NTM Lecture Series for Providers

April 27-28, 2023
NATIONAL JEWISH HEALTH

Treatment of Slowly Growing NTM

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DISCLOSURES:

Consultant: Genentech, Pfizer

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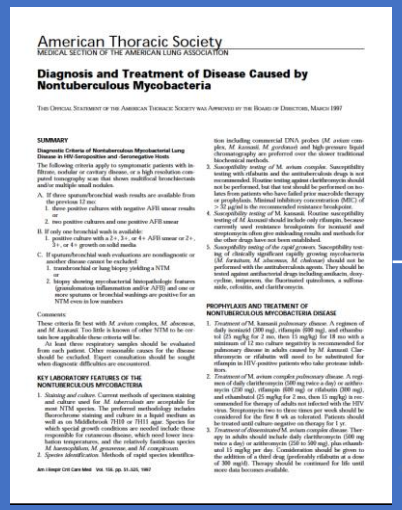
NTM Treatment Guidelines

1990

DIAGNOSIS AND TREATMENT OF DISEASE CAUSED BY NONTUBERCULOUS MYCOBACTERIA

1997



American Thoracic Society
MEDICAL SECTION OF THE AMERICAN LUNG ASSOCIATION

Diagnosis and Treatment of Disease Caused by Nontuberculous Mycobacteria

2007

American Thoracic Society Documents

An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases

2020

Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline

Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline: Executive Summary

2022

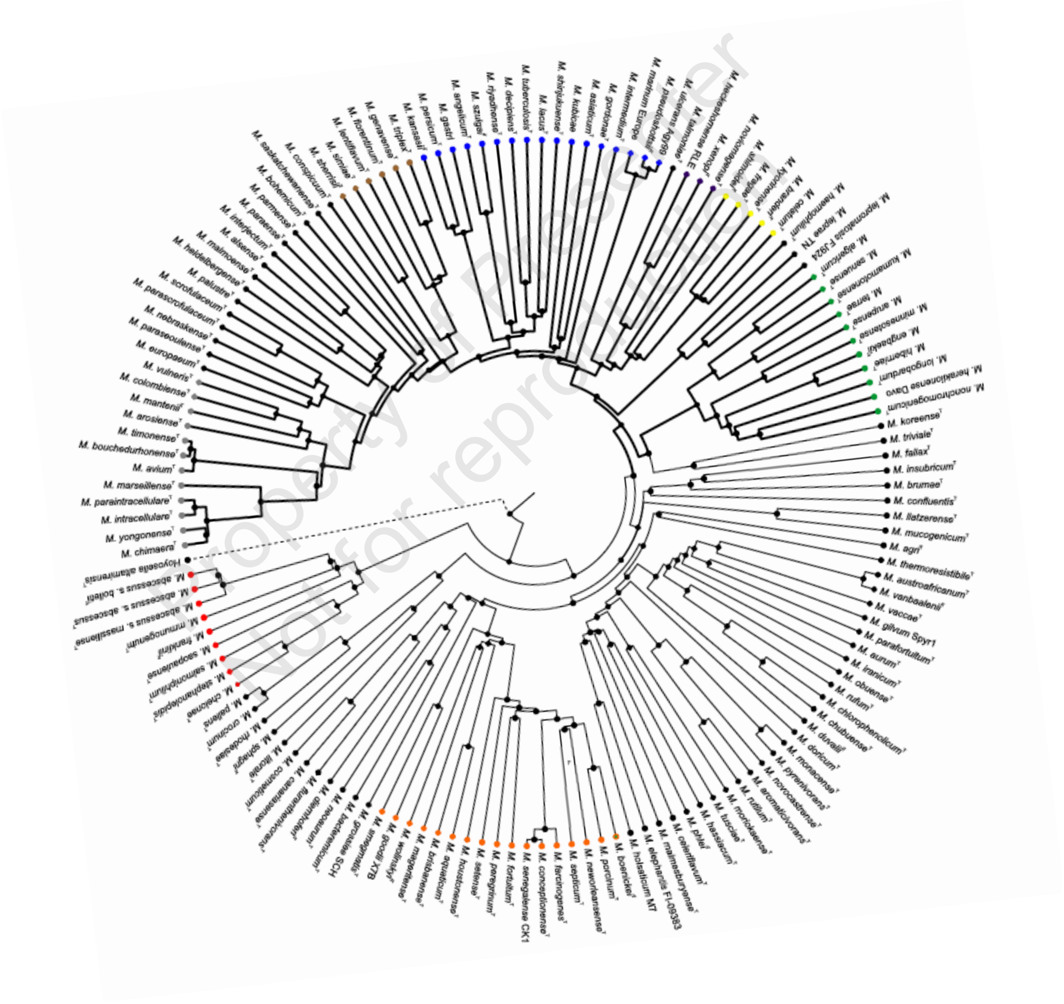
Review

Consensus management recommendations for less common non-tuberculous mycobacterial pulmonary diseases

Daley CL, et al. CID 2020;71:5-913 and Euro Respir J 2020;56:2000535
Lange C, et al. Lancet Infect Dis 2022;22:e178-190

NTM Treatment Guidelines

M. avium complex
M. kansasii
M. xenopi



M. malmoense
M. simiae
M. szulgai
M. genevense
M. gordonae

NTM-LD: Diagnostic Criteria

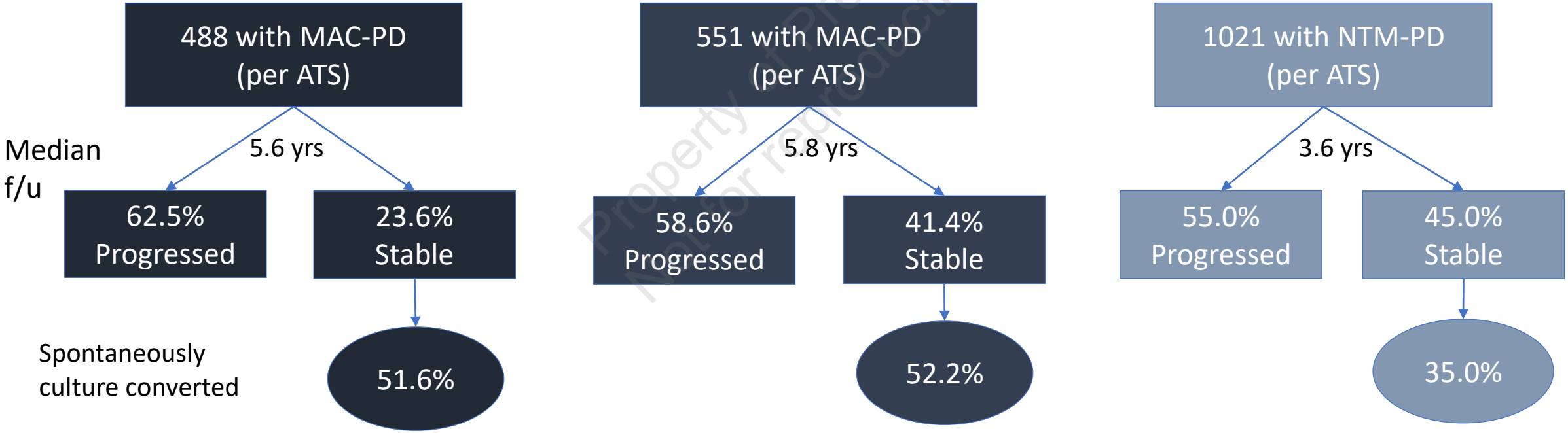
Clinical	Pulmonary or systemic symptoms	Both required
Radiological	Nodular or cavitary opacities on chest radiograph or high-resolution CT (HRCT) that shows bronchiectasis with multiple small nodules	
Appropriate exclusion of other diagnoses		
Microbiological	1. Positive cultures from ≥ 2 separate sputum samples. If results are non-diagnostic, consider repeat sputum AFB smears and cultures OR 2. Positive cultures from ≥ 1 bronchial wash or lavage OR 3. Transbronchial or other lung biopsy with mycobacterial histologic features (granulomatous inflammation or AFB) and positive culture for NTM OR biopsy showing mycobacterial histologic features (granulomatous inflammation or AFB) and ≥ 1 sputum or bronchial washings that are culture-positive for NTM	

Daley CL, et al. *CID* 2020;71:5-913; *Euro Respir J* 2020;56:2000535

Watchful waiting or initiation of treatment?

Guideline recommendation

In patients who meet the diagnostic criteria for NTM pulmonary disease, we suggest initiation of treatment rather than watchful waiting, especially in the context of positive acid-fast bacilli sputum smears and/or cavitary lung disease (conditional recommendation, very low certainty in estimates of effect).



Hwang JA, et al.
Eur Respir J 2017;49:1600537

Kwon BS, et al.
Resp Med 2019;150:45-50

Moon SM, et al.
Resp Med 2019;151:1-7.

Daley CL, et al. *CID* 2020;71:5-913; *Euro Respir J* 2020;56:2000535

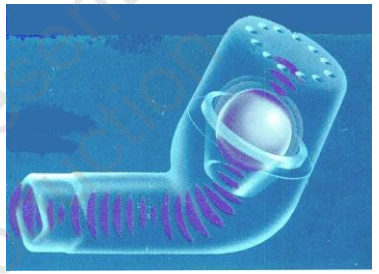
Risk Factors Associated with Progression

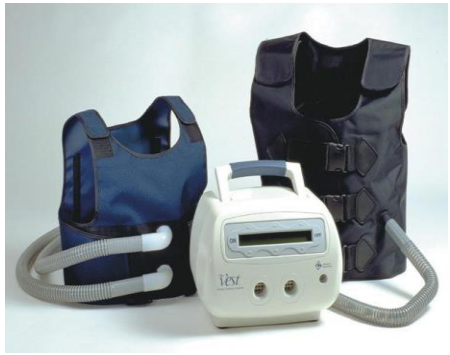
Host/Demographic Factors	Laboratory Factors	Radiographic Factors	Microbial Factors
• Male gender • Older age • Presence of co-morbidities • Low body mass index	• Elevated inflammatory indices (ESR, CRP) • Anemia • Low albumin	• Fibrocavitary • Extent of disease	• Bacterial load • Species

Hwang JA, et al. Eur Respir J 2017;49:1600537
Kwon BS, et al. Resp Med 2019;150:45-50
Moon SM, et al. Resp Med 2019;151:1-7.

