Macitentan Improves Health-Related Quality of Life in Pulmonary Arterial Hypertension: Results from the Randomized Controlled SERAPHIN Trial

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RATIONALE: Macitentan, a novel dual endothelin receptor antagonist with sustained receptor binding, in the SERAPHIN trial (NCT00660179) significantly reduced the risk of morbidity and mortality (primary endpoint) in patients with pulmonary arterial hypertension (PAH). Since PAH is a progressive disease that severely impairs patients’ health-related quality of life (HRQoL), we assessed the impact of macitentan treatment on HRQoL (exploratory endpoint) in SERAPHIN.

METHODS: SERAPHIN was the first event-driven, international, double-blind, placebo-controlled PAH outcomes trial. Patients (aged ≥12 years) with PAH in WHO functional class (FC) II–IV were randomized to oral macitentan 3 or 10 mg, or placebo once-daily. HRQoL was assessed among literate patients aged ≥14 years using the Short Form 36-item (SF-36v2), administered at baseline, month 6, month 12, and end-of-treatment visit, and changes from baseline were calculated for each SF-36 domain and component summary score (norm-based scores standardized to the 1998 US general population). In addition, Kaplan-Meier analyses assessing the time to first occurrence of a ≥5-point decrease from baseline (considered a clinically relevant change) in the physical (PCS) and mental component summary (MCS) scores across treatment groups over the entire treatment duration were performed, and treatment groups were compared using logrank tests.

RESULTS: Of 742 patients, 76% were female, median age was 45 (range 12–85) years, and most patients were in WHO FC II (52%) and III (46%). Median treatment duration was >2 years. Both doses of macitentan improved mean HRQoL scores from baseline to month 6 to a similar extent (Figure). Significant improvements compared to placebo were observed in the PCS and MCS scores and in 7 out of 8 domains (P<0.05, except general health perception). Data at month 12 will be presented. Both macitentan doses reduced the risk of deterioration of HRQoL scores, as measured by time to first occurrence of a ≥5-point decrease in the PCS score (3 mg: HR 0.70, 95% CI 0.54, 0.92, P=0.008; 10 mg: HR 0.65, 95% CI 0.50, 0.85, P=0.001) and the MCS score (3 mg: HR 0.81, 95% CI 0.63, 1.03, P=0.085; 10 mg: HR 0.79, 95% CI 0.61, 1.01, P=0.053) across the study duration.

CONCLUSIONS: At month 6, macitentan significantly improved HRQoL of PAH patients across 7 out of 8 domains and both summary component scores of the SF-36 questionnaire. Both macitentan 3 mg and 10 mg doses reduced the risk of deterioration of physical and mental components of HRQoL over the entire study duration.

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