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Title: Effects of anti-M1 prime monoclonal antibody, MEMP1972A following allergen challenge in patients with mild asthma

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Body: Background: Elevated serum IgE is associated with allergic asthma. Membrane IgE includes the M1 prime epitope, present in human IgE-switched memory B cells and plasmablasts. MEMP1972A, a therapeutic antibody specific for M1-prime that depletes M1-prime-expressing cells. Aim: To test proof-of-activity of MEMP1972A. Methods: This randomized, double-blind, controlled study (NCT01196039) assessed the activity and safety of MEMP1972A in adults with mild asthma after allergen inhalation challenge (AIC). Subjects (n=29) were randomized (1:1) to intravenous MEMP1972A (5 mg/kg) or placebo every 4 weeks for 12 weeks. The primary outcome was the area under the curve (AUC) of the late asthmatic response (LAR) at Wk 12. Secondary outcomes included early asthmatic response (EAR). Serum total IgE and allergen-specific IgE were measured to confirm mechanistic activity of MEMP1972A. Other exploratory biomarkers were measured eg sputum and blood eosinophils. Results: MEMP1972A treatment was well tolerated. At Wk 12, MEMP1972A reduced the LAR AUC by 36% (90% CI: -14, 69, p=0.21) and the EAR AUC by 26% (6, 43, p=0.046) vs placebo. AIC at screening and Wk 12 induced a ~2-fold increase in allergen-specific IgE which was abrogated by MEMP1972A and more than ~10-fold increase in sputum eosinophils, which was reduced by MEMP1972A at Wk 12. MEMP1972A reduced total IgE by ~20% at Wk

8, and blood eosinophils by ~45% at Wk 28 vs baseline. Conclusions: Attenuation of EAR, LAR, serum IgE, sputum and blood eosinophils following AIC is consistent with the mechanism of action of MEMP1972A. Depletion of the M1 prime-expressing B-cell lineage may be effective for the treatment of allergic asthma.