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Finding the best treatment for lung disease from infection with Mycobacterium abscessus

Submission date 26/10/2024	**Recruitment status** Recruiting	[_] Prospectively registered [X] Protocol [X] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 09/01/2025	**Overall study status** Ongoing	
Last Edited 08/09/2026	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims
Mycobacterium abscessus (MABS) are a group of rapid-growing, multi-drug resistant non-tuberculous mycobacteria (NTM) causing infections in humans, often chest infections. People who have underlying lung conditions such as cystic fibrosis (CF) or bronchiectasis are more likely to get MABS chest infection. The number of people who get MABS chest infections is small, but these infections are becoming more common. Some MABS chest infections can be cleared without treatment whereas other MABS chest infections can result in long-term MABS lung disease significantly impacting the person's quality of life. Currently, there are no guidelines for when to start treating MABS chest infections and the treatment regimens used can be administered for up to 2 years, but are often associated with significant side-effects. The aim of this study is to find out which combination of medications best treat Mycobacterium abscessus (MABS) chest infections. Initially, the study will evaluate the standard medications prescribed to treat MABS lung disease as these standard medications have not been properly tested for treating this disease. The researchers can also add new treatment groups and remove any treatment groups deemed ineffective. The data is analysed while the study is ongoing and these results can be used to change the trial design in real time. This means that the researchers can quickly identify effective treatment arms and potentially allocate more people to the successful treatments.

Who can participate?
1. Intervention Group: Patients who require medications to get rid of their MABS lung disease.
2. Observation Group: Patients who have not met the criteria to treat MABS lung disease infection or have chosen not to take the medications.

What does the study involve?
There are two phases of treatment for MABS: intensive therapy (IT) followed by consolidation therapy (CT). The initial interventional programme is randomised and open label. There are three stages of randomisation:
1. Randomisation to Short Intensive therapy (SI): At the start of the intensive phase, participants are randomised between one of three different intensive Arms A, B or C.
Arm A. Intravenous (IV) amikacin, IV tigecycline, IV cefoxitin OR imipenem PLUS oral azithromycin OR oral clarithromycin AND oral clofazimine.

Arm B. Inhaled amikacin (IA), IV tigecycline, IV cefoxitin OR imipenem PLUS oral azithromycin OR oral clarithromycin AND oral clofazimine.
Arm C. IV amikacin, IV tigecycline, IV cefoxitin OR imipenem PLUS oral azithromycin OR oral clarithromycin.
2. Randomisation to Prolonged Intensive or Immediate Consolidation (PI/IC): The second randomisation will ONLY be for participants who are still MABS positive at the end of short intensive therapy (based on respiratory sampling collected at 4 weeks) and are able to continue with intensive therapy. Randomisation will occur at the end of short intensive therapy and will allocate participants to either: Continue intensive therapy which will be followed by consolidation (participants remain on the same intensive therapy drug regimen if randomised to prolonged intensive therapy), OR immediately commence consolidation therapy.
3. Randomisation to Consolidation: This randomisation will allocate participants to the consolidation therapy arms a or b for 46 weeks.
Arm a. Oral clofazimine PLUS oral azithromycin OR oral clarithromycin in combination with one to three of the following oral antibiotics: oral linezolid, oral co-trimoxazole, oral doxycycline, oral moxifloxacin, oral bedaquiline (adults only), oral rifabutin.
Arm b. Inhaled amikacin (IA) AND oral clofazimine AND oral azithromycin OR oral clarithromycin in combination with one to three of the following oral antibiotics: oral linezolid, oral co-trimoxazole, oral doxycycline, oral moxifloxacin, oral bedaquiline (adults only), oral rifabutin.
Oral ethambutol can be added to any of the treatment arms if participants have mixed infection with slow-growing NTM.

What are the possible benefits and risks of participating?
We cannot promise the study will help you but the information we get from this study may help us learn more about the development, diagnosis and treatment of MABS lung disease in children and adults.
If a patient decides to participate in this study, they will have medical procedures and tests performed that may cause side effects. Participants may have none, some or all of the effects listed in the Participant information sheets, and they may be mild, moderate or severe. Participants are advised to speak to their study doctor if they notice any side effects or are worried about anything. The study doctor will also be routinely monitoring for side effects. There may be side effects that the study team do not expect or do not know about and that may be serious. Participants are advised to tell their study doctor or study team immediately about any new or unusual symptoms. If a severe side effect or reaction occurs, the study team may need to stop study treatments or procedures and the participant may not be able to continue in the study. If side effects occur the study team will advise the participant on the best way of managing these.
This research study involves exposure to a small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The dose from this study is comparable to that received from many diagnostic medical x-ray and nuclear medicines procedures. At this dose level, no harmful effects of radiation have been demonstrated as any effect is too small to measure. Therefore, the risk is believed to be low.
Treating MABS lung disease requires a complex mix of drugs. A list of the most common known side effects reported from the treatments is provided in the participant information sheets. These side effects are called common because between 1 in 10 people (10%) and 1 in 100 (1%) people reported these effects. Participants may find some of the side effects quite upsetting. Unfortunately, MABS lung disease treatment can be unpleasant and involves risk. The participant's treating doctor and study team will be monitoring participants' health very closely while they are on treatment. The unpleasant side effects of MABS treatment are well recognised and are the reason why we are doing this research; to provide patients with a better chance of treating the MABS infection while reducing the side effects. The side effects may go away

