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Oral presentation

sGC activation in pulmonary hypertension

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Impairments of the NO-sGC-cGMP pathway provoke acute and chronic vascular injury, including endothelial dysfunction, vasoconstriction and vascular remodeling in the pulmonary circulation. We evaluated the effects of the novel sGC activator Bay 41-2272 in three different models of acute and chronic pulmonary hypertension: 1. Ischemia-reperfusion injury induced pulmonary vascular dysfunction in isolated rabbit lungs, 2. Oleic acid induced lung vascular injury in an intact animal model and 3. chronic hypoxia induced pulmonary hypertension in mice. I/R provoked dramatic production of reactive oxygen species, acute pulmonary hypertension upon reperfusion, and increased pulmonary vascular permeability. Bay 41-2272 dose dependently reduced all three events resulting in significant organ protection. In oleic acid induced lung injury, pulmonary vasoconstriction as well as gas exchange properties of the injured lungs were beneficially influenced by the sGC activator. Finally, in chronic hypoxic pulmonary hypertensive mice, sGC activation effectively treated pulmonary hypertension and right heart hypertrophy – in part in an eNOS dependent manner – as proven by the investigations in NOS3 KO mice. In conclusion BAY 41-2272, a novel sGC activator, offers great therapeutical potential by restoration of the sGC-cGMP pathway which is impaired in different forms of acute and chronic pulmonary vasculopathy.