

Financial Disclosures

- PI for clinical trials with Insmed/Aradigm/Novartis/Chiltern/Hill Rom (all bronchiectasis/NTM related)
- Consultant (ended 9/2018)
 - AIT Therapeutics
 - Insmed

Case

- 59 y/o F without significant PMH
- Recurrent respiratory infections over 3 years;
- CXR revealed mild increase in airways disease;
- CT finally performed after 3 years of cough



CT Chest from 2016

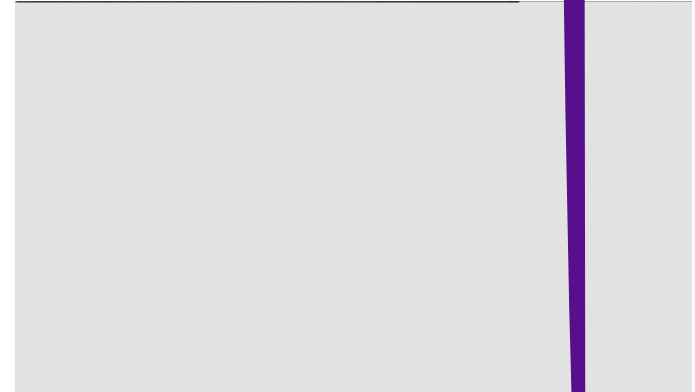
Case

- M. Abscessus subspecies abscessus
- Recurrent courses of combination of oral antibiotics with IV therapy for weeks to months
- IV tigecycline and IV amikacin with clofazimine and tedizolid for 3 months
- Then on oral therapy bedaquiline, clofazimine and inhaled amikacin

- And back on IV and then oral and back and forth.....

Mycobacterium abscessus

- Mycobacterium abscessus was first identified in a patient with a knee infection and SQ abscesses
- M. abscessus is the 2nd-3rd most common cause of lung disease due to NTM and the most common cause of lung disease due to a rapid grower
- The organism is highly resistant to antibiotics with current in vitro methods