Nonpharmacologic Therapy

- **Airway Clearance**
  - Regular exercise
  - Vibratory PEP
  - Chest percussion
  - Nebulized hypertonic saline
  - Chest wall oscillation
- **Pulmonary rehabilitation**
- **Nutrition**
- **GERD**
  - Lifestyle modifications



Best choice is what the patient will do

- Education
- Time commitment

Question #1

Which of the following infections is associated with the lowest culture conversion rate?

A. Extensively drug resistant TB (XDR-TB)

B. Macrolide resistant *Mycobacterium avium* complex

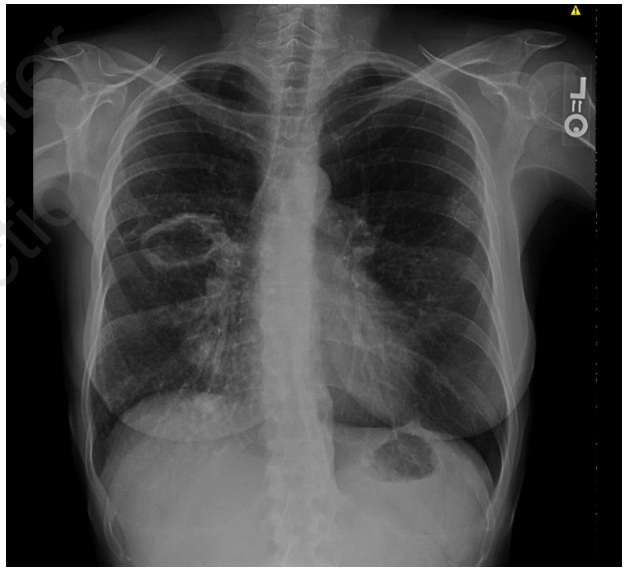
C. *Mycobacterium abscessus subspecies abscessus*

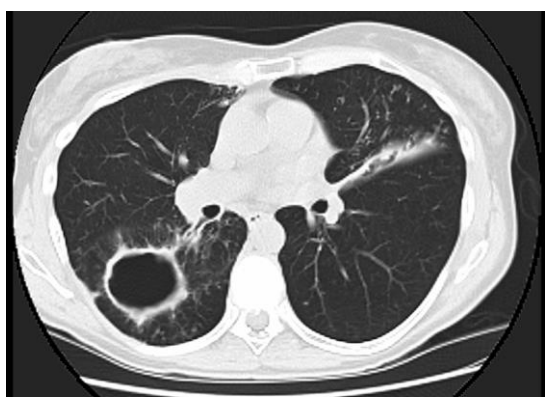
D. *Mycobacterium simiae*

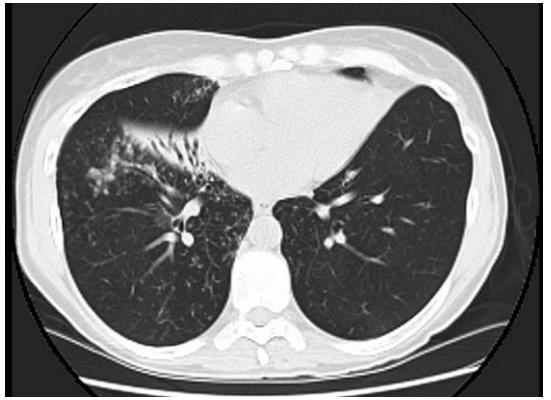
Treatment of MAC

- 65 year old Caucasian woman treated for *Mycobacterium avium* complex on two previous occasions with macrolide, rifampin, and ethambutol

- Now with AFB smear positive sputum specimen and culture positive for *M. intracellulare*







Mycobacterium avium Complex

10 Species

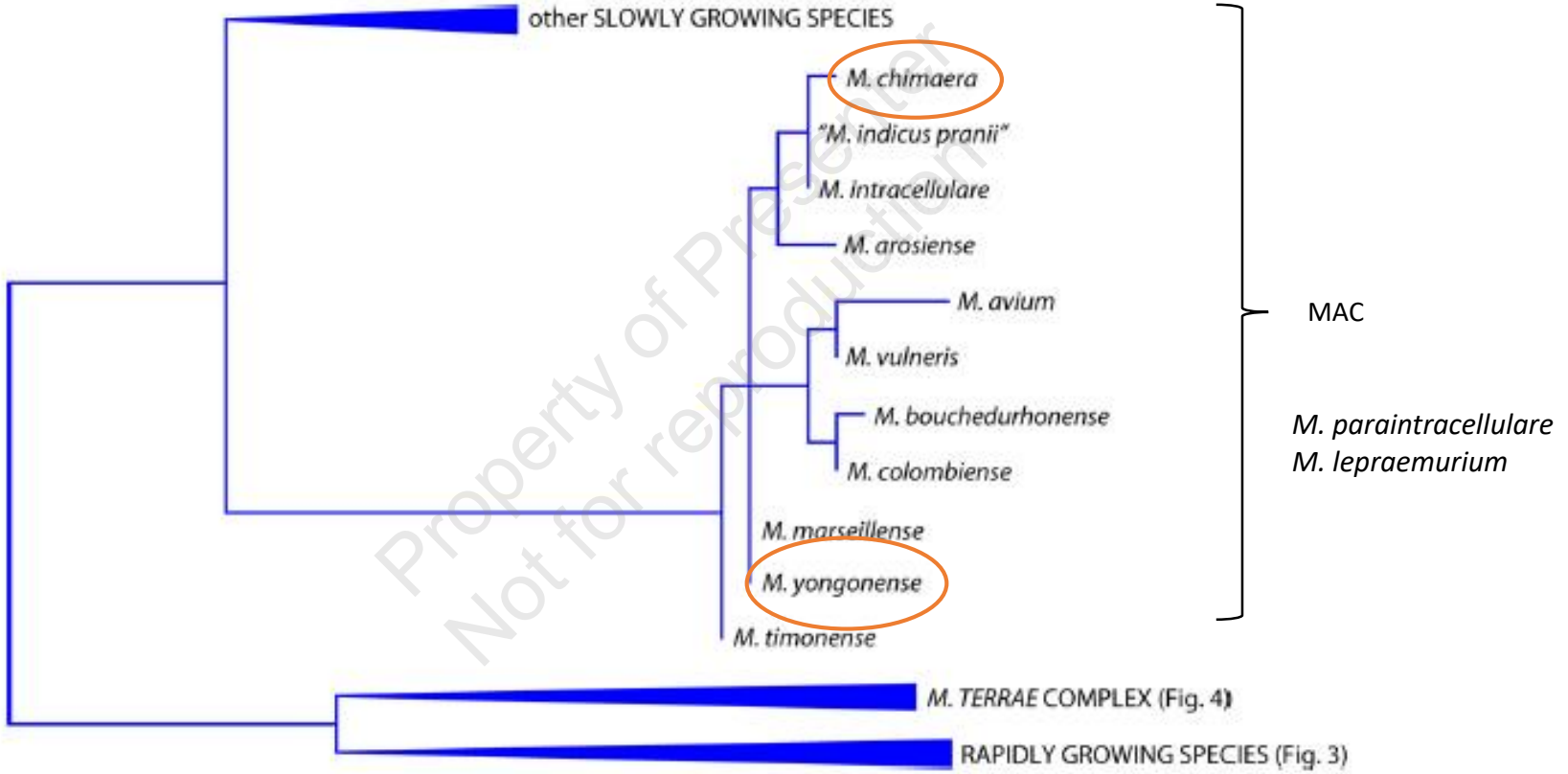


FIG 5 Phylogenetic tree, based on the 16S rRNA gene, for the species belonging to the *M. avium* complex.

Tortoli E, et al. J System Evol Micro 2004;54:1277-1285.
van Ingen J, et al. Int J Syst Evol Microb 2018;68:36666
Tortoli E. Clin Micro Rev 2014;27:727-752

Antimicrobial Susceptibility Testing

Species	Drugs
M. kansasii	Rifampicin Macrolide
MAC	Macrolide Amikacin
M. abscessus	Macrolide (including *erm*(41) gene) Amikacin

AST for MAC

Antimicrobial Agent	MIC, ug/ml		
	S	I	R
Clarithromycin	≤ 8	16	≥ 32
Amikacin (IV)	≤ 16	32	≥64
Amikacin (liposomal inhaled)	≤ 64	-	≥ 128

CLSI. M62 Performance Standards for Susceptibility Testing, 2018

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Daley CL, et al. CID 2020;71:5-913 and Euro Respir J 2020;56:2000535

Recommended Initial Treatment Regimens for MAC Pulmonary Disease

	No. of Drugs	Preferred Regimen[a]	Dosing Frequency	Duration
Nodular-bronchiectatic	3	Azithromycin (clarithromycin) Rifampin (rifabutin) Ethambutol	3 times weekly	12 months beyond culture conversion
Cavitary	≥ 3	Azithromycin (clarithromycin) Rifampin (rifabutin) Ethambutol Amikacin IV (streptomycin)[b]	Daily (IV aminoglycoside may be used 3 times weekly)	

a. Alternative drugs could include clofazimine, moxifloxacin, linezolid (tedizolid), bedaquiline
b. Consider for cavitary, extensive nodular bronchiectatic or macrolide resistant disease

