Ulster Med J 2025;**94(1):**28-30

Short Communication

Clinical Trials involving *Mycobacterium abscessus*: An update

J E. Moore and B C. Millar

Mycobacterium abscessus (*M. abscessus*) has now emerged as a significant bacterial pathogen in human infection, particularly in pulmonary disease, including in those with cystic fibrosis (CF)[1,2]. Several recent (2022-2023) reviews successfully describe (i) treatment options, including drug discovery[3-7] and (ii) pathogenesis of *M. abscessus*-related disease[1,8-11]. Due to its pathogenesis in disease, accompanied by its resistance to antibiotics and biocides used to disinfect healthcare facilities[12], as described in the above reviews, this makes *M. abscessus* a formidable challenge in terms of infection prevention and control, as well as with its antibiotic treatment and clinical management. Whilst there are numerous anti-*M. abscessus* approaches, strategies and innovations that have been proposed academically, as previously described[13], few of these will ever progress to being adopted as a clinically effective licenced treatment modality against this organism. Healthcare professionals therefore wish to learn about potential treatment options that are currently in the clinical trials pipeline, which could serve as new clinical interventions, as well as to inform their patients, about possibilities of becoming involved, if eligible. This review aims to highlight and briefly describe what trials involving *M. abscessus* are currently under examination in registered clinical trials globally.

The US National Library of Medicine Clinical Trials register[14] and the EU Clinical Trials register[15] were examined, using the key term "*Mycobacterium abscessus*". The US database returned 22 trials and the EU database returned 1 trial. These are listed in Table 1. Given that the sole EU listed trial had the same title as that in the US database, this was treated as a duplicate trial in two databases. Of these, 9 were observational and 13 were interventional.

Several of the observational studies examine patient registry data, optimisation of existing antibiotic interventions, genomic data and pharmacological PK/PD data. The interventional studies wish to explore novel interventions including nitric oxide, as well as anti-infectives including omadacycline, gallium, azithromycin, tigecycline, delpazolid, clofazamine, amikacin. What is currently missing from this list are interventional studies involving bacteriophage therapy, as is the case with *Pseudomonas aeruginosa* and cystic fibrosis.

More recently in May 2024, a case-control observational trial was initiated which hopes to identify new biological markers by characterizing the response/inflammation associated with the development and progression of *M. abscessus* lung disease in patients suffering from cystic fibrosis with the aim of increasing current knowledge available on the development and progression of lung disease [NCT06413459].

Readers can access current up-to-date information on each of the clinical trials listed, by accessing this via its assigned clinical trial number at clinicaltrials.gov.

Keywords: *Mycobacterium abscessus*, clinical trial, nitric oxide, antimicrobial resistance, cystic fibrosis, pulmonary disease.

Ethics Statement

Ethical approval was not required as no research was performed on any human or animal subject.

Author Contributions

CRediT authorship contribution statement:
John E Moore: Conceptualization; Formal analysis; Methodology; Roles/Writing - original draft; Writing - review & editing
Beverley C. Millar: Conceptualization; Formal analysis; Methodology; Roles/Writing - original draft; Writing - review & editing

Disclosure of Conflict of Interest

John E. Moore: None to declare
Beverley Cherie Millar: None to declare
The authors declare that the research was conducted in the absence of any commercial, financial or other relationships that could be construed as a potential conflict of interest.

Funding

This study was supported by internal funding.

J E. Moore and B C. Millar
Northern Ireland Public Health Laboratory,
Department of Bacteriology, Belfast City Hospital,
Belfast, BT9 7AD, Northern Ireland
School of Medicine, Dentistry and Biomedical Sciences,
The Wellcome-Wolfson Institute for Experimental Medicine,
Queen's University, Belfast, BT9 7BL, Northern Ireland
School of Biomedical Sciences, Ulster University,
Coleraine, BT52 1SA, Northern Ireland
Northern Ireland Regional Adult Cystic Fibrosis Centre,
Belfast City Hospital, Belfast, BT9 7AB, Northern Ireland

Professor John E. Moore,
Northern Ireland Public Health Laboratory,
Belfast City Hospital,
Lisburn Road,
Belfast, BT9 7AD,
Northern Ireland,
United Kingdom.

