assess Patients' Overall Disease Status

Pain and fatigue are readily identifiable symptoms of SCD – and often the focus of clinical trials.[1-4]

Current PRO assessments in SCD only focus on capturing domain-specific symptoms and impacts – such as pain, depression, and fatigue.[4,5]

However, patients with SCD can experience additional complications and symptoms that impact their health-related quality of life.[1,6]

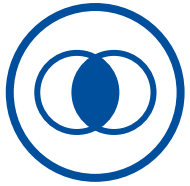
PRO, patient-reported outcome; SCD, sickle cell disease.

1. Kato GJ, et al. *Nat Rev Dis Primers.* 2018;4:18010. 2. Ballas SK, et al. *Blood.* 2012;120(18):3647-3656. 3. Ameringer S, et al. *Pediatr Oncol Nurs.* 2014;31(1):6-17. 4. Farrell AT, et al. *Blood Adv.* 2019;3(23):3982-4001. 5. Keller SD, et al. *Health Qual Life Outcomes.* 2014;12:125. 6. Rees DC, et al. *Lancet.* 2010;376(9757):2018-2031.

Clinical Global Impression of Change Is a Clinician-Reported Outcome That Assesses a Patient's Clinical Status

A single-item tool that evaluates a patient's status based on the treating physician's clinical judgment.[1]

Physicians are asked:
"Compared with the patient's clinical status at baseline before initiating treatment, the patient's overall condition is..." [1]



Analogous to the well-known Patient Global Impression of Change scale[2]

Rating		Description
1	Very much improved	• Nearly all better; good level of functioning; minimal symptoms • Represents a substantial change
2	Moderately improved	• Notably better with considerable reduction of symptoms • Increase in the level of functioning but some symptoms remain
3	Minimally improved	• Slightly better with little or no clinically meaningful reduction of symptoms • Represents little change in basic clinical status, level of care, or functional capacity
4	No change	• Symptoms remain essentially unchanged
5	Minimally worse	• Slightly worse but may not be clinically meaningful • Represents little change in basic clinical status or functional capacity
6	Moderately worse	• Clinically significant increase in symptoms and diminished functioning
7	Very much worse	• Severe exacerbation of symptoms and loss of functioning

Objective: To evaluate the impact of voxelotor on patient outcomes in SCD, as measured by the single-item CGI-C

CGI-C, Clinical Global Impression of Change; SCD, sickle cell disease.

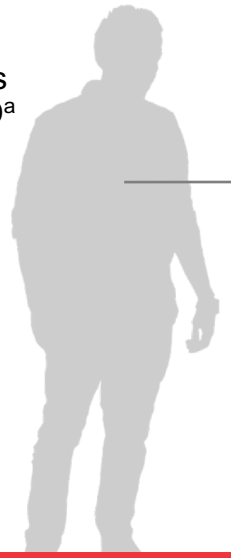
1. Busner J, Targum SD. *Psychiatry*. 2007;4(7):28-37. 2. Patients' Global Impression of Change (PGIC) Scale. Accessed November 5, 2020. https://chiro.org/LINKS/OUTCOME/Patients_Global_Impression_of_Change.pdf.

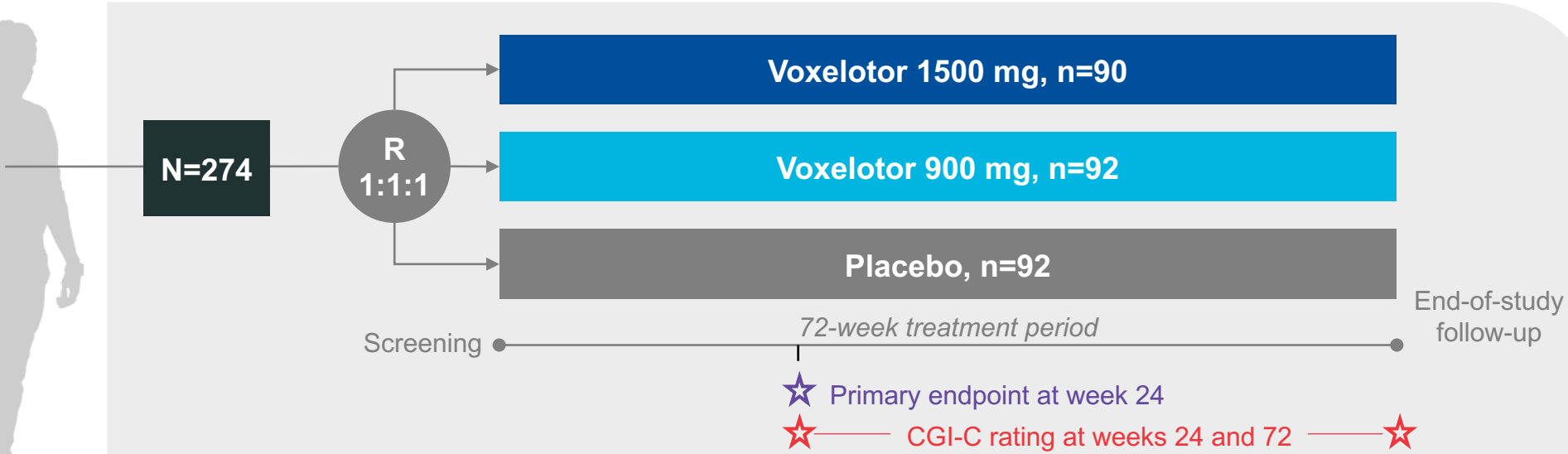
HOPE Trial: Study Design[1,2]

