Original Article

Investigation of *In vitro* Efficacy of New Generation Drugs Tedizolid and Omadacycline against Nontuberculous Mycobacteria

Seda Türkkal Arli[1], Nazli Ece Özçatalkaya[1], Elif Çiftçi[2], Şafak Ceren Uçak[3], Görkem Yaman[4], Dilek Satana[1]

[1]Department of Medical Microbiology, Istanbul Faculty of Medicine, Istanbul University, [2]Department of Medical Microbiology, Faculty of Medicine, Istanbul Nisantasi University, [3]Department of Medical Microbiology, Faculty of Dentistry, Istanbul Kent University, Istanbul, [4]Department of Medical Microbiology, Faculty of Medicine, Izmir Bakircay University, Izmir, Turkiye

Abstract

Background: Species-specific antimicrobial susceptibility testing is crucial for the effective treatment of nontuberculous mycobacteria (NTM). In this study, the *in vitro* antimicrobial activities of two next-generation antibacterial agents, tedizolid (TZD) and omadacycline (OMC) – which have demonstrated strong *in vitro* activity against NTM species but have not been comprehensively evaluated for NTM treatment in Turkiye – were investigated. **Methods:** In this study, antibiotic susceptibility testing for TZD and OMC was performed on a total of 104 NTM isolates (59 rapid-growing and 45 slow-growing) using the colorimetric microdilution method, in accordance with Clinical and Laboratory Standards Institute (CLSI) M24 and M62 standards. Minimum inhibitory concentration (MIC) ranges were 0.015–32 μg/ml for TZD and 0.003–64 μg/ml for OMC. For the interpretation of TZD susceptibility, the CLSI M62 breakpoints established for linezolid were used (≤8 μg/ml: susceptible, 16 μg/ml: intermediate, and ≥32 μg/ml: resistant). **Results:** Among the rapidly growing NTM isolates, only one *Mycobacterium fortuitum* isolate was found to be intermediate (1/29; 16 μg/mL), while one *Mycobacterium avium* isolate among the slowly growing species was classified as resistant (1/6; ≥32 μg/mL). The remaining 102 isolates were all found to be susceptible to TZD (≤8 μg/mL). Since no standardized breakpoint has yet been established for OMC, only the observed MIC values were reported. **Conclusions:** The findings demonstrated that TZD exhibits strong *in vitro* activity against NTM isolates, whereas OMC showed a variable activity profile, particularly among rapidly growing species. These results support the necessity of basing antibiotic selection for the treatment of NTM infections on species-specific susceptibility testing.

Keywords: Antituberculous susceptibility testing, microdilution, nontuberculous mycobacteria, omadacycline, tedizolid

Submitted: 10-Jan-2026 **Revised:** 19-Feb-2026 **Accepted:** 09-Mar-2026 **Published:** 27-Mar-2026

Introduction

Nontuberculous mycobacteria (NTM), which are part of the *Mycobacterium* genus, comprise over 200 species excluding *Mycobacterium tuberculosis*, the causative agent of tuberculosis, and *Mycobacterium leprae*, the causative agent of leprosy.[1] Today, the diagnosis and treatment of NTM infections are guided by recommendations from the Clinical and Laboratory Standards Institute (CLSI), as well as guidelines published by the American Thoracic Society and the Infectious Diseases Society of America (ATS/IDSA), with appropriate antibiotic selection and susceptibility testing.[2-4] This study aims to determine the *in vitro* antimicrobial susceptibility of NTM strains to tedizolid (TZD) and omadacycline (OMC) using the colorimetric microdilution method, in accordance with CLSI M24 and M62 guidelines, and to contribute data from Turkiye to the global literature.[4,5]

Access this article online

Quick Response Code:

Website: https://journals.lww.com/IJMY

DOI: 10.4103/ijmy.ijmy_25_26

Address for correspondence: Ms. Seda Türkkal Arli, Apartment 12, No. 14, Balaban Apartment, 405th Avenue, Demetlale Neighborhood, Yenimahalle 06170, Ankara, Turkey.
E-mail: sedaturkkal99@gmail.com

ORCID:
Seda Türkkal Arli: http://orcid.org/0009-0004-7815-1789

How to cite this article: Arli ST, Özçatalkaya NE, Çiftçi E, Uçak ŞC, Yaman G, Satana D. Investigation of *in vitro* efficacy of new generation drugs tedizolid and omadacycline against nontuberculous mycobacteria. Int J Mycobacteriol 2026;15:54-60.

