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Original Research

Characterization of Austrian severe asthma patients

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ABSTRACT

Introduction: The Severe Asthma Registry, founded by German Asthma Net (GAN) in 2011, is a prospective registry recording clinical parameters from participating centers in Germany, Austria and Switzerland. This article presents the baseline characteristics of severe asthma patients from Austrian centers.
Methods: We analyzed the baseline visit data of all patients recruited to the GAN Severe Asthma Registry from participating Austrian centers.
Results: Baseline visit data were available for 214 Austrian severe asthma patients from 6 Austrian centers from 2013 to 2022. Mean age was 53.7 years. Mean BMI was 26.4 kg/m2. More than a third (37.4%) of all patients had daily daytime asthma symptoms at baseline and had to use their reliever medication at least once per day. Forty-one percent of patients were classified as uncontrolled according to GINA and 24.8% as partially controlled at baseline visit. The median annual exacerbation frequency was 3 in the previous 12 months. At the time of baseline visit, 23.4% of all patients had regular treatment with oral corticosteroids. Furthermore, 23.9% had received any severe asthma monoclonal antibody prior to the baseline visit. There were no notable differences in baseline characteristics between patients categorized by smoking history or measurable type 2 inflammation.
Conclusions: This study provides the first multi-center characterization of Austrian severe asthma patients. Patients in this cohort had better asthma control and less frequent exacerbations compared to most international registries.

1. Introduction

Globally, there are over 300 million individuals who are afflicted by asthma [1]. Although severe asthma accounts for only 5–10% of all asthma cases, it leads to increased morbidity and significantly contributes to healthcare expenses and resource utilization [2,3]. Up to 30% of mild and moderate asthma patients have been reported to have uncontrolled asthma compared to 50% of patients with severe asthma [4]. To better understand the characteristics of patients with severe asthma and the effectiveness of treatments, we rely on data collected from registries and real-world studies. The Severe Asthma Registry, founded by the German Asthma Net (GAN) in 2011, is a prospective registry recording clinical parameters from participating centers in Germany, Austria and Switzerland [5]. To our knowledge, this is the first multi-center study characterizing Austrian severe asthma patients.

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Table 1
Patients characteristics at baseline. Values are presented as either percent, mean ± standard deviation or median (interquartile range), as indicated. * These data are the result of the analyses of the 64 patients (29.8%) in whom bronchodilator responsiveness testing at baseline was available. ICU, intensive care unit; ACQ-5, asthma control questionnaire 5-item scale; ACT, asthma control test; AQLQ, Asthma Quality of Life Questionnaire; FEV_1, forced expiratory volume in 1 s; FCV, forced vital capacity; FeNO, fraction of exhaled nitric oxide; DLCO, diffusion capacity for carbon monoxide; PBEC, peripheral blood eosinophil count.

Patients (n)	214
Sex, female (%)	47.2
Age at first visit (years, mean)	53.7 ± 15.4
BMI (kg/m^2, mean)	26.4 ± 5.4
Age at diagnosis (years, median)	39 (24–54)
Diagnosis before the age of 12y (%)	23.8
Any known relatives with asthma diagnosis (%)	29.4
Mother with asthma diagnosis (%)	12.6
Father with asthma diagnosis (%)	7.9
Siblings with asthma diagnosis (%)	6.5
Children with asthma diagnosis (%)	7.0
Smoking status	
Never smokers (%)	*46.7*
Former smokers (%)	*49.1*
Current smokers (%)	*3.3*
Packyears of former smokers (mean)	*17.8 ± 14.4*
Vaccination status	
Pneumococcal vaccination rate (%)	*46.3*
Seasonal flu vaccination rate (%)	*42.5*
Indicated inability to work because of asthma in the last 12 months (%)	31.3
Patients who indicate exertional dyspnoea (%)	73.8
Patients who indicate resting dyspnoea (%)	15.9
Patients who indicate chest tightness (%)	25.2
Patients who indicate cough (%)	55.1
Dry cough among patients indicating cough (%)	*45.8*
Productive cough among patients indicating cough (%)	*54.2*
Patients with wheezing determined by a physician (%)	35.5
Number of exacerbations in the past 12 months (median)	3 (2–5)
Patients with a history of exacerbation requiring intubation (%)	4.7
Patients with exacerbation(s) requiring physician assessment in the past 12 months (%)	40.2
Patients with exacerbation(s) requiring inpatient treatment in the past 12 months (%)	19.2
Patients with exacerbation(s) requiring ICU treatment in the past 12 months (%)	3.3
Patients with exacerbation(s) requiring intubation in the past 12 months (%)	0.5
ACQ-5 (points, median)	2.6 (1.5–3.8)
ACT (points, median)	17 (11–20.5)
AQLQ (points, median)	1.81 (1.38–2.53)
FEV_1 (% predicted, mean)	61.9 ± 22.0
FEV_1 (mL)	2017 ± 824
FEV_1/FVC ratio	0.65 (0.54–0.77)
Bronchodilator responsiveness (mL)*	+130 (45–280)
Bronchodilator responsiveness (%)*	+6.9 (2.6–11.9)
FeNO (ppb)	38.0 (22.0–63.5)
DLCO (% predicted)	75.8 ± 19.2
PBEC (cells/μL)	307 (110–606)

