Evaluation of Rescue Medication Use and Medication Adherence in Patients Initiating Umeclidinium/Vilanterol or Tiotropium/Olopatadine Within a Large US Health Insurer Database

Post No. P502 (A3313)


Background

The on-demand long-acting muscarinic antagonist/long-acting β2-agonist (LAMA/LABA) combination treatments u.meclidinium/vilanterol (UMEC/VLT) and tiotropium/olopatadine (TIO/OLO) have been directly compared in a previous randomized controlled trial. The reported superiority on lung function and a reduction in patient-reported rescue medication use with UMEC/VLT compared with TIO/OLO was significantly greater among patients with more severe lung function impairment who used rescue inhalers for chronic obstructive pulmonary disease.

This observational real-world study aimed to evaluate rescue medication use and medication adherence among patients initiating therapy with UMEC/VLT compared with TIO/OLO.

Methods

Study design and patients

This was a retrospective cohort study of commercial, Medicare Advantage with Part D, and Part D-only enrollees 65 years of age from the Optum Research Database.

Patients initiated UMEC/VLT or TIO/OLO between June 1, 2015, and November 30, 2016 (index date set as the first fill date) with 12 months of continuous enrollment pre- and post-index date (Figure 1).

• Patients were excluded if they had an inhalated corticosteroid (ICS) - or LABA-containing controller medication during the pre-index period, or any of the following on the index date pharmacy fills for both (UMEC/VLT or TIO/OLO) - multiple inhaled triple therapy (MITT: i.e., ICS, LAMA, and LABA), or missing demographic information.

Endpoints

• Rescue medication use was evaluated in the post-index period excluding fills on the index date.

• One unit of rescue medication (short-acting muscarinic antagonist (SAMA) or short-acting β2-agonist (SABA) controller medication) corresponds to one cartridge of a metered-dose inhaler (i.e., 333 µg) of added rescue medication.

• Medication adherence, defined as a proportion of days covered (PDC) ≥80%, was calculated using pharmacy claims for the index medication in the post-index period, including the index pharmacy fill.

• PDC was calculated by dividing the number of days with available index medication (based on days supplied for filled prescriptions) by the number of days between the index prescription claim and a pharmacy fill for an non-controller medication or the end of the 12-month post-index period, whichever occurred first.

Statistical analyses

• Inverse probability of treatment weighting (IPTW) was utilized to balance pre-index characteristics between treatment arms, and multivariable modeling was used to adjust for residual imbalances of pre-index characteristics following IPTW.

• Rescue medication use was evaluated in an intent-to-treat (ITT) analysis assessing non-inferiority (with a margin of 0.30 units) and superiority (with a margin of 0 of UMEC/VLT vs TIO/OLO).

• Weighted-ordinary least squares regression with bootstrapped standard errors, confidence intervals (CIs), and superiority criteria were used to model rescue medication use. This 95% C.I. and one-sided (p=0.025) bootstrapped P-values were used to determine if the non-inferiority and superiority criteria were met.

• On-treatment medication adherence was modeled using weighted logistic regression with a robust variance estimator (secondary objective).

• Patients were censored at the earliest of the time of a pharmacy fill for a non-index controller medication or the end of the 12-month post-index period.

Results

Study population

• The study population included 54,149 UMEC/VLT and 47,474 TIO/OLO initiators (Figure 2).

• The medication characteristics were similar between treatment cohorts after IPTW (Table 1).

Statistical analyses

• During the 12-month post-index period, the mean (SD) rescue medication use was similar between UMEC/VLT and TIO/OLO initiators: UMEC/VLT: 1.87 (3.88) units; TIO/OLO: 1.01 (2.70) units; P=0.067.

• In unadjusted analyses, UMEC/VLT met the pre-specified non-inferiority criteria (−0.24 units; 95% CI: −0.16, 0.08; P=0.01) but did not meet superiority criteria (P=0.27).

• After adjustment for residual imbalances between the cohorts, UMEC/VLT initiators had fewer mean units of rescue medication per patient per year than TIO/OLO initiators (−0.18 rescue medication use per patient per year) (P=0.002).

• In the adjusted ITT analysis, UMEC/VLT met the pre-specified non-inferiority and superiority criteria (P=0.001 and P<0.001, respectively, Figure 3).

• Medication adherence

• In the on-treatment analysis of medication adherence:

- Mean (SD) PDC was significantly higher among UMEC/VLT initiators compared with TIO/OLO initiators (1.03 (0.18) TIO/OLO vs 0.74 (0.21) P=0.02).

- The percentage of patients with PDC ≥80% was significantly greater among the UMEC/VLT cohort (28.6%) compared with the TIO/OLO cohort (27.2%); P=0.03).

- The adjusted odds of PDC ≥80% were 1.36 times higher among the UMEC/VLT cohort compared with the TIO/OLO cohort (95% CI: 1.24, 1.49; P=0.001).

Table 1: Pre-index patient demographics and clinical characteristics pre- and post-IPTW

<table>
<thead>
<tr>
<th>Variable</th>
<th>UMEC/VLT (n=54,149)</th>
<th>TIO/OLO (n=47,474)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>77.1 (11.2)</td>
<td>77.8 (11.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Gender, Male, %</td>
<td>61.3</td>
<td>60.4</td>
<td>0.01</td>
</tr>
<tr>
<td>CCI, mean (SD)</td>
<td>4.6 (3.8)</td>
<td>4.8 (3.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>CDS, mean (SD)</td>
<td>5.5 (3.7)</td>
<td>5.9 (4.3)</td>
<td>0.02</td>
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</table>

Figure 2. Patient enrollment

Figure 3. Non-inferiority and superiority of UMEC/VLT vs TIO/OLO on rescue medication use

Figure 3. Non-inferiority and superiority of UMEC/VLT vs TIO/OLO on rescue medication use

Compliance

In this real-world head-to-head comparison study within the LAMA/LABA class, patients initiating UMEC/VLT used significantly fewer units of rescue medication, meeting the pre-specified non-inferiority criteria, and had significantly higher adherence to their index medication than TIO/OLO initiators.

The real-world evidence provided by this study complements the findings of a head-to-head randomized trial that showed superior efficacy on key function and a reduction in rescue medication use with UMEC/VLT compared with TIO/OLO.

Conclusion

In this observational real-world study, UMEC/VLT was associated with significantly higher adherence to index therapy than TIO/OLO.

Disclosures

Drs. MI, RH, JD, HS, and AP were employees of Glaucus International (GI) and held stock options in GI, LSGB, and TIP. Dr. MI was also a consultant for LSGB and AP was a consultant for LSGB. Dr. RH was an employee of Optum at the time of the study which was contracted by GSK to conduct the study.

Acknowledgments

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