Evidence Table 14. Pharmacologic Therapy: Leukotriene Receptor Antagonists—Monotherapy/Effectiveness Studies

Abbreviations used in table:

AE	**adverse event**
BCD (or B)	**beclomethasone dipropionate**
CPAP	**continuous positive airway pressure**
ECP	**eosinophil cationic protein**
$FEF_{25\%-75\%}$	**forced midexpiratory flow**
FEV_1	**forced expiratory volume in 1 sec.**
FP (or F)	**fluticasone propionate**
FVC	**forced vital capacity**
GINA	**Global Initiative for Asthma Guidelines**
ICS	**inhaled corticosteroid**
ITT	**intent-to-treat**
LTRA	**leukotriene receptor antagonist**
M	**montelukast**
PC_{20}	**provocative concentration causing a 20% fall in FEV1**
PEF	**peak expiratory flow**
QoL	**quality of life**
RFD	**rescue-free days**
SAE	**severe adverse event**

*** indicates primary outcome**

Evidence Table 14. Pharmacologic Therapy: Leukotriene Receptor Antagonists—Monotherapy/Effectiveness Studies

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Rescue Medication Use	Lung Function	Exacerbations/Symptoms	Adverse Events
Malmstrom et al. (for the Montelukast/Beclomethasone Study Group). Oral montelukast, inhaled beclomethasone, and placebo for chronic asthma: a randomized, controlled trial. Ann Intern Med 1999;130(6): 487–495. (Merck Research Laboratories)	Multicenter, randomized, double-dummy, placebo-controlled, parallel-group trial followed by a double-blind placebo washout period (36 clinical centers in 19 countries; analyses adjusted for investigator effect)	To compare the clinical benefit of montelukast (M), placebo (P), and inhaled beclometha-sone (B)	895 (895?; all patients at least 1 measure-ment after baseline)	**Age** 15–85 yr, median 35 yr **Gender** 40% male, 60% female **Ethnicity** Caucasian 52%, Hispanic 32%, other 16%	Chronic asthma Duration 0.5–67 yr, median 17 yr 10% using theophylline 63% with history of allergic rhinitis 79% with history of exercise-induced asthma FEV_1, mean = 2.2 L FEV_1 % pred., mean = 65 Morning PEF, mean = 335 L/min Evening PEF, mean = 353 L/min Daytime asthma symptom score, mean = 3.4 (scale 0–6) $Beta_2$-agonist use, mean = 5.5 puffs/day Nocturnal awakenings, mean = 5.5 nights/week Eosinophil count, mean = 0.36 cells x 10^3/mcL	**Arm 1** M + placebo inhaler (n=387; 354 completers) **Arm 2** B + placebo tablet (n=251; 233 completers) **Arm 3** P (n=257; 215 completers)	10 mg once daily in evening + 2 puffs from inhaler at bedtime and in morning 100 mcg/puff twice daily + placebo tablet Placebo tablet + placebo inhaler All patients used salbutamol (100 mcg/puff) as needed.	12-week trial after a 2-week, single-blind placebo run-in period. Period 3 was a 3-week, double-blind placebo washout period involving a subset of patients (approximately 40).	Mean difference between B treatment and M treatment for beta-agonist use was –0.67 puffs/day (95% CI –1.10 to –0.245 puffs/day).	*Mean differences between B and M treatment were 5.8% (95%CI 3.0% to 8.5%) for FEV_1, 15.4 L/min (95% CI 8.1 to 22.5 L/min) for morning PEF, and 11.2 L/min (95% CI 4.2 to 18.3 L/min) for evening PEF. The M group had a faster and larger initial response than the B group; 7–10 days after initiation, effect of B treatment surpassed that of M. 22% of B group and 34% of M group did not show improvement in FEV_1. No difference was found between B and M groups in decrease in peripheral blood eosinophil count.	Mean differences between B and M treatment groups were –0.21 (95%CI –0.33 to –0.09) for daytime symptom scores and –0.70 (95% CI –1.098 to –0.32) for nocturnal awakenings. Percent of days with exacerbations was decreased by 42% with M treatment vs. P (p <0.05) and by 63% with B treatment vs. P (p <0.05). Days with asthma exacerbations were less frequent, and asthma-control days were more frequent in B vs. M treatment (p <0.05).	
Bisgaard and Nielsen. Bronchoprotec-tion with a leukotriene receptor antagonist in asthmatic preschool children. Am J Respir Crit Care Med 2000;162(1): 187–190.	Randomized, placebo-controlled, crossover study (Study was repeated with 6 of original sample to evaluate consistency of treatment response.)	To evaluate the effect of montelukast (M) on the bronchocon-strictor response to cold, dry air challenge in 3- to 5-yr-old children with asthma	16 (13 in ITT analysis)	**Age** 3.1–5.7 yr, mean = 4.5 yr **Gender** 69% male, 31% female **Ethnicity** Not reported	Hyperresponsive to cold, dry air challenge Duration of asthma 4–62 months, mean = 39 months Specific airway resistance, range 1.36–2.25, mean = 1.71 kPa % pred. range 103%–170%, mean = 129% 62% used inhaled budesonide, mean daily dose = 350 mcg Treatment regimen was unchanged for at least 2 months prior to study 54% had first-degree relative with atopic disease. 38% had concurrent atopic dermatitis. 23% had hay fever 23% were exposed to passive smoking at home	**Arm 1** M **Arm 2** Placebo (P)	5 mg chewable tablet Matching chewable tablet	Tablet was given between 8:00 and 9:00 a.m. daily for 2 days with cold, dry air challenge performed on 3rd day between 8:00 and 9:00 a.m. At least 1-week washout occurred between study periods. Terbutaline was used as rescue medication.	All children used terbutaline as rescue medication.	Specific airway resistance increased by 46% (95% CI 30% to 63%) after cold air challenge test with P treatment and by 17% (95% CI 3% to 31%) with M treatment (p <0.01 for difference between P and M groups). During second round (n=6), specific airway resistance increased by 52% (95% CI 28% to 75%) with P treatment and by 20% (95% CI 8% to 32%) with M treatment (p=0.02 for difference between groups).		