2. Methods

2.1. Dataset

We analyzed all patients recruited to the GAN Severe Asthma Registry from participating Austrian centers. Inclusion criteria in the GAN Severe Asthma Registry are written informed consent as well as a diagnosis of severe asthma in accordance with ERS/ATS definition [6] performed by a pediatric or adult respiratory specialist. This registry has been approved by the ethics committees of all participating centers and is being performed in accordance with the principles of the Declaration of Helsinki.

2.2. Statistical analysis

Data are presented as mean ± standard deviation for normally distributed data and median and interquartile ranges for non-normally distributed data. Categorical data are presented as number and/or percentage. Normality was tested using the Shapiro-Wilk test. When comparing baseline characteristics between patients with measurable type 2 inflammation signs and no measurable type 2 inflammation signs, statistical significance was tested using chi-square test for categorical data, unpaired 2-tailed *t*-test for normally distributed data and Mann-Whitney-U-test for non-normally distributed data. Pearson correlation analyses were used to measure linear dependence. Results were expressed as Pearson coefficient *r* with degrees of freedom and the two-tailed significance level.

P values of $< .05$ were considered statistically significant and *p* values of $< .001$ highly statistically significant. All statistical analyses were performed using SPSS Version 28 (IBM Corporation, Armonk, NY).

3. Results

Data were available for 214 Austrian severe asthma patients from 6 Austrian centers from 2013 to 2022. A detailed list of the centers at which patients were treated is provided in the Supplementary material (eTable 1). Since only six pediatric and adolescent patients (2.8%) were included in the registry, a separate analysis of these patients was not performed. Mean age was 53.7 years (±15.4) with an evenly balanced sex (47.2% female patients). Patients were on average overweight with a mean BMI of 26.4 kg/m^2 (±5.4). Median age of diagnosis was 39 years (24–54), with 23.8% of the patients being diagnosed before the age of 12 years. Half of the patients were former smokers with a mean smoking history of 17.8 packyears (±14.4). See Table 1 for an overview of baseline characteristics.

In 64 patients (29.8%) bronchodilator responsiveness testing was performed at baseline. Of these patients only 19 (29.7%) had positive bronchodilator responsiveness testing based on GINA criteria [7] (increase in FEV1 of greater than 12% and greater than 200 mL in adults or greater than 12% predicted in children) conducted in accordance with ATS/ERS recommendations [8,9]. There was no comprehensive data on previously performed bronchodilator responsiveness testing.

More than a third (37.4%) of all patients had daily daytime asthma symptoms at baseline and had to use their reliever medication at least once per day (see Fig. 1A and C). A third of patients reported to never have symptoms of night wakening while fifteen percent reported frequent nightly symptoms (see Fig. 1B). Forty-one percent of patients were classified as uncontrolled based on the GINA assessment of asthma control tool at baseline visit (see Fig. 1D). See eTable 2 in the Supplementary material for a detailed list of the questions asked.

Of the 67 patients (31.3%) who indicated inability to work because of asthma in the 12 months prior to baseline visit, 34 patients (15.9%) indicated an inability to work of <50 days, 8 patients (3.7%) 50–100 days, and 25 patients (11.7%) >100 days.

At the time of baseline visit 23.4% of patients had regular treatment with oral corticosteroids (OCS). See Table 2 for an overview of medications used at baseline visit.

Osteoporosis as a complication of OCS treatment (as assessed by the treating physician) was observed in 37 patients (17.3%) at baseline. See Table 4 for other OCS related complications.

