

A randomized, double-blind, placebo-controlled trial of the effect of zafirlukast on upper and lower respiratory responses to cat challenge

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Background: Zafirlukast, a leukotriene antagonist, has been shown to have protective effects against a variety of asthma triggers.

Objective: Our purpose was to evaluate zafirlukast's effects on upper and lower airway responses to cat allergen exposure with use of a well-characterized cat exposure model.

Methods: In a double-blind, placebo-controlled, cross-over trial 18 subjects with cat-induced asthma were randomly assigned to receive 1 week each of zafirlukast or placebo followed by a 1-hour cat challenge. Upper and lower respiratory symptoms were rated and spirometry and acoustic rhinometry were performed. Challenges were stopped early if the subject was too uncomfortable or had a >50% decrease in FEV₁.

Results: Overall changes in FEV₁ were significantly different with zafirlukast treatment ($P = .02$). Significant differences in FEV₁ change were detected at 15 and 30 minutes ($P = .027$ and $.05$, respectively) but not at 45 and 60 minutes. Changes in acoustic rhinometry were also significantly different at 15 and 30 minutes ($P = .05$ and $.0005$, respectively) but not at 45 and 60 minutes. Challenge length was significantly longer with zafirlukast versus placebo after adjustment for differences in allergen exposure ($P = .022$). Respiratory symptom scores were significantly different (lower respiratory, $P < .001$; upper respiratory, $P = .038$) through the first 30 minutes of the challenge after adjustment for allergen exposure.

Conclusions: Zafirlukast was significantly more effective than placebo in preserving pulmonary function and nasal anatomy and extending challenge length when cat-sensitive asthmatic subjects were exposed to high levels of cat allergen. (*J Allergy Clin Immunol* 2000;105:704-10.)

Key words: Zafirlukast, acoustic rhinometry, cat challenge, cat allergen

Abbreviations used

AR:	Acoustic rhinometry
BU:	Breath units
Fel d 1:	<i>Feline domesticus</i> allergen 1
LRSx:	Lower respiratory symptoms
MCA:	Minimum cross-sectional area
PD ₂₀ FEV ₁ :	Predicted dose inducing 20% fall in FEV ₁
URSx:	Upper respiratory symptoms

Leukotriene receptor antagonists comprise a new class of therapy for the treatment of asthma. Zafirlukast, a representative compound from this class, acts by competitively binding to the CysLT-1 receptor, inhibiting the effects of leukotriene D₄.¹ Studies have shown that zafirlukast blocks both early- and late-phase pulmonary responses to allergen challenge²⁻⁴ and acute responses to exercise⁵ and sulfur dioxide challenge⁶ among asthmatics. Nasal effects of zafirlukast have been less well studied, but the drug has been shown to be beneficial in the treatment of patients with ragweed-induced allergic rhinitis.⁷ In this study we used a well-characterized cat challenge model,^{8,9} which provides exposure to naturally generated cat allergen, to study the effects of zafirlukast on upper and lower airway responses during acute allergen exposure.

METHODS

Eighteen adult subjects with a history of cat-induced asthma who were in generally good health were recruited by advertisement. The study was approved by the Joint Committee for Clinical Investigation of Johns Hopkins University School of Medicine, and all participants gave written informed consent.

On recruitment, subjects were evaluated by questionnaire regarding their medical history and current medications. Exclusion criteria included a history of unstable asthma (defined as a recent hospitalization, an exacerbation requiring oral steroids within 4 weeks of study entry, or daily symptoms), a cat in the home, evidence of chronic disease other than asthma, upper respiratory infection within 2 weeks of study entry, and a history of severe reactions to cat exposure; smokers, pregnant women, and nursing mothers were also excluded.