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/ Off-Treatment Followup	Rescue Medication Use	Lung Function	Exacerbations/Symptoms	Adverse Events
Bleecker et al. Low-dose inhaled fluticasone propionate versus oral zafirlukast in the treatment of persistent asthma. J Allergy Clin Immunol 2000;105(6 Pt 1): 1123–1129. (GlaxoWellcome, Inc.)	Multicenter, randomized, double-blind, double-dummy trial	To provide comparative data on important objective and subjective measures related to clinical efficacy of the lowest recommended dose of the ICS fluticasone propionate (FP) compared with that of the recommended dose of oral zafirlukast (Z)	451 (ITT)	**Age** 12–68 yr, mean = 31 yr **Gender** 50% male, 50% female **Ethnicity** Caucasian 83%, African American 8%, other 9% **Smoking** No use of tobacco within the previous yr or a smoking history of >10 pack-yr	Persistent asthma Duration ≥6 months FEV_1, mean = 2.5 L PEF, mean = 362 L/min Albuterol use, mean = 4.67 puffs/day Symptom score, mean = 1.15	**Arm 1** Inhaled FP aerosol **Arm 2** Oral Z	88 mcg twice daily 20 mg twice daily	12 weeks after 8-to 14-day run-in period Albuterol as needed for symptom relief	Albuterol use was reduced by 2.39 puffs/day for FP treatment vs. 1.45 puffs/day for Z treatment (p <0.001), with differences in favor of FP by week 1.	*Treatment with FP resulted in greater increase in FEV_1 compared with Z (0.42 vs. 0.20 L, p <0.001), with differences in favor of FP by week 4. Differences occurred in favor of FP in morning PEF (49.9 vs. 11.68 L/min, p <0.001) and evening PEF (38.9 vs. 10.5 L/min, p <0.001), with differences in favor of FP by week 2.	Greater improvement in mean percentage of symptom-free days for FP vs. Z treatment (28.5 vs. 15.6, p <0.001), with differences in favor of FP by week 1 Greater decrease in symptom score for FP vs. Z treatment (–0.46 vs. –0.19, p <0.001), with differences in favor of FP after week 1 FP increased the percentage of nights with no awakenings by 21.2% vs. 8.0% with Z (p <0.001). No difference occurred in exacerbations (p=0.19): 4% with FP and 6% with Z.	Incidence of AE was similar between groups, with 10% in each group having ≥1 drug-related AE. Two patients in the zafirlukast group had SAE resulting in withdrawal; no patient in the FP group had SAE resulting in withdrawal.
Busse et al. (for the Fluticasone Propionate Clinical Research Study Group). Low-dose fluticasone propionate compared with montelukast for first-line treatment of persistent asthma: a randomized clinical trial. J Allergy Clin Immunol 2001;107(3): 461–468. (GlaxoWellcome, Inc.)	Multicenter, randomized, double-blind, double-dummy, parallel-group study (52 study sites; analyses adjusted for site)	To compare the efficacy and safety of low-dose fluticasone propionate (FP) and montelukast (M) as first-line maintenance therapy in symptomatic patients by using short-acting $beta_2$-agonists alone to treat persistent asthma	533 (ITT analysis)	**Age** 15–83 yr, mean = 34.9 yr **Gender** 44.8% male, 55.2% female **Ethnicity** 83% White, 10% African American, 7% other	Persistent asthma Duration ≥6 months FEV_1 % pred., range 50%–80%, mean = 65.5% All used short-acting $beta_2$-agonist for 3 months before screening. Symptom score, mean = 1.67 (0–5 range)	**Arm 1** FP + placebo capsule (n=271; 194 completers) **Arm 2** Oral (M) + placebo inhaler (n=262; 187 completers)	88 mcg twice daily through metered-dose inhaler + placebo capsule in evening 10 mg in evening + 2 puffs of placebo twice daily through metered-dose inhaler	24 weeks after 8- to 14-day run-in period Patients used inhaled albuterol as needed throughout study.	FP treatment as compared to M treatment resulted in greater decrease in rescue albuterol use (3.10 vs. 2.31 puffs/day, p <0.001) and percentage of RFDs (45.9 vs. 31.2, p <0.001).	*FP treatment as compared to M resulted in greater improvement in FEV_1 (0.51 vs. 0.33, p <0.001), in FVC (0.42 vs. 0.29, p=0.002), and in $FEF_{25\%–75\%}$ (0.66 vs. 0.41, p <0.001).	FP treatment as compared to M treatment resulted in greater improvement in asthma symptom scores (–0.85 vs. –0.60, p <0.001), percentage of symptom-free days (32.0 vs. 18.4, p <0.001), and nighttime awakenings/ night (–0.64 vs. –0.48, p=0.023). Physician assessment and patient satisfaction favored FP over M treatment (p <0.001). No difference was found in exacerbations (4% of FP group and 8% of M group).	No difference was found in incidence of AE (71% of FP group vs. 68% of M group); very few were drug related. No drug related SAE occurred.

