Title: The anti-IL-17A-antibody secukinumab does not attenuate ozone induced acute airway neutrophilia in healthy volunteers

Body: Background: Interleukin-17 (IL-17 or IL-17A) is linked to neutrophilic airway inflammation. Aim and Objective: To evaluate the effect of a novel anti-IL-17A antibody secukinumab (AIN457) on ozone-induced airway neutrophilia in healthy volunteers. Methods: 24 healthy volunteers with normal neutrophil levels in sputum and a proven inflammatory response to ozone 24 and 48 hours after the baseline ozone challenge (3 hours intermittent exercise with inhalation of 250 ppb ozone during the challenge) were randomized to secukinumab (10mg/kg bodyweight) or placebo or an open label prednisolone (50mg) arm in the ratio 2:1:1. Secukinumab or placebo was administered as an infusion whereas prednisolone was administered as an oral tablet. Sputum analyses were performed 24 and 48 hours following ozone challenges during the treatment phase at various time-points. Safety and pharmacokinetics were also assessed. Results: Administration of secukinumab was safe and well tolerated. Compared to placebo, secukinumab did not attenuate ozone-induced sputum neutrophilia 24 and 48 hours after ozone challenge. Prednisolone treatment resulted in an increase of neutrophils in sputum and in peripheral blood. No immunogenicity with secukinumab was observed. Mean half life of secukinumab was 29.8 days. Conclusions: Neutralizing IL-17A by secukinumab did not attenuate acute ozone-induced airway neutrophilia in healthy subjects. Study of the effects of anti-IL17A treatment on chronic neutrophilic airway diseases may be warranted in patients with disorders characterized by airway neutrophilia. The Abstract was funded by Novartis Institutes for BioMedical Research, Switzerland.