

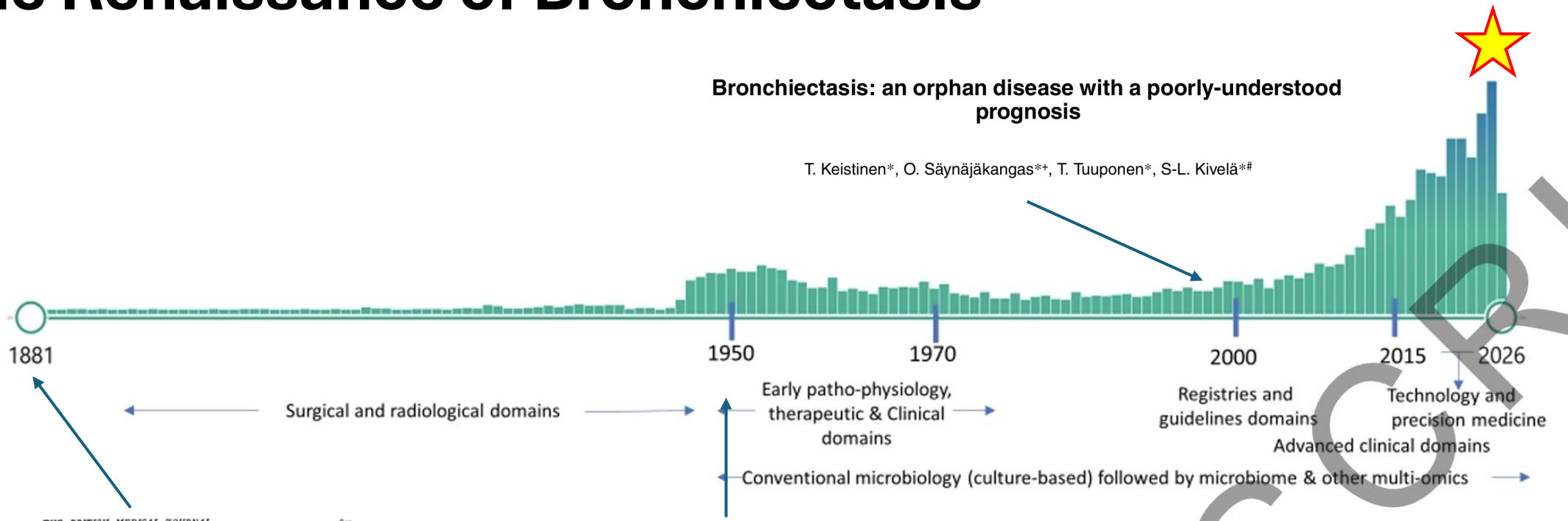
Year in Review: Key Updates in Bronchiectasis, 2025-2026

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Seoul National University Hospital

The Renaissance of Bronchiectasis

Bronchiectasis: an orphan disease with a poorly-understood prognosis

T. Keistinen*, O. Säynäjäkangas**+, T. Tuuponen*, S-L. Kivelä*##



May 28, 1881.] THE BRITISH MEDICAL JOURNAL. 837

LECTURES
ON
BRONCHIECTASIS.
Delivered at the Hospital for Consumption and Diseases of the
Chest, Brompton.

By C. THEODORE WILLIAMS, M.A., M.D., F.R.C.P.,
Physician to the Hospital.

LECTURE II.

LET us now take some well-marked examples of bronchiectasis, and verify our description of the disease as given in the last lecture.

CASE I.—Alfred H., aged 35, a labourer from Buckinghamshire, was admitted October 14th, 1880.

History.—He had been subject to bronchitis for four years, and in 1876 he had cough with expectoration streaked with blood, pain in the left side below the nipple, and night-sweats. The symptoms lasted one month, at the end of which time the night-sweats ceased, but the cough and expectoration remained, and were accompanied by shortness of breath. These symptoms had continued up to the present time, and the dyspnoea had gradually increased. In addition, he had had two attacks of pleuropneumonia similar to the one in 1876, the last occurring in June of this year.

On admission, his aspect was florid and healthy. He had lost about 7 lbs. in weight since July. Cough was frequent and convulsive. Expectoration was abundant; about a pint in twenty-four hours, partly frothy, partly mucous, with some large lumps of mucus-pus. It also contained colouring matter and a considerable amount of lung-tissue. The breath was very short on exertion. Both breath and expectoration were very foetid. His weight was 10 st. Bowels regular; tongue clean; and pulse normal.

Physical Signs (see Fig. 1).—On the left side were flattening and increased movement in the subclavian and lower mammary regions, the flattening being most marked in the latter (a). There was slight dulness to the second rib, with increased vocal vibration (a). Crepitation on cough was audible from the clavicle to the third rib (c). In the second intercostal space, close to the sternum, over a space as large as a five-shilling piece, was heard cavernous gurgle (b). He was ordered mixture antiseptica cum ammonia three times a day.

annexed those of an ordinary case of tubercular cavity (Fig. 2), where part of the right upper lobe is the seat of excavation. It will be noted that dulness is present, and that the cavernous sounds are chiefly audible in the middle portion of the first intercostal space, and not at its sternal end, as in Case 1.

Fig. 1.—Pitfalls (not stage). a denotes dulness; b denotes area of cavernous sounds.

Thorax (1950), 5, 233.

REDUCTION IN BRONCHIAL SUBDIVISION IN
BRONCHIECTASIS

BY
LYNNE McA. REID*
From the Royal Melbourne Hospital

Bronchiectasis, as the derivation of the word implies, is the name given to any condition in which there is dilatation of one or more bronchi. Since it is clear that increase in the diameter of a bronchus may result from a variety of conditions, among them infections and massive collapse, the term describes an anatomical abnormality rather than a single disease. A wide range exists both in the form and degree of the dilatation and in its distribution among the bronchi. As the reason for the diversity is not clearly understood, it is not possible at present to make a satisfactory classification of the miscellaneous conditions which are all grouped together as bronchiectasis. In this, as in any other disease, accurate study of the pathological anatomy is an essential step in its elucidation. But, although the abnormal morphology of the dilated bronchi is the outstanding feature, it has been imperfectly described.

During the examination of the large number of bronchograms and specimens seen in the routine work of a chest unit, it was noticed that the number of subdivisions of the bronchi between the hilum and the periphery of the lung differed from case to case, and was frequently much smaller than in the normal lung. It was decided to investigate this apparent reduction, and, in the event of its being demonstrated, to determine the fate of the missing subdivisions. This paper is a report on the findings.

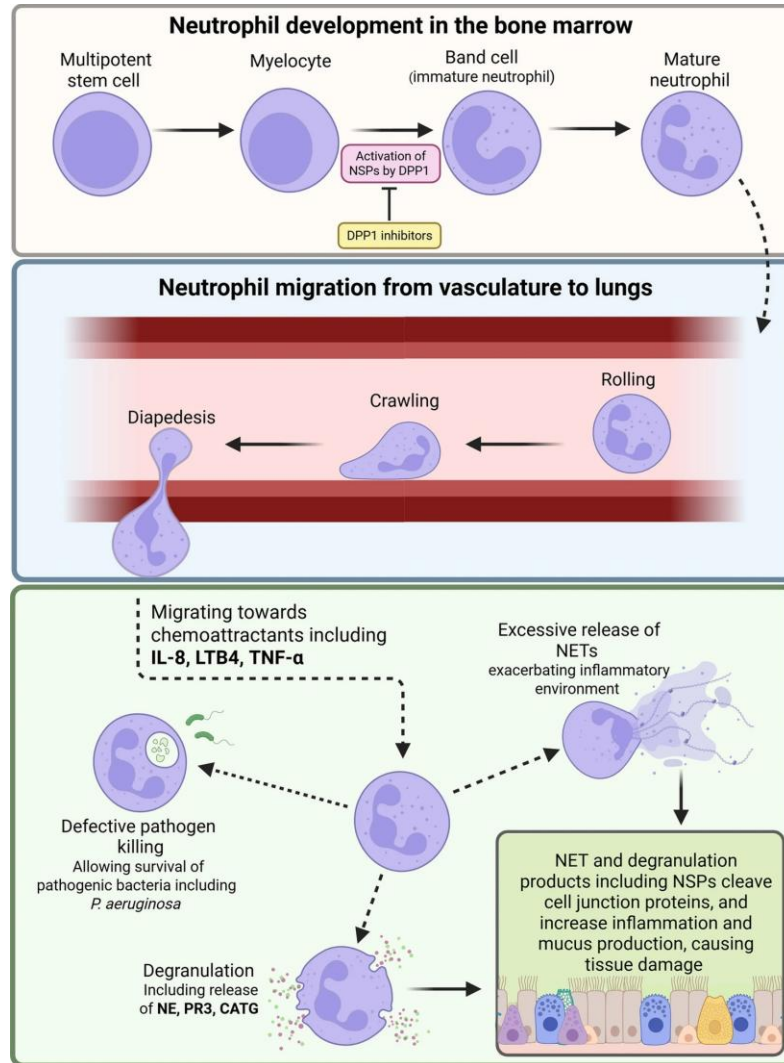
Vicious Vortex
BSI/FACED
EMBARC

Contents

- **Anti-inflammatory Drugs**
- **Novel Targets**
- **Mucoactive Agents**
- **Risk of Acute Exacerbations**
- **Endotypes**

