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

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Background

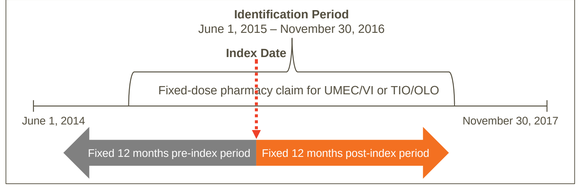
- The once-daily long-acting muscarinic antagonist/long-acting β_2-agonist (LAMA/LABA) combination treatments umeclidinium/vilanterol (UMEC/VI) and tiotropium/olodaterol (TIO/OLO) have been directly compared in a previous randomized controlled trial. The trial reported superiority on lung function and a reduction in patient-reported rescue medication use with UMEC/VI compared with TIO/OLO.[1]
- This observational real-world study aimed to evaluate rescue medication use and medication adherence among patients initiating therapy with UMEC/VI 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 ≥40 years of age from the Optum Research Database.
- Patients initiated UMEC/VI 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**).

Figure 1. Study design



- Patients were excluded if they had an inhaled 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/VI and TIO/OLO; multiple inhaler triple therapy (MITT; i.e. ICS, LABA, and LAMA); a claim for a non-index controller; 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 antagonists [SAMA]- or short-acting β_2-agonists [SABA]-containing medication) corresponds to one canister of a metered dose inhaler (i.e. 200 puffs) or approximately 100 doses of nebulized 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 a non-index controller medication or the end of the 12-month post-index period, whichever occurred first.

Statistical analyses

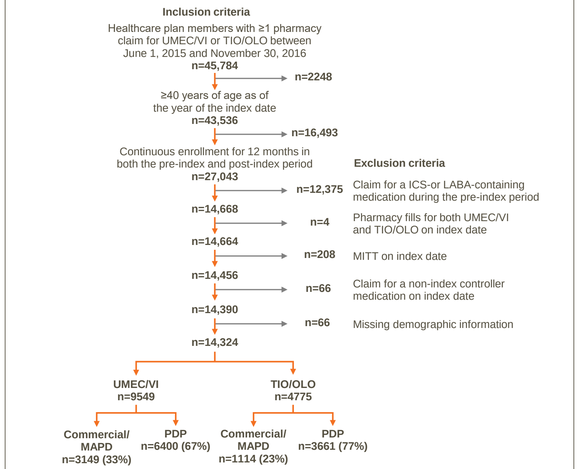
- Inverse probability of treatment weighting (IPTW) was utilized to balance pre-index characteristics between treatment cohorts, and multivariable modeling was used to adjust for residual imbalance of pre-index characteristics following IPTW.
- Rescue medication use was evaluated in an intent-to-treat (ITT) analysis assessing non-inferiority (with a margin of 0.30 units) and superiority (with a margin of 0 units) of UMEC/VI compared with TIO/OLO (primary objective).
  - Weighted ordinary least squares regression with bootstrapped standard errors, confidence intervals (CI) and *P*-values was used to model rescue medication use. The 95% CI and one-sided (α=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 9549 UMEC/VI and 4775 TIO/OLO initiators (**Figure 2**).
- Pre-index characteristics were similar between treatment cohorts after IPTW (**Table 1**).

Figure 2. Patient enrollment



MAPD, Medicare Advantage with Part D; PDP, Part D-only

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

	Pre-IPTW				Post-IPTW			
Variable	**UMEC/VI N=9549**	**TIO/OLO N=4775**	**Std diff (%)**	***P***	**UMEC/VI N=9549**	**TIO/OLO N=4775**	**Std diff (%)**	***P***
Age, mean (SD)	73.1 (9.5)	73.1 (8.5)	−0.72	0.681	73.0 (9.4)	73.4 (8.8)	−4.74	0.040
Male, %	46.9	46.9	0.03	0.986	47.0	46.0	1.93	0.351
Number of exacerbations*, †, mean (SD)	0.58 (0.95)	0.67 (1.10)	−8.07	0.025	0.60 (0.98)	0.60 (1.03)	−0.03	0.995
≥1 exacerbation*, †, n (%)	1211 (38.5)‡	446 (40.0)§	−3.23	0.353	1223 (38.8)‖	420 (37.7)**	2.41	0.590
CCI†, mean (SD)	2.0 (1.7)	2.2 (1.9)	−14.24	<0.001	2.03 (1.74)	2.09 (1.87)	−3.15	0.487
COPD Severity Score†, mean (SD)	24.1 (5.5)	25.6 (6.2)	−26.45	<0.001	24.4 (5.5)	24.4 (6.2)	0.36	0.942
Rescue medication units††, mean (SD)	3.8 (4.7)	4.2 (5.0)	8.83	<0.001	3.9 (4.8)	3.9 (4.8)	0.02	0.994
CDS, mean (SD)	5437.4 (3679.8)	5626.6 (3813.2)	5.05	0.005	5529.8 (3834.2)	5508.8 (3607.6)	0.56	0.790