Of the 51 Patients (23.9%) having received any severe asthma monoclonal antibody before baseline visit fourty-three patients (20.1%) have received one, seven patients (3.3%) two, and one patient (0.5%) three monoclonal antibodies (see Table 3). One patient had previously received Omalizumab, Mepolizumab and Benralizumab consecutively (switch). Seven patients had previously received both Omalizumab and Mepolizumab consecutively (switch). Eight patients had previously

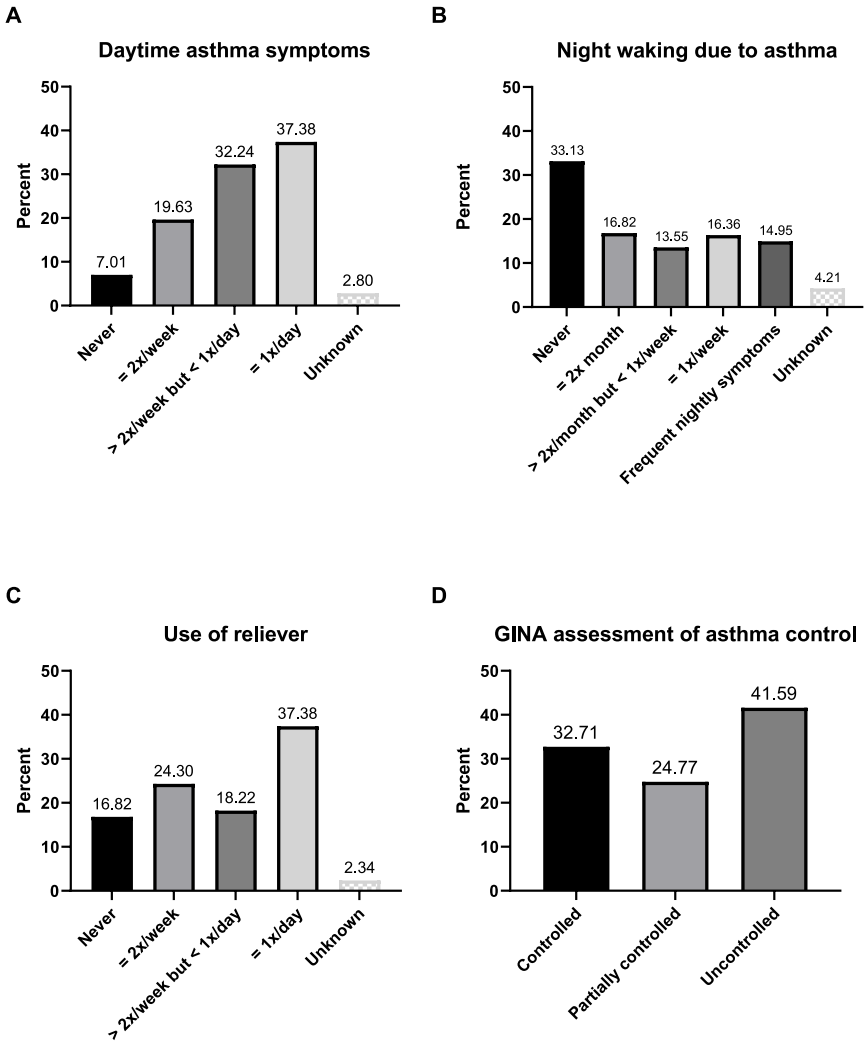

Fig. 1. Daytime asthma symptoms (A), night waking due to asthma (B), frequency of reliever use (C) and asthma control at based on the GINA assessment of asthma control tool (D) at baseline visit.

Table 2
Percentage of medications used at the time of the baseline visit. ICS, inhaled corticosteroids; LABA, long-acting beta2-agonist; LAMA, long-acting muscarinic antagonist; OCS, oral.

Any ICS containing inhaler	100
Any LABA containing inhaler	96
Any LAMA containing inhaler	61
Fixed dose ICS-LABA	79
Fixed dose ICS-LABA-LAMA	10.3
Leukotriene receptor antagonists	19.2
OCS	23.4
Theophylline	3.7

Table 3
Percentage of patients having previously received monoclonal antibodies (mAB) at any point before the baseline visit. * Switch between mABs (i.e. consecutive use of multiple mABs).

	Baseline
Any severe asthma mAB treatment	23.9
Omalizumab	12.1
Reslizumab	1.4
Mepolizumab	9.3
Benralizumab	2.8
Dupilumab	2.3
Omalizumab and Mepolizumab*	3.3
Omalizumab, Mepolizumab and Benralizumab*	0.5

received allergen immunotherapy. No patients had previously undergone bronchial thermoplasty.

Forty patients (18.7%) had taken part in a pulmonary rehabilitation program in the 12 months before baseline.

