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Efficacy of zafirlukast in the treatment of patients with bronchial asthma

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Zafirlukast is a drug newly used for the treatment of asthma. In this study, we examined the efficacy of zafirlukast on asthmatic patients and compared this efficacy between patients in different age groups and with different severities of pulmonary function. Patients concurrently inhaled long-acting β_2-agonist, corticosteroid or taken an oral aminophylline regimen, were treated with 20 mg oral zafirlukast twice daily for 6 weeks. In total, 32 asthmatic patients were included in the study. The primary efficacy measures included morning and evening peak expiratory flows (PEFs); secondary efficacy measures were the scoring of asthma symptoms including sleeping, coughing, and wheezing scores. Pulmonary functions including forced expiratory flow in 1 sec (FEV_1), forced vital capacity (FVC), and PEF rate (PEFR) were examined during each clinical visit. Results showed that oral zafirlukast administration resulted in improvements in morning and evening PEFs and asthma symptom scores with the following statistical p values: morning PEF (285.8 vs 308.4 L/min), $p = 0.003$; evening PEF (293.3 vs 312.1 L/min), $p = 0.007$; coughing score (1.03 vs 0.72), $p = 0.011$; and wheezing score (0.71 vs 0.51), $p = 0.009$. As to the pulmonary function during the clinical visit, only the improvement of PEFR reached a statistically significant level (74.3 vs 82, $p = 0.017$). We compared the efficacy between asthmatic patients of different ages and those with different severities of pulmonary function. In patients aged below 50 years, those with FEV_1 above 80% of the predicted value and FVC above 85% of the predicted value were more responsive to zafirlukast. In conclusion, we demonstrate the efficacy of zafirlukast in asthma therapy particularly for those patients who are younger and have better pulmonary function. When asthmatic patients do not respond to inhaled corticosteroid, long-acting β_2-agonist, or oral aminophylline, zafirlukast may provide an adjunct effect for asthma therapy.

Key words: Asthma, zafirlukast

Cysteinyl leukotrienes (C-LTs) are lipoxygenase products of arachidonic acid metabolism and have been postulated to play a significant role in the etiology of asthma [1,2]. The C-LTs cause constriction of human airway smooth muscle, increased secretion of bronchial mucus, and increased vascular permeability resulting in mucosal edema. They are synthesized by mast cells, eosinophils, basophils, macrophages and monocytes. They are present in the bronchoalveolar lavage fluid of patients with asthma, which suggests their participation in the events underlying asthma. Hence, considerable interest has been focused on developing C-LT receptor antagonists. A number of relatively potent and selective C-LT antagonists have been described in the literature [3,4]. Zafirlukast (Accolate) is a representative compound from a novel class of C-LT receptor antagonists. Results from *in vitro* and *in vivo* trials indicate that zafirlukast is one of the most potent and selective C-LT receptor antagonists described to date [5,6].

Asthma is usually treated by a stepwise increase in therapy. For patients whose asthma is poorly controlled with bronchodilators alone, it is recommended that they add inhaled prophylactic treatment, such as low-dose inhaled corticosteroids [7].

The possibility of poor inhaler technique and poor compliance with inhaled medications may mean that a prescribed dose of inhaled treatment may not actually be the dose received by the patient. In addition, it is sometimes recommended that even low doses of inhaled steroids be given by spacer devices or with mouth-rinsing to avoid problems such as oral candidiasis and dysphonia [8]. For these and other reasons, many patients dislike taking steroids. It would thus be desirable to introduce an alternative treatment which could be easily administered, effective, and safe in patients whose asthma is poorly controlled with bronchodilators alone, thereby avoiding the need to introduce inhaled prophylactic treatment.

Zafirlukast, a leukotriene receptor antagonist, has

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been shown to prevent the actions of C-LTs which are implicated in the inflammatory process of asthma [5].

The majority of experience has been at a dose of 20 mg twice per day in patients from Europe and North America with mild to moderate asthma. In these patient populations, zafirlukast (20 mg twice per day) has been shown to produce significant benefits in improving lung function, decreasing subjective asthmatic symptoms, and reducing bronchodilator use [9].

This trial was designed to assess the efficacy and safety of zafirlukast in asthma patients in Taiwan. The efficacy was measured by assessing the change in lung function following 6 weeks of treatment by monitoring complete blood counts, liver function test, and physical examinations. Efficacy between asthmatic patients of different ages and with a different severity of pulmonary functions was compared.