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/ Off-Treatment Followup	Rescue Medication Use	Lung Function	Exacerbations/Symptoms	Adverse Events
Busse et al. Fluticasone propionate compared with zafirlukast in controlling persistent asthma: a randomized double-blind, placebo-controlled trial. J Fam Pract 2001;50(7): 595–602. (GlaxoWellcome, Inc.)	Multisite, randomized double-blind, double-dummy, parallel-group study (34 sites in the United States; analyses adjusted for investigator effect)	To assess the clinical benefits of an ICS and a leukotriene modifier as first-line treatment for persistent asthma in patients who were symptomatic when using short-acting beta$_2$-agonists alone	338 (ITT analysis)	**Age** 12–75 yr **Gender** 50% male, 50% female **Ethnicity** Non-Hispanic White 86%, African American 10%, other 4%	Persistent asthma; majority had moderate asthma Most had asthma diagnosed for ≥10 yr. FEV$_1$, mean = 2.44 L Morning PEF, mean = 349 L/min Evening PEF, mean = 382 L/min All had used short-acting beta$_2$-agonist at least 6 weeks. Albuterol use, mean = 4.9 puffs/day Albuterol-free days, mean = 5.8% Symptom score, mean = 1.36 (0–5 range)	**Arm 1** Fluticasone propionate (FP) by inhaler + placebo capsule (n=113) **Arm 2** Oral zafirlukast (Z) + placebo by inhaler (n=111) **Arm 3** Placebo capsule and placebo by inhaler (n=114)	88 mcg twice daily + placebo capsule twice daily 20 mg capsule twice daily + 2 puffs of placebo by inhaler twice daily Placebo capsule + 2 puffs of placebo by inhaler twice daily	12 weeks after 8- to 14-day run-in period Albuterol as needed for symptom relief or corticosteroids for asthma exacerbations were permitted during the study.	FP treatment compared with placebo improved percentages of albuterol-free days (48.9% vs. 19.0%) and albuterol use (–2.8 vs. –1.3 puffs/day) (p <0.006). Z treatment compared with placebo improved percentage of albuterol-free days (37.5% vs. 19.0%) and albuterol use (–1.9 vs. –1.3 puffs/day). FP treatment compared with Z treatment improved the percentage of albuterol-free days and albuterol use (p <0.04).	*FP treatment improved pulmonary function more than Z treatment: 23.4% vs. 15.1% for FEV$_1$, 46.7 L/min vs. 15.2 L/min for morning PEF, and 33.3 L/min vs. 12.8 L/min for evening PEF (all p <0.05), with improvements significantly greater by day 4. Patients treated with FP also improved more than those treated with placebo (p <0.05).	FP treatment compared with placebo improved mean symptom scores (–0.65 vs. –0.43), percentages of symptom-free days (28.8 vs. 6.9), and nighttime awakenings, (–0.32 vs. –0.17) (all p <0.006). FP compared with Z treatment improved mean symptom scores, percentage of symptom-free days, and number of nighttime awakenings (p <0.04). Physician assessment of efficacy and patients' overall satisfaction favored FP over Z (p <0.025) or placebo (p <0.001). FP produced greater improvement in asthma QoL scores compared with Z or placebo (p <0.04). Most differences between FP and placebo were clinically meaningful; no differences between Z and placebo were clinically meaningful.	Percentages of patients who experienced AE were similar across treatment groups (67%–72%), with 12%–13% of AE in each group potentially related to study medication.
Nathan et al. A comparison of short-term treatment with inhaled fluticasone propionate and zafirlukast for patients with persistent asthma. Am J Med 2001;111(3): 195–202. (GlaxoWellcome, Inc.)	Multisite, randomized, double-blind, parallel-group study (25 centers in the United States; analyses adjusted for site)	To compare the effects of low-dose fluticasone (F) and zafirlukast (Z) on measures of clinical efficacy and safety over 4 weeks; in addition, the effect of switching patients from Z to F therapy was evaluated	294 (294)	**Age** 12–70 yr, mean = 32 yr **Gender** 44% male, 56% female **Ethnicity** Caucasian 85%, African American 10%, other 5%	Persistent asthma Morning predose FEV$_1$, mean = 2.5 L FEV$_1$ % pred., mean = 68.5 Morning PEF, 352 L/min Evening PEF, mean = 389 L/min Use of inhaled or oral short-acting beta$_2$-agonist for >6 weeks Daily albuterol use, mean = 4.4 puffs/day	**Arm 1** Inhaled F (n=144; 139 completers) **Arm 2** Oral Z (n=150; 138 completers)	2 puffs of 44 mcg morning and evening 20 mg morning and evening	4 weeks after 7- to 14-day screening period A 4-week open-label treatment period followed. No other asthma medications were permitted during the study.	F treatment more than Z treatment reduced albuterol use (–1.8 vs. –1.1 puffs/day, p=0.019).	*After weeks 3 and 4, F treatment improved morning PEF more compared to treatment with Z (p <0.033). At endpoint, mean change in morning PEF was greater in the F group than in the Z group (29.3 L/min, 8.2% change vs. 18.3 L/min, 5.3% change; p=0.022). No difference in change occurred in evening PEF or morning predose FEV$_1$ (p >0.20). During the open-label period, patients switched from Z to F had improvements in morning PEF (17.2 L/min), evening PEF (13.6 L/min), and FEV$_1$ (0.11 L) (all p <0.001).	F treatment increased the percentage of symptom-free days compared to treatment with Z (19.8% vs. 11.6%, p=0.025). No difference in change occurred in asthma symptom scores (p=0.085). During the open-label period, no difference in change occurred in percentage of symptom-free days. During the double-blind period, no difference occurred in percentage of patients with exacerbations.	No difference occurred in possible drug-related AE (4% of the F group and 10% of the Z group). No SAE occurred.

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Storms et al. Clinical safety and tolerability of montelukast, a leukotriene receptor antagonist, in controlled clinical trials in patients aged > or = 6 years. Clin Exp Allergy 2001; 31(1): 77–87. (Merck and Co., Inc.)	Pooled analysis from 11 multicenter, randomized, controlled Phase IIb and Phase III trials and 5 long-term extension studies	To summarize safety data and describe the tolerability of montelukast derived from 11 placebo-controlled, double-blind Phase IIb and Phase III clinical trials in patients with chronic asthma and from 5 extension studies	3,386 and 336 pediatric patients in trials; 2,031 adults and 257 children in extension studies	**Trials: Adults** **Age** 15–85 yr, mean = 37 yr **Gender** 49% male, 51% female **Ethnicity** Caucasian 79%, Hispanic 12%, Black 4%, other 6% **Trials: Children** **Age** 6–15 yr, mean = 11 yr **Gender** 65% male, 35% female **Ethnicity** Caucasian 80%, Hispanic 4%, Black 13%, other 3% (Similar percentages of each demographic group entered into the extensions.)	Chronic asthma: mild, moderate, and severe persistent Allergic rhinitis history: 77% of adults, 94% of children FEV_1 % pred., range 40–90	2 Phase IIb adult trials 8 Phase II adult trials 1 Phase III pediatric trial 5 extension studies	2–200 mg/day One 10 mg tablet/day One 5 mg chewable tablet/day in evening	6 and 3 weeks 4–16 weeks 8 weeks 1.5, 1.8, 2.5, & 4.1 yr, 10.3 months				*Percentages discontinuing trials due to clinical AE were 4.0% in placebo and 2.3% in montelukast groups for adults and 1.5% in placebo and 2.5% in montelukast groups for children. Incidence of clinical AE was comparable among placebo and montelukast patients in the adult and pediatric trials. No increase in AE occurred for those who received montelukast as high as 200 mg for 22 weeks.
Brabson et al. Efficacy and safety of low-dose fluticasone propionate compared with zafirlukast in patients with persistent asthma. Am J Med 2002;113(1): 15–21. (GlaxoWellcome, Inc.)	Multicenter randomized double-blind, double-dummy trial (44 sites in the United States)	To compare the efficacy and safety of fluticasone (F) with zafirlukast (Z) in patients with persistent asthma who had been treated previously with low doses of ICS	440 (378; ITT)	**Age** ≥12 yr, mean = 35.5 yr **Gender** 37% male, 63% female **Ethnicity** Caucasian 81%, Black 4%, other 15%	Stable persistent asthma Fixed daily dose of inhaled BCD 168–336 mcg (mean = 263 mcg) or triamcinolone acetonide 400–800 mcg (mean = 602 mcg) 38% treated by primary care physician; 52% treated by specialist FEV_1 % pred., mean = 73 PEF, mean = 87%	**Arm 1** F through metered-dose inhaler (n=224; 207 completers) **Arm 2** Z as single tablet (n=216; 171 completers)	44 mcg morning and evening 20 mg	6 weeks after 8-day run-in period Albuterol was used as needed for symptom relief.	Albuterol use was reduced by 0.6 puff/day in patients receiving F vs. an increase of 0.1 puff/day in patients receiving Z (p <0.001).	*Mean changes in FEV_1 were 0.24 L in the F group and 0.08 L in the Z group (p <0.001). F treatment increased morning peak flow compared with Z treatment (30 vs. 6 L/min, p <0.001).	F treatment resulted in greater (p=0.001) improvements in asthma symptom scores compared with Z treatment (diff = –0.17 on 0–4 scale). Fluticasone patients experienced more symptom-free days (22 vs. 8, p <0.001). Only 1% treated with F experienced exacerbation vs. 6% treated with Z (p=0.005). The completer rate was higher in the F group (92%) vs. the Z group (79%) (p <0.001). The percentage who withdrew due to lack of efficacy was higher in the Z group (13%) than in the F group (2%).	No SAE occurred in either group. At least 1 AE potentially related to treatment was experienced by 7% of F group patients and by 4% of Z group patients (p=0.14).