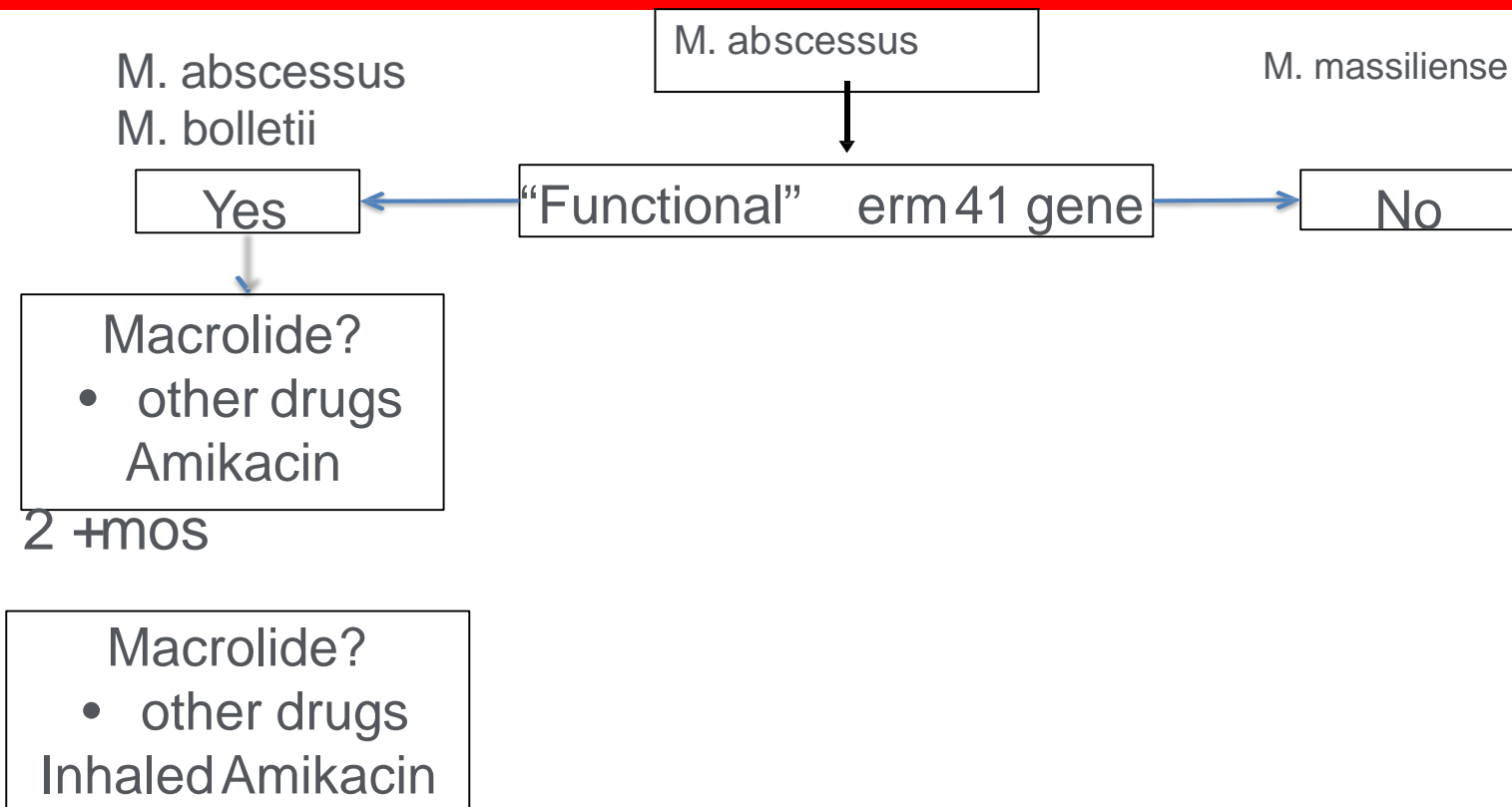


Isolated in 1950 from synovial fluid and buttock lesions in a 63 year old woman

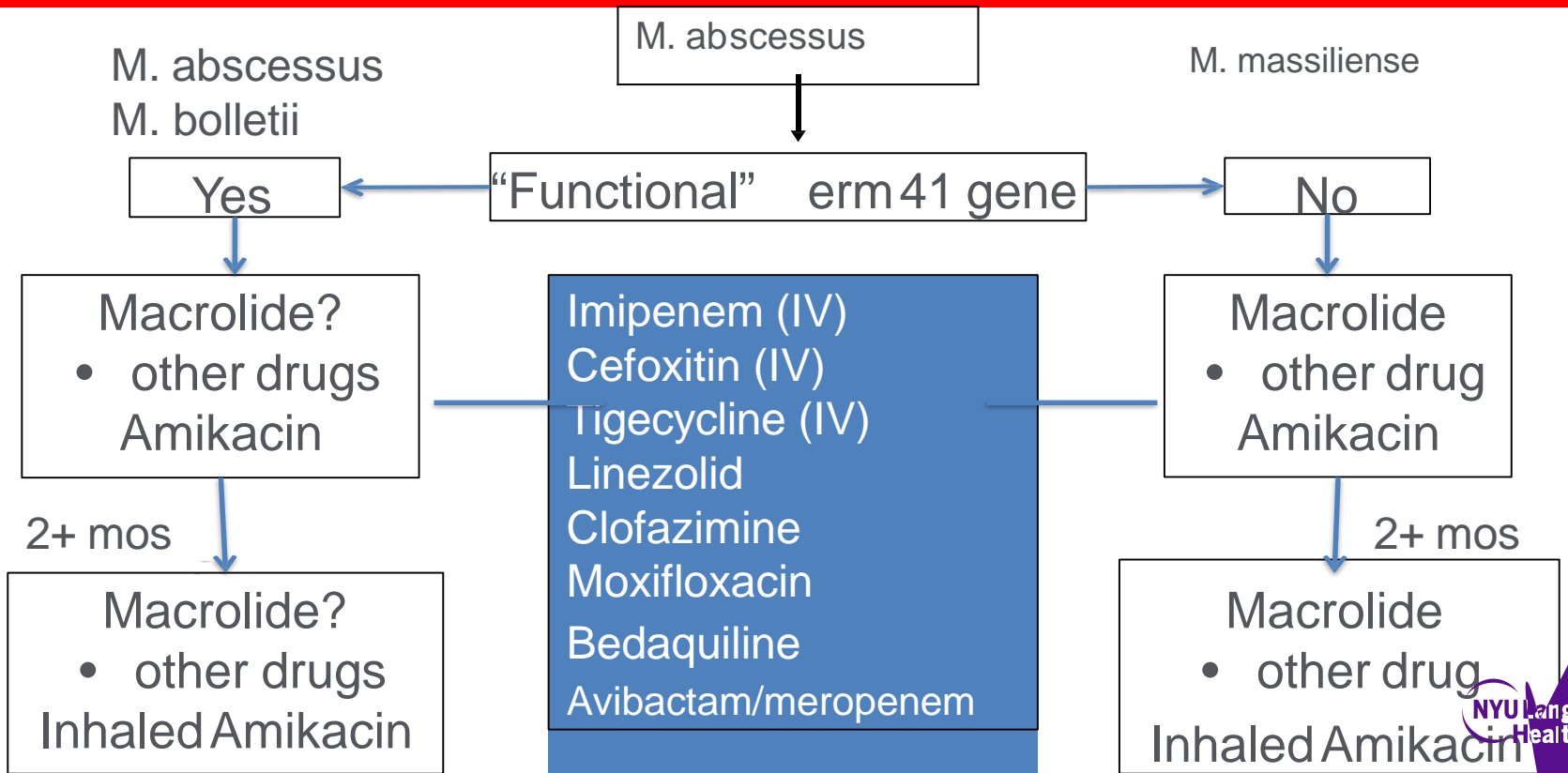
Current Common Options for Treatment

- Tigecycline IV
- Amikacin IV
- Cefoxitin IV
- Imipenem IV
- Moxifloxacin PO or IV
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Treatment of *M. abscessus*



Treatment of *M. abscessus* (Duration 12 months culture negativity)



DOES BEDAQUILINE WORK?

