

Challenging Clinical Cases of NTM-Lung Disease

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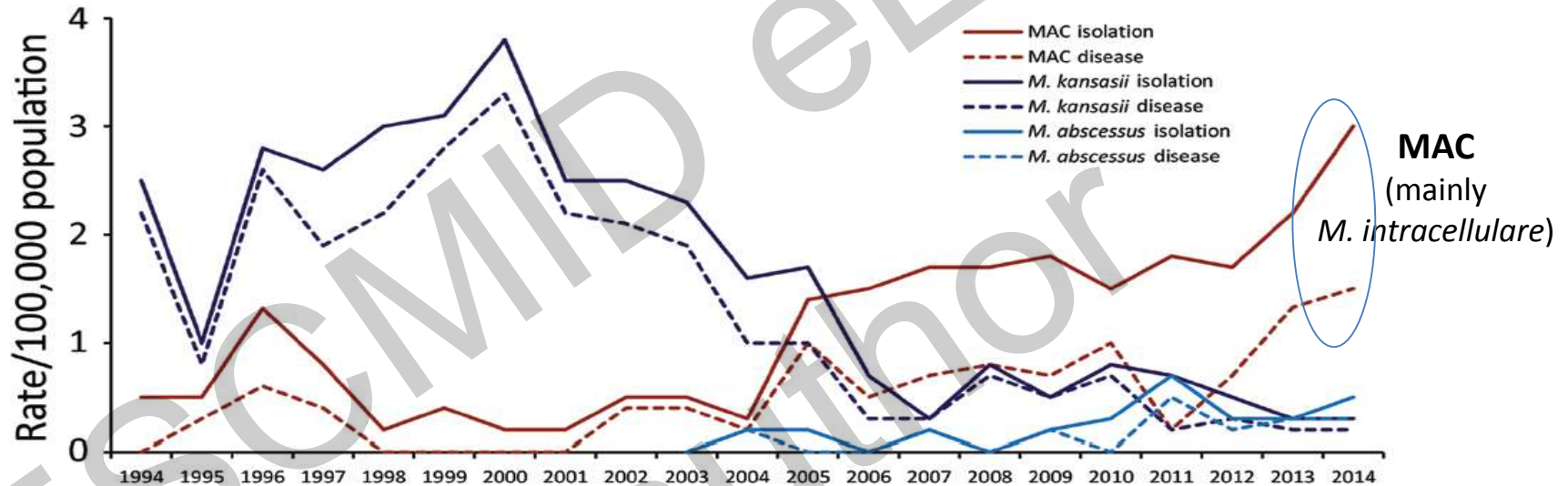
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**Update on diagnosis and treatment of non-tuberculous mycobacteria 29th
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Disclosures

I have no conflicts of interest related to the topic of this session

Pulmonary Infections with Nontuberculous Mycobacteria, Catalonia, Spain, 1994–2014