Daley CL, et al. CID 2020;71:905-913 and Euro Respir J 2020;56:2000535

Treatment Outcomes for MAC

	Culture Conversion	Microbiologic Recurrence	Reinfection
Macrolide susceptible			
Non cavitary Cavitary	70% - 80% 50% - 80%	25-48%	46-75%
Macrolide resistant			
No surgery/aminoglycoside* Some surgery/aminoglycoside Surgery + prolonged aminoglycoside*	5% 15% 80%	–	–

* ≥ 6 months parenteral aminoglycoside

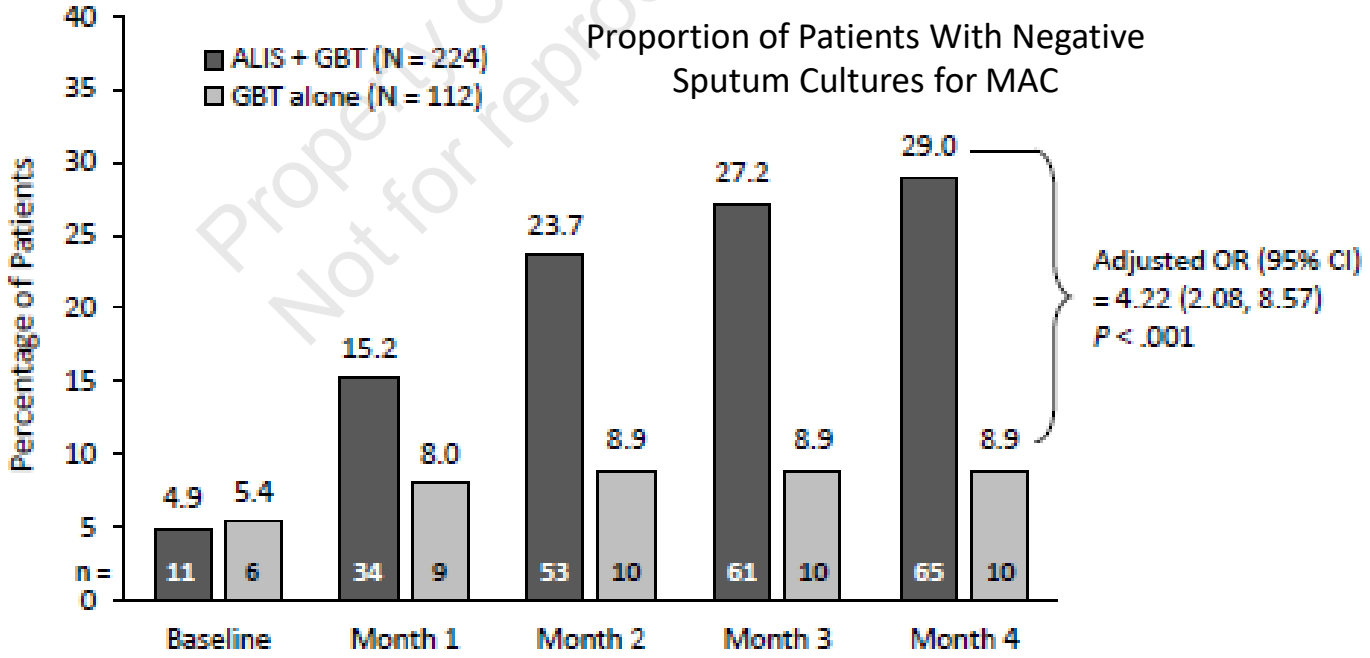
Griffith DE et al. *Am J Respir Crit Care Med.* 2006;174:928-934.
Jeong BH et al. *Am J Respir Crit Care Med.* 2015;191:96-103.
Moon SM et al. *Eur Respir J.* 2016;50:1602503.
Wallace R et al. *Chest.* 2014;146:276-282.
Koh WJ et al. *Eur Respir J.* 2017;50.
Morimoto K et al. *Ann Am Thorac Soc.* 2016;11:1904.
Boyle DP et al. *Ann Am Thorac Soc.* 2016;13:1956-1961

Treatment Refractory MAC Pulmonary Disease

Guideline recommendation

In patients with MAC pulmonary disease who have failed therapy after at least six months of guideline-based therapy, we recommend addition of amikacin liposome inhalation suspension (ALIS) to the treatment regimen rather than a standard oral regimen, only. (strong recommendation, moderate certainty in estimates of effect).

CONVERT Study – Randomized, controlled study of ALIS in treatment refractory MAC pulmonary disease



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Griffith D, et al. AJRCCM 2018;198:1559-1569

Sustainability and Durability of Culture Conversion

In patients who achieved culture conversion by month 6 in CONVERT:

- Was conversion sustained (negative results for 12 mos on treatment)
  - 63.1% of converters in the ALIS+GBT arm were sustained compared with 30.0% in GBT arm (P = .064)
- Was conversion durable (negative results for 3 mos and 12 mos after treatment)
  - 55.4% of converters in the ALIS + GBT arm remained culture negative at 3 months off of therapy compared with none in the GBT arm (P = .0017)
  - 46.2 % of converters in the ALIS +GBT arm remained culture negative at 12 months off of therapy compared with none in the GBT arm (P = <.0001)

Griffith D, et al. *Chest* 2021;160:831-842

Recommended Treatment Regimens for MAC Pulmonary Disease

	No. of Drugs	Preferred Regimen[a]	Dosing Frequency
Nodular-bronchiectatic	3	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol	3 times weekly
Cavitary	≥ 3	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol Amikacin IV (streptomycin)[b]	Daily (IV aminoglycoside may be used 3 times weekly)
Refractory[c]	≥ 4	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol Amikacin liposome inhalation suspension or IV (streptomycin)[b]	Daily (IV aminoglycoside may be used 3 times weekly)

a. Alternative drugs could include clofazimine, moxifloxacin, linezolid (tedizolid), bedaquiline
b. Consider for cavitary, extensive nodular bronchiectatic or macrolide resistant disease
c. Sputum culture positive after 6 months of guideline-based therapy

Daley CL, et al. CID 2020;71:905-913 and Euro Respir J 2020;56:2000535

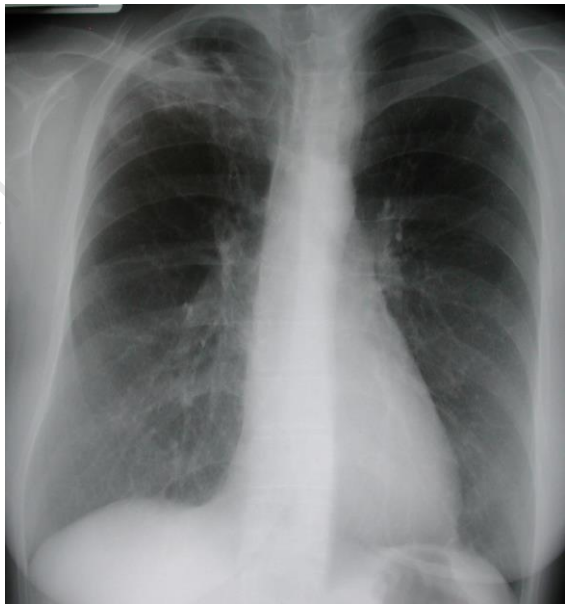
Other Interventions for Treatment Refractory MAC Pulmonary Disease

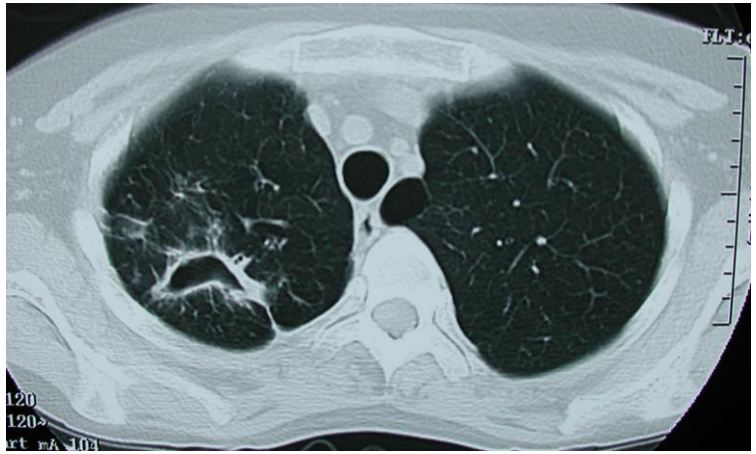
- Switching from intermittent therapy to daily therapy
- Adding additional medications
  - Amikacin liposome inhalation suspension
  - Clofazimine
  - Bedaquiline
  - Oxazolidinones (linezolid, tedizolid)
- Substituting medications
  - Rifabutin (substituting for rifampin)
- Surgery

