Meta-analysis of Asthma Control in Patients with Severe Eosinophilic Asthma Treated with Mepolizumab

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Introduction

- Mepolizumab is a monoclonal antibody that through a targeted blocking of interleukin-5 (IL-5) reduces eosinophil recruitment and survival. It is indicated as add-on maintenance therapy for patients with severe asthma aged 12 years or older with an eosinophilic phenotype.[1]
- Achieving asthma control is an important goal of asthma management. This can be measured through validated questionnaires like the Asthma Control Questionnaire (ACQ-5)[2] which addresses 5 main asthma symptoms (night symptoms, morning symptoms, activity limitation, shortness of breath and wheezing). The score ranges from 0 to 6, with higher scores indicating more active symptoms. ACQ-5 scores of 1.5 (or greater) indicate uncontrolled asthma, scores below 0.75 indicate Complete Asthma Control and scores between 0.75 and 1.5 indicate Partial Asthma Control. The minimally important clinical difference (MCID) is an improvement of 0.5 in ACQ-5 score.[3]
- The ability of the licensed dose of Mepolizumab 100 mg subcutaneous (SC), administered every 4 weeks, to achieve asthma control assessed by the Asthma Control Questionnaire-5 (ACQ-5) is of interest.

Objectives

- Identify patients that were uncontrolled at baseline in the MENSA and MUSCA studies, and who subsequently achieved complete or partial asthma control during the study period.
- Compare the proportions between treatment with Mepolizumab and Placebo over 24 weeks.

Methods

- This post-hoc analysis used data from two phase III trials comparing the licensed dose of mepolizumab 100 mg SC to placebo. In total, 468 patients treated with mepolizumab and 468 patients treated with placebo were part of this analysis.
- MENSA (NCT01691521) was a 32-week, randomized, double blind, placebo-controlled study in 576 patients with severe asthma (SA), treated with Mepolizumab, 100 mg SC (n=194) or 75 mg IV (n=191, not included in this analysis) or placebo (n=191). The primary endpoint was the annualized rate of exacerbations. The rate of exacerbations was reduced by 53% among those receiving subcutaneous Mepolizumab, as compared with those receiving Placebo.[4]
- MUSCA (NCT02281318) was a 24-week, randomized, double blind, placebo-controlled study in 551 patients with SA, treated with Mepolizumab 100 mg SC (n=274) or placebo (n=277). The primary endpoint was the mean change from baseline in the Saint George's Respiratory Questionnaire (SGRQ), assessing improvement in quality of life, with a treatment difference of -7.7 points compared to placebo (MCID for SGRQ is -4 points; lower scores indicating greater improvement).[5]

- Both studies recruited patients who were using high dose Inhaled Corticosteroid (ICS) plus a second controller and had at least 2 exacerbations in the previous year that required a minimum of 3 days of oral corticosteroids (OCS) treatment. They also required to have a blood eosinophil level of at least 150 cells/µL at screening or 300 cells/µL in the previous year.
- The proportion of uncontrolled patients achieving different levels of asthma control over the treatment period of each study was summarized and compared between treatment groups using a logistic regression model.

Table 1. Baseline characteristics

	Placebo (N=468)	Mepolizumab 100 mg (N=468)	Overall population (N=936)
Age, years, mean (SD)	50.9 (13.6)	50.4 (14.3)	50.6 (13.9)
Female, n (%)	283 (60)	265 (57)	548 (59)
Exacerbations in last year, n (%)			
2	273 (58)	248 (53)	521 (56)
3	94 (20)	96 (21)	190 (20)
≥4	101 (22)	124 (26)	225 (24)
Receiving maintenance OCS therapy, n (%)	111 (24)	116 (25)	227 (24)
Pre-bronchodilator FEV_1, mL, mean (SD)	1827.6 (647.93)	1822.0 (692.35)	1824.8 (670.15)
Blood eosinophil count, cells/µL, n geometric mean (SD Logs)	466 340 (0.93)	466 320 (0.97)	932 330 (0.95)
ACQ-5 score, n mean (SD)	462 2.21 (1.18)	465 2.25 (1.17)	927 2.23 (1.17)

