



UNIVERSITY OF
OXFORD



Radcliffe Department of Medicine



EMBARC

The European Bronchiectasis Registry

Asthma and Bronchiectasis

Professor James D Chalmers

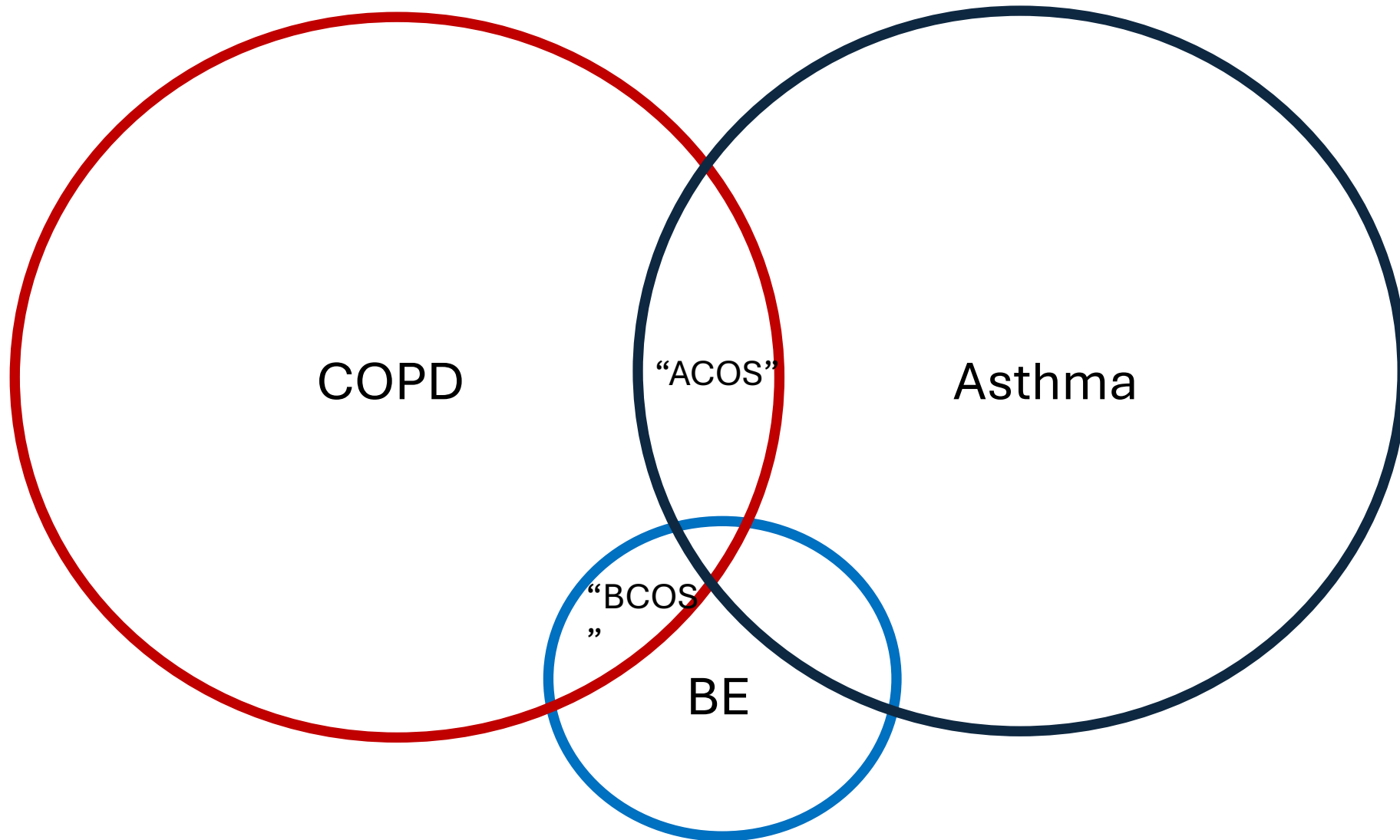
Rhodes Chair of Experimental Therapeutics, University of Oxford

Chair of EMBARC

Disclosures

I have received research grants or performed consultancy for the following companies

- Astrazeneca
- Boehringer Ingelheim
- Chiesi
- Expedition
- Genentech
- Gilead Sciences
- Grifols
- Insmad
- Joincare
- Antabio
- Genentech
- Novartis
- Zambon



ACOS= Asthma COPD overlap syndrome

BCOS= Bronchiectasis COPD overlap syndrome

Case

47 year old lady, works as a healthcare professional. Ex smoker (10 pack years), diagnosis of asthma for the past 14 years.

Cough, sputum production and intermittent breathlessness. Having 3-4 exacerbations per year treated with corticosteroids and often also antibiotics. She has just completed a course of antibiotics and steroids when she attends clinic.

Has chronic rhinosinusitis and a history of congenital heart disease.

Sputum culture 4 months ago *Haemophilus influenzae*. Two other negative cultures recently.

Case

Sputum very thick and difficult to expectorate

Exacerbations are associated with marked worsening in breathlessness, wheeze, change in sputum colour and thickness and often chest pain

She is treated with Fluticasone furoate/vilanterol and recently started a LAMA for her asthma. Also had montelukast for many years.

FEV1 1.8 litres (85% predicted)

Hb 143g/L (120-160)

WCC 6.3×10^9 /L (4-11)

Eos 0.25 (0-0.4)

Platelets 283 (150-400)

FVC 2.9 litres - ratio 62%

Creatinine 52 μ mol/L (44-80)

Sodium 141mmol/L (133-146)

Potassium 4.5mmol/L (3.5-5.3)

