SUPPLEMENT ARTICLE

Pharmacokinetics and Pharmacodynamics of Oral and Intravenous Omadacycline

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Oral and intravenous (IV) omadacycline formulations are approved in the United States for treating acute bacterial skin and skin structure infections and community-acquired bacterial pneumonia in adults. Oral omadacycline bioavailability is 34.5%; similar exposures are obtained following 300 mg oral and 100 mg IV doses. Oral administration should be in a fasted state, with dairy products, antacids, or multivitamins avoided for ≥4 hours after dosing. Low protein binding (21%), large volume of distribution (190 L), low systemic clearance (10 L/hour), and long elimination half-life (16–17 hours) support once-daily dosing. Omadacycline is excreted unchanged in feces (81.1%) and urine (14.4%), with low potential for drug–drug interactions. Dose adjustments are unnecessary for age, sex, and renal or hepatic impairment. Pharmacokinetic–pharmacodynamic studies identify $f\text{AUC}_{0-24}$/MIC ratio as the parameter that correlates with in vivo efficacy. Systemic exposure of omadacycline in epithelial lining fluid is greater than/equal to plasma concentrations in healthy adults.

Keywords. omadacycline; pharmacokinetics; pharmacodynamics; tetracyclines.

Omadacycline is an aminomethylcycline tetracycline antibiotic that is a semisynthetic derivative of minocycline with once-daily oral and intravenous (IV) administration in adults [1]. Omadacycline has in vitro activity against gram-positive and gram-negative aerobes, anaerobes, and atypical pathogens, including strains expressing tetracycline resistance through efflux and ribosomal protection mechanisms [2, 3]. Phase III clinical trials of omadacycline monotherapy demonstrated consistently favorable efficacy and safety profiles that supported the US Food and Drug Administration approval of omadacycline for the treatment of adults with acute bacterial skin and skin structure infections (ABSSSI), and community-acquired bacterial pneumonia (CABP) [1–3].

Pharmacokinetic and pharmacodynamic evaluations are integral parts of drug-development programs for antimicrobials [4, 5]. The present article reviews data regarding the pharmacokinetics and pharmacodynamics of oral and IV omadacycline administration. This information is useful for understanding rationales for omadacycline dosing regimens to treat ABSSSI and CABP safely and efficaciously.

PHARMACOKINETICS

Table 1 shows pharmacokinetic parameters for omadacycline, following single- and multiple-dose administration regimens

(every 24 hours or once daily; oral 300 mg and IV 100 mg) in representative studies [6–8].

Absorption and Loading Doses

Omadacycline is a compound with high aqueous solubility [9] but low gastrointestinal permeability [10]. Bioavailability for the omadacycline tablet formulation is 34.5%, necessitating a 300 mg oral dose to achieve similar exposures as a 100 mg IV dose [6]. Specifically, the area under the plasma concentration–time curve (AUC) from time zero to infinity ($\text{AUC}_{0-\infty}$) of omadacycline following administration of a single 300 mg oral dose was comparable with that following a single 100 mg IV dose (10.0 vs 10.3 µg × hour/mL; Figure 1) [6]. The median value for time to maximum plasma concentration (T_{max}) of oral omadacycline was 2.5–3.0 hours under fasting conditions [6].

The effect of a high-fat meal (kcal: 855; fat: 59%; protein: 14%; carbohydrate: 27%) with or without dairy (8 fl oz whole milk) on the relative bioavailability of oral omadacycline was evaluated in a 4-period-by-4-sequence crossover study in 31 healthy adults [11]. Subjects who fasted overnight and consumed a standard, high-fat, nondairy meal 3 hours after omadacycline administration had similar systemic exposure parameters (mean [coefficient of variation] $\text{AUC}_{0-\infty}$ and maximum plasma concentrations [C_{max}] of 10.2 [27.0%] µg × hour/mL and 0.6 [25.3%] µg/mL, respectively) as observed in other pharmacokinetic studies [6, 7]. A high-fat meal with dairy consumed 2 hours before dosing had the greatest impact, reducing exposure parameters of AUC and C_{max} by 59–63%, compared with fasting administration. AUC and C_{max} values for omadacycline reduced by 40–42% when a high-fat, nondairy meal was consumed 2 hours before dosing, whereas the rate and extent of absorption of omadacycline were not substantially decreased (ie, 15–17%) when this meal was

