Ambrisentan Therapy In Patients With Pulmonary Arterial Hypertension Receiving Concomitant Sildenafil Therapy: An Analysis Of The ARIES-3 Study

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Rationale: Ambrisentan (ABS) is an ETA-selective endothelin receptor antagonist approved for the treatment of pulmonary arterial hypertension (PAH). Clinical improvements have previously been reported in an open-label study of ABS in a diverse pulmonary hypertension patient population receiving a variety of background PAH therapies (ARIES-3).

Methods: 224 patients with pulmonary hypertension (WHO Groups 1, 3, 4, and 5) received 24-weeks of ABS therapy (5 mg once-daily) in the open-label ARIES-3 study; 139 of these patients had PAH. This post-hoc analysis examines the response of PAH patients who received ABS in addition to background sildenafil (20 to 100 mg sildenafil TID) therapy (ABS-S; n=58) to patients who received ABS monotherapy (ABS-M; n=58) at baseline. Change from baseline at week 24 is presented using last observation carried forward imputation for missing data. Kaplan-Meier estimates are presented for time-to-event analyses.

Results: Baseline characteristics were similar between subgroups, with the exception of cardiopulmonary hemodynamics, which were slightly worse in the ABS-S subgroup. Improvements in 6-minute walk distance (6MWD) were +25 m (95% CI: 11 to 40) in the ABS-S subgroup and in the ABS-M subgroups; whereas the decrease in B-type natriuretic peptide (BNP) was -34% (95% CI: -48% to -16%) in the ABS-S subgroup compared to -19% (95% CI: -37% to 5%) in the ABS-M subgroup. Improvements from baseline in BDI and WHO functional class were comparable between both subgroups. Kaplan-Meier estimates of survival were 96% (95% CI: 86% to 99%) in the ABS-S and 98% (95% CI: 88% to 100%) in the ABS-M subgroups; whereas, the risk of clinical worsening was 17% (95% CI: 10% to 30%) in the ABS-S subgroup and 5% (95% CI: 2% to 15%) in the ABS-M subgroup. Adverse events reported were generally comparable between the 2 subgroups, with peripheral edema being the most common event reported for each subgroup.

Conclusions: This post hoc analysis suggests that the safety and efficacy of ABS in PAH patients receiving concomitant sildenafil therapy is similar to PAH patients receiving ABS monotherapy.