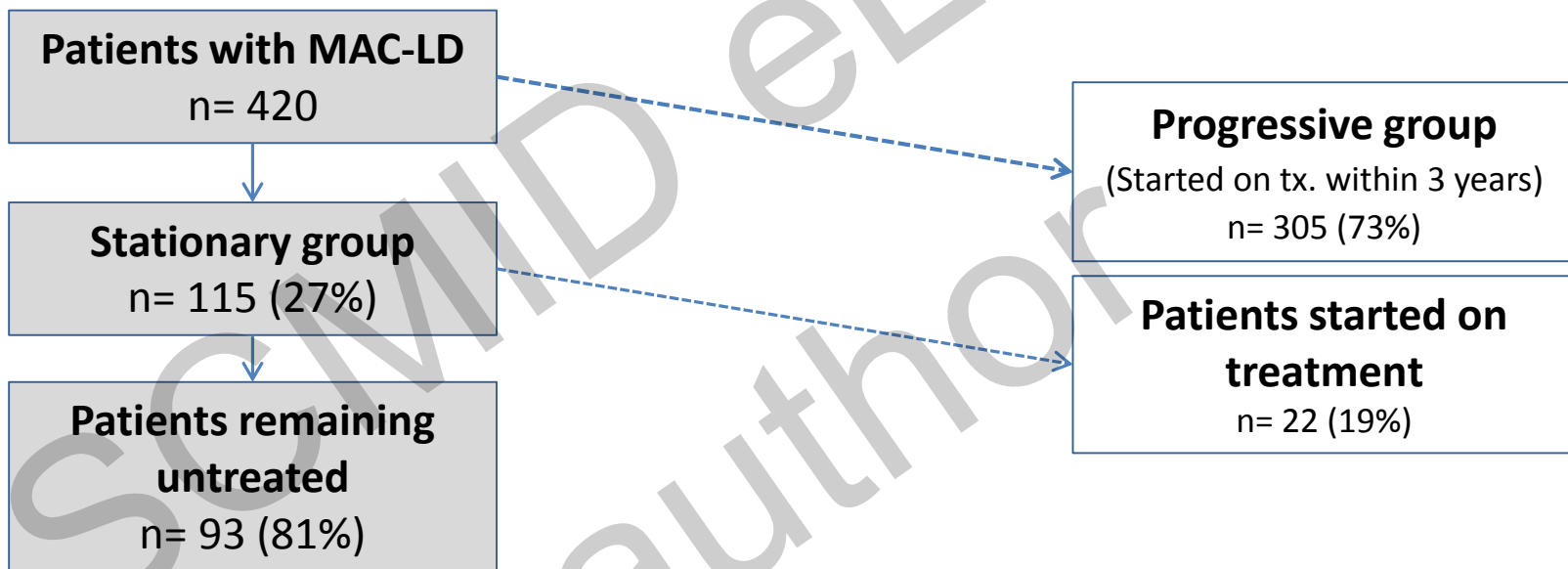


Santin M. EID 2018

Some Challenges on management of NTM-LD

- When to treat
- Tolerability of treatment
- Failures and recurrences

Natural history of *Mycobacterium avium* complex lung disease in untreated patients with stable course



Culture conversion 48 (52%)

Hwang et al. Eur Respir J 2017

Factors associated to progression of NTM-LD

Patient-related factors

- Severe systemic symptoms
- Low BMI
- Comorbidities
- Extensive disease
- Fibrocavitary disease

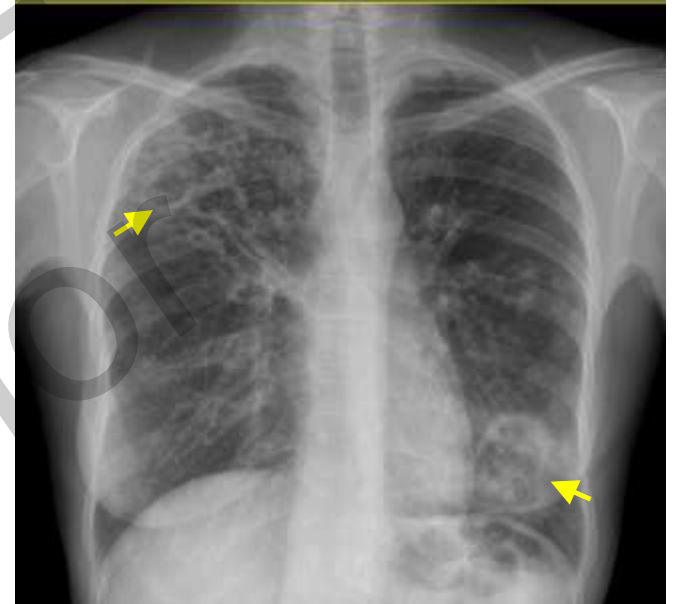
Mycobacterial factors

- Smear positivity
- ≥ 2 positive cultures
- Mycobacterial species

Case 1

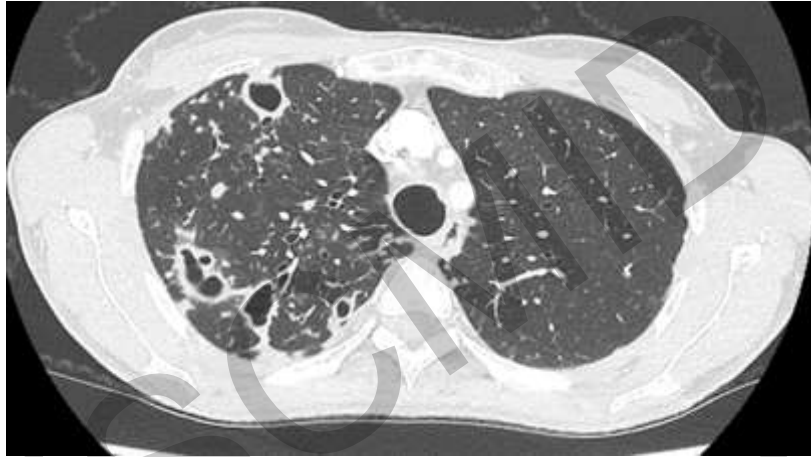
Intolerance: A major limitation of the NTM Therapy