After a physical examination, subjects underwent prick-puncture skin tests to cat, dog, dust mite, cockroach, molds (2 mold mixes including *Aspergillus*, *Penicillium*, *Mucor*, *Fusarium*, *Alternaria*, *Helminthosporium*, *Hormodendrum*, and *Botrytis* species), and grass

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(orchard), tree (oak and maple), and ragweed pollens. Skin tests to cats were graded on a scale of 0 to 4+ on the basis of the size of the wheal in relation to the histamine wheal. A positive skin test to cat allergen, defined as a wheal greater than one half the diameter of the histamine control and at least 3 mm larger than the diameter of the glycerin-saline solution control, was required for entry into the study. All subjects avoided short-acting antihistamines for 72 hours, long-acting antihistamines for 7 days, astemizole for 3 months, and tricyclic antidepressants for 6 weeks before skin testing.

Subjects then underwent spirometry (spirometer model DECpc [Warren Collins, Braintree, Mass]) and a methacholine challenge test with use of previously described methods.¹⁰ The methacholine challenge was considered positive if the predicted dose inducing a 20% decrease in FEV₁ (PD₂₀FEV₁) was less than 80 breath units (BU).

After the initial screening, subjects underwent a baseline cat challenge. Before all cat challenges, medications were restricted as follows: antihistamines (short acting, 72 hours; long acting [except astemizole], 7 days; astemizole, 3 months), short-acting inhaled β -adrenergic agonists (4 hours), salmeterol (24 hours), oral β -adrenergic agonists (short acting, 6 hours; long acting 24 hours), theophylline (24 hours), nasal or inhaled cromolyn sodium (48 hours), and nasal or inhaled corticosteroids (72 hours).

Cat exposure challenges were performed as previously described, in a 13.7-m³ room with 2 cats, a bed, and a small carpet.^{8,9} Before the challenge the cats were placed in a cage and bedding was shaken to disturb allergen. In addition, baseline symptom scores, spirometry, and acoustic rhinometry (AR)^{9,11} measurements were obtained. Patients were required to have an FEV₁ >70% of predicted to undergo a cat challenge. The subjects then enter the cat room for a 1-hour challenge. During the challenge upper respiratory symptoms (URsx; congestion, rhinorrhea, and pruritus) and lower respiratory symptoms (LRSx; tightness and wheezing) were scored every 5 minutes by the subject according to an arbitrary scale of 0 to 3. Repeat AR and spirometry were obtained at 15-minute intervals for the 1-hour challenge. At those times, bedding in the cat room was shaken once again to maintain high airborne allergen levels. Challenges were terminated early if the subject became too uncomfortable or had a drop in FEV₁ >50%. To determine the level of allergen exposure, air samples were collected during the challenge with use of a personal air sampling device (Gilian Instrument, Wayne, NJ) and airborne *Feline domesticus* allergen 1 (Fel d 1) was quantified (for the entire challenge) as previously described.^{8,12} To qualify for the study, each subject had to demonstrate a fall in FEV₁ of 15% or greater in the first 15 minutes of the screening cat challenge.

After the qualifying challenge, blood and urine specimens were obtained for hematologic analysis, clinical chemistry, urinalysis, and urine pregnancy tests. All laboratory values were checked before randomization to exclude subjects who had clinically significant deviations from the reference range, with the exception of abnormalities related to asthma or allergy.

Qualified subjects were then randomized to receive 1 week of treatment with either zafirlukast 20 mg twice daily or placebo. The active investigator and study coordinator were blinded to treatment identity. Patients were instructed to take the medication every 12 hours on an empty stomach, 1 hour before or 2 hours after a meal. The last dose of the week was to be taken 2 hours before the next cat challenge. The second cat challenge was then performed with the same protocol as the baseline challenge. This was followed by a 1-week washout period, after which subjects were treated for another week in a cross-over fashion, followed by another cat challenge. Adverse events were tabulated and reported for each treatment period.

The AR data from all challenges were collected and analyzed as previously described.⁹ The minimum cross-sectional areas (MCA) for each side were determined every 15 minutes. The percentage change from baseline was calculated at each time point, and the left

and right sides were averaged to determine the mean change in MCA. For symptom scores, each symptom was rated on a scale from 0 to 3, and scores were averaged to provide URSx and LRSx scores at each time point. These scores in turn were averaged to provide mean symptom scores for each 15-minute interval and for the entire challenge. Data for subjects who withdrew before a 15-minute time point were included for analysis at the next 15-minute time point.

