

# Montelukast improved pulmonary function and asthma-specific quality of life in aspirin-intolerant asthma

Dahlén SE, Malmström K, Nizankowska E, et al. Improvement of aspirin-intolerant asthma by montelukast, a leukotriene antagonist: a randomized, double-blind, placebo-controlled trial. *Am J Respir Crit Care Med.* 2002 Jan 1;165:9-14.

## QUESTION

In patients with aspirin-intolerant asthma (AIA) is montelukast effective for improving pulmonary function, asthma symptoms, and asthma-specific quality of life (QOL)?

## DESIGN

Randomized (unclear allocation concealment\*), blinded (clinicians and patients),\* placebo-controlled trial with 4-week follow-up.

## SETTING

8 centers in Europe and 2 in the United States.

## PATIENTS

80 patients (age range 22 to 72 y, 68% women) who had a diagnosis of AIA with characteristic symptoms of chronic rhinosinusitis, asthma, and aspirin intolerance and 90% of whom were receiving moderate-to-high doses of glucocorticosteroids. Before inclusion in the study, patients were required to show a 12% improvement in FEV<sub>1</sub> after inhalation of  $\beta$ -agonists, mild daytime asthma symptoms, and daily average use of  $\geq 1$  puff of  $\beta$ -agonists during a 2-week run-in period. Follow-up was 100%.

## INTERVENTION

Patients were allocated to montelukast (10 mg) ( $n = 40$ ) or placebo ( $n = 40$ ) taken orally once daily at bedtime.

## MAIN OUTCOME MEASURES

Pulmonary function (peak expiratory flow rate measured in the morning and evening and FEV<sub>1</sub> measured once per wk), asthma symptoms, daily use of  $\beta$ -agonists, and asthma-specific QOL.

## MAIN RESULTS

Analysis was by intention to treat. Improvement in pulmonary function was greater in the montelukast group than in the placebo group (Table). Improvement in asthma-specific QOL was greater in the montelukast group than in the placebo group (mean change from baseline for the average of 4 QOL domains 0.45 vs 0.08,  $P < 0.05$  for the difference). A greater decrease in rescue use of inhaled  $\beta$ -agonists occurred in the montelukast group than in the placebo group

(27.7% vs 1.6%,  $P < 0.05$ ). The percentage of study days with asthma exacerbations was lower in the montelukast group than in the placebo group (8.3% vs 21.7%,  $P < 0.05$ ). The groups did not differ for daytime asthma symptoms or awakenings per night.

## CONCLUSION

In patients with aspirin-intolerant asthma (90% of whom were receiving moderate-to-high doses of glucocorticosteroids), montelukast was effective for improving pulmonary function and asthma-specific quality of life.

Source of funding: Merck Research Laboratories.

For correspondence: Professor S.E. Dahlén, National Institute of Environmental Medicine, Stockholm, Sweden. E-mail se.dahlen@imm.ki.se. ■

\*See Glossary.

## Montelukast vs placebo for aspirin-intolerant asthma at 4 weeks†

| Outcomes   | Difference in LS means between groups (95% CI) |         | P value        |             |
|--|--|---------|----------------|-------------|
| FEV <sub>1</sub>   | 10.2% (4.9 to 15.5)                            |         | < 0.001        |             |
| Morning PEFR (L/min)                                     | 28.0 (14.4 to 41.6)                            |         | < 0.001        |             |
| Evening PEFR (L/min)                                     | 23.1 (9.5 to 36.7)                             |         | < 0.001        |             |
|  | Montelukast                                    | Placebo | RBI (CI)       | NNT (CI)    |
| Patients with $\geq 5\%$ improvement in FEV <sub>1</sub> | 52.5%  | 27.5%   | 91% (9 to 247) | 4 (3 to 30) |

†LS = least squares; PEFR = peak expiratory flow rate. Other abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

## COMMENTARY

Many drugs are known to be effective as monotherapy for asthma. As new agents are introduced into practice, questions about their value compared with that of existing medications are common. Resolving these issues poses substantial challenges.

Accumulating evidence suggests that the recently introduced leukotriene antagonists may have limited clinical value. One systematic review concluded that leukotriene antagonists are probably inferior to inhaled corticosteroids for most clinical outcomes in mild-to-moderate asthma (1). A second review concluded that insufficient evidence existed to recommend currently licensed doses of leukotriene antagonists as add-on therapy to inhaled corticosteroids (2). However, the authors of both reviews emphasized the relative paucity of high-quality trials on which to base firm recommendations.

AIA is a variant form of asthma that affects about 5% of patients. Patients with AIA produce substantially more cysteinyl-leukotrienes than do those with aspirin-tolerant asthma at baseline and after challenge with aspirin. It follows that leukotriene antagonists might be particularly effective for AIA. The study by Dahlén and colleagues

supports this conjecture by showing additional clinical benefits from montelukast in patients with AIA, 90% of whom were already taking corticosteroids.

The results are interesting, but caveats exist. With no direct comparison, we cannot conclude that leukotriene antagonists are superior to corticosteroids as the mainstay therapy in AIA. Furthermore, study patients were not allowed to take a long-acting  $\beta$ -agonist, so it remains unclear whether leukotriene antagonists are beneficial in AIA when added to what would usually be considered standard care.

Dennis E. Niewoehner, MD  
Veterans Affairs Medical Center  
Minneapolis, Minnesota, USA

## References

- Ducharme FM, Hicks GC. Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma. *Cochrane Database Syst Rev.* 2000;(3):CD:002314.
- Ducharme F, Hicks G, Kakuma R. Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma. *Cochrane Database Syst Rev.* 2002(1):CD003133.