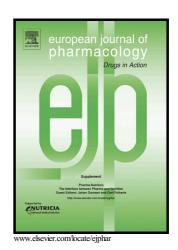
Author's Accepted Manuscript

Evaluation of the effects of RP5063, a novel, multimodal, serotonin receptor modulator, as single-agent therapy and co-administrated with sildenafil, bosentan, and treprostinil in a monocrotaline-induced pulmonary arterial hypertension rat model

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Evaluation of the effects of RP5063, a novel, multimodal, serotonin receptor modulator, as single-agent therapy and co-administrated with sildenafil, bosentan, and treprostinil in a monocrotaline-induced pulmonary arterial hypertension rat model

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Abstract

Pulmonary arterial hypertension (PAH), a condition that is defined by pulmonary vasculature constriction and remodeling, involves dysfunctional signaling of the serotonin (5-HT) receptors, 5-HT_{2/2B/7}. In a rat model of monocrotaline (MCT)-induced PAH, the effectiveness of RP5063 (RP), a dopamine and 5-HT receptor modulator, was evaluated as monotherapy and as an adjunct to standard PAH treatments. After a single 60 mg/kg dose of MCT, rats received vehicle (MCT+Veh; gavage twice-daily [b.i.d.]), RP (10 mg/kg; gavage b.i.d.), bosentan (B; 100 mg/kg; gavage BID), sildenafil (S; 50 mg/kg; gavage, BID), treprostinil (T; 100 ng/kg/min over 24 h intravenous), RP+B, RP+S, and RP+T for 28 days. Single-agent RP limited the functional and structural effects of PAH seen in the MCT+Veh group, with significant improvements in pulmonary hemodynamics, right ventricular (RV) hypertrophy, SO₂, and pulmonary blood vessel structural changes. These effects appeared comparable with those associated with B, S, and T.

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