

What's new in the NTM treatment guidelines?

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October 28, 2020

Financial Disclosures

- Consultant: Insmmed, Hill-Rom
- Advisory Board: Insmmed, Hill-Rom
- Clinical trial: Hill-Rom

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

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2007 NTM guidelines

2 societies

- American Thoracic Society
- Infectious Disease Society of America

2020 NTM guidelines

4 societies

- American Thoracic Society
- Infectious Disease Society of America
- European Respiratory Society
- European Society of Clinical Microbiology and Infectious Diseases

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- 22 PICO questions and 31 recommendations
- Focused on MAC, *M.abscessus*, *M.kansasii*, and *M.xenopi*

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Diagnostic criteria for NTM pulmonary disease

- Remains the same for the 2007 and 2020 guidelines
- Require both clinical and radiographic criteria for NTM
- Exclusion of other diagnosis
- Microbiologic criteria:
 1. Positive culture results from at least two separate sputum samples, **or**
 2. Positive culture from at least one bronchial wash or lavage, **or**
 3. Transbronchial or other lung biopsy with mycobacterial histologic features and positive culture for NTM or biopsy showing mycobacterial histologic features and one or more sputum or bronchial washings that are culture positive for NTM

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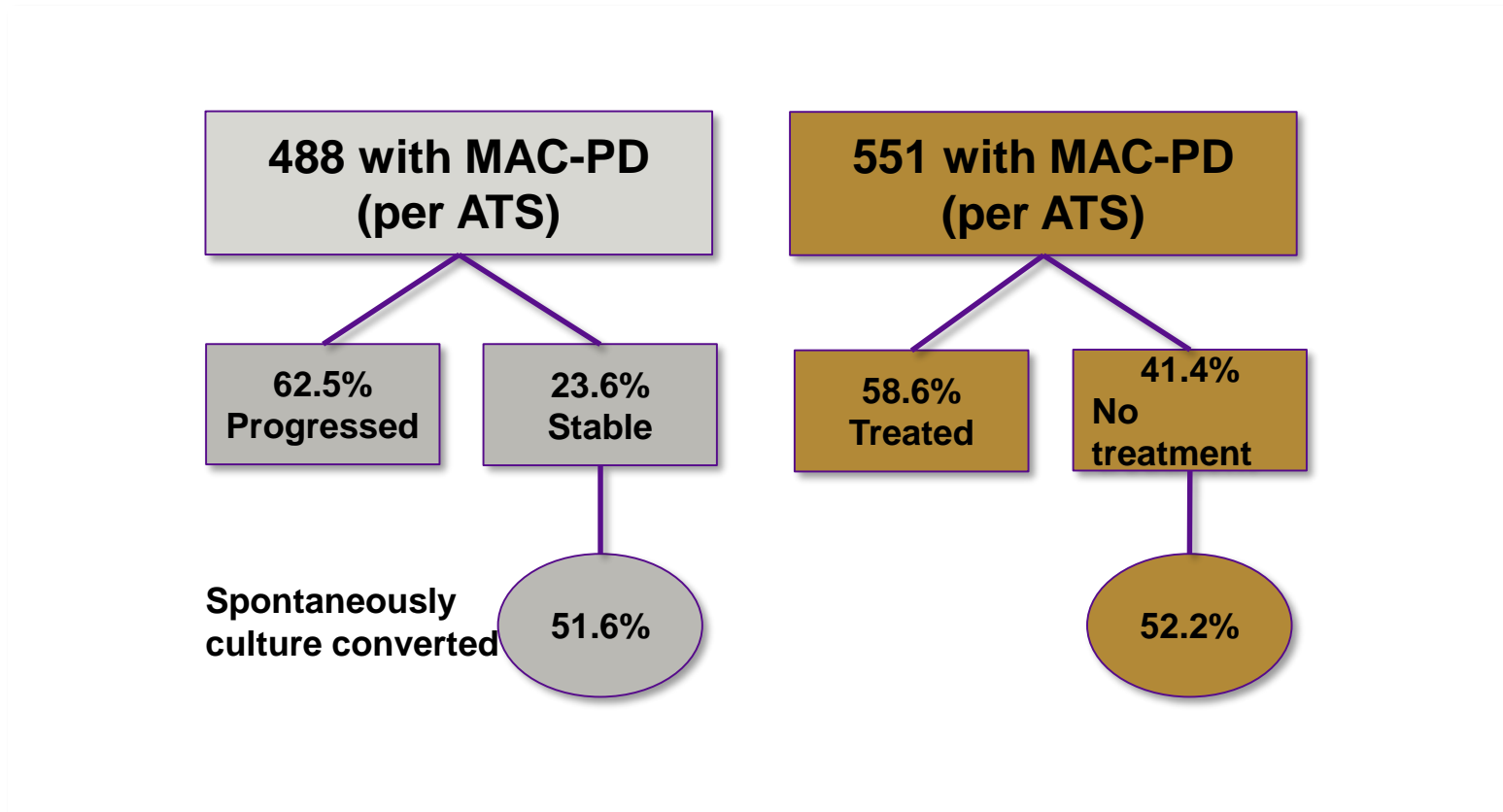
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Treatment of NTM pulmonary disease