Daley CL, et al. CID 2020;71:905-913 and Euro Respir J 2020;56:2000535

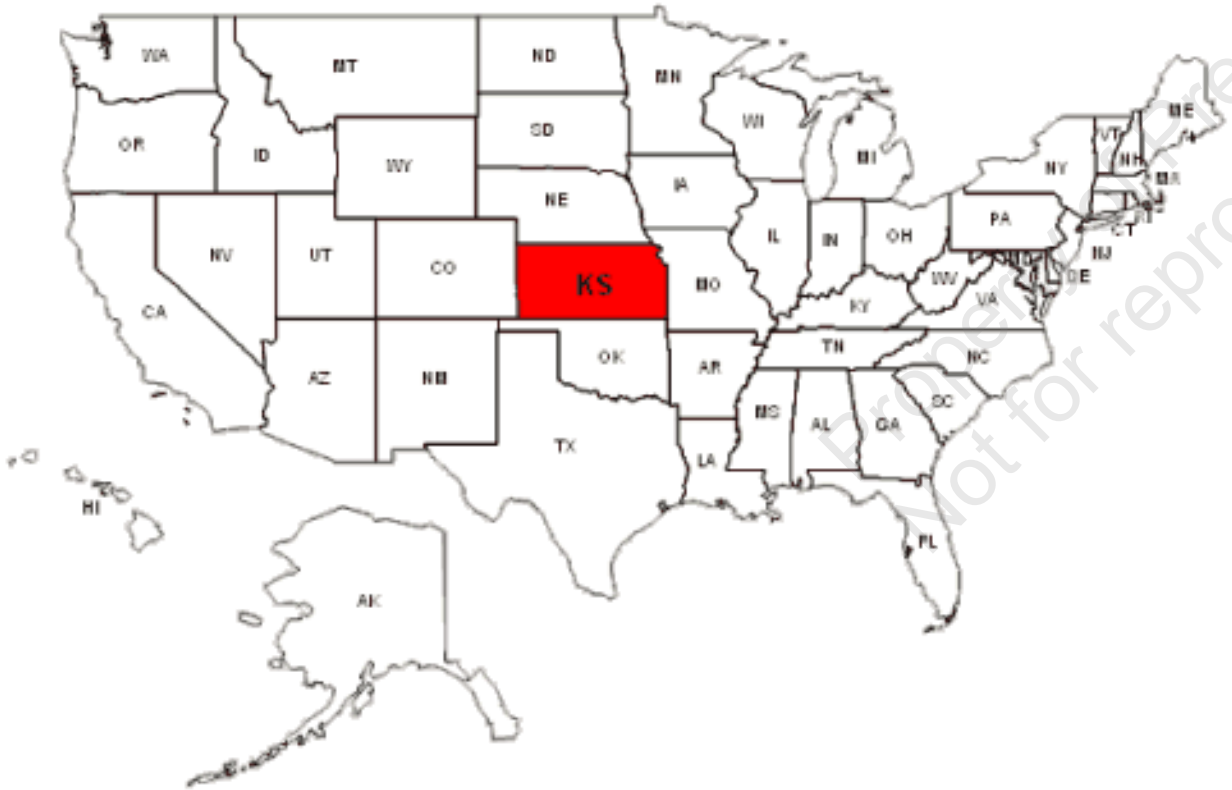
Treatment of *M. kansasii*

- 45 year old Caucasian woman with chronic cough
- Chest x-ray - abnormal
- Three sputum specimens obtained
- She was started on a 4-drug TB treatment regimen
- Sputum cultures grew *M. kansasii*





Mycobacterium kansasii



- First described by Buhler and Pollack as the “yellow bacilli” in 1953 and later named in 1955 by Hauduroy.
- Most cases are associated with progressive disease

Buhler VB, Pollack A. Am J Clin Pathol 1953;23:363-74

Mycobacterium kansasii Outcomes of Treatment

Study	N	Regimen	Duration mos	Conversion	Cure*	Failure	Recurrence
Ahn, 1983	40	H/R/E SM biw for 3 mo	12	Median – 5.5 weeks	ND	0	2.5%
Santin, 2009	75	H/R/E SM for 2-3 mo	12	ND	83%	0	6.6%
Sauret, 1995	14 14	H/R/E H/R/E	12 18	100%, mean-4.5±2.0	93% 100%	0	3.5% 0
Evans, 1996	47	H/R/E±Z	Mean-10.3	ND	79%	ND	0
BTS, 1994	173	R/E	9	89% by 3 mo	89%	1	9.7%

*Cure was nearly 100% when non-mycobacterial deaths and lost to follow-up patients are excluded

Outcomes With Clarithromycin-based Regimen

Study	N	Regimen	Mean Duration, months*	Mean Culture Conversion, months	Cure n (%) **	Failure n (%)	Recurrence n (%)
Griffith D, 2003	18	Clarithromycin Ethambutol Rifampin, given tiw	13.3±0.8	1.0 ± 0.9	14** (78)	0	0***
Shitrit D, 2006	56	Clarithromycin Ethambutol Rifampin, given daily	21.0±7.2	8.9 ± 10.3	56 (100)	0	ND

*At least 12 months of culture negativity
**Among completers, 100% cure rate
***Mean duration of follow-up was 46±8.0 mos

Griffith D, et al. CID 2003;37:1178-82
Shitrit D, et al. Chest 2006;129:771-76

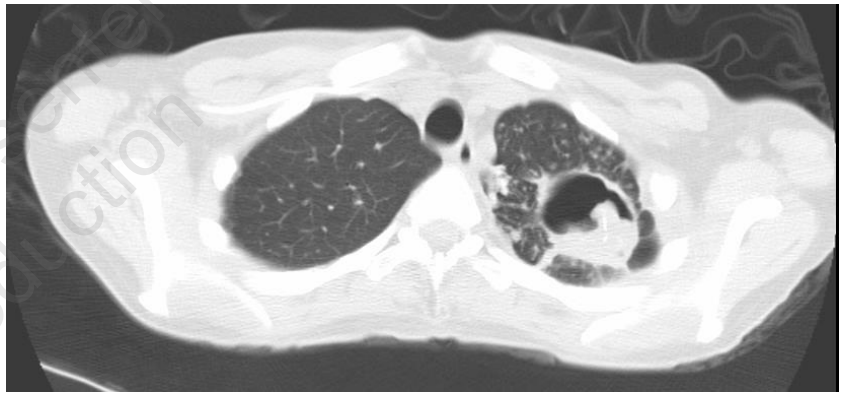
Recommended Treatment Regimens for *Mycobacterium kansasii*

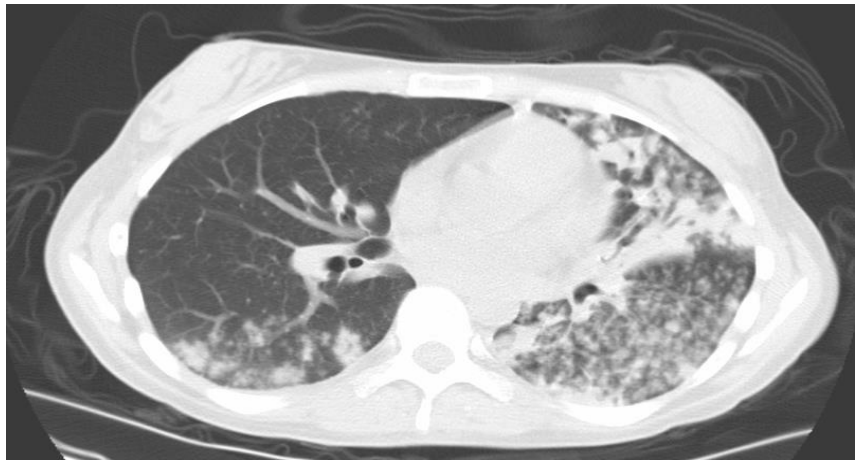
Phenotype	No. of Drugs	Preferred Regimen[a]	Dosing Frequency
Nodular-bronchiectatic or cavitary	3	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol	Daily
Nodular-bronchiectatic	3	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol	3 times weekly
Nodular-bronchiectatic or cavitary	3	Isoniazid Rifampicin (rifabutin) Ethambutol	Daily

Daley CL, et al. CID 2020;71:905-913 and Euro Respir J 2020;56:2000535

Treatment of *M. xenopi*

- 35 year old physician who developed cough, fever and progressive dyspnea
- Sputum specimens grew *M. xenopi* and *Aspergillus fumigatus*
- She was treated with azithromycin, moxifloxacin, rifampin, and amikacin
- Her fungal infection was treated with posaconazole
- She eventually underwent left upper lobe resection





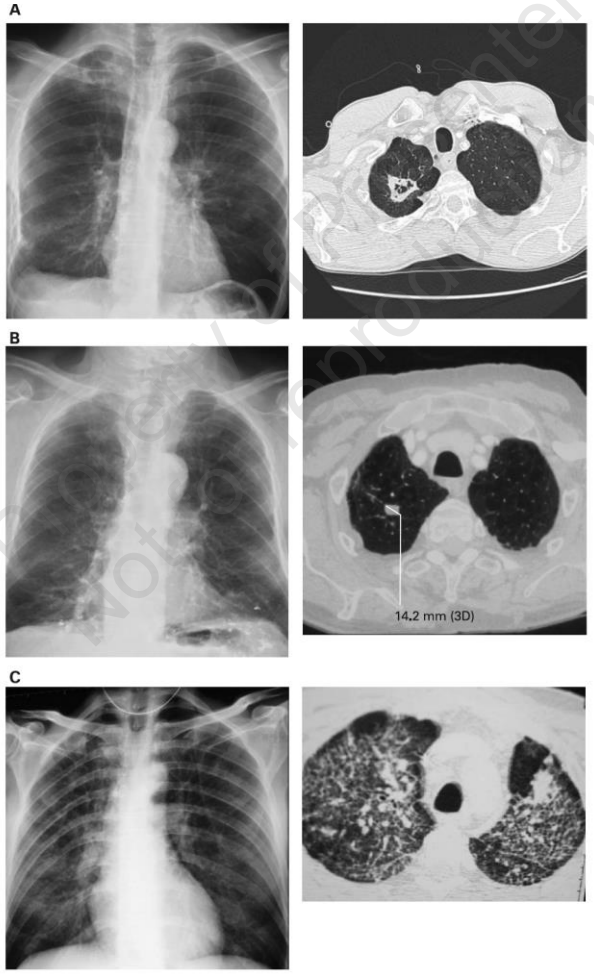
Mycobacterium xenopi

- Identified in 1959 from lesions on the skin of a South African toad, *Xenopus laevis*
- *M. xenopi* grows optimally at 45˚ C (113˚ F)
- 25/40 (51%) of patients met ATS criteria in the Netherlands

van Igen J. Emerg Infect Dis 2008;14:385

M. xenopi Pulmonary Infections in North-East France

- 13 hospitals in NE France (1983-2003)
- 136 patients
  - Cavitary – 39 (31%)
  - Solitary nodule – 41 (33%)
  - Infiltrative – 45 (36%)



