

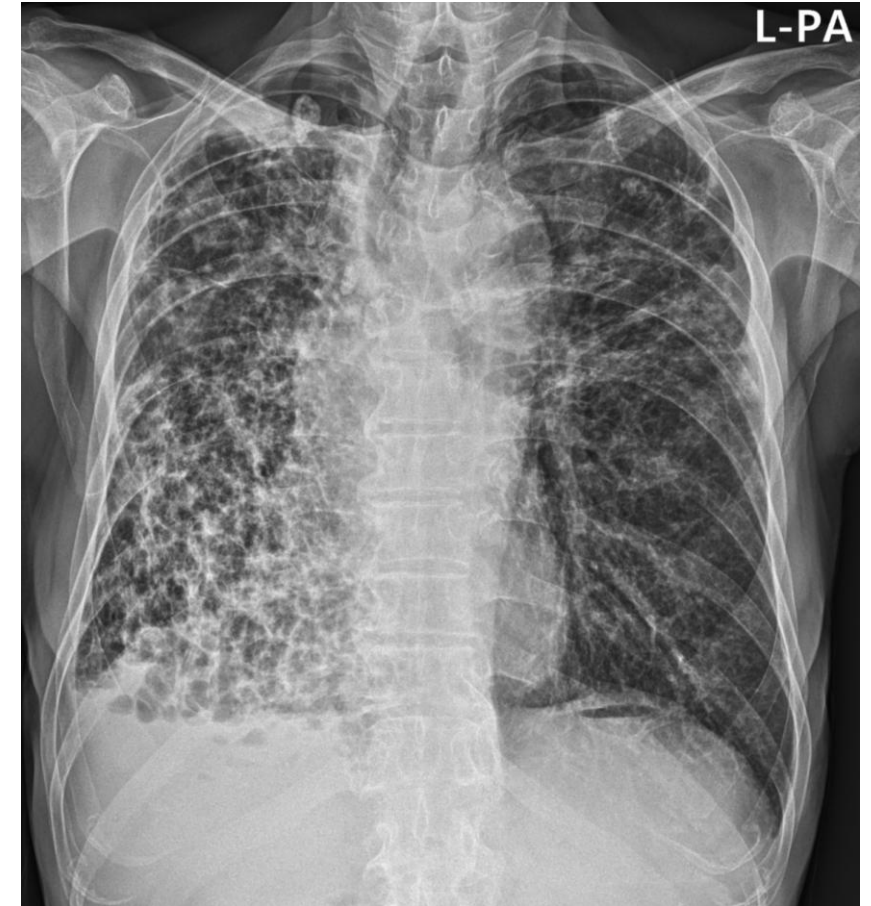
Disease Progression and Modification in Bronchiectasis

Hallym University College of Medicine

Hayoung Choi

Case study

- 77-year-old gentleman
 - First visited my clinic in late July 2026
 - TB was cured in his 20s
 - Bronchiectasis was diagnosed in 2008
 - Symptoms started to aggravate 7 years ago
 - 5 admissions in the last year
 - Anoro Elipta, Mucospect, Asima, Umkamin, Codeine
 - Sputum culture
 - AFB culture: negative
 - *P. aeruginosa*, ESBL+ *E.coli*



5 years ago



1 year ago



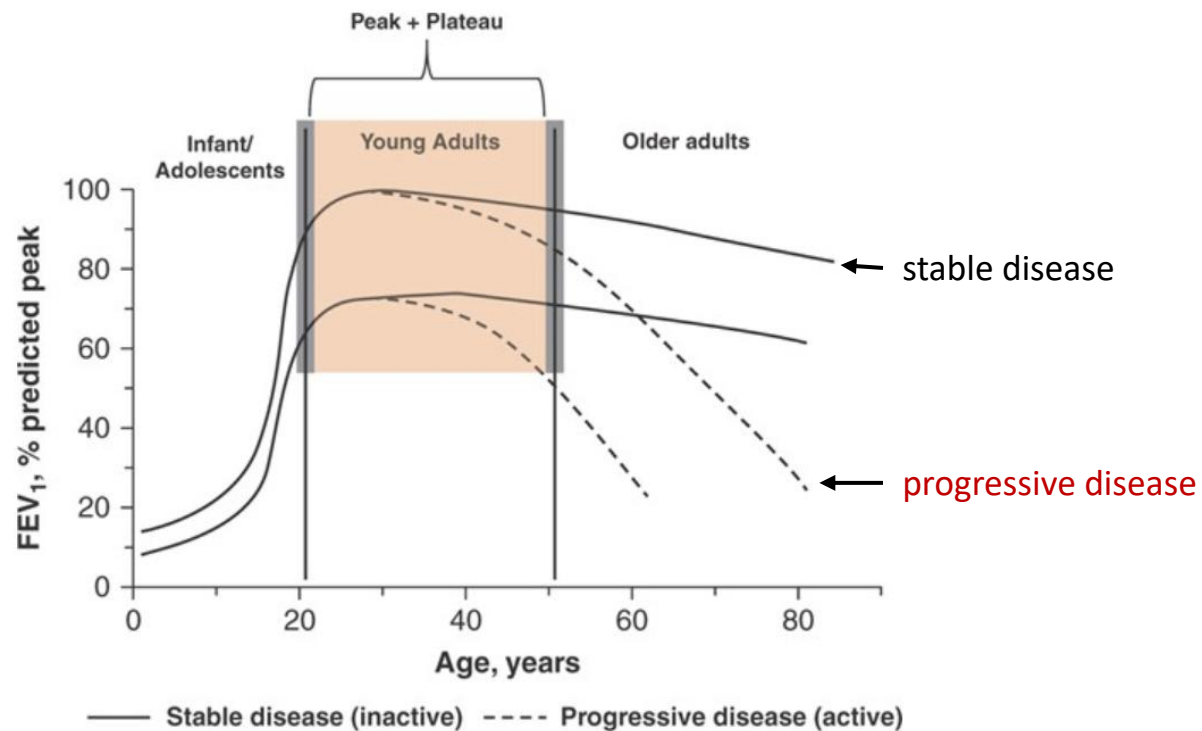
FEV1	2.22 L	67% of pred.
FVC	3.56 L	75% of pred.

1.71 L	53% of pred.
2.44 L	53% of pred.

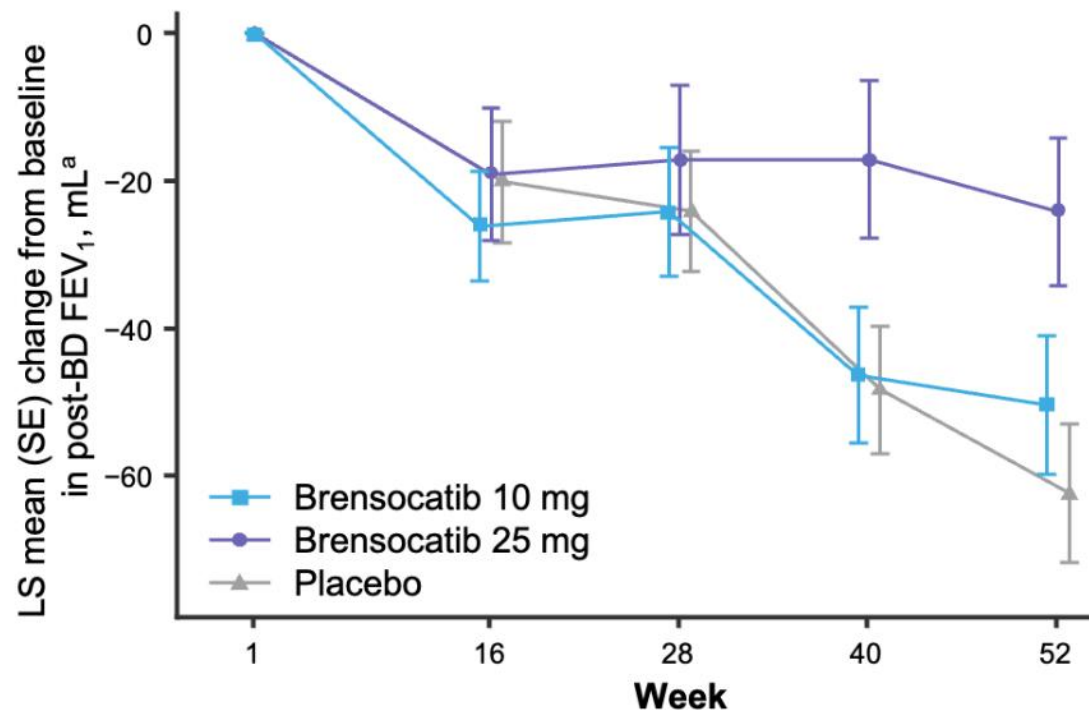
Disease progression

- **Definition**

A clinical term that refers to a progressive deterioration in an objective marker of pathology or lung function



Change in postbronchodilator FEV1 from baseline



Number of patients with observation

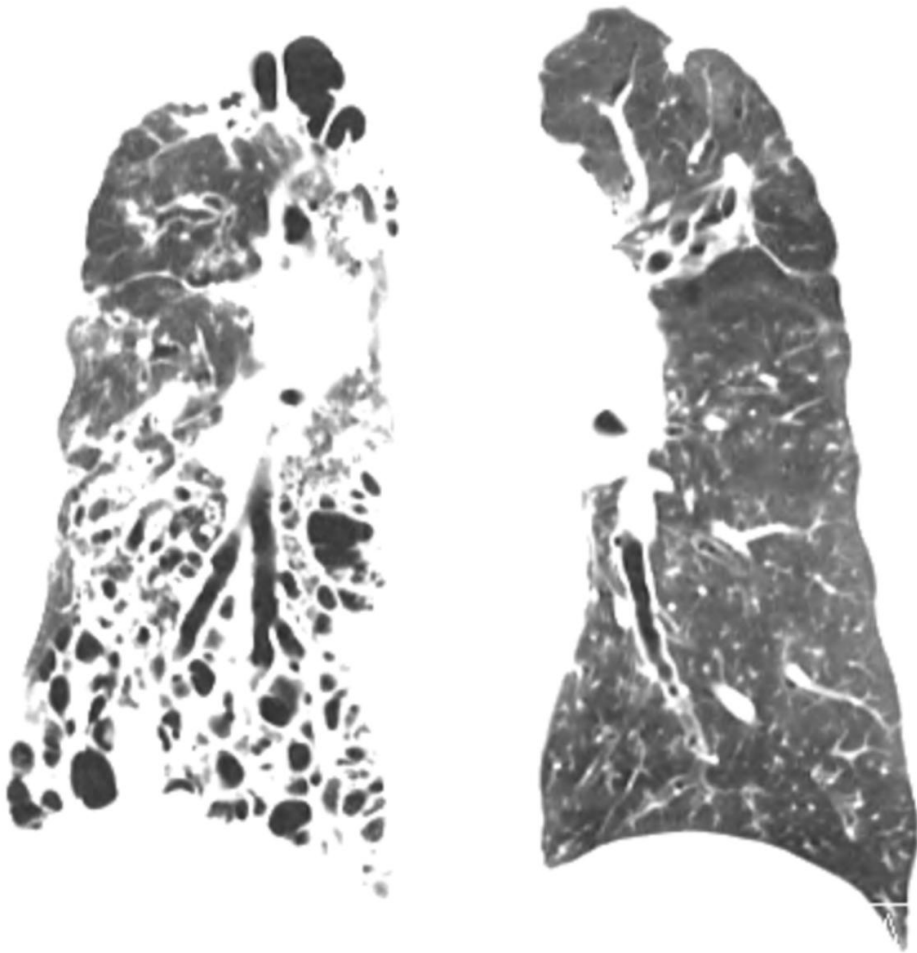
Brensocatib 10 mg	579	545	529	513	475
Brensocatib 25 mg	571	529	523	494	487
Placebo	563	522	513	494	468

