How Real-World Mepolizumab Users in the REALITI-A Study Relate to the Recruitment Criteria Applied in the Randomized, Placebo-Controlled Trials of Subcutaneous Mepolizumab in Severe Eosinophilic Asthma

Ramos-Barbón D[1], Bals R[2], Crimi N[3], Menzies D[4]*, Pek B[5]*, Pilette C[6], Steven G[7]*, Alfonso-Cristancho R[8], Jakes R[9], Maxwell AC[10], Price RG[11], Yang S[8], Howarth P[12]

[1]Hospital Santa Creu i Sant Pau, Barcelona, Spain; [2]Universitaetsklinikum des Saarlandes Innere V, Homburg, Saarland, Germany; [3]Azienda Ospedaliero Universitaria Policlinico Vittorio Emanuele, Catania, Sicily, Italy; [4]Glan Clwyd Hospital, Bodelwyddan, Rhyl, UK; [5]Centre hospitalier de Lanaudière, QC, Canada; [6]Cliniques universitaires Saint-Luc and Institute of Experimental and Clinical Research, UCLouvain, Brussels, Belgium; [7]Allergy, Asthma & Sinus Center SC, Greenfield, WI, USA; [8]Value Evidence and Outcomes, GSK, Collegeville, PA, USA; [9]Epidemiology, GSK, Upper Providence, PA, USA; [10]Real World Study Delivery, Value Evidence and Outcomes, GSK, Stevenage, Hertfordshire, UK; [11]Biostatistics, GSK, Stevenage, Hertfordshire, UK; [12]Global Medical, GSK House, Brentford, Middlesex, UK

Aims

Mepolizumab is an anti–interleukin-5 monoclonal antibody treatment approved for use in patients with insufficiently controlled severe eosinophilic asthma (SEA), despite use of standard-of-care therapies such as high-dose inhaled corticosteroids (ICS), bronchodilators, and/or requiring maintenance oral corticosteroids (OCS).[1,2]

Compared with real-world studies, randomized controlled trials (RCTs) conducted to prove efficacy and safety of new therapies typically have strictly defined inclusion and exclusion criteria. The key placebo-controlled studies of subcutaneous (SC) mepolizumab 100 mg in SEA required evidence of meeting the diagnosis criteria of severe eosinophilic asthma.[3-5] In contrast, minimal inclusion and exclusion criteria apply in the real world.

The REALITI-A study is a multinational, real-world cohort study, which recruited patients with asthma who were newly prescribed mepolizumab, to assess real-world clinical outcomes of patients receiving treatment with mepolizumab.[6]

Here, we aimed to evaluate participants in the REALITI-A study against the inclusion and exclusion criteria of the previously conducted mepolizumab RCTs, to determine the similarity of demographic and clinical characteristics of real-world participants to those in a controlled clinical trial setting.

Methods

REALITI-A (GSK ID: 204710)
Study design

- Real-world
- Observational
- Prospective
- Global
- Single-arm

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

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

Study enrollment period: **Dec 2016 to Oct 2019**

822 patients† *from* 84 centers in 7 countries *were* **evaluated against RCT criteria**

*Patients initiating mepolizumab at a dose differing from the approved dose of 100 mg SC have been excluded from this analysis; †patients treated.

All participants within the REALITI-A treated population (N=822) were assessed against the following RCT criteria for SEA:

- High-dose inhaled steroids* alongside another controller therapy‡ at baseline‡
- AND: Blood eosinophil level ≥150 cells/μL on entry (within 90 days prior to first dose/treatment index) or a historical blood eosinophil measure ≥ 300 cells/μL in the previous year
- OR: Daily maintenance oral steroids at baseline‡ (a surrogate marker of eosinophilic disease)

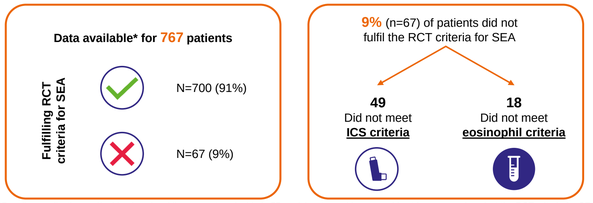
*High-dose inhaled steroids for clinical trials were defined as ≥1000 mcg/day (≥880 mcg/day per actuated dose of fluticasone propionate), which is different from current GINA high-dose ICS definition. Participants in REALITI-A were assessed against a criteria of >500 mcg/day fluticasone propionate. ‡Controller medications including long-acting beta-2 agonist (LABA), long-acting anticholinergic, leukotriene receptor antagonist, xanthine and nedocromil or cromolyn sodium. ‡Baseline defined as the period including the initiation date and 27 days prior.

