

Clinical remission in severe asthma with Biologic Therapy: an analysis from the UK Severe Asthma Registry: Online Supplement.

Definitions of severe asthma (ATS/ERS and GINA) ^{E1}

Definition of severe asthma: American Thoracic society/ European Respiratory Society

Severe asthma is defined as asthma which requires GINA step 4–5 asthma treatment (high dose inhaled corticosteroid (ICS) and long acting Beta-agonist (LABA) or leukotriene modifier/theophylline) and/or systemic corticosteroids (OCS) for 50% of the previous year to prevent it from becoming “uncontrolled” or which remains “uncontrolled” despite this therapy.

> Uncontrolled asthma is defined as at least one of the following:

1. Poor symptom control: Asthma Control Questionnaire (ACQ) consistently ≥ 1.5 , Asthma Control Test (ACT) < 20 (or “not well controlled” by NAEPP/GINA guidelines)
2. Frequent severe exacerbations: two or more bursts of systemic OCS (3 days each) in the previous year
3. Serious exacerbations: at least one hospitalisation, ICU stay or mechanical ventilation in the previous year
4. Airflow limitation: after appropriate bronchodilator withhold FEV1 ,80% predicted (in the face of reduced FEV1/FVC defined as less than the lower limit of normal)

> Controlled asthma that worsens on tapering of these high doses of ICS or systemic OCS (or additional biologics)

Definition of severe asthma: Global initiative for asthma (GINA) ^{E2}

Severe asthma is uncontrolled (poor symptom control, ≥ 2 exacerbations per year, requiring OCS, ≥ 1 severe exacerbation requiring hospitalisation) despite adherence factors with maximal optimized therapy and treatment of contributory factors, or that worsens when high dose treatment is decreased.

Definitions of remission set forth by the ‘expert consensus framework for asthma remission as a treatment goal’ ^(E3)

Clinical remission: on treatment

≥ 12 months:

- 1) Sustained absence of significant asthma symptoms using validated instrument AND
- 2) Optimisation and stabilization of lung function AND
- 3) Patient & HCP agreement regarding remission AND
- 4) No OCS for exacerbation or disease control

Clinical remission: off treatment

Same criteria but without asthma treatment in ≥ 12 months

Complete remission: on treatment

1. Meets definition for clinical remission AND
2. Current, objective evidence of the resolution of previous asthma-related inflammation* AND
3. In appropriate research settings: current negative bronchial hyperresponsiveness

Complete remission: off treatment

Same criteria but without asthma treatment in ≥ 12 months

NICE criteria for commencing biologics in the UK for uncontrolled asthma despite optimisation and assessment of adherence:

Benralizumab:^(E4)

Benralizumab, as an add-on therapy, is recommended as an option for treating severe eosinophilic asthma that is inadequately controlled in adults despite maintenance therapy with high-dose inhaled corticosteroids and long-acting beta-agonists, only if:

- the person has agreed to and followed the optimised standard treatment plan and
- the blood eosinophil count has been recorded as 300 cells per microlitre or more and the person has had 4 or more exacerbations needing systemic corticosteroids in the previous 12 months, or has had continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months (that is, the person is eligible for mepolizumab) or
- the blood eosinophil count has been recorded as 400 cells per microlitre or more with 3 or more exacerbations needing systemic corticosteroids in the past 12 months (that is, the person is eligible for reslizumab).

Dupilumab:^(E5)

Dupilumab as add-on maintenance therapy is recommended as an option for treating severe asthma with type 2 inflammation that is inadequately controlled in people 12 years and over, despite maintenance therapy with high-dose inhaled corticosteroids and another maintenance treatment, only if:

- the dosage used is 400 mg initially and then 200 mg subcutaneously every other week
- the person has agreed to and follows an optimised standard treatment plan
- the person has a blood eosinophil count of 150 cells per microlitre or more and fractional exhaled nitric oxide of 25 parts per billion or more, and has had at least 4 or more exacerbations in the previous 12 months
- the person is not eligible for mepolizumab, reslizumab or benralizumab, or has asthma that has not responded adequately to these biological therapies

Mepolizumab:^(E6)

Mepolizumab, as an add-on therapy, is recommended as an option for treating severe refractory eosinophilic asthma, only if:

- for adults who have agreed to and followed the optimised standard treatment plan and
- the blood eosinophil count has been recorded as 300 cells per microlitre or more and the person has had at least 4 exacerbations needing systemic corticosteroids in the previous 12 months, or has had continuous oral corticosteroids of at least the equivalent of prednisolone 5 mg per day over the previous 6 months or

- the blood eosinophil count has been recorded as 400 cells per microlitre or more and the person has had at least 3 exacerbations needing systemic corticosteroids in the previous 12 months (so they are also eligible for either benralizumab or reslizumab).

Omalizumab:^(E7)

Omalizumab is recommended as an option for treating severe persistent confirmed allergic IgE-mediated asthma as an add-on to optimised standard therapy in people aged 6 years and older:

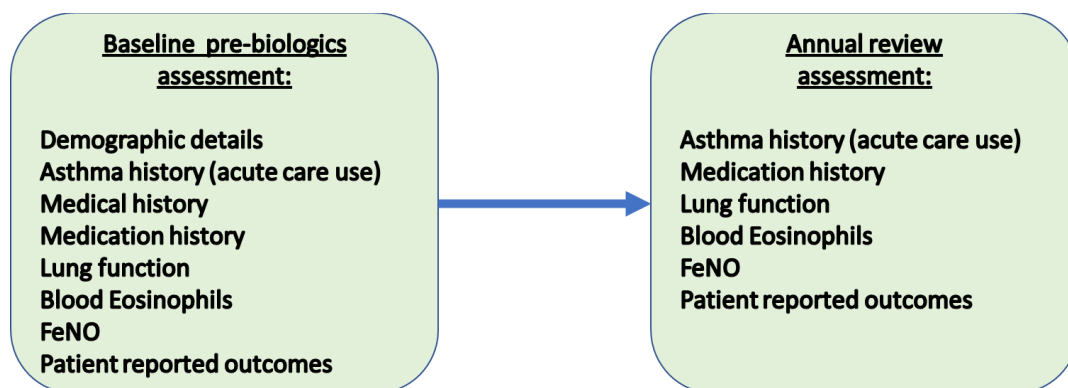
- who need continuous or frequent treatment with oral corticosteroids (defined as 4 or more courses in the previous year)

Reslizumab:^(E8)

Reslizumab, as an add-on therapy, is recommended as an option for the treatment of severe eosinophilic asthma that is inadequately controlled in adults despite maintenance therapy with high-dose inhaled corticosteroids plus another drug, only if:

- the blood eosinophil count has been recorded as 400 cells per microlitre or more
- the person has had 3 or more severe asthma exacerbations needing systemic corticosteroids in the past 12 months and

Assessments:



Data recorded at baseline assessment, includes demographic details, asthma/atopy history, comorbidities, exacerbation/acute care attendance in the last 12 months, medication history, biomarkers (blood eosinophil count (BEC) and fractional exhaled nitric oxide (FeNO) and lung function (GLI 2012 predictive values,^{E9}). Patient reported outcome measures (PROMs) completed at each assessment included asthma control assessment (ACQ5, asthma control questionnaire and quality of life measures (EuroQOL 5L5D). At annual review, acute care use, medication history,

biomarkers, lung function and PROMS are recorded. To reduce bias towards biologic classes, all biologics approved for use for severe asthma treatment in the UK were included in the analysis, including anti-IL5, anti-IL5R, anti-IL4 α r and anti-IgE.

Patient-reported outcome measures (PROMs) in this study addressed change in quality-of-life and asthma severity.

Asthma Control Questionnaire (ACQ5):

Asthma control. Asthma control was assessed by the five item asthma control questionnaire.^(E10) An ACQ5 score of 0.75 reflects adequate asthma control, whereas a score of 1.5 or over signals inadequate asthma control. The MCID is a reduction in ACQ5 score of 0.5 or greater.^(E11)

EuroQol:

Quality of life. The EuroQoL-5L5D Health scale is a visual analogue scale with which patients report their overall health,^(E12) 100 is the best health possible and 0 reflects the worst overall health. The EuroQoL-5L5D Index value reflects impairment of activities of daily living, the closer the score is to 1, the less the impairment of daily living. The change in Index Value following an intervention allows evaluation of the health economics of the intervention through calculation of quality-adjusted life years.

Figure S1: Flow diagram for construction of UKSAR cohort

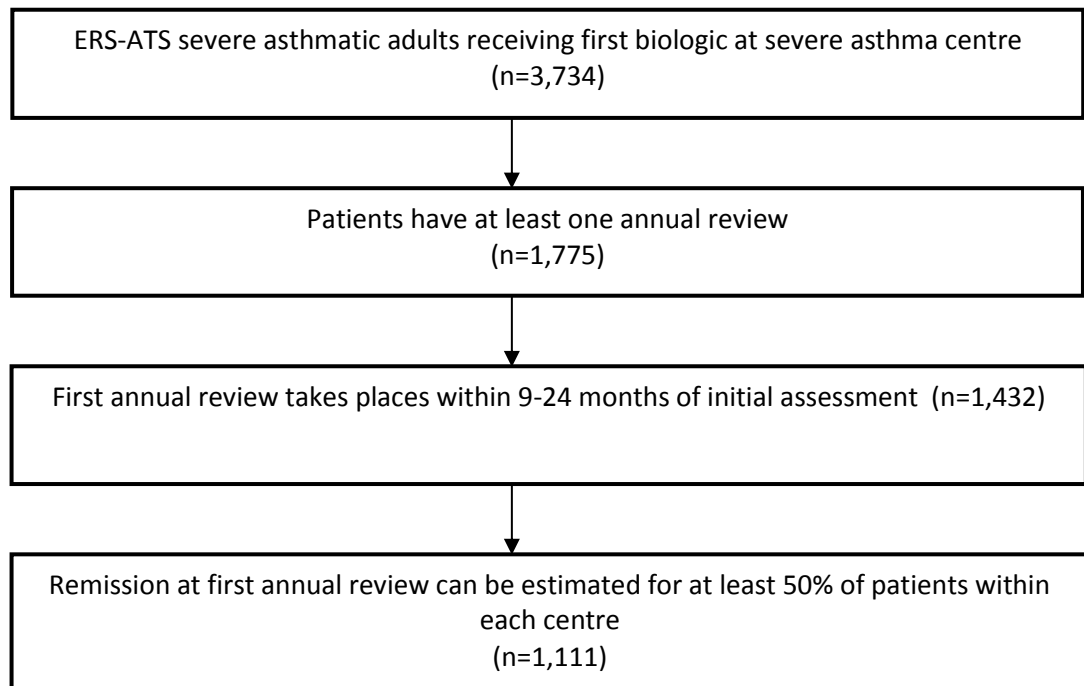


Table S1: Data completeness (whole cohort (n=1,111))

Variable	n (%) non-missing	n (%) missing
Time until Annual review (Years)	1,111 (100.0%)	0 (0.0%)
Sex	1,111 (100.0%)	0 (0.0%)
Age At First Assessment (Years)	1,111 (100.0%)	0 (0.0%)
Age at Onset of Symptoms (Years)	976 (87.8%)	135 (12.2%)
Duration Of Symptoms From Baseline (Years)	976 (87.8%)	135 (12.2%)
Ethnicity	1,109 (99.8%)	2 (0.2%)
Smoking Status	1,083 (97.5%)	28 (2.5%)
BMI (kg-m2)	1,099 (98.9%)	12 (1.1%)
Atopic Disease	1,111 (96.8%)	37 (3.2%)
Depression or Anxiety	1,111 (100.0%)	0 (0.0%)
Gastro-oesophageal Reflux	1,111 (100.0%)	0 (0.0%)
Nasal polyps	1,111 (100.0%)	0 (0.0%)
OCS bursts (Last Year)	1,086 (97.7%)	25 (2.3%)
Frequent exacerbator at baseline	1,086 (97.7%)	25 (2.3%)
Invasive Ventilations (Ever)	1,058 (95.2%)	53 (4.8%)
ED Attendances For Asthma (Last Year)	1,073 (96.6%)	38 (3.4%)
Hospital Admissions For Asthma (Last Year)	1,081 (97.3%)	30 (2.7%)
Highest Blood Eosinophil Count (N/10 ⁹ L) †	1,093 (98.4%)	18 (1.6%)
Blood Eosinophil Count (N/10 ⁹ L)	1,085 (97.7%)	26 (2.3%)
FeNO (ppb)	831 (74.8%)	280 (25.2%)
Composite Type 2 status	811 (73.0%)	300 (27.0%)
FEV ₁ (L)	1,089 (98.0%)	22 (2.0%)
FEV ₁ (% Predicted)	1,077 (96.9%)	34 (3.1%)
FVC (L)	1,062 (95.6%)	49 (4.4%)
FVC (% Predicted)	1,026 (92.3%)	85 (7.7%)
FEV ₁ /FVC	1,062 (95.6%)	49 (4.4%)
ACQ5 Score	954 (85.9%)	157 (14.1%)
Uncontrolled asthma	954 (85.9%)	157 (14.1%)
Puffs of SABA most days (ACQ Q6)	924 (83.2%)	187 (16.8%)
EuroQoL Health Scale	454 (40.9%)	657 (59.1%)
EuroQoL Utility	470 (42.3%)	641 (57.7%)
Maintenance OCS	1,106 (99.5%)	5 (0.5%)
Maintenance OCS (mg) *	634 (99.4%)	4 (0.6%)
Inhaled corticosteroids (ICS)	1,111 (100.0%)	0 (0.0%)
ICS Dose (BDP equivalent-µg) **	1,025 (92.9%)	78 (7.1%)
Theophylline	1,099 (98.9%)	12 (1.1%)
Short-acting β2-agonist (SABA)	1,099 (98.9%)	12 (1.1%)
Long-acting β2-agonist (LABA)	1,094 (98.5%)	17 (1.5%)
Leukotriene Receptor Antagonists	1,059 (95.3%)	52 (4.7%)
Maintenance Macrolides	1,087 (97.8%)	24 (2.2%)
Nebuliser	1,092 (98.3%)	19 (1.7%)
Biologic commenced	981 (88.3%)	130 (11.7%)
Biologic type commenced	981 (88.3%)	130 (11.7%)
ERS-ATS Severe Asthma	1,111 (100.0%)	0 (0.0%)
Hospital	1,111 (100.0%)	0 (0.0%)

† highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated.*among patients on oral corticosteroids**among patients on inhaled corticosteroids

BMI: Body Mass Index; OCS: Oral Corticosteroid Steroids; ED: Emergency Department; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; ICS: Inhaled Corticosteroid Steroids; BDP: Beclometasone Dipropionate; SABA: Short-Acting Beta Agonists; LABA: Long-Acting Beta Agonists; LAMA: Long-Acting Muscarinic Antagonist; ERS-ATS: European Respiratory Society-American Thoracic Society definition severe asthma 'asthma which requires treatment with GINA step 4-5 treatment or oral corticosteroids (OCS) for 50% of the last year to prevent it becoming uncontrolled'

