Leukotriene receptor antagonists: Focus on montelukast

ANTI-LEUKOTRIENE DRUGS
Cysteinyl-leukotrienes (CysLTs) are endogenous mediators of inflammation and play an important role in allergic airway disease by stimulating bronchoconstriction, mucus production, mucus oedema, inflammation, and airway infiltration by eosinophils, and dendritic cell maturation that prepares for future allergic response. By competitive binding to the Cys-LT(1) receptor, leukotriene receptor antagonist drugs such as montelukast block the effects of Cys-LTs and alleviate the symptoms of many chronic diseases, especially bronchial asthma and allergic rhinitis.

Recently published studies and case reports have demonstrated beneficial effects of LTRAs on other diseases commonly associated with asthma (exercise-induced asthma, rhinitis, chronic obstructive pulmonary disease, interstitial lung disease, chronic urticaria, atopic dermatitis, allergic fungal disease, nasal polyposis, and paranasal sinus disease) as well as other diseases not connected to asthma (migraine, respiratory syncytial virus postbronchiolitis, systemic mastocytosis, cystic fibrosis, pancreatitis, vulvovaginal candidiasis, cancer, atherosclerosis, eosinophils cystitis, otitis media, capsular contracture, and eosinophilic gastrointestinal disorders).1

MONTELUKAST
Montelukast sodium is a selective and orally-active leukotriene receptor antagonist with demonstrated effectiveness for treating allergic asthma and allergic rhinitis in adults and children as young as 12 months of age for allergic asthma and 6 months of age for allergic rhinitis. Leukotriene inhibitors are the first new class of medications for the treatment of persistent asthma that have been approved by the U.S. Food and Drug Administration in more than two decades. They also have been approved for the treatment of allergic rhinitis. Montelukast was also recently approved in the US for prevention of exercise-induced bronchoconstriction in patients who are ≥15 years of age.2

USE OF MONTELUKAST IN PRESCHOOL ASTHMATIC CHILDREN
It is well accepted that control of airway inflammation is crucial for overall asthma control. Hence, efficient anti-inflammatory therapy is important for disease control. Therefore, experts studied the effect of a treatment with montelukast on subjective and objective measures in preschool asthmatic children with insufficient control of airway inflammation, illustrated by increased fractional exhaled nitric oxide (FeNO). This study showed that montelukast could be considered the first line or add-on treatment in preschool children with mild to moderate asthma and elevated FeNO, showing decreased levels of FeNO, improved airway responsiveness to

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2. Neurphth chemotaxis and mucus production

Sources: Semin Respir Crit Care Med 23(4):399-410, 2002

**Figure 1. Leukotriene pathway diagram** -- the AA (arachidonic acid) cascade.
AMP, lung function and symptom scores.³

AN OBSERVATIONAL 12 MONTH STUDY OF ADD-ON MONTELUKAST THERAPY

This multicenter, 24-month, pre-post retrospective observational study included patients receiving current inhaled corticosteroid (ICS) therapy (alone or in combination with long-acting beta-agonist [LABA]), who received add-on treatment with montelukast for 12 consecutive months.

For the 696 patients who were included in the analyses, the proportion of patients experiencing an asthma attack declined from 31.5% in the year before to 10.1% (p < 0.001) the year after addition of montelukast therapy. Proportions of patients with an asthma-related emergency room visit, hospitalization, and oral corticosteroid use declined from 18.7% to 3.9%, 5.2% to 1.4%, and 17.5% to 5.9% (all p < 0.01), respectively.⁴

MONTELUKAST VS. INHALED LOW-DOSE BUDESONIDE IN MILD ASThma

Montelukast has demonstrated consistent benefit in controlling symptoms of asthma and may be an alternative, orally administered, nonsteroidal agent for treating mild asthma. Participants aged 5-15 years with recently diagnosed mild persistent asthma ( n = 62) were randomized to oral montelukast (5 mg daily) [ N (1) = 30] or inhaled budesonide (400 microg per day in two doses) [ N (2) = 32] in a single center, double-blind study. Montelukast may be used as an alternative to low dose inhaled corticosteroids for management of mild persistent asthma.⁵

EXERCISE-INDUCED BRONCHOCONSTRICTION (EIB)

Exercise-induced bronchoconstriction occurs in a large proportion of children with asthma, limiting everyday activities important for their physical and social development. Children 6 to 18 years of age were randomly allocated to receive daily 200 μg budesonide (twice daily, 100 μg per dose) + 9 μg formoterol (twice daily, 4.5 μg per dose; n = 20); 200 μg budesonide + 5 or 10 mg montelukast (once daily at bedtime; n = 20); 5 or 10 mg montelukast (n = 20); 200 μg budesonide (n = 20); or placebo (n = 20). Exercise-induced bronchoconstriction was significantly diminished after 4 weeks in all active treatment groups, and compared with placebo. However, exercise-induced bronchoconstriction protection improved more significantly in the budesonide + montelukast and montelukast groups compared with other therapeutic options.⁶

Single-dose montelukast in EIB

It has been previously established that montelukast provides protection against exercise-induced bronchoconstriction (EIB) after a single dose. Montelukast provides significant protection against EIB having an onset within 2 h following a single oral dose and lasting for at least 24 h.⁷

