

Identification of responders to inhaled corticosteroids in a chronic obstructive pulmonary disease population using cluster analysis

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*At the time that the analysis was conducted

SUPPLEMENTARY MATERIAL

Supplementary Table S1 Imbalances in baseline variables, as accounted for in the cluster analysis model

Patient characteristics	Cluster 1 Eosinophils >2.4%			Cluster 2 Eosinophils ≤2.4%, pack-years ≤46			Cluster 3 Eosinophils ≤2.4%, pack-years >46		
	VI (n=432)	FF/VI (n=1345)	p value	VI (n=244)	FF/VI (n=647)	p value	VI (n=142)	FF/VI (n=445)	p value
Age, years	65 (58–71)	65 (58–70)	0.7933	61.5 (54–70)	62 (55–69)	0.7681	65 (59–70)	65 (60–71)	0.7402
Female sex	163 (37.7)	530 (39.4)	0.5349	133 (54.5)	347 (53.6)	0.8150	48 (33.8)	164 (36.9)	0.5099
Body mass index	25.95 (22.91–29.42)	26.05 (22.95–30.10)	0.3185	26.39 (23.05–30.66)	26.13 (22.94–29.55)	0.4082	25.69 (23.23–29.81)	26.59 (23.15–30.34)	0.3637
Hispanic or Latino	68 (15.7)	230 (17.1)	0.5105	48 (19.7)	144 (22.3)	0.4028	32 (22.5)	62 (13.9)	0.0149
Current smoker	178 (41.2)	536 (39.9)	0.6179	125 (51.2)	318 (49.1)	0.5798	61 (43.0)	221 (49.7)	0.1638
Number of pack-years	41 (30–58.5)	40 (27–58)	0.4895	30 (20–38)	30 (20–40)	0.2931	62 (54–82)	61 (51–80)	0.4446
COPD duration in categories									
<5 years	174 (40.3)	577 (42.9)	0.1423	89 (36.5)	256 (39.6)	0.1587	52 (36.6)	185 (41.6)	0.1798
5 to <10 years	131 (30.3)	412 (30.6)	.	78 (32.0)	235 (36.3)	.	52 (36.6)	120 (27.0)	.
10 to <15 years	82 (19.0)	195 (14.5)	.	41 (16.8)	85 (13.1)	.	21 (14.8)	75 (16.9)	.
≥15 years	45 (10.4)	161 (12.0)	.	36 (14.8)	71 (11.0)	.	17 (12.0)	65 (14.6)	.
Exacerbations treated with steroid/antibiotics in the 12 months before screening visit									
0	40 (9.3)	89 (6.6)	0.0269	14 (5.7)	53 (8.2)	0.1979	9 (6.3)	45 (10.1)	0.3998
1	244 (56.5)	860 (63.9)	.	142 (58.2)	405 (62.6)	.	83 (58.5)	258 (58.0)	.
2	95 (22.0)	268 (19.9)	.	62 (25.4)	132 (20.4)	.	38 (26.8)	98 (22.0)	.

