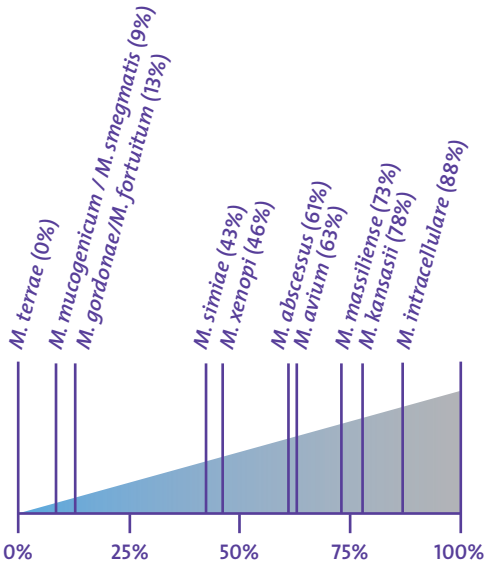
The decision to initiate treatment should be based on the potential risks and benefits of therapy to the individual.

In patients diagnosed with NTM-PD, **initiation of treatment** is recommended over **watchful waiting,** especially in the context of positive AFB sputum smears and/or cavitary lung disease.[1]

Drug susceptibility testing is performed for drugs used in treatment regimens where clear correlations exist between in vitro activity and the in vivo outcomes of treatment (e.g. for macrolides and amikacin in the treatment of Mycobacterium avium complex pulmonary disease (MAC-PD).[1]

The clinical relevance of the NTM species should be considered. The clinical relevance of commonly isolated NTM species, in terms of the percentage of patients with isolates of a species that meet diagnostic criteria for NTM-PD, varies greatly as shown below.[4]



Zweijpfenning et al.[4]

Key points

New international guidelines from ATS/ERS/ESCMID/IDSA provide recommendations on the management of four of the most common species MAC, *M. kansasii, M. xenopi* and *M. abscessus*.[1]

MAC
- Macrolide-based triple therapy for 12 months post-culture conversion
- ALIS for refractory patients

M. kansasii
- Triple therapy including a macrolide or isoniazid

M. abscessus
- **At least** triple therapy
- Consult experts for input

M. xenopi
- **At least** triple therapy with a macrolide or fluoroquinolone

References

1. Daley CL, et al. Eur Respir J 2020;56(1):2000535
2. Ratnatunga CN, et al. Front Immunol 2020;11:303
3. Griffith DE, et al. Am J Respir Crit Care Med 2007;175:367-416
4. Zweijpfenning SMH, et al. Semin Respir Crit Care Med 2018;39:336-42
5. Daley CL. Microbiology Spectrum, 2017;5:1-36

Abbreviations

AFB: acid-fast bacilli | **ALIS:** amikacin liposome inhalation suspension **ATS:** American Thoracic Society | **CT:** computed tomography | **GRADE:** Grading of Recommendations Assessment, Development, and Evaluation | **ERS:** European Respiratory Society | **ESCMID:** European Society of Clinical Microbiology and Infectious Diseases | **GBT:** guideline-based therapy | **IDSA:** Infectious Diseases Society of America | **MAC:** *Mycobacterium avium* complex | **NTM:** nontuberculous mycobacteria | **PD:** pulmonary disease | **PICO:** Population, Intervention, Comparator, Outcome

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NTM DIALOGUE

NTM DIALOGUE

Insights into the ATS/ERS/ESCMID/IDSA

NTM-PD guidelines 2020

Non-tuberculous mycobacteria (NTM) comprise over 190 species and subspecies that can produce opportunistic infections in both pulmonary and extrapulmonary sites.[1]

NTM infections can be difficult to diagnose and treat and are particularly prevalent in those with lung damage or disease, cancer and immuno-deficiencies.[2]

New international guidelines from ATS/ERS/ESCMID/IDSA provide best-practice guidance on the management of NTM pulmonary disease (NTM-PD), including diagnosis, drug susceptibility testing, initiation of therapy and treatment regimens.[1]

It covers four of the most common species:
- *Mycobacterium avium* complex (MAC)
- *Mycobacterium kansasii*
- *Mycobacterium xenopi*
- *Mycobacterium abscessus*

The recommendations were formulated using the GRADE approach, following systematic reviews conducted on 22 PICO questions[1]

This pocket guide gives an at-a-glance overview of the key recommendations from the 2020 NTM-PD guideline.

