Impact of Baseline Clinical Asthma Characteristics on the Response to Mepolizumab: A Post Hoc Meta-analysis of Two Phase III Trials

Poster No. 174

Liu MC[1], Taillé C[2–4], Lee JK[5], Smith SG[6], Mallett S[7], Martin N[8], Howarth P[8], Yancey SW[7], Lemiere C[9,10]

[1]Divisions of Allergy and Clinical Immunology, Pulmonary and Critical Care Medicine, Johns Hopkins Asthma and Allergy Center, Baltimore, MD, USA; [2]Service de Pneumologie, Hôpital Bichat, AP-HP-Nord, Paris, France; [3]INSERM U1152, Université de Paris, Paris, France; [4]INSERM 12, F-CRIN, Clinical Research Initiative In Severe Asthma: a Level for Innovation & Science (CRISALIS), France; [5]Evidence Based Medical Educator, Toronto Allergy and Asthma Clinic, Toronto, ON, Canada; [6]Respiratory Therapeutic Area, GSK, Research Triangle Park, NC, USA; [7]Clinical Statistics, GSK, Stockley Park, Uxbridge, Middlesex, UK; [8]Global Medical Affairs, GSK, Brentford, Middlesex, UK; [9]Faculty of Medicine, Université de Montréal, Montreal, QC, Canada; [10]Hôpital du Sacré-Cœur de Montréal, Montreal, QC, Canada

Aims

Severe asthma is a heterogeneous disease associated with a broad range of phenotypes and clinical characteristics.[1,2]

Mepolizumab is an anti–IL-5 monoclonal antibody approved as an add-on therapy for patients with a severe eosinophilic asthma phenotype.[3,4]

Compared with placebo, mepolizumab in addition to optimized standard of care has been shown to reduce exacerbation rates and OCS use whilst improving lung function, health-related quality of life, and asthma control in patients with severe eosinophilic asthma.[5–9]

This study aimed to investigate whether select baseline clinical characteristics could influence the efficacy of mepolizumab in patients with severe eosinophilic asthma.

Methods

MENSA & MUSCA

NCT01691521 & NCT02281318

Studies

Phase III
Randomized
Double-blind
Placebo-controlled
Multicenter
Global

Patients

576 (MENSA) **551** (MUSCA)

High-dose ICS plus ≥1 other controller therapies
≥2 clinically significant exacerbations* in prior year
Blood eosinophils ≥150 cells/μL (or ≥300 cells/μL in prior year)

Treatments

Standard of care therapy plus mepolizumab 100 mg SC† or placebo, every 4 weeks:

32 weeks (MENSA)
24 weeks (MUSCA)

Post hoc meta-analysis‡

208115

Endpoints

- Annualized rate of clinically significant exacerbations* — Primary§ endpoint
- Change from baseline to study end in pre-bronchodilator FEV_1
- Change from baseline to study end in SGRQ total score
- Change from baseline to study end in ACQ-5 score
- Proportion of patients achieving complete asthma control (ACQ-5 score <0.75)

Analysis Subgroups

936 patients from MENSA & MUSCA¶

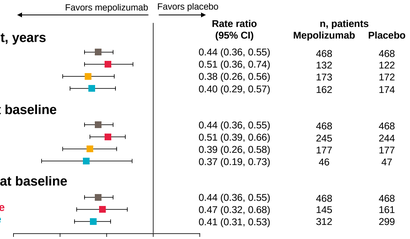
Subgroups:	Age at asthma onset	% predicted FEV_1 at baseline	Airway reversibility at baseline	Asthma control at baseline
	<18 years 18–<40 years ≥40 years	≤60% >60–80% >80%	Irreversible (<12% change in FEV_1) Reversible (≥12% change in FEV_1)	Uncontrolled (ACQ-5 score ≥1.5) Partial/complete control (ACQ-5 score <1.5)
Endpoints measured:				

*Requiring administration of systemic glucocorticoids for ≥3 days or an emergency department visit/hospitalization; †MENSA patients received mepolizumab 100 mg SC or 75 mg IV, whilst MUSCA patients received mepolizumab 100 mg SC: only MENSA/MUSCA patients who received mepolizumab 100 mg SC were included in the post hoc meta-analysis; ‡analyses were conducted separately for each study and subgroup; end-of-study treatment differences between mepolizumab 100 mg SC and placebo for each subgroup were combined across studies using an inverse variance weighted fixed-effects meta-analysis. All analyses included terms for treatment group, geographical region, baseline maintenance OCS use (yes/no) and exacerbations in the year prior to the study (2, 3, 4+; as an ordinal variable). Baseline % predicted pre-bronchodilator FEV_1 was also included as a covariate, with baseline FEV_1 instead used for analyses of FEV_1. Rate of exacerbations was analyzed using a negative binomial model; continuous endpoints were analyzed using mixed model repeated measures, with additional terms for baseline value, visit, visit by baseline value, and visit by treatment group; §primary endpoint for the 208115 post hoc analysis; ¶191 patients from MENSA who received mepolizumab 75 mg IV were not included in this analysis.