- 80 (59%) patients were treated
- Rifamycin, ethambutol, INH, clarithromycin, fluoroquinolones
- After 36 mos, 69% had died
  - Acute infiltrative form associated with poor prognosis (p=0.001)
  - **Rifamycin**-containing regimens were associated with better prognosis (p=0.006)

Andrejak C, et al. Thorax 2009;64:291-296

Activity of Different Combinations in Murine Model of *M. xenopi*

	Timepoint Relative to the Start of Treatment			
Group	Week 2	Week 4	Week 8	Week 12
Untreated	6.95	6.93	7.76	7.79
CLR/EMB/RIF	5.75	6.57	5.68	4.69
CLR/EMB/RIF/AMK	5.86	5.22	4.83	4.58
MXF/EMB/RIF	6.42	6.19	5.97	5.57
MXF/EMB/RIF/AMK	5.67	5.25	4.49	4.23
MXF/CLR		6.07		5.23

CLR-clarithromycin, EMB-ethambutol, RIF-rifampicin, AMK-amikacin, MXF-moxifloxacin

Andrejak C, et al. J Antimicrob Chemother 2013;68:659-665

Randomized, Controlled Trial of Moxi vs Clari in *M. xenopi*

- Randomized, controlled trial in France
  - **Clarithromycin**, ethambutol, rifampin vs.
  - **Moxifloxacin**, ethambutol, rifampin
- Enrolled 56 patients (2/3 of planned)
- Results (24 patients with 6-month conversion data available):
  - 89% culture conversion at 6 months
  - No difference between regimens

Andrejak C et al. AJRCCM 2016;193:A3733

Recommended Treatment Regimens For *M. xenopi*

Phenotype	No. of Drugs	Preferred Regimen[a]	Dosing Frequency
Nodular bronciectatic	≥ 3	Azithromycin and/or moxifloxacin Rifampicin (rifabutin) Ethambutol	Daily (aminoglycoside may be used 3 times weekly)
Cavitary	≥ 3	Azithromycin and/or moxifloxacin Rifampicin (rifabutin) Ethambutol Amikacin IV (cavitary)	Daily (aminoglycoside may be used 3 times weekly)

Daley CL, et al. CID 2020;71:905-913 and Euro Respir J 2020;56:2000535

Question #2

A 65 year old woman with chronic cough and nodular bronchiectasis has two sputum specimens which grow *Mycobacterium simiae*. What would be the most appropriate next step:

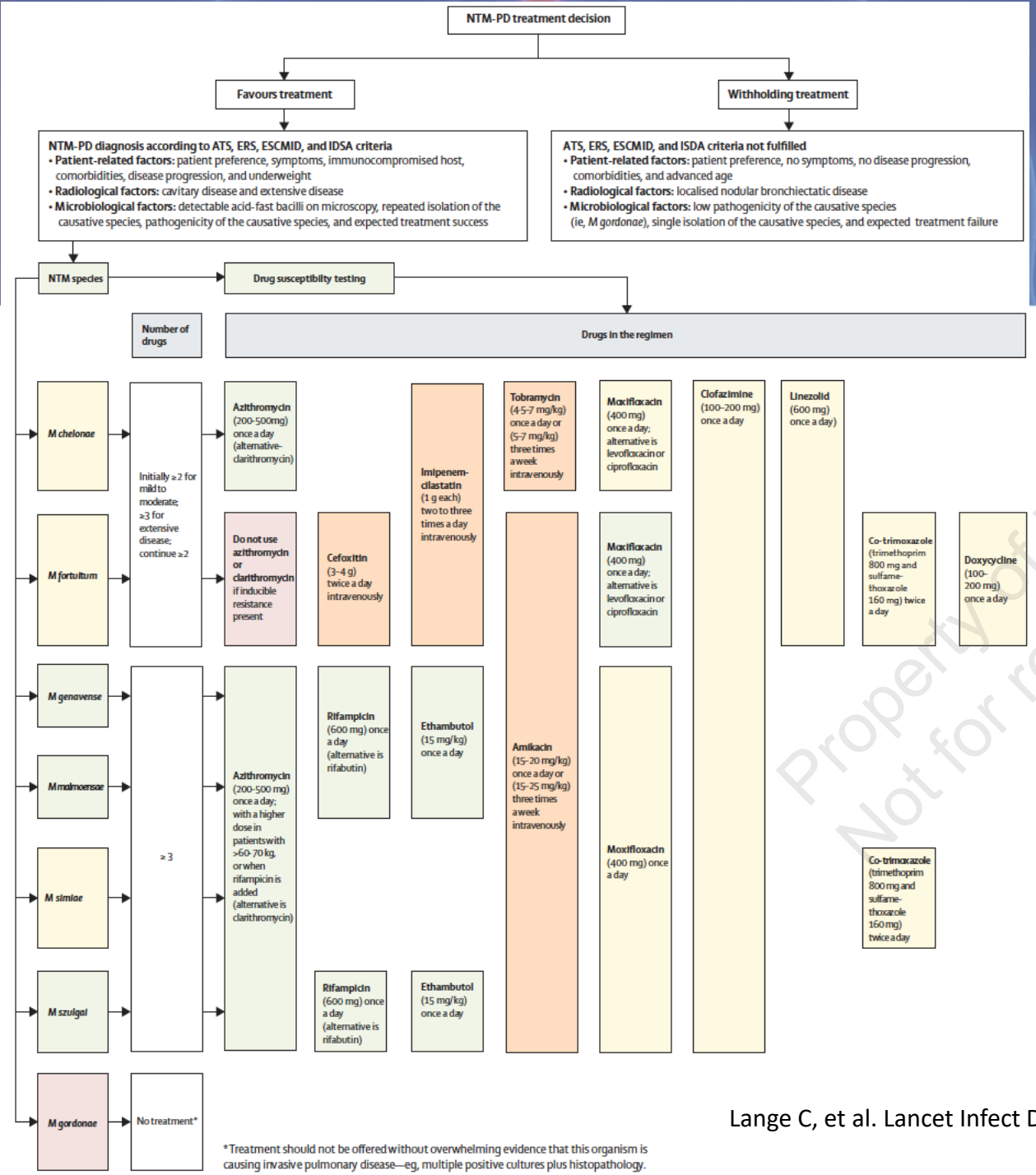
A. Initiate azithromycin, ethambutol, rifampin

B. Initiate moxifloxacin, clofazimine and trimethoprim-sulfamethoxazole

C. Follow without treatment for evidence of progressive disease

D. Discharge the patient as *M. simiae* is a water contaminant.

Treatment Algorithm for Other NTM



NTM species:
Green- high pathogenicity
Yellow – less pathogenic
Red – likely contaminant

Drug recommendations:
Green – drugs that are recommended
Yellow – drugs with less certainty
Orange – intravenous
Red - should not be used

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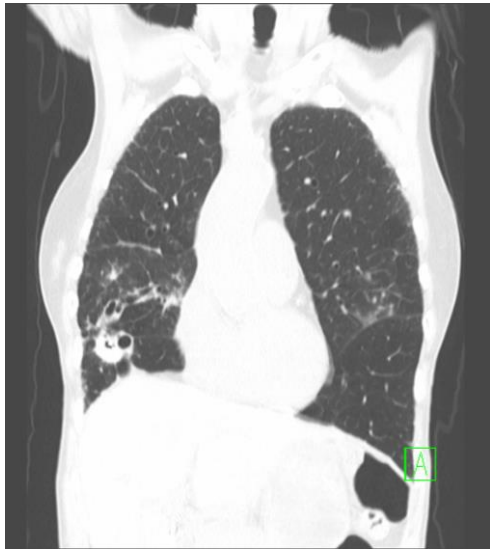
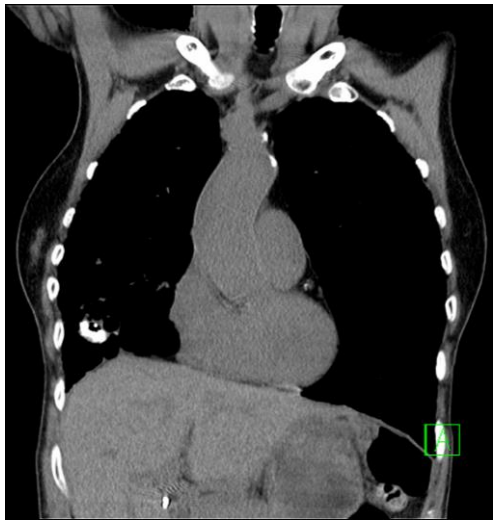
Lange C, et al. Lancet Infect Dis 2022;22.e178-90

Treatment of *M. malmoense*

- 68 year old women with Sjogren's syndrome and rheumatoid arthritis
- Presented with fatigue, minimal dry cough
- BAL grew *M. malmoense*
- Attempts at treatment unsuccessful due to drug-related toxicity
- Followed for over 5 years with no evidence of progression





Mycobacterium malmoense

- **Etymology:** mal.mo.en'se. N.L. neut. adj. *malmoense*, of or belonging to Malmö, Sweden, the source of the strains on which the original description is based
- **Effective publication:** Schröder KH, Juhlin I. *Mycobacterium malmoense* sp. nov. *International Journal of Systematic Bacteriology* 1977; **27**:241-246
  - First described in 4 patients from Malmo and Lund, Sweden
- **Systematic review:** two randomized controlled trials and three retrospective cohort studies. In addition, two systematic reviews were identified that addressed treatment outcomes or treatment recommendations for *M. malmoense* pulmonary disease.
- **Source:** Isolated from fresh water and soil
- **Distribution:** One of the most common NTM in northern Europe
- **Clinical forms:** Mainly pulmonary disease. Extrapulmonary and disseminated disease have also been described. 32/40 (80%) met ATS criteria for disease in the Netherlands
- **Risk factors for pulmonary disease:** Underlying pulmonary disease

https://www.bacterio.net/genus/mycobacterium

Lange C, et al. Lancet Infect Dis 2022;22.e178-90; Hoefsloot W, Eur Respir J, 2009; 34:926-931

