

# Asthma treatment: Clinical trials

0109

## COMPARISON OF ORAL VERSUS INHALED NONSTEROIDAL THERAPIES IN THE TREATMENT OF PATIENTS WITH MILD TO MODERATE ASTHMA

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The efficacy and safety of zafirlukast (ACCOLATE™) were compared with cromolyn sodium (INTAL®) and placebo in a multicenter, double-blind, double-dummy, parallel-group study. Patients (n=287) 12 to 71 years of age with self-assessed, mild-to-moderate asthma and a cumulative daytime asthma symptom score  $\geq 8$  over 7 consecutive days (range, 0 to 3 per day) were randomized to 13 weeks of treatment with zafirlukast (20 mg, bid), cromolyn sodium (2 puffs = 1600 µg, qid), or placebo. Albuterol was provided as rescue medication. Response to treatment was assessed by the percentage of patients who met  $\geq 1$  of the following response criteria: 50% reduction in daytime symptoms, first morning symptoms, or nocturnal awakenings without a 50% increase in  $\beta$ -agonist use, or a 50% decrease in  $\beta$ -agonist use without a 50% increase in daytime symptoms. More patients responded to treatment with zafirlukast (64%) and cromolyn sodium (68%) than with placebo (46%,  $p < 0.05$ ); no difference was observed between active treatments ( $p > 0.10$ ). The safety profile for active therapies was not clinically different than that of placebo. The proposed minimum dose of zafirlukast (20 mg, bid) was comparable in safety and efficacy to the optimum dose of cromolyn sodium (2 puffs, qid) in patients with mild-to-moderate asthma appropriate for first-line therapy.

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## LONG ACTING $\beta_2$ AGONISTS: A COMPARISON OF ORAL BAMBUTEROL AND INHALED SALMETEROL IN ASTHMATIC PATIENTS WITH NOCTURNAL SYMPTOMS

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The effect of bambuterol 20 mg at bedtime and of salmeterol 50 µg bid was compared in a multicentre study comprising a 2-week run-in and a 6-week double-blind double-dummy treatment period, with a randomized, parallel group design. 117 asthmatic patients (65F/52M) aged 20 to 70 years (mean 45) were randomized. They were to be treated with inhaled steroids 800 to 2,000 µg daily and/or oral steroids  $\leq 20$  mg/daily for at least 4 weeks, to have a nocturnal waking due to asthma symptoms with a need for rescue medication at least once during the run-in,  $\geq 15$  % overnight fall of peak expiratory flow (PEF) in 3 out of the last 7 days of the run-in, and  $40 \leq FEV_1 \leq 85$  % of predicted normal. The patients recorded morning and evening PEF, daily symptom score (0-3), rescue medication and subjective tremor score (0-3) in a diary. The primary variable was morning PEF, change from run-in. Main results were as follows:

	Bambuterol	Salmeterol	p value
FEV1 at visit 1(% pred)	64±12	65±13	NS
$\Delta$ PEF morning* (L/min)	28±51	29±52	NS
$\Delta$ PEF evening* (L/min)	20±53	23±53	NS
nocturnal awakening (%/week)			
- run-in	46±30	48±30	NS
- active treatment	18±25	25±31	NS

\* change from run-in, mean±SD.

Other efficacy variables (daily symptoms score, rescue medication, overnight fall of PEF) showed a similar improvement in both groups. Tremor scores were low and similar in both groups during the run-in and treatment periods (mean±SD: bambuterol 0,2±0,5 and 0,2±0,3; salmeterol 0,3±0,6 and 0,2±0,4). Five serious adverse events occurred during the study among which 4 deteriorations of asthma (salmeterol n=3, bambuterol n=1). In conclusion, similar efficacy and control of nocturnal and daily symptoms of asthma were obtained with oral bambuterol 20 mg at bedtime and inhaled salmeterol 50 µg bid in this group of moderate to severe asthmatic patients.

