Ambrisentan Therapy in Patients With Pulmonary Arterial Hypertension: 3-Year Outcome

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Purpose: Ambrisentan is an ETA-selective endothelin receptor antagonist (ERA) that is approved for the treatment of pulmonary arterial hypertension (PAH). Ambrisentan has been shown to improve 6-minute walk distance in two Phase 3, 12-week, placebo-controlled studies (ARIES-1 and ARIES-2). Three-year data from ARIES-E, the long-term extension study of ARIES-1 and ARIES-2, is presented.

Methods: This is an integrated analysis of 383 patients who received at least 1 dose of ambrisentan (2.5, 5, or 10 mg qd) in ARIES-1, ARIES-2, or ARIES-E. Patients who received placebo in the previous studies were randomized to ambrisentan in ARIES-E. The first 24 weeks of dosing in ARIES-E was a blinded, fixed-dose period. After 24 weeks, blinded dose adjustment was permitted. Baseline was defined as the time of randomization to ambrisentan. Patient survival information was also collected during a post-study follow-up.

Results: For the three combined dose groups at baseline, 3% of patients were WHO functional class I, 43% were class II, 46% were class III, and 8% were class IV. At 1-year, 350 patients (91%) were still alive, 25 (7%) were not alive and 8 (2%) had an unknown status (discontinued the study and had unknown survival status). At 2-years, 315 patients (82%) were still alive, 55 (15%) were not alive and 13 (3%) had an unknown status. At 3-years, 282 patients (74%) were still alive, 77 (20%) were not alive and 24 (6%) had an unknown status. Kaplan-Meier estimates of survival were 93% (95% CI: 91% to 96%) at 1 year, 85% (95% CI: 82% to 89%) at 2 years and 79% (95% CI: 75% to 83%) at 3 years. The 3-year safety profile of ambrisentan was consistent with previous data.

Conclusions: At 3 years, 74% of the patients initially taking ambrisentan for the treatment of PAH in ARIES-E were still alive.

Clinical Implications: These data continue to support the long-term use of ambrisentan in the treatment of PAH. (On behalf of the ARIES-E Study Group)

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