MONTELUKAST IN ALLERGIC RHINITIS: AN EVIDENCE-BASED REVIEW

Experts conducted a systematic review of studies that have evaluated montelukast in the treatment of seasonal AR (SAR) and perennial AR (PAR), with and without concomitant asthma. A general outcome was that patients treated with montelukast had significantly greater improvements in their symptoms of SAR and PAR than did patients who were given a placebo. The use of montelukast in combination with antihistamines such as loratadine or cetirizine has generally resulted in greater efficacy than when these agents were used alone, and in some studies has produced results comparable with intranasally applied corticosteroids. In patients with AR co-morbid with asthma, montelukast treatment has resulted in significant improvements in both, compared with placebo.⁸

MONTELUKAST IN TREATING PERENNIAL ALLERGIC RHINITIS

Perennial allergic rhinitis (PAR) is a chronic inflammatory nasal condition in individuals exposed year-round to allergens. This was a double-blind study of 15- to 85-year-old patients randomly allocated to montelukast, 10 mg (n=630), placebo (n=613), or the positive control cetirizine, 10 mg (n=122) for 6 weeks. Over 4 weeks, montelukast showed numerical improvement over placebo in Daytime Nasal Symptoms Score (DNSS) (least-squares mean difference of -0.04 [95% confidence interval (CI), -0.09, 0.01]); the difference between cetirizine and placebo was significant: -0.10 (95% CI, -0.19, -0.01). The Rhino-conjunctivitis Quality-of-Life score was significantly improved by montelukast (p < 0.05), but not by cetirizine, during 4 and 6 weeks. The treatment effect of montelukast, but not cetirizine, generally remained consistent through the 6 weeks of treatment. In pooled data, montelukast consistently improved Daytime Nasal Symptoms Score (DNSS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Composition</th>
<th>Packing</th>
<th>Administration</th>
</tr>
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<tbody>
<tr>
<td>MONTEY 10</td>
<td>Montelukast 10mg</td>
<td>10 x 10 Tablets</td>
<td>10mg OD</td>
</tr>
</tbody>
</table>

Sources: Semin Respir Crit Care Med.
versus placebo during all 6 weeks of treatment (-0.07 [95% CI, -0.10, -0.04]).

**MONTELUKAST WITH DESLORATAZINE OR LEVOCETIRIZINE IN PERSISTENT AR**

A randomized, double-blind, placebo-controlled crossover study was performed. Patients were assigned to 2 arms: 20 received montelukast, 10 mg/d, desloratadine, 5 mg/d, or both and placebo and 20 received montelukast, levocetirizine, or both, 5 mg/d, or placebo. The greatest improvement in nasal symptoms occurred after combination treatment. Decreases in the level of eosinophil cationic protein were greater after the combined use of montelukast and antihistamine than after each agent given alone. For persistent AR, the combination of montelukast and either desloratadine or levocetirizine is more effective than monotherapy with these agents.

**CORTICOSTEROIDS COMBINED WITH MONTELUKAST IN TREATMENT OF AR**

Topical corticosteroids are recommended as initial therapy in allergic rhinitis (AR) patients. Experts investigated clinical efficacy of monotherapy with topical steroid and combined therapy in AR patients. In this placebo-controlled and open study patients were divided to four groups. Group-1 received only intranasal mometasone furoate (MF) 200µg (n=25), group-2 received intranasal MF and oral desloratadine (DLR) 5mg (n=25), group-3 received levocetirizine in persistent AR.

**REFERENCES**

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**HIGHLIGHTS**

- Montelukast inhibits type 1 CysLT receptors found on immunocytes, smooth muscle and endothelium in the respiratory mucosa.
- The addition of montelukast to current ICS therapy improved long-term asthma control and resulted in substantial reductions in asthma-related resource use by patients with mild or moderate persistent asthma and concomitant seasonal AR who were persistent with montelukast therapy.
- Montelukast is as effective as inhaled budesonide in treatment of mild persistent asthma in children aged 5-15 years.
- Montelukast provides an effective and well tolerated oral treatment for allergic airway inflammation in patients with SAR or PAR without asthma, and in patients in whom AR is co-morbid with asthma.
- Montelukast provides protection against exercise-induced bronchoconstriction (EIB) after a single dose.
Effective Allergy Relief...

Monteley
Montelukast 10mg. Tab

- Works by blocking Leukotrienes – an underlying cause of allergic rhinitis
- Both Mast cells and eosinophils release leukotrienes
- Leukotrienes released during both early and late phase allergic responses
- Leukotrienes increases nasal airway resistance
- Well Tolerated with safety profile similar to that of Placebo
- Proven efficacy across many clinical studies

- Indicated for relief of symptoms of Allergic Rhinitis
- Effectively helps control Asthma
- Significantly reduces daytime nasal symptoms score in perennial and seasonal allergic rhinitis
- Approved to prevent exercise induced bronchoconstriction in patients aged 15 and above
- Indicated for prophylaxis & Chronic treatment of Asthma in patients aged 12 month & older

Dosage:
Adults and Adolescents 15 years and older:
One 10 mg tablet daily in the evening

Children:
6-14 years: One 5mg tablet
2-5 years: One 4mg tablet
12 months to 5 years: One 4mg oral granules packet
Preferably daily in the evening

A decisive choice for Allergy and Asthma
Monteley

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