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RISING STARS

0001 Characterising systemic inflammation in patients with bronchiectasis: data from the EMBARC BRIDGE study

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Introduction: Bronchiectasis is recognised as an inflammatory disease with neutrophils playing a key role. However, the systemic inflammatory mechanisms, including neutrophil-derived protein signatures, and their relationship to clinical characteristics remain unclear.

Aim: To characterise systemic inflammatory profiles in patients with bronchiectasis and investigate their associations with clinical outcomes.

Methods: Observational study of patients with stable bronchiectasis (BRIDGE study; NCT03791086), recruited from nine European sites (UK, Spain, Italy, Belgium, Netherlands, Germany, and Portugal). The Olink target 96 cardiovascular III panel was used to measure 92 serum proteins. Associations with clinical features were assessed using linear and negative-binomial regression, adjusted for age, gender, and BMI, with multiple-testing correction. In a mechanistic sub-study including bronchiectasis and healthy controls, neutrophil surface markers on peripheral blood neutrophils were measured by flow cytometry, with functional analysis of MPO release and NET formation.

Results: 484 patients with bronchiectasis were included (age 64 ± 14 (mean $\pm$ SD); 59 % female). Markers of systemic inflammation were strongly associated with higher BSI scores, worse lung function, greater symptom severity, and increased severe exacerbations during follow-up. Forty-two proteins were significantly ($p_{\text{adj}} < 0.05$) associated with BSI scores. Elevated levels of neutrophil related proteins including AZU-1, PRTN3, MPO, RETN, MMP9, and the neutrophil chemokine receptor CXCL16, as well as proteins related to endothelial dysfunction (SELE, vWF), tissue remodelling (GDF-15), and IL-33 signalling (ST2), were associated with higher disease severity using the BSI. Twenty-two and 28 proteins were significantly ($p_{\text{adj}} < 0.05$) associated with FEV₁ and FVC, respectively. Higher MPO, MMP9, RETN and CXCL16, and the endothelial activation markers SELE and OPG were associated with lower lung function. Symptom severity, measured by the MRC dyspnoea score, showed the broadest inflammatory signature, with 59 proteins significantly increased ($p_{\text{adj}} < 0.05$) in those reporting more severe breathlessness, including proteins linked to neutrophil activation (AZU1, MPO, PR3, and MMP9), endothelial dysfunction (SELE, LTBR, and PI3), and platelet activation (SELP, TR, and GP6). Reduced physical quality-of-life (QoL), assessed using the Bronchiectasis QoL Questionnaire, was significantly associated ($p_{\text{adj}} < 0.05$) with 44 proteins, including inflammatory and neutrophil-related markers (MPO, MMP9, PR3, GDF-15, and FABP4), and endothelial and coagulation proteins (vWF, SELE, tPA). Several proteins including MPO, PR3, MMP9, RETN, and SELE, were increased across multiple clinical outcomes. Severe exacerbations during follow-up, defined as those requiring hospitalisation, was significantly associated with elevation of 12 proteins after FDR adjustment, including increased levels of MPO and ST2, and lower levels of EGFR and the antioxidant PON3. In the mechanistic sub-study, bronchiectasis patients ($n = 30$) had significantly lower CD11b and increased CXCR2 on circulating neutrophils compared to controls ($n = 17$) ($p < 0.05$; Mann-Whitney), with CD11b positively correlating with FEV₁ and FVC ($p < 0.05$; Spearman R). MPO release under basal conditions was significantly reduced in bronchiectasis.

Conclusion: Systemic neutrophilic inflammation, endothelial activation, and dysregulated coagulation are strongly associated with impaired lung function, more severe dyspnoea, poorer QoL, and increased rate of severe exacerbations in bronchiectasis. Altered neutrophil phenotype and function in bronchiectasis further support a role for systemic immune dysregulation. These results highlight systemic pathways linked to disease burden and identify candidate biomarkers for risk stratification and potential therapeutic targets.

Conflict of interest No COI

0002 Early Mycobacterium abscessus Infection Drives Staged Epithelial Remodeling in Small Airways

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Background/Aims: Nontuberculous mycobacterial (NTM) infections, particularly *Mycobacterium abscessus* (*M. abscessus*), are increasingly associated with bronchiectasis. While disease is thought to originate in the peripheral airways, early host responses in the small airway epithelium remain poorly defined, particularly in models that preserve native airway features such as mucus. Here, we aimed to define early epithelial responses to *M. abscessus* infection using a mucus-preserving, human tissue-derived small airway model.

Methods: Primary human small airway epithelial (SAE) cells from six female donors (aged 47–71 years) without known respiratory disease were differentiated at an air–liquid interface (ALI) under optimized culture conditions selected based on comparative evaluation of multiple media. Cells were then infected apically with *M. abscessus* (ATCC 19977) at multiplicities of infection of 100 and 1000. Infection was performed without removal of apical mucus to preserve native airway conditions. Bulk transcriptomic profiling by RNA-seq and RT-qPCR was used to characterize epithelial responses across time points and infection loads. Barrier function was assessed by transepithelial electrical resistance (TEER).

Results: Bulk RNA-seq analysis revealed a staged epithelial response characterized by early suppression of differentiation and homeostasis programs, followed by induction of stress and remodeling pathways, and sustained activation of inflammatory and metabolic signaling. Acute-phase and proliferation-associated genes further increased at later time points, indicating amplification of epithelial responses. RT-qPCR confirmed upregulation of inflammatory mediators (CXCL8, IL-1 β , IL-6) and protease-related pathways, including CTSC (DPP-1), linking epithelial responses to pathways associated with neutrophil protease activation.

Despite marked transcriptional remodeling, TEER measurements showed no significant differences across conditions, indicating that epithelial barrier function is preserved during early infection. Consistent with this, minimal cell death was observed across conditions. Notably, low levels of bacteria were detected in the basal compartment despite intact barrier function, suggesting non-disruptive epithelial traversal, potentially through transcellular mechanisms. In contrast to prior reports of barrier disruption in NTM infection, these findings may reflect stage-dependent responses or model-specific features of early *M. abscessus* infection.

Conclusions: Using a mucus-preserving small airway model, early *M. abscessus* infection induces staged epithelial remodeling while maintaining barrier integrity. These findings provide insight into early epithelial responses to NTM infection in the small airway and support a model in which epithelial remodeling precedes barrier dysfunction in bronchiectasis pathogenesis.

Conflict of interest This work was supported by JSPS KAKENHI (JP21K20782), the Cystic Fibrosis Foundation (OLIVER23XX0), National Institutes of Health (NHLBI R01 HL163602), and the Japanese Society for Tuberculosis and Nontuberculous Mycobacteriosis Fellowship Grants (2024). Kenneth N. Olivier reports consulting, advisory, and/or investigator relationships with Mannkind Corporation, Spero Therapeutics, Paratek Pharmaceuticals, Insmed, Inc., AN2 Therapeutics, Beyond Air, Inc., ReCode Therapeutics, Verona Pharma, and CSL Behring. This work was also supported by Core grants NIH DK065988 and CF Foundation ESTHER24R0.

Results: Four PA-abundotypes were identified: PA-dominant (PD), Moderate PA-dominant (MPD), Other Microbe Dominant (OMD) and High Diversity (HD). Exacerbation risk was comparable across abundotypes, however, HD patients demonstrate reduced symptom burden, less severe disease and better lung function. Four separate, robust PA-interactotypes were identified: BC1 (characterized by PA-*Neisseria* interactions); BC2 (PA-*S. aureus* & *E. coli* interactions); BC3 (PA-*Streptococcus* interactions) and BC4 (mixed interactions). Further PA interactome analysis reveal core interactions with commensal taxa shared across all interactotypes while ancillary (variable) interactions remain interactotype-specific. Importantly, PA-abundotypes and PA-interactotypes are independent of one another capturing separate dimensions of PA-airway ecology. PA-abundance independently predicts disease severity, symptoms and reduced lung function. PA-interactotypes stratify exacerbation risk with BC3 as the lowest-risk group: BC1 and BC4 exhibit 1.45- and 1.44-higher fold rates (both $p < 0.05$), while BC2 shows a nonsignificant increase (1.32-fold; $p = ns$). PA-abundotypes remain stable during exacerbations while PA-interactotypes shift substantially suggesting dynamic responsiveness to acute clinical states. During PA-eradication, PA-abundotypes exhibit structured transitions reflecting treatment efficacy with HD representing an optimal pre-colistin state for highest likelihood of successful eradication, while transition to PD states is common. PA-interactotypes demonstrate no structured transition during eradication.

Conclusion: PA in bronchiectasis may be characterized by abundance and/or interactions, independent microbial traits contributing to clinical and treatment heterogeneity in bronchiectasis currently unappreciated in clinical practice. Abundotypes correlate with disease severity, symptoms, and lung function and addressed by standard therapy, while interactotypes vary during exacerbations and are not targeted by standard eradication regimes suggesting that current treatment approaches address only part (i.e. abundance) of PA biology with potential implications for antimicrobial therapeutics in bronchiectasis. Future work should assess the clinical benefit of targeting PA-interactions in addition to PA-abundance.

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ORAL COMMUNICATIONS

0005 An exploratory sputum DNA methylation analysis in patients with bronchiectasis

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Background/Aims: DNA methylation captures host exposures and regulates gene expression, overall influencing disease status. We previously reported an altered blood DNA methylation profile in severe bronchiectasis (BE). Here, we assessed whether DNA methylation is also altered in sputum.

Methods: Multicentre observational study including adult BE patients. Whole-genome sputum DNA methylation was analysed (Illumina 850k). Sputum cell proportions were estimated from methylation data. Differentially methylated regions (DMRs) associated with Bronchiectasis Severity Index (BSI) and its individual components were obtained using sex- and age-adjusted linear models. We also assessed the relevance of BSI clinical variables on methylation variability.

Results: We tested 91 patients: median age 70 IQR (64-78y), BSI 7 (6-12), 43 % chronic *Pseudomonas aeruginosa* (PsA) infection. Sputum mainly contained neutrophils (87 %), epithelial cells (6 %) and monocytes/macrophages (5 %). Before adjusting for cell composition, frequent exacerbations, FEV1 (%), chronic PsA, and overall BSI significantly contributed to methylation ($p < 0.05$). After adjustment, FEV1 (%) and chronic PsA still contributing to it. We identified 106 PsA-related DMRs mapped to 142 genes enriched in cell development pathways, and 142 FEV1-related DMRs mapped to 87 genes enriched in myeloid leukocyte activation and degranulation pathways. Most DMR-associated genes were in promoter regions.

Conclusions: Lung function and chronic PsA infection in BE patients are associated with sputum DNA methylation changes, independent of cell composition, and with potential effects on gene expression, highlighting the relevance of epigenetic alterations in BE.

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0006 Restoring near-normal F508del-CFTR function: a cell-permeable nanobody synergizes with CFTR modulators in primary airway epithelial cells from patients with cystic fibrosis

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Background/Aims: The most common cystic fibrosis (CF)-causing mutation, F508del, resides within nucleotide-binding domain 1 (NBD1) of the CFTR chloride channel. The current gold standard therapy for patients carrying at least one F508del allele is the triple combination therapy elexacaftor/tezacaftor/ivacaftor (ETI). Although ETI therapy restores F508del-CFTR function to ~50% of normal in patients, it does not stabilize the thermodynamically disrupted NBD1, and patients on ETI continue to exhibit persistent airway infection and inflammation. Furthermore, natural-history studies indicate that near-normal CFTR function is required to prevent CF-related lung disease. Here, we investigated a novel NBD1-targeting nanobody (NB1) that stabilizes F508del-CFTR and may enhance ETI efficacy, but whose functional impact has remained unclear due to challenges in intracellular delivery.

Methods: We synthesized a cysteine-containing NB1 and conjugated it to a CPP (R10) via a disulfide bond. CFBE41o- cells expressing F508del-CFTR were treated with NB1-R10, and uptake of fluorescently labeled NB1-R10 was assessed by live-cell microscopy and Western blot. Dose-response studies on the effect of NB1-R10 on F508del-CFTR function were conducted using transepithelial short circuit current (I_{sc}) measurements, quantifying CFTR inhibitor-172-sensitive I_{sc} (ΔI_{sc} CFTRinh-172) following cAMP-mediated activation. To assess CFTR maturation, Western blot analysis of whole-cell lysates was performed. Primary airway epithelial cultures were established from nasal brushings of three patients with CF homozygous for F508del. Intracellular uptake of NB1-R10 in these cultures was examined by live-cell microscopy. The effect of NB1-R10 monotherapy on F508del-CFTR function, as well as its synergism with ETI treatment, was assessed using I_{sc} measurements.

Results: Conjugation with R10 enabled dose-dependent intracellular delivery of NB1 in CFBE41o- cells, resulting in enhanced maturation and trafficking of F508del-CFTR to the apical cell membrane, and significantly enhanced F508del-CFTR channel function compared to vehicle-treated control. Furthermore, co-treatment with NB1-R10 and ETI led to a ~3.8-fold increase in F508del-CFTR function compared to ETI alone in CFBE41o- cells. In highly differentiated, patient-derived airway epithelial cultures, treatment with NB1-R10 demonstrated efficient intracellular uptake. I_{sc} measurements revealed significantly increased F508del-CFTR function compared to vehicle (ΔI_{sc} CFTRinh-172 = $-2.84 \pm 0.19 \mu A/cm^2$ vs. $-1.49 \pm 0.07 \mu A/cm^2$; $p < 0.0001$). ETI therapy alone restored F508del-CFTR function to 55% of normal levels (ΔI_{sc} CFTRinh-172 = $-23.01 \pm 1.17 \mu A/cm^2$ vs. $-41.52 \pm 5.42 \mu A/cm^2$). Notably, co-treatment with NB1-R10 and ETI significantly enhanced F508del-CFTR rescue compared to ETI alone (ΔI_{sc} CFTRinh-172 = $-36.85 \pm 1.54 \mu A/cm^2$; $p < 0.0001$), achieving ~89% of normal CFTR function.

Conclusions: Our results show that stabilization of F508del-CFTR via efficient delivery of NB1-R10 enhances the functional rescue of CFTR achieved by ETI in

airway epithelial cultures from patients with CF. This study highlights the utility of cell-permeable nanobodies for modulating protein function and underscores their therapeutic potential as next generation biopharmaceuticals for intracellular targeting.

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0007 Bronchiectasis in South America: Demographics, Clinical Characteristics and Comparison with the EMBARC European Registry

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Background/Aims: Bronchiectasis demonstrates substantial global heterogeneity in aetiology, microbiology and disease burden, yet data characterising South American populations remain scarce. The European Bronchiectasis Registry (EMBARC) has established a reference dataset for disease phenotyping in Europe ($n = 16,963$), but whether these findings apply to Latin American patients is unknown. We aimed to describe the clinical, functional and microbiological profile of patients with bronchiectasis across four South American countries and to compare key features with the EMBARC cohort.

Methods: Retrospective multicentre study of adult patients with bronchiectasis diagnosed by high-resolution computed tomography from Argentina, Peru, Paraguay and Uruguay. Data collected included demographics, aetiology, microbiology, pulmonary function, disease severity scores (FACED, E-FACED, BSI) and exacerbation history. Descriptive statistics were used. Comparisons with the EMBARC registry were performed at the aggregate level using published data.

Results: We enrolled 329 patients (age 56.6 ± 19.6 years; 69.3% female). Compared with EMBARC (67 years; 60.9% female), our cohort was significantly younger and had a higher proportion of women. The main aetiologies were post-infectious (38.0%), post-tuberculosis (30.1%) and idiopathic (28.3%). Post-tuberculosis aetiology was markedly more prevalent than in EMBARC (~4.9%), reflecting the historical tuberculosis burden in the region, while idiopathic aetiology was less frequent (28.3% vs. 38.1%). *Pseudomonas aeruginosa* was isolated in 63.8% of patients – more than double the rate in EMBARC (25.1%). Mean BMI was $24.5 \pm 5.3 \text{ kg/m}^2$. Severity scores were: FACED 3.0 ± 2.3 , E-FACED 6.2 ± 4.2 , BSI 3.1 ± 4.5 . The annual exacerbation rate was 0.60 ± 1.12 ; 13.9% experienced ≥ 2 exacerbations per year, compared with approximately 59% in EMBARC, a difference that may partly reflect retrospective data collection and varying local definitions. Inhaled antibiotics were used in 44.7% of patients, substantially higher than in EMBARC (~12–15%), consistent with the elevated prevalence of chronic *P. aeruginosa* infection.

Conclusions: This first multicentre study characterising bronchiectasis in South America reveals a distinct regional phenotype. A post-tuberculosis aetiology more than six times higher than in EMBARC underscores the need for region-specific epidemiological frameworks. The markedly elevated prevalence of chronic *P. aeruginosa* infection represents a defining feature of this population and a major driver of inhaled antibiotic use. These findings highlight the importance of developing Latin American registries and region-specific management strategies to complement global data.

0008 Epidemiology and Outcomes of Bronchiectasis in Alberta, Canada: A 15-Year Population-Based Study

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Background/Aims: Bronchiectasis is a chronic, progressive airway disease associated with recurrent exacerbations, impaired quality of life and substantial health care use. Although its burden is increasingly recognized internationally, no population-based epidemiologic study of adult bronchiectasis has been published from Canada. We aimed to define the incidence, prevalence, mortality, health care utilization, and direct health care costs of bronchiectasis in Alberta, overall and by airway disease phenotype.

Methods: We conducted a retrospective population-based cohort study using linked Alberta provincial administrative health datasets from 2010–2025 within a universal single-payer health system. Adults aged ≥ 18 years with bronchiectasis were identified using ICD-10-CA J47.x or ICD-9 494.x codes across inpatient, emergency department, and outpatient physician encounters, with cystic fibrosis excluded. Incident cases were defined using a 3-year washout period (April 1, 2007 to March 31, 2010). Patients were classified as COPD-associated bronchiectasis, asthma-associated bronchiectasis, or bronchiectasis without major airway comorbidity based on co-existing diagnostic codes. Outcomes included annual incidence and prevalence, all-cause and cause-specific mortality, respiratory-related health care utilization, complications, exacerbations, and direct health care costs. The Canadian Bronchiectasis and NTM Registry (CanBE-NTM) was used to validate study definitions. The study was approved by the University of Calgary Research Ethics Board (REB24-0209) with waiver of individual consent.

Results: We identified 12,426 adults with incident bronchiectasis (median age 67 years; 56.5% female), of whom 27% had COPD-associated disease and 13% had asthma-associated disease. Most diagnoses occurred in the outpatient setting (73.6%). Average annual incidence was 25.1 per 100,000 adults (95% CI 24.4–25.7) and remained relatively stable over time, whereas cumulative prevalence increased steadily, reaching 318.3 per 100,000 adults in 2024 (95% CI 312.7–324.0), more than double that in 2010. Incidence increased markedly with age, exceeding 100 per 100,000 among adults aged ≥ 75 years, and was higher in females across age groups. Health care burden differed substantially by phenotype. Respiratory-related hospitalization rates were 0.24 events/person-year overall and highest in COPD-associated bronchiectasis (0.62 events/person-year), with a similar pattern for respiratory-related emergency department visits (1.00 events/person-year in COPD-associated disease vs 0.28 in asthma-associated disease). Overall all-cause mortality during follow-up was 31.9%, with the worst outcomes in COPD-associated bronchiectasis, including 16.5% mortality within 1 year and 55.4% over follow-up. Mean total health care costs were \$13,393 CAD within 1 year, \$36,530 CAD over 5 years, and \$60,423 CAD over follow-up overall, rising to \$88,964 CAD over follow-up in COPD-associated bronchiectasis.

Conclusions: In this first Canadian population-based study of adult bronchiectasis, prevalence more than doubled over 15 years despite stable incidence, highlighting a growing chronic respiratory disease burden. Bronchiectasis was associated with substantial mortality, acute care use and health care costs, particularly among those with COPD overlap. These findings support improved disease recognition pathways, phenotype-specific management and health-system planning in Canada.

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0009 Sex differences in bronchiectasis – Data from the German Bronchiectasis Registry PROGNOSIS

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Background/Aims: The focus of scientific and clinical research is increasingly turning to gender differences in disease risk profiles and outcomes. These differences also exist in the context of infectious diseases, particularly in bronchiectasis (BE). Large BE registries help to highlight these differences, and this work aimed to identify differences between the sexes, in particular sex-specific risk factors for exacerbations, hospitalisation and death/transplantation.

Methods: The Prospective German Bronchiectasis Registry (PROGNOSIS) is a non-interventional registry, that collected longitudinal clinical data from adults with CT-confirmed BE. Differences between male and female patients were assessed by using Wilcoxon rank sum test, Pearson's Chi-squared test or Fisher's exact test depending on the variable and the false discovery rate (FDR) method was used to account for multiple testing. A negative binomial regression analysis was used to estimate rate ratios (RR) for hospitalization, exacerbation and a Firth's regression model for death/transplantation.

Results: 1289 patients (n = 791 female, 61.4%) were included. Median age was 63, males BMI was higher and females showed better lung function parameters (ppFEV₁ 77 vs. 65%, $p < 0.001$, ppFVC 90 vs. 78%, $p < 0.001$). Male subjects were more likely diagnosed with cardiovascular comorbidities (44.4% vs. 35.8%, $p = 0.002$), malignancies (17.5% vs. 11.0%, $p < 0.001$), diabetes mellitus (10.4% vs. 5.6%, $p = 0.001$) and COPD (30.3 vs. 18.6, $p < 0.001$), while females were more likely to suffer from osteoporosis (12.0% vs. 7.6%, $p = 0.012$). More male patients died from any cause (7.8 vs. 3.7, $p = 0.001$). Female were more likely diagnosed with idiopathic BE (31.0% vs. 24.9%, $p = 0.019$). Results of regression models showed risk-reduction for exacerbation with lower age in both sexes. An increased risk for females with BE for at least 11 years was found for frequent exacerbation and hospitalisation, whereas a lower BMI was found to decrease the risk for hospitalisations in men. Logistic regression for transplant/death revealed a higher risk with increased age, having osteoporosis and diabetes mellitus, and decreased FEV₁ only in females. Ultimately, the sensitivity analysis for the before mentioned outcomes did not yield a significant Odds Ratio (OR) for sex.

Conclusions: A number of significant disparities were identified between sexes, particularly females were more often diagnosed with idiopathic BE. Increased age, decreased FEV₁, osteoporosis and diabetes mellitus increased the risk for death/transplantation in females only. This means women should be closely monitored for their lung function and comorbidities. Validation of these sex-specific risk patterns in larger international registries of adults with BE is warranted.

Conflict of interest None

0010 Sputum microbiology in bronchiectasis and association with clinical outcomes: Data from the EMBARC registry

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Background/Aims: Patients with bronchiectasis are known to grow pathogens in their sputum during stable state and at exacerbation. Common pathogens include *Pseudomonas aeruginosa* and *Haemophilus influenzae*. Whilst *Pseudomonas* is known to be associated with an increased risk of exacerbations, hospitalisation and death, the association between other pathogens and clinical outcomes has not been previously described. This work describes the association between common pathogens grown in the sputum of bronchiectasis patients and exacerbations, hospitalisations and mortality.

Methods: Analysis was conducted of 18843 patients in the EMBARC registry. Sputum microbiology data for patients was examined, and each pathogen was coded as present or absent. A negative binomial model was used to analyse risk of exacerbations and hospitalisations for patients growing each pathogen. Cox proportional hazard regression was used to analyse risk of mortality for patients growing each pathogen. Univariate and multivariate analyses were performed with co-variables including age, gender, BMI FEV1, mMRC score, inhaled corticosteroid use, macrolide antibiotic use and inhaled antibiotics.

Results: The median age at consent in the cohort is 66 (55-74) with a female predominance (11023, 58.5%) and a median BMI of 24.4 (21.3-28.2). The most common pathogens grown were *Pseudomonas* (3175, 16.8%), *Haemophilus* (2775, 14.7%) and *Enterobacteriaceae* (1563, 8.3%) followed by *Staphylococcus*

aureus (1024, 5.4%), *Streptococcus pneumoniae* (1002, 5.3%) *Moraxella Catarrhalis* (664, 3.5%), *Aspergillus* (402, 2.1%) and *Stenotrophomonas* (311, 1.7%). On multivariate analysis, *Pseudomonas* (RR 1.27, 1.19-1.36, $p < 0.001$), *Streptococcus pneumoniae* (RR 1.24, 1.12-1.38, $p < 0.001$), *Stenotrophomonas* (RR 1.23, 1.03-1.47, $p = 0.03$), *Enterobacteriaceae* (RR 1.45, 1.33-1.59, $p < 0.001$), *Haemophilus* (RR 1.17, 1.10-1.26, $p < 0.001$) and *Aspergillus* (RR 1.43, 1.22-1.68, $p < 0.001$) are associated with an increased risk of exacerbations. Increased rates of hospitalisations were seen with *Pseudomonas* (RR 1.59, 1.44-1.75, $p < 0.001$), *Stenotrophomonas* (RR 1.56, 1.23-1.98, $p < 0.001$), and *Enterobacteriaceae* (RR 1.74, 1.54-1.97, $p < 0.001$) and a reduced rate of hospitalisation was seen with *Haemophilus* (RR 0.70, 0.63-0.78, $p < 0.001$) and *Staphylococcus aureus* (RR 0.74, 0.62-0.88, $p < 0.001$). *Pseudomonas* (HR 1.43, 1.23-1.66, $p < 0.001$) and *Enterobacteriaceae* (HR 1.43, 1.20-1.70, $p < 0.001$) were associated with an increased risk of mortality and *Moraxella* (HR 0.68, 0.50-0.94, $p = 0.02$) was associated with a reduced risk of mortality.

Conclusions: The data suggests that multiple gram negative pathogens are associated with an increased risk of poor outcomes. The data suggests similar outcomes with *Stenotrophomonas* and *Enterobacteriaceae* compared to *Pseudomonas*.

Conflict of interest None

0011 An Italian, Multicenter, Pragmatic, Randomized, Controlled Trial Assessing the Efficacy and Safety of Nocturnal Humidification Therapy in Patients With Bronchiectasis: the AIRVO-BX Study

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Background/Aims Bronchiectasis is a prototypical mucus-driven respiratory disease in which impaired mucociliary clearance leads to chronic infection, inflammation, and recurrent exacerbations. Controlling symptoms and preventing exacerbations are key goals of management. We hypothesized that nocturnal long-term humidification therapy (LHT), by improving mucus hydration and facilitating airway clearance when added to respiratory physiotherapy, may improve clinical outcomes in bronchiectasis patients.

Methods This multicentre, pragmatic, randomized, controlled, open-label study evaluated the efficacy and safety of nocturnal LHT in adults (≥ 18 years) with bronchiectasis and at least three exacerbations requiring antibiotic therapy in the 12 months prior to randomization despite optimized bronchiectasis management and respiratory physiotherapy enrolled across 16 Italian centers. Main exclusion criteria included COPD or asthma as the primary respiratory disease, cystic fibrosis, and traction bronchiectasis. Participants were randomized 1:1 from to receive nocturnal LHT (at least 4 hours/night) delivered via myAIRVO2 in addition to standard of care (SoC) daily or SoC alone, for 52 weeks. The primary endpoint was the annualized rate of bronchiectasis exacerbations (EX). Secondary endpoints included hospitalizations due to EX, QoL-Bronchiectasis Respiratory Symptom Scale, St George's Respiratory Questionnaire, Bronchiectasis Health Questionnaire, and Leicester Cough Questionnaire and adverse events.

Results Between June 20, 2019, and December 22, 2023, 130 subjects (female: 73.8%; median [IQR] age: 66.1 [53.0–73.7] years) were enrolled. Three participants did not meet inclusion criteria, leaving 127 participants for analysis: 65 were randomized to the LTHT group and 62 to the SoC group. Twenty participants did not complete the study (14 in the LTHT group and 6 in the SoC group). Reasons for discontinuation included non-adherence to LTHT (n = 2), withdrawal of consent before starting LTHT (n = 2), withdrawal of consent during the study (n = 1 in the SoC group); intolerance of LTHT (n = 5), worsening clinical conditions (n = 2 in the LTHT group), loss to follow-up (n = 5 in the SoC group and n = 1 in the LTHT group), and lack of perceived benefit (N = 2 in the LTHT group).

A 38 % reduction in exacerbations over 52 weeks was observed in the LTHT group compared to the SoC group. Overall, 89 EX occurred in the LTHT group and 139 in the SoC group, corresponding to 1.57 and 2.52 EX per patient-year, respectively (rate ratio 0.62; 95 % CI 0.44–0.88). Compared with baseline, significant improvements at 12 months were observed in the LTHT group versus the SoC group for QoL-BRSS 71.7 (66.9, 76.5) vs 60.6 (55.7, 65.4), $p = 0.002$; SGRQ 34.4 (30.6, 38.2) vs 44.1 (40.3, 48.0), $p < 0.001$; BHQ 65.2 (62.7, 67.6) vs 56.6 (54.2, 59.1), $p < 0.001$; LCQ 16.6 (15.6, 17.5) vs 14.5 (13.6, 15.5), $p = 0.003$. No serious device-related adverse events were reported. One patient in the SoC group died due to a respiratory cause. Interface-related nasal discomfort was reported by 5 patients in the LTHT group.

Conclusion Our findings support the role of nocturnal LTHT, in addition to respiratory physiotherapy in reducing exacerbations and improving symptoms and quality of life in bronchiectasis patients with frequent exacerbations.

Conflict of interest Fisher & Paykel Healthcare provided the myAIRVO2 devices along with the consumables used in this study and a Study Coordinator grant.

0012 Efficacy and Safety of Itepekimab in Patients with Non-Cystic Fibrosis Bronchiectasis

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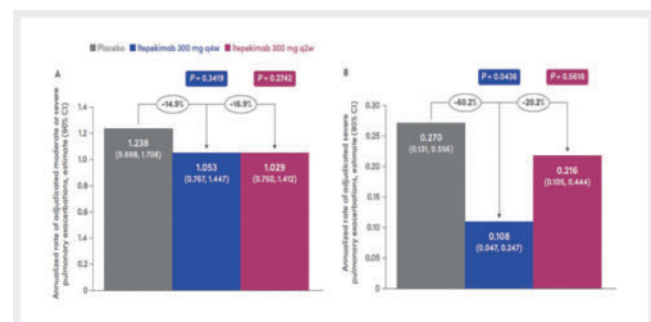
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Background/Aims: Patients with non-cystic fibrosis bronchiectasis (NCFB) often experience exacerbations that lead to declined lung function, worse quality of life, more hospitalizations, and increased mortality. Interleukin (IL)-33 is an epithelial cytokine that initiates and amplifies inflammation in response to cellular stress or damage. Itepekimab, a fully human monoclonal antibody, binds to IL-33 and inhibits its signaling. IL-33 drives both type 2 and non-type 2 inflammation, as well as mucus hypersecretion, and targets a number of pathways implicated in NCFB pathophysiology. Here, we present the results of a phase 2 trial that assessed efficacy and safety of itepekimab in adult patients with NCFB.

Methods: ACT18018 (NCT06280391) was a phase 2, randomized, double-blind, placebo-controlled, multinational trial that enrolled patients aged 18 to 85 years with a computed tomography (CT)-confirmed diagnosis of bronchiectasis and ≥ 2 moderate or ≥ 1 severe pulmonary exacerbations in the previous year. Patients received subcutaneous itepekimab 300 mg every 4 or 2 weeks (q4w or q2w) for a variable treatment period of at least 24 weeks, up to 52 weeks. The primary endpoint was the annualized adjudicated moderate or severe pulmonary exacerbation rate over the treatment period. Selected secondary endpoints included the annualized adjudicated severe pulmonary exacerbation rate (defined as requirement for hospitalization or intravenous antibiotics) over the treatment period, time to first exacerbation, least squares (LS) mean change vs placebo from baseline in pre-bronchodilator forced expiratory volume in 1 second (FEV₁), and LS mean change vs placebo from baseline in quality of life metrics (St. George's Respiratory Questionnaire [SGRQ] total score) at Week 24.

Results: In ACT18018, 314 patients were randomized to itepekimab q4w (n = 104), q2w (n = 108), or placebo (n = 102). Itepekimab vs placebo numerically reduced moderate or severe pulmonary exacerbation rates by 14.9 % (q4w; $P = 0.3419$) and 16.9 % (q2w; $P = 0.2742$) (► Fig. 1). Additionally, itepekimab vs placebo reduced severe exacerbation rates by 60.2 % (q4w; nominal $P = 0.0436$) and 20.2 % (q2w; nominal $P = 0.5618$) (► Fig. 1). At Week 24, LS mean change from baseline in pre-bronchodilator FEV₁ was 10 mL (q4w; $P = 0.7646$) and –40 mL (q2w; $P = 0.2202$) vs placebo. Week 24 LS mean change from baseline in SGRQ total score was –1.3 points (q4w; $P = 0.5378$) and –2.9 points (q2w; $P = 0.1800$) vs placebo. Itepekimab was generally well tolerated. Treatment-emergent adverse events occurred in 81.6 % (itepekimab q4w), 82.2 % (itepekimab q2w), and 82.4 % (placebo) of patients. The proportion of patients experiencing serious adverse events was similar between groups.



► Fig. 1 Annualized rate of adjudicated (A) moderate or severe exacerbations and (B) annualized rate of adjudicated severe exacerbations. Id 29142072

Conclusions: Itepekimab numerically reduced moderate or severe pulmonary exacerbation rates in adults with NCFB, and showed greatest efficacy in reducing severe exacerbations. Itepekimab was well tolerated and demonstrated an acceptable safety profile.

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0013 Improving ciliary function in DNAI1-deficient respiratory cells by mRNA therapy

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Background/Aims: Primary ciliary dyskinesia (PCD) is a rare genetic disorder characterised by dysfunctional motile cilia. The hallmark symptom is a chronic mucopurulent airway disease. Recurrent airway infections lead to irreversible lung damage (bronchiectasis), which may progress to respiratory failure. Currently, there is no causal therapy for this genetic disease and evidence-based treatment options are limited. Recently, mRNA therapy has emerged as a promising option for treating various diseases for which there is a high level of unmet medical need.

In individuals with PCD, *DNAI1* is one of the most frequently affected genes and is therefore a leading cause of bronchiectasis associated with PCD. Disease-causing variants in *DNAI1* result in a major structural defect of respiratory cilia, specifically of the outer dynein arm complex. This leads to severely reduced ciliary beating and consequently to impaired mucociliary airway clearance of affected individuals. The aim of this study was to improve ciliary function in human nasal epithelial cells from individuals with PCD due to *DNAI1*-deficiency using a selective organ targeting (SORT) lipid nanoparticle (LNP) containing an optimized *DNAI1* mRNA.

Methods: Human nasal epithelial cells were obtained *via* nasal brush biopsies and cultured at an air-liquid interface. Following differentiation into a pseudostratified epithelium *in vitro*, the cells were transfected basolaterally or *via* aerosol delivery with SORT-LNP-*DNAI1* mRNA. Ciliary function was assessed using high-speed video microscopy, and protein localisation was evaluated using high-resolution immunofluorescence microscopy with anti-DNAI1 antibodies.

Results: Following treatment with SORT-LNP-*DNAI1* mRNA, we successfully transfected *DNAI1*-deficient multiciliated cells and restored ciliary beat frequency, as demonstrated by high-speed video microscopy. Immunofluorescence analysis also confirmed the restored localisation of *DNAI1* and *DNAI1*-dependent proteins of the outer dynein arm complex, such as axonemal heavy chain dynein 5 (DNAH5), in a subset of ciliary axonemes of *DNAI1*-deficient individuals.

Conclusions: In summary, we have provided *in vitro* proof of concept for the restoration of ciliary motility in human nasal epithelial cells from individuals with PCD and disease-causing *DNAI1* variants. This supports the potential of SORT-LNP-*DNAI1* mRNA delivery as a mutation-agnostic therapeutic strategy.

Conflict of interest Research funding from ReCode Therapeutics

0014 In vitro neutrophil migration into non-CF bronchiectasis sputum imprints a dysfunctional phenotype identical to in vivo

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Background/Aims: Non-cystic fibrosis bronchiectasis (NCFBE) patients despite having diverse etiologies, follow a common disease path featuring small airway mucoobstruction, inflammation, infection and mesenchymal remodeling with loss of elastic tissue, diagnosed by X-ray or computed tomography imaging as bronchiectasis. Here, we tested the hypothesis that this common disease path is driven by the reprogramming of naïve blood neutrophils that are continuously recruited to NCFBE airways and adopt a dysfunctional phenotype therein.

Methods: Blood and sputum were collected from pediatric and adult patients with NCFBE after obtaining informed consent and cells processed for analysis by flow cytometry. In addition, airway supernatant (ASN) was generated by dual centrifugation of sputum to generate a cell- and bacteria-free fraction, which we used for immune mediator profiling (Mesoscale), and as the apical fluid in a biomimetic small airway model we previously developed to enable mass transmigration and conditioning of blood neutrophils by CF ASN [1–3].

Results: We included 21 NCFBE subjects, whose mean age of 37 years, with 71.4 % females [Table 1]. NCFBE etiology included 11 PCD and 3 idiopathic cases, with the remaining 8 attributed to CFTR mutation, IBD, GVHD, connective tissue disease, or aspiration/GERD. Infection status among the 21 patients was heterogenous, including *P. aeruginosa*, MSSA, MRSA, and multiple *Mycobacterium* species; 38.1 % of patients exhibited polymicrobial infections. Direct analysis of NCFBE sputum cells revealed a dominant presence of CD16lo, CD63hi, and CD66bhi neutrophils [Fig 1A], indicative of a loss of key phagocytic receptor concomitant with an excessive release of neutrophil elastase- and myeloperoxidase-rich primary granules and secondary granules. This phenotype was discovered in CF by our group and termed “GRIM” (for granule-releasing, immunomodulatory and metabolically active), and was found responsible for mucus induction, chronic leukocyte recruitment and bacterial tolerance. *In vitro* transmigration into NCFBE ASN of naïve blood neutrophils from either healthy control or NCFBE donors (n = 3) led to the appearance of GRIM neutrophils, signaling a dominant reprogramming effect of the airway milieu (represented by NCFBE ASN). The sputum from NCFBE patients on brensocatib was still indicative of GRIM neutrophil reprogramming suggesting that this pathological process is not fully countered by this drug. Immune mediator profiling

of NCBE sputum supernatant confirmed a pro-neutrophilic signature, featuring notably high IL- β , G-CSF and TNF α levels [Fig. 1B].

Conclusions: Combined analysis of NCFBE sputum and blood using direct immunophenotyping and the use of our biomimetic small airway model identify a pathophysiological path to blood neutrophil recruitment and GRIM reprogramming, similar to what we previously described in CF. These studies highlight key therapeutic targets and a new approach methodology to test candidate drugs in NCFBE.

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Conflict of interest None to report.

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0015 Phase 3b ENCORE study of amikacin liposome inhalation suspension in new occurrence of Mycobacterium avium complex lung infection

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Background/Aims: *Mycobacterium avium* complex lung disease (MAC-LD) is a chronic infection associated with high symptom burden, impaired health-related quality of life (HRQOL), and a 5-year all-cause mortality rate up to 42%. A substantial proportion of patients who receive multidrug therapy do not achieve treatment success, and the optimal drugs, regimens, and recommended duration of therapy for the treatment of MAC-LD have not been evaluated in specifically designed clinical studies. Additionally, most studies in MAC-LD have focused on microbiologic endpoints such as culture conversion, but experience with validated, patient-reported outcome (PRO) tools as primary endpoints is limited in this population. Amikacin liposome inhalation suspension (ALIS) is an aminoglycoside approved as part of a multidrug therapy for adults with limited or no alternative treatment options for refractory MAC-LD; it has now been evaluated in clinical trials for patients with a new occurrence of MAC-LD who have not received antibiotics. Here, we present data from ENCORE, a phase 3b, active comparator, placebo-controlled trial, which evaluated the efficacy and safety of 12 months of ALIS with multidrug therapy in adults with a new occurrence of MAC-LD who have not received antibiotics.

Methods: ENCORE (NCT04677569) was the largest (N = 425), randomized, controlled, double-blind, superiority multicenter trial to date in an adult population with noncavitary lung disease and a new or recurrent diagnosis of MAC-LD. Patients had respiratory symptoms attributable to current MAC lung infection (average Quality of Life-Bronchiectasis Respiratory Domain [QOL-B RD] score ≤ 85) and positive sputum cultures for MAC within 6 months of screening and again at screening. Patients who had received mycobacterial antibiotic treatment for their current MAC lung infection were excluded. Eligible patients were randomized 1:1 to receive ALIS 590 mg or active comparator (empty liposome control) plus azithromycin 250 mg and ethambutol 15 mg/kg (all once daily) for 12 months. The primary endpoint was the change from baseline to Month 13 in respiratory symptom score (RSS), which was derived from the QOL-B RD and validated to assess respiratory symptoms in adults with new or recurrent diagnosis of MAC-LD. Data were reported with descriptive statistics.

Results: The ENCORE study met the primary endpoint; a statistically significant improvement in RSS was observed with ALIS vs comparator (least squares mean change from baseline to Month 13: 17.77 vs 14.66; treatment difference: 3.11 points; $P=0.0299$). The proportions of patients achieving culture conversion by Month 13 and durable culture conversion at Month 15 were statistically significantly increased with ALIS vs comparator (82.4% vs 55.6% and 76.2% vs 47.6%, respectively; $P<0.0001$). Additional PROs will be presented. No new safety signals were observed.

Conclusions: The ENCORE study demonstrated superior respiratory symptom improvement and microbiological efficacy with ALIS vs comparator in patients with a new occurrence of MAC-LD who have not received antibiotics; the outcome of HRQOL measures will be presented to further characterize the clinical benefit of ALIS in MAC-LD.

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0016 Redefining Cystic Fibrosis in Chinese Patients with Bronchiectasis

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Background/Aims: Cystic fibrosis (CF) is considered rare in China, and routine screening is seldom performed in adults with bronchiectasis. Whether the apparent rarity of CF reflects true population prevalence or systematic under-recognition remains unclear. Diagnosis of CF and CFTR-related disorders (CFTR-RD) relies on clinical manifestations, sweat testing, and CFTR variant interpretation, which is largely defined by the CFTR2 project and may underrepresent non-European variants. This study aimed to define the frequency, variant spectrum, and clinical features of CF in Chinese bronchiectasis populations and to investigate mutation-specific mechanisms and therapeutic responses.

Methods: We conducted systematic CF screening in Chinese adults with bronchiectasis using clinical assessment, sweat chloride testing, and whole-exome sequencing (WES). Unclassified CFTR variants were functionally characterized through in vitro and in vivo assays, including electrophysiological analyses,

minigene assays, and evaluation of CFTR modulator responses. Patient-derived airway organoids and CFTR knock-in mice were used for mechanistic studies, and single-cell RNA sequencing was performed to assess airway epithelial cell composition and transcriptional changes.

Results: Among 1116 patients with bronchiectasis, 37 (3.4%) were diagnosed with CF (sweat chloride ≥ 60 mmol/L). WES identified 31 CFTR variants, 22 of which were absent from CFTR2. Functional analysis of CFTR protein transcription, translation, and trafficking was performed to reclassify previously unclassified variants, confirming CF in 4 additional patients (0.4%) and CFTR-related disorders in 23 (2.1%). Compared with idiopathic bronchiectasis, CF patients exhibited a younger age at diagnosis, earlier symptom onset, increased rates of malnutrition and exacerbations, and upper-lobe predominant cystic bronchiectasis with frequent NTM infection. Mechanistically, the CFTR G970D mutation, the most prevalent variant in Chinese patients with CF, impaired CFTR protein processing and function. Single-cell transcriptomic analysis further demonstrated that CFTR G970D reshapes airway epithelial cell composition by skewing basal cell differentiation toward secretory lineages and enhancing inflammatory signaling. The CFTR G970D (G965D in mice) mutation significantly exacerbated lung inflammatory responses, mucus retention, and airway dysfunction caused by chronic *Pseudomonas aeruginosa* infection, and impaired host bacterial clearance. Importantly, Elexacaftor–Tezacaftor–Ivacaftor restored CFTR chloride channel function and alleviated chronic *Pseudomonas aeruginosa* infection in G970D models.

Conclusions: This study defines the prevalence, genetic landscape, and clinical characteristics of CF in Chinese bronchiectasis populations, reveals mutation-specific pathogenic mechanisms involving epithelial remodeling and inflammation, and provides evidence supporting targeted therapeutic strategies, including CFTR modulators, for the precision management of CF and CF-related bronchiectasis in China.

Conflict of interest The authors declare no conflicts of interest.

0017 Sputum Multi-omics Integration Identifies Three Mechanistically Distinct Endotypes with Differential Exacerbation Risk in Bronchiectasis

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Background/Aims: Bronchiectasis is a clinically heterogeneous disease driven by fundamental differences in the molecular biology of the airway microenvironment. Single-omic approaches or clinical indicators alone are insufficient to capture this complexity, highlighting the urgent need for a multi-omics molecular endotyping framework that reflects distinct inflammatory mechanisms. To integrate sputum transcriptomics, proteomics, and metabolomics to identify biologically distinct molecular endotypes and elucidate their underlying mechanistic pathways, thereby providing a molecular foundation for precision stratification in bronchiectasis.

Methods: Ninety-four patients with stable bronchiectasis were enrolled as a discovery cohort. Sputum cell transcriptomics (RNA sequencing, two batches, n = 94), sputum supernatant proteomics (data-independent acquisition mass spectrometry, 10,405 proteins identified), and untargeted metabolomics (1,780 metabolites identified) were simultaneously collected, with 16S rRNA microbiome sequencing being performed on 73 paired samples. Similarity Network Fusion was applied to integrate the three omics layers, with spectral clustering used to identify molecular endotypes. Clustering stability was vali-

dated by Bootstrap resampling and subsampling-based Adjusted Rand Index. Endotype-specific molecular mechanisms were systematically characterized through differential gene expression analysis, GO/KEGG pathway enrichment, Gene Set Enrichment Analysis, single-sample GSEA, and xCell immune cell deconvolution. Cross-omics mechanistic causal chains were constructed via transcriptome-proteome, proteome-metabolome, and microbiome-metabolome correlation analyses.

Results: Similarity Network Fusion has identified three molecularly distinct endotypes with significantly different cumulative acute exacerbation (AE) incidence rates (Log-rank $P = 0.024$). The Th2-M2 polarization endotype ($n = 23$) was characterized by M2 macrophage polarization, Th2 inflammatory axis activation, enrichment of antioxidant metabolites (uric acid and γ -glutamyl-cysteine), and preserved commensal microbiota, with the strongest MRC1 transcriptome-proteome correlation among the three endotypes ($r = 0.75$, $P < 0.001$), and the lowest AE risk. Endotype 2 -- the PA-tryptophan reprogramming endotype ($n = 34$) was defined by *Pseudomonas aeruginosa* (PA) dominance (relative abundance 33.29%) driving systemic activation of the tryptophan-tryptophan metabolic axis and neutrophil effector protein degranulation. Notably, myeloperoxidase protein levels were markedly elevated without a corresponding transcriptional up-regulation (transcriptome-proteome correlation $r = 0.045$, $P > 0.05$), indicating that effector protein accumulation arises from migratory neutrophil degranulation rather than local transcriptional induction. This endotype carried the highest AE risk (HR = 2.76 vs. Th2-M2 polarization endotype, 95% CI: 1.30–5.87, $P = 0.008$). Endotype 3 -- the metabolic failure-transcriptional silencing endotype ($n = 37$) was characterized by the concurrent collapse of aerobic and anaerobic metabolism (profound negative enrichment of glycolysis and oxidative phosphorylation pathways), profound transcriptional silencing (only 32 upregulated genes), and enrichment of obligate anaerobes, providing a molecular explanation of "metabolic exhaustion" for the clinically observed structural-inflammation dissociation phenomenon.

Conclusions: Through sputum multi-omics Similarity Network Fusion integration, this study has identified three novel bronchiectasis endotypes with distinct mechanistic pathways and differential prognostic trajectories, systematically characterizing their cross-omics molecular features and causal mechanisms. These findings provide a translatable molecular foundation for precision endotyping and targeted therapeutic intervention in bronchiectasis.

Conflict of interest None declared.

POSTER PRESENTATIONS

SESSION: Allied Healthcare & Patients

0018 Identifying international research priorities for bronchiectasis

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Background/Aims: Bronchiectasis is a chronic, progressive, and increasingly recognised lung disease affecting both children and adults. Despite major ad-

vances in understanding disease mechanisms, phenotypes, and emerging therapeutics, people living with bronchiectasis continue to face delayed diagnosis, limited treatment options, and fragmented care systems. A unified, international research agenda, shaped through meaningful collaboration between consumers, carers, health professionals, and researchers, has been lacking.

The aim of this study was to collaboratively identify and prioritise the most important research questions in bronchiectasis to inform the future direction of global research efforts.

Methods: The priority setting was conducted in multiple stages using a modified James Lind Alliance framework. Stakeholders included people living with bronchiectasis, family members and caregivers, multidisciplinary healthcare professionals, and researchers.

Stage one involved an open-ended questionnaire inviting participants to identify the key research issues most important to them across five priority areas: populations at risk; early detection and diagnosis; treatment and management; bronchiectasis with comorbid and coexistent disease; and understanding mechanisms of disease. Responses were analysed using thematic analysis to identify key topics within each area.

Stage two involved two consensus workshops held at the World Bronchiectasis Conference 2025: one for consumers (patients, family members, and caregivers) and one for multidisciplinary professionals. Participants ranked the key research topics and collaboratively developed targeted research questions to inform future research.

Results: A total of 379 participants completed the questionnaire. Twenty-seven participants attended the face-to-face multidisciplinary professional workshop, and 28 participated in the consumer workshop.

A final consensus list of the top 15 research priorities was identified across the five priority areas.

The top research priorities included:

- **Populations at risk:** infectious risk factors, coexisting respiratory conditions, and early life exposures
- **Early detection and diagnosis:** clinician awareness and education, screening and monitoring tools, and early detection biomarkers
- **Treatment and management:** airway clearance and physiotherapy, access to new treatments and innovation, and self-management and patient empowerment
- **Comorbid and coexistent disease:** managing bronchiectasis alongside other respiratory conditions, integrated care for multimorbidity, comorbidity interactions and impacts on disease, medication overlap and management challenges
- **Mechanisms of disease:** inflammatory and immune mechanisms, and disease progression and clinical trajectories

Conclusions: This international priority setting partnership identified key research priorities that reflect the perspectives of people living with bronchiectasis, carers, and multidisciplinary professionals. These findings provide a clear, stakeholder-informed framework to guide future research investment, collaboration, and translation, with the potential to improve outcomes for people living with bronchiectasis globally.

0019 Learning Points from Patient Experiences of Video-Supported Recruitment: A SWAT within the BOAT Trial

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Background Enhancing patient engagement in clinical research is essential for improving recruitment, retention, and diversity within bronchiectasis trials. People living with bronchiectasis often experience substantial treatment burdens, fluctuating symptoms, and limited access to clear, accessible information about research opportunities. The UK-wide BOAT trial (Bronchiectasis: Optimising Azithromycin Therapy) investigates azithromycin deprescribing and incorporates an embedded Study Within A Trial (SWAT) evaluating a novel multilingual video animation. This SWAT aims to determine whether an accessible, patient-centred video can support understanding, improve engagement, and address barriers to trial participation.

Aim: To explore patient perspectives on receiving trial information and to evaluate the influence of a co-designed video animation on engagement and recruitment to the BOAT trial.

Methods: A mixed-methods SWAT was embedded within the host trial. The video animation was co-produced with pharmacists, clinicians, and patient contributors from Asthma + Lung UK, ensuring relevance, clarity, and lived-experience alignment. Developed iteratively with Media Borne, the animation included closed captions translated into English, Urdu, Polish, Bengali and Welsh to widen accessibility.

Trial sites alternated recruitment between: (1) paper-based participant information sheets (PIS), and (2) PIS plus video animation.

Quantitative data monitored patient demographics and recruitment rates. Semi-structured qualitative interviews explored participant experiences of receiving trial information, decision-making processes, and perceptions of the animation. Interviews were analysed using reflexive thematic analysis.

