

Disease Stability Is Achievable in a Wide Spectrum of Patients with Chronic Obstructive Pulmonary Disease Receiving Mepolizumab: Pooled Results from Phase III Randomised Controlled Trials

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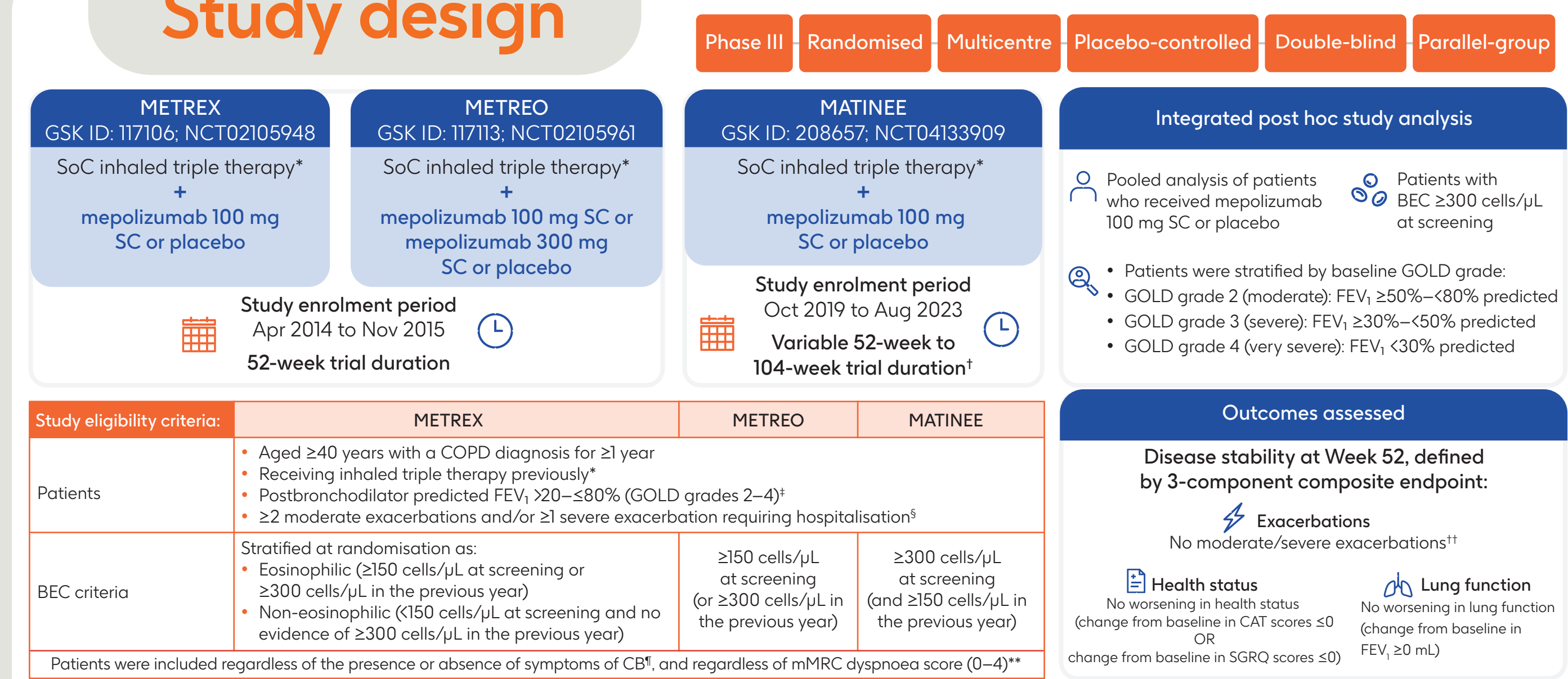
Background

- Patients with COPD and type 2 inflammation characterised by an eosinophilic phenotype are more likely to experience frequent and severe exacerbations^{1,2}
- COPD activity translates to exacerbations, which drive disease progression characterised by worsening symptoms and deteriorating lung function^{3–5}
- Disease stability, defined as a sustained state of low disease activity, as indicated by no worsening in symptoms or lung function and no exacerbations, following optimisation of management, is an emerging, ambitious, and achievable treatment goal in COPD^{3,6}
- Mepolizumab is a humanised monoclonal antibody that specifically binds to IL-5, a central cytokine in type 2 inflammation,⁷ and has been approved in several regions for add-on maintenance treatment of inadequately controlled COPD and an eosinophilic phenotype^{8,9}
- Three Phase III trials, METREX, METREO, and MATINEE, demonstrated the efficacy of mepolizumab as an add-on to inhaled triple therapy in a wide spectrum of patients with COPD, a history of exacerbations, and an eosinophilic phenotype^{10,11}

