

S109 TARGETING THE PROSTACYCLIN PATHWAY IN THE TREATMENT OF CONNECTIVE TISSUE DISEASE ASSOCIATED PULMONARY ARTERIAL HYPERTENSION (PAH): INSIGHTS FROM THE RANDOMISED CONTROLLED GRIPHON TRIAL WITH SELEXIPAG

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Rationale Despite available therapies, patients with connective tissue disease-associated PAH (PAH-CTD) have a poor prognosis. The global phase III GRIPHON study (NCT01106014) enrolled 1,156 patients including 334 with PAH-CTD. Compared with placebo, selexipag reduced the risk of the primary composite outcome of morbidity/mortality up to end of treatment by 41% (hazard ratio [HR] 0.59; 99% CI: 0.37–0.96) among patients with PAH-CTD. We examined the effect of selexipag vs placebo in the PAH-CTD subgroups: PAH associated with systemic sclerosis (PAH-SSc), systemic lupus erythematosus (PAH-SLE) and mixed CTD (PAH-MCTD).

Methods Patients (18–75 years) were randomised 1:1 to placebo or selexipag. HRs (95% CI) were calculated using Cox regression models to determine the effect of selexipag vs placebo on morbidity/mortality.

Results Of the 334 patients enrolled with PAH-CTD, 170 had PAH-SSc, 82 PAH-SLE, and 47 PAH-MCTD; CTD sub-classification was not reported in 35 patients. Across the subgroups, the majority of patients were female (84–99%) and were receiving an endothelin receptor antagonist, a phosphodiesterase type-5 inhibitor or both at baseline (73–83%). In the PAH-SSc, PAH-SLE and PAH-MCTD subgroups, the mean (SD) age was 60.0 (10.6), 39.0 (11.3) and 48.0 (14.7) years, respectively, and 65%, 33%, and 45% were in WHO functional class III, respectively. Selexipag reduced the risk of morbidity/mortality events by 44% (HR 0.56; 95% CI: 0.34–0.91) in PAH-SSc, 34% (HR 0.66; 95% CI: 0.30–1.48) in PAH-SLE, and 53% (HR 0.47; 95% CI: 0.15–1.48) in PAH-MCTD (Figure). The treatment effect was consistent across the subgroups (interaction test indicated no heterogeneity; $p = 0.6737$). By the end of study, 22 PAH-SSc, 7 PAH-SLE and 3 PAH-MCTD patients in the placebo, and 17 PAH-SSc, 4 PAH-SLE, 8 PAH-MCTD patients in the selexipag group had died. Common prostacyclin-associated side effects observed with selexipag in PAH-CTD patients generally occurred at a similar incidence to PAH-non-CTD patients and within the PAH-CTD subgroups.

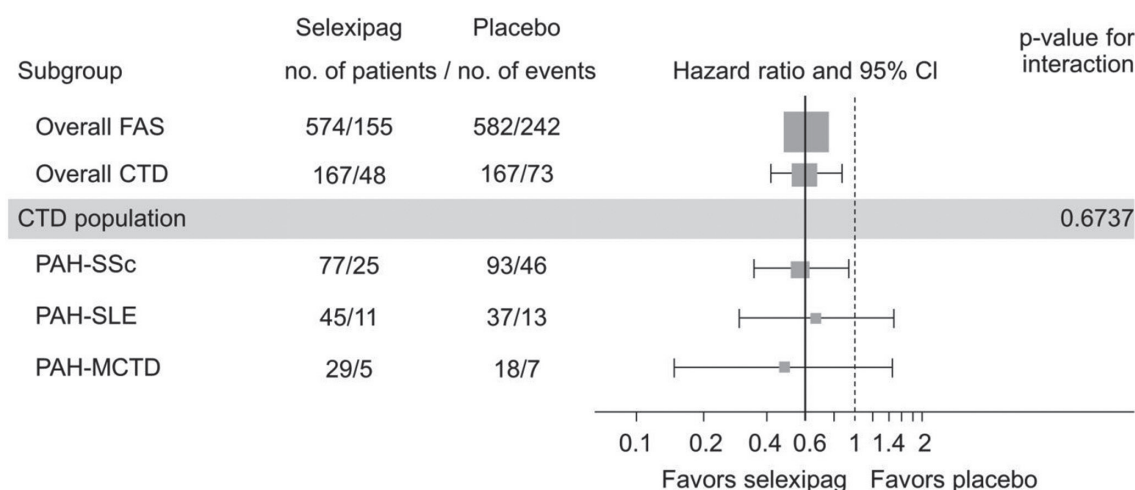
Conclusion GRIPHON included the largest randomised cohort of patients with PAH-CTD to date. The treatment effect of selexipag on time to first morbidity/mortality event was consistent across the subgroups, suggesting that selexipag is an effective therapeutic option in these difficult-to-treat patients.

Please refer to page A270 for declarations of interest in relation to abstract S109.

S110 2-D SEGMENTAL LONGITUDINAL STRAIN RATES CORRELATE WITH PROGNOSTIC INDICATORS IN IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION

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'Other' CTD (n=35) not shown.

CI, confidence interval; CTD, connective tissue disease; FAS, full analysis set; MCTD, mixed connective tissue disease; PAH, pulmonary arterial hypertension; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

Abstract S109 Figure 1