LFTs all in the normal range

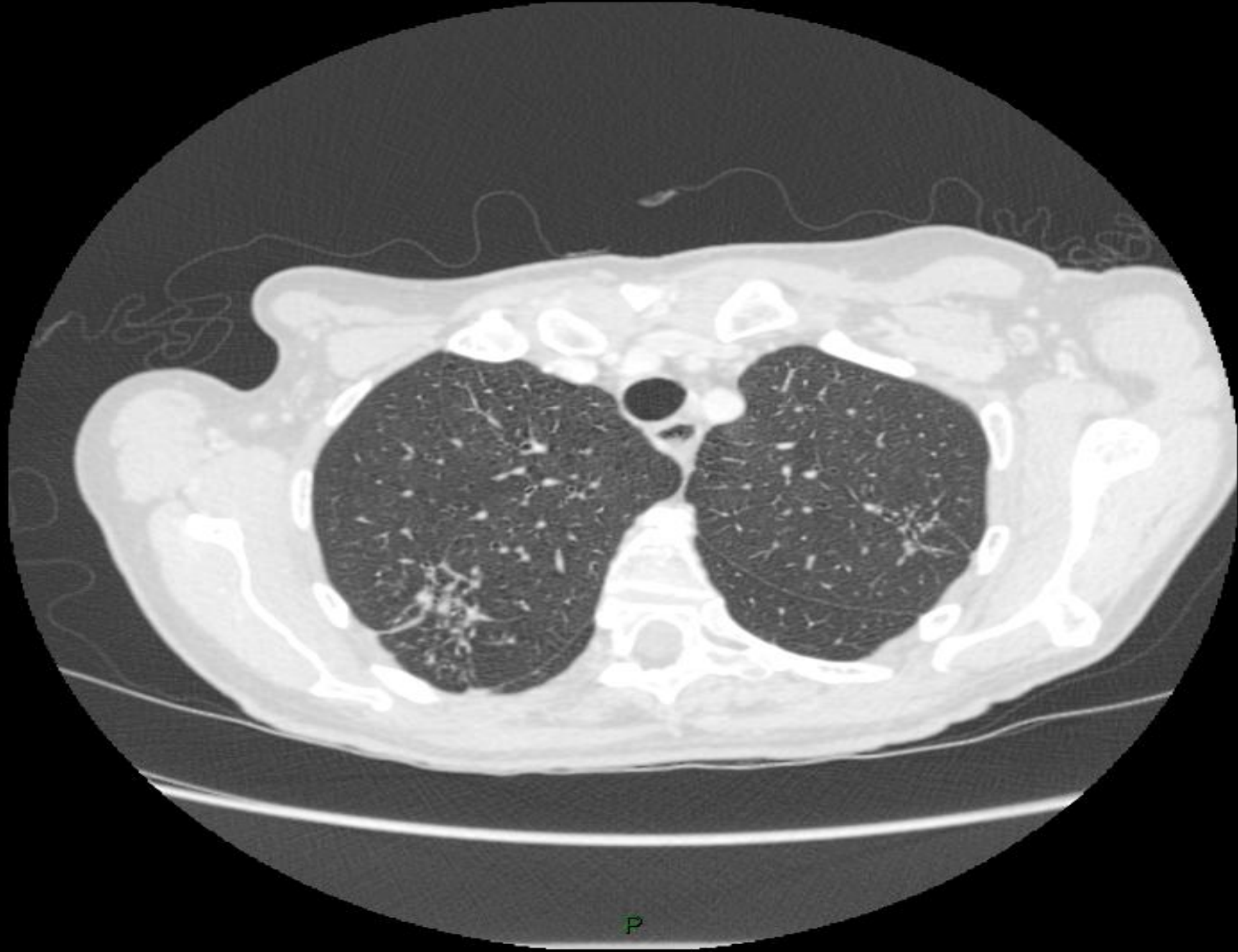
Nasal nitric oxide:110nl/min

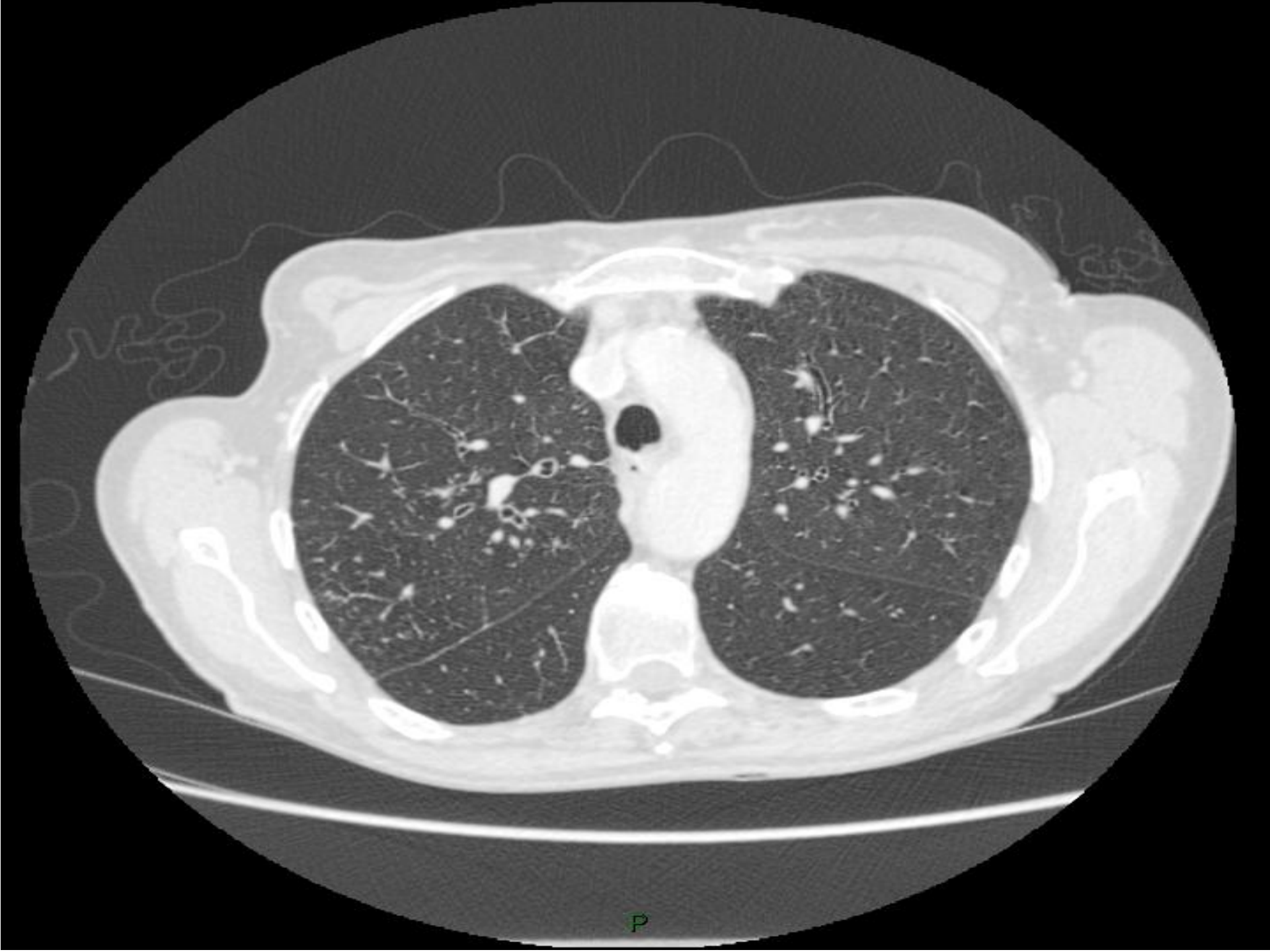
Case

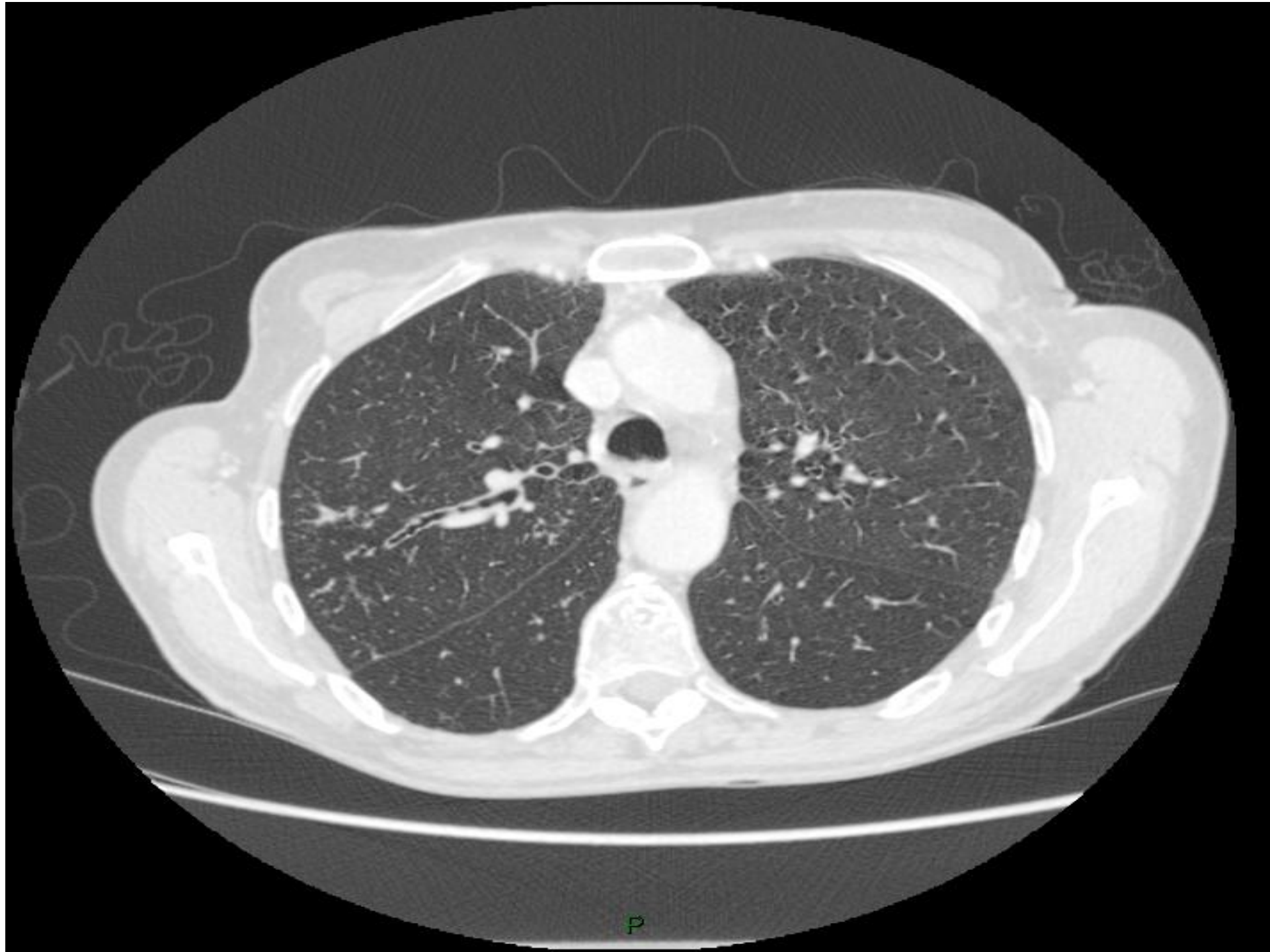


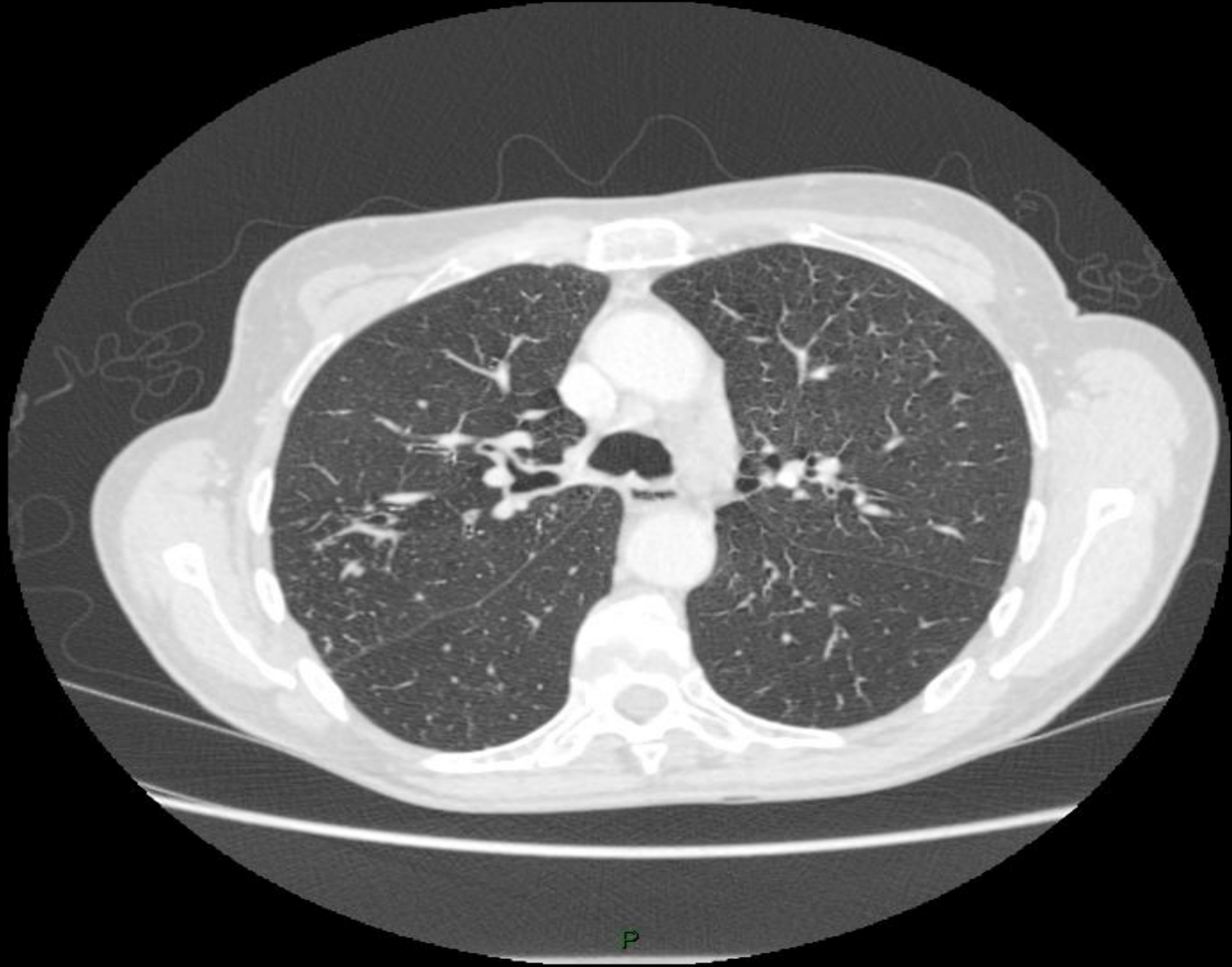
University
of Dundee

We suspected bronchiectasis based on the referral information and so organised a High resolution CT scan in advance of her clinic appointment







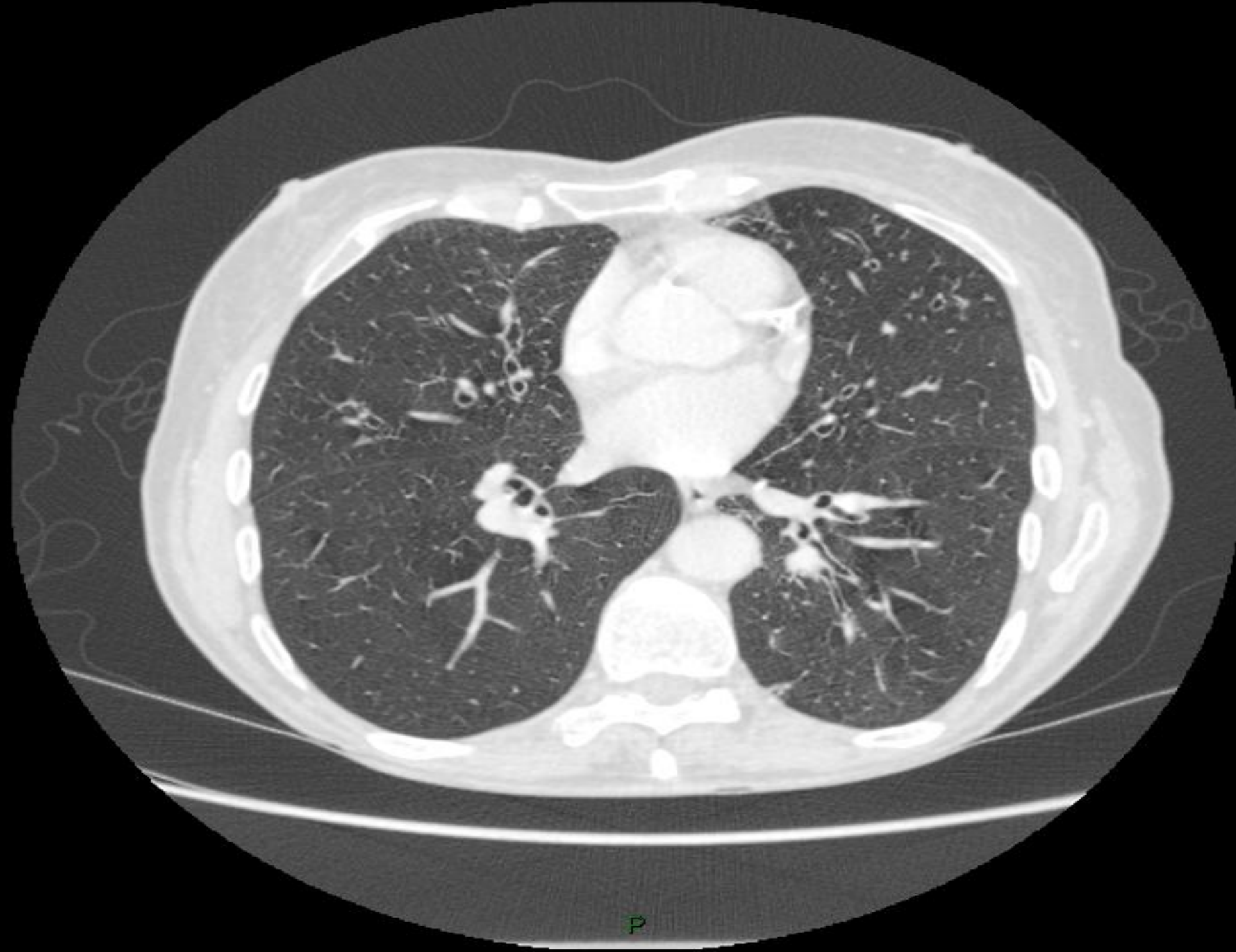
















Results

IgE to Aspergillus: 7.86ku/L

IgG to Aspergillus 57.1mg/L (0-40)

Total IgE- 560ku/L (0-100)

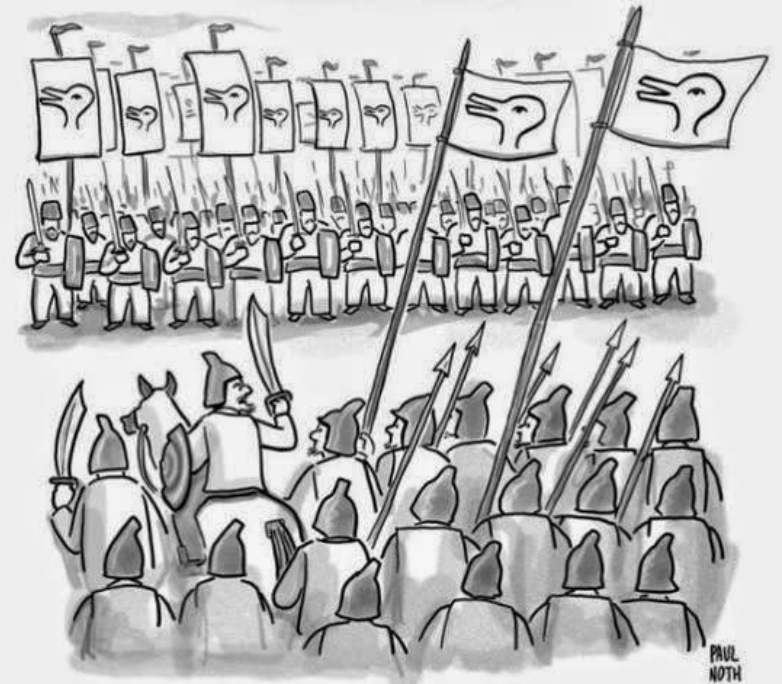
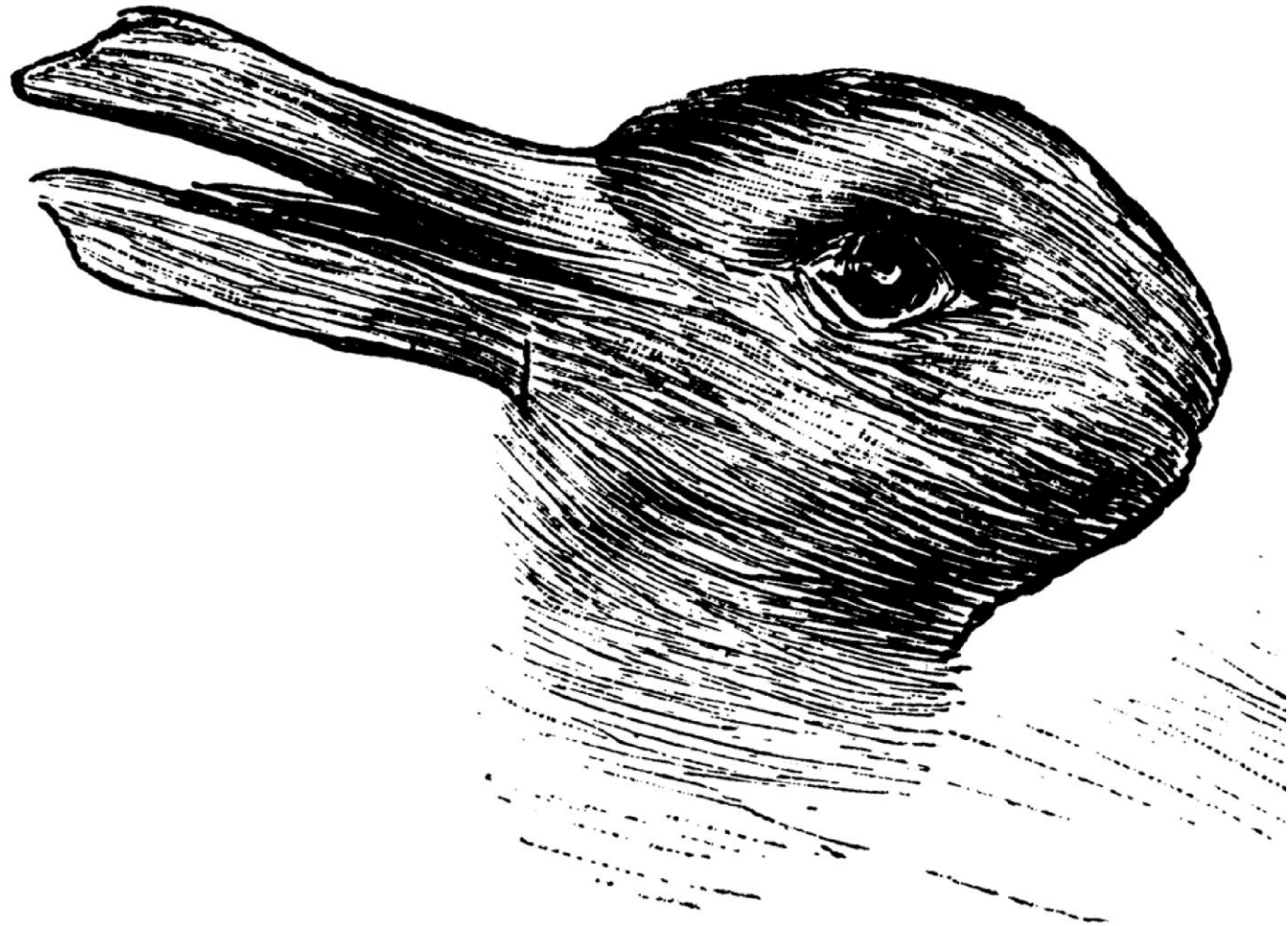
Serum immunoglobulins and functional antibody responses to pneumococcus = normal

