



ELSEVIER

LETTERS TO THE EDITOR

Montelukast is an effective monotherapy for mild asthma and for asthma with co-morbid allergic rhinitis

Dear Sir,

The IPCRG is to be acknowledged for their new guidelines for General Practitioners (GPs) on the management of chronic airways diseases in the February issue of the Primary Care Respiratory Journal. It is vital that such guidelines be based on scientific evidence and regulatory licenses. However, the recommendations for asthma [1] fall short with regard to the leukotriene receptor antagonist, montelukast, an anti-inflammatory and bronchodilatory medicine used in persistent asthma as a monotherapy or add-on therapy, and used in co-morbid asthma and allergic rhinitis.

The assertion of a lack of pediatric monotherapy data on leukotriene modifiers in mild persistent asthma is inaccurate. The MOSAIC trial [2] was a 12-month, non-inferiority study that compared the relative benefit of montelukast and fluticasone in children with mild persistent asthma. The results showed that the mean difference between the two treatments in the percentage of asthma rescue-free days (a primary endpoint assessing outcomes of relevance to the patient) was clinically comparable between the two therapies (difference of <1 day/month). In post-hoc analyses of the primary endpoint, there was a large degree of overlap (84.3% [95% CI of 77.0 to 91.6]) in the response of patients treated with either therapy. Several secondary endpoints, however, favored fluticasone.

Other studies have also shown that montelukast is an appropriate monotherapy for children. Importantly, montelukast was effective as a monotherapy controller in reducing asthma exacerbations in 2- to 5-yr olds with intermittent asthma [3]. In children with mild-to-moderate

asthma, significant improvements in asthma symptoms were reported in 2- to 5-yr olds and in airway obstruction in 6- to 14-yr olds [4,5].

Separately, guidance on therapy for patients with co-morbid asthma and allergic rhinitis is missing in the IPCRG asthma guidelines. This is puzzling, since not only does the IPAG/IPCRG's previous guidance on asthma rightly state that management of rhinitis may improve co-morbid asthma [6], but the current IPCRG guideline on allergic rhinitis [7] also recommends a leukotriene modifier as a preferred option for allergic rhinitis patients with asthma.

Several treatment options must be considered by the GP seeking the right therapeutic balance of efficacy, safety (especially in pediatrics), adherence, and ease-of-use for the control and management of asthma. Such an approach would come closest to optimizing care for individual patients.

Conflict of interest declaration

The author is an employee of Merck and Co. Inc.

References

- [1] van der Molen T, Ostrem A, Stallberg B, Ostergaard MS, Singh RB. International Primary Care Respiratory Group (IPCRG) Guidelines: Management of Asthma. *Prim Care Resp J* 2006;15(1):35–47.
- [2] Garcia Garcia ML, Wahn U, Gilles L, Swern A, Tozzi CA, Polos P. Montelukast, compared with fluticasone, for control of asthma among 6- to 14-year-old patients with mild asthma: the MOSAIC study. *Pediatrics* 2005;116:360–9.
- [3] Bisgaard H, Zielen S, Garcia-Garcia ML, et al. Montelukast reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. *Am J Respir Crit Care Med* 2005;171:315–22.
- [4] Knorr B, Franchi LM, Bisgaard H, et al. Montelukast, a leukotriene receptor antagonist, for the treatment of persistent asthma in children aged 2 to 5 years. *Pediatrics* 2001;108(3):E48.

- [5] Knorr B, Matz J, Bernstein JA, et al. Montelukast for chronic asthma in 6- to 14-year-old children: a randomized, double-blind trial. Pediatric Montelukast Study Group. *JAMA* 1998;279:1181–6.
- [6] International Primary Care Airways Group (IPAG). Chronic Airways Disease: A Guide for Primary Care Physicians. IPAG Diagnosis & Management Handbook. 2005.
- [7] Price D, Bond C, Bouchard J, Costa R, Keenan J, Levy ML, et al. International Primary Care Respiratory Group (IPCRG) Guidelines: Management of Allergic Rhinitis. *Prim Care Resp J* 2006;15(1):58–70.

Dr Peter G. Polos*
 Senior Medical Director, Merck & Co., Inc.,
 Whitehouse Station, New Jersey, NJ 08889, USA
 *Tel.: +1 908 423 3473; fax: +1 908 823 3423.
 E-mail address: Peter.Polos@merck.com

4 May 2006

doi:10.1016/j.pcrj.2006.07.003

The role of Montelukast as monotherapy in paediatric asthma – IPCRG Guideline authors' response

Dear Sir,

We would like to thank Dr Polos for his critical reading of the IPCRG guidelines. The process of making guidelines for a worldwide primary care audience should be reliable, fair, and independent. Moreover, suggestions for treatment should be evidence-based, acceptable to physicians who need to have a degree of ownership of them, and guidelines need to be within reach of the public whom they serve as primary care physicians. Dr Polos states that there is evidence for the treatment of paediatric asthma with the leukotriene antagonist (LTRA) Montelukast. Indeed the study from Knorr et al. in children between 2 and 5 years old shows a favourable effect for montelukast as compared to placebo [1], and the Bisgaard et al. study in the same age group shows a reduction in the number of exacerbations [2].

However, based on these two studies alone, the IPCRG Guideline Committee did not feel that there was substantial and sufficient evidence to recommend Montelukast as monotherapy in children between the age of 2 and 5 years. We had several reasons for this decision. These studies [1,2] were not performed in primary care, which meant that we could not extrapolate these results to the very variable group of patients in primary care. Secondly, we still need a direct comparison between the effect of inhaled corticosteroids (ICS) in this age group and the effect of LTRAs. In the older age group of 6–14 years, the MOSAIC study showed a non-inferiority between Montelukast monotherapy and low dose ICS. However, this study has been heavily criticised [3]. An independent direct comparison

between montelukast and low dose ICS [4] also in the older age group showed clearly that low dose ICS treatment has superior effects on inflammation, clinical, and pulmonary outcomes as compared to Montelukast. Although the benefit of prescribing a tablet once-daily – as opposed to the complicated requirements of learning how to inhale both short-acting beta-agonists and corticosteroids – is very clear to us as primary care physicians, we still believe that monotherapy with LTRAs has not been proven enough for it to be recommended in global primary care guidelines. What we need is evidence on a primary care level with primary care patients, and we would encourage MSD to perform a direct comparison between Montelukast and ICS in the preschool age group.

References

- [1] Knorr B, Franchi LM, Bisgaard H, et al. Montelukast, a leukotriene receptor antagonist, for the treatment of asthma in children aged 2 to 5 years. *Pediatrics* 2001;108(3):E48.
- [2] Bisgaard H, Zielen S, Garcia-Garcia M, et al. Montelukast reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. *Am J Respir Crit Care Med* 2005;171:315–22.
- [3] Goodman DC. When an asthma drug has an inferiority complex: a noninferiority trial. *Pediatrics* 2005;116(2):493–5.
- [4] Zeiger RS, Bird SR, Kaplan MS, et al. Short-term and long-term asthma control in patients with mild persistent asthma receiving montelukast or fluticasone: a randomized controlled trial. *Am J Med* 2005;118(6):649–57.

Thys van der Molen*
 Department of General Practice, University
 Medical Center, Groningen, Antonius Deusinglaan 1,
 9713 AV, Groningen, The Netherlands
 C.P. Onno van Schayck
 Care and Public Health Research institute (Caphri),
 University of Maastricht, The Netherlands