Clinical remission with mepolizumab in severe asthma: impact of lung function parameters

Digital poster
Supplemental data
Narrated summary

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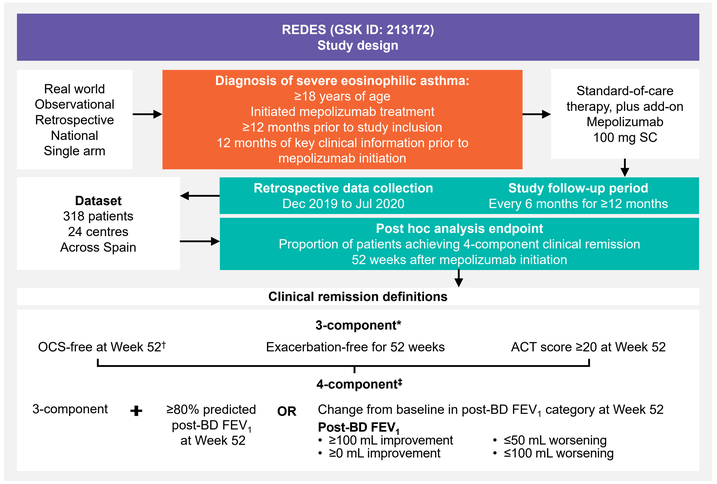
Aims

- Mepolizumab, a precision medicine for the treatment of severe asthma,[1] has been shown to improve outcomes in patients in real-world studies, including the REDES study.[2–4]
- Use of precision medicine, including the introduction of biologic agents, for the treatment of other chronic inflammatory diseases has facilitated the adoption of clinical remission as a treatment goal.[5–7]
- On-treatment clinical remission is now being discussed as an achievable treatment goal for some patients with severe asthma[8,9]; the definition of clinical remission is currently an evolving concept:
  - Consideration of whether lung function outcomes should be included in a remission definition is ongoing, in part due to the natural age-related loss of lung capacity.[8]
  - There is also the question of how best to define a lung function remission component.
- In a recent post hoc analysis of the real-world REDES study, during which patients with severe asthma received 52 weeks of mepolizumab treatment, clinical remission definitions were met by 37% (96/260) of patients in the absence of a lung function parameter and 30% (43/144) of patients when a lung function parameter was included.[9]
- The objective of this post hoc analysis of the REDES study was to expand on the previous findings to assess the impact of including various differing lung function parameters within a 4-component clinical remission definition.

Methods



Patients were excluded from the analysis of the 3-component definition if they had missing ACT scores at Week 52; †not receiving OCS at baseline and remained off OCS at Week 52 or tapered off during the study; ‡patients were excluded from the analysis of the 4-component definition with ≥80% predicted post-BD FEV_1 criteria if they were missing predicted post-BD FEV_1 scores at Week 52; patients were excluded from the analysis of the 4-component definition with change from baseline in post-BD FEV_1 criteria if they were missing change in post-BD FEV_1 at Week 52

Results

- Study populations for analysis of 3-component definition of clinical remission:

Patients with data for OCS use, exacerbations and ACT score ≥20 at Week 52 (3-component population)	n=260

- Study populations for analysis of 4-component definition of clinical remission:

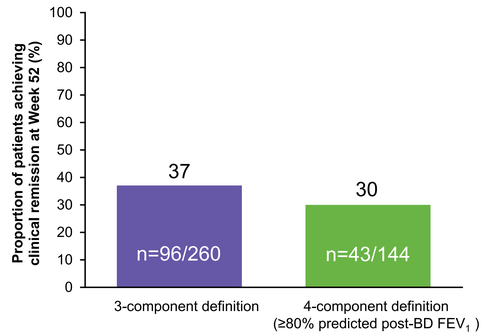
Patients in 3-component population with ≥80% predicted post-BD FEV_1 data at Week 52	n=144
Patients in 3-component population with data for change from baseline in post-BD FEV_1 category at Week 52	n=125

Table 1: **Baseline demographics and clinical characteristics among patients with ≥80% predicted post-BD FEV_1 data at Week 52 (n=144)**

	n=144
Age, years, mean (SD)	58.6 (12.8)
Age at asthma diagnosis, years, mean (SD)	33.7 (18.3)
Female, n (%)	108 (75)
BMI, kg/m², mean(SD)	28.2 (5.2)
Exacerbations in the 12 months pre-mepolizumab, mean (SD)	4.2 (3.1)
Baseline ACT score, mean (SD)	14.4 (5.0)
Baseline ACT score <20, n (%)	115 (85)
Baseline ACT score ≥20, n (%)	21 (15)
OCS dependent* in the 12 months pre-mepolizumab, n (%)	60 (42)
Baseline OCS dose, median (IQR)	10.0 (5.0, 15.0)
Baseline BEC†, cells/µl, geometric mean (SD log)	545 (0.725)
Baseline % predicted post-BD FEV_1, mean (SD)	76.2 (23.9)
Atopic sensitisation, n (%)	57 (40)
Comorbidities, n (%)	
CRSwNP	64 (44)
Bronchiectasis	36 (25)
GERD	35 (24)
Anxiety	33 (23)