Results: Seven interviews were included in the interim analysis. Four themes were identified:

1. Impact of Living with Bronchiectasis: Participants described substantial physical and social consequences of their condition, including breathlessness, fatigue, chronic cough, recurrent infections, embarrassment, reduced activity, and loss of independence. Some reported prior misdiagnoses or diagnostic delays, shaping their desire for better understanding of the condition and, for some, strong interest in contributing to research that may support future patients.
2. Motivations for Trial Participation: Engagement was primarily driven by trust in clinicians, especially GP recommendation. Motivation to help other people, confidence in the NHS, and the prospect of closer monitoring were also strong motivators. The video animation had limited influence on the decision to participate, as many had already formed their decision before viewing it or had not viewed it during recruitment.
3. Preferences for Receiving Trial Information: While some viewed the animation as clear and quicker to understand than written documents, most preferred verbal explanation complemented by written materials for later reference. Participants expressed openness to video content if easily accessible online and suggested it may be particularly useful for younger or newly diagnosed individuals.
4. Variable Exposure and Recall of the Animation: Inconsistent integration of the video into site recruitment pathways resulted in several participants not receiving or recalling the animation. Among those who did view it, feedback was positive, describing it as reassuring, accessible, and a helpful summary—though rarely decisive for participation.

Conclusions: This interim analysis suggests that while the video animation is positively received and may enhance the accessibility of trial information, its impact on recruitment is limited without consistent clinical endorsement. Trust in clinicians remains the dominant driver of engagement in bronchiectasis trials. To maximise utility, future recruitment strategies should embed video resources directly into clinical discussions, ensure consistent site implementa-

tion, and provide early access to multimedia materials before consenting processes. These insights will inform development of patient-centred engagement tools to support inclusive participation in bronchiectasis research.

Conflict of interest The authors declare no conflict of interest.

0020 Early Real-World Experience with Brinsupri† on Airway Clearance and Clinical Symptoms in Bronchiectasis

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Background/Aims: Bronchiectasis management is traditionally centered on addressing impaired mucus clearance and chronic inflammation with breathing techniques and airway clearance techniques (ACTs). The introduction of Brinsupri[®], a targeted anti-inflammatory shown to decrease exacerbations is unclear on its potential role on mucus characteristics for this population. This study evaluates early real-world experiences with Brinsupri[®]; detailing changes in symptoms and mucus production, while assessing the synergistic and continued role of ACTs in a combined regimen.

Methods: An online cross-sectional survey was shared via social media platforms to bronchiectasis patients (N = 333). Analyses were descriptive, focusing on a subset of 48 patients currently prescribed Brinsupri[®] to assess changes in clinical status and ACT habits.

Results:

- **Dosing:** 80 % of users are on 25 mg once daily with 55.1 % using for 3-6 months, 24.50% using for 1-3 months.
- **Symptoms:** Reported improvements include reduced cough (43.8 %), fewer flare-ups (41.7 %), and improved energy (41.7 %).
- **Mucus Rheology:** 37.5 % reported reduced mucus production, while 25.0% found mucus thinner or easier to clear.
- **ACT Perception & Synergy:** ACT feels "easier" for 43.8 % of users. However, 81.3 % maintained their original ACT routine, and 83.3 % reported total daily clearance time stayed the same.
- **OPEP Value:** Aerobika® OPEP use remained unchanged for 69.4 % of users. Key benefits cited include easier mucus clearance (59.7 %) and feeling lungs are "clearer" post-treatment (45.4 %).
- **Preventive Commitment:** **84.3 %** of patients would continue OPEP use preventively even if symptoms significantly improved.

Conclusions: Brinsupri[†] offers significant clinical gains, yet, from the patient feedback in this survey, it does not routinely replace the need for mechanical clearance. The medication enhances ACT by self-reported reduction in mucus production and making it easier to clear, but the high self-reported adherence to the Aerobika[®] OPEP device underscores its essential, synergistic role in maintaining bronchial hygiene alongside pharmacological advancements.

Conflict of interest Judy Schloss and Dominic Coppolo are employees of Monaghan Medical Corporation. Linda Esposito is the owner of her consulting business "BE Clear with Bronchiectasis. Jason Suggett is employed by Trudell Medical.

0021 Redefining Bronchiectasis Care: What Patients Experience in a CF-Inspired Multidisciplinary Clinic

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DOI 10.1055/s-0046-1826036

Background Bronchiectasis is a chronic respiratory condition requiring long-term medical management, airway clearance, nutritional optimisation, and patient education to support self-management and reduce exacerbations. In

cystic fibrosis (CF), multidisciplinary team (MDT) clinic models are well established and have demonstrated benefits in care coordination, patient education, and treatment adherence. Bronchiectasis shares many clinical and self-management challenges with CF, including chronic infection, sputum burden, complex medication regimens, and the need for regular allied health input. Translating CF MDT models to bronchiectasis care may therefore address similar unmet needs; however, patient satisfaction with such models in bronchiectasis has not been well described.

Aim To evaluate patient satisfaction with a bronchiectasis MDT clinic explicitly modelled on established CF MDT clinics, with a focus on nursing and allied health contributions to education, self-management, and continuity of care.

Methods Patients attending a dedicated bronchiectasis MDT clinic were invited to complete a patient satisfaction survey following their appointment. The clinic structure was intentionally based on the CF MDT framework, providing coordinated, same-day access to a respiratory specialist physician, nurse practitioner, respiratory physiotherapist, and dietitian. Care focused on patient-centred education regarding bronchiectasis, airway clearance techniques, nutritional assessment, medication optimisation, and the development and reinforcement of individualised exacerbation action plans. Survey domains included disease understanding, confidence in self-management, medication access and adherence, and overall satisfaction with MDT care.

Results Patients reported high levels of satisfaction with the MDT clinic model. Education delivered by nursing and allied health staff improved patient understanding of bronchiectasis and its chronic nature. Physiotherapy input increased confidence in airway clearance techniques, while dietetic review supported nutritional optimisation and management of weight and energy balance. Nurse practitioner involvement was highly valued for continuity of care, reinforcement of action plan use, and facilitation of streamlined access to repeat prescriptions. Patients reported improved medication adherence and increased confidence in recognising and responding to exacerbations.

Conclusion A bronchiectasis MDT clinic modelled on established CF care frameworks is associated with high patient satisfaction and perceived improvements in education, self-management, and medication adherence. Nursing and allied health professionals play a central role in delivering coordinated, patient-centred care. Adapting CF MDT models to bronchiectasis represents a practical and effective approach to addressing the complex needs of this population

Conflict of interest Nil

0022 Prevalence, clinical effects and treatment options for urinary incontinence in people with bronchiectasis: a systematic review

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Background/Aims: Urinary incontinence is a recognised comorbidity of people with bronchiectasis, but the prevalence, clinical impact and treatment options for management in this population are unclear. This study aimed to establish the prevalence of urinary and faecal incontinence, the measurement tools used to assess presence, the clinical impact and breadth of treatment options.

Methods: A search of five electronic databases (Medline, Embase, CINAHL, Pubmed and Web of Science) was undertaken in December 2024 and updated in September 2025. All study designs were of interest. Two independent reviewers undertook screening, risk of bias assessment and data extraction.

Results: Of the 1825 studies screened, five met the inclusion criteria (n = 246 patients), with the majority (80%) reporting on adult females with bronchiectasis. The pooled prevalence of urinary incontinence was 44% (95% CI 32% to 57%). Faecal incontinence was not reported. A mix of measurement tools were

used to assess the presence of incontinence. One study reported the duration of symptoms, with 88 % and 40 % of patients experiencing symptoms for greater than 5 years or greater than 10 years respectively. Cough-induced incontinence was observed, together with a negative impact on quality of life, with substantial impairment. A mix of interventions were applied: 1) Pelvic floor exercises (2 studies); 2) Bladder retraining (1 study); or an unspecified intervention (2 studies); between 25 % and 68 % of patients reported improvement in symptoms following these interventions.

Conclusions: The prevalence of urinary incontinence in bronchiectasis and negative clinical impact supports the need for consistent screening and implementation of treatment options in people with bronchiectasis. A greater understanding of this comorbidity may be furthered by use of standardised assessment tools.

Conflict of interest None

0023 Telehealth healthcare delivery in adults with bronchiectasis: a systematic review

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Background/Aims: Adults with bronchiectasis require specialist management from healthcare providers and this clinical care may be delivered via telehealth. This review aims to examine the feasibility and clinical effectiveness of telehealth as a mode of delivery in adults with bronchiectasis.

Methods: Five electronic databases were searched for eligible studies (randomised, non-randomised controlled trials and uncontrolled interventional studies) investigating telehealth interventions delivering healthcare to adults with bronchiectasis. Data on measures of feasibility (uptake, adherence, adverse events), satisfaction and clinical effects (health-related quality of life (HRQOL), symptoms) were extracted. Best evidence synthesis was reported as effect size (*d*) or mean difference (MD, 95 % confidence interval).

Results: Nine studies were included (one randomised controlled trial, one non-randomised controlled trial and six uncontrolled trials; total *n* = 156 participants). Interventions delivered were pulmonary rehabilitation (*n* = 4 studies), physical activity/exercise (*n* = 1 study), airway clearance therapy (*n* = 3 studies) and multidisciplinary interventions following emergency department presentations (*n* = 1 study). Studies reported high adherence to interventions (75 to 100 %), high patient satisfaction (81 to 100 %) with no intervention-related adverse events. Telehealth pulmonary rehabilitation (*n* = 49 participants) demonstrated improvements in HRQOL with small to large effect sizes at end-intervention (Chronic Respiratory Questionnaire domains: *d* range 0.23 to 1.78). There were mixed effects on anxiety and depression with negligible to large effect sizes at end-intervention (Anxiety [*d* range 0.0 to 1.1]; Depression [*d* range 0.04 to 0.71]). Airway clearance therapy via telehealth improved HRQOL at 12-weeks measured with St George's Respiratory Questionnaire impact domain (-5.9 [-11.9 to 0.0]) and total score (-5.8 [-10.8 to -0.9]); and the Quality of Life-Bronchiectasis vitality (0.8 [0.2 to 1.5]) and treatment burden (0.9 [0.1 to 1.8]) domains.

Conclusions: Telehealth pulmonary rehabilitation and airway clearance interventions are safe, feasible and may be clinically effective for adults with bronchiectasis. There are few data on telehealth delivery of other healthcare interventions for adults with bronchiectasis.

Conflict of interest None

0024 Telehealth physiotherapy for adults with bronchiectasis: a controlled trial

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Background/Aims: Physiotherapy-led airway clearance therapy, exercise therapy and self-management improves outcomes in people with bronchiectasis, however access to specialised respiratory physiotherapy is limited. This pilot study aimed to establish the feasibility and clinical effects of a telehealth physiotherapy model of care for people with bronchiectasis.

Methods: Adults with bronchiectasis were recruited from two tertiary hospitals. Participants self-selected the intervention or the control group in this parallel group controlled study. Over 12 months, the intervention group received four telehealth physiotherapy sessions which included airway clearance therapy, exercise advice and/or pulmonary rehabilitation referral and self-management education in addition to usual medical care while the control group received usual care only. Evaluation was based on the RE-AIM framework which measured Reach (uptake, program completion), Effectiveness (health-related quality of life [Leicester cough questionnaire (LCQ), Quality of Life-Bronchiectasis (QOL-B)]), Adoption (preference, patient experience and perceptions via semi-structured interviews), Implementation (fidelity, goal achievement) and Maintenance (individual: participant program engagement; and organisational: ongoing offer of telehealth physiotherapy service).

Results: 21 of 123 eligible participants were recruited (18 intervention; 3 control) with a median (IQR) age of 64 (54 to 74) years and a median (IQR) Bronchiectasis Severity Index of 7 (4.0 to 9.5). A total of 17 out of 18 participants completed the *a priori* number of sessions. Between-group analysis was not possible for HRQOL measures due to disparity in group sizes. The within-group analysis for the intervention group showed improvement in all LCQ domains and total score (all *p* < 0.05) and improved QOL-B physical function (MD -15.4; 95 % CI [-28.2 to -2.7]), emotional function (-8.3 [-15.9 to -0.7]) and respiratory symptoms (-13.6 [-22.8 to -4.5]). Participant self-selection of group allocation showed a clear preference for telehealth compared to usual care. Patient interviews revealed that preconceived ideas of telehealth physiotherapy was influenced by prior experience; skilled clinicians, individualised tailored care and workable technology drives acceptance of the model; telehealth is a convenient model of physiotherapy delivery and is a viable option when support for delivery is offered. Fidelity of assessment and treatment was greater than 90 % for 10/17 items. A high rate of participant goals were achieved (88 to 100 %). Approximately 85 % of participants reported ongoing engagement with an airway clearance routine at 12 months. One of the two sites provided funding for staffing and equipment to expand the service on an ongoing basis.

Conclusions: Telehealth physiotherapy appears to be a feasible option for clinical care but further clarification is required to determine the clinical impact of this service.

Conflict of interest None

0025 Pediatric to adult transition pathway in a PCD Clinic: impacts on patients and their families

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DOI 10.1055/s-0046-1826040

Background/Aims: Primary ciliary dyskinesia (PCD) is a rare genetic disease that has been underdiagnosed. New technology has allowed for increased awareness and earlier diagnosis of the disease, leading to positive effects on long-term health. However, in British Columbia (BC) there are no specialized adult PCD clinics to support the transition of pediatric patients into adult care. The PCD clinic at BC Children's Hospital (BCCH) follows 59 children between

16 months – 22 years old. Previously, individuals with PCD were followed by primary care providers after they aged out of the pediatric system. If no provider was in service, young adults remained in pediatric care. Therefore we tested a transition pathway in patient's representative of key age groups (► Table 1).

► Table 1			
	Mia: 12-14 yrs	Ava: 15-16 yrs	Ian: 19 – 24 yrs
Key findings	Able to ask questions	Engaged, beginning to show independence in therapies	Invested in results/ outcomes of appointments
Challenges	Describing rationale for specific therapies	Logistics regarding cleaning equipment or picking up prescriptions	Gaining independence from parents
Qualitative response	<i>“As she has grown over at the age of 8, it’s made a difference to talk to her not like a little kid, but trying to explain more the condition and what it means. Having the team speak to her versus parents makes a huge difference. The team can use layman terms to explain exactly what it means and it’s super helpful. It’s hard for me (mom) to explain things.”</i>	<i>“Fear around my PCD diagnosis is not a vulnerability, rather it is an opportunity for me to embrace curiosity as my greatest power.”</i>	<i>“PCD has impacted my life and it’s something that I can’t change, but with the consistent support of my PCD team and my family, I feel confident in maintaining my health as I move into adult care.”</i>

Methods: A quality improvement project was undertaken to develop a transition pathway for pediatric patients with PCD and Bronchiectasis. The pathway focused on three areas:

- Understanding PCD
- Managing PCD
- Living with PCD

This pathway was implemented into our clinic in 2025 and has been used in ages 12 – 22 years. An informal survey was distributed across three age groups: 12 – 14 years ‘Mia’, 15 – 16 years ‘Ava’, and 19 – 24 years ‘Ian’ (post transition).

Results: The pathway highlight’s themes that are specific to PCD with respect to symptomology and pathophysiology.

Conclusions: Feedback from patients supports the importance of implementation of transition pathways in PCD clinics due to the nuance of the disease and multi-faceted needs of this patient population and further data will be collected.

The survey highlights teaching focuses on increasing time dedication are the following areas: navigating the health care system, accessing results, and understanding long-term impacts.

Challenges in our clinic continue to be that there is no accredited adult service to transition patients to, which is important for continuity of care and ensuring strong attachment to adult services. Positive impacts are demonstrated by both patients and their caregivers.

Conflict of interest None.

0026 Real-World Airway Clearance Practices in Bronchiectasis- A Patient Reported Survey

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DOI 10.1055/s-0046-1826041

Background/Aims: Bronchiectasis is characterized by impaired mucociliary clearance, inflammation, chronic infection, and progressive airway damage, forming a self-perpetuating “vicious vortex.” Airway clearance techniques (ACTs) are time-intensive but remain central to management. This study aimed to quantify real-world ACT burden perception and evaluate current ACT practices, and the specific role of Oscillating Positive Expiratory Pressure (OPEP) therapy in maintaining respiratory health.

Methods: A cross-sectional, patient-reported survey (shared via social media platforms) of individuals with bronchiectasis (N = 333 with 95.8 % female; 71.2 % aged 60–79) was conducted in March of 2026. Participants reported on their demographics and clinical background, existing comorbidities, current ACT methods, treatment frequency, escalation and care practices.

Results:

Treatment Burden: Over 51 % of respondents spend more than 45 minutes daily on ACT, with 52.6 % performing clearance twice daily every day of the week.

Adherence & OPEP Utility: 83.2 % currently use an OPEP device. Despite the time burden, 75.8 % use their OPEP device 5–7 days per week. Adherence is high, with 56.7 % of users skipping sessions “rarely” or “never”.

Modality Preference: Nebulized saline (85.3 %) and OPEP devices like the Aerobika® (78.7 %) are the most frequently used methods.

Escalation of Care: Only 26.1 % of the participants had a written action plan for symptom flares, but 55.0 % reported increasing saline nebulization and 52.6 % increased Aerobika® OPEP use during a flare.

Aerobika® OPEP users provided clinically meaningful benefits, including easier mucus clearance (59.7 %), increased mucus expectoration (44.3 %), and a subjective sense of lung clearance (45.4 %).

Preventive Value: Notably, 84.3 % of patients indicated they would continue using their OPEP device preventively even if their symptoms were significantly improved.

Conclusions: The burden of ACT in bronchiectasis remains high, requiring significant daily time commitments. The Aerobika® OPEP device is a favored, highly utilized tool that patients view as essential for long-term maintenance, demonstrating a strong perceived need for continued preventive clearance regardless of symptomatic status. These findings support the continued central role of nebulized saline and OPEP therapy as a foundational component of bronchiectasis management.

Conflict of interest Judy Schloss and Dominic Coppolo are employees of Monaghan Medical Corporation. Linda Esposito is the owner of her consulting business ‘BE Clear with Bronchiectasis. Jason Suggett is employed by Trudell Medical.

0027 Living Life with Bronchiectasis: A patient experience survey from the LiveBE study

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DOI 10.1055/s-0046-1826042

Background/Aims: LiveBE set out to improve our understanding of how the lives of people with bronchiectasis are changed by their disease. This study aimed to take a holistic view of the patient with bronchiectasis; to help guide our clinical understanding of their needs and in turn aim to improve the lives of patients with bronchiectasis.

Methods: Initial question design was from clinicians working with patients with bronchiectasis. This was built upon by a review of the literature and devel-

oped through consultation with 3 patients with bronchiectasis. Following ethical approval our questionnaire was distributed by post to patients whom have expressed an interest in taking part in research and recruitment also took place through clinics and posters.

The questionnaire was predominately quantitative in nature with an open question at the end. It was divided into sections including: basic demographics, time to diagnosis and current symptom burden via the CAAT score; how living with bronchiectasis affects home life, outdoor life, social and relaxation, mental health, the health professional relationship, work and non-respiratory symptoms. The average time taken to complete was 15 minutes and 34 seconds.

Results: At the time of writing we report preliminary results from 98 patients with an average age of 72 years; 62 % were female and 38 % male. 41 % of those questioned reported symptoms for over 10 years yet only 22 % of those had a diagnosis for over 10 years. 69 % of patients reported they felt they had control of their bronchiectasis "all" or "most" of the time, 32 % felt their ability to control their bronchiectasis had improved over time. 21 % had regular contact with children under the age of 5. 64 % of these reported that these interactions either had "no" or "a positive" impact on their bronchiectasis. Regarding changes to daily home life the majority of people had not had to alter their home or their diet, however, 48 % had changed their social activities; the main reason stated was "because symptoms made the activity difficult". 73 % of patients reported that they intentionally exercised to increase their heart rate with 70 % of this group finding this had a positive impact on their bronchiectasis. 30 % reported their bronchiectasis had impacted their mental health with "anxiety- future worry" the most commonly reported. 44 of our patients reported some urinary incontinence; 33 were female and 11 male, similar to the overall split. Both stress and urge incontinence symptoms were reported. Of these only 40 % have discussed this with a medical professional and 30 % have been offered treatment. Recurring themes from our open question "if there was one thing you could change about your health" were to have healthier lung function and more energy.

Conclusions: Key outcomes for further exploration include how to help patients feel more in control of their disease, how to support and promote healthy exercise opportunities and to encourage patients to discuss all symptoms that may be interlinked with bronchiectasis not just respiratory.

Conflict of interest None

SESSION: BASIC SCIENCE 1

0028 Early Insights into Immunological and Transcriptomic Signatures Related to Radiological Severity in Nontuberculous Mycobacterial Pulmonary Disease (NTM-PD)

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DOI 10.1055/s-0046-1826043

Background/Aims: Neutrophils may play a role in controlling non-tuberculous mycobacterial (NTM) infection, but they are also implicated in host tissue damage such as bronchiectasis. Nontuberculous mycobacterial pulmonary disease (NTM-PD) is clinically heterogeneous, and current tools for assessing severity-

ty-such as symptoms, sputum smear status, blood biomarkers like CRP, and radiological findings-lack sensitivity and are prone to variability. Radiology, particularly chest CT scans, is commonly used to assess disease extent (e.g., bronchiectasis), but for safety reasons, cannot be performed frequently. Therefore, there is a need for simple, non-invasive biomarkers to predict disease severity, treatment response, or progression if left untreated.

Methods: This observational study was conducted at the Grove Centre, Royal Free Hospital, London. Ethical approval was obtained from the NHS Research Ethics Committee, and all participants provided informed consent. I assessed neutrophil-related proteins (including neutrophil elastase, MMP-8/9, S100A8/A9, and HNP1-3) and humoral immune response indicators (serum and sputum IgG and specific IgA antibodies) in adults with NTM-PD. Whole-blood transcriptomic analysis identified gene expression profiles associated with radiological severity. Validated CT scoring was used to assess the severity of bronchiectasis. Health status was evaluated using standardized questionnaires for respiratory symptoms and quality of life.

Results: I examined the relationship between neutrophil markers, humoral immune response indicators, and health status with radiological lung disease severity. Radiological severity positively correlated with serum levels of neutrophil elastase, S100A8/A9, MMP-8/9, and anti-GPL-core IgA antibodies. Transcriptomic profiling revealed gene-expression trends that aligned with findings related to neutrophil and humoral immune responses. *KANSL1* and *PLEKHM1* were upregulated in patients with higher CT scores, while *IER3* was more expressed in those with milder disease.

Conclusions: This study provides novel insights into immunological and transcriptomic markers that may reflect disease severity in NTM-PD. Further validation in larger, multi-centre longitudinal studies is required to confirm these associations and guide biomarker-based treatment approaches.

Acknowledgment: This work was conducted as part of a PhD research project sponsored by King Saud University, Riyadh, Saudi Arabia, and the Cultural Bureau of the Royal Embassy of Saudi Arabia in the United Kingdom.

Conflict of interest : The authors declare no conflicts of interest.

0029 Feasibility and Safety of Outpatient Parenteral Antibiotic Therapy (OPAT) in Adults with Cystic Fibrosis, Bronchiectasis, Primary Ciliary Dyskinesia and NTM Pulmonary Disease – a Single-Center, Retrospective Cohort Study

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Introduction: Outpatient parenteral antibiotic therapy (OPAT) is an established alternative to inpatient care for adults with cystic fibrosis (CF) requiring intravenous antibiotics who are clinically stable or stabilized after initial hospitalization. While port-a-caths and peripherally inserted central catheters (PICC) were traditionally used, midline catheters have become first-line at our institution. Indications have recently expanded to include bronchiectasis, primary ciliary dyskinesia (PCD), and nontuberculous mycobacterial pulmonary disease (NTM-PD).

Objective: To evaluate the feasibility and safety of OPAT across different indications and vascular access types.

Methods: We retrospectively analyzed adults with CF, bronchiectasis, PCD, or NTM-PD who received ≥ 1 OPAT course between September 2016 and October 2025. Data included demographics, clinical status, microbiology, treatment details, catheter type, adverse events (AE), early discontinuation, and 30-day hospital (re-)admission. Data were stored in a FileMaker Pro database and ana-

lyzed descriptively using SPSS. Group differences were assessed with chi-squared and Kruskal–Wallis tests ($p < 0.05$).

Results: A total of 602 OPAT courses in 233 patients were analyzed, corresponding to 22.2 inpatient years. CF patients were younger (median 26 years) than those with PCD (36), bronchiectasis (57), and NTM-PD (62). *Pseudomonas aeruginosa* was the most common pathogen (64%). Median OPAT duration was 10 days for CF, bronchiectasis, and PCD, and 37 days for NTM-PD ($p < 0.001$). AE rates were highest in NTM-PD (48%), compared to CF (10%), bronchiectasis (8%), and PCD (14%) ($p < 0.001$), driven mainly by ototoxicity, catheter occlusion, and gastrointestinal symptoms. Early discontinuation (4%) and hospital (re-)admission (0.8%) were low overall. PICC was most commonly used (52%), followed by port-a-cath (29%) and midline (18%). AE rates showed a non-significant trend toward higher incidence with midlines (17%) versus PICC (12%) and port-a-cath (7%) ($p = 0.072$), primarily due to catheter occlusion. Early discontinuation was also higher with midlines (8%) compared to PICC (4.2%) and port-a-cath (0.6%) ($p = 0.009$). Hospital (re-)admission did not differ by access type.

Conclusion: OPAT is feasible and safe across chronic respiratory diseases. Higher catheter-related complications with midlines highlight the need for careful patient selection and targeted education on catheter management.

Conflict of interest Felix C. Ringshausen reports participation on an advisory and trial boards for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmid, Parion Sciences, and Sanofi; clinical trial participation for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmid, Parion Sciences, Ruhr University-Bochum, University of Dundee and Vertex Pharmaceuticals; research grants from German Center for Lung Research (DZL), German Center for Infection Research (DZIF), Mukoviszidose Institute, Novartis and Insmid; and has provided speaker services for Boehringer Ingelheim, Cliniqo GmbH, iIDE Werbeagentur GmbH, Insmid, med update GmbH and Sanofi; leadership or fiduciary roles as co-chair of the German Bronchiectasis Registry PROGNOSIS, member of the steering committee of the European Bronchiectasis Registry EMBARC and PI of the German Center for Lung Research.

0030 Mucus is hyperconcentrated in children with bronchiectasis compared to healthy children

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Background/Aims: Abnormal mucus accumulation plays a key role in bronchiectasis pathophysiology. Recent studies have characterised mucus hyperconcentration and altered rheological properties in adults with bronchiectasis, but mucus properties have not been investigated in children with bronchiectasis. Our aim was to measure mucus concentrations and biophysical properties, and explore relationships with immune cells, bronchiectasis aetiology, age, lung function and respiratory symptoms.

Methods: We prospectively collected induced sputum samples from children and adolescents with bronchiectasis ($n = 35$; mean 11.2, SD 3.4 years; 54% male) and healthy children ($n = 9$, mean 8.6, SD 3.8 yrs; 56% male). Mucus concentration (a measure of mucus percent solids) was calculated by measuring dry-to-wet ratio in triplicate using an ultramicrobalance (Mettler Toledo). Elastic and viscous moduli of sputum were determined by cone and plate rheology (TA Instruments). Total immune cells in sputum were quantified by trypan

blue cell counts. We prospectively performed spirometry and multiple breath washout lung function and assessed self-reported symptom data in children with bronchiectasis through the Bronchiectasis Exacerbation and Symptom Tool questionnaire.

Results: Children with bronchiectasis had higher mucus concentrations (1.42, SD 0.84) compared to healthy children (0.74, SD 0.20; Wilcoxon rank-sum; $p = 0.007$). Mucus concentration correlated with elastic modulus (Spearman $r_s = 0.47$, $p = 0.002$), viscous modulus ($r_s = 0.47$, $p = 0.002$) and complex viscosity ($r_s = 0.44$, $p = 0.003$). Immune cells strongly correlated with mucus concentration ($r_s = 0.88$, $p < 0.001$). Mucus concentration was heterogeneous and evenly spread amongst the different bronchiectasis aetiologies. Mucus concentration correlated with age in children with bronchiectasis ($r_s = 0.55$, $p < 0.001$) but not in healthy children. In the bronchiectasis cohort, mucus concentration correlated with lung clearance index z-scores ($r_s = 0.34$, $p = 0.046$) and respiratory symptoms ($r_s = 0.35$, $p = 0.04$), but not with FEV₁ z-scores ($r_s = 0.23$, $p = 0.20$).

Conclusions: Mucus is hyperconcentrated in children with bronchiectasis and may contribute to disease pathophysiology and clinical burden. Patient-reported respiratory symptoms may help to identify children who could benefit most from mucus-targeted therapies [1].

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Conflict of interest Nil relevant

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0031 Evaluation of Serum Azurocidin (AZU-1) as a potential biomarker of disease activity and predictor of exacerbations in adults with bronchiectasis: Data from the German Bronchiectasis Registry PROGNOSIS

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Background: Azurocidin (AZU-1) is a neutrophil-derived glycoprotein stored in azurophilic granules together with proteinase 3 and neutrophil elastase. It exhibits cytotoxic activity against gram-negative bacteria and contributes to monocyte recruitment. Previous studies have suggested a potential role for AZU-1 as a biomarker of disease activity and exacerbation risk in pulmonary diseases. Since neutrophilic inflammation is a central driver of bronchiectasis progression, AZU-1 may serve as a marker of dysregulated neutrophil activity in this disease. In contrast to sputum-based assays, which are often limited by sample availability and variable quality, serum biomarkers are readily accessible and suitable for routine clinical use. We therefore evaluated AZU-1 as a serum biomarker of disease activity and future exacerbations in adults with bronchiectasis and compared its performance with C-reactive protein (CRP) and interleukin-6 (IL-6).

Methods: Serum samples from 392 adults with bronchiectasis enrolled in the German Bronchiectasis Registry PROGNOSIS (ClinicalTrials.gov: NCT02574143; ethics approval: 6656/2015) were analyzed. Samples were collected at the baseline visit and stored in the Hannover Unified Biobank. Serum concentrations of AZU-1 (ELISA, Thermo Scientific, lot 2474091024), CRP (ECLIA, Roche, lot 864924), and IL-6 (ECLIA, Roche, lot 802128) were measured and linked to the corresponding clinical registry data. Baseline characteristics were analyzed descriptively. Group differences were assessed using the Kruskal-Wallis test, and associations between biomarkers and clinical variables were explored using Spearman's rank correlation analysis.

Results: Disease severity was heterogeneous, with 35.5 % of patients classified as having mild, 34.2 % moderate, and 30.4 % severe disease according to the Bronchiectasis Severity Index (BSI). Radiologically, 68.4 % showed involvement of at least three lobes or cystic bronchiectasis. Chronic sputum production was reported by 74.7 % of patients, and 39.4 % had chronic *Pseudomonas aeruginosa* infection. In exploratory analyses, CRP and IL-6 demonstrated consistent correlations with measures of disease activity and severity, including BSI (CRP: $r = 0.339$; IL-6: $r = 0.327$; $p < 0.01$), mMRC dyspnea score, and exacerbation frequency. Both biomarkers were also inversely associated with lung function (ppFEV1 and ppFVC) and several domains of health-related quality of life. By contrast, AZU-1 showed weak or no significant associations with most clinical parameters. AZU-1 showed a significant inverse correlation with age ($r = -0.138$) and, in contrast to CRP and IL-6, a significant positive correlation with exacerbations during follow-up ($r = 0.180$); however, both effect sizes were small.

Conclusions: AZU-1 appears to have limited value as a standalone serum biomarker of disease activity in bronchiectasis, whereas CRP and IL-6 remain more closely associated with established clinical measures. However, the observed relationship between AZU-1 and future exacerbations warrants further investigation. Prospective studies incorporating longitudinal sampling are required to evaluate the potential of AZU-1 as a prognostic serum biomarker.

Conflict of interest Raphael Ewen reports clinical trial participation for Boehringer Ingelheim and Insmed; research grants from German Center for Lung Research (DZL); speaker services for Boehringer Ingelheim and iIDE Werbeagentur GmbH. Felix C. Ringshausen reports participation on an advisory and trial boards for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmed, Parion Sciences, and Sanofi; clinical trial participation for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmed, Parion Sciences, Ruhr University-Bochum, University of Dundee and Vertex Pharmaceuticals; research grants from German Center for Lung Research (DZL), German Center for Infection Research (DZIF), Mukoviszidose Institute, Novartis and Insmed; and has provided speaker services for Boehringer Ingelheim, Cliniqo GmbH, iIDE Werbeagentur GmbH, Insmed, med update GmbH and Sanofi; leadership or fiduciary roles as co-chair of the German Bronchiectasis Registry PROGNOSIS, member of the steering committee of the European Bronchiectasis Registry EMBARC and PI of the German Center for Lung Research.

0032 Impact of geographic and climatic variables and environmental atmospheric pollutants on pulmonary NTM infections: an Italian nationwide case-control study

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Background/Aims: Nontuberculous mycobacteria (NTM) are environmental pathogens that may cause pulmonary disease. The impact of geographic and climatic variables, as well as environmental pollutants, on the development of NTM pulmonary disease (NTM-PD) remains largely unknown. The aim of this study was to assess whether NTM-PD is associated with geographic and climatic parameters and exposure to environmental pollutants (PM2.5, PM10, ammonia, CO, NO2, NO, nonmethane VOCs, O3, total elemental carbon, peroxyacyl nitrates, SO2 and dust).

Methods: We conducted a case-control study evaluating meteorological, geographic conditions and pollutant concentrations during the 12 months before the first NTM isolate in the municipalities of residence of 1,296 adults with NTM-PD enrolled in an Italian multicenter observational study (2017–2024). These cases were compared with a random sample of 6,480 adults from the general population.

Results: Patients with NTM-PD more frequently resided in areas characterized by higher concentrations of most pollutants, with the exception of dust (Figure 1). Conversely, O3 concentrations were significantly lower in the areas of residence of NTM patients. Densely populated areas and those located farther from coastal regions were associated with a higher risk of NTMPD. Hotter climates with limited ventilation were also associated with an increased risk of NTM infection.

Conclusions: environmental pollution, climate change, urbanization, and distance from coastal regions may adversely influence the risk of NTM infection.

Conflict of interest this study was supported by an unrestricted grant by Insmed

0033 STAKEHOLDER ACCEPTABILITY OF PATIENT-DERIVED ORGANOIDs FOR PERSONALISED MEDICINE IN CYSTIC FIBROSIS

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Background/Aims: Patient-derived organoids are emerging as powerful human-relevant models for disease modelling, drug discovery and personalised medicine. In cystic fibrosis (CF), organoid-based functional assays can directly measure CFTR activity and predict responses to CFTR modulator therapies. Similarly, in rare childhood cancer, patient-derived organoids are increasingly used to characterise tumour biology and predict individual patient treatment response. As these technologies move toward translational and clinical implementation, understanding the perspectives of healthcare professionals and scientists who may adopt them is important. We therefore evaluated acceptability of organoid-based approaches in CF and related disease research in these stakeholders.

Methods: A cross-sectional online questionnaire study was conducted to assess attitudes towards organoid technologies in research and clinical settings. The survey was adapted from our previous work assessing the views of people living with CF [1]. Acceptability was assessed across three domains: willingness to use organoids, perceived impact on patient outcomes, and perceived advantages and limitations. Participants were also asked to identify potential barriers to clinical implementation. Between December 2023 and April 2025, participants were recruited through professional mailing lists, poster and electronic advertisements across Australian university and healthcare institutions.

Results: A total of 107 participants completed the questionnaire, including scientists without a clinical background (29.0%), medical professionals (30.8%), nurses (22.4%), and allied health professionals. CF was a primary area of work for 54.2% of respondents and cancer for 15.9%. Overall, 80.4% of participants considered organoid technology acceptable for use in research and clinical contexts (decisional balance score > 1.0). Respondents rated the potential of organoid models to accelerate the discovery of effective treatments for rare diseases as the most important advantage. The highest-rated limitation was that treatments identified through organoid testing may be unavailable or unaffordable.

Conclusions: Healthcare professionals and scientists demonstrate strong acceptance of patient-derived organoids for drug discovery and precision medicine. These findings support integration of organoid-based functional testing into translational research and clinical decision-support frameworks for cystic fibrosis, cancer and other rare diseases. Consideration of organoid-based assays should be embedded early in health policy and system planning to enable effective implementation.

Conflict of interest None

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0034 Modern Approaches to Paediatric Bronchiectasis: From Early Recognition to Precision Therapy

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Background/Aims: Paediatric bronchiectasis is a chronic respiratory disease characterised by irreversible bronchial dilatation, recurrent infection, persistent airway inflammation, and impaired mucociliary clearance. Increasing clinical awareness and improved imaging techniques have led to greater recognition of this condition in children worldwide. However, delayed diagnosis remains common because symptoms frequently mimic recurrent wheezing disorders and poorly controlled asthma. This review aims to summarise current concepts in paediatric bronchiectasis, with emphasis on early recognition, pathophysiology, multidisciplinary management, and emerging therapeutic approaches that may improve long-term respiratory outcomes.

Methods: A narrative review of recent peer-reviewed literature, international respiratory guidelines, and paediatric bronchiectasis studies was conducted. Key areas reviewed included airway inflammation, microbiology, diagnostic imaging, airway clearance therapy, antimicrobial management, and preventive respiratory care.

Results: Persistent wet cough lasting longer than four weeks remains the most important clinical indicator of paediatric bronchiectasis and should prompt early evaluation. High-resolution computed tomography remains the diagnostic gold standard. Common underlying causes include severe respiratory infections, immunodeficiency disorders, aspiration syndromes, primary ciliary dyskinesia, and cystic fibrosis. Evidence suggests that early diagnosis and structured airway clearance programmes may reduce exacerbation frequency and preserve lung function during childhood. Current management requires coordinated multidisciplinary care involving physiotherapy, vaccination, nutritional optimisation, prompt antimicrobial therapy, and regular pulmonary follow-up. Emerging research into airway microbiome modulation, biologic therapies, and precision medicine may further improve future outcomes.

Conclusions: Paediatric bronchiectasis is increasingly recognised as a preventable and treatable chronic lung disease when identified early. Greater awareness among healthcare professionals and timely evidence-based intervention are essential to reducing long-term respiratory morbidity and improving quality of life. Persistent wet cough in children should never be overlooked, as early intervention may prevent irreversible lung damage.

Conflict of interest The author declares no conflict of interest.

SESSION: BASIC SCIENCE 2

0035 Bronchoalveolar oxysterols are associated with disease severity and lung function decline in bronchiectasis

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Background/Aims: Bronchiectasis is a chronic lung disease characterised by structural damage and irreversible dilation of the bronchi, in which chronic inflammation plays a central role in disease pathophysiology. We recently demonstrated that oxidised cholesterol (oxysterols) are produced locally in the lung during respiratory infections and are associated with inflammation. In this study we hypothesised that oxysterols are also biomarkers for inflammatory lung diseases. Therefore we investigated the association between oxysterol concentrations and clinical outcomes including exacerbations and lung function decline in patients with bronchiectasis.

Methods: In this retrospective study, bronchoalveolar lavage (BAL) samples were collected from 38 patients with confirmed bronchiectasis and 12 healthy controls. Oxysterol concentrations were quantified using targeted liquid chromatography/mass spectrometry (LC/MS). A panel of six oxysterols including 25-hydroxycholesterol (25-OHC), 7 α ,25-dihydroxycholesterol (7 α ,25-OHC), 27-hydroxycholesterol (27-OHC), 7 β -hydroxycholesterol (7 β -OHC), and 7-ke-tocholesterol (7-KC) were assessed for their relationships with markers of disease severity, hospitalisation, exacerbation frequency, bacterial colonisation (including *Pseudomonas aeruginosa*), radiological severity, lung function, and the Bronchiectasis Severity Index.

Results: Concentrations of 7 α ,25-OHC, 7 β -OHC, and 7-KC were significantly elevated in the BAL of patients with bronchiectasis compared with healthy controls. Among demographic factors, older age was strongly correlated with higher 7 α ,25-OHC concentrations ($r = 0.69$, $P = 0.016$), and a lower BMI significantly associated with higher 7-KC levels ($r = -0.466$, $P = 0.025$). No significant differences in oxysterol concentrations were observed between males and females in this cohort. Regarding disease outcomes, we found that higher concentrations of the oxysterols 7 β -OHC and 7-KC were associated with reduced lung function, reflected by lower FEV₁ % predicted ($r = -0.41$, $P = 0.018$; $r = -0.387$, $P = 0.024$, respectively). In addition, 7 β -OHC concentrations positively correlated with higher Bronchiectasis Severity Index ($r = 0.348$, $P = 0.047$). Concentrations of 7-KC were also associated with an increased number of bacterial species colonising the airways and with more frequent exacerbations over the previous 12 months ($P = 0.037$ and $P = 0.02$, respectively). No significant associations were found between oxysterol concentrations and radiological severity.

Conclusions: These data demonstrated that BAL-derived oxysterols are promising biomarkers of disease severity in adults with bronchiectasis.

Conflict of interest No conflict of interest

0036 An incidental finding of infected bronchiectasis in a patient with an Asthma COPD overlap exacerbation a 10-year follow up.

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DOI 10.1055/s-0046-1826051

Background/Aims: The aim of our study is to present a case of a patient that for years was treated for asthma until it overlapped to COPD and thorough examination showed underlying bronchiectasis.

Methods: A now 66-year-old female patient considered and treated for decades as Asthma in outpatient setting with a sudden drop in lung function in the past 4 years, with irreversible obstruction seen on spirometry, purulent sputum and increased number of exacerbations requiring hospitalization.

Results: The patient was followed up and treated as Asthma in secondary healthcare institution since youth until year 2014 when a sudden drop of FEV1 was noted on a spirometry and the patient was referred to tertiary healthcare. The initial x-ray showed a consolidation near the left Hyllus which afterwards on the control x-ray showed that it had underlying traction bronchiectasis underneath it. The fixed obstruction was first noted in 2016. Until then the patient was treated with ICS/Formoterol but afterwards LAMA was added and this combination was in compliance with GOLD guidelines for that time. The number of exacerbations requiring hospitalization did not exceed 1 every 2 years (even during the Covid pandemic) and the FEV1 during exacerbation did not go below 45 % and the FEV1 while not exacerbated was always above 50 %. However, a reduction below 60 % of FVC was noted on several occasions and a body plethysmography noted an increase in RV and RV/TLC ratio explaining the reduction in FVC. In 2025 during an exacerbation with fever, yellowish like sputum and a drop of FEV1 to around 30 % a positive culture of *Pseudomonas aeruginosa* was present which was still sensitive or intermediate to most antibiotics and was treated accordingly. A CT was also done showing now bronchiectasis on both lungs, with the right lung never noted before on x-rays. After the hospitalization the FEV1 was improved. Another hospitalization followed due to exacerbation followed in 2026 with a 7 months gap but not *Pseudomonas* was isolated again in the meantime. After the hospitalization 2025 the patient was also put on prophylaxis with 250mg Azithromycin.

Conclusions: ACO and inflamed bronchiectasis commonly coexist and amplify each other via chronic inflammation, mucus stasis, and infection. Recognizing bronchiectasis in ACO requires adding infection-directed and airway-clearance strategies to standard ACO care.

Conflict of interest None, there are no competing interests

0037 Rapidly Progressive Cystic Bronchiectasis in Suspected Primary Ciliary Dyskinesia: A Challenging Case with Recurrent Severe Exacerbations (Case Report)

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DOI 10.1055/s-0046-1826052

Background/Aims: To present a case of severe bilateral cystic bronchiectasis with rapid progression over two years and high clinical suspicion of primary ciliary dyskinesia (PCD), emphasizing the importance of timely etiological diagnosis.

Methods: A retrospective analysis of clinical, radiological, and microbiological data from 2013 to early 2026 was performed, with focus on 2024–2026. Evaluation included high-resolution computed tomography (HRCT), serial sputum cultures, and cardiopulmonary assessment including echocardiography.

Results: A 42-year-old non-smoking male with chronic productive cough and bronchiectasis since childhood presented with recurrent lower respiratory tract infections, initially managed in outpatient settings. Clinical deterioration became evident in 2017 with hemoptysis, purulent sputum, and dyspnea, when *Pseudomonas aeruginosa* was isolated. Eradication was not achieved despite prolonged inhaled tobramycin therapy.

In 2021, the patient was hospitalized for COVID-19 pneumonia, followed by gradual functional decline. Marked worsening occurred during 2025–early 2026, with seven hospitalizations due to severe exacerbations. HRCT demonstrated progression in the extent and size of cystic bronchiectasis, with persistent *Pseudomonas aeruginosa* colonization.

During the most recent hospitalization (February 2026, 23 days), the patient developed type 2 respiratory failure requiring non-invasive ventilation. Imaging and echocardiography suggested secondary pulmonary hypertension.

Extensive etiological workup excluded common causes, including cystic fibrosis and immunodeficiency. Clinical suspicion of PCD was raised based on early disease onset and progressive course, despite absence of classical features such as situs inversus and hearing impairment. Definitive diagnostic testing (nasal nitric oxide, ciliary function analysis, genetic testing) remains unavailable.

Conclusions: This case highlights the severe consequences of delayed etiological diagnosis in bronchiectasis. PCD should be considered in patients with early-onset disease, rapid progression, and poor response to standard therapy, even without classic features. Limited access to specialized diagnostics remains a major barrier, underscoring the need for wider availability of genetic and functional testing.

Conflict of interest None, there are no competing interests.

0038 Defining the Role of Dipeptidyl Peptidase-1 in Murine Lung Immune Regulation

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DOI 10.1055/s-0046-1826053

Introduction/Aim: Dipeptidyl peptidase-1 (DPP1) is a protease that activates neutrophil serine proteases that drive lung immune responses. While neutrophilic inflammation is central to many lung diseases, the broader effects of DPP1 on protease networks and immune regulation are unclear. Therefore, we aim to characterise how DPP1 modulates lung proteolytic and immune pathways under homeostatic and inflammatory conditions in a murine model.

Method: DPP1 activity was modulated using the clinically approved inhibitor brensocatic. To assess DPP1's role under inflammatory versus basal conditions, mice received oral gavage of brensocatic (30 mg/kg/day) or vehicle for 10 days prior to an intratracheal instillation of lipopolysaccharide (LPS) or saline (PBS). Lungs were collected at 24h and 72h post-instillation ($n = 3-4$ /group). Enrichment-free shotgun proteomics coupled with N-terminomics was applied to profile global protein abundance and DPP1-dependent proteolytic events.

Conflict of interest None

0041 Cigarette smoke extract and LPS trigger RIPK1/RIPK3/MLKL-mediated necroptosis and fibrotic lung injury

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DOI 10.1055/s-0046-1826056

Background/Aims: Chronic cigarette smoke exposure is a major contributor to the development of pulmonary inflammation. Recent studies highlighted the role of necroptosis in chronic pulmonary inflammation. However, the precise molecular mechanism linking the regulated cell death pathway to chronic pulmonary inflammation remains unclear. The present study investigated the effect of cigarette smoke extract (CSE) with intermittent lipopolysaccharide (LPS) exposure on RIPK1-mediated necroinflammation and its association with fibrotic remodelling in the mouse lung.

Methods: The mice were exposed to CSE with intermittent fortnightly LPS through the systemic route for 60 consecutive days, and lung tissues were evaluated for molecular markers to understand the mechanistic consequences of RIPK1-mediated necroinflammation and its related signalling in chronic pulmonary inflammation.

Results: Chronic CSE and LPS exposure induced a significant increase in necroinflammation through activation of the RIPK1/RIPK3/MLKL signalling. Activation of these signalling results in redox imbalance, fibrotic remodelling, and disruption of tight junction proteins, ultimately triggering lung tissue damage.

Conclusions: These outcomes have emphasised the importance of RIPK1-dependent necroptotic signalling in chronic pulmonary inflammation and fibrotic lung damage.

Conflict of interest The authors declare no conflict of interest.

0042 AIR-BREES: Airway Inhalation Risks—a Bronchiectasis Respiratory Environmental Exposure Survey

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DOI 10.1055/s-0046-1826057

Background: The concept of identifying and targeting modifiable disease mechanisms in bronchiectasis was introduced as the 'treatable traits' model. Within this framework, treatable traits in bronchiectasis are categorized into aetiological, pulmonary, non-pulmonary and environment/lifestyle domains. Aiming to address these treatable traits, the 2025 ERS Guideline for the management of bronchiectasis recommends a multimodal treatment approach. However, the environmental and lifestyle domain has received limited attention. Workplace exposures have been shown to contribute substantially to the burden of several nonmalignant lung diseases in adults. Bronchiectasis have been notably absent from this literature and no study has systematically evaluated environmental exposures across the lifespan of individuals with bronchiectasis. In this study, we aimed to investigate whether environmental and occupational exposures are associated with distinct bronchiectasis phenotypes.

Methods: In an exploratory cross-sectional survey study, we recruited adult patients with bronchiectasis attending outpatient clinics at Ghent University Hospital and VITAZ Hospital (Belgium) between June 2025 and February 2026. Environmental and occupational exposures were assessed using a questionnaire covering lifetime occupational history, smoking, home environment, hobbies, and animal contact. Jobs were classified by an occupational medicine expert into exposure categories. Clinical data were extracted from electronic medical records. Associations between exposures and disease outcomes were analyzed

using Fishers exact or Wilcoxon rank sum tests, and linear, Poisson, and logistic regression models. Models were adjusted for age, sex, smoking, and *Pseudomonas aeruginosa* colonization when appropriate.

Results: Among 79 bronchiectasis patients, the mean age was 55 years and 73 % were women. Cigarette smoking, expressed as pack-years, was associated with lower DL_{CO} (− 0.4 % pred per pack-year, p = 0.004) and higher BACI score (+ 0.07 per pack-year, p = 0.043). Twenty-two patients (28 %) were colonised with *Pseudomonas aeruginosa*. Colonised patients had significantly worse lung function with lower FEV₁ (75 % pred vs 94 % pred, p < 0.001) and DL_{CO} (68 % pred vs 83 % pred, p = 0.018). Also, they had been more often hospitalized in the past year (36 % vs 11 %, p = 0.011), and tended to have had more exacerbations in the past year (p = 0.072).

Occupational silica/metal dust exposure (n = 9; 12 % of patients), typical for jobs such as welding, metalworking, and construction work, was associated with lower FEV₁ (− 25.1 % pred, p = 0.004) and higher BACI score (+ 4.75, p = 0.022), even after adjustment for age, sex, smoking and *P. aeruginosa* colonisation. Notably, in the adjusted model the effect size of silica/metal dust exposure (− 15.0 %) was comparable to that of *P. aeruginosa* colonization (− 19.0 %), and appeared independent (see Figure).

Occupational spray exposure (n = 6, 8 % of patients), typical for professions such as professional cleaning and hairdressing, resulted in higher exacerbation (IRR [Incidence Rate Ratio] 2.01, p = 0.010) and hospitalisation rates in the past year (IRR 3.19, p = 0.040), even after adjustment for age, sex, smoking, and *P. aeruginosa* colonization.

Conclusions: Beyond the well-known risk factors of smoking and *Pseudomonas aeruginosa* colonisation, two additional environmental risk factors were identified, with potential implications for patient counselling and exposure prevention. The modest sample size limits statistical power, and findings should therefore be interpreted with caution and confirmed in larger cohorts.

0043 Pseudomonas aeruginosa infection increases sputum viscoelasticity and chronic inflammation in bronchiectasis

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This study was designed to determine the impact of PA infection on sputum viscoelastic properties, inflammation markers, the proteome and microbiome in patients with BE.

Results: Sputum elasticity, viscosity and concentration were significantly increased in BE patients with PA infection compared to patients without PA infection and healthy controls. Increased sputum viscoelasticity and concentration in BE with PA infection were associated with elevated markers of neutrophilic inflammation, including IL-1b, myeloperoxidase (MPO), and neutrophil serine proteases activity. Sputum metagenome analysis revealed that PA infection was correlated with reduced microbiome diversity and PA relative abundance in BE.

