

# The Art & Science of Treating NTM Lung Disease: Managing Difficult Treatments & How to Get Patients Back on Track

MC, MAC and Me: What a long strange trip it's been

David E. Griffith, MD  
Professor of Medicine  
University of Texas Health Science Center  
Tyler, TX



# Conflict of Interest/Disclaimer

- I was a co-investigator on INS-112, a study of amikacin liposome inhalation suspension for treatment of refractory *M. avium* complex and *M. abscessus* lung diseases
- I am a co-investigator on INS-212 CONVERT and INS-312 CONVERT studies of amikacin liposome inhalation suspension for treatment of *M. avium* complex lung disease
- I am a co-investigator on an Insmed sponsored IIR study of amikacin liposome inhalation suspension for treatment of *M. abscessus* lung disease

# MC, her own self



# Caveat Ausculator

- UTHSCT EMR introduced in mid 2000's, all prior paper medical records destroyed



# MC

- Born 1941, lifetime East TX resident
- Worked for small town newspaper, keeper and guardian of local history
- Approximately 20 pack year history of cigarette smoking, quit in mid 1980's
- Developed persistent cough mid '90's, diagnosed with "bronchitis"
- 18-24 months later, diagnosed with MAC lung disease

# In the beginning...

- Chest CT scan with “extensive cylindrical and saccular bronchiectasis” with RML destruction
- Mixed nodular/bronchiectatic and cavitary picture
- Sputum 4+ AFB smear and culture positive for MAC, macrolide susceptible
- Spirometry with mild restriction

# MC Microbiology

- > 100 sputum AFB cultures between 2004 and 2018
- Initially all strongly (3-4+) smear and culture positive
- 8 month gap with no cultures 7/12 to 3/13, patient participating in Insmmed Arikayce study 112

# Initial Treatment Phase

## Treatment

- 1997 Started MAC therapy with TIW clarithromycin, rmp, ethambutol
- 1998 RML lobectomy for hemoptysis
- Peri-operative amikacin
- 1998 to '06: Some combination of macrolide, rifamycin, and ethambutol; daily, TIW
- Gaps in therapy and follow-up

## Meanwhile....

- Macrolide susceptible isolate
- Sputum remains strongly AFB smear and culture positive throughout these years
- Late 1990's MI without fixed CAD
- Develops clarithromycin intolerance
- Macrolide resistance emerges sometime in early 'oughts



# Middle phase: the dark star years

## Treatment

- 6/08-7/12: FQ, rmp, emb, inhaled amikacin
- Radiographically and clinically (PFT's) remarkably little change
- Major challenge is cough

## Meanwhile...

- Sputum remains strongly AFB smear and culture positive
- '08 daughter-in-law dies from severe strep infection
- '09 husband has CVA, severely debilitated
- '09 second MI without fixed CAD

# Dark star crashing: A glimmer of hope?

## Treatment

- 7/12 to 3/13: Arikayce study, emb, moxifloxacin, rmp
- 3/13 to 3/14: emb, cipro, rmp

## Meanwhile...

- MAC isolate amikacin resistant
- Insurance would not cover moxi
- Sputum AFB culture negative more often than positive after completing Arikayce study
- '13 husband dies
- '14 kitchen fire

# Recent therapy: I need a miracle every day...

## Treatment

- 3/14-2/16: Bedaquiline, strep IV, emb
- 2/16-2/17: Bedaquiline, inhaled amikacin, emb, azithromycin
- 2/17 ALIS added to bedaquiline, emb, azithromycin

## Meanwhile...

- Port placed with complications
- \$1000-\$2000/month co-paycoBedaquiline
- **(ATAMH)**:Patient found to have macrolide susceptible MAC isolate
- Sputum negative more often than positive after starting bedaquiline
- '15 and '16 pneumonia
- '16 house hit by lightning, kitchen flooded
- ALIS approved for compassionate use

