COMPARISON OF MONTELUKAST VERSUS SALMETEROL AS ADD-ON TO INHALED FLUTICASONE IN AT-RISK ASTHMATIC CHILDREN POSSESSING THE HOMOZYGOUS ARGinine-16 B₂-ADRENOCEPTOR GENOTYPE- A RANDOMIZED CONTROLLED TRIAL

K. Basu^{1,2}, H.P. Donald², B.J. Lipworth³, R. Tavendale⁴, D.F. Macgregor², S.A. Ogston⁵, C.N. Palmer⁴, S. Mukhopadhyay^{1,2}

¹Academic Department of Paediatrics, Brighton and Sussex Medical School, University of Sussex, Brighton,

²Children's Asthma and Allergy Unit, Perth Royal Infirmary, NHS Tayside, ³Asthma and Allergy Research Group, Division of Medicine and Therapeutics, ⁴Population Pharmacogenetics Group, Biomedical Research Institute, ⁵Division of Clinical and Population Sciences and Education, University of Dundee, Dundee, UK

Background and aims: Although clinical response is often variable, salmeterol is at least as effective as montelukast as add-on controller in children with asthma. However, children taking salmeterol, homozygous for the arginine-16 (Arg16) allele of ADRB2, have more frequent asthma exacerbations. We therefore investigated long term asthma control in genetically susceptible children with Arg/Arg-16 who were randomized to receive montelukast or salmeterol as add-on to inhaled steroid.

Methods: 62 asthmatic children with the Arg/Arg16 genotype were randomly assigned to receive fluticasone (as Flixotide®) plus either oral montelukast, or salmeterol (as Seretide®) with placebo montelukast. The primary end-point was school absence over one year. The study was funded by an unrestricted educational grant from MSD, UK.

Results: Reliever use was significantly decreased with montelukast compared with salmeterol (0.47(95%CI, 0.16-0.79;p=0.004)). Symptom scores improved with montelukast compared with salmeterol (morning cough: 0.51(95%CI,0.09-0.92;p=0.018); morning wheeze: 0.55(95% CI,0.25-0.86;p=0.001); morning dyspnoea: 0.29(95%CI,0.06-0.53;p=0.008); night wheeze: 0.46(95%CI,0.15-0.77;p=0.004); night dyspnoea: 0.44(95% CI,0.16-0.73;p=0.001). A significant improvement in pediatric asthma-related quality of life scores was observed with montelukast compared to salmeterol (activity limitation score: -0.55(95%CI,-0.918- -0.18;p=0.004), symptom score: -0.53(95%CI,-0.92- -0.14;p=0.009), emotional function score -0.523(95% CI,-0.84- -0.20;p=0.002)). No significant difference was observed in school absences (0.40(95% CI,-0.07-0.87;p=0.097)) between the treatment groups.

Conclusions: In children with Arg/Arg-16 genotype, montelukast may be more effective than salmeterol as add-on controller. This contrasts with the overall population of asthmatic children where salmeterol is more effective than montelukast. There is need to explore the feasibility and cost-effectiveness of ADRB2 genotype-directed choice of controller therapies in asthmatic children.