SD=standard deviation; FEV_1= forced expiratory volume at 1 second

Table 2. Complete/Partial Asthma Control at end of study in patients uncontrolled at baseline

Patient Group – Outcome	Placebo N=468	Mepolizumab 100mg N=468	Odds Ratio (95% CI)
Uncontrolled at baseline, n (%)	**314 (67%)**	**334 (71%)**	
Patients uncontrolled at baseline – Complete Control	12%	25%	2.28 (1.47,3.54)
Patients uncontrolled at baseline – Complete or Partial Control	30%	49%	2.54 (1.78,3.63)

Figure 1. Uncontrolled patients at baseline that achieve complete Asthma Control over first 24 weeks of each study

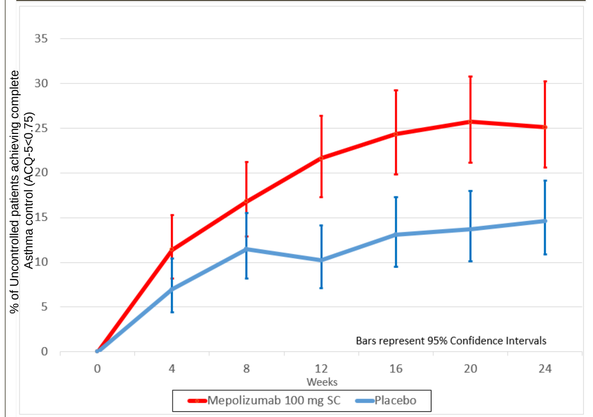
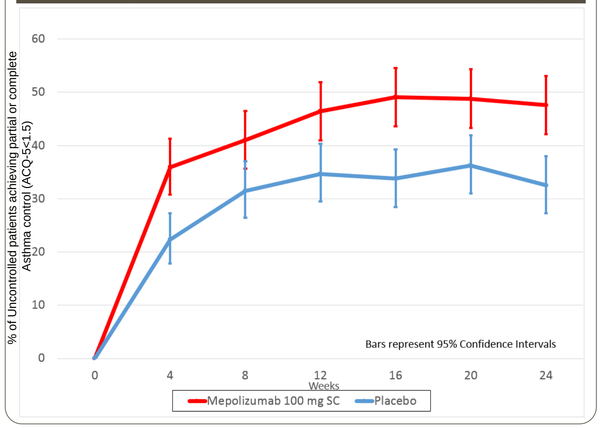


Figure 2. Uncontrolled patients at baseline that achieve partial or complete Asthma Control over first 24 weeks of each study



Results

- At baseline 69% (n=648) of all subjects had uncontrolled asthma, 21% had partially controlled asthma and 9% were controlled at baseline.
- In this meta-analysis, following 32 weeks of treatment in MENSA and 24 weeks in MUSCA, of patients with uncontrolled asthma at baseline:
  - 25% (Mepolizumab) vs 12% (Placebo) achieved complete control (Odds Ratio (OR) 2.28, 95%CI 1.47,3.54).
  - 49% (Mepolizumab) vs 30% (Placebo) achieved partial or complete asthma control (OR 2.54, 95%CI 1.78,3.63).
- Clinically significant and persistent improvement vs placebo in the proportion of patients achieving complete asthma control / partial or complete asthma control was observed after 3 doses (at 12 weeks, Figures 1 and 2).

Conclusions

- Achieving and maintaining asthma control is an important goal of asthma management. Despite GINA step 4-5 recommended treatment with high dose ICS plus a second controller, 69% of the severe eosinophilic asthma patients in MENSA and MUSCA studies were uncontrolled based on ACQ-5 score at baseline.
- Among these patients Mepolizumab significantly increased the odds of achieving complete asthma control at the end of the treatment period compared to placebo.
- Additionally, of these patients almost half treated with Mepolizumab were controlled or partially controlled (49%) at the end of the study compared to just under a third (30%) in the Placebo group.
- These findings support a significant and meaningful benefit with Mepolizumab in achieving asthma control compared to placebo in this population.

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