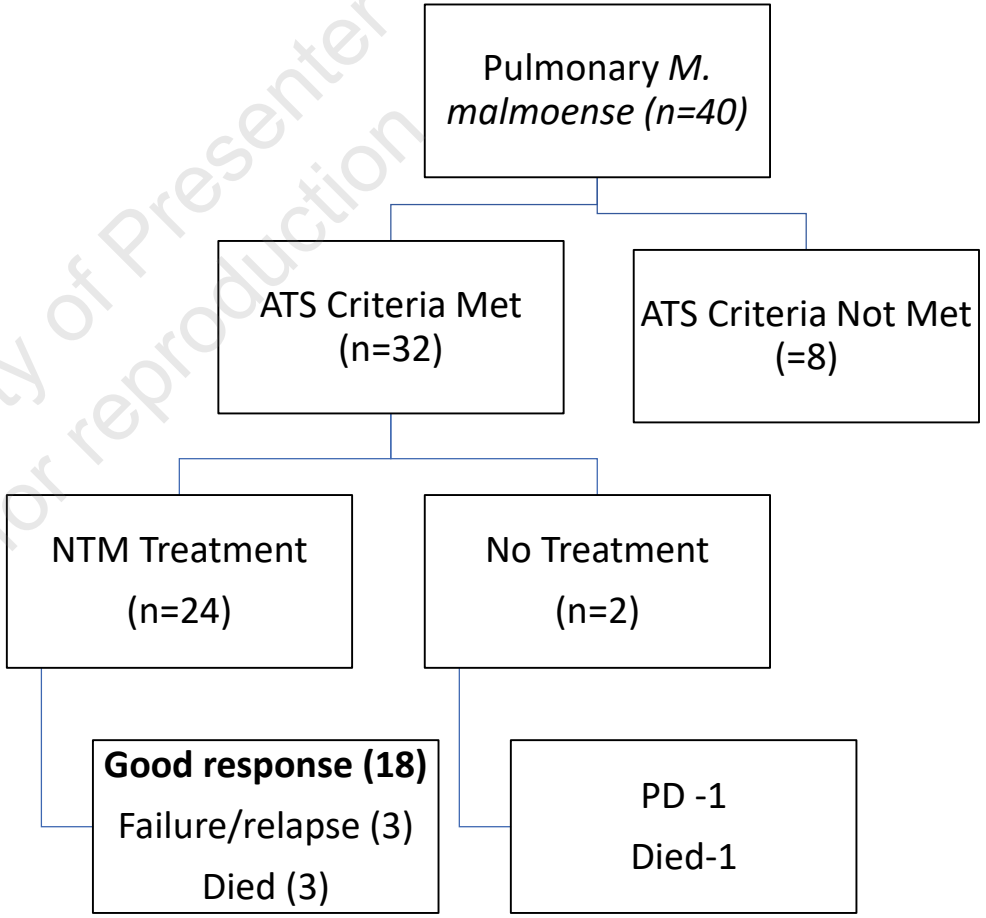
MIC_{50} and MIC_{90} for *M. malmoense*

Drug	*M. malmoense (n=31)*
Clarithromycin	**0.12/1**
Ciprofloxacin	**1/4**
Moxifloxacin	**<0.12/1**
Linezolid	2/8
Clofazimine	**0.06/0.12**
Amikacin	**<1/2**
Tobramycin	NT
Co-trimoxazole	**1/2**
Doxycyline	16/>16

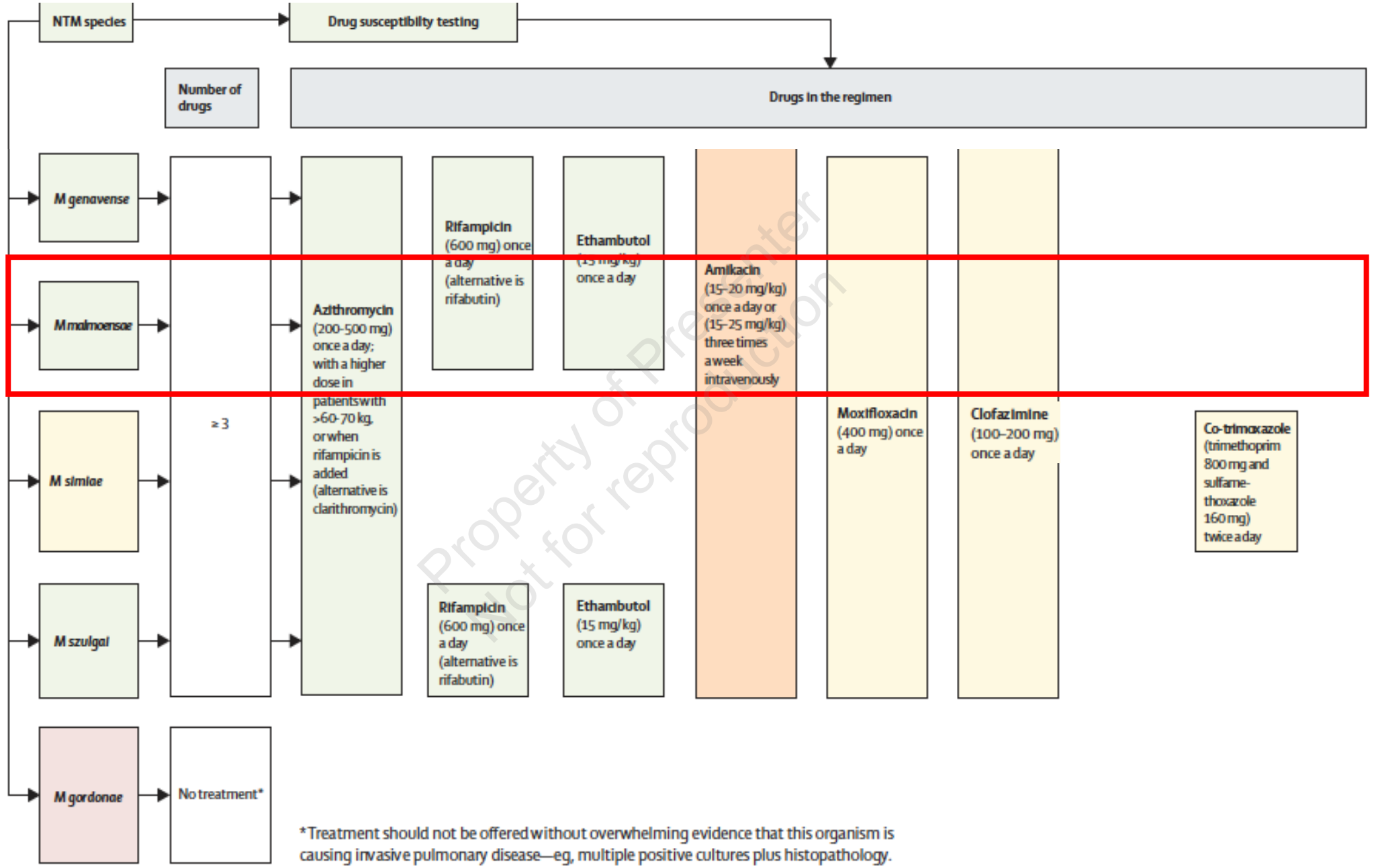
Lange C, et al. Lancet Infect Dis 2022;22.e178-90

Treatment Outcomes - Pulmonary Infection with *M. malmoense*

- Patients with pulmonary *M. malmosense* in the Netherlands
- Retrospective design
- Regimens included various combinations including macrolides and fluoroquinolones
- Mean duration of therapy – 12 months (1-26)



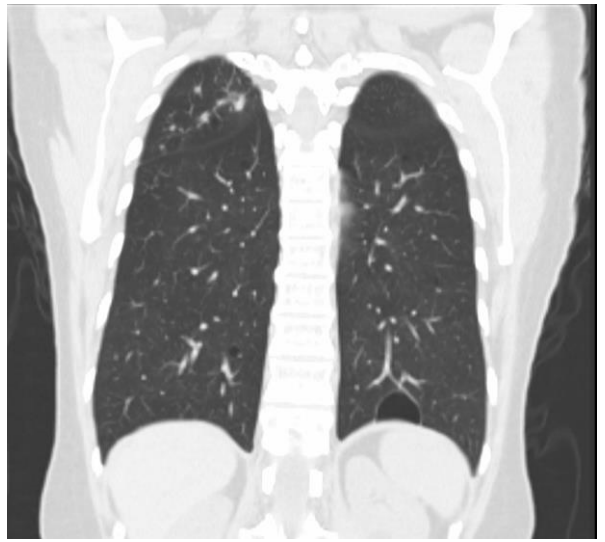
Hoefsloot W, et al. Eur Respir J 2009;34:926-931

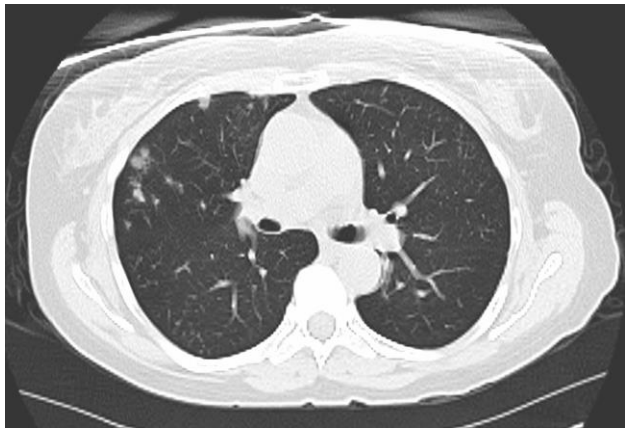


*Treatment should not be offered without overwhelming evidence that this organism is causing invasive pulmonary disease—eg, multiple positive cultures plus histopathology.