Results

Clinically significant exacerbations were reduced by 49–63% with mepolizumab vs placebo, across age at onset, lung function, and airway reversibility subgroups

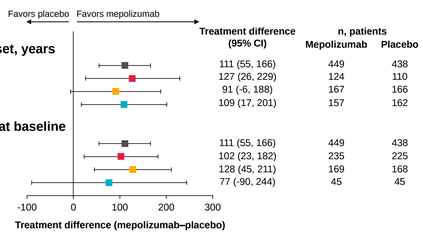
Annualized rate of on-treatment clinically significant exacerbations



	Rate ratio (95% CI)	n, patients Mepolizumab	Placebo
Age at asthma onset, years			
ITT population	0.44 (0.36, 0.55)	468	468
<18	0.51 (0.36, 0.74)	132	122
18–<40	0.38 (0.26, 0.56)	173	172
≥40	0.40 (0.29, 0.57)	162	174
% predicted FEV_1 at baseline			
ITT population	0.44 (0.36, 0.55)	468	468
≤60%	0.51 (0.39, 0.66)	245	244
>60–80%	0.39 (0.26, 0.58)	177	177
>80%	0.37 (0.19, 0.73)	46	47
Airway reversibility at baseline			
ITT population	0.44 (0.36, 0.55)	468	468
Irreversible	0.47 (0.32, 0.68)	145	161
Reversible	0.41 (0.31, 0.53)	312	299

Lung function improved with mepolizumab vs placebo, across all age at asthma onset and the majority of lung function subgroups

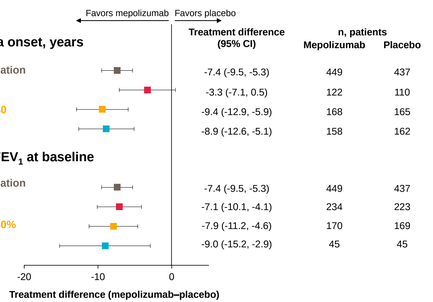
Change from baseline to study end in pre-bronchodilator FEV_1, mL



	Treatment difference (95% CI)	n, patients Mepolizumab	Placebo
Age at asthma onset, years			
ITT population	111 (55, 166)	449	438
<18	127 (26, 229)	124	110
18–<40	91 (-6, 188)	167	166
≥40	109 (17, 201)	157	162
% predicted FEV_1 at baseline			
ITT population	111 (55, 166)	449	438
≤60%	102 (23, 182)	235	225
>60–80%	128 (45, 211)	169	168
>80%	77 (-90, 244)	45	45

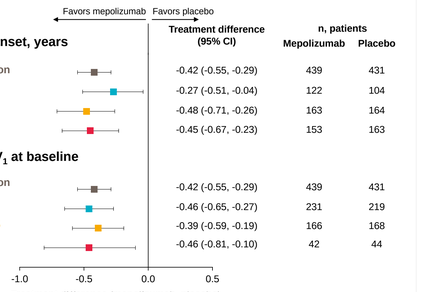
Health-related quality of life and asthma control improved with mepolizumab vs placebo, across most baseline characteristics subgroups

Change from baseline to study end in SGRQ total score



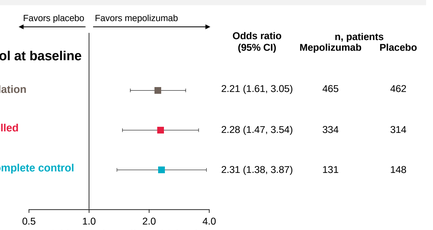
	Treatment difference (95% CI)	n, patients Mepolizumab	Placebo
Age at asthma onset, years			
ITT population	-7.4 (-9.5, -5.3)	449	437
<18	-3.3 (-7.1, 0.5)	122	110
18–<40	-9.4 (-12.9, -5.9)	168	165
≥40	-8.9 (-12.6, -5.1)	158	162
% predicted FEV_1 at baseline			
ITT population	-7.4 (-9.5, -5.3)	449	437
≤60%	-7.1 (-10.1, -4.1)	234	223
>60–80%	-7.9 (-11.2, -4.6)	170	169
>80%	-9.0 (-15.2, -2.9)	45	45

