Inhaled Conventional Amikacin for Nontuberculous Mycobacteria Pulmonary Disease

전 병 우

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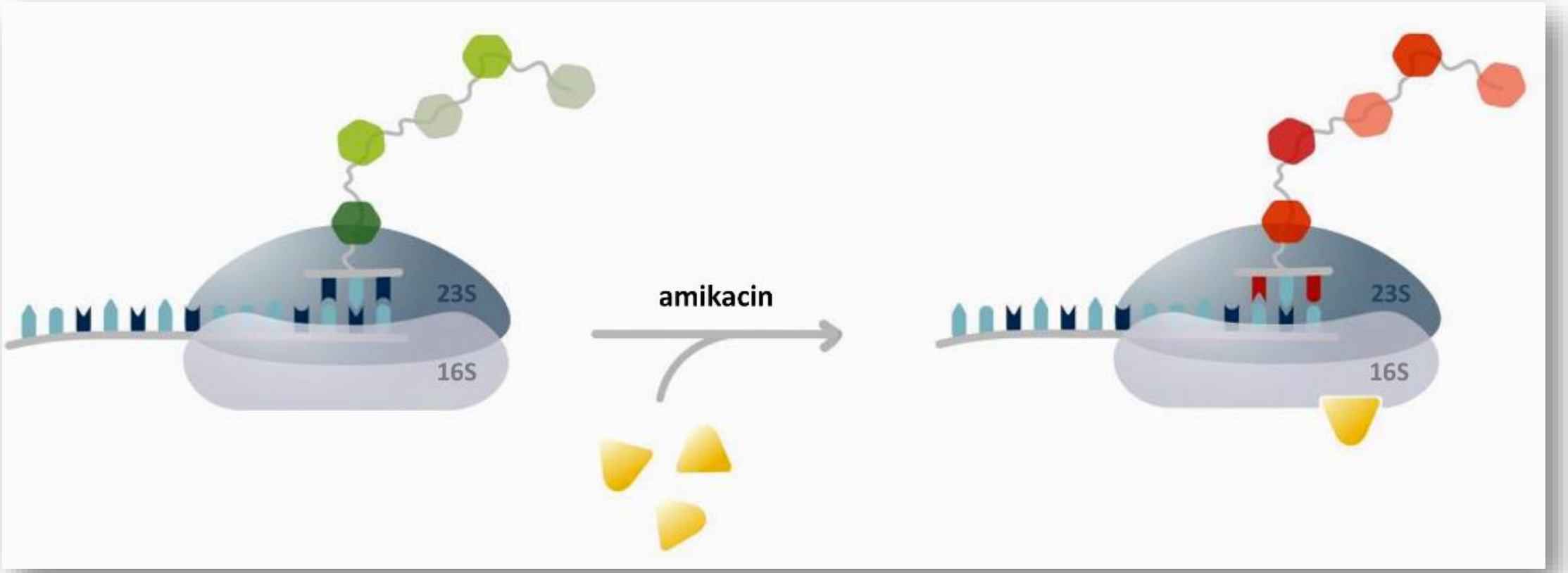
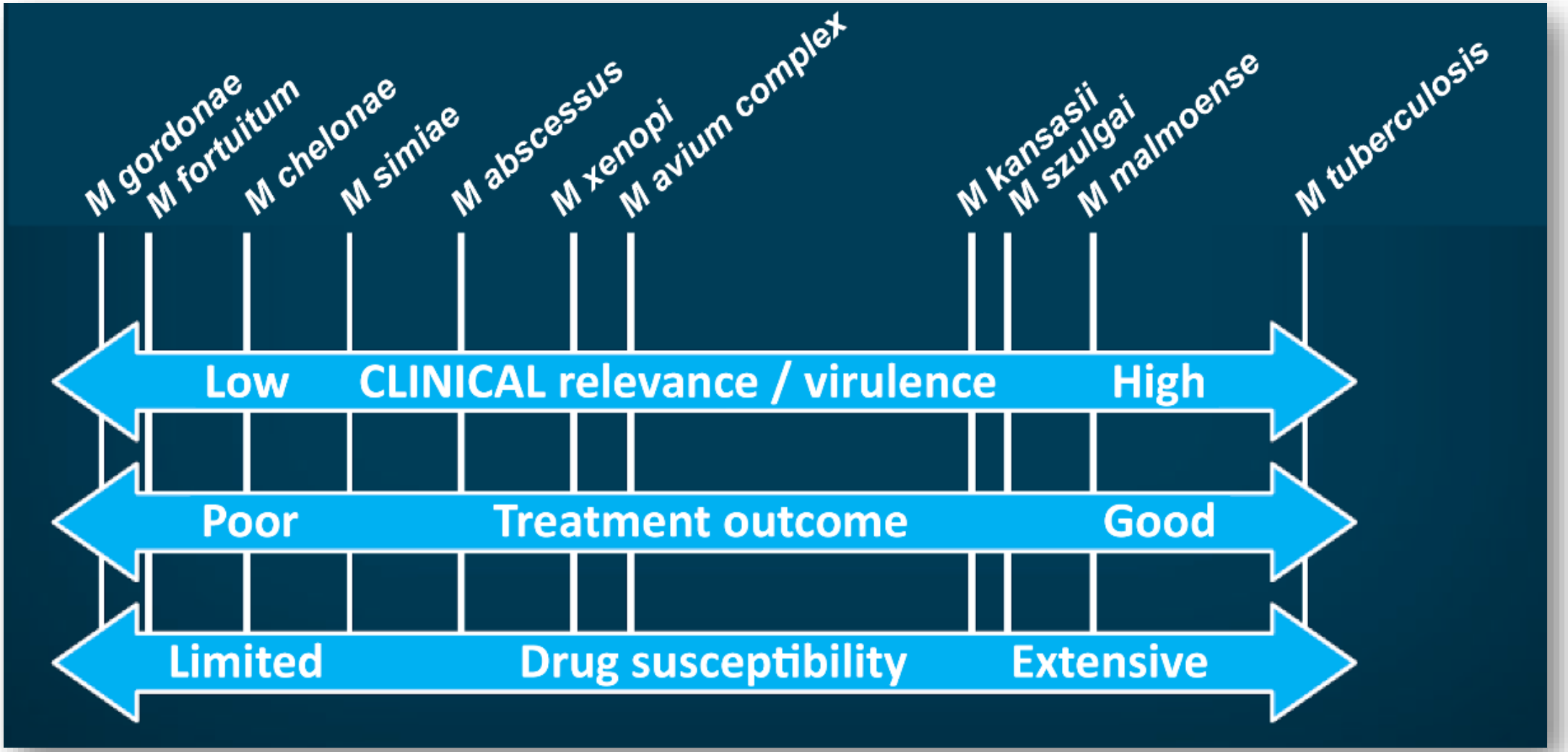
Mechanism of action of amikacin

- Derivatives of kanamycin (adding of a hydroxy-aminobutyric acid)
- Binding to the decoding A-site located on the 16S RNA
- Leading to mistranslation of proteins



Universal regimen for *Mycobacterial* pulmonary disease (PD)?



Jakko et al. Infect Genet Evol 2012;12(4):832-7

Duration of aminoglycoside injection and outcome in cavitary *M. avium* complex-PD

- 101 cavitary *M. avium* complex-PD patient
- Aminoglycoside ≥ 3 months (n = 75) vs. < 3 months (n = 26)

Factor for treatment success	Success (n = 64)	Univariate	Multivariate	
			aOR (95% CI)	*P* value
Male	36%	<0.001	0.21 (0.08-0.54)	0.001
Current or past smoker	27%	0.003	-	-
Diabetes	5%	0.008	0.21 (0.05-0.94)	0.041
Fibrocavitary form	28%	0.020	-	-
Aminoglycoside Injection ≥3 mo	81%	0.035	3.60 (1.25-10.39)	0.018

Injection Duration (mo)	n	Multivariate	
		aOR (95% CI)	*P* value
0-1.4	8	1.0 (ref)	-
1.5-2.9	18	3.79 (0.50-28.55)	0.195
3.0-4.4	28	10.56 (1.49-74.87)	0.018
4.5-5.9	18	24.53 (2.73-220.26)	0.004
6.0-7.4	14	15.48 (1.65-146.19)	0.016
7.5-30	15	1.52 (0.18-12.84)	0.700

Kim et al. Clin Infect Dis 2019;68(11):1870-1876

Role of amikacin in *M. abscessus*-PD treatment

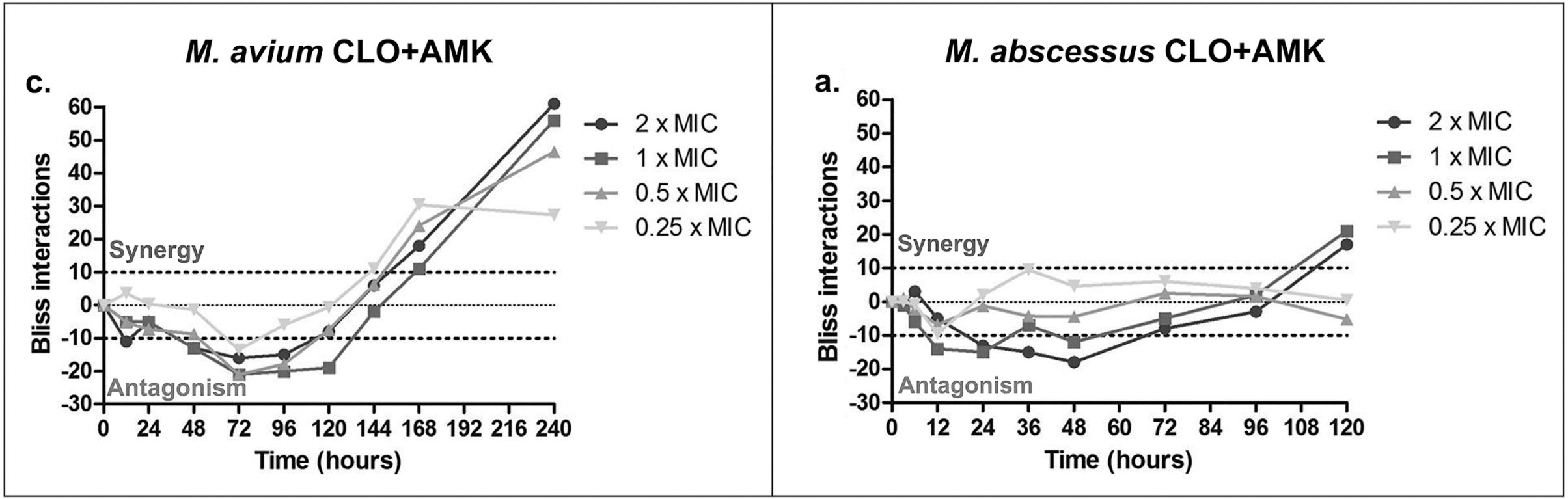
- 14 studies involving 303 *M. abscessus*-PD patients
- Treatment success rate: 33.0% for *M. abscessus* subsp. *abscessus*
- Parenteral amikacin (aOR 1.44, 95% CI 1.05–1.99) was related to treatment success

