European Respiratory Society
Annual Congress 2012

Abstract Number: 2451

Publication Number: P2130

Abstract Group: 5.1. Airway Pharmacology and Treatment

Keyword 1: Asthma - management **Keyword 2:** Bronchodilators **Keyword 3:** Animal models

Title: Protection against allergen-induced airway hyperresponsiveness (AHR) by olodaterol in guinea pigs is synergistically enhanced by tiotropium

Ms. Marieke 18026 Smit marieke.smit@rug.nl [1,2], Ms. Annet 18027 Zuidhof a.b.zuidhof@rug.nl [1,2], Ms. Sophie 18028 Bos i.s.t.bos@rug.nl [1,2], Dr. Harm 18029 Maarsingh h.maarsingh@rug.nl [1,2], Dr. Reinoud 18030 Gosens r.gosens@rug.nl [1,2], Prof. Dr Johan 18033 Zaagsma j.zaagsma@rug.nl [1,2] and Prof. Dr Herman 18034 Meurs h.meurs@rug.nl [1,2]. [1] Department of Molecular Pharmacology, University of Groningen, Netherlands and [2] Groningen Research Institute for Asthma and COPD, University of Groningen, Netherlands .

Body: The ultra-long acting β_2-agonist olodaterol has shown to be effective in asthma and COPD. Increased cholinergic tone, common to these diseases, may reduce β_2-agonist responsiveness. In a guinea pig model of asthma, we investigated the protection of allergen (ovalbumin, OA)-induced AHR by olodaterol, alone and in combination with the long acting anticholinergic tiotropium. Airway responsiveness (PC_{100}) was assessed at baseline (24h before OA) and after the early (EAR, 6h after OA) and late (LAR, 24h after OA) asthmatic reactions. 1h before OA, animals were treated with PBS (control), 1 mM olodaterol and/or 0.1 mM tiotropium (nebulizer concentrations, 3 min). OA induced AHR to histamine after the EAR (4.9-fold decrease in PC_{100} compared to baseline), which was fully protected by olodaterol (2.3-fold increase in PC_{100}) and tiotropium (1.3-fold increase). When combined, a synergistic 4.8-fold increase in PC_{100} was observed. After the LAR, AHR (2.8-fold decrease), was also protected by olodaterol, tiotropium and their combination (1.5-, 1.3- and 1.6-fold increase in PC_{100}, respectively). OA-induced infiltration of inflammatory cells, measured by BAL after the LAR, was not affected by any treatment. In conclusion, in a guinea pig model of asthma olodaterol and tiotropium protect against allergen-induced AHR after the EAR and LAR, without affecting inflammatory cell influx. Synergism between the drugs was found after the EAR, indicating that acetylcholine reduces the effectiveness of the β_2-agonist and that the combination of olodaterol and tiotropium may be beneficial in the treatment of allergic asthma. (supported by Boehringer Ingelheim Pharma).