

Supplementary data

Table S1. List of study endpoints

Item	Endpoint
Primary	
1	The proportion of patients diagnosed with ACO at least once at the time of registration, 1 year later, and 2 years later among all patients
2	The numbers and proportions of patients diagnosed with ACO and non-ACO, among patients having the data necessary for ACO diagnosis at registration
Secondary	
1	Comparison of patient demographics, clinical characteristics, symptoms, and the results of examinations/tests required for the diagnostic criteria for ACO at the time of registration, among patients diagnosed with ACO, those diagnosed with non-ACO, and those patients lacking the data necessary for definitive ACO diagnosis at the time of registration
	Evaluations:
	<ul style="list-style-type: none">• Patient demographics (sex, BMI, age, smoking history, family history of allergic diseases [within the second-degree relative excluding his/her partner], past history of allergic disease [including history of asthma before and after 40 years old], FEV₁/FVC after inhalation of a bronchodilator, duration of COPD, comorbidity/concomitant disease, COPD stage, and medication)• Clinical characteristics (presence or absence of emphysema on CT, presence or absence of lung diffusion impairment [%D_{LCO} < 80% or %D_{LCO}/V_A < 80%], the frequency of exacerbation events in the past year, proportion of patients with exacerbation, severity of exacerbation, and FEV₁ after bronchodilator administration)• Symptoms (questionnaire scores [ACQ, CAT, and mMRC], presence or absence of symptoms [variable and paroxysmal] based on interview)• Implementation of examinations/tests required for the ACO diagnostic criteria (concomitant perennial allergic rhinitis, airway reversibility, peripheral blood eosinophil count, FeNO, total IgE, and specific IgE to perennial inhalant antigens)

2 Comparison of patient demographics, clinical characteristics, symptoms, and the implementation rate and results of examinations/tests required for the diagnostic criteria for ACO at each time point (registration, 1 year, 2 years) between patients diagnosed with ACO at the time of registration and those diagnosed with non-ACO consistently throughout 2 years

Evaluations:

- Patient demographics (sex, BMI, age, smoking history, family history of allergic diseases [within the second-degree relative excluding his/her partner], past history of allergic disease [including history of asthma before and after 40 years old], FEV₁/FVC after inhalation of a bronchodilator, duration of COPD, comorbidity/concomitant disease, COPD stage, medication, and duration of asthma)
- Clinical characteristics (number and frequency of exacerbation events in the past year, proportion of patients with exacerbation, severity of exacerbation, and FEV₁ after bronchodilator administration)
- Symptoms (questionnaire scores [ACQ, CAT, and mMRC] and presence or absence of symptoms [variable and paroxysmal] based on interview)
- Implementation of examinations/tests required for the ACO diagnostic criteria (concomitant perennial allergic rhinitis, peripheral blood eosinophil count, and FeNO)

3 Comparison of patient demographics, clinical characteristics, symptoms, and the results of examinations/tests required for the diagnostic criteria for ACO at the time of registration between the following patient groups:

(i) Those diagnosed with ACO for at least one time point (registration, 1 year, 2 years) during the study, and those diagnosed with non-ACO consistently throughout 2 years

(ii) Those diagnosed with ACO consistently throughout 2 years, those diagnosed with non-ACO consistently throughout 2 years, and those who transitioned from non-ACO to ACO during the study

Evaluations:

- Evaluations are identical to those specified for secondary endpoint 1

4 The ratio of patients who underwent examinations/tests required for each ACO diagnostic criterion and the ratio of patients who met each criterion ($[\text{number of patients who met each ACO diagnostic criterion}]/[\text{number of patients tested}]$) at each time point (registration, 1 year, 2 years) for the patient group diagnosed with ACO, the group diagnosed with non-ACO, and in the population lacking the data necessary for ACO diagnosis at the time of registration. In the latter group, the reasons for the lack of available data will also be investigated

5 Comparison of the symptoms and the results from examinations/tests required for the ACO diagnostic criteria, between patients with and without change in the ACO diagnosis at the time of registration and 1 year later, for each of the following groups:

(i) Those diagnosed with ACO and non-ACO at 1 year, among patients diagnosed with ACO at the time of registration

(ii) Those diagnosed with non-ACO and ACO at 1 year, among patients diagnosed with non-ACO at the time of registration

Evaluations:

- Symptoms (questionnaire scores [ACQ, CAT, and mMRC]) and results from examinations/tests required for the ACO diagnostic criteria (peripheral blood eosinophil count, and FeNO)
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6 Among patients who have data necessary for the diagnosis of ACO at all time points during the evaluation period, the numbers and proportions of patients diagnosed with ACO consistently throughout 2 years, patients who transitioned between ACO and non-ACO during the 2-year study, and patients diagnosed with non-ACO consistently throughout 2 years

7 Comparison of the implementation rate and results of each examination/test required for the ACO diagnostic criteria at registration, for each of the following groups:

(i) Those diagnosed with ACO at registration, and having variability of respiratory symptoms

(ii) Those diagnosed with non-ACO at registration, and having variability of

respiratory symptoms

(iii) Those diagnosed with ACO at registration, and having no variability of respiratory symptoms

(iv) Those diagnosed with non-ACO at registration, and having no variability of respiratory symptoms

Exploratory

- 1 Comparison of patient demographics, clinical characteristics, and the implementation rate and results of examinations/tests required for the ACO diagnostic criteria at the time of registration, between the groups with and without asthma (physician-diagnosed) at registration, and the proportions of ACO and non-ACO patients in each of these groups

Evaluations:

- Evaluations are identical to those specified for secondary endpoint 1
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- 2 Comparison of patient demographics, clinical characteristics, and the implementation rate and results of examinations/tests required for the ACO diagnostic criteria at the time of registration, between the patient groups using and not using ICS at registration, and the proportions of ACO and non-ACO patients in each of these groups
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- 3 A distribution chart of ACQ scores relative to CAT scores in each of the patient groups diagnosed with ACO and non-ACO at registration
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ACO asthma-COPD overlap, ACQ asthma control questionnaire, BMI body mass index, CAT COPD assessment test, COPD chronic obstructive pulmonary disease, CT computed tomography, D_{LCO} diffusion capacity for carbon monoxide, FeNO fractional exhaled nitric oxide, FEV₁ forced expiratory volume in one second, FVC forced vital capacity, ICS inhaled corticosteroids, Ig immunoglobulin, JRS Japanese Respiratory Society, mMRC modified Medical Research Council questionnaire, V_A alveolar volume