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Israel et al. Effects of montelukast and beclomethasone on airway function and asthma control. J Allergy Clin Immunol 2002; 110(6): 847–854. (Merck and Co., Inc., Whitehouse Station, NJ; and USHH-Merck and Co., Inc., West Point, PA)	Multicenter, randomized, double-blind, placebo-controlled, parallel-group study (64 centers in the United States)	To compare the effects of montelukast (M) and beclometha-sone (BCD), as judged by days of asthma control	782 (752; ITT)	**Age** 15–74 yr, mean = 33.2 yr **Gender** 48% male, 52% female **Ethnicity** Caucasian 85%, Black 6%, Hispanic 5%, other 4% **Smoking** Nonsmoker for ≥1 yr with smoking history ≤7 pack-yr	Persistent asthma Duration ≥1 yr, mean = 19 yr FEV_1, mean = 2.5 L FEV_1, % pred., mean = 66.7 Reversibility %, mean = 28.8 Daily beta$_2$-agonist use, mean = 5.7 puffs/day	**Arm 1** Montelukast sodium (M) (n=339; 328 completers) **Arm 2** BCD (n=332; 318 completers) **Arm 3** Placebo (n=111; 106 completers)	10 mg tablet once daily in evening 200 mcg (4 puffs) twice daily by inhalation	6 weeks following 2-week single-blind placebo baseline period Inhaled albuterol for symptomatic relief and short-acting antihis-tamines were permitted. Up to 2 uses of rescue oral corticosteroid were permitted.	Both treatments reduced average albuterol use compared to placebo (p <0.001), with no difference between M (–30.3%) and BCD (–31.9%). The percentage of patients who used rescue corticosteroids did not differ between treatment groups (p=0.473). M was better than placebo (2.7% vs. 7.2%, p=0.037), but BCD was not (3.6% vs. 7.2%, p=0.127).	Improved FEV_1 of the M group (0.24 L) and BCD group (0.38 L) differed from the placebo group (0.10 L, p <0.001), with the effect of BCD greater than that of M (p <0.001).	*Percentage overlap of days of asthma control for treatments was 97.7%. Means were 41.4% for M and 41.1% for BCD (p=0.929) vs. 26.8% for placebo (p <0.001). Fewer patients in the M group than in the placebo group had an asthma attack (3% vs. 8.1%, p <0.025), with no difference between the 2 treatments (3% vs. 3.9%). No difference was found between treatment groups in percentage of days of sustained asthma control (33.4% for M, 32.1% for BCD), with both greater than placebo (19.3%, p <0.05).	Laboratory AE occurred for 3.9% of the M group, 3.0% of the BCD group, and 4.5% of the placebo group (p >0.05).
Kanniess et al. Montelukast versus fluticasone: effects on lung function, airway responsiveness and inflammation in moderate asthma. Eur Respir J 2002; 20(4): 853–858. (GlaxoSmithKline, Germany)	Randomized, double-blind, crossover design	To compare montelukast (M) with low-dose fluticasone	40 (40)	**Age** 18–60 yr, mean = 37 yr **Gender** 60% male, 40% female **Ethnicity** Not reported **Smoking** 100% nonsmokers	Moderate, allergic bronchial asthma No ICS or systemic corticosteroids within 3 or 6 months or antihistamines or theophylline within 4 weeks FEV_1, mean = 2.79 L FEV_1 % pred., mean = 74.0 FVC % pred., mean = 93.1 PC_{20} methacholine (Mch) geometric mean = 0.180 mg/mL Sputum eosinophils, geometric mean = 4.28% Tryptase in sputum, geometric mean = 8.0 pg/mL	**Arm 1** F + placebo tablet **Arm 2** M + placebo inhaler	100 mcg twice daily 10 mg at nighttime	Two 4-week periods with a 3- to 8-week washout interval after a 1- to 2-week screening period Salbutamol was permitted as rescue medication.	Use of rescue medication decreased after both treatments (p <0.05), with no difference between treatments.	*FEV_1 increased (p <0.001) after F (0.50 L) and after M (0.37 L), with no difference between treatments. PC_{20} of methacholine increased 1.33, doubling concentrations after F (p <0.001), but there was no effect after M (p=0.39). Changes differed between drugs. Percent of eosinophils decreased after F by a factor of 2.7 (p <0.001), but not after M (p=0.16), with difference between groups. Level of nitric oxide decreased (p <0.01) after F, but not after M, with difference (p <0.001) between treatments.	(Based on diary data of 38 patients) F reduced daytime symptoms (1.5 to 0.8, p=0.05) compared to baseline. Neither treatment had an effect on nighttime symptoms (p >0.15).	

