Mepolizumab Reduces Exacerbations and Improves Health-Related Quality of Life in Patients With Severe Asthma and Nasal Polyps, Sinusitis, or Allergic Rhinitis

Poster No. 079

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Aims

- Allergic rhinitis (AR), sinusitis, and nasal polyps (NP) are common upper airway comorbidities in patients with severe asthma[1,2] associated with poor asthma control and health-related quality of life (HRQoL), and increased exacerbation risk.[3–5]
- Mepolizumab reduces the annual rate of asthma exacerbations and improves symptom control, HRQoL, and lung function, in addition to reducing corticosteroid dependence in patients with severe eosinophilic asthma.[6–9]
- A previous post hoc meta-analysis of patients with severe eosinophilic asthma suggested that mepolizumab is effective in patients with comorbid upper airway disease[10]; however, further investigation in patients with specific upper airway comorbidities is required.
- In this analysis, we examined the impact of mepolizumab on clinically significant exacerbations, symptom control, HRQoL, and lung function in patients with severe eosinophilic asthma and specific upper respiratory comorbidities.

Methods

DREAM,[6] SIRIUS,[7] MENSA,[8] & MUSCA[9]
Study design

- Randomized
- Double-blind
- Placebo-controlled
- Multicenter
- Phase III studies*

DREAM (NCT01000506)
SIRIUS (NCT01691508)
MENSA (NCT01691521)
MUSCA (NCT02281318)

≥12 years of age

Severe eosinophilic asthma:

High-dose ICS plus additional controller therapies

≥2 exacerbations in the prior year (not required in SIRIUS)

Eosinophilic inflammation

Mepolizumab SC or IV† (n=1189)

Placebo SC or IV (n=689)

Q4W in addition to:

SoC

Treatment period: **52** weeks (DREAM); **24** weeks (SIRIUS & MUSCA); **32** weeks (MENSA)

Post hoc meta-analysis

Endpoints

- Annual rate of clinically significant **exacerbations**‡
- Change from baseline in **SGRQ total score** at study end
- Change from baseline in **ACQ-5 score** at Week 24
- Change from baseline in **pre-bronchodilator FEV$_1$** at Week 24

Subgroups

- NP
- Sinusitis
- AR

*DREAM is a Phase IIb/III study; †all mepolizumab doses from studies were included for analysis (75 mg, 250 mg, and 750 mg IV; 100 mg SC); ‡defined as worsening of asthma requiring use of OCS or systemic corticosteroids for ≥3 days and/or an ED visit and/or hospitalization. ACQ-5, Asthma Control Questionnaire 5; ED, emergency department; FEV$_1$, forced expiratory volume in 1 second; ICS, inhaled corticosteroids; IV, intravenous; OCS, oral corticosteroids; Q4W, once every 4 weeks; SC, subcutaneous; SGRQ, St George's Respiratory Questionnaire; SoC, standard of care

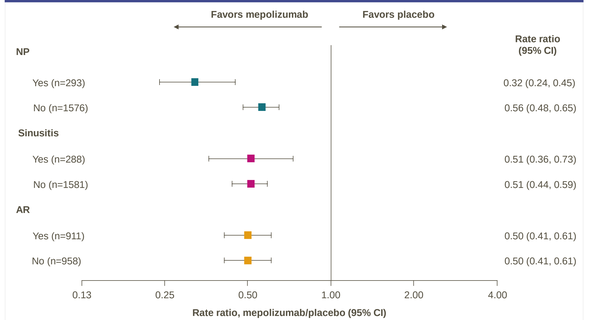
Results

Baseline demographics and clinical characteristics

	NP		Sinusitis		AR	
	Yes (N=293)	No (N=1576)	Yes (N=288)	No (N=1581)	Yes (N=911)	No (N=958)
Age, years	50.5 (12.1)	49.8 (13.2)	51.2 (12.5)	49.6 (13.1)	48.3 (13.1)	51.3 (12.7)
Female, %	50	61	57	60	59	59
BMI, kg/m^2	27.5 (5.4)	28.3 (6.2)	27.5 (6.4)	28.3 (6.0)	28.4 (6.3)	28.0 (5.8)
Blood eosinophil count, cells/μL*	410 (0.98)	270 (0.95)	370 (1.04)	280 (0.95)	330 (0.94)	260 (0.98)
Exacerbations in previous year, n (%)						
≤2	150 (51)	803 (51)	113 (39)	840 (53)	458 (50)	495 (52)
3	57 (19)	349 (22)	75 (26)	332 (21)	198 (22)	211 (22)
≥4	86 (29)	424 (27)	100 (35)	409 (26)	255 (28)	252 (26)
On maintenance OCS, n (%)	116 (40)	477 (30)	130 (45)	465 (29)	269 (30)	325 (34)
% predicted pre-bronchodilator FEV$_1$	59.3 (16.4)	59.8 (16.8)	61.2 (17.4)	59.4 (16.6)	62.0 (17.0)	57.6 (16.2)
SGRQ total score†	46.9 (19.4)	46.6 (18.9)	46.7 (19.0)	46.8 (19.0)	46.8 (19.4)	46.6 (18.7)
ACQ-5 score	2.25 (1.18)	2.26 (1.16)	2.25 (1.26)	2.27 (1.14)	2.24 (1.20)	2.29 (1.13)

