Response to montelukast among subgroups of children aged 2 to 14 years with asthma

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Background: Determining who responds to asthma therapies, particularly leukotriene modifiers, continues to be explored.
Objective: We sought to identify patient characteristics predictive of response to montelukast.
Methods: We used data from 2 clinical trials in which children with asthma received either montelukast or placebo. Symptoms, β-agonist use, and unanticipated health resource use caused by asthma were recorded in validated daily diaries for children 2 to 5 (n = 689) and 6 to 14 (n = 336) years old. We defined primary end points of days without asthma in 2- to 5-year-old patients (24 hours without symptoms, β-agonist use, or asthma attack) and change in percent predicted FEV_1 in 6- to 14-year-old children. Asthma attack was defined by the use of rescue oral corticosteroids or by an unscheduled visit to a medical provider. Patients were grouped according to baseline characteristics, such as family history of asthma, personal history of allergy, frequency of asthma symptoms, eosinophilia, and concomitant use of inhaled corticosteroids or cromolyn. We examined the stratum-specific effects of montelukast on the percentage of days without asthma, change in percent predicted FEV_1, asthma attack, and a variety of secondary symptom and FEV_1 end points.
Results: We did not identify characteristics that predicted response to montelukast in either preschool or 6- to 14-year-old children. These findings were consistent across all symptom and FEV_1 outcomes. There was also no differential response to montelukast in either age group when asthma attack was the outcome.
Conclusion: The patient characteristics studied do not appear to provide an indication of who will benefit most from treatment with montelukast. (J Allergy Clin Immunol 2003;111: 757-62.)

Key words: *Asthma, montelukast sodium, preschool children*

The aim of this study was to identify patients most likely to exhibit a beneficial treatment response when taking montelukast. No asthma treatment currently available provides benefit to all patients, and a substantial number of patients will not respond to any given therapy. Heterogeneous response has been documented for asthma treatments, including β-agonists,[1] inhaled corticosteroids,[2,3] and leukotriene receptor antagonists.[2] This issue is further complicated in young children who present with asthma-like symptoms that might represent other disease pathologies. Therefore it is a critical clinical question whether a particular therapy will be effective in an individual child with symptoms of asthma, and examination of this question is pertinent.

Certain patient characteristics are predictive of the continuation to adult asthma. Several studies have shown that patients with a family history of asthma,[4,5] a personal history of atopy,[5-7] and more severe or frequent symptoms[5,8] are among those most likely to remain asthmatic. Algorithms have been suggested to predict the likely prognosis of preschool wheezing but still need validation.[9,10] However, it is important to emphasize that there is no evidence that such predictors of asthma also predict a response to treatment. Furthermore, even among children who will eventually outgrow asthma, treatment should be chosen on the basis of the likelihood of relieving the immediate symptoms rather than a statistical probability of the prognosis.

Roorda et al[11] reported on factors predicting response to an inhaled corticosteroid among preschool children with asthma. In this study of children aged 12 to 47 months, those who had a family history of asthma or were at least 2 years old displayed greater response to treatment. To our knowledge, this is the only study to have examined patient characteristics as predictors of response to inhaled corticosteroids among children.

Likewise, we looked for patient characteristics to predict which children are likely to better respond to treatment with montelukast sodium, a leukotriene receptor antagonist approved for childhood asthma. Using data from 2 randomized clinical trials of montelukast in children with asthma aged 2 to 5 and 6 to 14 years, we examined the response to montelukast treatment within subgroups defined by patient characteristics, including several characteristics that predict continuation to adult asthma.[12,13] Both randomized studies demonstrated improvements in asthma symptoms, quality of life, and lung function in children taking montelukast.[12,13] Understanding which patients are most likely to benefit from montelukast could help contribute to the successful clinical management of children with asthma.