Funding source: The study was supported by German Federal Ministry of Research, Technology and Space (82DZL009C1).

Conflict of interest None

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Aims: Describe clinical outcomes of a cohort of individuals with CFTR-related bronchiectasis and NTM-LD with or without access to highly effective modulator therapy (HEMT). Using dual RNA sequencing, elucidate differential recruited macrophage control of a clinical *M. avium* strain in individuals with bronchiectasis and varying CFTR function.

Methods: A demographically diverse prospective cohort and biobank of bronchiectasis patients, half with NTM-LD and ~10% with CFTR dysfunction without systemic CF disease, was established in 2024 under Institutional Review Board approval with participant informed consent. Demographics and clinical characteristics pre- and post-HEMT prescription were summarized descriptively. Peripheral blood monocyte cells (PBMCs) were collected from participants and differentiated into macrophages to evaluate recruited moMac, and infected with a clinical *M. avium* strain for up to 3 days. Cells were isolated to determine growth restriction (via colony forming units) and RNA isolation of both the host and mycobacteria. Quality control, dual rRNA depletion, library preparation, Illumina sequencing (2x150 bp; minimum 30M reads per sample) were performed by Azenta Life Sciences US, Inc. Trimmed reads are aligned to GRCh38 reference genome (STAR aligner v2.5.2b) for host library and *M. avium* reference ASM974144v1 (Bowtie2 aligner v2.6). Differential gene expression (DE) was evaluated using DESeq2, with further ontology and pathway analysis with EnrichR.

Results: Of 15 individuals diagnosed with CFTR-related bronchiectasis and active NTM-LD, 9 (60%) were prescribed HEMT, all of which demonstrated clinical improvement and 8 stopped or deferred antimicrobials. Among the 6 not prescribed HEMT, 3 of 5 were on or recommended guideline-directed antimicrobial therapy. Ex vivo infection of moMac demonstrated transcriptional upregulation of genes involved in monocyte chemotaxis, foam cell formation, and at 72 hours, type 2 interferon signaling. Differential gene regulation was observed between those with and without CFTR dysfunction, with analysis ongoing.

Conclusions: Individuals with CFTR-related bronchiectasis may derive multifaceted benefit from HEMT, including improved control of NTM lung infection. CFTR dysfunction in recruited moMac likely defines a distinct endotype underlying bronchiectasis and NTM susceptibility. We are testing the hypothesis that differential gene regulation will be observed between those with and without CFTR dysfunction.

Conflict of interest This work was funded through the American Thoracic Society, Cystic Fibrosis Foundation, and the Research Allocation Program through the University of California, San Francisco.

0045 Bronchoalveolar lavage as a diagnostic tool for assessing disease activity in bronchiectasis

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Pneumologie 2026; 89: e3–e89 2026; 89: | © 2026. Thieme. All rights reserved.

Results: In this interim analysis of this cross-sectional group of 83 patients (clinically stable state), the mean age was 62.2 (SD +/- 14.4) years, with a predominance of female subjects (68.7%). Most subjects were non-smokers (91.6%). A large proportion of subjects had underlying conditions including COPD (32.5%) and bronchial asthma (33.7%). Mean lung function showed moderate impairment (FEV1 64.8% and FVC 75.3% predicted). Most subjects (66.2%) experienced ≥ 1 antibiotic treated exacerbation within the previous 12 months.

31 subjects couldn't be evaluated mainly caused by bad recovery in the BAL but could be included in the microbiome analysis.

Surprisingly bronchoalveolar lavage (BAL) revealed relevant neutrophilia ($> 15\%$) in 42.3% of patients, only 11.5% of these showed systemic neutrophilia ($> 6400/\mu\text{g}$). More than half of the cohort showed pathogenic germs despite their clinically stable state (62.5%).

These pathogens were not consistently reflected in sputum. *Pseudomonas aeruginosa* dominated with 32% followed by *Staph. aureus* (15.2%), *Haemophilus influenzae* (13%), *E. coli* (6.5%) and other pathogens (32%). A high rate of *Candida* was detected in the sputum (26.5%), which couldn't be reflected in bronchial secretion (8.4%) and BAL (7.2%).

Conclusions: Clinically stable patients with bronchiectasis need to be followed up regularly. In line with the data from Prognosis registry, there are initial indications that BAL may be superior to systemic markers for assessing disease activity. Especially the high rate of *Candida* in sputum samples highlights the careful need of interpreting microbiological samples and shows the difficulties in getting high quality sputum samples versus BAL without cross contamination from the oropharyngeal flora.

Conflict of interest None

0046 A secreted factor of *Pseudomonas aeruginosa* rapidly kills non-tuberculous mycobacteria in biofilms in vitro

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DOI 10.1055/s-0046-1826061

Background/Aims NTM infections are increasing in prevalence worldwide, with an incidence of $\sim 10\%$ in those with bronchiectasis. These infections are incredibly difficult to treat, with a mere 36% antibiotic success rate for *Mycobacterium abscessus* subsp. *abscessus*, highlighting the urgent need for novel antimicrobial strategies. Nontuberculous mycobacteria can be found in the lungs alongside *Pseudomonas aeruginosa*, and previous studies indicate an antagonistic relationship between these organisms. We therefore investigated competitive interactions between *P. aeruginosa* and *M. abscessus* as a tool for the development of antimicrobial strategies against this difficult to treat organism.

Methods We first grew dual-species biofilms of *P. aeruginosa* and *M. abscessus* for 7 days in LB broth with daily replacement of media. We evaluated the live proportion of each species and changes to biofilm architecture using viability plating on selective agar and confocal laser scanning microscopy. We then collected sterile filtered supernatant from *P. aeruginosa* grown either planktonically or in a biofilm. This supernatant was used as the growth medium for fresh NTM cultures to investigate its ability to potentiate killing of other NTM species. Supernatant was further fractionated via solid phase extraction to identify active fractions before running untargeted metabolomics via liquid chromatography-mass spectrometry (LC-MS) and identifying target molecules via tandem mass spectrometry.

Results We found that coculture of these organisms results in a rapid decline of detectable *M. abscessus*, with a $6 \log_{10}$ reduction by day 3 of coculture. Filtered supernatant from *P. aeruginosa* biofilms, but not planktonic cultures,

mediated killing for a variety of rapid- and slow-growing NTM species including *M. fortuitum*, *M. chelonae*, *M. avium*, *M. intracellulare*, and *M. chimaera* when used as a growth medium. Fractionation via solid phase extraction in C18 columns indicated that the factor responsible for killing is a base and is non-polar at a neutral pH. Mass spectrometry identified > 900 molecules highly enriched in *P. aeruginosa* biofilm fractions not present in planktonic or media controls. Potential molecules will be further investigated for their anti-NTM potential.

Conclusions Our data indicate that a secreted factor from *P. aeruginosa* rapidly kills *M. abscessus*, alongside a variety of mycobacterial species. Identification of this factor presents an opportunity for development of a new antimicrobial molecule, and for the identification of conserved vulnerable pathways in the nontuberculous mycobacteria. These results highlight how microbial competition in polymicrobial airway communities may shape pathogen persistence and reveal a conserved vulnerability in NTM that could be exploited for therapeutic development.

0047 Clinical and Microbiological Characteristics of Hospitalized Patients with Bronchiectasis – A One-Year Retrospective Analysis in North Macedonia

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DOI 10.1055/s-0046-1826062

Aim To analyze the demographic characteristics, comorbidities, microbiological findings, and hospitalization patterns of patients with bronchiectasis hospitalized during the period 01.01.2025–01.01.2026.

Materials and Methods A retrospective analysis was conducted using hospital records of patients diagnosed with bronchiectasis who were hospitalized between 01.01.2025 and 01.01.2026. Evaluated parameters included chest CT findings, microbiological analysis of sputum using PCR or bronchoalveolar lavage (BAL), arterial blood gas analysis for assessment of partial respiratory failure, and spirometry for confirmation of chronic obstructive pulmonary disease (COPD).

Results During the study period, a total of 60 hospitalizations were recorded among 39 patients with bronchiectasis. The patients' age ranged from 32 to 84 years, with a mean age of approximately 63 years. There were 25 male patients (64.1%) and 14 female patients (35.9%).

Regarding age distribution, 2 patients (2.5%) were aged 20–40 years, 4 patients (6.9%) were 40–50 years, 3 patients (6.7%) were 50–60 years, 13 patients (33.8%) were 60–70 years, and 17 patients (49.9%) were older than 70 years. Ten patients experienced multiple hospitalizations due to exacerbations, of whom 7 were male and 3 female. Four patients had three hospitalizations each, five patients had two hospitalizations each, and one patient had nine hospitalizations.

The most common comorbidities were chronic obstructive pulmonary disease (COPD) and respiratory failure, present in 28 patients. Asthma was present in 4 patients, lung cancer in 1 patient, and pulmonary thromboembolism in 1 patient. Five patients had no comorbidities.

Microbiological analysis revealed that *Pseudomonas aeruginosa* infection was isolated in 15 patients (9 males, 60%; 6 females, 40%). *Acinetobacter baumannii* infection and *Aspergillus fumigatus* infection were identified in 2 patients.

Conclusion Bronchiectasis represents a significant cause of recurrent hospitalizations, particularly in older patients and those with comorbid COPD and respiratory failure. The frequent isolation of *Pseudomonas aeruginosa* highlights the importance of timely microbiological diagnostics and targeted therapy to reduce exacerbations and hospital admissions.

Conflict of interest I have no conflict of interest

0048 Relationship between the Severity of the Clinical Course of primary bronchiectasis (BE) and Family and Genetic History

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Introduction: No scientific research on bronchiectasis has yet been conducted in Azerbaijan. Since 2024, the Institute of Pulmonology has begun an exploratory study covering the etiological, clinical, laboratory, and therapeutic aspects of the disease.

Study Objective: To evaluate the relationship between Primary BE severity and family and genetic history.

Materials and Methods: A total of 216 patients aged 18 to 65 years were examined. Of these, 120 were women and 96 were men. Of these, 122 had primary bronchiectasis, and 94 had secondary bronchiectasis. A questionnaire was compiled for each patient, including family and genetic history, clinical course of the disease, results of radiographic and microbiological studies, spirometry, ECG, and echocardiography, treatment, and follow-up.

Study Results: A study of etiologic factors revealed a number of unique features. Consanguineous marriage was noted in 96 cases. Of these, first-cousin marriages accounted for 75 (61.4%). Between second cousins 21 (17.2%) of cases. In the remaining 26 (21.3%) observations, severe chronic diseases were noted: diabetes mellitus 10, anemia 11, bronchial asthma 5. In addition, gestosis with forced cesarean section was noted in 8 cases. The most common pathology in primary BE was Kartagener syndrome (73-60%), and in 9 (7.3%) observations the disease was present in 2 children of the family. Cystic hypoplasia was detected in 26 (21.3%) of patients, cystic fibrosis in 23 (19%) of cases. The first episodes of bronchopulmonary disease were noted in the neonatal period in 67 (55%) cases, in 55 (45%) patients the onset of the disease occurred at the age of 2-5 years. At the time of the initial examination, the condition of 74 (61%) patients was severe due to BOS, chronic *Pseudomonas aeruginosa* infection, pulmonary heart failure. In 48 (39%) cases, the disease course was considered moderate. However, the presence of *Pseudomonas aeruginosa* was a poor prognostic indicator of the pathological process.

Conclusion: A history of consanguineous marriage, genetically determined pathology, congenital respiratory tract malformations, and chronic *Pseudomonas aeruginosa* infection were considered indicators of severe primary BE.

0049 Florensocatic (dipeptidyl peptidase-1 inhibitor) Phase I study in healthy Caucasian subjects

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DOI 10.1055/s-0046-1826064

Background/Aims: Florensocatib, a dipeptidyl peptidase-1 inhibitor (DPP1i) under development for non-cystic fibrosis bronchiectasis (NCFBE), has completed two Phase I and one Phase II studies in China, with a Phase III trial ongoing. Additionally, a global Phase III study is planned.

Recently, a Phase I study was conducted to evaluate the safety, pharmacokinetics and pharmacodynamics of florensocatic in Caucasian healthy subjects.

Methods: A single-ascending-dose (SAD) and multiple-ascending-dose (MAD) study was conducted in healthy Caucasian subjects receiving 10, 20, or 40 mg oral florensoctatib or placebo. In the 10-mg and 20-mg cohorts, 7 subjects per dose received florensoctatib and 3 received placebo, administered as a single dose followed by 28 days of once-daily dosing under fasted conditions. In the

40-mg cohort, 15 subjects received florensocatin and 5 received placebo as single and multiple (fasted) doses, including an additional food-effect period. PK assessments included plasma and urine sampling; pharmacodynamic (PD) biomarkers (neutrophil elastase [NE] and azurocidine 1 [AZU-1]) were measured in blood; and safety was monitored throughout the study.

Results: Under fasted conditions, florensocatib was rapidly absorbed (median $t_{\max}$ 0.75 – 2.5 h) and slowly eliminated (mean $t_{1/2}$ 20 – 30 h) following single-dose administration in healthy Caucasian subjects. Across the 10 – 40 mg dose range, $C_{\max}$ and AUC increased dose-proportionally after both single and multiple dosing. Food intake delayed absorption and reduced $C_{\max}$ by ~31 %, while AUC was unchanged. Steady-state is expected after 5 days of once-daily dosing, with limited systemic accumulation.

NE activity showed a dose-dependent reduction over time, with the greatest mean decrease of > 50% after 28 days of 40 mg dosing. AZU-1 showed strong inhibition across all active doses, with greatest mean reduction of 85-91% on Day 28 (last day of daily dosing).

Florensocatib was safe and well tolerated across all dose levels.

Conclusions: This Phase I study demonstrates that single and multiple doses of florensoctatib are safe and well tolerated in Caucasian subjects, with favorable PK profile and robust PD response. Overall, the study results provide confidence to progress florensoctatib to global phase III and support selection of 40 mg daily dose as clinically relevant dose.

Conflict of interest James D. Chalmers reports grants or contracts from AstraZeneca, Chiesi, Genentech, Gilead Sciences, GlaxoSmithKline, Inmed, Grifols, Trudell, Verona and Boehringer Ingelheim, and consulting fees from AstraZeneca, Biomx, Chiesi, CSL Behring, Expedition, GlaxoSmithKline, Inmed, Grifols, Boehringer Ingelheim, Pfizer, Sanofi/Regeneron and Zambon. Merete B. Long has received consulting fees from Grifols. All other authors are employees or intern of Chiesi, which is sponsoring the study.

0050 Validation of a Privacy-Preserving Cough Monitoring Smartwatch Against Human-Annotated Ground Truth in Adults with Chronic Cough: A Decentralized, Real-World Study

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Background/Aims: Objective cough frequency monitoring is increasingly recognized as a valuable endpoint in respiratory clinical trials, including in bronchiectasis. However, existing cough monitoring approaches often rely on continuous audio recording, raising significant privacy concerns for participants, investigators, and ethics review boards. The Hyfe CoughMonitor (HCM) is a wrist-worn system that passively detects coughs using an on-device algorithm and records only the timestamp of each cough event. No audio is recorded, stored, or transmitted at any point, making it impossible to reconstruct speech or listen to participant conversations. This study aimed to validate the accuracy of the HCM against human-annotated ground truth cough counts in adults with chronic cough from diverse etiologies under real-world conditions.

Methods: This was a prospective, decentralized, observational device validation study conducted in the United States (NCT06775301). Thirty-one adults (23 female; mean age 57, range 34-81) with problematic cough were enrolled. Etiologies included unexplained/refractory chronic cough (n = 13), asthma (n = 5), bronchiectasis (n = 4), gastroesophageal reflux disease (n = 4), nontuberculous mycobacterial lung disease (n = 2), and others. Participants simultaneously wore the HCM on one wrist and a separate audio recording device on

the other for 24 hours under normal daily living conditions. The HCM generated cough timestamps without recording audio, while the audio device provided the reference dataset. Audio recordings were segmented into one-minute chunks and independently annotated by two blinded human annotators using a validated standard operating procedure. Disagreements were adjudicated by a third expert reviewer to establish ground truth. Agreement between HCM and ground truth was assessed using Lin's Concordance Correlation Coefficient (LCCC). Event-level performance was evaluated using sensitivity and false positive rate for cough-seconds, defined as seconds containing at least one cough.

Results: Subjects were adherent to the monitoring protocol 99.7% of the time. A total of 730.8 person-hours were analyzed, encompassing 18,305 ground truth coughs and 10,599 ground truth cough-seconds. Inter-annotator agreement was high (Pearson's $r = 0.985$ for coughs). Hourly LCCC between HCM and ground truth was 0.975 for coughs and 0.968 for cough-seconds, both indicating substantial agreement. Median event-level sensitivity for cough-seconds was 90.5%, and the median false positive rate was 1.56 per hour. No adverse events were reported.

Conclusions: The Hyfe CoughMonitor demonstrated high agreement with human-annotated ground truth for continuous cough monitoring across diverse cough etiologies, including bronchiectasis, in real-world ambulatory settings. Its fully privacy-preserving design, which records no audio and transmits only cough timestamps, eliminates the risk of capturing participant conversations, addressing a critical barrier to the adoption of continuous cough monitoring in clinical trials. These findings support the use of the HCM as an accurate and privacy-preserving objective endpoint measure for cough frequency and its dynamics.

Conflict of interest all authors are employees or received consultancy fees from Hyfe Inc.

SESSION: Theme: Comorbidities, Immunology & Inflammation 1

0051 Identification of novel autoantibodies to unlock targeted treatments and diagnostics in idiopathic non-cystic fibrosis bronchiectasis

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Background/Aims: The pathogenesis of bronchiectasis is poorly understood, due to disease heterogeneity, with an unmet clinical need for new biomarkers and endotype-targeted therapies. About 40% of bronchiectasis cases have no identified aetiology and are in need of better clinical characterisation. One of the known aetiologies of a subset (~6%) of bronchiectasis cases is autoimmune disease linked to autoantibodies, such as rheumatoid arthritis. Furthermore, recent studies suggest that other lung diseases, including idiopathic pulmonary fibrosis and a subset of patients with severe COVID-19, show clear evidence of autoantibodies. We hypothesize that these antibodies form in the adaptive immune response against self-antigens and can initiate and/or perpetuate airway damage in idiopathic bronchiectasis. This study aimed to identify novel pathogenic autoantibodies in idiopathic bronchiectasis as a potential mechanism of disease, to inform targeted diagnostics and therapies.

Methods: We performed a targeted assessment of IgG autoantibodies against six antigens identified from a literature review of all autoantibodies in other

chronic respiratory diseases. Autoantigen targets were as follows: cyclic citrullinated peptide (CCP), bactericidal/permeability-increasing protein (BPI), cytokeratin 18 (CK18), interferon (IFN)- α 2, IFN- γ and IFN- ω . Serum samples from the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) biobank were tested for autoantibodies using high-throughput enzyme-linked immunosorbent assay (ELISA). Positivity was defined as optical density (OD) greater than the mean + 3 standard deviations of healthy controls. Total IgG was also tested on high-throughput ELISA.

Results: A total of 701 cases and 700 controls were included in the study. Preliminary data revealed a statistically significantly higher OD in the bronchiectasis cases versus healthy controls ($p < 0.0001$) across all autoantibodies. The proportion of cases that were positive ranged from 6-19%, versus 1.3-2.1% in controls across the six different autoantibodies. Anti-CCP, BPI and CK18 autoantibodies were most frequently positive, whereas anti-interferon autoantibodies were less common. When assessing for all six autoantigens together, 189/701 (27%) cases and 27/700 (4%, $p < 0.0001$) controls had at least one positive autoantibody. Within this group, 31 (16%) cases and 7 (26%) controls were positive for all six autoantibodies, corresponding to 4% (31/701) and 1% (7/700) of the total cohorts, respectively. The most unique autoantibodies with no individuals positive for any other autoantibodies in each group were 23/189 (12%) cases with anti-CK18 autoantibodies and 5/27 (19%) controls, corresponding to 3% and 0.7% of the full case or control cohorts. Mean total IgG was 11.1 g/L and 10.2 g/L in cases and controls, respectively. Linear regression of total IgG versus antigen-specific IgG showed only weak positive correlation with a low R^2 of ≤ 0.10 for any autoantigen, suggesting the variation in antigen-specific IgG was not explained by total IgG concentrations.

Conclusions: These preliminary findings support a potential autoimmune mechanism in idiopathic bronchiectasis beyond the known frequency and established aetiologies of autoimmune disease comorbidity, and provide a rationale for further mechanistic studies. Planned analyses including multivariate analysis of detailed clinical metadata to identify any potential linkage to a clinical endotype are ongoing.

Conflict of interest None to declare.

0052 The Progressive Burden of Bronchiectasis: Comparing Quality of Life Outcomes Between Hospitalised and Non-Hospitalised Patients in BronchUK

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Background/Aims: Background: Bronchiectasis is a chronic respiratory condition that significantly impairs health-related quality of life (QoL). Despite its rising prevalence, longitudinal data on the progression of this burden remain limited.

Objective: This study aims to document the five-year trajectory of QoL in patients with bronchiectasis, specifically comparing outcomes between previously hospitalised and non-hospitalised individuals at baseline to evaluate the impact of disease severity.

Methods: Utilizing data from the BronchUK registry (n = 1,119 at baseline), we identified 251 patients with full follow up to year 5 visit where QoL was assessed annually using four validated instruments: the Bronchiectasis-specific Quality of Life Questionnaire (QoL-B), St. George's Respiratory Questionnaire (SGRQ), EuroQol 5-Dimension (EQ-5D-3L), and Hospital Anxiety and Depression Scale (HADS).

Results: At baseline, previously hospitalised patients (N = 133) demonstrated significantly worse QoL scores across nearly all domains compared to non-hospitalised patients (N = 118, eg QoLB Respiration 51 vs 65, SGRQ 49 vs 38; all $p < 0.001$). Over 5 years, both groups experienced a progressive decline in health status. Notably, non-hospitalised patients showed a "catch-up" trend, exhibiting a steady deterioration that narrowed the QoL gap with the hospitalised cohort over time. Longitudinally the SGRQ worsened across both groups but did not reach minimally clinically important difference (MCID of 4 points) from baseline (49 to 52 prev hospitalised vs 38 to 40/43 in non hospitalised) (Figure 1 & 2) Strong associations were found between the QoL-B, SGRQ, and EQ-5D-3L instruments.

Conclusions: Bronchiectasis imposes a substantial and progressive multidimensional burden. The significant decline in QoL among patients who had not been hospitalised at baseline emphasizes the need for early diagnosis and proactive management strategies to preserve well-being throughout the disease course.

Conflict of interest None

0053 Phenotyping eosinophilic inflammation spectrum in bronchiectasis: data from a single centre in Greece

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Background/Aims: Endophenotyping in bronchiectasis (BE) provides deeper insight into disease traits and is fundamental to the implementation of precision medicine. An eosinophilic endotype, defined by blood eosinophil count (BEC) ≥ 300 cells/ μ L, and bronchiectasis with coexisting asthma (BE + A) are increasingly recognised; however, their clinical impact remains unclear. This study compares the impact of eosinophilic inflammation on clinical status in eosinophilic BE versus BE + A.

Methods: We conducted a retrospective, observational, single-centre study of patients attending our BE clinic between 2023 and 2025. Patients with BEC ≥ 300 cells/ μ L, with or without coexisting asthma, were included. Clinical characteristics and disease severity were assessed. BEC and spirometry were obtained during clinical stability. Exacerbations were tracked over a 12-month follow-up.

Results: 95 patients with available BEC data were evaluated. Eosinophilic BE was identified in 13 patients (14%). The most common aetiologies were post-in-

fectious and idiopathic. 21 patients (22%) had BE + A, of whom 9 (9.5%) exhibited BEC ≥ 300 cells/ μ L. Patients with BE + A and blood eosinophilia had a higher mean BEC (462.2 ± 53.5 cells/ μ L) compared to those with eosinophilic BE alone (377.5 ± 19.8 cells/ μ L). No significant differences were observed between groups regarding disease severity, exacerbation rate or lung function. Respiratory symptoms, such as cough, sputum production and wheezing, were also comparable.

Conclusions: Eosinophilic BE and BE + A with blood eosinophilia appear to represent similar clinical phenotypes. Nevertheless, the study is limited by the small number of patients in each group.

Conflict of interest no

0054 Case Report: Broncholithiasis in a Patient with Bronchiectasis and COPD

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Background/Aims: Broncholiths are calcified endobronchial concretions, often originating from peribronchial lymph nodes that erode into the airway. They represent a rare but challenging complication in patients with chronic lung diseases such as bronchiectasis. Their presence can perpetuate cycles of infection, inflammation, and hemoptysis, and management decisions are complex, particularly in patients with significant comorbidities.

Methods: We report the case of a 66-year-old patient with a medical history including COPD (GOLD IV, group E) under long-term oxygen therapy and non-invasive ventilation and Bronchiectasis with a prior Resection of the left lower lobe, the inferior lingular segment and the middle lobe. He presented to the emergency department with acute-on-chronic dyspnea and hemoptysis.

Results: Chest imaging, including a radiograph and subsequent high-resolution CT, confirmed extensive, stable bilateral cylindrical and sacciform bronchiectasis. The CT scan also revealed a critical new finding: the presence of broncholiths (calcified endobronchial concretions), which were noted to be slightly progressive. A 4 mm broncholith was specifically localized within a subsegmental bronchus of the right lower lobe, (Figure 1) a finding that had increased in size from 2 mm on a prior CT.

Bronchoscopy was performed to identify the source of the hemoptysis and to assess the broncholiths. The procedure confirmed the presence of significant mucus hypersecretion. Broncholiths were visualized in the subsegments of R7 and R10. (Figure 2) However, their complete endoscopic removal was deemed only partially possible, and due to the high risk of complications such as bleeding, a decision was made in consultation with the patient to not pursue a more aggressive, anesthesia-assisted removal.

Microbiological analysis of tracheal secretions identified *Pseudomonas aeruginosa* (3-Multidrug-Resistant-Gram-Negative Bacteria), sensitive to Meropenem and Tobramycin, which were respectively i.v. and als Inhalation prescribed, leading in addition to conventional intensive inhaled and mucolytic medication to clinical improvement. A subsequent culture identified *Achromobacter xylosoxidans*, but therapy was continued due to the favorable clinical response. The patient's dyspnea and productive cough gradually improved.

Conclusions: This case highlights the diagnostic and therapeutic challenges associated with broncholiths in a patient with severe, pre-existing airway disease. The management strategy consequently focused on treating the associated infectious exacerbation with targeted antibiotics, achieving clinical stabilization without direct intervention on the broncholiths themselves.

Conflict of interest None

0055 Cachexia is associated with Distinct Microbiome Signatures in the Lower Airway of Patients with Bronchiectasis

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Background/Aims: Cachexia affects the quality of life and clinical course for our patients with bronchiectasis and non-tuberculous mycobacterial (NTM) lung disease. The diagnosis of cachexia may inform treatment decisions as it is associated with acceleration of disease and portends a poor prognosis. While there is growing understanding of the systemic inflammatory and metabolic processes underlying cachexia, the role of the lower airway microbiome in the development of cachexia in bronchiectasis has not been described.

Methods: Participants enrolled in the NYU Bronchiectasis and NTM Research Registry undergoing clinically indicated bronchoscopy with bronchoalveolar lavage (BAL) were consented for collection of BAL and supraglottic samples. Clinical data were abstracted from the electronic medical record. Subjects were divided into two groups: cachexia (5% weight loss over 6 months, > 2% weight loss with BMI < 20 over 6 months, or BMI < 18.5, N = 55) and non-cachexia (N = 89). 16S rRNA and cDNA sequencing was performed on BAL specimens. Statistical analysis utilized QIIME 2 and EdgeR to assess diversity and taxonomic analysis.

Results: We identified no significant differences in demographics, lung function, comorbidities, or symptoms (Table 1). In comparison to the non-cachexia group, the cachexia group has significantly lower BMI and an increased rate of cavitory disease on imaging (Table 1). There are no significant differences in bronchoalveolar lavage clinical culture of pathologic organisms including NTM, *Pseudomonas*, *Haemophilus*, and *Aspergillus*, though the non-cachexia group has a higher rate of oral commensals in clinical culture (Table 2).

Evaluation of the lower airway microbiome demonstrated no significant differences in bacterial load, alpha diversity (Figure 1A-B) or beta diversity by PCoA between the cachexia and non-cachexia groups (Figure 1C-D). However, differential taxonomic analysis of 16S rRNA data demonstrates differential enrichment of pathogenic and commensal taxa between the groups: The cachexia group is enriched for *Nocardia*, *Mycoplasma*, *Mycobacteria*, and *Serratia*, whereas the non-cachexia group is enriched for *Moraxella*, *Stenotrophomonas*, *Legionella*, and *Proteus*. Notably, there is enrichment of oral taxa *Gemella*, *Peptostreptococcus*, and *Prevotella* in the non-cachexia group (Figure 1E). Analyzing the metatranscriptome, multiple species of *Nocardia*, *Metamycobacterium salinarum* (an oral commensal), and *Mycobacterium monacense* (*Mycobacterium*) were again enriched in the cachexia group. Interestingly, an oral commensal, *Streptococcus viridans*, was also enriched in the cachexia group (Figure 1F).

Conclusions: There are overlapping signals across microbiome analyses of certain taxa, particularly from the class *Actinomycetes*, which may be associated with cachexia in bronchiectasis and NTM lung disease. This was independent of clinical cultures, in which these taxa are fastidious, and the mechanisms underlying cachexia require further investigation. Although these findings require replication in larger cohorts, they suggest that distinct lower airway microbiome signatures may prognosticate cachexia risk and represent potential therapeutic targets in bronchiectasis and NTM lung disease.

Conflict of interest None Applicable

SESSION: Theme: Comorbidities, Immunology & Inflammation 2

0056 Serum Club Cell Protein 16 (CC16) and its Association with Bronchiectasis Severity and Activity – Data from the German Bronchiectasis Registry PROGNOSIS

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Background: Club cell protein 16 (CC16), also known as SCGB1A1 protein, secretoglobin, or uteroglobin, is secreted by club cells – non-ciliated, secretory epithelial cells located in the small airways that contribute to maintenance of the bronchial epithelial barrier. Dysregulation of CC16 has been implicated in the pathogenesis of various pulmonary diseases. Functionally, CC16 exerts anti-inflammatory effects, although its biological role remains incompletely understood. Circulating CC16 levels appear to increase in conditions associated with acute lung injury, while reduced levels have been reported in chronic inflammatory lung diseases such as COPD.

Objective: To evaluate associations between CC16 serum levels and clinical markers of disease severity and activity in adults with bronchiectasis, and to assess its potential as a biomarker for disease severity, activity, and future exacerbation risk.

Methods: We analyzed serum samples from 400 consecutively enrolled adult participants in the German bronchiectasis registry PROGNOSIS. Samples were stored at –80 °C in the Hannover Unified Biobank prior to analysis. CC16 concentrations were quantified using a standardized ELISA (BIOZOL Diagnostica, Hamburg, Germany). Results were compared with routinely measured levels of C-reactive protein (CRP) and interleukin-6 (IL-6). Baseline characteristics were summarized descriptively. Group differences were assessed using Mann-Whitney U and Kruskal-Wallis tests, and correlations were evaluated using Spearman's rank correlation coefficients.

Results: A total of 392 participants were included in the final analysis; 8 were excluded due to missing data. One-year follow-up data on exacerbation rates were available for 186 individuals. The mean (SD) age was 55 (17) years, and 61 % were female. Mean (SD) percent predicted FEV₁ was 76 (27). The median (IQR) Bronchiectasis Severity Index (BSI) was 6 (4–9), consistent with moderate disease severity. The most common etiologies were idiopathic (33 %), asthma (19 %), and primary ciliary dyskinesia (17 %). *Pseudomonas aeruginosa* was the most frequently detected pathogen (35 %), followed by *Staphylococcus aureus*

(28 %) and *Haemophilus influenzae* (18 %). CC16 serum levels showed weak but statistically significant positive correlations with age ($p = 0.281$; $p < 0.001$), percent predicted FEV₁ ($p = 0.140$; $p = 0.006$), and QOL-B respiratory symptom scale (RSS) ($p = 0.112$; $p = 0.035$). Weak but significant negative correlations were observed with exacerbation rates at baseline ($p = -0.102$; $p = 0.044$) and at 1-year follow-up ($p = -0.182$; $p = 0.013$). No associations were identified with sputum volume or sputum color. CRP and IL-6 demonstrated weak to moderate correlations with multiple markers of disease severity and activity at baseline – most notably BSI ($p = 0.339$ and $p = 0.327$; $p < 0.001$, each) and QOL-B scales (RSS, $p = -0.298$ and $p = -0.310$; $p < 0.001$, each) – but not with the exacerbation rate at follow-up. The exacerbation rate at 1-year follow-up showed the strongest correlation with the baseline exacerbation rate ($p = 0.423$; $p < 0.001$).

Conclusion: CC16 serum levels were weakly associated with disease severity and activity in bronchiectasis at baseline. Moreover, lower CC16 levels demonstrated a weak but statistically significant association with future exacerbation risk, warranting further investigation into its potential role as a prognostic biomarker.

Conflict of interest Meret Moormann reports no conflicts of interest. Felix C. Ringshausen reports participation on an advisory and trial boards for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmad, Parion Sciences, and Sanofi; clinical trial participation for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmad, Parion Sciences, Ruhr University-Bochum, University of Dundee and Vertex Pharmaceuticals; research grants from German Center for Lung Research (DZL), German Center for Infection Research (DZIF), Mukoviszidose Institute, Novartis and Insmad; and has provided speaker services for Boehringer Ingelheim, Cliniqo GmbH, i!DE Werbeagentur GmbH, Insmad, med update GmbH and Sanofi; leadership or fiduciary roles as co-chair of the German Bronchiectasis Registry PROGNOSIS, member of the steering committee of the European Bronchiectasis Registry EMBARC and PI of the German Center for Lung Research.

0057 Single-cell RNA sequencing of induced sputum to characterise airway immune cells in paediatric bronchiectasis

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Background/Aims: Childhood bronchiectasis provides a critical window to investigate early disease processes before the establishment of advanced disease. Airway inflammation is one important pathophysiological process that is poorly characterised in early bronchiectasis. Single cell RNA sequencing (scRNAseq) is a method of investigating the signalling pathways of individual cell populations. However, most respiratory scRNAseq datasets are captured using invasive sampling methods, including tissue biopsy and bronchoalveolar lavage. Datasets using non-invasive induced sputum sampling are lacking, and there are no scRNAseq datasets of paediatric bronchiectasis. Therefore, we aimed to apply scRNAseq to profile airway immune cells in a prospective longitudinal cohort of paediatric bronchiectasis.

Methods: Induced sputum samples were collected from children aged 6–18 years with CT-confirmed non-cystic fibrosis bronchiectasis. Sputum was induced using nebulised hypertonic saline for up to 30 minutes. For each sample, a subset of sputum cells ($n = 500,000$) underwent fluorescence-activated cell sorting (FACS) to capture live leukocytes, determined by two viability stains (CalceinVioletAM and FVS780) and CD45 + expression. From this, up to 30,000 captured live leukocytes were loaded onto the Honeycomb Biotechnologies HIVE CLX platform and stored at -20°C for up to 6 months. Sample were batch

processed for scRNAseq library preparation in-house, according to manufacturer's protocols. Libraries were sequenced at the Australian Genome Research Facility. Quality control and downstream analyses of sequencing data were performed using the R package Seurat.

Results: To date, FACS was performed on 13 induced sputum samples (median age = 12.5 years, range = 9.1–16.2 years) and 10 samples have undergone scRNAseq library preparation and sequencing. The dataset featured a total of 477,723 cells, which were first clustered in PCA-reduced space. Clusters with combined features of low number of unique genes (< 150 genes), high mitochondrial gene content ($> 25\%$), and expression of non-immune markers, consistent with low-quality or ambient RNA-driven cells, were excluded. Preliminary annotation of the 122,821 high quality cells (median 10,534 cells per sample, 9,063 interquartile range, IQR) identified major airway leukocyte populations of macrophage lineage ($n = 39,548$, 32.2 %), neutrophils ($n = 24,441$, 19.9 %) and T cells ($n = 859$, 0.7 %). High-quality cell retention was at least ten-fold higher using the new HIVE-CLX platform compared to our previous efforts with the HIVE V1 platform (18 samples, median 535 cells per sample, IQR 680).

Conclusions: Our pipeline demonstrates that the key airway immune populations responsible for regulation of airway inflammation – macrophages, neutrophils, and T cells – can be captured from paediatric bronchiectasis sputa through the HIVE CLX platform. Ongoing analyses will define inflammatory pathways, cellular differentiation trajectories, and cell–cell communication networks in these samples. This unique, high-resolution dataset will allow for the mapping of immune cell functions in paediatric bronchiectasis to investigate inflammatory mechanisms.

Conflict of interest No conflicts to declare.

0058 Efficacy and Safety of Brensocatib in Patients With Non-Cystic Fibrosis Bronchiectasis and Comorbid Chronic Rhinosinusitis: A Subgroup Analysis of the ASPEN Trial

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Background/Aims: Brensocatib is an oral, competitive, and reversible dipeptidyl peptidase-1 inhibitor that targets neutrophilic inflammation and is approved in the US, EU, and UK for the treatment of NCFB in patients > 12 years (EU and UK: with ≥ 2 pulmonary exacerbations [PEx] in ≤ 12 months). In the randomized ASPEN trial (NCT04594369), brensocatib 10 mg and 25 mg significantly reduced exacerbation burden over 52 weeks vs placebo in patients with NCFB; brensocatib 25 mg significantly reduced also lung function decline and nominally significantly improved patient-reported symptoms. Among patients with bronchiectasis, patients with comorbid CRS have greater disease severity and potentially worse clinical outcomes than those without, necessitating exploration of brensocatib effects in this subgroup. In this post hoc analysis of ASPEN, we report findings from patient subgroups in the ASPEN trial based on the presence or absence of comorbid CRS at baseline.

Methods: ASPEN enrolled patients with NCFB and a history of PEx in the 12 months prior to screening (adults [18–85 years], ≥ 2 ; adolescents [12–< 18 years], ≥ 1). Patients were randomized to receive once-daily brensocatib (10 mg/25 mg) or matching placebo for 52 weeks (adults, 1:1:1; adolescents, 2:2:1). Endpoints analyzed for subgroups with and without comorbid CRS were annualized PEx rate, time to first PEx, proportion remaining PEx-free, annualized

rate of severe PEx, change from baseline in FEV₁ and FVC, and QOL-B RSS (adult patients only) at 52 weeks, and safety.

Results: Patients with comorbid CRS appeared to have greater disease severity at baseline, reflected in higher exacerbation history, increased history of asthma (31.3 % vs 17.6 %), lower postbronchodilator % predicted FEV₁ (mean [SD]: 71.8 [21.1] vs 73.6 [23.6]), higher Bronchiectasis Severity Index score (mean [SD]: 8.0 [3.7] vs 7.0 [3.6]), and greater chronic macrolide (37.5 % vs 17.6 %) or inhaled steroid (64.1 % vs 57.6 %) use than patients without comorbid CRS (Table). Higher rates of on-study exacerbations and greater lung function decline, as measured by FEV₁ and FVC, were observed in patients with CRS vs without. Brensocatib 10 mg and 25 mg reduced exacerbation rate, prolonged the time to first exacerbation, and increased the odds of remaining exacerbation-free vs placebo in patients with and without comorbid CRS (Table). Both doses of brensocatib reduced lung function decline vs placebo, regardless of comorbid CRS. Brensocatib 10 mg and 25 mg improved QOL-B RSS vs placebo in adult patients with and without comorbid CRS. TEAEs were consistent with the overall ASPEN results. A greater proportion of TEAEs were observed in patients with vs without comorbid CRS across all treatment arms (Table).

Conclusions: Consistent with the overall ASPEN population, brensocatib reduced exacerbation rates vs placebo, regardless of comorbid CRS. Both doses reduced also lung function decline vs placebo in patients with and without comorbid CRS. Patients with CRS presented with greater disease severity at baseline and during the study.

Conflict of interest This study was funded by Insmmed Incorporated Michal Shteinberg: grants from GSK, the Tel Aviv league for lung diseases, and Trudell Medical International; consulting fees from AstraZeneca, Boehringer Ingelheim, Dexcel, GSK, Kamada, Synchrony Medical, Trumed, Vertex, and Zambon; honoraria or travel fees from AstraZeneca, Boehringer Ingelheim, GSK, Insmmed, Kamada, Rafa, and Sanofi; devices from Trudell Medical International. Timothy R. Aksamit: clinical trial design and participation with AstraZeneca, Insmmed Incorporated, Johnson & Johnson, Redhill Biopharma, Spero Therapeutics, and Zambon; work with Hillrom and RespirTech; no personal honoraria or research support; support to the Mayo Foundation for Medical Education and Research; Medical Director of Bronchiectasis and NTM 360 for the COPD Foundation. James D. Chalmers: grants and personal fees from AstraZeneca, Boehringer Ingelheim, GSK, Insmmed Incorporated, and Zambon; a grant from Gilead; personal fees from Chiesi and Novartis. Xiaodan Wei, Melanie Lauterio, and Ariel Teper are employees and shareholders of Insmmed Incorporated. Felix C. Ringshausen: grants or contracts from any entity from German Center for Infection Research (DZIF), German Center for Lung Research (DZL), Mukoviszidose Institute, and Novartis; consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Insmmed, and Parion Sciences; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Cliniqo GmbH, ilDE Werbeagentur GmbH, Insmmed, med update GmbH, and Sanofi; participation in a data safety monitoring board or advisory board for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmmed, and Parion Sciences; leadership or fiduciary role in other board, society, committee, or advocacy group, paid or unpaid as cochair of the German Bronchiectasis Registry PROGNOSIS, member of the steering committee of the European Bronchiectasis Registry EMBARC, and PI of the German Center for Lung Research; other financial or nonfinancial interests (fees for clinical trial participation paid to institution) from AstraZeneca, Boehringer Ingelheim, Insmmed, Parion Sciences, Ruhr University Bochum, University of Dundee, and Vertex. Medical writing support was provided by Ashley Oney, MD, of Envision Spark, an Envision Medical Communications Agency, and funded by Insmmed Incorporated.

0059 Efficacy and Safety of Brensocatib in Patients With Non-cystic Fibrosis Bronchiectasis (NCFB) by ROSE Criteria: A Post Hoc Analysis of the ASPEN Trial

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Background/Aims (138) Brensocatib is an oral inhibitor of dipeptidyl peptidase 1, targeting neutrophilic inflammation approved in the US, EU, and UK for the treatment of NCFB in patients > 12 years (EU and UK: with ≥ 2 pulmonary exacerbations [PEx] in ≤ 12 months). In the randomized ASPEN trial (NCT04594369), 10-mg and 25-mg brensocatib reduced exacerbation burden over 52 weeks vs placebo in patients with NCFB; 25-mg brensocatib also significantly reduced lung function decline and nominally significantly improved patient-reported symptoms. Many patients with NCFB have comorbid respiratory diseases, such as COPD; coexistence of both conditions is associated with a more severe clinical presentation and worse outcomes necessitating an exploration of brensocatib effects. The “ROSE” consensus definition provides a standardized diagnostic criteria to define the association of COPD and NCFB. We report ASPEN subgroup results in patients who met the ROSE criteria at baseline.

Methods (118) ASPEN enrolled patients with clinical and CT confirmed NCFB; a history of PEx in the 12 months before screening (adults [18–85 years], ≥ 2; adolescents [12–<18 years], ≥ 1). Patients were randomized to once-daily brensocatib (10 mg/25 mg) or matching placebo for 52 weeks (adults, 1:1:1; adolescents, 2:2:1). The ROSE criteria were defined as radiographic NCFB, at least 2 characteristic respiratory symptoms, obstructive pattern with FEV₁/FVC ratio less than 0.7, and former smokers with more than 10 pack-years. Current smokers were excluded from the trial. Endpoints analyzed for subgroups with and without ROSE criteria included PEx rate, time to first PEx, patients remaining PEx-free, change in postbronchodilator FEV₁, FVC, and QOL-B RSS (adult patients only) at 52 weeks, and safety.

Results (183) Baseline demographic and clinical characteristics were mostly balanced across treatment arms. Patients meeting the ROSE criteria (n = 140) were older (mean [SD], 67.9 years [9.1] vs 59.5 years [16.0]), mostly male (66.4 % vs 40.7 %), had a higher incidence of COPD history (42.9 % vs 12.8 %), and had clinical characteristics consistent with more severe disease (higher BSI, increased PEx in the 12 months before screening, lower ppFEV₁, higher inhaled corticosteroid use) than patients not meeting the ROSE criteria (n = 1581, Table). Higher rates of on-study exacerbations and greater lung function decline, as measured by FEV₁ and FVC, were observed in patients meeting the ROSE criteria. Brensocatib 10 mg and 25 mg reduced exacerbation rate, prolonged time to first exacerbation, and increased the odds of remaining exacerbation-free vs placebo, in both subgroups (Table). Both doses of brensocatib reduced lung function decline vs placebo, in both subgroups. Brensocatib 10 mg and 25 mg improved QOL-B RSS vs placebo in adult patients not meeting ROSE criteria. Adverse events were consistent with overall ASPEN results, with more serious adverse events observed in patients meeting ROSE criteria across all treatment arms (Table).

Conclusions (60) Patients with NCFB-COPD association in ASPEN defined by ROSE criteria presented with more severe disease at baseline and greater disease activity during the study than those without ROSE. Consistent with overall findings of ASPEN, brensocatib 10 and 25 mg reduced PEx burden and 25-mg

spatial distribution of emphysema, as these represent critical confounders of bronchus–artery dimensions and may lead to underestimation of bronchial dilatation.

Conflict of interest None

SESSION: Cystic Fibrosis and Bronchiectasis 1

0062 Clinical and Radiological Profile of Cystic Fibrosis Associated Bronchiectasis: A Descriptive Study of 19 Patients in Morocco

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Background/Aims: Cystic fibrosis (CF) remains a diagnostic and therapeutic challenge in Morocco. Chronic airway infections, particularly with *Pseudomonas aeruginosa*, accelerate the progression of bronchiectasis and contribute to lung function decline. Given that the consanguinity rate in Morocco is approximately 20%, the prevalence of autosomal recessive disorders such as CF may be higher than previously recognized. This study aims to describe the clinical, diagnostic, and radiological characteristics of Moroccan CF patients presenting with bronchiectasis, providing insight into disease patterns in this population.

Methods: We conducted a retrospective study of 50 patients with cystic fibrosis, of whom 19 had confirmed bronchiectasis, followed at Harouchi hospital in Casablanca, Morocco. Inclusion criteria required a diagnosis of CF confirmed by sweat chloride testing (>60mmol/L) and/or genetic analysis, alongside radiological evidence of bronchiectasis on computed tomography (CT) scan. All 19 patients included had at least one positive respiratory culture for *Pseudomonas aeruginosa*.

Results: The median age of the cohort was 10.2 years, with a male-to-female ratio of 8:11. Genetic confirmation of cystic fibrosis was obtained in six patients. A history of consanguinity was noted in ten cases, reflecting a potential genetic predisposition within the cohort. Clinically, all patients presented with chronic cough and recurrent respiratory infections since early childhood, highlighting the persistent and progressive nature of the disease. Pancreatic insufficiency was documented in nine patients, indicating significant extrapulmonary involvement. All patients (100%) experienced recurrent pulmonary exacerbations, underscoring the severity of respiratory disease in this group. Chest computed tomography (CT) scans revealed a predominance of cylindrical bronchiectasis in the majority of cases. From a microbiological standpoint, all 19 patients (100%) were chronically colonized with *Pseudomonas aeruginosa*, a finding consistent with advanced disease and associated with increased morbidity and poorer clinical outcomes.

Conclusions: In this cohort, cystic fibrosis–associated bronchiectasis is characterized by early-onset, severe respiratory involvement, frequent pulmonary exacerbations, and a high prevalence of *Pseudomonas aeruginosa* colonization. The notable rate of consanguinity and the limited genetic confirmation highlight gaps in diagnostic resources and genetic screening. These findings emphasize the need for earlier diagnosis, improved access to molecular testing, and comprehensive multidisciplinary management, including optimized antimicrobial strategies, to reduce disease burden and improve outcomes in this population.

Conflict of interest No potential conflict of interest was reported.

0063 Unsupervised home spirometry versus supervised clinic spirometry: Analysis of longitudinal participant-level data from the CLEAR trial in patients with bronchiectasis

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Background/Aims: Lung function measurement is central to assessing disease severity and monitoring progression in bronchiectasis. Although home spirometry is convenient for remote monitoring, there is limited evidence for its validity and reliability. In an a priori defined sub-study in the CLEAR trial (ISRCTN89040295), we assessed the validity, reliability, and responsiveness of home spirometry in adults with bronchiectasis, guided by the PANACEA multidimensional evaluation framework.

Methods: Participants performed supervised “clinic” spirometry, using the SpiroSensePro spirometer, at five scheduled visits and unsupervised “home” spirometry, using the mySpiroSense spirometer, weekly and at the start and end of pulmonary exacerbations over 52 weeks. We evaluated: agreement between clinic and home spirometry; longitudinal variation in clinic and home spirometry; responsiveness of home spirometry to changes in lung function across pulmonary exacerbations; measurement quality of clinic and home spirometry; adherence to weekly home spirometry; and patient experience of home spirometry. Agreement was evaluated using Bland–Altman analysis; variation and responsiveness were summarised descriptively and with agreement metrics. Quality, adherence and patient experience were summarised descriptively.

Results: Of the 288 participants in the CLEAR trial, 257 had home spirometry data available. Agreement between clinic and home measurements was good; mean FEV₁ values were similar, with a mean difference of 20 mL (95% CI: -130.0, 170.0) representing less than 1% difference in home spirometry compared to clinic spirometry. Comparable findings were observed in other lung function measurements. Variability between clinic and home measurements was initially high (FEV₁ CV 21.0%) but decreased over time, with improved agreement by visit 5 (CV 11.7%; ICC 0.90). Among 462 exacerbations, 195 had home spirometry data within 7 days of exacerbation start and end dates. FEV₁ (L) was 2.11 (0.83) pre-exacerbation (stable), decreasing to 2.08 (0.81) at the start of exacerbation and increasing to 2.10 (0.78) at the end of exacerbation. A 100 mL decline in FEV₁ occurred in 48% of exacerbations; 35% returned and 65% did not return to within 100 mL of pre-exacerbation stable values by exacerbation end. Most spirometry sessions met ATS/ERS quality criteria, although performance was lower in home compared with clinic testing (FEV₁: 75% vs 84%). Adherence to weekly home spirometry declined over time (57% at week 1 to 39% at week 52). Patient-reported experience was generally positive.

Conclusions: Home spirometry demonstrated good agreement compared to clinic spirometry. Reliability of home spirometry improved over time, albeit

patients were less adherent. Home spirometry was responsive to exacerbations. With appropriate patient support, patient confidence in self-management may be enhanced, supporting the use of home spirometry as a practical tool for remote monitoring and decentralised clinical trials in bronchiectasis.

