Synopsis of the
Non-Interventional Study Report

CHARACTERISATION OF PATIENTS WITH SEVERE ASTHMA IN PRIMARY AND SECONDARY CARE SETTINGS IN EUROPE REPORTED TO BE ELIGIBLE FOR BIOLOGICAL THERAPY (RECOGNISE STUDY)

Medicinal product(s): Not applicable

Indication: Severe asthma

Sponsor: AstraZeneca PLC

Study code: D3250R00039

Study dates: FPFV: 26 APR 2018
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Synopsis

Title:	Characterisation of patients with severe asthma in primary and secondary care settings in Europe reported to be eligible for biological therapy (RECOGNISE STUDY)
Version identifier of final study report:	Version 1.0
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Active substance	N/A
Medicinal product:	N/A
Product reference	N/A
Dose and mode of administration	N/A
Duration of treatment	N/A
Marketing authorisation holder(s)	AstraZeneca PLC
Study sites	In total, 140 sites from 12 countries across Europe participated in the study: 4 from Bulgaria, 10 from Czech Republic, 10 from Germany, 23 from Greece, 20 from Hungary, 11 from Poland, 14 from Romania, 15 from Slovenia (phase 1), and 7 from France, 15 from Italy, 3 from the Netherlands, 8 from Spain (phase 2).
Number of patients	Planned number of patients with severe asthma: approx. 1,500 Enrolled number of patients: 1,025
Research question and objectives	The RECOGNISE study was designed to describe the characteristics of patients with severe asthma. The primary objective of the study is to describe the characteristics of patients with severe asthma who are reported by investigators to be eligible and non-eligible for biological therapy. Secondary objectives are to describe the proportion of patients eligible for biological therapy, to describe the characteristics of patients by chronic OCS treatment, to estimate the proportion of patients objectively meeting label criteria for biologics, to describe the reasons for eligibility for biological therapy (according to the investigator), to describe the reasons for referral of patients to specialized care for further clinical assessment, and to describe the severity of asthma exacerbations and Healthcare Resource Utilization (HCRU) by oral corticosteroid (OCS) bursts ($\geq$ 2 OCS bursts in the

	previous year).
Methodology	This study is a multi-country, multicentre, observational, cross-sectional, one-visit study to primarily describe the characteristics of patients with severe asthma who could be considered or not suitable for referral to further clinical assessment for biologic therapy, among all patients with severe asthma assessed in primary and secondary care settings in Europe. All study assessments were completed on the same day (both patient-reported outcomes and variables collected by the investigator).
Main inclusion criteria	Inclusion criteria were: 1. Male or female patients aged 18 years or older with physician's confirmed diagnosis of asthma 2. Diagnosis of asthma defined as severe according to American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines: Asthma requiring high-dose ICS plus at least one of the following additional controller(s) for 12 months (GINA Step 4/5): LABA, leukotriene modifier, theophylline, or continuous or near continuous OCS [i.e., maintenance OCS for ≥50% of the previous year]) (controlled or uncontrolled). NB: High dose ICS defined according to GINA. 3. At least one documented blood EOS (%) or absolute count in the last 12 months This inclusion criterion did not apply to the Netherlands 4. Twelve months of documented baseline data in the medical records or asked on study visit including asthma medication, especially OCS treatment, and history of asthma exacerbations (number and severity) 5. Evidence of one pre-bronchodilator forced expiratory volume in the first second (FEV1) in last 12 months or on study visit day (for Italy: at any time in the previous history) For France and Spain: Evidence of one pre-bronchodilator forced expiratory volume in the first second (FEV1) or PEF measurement at any time in the previous history This inclusion criterion did not apply to the Netherlands 6. Patients must be able and willing to read and understand written instructions, and to complete the questionnaires required by the protocol 7. After full explanation, patients must have signed an informed consent document indicating that they understand the purpose of and the procedures required for the study and are willing to participate in the study Exclusion criteria were: 1. Other respiratory conditions including: chronic obstructive

