Title: Study design supporting the effectiveness of inhaled extra-fine beclomethasone/formoterol at the level of small airways of asthmatics

Body: Background. We made an attempt to establish in what way does treatment with inhaled extra-fine beclomethasone/formoterol (I-EF-BDP/F) formulation differ from other combined preparations of ICS and long acting beta-agonist (LABA). Methods. This was real life clinical observation of asthmatics switched to I-EF-BDP/F (Foster, Chiesi Pharma, Italy) from dry powder inhalers of fluticasone/salmeterol and budesonide/formoterol. Effects of 8-weeks treatment were documented by spirometry and airway / systemic inflammation: exhaled breath temperature (EBT), blood eosinophils (Eos) and C-reactive protein (CRP). Results. 59 patients completed the study (mean age 51 ± SD 12 years, 38 women). They did not show significant pre/post changes in the inflammatory indices (EBT, Eos and CRP). However, when we ranked them according to the pre/post treatment differences in forced vital capacity % predicted (FVC, a simple indicator of small airways involvement), the subjects above the 75th percentile (“top responders”, n=15), demonstrated significant drop in EBT [ºC] (34.04±0.30 vs. 33.57±0.33, P=0.003) and Eos [cells/µL] (381.7±91.2 vs. 244.2±43.2, P=0.018). The pre/post EBT and CRP differences of the “top responders” significantly exceeded those of the patients below the 25th percentile of FVC: P=0.04 and 0.05 respectively. Conclusion. Subjects demonstrating highest improvement in FVC after transition to I-EF-BDP/F from other combined ICS/LABA preparations had prominent decrease in the level of inflammation. As FVC is a simple indicator of small airway involvement, these results support the notion that I-EF-BDP/F may exert its effects
in the small airway.