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METHODS

Study subjects were enrolled in 2 clinical trials of montelukast in the treatment of asthma in 2- to 5-year-old (n = 689) and 6- to 14-year-old (n = 336) children. Further details of the trial designs and findings can be found in the primary articles.[12,13] After a 2-week placebo run-in period, patients were randomized to montelukast or placebo and followed for 12 weeks (2- to 5-year-old patients) or 8 weeks (6- to 14-year-old patients). Subjects had a history of physician-diagnosed asthma and were required to meet minimum levels of asthma symptoms and β-agonist use during the placebo baseline period. All patients were in good health, other than having asthma, on the basis of the results of medical history, physical examination, and routine laboratory testing. Up to 50% of the 2- to 5-year-old patients were permitted concomitant use of inhaled corticosteroids or inhaled cromolyn at a constant dose during the study; up to 40% of the 6- to 14-year-old patients were permitted concomitant use of inhaled corticosteroids. As-needed treatment with β-agonists (oral, inhaled, or nebulized, according to each investigator's usual clinical practice) was permitted. Oral corticosteroid rescue for worsening asthma was permitted according to a predefined plan. Each institution's ethical review board approved the study protocol, and informed consent was obtained from each patient.

Validated asthma-specific daily diary records[14,15] were used to ascertain symptoms and β-agonist use during the placebo run-in and treatment periods. Diaries were completed by caregivers for the 2- to 5-year-old patients. Diary card questions were read by caregivers to 6- to 8-year-old patients, and their responses were recorded. Patients aged 9 to 14 years answered and recorded diary card questions under caregiver supervision. In addition, data were collected on resource use that resulted from worsening asthma, including rescue oral corticosteroid use and unscheduled doctor, hospital, or emergency department visits. Episodes of worsening asthma were also ascertained from adverse event reports.

In both trials patient demographic data were collected at baseline, including age, race, sex, weight, and height. Also assessed at baseline were the following: smoking in the patient's household, patient's family history of asthma, the duration of asthma in the patient, and the presence of allergic manifestations, including rhinitis, conjunctivitis, and, in 2- to 5-year-old children, eczema, as well as the presence antibodies to common inhalant allergens. Diagnoses of rhinitis, conjunctivitis, and eczema were based on responses to a health history questionnaire. In 2- to 5-year-old patients, serologic testing for allergens (RAST) was performed at screening and included testing for dog and cat dander, cockroach, *Alternaria alternata*, and dust mites.

Among patients aged 6 to 14 years, spirometry (FEV_1) was performed at each clinic visit between 6 and 9 AM. Inhaled β-agonists and short-acting antihistamines were withheld for at least 6 and 48 hours, respectively, before spirometry. Patients receiving scheduled concomitant inhaled corticosteroids withheld their morning dose until completion of a clinic visit. The largest FEV_1 from a set of 3 acceptable maneuvers at each clinic visit was recorded as the true value. Each clinic center transmitted the spirometry data electronically to the central spirometry quality control center, where the data were reviewed to ensure uniform adherence to American Thoracic Society standards of acceptability and reproducibility.[16]

We conducted parallel separate analyses on the data from the 2 clinical trials. For the 2- to 5-year-old patients, the primary end point was days without asthma, which was defined as a 24-hour period without any symptoms, β-agonist use, or asthma attacks. Asthma attacks were defined as any episode of worsening asthma that resulted in rescue oral corticosteroid use or in an unscheduled visit to the doctor, hospital, or emergency department. Change from baseline in the percent predicted FEV_1 was the primary end point among the 6- to 14-year-old patients. For both studies, we included asthma attacks as a secondary end point. Other secondary end points included daytime asthma symptoms, overnight asthma symptoms, 24-hour asthma symptoms, 24-hour individual symptoms (cough, wheeze, difficulty breathing, and activity limitation), and 24-hour use of β-agonists. Symptom end points were evaluated as the percentage of days in the treatment period with symptoms (any level), as well as the mean symptom score over the treatment period. In the 6- to 14-year-old patients we additionally included analyses of change from baseline in FEV_1 in liters, percentage change in FEV_1 in liters, and a 2-level variable comparing the highest and lowest quartiles of FEV_1 in liters.

The effect of montelukast treatment on end points was evaluated within dichotomous subgroups of the following baseline characteristics: duration of asthma, family history of asthma, personal history of allergic rhinitis or conjunctivitis, concomitant use of corticosteroids, concomitant use of cromolyn, and eosinophilia (>5%). Among the 2- to 5-year-old patients, we also studied montelukast treatment effects within strata of eczema, abnormal RAST results (positive result with any tested allergens), and smoking in the household. Data differed slightly in the 2 trials; data on RAST results, eczema, and smoking in the household were not collected in the study of 6- to 14-year-old patients, and spirometry results were not collected in the 2- to 5-year-old patients.

