European Respiratory Society
Annual Congress 2013

Abstract Number: 337

Publication Number: P489

Abstract Group: 4.3. Pulmonary Circulation and Pulmonary Vascular Disease

Keyword 1: Circulation **Keyword 2:** Pulmonary hypertension **Keyword 3:** Pharmacology

Title: Imatinib lowers the pulmonary vascular tone in human and guinea pig lung tissue

Nina A. 2347 Maihöfer nina.maihoefer@rwth-aachen.de [1], Dr. Marco 2348 Schlepütz mschlepuetz@ukaachen.de [1], Dr. Jan W. 2349 Spillner jspillner@ukaachen.de MD [2], Thomas 2350 Schröder thomas.schroeder@luisenhospital.de [3], Prof. Dr Rüdiger 2351 Autschbach rautschbach@ukaachen.de MD [2], Dr. Saskia 2352 Westphal swestphal@ukaachen.de MD [4], Dr. Alberto 2353 Perez-Bouza alberto.perez_bouza@ukb.uni-bonn.de MD [5], Dr. Till 2355 Braunschweig tbraunschweig@ukaachen.de MD [4], Dr. Gereon 2356 Schaelte gschaelte@ukaachen.de MD [6], Prof. Dr Rolf 2357 Rossaint rrossaint@ukaachen.de MD [6], Prof. Dr Stefan 2358 Uhlig suhlig@ukaachen.de [1], Dr. Christian 2359 Martin chmartin@ukaachen.de [1] and Dr. Annette D. 2360 Rieg arieg@ukaachen.de MD [1,6]. [1] Institute of Pharmacology and Toxicology, University Hospital Aachen, Aachen, Germany ; [2] Department of Cardiac and Thorax Surgery, University Hospital Aachen, Aachen, Germany ; [3] Department of Surgery, Luisenhospital Aachen, Aachen, Germany ; [4] Institute of Pathology, University Hospital Aachen, Aachen, Germany ; [5] Institute of Pathology, Universtiy Hospital Bonn, Bonn, Germany and [6] Department of Anaesthesiology, University Hospital Aachen, Aachen, Germany .

Body: Introduction: In pulmonary hypertension, imatinib impedes proliferation and ameliorates pulmonary haemodynamics. However, the relaxant potential of imatinib is virtual unknown. Aims and objectives: We wanted to elucidate whether and how imatinib may modulate the tone of pulmonary arteries (PAs) and pulmonary veins (PVs). Methods: Imatinib-induced relaxation was studied by videomicroscopy in precision-cut lung slices (PCLS) from humans and guinea pigs (GPs); baseline luminal vessel area was defined as 100%. Intracellular cAMP was measured by ELISA and imatinib-induced changes of pre- and postcapillary resistances were studied in the isolated perfused lung (GP). Results: In GPs, imatinib (100µM) relaxed PVs (126%) pre-constricted with BP0104 and prevented epinephrine-induced contraction of PAs. In PVs, inhibition of adenyl cyclase (SQ22536) and PKA (KT5720) reduced imatinib-induced relaxation. Conversely, imatinib increased cAMP. Further, inhibition of KATP-channels (glibenclamide), BKCa2+-channels (iberiotoxin) and Kv-channels (4-aminopyridine) diminished imatinib-induced relaxation. In the isolated perfused lung (GPs), imatinib (10µM) lowered the BP0104-induced increase of postcapillary resistances. Moreover, imatinib (100nM; 100µM) relaxed human pre-constricted PAs up to 125% and 167% dependent on the activation of KATP-, BKCa2+- and Kv-channels. Conclusion: Imatinib relaxes pulmonary vessels by cAMP/PKA (GPs) and the activation of KATP-, BKCa2+- and Kv-channels (GPs; humans). These data suggest the use of imatinib in acute pulmonary hypertension. Since imatinib combines long-term antiproliferative and short-term vasodilatory effects, it may represent a new approach to treat pulmonary hypertension.