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Conflict of interest DM has received grants from NIHR, Innovate UK, MRC, Novavax, Northern Ireland HSC R&D, Randox and Wellcome Trust; consultancy fees from Bayer, Aptarion, Direct Biologics, Healios, Novartis, MSD; has a patent for novel treatment for inflammatory disease with Queen's University Belfast; previous Co-Director of Research for the Intensive Care Society; is a member of two Data Safety Monitoring Boards (Vir Biotechnology, Inc; Faron Pharmaceuticals); previous Director of the MRC/NIHR EME programme; is Scientific Director for Programmes in NIHR; spouse has received consultancy fees from Insmmed; spouse has received payments for participation in grant review panels from California Inst For Regenerative Medicine. JN is Chair of the EME Funding Board. DL has received grants from Northern Ireland Chest Heart & Stroke, Academy of Medical Sciences, Belfast HSC Trust, HSC R&D; has received hono- raria for presentation at an event from Glaxosmithkline. JS has received grants from HSC R&D Doctoral Research Fellowship and Belfast Health and Social Care Trust Charitable Funds. WDCM has received grants from NIHR; is a chair of two Data Safety Monitoring Boards; is President of the Association for Respiratory Technology and Physiology, is Associate Editor of ERJ Open Research. ADS has received grants from Bayer, Gilead, Pfizer, Astrazeneca, Insmmed, Novartis; fees from Boehringer, Bayer, Gilead, Pfizer GSK, Insmmed, Astrazeneca, Novartis, Sanofi, 30T in work unrelated to this manuscript; has received fees from Bayer, Gilead, Pfizer GSK, Insmmed, Astrazeneca, Innogen, Sanofi and Fisher&Paykel for speaker fees; support for attending meetings and/or travel from Astra Zeneca, Chiesi, GSK and Insmmed. JDC has received grants from Astrazeneca, Boehringer Ingelheim, Chiesi, Grifols, Genentech, Gilead, Insmmed, Trudell; has received consultancy fees from Astrazeneca, Glaxosmithkline, Grifols, Boehringer Ingel- heim, Janssen, Zambon, Chiesi, Insmmed, Novartis, Pfizer, Antabio. FC was Trus- tee, now Volunteer for Primary Ciliary Dyskinesia Support UK and is Trustee for Ciliopathy Alliance UK. JMB has received grants from NIHR, Northern Ireland Chest Heart & Stroke, European Cystic Fibrosis Society, and Northern Ireland HSC R&D. RM, RHM, BON, JSE, MC, AJ, RA have no conflicts to disclose.

0064 Association of Inhaled Corticosteroid Use and Clinical Outcomes in Patients with Bronchiectasis

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Background/Aims: Data from the US Bronchiectasis and NTM Research Reg- istry (BRR) indicate that approximately 40% of patients with bronchiectasis are prescribed inhaled corticosteroids (ICS) ^{1,2}. The association of ICS with bron- chiectasis outcomes has not been sufficiently evaluated to date. European Bronchiectasis Registry (EMBARC) analysis found that baseline ICS use in bron- chiectasis is associated with increased risk of exacerbations and mortality³.

However, US BRR analysis did not find ICS therapy to be a predictor of increased mortality². We hypothesize that baseline ICS therapy in bronchiectasis is asso- ciated with worse clinical outcomes, including decline in spirometry and more exacerbations.

Methods: Adult patients enrolled in the BRR with known data for ICS therapy were retrospectively analyzed. Patients were excluded if baseline and first an- nual follow-up exacerbations, hospitalizations, respiratory cultures and spirom- etry were unknown or missing. Baseline demographics, first annual follow-up and clinical characteristics were described across baseline ICS prescription status (documented vs. not). First annual follow-up clinical characteristics were further evaluated within two subgroups: 1) baseline nontuberculous mycobac- teria (NTM) and 2) baseline *Pseudomonas aeruginosa* (PsA) isolation. Inferential analyses across ICS groups were performed using Wilcoxon and Chi-square tests. Statistical significance was defined as $\alpha < 0.05$ with multiplicity controlled using the Benjamini–Hochberg false discovery rate.

Results: Among 7,971 patients in the BRR with available data, 1,050 met in- clusion criteria, of whom 283 (27%) were prescribed ICS at baseline (Figure 1). The cohort was predominantly female (80.3%). At baseline, patients prescribed ICS had lower baseline forced expiratory volume in 1 second (FEV₁) % predicted (70% vs 78%, $p < 0.001$), were more likely to have ≥ 1 pulmonary or exacerba- tion-related hospitalization in the prior 2 years (25.8% vs 17%, $p = 0.005$) and were less likely to have NTM isolated (46.3% vs 64.4%, $p < 0.001$) compared to those without ICS use (Table 1).

At 1-year follow-up, patients with baseline ICS therapy had lower FEV₁ % pre- dicted (72% vs 77%, $p = 0.002$) and were more likely to have had ≥ 1 exacerba- tion (58.3% vs 42.1%, $p < 0.001$), ≥ 1 exacerbation-related hospitalization (20.5% vs 10.2%, $p < 0.001$) and isolation of PsA (37.7% vs 28.0%, $p = 0.01$) compared to those without ICS use (Table 2).

Among patients with baseline NTM positivity, the ICS therapy group had lower FEV₁ % predicted, higher exacerbation burden, and were more likely to have PsA and *Staphylococcus aureus* isolation at 1-year follow-up (all p-values < 0.01). Among those with baseline PsA positivity, there were no significant differences in spirometry, exacerbation or microbiology at 1-year follow-up based on ICS therapy.

Conclusions: To our knowledge, this is the first study to systematically evalu- ate the clinical association of ICS therapy in patients with bronchiectasis using US national registry data. Patients prescribed ICS therapy were sicker at baseline and had worse clinical outcomes, including a lower FEV₁ % predicted, higher exacerbation rates, and increased incidence of PsA isolation at 1-year follow-up. These findings suggest that ICS therapy may need to be used with caution in bronchiectasis and/or NTM. Baseline ICS therapy may reflect treatment of co- existing asthma/COPD. Further studies are needed to determine whether spe- cific subgroups would benefit from ICS therapy.

Conflict of interest None

0065 MCCSA2 a Combination of the b- agonist Formoterol and the Cholinergic Agonist Methacho- line Induce Synergistic Activation of Mucociliary Clearance in a CFTR Independent Manner

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Background/Aims: Mucociliary clearance (MCC), mediated by the actions of diverse conducting airway and submucosal gland epithelial cells, plays a critical role as an innate lung defense mechanism. In cystic fibrosis (CF) impaired mu- cus clearance and chronic mucus hypersecretion causes airway obstruction and infection, with a progressive development of bronchiectasis. Disrupted MCC also contributes significantly to the pathophysiology of idiopathic bronchiec- tasis and other common pulmonary disorders, including COPD, asthma, and primary ciliary dyskinesia. Although CFTR modulator (CFTRm) drugs provide substantial benefit to people with CF (pwCF), many continue to experience

respiratory morbidity likely because they are left with significant bronchiectasis. Our prior work demonstrates that low dose cholinergic + β -adrenergic agonists, accelerate MCCV and increase ASL more than their predicted additive effects (synergistic). *In vitro*, *ex vivo* and *in vivo* data from wild type and transgenic CF models provides evidence that a combination of formoterol, β adrenergic, and methacholine, cholinergic agonist drugs (MCCSA2) synergistically increases MCC without causing bronchoconstriction.

Methods: We conducted a SAD study in healthy volunteers (HV) and pwCF. We tested a fixed nebulized dose of formoterol 20mg or formoterol in combination with 1mg, 3mg or 12mg of methacholine (MCCSA2), administered simultaneously, in twelve (n = 12) HV followed by twenty-four (n = 24) pwCF on CFTRm (Trikafta).

Results: At baseline, no significant differences in spirometry were observed between HV and pwCF. A significant difference in lung clearance index (LCI) is observed between healthy controls and pwCF ($LCI_{2.5} \text{ HC} - 7.9 \pm 1.05$ vs pwCF- 14.56 ± 0.74 , $p < 0.0001$). Following the administration of MCCSA2 no adverse events or signs of intolerance were noted up to 2 hours following dosing in both HV and pwCF. Mild improvement in FEV₁ was observed in both HV and pwCF.

Conclusions: Despite the small number of subjects, positive trends for acute increases in lung function were noted (FEV₁/FVC ratio and FEF_{25%-75%}) ($p < 0.10$ and $p < 0.07$ respectively). All treatment groups produced sputum and with a trend for larger amounts with the highest MCCSA2 dose ($p < 0.056$). All MCCSA2 treatment groups mobilized sputum with a significantly higher solids content ($p < 0.024$). In conclusion, MCCSA2 increases MCC in a CFTR independent manner in WT and CF models. A single dose of MCCSA2 was safe in HV and pwCF. Early signals of efficacy in MCC function are detected with a single dose.

Conflict of interest Yes. Isaac Cohen serves as the CEO of MCC Therapeutics, Inc.

0066 Pediatric simulations of verducatib (B1 1291583) in adolescents to support Phase III dose selection

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Background/Aims: Bronchiectasis, a chronic inflammatory lung disease, is driven by dipeptidyl peptidase 1 (DPP1)-activated neutrophil serine proteases. Verducatib, a DPP1 inhibitor, reduced pulmonary exacerbation risk in people with non-cystic fibrosis bronchiectasis (NCFBE) in the Phase II AIRLEAF® study. Verducatib had similar safety, pharmacokinetic (PK), and pharmacodynamic profiles in those with cystic fibrosis bronchiectasis (CFBE; Phase II CLAIRAFLY®) compared with those with NCFBE (AIRLEAF®). To support the inclusion of adolescents (aged 12 to <18 years) in the Phase III AIRTIVITY™ study, population PK (popPK) modeling and simulation approaches were used.

Methods: PopPK analysis, including covariates, was performed using NONMEM®. Individual parameter estimates of primary and secondary PK parameters for the Phase II population were derived from the final model. Steady-state exposure of verducatib was simulated for a representative US adult population (N = 10,000) sampled from the National Health and Nutrition Examination Survey (NHANES) database. These simulations used the Phase III dose of 2.5 mg once daily to establish the reference exposure range for the adolescent population. Adolescent exposure was simulated based on a uniform distribution of body weights, with 1,000 adolescents simulated at each weight level to ensure representation between 12 and 18 years old. The target for pediatric exposure was within the 95 % prediction interval of the adult AUC_(24h,ss) for 2.5 mg once daily. Sample size calculations were performed using stochastic simulation and estimation with the verducatib PK model in NONMEM®. The appropriate sample size was defined as the number of people needed to detect a 95 % confidence interval within 60–140 % of the geometric mean estimate with ≥ 80 % power for clearance and central volume of distribution.

Results: Distributions of simulated pediatric verducatib AUC_(24h,ss) versus body weight showed that adolescents weighing ≥ 35 kg had similar exposure to adults receiving verducatib 2.5 mg. The sample size calculations indicated that a sample size of approximately 50 adolescents is needed to estimate key PK parameters for verducatib with ≥ 80 % power in the adolescent population of AIRTIVITY™.

Conclusions: Pediatric simulations and sample size calculations support the use of verducatib 2.5 mg in adolescents aged 12 to <18 years weighing ≥ 35 kg with CFBE and NCFBE in AIRTIVITY™, and have informed the study design of AIRTIVITY™. Study recruitment began in June 2025.

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AH and MVE are employees of Pharmetheus AB, the research organization that was contracted to conduct this analysis. **AG, ATE,** and **GB** are employees of Boehringer Ingelheim and report contribution to the submission of a pending patent related to the verducatib asset.

0067 Impaired B-cell responses to P. aeruginosa and their impact on antibody production in bronchiectasis; a substudy in the EMBARC-BRIDGE cohort

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Introduction: B-cells are responsible for antigen specific antibody production that are critical components of the adaptive immune system that help defend the airways against invading pathogens such as *P. aeruginosa* (PA). Dysregulation of these airway antibodies have been associated with increased exacerbations in patients with bronchiectasis (BE).

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from healthy controls (HC) and patients with CT confirmed BE from the EMBARC-BRIDGE study. PBMCs were stimulated with vehicle or PA PA01 for 72h at 37 °C 5 % CO₂. Cell supernatant was collected and antibody titre was measured by ELISA and cytokine concentration by multiplex MSD™. Antibody binding measured against 44 PA clinical isolates from BE patients with chronic PA infection, with PA growth measured at A600nm for 24h. Biofilm formation was measured by crystal violet staining after 24h and genetic characterisation performed by illumina whole genome sequencing and alignment to the PA01 reference genome. Cells were stained for B-cell markers and analysed using flow cytometry.

Results: PA antibody concentration in response to PA01 showed a decrease in PA antibody concentration released from stimulated (n = 20 [2.036e-006 $\pm$ 2.729e-006] ([mean $\pm$ SD] units/ml) compared to unstimulated BE PBMCs, (n = 19 [9.445e-006 $\pm$ 8.895e-006] $P = 0.0006$) and HC PBMCs (n = 18, stimulated; [2.287e-006 $\pm$ 2.379e-006], unstimulated; [1.013e-005 $\pm$ 8.727e-006], $P = 0.0012$). Binding capabilities of PA antibodies against PA isolates (n = 44) showed a significant decrease in PA antibody binding in stimulated BE PBMCs ([2.241e-005 $\pm$ 1.21e-005]) compared to stimulated HC PBMCs ([1.209e-005 $\pm$ 1.904e-005], $P < 0.001$). There was also a significant decrease in PA antibody binding in stimulated compared to unstimulated HC PBMCs ([3.024e-005 $\pm$ 3.691e-005], $P = 0.0018$).

Magnitude of PA antibody binding from BE and HC PBMCs was not significantly associated with isolate biofilm formation, total growth or MIC of ciprofloxacin ($R^2 \leq 0.061$, $P \geq 0.422$). PA antibody binding was significantly changed by exoenzyme type with $exoS^+$ ($n = 22$) and $exoU^+$ ($n = 21$) isolates having decreased binding against unstimulated BE ($exoS^+$; $P = 0.0383$, $exoU^+$; $P = 0.0231$) and HC PBMCs ($exoS^+$; $P = 0.0026$, $exoU^+$; $P = 0.0009$) as well as $exoY^+$ ($n = 36$) isolates in unstimulated HC PBMCs ($P = 0.0436$).

B-cell marker analysis showed that stimulated BE PBMCs had decreased B-cells with CD20 marker at 72h ($n = 16$ [1376 ± 1060], $P = 0.045$) with a trend towards a decrease in unstimulated bronchiectasis ($n = 16$ [1624 ± 1152], $P = 0.142$) compared to HC PBMCs, indicating a possible reduction in mature B-cells. There was also a significant reduction in B-cells with CD20 + marker at 72h compared to 0h in stimulated BE (0h; $n = 5$, 72h; $n = 16$, $P = 0.019$). Stimulated BE PBMCs also exhibited a trend towards decreased B-cells with CD27 marker ($n = 16$, [474.3 ± 212.7], $P = 0.055$) compared to stimulated HC, indicating a possible reduction in memory B-cells. There were no significant differences between BE and HC B-cells (CD19+) and B-cells with CD10, CD80 and ICAM-1 markers.

Conclusion: We have demonstrated decreased antibody responses to PA in patients with BE, driven by a reduction in mature and possible reduction in memory B-cells. Decreased antibody binding with $exoS^+$ and $exoU^+$ in clinical PA isolates indicate that a combination of immune dysfunction and bacterial evasion may contribute to susceptibility to PA infection in people with BE.

0068 Plasma Proteomic Signatures for Incident Bronchiectasis: Causal Validation, Severity Stratification, and Predictive Modeling

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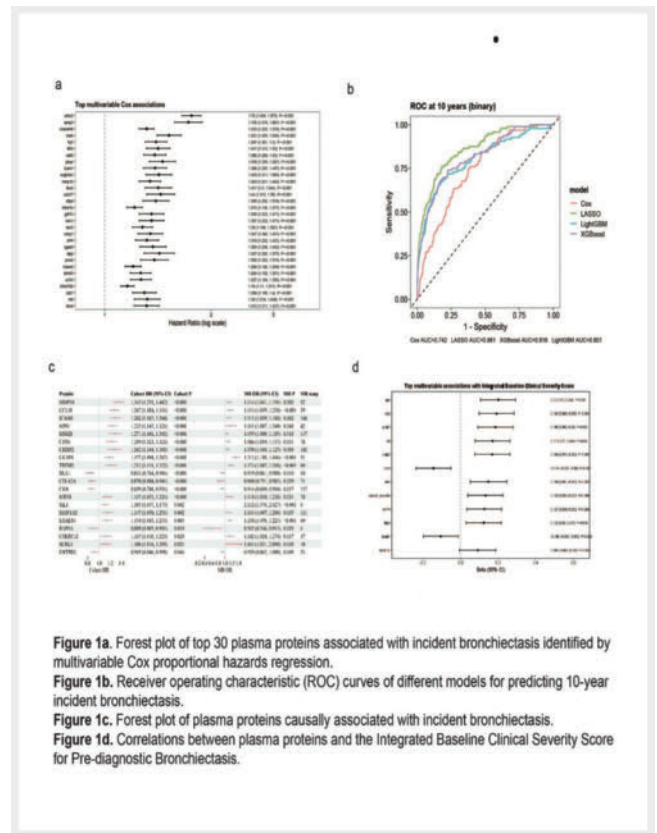
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Background/Aims: Bronchiectasis is a chronic respiratory disease with irreversible airway dilation, lacking robust plasma biomarkers for early onset prediction and pre-diagnostic severity stratification. This study aimed to identify proteomic biomarkers associated with incident bronchiectasis via integrated profiling, validate causal effects, and develop predictive models for clinical utility.

Methods: We analyzed 44,105 UK Biobank participants (568 incident bronchiectasis cases, 43,537 controls) with plasma proteins quantified by the Olink platform. Multivariable Cox proportional hazards regression screened proteins linked to disease onset time; two-sample Mendelian randomization (MR) validated causal associations using FinnGen GWAS data. A self-constructed Baseline Bronchiectasis Severity Score (BBS Score) was used to explore protein correlations with pre-diagnostic severity via multivariable linear regression. Four models (Cox, LASSO-Cox, XGBoost, LightGBM) were built to predict 10-year onset risk, with performance compared by time-dependent ROC curves.

Results: Multivariable Cox regression identified 30 plasma proteins significantly associated with incident bronchiectasis (all $P < 0.001$) (► Figure 1a). LASSO-Cox achieved the highest 10-year predictive performance (AUC = 0.861), outperforming XGBoost (0.816), LightGBM (0.801), and traditional Cox regression (0.742) (► Figure 1b). MR validation confirmed 21 proteins with causal associations to bronchiectasis onset (► Figure 1c). Fourteen proteins correlated with the BBS Score—pro-inflammatory and tissue remodeling proteins (e.g., GGH, CTSD, TNF) showed strong positive correlations ($\beta > 0.16$, $P < 0.001$), while CDSN and TPSAB1 were negatively correlated ($P < 0.05$) (► Figure 1d).



► Fig. 1

Conclusions: This study identified plasma proteomic signatures for incident bronchiectasis, with 21 proteins validated as causal biomarkers and 14 linked to pre-diagnostic severity via the BBS Score. The LASSO-Cox model exhibited excellent predictive performance for 10-year disease risk, providing novel biomarkers and a robust tool for early risk stratification and precision management of bronchiectasis.

Conflict of interest The authors declare no competing interests.

0069 BRACE – a multicentre UK audit of multidisciplinary bronchiectasis care

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Background/Aims: Effective management of patients with bronchiectasis requires systematic multidisciplinary assessment, both of aetiological factors and contemporaneous markers of severity and complication. Guidelines exist to direct practitioners in management both at diagnosis and during disease monitoring, but multicentre audit data about levels of compliance with recommended practice are lacking.

The BRACE audit evaluates clinical characteristics, aetiological patterns and adherence to guideline-recommended investigations and interventions in adults with bronchiectasis.

Methods: An audit was conducted across 16 UK centres. We report an interim analysis comprising demographics, aetiology, clinic type, investigations, multidisciplinary interventions and outcomes for 617 adults. Full baseline testing data were available for $n = 483$.

Results: Patients had a mean age of 69 years (range 19–94); 38 % were male. 26 % were seen in general respiratory clinics, 74 % in specialist bronchiectasis clinics. The most common aetiologies were idiopathic and post-infectious. Significant proportions had asthma, chronic obstructive pulmonary disease, or autoimmune conditions as contributors to their disease. Tuberculosis-related bronchiectasis was rare (<5 %).

Among 483 patients with full data, major gaps in guideline-recommended assessment were identified, including the following:

- 13 % lacked measurement of immunoglobulin levels;
- 27 % had not had protein electrophoresis testing;
- 15 % had no measurement of total IgE;
- 20 % lacked assessment of *Aspergillus* immunology;
- 34 % had no functional antibody assessment;
- 31 % lacked Nontuberculous mycobacterial (NTM) testing.

Over the previous 12 months, a mean of 2.21 routine bacterial sputum cultures were sent. 50 % had ≥ 2 isolates of *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, enteric Gram-negative organisms, or NTM. Patients had a mean of 0.5 hospitalisations and 2.2 outpatient-treated exacerbations per year.

19.1 % of patients had been to pulmonary rehabilitation. 37.5 % of those with an underweight BMI (<18.5) had seen a dietician and 5.9 % of those with an overweight BMI (>25) had been referred a weight management service.

Conclusions: This audit highlights significant microbiological burden and high exacerbation frequency, along with persistent gaps in adherence to guideline-recommended investigations. Despite specialist care being delivered to the majority of patients, incomplete immunological and microbiological assessment is common. Simultaneously, multidisciplinary services are under-used, as exemplified by the data relating to dietetic weight management services. These areas are identified as key targets for quality-improvement initiatives and standardisation of bronchiectasis care pathways.

Conflict of interest JK – none MC – none ADS – This work was supported by an educational grant to INSPIRE and Newcastle University from Inmed Incorporated

0070 Navigating Therapeutic Dilemmas: Management of *Pseudomonas aeruginosa* Pneumonia in a Patient with Severe Immune Thrombocytopenia and Underlying Bronchiectasis—A Case Report

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Background/Aims: Managing severe immune thrombocytopenia (ITP) in the setting of active life-threatening infection presents a profound therapeutic challenge. The use of immunosuppressive corticosteroids is often contraindicated, necessitating alternative strategies to elevate platelet counts while combating infection.

Results: A 52-year-old woman with ITP and bronchiectasis developed acute respiratory deterioration with a platelet count nadir of $6 \times 10^9/L$, creating a therapeutic dilemma between infection control and bleeding risk. After empirical therapies failed, *Pseudomonas aeruginosa* was identified as the probable causative agent via metagenomic next-generation sequencing of bronchoalveolar lavage fluid, supported by imaging and inflammatory markers. To address both threats without systemic immunosuppression, a combined regimen of piperacillin-tazobactam, eltrombopag, and intravenous immunoglobulin was initiated. This approach led to clinical and hematological recovery, with resolution of pneumonia and platelet recovery above $50 \times 10^9/L$, culminating in successful discharge.

Conclusions: Faced with the dual challenge of severe thrombocytopenia and active *Pseudomonas aeruginosa* pneumonia, this case illustrates a critical therapeutic strategy:

employing a thrombopoietin receptor agonist to support hemostasis without compromising immunity, alongside targeted antimicrobial therapy. This approach navigates the central dilemma of avoiding immunosuppression while controlling infection and hemorrhage. It underscores the need for tailored management and further research in this high-risk clinical intersection.

Conflict of interest The authors declare that they have no competing interests.

0071 A rare X-linked cause of bronchiectasis

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Background/Aims: Bronchiectasis is a common chronic respiratory disease with multiple underlying causes. Identifying subacute etiologies is essential for optimal patient management. Primary ciliary dyskinesia (PCD) is a heterogeneous genetic disorder that is commonly associated with bronchiectasis and a progressive decline in lung function. More than 55 genes have been linked to PCD, and mutations in the OFD1 gene represent a rare X-linked cause of ciliopathy-associated bronchiectasis.

Case description: A 33-year-old man was referred to pulmonology in 2016 for recurrent respiratory infections since childhood, chronic wet cough, dyspnea, and hemoptysis. There was no relevant family history, and he has a healthy daughter. Chest-CT revealed extensive bilateral bronchiectasis and hypertrophic left bronchial artery. Pulmonary function tests showed moderately severe obstructive ventilatory impairment. Several etiological tests were performed, but the results were inconclusive. Despite optimized treatment and pulmonary rehabilitation, he developed recurrent hemoptysis requiring embolization. In the following years, he experienced multiple exacerbations and hospitalizations with progressive loss of left lung volume, leading to long-term oxygen therapy and nocturnal noninvasive ventilation, and he was listed for lung transplantation. In 2023, he was referred for specialized bronchiectasis consultation. Medical therapy was optimized, *Pseudomonas aeruginosa* eradicated, airway clearance techniques reviewed, and respiratory rehabilitation intensified, resulting in significant clinical, functional (FEV₁ improved from 27 % to 36 %), and radiological improvements. Currently, supplemental oxygen is only needed during strenuous activity. Genetic testing revealed a rare X-linked OFD1 mutation, and the patient was referred for counseling.

Conclusions: This case highlights the importance of subspecialized bronchiectasis consultation to optimize management and identify rare etiologies, such as PCD. Early recognition and multidisciplinary management can reduce PCD morbidity. Therapies to correct ciliary dysfunction are in preclinical or early-stage trials, making accurate diagnosis of PCD essential to ensure patients can access new treatments as soon as they become available.

0072 Platelet count, clinical outcomes, and antibiotic and anti-inflammatory treatment in adults with bronchiectasis

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Background/Aims: Platelets are a key inflammatory marker in chronic respiratory diseases. To investigate the associations between platelet count (PC) and clinical characteristics, the efficacy of inhaled antibiotics or anti-inflammatory therapy in bronchiectasis.

Methods: We collected peripheral blood from adults with bronchiectasis to measure PC and assess its association with disease severity and clinical outcomes. Post-hoc analyses evaluated changes in PC before and after inhaled antibiotic or oral anti-inflammatory therapy and its potential to predict treatment outcomes.

Results: In the retrospective cohort study of 316 adults with bronchiectasis, higher modified Reiff score, leukocyte count and lymphocytes percentage were independently associated with higher PC, which remained stable at exacerbation onset. Detection of any pathogenic bacteria or *Pseudomonas aeruginosa* predicted shorter time to the first exacerbation, irrespective of the presence/absence of thrombocytosis. In two double-blind placebo-controlled randomized trials, PC decreased significantly throughout inhaled tobramycin and oral dipeptidylpeptidase-1 inhibitor treatment compared with baseline. Inhaled tobramycin reduced *Pseudomonas aeruginosa* density and improved symptoms while dipeptidylpeptidase-1 inhibitor decreased the exacerbation frequency, independent of the baseline PC.

Conclusions: PC reflects disease severity in bronchiectasis but does not predict responses to inhaled antibiotics or oral anti-inflammatory therapy.

Conflict of interest: All authors declared no potential conflict of interest related to this manuscript.

SESSION: Cystic Fibrosis and Bronchiectasis 2

0073 Novel Polymeric Reducing Agents as Mucus Modulators in Cystic Fibrosis

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Background/Aims: A prominent feature of cystic fibrosis (CF) lung disease is airway mucus obstruction, due to abnormal viscoelastic properties of CF mucus leading to impaired mucociliary clearance. The secreted mucins MUC5AC and MUC5B form complex polymeric networks via covalent disulfide bonds. These crosslinks play an important role for the viscoelastic properties of mucus in the airways. In CF, increased oxidation of free thiol groups of mucin monomers by reactive oxygen species released by leukocytes in chronic airway inflammation leads to abnormal crosslinking and stiffening of mucus. Targeting these excess crosslinks is a promising mucolytic strategy. The only reducing agent approved for clinical use N-acetylcysteine (NAC) lacks potency and clinical efficacy resulting in an unmet medical need for more effective mucolytic therapies. The aim of this study was to test the mucolytic activity of a novel thiol-containing polymeric reducing agent (dPGS-SH), by assessing its effects on viscoelastic properties and multimer size of sputum samples and mucus transport and viscoelasticity on primary human nasal epithelial cultures from patients with CF.

Methods: Sputum samples from patients with CF were treated with the novel mucolytic agent dPGS-SH, NAC and dithiothreitol (DTT) and MUC5B and MUC5AC expressions were analysed by Western blots to monitor relative change in mucin mass and multimeric organization. Viscoelasticity of treated sputum samples was determined using a cone-plate rheometer. To investigate the effect of dPGS-SH-mediated mucolysis in vitro, primary CF airway cultures grown at

air-liquid interface were treated apically with dPGS-SH for 24 h. Mucociliary transport was measured by particle tracking using video microscopy and magnetic microwire rheology was performed to analyse effects on viscoelastic properties of the native mucus layer.

Results: The novel mucolytic agent dPGS-SH showed stronger reducing activity of high-molecular weight mucin multimers in Western blot analysis compared to NAC and demonstrated dose-dependent reduction of MUC5B and MUC5AC polymer size. Further, dPGS-SH decreased the storage modulus (G') in rheological measurements of CF sputum. Analysis of particle tracking of fluorescent beads added to the mucus layer showed that dPGS-SH treatment increased mucociliary transport velocity on CF airway cultures compared to PBS treated cultures. Magnetic microwire rheology showed improvement of compliance and viscosity of the native mucus layer in dPGS-SH treated CF nasal epithelial cultures grown at air-liquid interface.

Conclusions: Our results in CF sputum and in the intact native mucus layer of CF nasal epithelial cultures support dPGS-SH as potent novel mucolytic and provide the rationale for advancing preclinical testing of this novel reducing agent to *in vivo* studies of mouse models of muco-obstructive lung disease. Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – SFB 1449 – 431232613; sub-project C04.

0074 ATL-105, a novel multimodal serine protease inhibitor with immunomodulatory and anti-infective properties for the treatment of non-CF bronchiectasis

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Background/Aims: Non-cystic fibrosis bronchiectasis (NCFB) is a lung disease marked by chronic neutrophilic inflammation, excessive neutrophil serine proteases (NSPs), and frequent lung infections. NSPs are linked to disease progression and poor outcomes, making them a key therapeutic target. ATL-105 is a new recombinant version of alpha-1 antitrypsin (AAT) with high activity and optimized for inhalation designed to act locally in the lungs, bypassing systemic circulation. It broadly targets key drivers of NCFB pathogenesis by inhibiting NSPs in the lungs, modulating cytokines, inhibiting bacterial virulence factors and exerting antiviral activity through TMPRSS2 inhibition, thereby disrupting the vicious vortex of inflammation, infection, impaired mucus clearance, and tissue damage.

Methods: Inhibition of NSPs and TMPRSS2 was assessed using recombinant proteases with fluorogenic substrates. Effects on inflammation mediators were evaluated in cytokine-stimulated HL60 cells and LPS-stimulated human monocytes via cytometric bead arrays. Antiviral activity against Influenza A virus and common cold viruses was measured by intracellular viral proteins. Bacteriostatic effects against proteases from *S. aureus* and *P. aeruginosa* were assessed using V8 enzyme and agar diffusion assays. In vivo efficacy was investigated in LPS-induced lung inflammation in C57BL/6J mice after pulmonary ATL-105 application. Stability and NE-neutralizing capacity were evaluated pre- and post-nebulization using a novel proprietary mesh nebulizer device. Aerosol properties and regional lung deposition were analyzed by particle sizing, imaging, and computational modeling.

Results: ATL-105 inhibits NE with IC_{50} of 21 nM, superior to plasma AAT (ProLactin®, IC_{50} of 66 nM). Similarly, ATL-105 inhibits PR3 and CatG with IC_{50} of 87 nM and 55 nM, respectively. In vitro, ATL-105 reduced the production of the pro-inflammatory cytokine IL-8 in HL-60 cells while increasing the levels of the anti-inflammatory mediator IL-10 in LPS-activated human monocytes. ATL-105 effectively inhibited TMPRSS2, a human alveolar protease involved in viral cell entry, resulting in reduced viral replication in vitro of influenza A virus and common cold viruses that can trigger disease exacerbations in NCFB. Furthermore, ATL-105 exhibited bacteriostatic activity against *S. aureus* and *P. aeruginosa*, two clinically relevant pathogens. In an LPS mouse model, pulmonary

delivery of ATL-105 led to a dose-dependent inhibition of NE activity in bronchoalveolar lavage fluid and improved inspiratory resistance and compliance. The compound remained stable during nebulization, retaining structural integrity and activity. Aerosol droplets with a mass median aerodynamic diameter of 4 to 5 µm were observed, optimal for efficient lung deposition. In silico imaging confirmed effective intrathoracic deposition, with over 60 % of the administered dose reaching disease-relevant regions of the distal and peripheral airways.

Conclusions: ATL-105 has demonstrated broad effects against several disease drivers of NCFB, making it a promising candidate for effective NCFB therapy. Further supported by its suitability for pulmonary delivery, clinical development is warranted. A clinical phase 1b proof-of-concept trial in NCFB patients is in preparation; the development strategy has been agreed with EU and US regulators.

Conflict of interest No conflict of interest

0075 Multidimensional Assessment of the Clinical Evolution of Asthma-Bronchiectasis Overlap

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Background/Aims: Asthma-bronchiectasis overlap (ABO) is a high-burden disease characterized by the coexistence of asthma and bronchiectasis, yet its disease progression patterns remain incompletely understood. Previous studies have lacked multidimensional dynamic evaluations of long-term evolution in ABO compared to bronchiectasis alone, and the clinical evolution of these two conditions remains unclear.

Methods: A retrospective cohort study included patients with ABO and bronchiectasis alone from The First Affiliated Hospital of Guangzhou Medical University between 2011 and 2024, with follow-up assessments. Imaging progression was evaluated using modified Reiff scores and Bhalla scores based on chest HRCT. Changes in pulmonary function tests, acute exacerbation frequency, and symptom scores were tracked. Evolution patterns were analyzed through stratified comparisons and multivariate regression models.

Results: At baseline, patients with bronchiectasis alone exhibited more significant structural lung damage, while ABO patients showed more severe obstructive ventilatory dysfunction. During follow-up, both ABO and bronchiectasis alone patients demonstrated progressive imaging severity, with no statistically significant difference in annual progression rates. Pulmonary function trends diverged between groups. ABO patients showed overall improvement over time, whereas bronchiectasis alone patients experienced a decline. In ABO patients, imaging findings worsened compared to baseline, while pulmonary function improved and acute exacerbation frequency decreased. Structural lesion progression in ABO was independent of pulmonary function and clinical symptom improvement. A history of severe acute exacerbations at baseline and elevated mMRC scores predicted accelerated deterioration in modified Bhalla total scores, lobe involvement, and bronchial dilation severity.

Conclusions: ABO patients exhibit a unique disease progression pattern, with structural lesion progression occurring independently of pulmonary function and clinical symptom improvement. Future management requires a multidimensional assessment system to guide precision therapy.

Conflict of interest All authors declared no potential conflict of interest related to this manuscript.

0076 Clinical implications of traction bronchiectasis in IPF and fibrotic RA-ILD – A retrospective single-center cohort study

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Background/Aims: Bronchiectasis is a common feature in idiopathic pulmonary fibrosis (IPF) and rheumatoid arthritis-associated interstitial lung disease (RA-ILD). While these so-called traction bronchiectasis are often considered a secondary phenomenon in fibrosing ILD, their prognostic significance and relationship to respiratory pathogen detection and outcomes remain unclear.

Methods: Bronchiectasis is a common feature in idiopathic pulmonary fibrosis (IPF) and rheumatoid arthritis-associated interstitial lung disease (RA-ILD). While these so-called traction bronchiectasis are often considered a secondary phenomenon in fibrosing ILD, their prognostic significance and relationship to respiratory pathogen detection and outcomes remain unclear.

Results: 267 IPF and 56 RA-ILD patients were included. Median modified Brody score was 11.5 (IQR 7–16; max possible range 0–72). Higher Brody scores strongly correlated with fibrotic extent ($R=0.6$, $P<0.001$). Higher scores had significantly lower baseline FVC and DLCO ($P<0.001$), but no differences in PFT trajectories over time. In multivariable Cox regression, higher bronchiectasis scores were independently associated with mortality (HR 1.03 per point [95 %CI 1.01–1.06], $P=0.003$); fibrosis extent showed similar results (HR 1.02, CI 1.00–1.03, $P=0.017$). Pathogens were found at a median of 3 months after baseline in 50.9 % (IPF) and 46.4 % (RA-ILD), without association with survival, symptoms or Brody scores. *Staphylococcus aureus* was most common (28.9 %); *Pseudomonas aeruginosa* was rare (1.9 %).

Conclusions: In both IPF and RA-ILD, higher bronchiectasis scores were associated with fibrosis extent and mortality, but not classical clinical bronchiectasis features. This supports traction bronchiectasis as a marker of fibrotic remodeling rather than a distinct syndrome.

Conflict of interest None

0077 Oscillometry in the assessment of disease activity and severity in bronchiectasis

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Background/Aims: Bronchiectasis is a heterogeneous disease characterized by permanent bronchial dilation and respiratory symptoms, including cough, sputum production and exacerbations. While disease severity is traditionally assessed using composite clinical, functional, and radiological scores, increasing attention is being paid to the concept of disease activity. Spirometry is routinely used in bronchiectasis and is included in severity scores, but has limited sensitivity for small airway dysfunction. In contrast, impulse oscillometry

(Forced Oscillation Technique, FOT) can detect early peripheral airway abnormalities, including increased resistance (R5, R5–R20) and reduced reactance (X5). However, evidence in bronchiectasis remains limited and is mainly focused on disease severity rather than activity. Identifying active disease may enable timely therapeutic interventions to prevent progression and irreversible lung damage. Therefore, this study aimed to evaluate whether oscillometric parameters and their post-bronchodilator (BD) variability are associated with disease activity in bronchiectasis, including in patients with normal spirometry, and to assess the potential of oscillometry in complementing severity assessment.

Methods: A prospective observational study was conducted in adults with bronchiectasis. All subjects underwent FOT and spirometry before and after bronchodilation, along with assessment of systemic inflammatory markers (iron, ferritin, complete blood count, C-reactive protein, fibrinogen, albumin). Non-parametric tests and Spearman correlations were used to evaluate associations between oscillometry parameters and markers of disease activity, including ≥ 2 exacerbations/year, daily sputum production, respiratory/systemic symptoms, CT signs of activity, and inflammatory biomarkers.

Results: A total of 43 patients with bronchiectasis were enrolled (mean age 64.5 years, 62.8% female). Overall, 27.9% experienced ≥ 2 exacerbations in the previous year and 60.5% reported daily sputum production. Patients with ≥ 2 exacerbations showed reduced post-BD variability in R5tot%, R5tot, X5tot and AXtot compared with non-exacerbators (all $p < 0.05$), suggesting lower mechanical reversibility in more active disease, not captured by spirometry. A similar pattern of reduced variability (R5tot%, X5tot%, Fres tot%) was observed in patients with respiratory symptoms (all $p < 0.05$), while in those with daily sputum production and CT features of active disease (e.g. mucus plugs, tree-in-bud pattern) only some oscillometric variability indices confirmed this pattern. Oscillometric parameters confirmed were associated with severity indices (BSI, mMRC) and with *Pseudomonas aeruginosa* colonization, showing increased R5, AX and Fres and more negative X5 in more severe forms (all $p < 0.05$). A systemic inflammatory condition (elevated fibrinogen or inflammatory pattern at electrophoresis) correlated with reduced X5tot% variability ($p = 0.047$ and 0.027 respectively). No significant differences were observed according to hospitalization history.

Conclusions: Bronchiectasis is a heterogeneous inflammatory disease in which early recognition of disease activity may enable timely therapeutic interventions. Forced oscillation technique confirmed its association with disease severity and demonstrated reduced post-bronchodilator variability of R5tot% and X5tot%, even in the absence of spirometric abnormality. These findings suggest that oscillometry may represent a sensitive marker of small airway dysfunction and a valuable tool for the integrated assessment of disease activity alongside clinical, radiological, and laboratory parameters.

0078 The LTAP-Treated Bronchiectasis Phenotype: Severity, Exacerbation Burden and Microbiological Risk in a Large Tertiary Centre Cohort

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Background Long-term antibiotic prophylaxis (LTAP) is widely used to reduce exacerbations in bronchiectasis, yet the clinical and microbiological phenotype of patients selected for LTAP in real-world practice remains poorly characterised. Defining this phenotype may improve treatment stratification and pathway design.

Methods: We performed a cross-sectional analysis of 460 adults attending a tertiary bronchiectasis centre. Patients receiving LTAP were compared with those not on prophylaxis. LTAP regimens included macrolides, nebulised antibiotics, oral non-macrolides or combination therapy. Clinical variables included FEV₁ % predicted, annual exacerbation frequency and chronic *Pseudomonas aeruginosa* infection. Group comparisons used χ^2 , Fisher's exact or Mann-Whitney U tests. Multivariable logistic regression (adjusted for age and sex) identified

fied independent predictors of LTAP use. Sensitivity analysis excluded patients with macrolide contraindications.

Results: LTAP was prescribed in 159 patients (34.6%). Compared with non-LTAP patients, those receiving LTAP had more severe airflow limitation (median FEV₁ 51% vs 68%, $p < 0.001$), higher exacerbation frequency (median 3 vs 1/year, $p < 0.001$), and a greater likelihood of ≥ 3 exacerbations/year (62.3% vs 21.4%, $p < 0.001$). Chronic *Pseudomonas aeruginosa* infection was significantly more prevalent in the LTAP group (38.4% vs 12.1%, $p < 0.001$). Microbiological profiles differed significantly, with increased *Pseudomonas* and reduced *Haemophilus influenzae* isolation among LTAP patients ($p = 0.002$).

On multivariable analysis, severe airflow limitation (OR 3.9, 95% CI 2.3–6.7), ≥ 3 exacerbations/year (OR 4.8, 95% CI 2.9–8.1) and chronic *Pseudomonas* infection (OR 3.5, 95% CI 1.9–6.4) independently predicted LTAP use. Results were consistent on sensitivity analysis.

Conclusion: LTAP use identifies a distinct, high-risk bronchiectasis phenotype characterised by advanced disease, frequent exacerbations and adverse microbiology. Rather than reflecting prescribing variation alone, LTAP appears to mark underlying disease severity and biology, supporting phenotype-based treatment stratification in bronchiectasis care.

Conflict of interest Nil

0079 Patient-focused Target Product Profiles for the development of phage therapies to treat lung infections in cystic fibrosis

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Background/Aims: Despite advances in cystic fibrosis (CF) care, lung infections remain a leading cause of morbidity and mortality for people with CF (pwCF). Phage therapy offers a potential solution by specifically targeting pathogenic bacteria, including antibiotic-resistant strains. In addition, phage therapy appears to pose less risk of cumulative toxicity associated with repeated conventional antibiotic use which may help minimise complications in organs such as the liver, kidneys, and auditory/vestibular system, - an important consideration in an ageing CF population.

The CF AMR Syndicate joined forces with the TRAILFINDER-CF Innovation Hub to deliver patient-focused Target Product Profiles (TPPs) intended to catalyse the development of phage-based therapies for CF lung infections. A TPP describes the desired characteristics a therapeutic should have to address a specific clinical need.

Methods: The TPP development process began with focus groups and one-to-one interviews with pwCF and their loved ones, followed by input from CF clinical care teams and phage therapy innovators, alongside a clinical trial landscape review. These interactions explored phage therapy awareness; integration into current treatment strategies; and barriers to clinical adoption. Clinical trial endpoints and outcome measures, preclinical data requirements, as well as regulatory and safety considerations were also explored. Findings were synthesised to produce an initial set of TPPs, which were subsequently refined through multi-stakeholder input via a consensus survey and a virtual symposium where survey results were discussed to finalise the documents.

Results: The following TPPs have been developed for both conventional and modified phage therapy: (1) A patient-focused TPP capturing the needs and priorities of pwCF that should be addressed by any phage-based therapeutic; (2) A TPP for phage therapy for the treatment of chronic lung infections; (3) A TPP for phage therapy to eradicate new lung infections. The TPPs are pathogen-agnostic and designed to apply to pathogens commonly associated with CF, and they may also be relevant to related respiratory conditions where chronic infection is common, such as in non-CF bronchiectasis.

Conclusions: Extensive stakeholder engagement, including input from pwCF, clinicians, researchers, and industry experts, has informed and refined the final TPPs. The resulting consensus-driven TPP document define the desired characteristics of phage therapies for CF lung infections and aim to guide and accelerate innovation aligned with real world needs. Although developed with a focus on CF, these TPPs may also serve as a framework for the development of phage therapies targeting lung infections in related conditions such as non-CF bronchiectasis.

Conflict of interest None to declare

0080 Patient engagement and collaboration in the design of the Phase III AIRTIVITY® study in people living with bronchiectasis

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Background/Aims: Seeking input from people with lived experience of disease before initiating a clinical study can help optimise the study's design and execution. During protocol development, collaboration with people with lived experience can support patient centricity and improve the feasibility of study assessments, leading to a study that not only has the potential to generate high-quality data, but appropriately aligns with patients' day-to-day lives. Furthermore, drugs developed through patient-centric study designs are more likely to obtain regulatory approval than those developed without such designs. [1] We present the outcomes of engagement and collaboration with patient experts and people with lived experience of bronchiectasis in the design of the Phase III AIRTIVITY™ study (NCT06872892).

Methods: AIRTIVITY™ is assessing the efficacy, safety and tolerability of verducatib 2.5 mg in people with bronchiectasis. To ensure patient centricity in AIRTIVITY™ and highlight the importance of the patient voice in its development, the sponsor of AIRTIVITY™ (Boehringer Ingelheim) engaged with a panel of advisors to discuss aspects of the AIRTIVITY™ study design and identify potential challenges to its feasibility. Three online meetings were held between June and December 2024 to seek advisors' input regarding the proposed study design. Eight multinational advisors (six people with lived experience of bronchiectasis and two representatives of people living with lung conditions [including asthma and chronic obstructive pulmonary disease]) provided feedback on the AIRTIVITY™ study design. The sponsor then incorporated this feedback into the AIRTIVITY™ study design, where possible.

Results: Advisory board discussion outcomes are summarised in Table 1. Advisors' feedback was incorporated into several aspects of the AIRTIVITY™ study design, including: i) the visit schedule (monthly on-site or telephone contact points between participants and study site), ii) the length of the AIRTIVITY™ study (up to 1.5 years in length) and iii) determining which study procedures can be performed remotely to reduce on-site visit time (patient-reported outcome measure questionnaires and sputum collection may be performed at home, before an on-site visit).

Conclusions: Collaboration from people with lived experience of bronchiectasis and those representative of the lung disease community was essential to finalise the study design of AIRTIVITY™, and the effects of this input will be relevant throughout the conduct of AIRTIVITY™. Engagement from the advisory panel helped identify practical barriers to participation, such as visit burden,

fatigue during clinic assessments and logistical challenges associated with everyday data collection—barriers highly relevant to people with chronic diseases like bronchiectasis. Addressing these aspects during protocol development contributed to an enhanced patient-centred study design. If executed early, engagement with people with lived experience has the potential to improve clinical trial feasibility, reduce participation burden, support adherence to study procedures and improve participant retention. This, in turn, is expected to enhance the study's data quality. Integrating patient perspectives into clinical research design is therefore essential to advancing patient centricity and improving drug development. We propose that clinical research should routinely incorporate the perspectives of those with lived disease experience to optimise study design feasibility and practicality.

Conflict of interest This research was supported and funded by Boehringer Ingelheim International GmbH. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (IC-MJE). The authors did not receive payment related to the development of the abstract. Ally Zoras, MSc, of Nucleus Global provided writing, editorial support and formatting assistance, which was contracted and funded by Boehringer Ingelheim. Boehringer Ingelheim was given the opportunity to review the abstract for medical and scientific accuracy as well as intellectual property consideration. JDC reports support for the present publication from Boehringer Ingelheim; grants or contracts from AstraZeneca, Boehringer Ingelheim, Genentech, Gilead Sciences, GlaxoSmithKline, Grifols, Insmed and Trudell Medical Group; consulting fees from Antabio, AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, CSL Behring, Expedition Therapeutics, Enterprise Therapeutics, GlaxoSmithKline, Grifols, Insmed, Melodia, Pfizer, Trudell Medical Group, UCB, Vast Therapeutics and Zambon; and is the current Chief Editor of the *European Respiratory Journal*. RTS reports support for the present publication from Boehringer Ingelheim and is a retiree of GlaxoSmithKline. RTS reports personal fees from AstraZeneca, Boehringer Ingelheim, the COPD Foundation, ENA Respiratory, GlaxoSmithKline, the Global Allergy and Airways Patient Platform, Global Skin, ItalyAndBeyond, Janssen, Roche, Renovion and Samay Health. RTS also discloses share options in ENA Respiratory. EB, FH, and SP report support for the present publication from Boehringer Ingelheim and have nothing else to disclose. LE reports support for the present publication from Boehringer Ingelheim and reports consultancy fees from Monaghan Medical Corporation. DH, TLN and WS are all employees of Boehringer Ingelheim. WS also reports contribution to the submission of a pending patent related to the verducatib asset.

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0081 Compartmentalized PDE3/4 Modulation by Inhaled KIT2014 Improves Airway Epithelial Function and Limits Inflammation in Non-Cystic Fibrosis Bronchiectasis-relevant models

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Background/Aims: Non-cystic fibrosis bronchiectasis (NCFBE) is a chronic respiratory disease characterized by irreversible airway dilation, persistent neutrophilic inflammation, and impaired mucociliary clearance, leading to mucus obstruction in distal airways and recurrent infections. The disease is sustained by a self-perpetuating cycle of mucus retention, inflammation, and tissue damage (Cole's vicious cycle). Current therapies remain largely sympto-

matic and do not address underlying epithelial dysfunction, partly due to the limited translational relevance of preclinical models.

KIT2014 is an inhaled cell-penetrating peptide targeting the A-kinase anchoring protein (AKAP) scaffold function of phosphoinositide 3-kinase gamma (PI3K γ). By disrupting the PI3K γ -protein kinase A interaction (PKA), KIT2014 limits the activity of PI3K γ -anchored phosphodiesterases 3 and 4 (PDE3/4), leading to a localised increase in intracellular cAMP. This enables compartment-restricted modulation of cAMP signaling in airway epithelial and inflammatory cells, with potential benefits on mucociliary clearance, epithelial integrity, and inflammation.

Methods: The pharmacological activity of KIT2014 was evaluated across complementary translational models.

Inflammatory biomarkers were profiled in human bronchial epithelial cells under pro-inflammatory stimulation (BioMAP®). In vitro studies in differentiated human airway epithelial cultures (MucilAir™, air-liquid interface) assessed ciliary beating frequency (CBF), mucociliary clearance (MCC), and epithelial integrity (TEER).

In vivo activity was evaluated in a murine model of lipopolysaccharide (LPS)-induced acute lung injury, assessing lung tissue damage, neutrophil infiltration and bronchoalveolar lavage inflammatory markers following inhaled administration of KIT2014.

Clinical translation was supported by a Phase 1 randomized, placebo-controlled, double-blind study in 56 healthy subjects across single and multiple ascending dose cohorts, evaluating safety and pharmacokinetics.

Results: In a human bronchial epithelial inflammation model (BioMAP® BE3C), KIT2014 reduced selected pro-inflammatory cytokines involved in epithelial activation and leukocyte recruitment.

In differentiated human airway epithelial cultures, KIT2014 increased ciliary beating frequency at early timepoints while preserving epithelial barrier integrity (TEER $\geq 200 \Omega \cdot \text{cm}^2$) and showing no cytotoxicity.

In the murine LPS-induced lung injury model, KIT2014 reduced neutrophil infiltration, with a reduction up to 2.3-fold (57 %) in LY6G-positive cells in lung tissue, and attenuated structural lung damage, with a ~24 % reduction in lung injury score and a decrease in morphological damage up to 1.7-fold, compared to the diseased control group.

In a first-in-human Phase 1 study, inhaled KIT2014 was safe and well tolerated, with no serious adverse events and negligible systemic exposure following repeated dosing up to 2 mg.

Conclusions: Scaffold-based, compartmentalised modulation of cAMP signaling by KIT2014 restores key epithelial functions, including ciliary activity and CFTR channel function (Ghigo et al., *Sci Transl Med* 2022), while exerting anti-inflammatory effects in vivo.

However, the LPS-induced model primarily reproduces acute neutrophilic inflammation and lacks key features of NCFBE, including mucus obstruction, airway dilation, and ciliary dysfunction, thus failing to recapitulate a stable bronchiectatic phenotype. These limitations highlight the importance of human-relevant systems, such as air-liquid interface epithelial models, and improved in vivo approaches to better evaluate therapeutic candidates.

Despite the lack of fully translatable models, the combined epithelial and anti-inflammatory effects observed, together with a favorable clinical safety profile, support the continued development of KIT2014 as a potential disease-modifying therapy for NCFBE.

Conflict of interest KIT2014 is a proprietary asset of Kither Biotech S.r.l. This work was supported by Kither Biotech S.r.l.