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## 0.5% NEDOCROMIL SODIUM NEBULISER SOLUTION IN MILD-TO-MODERATE ASTHMA PATIENTS

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Using a double-blind, placebo controlled, parallel group study design, we have evaluated the efficacy and safety of 0.5% nedocromil sodium (Tilade®) nebuliser solution in mild-to-moderate asthma patients. Nebuliser solutions, administered four times daily for 12 weeks, were randomly allocated to 188 symptomatic asthma patients (age range 12-81; mean 33 years). Eight centres took part, with 94 patients in each treatment group. Both treatments were safe and well tolerated. All the diary card and clinic variables showed differences in favour of nedocromil sodium compared with placebo, these being statistically significant for:

	baseline	weeks 3-12†	p-value
summary score‡			
nedocromil sodium	3.41	2.49	0.028
placebo	3.32	2.95	
sleep difficulty			
nedocromil sodium	0.98	0.70	0.028
placebo	0.98	0.89	
a.m. peak flow (L/min)			
nedocromil sodium	386	411	0.050
placebo	376	390	
p.m. peak flow (L/min)			
nedocromil sodium	406	442	0.002
placebo	407	409	
FEF <sub>25-75</sub> (L/sec)			
nedocromil sodium	1.98	2.20	0.011
placebo	1.99	2.03	

† primary time period of assessment

‡ main efficacy variable (daytime asthma + sleep difficulty)

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## IMPROVEMENTS IN QUALITY OF LIFE IN CHRONIC ORAL STEROID-DEPENDENT ASTHMA PATIENTS USING FLUTICASONE PROPIONATE ARE MAINTAINED ONE YEAR LATER

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The purpose of this study was to assess quality of life (QOL) associated with long-term use of fluticasone propionate (FP) in chronic oral steroid-dependent patients. Previously, we reported that patients receiving inhaled fluticasone propionate (1000mcg or 750mcg twice daily) experienced significant improvements in key dimensions of QOL (Jolicoeur, L. et al. JACI 1994; 93: 185.). Following this study, ninety-one (91) patients were entered into an open-label extension receiving FP in doses of 250-1000mcg twice daily. Patients completed the Medical Outcomes Study Short Form 36 and Sleep Scale at pre-study, and at 4, 8, and 12 months of extension. QOL scale scores range from 0-100 with higher scores reflecting better QOL.

	Pre-study	Month 4	Month 8	Month 12
Physical Functioning	60.8	73.5	73.8	73.3
Role-Physical	48.1	66.5	63.4	62.2
General Health	53.5	63.4	63.3	62.9
Vitality	51.9	60.4	60.0	60.1
Change in Health	58.1	85.6	85.8	85.5
Sleep	48.9	62.2	63.2	61.2

Patients experienced an improvement in six QOL dimensions, ranging from 8 to 27 points, after receiving FP for 1 year. Overall, long-term use of FP in patients previously requiring oral steroids improves QOL and continually maintains this improvement.

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## EFFECTS OF AN INHALED STEROID ON GENERIC QUALITY OF LIFE IN ASTHMA OR COPD

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In a four-year prospective controlled study we examined the influence of beclomethasone dipropionate (BDP) 400 µg, two times daily, on quality of life in 56 patients with asthma or COPD. During the first two years, patients only received bronchodilator therapy with salbutamol or ipratropium bromide. During the third and fourth years, additional treatment with BDP was given. 56 Patients (28 asthma, 28 COPD) with an annual decline in the forced expiratory volume in one second (FEV<sub>1</sub>) of at least 80 ml/yr in combination with at least two exacerbations per year during bronchodilator therapy alone participated. Quality of life was assessed at the start and after two and four years by means of the Inventory of Subjective Health (ISH) and the Nottingham Health Profile (NHP). BDP significantly improved the course of lung function (FEV<sub>1</sub>) ( $p < 0.0001$ ). However, it did not improve the ISH score or the six dimensions of the NHP, neither in asthma, nor in COPD. BDP temporarily decreased respiratory symptoms during months 4-6 of BDP treatment in asthma ( $p < 0.01$ ) and during months 7-12 in COPD ( $p < 0.05$ ). A weak correlation was found both cross-sectionally and longitudinally between (change in) symptoms and quality of life on the one and the (change in) FEV<sub>1</sub> on the other hand. It was concluded that although BDP significantly improved the course of lung function and temporarily decreased the severity of symptoms, it did not improve general well-being of patients with asthma or COPD.

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