Voxelotor is a HbS polymerization inhibitor that was approved by the US Food and Drug Administration for the treatment of SCD in adults and pediatric patients 12 years of age and older[3]

Phase 3, randomized, double-blind, placebo-controlled, multicenter trial evaluating the efficacy and safety of voxelotor

- 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





Selected exploratory endpoint	Primary efficacy endpoint	Key secondary efficacy endpoints
• **CGI-C:** Proportion of patients rated "very much improved" or "moderately improved" compared with baseline at timepoints including week 24 and week 72	• **Hb response rate:** percentage of participants with Hb increase of **>1.0 g/dL** at 24 weeks	• **Hemolysis markers:** change from baseline to week 24 • **Hb level:** change from baseline to week 24 • **Annualized incidence of VOCs:** final analysis at 72 weeks

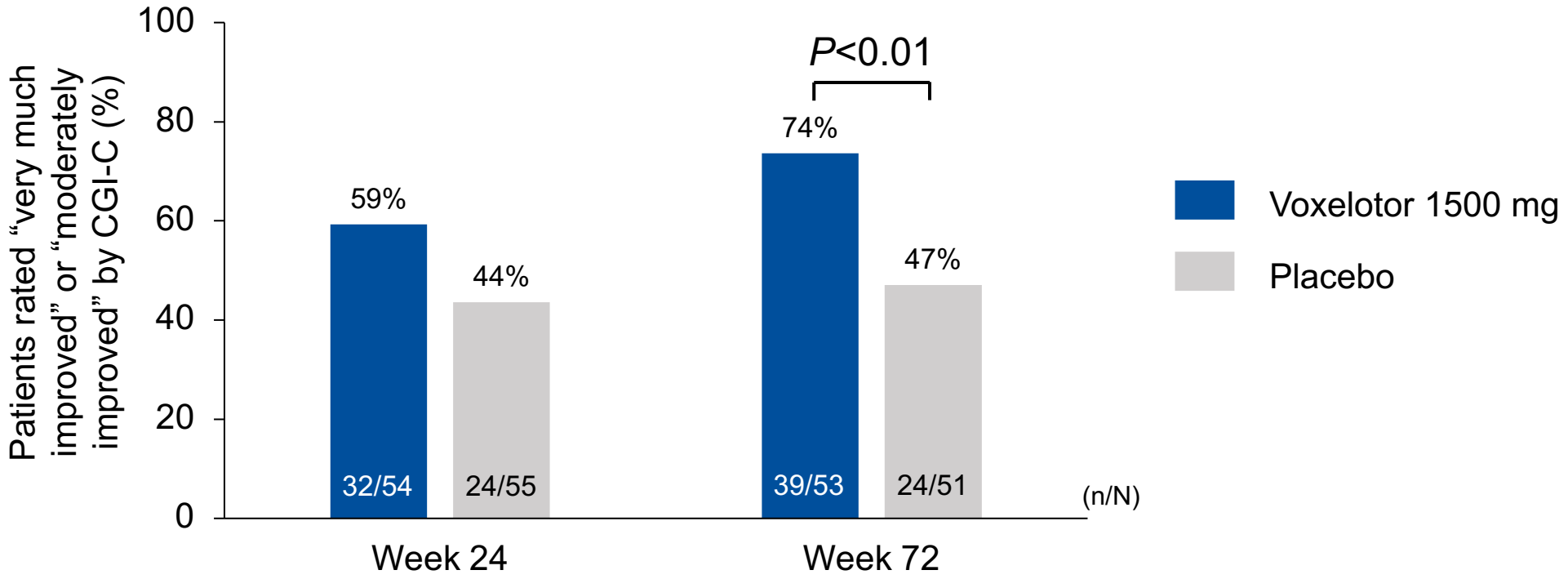
[a]Eligible genotypes: HbSS, HbSβ^0, HBSβ$^+$, HbSC, and other documented variants.