0082 Characterizing CFTR-Related Disorder Bronchiectasis and Response to Modulator Therapy: A Prospective Multicenter Registry Cohort

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Background/Aims: Bronchiectasis due to cystic fibrosis (CF) is well characterized, yet the clinical significance of partial cystic fibrosis transmembrane conductance regulator (CFTR) dysfunction in people with non-CF bronchiectasis, and whether modulator therapy improves outcomes, is poorly understood. CFTR-related disorder (CFTR-RD) encompasses partial CFTR dysfunction that manifests as single-organ disease, including bronchiectasis, without meeting diagnostic criteria for CF. Incomplete CFTR variant reporting in non-White populations and complexities of functional testing can result in underdiagnosis of CF and CFTR-RD, precluding access to potentially life-altering commercially available highly effective modulator therapy (HEMT). Here, we aim to describe a prospective multi-center cohort of clinically diagnosed or suspected CFTR-related bronchiectasis prescribed modulator therapy and evaluate clinical outcomes 6 months after initiating therapy.

Methods: Adult patients enrolled in the United States Bronchiectasis and NTM Research Registry (BRR) were included if they were clinically diagnosed with CFTR-RD with single-organ disease (e.g., bronchiectasis) and were prescribed HEMT. The cohort was further restricted to those with pre-modulator sweat chloride (CL) concentration of ≥ 30 and ≤ 60 mEq/L and full 6-month post-modulator clinical data (i.e., body mass index, spirometry, exacerbation events). Baseline characteristics were summarized descriptively. Pre- versus post-modulator findings were assessed by Wilcoxon signed rank sum and McNemar's test for continuous and categorical variables, respectively, adjusted with the Benjamini-Hochberg false discovery rate ($q < 0.05$). Exacerbation rates were modeled using Poisson and negative binomial GEE, adjusted for age, sex, and FEV1, with negative binomial specification used to assess robustness.

Results: Clinical data was extracted from 41 patients over 7 participating academic centers, with a median age of 67 (IQR 57.0 – 73.0), majority female (78.0 %), predominantly commercially insured (88.9 %), all non-Hispanic White (100 %). The majority were prescribed combination HEMT, with 3 prescribed ivacaftor alone (► Fig. 1). At this time, 36 of 41 participants had clinical outcomes available 6 months after HEMT initiation, with 34 (94.4 %) noted to have improvement in general well-being and significant improvement of cough ($P = 0.001$). The majority took full dose therapy during the study period, with 5 individuals requiring dose modification and 2 ending therapy due to tolerability or drug interactions. While all 41 were clinically considered to have CFTR-related bronchiectasis, sweat CL was either < 30 mEq/L or the potential disease-causing variant was unclear. The cohort was thus restricted to 30 (73.2 %) individuals meeting expert standards for CFTR-RD diagnosis, 26 of whom had available 6 month post-modulator data. Demographics were similar to the larger cohort. Cough was significantly reduced ($p = 0.009$), as were bronchitis and pneumonia (none post-modulator from 3-5 pre-modulator).

Adjusted exacerbation rates declined 90 % in the 6 months post-modulator compared to pre-modulator (IRR 0.10, 95 % CI 0.04–0.29, $p < 0.001$; $n = 19$ with no missing data).

		N	41
Demographics			
Age, median [IQR]	41	67.0 [57.0-73.0]	
Female, n (%)	41	32 (78.0)	
non-Hispanic White, n (%)	35	35 (100.0)	
Insurance	36		
Commercial		32 (88.9)	
Medicaid/Uninsured		4 (11.1)	
CFTR Variant			
F508del		20 (46.5)	
R117H		3 (6.7)	
5T		5 (11.6)	
D1152H		1 (2.3)	
G551D		1 (2.3)	
Other		13 (30.2)	
Modulator			
Elxacaftor/Tezacaftor/Ivacaftor (ETI)		33 (80.5)	
Ivacaftor		3 (7.3)	
Vanzacaftor/Tezacaftor/Deutivacaftor (VTD)		5 (12.2)	
Restricted Cohort		N	30
Clinical Characteristics			
BMI, median [IQR]	30	20.9 [19.5-23.0]	
Sweat Cl, median [IQR]	30	43.5 [38.0-53.0]	
FVC %predicted, median [IQR]	21	79 [67-102]	
FEV1 %predicted, median [IQR]	23	68 [56-91]	
FEV1/FVC, median [IQR]	21	0.87 [0.77-0.93]	
Median number of exacerbations experienced in the past year [IQR]	28	1 [0-2]	
Model-based estimates, adjusted for age, sex, FEV1 %predicted (N = 19 full data)			
	Rate Ratio	95% CI (p-value)	
Poisson GEE	0.10	0.04-0.29 (<0.001)	
Negative binomial GEE	0.11	0.04-0.29 (<0.001)	

► Fig. 1

Conclusions: CFTR-related bronchiectasis is an emerging endotype deserving of targeted therapy. In a cohort of individuals with access to HEMT, treatment was well-tolerated and associated with improvement of respiratory-related symptoms including significant reduction of exacerbations. Further work is required to define which patients with CFTR-RD benefit from HEMT, and the longitudinal benefit and tolerability in this population.

Conflict of interest The authors would like to acknowledge that the Bronchiectasis and NTM Research Registry is supported in part by corporate donors, all of which can be found on the Supporters page of the Association website. It should also be noted that this work would not have been possible without the comprehensive chart reviews and recording of data by the dedicated research coordinators and principal investigators at each participating site.

SESSION: INFECTIONS

0083 Bacteriological Profile of Sputum Pyogenic Cultures, Associated Comorbidities, and Complications in Patients with Bronchiectasis Admitted to a Tertiary Care Respiratory Unit in Sri Lanka: A Descriptive Case Series- Preliminary report

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Background/Aims: Bronchiectasis is a chronic suppurative airway disease characterised by permanent, abnormal bronchial dilatation resulting from recurrent infection and inflammation. Although its global prevalence is rising, particularly across Asia, local epidemiological and microbiological data from Sri Lanka remain entirely absent from the published literature. This knowledge

gap impedes rational empirical antibiotic prescribing, complication surveillance, and guideline development in the local setting.

This study aimed to: (1) identify the most common microorganisms isolated on sputum pyogenic culture in hospitalised bronchiectasis patients; (2) document the prevalence of associated comorbidities; (3) determine the prevalence of pulmonary hypertension and long-term oxygen therapy (LTOT) dependency; and (4) ascertain the proportion of patients with High-Resolution Computed Tomography (HRCT)-confirmed diagnoses.

Methods: A descriptive case series was conducted in the Respiratory Unit of a tertiary care hospital in Sri Lanka over a consecutive one-month period, as a preliminary study with a total study duration of five months. All adult patients (aged ≥ 18 years) admitted with a diagnosis of bronchiectasis were enrolled. Data on sputum pyogenic culture results, antibiotic sensitivity profiles, comorbidities, echocardiographic findings, LTOT status, and HRCT results were collected using a structured Case Record Form. Descriptive statistics were applied, with categorical variables reported as frequencies and percentages.

Results: Thirteen patients were enrolled (9 female [69.2 %], 4 male [30.8 %]). *Pseudomonas aeruginosa* was the predominant pathogen, isolated in 7 patients (53.8 %). Coliform organisms were isolated in 5 patients (38.5 %), *Klebsiella pneumoniae* in 1 (7.7 %), and polymicrobial growth of Coliform and *Staphylococcus aureus* in 1 patient (7.7 %). Pulmonary tuberculosis was the most prevalent comorbidity (53.8 %), followed by hypertension (46.2 %) and bronchial asthma (38.5 %). None of the patients had documented pulmonary hypertension or were on LTOT. HRCT had been performed in only 5 patients (38.5 %). Among *Pseudomonas* isolates, ceftazidime (100 %), imipenem (71.4 %), and netilmicin (71.4 %) demonstrated the highest sensitivity rates, while ciprofloxacin and gentamicin sensitivity had not been adequately tested due to the poor availability of these drugs in the government sector.

Conclusions: *Pseudomonas aeruginosa* is the dominant pathogen in hospitalised bronchiectasis patients in this Sri Lankan tertiary care setting, consistent with broader Asian registry data. A post-tuberculosis aetiology appears highly prevalent. Critically, fewer than 40 % of patients had HRCT-confirmed diagnoses, indicating a significant diagnostic gap. The lack of internationally recognised, suitable antibiotics for bronchiectasis treatment represents an identified treatment gap. These findings have direct implications for empirical antibiotic stewardship and highlight the urgent need to improve adherence to international diagnostic standards, or alternatively to develop locally applicable guidelines for Sri Lanka.

Conflict of interest None

0084 50 shades of green: Longitudinal dynamics of sputum colour and associated clinical outcomes in bronchiectasis

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Background: Sputum colour is a marker of neutrophilic airway inflammation and correlates with disease severity in European bronchiectasis cohorts, but its longitudinal behaviour and clinical significance remain unclear. We sought to examine sputum colour in Canadian and UK cohorts to assess its stability over time and relationship to disease severity and activity.

Methods: Adults with non-CF bronchiectasis in the Calgary Biobank (CAN) and Liverpool POSTED (UK) cohorts were prospectively followed for up to 20 years. Sputum colour was assessed using the investigator-rated Murray 4-point chart (both cohorts) and patient-reported BEST score (UK only). Clinical features and outcomes were compared across sputum-colour scores and variability subgroups, and changes in Murray and BEST scores were analysed in relation

to outcomes. Agreement between BEST colour and Murray colour was assessed using assessed using quadratic weighted Cohen's kappa. Negative binomial models were used to estimate incidence rate ratios (IRRs) for antibiotic initiation within 30 days of a change in sputum colour or BEST score, with robust variance estimation clustered by patient identifier. Results are presented as IRRs (outcome defined such that higher values represent sooner antibiotic initiation) with 95 % confidence intervals

Measurements and Main Results: A total of 1193 sputum samples from 86 participants (range 5 to 88 samples per individual) were included across the two independent bronchiectasis cohorts. In the Canadian cohort, 39 patients provided 446 sputum samples, median (range) 7 (5-88) samples per patient across a median (range) 7 (1-22) years follow up. In general, participants in the Calgary cohort were younger (mean age 55.5 vs 69.9 years, $p < 0.001$) and had more severe disease characteristics including a mean Bronchiectasis Severity Index (BSI), 12.0 vs 8.0, $p < 0.001$.

Across both cohorts, purulent sputum was associated with lower lung function, higher BSI scores, more exacerbations, and chronic *P. aeruginosa* (all $p < 0.05$). Sample-Sample sputum colour was stable in ~90 % of samples, but patients with variable colour had more severe disease than those with persistently mucoid sputum. Investigator-patient discordance was common, quadratic weighted Cohen's Kappa (κ) of 0.36 (95 % CI, 0.22-0.50). Sample-Sample change in Murray Chart did not predict time to next exacerbation (TTNE), adjusted IRR [95 % CI] 0.96 [0.65-1.42], $p = 0.84$, whereas change in colour component of BEST (adjusted IRR [95 % CI] 1.95 [1.50-2.53], $p < 0.001$) and change in total BEST score (adjusted IRR [95 % CI] 2.05 [1.15-3.66], $p = 0.02$) were associated with shorter TTNE and greater antibiotic use.

Conclusions: This international study demonstrates that sputum colour is a prognostic biomarker with defined short- and long-term stability. Colour variability on the Murray score helps stratify disease severity. Patient-reported colour shows frequent discordance with investigator ratings, but only patient-reported colour changes are associated with short-term disease outcomes.

Conflict of interest nil

0085 Intra-host *Pseudomonas aeruginosa* dynamics under antibiotic pressure in COPD and non-CF bronchiectasis: results from an observational trial.

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Background: Antibiotic eradication therapy is a frequent intervention in *Pseudomonas*-driven exacerbations of COPD and non-cystic fibrosis bronchiectasis (NCFBE). However, the impact of intra-patient heterogeneity of *P. aeruginosa* on eradication outcomes remains unclear.

Methods: We enrolled 30 patients with COPD and/or NCFBE with known or newly detected *P. aeruginosa* colonization into an observational study. The analysis cohort consisted of 22 participants undergoing in-hospital antibiotic eradication. Respiratory samples were collected prior to, during and after eradication

therapy and extensive culture was performed to collect up to 10 randomly selected *P. aeruginosa* isolates per sample. The isolates underwent phenotypic resistance testing as well as whole-genome sequencing.

Results: *Pseudomonas*-positive cultures could be obtained in 11 out of 22 patients within the time frame of antibiotic treatment. Extended susceptibility testing indicated low levels of resistance prior to the initiation of eradication therapy and minimal intra-host phenotypic resistance variability. Whole-genome sequencing revealed that in all cases in which three or more longitudinal *Pseudomonas*-positive samples could be obtained during antibiotic therapy ($n = 4$), patients were colonized with a single clonal lineage. In most isolates, no concordance was identified between phenotypic and genotypic resistance profiles. Short-term eradication success (negative result in the final culture at the conclusion of antibiotic treatment) was observed in most patients (10/11).

Conclusion: *P. aeruginosa* colonization in COPD/NCFBE patients may primarily involve a single clonal lineage and exhibit low intra-host resistance heterogeneity. While limited by the sample size of our cohort, these findings suggest that susceptibility testing of a single isolate can inform eradication therapy in these selected patients.

0086 Evolving Multidrug-Resistant *Pseudomonas aeruginosa* and Nontuberculous Mycobacterial Infections in Cystic Fibrosis Bronchiectasis Through Bilateral Lung Transplantation

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Background/Aims: Cystic fibrosis (CF) patients with bronchiectasis harboring multidrug-resistant (MDR) *Pseudomonas aeruginosa* and nontuberculous mycobacterial (NTM) infections represent among the highest-risk candidates for lung transplantation. Uncontrolled NTM may necessitate transplant inactivation, while post-transplant immunosuppression can drive resistance evolution and polymicrobial superinfection. We present the infectious disease management of a CF bronchiectasis patient with extensively drug-resistant (XDR) *P. aeruginosa* and refractory *Mycobacterium avium* complex (MAC), emphasizing treatment duration, resistance evolution, and tailored perioperative prophylaxis.

Methods: Retrospective single-patient case review of microbiological data, antimicrobial susceptibility profiles, treatment durations, imaging, and clinical outcomes from pre-transplant evaluation through 28 months post-bilateral orthotopic lung transplantation (BOLT).

Results: A male in his mid-50s with CF bronchiectasis ($\Delta F508/2789 + 5G > A$), *P. aeruginosa* colonization since 2010, and MAC (culture-positive since 2019 despite ~4 years of multidrug therapy) was listed for BOLT in December 2022. Transplant was inactivated in February 2023 when *P. aeruginosa* demonstrated XDR phenotype (susceptible only to cefiderocol; resistant to meropenem, cefepime, ceftazidime, piperacillin-tazobactam, ceftolozane-tazobactam, aztreonam, ciprofloxacin, levofloxacin, tobramycin) and MAC showed a positive AFB smear indicating high organism burden.

A six-drug MAC regimen was developed with national NTM experts: azithromycin 250 mg, ethambutol 1200 mg, rifabutin 300 mg, clofazimine 100 mg, tedizolid 200 mg daily, and inhaled amikacin 590 mg daily (previously discontinued due to MIC 128). After negative AFB smears/cultures for > 3 months, the patient was reactivated. Pre-transplant *Aspergillus fumigatus* (BAL antigen 7.728; serum negative) required isavuconazole 372 mg daily.

Tailored perioperative prophylaxis included cefiderocol 2g IV q8h and IV amikacin 30 mg/kg (14 days each), intraoperative amikacin/amphotericin B pleural irrigations, and oral vancomycin for *C. difficile* prevention. BOLT was performed October 15, 2023 (CMV D - /R +). Transplanted lungs showed bronchiectasis with necrotizing granulomatous inflammation; AFB/GMS stains were negative. Allograft cultures grew pan-susceptible *P. aeruginosa* (donor-derived, < 10K CFU/

mL) and *C. krusei*, treated with piperacillin-tazobactam continuous infusion (14 days) and inhaled tobramycin (30 days).

Rifabutin was discontinued day 12 post-transplant (CYP3A4 interactions with tacrolimus/isavuconazole). MAC therapy continued with 4 drugs and was completed 12 months post-last positive culture; total MAC treatment: ~5 years. All post-transplant NTM cultures remained negative through 28 months of follow-up.

The post-transplant course was complicated by failure to thrive (BMI 16–18 kg/m², weight 45–50 kg), pancytopenia, and suspected drug-induced neurotoxicity prompting everolimus discontinuation. By September 2025, BAL cultures demonstrated MDR *P. aeruginosa* re-emergence (susceptible only to piperacillin-tazobactam; intermediate to tobramycin) alongside *Providencia rettgeri* (10–50K CFU/mL), *Achromobacter xylosoxidans* (10–50K CFU/mL), *Aspergillus flavus*, and *C. difficile* colitis. Treatment required piperacillin-tazobactam IV (14 days), inhaled tobramycin, voriconazole, and oral vancomycin (10 days).

Conclusions: Lung transplantation is feasible in CF bronchiectasis with concurrent XDR *P. aeruginosa* and refractory MAC through aggressive pre-transplant optimization and individualized perioperative prophylaxis. MAC was cured after ~5 years of combination therapy; however, *P. aeruginosa* resistance evolved in the allograft with emerging polymicrobial infections, underscoring the need for longitudinal susceptibility surveillance and multidisciplinary collaboration.

Conflict of interest None

0087 Etiological and Microbiological Phenotypes of Non-Cystic Fibrosis Bronchiectasis in Vietnam: A High Tuberculosis-Burden Cohort

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Background/Aims: Data on bronchiectasis phenotypes in Vietnam remain limited. We aimed to describe the clinical, radiological and microbiological characteristics of bronchiectasis in a two-center Vietnamese cohort, with particular attention to post-tuberculosis (post-TB) disease.

Methods: We conducted a retrospective two-center study of patients with bronchiectasis managed at Cho Ray Hospital and University Medical Center, Ho Chi Minh City, from 2024 to 2025. Continuous variables were summarized as median [IQR] and categorical variables as n (%). Exploratory subgroup analyses compared post-TB versus non-post-TB bronchiectasis, and *Pseudomonas* versus other identified bacterial isolates.

Results: Ninety-five patients were included. Median age was 59 years [44.8–68.3], and 72/91 (79.1 %) were female. Dyspnea was present in 56/82 (68.3 %), bilateral disease in 58/88 (65.9 %), and the median number of involved lobes was 3 [2–4]. Median FEV1 was 78 % predicted [64.0–87.5], median Bronchiectasis Severity Index (BSI) was 4 [3–6], and median Reiff score was 4 [2–7]. Among 78 patients with recorded etiology, idiopathic bronchiectasis accounted for 29/78 (37.2 %) and post-TB bronchiectasis for 22/78 (28.2 %). Post-TB patients were more often male (38.1 % vs 13.2 %, *p* = 0.025), more frequently ever-smokers (25.0 % vs 2.1 %, *p* = 0.008), and had higher white blood cell counts (10.03 [7.60–11.47] vs 7.06 [5.76–8.20], *p* < 0.001), but showed no clear differences in FEV1, BSI or Reiff score. Bacterial culture was positive in 43/65 (66.2 %). Among 23 cases with identified bacterial isolates, *Pseudomonas* was the most common organism (10/23, 43.5 %) and was associated with higher BSI (6.5 [5.25–9.0] vs 4.0 [3.0–4.0], *p* = 0.004) and higher Reiff score (6.0 [4.25–8.5] vs 3.0 [3.0–5.0], *p* = 0.021).

Conclusions: Post-TB bronchiectasis represents a substantial phenotype in this Vietnamese two-center cohort. While etiology alone was not clearly asso-

ciated with greater functional or composite severity, *Pseudomonas* isolation identified patients with more severe structural and clinical disease.

Conflict of interest none

0088 Treatment Outcomes in Chronic Pulmonary Aspergillosis: A Single-Center Retrospective Analysis

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DOI 10.1055/s-0046-1826103

Background/Aims: Chronic pulmonary aspergillosis (CPA) comprises a spectrum of progressive lung diseases occurring in patients with structural lung disease, including bronchiectasis and impaired host response to *Aspergillus* species, most commonly *Aspergillus fumigatus*. The most severe phenotypes include cavitary chronic pulmonary aspergillosis (CCPA), chronic fibrocavitary pulmonary aspergillosis (CFPA), and subacute invasive pulmonary aspergillosis (SAIA). Despite antifungal therapy, CPA remains associated with significant morbidity and mortality. This study aimed to characterize CPA patients treated at a Evangelische Lungenklinik Berlin a tertiary care center and evaluate clinical outcomes.

Methods: We conducted a retrospective analysis of patients treated at Evangelische Lungenklinik Berlin between 2018 and 2025. The hospital database was screened for aspergillosis cases using ICD-10 codes (B44.0–B44.9). Patients fulfilling the 2016 ESCMID/ERS diagnostic criteria for CPA were included. Cases of simple aspergilloma and *Aspergillus* nodules were excluded from outcome analyses. Clinical data, treatment regimens, complications, and survival were assessed. Survival analysis was performed using the Kaplan–Meier method.

Results: Of 235 patients with ICD-10 codes suggestive of aspergillosis, 54 met diagnostic criteria for CPA. After exclusion of simple aspergilloma (*n* = 12) and *Aspergillus* nodules (*n* = 3), 39 patients were included in the final analysis (CCPA *n* = 28; CFPA *n* = 7; SAIA *n* = 4).

Median age was 63 years (range 30–87), and 64 % were male. Median follow-up was 1.68 years (range 0.07–5.6). All 39 patients received primary antifungal therapy with triazoles.

Comorbidities were common, with COPD (30.8 %) being the most frequent, followed by lung cancer (23.1 %) and bronchial asthma (20.5 %). Other relevant conditions included prior tuberculosis (15.4 %), emphysema (15.4 %), nontuberculous mycobacterial disease (12.8 %), bronchiectasis (10.3 %) and sarcoidosis (5.1 %).

Treatment modification occurred in 15 patients (38 %), mainly due to adverse drug effects (*n* = 13; 33 %). Hemoptysis was observed in 11 patients (28 %). Six patients (15 %) required surgical intervention, and four (10 %) underwent pulmonary artery embolization.

More than 70 % of patients demonstrated clinical and radiological response within 3–6 months. Estimated median survival was 3.5 years.

However, overall prognosis remained limited: 16 patients (41 %) died during follow-up, with a median time to death of 10.2 months after diagnosis.

Conclusions: CPA is associated with substantial morbidity, frequent complications such as hemoptysis, and a high rate of treatment modification due to drug-related toxicity. Although most patients initially respond to antifungal therapy, long-term prognosis remains poor.

These findings highlight the need for improved therapeutic strategies and better identification of prognostic factors. Interpretation is limited by the retrospective single-center design and relatively short follow-up, underscoring the need for prospective multicenter studies.

Conflict of interest no conflict of interest

0089 Optimising paediatric to adult transition clinics for patients with Non-Cystic Fibrosis Bronchiectasis: A thematic analysis of data collected from service users and healthcare professionals

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Background Non-Cystic Fibrosis Bronchiectasis (NCFB) is a chronic respiratory condition characterised by dilatation of bronchi, recurrent infections and a productive cough. There are many aetiologies of NCFB, with a significant proportion diagnosed in childhood. Effective transition from paediatric to adult services is important for patient experience, future self-management and longer-term health.

Aims

1. To explore, understand and describe the views of service users (patients, parents/carers), and health care professionals (HCPs) who have accessed the current bronchiectasis transition service at a tertiary NHS Hospital.
2. To use the data to inform development of resources and procedures to optimise transition.

Methods Questionnaires including both quantitative and qualitative elements were designed for patients, parents/carers and HCPs; exploring views of the current service and suggestions for development. Questionnaires were issued to service users via several methods to maximise response rate (post, text message, phone call, in person). Surveys to healthcare professionals were disseminated via email and findings were further explored in an online focus group. Thematic analysis was used to analyse qualitative data.

Results

Service Users: 22 patients were invited to complete the survey with a 50% response rate. Data was also collected from 6 parents/carers. Age of first attendance at transition clinic was 16-18 years. Patients had attended 1 (n=6) or 2 (n=5) transition clinic appointments; 91% of respondents felt this was sufficient. 100% of responders felt that transition appointments were useful. Analysis of qualitative data identified three core themes:

Communication: service users felt welcomed, at ease, recognised good links between the teams and felt both being present in appointments helped the transition.

Preparedness: most reported feeling prepared and well informed, with improvement suggestions including more appointments and an information resource.

Service differences: variations in service delivery were noted as significant changes to get used to.

Healthcare Professionals: 8 HCPs responded (100%), including doctors, nurses and physiotherapists. 75% felt that the current transition pathway improved care, however, only 25% agreed the existing structure was "optimal", acknowledging the need for service user involvement in changes. Key emerging themes included:

Optimal service delivery: HCPs wanted to start the transition process earlier, emphasise the importance to young adults, use recognised systems and develop SOPs and resources for service users. Service user involvement was considered essential to ensure appropriate change. HCPs indicated that 1 to 3 transition clinic appointments would be suitable for most patients, with both adult and paediatric teams present, on both sites.

Service differences: highlighting that paediatric and adult clinics are run differently, with variation in which HCPs form part of the core team, how patients

access the service, how frequently patients are seen and where they are seen. Ensuring smooth transition is key.

Conclusions This data highlights requirements for a thorough preparation process for the transition of high quality, individualised bronchiectasis care from paediatric to adult services. These findings have informed the design and implementation of a revised standard practice at our trust, changes in clinic frequency and location and creation of a simple transition leaflet for service users.

Conflict of interest None

0090 Recognising Diffuse Panbronchiolitis in Multicultural Bronchiectasis Populations: The Diagnostic Value of Nasal Nitric Oxide

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Background Diffuse panbronchiolitis (DPB) is a chronic inflammatory airway disease most commonly described in East Asian populations. Outside these regions, DPB may be under-recognised and misclassified as idiopathic or post-infectious bronchiectasis. Nasal nitric oxide (nNO) measurement is widely used as a screening tool for primary ciliary dyskinesia (PCD), where levels are characteristically low; however, reduced nNO has also been described in DPB and may not be widely appreciated in clinical services caring predominantly for Caucasian populations.

Methods: We present a case series of three adult patients of Asian background (2 x Vietnamese, 1 x Chinese) referred to a tertiary bronchiectasis service. All presented with chronic productive cough, longstanding rhinosinusitis, and radiological bronchiectasis, and were initially managed as standard bronchiectasis. As part of further evaluation for persistent symptoms, nasal nitric oxide was measured using a chemiluminescence analyser.

Results: All three patients demonstrated significantly reduced nasal nitric oxide levels, within a range commonly associated with PCD, contributing to diagnostic uncertainty. However, the overall clinical phenotype (including ethnicity, upper and lower airway involvement, imaging findings, and disease course) was more consistent with diffuse panbronchiolitis. Recognition of this pattern prompted initiation of long-term macrolide therapy in all patients. Each experienced substantial symptomatic improvement, reduced exacerbation frequency, and improved functional status following treatment.

Conclusion: This case series highlights that low nasal nitric oxide is not specific to PCD and may also be observed in diffuse panbronchiolitis. In bronchiectasis clinics serving predominantly Caucasian populations, this association may be under-recognised, risking misdiagnosis and delayed effective therapy. Nasal nitric oxide measurement may be a useful adjunct in the diagnostic work-up of complex bronchiectasis, provided results are interpreted in clinical context. Early identification of DPB is essential given its favourable response to macrolide therapy.

0091 UK Clinician Access, Utilisation and Eligibility Perspectives Genetic testing in Bronchiectasis: A National Survey

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Background/Aims: Genomic testing is increasingly recognised as an important component of bronchiectasis evaluation, particularly for identifying underlying ciliopathies, immunodeficiencies and other genetic contributors. The NHS England R189 “Respiratory Ciliopathies including non-CF bronchiectasis” gene panel provides a comprehensive approach, yet uptake remains variable, and concerns have been raised regarding the suitability and restrictiveness of current eligibility criteria. Although it is accessible only to clinicians in England we asked all devolved nations (Wales, Scotland & N. Ireland) view on their (equivalent) access to genetic testing. To inform future service development, we conducted a national survey of clinicians managing bronchiectasis to evaluate access, utilisation, and perceived appropriateness of R189 criteria (see <https://panelapp.genomicsengland.co.uk/panels/550/>)

Methods: An anonymous online survey was distributed to bronchiectasis-treating clinicians across the UK. Respondents reported their clinic size, region, perceived access to extended genetic testing, frequency of ordering the R189 panel, and views on the panel’s usefulness and eligibility criteria. Free-text comments were analysed thematically.

Results: Sixteen clinicians responded, representing England (10), Scotland (4), Wales (1), and Northern Ireland (1). Clinic sizes ranged from “1–249 patients” to “750+ patients”.

Access to R189 testing (or similar) varied widely.

- Easy access: 9 clinicians
- Some access but administrative/MDT barriers: 5 clinicians
- Very limited access: 2 clinicians
- No access due to cost: 1 clinician

Several respondents highlighted administrative workload, MDT approval, and pathway inconsistency as barriers to routine use.

Frequency of ordering extended genetic testing

- Regularly (1–5 requests/month): 6 clinicians
- Rarely: 9 clinicians
- Never due to access issues: 1 clinician

Thus, even clinicians with easy access may order tests infrequently, citing uncertainty regarding criteria, perceived yield, or competing clinical priorities. Perceptions of the R189 panel; All 16 clinicians considered the panel clinically useful.

However, 13 of 16 clinicians felt that eligibility criteria are too narrowly focused on childhood-onset symptoms, particularly chronic respiratory symptoms “since infancy”. Only 3 respondents believed the criteria were appropriate.

Key Themes from Qualitative Analysis

A) Eligibility criteria too restrictive for adult presentations (dominant theme); Clinicians consistently described that:

- Many adults with PCD, CFTR-related disease or immunodeficiency do not recall early symptoms.
- Adult-onset or late-diagnosed bronchiectasis is common.
- Restrictive criteria risk “missing” a substantial proportion of genetic disease in adults.

Several clinicians stressed that childhood-onset frameworks reflect outdated assumptions and ignore the heterogeneous and often subtle early manifestations of genetic disease.

B) Mismatch between panel scope and entry criteria; Respondents noted that the majority of genes on R189 relate to PCD, but the panel also includes multiple immunodeficiency-related and other bronchiectasis genes.

Criteria focused on PCD phenotype therefore “do not match the purpose of the panel”.

One clinician described the need to “broaden the panel’s clinical indications to match the genetic content”.

C) Suggested expansions to R189 eligibility; Commonly proposed additional criteria included:

- Severe bronchiectasis in adults < 50 years
- Any idiopathic bronchiectasis, regardless of age
- Family history of bronchiectasis or ciliopathies
- Recurrent infections or immunodeficiency features
- Complex microbiology (e.g., NTM, fungi)
- “Unexpectedly severe” or rapidly progressive disease at any age

Several clinicians strongly advocated testing all “younger adults with idiopathic bronchiectasis”.

D) Pathway challenges and reliance on other services

Some clinicians described reliance on immunology or PCD services for access. Others highlighted delays, variable interpretation by genetics labs, and requests for unnecessary referrals

Conclusions: This national survey demonstrates strong clinician support for the R189 gene panel, but widespread concern that current eligibility criteria are overly restrictive and misaligned with real-world bronchiectasis presentations. Respondents recommend broadening criteria to include adult-onset, idiopathic and severe disease, incorporating family history and immunodeficiency features, and addressing pathway-related barriers. Optimising access and criteria will improve diagnostic equity and better reflect the heterogeneous nature of bronchiectasis.

Conflict of interest None

0092 Knowledge, Attitudes, and Practices Regarding Clinical Management of Bronchiectasis Among Doctors Managing Adult Respiratory Illnesses in Sri Lanka: A Cross-Sectional Study

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Background/Aims: Bronchiectasis is a chronic progressive respiratory disease with rising global prevalence, particularly in Asia and low- and middle-income countries (LMICs). Sri Lanka bears a substantial burden of post-tuberculous respiratory disease; however, physician knowledge, attitudes, and practices (KAP) regarding bronchiectasis management remain entirely unstudied in this context. . KAP studies provide a structured methodology for characterising gaps between theoretical knowledge, prevailing attitudes, and actual clinical behaviour. There is no equivalent study has been published for Sri Lanka or South Asia prior to this investigation

This study assess Knowledge Attitude and Practices of doctors managing adult respiratory illnesses in Sri Lanka regarding bronchiectasis clinical management based on British Thoracic Society (BTS) guidelines, identify service infrastructure gaps, and determine factors associated with adequate knowledge.

Methods: A cross-sectional descriptive study was conducted among 98 doctors across all 9 provinces of Sri Lanka (Uva Province: no responses) using a validated, self-administered electronic questionnaire based on BTS guidelines. Knowledge (7 items, max score 7), attitude (5 Likert items, max 25), and practice (5 scored + 3 descriptive items) were assessed. Non-parametric tests (Mann-Whitney U, Kruskal-Wallis, Spearman’s ρ) and binary logistic regression were applied; SPSS version 26 was used throughout.

Results: Mean knowledge score was $5.84 \pm 0.82/7$; 65.3% demonstrated good knowledge (score 6–7) and 34.7% moderate knowledge. Attitude was predominantly neutral (48.0%) or positive (43.9%; mean $19.68 \pm 3.43/25$). Practice

levels were predominantly good (90.8%). Respiratory specialty (OR = 3.30, 95% CI: 1.32–8.24, $p = 0.011$) was an independent predictor of adequate knowledge, while prior training showed a positive but non-significant association (OR = 2.14, 95% CI: 0.86–5.35, $p = 0.102$). Critical service gaps included HRCT unavailability in 40.8%, absent chest physiotherapy in 22.4%, and lacking sputum culture capacity in 15.3% of settings.

Conclusions: Sri Lankan physicians demonstrate satisfactory overall KAP; however, significant specialty-related knowledge disparities and healthcare infrastructure deficits persist. The lowest item accuracy was for first question regarding knowledge as what is the least likely cause of adult bronchiectasis (acute viral URTI as least likely cause: 54.1%), reflecting gaps in differential etiology understanding. Targeted CME for non-respiratory specialists and urgent investment in diagnostic infrastructure are essential to optimize bronchiectasis care in Sri Lanka.

Conflict of interest None

0093 Diagnostic Detectives: outcomes from the case files of a regional bronchiectasis diagnostic clinic

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Background/Aims: Recent updates to ERS Bronchiectasis guidelines highlight the importance of aetiological classification. Despite this, almost 40% are classed as idiopathic in EMBARC data. As the regional Cystic Fibrosis (CF) and Primary Ciliary Dyskinesia (PCD) centre and a provider of non-CF bronchiectasis care, we have developed a pan-Wales multi-disciplinary diagnostic service for “unexplained” bronchiectasis in younger (<50 years) groups or with other features of multi-system disease (► **Tab. 1**).

► **Table 1** Clinic demographics

	(n) (%)
Total	46 (100%)
Male	19 (41%)
Mean age (range)	41.7 (18-90)
Mean FEV1 (%pred)	81
Ps. Aeruginosa	9 (20%)
CFTR gene variants	11 (24%)
SCC > 30mmol/L	14 (30%)
Nasal FeNO < 200ppb	4 (9%)

Methods: Our service has been running since 2023, and we have reviewed outcomes of referrals since initiation. Structured clinical assessment, blood and respiratory sample testing, lung function, FeNO (nasal and lower airway), radiography, sweat chloride testing (SCC) and genetic testing (CF50, extended CFTR genotyping and R189 ciliopathy panel) are available where indicated. Specialist physiotherapists and dieticians are integrated into clinic.

Following initial consultation and work up, either virtual or in-person follow up is arranged to review and discuss results. Following this, attendees are either retained under our service, referred onwards for further specialist testing or discharged back to the referring team.

Results: 46 individual referrals have been seen. Most referrals originate from secondary care respiratory clinics **31/46 (67%)**.

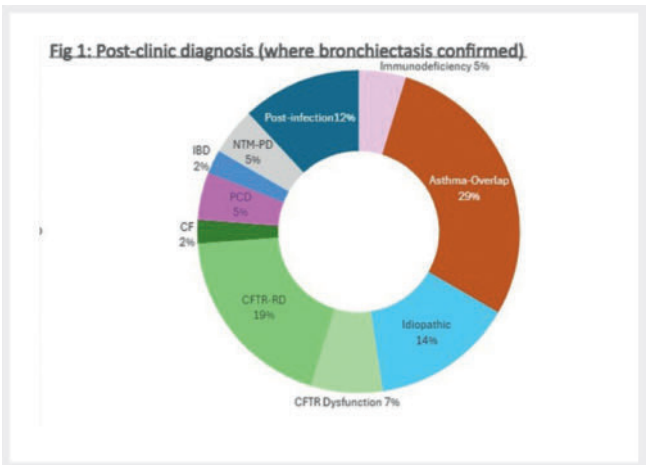
Bronchiectasis has been confirmed in **42/46**, suspected aetiology identified in **36/42 (86%)**, and following review, treatment modifications made in **32/42 (76%)**.

Among those with bronchiectasis, we have frequently identified altered CFTR function (raised SCC) or CFTR gene variants amongst attendees. As per ECFS diagnostic criteria, **1** late diagnosis of Cystic Fibrosis was made (now trialling CFTR modulator therapy) and **8** diagnosed with CFTR-related disorders. A further **3** had persistent (2+) elevated SCC (>30mmol/L) not meeting diagnostic criteria for either CF or CFTR-RD.

Coexisting airways disease was also common. As per NICE/BTS diagnostic criteria, asthma was diagnosed or confirmed in **12/42 (29%)**. Asthma therapy was uptitrated in **10/12 (83%)**, and **3/5** meeting NICE criteria for consideration of biologic therapies are trialling this following asthma MDT discussion.

Onward referral to a national diagnostic centre resulted in **2** PCD diagnoses.

Conclusions: Our specialist diagnostic service has helped identify associated pathology for most referrals and provide access to multi-disciplinary support. A unified cross-respiratory approach improves access to targeted treatment including biologic therapies with existing guidance utilised when being considered in people with bronchiectasis (► **Fig. 1**).



► **Fig. 1**

Altered CFTR function in respiratory disease other than CF has been recognised previously and requires further evaluation as a “treatable trait.”

Building links between adult respiratory services and newborn screening services to recognise CF-screen positive, inconclusive diagnosis (CF-SPID) presenting to adult services is a future priority (locally not recorded in adult health records). As an additional potential indicator of CFTR dysfunction this may help with endotyping or prompting referrals for further testing.

Conflict of interest No conflicts of interest have been identified

0094 Importance of Understanding the Patient Experience in Healthcare: An Example of the Integrated Patient Journey in Non-Cystic Fibrosis Bronchiectasis

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Introduction: Non-cystic fibrosis bronchiectasis (NCFB) is a chronic, under-recognized condition that places a substantial burden on patients and healthcare systems [1]. To better align clinical development and support strategies with patient realities, we created an Integrated Patient Journey (IPJ) that incorporates the patient voice alongside clinical and real-world evidence.

Methods: The IPJ was constructed using published literature, real-world data, patient-reported outcome measures (PROMs), and qualitative insights from semi-structured patient interviews. To supplement existing evidence, six in-

interviews were conducted with NCFB patients, facilitated with the help of the COPD foundation. These interviews explored unmet needs, barriers to screening and diagnosis, challenges in follow-up care, and other impactful qualitative dimensions of the individual patient experience. Findings were mapped into a standardized three-stage framework, Diagnosis, Treatment, and Follow-Up, capturing not only medical touchpoints but also emotional, financial, and social experiences. This approach provided a structured view of barriers, unmet needs, and opportunities across the patient pathway.

Results: Once diagnosed, patients reported a high treatment burden, frequent adherence challenges, and limited support for the emotional and social impact of disease management (► Fig. 1). These results highlight opportunities to address.



► Fig. 1

Conclusion: By embedding patient perspectives into a systematic framework, the IPJ demonstrates how the patient voice can generate actionable insights that go beyond clinical endpoints, including the development of novel endpoints that reflect patient-prioritized outcomes, improve alignment with the real-world needs of patients, and inform strategies that enhance both patient outcomes and healthcare value. These results demonstrate that integrating lived experience is not optional but essential for advancing patient-centered care and development.

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Disclosures: All authors are employees of Sanofi and may hold stocks/stock options in the company

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0095 Caregiver Perspectives on Pediatric Non-Cystic Fibrosis Bronchiectasis Clinical Trial Design: Insights from US Caregiver Panels

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Background/Aims Non-cystic fibrosis bronchiectasis (NCFB), including Primary Ciliary Dyskinesia (PCD), represents a significant burden for pediatric patients and their families. Currently, limited data exists regarding caregiver perspectives on clinical trial participation. Understanding family priorities, concerns, and preferences is essential for designing patient-centered trials that optimize recruitment, retention, and participant experience. This study ex-

plored caregiver perspectives on clinical trial design elements, participation barriers, and ideal treatment characteristics for children with NCFB.

Methods Two US caregiver panels (one for adolescents, one for younger children) were conducted in Q4 2025 with support from the Bronchiectasis and nontuberculous mycobacteria (NTM) Association. Panel 1 included 3 caregivers of children aged 12–18 years (n = 4), and Panel 2 included 2 caregivers (parents) of a child aged 10 years (n = 1). All adolescent children were diagnosed with PCD. Children had varied clinical trial experience (0–4 prior trials). Semi-structured discussions explored study logistics and scheduling preferences, procedure tolerability, daily symptom tracking feasibility, decision-making factors, placebo design acceptability, support needs, and ideal treatment characteristics.

Results

Study Design Preferences: Monthly clinic visits of 1.5–2 hours were considered manageable across both age groups. Caregivers emphasized the importance of evening or weekend scheduling or offering summertime visits to reduce school disruption. Home visits for blood draws were strongly preferred. Concerns were raised regarding radiation exposure from imaging procedures. Daily symptom tracking via personal smartphone application (approximately 2 minutes per day, completed in the evening) was deemed manageable when supported by reminder notifications.

Decision-Making Factors: Child safety and comfort were paramount priorities across both panels. Caregivers required clear information about medication mechanism of action, expected benefits, and potential side effects. Trust in the medical team, particularly involvement of the child's regular pulmonologist, was critical for participation confidence. Placebo-controlled designs were understood as scientifically necessary but emotionally challenging; guaranteed access to active treatment post-trial would significantly increase acceptability. **Support Needs:** Caregivers preferred healthcare professionals rather than parents to administer procedures such as injections and blood draws. Age-appropriate educational materials for children, quick access to the clinical team for questions or emergencies, and consistency and empathy in staff interactions were identified as key support requirements.

Ideal Treatment Characteristics: Improved symptom control—including enhanced mucus clearance, cough reduction, and exercise tolerance was highly valued. Oral or inhaled administration was preferred over injections. Enhanced quality of life outcomes, including improved stamina, physical activity capacity, and social participation, were primary goals.

Participation Motivators: Direct benefit to the child's health and quality of life was the primary motivator. Hope for slowing disease progression through physical activity limiting symptoms and daily treatment burden reduction were also important. Contributing to research for future patients was mentioned as a secondary motivation.

Conclusions Caregivers of children with NCFB prioritize child safety, treatment burden reduction, and clear communication when considering clinical trial participation. Study designs incorporating flexible scheduling, home-based procedures, involvement of trusted pulmonologists, and minimally invasive monitoring approaches are most acceptable to families. These thematic findings provide insights for designing patient-centered pediatric NCFB trials that address family needs while advancing therapeutic development.

Conflict of interests The caregiver panels were facilitated with support from the Bronchiectasis and NTM Association. The authors would like to acknowledge that the Bronchiectasis and NTM Association and its programs are supported in part by corporate donors, all of which can be found on the Supporters page of the Association website. This work was funded by Sanofi. AM, FV and PAK are employees of Sanofi and may hold shares and/or stock options.

0096 Improving access to airway clearance devices in bronchiectasis: A service evaluation of Aerobika provision through a Mater Foundation initiative

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DOI 10.1055/s-0046-1826111

Background Bronchiectasis is a chronic respiratory condition characterised by abnormal airway dilatation, airway inflammation, and recurrent infection, commonly presenting with persistent productive cough and sputum production. It is associated with recurrent exacerbations and reduced health-related quality of life.

Airway clearance therapy is a cornerstone of bronchiectasis management, supporting sputum clearance, symptom control, and self-management. Positive expiratory pressure (PEP) devices are commonly prescribed; however, access to subsidised devices is often limited for patients with non-cystic fibrosis bronchiectasis, who are typically required to self-fund airway-clearance equipment. A Mater Foundation initiative enabled the provision of Aerobika (oscillating PEP) devices to patients attending a tertiary bronchiectasis outpatient clinic. This service evaluation aimed to assess patient experience, including satisfaction, usability, and perceived benefit of Aerobika devices provided through this initiative.

Methods A single-centre quality assurance service evaluation was conducted in a respiratory outpatient bronchiectasis clinic. Adults with non-cystic fibrosis bronchiectasis who had been provided with an Aerobika device were invited to complete a short anonymous questionnaire. The survey assessed satisfaction, usability, perceived benefit, and integration of the device into airway clearance routines, as well as perceived changes in airway clearance frequency and access to the device. Surveys were completed via Microsoft Forms. Data were analysed descriptively.

Results Ten patients completed the survey. Mean satisfaction with the Aerobika device was 74 %. All patients (100 %) reported that the device was easy to use. The majority (70 %) reported that the Aerobika helped clear sputum from their chest, fit easily into their daily routine, and supported management of their chest symptoms. 60 % of patients reported performing airway clearance more often since receiving the device.

Qualitative feedback identified key facilitators of use, including ease of use, ease of cleaning, lightweight design, and the ability to feel vibrations in the chest during use. Reported barriers were minimal, with some participants noting that the device could be difficult to take apart for cleaning, particularly for those with hand difficulties.

Conclusions Provision of Aerobika devices through a hospital foundation initiative was associated with high patient satisfaction and positive patient-reported experiences. Patients reported that the device was easy to use, integrated well into daily routines, and supported airway clearance and symptom management.

These findings highlight the potential benefit of initiatives that improve access to subsidised airway clearance devices for patients with bronchiectasis who would otherwise be required to self-fund, supporting adherence, self-management, and addressing inequities in access to recommended therapies.

0097 Unity is strength: early results from a joint pulmonology–infectious diseases outpatient clinic for the management of infectious complications of bronchiectasis at the Alessandria University Hospital

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Background The management of bacterial and mycobacterial superinfections in bronchiectasis requires a multidisciplinary diagnostic and therapeutic approach. At the AOU SS Antonio e Biagio e Cesare Arrigo in Alessandria, a monthly outpatient service jointly run by a pulmonologist and an infectious diseases specialist has been established. During visits, patients undergo a combined clinical evaluation, with the possibility of performing on-site simple spirometry using a portable device and initiating a dedicated respiratory physiotherapy program.

Methods: All patients attending the outpatient clinic were enrolled. Demographic, microbiological, and respiratory function data were collected. Diagnostic and therapeutic pathways decided through a multidisciplinary approach were also analyzed.

Results: Since June 2024, a total of 54 patients, equally distributed between males and females and with a mean age of 69 years, have received at least one joint evaluation. Eighteen patients had isolation of non-tuberculous mycobacteria (NTM) from respiratory samples, most commonly *Mycobacterium avium* (12 cases), followed by *M. abscessus subsp. abscessus* (5), *M. xenopi* (4), *M. intracellulare* (2), and *M. celatum* (1). Twentyfour patients had isolation of Gram-negative bacteria, including *Pseudomonas aeruginosa* in five cases. In ten cases, both Gram-negative bacteria and NTM were isolated. Thirtyeight patients underwent simple spirometry during at least one visit to assess respiratory function. Fortyseven patients received at least one therapeutic intervention following joint evaluation, including modification of bronchodilator therapy, initiation of respiratory physiotherapy, or a course of antibacterial treatment (Diagram 1).

Conclusions: In our setting, the multidisciplinary management of patients with bronchiectasis allows for a comprehensive and global approach, ensuring accurate assessment of respiratory function and optimization of therapeutic strategies, including pharmacological treatments. It also enables patients to access care more rapidly. Collaboration between the two specialists results in therapeutic modifications in most cases. Increasing the sample size and longitudinal follow-up will be necessary to obtain statistically significant data.

Conflict of interest none

0098 Nationwide trends in incidence and management of bronchiectasis in Korea

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Background/Aims: Bronchiectasis is a chronic structural airway disease associated with substantial morbidity, mortality, and healthcare utilization, and known to exhibit distinct patterns across different countries. Although treatment strategies have advanced substantially in recent years, real-world prescribing and treatment patterns remain poorly characterized in Korea. We aimed to describe nationwide trends in incidence, diagnostic evaluation, and pharmacologic management of bronchiectasis in Korea using National Health Insurance (NHI) claims database

Methods: We did retrospective cohort study using the Korean NHI claims database from 2015 to 2022. Adults with incident bronchiectasis except cystic fibrosis were identified using ICD-10 codes, requiring a two-year washout period without prior codes. We evaluated annual incidence, diagnostic tests, and prescription patterns, and also evaluated the exacerbation by episodes of short-term antibiotics and systemic steroid, and hospitalization including intensive care unit (ICU) admission and emergency room (ER) visit.

Results: Between 2017 and 2022, total of 320,975 incident cases of bronchiectasis were identified, and the number of incident cases showed a gradual decline over time, decreasing from 33,284 in 2017 to 23,801 in 2022. Among them, 278,166 (86.7%) were aged 50 years or older, indicating that the disease

was predominantly observed in the elderly population, and 182,240 (57%) were female. The most common comorbidities were asthma in 106,165 patients (33%) and chronic obstructive pulmonary disease (COPD) in 98,193 patients (31%). Computed tomography was performed in 209,693 cases (65%), whereas pulmonary function tests were conducted in only 93,320 patients (29%), and pulmonary rehabilitation was documented in just 1,202 cases. Regarding pharmacologic treatment, only 14,608 cases (4.6%) used inhalers other than relievers, and 21,474 cases (6.7%) were prescribed mucolytics. Long-term macrolide therapy was identified in 2,120 cases, non-macrolide long-term antibiotic therapy in 2,408 cases, and long-term systemic corticosteroid use in 6,502 cases. Also, 145,307 cases (45%) experienced three or more episodes of short-term antibiotic use within a year, and 91,266 cases (28.4%) had three or more episodes of short-term systemic corticosteroid use. In addition, a substantial proportion of patients experienced severe clinical events, with 113,544 cases (35%) requiring hospitalization, 57,240 cases (18%) visiting the emergency room, and 8,718 cases (2.7%) requiring intensive care unit (ICU) admission.

Conclusions: Although the incidence of bronchiectasis in Korea showed a declining trend over the study period, pulmonary function test and pulmonary rehabilitation remained substantially underutilized. The majority of patients did not receive regular treatment including maintenance inhaler, and long-term macrolide use was infrequent. In contrast, considerable proportion of patients experienced frequent exacerbation-like episodes, with short-term antibiotics and systemic corticosteroids and hospitalization. These findings reveal a significant gap between the high burden of acute events and the low utilization of maintenance therapies, underscoring the need for greater attention to proactive bronchiectasis management.

Conflict of interest none declared

SESSION: NTM 1

0099 Molecular identification and resistance profile of respiratory NTM strains in a single center over a five-year period

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Background/Aims: Several nontuberculous mycobacteria (NTM) species are regarded as non-pathogenic to humans, but especially species of the *M. abscessus* complex (MABC) and *M. avium* complex (MAC) cause infections in patients with underlying lung disease or immunosuppression.

In this single-center study, we analyzed 71 NTM strains over a five-year period, from January 2021 to January 2026. We included MABC and MAC, and included only the first isolate for each patient. All strains were cultured from respiratory samples from patients with underlying lung diseases such as bronchiectasis and/or cystic fibrosis. We aimed to assess, retrospectively, the distribution of individual species within the aforementioned groups and their observed molecular mechanisms of resistance to aminoglycosides and macrolides.