	Total[#]		*M. abscessus* subsp. *abscessus* pulmonary disease[¶]		*M. abscessus* subsp. *massiliense* pulmonary disease[+]	
	Adjusted OR[§] (95% CI)	p-value	Adjusted OR[§] (95% CI)	p-value	Adjusted OR[§] (95% CI)	p-value
Clarithromycin	0.81 (0.47–1.40)	0.438	0.33 (0.13–0.84)	0.020	3.85 (0.50–29.6)	0.190
Azithromycin	1.61 (0.93–2.78)	0.085	3.29 (1.26–8.62)	0.016	0.23 (0.02–2.42)	0.226
Cefoxitin	0.61 (0.35–1.07)	0.080	1.22 (0.53–2.86)	0.640	0.39 (0.04–4.12)	0.429
Imipenem	2.65 (1.36–5.10)	0.005	7.96 (1.52–41.6)	0.018	10.2 (0.08–1364.6)	0.353
Amikacin	2.03 (0.74–4.11)	0.181	1.44 (1.05–1.99)	0.020	0.38 (0.01–53.1)	0.698
Fluoroquinolone	0.62 (0.36–1.01)	0.076	1.24 (0.46–3.33)	0.680	3.12 (0.27–35.9)	0.362
Ethambutol	0.48 (0.23–1.02)	0.060	0.54 (0.15–1.96)	0.355	0.62 (0.01–556.3)	0.890
Rifampicin	0.70 (0.29–1.70)	0.425	1.21 (0.16–9.35)	0.904	0.67 (0.01–788.6)	0.912

Kwak et al. Eur Respir J 2019;54(1):1801991

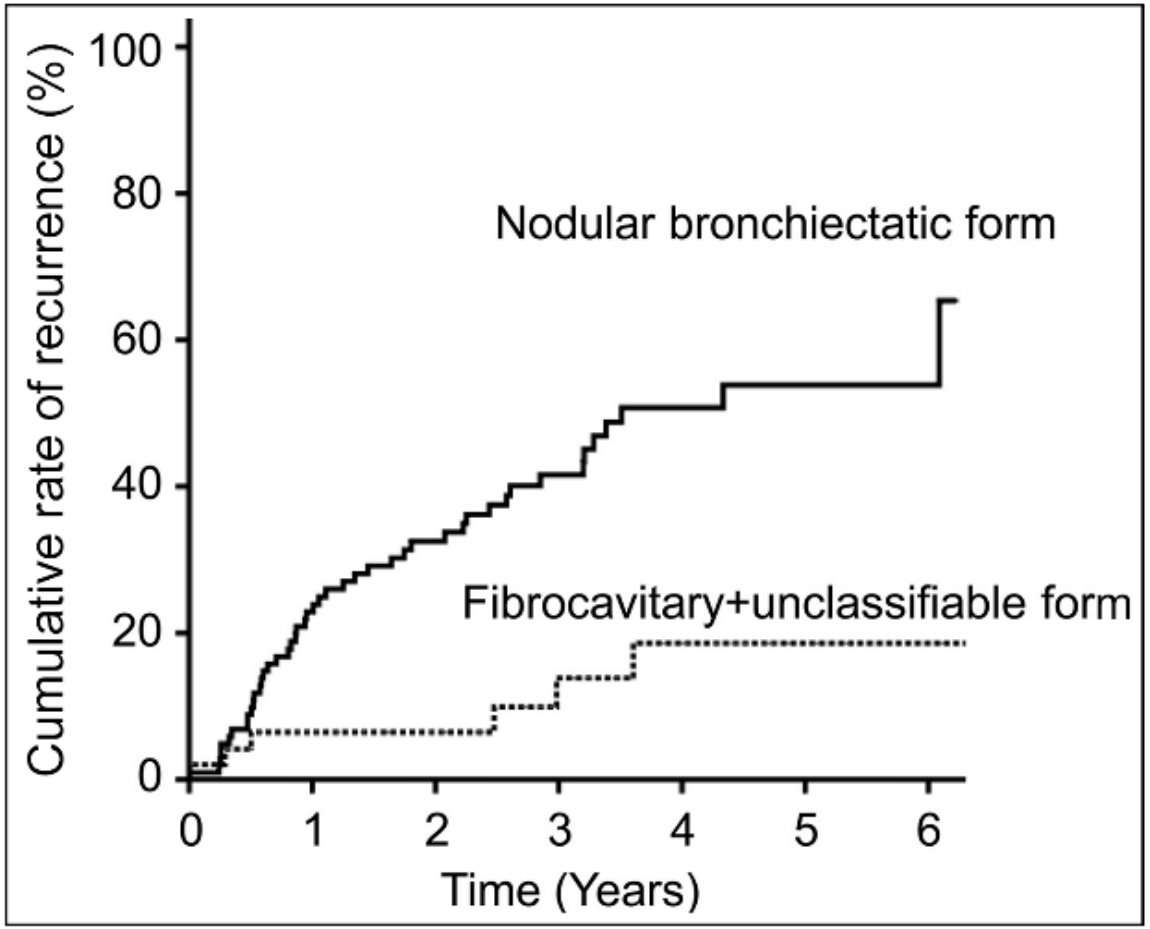
Amikacin synergism with other drugs

Time course of Bliss interactions of clofazimine and amikacin in of *M. avium* and *M. abscessus*