Anti-inflammatory drugs; DPP-1 inhibitors

DPP-1 (cathepsin C) inhibitors



Brensocatib → ASPEN trial (Phase III)

HSK31858 → SAVE-BE trial (Phase II)

BI1291583 → AIRLEAF trial (Phase II)

Phase 3 Trial of the DPP-1 Inhibitor Brensocatib in Bronchiectasis

J.D. Chalmers,¹ P.-R. Burgel,^{2,3} C.L. Daley,^{4,5} A. De Soyza,^{6,7} C.S. Haworth,^{8,9} D. Mauger,¹⁰ M.R. Loebinger,^{11,12}
P.J. McShane,¹³ F.C. Ringshausen,¹⁴⁻¹⁶ F. Blasi,^{17,18} M. Shteinberg,^{19,20} K. Mange,²¹ A. Teper,²¹ C. Fernandez,²¹
M. Zambrano,²¹ C. Fan,²¹ X. Zhang,²¹ and M.L. Metersky,²² for the ASPEN Investigators*

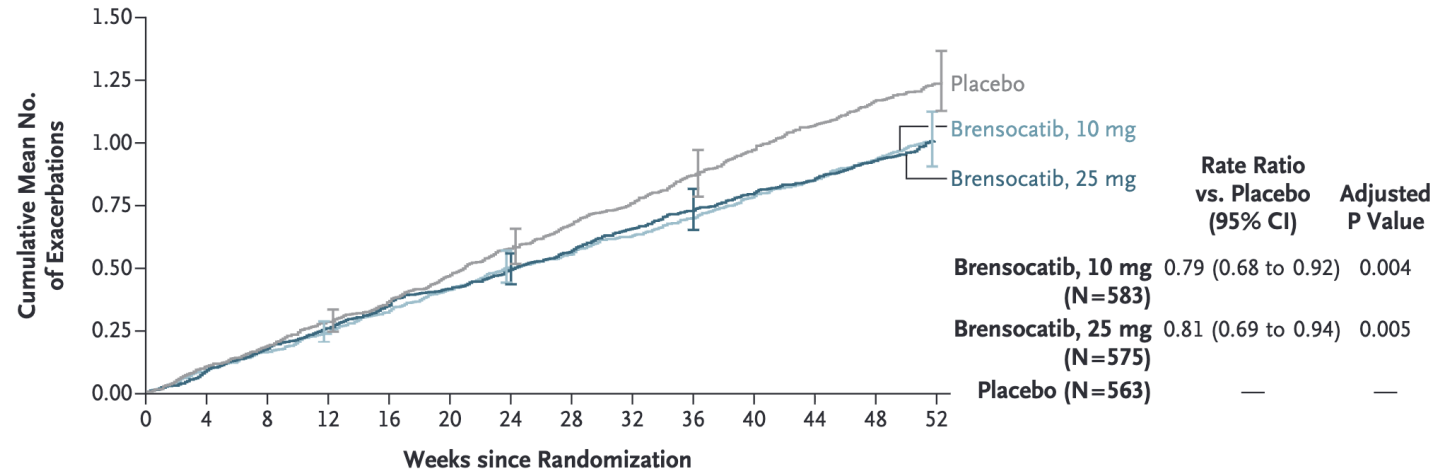
ASPEN trial

N=1,721

52wk, placebo:10mg:25mg = 1:1:1

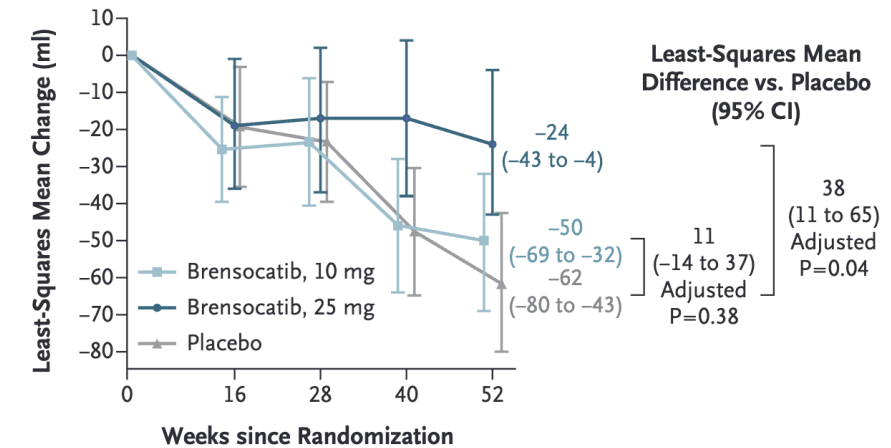
Primary outcome: annual exacerbation rate

Exacerbations over the 52-Wk Treatment Period



~20% ↓

Change in Postbronchodilator FEV₁ from Baseline



Hyperkeratosis

: placebo/10mg/25mg = 0.7% / 1.4% / 3.0%

Pneumonia

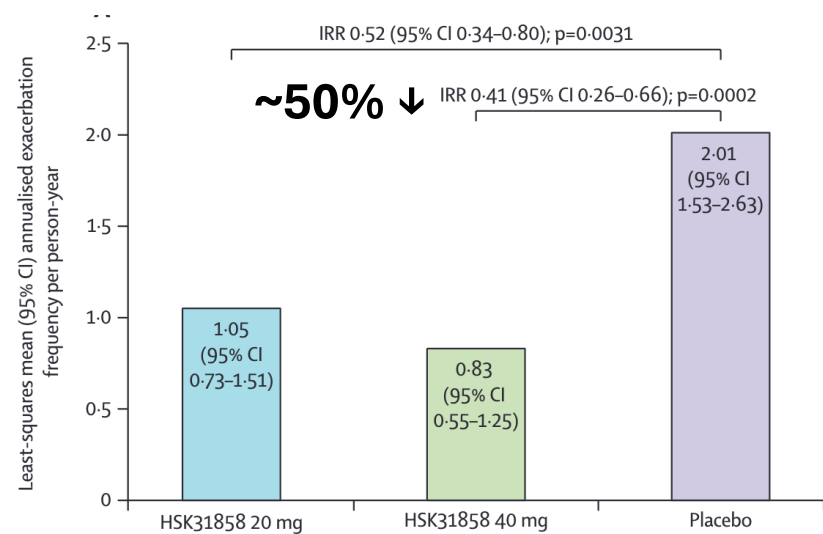
: placebo/10mg/25mg = 5.9% / 4.0% / 4.7%

QOL-B

: placebo/10mg/25mg = 4.81 / 6.84 / 8.58 < MCID 8

Effects of the DPP-1 inhibitor HSK31858 in adults with bronchiectasis in China (SAVE-BE): a phase 2, multicentre, double-blind, randomised, placebo-controlled trial

Nan-Shan Zhong*†, Rong Qiu*, Jie Cao*, Yan-Ming Huang*, Hua Zhou*, Xing-Xiang Xu*, Jin-Fu Xu*, Huan Ye, Zhi-Ren Yang, Ling-Yun Gao, Yao Shen, Zu-Ke Xiao, Shi-Guang Xie, Dian-Jie Lin, Li Zhao, Hao Xiong, Xian-Ming Zhang, Fang-Qiong Li, Wei-Jie Guan†, James D Chalmers‡, on behalf of the SAVE-BE trial investigators§



Why?

