**Clinical Study Report Synopsis**
Drug Substance Budesonide
Study Code NIS-RCN-PUL-2008/1

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|---|---|---|---|
| Drug Substance | Budesonide | SYNOPSIS | (for national authority use only) |
| Study Code | NIS-RCN-PUL-2008/1 | | |
| Date | 30th July 2009 | | |

# A Non-interventional Study of cough variant asthma treatment with Pulmicort®Respules® in patient aged 5-year old or younger in outpatient department

**Study dates:**

**First subject enrolled** 4th April, 2008

**Last subject completed** 22th March, 2009

**Phase of development**

Post-market non-interventional study

## Objectives

### Primary

To show the efficacy of Pulmicort® Respules® in cough variant asthma (CVA) treatment in patient aged 5-year old or younger in outpatient department

### Secondary

- Compliance of the patient suffered from cough variant asthma treated with Inhaled Corticosteroid (ICS)
- Impact of ICS on patient's nocturnal symptom
- Impact of ICS on patient's quality of life
- Overall assessment of investigator to ICS treatment of CVA

## Study design

Open label, non-interventional

## Target patient population and sample size

Patient aged 5-year old or younger who has been diagnosed as CVA and decided by physician to use Pulmicort® Respules® inhalation. Totally 914 CVA patients were recruited.

## Investigational product, dosage

Pulmicort® Respules® 1mg/vial, initial dosing 1-2 mg daily nebulization

## Comparator, dosage and mode of administration

NA

## Duration of treatment

7 weeks

## Variables

### Primary variables

Evaluation of daytime symptom score (0-3) under treatment with Pulmicort® Respules® at week 7 compared to those at week 1

### Secondary variables

- Days of complying or against with doctor's advice and its reasons

- Evaluation of symptoms score under treatment with Pulmicort® Respules® at week 7 compared to those at week 1 (i.e. overall score, nocturnal score, impact of CVA related disease on symptom score and as- needed bronchodilator usage at week 7 compared to those at week 1)
- We had no variable collected for impact of ICS on patient's quality of life
- Disease control levels under treatment with Pulmicort® Respules® at week 7 compared to those at screening and their consistency with patients self-evaluation (including impact of concomitant drug on CVA control level)

**Statistical methods**

Descriptive statistics

**Description of analysis set**

All 914 patients were enrolled into study, while 11 patients were excluded due to protocol breach. Remaining 903 patients were included into intention to treat outcome variables analysis.

**Patient population**

914 patients (≤ 5yr) were recruited from 39 centres nationally. Among these, 11 patients were not included into variables analysis set due to protocol breach. The withdraw rate of the remaining 903 patients is 8.97% (81/903). Table S2 showed the patients disposition.

**Table S2 Patient population and dispositions**

| | | **Total** |
|---|---|---|
| Sex N( %) | Male | 536 (59.36) |
| | Female | 367 (40.64) |
| Age (yrs) | Mean (SD) | 2.8 (1.2) |
| Disposition | | |
| Patients completed 1 week (visit2)** | | 903 (100) |
| After 3 weeks (visit 3) ** | | 886 (98.12) |
| After 5 weeks (visit 5) ** | | 854 (94.57) |
| After 7 weeks (visit 7) ** | | 822 (91.03) |
| Cases of discontinuation in advance** | | 81 (8.97) |
| Cases of protocol breach* | | 11 (1.20) |

*The ratio of Protocol breach cases was calculated based on total recruited subjects of 914.
**The ratio of completed and discontinuation cases were calculated based on patients included for analysis.

**Summary of efficacy results**

Table S3 showed efficacy results.

**Table S3 Efficacy results**

| Efficacy variables | | Screening | Week 1 | Week 7 | Improvement |
|---|---|---|---|---|---|
| Primary efficacy variables | | | | | |
| Mean daytime symptom score | | -- | 2.4 | 0.3 | -2.1 |
| Secondary efficacy variables | | | | | |
| Compliance (≥80%) | | -- | 869 (96.23%) | 790 (87.49%) | |
| Mean of nocturnal symptom score | | -- | 1.5 | 0.2 | -1.3 |
| Ratio of patients taking bronchodilator | | -- | 39.42% | 2.99% | -36.43% |
| Median of bronchodilator usage days | | -- | 5.8 | 3.9 | -1.9 |
| Investigator assessment of CVA control | Effectively controlled | 34% | 83.5% | 89.92% | 55.92% |
| | Uncontrolled | 66% | 16.17% | 1.11% | -64.89% |
| Self-assessment of CVA control | Effectively controlled | -- | 82.83% | 89.59% | 6.76% |
| | Uncontrolled | -- | 17.05% | 1.55% | -15.5% |

--No data.

The overall symptom scores had a declining tendency as treatment went on. The number of patients who needed bronchodilator for reliever therapy decreased significantly after pulmicort respules treatment. For those patients who needed bronchodilator for reliever therapy, the mean days for as-needed bronchodilator usage decreased. The overall treatment compliance during the study was around 90%. The nocturnal symptom scores decreased along with the treatment. The effective control rate of CVA judged by investigator was 34% at screening and increased significantly to 89.92% at week 7 and the uncontrolled rate decreased significantly from 66% at screening to 1.11% at week 7. The effectively controlled rate of self-assessment also increased from 82.83% at week 1 to 89.59% at week 7 and the uncontrolled rate decreased from 17.05% at week 1 to 1.55% at week 7.

**Table S4 Correlation between influencing factors and CVA**

| factors | CVA symptom control | | CVA recurrence | |
|---|---|---|---|---|
| | **Odds Ratio** | **P value** | **Odds Ratio** | **P value** |
| Compliance | 2.698 | 0.0033 | 0.439 | 0.0016 |
| Baseline disease | 1.046 | 0.8102 | 0.457 | <0.0001 |
| Antibiotics | 0.954 | <0.0001 | 1.026 | 0.0185 |

The possibility to be effectively controlled for CVA patients with good compliance was 2.698 times over that for patients with poor compliance, and patients with good compliance had lower possibility of CVA recurrence (OR=0.439).

Patients with mild baseline disease had lower possibility of CVA recurrence. History of antibiotics usage may lead to slightly poor symptom control and slightly high CVA recurrence.

**Summary of safety results**

In this non-interventional study, the reporting of adverse events (including serious adverse event) during the study was spontaneous. There was no spontaneous report of adverse events in the study.