Sputum culture: Haemophilus influenzae

Sputum x 3 for NTM= all negative by microscopy

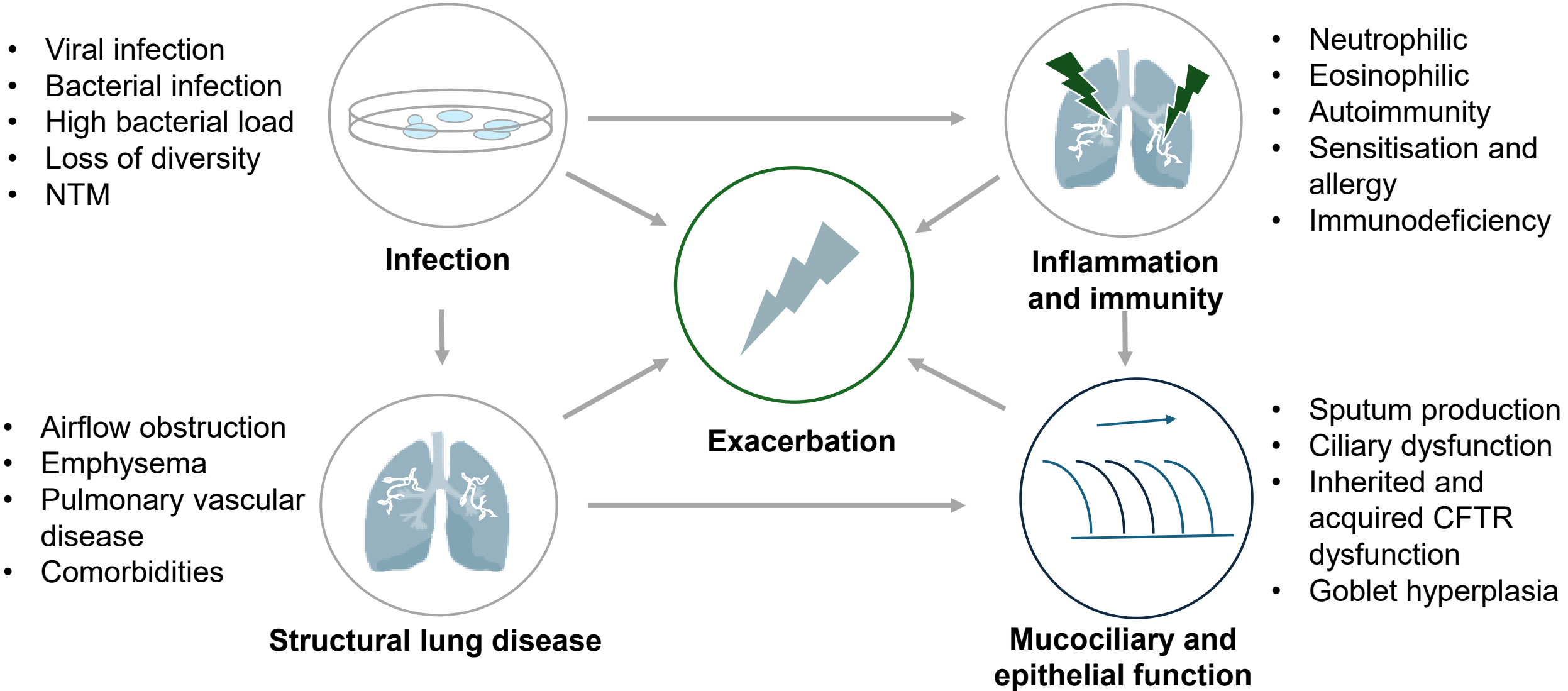
Culture x 1 positive for *Mycobacterium fortuitum*

Culture x 2 negative



“There can be no peace until they renounce their Rabbit God and accept our Duck God.”

Disease labels versus treatable traits¹



Bronchiectasis in severe asthma

184 patients referred to severe asthma clinic (Spain).
CT scans found bronchiectasis in 86 (47%)

Bronchiectasis was associated with more hospitalisations
OR 2.09, 95% CI 1.08–4.05 and higher blood eosinophils

Predictors of Bronchiectasis in Subjects With Severe Asthma

Predictor	OR	95% CI
Atopic dermatitis	0.188	0.041–0.875
Hypersensitivity to nonsteroidal anti-inflammatory drugs	2.243	1.000–5.032
Gastroesophageal reflux disease	1.892	1.050–3.408

How common is asthma in people with bronchiectasis?

	EMBARC cohort (n=16 963)	UK (n=8163)	Southern Europe (n=4295)	Northern and western Europe (n=3444)	Central and eastern Europe (n=1061)
Age, years	67 (57-74)	69 (61-75)	66 (54-74)	65 (52-73)	62 (53-70)
Age >65 years	9943 (58.6%)	5465 (66.9%)	2174 (50.6%)	1841 (53.5%)	463 (43.6%)
Female	10335 (60.9%)	4938 (60.5%)	2766 (64.4%)	2101 (61.0%)	530 (50.0%)
Male	6628 (39.1%)	3225 (39.5%)	1529 (35.6%)	1343 (39.0%)	531 (50.0%)
BMI, kg/m ² *	24.9 (21.7-28.7)	25.7 (22.4-29.8)	24.3 (21.4-27.7)	23.8 (21.4-27.7)	24.8 (21.2-28.4)
Comorbidities					
Cardiovascular diseases	5509 (32.5%)	2413 (29.6%)	1397 (32.5%)	1135 (33.0%)	564 (53.2%)
Stroke	600 (3.5%)	388 (4.8%)	79 (1.8%)	101 (2.9%)	32 (3.0%)
Liver disease	103 (0.6%)	35 (0.4%)	15 (0.3%)	40 (1.2%)	13 (1.2%)
Osteoporosis	2228 (13.1%)	1255 (15.4%)	460 (10.7%)	398 (11.6%)	115 (10.8%)
Depression	2377 (14.0%)	1401 (17.2%)	493 (11.5%)	350 (10.2%)	133 (12.5%)
Anxiety	2428 (14.3%)	1290 (15.8%)	660 (15.4%)	339 (9.8%)	139 (13.1%)
Neoplastic disease	1863 (11.0%)	885 (10.8%)	435 (10.1%)	429 (12.5%)	114 (10.7%)
Chronic renal failure	667 (3.9%)	280 (3.4%)	173 (4.0%)	199 (5.8%)	15 (1.4%)
Diabetes	1724 (10.2%)	880 (10.8%)	403 (9.4%)	302 (8.8%)	139 (13.1%)
Asthma	5267 (31.0%)	3208 (39.3%)	811 (18.9%)	1046 (30.4%)	202 (19.0%)
COPD	4324 (25.5%)	2225 (27.3%)	828 (19.3%)	862 (25.0%)	409 (38.5%)
Smoking					
Never	9096 (53.6%)	4191 (51.3%)	2436 (56.7%)	1942 (56.4%)	527 (49.7%)
Ex-smoker	6785 (40.0%)	3591 (44.0%)	1501 (34.9%)	1328 (38.6%)	365 (34.4%)
Current	1082 (6.4%)	381 (4.7%)	358 (8.3%)	174 (5.1%)	169 (15.9%)
Severity of illness					
Modified MRC dyspnoea score	1 (0-2)	1 (1-2)	1 (0-2)	1 (0-2)	2 (1-3)
Does not produce daily sputum	4752 (28.0%)	2203 (27.0%)	1598 (37.2%)	947 (27.5%)	302 (28.5%)
Quality of life bronchiectasis respiratory symptom score†	63 (44-77.8)	59.3 (40.7-77.8)	70.4 (51.9-83.3)	62.9 (44.4-77.7)	59.3 (40.7-74.1)

Data are median (IQR) and n (%). COPD=chronic obstructive pulmonary disease. MRC=Medical Research Council. Data were complete for all 16963 participants except where indicated. * There were 15 792 participants in the EMBARC cohort (7461 in UK, 4113 in southern Europe, 3182 in western and northern Europe, and 1036 in central eastern Europe) with available data for BMI. † There were 11 152 participants in the EMBARC cohort (7131 in UK, 1130 in southern Europe, 2367 in western and northern Europe, and 524 in central eastern Europe) with available quality of life bronchiectasis respiratory symptom score.

Table 1: Patient characteristics overall and by European region

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline (Intention-to-Treat Population).*

Characteristic	Brensocatib, 10 mg (N=583)	Brensocatib, 25 mg (N=575)	Placebo (N=563)
Age			
Mean — yr	59.8±15.9	60.6±15.8	60.0±15.4
Distribution — no. (%)			
≥75 yr	83 (14.2)	84 (14.6)	93 (16.5)
18 to 74 yr	483 (82.8)	475 (82.6)	462 (82.1)
<18 yr	17 (2.9)	16 (2.8)	8 (1.4)
Female sex — no. (%)	385 (66.0)	360 (62.6)	362 (64.3)
Race or ethnic group — no. (%)†			
White	431 (73.9)	430 (74.8)	405 (71.9)
Asian	63 (10.8)	64 (11.1)	64 (11.4)
More than one race or ethnic group	25 (4.3)	20 (3.5)	21 (3.7)
American Indian or Alaska Native	8 (1.4)	6 (1.0)	9 (1.6)
Black or African American	2 (0.3)	5 (0.9)	3 (0.5)
Native Hawaiian or Pacific Islander	1 (0.2)	0	1 (0.2)
Other	5 (0.9)	4 (0.7)	1 (0.2)
Unknown or not reported	48 (8.2)	46 (8.0)	59 (10.5)
Body-mass index‡	25.5±5.4	25.4±5.1	25.1±4.9
Most common causes of bronchiectasis — no. (%)§			
Idiopathic or other	331 (56.8)	354 (61.6)	321 (57.0)
Injury: pneumonia or childhood infection	173 (29.7)	156 (27.1)	174 (30.9)
Cilia abnormalities: primary ciliary dyskinesia	47 (8.1)	38 (6.6)	33 (5.9)
Long-term use of antibiotics — no. (%)			
Macrolides	110 (18.9)	114 (19.8)	105 (18.7)
Inhaled antibiotics	41 (7.0)	40 (7.0)	36 (6.4)
Use of inhaled glucocorticoids — no. (%)			
<i>Pseudomonas aeruginosa</i> -positive sputum sample — no. (%)	324 (55.6)	324 (56.3)	352 (62.5)
203 (34.8)	205 (35.7)	199 (35.3)	
Exacerbations in previous 12 mo — no. (%)			
≥1	411 (70.5)	412 (71.7)	396 (70.3)
≥3	172 (29.5)	163 (28.3)	167 (29.7)
Bronchiectasis Severity Index score — points	7.1±3.5	7.1±3.6	7.1±3.6
Hospitalized for exacerbation in previous 24 mo — no. (%)			
146 (25.0)	133 (23.1)	142 (25.2)	
Postbronchodilator FEV ₁ — % of predicted value**			
74.3±23.4	74.3±24.6	71.9±22.2	
Blood eosinophil count — no. (%)			
<300 cells/mm ³	465 (79.8)	461 (80.2)	452 (80.3)
≥300 cells/mm ³	115 (19.7)	111 (19.3)	106 (18.8)
Missing data	3 (0.5)	3 (0.5)	5 (0.9)
History of COPD — no. (%)			
77 (13.2)	83 (14.4)	102 (18.1)	
History of asthma — no. (%)			
101 (17.3)	109 (19.0)	111 (19.7)	

Asthma and lower airway disease

Bronchiectasis and asthma: Data from the European Bronchiectasis Registry (EMBARC)

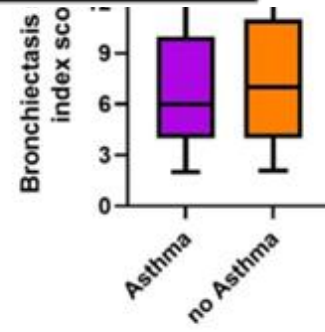
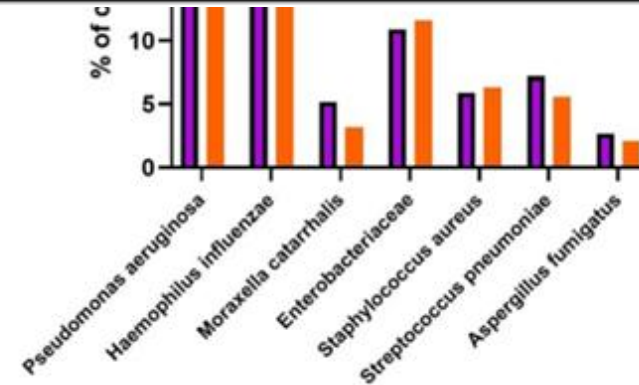
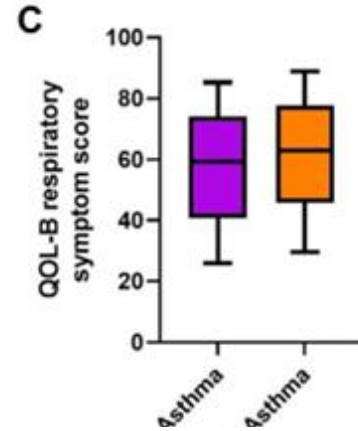
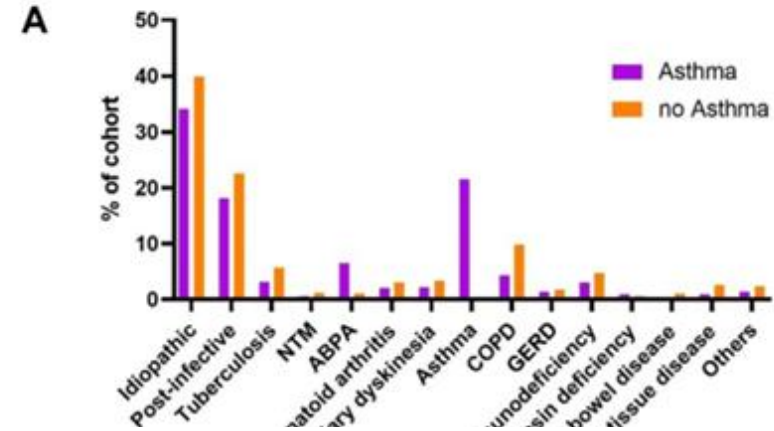