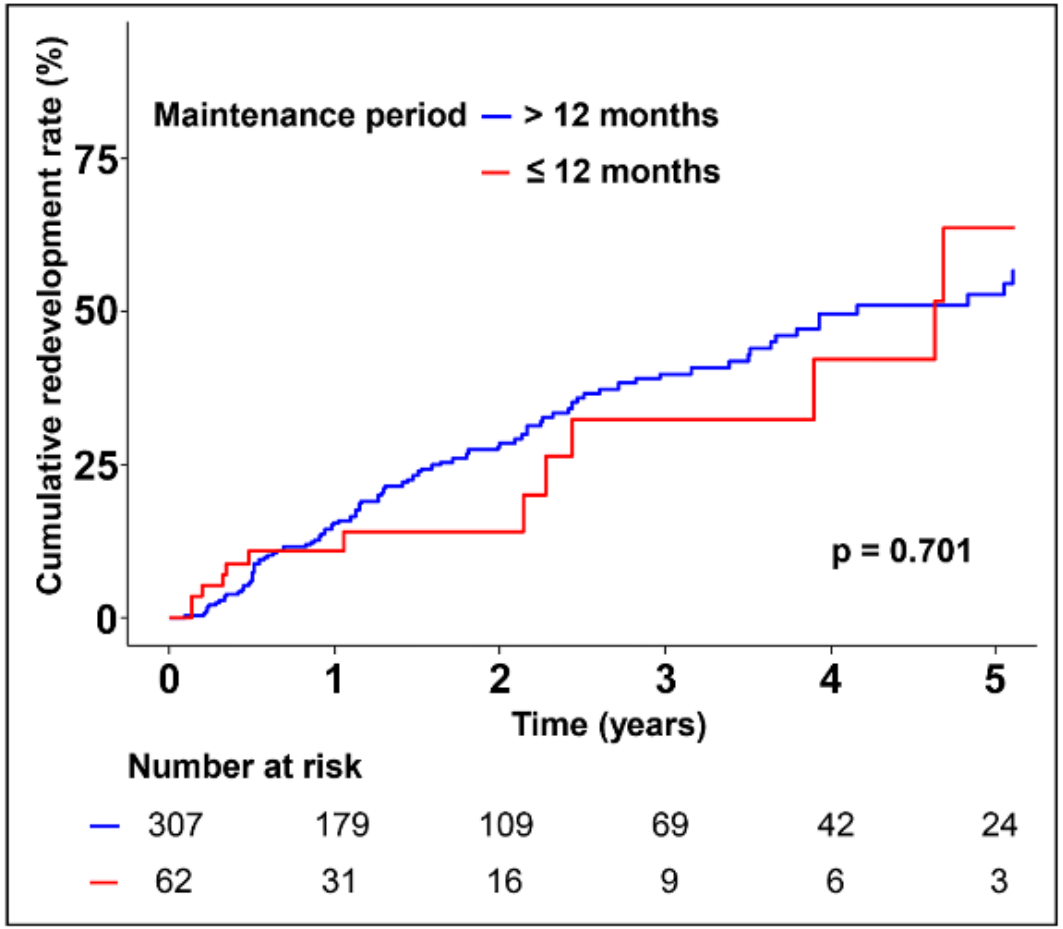


Ferro et al. Antimicrob Agents Chemother 2015;60(2):1097-105

Frequent recurrence of NTM-PD



서울아산병원 31% (50 / 158), MAC



삼성서울병원 32% (205 / 631), MAC

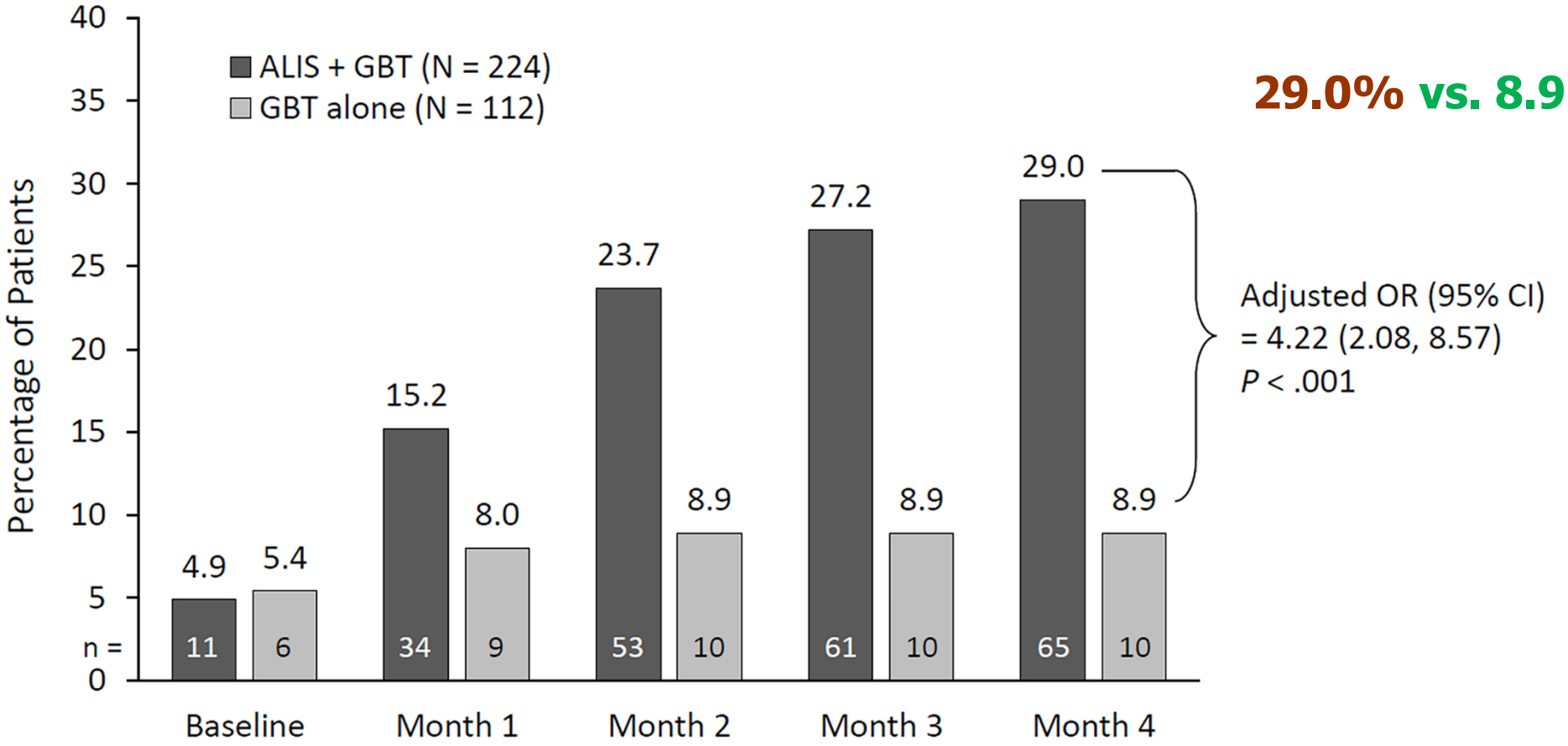
Unpublished data 삼성서울병원

Lee et al. Antimicrob Agents Chemother 2015;59(6):2972-7

Amikacin Liposome Inhalation Suspension

- *M. avium* complex -

Sputum culture conversion by study month



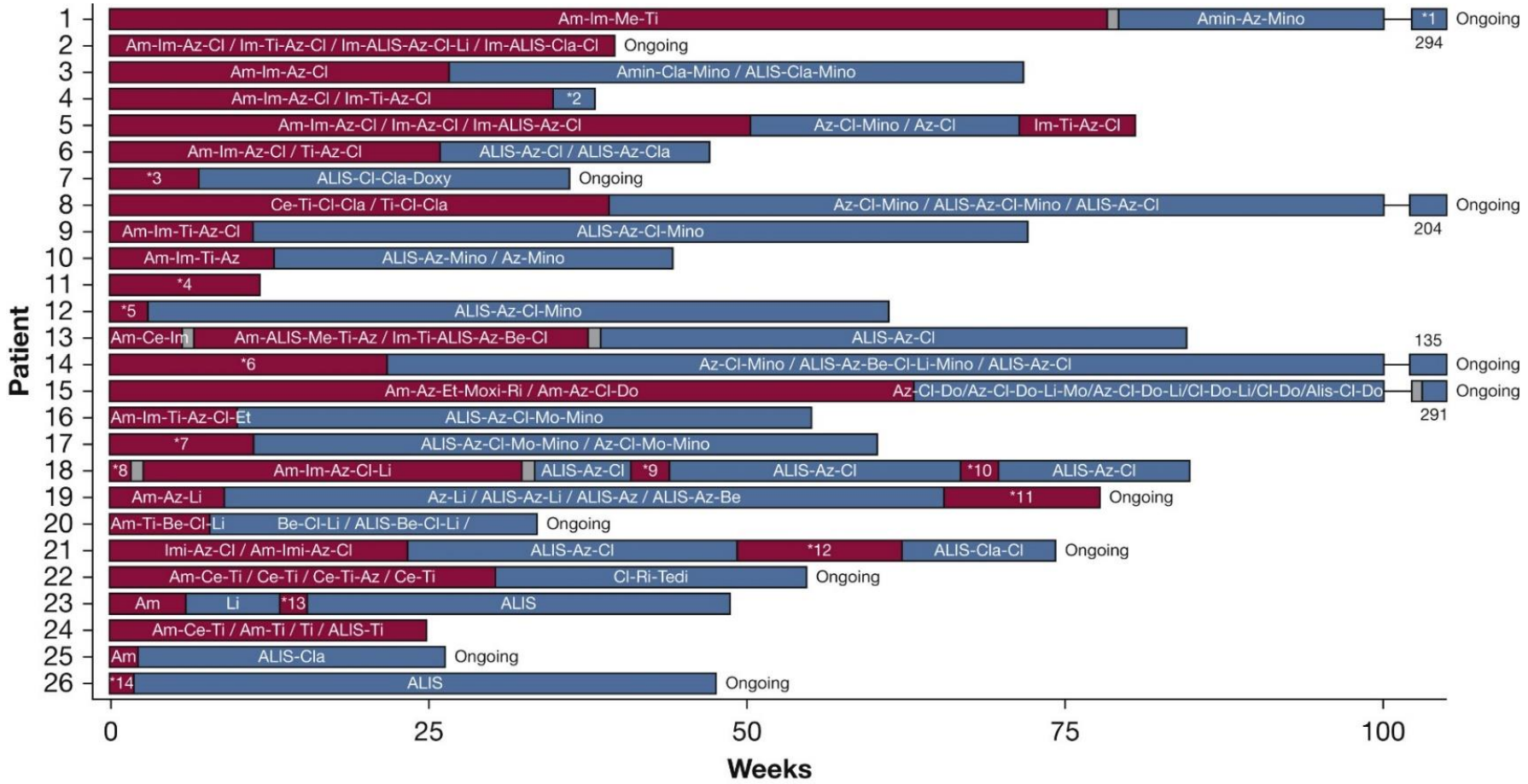
29.0% vs. 8.9%

Griffith et al. Am J Respir Crit Care Med 2018;198(12):1559-1569

Amikacin Liposome Inhalation Suspension

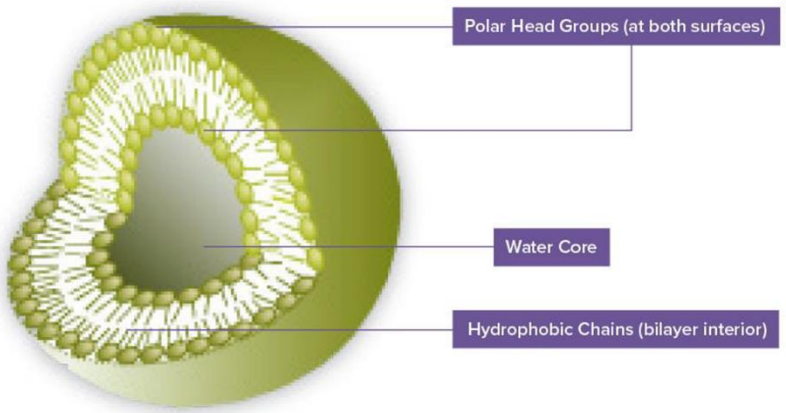
- *M. abscessus* -

- Netherlands, Belgium, France, Italy, Australia: 25 *M. abscessus*-patients treated with ALIS
- Mean duration of ALIS: 13.6 months, favorable outcome 60% (15/25)



Zweijpfenning et al. CHEST 2022, Online ahead of print

Amikacin Liposome Inhalation Suspension (ALIS)