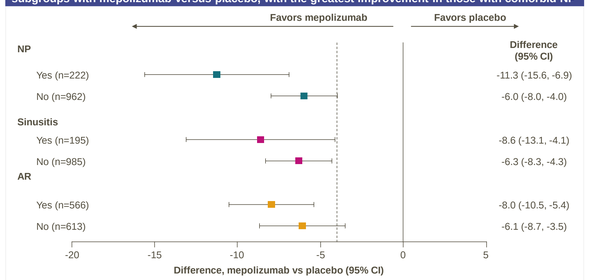
Values are presented as mean (SD) unless otherwise stated. *Data are presented as geometric mean (SD on log-transformed scale) for blood eosinophil count; †SGRQ data were not collected in the DREAM study. BMI, body mass index; SD, standard deviation

Mepolizumab versus placebo reduced the annual rate of clinically significant exacerbations by approximately 50% in all patients, with the largest reductions observed in patients with comorbid NP



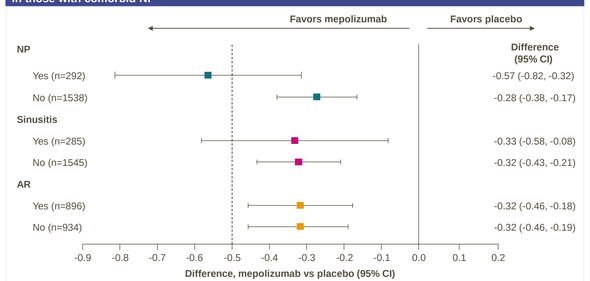
CI, confidence interval

Improvements from baseline to study end in SGRQ total score were above the MCID in all patient subgroups with mepolizumab versus placebo, with the greatest improvement in those with comorbid NP



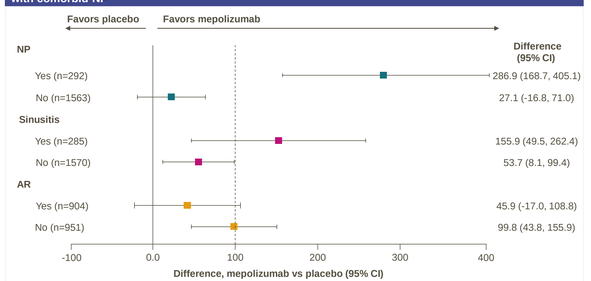
The MCID for SGRQ is 4.0 (as indicated by dashed line). MCID, minimum clinically important difference

Improvements from baseline to Week 24 in ACQ-5 score were largest with mepolizumab versus placebo in those with comorbid NP



The MCID for ACQ-5 is 0.5 (as indicated by dashed line).

Improvements in FEV$_1$ from baseline to Week 24 were largest with mepolizumab versus placebo in those with comorbid NP



The MCID for FEV$_1$ is 100 mL (as indicated by dashed line).

Conclusions

- In this hypothesis-generating analysis, patients with severe eosinophilic asthma and comorbid NP, sinusitis, or AR demonstrated clinically relevant improvements in asthma exacerbation rates with mepolizumab treatment, with the largest response (68% reduction) seen in those with comorbid NP.
- Baseline blood eosinophil counts were higher in patients with upper airway comorbidities than those without; similarly, improvements in HRQoL were numerically greater in patients with upper airway comorbidities than those without.
- The increased benefit we observed in patients with NP is similar to previous findings among patients with severe asthma and NP receiving other biologics[11] and with severe asthma and comorbid upper airway disease receiving mepolizumab.[10]
- Patients with comorbid NP reported the highest baseline blood eosinophil counts (geometric mean of 410 cells/μL). Higher baseline blood eosinophil counts have previously been associated with an increased response to mepolizumab treatment.[12]
- These results suggest that patients with severe eosinophilic asthma with and without comorbid NP, sinusitis, or AR benefit from mepolizumab treatment, although patients with NP may benefit to an even greater degree.

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Disclosures

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