

European Respiratory Society Annual Congress 2012

Abstract Number: 3896

Publication Number: P4843

Abstract Group: 5.1. Airway Pharmacology and Treatment

Keyword 1: Allergy **Keyword 2:** Anti-inflammatory **Keyword 3:** Pharmacology

Title: Combining corticosteroids and NK1R antagonists: A new drugs combination to treat allergic diseases

Prof. Karim 25615 Maghni karim.maghni@umontreal.ca ¹, Mrs. Lucero 25616 Castellanos lucero.castellanos@rtss.qc.ca ¹, Ms. Sandra 25617 Favret sandra.favret@umontreal.ca ¹ and Dr. Mélanie 25618 Welman mwelman@rtss.qc.ca ¹. ¹ Research Center, Sacré-Coeur Hospital of Montreal, Université de Montréal, QC, Canada, H4J1C5 .

Body: Introduction. Recently, using the rat mast cell/basophil cell line RBL-2H3, a major model system for the study of FcεRI intracellular signaling pathways, we found that optimal pharmacological blocking of autocrine activation of the neurokinin-1 receptor (NK1R) in response to FcεRI clustering suppresses antigen-induced 50 % of maximal cell degranulation, and decreases by nearly 50 % antigen-induced maximal cell activation. Aim. To determine whether combining corticosteroids and NK1R antagonist may be a powerful therapeutic combination to control IgE-FcεRI complex responses in allergic diseases. Methodology. IgE-sensitized RBL-2H3 cells were incubated with various concentrations of corticosteroids in combination or not with NK1R antagonist prior to FcεRI clustering. Cells degranulation and cysteinyl-leukotrienes (Cys-LTs) production were examined. Results: Maximal concentrations of respective corticosteroids decreased by nearly 50 % allergen-induced maximal degranulation and Cys-LTs production in basophils. Pharmacological blocking of NK1R alone has also produced similar inhibitory effects in basophils. Interestingly, the combination of corticosteroids and NK1R antagonist improved both time response and concentration efficacy of corticosteroids with nearly total inhibition of basophil allergic responses. Conclusion: Combining corticosteroids and NK1R antagonist (patent WO2007/096782) is a promising therapeutic combination to increase corticosteroids efficacy while decreasing effective doses, and may give a second “breath” to corticosteroids patents that are no longer protected. Supported by the Canadian Institutes of Health Research.