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

Progression of NTM Pulmonary Disease

In Those Who Meet ATS/IDSA Diagnostic Criteria



Hwang JA et al. *Eur Respir J.* 2017
Byoung SK et al. *Resp Med.* 2019

Who to Treat?

Risk Factors Associated with Progression

Host/Demographic Factors	Laboratory Factors	Radiographic Factors	Microbial Factors
<ul style="list-style-type: none">• Male gender• Older age• Presence of comorbidities• Low body mass index	<ul style="list-style-type: none">• Elevated inflammatory indices (ESR, CRP)• Anemia• Hypoalbuminemia	<ul style="list-style-type: none">• Fibrocavitary• Extent of disease	<ul style="list-style-type: none">• Bacterial load• Species

Hwang JA et al. *Eur Respir J.* 2017

Kwon BS et al. *Resp Med.* 2019

Moon SM et al. *Resp Med.* 2019

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- For patients with MAC or *m. abscessus*, we suggest susceptibility-based treatment for macrolides and amikacin (*conditional recommendation, very low certainty in estimates of effect*).

Antimicrobial Agent	MIC, ug/mL			Comments
	S	I	R	
First Line				
Clarithromycin	≤ 8	16*	≥ 32	Class drug for macrolides
Amikacin (IV)	≤ 16	32	≥64	
Amikacin (liposomal inhaled)	≤ 64	-	≥ 128	

Woods et al, *CLSI Supplement*, 2018.

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Treatment of macrolide-susceptible MAC

- We recommend a 3-drug regimen that includes a macrolide over a 3-drug regimen without a macrolide (*strong recommendation, very low certainty in estimates of effect*).

	Culture Conversion
Macrolide susceptible	
Non cavitary	80%
Cavitary	50%-80%
Macrolide resistant	
No surgery/aminoglycoside*	5%
Some surgery/aminoglycoside	15%
Surgery + prolonged aminoglycoside*	80%

Griffith DE et al. *Am J Respir Crit Care Med.* 2006
 Jeong BH et al. *Am J Respir Crit Care Med.* 2015
 Moon SM et al. *Eur Respir J.* 2016

Wallace R et al. *Chest.* 2014
 Koh WJ et al. *Eur Respir J.* 2017
 Morimoto K et al. *Ann Am Thorac Soc.* 2016

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Treatment of macrolide-susceptible MAC

- We suggest azithromycin-based treatment regimens rather than clarithromycin-based regimens (*conditional recommendation, very low certainty in estimates of effect*).
- We suggest a treatment regimen with at least 3 drugs (including a macrolide and ethambutol) over a regimen with 2 drugs (a macrolide and ethambutol) (*conditional recommendation, very low certainty in estimates of effect*).