Methods

Study setting

In this study, a total of 104 nontuberculous mycobacteria (NTMs), 59 of which were rapidly growing mycobacteria (RGM) and 45 were slow-growing mycobacteria (SGM), were isolated from clinical samples sent to the Istanbul University, Istanbul Faculty of Medicine, Department of Medical Microbiology, Mycobacteriology Laboratory, and Düzen Private Laboratory routinely collect clinical patient samples for examination. Collection strains isolated from samples accepted between 2018 and 2023 were identified using the MALDI-TOF MS system. As a quality control strain, *Staphylococcus aureus* ATCC 29213 was used according to the recommendations of the CLSI M62 guideline, and it was tested concurrently using the broth microdilution method.[5]

Study design and reporting compliance

Preparation of drug stock solutions

TZD (TR-700, Selleckchem) and OMC tosylate (PTK 0796 tosylate, Amadacycline tosylate, Selleckchem) were obtained as pure powder from the manufacturer in amounts of 25 mg and 5 mg, respectively. The amount of antimicrobial agents to be used was calculated based on the formula:

$$\text{Weight (mg)} = (\text{Volume [mL]} \times \text{Concentration [µg/mL]})/\text{Potency (µg/mg)}.$$

Potency values were determined according to the information provided by the manufacturer. The drug amounts calculated in grams were weighed using an analytical balance and diluted with appropriate solvents recommended by the manufacturer. As a result, stock solutions were prepared.[4] The basic properties and initial concentrations of the antimicrobial agents used are presented in Table 1.

Broth microdilution method

Antimicrobial susceptibility testing of NTM isolates was performed using the broth microdilution method in accordance with the guidelines of the CLSI. For rapidly growing mycobacterial isolates, cation-adjusted Mueller-Hinton broth II (CAMHB II) was used, while for slowly growing isolates, Middlebrook 7H9 broth supplemented with 5% Oleic Albumin Dextrose Catalase, Growth Supplement (OADC) was preferred. Separate 96-well U-bottom microplates were prepared for the tested agents, TZD and OMC, with 100 µL of the appropriate broth medium added to each well. Stock solutions, previously dissolved in dimethyl sulfoxide, were diluted in the relevant broth medium to achieve a concentration four times higher than the starting concentration, and 100 µL of this solution was added to the first wells of the microplates. A serial dilution was then performed. In addition to the test groups containing the isolates, solvent control, negative control (medium only), and positive control (medium + isolate) groups were included in appropriate wells. Bacterial suspensions adjusted to a 0.5 McFarland standard were further diluted 1:100 in the appropriate broth medium and inoculated into all wells at a volume of 100 µL (except for the negative control wells). The microplates were sealed with tape to prevent evaporation and incubated at 37°C for 48 h for rapidly growing isolates and for 7–8 days for slowly growing isolates. At the end of the incubation period, 30 µL of resazurin solution was added to all wells, followed by a second incubation period of 2–5 days for rapidly growing species and 7–14 days for slowly growing species. A color change in the positive control wells from blue to pink or purple was considered indicative of microbial growth. The lowest concentration at which no color change was observed was recorded as the minimum inhibitory concentration (MIC) for the tested antimicrobial agent.[4]

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Istanbul University, Istanbul Faculty of Medicine (protocol code 1352188 and date of approval: October 31, 2022).

Patient consent agreement

Patient consent is not required.

Type of sampling and reasons for selection

NTM isolated from various clinical samples sent to the laboratory for routine examination due to suspected tuberculosis were included in the study.

Inclusion and exclusion criteria

NTM isolated from samples sent to the laboratory with suspected tuberculosis were included in the study. If *M. tuberculosis* was isolated from the sample, the sample was not included in the study.

Statistical analysis

All statistical analyses were performed using GraphPad Prism version 8.0.1 (GraphPad Software, San Diego, CA, USA). Continuous variables were expressed as median and interquartile range (IQR), given the nonnormal distribution of MIC values. Paired comparisons between TZD and OMC MIC

Table 1: General characteristics and initial concentrations of the drugs used

	TZD	OMC
MIC range used (µg/mL)	32–0.015	64–0.03
Required drug concentration for one isolate (µg/mL)	128 (32×4)	256 (64×4)
Potency value (%)	100	100
Weight (mg)=Volume (mL) × Concentration (µg/mL)/potency (µg/mg)	1 mL×128 µg/mL=128 µg*	1 mL×256 µg/mL=256 µg*
Solvent (1 mL)	DMSO	DMSO

*Because the weighed amount was too small to be measured accurately on an analytical balance, at least 100 times the amount was weighed.
MIC: Minimum inhibitory concentration, DMSO: Dimethyl sulfoxide, TZD: Tedizolid, OMC: Omadasiklin

values for the same isolates were conducted using the Wilcoxon signed-rank test based on raw MIC values. A two-tailed $P < 0.05$ was considered statistically significant. Comparisons of categorical MIC distributions and proportions of isolates demonstrating elevated MIC values across species were analyzed using the Chi-square (χ^2) test. When the expected cell counts were small, appropriate corrections were applied. MIC_{50} and MIC_{90} values were calculated descriptively and were not subjected to inferential statistical testing.

