Name of Sponsor/Company
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Title of Study
Does extra fine HFA-BDP suppress small airways inflammation in COPD?

Investigators
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Study centre(s)
Asthma & Allergy Research Group, Ninewells Hospital, Dundee

Publication (reference)
SHORT P, WILLIAMSON P, LIPWORTH BJ. Effects of extra-fine inhaled and oral corticosteroids on alveolar nitric oxide in COPD. Lung 2012;190:395-401

Date of first enrolment	**Phase of development**
18.03.2009	Phase IV
Date of last completed	
11.10.2011	

Objectives
To establish whether extra-fine particle BDP (Qvar) can achieve suppression of small airways inflammation and obstruction in COPD.

Methodology
A double-blind randomized, controlled, crossover trial with an open-label systemic steroid comparator. After a 2 week steroid washout period, participants were randomized to 3 weeks of 100 mcg of HFA-BDP twice daily and then 3 weeks of 400 mcg of HFA-BDP twice daily, or matched placebos with subsequent crossover. All patients then received 1 week open-label, 25 mg/day of prednisolone. Exhaled nitric oxide, plasma cortisol, and lung function were recorded. CANO was corrected for axial diffusion.

Number of patients planned
24 enrolled to complete 14 adults

Number of patients analysed
16

Diagnosis and main criteria for inclusion
Chronic obstructive pulmonary disease (COPD) patients with a FEV1/FVC ratio <0.7, FEV1 <80% predicted with CANO>2 ppb

Test product dose

Group 1
HFA-BDP 100 µg b.i.d. (3 weeks)
HFA-BDP 400 µg b.i.d. (3 weeks)

Group 2
Placebo 1 puff b.i.d. (3 weeks)
Placebo 4 puffs b.i.d. (3 weeks)

Duration of treatment
12 weeks (2 treatment periods of 6 weeks)

Reference therapy
Placebo (see Test Product Dose)

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Criteria for evaluation

Primary Endpoint
CANO

Secondary Endpoints
Spirometry, Whole Body Plethysmography, Impulse Oscillometry, SGRQ, patient diary cards, FENO, JNO, induced sputum analysis. FBC, SPD, CRP, hsCRP, IL-6, TNFα, glucose, overnight urinary cortisol/creatinine ratio, 8am serum cortisol.

Statistical methods
Data were assessed for normality using the Shapiro-Wilk test and through inspection of Boxplots.

Non-Gaussian data were log-transformed before analysis. Analysis of variance (ANOVA) of repeated measures was performed with Bonferroni correction for multiple comparisons.

Analyses were performed per-protocol using SPSS version 17 (SPSS Inc., Chicago, IL).

Summary Conclusions

Results
There were no significant differences seen with either dose of HFA-BDP compared with placebo. Oral prednisolone significantly reduced FENO and JNO but not CANO. Plasma cortisol was significantly suppressed by oral prednisolone only.

Conclusion
Whilst CANO remains a biomarker of interest in COPD, it is not suppressed by systemic or extra-fine particle ICS. CANO is not a useful marker for monitoring response of small airway disease to therapies in COPD.

Date of the report: 04/08/2015