Preliminary Results of Bedaquiline as Salvage Therapy for Patients With Nontuberculous Mycobacterial Lung Disease
Philly, J, et al CHEST 2015; 148(2):499-506.

- Bedaquiline is an oral antimycobacterial agent belonging to the diarylquinolines class
- It appears to be effective for the treatment of MDRTB but has not been tested for NTM disease

- Preliminary Results of Bedaquiline as Salvage Therapy for Patients With Nontuberculous Mycobacterial Lung Disease Philley, J, et al CHEST 2015; 148(2):499-506
- A case series of off-label use of bedaquiline caused by MAC or Mab.
- 10 patients were reviewed (6 MAC, 4 Mab)
- Patients had refractory disease and were treated for 1-8 years prior to starting bedaquiline
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Emerging Pharmacologic Therapies -- Bedaquiline

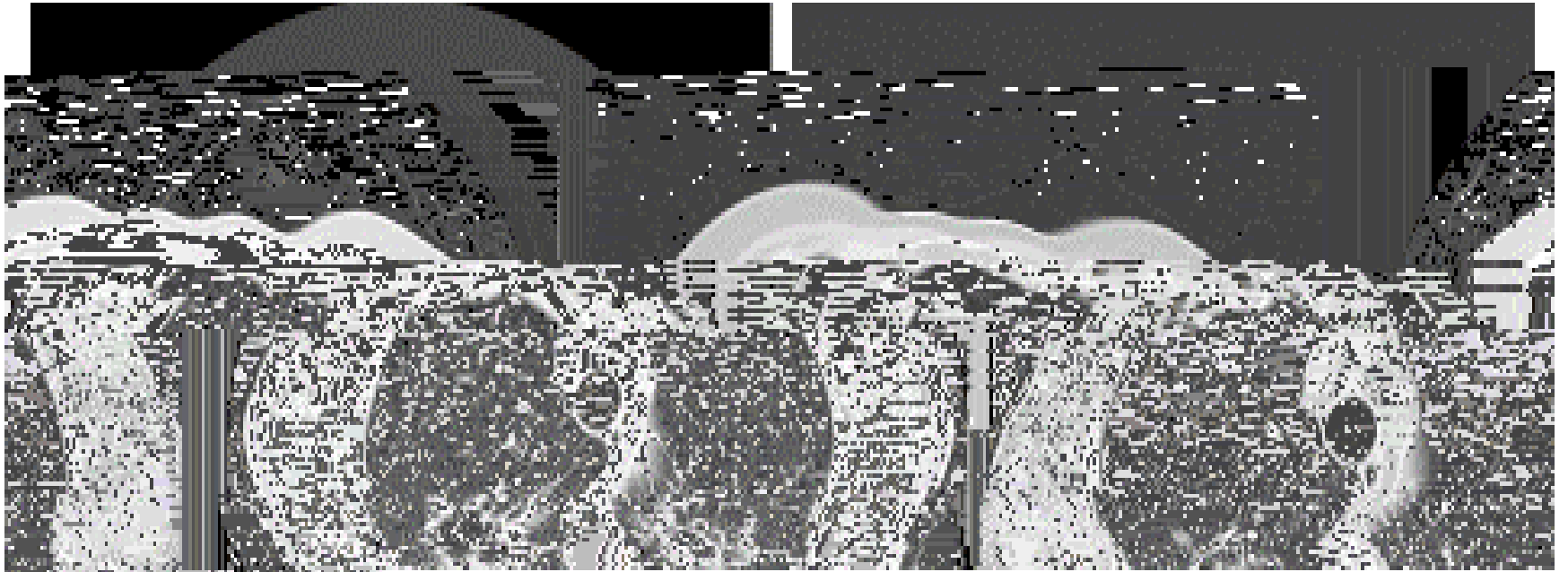
- A bedaquiline/ clofazimine combination regimen might add activity to the treatment of clinically relevant non-tuberculous mycobacteria

Ruth M, J Antimicrob Chemother 2019; Ijakko van Ingen

- In TK assays, bedaquiline showed a bacteriostatic effect. Clofazimine extended the bacteriostatic activity of bedaquiline.

A New Approach –Avibactam with Carbapenems??

- Combination of avibactam and carbapenems exhibit enhanced potencies against drug resistant *Mycobacterium abscessus*.
 - Kaushik, A et al. *J Antimicrob Chemother* 2014; 58: 1000-1008



Emerging Pharmacologic Therapies – tetracycline anaologs

Bax H, et al. J Antimicrob Chemother 2019 (Netherlands)

Kaushi, A, et al Antimicrobial Agents and Chemotherapy 2019 (Hopkins)

- **New Tetracycline Analogs**
 - Omadacycline (oral) / Eravacycline (IV)
 - In vitro data against drug resistant M. Abscessus
 - Promising alternative to IV Tigecycline



Surgery

- Indications for surgery

