

Online supplement in relation to:

Distribution of Type 2 biomarkers and association with severity, clinical characteristics and co-morbidities in the BREATHE real-life asthma population

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Table S1: Symptoms, quality-of-life, comorbidities and medication in patients with severe eosinophilic and non-eosinophilic asthma

Variable	B-EOS <0.3	B-EOS ≥0.3	p-value	S-EOS <0.3	S-EOS ≥0.3	P
N	53	32		39	39	
ACQ5	2.2 (1.1-3.0)	2.4 (1.7-3.3)	0.4¥	2.2 (1.2-3.0)	2.4 (1.8-3.0)	0.6¥
ACQ5>1.5	37/53 (70%)	26/32 (81%)	0.2¤	28/39	33/39	0.2¤
ACT	17 (12-20)	14 (11-19)	0.1¥	16 (12-20)	14 (11-18)	0.3¥
ACT≤19	35/53 (66%)	23/32 (72%)	0.4¤	27/39	29/39	0.6¤
mMRC	2.0 (0.9)	2.0 (0.9)	0.7¥	2.1 (0.9)	2.0 (0.9)	0.8¥
Exacerbations previous year	1.4 (1.6) / 1 (0-2.0)	1.8 (2.0) / 1 (0-4)	0.4‡/0.5¥	1.2 (1.5) / 1 (0-2)	2.2 (2.0) / 1 (0-5)	0.02‡/0.05¥
ER visits	0.60 (0.97) / 0 (0-1)	0.44 (0.84) / 0 (0-1)	0.4‡/0.5¥	0.64 (1.1) / 0 (0-1)	0.55 (0.93) / 0 (0-1)	0.7‡/0.8¥
Hospitalizations	0.51 (0.93) / 0 (0-1)	0.38 (0.83) / 0 (0-1)	0.5‡/0.4¥	0.38 (0.78) / 0 (0-1)	0.70 (1.2) / 0 (0-1)	0.2‡/5¥
Quality of life						
SF12						
PCS	44 (34-52)	41 (38-44)	0.6¥	44 (36.0-50.3)	40.0 (34.2-46.4)	0.5¥
MCS	46 (40-55)	55 (49-58)	0.007¥	47 (42-53)	54 (48-59)	0.03¥
miniAQLQ overall	4.9 (1.4)	5.0 (1.1)	0.9‡	4.9 (1.4)	4.9 (1.2)	1.0‡
miniRQLQ overall	1.4 (0.9)	1.5 (1.1)	0.8‡	1.4 (1.0)	1.5 (1.1)	0.7‡
Co-morbidities						
Nijmegen	17.0 (9.0)	17.3 (9.5)	0.8‡	18.3 (10.2)	16.8 (9.0)	0.5‡
SNOT22	22.9 (15.3)	21.9 (17.1)	0.9‡	25.1 (16.8)	18.3 (12.9)	0.6‡
Epworth sleepiness scale	5.2 (3.1)	6.8 (4.2)	0.1‡	6.1 (3.9)	5.6 (3.9)	0.6‡
Medication						
LABA, µg	40 (36-40)	36 (24-40)	0.3¥	39 (24-100)	36 (24-40)	0.4¥
ICS, budesonide equivalents, µg	1788 (433)	1819 (460)	0.7‡	1723 (333)	1894 (594)	0.2‡
OCS for asthma, n	6/53 (11%)	4/32 (13%)	0.9§	3/39 (8%)	8/39 (21%)	0.1§
OCS for asthma, mg	12.5 (5-15)	5 (5-7.5)	0.1¥	12.5 (5.0-17.5)	7.5 (5.0-13.8)	0.6¥

Data are presented as numbers (n), n/N (%), mean±SD or median (IQR). ACQ-5: Asthma Control Questionnaire; ACT: Asthma Control Test; MRC: Medical Research Council dyspnea scale; SF-12: Health condition questionnaire; PCS: physical component score; MCS: mental component score; miniAQLQ: Mini Asthma Quality of Life Questionnaire; miniRQLQ: Mini Rhinoconjunctivitis Quality of Life Questionnaire; Nijmegen: Hyperventilation; SNOT22: Sino-Nasal Outcome Test; LABA: long-acting β -agonist; ICS: inhaled corticosteroids; OCS: oral corticosteroids. Statistical tests: ¤: chi-square §: fishers exact test, ‡: Welch's ANOVA, ¥: Kruskal Wallis.

