Omadacycline is Efficacious in a Treatment Model of Inhalational Anthrax in New Zealand White Rabbits

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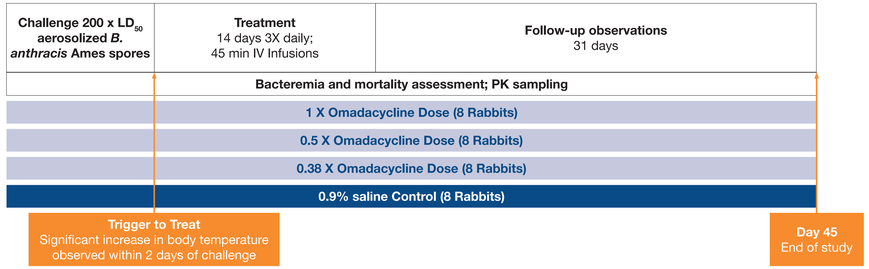
Background

- *Bacillus anthracis* causes cutaneous, respiratory, and intestinal anthrax. It is among the agents most likely to be used in a biologic attack and is in the category of agents of greatest risk to public health and security
- *B. anthracis* can be engineered to be resistant to tetracycline and other antibiotics
- Omadacycline has previously been shown to have potent *in vitro* activity against *B. anthracis* and to be efficacious in a preclinical post-exposure prophylaxis and a delayed treatment mouse model of inhalational anthrax

Methods

Figure 1. Study Design



- The treatment regimens were derived via mathematical modeling and analyses using data from iterative pharmacokinetic (PK) studies in NZW rabbits to closely match the concentration-time curve observed in humans administered 200 mg IV day 1, followed by 100 mg IV maintenance (humanized treatment)
- NZW rabbit plasma of omadacycline-treated infected rabbits was collected at different timepoints during the study for PK analysis and exposures were confirmed to be within expected targets

Table 1. Omadacycline humanized treatment regimen in New Zealand White Rabbits

Day of Treatment	1			2 to 14		
Time (hr)*	0	7	14	0	7	14
Dose Fraction						
1 X (mg/kg)	5.0	4.0	4.0	4.0	3.0	2.0
0.5 X (mg/kg)	2.5	2.0	2.0	2.0	1.5	1.0
0.38 X (mg/kg)	1.9	1.5	1.5	1.5	1.1	0.8

*Omadacycline administration via 45-minute IV infusions.

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Omadacycline treatment results in survival of all rabbits infected with *B. anthracis*

Objectives

Determine the efficacy of three omadacycline dosing regimens, which correspond to the human standard dose (1 X) and fractions of this dose (0.5 X and 0.38 X), for treatment against inhalation anthrax caused by *B. anthracis*, as measured by survival

Compare efficacy of omadacycline treatment to negative (untreated) control

Conclusions

100% efficacy was observed with all tested doses of omadacycline

These results support the continued development of omadacycline for treatment of anthrax

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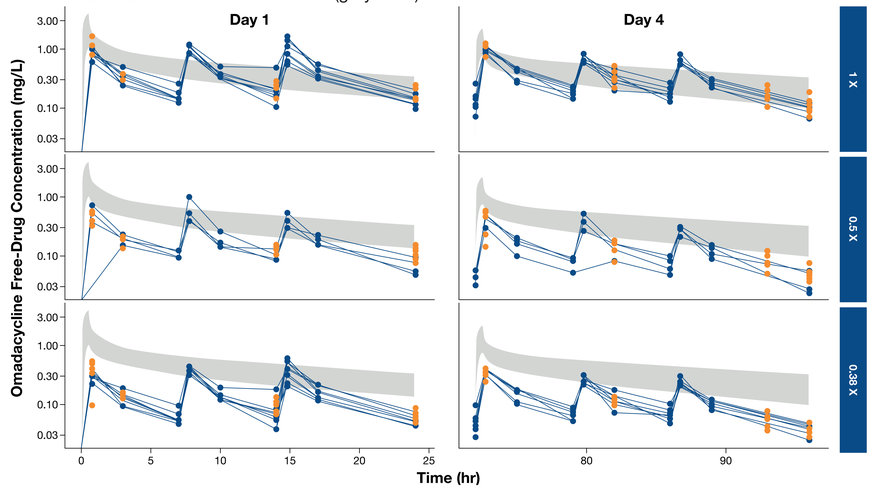
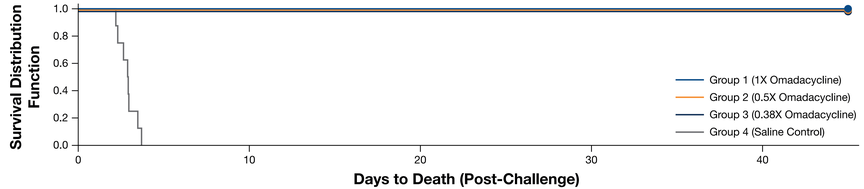
Results

Figure 2. Omadacycline Free-Drug Plasma Concentration Versus Time on Day 1 (loading) and Day 4 (steady state) for NZW Rabbits (uninfected rabbits=blue circles and lines; infected rabbits=orange circles) Overlaid with Profile in Humans (gray zone)



- All of the rabbits in the omadacycline treatment groups survived the entire 45-day post-challenge observation period, while all of the animals in the vehicle control group died within 3 days (**Figure 3**)

Figure 3. Kaplan-Meier Survival Data: Efficacy of Omadacycline Treatment vs Inhalational Anthrax in New Zealand White Rabbits



Survival rates for Groups 2 and 3 were slightly offset from 1.0 to distinguish between Groups 1 to 3.

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