Comparative Efficacy of Umeclidinium/Vilanterol, Umeclidinium, and Salmeterol in Symptomatic Patients With Chronic Obstructive Pulmonary Disease Free of Inhaled Corticosteroids: The EMAX Trial

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Background

- Long-acting muscarinic antagonists (LAMA), such as UMEC and VI, when added to LABA significantly improved symptoms compared to LABA monotherapy.
- UMEC/VI combination therapy may be considered an initial therapy in symptomatic patients with chronic obstructive pulmonary disease (COPD) free of inhaled corticosteroids (ICS) due to superior effects in bronchodilation compared to BID LABA/ICS maintenance therapy.
- UMEC/VI combination therapy provides incremental improvements in symptoms compared to monotherapy; however, the magnitude of this benefit remains uncertain because between-class comparator trials have consistently shown significant improvements with UMEC/VI versus UMEC and VI.
- Potentially, UMEC/VI could be used as an initial therapy in COPD patients free of ICS.

Methods

- **Study design**: This was a double-blind, parallel-group study of 24 weeks duration in patients aged ≥40 years with symptomatic COPD (GOLD stage 1 to 3) and previously untreated with bronchodilator therapy. Patients were randomized into three groups: UMEC/VI (umeclidinium at 63.25 µg and vilanterol at 25 µg), UMEC (umeclidinium at 63.25 µg), or SAL (salmeterol at 50 µg) with a 1:1:1 ratio. Participants were on their first month in lung function and a range of COPD symptom measures versus UMEC and SAL.

- **Patient characteristics**: Patients were aged 40 to 80 years with a smoking history of at least 10 pack-years, a COPD diagnosis, and pre- and post-albuterol forced expiratory volume in 1 second (FEV1) of ≤ 100% predicted. A post-albuterol FEV1/FVC ratio of < 0.7, a post-albuterol FEV1 of ≤ 80% predicted, and a history of moderate/severe COPD exacerbations were included.

- **Randomization**: Eligible patients were randomized into three groups: UMEC/VI (umeclidinium at 63.25 µg and vilanterol at 25 µg), UMEC (umeclidinium at 63.25 µg), or SAL (salmeterol at 50 µg) with a 1:1:1 ratio.

- **Outcomes**: The primary outcome was change from baseline in trough FEV1 over 24 weeks. Secondary outcomes included changes in post-albuterol FEV1 and forced vital capacity (FVC), impact on health-related quality of life, and exacerbations.

Results

- **Patient demographics and clinical characteristics**: Table 1 shows patient demographics and clinical characteristics across the three treatment groups. Patients were well-balanced across the groups in terms of age, sex, smoking history, and GOLD stage.

- **Symptom improvement**: Figure 1 shows a significant improvement in trough FEV1 from baseline with UMEC/VI versus both UMEC and SAL at Week 24 (LS mean (95% CI) change from baseline: UMEC/VI vs UMEC: 122 mL (106, 138), UMEC/VI vs SAL: 189 mL (152, 225), both P < 0.001). Table 2 summarizes the tolerability outcomes.

- **Exacerbations**: Table 3 summarizes the exacerbation outcomes. The risk of a moderate/severe exacerbation to Day 168 was 13%, 16%, and 19% for UMEC/VI, UMEC, and SAL, respectively. The risk of a severe exacerbation to Day 168 was 1%, 1%, and 1% for UMEC/VI, UMEC, and SAL, respectively. UMEC/VI significantly reduced the risk of moderate/severe exacerbations compared to UMEC and SAL.

- **Safety**: No serious adverse events were reported. Few additional patients (<1%) with GOLD grade 1 were randomized into the UMEC and SAL groups.

Conclusions

- UMEC/VI provided significant improvements in trough FEV1 compared to UMEC and SAL with no significant safety concerns.

References


Disclosures

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