More than half of the patients (60.7%) had frequent patient reported lower respiratory tract infections (defined as >2x/year and any etiology) at the time of baseline visit. A clinical diagnosis of any allergy (requiring either a positive scin prick test [SPT] or positive specific IgE [sIgE] to an allergen as well as symptoms linked to exposure of the allergen) was present in 128 patients (59.8%). See Table 5 for a detailed list of allergic diseases. SPT data and sIgE data were available in 155 (72.4%) and 182 (85.0%) patients, respectively. Eighty-seven patients (56.1% of patients with available SPT data) had a positive SPT for seasonal and 97 patients (62.6%) for perennial aeroallergens. Eighty-one patients (44.5% of patients with available sIgE data) had positive sIgE against seasonal and 96 patients (52.7%) against perennial aeroallergens. Chronic rhinosinusitis could be observed in 40.7% and chronic rhinosinusitis with nasal polyps (CRSwNP) in 27.1% of patients. Arterial hypertension was diagnosed in 31.8%. Almost a quarter of the

Table 4
Percentage of patients (overall population) with OCS related complications (as assessed by the treating physician).

OCS related complications	Baseline
Osteoporosis	17.3
Skin changes	20.6
Diabetes	3.7
Cataract	5.6
Other (unspecified)	10.7

Table 5
Percentage of patients with comorbidities at baseline visit.

Chronic rhinosinusitis (any)	40.7
Chronic rhinosinusitis with nasal polyps	27.1
Allergy (any)	59.8
Allergic rhinoconjunctivitis	50.5
Food allergies	12.1
Atopic dermatitis	5.6
Urticaria	5.1
Aspirin-exacerbated respiratory disease	13.6
Patient reported lower respiratory tract infections >2x/year	60.7
Chronic obstructive pulmonary disease	14.5
Alpha-1 antitrypsin deficiency	0.9
Hypereosinophilic syndrome	3.3
Gastroesophageal reflux disease	24.3
Inducible laryngeal obstruction	0.9
Eosinophilic pneumonia	0.9
Bronchiectasis	3.7
Depression	10.3
Atelectasis	3.7
Arterial hypertension	31.8
Other cardiovascular diseases (not specified)	18.7

patients had gastroesophageal reflux disease (GERD). A concomitant diagnosis of chronic obstructive pulmonary disease (COPD) was present in 14.5% of all patients. See Table 5 and Fig. 2 for comprehensive list of recorded comorbidities.

Smoking history in packyears did not correlate with asthma control scores, peripheral blood eosinophilia, bronchodilator responsiveness and FeNO. Smoking history in packyears did show a weak, but statistically significant positive correlation with age at diagnosis $r(157) = 0.17$, $p = .033$. Smoking history in packyears showed a weak, but statistically significant, negative correlation with FEV_1 in percent predicted $r(205) = -0.20$, $p = .004$, FEV_1/FVC ratio $r(163) = -0.24$, $p = .002$ and diffusion capacity of the lungs for carbon monoxide (DLCO) in percent predicted $r(61) = -0.36$, $p = .004$. Smoking history in packyears showed a statistically highly significant positive correlation with intrathoracic gas volume in percent predicted $r(85) = 0.37$, $p < .001$ (see Table 6).

4. Discussion

Compared to recently published international severe asthma registry data (United Kingdom, Italy, South Korea, Australia and United States of America) Austrian patients are similar in age but more often male (40.7% international patients versus 52.8 Austrian patients) and more likely to be former smokers (33.5% of international patients versus 49.1% of Austrian patients) [10]. It is unclear why patients in this study are more frequently male. In the German GAN cohort sex was 43% male [11]. A separate analysis of South Korean severe asthma patients showed data on male sex and smoking status comparable to the combined international registry [12]. A recent study from the Italian severe asthma registry showed a prevalence of smoking history in line with the Austrian data presented here [13]. The difference in smoking history among severe asthma patients may be due to two reasons. Firstly, the smoking rate in Austria [14] is higher than in the United Kingdom [15], Australia [16] and the United States of America [17], although the rate of former smokers is comparable between Austria and Australia. Secondly, it might possibly be that in those countries' patients presenting with clinical symptoms of asthma and a smoking history are more likely to be diagnosed as COPD. Almost 15% of the Austrian patients with severe asthma as diagnosed by a respiratory specialist in this registry had a concomitant diagnosis of COPD. Smoking history correlated with functional markers for emphysema and fixed airway obstruction but not with PBEC nor FeNO suggesting that these patients, despite evidence for smoking related COPD and emphysema, have similar asthma pathophysiology. A real-life single-center study of Austrian severe eosinophilic asthma patients showed, that benralizumab is equally effective in patients with a smoking history of >10 packyears [18].

