TiO TROPIUM + O LO DATEROL SHOWS CLINICALLY MEANINGFUL IMPROVEMENTS IN QUALITY OF LIFE VERSUS PLACEBO

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Disclosures – consultant: Boehringer Ingelheim, Meda, Mylan, Teva; Speaker Bureau: Boehringer Ingelheim, Meda, Mylan, Teva, Thermo Fisher Scientific; organizational: former AAPA liaison to NIH/NAEPP-CC, current AAPA liaison to NIH/NIAID-food allergy, peanut allergy prevention-CC

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Introduction

Background

• Combination therapies are recommended for treatment of moderate to severe COPD¹

• Stiolto®, the combination of tiotropium (a LAMA) plus olodaterol (a LABA), is approved for once-daily maintenance treatment in COPD

• Data from the Phase III TONADO® studies of tiotropium + olodaterol demonstrated significant improvements in lung function compared to monocomponents, with no additional safety concerns²

Aim

• To evaluate quality of life and lung function after 12 weeks of treatment with tiotropium + olodaterol (2.5/5 µg; 5/5 µg) and tiotropium (5 µg) compared to placebo in patients with moderate to severe COPD

LAMA, long-acting muscarinic antagonist; LABA, long-acting β₂-agonist

OTEMTO® 1 and 2 study design and methods

- OTEMTO® 1 (NCT01964352) and 2 (NCT02006732) were replicate, randomized, double-blind, parallel-group, placebo-controlled, Phase IIIb studies.

- Patients were aged ≥40 years with a diagnosis of moderate to severe COPD (GOLD 2–3).

- Primary end points measured at 12 weeks were:
  - SGRQ total score
  - FEV₁ AUC₀–₃ response (change from baseline)
  - Trough FEV₁ response

- Data are presented for tiotropium + olodaterol 5/5 µg and tiotropium 5 µg (licensed doses).

R, randomization; GOLD, Global initiative for chronic Obstructive Lung Disease; SGRQ, St. George’s Respiratory Questionnaire; FEV₁, forced expiratory volume in 1 s; AUC₀–₃, area under the curve from 0 to 3 h.
## Demographics and baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>OTEMTO® 1</th>
<th>OTEMTO® 2</th>
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<tbody>
<tr>
<td>Patients, n</td>
<td>812</td>
<td>809</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>481 (59.2)</td>
<td>506 (62.5)</td>
</tr>
<tr>
<td>Mean (SD) age, years</td>
<td>64.9 (8.4)</td>
<td>64.6 (8.4)</td>
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<tr>
<td>Smoking status, n (%)</td>
<td></td>
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<tr>
<td>Ex-smoker</td>
<td>417 (51.4)</td>
<td>441 (54.5)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>395 (48.6)</td>
<td>368 (45.5)</td>
</tr>
<tr>
<td>Mean (SD) pre-bronchodilator FEV₁, L</td>
<td>1.333 (0.496)</td>
<td>1.361 (0.488)</td>
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<tr>
<td>Mean (SD) post-bronchodilator FEV₁, L</td>
<td></td>
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<tr>
<td>FEV₁, L</td>
<td>1.521 (0.509)</td>
<td>1.551 (0.499)</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>55.3 (12.8)</td>
<td>54.9 (12.8)</td>
</tr>
<tr>
<td>GOLD, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1 (0.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>2</td>
<td>529 (65.1)</td>
<td>513 (63.4)</td>
</tr>
<tr>
<td>3</td>
<td>278 (34.2)</td>
<td>292 (36.1)</td>
</tr>
<tr>
<td>4</td>
<td>4 (0.5)</td>
<td>4 (0.5)</td>
</tr>
<tr>
<td>Baseline pulmonary medication, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>639 (78.7)</td>
<td>601 (74.3)</td>
</tr>
<tr>
<td>ICS</td>
<td>311 (38.3)</td>
<td>297 (36.7)</td>
</tr>
<tr>
<td>LAMA</td>
<td>285 (35.1)</td>
<td>275 (34.0)</td>
</tr>
<tr>
<td>SAMA</td>
<td>72 (8.9)</td>
<td>52 (6.4)</td>
</tr>
<tr>
<td>LABA</td>
<td>309 (38.1)</td>
<td>320 (39.6)</td>
</tr>
<tr>
<td>SABA</td>
<td>420 (51.7)</td>
<td>398 (49.2)</td>
</tr>
</tbody>
</table>

Data are for treated population

ICS, inhaled corticosteroid; SAMA, short-acting muscarinic antagonist; SABA, short-acting β-agonist
**FEV₁ AUC₀⁻³ and trough FEV₁ responses after 12 weeks**

Data are for the full analysis set

* *p<0.0001 vs placebo

**FEV₁ AUC₀⁻³ response**

- **Tiotropium 5 µg**
- **Tiotropium + olodaterol 5/5 µg**

**Trough FEV₁ response**

- **Tiotropium 5 µg**
- **Tiotropium + olodaterol 5/5 µg**
**SGRQ total score responses after 12 weeks**

- **SGRQ responders** (improvement ≥4.0 units)
- Placebo
- Tiotropium 5 µg
- Tiotropium + olodaterol 5/5 µg

**Change from baseline in SGRQ total score**

- **SGRQ responders (%)**

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**p<0.01; ***p<0.0001 vs placebo;**

++ p<0.01 vs tiotropium 5 µg (nominal p value)

SGRQ data combined from OTEMTO® 1 and 2

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**p<0.01; ***p<0.0001 vs placebo;**

+ p<0.05 vs tiotropium 5 µg (nominal p value)
Safety and conclusions

These studies showed that tiotropium + olodaterol 5/5 µg produced a clinically meaningful improvement in quality of life versus placebo, while confirming its effects on lung-function parameters and safety.

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=406)</th>
<th>Tiotropium 5 µg (n=406)</th>
<th>Tiotropium + olodaterol 5/5 µg (n=405)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All adverse events (AEs), n (%)</td>
<td>198 (48.8)</td>
<td>183 (45.1)</td>
<td>178 (44.0)</td>
</tr>
<tr>
<td>Treatment-related\textsuperscript{a} AEs, n (%)</td>
<td>22 (5.4)</td>
<td>13 (3.2)</td>
<td>18 (4.4)</td>
</tr>
<tr>
<td>AEs leading to discontinuation, n (%)</td>
<td>21 (5.2)</td>
<td>10 (2.5)</td>
<td>4 (1.0)</td>
</tr>
<tr>
<td>Serious AEs, n (%)</td>
<td>15 (3.7)</td>
<td>18 (4.4)</td>
<td>16 (4.0)</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Investigator defined
Safety data combined from OTEMTO\textsuperscript{®} 1 and 2