shortly after treatment ends. However, sometimes side effects can be serious, long-lasting or permanent. The study doctor will advise the participant on the best way of managing any side effects.
The effects of treatments used for MABS lung disease on the unborn child and the newborn baby are not known. Because of this, it is important that participants are not pregnant or breastfeeding and do not become pregnant during the course of the research project. Patients must not participate in the research if they are pregnant, trying to become pregnant, or breastfeeding. If the participant is female and childbearing is a possibility, they will be required to undergo a pregnancy test before commencing and during the study if they are receiving study drugs. Male participants are advised not to father or donate sperm while they are on study drugs and for at least 3 months after the last dose of study medication. Both male and female participants are strongly advised to use effective contraception during the course of the research and for a period of 3 months after completion of the research.

Where is the study run from?
Nottingham University Hospitals NHS Trust (UK)

When is the study starting and how long is it expected to run for?
January 2019 to December 2026

Who is funding the study?
University of Queensland (Australia)

Who is the main contact?

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04310930

Clinical Trials Information System (CTIS)

2020-000050-10

Integrated Research Application System (IRAS)
1007146

Central Portfolio Management System (CPMS)
61990

Protocol serial number
FORMaT001

Study information

Scientific Title
A multi-centre, randomised, multi-arm, adaptive platform trial in people with or without cystic fibrosis Finding the Optimal Regimen for Mycobacterium abscessus Treatment (FORMaT)

Acronym
FORMaT

Study objectives
Current study hypothesis as of 11/06/2025:

A1: To determine the probability of microbiological clearance with acceptable toxicity for treatment combinations tested inclusive of both intensive and consolidation phases for patients with MABS-PD.
Nested study A1.1: SHORT INTENSIVE THERAPY Compare the efficacy of intensive therapies on clearance of MABS with tolerance at 6 weeks.
Nested study A1.1.1. SHORT INTENSIVE THERAPY Compare clearance of MABS with tolerance with the use of inhaled amikacin and the use of intravenous amikacin.
A1.1.2 SHORT INTENSIVE THERAPY Compare clearance of MABS with tolerance between standard intravenous therapies given with and without clofazimine.
A1.2: DURATION OF INTENSIVE THERAPY FOR PATIENTS WITH POSITIVE MABS CULTURES AFTER 4 WEEKS OF INTENSIVE: Compare clearance with tolerance at 10 weeks between those allocated to prolonged intensive therapy and to immediate consolidation following short intensive.
A1.3: CONSOLIDATION THERAPY Compare clearance with tolerance of MABS of consolidation therapy of those allocated to oral only and those allocated to oral therapy plus inhaled amikacin.

1. To examine the probability of microbiological clearance at Final Outcome (irrespective of toxicity) for participants according to treatment path.
2. To describe the safety of the treatment combinations in patients with MABS.
3. To examine the change in Forced Expiratory Volume in one second (FEV1) z-score at Final Outcome compared with Screening in patients who do and who do not clear MABS at Final Outcome.
4. To phenotype the structural abnormalities of chest Computed Tomography (CT)s of MABS patients and examine changes in chest CT scores (bronchiectasis, trapped air, % disease) between Screening and Final Outcome between those who clear and those who do not clear MABS at Final Outcome.
5. To examine the predictive value of structural abnormalities on Screening CTs for sputum conversion and for progression of structural changes in relation to therapy.

6. To examine change in 6MWD for adult participants from Screening to Final Outcome according to treatment pathway and in participants who do and do not clear MABS at Final Outcome.
7. To examine the change in Health-Related Quality of Life (HRQoL) for participants with CF (using the Cystic Fibrosis Questionnaire-Revised (CFQ-R)) at Final Outcome compared with Screening according to treatment path and in those that do and those that do not clear MABS at Final Outcome.
8. To examine general HRQoL at Final Outcome compared with Screening according to treatment path and in those who do and who do not clear MABS at Final Outcome.
9. To examine the cost effectiveness of the proposed treatment combinations across both intensive and consolidation phases of the trial.
10. To examine causes for early withdrawal from MABS-PD treatment due to reasons other than poor tolerance as defined in the primary objectives.

