Seasonal Efficacy of Mepolizumab in Patients With Severe Eosinophilic Asthma – Meta-analysis From Two Phase 3 Trials

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Aims

For patients with asthma, the risk of having an exacerbation can be influenced by allergen sensitization and seasonal triggers.[1,2] Since many aeroallergens and respiratory viruses appear in seasonal patterns, asthma exacerbations are often observed in similar seasonal cycles.[3,4]

Mepolizumab is an anti-interleukin-5 monoclonal antibody approved as an add-on therapy for severe eosinophilic asthma.[5] Compared with placebo, mepolizumab in addition to optimized standard of care has been shown to reduce exacerbation rates for patients with severe eosinophilic asthma.[6–9] However, studies assessing the effect of mepolizumab on seasonal exacerbations are limited.

This study aimed to investigate the effect of the licensed dose of mepolizumab (100 mg subcutaneous [SC]) on seasonal exacerbations.

Methods

MENSA & MUSCA → **Post hoc meta-analysis‡**

Studies

Randomized · Double-blind · Placebo-controlled · Multicenter · Global

Phase III

Patients

576 (MENSA)

551 (MUSCA)

Severe eosinophilic asthma:

- High-dose ICS plus ≥1 other controller therapies
- ≥2 clinically significant exacerbations* in prior year
- Blood eosinophils ≥150 cells/μL†

Treatments

Standard of care therapy plus:

Placebo OR Mepolizumab 100 mg SC — Every 4 weeks — 32 weeks (MENSA) / 24 weeks (MUSCA)

Patients

911 (MENSA & MUSCA)

Receiving mepolizumab 100 mg SC or placebo

Sensitive to ≥1 tested allergen

Endpoints

Mepolizumab 100 mg SC vs Placebo

Annualized rate of clinically significant exacerbations*

Subgroups‡

Allergen sensitivity:

- Sensitive to ≥1 allergen (yes/no)
- Sensitive to ≥1 seasonal allergen (yes/no)

Of the 1127 patients enrolled in MENSA and MUSCA, 911 were included in this meta-analysis; 194 MENSA patients receiving mepolizumab 75 mg IV and 22 MENSA/MUSCA patients without ≥1 result for perennial or seasonal allergen sensitivities were excluded.

*Requiring administration of systemic glucocorticoids for ≥3 days or an emergency department visit/hospitalization; †or ≥300 cells/μL in the previous year; ‡GSK ID 208115, NCT01691521, and NCT02281318; ‡analysis of the number of exacerbations was performed separately for each subgroup using generalized estimating equation models. A negative binomial distribution was assumed with covariates of study ID, treatment, season, interaction of treatment by season and logarithm of time in season as an offset variable.

ICS, inhaled corticosteroids

Results

Patient population

Baseline demographics and characteristics	Placebo N=457	Mepolizumab N=454	Total N=911
Mean (SD) age, years	50.8 (13.6)	50.2 (14.2)	50.5 (13.9)
Female, n (%)	277 (61)	254 (56)	531 (58)
Mean (SD) asthma duration, years	19.6 (14.9)	19.8 (13.8)	19.7 (14.4)
Exacerbations in previous year, n (%)			
2	266 (58)	237 (52)	503 (55)
3	93(20)	93 (20)	186 (20)
≥4	98 (21)	124 (27)	222 (24)
Using maintenance OCS, n (%)	107 (23)	111 (24)	218 (24)
Mean (SD) % predicted pre-bronchodilator FEV_1	60.06 (17.10)	59.02 (16.72)	59.54 (16.91)
Mean (SD) SGRQ total score	46.5 (19.40)	47.2 (18.55)	46.8 (18.97)
Mean (SD) ACQ-5 score	2.19 (1.17)	2.22 (1.17)	2.21 (1.17)
Geometric mean (SD log) blood eosinophil count, cells/μL	340 (0.92)	320 (0.96)	330 (0.94)

ACQ-5, Asthma Control Questionnaire 5; OCS, oral corticosteroids; SD, standard deviation

Patient population (continued)