Results

In this study, the species and numbers of rapidly growing isolates were as follows: *Mycobacterium fortuitum* (29), *Mycobacterium abscessus* (21), *Mycobacterium peregrinum* (3), *Mycobacterium chelonae* (3), *Mycobacterium neoaurum* (1), and the *Mycobacterium farcinogenes–senegalense* group (1). Among the slowly growing isolates (45), the species and their counts were *Mycobacterium lentiflatum* (15), *Mycobacterium avium* complex (MAC) (14) – including *M. avium* (6), *Mycobacterium intracellulare* (4), and *Mycobacterium chimera* (4) – *Mycobacterium simiae* (4), and *Mycobacterium kansasii* (3).

For *M. fortuitum* (n = 29), the median MIC of TZD was 0.5 µg/mL (IQR: 0.19–0.50), which was comparable to OMC (median: 0.5 µg/mL, IQR: 0.13–4.0). The MIC_{50}/MIC_{90} values were 0.5/2 µg/mL for TZD and 0.5/16 µg/mL for OMC. The median fold difference (OMC/TZD) was 1 (IQR: 0.5–4). Although OMC demonstrated a higher MIC_{90}, the paired comparison did not reach statistical significance (P = 0.0696). In contrast, for *M. abscessus* (n = 21), TZD exhibited lower MIC values compared with OMC. The median MIC was 0.25 µg/mL (IQR: 0.13–0.50) for TZD and 0.5 µg/mL (IQR: 0.25–4.0) for OMC. The MIC_{50}/MIC_{90} values were 0.25/0.5 µg/mL for TZD and 0.5/4 µg/mL for OMC. The median fold difference was 2 (IQR: 1–8), indicating higher MIC values for OMC. This difference was statistically significant (P = 0.0006). For *M. lentiflatum* (n = 15), TZD demonstrated markedly lower MIC values compared with OMC. The median MIC was 0.25 µg/mL (IQR: 0.03–0.5) for TZD and 4 µg/mL (IQR: 1–16) for OMC. The MIC_{50}/MIC_{90} values were 0.25/1 µg/mL and 4/64 µg/mL, respectively. The median fold difference was 16 (IQR: 4–64), and the difference was highly statistically significant (P = 0.0017). For *M. avium* (n = 6), median MIC values were 0.25 µg/mL (IQR: 0.06–1) for TZD and 0.125 µg/mL (IQR: 0.03-64) for OMC. Although the MIC_{90} values were 32 µg/mL and 64 µg/mL, respectively, paired analysis did not demonstrate a statistically significant difference between the two agents (P = 0.8438). The wide IQR reflects substantial variability among isolates. For *Mycobacterium gordonae* (n = 9), TZD showed substantially lower MIC values than OMC. The median MIC was 0.06 µg/mL (IQR: 0.06–0.125) for TZD and 2 µg/mL (IQR: 0.5–8) for OMC. The MIC_{50}/MIC_{90} values were 0.06/0.25 µg/mL and 2/16 µg/mL, respectively. The median fold difference was 32 (IQR: 8–64), and the difference was statistically significant (P = 0.0078) [Table 2].

