Therapeutic Switch From Omalizumab to Mepolizumab in Patients With Uncontrolled Severe Eosinophilic Asthma: Treatment Effect by Exacerbations in Previous Year and Maintenance Use of OCS

Poster No. 077

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Aims

- Mepolizumab is approved for the treatment of patients with severe eosinophilic asthma.[1]
- In the OSMO study,[2] omalizumab-treated patients with uncontrolled severe eosinophilic asthma were switched to mepolizumab treatment and experienced significant and clinically relevant improvements in asthma control, health-related quality of life and asthma exacerbations.
- The aim of this post hoc analysis of the OSMO study was to determine the relationship between prior exacerbation history (previous 12 months) and maintenance oral corticosteroid (OCS) use at baseline on the treatment response to mepolizumab.

Methods

OSMO
study design

Switch study
Open-label
Single-arm
Multicenter
Phase IV study

145
patients
(ITT population)
≥12 years of age

Severe eosinophilic asthma:
≥2 exacerbations in previous year
Uncontrolled despite omalizumab treatment for ≥4 months (plus standard of care therapy)

Standard of care therapy plus:
Mepolizumab **100** mg SC
Every 4 weeks up to:
32 weeks

Post hoc analysis*

Endpoints

- Mean changes from baseline in **ACQ-5 score**†
- Mean change from baseline in **SGRQ total score**†
- Mean change from baseline in **pre-bronchodilator FEV_1**†
- Annualized rate of clinically significant **exacerbations**‡

Subgroup analysis

Number of exacerbations in prior 12 months:
≤2 vs 3 vs ≥4

Maintenance OCS:
Using vs Not using

*GSK ID 204471, NCT02654145; †analyses performed using MMRM with covariates of region, baseline maintenance OCS therapy (OCS vs no OCS), exacerbations in the year prior to the study (as an ordinal variable) and visit; ‡analyses of number of exacerbations performed using GEE model assuming a negative binomial distribution with a covariate of treatment period (either pre-treatment [during 12 months prior to screening visit] or on and off treatment [defined as exacerbations between the first dose and study conclusion regardless of treatment discontinuation]) and logarithm of time as an offset variable.

ACQ-5, Asthma Control Questionnaire 5; FEV_1, forced expiratory volume in 1 second; GEE, generalized estimating equation model; ITT, intent-to-treat; MMRM, mixed model repeated measures; SC, subcutaneous; SGRQ, St George's Respiratory Questionnaire

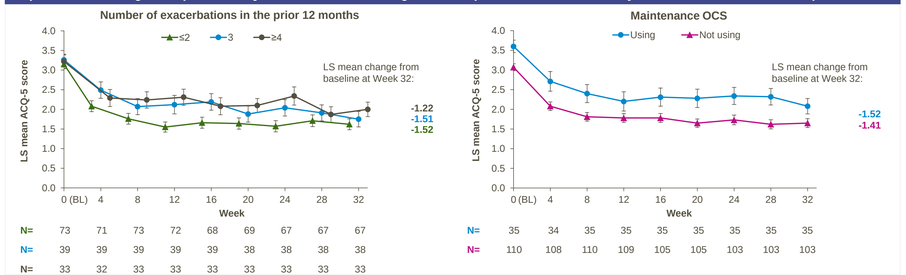
Results

Baseline demographics and disease characteristics

	Number of exacerbations in prior 12 months			Maintenance OCS	
	≤2 (N=73)	3 (N=39)	≥4 (N=33)	Using (N=35)	Not using (N=110)
Age, years, mean (SD)	52.6 (14.5)	53.1 (13.4)	56.4 (13.0)	56.2 (10.5)	52.8 (14.7)
Female (%)	53	64	67	54	61
Asthma duration, years, mean (SD)	25.2 (16.6)	27.4 (19.1)	24.2 (14.7)	24.0 (14.6)	26.1 (17.5)
Prior duration of omalizumab treatment, months, median (range)	29.6 (5–161)	40.3 (6–129)	20.2 (4–92)	43.2 (5–129)	29.0 (4–161)
On maintenance OCS at baseline* n (%) Dose (mg/day), median (range)	14 (19) 10.0 (4–40)	12 (31) 12.5 (5–30)	9 (27) 8.8 (5–40)	35 (100) 10.0 (4–40)	N/A
Exacerbations in previous year, mean (SD)	N/A	N/A	N/A	3.8 (3.87)	3.1 (2.12)
Exacerbations requiring hospitalization and/or ER visits, n (%)	8 (11)	17 (44)	18 (55)	13 (37)	30 (27)
Pre-bronchodilator FEV_1, % predicted, mean (SD)	60.6 (18.8)	58.3 (17.7)	58.6 (16.5)	55.4 (17.9)	60.8 (17.9)
SGRQ total score, mean (SD)	52.5 (15.7)	58.0 (18.5)	64.0 (17.3)	63.7 (13.2)	54.3 (18.0)
ACQ-5 score, mean (SD)	3.1 (0.94)	3.3 (0.82)	3.2 (1.09)	3.6 (0.91)	3.1 (0.91)
Blood eosinophil count, cells/μL, geo. mean (SD†)	330 (1.2)	260 (1.1)	260 (1.1)	160 (1.6)	360 (0.9)