Patients and Methods

Trial design

This was a single center, open, and noncomparative trial. Prospective patients were observed during a 1-week screening period. It was possible for the 1-week screening period to be extended by an additional week if a patient needed more time to meet the criteria for symptoms and/or the forced expiratory flow in 1 sec (FEV_1) predicted value. Patients who fulfilled the asthma symptom criteria [10] were selected for therapy with zafirlukast for a period of 6 weeks. Patients could continue using their current treatment throughout the trial including inhaled β_2-agonists, corticosteroids and aminophyllines. The trial medication zafirlukast was provided by Astra/Zeneca Pharmaceuticals, Taiwan, at a dosage of 20 mg/tablet.

Patient population

A total of 32 patients were included in the study. Both male and female patients with reversible obstructive airway disease (asthma) were eligible for the trial. Female patients could not be pregnant at the start of the trial, nor intend to become pregnant during the trial period. Each patient had to be: 1. aged 12 to 70 years inclusive; and 2. using one of the following asthma treatment regimens: inhaled β_2-agonists, inhaled corticosteroids (beclomethasone or budesonide up to 800 µg/day, or fluticasone up to 500 µg/day), or other antiasthmatic therapy, except for oral steroids. For inclusion in the treatment period, each patient had to: 1. have an FEV_1 ≥60 % of the predicted value demonstrated at screening or at any time between screening and the start of treatment; 2. have asthma symptoms in the last 7 days of the screening period; and 3. demonstrate the ability to comply with the trial regimen and to use the peak flow meter and diary card correctly.

Prospective patients were excluded from entry to the screening period if any of the following conditions applied:

1. Evidence of hepatic disease other than Gilbert's syndrome from the physical examination or medical history;
2. Evidence (from the physical examination or medical history) of any disease that affects gastrointestinal absorption;
3. Evidence of any significant respiratory disease, other than reversible airways obstruction;
4. Use of short course of oral steroids or regular oral steroids within 1 month prior to screening;
5. Upper or lower respiratory tract infection within 6 weeks prior to screening;
6. Participation in another trial with another new chemical entity in the 4 weeks prior to screening;
7. Evidence of drug or alcohol abuse;
8. Evidence of risk of transmitting through blood or other body fluids the agents responsible for the acquired immunodeficiency syndrome (AIDS) or other sexually transmitted diseases or hepatitis; or
9. Currently be breast feeding.

Patients should not have had any known travel or holiday commitments that would prevent attendance at the clinic as required by the protocol. Patients were withdrawn from the trial for any of the following reasons:

1. Deterioration of the condition under treatment (if the investigator considered it would be in the patient's best interests not to continue);
2. Inappropriate patient compliance with the dosing regimen or with the trial rules and procedures;
3. Serious adverse effects (patients hospitalized for asthma exacerbation would not necessarily be withdrawn); or
4. Patients unwilling or unable to continue (drop-outs).

Diary cards and peak flow meters

At the beginning of the screening period, patients were given both a booklet of diary cards and a mini-Wright peak flow meter that had the American Thoracic Society Scale (Clement Clarke International, Harlow, Essex, UK), and they were instructed in their proper use. Peak flow meters were supplied by Astra/Zeneca Pharmaceuticals specifically for this trial; no other peak flow meter was used. The diary card was used to record

day-time asthma symptom scores, night-time awakenings, morning asthma symptoms, PEF twice daily and β_2-agonist usage throughout the day. The diary card data was reviewed by the investigator to determine eligibility and to assess the control of asthma and the occurrence of exacerbation of asthma during the trial. It was also used to determine patients' compliance with the trial scheme. Each diary card recorded data for 1 week, Monday to Sunday inclusive. In subsequent visits to the clinic, any card containing data entries for Sunday were collected and the remaining cards, including the card currently in use, were returned to the patient. This was to ensure continuity of data recording by the patient. All suitable patients, who received 6 weeks of treatment, were scheduled for four visits to the Allergy Clinic, Cathay General Hospital, Taipei.

Visit 1 (beginning of screening period)
After learning the details of the trial, patients were assessed for all inclusion/exclusion criteria and completed appropriate case report forms; they then made an appointment for 1 week later (or as appropriate if further lung function tests were planned).