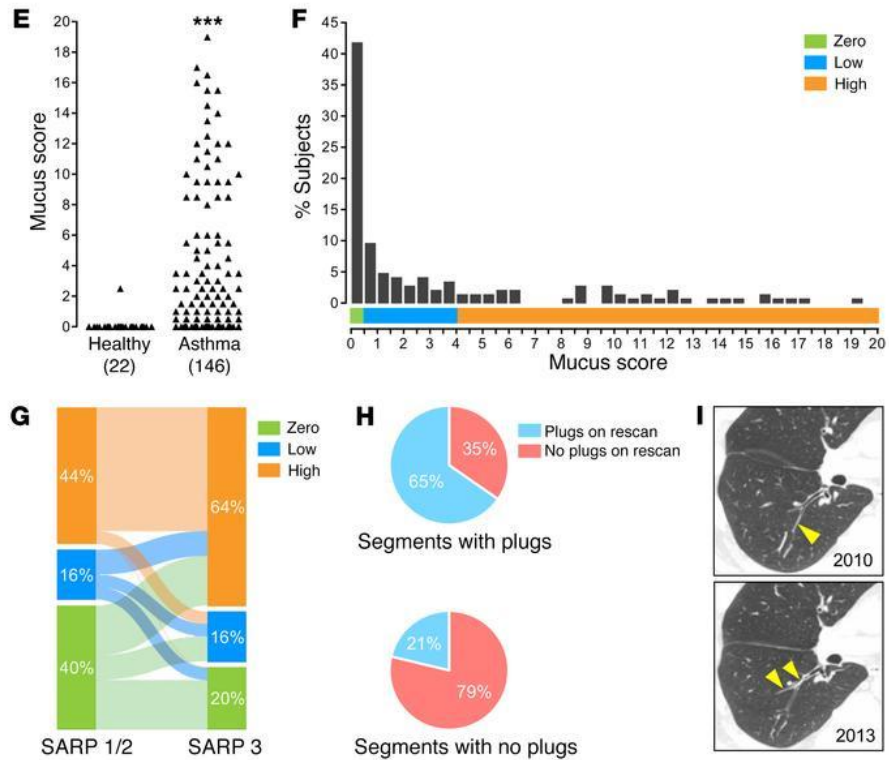
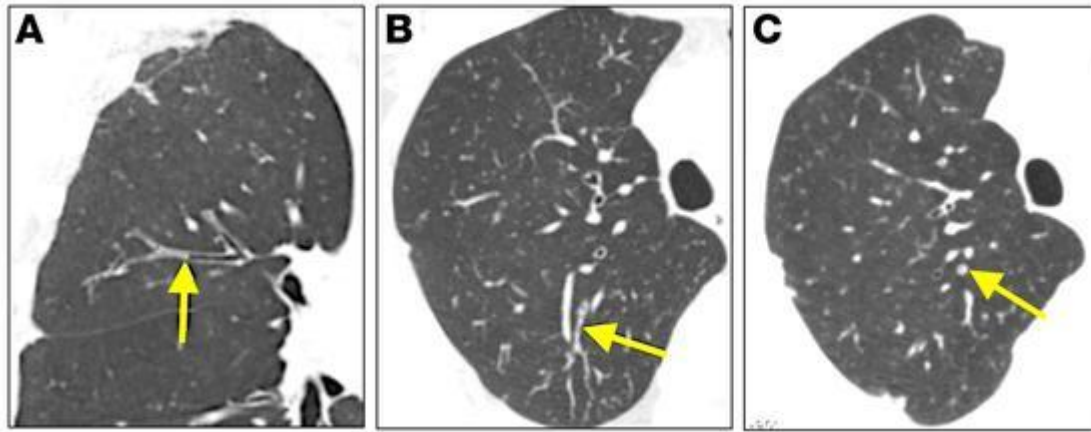
Eva Polverino, MD,^a Katerina Dimakou, PhD,^b Letizia Traversi, MD,^a Apostolos Bossios, PhD,^{c,d} Charles S. Haworth, Michael R. Loebinger, PhD,^f Anthony De Soyza, PhD,^{g,h} Montserrat Vendrell, MD,ⁱ Pierre-Régis Burgel, PhD,^{l,j,k} Pontus Mertsch, MD,^{l,m} Melissa McDonnell, PhD,ⁿ Sabina Škr gat, MD,^{o,p,q} Luis Maiz Carro, MD,^r Oriol Sibila, PhD Menno van der Eerden, PhD,^u Paula Kauppi, PhD,^v Adam T. Hill, MD,^w Robert Wilson, MD,^e Branislava Milenkovic, PhD, Rosario Menendez, MD,^z Marlene Murriss, MD,^{aa} Tonia Digalaki, MD,^b Megan L. Crichton, PhD,^{bb} Sermin Borecki, PhD, Dusanika Obradovic, PhD,^{dd,ee} Adam Nowinski, PhD,^{ff} Adelina Amorim, MD,^{gg} Antoni Torres, MD,^{hh} Natalie Lorent, PhD, Tobias Welte, MD,^{ii,kk,ll} Francesco Blasi, MD,^{mm,nn} Eva Van Braeckel, PhD,^{oo,pp} Josje Altenburg, PhD,^{qq} Amelia Shoemark, PhD,^{bb} Michal Shteinberg, PhD,^{rr,ss} Wim Boersma, MD,^{tt} J. Stuart Elborn, MD,^{uu}

TABLE III. Relationship between asthma and clinical outcomes in bronchiectasis patients

Outcome	Unadjusted	Adjusted*	Fully adjusted†
Exacerbations	1.24 (1.18-1.29)	1.26 (1.21-1.32)	1.07 (1.02-1.12)
Hospitalizations	1.09 (1.02-1.16)	1.18 (1.10-1.27)	1.07 (0.99-1.16)
Mortality	0.71 (0.62-0.82)	0.75 (0.66-0.86)	0.77 (0.67-0.89)

Parameter	Asthma with bronchiectasis	Bronchiectasis without asthma	P value
Any test performed	3456	6025	
Elevated peripheral eosinophil count, n/N (%)	574/2804 (20.5%)	433/5441 (8.0%)	< .0001
IgE groups	2755	5135	
<150	1837 (66.7%)	4361 (84.9%)	< .0001
150-300	279 (10.1%)	351 (6.8%)	
301-500	193 (7.0%)	169 (3.3%)	
501-750	122 (4.4%)	76 (1.5%)	
751-1000	71 (2.6%)	53 (1.0%)	
1000-2000	121 (4.4%)	68 (1.3%)	
>2000	132 (4.8%)	57 (1.1%)	
Raised specific IgE to <i>Aspergillus</i>	697/2337 (29.8%)	413/4028 (10.3%)	< .0001
Diagnostic criteria for ABPA at baseline	265 (7.7%)	103 (1.7%)	< .0001

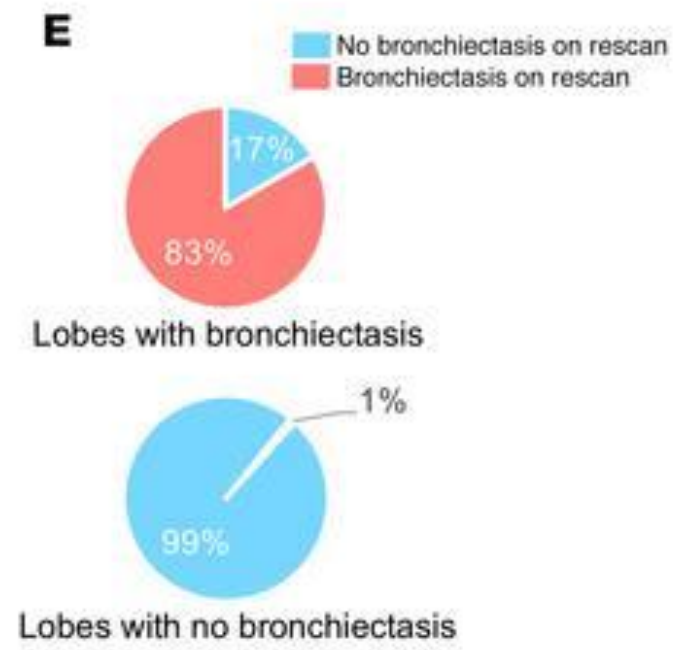
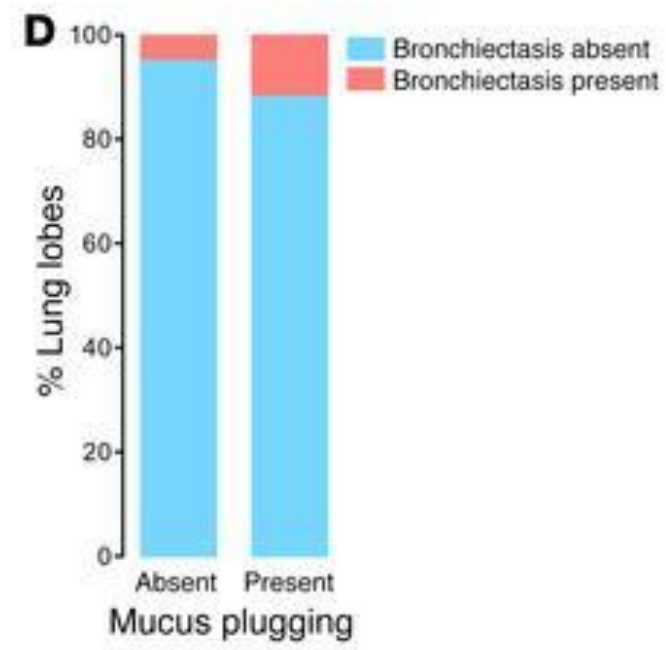
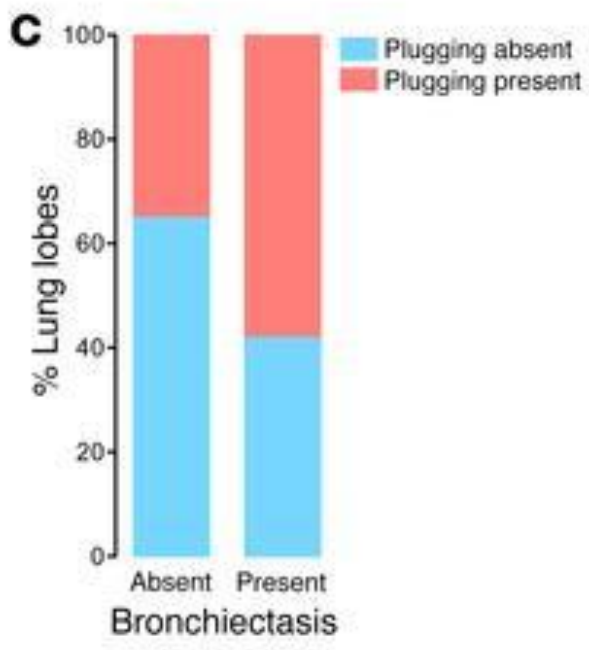
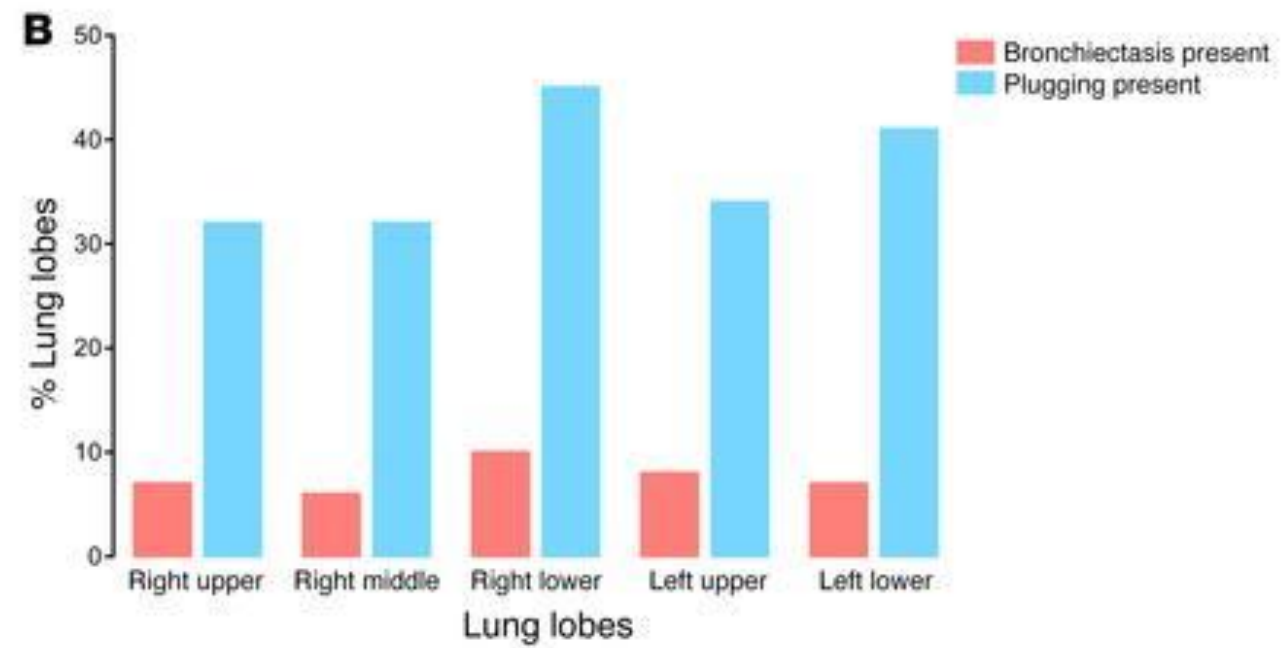
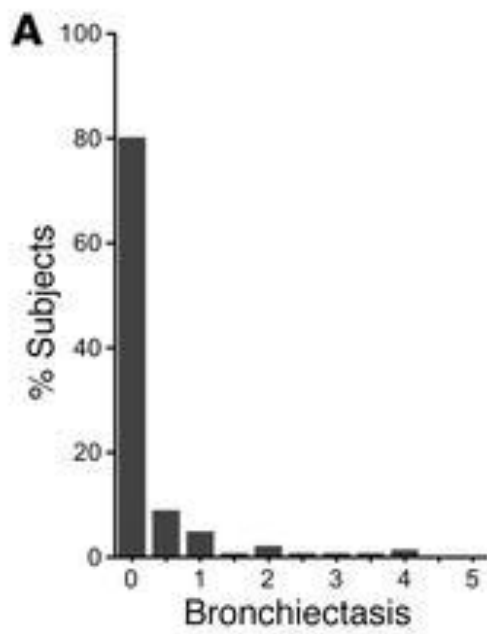




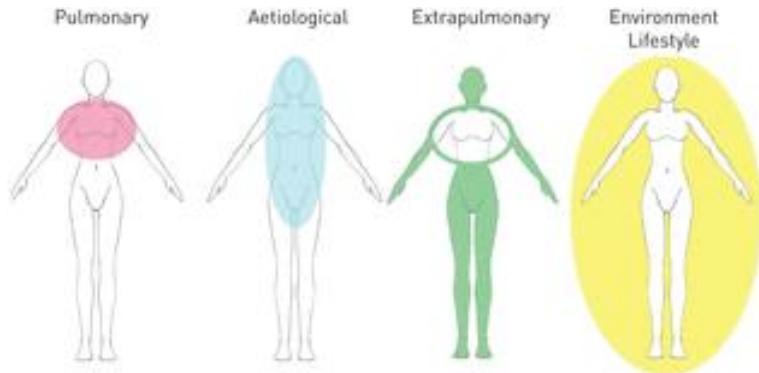
US SARP study

Sputum eosinophilia was associated with mucus plugging.

