STUDY REPORT SYNOPSIS

Real-World Treatment Patterns and Patient reported outcome in COPD (REMIND)

A secondary database study using COPD cohort study in Japan to investigate health status of COPD patients with different inhaler treatment

Milestones: [redacted]

Phase of development: Post-Marketing

Sponsor: AstraZeneca

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This study was performed in accordance with ethical principles that are consistent with the Declaration of Helsinki and "Ethical Guidelines for Medical and Biological Research Involving Human Subjects".

Background/rationale: Chronic obstructive pulmonary disease (COPD) is a complex and progressive respiratory disease characterized by expiratory airflow limitation. According to World Health Organization (WHO), COPD is the third leading cause of death worldwide, causing 3.23 million deaths in 2019. In Japan, although more than 5 million of patients are estimated to have COPD, the large of the population are under-diagnosed and under-treated. In Japan, triple therapy (inhaled corticosteroid [ICS]+long acting muscarinic antagonist [LAMA]+long acting β2 agonist [LABA]) has been added to the algorithm of stable COPD management in addition to LAMA and LABA by the latest COPD guideline published in 2022 by Japanese Respiratory Society (JRS). Specifically, the guideline recommends that for COPD patients who are still symptomatic and/or have frequent exacerbations with current treatment to receive step up treatment, such as from single (LAMA) therapy to dual bronchodilator (LAMA+LABA) therapy, or from dual (LAMA+LABA or ICS+LABA) therapy to triple (ICS+LAMA+LABA) therapy in alignment with the recommendation by Global Initiative for Chronic Obstructive Lung Disease (GOLD). Although many physicians believe that improvement of symptoms is important in COPD treatment, previous reports in Japan showed that more than 70% of COPD patients receiving regular COPD treatment had persistent symptom in the real-world. This indicates that many physicians may not recognize the real patient symptoms and, as a result, continue to prescribe the same medications. Furthermore, over the past decade, the number of inhalation therapy options have increased, but patients are reporting COPD symptoms even though receiving each inhalation treatment in real-world settings has not been extensively evaluated. In addition, the escalation of inhaler treatment and subsequent change in symptoms in symptomatic COPD patients is unknown. This retrospective observational study aims to report distribution of the proportion of symptomatic COPD patients classified by the COPD Assessment Test (CAT) managed with single or dual inhaler treatment using the data at cohort entry in the COPD cohort study, and treatment change and longitudinal CAT score by each inhaler treatment was also evaluated using the data during the follow-up period.

Objectives:

Primary objective:

1) To describe the proportion of symptomatic (CAT ≥10) and non-symptomatic (CAT <10) COPD patients in each of 3 different inhaler treatment categories* at cohort entry

Secondary objectives:

1) To describe changes of inhaler treatment categories during 1-year follow-up period in symptomatic (CAT ≥10)/non-symptomatic (CAT <10) COPD patients by 3 different inhaler treatment categories* at cohort entry
2) To describe the COPD symptom status assessed with the CAT after 1-year follow-up period in symptomatic (CAT ≥10)/non-symptomatic (CAT <10) COPD patients by 3 different inhaler treatment categories* at cohort entry
3) To describe the change of COPD symptom status assessed with the CAT after 1-year follow-up period by 3 different inhaler treatment categories* at cohort entry

Exploratory objectives:

1) To describe the level of dyspnea by each of 3 different inhaler treatment categories* at cohort entry
2) To describe the proportion of the CAT severity categories (0–9, 10–19, 20–29 and 30–40) in COPD patients by each of 3 different inhaler treatment categories* at cohort entry
3) To describe the proportion of COPD patients with minimally symptoms (categorized with combination of CAT [0–9, 10–19, 20–29, 30–40] and modified Medical Research Council [mMRC] [0–1, ≥2]) by each of 3 different inhaler treatment categories* at cohort entry
4) To describe the proportion of symptomatic/non-symptomatic COPD patients during coronavirus disease 2019 (COVID-19) pandemic (from March 2020 to at the end of the COPD cohort study) by each of different inhaler treatment categories* at cohort entry
5) To describe the proportion of symptomatic/non-symptomatic COPD patients during COVID-19 pandemic (from March 2020 to at the end of the COPD cohort study) by each

of 3 different inhaler treatment categories* at 2-year follow-up
6) To describe the change of COPD symptom status assessed with CAT during COVID-19 pandemic (from March 2020 to at the end of the COPD cohort study) by 3 different inhaler treatment categories* at cohort entry

* LAMA, LAMA+LABA or ICS+LABA

Study design: Retrospective, observational study to investigate longitudinal COPD symptoms and change of inhaler treatment categories (LAMA, LAMA+LABA or ICS+LABA) during follow-up period in COPD patients registered in the COPD cohort study.

Data source: The data derived from the COPD cohort study (NCT03577795) which were consisted of the enrollment period (from June 2018 to December 2018) and maximum 2-year follow-up period.

Study population: The COPD patients received the following inhaler treatments at cohort entry; LAMA, LAMA+LABA or ICS+LABA.

Inclusion criteria:
1) Patients receiving any of following inhaler treatments; LAMA, LAMA+LABA (both single and dual inhaler) or ICS+LABA (both single and dual inhaler) at cohort entry

Exclusion criteria:
1) Patients enrolled at the sites participating in the COPD cohort study where there was no agreement on secondary use of data for this study

Statistical methods: All analysis was performed in the full analysis set (FAS) that included all patients who met the inclusion criteria and did not meet the exclusion criteria.
This study was a descriptive study, and no comparative test was conducted. In general, for categorical variables, number and percentage of patients were calculated. For quantitative variables, number of patients, mean, standard deviation (SD), median, maximum, minimum and quartiles were calculated.
For the primary objective, proportion of COPD patients with CAT (≥10, <10) at cohort entry per inhaler treatment categories were tabulated with 95% Clopper-Pearson confidence interval (CI). For the secondary objectives, proportion of COPD patients with changes of inhaler treatment after 1 year per CAT (≥10, <10) and inhaler treatment categories (objective 1), and proportion of COPD patients with CAT (≥10, <10) at 1-year follow-up were analyzed in the same manner as the primary objective.