Asthma control at baseline based on GINA criteria seems better in Austrian patients than in comparable international data. In the international severe asthma registry 23.3% were classified as well controlled at baseline, albeit based on ACT scoring and not GINA criteria [10]. In the predominantly German overall GAN cohort only 13.3% of adult asthma patients were classified as having controlled asthma based on GINA criteria [5]. In comparison, 32.7% of patients in the Austrian GAN cohort were classified as having controlled asthma based on GINA criteria. Less Austrian patients (24.3% of adult patients) received OCS at baseline visit than in the predominantly German overall GAN cohort (38.0% of adult patients) [5]. It is plausible, that the higher rate of OCS use in patients from German centers compared to the patients from Austrian centers is mainly due to the higher rate of patients having not well controlled asthma. It is unclear, why in the overall and mostly German cohort more patients have unsatisfactory asthma control, as both cohorts derive from the same registry with identical inclusion criteria. One possible explanation is that the data analyzed in the overall GAN cohort was collected from 2011 until 2020 [5] and the data analyzed in the cohort of Austrian centers presented here was collected until 2022. Between 2020 and 2022, targeted treatment options with monoclonal antibodies have been more widely available and with broader indications. There might also be a selection bias because most Austrian patients were recruited from tertiary care asthma clinics.

The exacerbation risk was comparable with 40.2% of the Austrian patients having had at least one exacerbation which in the 12 months before baseline compared to 40.8% in the international severe asthma registry data [10]. The rate of patients requiring hospitalization for an exacerbation in the previous 12 months was lower in Austrian patients at 19.2% compared to 26.8% in international registries, as was the rate requiring invasive ventilation (0.5% of Austrian patients in the previous 12 months versus 5.5% internationally) [10]. The latter difference might be due to a difference in threshold when to abandon non-invasive ventilation attempts rather than a difference in severity of exacerbations but use of non-invasive ventilation for asthma exacerbations is not recorded in the current form of the registry.

Baseline characteristics did not differ between patients grouped based on the presence of measurable type 2 inflammation as defined by the 2022 GINA guidelines [7]. An analysis of UK severe asthma patients showed a higher BMI, a higher smoking rate as well as more severe airflow obstruction (based on FEV_1/FVC ratio) in patients without measurable type 2 inflammation [19]. These differences were not seen in our cohort. Only exacerbations requiring inpatient treatment were statistically significantly more likely in patients with measurable type 2 inflammation. Mean diffusion capacity for carbon monoxide in percent predicted was clinically meaningfully lower in the group with no measurable type 2 inflammation but this was not statistically significant ($p = .051$). These results could be conclusive with the current paradigm that patients without measurable type 2 inflammation are not a separate entity of asthma patients but rather patients with the same pathophysiology in whom type 2 inflammation has not yet been measured, possibly due to the inability to pause ICS.

Bronchodilator responsiveness was positive in only 30% of tested patients in both the current Austrian study as well as in the analysis of the German GAN cohort [20]. Bronchodilator responsiveness showed no