Change from baseline to study end in ACQ-5 score



	Treatment difference (95% CI)	n, patients Mepolizumab	Placebo
Age at asthma onset, years			
ITT population	-0.42 (-0.55, -0.29)	439	431
<18	-0.27 (-0.51, -0.04)	122	104
18–<40	-0.48 (-0.71, -0.26)	163	164
≥40	-0.45 (-0.67, -0.23)	153	163
% predicted FEV_1 at baseline			
ITT population	-0.42 (-0.55, -0.29)	439	431
≤60%	-0.46 (-0.65, -0.27)	231	219
>60–80%	-0.39 (-0.59, -0.19)	166	168
>80%	-0.46 (-0.81, -0.10)	42	44

Proportion of patients achieving complete asthma control



	Odds ratio (95% CI)	n, patients Mepolizumab	Placebo
Asthma control at baseline			
ITT population	2.21 (1.61, 3.05)	465	462
Uncontrolled	2.28 (1.47, 3.54)	334	314
Partial/complete control	2.31 (1.38, 3.87)	131	148

Conclusions

- Mepolizumab was associated with clinical benefits in patients with varying age at asthma onset, lung function, airway reversibility, and asthma control at baseline.
- These results indicate that mepolizumab is likely to be beneficial for patients with severe eosinophilic asthma who have a broad range of baseline clinical characteristics.

References

1. Chung KF, et al. *Eur Respir J* 2014;43(2):343–73.
2. Wenzel S. *Clin Exp Allergy* 2012;42(5):650–8.
3. Food and Drug Administration. Nucala (mepolizumab) key highlights of prescribing information 2020. Available from: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Nucala/pdf/NUCALA-PI-PIL.PDF [last accessed December 2020].
4. European Medicines Agency. Nucala summary of product characteristics 2019. Available from: https://www.ema.europa.eu/en/documents/product-information/nucala-epar-product-information_en.pdf [last accessed December 2020].
5. Pavord ID, et al. *Lancet* 2012;380(9842):651–9.
6. Bel EH, et al. *N Engl J Med* 2014;371:1189–97.
7. Ortega HG, et al. *N Engl J Med* 2014;371(13):1198–207.
8. Chupp GL, et al. *Lancet Respir Med* 2017;5:390–400.
9. Lugogo N, et al. *Clin Ther* 2016;38(9):2058–70 e1.

Abbreviations

ACQ-5, Asthma Control Questionnaire-5 item; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroids; IL, interleukin; ITT, intent-to-treat; IV, intravenous; OCS, oral corticosteroids; SC, subcutaneous; SGRQ, St George's Respiratory Questionnaire.

Disclosures

- This analysis and the parent studies were funded by GlaxoSmithKline (GSK; meta-analysis: 208115 [MEA115588/NCT01691521; 200862/NCT02281318]).
- On behalf of all authors, an audio recording of this poster was prepared by MCL, who did not receive any payment for this recording.
- MCL reports personal fees for advisory board attendance from GSK, Gossamer Bio, and AstraZeneca; research grants from GSK and Gossamer Bio. CT has received personal fees for consultancy services, speaking at conferences, and participation in clinical research projects (as an investigator) with GSK, AstraZeneca, Novartis, Roche, Sanofi, Chiesi, and Teva. JKL reports grants and personal fees from Novartis, Pfizer, Genentech, Regeneron, AstraZeneca, and Sanofi, as well as personal fees from GSK, Merck, Takeda, and CSL. SGS, SM, NM, PH, and SWY are current employees of GSK, and hold stocks/shares in GSK. CL has received personal fees for consultancy services and participation in clinical research projects (as an investigator) with GSK, AstraZeneca, Novartis, Sanofi, and Teva Innovation; research grants from GSK and Sanofi.
- Editorial support (in the form of writing assistance, assembling tables and figures, collating and incorporating author comments, grammatical editing, and referencing) was provided by Bianca Paris, PhD, at Fishawack Indicia Ltd, UK, part of Fishawack Health and was funded by GSK.

Scan the QR code or go to http://tago.ca/aaaai_7 to access a downloadable version of this poster and the associated audio recording

Prepared for the American Academy of Allergy Asthma & Immunology Annual Meeting 2021