Table S2: Summary statistics for scalar variables (whole cohort (n=1,111))

Variable	Mean (SD)	Median (IQR)
Time until Annual review (Years)	1.2 (0.3)	1.1 (1.0,1.3)
Age At First Assessment (Years)	50.8 (14.5)	52.0 (41.0,61.0)
Age at Onset of Symptoms (Years)	25.7 (19.9)	21.0 (7.0,41.0)
Duration Of Symptoms From Baseline (Years)	25.1 (17.3)	23.0 (10.0,37.0)
BMI (kg-m ²)	30.8 (7.4)	29.8 (26.1,34.8)
OCS bursts (Last Year)	5.9 (4.0)	5 (3,8)
ED Attendances For Asthma (Last Year)	1.7 (3.9)	0 (0,2)
Hospital Admissions For Asthma (Last Year)	1.1 (2.1)	0 (0,1)
Highest Blood Eosinophil Count (N/10 ⁹ L) †	0.94 (1.11)	0.70 (0.44,1.10)
Blood Eosinophil Count (N/10 ⁹ L)	0.50 (0.57)	0.40 (0.20,0.65)
FeNO (ppb)	57.8 (49.0)	43.0 (24.0,75.0)
FEV ₁ (L)	2.1 (0.8)	2.0 (1.5,2.6)
FEV ₁ (% Predicted)	67.3 (21.3)	66.9 (52.1,81.5)
FVC (L)	3.3 (1.0)	3.1 (2.5,3.9)
FVC (% Predicted)	85.9 (19.1)	85.9 (73.4,97.8)
FEV ₁ /FVC	63.1 (18.7)	63.6 (53.7,72.1)
ACQ5 Score	3.0 (1.4)	3.2 (2.0,4.0)
EuroQoL Health Scale	56.5 (21.3)	60.0 (40.0,70.0)
EuroQoL Utility	0.7 (0.3)	0.8 (0.6,0.9)
Maintenance OCS (mg) *	12.9 (8.7)	10 (8,15)
ICS Dose (BDP equivalent-µg) **	1950.5 (640.1)	2000 (1600,2000)

† highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated

* among patients on OCS

** among patients on inhaled corticosteroids

SD: Standard Deviation; IQR: InterQuartile Range; BMI: Body Mass Index; ED: Emergency Department; FEV₁: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; FeNO: Fractional exhaled Nitric Oxide; ACQ: Asthma Control Questionnaire; OCS: Oral Corticosteroids; ICS: Inhaled Corticosteroids; BDP: Beclometasone Dipropionate

Table S3. Baseline demographics of the whole cohort at initial assessment prior to commencing biologics (n=1,111)

Variable	n	Category	Result
Time to first Annual Review (Years)	1,111		1.1 (1.0,1.3)
Time to first Annual Review (Months)	1,111	>=9 & <12 months	352 (31.7%)
		>=12 & <18 months	587 (52.8%)
		>=18 & <=24 months	172 (15.5%)
Sex	1,111	Female	667 (60.0%)
Age At First Assessment (Years)	1,111		52.0 (41.0,61.0)
Ethnicity	1,109	White	966 (87.1%)
		Non-White	143 (12.9%)
Smoking Status	1,083	Never	723 (66.8%)
BMI (kg-m2)	1,099		29.8 (26.1,34.8)
BMI ≥30kg-m2		≥30	540 (49.1%)
Atopic Disease	1,111		567 (51.0%)
Depression or Anxiety	1,111		129 (11.6%)
Gastro-oesophageal Reflux	1,111		224 (20.2%)
Nasal polyps	1,111		237 (21.3%)
OCS bursts (Last Year)	1,086		5 (3,8)
Any OCS bursts (Last Year)	1,086		1,020 (93.9%)
Frequent exacerbator at baseline	1,086	≥3 exacerbations in last year	906 (83.4%)
Invasive Ventilations (Ever)	1,058		101 (9.5%)
ED Attendances For asthma (Last Year)	1,073		0 (0,2)
Any ED Attendance for asthma (Last Year)	1,073		435 (40.5%)
Any Hospital Admissions for asthma (Last Year)	1,081		431 (39.9%)
Hospital Admissions for asthma (Last Year)	1,081	≥2	253 (23.4%)
Highest Blood Eosinophil Count recorded (N/10 ⁹ L) †	1,093		0.70 (0.44,1.10)
Blood Eosinophil Count (N/10 ⁹ L)	1,085		0.40 (0.20,0.65)
Blood Eosinophil Count (N/10 ⁹ L)	1,085	<0.15	219 (20.2%)
		≥0.15 & <0.30	131 (12.1%)
		≥0.30 & ≤0.45	264 (24.3%)
		>0.45	471 (43.4%)
FeNO (ppb)	831		43.0 (24.0,75.0)
FeNO	831	<20ppb	167 (20.1%)
		≥20 & <50ppb	299 (36.0%)
		≥50ppb	365 (43.9%)
Composite T2-Group	811	Eos Low (<0.15) / FeNO Low (<20)	48 (5.9%)
		Eos High (≥0.15) / FeNO Low (<20)	111 (13.7%)
		Eos Low (<0.15) / FeNO High (≥20)	126 (15.5%)
		Eos High (≥0.15) / FeNO High (≥20)	526 (64.9%)
Clinic FEV ₁ (L)	1,089		2.0 (1.5,2.6)
Clinic FEV ₁ (% Predicted)	1,077		66.9 (52.1,81.5)
Clinic FVC (L)	1,062		3.1 (2.5,3.9)
Clinic FVC (% Predicted)	1,026		85.9 (73.4,97.8)
Clinic FEV ₁ /FVC	1,062		63.6 (53.7,72.1)
ACQ5 Score	954		3.2 (2.0,4.0)
Uncontrolled Asthma	954	ACQ5≥1.5	807 (84.6%)
Maintenance OCS	1,106		638 (57.7%)
Maintenance OCS (mg)	1,102634		10 (8,15)
Inhaled corticosteroids (ICS)	1,111		1,103 (99.3%)
ICS Dose (BDP equivalent-µg)	1,025		2000 (1600,2000)
Theophylline	1,099		299 (27.2%)
Long-acting β2-agonist (LABA)	1,094		1,013 (92.6%)
Long acting anti-muscarinic agent (LAMA)	1,095		709 (64.7%)
Leukotriene Receptor Antagonists	1,059		548 (51.7%)

Maintenance Macrolides	1,087		100 (9.2%)
Biologic type commenced	981	Anti-IL5	828 (84.4%)
		Anti-IgE	150 (15.3%)
		Anti-IL4 R α	3 (0.3%)
ERS-ATS Severe Asthma	1,111	Yes	1,111 (100.0%)

‡ Median (IQR) or count (%) as appropriate; † highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated. *among patients on oral corticosteroids**among patients on inhaled corticosteroids

BMI: Body Mass Index; OCS: Oral Corticosteroid Steroids; ED: Emergency Department; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; ICS: Inhaled Corticosteroid Steroids; BDP: Beclometasone Dipropionate; SABA: Short-Acting Beta-2 Agonists; LABA: Long-Acting Beta-2 Agonists; LAMA: Long-Acting Muscarinic Antagonist; ERS-ATS: European Respiratory Society-American Thoracic Society

Table S4: Baseline demographics of the primary remission/non-remission‡ cohort (n=830)

Variable	n	Category	Result
Time to first Annual Review (Years)	830		1.1 (1.0,1.3)
Time to first Annual Review (Months)	830	>=9 & <12 months	279 (33.6%)
		>=12 & <18 months	430 (51.8%)
		>=18 & <=24 months	121 (14.6%)
Sex	830	Female	489 (58.9%)
Age At First Assessment (Years)	830		52.0 (42.0,61.0)
Age at Onset of Symptoms (Years)	737		22.0 (7.0,41.0)
Age Of Onset of Symptoms (Years)	737	≥40	209 (28.4%)
Duration Of Symptoms From Baseline (Years)	737		23.0 (11.0,37.0)
Duration Of Symptoms From Baseline (Years)		<20	308 (41.8%)
		≥12 & <18	147 (19.9%)
		≥18	282 (38.3%)
Ethnicity	828	White	724 (87.4%)
Smoking Status	809	Never	539 (66.6%)
BMI (kg-m2)	823		30.0 (26.3,34.8)
BMI (kg-m2)	823	<25	144 (17.5%)
		≥25 & <30	271 (32.9%)
		≥30	408 (49.6%)
Atopic Disease	830		427 (51.4%)
Depression or Anxiety	830		88 (10.6%)
Gastro-oesophageal Reflux	830		144 (17.3%)
Nasal polyps	830		171 (20.6%)
OCS bursts (Last Year)	817		5 (3,8)
Any OCS bursts (Last Year)	817		762 (93.3%)
Frequent exacerbator at baseline	817	≥3 exacerbations in last year	668 (81.8%)
Invasive Ventilations (Ever)	798		76 (9.5%)
ED Attendances For asthma (Last Year)	807		0 (0,2)
Any ED Attendance for asthma (Last Year)	807		293 (36.3%)
Hospital Admissions for asthma (Last Year)	814		0 (0,1)
Any Hospital Admissions for asthma (Last Year)	814		315 (38.7%)
Hospital Admissions for asthma (Last Year)	814	≥2	183 (22.4%)
Highest Blood Eosinophil Count recorded (N/10 ⁹ L) †	821		0.70 (0.45,1.08)
Blood Eosinophil Count (N/10 ⁹ L)	819		0.40 (0.20,0.62)
Blood Eosinophil Count (N/10 ⁹ L)	819	<0.15	175 (21.4%)
		≥0.15 & <0.30	96 (11.7%)
		≥0.30 & ≤0.45	196 (23.9%)
		>0.45	352 (43.0%)
FeNO (ppb)	638		43.0 (24.0,74.0)
FeNO (ppb)	638	<20ppb	123 (19.3%)
		≥20 & <50ppb	234 (36.7%)
		≥50ppb	281 (44.0%)
Composite Type 2 status	627	Eos Low (<0.15) / FeNO Low (<20)	40 (6.4%)
		Eos High (≥0.15) / FeNO Low (<20)	79 (12.6%)
		Eos Low (<0.15) / FeNO High (≥20)	107 (17.1%)
		Eos High (≥0.15) / FeNO High (≥20)	401 (64.0%)
FEV ₁ (L)	818		2.0 (1.5,2.6)
FEV ₁ (% Predicted)	811		67.2 (52.5,81.9)
FVC (L)	802		3.2 (2.5,3.9)
FVC (% Predicted)	772		85.5 (74.1,97.7)
FEV ₁ /FVC	802		64.0 (54.3,72.3)
ACQ5 Score	736		3.0 (2.0,4.0)
Uncontrolled Asthma	736	ACQ5≥1.5	622 (84.5%)
EuroQoL Health Scale	350		60.0 (44.0,73.0)
EuroQoL Utility	362		0.7 (0.5,0.9)
Maintenance OCS	826		475 (57.5%)

Maintenance OCS (mg) *	474		10 (8,15)
Inhaled corticosteroids (ICS)	830		827 (99.6%)
ICS Dose (BDP equivalent-μg) **	775		2000 (1600,2000)
Theophylline	821		216 (26.3%)
Short- acting β2-agonist (SABA)	823		785 (95.4%)
Long-acting β2-agonist (LABA)	818		763 (93.3%)
Long acting anti-muscarinic agent (LAMA)	821		525 (63.9%)
Leukotriene Receptor Antagonists	799		407 (50.9%)
Maintenance Macrolides	816		69 (8.5%)
Nebuliser	819		180 (22.0%)
ERS-ATS Severe Asthma	830	Yes	830 (100.0%)

‡ ACQ5 <1.5, no mOCS or OCS bursts, FEV₁ above LLN or <100mls less than pre-biologic FEV

† Median (IQR) or count (%) as appropriate; † highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated

* among patients on oral corticosteroids

** among patients on inhaled corticosteroids

BMI: Body Mass Index; OCS: Oral Corticosteroid Steroids; ED: Emergency Department; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; ICS: Inhaled Corticosteroid Steroids; BDP: Beclometasone Dipropionate; SABA: Short-Acting Beta Agonists; LABA: Long-Acting Beta Agonists; LAMA: Long-Acting Muscarinic Antagonist; ERS-ATS: European Respiratory Society-American Thoracic Society

Table S5: Data completeness of the primary remission cohort by remission status‡ (n=830)