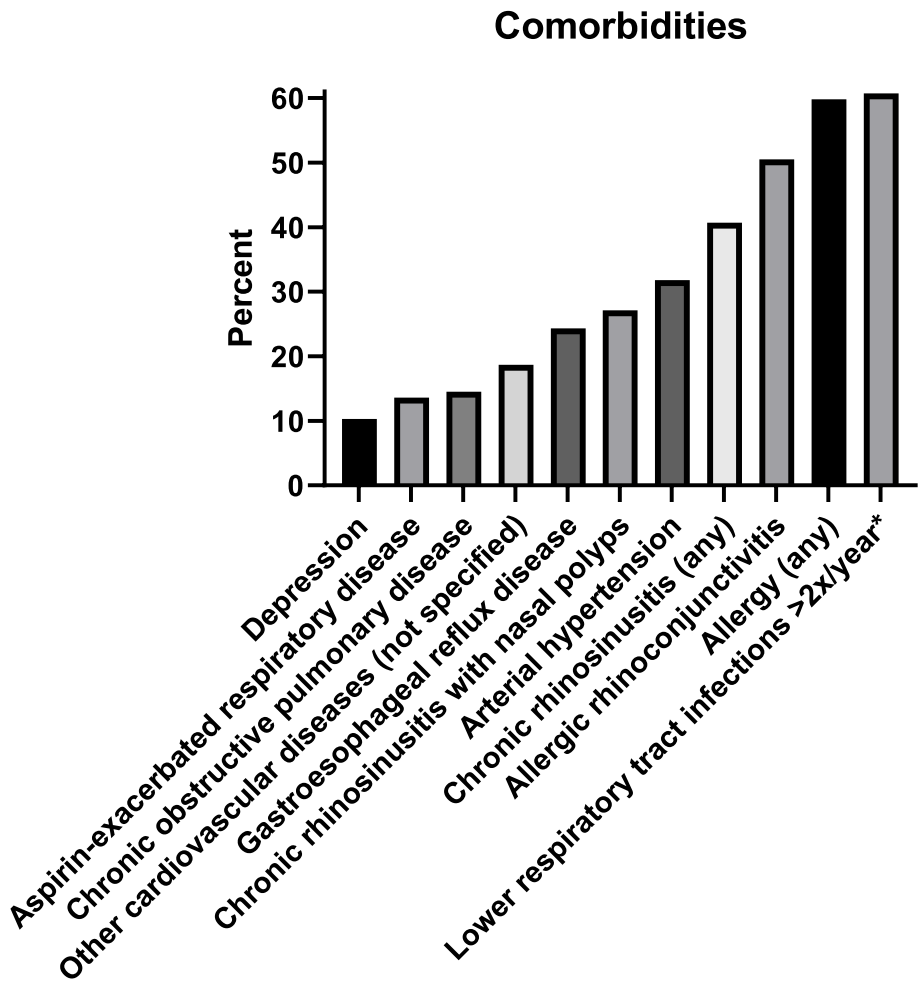

Fig. 2. Percent of patients with comorbidities at baseline visit. Only comorbidities >10% are shown in this figure. * Patient reported lower respiratory tract infections >2x/year.

correlation with smoking history in either study [20]. Also, bronchodilator responsiveness did not differ between patients with and without measurable type 2 inflammation in this cohort. Previous studies have demonstrated that treatment success with benralizumab [18,21,22] and dupilumab [23] is independent of positive bronchodilator responsiveness.

Surprisingly, there was no difference in the percentage of patients who had received any type of severe asthma mAB, as there are fewer mAB indications and treatment possibilities for patients with no measurable type 2 inflammation. This might be due to the low percentage of patients having received monoclonal antibodies until baseline visit in either group. It will be important to compare these groups in the planned analysis of the annual follow-up visits as it is to be expected that, based on current guidelines, more patients in the group with measurable type 2 inflammation would fulfill treatment indications for severe asthma mAB treatment.

Treatment with LAMA at baseline visit was almost twice as frequent (61%) compared to an analysis of the Italian severe asthma registry (SANI, 35.9%) [24]. In a different Italian severe asthma registry (RItA) use of LAMA was 31.2% at baseline and increased only to 35,2% at one year follow up [25]. The reason for this difference in prescription practice is unclear as other baseline characteristics are comparable. LAMA use in our predominantly adult patients was comparable to adult patients in the German GAN cohort (56.2%) [5]. Considering treatment with LAMA is recommended for patients with insufficient asthma control under at least medium dose ICS-LABA [7].

This study provides the first characterization of Austrian severe asthma patients. Data of national and international registries are important to increase understanding of asthma pathophysiology and phenotypes. Furthermore, they provide helpful information about treatment and its effectivity. Despite the moderate sample size, the amount of data collected per patient, as well as high data quality, allow the results presented here to help reframe paradigms. Three characteristics which are traditionally often seen as attributes that make an asthma diagnosis less likely, smoking history, negative bronchodilator response and no measurable type 2 inflammation, are relatively prevalent in our severe asthma cohort but have no effect on asthma control or other baseline characteristics. At the time of inclusion in the GAN Severe Asthma Registry asthma control of two-thirds of the patients was either only partially controlled or uncontrolled. While slightly better than

