Abstract to be submitted to the European Respiratory Society Annual Meeting, Vienna 1-5th September 2012

Title: Poly:IC Causes Exacerbation In A Murine Allergic Inflammation Model Driven By House Dust Mite In Freund’s Complete Adjuvant

Authors: Raquel Otal, Elena Calama, Félix Gil, Montserrat Miralpeix and Jorge De Alba.

Department: Respiratory Pharmacology Section. Respiratory Therapeutic Area-Discovery. Almirall SA. Barcelona, Spain.

Abstract

RATIONALE: RNA viruses are major causes of respiratory infections and known to exacerbate asthma and other respiratory diseases. The objective of the study was to use poly I:C, a synthetic analogue dsRNA, to elicit exacerbation in a model of allergic inflammation driven by house dust mite (HDM) in Freund’s Complete Adjuvant (FCA). This HDM-CFA model is characterized by airway hyperresponsiveness (AHR) and a mixed T-helper phenotype (1).

METHODS: BALB/c mice (male, 18-20g) were sensitised subcutaneously on day 0 with 100µg of house dust mite (Dermatophagoides pteronyssinus (Der p)) extract in complete Freund’s adjuvant as previously described (1). On day 14, mice were exposed to saline or HDM (25µg) via intranasal instillation. A dose of Poly I:C that elicited submaximal inflammatory response (30 µg) was administered by intranasal instillation at different times around the HDM challenge, 24hrs before (-24hr), at the same time (0hrs) and after (+6hours,+24hours). 24 hours post-HDM challenge, non-invasive whole-body plethysmography was used to assess AHR stimulated by aerosolised methacholine (MCh, 0-16mg/ml). 48 hours after HDM challenge bronchoalveolar lavage fluid (BALF) was collected for the measurement of inflammatory cells.

RESULTS: Poly I:C administered at different time points, caused a significant exacerbation in BALF neutrophils (-24, 0 and +6), macrophages (-24, 0 and +6) and lymphocytes (-24 and 0) in the HDM challenged animals when compared with Poly I:C or HDM alone. When administered 24hrs before the challenge, the AHR associated to MCh was also significantly exacerbated.

CONCLUSIONS: Poly I:C exacerbates the inflammation and AHR in a murine model that mimics certain aspects of persistent asthma. The time of poly I:C administration with respect to HDM challenge seems to be key in the degree of exacerbation observed . This model could be used to investigate new mechanisms of action underlying viral exacerbation in persistent asthma and for the assessment and evaluation of novel therapies for such condition.


‘The U-BIOPRED consortium receives funding from the European Community and from the European Federation of Pharmaceutical Industries and Associations as an IMI JU funded project.’

http://www.ubiopred.european-lung-foundation.org