Brensocatib 25 mg showed a **38 mL less** FEV₁ decline vs placebo

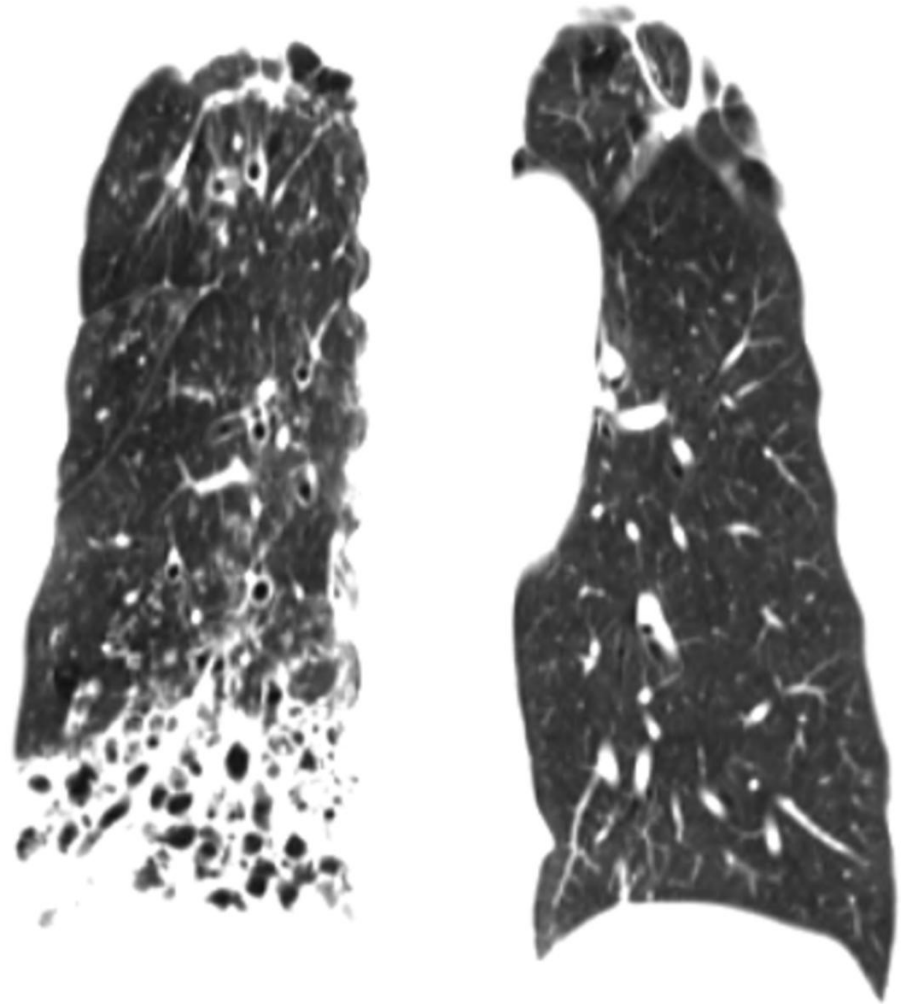
	Brensocatib 10 mg	Brensocatib 25 mg	Placebo
LS mean change from baseline in post-BD FEV ₁ at week 52, mL	-50	-24	-62
LS mean difference vs placebo in post-BD FEV ₁ , mL	11	38	—
P value vs placebo	0.3841	0.0054 ^b	—

^a% predicted FEV₁ analyzed using a linear repeated measures model in the ITT analysis set. ^bP value is statistically significant when adjusted for multiplicity control. BD, bronchodilator; FEV₁, forced expiratory volume in 1 second; ITT, intention-to-treat; LS, least squares.

Paradigm shift: reactive to proactive



Feb 2026

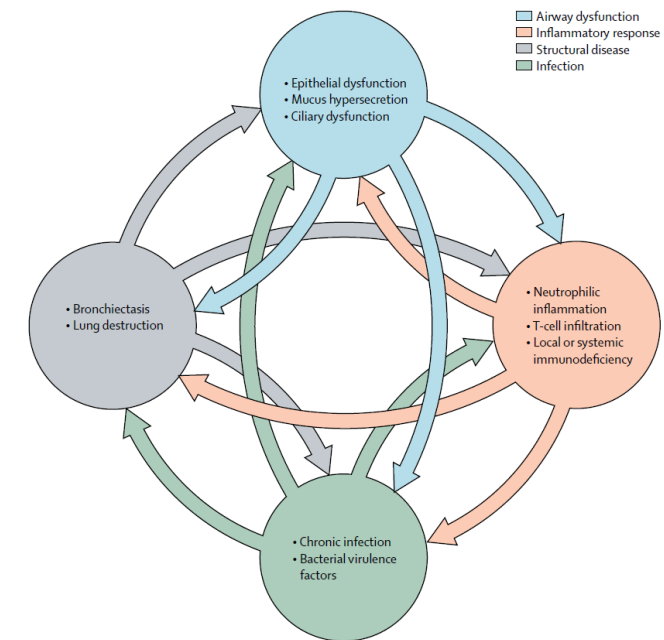
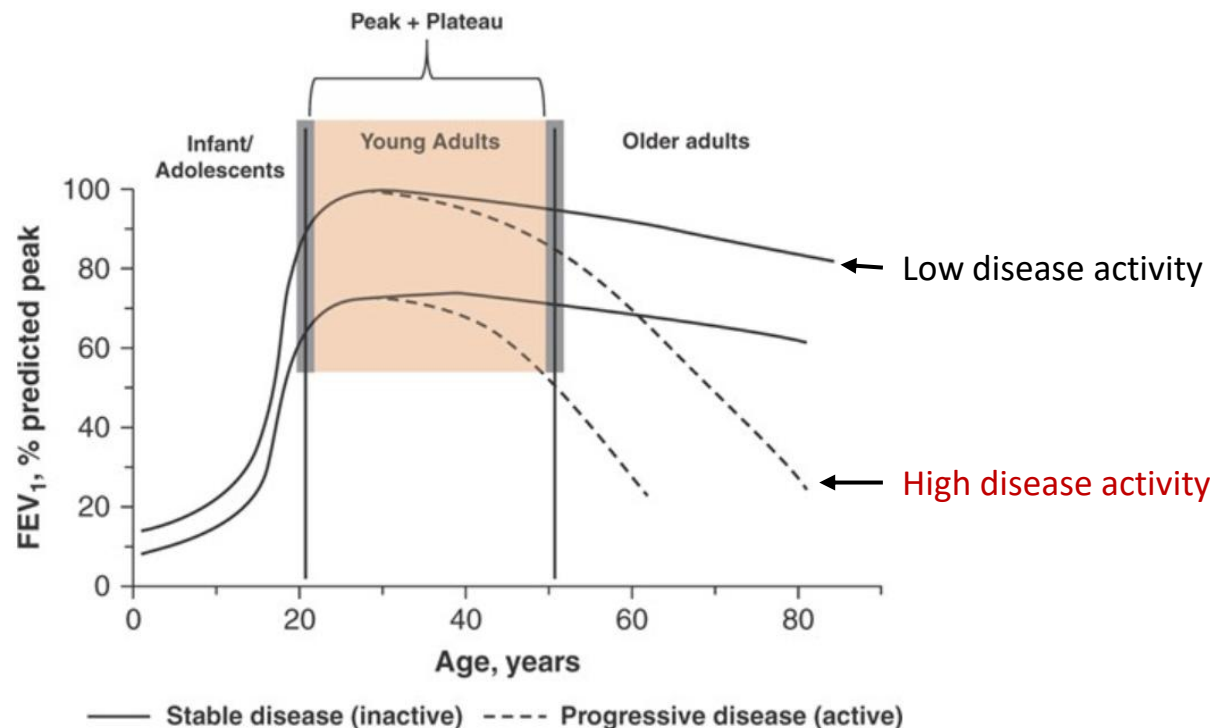


May 2019

Disease activity

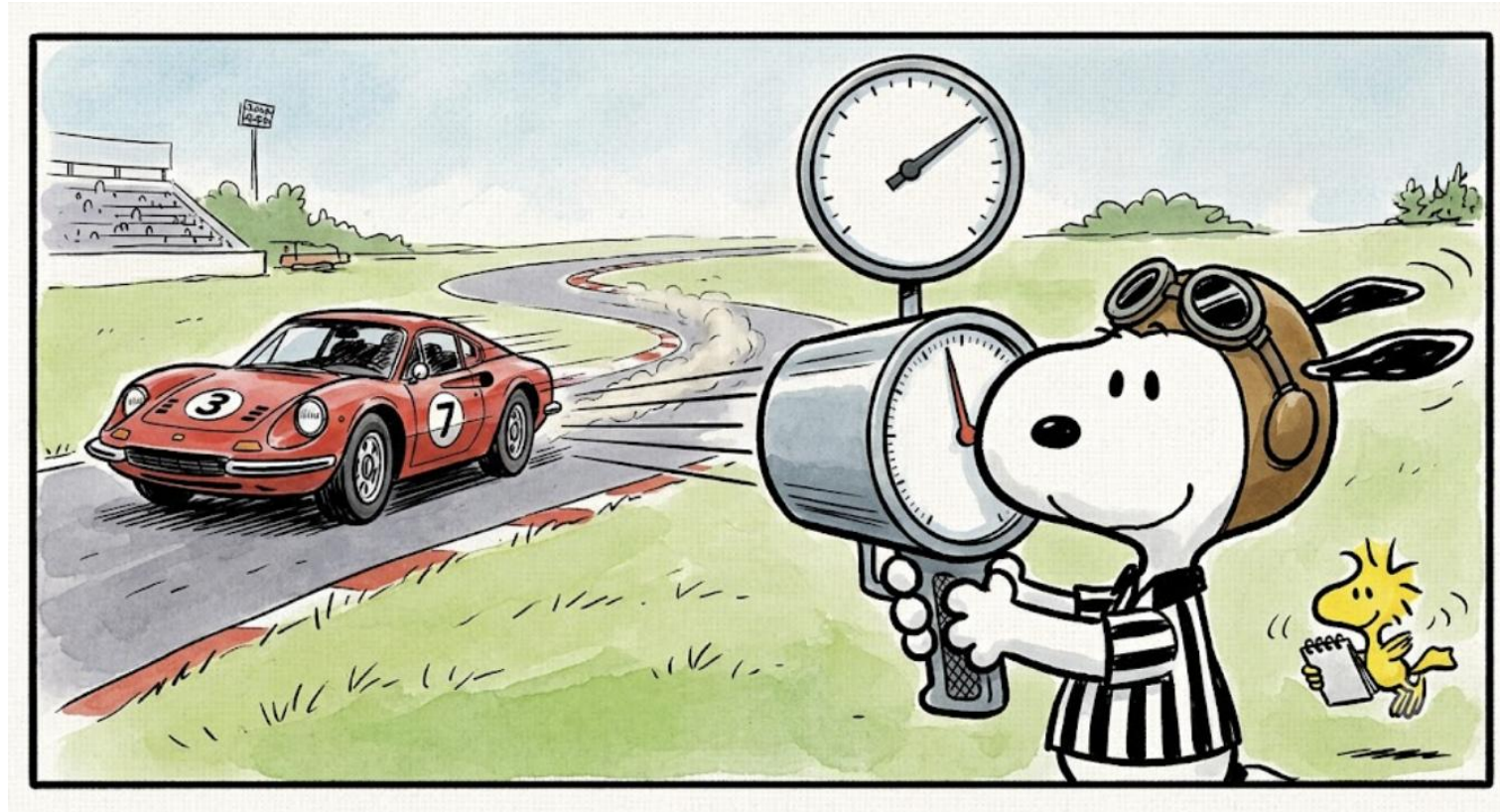
- **Definition**

A biological term that relates to the **level of activation of the pathophysiological processes** that cause the disease; it can ideally be identified and quantified by validated **biomarkers**