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/ Off-Treatment Followup	Rescue Medication Use	Lung Function	Exacerbations/Symptoms	Adverse Events
Baumgartner et al. Distribution of therapeutic response in asthma control between oral montelukast and inhaled beclomethasone. Eur Respir J 2003;21(1): 123–128.	Multicenter, randomized, double-blind, double-dummy, placebo-controlled, parallel group study (16 centers in 8 countries)	To compare the effective-ness of montelukast (M) and inhaled beclometha-sone (B) in the treatment of adult patients	730 (679; ITT for efficacy)	**Age** ≥15 yr, mean = 35.7 yr **Gender** 34% male, 66% female **Ethnicity** Not reported **Smoking** Nonsmokers for ≥1 yr	Chronic asthma Duration ≥1 yr, mean = 18.6 yr FEV_1, mean = 2.21 L FEV_1 % pred., mean = 68 Beta-agonist use, mean = 5.2 puffs/day	**Arm 1** Oral M (n=313; 219 completers) **Arm 2** Inhaled B (n=314; 295 completers) **Arm 3** Placebo (n=103; 93 completers)	10 mg once daily 200 mcg (4 puffs) twice daily	6 weeks after 2-week single-blind placebo run-in period Short-acting inhaled beta-agonist was used as needed throughout study.	Percent reduction in beta-agonist use was greater (p <0.05) for patients taking B (45.7%) than for patients taking M (35.7%), with both greater than placebo (15.7%, p <0.05).	Overlap in change in FEV_1 between active treatment groups was 96%. No difference was found between change in M (12.1%) and B (13.9%) groups, with both greater than the placebo group (6.4%, p <0.05).	*Overlap in percentage of asthma-control days between active treatment groups was 89%. The mean in the M (50.7%) and B (57.9%) groups was greater than in the placebo group (40.0%, p <0.05). Difference favored the B group over the M group (diff 7.2, p <0.05). Percent of patients with ≥1 asthma attack did not differ between M (6%) and B (4%) groups; both groups had fewer attacks than the placebo group (15%, p <0.05).	AE were more frequent in the placebo group (54%) than in the M (39%) and B (42%) groups. A higher percentage of patients discontinued because of AE in the placebo group (2.9%) compared with the M (0%) and B (1%) groups.
Bisgaard. A randomized trial of montelukast in respiratory syncytial virus post-bronchiolitis. Am J Respir Crit Care Med 2003; 167(3):379–383. (University Hospital of Copenhagen, Denmark)	Multicenter randomized, double-blind, placebo-controlled, parallel-group study (11 pediatric centers that were secondary referral centers)	To assess the effect of cys-LT receptor antagonists on the post-infectious course of respiratory syncytial virus	130 (116 for treatment period, 87 for followup period)	**Age** 3–36 months, mean = 9.5 months **Gender** 48% male, 52% female **Ethnicity** Not reported Tobacco exposure, 42% Pets at home, 43% Atopic heredity, 38%	Moderate-to-severe symptoms requiring hospital admission Admission 2–7 days, median 4.5 days Treatment: O_2, 29%; CPAP, 16%; beta-agonist, 81%	**Arm 1** Montelukast (n=65; 55 completers) **Arm 2** Placebo (n=65; 61 completers)	5 mg tablet in evening	28 days, beginning a median of 3 days after admission			*Infants given montelukast were free of daytime and nighttime symptoms 6 of 28 days vs. 1 of 28 days for infants given placebo (p=0.015). More infants reported ≥1 symptom-free day and night on active treatment (p=0.045). Daytime cough was reduced on active treatment vs. placebo (p=0.04). Exacerbations occurred in 4 infants given montelukast and 10 given placebo (p=0.08). Time to exacerbation was 8 vs. 23 days (p=0.044).	Three infants given montelukast were withdrawn due to symptom severity vs. 8 infants given placebo (p=0.11).

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Ducharme. Inhaled glucocorticoids versus leukotriene receptor antagonists as single agent asthma treatment: systematic review of current evidence. BMJ 2003;326(7390): 621–625.	Systematic review of randomized controlled trials (All were parallel group designs; 10 used double-blinding, while 3 were open label; 10 were of high methodolo-gical quality.)	To compare the safety and efficacy of anti-leukotrienes and inhaled glucocorticoids as mono-therapy in people with asthma	13 trials; 5,109 subjects Sample sizes ranged from 20 to 666, with mean of 393	**Age** 1 pediatric trial with mean age = 10 yr; 12 adult trials with mean age ranging from 30 to 41 yr **Gender** Males ranged from 35% to 65% in the various trials **Ethnicity** Not reported **Smoking** Not reported	4 trials focused on patients with mild asthma. 8 trials had patients with moderate obstruction. 1 trial failed to report severity.	**Arm 1** Anti-leukotrienes: Montelukast (8 trials), zafirlukast (4 trials), or pranlukast (1 trial) **Arm 2** ICS Beclomethasone dipropionate (BCD) (8 trials), fluticasone propionate (5 trials), or budesonide (1 trial) One trial used two ICS arms.	10 mg once daily (7 trials), 20 mg twice daily (4 trials), 5 mg once daily (1 trial), 450 mg once daily (1 trial) 100 mg twice daily (4 trials), 100 mg 3 times daily (1 trial), 200 mg/day (1 trial), 200 mg twice daily (4 trials), 200–250 mg twice daily (1 trial), 400 mg/day (3 trials)	Ranged from 4 to 37 weeks: 4 weeks (2 trials), 6 weeks (4 trials), 12 weeks (3 trials), 16 weeks (1 trial), 24 weeks (2 trials), 37 weeks (1 trial)	Within 6 weeks, patients in the inhaled glucocorticoid group, compared to the anti-leukotriene group experienced less rescue use of beta$_2$-agonists (–0.78, 95% CI –0.55 to –1.00 puffs/day; 6 trials).	Within 6 weeks, patients in the inhaled glucocorticoid group compared to the anti-leukotriene group experienced greater improvement in FEV_1 (WMD 130 mL, 95% CI 80 mL to 170 mL; 8 trials) and morning PEF (WMD 19 L/min, 95% CI 14 L to 25 L; 7 trials).	*Patients treated with LTRAs were 60% more likely to experience exacerbation requiring systemic glucocorticoids than those treated with inhaled glucocorticoids (RR 1.6, 95% CI 1.2 to 2.2; 11 trials). The magnitude of effect was not related to LTRA, inhaled glucocorticoid preparation, or baseline severity (all p >0.10). Within 6 weeks, patients in the inhaled glucocorticoid vs. the anti-leukotriene group experienced fewer nocturnal awakenings per week (WMD –0.56, 95% CI –0.28 to –0.77; 5 trials) and fewer days with symptoms (–9%, 95% CI –5% to –13%; 3 trials). Anti-leukotriene was associated with increased risk of withdrawal due to poor asthma control (RR 2.5, 95% CI 1.8 to 3.5; 12 trials).	No difference occurred in the number of patients who experienced any AE (RR 1.0, 95% CI 0.9 to 1.1; 11 trials).
Jayaram et al. Steroid naive eosinophilic asthma: anti-inflammatory effects of fluticasone and montelukast. Thorax 2005;60(2): 100–105. (GlaxoWellcome, Inc.)	Multicenter, randomized, double-blind, double-dummy, parallel group placebo and active controlled trial (4 centers)	To compare the magnitude of anti-inflammatory effects of montelukast with fluticasone in subjects with asthma and sputum eosinophilia	50 (49)	**Age** 34.7 yr **Gender** 41% male, 59% female **Ethnicity** Not reported **Smoking** 10% current smoker, 14% exsmoker, 76% nonsmoker	Persistent symptomatic asthma Had taken only short-acting bronchodilator for at least 2 months FEV_1 % pred., 75.9 (prebronchodilator) Change in FEV_1 after bronchodilator, mean = 18.8% 86% atopic Salbutamol use, mean = 3.1 puffs/day Symptom score, mean = 24.0 (range 5–35) All had induced sputum eosinophilia ≥3.5%.	**Arm 1** Fluticasone (F) by inhaler + placebo tablet (n=18; 17 completers; 18 analyzed) **Arm 2** Montelukast (M) + placebo inhaler (n=19; 18 completers; 19 analyzed) **Arm 3** Placebo (n=13; 11 completers; 12 analyzed)	50 mcg, 2 puffs in morning and 3 puffs in evening + placebo tablet in evening 10 mg tablet in evening and placebo inhaler Placebo tablet and placebo inhaler	8 weeks If exacerbation occurred, F (125 mcg, 2 puffs/day) was added to treatment.		*F resulted in greater reduction in sputum eosinophils (geometric mean = 11.9–1.7) vs. M (10.7–6.9; p=0.04) or Placebo (15.4–7.8; p=0.002) treatment. Mean difference for F vs. M treatment was –2.3%, 95% CI –5.2 to 01.0) and for F vs. Placebo treatment was –4.0% (95% CI –10.2 to –1.6). Median reduction in sputum eosinophilia after F on day 7 was 72.7% vs. 56.2% with M and 34.9% with Placebo. F treatment resulted in greater improvement in FEV_1 (475 mL; 2.6–3.0 L) vs. M (156 mL; 2.8–2.8 L; p=0.02) and vs. Placebo treatment (125 mL; 2.4-2.4L; p=0.01). Mean difference between F and M treatment was 373 mL (95% CI 26 to 729 mL, p=0.03) and between F and Placebo was 458 mL (95% CI 73 to 842; p=0.02).		