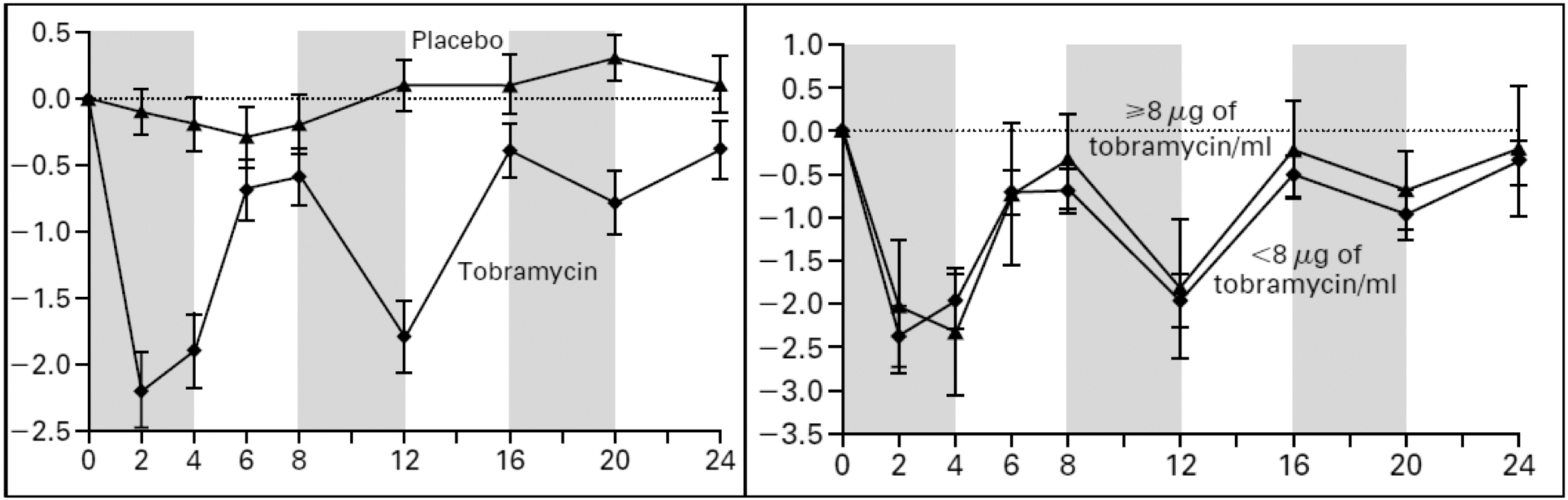


Instruction	When	Parts cleaned	Method	How Long	Comments
Wipe	After each use	• Medication Reservoir and Aerosol Chamber • Mouthpiece	Wipe with clean disposable paper towel.	1 second per part	Wipe to remove residual medicine and then dispose of paper towel in trash with solid waste.
Rinse	Prior to first use, then after each use	• Aerosol Head • Medication Cap and Seal • Blue Valve • Medication Reservoir and Aerosol Chamber • Mouthpiece	Warm running tap water.	10 seconds	Rinse each side of the Aerosol Head for 10 seconds.
Clean	Prior to first use, then after each use	• Aerosol Head • Medication Cap and Seal • Blue Valve • Medication Reservoir and Aerosol Chamber • Mouthpiece	Soak each piece in warm soapy water. While soaking swish or shake each piece.	5 minutes	Use 3 to 5 drops of clear liquid dish soap in a bowl with enough warm water to cover all pieces. Soak longer if Handset has dried or if visibly dirty.
Rinse	Prior to first use, then after each use	• Aerosol Head • Medication Cap and Seal • Blue Valve • Medication Reservoir and Aerosol Chamber • Mouthpiece	Warm running tap water.	Until soap is removed.	Check each part and soak for another 5 minutes if any part looks dirty.
Disinfect	Prior to first use, then after each use	• Aerosol Head • Medication Cap and Seal • Blue Valve • Medication Reservoir and Aerosol Chamber • Mouthpiece	Boil in **distilled** water.	5 minutes	Air-dry in a dust-free environment.

ALIS 사용이 현실적으로 어려운 이유

- 고가의 약제 (4주 사용시 약제 비용 단독 2~3천만원 소요)
- 복잡한 사용법과 장비
- 제품 구매 절차의 복잡함 (접근성 감소)
- 비용-대비 만족스럽지 못한 치료 성적
- 여전히 발생하는 약제 부작용
- 국내 식약처 허가되지 않은 상태

Intermittent administration of inhaled tobramycin in cystic fibrosis



Mean change in the density of *P. aeruginosa* in samples of expectorated sputum (log_{10} CFU/g, week)

..well tolerated and improved pulmonary function, decreased the density *of P. aeruginosa* in sputum, and decreased the risk of hospitalization..

Ramsey et al. N Engl J Med 1999;340(1):23-30

Current Guidelines,

Conventional Amikacin Inhalation (AmkInh)

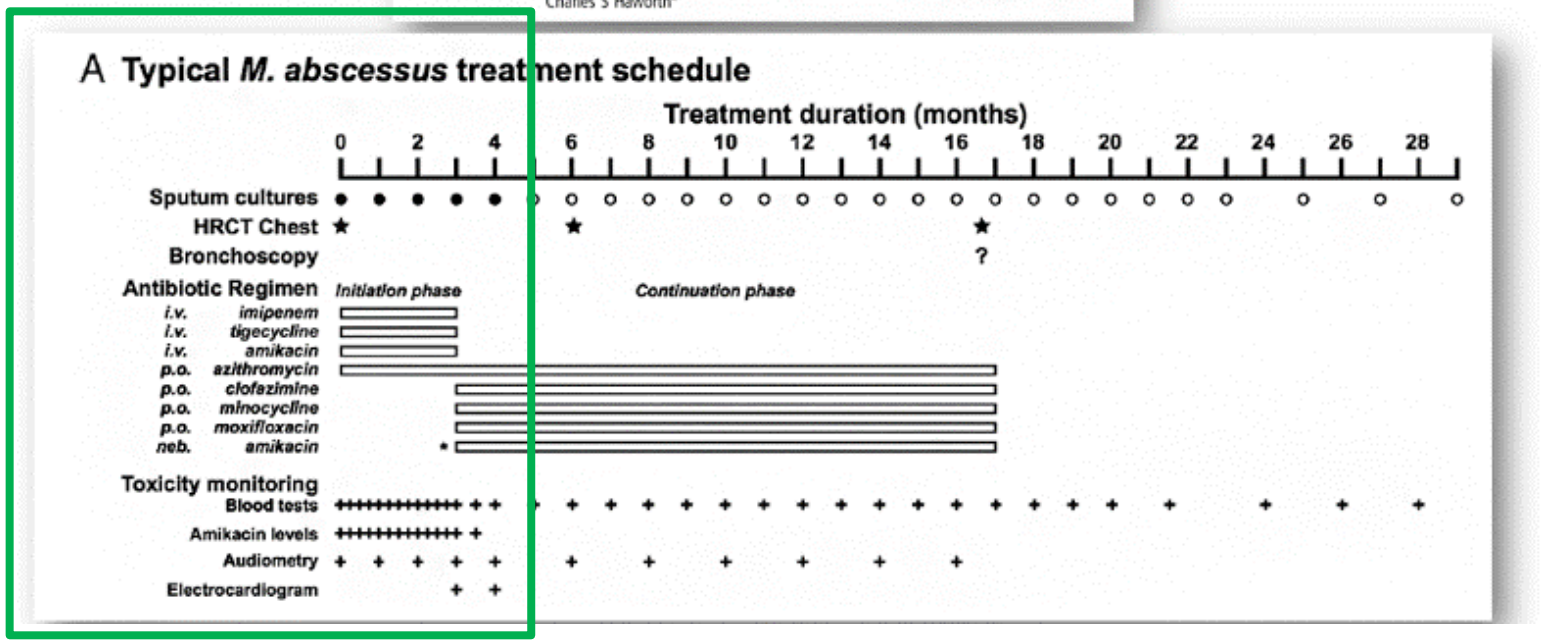
US Cystic Fibrosis Foundation
European Cystic Fibrosis Society, 2016

Supplement

OPEN ACCESS

US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis

R Andres Floto,[1,2] Kenneth N Olivier,[3] Lisa Saiman,[4] Charles L Daley,[5] Jean-Louis Herrmann,[6,7] Jerry A Nick,[8] Peadar G Noone,[9] Diana Bilton,[10] Paul Corris,[11] Ronald L Gibson,[12] Sarah E Hempstead,[13] Karsten Koetz,[14] Kathryn A Sabadosa,[13] Isabelle Sermet-Gaudelus,[15] Alan R Smyth,[16] Jakko van Ingen,[17] Richard J Wallace,[18] Kevin L Winthrop,[19] Bruce C Marshall,[20] Charles S Haworth[2]



AmkInh: *M. abscessus and* MAC, 250–500 mg/dose once or twice daily

Floto et al. Thorax 2016;71 Suppl 1(Suppl 1):i1-22

British Thoracic Society, 2017

- **AmkInh: *M. abscessus* in continuation phase or severe MAC**

Regimens in continuation phase
Nebulized amikacin and oral Clarithromycin 500 mg twice daily or Azithromycin 250-500 mg daily and 1-3 of the following antibiotics guided by DST results and patient tolerance oral clofazimine 50-100 mg daily oral linezolid 600 mg daily or twice daily oral minocycline 100 mg twice daily oral moxifloxacin 400 mg daily oral co-trimoxazole 960 mg twice daily

"..For individuals with M. abscessus that demonstrate macrolide resistance..

"the continuation phase regimen should include nebulised amikacin in combination with.. Grade D"

Haworth et al. Thorax 2017;72(Suppl 2):ii1-ii64

ATS/ERS/ESCMID/IDSA, 2020

- **AmkInh: *M. abscessus* in continuation phase or refractory MAC**

"..*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*.."

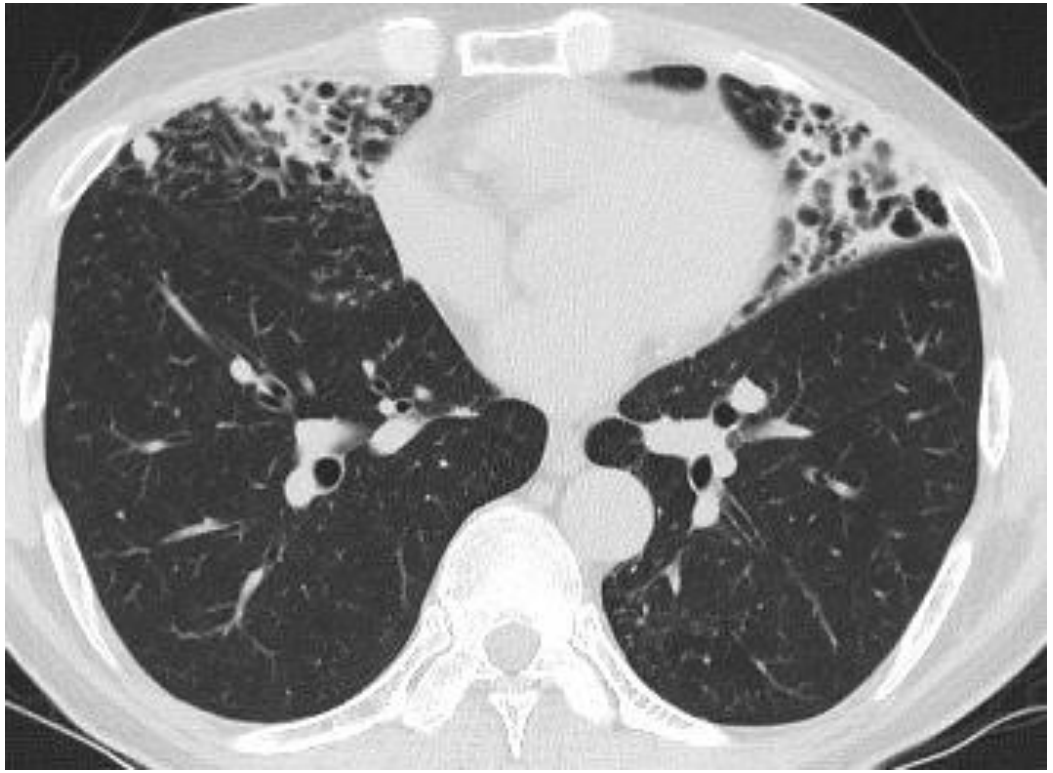
"..where ALIS is not yet available,
addition of inhaled parenteral amikacin is a reasonable alternative.."

