P228 EFFICACY AND SAFETY OF FLUTICASONE PROPIONATE/FORMOTEROL IN PAEDIATRIC PATIENTS WITH ASTHMA

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10.1136/thoraxjnl-2014-206260.356

Background Fluticasone propionate (FP) and formoterol (FORM) have been combined in a single inhaler (FP/FORM; *flutiform*[®]) for the treatment of adolescents and adults with asthma. This study assessed the efficacy and safety of FP/FORM in paediatric asthma patients.

Methods A total of 512 patients aged 5 to <12yrs were randomised 1:1:1 to 12 weeks of treatment with either FP/FORM (100/10 µg BID), FP (100 µg BID) or fluticasone propionate/salmeterol (FP/SAL) (100/50 µg BID) in a double-blind, parallel group, multicentre study. The objectives were to demonstrate superiority of FP/FORM to FP and non-inferiority to FP/SAL. The primary endpoint was the change from predose FEV₁ at baseline to 2-hour postdose FEV₁ over the 12 weeks. The two key secondary endpoints were FEV₁ AUC_{0-4h} at Week 12 and change from pre-dose FEV₁ over the 12 weeks.

Results FP/FORM was superior to FP for change from predose FEV₁ at baseline to 2-hour postdose FEV₁ (treatment difference = 0.07 L; 95% CI: 0.03, 0.11; p < 0.001) and FEV₁ AUC_{0-4h} at Week 12 (treatment difference = 0.09 L; 95% CI: 0.04, 0.13; p < 0.001). FP/FORM was non-inferior to FP/SAL for change from predose FEV₁ at baseline to 2-hour postdose FEV₁ (treatment difference = -0.00 L; 95% CI: -0.04, 0.04; p < 0.001), AUC_{0-4h} at Week 12 (treatment difference = 0.01 L; 95% CI: -0.03, 0.06; p < 0.001) and change from predose FEV₁ (treatment difference = -0.02 L; 95% CI: -0.06, 0.02; p < 0.001). The safety and tolerability profiles of all treatments were similar.

Conclusion In children 5 to <12yrs with asthma, FP/FORM was superior to FP, and non-inferior to FP/SAL for improvements in lung function, with a similar tolerability profile to both FP and FP/SAL.

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P229 ONCE-DAILY TIOTROPIUM RESPIMAT® AS ADD-ON TO AT LEAST MEDIUM- TO HIGH-DOSE ICS, WITH OR WITHOUT LABA, IMPROVES LUNG FUNCTION IN PATIENTS WITH SYMPTOMATIC ASTHMA, INDEPENDENT OF ALLERGIC STATUS

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10.1136/thoraxjnl-2014-206260.357

Background A substantial number of patients have symptomatic asthma despite treatment according to guidelines. Several studies have confirmed that tiotropium Respimat[®], a once-daily long-acting anticholinergic bronchodilator, improves lung function in symptomatic patients receiving at least medium-dose inhaled corticosteroids (ICS) + long-acting β₂-agonist (LABA) (Kerstjens *et al.* NEJM 2012;367:1198–207; Bateman *et al.* JACI 2011;128:315–22). Here we examine whether the atopic and/or allergic status of patients in these trials influenced their response to tiotropium Respimat[®].

Method Two 48-week trials of tiotropium Respimat[®] 5 µg (PrimoTinA-asthma[®]: NCT00776984, NCT00772538) in patients (n = 912) on high-dose ICS + LABA; two 24-week trials of tiotropium Respimat[®] 5 µg and 2.5 µg (MezzoTinA-asthma[®]: NCT01172808, NCT01172821) in patients (n = 2100) on moderate-dose ICS. Pre-planned analyses (pooled populations) were performed in two subgroups defined at baseline as total serum immunoglobulin E (IgE) ≤ or >430 µg/L or blood eosinophils ≤ or >0.6×10⁹/L or clinical judgement of allergic status ('No' or 'Yes'). All tiotropium doses were delivered via the Respimat[®] SoftMist[™] inhaler.

Results Tiotropium Respimat[®] 5 µg or 2.5 µg improved peak and trough forced expiratory volume in 1 second versus placebo (Table) independent of IgE, eosinophil count and clinical judgement.

Abstract P229 Table 1

Adjusted mean difference for tiotropium Respimat [®] from placebo (mL)		Interaction p value ^a		Interaction p value ^a		Clinical judgement 'No' or 'Yes'		Interaction p value ^a	
		IgE ≤/ >430 µg/L			Eosinophils ≤/ >0.6×10 ⁹ /L				
PrimoTinA-asthma [®]	n ^b	336/377			654/175			335/516	
	Peak FEV ₁ (0–3h)		0.742			0.7021			0.2114
	Trough	148/102			115/58			76/130	
	FEV ₁	127/89	0.6209		103/52	0.7542		94/91	0.4099
MezzoTinA-asthma [®]	n ^b	356/610			769/201			349/624	
	Peak FEV ₁ (0–3h)		0.9677			0.2375			0.6233
	Trough	168/193			170/240			180/189	
	FEV ₁	139/152	0.8437		137/182	0.5148		138/153	0.6727
Tiotropium Respimat [®] 2.5 µg	n ^b	364/614			779/203			349/635	
	Peak FEV ₁ (0–3h)		0.9677			0.2375			0.6233
	Trough	197/237			236/176			243/213	
	FEV ₁	167/188	0.8437		185/158	0.5148		209/164	0.6727

^aFor treatment×subgroup interaction; ^bValues for active and placebo groups combined
FEV₁, forced expiratory volume in 1 second