Variable	Non remission (81.7% (678))		Remission (18.3% (152))	
	n (%) non-missing	n (%) missing	n (%) non-missing	n (%) missing
Time until Annual review (Years)	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)
Sex	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)
Age At First Assessment (Years)	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)
Age at Onset of Symptoms (Years)	600 (88.5%)	78 (11.5%)	137 (90.1%)	15 (9.9%)
Duration Of Symptoms From Baseline (Years)	600 (88.5%)	78 (11.5%)	137 (90.1%)	15 (9.9%)
Ethnicity	676 (99.7%)	2 (0.3%)	152 (100.0%)	0 (0.0%)
Smoking Status	663 (97.8%)	15 (2.2%)	146 (96.1%)	6 (3.9%)
BMI (kg-m2)	671 (99.0%)	7 (1.0%)	152 (100.0%)	0 (0.0%)
Atopic Disease	678 (98.0%)	14 (2.0%)	152 (100.0%)	0 (0.0%)
Depression or Anxiety	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)
Gastro-oesophageal Reflux	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)
Nasal polyps	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)
Rescue Steroids In Last Year	667 (98.4%)	11 (1.6%)	150 (98.7%)	2 (1.3%)
Frequent exacerbator at baseline	667 (98.4%)	11 (1.6%)	150 (98.7%)	2 (1.3%)
Invasive Ventilations (Ever)	650 (95.9%)	28 (4.1%)	148 (97.4%)	4 (2.6%)
A&E Attendances For Asthma In Last Year	661 (97.5%)	17 (2.5%)	146 (96.1%)	6 (3.9%)
Hospital Admissions For Asthma In Last Year	666 (98.2%)	12 (1.8%)	148 (97.4%)	4 (2.6%)
Highest Blood Eosinophil Count (N/10 ⁹ L) †	671 (99.0%)	7 (1.0%)	150 (98.7%)	2 (1.3%)
Blood Eosinophil Count (N/10 ⁹ L)	670 (98.8%)	8 (1.2%)	149 (98.0%)	3 (2.0%)
FeNO (ppb)	504 (74.3%)	174 (25.7%)	134 (88.2%)	18 (11.8%)
Composite T2 status	496 (73.2%)	182 (26.8%)	131 (86.2%)	21 (13.8%)
FEV1 (L)	667 (98.4%)	11 (1.6%)	151 (99.3%)	1 (0.7%)
FEV1 (% Predicted)	660 (97.3%)	18 (2.7%)	151 (99.3%)	1 (0.7%)
FVC (L)	653 (96.3%)	25 (3.7%)	149 (98.0%)	3 (2.0%)
FVC (% Predicted)	629 (92.8%)	49 (7.2%)	143 (94.1%)	9 (5.9%)
FEV1/FVC	653 (96.3%)	25 (3.7%)	149 (98.0%)	3 (2.0%)
ACQ5 Score	598 (88.2%)	80 (11.8%)	138 (90.8%)	14 (9.2%)
Puffs of SABA most days (ACQ Q6)	582 (85.8%)	96 (14.2%)	129 (84.9%)	23 (15.1%)
EuroQoL Health Scale	273 (40.3%)	405 (59.7%)	77 (50.7%)	75 (49.3%)
EuroQoL Utility	285 (42.0%)	393 (58.0%)	77 (50.7%)	75 (49.3%)
Maintenance OCS	674 (99.4%)	4 (0.6%)	152 (100.0%)	0 (0.0%)
Maintenance OCS (mg) *	397 (99.7%)	1 (0.3%)	77 (100.0%)	0 (0.0%)
Inhaled corticosteroids (ICS)	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)
ICS Dose (BDP equivalent-µg) **	632 (93.2%)	46 (6.8%)	143 (94.7%)	8 (5.3%)
Theophylline	673 (99.3%)	5 (0.7%)	148 (97.4%)	4 (2.6%)
Short-acting β2-agonist (SABA)	673 (99.3%)	5 (0.7%)	150 (98.7%)	2 (1.3%)
Long-acting β2-agonist (LABA)	667 (98.4%)	11 (1.6%)	151 (99.3%)	1 (0.7%)
Long acting anti-muscarinic agent (LAMA)	670 (98.8%)	8 (1.2%)	151 (99.3%)	1 (0.7%)
Leukotriene Receptor Antagonists	653 (96.3%)	25 (3.7%)	146 (96.1%)	6 (3.9%)
Maintenance Macrolides	665 (98.1%)	13 (1.9%)	151 (99.3%)	1 (0.7%)
Nebuliser	670 (98.8%)	8 (1.2%)	149 (98.0%)	3 (2.0%)
Biologic commenced	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)
Biologic type commenced	609 (89.8%)	69 (10.2%)	138 (90.8%)	14 (9.2%)
ERS-ATS Asthma	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)
Hospital	678 (100.0%)	0 (0.0%)	152 (100.0%)	0 (0.0%)

‡ ACQ5 <1.5, no mOCS or OCS bursts, FEV₁ above LLN or <100mls less than pre-biologic FEV₁

† highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated

*among patients on OCS

** among patients on inhaled corticosteroids

BMI: Body Mass Index; OCS: Oral Corticosteroid Steroids; ED: Emergency Department; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; ICS: Inhaled Corticosteroid Steroids; BDP: Beclometasone Dipropionate; SABA: Short-Acting Beta Agonists; LABA: Long-Acting Beta Agonists; LAMA: Long-Acting Muscarinic Antagonist; ERS-ATS: European Respiratory Society-American Thoracic Society

Table S6: Summary statistics for scalar variables in the primary remission cohort by remission status‡ (n=830)

Variable	Non remission (81.7% (678))		Remission (18.3% (152))	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Time until Annual review (Years)	1.2 (0.3)	1.1 (1.0,1.4)	1.1 (0.3)	1.1 (1.0,1.2)
Age At First Assessment (Years)	49.7 (14.4)	51.0 (41.0,59.0)	55.2 (13.2)	55.0 (48.0,65.0)
Age at Onset of Symptoms (Years)	23.9 (18.8)	20.0 (6.0,39.0)	33.6 (21.4)	32.0 (14.0,52.0)
Duration Of Symptoms From Baseline (Years)	25.7 (17.1)	24.5 (12.0,37.0)	21.6 (16.6)	20.0 (8.0,32.0)
BMI (kg-m ²)	31.4 (7.3)	30.5 (26.6,35.1)	29.2 (7.2)	27.9 (25.4,31.8)
Rescue Steroids In Last Year	6.1 (4.1)	5 (3,8)	4.7 (3.1)	4 (3,6)
A&E Attendances For Asthma (Last Year)	1.6 (3.9)	0 (0,2)	0.6 (1.8)	0 (0,0)
Hospital Admissions For Asthma (Last Year)	1.2 (2.1)	0 (0,1)	0.6 (1.2)	0 (0,1)
Highest Blood Eosinophil Count (N/10 ⁹ L) †	0.88 (1.11)	0.68 (0.40,1.00)	1.13 (1.25)	0.79 (0.58,1.33)
Blood Eosinophil Count (N/10 ⁹ L)	0.49 (0.64)	0.39 (0.18,0.60)	0.52 (0.50)	0.46 (0.22,0.70)
FeNO (ppb)	55.1 (46.9)	41.0 (22.0,72.0)	64.0 (45.8)	51.0 (35.0,81.0)
FEV ₁ (L)	2.0 (0.8)	2.0 (1.5,2.6)	2.2 (0.9)	2.1 (1.6,2.7)
FEV ₁ (% Predicted)	66.8 (20.7)	67.0 (52.4,81.2)	72.2 (23.5)	68.6 (55.0,88.2)
FVC (L)	3.2 (1.0)	3.1 (2.5,3.9)	3.4 (1.1)	3.3 (2.7,4.2)
FVC (% Predicted)	85.1 (18.8)	85.2 (73.8,97.0)	89.3 (19.8)	86.7 (75.8,99.4)
FEV ₁ /FVC	63.5 (21.3)	63.7 (54.3,72.2)	63.6 (12.9)	64.5 (54.4,73.6)
EuroQoL Health Scale	54.6 (20.1)	60.0 (40.0,70.0)	67.4 (19.8)	75.0 (50.0,85.0)
EuroQoL Utility	0.6 (0.3)	0.7 (0.5,0.8)	0.8 (0.2)	0.9 (0.8,1.0)
ACQ5 Score	3.2 (1.3)	3.2 (2.2,4.2)	2.2 (1.4)	2.0 (1.2,3.4)
Maintenance OCS (mg) *	13.5 (9.1)	10 (8,15)	10.0 (5.2)	10 (7,10)
ICS Dose (BDP equivalent-µg) **	1961.0 (624.6)	2000 (1600,2000)	2005.8 (767.9)	2000 (1600,2000)

‡ ACQ5 <1.5, no mOCS or OCS bursts, FEV₁ above LLN or <100mls less than pre-biologic FEV₁

† highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated

* among patients on OCS

* among patients on inhaled corticosteroids

SD: Standard Deviation; IQR: InterQuartile Range; BMI: Body Mass Index; ED: Emergency Department; FEV₁: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; FeNO: Fractional exhaled Nitric Oxide; ACQ: Asthma Control Questionnaire; OCS: Oral Corticosteroids; ICS: Inhaled Corticosteroids; BDP: Beclometasone Dipropionate

Table S7: Clinical characteristics and outcomes at baseline and after 1 year on biologics

	N	Baseline	Annual Review 1	p-value
Time to first annual review (years)	1,111	-	1.1 (1.0,1.3)	-
BMI (kg/m ²)	955	30.0 (26.1,35.0)	29.9 (26.1,35.1)	0.011
Rescue Steroids In Last Year	1040	5 (3,8)	1 (0,3)	<0.001
Any Rescue Steroids in Last Year	1040	975 (93.8%)	656 (63.1%)	<0.001
Frequent exacerbator (≥3 exacerbations in last year)	1040	864 (83.1%)	302 (29.0%)	0.002
ED attendances for asthma (last year)	1015	0 (0,2)	0 (0,0)	<0.001
Any ED attendance for asthma (last year)	1015	397 (39.1%)	139 (13.7%)	<0.001
Hospital admissions for asthma (last year)	984	0 (0,1)	0 (0,0)	<0.001
Any hospital admission for asthma (last year)	984	395 (40.1%)	140 (14.2%)	<0.001
Blood eosinophil count (10 ⁹ /L)	738	0.37 (0.16,0.61)	0.06 (0.00,0.14)	<0.001
FEV1 (L)	941	2.0 (1.5,2.6)	2.2 (1.6,2.7)	<0.001
FEV1 (% predicted)	929	67.4 (52.4,81.9)	73.3 (58.7,87.5)	<0.001
FVC (L)	870	3.2 (2.5,3.9)	3.2 (2.5,4.0)	0.507
FVC (% predicted)	831	86.2 (74.0,98.3)	87.8 (74.5,100.0)	0.065
FEV1/FVC	868	63.6 (53.6,72.3)	68.0 (58.7,75.7)	<0.001
FeNO (ppb)	567	43.0 (23.0,73.0)	36.0 (16.0,69.0)	<0.001
ACQ5 Score	851	3.0 (2.0,4.0)	2.0 (0.8,3.2)	<0.001
ACQ5≥1.5	851	721 (84.7%)	514 (60.0%)	<0.001
ACQ6 Score	806	3.0 (2.0,4.0)	1.8 (0.8,3.2)	<0.001
ACQ6 ≥1.5	806	690 (85.6%)	491 (60.9%)	<0.001
ACQ7 Score	806	3.1 (2.2,4.0)	2.1 (1.3,3.3)	<0.001
ACQ7 ≥1.5	806	712 (88.3%)	549 (68.1%)	<0.001
Reported number of SABA puffs most days (ACQ Q6)	806			
None		96 (11.9%)	203 (25.2%)	<0.001
1-2 puffs		120 (14.5%)	168 (20.8%)	
3-4 puffs		155 (19.2%)	135 (16.8%)	
5-8 puffs		165 (20.5%)	135 (16.8%)	
9-12 puffs		123 (15.3%)	85 (10.6%)	
13-16 puffs		73 (9.1%)	36 (4.5%)	
>16 puffs		74 (9.2%)	44 (5.5%)	
Maintenance OCS	1085	625 (57.6%)	517 (47.7%)	<0.001

Median (IQR) or count (%) as appropriate 'Last Year' refers to measures assessed using clinical records in the 12 months prior to either baseline visit to the severe asthma clinic or at annual review, otherwise measures were as observed or recorded at the relevant time-point.

BMI: Body Mass Index; OCS: Oral Corticosteroid Steroids; ED: Emergency Department; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; SABA: Short-Acting Beta Agonists

Table S8: Baseline pre-biologics characteristics of those who meet remission versus those who do not meet remission at annual review (remission criteria ACQ5 <1.5, no mOCS or OCS bursts, FEV₁ above LLN or <100mls less than pre-biologic FEV₁).

Baseline variable	n	Category	Non-remission	Remission	p-value
	830		81.7% (678)	18.3% (152)	
Time to first Annual Review (Years)	830		1.1 (1.0,1.4)	1.1 (1.0,1.2)	0.097
Sex	830	Female	412 (60.8%)	77 (50.7%)	0.022
		Male	266 (39.2%)	75 (49.3%)	
Age At First Assessment (Years)	830		51.0 (41.0,59.0)	55.0 (48.0,65.0)	<0.001
Age At First Assessment (Years)	830	18-34	111 (16.4%)	12 (7.9%)	0.005
		35-54	296 (43.7%)	61 (40.1%)	
		>=55	271 (40.0%)	79 (52.0%)	
Age at Onset of Symptoms (Years)	737		20.0 (6.0,39.0)	32.0 (14.0,52.0)	<0.001
Age of Onset of Symptoms (Years)	737	<12	202 (33.7%)	29 (21.2%)	0.012
		≥12 & <18	57 (9.5%)	12 (8.8%)	
		≥18	341 (56.8%)	96 (70.1%)	
Age Of Onset of Symptoms (Years)	737	(≥40)	146 (24.3%)	63 (46.0%)	<0.001
Duration Of Symptoms From Baseline (Years)	737		24.5 (12.0,37.0)	20.0 (8.0,32.0)	0.008
Ethnicity	828	White	583 (86.2%)	141 (92.8%)	0.028
		Non-White	93 (13.8%)	11 (7.2%)	
Smoking status	809	Never	430 (64.9%)	109 (74.7%)	0.023
		Current/Ex-smoker	233 (35.1%)	37 (25.4%)	
BMI (kg-m2)	823		30.5 (26.6,35.1)	27.9 (25.4,31.8)	0.001
BMI (kg-m2)	823	<25	110 (16.4%)	34 (22.4%)	<0.001
		≥25 & <30	204 (30.4%)	67 (44.1%)	
		≥30	357 (53.2%)	51 (33.6%)	
Atopic Disease	830		355 (52.4%)	72 (47.4%)	0.226
Depression or Anxiety	830		85 (12.5%)	3 (2.0%)	<0.001
Gastro-oesophageal Reflux	830		119 (17.6%)	25 (16.4%)	0.745
Nasal polyps	830		123 (18.1%)	48 (31.6%)	<0.001
OCS bursts (Last Year)	817		5 (3,8)	4 (3,6)	<0.001
Any OCS bursts (Last Year)	817		624 (93.6%)	138 (92.0%)	0.493
Frequent Exacerbator at baseline	817	Yes (≥3 in Last Year)	554 (83.1%)	114 (76.0%)	0.043
Invasive Ventilations (Ever)	798		68 (10.5%)	8 (5.4%)	0.058
Any ED Attendance for asthma (Last Year)	807		259 (39.2%)	34 (23.3%)	<0.001
Any Hospital Admissions for asthma (Last Year)	814		270 (40.5%)	45 (30.4%)	0.022
Highest Blood Eosinophil Count (N/10 ⁹ L) †	821		0.68 (0.40,1.00)	0.79 (0.58,1.33)	<0.001
Highest Blood Eosinophil Count (N/10 ⁹ L) †	821	<0.15	13 (1.9%)	4 (2.7%)	0.006
		≥0.15 & <0.3	27 (4.0%)	4 (2.7%)	
		≥0.3 & <0.5	157 (23.4%)	20 (13.3%)	
		≥0.5 & <1.0	292 (43.5%)	61 (40.7%)	
		≥1.0	182 (27.1%)	61 (40.7%)	
Blood Eosinophil Count (N/10 ⁹ L)	819		0.39 (0.18,0.60)	0.46 (0.22,0.70)	0.011
FeNO (ppb)	638		41.0 (22.0,72.0)	51.0 (35.0,81.0)	0.002
FeNO (ppb)	638	<20	111 (22.0%)	12 (9.0%)	0.001
		≥20 & <50	184 (36.5%)	50 (37.3%)	
		≥50	209 (41.5%)	72 (53.7%)	
Composite Type 2 status	627	Eos Low (<0.15) / FeNO Low (<20)	38 (7.7%)	2 (1.5%)	0.004
		Eos High (≥0.15) / FeNO Low (<20)	69 (13.9%)	10 (7.6%)	
		Eos Low (<0.15) / FeNO High (≥20)	86 (17.3%)	21 (16.0%)	
		Eos High ≥0.15) / FeNO High (≥20)	303 (61.1%)	98 (74.8%)	
FEV ₁ (L)	818		2.0 (1.5,2.6)	2.1 (1.6,2.7)	0.073
FEV ₁ (% Predicted)	811		67.0 (52.4,81.2)	68.6 (55.0,88.2)	0.027
FVC (L)	802		3.1 (2.5,3.9)	3.3 (2.7,4.2)	0.048
FVC (% Predicted)	772		85.2 (73.8,97.0)	86.7 (75.8,99.4)	0.065

