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## The Impact of Time from Diagnosis at Baseline on Long-Term Outcome in the GRIPHON Study: Selexipag in Pulmonary Arterial Hypertension (PAH)

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**Background:** Newly diagnosed PAH patients have a poor prognosis (Humbert M, et al. Eur Respir J 2010; 36:549–555 and D’Alonzo GE, et al. Ann Intern Med 1991; 115:343–349). In the randomized, event-driven, long-term GRIPHON trial, the oral IP prostacyclin receptor agonist selexipag significantly reduced the risk of morbidity/mortality events compared with placebo in PAH patients. This post-hoc analysis explores whether early initiation of selexipag, with regards to time from diagnosis, improves outcomes for PAH patients.

**Methods:** The treatment effect of selexipag versus placebo on the primary endpoint (composite morbidity / mortality) was evaluated for patients categorized based on their time from diagnosis at baseline using a 6-month threshold to define the newly diagnosed patients (4. Simonneau G, et al. Eur Respir J 2015; 46:1711-20): patients treated earlier (time from diagnosis  $\leq$  6 months) and later (time from diagnosis  $>$  6 months). Kaplan-Meier estimates by treatment arm and subgroup were calculated. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using Cox proportional-hazard models and consistency of treatment effect across subgroups was assessed using an interaction test.

**Results:** When patients were categorized by time from diagnosis, patients treated with selexipag earlier (time from diagnosis  $\leq$  6 months; N=404) were younger and more likely to be in WHO FC II, treatment-naïve and from Asia/ Eastern Europe than those treated later (time from diagnosis  $>$  6 months; N=752). Selexipag reduced the risk of morbidity/mortality in patients treated earlier (HR 0.45 [95% CI: 0.33-0.63]) and later (HR 0.70 [95% CI: 0.54-0.91]), with a more pronounced treatment effect in those treated earlier (interaction p-value 0.0391). Consistent results were observed in subgroup analyses by background PAH therapy.

**Conclusions:** Consistent with other studies suggesting that earlier initiation of treatment for PAH results in a more pronounced treatment effect, this analysis shows that outcome was better in patients who were treated with selexipag closer to the time of diagnosis. This pattern was observed in all background PAH therapy subgroups.



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