Charles et al. Eur Respir J 2020; 56: 2000535

AmkInh 환자 적용 적용사례

CASE 1 – 난치성 MAC, clarithromycin resistance

- M/65 *M. avium* recurrence, clarithromycin resistance
- azithromycin ethambutol rifabutin clofazimine amikacin inhalation (TIW) for 14 months, microbiological cure



검사일자	순번	도말	액체	고체	검체	동정
2019-01-12	1				M31(sputum)	
2019-04-12	1				M31(sputum)	
2019-09-03	1	1+	(+)	1+	M31(sputum)	M. avium
2019-10-15	1	trace	(+)		M31(sputum)	M. avium
2019-12-02	1		(+)		M31(sputum)	M. avium
2019-12-20	1	trace	(+)	trace	M31(sputum)	M. avium
2020-01-18	1				M31(sputum)	
2020-02-25	1		(+)		M31(sputum)	M. avium
2020-06-02	1				M31(sputum)	
2020-08-18	1				M31(sputum)	
2020-10-19	1				M31(sputum)	
2020-12-22	1				M31(sputum)	
2021-03-23	1				M31(sputum)	

CASE 2 – subsp. *M. massiliense*에서 유지 요법

- F/60 subsp. *M. massiliense*, susceptible to clarithromycin
- Initial phase: (iv) amikacin imipenem azithromycin
- Continuation phase: amikacin inhalation azithromycin
- Total treatment period: 12 months, microbiological cure

검사일자	순번	도말	액체	고체	검체	동정
2017-07-04	1				M31(sputum)	
2017-09-26	1				M31(sputum)	
2017-12-05	1				M31(sputum)	
2018-05-15	1		(+)	trace	M31(sputum)	M. massiliense
2018-08-14	1		(+)	trace	M31(sputum)	M. massiliense
2019-01-08	1	trace	(+)	trace	M31(sputum)	M. massiliense
2019-09-04	1	trace			M31(sputum)	
2020-03-10	1				M31(sputum)	
2020-11-24	1				M31(sputum)	
2020-12-01	1				M31(sputum)	
2020-12-02	1				M31(sputum)	
2020-12-03	1				M31(sputum)	
2020-12-08	1				M31(sputum)	
2020-12-16	1				M31(sputum)	
2021-04-21	1			trace	M31(sputum)	Unidentified
2021-08-11	1				M31(sputum)	
2021-10-12	1				M31(sputum)	

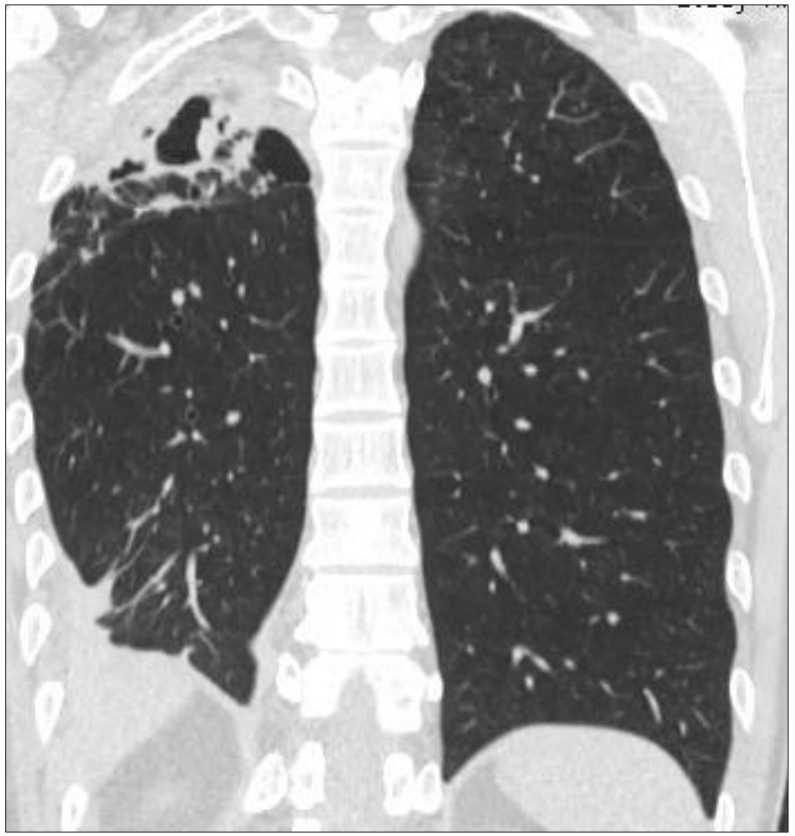
CASE 3 – subsp. *abscessus*에서 유지 요법

- M/58 subsp. *abscessus*, clarithromycin inducible resistance
- Initial phase: (iv) amikacin imipenem tigecycline azithromycin clofazimine linezolid
- Continuation phase: amikacin inhalation azithromycin clofazimine linezolid
- Total treatment period: 19 months, microbiological cure

검사일자	순번	도말	액체	고체	검체	동정
2019-02-13	1	trace	(+)	trace	M31(sputum)	M. abscessus
2019-02-13	2	1+	(+)	trace	M31(sputum)	M. abscessus
2019-02-13	3	trace			M31(sputum)	
2019-03-20	1	2+	(+)	trace	M31(sputum)	M. abscessus
2019-03-21	1	trace	(+)	trace	M31(sputum)	M. abscessus
2019-03-27	1		(+)	trace	M31(sputum)	M. abscessus
2019-04-03	1	trace			M31(sputum)	
2019-04-10	1	trace			M31(sputum)	
2019-04-17	1	trace			M31(sputum)	
2019-05-15	1	1+			M31(sputum)	
2019-09-11	1				M31(sputum)	
2019-12-18	1				M31(sputum)	
2020-02-19	1				M31(sputum)	
2020-06-30	1				M31(sputum)	
2020-10-20	1				M31(sputum)	
2020-12-22	1				M31(sputum)	
2021-03-23	1				M31(sputum)	

CASE 4 – subsp. *abscessus*에서 유지 요법

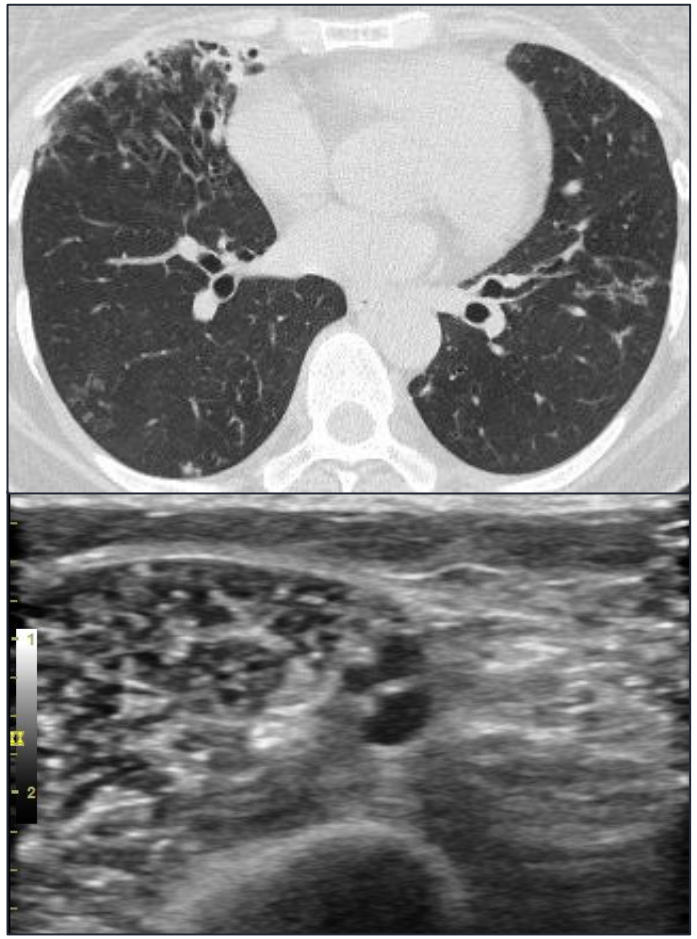
- M/46 subsp. *abscessus*, clarithromycin inducible resistance
- Initial phase: (iv) amikacin imipenem tigecycline azithromycin clofazimine
- Continuation phase: amikacin inhalation azithromycin clofazimine
- Total treatment period: 16 months, microbiological cure



검사일자	순번	도말	액체	고체	검체	동정
2019-10-29	1	trace	(+)	trace	M31(sputum)	M. abscessus
2019-10-29	2	1+	(+)	1+	M31(sputum)	M. abscessus
2019-11-26	1		(+)		M31(sputum)	M. avium
2020-07-28	1	trace			M31(sputum)	
2020-07-31	1				M31(sputum)	
2020-08-01	1				M31(sputum)	
2020-08-02	1				M31(sputum)	
2020-08-07	1				M31(sputum)	
2020-08-16	1				M31(sputum)	
2020-08-23	1				M31(sputum)	
2020-10-22	1				M31(sputum)	
2020-12-24	1				M31(sputum)	
2021-02-25	1				M31(sputum)	
2021-04-29	1				M31(sputum)	
2021-07-01	1				M31(sputum)	
2021-09-02	1	trace			M31(sputum)	
2021-12-03	1				M31(sputum)	

