Evaluation of Time-to-Triple Therapy in Patients Diagnosed With COPD Initiating Maintenance Therapy With a Fixed-Dose Combination of LAMA/LABA Versus ICS/LABA Within a Large US Health Insurer Database

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Background

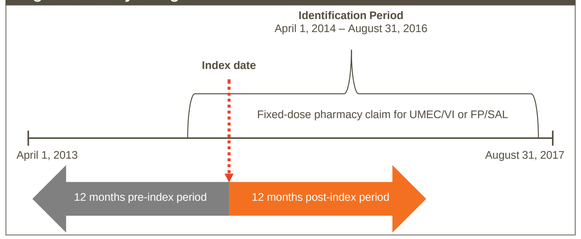
- Since 2017, Global initiative for chronic Obstructive Lung Disease (GOLD) strategy documents have recommended inhaled corticosteroid/long-acting β_2-agonist (ICS/LABA) as initial maintenance therapy for only a minority of patients.[1] Despite this, ICS/LABA fixed-dose combination therapy has continued to be a mainstay for patients initiating treatment for chronic obstructive pulmonary disease (COPD) in clinical practice.[2-4]
- Recent clinical trial data suggest that long-acting muscarinic antagonist (LAMA)/LABA combination treatment can significantly improve lung function and reduce exacerbation rates compared with ICS/LABA.[5,6] However, little is known about how this impacts escalation to multiple-inhaler triple therapy (MITT; ICS+LABA+LAMA).
- This study examined escalation to MITT in patients initiating LAMA/LABA compared with patients initiating ICS/LABA using real-world data.
- The primary objective of the study (previously presented) was to evaluate medication adherence, measured by proportion of days covered, of umeclidinium/vilanterol (UMEC/VI) and the ICS/LABA fluticasone propionate/salmeterol (FP/SAL) as initial maintenance therapy in patients diagnosed with COPD.[7]
- A secondary study objective (the focus of this poster) was to evaluate the incidence of escalating to MITT among patients diagnosed with COPD initiating maintenance treatment with UMEC/VI compared with FP/SAL.

Methods

Study design

- This was a retrospective observational study in a population of patients diagnosed with COPD enrolled in commercial or Medicare Advantage with Part D (MAPD) health plans using claims from the Optum Research Database.
- Patients ≥40 years of age who initiated once-daily UMEC/VI (62.5/25 mcg) or twice-daily FP/SAL (250/50 mcg) between April 1, 2014 and August 31, 2016 were identified. The index date was the first fill date for UMEC/VI or FP/SAL (**Figure 1**).

Figure 1. Study design



- Patients had 12 months of pre- and post-index continuous enrollment and at least one medical claim containing a COPD diagnosis code in any position during the pre-index period.
- Exclusion criteria were: an asthma diagnosis in the pre-index period or on the index date; ICS-, LABA-, or LAMA-containing therapy during the pre-index period; missing demographic information; or pharmacy fills for both UMEC/VI and FP/SAL, MITT, a non-index therapy, or a COPD exacerbation on the index date.
- MITT was defined as the occurrence of at least one day of overlapping supply of ICS, LABA, and LAMA.

Statistical analysis

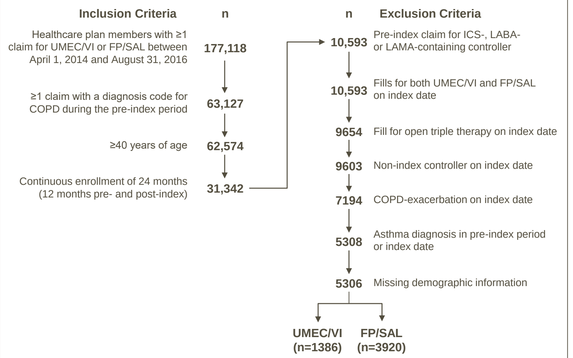
- Inverse probability of treatment weighting (IPTW) of pre-index characteristics was used to control for possible confounding of the association between study outcomes and index treatment.
- An intent-to-treat analysis using Kaplan–Meier and weighted Cox proportional hazards regression was performed. Variables that were not balanced following IPTW (standardized difference >0.10 or *P*-value <0.05) were included in the multivariable adjusted model.
- To test the proportional hazards assumption a proportional hazards test (log[time] with Schoenfeld residuals) was conducted.

Results

Study population

- A total of 1386 UMEC/VI and 3920 FP/SAL initiators met all study selection criteria (**Figure 2**).

Figure 2. Patient identification and attrition



- Following IPTW, most pre-index characteristics were adequately balanced between treatment groups (**Table 1**), although some variables remained unbalanced (methylxanthines use, short-acting muscarinic antagonist [SAMA] nebulized use, SAMA/short-acting β_2-agonist [SABA] combination inhaled units [categorized], all-cause inpatient costs [categorized], and all-cause other medical costs [categorized]).

