Observational Study Report Synopsis

Study Code	D589BR00033
Version	1.0
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Research Study in patients with COPD in high risk population in Japan: Proportion of overlap between COPD and asthma, and the relationship with COPD exacerbation

Sponsor: AstraZeneca K.K.

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Background/Rationale:

Asthma-COPD overlap syndrome (ACOS) was recently described by a joint project of The Global Initiative for Asthma (GINA) and The Global Initiative for Chronic Obstructive Lung Disease (GOLD). Using this GINA-GOLD approach, we investigated the proportion of ACOS in COPD patients and the clinical characteristics of patients with ACOS, including exacerbation history and eosinophilic inflammation compared to patients with COPD alone.

Objectives and Hypotheses:

(a) Primary objective

To clarify the proportion of ACOS defined by GINA and GOLD in patients with COPD receiving outpatient treatment and follow-up by physicians in Japan.

(b) Main secondary objectives

1. To explore the features of history of COPD exacerbations, symptoms, eosinophilic inflammation and patient background in patients with ACOS.
2. To clarify the history of COPD exacerbations in patients with COPD.
3. To evaluate the degrees of eosinophilic inflammation of the respiratory tract in patients with COPD.
4. To evaluate the symptoms in patients with COPD.

Study Design:

Cross-sectional survey

Patients:

- Outpatients in each center were recruited according to a protocol regulating consecutive recruitment.

- Inclusion criteria: physician-diagnosed COPD ($FEV_1/FVC < 0.7$ confirmed by past medical records); age ≥40 years at time of COPD diagnosis; current or ex-smoker with

a history of ≥10 pack-years; past (≥1 year) medical records detailing COPD (including spirometry results); and the availability of either spirometry data from at least two different time-points excluding any with COPD exacerbations during the previous 3 years or airway reversibility test results.

- Major exclusion criteria: current COPD exacerbations; past/present history of lung cancer; current enrolment in any other interventional study/clinical trial; and unable to understand the study procedure/answer the questionnaires.

Methods:

A multicenter, cross-sectional study using data from the medical records of COPD patients with follow-up by physicians was performed in 38 Japanese sites (NCT02413359). Each site recruited outpatients with physician-diagnosed COPD, a smoking history ≥10 pack-years and lung function data in their medical records, according to the protocol regulating consecutive recruitment. ACOS patients were identified as having ≥3 symptomatic features of asthma and/or variability of FEV1 (≥12% and ≥200mL (primary definition, PD) or ≥12% and ≥400mL (secondary definition, SD).

Results:

A total of 1,008 COPD patients (mean age, 73.5 years; mean FEV1, 56.71% of predicted normal; mean pack-years, 56.9 pack-years) were included in the analysis set. 59.0% and 32.5% of the patients were classified as ACOS according to PD and SD, respectively. There was no statistically significant difference in the COPD exacerbation rate over the previous year between the ACOS and COPD alone groups (exacerbation rate per year, 0.4891 vs. 0.5109 for PD, 0.4939 vs. 0.5000 for SD). The percentage of blood eosinophils was higher in patients with ACOS compared with COPD alone patients (mean percentage, 3.96% vs. 3.19%, P=0.0003 for PD; 4.37% vs. 3.31%, P<0.0001 for SD). Although FeNO levels showed no significant difference between the ACOS and COPD alone groups under PD, there was a statistically significant difference in the ACOS group compared to the COPD alone group under SD (mean value, 31.82ppb vs. 24.48ppb, P=0.0183). The ACOS group was younger, had higher BMI, better lung function and shorter duration of COPD than the COPD alone group.