CASE 5 – 도관 유지가 어려운 subsp. *abscessus* 환자

- F/57 subsp. abscessus
- Totally occluding thrombus in the left upper arm basilic vein, after PICC

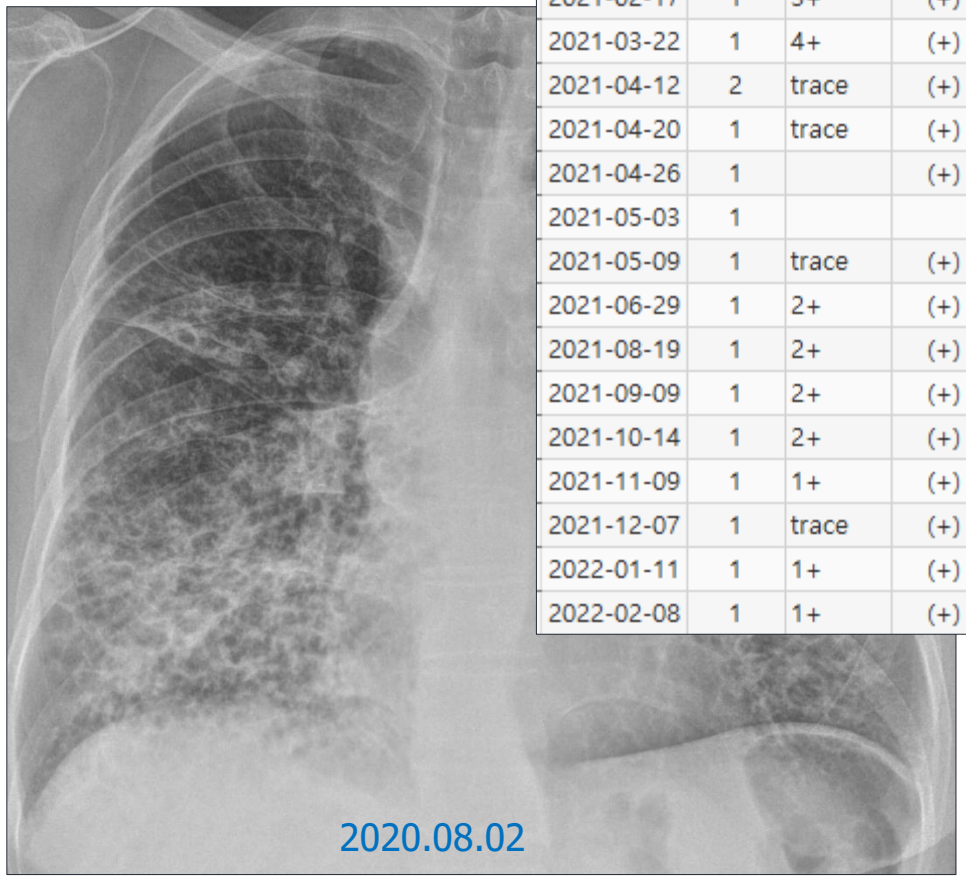


검사일자	순번	도말	액체	고체	검체	동정
2020-12-10	1	2+	(+)	1+	M31(sputum)	M. abscessus
2021-02-04	1	2+	(+)	trace	M31(sputum)	M. abscessus
2021-04-08	1	1+	(+)	1+	M31(sputum)	NTM
2021-05-20	1	1+	(+)	trace	M31(sputum)	M. abscessus
2021-06-11	1		(+)	trace	M31(sputum)	NTM
2021-06-15	1	trace	(+)		M31(sputum)	M. abscessus
2021-06-21	1			trace	M31(sputum)	NTM
2021-07-22	1	1+	(+)	trace	M31(sputum)	NTM
2021-09-02	1	1+	(+)	trace	M31(sputum)	M. abscessus
2021-10-14	1	2+	(+)	trace	M31(sputum)	M. abscessus
2021-10-25	1		(+)	trace	M31(sputum)	M. abscessus
2021-10-26	1				M31(sputum)	
2021-11-01	1				M31(sputum)	
2021-11-02	1				M31(sputum)	
2021-11-08	1				M31(sputum)	
2021-11-09	1				M31(sputum)	
2021-12-22	1				M31(sputum)	

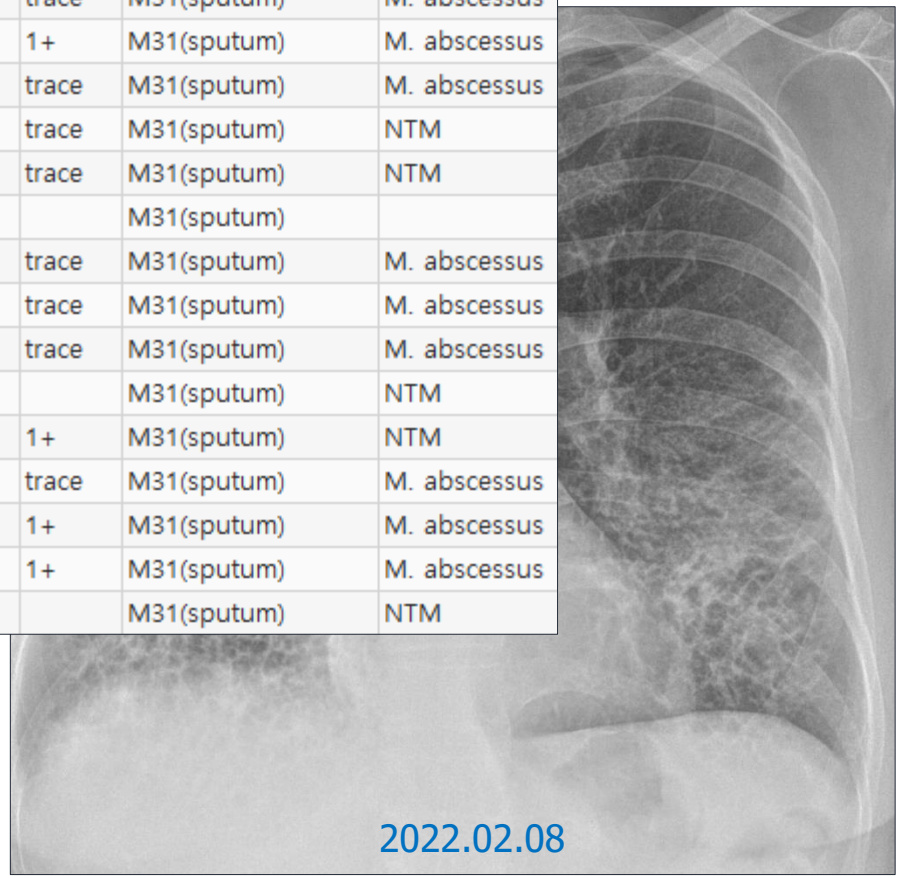
CASE 6 – 난치성 subsp. *abscessus* 에서 억제 요법

- F/69 subsp. subsp. *abscessus*, cl
- Initial phase: (iv) amikacin imipe
- Continuation phase: amikacin inh

검사일자	순번	도말	액체	고체	검체	동정
2021-01-04	1	2+	(+)	trace	M31(sputum)	NTM
2021-01-11	1	1+	(+)	trace	M31(sputum)	M. abscessus
2021-02-17	1	3+	(+)	trace	M31(sputum)	M. abscessus
2021-03-22	1	4+	(+)	1+	M31(sputum)	M. abscessus
2021-04-12	2	trace	(+)	trace	M31(sputum)	M. abscessus
2021-04-20	1	trace	(+)	trace	M31(sputum)	NTM
2021-04-26	1		(+)	trace	M31(sputum)	NTM
2021-05-03	1				M31(sputum)	
2021-05-09	1	trace	(+)	trace	M31(sputum)	M. abscessus
2021-06-29	1	2+	(+)	trace	M31(sputum)	M. abscessus
2021-08-19	1	2+	(+)	trace	M31(sputum)	M. abscessus
2021-09-09	1	2+	(+)		M31(sputum)	NTM
2021-10-14	1	2+	(+)	1+	M31(sputum)	NTM
2021-11-09	1	1+	(+)	trace	M31(sputum)	M. abscessus
2021-12-07	1	trace	(+)	1+	M31(sputum)	M. abscessus
2022-01-11	1	1+	(+)	1+	M31(sputum)	M. abscessus
2022-02-08	1	1+	(+)		M31(sputum)	NTM