Among RGM, *M. fortuitum* displayed a broader MIC distribution of TZD. While the majority of isolates clustered between 0.25 and 1 µg/mL, one isolate demonstrated a higher MIC of 16 µg/mL. Although the proportion of isolates with elevated MIC values was slightly higher in *M. fortuitum* compared with other RGM species, this difference did not reach statistical significance (P = 0.305). Despite this outlier, the overall MIC_{90} remained low (2 µg/mL), indicating generally preserved *in vitro* activity. No other RGM species demonstrated similarly elevated MIC values for TZD. On the other hand, *M. fortuitum*, *M. abscessus*, and *M. chelonae* displayed broader MIC distribution of OMC. While most isolates clustered between 0.25 and 4 µg/mL, three isolates of *M. fortuitum*, one isolate of *M. abscessus*, and two isolates of *M. chelonae* demonstrated elevated MIC values of 32 µg/mL. Although the proportion of isolates with higher MIC values was numerically greater in these species, the difference was not statistically significant among RGM isolates (P = 0.285). Among SGM, *M. avium* demonstrated the broadest MIC range of TZD, including one isolate with an elevated MIC ≥32 µg/mL. The proportion of isolates with elevated MIC values was significantly higher in *M. avium* compared with other SGM species (P = 0.009). Although most isolates remained within lower concentration ranges of TZD, this finding indicates occasional upper-range variability within the species. On the other hand, *Mycobacterium lentiflavum*, *M. avium*, *M. intracellulare*, *M. simiae,* and *M. kansasii* demonstrated broader MIC ranges of OMC. Three isolates of *M. avium* and two isolates from other SGM species exhibited elevated MIC values ≥64 µg/mL OMC. Although the proportion of isolates with high-level MIC values appeared numerically greater in these species, the difference was not statistically significant among SGM isolates (P = 0.387). Overall, TZD demonstrated a more consistent and narrower MIC distribution across both RGM and SGM compared with OMC. Elevated MIC values were infrequent with TZD and were largely confined to isolated outliers, most notably in *M. fortuitum* among RGM and *M. avium* among SGM. In contrast, OMC exhibited broader interspecies variability, with high-level MIC values (≥32–64 µg/mL) observed in multiple RGM and SGM species, particularly *M. fortuitum*, *M. lentiflavum*, and *M. avium*. Although not all interspecies differences reached statistical significance, the overall distribution patterns suggest more stable *in vitro* activity of TZD, whereas OMC showed greater heterogeneity in upper-range MIC values. These findings highlight notable species-dependent differences in antimicrobial activity and underscore the importance of species-level susceptibility profiling when evaluating therapeutic options.

The MIC values of both rapidly and slowly growing mycobacterial species for TZD are presented in Table 3.

The MIC values of both rapidly and slowly growing mycobacterial species for OMC are presented in Table 4.

Table 2: Comparative minimum inhibitory concentrations of omadacycline and tedizolid for clinical isolates of slowly growing mycobacteria and rapidly growing mycobacteria

Organism	*n*	TZD Median, (IQR)	OMC Median, (IQR)	TZD MIC_{50}/ MIC_{90}	OMC MIC_{50}/ MIC_{90}	Median fold difference (IQR)	*P**
RGM							
Mycobacterium fortuitum	29	0.5 µg/mL (0.19–0.50)	0.5 µg/mL (0.13–4.0)	0.5/2	0.5/16	1 (0.5–4)	0.0696
Mycobacterium abscessus	21	0.25 µg/mL (0.13–0.50)	0.5 µg/mL (0.25–4.0)	0.25/0.5	0.5/4	2 (1–8)	0.0006
SGM							
Mycobacterium lenfilatum	15	0.25 µg/mL (0.03–0.50)	4.00 µg/mL (0.50–16.0)	0.25/1	4/64	16 (4–64)	0.0017
Mycobacterium gordonae	9	0.06 µg/mL (0.05–0.13)	2.00 µg/mL (0.50–6.00)	0.06/0.25	2/16	32 (8–64)	0.0078
Mycobacterium avium	6	0.25 µg/mL (0.05–0.75)	0.13 µg/mL (0.03–64)	0.25/1	0.125/64	1 (0.125–256)	0.8438

*Wilcoxon signed-rank test based on MIC values. RGM: Rapidly growing mycobacteria, SGM: Slowly growing mycobacteria, OMC: Omadacycline, TZD: Tedizolid, IQR: Interquartile range, MIC: Minimum inhibitory concentrations

Table 3: Minimum inhibitory concentration values of rapidly and slowly growing mycobacterial isolates against tedizolid

	MIC values against TZD (µg/mL)												
	n	≥32	16	8	4	2	1	0.5	0.25	0.125	0.06	0.03	≤0.015
RGM													
Mycobacterium fortuitum	29		1		2	1	2	10	6	3	3	1	
Mycobacterium abscessus	21						1	5	7	4	2		2
Mycobacterium chelonae	3					1			2				
Mycobacterium peregrinum	3						1	1	1				
Mycobacterium elephantis	1								1				
Mycobacterium neoarum	1									1			
Mycobacterium farcinogenes	1									1			
SGM													
Mycobacterium lentiflavum	15						3	4	1	2	1	3	1
Mycobacterium gordonae	9								1	2	4	1	1
Mycobacterium avium	6	1					1		2		1		1
Mycobacterium intracellulare	4					1	2			1			
Mycobacterium chimera	4				1			1	2				
Mycobacterium simiae	4					2			2				
Mycobacterium kansasii	3							2	1				