***Corresponding author:** Professor John E. Moore
E-mail: jemoore@niphl.dnet.co.uk

Table 1: Current clinical trials targeting Mycobacterium abscessus (n=22)
(Source: ClinicalTrials.gov)

NCT01354912	The Incidence of Nontuberculous Mycobacterial Pulmonary Infection in Bilateral Bronchiectasis and Bronchiolitis	Bronchiectasis; Bronchiolitis	OBSERVATIONAL:
NCT03597347	Trial of Inhaled Molgramostim in Cystic Fibrosis Subjects With Nontuberculous Mycobacterial Infection	Mycobacterium Infections, Nontuberculous Cystic Fibrosis (CF)	INTERVENTIONAL: DRUG: Molgramostim nebulizer solution: DEVICE: PARI eFlow nebulizer system.
NCT03339063	The Italian Registry of Pulmonary Nontuberculous mycobacteria	Nontuberculous Mycobacteria	OBSERVATIONAL:
NCT04310930	Finding the Optimal Regimen for Mycobacterium abscessus Treatment	Pulmonary Disease Due to Mycobacteria (Diagnosis)	INTERVENTIONAL: DRUG: Amikacin, Tigecycline, Imipenem, Cefoxitin, Azithromycin, Clarithromycin, Clofazimine, Ethambutol, Amikacin, Linezolid, co-trimoxazole, Doxycycline, Moxifloxacin, Bedaquiline, Rifabutin.
NCT04685720	A Pilot Study to Assess the Effect of Intermittent iNO on the Treatment of NTM Lung Infection in CF and Non-CF Patients	Non-Tuberculous Mycobacterial Pneumonia; Cystic Fibrosis; Mycobacterial Pneumonia; Mycobacterium abscessus Infection; Mycobacterium avium Complex	INTERVENTIONAL: DEVICE: LungFit
NCT05101915	Study of a Nebulised Nitric Oxide Generating Solution in Patients With Mycobacterium abscessus	Cystic Fibrosis	INTERVENTIONAL: DRUG: RESP301.
NCT04922554	Oral Omadacycline vs. Placebo in Adults With NTM Pulmonary Disease Caused by Mycobacterium abscessus Complex (MABc)	Mycobacterium Infections, Nontuberculous;Mycobacterium abscessus Infection; Nontuberculous Mycobacterial Lung Disease; Nontuberculous Mycobacterial Pulmonary Infection	INTERVENTIONAL: DRUG: Omadacycline Oral Tablet; DRUG: Placebo.
NCT04294043	IV Gallium Study for Patients With Cystic Fibrosis Who Have NTM (ABATE Study)	Nontuberculous Mycobacterium Infection	INTERVENTIONAL: DRUG: Gallium nitrate.
NCT00599079	Azithromycin in the Treatment of M. avium Complex Lung Disease	Mycobacterium avium Complex Lung Disease	INTERVENTIONAL: DRUG: Azithromycin.
NCT00600600	Tigecycline for Treatment of Rapidly Growing Mycobacteria	Mycobacterium abscessus Lung Disease;Rapidly Growing Mycobacterial Lung Disease	INTERVENTIONAL: DRUG: Tigecycline.
NCT02832843	Genome-Wide Association Study in Patients With Nontuberculous Mycobacterial Lung Disease	Mycobacterium Infections, Nontuberculous	OBSERVATIONAL:
NCT06004037	Study to Evaluate the Efficacy of Delpazolid as Add-on Therapy in Refractory Mycobacterium abscessus Complex	Nontuberculous Mycobacterium Infection; Mycobacterium abscessus Infection	INTERVENTIONAL: DRUG: Delpazolid.
NCT05354583	Treatment Outcome Between Mycobacterium abscessus Infection in Chronic Lung Disease and Acquired Interferon-gamma Autoantibody Syndrome	Mycobacterium abscessus Infection; Adult-Onset Immunodeficiency With Acquired Anti-Interferon-Gamma Autoantibodies; Nontuberculous Mycobacterial Pulmonary Infection	OBSERVATIONAL: DRUG: Appropriate treatment.
NCT05676138	PK and PD of Antibiotics for Treatment of Mycobacterium Abscessus Pulmonary Disease	Nontuberculous Mycobacterial Pulmonary Infection	OBSERVATIONAL: I
NCT05294146	Pharmacokinetic Study With a Loading Dose of Clofazimine in Adult Patients With Nontuberculous Mycobacterial Disease	Nontuberculous Mycobacterial Diseases	INTERVENTIONAL: DRUG: Clofazimine.

NCT01528930	Inhaled Amikacin Treatment for Nontuberculous Mycobacterial Lung Disease	Pulmonary Non-tuberculous Mycobacterial Lung Disease	INTERVENTIONAL: DRUG: Amikacin.
NCT03208764	Inhaled Nitric Oxide for Patients With MABSC	Mycobacterium abscessus Infection	INTERVENTIONAL: DRUG: Nitric Oxide.
NCT02005094	The Role of Inflammasome in Inflammatory Macrophage in Mycobacterium avium Complex-lung Disease and Mycobacterium abscessus-lung Disease		OBSERVATIONAL:
NCT04024423	Healthcare-associated Links in Transmission of Nontuberculous Mycobacteria in Cystic Fibrosis	Cystic Fibrosis;Nontuberculous Mycobacterium Infection	OBSERVATIONAL:
NCT03038178	Liposomal Amikacin for Inhalation (LAI) in the Treatment of Mycobacterium abscessus Lung Disease	Mycobacterium Infections, Nontuberculous;Mycobacteria, Atypical	INTERVENTIONAL: DRUG: LAI plus multi-drug regimen.
NCT04163601	Liposomal Amikacin Inhalation in M. abscessus Patients	M.abscessus Pulmonary Disease	OBSERVATIONAL:
NCT00018044	Study of Mycobacterial Infections	Mycobacterium Infections	OBSERVATIONAL:

REFERENCES

1. López-Roa P, Esteban J; Muñoz-Egea MC. Updated review on the mechanisms of pathogenicity in *Mycobacterium abscessus*, a rapidly growing emerging pathogen. *Microorganisms*. 2022;11:90. doi: 10.3390/microorganisms11010090.
2. Johansen MD, Herrmann JL, Kremer L. Non-tuberculous mycobacteria and the rise of *Mycobacterium abscessus*. *Nat Rev Microbiol*. 2020;18:392-407. doi: 10.1038/s41579-020-0331-1.
3. Andersson V, Fröberg G, Dahl VN, Chryssanthou E, Giske C, *et al*. The *in vitro* activity of carbapenems alone and in combination with β-lactamase inhibitors against difficult-to-treat mycobacteria; *Mycobacterium tuberculosis*, *Mycobacterium abscessus*, and *Mycobacterium avium* complex: A systematic review. *Int J Mycobacteriol*. 2023;12(3):211-25.
4. Alcaraz M, Edwards TE, Kremer L. New therapeutic strategies for *Mycobacterium abscessus* pulmonary diseases - untapping the mycolic acid pathway. *Expert Rev Anti Infect Ther*. 2023;21(8): 813-29.
5. Ganapathy US, Dick T. Why matter matters: Fast-tracking *Mycobacterium abscessus* drug discovery. *Molecules*. 2022;27(20): 6948.
6. Broncano-Lavado A, Senhaji-Kacha A, Santamaría-Corral G, Esteban J, García-Quintanilla M. Alternatives to antibiotics against *Mycobacterium abscessus*. *Antibiotics* (Basel). 2022; 11(10): 1322. doi: 10.3390/antibiotics11101322.
7. Recchia D, Stelitano G, Stamilla A, Gutierrez DL, Degiacomi G, Chiarelli LR, *et al*. *Mycobacterium abscessus* infections in cystic fibrosis individuals: A review on therapeutic options. *Int J Mol Sci*. 2023;24(5):4635. doi: 10.3390/ijms24054635.
8. Lagune M, Kremer L, Herrmann JL. *Mycobacterium abscessus*, a complex of three fast-growing subspecies sharing virulence traits with slow-growing mycobacteria. *Clin Microbiol Infect*. 2024:30(6):726-31. Epub 2023 Oct 4..
9. Parmar S, Tocheva EI. The cell envelope of *Mycobacterium abscessus* and its role in pathogenesis. *PLoS Pathog* 2023;19(5):e1011318. doi: 10.1371/journal.ppat.1011318.
10. Bar-Oz M, Meir M, Barkan D. Virulence-associated secretion in *Mycobacterium abscessus*. *Front Immunol*. 2022;13:938895. doi: 10.3389/fimmu.2022.938895.
11. Ferrell KC, Johansen MD, Triccas JA, Counoupas C. Virulence mechanisms of *Mycobacterium abscessus*: Current knowledge and implications for vaccine design. *Front Microbiol*. 2022:13:842017. doi: 10.3389/fmicb.2022.842017.
12. Caskey S, Moore JE, Rendall JC. *In vitro* activity of seven hospital biocides against *Mycobacterium abscessus*: Implications for patients with cystic fibrosis. *Int J Mycobacteriol*. 2018;7(1): 45-7. doi: 10.4103/ijmy.ijmy_197_17.
13. Millar BC, Moore JE. Antimycobacterial strategies to evade antimicrobial resistance in the nontuberculous mycobacteria. *Int Mycobacteriol*. 2019; 8(1):7-21.
14. National Library of Medicine. ClinicalTrials.gov: a place to learn about clinical studies frm around the world. [Internet]. Bethesda: National Library of Medicine. [cited 2025 Jan 9]. Available from: www.clinicaltrials.gov
15. EU Clinical Trials Register: contains information on interventional clinical trials on medicines conducted in the European Union(EU), or the European Economic Area (EEA) which started after 1 May 2004. [Internet]. Amsterdam, The Netherlands. [cited 2025 Jan 9]. Available from: www.clinicaltrialsregister.eu.