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Jenkins et al. Traditional and patient-centered outcomes with three classes of asthma medication. Eur Respir J 2005; 26(1):36–44. (Australian Federal Government, AstraZeneca, Aventis Pharma, GlaxoSmithKline, Merck Sharp and Dohme, New South Wales State Department of Health)	Randomized double-blind, double-dummy crossover design	To examine the relation-ship between clinical and subjective variables in the assess-ment of response to treatment with 3 different classes of medication	58 (53)	**Age** 16–70 yr, mean = 38.5 yr **Gender** 60% male, 40% female **Ethnicity** Not reported **Smoking** 19% former smokers	Mild-to-moderate persistent, suboptimally controlled asthma 67% taking ICS prior to enrollment FEV_1 % pred., mean = 76.1 FEV_1/FVC ratio, mean = 0.72	**Arm 1** Encapsulated montelukast plus placebo Turbuhaler **Arm 2** Eformoterol plus placebo capsule	10 mg nocte 12 mcg b.i.d. Reliever salbutamol was permitted throughout the study.	2-week run-in period; two 6-week treatment periods separated by 1-week washout periods; 6-week single-blind fluticasone propionate 250 mcg b.i.d. plus placebo capsules	*Mean morning PEF was significantly higher with eformoterol (453 L/min) and with fluticasone (468 L/min) than with montelukast (428 L/min; both p <0.001). No difference was found between eformoterol and fluticasone. No difference in clinic FEV_1 % pred. was found between montelukast and eformoterol, with the effect of fluticasone better than both. Fluticasone >eformoterol for lung function factor derived from PCA.	*Median nighttime symptom score was lower with eformoterol and with fluticasone compared with montelukast (p <0.001 and p=0.01, respectively). No difference was found in daytime symptom scores between eformoterol and fluticasone compared with montelukast (p=0.054 and p=0.06, respectively). Better asthma control occurred with both eformoterol and fluticasone than with montelukast. Mean absolute improvement in QoL scores with eformoterol and fluticasone was not clinically important. Eformoterol >fluticasone for symptom/relievers use factor and equivalent for patient-centered factor derived from PCA.	Five severe exacerbations occurred (n=3 with montelukast; n=1 with eformoterol; n=1 with washout after eformoterol), and 11 moderate exacerbations occurred (n=8 with run-in, n=2 with eformoterol, n=1 with fluticasone).
Straub et al. The effect of montelukast on lung function and exhaled nitric oxide in infants with early childhood asthma. Eur Respir J 2005; 25(2):289–294.	Randomized, double-blind, placebo-controlled trial	To investigate the therapeutic effect of montelukast (M) in a well-defined group of very young children with recurrent wheeze and a positive family history of asthma and allergy	24 (24)	**Age** Mean = 18.3 months **Gender** 54% male, 46% female **Ethnicity** Not reported	Mild disease activity $FEV_{0.5}$, 175 mL Symptom score, range 0–9; median = 4.5 (possible range, 0–18) Fractional exhaled nitric oxide, mean = 31.6 ppb Sensitive only to food allergens, 66.7%; sensitive only to aeroallergens 16.7%; and sensitive to both food and aeroallergens, 16.7% All had history of recurrent wheeze. All had positive family history of asthma.	**Arm 1** M (n=12) **Arm 2** Placebo (n=12)	4 mg daily 1 placebo tablet daily	4 weeks	Mean $FEV_{0.5}$ improved in the M group (189.0 to 214.4 mL; p=0.038) but not in the placebo group (161.0 to 166.6 mL, p=0.026). Fractional exhaled nitric oxide decreased in the M group (29.8 to 19.0 ppb, p=0.01) but not in the placebo group (33.4 to 34.5 ppb, p=0.25). Difference in change between the groups was significant (p=0.04).	Median score in the M group improved from 5.5 to 1.5 (p=0.04) but not in the placebo group (3.0 to 4.0, p=0.35).	