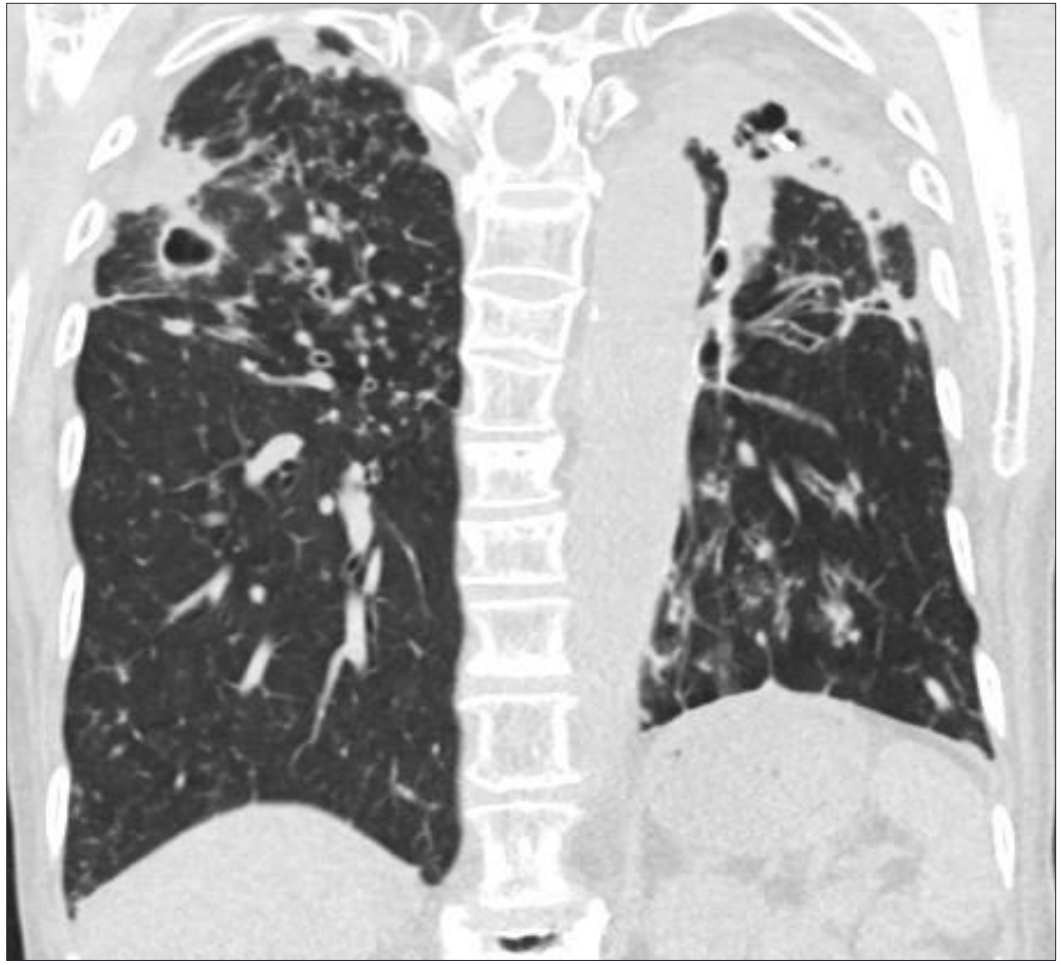
2020.08.02



2022.02.08

CASE 7 – 경구 약제 부작용, 거동 제한으로 주사치료 어려운 경우

- F/73 subsp. subsp. *abscessus*, clarithromycin inducible resistance
- L-spine compression fracture, Nerve root compression d/t disc extrusion



Reference 1: Case series

AmkInh for refractory *M. avium*-PD

- USA, 6개월 이상 치료 받은 MAC-PD 6명: macrolide based oral agents + AmkInh (15 mg/kg daily)
- Symptomatic improvement 100% (6/6) negative culture 67% (4/6), after 6-months of AmkInh

Pt. No	Sex, Age (Years)	NTM Species	Radiographic Pattern	Duration of therapy prior to starting amikacin (months)	Amikacin Therapeutic Regimen	Duration of Inhaled Amikacin (months)	Current Therapeutic Regimen	Current Patient Status	Current Sputum Culture Status
1	F, 73	MAC	nodular infiltrates, bronchiectasis in RUL, RML, lingula	96	CLA, RIF, EMB, inhaled amikacin	9	no oral antibiotics since 7/05; no inhaled amikacin since 6/06.	rare cough, wt loss, sweats, fatigue; abdominal cramps	negative for 21 months; now positive (MAC)
2	F, 67	MAC	bilateral bronchiectasis, cavitary lesion RUL and bilateral apical fibrosis/scarring	12	AZI, RIF, EMB, inhaled amikacin	4	n/a	progressive disease; died	persistent positive at death
3	F, 66	MAC, *M. chelonae*	bronchiectasis RML, RLL, LLL, lingula; bilateral apical fibrosis/scarring, centrilobular nodules	48	AZI, RIF, EMB, inhaled amikacin	52	AZI 500 mg/d since 4/06	status post multiple lobectomies; cough and exertional dyspnea; daily low grade fevers	negative for 6 months., now positive; *M. chelonae* (resistant to amikacin
4	F, 71	MAC	bronchiectasis and centrilobular nodules in posterior segments of both upper lobes, RML, lingula and lower lobes	36	CLA, inhaled amikacin	16	no antibiotics since 11/05	rare cough	negative for 7 months; now positive; MAC (resistant to EMB, RIF)
5	F, 52	MAC, *M. chelonae*	LUL wedge resection for MAC; bronchiectasis in LLL, RUL; R apical scarring, nodules in LLL, LUL, lingula	0.5	AZI, inhaled amikacin (thrombocytopenia on RIF/EMB)	13	inhaled amikacin 1000 mg/d and AZI 250 mg/d since 5/05	improved with some cough, no purulence	negative for 6 mo.
6	F, 54	MAC	bronchiectasis w/bronchial wall thickening RLL, RUL.	13	AZI, inhaled amikacin	8	AZI 500 mg 2/wk, inhaled amikacin 1000 mg 3/wk	rare cough, clinically well	no cough sputum (despite sputum induction)

Davis et al. BMC Pulm Med 2007;7:2

Reference 2: Case series

AmkInh for refractory NTM-PD

- USA, 3개월 이상 표준치료 임상적 방사선학적 악화, 혹은 경구 항생제 부작용 많은 환자 9명
- AmkInh (100~300mg twice-daily), Mean duration: 75 days (range 18–277 days)
- Favorable outcome 98% (8/9)

Patient no.	Age (years) and gender	Cancer, disease status	Chemotherapy/ radiation[a]	Co-morbidities (smoking)	ANC/ALC, cells/microliter[b]	Signs and symptoms	Mycobacterial spp., lung involved	Concurrent antimicrobials	Response, duration of aeAMK therapy
1	74, female	Breast, remission	790/4,359	None (−)	8,250/1,710	Chronic cough, dyspnea	*M. kansasii*, RLL, LLL, LUL, lingula	CLR, ETM, RIF	CR, 92 days[c]
2	73, female	Gastric adenocarcinoma, remission	2,240/2,177	Polyserositis (+)	12,700/1,380	Chronic cough, dyspnea	*M. intracellulare*, RLL, LLL, lingula	CIP, CLR	CR, 75 days
3	73, female	None	NA	None (−)	3,600/1,410	Chronic cough, night sweats	*M. avium*, RML, RLL, LLL	ETM, RIF	CR, 201 days[c]
4	69, male	None	NA	COPD (+)	1,840/1,060	None	*M. abscessus*, RML, RLL, LUL, lingula	MOX, CLR	CR, 133 days
5	62, female	None	NA	COPD (−)	4,750/1,590	Chronic cough	*M. kansasii*, RML, RLL	AZT, ETM, RIF	CR, 54 days
6	60, female	Lung squamous carcinoma, advanced	19/229	None (+)	28,420/970	Cough, fever	*M. abscessus*, LUL, LLL	CLR, TMP-SMX	PR, 18 days
7	55, female	Breast, remission	None	None (+)	5,070/1,650	Chronic cough	*M. abscessus*, RUL, RLL, LUL, LLL, lingula	CLR	CR, 59 days
8	53, male	AML, HSCT, partial remission	764/NA	BOOP (−)	9,110/1,520	Cough	*M. intracellulare*, *M. abscessus*, LLL	AZT, CIP, ETM	CR, 38 days
9	51, female	Breast, remission	Active therapy/851	None (+)	4,190/2,280	None	*M. kansasii*, RLL, LUL	CLR, MOX	CR, 277 days[c]

A Safdar et al. Eur J Clin Microbiol Infect Dis 2012;31(8):1883-7

Reference 3,4,5: Observational studies

AmkInh for NTM-PD

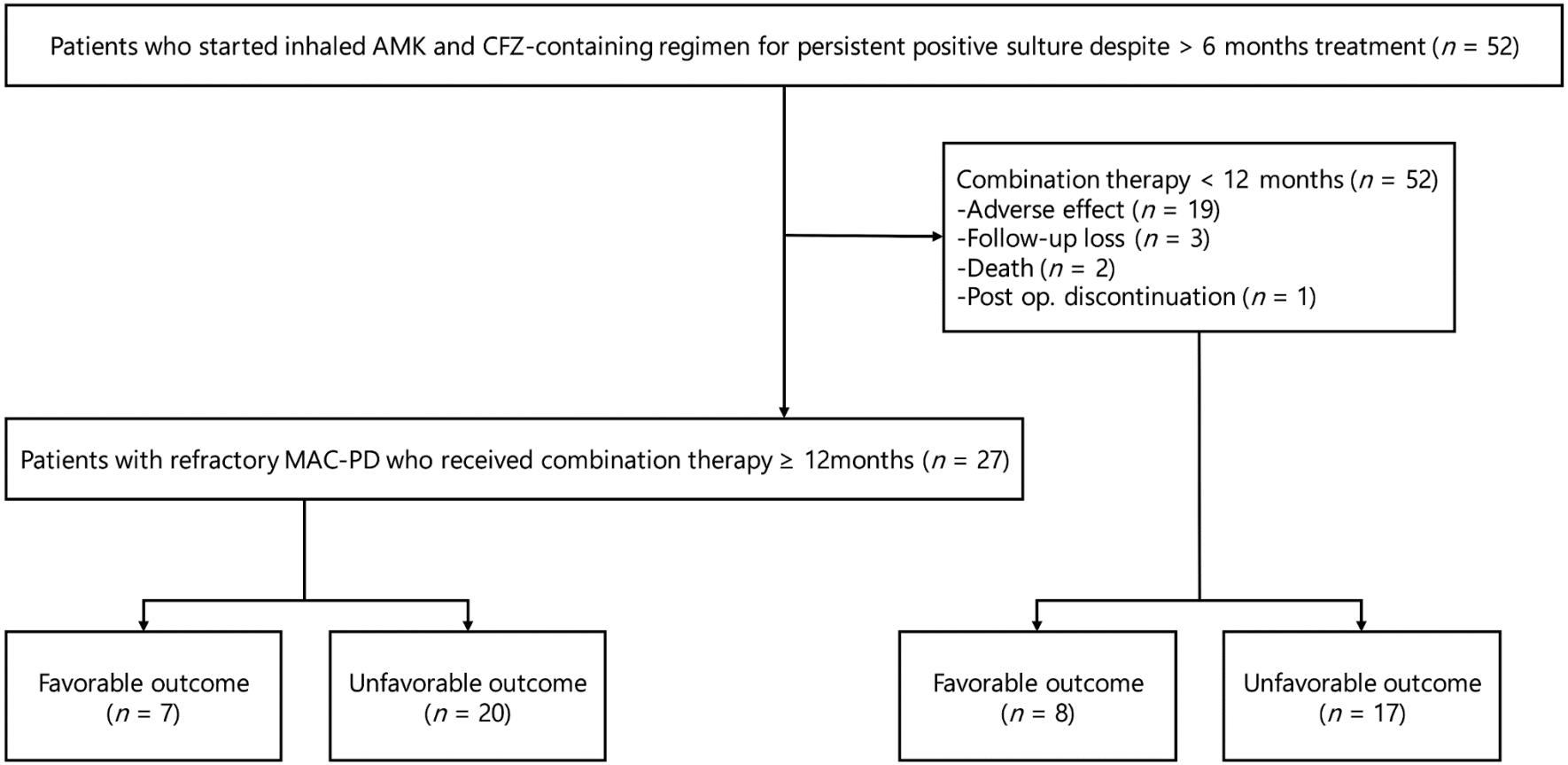
Author (yr)	No.	Species	Previous Tx	Dosage	AmkInh Duration	Sputum conversion
Olivier (2014) NIH Clinical Center, USA	20	MAC (5) *M. abscessus* (15)	60 mo. (range 6-190)	250 mg+ 3ml saline (once daily-> 250m twice daily -> 500mg twice daily)	19 mo. (range 1-50)	One negative 40% Negative conversion 25%*
Yagi (2017) Keio University, Japan	23	MAC (21) *M. abscessus* (2)	61 mo. (IQR, 30-104)	15 mg/kg, once daily	7 mo (range 5-36)	Negative conversion 43%¶
Jhun (2018) Samsung medical, South Korea	77	MAC (20) *M. abscessus* (48) Mixed (9)	38 mo. (IQR, 16-61)	250 mg -> 500 mg once daily OR, 500 mg three times weekly	12 mo. (IQR, 7-12)	One negative 34% Negative conversion 18%#