Patient characteristics	Cluster 1 Eosinophils >2.4%			Cluster 2 Eosinophils ≤2.4%, pack-years ≤46			Cluster 3 Eosinophils ≤2.4%, pack-years >46		
	VI (n=432)	FF/VI (n=1345)	p value	VI (n=244)	FF/VI (n=647)	p value	VI (n=142)	FF/VI (n=445)	p value
≥3	53 (12.3)	128 (9.5)	.	26 (10.7)	57 (8.8)	.	12 (8.5)	44 (9.9)	.
Number of hospitalised exacerbations in the 12 months before screening visit									
0	351 (81.3)	1,077 (80.1)	0.6166	198 (81.1)	498 (77.0)	0.4043	123 (86.6)	346 (77.8)	0.0136
1	70 (16.2)	221 (16.4)	.	36 (14.8)	116 (17.9)	.	14 (9.9)	90 (20.2)	.
≥2	11 (2.5)	47 (3.5)	.	10 (4.1)	33 (5.1)	.	5 (3.5)	9 (2.0)	.
COPD type									
Bronchitis	291 (67.4)	875 (65.1)	0.3801	184 (75.4)	451 (69.7)	0.0934	77 (54.2)	293 (65.8)	0.0125
Emphysema	232 (53.7)	799 (59.4)	0.0367	104 (42.6)	323 (49.9)	0.0518	97 (68.3)	269 (60.4)	0.0923
On-treatment pneumonia vaccine	29 (6.7)	90 (6.7)	0.9876	27 (11.1)	48 (7.4)	0.0804	6 (4.2)	27 (6.1)	0.4067
On-treatment influenza vaccine	91 (21.1)	323 (24.0)	0.2070	55 (22.5)	145 (22.4)	0.9670	28 (19.7)	91 (20.4)	0.8503
History of:									
Cardiovascular disease	274 (63.4)	834 (62.0)	0.5965	137 (56.1)	382 (59.0)	0.4347	92 (64.8)	290 (65.2)	0.9341
Cardiac disorders	85 (19.7)	221 (16.4)	0.1202	36 (14.8)	77 (11.9)	0.2538	30 (21.1)	77 (17.3)	0.3042
Coronary artery disease	45 (10.4)	141 (10.5)	0.9686	21 (8.6)	44 (6.8)	0.3553	20 (14.1)	53 (11.9)	0.4942
Congestive heart failure	7 (1.6)	22 (1.6)	0.9826	4 (1.6)	15 (2.3)	0.5315	1 (0.7)	10 (2.2)	0.2378
Myocardial infarction	30 (6.9)	74 (5.5)	0.2664	7 (2.9)	19 (2.9)	0.9573	11 (7.7)	24 (5.4)	0.3025
Arrhythmia	27 (6.3)	65 (4.8)	0.2474	12 (4.9)	32 (4.9)	0.9863	6 (4.2)	20 (4.5)	0.8921
Vascular disorders	203 (47.0)	644 (47.9)	0.7472	103 (42.2)	300 (46.4)	0.2665	71 (50.0)	220 (49.4)	0.9072