# MC: Anti-mycobacterial medications 1998-2018

- Clarithromycin (rash)
- Azithromycin
- Rifampin
- Rifabutin (rash)
- Ethambutol
- Amikacin (IV and inhaled)
- Streptomycin (IV, hearing loss requiring hearing aids)
- Clofazimine (nausea)
- ALIS
- Bedaquiline
- Moxifloxacin
- Ciprofloxacin



# Microbiological Success!: The Golden Road to Unlimited Devotion

## Treatment

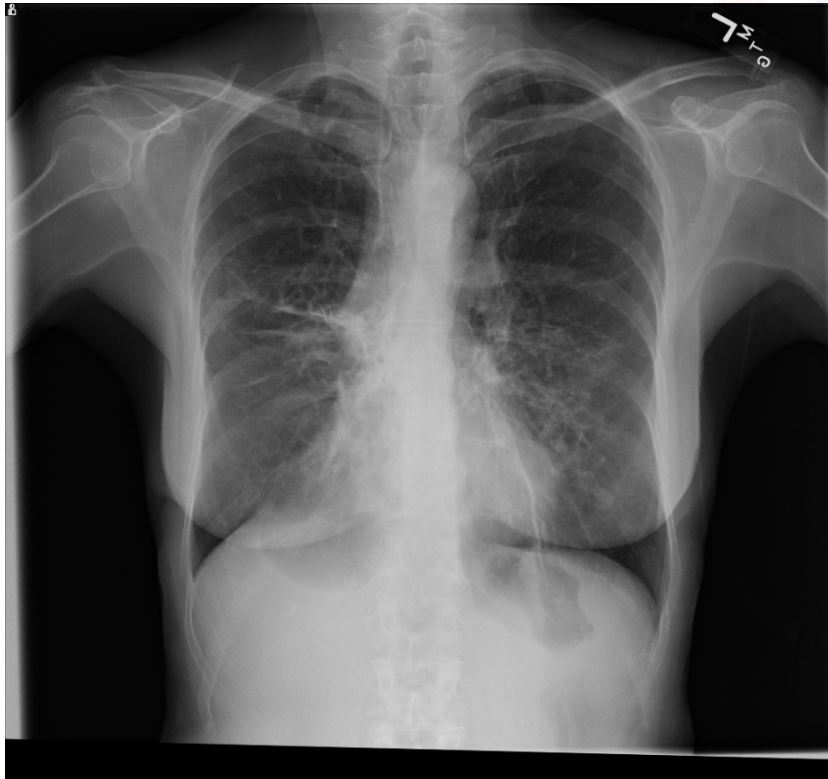
- 2/17- 2/18: Bedaquiline, emb, azi, ALIS
- MAC medications stopped intentionally for first time in 20 years
- 10/09 FVC 2.05 L (64% pred)  
FEV1 1.6 L (66% pred)

## Meanwhile....

- Sputum AFB culture negative for 12 consecutive months on therapy
- Sputum remains AFB culture negative since stopping MAC medications
- 1/18 FVC 1.78 L (62% pred)  
FEV1 1.11 L (51% pred)
- Severe cough, occasional hemoptysis