How to assess disease activity

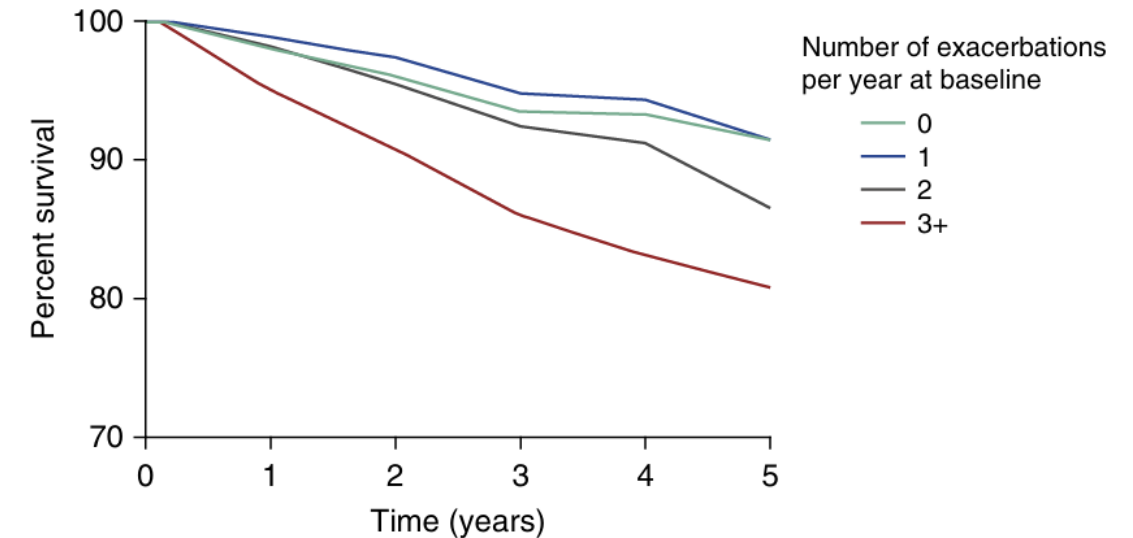
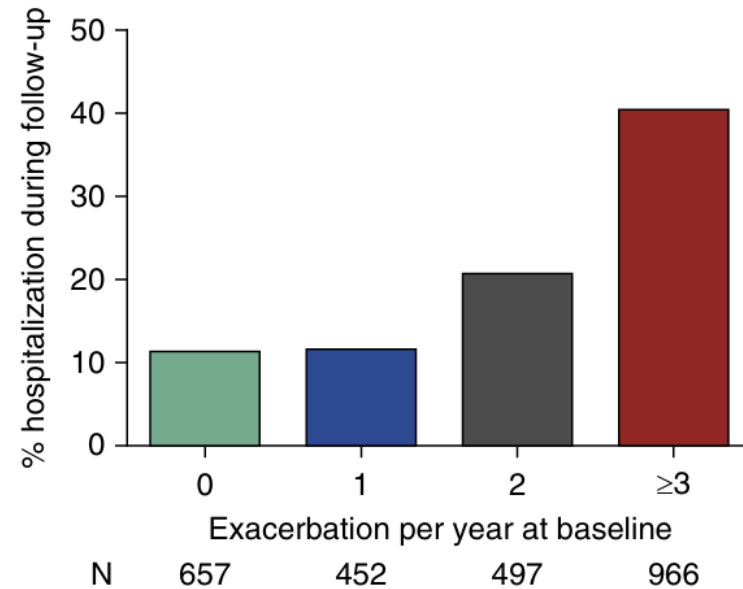
- Validated **biomarkers** – currently lacking in bronchiectasis



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Exacerbation – frequent exacerbator phenotype

- **≥3 exacerbations** at baseline
 - **Adjusted risk** for future exacerbation = **5.2**



Numbers at risk						
0	657	654	600	554	522	153
1	452	444	402	381	351	134
2	497	490	437	407	376	196
3 or more	966	958	836	771	694	365

The frequent exacerbator phenotype in bronchiectasis revisited: Data from EMBARC registry



[Oriol Sibila](#), [Lidia Perea](#), [Pierre Regis Burgel](#), [Eva Polverino](#), [Rebecca C Hull](#), [Merete B Long](#), [Sanjay H Chotirmall](#), [Michal Shteinberg](#), [Jennifer Pollock](#), [Jamie Stobo](#), Holly Lind, Charles Haworth, Katerina Dimakou, Apostolos Bossios, Michael R Loebinger, Raja Dhar, Jin-Fu Xu, Pontus Mersch, Jessica Rademacher, Hayoung Choi, Natalie Lorent, Francesco Blasi, Montserrat Vendrell, Pieter Goeminne, Felix Ringshausen, Anthony De Soyza, Stefano Aliberti, James D Chalmers ✉

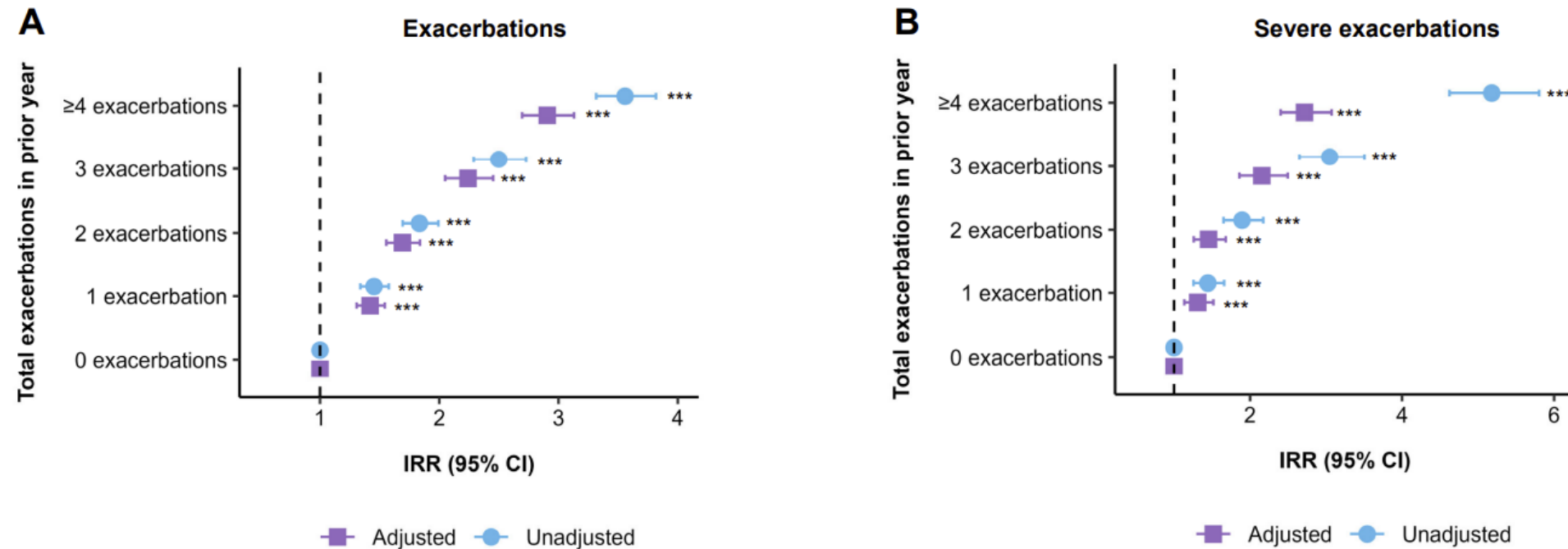


Figure 1. Effect of prior exacerbations on the risk of exacerbation and severe exacerbations during follow-up.

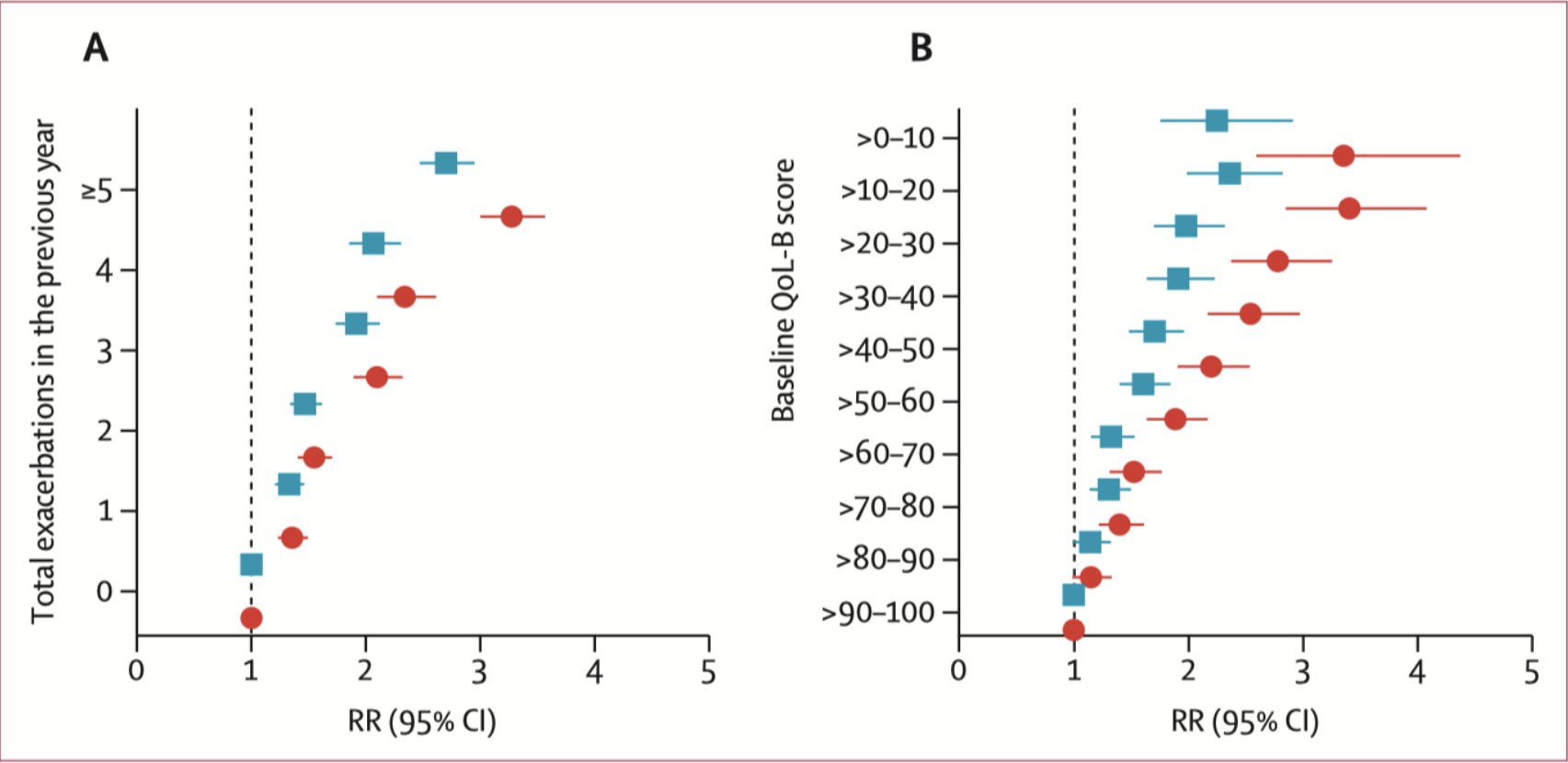
Symptoms, risk of future exacerbations, and response to long-term macrolide treatment in bronchiectasis: an observational study



Oriol Sibila, Jamie Stobo, Lidia Perea, Yong-Hua Gao, Jin-Fu Xu, Holly Lind, Kateryna Viligorska, Arietta Spinou, Eva Polverino, Felix C Ringshausen, Montserrat Vendrell, Pierre-Régis Burgel, Charles S Haworth, Michael R Loebinger, Natalie Lorent, Raja Dhar, Hayoung Choi, Sanjay H Chotirmall, Anthony De Soyza, John R Hurst, Jeremy S Brown, Menno van der Eerden, Paula Kauppi, Emma D Johnson, Raul Mendez, Katerina Dimakou, Apostolos Bossios, Antoni Torres, Francesco Blasi, Michal Shteinberg, Stuart J Elborn, Pieter C Goeminne, Stefano Aliberti, Lata Jayaram, Noel Karalus, Steven L Taylor, Megan L Martin, Lucy D Burr, Conroy Wong, Lotte Terpstra, Josje Altenburg, Wim Boersma, James D Chalmers