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Previous study hypothesis:

E.2.1: To determine the probability of microbiological clearance with acceptable toxicity for treatment combinations tested inclusive of both intensive and consolidation phases for patients with MABS-PD.
A1.1: SHORT INTENSIVE THERAPY Compare the efficacy of intensive therapies on clearance of MABS with tolerance at 6 weeks.
A1.1.1. Compare clearance of MABS with tolerance with the use of inhaled amikacin and the use of intravenous amikacin.
A1.1.2 Compare clearance of MABS with tolerance between standard intravenous therapies given with and without clofazimine.
A1.2: DURATION OF INTENSIVE THERAPY FOR PATIENTS WITH POSITIVE MABS CULTURES AFTER 4 WEEKS OF INTENSIVE: Compare clearance with tolerance at 10 weeks between those allocated to prolonged intensive therapy and to consolidation following short intensive.
A1.3: CONSOLIDATION THERAPY Compare clearance with tolerance of MABS of consolidation therapy of those allocated to oral only and those allocated to oral therapy plus inhaled amikacin.

1. The probability of microbiological clearance of MABS irrespective of toxicity for participants according to treatment path.
2. The safety of the treatment combinations in patients with MABS.
3. The relative change in FEV1 z-score between treatment groups.
4. Change in % Bronchiectasis scored using PRAGMA in chest CTs between Day 0 (screening) and at 12 weeks and at final outcome and between those who clear and those who do not clear MABS.
5. Change in % Air Trapping scored using PRAGMA in chest CTs between Day 0 (screening) and at 12 weeks and at final outcome and between those who clear and those who do not clear MABS.
6. Change in % Disease scored using PRAGMA in chest CTs between Day 0 (screening) and at 12 weeks and at final outcome and between those who clear and those who do not clear MABS.
7. The predictive value of structural abnormalities at Day 0 (screening) CTs for sputum conversion and for progression of structural changes in relation to therapy.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 14/01/2025, London - Brighton & Sussex Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8140; brightonandsussex.rec@hra.nhs.uk), ref: 24/LO/0838

Primary study design
Interventional

Study design
Adaptive platform trial - Interventional randomized parallel-group controlled trial

Study type(s)
Diagnostic, Efficacy, Quality of life, Safety, Treatment, Other

Health condition(s) or problem(s) studied
Mycobacterium abscessus pulmonary disease

Interventions
There are two phases of treatment for Mycobacterium abscessus (MABS): intensive therapy (IT) followed by consolidation therapy (CT). The initial interventional programme is randomised and open label. There are three stages of randomisation:
1. Randomisation to Short Intensive therapy (SI): At the start of the intensive phase, participants are randomised between one of three different intensive Arms A, B or C.
Arm A. Intravenous (IV) amikacin, IV tigecycline, IV cefoxitin OR imipenem PLUS oral azithromycin OR oral clarithromycin AND oral clofazimine.
Arm B. Inhaled amikacin (IA), IV tigecycline, IV cefoxitin OR imipenem PLUS oral azithromycin OR oral clarithromycin AND oral clofazimine.
Arm C. IV amikacin, IV tigecycline, IV cefoxitin OR imipenem PLUS oral azithromycin OR oral clarithromycin.
2. Randomisation to Prolonged Intensive or Immediate Consolidation (PI/IC): The second randomisation will ONLY be for participants who are still MABS positive at the end of short intensive therapy (based on respiratory sampling collected at 4 weeks) and are able to continue with intensive therapy. Randomisation will occur at the end of short intensive therapy and will allocate participants to either: Continue intensive therapy which will be followed by consolidation (participants remain on the same intensive therapy drug regimen if randomised to prolonged intensive therapy), OR immediately commence consolidation therapy.
3. Randomisation to Consolidation: This randomisation will allocate participants to the consolidation therapy arms a or b for 46 weeks.

Arm a. Oral clofazimine PLUS oral azithromycin OR oral clarithromycin in combination with one to three of the following oral antibiotics: oral linezolid, oral co-trimoxazole, oral doxycycline, oral moxifloxacin, oral bedaquiline (adults only), oral rifabutin.
Arm b. Inhaled amikacin (IA) AND oral clofazimine AND oral azithromycin OR oral clarithromycin in combination with one to three of the following oral antibiotics: oral linezolid, oral co-trimoxazole, oral doxycycline, oral moxifloxacin, oral bedaquiline (adults only), oral rifabutin.
Oral ethambutol can be added to any of the treatment arms if participants have mixed infection with slow-growing NTM.