We evaluated the response to montelukast as a function of pretreatment asthma symptom frequency as follows. Patients who reported having daytime or nighttime symptoms on at least 75% of days during the 2-week placebo run-in period were classified as having frequent symptoms. Those who reported having symptoms on less than 75% of run-in days were considered to have less frequent symptoms. This classification scheme is similar to that used by Roorda et al[11] in their study of response to fluticasone.

ANOVA was used to compare least-square mean differences in continuous end point levels, days without asthma, and change in percent predicted FEV_1 between the placebo and montelukast groups. Logistic regression was used to compare the odds of asthma attack in the 2 treatment groups. Differential response to montelukast was evaluated on the basis of the statistical significance of interaction terms included in the regression models. Subjects with missing data were excluded from the specific analyses for which they lacked data. All analyses were based on intention-to-treat criteria. We included baseline variables as covariates in the regression models if they appeared to differ between treatment groups. All significance testing was 2 tailed. A P value of .05 or less was considered statistically significant.

RESULTS

Randomization was successful in evenly distributing most patient's baseline characteristics across allocated treatment groups in the 2 studies (Table I). Modest differences between treatment groups were apparent in the 2- to 5-year-old patients for abnormal RAST results, activity-induced asthma, and eosinophilia at baseline. In the 6- to 14-year-old patients, differences were observed for the sex of the child, concomitant inhaled corticosteroid use, and eosinophilia.

Among the 2- to 5-year-old patients, there was not statistical evidence that the effect of treatment with montelukast was modified by the presence of any baseline variable (Table II). Statistically nonsignificant treatment differences in days without asthma were observed according to the presence of eczema and the frequency of

TABLE I. Baseline characteristics of study populations

Characteristic	2- to 5-Year-old patients		6- to 14-Year-old patients	
	Placebo (n = 227)	Montelukast (n = 458)	Placebo (n = 132)	Montelukast (n = 197)
Mean (SD)				
Age (y)	3.6 (1.1)	3.6 (1.1)	10.9 (2.3)	10.9 (2.2)
Height (cm)	102 (11)	102 (10)	149 (13)	148 (14)
Weight (kg)	17.5 (4.1)	17.6 (4.3)	46.1 (16.5)	44.8 (15.1)
Duration of asthma (y)	2.4 (1.3)	2.4 (1.3)	6.9 (3.4)	6.8 (3.5)
Days with no nighttime symptoms (%)	34 (28)	36 (29)	79 (26)	77 (28)
Days with no symptoms in 24-h period (%)	12 (16)	11 (15)	12 (16)	10 (15)
Days with no β-agonist use in 24-h period (%)	19 (20)	18 (19)	17 (20)	16 (20)
Days with no symptoms or β-agonist use in 24-h period (%)	10 (14)	9 (14)	8 (14)	7 (13)
FEV_1 (L)	—	—	1.8 (0.5)	1.8 (0.6)
FEV_1 (% predicted)	—	—	71.5 (10.5)	71.0 (11.4)
Percentage (n)				
Family history of asthma	63 (143)	61 (279)	72 (95)	74 (145)
Male sex	57 (130)	59 (271)	61 (80)	67 (131)
Abnormal RAST result	52 (112)	48 (210)	—	—
Exercise-induced asthma	81 (183)	77 (352)	95 (125)	93 (183)
Personal history of conjunctivitis or rhinitis	61 (138)	63 (290)	93 (123)	95 (188)
Concomitant corticosteroid or cromolyn use	40 (91)	41 (186)	33 (44)	40 (78)
Smoking in household	37 (83)	39 (176)	—	—
Eosinophilia	55 (122)	50 (223)	60 (79)	57 (112)

TABLE II. Percentage of days without asthma* with montelukast compared with placebo within categories of several baseline characteristics among 2- to 5-year-old children

