Real-World Benefits of Mepolizumab in Patients with Severe Asthma and Comorbid Chronic Rhinosinusitis with Nasal Polyps (CRSwNP): Post Hoc Analysis of REALITI-A

Poster No. 48

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Introduction

Comorbid CRSwNP is common in patients with severe eosinophilic asthma (34-57%)[1–6] and is associated with increased asthma severity and worse symptom control compared with patients without comorbid CRSwNP.[1–3]

Mepolizumab is a humanized monoclonal antibody that targets IL-5, providing a precision medicine approach for the treatment of severe eosinophilic asthma.[7,8] In clinical trials and real-world studies, including the international REALITI-A study, mepolizumab treatment reduced exacerbation rates and OCS use, while improving asthma symptoms in patients with severe eosinophilic asthma.[4,5,9–13]

The treatment benefit patients experienced with mepolizumab in clinical and real-world trials was generally greater in patients with CRSwNP versus without CRSwNP.[14–17] The benefits of mepolizumab at 1 year of follow-up have been reported and to date examination of the effect of CRSwNP on mepolizumab efficacy in the REALITI-A study is based on the same follow-up period.

The objective of this post hoc analysis of the REALITI-A full study population at 2 years was to assess whether the presence of NP influenced real-world mepolizumab treatment outcomes in patients with severe eosinophilic asthma over a longer time period.

Methods

REALITI-A (GSK ID: 204710)
Study design

- Real-world
- Observational
- Prospective
- International
- Single-arm

Clinical diagnosis of asthma:
≥18 years of age
Newly prescribed mepolizumab
≥12 months relevant medical records prior to enrollment

Standard-of-care therapy, plus add-on:
Mepolizumab 100 mg SC
Initiation of mepolizumab was at the **physician's discretion**

Study enrollment period
Dec 2016 to Oct 2019

Pre-treatment period
12 months prior to enrollment

Follow-up period
24 months

Dataset
Treated: 822* patients
84 centers
7 countries

Outcomes

- Rate of CSEs†
- Change from baseline in daily OCS use‡
- Change from baseline§ in ACQ-5 score‖
- Change from baseline§ in clinic FEV_1‖

stratified (post hoc) to:
CRSwNP status at enrollment
With
Without

*One patient was excluded from the treated population after initiating mepolizumab at 300 mg SC (approved dose for EGPA); †CSEs were defined as asthma deterioration requiring OCS for ≥3 days, or an SCS administration (or doubling the dose in patients on maintenance OCS), or an emergency room visit or hospitalization. The rate of CSEs was analyzed using a GEE model assuming a negative binomial distribution, with a covariate of treatment period (pre-treatment and follow-up). The variance of the estimated mean was corrected for within-patient correlation and the logarithm of time was included as an offset variable; ‡baseline was defined as the 28 days preceding mepolizumab initiation, prednisone equivalent; §baseline was defined as the 90 days preceding mepolizumab initiation; ‖analysis performed using MMRM with covariates of time point, country, baseline OCS therapy (use/no use), and ordinal exacerbations during the pre-treatment period (0, 1, 2, 3, ≥4).

Results

Table 1. Patient demographics and clinical characteristics at enrollment

	Treated population (N=822)	CRSwNP status at enrollment	
		With CRSwNP (n=323)	Without CRSwNP (n=499)
Age, years, mean (SD)	54 (13.6)	54 (12.9)	54 (14.0)
Female, n (%)	521 (63)	170 (53)	351 (70)
Asthma duration, years, mean (SD)	n=801 19.7 (15.7)	n=317 20.8 (15.2)	n=484 18.9 (15.9)
Smoking history, n (%) Never smoked Former smoker Current smoker	n=816 503 (62) 290 (36) 23 (3)	n=321 208 (65) 111 (35) 2 (<1)	n=495 295 (60) 179 (36) 21 (4)
Patients with mOCS use*, n (%) mOCS dose, mg/day, median (IQR)	320 (39) n=297 10.0 (5.0, 14.7)	135 (42) n=129 7.5 (5.0, 10.8)	185 (37) n=168 10.0 (5.0, 16.3)
BEC, cells/μL†, geometric mean (SD log)	n=614 350 (1.253)	n=264 440 (1.204)	n=350 295 (1.264)
Rate of clinically significant exacerbations, events/year	n=821 4.3	n=323 4.2	n=498 4.3
ACQ-5 score†, LS mean (95% CI)	n=781 2.87 (2.78, 2.96)	n=307 2.72 (2.58, 2.86)	n=474 2.96 (2.85, 3.08)
Clinic FEV_1†, mL, LS mean (95% CI)	n=398 1966 (1890, 2042)	n=186 2114 (2005, 2224)	n=212 1821 (1692, 1949)

*Prednisone-equivalent dose in the 28 days prior to and including the mepolizumab initiation date. Of the patients receiving mOCS, information on daily dose data was not available for 23; †latest record in the 90 days prior to mepolizumab initiation.