After the first 60 patients have completed short IT, an interim analysis will be conducted, and Bayesian adaptive randomisation will be implemented. New interventions may be added or existing treatment arms stopped due to lack of benefit or unacceptable toxicity at interim analyses. Subsequent interim analyses will be performed after every 100 intervention

participants are recruited to the trial. The FORMaT trial may include placebo-controlled double-blind randomised interventions in the future, but the initial intervention program is randomised but open-label. Randomisation will be performed via the REDCAP trial database after the relevant randomisation stratification factors are entered into the database.

Details of medications and dosing in both adults and children can be found in the drug dosing regimen tables contained in the relevant sections of the FORMAT intervention program Appendix A1 and Appendix A2 modules, which are available online.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Amikacin, tigecycline, imipenem, cilastatin, cefoxitin, azithromycin, clofazimine, ethambutol, clarithromycin, linezolid, trimethoprim, sulfamethoxazole, doxycycline, moxifloxacin, bedaquiline, rifabutin

Primary outcome(s)
Current primary outcome measure as of 11/06/2025:

The primary outcome of the Intervention Program is microbiological clearance of MABS with good tolerance of the interventions.
Definition of MABS clearance at final outcome:
Negative MABS cultures from four consecutive sputum samples with one of those sputum specimens collected four weeks after the completion of consolidation therapy, or a MABS negative Bronchoalveolar Lavage (BAL) collected four weeks after completion of consolidation.
Definition of tolerance:
Tolerance is based on the Common Terminology Criteria for Adverse Events (CTCAE version 5.0). Only adverse events that are attributed as either “possibly-“, “probably-“, or “definitely-“ related to study drug will be assessed in the determination of tolerance. “Good” tolerance is defined as no adverse events occurring or only adverse events coded as CTCAE grades 1 and 2. “Poor” tolerance is defined as any adverse events attributed as possibly-, probably-, or definitely-related to study drug coded as CTCAE grades 3, 4, or 5.

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Previous primary outcome measure:

MABS clearance during short intensive therapy. The number of patients in each group with microbiological clearance of MABS with good tolerance. MABS clearance is defined as 3 MABS negative sputum samples or ONE MABS negative BAL collected at Week 4 of Short Intensive therapy and interpreted at Week 6 of short intensive therapy. Good treatment tolerance is defined as no AE’s related to study treatment and/or AEs of CTCAE grades 1 or 2 related to study treatment.

Key secondary outcome(s)
Current secondary outcome measures as of 25/06/2025:

1. Probability of MABS clearance at Final Outcome irrespective of toxicity according to participant's treatment pathway.
2. Safety of treatment combinations, including changes in microbiological resistance.
3. Change in FEV1 z-score at Final Outcome compared with Screening in participants who do and do not clear MABS at Final Outcome.
4. Phenotype of the structural abnormalities of chest CTs and changes in chest CT scores between Screening and Final Outcome between participants who clear or do not clear MABS at Final Outcome.
5. Predictive value of structural abnormalities on Screening CT scans for sputum conversion and for progression of structural changes in relation to treatment.
6. Change in 6-minute walk distance (6MWD) for adult participants from Screening to Final Outcome according to treatment pathway and in participants who do and do not clear MABS at Final Outcome.
7. Change in HRQoL for participants from Screening to Final Outcome according to treatment pathway and in participants who do and do not clear MABS at Final Outcome.
8. Cost effectiveness of the treatment combinations across intensive and consolidation phases of the trial.
9. Causes for early withdrawal from MABS-PD treatment due to reasons other than poor tolerance as defined in the primary objectives.

Exploratory outcomes:
1. Participant's MABS clearance status 12 months after Final Outcome.

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Previous secondary outcome measures:

1. Efficacy of inhaled Amikacin during intensive therapy in comparison to intravenous Amikacin in the treatment of MABS-PD. The number of patients in each group with microbiological clearance of MABS with good tolerability at completion of short intensive therapy with the use of inhaled amikacin (Arm B) and with the use of IV amikacin (Arm A) given during the intensive phase. Assessment of MABS clearance and treatment tolerance are as in point 1.
2. Efficacy of additional clofazimine during short intensive therapy in comparison to no additional clofazimine for treatment of MABS-PD. The number of patients in each group with microbiological clearance of MABS with good tolerability at completion of short intensive therapy with the use of additional clofazimine (Arm A) and without the use of additional clofazimine (Arm C) given during the intensive phase. Assessment of MABS clearance and treatment tolerance are as in point 1.
3. Comparison of microbiological clearance of MABS with good tolerability at 12 weeks in patients with MABS-positive cultures at 6 weeks and allocated to prolonged intensive therapy and those allocated to consolidation therapy. The number of patients in each group with clearance of MABS at 12 weeks with good tolerance. MABS clearance at 12 weeks is defined as 3 MABS negative sputum samples or ONE MABS negative BAL collected at Week 10 of Prolonged Intensive therapy and interpreted at Week 12 of Prolonged intensive therapy. Good treatment tolerance is defined as no AE's related to study treatment and/or AEs of CTCAE grades 1 or 2 related to study treatment.
4. Comparison of MABS clearance at Final Outcome between those allocated to consolidation therapy with oral treatment and those allocated to consolidation with oral therapy and additional inhaled amikacin. The number of patients with microbiological clearance of MABS with good tolerability between those allocated to consolidation therapy with oral treatment and those allocated to consolidation therapy with oral therapy and additional inhaled amikacin. MABS clearance at Final Outcome is defined as 4 consecutive MABS negative sputum samples

with at least ONE of these collected 4 weeks after ceasing consolidation therapy OR ONE MABS negative BAL collected 4 weeks after ceasing Consolidation therapy. Good treatment tolerance is defined as no AE's related to study treatment and/or AEs of CTCAE grades 1 or 2 related to study treatment.
5. The probability of microbiological clearance of MABS at time point final, irrespective of toxicity for participants according to treatment path. [Time Frame: 6 weeks, 12 weeks, at end of consolidation and at final outcomes]. Definitions of MABS clearance at time point final is as per Point 5.
6. The safety of the treatment combinations in patients with MABS. The number of participants with treatment-related adverse events as assessed by CTCAE version 5 at the completion of short IT, at the completion of prolonged IT, at the completion of CT and at final outcomes.
7. The relative change in FEV1 z-score between treatment groups for time point final compared with time point start in patients who do and who do not clear MABS at time point final.
8. Relative change in FEV1 z score compared between treatment groups.
9. Change in % Bronchiectasis scored using PRAGMA in chest CTs between Day 0 (screening) and at 12 weeks and at final outcome and between those who clear and those who do not clear MABS.
10. Change in Health-Related Quality of Life (HRQoL) for participants with CF (using the Cystic Fibrosis Questionnaire-Revised (CFQ-R)) between Final Outcome and Screening; between end of Prolong Intensive Therapy and Screening; and between end of Short Intensive therapy and Screening; according to treatment path and in those that do and those that do not clear MABS at Final Outcome. MABS clearance at Final Outcome is as per Point 5.
11. Change in general HRQoL between Final Outcome and Screening; between end of Prolong Intensive Therapy and Screening; and between end of Short Intensive therapy and Screening; according to treatment path and in those who do and who do not clear MABS at Final Outcome. MABS clearance at Final Outcome is as per Point 5.
12. The cost-effectiveness of the proposed treatment combinations across both intensive and consolidation phases of the trial by using the Health Utilisation and Costs Questionnaire administered at Screening, end of Intensive Therapy Phases and at Final Outcome.
13. Total cost between treatments calculated as the sum product of health resource utilisation and resource unit price during the treatment period.
14. The change in 6-minute walk distance for adult participants from the date of randomization to up to 62 weeks according to treatment path and in participants who do and do not clear MABS at time point final.

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 25/06/2025:

Eligibility criteria for the FORMaT trial can be applied at two levels:
1. Eligibility into the Intervention Program, or;
2. Eligibility into the Observational Cohort.
Potential participants can only be enrolled in either the Intervention Program or the Observational Cohort at any one time. Provided the eligibility criteria are met, potential participants may either:

1. Enrol directly into the Intervention Program, or;
2. Enrol into the Observational Cohort and transition into the Intervention Program once they satisfy the inclusion criteria for this program which can occur at any time during the trial.

Eligibility into the FORMaT trial will be assessed at screening. Observational Cohort participants who go on to meet the Intervention Program eligibility criteria can transition from the Observational Cohort to the Intervention Program.

INTERVENTION PROGRAM ELIGIBILITY
Potential participants are eligible for the Intervention Program if the criteria below are met. Eligible participants with mixed NTM infections (slow growers + MABS) or with recurrence of MABS infection following completion of previous treatment will be eligible if they meet the inclusion and exclusion criteria listed below. For eligible participants with mixed NTM infections additional therapy combinations are available as detailed in the relevant appendices.