Statistical analysis

Drug and placebo challenges were compared with regard to URSx scores, LRSx scores, change in FEV₁, challenge length, and change in nasal cross-sectional area as measured by AR. Data were analyzed before and after adjustment for differences in allergen level between the drug and placebo challenges. An α level $\geq .05$ was considered significant.

In the unadjusted analyses, differences in median challenge outcome measures were tested with the Wilcoxon matched-pairs signed rank test at each time point. Subjects who prematurely exited the cat room had all missing observations replaced by their last nonmissing values (ie, last value carried forward). To compare challenge outcomes over the duration of the entire challenge, curves were generated for each variable and the area under these curves was compared with use of the Wilcoxon matched-pairs signed rank test.

In the allergen-adjusted analyses, challenge length was analyzed with use of a stepwise Cox-proportional hazards model with allergen exposure, skin test grade response, treatment sequence, and visit as covariates. Nonsignificant terms were dropped if $P > .15$. URSx and LRSx scores were analyzed with a repeated-measures model using all nonmissing data collected every 5 minutes through 30 minutes, which allowed for the most complete data set because many subjects left before the first half hour and the data were censored from the time they left the room. This repeated-measures analysis estimated the rate of change in the symptom scores over time as a function of treatment. Allergen exposure, treatment sequence, and visit were included as covariates. Subject was included as a random effect (thus each subject was used as his or her own control, which adjusts for individual differences in sensitivity). Change in FEV₁ and change in nasal cross-sectional area were reanalyzed with use of a similar repeated-measure model using all nonmissing 15- and 30-minute data.

RESULTS

Subjects and baseline challenges

Eighteen subjects were enrolled. Demographic data are shown in Table I. Ages ranged from 20 to 55 years (median 32.5 years). Eleven of the subjects were female and 7 were male. Cat skin test wheal size ranged from 4 to 16 mm (median 10 mm). Baseline FEV₁ ranged from 71% to 115% of predicted (median 85%). Sixteen of the 18 subjects had methacholine reactivity, with PD₂₀FEV₁ values ranging from 0.6 to 49.5 BU (median 20.8 BU). Six of the subjects took daily maintenance medication for their asthma. All subjects had a history of asthma, 17 had a history of rhinitis, and 17 had other positive skin tests.

Responses to the baseline challenges are also shown in Table I. FEV₁ changes at 15 minutes ranged from 17% to 70% (median 35.5%) and maximum FEV₁ changes ranged from 17% to 70% (median 43.2%). Mean LRSx scores ranged from 0.5 to 2.67 (median 1.59) and mean URSx scores ranged from 0.11 to 2.67 (median 1.22). Mean maximum changes in MCA ranged from 0% to

TABLE I. Demographic characteristics and baseline challenges

Median age (y [range])	32.5 (20-55)
Sex	7 male, 11 female
Median cat wheal (mm [range])	10 (4-16)
Median baseline FEV ₁ (% predicted [range])	85 (71-115)
Median PD ₂₀ FEV ₁ (BU [range])	20.8 (0.6-49.5)
Subjects who were methacholine reactive	16/18
Subjects who were on maintenance asthma medications	6/18
Subjects with other positive skin tests	17/18
Subjects with history of allergic rhinitis	17/18
Response to baseline challenges	
Median challenge length (min [range])	15 (11-30)
Median decrease in FEV ₁ at 15 min (range)	35% (17%-70%)
Median maximum decrease in FEV ₁ (range)	43.2% (17%-70%)
Median LRSx (range)	1.59 (0.5-2.67)
Median URSx (range)	1.22 (0.11-2.67)
Median maximum change in MCA (range)	27% (0%- 81%)

TABLE II. Comparison of challenge outcome measures (unadjusted for allergen levels)