*Exacerbations identified during the 12-month pre-index period, excluding the index date; †UMEC/VI: N=3149; TIO/OLO: N=1114; ‡Mod: 33.2%; Sev: 8.7%; §Mod: 34.7%; Sev: 10.1%; ‖Mod: 33.5%; Sev: 9.0%; **Mod: 32.7%, Sev: 8.5%; ††Inhaled+nebulized. Covariates with residual imbalance following IPTW that were included in the adjusted model were age (categorized), enhanced alternative, employer group pharmacy plan type, mail order index pharmacy fill, ≥90-day index fill, and baseline medication use (i.e. methylxanthine, nebulized SAMA, nebulized SABA, and nebulized SAMA/SABA).
CCI, Charlson Comorbidity Index; CDS, Chronic Disease Score; COPD, chronic obstructive pulmonary disease; IPTW, inverse probability of treatment weighting; Mod, moderate; SD, standard deviation; Sev, severe; Std diff, standardized difference

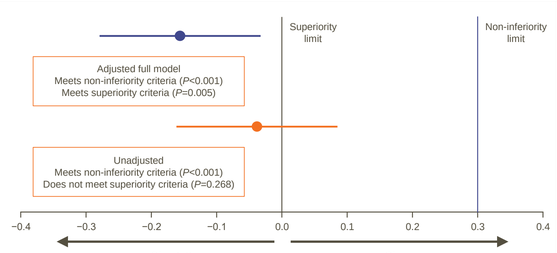
Rescue medication use

- During the 12-month post-index period, the mean (SD) rescue medication use was similar between UMEC/VI and TIO/OLO initiators (UMEC/VI: 1.87 [3.88] units; TIO/OLO: 1.91 [3.75] units; *P*=0.607).
  - In unadjusted analyses, UMEC/VI met the pre-specified non-inferiority criteria (−0.04 units; 95% CI: −0.16, 0.08; *P*<0.001) but did not meet superiority criteria (*P*=0.27).
  - After adjustment for residual imbalances between the cohorts, UMEC/VI initiators had fewer mean units of rescue medication per patient per year than TIO/OLO initiators (−0.16; 95% CI: −0.28, −0.04).
- In the adjusted ITT analysis, UMEC/VI met the pre-specified non-inferiority and superiority criteria (*P*<0.001 and *P*=0.005, respectively; **Figure 3**).

Medication adherence

- In the on-treatment analysis of medication adherence:
  - Mean (SD) PDC was significantly higher among UMEC/VI initiators compared with TIO/OLO initiators (UMEC/VI: 0.50 [0.33]; TIO/OLO: 0.47 [0.32]; *P*<0.001).
  - The percentage of patients with PDC ≥80% was significantly greater among the UMEC/VI cohort (28.6%) compared with the TIO/OLO cohort (22.7%; *P*<0.001).
  - The adjusted odds of PDC ≥80% were 1.36 times higher among the UMEC/VI cohort compared with the TIO/OLO cohort (95% CI: 1.24, 1.49; *P*<0.001).

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



The pre-specified non-inferiority and superiority margins were 0.30 and 0 units of rescue medication, respectively. One-sided (α=0.025) bootstrapped *P*-values were used to determine if the non-inferiority and superiority criteria were met; *P*<0.025 was considered statistical evidence that UMEC/VI was non-inferior and/or superior to TIO/OLO on units of rescue medication.

Limitations

- This study was dependent on codes contained in claims data, which do not guarantee that patients took their medication.
- Survivor bias may have been introduced by the requirement for patients to have been continuously enrolled for 12 months after the index date, which could exclude patients with more severe or advanced COPD who did not survive.

Conclusions

- In this real-world head-to-head comparison study within the LAMA/LABA class, patients initiating UMEC/VI used significantly fewer units of rescue medication, meeting the pre-specified superiority 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 lung function and a reduction in rescue medication use with UMEC/VI compared with TIO/OLO.[1]

Reference

1. Feldman GJ, et al. *Adv Ther* 2017;34(11):2518–33.

Disclosures

- CM, BH, RR, and RHS are employees of GlaxoSmithKline (GSK) and hold stocks/shares in GSK. LGSB, EK, LL, and JT are employees of Optum and LS was an employee of Optum at the time of the study, which was contracted by GSK to conduct the study.

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