Efficacy of Drug Regimens Containing Omadacycline in a Murine Model of *Mycobacterium avium* Chronic Lung Infection

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Background

MAC is the most common non-tuberculous mycobacteria and most frequent causative pathogen of NTM pulmonary disease.[1,2]

MAC is often associated with comorbidities, chronic infections, and high mortality rates, and new treatment options are needed.[1,2]

Omadacycline is an IV and oral aminomethylcycline antibiotic, FDA-approved for the treatment of adults with community acquired bacterial pneumonia and acute bacterial skin and skin structure infections caused by susceptible microorganisms.[3]

Omadacycline has broad-spectrum antibacterial activity, including vs MAC *in vitro*.[4]

The safety and efficacy of omadacycline for treatment of MAC has not been established.

Methods

In an aerosol infection murine model of MAC PD caused by *M. avium* ATCC 700898, ten different treatment regimens were evaluated:

- Omadacycline alone or in dual, triple, or quadruple combinations with SOC agents CLR, RIF, EMB, and CFZ.

Treatment efficacy was assessed based on the mean $\log_{10}$ reduction of bacterial colony forming units in the lung and spleen over 4 months compared to untreated control.

ANOVA with Holm-Sidak test or mixed effects analysis with Benjamini procedure (normal distribution, Geisser-Greenhouse correction) was applied to compare efficacy of combinations ($p<0.05$ indicating significance).

Results

- OMC treatment alone reduced *M. avium* CFU by 1 and 0.2 $\log_{10}$ in lung and spleen, respectively, at 4 months (M4).
- OMC-CFZ or OMC-CLR had enhanced activity compared to OMC alone.
- Among ≥3 drug combinations, OMC-CLR-CFZ was the most potent, followed by OMC-SOC, SOC alone, and OMC-CLR-EMB.

Omadacycline, alone or in combination, showed efficacy against *M. avium* in a murine chronic infection model

Objectives

To determine the efficacy of omadacycline alone or in combination with other antimycobacterial agents against *M. avium* complex in a murine model of aerosol infection

Conclusions

This is the first study demonstrating omadacycline efficacy against *M. avium* in mice.

These data suggest that further evaluation of omadacycline for the treatment of MAC PD is warranted.

Abbreviations: ANOVA, analysis of variance; CLR, clarithromycin; CFU, colony-forming units; CFZ, clofazimine; EMB, ethambutol; IV, intravenous; M1, month 1; MAC, *Mycobacterium avium* complex; NTM, nontuberculous mycobacteria; OMC, omadacycline; PD, pulmonary disease; RIF, rifampin; SOC, standard of care

References: 1. Daley CL, Winthrop KL. *J Infect Dis*. 2020;222:S199-S211 **2**. Kwon YS, et al. *Tuberc Respir Dis (Seoul)*. 2019;82:15-26. **3**. NUZYRA® (omadacycline) prescribing information. Available at https://www.nuzyra.com/nuzyra-pi.pdf (accessed 17 Nov 2025). **4**. Brown-Elliott BA, et al. *Antimicrob Agents Chemother*. 2021;65: e01947-20.

Funding and Disclosures: This work was funded by Paratek Pharmaceuticals. JVP, AWS are employees and shareholders of Paratek Pharmaceuticals. Medical editorial assistance, funded by Paratek Pharmaceuticals, was provided by AIM Biomedical (Clayton, MO).

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Results (continued)

- All regimens demonstrated significant efficacy in the lung and spleen by M1 except for OMC alone, which demonstrated significant efficacy by M2.
- OMC efficacy was similar to RIF over time when included in the SOC regimen (**Fig 1**, **2**).
- No drug-resistant isolates were recovered after 4 months, regardless of treatment.

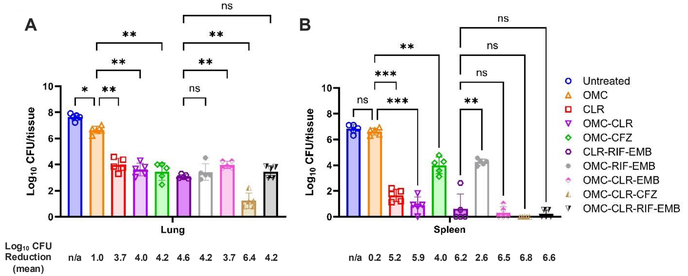

Figure 1: Mean reduction in bacterial tissue burden by treatment group after four months of treatment compared to untreated mice in the (**A**) lung and (**B**) spleen. Each symbol represents an individual animal; mean and standard deviation are shown. One-way ANOVA with Holm-Sidak multiple comparison test: $p<0.05$*, $p<0.01$**, $p<0.001$***, ns, not significant.

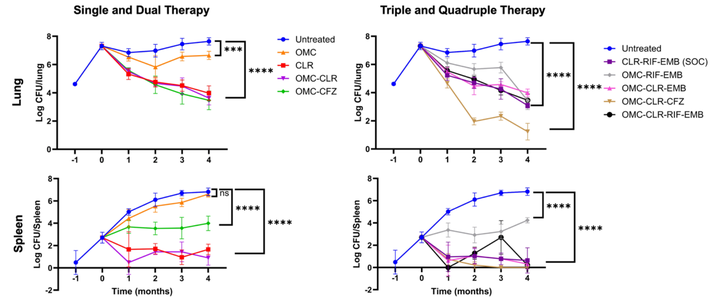

Figure 2: Total lung CFU count of 10 groups of *M. avium*-infected mice treated for 4 months. Data are presented as mean and standard deviation. Mixed effects analysis with Benjamini procedure: ***$p<0.001$, ****$p\leq0.0001$.

Poster 67431 presented at the 1st Interdisciplinary Meeting on Antimicrobial Resistance and Innovation, Las Vegas, NV, January 28–30, 2026