Baseline characteristic	Least-square mean value during 12-wk treatment period (% of days without asthma		Least-square mean (95% CI) difference between treatment groups	*P* value for interaction between treatment and the baseline characteristic†
	Placebo	Montelukast		
Family history of asthma (n = 422)	27	33	6.5 (1.0 to 13)	
No family history of asthma (n = 263)	28	34	5.6 (–1.5 to 13)	.84
Smoking in household (n = 259)	27	32	4.9 (–2.3 to 12)	
No smoking in household (n = 425)	27	34	7.0 (1.5 to 13)	.65
Duration of asthma, 0.5-2 y (n = 306)	28	33	5.1 (–0.8 to 11)	
Duration of asthma, 3-5 y (n = 379)	27	34	7.4 (1.0 to 14)	.60
Concurrent use of corticosteroids (n = 189)	24	34	9.6 (1.4 to 18)	
No concurrent use of corticosteroids or cromolyn (n = 408)	29	34	5.1 (–0.5 to 11)	.38
Concurrent use of cromolyn (n = 88)	24	28	4.4 (–8.3 to 17)	
No concurrent use of corticosteroids or cromolyn (n = 408)	29	34	5.1 (–0.5 to 11)	.91
Personal history of conjunctivitis or rhinitis (n = 428)	26	32	6.1 (0.6 to 12)	
No personal history of conjunctivitis or rhinitis (n = 257)	28	35	6.4 (–0.6 to 14)	.94
Eczema (n = 137)	27	27	0.2 (–9.4 to 9.9)	
No eczema (n = 548)	27	35	7.7 (2.8 to 13)	.18
Abnormal RAST result (n = 322)	28	34	5.9 (0.4 to 12)	
No abnormal RAST result (n = 335)	27	33	6.4 (0.04 to 13)	.92
Eosinophilia at baseline (n = 345)	28	34	5.5 (–0.5 to 12)	
No eosinophilia at baseline (n = 325)	27	33	5.9 (–0.5 to 12)	.93
Frequent‡ 24-h symptoms (n = 528)	21	28	7.6 (3.1 to 12.2)	
Less frequent 24-h symptoms (n = 157)	49	51	1.2 (–7.2 to 9.6)	.19

Least-square mean differences within strata are presented, as are the *P* values for interaction.

*Days without asthma was defined as a 24-hour period without symptoms, β-agonist use, or asthma attack.

†The test for interaction compares the stratum-specific least-square mean differences between treatment groups. A statistically nonsignificant value ($P > .05$) indicates that there was not statistical evidence for differences between the stratum-specific least-square mean treatment differences.

‡Frequent 24-hour symptoms was defined as having reported daytime or nighttime symptoms on at least 75% of days during the placebo run-in period; less frequent 24-hour symptoms was having symptoms on less than 75% of run-in days.

TABLE III. Change in the percent predicted FEV_1 from baseline over the treatment period with montelukast compared with placebo within categories of several baseline characteristics among 6- to 14-year-old patients

Baseline characteristic	Least-square mean change over 12-wk treatment period (change in % predicted FEV_1)		Least-square mean (95% CI) difference between treatment groups	*P* value for interaction between treatment and the baseline characteristic*
	Placebo	Montelukast		
Family history of asthma (n = 240)	2.8	5.6	2.8 (0.6 to 4.9)	
No family history of asthma (n = 89)	3.1	7.4	4.3 (0.8 to 7.7)	.47
Duration of asthma, 0-7 y (n = 176)	1.8	5.2	3.4 (0.9 to 5.9)	
Duration of asthma, 8-14 y (n = 153)	4.1	7.0	2.9 (0.3 to 5.6)	.81
Concurrent use of corticosteroids† (n = 122)	2.1	5.8	3.7 (0.7 to 6.8)	
No concurrent use of corticosteroids (n = 207)	3.3	6.2	2.9 (0.7 to 5.2)	.68
Personal history of conjunctivitis or rhinitis (n = 311)	2.7	5.7	3.0 (1.2 to 4.9)	
No personal history of conjunctivitis or rhinitis (n = 18)	5.3	12.8	7.6 (0.1 to 15.1)	.25
Eosinophilia at baseline (n = 203)	2.6	6.8	4.2 (1.9 to 6.6)	
No eosinophilia at baseline (n = 126)	3.3	5.0	1.7 (–1.1 to 4.5)	.18
Frequent‡ 24-h symptoms (n = 269)	2.5	6.1	3.6 (1.6 to 5.6)	
Less frequent 24-h symptoms (n = 60)	4.5	5.8	1.4 (–2.8 to 5.6)	.36

Least-square mean differences within strata are presented, as are the *P* values for interaction.
*The test for interaction compares the stratum-specific least-square mean differences between treatment groups. A statistically nonsignificant value ($P > .05$) indicates that there was not statistical evidence for differences between the stratum-specific least-square mean treatment differences.
†There was no concomitant use of cromolyn in the 6- to 14-year-old population.
‡Frequent 24-hour symptoms were defined as having reported daytime or nighttime symptoms on at least 75% of days during the placebo run-in period; less frequent 24-hour symptoms were defined as having symptoms on less than 75% of run-in days.

