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CHANGE IN USE OF ASTHMA AND ALLERGY DRUGS AFTER START OF MONTELUKAST OR OTHER CONTROLLERS IN ITALIAN CHILDREN WITH ASTHMA AND ALLERGIC RHINITIS

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BACKGROUND

- Leukotrienes are leukocyte-generated lipid mediators that promote eosinophil and mast-cell induced bronchoconstriction and inflammation associated with asthma.
- Recognition of the importance of leukotrienes in the pathogenesis of asthma has led to the development of leukotriene synthesis inhibitors and leukotriene receptor antagonists (LTRA). Montelukast is the only LTRA with proven efficacy in children 2-14 years.
- Montelukast improves pulmonary function, reduces symptoms, decreases night-time awakenings, and decreases the need for rescue medications as compared to placebo.
- Therapy with inhaled corticosteroids (ICS) is the recommended first choice treatment to reduce inflammation and symptoms in children with mild to severe asthma according to the GINA guidelines. However, people with asthma who remain symptomatic despite use of ICS should receive additional controller therapy. The dose of ICS can be increased or long-acting B-agonists (LABA) or LTRA can be added on to ICS treatment.
- Montelukast offers significant benefits when added to inhaled corticosteroids (according to secondary end-point analyses) and may allow for tapering off of ICS and reduction in B-agonist use
- LTRA inhibit the production of cysteinyl leukotrienes, important pro-inflammatory mediators in asthma that are unaffected by steroid treatment; they are particularly effective in allergen, exercise, and aspirin induced asthma. In patients with seasonal allergic rhinitis and concomitant asthma, LTRAs improve nasal, eye, and throat symptoms as well as quality of life.

RATIONALE

- Clinical trial data assess the efficacy of a drug under protocol-drive circumstances with better adherence than in real life practice. Observational studies supplement clinical trial data since they provide information on effectiveness in a real-world clinical practice setting with more heterogeneous patient populations and poorer adherence.
- There is limited evidence from observational studies on effectiveness of montelukast added to ICS vs. other asthma controllers in children with asthma and allergic rhinitis initiating GINA stage 3 therapy requiring high dose ICS, addition of LABA to ICS or addition of montelukast to ICS

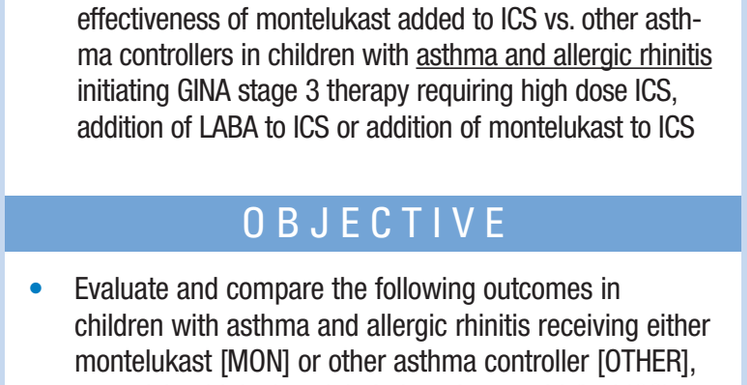
OBJECTIVE

- Evaluate and compare the following outcomes in children with asthma and allergic rhinitis receiving either montelukast [MON] or other asthma controller [OTHER], comprising high-dose inhaled corticosteroid (h-d ICS) or ICS + long-acting beta agonist (LABA):
  - Asthma-rescue/acute and allergy medication use and cost

METHODS

Study Design

- 2-year retrospective pre-post cohort study in children with asthma and allergic rhinitis



* ~55% of this group also received ICS
**Other Controller (h-d ICS, ICS+LABA)

n=Children with asthma and allergic rhinitis

METHODS (CONT'D)

Setting

- Italy is one of the few countries in which a specific primary care system is devoted to children up to the age of 14 years. Within the framework of the National Health Service (NHS), every child is registered at birth and receives free medical care from one of the approximately 6,000 family paediatricians working for the NHS.
- PEDIANET is a network of family paediatricians who share a common project of epidemiological and clinical research on the care of children. They all maintain computerized medical records.
- A central PEDIANET database is kept in the city of Padua with the longitudinal medical records of children who are or have been registered with the collaborating paediatricians (n=109).
- For the purpose of this study, the data was collected and handled anonymously in compliance with the Italian law on privacy.