Diagnosis

Diagnosis of NTM-PD requires clinical, radiological and microbiological criteria.[1]

Clinical
- Pulmonary symptoms (e.g. cough, sputum production, haemoptysis, dyspnoea, chest pain)[3]
- Appropriate exclusion of other diagnoses

Radiological
- Nodular or cavitary opacities on chest radiograph, or bronchiectasis with multiple small nodules on high-resolution CT scan

Microbiological

One of the following:
- Positive culture results from at least two sputum samples*
- Positive culture results from at least one bronchial wash or bronchoalveolar lavage
- Transbronchial or other lung biopsy with mycobacterial histological features† and positive culture for NTM
- Transbronchial or other lung biopsy with mycobacterial histological features† and one or more sputum or bronchial washings culture positive for NTM

*Isolates should be the same NTM species in order to meet disease criteria; †granulomatous inflammation or acid-fast bacilli

M. kansasii

Management of *M. kansasii*

Treatment regimen

Rifampicin susceptible disease

- Triple therapy including rifampicin, ethambutol, and either isoniazid or a macrolide

Rifampicin resistant disease or intolerance to first-line therapy

- Include a fluoroquinolone (e.g. moxifloxacin)

Frequency

Nodular/bronchiectatic disease treated with triple therapy including a macrolide

- Treatment daily or 3 times per week

Cavitary disease treated with triple therapy including a macrolide

- Daily treatment

All patients treated with triple therapy including isoniazid

- Daily treatment

Aminoglycosides

Parenteral amikacin/streptomycin not recommended for routine treatment unless it is impossible to use a rifampicin-based regimen or severe disease is present.

Duration

At least 12 months in total

MAC

Management of MAC

Treatment regimen

Treatment regimen should contain AT LEAST 3 antimicrobials

Macrolide susceptible disease

- Triple therapy including a macrolide*, ethambutol and rifampicin

Cavitary disease/macrolide resistant disease

- As above, plus parenteral amikacin or streptomycin as initial therapy for 2–3 months**

*Azithromycin or clarithromycin; preferably azithromycin to reduce the risk of drug-drug interaction | **Not inhaled amikacin or ALIS

Separately, outside of the guidelines,[5] it is recommended that patients on treatment are monitored regularly for culture conversion[5] to plan ahead for possible refractory disease at 6 months

Frequency

Nodular/bronchiectatic disease

- Treatment 3 times per week

Severe or cavitary disease

- Daily treatment

Refractory disease

(failure after at least 6 months of GBT)

Add Amikacin Liposomal Inhalation Suspension (ALIS) to current treatment regimen.

Duration

At least 12 months after culture conversion

M. xenopi

Management of *M. xenopi*

Treatment regimen

Patients should be treated aggressively given the high mortality of the disease

***M. xenopi* PD**

- A multidrug treatment regimen that includes **at least** three drugs: rifampicin, ethambutol, and either a macrolide and/or a fluoroquinolone (moxifloxacin recommended)

Cavitary or advanced/ severe bronchiectatic disease

- Add parenteral amikacin to the treatment regimen and obtain expert consultation

Frequency

Daily treatment

Duration

At least 12 months after culture conversion

M. abscessus

Management of *M. abscessus*

Treatment regimen

Treatment regimens should be designed in collaboration with experts.

***In vitro* macrolide susceptibility testing should be performed, including detection of a functional or non-functional erm(41) gene.**

The multidrug regimen should include at least three active drugs (guided by *in vitro* susceptibility).

Strains without inducible or mutational resistance

- A macrolide-containing multidrug treatment regimen

Strains with inducible or mutational macrolide resistance

- Continue to include a macrolide if the drug is being used for its immunomodulatory properties (but do not count it as an active drug in the multidrug regimen)

Duration

Duration of therapy should be determined with expert input.

Consider subgroups, e.g. nodular/ bronchiectatic versus cavitary disease, different *M. abscessus* subspecies and drug susceptibility.

Surgery

Surgical resection may be appropriate for selected patients, such as those with failure of medical management, cavitary disease, drug resistant isolates, or complications such as severe bronchiectasis. The decision to proceed must be weighed against the risks and benefits of surgery, and expert consultation is required.