Aims

This pooled post hoc analysis of results from the MATINEE, METREX, and METREO studies assessed the effect of mepolizumab on disease stability in patients with COPD with BEC ≥300 cells/μL overall and by GOLD grade (2–4)

Study design



Demographics

	All patients (n=1146 [†] ; 100%)		GOLD 2 (n=483; 42.1%)		GOLD 3 (n=504; 44.0%)		GOLD 4 (n=148; 12.9%)	
	Mepolizumab 100 mg (n=568)	Placebo (n=578)	Mepolizumab 100 mg (n=238)	Placebo (n=245)	Mepolizumab 100 mg (n=256)	Placebo (n=248)	Mepolizumab 100 mg (n=69)	Placebo (n=79)
Male, n (%)	379 (67)	391 (68)	156 (66)	167 (68)	168 (66)	155 (63)	51 (74)	65 (82)
Age, mean (SD)	65.7 (8.2)	66.1 (8.3)	66.2 (9.0)	66.0 (8.3)	66.2 (8.2)	66.2 (8.3)	65.2 (6.0)	63.5 (6.9)
Moderate/severe exacerbations 12 months prior to screening, mean (SD)	2.4 (1.2)	2.3 (1.1)	2.4 (1.2)	2.2 (0.9)	2.5 (1.2)	2.4 (1.2)	2.3 (1.3)	2.4 (1.1)
Smoking status								
Current smoker, n (%)	160 (28)	162 (28)	66 (28)	65 (27)	74 (29)	72 (29)	18 (26)	23 (29)
Former smoker, n (%)	407 (72)	408 (71)	172 (72)	177 (72)	181 (71)	172 (69)	51 (74)	56 (71)
Symptoms of CB [§]								
Patients with assessment, n	551	568	232	240	245	243	69	79
Yes, n (%)	376 (68)	382 (67)	160 (69)	165 (69)	166 (68)	159 (65)	48 (70)	54 (68)
No, n (%)	175 (32)	186 (33)	72 (31)	75 (31)	79 (32)	84 (35)	21 (30)	25 (32)
mMRC dyspnoea scale, n (%)								
<2	129 (22)	112 (20)	63 (26)	75 (31)	38 (15)	43 (17)	8 (12)	10 (13)
≥2	447 (77)	452 (80)	174 (73)	170 (69)	215 (84)	205 (83)	61 (88)	68 (86)
CAT total score								
Patients with assessment, n	547	564	231	240	243	240	69	78
Mean (SD)	19.2 (7.2)	19.2 (7.1)	17.8 (7.0)	17.9 (7.0)	20.1 (7.1)	19.8 (7.1)	20.7 (7.1)	21.1 (6.1)
SGRQ total score								
Patients with assessment, n	549	567	231	240	244	242	69	79
Mean (SD)	54.9 (17.5)	54.0 (17.5)	50.1 (17.7)	48.8 (17.7)	57.6 (16.6)	56.5 (17.0)	61.5 (16.8)	61.9 (13.8)

*In total, 11 patients (5 mepolizumab/6 placebo) had mild airflow obstruction (GOLD grade 1 [mild]: FEV₁ ≥80% predicted) as FEV₁ ≥80% predicted was not excluded from the studies; †determined by answers to items related to cough and sputum in the SGRQ at screening

Results

Figure 1: A greater proportion of patients achieved disease stability with mepolizumab versus placebo using both CAT- and SGRQ-based definitions. This effect was observed across all GOLD subgroups at Week 52. A statistically significant treatment difference was observed for disease stability (SGRQ-defined) in the overall population, favouring mepolizumab