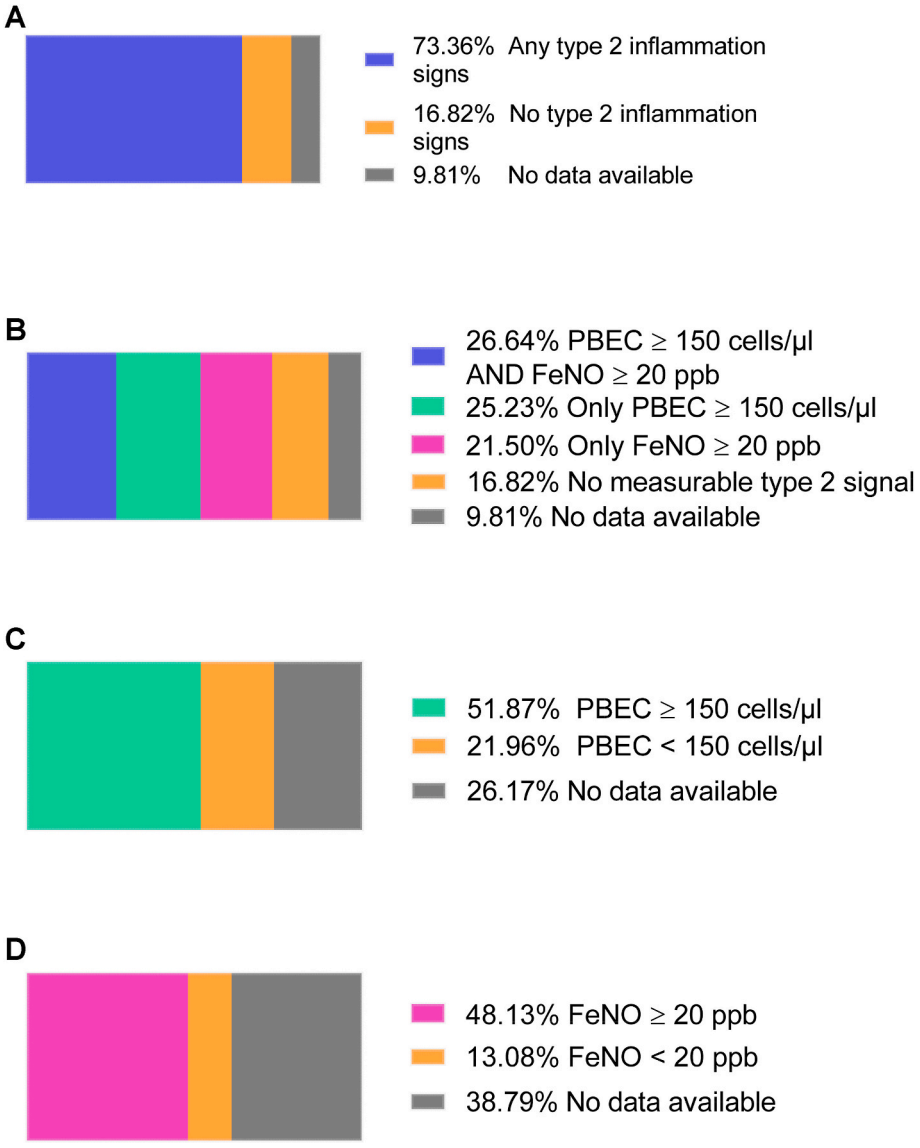

Fig. 3. Percent of patients with measurable type 2 inflammation signs. N = 214 for all graphs. A: Percent of patients with any type 2 inflammation signs defined as PBEC ≥150 cells/µl and/or FeNO ≥20 ppb; B: Percent of patients with a type 2 inflammation signs and specified which type 2 inflammation signs; C: Percent of patients with a PBEC ≥150 cells/µl; D: Percent of patients with a FeNO ≥20 ppb. PBEC, peripheral blood eosinophil count; FeNO, fraction of exhaled nitric oxide; We compared baseline characteristics between patients with measurable type 2 inflammation signs (n = 157) and patients with no measurable type 2 inflammation signs (n = 36) in patients for whom data on either PBEC and/or FeNO was available (n = 193). Patients with exacerbation(s) requiring inpatient treatment in the past 12 months were more common in the group with any type 2 inflammation signs (19.7%) compared to the group with no measurable type 2 inflammation signs (13.7%, p=.011). Mean diffusion capacity for carbon monoxide in percent predicted was lower in the group with any type 2 inflammation signs (78.4 ± 17.6) compared to the group with no measurable type 2 inflammation signs (66.7 ± 22.6) but this difference was not statistically significant (p=.051). Otherwise, no relevant differences between these groups could be detected. See also Table 7 for a detailed summary.

Table 6
Pearson correlation between smoking history in packyears and other variables. ACT, asthma control test; ACQ-5, asthma control questionnaire 5-item scale; FEV_1, forced exiratory volume in 1 s; FCV, forced vital capacity; ITGV, intrathoracic gas volume; DLCO, diffusion capacity for carbon monoxide; PBEC, peripheral blood eosinophil count; FeNO, fraction of exhaled nitric oxide; In 193 patients (90.2%) some testing for type 2 inflammation was available. Data from PBEC was available for 158 patients (73.8%) and FeNO for 131 patients (61.2%). Evidence for type 2 inflammation as suggested by GINA [7] (PBEC ≥150 cells/μl and/or FeNO ≥20 ppb) was identified in 157 patients (73.4%). Data on sputum eosinophils were not available. About half of all patients had a PBEC ≥150 cells/μl (51.9%). This was similar for FeNO ≥20 ppb (48.1%) (See also Fig. 3).