Patients with maintenance treatment with OCS for ≥6 months in the last year; †where BEC of zero was recorded, a small value (minimum of all non-missing results/2) was added prior to log transformation. All parameters collected at a pre-treatment visit prior to mepolizumab initiation unless otherwise specified

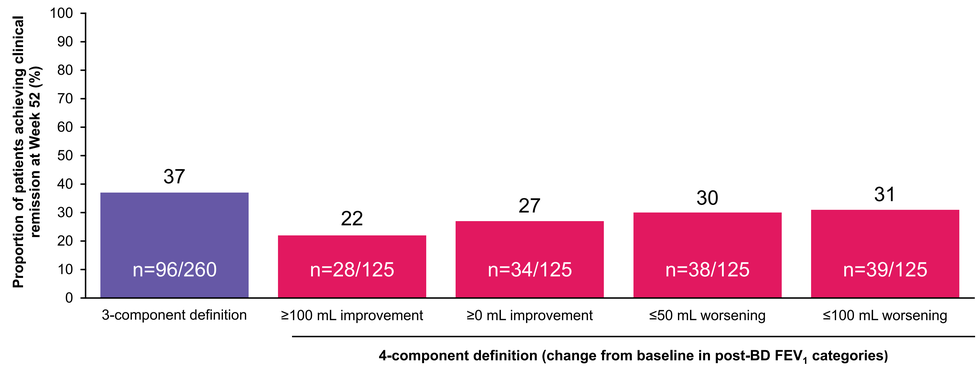
Figure 1: **The addition of ≥80% predicted post-BD FEV_1 criteria to the composite 3-component definition reduced the proportion of patients with clinical remission at Week 52 from 37% to 30%**



Conclusion

- This post hoc analysis using data from the real-world REDES study supports clinical remission as an achievable goal in a subset of patients with severe asthma receiving mepolizumab.
  - As expected, the inclusion of a lung function parameter within the 4-component clinical remission definition reflects more stringent criteria, with marginally fewer patients defined as in clinical remission compared with the 3-component definition.
  - These data may feed into the discussion on whether lung function should be factored into the definition of clinical remission in asthma or reserved as a validation factor.
- A similar proportion of patients achieved a 4-component definition of clinical remission when using the ≥80% predicted FEV_1 or ≤50 mL worsening from baseline in post-BD FEV_1 parameter.
  - A ~50 mL loss of FEV_1 may reflect a loss similar to the natural loss of lung function occurring annually with age in individuals without lung disease.[10]
- These findings support clinical remission in severe asthma as a realistic real-world goal, provide insight into the variation in this outcome if different levels of lung function benefit were to be incorporated into the definition, and should aid development of a standardised definition of asthma remission on therapy.

Figure 2: **With incorporation of change from baseline in post-BD FEV_1 categories, the proportion of patients achieving clinical remission ranged from 22% to 31%, increasing sequentially as the level of improvement in post-BD FEV_1 required decreased**



Abbreviations

ACT, Asthma Control Test; BEC, blood eosinophil count; ; BD, bronchodilator; BMI, body mass index; CRSwNP, chronic rhinosinusitis with nasal polyps; FEV_1, forced expiratory volume in 1 second; geo., geometric; GERD, gastroesophageal reflux disease; IQR, interquartile range; OCS, oral corticosteroid; SC, subcutaneous; SD, standard deviation.

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MGSH's listed affiliation was at the time of the study and has since left GSK.

JO has served on adjudication committees or data and safety monitoring boards for AstraZeneca, GSK, Novartis and Sanofi; received consultancy fees from AstraZeneca, GSK and Sanofi; and received grants and personal fees from GSK; **TCD** declares honoraria for speakers' bureau from ALK, DIATER, GSK, LETI, Novartis and Sanofi; **EMM** declares honoraria for speakers' bureau from ALK, AstraZeneca, BIAL, Boehringer Ingelheim, Chiesi, GSK, Novartis, Teva and Sanofi; **MGSH** was an employee of GSK at the time of study and held stock/shares in GSK; **DBC, RGP, AR, SZ** and **PH** are all employees of GSK and hold stocks/shares in GSK; **GC** has acted as a consultant for AstraZeneca, Genentech, Boehringer Ingelheim and Teva; attended a speaker's bureau with AstraZeneca, Genentech and Circassia; received speaker fees from Amgen, Sanofi-Genzyme and Regeneron, received research grants from AstraZeneca and institutional grants from AstraZeneca, Genentech, Boehringer Ingelheim and GSK; has clinical trial funding from Amgen, Sanofi-Genzyme and Regeneron, and is an advisory board member for Amgen, Sanofi-Genzyme and Regeneron; **CDR** has received funding for travel or speaker fees from ALK, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Menarini, Novartis, Stallergenes and Pfizer.

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