FEV ₁ /FVC	802		63.7 (54.3,72.2)	64.5 (54.4,73.6)	0.498
ACQ5 Score	736		3.2 (2.2,4.2)	2.0 (1.2,3.4)	<0.001
Uncontrolled Asthma	711	ACQ5 ≥1.5	531 (88.8%)	91 (65.9%)	<0.001
EuroQoL Health Scale	350		60.0 (40.0,70.0)	75.0 (50.0,85.0)	<0.001
EuroQoL Utility	362		0.7 (0.5,0.8)	0.9 (0.8,1.0)	<0.001
Maintenance OCS	826		398 (59.1%)	77 (50.7%)	0.059
Maintenance OCS (mg)*	474		10 (8,15)	10 (7,10)	0.001
Inhaled corticosteroids (ICS)	830		676 (99.7%)	151 (99.3%)	0.500
ICS Dose (BDP equivalent-ug)**	775		2000 (1600,2000)	2000 (1600,2000)	0.556
Theophylline	821		184 (27.3%)	32 (21.6%)	0.153
SABA	823		643 (95.5%)	142 (94.7%)	0.644
Long-acting β2-agonist (LABA)	818		619 (92.8%)	144 (95.4%)	0.258
Long acting anti-muscarinic agent (LAMA)	821		420 (62.7%)	105 (69.5%)	0.113
Leukotriene Receptor Antagonists	799		327 (50.1%)	80 (54.8%)	0.303
Maintenance Macrolides	816		60 (9.0%)	9 (6.0%)	0.202
Nebuliser	819		164 (24.5%)	16 (10.7%)	<0.001

*among patients on oral corticosteroids

**among patients on inhaled corticosteroids

‡ Median (IQR) or count (%) as appropriate; † highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated

OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; ED: Emergency Department; OCS: Oral Corticosteroid Steroids; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; SABA: Short-Acting Beta-2 Agonists; ICS: Inhaled Corticosteroid Steroids; LABA: Long-Acting Beta-2 Agonists; LAMA: Long-Acting Muscarinic Antagonist

Table S9: Odds ratios associated with remission‡ for selected covariates (plus 10 unit increase for age and symptom duration, 1 unit increase in BMI)

Variable	Category	Unadjusted model		Adjusted for time to first Annual Review, hospital		Adjusted for time to Annual Review, hospital, baseline ACQ5, baseline exacerbations (ie baseline morbidity)	
		N	OR (95%CI, p-value)	N	OR (95%CI, p-value)	N	OR (95%CI, p-value)
OR: Odds Ratio; CI: Confidence							
Sex	Male	830	1	830	1	726	1
	Female		0.66 (0.46,0.94), p=0.021		0.64 (0.45,0.93), p=0.018		0.76 (0.51,1.15), p=0.199
Age at first assessment (years)	Increase of 10 years	830	1.31 (1.15,1.50), p<0.001	830	1.31 (1.15,1.50), p<0.001	726	1.25 (1.07,1.45), p=0.004
	18-34	830	1	830	1	726	1
	35-54		1.90 (0.99,3.67), p=0.055		1.94 (0.99,3.80), p=0.053		1.94 (0.93,4.03), p=0.077
>=55	2.69 (1.41,5.15), p=0.003		2.62 (1.35,5.10), p=0.005		2.18 (1.05,4.56), p=0.037		
Duration of symptoms at baseline (years)	Increase of 10 years	737	0.86 (0.76,0.97), p=0.011	737	0.86 (0.76,0.97), p=0.013	667	0.92 (0.81,1.05), p=0.226
	<10	737	1	737	1	667	1
	10-19		0.49 (0.27,0.87), p=0.015		0.54 (0.29,0.97), p=0.040		0.66 (0.34,1.28), p=0.224
	20-29		0.61 (0.35,1.05), p=0.073		0.64 (0.37,1.14), p=0.128		0.77 (0.41,1.44), p=0.410
	>=30		0.51 (0.32,0.82), p=0.006		0.51 (0.31,0.84), p=0.008		0.70 (0.40,1.22), p=0.210
Ethnicity	White	828	1	828	1	724	1
	Non-White		0.51 (0.26,0.98), p=0.043		0.53 (0.26,1.07), p=0.077		0.59 (0.26,1.34), p=0.207
BMI (kg-m2)	Increase of 1 kg-m2	823	0.96 (0.93,0.98), p=0.001	823	0.95 (0.92,0.98), p<0.001	722	0.96 (0.94,0.99), p=0.016
	Not overweight (<25)	823	1	823	1	722	1
	Overweight (>=25 & <30)		1.03 (0.64,1.66), p=0.899		1.00 (0.61,1.63), p=0.992		0.98 (0.56,1.71), p=0.945
	Obese (>=30)		0.46 (0.28,0.74), p=0.002		0.39 (0.24,0.65), p<0.001		0.53 (0.30,0.93), p=0.026
Smoking status	Never smoker	809	1	809	1	710	1
	Current/ex-smoker		0.61 (0.40,0.91), p=0.017		0.53 (0.34,0.82), p=0.004		0.64 (0.39,1.03), p=0.066
Depression/anxiety	No	830	1	830	1	726	1
	Yes		0.13 (0.04,0.42), p=0.001		0.13 (0.04,0.43), p=0.001		0.11 (0.02,0.50), p=0.004
Composite Type 2 status	Eos Low (<0.15) / FeNO Low (<20)	627	1	627	1	556	1
	Eos High (>=0.15) / FeNO Low (<20)		2.83 (0.59,13.61), p=0.194		3.26 (0.67,15.93), p=0.144		3.79 (0.73,19.75), p=0.113
	Eos Low (<0.15) / FeNO High (>=20)		4.61 (1.03,20.66), p=0.046		5.33 (1.17,24.34), p=0.031		6.23 (1.28,30.34), p=0.023
	Eos High (>=0.15) / FeNO High (>=20)		6.34 (1.50,26.78), p=0.012		7.44 (1.73,31.95), p=0.007		7.48 (1.64,34.16), p=0.009
OCS bursts (year prior to biologics)	0	817	1	817	1	726	1
	1		2.03 (0.81,5.04), p=0.129		1.54 (0.60,3.94), p=0.363		1.44 (0.54,3.87), p=0.465
	2		0.66 (0.25,1.73), p=0.394		0.52 (0.19,1.43), p=0.203		0.57 (0.20,1.65), p=0.302
	>=3		0.70 (0.35,1.37), p=0.292		0.50 (0.24,1.06), p=0.070		0.62 (0.28,1.38), p=0.244
Maintenance OCS	No	826	1	826	1	722	1
	Yes		0.74 (0.52,1.05), p=0.092		0.84 (0.57,1.24), p=0.390		0.83 (0.52,1.30), p=0.408
Biologic Therapy Type	Anti-IL5	745	1	745	1	674	1
	Anti-IgE		0.22 (0.09,0.55), p=0.001		0.25 (0.10,0.64), p=0.004		0.22 (0.08,0.65), p=0.006
ACQ5	<1.5	736	1	736	1	726	1
	>=1.5		0.23 (0.15,0.36), p<0.001		0.19 (0.12,0.31), p<0.001		0.20 0.20 (0.12,0.32), p<0.001

‡ ACQ5 <1.5, no mOCS or OCS bursts, FEV₁ above LLN or <100mls less than pre-biologic FEV₁

Figure S2: Estimated adjusted probability of achieving clinical remission* at the means for selected covariates

‡ ACQ5 <1.5, and no mOCS or OCS bursts and, FEV₁ above LLN or <100mls less than pre-biologic FEV₁ CI: Confidence Interval; BMI: Body Mass Index; Eos: Blood eosinophil count (N/10⁹L); FeNO: Fractional exhaled Nitric Oxide; OCS: Oral Corticosteroids; mOCS; maintenance OCS; ACQ: Asthma Control Questionnaire; FEV₁; Forced Expiratory Volume (1 second)

Baseline covariate

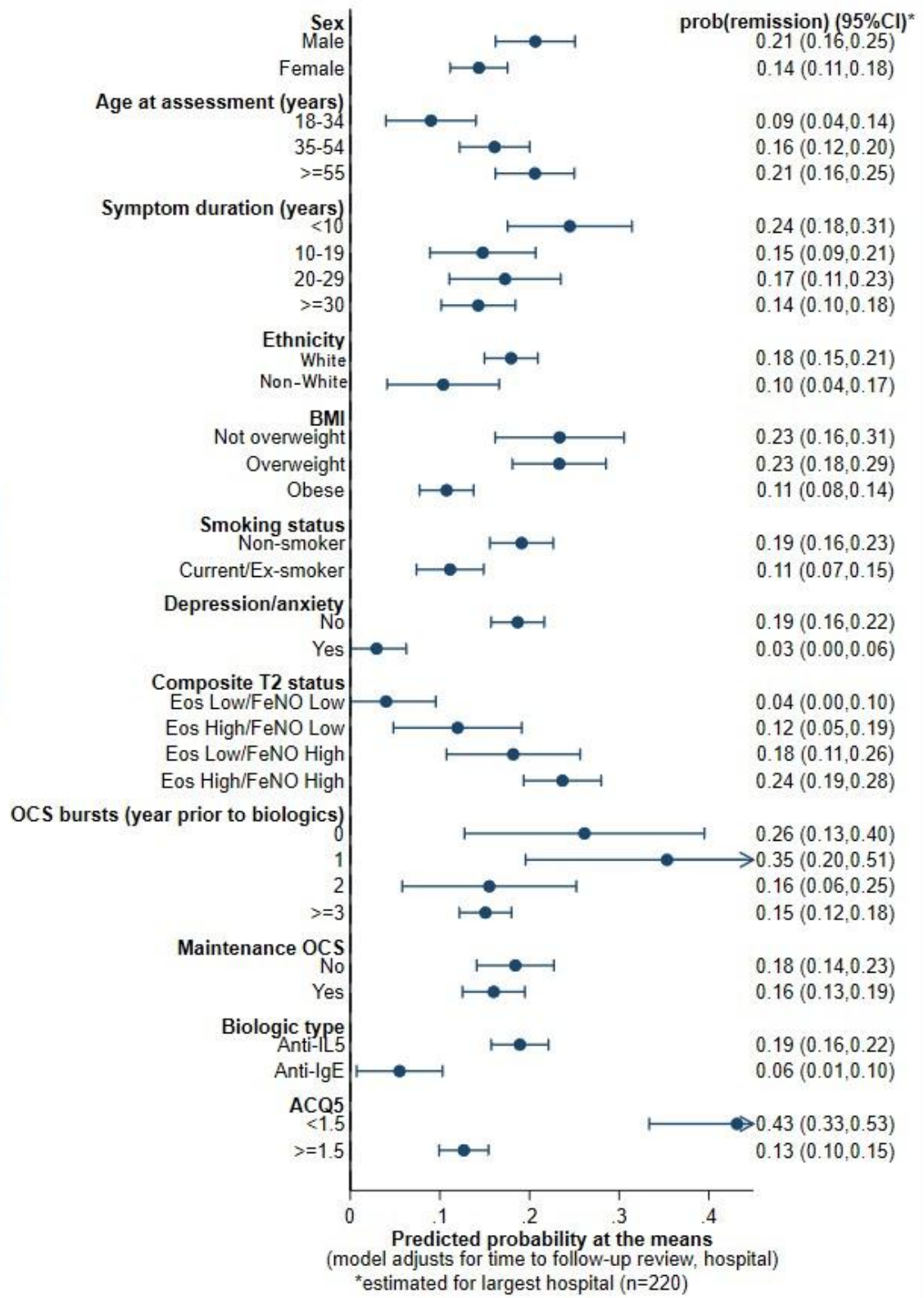


Table S10: Individual area under the curve for each variable included in the regression model.

Variable	Individual AUC (95% CI)
Hospital	0.618 (0.567,0.669)
Time to Follow-up	0.618 (0.567,0.669)
Age At Initial Assessment (Years)	0.655 (0.605,0.706)
Gender	0.644 (0.591,0.696)
Duration Of Symptoms At Baseline (Years)	0.661 (0.614,0.709)
Ethnicity	0.627 (0.576,0.677)
BMI (kg-m2)	0.683 (0.636,0.730)
Smoking Status	0.666 (0.617,0.715)
Depression or Anxiety	0.652 (0.604,0.700)
T2-Group	0.652 (0.600,0.704)
Exacerbations (Last Year)	0.657 (0.615,0.700)
Maintenance OCS	0.630 (0.581,0.678)
Biologic Therapy Type	0.651 (0.603,0.700)
Baseline ACQ5	0.709 (0.661,0.756)

Table S11: Remission criteria ACQ <1.5 AND no OCS bursts or mOCS >5mg/day AND FEV₁ above LLN or <5% from pre-biologics FEV₁: baseline characteristics of those who meet remission at annuak review and those who do not.