Treatment of *M. simiae*

- 66 year old woman from Alaska
- Presented with myalgias, night sweats, fatigue, jaw pain and cough
- Sputum cultures grew MAC so she was treated with azithromycin, rifampicin, and ethambutol
- After two months of therapy, all cultures positive for *M. simiae*
- Still culture positive after 6 months so 8 weeks of IV amikacin given
- Despite 18 months of therapy all cultures remained positive for *M. simiae!*





Mycobacterium simiae

- **Etymology:** si'mi.ae. L. masc./fem. n. *simia*, an ape; L. gen. masc./fem. n. *simiae*, of an ape
- **Effective publication:** Karassova V, Weissfeiler J, Krasznay E. Occurrence of atypical mycobacteria in Macacus rhesus. *Acta Microbiol Acad Sci Hung* 1965; **12**:275-282.
  - First isolated from rhesus macaques in 1965
- **Systematic review:** 11 case reports and case series - 197 patients with *M. simiae* pulmonary disease.
- **Source:** Isolated from water and soil. Found in water networks.
- **Distribution:** Worldwide. Particularly common in Isolated arid regions (Israel, Lebanon, Iran, India, Cuba, desert SW of US)
- **Clinical forms:** Pulmonary and extrapulmonary disease. Only 4 to 21% of people with *M. simiae* isolates fulfill diagnostic criteria for pulmonary disease
- **Risk factors for pulmonary disease:** COPD, bronchiectasis, smoking

https://www.bacterio.net/genus/mycobacterium
Lange C, et al. Lancet Infect Dis 2022;22.e178-90

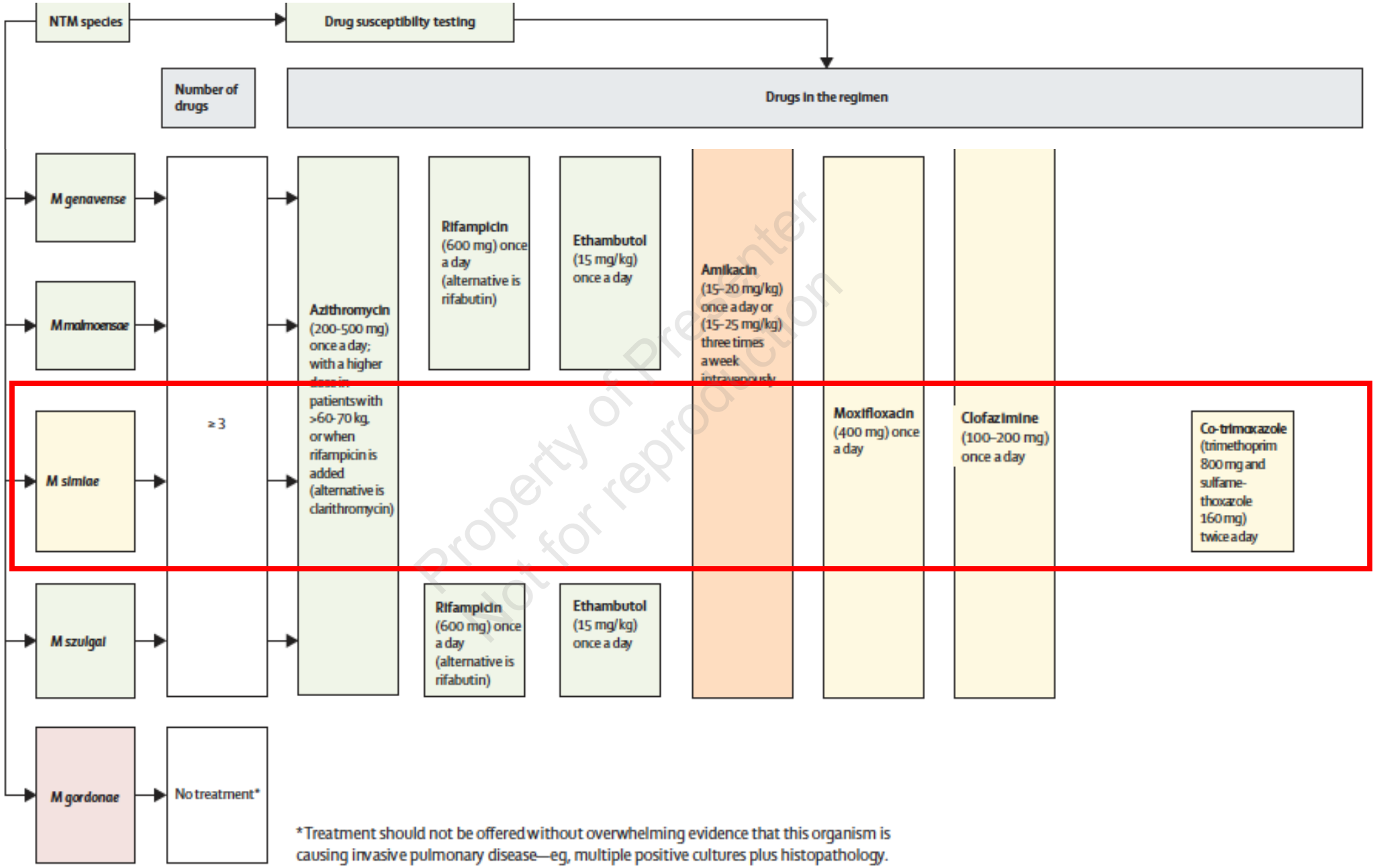
MIC_{50} and MIC_{90} for *M. simiae*

Drug	*M. simiae (n=21)*
Clarithromycin	**4/8**
Ciprofloxacin	16/>16
Moxifloxacin	**2/>8**
Linezolid	16/32
Clofazimine	**<0.12/0.25**
Amikacin	**8/16**
Tobramycin	NT
Co-trimoxazole	**4/>8**
Doxycyline	16/16

Lange C, et al. Lancet Infect Dis 2022;22.e178-90

Treatment Outcomes for *M. simiae*

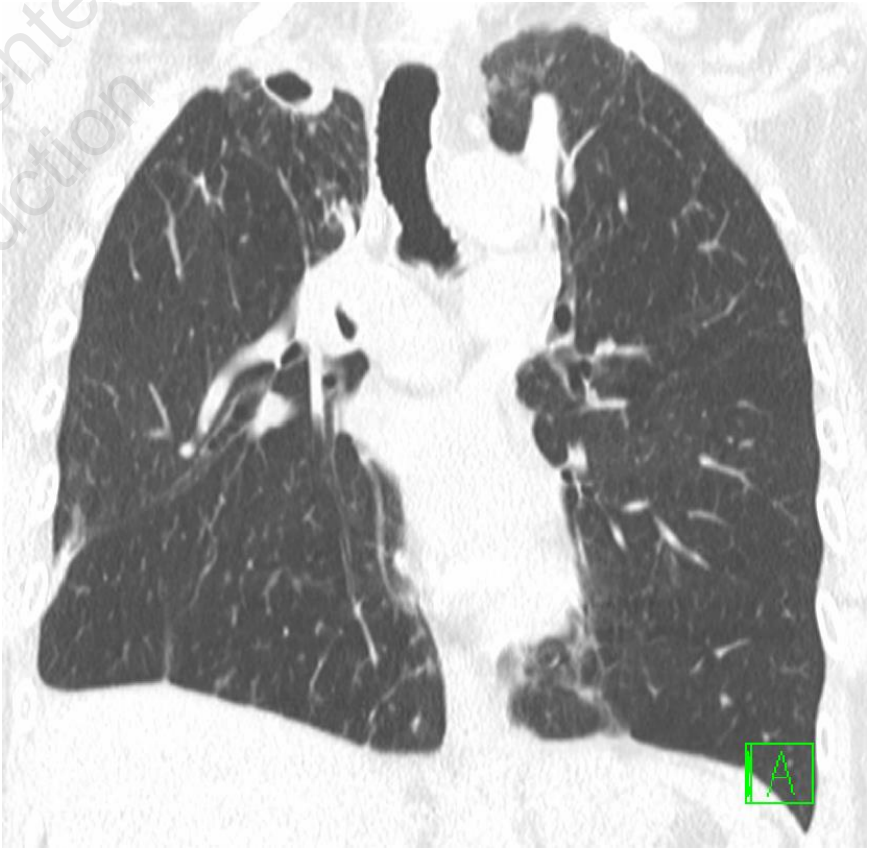
Study	Country	N	Regimen	Outcomes
Barzilai A, 1998	Israel	3	**Clarithromycin** Ciprofloxacin Ethambutol	Successful in AIDS patients with disseminated *M. simiae* after 24 months f/u. Also started on ART
Van Ingen J, 2008	Netherlands	3	**Macrolide** Ethambutol Other	One improved, One relapsed One died
Qvist T, 2013	Denmark	1	**Clarithromycin** Moxifloxacin Trim-Sulfa	Negative cultures at one year in bilateral lung transplant recipient
Shitrit D, 2008	Israel	102	**Clarithromycin** Ethambutol Rifampin	No failures/relapses during median of 24 mos f/u
Baghaei P, 2012	Iran	26	**Clarithromycin** Ofloxacin Trim-Sulfa	24 (92%) “cured” No recurrences over 2 yrs f/u



*Treatment should not be offered without overwhelming evidence that this organism is causing invasive pulmonary disease—eg, multiple positive cultures plus histopathology.