24-hour symptoms (symptoms or β-agonist use). In patients without eczema, those assigned montelukast had 7.7% more days without asthma in the treatment period than those assigned placebo, whereas there was no difference in the percentage of days without asthma according to treatment status in patients with eczema (*P* value for interaction = .18). Patients taking inhaled corticosteroids had a montelukast-placebo treatment difference of 9.6%, whereas patients not taking either corticosteroids or cromolyn had a treatment difference of 5.1% (*P* value for interaction = .38). More frequent 24-hour symptoms during the placebo run-in period predicted a greater response to montelukast treatment that was again statistically nonsignificant. Montelukast-placebo treatment differences for days without asthma were 7.6% and 1.2% for patients in the top and lower 3 quartiles, respectively, of frequent 24-hour symptoms. Treatment effects were similar across levels of all other baseline variables.

Similarly, in the 6- to 14-year-old patients, the effect of montelukast on changes in percent predicted FEV_1 were not significantly modified by baseline variables (Table III). Patients who did not report a personal history of conjunctivitis or rhinitis had a nonsignificantly greater response to treatment than did patients who reported a personal history of either allergic condition. Respective montelukast-placebo differences in change in percent predicted FEV_1 were 3.0% and 7.6% for those who did and did not report a personal history. Findings were similar for other FEV_1 outcomes.

Analyses with alternative end points also did not detect differential response to treatment with montelukast in either trial population. Response to montelukast did not differ when we examined the degree to which treatment with montelukast prevented asthma attacks within subgroups of the same patient characteristics previously described (data not shown). In the 6- to 14-year-old patients, we included an analysis using days without symptoms or β-agonist use as the outcome and found no evidence of differential response according to any baseline characteristic. In both the 2- to 5- and 6- to 14-year-old patients, we studied treatment effects on additional outcome variables, including percentage of symptom-free days, percentage of days without β-agonist use, and percentage of days without specific daytime and nighttime symptoms. We examined mean symptom scores, including mean 24-hour symptom scores, mean daytime symptom scores, and mean scores for nighttime symptoms and individual daytime symptoms (eg, cough and wheeze). For all of these end points, there was no statistical evidence that the response to montelukast differs in patients on the basis of any baseline characteristics measured in both the 2- to 5- and 6- to 14-year-old populations. Finally, adjusting for variables that differed slightly across treatment groups (Table I) did not appreciably change the regression results.

DISCUSSION

The ability to predict which patients are more likely to successfully respond to therapy would greatly aid clinical decision making. We studied whether baseline characteristics of children with asthma contributed to their response to montelukast treatment. We were unable to identify any baseline characteristic that predicted response to mon-

telukast in preschool or 6- to 14-year-old children. Our data afforded the opportunity to examine major patient characteristics of interest, such as family history of asthma, personal history of allergy, and use of other asthma medications. The findings were consistent across a variety of symptom and FEV_1 outcome variables and suggest that patient characteristics are unlikely to contribute meaningfully to decisions about prescribing montelukast.

Study data were from 2 randomized, double-blind, placebo-controlled clinical trials of montelukast treatment among children with asthma.[12,13] Separate studies were conducted in 2- to 5- and 6- to 14-year-old patients. We did not attempt to pool data from the 2 trials because they differed slightly with respect to data collection and eligibility requirements. Still, the 2 study populations appeared similar with respect to their underlying severity of disease. With the exception of more frequent nighttime symptoms among the preschool children, symptom frequencies for the 2 age groups were nearly identical, as shown in Table I. In both trials montelukast was associated with statistically significant decreases in asthma symptoms and health care resource use for the treatment of asthma. Baseline characteristics included in the analysis were those measured as part of the primary clinical trials and included characteristics that have been shown to predict persistence of childhood asthma, such as family history of asthma, eosinophilia, and personal history of allergy. Our findings demonstrate that characteristics predictive of asthma prognosis are not, in general, predictive of response to montelukast.

