

# European Respiratory Society Annual Congress 2013

**Abstract Number:** 2140

**Publication Number:** P1588

**Abstract Group:** 5.1. Airway Pharmacology and Treatment

**Keyword 1:** Bronchodilators **Keyword 2:** Pharmacology **Keyword 3:** Airway smooth muscle

**Title:** Combination study of tiotropium and olodaterol in human precision-cut lung slices

Dr. Marco 18260 Schlepütz mschlepuetz@ukaachen.de<sup>1</sup>, Mrs. Nina 18261 Maihöfer nmaihofer@ukaachen.de<sup>1</sup>, Dr. Annette D. 18262 Rieg arieg@ukaachen.de MD<sup>1</sup>, Dr. Saskia 18263 Westphal swestphal@ukaachen.de MD<sup>2</sup>, Dr. Alberto 18264 Perez-Bouza alberto.perez\_bouza@ukb.uni-bonn.de MD<sup>3</sup>, Dr. Till 18272 Braunschweig tbraunschweig@ukaachen.de MD<sup>2</sup>, Mr. Thomas 18376 Schröder thomas.schroeder@luisenhospital.de<sup>4</sup>, Dr. Jan W. 18378 Spillner jspillner@ukaachen.de MD<sup>5</sup>, Prof. Dr Rüdiger 18379 Autschbach rauschbach@ukaachen.de MD<sup>5</sup>, Dr. Michael P. 18415 Pieper michael\_paul.pieper@boehringer-ingelheim.com<sup>6</sup>, Prof. Dr Stefan 18421 Uhlig suhlig@ukaachen.de<sup>1</sup> and Dr. Christian 18422 Martin chmartin@ukaachen.de<sup>1</sup>. <sup>1</sup> Institute of Pharmacology and Toxicology, RWTH Aachen University, Aachen, Germany ; <sup>2</sup> Institute of Pathology, RWTH Aachen University, Aachen, Germany ; <sup>3</sup> Institute of Pathology, University Hospital Bonn, Bonn, Germany ; <sup>4</sup> Department of Surgery, Luisenhospital Aachen, Aachen, Germany ; <sup>5</sup> Department of Cardiothoracic and Vascular Surgery, RWTH Aachen University, Aachen, Germany and <sup>6</sup> Div. Research Germany, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riß, Germany .

**Body:** In COPD, monotherapy often fails to improve health status. Hence, combinations of bronchodilators are recommended. The pharmacological impact of drugs on bronchoconstriction (BC) can be determined in vitro by precision-cut lung slices (PCLS). So, the present aim was to characterize the combined effect of tiotropium and the novel LABA olodaterol on BC in human lung tissue. PCLS were prepared from lung lobes received from cancer patients. BC in PCLS was monitored by videomicroscopy. First, concentration-response curves with carbachol (CCh,  $10^{-8}$ – $10^{-3}$ M) were performed in the presence and absence of tiotropium ( $10^{-11}$ – $10^{-8}$ M) or olodaterol ( $10^{-10}$ – $10^{-7}$ M). For the combined effect of tiotropium and olodaterol, concentration-response curves with CCh were conducted at  $10^{-9.5}$ M tiotropium or  $10^{-9}$ M olodaterol alone and in their combination. Tiotropium concentration-dependently inhibited CCh-induced BC and a suitable inhibitory concentration for the combination study was found at  $10^{-9.5}$ M. The functional antagonist olodaterol also inhibited CCh-induced BC and an appropriate inhibitory concentration for the combination study was determined to  $10^{-9}$ M. In the combination study half-maximal effective concentrations ( $\log EC_{50}$ ) for CCh-induced BC were  $-5.9 \pm 0.2$  under control conditions,  $-5.7 \pm 0.1$  at  $10^{-9.5}$ M tiotropium,  $-5.4 \pm 0.2$  at  $10^{-9}$ M olodaterol and  $-4.6 \pm 0.2$  for the combination of tiotropium and olodaterol. In vitro the combination of tiotropium and olodaterol was more effective to inhibit BC than each bronchodilator alone. Since those studies were performed in human tissue, correlation to the in vivo situation may be allowed and the combination of tiotropium and olodaterol may be beneficial in the treatment of patients.