RGM: Rapidly growing mycobacteria, SGM: Slowly growing mycobacteria, MIC: Minimum inhibitory concentration, TZD: Tedizolid

Table 4: Minimum inhibitory concentration values of rapidly and slowly growing mycobacterial isolates against omadacycline

	MIC values against OMC (µg/mL)												
	n	≥64	32	16	8	4	2	1	0.5	0.25	0.125	0.06	≤0.03
RGM													
Mycobacterium fortuitum	29		3	1	1	3	1	5	2	5	7	1	
Mycobacterium abscessus	21		1			6	1	1	5	3	2	1	1
Mycobacterium chelonae	3		2	1									
Mycobacterium peregrinum	3									2	1		
Mycobacterium elephantis	1							1					
Mycobacterium neoarum	1											1	
Mycobacterium farcinogenes	1							1					
SGM													
Mycobacterium lentiflavum	15	3		1	1	4		2	1		1		2
Mycobacterium gordonae	9			1	1	1	2	1	2			1	
Mycobacterium avium	6	2									2		2
Mycobacterium intracellulare	4	2						1				1	
Mycobacterium chimera	4		1		1	1	1						
Mycobacterium simiae	4	2				1		1					
Mycobacterium kansasii	3	2					1						

RGM: Rapidly growing mycobacteria, SGM: Slowly growing mycobacteria, MIC: Minimum inhibitory concentration, OMC: Omadacycline

Discussion

Antibiotic susceptibility testing (AST) in accordance with CLSI and ATS/IDSA guidelines is utilized to determine appropriate treatment regimens for NTM infections.[2-4] However, AST is generally recommended for clinically significant pathogenic species, as each NTM species exhibits a distinct antimicrobial susceptibility profile. Therefore, species-level identification of isolates is crucial for effective treatment.[6] On the other hand, discrepancies between *in vitro* AST results and clinical responses introduce uncertainties in treatment planning.[2] The limitations of current therapeutic options highlight the need for more effective, tolerable agents suitable for long-term use and innovative pharmaceutical developments. In this context, TZD and OMC have emerged as promising alternative treatment options due to their strong *in vitro* activity against NTM species.[6]

Oxazolidinones are synthetic agents that inhibit protein synthesis and are effective against Gram-positive bacteria, including mycobacteria.[7,8] Linezolid, the first Food and Drug Administration-approved member of this class, is used in the treatment of NTM and tuberculosis; however, its long-term use is limited by toxicity and high MIC values, which reduce its efficacy.[7-9] TZD phosphate, developed to overcome these limitations, offers lower toxicity, the convenience of once-daily dosing, and potent *in vitro* activity, making it a promising alternative for NTM infections.[10,11]

In this study, the antimicrobial susceptibility of a total of 104 NTM isolates – comprising 59 rapidly growing and 45 slowly growing strains – was evaluated against TZD. The MIC range for TZD was determined as ≤0.015 to ≥32 µg/mL. For susceptibility interpretation, the breakpoint values recommended for linezolid in the CLSI M62 document were used as a reference, based on available literature data (susceptible ≤8 µg/mL, intermediate 16 µg/mL, resistant ≥ 32 µg/mL).[5]

Among the slowly growing mycobacteria, one *M. avium* isolate within the MAC group was found to be resistant (1/6; ≥32 µg/mL), while the remaining isolates were susceptible (13/14; ≤8 µg/mL). All *M. kansasii* isolates were determined to be susceptible to TZD (3/3; ≤8 µg/mL). Due to better growth conditions for these species, testing was performed using Middlebrook 7H9 broth supplemented with 5% OADC.[12,13] Similar studies have reported high MIC values for MAC (Zhang *et al*.;[14] $MIC_{50:}$ 16 µg/mL, $MIC_{90:}$ 32 µg/mL) and susceptibility for *M. kansasii* (18/18; ≤8 µg/mL), noting that linezolid MIC values were 4–8 times higher compared to TZD.[14] Brown-Elliott and Wallace[10] reported an MIC_{90} > 32 µg/mL for 100 MAC isolates and 64 µg/mL for linezolid, whereas *M. kansasii* isolates showed an MIC_{50} of 0.5 µg/mL and were all susceptible. In the literature, TZD MIC values for MAC are generally higher than those for linezolid, but *M. kansasii* isolates – including those in our study – are consistently considered susceptible. These findings suggest that TZD may serve as an alternative to linezolid for slowly growing species. In addition, all isolates of *M. lentiflavum* (15/15), *M. gordonae* (9/9), and *M. simiae* (4/4) were found to be susceptible to TZD.

