# Omadacycline Exposure After a Light Meal

Kelly Wright, PharmD, BCPS; Alisa W. Serio, PhD; Amy Manley, MS; Stephen A. Bai, PhD; Surya Chitra, PhD

Paratek Pharmaceuticals, Inc., King of Prussia, PA, USA

## Background

Omadacycline is a novel aminomethylcycline antibiotic approved to treat adults with community-acquired bacterial pneumonia (CABP) or acute bacterial skin and skin structure infection (ABSSSI)<sup>1</sup>

Patients taking omadacycline are instructed to fast for 4 h before and 2 h after oral dosing (no dairy products, antacids, or multivitamins for 4 h)<sup>1</sup>

The effect of a light meal on omadacycline pharmacodynamics (PD) is unknown

## Methods

A phase 1, open-label, single sequence study enrolled 12 participants who received a single oral 300 mg dose of omadacycline while fasting and approximately 60-90 min after having orange juice and toast<sup>2</sup>

Washout period: ≥4 days between the last dose in one period and the first dose in the next period

Concentration-time profiles for Days 2 and 5 for 5-day dosing regimens were simulated from Day 1 data

**Regimens: A:** 300 mg QD Days 1–5; **B:** 600 mg Day 1, then 300 mg QD Days 2–5; C: 450 mg QD Days 1–2, then 300 mg QD Days 3–5; D: 450 mg QD Days 1–5

Unbound plasma areas under the curve (fAUC; based on 20% plasma protein binding of omadacycline) to minimum inhibitory concentration (MIC) ratio targets were simulated for each regimen using the MIC that inhibits 90% (MIC<sub>90</sub>) of isolates<sup>3</sup>

MIC<sub>90</sub>: Staphylococcus aureus 0.25 mg/L, Streptococcus pyogenes 0.12 mg/L, and Streptococcus pneumoniae 0.12 mg/L<sup>3</sup>

Efficacy targets were previously derived from in vivo models. Stasis targets for common ABSSSI pathogens S. aureus (median target = 21.9) and S. pyogenes (median target = 33.3) and a 1-log<sub>10</sub> reduction target for a common CABP pathogen, S. pneumoniae, (median target = 17.4) were applied to simulated exposures<sup>4,5</sup>

Funding and disclosures KW, AWS, AM, SAB, and SC: Employee – Paratek Pharmaceuticals, Inc. This study was funded by Paratek Pharmaceuticals, Inc. Medical editorial assistance, funded by Paratek Pharmaceuticals, Inc., was provided by Innovative Strategic Communications.

## Effect of a Light Meal on the Pharmacodynamics of Omadacycline

## Objectives

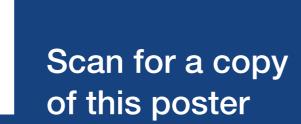
To simulate the effect of a light meal on omadacycline PD using phase 1 study data

To compare simulated omadacycline exposures to efficacy targets for common ABSSSI and CABP pathogens S. aureus, S. pyogenes, and S. pneumoniae

## Conclusions

Omadacycline exposures remained above efficacy targets for key ABSSSI and CABP pathogens for all regimens except regimen A on Day 2 in fed state against S. aureus, which then exceeded the target on Day 5







### Results

All four regimens exceeded median fAUC/MIC<sub>90</sub> ratio targets for stasis against S. aureus and S. pyogenes and 1-log<sub>10</sub> reduction for S. pneumoniae, except for Regimen A on Day 2 in a fed state against S. aureus, which increased above the target by Day 5

		fAUC/MIC <sub>90</sub>			
		Day 2		Day 5	
Pathogen	Regimen*	Fasted	Fed	Fasted	Fed
S. aureus		Median target for stasis = 21.9			
	A: 300 mg	27.2	20.0	31.5	25.1
	B: 600/300 mg	38.2	28.2	32.2	25.7
	C: 450/300 mg	36.4	26.8	32.7	26.1
	D: 450 mg	36.4	26.8	42.1	33.5
S. pyogenes		Median target for stasis = 33.3			
	A: 300 mg	54.4	40.0	63.0	50.2
	B: 600/300 mg	76.4	56.4	64.4	51.4
	C: 450/300 mg	72.8	53.6	65.4	52.2
	D: 450 mg	72.8	53.6	84.2	67.0
S. pneumoniae		Median target for 1-log <sub>10</sub> reduction = 17.4			
	A: 300 mg	54.4	40.0	63.0	50.2
	B: 600/300 mg	76.4	56.4	64.4	51.4
	C: 450/300 mg	72.8	53.6	65.4	52.2
	D: 450 mg	72.8	53.6	84.2	67.0

\*Regimens were **A:** 300 mg QD Days 1–5; **B:** 600 mg Day 1, then 300 mg QD Days 2–5; **C:** 450 mg QD Days 1–2, then 300 mg QD Days 3–5; and **D**: 450 mg QD Days 1–5. Omadacycline MIC for S. aureus: MIC<sub>90</sub>: 0.25 mg/L and Streptococcus spp.: MIC<sub>90</sub>: 0.12 mg/L

fAUC/MIC ratios were approximately 25% lower on Days 2 and 5 after a light meal compared with fasted

Ratios increased with simulated higher doses or loading doses

Similar increases were observed regardless of the loading dose strategy employed

#### References

- 1. NUZYRA® (omadacycline) Prescribing Information. King of Prussia, PA: Paratek Pharmaceuticals, Inc., 2020.
- 2. Hunt TL, et al. Eur J Drug Metab Pharmacokinet. 2021;46:85–92.
- 3. Pfaller MA, et al. Antimicrob Agents Chemother. 2020;64:e02488–19.
- 4. Lepak AJ, et al. Antimicrob Agents Chemother. 2017;61:e02368-16.
- 5. Lepak AJ, et al. Antimicrob Agents Chemother. 2019;63:e00624–19.