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Characterisation of exacerbations of severe eosinophilic asthma (SEA) on mepolizumab compared to placebo

Asthma - mechanism, Inflammation, Asthma - management

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Mepolizumab reduces exacerbations of SEA. The nature of exacerbations on mepolizumab is unclear. We have tested the hypothesis that these exacerbations differ in inflammatory profile, symptoms, FEV1 and response to oral corticosteroids (OCS).

Methods

A RCT of mepolizumab in SEA was conducted (Haldar, NEJM 2009;360). Subjects were reviewed at exacerbation, prior to starting treatment or as soon as possible after. Spirometry, Asthma Control Questionnaire (ACQ5), visual analogue scale (VAS) (cough, breathlessness, wheeze) and induced sputum counts were measured.

Results

177 exacerbations were assessed-101 prior to treatment (pre-treatment) and 76 after starting OCS (treated) with no difference in the duration of OCS in the treated groups.

Pre-treatment increase from baseline VAS was 39 vs 20mm (p<0.01), change in ACQ5, 1.0 vs 0.59 (p=0.09)

and geometric mean sputum eosinophils 5.9 vs 2.3%, (p=0.03) in placebo vs mepolizumab arms respectively.

There was a reduction in ACQ5 and VAS after starting OCS in the placebo but not in the mepolizumab arm(Table). Change in FEV1 did not differ between groups, before or after treatment.

	Placebo			Mepolizumab		
	Pre-treatment	Treated	Mean dif.	Pre-treatment	Treated	Mean dif.
Δ FEV1 (L)	-0.11 (-0.25-0.01)	-0.14 (-0.27-0.02)	0.03 (-0.16-0.22)	-0.16 (-0.32-0.0)	-0.27 (-0.52-0.02)	0.13 (-0.12-0.38)
Δ Mean VAS (mm)	39 (33-45)	8 (-6-21)	31 (19-44)	20 (11-29)	30 (18-42)	-10 (-27-6)
Δ ACQ5	1.0 (0.8-1.3)	0.3 (-0.2-0.8)	0.7 (0.2-1.2)	0.6 (0.1-1.0)	1.0 (0.2-1.7)	-0.4 (-1.2-0.4)
Data shown as mean (95% CI). Δ Change from stable baseline						

Conclusion

Exacerbations on mepolizumab have less severe symptoms and tend to be less eosinophilic.

Our data suggests an impaired symptomatic response to OCS for patients treated with mepolizumab compared to placebo. Further work is required to determine if different treatment approach is needed.