CGI-C, Clinical Global Impression of Change; 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; ULN, upper limit of normal; 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. Oxbryta. Prescribing information. Global Blood Therapeutics, Inc; 2019.

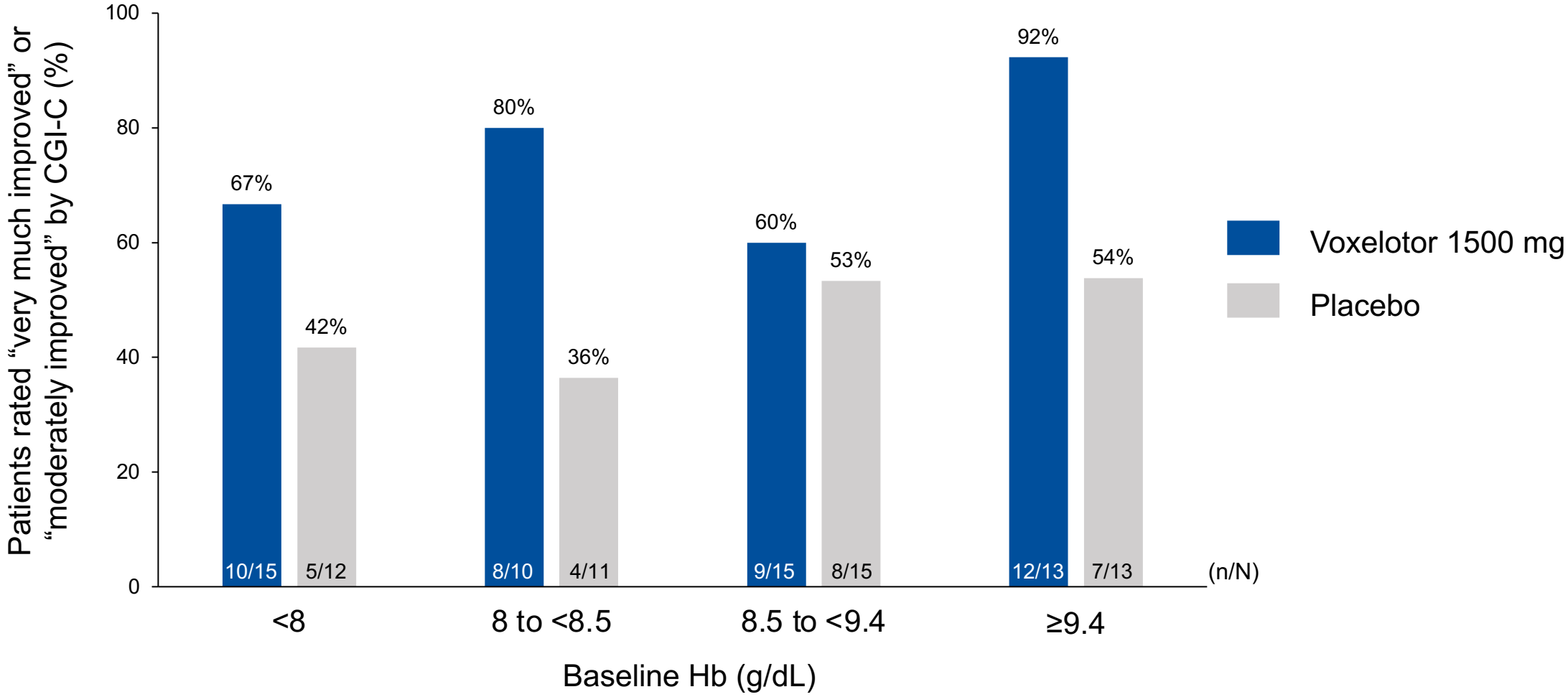
Voxelotor Was Associated with Greater Improvements in Patient SCD Status as Measured by CGI-C at Week 72

Clinicians rated the overall change in the patient's SCD status since the start of the study.