Pneumonia	91 (21.1)	309 (23.0)	0.4085	51 (20.9)	137 (21.2)	0.9290	30 (21.1)	122 (27.4)	0.1363
Eye disorders	53 (12.3)	172 (12.8)	0.7775	20 (8.2)	67 (10.4)	0.3330	19 (13.4)	76 (17.1)	0.2975
Metabolism disorders	178 (41.2)	551 (41.0)	0.9305	84 (34.4)	237 (36.6)	0.5411	58 (40.8)	186 (41.8)	0.8410
Endocrine disorders	0	3 (0.2)	0.3259	103 (42.2)	300 (46.4)	0.2665	1 (0.7)	0	0.0764
Baseline WBC, GI/L	6.90 (5.80–7.90)	7.00 (5.80–8.20)	0.3754	7.20 (6.10–8.50)	7.30 (6.10–8.60)	0.6452	7.30 (6.10–8.60)	7.50 (6.20–9.00)	0.3785
Baseline lymphocytes, %	27.70 (22.30–33.20)	27.10 (22.30–32.90)	0.3688	26.05 (21.20–30.95)	25.80 (21.10–31.30)	0.9552	26.15 (20.20–30.30)	24.60 (19.40–29.90)	0.3287
Baseline eosinophils, GI/L	0.27 (0.21–0.39)	0.28 (0.21–0.40)	0.4070	0.11 (0.07–0.14)	0.11 (0.07–0.14)	0.3163	0.10 (0.07–0.14)	0.11 (0.08–0.15)	0.0444
Baseline eosinophils, %	4.00 (3.10–5.50)	4.10 (3.10–5.60)	0.5792	1.60 (1.05–2.00)	1.50 (1.00–2.00)	0.2928	1.40 (1.00–2.00)	1.50 (1.00–2.00)	0.0877
Baseline neutrophils, GI/L	4.15 (3.39–5.02)	4.20 (3.37–5.16)	0.3105	4.69 (3.83–5.88)	4.84 (3.81–6.01)	0.5918	4.82 (3.79–5.84)	5.03 (3.90–6.34)	0.2992
Baseline neutrophils, %	61.00 (55.10–66.40)	61.10 (55.00–66.90)	0.2884	66.50 (60.50–72.20)	66.40 (60.80–71.30)	0.8773	66.60 (61.40–73.60)	67.20 (62.40–72.50)	0.3648
Baseline haemoglobin, G/L	145.00 (135.0–154.0)	145.00 (136.0–153.0)	0.7118	145.00 (137.0–154.0)	145.00 (136.0–154.0)	0.8750	147.00 (137.0–157.0)	147.00 (138.0–156.0)	0.9849
Baseline urea/BUN, mmol/L	5.50 (4.50–6.80)	5.50 (4.50–7.00)	0.7234	5.20 (4.10–6.80)	5.20 (4.30–6.40)	0.7135	5.40 (4.50–6.50)	5.50 (4.50–6.60)	0.9037
Lung function at screening									
Pre-bronchodilator FEV ₁ , L	1.09 (0.82–1.37)	1.10 (0.81–1.42)	0.8555	1.07 (0.79–1.42)	1.13 (0.82–1.42)	0.5026	1.07 (0.74–1.45)	1.02 (0.76–1.38)	0.4270

