P3998

Omadacycline is efficacious as therapeutic treatment against inhalation anthrax in a blinded, randomized, pivotal study in New Zealand White rabbits

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Background

- The Tier 1 biothreat agent *Bacillus anthracis* causes anthrax and can be engineered to be antibiotic resistant[1–3]
- Omadacycline is a semisynthetic tetracycline-class antibiotic available as once-daily PO and IV formulations, FDA-approved for adults with CABP and ABSSSI[4]
- Omadacycline has shown potent *in vitro* activity against *B. anthracis* and was efficacious in preclinical models[5–7]
- Omadacycline is recommended by the Centers for Disease Control and Prevention as an alternative therapeutic agent for anthrax PEP[1]

Methods

- PK of omadacycline in NZWRs was used to derive treatment regimens simulating human exposures (**Figure 2**)
  - Human IV regimen denoted "1X": 200 mg IV day 1; 100 mg daily thereafter
- NZWR were challenged with aerosolized *B. anthracis* spores and randomized to treatment at the time of trigger, which was a significant increase in body temperature
- Anthrax-infected NZWR were treated with 0.15X or 0.05X fractions of the 1X humanized dose of omadacycline (12 NZWR / group) compared with saline control (6 NZWR) via IV infusion, 3x/day for 14 days
  - See also **Additional Information**
- Primary endpoint was survival through 45 d

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Abbreviations

ABSSSI, acute bacterial skin and skin structure infection; CABP, community-acquired bacterial pneumonia; FDA, US Food and Drug Administration; IV, intravenous; mITT, modified intent-to-treat; NA, not applicable; NZWR, New Zealand White rabbit; OMC, omadacycline; PEP, post-exposure prophylaxis; PK, pharmacokinetics; PO, oral; q24, every 24 h

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Objectives

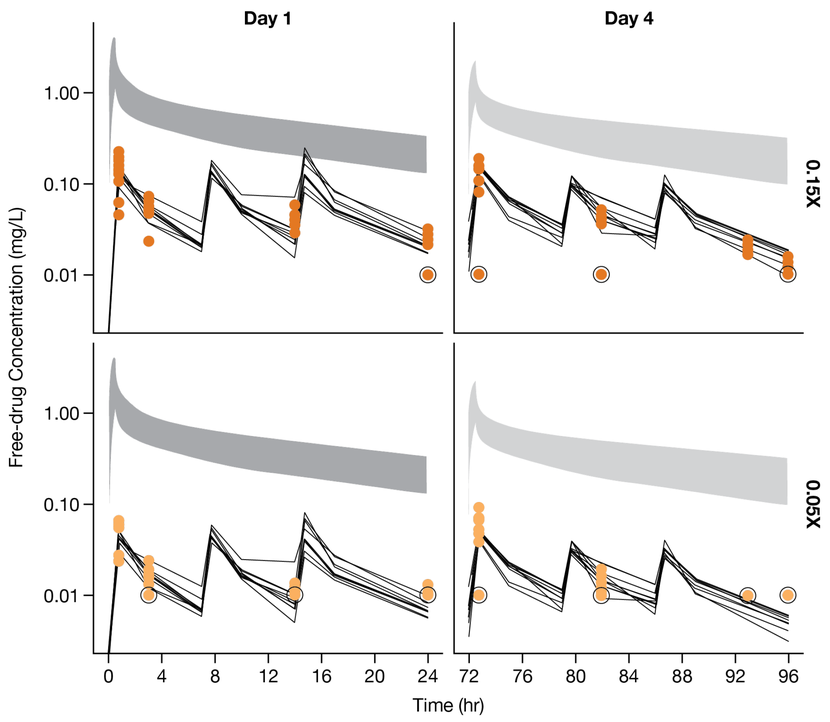
- Investigate the effectiveness of omadacycline as therapeutic treatment in the NZWR model of inhalation anthrax

Omadacycline demonstrated significant efficacy against inhalation anthrax in NZWR

- Omadacycline was efficacious at concentrations well below the predicted human exposures
- Omadacycline may be an option for treatment in the event of an anthrax attack or public health emergency

Results

Figure 2: OMC concentration–time profiles in *B. anthracis*-infected NZWRs vs predicted human exposure



Concentrations in infected rabbits are represented by orange dots. Concentration observations reported as below the limit of quantitation are circled in black. Black lines show concentration–time profiles from uninfected rabbits administered the 1X regimen, scaled to the corresponding multiple of 0.15X or 0.05X. The omadacycline profile in humans administered OMC 200 mg IV q24h for one dose followed by 100 mg IV q24h is represented by the gray zone (5th–95th percentile).