Table 1. Demographics and pre-index clinical characteristics pre- and post-IPTW

Demographics	Pre-IPTW				Post-IPTW			
	UMEC/VI (N=1386)	FP/SAL (N=3920)	Std diff. (%)	*P*-value	UMEC/VI (N=1386)	FP/SAL (N=3920)	Std diff. (%)	*P*-value
Age, mean (SD)	68.52 (10.48)	69.49 (10.49)	−9.30	0.003	69.47 (10.59)	69.15 (10.53)	3.04	0.497
Female, %	45.31	53.62	−16.68	<0.001	50.99	51.50	−1.02	0.823
Insurance type								
Commercial, %	33.62	24.06	21.23	<0.001	26.94	26.76	0.40	0.920
MAPD, %	66.38	75.94	−21.23	<0.001	73.06	73.24	−0.40	0.920
Geographic region								
Northeast, %	14.43	17.70	−8.92	0.005	17.23	16.88	0.95	0.845
Midwest, %	26.77	31.63	−10.72	<0.001	30.62	30.29	0.72	0.878
South, %	51.37	41.10	20.72	<0.001	42.28	43.73	−2.93	0.510
West, %	7.43	9.57	−7.66	0.017	9.86	9.10	2.60	0.620
Charlson comorbidity score, mean (SD)	2.16 (1.66)	2.33 (1.78)	−10.07	0.001	2.31 (1.77)	2.30 (1.78)	0.42	0.928
Chronic disease score, mean (SD)	5077.14 (3743.13)	5316.92 (3632.34)	−6.50	0.036	5358.00 (3964.69)	5225.13 (3620.08)	3.50	0.496
COPD severity score, mean (SD)	23.86 (5.27)	24.04 (5.80)	−3.15	0.301	24.21 (4.97)	23.98 (6.03)	4.06	0.267
COPD exacerbations, %	33.19	30.26	6.31	0.042	32.83	31.15	3.61	0.409
COPD medication in pre-index period								
SABA, %	49.13	54.52	−10.79	<0.001	54.00	53.37	1.27	0.780
Systemic corticosteroids, %	48.56	47.88	1.35	0.666	47.63	48.06	−0.87	0.849

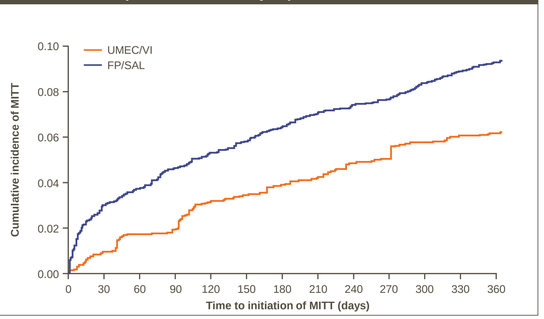
SD, standard deviation; Std diff., standard difference

- The post-IPTW mean (SD) age was 69.2 (10.6) years, 51.4% were female, and 73.2% were MAPD enrollees.

Incidence of escalation to MITT

- Over the 12-month post-index period, the MITT incidence rate was 0.02 and 0.03 per 100 person-days for UMEC/VI and FP/SAL initiators, respectively, with a weighted incidence rate ratio of 0.65 (95% confidence interval [CI]: 0.47, 0.90; *P*=0.010).
- The average adjusted risk of MITT initiation was 35% lower among UMEC/VI initiators versus FP/SAL initiators (hazard ratio [HR] 0.65; 95% CI: 0.47, 0.89; *P*=0.008) (**Figure 3**).
- Although the UMEC/VI and FP/SAL Kaplan–Meier curves do not cross during the 365-day post-index period (**Figure 3**), a proportional hazards test revealed that there was significant variation in the curves over this period (*P*=0.005).
  - During the first 90 days there was a significant difference in the adjusted rate of MITT initiation between cohorts (adjusted HR 0.41; 95% CI: 0.25, 0.67; *P*<0.001); The difference between cohorts was not significant during days 91–365 (adjusted HR 0.88; 95% CI: 0.58, 1.33; *P*=0.539).

Figure 3. Kaplan–Meier analysis of time to initiation of MITT in the UMEC/VI and FP/SAL cohorts (intent-to-treat analysis)



  - In a 30-day (monthly) analysis, UMEC/VI initiators had a significantly lower adjusted rate of MITT initiation compared with FP/SAL initiators in Months 1 (*P*<0.001), 3 (*P*=0.030), and 12 (*P*=0.022).

Limitations

- Limitations of this study include those typically associated with claims studies, including medication use being based on observed pharmacy dispensing, which may not be representative of the patients' actual drug-taking.

Conclusion

- Patients with COPD who initiate maintenance therapy with UMEC/VI have a 35% lower risk of MITT escalation compared with patients who initiated FP/SAL.
- Patients initiating UMEC/VI have previously been shown to have significantly higher medication adherence (measured by proportion of days covered) compared with FP/SAL, which may be related to the increased length of time observed for patients initiating UMEC/VI progressing to triple therapy compared with patients who initiated FP/SAL.[7]

References

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease; 2017; 2. Gruffydd-Jones K, et al. *Npj Prim Care Respir Med* 2016;26:16002; 3. Souliotis K, et al. *PLoS One* 2016;11(5):e0154960; 4. Drivenes E, et al. *BMC Fam Pract* 2014;15:42; 5. Horita N, et al. *Cochrane Database Syst Rev* 2017;2:CD012066; 6. Rodrigo GJ, et al. *Int J Chron Obstruct Pulmon Dis* 2017;12:907–22; 7. Moretz C, et al. *J Manag Care Spec Pharm* 2018;24(10):S1–S112.

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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