Visit 2 (review of screening period and start of treatment)
The use of the diary card and peak flow meter was assessed. If the patient had used either of these incorrectly, we provided further instructions and extended the screening period for an additional week. The diary card data were reviewed for completeness. The total day-time asthma symptom score in the last 7 days of the screening period for the patient should be such that he/she was eligible. If the patient was eligible for treatment, pulmonary function data, and sera and sputum samples were collected. Patients were instructed to take the trial medication and to record all adverse events; they then received all trial medication and made an appointment for visit 3 weeks later.

Visit 3 (treatment period)
The diary card data were reviewed for completeness. Changes in each patient's current medical condition were assessed. We recorded any adverse events. The unused trial medication from visit 2 was collected. We dispensed further trial medication, and then made an appointment for visit 4, 3 weeks later.

Visit 4 (end of the trial or withdrawal)
A complete physical examination was made. Changes in each participant's current medical condition were assessed and any changes such as adverse events were recorded. Pulmonary function data, and sera and sputum samples were collected. The diary card data were reviewed for completeness.

Clinical evaluation
Pulmonary function tests, consisting of forced vital capacity (FVC), forced expiratory flow in 1 sec (FEV_1), and forced expiratory flow rate (FEFR), were performed by using standard procedures. A spirometer that met the American Thoracic Society standards was used; the calibration was checked each day of use and recorded. These records were checked by the trial monitor. FEV_1 was obtained from the full expiratory volume-time curve. If the spirometer produced a print-out on thermal paper, a photocopy was taken and filed with the case report forms. The time of the last use of β_2-agonists before the lung function tests was recorded. If this was less than 4 h, the spirometry test was deferred until 4 h had elapsed since the last use of a β_2-agonist. The time of day that any given patient underwent lung function tests was recorded and standardized throughout the trial to ensure that tests did not vary by more than ±2 h from visit to visit. FEV_1 was recorded at all visits.

The daily peak flow was also measured at each clinic visit under the supervision of the investigator. This was measured by using a peak flow meter available at the clinic. For each patient, the same peak flow meter was used. The use of a β_2-agonist was withheld for 4 h before the spirometry test. The best of three blows was recorded. This was measured using a mini-Wright peak flow meter in the morning and in the evening. Three measurements were made and the greatest of the three was recorded on the diary card. Measurements were made before the use of bronchodilator inhalers.

Day-time asthma symptom scores were used to determine asthma severity at the end of the screening period; each patient had asthma symptoms in the last 7 days of the screening period. If the screening period was extended to allow for further instruction about completion of the diary card or use of the peak flow meter, then the last 7 days of the extended period were used for the assessment.

Patients' completed diary cards scored the severity of their daytime symptoms according to the following system: 0 = no symptoms, the patient had no symptoms of asthma; 1 = mild symptoms, the symptoms did not interfere with normal activities such as mild wheezing; 2 = moderate symptoms, the symptoms interfered with some activities such as prevented playing sports but no other activity; and 3 = severe symptoms, the symptoms interfered with most activities, for example the patient was confined to home. The diary card was also used to record the number of times that each patient awoke because

of an asthma attack during each night of the trial.

The patients also recorded whether or not asthma symptoms were present on awakening each morning during the trial, as well as the total number of β_2-agonist doses taken each day. A dose was one actuation of the device. Safety was determined during each visit by means of a review of the patient's state of health, an interview for subjective symptomatology, routine clinical laboratory tests, review of the diary cards and the recording of adverse events.

The total number of tablets at visits 3 and 4 that should have been taken since the previous visit was calculated. All adverse events were recorded on the case report forms provided; a description of the event, severity, duration, seriousness, outcome, including the date of resolution, was provided along with the investigator's assessment of the relationship to the trial treatment.

Statistical analysis

The diary card efficacy parameters (morning and evening PEF, day-time symptoms, night-time awakening, β_2-agonist usage) were summarized statistically as the mean of each week and consisted of the mean, standard deviation, median, minimum, maximum, and number of patients. The percentage of change from the baseline to each follow-up week (weeks 1 to 6) and the endpoint were evaluated. A Wilcoxon signed ranks test was used to compare these parameters.