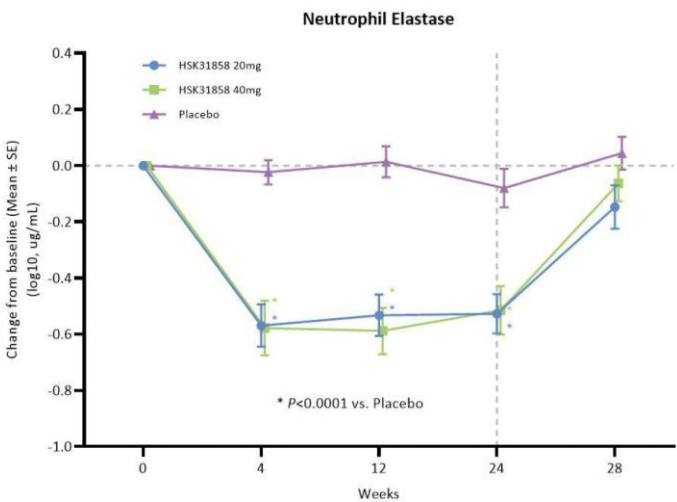
- Sputum NE >20ug/mL 54% (> 33% in WILLOW trial)
- Higher AE rate in placebo

SAVE-BE trial

N=244

26 wk, placebo:20mg:40mg = 1:1:1

Primary outcome: annual exacerbation rate

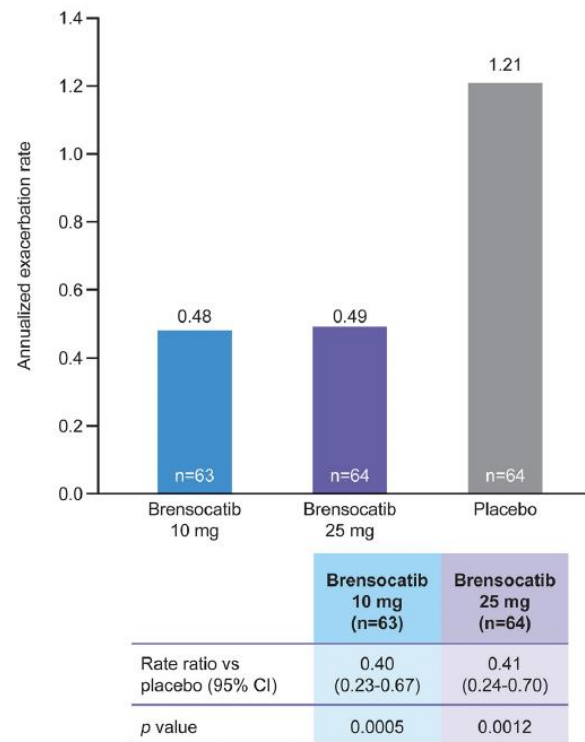


	Placebo (n=75)	20 mg HSK31858 (n=74)	p value for 20 mg HSK31858 vs placebo	40 mg HSK31858 (n=75)	p value for 40 mg HSK31858 vs placebo
Adverse events of special interests					
Dermatological disorders	0	1 (1%)	0.99	2 (3%)	0.50
Periodontal disorders	3 (4%)	3 (4%)	1.0	1 (1%)	0.62
Life-threatening infections	0	0	..	0	..

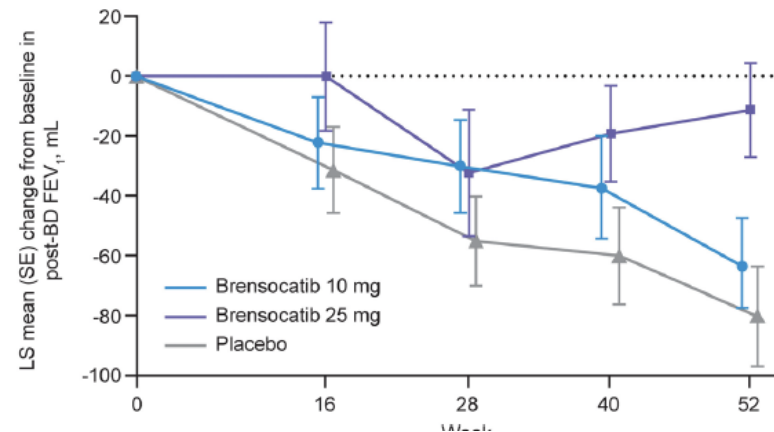
Efficacy and Safety of Brensocatib in Participants of Asian Race with Non-cystic Fibrosis Bronchiectasis: A Subgroup Analysis of the ASPEN Trial

Doreen Addrizzo-Harris · James D. Chalmers · Stefano Aliberti · Pierre-Régis Burgel · Brian M. Morrissey · Xiangmin Zhang · Chunpeng Fan · Melanie Lauterio · Sebastian Fucile · Dianne Griffis · Ariel Teper

Subgroup analysis in ASPEN study
: N = 191 of Asians



~60% ↓



	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	

	Brensocatib 10 mg (n=60) ^a	Brensocatib 25 mg (n=60) ^a	Placebo (n=60) ^a
Change from baseline in QOL-B RSS at week 52, LS mean (SE), points	2.53 (1.66)	4.28 (1.63)	-3.21 (1.96)
LS mean difference vs placebo (95% CI)	5.74 (0.66-10.82)	7.49 (2.48-12.50)	-
p value	0.0267	0.0034	

Cathepsin C (dipeptidyl peptidase 1) inhibition in adults with bronchiectasis: AIRLEAF, a phase II randomised, double-blind, placebo-controlled, dose-finding study

James D. Chalmers¹, Michal Shteinberg^{2,3}, Marcus A. Mall^{4,5,6}, Anne E. O'Donnell⁷, Henrik Watz⁸, Abhya Gupta⁹, Edith Frahm¹⁰, Anastasia Eleftheraki¹⁰, Johanna Rauch¹¹, Sanjay H. Chotirmall^{12,13}, April W. Armstrong¹⁴, Peter Eickholz¹⁵, Naoki Hasegawa¹⁶, Wiebke Sauter⁹ and Pamela J. McShane¹⁷