	Zafirlukast (median [range])	Placebo (median [range])	Statistical significance
Challenge length (min)	30 (14-60)	24 (7-60)	<i>P</i> = .08
Decrease in FEV ₁ at 15 min (%)	16.25 (0-45)	21.5 (5.5-57)	<i>P</i> = .027
Mean change FEV ₁ (%)	26.5 (0-45)	33.12 (1.5-57)	<i>P</i> = .02
Maximum change in FEV ₁ (%)	33 (0-47)	39.5 (6-57)	<i>P</i> = .098
Mean LRSx score	1.44 (0-2.83)	1.56 (0-2.92)	<i>P</i> = .43
Mean URSx score	1.43(0-2.86)	1.49 (0.22-2.86)	<i>P</i> = .9
Maximum change MCA (%)	32.6 (0-66)	41.3 (9.3-75.8)	<i>P</i> = .13
Fel d 1 level (ng/m ³)	4849 (2,561-22,006)	5,786 (878-26,226)	<i>P</i> = .76

81% (median 27%). The challenge lengths ranged from 11 to 30 minutes (median 15 minutes). Three subjects lasted less than 15 minutes, 9 subjects lasted 15 minutes, and 6 subjects lasted between 15 and 30 minutes. None of the subjects stayed in their baseline challenge more than 30 minutes.

Challenge outcomes after treatment

Although airborne Fel d I levels were overall similar in the zafirlukast and placebo challenges (Table II), there were several subjects for whom allergen levels were considerably higher or lower in one challenge compared with the other. Therefore data were further analyzed to take these differences into account as discussed in the statistical analysis section. The results presented include both the raw data and any differences resulting from allergen adjustment.

Fig 1 is a Kaplan-Meier curve depicting challenge lengths for the zafirlukast, placebo, and baseline challenges. Challenge length tended to be longer after zafirlukast (zafirlukast range 14 to 60 minutes, median 30 minutes; placebo range 7 to 60 minutes, median 24 minutes), although these differences were not significant (*P* = .08). While receiving zafirlukast, 1 subject lasted less than 15 minutes, 4 subjects lasted 15 minutes, 6 subjects lasted between 15 and 30 minutes, 2 subjects lasted between 30 and 45 minutes, and 5 subjects lasted 60 minutes. While receiving placebo, 3 subjects lasted less than 15 minutes, 4 subjects lasted 15 minutes, 8 subjects lasted between 15 and 30 minutes, and the remaining 3 subjects

lasted 60 minutes. Challenge length was longer during zafirlukast administration in 11 subjects and during placebo administration in 4 subjects, with the remaining 3 subjects having equal challenge lengths while receiving zafirlukast and placebo.

When challenge length data were reanalyzed to adjust for differences in allergen level and sensitivity (Table III), zafirlukast was found to significantly extend challenge length with a *P* value of .022 (risk ratio 0.37). By the assumptions of the Cox proportional hazards model, this implies that the likelihood of withdrawing from the cat room at a point in time after zafirlukast treatment was 0.37 times the likelihood of withdrawing at that time after placebo treatment. The statistical significance of allergen exposure was *P* = .0003 and a 10-fold increase in allergen level (a unit increase in log₁₀[Fel d 1 level]) was associated with a relative risk ratio of 19.2. When the effect of cat sensitivity on challenge length was assessed, there was no significant difference between grades 2 and 3 skin tests, but grade 4 was significantly different from grades 2 and 3 (*P* = .0085, relative risk 3.98).

Fig 2 illustrates the relationship between challenge length and allergen level by plotting the ratio of both allergen level and challenge length for each subject. Most subjects did as well or better on zafirlukast than on placebo, and 3 of the 4 subjects who had longer challenges while receiving placebo also had much higher allergen exposures while receiving zafirlukast. In the graph, the 3 leftmost subjects were exposed to more allergen after zafirlukast treatment than after placebo

