Evaluating Time-to-First COPD Exacerbation in Patients Diagnosed With COPD Initiating Maintenance Therapy With Inhaled Fixed-Dose Combinations of LAMA/LABA or ICS/LABA Within a Large US Health Insurer Database

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Background

- Initiated oral corticosteroids (ICS) with long-acting β2-agonist (LABA) combination therapies are currently prescribed across all Global Initiative for Chronic Obstructive Lung Disease (GOLD) severity levels.1
- Long-acting muscarinic antagonist (LAMA) monotherapy has been used as an initial maintenance therapy for highly symptomatic GOLD group D patients. 2

- Recent data from observational, nonrandomized studies using the LAMA/LABA combination therapies can significantly improve lung function and reduce exacerbation rates compared with ICS/LABA. 3
- Exacerbation rates in patients with chronic obstructive pulmonary disease (COPD) initiating maintenance therapy with ICS/LABA versus ICS/LABA have not previously been compared using real-world data.

- This retrospective study compared the use of the LAMA/LABA combinations (umeclidinium/vilanterol, (UMEC/VI), tiotropium/olodaterol [DPI/FI/SAL], all initial maintenance therapy in patients diagnosed with COPD.

- The primary objective of the study (methodology published) was to evaluate medication adherence, measured by proportion of days covered. 6

- A secondary objective of this paper was to evaluate time-to-first exacerbation among patients initiating UMEC/VI versus FPI/SAL.

Methods

Study design:

- A retrospective observational study in a population diagnosed with COPD enrolled in either commercial or Medicare Advantage (MA) or Medicare fee-for-service (FFS) health plans. Data from the Optum Research Database were utilized for this study.

Study population:

- Patients aged 40 years who initiated maintenance therapy with UMEC/VI or FPI/SAL between April 1, 2014 and August 31, 2016 were included. The index date was defined as the first date of treatment sensitivity analyses.

Figure 1. Study Design

- Patients had 12 months of pre- and post-index continuous enrollment.
- At least one medical claim containing a diagnosis of chronic obstructive pulmonary disease (COPD) during the pre-index period.
- Exclusion criteria included an asthma diagnosis in the pre-index period or on the index date. 7

Results

- Approximately 69% of patients with COPD initiating maintenance therapy during the pre-index period, mean, demographic, and clinical characteristics were similar between the two groups.

- Exacerbation rates were calculated using Kaplan-Meier and weighted Cox proportional hazards regression of time to first (ITT) and on-treatment (sensitivity) analyses. For the on-treatment analysis, patients were censored at the time of discontinuation, at the time of a pharmacy fill for a non-index controller medication, or at the end of the 12-month post-index period, whichever occurred first.

- Inverse probability of treatment weighting (IPTW) of pre-index characteristics was used to control for potential confounding of the association between study outcomes and index treatment.

- Kaplan-Meier and weighted Cox proportional hazards regression was performed in models with and without IPTW. Variables that were not balanced following IPTW (standardized difference ≥10 or Pearson χ2 was included in the multivariable adjusted model).

- Time-to-first moderate/severe exacerbation was evaluated in intent-to-treat (ITT) and on-treatment (sensitivity) analyses. For the on-treatment analysis, patients were censored at the time of discontinuation, at the time of a pharmacy fill for a non-index controller medication, or at the end of the 12-month post-index period, whichever occurred first.

- Following IPTW, most pre-index characteristics were adequately balanced between treatment groups (Table 1), although there were moderate unbalanced characteristics (mean difference in age using murine mucosal antigen [SAA] reduced salbutamol 0.87mg [SABA] combination therapies vs UMEC/VI), other medical costs [spacer].

- The post-ITPM mean, standard deviation (SD) age was 66.2 (14.5) years. 11.4% were female and 72.3%, were MAPF smokers. Approximately a third of patients experienced a COPD exacerbation in the pre-index period.

Table 1. Demographic and baseline characteristics pre-index and post-ITPM

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>UMEC/VI (n=4508)</th>
<th>FPI/SAL (n=5308)</th>
<th>Pre-ITPM adjustment</th>
<th>Post-ITPM adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.66 (14.5)</td>
<td>65.10 (14.3)</td>
<td>0.94 (0.21)</td>
<td>0.93 (0.20)</td>
</tr>
<tr>
<td>Female, %</td>
<td>27.5</td>
<td>26.9</td>
<td>0.72 (0.30)</td>
<td>0.73 (0.30)</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>54.0</td>
<td>57.2</td>
<td>0.75 (0.31)</td>
<td>0.75 (0.31)</td>
</tr>
<tr>
<td>Baseline symptom index (days)</td>
<td>33.62 (50.99)</td>
<td>30.26 (46.70)</td>
<td>0.036 (0.003)</td>
<td>0.036 (0.003)</td>
</tr>
<tr>
<td>Baseline exacerbation index (days)</td>
<td>12 (95)</td>
<td>11 (95)</td>
<td>0.928 (0.017)</td>
<td>0.928 (0.017)</td>
</tr>
</tbody>
</table>

Figure 3. Kaplan-Meier weighted Cox proportional hazards regression of time-to-first exacerbation (ITT) and FPI/SAL. (A) ITT and (B) Mortality sensitivity analyses

- Incidence of first ITT exacerbation

  - In the ITT analysis, the incidence rate for moderate/severe exacerbation per 100 person days was 69.47 (10.36); 95% CI, 65.02–74.46.

  - The adjusted hazard ratio (HR) of a moderate/severe exacerbation in the UMEC/VI cohort relative to the FPI/SAL cohort was 0.75 (95% CI, 0.59–0.98); p = 0.036.

  - The difference in HR for a severe COPD exacerbation per 100 person days was 0.62 (95% CI, 0.44–0.86).

- Incidence of first on-treatment exacerbation (sensitivity analysis)

  - For the on-treatment analysis, the incidence rate for moderate/severe exacerbation per 100 person days was 69.15 (10.53); 95% CI, 65.19–74.30.

  - The adjusted hazard ratio (HR) of a moderate/severe exacerbation in the UMEC/VI cohort relative to the FPI/SAL cohort was 0.75 (95% CI, 0.60–0.94); p = 0.017.

  - The difference in HR for a severe COPD exacerbation per 100 person days was 0.62 (95% CI, 0.50–0.78).

- The Kaplan-Meier weighted Cox proportional hazards regression with the FPI/SAL cohort (Figure 3).

Conclusions

- This study found that patients with COPD who initiated treatment with UMEC/VI had a numerically lower rate of first exacerbation. Patients who remained on treatment had a significant 30% reduced risk of a first exacerbation with FPI/SAL versus UMEC/VI.

- This finding may support the use of LAMA/LABA as a first-line therapy in symptomatic patients.

Acknowledgments

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References


Disclosures

- GSK holds patents and has equity interests in the development of combination therapies for moderate/severe COPD.
- All authors have no conflict of interest.
- Dr. C. Moretti is an employee of GSK at all times of the study, which was conducted by GSK.

Limitations

- Limitations of this study include those frequently associated with claims data studies, such as the reliability of diagnosis codes, and a potential sample bias resulting from the requirement for patients to have been enrolled for 12 months post-index.

- The findings may support the use of LAMA/LABA as a first-line therapy in symptomatic patients.