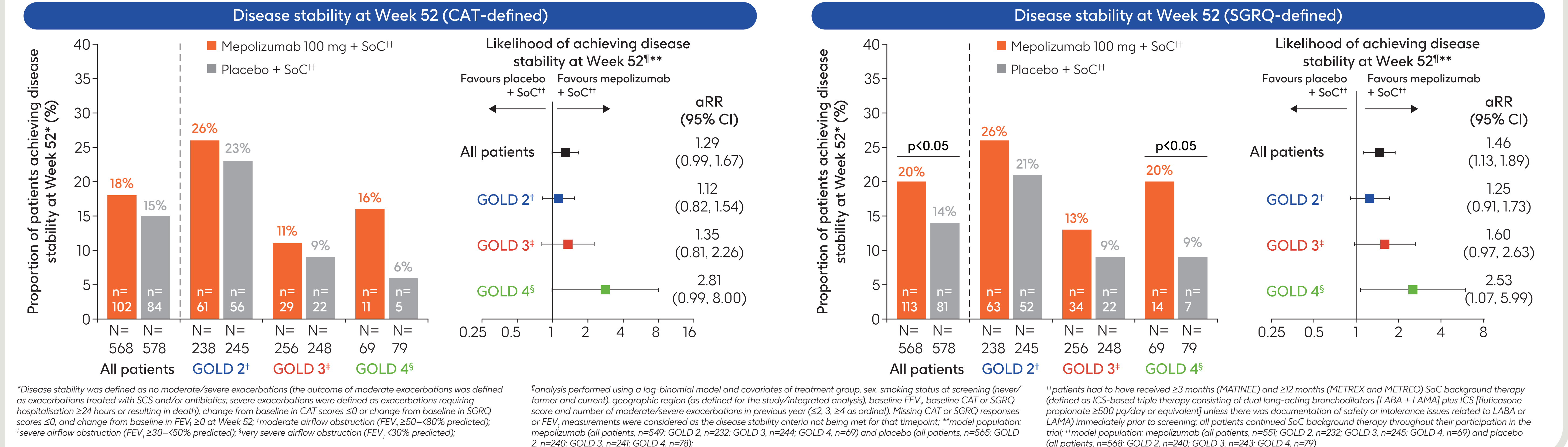


Figure 2: In the overall population, exacerbations were the most prominent driver of the numerical differences between mepolizumab and placebo in achieving disease stability at Week 52

		All patients	GOLD 2*	GOLD 3*	GOLD 4*
⚡ Exacerbation-free at Week 52	Mepolizumab	52% (n=295/568)	64% (n=152/238)	43% (n=111/256)	42% (n=29/69)
	Placebo	42% (n=242/578)	56% (n=137/245)	30% (n=75/248)	37% (n=29/79)
📄 Stability in CAT score [§] at Week 52	Mepolizumab	54% (n=309/568)	60% (n=143/238)	50% (n=127/256)	55% (n=38/69)
	Placebo	53% (n=306/578)	61% (n=150/245)	47% (n=117/248)	44% (n=35/79)
📄 Stability in SGRQ score [§] at Week 52	Mepolizumab	57% (n=326/568)	63% (n=151/238)	52% (n=133/256)	54% (n=37/69)
	Placebo	55% (n=320/578)	60% (n=148/245)	52% (n=128/248)	52% (n=41/79)
🫁 Stability in FEV ₁ ** at Week 52	Mepolizumab	45% (n=256/568)	50% (n=119/238)	39% (n=99/256)	49% (n=34/69)
	Placebo	43% (n=247/578)	49% (n=119/245)	37% (n=92/248)	42% (n=33/79)

*FEV₁ ≥50–<80% predicted; †FEV₁ ≥30–<50% predicted; ‡FEV₁ <30% predicted; §change from baseline in CAT scores ≤0; ¶change from baseline in SGRQ scores ≤0; **change from baseline in FEV₁ ≥0

Conclusions

This integrated analysis of patients with COPD, a history of exacerbations, and BEC ≥300 cells/μL pooled from three Phase III RCTs showed that greater proportions of patients receiving mepolizumab achieved disease stability versus placebo

Mepolizumab was associated with disease stability in patients with a wide spectrum of airflow obstruction at screening, observed across all GOLD 2–4 subgroups. Greater disease stability was observed using the SGRQ-defined measure compared with CAT, likely reflecting its increased sensitivity to change, given its greater complexity and broader coverage of health-related quality of life domains

In the overall population, exacerbations were the main driver of the difference in achieving disease stability between groups; previous analyses have shown lung function improvements may occur over a longer timeframe.¹² Patterns across GOLD subgroups were variable

Patients achieved disease stability in greater proportions with GOLD 2 airflow obstruction than with GOLD 3 or 4. Earlier intervention with targeted therapy may therefore offer an opportunity to improve outcomes

Abbreviations

aRR, adjusted risk ratio; BEC, blood eosinophil count; CAT, COPD Assessment Test; CB, chronic bronchitis; CI, confidence interval; COPD, chronic obstructive pulmonary disease; COVID-19, Coronavirus Disease 2019; FEV₁, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroid; IL-5, interleukin-5; LABA, long-acting β₂-agonist; LAMA, long-acting muscarinic antagonist; mMRC, modified Medical Research Council; RCT, randomised controlled trial; SC, subcutaneous; SCS, systemic corticosteroid; SD, standard deviation; SGRQ, St George's Respiratory Questionnaire; SoC, standard of care

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