Baseline variable	n		Non-remission	Remission	p-value
	830		81.7% (678)	18.3% (152)	
Time until Annual Review (Years)	830		1.1 (1.0,1.4)	1.1 (1.0,1.2)	0.067
Time until Annual Review (Years)	830	>=9 & <12 months	223 (32.9%)	56 (36.8%)	0.175
		>=12 & <18 months	349 (51.5%)	81 (53.3%)	
		>=18 & <=24 months	106 (15.6%)	15 (9.9%)	
Sex	830	Female	413 (60.9%)	76 (50.0%)	0.013
Age At First Assessment (Years)	830		51.0 (41.0,59.0)	55.0 (48.0,65.0)	<0.001
Age at Onset of Symptoms (Years)	737		20.0 (6.0,39.0)	33.5 (14.0,52.0)	<0.001
Age Of Onset of Symptoms (Years)	737	(≥40 years)	146 (24.3%)	63 (46.3%)	<0.001
Duration Of Symptoms From Baseline (Years)	737		25.0 (12.0,37.0)	20.0 (8.0,31.5)	0.007
Duration of Symptoms From Baseline (Years)	737	<20	243 (40.4%)	65 (47.8%)	0.227
		20-29	120 (20.0%)	27 (19.9%)	
		>=30	238 (39.6%)	44 (32.4%)	
Ethnicity	828	White	583 (86.2%)	141 (92.8%)	0.028
Smoking status	809	Never smoked	430 (64.9%)	109 (74.7%)	0.023
BMI (kg-m2)	823		30.5 (26.6,35.2)	27.8 (25.3,31.6)	<0.001
BMI (kg-m2)	823	<25	109 (16.2%)	35 (23.0%)	<0.001
		≥25 & <30	204 (30.4%)	67 (44.1%)	
		≥30	358 (53.4%)	50 (32.9%)	
Atopic Disease	830		355 (52.4%)	72 (47.4%)	0.226
Depression or Anxiety	830		85 (12.5%)	3 (2.0%)	<<0.001
Gastro-oesophageal Reflux	830		119 (17.6%)	25 (16.4%)	0.745
Nasal polyps	830		124 (18.3%)	47 (30.9%)	0.001
OCS bursts (Last Year)	817		5 (3,8)	4 (3,6)	<0.001
Any OCS bursts (Last Year)	817		624 (93.6%)	138 (92.0%)	0.493
Frequent Exacerbator at baseline	817	Yes (≥3 in Last Year)	554 (83.1%)	114 (76.0%)	0.043
Invasive Ventilations (Ever)	798		68 (10.5%)	8 (5.4%)	0.058
Any ED Attendance for asthma (Last Year)	807		259 (39.2%)	34 (23.3%)	<0.001
Any Hospital Admissions for asthma (Last Year)	814		270 (40.5%)	45 (30.4%)	0.022
Highest Blood Eosinophil Count (N/10 ⁹ L) †	821		0.68 (0.41,1.00)	0.79 (0.58,1.33)	0.001
Blood Eosinophil Count (N-109L)	819		0.40 (0.18,0.60)	0.46 (0.22,0.70)	0.127
Blood Eosinophil Count (N-109L)	819	<0.15	148 (22.1%)	27 (18.1%)	0.102
		≥0.15 & <0.30	76 (11.3%)	20 (13.4%)	
		≥0.30 & ≤0.45	169 (25.2%)	27 (18.1%)	
		>0.45	277 (41.3%)	75 (50.3%)	
FeNO (ppb)	638		41.0 (22.0,72.0)	51.0 (35.0,81.0)	0.002
FeNO (ppb)	638	<20ppb	111 (22.0%)	12 (9.0%)	0.001
		≥20 & <50ppb	185 (36.6%)	49 (36.8%)	
		≥50ppb	209 (41.4%)	72 (54.1%)	
Composite Type 2 status	627	Eos Low (<0.15) / FeNO Low (<20)	38 (7.6%)	2 (1.5%)	0.004
		Eos High (≥0.15) / FeNO Low (<20)	69 (13.9%)	10 (7.7%)	
		Eos Low (<0.15) / FeNO High (≥20)	86 (17.3%)	21 (16.2%)	
		Eos High (≥0.15) / FeNO High (≥20)	304 (61.2%)	97 (74.6%)	
FEV ₁ (L)	818		2.0 (1.5,2.6)	2.1 (1.6,2.7)	0.048
FEV ₁ (% Predicted)	811		66.9 (52.4,81.2)	68.6 (55.0,88.2)	0.024
FVC (L)	802		3.1 (2.5,3.9)	3.3 (2.7,4.2)	0.0129
FVC (% Predicted)	772		85.2 (73.6,97.0)	86.7 (76.2,99.4)	0.055
FEV ₁ /FVC	802		63.7 (54.3,72.2)	64.5 (54.4,72.6)	0.530
ACQ5 Score	736		3.2 (2.2,4.2)	2.0 (1.2,3.4)	<0.001
Uncontrolled Asthma	736	ACQ5 ≥1.5	532 (89.0%)	90 (65.2%)	<0.001
EuroQoL Health Scale	350		60.0 (40.0,70.0)	75.0 (50.0,85.0)	<0.001
EuroQoL Utility	362		0.7 (0.5,0.8)	0.9 (0.8,1.0)	<0.001

Maintenance OCS	826		397 (58.9%)	78 (51.3%)	0.087
Maintenance OCS (mg) *	474		10 (8,15)	10 (6,10)	0.001
Inhaled corticosteroids (ICS)	830		676 (99.7%)	151 (99.3%)	0.500
ICS Dose (BDP equivalent-μg) **	775		2000 (1600,2000)	2000 (1600,2000)	0.619
Theophylline	821		184 (27.3%)	32 (21.6%)	0.153
Short-acting β2-agonist (SABA)	823		643 (95.5%)	142 (94.7%)	0.644
Long-acting β2-agonist (LABA)	818		620 (93.0%)	143 (94.7%)	0.439
Long acting anti-muscarinic agent (LAMA)	821		421 (62.8%)	104 (68.9%)	0.163
Leukotriene Receptor Antagonists	799		328 (50.2%)	79 (54.1%)	0.397
Maintenance Macrolides	816		60 (9.0%)	9 (6.0%)	0.222
Nebuliser	819		164 (24.5%)	16 (10.7%)	<0.001

*among patients on oral corticosteroids

**among patients on inhaled corticosteroids

‡ Median (IQR) or count (%) as appropriate; † highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated

OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; ED: Emergency Department; OCS: Oral Corticosteroid Steroids; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; SABA: Short-Acting Beta Agonists; ICS: Inhaled Corticosteroid Steroids; LABA: Long-Acting Beta Agonists; LAMA: Long-Acting Muscarinic Antagonist

Figure S3: Reasons for not meeting remission criteria after 1 year on biologic therapy. Remission definition: ACQ5 <1.5, no mOCS or OCS bursts, FEV₁ above LLN or ≤5% less than pre-biologic FEV₁



ACQ: Asthma Control Questionnaire; mOCS: maintenance Oral Corticosteroid Steroids; FEV₁: Forced Expiratory Volume (1 second); LLN: Lower Limit of Normal

Table S12: Remission criteria ACQ <1.5 AND no OCS bursts or mOCS >5mg/day AND FEV₁ above LLN or no lower than pre-biologics: baseline characteristics of those who meet remission at annual review and those who do not.

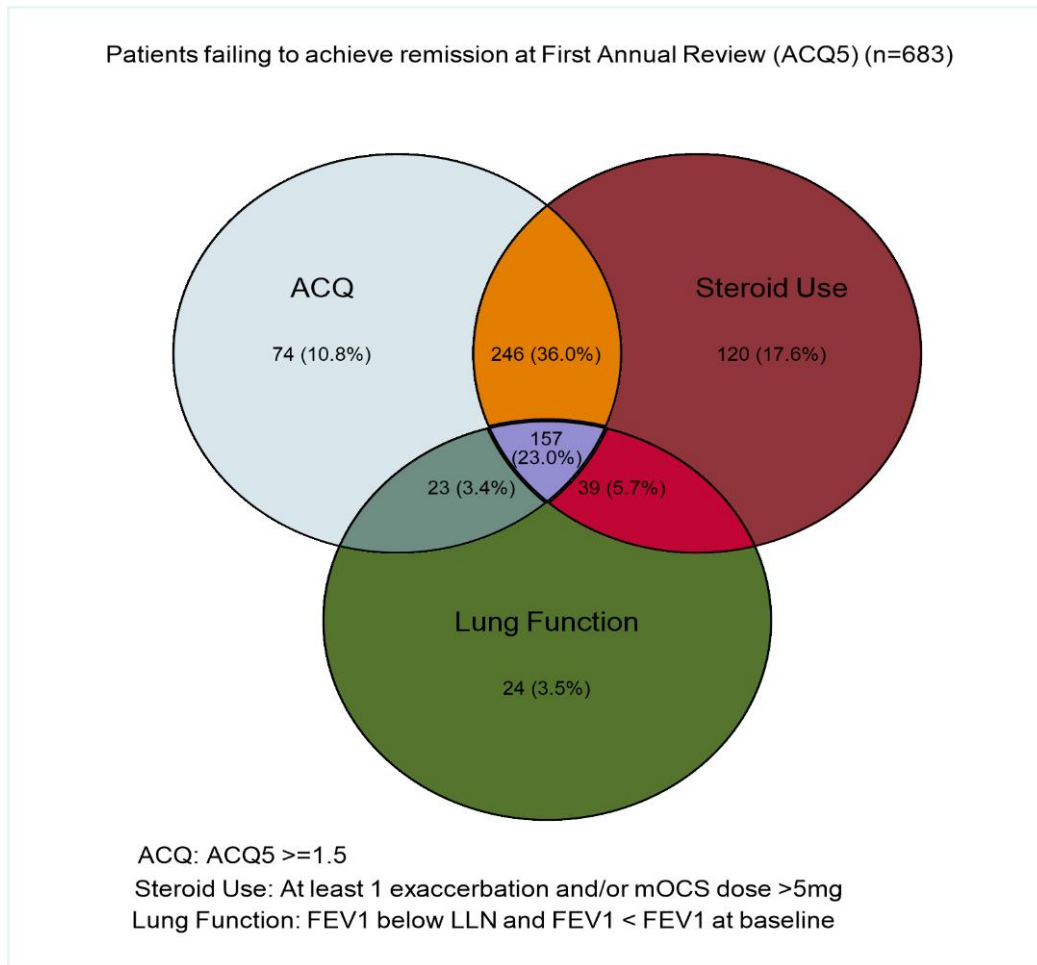
	n	Category	Non-remission	Remission	p-value
	830		82.3% (683)	17.7% (147)	
Time until Annual Review (Years)	830		1.1 (1.0,1.4)	1.1 (1.0,1.2)	0.054
Time until Annual Review (Years)	830	>=9 & <12 months	225 (32.9%)	54 (36.7%)	0.151
		>=12 & <18 months	351 (51.4%)	79 (53.7%)	
		>=18 & <=24 months	107 (15.7%)	14 (9.5%)	
Sex	830	Female	414 (60.6%)	75 (51.0%)	0.032
Age At First Assessment (Years)	830		51.0 (41.0,59.0)	55.0 (48.0,65.0)	<0.001
Age at Onset of Symptoms (Years)	737		20.0 (6.0,39.0)	33.5 (15.0,52.0)	<0.001
Age Of Onset of Symptoms (≥40 years)	737		148 (24.5%)	61 (46.2%)	<0.001
Duration Of Symptoms From Baseline (Years)	737		25.0 (12.0,37.0)	20.0 (8.0,31.0)	0.004
Duration Of Symptoms From Baseline (Years)	737	0-19	245 (40.5%)	63 (47.7%)	0.210
		20-29	120 (19.8%)	27 (20.5%)	
		>=30	240 (39.7%)	42 (31.8%)	
Ethnicity	828	White	587 (86.2%)	137 (93.2%)	0.020
Smoking status	809	Never smoked	433 (64.8%)	106 (75.2%)	0.018
BMI (kg-m2)	823		30.5 (26.6,35.2)	27.8 (25.3,31.4)	<0.001
BMI (kg-m2)	823	<25	111 (16.4%)	33 (22.4%)	<0.001
		≥25 & <30	204 (30.2%)	67 (45.6%)	
		≥30	361 (53.4%)	47 (32.0%)	
Atopic Disease	830		358 (52.4%)	69 (46.9%)	0.195
Depression or Anxiety	830		86 (12.6%)	2 (1.4%)	<0.001
Gastro-oesophageal Reflux	830		120 (17.6%)	24 (16.3%)	0.718
Nasal polyps	830		124 (18.2%)	47 (32.0%)	<0.001
OCS bursts (Last Year)	817		5 (3,8)	4 (3,6)	<0.001
Any OCS bursts (Last Year)	817		629 (93.6%)	133 (91.7%)	0.413
Frequent Exacerbator at baseline	817	Yes (≥3 in Last Year)	559 (83.2%)	109 (75.2%)	0.023
Invasive Ventilations (Ever)	798		70 (10.7%)	6 (4.2%)	0.017
Any ED Attendance for asthma (Last Year)	807		261 (39.2%)	32 (22.7%)	<0.001
Any Hospital Admissions for asthma (Last Year)	814		272 (40.5%)	43 (30.1%)	0.020
Highest Blood Eosinophil Count (N/10 ⁹ L) †	821		0.69 (0.41,1.00)	0.79 (0.58,1.33)	<0.001
Blood Eosinophil Count (N/10 ⁹ L)	819		0.39 (0.18,0.60)	0.47 (0.20,0.70)	0.086
Blood Eosinophil Count (N/10 ⁹ L)	819	<0.15	148 (21.9%)	27 (18.8%)	0.049
		≥0.15 & <0.30	78 (11.6%)	18 (12.5%)	
		≥0.30 & ≤0.45	172 (25.5%)	24 (16.7%)	
		>0.45	277 (41.0%)	75 (52.1%)	
FeNO (ppb)	638		41.0 (22.0,72.0)	53.0 (36.0,81.0)	<0.001
FeNO (ppb)	638	<20ppb	113 (22.2%)	10 (7.8%)	<0.001
		≥20 & <50ppb	186 (36.5%)	48 (37.2%)	
		≥50ppb	210 (41.3%)	71 (55.0%)	
Composite Type 2 status	627	Eos Low (<0.15) / FeNO Low (<20)	38 (7.6%)	2 (1.6%)	0.002
		Eos High (≥0.15) / FeNO Low (<20)	71 (14.2%)	8 (6.3%)	
		Eos Low (<0.15) / FeNO High (≥20)	86 (17.2%)	21 (16.7%)	
		Eos High (≥0.15) / FeNO High (≥20)	306 (61.1%)	95 (75.4%)	
FEV ₁ (L)	818		2.0 (1.5,2.6)	2.1 (1.6,2.7)	0.047
FEV ₁ (% Predicted)	811		66.9 (52.4,81.1)	68.7 (55.0,88.9)	0.018
FVC (L)	802		3.1 (2.5,3.9)	3.3 (2.7,4.2)	0.038
FVC (% Predicted)	772		85.1 (73.8,97.0)	87.1 (76.2,99.4)	0.018
FEV ₁ /FVC	802		63.7 (54.3,72.2)	64.6 (55.0,73.7)	0.43
ACQ5 Score	736		3.2 (2.2,4.2)	2.0 (1.2,3.2)	<0.001
Uncontrolled Asthma	736	ACQ5 ≥1.5	536 (88.9%)	86 (64.7%)	<0.001
EuroQoL Health Scale	350		55.0 (40.0,70.0)	75.0 (50.0,85.0)	<0.001
EuroQoL Utility	362		0.7 (0.5,0.8)	0.9 (0.8,1.0)	<0.001
Maintenance OCS	826		401 (59.1%)	74 (50.3%)	0.053
Maintenance OCS (mg) *	474		10 (8,15)	10 (7,10)	0.004

ICS	830		681 (99.7%)	146 (99.3%)	0.478
ICS Dose (BDP equivalent- μ g) **	775		2000 (1600,2000)	2000 (1600,2000)	0.426
Theophylline	821		185 (27.3%)	31 (21.7%)	0.166
Short-acting β 2-agonist (SABA)	823		648 (95.6%)	137 (94.5%)	0.569
Long-acting β 2-agonist (LABA)	818		624 (92.9%)	139 (95.2%)	0.304
Long acting anti-muscarinic agent (LAMA)	821		423 (62.7%)	102 (69.9%)	0.101
Leukotriene Receptor Antagonists	799		330 (50.2%)	77 (54.6%)	0.337
Maintenance Macrolides	816		61 (9.1%)	8 (5.5%)	0.154
Nebuliser	819		166 (24.6%)	14 (9.7%)	<0.001

*among patients on oral corticosteroids**among patients on inhaled corticosteroids[†] Median (IQR) or count (%) as appropriate; † highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated.

OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; ED: Emergency Department; OCS: Oral Corticosteroid Steroids; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; SABA: Short-Acting Beta Agonists; ICS: Inhaled Corticosteroid Steroids; LABA: Long-Acting Beta Agonists; LAMA: Long-Acting Muscarinic Antagonist

Figure S4: Reasons for not meeting remission criteria after 1 year on biologic therapy. Remission definition: ACQ5 <1.5, no mOCS or OCS bursts, FEV₁ above LLN or ≤less than pre-biologic FEV1



ACQ: Asthma Control Questionnaire; mOCS: maintenance Oral Corticosteroid Steroids; FEV₁; Forced Expiratory Volume (1 second); LLN: Lower Limit of Normal

Table S13: Remission criteria ACQ <1.5 AND no OCS bursts or mOCS >5mg/day: baseline characteristics of those who meet remission at 1 year and those who do not

	n	Category	Non-remission	Remission	p-value
	925		78.8% (729)	21.2% (196)	
Time until Annual Review (Years)	925		1.1 (1.0,1.4)	1.1 (1.0,1.3)	0.035
Sex	925	Female	445 (61.0%)	100 (51.0%)	0.011
Age At First Assessment (Years)	925		51.0 (40.0,59.0)	55.0 (48.0,65.0)	<0.001
Age at Onset of Symptoms (Years)	818		20.0 (6.0,38.5)	35.0 (14.0,50.0)	<0.001
Age Of Onset of Symptoms (≥40 years)	818		155 (24.1%)	81 (46.6%)	<0.001
Duration Of Symptoms From Baseline (Years)	818		25.0 (12.0,38.0)	20.0 (8.0,32.0)	0.003
Duration of symptoms From Baseline (Years)	818	0-19	260 (40.4%)	80 (46.0%)	0.175
		20-29	123 (19.1%)	37 (21.3%)	
		≥30	261 (40.5%)	57 (32.8%)	
Ethnicity	923	White	623 (85.7%)	178 (90.8%)	0.060
Smoking status	903	Never smoked	460 (64.4%)	140 (74.1%)	0.012
BMI (kg-m2)	917		30.7 (26.6,35.2)	27.8 (24.9,31.8)	<0.001
BMI (kg-m2)	917	<25	119 (16.5%)	50 (25.6%)	<0.001
		≥25 & <30	215 (29.8%)	78 (40.0%)	
		≥30	388 (53.7%)	67 (34.4%)	
Atopic Disease	925		382 (52.4%)	92 (46.9%)	0.166
Depression or Anxiety	925		100 (13.7%)	5 (2.6%)	<0.001
Gastro-oesophageal Reflux	925		138 (18.9%)	34 (17.3%)	0.613
Nasal polyps	925		134 (18.4%)	62 (31.6%)	<0.001
OCS bursts (Last Year)	908		6 (4,8)	4 (3,6)	<0.001
Any OCS bursts (Last Year)	908		672 (94.1%)	178 (91.8%)	0.232
Frequent Exacerbator at baseline	908	Yes (≥3 in Last Year)	602 (84.3%)	151 (77.8%)	0.033
Invasive Ventilations (Ever)	888		76 (10.9%)	10 (5.2%)	0.019
Any ED Attendance for asthma (Last Year)	898		296 (41.7%)	50 (26.6%)	<0.001
Any Hospital Admission for asthma (Last Year)	908		299 (41.7%)	58 (30.4%)	0.004
Highest Blood Eosinophil Count (N/10 ⁹ L) †	912		0.68 (0.40,1.00)	0.79 (0.55,1.33)	<0.001
Blood Eosinophil Count (N/10 ⁹ L)	908		0.40 (0.20,0.60)	0.46 (0.21,0.72)	0.082
Blood Eosinophil Count (N/10 ⁹ L)	819	<0.15	148 (20.7%)	37 (19.2%)	0.179
		≥0.15 & <0.30	85 (11.9%)	22 (11.4%)	
		≥0.30 & ≤0.45	181 (25.3%)	37 (19.2%)	
		>0.45	301 (42.1%)	97 (50.3%)	
FeNO (ppb)	704		39.0 (22.0,72.0)	51.0 (33.0,80.0)	0.001
FeNO (ppb)	704	<20ppb	121 (22.5%)	19 (11.4%)	0.002
		≥20 & <50ppb	198 (36.9%)	59 (35.3%)	
		≥50ppb	218 (40.6%)	89 (53.3%)	
Composite Type 2 status	691	Eos Low (<0.15) / FeNO Low (<20)	38 (7.2%)	3 (1.8%)	0.007
		Eos High (≥0.15) / FeNO Low (<20)	79 (15.0%)	15 (9.2%)	
		Eos Low (<0.15) / FeNO High (≥20)	84 (15.9%)	27 (16.6%)	
		Eos High (≥0.15) / FeNO High (≥20)	327 (61.9%)	118 (72.4%)	
FEV ₁ (L)	907		1.9 (1.5,2.6)	2.1 (1.5,2.7)	0.023
FEV ₁ (% Predicted)	899		66.4 (51.6,80.6)	70.7 (55.6,87.9)	0.004
FVC (L)	887		3.1 (2.5,3.9)	3.2 (2.7,4.2)	0.016
FVC (% Predicted)	853		84.6 (72.6,96.7)	86.9 (76.2,99.4)	0.012
FEV ₁ /FVC	887		63.7 (54.3,71.9)	64.5 (56.4,73.4)	0.427
ACQ5 Score	822		3.4 (2.2,4.2)	2.2 (1.2,3.2)	<0.001
Uncontrolled asthma	822	ACQ5 ≥1.5	579 (89.9%)	117 (65.7%)	<0.001
EuroQoL Health Scale	389		55.0 (40.0,70.0)	70.0 (50.0,80.0)	<0.001
EuroQoL Utility	404		0.7 (0.5,0.8)	0.9 (0.8,1.0)	<0.001
Maintenance OCS	920		422 (58.2%)	101 (51.8%)	0.109
Maintenance OCS (mg) *	521		10 (8,15)	10 (6,10)	<0.001
ICS	920		422 (58.2%)	101 (51.8%)	0.109
ICS Dose (BDP equivalent-µg) **	521		2000 (1600,2000)	2000 (1600,2000)	0.896
Theophylline	914		202 (27.9%)	38 (20.1%)	0.031

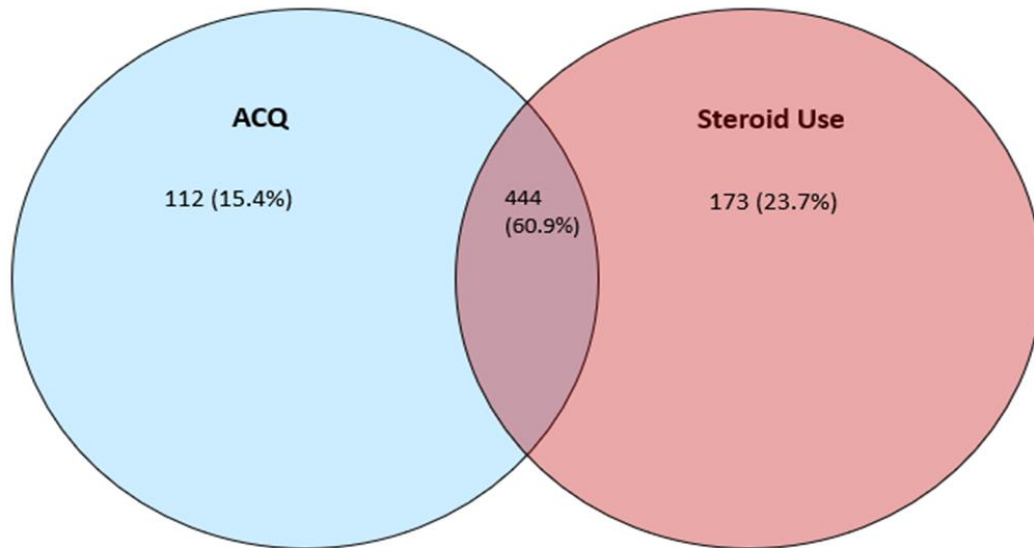
Short-acting β2-agonist (SABA)	918		693 (95.7%)	185 (95.4%)	0.829
Long-acting β2-agonist (LABA)	912		668 (93.2%)	183 (93.8%)	0.736
Long acting anti-muscarinic agent (LAMA)	916		455 (63.0%)	125 (64.4%)	0.717
Leukotriene Receptor Antagonists	888		359 (51.4%)	98 (51.9%)	0.904
Maintenance Macrolides	908		70 (9.8%)	12 (6.2%)	0.119
Nebuliser	913		179 (24.8%)	23 (12.0%)	<0.001

*among patients on oral corticosteroids**among patients on inhaled corticosteroids[†] Median (IQR) or count (%) as appropriate; [†] highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated.

OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; ED: Emergency Department; OCS: Oral Corticosteroid Steroids; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; SABA: Short-Acting Beta Agonists; ICS: Inhaled Corticosteroid Steroids; LABA: Long-Acting Beta Agonists; LAMA: Long-Acting Muscarinic Antagonist

Figure S5: Reasons for not meeting remission criteria after 1 year on biologic therapy. Remission definition: ACQ5 <1.5, no mOCS or OCS bursts

Patients failing to achieve remission at First Annual Review (ACQ5) (n=729)



ACQ: ACQ5 \geq 1.5

Steroid Use: At least 1 exacerbation and/or mOCS dose $>$ 5mg

ACQ: Asthma Control Questionnaire; mOCS: maintenance Oral Corticosteroid Steroids

Table S14: Remission criteria ACQ <1.5 AND no OCS bursts or mOCS >5mg/day AND no SABA use: baseline characteristics of those who meet remission at annual review and those who do not

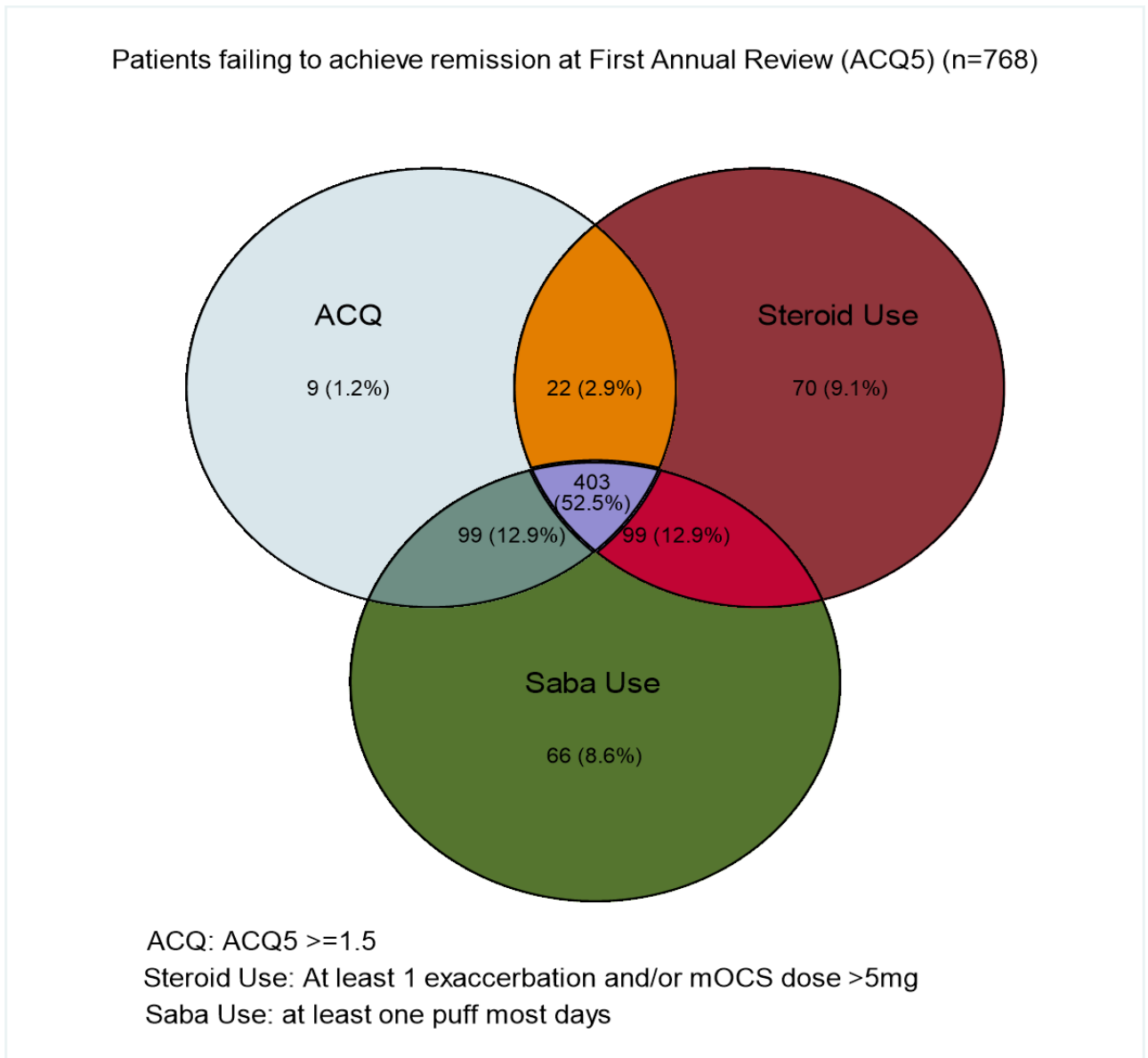
	n	Category	Non-remission	Remission	p-value
	891		86.2% (768)	13.8% (123)	
Time until Annual Review (Years)	891		1.1 (1.0,1.4)	1.1 (1.0,1.3)	0.023
Time until Annual Review (Years)	891	>=9 & <12 months	226 (29.4%)	49 (39.4%)	0.031
		>=12 & <18 months	409 (53.3%)	61 (49.6%)	
		>=18 & <=24 months	133 (17.3%)	13 (10.6%)	
Sex	891	Female	463 (60.3%)	63 (51.2%)	0.058
Age At First Assessment (Years)	891		51.0 (41.0,60.0)	55.0 (48.0,65.0)	<0.001
Age at Onset of Symptoms (Years)	785		20.0 (6.0,40.0)	40.0 (17.0,53.0)	<0.001
Age Of Onset of Symptoms (≥40 years)	785		171 (25.3%)	56 (51.9%)	<0.001
Duration Of Symptoms From Baseline (Years)	785		24.0 (12.0,38.0)	19.5 (7.5,31.0)	0.002
Duration of symptoms From Baseline (Years)	785	0-19	276 (40.8%)	54 (50.0%)	0.196
		20-29	134 (19.8%)	18 (16.7%)	
		>=30	267 (39.4%)	36 (33.3%)	
Ethnicity	889	White	657 (85.8%)	112 (91.1%)	0.111
Smoking status	869	Never smoked	485 (64.5%)	87 (74.4%)	0.036
BMI (kg-m2)	885		30.5 (26.6,35.2)	26.7 (24.7,30.5)	<0.001
BMI (kg-m2)	885	<25	133 (17.4%)	33 (27.0%)	<0.001
		≥25 & <30	227 (29.8%)	54 (44.3%)	
		≥30	403 (52.8%)	35 (28.7%)	
Atopic Disease	891		397 (51.7%)	58 (47.2%)	0.436
Depression or Anxiety	891		97 (12.6%)	1 (0.8%)	<0.001
Gastro-oesophageal Reflux	891		147 (19.1%)	23 (18.7%)	0.908
Nasal polyps	891		147 (19.1%)	46 (37.4%)	<0.001
OCS bursts (Last Year)	874		6 (3,8)	5 (3,6)	<0.001
Any OCS bursts (Last Year)	874		707 (93.9%)	109 (90.1%)	0.118
Frequent Exacerbator at baseline	874	Yes (≥3 in Last Year)	631 (83.8%)	95 (78.5%)	0.150
Invasive Ventilations (Ever)	855		81 (11.0%)	3 (2.5%)	0.002
Any ED Attendance for asthma (Last Year)	864		311 (41.6%)	31 (26.5%)	0.001
Any Hospital Admission for asthma (Last Year)	874		312 (41.3%)	35 (29.4%)	0.003
Highest Blood Eosinophil Count (N/10 ⁹ L) †	878		0.67 (0.40,1.00)	0.90 (0.55,1.41)	<0.001
Blood Eosinophil Count (N/10 ⁹ L)	874		0.40 (0.20,0.62)	0.44 (0.20,0.78)	0.410
Blood Eosinophil Count (N/10 ⁹ L)	819	<0.15	149 (19.8%)	26 (21.5%)	0.173
		≥0.15 & <0.30	81 (10.8%)	15 (12.4%)	
		≥0.30 & ≤0.45	195 (25.9%)	20 (16.5%)	
		>0.45	328 (43.6%)	60 (49.6%)	
FeNO (ppb)	671		42.0 (23.0,74.0)	50.0 (35.5,75.5)	0.026
FeNO	671	<20ppb	120 (21.2%)	11 (10.6%)	0.038
		≥20 & <50ppb	205 (36.2%)	40 (38.5%)	
		≥50ppb	242 (42.7%)	53 (51.0%)	
Composite Type 2 status	658	Eos Low (<0.15) / FeNO Low (<20)	33 (5.9%)	2 (2.0%)	0.067
		Eos High (≥0.15) / FeNO Low (<20)	83 (14.9%)	8 (7.9%)	
		Eos Low (<0.15) / FeNO High (≥20)	87 (15.6%)	20 (19.8%)	
		Eos High (≥0.15) / FeNO High (≥20)	354 (63.6%)	71 (70.3%)	
FEV ₁ (L)	873		1.9 (1.4,2.6)	2.2 (1.7,2.8)	0.002
FEV ₁ (% Predicted)	865		65.8 (51.4,79.8)	74.1 (59.1,89.7)	<0.001
FVC (L)	853		3.1 (2.5,3.9)	3.3 (2.8,4.3)	0.007
FVC (% Predicted)	819		84.3 (72.4,96.7)	87.8 (79.6,100.6)	0.004
FEV ₁ /FVC	853		63.5 (53.6,71.7)	65.9 (58.6,74.4)	0.030
ACQ5 Score	788		3.2 (2.2,4.0)	1.8 (0.9,2.8)	<0.001
Uncontrolled Asthma	788	ACQ5 ≥1.5	604 (89.3%)	65 (58.0%)	<0.001
EuroQoL Health Scale	358		55.0 (40.0,70.0)	75.0 (50.0,80.0)	<0.001
EuroQoL Utility	375		0.7 (0.5,0.8)	0.9 (0.8,1.0)	<0.001
Maintenance OCS	886		444 (58.1%)	59 (48.4%)	0.043
Maintenance OCS (mg) *	501		10 (8,15)	10 (6,10)	<0.001
ICS	891		764 (99.5%)	122 (99.2%)	0.687
ICS Dose (BDP equivalent-µg) **	830		2000 (1600,2000)	2000 (1600,2000)	0.083