Allergen sensitivity	Placebo N=457	Mepolizumab N=454	Total N=911
Sensitivity to ≥1 allergen			
Positive atopic status, n (%)	216 (47)	215 (47)	431 (47)
Positive perennial allergens*, n (%)			
0	241 (53)	239 (53)	480 (53)
1	28 (6)	41 (9)	69 (8)
2	94 (21)	82 (18)	176 (19)
≥3	94 (21)	92 (20)	186 (20)
Sensitivity to ≥1 seasonal allergen			
Positive atopic status, n (%)	146 (32)	144 (32)	290 (32)
Positive seasonal allergens†, n (%)			
0	311 (68)	310 (68)	621 (68)
1	49 (11)	59 (13)	108 (12)
2	29 (6)	30 (7)	59 (6)
≥3	68 (15)	55 (12)	123 (14)

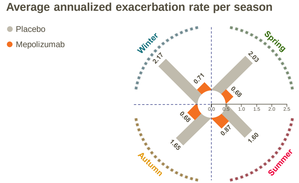
*Perennial allergens tested: *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, dog dander, cat dander, *Alternaria tenuis*; †seasonal allergens tested: elm, olive tree, oak white, thistle, wild rye, Bermuda grass, western ragweed pollen.

Patients receiving mepolizumab versus placebo experienced a reduction in exacerbation rate across all seasons; those receiving placebo experienced larger seasonal variations in exacerbation rate

Sensitivity to ≥1 allergen

Sensitivity: NO

Average annualized exacerbation rate per season

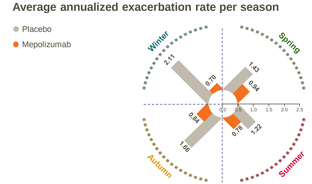


Season	Rate ratio (95% CI)
Spring	0.34 (0.19, 0.62)
Summer	0.54 (0.33, 0.91)
Autumn	0.41 (0.25, 0.69)
Winter	0.32 (0.17, 0.62)

Rate ratio mepolizumab/placebo (95% CI)

Sensitivity: YES

Average annualized exacerbation rate per season



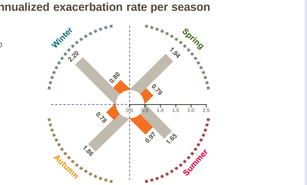
Season	Rate ratio (95% CI)
Spring	0.66 (0.42, 1.01)
Summer	0.64 (0.36, 1.13)
Autumn	0.51 (0.30, 0.85)
Winter	0.33 (0.19, 0.58)

Rate ratio mepolizumab/placebo (95% CI)

Sensitivity to ≥1 seasonal allergen

Sensitivity: NO

Average annualized exacerbation rate per season

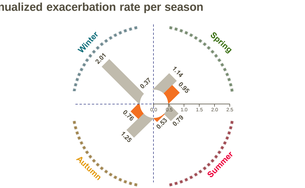


Season	Rate ratio (95% CI)
Spring	0.41 (0.27, 0.62)
Summer	0.59 (0.39, 0.89)
Autumn	0.42 (0.27, 0.65)
Winter	0.37 (0.22, 0.60)

Rate ratio mepolizumab/placebo (95% CI)

Sensitivity: YES

Average annualized exacerbation rate per season



Season	Rate ratio (95% CI)
Spring	0.83 (0.42, 1.63)
Summer	0.67 (0.25, 1.77)
Autumn	0.61 (0.30, 1.22)
Winter	0.18 (0.07, 0.47)

Rate ratio mepolizumab/placebo (95% CI)

For all radial plots, each increment of the radial axis represents 0.1 exacerbations/year, with the outer ring representing a possible maximum of 2.5 exacerbations/year. For patients enrolled in the Northern Hemisphere, seasons were classified as spring (March/April/May), summer (June/July/August), autumn (September/October/November), winter (December/January/February).
For patients enrolled in the Southern Hemisphere, 6 months were added to the exacerbation start date to classify the season. CI, confidence interval

Conclusions

- Mepolizumab reduces exacerbation rates for patients with severe eosinophilic asthma, irrespective of the season or allergen sensitization.
- The rate of exacerbations among patients receiving mepolizumab was relatively consistent across all seasons. However, the response to mepolizumab versus placebo was larger in the winter, owing to patients in the placebo group experiencing more exacerbations in this season.
- Our results suggest that although perennial and seasonal allergies can influence exacerbations over a 12-month period, patients with severe eosinophilic asthma may experience clinical benefit with mepolizumab, irrespective of the season.

References

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