Prior
Exacerbations



Higher
Symptom
burden

Future exacerbation risk

Future exacerbation risk

Higher
Symptom
burden



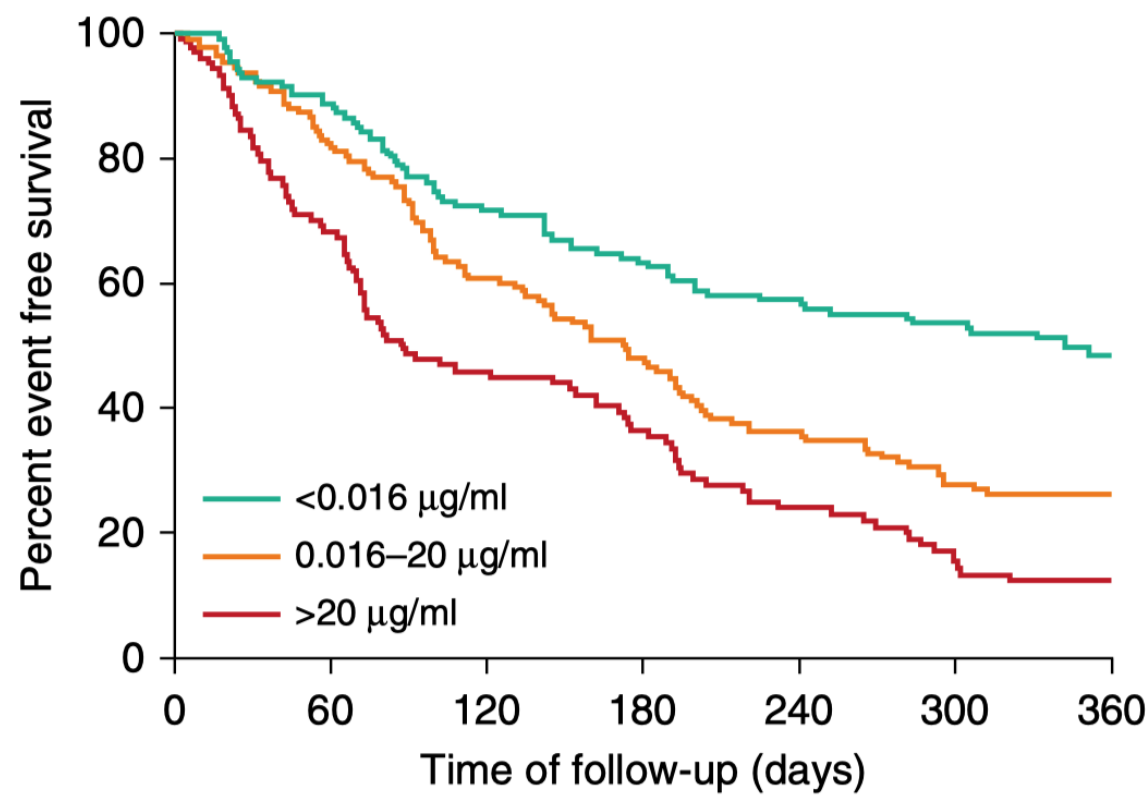
More exacerbations



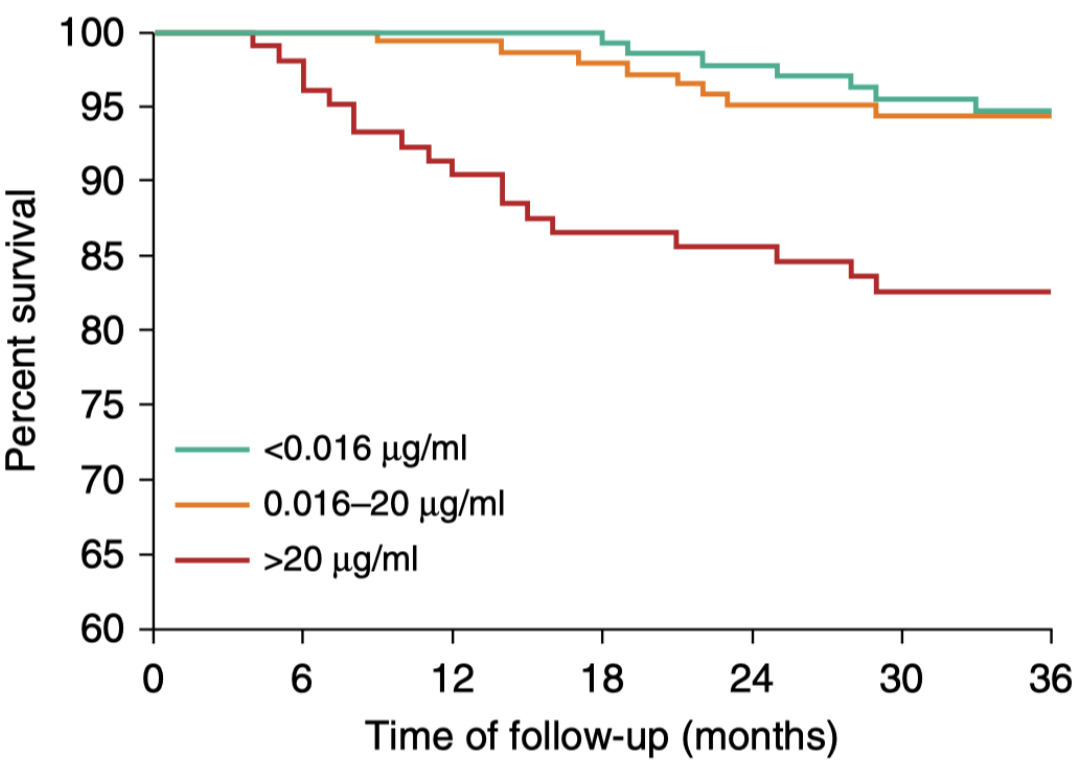
	Number of exacerbations in the previous year				
	0	1	2	3	4
All study population					
–40 points below mean	1.71 (1.54–1.88)	1.89 (1.71–2.07)	2.09 (1.91–2.28)	2.32 (2.12–2.51)	2.56 (2.36–2.77)
–30 points below mean	1.55 (1.41–1.70)	1.72 (1.57–1.87)	1.90 (1.75–2.06)	2.11 (1.94–2.27)	2.33 (2.16–2.50)
–20 points below mean	1.41 (1.29–1.54)	1.56 (1.44–1.69)	1.73 (1.60–1.86)	1.92 (1.78–2.05)	2.12 (1.97–2.26)
–10 points below mean	1.29 (1.18–1.40)	1.42 (1.31–1.54)	1.57 (1.46–1.69)	1.74 (1.62–1.86)	1.93 (1.80–2.05)
Mean score	1.17 (1.07–1.27)	1.29 (1.19–1.39)	1.43 (1.33–1.54)	1.58 (1.48–1.69)	1.75 (1.64–1.87)
10 points above mean	1.06 (0.98–1.15)	1.18 (1.09–1.27)	1.30 (1.21–1.40)	1.44 (1.34–1.54)	1.59 (1.49–1.70)
20 points above mean	0.97 (0.88–1.05)	1.07 (0.98–1.16)	1.18 (1.09–1.28)	1.31 (1.21–1.41)	1.45 (1.34–1.56)
30 points above mean	0.88 (0.80–0.96)	0.97 (0.89–1.06)	1.08 (0.99–1.17)	1.19 (1.10–1.29)	1.32 (1.21–1.43)
40 points above mean	0.80 (0.72–0.88)	0.89 (0.80–0.97)	0.98 (0.89–1.07)	1.08 (0.99–1.18)	1.20 (1.09–1.31)
Expected number of exacerbations in 1 year are estimated from the negative binomial regression model for the participants included from the EMBARC study population. Baseline QoL-B-RSS (relative to mean=59.5). QoL-B-RSS=quality-of-life bronchiectasis questionnaire respiratory symptoms score.					
Table 2: Expected number of exacerbations in 1 year (95% CI)–given the number of exacerbations in the previous year and baseline QoL-B-RSS score					

Neutrophilic inflammation in bronchiectasis

Time to the next exacerbation



Mortality

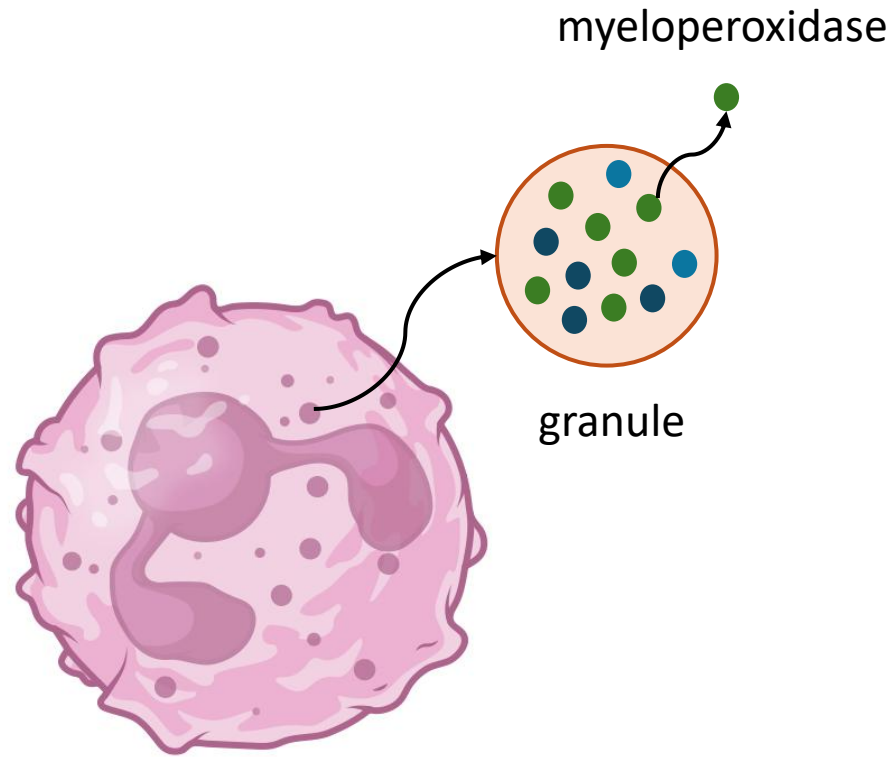


Assessment of airway neutrophils by sputum colour: correlation with airways inflammation