Mucus plugged airways more likely to develop bronchiectasis during follow-up



Mucociliary clearance : CISCO



[Chest Infections Original Research]



Check for updates

Inflammatory and Mucociliary Dysfunction-Based Endotypes Across the Spectrum of Chronic Airway Diseases

Erin Cant, PhD; Mathieu Bottier, PhD; Morven Shuttleworth, PhD; Jamie Stobo, MSc; Lidia Perea, PhD; Simon Finch, PhD; Merete Long, PhD; Hollian Richardson, PhD; Daniela Alferes de Lima Headley, PhD; Jeffrey T. J. Huang, PhD; Amelia Shoemark, PhD; and James D. Chalmers, PhD



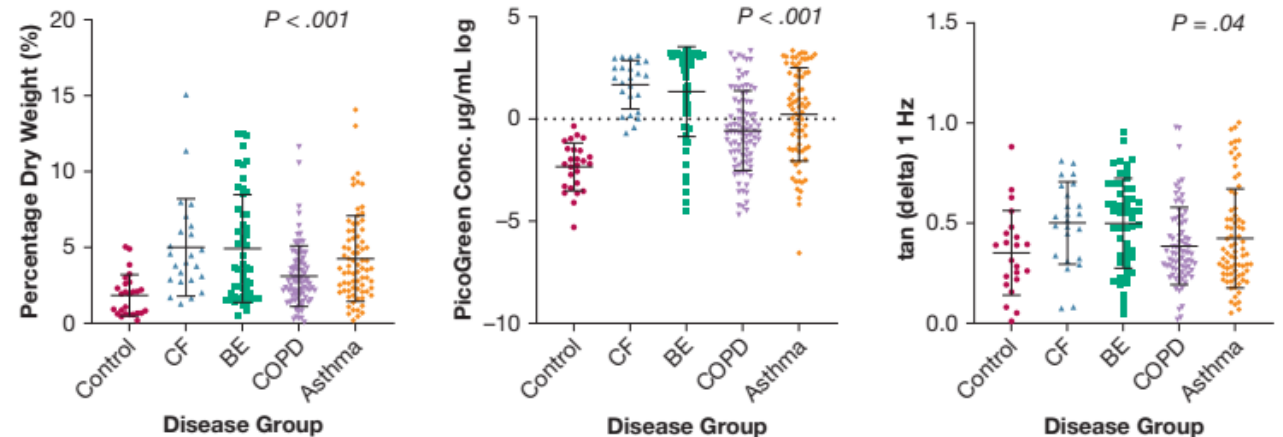
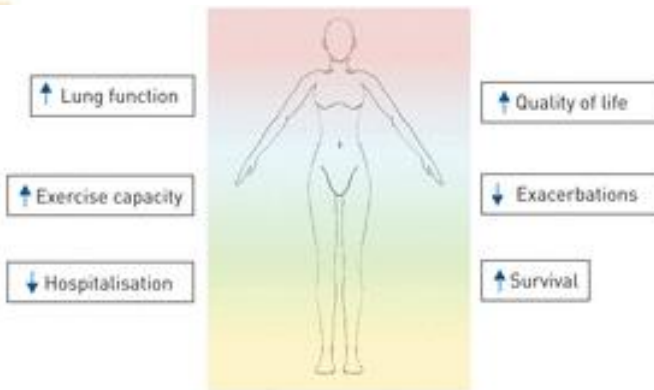
Treatable traits: toward precision medicine of chronic airway diseases

PRECIS



CrossMark

Alvar Agusti¹, Elisabeth Bel², Mike Thomas³, Claus Vogelmeier⁴, Guy Brusselle^{5,6}, Stephen Holgate⁷, Marc Humbert⁸, Paul Jones⁹, Peter G. Gibson¹⁰, Jørgen Vestbo¹¹, Richard Beasley¹² and Ian D. Pavord¹³



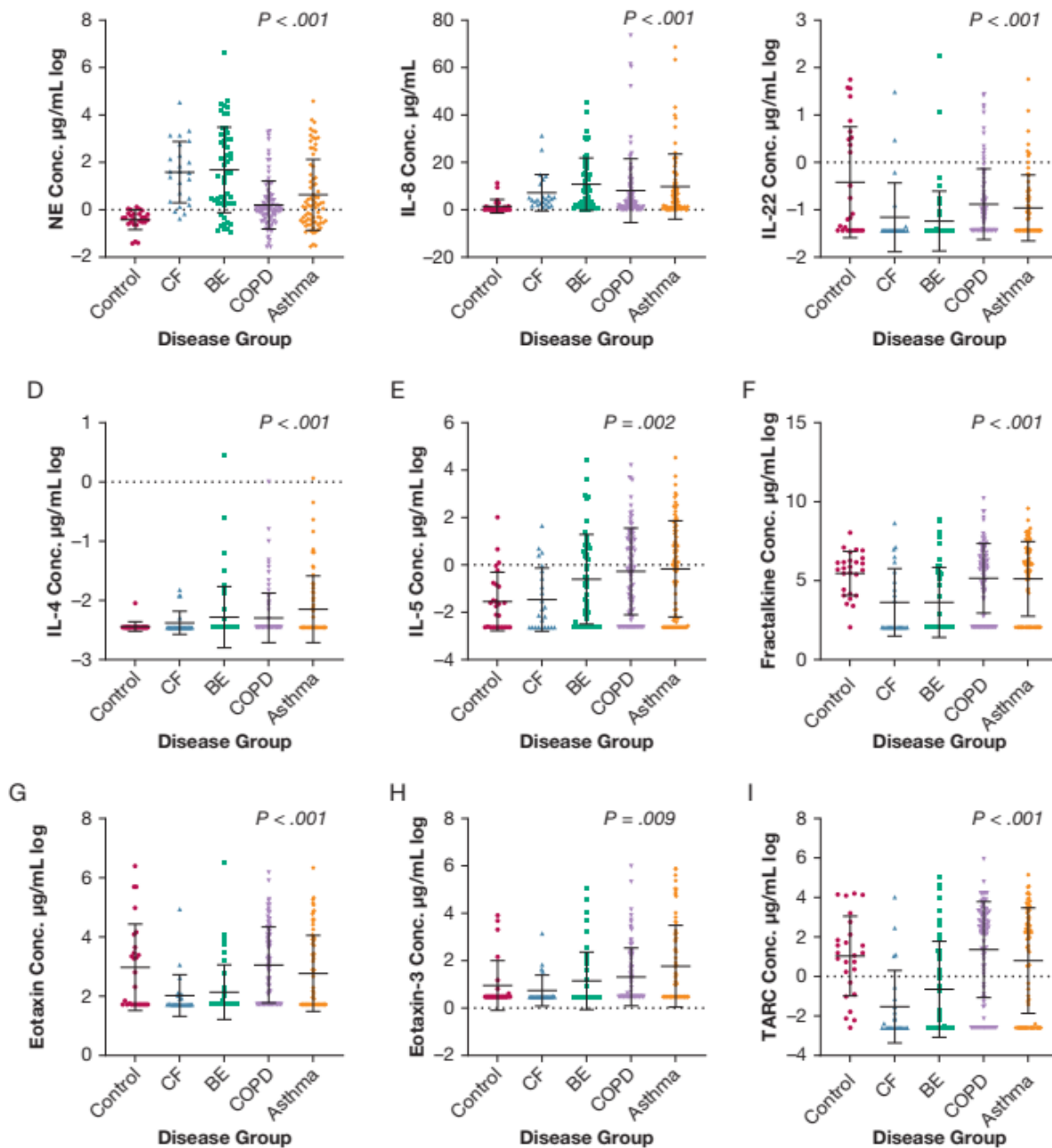


TABLE 2] Clinical Characteristics and Diseases of Participants Compared Between 2 Clusters Based on Sputum Physical Properties and Inflammatory Markers

	Cluster 1 (Neutrophilic; n = 139)	Cluster 2 (Th 2; n = 106)
Condition ($P = 4.07 \times 10^{-6}$)		
Asthma	36 (25.9%)	40 (37.8%)
BE	42 (30.2%)	12 (11.3%)
CF	21 (15.1%)	3 (2.8%)
COPD	40 (28.8%)	51 (48.1%)
MRC Dyspnoea score ($P = .520$)		
1	28 (20.1%)	20 (18.9%)
2	36 (25.9%)	34 (32.0%)
3	39 (28.1%)	29 (27.4%)
4	26 (18.7%)	18 (17.0%)
5	10 (7.2%)	5 (4.7%)
No. of exacerbations in the past year ($P = .729$)		
Minimum	0	0
Q1	1	0
Median	2	2
Mean	2.223	2.302
Q3	3	3
Maximum	12	13
No. of severe exacerbations (hospitalizations) ($P = .735$)		
Minimum	0	0
Q1	0	0
Median	0	0
Mean	0.259	0.2453
Q3	0	0
Maximum	4	3

Categorical data are presented as No. of participants (%). Continuous data are presented as minimum, lower quartile (Q1), median, mean, upper quartile (Q3), and maximum. Unadjusted 2-sided P values comparing distribution of characteristics between clusters are provided. BE = bronchiectasis; CF = cystic fibrosis; Th2 = T helper 2.



Real-world effectiveness of biologic therapies in severe asthma patients ineligible for phase 3 randomised controlled trials of biologics: an analysis from the UK Severe Asthma Registry

Paul E. Pfeffer ^{1,2}, Jola Karaj¹, Thomas Brown ³, Hassan Burhan⁴, Rekha Chaudhuri⁵, Kathryn Prior⁶, Salman Siddiqui⁷, Liam Heaney⁸, David J. Jackson^{9,10}, Mitesh Patel¹¹, Pujan H. Patel^{12,13}, Hitasha Rupani ¹⁴ and John Busby¹⁵ on behalf of the UK Severe Asthma Registry

- UK registry
- 1421 patients with severe asthma
- 382 patients with comorbidities other than asthma incl BE
- No differential effect of biologics

Real-World Effectiveness of IL-5/5Ra Targeted Biologics in Severe Eosinophilic Asthma With Comorbid Bronchiectasis

Sarah A. Bendien, MD ^{a,*} · Johannes A. Kroes, MSc ^{b,*} · Lotte H.G. van Hal, MSc ^b · ... · Anke-Hilse Maitland-van der Zee, PhD ¹ · Anneke ten Brinke, MD, PhD ^P on behalf of the Registry of Adult Patients With Severe Asthma for Optimal Disease Management Team ...
Show more

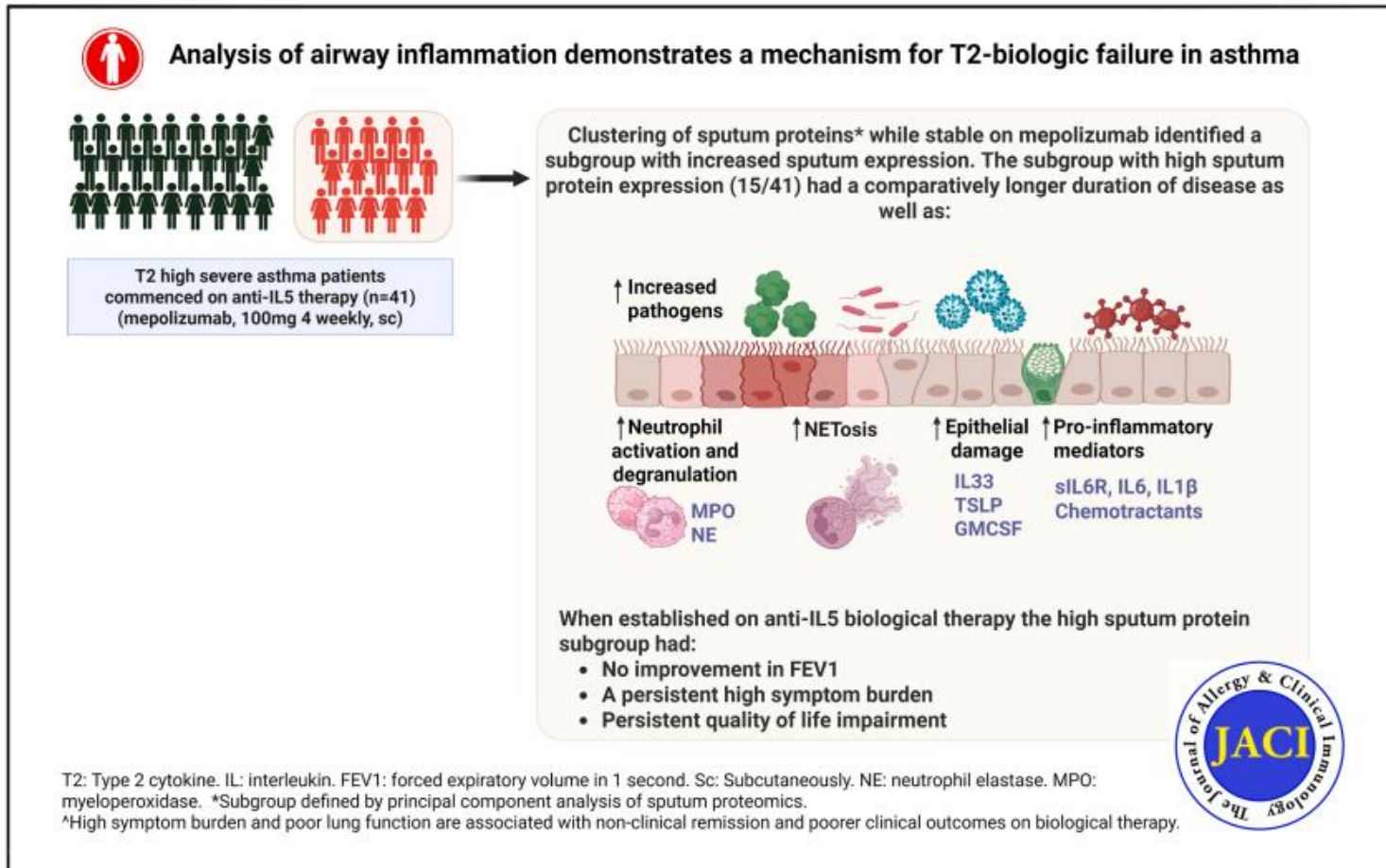
- N=97 patients with asthma and bronchiectasis
- Anti-IL-5/5Rα therapy significantly reduced exacerbation frequency, daily maintenance oral corticosteroid (OCS) dose, and cumulative OCS exposure over 12 months.
- It also improved asthma symptom scores, pulmonary function parameters, and reduced healthcare utilization.