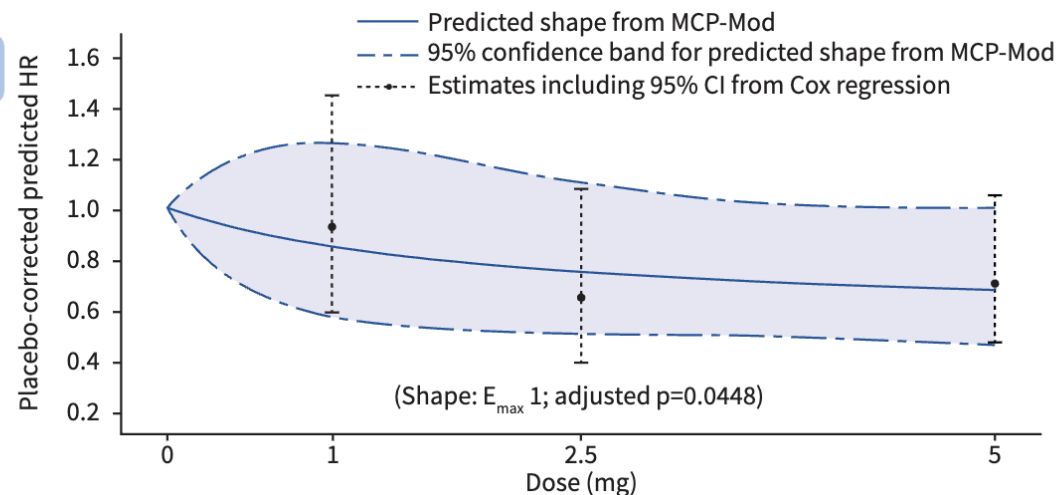
AIRLEAF trial

N=322

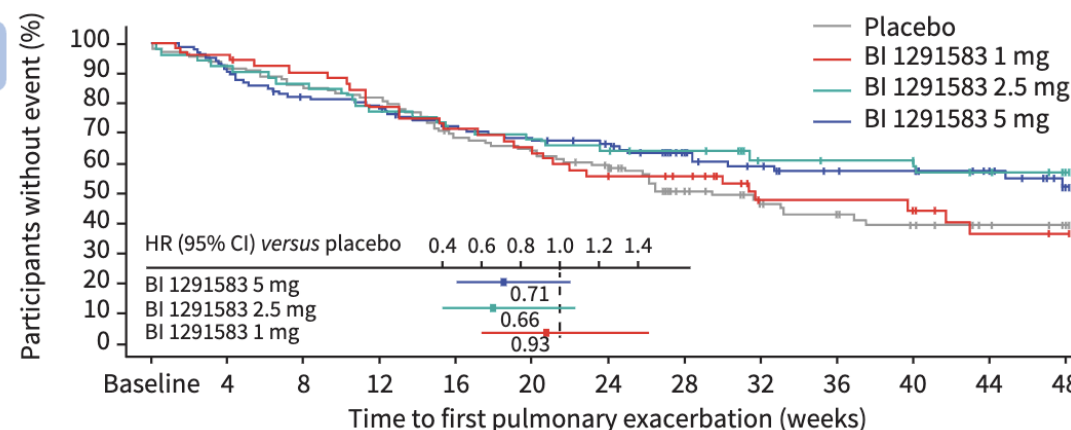
24-48 wk, placebo:1mg:2.5mg:5mg = 1:1:1:1

Primary outcome: annual exacerbation rate

1



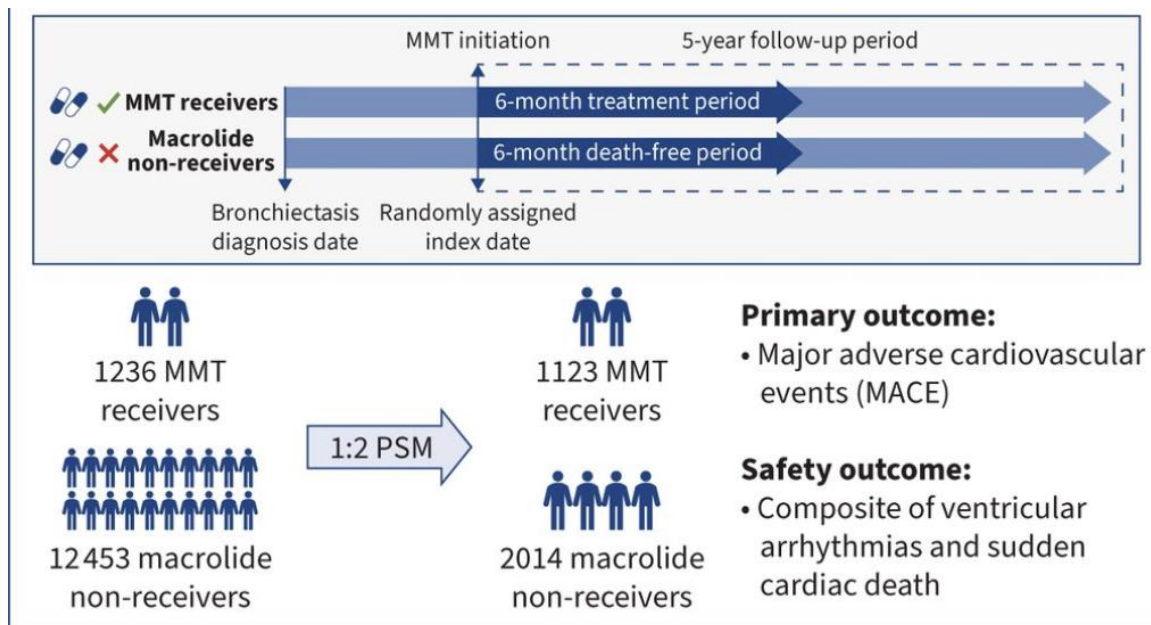
2



Anti-inflammatory drugs; Macrolide

Cardiovascular Risk & Benefit of Macrolide in BE

Retrospective cohort study (22,895 BE patients in HK between 2001 and 2018)



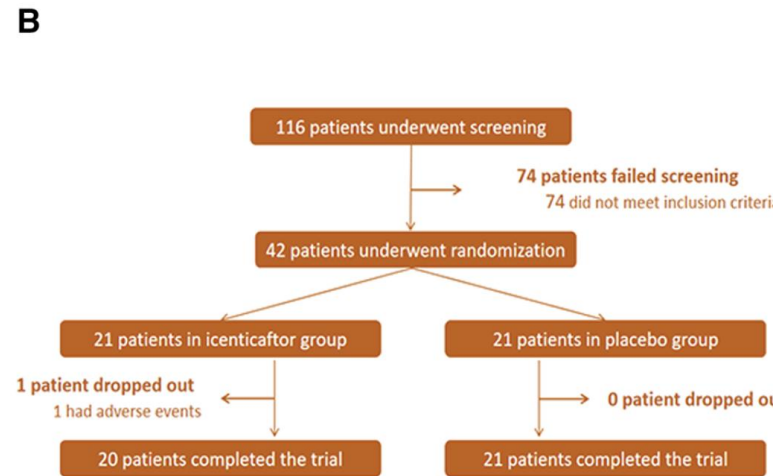
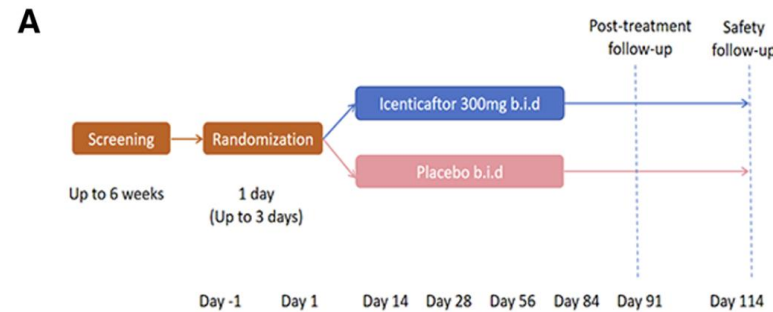
	Events, n (incidence rate per 1000 person-years)			Hazard ratio (95% CI)	p-value
	MMT receivers	Macrolide non-receivers			
Primary outcome					
MACE	70 (16.38)	169 (24.11)		0.68 (0.52–0.90)	0.007
Secondary outcomes					
All-cause mortality	476 (109.95)	948 (132.04)		0.83 (0.74–0.93)	<0.001
Cardiovascular death	28 (6.47)	54 (7.52)		0.86 (0.54–1.35)	0.51
AMI	23 (5.33)	73 (10.28)		0.52 (0.33–0.83)	0.006
Stroke	32 (7.46)	79 (11.15)		0.61 (0.45–1.01)	0.059
Safety outcome					
Ventricular dysrhythmia or sudden cardiac death	31 (7.17)	55 (7.67)		0.93 (0.60–1.44)	0.746
Negative control outcome					
Hip fracture hospitalisation	27 (6.31)	53 (7.46)		0.85 (0.54–1.35)	0.496

Novel Targets for BE

The CFTR potentiator icentricafor for treatment of bronchiectasis: an international phase 2, double-blind, randomized placebo-controlled trial

Wei-Jie Guan^{1,2}, Charles S. Haworth³, Harm A.W.M. Tiddens^{4,5,6}, Michael R. Loebinger^{7,8}, Adam T. Hill⁹, Oriol Sibila^{10,11,12}, Felix C. Ringshausen^{13,14,15}, Bridget D. Stuart¹⁶, Yingying Wang¹⁷, J. Stuart Elborn¹⁸, Nan-Shan Zhong^{1,2}, James D. Chalmers^{19,20,*}

N=42 (early termination d/t COVID and sponsor)
BE with at least one sputum pathogenic bacteria
Primary endpoint: bacterial load



C

Changes from baseline in the primary endpoint at different time points (PD analysis set)

	Icenticafor group		Placebo group		Treatment difference		
Time points	LSM	SE	LSM	SE	LSM	SE	80% CI
Week 4	0.23	0.32	0.42	0.30	-0.29	0.36	-0.76, 0.17
Week 8	0.43	0.34	0.39	0.32	0.04	0.38	-0.46, 0.54
Week 12	0.10	0.39	0.49	0.34	-0.39	0.45	-0.98, 0.20

D

Study end points at baseline and day 84 (PD analysis set)