R A Stockley, D Bayley, S L Hill, A T Hill, S Crooks, E J Campbell



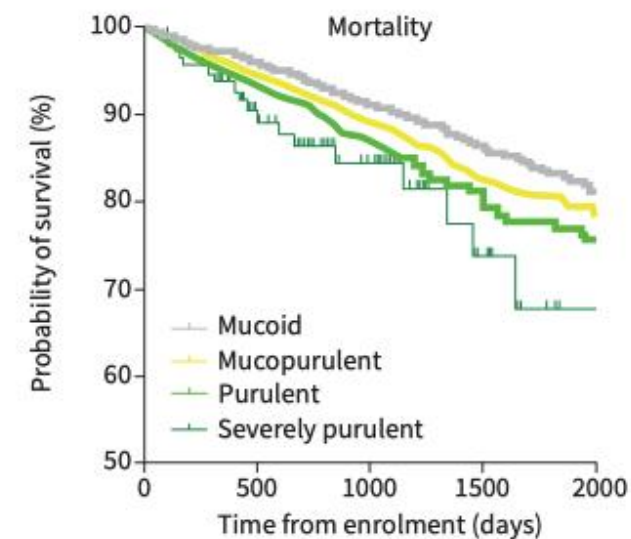
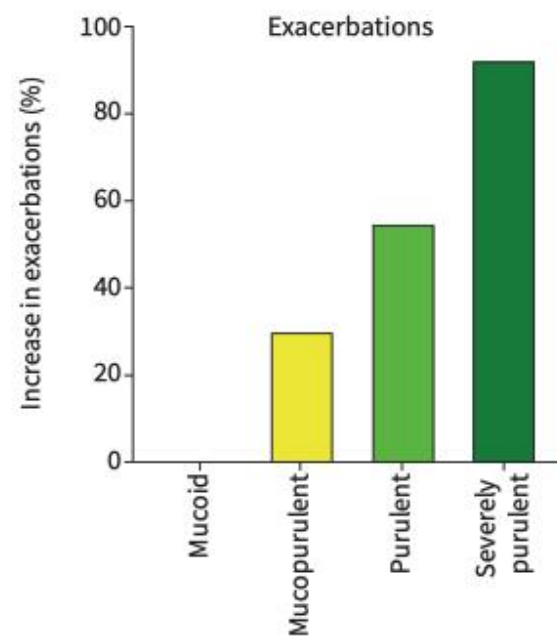
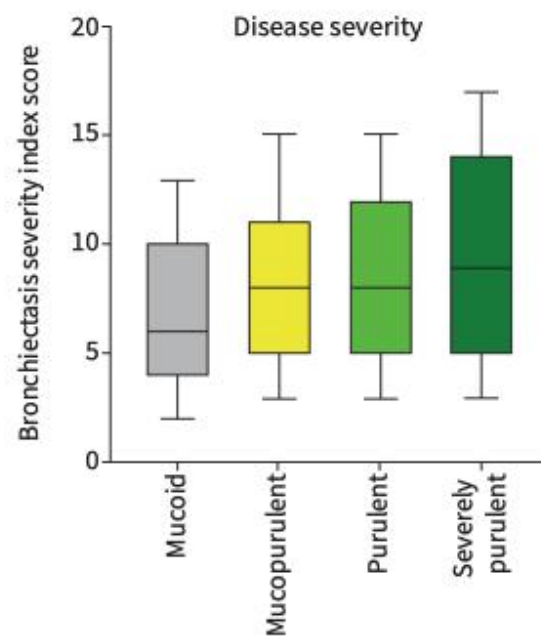
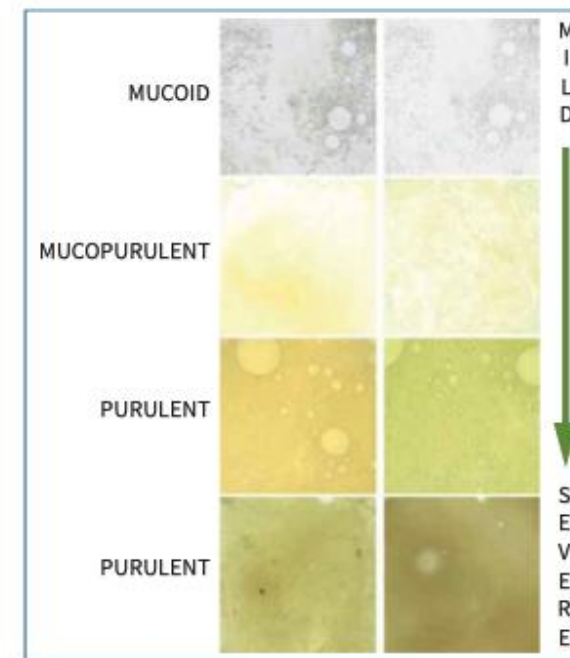
purulent sputum



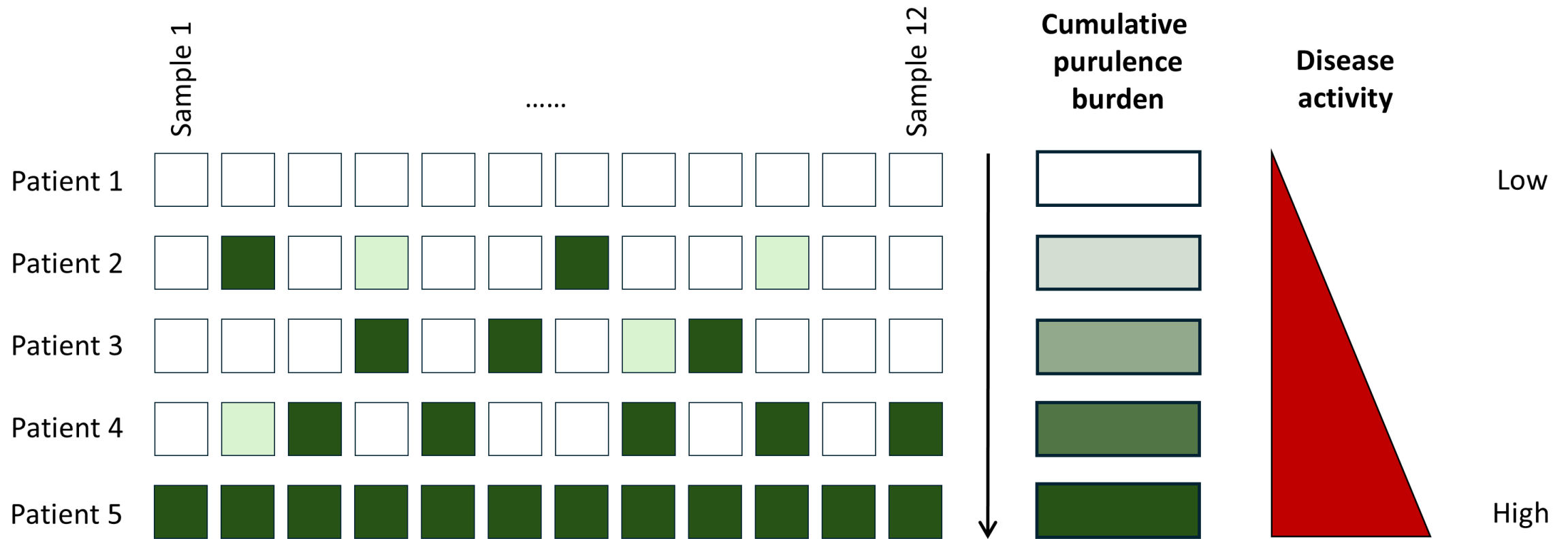
neutrophil



13484 patients with
bronchiectasis from
31 countries



Cumulative burden of sputum purulence





This article appears in:

ERJ Open Research

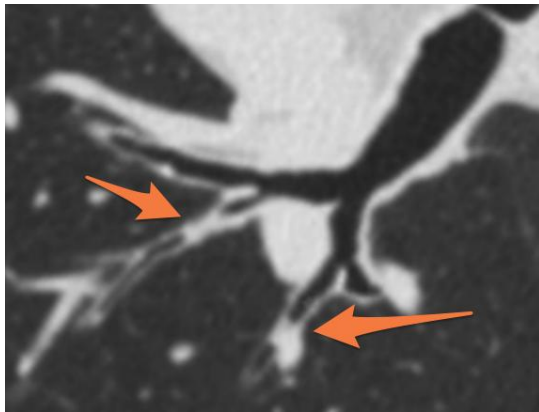
Early View

Mucus plugging, disease severity, and sputum myeloperoxidase concentration in bronchiectasis

Sun-Hyung Kim | Ki Man Lee | Jin Young Yoo [Show More](#) 

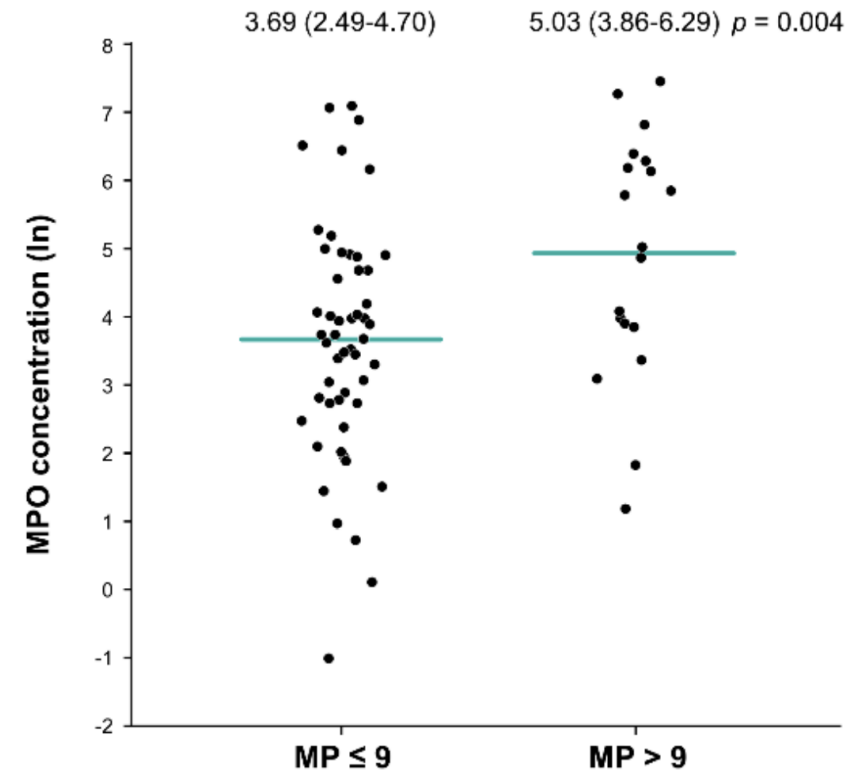
ERJ Open Research 2024 00279-2024; DOI: <https://doi.org/10.1183/23120541.00279-2024>

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Mucus plugging

- High (> 9 bronchopulmonary segments) vs. Low (≤ 9 segments)
- High MP group had higher disease severity (modified Reiff score, FACED score)



Serum C-reactive protein (CRP)

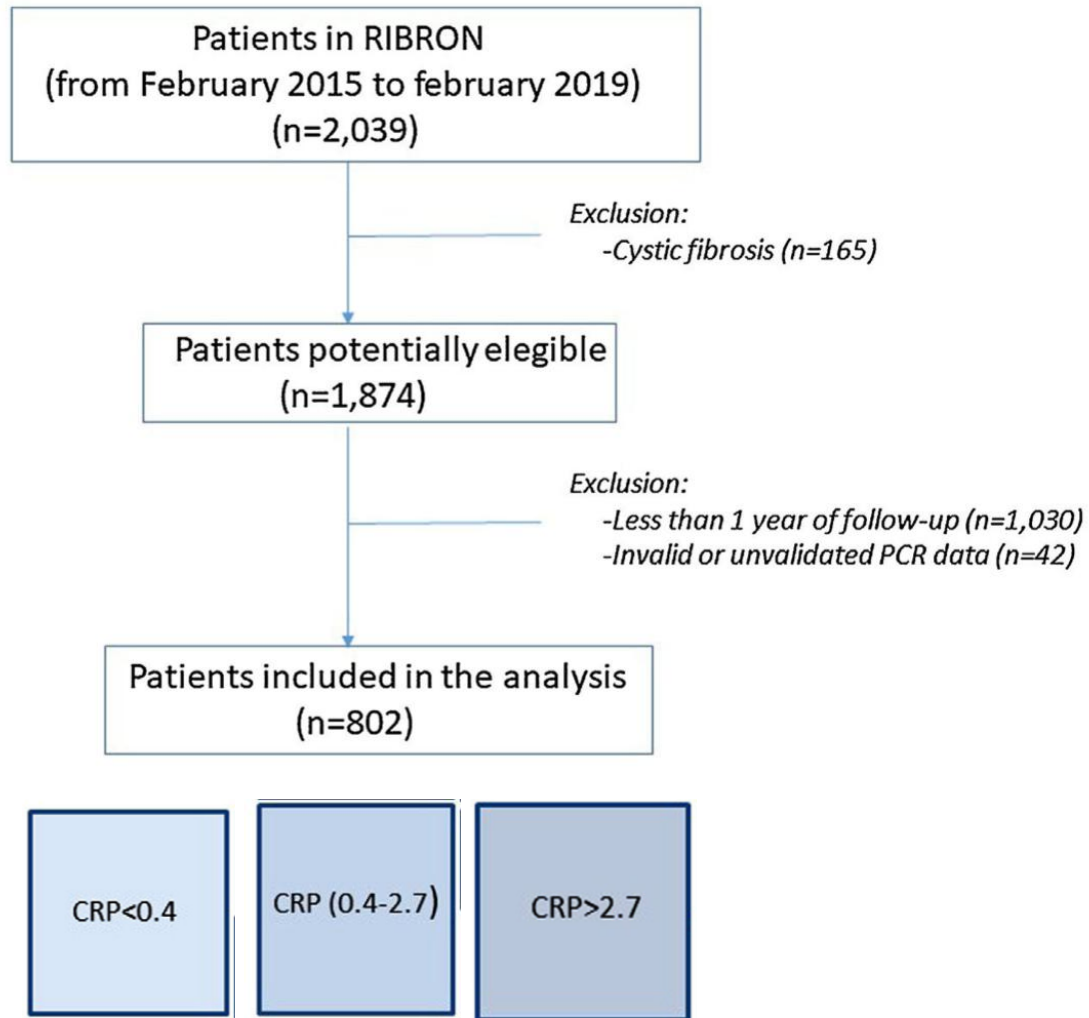


Table 3

Risk Factors for the Presence of at Least One Severe Exacerbation in the First Year of the Follow-up.

