

MEETING ABSTRACT

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Mechanisms of asthma and allergic disease – 1093. A novel human anti-VCAM-1 Monoclonal antibody Ameliorates airway inflammation and remodeling in murine asthma model

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Background

Asthma is a chronic inflammatory disease induced by Type 2 helper T cells (Th2) and eosinophils. Vascular cell adhesion molecule-1 (VCAM-1) is the regulatory receptor implicated with recruiting eosinophils and lymphocytes to pathologic site in asthma. A monoclonal antibody (mAb) against VCAM-1 may attenuate allergic inflammation and pathophysiologic features of asthma. We evaluated whether a recently developed human anti-VCAM-1 mAb can inhibit pathophysiologic features of asthma in a murine asthma model induced by ovalbumin (OVA).

Methods

We evaluated whether human anti-VCAM-1 mAb binds to human or mouse VCAM-1. Leukocyte adhesion inhibition assay was performed to evaluate the *in vitro* blocking activity of human anti-VCAM-1 mAb. OVA sensitized BALB/c mice were treated with human anti-VCAM-1 mAb or isotype control Ab before intranasal OVA challenge. We evaluated airway hyperresponsiveness (AHR) and cell counts in bronchoalveolar lavage (BAL) fluid, measured inflammatory cytokines, and examined histopathological features, including VCAM-1 immunohistochemistry.

Results

The human anti-VCAM-1 mAb bound to human and mouse VCAM-1 molecules and inhibited adhesion of human leukocytes *in vitro*. AHR and inflammatory cell counts in BAL fluid were reduced in mice treated

with human anti-VCAM-1 mAb as compared to a control Ab. The levels of interleukin (IL)-5 and IL-13, and transforming growth factor- β in lung tissue were decreased in treated mice. Human anti-VCAM-1 mAb reduced goblet cell hyperplasia and peribronchial fibrosis. *In vivo* VCAM-1 expression decreased in treated group.

Results

Human anti-VCAM-1 mAb can attenuate allergic inflammation and pathophysiological features of asthma in OVA induced murine asthma model. This data suggested that human anti-VCAM-1 mAb could be an additional anti-asthma therapeutic medicine.

Author details

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