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Garcia-Garcia et al. Montelukast, compared with fluticasone, for control of asthma among 6- to 14-year-old patients with mild asthma: the MOSAIC study. Pediatrics 2005;116(2): 360–369. (Merck and Co.)	Multicenter, randomized, double-blind, double-dummy, parallel-group design (104 sites in 24 countries)	To compare the efficacy of orally administered montelukast (M) with that of inhaled fluticasone (F) in the percentage of asthma RFDs among 6- to 14-yr-old patients with mild persistent asthma	994 (966; ITT analysis)	**Age** 5–15 yr, median 9 yr **Gender** 62% male, 38% female **Ethnicity** 63.6% White, 21.2% Hispanic, 5.9% Asian, 0.6% Black, 7.2% multiracial, 1.5% other **Weight** 106–181 kg, median 136 kg **Height** 106–181 cm, median 135 cm	Mild persistent at step 2 of GINA guidelines Clinical history of ≥12 months 61.7% had history of allergic rhinitis. FEV_1 % pred., range 34–129, median = 86.8 FEV_1 range, 0.5–4.6 L; median = 1.8 L During 4-week run-in: asthma RFDs, range 0%–100%, median = 64%; days with beta-receptor agonist use, range 0%–100%, median = 35.6%	**Arm 1** M plus placebo inhaler (n=495; n=459 completers) **Arm 2** FI plus placebo tablet (n=499; n=466 completers)	5 mg tablet once at bedtime (10 mg if patient turned 15 during study) 2 puffs of 50 mcg morning and evening All patients received open-label salbuterol inhaler to be used as needed.	12 months after 4-week run-in period	Percentage of days with beta-receptor agonist use was 15.4% in the M group and 12.8% in the F group (p=0.003), a decrease of 22.7% in the M group and 25.4% in the F group. The percentage of patients with additional asthma rescue medication was 20.7% in the M group vs. 13.5% in the F group (RR = 1.56, 95% CI 1.17 to 2.06).	Percentage of predicted FEV_1 increased from 88.1% to 89% in the M group and from 88.9% to 91.7% in the F group; difference of 2.2% in favor of fluticasone (p=0.004).	*Percentage of RFDs was 84% in the M group and 86.7% in the F group, change from baseline was 22.4% vs. 25.2%, a difference of <1 day/month and above the noninferiority limit. The percentage with asthma attack was 32.2% in the M group vs. 25.6% in the F group (RR = 1.26, 95% CI 1.04 to 1.53). Mean asthma-related QoL score increased from 5.4 to 6.3 in the M group and from 5.3 to 6.4 in the F group (p=0.036).	No difference in AE (4.4% of the M group and 3.2% of the F group) occurred. No SAE occurred in either group.
Ostrom et al. Comparative efficacy and safety of low-dose fluticasone propionate and montelukast in children with persistent asthma. J Pediatr 2005;147(2): 213–220. (GlaxoSmithKline, Inc.)	Multisite randomized, double-blind, double-dummy, parallel-group study (43 clinical centers in the United States; investigator controlled in analysis)	To evaluate efficacy, safety, health outcomes, and cost-effectiveness of treatment with fluticasone propionate (FP) versus montelukast (M) in children with persistent asthma	342 (ITT analysis)	**Age** 5–12 yr, mean = 9.3 yr **Gender** 65% male, 35% female	Persistent asthma Duration ≥6 months FEV_1 % pred., range 60%–85%, mean = 75.9% FEV_1, mean = 1.65 L Morning PEF, mean = 230 L/min Evening PEF, mean = 242 L/min All used short-acting $beta_2$-agonist over the 3 months before screening. Daytime asthma symptom score, mean = 1.59 (0–5 range) Nighttime asthma symptom score, mean = 0.69 (0–3 range) % symptom-free days, mean = 18.8 Total albuterol use: mean = 2.39 puffs/day; daytime mean = 1.73 puffs/day; nighttime mean = 1.65 puffs/day % RFDs, mean = 25.4	**Arm 1** FP + placebo capsule (n=172; 150 completers) **Arm 2** Oral M + placebo inhaler (n=172; 134 completers)	50 mcg twice daily through multidose powder inhaler + placebo capsule once daily 5 mg once daily + placebo inhaler twice daily	12 weeks after 8- to 14-day run-in period Patients used inhaled albuterol as needed throughout the study.	FP vs. M treatment decreased mean total albuterol use (–1.43 vs. –1.23, p=0.018) and mean nighttime albuterol use (–0.39 vs. –0.21, p <0.001) but not mean daytime albuterol use (–1.01 vs. –0.92, p=0.10). FP vs. M treatment increased percentage of RFDs (45.1 vs. 35.0; p=0.002).	*FP vs. M treatment resulted in greater increase in mean percent FEV_1 (10.62 vs. 4.60; p=0.002), morning PEF (39.9 vs. 23.0; p=0.004), and evening PEF (35.5 vs. 20.4; p=0.020). Results were consistent when analyzed for each of 2 severity groups separately.	FP vs. M treatment resulted in greater decrease in nighttime asthma symptom scores (–0.40 vs. –0.19; p <.001) and with no difference for daytime asthma symptom score (–0.891 vs. –0.75, p=0.20) or percentage of symptom-free days (37.7 vs. 31.3; p=0.087). Mean daily total asthma-related cost/patient in FP treatment was one-third that of M treatment ($1.25 vs. $3.49). Mean total asthma-related daily cost per successfully treated patient (achieving ≥15% FEV_1 improvement) was $4.03 for FP and $17.45 for M.	Incidence of drug-related AE was similar in FP (7%) and M (6%) treatment. No SAE occurred in FP group; 1 in the M group required non-drug-related hospitalization. Drug-related withdrawals occurred in 2 patients in the FP group and 1 patient in the M group.