- A 47 y/o female with bronchiectasis
- 1 year of cough with no systemic symptoms
- Sputum smear: AFB (++) , Xpert (-)
- Culture (x3): *M. intracellulare*
- Tx: **Clari + RIF + EMB**



Case 1

Intolerance: A major limitation of the NTM Therapy



Case 1

Intolerance: A major limitation of the NTM Therapy

Two weeks later, tx. was discontinued because of:

- Dizziness
- Bad taste
- Pyrosis
- Nausea
- ENT: Vestibular dysfunction (**Clari**)



How to continue Tx?

- Azithromycin-containing regimen:
 - Azithro + EMB + RMP
- Macrolide-free regimen:
 - EMB + RMP/RBT
 - EMB + RMP/RBT + FQ
 - EMB + RMP/RBT + Clofazimine
 - EMB + RMP/RBT + injectable or inhaled agent (ALIS)

Case 1

Intolerance: A major limitation of the NTM Therapy

- Tx completed (15 m.) with **Azithro**
- Microbiologic and clinical response
- Dizziness improved



Modification of anti-NTM Therapy

	Patients	Tx modification
• Wallace RJ	50 pts MAC-LD treated with Clarithromycin	41% at least 1 drug discontinued
• Jenkins PA	371 pts NTM-LD	20% Tx changed
• Jarand J	107 pts M. abscessus-LD	65% at least 1 drug discontinued (mainly Amik)
• Santin M (non published data)	32 pts NTM-LD	23% at least 1 drug discontinued

Wallace RJ. AJRCCM 1996; Jenkins PA. Thorax 2008; Jarand J. CID 2011

Intermittent vs. daily therapy

Treatment Episodes With Initial Intermittent or Daily Macrolide/Azalide-Based Therapy For NB MAC Lung Disease (Wallace RJ. Chest 2014)

Episode	tiw, No. (%)	Daily, No. (%)
Regimen modification ^a		
Clarithromycin	3 of 74 (4)	14 of 21 (67)
Azithromycin	2 of 72 (3)	10 of 13 (77)
Clarithromycin + azithromycin	5 of 180 (3)	24 of 34 (71)

Modification of Initial Antibiotic Treatment (Jeong BH AJRCCM 2015)

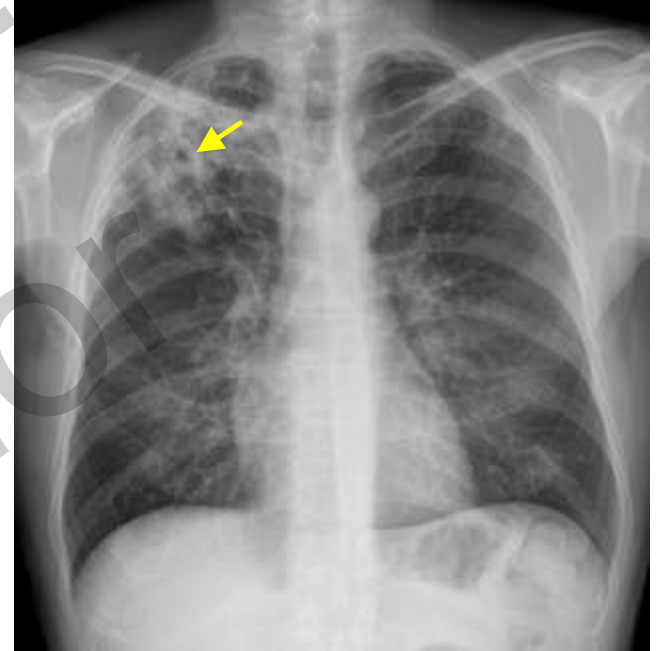
	Daily Therapy (n = 99)	Intermittent Therapy (n = 118)	P Value
Early discontinuation of antibiotic treatment	15 (15%)	13 (11%)	0.366
Dose reduction of CLR	11/95 (12%)	1/26 (4%)	0.458
Change from AZM to CLR	0/12 (0%)	3/116 (3%)	NA
Discontinuation of RIF or RFB	4/99 (4%)	7/118 (6%)	0.527
Discontinuation of EMB	24/99 (24%)	1/118 (1%)	<0.001
Discontinuation of streptomycin	4/60 (7%)	—	NA
Total	46/99 (46%)*	25/118 (21%)	<0.001