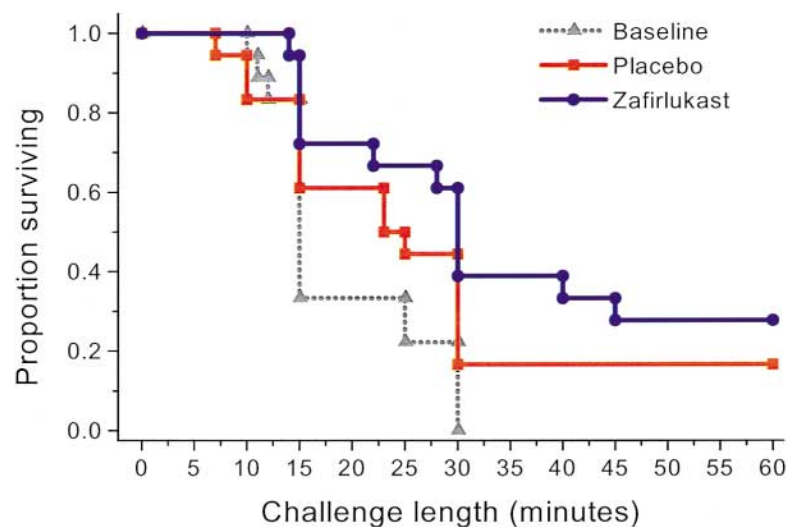


FIG 1. Kaplan-Meier curves comparing challenge length for baseline and zafirlukast and placebo challenges.

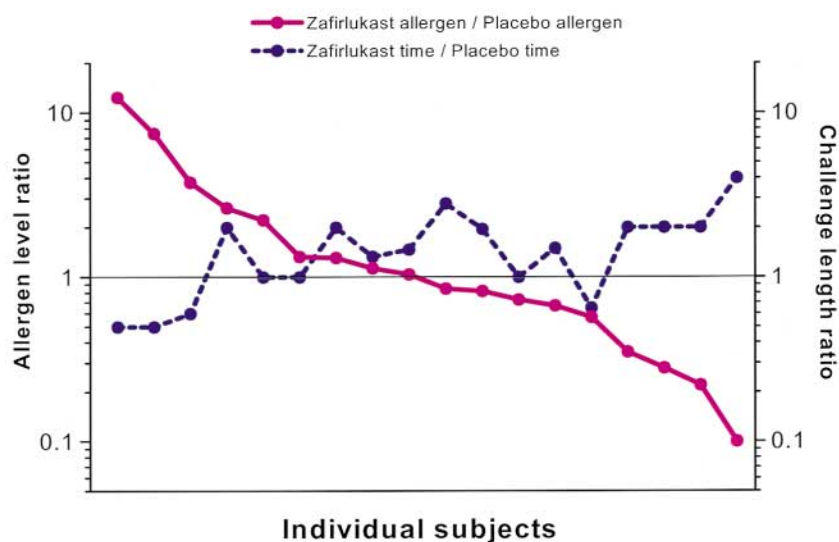


FIG 2. Relative allergen exposure and challenge length between treatments. Line (•) represents ratio of allergen level in zafirlukast versus placebo challenges. Gray line represents ratio of challenge length in the zafirlukast versus placebo challenges.

TABLE III. Comparison of challenge outcome measures (adjusted for allergen levels)

	Estimated improvement due to zafirlukast (95% CI)	Statistical significance	Estimated incremental effect of $\log_{10}(\text{Fel d 1})$ (95% CI)	Statistical significance
Cox proportional hazards	Risk ratio		Risk ratio	
Challenge length (min)	0.37 (0.16-0.87)	$P = .0223$	19.2 (3.91-93.9)	$P < .001$
Repeated-measures analysis	Per 15 minutes		Per 15 minutes	
Percent FEV ₁ at 0-30 min	+9.1 (3.33-14.7)	$P = .003$	17.2 (5.5-28.9)	$P < .001$
LRSx at 0-30 min	0.57 (0.80-0.34)	$P < .001$	0.83 (0.33-1.34)	$P = .002$
URSx at 0-30 min	0.16 (-0.04-0.29)	$P = .010$	0.022 (-0.25-0.30)	$P = .873$
Percent change MCA at 0-30 min	-0.62 (-5.8-4.6)	$P = .817$	0.84 (-13.2-11.5)	$P = .895$

CI, Confidence interval.