# MC Radiography

2007

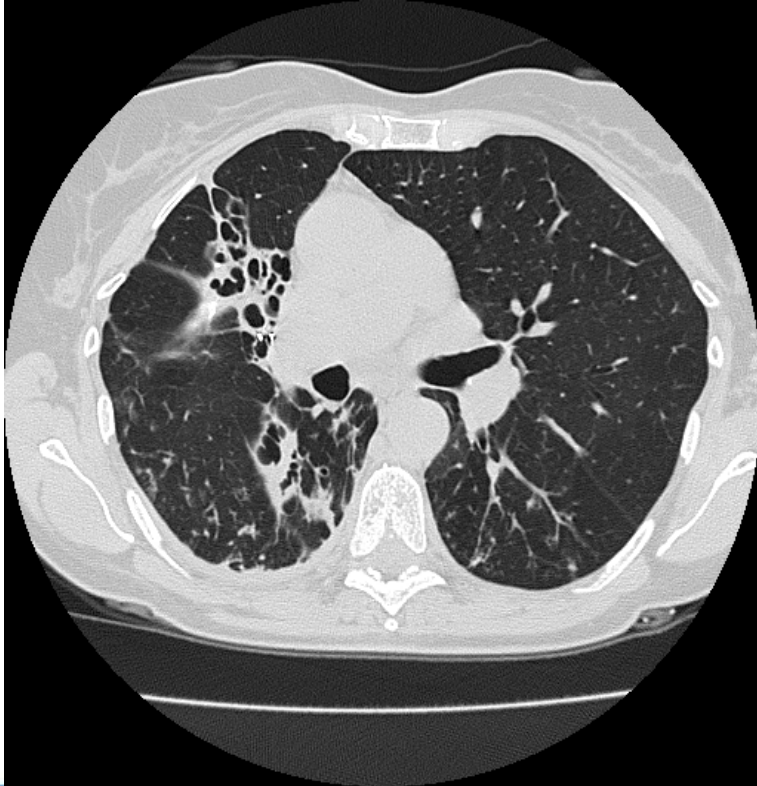


2018

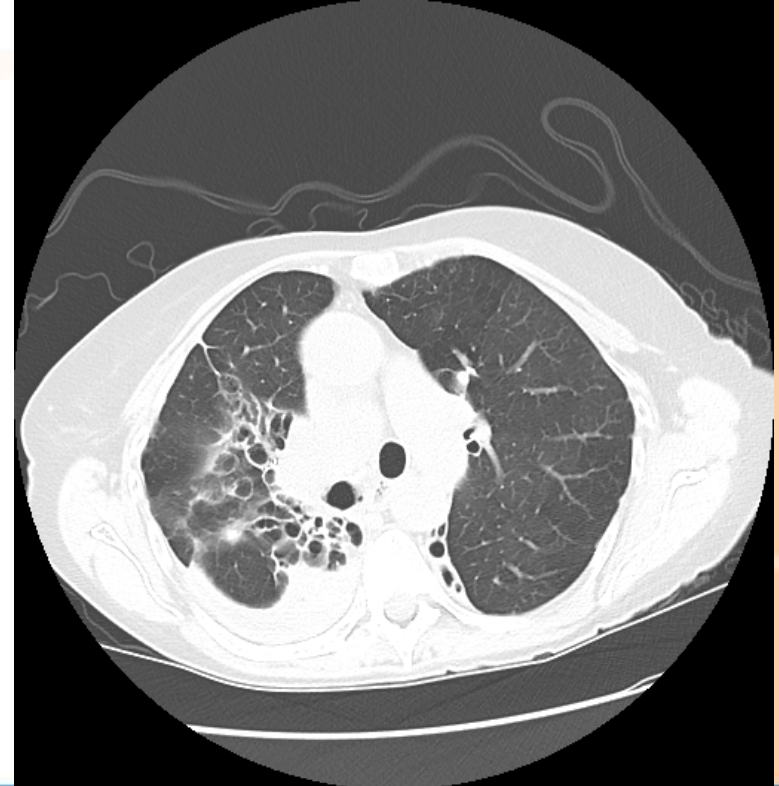


# MC Radiography

2007



2017



# Bacterial Species Isolated from MC sputum

- *Klebsiella*
- *Serratia*
- *Achromobacter*
- *Enterobacter*
- *Pseudomonas*
- *Stenotrophomonas*
- *Pantoea Agglomerans*



# Strategies attempted for controlling cough with, at best, transient success

- LABA: nebulized and inhaler
- LAMA: nebulized and inhaler
- ICS: nebulized and inhaler
- Oral steroid
- IV, oral and inhaled antibiotic
- Roflumilast
- Hypertonic Saline
- Hydrocodone

# Management Challenges in NTM: Impediments, opportunities and luck...

- Acquired drug resistance
- Drug Toxicity and Side Effects
- Limited Drug Choices
- Drug costs and availability (ALIS, bedaquiline)
- Co-morbidities



# MC and Some of Us We will get by.....



UT HEALTH  
NORTHEAST