Methods: Determination of the subspecies and molecular mechanisms of resistance to macrolides and aminoglycosides was performed using the GenoType NTM-DR® (Hain Lifescience GmbH/Bruker). This commercial test identifies common NTM species /subspecies and detects common mutations for resistance to aminoglycosides via analysis of the *rrs* gene, and to macrolides via the *rrl* and *erm*(41) genes. Further molecular analyses, e.g. whole genome sequencing, were performed in individual cases.

Results: Strain distribution within the MABC: *M. abscessus* subsp. *abscessus* (N = 18) *M. abscessus* subsp. *massiliense* (N = 5), and *M. abscessus* subsp. *bolletii*

(N = 3). Strain distribution within the MAC: *M. avium* (N = 12), *M. intracellulare* (N = 11), *M. chimerae* (N = 21).

Resistance profile: For MABC and MAI, aminoglycoside resistance was only rarely detected (<2% overall). Resistance to macrolides was predominantly seen in MABC: *M. abscessus* subsp. *abscessus* (78% of isolates within species), *M. abscessus* subsp. *massiliense* (0%), and *M. abscessus* subsp. *bolletii* (100%). Further, the detailed molecular resistance distribution will be shown, together with corresponding phenotypic resistance testing of the reference laboratory for selected strains that were previously tested with GenoType NTM-DR®.

Conclusions: MABC and MAI strains over this five-year period show different resistance profiles between species, but also within the same species. Due to limited treatment options and long-term therapy, resistance profiling is fundamental in order to select a successful treatment regimen for each patient. Together with the variability in resistance profiles, rapid molecular resistance typing for certain antibiotics aids/guides in this selection, with phenotypic testing adding further information that currently exceeds genotypic testing.

Conflict of interest None

0100 Species Distribution and Geographic Clustering of Nontuberculous Mycobacterial Isolates at UC Irvine Medical Center, 2020–2024

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Background Nontuberculous mycobacteria (NTM) infections are increasing in prevalence, yet regional data on species distribution, temporal trends, and geographic clustering remain limited. We characterized NTM species distribution, sex-based differences, temporal shifts, and geographic patterns in Southern California.

Methods We conducted a retrospective analysis of NTM-positive cultures from UC Irvine Medical Center (2020–2024). Isolates were classified by species and growth rate (SGM vs. RGM) and mapped by patient ZIP code. Demographics including age and sex were recorded at the isolate level. This study was approved by the UC Irvine IRB (STUDY0000035).

Results A total of 756 NTM isolates were identified across 155 ZIP codes. The median age was 68.8 years (IQR 56.5–77.5), with 51.5% aged 60–79 years. Males comprised 56.6% of isolates (M:F 1.31:1).

Species distribution. MAC predominated (n = 298, 39.4%), followed by unspecified NTM (n = 224, 29.6%), *M. gordonae* (n = 97, 12.8%), *M. abscessus* complex (n = 51, 6.7%), *M. chelonae* (n = 30, 4.0%), *M. kansasii* (n = 15, 2.0%), and *M. fortuitum* group (n = 14, 1.9%). Among speciated isolates (n = 532), SGM predominated (80.1%) over RGM (19.9%).

Temporal trends. Annual isolate volume increased 67% over the study period (162 in 2020 to 270 in 2024). The proportion of RGM among speciated isolates more than doubled, from 11.9% in 2020 to 27.8% in 2024, driven by increases in *M. abscessus* complex and *M. chelonae*. *M. gordonae* rose from 8.6% to 20.0% of annual isolates. MAC's relative share declined from 52.5% to 28.9% despite stable absolute counts.

Sex-based differences. *M. abscessus* complex was the only species group with female predominance (54.9% female; M:F 0.82:1), contrasting with male predominance for MAC (1.12:1), *M. gordonae* (1.69:1), *M. kansasii* (4.00:1), and *M. fortuitum* (3.67:1). Among female isolates, *M. abscessus* represented 8.6% of all NTM compared with 5.5% among males.

Geographic distribution. Distribution was heterogeneous: median 3 isolates per ZIP code (IQR 1–6; range 1–31), with 24 ZIP codes (15.5%) containing ≥ 10 isolates. Among ZIP codes with ≥ 2 isolates (n = 107), median MAC proportion was 40.0% (IQR 15.5–54.7%). The highest-burden ZIP codes (92804, 92840, 92802) clustered in central Orange County. *M. abscessus* complex was distributed across 29 ZIP codes with concentration in select areas.

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Background/Aims: Nontuberculous mycobacterial (NTM) pulmonary disease (PD) is a chronic infectious disease often associated with low body mass index and weight loss. However, a comprehensive nutritional status (NS) assessment in these patients has not been conducted.

This study aims to perform a full nutritional evaluation in patients with a new diagnosis of NTM-PD.

Methods: We conducted a multicenter observational study including 8 NTM-PD referral centers in Italy. Participation in the study consists of pneumological/infectious disease visits, as per normal clinical practice, and a nutritional assessments. Nutritional assessments included anthropometric measurements, questionnaires on nutritional status and physical activity, bioimpedance (BIA), dynamometry and gait speed 4 meters, to evaluate body composition and physical performance. Pulmonary function tests were also collected.

Results: Seventy patients with NTM-PD (77 % female, mean age 69 years) were included. The most frequently isolated species was *Mycobacterium avium* complex (74 %), followed by *M. abscessus* complex, with other species being rare. Radiologically, 70 % presented a nodular-bronchiectatic pattern and 29 % cavitory disease. Antimycobacterial therapy was initiated in 73 % of cases.

Pulmonary function impairment was generally mild, with obstructive and restrictive patterns observed in 36 % and 13 % of patients, respectively. Physical performance assessment revealed reduced exercise capacity, with 26 % of patients showing impaired gait speed and 46 % reduced handgrip strength. According to International Physical Activity Questionnaire, 21.7 % and 36.2 % of patients had an inactive and moderately active lifestyle, respectively.

Nutritional assessment highlighted a high burden of undernutrition, with a mean BMI of 20.8 kg/m² and 22 % of patients underweight; 21.7 % reported recent weight loss. Anthropometric and BIA parameters indicated reduced muscle mass and energy reserves in a significant proportion of patients. Malnutrition risk was identified in more than one-third of patients by MUST and MNA, while 40.6 % met criteria for sarcopenia (predominantly probable). Regarding nutritional phenotypes, the majority of patients were normally nourished or overweight and non-sarcopenic (42.0 %), followed by sarcopenic (33.3 %), underweight/malnourished (20.3 %), sarcopenic obese (2.9 %) and obese (1.5 %) individuals.

Cavitory disease was associated with worse nutritional status, higher malnutrition risk, and increased prevalence of severe sarcopenia compared with nodular-bronchiectatic disease. Over half of patients required nutritional interventions, particularly those with sarcopenic or undernourished phenotypes.

Conclusions: patients with NTM-PD at diagnosis show a high prevalence of impaired nutritional status and physical performance, with more than 20 % underweight and 40 % at risk of malnutrition or malnourished and requiring a nutritional intervention, despite coming from a high-income country. Sarcopenia is also highly prevalent despite the population not being elderly and lacking major comorbidities.

Conflict of interest the study was supported by an unrestricted grant from Insmmed

0104 Solitary Pulmonary Nodules in Nontuberculous Mycobacterial Infection: An Underrecognized Presentation in Bronchoscopy Practice

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Background/Aims: Nontuberculous mycobacterial (NTM) lung disease is usually associated with bronchiectasis and multifocal nodular abnormalities. Pres-

entation as a solitary pulmonary nodule (SPN), particularly in patients without bronchiectasis, is less well recognized and may mimic malignancy.

Methods: We retrospectively reviewed 680 patients who underwent outpatient bronchoscopy at Cleveland Clinic Florida from July 2022 through July 2024, after excluding those with prior NTM treatment. Patients with bronchoalveolar lavage (BAL) acid-fast bacilli (AFB) culture-positive NTM were identified, and radiographic patterns, microbiologic sampling practices, and clinical suspicion for NTM were compared by bronchiectasis status.

Results: Of 27 patients with BAL culture-confirmed NTM, 8 (29.6 %) presented with an SPN and 11 (40.7 %) with multiple nodules. SPNs occurred only in patients without underlying bronchiectasis. Radiographic features were heterogeneous and frequently overlapped with malignancy, including spiculation, lobulation, central cavitation, ground-glass change, and satellite lesions. *Mycobacterium avium* complex predominated.

Coexisting malignancy was identified in a subset of patients with BAL culture-positive NTM (10.3 %), indicating that NTM infection and lung cancer may not be mutually exclusive in patients undergoing bronchoscopy for pulmonary nodules. Malignancy was present in 42.3 % of the overall bronchoscopy cohort, underscoring the high pretest probability of cancer.

Compared with patients with bronchiectasis, those without bronchiectasis were less likely to undergo microbiologic sampling (65.5 % vs 88.0 %, $P=0.0011$) and less likely to have preprocedural suspicion for NTM (20.0 % vs 100 %, $P=0.0171$), despite similar BAL AFB culture positivity rates (6.4 % vs 6.7 %).

Conclusions: In this outpatient bronchoscopy cohort, nearly one-third of culture-confirmed NTM cases presented as SPNs and were seen only in patients without bronchiectasis. These lesions often mimicked malignancy, yet NTM was less frequently suspected and microbiologic evaluation was less often pursued. BAL with mycobacterial cultures during bronchoscopy for selected SPNs may merit consideration, particularly in higher-prevalence regions.

Conflict of interest None

0105 Pulmonary Rehabilitation in Nontuberculous Mycobacterial Pulmonary Disease: A Prospective Cohort Study

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Background/Aims: Nontuberculous mycobacterial pulmonary disease (NTM-PD) is a chronic, progressive condition in which antibiotic regimens frequently fail to achieve sustained cure, leaving patients with persistent symptoms and functional decline. In this context, the potential role of non-pharmacological interventions has gained increasing attention, although high-quality evidence supporting pulmonary rehabilitation (PR) in patients with NTM-PD remains scarce. We report the results of a prospective observational cohort study evaluating the effects of an 8-week structured PR program on pulmonary function, exercise capacity, quality of life (QoL), and radiological severity.

Methods: A prospective single-arm cohort study was conducted at a tertiary university hospital in South Korea (ClinicalTrials.gov ID: NCT06838442). Patients with NTM-PD participated in a pragmatic 8-week supervised PR program consisting of five biweekly sessions comprising patient education, airway clearance therapy (including diaphragmatic breathing, huffing, and high-frequency chest wall oscillation), and aerobic and resistance exercise training. Assessments were performed at baseline (D0), program completion (W8), and

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SESSION: NTM 2

0107 Quantification of structural lung abnormalities in a cohort bronchiectasis patients with and without Nontuberculous Mycobacteria using the manual BEST-NTM score

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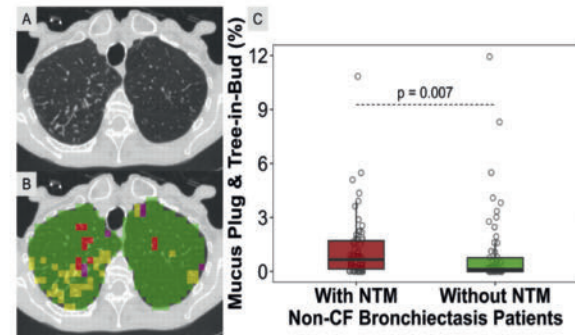
DOI 10.1055/s-0046-1826122

Background: Nontuberculous Mycobacteria (NTM) pulmonary disease is associated with a spectrum of structural abnormalities on chest computed tomography (CT). However, the prevalence of specific structural abnormalities and their differences between bronchiectasis patients with and without NTM remain incompletely characterized. A scoring tool that can detect NTM specific structural lung abnormalities could be used as a sensitive outcome in clinical care and randomized clinical trials.

Aim: This study aimed to validate the previously developed manual Bronchiectasis Scoring Technique specific for NTM (BEST-NTM) [1] to quantify NTM specific structural lung abnormalities, by comparing abnormalities in a clinical cohort of bronchiectasis patients with and without NTM.

Methods: In this retrospective cohort study, 123 consecutive patients in a large non-CF bronchiectasis clinic were included, in whom 63 were culture positive for NTM and 60 were culture negative. Chest CT scans were evaluated using the quantitative BEST-NTM scoring, with results expressed as percentage of total lung volume. Assessed structural abnormalities included atelectasis & consolidation, bronchiectasis, mucus plug & tree-in-bud, bronchial wall thickening, cavity wall, cavity, ground-glass opacities, and emphysema & bullae. Between-group comparisons were performed using Mann-Whitney U-tests, with $p < 0.05$ considered significant.

Results: The BEST-NTM score identified bronchiectasis (median 2.00 %, range 0.17 % – 8.42 %), atelectasis & consolidation (median 1.30 %, range 0.00 % – 15.50 %), and mucus plug & tree-in-bud (median 0.66 %, range 0.00 % – 10.84 %) as the most prevalent structural abnormalities in patients with NTM. Mucus plug & tree-in-bud was significantly higher in patients with NTM ($p = 0.007$) compared to those without NTM (► **Table 1** & ► **Fig. 1**). Other structural abnormalities were minimal and showed no significant differences ($p > 0.05$). Cavitation was observed in only 7 (9 %) bronchiectasis patients with NTM.



► **Figure 1 (A & B)** Example image of annotated structural abnormalities using the manual quantitative BEST-NTM score: magenta = atelectasis/consolidation, red = bronchiectasis, yellow = mucus plug/tree-in-bud, and green = no abnormalities. **(C)** Box plot of the manual BEST-NTM score for mucus plug/tree-in-bud. Mucus plug/tree-in-bud was significantly higher in patients with NTM ($p = 0.007$) compared to those without NTM.

► **Table 1** Demographics of the included clinical cohort of bronchiectasis patients with and without NTM

	Non-CF Bronchiectasis Patients		P – Value *
	With NTM	Without NTM	
N	63	60	
Age (years)	71 (63 – 75)	73 (64 – 78)	$p = 0.555$
Sex (male / female)	53 / 10	47 / 13	$p = 0.410^{\dagger}$
Atelectasis/consolidation (%)	1.30 (0.82 – 2.88)	1.08 (0.42 – 2.53)	$p = 0.209$
Bronchiectasis (%)	2.01 (1.07 – 3.46)	1.38 (0.87 – 3.02)	$p = 0.197$
Mucus plug/tree-in-bud (%)	0.66 (0.11 – 1.75)	0.12 (0.00 – 0.79)	$p = 0.007$
Bronchial wall thickening (%)	0.00 (0.00 – 0.14)	0.00 (0.00 – 0.02)	$p = 0.607$
Cavity wall (%)	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	$p = 0.374$
Cavity (%)	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	$p = 0.522$
Ground glass opacity (%)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.10)	$p = 0.615$
Emphysema/bullae (%)	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	$p = 0.176$

Median (Q1 – Q3); * Mann-Whitney U-test; [†] Chi-Square test

Conclusion: Bronchiectasis, atelectasis & consolidation, and mucus plug & tree-in-bud are the most prevalent structural abnormalities in patients with NTM. Among these, only mucus plug & tree-in-bud was significantly associated with NTM, highlighting the relevance of mucus accumulation in active NTM infections. These results are consistent with an automated CT analysis [2] pre-

viously performed in the same cohort, and a prior study using BEST-NTM in a randomized clinical trial with exclusively NTM positive patients [1]. Our results strongly support the potential of NTM-specific quantitative chest CT assessments to guide clinical care and assist in the development of novel NTM therapies.

Conflict of interest : No conflict of interest.

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0108 Nontuberculous Mycobacteria Commonly Detected in Bronchoscopy Patients Without Prior Clinical Suspicion in an Endemic Region

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Objective: To determine the incidence of nontuberculous mycobacteria (NTM) detected via bronchoalveolar lavage (BAL) in a large outpatient bronchoscopy cohort, and to assess the diagnostic yield of routine NTM screening in an NTM-endemic region.

Background/Aims: Early detection of NTM lung disease (NTM-LD) may provide an opportunity for intervention prior to irreversible lung damage; however, there are currently no widely accepted guidelines for routine screening. Existing diagnostic strategies rely on presence of respiratory symptoms and suggestive radiographic findings, and risk factors such as immunosuppression or underlying lung disease (2,3,4,6), with bronchoscopic evaluation typically reserved for patients unable to produce adequate sputum (1,2,3). We aim to determine the utility of universal BAL acid-fast bacilli (AFB) cultures in all patients undergoing bronchoscopy, regardless of indication or symptom status, in an endemic region where the burden of undiagnosed disease may be substantial.

Methods: We conducted a retrospective study of 680 patients undergoing outpatient bronchoscopy with BAL at Cleveland Clinic Florida between July 2022 and July 2024. Patients with prior history of tuberculosis or NTM-LD were excluded. The primary outcome was the incidence of new NTM identification in this cohort. Positive cases were further characterized by NTM species/subspecies, symptom status, and presence of bronchiectasis. NTM identification was established using the 2020 ATS/ERS/ESCMID/IDSA diagnostic criteria (3), defined by either microbiologic evidence (positive BAL AFB culture) or combined microbiologic and histopathologic findings (positive BAL AFB culture with granulomatous inflammation on biopsy).

Results: Of the 680 patients who underwent bronchoscopy, 453 had BAL AFB culture testing performed. Among these, 27 patients (6%) met diagnostic criteria for NTM. 1/27 (3.7%) of the positive cases had bronchiectasis. 20/27 (74.1%) underwent bronchoscopy without suspicion of NTM and 13/27 (48%) reported being asymptomatic on initial evaluation. *Mycobacterium avium* complex (MAC) was present in 21/27 (77.8%) of the positive cases (7 with *M. intracellulare*/*M. chimaera*, 1 with only *M. intracellulare*, and 13 not speciated further). *Mycobacterium abscessus* (MAb) subspecies *massiliense* was seen in 4/27 (14.81%) of the positive cases. There was 1 case of MAC/MAb coinfection and 1 case of *Mycobacterium interjectum*, each making up 3.7% of positive cases.

Conclusions: In this cohort, 27 cases of NTM were identified among 453 patients with available BAL AFB cultures collected during bronchoscopies performed for various reasons. As expected, MAC was the predominant species identified, followed by MAb subspecies *massiliense*. Notably, the majority of cases were identified in patients without bronchiectasis and without prior clinical suspicion, and only about half of the patients reported having symptoms on evaluation. Though our data set is small, this poses the question of whether

we can diagnose a subset of patients who might progress to develop NTM-LD earlier in their disease course. If so, it highlights a potential role for routine BAL AFB culture screening in patients undergoing bronchoscopy, regardless of indication or symptom status, in NTM-endemic regions.

Conflict of interest No conflicts of interest to disclose

0109 Identifying Vulnerable Patients in NTM PD: Respiratory Comorbidity and Treatment Intolerance Drive Mortality Risk

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DOI 10.1055/s-0046-1826124

Background Non-tuberculous mycobacterial pulmonary disease (NTM-PD) is increasingly recognised in ageing populations with complex respiratory comorbidity. Mortality predictors in real-world cohorts remain poorly defined, particularly in patients with co-existing chronic lung disease.

Methods A retrospective cohort study was conducted at a UK tertiary respiratory centre, including all patients diagnosed with NTM-PD between 2020 and 2024. Demographic, clinical, microbiological, radiological and treatment-related variables were collected. The primary outcome was all-cause mortality. Survival was assessed using Kaplan–Meier methods, and multivariable Cox proportional hazards modelling was performed using pre-specified clinically relevant covariates.

Results Forty-eight patients were included (mean age 68.5 years; 58 % male) with a median follow-up of 24 months. Thirteen deaths occurred (27.1 %). Independent predictors of mortality included:

- **Age > 75 years** (HR 3.2, 95% CI 1.4–7.1)
- **Cavitory disease** (HR 2.8, 95% CI 1.2–6.5)
- **Chronic obstructive pulmonary disease** (HR 2.5, 95% CI 1.1–5.7)
- **Poor treatment adherence** (HR 3.5, 95% CI 1.6–7.6)
- **Mycobacterium chimaera infection** (HR 2.1, 95% CI 1.0–4.4)

Treatment discontinuation due to adverse events occurred in 29.2% and was associated with increased mortality. Culture conversion was achieved in 58.3% and was protective (HR 0.4, 95% CI 0.2–0.9).

Conclusion Mortality in NTM-PD was strongly associated with advanced age, cavitory disease, COPD comorbidity, treatment intolerance and poor adherence. *M. chimaera* infection identified a higher-risk phenotype. These findings highlight a clinically recognisable vulnerable subgroup and support early risk stratification, adherence-focused interventions and targeted multidisciplinary review in NTM-PD care pathways.

Conflict of interest Nil

0110 Automatic Mucus Plug Quantification in Bronchiectasis Patients with NTM Infection

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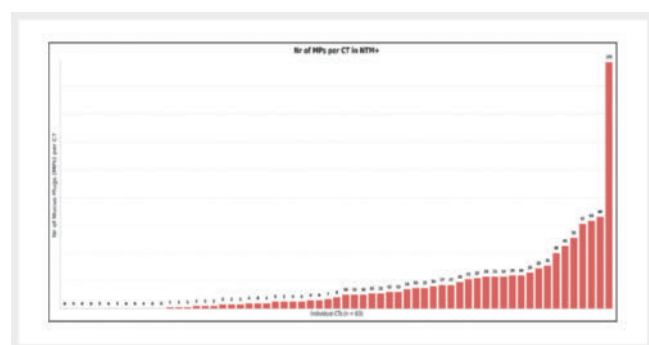
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DOI 10.1055/s-0046-1826125

Background/Aims: Bronchiectasis (BE) and nontuberculous mycobacteria (NTM) pulmonary disease are condition of rising incidence that frequently co-exist. Mucus plug (MP) is a radiologically quantifiable biomarker of airway disease and severity. Automated validated artificial intelligence (AI)-based algorithms such as LungQ®-MP allow objective, reproducible quantification of MP (count and plug volume in mL). In this retrospective observational study, we aimed to assess and to compare MP burden, automatically detected and quan-

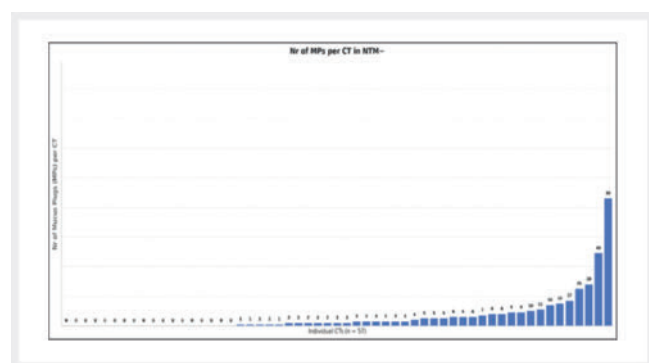
tified, in patient with (NTM+) and without (NTM-) NTM present in airway cultures. We hypothesized that NTM+ patients would demonstrate a greater and more severe MP burden compared to NTM- patients.

Methods: Chest CT scans from patients managed in a single center BE clinic that met the technical requirements were analysed using LungQ® (Thirona, Nijmegen, the Netherlands), a validated fully automated AI-based tool. LungQ®-MP detects a MP that completely blocks the lumen of an airway and automatically counts, and computes the total volume (mL) of MPs. LungQ®-bronchus-artery (BA) segments the bronchial tree and identifies for each bronchus the matching artery. For each BA-pair it computes the following diameters: bronchus outer and inner diameter (B_{out} and B_{in}), arterial diameter (A), and bronchial wall thickness (B_{wt}). Next, it computes the following ratios to assess bronchial dilatation (B_{out}/A and B_{in}/A) and bronchial wall thickening (B_{wt}/A and B_{wa}/B_{oa} (bronchus wall area/bronchus outer area) for each segmental generation. NTM status was defined by respiratory culture results (sputum of bronchoalveolar lavage); any patient with at least one positive NTM culture was classified as NTM+. MP number and volume were compared between groups using zero-inflated statistical models. Results are shown as median [IQR] unless stated otherwise.

Results: A total of 120 subjects were included: 63 NTM+ (mean age 69.4 years, ranges 31-89; 84.1% female) and 57 were NTM- (mean age 69.3 years, range 21-89; 63.2% female). Groups were comparable for age, BMI, tobacco history, and BE ethology. LungQ-MP detected a greater MP burden in the NTM+ group: MP count was 8 versus 2 in the NTM- group ($p < 0.001$) (► **Figure 1, 2**), and total MP volume was 0.36 mL versus 0.09 mL ($p < 0.002$). The highest number of detected MP in a single CT was 177 in the NTM+ versus 86 in the NTM- group (► **Figure 1** and **Figure 2**). In contrast, BA ratios and B_{wa}/B_{oa} across segmental generations G_{1-6} did not differ significantly between groups ($p > 0.005$ for all).



► **Figure 1** Distribution of MPs in NTM+ patients (n=63). Each bar represents one CT scan, sorted in ascending order within each group by total number MPs. Values are displayed on top of each bar.



► **Figure 2** Distribution of MPs in NTM- patients (n=57). Each bar represents one CT scan, sorted in ascending order within each group by total number MPs. Values are displayed on top of each bar.

Conclusions: NTM+ BE patients carry a significantly greater MP burden, in both number and total volume, compared to NTM- patients. This difference was not reflected in airway structural dimensions and ratios, suggesting that MP quantification may be a more sensitive CT biomarker of NTM associated airway disease than bronchial structural measures alone. Prospective studies should evaluate whether automated MP quantification can improve early identification of NTM pulmonary disease and reduce the need for invasive diagnostic procedures in patients unable to produce adequate sputum for cultures.

Conflict of interest Harm Tiddens is the Chief Medical Officer at Thirona B.V.

0111 Epidemiology and Spatial Distribution of Non-Tuberculous Mycobacteria in a North Italian Region

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DOI 10.1055/s-0046-1826126

Background: NTM identification is increasing in industrialized countries due to a progressive implementation of diagnostic techniques. A role of the environmental risk factors both in contamination and active disease has been proposed, but the real impact is still not fully understood. However, some data suggest an association with disease occurrence in specific populations. We described the spatial distribution of NTM that were identified in our Region in order to identify potential clusters.

Methods: Cases were identified from NTM reports to public health authorities in Piemonte Region, Italy, from 2017 to 2021. Incidence rate of NTM was calculated for each city and for administrative units. Moreover, spatial statistics were applied in order to find case excess in urban agglomerations. Analysis was performed using SAS 9.4 and R (SATSCAN package) software.

Results: Among a general population of 4.252.279, we identified 361 cases in five years, with an incidence rate of 1,486 events per 100,000 people/year. As expected, major number of NTM are reported in bigger cities, in particular Torino (n: 132 cases), Novara (n: 12), Asti (n: 8) and Alessandria (n: 5). No significant differences are found considering incidence rates. On the other hand, a raw georeferencing-based data analysis shows six cluster with a major risk of infection, where one among them (Torino-Crugliasco) has a statistical significance (n: 136).

Conclusions: Those preliminary results show that a territorial-based approach could identify significative NTM clusters. We aim to proceed with analysis of environmental risk factors, in order to relate NTM cases to specific contaminants. Clinical data will also be considered to stratify NTM isolation and NTM diseases in our analysis.

Conflict of interest none

0112 When a diagnosis doesn't follow the script: a case report of a M. abscessus pulmonary disease mimicking a rare condition in a bronchiectatic patient

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DOI 10.1055/s-0046-1826127

Background: NTM PD diagnosis and management put major challenge in bronchiectatic patients, where chronic lung inflammation and the consequent parenchymal alterations can hide other conditions. M. abscessus is a difficult-to-treat pathogen that can colonize low respiratory tract, especially in patients with chronic pulmonary inflammatory disease, and consequently contribute itself on lung damage progression. Lipoid pneumonia (LP) is a rare condition, typically associated with eating disorders, caused by the deposit of inhaled greasy materials in the airways after laxatives intoxication, lipidic-based dietary integrators and self-induced vomiting.

Case description: 54 years old female patient in follow up at our Pneumology Unit after a diagnosis of LP related to an eating disorder. The patient had an history of recurrent pneumonia, and low weight (BMI reported around 15 Kg/m² at the first examination). LP diagnosis was made after an atypical inferior right lobe resection in 2023, when a lymphoistiocytoid inflammation, associated to small granulomatous lesions without central necrosis, and large amounts of lipidic inclusions were found, despite the absence of peripheral fibrosis. Mycobacterial and standard cultures were found negative. After the resection of the mostly involved lobe, in the following two years the patient suffered at least 2-3 lower respiratory tract infections, and BMI decreased to 13 Kg/m². In November 2025, a new CT scan revealed a complete atelectasis of the medium lobe due to an extension of inflammatory disease. Contemporarily, the patient reported mild fever and cough. A criobiopsy of one lesion was performed, showing an interstitial lymphoistiocytic inflammation, suppurate mucus and some granulomatous lesions with endoalveolar macrophage cells. In order to attribute the real cause of the patient's condition to a specific condition, a second opinion has been asked to a pulmonary disease- focused Pathology Unit. The colleagues compared the two histologic preparations and opted for a possible mycobacterial infection as the main cause of the disease, where the lipidic inclusions could have been in both preparations an aspiration of oily materials. Finally, a strain of macrolide-resistant M. abscessus subsp. abscessus grew from the culture of material sampled after the criobiopsy. Consequently, the patient started an antibiotic polychemotherapy, currently ongoing during the intensive phase with good tolerance and reduction of fever occurrence.

Discussion: This case shows how the diagnosis of an acute illness in a chronic inflammatory pulmonary condition can be hard. Even if the histopathological preparations have never been pathognomonic for any condition, the classical granulomatous lesions associated with mycobacterial diseases have never been shown, while the presence of lipidic material mimicked a most likely condition in this patient. Our experience shows also that targeted criobiopsy could provide a more accurate sampling, rather than the analysis of a single section of the pulmonary parenchyma involved in a standard lobectomy. More studies are needed to investigate further those aspects.

Conflict of interest none

0113 NTM mapping in the Rotterdam region in the Netherlands

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DOI 10.1055/s-0046-1826128

Background Non-tuberculous Mycobacteria (NTM) isolates have been identified with increasing frequency over the past decades. The exact prevalence of NTM disease remains unknown and shows strong geographic heterogeneity. Data on the prevalence of NTM and its clinical relevance in the Netherlands are lacking.

The primary aim of this study was to obtain a comprehensive overview of all isolates, patient characteristics, the occurrence of NTM disease especially NTM Lung Disease (NTM-LD) and its treatment and outcomes. Furthermore, we aimed to identify previously unrecognized risk factors for NTM disease.

Methods A retrospective descriptive observational study was performed. All NTM isolates from a large teaching hospital in the Rotterdam region in the

Netherlands were mapped from January 2019 till December 2023. Clinical data from patients with positive NTM cultures were collected and analyzed.

Results Over 5 years NTM isolates were cultured from 61 patients, with specimens originating from the lung (49/61, 80.4%), skin (6/61, 9.8%), lymph nodes (3/61, 4.9%) and miscellaneous sites (3/61, 4.9%). All patients with pulmonary NTM isolates were assessed against ATS criteria for NTM-LD (i.e. compatible symptoms, radiology and microbiology). Of the 49 patients with a pulmonary NTM isolate, 17 (34.7%) met criteria for NTM-LD.

MAC was the most frequently identified species found in NTM-LD (7/17, 41.2%), followed by *Mycobacterium malmoense* (2/17), *Mycobacterium fortuitum* (2/17), *Mycobacterium kansasii* (1/17) and other NTM species (5/17).

Allmost all patients with NTM-LD had identifiable risk factors, with bronchiectasis being the most prevalent. No previously unreported risk factors were identified. Of the 17 patients with NTM-LD, 6 (35.3%) were treated with antibiotics, of whom only 2 patients achieved cure. Moreover, 3 patients achieved cure without antibiotic treatment. Mortality rate was high in patients with NTM-LD: The 3-year mortality rate was 23.5% (4/17).

Conclusions This study provides a comprehensive overview of NTM isolates in the region of Rotterdam in the Netherlands and elucidates their clinical significance, especially regarding NTM-LD.

Antibiotic treatment was administered to a limited number of patients with NTM-LD. The mortality rate in NTM-LD patients was remarkably high.

Conflict of interest none

0114 Changes in Complete Blood Count During 12 Months of Treatment for Mycobacterium avium complex Pulmonary Disease: A MAC 2v3 analysis

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DOI 10.1055/s-0046-1826129

Background/Aims: *Mycobacterium avium* complex pulmonary disease (MAC-PD) is a chronic infection with increasing incidence and complex management requiring treatment with two or more antibiotics. There is increasing interest in identifying additional MAC-PD outcome measures for both clinical management and clinical trial endpoints, given limitations of using mycobacterial cultures alone. Limited data are available on baseline or changes in complete blood count (CBC) analytes in MAC-PD, which are routinely collected in this population during treatment. In an exploratory analysis, we aimed to describe baseline CBC analytes and evaluate changes during therapy and their correlation with microbiological response to identify potential candidate outcome measures.

Methods: The recently completed MAC2v3 pragmatic trial randomized non-cavitary, treatment-naïve people with MAC-PD to azithromycin and ethambutol + /- rifampin thrice weekly for 12 months. CBCs and mycobacterial cultures were collected as needed as part of routine care. We included participants with CBC at baseline and at least one post-baseline time point, and >2 post-baseline mycobacterial cultures. We collected all CBC results at baseline and during 0-4 months, 4-8 months and 8-12 months of therapy; here we utilized the latest CBC in each time-frame. We calculated descriptive statistics and Mann-Whitney U Test p-values to evaluate changes in CBC values between those with and without documented confirmed negative cultures (at least 2 consecutive post-baseline negative mycobacterial cultures without a subsequent positive result) during the first 12 months of therapy. CBC analytes with p-value < 0.1 were considered as potential outcome measure candidates.

Results: 270 participants met inclusion criteria, with CBCs available for 78.1% at 0-4 months, 81.1% at 4-8 months, and 76.7% at 8-12 months of therapy. Most were female (83.0%), Non-Hispanic White (81.1%) and had bronchiectasis (88.5%). The median age was 70.0 years (range 29.6-90.6 years) with 46.7% randomized to receive rifampin. At baseline, 36.7% were lymphopenic, 14.4%

were anemic, and 27.4% had mild monocytosis. No participants had neutropenia < 1.0 K/cu mm. At baseline, statistically significant differences were seen between those who met criteria for negative cultures and those who did not (Table 1) with regards to thrombocytopenia (4.8% with negative cultures vs. 0% without negative cultures) and monocytosis (10.8% with negative cultures vs. 2.9% without negative cultures), in addition to median eosinophil count (0.11 K/cu mm with negative cultures vs. 0.18 K/cu mm without negative cultures) and eosinophil percent (2.0% with negative cultures vs. 2.9% without negative cultures). Changes in eosinophil count ($p = 0.064$) and monocyte percent ($p = 0.070$) met the criteria for further consideration as candidate outcome measures (Table 2).

Conclusions: We identified baseline differences in CBC analytes between those who met criteria for negative cultures and those who did not after initiation of therapy for MAC-PD. Changes in eosinophil count and monocyte percent may be potential candidates for outcome measures. More research is needed regarding changes in these CBC analytes over time by treatment regimens, MAC-PD severity and underlying disease.

Conflict of interest Varley: Research: this work was supported by National Heart, Lung, and Blood Institute: K23 HL161495. Hawkins: None Henkle: Advisory Board: Insmmed, AN2; Consultant: COPD Foundation Winthrop: Research: Insmmed, AN2, Mannkind, Verona, Merck, Boehringer Ingelheim; Consultant: Insmmed, Paratek, AN2, Spero, Mannkind, Zambon, Boehringer Ingelheim

SESSION: PCD AND PAEDIATRICS 1

0115 Clinical and Etiological Profile of Bronchiectasis in Morocco

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DOI 10.1055/s-0046-1826130

Background/Aims: Bronchiectasis is a chronic respiratory condition characterized by irreversible dilation of the bronchi resulting from persistent airway inflammation and recurrent infections. Although its burden is increasingly recognized worldwide, the epidemiology and etiological spectrum of bronchiectasis in North African countries remain poorly documented. Identifying the clinical and etiological characteristics of bronchiectasis is essential to guide diagnostic strategies and optimize patient management. This study aims to describe the clinical presentation, radiological features, and underlying etiologies of bronchiectasis in a cohort of Moroccan patients.

Methods: Patients diagnosed, between 2019 and 2024, with bronchiectasis based on computed tomography (CT) findings were retrospectively analyzed. Demographic data and clinical manifestations were collected. Etiological investigations included immunological assessments, HIV test, screening for cystic fibrosis, evaluation for primary ciliary dyskinesia and other relevant diagnostic tests when indicated.

Results: A total of 102 patients were included, with a median age of 8 years and a male-to-female ratio of 46:56. Chronic productive cough and recurrent respiratory infections were the most common presenting symptoms. CT imaging revealed predominantly cylindrical bronchiectasis. The main identified etiologies included primary immunodeficiencies (27.5%), HIV (13%), cystic fibrosis (8%) and idiopathic bronchiectasis (7%).

Conclusions: Bronchiectasis in Moroccan patients presents with heterogeneous etiologies, with genetic disorders representing important contributors. These findings highlight the importance of systematic etiological investigation, including immunological and genetic assessments, to improve diagnosis and management of bronchiectasis in Morocco.

Conflict of interest No potential conflict of interest was reported.

0116 From underdiagnosis to genetic confirmation: unveiling Primary Ciliary Dyskinesia in Morocco

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DOI 10.1055/s-0046-1826131

Background/Aims: Primary ciliary dyskinesia (PCD) is a rare, genetically heterogeneous disorder caused by mutations in over 50 genes affecting motile cilia, leading to impaired mucociliary clearance and recurrent respiratory disease from early childhood. Despite growing recognition worldwide, PCD remains largely underdiagnosed in many low and middle income countries, including Morocco, where the high prevalence of consanguinity increases the risk of autosomal recessive disorders. Early diagnosis is critical to optimize management and prevent long-term complications.

This study aims to describe Moroccan patients with genetically confirmed PCD, emphasize the role of genetic testing in establishing a definitive diagnosis and highlight the need for improved recognition and care for patients who remain undiagnosed in Morocco.

Methods: We evaluated patients presenting with unexplained recurrent respiratory infections. After excluding major differential diagnoses, all patients underwent a standardized workup including serum immunoglobulin measurements (IgG, IgA, IgM, IgE), lymphocyte subset analysis, sweat testing for cystic fibrosis, and HIV screening. In patients with persistent clinical suspicion of PCD, whole-exome sequencing (WES) was performed to identify pathogenic variants in genes implicated in motile ciliopathies.

Results: Eight patients (5 males, 3 females) with a median age of 12.7 years were included. All patients presented with chronic productive cough and recurrent respiratory infections from early childhood. Chest CT confirmed bronchiectasis in seven cases, and situs inversus was observed in one patient. Seven patients came from consanguineous families. Immunological evaluation was normal in six patients, while two exhibited concomitant immunodeficiencies: one female with combined immunodeficiency and one male with Wiskott-Aldrich syndrome. Whole-exome sequencing identified homozygous pathogenic variants in genes associated with primary ciliary dyskinesia in all patients, confirming the diagnosis. Notably, genetic testing in the broader Moroccan population suggests the presence of multiple PCD related variants needing to be studied, though only confirmed cases are reported here.

Conclusions: PCD should be considered in the differential diagnosis of patients with recurrent respiratory infections, especially when immunological evaluations are inconclusive. Coexistence with other immunodeficiencies may complicate diagnosis. In highly consanguineous populations like Morocco, genetic testing is essential for timely and accurate diagnosis. Early identification of PCD can improve patient management, reduce complications, and guide national strategies for diagnosis and care. Importantly, increasing awareness of PCD among healthcare providers and the public is crucial to ensure early recognition and intervention in this underdiagnosed population.

Conflict of interest No potential conflict of interest was reported.

0117 Longitudinal lung clearance index measurements in children and adolescents with bronchiectasis

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DOI 10.1055/s-0046-1826132

Background/Aims: Sensitive surveillance methods are needed to accurately assess disease severity and progression in children with bronchiectasis. The lung clearance index (LCI) is a sensitive marker of lung disease in children with cystic fibrosis but has not been extensively studied in children with bronchiectasis. We aimed to determine the sensitivity, variability and progression of LCI compared with spirometry (FEV₁) in children with bronchiectasis.

Methods: We prospectively performed multiple breath washout (MBW) and spirometry in 53 children and adolescents with bronchiectasis (192 visits; range 3.35-17.46 years; 26 males) and 60 healthy controls (151 visits; 2.32-17.66 years; 26 males) as part of the BRIGHT longitudinal cohort study. Nitrogen MBW data were collected using the Eco Medics Exhalyzer® D device and analysed using Spiroware 3.3.1. Lung function data were collected according to international guidelines and presented as global lung function initiative z-scores. Percentage change in LCI between consecutive visits was calculated within each participant. Bland-Altman analysis was used to assess agreement, with mean difference and 95 % limits of agreement (mean ± 1.96 SD) reported. Longitudinal MBW outcomes (≥ 2 measurements) were analysed using mixed-effects models in children with bronchiectasis (162 observations in 32 individuals; median follow-up 1.8 years) and healthy controls (91 observations in 24 individuals; median follow-up 1.9 years).

Results: LCI was significantly elevated (worse) in children with bronchiectasis (median 1.36 (IRQ 2.89) z-score) compared with healthy controls (0.4 (IRQ 1.08) z-score, Wilcoxon rank-sum: $z = -4.05$, $p < 0.0001$). At stable baseline visits, 41 % (20/49) of children with bronchiectasis had an abnormal LCI z-scores (> 1.64) compared to 21 % (5/24) with abnormal FEV₁ z-scores (< -1.64). LCI z-scores correlated with age (Spearman $r_s = 0.41$, $p < 0.0001$) in children with bronchiectasis but not healthy controls ($r_s = -0.003$, $p = 0.97$). Limits of agreement were wider in bronchiectasis (-19.2 % to 18.2 %) compared to healthy controls (-16.2 % to 11.8 %), indicating greater visit-to-visit variability. Children with bronchiectasis had significantly higher LCI z-score over time compared with healthy controls ($\beta = 1.69$, 95 % CI 0.71-2.67, $p = 0.001$), but LCI did not change significantly over the follow-up period (age $\beta = 0.08$, $p = 0.25$).

Conclusions: Preliminary results suggest that LCI is more sensitive than FEV₁ for detecting lung function abnormalities in children with bronchiectasis. LCI tracks higher in children with bronchiectasis than healthy controls, but LCI does not appear to worsen or improve over a 20-month period in children with bronchiectasis being treated at a tertiary hospital. These findings support further research to assess the utility of LCI for clinical monitoring and as an outcome measure for clinical trials in children with bronchiectasis.

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Conflict of interest Nil

0118 One Mutation, Three Lives: Variable Expression of Primary Ciliary Dyskinesia Type 7 in Siblings

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Introduction: Primary Ciliary Dyskinesia (PCD) type 7 is a rare autosomal recessive disorder caused by mutations in the DNAH11 gene, leading to abnormal motile ciliary function. The disease is characterized by recurrent respiratory infections, chronic sinusitis, bronchiectasis, situs inversus as part of Kartagener syndrome, and may also be associated with complex congenital cardiac malformations.

Case Series: Three brothers aged 12, 19, and 21 years, all with a molecular diagnosis of PCD type 7, are followed at our clinic for recurrent respiratory infections and bronchiectasis. Despite sharing the same molecular diagnosis, the three brothers, born to consanguineous parents, presented variable clinical phenotypes. The common manifestations included recurrent respiratory and ear infections, hearing loss, lower lobe cylindrical bronchiectasis and a restrictive pattern in spirometry. The index case, a 12 year-old male, presented with newborn respiratory distress syndrome and a respiratory infection due to *Serratia marcescens*. Imaging studies revealed situs inversus totalis and an atrial septal defect with a left-to-right shunt, consistent with Kartagener syndrome. Genetic testing confirmed a homozygous mutation in the DNAH11 gene, also present in the other two individuals. The eldest brother, a 21-year-old male, presented with a polymalformative syndrome, complex congenital heart disease, polysplenia and severe right-sided pelvicalyceal dilation. Cardiac anatomy revealed atrial and ventricular septal defects and double-outlet right ventricle with pulmonary stenosis, resulting in a functional single right ventricle physiology. The patient had previously undergone a bidirectional cavopulmonary connection with a bilateral Glenn shunt. He also had congenital profound sensorineural hearing loss, associated with a homozygous W24X mutation, confirming DFNB1A nonsyndromic autosomal recessive deafness. The 19-year-old male, also genetically confirmed, exhibited a milder clinical phenotype, characterized by sensorineural hearing loss, persistent bronchorrhea, and recurrent respiratory infections. There is also a history of a sister who died at 10 days of age, with suspected single ventricle physiology.

Conclusions: Primary Ciliary Dyskinesia type 7 is a rare genetic disorder. This case series is important as it highlights the phenotypic variability and multisystem manifestations associated with the condition, even among siblings sharing the same molecular diagnosis.

Conflicts of interest The authors declare no conflicts of interest.

0119 Dupilumab for chronic rhinosinusitis with nasal polyps in adults with primary ciliary dyskinesia: a case series

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Background: Primary ciliary dyskinesia (PCD) is a rare genetic multisystem disorder predominantly affecting the respiratory tract. In the upper airways, PCD is frequently associated with chronic rhinosinusitis with nasal polyps (CRSwNP), which can substantially impair health-related quality of life. Current treatment approaches are largely derived from general otorhinolaryngological recommendations and are not disease-specific. Dupilumab, a monoclonal antibody targeting type 2 inflammation, is approved as add-on therapy for adults with severe CRSwNP inadequately controlled by systemic corticosteroids and/or surgery. However, patients with PCD have not been specifically studied in pivotal trials. We therefore assessed the clinical effectiveness of dupilumab in

adults with PCD-related CRSwNP and explored potential clinical, radiological, functional, and inflammatory markers associated with treatment response.

Methods: We report a case series of 15 adults with confirmed PCD or Kartagener syndrome and concomitant CRSwNP treated with dupilumab 300 mg subcutaneously every 2 weeks. PCD diagnosis was based on biallelic pathogenic variants in PCD-associated genes and/or characteristic ultrastructural defects on transmission electron microscopy in the context of a compatible clinical phenotype. All patients received standard of care including nasal irrigations, intranasal corticosteroids, and physiotherapy, but remained symptomatic despite repeated endoscopic sinus surgery and polypectomy. Baseline assessment included SNOT-22, cone-beam CT of the paranasal sinuses with Lund–Mackay scoring, percent predicted FEV1 (ppFEV1), blood eosinophil count, total serum IgE, and fractional exhaled nitric oxide (FeNO). Response was reassessed after 6 months. Treatment response was defined as improvement in SNOT-22 and/or Lund–Mackay score together with concordant physician- and patient-reported global benefit.

Results: Of 15 patients, 5 (33 %) discontinued dupilumab prematurely because of lack of clinical benefit ($n = 3$) or adverse events ($n = 2$). Reported adverse events included one allergic/anaphylactoid reaction with rash and progressive dyspnea and one episode of chills with suspected onset of pulmonary exacerbation. One patient underwent lung transplantation; 9 patients completed at least 6 months of treatment. Among these, sinonasal symptom burden improved significantly, with median SNOT-22 decreasing from 59 to 32 ($p = 0.011$). No significant changes were observed in ppFEV1 (median 55 % to 56 %) or Lund–Mackay score (median 12 to 13). Overall, 6 patients (40 %) were classified as responders and continued treatment. The transplanted patient also continued dupilumab after transplantation with sustained benefit. Responders tended to be older and had higher baseline eosinophil counts, total IgE, and FeNO, with FeNO showing the clearest difference (11 vs 4 ppm, $p = 0.008$). Concomitant asthma was not associated with response.

Conclusions: Adults with PCD and CRSwNP may experience clinically relevant improvement in sinonasal symptoms during dupilumab therapy, particularly in the presence of biomarkers suggestive of type 2 inflammation. However, response was heterogeneous, and neither lung function nor radiological scores improved significantly. Further studies are needed to identify predictors of benefit from biologic therapy in this distinct patient population.

Conflict of interest Raphael Ewen reports clinical trial participation for Boehringer Ingelheim and Insmed; research grants from German Center for Lung Research (DZL); speaker services for Boehringer Ingelheim and i!DE Werbeagentur GmbH. Felix C. Ringshausen reports participation on an advisory and trial boards for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmed, Parion Sciences, and Sanofi; clinical trial participation for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmed, Parion Sciences, Ruhr University-Bochum, University of Dundee and Vertex Pharmaceuticals; research grants from German Center for Lung Research (DZL), German Center for Infection Research (DZIF), Mukoviszidose Institute, Novartis and Insmed; and has provided speaker services for Boehringer Ingelheim, Cliniqo GmbH, i!DE Werbeagentur GmbH, Insmed, med update GmbH and Sanofi; leadership or fiduciary roles as co-chair of the German Bronchiectasis Registry PROGNOSIS, member of the steering committee of the European Bronchiectasis Registry EMBARC and PI of the German Center for Lung Research.

0120 A systematic review of growth-related parameters and nutritional status of patients with primary ciliary dyskinesia (PCD)

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Background/Aims: Growth, nutritional status, and intake are crucial for the management and prognosis of chronic lung diseases, particularly in those with bronchiectasis. In patients with primary ciliary dyskinesia (PCD), increased respiratory load, recurrent or chronic infections, and increased mucus production lead to increased metabolic demands, as well as appetite loss; however, research on nutrition in this population is limited. In this study, we systematically reviewed the existing literature and summarised the evidence on growth, nutritional status, and intake of patients with PCD.

Methods: We conducted searches in MEDLINE, Embase, Scopus, and PubMed, limited to the past 20 years, due to changes in the diagnosis of PCD. Eligible studies included cross-sectional, case-control, prospective studies, and case series with > 5 people that reported on the growth, nutritional status, or intake of PCD patients. We performed additional searches through reference list checking and in medRxiv for relevant preprints. The review was registered in PROSPERO (CRD420251065699).

Results: Fifty studies were included in the qualitative synthesis. We observed variability in growth-related outcomes: some studies reported reduced z-scores for height, body weight, or body mass index, while others reported no growth differences in patients with PCD. The prevalence of undernutrition was reported in 4 to 11 %, whereas underweight ranged from 0 to 50 %; overweight and obesity ranged from 3 to 25 %. Only four studies reported on nutrition-related topics in patients with PCD. They showed average to high intake of energy and protein, while for most micronutrients and vitamins, the intakes or measured blood levels were within the normal ranges, except for vitamin D, for which intake and blood levels were below the recommendation, similar to evidence from patients with bronchiectasis. The prevalence of vitamin D insufficiency in patients with PCD was 54 %, while deficiency was reported in 18 to 26 % of study participants. In one of the included studies, few participants reported a recommendation for increased caloric intake from their physician or the use of hyper-caloric drinks.

Conclusions: In our systematic review, we saw considerable variability in growth-related outcomes and limited data on the nutritional intake of patients with PCD. The findings we noted related to malnutrition and vitamin D insufficiency/deficiency are alarming and warrant further investigation. While some patients with PCD might be susceptible to malnutrition, further affecting their lung health and immune function, others might need further assessment to reduce the risk of overweight, which also negatively impacts their lung health. Overall, the results of our systematic review highlight the need for timely and frequent assessment of nutrition and growth, including assessment of vitamin D status as standards of care for PCD, to promote healthy weight and adequate nutrient intake.

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Conflict of interest The authors have no conflicts of interest to declare.

SESSION: PCD AND PAEDIATRICS 2

0121 Nutritional supplement use among people with primary ciliary dyskinesia

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Background/Aims: Primary ciliary dyskinesia (PCD) is a rare genetic disease characterised by impaired mucociliary airway clearance leading to recurrent respiratory infections, bronchiectasis, chronic rhinosinusitis, and hearing im-

pairment, as well as manifestations from other organ systems. Nutritional status plays a crucial role in promoting respiratory health and effective infection management; yet, nutrition in respiratory disease remains largely underexplored. Limited data from other respiratory conditions show a high prevalence of nutritional supplement use, despite a lack of evidence about the usefulness and safety of supplements and their potential interaction with prescribed medications. To date, no study has assessed the use of supplements in less common respiratory conditions, such as PCD. In this project, we aimed to longitudinally describe supplement use in people with PCD.