Results

Demographics

Thirty-two patients were enrolled in the study, among which four patients withdrew due to respiratory tract

Table 1. Profiles and pretrial baseline data of patients who signed informed consent

Group	Patient no.	Age (yr)	Sex	FEV_1 (%)[b]	FVC (%)	PEFR (%)	FEV_1/FVC (%)
A	1	37	F	96	103	86	98
	2	41	F	127	119	127	113
	3	35	M	86	89	60	104
	4	37	F	97	93	96	110
	5	31	F	82	77	61	110
	6	30	F	113	115	96	103
	7	29	F	98	93	81	109
	8	33	F	94	115	81	85
	9	32	F	105	105	110	105
	10	35	M	88	110	70	83
	11	31	F	93	102	84	95
	12	36	F	107	99	92	113
	13	40	F	63	54	90	123
	14	42	F	97	89	55	84
	15	48	M	88	72	109	127
	16	43	F	65	73	45	95
	17	31	F	61	53	65	120
	18[a]	49	F	93	-	66	-
	19[a]	25	M	80	-	64	-
	20[a]	28	M	71	-	60	-
B	21	69	M	66	62	64	109
	22	68	F	56	46	49	132
	23	60	M	85	99	95	88
	24	58	M	88	74	81	124
	25	50	F	60	54	35	96
	26	58	M	105	105	86	104
	27	65	M	72	85	58	100
	28	57	F	92	91	83	109
	29	57	F	90	85	60	113
	30	55	M	60	45	85	90
	31	68	M	86	78	42	114
	32[a]	50	M	73	-	60	-

Abbreviations: FEV_1 = forced expiratory flow in 1 sec; FVC = forced vital capacity; PEFR = peak expiratory flow rate

[a]Early withdrawal due to acute exacerbation.

[b]Percentage of predicted value.

Table 2. Changes of pulmonary function in clinic visit from baseline to 3 weeks (group A) and 6 weeks (group B) of zafirlukast treatment

Group A	No. of cases	After 3 weeks of zafirlukast (visit 3) mean (±SD)	Baseline (visit 1) mean (±SD)	p^a
FEV_1 (%)[b]	28	84.8 (±22.9)	87.0 (±15.6)	0.348
PEFR (%)	28	79.6 (±27.8)	74.3 (±24.3)	0.086
Group B	**No. of cases**	**After 6 weeks of zafirlukast (visit 4) mean (±SD)**	**Baseline (visit 2) mean (±SD)**	p^a
FEV_1 (%)	27	85.4 (±21.8)	87 (±15.6)	0.43
PEFR (%)	27	82 (±25.4)	74.3 (±24.3)	0.017

[a]Test statistics based on Wilcoxon signed rank test.
[b]Percentage of predicted value.

Table 3. Change from baseline in diary card assessment within the first 3 weeks (group A) and the fourth to sixth weeks (group B)

Group A	No. of cases	Mean value (±SD) of diary card records from visits 2 to 3	Mean value (±SD) of diary card records from visits 1 to 2	p^a
Morning PEF (L/min)	24	307.9 (±84.9)	285.8 (±85.6)	0.001
Evening PEF (L/min)	24	310.8 (±82.2)	293.3 (±83.3)	0.002
Sleep score	24	0.69 (±0.82)	0.92 (±0.95)	0.028
Coughing score	22	0.76 (±0.6)	1.03 (±0.63)	0.006
Wheezing score	22	0.43 (±0.59)	0.73 (±0.63)	0.001
Group B	**No. of cases**	**Mean value (±SD) of diary card records from visits 3 to 4**	**Mean value (±SD) of diary card records from visits 1 to 2**	p^a
Morning PEF (L/min)	24	308.4 (±87.4)	285.8 (±85.6)	0.003
Evening PEF (L/min)	23	312.1 (±83.8)	293.3 (±83.3)	0.007
Sleep score	23	0.68 (±0.77)	0.92 (±0.95)	0.1
Coughing score	22	0.72 (0.56)	1.03 (0.63)	0.011
Wheezing score	22	0.51 (0.57)	0.73 (0.63)	0.009

[a]Test statistics based on Wilcoxon signed rank test.

infections during this study period. Of all remaining patients, 10 (36%) were male, and 18 (64%) were female; all patients were Oriental. The mean age for patients was 45.6 years (range: 29-69). The patients' profile and baseline data are summarized in Table 1.

