Comparative Real-World Effectiveness of Triple Therapy Versus Dual Bronchodilation on Lung Function Decline in Frequently Exacerbating Patients with COPD

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BACKGROUND

• The mainstay of therapeutic management in COPD is long-acting inhaled bronchodilators (LAMA and/or LABA)1
• Addition of Inhaled Corticosteroids (ICS) to LAMA+LABA is recommended in patients at risk for further exacerbations1
• Randomized controlled clinical trials (RCTs) have shown that patients on triple therapy (ICS+LAMA+LABA vs LAMA+LABA or TT) have a higher exercatory volume in 1 second (FEV1) after one year, compared to those using dual bronchodilation (LAMA+LABA or DB)2,3
• Part of the patients in the RCTs stepped down from ICS4

AIM

To compare the real world effectiveness of triple therapy with ICS+LAMA+LABA vs LAMA+LABA on lung function decline among frequently-exacerbating COPD patients.

DESIGN & METHODOLOGY

Design: Matched historical cohort study.

Data sources: The Clinical Practice Research DataLink (CPRD, www.cprd.com) and Optimum Patient Care Research Database (OPCRD, opcdr.co.uk)

Index date: step-up from no maintenance therapy or LAMA

• COPD diagnosis
• ≥ 2 exacerbations
• Age ≥ 40 years
• Smoker history
• No other chronic resp. conditions

Baseline period (1 year)

Outcome period

Figure 1 – Study design

Table 1 – Patient records selection flow

COPD diagnosis (read code)

Stopped up to LAMA+LABA or Triple therapy

Age ≥ 40 at diagnosis

Smoking history

≥ 2 exacerbations in baseline

≥ 2 FEV1 measurements during follow-up

Matched patients

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RESULTS

Table 2 – Characteristics of matched patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>LAMA/LABA (N=151)</th>
<th>Triple therapy (N=252)</th>
<th>Matched pair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.3 (7.5)</td>
<td>68.9 (7.9)</td>
<td>69.2 (7.9)</td>
</tr>
<tr>
<td>Male gender</td>
<td>105 (69.7)</td>
<td>130 (51.7)</td>
<td>119 (59.7)</td>
</tr>
<tr>
<td>GOLD Grade</td>
<td>3 (2)</td>
<td>1 (0)</td>
<td>1 (0)</td>
</tr>
<tr>
<td>Exacerbations</td>
<td>329 (22.4)</td>
<td>368 (21.5)</td>
<td>355 (22.9)</td>
</tr>
<tr>
<td>LAMA use</td>
<td>97 (64.3)</td>
<td>239 (43.4)</td>
<td>231 (43.4)</td>
</tr>
<tr>
<td>Smoking status</td>
<td>55 (36.7)</td>
<td>131 (25.1)</td>
<td>127 (25.1)</td>
</tr>
<tr>
<td>Blood eosinophil count, most recent within 5 years</td>
<td>56 (37.2)</td>
<td>83 (71.9)</td>
<td>76 (71.9)</td>
</tr>
</tbody>
</table>

Statistical analysis:

Multilevel model for change, where the intercept and slope (rate of FEV1 decline over time) were modelled as random effects (allowing these to vary across individuals). The level-2 component was the mean population difference in lung function decline with therapy. A time-varying predictor of treatment was used, representing the last therapy kind the patient was on in the 120 days preceding each FEV1 measurement. Therefore, estimates for other therapies than TT or DB are also available.

Table 2 – Characteristics of matched patients

Table 3 – FEV1 trajectories and average rates of decline by therapy, with 95% confidence intervals

CONCLUSION

We observed a reduction of lung function decline with TT compared to DB of 15.2 mL (-23.3, 32.8) consistent with the results supporting the efficacy of TT from RCTs. This difference was more prominent in current smokers.

Effect modification

Age at index date, gender and blood eosinophil count did not modify the effect of treatment on lung function decline significantly. Smoking status at baseline did modify the comparative effectiveness significantly (P=0.044); the difference between TT and DB was 20 mL/year larger in current smokers compared to former smokers.

Figure 3 – Predicted FEV1 trajectories, by smoking status and therapy, with 95% confidence intervals

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