INTERVENTION PROGRAM INCLUSION CRITERIA
1. Positive MABS-PD diagnosis meeting all three American Thoracic Society clinical, radiological and microbiological diagnostic criteria for MABS-PD. Defined as:
a. Clinical: Pulmonary symptoms and exclusion of other diagnoses.
b. Radiological: Nodular or cavitary opacities on chest radiograph or a chest high-resolution computed tomography (HRCT) scan showing multifocal bronchiectasis with multiple small nodules.
c. Microbiological: MABS positive culture results from at least two separate expectorated sputum samples.
or
Positive culture results from at least one bronchial wash or lavage.
or
Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or acid-fast bacilli (AFB)) and positive culture for NTM or biopsy showing mycobacterial histopathologic features (granulomatous inflammation or AFB) and one or more sputum or bronchial washes that are culture positive for NTM.
Screening samples must be collected within the timeframes stated in the relevant appendix.
2. Male or female participants of any age.
3. Participant has not received treatment for MABS-PD in the 12 months preceding assessment of eligibility or as specified in the relevant appendix (this includes drugs prescribed for the treatment of other mycobacteria and/or other indications that may have activity against MABS, as specified in the FORMaT Prohibited Drug List Standard Operating Procedure (SOP)).
4. Informed consent signed by participant or parent/legal guardian if participant is under 18 years of age.
5. Ability to comply with study visits, therapies and study procedures as judged by the site investigator.

OBSERVATIONAL COHORT INCLUSION CRITERIA
To be eligible to participate in the Observational Cohort the following criteria must be met:
1. Male and female participants of any age with at least one positive respiratory culture for MABS.
2. Informed consent signed by participant or parent/legal guardian if participant is under 18 years of age.
3. Ability to comply with study visits and study procedures as judged by the site investigator.

ADDITIONAL ELIGIBILITY CRITERIA
Mixed NTM infections

Participants who have cultured slow growing NTM of the same species two or more times in the 24 months prior to screening, with one of those cultures within the 6 months prior to screening, will be considered to have mixed NTM infection at the time of screening. The participants must meet all other inclusion criteria and no exclusion criteria to be eligible for participation. Ethambutol may be used in addition to trial therapies to cover mixed NTM infections considered to require treatment by their clinician.

Appendix specific sub-studies and integrated studies
Appendix specific sub-studies and integrated studies may have additional eligibility criteria which are described in each of the relevant appendices.

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Previous inclusion criteria:

Intervention Programs:
Eligible participants with mixed NTM infections (slow growers + MABS) or with recurrence of MABS infection following completion of previously successful treatment defined as remaining free of positive respiratory cultures for MABS over 12 months post-treatment, will be eligible if they met the inclusion criteria listed below:
1. Positive MABS-PD diagnosis meeting all three American Thoracic Society clinical, radiological and microbiological diagnostic criteria for MABS-PD. Defined as:
1.1. Clinical: Pulmonary symptoms and exclusion of other diagnoses
1.2. Radiological: Nodular or cavitary opacities on chest radiograph or a chest high-resolution computed tomography (HRCT) scan showing multifocal bronchiectasis with multiple small nodules
1.3. Microbiological: MABS positive culture results from at least two separate expectorated sputum samples, Or
1.4. Positive culture results from at least one bronchial wash or lavage, Or
1.5. Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or acid-fast bacilli [AFB]) and positive culture for NTM or biopsy showing mycobacterial histopathologic features (granulomatous inflammation or AFB) and one or more sputum or bronchial washes that are culture positive for NTM.
2. Male or female participants in Denmark aged 18 years and older, in other countries children are included.
3. Participant has not received treatment for MABS-PD in the 12 months preceding assessment of eligibility.
4. Informed consent signed by the participant or parent/legal guardian if the participant is under 16 years of age.
5. Ability to comply with study visits, therapies and study procedures as judged by the site investigator.

Observational Cohort:
1. Male and female participants of any age with at least one positive respiratory culture for MABS
2. Informed consent signed by the participant or parent/legal guardian if the participant is under 16 years of age
3. Ability to comply with study visits and study procedures as judged by the site investigator

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
All

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 25/06/2025:

INTERVENTION PROGRAM EXCLUSION CRITERIA
1. Participants receiving current treatment for MABS (this includes drugs prescribed for the treatment of other mycobacteria and/or other indications that may have activity against MABS, as specified in the FORMaT Prohibited Drug List SOP), except for participants taking azithromycin as part of routine treatment for CF or chronic infection-related pulmonary disease, or as specified in the relevant appendix.
2. Participants who have a QTc interval of >500 milliseconds (QT interval corrected based on Fridericia method).
3. Participants who are pregnant or planning to continue breast feeding.
4. Known hypersensitivity or contraindication to any of the therapies for which no alternative option(s) have been provided.