Treatment of *M. szulgai*

- 82 year old woman with chronic cough but otherwise very active and healthy
- Previously treated for macrolide resistant, cavitary, MAC pulmonary disease with VATS right upper lobectomy
- Now growing M. szulgai with new upper lobe cavity



Mycobacterium szulgai

- **Etymology:** szul'ga.i. N.L. gen. masc. n. *szulgai*, of Szulga, named after T. Szulga, a Polish microbiologist
- **Effective publication:** Marks J, Jenkins PA, Tsukamura M. *Mycobacterium szulgai*--a new pathogen. *Tubercle* 1972; **53**:210-214.
  - First described in 1972 seven patients with pulmonary and extrapulmonary disease
- **Systematic review:** 25 retrospective case reports and case series - 44 patients with *M. szulgai* pulmonary disease.
- **Source:** Rarely isolated from water supply networks and soil. Accounts for <1% of NTM isolates
- **Distribution:** Worldwide.
- **Clinical forms:** Mainly caused pulmonary disease mimicking TB. Of the 21 patients, 16 (76%) met the American Thoracic Society diagnostic criteria and were thus likely to have *M. szulgai* disease.
- **Risk factors for pulmonary disease:** COPD, smoking

https://www.bacterio.net/genus/mycobacterium

Lange C, et al. Lancet Infect Dis 2022;22.e178-90

MIC_{50} and MIC_{90} for *M. szulgai*

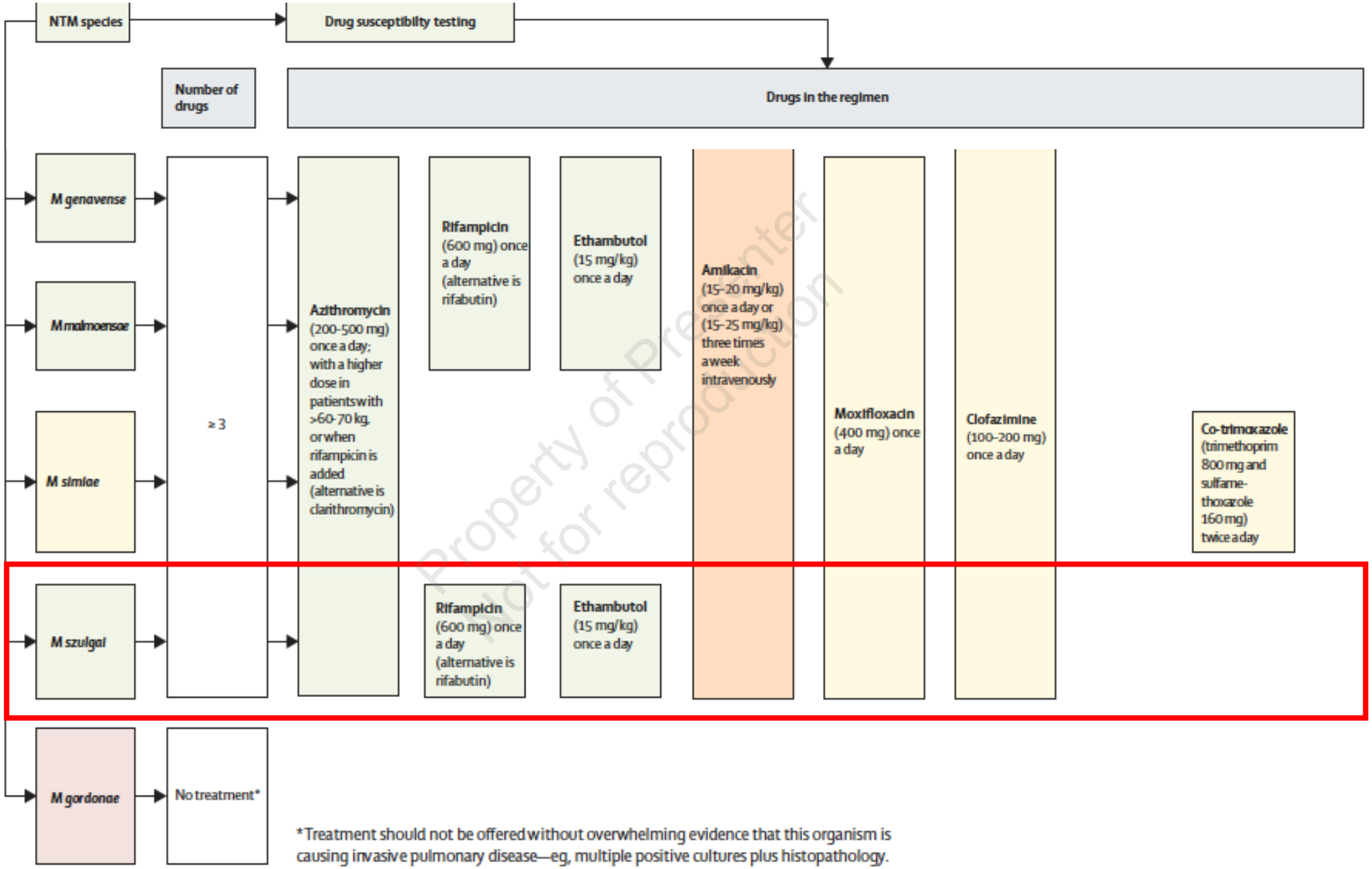
Drug	*M. szulgai (n=9)*
Clarithromycin	**0.25/2**
Ciprofloxacin	8/>16
Moxifloxacin	**1/4**
Linezolid	2/4
Clofazimine	**0.06/0.12**
Amikacin	**4/16**
Tobramycin	NT
Co-trimoxazole	**0.25/2**
Doxycyline	4/>16

Lange C, et al. Lancet Infect Dis. 2022;22:e178-e190

Mycobacterium szulgai

- A systematic literature review identified 25 retrospective case reports and case series, including a total of 44 patients with *M szulgai* pulmonary disease
- Most patients were treated with a combination of rifampicin, ethambutol, and clarithromycin or azithromycin.
- Treatment duration was variable; 12 months was most frequently used (range 5–18 months).
- The outcome was favorable in 85% of patients treated with rifampicin, clarithromycin, and azithromycin combination regimens; no relapses were observed among the five (11%) patients that post-treatment follow-up was available for.
- The cure rate was 81% among 21 patients treated with clarithromycin and azithromycin sparing regimens

Lange C, et al. Lancet Infect Dis. 2022;22:e178-e190



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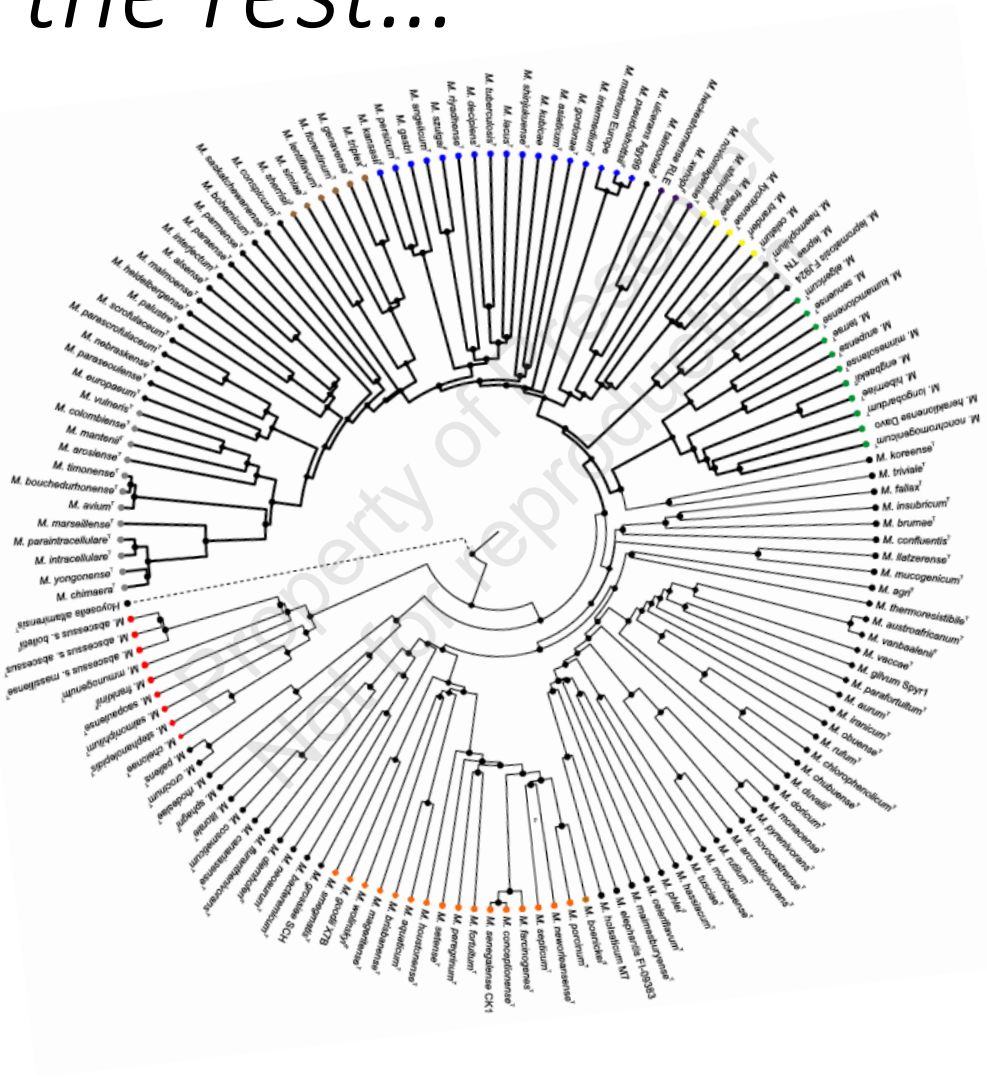
What about all the rest…



Tortoli E, et al. Inf Gen Evol 2017;56:19

http://www.bacterio.net/mycobacterium.html