Variable	OR (CI95%)	P Value
Chronic bronchial infection by <i>P. aeruginosa</i>	1.6 (1.1–2.7)	.041
FEV1% predicted	0.97 (0.96–0.99)	.0001
Severe exacerbations (previous year)	1.15 (1.3–1.8)	.0001
Dyspnea (mMRC)	1.23 (1.1–1.6)	.017
CRP (mg/L)		
1st tertile	1	
2nd tertile	2.9 (1.4–5.9)	.0001
3rd tertile	4.2 (2.2–8.2)	.0001

Disease modification

- **Mitigation**

- Reduce the number of exacerbations
- Treat *Pseudomonas*
- Manage complications
- Increase exercise capacity



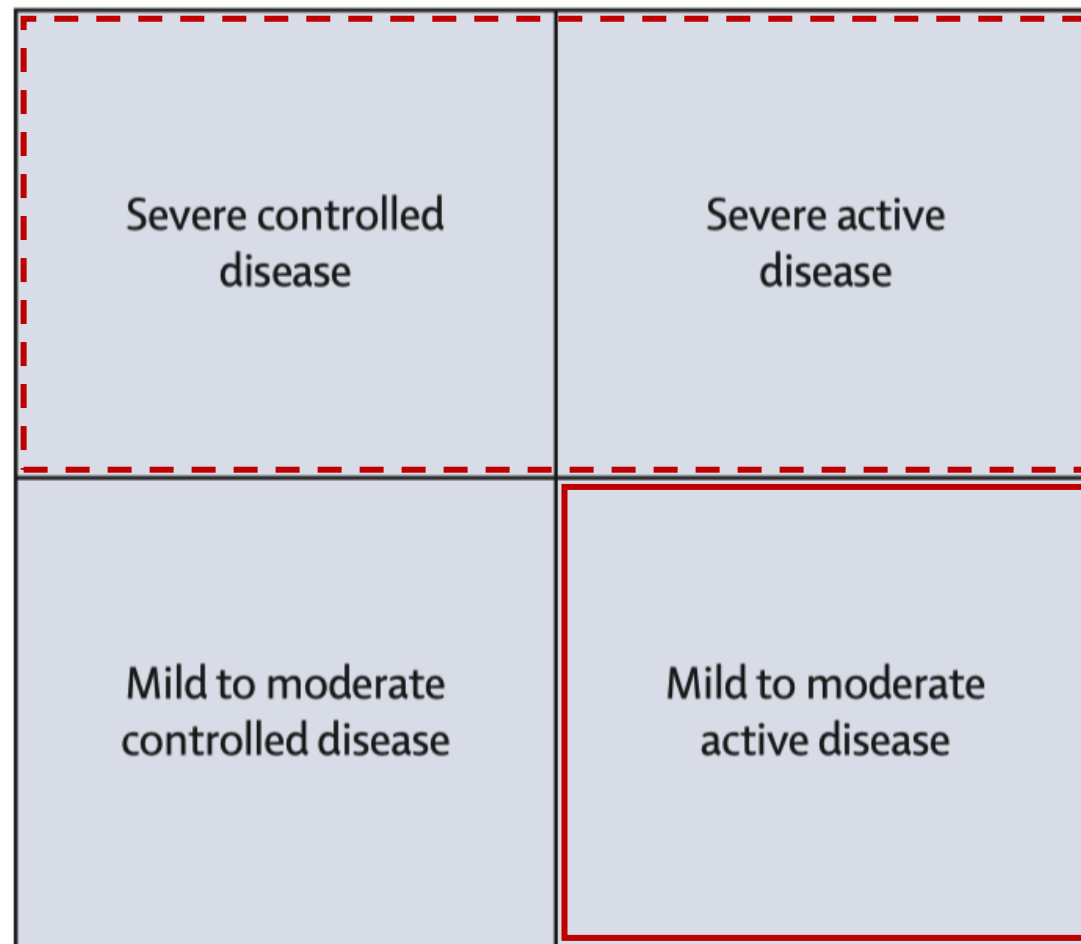
- **Modification**

- Prevent exacerbations
- Preserve lung function
- Prevent airway damage
- Prevent complications
- Avoid *Pseudomonas* and other infections



- FEV₁
- Extent of radiological dilatation
- Emphysema

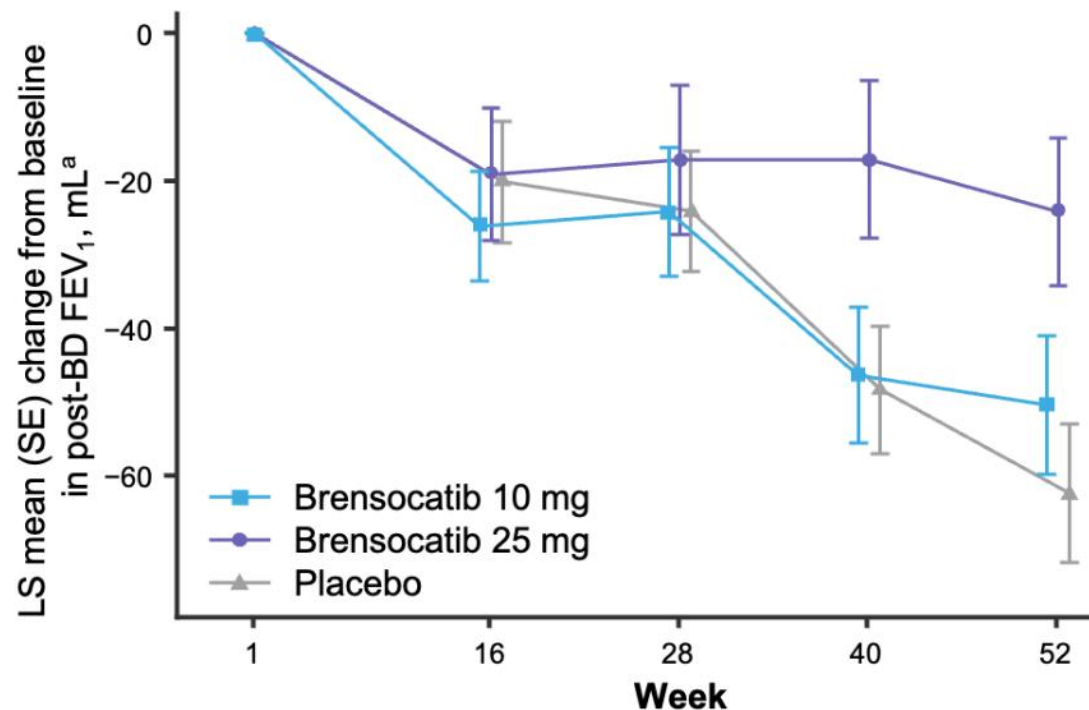
Disease severity



Disease activity

- Sputum purulence
- Frequency of exacerbations
- Severity of daily symptoms
- Neutrophil elastase concentrations and blood or sputum eosinophil counts

Change in postbronchodilator FEV1 from baseline



Number of patients with observation

Brensocatib 10 mg	579	545	529	513	475
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Placebo	563	522	513	494	468

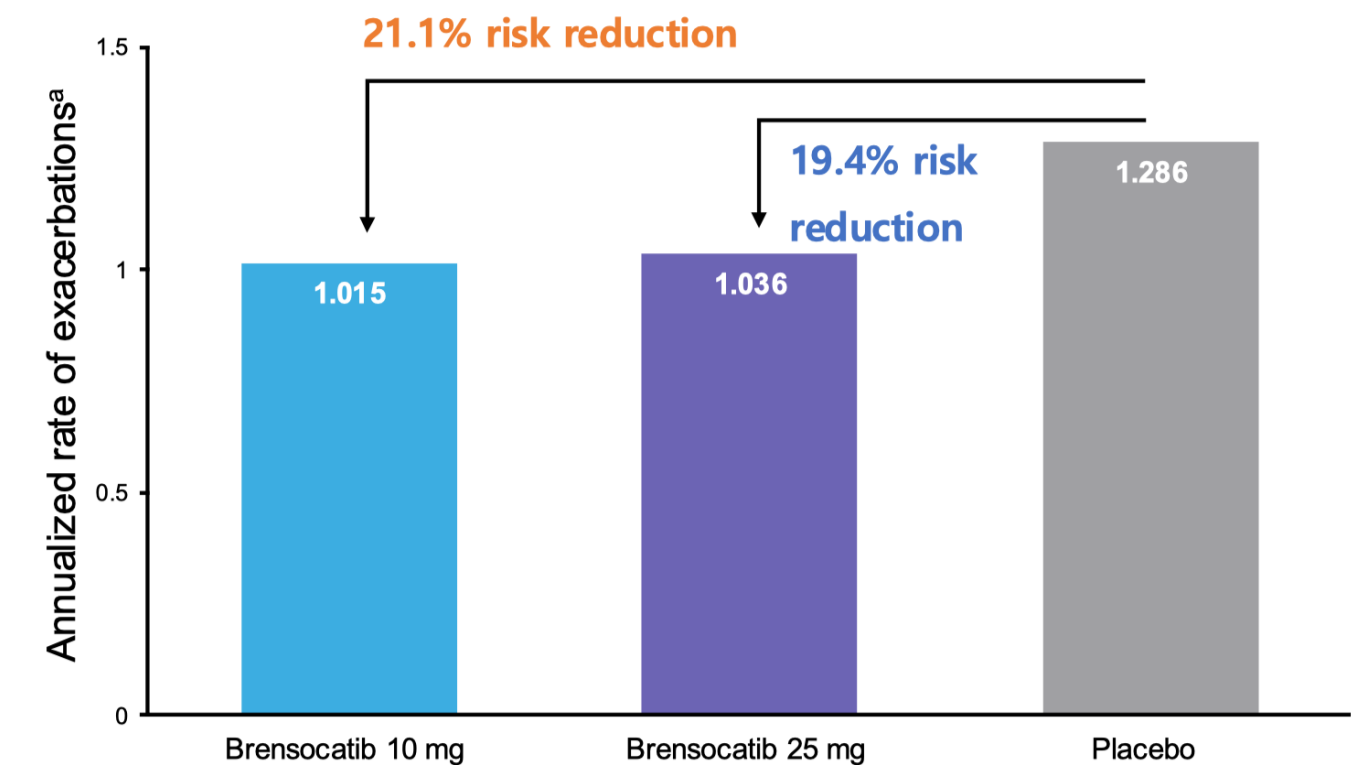
Brensocatib 25 mg showed a **38 mL less** FEV₁ decline vs placebo

	Brensocatib 10 mg	Brensocatib 25 mg	Placebo
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LS mean difference vs placebo in post-BD FEV ₁ , mL	11	38	—
P value vs placebo	0.3841	0.0054 ^b	—

^a% predicted FEV₁ analyzed using a linear repeated measures model in the ITT analysis set. ^bP value is statistically significant when adjusted for multiplicity control. BD, bronchodilator; FEV₁, forced expiratory volume in 1 second; ITT, intention-to-treat; LS, least squares.