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Macrolide-susceptible MAC

- In patients with noncavitary nodular/bronchiectatic macrolide-susceptible MAC pulmonary disease, we suggest a 3 times a week macrolide-based regimen rather than a daily macrolide based regimen (*conditional recommendation, very low certainty in estimates of effect*).
- In patients with cavitary or severe/advanced nodular bronchiectasis macrolide-susceptible MAC pulmonary disease, we suggest a daily macrolide-based regimen (*conditional recommendation, very low certainty in estimates of effect*).

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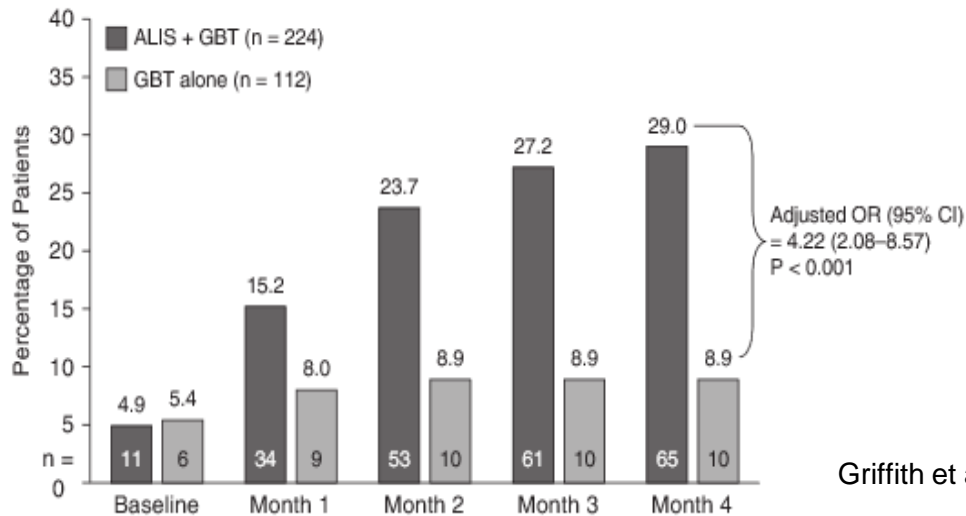
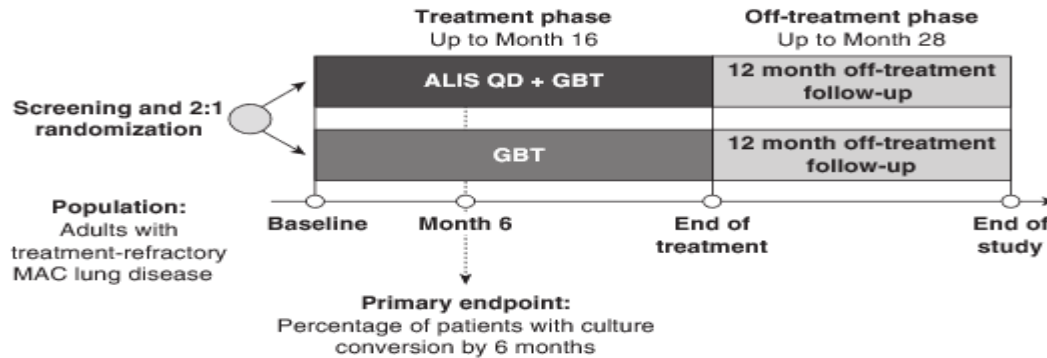
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Inhaled liposomal amikacin

- In patients with newly diagnosed MAC pulmonary disease, we suggest neither inhaled amikacin (parental) nor amikacin liposome inhalation suspension (ALIS) be used as part of the initial treatment regimen (*conditional recommendation, very low certainty in estimates of effect*).
- In patients with MAC pulmonary disease who have failed therapy after at least 6 months of guideline-based therapy, we recommend addition of ALIS to the treatment regimen rather than a standard oral regimen, only (*strong recommendation, moderate certainty in estimates of effect*).