Figure 1. The rate of CSEs during the 2 year follow-up period was lower than prior to mepolizumab initiation, with numerically greater reductions in patients with CRSwNP versus without CRSwNP

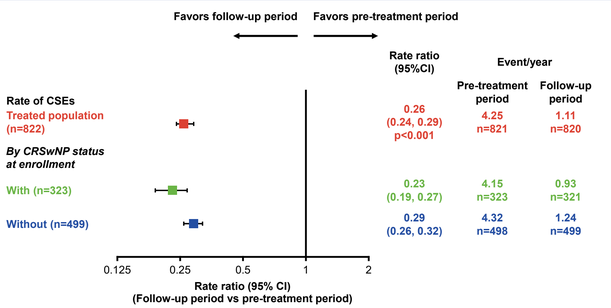


Figure 2. There was a 100% reduction in the median daily dose of mOCS at week 101–104 following mepolizumab initiation for patients with and without CRSwNP at enrollment and greater than half of patients discontinued mOCS at week 101–104

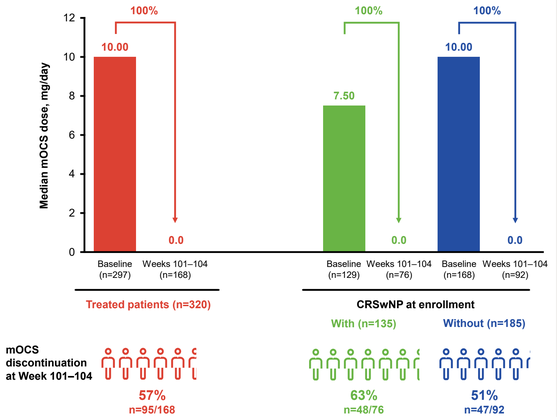
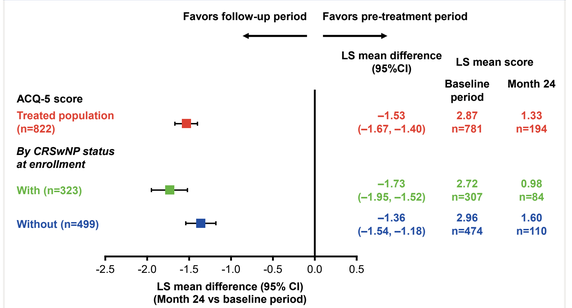


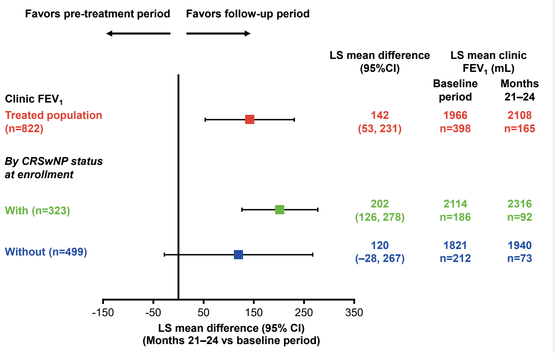
Figure 3. Patients had improvements in ACQ-5 score following 2 years of mepolizumab treatment compared with baseline, with numerically greater improvements seen for patients with CRSwNP versus without CRSwNP



Conclusions

- This post hoc analysis using data from the real-world REALITI-A study population at 2 years showed that mepolizumab reduced CSEs and OCS use, in addition to improving symptoms and lung function in patients with severe eosinophilic asthma both with and without comorbid CRSwNP.
  - There was a nominally greater treatment benefit with mepolizumab in all outcomes evaluated in patients with comorbid CRSwNP versus patients without comorbid CRSwNP, supporting previous clinical study results.[10–14]
  - As data were collected during standard routine or unscheduled clinical care there may be missing information, which potentially impacted CIs for the outcomes in the with/without subgroup analysis.
- These results suggest that patients with severe eosinophilic asthma both with and without comorbid CRSwNP benefit from treatment with mepolizumab, and that patients with severe asthma and CRSwNP represent a clinically identifiable phenotype particularly suited to mepolizumab therapy.

Figure 4. Following 2 years of mepolizumab treatment, there was an increase in clinic FEV_1 in all treated patients compared with baseline, with numerically greater improvements in patients with CRSwNP versus without CRSwNP



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Abbreviations

ACQ-5, Asthma Control Questionnaire-5; BEC, blood eosinophil count; CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; CSE, clinically significant asthma exacerbation; EGPA, eosinophilic granulomatosis with polyangiitis; FEV_1, forced expiratory volume in 1 second; GEE, generalized estimating equation; IL, interleukin; IQR, interquartile range; log, logarithm; LS, least squares; MMRM, mixed model repeated measures; mOCS, maintenance OCS; OCS, oral corticosteroid; SC, subcutaneous; SCS, systemic corticosteroid; SD, standard deviation.

Disclosures

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