Efficacy assessments

The descriptive statistics of the clinical visit pulmonary function are summarized in Table 2 (by visit). The mean baseline peak expiratory flow (PEF) rate (±SD) was 74.3% ±24.3% of the predicted value (range: 42%-123%) and the mean endpoint PEF rate (PEFR) (±SD) was 82% ±25.4% of the predicted value (range: 33%-137%). The mean change of the endpoint from baseline in PEFR was 10.3%, and the increments were statistically significant at the endpoint ($p = 0.017$). The descriptive statistics of the clinical visit FEV_1 are summarized in Table 2. Changes from the baseline in the clinical visit FEV_1 were not statistically significant.

The mean value during each visit for morning PEF was calculated. Descriptive statistics of morning PEF are summarized in Table 3. The mean baseline (visit 1-2) morning PEF (±SD) was 285.8 ±85.6 L/min (range: 123-477 L/min). The mean endpoint (visit 3-4) morning PEF (±SD) was 308.4 ±87.3 L/min (range: 153-455 L/min). The mean change of the endpoint from the baseline in morning PEF was 22.6, and the increments were statistically significant at the endpoint ($p = 0.003$). The mean value during each visit for evening PEF was calculated. Descriptive statistics of evening PEF are summarized in Table 3. The mean baseline (visit 1-2) evening PEF (±SD) was 293.3 ±83.3 L/min (range: 118-444 L/min). The mean endpoint (visit 3-4) evening PEF (±SD) was 312.1 ±83.7 L/min (range: 156-461 L/min). The mean change of the endpoint from the baseline in evening PEF was 18.8, and the increments were statistically significant at the endpoint ($p = 0.007$).

The descriptive statistics of the sum of the score of night-time awakenings during each visit are summarized in Table 3. The mean baseline (visit 1-2) score of night-time awakenings was 0.92 ±0.95 (range: 0-3). The mean endpoint (visit 3-4) score of night-time awakenings was 0.68 ±0.77 (range: 0-2.6). The result of changes in night-time awakenings of the endpoint from the baseline was -0.24, which is not statistically significant. The descriptive statistics of the sum of the

score of coughing during each visit are summarized in Table 3. The mean baseline (visit 1-2) score of coughing was 1 ±0.63 (range: 0.2-2.5). The mean endpoint (visit 3-4) score of coughing was 0.72 ±0.56 (range: 0-1.6). The result for changes in coughing of the endpoint from the baseline was -0.28, which indicates statistically significant decrements in coughing at the endpoint (p = 0.006). The descriptive statistics of the sum of the score of wheezing during each visit are summarized in Table 3. The mean baseline (visit 1-2) score of wheezing was 0.73 ±0.63 (range: 0-2.1). The mean endpoint (visit 3-4) score of wheezing was 0.51 ±0.57 (range: 0-2). The result for changes in wheezing of the endpoint from the baseline was -0.22, which indicates a statistically significant decrements in wheezing at the endpoint (p = 0.009).

Zafirlukast effect on different age groups of asthmatic patients

We analyzed the results in this study based on age. Asthmatic patients were divided into two groups. One group consisted of patients over 50 years old, and the other of those under 50. We found that patients under 50 had better response to zafirlukast. After the 6-week treatment, with zafirlukast, lung function (morning and evening PEF) and asthma symptoms (night-time awakening, coughing, wheezing) showed significant improvement in patients under 50 (Table 4). Although zafirlukast treatment also improved the lung function (morning and evening PEF) and asthma symptoms (night-time awakening, cough, wheezing) of patients over 50, the improvements were not statistically significant.

Effect of zafirlukast on patients with different severities of asthmatic

We analyzed the results of this study based on the baseline FEV_1. Asthmatic patients were divided into two groups: one consisted of patients with baseline FEV_1 values over 80%, which is the percentage of the predicted value, and the other of those under 80%. We found that patients whose baseline FEV_1 was over 80% of the predicted value responded better to zafirlukast. After treatment, with zafirlukast the lung function (morning and evening PEF) and asthma symptoms (night-time awakening, coughing, wheezing) showed significant improvement in patients with baseline FEV_1 over 80% of the predicted value (Table 4). Zafirlukast treatment also improved the lung function (morning and evening PEF) and asthma symptoms (night-time awakening, coughing, wheezing) in patients with baseline FEV_1 under 80% of the predicted values, but the improvements were not statistically significant.