Annualized rate of adjudicated exacerbations over 52 weeks

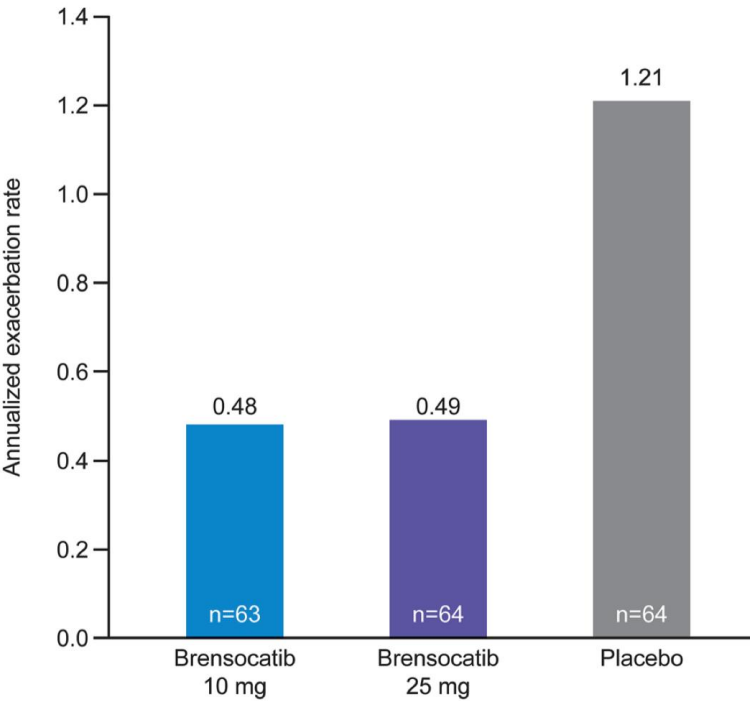
Primary endpoint



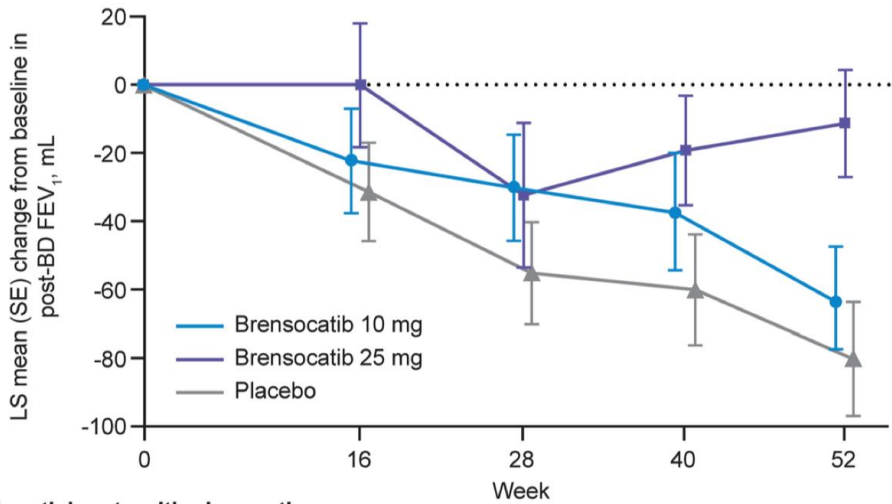
	Brensocatib 10 mg n= 583	Brensocatib 25 mg n= 575
Rate ratio vs placebo (95% CI)	0.789 (0.680–0.916)	0.806 (0.694–0.936)
P value	0.0019 ^b	0.0046 ^b

^aExacerbations were adjudicated events in the ITT analysis set analyzed using a negative binomial model. ^bP value is statistically significant when adjusted for multiplicity control. ITT, intention-to-treat.

ASPEN trial subgroup analysis of Asian race (n=191)



	Brensocatib 10 mg (n=63)	Brensocatib 25 mg (n=64)
Rate ratio vs placebo (95% CI)	0.40 (0.23-0.67)	0.41 (0.24-0.70)
p value	0.0005	0.0012



No. of participants with observations

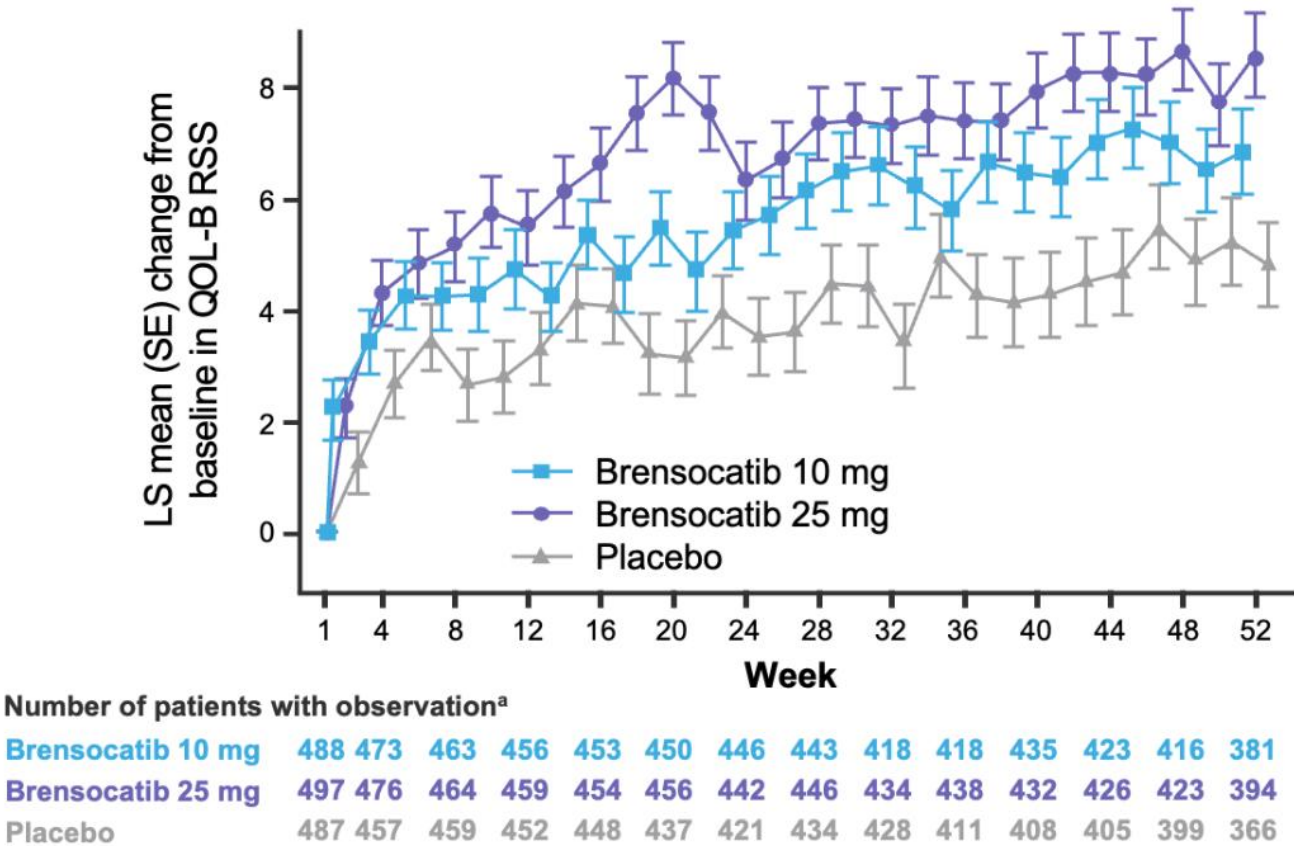
Brensocatib 10 mg	63	63	61	61	57
Brensocatib 25 mg	64	62	60	57	57
Placebo	64	57	56	53	52

	Brensocatib 10 mg (n=63) ^a	Brensocatib 25 mg (n=63) ^a	Placebo (n=58) ^a
Change from baseline in post-BD FEV ₁ at week 52, LS mean (SE), mL	-62 (14.8)	-11 (15.6)	-80 (16.6)
LS mean difference vs placebo (95% CI)	18 (-27 to 63)	69 (24-114)	-
p value	0.4368	0.0029	

Change in QOL-B Respiratory Symptoms from baseline

Secondary endpoint

Brensocatib 25 mg showed a nominally significant improvement in QOL-B RSS of 3.8 points vs placebo



LS mean change from baseline in QOL-B RSS at week 52

LS mean difference vs placebo in QOL-B RSS

P value vs placebo^b

Brensocatib 10 mg	Brensocatib 25 mg	Placebo
6.841	8.575	4.809
2.031	3.766	–
0.0594	0.0004 ^c	–

^aAdult patients only. ^bP value vs placebo calculated using a linear repeated measures model in the ITT analysis set. ^cNominally significant P value. LS, least squares; QOL-B RSS, Quality of Life-Bronchiectasis questionnaire Respiratory Symptoms Domain score.

Broad Immunomodulatory Effects of the Dipeptidyl Peptidase-1 Inhibitor Brensocatib in Bronchiectasis

Data from the Phase 2, Double-Blind, Placebo-controlled WILLOW Trial

Emma D. Johnson¹, Merete B. Long¹, Lidia Perea^{1,2}, Vivian H. Shih³, Carlos Fernandez³, Ariel Teper³, David Cipolla³, Eve McIntosh¹, Rachel Galloway¹, Zsafia Eke¹, Morven Shuttleworth¹, Rebecca Hull¹, Arietta Spinou⁴, Anthony De Soyza⁵, Felix C. Ringshausen^{6,7}, Pieter Goeminne⁸, Natalie Lorent⁹, Charles Haworth¹⁰, Michael R. Loebinger¹¹, Francesco Blasi^{12,13}, Michal Shteinberg^{14,15}, Stefano Aliberti^{16,17}, Eva Polverino¹⁸, Oriol Sibila², Amelia Shoemark¹, Kevin Mange³, Jeffrey T. J. Huang¹, Jamie Stobo¹, and James D. Chalmers¹