Patient characteristics	Cluster 1 Eosinophils >2.4%			Cluster 2 Eosinophils ≤2.4%, pack-years ≤46			Cluster 3 Eosinophils ≤2.4%, pack-years >46		
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Pre-bronchodilator % predicted FEV ₁	39.60 (30.50–49.00)	39.90 (29.85–50.30)	0.4990	41.00 (30.90–50.70)	41.80 (31.60–51.80)	0.4433	38.60 (27.20–51.70)	37.95 (28.65–49.75)	0.5792
Post-bronchodilator FEV ₁ , L	1.25 (0.99–1.56)	1.24 (0.95–1.57)	0.8680	1.21 (0.92–1.54)	1.23 (0.97–1.55)	0.4154	1.21 (0.87–1.60)	1.15 (0.90–1.57)	0.7544
Post-bronchodilator % predicted FEV ₁	46.00 (36.10–54.90)	45.50 (35.30–56.30)	0.7880	45.75 (35.10–55.50)	46.60 (37.10–56.90)	0.2969	43.75 (31.45–56.25)	44.10 (32.90–54.65)	0.8822
Post-bronchodilator FEV ₁ /FVC	44.35 (36.70–52.55)	45.40 (36.90–54.40)	0.1415	46.30 (37.20–55.60)	47.10 (37.90–55.30)	0.7017	44.00 (33.50–54.05)	42.90 (35.70–51.35)	0.8223
Lung function at baseline									
Post-bronchodilator FEV ₁ , L	1.19 (0.88–1.53)	1.16 (0.86–1.53)	0.9218	1.11 (0.83–1.48)	1.19 (0.90–1.49)	0.1669	1.11 (0.80–1.53)	1.09 (0.82–1.48)	0.7553
Post-bronchodilator % predicted FEV ₁	42.50 (32.75–53.45)	42.80 (31.90–54.00)	0.6827	43.35 (31.85–51.85)	44.00 (34.60–54.30)	0.2510	41.30 (29.00–54.90)	41.20 (30.00–52.30)	0.9991
Reversibility at screening									
Percent reversibility, %	14.35 (6.15–24.20)	12.60 (4.80–22.90)	0.1396	11.20 (2.70–20.00)	10.80 (3.30–19.40)	0.9218	10.05 (3.95–20.15)	13.10 (5.60–23.10)	0.1047
Reversibility, mL	150.0 (60.0–245.0)	130.0 (50.00–230.0)	0.1198	120.0 (30.0–200.0)	120.0 (40.0–200.0)	0.8202	110.0 (50.0–190.0)	130.0 (60.0–230.0)	0.1065
Reversibility subgroup (≥12% and ≥200 mL increase)	157 (36.3)	421 (31.3)	0.0517	62 (25.4)	162 (25.0)	0.9093	32 (22.5)	138 (31.0)	0.0525
Medication use									
Drugs used in diabetes	37 (8.6)	147 (10.9)	0.1605	22 (9.0)	60 (9.3)	0.9057	14 (9.9)	36 (8.1)	0.5108
Antithrombotic agents	133 (30.8)	353 (26.2)	0.0654	51 (20.9)	127 (19.6)	0.6718	46 (32.4)	121 (27.2)	0.2315
Antihaemorrhagics	0	8 (0.6)	0.1081	0	2 (0.3)	0.3846	1 (0.7)	1 (0.2)	0.3932
Anti-anaemic preparations	23 (5.3)	64 (4.8)	0.6355	12 (4.9)	23 (3.6)	0.3503	8 (5.6)	16 (3.6)	0.2855
Cardiac Therapy	27 (6.3)	90 (6.7)	0.7476	15 (6.1)	29 (4.5)	0.3063	11 (7.7)	23 (5.2)	0.2522
Antihypertensives	24 (5.6)	63 (4.7)	0.4652	7 (2.9)	20 (3.1)	0.8629	8 (5.6)	27 (6.1)	0.8493
Diuretics	88 (20.4)	256 (19.0)	0.5406	53 (21.7)	137 (21.2)	0.8590	30 (21.1)	97 (21.8)	0.8657
Peripheral vasodilators	3 (0.7)	17 (1.3)	0.3290	1 (0.4)	5 (0.8)	0.5547	3 (2.1)	5 (1.1)	0.3761
Vasoprotectives	9 (2.1)	43 (3.2)	0.2321	7 (2.9)	16 (2.5)	0.7397	3 (2.1)	13 (2.9)	0.6064
Beta blocking agents	49 (11.3)	130 (9.7)	0.3136	24 (9.8)	52 (8.0)	0.3913	14 (9.9)	43 (9.7)	0.9452
Calcium channel blockers	64 (14.8)	219 (16.3)	0.4683	43 (17.6)	94 (14.5)	0.2535	20 (14.1)	65 (14.6)	0.8776
Agents acting on the renin–angiotensin system	129 (29.9)	415 (30.9)	0.6966	71 (29.1)	202 (31.2)	0.5399	48 (33.8)	144 (32.4)	0.7496
Lipid modifying agents	125 (28.9)	392 (29.1)	0.9334	51 (20.9)	136 (21.0)	0.9691	40 (28.2)	137 (30.8)	0.5540
Anti-inflammatory and antirheumatic products	172 (39.8)	471 (35.0)	0.0711	63 (25.8)	179 (27.7)	0.5805	48 (33.8)	161 (36.2)	0.6065
Drugs for treatment of bone disease	17 (3.9)	54 (4.0)	0.9414	15 (6.1)	26 (4.0)	0.1762	3 (2.1)	16 (3.6)	0.3847
Psycholeptics	55 (12.7)	203 (15.1)	0.2255	31 (12.7)	79 (12.2)	0.8413	20 (14.1)	62 (13.9)	0.9637

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Psychoanaleptics	66 (15.3)	224 (16.7)	0.5006	31 (12.7)	84 (13.0)	0.9121	22 (15.5)	72 (16.2)	0.8459
Antihistamines for systemic use	45 (10.4)	171 (12.7)	0.2037	14 (5.7)	59 (9.1)	0.1008	12 (8.5)	42 (9.4)	0.7230

Data are number (%) or median (intra-quartile range) unless otherwise stated.

BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; FF, fluticasone furoate; FVC, forced vital capacity; VI, vilanterol; WBC, white blood cells.