Some of the variables we considered have been suggested to predict continuation to adult asthma in children with physician-diagnosed asthma.[4-8] However, it is essential to distinguish the prediction of asthma prognosis from the prediction of treatment response. Furthermore, it is critical to emphasize that even if we could with certainty predict the course of asthma in individuals, asthma symptoms should be appropriately treated, irrespective of a child's propensity to have adult asthma.[17,18] Even among children whose asthma will eventually resolve, treatment is likely to diminish current symptoms,[19,12] improve quality of life,[12,13] and decrease the risk of hospitalizations.[20]

The motivation for this study was to identify patients most likely to exhibit a beneficial treatment response when taking montelukast. No asthma treatment currently available provides benefit to all patients, and a substantial number of patients will not respond to any given therapy. Large variability in patient response to inhaled corticosteroids was recently demonstrated by Szefler et al.[3] In this study fewer than half of the patients allocated to either fluticasone or beclomethasone responded with a greater than 15% increase in FEV_1. Similarly, data presented by Malmstrom et al[2] illustrate broad FEV_1 response distributions for asthmatic patients treated with either montelukast or beclomethasone. Pediatric data on bronchoprotection from long-acting β_2-agonists also show pronounced heterogeneity.[21]

Roorda et al[11] recently studied the response to an inhaled corticosteroid, fluticasone propionate, among children aged 12 to 47 months with asthma. The effects of fluticasone on symptom-free days and exacerbations over follow-up were examined within strata of age, symptom frequency, family history of asthma, personal history of rhinitis or eczema, and prior history of exacerbation. Study investigators concluded that response to fluticasone was most beneficial in children with a family history of asthma in children aged 2 years or older and in children with more frequent symptoms at baseline.

Our analysis differs from that of Roorda et al[11] in the method of assessing differential response. We included a formal statistical test for differential response (ie, interaction or effect modification), whereas Roorda et al compared effect estimates across subgroup categories. Comparisons across subgroup categories are not as specific as statistically testing for differences. It is thus possible that some of the differences in response cited by the authors would not have achieved statistical significance under formal testing for differential response and might simply represent random variation caused by small samples.[22] Still, the absolute differences observed in the study by Roorda et al[11] were sizable, suggesting clinically important differences.

Whereas the method used by Roorda et al[11] might have resulted in spurious apparent differential response, our method might have failed to detect true differential response because of relatively small sample sizes within subgroups.[22] Based, in part, on the difficulty of assessing differential response on a statistical basis through either subgroup comparisons of statistical significance or formal testing, it is increasingly recommended that subgroup analyses from clinical trials contribute primarily to qualitative comparisons of effect estimates across subgroups.[22,23] However, the response differences seen in our study were modest and suggest insignificant clinical differences.

The issue of multiple comparisons is another common criticism of subgroup analyses. In our study we identified 9 baseline characteristics on which we subgrouped the 2- to 5-year-old patients and identified 6 baseline characteristics for the 6- to 14-year-old patients. These 15 subgroups were used for 2 end points, making a total of 30 comparisons. At a 5% type I error rate per comparison, we can expect to find one spuriously significant association in every 20 comparisons.[24] Statistical tests are available to adjust significance levels for multiple comparisons[24]; however, the use of these tests is debated.[25] As presented, our analysis does not support differential response to montelukast according to the baseline variables we considered. Additionally, adjusting for multiple comparisons would only further highlight the absence of differential response observed in these data.

Our findings corroborate those from other subgroup analyses of montelukast treatment in children and adults. Results from the primary trial analysis of 2- to 5-year-old patients indicated no difference in response to montelukast according to study center, age, sex, or race.[12] Among 6- to 14-year-old patients, no treatment differences were observed according to categories of age, ethnicity, Tanner stage, or history of exercise-induced asth-

ma.[13] In adults Reiss et al[26] reported similar montelukast benefits across categories of age, sex, race, history of allergic rhinitis, history of exercise-induced asthma, study center, and concomitant use of inhaled corticosteroids. Finally, in subjects aged 15 years or older, baseline peak expiratory flow variability was not associated with montelukast-associated decreases in peak expiratory flow variability over follow-up.[27]

The heterogeneity of the clinical response to pharmacotherapy is of great practical interest. We did not find evidence of differential patient response to montelukast sodium according to baseline characteristics among children aged 2 to 14 years. It is possible that additional phenotype information would enable better prediction of treatment response, although our data included most commonly available clinical indices. The present study contributes to our understanding of when patient characteristics will and will not provide an indication of treatment response.

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