Case 2

When the initial tx “is not working”

- A 51 y/o male smoker with COPD, presented with minor haemoptysis
- HRCT scan: URL cavitary infiltrate
- Sputum smear: AFB (+), Xpert (-)
- Culture (x4): ***M. intracellulare***
- Initial tx: Daily **Clari + RMP + EMB**
- Cultures at mths. 1, 2, 3 & 5:

M. intracellulare



What to do?

- To switch from Clarithro to Azithro?
- To switch from RMP to RBT?
- To add an parenteral agent?
- To check for susceptibility to Clari?

Case 2

When the initial tx “is not working”

- Cultures at mths. 1, 2, 3 & 5:
M. intracellulare
- 2nd tx: **Clari + RBT + EMB + Amik**
(19-month tx, with 4 months of Amik)
- Cultures:
 - Month 6 Positive
 - Month 7 Negative



Case 3

Recurrence (Relapse or Reinfection?)

2007

A 72 y/o female with bronchiectasis,
presented with cough and low-grade fever

– Sputum culture (x3): ***M. intracellulare***

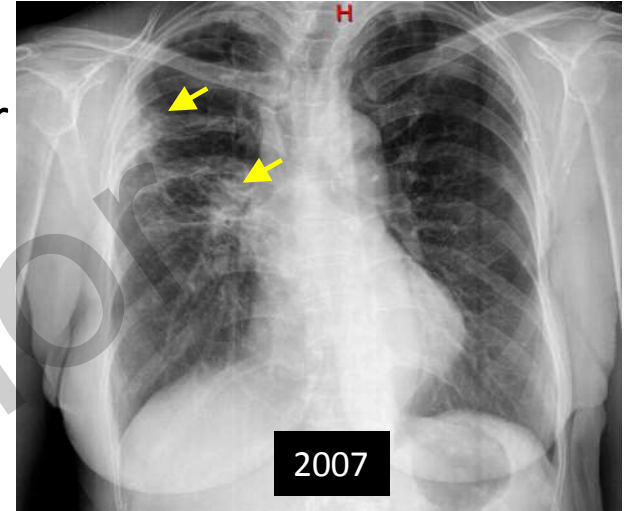
– Tx: 1st Clari+EMB+RBT (daily)

2nd Azithro+EMB+RBT (daily)

3rd Azithro+EMB (tiw)

– Cultures at mths. 4 & 5: Negative

– 3 months later: ***M. intracellulare***



What to do?

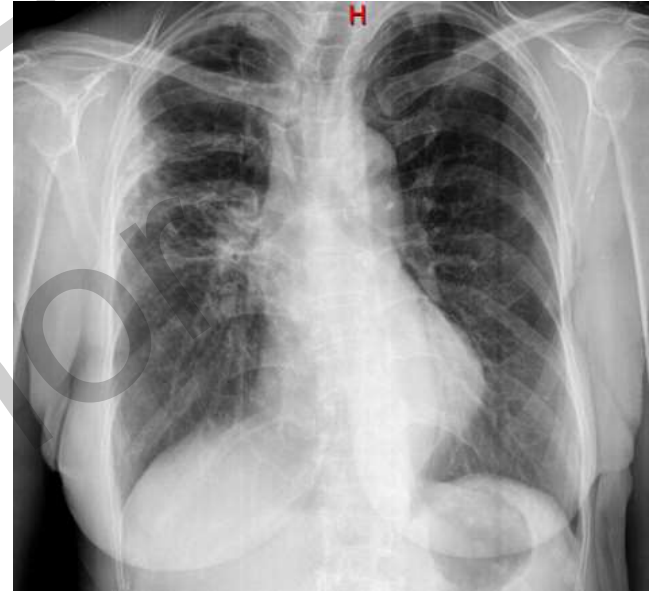
- To discontinue treatment?
- To perform more cultures and check for susceptibility to Clari?
- And meanwhile,...
 - Go back to a daily regimen?
 - Add an injectable/inhaled agent?
 - Add a FQ or Clofazimine?