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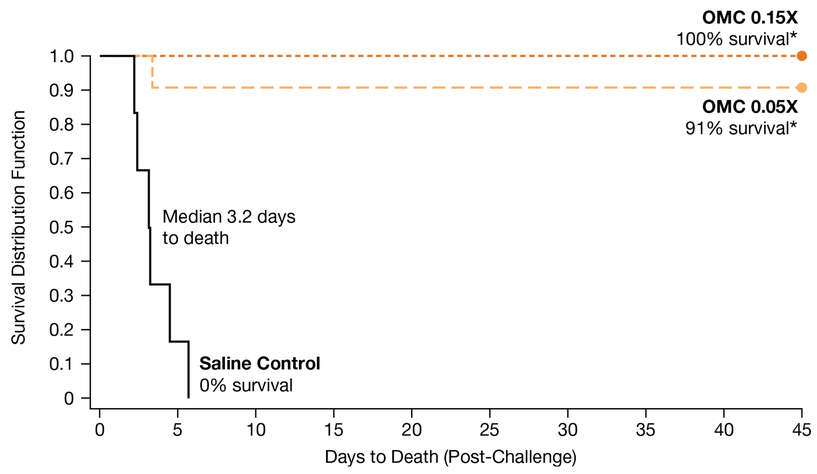
Results

- In the mITT population, the 0.15X omadacycline group had 100% (12/12) survival, the 0.05X omadacycline group had 91% (10/11) survival, and the saline control group had 0% (0/6) survival (median time to death: 3.2 days; **Figure 1**)

Figure 1: Survival of NZWR exposed to *B. anthracis*



Times to death for surviving animals were right-censored at the end of the study. *Times to death for the treated groups were significantly greater than that of the saline control group (log-rank test p<0.0001 for both OMC 0.15X and OMC 0.05X). Omadacycline minimum inhibitory concentration = 0.06 mg/L for *B. anthracis* Ames strain.

- *B. anthracis* was not detected in any blood or tissues of surviving omadacycline-treated NZWR post challenge (**Table 1**).

Table 1: Presence of *B. anthracis* in blood cultures and tissues of surviving NZWR versus those that succumbed from *B. anthracis* infection, mITT population

% (n/N)	Surviving NZWR		NZWR succumbing to *B. anthracis* infection	
	OMC 0.15X (N=**12**/12)	OMC 0.05X (N=**10**/11)	OMC 0.05X (N=**1**/11)	Saline Control (N=**6**/6)
Positive *B. anthracis* blood cultures post challenge				
Day 7	0 (0/12)	0 (0/10)	NA	NA
Day 14	0 (0/12)	0 (0/10)		
Day 28	0 (0/12)	0 (0/10)		
Day 45	0 (0/12)	0 (0/10)		
Terminal time point	NA	NA	100 (1/1[b])	100 (5/5[a])
Positive *B. anthracis* tissue (end of study or terminal time point)				
Brain	0 (0/12)	0 (0/10)	100 (1/1[b])	100 (6/6)
Lung	0 (0/12)	0 (0/10)	100 (1/1[b])	100 (6/6)
Spleen	0 (0/12)	0 (0/10)	100 (1/1[b])	100 (6/6)
Mediastinal lymph node	0 (0/12)	0 (0/10)	100 (1/1[b])	100 (6/6)

[a]One terminal sample unable to be obtained.
[b]The one rabbit in the 0.05X OMC group that succumbed was bacteremic at the terminal time point (lower bacterial level than the controls) and showed bacterial burden in all tissues assessed (lower bacterial levels than the controls, and BLLOQ [below the lower limit of quantification] in the mediastinal lymph node).

References

1. Bower WA, et al. *MMWR Recomm Rep*. 2023;72(6):1–47.
2. CDC. Bioterrorism and anthrax: The threat. https://www.cdc.gov/anthrax/bioterrorism/index.html. Accessed August 26, 2024.
3. CDC. Bioterrorism agents/diseases. https://emergency.cdc.gov/agent/agentlist-category.asp. Accessed August 26, 2024.
4. Gallagher JC. *Clin Infect Dis.* 2019;69(Suppl 1):S1–S5.
5. Heine HS, et al. *Antimicrob Agents Chemother*. 2024;68:e0059524.
6. Henning L, et al. *ASM Microbe*. 2023; Houston, TX: P3984.
7. Pfefferle D, et al. *Global Congress of ESCMID*. 2025; Vienna, Austria: P3784.

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