



**Guideline topic: Pharmacological management of asthma**  
**Evidence table 4.4d: Leukotriene receptor antagonists with short-acting beta-agonists**

Author	Year	Study type	Quality rating	Population	Outomes measured	Effect size	Confidence intervals / p values	Comments
<b>Adults</b>								
Altman <sup>1</sup>	1998	Randomised placebo controlled, double-blind comparing placebo with 10, 100, 200 mg once daily in evening, or 10 or 50 mg bd (6gps)	++	Similar to Noonan	Similar to Noonan	Results similar as above in terms of changes in FEV1, PEFR, global assessment and beta-agonist usage, with no dose response observed.  Activity domain is significantly improved, but not on environment for QoL (for pooled data) Note 10 mg/day no sign increase	CI provided in Tables	Similar to Noonan

						in am PEFR.		
Fish <sup>2</sup>	1997	13 week randomised, double-blind, placebo-controlled, parallel group comparing zafirlukast 20mg bd vs placebo	+	N=762 (12-76 years) 514 ZAF; 248: PLAC As needed beta-agonist Asthma score >8 over 7 consec days	Symptom score beta-agonist use AM/PM usage FEV1 daily PEFR adverse events	Total symptom score reduction: 27 vs 13  (Z vs P) p<0.05  beta-agonist use; 3.1 vs 3.9 puffs/day p<0.01  FEV1; 3.0 vs 2.95 p<0.05  AM PEFR; 418 vs 405 p<0.05	Mean + - SEM shown; No. 95% CI shown	Study has power to detect diff of 10% in FEV1.  Changes achieved are small  Placebo effect
Kemp <sup>3</sup>	1999	13 wk randomised placebo controlled parallel multicenter; 4 separate randomised trials	+	N=261 As needed beta-agonist Steroid naïve FEV1 <60%	Trials analysed separately and together also!!  FEV1; am PEFR; Asthma symptoms	64% increase in >10% FEV1 vs 50% for placebo  FEV1 diff (95%CI) 0.01, 0.27 p=0.039  AM PEF 0.1, 7.0 p<0.001  Daytime symptom score -2.7, -0.7p=0.001  beta-agonist use-1.8, -0.6p<0.001	Mean SEM and 95% CI shown	Small changes Placebo effect
Nathan <sup>4</sup>	1998	13 wk double-blind multicenter	++	N=454 (Z231; P223)	Daytime symptoms; -23%	Mean +- shown; No 95% CI	Study has power to detect 0.2	

		placebo controlled parallel group. ZAF 20 mg bd vs placebo		374 completed; >12 years; FEV1 45-80% pred; reversibility of 15% with beta-agonist; symptomatic.  No oral/inhaled steroids Asthma symptoms B2-agonist use Nasal congestion score  PEFR am/pm  FEV1  AQLQ	vs-16%  Night time: -18.7% vs 8.7%  beta-agonist: -23.7% vs -0.6%  AM PEFR:24.1 vs 13.1 p<0.01 FEV1 change; 0.05 NS  QoL: overall p=0.004 (0.26 unit change)  Blood eos: sign greater fall with ZAF	shown.	unit diff in asthma symptom, score  Small changes observed; no sign changes in FEV1  Placebo effect	
Noonan <sup>5</sup>	1998	Randomised parallel group, double blind, comparing 2, 10 or 50 mg/daily pm dose	++	Chronic asthma (28-65 yrs); 40-80% pred FEV1; <15% increase in FEV1 with beta agonist; weekly daytime symptom score of >32; >1 puff of Ventolin/day; in 20% inhaled steroid permitted.	1] Morning and evening FEV1  2] Asthma symptoms and beta agonist use  3] PEFR	Changes in AM FEV1 not different across doses but sign diff from placebo (MEAN% CHANGE: 6.2, 14.7, 13.5, 13.1) But no sign change in afternoon FEV1.  Improved, no dose response,	CI provided in Tables  P<0.05 of placebo.  p<0.05	Nearly all patients completed. Main emphasis on dose response; prob on basis of this study the 10 mg dose was used. Interest in evening FEV1 not improved: the 24 hour effect worn off then?

					4] Global evaluation 5] Asthma specific QoL	except 2mg showed no effect Both am and pm PEFR sign increased equally amongst the doses. Physician ge sign with 10 & 50 mg doses of placebo Improved in symptom, environment and emotion, not activity.	p<0.05  p<0.05	A power of 80% for 11% change in FEV1 required 50 in each group (70 actual in each group).  Good evidence that there is a bronchodilator effect of montelukast, with improved asthma control in patients with asthma not on IS (only 20% were on IS)
Reiss <sup>6</sup>	1998	Randomised, double blind, placebo, parallel group. Comparing placebo to Montelukast 10 mg/pm dose)	++	>15 years; 15% increase in FEV1 after beta agonist; moderate symptom score; at least 1 puff ventolin per day. 23% on inhaled steroids	FEV1 and saytime symptom scores were 1 ary end-points	13.1% increase vs placebo of 4.2% FEV1 Improvements in a, {EFR; reduction in beta-agonist use; daytime symptom score; improved QoL across all measures.	Mean diff of 8.9% (CI 6.8 to 11%)  p<0.001	Note 14.3% discontinuation in MON and 8.6% in placebo. Results applicable to Step 2 or 3.
Spector <sup>7</sup>	1994	6 wk randomised double-blind, placebo controlled, parallel group comparing	+	N=276 (10 mg:68; 20 mg:68; 40 mg:70; placebo: 70). FEV1 40- 75%; FEV1 increased by	Asthma symptom score PEF am/pm Inhaler use FEV1	Symptoms: -28% - 8%, 09%, 010%  Inhaler use: -31%, -18%, -20%, -15%	Mean +-  SEM shown	Well -balanced group  Changes biggest with 40 mg dose

	10, 20 or 40 mg ZAF per day with placebo	15% with beta-agonist; 18-65 years; asthma score of >10	AM PEF: 6%, 6%, 7%, 2% FEV1: 11%, 6%, 7%, 1%	Dose response with serum levels of ZAF  Effectsd fairly modest, again a placebo response
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