Analysis of airway inflammation demonstrates a mechanism for T2-biologic failure in asthma



P. Jane McDowell, PhD, Adnan Azim, PhD, John Busby, PhD, Sarah Diver, PhD, Freda Yang, MD, Catherine Borg, MSc, et al

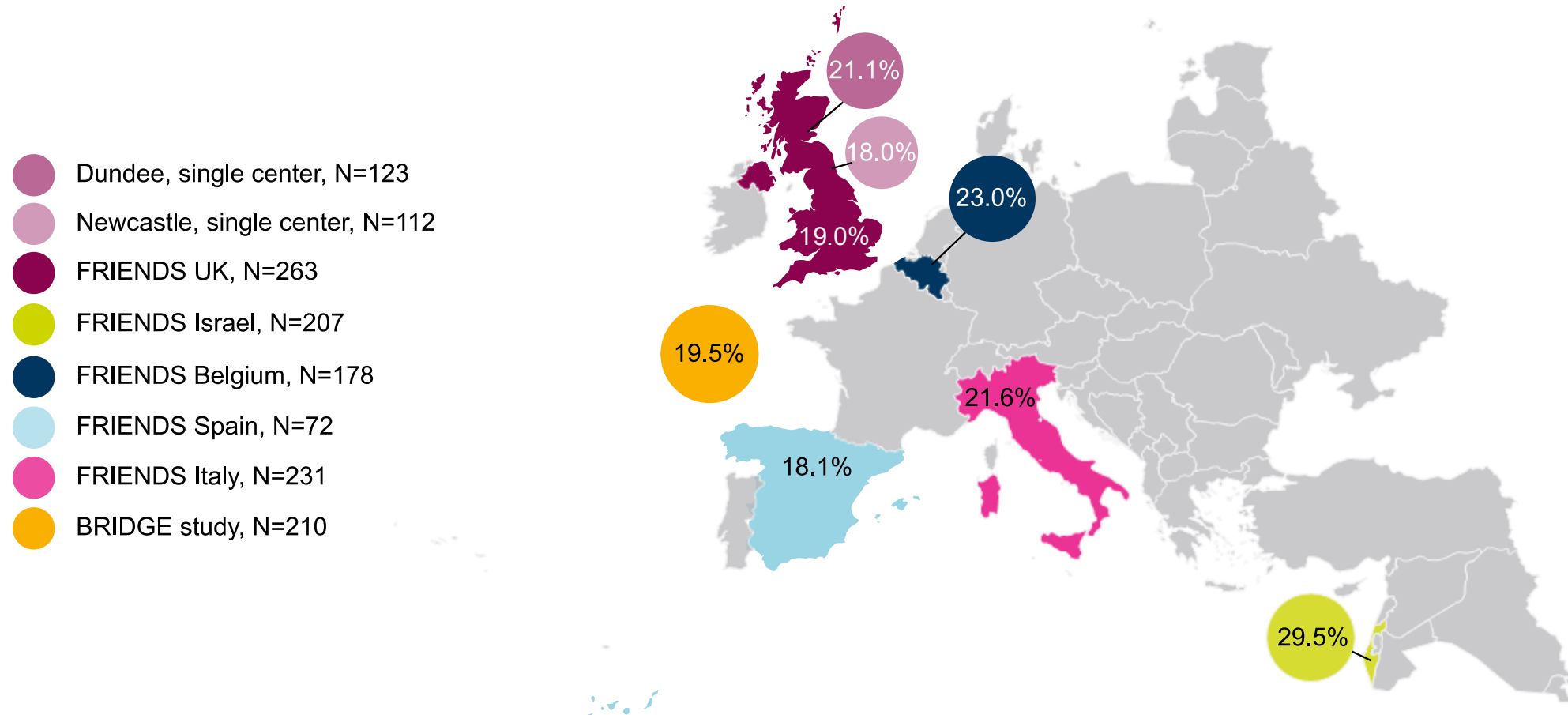
GRAPHICAL ABSTRACT



- Asthma is not a predominantly neutrophilic disease
- Enrol patients with Th2 biologic failure
- NETs and NE significantly different between clusters

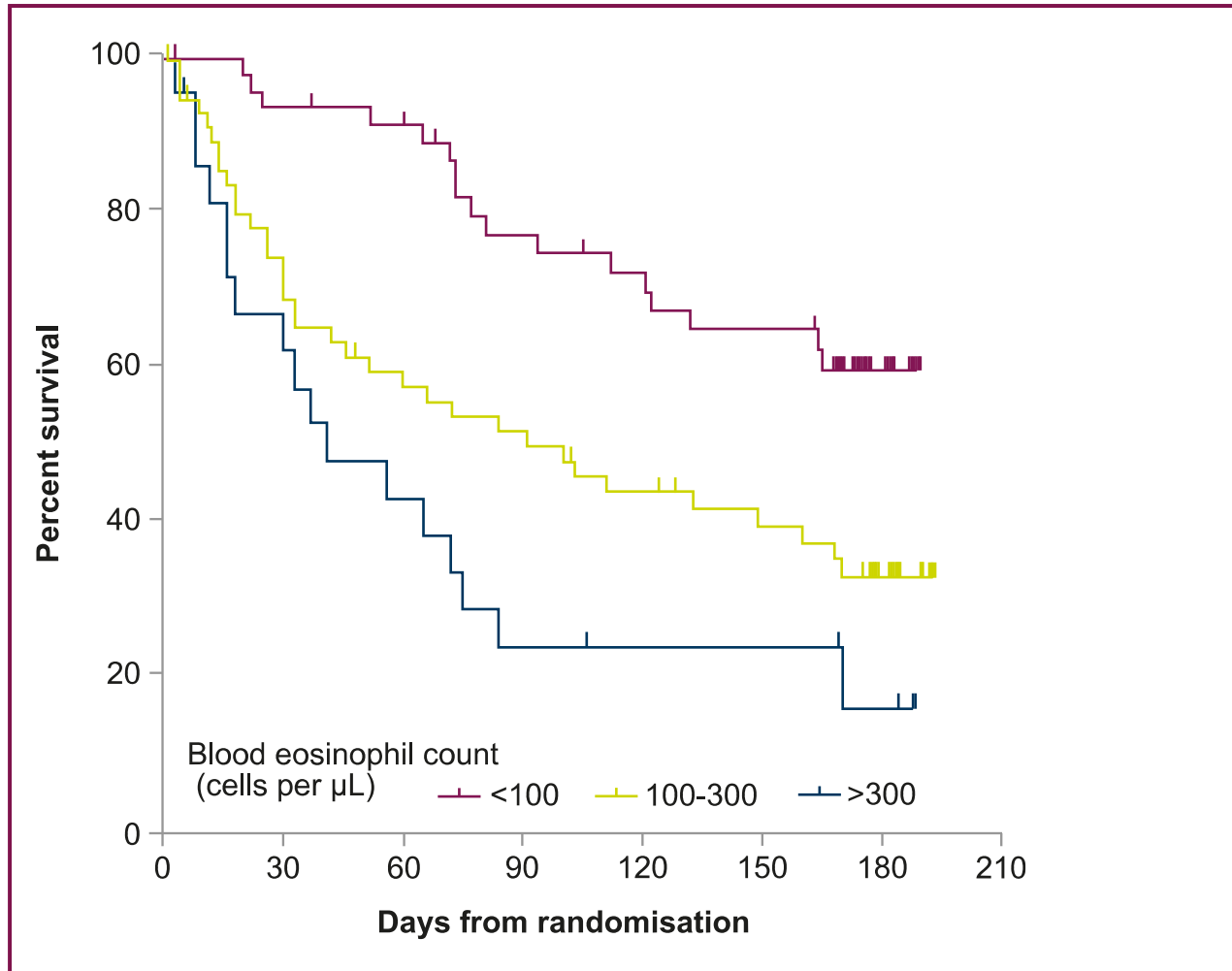
Prevalence of eosinophilic bronchiectasis

Patients with blood eosinophilia (%)



Defined by blood eosinophils >300 cells/ μ l

Eosinophil counts and exacerbations



Compared with eosinophil counts <100 cells/ul

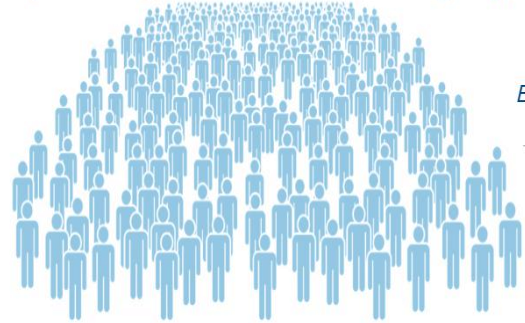
- Eos=100–300 cells/ul:
RR 2.35, 95%
CI 1.16-4.78, $p=0.018$
- Eos >300 cells/ul:
RR 3.47, 95%
CI 1.47-8.18, $p=0.004$

Inhaled corticosteroids in bronchiectasis

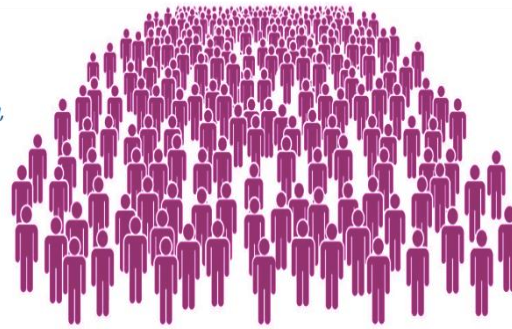


EMBARC

(The European Bronchiectasis Registry)



Exclusion of those with known asthma, COPD and/or ABPA *



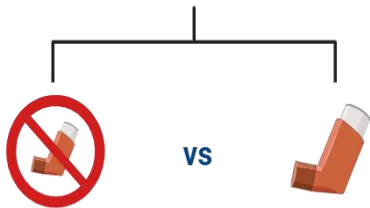
Further exclusion of those without blood eosinophil data



A multicentre, prospective, observational cohort of ~20,000 bronchiectasis patients from >30 countries

9,715 individuals included for analysis

4,385 individuals included for analysis



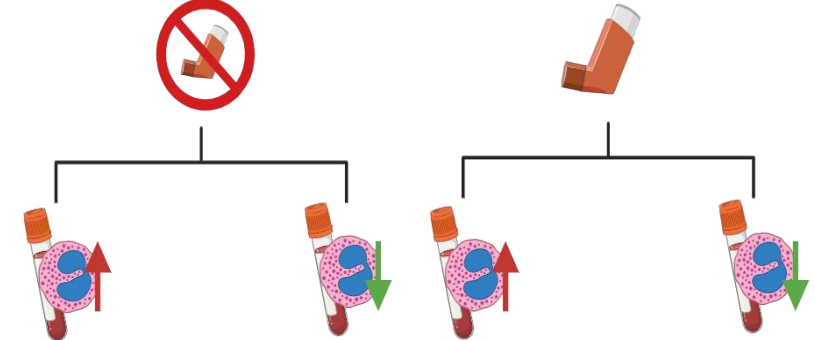
Demographic and clinical comparisons between those receiving / not receiving ICS



Demographic and clinical comparisons between those receiving / not receiving ICS

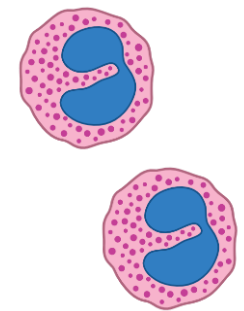


Negative binomial modelling for exploration of treatment outcomes associated with ICS use over long-term follow-up among those with a primary diagnosis of bronchiectasis minus eosinophilic comorbidities

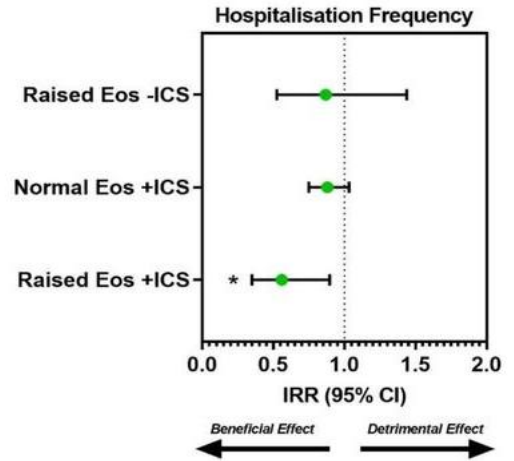
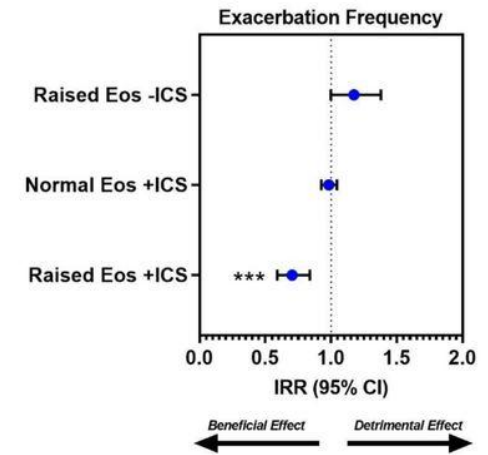
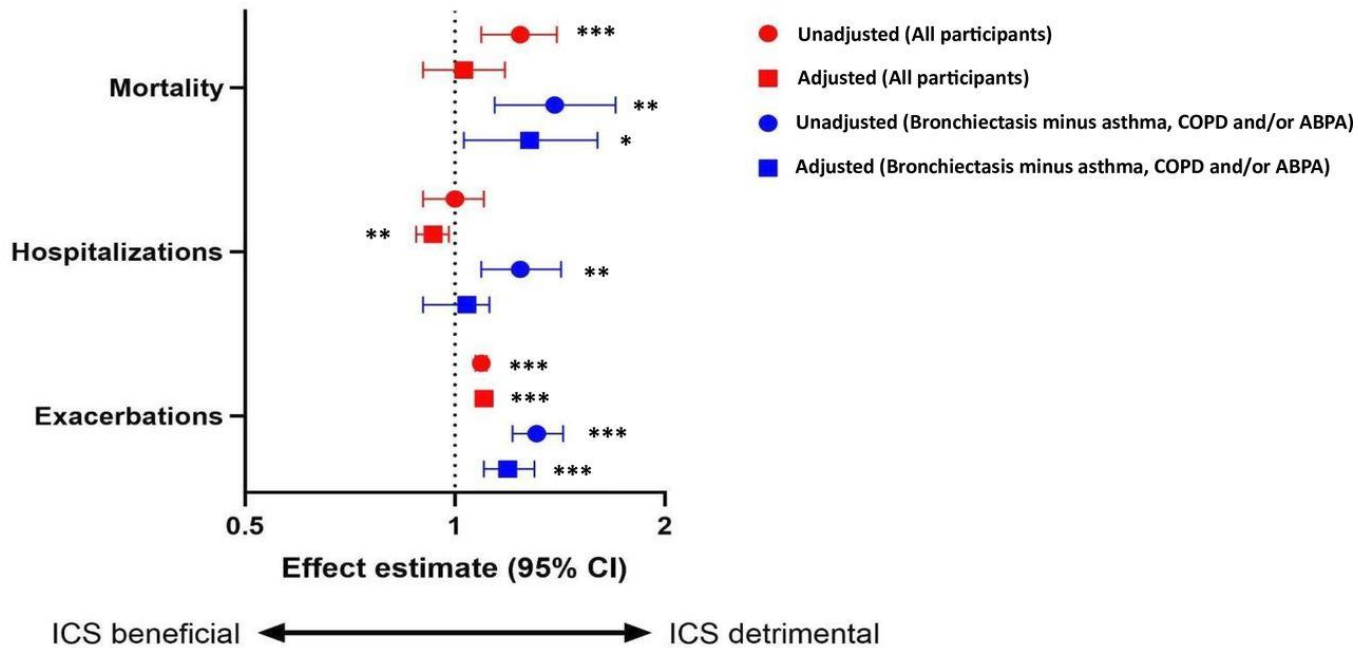