Results: A total of 414 patients were included in FAS. Among them, 76 patients were treated with LAMA, 261 patients were treated with LAMA+LABA, and 77 patients were treated with ICS+LABA. When calculating the proportions of patients below, the denominator was the number of patients excluding missing patients subtracted from the number of included patients.
The proportion of patients with CAT ≥10 at cohort entry was 32.9% [95% CI: 22.5%–44.6%] (25/76 patients) in patients treated with LAMA, 55.0% [95% CI: 48.7%–61.2%] (143/260 patients) in patients treated with LAMA+LABA, and 50.0% [95% CI: 38.3%–61.7%] (38/76 patients) in patients treated with ICS+LABA. The proportion of patients with CAT <10 at cohort entry was 67.1% [95% CI: 55.4%–77.5%] (51/76 patients) in patients treated with LAMA, 45.0% [95% CI: 38.8%–51.3%] (117/260 patients) in patients treated with LAMA+LABA, and 50.0% [95% CI: 38.3%–61.7%] (38/76 patients) in patients treated with ICS+LABA.
In patients with CAT ≥10 at cohort entry, the proportion of patients with a step up in their inhaler treatment category after 1 year was 12.0% (3/25 patients) in patients treated with LAMA, 10.5% (15/143 patients) in patients treated with LAMA+LABA, and 5.3% (2/38 patients) in patients treated with ICS+LABA. The proportion of patients whose inhaler treatment category remained uncharged after 1 year was 76.0% (19/25 patients) in patients

treated with LAMA, 81.8% (117/143 patients) in patients treated with LAMA+LABA, and 84.2% (32/38 patients) in patients treated with ICS+LABA. No step down in inhaler treatment category after 1 year was reported in patients treated with LAMA+LABA, or ICS+LABA. The proportion of patients without inhaler treatment after 1 year was 12.0% (3/25 patients) in patients treated with LAMA, 7.7% (11/143 patients) in patients treated with LAMA+LABA, and 10.5% (4/38 patients) in patients treated with ICS+LABA.
In patients with CAT <10 at cohort entry, the proportion of patients with a step up in their inhaler treatment category after 1 year was 11.8% (6/51 patients) in patients treated with LAMA, 12.0% (14/117 patients) in patients treated with LAMA+LABA, and 5.3% (2/38 patients) in patients treated with ICS+LABA. The proportion of patients whose inhaler treatment category remained uncharged after 1 year was 82.4% (42/51 patients) in patients treated with LAMA, 82.9% (97/117 patients) in patients treated with LAMA+LABA, and 89.5% (34/38 patients) in patients treated with ICS+LABA. No step down in inhaler treatment category after 1 year was reported in patients treated with LAMA+LABA, or ICS+LABA. The proportion of patients without inhaler treatment after 1 year was 5.9% (3/51 patients) in patients treated with LAMA, 5.1% (6/117 patients) in patients treated with LAMA+LABA, and 5.3% (2/38 patients) in patients treated with ICS+LABA.
In addition, in patients with CAT ≥10 at cohort entry, the proportions of patients with CAT ≥10 and CAT <10 after 1 year were 84.2% [95% CI: 60.4%–96.6%] (16/19 patients) and 15.8% [95% CI: 3.4%–39.6%] (3/19 patients), respectively, in patients treated with LAMA, 73.6% [95% CI: 64.8%–81.2%] (89/121 patients) and 26.4% [95% CI: 18.8%–35.2%] (32/121 patients), respectively, in patients treated with LAMA+LABA, and 66.7% [95% CI: 46.0%–83.5%] (18/27 patients) and 33.3% [95% CI: 16.5%–54.0%] (9/27 patients), respectively, in patients treated with ICS+LABA. In patients with CAT <10 at cohort entry, the proportions of patients with CAT ≥10 and CAT <10 after 1 year were 13.0% [95% CI: 4.9%–26.3%] (6/46 patients) and 87.0% [95% CI: 73.7%–95.1%] (40/46 patients), respectively, in patients treated with LAMA, 30.4% [95% CI: 21.7%–40.3%] (31/102 patients) and 69.6% [95% CI: 59.7%–78.3%] (71/102 patients), respectively, in patients treated with LAMA+LABA, and 20.7% [95% CI: 8.0%–39.7%] (6/29 patients) and 79.3% [95% CI: 60.3%–92.0%] (23/29 patients), respectively, in patients treated with ICS+LABA.
The mean changes (SD) in the CAT scores from cohort entry to 1-year follow-up were almost unchanged in each category (0.2 [4.3] in patients treated with LAMA, 0.6 [5.9] in patients treated with LAMA+LABA, and 0.0 [5.9] in patients treated with ICS+LABA, respectively).

Conclusion: This study showed that there were patients whose symptoms persisted (defined as CAT ≥10) although the study population was COPD patients treated with inhaler treatment. In addition, many symptomatic patients with COPD using inhaler treatment remained on the same treatment without escalation at 1-year follow-up and remained symptomatic.
There is a need to review patients' symptoms and adjust treatment including escalation regularly.

Publications:
Not applicable