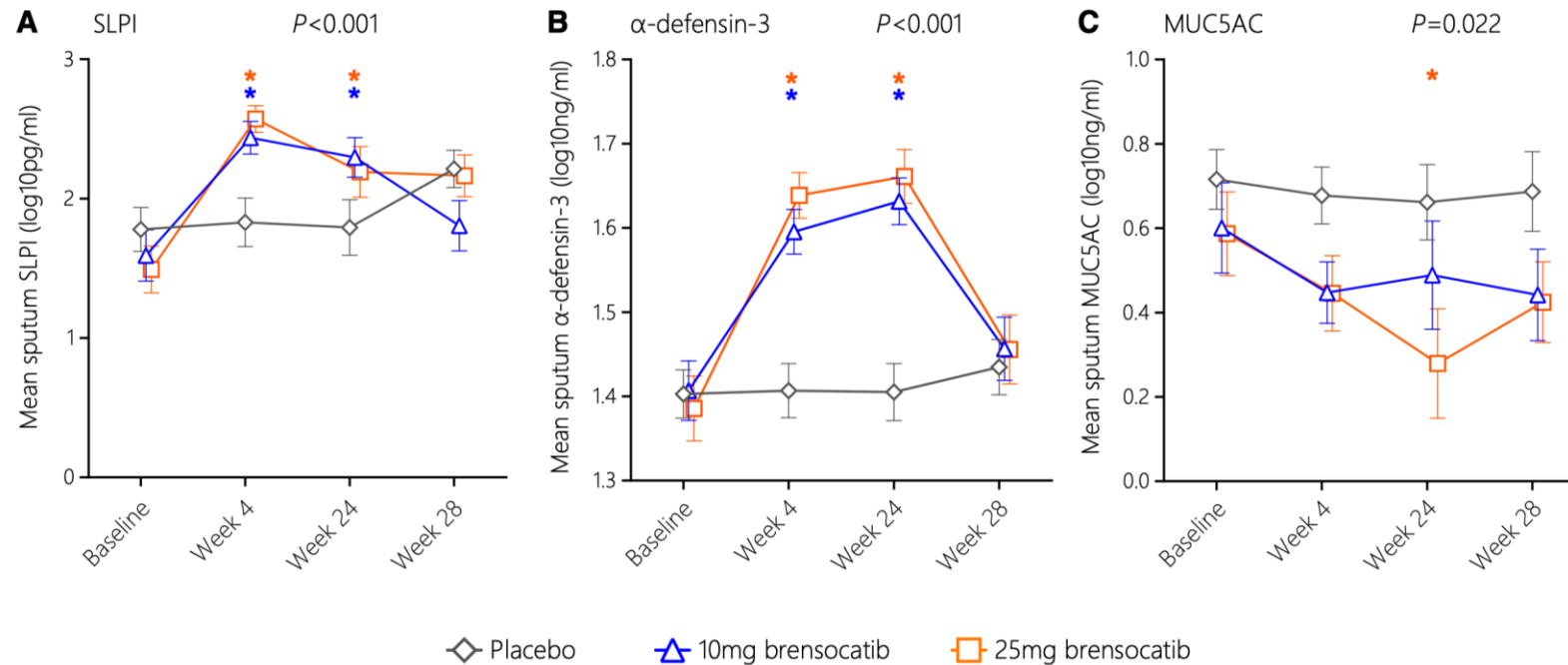
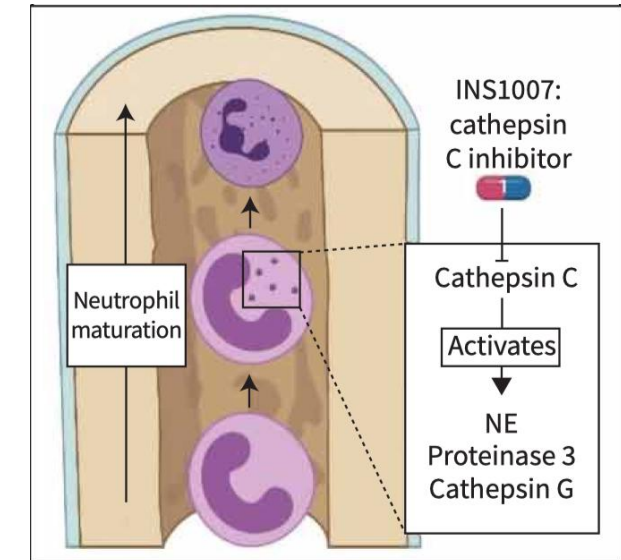
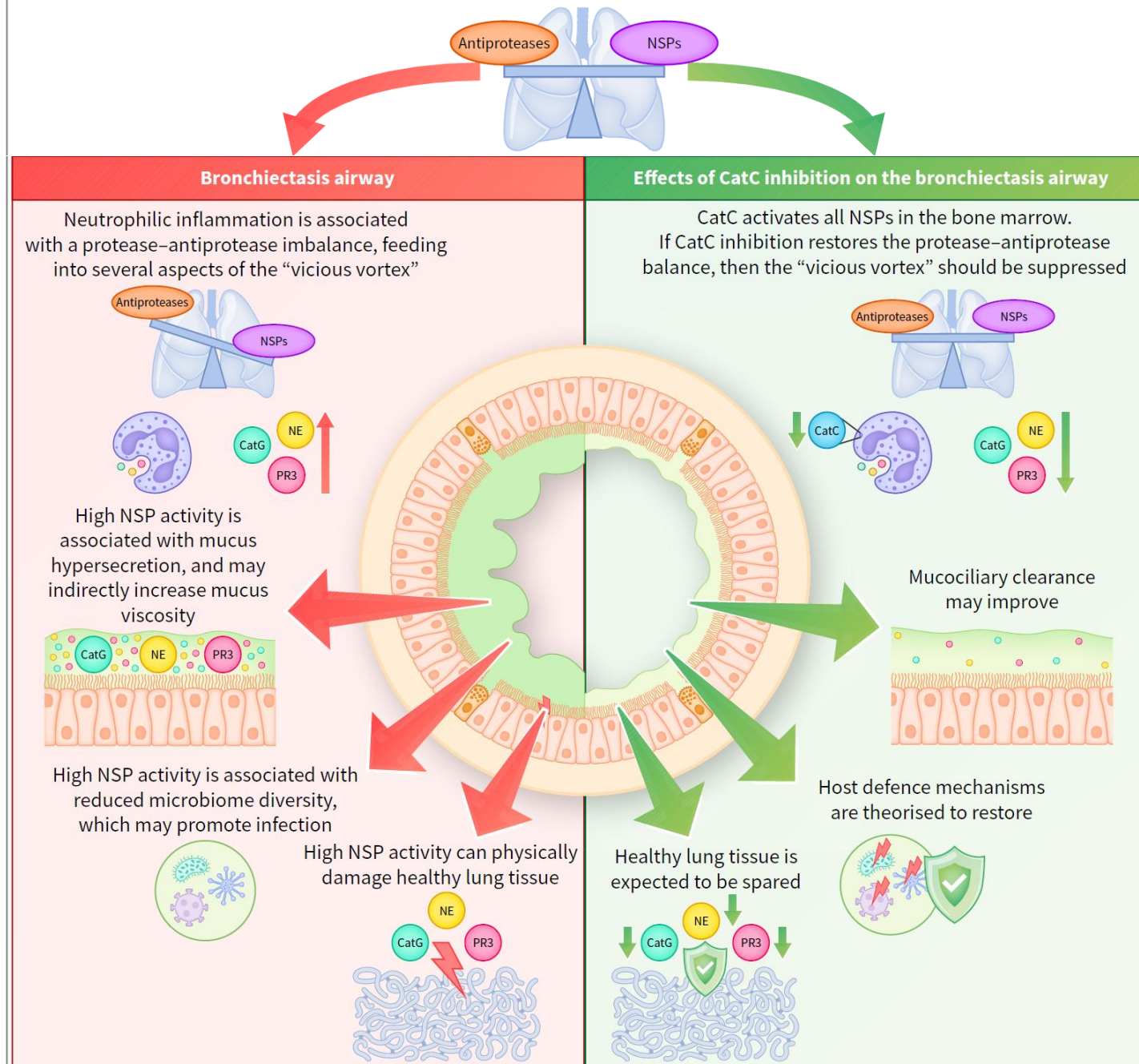


Figure 1. (A–C) Mean and SE of log₁₀-transformed concentrations across the time points by treatment group for (A) SLPI, (B) α -defensin-3, and (C) MUC5AC. Two-sided false discovery rate-adjusted *P* values for the likelihood ratio test for any differences between the treatment arms over time are presented (asterisks mark significant differences from placebo in each treatment group at each time point). MUC5AC = mucin-5AC; SLPI = secretory leukoprotease inhibitor.

Targeting neutrophil serine proteases in bronchiectasis

In a healthy state, both proteases and antiproteases are important for protecting the lung against environmental threats

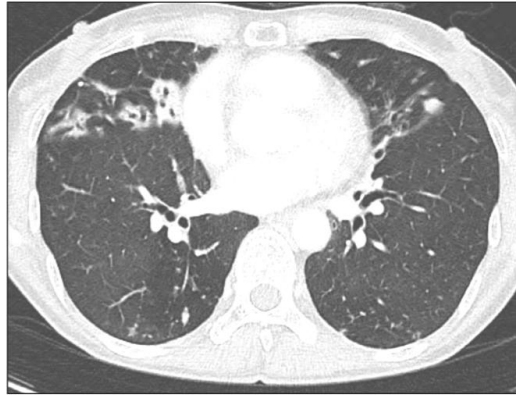


Targeting disease modification in the era of anti-inflammatory treatments

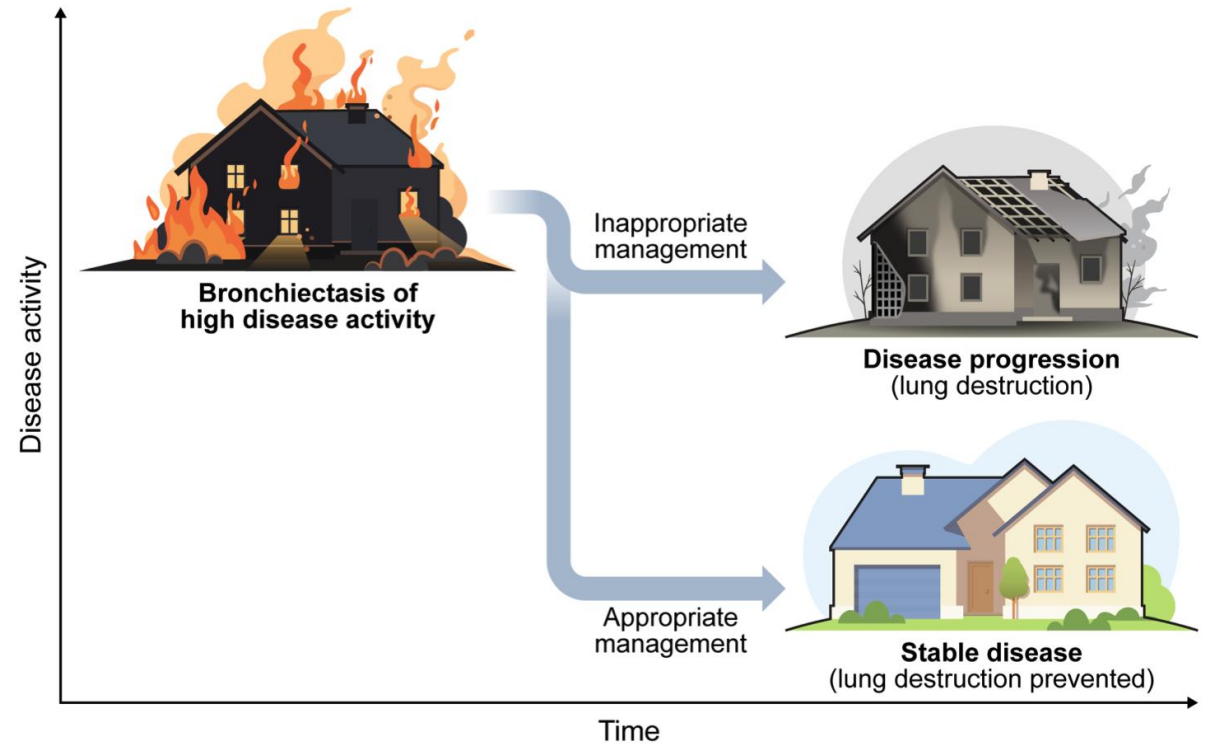
(A) High disease severity and low disease activity



(B) Low disease severity and high disease activity



(C) Concept of bronchiectasis management focusing on disease activity



Take home messages

- Now it is time to discuss **disease progression** in bronchiectasis.
- **Disease activity** helps us identify progressive disease.
- Symptoms, sputum purulence, exacerbation, chest CT findings, and sputum and serum inflammatory markers are **potential activity markers**—a validated biomarker is lacking.
- Focus on patients with **high disease activity** (at risk for future complications).
- **Disease modification** in bronchiectasis would be achieved by novel anti-inflammatory treatments and beyond.