Variable	Icenticafor group (N=21)			Placebo group (N=21)		
	Baseline	Day 84	Difference	Baseline	Day 84	Difference
Logarithmic (CFU/ml) of PPM						
No.	13	13	13	19	19	19
Mean (SD)	6.74 (1.03)	6.55 (1.66)	-0.19 (1.46)	6.75 (1.68)	7.09 (1.15)	0.34 (1.65)
QoL-B-RSS						
No.	13	13	13	20	20	20
Mean (SD)	56.98 (14.86)	59.83 (15.11)	2.85 (9.46)	57.78 (14.93)	61.30 (11.30)	3.52 (11.98)
Fibrinogen concentration (g/L)						
No.	19	19	19	19	19	19
Mean (SD)	4.53 (0.55)	4.33 (0.75)	-0.19 (0.63)	4.85 (0.68)	4.72 (0.72)	-0.13 (0.48)
Rescue medication use (puffs)*						
No.	16	16	16	20	20	20
Mean (SD)	1.41 (3.06)	1.04 (2.32)	-0.67 (1.07)	0.35 (0.63)	0.49 (1.09)	0.14 (0.90)
FEV₁ (L)						
No.	17	17	17	19	19	19
Mean (SD)	1.87 (0.76)	1.92 (0.82)	0.05 (0.17)	2.01 (0.62)	2.03 (0.63)	0.02 (0.13)
FVC (L)						
No.	17	17	17	19	19	19
Mean (SD)	2.95 (0.96)	2.93 (0.98)	-0.02 (0.18)	3.01 (0.88)	3.04 (0.90)	0.03 (0.22)
FEV₁/FVC (%)						
No.	17	17	17	19	19	19
Mean (SD)	63.1 (14.0)	64.6 (13.7)	1.5 (2.9)	67.5 (10.3)	67.2 (8.7)	-0.3 (3.6)

Safety and antimicrobial efficacy of CSL787, a novel nebulized IgG therapy, in patients with bronchiectasis: results from a randomized phase 1 trial

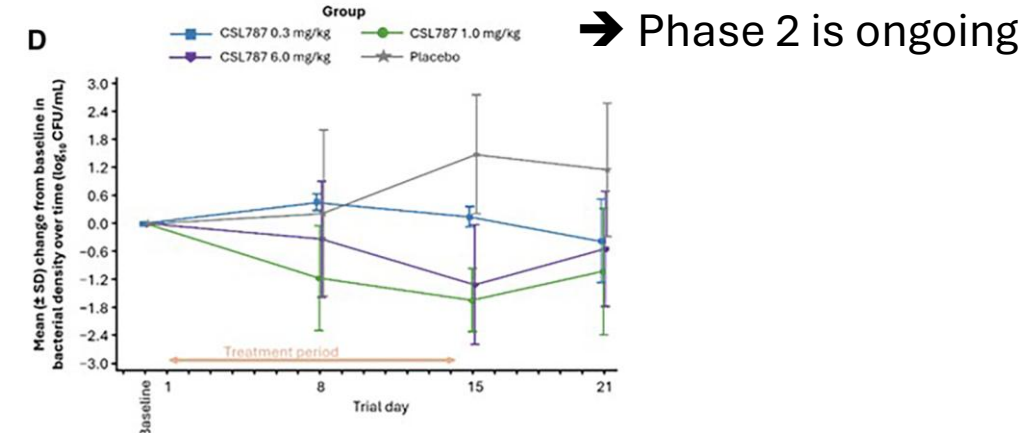
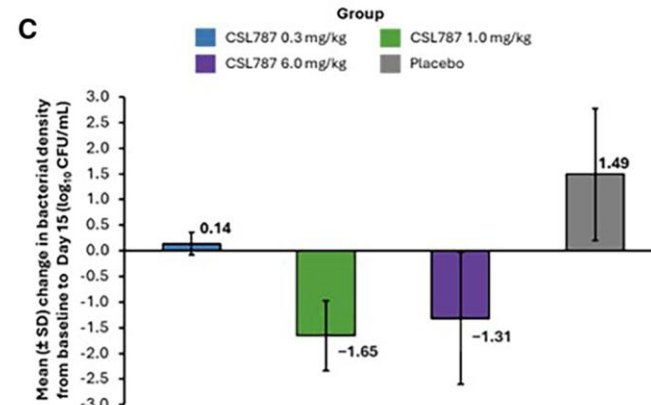
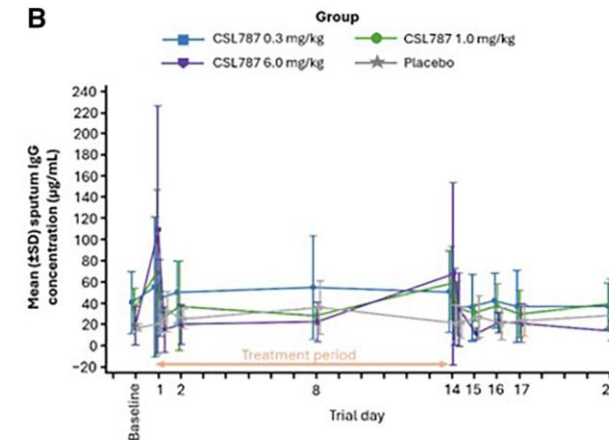
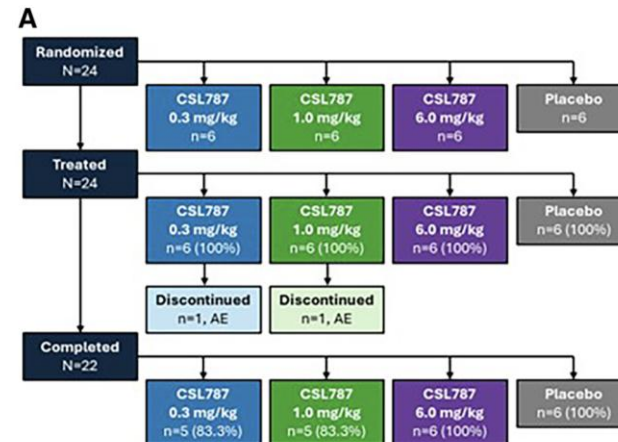
Damian G. Downey^{1,10}, Ilka Schulze², Andreas Eich^{3,10}, Dave Singh^{4,5,10}, Michael Larbig⁶, Oliver Vit⁶, Laurent B. Nicolas⁷, Sanjay H. Chotirmall^{8,9,10}, James D. Chalmers^{10,11,*}

N=22, 1 dose of nebulization/day for 14days
BE with at least one sputum pathogenic bacteria
Primary outcome: treatment-emerge adverse event