Theophylline	880	204 (26.7%)	21 (17.9%)	0.042
Short-acting β2-agonist (SABA)	884	729 (95.7%)	116 (95.1%)	0.769
Long-acting β2-agonist (LABA)	878	705 (93.3%)	112 (91.8%)	0.559
Long acting anti-muscarinic agent (LAMA)	882	472 (62.1%)	77 (63.1%)	0.831
Leukotriene Receptor Antagonists	854	369 (50.2%)	65 (54.6%)	0.371
Maintenance Macrolides	875	69 (9.2%)	6 (5.0%)	0.126
Nebuliser	879	173 (22.8%)	9 (7.5%)	<0.001

*among patients on oral corticosteroids**among patients on inhaled corticosteroids[†] Median (IQR) or count (%) as appropriate; † highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated

OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; ED: Emergency Department; OCS: Oral Corticosteroid Steroids; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; SABA: Short-Acting Beta Agonists; ICS: Inhaled Corticosteroid Steroids; LABA: Long-Acting Beta Agonists; LAMA: Long-Acting Muscarinic Antagonist

Figure S6: Reasons for not meeting remission criteria after 1 year on biologic therapy. Remission definition: ACQ5 <1.5, no mOCS or OCS bursts, no daily SABA use



ACQ: Asthma Control Questionnaire; mOCS: maintenance Oral Corticosteroid Steroids; SABA: Short-Acting Beta Agonists

Table S15: Remission criteria ACQ <1.5 AND no OCS bursts or mOCS >5mg/day AND ≤2 SABA/day: baseline characteristics of those who meet remission at annual review and those who do not.

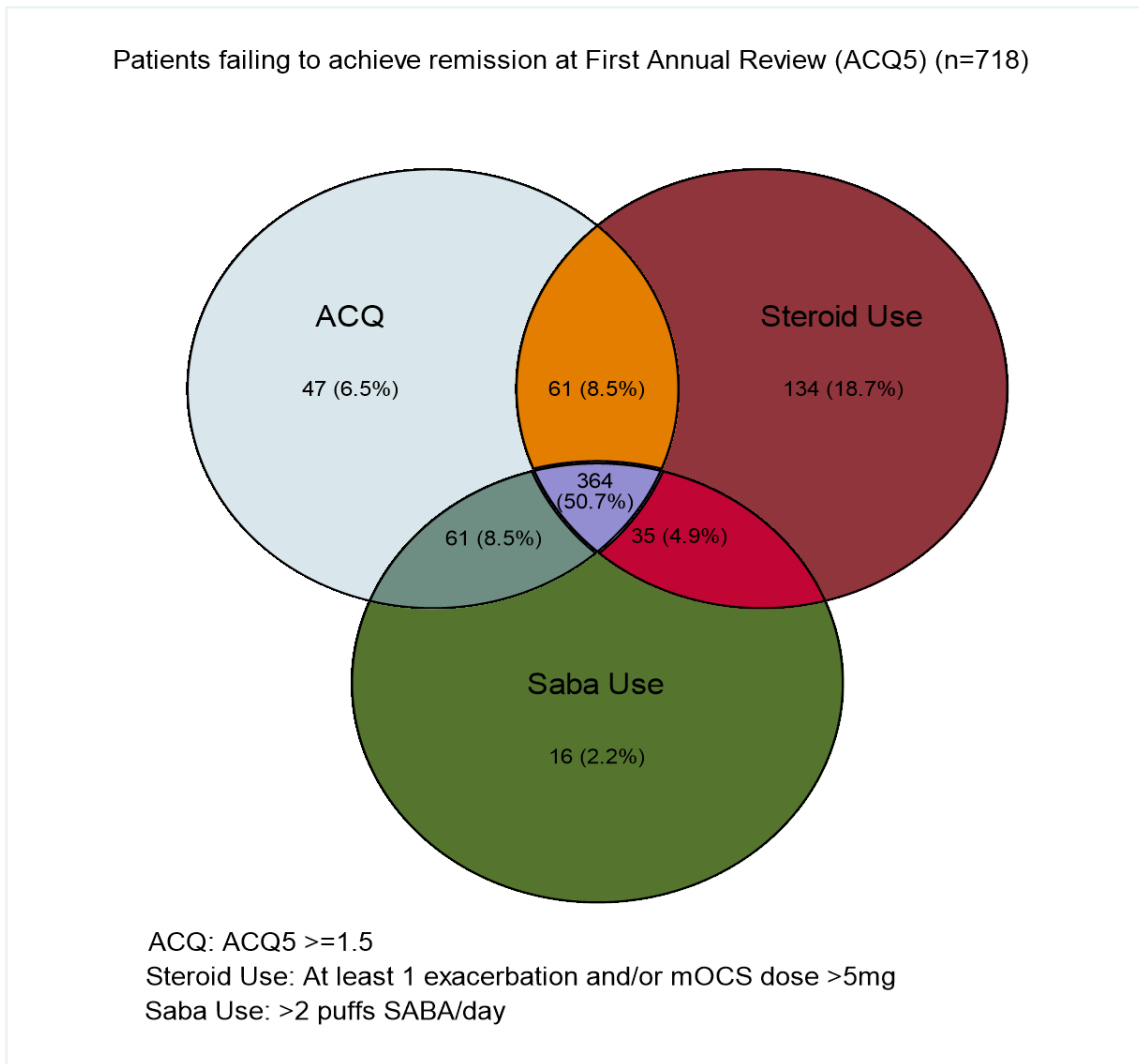
	n		Non-remission	Remission	p-value
	891		80.6% (718)	19.4% (173)	
Time until Annual Review (Years)	891		1.1 (1.0,1.4)	1.1 (1.0,1.3)	0.020
Sex	891	Female	437 (60.9%)	89 (51.4%)	0.024
Age At First Assessment (Years)	891		51.0 (40.0,59.0)	56.0 (48.0,65.0)	<0.001
Age at Onset of Symptoms (Years)	785		20.0 (5.5,39.0)	36.0 (16.0,52.0)	<0.001
Age of Onset of Symptoms (Years)	785	<12	221 (35.0%)	32 (20.9%)	0.002
		≥12 & <18	62 (9.8%)	13 (8.5%)	
		≥18	349 (55.2%)	108 (70.6%)	
Age Of Onset of Symptoms (≥40 years)	785		153 (24.2%)	74 (48.4%)	<0.001
Duration Of Symptoms From Baseline (Years)	785		24.0 (12.0,38.0)	20.0 (8.0,32.0)	0.005
Ethnicity	889	White	613 (85.6%)	156 (90.2%)	0.115
Smoking status	869	Never	450 (64.0%)	122 (73.5%)	0.021
BMI (kg-m2)	885		30.6 (26.6,35.3)	27.5 (24.9,30.9)	<0.001
BMI (kg-m2)	885	<25	122 (17.1%)	44 (25.6%)	<0.001
		≥25 & <30	208 (29.2%)	73 (42.4%)	
		≥30	383 (53.7%)	55 (32.0%)	
Atopic Disease	891		377 (52.5%)	78 (45.1%)	0.080
Depression or Anxiety	891		95 (13.2%)	3 (1.7%)	<0.001
Gastro-oesophageal Reflux	891		138 (19.2%)	32 (18.5%)	0.828
Nasal polyps	891		134 (18.7%)	59 (34.1%)	<0.001
OCS bursts (Last Year)	874		6 (4,8)	4 (3,6)	<0.001
Any OCS bursts (Last Year)	874		661 (94.0%)	155 (90.6%)	0.111
Frequent Exacerbator at baseline	874	Yes (≥3 in Last Year)	595 (84.6%)	131 (76.6%)	0.012
Invasive Ventilations (Ever)	855		77 (11.2%)	7 (4.2%)	0.006
Any ED Attendance for asthma (Last Year)	864		298 (42.6%)	44 (26.7%)	<0.001
Any Hospital Admission for asthma (Last Year)	874		300 (42.5%)	47 (28.0%)	<0.001
Highest Blood Eosinophil Count (N/10 ⁹ L) †	878		0.67 (0.40,1.00)	0.79 (0.55,1.33)	<0.001
Blood Eosinophil Count (N/10 ⁹ L)	874		0.40 (0.20,0.62)	0.46 (0.20,0.76)	0.128
Blood Eosinophil Count (N/10 ⁹ L)	819	<0.15	140 (19.9%)	35 (20.5%)	0.155
		≥0.15 & <0.30	79 (11.2%)	17 (9.9%)	
		≥0.30 & ≤0.45	183 (26.0%)	32 (18.7%)	
		>0.45	301 (42.8%)	87 (50.9%)	
FeNO (ppb)	671		41.0 (22.0,72.0)	51.0 (35.0,81.0)	0.002
FeNO (ppb)	671	<20ppb	116 (22.1%)	15 (10.3%)	0.003
		≥20 & <50ppb	192 (36.6%)	53 (36.3%)	
		≥50ppb	217 (41.3%)	78 (53.4%)	
Composite Type 2 status	658	Eos Low (<0.15) / FeNO Low (<20)	32 (6.2%)	3 (2.1%)	0.011
		Eos High (≥0.15) / FeNO Low (<20)	80 (15.5%)	11 (7.7%)	
		Eos Low (<0.15) / FeNO High (≥20)	81 (15.7%)	26 (18.2%)	
		Eos High (≥0.15) / FeNO High (≥20)	322 (62.5%)	103 (72.0%)	
FEV ₁ (L)	873		1.9 (1.4,2.6)	2.0 (1.6,2.7)	0.031
FEV ₁ (% Predicted)	865		66.5 (51.5,80.1)	69.0 (55.6,88.0)	0.005
FVC (L)	853		3.1 (2.5,3.9)	3.2 (2.7,4.2)	0.035
FVC (% Predicted)	819		84.6 (72.9,96.7)	86.8 (75.7,100.0)	0.029
FEV ₁ /FVC	853		63.7 (54.0,71.8)	64.4 (56.5,73.4)	0.49
ACQ5 Score	788		3.2 (2.2,4.0)	2.2 (1.0,3.2)	<0.001
Uncontrolled Asthma	788	ACQ5 ≥1.5	567 (89.9%)	102 (65.0%)	<0.001
EuroQoL Health Scale	358		55.0 (40.0,70.0)	70.0 (50.0,80.0)	<0.001
EuroQoL Utility	375		0.7 (0.5,0.8)	0.9 (0.8,1.0)	<0.001
Maintenance OCS	886		410 (57.4%)	93 (54.1%)	0.426
Maintenance OCS (mg) *	501		10 (8,15)	10 (6,10)	<0.001
ICS	830		715 (99.6%)	171 (98.8%)	0.243
ICS Dose (BDP equivalent-µg) **	830		2000 (1600,2000)	2000 (1600,2000)	0.671
Theophylline	880		191 (26.8%)	34 (20.5%)	0.095
Short-acting β2-agonist (SABA)	884		682 (95.7%)	163 (95.3%)	0.850
Long-acting β2-agonist (LABA)	878		657 (93.1%)	160 (93.0%)	0.987