Discussion

The results of this study demonstrate that zafirlukast is effective in treating asthmatic patients. Patients showed significant improvements in both morning and evening PEF values, as well as in asthma symptoms including night-time awakenings, coughing and wheezing. These improvements occurred as early as 1 week after initiation of drug use, and continued throughout the 6-week treatment period. Similar findings that zafirlukast is efficacious in different sex and racial groups and provides a benefit to patients with either mild and moderate persistent asthma have been reported [11]. Although the effect of zafirlukast on asthma symptoms was observed within the first week of treatment, there was no improvement of FEV_1 throughout the entire course of the treatment. This discrepancy might be due to the time difference of the clinical visits. It has been reported that a morning dip of pulmonary function is a common phenomenon in asthma. The measurement of FEV_1 in the morning clinic was lower than that in the

Table 4. Change from baseline in diary card assessment for different groups of patients

Patient group	Morning PEF (L/min)		Evening PEF (L/min)		Wheezing score		Cough score		Sleep score	
	Visits 2-3	Visits 3-4	Visits 2-3	Visits 3-4	Visits 2-3	Visits 3-4	Visits 2-3	Visits 3-4	Visits 2-3	Visits 3-4
All	***	***	***	***	***	**	***	***	**	ns
Age ≥50	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
Age <50	***	***	***	**	***	**	ns	**	**	**
FEV1 ≥80%	**	**	**	**	***	**	**	ns	**	**
FEV1 <80%	**	ns	**	ns	ns	ns	ns	ns	ns	ns
FVC ≥85%	***	***	**	**	***	**	**	ns	**	ns
FVC <85%	ns	ns	**	ns	ns	ns	ns	ns	ns	**

Abbreviation: ns = not significant.

Note: Test statistics based on Wilcoxon signed rank test.

** $p < 0.05$ between treatments.

*** $p < 0.01$ between treatments.

afternoon, which might have caused the variation of pulmonary function in the clinical visit.

Substantial evidence exists for the key role of C-LTs in the pathogenesis of asthma. First, the C-LTs contract airway smooth muscles and are 100- to 1000-fold more potent than histamine in this respect. Second, the C-LTs act on the vasculature to produce vasodilation and increase vascular permeability, processes that are likely relevant to the movement and recruitment of leukocytes to the site of an inflammatory response and that result in airway tissue edema; these changes can decrease airway caliber. Third, the C-LTs potently stimulate mucous secretion and interfere with mucociliary clearance, which further alters airway patency [12-14]. In patients who exhibit exercise induced asthma, there is a significant increase in urinary LTE_4 excretion in relation to the exercise challenge. Inhibitors of the synthesis of leukotriene-receptor antagonists have been shown to protect against exercise-induced bronchoconstriction and to decrease urinary secretion of LTE_4 [15,16].

The numbers of 15-lipoxygenase-positive cells in bronchial mucosal biopsies from patients with asthma were found to be significantly higher than those in healthy subjects. C-LTs play a direct role in the development of airway hyper-responsiveness.

The leukotriene modifiers are the first new drugs for the treatment of asthma to be introduced in more than 20 years, and their exact role remains to be determined. Despite their novelty, however, there are data to support their use in patients with persistent asthma, whether it is mild, moderate, or severe. In patients with moderate-to-severe chronic persistent asthma, leukotriene-modifier therapy can be combined with inhaled glucocorticoids to maintain control of asthma with lower doses of inhaled glucocorticoids, or it can be added to an existing regimen to achieve better control of asthma.

The efficacy of zafirlukast has been demonstrated in clinical trials, and it has been shown to be superior to placebos in improving pulmonary functions and asthma symptom scores [11]. Previous studies have shown that maintenance treatment with inhaled glucocorticoids was clinically superior to the regular administration of the leukotriene receptor antagonist, and treatment with inhaled salmeterol provided significantly greater improvement over oral zafirlukast [17]. It can be speculated that a certain number of asthmatic patients have a better response to zafirlukast.

This study demonstrates that patients aged lesser than 50, with an FEV_1 above 80% of the predicted value and an FVC above 85% of the predicted value show significantly greater responsiveness of improved pulmonary functions and symptom control with zafirlukast treatment. Additional studies, particularly with comparison of responders and nonresponders are needed to clarify the role of zafirlukast in the therapeutic management of asthma.

In conclusion, we demonstrate the efficacy of zafirlukast in asthma therapy particularly in those patients with better pulmonary functions and who are younger. When asthmatic patients do not respond to inhaled corticosteroids, inhaled long-acting β_2-agonists or oral aminophyllines, zafirlukast may provide an adjunct effect for asthma therapy.

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