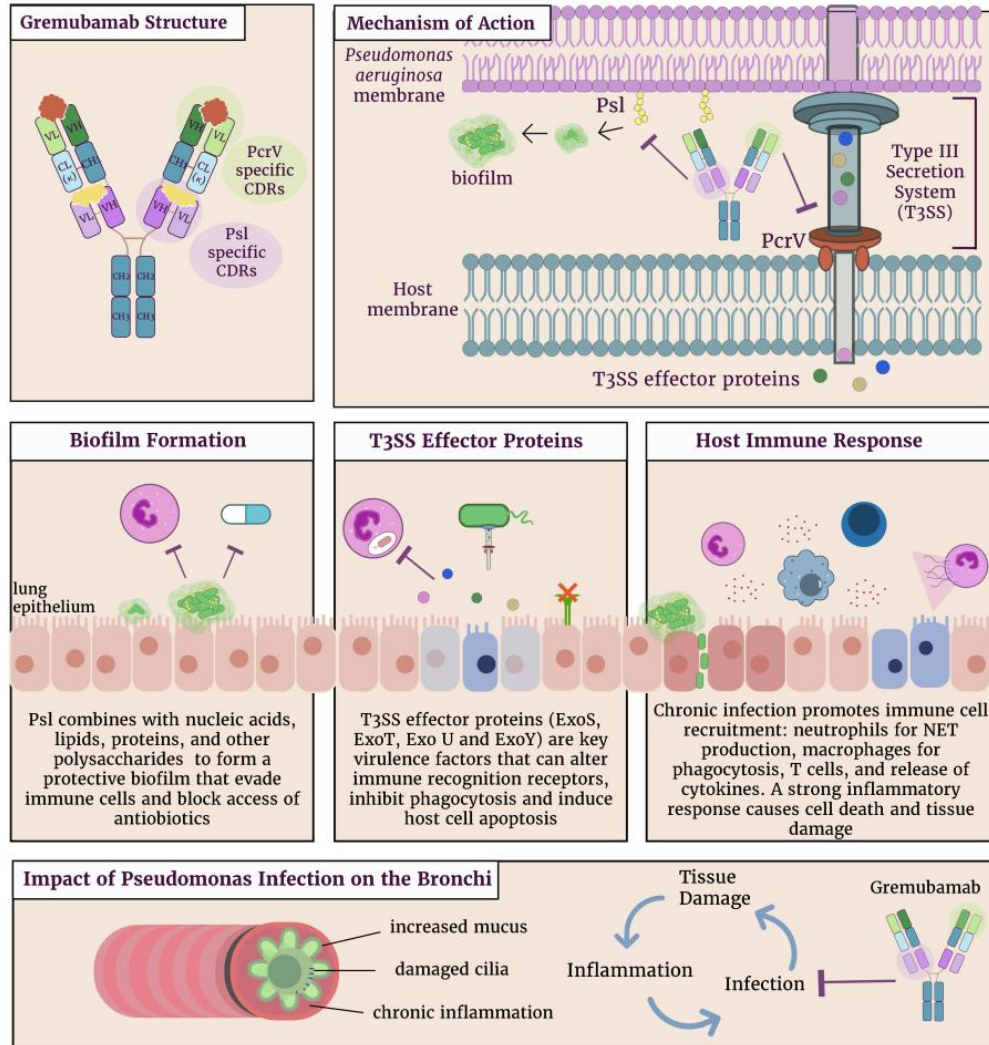
CSL787 = polyclonal IgG from healthy donor plasma → formulated for inhalation

MoA

- Opsono-phagocytosis
- Neuralization
- Immunomodulation



Targeting Pseudomonas



Gremubamab → AZD0292 (longer half life)

Phase I (NCT06311760)

N=32 ; placebo vs 100,300,1000,2000mg of AZD0292

No fetal/severe TEAEs

(slightly higher TEAEs in high dose groups; skin problems)

→ Phase 2 is ongoing

Mucoactive agents

Hypertonic Saline or Carbocisteine in Bronchiectasis

J.M. Bradley,¹ B. O'Neill,² D.F. McAuley,¹ J.D. Chalmers,³ A. De Soyza,⁴ A.T. Hill,^{5,6} M. Carroll,⁷ M.R. Loebinger,^{8,9} J. Duckers,¹⁰ M. Clarke,^{11,12} R.H. McLeese,¹³ K. Ferguson,^{14,15} A. Jackson,¹² C. Campbell,¹² C. McDowell,¹² A. Agus,¹² J. Norrie,¹¹ F. Copeland,¹⁶ D.G. Downey,^{1,15} R. Convery,¹⁷ M. Kelly,¹⁴ W. Flight,¹⁸ N.P. Talbot,¹⁸ J.R. Hurst,¹⁹ J. Steer,²⁰ M. Anwar,²¹ M. Shahidi,²² T. Gatheral,²³ M. Etumi,²⁴ A.L. Sullivan,²⁵ A.A. Ionescu,²⁶ V. Patil,²⁷ M. Bhattacharya,²⁸ S. Caskey,¹⁵ D. Cosgrove,¹⁷ C. Hagan,¹⁷ A. Shoemark,³ T. McManus,¹³ G. Davies,⁴ and J.S. Elborn,¹ for the CLEAR Investigator Team*

CLEAR trial
N=288
52wks, Hypertonic saline/Carbocisteine 2x2 factorial
Primary outcome: # of exacerbations

Outcome	HTS (N = 126)	No HTS (N = 141)	Mean Difference or Hazard Ratio, HTS vs. No HTS (95% CI)	Carbocisteine (N = 129)	No Carbocisteine (N = 138)	Mean Difference or Hazard Ratio, Carbocisteine vs. No Carbocisteine (95% CI)
	mean (95% CI)	mean (95% CI)		mean (95% CI)	mean (95% CI)	
Primary outcome: no. of pulmonary exacerbations over 52 wk†	0.76 (0.58 to 0.95)	0.98 (0.78 to 1.19)	−0.25 (−0.57 to 0.07)	0.86 (0.66 to 1.06)	0.90 (0.70 to 1.09)	−0.04 (−0.36 to 0.28)
Secondary outcomes						
Health-related quality-of-life measures‡						
QoL-B respiratory symptoms	59.8 (57.0 to 62.6)	60.5 (57.9 to 63.1)	−0.7 (−4.6 to 3.1)	60.0 (57.2 to 62.8)	60.3 (57.7 to 62.9)	−0.3 (−4.2 to 3.5)
SGRQ total score	42.5 (39.9 to 45.0)	42.7 (40.4 to 45.1)	−0.3 (−3.8 to 3.2)	42.8 (40.2 to 45.3)	42.5 (40.1 to 44.9)	0.3 (−3.2 to 3.8)
EQ-5D-5L utility index	0.73 (0.68 to 0.78)	0.72 (0.67 to 0.77)	0.01 (−0.06 to 0.08)	0.75 (0.70 to 0.80)	0.70 (0.65 to 0.75)	0.05 (−0.02 to 0.13)
EQ-VAS score	70.9 (68.0 to 73.8)	68.4 (65.6 to 71.1)	2.6 (−1.5 to 6.7)	71.2 (68.3 to 74.1)	68.1 (65.4 to 70.9)	3.1 (−1.1 to 7.2)
No. of days from randomization to next pulmonary exacerbation§	256.5 (229.4 to 283.6)	239.2 (214.7 to 263.7)	0.80 (0.56 to 1.14)	244.8 (219.2 to 270.4)	249.8 (224.0 to 275.6)	1.17 (0.83 to 1.67)
No. of days of antibiotic treatment for exacerbations over 52 wk¶	18.9 (13.3 to 24.6)	21.7 (15.5 to 27.8)	−0.14 (−0.5 to 0.3)	19.6 (13.8 to 25.3)	21.2 (15.1 to 27.2)	−0.08 (−0.5 to 0.3)
Change in lung function from base-line						
FEV ₁ — liters	−0.01 (−0.10 to 0.08)	−0.02 (−0.10 to 0.06)	0.01 (−0.1 to 0.1)	−0.003 (−0.09 to 0.09)	−0.03 (−0.12 to 0.05)	0.03 (−0.09 to 0.2)
FEV ₁ — % of predicted	1.6 (−1.9 to 5.2)	−0.0 (−3.1 to 3.1)	1.6 (−3.1 to 6.4)	1.6 (−1.9 to 5.1)	−0.05 (−3.2 to 3.1)	1.7 (−3.2 to 6.5)
FVC — liters	−0.0 (−0.11 to 0.11)	−0.06 (−0.16 to 0.03)	0.06 (−0.08 to 0.2)	−0.02 (−0.13 to 0.08)	−0.05 (−0.15 to 0.05)	0.02 (−0.1 to 0.2)
FEF _{25–75} z score	−1.3 (−3.0 to 0.3)	−0.4 (−1.9 to 1.0)	−0.9 (−3.2 to 1.4)	−0.6 (−2.3 to 1.0)	−1.0 (−2.5 to 0.5)	0.4 (−1.9 to 2.7)

No significant difference
Effect of standard care ?