For rapidly growing species, testing was performed using CAMHB II medium. All *M. abscessus* (21/21) and *M. chelonae* (3/3) isolates were found to be susceptible to TZD. Among *M. fortuitum* isolates, one was identified as intermediate susceptible (1/29; 16 µg/mL). Brown-Elliott and Wallace[10] reported susceptibility for *M. fortuitum* (n = 20) and *M. chelonae* (n = 22) with MIC_{50} and MIC_{90} values of 1 µg/mL and 2 µg/mL, respectively. Linezolid MIC values were reported to be 2–8 times higher.[10] Similarly, Zhang *et al*.[14] found all *M. abscessus* complex isolates (35/35), *M. fortuitum* (21/21), and *M. chelonae* (1/1) susceptible to TZD. In addition, TZD susceptibility was demonstrated for *M. peregrinum* (n = 3; $MIC_{50:}$ 0.5 µg/mL), *Mycobacterium elephantis* (n = 1; MIC: 0.25 µg/mL), *M. neoaurum* (n = 1; MIC: 0.125 µg/mL), and *M. farcinogenes–senegalense* group (n = 1; MIC: 0.125 µg/mL). These rare species data provide valuable contributions to the existing literature.

Tigecycline (TGC), a member of the tetracycline antibiotic class, is included in treatment protocols due to its potent *in vitro* activity against RGM such as the *M. abscessus* complex.[15,16] However, its use is limited by the requirement for intravenous administration and frequent gastrointestinal side effects during prolonged therapy.[17,18] In contrast, OMC from the same class offers a more advantageous alternative with both oral and parenteral formulations, better tolerability, and a broad spectrum of activity.[19,20] Indeed, recent studies have demonstrated clinical success of OMC in treating *M. abscessus* infections,[21] suggesting that it may be a more feasible option compared to TGC.

In this study, the MIC range of OMC against a total of 104 NTM isolates was determined as 0.003–64 µg/mL. Since CLSI has not yet established breakpoint values for OMC, the obtained MIC values were reported. For the 45 slowly growing NTM isolates, the MIC range for OMC was found to be <0.03 to >64 µg/mL; notably, MIC_{90} values reached high levels (>64 µg/mL), particularly among MAC and *M. lentiflavum* isolates. Data on OMC susceptibility for these species are quite limited in the literature. Brown-Elliott and Wallace[22] reported OMC MIC_{50} and MIC_{90} values generally >16 µg/mL in slowly growing species. A standardized susceptibility testing method for OMC has not yet been developed by CLSI. Variability in MIC results for the same species depending on different culture media, especially among slowly growing species, suggests that tetracycline stability and incubation time may influence test outcomes. This highlights the need for novel methodological approaches to standardize OMC susceptibility testing.[23]

For 59 rapidly growing mycobacterial isolates, the MIC range for OMC was determined as ≤ 0.03–32 µg/mL. Among *M. abscessus* isolates (n = 21), the MIC_{50} and MIC_{90} values were 0.5 µg/mL and 4 µg/mL, respectively;

for *M. fortuitum* (n = 29), these values were 0.5 µg/mL and 16 µg/mL; and for *M. chelonae* (n = 3), the MIC_{50} was 32 µg/mL. Similarly, in a study by Shoen *et al*.,[24] OMC MIC_{90} values against *M. abscessus*, *M. chelonae*, and *M. fortuitum* were reported as 2, 0.25, and 0.5 µg/mL, respectively. Kaushik *et al*.[25] also evaluated the efficacy of OMC and eravacycline against drug-resistant *M. abscessus* complex, reporting an OMC MIC_{90} value of 2 µg/mL. Both studies found TGC and MIC values to be similar to those of OMC. However, in the present study, two *M. chelonae* isolates exhibited elevated MIC values of 32 µg/mL, which contrasts with the literature and is likely attributable to differences in incubation temperature. Brown and Wallace.,[22] in their study of 70 rapidly growing mycobacterial species, reported an MIC range of 0.03–1 µg/mL, with an MIC_{50} of 0.12 µg/mL for *M. abscessus* subspecies *massiliense* and an MIC_{90} of 0.5 µg/mL for *M. chelonae*. In this study, TGC also demonstrated MIC values comparable to OMC among rapidly growing species.