Results

Summary of Baseline disease characteristics within the mepolizumab development program

	Randomized controlled trials			Real-world studies
	MENSA (N=576)	MUSCA (N=551)	SIRIUS* (N=135)	REALITI-A† (N=822)
Exacerbations in previous year, mean (SD)	3.6 (2.58)	2.8 (1.75)	3.1 (3.10)	n=821 4.4 (4.10)
≥2 exacerbations in previous year, n (%)	575 (>99)	549 (>99)	91 (67)	663 (81)
Eosinophil count on entry, geometric mean (SD logs), cells/μL	290 (0.99)	320 (1.02)	240 (1.128)	n=606‡ 357 (1.25)
Maintenance OCS use, n (%)	144 (25)	131 (24)	135 (100)	318 (39)
IgE, geometric mean (SD logs), U/mL	159.3 (1.50)	176.9 (1.46)	115.7 (1.27)	n=674‡ 183.0 (1.61)
ACQ-5 score, mean (SD)	2.2 (1.20)	2.2 (1.13)	2.1 (1.22)	n=780‡ 2.9 (1.32)
Pre-bronchodilator % predicted FEV_1, mean (SD)	61.0 (17.99)	58.6 (16.04)	58.7 (17.75)	n=395‡ 67.5 (21.14)
Smoking history, n (%)				n=815
Never smoked	417 (72)	403 (73)	82 (61)	490 (60)
Former smoker	159 (28)	147 (27)	53 (39)	300 (37)
Current smoker	0	1 (<1)	0	25 (3)
Medical conditions (past or ongoing), n (%)				
Hay fever	294 (51)	290 (53)	73 (54)	400 (49)
Chronic sinusitis	188 (33)	194 (35)	75 (56)	329 (40)
Nasal polyps	174 (30)	182 (33)	65 (48)	321 (39)
COPD	0	0	0	81 (10)
Other lung disease	0	0	0	122 (15)

*OCS sparing study, all patients required to be receiving maintenance OCS with no requirement for a prior history of exacerbations. Baseline results provided from all subjects within the RCTs. †Within the REALITI-A real-world study there were no protocol required assessments (including no requirement for maximum post-bronchodilator testing, lab measurements or questionnaires). N varies for each characteristic. ‡Baseline of REALITI-A study is the latest record prior to treatment index, but not more than 90 days prior to index date.
ACQ-5, asthma control questionnaire-5; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; IgE, immunoglobulin E; OCS, oral corticosteroids; SD, standard deviation.



*Baseline medication and/or blood eosinophils were not evaluable in 55 participants, and hence could not be assessed against the RCT criteria for SEA

Demographics and clinical characteristics by alignment with RCT criteria for SEA

	Meeting RCT criteria (N=700)	Not meeting RCT criteria (N=67)
Age, mean (SD), years	53.8 (13.5)	55.8 (13.8)
Female, %	62	69
BMI, mean (SD), kg/m²	28.9 (7.2)	28.1 (6.4)
Country		
Italy	30%	33%
UK	26%	10%
USA	9%	24%
Spain	12%	10%
Germany	12%	4%
Canada	6%	13%
Belgium	5%	4%
Asthma duration, mean (SD), years	19.9 (15.6)	18.4 (16.6)
Daily maintenance ICS dose, mean (SD), mcg/day	1297 (620)	675 (396)
Exacerbations in the previous year, mean (SD)	4.5 (4.1)	2.9 (2.4)
Eosinophil count on entry, geometric mean (SD logs), cells/μL	379 (1.20)	193 (1.57)
Maintenance OCS use, n (%)	318 (45)	0
ACQ-5 score, mean (SD)	2.9 (1.3)	2.8 (1.4)
Pre-bronchodilator % predicted FEV_1, mean (SD)	67.4 (21.4)	68.3 (19.2)

Percentages may not add up to 100% owing to rounding. *BEC on entry (within 90 days prior to first dose/treatment index). BMI, body mass index

Conclusions

- Most patients treated with mepolizumab in real-world settings met the criteria for SEA, which is consistent with the populations of RCTs in which the efficacy of mepolizumab has been proven.
- Among patients who did not meet the RCT criteria for SEA, the main reasons were low blood eosinophil levels and low ICS use. However, these patients did experience exacerbations and had uncontrolled symptoms.
- In the real-world setting, as reflected by entrants into REALITI-A, there is more complex SEA being treated with mepolizumab than in the clinical trials, as suggested by the presence of co-existent lung disease.