Hypertonic Saline or Carbocisteine in Bronchiectasis

J.M. Bradley,¹ B. O'Neill,² D.F. McAuley,¹ J.D. Chalmers,³ A. De Soyza,⁴ A.T. Hill,^{5,6} M. Carroll,⁷ M.R. Loebinger,^{8,9} J. Duckers,¹⁰ M. Clarke,^{11,12} R.H. McLeese,¹³ K. Ferguson,^{14,15} A. Jackson,¹² C. Campbell,¹² C. McDowell,¹² A. Agus,¹² J. Norrie,¹¹ F. Copeland,¹⁶ D.G. Downey,^{1,15} R. Convery,¹⁷ M. Kelly,¹⁴ W. Flight,¹⁸ N.P. Talbot,¹⁸ J.R. Hurst,¹⁹ J. Steer,²⁰ M. Anwar,²¹ M. Shahidi,²² T. Gatheral,²³ M. Etumi,²⁴ A.L. Sullivan,²⁵ A.A. Ionescu,²⁶ V. Patil,²⁷ M. Bhattacharya,²⁸ S. Caskey,¹⁵ D. Cosgrove,¹⁷ C. Hagan,¹⁷ A. Shoemark,³ T. McManus,¹³ G. Davies,⁴ and J.S. Elborn,¹ for the CLEAR Investigator Team*

CLEAR trial

N=288

52wks of standard care

+ Hypertonic saline/Carbocisteine 2x2 factorial

Primary outcome: # of exacerbations

Event	HTS (N=146)		No HTS (N=142)		Risk Ratio, HTS vs. No HTS (95% CI)	Carbocisteine (N=144)		No Carbocisteine (N=144)		Risk Ratio, Carbocisteine vs. No Carbocisteine (95% CI)
	no. of events	no. with event (%)	no. of events	no. with event (%)		no. of events	no. with event (%)	no. of events	no. with event (%)	
Primary outcome: serious adverse events	17	16 (11)	22	19 (13)	0.8 (0.4–1.5)*	24	20 (14)	15	15 (10)	1.3 (0.7–2.5)†
Related to trial drug	1	1 (1)	0	0		1	1 (1)	0	0	
Respiratory, thoracic, and mediastinal disorders	1	1 (1)	0	0		1	1 (1)	0	0	
Unexpected reaction related to HTS or carbocisteine‡	0	0	0	0		0	0	0	0	
Secondary outcome: adverse events	274	100 (68)	238	94 (66)	1.0 (0.9–1.2)§	284	103 (72)	228	91 (63)	1.1 (1.0–1.3)¶
Related to HTS or carbocisteine‡	69	43 (29)	22	15 (11)		63	40 (28)	28	18 (12)	
Eye disorders	3	2 (1)	0	0		3	2 (1)	0	0	
Gastrointestinal disorders	24	17 (12)	14	11 (8)		32	23 (16)	6	5 (3)	
General	2	2 (1)	1	1 (1)		2	2 (1)	1	1 (1)	
Infections and infestations	1	1 (1)	0	0		0	0	1	1 (1)	
Nervous system disorders	2	2 (1)	1	1 (1)		3	3 (2)	0	0	
Respiratory, thoracic, and mediastinal disorders	35	27 (18)	3	1 (1)		18	15 (10)	20	13 (9)	
Skin and subcutaneous tissue disorders	1	1 (1)	3	3 (2)		4	4 (3)	0	0	
Vascular disorders	1	1 (1)	0	0		1	1 (1)	0	0	

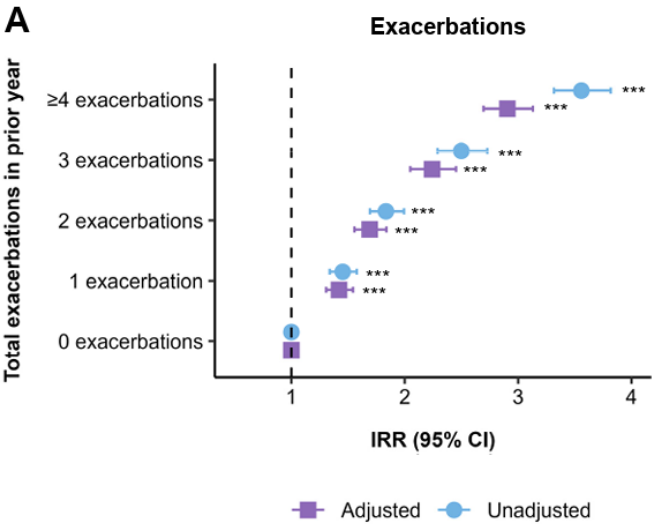
Higher adverse events
(no different SAE)

Risk of Acute Exacerbations

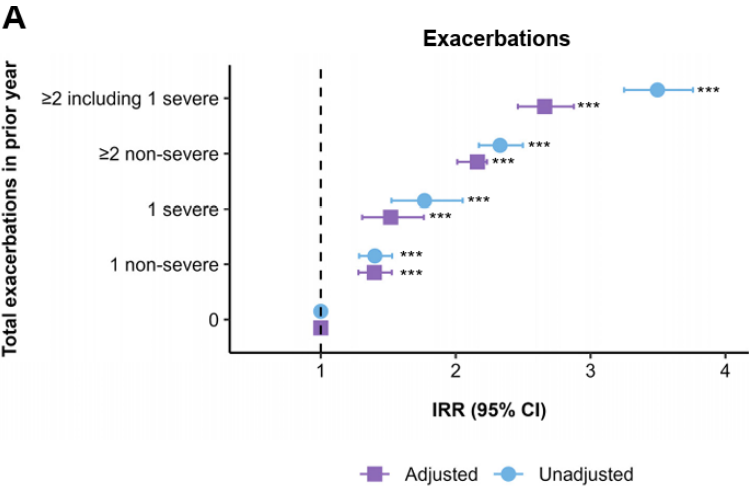
Frequent Exacerbator Phenotype in BE

N=19,324 in EMBARC

Previous definition ≥ 3 exacerbations



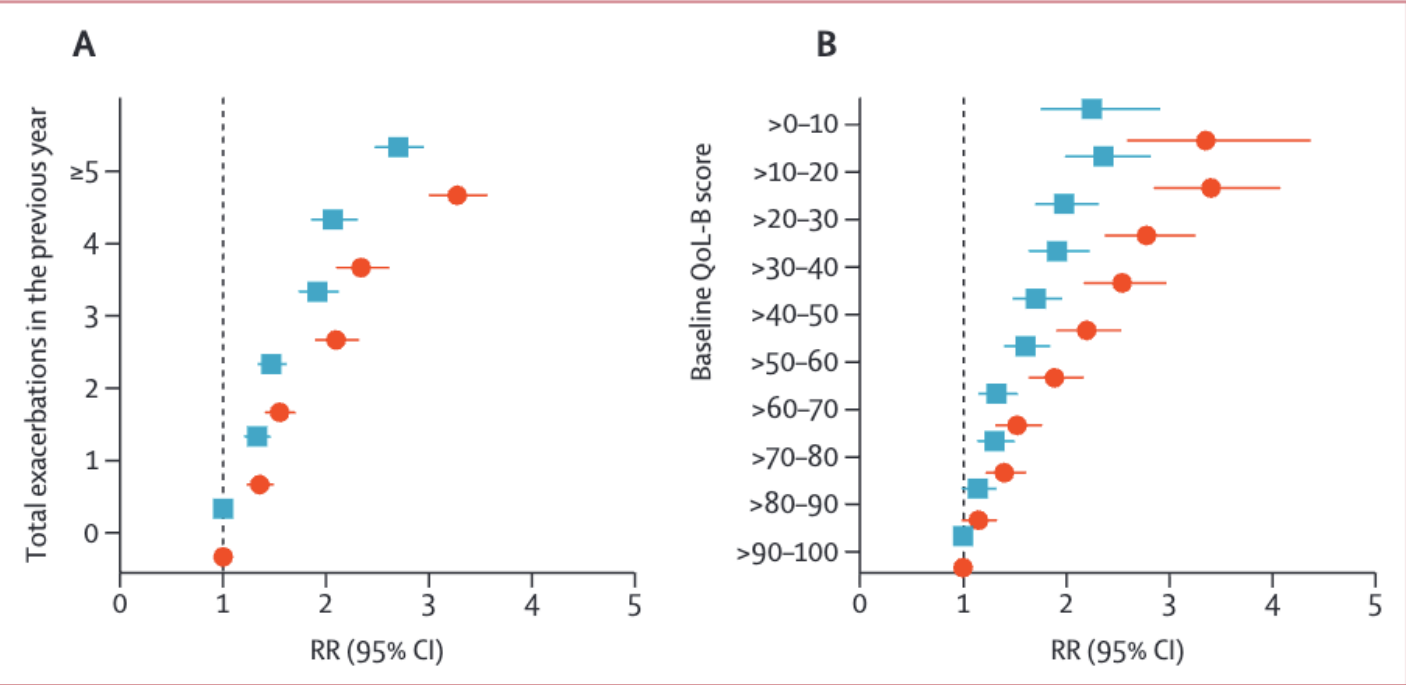
No ceiling



Prior severe
→ next severe

Symptoms Predicting Acute Exacerbations

N=9,466 in EMBARC



Each 10-point fall in QoL-B
→ 10% higher exacerbation rate

	Number of exacerbations in the previous year				
	0	1	2	3	4
-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)