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Szefler et al. Characterization of within-subject responses to fluticasone and montelukast in childhood asthma. J Allergy Clin Immunol 2005;115(2): 233–242. (National Heart, Lung, and Blood Institute)	Randomized crossover study	To examine the variability of response to ICSs and LTRAs in children with asthma to identify patient features that would serve as indicators for selection of the medication most likely to achieve a favorable response in individual patients	144 (126)	**Age** 6–17 yr **Gender** Not reported **Ethnicity** Not reported	Mild-to-moderate asthma Improvement in FEV_1 of 12% or greater after maximal bronchodilation or methacholine PC_{20} of 12.5 mg/mL or less No corticosteroid treatment within 4 weeks, no leukotriene-modifying agents within 2 weeks, no history of respiratory tract infection within 4 weeks Asthma symptoms or rescue bronchodilator use, on average, 3 or more days/week during previous 4 weeks	**Arm 1** Fluticasone propionate + placebo tablet (FP) **Arm 2** Montelukast + placebo inhaler (M) Study n=144; 127 completers	100 mcg per inhalation; 1 inhalation twice daily 1 tablet at night; 5 mg for those 6–14 yr of age and 10 mg for those 15–18 yr of age	Two 8-week periods after a 5- to 10-day characterization period First 4 weeks of 2nd treatment period were considered sufficient for washout of medication used in first period.		Agreement in responses to 2 medications at end of 8-week periods; concordance correlation of 0.55 (95% CI 0.43 to 0.65; n=126) *Mean FEV_1 improvement was 6.8% for FP and 1.9% for M treatment groups (mean diff. 4.9%, p <0.001). Defining response as $FEV_1 \geq 7.5\%$, 17% responded to both FP and M; 23% responded to FP only; 5% responded to M only; and 55% responded to neither. Difference in response (FP – M) was associated with lower prebronchodilator FEV_1 % predicted and FEV_1/FVC ratio, lower methacholine PC_{20} value, higher bronchodilator use, higher FEV_1 response to bronchodilator, higher exhaled nitric oxide level, higher ECP level, and nonminority race. Multivariable regression model for difference in response (FP – M) included baseline prebronchodilator FEV_1/FVC ratio, baseline $\log_2$ ECP value, body mass index, and $\log_2$ PC_{20} value.	
Zeiger et al. Short-term and long-term asthma control in patients with mild persistent asthma receiving montelukast or fluticasone: a randomized controlled trial. Am J Med 2005;118(6): 649–657. (Merck & Co., Inc.)	Multicenter, randomized, 2-part, parallel-group trial (39 sites) Mild Asthma Montelukast versus Inhaled Corticosteroid (MIAMI) study	To determine whether montelukast is as effective as fluticasone (F) in controlling mild persistent asthma, as determined by RFDs	400 (176 in ITT analysis for double-blind period; 329 for open-label period)	**Age** 15–85 yr, mean = 35.2 yr **Gender** 31% male, 69% female **Ethnicity** 80.8% White, 7.9% Black, 2.6% Asian, 8.7% other	Mild persistent asthma Age at first treatment, mean = 20.6 yr Atopy, 80% FEV_1, mean = 3.3 L FEV_1 % pred., mean = 94 Albuterol use, mean = 3.5 days/week Daytime asthma symptoms, mean = 3.6 days/week Nighttime awakenings, 65.5% ≤2/month, 34.5% >2/month RFDs, mean = 58.1% of days in run-in period	**Arm 1** Inhaled F (n=191; 173 completed double-blind therapy; 177 entered open-label period; 151 completers) **Arm 2** Montelukast (M) (n=189; 177 completed double-blind therapy; 173 entered open-label period; 138 completers)	2 puffs of 44 mcg twice daily + placebo tablet 10 mg once nightly + placebo inhaler	12-week double-blind period and 36-week open-label period (10% of participants switched therapies to preserve masking in preceding period); 3-week placebo run-in period	*M was as effective treatment as F with respect to mean percentage of RFDs during the 12-week double-blind period. Mean percentage of asthma RFDs days was 74.9% for F group and 73.1% for M group (diff. 1.8%, 95% CI –3.2% to 6.8%; 0.5 days/month). During double-blind period, those in lowest quartile of FEV_1 (≤86%) had more RFDs with F than with M treatment. During open-label period, mean percentage of RFDs was greater for F group vs. M group (77.3% vs. 71.1%; diff 6.2%, 95% CI 0.8% to 11.7%). Those in the highest quartile of days of albuterol use at baseline (5–6 days/week) had more RFDs with F than with M during the open-label period, whereas those in the lower 3 quartiles (≤4 days/week) F and M groups were comparable over the 48-week study. No difference was found between F and M groups in increase in morning PEF during either period.	During the 12-week double-blind period, the F group had increase in FEV_1 (2.6%, 95% CI 1.2 to 3.9) vs. the M group (–0.3%, 95% CI –1.6 to 1.0), with mean difference of 2.9% (94% CI 1.3 to 4.4, p <0.001). No difference between F and M groups occurred in morning PEF or total eosinophil counts.	During the 12-week double-blind period, no difference was found between F and M groups in change in asthma symptoms score (p=0.08), asthma control score (p=0.09), or asthma-specific QoL score (p=0.20). During the open-label period, F vs. M treatment group showed improved asthma symptom score (diff. –2.09, 95% CI –3.2 to 0.8, p=0.002), with no difference in change in control score (diff. –0.1, 95% CI –0.2 to 0.1) or asthma-specific QoL score (diff 0.1, 95% CI –0.0 to 0.3, p=0.11).

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Zeiger et al. Response profiles to fluticasone and montelukast in mild-to-moderate persistent childhood asthma. J Allergy Clin Immunol 2006;117(1): 45–52. (National Heart, Lung, and Blood Institute)	Multicenter, double-blind, randomized, crossover trial (Stratified by clinical center, age, and FEV_1 percent predicted)	To determine intraindividual and interindi-vidual response profiles and predictors of response to an ICS and an LTRA	144 (127)	**Age** 6–17 yr with 33% 6–9 yr **Gender** 59% male, 41% female **Ethnicity** 48% minority	Mild-to-moderate persistent asthma Absence of leukotriene modifier agents within 2 weeks In previous 4 weeks: asthma symptoms or rescue bronchodilator use on average of 3 or more days/week, no corticosteroid therapy, no respiratory tract infection FEV_1 % pred. $\geq$70% $\geq$12% FEV_1 reversibility after maximum bronchodilation or methacholine dose required to reduce baseline FEV_1 by 20%	**Arm 1** Fluticasone propionate (FP) **Arm 2** Montelukast (M) (n=127 completed both arms of treatment)	100 mcg/ inhalation; 1 inhalation twice daily 1 tablet at night; 5 mg for those 6–12 yr of age and 10 mg for those 15–18 yr of age	5–10 day run-in period; 16-week trial, with two 8-week treatment periods First 4 weeks of second treatment period was washout period for the 1st treatment. Subjects received an active drug and a matching placebo for the alternative drug.		Greater improvement occurred after FP vs. M treatment in prebronchodilator FEV_1/FVC (82.2 vs. 79.0, p <0.0001), FEV variability (7.5 vs. 8.5, p=0.03), morning PEF (334.2 vs. 324.8, p=0.0002), R5 (0.60 vs. 0.63, p=0.003), and area of reactance (1.25 vs. 1.53, p=0.0003). Decrease occurred in exhaled nitric oxide after both FP and M treatment (20.6 and 30.9, p <0.001), with the decrease greater after FP (p=0.0028). Higher exhaled nitric oxide levels at baseline discriminated asthma control day response to treatments, with greater responses to FP than to M treatment (p=0.011).	Asthma control days were increased by both FP (2.8 days/week) and M (2.1 days/week) treatment, with a concordance correlation of 0.70 (95% CI 0.60 to 0.78) and difference between FP and M (p <0.001). 29.3% achieved $\geq$1 more day/week with FP vs. M treatment; 12.2% achieved $\geq$1 more day/week with M vs. FP treatment. Both FP and M treatment increased Asthma Control Questionnaire scores (0.59 and 0.76, p <0.001), favoring FP (p=0.009).