## P88 REAL-LIFE EXPERIENCE OF OMALIZUMAB IN CHILDREN WITH SEVERE ASTHMA

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**Introduction** Therapeutic options for children with severe asthma are limited. Clinical studies support the use of the anti-IgE antibody, omalizumab, in children with severe atopic asthma. However, children included in these studies had less severe disease than those in whom omalizumab is currently recommended. Little is known about the clinical efficacy of omalizumab in children with severe therapy resistant asthma (STRA).

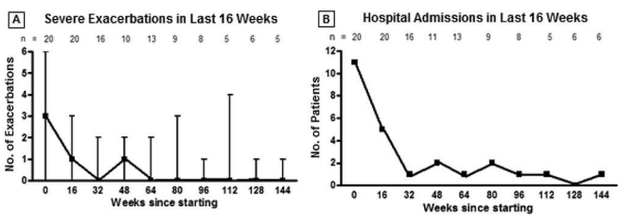
**Objectives** To determine the short-term (16 weeks) and long-term (beyond 16 weeks) efficacy of omalizumab, and predictors of a successful therapeutic response in children with STRA in a clinical setting.

**Methods** This was an observational, prospective study of children with STRA who were commenced on omalizumab. Spirometry, bronchodilator reversibility (BDR), exhaled nitric oxide ($FE_{NO}$), asthma control test (ACT), mini asthma-related quality of life questionnaire (AQLQ), severe exacerbations (requiring a course of oral corticosteroids (OCS) for ≥3 days) and number of unscheduled healthcare visits (UHCV) and hospital admissions were recorded before and every 4 weeks after commencing treatment. Every 16 weeks, patients underwent a more thorough assessment to determine if the treatment should be continued.

**Results** 33 children (22 male) aged 5–16 years were commenced on omalizumab. At 16 weeks there were significant improvements in mini-AQLQ; ACT; $FE_{NO}$; maintenance OCS dose; severe exacerbations and UHCVs.

20/33 (60.6%) children continued omalizumab beyond the initial 16 weeks (up to 192 weeks). Compared to those who discontinued, at baseline these children had higher mini-AQLQ (4.28 vs. 3.05) and ACT (11 vs. 8), were younger (11 vs. 13 years) and were more likely to have been admitted to hospital (57.9% vs. 0%) and have had a severe exacerbation (95% vs. 50%) in the 16 weeks before starting omalizumab. Maximal reduction in number of exacerbations and hospital admissions was evident at 32 weeks; this was maintained for up to 144 weeks (Figure 1).

**Conclusion** This is the first longitudinal study demonstrating long-term clinical efficacy of omalizumab as add-on therapy in children with STRA. Omalizumab was most effective in those with an exacerbation-prone phenotype at baseline, highlighting the importance of thorough patient characterisation when considering this treatment option.




**Abstract P88 Figure 1. Number of exacerbations(A) and incidence of hospital admissions (B) over timeduring treatment with omalizumab in children with severe therapy resistant asthma. Data shown is only for those who continued omalizumab beyond 16 weeks. Median and range shown for continuous data.**

## P89 NOVEL MECHANISMS OF IMMUNOMODULATION BY VITAMIN D AND -1-ANTITRYPSIN

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Vitamin D deficiency/insufficiency has been associated with poor respiratory health and a predisposition to respiratory disease. Local activation of vitamin D in the airways is important for antimicrobial defenses and suppression of inflammatory responses via the generation of a tolerogenic immune environment. One of the most highly unregulated proteins by vitamin D in CD4+ T-cells is the serine protease inhibitor -1-antitrypsin. In addition to controlling the pro-inflammatory effects of neutrophil elastase, -1-antitrypsin also acts via other pathways as an immunomodulator. We have identified a novel axis of immune modulation by vitamin D; where -1-antitrypsin is able to induce IL-10 production in PBMCs via an interaction with the complement component C3a. Our *in vitro* findings are supported by *in vivo* correlations of serum vitamin D, -1-antitrypsin, C3a and IL-10 in the airways of both asthmatics and healthy controls from a paediatric cohort. We propose that vitamin D is an upstream regulator of the -1-antitrypsin/C3a/IL-10 axis, providing attractive therapeutic options to promote tolerance in a range of inflammatory diseases.

# Clinical TB

## P90 VITAMIN D STATUS IMPROVES FOLLOWING RECOVERY FROM TUBERCULOSIS

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**Introduction and Objectives** Vitamin D deficiency associates with active tuberculosis, but the question of whether this arises as a cause or as a consequence of disease is controversial. Paired comparison of vitamin D status of TB patients at diagnosis and following recovery has potential to inform the debate, but such studies have not previously been conducted.

**Methods** We conducted a longitudinal study comparing serum concentrations of vitamin D metabolites in TB patients at long-term follow-up vs. diagnosis. Participants diagnosed with pulmonary TB in 2007–9 were invited to attend a follow-up visit in 2012. Concentrations of 25-hydroxyvitamin D (25[OH]D, the measure of vitamin D status), 1 ,25-dihydroxyvitamin D (1,25 $[OH]_2D$), 24R,25-dihydroxyvitamin D (24,25$(OH)_2D$), 4 ,25-dihydroxyvitamin D (4,25$[OH]_2D$), calcium, albumin, parathyroid hormone (PTH) and vitamin D binding protein (DBP) were determined in serum samples collected at follow-up and at the