Data are shown as median (range or IQR).
*4 *M. abscessus* + 1 MAC
¶ 2 *M. abscessus* + 8 MAC
# 6 *M. abscessus* + 3 MAC + 5 mixed

Olivier KN, et al. Ann Am Thorac Soc 2014;11:30
Yagi K, et al. BMC Infect Dis 2017;17:558
Jhun BW, et al. AAC 2018;62: e00011

Outcomes of AmkInh and Clofazimine-Regimens for Refractory MAC-PD

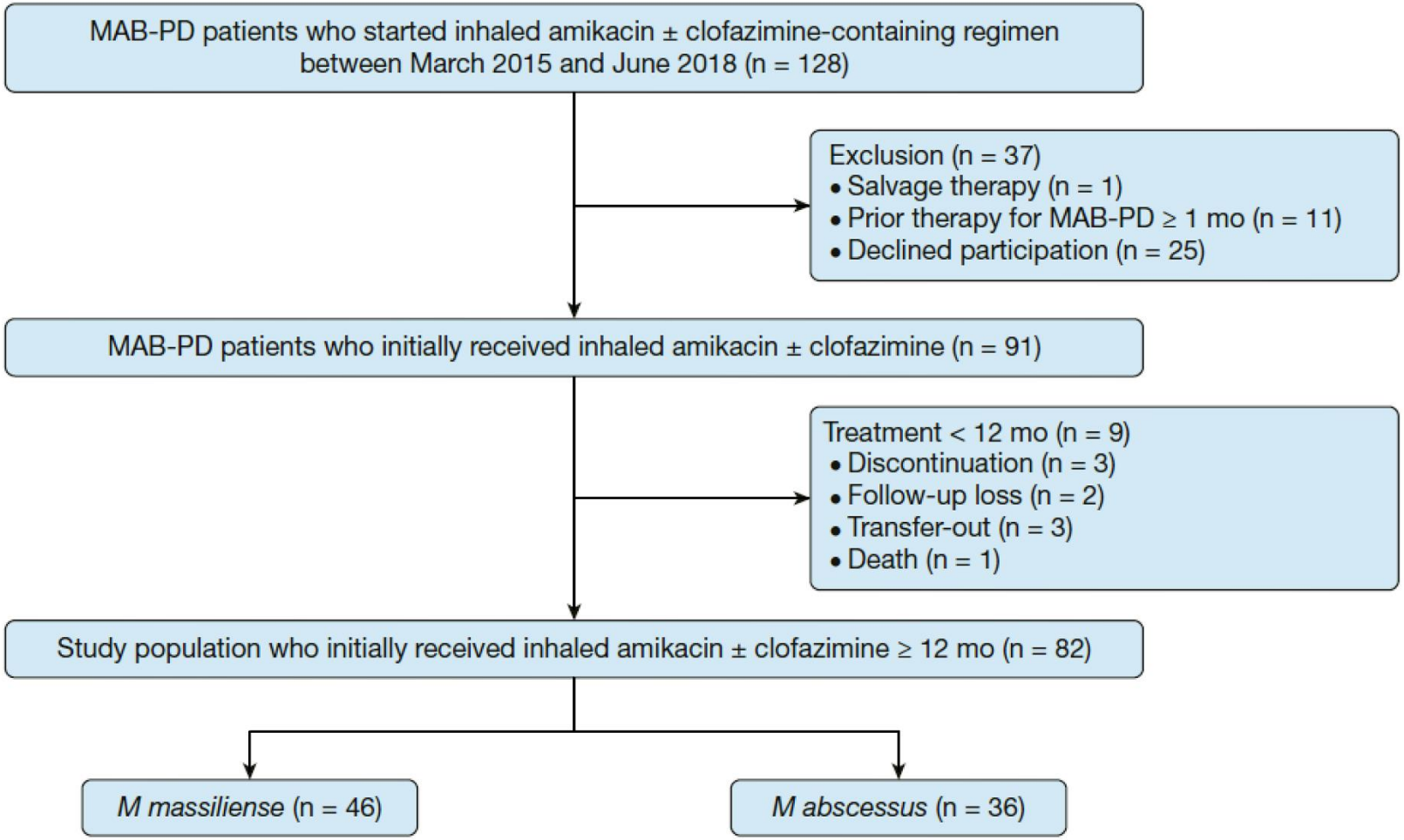
- SMC, refractory MAC-PD with previous treatment of 28.5 (IQR 20.3–55.5) mo.
- AmkInh and Clofazimine-Regimens: 15.4 (IQR 12.5–21.2) mo.
- Culture conversion 33%, time to culture conversion: 3.0 (IQR 1.0–9.2) mo.
- Microbiological cure 23%, Favorable outcome (cure + clinical cure) 29%



Kim et al. Clin Med 2020;9(9):2968

AmkInh-containing regimens for *M. abscessus*

- SMC, prospective observational cohort, 82 *M. abscessus*-PD,
- Total duration of AmkInh-containing regimens: 18 (IQR 15-22) mo.



Kang et al. CHEST 2021;160(2):436-445

AmkInh-containing regimens for *M. abscessus*

	subsp. *abscessus* (n = 36)	subsp. *massiliense* (n = 46)
Initial phase	4 weeks	1-2 weeks
	IV amikacin (100%) IV imipenem (100%) IV tigecycline (28%)	IV amikacin (100%) IV imipenem (100%)
Continuation phase	>12 mo of (-) culture	>12 mo of (-) culture
	amikacin inhalation (100%) azithromycin (100%) clofazimine (100%) linezolid (42%)	amikacin inhalation (100%) azithromycin (100%) clofazimine (65%) linezolid (4%)
Microbiological cure	31% (11/36)	96% (44/46)

Kang et al. CHEST 2021;160(2):436-445

Adverse effects associated with amikacin in NTM-PD

Author	No.	Route	Stopped	Renal injury	Hearing loss	Tinnitus	Vertigo	Hoarseness Dysphonia
Jorup	31	iv	-	3%	-	-	-	-
Parenti	37	iv	14%	-	-	-	-	-
DeLalla	12	iv	-	-	-	-	-	-
Roger	15	iv	7%	7%	-	-	-	-
Lyu	41	iv	-	2%	10%	-	-	-
Ellender	45	iv	-	-	7%	-	2%	-
Zweijpfenning	19	iv	16%	-	37%	42%	-	-
Davis	6	Inh	17%	-	-	-	-	-
Olivier	20	Inh	35%	5%	10%	-	5%	5%
Yagi	23	Inh	4%	-	-	4%	-	19%
Jhun	77	Inh	27%	-	19%	5%	-	1%
Kang	82	Inh	16%	4%	8%	-	-	1%
Olivier	44	ALIS	16%	2%	4%	11%	-	43%
Griffith	224	ALIS	17%	3%	5%	8%	1%	46%
Winthrop	163	ALIS	16%	2%	8%	4%	3%	43%

NTM 폐질환에서 **AmkInh** 사용 해볼 수 있는 상황

- 난치성 MAC 폐질환 환자에서 사용 (특히, synergism with clofazimine)
- *M. abscessus* 폐질환, 특히 subsp. *massiliense* 환자에서 유지 약제로 사용
- 도관 합병증 혹은 환자의 거동 제한 등에 의해, 장기간 amikacin 주사 (intravenous or intramuscular) 사용이 어려운 상황에서 대체하여 사용

요 약

- Conventional amikacin 흡입은 NTM 폐질환 치료 시에 임상 의사가 시도해 볼 수 있는 치료법 중의 한 가지가 될 수 있다. 아직은 적용할 수 있는 상황이 제한적이고, 적절한 용법이 정립되지 않았기 때문에 더 많은 연구가 필요하다.

- 그러나, NTM 폐질환 치료에 사용할 수 있는 효과적인 약제가 극명히 부족한 임상 상황을 고려한다면, conventional amikacin 흡입과 같은 전략을 부가적으로 진료현장에서 활용하는 것이 좋다고 생각한다.

- 따라서, 많은 사용 경험을 바탕으로, 적절한 사용법과 치료 전략을 수립하고, 적합한 대상자를 선별해 나가는 것이 좋을 것으로 생각한다.