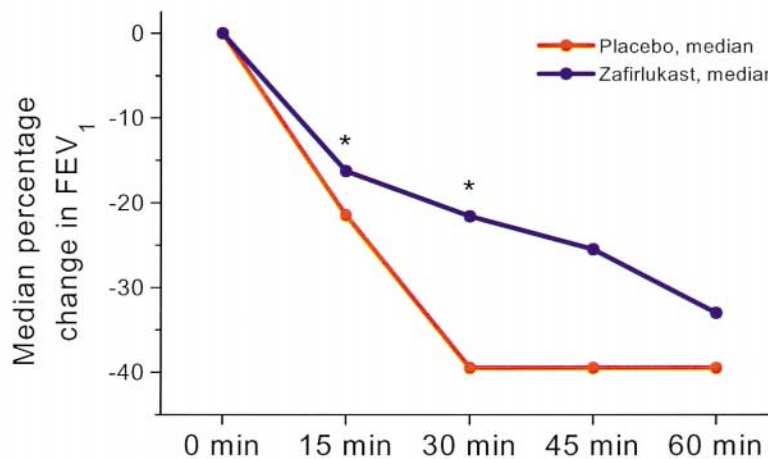


FIG 3. Median percent change from baseline in FEV₁ over time. Median percent changes were 16.2%, 21.6%, 25.5%, and 33% for active drug and 21.5%, 39.5%, 39.5%, and 39.5% for placebo. Asterisk, Statistically significant differences were detected at the 15- and 30-minute time points ($P < .05$) without adjustment for differences in allergen exposure.

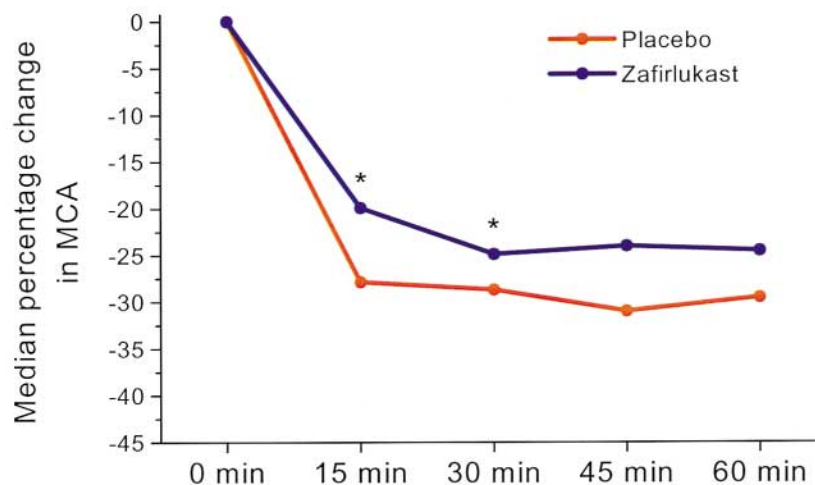


FIG 4. Median percent change from baseline in MCA over time. Median percent changes were 19.9%, 24.8%, 24%, and 24.5% for active drug and 27.85%, 28.7%, 31%, and 29.5% for placebo. Asterisk, Statistically significant differences were detected at the 15- and 30-minute time points ($P < .05$) without adjustment for differences in allergen exposure.

treatment and spent less time in the cat room. The 4 right-most subjects were exposed to less allergen after zafirlukast treatment and spent more time in the cat room. Of the remaining 11 subjects who had comparable allergen levels between treatments, 7 stayed in the room longer after zafirlukast treatment, 3 stayed the same amount of time, and 1 stayed less time.