Although OMC exhibits *in vitro* MIC values similar to TGC, it is considered a potential therapeutic agent against RGM due to its oral bioavailability, better tolerability, and favorable pharmacokinetic properties. However, CLSI has not yet established a standardized MIC testing method for these pathogens. This gap complicates accurate determination of MIC values,[22] and the variability observed in our study is thought to stem from factors such as isolate origin, sample size, incubation conditions, and limitations in testing methodologies.

There are no comparative literature data available on the *in vitro* susceptibility to OMC of other rapidly growing mycobacterial species included in our study, namely *M. peregrinum* (n = 3; MIC_{50}: 0.25 µg/mL), *M. elephantis* (n = 1; MIC: 1 µg/mL), *M. neoaurum* (n = 1; MIC: 0.06 µg/mL), and *M. farcinogenes* (n = 1; MIC: 1 µg/mL). In this respect, our study contributes to the literature by providing MIC data for these rare species.

Rationale of the study

Species-specific antimicrobial susceptibility testing is crucial for the effective treatment of nontuberculous mycobacteria (NTM). In this study, the *in vitro* antimicrobial activities of two next-generation antibacterial agents, TZD and OMC – which have demonstrated strong *in vitro* activity against NTM species but have not been comprehensively evaluated for NTM treatment in Turkiye – were investigated.

Outcomes of the study

In conclusion, this study demonstrated that TZD exhibits strong *in vitro* activity against NTM species, whereas OMC showed variable results among rapidly growing strains. Species-specific susceptibility testing is essential for the treatment of NTM infections; however, considering that *in vitro* results do not always correlate with clinical outcomes, further comprehensive evaluation of drug efficacy through animal models and clinical trials is warranted.

Limitations of the study

The results in this study were obtained using *in vitro* microdilution. The gene profiles of the resistant strains that could cause resistance could not be determined at the molecular level due to material limitations.

Consent for publication

"Not applicable" for nonhuman studies.

Financial support and sponsorship

This research was funded by the Istanbul University Scientific Research Project Foundation, grant number: 39625.

Conflicts of interest

There are no conflicts of interest.

References

1. Tarashi S, Siadat SD, Fateh A. Nontuberculous mycobacterial resistance to antibiotics and disinfectants: Challenges still ahead. Biomed Res Int 2022;2022:8168750:1-12.
2. Pennington KM, Vu A, Challener D, Rivera CG, Shweta FN, Zeuli JD, *et al*. Approach to the diagnosis and treatment of non-tuberculous mycobacterial disease. J Clin Tuberc Other Mycobact Dis 2021;24:100244.
3. CLSI. Susceptibility Testing of Mycobacteria, Nocardiae, and Other AerobicActinomycetes; Approved Standard—Second Edition. CLSI document M24-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2011. Available from: https://cdn.bfldr.com/YLD4EVFU/at/hqj6p2j7grxcmr96v43sjwk/m24ed3_sample.pdf. [Last accessed on 2023 Jan 24].
4. CLSI. Susceptibility Testing of Mycobacteria, Nocardia spp., and Other AerobicActinomycetes. 3rd ed. CLSI Standard M24. Wayne, PA: Clinical and LaboratoryStandards Institute; 2018. Available from: https://clsi.org/standards/products/microbiology/documents/m24/. [Last accessed on 2026 Feb 18].
5. CLSI. Performance Standards for Susceptibility Testing of Mycobacteria, Nocardiaspp., and Other Aerobic Actinomycetes. 1st ed. CLSI supplement M62. Wayne, PA: Clinical and Laboratory Standards Institute; 2018. Available from: https://clsi.org/shop/standards/m24s/. [Last accessed on 2026 Feb 18].
6. Alffenaar JW, Märtson AG, Heysell SK, Cho JG, Patanwala A, Burch G, *et al*. Therapeutic drug monitoring in non-tuberculosis mycobacteria infections. Clin Pharmacokinet 2021;60:711-25.
7. Marfil E, Ruiz P, Martínez-Martínez L, Causse M. Comparative study of *in vitro* activity of tedizolid and linezolid against *Mycobacterium avium* complex. J Glob Antimicrob Resist 2022;30:395-8.
8. Wen S, Gao X, Zhao W, Huo F, Jiang G, Dong L, *et al*. Comparison of the *in vitro* activity of linezolid, tedizolid, sutezolid, and delpazolid against rapidly growing mycobacteria isolated in Beijing, China. Int J Infect Dis 2021;109:253-60.
9. Ruth MM, Koeken VA, Pennings LJ, Svensson EM, Wertheim HF, Hoefsloot W, *et al*. Is there a role for tedizolid in the treatment of non-tuberculous mycobacterial disease? J Antimicrob Chemother 2020;75:609-17.
10. Brown-Elliott BA, Wallace, RJ. *In vitro* susceptibility testing of tedizolid against nontuberculous mycobacteria. Am Soc Microbiol J Clin Microbiol 2017;55:1747-54. [doi: 10.1128/JCM.00274-17].
11. Johnson TM, Byrd TF, Drummond WK, Childs-Kean LM, Mahoney MV, Pearson JC, *et al*. Contemporary pharmacotherapies for nontuberculosis mycobacterial infections: A narrative review. Infect Dis Ther 2023;12:343-65.
12. Jaffré J, Aubry A, Maitre T, Morel F, Brossier F, Robert J, *et al*. Rational choice of antibiotics and media for *Mycobacterium avium* complex drug susceptibility testing. Front Microbiol 2020;11:81.
13. Lin S, Hua W, Wang S, Zhang Y, Chen X, Liu H, *et al*. *In vitro*