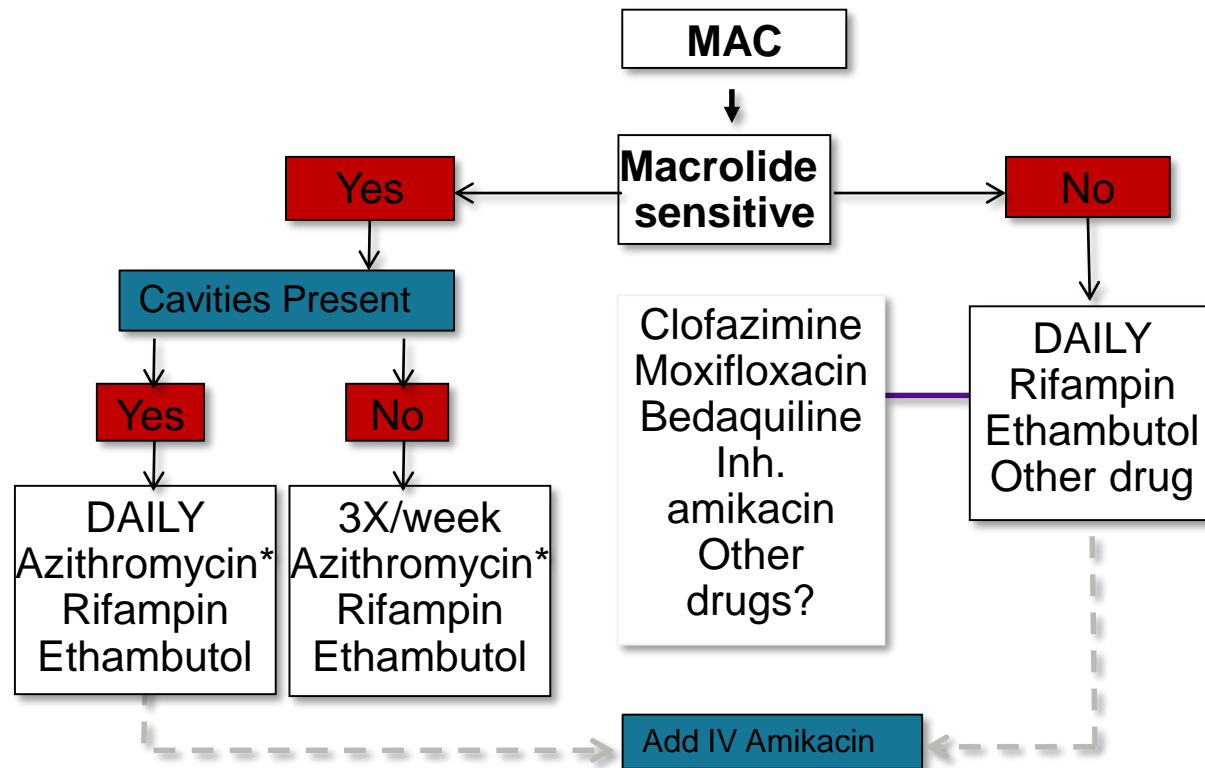
Amikacin Liposome Inhalation Suspension for Treatment-Refractory Lung Disease Caused by *Mycobacterium avium* Complex (CONVERT)

A Prospective, Open-Label, Randomized Study



Griffith et al, AM J Resp Crit Care Med, 2018

Treatment of Pulmonary *Mycobacterium avium* Complex



* clarithromycin is an alternative

Duration: 12 mos culture negativity

Major points

- Diagnostic criteria for NTM pulmonary disease remains the same.
- Treatment may be preferred over watchful waiting, specifically in those who have risk factors for progression.
- Azithromycin is preferred over clarithromycin.
- Inhaled liposomal amikacin is approved for those with refractory MAC.
- Susceptibilities can help direct treatment in NTM.

THANK YOU!

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