OBSERVATIONAL COHORT EXCLUSION CRITERIA
Potential participants will be ineligible to participate in the Observational Cohort if any of the following criterion are met:
Receiving active treatment for MABS within the previous 12 months (this includes drugs prescribed for the treatment of other mycobacteria and/or other indications that may have activity against MABS, as specified in the FORMaT Prohibited Drug List SOP, except for participants taking azithromycin as part of routine treatment for CF or chronic infection-related pulmonary disease).

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Previous exclusion criteria:

Intervention Program:
1. Participants receiving current treatment for MABS within the previous 12 months (this includes drugs prescribed for treatment of other mycobacteria and/or other indications that may have activity against MABS, as specified in FORMaT SOP 14, except for participants taking azithromycin as part of routine treatment for CF or chronic infection-related pulmonary disease)
2. Positive pregnancy test at any time during the FORMaT trial for females of childbearing potential
3. Breast-feeding
4. An unwillingness to comply with the acceptable methods of contraception, as described below
5. Participants with a QTc interval >500 milliseconds (QT interval corrected based on Fridericia method)
6. Known hypersensitivity to any of the therapies for which no alternative option(s) have been

provided. This includes:
6.1. Amikacin
6.2. Tigecycline
6.3. Macrolide antibiotics
6.4. Clofazimine

Observational Cohort:
Receiving active treatment for MABS within the previous 12 months (this includes drugs prescribed for the treatment of other mycobacteria and/or other indications that may have activity against MABS, as specified in FORMaT Standard Operating Procedure (SOP) 14, except for participants taking azithromycin as part of routine treatment for cystic fibrosis (CF) or chronic infection-related pulmonary disease)

Date of first enrolment
02/03/2020

Date of final enrolment
30/11/2026

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Australia

Belgium

Denmark

France

Israel

Singapore

Taiwan

Study participating centre
University Hospitals Bristol and Weston NHS Foundation Trust
Bristol Royal Hospital for Children
Upper Maudlin Street

Bristol
England
BS2 8BJ

Study participating centre
Alder Hey Children's NHS Foundation Trust
Eaton Road
Liverpool
England
L12 2AP

Study participating centre
NHS Lothian
Royal Hospital for Children and Young People
50 Little France Crescent
Edinburgh
Scotland
EH16 4TJ

Study participating centre
NHS Lothian
Western General Hospital
Crewe Road South
Edinburgh
Scotland
EH4 2XU

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
England
SO16 6YD

Study participating centre
Manchester University NHS Foundation Trust
Wythenshawe Hospital
100 Southmoor Road

Wythenshawe
England
M23 9LT

Study participating centre
Manchester University NHS Foundation Trust
Royal Manchester Children's Hospital
Oxford Street
Manchester
England
M13 9WL

Study participating centre
Nottingham University Hospitals NHS Trust
Welcome Wolfson Adult CF Centre (City Hospital Campus)
Hucknall Rd
Nottingham
England
NG5 1PB

Study participating centre
Nottingham University Hospitals NHS Trust
Queens Medical Centre
Derby Rd, Lenton
Nottingham
England
NG7 2UH

Study participating centre
Birmingham Women's and Children's NHS Foundation Trust
Birmingham Children's Hospital
Steelhouse Ln
Queensway
Birmingham
England
B4 6NH

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Birmingham Heartlands Hospital
Bordesley Green E

Birmingham
England
B9 5SS

Study participating centre
Cardiff and Vale University Health Board
Study Centre Name: University Hospital Llandough
Address: UHL, Penlan Rd, Llandough
Penarth
Wales
CF64 2XX

Study participating centre
Cardiff and Vale University Health Board
Noah's Ark Childrens Hospital for Wales
Heath Park Way
Cardiff
Wales
CF14 4XW

Study participating centre
NHS Greater Glasgow and Clyde
Queen Elizabeth University Hospital, Glasgow
1345 Govan Road
Glasgow
Scotland
G51 4TF

Study participating centre
Belfast Health and Social Care Trust
Belfast City Hospital
Lisburn Road
Belfast
Northern Ireland
BT9 7AB

Study participating centre
Prince Charles Hospital
627 Rode Rd

Chermside
Australia
QLD 4032

Study participating centre
Queensland Children's Hospital
501 Stanley Street
Brisbane
Australia
QLD 4101

Study participating centre
Mater Private Hospital
301 Vulture Street
Brisbane
Australia
QLD 4101

