Incidence of Vaso-occlusive Crisis Does Not Increase With Achieving Higher Hemoglobin Levels on Voxelotor Treatment or After Discontinuation: Analyses of the HOPE Study

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BACKGROUND

• Sickle cell disease (SCD) is an inherited disorder in which pathophysiology is driven by hemoglobin (Hb) polymerization and red blood cell sickling, leading to chronic hemolytic anemia, and intermittent vaso-occlusive with subsequent ischemic-reperfusion injury.

• Hemolytic anemia is associated with innate immune system and endothelial cell activation resulting in an inflammatory, pro-adhesive state that leads to vaso-occlusive crisis (VOC) and damage to organs.1,2

• Voxelotor is a first-in-class sickle hemoglobin (HbS) polymerization inhibitor in development for the treatment of SCD (Figure 1).2

OBJECTIVES

• Study Design

• In the phase 3 HOPE trial, voxelotor 1500 mg and 900 mg daily demonstrated robust, reliable, and sustained dose-dependent improvements in patients’ Hb levels, with numerically fewer VOCs compared with placebo, which suggests that viscosity was not increased with voxelotor treatment.3

Figure 2. Voxelotor Inhibits HbS Polymerization and Is Potentially Disease Modifying

RESULTS

Baseline Characteristics

• Baseline characteristics were similar among patients receiving voxelotor 1500 mg and 900 mg and those receiving placebo, as previously reported.4

Figure 1. Voxelotor Inhibits HbS Polymerization and Is Potentially Disease Modifying

METHODS

Study Design

• A post hoc analysis of data from the HOPE trial (a phase 3, randomized, placebo-controlled, double-blind, multicenter study) was conducted to compare VOC incidence by Hb level and Hb occupied among patients with SCD who were aged 12 to 65 years and receiving 2 different doses of voxelotor or placebo (Figure 2).

Key Eligibility Criteria

• ≥ 18 years of age at randomization
• History of SCD events
• HbSS, HbSC, and other genotypes: HbSS, HbS+β, HbSC, and other genetic conditions
• Randomized to receive 2 different doses of voxelotor or placebo (Figure 2).1,2

• Analyses of the HOPE Study were conducted to compare VOC incidence among patients with SCD who were aged 12 to 65 years and receiving 2 different doses of voxelotor or placebo (Figure 2).1,2

Key Findings

• Rates of VOCs Associated With Reduced Rates of VOCs

1. Patients who received voxelotor experienced the lowest VOC rates and fewer VOCs compared with those receiving placebo, consistent with a treatment-induced inhibition of HbS polymerization (Figure 4).3

2. Among patients receiving voxelotor, the <20% Hb occupancy group (n=49) included 21 patients treated with voxelotor 900 mg and 28 treated with voxelotor 1500 mg. The 20% to <30% Hb occupancy group (n=62) included 50 patients treated with voxelotor 900 mg and 32 patients treated with voxelotor 1500 mg. The ≥30% Hb occupancy group (n=87) included 46 patients treated with voxelotor 900 mg and 46 treated with voxelotor 1500 mg. The 20% to <30% Hb occupancy group (n=62) included 50 patients treated with voxelotor 900 mg and 32 patients treated with voxelotor 1500 mg.

3. Among patients receiving voxelotor, the <20% Hb occupancy group (n=49) included 21 patients treated with voxelotor 900 mg and 28 treated with voxelotor 1500 mg. The 20% to <30% Hb occupancy group (n=62) included 50 patients treated with voxelotor 900 mg and 32 treated with voxelotor 1500 mg. The ≥30% Hb occupancy group (n=87) included 46 patients treated with voxelotor 900 mg and 46 treated with voxelotor 1500 mg.

CONCLUSIONS

• There was no evidence that increased Hb with voxelotor treatment led to an increased risk of VOC. Patients who achieved the greatest absolute Hb levels after 24 weeks of treatment with voxelotor had numerically fewer VOCs than patients who received placebo.

• Patients who reached a Hb occupancy of ≥20% and those with Hb levels of ≥12 g/dL with voxelotor experienced the lowest VOC rates and fewer VOCs compared with those receiving placebo, consistent with a treatment-induced inhibition of HbS polymerization (Figure 4).3

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REFERENCES


