**ASTHMA**

BENRALIZUMAB, AN ANTI-INTERLUKIN 5 RECEPTOR A MONOCLONAL ANTIBODY, VERSUS PLACEBO FOR UNCONTROLLED EOSINOPHILLIC ASTHMA: A PHASE 2B RANDOMISED DOSE RANGING STUDY *(Castro et al, Lancet Respir Med 2014; 2: 878-90)*

http://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600(14)70201-2.pdf

Bernalizumab is a human monoclonal antibody that targets Il-5 receptor 5 α. This was a double blind randomised placebo-controlled study; the primary outcome was to compare the annual asthma exacerbation rate between eosinophilic and non-eosinophilic asthmatics. Eosinophilic patients were randomised to placebo/2/20/100 mg and non-eosinophilic received 100mg only. 964 patients were screened and 604 patients were randomised. For the eosinophilic group, all doses showed a decrease in average ACQ6. The 100mg dose in this group also had a lower exacerbation rate than placebo (p=0.09). Treatment was most effective in patients with blood eosinophil count > 300; this subgroup had lower exacerbations and FEV1 improvements when compared to placebo. For the non-eosinophilic patients there was an improvement in asthma control and lung function.

**Final statement:** Bernalizumab proves to decrease ACQ6 in eosonhipllic asthmatics (particularly >300).

CLASSIFICATION OF CHILDHOOD ASTHMA PHENOTYPES AND LONG-TERM CLINICAL RESPONSES TO INHALED ANTI-INFLAMATORY MEDICATIONS *(Howrylak et al, J Allergy Clin Immunol. 2014; 133(5): 1289-1301)*

http://www.jacionline.org/article/S0091-6749(14)00203-6/abstract

The Childhood Asthma Management Program (CAMP) randomised children (5-12years) with mild-moderate persistent asthma to budesonide, nedocromil or matching placebo for 48 weeks. This patient data was used for this study to identify different asthma phenotypes; with 18 selected baseline variables and a spectral clustering analysis, 5 clusters were identified.

1. Mild asthma, low atopy, airway obstruction and exacerbations.

2. & 3. Were both atopic with medium rates of exacerbations. They were separated by degree of airway obstruction. Clusters 1-3 showed a reduction in exacerbations with budesonide and no change with nedocromil.

4 & 5 both had high levels of airways obstruction and exacerbations. They were separated by moderate and high atopy respectively. Clusters 4-5 had a larger proportion of patients requiring at least one course of steroids within 12 months of randomisation. Cluster 4 patients had a reduction in exacerbations with either budesonide or nedocromil. Cluster 5 showed no reduction in exacerbation with either medication.

**Final statement:** Mild asthmatics showed a reduction in exacerbations with budesonide. More sever asthmatics with moderate atopy showed a reduction in exacerbations with either budesonide or nedocromil.

EXHALED BIOMARKERS AND GENE EPRESSION AT PRESCHOOL AGE IMPROVE ASTHMA PREDICTION AT 6 YEARS OF AGE *(Klaassen et al, Am J Respir Crit Care Med Vol 191, Iss 2, pp 201-207, Jan 15, 2015)*

http://www.atsjournals.org/doi/abs/10.1164/rccm.201408-1537OC?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed&#.VgKjPt9VhBc

The Asthma Detection and Monitoring (ADEM) project is a longitudinal study using airway biomarkers with clinically available tools to predict asthma at 6 years of age among preschool wheezing toddlers. 202 children between ages 2-4 were followed up to the age of 6. The asthma predictive index (API) was poor at predicting asthma. The addition of exhaled breath condensate (EBC) levels of volatile organic compounds improved prediction area under the curve (AUC) to 86% (p=0.0002). A combination of VOCs + API + gene expression had an AUC of 95%, a PPV of 90%, a NPV of 89%, a sensitivity of 88% and a specificity of 88%.

**Final statement:** A combination of Asthma Predictive Index volatile organic compounds and gene expression improves the ability to predict asthma at 6 years of age.

GENE EXPRESSION IN RELATION TO EXHALED NITRIC OXIDE IDENTIFIES NOVEL ASTHMA PHENOTYPES WITH UNIQUE BIOMOLECULAR PATHWAYS *(Modena et al, Am J Respir Crit Care Med Vol 190, Iss 12, pp 1363-1372)*

http://www.atsjournals.org/doi/abs/10.1164/rccm.201406-1099OC?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed#.VgKkkt9VhBc

This study looked to identify clinically distinct asthma phenotypes by clustering bronchial airway epithelial cells (BAEC) samples according to the expression of certain genes correlated with fractionated exhaled nitric oxide (FeNO). 155 participants were analysed and 5 clusters identified.

1. This group had the lowest FeNO (18ppb).

2. This group had the highest FeNO (55ppb), including moderate-severe child onset asthmatics, highly obstructed and obese.

3. This group had a median FeNO of 39ppb; more than 50% had severe asthma with later onset and shorter duration.

4. This group had a normal FeNO, but a high degree of health care utilisation, moderate systemic steroid use and early asthma onset, with the highest BMI.

5. This group had a median FeNO of 38ppb, 50% were African American, early onset disease, high IgE and a high proportion of intubations.

**Final statement:** This study found several genes that are negatively and positively associated with FeNO.

ORAL GLUCOCORTICOID-SPARING EFFECT OF MEPOLIZUMAB IN EOSINOPHILIC ASTHMA *(Bel et al, N Engl J Med 2014; 317: 1189-97)*

http://www.nejm.org/doi/full/10.1056/NEJMoa1403291

This was a multi-centre randomised, double blind, placebo controlled study looking at the steroid sparing effect of mepolizumab. In the study there was a steroid reduction and maintenance phase. The odds for a reduction in the mepolizumab group vs placebo was 2.39 (p=0.008). The median reduction from baseline daily steroid dose was 50% in the mepolizumab group. There was no difference in total cessation of oral steroid use.

**Final statement:** Mepolizumab was shown to reduce maintenance steroid doses.