Title of Study

An open-label randomized pilot trial to evaluate tolerability, safety and applicability of AKITA Inhaled Budesonide Suspension in children aged 3-11 years with mild to moderate asthma

Study Period		**Phase of Development**
Date of first enrolment	14 March 2011	2
Date of last completed	18 Janury 2012	

Objectives

To evaluate the airway tolerability/efficacy, safety and applicability of nebulized Budesonide delivered with AKITA in children aged 3-11 years with asthma in comparison to delivery with conventional jet nebulizer

Methodology

Open-label, randomized, observational, two-armed, multicenter pilot trial

Number of Subjects (Planned and Analysed)

Planned: 40 (20 investigational product, 20 comparator, each 10 age 3-5, 10 age 6-11)

Actual: 43 screened, 41 randomized, 41 analyzed

Criteria for Inclusion

Children aged 3-11years with mild to moderate asthma for at least 6 months and currently stable.

Main further inclusion criteria:

- Informed consent
- Asthma treated for at least 3 months with inhaled (ICS) corticosteroids (MDI/DPI)

Specific inclusion criteria for children aged 6-11 years:

- FEV_1 >= 50% predicted at screening or baseline
- Increase of FEV_1 at least 12% within 15-30 minutes after salbutamol inhalation

Main exclusion criteria:

- History of allergy or adverse experience with budesonide
- Upper respiratory tract infection within 4 weeks of Screening
- Emergency room visit for treatment of asthma exacerbation within 4 weeks of Screening
- Hospitalization for asthma within 3 months of Screening
- Use of inhaled LABA, theophylline, anti-IgE, or oral corticosteroids within 3 months of Screening.
- Treatment with other investigational asthma treatment within 30 days prior to Screening.
- Evidence of chronic lung diseases other than asthma
- History of medication noncompliance

- History of significant medical illness or condition that in the Investigator's opinion places the subject at undue risk by participating in the study
- Past episode of anaphylaxis with severe respiratory symptoms
- Taking oral or i.v. corticosteroids for any disease indication

Test Product, Dose and Mode of Administration

Budesonide nebuliser suspension, 2 mL of 1 mg/2 mL budesonide, administered via AKITA JET nebulizer twice daily. Per dose, only a portion of the fill dose approximately 15 breaths (range 7-23 breaths), or 250 µL = 125 µg of budesonide aerosolised. Daily aerosolised dose of 250 µg budesonide resulting in approx. 40µg deposited dose (80µg deposited daily dose).

Duration of Treatment

2 weeks screening, 12 weeks treatment, 2 weeks follow-up

Reference Therapy, Dose and Mode of Administration

Budesonide nebulizer suspension, 2mL of 0.5 mg/2 mL Budesonide, administered via conventional jet nebulizer (Pari LC SPRINT), twice daily. Note: comparator used approved maintenance dose (500µg BID) given via nebulizer and the Pari LC SPRINT achieved the same deposited dose of approx. 40µg per application or 80µg deposited per day.

Criteria for Evaluation

Efficacy

- Change and percent change in FEV_1 (age group 6-11 years)
- Changes in PEF (age group 6-11 years)
- Changes in Children Asthma Control Test (C-ACT)
- Changes in asthma symptom scores
- Change in FEV_1 % predicted from Baseline
- FeNO level
- Change in average number of puffs of Salbutamol per day from Baseline
- Change and percent change in number of nocturnal awakenings from Baseline
- Number of days of hospitalization
- Absenteeism from kindergarten/preschool/school

Safety

- The number and percent of subjects with at least one treatment emergent AE (TEAE)
- The number and percent of subjects with TEAEs by System Organ Class and preferred term
- The number and percent of subjects with TEAEs by intensity
- The number and percent of subjects with TEAEs by relationship to study drug
- The number and percent of subjects with SAEs
- The number and percent of subjects with hospitalizations or emergency room visits
- Changes in vital signs

- Changes in weight and Body Mass Index
- Changes in physical examination
- Laryngeal / oropharyngeal symptoms

Statistical Methods

The study was conducted as an open-label pilot study. Statistical methods were descriptive:

Continuous variables were summarized by number of observations, arithmetic mean, standard deviation, minimum, lower quartile, median, upper quartile, maximum. Categorical data were described using absolute and relative frequencies.

Results were presented for the full analysis set by treatment and also for subgroups by age group. A conservative imputation method for missing data was used.

Summary – Conclusions

Efficacy Results

The change from baseline during the treatment period across all the efficacy parameters, presents a trend in favour of the AKITA JET group: FEV_1 /predicted FEV_1 (6.0% AKITA JET group versus 4.8% Pari Boy group), PEF (6.8 L/min versus 3.9 L/min), C-ACT score (2.3 versus 0.1), FeNO (-11.1 ppb versus +2.1 ppb), asthma symptom scores (-0.2 versus 0.0), nocturnal awakenings (-2.2 versus 1.4 days with awakenings), absenteeism from school and kindergarten (0.0 versus 0.1 days) and salbutamol puffs (-0.1 versus +0.2 puffs/day).

Safety Results

The adverse event profiles of the AKITA JET and Pari Boy groups were comparable.

Hoarseness, voice alteration and pharyngeal thrush have been defined as typical side effects of oropharyngeal budesonide deposition by inhalation using nebulizers. None of these events occurred in the AKITA JET group and the only case of hoarseness occurred in a patient of the Pari Boy group.

There were no clinically significant changes in vital signs and no notable differences in changes in physical examination, weight and BMI between the treatment groups.

The AKITA JET nebulizer has been used with a compliance rate of about 91%, very similar to that of the conventional nebulizer Pari Boy (90%). One patient from each treatment group dropped out. All other patients used the devices until termination.

Conclusions

Despite small patient numbers, this study suggests that the AKITA JET device has been accepted by children and parents and shows a trend to better efficacy and acceptable safety. The actual doses utilized with the AKITA JET were less than for the conventional nebulizer tested.

Since the generation of the original study report, Activaero GmbH has been acquired by Vectura.