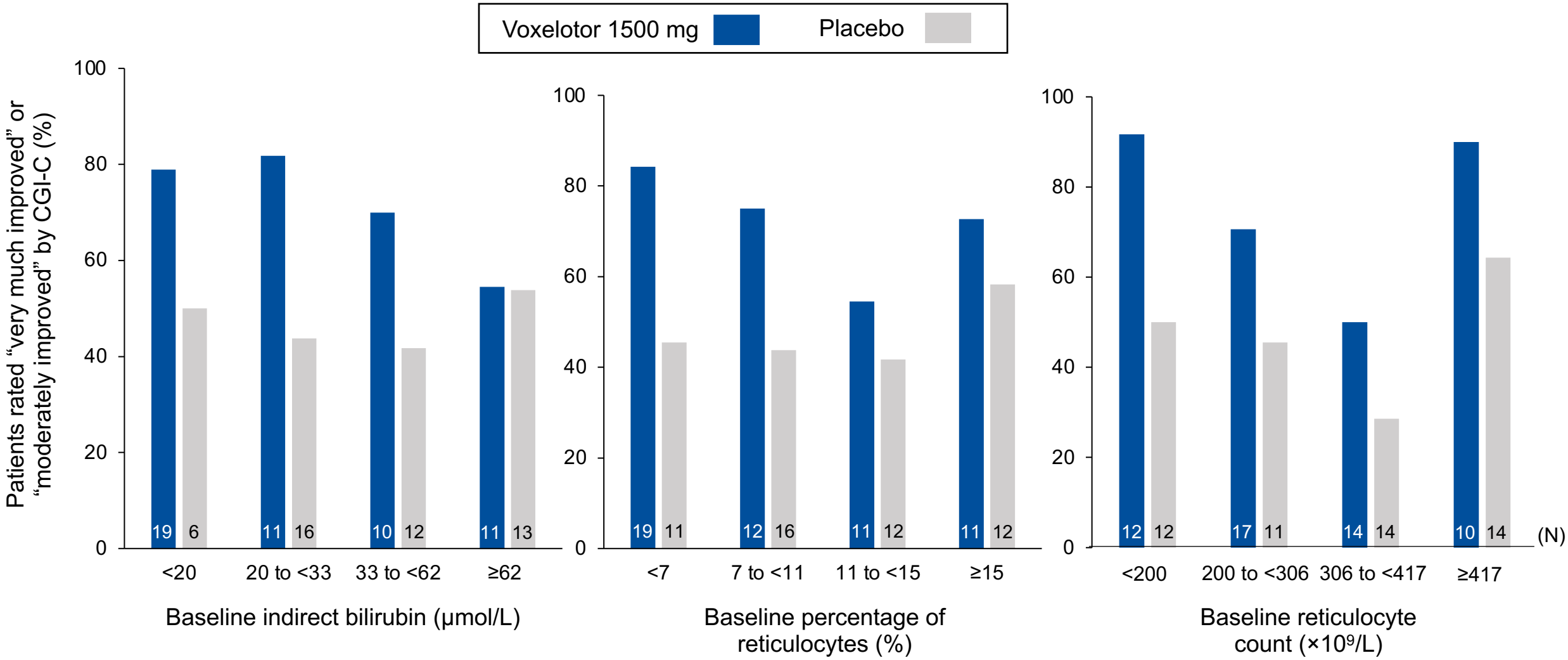
CGI-C, Clinical Global Impression of Change; SCD, sickle cell disease.

Voxelotor Was Associated with Greater Improvements in CGI-C Score at Week 72 Regardless of Baseline Hb



CGI-C, Clinical Global Impression of Change; Hb, hemoglobin.

Voxelotor Was Associated with Greater Improvements in CGI-C Score at Week 72 Regardless of Hemolysis Markers



CGI-C, Clinical Global Impression of Change.

Conclusions

Voxelotor 1500 mg resulted in improved health status in patients with SCD as assessed by the CGI-C, a clinician-reported outcome.

Improvements were observed regardless of baseline Hb levels and baseline markers of hemolysis.

The CGI-C provides an overall clinician-determined summary measure of a patient's SCD status that takes into account all available information, including the patient's history, their symptoms, and the impact of those symptoms on daily functioning.[1]

CGI-C assessments are being included in ongoing studies of voxelotor.

CGI-C, Clinical Global Impression of Change; Hb, hemoglobin; SCD, sickle cell disease.

1. Busner J, Targum SD. *Psychiatry*. 2007;4(7):28-37.

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