Exacerbation Reduction in Patients Based Upon Baseline Eosinophil Counts and FEV_1 Reversibility

Poster No. 080

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Aims

Mepolizumab has been shown to reduce the rate of clinically significant exacerbations, as well as improve asthma control compared with placebo in patients with severe eosinophilic asthma.[1–4]

Previous studies show that baseline blood eosinophil count is predictive of response to mepolizumab.[1,2,5,6]

Separately, supervised cluster analysis of the DREAM study[1] suggested that airway reversibility may be associated with improved response to mepolizumab.[7]

The aim of this post hoc analysis of the DREAM study was to evaluate the efficacy of mepolizumab in patients with severe eosinophilic asthma over a 52-week period according to baseline blood eosinophil count and forced expiratory volume in 1 second (FEV_1) reversibility.

Methods

DREAM › **Post hoc analysis**

Study design

Randomized · Double-blind · Dose-ranging · Multicenter

Phase IIb/III (NCT01000506)

Patients

604 patients in the ITT population*

≥12 years of age

Severe eosinophilic asthma:

≥2 exacerbations in previous year

Reversible: an increase in FEV_1 of ≥12% and ≥200 mL following administration of bronchodilator†

Non-reversible: a post-bronchodilator increase in FEV_1 of <200 mL or a ≥200 mL increase that is <12% from pre-bronchodilator FEV_1

Treatments

Placebo · Mepolizumab 75 mg IV · Mepolizumab 250 mg IV · Mepolizumab 750 mg IV

Plus: SoC

Every 4 weeks for: 52 weeks

Endpoint

Mepolizumab IV vs Placebo

Annualized rate of clinically significant exacerbations†

Analysis‡

Stratified by reversibility and baseline blood eosinophil count:

- reversible + <150 cells/µL
- reversible + ≥150 cells/µL
- reversible + <300 cells/µL
- reversible + ≥300 cells/µL
- Non-reversible + <150 cells/µL
- Non-reversible + ≥150 cells/µL
- non-reversible + <300 cells/µL
- non-reversible + ≥300 cells/µL

All mepolizumab doses were combined for this analysis. *Patients in the ITT population with baseline blood eosinophil count and reversibility data were analyzed; †albuterol/salbutamol; ‡exacerbations were defined as worsening of asthma requiring use of OCS or systemic corticosteroids for ≥3 days and/or hospitalization and/or an ER visit. For patients receiving maintenance OCS, an exacerbation requiring OCS was defined as the use of oral/systemic corticosteroids at least double the existing maintenance dose for ≥3 days.
ER, emergency room; FEV_1, forced expiratory volume in 1 second; ITT, intent-to-treat; IV, intravenous; OCS, oral corticosteroids; SoC, standard of care

