Mepolizumab and the response to oral prednisolone in patients with severe eosinophilic asthma

1 University of Oxford - Oxford (United Kingdom), 2 University of Leicester - Leicester (United Kingdom), 3 Queen's University Belfast - Belfast (United Kingdom)

R. Shrimanker ¹, B. Hargaden ², P. Bradding ², A. Wardlaw ², C. Brightling ², R. Green ², M.Bafadhel ¹, L. Heaney ³, I. Pavord ¹, P. Haldar ²



Introduction

Mepolizumab, an anti-IL-5 antibody treatment, reduces circulating and airway eosinophils and reduces the rate of exacerbations requiring oral corticosteroid treatment in severe eosinophilic asthma¹.

The response to oral corticosteroids in asthma is related to the presence of eosinophilic airways inflammation².

We have tested the hypothesis that mepolizumab treatment is associated with a reduced response to oral corticosteroids in patients with severe eosinophilic asthma.

Methods

We carried out a retrospective analysis of a placebo controlled double blind trial of mepolizumab 750 mg IV given every four weeks for 52 weeks³.

The study involved 61 patients with severe asthma, an induced sputum eosinophil count of >3% at screening or at some point over the previous 12 months and two or more exacerbations of asthma treated with systemic corticosteroids in the last year. 29 patients were treated with mepolizumab.

Participants received 2 weeks of oral prednisolone treatment, 0.5mg/kg, at stable state before starting mepolizumab treatment and on mepolizumab after 12 months treatment. FEV1, asthma control questionnaire (ACQ5) and visual analogue scale (VAS) for breathlessness, wheeze and cough was measured





Results

28 participants on mepolizumab treatment who received 2 weeks of prednisolone before mepolizumab and on mepolizumab were evaluated.

Prednisolone was associated with a significantly greater improvement in mean VAS prior to mepolizumab compared to on mepolizumab (14.6mm vs 2.8mm, p=0.03).

There was a small improvement in ACQ5 with prednisolone before mepolizumab treatment (0.3, p=0.05) but not on mepolizumab treatment (0.17, p=0.3). There was no significant change in FEV1 with prednisolone treatment either before or on mepolizumab treatment (table and figure).

Table. Changes in VAS, ACQ5 and FEV1 in response to prednisolone prior to and on mepolizumab treatment

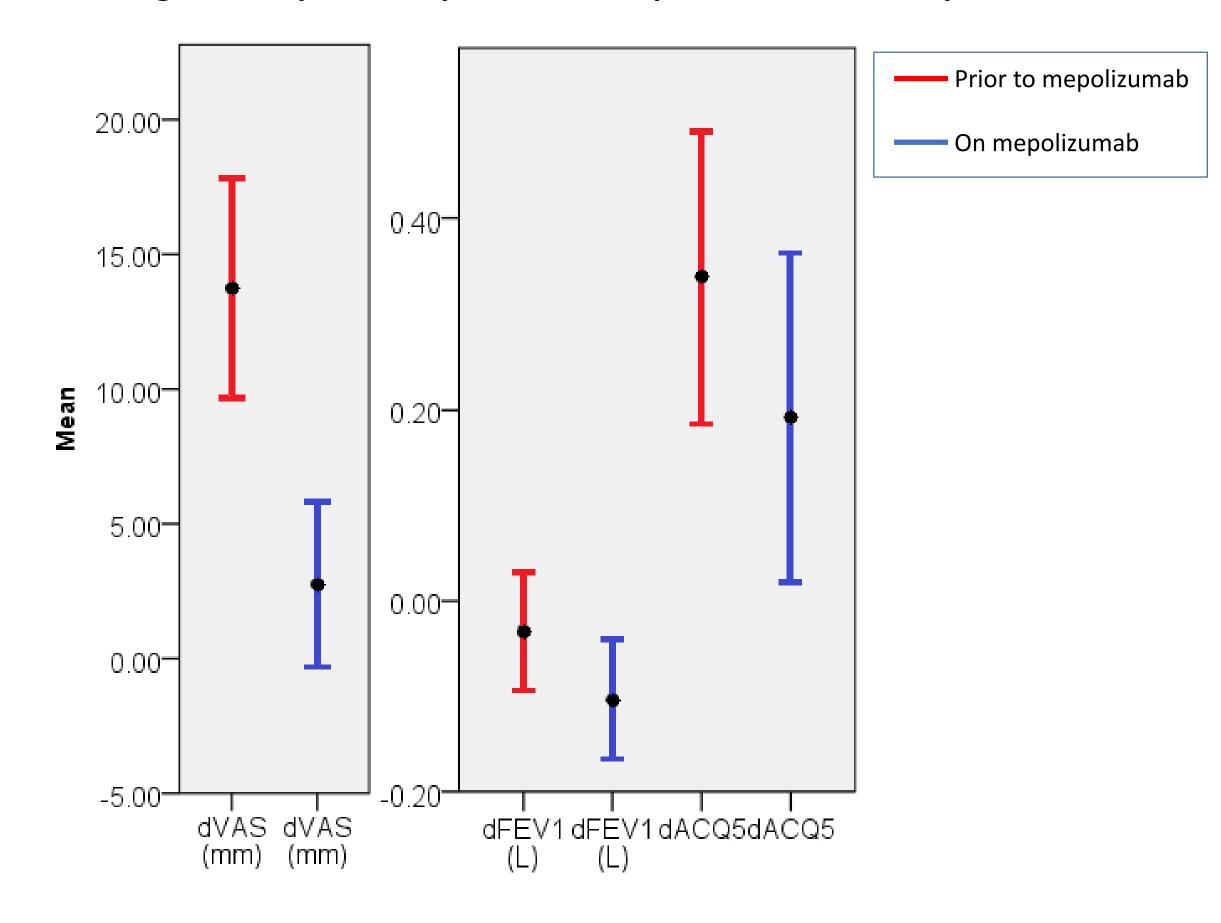
Response to prednisolone	Prior to mepolizumab	On mepolizumab	Between group difference	p
Mean Δ VAS (mm)	14.6	2.8	11	0.03
	(6.4-22.9)	(-3.5-9.1)	(0.9-21)	
Mean ∆ ACQ5	0.3	0.17	0.13	0.34
	(0-0.6)	(-0.25)	(-0.1-0.4)	
Mean △ FEV1 (L)	0.07	0.1	-0.07	0.5
	(-0.2-0.1)	(-0.2-0.0)	(-0.1-0.3)	

 Δ Difference between pre and post steroid visits. Data shown as mean (95%CI)

References

- 1. Pavord, I.D., et al., *Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial.* Lancet, 2012. **380**(9842): p. 651-9
- 2. Haldar, P., et al., *Mepolizumab and exacerbations of refractory eosinophilic asthma*. N Engl J Med, 2009. **360**(10): p. 973-84.
- 3. Little, S.A., et al., Non-invasive markers of airway inflammation as predictors of oral steroid responsiveness in asthma. Thorax, 2000. **55**(3): p. 232-4.

Figure. Response to prednisolone prior to and on mepolizumab



Error bars show SEM. d- change between pre and post steroid treatment visits. VAS – visual analogue scale. ACQ5 – asthma control questionnaire 5. FEV1 – forced expiratory volume in 1 second

Conclusions

- Treatment with mepolizumab is associated with an attenuated symptom response to prednisolone treatment in severe eosinophilic asthma.
- This mechanism is likely to be independent of changes in airflow limitation.

Funding

Poster available at this link