Table S2: Baseline characteristics and biomarkers across asthma severity and -control

Variable	Mild-moderate asthma \ddagger			Severe asthma		
	Controlled	Uncontrolled	p	Controlled	Uncontrolled	p
Patients total, n	153	266		16	74	
Age (years)	40 (18)	42 (17)	0.2‡	49 (12)	49 (14)	0.9‡
Sex (female)	77 (50%)	136 (64%)	0.001¤	9 (56%)	38 (51%)	0.5¤
BMI (kg/m^2)	24.9 (4.4)	26.4 (5.7)	0.02‡	26.1 (5.1)	28.4 (5.9)	0.1‡
Smoking (packyears)	0 (0-4)	0 (0-9)	0.1§	2.5 (0-10)	0 (0-8)	0.5§
Atopy	76 (50%)	94 (45%)	0.5¤	11 (69%)	41 (55%)	0.9¤
Lung function						
FEV1 (L)	3.5 (1.0)	3.1 (0.9)	0.0001‡	2.8 (0.7)	2.8 (0.8)	1.0‡
FEV1 % predicted	96 (15)	92 (17)	0.01‡	86 (19)	85 (22)	0.9‡
FVC (L)	4.7 (1.3)	4.1 (1.1)	<0.0001‡	4.1 (0.9)	3.8 (1.0)	0.3‡
FVC % predicted	108 (14)	102 (17)	0.0009‡	104 (18)	97 (21)	0.2‡
Biomarkers						
Blood eosinophils ($\text{cells} \cdot 10^9/\text{L}$)	0.16 (0.10-0.25)	0.18 (0.10-0.32)	0.1§	0.17 (0.10-0.29)	0.24 (0.13-0.45)	0.2§
Blood eosinophils $\geq 0.3 \text{ cells} \cdot 10^9/\text{L}$	34/153 (22%)	78/266 (29%)	0.4	4/16 (25%)	28/69 (41%)	0.2§
Sputum eosinophils (%)	1.1 (0.25-3.8)	1.8 (0.25-5.8)	0.1§	0.6 (0.13-6.8)	3.5 (1.0-7.4)	0.1§
Sputum eosinophils $\geq 3\%$	37/106 (35%)	71/195 (36%)	0.07¤	4/12 (33%)	36/67 (54%)	0.2§
Sputum neutrophils (%)	25.8 (10.8-61.3)	42.0 (17.8-66.5)	0.03§	41.2 (19.4-62.6)	49.8 (23.8-72.3)	0.3§
Sputum neutrophils $\geq 61\%$	28/106 (26%)	55/195 (28%)	0.4¤	3/12 (25%)	22/67 (33%)	0.8§
IgE total (IU/ml)	57 (24-167)	57 (18-210)	0.8§	163 (97-391)	129 (47-252)	0.1§
IgE total $\geq 150 \text{ IU/ml}$	42/153 (27%)	82/266 (31%)	0.9¤	11/16 (69%)	32/74 (43%)	0.5¤
FeNO (ppb)	17 (10-28)	16 (9-36)	0.6§	19 (13-26)	16 (10-44)	0.8§
FeNO $\geq 25 \text{ ppb}$	16/153 (10%)	45/266 (17%)	0.2¤	5/16 (31%)	29/74 (39%)	0.2§

Data are presented as numbers (n), n/N (%), mean \pm SD, or median (IQR). BMI: body mass index; FEV1: forced expiratory volume in 1 sec; FVC: forced vital capacity.

Uncontrolled: ACQ5 >1.5 or ACT < 19. ¤: 6 patients with mild-moderate asthma had no ACQ5 or ACT score available and were thus excluded.

Statistical tests: ¤: chi-square §: fishers exact test, ‡: Welch's ANOVA, ¥: Kruskal Wallis.

Table S3:

		Mild-moderate Asthma, n=291		Severe asthma, n=73	
		B-EOS		B-EOS	
		>= 0.3	< 0.3	>= 0.3	< 0.3
S-EOS	>= 3%	42 (14%)	64 (22%)	21 (29%)	16 (22%)
	<3%	36 (12%)	149 (51%)	8 (11%)	28 (38%)

Table S4 identification of airway eosinophilia using conventional T2 biomarkers

	All		Severe		Moderate	
	Kappa	P	Kappa	P	Kappa	p
B-EOS (≥ 0.3)	0.25	<0.0001	0.34	0.003	0.21	0.0002
FeNO (≥ 25 ppb)	0.24	<0.0001	0.34	0.003	0.20	0.0005
IgE ≥ 150 IE	0.11	0.03	0.21	0.08	0.07	0.25