Long acting anti-muscarinic agent (LAMA)	882		439 (61.7%)	110 (64.3%)	0.532
Leukotriene Receptor Antagonists	854		348 (50.7%)	86 (51.5%)	0.845
Maintenance Macrolides	875		67 (9.5%)	8 (4.7%)	0.043
Nebuliser	879		167 (23.5%)	15 (8.9%)	<0.001

*among patients on oral corticosteroids**among patients on inhaled corticosteroids[‡] Median (IQR) or count (%) as appropriate; † highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated

OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; ED: Emergency Department; OCS: Oral Corticosteroid Steroids; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; SABA: Short-Acting Beta Agonists; ICS: Inhaled Corticosteroid Steroids; LABA: Long-Acting Beta Agonists; LAMA: Long-Acting Muscarinic Antagonist

Figure S7: Reasons for not meeting remission criteria after 1 year on biologic therapy. Remission definition: ACQ5 <1.5, no mOCS or OCS bursts, ≤2 puffs SABA/day



ACQ: Asthma Control Questionnaire; mOCS: maintenance Oral Corticosteroid Steroids; SABA: Short-Acting Beta Agonists

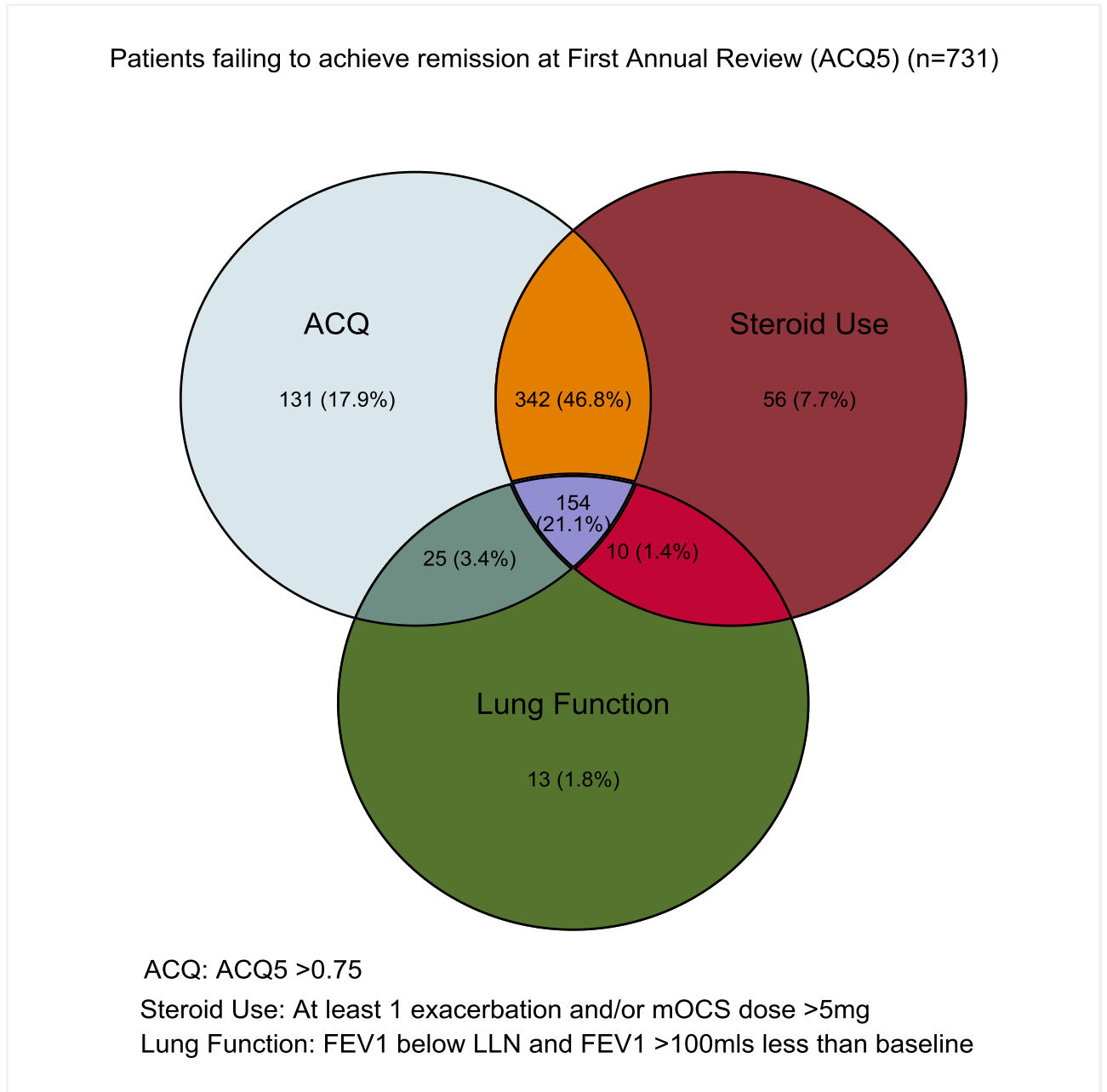
Table S16: Remission criteria ACQ5 ≤ 0.75 AND no OCS bursts or mOCS $>5\text{mg/day}$ AND FEV₁ above LLN or $<100\text{mls}$ less than pre-biologic FEV₁: baseline characteristics of those who meet remission at 1 year and those who do not

	n		Non-remission	Remission	p-value
	830		88.1% (731)	11.9 % (99)	
Time until Annual Review (Years)	830		1.1 (1.0,1.4)	1.1 (1.0,1.2)	0.168
Sex		Female	437 (59.8%)	52 (52.5%)	0.168
Age At First Assessment (Years)	830		51.0 (41.0,60)	55.0 (47.0,66.0)	0.001
Age at Onset of Symptoms (Years)	737		21.0 (6.0,40.0)	31.0 (16.0,52.0)	<0.001
Duration Of Symptoms From Baseline (Years)	737		24.0 (11.0,37.0)	20.0 (8.0,33.0)	0.057
Ethnicity	828	White	629 (86.3%)	95 (96.0%)	0.006
Smoking status	809	Never smoked	468 (65.5%)	71 (74.7%)	0.179
BMI (kg-m2)	823		30.3 (26.6,35.1)	27.3 (25.0,31.0)	<0.001
Atopic Disease	830		382 (52.3%)	45 (45.5%)	0.202
Depression or Anxiety	830		88 (12.0%)	0(0.0%)	<0.001
Gastro-oesophageal Reflux	830		128 (17.5%)	16 (16.2%)	0.739
Nasal polyps	830		136 (18.6%)	35 (35.4%)	<0.001
OCS bursts (Last Year)	817		5 (3,8)	4 (2,6)	0.001
Any OCS bursts (Last Year)	817		676 (94.0%)	86 (87.8%)	0.020
Frequent Exacerbator at baseline	817	Yes (≥ 3 in Last Year)	595 (82.8%)	73 (74.5%)	0.047
Invasive Ventilations (Ever)	798		0 (0,0)	0 (0,0)	0.059
Any ED Attendance for asthma (Last Year)	807		276 (38.8%)	17 (17.9%)	<0.001
Any Hospital Admissions for asthma (Last Year)	814		289 (40.3%)	26 (26.8%)	0.010
Highest Blood Eosinophil Count (N/10 ⁹ L) †	821		0.69 (0.43,1.00)	0.90 (0.60,1.41)	<0.001
Blood Eosinophil Count (N/10 ⁹ L)	819		0.39 (0.18,0.60)	0.53 (0.21,0.78)	0.028
Blood Eosinophil Count (N/10 ⁹ L)	819	<0.15	158 (21.9%)	17 (17.5%)	0.018
		≥ 0.15 & <0.30	82 (11.4%)	14 (14.4%)	
		≥ 0.30 & ≤ 0.45	183 (25.3%)	13 (13.4%)	
		>0.45	299 (41.4%)	53 (54.6%)	
FeNO (ppb)	638		42.0 (23.0,71.0)	54.0 (38.0,88.0)	0.001
FeNO (ppb)	638	$<20\text{ppb}$	118 (21.4%)	5 (5.7%)	0.001
		≥ 20 & $<50\text{ppb}$	203 (36.8%)	31 (35.6%)	
		$\geq 50\text{ppb}$	230 (41.7%)	51 (58.6%)	
Composite Type 2 status	627	Eos Low (<0.15) / FeNO Low (<20)	40 (7.4%)	0(0.0%)	0.002
		Eos High (≥ 0.15) / FeNO Low (<20)	74 (13.7%)	5 (5.9%)	
		Eos Low (<0.15) / FeNO High (≥ 20)	93 (17.2%)	14 (16.5%)	
		Eos High (≥ 0.15) / FeNO High (≥ 20)	335 (61.8%)	66 (77.6%)	
FEV ₁ (L)	818		2.0 (1.4,2.6)	2.2 (1.7,2.8)	0.001
FEV ₁ (% Predicted)	811		66.5 (52.0,81.1)	74.1 (61.1,89.9)	<0.001
FVC (L)	802		3.1 (2.5,3.9)	3.3 (2.8,4.3)	0.014
FVC (% Predicted)	772		85.1 (73.4,97.1)	87.2 (79.8,102.9)	0.011
FEV ₁ /FVC	802		63.6 (53.6,72.1)	66.4 (58.1,74.1)	0.072
ACQ5 Score	736		3.2 (2.2,4.0)	1.7 (0.7,3.0)	<0.001
Uncontrolled asthma	736	ACQ5 ≥ 1.5	569 (88.4%)	53 (57.6%)	<0.001
EuroQoL Health Scale	350		60.0 (40.0,70.0)	80.0 (60.0,85.0)	<0.001
EuroQoL Utility	362		0.7 (0.5,0.8)	0.9 (0.8,1.0)	<0.001
Maintenance OCS	826		424 (58.3%)	51 (51.5%)	0.199
Maintenance OCS (mg) *	474		10 (8,15)	10 (5,10)	0.001
ICS	830		729 (99.7%)	98 (99.0%)	0.252
ICS Dose (BDP equivalent- μg) **	775		2000 (1600,2000)	2000 (1600,2000)	0.469
Theophylline	821		194 (26.8%)	22 (22.9%)	0.422
Short-acting $\beta 2$ -agonist (SABA)	823		694 (95.6%)	91 (93.8%)	0.433
Long-acting $\beta 2$ -agonist (LABA)	818		670 (93.1%)	93 (94.9%)	0.494
Long acting anti-muscarinic agent (LAMA)	821		462 (63.9%)	63 (64.3%)	0.941
Leukotriene Receptor Antagonists	799		354 (50.2%)	53 (56.4%)	0.261
Maintenance Macrolides	816		62 (8.6%)	7 (7.1%)	0.618
Nebuliser	819		170 (23.5%)	10 (10.4%)	0.004

*among patients on oral corticosteroids**among patients on inhaled corticosteroids[†] Median (IQR) or count (%) as appropriate; † highest recorded according to prior medical records. 'Last Year' refers to measures assessed using clinical records in the 12 months prior to initial presentation at the severe asthma centre, other measures were as observed or recorded at initial presentation unless otherwise indicated

OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; ED: Emergency Department; OCS: Oral Corticosteroid Steroids; FeNO: Fractional Exhaled Nitric Oxide; ppb: Parts per Billion; FEV₁: Forced Expiratory Volume (1 second); FVC: Forced Vital Capacity; ACQ: Asthma Control Questionnaire; SABA: Short-Acting Beta Agonists; ICS: Inhaled Corticosteroid Steroids; LABA: Long-Acting Beta Agonists; LAMA: Long-Acting Muscarinic Antagonist

Figure S8: Reasons for not meeting remission criteria after 1 year on biologic therapy. Remission definition: ACQ5 \leq 0.75, no mOCS or OCS bursts, FEV₁ above LLN or <100mls less than pre-biologic FEV₁



ACQ: Asthma Control Questionnaire; mOCS: maintenance Oral Corticosteroid Steroids; FEV₁; Forced Expiratory Volume (1 second); LLN: Lower Limit of Normal

References online supplement:

- E1. Chung FK, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014; 43: 343–373
- E2. Global initiative for asthma: GINA Difficult to treat and severe asthma, April 2019. URL [GINA-Severe-asthma-Pocket-Guide-v2.0-wms-1.pdf \(ginasthma.org\)](https://ginasthma.org/GINA-Severe-asthma-Pocket-Guide-v2.0-wms-1.pdf) (Accessed 08/08/2023)
- E3. Menzies-Gow A, Bafadhel M, Busse WW, Casale TB, Kocks JWH, Pavord ID, et al. An expert consensus framework for asthma remission as a treatment goal. *Journal of Allergy and Clinical Immunology*. 2020 Mar 1;145(3):757–65.
- E4. National Institute for Health and Care Excellence (NICE), Guidance for Benralizumab, Accessed 21 April 2023, URL: <https://www.nice.org.uk/guidance/TA565/chapter/1-Recommendations>
- E5. National Institute for Health and Care Excellence (NICE), Guidance for Dupilumab, Accessed 21 April 2023, URL: <https://www.nice.org.uk/guidance/TA751/chapter/1-Recommendations>
- E6. National Institute for Health and Care Excellence (NICE), Guidance for Mepolizumab, Accessed 21 April 2023, URL: <https://www.nice.org.uk/guidance/TA671/chapter/1-Recommendations>
- E7. National Institute for Health and Care Excellence (NICE), Guidance for Omalizumab, Accessed 21 April 2023, URL: <https://www.nice.org.uk/guidance/ta278/chapter/1-Guidance>
- E8. National Institute for Health and Care Excellence (NICE), Guidance for Reslizumab, Accessed 21 April 2023, URL: <https://www.nice.org.uk/guidance/TA479/chapter/1-Recommendations>
- E9. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: The global lung function 2012 equations. *European Respiratory Journal*. 2012 Dec 1;40(6):1324–43.
- E10. Juniper EF, O’Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J*. 1999;14(4):902–7.
- E11. Juniper EF, Bousquet J, Abetz L, Bateman ED. Identifying “well-controlled” and “not well-

controlled" asthma using the Asthma Control Questionnaire. *Respir Med.* 2006 Apr 1;100(4):616–21.

E12. EuroQol 5 Dimension, 5 level (EQ-5D-5L). Accessed 21 April 2023, URL: <https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/>