Fig 3 shows the median percent change in FEV₁ in the challenges after active and placebo treatment. The overall change in FEV₁ (Table II) was significantly less after zafirlukast treatment ($P = .02$). The median decreases in FEV₁ at 15, 30, 45, and 60 minutes were 16.2%, 21.6%, 25.5%, and 33% with zafirlukast and 21.5%, 39.5%, 39.5%, and 39.5% with placebo. At 15 and 30 minutes

there were significant differences in favor of zafirlukast ($P = .027$ and $.05$, respectively) but not at 45 and 60 minutes ($P = .089$ and $.11$, respectively). The maximum fall in FEV₁ was less after zafirlukast but was not significant ($P = .098$). When the fall in FEV₁ was reanalyzed to adjust for allergen level, zafirlukast was estimated to significantly attenuate the rate of drop in FEV₁ by 9.1% every 15 minutes ($P = .003$, Table III). The statistical significance of allergen level on FEV₁ was $P < .001$, and a 10-fold increase in allergen level was estimated to decrease FEV₁ by 17.2% every 15 minutes.

The overall change in MCA was significantly reduced in the zafirlukast group ($P = .04$) (Fig 4). The median changes in MCA at 15, 30, 45, and 60 minutes were

19.9%, 24.8%, 24%, and 24.5% for zafirlukast and 27.8%, 28.7%, 31%, and 29.5% for placebo. These were significantly different at 15 and 30 minutes ($P = .05$ and $.0005$, respectively) but not at 45 and 60 minutes ($P = .08$ and $.07$, respectively). The mean maximum percent change in MCA ranged from 0 to 66 (median 32.6) for those on zafirlukast and from 9.3 to 75.8 (median 41.3) for those on placebo. When the percent change in MCA was reanalyzed to adjust for differences in allergen level, no significant effects were found.

LRSx and URSx scores were similar in the 2 treatment groups (Table II) and showed no significant treatment differences when scores were analyzed without adjustment for differences in allergen exposure ($P = .43$ and $.90$, respectively). However, when the scores were reanalyzed to adjust for differences in allergen level (Table III), zafirlukast significantly reduced the rate of increase in LRSx and URSx scores ($P < .001$ and $.010$, respectively). The rate of change in LRSx and URSx scores with zafirlukast treatment was estimated to be 0.57 and 0.16 symptom score units less per 15 minutes. Allergen level was found to have a significant effect on LRSx scores ($P = .002$) but not on URSx scores ($P = .873$). Treatment order was not statistically significant ($P = .072$ and $.527$), although the difference with second blinded challenge showed significantly lower rates of change (-0.27 and -0.18 per 15 minutes and $P = .041$ and $.0078$, respectively).

Three of the 18 subjects had mild adverse effects during treatment with zafirlukast, including diarrhea for 1 week in 1 subject, diarrhea for 1 day and nausea for 2 days in another subject, and mild mouth dryness for 1 week in another subject. None of these effects caused prolonged harm or discomfort and all resolved without medical intervention. None of the subjects were withdrawn from the study as a result of adverse events or noncompliance.

DISCUSSION

This study shows that treatment with zafirlukast significantly reduces both upper and lower respiratory responses to cat exposure. Zafirlukast produced an overall attenuation in FEV₁ change, with significant differences in FEV₁ change at 15 and 30 minutes. When differences in allergen exposure were taken into account, there were also significant changes in challenge duration and symptom scores in favor of zafirlukast. However, in spite of these positive results, it is likely that the overall effect of the medication on allergen-induced asthma may have been underestimated in this study by several factors.

First, the study was designed to include only asthmatic patients with a high degree of reactivity to cat allergen because entrance required a $>15\%$ decrease in FEV₁ in the first 15 minutes of the cat challenge. Second, the allergen levels encountered in the challenges in this study are extraordinary. It is likely that the greater effect of zafirlukast in the first half of the challenge was due in part to the very high allergen level encountered, with the intense exposure eventually overwhelming the positive

effects of the medication. In addition, because very few challenges lasted for more than 30 minutes, the analysis after that point included very few subjects. For example, actual data were available for all subjects at 15 minutes, for 11 subjects at 30 minutes, and for only 3 subjects at 45 and 60 minutes. These small numbers for analysis beyond 30 minutes are another likely reason that there were no statistically different outcomes in the second half of the challenge.

