Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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1. ABSTRACT

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: *Stiolto® Respimat®; Anoro® Ellipta®*			
Name of active ingredient: Olodaterol and Tiotropium Bromide *(ATC R03AL06);* Umeclidinium and Vilanterol (ATC R03AL03)			
Report date: DD Month YYYY	**Study number:** 1237-0090	**Version/Revision:**	**Version/Revision date:**
Title of study:	The Role of Inhaler Device in the Treatment Persistence with Dual Bronchodilators in Patients with COPD		
Keywords:	*COPD, non-interventional study, treatment persistence*		
Rationale and background:	Adherence to COPD therapies involves patients initiating their prescribed therapy, implementing it as prescribed (i.e., correctly administering the prescribed dose at the physician directed frequency), and persisting with treatment **(P19-09366; R18-2765).** Inadequate peak inspiratory flow rates to use many dry-powder inhalers (DPIs) may lead to improper inhalation that prevents successful drug delivery to the lungs, which may affect treatment efficacy or treatment adherence. The question if different devices, DPI and Soft Mist Inhalers (SMI), played a role in treatment persistence remains to be answered. In this study we aimed to compare the persistence in using two different medications from the same drug class (LAMA/LABA FDC) which are delivered through different devices, a DPI and an SMI.		
Research question and objectives:	In the present study we aimed to evaluate whether persistence of two combination therapies in same drug class (LAMA/LABA as a fixed dose combination) delivered through different devices (a DPI or an SMI) differ. We therefore compared relative treatment persistence between patients prescribed *Olodaterol/Tiotropium Bromide* delivered with the Respimat SMI and *Umeclidinium/Vilanterol* delivered with the Ellipta DPI using a 1:2 propensity score matched analysis within an administrative claims database in the US.		
Study design:	New-user cohort design with propensity scores used to match up to 2 *Umeclidinium/Vilanterol* initiators to each *Olodaterol/Tiotropium Bromide* initiator.		
Setting:	Data was utilized from Truven MarketScan claims database that captures longitudinal, individual-level administrative claims data from the United States. Patient identification period was between 17 November 2015 and 31 March 2018.		

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Subjects and study size, including dropouts:	Patients initiating *Olodaterol/Tiotropium Bromide* or *Umeclidinium/ Vilanterol* between 17 November 2015 and 31 March 2018 built the pre-matched cohort. The following exclusion criteria were applied: • Aged <40 years. • Enrolment with medical and pharmacy coverage prior to the cohort entry < 180 days. • Never had COPD diagnosis on the cohort entry date or prior to cohort entry. • A record for dispensed *Olodaterol/Tiotropium Bromide* delivered with Respimat inhalator or *Umeclidinium/Vilanterol* delivered with the Ellipta Inhaler during the 180-day baseline prior to cohort entry. • Diagnosis of asthma any time prior to cohort entry. • Diagnosis of lung cancer any time prior to cohort entry. • Diagnosis of lung transplant any time prior to cohort entry. There were 14,751 new users of *Olodaterol/Tiotropium Bromide* or *Umeclidinium/Vilanterol* who satisfied the inclusion criteria. Among them, 3,889 initiated *Olodaterol/Tiotropium Bromide* and 10,862 initiated *Umeclidinium/ Vilanterol*).		
Variables and data sources:	**Exposures** • *Olodaterol/Tiotropium Bromide* (Stiolto®) delivered via Respimat inhaler • *Umeclidinium/Vilanterol* (Anoro®) delivered via Ellipta Inhaler **Outcome** Discontinuation of index treatment (*Olodaterol/Tiotropium Bromide* or *Umeclidinium/Vilanterol*), defined as persistence of treatment (no refill claim within 60 days (allowable grace period) after end of <n> days supply). Addition of another drug will not count as a discontinuation. **Covariates**		

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	Information on demographics, concomitant medications, comorbidities/symptoms, lifestyle and respiratory function procedures were collected. All data was utilized from Truven MarketScan claims database.		
Results:	The rate of discontinuation was 1,826 per 1,000 person-years in the Olo/Tio group compared to 1,647 per 1,000 person-years in the reference group resulting in a rate difference of appr. 179 per 1,000 person-years. The adjusted hazard ratio of discontinuation associated with Olo/Tio relative to Umec/Vi was 1.11 (95% CI: 1.06-1.16). Different sensitivity analyses did not have a meaningful impact on the results.		
Discussion:	Discontinuation of treatment was slightly higher in users of Olo/Tio delivered with the Respimat soft mist inhaler than in those of Umec/Vi delivered with the Ellipta dry powder inhaler. The clinical meaning of the differences is not clear so far.		
Marketing Authorisation Holder(s):	Boehringer Ingelheim International GmbH Binger Straße 173 55216 Ingelheim am Rhein, Germany		
Names and affiliations of principal investigators:	[redacted] MPH, PhD [redacted]		

[redacted]
[redacted]