Methods: We used data from the Living with PCD study and the Swiss population-based PCD registry (CH-PCD). Participants were asked to complete adapted versions of the FOLLOW-PCD questionnaire in two separate timepoints (t1: 2020-2021 and t2: 2022-2023), either online or sent by post. In both timepoints and for both studies, the questionnaire included identical supplement-related questions and specifically inquired about the use of oral caloric nutrition and nutritional supplements in the past period of at least 3 months, without distinguishing whether these were prescribed or not. We defined nutritional supplements as those reported to these questions including, among others, vitamins, minerals, and herbs. We described supplement use and whether it changed over time by comparing participant responses across the two timepoints.

Results: 344 people with PCD (63 % female; median age 36 years old; 67 % adults) responded to the questionnaire in both timepoints, with a median interval of 2.5 years (interquartile range, 2.1–2.6 years). 7 % of participants overall and 6–9 % of adults (depending on the timepoint) reported using oral caloric nutrition supplements. Half of the participants reported using nutritional supplements (t1: n = 171, 50 % and t2: n = 187, 54 %). The median number of supplements reported per person was 1 (range 0–19). Significant variation was noted with age, with 59 % of adults reporting use of nutritional supplements, compared to 44 % of children or adolescents. Participants most frequently reported taking vitamins, as multivitamins or individual vitamins (t1: n = 139, 40 % and t2: n = 154, 45 %). The percentage of participants who used ≥ 5 nutritional supplements was low and stable over time (t1: n = 13, 4 % and t2: n = 15, 4 %). When comparing the within-person responses across the two timepoints, the majority of participants provided the same answer regarding their use of oral caloric nutrition supplements (87 %, n = 299) and nutritional supplements (65 %, n = 222) over time.

Conclusions: In this first study focusing on supplement use in PCD, half of the participants reported using nutritional supplements regularly and consistently over time, while the use of oral caloric nutrition supplements was less frequent but highly stable. Given the high frequency and potential interactions between supplements and prescribed medications, the regular assessment of supplement use needs to be introduced as part of nutritional support and standard of care for PCD to ensure the appropriate use of these products.

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Conflict of interest The authors have no conflicts of interest to declare.

0122 Automatic reanalysis of genetic data from patients with Primary Ciliary Dyskinesia

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Background/Aims: Primary ciliary dyskinesia (PCD) is a heterogeneous genetic disorder characterized by structural and functional abnormalities of motile cilia, leading to chronic pulmonary symptoms and progressive lung damage. PCD is inherited predominantly in an autosomal recessive manner, caused by pathogenic variants in more than 50 genes. Currently, 20-30 % of patients with a clear PCD-phenotype remain genetically unsolved, making regular reanalysis necessary. As variant interpretation has become the bottleneck in genetic diagnostics, this study aims to investigate automated variant classification capability to improve the reanalysis of genetically unsolved PCD patients.

Methods: HerediClassify was validated on 42 manually classified variants from 30 patients. A reanalysis cohort (n = 159, including 121 adults and 38 pediatric patients) and a first-analysis cohort (n = 66, including 42 adults and 24 pediatric patients) with a PCD phenotype were analyzed using the automated classification tool HerediClassify, which screened 908 genes associated with PCD or its differential diagnosis. Based on clinical records, phenotypic features were assessed using the PICADAR score (Primary CiliAry Dyskinesia Rule) in children and the modified PICADAR score in adults. Symptoms not documented were interpreted as absent. For all PICADAR-positive cases, the PP4 criterion for disease-specific phenotype was applied automatically by HerediClassify to variants in PCD-associated genes.

Results: In the validation cohort, HerediClassify classified 83 % of variants correctly. The proportion of PICADAR-positive cases was lower in adults than in pediatric patients in both cohorts: 25 % vs. 50 % in the reanalysis cohort and 27 % vs. 32 % in the first-analysis cohort. In the reanalysis cohort, which included patients who had remained without a genetic diagnosis following routine diagnostic workup, one additional patient was genetically diagnosed with a compound heterozygous variant in *CCDC40*. In the first-analysis cohort, HerediClassify correctly identified 71 % of patients that had been diagnosed manually. The five diagnosed patients in the first-analysis cohort had variants in *RSPH3*, *ZMYND10*, *CCDC40*, *ODAD4*, and *RSPH1*. Without the inclusion of phenotypic evidence, the disease-causative variant in 50 % of patients would not have been identified by HerediClassify.

Conclusions: In this study, we demonstrate that HerediClassify is suitable for automated variant classification in PCD through its high concordance with manual variant classification. Therefore, automated variant classification can efficiently enhance reanalysis by identifying high-priority variants.

The systematic inclusion of phenotype-specific information, such as the PICADAR score for disease-specific phenotypes, substantially improves the interpretation of genetic data by both manual and automated approaches and should be considered standard practice.

Conflict of interest None

0123 Cardiorespiratory responses during the modified Shuttle walk test in children with chronic suppurative lung diseases. Comparisons with healthy, age-matched peers.

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Background: While children with CSLDs show normal pulmonary function at rest, chronic inflammation may compromise cardiorespiratory efficiency during high-intensity exertion. The cardiopulmonary exercise test is the gold standard for assessing maximal exercise capacity. However, its high costs and specialized equipment make it impractical for clinical use. The modified Shuttle walk test (MSWT) offers an alternative for evaluating exercise capacity in the pediatric cystic fibrosis population. Limited data are reported for other chronic suppurative lung diseases (CSLDs), such as protracted bacterial bronchitis (PBB) and non-cystic fibrosis bronchiectasis (NCFB).

Aim: To compare cardiorespiratory responses during the MSWT between children with CSLDs and healthy, age-matched peers.

Methods: Fourteen children (CSLDs, $n = 14$) aged 6 to 12 years with CSLDs were matched on age, height, and weight to healthy peers (HP, $n = 14$). Exercise capacity was assessed using the MSWT. Furthermore, baseline assessments included anthropometric characteristics, respiratory muscle strength (Maximal Inspiratory Pressure, MIP/Maximal Expiratory Pressure, MEP), and handgrip strength. Handgrip strength (in kilograms) was normalized to body weight. Physical activity levels and sedentary behaviors were assessed using the Youth Activity Profile (YAP) questionnaire.

Results: CSLDs included 7 children with NCFB and 7 with PBB. The CSLDs and HP did not differ in age, height, and weight [mean age in years: 8.3 ± 1.7 versus 8.4 ± 1.6 ; height in cm: 132.6 ± 9 versus 129.6 ± 9.8 ; median weight in Kg: 30.5 (IQR: 26–35.8) versus 29.8 (IQR: 23.6–38.2), $p > 0.05$]. The CSLDs exhibited significantly lower respiratory muscle strength (MIP: 68.5 ± 23.6 versus 98.7 ± 16.6 , $p < 0.001$; MEP: 84.6 ± 18.8 versus 109.6 ± 14.2 cmH₂O, $p < 0.001$) compared to the HP. CSLDs and HP did not differ in the total meters covered during the MSWT (629.5 ± 106.9 versus 671.4 ± 110.6 , $p = 0.317$) and the maximum heart rate (159.6 ± 13.3 versus 163.9 ± 5.7 bpm, $p = 0.275$). However, CSLDs demonstrated lower minimum oxygen % saturation (90.9 ± 4.3 versus 97.1 ± 0.3 , $p < 0.001$) compared to the HP. Similarly, at the iso-level (7th level of MSWT), CSLDs demonstrated lower oxygen % saturation (95.4 ± 3.5 versus 97.6 ± 0.5 , $p = 0.034$) compared to the HP. Most of the children ($n = 22$) were right-handed. Relative handgrip strength did not differ between groups for both dominant ($p = 0.07$) and non-dominant ($p = 0.119$) hand. Physical activity and sedentary behaviors did not differ between groups ($p < 0.05$).

Conclusions: The exercise capacity was comparable between groups. However, the MSWT revealed marked oxygen desaturation during high exertion. These findings suggest that although CSLDs maintain exercise performance, cardiorespiratory strain is evident, highlighting the need for monitoring during exercise.

Conflict of interest The authors declare no conflicts of interest.

0124 User satisfaction and co-designing a website for physiotherapy management for children with chronic suppurative lung diseases

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Background: The development of evidence-based, child-centered digital tools requires structured consensus processes and real-world usability testing to ensure clinical relevance and users' adherence. Websites developed for children with chronic suppurative lung diseases (CSLDs), including cystic fibrosis (CF), have demonstrated that accessible, evidence-based digital platforms can enhance disease knowledge, support symptom recognition, and promote adherence to self-management practices. However, their effectiveness largely depends on age-appropriate design, cultural adaptation, and systematic user involvement in their development.

Aims: To present the co-design of an informative website for children aged 6–12 years, specifically targeting the physiotherapy needs and the users' satisfaction.

Methods: We adopted a user-centered, participatory approach involving healthcare professionals (HCPs) and parents of children with CSLDs during website development. Initially, a comprehensive list of the website's content and functions was developed through two separate Focus Group studies (FGs). One study included HCPs and another study included parents. Afterward, we conducted user experience testing (UET) and sessions with parents and children who navigated the website remotely to pilot the usability and completeness of the newly developed website, named www.fysao.gr. Furthermore, parents completed a modified version of the Mobile Application Rating Scale (uMARS), with modifications to the questions, using a three-point Likert scale to assess engagement (4 questions), functionality (1 question), aesthetics (2 questions), information quality (3 questions), and overall satisfaction (2 questions).

Results: Seven HCPs (3 physiotherapists; 4 pediatric pulmonologists) participated in one FG, and six parents (2 have children with CF, 3 with bronchiectasis, 1 with primary ciliary dyskinesia) participated in the other FG. The FGs identified ten main themes as high priority to be included in the website. Those included evidence-based medical and physiotherapy information (95.9%), gamification (95.9%), interactive features (95.9%), reminders (89.8%), training modules for children, parents, and HCPs ($\geq 89.8\%$), multilingual access (89.8%), strict privacy policies (87.8%), and free access (95.9%). During UET, 24 parents completed the evaluation. The website received high usability and satisfaction ratings: 100% rated it as pleasant and accurate; 92.9% easy to learn; 78.6% clear and high-quality layout and aesthetic. The mean overall rating was 4.86/5 units, and all participants (100%) would recommend it.

Conclusions: The website "FysAQ" demonstrates high user satisfaction. It integrates evidence-based content, gamification, interactivity, and accessibility features, representing it as a user-centered digital health tool for future clinical implementation.

Conflict of interest authors state that they have no conflict of interest.

0125 Using 6-Minute Walk Test and Chester Step Test for Detecting Exertional Desaturation in Children with Chronic Suppurative Lung Disease: A Pilot Study.

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Background: Impaired exercise capacity is evident in children with chronic suppurative lung diseases (CSLDs) compared to healthy peers. Field tests, such as the six-minute walk test (6MWT) and the Chester step test (CST), are useful for assessing functional and exercise aerobic capacity, respectively. However, little is known regarding the ability of these tests to detect exercise-induced desaturation with minimum exertion in children with non-cystic fibrosis bronchiectasis (NCFB) and protracted bacterial bronchitis (PBB).

Aim: To evaluate the cardiorespiratory responses during both the 6MWT and CST in children with NCFB and PBB.

Methods: Children aged 6–12 years diagnosed with PBB or NCFB were included. Anthropometric characteristics, body composition (measured through TANITA-RD45) and performance during the 6MWT and CST were assessed on the same day. All children performed both tests twice, in a randomized sequence, with continuous monitoring of SpO₂ and heart rate (HR) using the MIR Spirodoc oximeter. The Dalhousie Pictorial Scale was used to assess breathless-

ness and lower-limb fatigue. A 30-minute rest interval was provided between each trial of both the 6MWT and CST. All parameters were recorded continuously from rest up to each minute of the 6-minute recovery for both tests. Systolic and diastolic blood pressure were measured at rest, at the end of the test, and at the end of recovery. Rest, final, minimum and maximal values were analyzed. Desaturation was defined as a decrease of at least 4 % of SpO₂.

Results: Twenty children (10 boys and 10 girls) with a mean (SD) age of 8.65 (1.69) years were included; 13 with NCFB and 7 with PBB. Mean (SD) height and weight were 133.95 (9.19) cm and 33.52 (10.34) kg, respectively. Mean (SD) values of body mass index (BMI) were 18.35 (3.43); fat mass 8.7 (4.19) kg; fat free mass (FFM) 24.81 (6.58) kg; fat free mass index (FFMI) 13.9 (2.69). SpO₂ was >97 % for all participants at rest. None required supplemental oxygen. No adverse events were reported during tests. All children completed the 6MWT. Distance covered was mean (SD) 670.5 (104.52) meters. During 6MWT, desaturation was reported for 14 children. For the CST, six children reached level 5, four reached level 4, six reached level 3, two reached level 2, and two completed only level 1. Fatigue and inability to follow the pace were the main reasons for CST termination. Mean (SD) steps performed during CST was 165.95 (74.9). Mean (SD) values for final heart rate were different between tests (6MWT: 149.1 ± 19.5 versus CST: 162 ± 19.2 bpm; $p = 0.015$). During CST, desaturation was reported over level 3 for 10 children ($n = 2$ level 3; $n = 4$ level 4; $n = 4$ level 5). Minimum SpO₂ values were different between the 6MWT and CST ($92.3 \pm 3.25\%$ vs $95.11 \pm 2.37\%$; $p = 0.012$, respectively), whereas final SpO₂ did not differ between tests ($97.15 \pm 1.87\%$ vs $96.75 \pm 2.1\%$; $p > 0.05$, respectively).

Conclusions: CST imposes greater physiological loads and may not be feasible for all children to complete. The 6MWT can detect oxygen desaturation at comparatively lower levels of exertion.

Conflict of interest The authors declare no conflicts of interest.

0126 Diagnostic Pitfall in High-Speed Video Analysis of Primary Ciliary Dyskinesia: A TTC12-Related Case with Mixed Ciliary Activity

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Background/Aims: Primary ciliary dyskinesia (PCD) is a genetically heterogeneous disorder. Its diagnosis relies on a combination of high-speed video analysis (HSVA), transmission electron microscopy (TEM), immunofluorescence (IF), and genetic testing. However, heterogeneous ciliary motility may complicate HSVA interpretation and lead to potential misdiagnosis.

Methods: We report a patient presenting with recurrent respiratory infections, bronchiectasis, and sinusitis. Nasal epithelial samples were obtained for HSVA and TEM, and peripheral blood was collected for whole-exome sequencing (WES).

Results: This study reports a case of a patient presenting primarily with recurrent respiratory tract infections, bronchiectasis, and sinusitis. The patient comes from a close-knit family; the patient's maternal grandmother and paternal grandfather were half-siblings (same mother, different fathers). The patient's nasal nitric oxide (nNO) level was 124 ppb. A sinus CT scan revealed inflammation of the bilateral maxillary sinuses, the right ethmoid sinus, and the sphenoid sinus, and the chest CT scan showed bronchiectasis in the lingular segment of the left upper lobe, the left lower lobe, and the right middle lobe. Peripheral airway resistance was normal, and no abnormalities in lung compliance were observed.

Initial HSVA interpretation focused predominantly on motile cilia, leading to misclassification of immotile cilia as non-viable and an overall conclusion of normal ciliary motility. TEM did not reveal definitive ultrastructural abnormalities, and PCD was initially considered unlikely.

However, whole-exome sequencing subsequently revealed a homozygous variant in TTC12 (NM_017868.4:c.1799T>A), with both parents confirmed as heterozygous carriers. Immunofluorescence demonstrated preserved DNAH5

and absence of DNALI1, consistent with an isolated inner dynein arm defect. This is consistent with the characteristics of TTC12 deletion.

Conclusions: This case highlights a diagnostic pitfall in HSVA interpretation, where heterogeneous ciliary motility may lead to selection bias and false-negative results. Additionally, TTC12-associated PCD may present with a phenotype characterized primarily by defects in the inner motile arm and atypical TEM findings. This case underscores the importance of integrating multimodal diagnostic approaches in the diagnosis of PCD and highlights the potential value of immunofluorescence in identifying specific subtypes.

Conflict of interest NO

0127 Diagnostic Overlap Between PCD and CFTR Dysfunction: An Unresolved Case with Discordant Findings

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Background/Aims: Primary Ciliary Dyskinesia (PCD) and CFTR-related disorders may present with overlapping clinical features, including bronchiectasis and chronic sinusitis. Distinguishing between these entities remains challenging, particularly in adults with inconclusive diagnostic results. We present a case highlighting the limitations of current diagnostic tools and the complexity of differentiating between these conditions.

Methods: We describe a 46-year-old female, followed from age 35, with a history of bronchiectasis since childhood and recurrent otitis in early life. Family history was notable for two daughters with frequent respiratory infections. Diagnostic work-up included pulmonary function tests, high-resolution computed tomography (HRCT), sweat chloride testing, CFTR gene sequencing, β -adrenergic sweat secretion test (evaporimetry), nasal nitric oxide (nNO) measurement, digital highspeed videomicroscopy (HSVM), transmission electron microscopy (TEM), immunofluorescence (IF), and whole exome sequencing (WES).

Results: Pulmonary function tests demonstrated severe airflow obstruction (FEV1 46 % predicted). HRCT revealed varicose bronchiectasis predominantly affecting the middle lobe. Sweat chloride values revealed discordant results (74 mmol/L in 2017-increased; 54 mmol/L in 2024-intermediate). Initial CFTR mutation screening for common variants was negative, but a heterozygous CFTR variant (c.3205G>A, p.Gly1069Arg) was identified in extended phase II sequencing. Fecal elastase was normal. Functional CFTR assessment by β -adrenergic sweat secretion showed absent response, supporting CFTR dysfunction. HSVM analysis showed low-normal mean beat frequency (7.75 Hz, range: 0.0-17.0; Ref mean: 12.75 Hz; range: 7.0-19.0) with the beat pattern evidencing 68.2 % of dyskinetic motion. TEM demonstrated class-2 abnormalities, suggestive of PCD. nNO levels were within the normal range (190 nL/min) and the PICADAR score was 5. WES testing detected variants of uncertain significance in genes associated with autosomal recessive PCD (DNAAF4, GAS2L2, TTC12) and IF analysis revealed reduced expression of the respective ciliary proteins. Further familial evaluation is ongoing.

Conclusions: This case illustrates a diagnostic overlap between PCD and CFTR dysfunction, with discordant results. While HSVM, IF and ultrastructural findings supported ciliary dysfunction, normal nNO levels and an intermediate

PICADAR score introduced a diagnostic uncertainty within current ERS diagnostic guidelines. Conversely, abnormal CFTR testing supported CFTR dysfunction. Findings highlight the limitations of current diagnostic algorithms and underscore the importance of integrated and family-based evaluation in complex cases, where diagnostic classification remains unresolved.

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Conflict of interest The authors declare no conflicts of interest.

SESSION: PCD AND PAEDIATRICS 3

0128 A family with primary ciliary dyskinesia (PCD) from pathogenic variants in HYDIN – a case series

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Background/Aims: Primary ciliary dyskinesia (PCD) is an inherited disorder resulting in abnormal ciliary structure and function. PCD is caused by pathogenic mutations in at least 50 genes, and clinical manifestations can vary greatly in pattern and severity according to the genotype. DNAH5 is by far the most frequently identified genetic variant leading to PCD. Variants in HYDIN are less frequently identified. There are at least 42 known cases of PCD caused by pathogenic variants in HYDIN described in the ERN-LUNG International PCD Registry.

Methods: We examined a sibship attending our centre who are all affected by PCD caused by pathogenic variants in HYDIN. Here we describe the clinical and radiological features of this group, how they compare both with each other and with individuals with PCD caused by different genetic variants.

Results: 5 siblings (4 female) in this family are all affected by PCD due to pathogenic mutations in HYDIN. Each is affected by a pathogenic in-frame deletion of the 17th coding exon as well as a frameshift deletion in exon 17. The latter was considered to be a variant of uncertain significance (VUS) until genetic testing of both parents confirmed the pathogenicity of this variant. Though neither parent are affected by PCD, it was noted that a paternal grandparent suffered from recurrent respiratory tract infections (RTIs).

All siblings were born at term and demonstrated situs solitus. 2 sisters experienced neonatal respiratory distress. Median PICADAR (Primary Ciliary Dyskinesia Rule) score was 6. All experienced chronic cough, recurrent RTIs, and chronic rhinosinusitis from early childhood. Two experienced recurrent episodes of otitis media. One sibling was tested for PCD with transmission electron microscopy (TEM) and high speed video-microscopy analysis (HSVA), which were normal. Due to difficulties in diagnosing PCD related to HYDIN mutations, none received a definite diagnosis of PCD until well into adulthood.

Clinically, though all siblings continue to experience a chronic productive cough, phenotypic characteristics vary in terms of frequency of RTIs and extent of sinus disease. Subfertility has affected at least one sibling who has attempted to conceive. Radiological severity of bronchiectasis is mild, and predominantly affects the right middle lobe, left lower lobe, and lingula. Sputum microbiology is varied, with three siblings having a previous growth of *Pseudomonas aeruginosa*. All have low nasal nitric oxide levels. Lung function remains relatively well preserved, with a median FEV1 of 107%.

Conclusions: This family of five siblings with PCD secondary to pathogenic variants in HYDIN display clinical characteristics of PCD of varying severity, and differ from the typical phenotype seen in PCD resulting from other genetic variants. Their cases highlight the significant genetic and clinical heterogeneity of PCD, and underline the need for individualised care even within a general PCD population, particularly in regions where the genetic landscape of PCD has yet to be fully elucidated.

Conflict of interest The authors declare they have no conflicts of interest.

0129 Comparison of cut-off values for nasal nitric oxide measurements in children under four years of age

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Background/Aims: Primary Ciliary Dyskinesia (PCD) is a rare genetic disorder resulting in malfunctioning of the motile cilia. Due to its heterogeneous clinical presentation, the diagnosis is often delayed leading to irreversible structural lung damage. The diagnostic process is multifactorial and one step is the measurement of nasal nitric oxide (nNO), which is known to be markedly decreased in the majority of patients with PCD. However, performance in young children can be challenging and there are no reliable cut-off values for patients under 5 years of age. A recent study examined cut-off values for young children using tidal breathing technique (Leigh MW et al., Eur Respir J 2026; in press). The aim of this study was to evaluate the applicability of these recently published cut-off values in our population of PCD patients and healthy controls.

Methods: In this study, nNO measurements performed with tidal breathing by children presenting in our outpatient clinic and healthy controls were retrospectively analyzed according to the published technical standard by Beydon et al., 2023. The children were divided into two groups: children with and without PCD according to the 2025 ERS diagnostic guidelines. The latter group included healthy controls or children with chronic cough excluding those with cystic fibrosis or inborn errors of immunity. Ideal cut-off values were calculated using receiver operating characteristics analysis for three age groups (<9 months; ≥9- <24 months; ≥24- <48 months) and compared to the published cut-off values.

Results: For preliminary analysis we included a total of 58 measurements, 23 from children with PCD and 35 from children without PCD. Children <9 months (n = 17) showed an ideal cut-off at 6.3nl/min (sensitivity and specificity 100%). In the study of Leigh et al. a cut-off at 18nl/min is suggested which showed a sensitivity of 100% and a specificity of 62.5% in our population. For children ≥9 and <24 months (n = 13) a cut-off of 23nl/min was suggested by Leigh et al., which is similar to the ideal cut-off of 23.5nl/min in our cohort and showed a sensitivity and specificity of 100%. For children ≥24 and <48 months (n = 28) our data suggests an ideal cut-off at 59nl/min with a sensitivity of 93.3% and a specificity of 92.3%. This is higher than the suggested cut-off by Leigh et al. with 45nl/min, which showed a sensitivity of 86.7% and a specificity of 92.3% in our study population.

Conclusions: In line with the published data we were able to show that cut-off values for nNO measurements need to be adapted to the age of young children, as nNO values rise within the first years of life. However, our limited data suggests slightly different cut-off values in our population than previously suggested by Leigh et al. An extended analysis including a higher number of children will be available at the World Bronchiectasis Conference. The definition of reliable cut-off values is important to identify patients with PCD at an early age and therefore enable early intervention and treatment to slow down disease progression.

Conflict of interest None

0130 An Optimized Immunofluorescence Panel Improves Diagnostic Accuracy for Primary Ciliary Dyskinesia

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0132 In Vitro Gene Therapy Study of Primary Ciliary Dyskinesia Based on DNAI1-mRNA Lipid Nanoparticles

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DOI 10.1055/s-0046-1826147

Background/Aims: Primary Ciliary Dyskinesia (PCD) is a common hereditary respiratory disease, mainly caused by defects in ciliary ultrastructure or abnormalities in ciliary motility. DNAI1 is a major pathogenic mutant gene associated with PCD, accounting for approximately 2%–10% of all PCD cases. Currently, there are no etiologically targeted therapeutic strategies for this disease. This study aimed to evaluate the therapeutic potential and efficacy of the DNAI1-mRNA lipid nanoparticle (mRNA-LNP) delivery system in treating DNAI1-mutant PCD in vitro.

Methods: Airway epithelial cells were isolated from PCD patients carrying biallelic pathogenic variants of DNAI1, and an air-liquid interface (ALI) differentiation culture model was established. Three DNAI1-mRNA-LNP formulations (RC04, RC05, RC06) with distinct lipid carrier structures were designed and prepared. Single or multiple gene delivery was performed on day 14 of ALI model differentiation. High-speed video microscopy analysis (HSVA) combined with image analysis software was used to quantitatively measure ciliary beat frequency (CBF) and the proportion of functionally beating cilia. Immunofluorescence staining was applied to verify the expression efficiency of the DNAI1 protein.

Results: Partial restoration of ciliary motility was observed in ALI models treated with mRNA-LNP delivery. Significant differences in the proportion of beating cilia were noted among different LNP-treated groups: the RC06 group exhibited the optimal performance, with a recovered cell proportion of $5.8\% \pm 0.9\%$, followed by the RC04 group ($2.2\% \pm 0.6\%$) and the RC05 group ($1.8\% \pm 0.8\%$). The CBF of recovered cilia ranged from 9.2 to 14.6 Hz, which was significantly higher than that of the control group and close to the reference value of normal human airway cilia. Additionally, the multiple-dosing group showed a higher proportion of ciliary recovery and a more stable CBF distribution compared with the single-delivery group. Immunofluorescence results demonstrated specific expression of the DNAI1 protein in the negative control (NC) group, RC04 group, and RC06 group—with the highest expression level in the RC06 group (significantly higher than that in the RC04 group)—whereas no obvious DNAI1 protein expression was detected in the empty LNP control group.

Conclusions: This study confirms that the mRNA-LNP system can effectively deliver the DNAI1 gene and partially restore the ciliary beating function of PCD patients in the in vitro ALI model, providing experimental evidence for the etiological treatment of DNAI1-mutant PCD.

Conflict of interest The authors declare that they have no known competing interests.

0133 In Vitro Gene Therapy Study of Primary Ciliary Dyskinesia Based on DNAI1-mRNA Lipid Nanoparticles

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DOI 10.1055/s-0046-1826148

Background/Aims: Primary Ciliary Dyskinesia (PCD) is a common hereditary respiratory disease, mainly caused by defects in ciliary ultrastructure or abnormalities in ciliary motility. DNAI1 is a major pathogenic mutant gene associated with PCD, accounting for approximately 2%–10% of all PCD cases. Currently, there are no etiologically targeted therapeutic strategies for this disease. This study aimed to evaluate the therapeutic potential and efficacy of the DNAI1-mRNA lipid nanoparticle (mRNA-LNP) delivery system in treating DNAI1-mutant PCD in vitro.

Methods: Airway epithelial cells were isolated from PCD patients carrying biallelic pathogenic variants of DNAI1, and an air-liquid interface (ALI) differentiation culture model was established. Three DNAI1-mRNA-LNP formulations (RC04, RC05, RC06) with distinct lipid carrier structures were designed and prepared. Single or multiple gene delivery was performed on day 14 of ALI model differentiation. High-speed video microscopy analysis (HSVA) combined with image analysis software was used to quantitatively measure ciliary beat frequency (CBF) and the proportion of functionally beating cilia. Immunofluorescence staining was applied to verify the expression efficiency of the DNAI1 protein.

Results: Partial restoration of ciliary motility was observed in ALI models treated with mRNA-LNP delivery. Significant differences in the proportion of beating cilia were noted among different LNP-treated groups: the RC06 group exhibited the optimal performance, with a recovered cell proportion of $5.8\% \pm 0.9\%$, followed by the RC04 group ($2.2\% \pm 0.6\%$) and the RC05 group ($1.8\% \pm 0.8\%$). The CBF of recovered cilia ranged from 9.2 to 14.6 Hz, which was significantly higher than that of the control group and close to the reference value of normal human airway cilia. Additionally, the multiple-dosing group showed a higher proportion of ciliary recovery and a more stable CBF distribution compared with the single-delivery group. Immunofluorescence results demonstrated specific expression of the DNAI1 protein in the negative control (NC) group, RC04 group, and RC06 group—with the highest expression level in the RC06 group (significantly higher than that in the RC04 group)—whereas no obvious DNAI1 protein expression was detected in the empty LNP control group.

Conclusions: This study confirms that the mRNA-LNP system can effectively deliver the DNAI1 gene and partially restore the ciliary beating function of PCD patients in the in vitro ALI model, providing experimental evidence for the etiological treatment of DNAI1-mutant PCD.

Conflict of interest The authors declare that they have no known competing interests.

SESSION: REGISTRIES & TRIALS 1

0134 Florensocatic, an inhibitor of dipeptidyl peptidase-1, for the treatment of non-cystic fibrosis bronchiectasis: Rationale and Design of the FABLE Phase III trial

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Background/Aims: Non-cystic fibrosis bronchiectasis (nCFBE) is a chronic, progressive disease characterized by persistent neutrophilic airway inflammation, recurrent lung infections and frequent pulmonary exacerbations (PE). Current treatment options for nCFBE are primarily supportive, underscoring an unmet need. Inhibiting dipeptidyl peptidase 1 (DPP1), an enzyme responsible for activating neutrophil serine proteases has emerged as a promising therapeutic approach to reduce PE and improve clinical outcomes in patients with nCFBE. Florensocatic, a Phase II randomized placebo-controlled study, report-

ed significantly reduced PE and sputum volume, and improved purulence with 24 weeks treatment in patients with nCFBE. FABLE is a phase III, double-blind, placebo-controlled study, aimed to evaluate the long-term efficacy and safety of florensocatib in patients with nCFBE.

Methods: A total of approximately 904 patients with nCFBE will be randomized to receive oral florensocitib tablets 40mg/day or placebo. In the Main (double-blind) phase, participants will be treated for a variable follow-up duration (52 to 78 weeks).

The primary endpoint is the annualised rate of adjudicated PEs. Key secondary endpoints include time to first adjudicated PE and annualized rate of severe adjudicated PE, change from baseline in quality of life, St. George's Respiratory Questionnaire (SGRQ) total score, and change from baseline in post-bronchodilator FEV₁ and FVC. Inclusion criteria include consenting participants with chest-CT confirmed nCFBE, a history of recurrent PEs requiring antibiotics over the prior 12 months, and a post-bronchodilator FEV₁ ≥ 30 % of the predicted value. Key exclusion criteria include PE ≤ 4 weeks prior to screening, cystic fibrosis, alpha-1 antitrypsin deficiency, active nontuberculous mycobacterial or other uncontrolled respiratory infections, immunocompromised status, and comorbidities that could interfere with participant safety or study results.

Participants completing the Main phase with $\geq 70\%$ treatment compliance will be eligible to enter an open-label extension (OLE), during which all participants will receive florensocatinb 40mg/day for up to 52 additional weeks, until market approval or study termination, whichever occurs first. Safety and efficacy will continue to be evaluated throughout the OLE.

A biomarker sub-study will enrol participants (n = 100-150) who provide additional consent to collect extra blood and sputum samples and undergo additional CT scans. The sub-study will evaluate the effect of florensocitab on the progression of lung damage and biomarker activity in blood and sputum during both Main and OLE phases.

Results: This trial is in the planning phase, with a total duration expected to be up to 138 weeks.

Conclusions: FABLE phase III study will provide long-term, robust evidence on the efficacy and safety of florensoctatib, contributing with critical insights to address the unmet clinical need for treatment of adults and adolescents with nCFBE.

Conflict of interest -**James D. Chalmers** reports grants or contracts from AstraZeneca, Chiesi, Genentech, Gilead Sciences, GlaxoSmithKline, Insmmed, Grifols, Trudell, Verona and Boehringer Ingelheim, and consulting fees from AstraZeneca, Biomx, Chiesi, CSL Behring, Expedition, GlaxoSmithKline, Insmmed, Grifols, Boehringer Ingelheim, Pfizer, Sanofi/Regeneron and Zambon. -**Felix C. Ringshausen** reports participation on an advisory and trial boards for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmmed, Parion Sciences, and Sanofi; clinical trial participation for AstraZeneca, Boehringer Ingelheim, Chiesi, Insmmed, Parion Sciences, Ruhr University-Bochum, University of Dundee and Vertex Pharmaceuticals; research grants from German Center for Lung Research (DZL), German Center for Infection Research (DZIF), Mukoviszidose Institute, Novartis and Insmmed; and has provided speaker services for Boehringer Ingelheim, Cliniqo GmbH, i!DE Werbeagentur GmbH, Insmmed, med update GmbH and Sanofi; leadership or fiduciary roles as co-chair of the German Bronchiectasis Registry PROGNOSIS, member of the steering committee of the European Bronchiectasis Registry EMBARC and PI of the German Center for Lung Research. -**All other authors** are employees of Chiesi, which is sponsoring the study.

0135 Subgroup analysis: AIRLEAF® Phase II study of a dipeptidyl peptidase 1 (DPP1, or CatC) inhibitor, verducatib, in adults with non-cystic fibrosis bronchiectasis

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Background/Aims: AIRLEAF®, a Phase II study, evaluated the efficacy, safety and optimal dosing of the DPP1 inhibitor verducatib in adults with bronchiectasis. [1] Verducatib treatment reduced the risk of experiencing a pulmonary exacerbation (PEx), most notably with the 2.5 mg dose, the dose taken forward into the Phase III AIRTYVITY™ study.

Methods: This double-blind, placebo-controlled study randomised 322 participants to verdutacitab (1/2.5/5 mg) or placebo for up to 48 weeks. The subgroups evaluated here are 1 PEX with St. George's Respiratory Questionnaire (SGRQ) Symptoms score >40 vs ≥2 PEXs in the year prior to screening, baseline *Pseudomonas aeruginosa* status, maintenance use of macrolides at baseline and aetiology (idiopathic/post-infectious vs all others).

Results: All subgroups in the 2.5 mg dose group had reductions in risk and rate of PExs, consistent with the overall study population (**Table 1**). Hazard ratios ranged from 0.47 to 0.82, illustrating consistent prolongation of time to first PEx. Particularly, estimates of the benefit for unique populations included in AIRLEAF®, such as 1 PEx plus high symptom score, were consistent with the overall population.

Conclusions: These results support the use of the 2.5 mg dose across all subgroups in AIRTIVITY™.

Conflict of interest DISCLOSURE STATEMENT This study was supported and funded by Boehringer Ingelheim International GmbH. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors did not receive payment related to the development of the abstract. Amy Bohm, MBio, of Nucleus Global provided writing, editorial support and formatting assistance, which was contracted and funded by Boehringer Ingelheim. Boehringer Ingelheim was given the opportunity to review the abstract for medical and scientific accuracy as well as intellectual property consideration. **JDC** reports support for the present publication from Boehringer Ingelheim; grants or contracts from AstraZeneca, Boehringer Ingelheim, Genentech, Gilead Sciences, GlaxoSmithKline, Grifols, Insmad and Trudell Medical Group; consulting fees from Antabio, AstraZeneca, Boehringer Ingelheim, Chiesi Farmaceutici, CSL Behring, Expedition therapeutics, Enterprise therapeutics, GlaxoSmithKline, Grifols, Insmad, Melodia, Pfizer, Trudell Medical Group, UCB, Vast Therapeutics and Zambon; and is the current Chief Editor of the *European Respiratory Journal*. **MS** reports support for the present publication from Boehringer Ingelheim; grants or contracts from GSK, Tel Aviv League for Lung Diseases and Trudell Medical Group; consultancy fees from AstraZeneca, Boehringer Ingelheim, Dexcel, GSK, Insmad, Kamada, Syn-

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0136 Long term outcomes of patients with Nocardia isolation in respiratory secretions – a retrospective cohort study

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Background/Aims: Nocardia species are a rare cause of pulmonary infections, usually seen in immunocompromised patients and patients with chronic lung disease. In immunocompromised patients, antimicrobial treatment is usually undertaken due to concern of invasive disease. However, in many cases Nocardia isolation in sputum is not related to significant disease and is considered a colonizer, in such cases treatment might be unnecessary.

Aim – assessing the long-term outcomes of patients with Nocardia isolation in sputum, comparing outcomes of patients who did not receive targeted treatment for Nocardia with the outcomes of those who did.

Methods: We performed a single-center retrospective cohort study including patients with Nocardia isolated from respiratory specimens between 2010 and 2021. Demographic and clinical data were obtained from electronic medical records. Treatment was defined as initiation of antimicrobial therapy targeting Nocardia species within six months of the positive respiratory specimen. Chest CT scans were manually reviewed by readers blinded to treatment allocation. Outcomes were compared between treated and untreated patients.

Results: 120 Patients had Nocardia species isolated from respiratory samples, with a mean follow up of 42 (19) months. In the 6 months following the first Nocardia isolation 23 (20%) patients received targeted treatment for Nocardia and 97 (80%) did not. Respiratory symptoms at presentation were similar between the treated and untreated groups (51% and 52% respectively, P=0.855) as were immunodeficiency states (13% and 17% respectively, P=0.761). Two patients received treatment aimed for Nocardia later than 6 months after first isolation. There was no difference in the rate of pulmonary hospitalization (P=0.402 HR=1.478 95% CI 0.592-3.69) or in the composite endpoint of death or hospitalization from any cause (P=0.248 HR 1.68 95% CI 0.697-4.049), between patients that did or did not receive treatment.

Conclusions: Most patients with Nocardia isolated from sputum did not receive targeted therapy and showed no evidence of progression to severe pulmonary nocardiosis. These findings provide reassurance that a watchful waiting approach may be appropriate in selected patients with Nocardia isolation in sputum who lack clinical or radiological features of severe disease.

Conflict of interest There are no relevant conflicts of interests to any of the authors

0137 The Australian Bronchiectasis Registry: Demographic and Aetiological Characteristics of a National Adult and Paediatric Cohort

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Background/Aims: Bronchiectasis is an increasingly recognised disease worldwide; however, gaps remain in understanding the prevalence and burden of disease in Australia.

The Australian Bronchiectasis Registry (ABR) was established in 2016 as a national, multicentre registry to capture longitudinal clinical data on people living with bronchiectasis across metropolitan and regional settings. By integrating

data across paediatric and adult cohorts, the ABR provides a unique opportunity to characterise bronchiectasis in Australia across the care continuum. This analysis aimed to describe the demographic and aetiological characteristics of participants enrolled in the ABR.

Methods: The ABK is a prospective, observational, multicentre registry established by the Australian Bronchiectasis Consortium and Lung Foundation Australia (LFA), with support from the European and US Bronchiectasis Registries. Individuals are eligible if they have a computed tomography (CT) chest scan consistent with the diagnosis of bronchiectasis, or for paediatric participants, a documented diagnosis of chronic suppurative lung disease (CSLD), where symptoms and/or signs of CSLD are present, with or without CT features. Participants must not have had a prior heart and/or lung transplant. Informed consent is obtained from the participant, parent, or guardian.

Data is collected at registration, annual review, and during exacerbations, and entered locally using a REDCap platform hosted by the University of Sydney.

This cross-sectional analysis included participants enrolled between March 2016 and March 2026. Descriptive statistics were used to summarise baseline characteristics.

Results: As of 31 March 2026, the ABR captured records for 1,885 participants from 18 sites. Age at registration was available for 1,854 participants, of whom 1,103 were adults (≥ 18 years) and 751 were children and adolescents (0–17 years). Participant sex was recorded for 99.4% of the cohort ($n = 1,873$); 58.6% were female, 41.4% were male, and 0.05% identified as other.

Enrolment was highest in Queensland, New South Wales, and the Northern Territory, reflecting the distribution of contributing sites.

In adults, the most common aetiologies were idiopathic (30.0%) and post-infective (29.7%), followed by non-tuberculous mycobacterial (NTM) disease (14.0%), with the higher proportion of NTM likely reflecting the contribution of a large cohort from an NTM specialist centre. In paediatric participants, bronchiectasis was predominantly post-infective (70.0%), with lower proportions of idiopathic disease (15.7%) and primary ciliary dyskinesia (4.6%). The high proportion of idiopathic bronchiectasis across both adult and paediatric cohorts highlights an opportunity for the ABR to support improved characterisation of patient populations and underlying aetiologies.

Conclusions: The ABR provides a secure national platform for capturing longitudinal data on people living with bronchiectasis across both paediatric and adult populations. This unique dataset enables insights into differences in disease characteristics across the continuum of care and supports future research and quality improvement initiatives.

While enrolment has temporarily plateaued during a planned database redevelopment, ongoing clinician and patient engagement remains strong. Future efforts will focus on enhancing data completeness, developing targeted outcome measures, and expanding site participation to support continued registry growth and impact.

Conflict of interest The ABR is generously supported by Boehringer Ingelheim.

0138 Effectiveness of inhaled colistin in bronchiectasis: a real-world analysis from the REPAIR registry.

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Background/Aims: Bronchiectasis is characterized by recurrent exacerbations and chronic bronchial infection, leading to significant morbidity and healthcare utilization. Inhaled antibiotics are widely used, but real-world data comparing different formulations remain limited. We aimed to evaluate the effectiveness of inhaled colistin and compare outcomes between nebulized and dry powder formulations.

Methods: Multicentre observational study using data from the REPAIR registry. We included bronchiectasis patients receiving inhaled colistin. A baseline descriptive analysis was performed. Longitudinal changes were assessed using generalized linear mixed models with negative binomial distribution. A univariable analysis compared nebulized versus dry powder colistin at 6 months. Outcomes included exacerbations, hospitalizations, emergency visits, days of hospitalization, CAT score, microbiological isolation, adverse events, and mortality.

Results: A total of 244 patients were included (76.6% female, mean age 66.9 ± 15.2 years). Chronic bronchial infection was present in 49.6%, with *Pseudomonas aeruginosa* in 74.6%. Longitudinal analysis showed a significant reduction in ambulatory exacerbations (IRR 7.78; $p < 0.001$), emergency visits (IRR 3.17; $p = 0.037$), hospitalizations ($p = 0.004$), and days of hospitalization ($p = 0.030$). No significant interaction between time and colistin formulation was observed. CAT score did not significantly change over time (mean difference -1.33; $p = 0.515$). In the comparison between formulations, no significant differences were observed in exacerbations, hospitalizations, or emergency visits. However, microbiological isolation after initiating inhaled antibiotic therapy was more frequent in the dry powder group (70.0% vs 41.4%; $p = 0.048$). No significant differences in adverse events or mortality were found.

Conclusions: Inhaled colistin is associated with a significant reduction in exacerbations and hospitalizations in bronchiectasis patients. No differences were observed between nebulized and dry powder formulations in clinical outcomes, although dry powder may be associated with higher microbiological isolation. These findings support the effectiveness of inhaled colistin in real-world practice.

Conflict of interest We declare no conflicts of interest.

0139 Clinical outcome burden in people with bronchiectasis by baseline pulmonary exacerbation frequency: A real-world data analysis

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Background/Aims: Bronchiectasis is a chronic inflammatory lung disease that is characterised clinically by cough, sputum production, and respiratory infections, and radiologically by the identification of abnormally dilated bronchi. This study evaluates clinical outcomes in a large United States (US) cohort following a new diagnosis of bronchiectasis, by baseline pulmonary exacerbation (PEX) frequency.

Methods: This non-interventional study utilised existing US healthcare claims data in the Optum® Clinformatics® Data Mart from individuals with an incident bronchiectasis diagnosis (2017–2022) and who were continuously registered for 365 days prior to diagnosis. Individuals were grouped by baseline PEX frequency (0, 1, 2, and ≥ 3) and followed for up to 7 years and 9 months. A baseline PEX was defined as a PEX that occurred in the 12 months prior to bronchiectasis diagnosis; baseline PEXs were categorised as an emergency department visit, or hospitalisation with a primary or secondary diagnosis code for a respiratory disease, or an outpatient visit with a diagnosis code for a respiratory disease followed by a prescription for specific antibiotics, including macrolides, within 7 days. Clinical outcome burden was assessed in Year 1 and across the follow-up period and included occurrence of PEXs, severe PEXs, lung transplantation, lung resection, and death.

Results: This analysis included 75,731 individuals, with a mean age of 74.2 years. Most individuals were female (58.4%), white (57.6%), and insured through Medicare Advantage (88.6%). The proportion of people with no baseline PEXs was 32.3%, 39.1% with 1 PEX, 16.1% with 2 PEXs, and 12.4% with ≥ 3 PEXs. In Year 1, the proportion of people experiencing outcome events generally increased progressively based on baseline PEX frequency, with the following ranges reported for subgroups of 0 to ≥ 3 baseline PEXs (Table): any PEXs (29.3–67.4%), severe PEXs (14.3–49.1%), all-cause deaths (7.8–27.5%) and respiratory-related deaths (4.0–20.1%). This increase was also seen in overall follow-up, and a greater proportion of people experiencing these outcomes than at Year 1, with the following ranges reported across the PEX subgroups: any PEXs (50.8–77.0%), severe PEXs (30.9–64.7%), all-cause deaths (21.4–48.7%) and respiratory-related deaths (9.6–33.0%). Lung transplantations and resections were uncommon (<1% and <3%, respectively, across all subgroups at both time points). At Year 1 and in the overall follow-up group, people with 1 PEX at baseline still had a higher event burden compared with those with no PEXs (proportion range across non-surgical events at Year 1: 12.8–61.6% vs. 4.0–29.3%, respectively; overall follow-up range: 20.3–74.3% vs. 9.6–50.8%, respectively).

Conclusions: In the US, the clinical burden in people with incident bronchiectasis increased according to number of baseline PEXs in the 12 months prior to diagnosis. About 30% of those with 0 baseline PEX experienced at least one PEX within the first year of follow-up. Those with a single baseline PEX—the largest subgroup—experienced more clinical outcome events than those with no prior PEX. Acknowledging high baseline PEX frequency as an important indicator of future clinical outcomes, our findings demonstrate that even limited exacerbation history can result in high clinical burden.

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Boehringer Ingelheim; and payment or honoraria from The France Foundation. CB, BP, ML, and WKM are employees of Boehringer Ingelheim.

0140 InhalEd ColiFin® in adult bRronchiectasis pAtients with new asymptomatic PseuDomonas aeruglnosa infeCtion– an open-lAbel, proof of concepT- randomizEd controlled trial (ERADICATE)

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Background/Aims: Chronic bacterial infections with *Pseudomonas aeruginosa* (PA) have a negative impact on morbidity and mortality in bronchiectasis. Despite a lack of evidence, guidelines recommend early eradication.

Methods: ERADICATE is a multicentric open-label, proof-of-concept randomized controlled trial. 66 patients with new detection of PA in sputum will be randomized in a 2:1 ratio to either inhalation of colistimethate sodium 2 million I.U. t.i.d. for 28 days, or continuation of standard of care without receiving an eradication attempt. Both groups receive a follow-up of 28 weeks after randomization.

Objectives and end-points: Primary objective is to evaluate the efficacy of colistimethate sodium inhalation for 28 days versus standard of care on sputum culture negativity for PA 28 weeks after randomization. Secondary endpoints are to evaluate safety of colistimethate sodium treatment and effects on exacerbations, lung function, quality of life and microbiological aspects.

Key inclusion and exclusion criteria: The trial will enroll patients ≥ 18 years with CT-confirmed diagnosis of bronchiectasis and new or first-time detection

Methods: We analyzed data from the European Bronchiectasis Registry (EM-BARC), including 30 countries across Europe and Asia. The association between baseline exacerbation history and future exacerbations was tested using negative binomial regression. Severe exacerbations were defined as those requiring hospitalization.

Results: A total of 19,324 patients with bronchiectasis were included. Each prior exacerbation was associated with an increased risk of exacerbations and hospitalizations. Incidence Rate Ratio (IRR) for future exacerbations was 1.45 (95%CI 1.34-1.58, $p < 0.001$) for one exacerbation, 1.84 (95%CI 1.69-1.99, $p < 0.001$) for two exacerbations, 2.50 (95%CI 2.29-2.73, $p < 0.001$) for three exacerbations and 3.56 (95%CI 3.32-3.82, $p < 0.001$) for patients with four or more prior exacerbations. Additionally, one prior severe exacerbation was associated with increased risk of exacerbation (IRR = 1.52, 95%CI 1.45-1.60, $p < 0.001$) and strongly associated with future severe exacerbations (IRR = 3.96, 95%CI 3.71-4.22, $p < 0.001$). The frequent exacerbator phenotype was consistent across different etiologies and geographic regions.

Conclusions: The frequent exacerbator phenotype is highly consistent across patient subgroups and regions. Each prior exacerbation is associated with a progressively higher risk with no definitive threshold defining high risk.

Conflict of interest LP reports participation on an Advisory Board from Insmmed. OS reports consulting fees from Insmmed and Boehringer Ingelheim. JC reports grants or contracts from Grifols; consulting fees from Antabio, AstraZeneca, Boehringer Ingelheim, Chiesi, Glaxosmithkline, Grifols, Insmmed, Janssen, Novartis, Pfizer, and Zambon; and leadership or fiduciary roles as Chair of ERS Bronchiectasis Guideline Task Force, Chief Editor of ERJ, and Chair of EM-BARC Clinical Research Collaboration. The extended list of CoIs from all the authors will be included in the work.

0143 Final pooled data from Phase II studies (AIRLEAF®, CLAIRLEAF®) of the dipeptidyl peptidase 1 (or Cathepsin C) inhibitor verducatib in bronchiectasis

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Background/Aims: Verducatib (BI 1291583), a dipeptidyl peptidase 1 inhibitor, reduced the risk of adults with bronchiectasis experiencing a pulmonary exacerbation (PEX) in the Phase II AIRLEAF® study. [1] Upon completion of treatment in AIRLEAF®, participants were eligible to enter the double-blind part of the CLAIRLEAF® rollover study (ongoing) to assess long-term safety and efficacy. Here, we present the final pooled data from all participants who received verducatib in the AIRLEAF® or CLAIRLEAF® (excluding those who rolled over from CLAIRFLY®) studies.

Methods: In AIRLEAF®, 322 participants received one of three verducatib doses (1/2.5/5 mg) or placebo once daily for 24–48 weeks. [1] Upon entering CLAIRLEAF®, those on active therapy in AIRLEAF® remained on the same blinded verducatib dose. Those in the placebo group in AIRLEAF® were blindly randomised (1:1:1) to a verducatib dose. As with the pre-specified analysis of the interim pooled data, [2] in this final analysis, data from AIRLEAF® and CLAIRLEAF® were pooled to allow analyses with observational data up to Week 104. The analysis included 296 participants. For the efficacy analysis, the 2.5 and 5 mg verducatib doses were compared against the subtherapeutic 1 mg dose [1] (due to the absence of a placebo group). The efficacy endpoints assessed were time to first PEX and PEX rate, both up to Week 104. Safety analyses were descriptive and based on treatment-emergent adverse events.

Results: The comparison of the 2.5 mg versus 1 mg dose of verducatib on time to first PEX revealed a 24% risk reduction (hazard ratio [HR] 0.76; 95% confidence interval [CI] 0.51–1.14); the effect of the 5 mg dose was a 13% reduction (HR 0.87; 95% CI 0.61–1.24). The 2.5 mg dose showed a 33% decrease (rate ratio [RR] 0.67; 95% CI 0.45–0.99) in PEX rate versus the 1 mg dose, whereas the 5 mg dose showed a 7% decrease (RR 0.93; 95% CI 0.67–1.31). The pooled safety data up to 104 weeks of exposure continue to support the known verducatib safety profile to date.

