Abstract: 4973

Efficacy and safety of selexipag in pulmonary arterial hypertension (PAH) patients with and without significant cardiovascular (CV) comorbidities

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Introduction: Many PAH patients today have a number of CV comorbidities, yet data on the efficacy and safety of therapies in such patients remain scarce. Most recent PAH clinical trials also include patients with comorbidities.

Purpose: To assess the long-term efficacy and safety of the oral, selective IP prostacyclin receptor agonist, selexipag, in PAH patients with and without significant CV comorbidities using post hoc analysis of GRIPHON data.

Methods: GRIPHON enrolled 1156 PAH patients randomised 1:1 to placebo:selexipag. The present analysis includes patients with right heart catheterisation within 1 year of randomisation who were categorised as with or without CV comorbidities. Patients with CV comorbidities were defined as having =3 of the following: body mass index (BMI) >30 kg/m², history of essential hypertension, diabetes mellitus, or historical evidence of significant coronary artery disease; if PAWP/LVEDP was >12 but <15 mmHg, pulmonary vascular resistance (PVR) had to be >500 dyn.sec/cm5; if PAWP/LVEDP was <12, then PVR had to be >300 dyn.sec/cm5. Selexipag effect on time to first morbidity/mortality (M/M) event up to end of treatment was assessed for both subgroups. Baseline (BL) adjusted treatment hazard ratios with 95% CIs were calculated using Cox models. Model building involved stepwise backward elimination of BL covariates.

Results: 752 PAH patients could be categorised based on these criteria (99 with CV comorbidities, 653 without). At BL, patients with CV comorbidities were older (median [range] 60 [28–80] vs 46 [18–78] yrs), had higher BMI (mean [SD] 33.3 [7.23] vs 26.0 [5.64] kg/m²) and lower 6-minute walk distance (mean [SD] 319 [95.7] vs 354 [79.3] m) vs those without. A greater proportion were from Western Europe/Australia/North America (60.6% vs 38.9%) and in WHO functional class III (69.7% vs 49.9%). At
BL, 82.8% of patients with CV comorbidities were receiving PAH therapies vs 75.7% of those without. As expected, at BL a higher proportion of patients with CV comorbidities (vs without) had previous/concomitant cardiac disease (62.6% vs 43.0%), metabolism/nutrition disorders (75.8% vs 31.2%), respiratory/thoracic/mediastinal disorders (59.6% vs 37.5%) and vascular disorders (76.8% vs 37.4%). Selexipag reduced the risk of M/M events vs placebo in both subgroups (Figure), with no evidence of an inconsistent treatment effect (interaction p-value=0.1544). Adverse events leading to treatment discontinuation were reported in 35.4% (25.9% selexipag, 46.7% placebo) of those with CV comorbidities and 35.0% (32.0% selexipag, 38.0% placebo) of those without. Common prostacyclin associated side effects observed with selexipag (headache, diarrhoea, nausea) were reported at a similar incidence in both subgroups.

Conclusions: Selexipag had a beneficial effect on long-term outcome in PAH patients both with and without CV comorbidities. Safety in both groups was consistent with the known profile of selexipag.

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*The model contains terms for: treatment, PAH status (patients with or without CV comorbidities), and their interaction, geographical region, aetiology, WHO Functional Class and 6-minute walk distance.*