Title of the Study: Comparison of a Four-Times-a-Day Dosing Frequency to a Twice-a-Day Regimen in Subjects Requiring a Low-Dose Inhaled Steroid, Budesonide, to Control Mild to Moderate Asthma

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Study Site: Hôpital du Sacré-Coeur
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Study Period: November 1990 through August 1993

Clinical Phase: 4

Objectives: To compare the efficacy of twice daily to four times daily dosing with Pulmicort® Turbuhaler® for control of asthma exacerbations, and to compare patient compliance for the two dosing regimens

Study Design: Randomised, open-label, single-blind, parallel group design

Number of Patients: Fifty-eight patients (38F/20M), mean age 50 (SD 13), 29 per treatment
Investigational and Reference Therapies: Pulmicort® Turbuhaler®: 400, 800 or 1200 µg daily, dosed BID or QID
Lot No.: RE 35, SL 88, SF 59, QD 16, QI 20, RF 113, RE 105, QH 66, QM 82, RB 57, QH 37

Duration of Treatment: According to the protocol, treatment was to continue until exacerbation, but not to exceed 48 weeks (actual duration was 7.3 months (SD = 4.1))

Assessment Methods: Spirometry at all visits; methacholine provocation tests and Cortrosyn® tests at baseline, 24 weeks, and at termination; swabs for Candida albicans at 0, 6, 14, 24, 36, and 48 weeks (additional tests optional); exacerbations identified on the basis of daily diary recordings, which included morning and evening PEFR, asthma symptoms, and medication use
Diagnosis and Criteria for Inclusion: Male or female outpatients; 18 through 70 years of age; mild to moderate asthma optimally controlled on a daily dose of 400 through 1200 µg inhaled steroid from a pMDI (or 800 through 2400 µg from Beclovent®/Rotahaler®); written informed consent; willing and capable of following study directions and completing a daily diary; clinically stable at study entry and during the two-week baseline period as defined by no nocturnal awakenings due to asthma, no recent modification in the need for asthma medications, no acute viral infections, and daily fluctuations in peak expiratory flow rates < 20 %; FEV₁ reversibility ≥ 20% 30 minutes after administration of a β₂-agonist documented within the last year; PC₂₀ value ≤ 16 mg/ml as determined at a methacholine provocation test at visit 1 or 2 (otherwise eligible patients were excluded at visit 1 or 2 if PC₂₀ was not in acceptable range); pregnant or lactating women, or women not using adequate contraception; smokers; use of oral steroids in the 3 months preceding study start; diabetes; history of sudden deterioration in asthma symptoms; emergency room visit in the last 3 months or hospitalisation in the last year for asthma; any condition such as alcohol or drug abuse likely to affect study compliance.

Statistical Methods: The confidence interval test, chi square, unpaired t-test, analysis of variance with orthogonal contrasts, and Kaplan-Meier survival curves were used in the analysis of the results. Sub-group analyses were performed for the different doses levels.

Summary of Results: The number of exacerbations in the QID group (11) was significantly less than in the BID group (17) (p = 0.05). Compliance with the BID regimen (95% (SD 16)) was significantly higher than with QID dosing (83% (SD 16)). The number of reports of throat side effects, including candidiasis, was significantly higher in the QID group (p = 0.05). No serious adverse events were reported.
Conclusions: Under the conditions of this study, QID dosing of budesonide administered with Turbuhaler® resulted in fewer exacerbations than was seen with BID dosing for patients requiring low to moderate (400 through 1200 µg/day) doses of inhaled steroid to stabilize their asthma symptoms. Compliance was superior on the BID regimen, but was good in both treatment groups. The frequency of throat side effects and positive tests for Candida albicans was higher in patients on the QID regimen as compared to the BID regimen.

Signatures:

Author: [Signature]
Date: [Date]

Statistician: [Signature]
Date: [Date]