Conclusions: This pooled analysis demonstrates consistent positive effects of the 2.5 mg verducatib dose on PEXs, and provides supportive evidence for the long-term efficacy and safety of verducatib in people with bronchiectasis. The 2.5 mg dose is being investigated in the Phase III AIRTIVITY™ study.

Conflict of interest Please see attached file.

References

- [1] Chalmers JD et al. Eur Respir J 2025; 65: PMID: 2401551
- [2] Shteinberg M et al. Presented at ERS. 2025; Poster PA4960

0144 Comparison of Aerobika versus other PEP therapies, in addition to inhaled hypertonic saline, among adult patients in the U.S. Bronchiectasis Research Registry

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Background/Aims: Airway clearance therapies, including positive expiratory pressure (PEP) devices and adjunctive treatments such as hypertonic saline (HS), are central to bronchiectasis disease management. However, variation exists in the types of PEP devices used in clinical practice, and comparative data on their real-world effectiveness remain limited. This study of adult patients enrolled in the U.S. Bronchiectasis Research Registry and NTM (BRR) aimed to evaluate differences in patient characteristics and clinical outcomes among persons with bronchiectasis (pwBE) using Aerobika® in combination with HS versus those using other PEP devices with HS.

Methods: Adult pwBE enrolled in the BRR and prescribed positive expiratory pressure (PEP) devices and hypertonic saline (HS) at baseline were retrospectively analyzed. Patients with unknown exacerbation, spirometry, imaging and culture data at baseline and first annual follow-up were excluded. Patients were categorized as using Aerobika[®] and HS vs. other PEP measures and HS, where other PEP devices included: Acapella[®] device, Lung Flute, flutter valve, Volara System, and others collected in the BRR. Demographics, co-existing conditions, and baseline and first annual follow-up clinical characteristics were summarized descriptively for both groups. Differences between groups were assessed using standardized mean differences (SMDs), which can generally be interpreted as: <0.1 = well balanced, 0.10 - 0.20 = small imbalance, and >0.20 = moderate to large imbalance.

Results: 350 patients were included, with most patients prescribed Aerobika® + HS (n = 304, 87 %). PwBE using Aerobika® + HS and those using other PEP devices + HS were generally similar across many baseline clinical characteristics, including age, lung function (FEV₁), and BMI, with most standardized mean differences (SMDs) indicating good balance (Table). However, notable imbalances were observed in select demographic variables, particularly sex and race/ethnicity distributions, with those prescribed Aerobika® + HS more likely to be female (87 % vs. 76 %, SMD = 1.32) and white (90 % vs. 85 %, SMD = 1.35), and less likely to carry a diagnosis of asthma (23 % vs. 30 %, SMD = 0.49) and/or GERD (55 % vs. 59 %, SMD = 0.90). Those prescribed Aerobika® + HS had more diffuse disease and were more likely to have isolated *Pseudomonas aeruginosa* (PsA) (30 % vs. 28 %, SMD = 0.63) and NTM (69 % vs. 64 %, SMD = 1.10), and had greater median number of lobes involved on CT imaging (5 [IQR: 3-6] vs. 3 [IQR: 2-5.5], SMD = 0.46). Consistent with this disease severity, patients prescribed Aerobika® + HS were more likely to have had at least one exacerbation but less likely to have isolated PsA at first annual follow-up.

Conclusions: Aerobika® is the most common PEP device prescribed among patients enrolled in the BRR. Compared to those prescribed other PEP devices, patients prescribed Aerobika® + HS had a greater disease severity at baseline. The observed baseline imbalances suggest potential bias by indication and/or PEP prescribing habits across centers. Prospective and controlled studies adjusting for these limitations are needed to better determine whether specific PEP devices confer differential clinical benefits in bronchiectasis management.

Conflict of interest No conflicts related to this study exist among the authors

0145 First International Multicenter Validation of the Chronic Airways Assessment Test (CAAT)TM in Bronchiectasis

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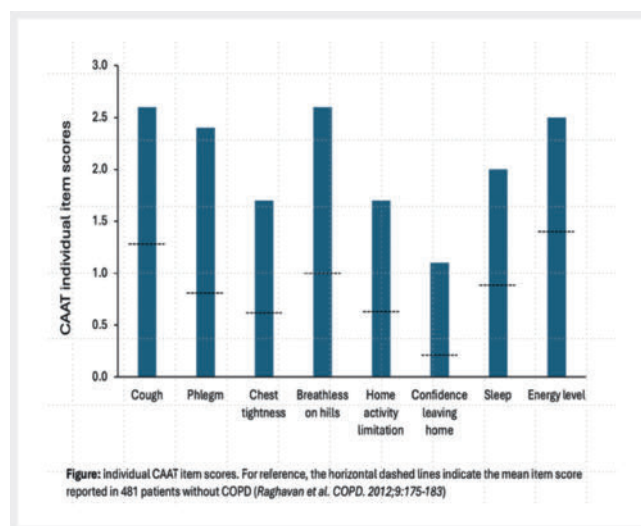
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Background/Aims: The Chronic Airways Assessment Test (CAAT™) is an evolution of the COPD Assessment Test (CAT™), adapted for broader airway disease use. It was validated as a patient-reported measure of symptom burden and health status in COPD, and as a cross-disease measure of disease impact in asthma (Tomaszewski et al. *Respir Res.* 2023;24:106; Jones et al *ERJ Open Res.* 2025;11:01359-02024). The CAAT is a brief 8-item measure used to assess the impact of disease on daily life, monitor disease severity and changes over time, and support clinical decision-making (e.g., its inclusion within the 2025 GOLD strategy). Items are scored on a Likert scale from 0 to 5; total score ranges from 0 to 40 with higher scores reflecting higher disease impact. The mean CAT scores reported in a large sample of people without COPD was 6.9 (Raghavan et al. *COPD.* 2012;9:175-183). We report the first cross sectional multicentre validation of the CAAT in people with bronchiectasis

Methods: People with bronchiectasis enrolled from the pooled from the ongoing EMBARC-BRIDGE (NCT03791086) study (n = 192) and a US cohort at the University of Alabama (n = 44). Participants with self-reported or physician report COPD comorbid asthma or COPD (n = 109) were excluded to define the final analysis cohort (n = 238). Exacerbation history, post bronchodilator, Forced Expiratory Volume in 1 second (FEV₁) and CAAT scores were collected. Descriptive statistics and internal consistency reliability on the CAAT total scores and individual item scores was conducted.

Results: Among the 236 participants (male vs female: 72/164), mean age was 64.3 years (standard deviation [SD] 15.3). Of 185 EMBARC BRIDGE participants with available smoking data, 63.8% were never smokers, 31.9% were former smokers and 4.3% were current smokers. Median FEV₁ percent predicted was 87.8% (IQR 70-100%), and median number of exacerbations in the previous year was 1 (interquartile range [IQR] 0-3). Baseline mean CAAT score was 16.1 (SD 8.8), Bronchiectasis Severity Index (BSI) score was 5.7 (SD 3.4). Individual CAAT item scores are shown in the ► **Fig. 1:** the highest scores were observed for Cough, Sputum, Breathlessness on hills, and Energy items.



► Fig. 1

Conclusions: Total CAAT scores were clearly higher in this bronchiectasis cohort than those reported in people without COPD. The CAAT demonstrated good internal consistency in this bronchiectasis population, supporting its reliability as a measure of respiratory symptoms and impacts.

This was not just due to cough, sputum and breathlessness, but also sleep and energy which may reflect systemic effects of the disease. These results support continued efforts to develop and validate the CAAT instrument for disease monitoring, HRQL assessment, and, potentially, therapeutic development.

Conflict of interest RTS, JDC, GMS and PWJ report relationships with multiple pharmaceutical companies involved in respiratory therapeutics, including re-

search funding, consulting fees, and personal fees, outside the submitted work. FF, PD and GH are employed by PPD™ Evidera™ Patient-Centered Research, part of Thermo Fisher Scientific, a consultancy that received research funding from GAAPP to conduct this analysis.

0146 Nocturnal digital cough monitoring in people with Primary Ciliary Dyskinesia and Cystic Fibrosis – First results of an international multi-centre observational study

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DOI 10.1055/s-0046-1826161

Background/Aims: Cough is recognized as a marker of poor disease control and an early sign of pulmonary exacerbation in chronic lung diseases. This study evaluates continuous nocturnal cough monitoring in people with primary ciliary dyskinesia (PCD) and cystic fibrosis (CF) to characterize the natural history of nighttime cough under standard-of-care treatment.

Methods: This international, multicenter, prospective observational study evaluates continuous objective cough monitoring using a therapy management application (PARI Connect app) over 24 weeks in patients aged > 12 years. The study aims to enroll 30 individuals with PCD and 250 with CF. Subjective cough severity is recorded daily via an integrated visual analogue scale. Clinical and sociodemographic characteristics, disease-specific outcomes, and cough-related quality of life are assessed at baseline and at 3 and 6 months.

Results: To date, 130/280 participants have been enrolled, 57.5% female; median age 31.0y [IQR 21.5–37.0]; median FEV₁ 79.0%pred [IQR 58.0–94.0]. Among participants with CF, 95/107 (88.8%) receive CFTR modulator therapy, predominantly elexacaftor/tezacaftor/ivacaftor (88/95; 92.6%). No pulmonary exacerbations in the preceding 12 months were reported by 68/122 CF or PCD participants (55.7%). 76 participants had a 3-months visit and 25 participants a 6-months visit. A median duration of 8.1 hours (PCD 9.3, CF 8.0) of cough monitoring per night were recorded with a mean nocturnal cough frequency of 11.3 (SD 30.3) in PCD and 9.6 (SD 38.1) in CF, respectively. Subjective daily cough frequency differed between PCD (median 3.9) and CF (median 0.5). Patient-level analyses of cough frequency are ongoing and will be available at the World Bronchiectasis Conference.

Conclusions: This study will generate evidence to support the use of noninvasive cough monitoring as a marker of disease control and will critically evaluate its utility as a remote digital endpoint in future therapeutic trials.

Conflict of interest Funded by a Vertex pharmaceuticals independent innovation grant.

0147 The Impact of Proton Pump Inhibitor (PPI) Use on Exacerbation Rates in Patients with Bronchiectasis: An Analysis of the US Bronchiectasis and NTM Research Registry

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Background/Aims: Proton pump inhibitors (PPIs) are commonly prescribed in bronchiectasis, often for gastroesophageal reflux disease (GERD), but may alter the aerodigestive microbiome and susceptibility to respiratory infection. We aimed to determine whether baseline PPI prescription was associated with future bronchiectasis exacerbations and airway microbiome differences.

Methods: We conducted a retrospective analysis of the U.S. Bronchiectasis and NTM Research Registry. Three cohorts were evaluated: a baseline descriptive cohort (N = 3,236), a 24-month longitudinal cohort for exacerbation modeling (N = 363), and a bronchoscopy microbiome sub-study (N = 200). Multivariable negative binomial regression assessed the association between baseline PPI prescription and total exacerbations over 24 months, adjusting for smoking, clinician-documented GERD, H2-blocker use, chronic *Pseudomonas aeruginosa* infection, baseline exacerbation history, change in ppFEV₁ and follow-up time. In the microbiome sub-study, paired supraglottic and bronchoalveolar lavage samples underwent 16S rRNA gene sequencing. All participants provided consent under registry and site-specific protocols approved by institutional review boards.

Results: Among 3,236 participants with baseline medication and exacerbation data, 815 (25.2%) had a recorded PPI prescription. PPI users had greater baseline disease burden, including more prior exacerbations, more prior pulmonary hospitalizations, and higher modified Bronchiectasis Severity Index scores, while baseline lung function and standard culture-based microbiology were broadly similar between groups. In the longitudinal cohort, 102/363 (28.1%) had baseline PPI exposure. Over 24 months, baseline recorded PPI prescription was independently associated with a higher exacerbation rate (incidence rate ratio 1.48, 95% CI 1.09–2.00). In the microbiome sub-study, PPI exposure was associated with significantly lower supraglottic alpha diversity, whereas BAL alpha diversity did not differ significantly by PPI status. There were no significant global beta-diversity differences in either supraglottic or BAL samples. However, differential abundance analyses demonstrated taxon-specific compositional shifts. In supraglottic samples, PPI exposure was associated with enrichment of genera containing potential pathogens, including *Pseudomonas*, *Enterococcus*, *Bacteroides*, and *Clostridium*, whereas *Actinomyces*, *Acinetobacter*, and *Staphylococcus* were enriched in those without PPI exposure. In BAL, PPI exposure was associated with enrichment of *Proteus*, *Nocardia*, and *Achromobacter*, while *Stenotrophomonas*, *Prevotella*, and *Moraxella* were enriched in non-users. Several taxa showed concordant enrichment patterns across upper and lower airway compartments, supporting aerodigestive microbial perturbation.

Conclusions: In bronchiectasis, baseline recorded PPI prescription was independently associated with higher subsequent exacerbation rates. Exploratory microbiome analyses showed reduced supraglottic diversity and taxon-specific upper and lower airway compositional shifts consistent with altered aerodigestive microbial ecology. These findings support biological plausibility for the observed clinical association and suggest that indication-based PPI use should be regularly reassessed in this population.

Conflict of interest This work used data from the Bronchiectasis and NTM Research Registry. The authors would like to acknowledge that the Bronchiectasis and NTM Research Registry is supported in part by corporate donors, all of which can be found on the Supporters page of the Association website. It should also be noted that this work would not have been possible without the comprehensive chart reviews and recording of data by the dedicated research coordinators and PIs at each of the participating Bronchiectasis and NTM Research Registry sites. Amanda E. Brunton is an employee of the Bronchiectasis and NTM Association.

0148 Induced sputum collection using Lung Flute® ECO in suspected NTM pulmonary disease with bronchiectatic features: a prospective interim analysis

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Background/Aims: Patients with bronchiectatic features and suspected NTM pulmonary disease (NTM-PD) often require repeated microbiological assessment, yet many are unable to expectorate sputum spontaneously. Although limited data are available for the use of Lung Flute® ECO in pulmonary tuberculosis, evidence in NTM-PD is scarce. We prospectively evaluated the feasibility, microbiological yield, and safety of induced sputum collection using Lung Flute® ECO in this setting.

Methods: This interim analysis of an ongoing prospective observational study included adults with radiological findings suspicious for NTM-PD who had been unable to submit sputum for at least 8 weeks. Patients used Lung Flute® ECO once weekly for three consecutive attempts per cycle, and the cycle was repeated every 12 weeks until diagnosis, for up to four cycles (maximum 12 attempts). The primary endpoint was induced sputum submission rate. Secondary endpoints included microbiological yield and adverse events. Sputum quality was assessed using the Miller–Jones classification.

Results: Twelve patients were included. Median age was 71 years (range, 54–83), and 11 were female. Baseline pulmonary function was generally preserved, with a median predicted FEV1 of 90.5 %. At least one induced sputum sample was obtained in 11 of 12 patients (91.7 %). On an assessment basis, evaluable sputum samples were obtained in 100 of 108 attempts (92.6 %). Among submitted samples, Miller–Jones quality was M2 in 36, P1 in 29, M1 in 26, P2 in 7, and P3 in 2. No acid-fast smear-positive sample was observed. Culture positivity was documented in 13 of 100 submitted samples, corresponding to 7 of 12 patients. Five patients met criteria for confirmed disease, while 2 additional patients were classified as probable disease. In one additional patient, bronchoscopy was prioritized because of clinical deterioration requiring treatment, and the diagnosis was subsequently established bronchoscopically. Adverse events were observed in 5 patients and were generally mild, including cough, dyspnea, dizziness, headache, and throat discomfort. No serious adverse events were observed.

Conclusions: In this selected cohort of patients with suspected NTM-PD and bronchiectatic features who were unable to expectorate spontaneously, induced sputum collection using Lung Flute® ECO achieved a high sputum submission rate and yielded culture-positive specimens despite uniformly smear-negative samples. This non-invasive approach may facilitate microbiological diagnosis with acceptable safety.

Conflict of interest Kazuya Tone has received lecture fees from Inmed GK, Sanofi K.K., AstraZeneca K.K., Asahi Kasei Corporation, Boehringer Ingelheim, Kyorin Pharmaceutical Co., Ltd., and Teijin Healthcare Ltd., and is affiliated with an endowed course supported by Inmed GK. No other conflicts of interest to declare.

0149 Finding the Optimal Regimen for Mycobacterium abscessus Treatment (FORMaT) Trial: First Interim Analysis of 61 Intervention Participants after Short Intensive Therapy

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DOI 10.1055/s-0046-1826164

Background/Aims: Treatment for Mycobacterium abscessus pulmonary disease (MABC-PD) is characterised by prolonged use of multiple, expensive antibiotics that exhibit substantial toxicity and poor effectiveness. The Finding the Optimal Regimen for Mycobacterium abscessus Treatment (FORMaT) adaptive platform trial (APT) aims to find the best treatment for MABC-PD. There is an intensive treatment phase using intravenous (IV) and oral antimicrobials (see Table 1) followed by a consolidation treatment phase each with separate randomisations. An Observational Cohort simultaneously recruits participants with positive mycobacterium abscessus (MABC) respiratory cultures who do not meet American Thoracic Society (ATS) criteria for treatment.

Methods: Inclusion Criteria for the APT: positive MABSC-PD diagnosis based on ATS criteria; any age and sex; no MABSC-PD treatment in 12 months prior; and for Observational Cohort: ≥ 1 MABSC positive respiratory culture; any age and sex; no active MABC-PD treatment in 12 months prior. The first interim analysis in May 2026 will analyse data from 61 APT participants who have completed 6 weeks intensive therapy using Sequential Multiple Assignment Randomised Trial approach, thus providing the first randomised assessment of standard of care treatments. Following interim analysis, a new treatment arm using combined B-lactam antimicrobials will be initiated.

The APT has 3 nested trials – the first compares efficacy and tolerance of the 3 intensive therapy arms at 6 weeks. The primary outcome measures are: MABC clearance – defined as 3 negative respiratory samples (sputum/induced sputum) or 1 negative bronchoalveolar lavage collected at Week 4 and interpreted at Week 6; and Treatment tolerance – defined as no adverse events (AEs) or AEs possibly/probably/definitely related to study drugs graded 1 or 2 based on the Common Terminology Criteria for Adverse Events Version 5.0.

Results: To date 61 intervention participants and 64 observation participants have been recruited. Table 2 outlines the baseline demographics of the participants.

Conclusion: Interim analysis outcomes will be presented. The novel treatment arm – sulbactam-durlobactam (in-kind from industry partner) in combination with IV ceftriaxone and oral amoxicillin, azithromycin and clofazimine, will be introduced to the FORMaT APT after interim analysis is completed.

Conflict of interest Nil conflicts of interest(s) to declare.

SESSION: Respiratory Physiotherapy and Airway Clearance

0150 Feasibility and Clinical Utility of Forced Oscillation Technique (FOT) as an Outcome Measure for Airway Clearance Efficacy in Non-Cystic Fibrosis Bronchiectasis: A Pilot Study

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Background/Aims: Airway clearance techniques (ACT) are recommended by the 2025 ERS guidelines in non-cystic fibrosis bronchiectasis (non-CF BE), but robust outcome measures to assess their acute mechanical efficacy are still lacking. The Forced Oscillation Technique (FOT) is a non-invasive, effort-independent method sensitive to central and peripheral respiratory mechanics, and is a candidate outcome measure. The aim of this study is to assess the feasibility and clinical usefulness of FOT as an outcome measure of the efficacy of a single airway clearance session in adults with non-CF bronchiectasis.

Methods: Prospective single-centre pilot study. Adults with clinically stable non-CF bronchiectasis of mild-to-moderate severity were enrolled. FOT measurements at 5 Hz were performed before and 15 minutes after a 60-minute airway clearance session carried out with the patient's habitual technique. Primary outcomes: pre-post change in 5-Hz Rrs, Xrs and Δ Xrs. Secondary outcomes: dyspnoea (Borg CR-10), global respiratory well-being (3-point Likert scale), sputum volume, and feasibility (proportion of ERS-compliant FOT acquisitions). Descriptive and exploratory analyses (Wilcoxon signed-rank test, Spearman's correlation, effect sizes).

Results: Five patients were enrolled (4 women, 1 man; median age 59 years; median BSI 3, range 0–8). No 5-Hz FOT parameter showed statistically significant pre-post changes. A large effect size was detected for Δ Xrs ($r = -0.73$; $p = 0.188$) in the direction opposite to that expected, with the marker of tidal expiratory flow limitation increasing in 4 of 5 patients. Perceived dyspnoea worsened concordantly (median Δ Borg + 2 points; 5/5), in apparent dissociation with global respiratory well-being (Likert + 1 in 5/5; ceiling effect). The exploratory Δ Rrs_tot- Δ Borg correlation was $\rho = -0.949$ ($p = 0.014$), with a marked leverage effect. Feasibility was acceptable: 65.7 % ERS-compliant acquisitions (95 % CI 47.8–80.9 %); median pre + post FOT time 11 minutes; no adverse events.

Conclusions: FOT is applicable, safe and technically acceptable for outpatient monitoring of an airway clearance session in stable non-CF patients. Its sensitivity in detecting an acute mechanical benefit 15 minutes after session end is not confirmed; the signal of a possible Δ Xrs increase generates the hypothesis of a transient post-session "mechanical turbulence". Confirmatory studies should adopt richer post-session timing, stratification by disease severity and technique, and integration with quantitative imaging.

Conflict of interest The authors declare no conflicts of interest.

0151 Physiotherapy Support Staff in Airway Clearance: A Competency-Led Approach

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Background Airway clearance techniques (ACTs) are a core component of bronchiectasis management, with strong evidence demonstrating improvements in sputum clearance, symptom burden and exacerbation risk (Herrero Cortina et al., 2023). However, real-world practice shows substantial variation in ACT delivery, review frequency and service capacity (Herrero Cortina et al., 2023). Reviews consistently highlight the need for skilled physiotherapists to individualise ACT selection based on patient-specific physiological factors (Belli et al., 2021). Workforce pressures within UK respiratory pathways further challenge consistent ACT provision, signalling the need for safe and effective skill-mix models.

Methods A narrative synthesis of evidence was undertaken, integrating:

- international bronchiectasis ACT guidelines (ERS 2023)
 - reviews of ACT mechanisms and therapist-dependent factors (Belli et al., 2021; Reychler et al., 2026)
 - physiotherapy ACT utilisation data (Phillips et al., 2021)
 - patient-reported barriers and enablers to ACT adherence (Franks et al., 2022)
 - UK guidance on physiotherapy support staff delegation and scope of practice
- Themes were synthesised to construct a theoretical model outlining which ACT-related tasks can be safely delegated to support staff under physiotherapist supervision.

Results

The synthesis identified:

- Robust evidence from 30 RCTs summarised in the ERS statement demonstrating ACT-related improvements in sputum clearance, quality of life and exacerbation reduction (Herrero Cortina et al., 2023).

- Marked variation and gaps in ACT delivery, largely driven by service pressures rather than evidence limitations.
- Key determinants of ACT selection—secretion burden, airway stability, comorbidities, patient capacity and preference—requiring physiotherapist-led assessment and clinical reasoning (Belli et al., 2021).
- Clear opportunities for support staff involvement in ACT education, technique reinforcement, device support and adherence monitoring, consistent with UK delegation standards.
- Patient-centred needs indicating improved adherence when supported through structured follow-up and individualised teaching (Franks et al., 2022).

The resulting model positions physiotherapists as responsible for assessment and treatment planning, with PTAs delivering delegated ACT support within defined competency boundaries.

Conclusion Integrating support staff into delegated aspects of ACT delivery offers a scalable, evidence-aligned approach to addressing workforce pressures while maintaining safety and quality. The proposed competency-led model is theoretically robust, consistent with UK physiotherapy delegation frameworks, and well suited for piloting within bronchiectasis services to enhance access, adherence and continuity of ACT care.

Conflict of interest None

0152 Association Between Airway Clearance Technique Adherence and Exacerbation Risk in Children and Adolescents With Non-Cystic Fibrosis Bronchiectasis: A Retrospective Cohort Study

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Background: Airway clearance techniques (ACT) are central to the management of non-cystic fibrosis bronchiectasis (NCFB), but pediatric evidence linking adherence to clinical outcomes is limited.

Aims: To evaluate the association between self-reported ACT adherence and exacerbation risk in children and adolescents with NCFB.

Methods: In this retrospective cohort study, we included all children and adolescents diagnosed with NCFB between 2019 and 2025 at a tertiary pediatric respiratory center. ACT adherence was categorized as high ($\geq 80\%$), moderate (36–79 %), or low ($< 35\%$). The total number of exacerbations in the first year after diagnosis was analyzed using multivariate negative binomial regression. Severe exacerbations (requiring emergency department visits or hospitalization) were assessed using binary logistic regression due to the low frequency of events. Models were adjusted for etiology, sex, *Pseudomonas aeruginosa* status, age at diagnosis, FEV₁ % predicted, and BMI z-score. Results presented as IRR (Incidence Rate Ratio) and OR (Odds Ratio).

Results: A total of 102 patients were included (median age at diagnosis 9.6 years [IQR 6–12.9], 55.9 % male). The most common etiologies were post-infectious (49 %) and primary ciliary dyskinesia (23.5 %). Median FEV₁ % predicted was 99 (IQR 81–110). High, moderate, and low ACT adherence were reported in 42.1 %, 31.4 %, and 26.5 % of patients, respectively. High ACT adherence was independently associated with fewer total number of exacerbations compared to low adherence (IRR 0.44, 95 % CI 0.24–0.83, $p = 0.012$), after adjustment for aetiology, sex, *Pseudomonas aeruginosa* status, age at diagnosis, FEV₁ % pre-

dicted, and BMI z-score. Moderate adherence was not independently associated with fewer total number of exacerbations compared to low adherence (IRR 0.81, 95% CI 0.43–1.54, $p = 0.525$). ACT adherence was not independently associated with severe exacerbations ($p = 0.253$). Higher BMI z-score at diagnosis was independently associated with lower odds of severe exacerbations (OR 0.52, 95% CI 0.32–0.85, $p = 0.009$). No other covariates were significantly associated with severe exacerbations.

Conclusions: High ACT adherence is independently associated with reduced total number of exacerbations in pediatric NCFB, highlighting the clinical importance of adherence optimization.

Conflict of interest The authors declare no conflicts of interest.

0153 Airway Clearance Technique of Oscillation and Lung Expansion in Bronchiectasis with exacerbation: a multicenter randomized controlled clinical trial

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DOI 10.1055/s-0046-1826168

Background/Aims: Airway clearance technique plays a vital role in bronchiectasis management. A novel technique, oscillation and lung Expansion (OLE), continuously delivers high-frequency oscillation and positive expiratory pressure. We aimed to assess the efficacy of OLE in bronchiectasis with exacerbation.

Methods: A multicenter randomized controlled trial was set up. Subjects with bronchiectasis and suffering a hospitalization due to exacerbation were recruited and randomly assigned to OLE and postural drainage (PD) group. The primary endpoint was length of stay, and secondary endpoints were 24-hour sputum volume, the change of bronchiectasis exacerbation and symptom tool (BEST), Bronchiectasis Health Questionnaire (BHQ), Quality of Life–Bronchiectasis (QOL-B) and Leicester Cough Questionnaire (LCQ). This trial is registered in ClinicalTrials.gov, NCT06393257.

Results: 99 subjects were enrolled in this study, 50 in OLE group and 49 in PD group. The length of stay in OLE group was significantly shorter than PD group (5.1 d vs 7.2 d, $P < 0.001$). The 24-hour sputum volumes of subjects in OLE group were significantly higher than that of subjects in PD group at the initial stage of trial. No significant difference was observed in change of BEST, BHQ, QOL-B and LCQ scores between two groups.

Conclusions: The OLE technique showed significant benefits in reducing the length of hospital stays and facilitating the airway clearance for exacerbated bronchiectasis patients, which might be widely applied to the management of stable bronchiectasis in the future.

Conflict of interest The authors declare no conflict of interests.

0154 Mechanical insufflator exsufflation as means for airway clearance in children with non CF- bronchiectasis – a case report

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DOI 10.1055/s-0046-1826169

Background/Aims: Children with Bronchiectasis are recommended to perform regular Airway clearance technique (ACT), yet no high-quality evidence demonstrates superiority for one technique/ device over the other. ERS guidelines emphasize a personalized approach both for the type and frequency of ACT.

Mechanical insufflation–exsufflation (MI-E), is an airway clearance modality that delivers positive pressure followed by rapid negative pressure to simulate a physiologic cough. It is widely used in neuromuscular disorders to improve secretion clearance and reduce pulmonary complications. However, its role in children with non-cystic fibrosis bronchiectasis remains less clearly defined. We present two paediatric patients, Y (3 years old) and M (9 years old), both with a confirmed diagnosis of non-CF bronchiectasis and a history of frequent pulmonary exacerbations. Prior to the intervention, both patients were treated with Positive Expiratory Pressure (PEP) therapy as part of their routine airway clearance regimen.

Due to ongoing frequent exacerbations, the pulmonary team elected to incorporate MI-E into their daily airway clearance protocol. To facilitate adaptation and ensure proper technique, each patient attended weekly outpatient sessions at the pulmonary institute for six consecutive weeks. During this period, both the patients and their caregivers were gradually trained in integrating MI-E into their home airway clearance routine.

Methods: This retrospective case analysis compared clinical data from the 12 months prior to initiation of MI-E with the first 12 months following its incorporation into the patients' airway clearance regimen.

A pulmonary exacerbation was defined as a clinical deterioration characterized by increased cough and/10% decline in FEV1 or increased sputum production, requiring antibiotic treatment as documented by the treating pulmonologist. Data were extracted from the electronic medical records and included the number of exacerbations, antibiotic use (oral and intravenous), and documented patient and caregiver remarks regarding pulmonary symptoms and perceived benefit of MI-E.

Results: In the 12 months preceding initiation of MI-E, M experienced 4 pulmonary exacerbations and Y experienced 3. During the first year following incorporation of MI-E into their airway clearance regimen, exacerbations decreased to 2 in M and 1 in Y. Similarly, antibiotic use declined in both patients. Each girl required 4 antibiotic courses in the year prior to MI-E, compared with 2 courses in M and 1 course in Y during the first year with MI-E. In M, sputum volume was objectively measured during outpatient treatment sessions. expectorated mucus volume was 15 mL with Positive Expiratory Pressure (PEP) alone, compared to 25 mL when MI-E was combined with PEP.

Subjective reports also reflected clinical improvement. M described easier airway clearance sessions, reduced coughing, and increased participation in dancing classes and training. Following home initiation of MI-E, Y's parents reported reduced coughing and improved sleep quality, which enabled the family to undertake an extended vacation.

Conclusions: MI-E showed clinical improvement for these girls with bronchiectasis, suggesting the potential role within individualized airway clearance regimens. Larger controlled trials are needed to better define its use, short- and long-term use.

Conflict of interest The authors have no conflict of interest to declare

0155 Effectiveness of mucolytic-assisted respiratory physiotherapy in optimizing airway clearance among patients with chronic bronchiectasis: A case report in Nairobi, Kenya.

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Background/Aims: Bronchiectasis is a chronic respiratory disease characterized by progressive structural lung damage, abnormal widening of the bronchi (1), chronic airway inflammation, chronic cough, mucus hypersecretion, impaired mucociliary clearance and recurrent pulmonary exacerbations (2). Treatment of bronchiectasis heavily depends on proper airway clearance techniques (ACT) and antibiotic therapy. (3)

The goals of ACTs are to improve symptoms, reduce bacterial load, and improve HRQOL by reducing mucus plugging and cough hyperreactivity (4)

Despite benefits of ACTs, access to this treatment in bronchiectasis is inadequate, with marked variation in clinical practice and inconsistent clinician recommendations for airway clearance techniques (5).

Aim Demonstrate the impact of combining mucolytic therapy with Respiratory PT led ACTs in a patient with bronchiectasis (► Table 1, 2).

► Table 1

Category	Mechanism	Intervention	Frequency
Mucolytics	Decrease mucous viscosity	N-acetylcysteine	600mg BD
Expectorants	Induce mucous expulsion through coughing	Hypertonic saline	3% BD
ACTs	Loosen and mobilize mucous	ACBT	5 breaths, 2 huffs BD
PEP	Generating airflow behind and push mucous upwards	Aerobika	BD, 3 resistances
Breathing retraining	Reduce hyperventilation	Diaphragmatic breathing	BD, AM and PM when in bed
Laryngeal hypersensitivity suppression	Reduce chronic cough	Sniff-puff techniques Sucking Ice/ boiled sweets Sipping water regularly	BD BD Regularly

► Table 2

Pre-intervention		Post-intervention
Ease of expectoration	Difficult	Improved
Mucous viscosity	Thick, sticky	Reduced
Mucous load	High	Reduced
Chest infection	Frequent	Non
HROL (QOL-B)	41	82

Methods:

Bronchiectasis and mucolytics (8)

Results:

Conclusions: ◊Mucolytic-assisted physiotherapy can reduce sputum viscosity and bacterial load

◊Combining mucolytic with ACTs and OPEP/PEP improves clearance and adherence

◊Individual care and patient education are essential in long-term management of Bronchiectasis

Conflict of interest None

0156 Real-World evidence of Simeox airway clearance device in Muco-Obstructive Lung Diseases: Results of the German Prospective Multicenter IMPROVE Study

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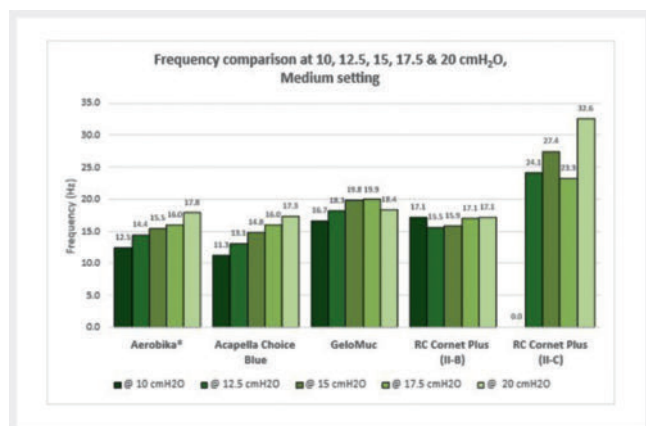
Background/Aims: Muco-obstructive lung diseases (MOLDs), including chronic obstructive pulmonary disease (COPD) and non-cystic fibrosis bronchiectasis (NCFB), are characterized by persistent mucus production, impaired airflow, and reduced quality of life (QoL). Although standard airway clearance techniques (ACTs) like nebulizers and positive expiratory pressure (PEP/oPEP) devices are commonly recommended, respiratory symptoms may persist. Simeox, a CE-marked medical device, aims to liquefy and mobilize bronchial mucus by generating intrapulmonary oscillatory vibrations during exhalation. This study collected real-world clinical data on Simeox use as an adjunct to standard ACTs in adult patients with stable MOLD.

Methods: IMPROVE was a national, multicenter, prospective, observational post-market clinical follow-up (PMCF) study conducted in Germany. Ethics approval was obtained at each site, and all patients provided written informed consent before participation. Clinically stable adults with MOLD, compliant for ≥ 3 months or intolerant to PEP/oPEP and nebulizers, were enrolled at the study site. After remote training by respiratory physiotherapists, patients used Simeox at home for 20 consecutive days (1–3 sessions/day) while continuing standard ACTs.

The primary endpoint was change from baseline in St. George's Respiratory Questionnaire (SGRQ) total score at Day 20. Secondary endpoints included SGRQ domain scores, COPD Assessment Test (CAT), modified Medical Research Council (mMRC) dyspnea scale, sputum-related outcomes, device adherence, usability, patient satisfaction, and safety. An SGRQ responder was defined as a ≥ 4-point decrease (MCID). Main analysis was conducted in the full analysis set (FAS). Data are presented as mean (SD).

Results: A total of 85 patients were included in the FAS (NCFB: 41; COPD: 31; others 13). Baseline characteristics: age 62.4 (11.7) years, BMI 25.4 (6.4), 62.4% female, FEV1% predicted 63.7 (25.5). Main comorbidities: 51% asthma, arterial hypertension 37%, 19% emphysema, GERD 13%, dyslipidemia 12%, diabetes 11%, chronic rhinosinusitis 11%. Treatments: 99% nebulizers, 93% PEP/oPEP, 77% SABA, 67% ICS/LABA, 60% LAMA, 46% SAMA, 44% ICS, 37% LABA. The ANCOVA-adjusted mean change in SGRQ total score was – 3.8 (SD 9.5; 95% CI – 5.8 to – 1.7; p = 0.0004) with a responder rate of 52.4% (COPD: 58.1%; NCFB: 47.5%). Improvements were greatest in the SGRQ Symptoms domain across the entire population (mean – 7.0, p < .0001) and for each subgroup. The mean change in CAT total score was – 3.1 (SD 6.4), p < .0001. Mean mMRC dyspnea score improved by – 0.4 (0.9), p < .0001. Most patients reported improvement in sputum clearance (91.7%) and chest congestion (83.5%). Compliance was high, with 90.6% of compliers. Usability was rated as “very appropriate” by 85.9% of participants, and more than 70% expressed an intention to continue Simeox therapy.

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► Fig. 2

The findings demonstrate that OPEP devices employing different mechanical designs may exhibit variability in laboratory-measured performance parameters under controlled conditions. These observations reflect differences in device mechanics and operating principles.

While these data highlight significant mechanical variability between OPEP designs, the clinical impact of these differences remains hypothetical. Further prospective clinical research is warranted to investigate whether the observed technical parameters correlate with enhanced secretion mobilization in specific patient populations.

Selection of an OPEP device should be based on multiple factors, including, the device's intended use, available clinical evidence, usability considerations, and patient preferences, in accordance with clinical judgment.

Conflicts of interest Sivagurunathan Sutharsan received personal fees or grants from Galapagos, Proteostasis Therapeutics, CeltaSys, Vertex Pharmaceuticals, Boehringer Ingelheim, Corbus Pharmaceuticals, Insmid Germany GmbH, Medical Trudell, and Ionis Pharmaceuticals outside the submitted work. Laboratory support was provided by Trudell Medical International.

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SESSION: TREATMENTS

0159 Real-World Outcomes of Nebulized Levofloxacin in Chronic Bronchial Infection and Non-Cystic Fibrosis Bronchiectasis: A Comparative Analysis from the INBREATHING Registry

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Background/Aims: Inhaled antibiotics(IAs) improve bacterial control in non-cystic fibrosis bronchiectasis (NCFB) with chronic bronchial infection(CBI). Nebulized levofloxacin(NL) has broad antibacterial activity, but real-world evidence in NCFB is scarce. This study compared the effectiveness, safety, and resistance profile of NL versus other IAs in CBI.

Methods: Retrospective sub-analysis of the multicenter INBREATHING registry including NCFB patients with CBI treated with IAs across 15 Spanish centers. Patients receiving NL(n = 81) were compared with those treated with other IAs(n = 285). Clinical, functional, microbiological data and adverse events were collected. Exacerbations and hospitalizations in the year before and at 6 and 12 months after treatment initiation were analyzed using appropriate paired and between-group statistical tests.

Results: Levofloxacin-treated patients were younger(68vs.73years) and more often female(66.7 %vs.51.2 %). *Pseudomonas aeruginosa* was the predominant pathogen in both groups. Levofloxacin was mainly used as second or third-line therapy. Levofloxacin significantly reduced exacerbations at 6 (2[1–3]vs.0[0–1];p<0.001) and 12 months compared with the prior year(p<0.001, **Figure 1**), as well as hospitalizations at 6 months (p = 0.001). Combined exacerbations and hospitalizations were significantly reduced at both time points(p<0.001). Effectiveness was comparable to other IAs(**Figure 1**). Intolerance was similar(19.8 %vs.20.4 %), while resistance development was lower with levofloxacin(10.9 % vs.24.7 %;p = 0.046).

Conclusions: In this large real-world cohort, NL was safe and effective, significantly reducing exacerbations and hospitalizations in NCFB patients with CBI, with a lower resistance rate than other IAs. These findings support its use as a valuable therapeutic option.

0160 Multi-Target Mechanisms of Kale as a Dietary Intervention in Bronchiectasis: A Network Pharmacology and Molecular Simulation Study

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Background/Aims: Bronchiectasis is a chronic airway disease characterized by persistent neutrophil-dominated inflammation, recurrent infection, and irreversible bronchial dilation. Current treatments primarily focus on symptom

control and infection management, with limited options targeting underlying inflammatory mechanisms. Kale, a nutrient-dense cruciferous vegetable, contains multiple bioactive compounds with known anti-inflammatory and antioxidant properties. However, its potential role in bronchiectasis remains unclear. This study aimed to investigate the potential mechanisms of kale in bronchiectasis from a dietary perspective using a network pharmacology approach combined with molecular simulation techniques.

Methods: Bioactive compounds of kale were identified through a systematic literature search of published studies, and their potential targets were predicted using SwissTargetPrediction and SuperPred platforms. Bronchiectasis-associated targets were collected from GeneCards, TTD, MalaCards, OMIM, GWAS Catalog, and Open Targets. The overlapping targets between kale and bronchiectasis were identified and used to construct a protein–protein interaction (PPI) network via STRING, which was visualized using Cytoscape. Key hub targets were screened based on topological analysis. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses were performed to identify the main biological processes and signaling pathways. Molecular docking was conducted to evaluate the binding affinities between key bioactive compounds and core targets. Furthermore, molecular dynamics simulations were performed to assess the stability of the ligand–target complexes.

Results: A total of 18 bioactive compounds and 263 predicted targets were identified for kale, along with 760 bronchiectasis-associated targets, yielding 38 overlapping targets. The protein–protein interaction (PPI) network analysis identified CXCR4, MMP2, and STAT1 as key hub targets, which are mainly involved in inflammatory signaling, extracellular matrix remodeling, and immune regulation. GO biological process enrichment analysis indicated that these overlapping targets were significantly associated with neutrophil activation, leukocyte migration, and responses to oxidative stress and bacterial stimuli. KEGG pathway analysis highlighted significant enrichment in neutrophil extracellular trap (NET) formation, chemokine signaling pathway, HIF-1 signaling pathway as central mechanisms. Among the selected representative compounds, molecular docking analysis was performed between key bioactive compounds and core targets. The results showed that 5-caffeoylquinic acid exhibited favorable binding affinity with STAT1 (–7.6 kcal/mol), while kaempferol demonstrated strong binding to CXCR4 (–7.8 kcal/mol). In addition, both quercetin and caffeic acid showed stable binding interactions with MMP2 (–7.9 and –6.6 kcal/mol, respectively). Molecular dynamics simulations further supported the reliability of the molecular docking results, suggesting stable interactions between the key bioactive compounds and core targets.

Conclusions: This study systematically revealed that kale may exert beneficial effects in bronchiectasis through multi-component, multi-target, and multi-pathway mechanisms, particularly involving neutrophil-driven inflammation, chemokine signaling, and oxidative stress pathways. These findings highlight the potential role of kale as a complementary dietary strategy in bronchiectasis management. However, further experimental and clinical studies are required to validate these findings.

Conflict of interest The authors declare that they have no competing interests.

0161 Impact of inhaled corticosteroids on survival in patients with bronchiectasis

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Background/Aims: The use of inhaled corticosteroids (ICS) in patients with bronchiectasis remains controversial, as some studies suggest a potential link to increased morbidity and mortality. This study evaluated the association between ICS use and mortality risk in patients with bronchiectasis, identifying susceptible subgroups and optimal cumulative doses.

Methods: This nationwide cohort study utilized the Korean National Health Insurance Service-National Sample Cohort (NHIS-NSC) database (2002–2019). Eligible participants were patients with bronchiectasis who received at least two respiratory inhaler prescriptions per year. Time-dependent Cox regression models were employed to assess the association between ICS exposure and survival. ICS exposure was defined by three metrics: usage status (users vs. non-users), cumulative dose (continuous), and cumulative dose tertiles.

Results: Among 2,279 patients, 520 (23 %) died during a mean follow-up of 5.4 years. In the total population, ICS use, cumulative dose, and dose tertiles showed no significant association with mortality. However, subgroup analyses revealed a significantly lower mortality risk among female ICS users compared to non-users [adjusted hazard ratio (aHR) 0.68; 95 % confidence interval (CI) 0.50–0.92]. In this subgroup, both higher cumulative dose (aHR 0.96; 95 % CI 0.93–0.99) and the highest dose tertile (aHR 0.61; 95 % CI 0.39–0.96) were associated with improved survival. Among patients with comorbid asthma, ICS users had a lower mortality risk than non-users (aHR 0.81; 95 % CI 0.67–0.99), though no dose-response relationship was observed. Similarly, in patients with comorbid coronary heart disease, ICS use (aHR 0.70; 95 % CI 0.52–0.93) and higher cumulative doses (aHR 0.97; 95 % CI 0.94–0.99) were associated with reduced mortality; specifically, the middle tertile showed a lower risk (aHR 0.62; 95 % CI 0.42–0.92) compared to the lowest tertile, while the highest tertile did not reach significance.

Conclusions: ICS use was not associated with increased all-cause mortality in patients with bronchiectasis. Our findings suggest that ICS may improve survival in specific subgroups, including female patients and those with comorbid asthma or coronary heart disease. Identifying optimal indications for ICS will facilitate personalized therapeutic strategies for bronchiectasis.

Conflict of interest This work was supported by the National Research Foundation of Korea (NRF2020R1A5A2019210).

0162 Incidence, Timing, and Risk Factors for Hepatotoxicity During First-Line Anti-Tuberculosis Therapy in a Multi-Health-System Real-World Cohort

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Background Anti-tuberculosis drug-induced liver injury (DILI) is a leading cause of treatment interruption and adverse outcomes during first-line therapy with isoniazid, rifampin, pyrazinamide, and ethambutol. Reported incidence varies widely (3–16 %), reflecting differences in study populations, monitoring protocols, and DILI definitions. Contemporary, large-scale, multi-center estimates derived from real-world electronic health record (EHR) data remain scarce. We aimed to establish a well-characterized retrospective cohort to evaluate the incidence, timing, and risk factors for hepatotoxicity during standard anti-tuberculosis therapy.

Methods Using the TriNetX Global Collaborative Network, we constructed a retrospective cohort of adults (≥ 18 years) with ICD-10-coded active tuberculosis (A15–A19) who received standard first-line therapy across 127 healthcare organizations, yielding 20,334 patients. An analytic hepatotoxicity cohort was defined by requiring ALT/AST measurements and/or ICD-10 codes for abnormal liver function or inflammatory liver disease (K75, R94.5), resulting in 17,191 patients from 116 organizations (mean age 62 years). Liver enzyme data completeness was high: ALT and AST were available for 99 % and 98 % of patients, respectively, total bilirubin for 94 %, and albumin for 81 %. Among these, 3,577 patients (20.8 %) had documented pre-existing chronic liver disease or viral hepatitis. Using this licensed de-identified dataset, we will construct longitudinal medication and laboratory timelines, apply consensus DILI criteria based on ALT/AST elevations relative to upper limits of normal, and evaluate incidence, time to onset, and risk factors using multivariable regression models adjusting for age, sex, baseline liver disease, and concomitant hepatotoxic medications.

This study uses de-identified data and was determined exempt by the UC Irvine Institutional Review Board.

Results Of 20,334 adults receiving first-line anti-tuberculosis therapy, 17,191 (84.5%) met criteria for the analytic hepatotoxicity cohort based on available liver enzyme monitoring and/or liver-related diagnostic codes. This high capture rate across 116 healthcare organizations confirms the feasibility of leveraging routinely collected EHR data for rigorous DILI assessment. The cohort spans diverse geographic regions and practice settings, providing a large, heterogeneous population well-suited to estimate real-world hepatotoxicity incidence. The substantial proportion with pre-existing liver disease (20.8%) will enable subgroup analysis of this high-risk population. Planned analyses will apply standardized DILI thresholds to characterize incidence, time to onset from treatment initiation, and independent risk factors for hepatotoxicity.

Conclusions This multi-center real-world cohort of over 17,000 patients with high laboratory data completeness establishes a robust platform for estimating the incidence, timing, and risk profiles of anti-tuberculosis DILI from routinely collected EHR data. The scale and diversity of this cohort address key limitations of prior single-center studies. Planned analyses will refine contemporary risk estimates and may inform liver enzyme monitoring strategies and regimen selection for patients initiating treatment for active tuberculosis.

Disclosures The authors report no conflicts of interest. No commercial funding was received for this study.

0163 Inhaled Tranexamic Acid Dosing and Environmental Medication Loss From Three Jet Nebulizer Configurations

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Background/Aims: Nebulized tranexamic acid (TXA) has shown clinical benefit when used to control hemoptysis in bronchiectasis. However, the delivered dose available for pulmonary deposition during nebulization remains incompletely characterized between different types of nebulizers. Constant Output (CO) and standard jet (SJ) nebulizers generate aerosol throughout the respiratory cycle, resulting in variability and inefficiencies in lung delivery. In addition, aerosol produced during exhalation contributes to fugitive emissions of medication creating potential secondary exposure for nearby individuals. Breath Actuated (BA) nebulizers only release medication on inhalation greatly mitigating excess environmental loss and decreasing variable delivery. To date, neither the respirable dose profile nor the magnitude of environmental TXA loss has

been quantified. This bench study aimed to characterize respirable output and fugitive emissions as environmental aerosol loss during nebulized TXA administration to better define dosing efficiency and occupational safety considerations in bronchiectasis management.

Methods: The AirLife† Misty Max 10 and two configurations of the AeroEclipse® II BAN® Nebulizers were evaluated (n = 5 each): (1) breath-actuated mode (BA) and (2) continuous mode (CM) with filter kit. Each device was filled with 5 mL total volume consisting of 2.5 mL TXA (1000 mg/10 mL) and 2.5 mL NS (nominal dose (ND) 2500 mg TXA). The nebulizer was connected to a breathing simulator (ASL 5000, IngMar Medical) configured at 10 breaths/min, tidal volume 500 mL, and a 1:2 I:E ratio. All nebulizers were run at 7.3–8.0 L/min at 50 psi. Emitted aerosols were captured on an inhalation filter at 1-minute intervals until sputter to determine delivered mass. TXA quantification was performed using validated HPLC-UV spectrophotometry. Fine droplet mass ($FDM_{<4.7\mu m}$) was calculated as the product of total emitted mass and fine droplet fraction measured by laser diffractometry. Environmental loss was calculated as ND minus recovered inhaled mass and residual mass recovered from the nebulizer post run.

Results: BA mode on the AeroEclipse® II BAN® Nebulizer had a mean $FDM_{<4.7\mu m}$ of 99.1 ± 5.7 mg, a mean treatment time of 16 min 50 sec, and a calculated environmental loss (EL) of 16.5 ± 12.0 mg (6.6%).

AeroEclipse® II BAN® Nebulizer with a filter kit (CN) reduced the mean treatment time to 6 min 58 sec and increased mean $FDM_{<4.7\mu m}$ to 131.3 ± 8.9 mg. EL was minimal 1.8 ± 4.0 mg (0.7%).

The AirLife† Misty Max 10 (CO/SJ) demonstrated lower delivery efficiency with mean $FDM_{<4.7\mu m}$ of 31.1 ± 2.8 mg and a mean treatment time of 8 min 36 sec. Calculated EL was substantially higher at 91.1 ± 10.2 mg (36.4%).

Conclusions: Nebulizer selection significantly altered TXA delivery efficiency, respirable mass dose, and environmental loss. Continuous filtered delivery produced the highest respirable mass with minimal fugitive, whereas use of a CO standard jet nebulizer resulted in substantial environmental loss exceeding one-third of the nominal dose. Device selection substantially influences both therapeutic delivery and potential second-hand exposure during off-label TXA nebulization, with important implications for treatment environments and occupational safety.

Conflict of interest Judy Schloss and Dominic Coppolo are employees of Monaghan Medical Corporation. Jason Suggett is and employee of Trudell Medical International and Jolyon Mitchell is a consultant for Trudell Medical International.

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