Case 3

Recurrence (Relapse or Reinfection?)

2007

- 3 months later: *M. intracellulare* (2 of 3 consecutive sputums, susceptible to Clari) and multiple cultures negative thereafter
- Tx: discontinued after 19 months (12 months with culture negative)



Microbiologic Recurrence

Measure	Still on Therapy ^a	After Completion of Therapy ^b
MR after sputum conversion	25 of 180 (14)	74 of 155 (48)
Genotyping on ≥ 2 MR isolates	21 of 25 (84)	53 of 74 (72)
→ New infection	10 of 21 (48)	40 of 53 (75)
True relapse	11 of 21 (52)	13 of 53 (25)
Genotyping of single MAC isolates	22 of 23 (93)	37 of 45 (82)
→ New infection	18 of 23 (78)	28 of 37 (76)
True relapse	5 of 23 (22)	9 of 37 (24)

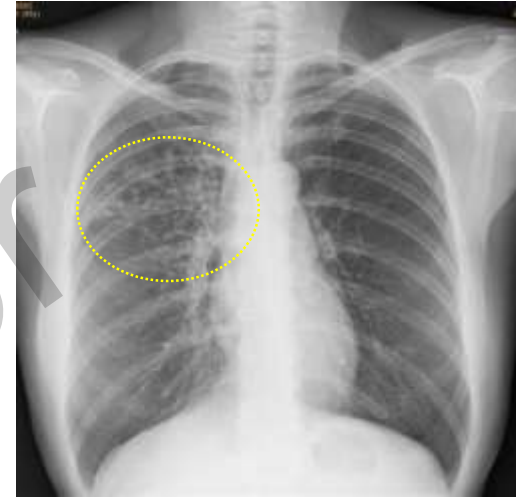
(Wallace RJ. Chest 2014)

Case 4

When no “reliable” choices are available

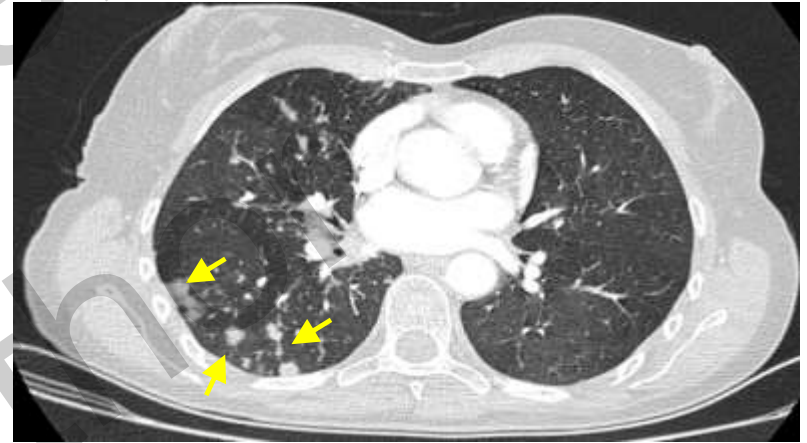
2012

- A 52 y/o female with bronchiectasis and isolation of *M. avium* (x5) and *M. abscessus* (x3) in 1 the last year
- Tx: **Clari + Moxi + Amik** i.m. x 2 mths
- Sputum culture at month 3: *M. abscessus* (x2) **Clari-Resistant**
- Referred to the TB Unit of the BUH



Case 4

When no “reliable” choices are available



We considered...

- Amik + Tigecycline + B-lactam + Linezolid /Tedizolid +/- Moxi
- Add ALIS (not available)
- New drugs: BDQ
- Surgery
- Intermittent oral/inhaled therapy (alleviate symptoms)
- Not treatment

Case 4

When no “reliable” choices are available

She refused treatment

2013-2018 (No treatment)

Multiple cultures negative. A few isolates of *M. abscessus* (x3) *M. intracellulare* (x2) and other species



Summary

- An observational period for progression may be advisable before starting therapy in patients with NTM-LD (nodular/bronchiectatic disease)
- Therapy should be based on the guidelines
- Recurrences, either during or after discontinuing therapy more often represent a new infection
- Surgery represents a reliable alternative for patients with refractory NTM-LD
- Intermittent symptoms-guided therapy is an option when the aim of treatment is to alleviate symptoms



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