



**Guideline topic: Pharmacological management of asthma**  
**Evidence table 4.4c: Inhaled corticosteroid vs leukotriene receptor antagonists**

Author	Year	Study type	Quality rating	Population	Outcomes measured	Effect size	Confidence intervals / p values	Comments
<b>Adults</b>								
Malmstrom <sup>1</sup>	1999	Randomised, double-blind, double dummy. Parallel group 12 week treatment period	++	N=895 Adult > 15y 36 centres  Beclomethasone 200ug bd vs montelukast 10 mg od	A] change in FEV1 B] symptom score C] am PEF D] pm PEF E] nocturnal awakenings F] beta-agonist use	Mean difference for BDP vs montelukast 5.8% -0.2 15L/min 11L/min -0.7 -0.67 puffs/d	(95% CI 3-8%) (95% CI -0.3 to -0.1) (95% CI 8-23L/min) (95% CI 4-18L/min) (95% CI -1.1 to -0.3) (95% CI -1.1 to -0.3)	Although both BDP and montelukast significantly improved asthma control compared to placebo, BDP was more effective than montelukast.
<b>Young People</b>								
Bleecker <sup>2</sup>	2000	Randomised, double-blind, double-dummy. Parallel group	++	N=451 Age 12 – Adult 41 centres Fluticasone 88ug bd	1] change in FEV1 2] am PEF 3] pm PEF 4] Symptom-	FP vs zafirlukast 0.42 vs 0.20 49 vs 11 39 vs 11	p< 0.001 p< 0.001 p< 0.001 p< 0.001	FP was more effective than zafirlukast in

		12 week treatment period++		Vs zafirlukast 20 mg bd	free days 5] Salbutamol use	29 vs 16 -2.4 vs -1.5		asthma control
<b>Children</b>								
Knorr <sup>3</sup>	1998	Multicenter, doubleblind, placebo controlled RCT	++	336 asthmatic children 6-14 years  8 weeks of placebo versus montelukast 5md OD	1] FEV1 2] PEFr am and pm 3] beta2 agonist usage 4] day/night asthma symptoms 5] astj,a exacerbatopm (daus )%) 6] use of oral steroid (proportion) 7] global-parent/patient 8] global-physician 9] QOLY 10] Blood eosinophils (cells*10 <sup>9</sup> )	Compared with placebo  1] montelukast improved FEV1 4.65% 2] am PEFr improved 9.93 L/min pm PEFR no improvement 3] reduced mean of 22%, p=0.01 4] day score reduced by 0.05 night score reduced by 0.29 5] 25.6 (placebo) vs 20.58 (monte) 6] 15.8 (placebo) vs 12.1 (monte) 7] 1.72 (placebo) vs 1.46 (monte) 8] 1.96 (placebo) vs 1.68 (monte) combined global score only significant p=0.94 9] all domains	1] 95% ci; 1.92,7.4 2] am PEF p=0.03 pm p=NSD 3] p=0.01 4] day, p=0.27 night, p=0.48 5] p=0.049 6] p=0.41 7] p=0.06 8] p=0.06 9] p<0.05 10] p=0.02	Modest benefits

						10 reduced 0.06 compared to placebo		
Bisgaard <sup>4</sup>	1999	RCT, crossover, double blind	+	26 asthmatic children, 6-15 years, 11 on ICS, 15 ICS naïve  Given 2 weeks montelukast 5mg or placebo then crossover	1] Exhaled NO  2] FEV1 and MMEF	*only those not on ICS (n=15)  1] 18% fall ENO 9placebo)  33.1% fall ENO (monte)  2] NS tendency for better values with montelukast		Small subgroup analysis for children on ICS
Simons <sup>5</sup>	2001	RCT, multicentered, placebo cotrolled, crossover study	++	279 Asthmatic children 6-14 years with symptoms despite BUD 400mcg/day.  Children given montelukast 5mg OD or placebo for 4 weeks and then 'crossed over' treatments	1] FEV1 compared with baseline  2] Home PEFR monitoring  3] asthmat attack rates  4] beta2 agonist usage  5] QOLY  6] parent's gloal assessment  7] NS different from placebo  8] 8% reduction greater than	1] 95%ci- (0.1,2.7]  2] Home PEFR monitoring  3] montelukast 12.2% VERSUS 15.9% for placebo, p< 0.001  4] montelukast reduced beta2 use by means 0.33puffs;/day, p=0.013  5] NS different from placebo	1] 95% ci-(0.1,2.7)  2] 95%ci; (1.4,18.1) for am and 2.4,1.9] for pm  P< 0.001	No washout period in crossover study but outcome measured in 2 <sup>nd</sup> half of each study period.  Benefits of additional montelukast while statistically significant are at best modest

					placebo	6] NS different from placebo	
						7] NS different from placebo	
						8] 8% reduction greater than placebo	Severe asthma FEV1 77%

1. Malmstrom K, Rodriguez-Gomez G, Guerra J, Villaran C, Pineiro A, Wei LX, et al. Oral montelukast, inhaled beclomethasone, and placebo for chronic asthma. A randomized, controlled trial. Montelukast/Beclomethasone Study Group. *Ann Intern Med* 1999;130(6):487-95.
2. Bleecker ER, Welch MJ, Weinstein SF, Kalberg C, Johnson M, Edwards L, 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):1123-9.
3. Knorr B, Matz J, Bernstein JA, Nguyen H, Seidenberg BC, Reiss TF, et al. Montelukast for chronic asthma in 6- to 14-year-old children: a randomized, double-blind trial. Pediatric Montelukast Study Group. *JAMA* 1998;279(15):1181-6.
4. Bisgaard H, Loland L, Oj JA. NO in exhaled air of asthmatic children is reduced by the leukotriene receptor antagonist montelukast. *Am J Respir Crit Care Med* 1999;160(4):1227-31.
5. Simons FE, Villa JR, Lee BW, Teper AM, Lyttle B, Aristizabal G, et al. Montelukast added to budesonide in children with persistent asthma: a randomized, double-blind, crossover study. *J Pediatr* 2001;138(5):694-8.