assessment of 17 antimicrobial agents against clinical *Mycobacterium avium* complex isolates. BMC Microbiol 2022;22:175.
14. Zhang H, Hua W, Lin S, Zhang Y, Chen X, Wang S, *et al*. *In vitro* susceptibility of nontuberculous mycobacteria to tedizolid. Infect Drug Resist 2022;15:4845-52.
15. Daley CL, Iaccarino JM, Lange C, Cambau E, Wallace RJ Jr., Andrejak C, *et al*. Treatment of nontuberculous mycobacterial pulmonary disease: An official ATS/ERS/ESCMID/IDSA clinical practice guideline. Eur Respir J 2020;56:2000535: 1-70.
16. Daley CL, Flume PA, van Ingen J, Khare R, Mingora CM, Nguyen MH, *et al*. A systematic review of tetracyclines for nontuberculous mycobacteria: Focus on rapidly growing mycobacteria. Eur Respir Rev 2025;34:250038.
17. Morrisette T, Molina KC, Da Silva B, Mueller SW, Damioli L, Krsak M, *et al*. Real-world use of tedizolid phosphate for 28 days or more: A case series describing tolerability and clinical success. Open Forum Infect Dis 2022;9:ofac028.
18. Chen J, Zhao L, Mao Y, Ye M, Guo Q, Zhang Y, *et al*. Clinical efficacy and adverse effects of antibiotics used to treat *Mycobacterium abscessus* pulmonary disease. Front Microbiol 2019;10:1977.
19. Zhanel GG, Esquivel J, Zelenitsky S, Lawrence CK, Adam HJ, Golden A, *et al*. Omadacycline: A novel oral and intravenous aminomethylcycline antibiotic agent. Drugs 2020;80:285-313.
20. Watkins RR, Deresinski S. Omadacycline: A novel tetracycline derivative with oral and intravenous formulations. Clin Infect Dis 2019;69:890-6.
21. Morrisette T, Alosaimy S, Philley JV, Wadle C, Howard C, Webb AJ, *et al*. Preliminary, real-world, multicenter experience with omadacycline for *Mycobacterium abscessus* infections. Open Forum Infect Dis 2021;8:ofab002.
22. Brown-Elliott BA, Wallace RJ Jr. *In vitro* susceptibility testing of omadacycline against nontuberculous mycobacteria. Antimicrob Agents Chemother 2021;65:e01947-20.
23. Chapagain M, Pasipanodya JG, Athale S, Bernal C, Trammell R, Howe D, *et al*. Omadacycline efficacy in the hollow fibre system model of pulmonary *Mycobacterium avium* complex and potency at clinically attainable doses. J Antimicrob Chemother 2022;77:1694-705.
24. Shoen C, Benaroch D, Sklaney M, Cynamon M. *In vitro* activities of omadacycline against rapidly growing mycobacteria. Antimicrob Agents Chemother 2019;63:e02522-18.
25. Kaushik A, Ammerman NC, Martins O, Parrish NM, Nuermberger EL. *In vitro* activity of new tetracycline analogs omadacycline and eravacycline against drug-resistant clinical isolates of *Mycobacterium abscessus*. Antimicrob Agents Chemother 2019;63:e00470-19.