Negative binomial modelling for exploration of treatment outcomes associated with ICS use over long-term follow-up among those with a primary diagnosis of bronchiectasis stratified by baseline blood eosinophil count

ICS use and outcomes in real life

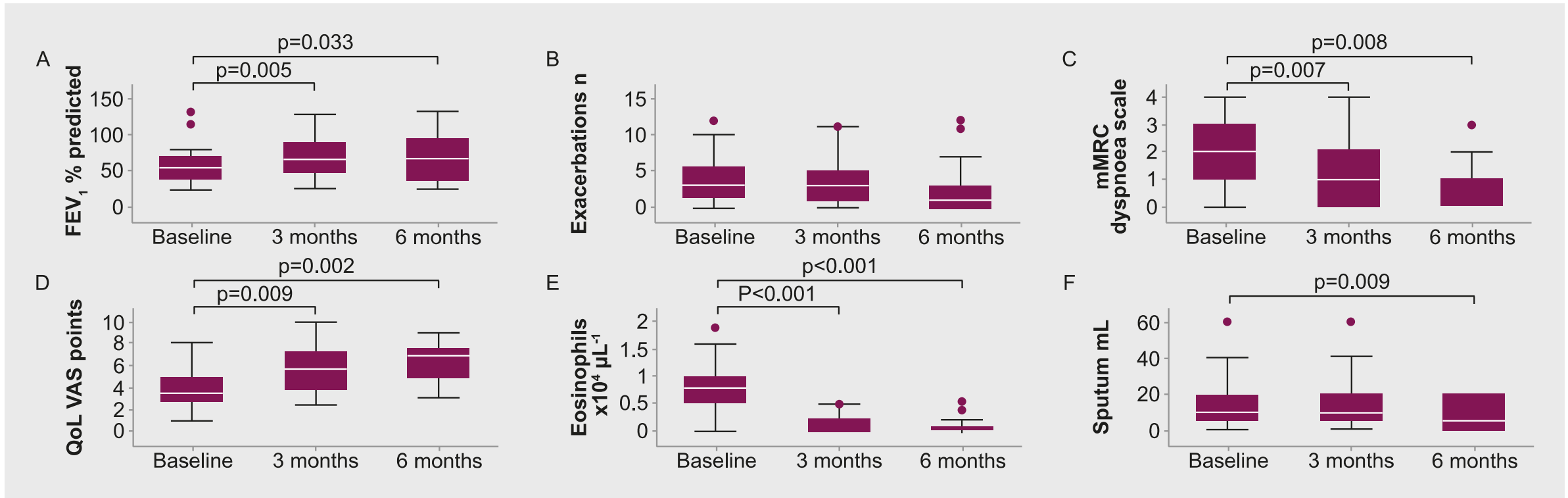


Poorer outcomes in users of ICS



Anti-IL5 or Anti-IL-5R treatment for bronchiectasis?

- Case series of 21 patients treated with anti-IL5 or anti-IL-5 receptor monoclonal antibody therapy
- Refractory disease despite standard of care for bronchiectasis
- Marked improvements in FEV₁, exacerbation rates, dyspnoea and quality of life



FEV₁: forced expiratory volume in 1 second; IL-5: interleukin-5; IL-5R: interleukin-5 receptor; mMRC: modified Medical Research Council; QOL: quality of life; VAS: visual analogue scale
Rademacher J et al. *Eur Respir J* 2020; **55**: 1901333

A Multicentre, Randomised, Double-blind, Parallel-group, Placebo-controlled, 52 Week, Phase III Study With an Open-label Extension to Evaluate the Efficacy and Safety of Benralizumab in Patients With Non-Cystic Fibrosis Bronchiectasis (MAHALE)



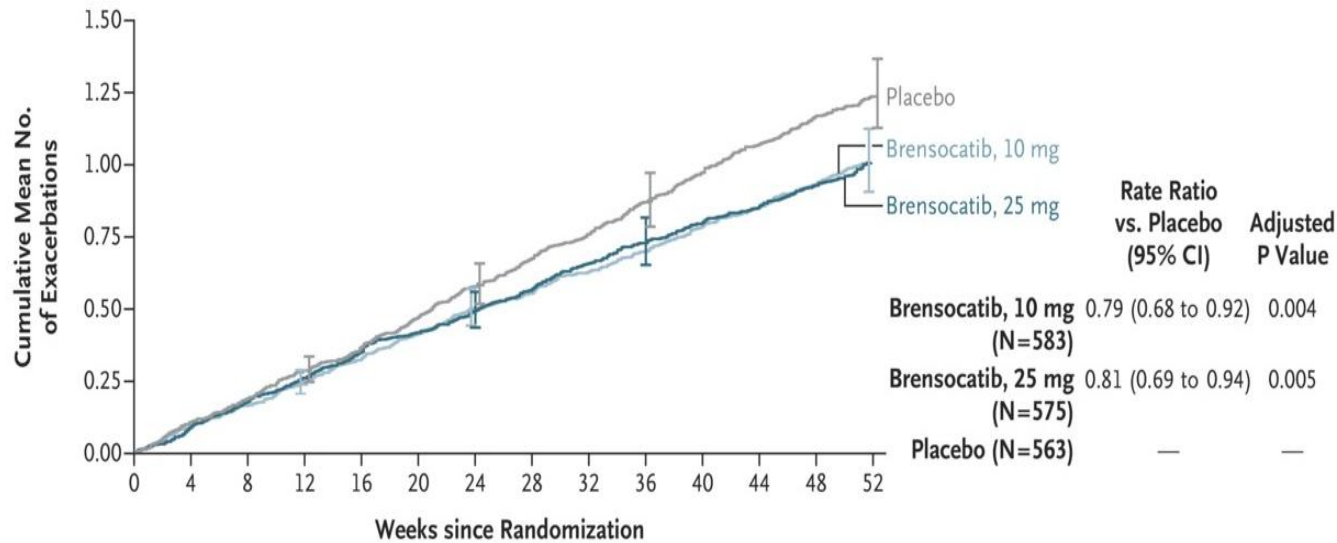
- Benralizumab 30mg SC every 4 weeks vs placebo
- Planned to enrol 420 patients. Terminated due to COVID-19 pandemic.
- Patients with low eosinophils included as per regulatory requirements
- Only 100 patients enrolled. 80 low eos, 20 high eos

- Overall 54 randomized to Benralizumab and 46 to placebo

- **No effect on exacerbations (rate ratio 1.14 95% CI 0.71-1.82)**
- Study unpowered and did not enrol the target population

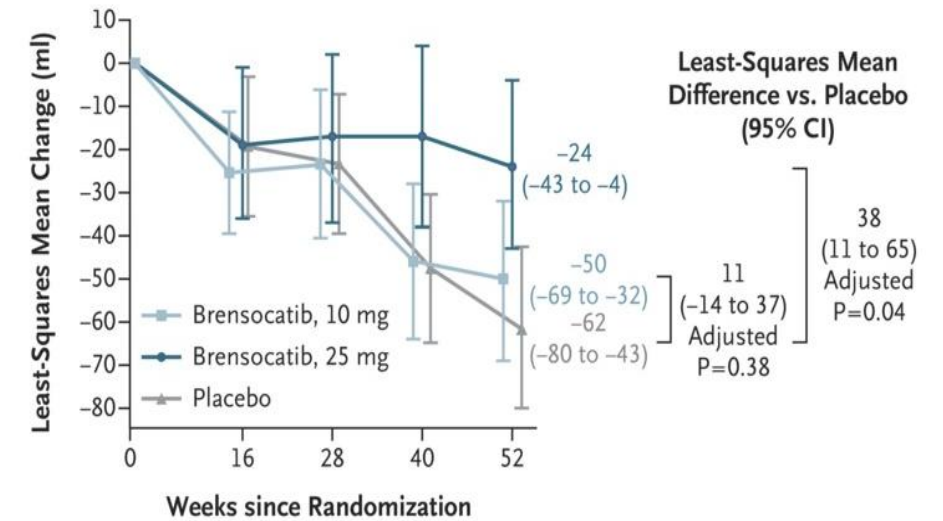
DPP1 inhibition reduces exacerbations

Exacerbations over the 52-Wk Treatment Period



No. at Risk	0	4	8	12	16	20	24	28	32	36	40	44	48	52
Brensocaticib, 10 mg	583	582	582	576	570	565	564	555	546	540	533	529	522	516
Brensocaticib, 25 mg	575	572	568	566	563	552	550	543	540	537	528	523	520	515
Placebo	563	562	556	551	547	544	539	534	529	522	519	509	507	499

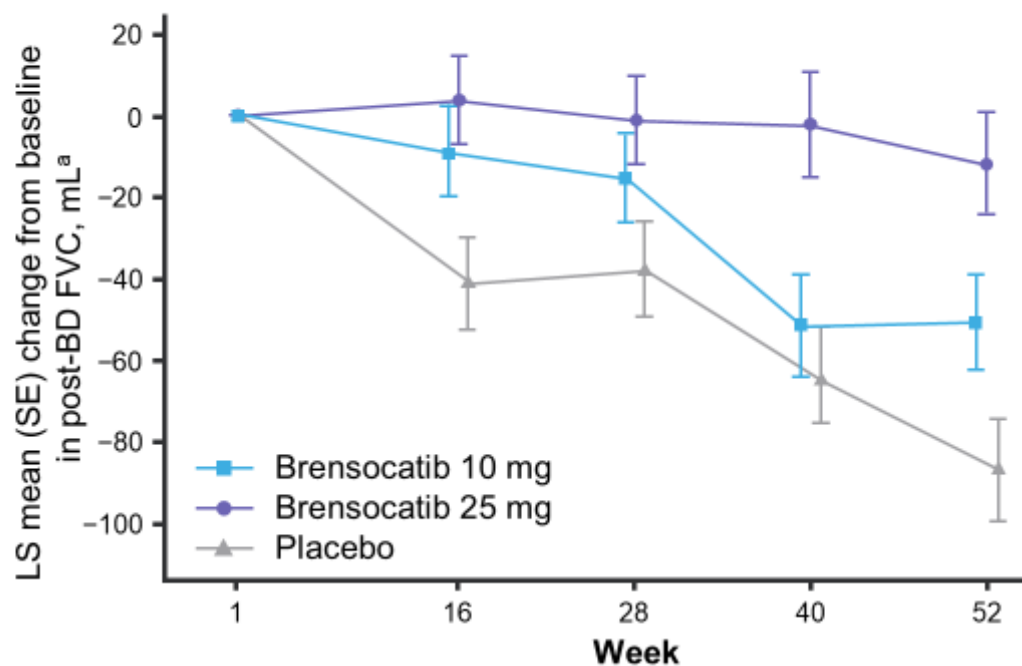
Change in Postbronchodilator FEV₁ from Baseline



No. with Data	0	16	28	40	52
Brensocaticib, 10 mg	579	545	529	513	475
Brensocaticib, 25 mg	571	529	523	494	487
Placebo	563	522	513	494	468

Change From Baseline in Post-Bronchodilator FVC at Week 52

Exploratory endpoint



Number of patients with observation

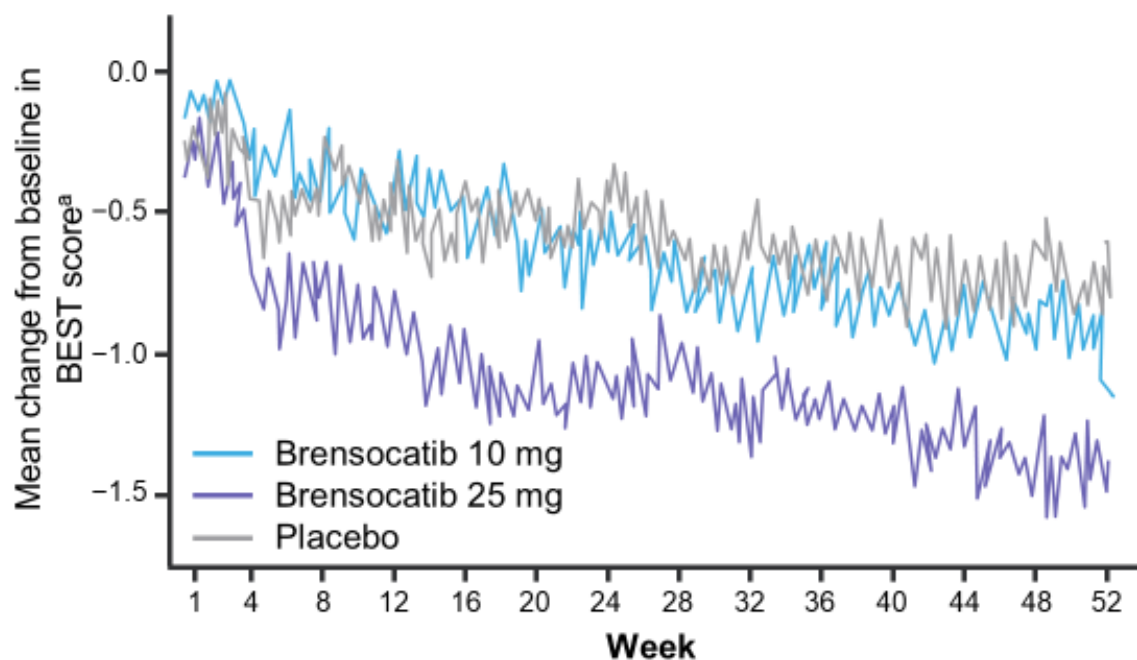
	1	16	28	40	52
Brensocatib 10 mg	579	545	529	513	475
Brensocatib 25 mg	571	529	523	494	487
Placebo	563	522	513	494	468

	Brensocatib 10 mg	Brensocatib 25 mg	Placebo
LS mean change from baseline in post-BD FVC at week 52, mL	-51	-12	-87
LS mean difference vs placebo in post-BD FVC, mL	36	75	-
<i>P</i> value vs placebo	0.0331 ^b	<0.0001 ^b	-

^aFVC analyzed using a linear repeated measures model in the ITT analysis set. ^bNominally significant *P* value. BD, bronchodilator; FVC, forced vital capacity; ITT, intention-to-treat; LS, least squares.

