**EFFECT OF MACITENTAN ON HAEMODYNAMICS IN INEFFICIENT VENTRICULO-ARTERIAL COUPLING**


Introduction and objectives Macitentan, a novel dual endothelin receptor antagonist (ERA), significantly reduced morbidity and mortality in pulmonary arterial hypertension (PAH) patients in the SERAPHIN trial (NCT00660179), the first event-driven outcomes trial in PAH. A substudy in SERAPHIN investigated the effect of macitentan on patients’ cardiac haemodynamics.

Methods 742 PAH patients were randomised to placebo, macitentan 3 mg, or macitentan 10 mg once-daily. Stable background PAH therapy, except injectable prostanoids and other ERAs, were allowed. At selected centres, patients underwent right heart catheterisation at randomisation and Month 6. Changes from baseline to Month 6 for mean right atrial pressure (mRAP), mean pulmonary arterial pressure (mPAP), pulmonary vascular resistance (PVR), cardiac index (CI) and mixed venous oxygen saturation (SvO2) were calculated for all patients and stratified in an exploratory analysis for background PAH therapy and baseline WHO functional class I/II vs III/IV. Median treatment effects (95% CI) between placebo and macitentan are reported.

Results 187 patients participated in the substudy (51% were treatment-naïve and 56% in WHO FC III/IV). Baseline median values for all patients on placebo (n = 68), macitentan 3 mg (n = 62) and 10 mg (n = 57) were: mRAP 7.0, 8.0, 7.0 mmHg; mPAP 32.0, 54.0, 52.3 mmHg; PVR 800, 785, 789 dyn·sec/cm5; CI 2.49, 2.23, 2.47 L/min/m2; and SvO2 66.0, 64.5, 66.5%, respectively. Overall, haemodynamic parameters improved at Month 6 with macitentan and worsened with placebo. Beneficial treatment effects with macitentan were statistically significant (P < 0.05) for PVR and CI for both subgroups, except for PVR in treatment naïve patients treated with macitentan 3mg (Table).

Conclusions Macitentan significantly improved cardio-pulmonary haemodynamics in PAH patients. Improvements in PVR and CI were consistent irrespective of background PAH therapy and baseline WHO FC.

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**INEFFICIENT VENTRICULO-ARTERIAL COUPLING CONTRIBUTES TO REDUCED EXERCISE CAPACITY IN PULMONARY HYPERTENSION**

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Introduction Venticulo-arterial (VA) coupling (Ees/Ea) in the right heart is defined by RV end-systolic elastance (Ees) and pulmonary arterial effective elastance (Ea) with Ees/Ea representing the mechanical efficiency of forward flow from the RV. Ees/Ea may influence exercise capacity in pulmonary hypertension (PH) because patients exhibit cardiac limitation at peak oxygen uptake (peak VO2) and suffer impaired exercise cardiac output adaptation. We hypothesised that Ees/Ea in the RV represents a