European Respiratory Society
Annual Congress 2013

Abstract Number: 1175

Publication Number: 3537

Abstract Group: 5.3. Allergy and Immunology

Keyword 1: Allergy **Keyword 2:** Asthma - management **Keyword 3:** Immunology

Title: QGE031 high affinity anti-IgE: Tolerability, safety, pharmacokinetics and pharmacodynamics in atopic subjects

Dr. Jonathan 1402 Arm jonathan.arm@novartis.com MD [1], Dr. Ivan 1766 Bottoli ivan.bottoli@novartis.com [2], Dr. Andrej 1767 Skerjanec andrej.skerjanec@novartis.com [3], Dr. Andrea 1768 Groenewegen andrea.groenewegen@novartis.com [4], Dr. Phil 1769 Lowe phil.lowe@novartis.com [5] and Dr. Suzanne 1770 Maahs suzanne.maahs@novartis.com [6]. [1] Translational Medicine, Novartis Institutes for Biomedical Research, Cambridge, MA, United States, 02139 ; [2] Primary Care, Novartis Pharma AG, Basel, Switzerland ; [3] Preclinical Safety, Novartis Pharma AG, Basel, Switzerland ; [4] Biomarker Development, Novartis Pharma AG, Basel, Switzerland ; [5] Modelling and Simulation, Novartis Pharma AG, Basel, Switzerland and [6] Clinical Sciences and Innovation, Novartis Institutes for Biomedical Research, East Hanover, NJ, United States .

Body: QGE031, a human anti-IgE with higher affinity than omalizumab (OMA), was evaluated in atopic subjects (18-55 years) in single escalating intravenous (IV) and multiple ascending subcutaneous (SC) dose trials. Subjects in the IV trial received 0.1-10 mg/kg QGE031 (n=36), placebo (PB, n=29) or SC OMA (n=8). Subjects in the SC trial received 2-4 doses of 0.2-4 mg/kg QGE031 (n=70), PB (n=28) or OMA (n=12). Outcomes included safety, tolerability, PK, free and total IgE, expression of FcεRI and IgE and, in the SC study, skin prick testing (SPT). No deaths or serious adverse events occurred. In the IV trial, subject discontinuation rate was 17.8% (unrelated to adverse events, AEs). Urticaria occurred in 4/73 subjects; 3 at the higher IV doses and 1 on PB. For the SC trial, 2 subjects receiving 2 mg/kg QGE031 withdrew (due to symptoms considered unrelated to drug). Four urticarial events (1 in the 0.6 mg/kg and 3 in PB group) occurred in 3 subjects. PK analyses of both IV and SC dosing showed minimal IgE mediated drug disposition, rapid capture of IgE and a biexponential distribution/elimination. QGE031 reduced free IgE below the quantification level for all doses and elicited dose-and time-dependent suppression of basophil FcεRI, surface IgE expression and SPT responses. QGE031 showed 9-fold increase in PKPD potency (95% CI 6.1-14 fold) than OMA. The extent and duration of PD effects were dependent upon baseline IgE, but robust PD responses were observed in all groups including those with high baseline IgE. QGE031 was well tolerated with no serious AEs and reduced free circulating IgE, FcεRI, surface IgE, and SPT responses significantly greater and for a longer duration than OMA.