Prior 0/yr + severe Sx = 1.55/yr
Prior 3/yr + average Sx = 1.58/yr

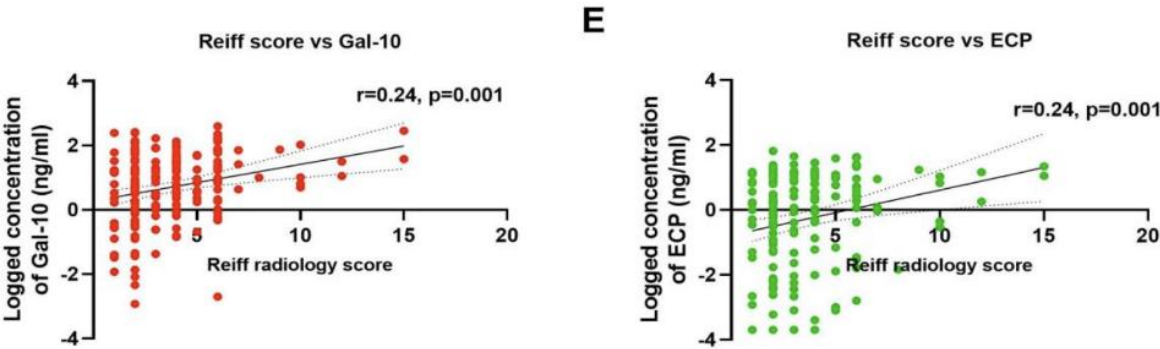
Endotypes

Clinical, molecular and microbial characterisation of the eosinophilic endotype of bronchiectasis: data from the EMBARC-BRIDGE study

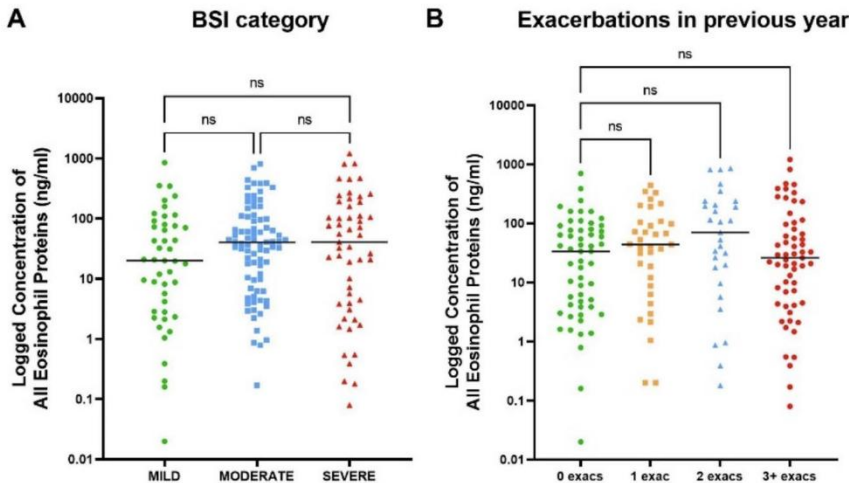
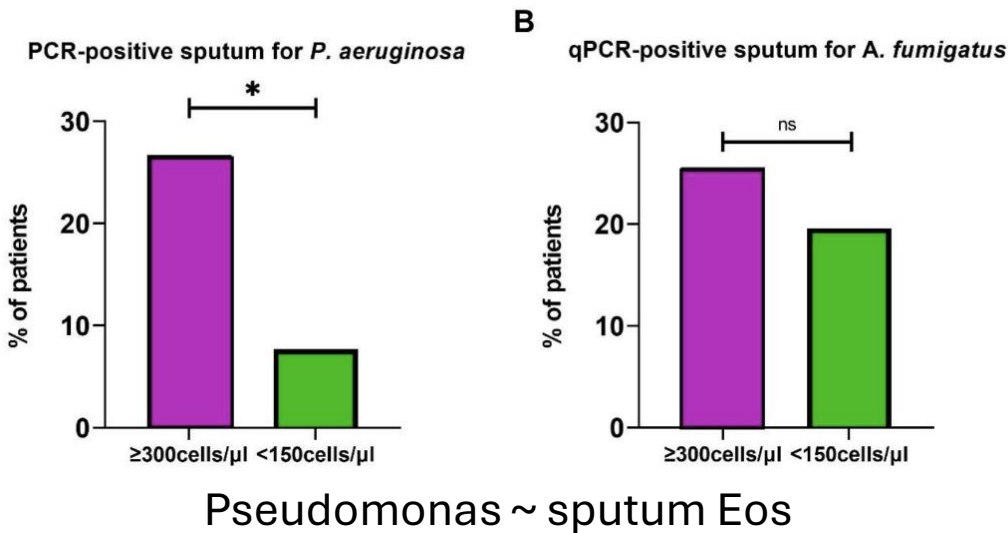
Jennifer Pollock,¹ Jeffrey T J Huang,¹ Morven Shuttleworth,¹ Merete B Long,¹ Hollian Richardson,¹ Daniela Alferes de Lima,¹ Elena Kuzmanova,¹ Clare Clarke,¹ Michal Shteinberg ^{2,3} Stefano Aliberti,^{4,5} Charles Haworth,⁶ Sanjay Haresh Chotirmall ^{7,8} Eva Polverino,⁹ Pieter C Goeminne,¹⁰ Michael Loebinger,^{11,12} Natalie Lorent,^{13,14} Felix C Ringshausen ¹⁵ Oriol Sibila,¹⁶ Eva Rodriguez-Suarez,¹⁷ Christopher McCrae,¹⁸ Amelia Shoemark ¹, James D Chalmers ^{1,19}

Eosinophilic BE (BEC > 300 cells/uL) = 20~30%
Higher BEC ~ eosinophilic endotype of BE?
Eosinophilic protein profiles from sputum (N=180)

blood Eos ~ sputum Eos: **weak correlation** (r = 0.33)



Sputum Eos protein ~ radiologic severity



Sputum Eos Protein <> BSI/exacerbation

Upper-Airway Microbiome, Mucociliary Function, and Clinical Outcomes in Bronchiectasis

Data from the EMBARC-BRIDGE Study

Hayoung Choi¹, Hollian Richardson², Chandani Hennayake², Morven Shuttleworth², Erin Cant², Mathieu Bottier³, Arietta Spinou⁴, Kara Robertson², Merete B. Long², Anthony De Soya⁵, Felix C. Ringshausen^{6,7}, Pieter Goeminne⁸, Natalie Lorent^{9,10}, Charles Haworth¹¹, Josje Altenburg¹², Michael R. Loebinger¹³, Daniela Alferes de Lima Headley², Alison J. Dicker¹⁴, Francesco Blasi^{15,16}, Michal Shteinberg^{17,18}, Stefano Aliberti^{19,20}, Eva Polverino²¹, Oriol Sibila²², Amelia Shoemark², and James D. Chalmers²

Nasopharyngeal swabs (N=344)
- Microbiome, mucociliary function

Pseuomonas in nasal swab (>0%)
No Pseuomonas in nasal swab

→ Pseudomonas in sputum 25.8%
→ Pseudomonas in sputum 10.0%

Group	Exacerbation		Severe Exacerbation	
	IRR (95% CI)	P Value	IRR (95% CI)	P Value
No dysbiosis	1.0 (Reference)	0.14	1.0 (Reference)	0.027
Dysbiosis	1.36 (0.90–2.05)		3.16 (1.14–8.78)	

Definition of abbreviation: IRR = incident rate ratio.
Dysbiosis was defined as a relative abundance of pathogenic taxa >10%, including *Pseudomonas*, *Haemophilus*, and *Staphylococcus*.

Worse symptoms
Higher epithelial disruption in dysbiosis group

Summary

- DPP-1 inhibitors: brensocatib, flensocatib, BI1291583 + Macrolide
- Novel targets: icenticaftor, CSL787, AZD0292
- Mucoactive agents: hypertonic saline vs carbocysteine
- Risk of acute exacerbations: severity of AE, symptoms
- Endotypes: sputum Eos proteins, upper-airway microbiome