Sotatercept for the treatment of pulmonary arterial hypertension: PULSAR open-label extension

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This report characterises the longer-term safety and efficacy of sotatercept in adult participants with pulmonary arterial hypertension from the PULSAR open-label extension period
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Abstract

Background In participants with pulmonary arterial hypertension, 24 weeks of sotatercept resulted in a significantly greater reduction from baseline in pulmonary vascular resistance than placebo. This report characterises the longer-term safety and efficacy of sotatercept in the PULSAR open-label extension. We report cumulative safety, and efficacy at months 18–24, for all participants treated with sotatercept.

Methods PULSAR was a phase 2, randomised, double-blind, placebo-controlled study followed by an open-label extension, which evaluated sotatercept on top of background pulmonary arterial hypertension therapy in adults. Participants originally randomised to placebo were re-randomised 1:1 to sotatercept 0.3 or 0.7 $mg \cdot kg^{-1}$ (placebo-crossed group); those initially randomised to sotatercept continued the same sotatercept dose (continued-sotatercept group). Safety was evaluated in all participants who received ⩾1 dose of sotatercept. The primary efficacy endpoint was change from baseline to months 18–24 in pulmonary vascular resistance. Secondary endpoints included 6-min walk distance and functional class. Two prespecified analyses, placebo-crossed and delayed-start, evaluated efficacy irrespective of dose.

Results Of 106 participants enrolled in the PULSAR study, 97 continued into the extension period. Serious treatment-emergent adverse events were reported in 32 (30.8%) participants; 10 (9.6%) reported treatment-emergent adverse events leading to study discontinuation. Three (2.9%) participants died, none considered related to study drug. The placebo-crossed group demonstrated significant improvement across primary and secondary endpoints and clinical efficacy was maintained in the continued-sotatercept group.

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Conclusion These results support the longer-term safety and durability of clinical benefit of sotatercept for pulmonary arterial hypertension.