Correlation between the listed variables and smoking history in packyears		
Age at diagnosis	$r(157) = .17$	$p = .033$
ACT	$r(186) = -.13$	$p = .078$
ACQ-5	$r(121) = .17$	$p = .056$
FEV_1 percent predicted	$r(205) = -.20$	$p = .004$
FEV_1/FVC ratio	$r(163) = -.24$	$p = .002$
ITGV percent predicted	$r(85) = .37$	$p < .001$
Bronchodilator responsiveness of FEV_1 in percent	$r(73) = -.15$	$p = .214$
DLCO percent predicted	$r(61) = -.36$	$p = .004$
PBEC	$r(84) = -.10$	$p = .377$
FeNO	$r(129) = -.03$	$p = .725$

previously published international data, there is vast room for improvement. Analyses of the annual follow up data are warranted to assess if those needs are being met.

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CRediT authorship contribution statement

Andreas Renner: Conceptualization, Data curation, Formal analysis, Methodology, Visualization, Writing – original draft. **Slagjana Stoshikj:** Investigation, Writing – review & editing. **Wolfgang Pohl:** Investigation, Writing – review & editing. **Christina Bal:** Investigation, Writing – review & editing. **Matthias Reisinger:** Investigation, Writing – review & editing. **Judith Löffler-Ragg:** Investigation, Writing – review & editing. **Angela Zacharasiewicz:** Investigation, Writing – review & editing. **Roland Buhl:** Conceptualization, Writing – review & editing. **Eckard Hamelmann:** Conceptualization, Writing – review & editing. **Christian Taube:** Conceptualization, Writing – review & editing. **Stephanie Korn:** Conceptualization, Writing – review & editing. **Marco Idzko:** Conceptualization, Investigation, Project administration, Writing – review & editing, All authors approved submission of the manuscript for publication.

Declaration of competing interest

Andreas Renner: None.

Slagjana Stoshikj: Speaker fees from AstraZeneca, all outside the submitted work.

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Judith Löffler-Ragg: None.

Angela Zacharasiewicz: None.

Table 7
Differences in patients characteristics at baseline between patients with any type of type 2 inflammation signs defined as peripheral blood eosinophilic count ≥150 cells/μl and/or of fraction of exhaled nitric oxide ≥20 ppb and patients with no measurable type 2 inflammation signs in patients for whom data on either peripheral blood eosinophilic count and/or fraction of exhaled nitric oxide was available (n = 193). Values are presented as either percent, mean ± standard deviation or median (interquartile range), as indicated. Statistical significance was calculated using chi-square test for categorical, unpaired 2-tailed *t*-test for normally distributed, and Mann-Whitney-U-test for non-normally distributed data.ACQ-5, asthma control questionnaire 5-item scale; ACT, asthma control test; AQLQ, Asthma Quality of Life Questionnaire; FEV_1, forced expiratory volume in 1 s; FCV, forced vital capacity; DLCO, diffusion capacity for carbon monoxide; mAB, monoclonal antibody.

Differences in baseline characteristics based on type 2 inflammation	Any type 2 inflammation signs (n = 157)	No type 2 inflammation signs (n = 36)	Statistical significance
Sex, female (%)	47.4	55.6	$p = .681$
Age at diagnosis (years, mean)	37.7 ± 18.4	39.6 ± 22.5	$p = .623$
BMI (kg/m^2, mean)	26.6 ± 5.1	25.5 ± 4.5	$p = .433$
Former smokers (%)	50.6	44.4	$p = .773$
Packyears of former smokers (mean)	10.4 ± 16.2	6.5 ± 11.6	$p = .169$
Number of exacerbations in the past 12 months (median)	3 (2–6)	3 (2–4)	p=.363
Patients with exacerbation(s) requiring physician assessment in the past 12 months (%)	38.2	36.1	p=.660
Patients with exacerbation(s) requiring inpatient treatment in the past 12 months (%)	19.7	13.7	p=.011
ACQ-5 (points, median)	2.4 (1.4–3.5)	2.8 (1.5–3.8)	p=.640
ACT (points, median)	17.0 (11.5–20.0)	18.0 (10.0–22.0)	p=.465
AQLQ (points, median)	1.86 (1.47–2.63)	1.72 (1.31–2.44)	p=.557
FEV_1 (% predicted, mean)	62.2 ± 22.3	63.5 ± 22.1	p=.752
FEV_1 (mL, mean)	2031 ± 867	1991 ± 719	p=.798
FEV_1/FVC ratio (median)	0.65 (0.52–0.77)	0.66 (0.55–0.77)	p=.526
Bronchodilator responsiveness (mL, median)	+130 (60–275)	+55 (20–400)	p=.326
Bronchodilator responsiveness (%, median)	+6.9 (2.9–11.7)	+3.3 (1.6–17.9)	p=.649
DLCO (% predicted, mean)	78.4 ± 17.6	66.7 ± 22.6	$p = .051$
Patients who had received any severe asthma mAB treatment (%)	23.6	22.2	$p = .567$

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Appendix A. Supplementary data

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