Improvements in COPD Symptoms With Umeclidinium/Vilanterol Analyzed by Baseline CAT Score: A Post Hoc Analysis of the EMAX Trial

EMAX TRIAL

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Background

- The Global Initiative for Obstructive Lung Disease strategy report recommends dual bronchodilator treatment as initial maintenance therapy in symptomatic patients with COPD at low risk of exacerbations only if they have severe symptoms.[1]
- COPD Assessment Test (CAT) scores ≥20 indicate a high impact of COPD on a patient's health.
- Subgroup analyses of the Early MAXimization of bronchodilation for improving COPD stability (EMAX) trial showed consistent symptom improvements with dual- versus mono-bronchodilator therapy irrespective of baseline CAT score.[2]
  - However, analyses by pre-specified subgroups are typically based on artificially determined thresholds, and the relationship between improvements and baseline CAT score is more likely to be described by a continuous function.
- This post hoc analysis of the EMAX trial evaluated improvements in patient-reported symptom severity and lung function with dual- versus mono-bronchodilator therapy, using fractional polynomials to model baseline CAT score as a continuous variable to examine the thresholds at which treatment differences are observed.

Methods

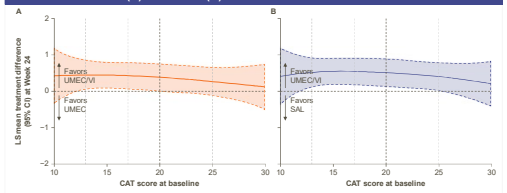
- The 24-week, double-blind, parallel-group EMAX trial randomized patients with symptomatic COPD and low exacerbation risk not receiving inhaled corticosteroids 1:1:1 to umeclidinium/vilanterol (UMEC/VI) 62.5/25 mcg once daily, UMEC 62.5 mcg once daily, or salmeterol (SAL) 50 mcg twice daily over 24 weeks.[3]
- Improvements in self-administered computerized Transition Dyspnea Index (SAC-TDI), Evaluating Respiratory Symptoms: COPD (E-RS) total score, daily rescue medication use, and trough forced expiratory volume in 1 second (FEV_1) were assessed using fractional polynomial modeling with continuous transformations of baseline CAT score covariates.

Results

Symptoms

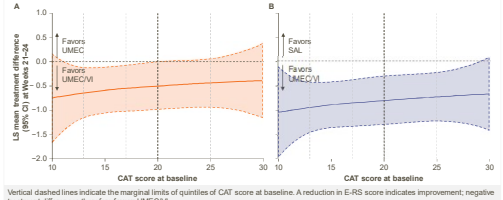
- Numerically greater improvements in SAC-TDI focal score at Week 24 and E-RS total score at Weeks 21–24 were observed with UMEC/VI versus UMEC across baseline CAT scores, with the greatest benefits observed at CAT scores of approximately 10–20, with a trend for a smaller effect at higher scores (**Figures 1A and 2A**).
  - Similar trends were observed versus SAL, with the greatest benefits seen across a wider range of CAT scores (**Figures 1B and 2B**).

Figure 1. Improvements in SAC-TDI focal score at Week 24 by baseline CAT score with UMEC/VI versus (A) UMEC and (B) SAL



Vertical dashed lines indicate the marginal limits of quintiles of CAT score at baseline.

Figure 2. Improvements in 4-weekly E-RS total score at Weeks 21–24 by baseline CAT score with UMEC/VI versus (A) UMEC and (B) SAL



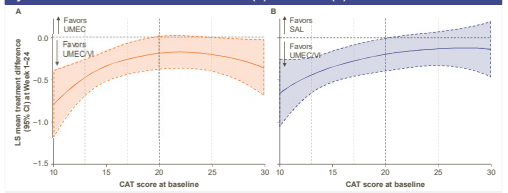
Vertical dashed lines indicate the marginal limits of quintiles of CAT score at baseline. A reduction in E-RS score indicates improvement; negative treatment differences therefore favour UMEC/VI.

- Rescue medication use over Weeks 1–24 showed greater variation in treatment differences with UMEC/VI versus UMEC and SAL across CAT scores than other endpoints. Numerically greater improvements in rescue medication use were observed with UMEC/VI versus both UMEC and SAL, with the greatest benefits at CAT scores of <20 (**Figure 3**).

Lung function

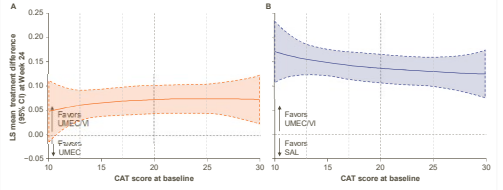
- UMEC/VI demonstrated greater improvements versus UMEC and SAL for trough FEV_1 at Week 24 across baseline CAT scores (**Figure 4**).

Figure 3. Improvements in rescue medication use (puffs/day) across Weeks 1–24 by baseline CAT score with UMEC/VI versus (A) UMEC and (B) SAL



Vertical dashed lines indicate the marginal limits of quintiles of CAT score at baseline. A reduction in rescue medication puffs/day indicates improvement; negative treatment differences therefore favour UMEC/VI.

Figure 4. Improvements in trough FEV_1 at Week 24 by baseline CAT score with UMEC/VI versus (A) UMEC and (B) SAL



Vertical dashed lines indicate the marginal limits of quintiles of CAT score at baseline.

Conclusions

- Greater improvements in symptoms and lung function were seen with UMEC/VI versus UMEC or SAL, irrespective of baseline CAT score.
- Patients with lower baseline CAT scores had the greatest improvements in daily symptoms with UMEC/VI versus UMEC and SAL, as indicated by E-RS score and reduced rescue medication use over the 24-week study period.
- Dual bronchodilators may be considered as initial maintenance therapy for symptomatic patients with COPD across a broad range of symptom severities.
- Fractional polynomial modeling is a promising addition to traditional subgroup analyses and may reveal non-linear associations relevant to treatment decisions.

Table 1. Baseline characteristics

Characteristic	ITT (N=2425)
Age, years, mean (SD)	64.6 (8.5)
Female, n (%)	988 (41)
Current smoker at screening, n (%)	1203 (50)
Moderate COPD exacerbation history in prior year*, n (%)	393 (16)
Post-salbutamol % predicted FEV_1, mean (SD)	55.4 (12.7)
Baseline CAT score, n (%)	
<20	1352 (56)
≥20	1073 (44)
Baseline CAT score, mean (SD)	19.2 (6.1)
BDI score, mean (SD)	7.0 (1.9)
Baseline E-RS total score	10.6 (5.7)

*Number of exacerbations requiring oral or systemic corticosteroids and/or antibiotics (moderate) in 12 months prior to screening (patients with >1 moderate exacerbation or with a severe exacerbation [requiring hospitalization] were excluded).
BDI, Baseline Dyspnea Index

References

1. Global Initiative for Obstructive Lung Disease (GOLD); Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. 2020.
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3. Maltais F, et al. *Respir Res* 2019;20:238.

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