Change From Baseline in Average Daily BEST Score

Exploratory endpoint



Number of patients with observation^a

Brensocatib 10 mg	558	553	555	547	544	534	528	520	515	506	504	505	497	488
Brensocatib 25 mg	557	552	542	540	534	529	517	520	522	513	507	505	499	494
Placebo	549	549	541	534	527	520	517	508	505	499	493	490	485	477

	Brensocatib 10 mg	Brensocatib 25 mg	Placebo
LS mean change from baseline in 52-week average daily BEST score	-0.594	-0.999	-0.426
LS mean difference vs placebo in BEST score	-0.168	-0.572	—
<i>P</i> value vs placebo	0.1696	<0.0001 ^b	—

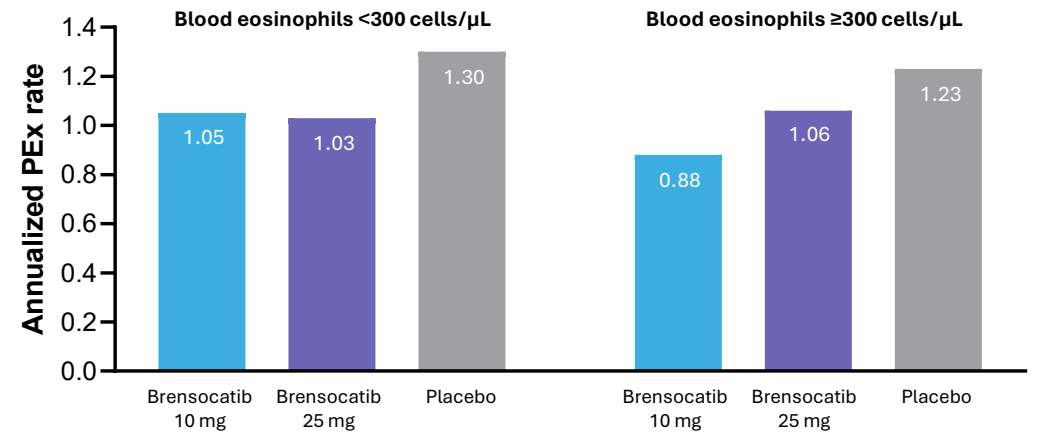
^aAverage daily change in the BEST score analyzed with an analysis of covariance model in adult patients in the ITT analysis set. ^bNominally significant *P* value. BEST, Bronchiectasis Exacerbation and Symptoms Tool.

Asthma and Bronchiectasis overlap with DPP1 inhibitors

No efficacy in patients with underlying asthma

	Asthma Yes		Asthma No	
	Brensocatib 10 mg n=101	Brensocatib 25 mg n=109	Brensocatib 10 mg n=482	Brensocatib 25 mg n=4521
RR vs placebo (95% CI)	0.96 (0.71-1.30)	0.99 (0.72-1.34)	0.75 (0.63-0.89)	0.76 (0.64-0.90)

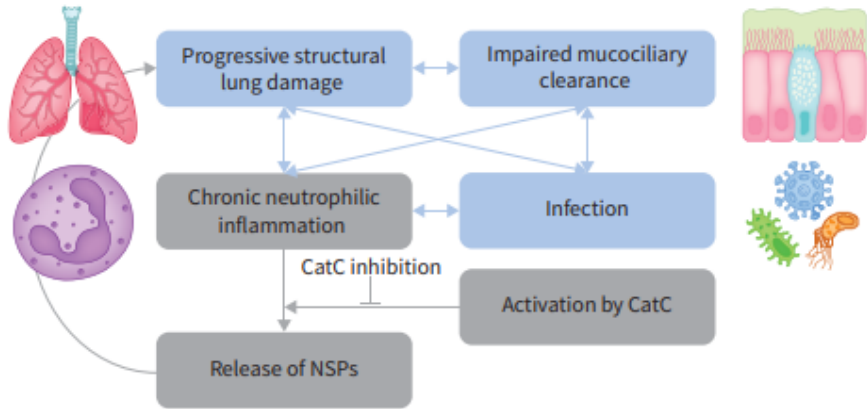
No Differential effect by Eosinophil count



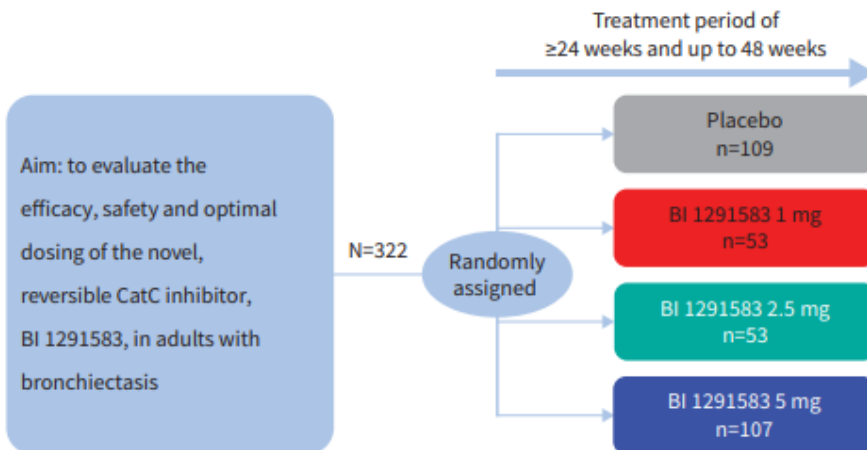
	Blood eosinophils <300 cells/μL		Blood eosinophils ≥300 cells/μL	
	Brensocatib 10 mg n=465	Brensocatib 25 mg n=461	Brensocatib 10 mg n=115	Brensocatib 25 mg n=111
RR vs placebo (95% CI)	0.806 (0.681-0.954)	0.794 (0.671-0.939)	0.720 (0.522-0.994)	0.863 (0.618-1.203)

AIRLEAF- the treatable traits trial

Bronchiectasis: the vicious vortex

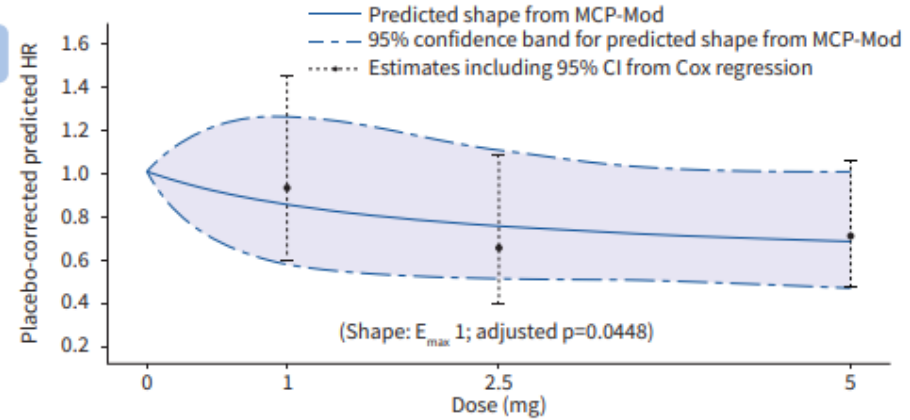


AIRLEAF phase II trial design

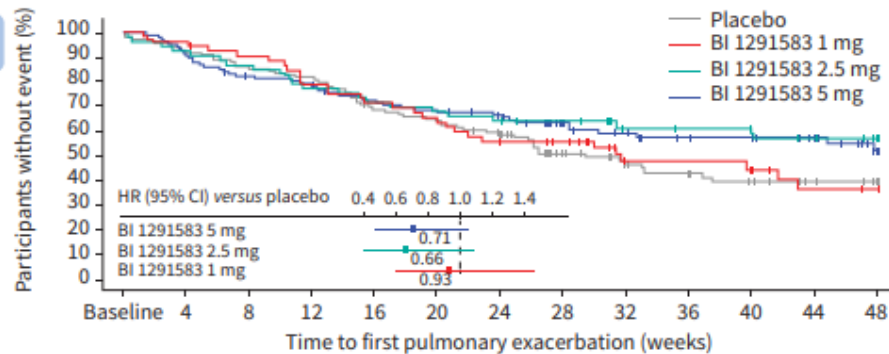


AIRLEAF results

1



2



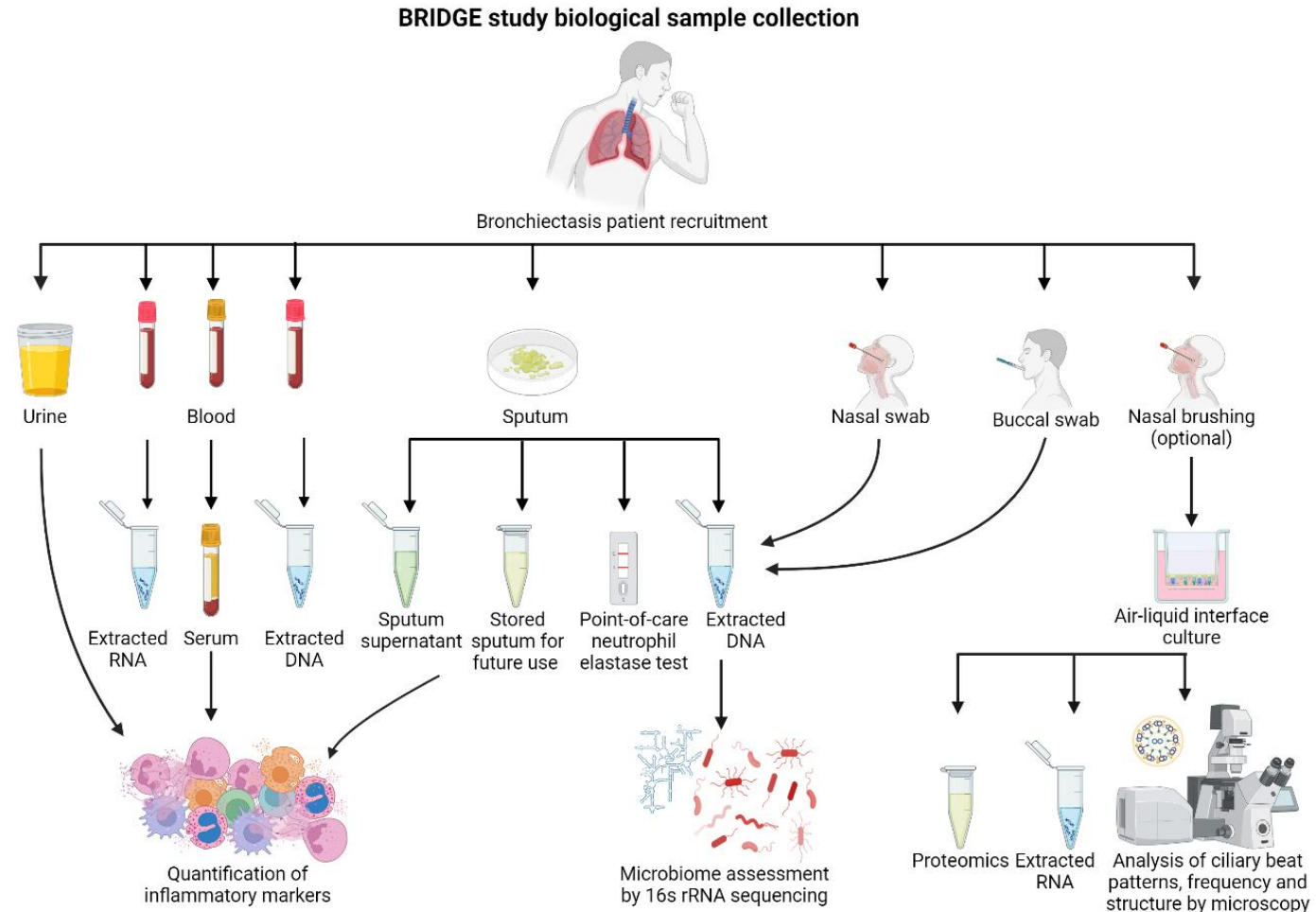
The safety profile of BI 1291583 was similar to placebo

The AIRTIVITY phase III trial is planned to begin in 2025

Bronchiectasis resources!



- Get bronchiectasis clinical samples and data for your research
- www.bronchiectasis.net
- Open to researchers



Respiratory Research Group



University
of Dundee



Acknowledgements



Oriol Sibila (Barcelona)
Stefano Aliberti (Milan)
Felix Ringshausen (Hannover)
Raja Dhar (Kolkatta)
Sanjay Chotirmall (Singapore))
Jeffrey Huang (Dundee)
Eva Polverino (Barcelona)
Matthieu Bottier (London)
Charles Haworth (Cambridge)
Yonghua Gao (Shanghai)
Jin-fu Xu (Shanghai)
Stuart Elborn (Belfast)
Michael Tunney (Belfast)
Michael Loebinger (London)
Tony De Soyza (Newcastle)
Burkhard Tuemmler (Hannover)
Arietta Spinou (London)
And many many more.....

University of Dundee

Amelia Shoemark
Merete Long
Rebecca Hull
Amy Gilmour
Chloe Hughes
Morven Shuttleworth
Daniella Alferes Da Lima
Ashley Giam
Simon Finch
Hani Abo Leyah
Erin Cant
Lucy Bidgood
Ben New
Ashleigh Fobister
Yonghua Gao

Emma Johnson
Chandi Hennayake
Kara Robertson
Emily Ward
Zsofia Eke
Eve MacIntosh
Hollian Richardson
Mattia Nigro
Hayoung Choi
Hannah Dickson
Holly Lind
Rachel Galloway
Kateryna Vilgorska
Jamie Stobo
Rachel Galloway