	pulmonary disease (as main diagnosis), bronchiectasis, idiopathic pulmonary fibrosis, pulmonary hypertension, alpha-1-antitrypsin-deficiency, and malignancy of any kind (NB: the following conditions are permitted: nasal polyposis, allergic rhinitis, atopic dermatitis, non-idiopathic pulmonary fibrosis) 2. Concurrent biologics for asthma except for stable allergen immunotherapy (defined as a stable dose and regimen at the time of the study visit). Acceptable washout periods for other asthma biologics: • Other eosinophil lowering products indicated for asthma (including mepolizumab, reslizumab or benralizumab): at least 4 months • Prior omalizumab use: at least 1 month 3. An acute or chronic condition that, in the investigator's opinion, would limit the patient's ability to complete questionnaires or participate in this study or impact the interpretations of results 4. Patient is participating in an ongoing randomised clinical trial or participation in an observational trial that might, in the investigator's opinion, influence the assessment for the current study
Statistical methods	All analyses were descriptive and performed with appropriate statistical methods: categorical variables by frequency tables, and continuous variables by sample statistics (mean, standard deviation, quartiles, median, minimum and maximum). For continuous endpoint variables, 95% confidence intervals for mean or proportion were also presented. In case of repeated evaluations for a given characteristic (in the last 12 months), the most recent one (including time of enrolment) was selected. Data were summarized for the total population as well as by subgroups.
Results Summary	Three-quarters of patients (n=770) were considered eligible for biological therapy by the investigator and 24% (n=249) were considered non-eligible (for 0.6% [n=6] eligibility per investigator was not assessed). Median age at diagnosis was 40.5 years in patients eligible and 46 years in patients non-eligible for biological therapy. Most patients were female (69.2% of eligible and 67.9% of non-eligible patients). Almost all patients were white. More than half (51.4% and 55.4%) was not employed. The smoking status was similar in eligible and non-eligible patients (28.8% and 30.9% were former or current smokers with a median number of pack years of 15 and 16, respectively). Median total eosinophil count was 324.5 cells/µl for eligible (n=330) and 180 cells/µl for non-eligible (n=106) patients. Median total white blood cell count was 7,550 cells/µl (n=435)

	and 7,720 cells/µl (n=137), with 4% (n=433) and 3% (n=137) eosinophils, respectively. Median IgE count was 161 UI/ml for eligible (n=166) and 97.5 UI/ml for non-eligible (n=30) patients. Median FeNO was 31 ppm (n=48) and 22.5 ppm (n=14), respectively. Chronic OCS use (defined as treatment maintenance with OCS for ≥ 50% of the previous year) was documented for 27.5% of eligible and 18.1% of non-eligible patients; short courses of systemic corticosteroids (≥ 3 days) for 76.8% and 45.0%, respectively. Median pre-bronchodilator FEV1 was 1,730 ml and 1,675 ml, respectively. Most patients (95.0% and 94.0%) were adherent with asthma medication; 49.9% and 30.1% had a history of atopy. Asthma medication used currently or in the last 12 months was documented for 95.8% of eligible and 79.9% of non-eligible patients. Based on the ATC Classification System, most frequently used asthma medications were 'drugs for obstructive airway diseases' and corticosteroids (across different therapeutic subgroups), with most of these being more common in eligible patients. Asthma exacerbations in the last 12 months were documented for 86.6% of eligible and 53.0% of non-eligible patients with on average (median) 2 and 1 exacerbations, respectively. Most patients (97.5% and 96.0%) visited a physician in the last 12 months; 64.9% and 74.3% visited a general practitioner (with 5 and 6 visits on average [median]), and 95.2% and 76.3% visited a specialist, mainly an asthma specialist (93.4% and 68.3%; 4 and 3 visits). Hospitalisations in the last 12 months were reported for 21.3% and 13.3% (with a duration of 6 and 8 hospital days on average), 19.5% and 8.8% had an emergency visit (1 visit on average for both eligible and non-eligible patients), and 14.8% and 11.6% were on sick leave (for 14 days on average for both subgroups). Most frequent comorbidities were osteoporosis, gastrointestinal diseases and cataracts (OCS-related), as well as diabetes, COPD and congestive heart failure (part of Charlson Comorbidity Index). CCI and age-adjusted CCI (ACCI) were somewhat lower in eligible patients (43.8% of eligible and 37.3% of non-eligible patients had an ACCI of 0 or 1; median CCI and ACCI were 0 and 2 for both subgroups). Based on the St George's Respiratory Questionnaire (SGRQ), impairment seemed to be greater in eligible patients, indicating worse HRQoL in this subgroup (the mean total score was 55.0% in eligible and 42.3% in non-eligible patients). Asthma was, based on the ACQ-6, less well controlled in eligible patients (mean scores of 2.7 and 2.0, with 84.0% and 61.0% having not well controlled asthma [scoring ≥ 1.5]). In the phase 1 countries Bulgaria, Czech Republic, Greece,