Study participating centre
Gold Coast University Hospital
1 Hospital Boulevard
Southport
Australia
QLD 4215

Study participating centre
Sunshine Coast University Hospital
6 Doherty Street
Sunshine Coast
Australia
QLD 4575

Study participating centre
Gallipoli Medical Research Facility
121 Newdegate Street
Greenslopes
Australia
QLD 4120

Study participating centre
Royal Adelaide Hospital
Lot 102 Port Rd
Adelaide
Australia
SA 5000

Study participating centre
Royal Melbourne Hospital
300-328 Grattan St
Parkville
Australia
VIC 3052

Study participating centre
Royal Perth Hospital
197 Wellington Street
Perth
Australia
WA 6000

Study participating centre
Princess Alexandra Hospital
Lot 2, 199 Ipswich Rd
Woolloongabba
Australia
QLD 4102

Study participating centre
Royal Prince Alfred Hospital
12 Missenden Rd
NSW 2050
Australia
Camperdown

Study participating centre
John Hunter Hospital
38 Lookout Rd
New Lambton Heights
Australia
NSW 2305

Study participating centre
Sir Charles Gairdner Hospital
12 Hospital Ave
Nedlands
Australia
WA 6009

Study participating centre
Perth Children's Hospital
15 Hospital Ave
Nedlands
Australia
WA 6009

Study participating centre
Alfred Hospital
55 Commercial Rd
Melbourne
Australia
VIC 3004

Study participating centre
Westmead Children's Hospital
Corner Hawkesbury Road and Hainsworth Street
Westmead
Australia
NSW 2145

Study participating centre
Macquarie University Hospital
3 Technology Place
Macquarie University
Macquarie Park
Australia
NSW 2109

Study participating centre

Westmead Adult's Hospital
Corner of Hawkesbury Road and Darcy Road
Westmead
Australia
NSW 2145

Study participating centre
St George Hospital
28A Gray Street
Korgarah
Australia
NSW 2217

Study participating centre
Austin Hospital
145 Studley Road
Heidelberg
Australia
VIC 3084

Study participating centre
Rigshospitalet
Blegdamsvej 9
Copenhagen
Denmark
2100

Study participating centre
Tan Tock Seng Hospital
11 Jin Tan Tock Seng
Singapore
Singapore
308433

Study participating centre
Singapore General Hospital Outram Road
Singapore
Singapore
169608

Study participating centre
National University Hospital Singapore
5 Lower Kent Ridge Road
Singapore
Singapore
119074

Study participating centre
Rambam Health Care Campus
HaAliya HaShniya St 8
Haifa
Israel
3109601

Study participating centre
Carmel Medical Centre
Mikhal Street 7
Haifa
Israel
3436212

Study participating centre
Hadassah Ein Kerem Hospital
Kalman Ya'akov Man St
Jerusalem
Israel
9987500

Study participating centre
Schneider
Kaplan Street 14
Peta Tikva
Israel
4920235

Study participating centre
Soroka Medical Centre
Ytizhack I, Rager Blvd 151

Beer-Sheeva
Israel
8410101

Study participating centre
Sheba Medical Centre
Derech Sheba 2
Ramat Gan
Tel Aviv
Israel
5266202

Study participating centre
National Taiwan University Hospital
No. 7, Zhongshan S Rd
Zhongzheng District
Taipei
Taiwan
100

Study participating centre
Kaoshiung Medical University Hospital
No. 100, Ziyou 1st Road
Kaohsiung City
Taiwan
80756

Sponsor information

Organisation
Nottingham University Hospitals NHS Trust

ROR
https://ror.org/05y3qh794

Funder(s)

Funder type
University/education

Funder Name
University of Queensland

Alternative Name(s)
The University of Queensland, UQ Australia, University of Queensland in Australia, University of Queensland - Australia, The University of Queensland | Brisbane QLD, uniofqld, UQ

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Australia

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publicly available repository. Data shared on this platform will be aggregated anonymised data. The data will become available at the end of each trial/iteration of the trial. The data will be available on the publicly available repository indefinitely or for as long as funding is available to support the repository. A written request from any researchers to the FORMaT trial Chief investigator and/or their delegate will be required to obtain approval and access to the data. The data can be requested to be used for any NTM or NTM-relevant research. Consent from participants is obtained to share the aggregated anonymised data on a public repository for use in future research.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		21/09/2025	22/09/2025	Yes	No
Protocol file	version 4.1	27/11/2024	12/05/2026	No	No
Statistical Analysis Plan		05/05/2026	12/05/2026	No	No
Study website		11/11/2025	11/11/2025	No	Yes