Population

- Italian children (<14 years) with asthma and allergic rhinitis registered for ≥2 years with pediatrician during period July 2001–October 2004
- Received ≥2 consecutive asthma-controller prescriptions* after July 1, 2001 in addition to existing therapy
  - *Controllers: high-dose ICS defined as 800 µg beclomethasone, > 400 µg budenoside, > 1250 µg flunisolide and > 500 µg fluticasone per day (www.gina.org), LABAs (formoterol, salmeterol) or LTRAs (only montelukast during study period)
- Continuous eligibility (>1 year of follow-up prior and after the index date)
- No chronic obstructive pulmonary disease, cystic fibrosis or bronchopulmonary dysplasia

Outcomes

- Pre-post differences in mean per-child-per-month prescription costs and rates of
  - rescue medications (short-acting beta agonist)
  - acute medications (antibiotics, oral corticosteroids)
  - allergy medications (antihistamines, nasal steroids)
  - other respiratory medications (e.g., cromones)
- All data were obtained from the computerized medical charts and costs were obtained from the Italian drug tariff (2004 values)

Statistical Analyses

- Multivariate linear regression adjusting for baseline characteristics including age, severity (based on prior medication use), sinusitis and gender

RESULTS

Table 1: Baseline Treatment Patterns

	N	% (of total)
MONTELUKAST	**23**	**26.1%**
ICS+Montelukast	18	20.5%
Montelukast monotherapy	5	5.7%
OTHER	**65**	**73.9%**
High-dose ICS	33	37.5%
ICS+LABA	31	35.2%
LABA monotherapy	1	1.1%
TOTAL	**88**	**100%**

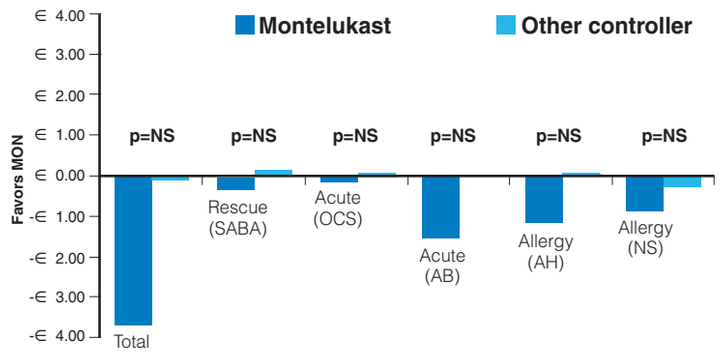
RESULTS (CONT'D)

Table 2: Baseline[1] Patient Characteristics

	Montelukast* N=23	OTHER** N=65	P-value
Female (%)	26.2%	34.8%	0.43
Age (mean, SD)	7.8	8.4	0.40
Asthma severity			
Intermittent	76.9%	47.8%	0.009
Mild	20.0%	30.4%	
Moderate		8.7%	
Severe	3.1%	13.0%	
Sinusitis	10.8%	17.4%	0.41
Prior hospitalizations for asthma	0 %	0 %	NA

NOTES: [1]At the time of 2nd asthma controller introduction;
*55% added to ICS
** includes h-d ICS and ICS+LABA; LABA alone negligible

Figure 1: Cost Difference between Post and Pre Controller Treatment Periods — Children (<14) [Mean Euro per patient/per month]



NOTES: Total includes rescue, acute, allergy medications. OCS= oral steroids; AB=antibiotics, AH=antihistaminics; NS=nasal steroids
p-value: NS=non-significant adjusted

CONCLUSIONS

- Substantial decreases in total use and costs of asthma-rescue/acute and allergy medication were observed over a 2-year period among asthmatic children <14 years of age with a recorded diagnosis of asthma and allergic rhinitis who were adding montelukast compared to those treated with either h-d ICS or ICS+LABA.
- Future studies focusing on children with asthma and allergic rhinitis of larger sample size may provide further evidence regarding the effectiveness of montelukast in children with asthma and allergic rhinitis.

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