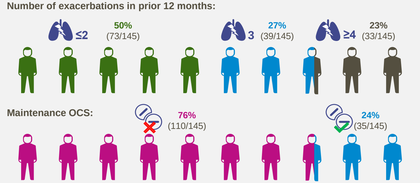
*Maintenance OCS use was considered as regular daily treatment with OCS at baseline to maintain patients' asthma control. No titration of maintenance OCS was permitted in this study (all patients were to maintain their background asthma controller medication – with the exception of discontinuing omalizumab and initiating/switching to mepolizumab treatment). Dose (mg/day) defined as prednisolone equivalent; †SD of transformed log. ER, emergency room; SD, standard deviation

Mepolizumab 100 mg SC improved ACQ-5 score at 32 weeks regardless of prior exacerbation history or maintenance OCS use in patients



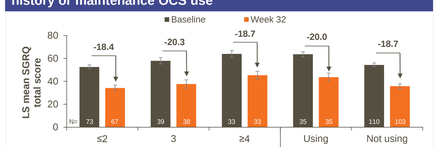
The MCID for ACQ-5 is 0.5, with higher scores indicating worse asthma control. Numbers of patients are shown at the bottom of each graph. Vertical bars reflect standard errors.
BL, baseline; LS, least squares; MCID, minimal clinically important difference

Proportion of patients in each subgroup*



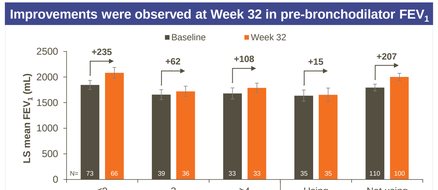
*The ITT population contained a total of 145 patients.

Mepolizumab 100 mg SC markedly improved SGRQ total score at Week 32 compared with baseline regardless of prior exacerbation history or maintenance OCS use



LS mean change from baseline is shown in bold font. The MCID for SGRQ is 4.0, with higher numbers indicating worse asthma health status. Numbers of patients are at the bottom of the bars. Vertical bars reflect standard errors.

Improvements were observed at Week 32 in pre-bronchodilator FEV_1

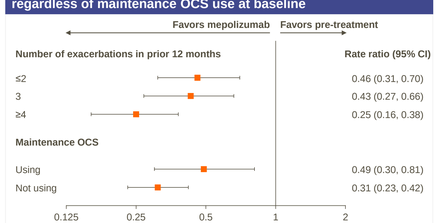


LS mean change from baseline is shown in bold font. Numbers of patients are at the bottom of the bars. Vertical bars reflect standard errors.

Conclusions

- Patients with severe eosinophilic asthma previously uncontrolled by omalizumab experienced improvements in clinical outcomes when they were directly switched to mepolizumab 100 mg SC treatment.
- Regardless of prior exacerbation history and maintenance OCS use, clinically significant improvements (exceeding the MCID) were observed in ACQ-5 score and SGRQ total score.
- Improvements in FEV_1 were observed regardless of prior exacerbation history (no consistent trend identified); greater improvements in FEV_1 were observed in patients not using versus those using maintenance OCS at baseline.
- Reductions in exacerbations were observed regardless of prior exacerbation history and maintenance OCS use, with a trend for higher exacerbations reduction in patients with ≥4 exacerbations and in those not using maintenance OCS.
- However, these data should be interpreted with caution given that this was a non-planned post hoc analysis.

Mepolizumab reduced the annualized rate of clinically significant exacerbations in all exacerbation history subgroups and regardless of maintenance OCS use at baseline



*Rate ratio (mepolizumab/pre-treatment). The pre-treatment period included exacerbations during the 12 months prior to the screening visit; the on + off treatment period included exacerbations between the first dose of mepolizumab and the end of the study (regardless of treatment discontinuation). CI, confidence interval

References

1. GlaxoSmithKline. NUCALA prescribing information. 2019.
2. Chapman KR, et al. *Allergy* 2019;74:1716–26.

Disclosures

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