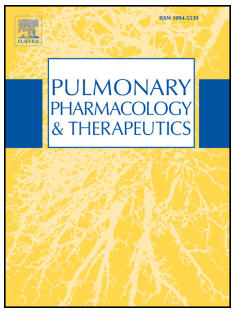

Modeling of pharmacokinetics, efficacy, and hemodynamic effects of macitentan in patients with pulmonary arterial hypertension

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Modeling of pharmacokinetics, efficacy, and hemodynamic effects of macitentan in patients with pulmonary arterial hypertension

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Abstract

Background: Macitentan is the first endothelin receptor antagonist with demonstrated efficacy on morbidity and mortality in pulmonary arterial hypertension (PAH) in the pivotal study SERAPHIN.

Methods: The pharmacokinetics (PK) of macitentan and its active metabolite, ACT-132577, were characterized in a population model. Efficacy and hemodynamics (pharmacodynamics, PD) were related to PK based on PK/PD modeling.

Results: Sex, age, and body weight influenced the PK to a statistically significant extent. Model-based simulations showed that these variables are clinically not relevant. Concomitant use of PAH medication (PDE-5 inhibitors) did not influence macitentan trough concentration to a relevant extent.

Efficacy and hemodynamics showed clear differences from placebo for macitentan concentrations on 3 and 10 mg with consistent superior effects for 10 mg. After 6 months, PAH