Demographics and clinical characteristics by alignment with RCT criteria for SEA (continued)

	Meeting RCT criteria (N=700)	Not meeting RCT criteria (N=67)
Smoking history		
Never smoked	60%	61%
Current smoker	3%	5%
Former smoker	37%	35%
Medical history reported during 12 months prior to the enrollment date		
Any	94%	91%
Recognised to be associated with asthma		
Any asthma-related	81%	84%
Hay fever	48%	49%
Chronic sinusitis	40%	37%
Nasal polyps	40%	43%
Any drug hypersensitivity	31%	45%
Nasal polypectomy	28%	36%
Atopic dermatitis	10%	7%
Anaphylaxis	7%	4%

Multiple concurrent medical conditions may be reported by a single participant,

References

1. Nucala EMA SmPC. Available from: https://www.ema.europa.eu/en/documents/variation-report/nucala-h-c-3860-ii-0013-g-epar-assessment-report-variation_en.pdf. 2019 [last accessed July 13, 2020].
2. Nucala US product information. Available from: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Nucala/pdf/NUCALA-PI-PIL-IFU-COMBINED.PDF. Revised 9/2019 [last accessed July 13, 2020].
3. Chupp GL, et al. *Lancet Respir Med* 2017;5(5):390–400.
4. Ortega HG, et al. *N Engl J Med* 2014;371(13):1198–207.
5. Bel EH, et al. *N Engl J Med* 2014;371:1189–97.
6. Harrison T, et al. *Eur Respir J* 2020;56(4):2000151.

Disclosures

- This study was funded by GlaxoSmithKline (GSK ID: 204710).
- On behalf of all authors, an audio recording of this poster was prepared by DR-B, who did not receive any payment for this recording.
- *DM, GS and BP contributed to this study and the parent abstract but were not available to provide feedback on and/or approve this poster due to competing priorities with the ongoing pandemic.
- **DR-B** reports personal fees from GlaxoSmithKline, AstraZeneca, TEVA Pharmaceuticals, personal fees and nonfinancial support from Novartis and Chiesi, nonfinancial support from Boehringer Ingelheim, and personal fees from BIAL Pharmaceuticals, outside the submitted work. **RB** reports grants and personal fees from AstraZeneca, Boehringer Ingelheim, and Novartis, personal fees from GSK, Grifols, and CSL Behring, and grants from the German Federal Ministry of Education and Research (BMBF) Competence Network Asthma and COPD (ASCONET). **NC**, **DM**, and **BP** received research grants from GSK, AstraZeneca, Sanofi-Genzyme, Novartis, Hoffman-Laroche, and Merck. **CP** has received fees for advisory boards, speaker meetings, and research grants from GSK, AstraZeneca, Chiesi, Novartis, Teva, and ALK-Abello. **GS** has served as a speaker or advisor for Aimmune, ALK, Allergy & Asthma Network, AstraZeneca, Boehringer Ingelheim, and Optinose; and has been an investigator for 3M, AstraZeneca, Chiesi, GSK, Lupin, Menlo, Merck, NeRRE, Novartis, Pearl Therapeutics, Sanofi, Teva, and Watson. **RA-C**, **RJ**, **ACM**, **RGP**, **SY,** and **PH** are employees of GSK and hold stock/share options in GSK.
- Editorial support (including preparation of the draft poster under the direction and guidance of the authors, collating and incorporating authors' comments for each draft, assembling tables and figures, grammatical editing and referencing) was provided by Nathan Ley, PhD, at Fishawack Indicia Ltd, UK, and was funded by GSK.

Scan the QR code or click on https://tago.ca/-ATS22 to access a downloadable version of this poster and the associated audio recording

Presented at the American Thoracic Society Annual Meeting, Virtual, May 14–19, 2021