	Hungary, Poland, Romania and Slovenia, 81% were considered eligible for biological therapy by the investigator. Proportions ranged from 64% in the Czech Republic to 91% in Slovenia. In the phase 2 countries France, Italy, Netherlands and Spain together with the phase 1 country Germany, 52% were considered eligible. Here, proportions ranged from 8% in the Netherlands to 96% in Spain. Based on currently approved EU labels for omalizumab, mepolizumab, reslizumab, benralizumab and dupilumab, 62% of patients were eligible for biological therapy; 64% in phase 1 countries and 55% in phase 2 countries (incl. Germany). Clinical judgement and label criteria did not agree in phase 1 countries (not incl. Germany) according to McNemar's test. Main reasons for eligibility for biological therapy according to the investigator were 'corticosteroid treatment (high dose, long-term use & side effects), 'high-risk patients' and 'add-on specialist treatment' in phase 1 countries (incl. Germany); and 'lack of control', 'allergic uncontrolled asthma', 'OCS maintenance treatment', and 'high blood eosinophils' in phase 2 countries. It should be noted that data collection regarding this point differed during the first and second phase of the study with different options of specified answers given in the eCRF. Moreover, the majority of participating investigators were pulmonologists in phase 1 and general practitioners (GP) in phase 2. Main reasons for referral to specialized care for further clinical assessment were 'optimizing treatment' and 'difficulty to attain asthma control' in phase 2 countries (not incl. Germany; not assessed during the first phase). One-quarter of patients (n=261) was dependent on chronic OCS use (maintenance OCS for $\geq$ 50% of the previous year). Unemployment was with 59.4% higher in these patients. Median total eosinophil count was 332 cells/µl (n=124); median total white blood cell count was 7,300 cells/µl (n=135), with 4% (n=138) eosinophils. Median IgE count was 107.4 UI/ml (n=59), and median FeNO 56 ppm (n=11). 75.1% of patients also had short courses of systemic corticosteroids (for $\geq$ 3 days) in the last year. Median pre-bronchodilator FEV1 was 1,620 ml. Adherence with asthma medication was documented for 89.7%; 50.6% had a history of atopy. Asthma exacerbations in the last 12 months were documented for 87.0% with on average (median) 2 exacerbations. Doctor's visits in the last 12 months were documented for 93.5%; 69.3% visited a GP (6 visits on average [median]), and 90.0% a specialist, mainly an asthma specialist (87.7%; 4 visits). Hospitalisations in the last 12 months were documented for 21.5% (on average 8 hospital days); 23.9% had an emergency visit (1 visit on average), and 10.0% were on sick leave (for 13.5 days on average). OCS-related comorbidities were somewhat more frequent in patients

	with chronic OCS use, as were diabetes and COPD. Correspondingly, CCI and ACCI were somewhat higher. Moreover, impairment (based on SGRQ) was greater, and asthma control worse (based on ACQ-6). In phase 2 countries (not incl. Germany), 43% of patients (n=61) had a history of two or more OCS bursts in the last 12 months. Of these, 74% had uncontrolled asthma. GP visits were, with on average 10 visits [median] in the last 12 months, more common in these patients, whereas hospitalisations were with an average of 4 hospital days shorter.
Conclusion(s)	Taken together, these results suggest that a significant proportion of patients suffering from severe asthma, particularly patients with Th2 inflammation, can benefit from biological treatment. For these patients, whose disease previously remained uncontrolled, effective treatments are now available, and the need for systemic corticosteroids may be reduced.
Publication(s)	N/A
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