When challenge length was compared between the 2 groups, the median challenge time was longer in the zafirlukast group but the difference was not significant ($P = .08$). Reasons for discontinuing the challenge included an FEV₁ change of 50% or the presence of excessive symptoms. In the baseline challenges none of the subjects lasted a full hour, whereas 5 and 3 subjects lasted an entire hour during the zafirlukast and placebo challenges, respectively. When differences in allergen level and subject sensitivity were taken into account, there was a significant difference between the zafirlukast and placebo challenges. In addition, for 3 of the 4 subjects who had a longer challenge while receiving placebo, allergen levels were considerably lower during their placebo challenges.

Differences were seen in subjective symptoms (LRSx and URSx) only after adjustment for allergen level and analysis of the rate of change in symptoms over time. Although we have previously reported a relatively strong correlation between FEV₁ change and LRSx scores,⁹ this was not seen in this study ($r = 0.18$, $P = .29$). Again, these results may also be affected by the extremely high allergen levels. The allergen levels in the cat room were in the several thousand nanograms per cubic meter range, and it may be that at these levels subjects are less able to detect differences in subjective symptoms. It is possible that with lower levels, similar to those found among homes with cats (10 to 200 ng/m³),¹³ treatment differences in subjective symptoms would be more apparent. To fully evaluate the effects of zafirlukast on allergen-related symptoms, additional studies at lower antigen levels are needed.

Other clinical trials have shown that zafirlukast is effective in reducing asthmatic responses to allergen challenge.²⁻⁴ By use of aerosolized bronchoprovocation, Findlay et al³ evaluated 15 cat-allergic asthmatics and found that zafirlukast, compared with placebo, produced a mean 10-fold increase in interpolated PD₂₀FEV₁ on inhalation of increasing concentrations of cat allergen. Corren et al¹⁴ also looked at the effects of zafirlukast on cat-induced asthma in a cat exposure model similar to the one used in this study. Their results showed a significant difference between zafirlukast and placebo in FEV₁ and asthma symptom scores but no difference in nasal symptom scores and nasal or induced sputum cellular components. Our results are in general agreement with both studies, although the allergen exposure in our challenges was somewhat more intense than that in the studies by Findlay et al and Corren et al.

Less is known about the effects of zafirlukast on upper respiratory responses. In this study zafirlukast signifi-

cantly lowered the percentage change in MCA as measured by AR. This was seen at all time points during the challenge, with significant differences at 15 and 30 minutes, and was not affected by adjustment for allergen level. URSx scores were reduced by zafirlukast only after adjustment for time and allergen level. Furthermore, although zafirlukast had a statistically significant effect on both symptom scores, the magnitude of the effect on the URSx scores was about one third that of LRSx scores. As a comparison, Donnelly et al⁷ conducted a 2-day, 8-hour challenge during ragweed season to study the effects of zafirlukast in 164 subjects with ragweed-induced rhinitis. They showed that symptom scores for nasal congestion improved most consistently the evening after the start of treatment and that subjects had less sneezing and rhinorrhea. Our study differs in that we looked at more acute reactions to a shorter and more intense challenge.

In addition, our study may have underestimated the effects on nasal responses because it was primarily an asthma study. Subjects were recruited on the basis of the intensity of their asthmatic response and were not required to have a nasal response. It is therefore possible that if we conducted another study primarily in subjects with cat-induced rhinitis the effect of zafirlukast on upper respiratory responses might be better appreciated.

In conclusion, the results of this study show that zafirlukast helps to preserve pulmonary function and nasal anatomy in cat-sensitive asthmatic subjects challenged with high levels of cat allergen. Zafirlukast significantly reduced changes in FEV₁ and MCA and allowed subjects with significant asthmatic responses to last longer during cat challenges. Upper and lower respiratory symptom scores were also significantly reduced after use of time as a covariate and adjustment for allergen level. The true clinical relevance of these findings remains to be determined, although it is likely that the effects of the medication would be even more pronounced at more natural levels of airborne allergen.

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