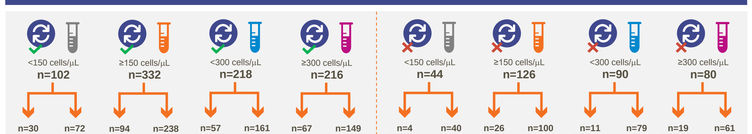
Results

Patient population at baseline

	Reversible				Non-reversible			
	<150 cells/µL	≥150 cells/µL	<300 cells/µL	≥300 cells/µL	<150 cells/µL	≥150 cells/µL	<300 cells/µL	≥300 cells/µL
Age, years	50 (11)	48 (11)	49 (11)	47 (12)	52 (9)	49 (12)	50 (11)	50 (11)
Female, n (%)	61 (60)	219 (66)	138 (63)	142 (66)	28 (64)	70 (56)	53 (59)	45 (56)
Ethnicity, n (%)								
Hispanic or Latino	13 (13)	30 (9)	23 (11)	20 (9)	5 (11)	12 (10)	11 (12)	6 (8)
Not Hispanic or Latino	89 (87)	302 (91)	195 (89)	196 (91)	39 (89)	114 (90)	79 (88)	74 (93)
Asthma duration, years	18 (15)	18 (14)	18 (14)	18 (14)	20 (15)	22 (15)	21 (15)	21 (15)
Exacerbations in previous year	3.4 (2.9)	3.8 (3.6)	3.5 (3.5)	3.8 (3.3)	3.7 (1.9)	3.3 (2.1)	3.5 (2.2)	3.4 (1.9)
Smoking status, n (%)								
Never smoked	76 (75)	269 (81)	165 (76)	180 (83)	30 (68)	96 (76)	62 (69)	64 (80)
Former smoker	26 (25)	63 (19)	53 (24)	36 (17)	14 (32)	30 (24)	28 (31)	16 (20)
On maintenance OCS therapy, n (%)	28 (27)	102 (31)	65 (30)	65 (30)	20 (45)	36 (29)	31 (34)	25 (31)
Pre-bronchodilator FEV_1, L	1.95 (0.71)	1.89 (0.62)	1.93 (0.68)	1.88 (0.60)	1.74 (0.65)	1.84 (0.73)	1.84 (0.74)	1.80 (0.67)
Pre-bronchodilator FEV_1, % predicted	61.0 (15.2)	60.1 (15.2)	60.9 (15.0)	59.7 (15.4)	58.4 (15.5)	57.8 (18.6)	58.9 (17.7)	56.9 (18.0)
FEV_1 reversibility, %	29.7 (20.24)	30.3 (23.18)	30.9 (20.85)	29.4 (24.08)	11.6 (9.77)	14.0 (12.85)	12.5 (13.31)	14.4 (10.69)
ACQ-6 score	2.5 (1.0)	2.4 (1.1)	2.4 (1.0)	2.5 (1.2)	2.1 (1.0)	2.0 (1.1)	2.1 (1.1)	2.1 (1.1)
Blood eosinophil count, cells/µL, geometric mean (SD logs)	70 (0.75)	390 (0.60)	120 (0.78)	560 (0.44)	60 (0.99)	390 (0.64)	110 (0.95)	560 (0.52)
FeNO, ppb, geometric mean (SD logs)	25.1 (0.86)	35.7 (0.75)	27.4 (0.80)	39.5 (0.73)	24.5 (0.78)	30.1 (0.80)	25.4 (0.78)	32.6 (0.80)

Values are presented as mean (SD) unless otherwise stated. ACQ, Asthma Control Questionnaire; FeNO, fractional exhaled nitric oxide; ppb, parts per billion; SD, standard deviation

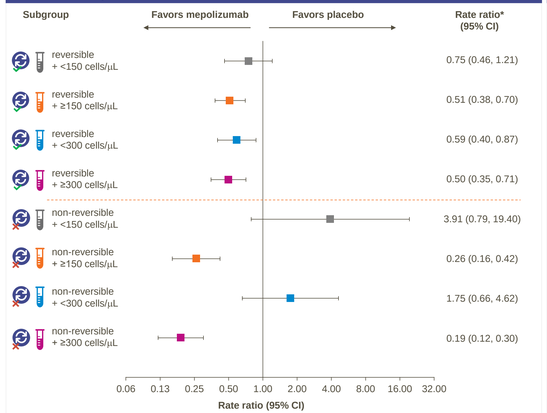
Patient subgroups



Conclusions

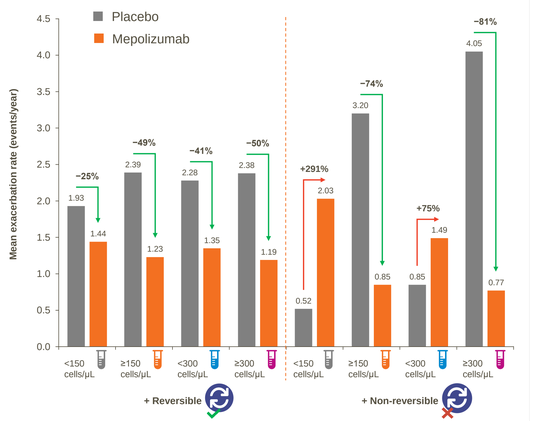
- Previous analyses have shown an association between exacerbation reduction with mepolizumab and higher baseline eosinophil counts.
- This exploratory analysis reaffirms that baseline blood eosinophil counts remain the most useful predictor of improved response to mepolizumab treatment in terms of exacerbations.
- Based on this analysis the role of airway reversibility in predicting response to mepolizumab treatment is still unclear and may not have additional impact, although the low numbers of patients receiving placebo in this analysis (particularly among non-reversible patients) is a limitation.
  - In cases where patients performed worse with mepolizumab compared with placebo, this was driven mainly by a relatively small number of patients with baseline blood eosinophils <150 cells/µL (ie, outside the specific population for which mepolizumab is approved).
- Furthermore, it is possible that some patients classified as non-reversible may also have had airflow variability or hyper-responsiveness.

Reductions in the rate of clinically significant exacerbations over 52 weeks favored mepolizumab versus placebo in those with higher baseline blood eosinophil count, and this effect was more pronounced in those who were not reversible



*Ratio of exacerbation rates among patients receiving mepolizumab to exacerbation rates among patients receiving placebo.
CI, confidence interval

There were fewer clinically significant exacerbations over 52 weeks with mepolizumab versus placebo in those with higher baseline blood eosinophil count, and this effect was increased in those without reversibility



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