Table 1. Omadacycline Pharmacokinetic Parameters Following Administration of Single and Multiple Oral and Intravenous Dosing Regimens [6–8]

Parameter	Oral Tablet		Intravenous Infusion	
	Single Dose [6] 300 mg	Steady State [7] 300 mg Once Daily	Single Dose [6] 100 mg	Steady State [8] 100 mg Once Daily
C_{max}, μg/mL	0.50 (19.8)	0.81 (25.9)	1.8 (36.8)	2.1 (32.1)
T_{max}, hours	3.0	2.5	0.5	NR
AUC, μg × h/mL[a]	10.3 (24.3)	9.27 (26.8)	10.0 (15.5)	12.1 (26.5)
$t_{1/2}$, hours	16.8 (9.3)	15.5 (10.7)	16.8 (9.3)	16.0 (21.9)

Data are presented as mean (% coefficient of variation) except for T_{max}, which is median.

Abbreviations: AUC, area under the concentration–time curve; C_{max}, maximum concentration; NR, not reported; $t_{1/2}$, elimination half-life; T_{max}, time to reach C_{max}.

[a]AUC is AUC from zero to infinity for single-dose administration and 24-hour AUC for multiple-dose administration.

consumed 4 hours before dosing. Mean values for the elimination half-life ($t_{1/2}$) of omadacycline were similar across treatment groups (range: 13.5–13.8 hours). Median T_{max} was slightly prolonged in fed, compared with fasting, subjects (2.9 hours vs 2.5 hours).

Compared with healthy subjects in a fasted state, a 19–25% reduction in systemic exposure (AUC and C_{max}) was observed when a light meal (toast and orange juice) was consumed before receiving a 300 mg oral dose of omadacycline (Hunt, T: Personal Communication: A phase I, open-label, 3-period, single-sequence study to evaluate the effect of verapamil extended release and a light meal on the pharmacokinetics, safety, and tolerability of omadacycline in healthy adult subjects. Protocol PTK0796-DDI-17106, 2018). No differences in T_{max} were observed between fed and fasting subjects (2.75 hours, both groups).

A population pharmacokinetic analysis of plasma concentration–time data following IV and oral administration of omadacycline (10 phase I clinical trials; 319 subjects) recommended the restriction of food intake for ≥4 hours before
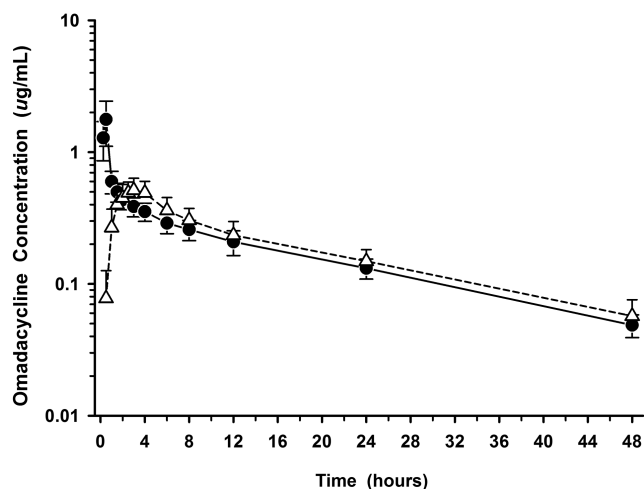

Figure 1. Mean (± standard deviation) plasma concentration–time profiles of omadacycline after 100 mg intravenous (closed circles) and 300 mg oral (open triangles) administration. Data on the *y*-axis are the log scale. Adapted by authors from Sun et al [6].

and 2 hours after the oral tablet formulation [12]. Ideally, oral omadacycline should be taken in a fasted state (ie, no food or drink, except water, for ≥4 hours before and 2 hours after a dose). The consumption of dairy-containing products and divalent or trivalent cation-containing products (eg, antacids or vitamin products containing calcium, magnesium, aluminum, iron, bismuth, or zinc) should be avoided for at least 4 hours after oral administration.

A 3-period crossover study evaluated plasma pharmacokinetics of omadacycline after the first and fifth doses of once-daily oral regimens of 300 mg, 450 mg, and 600 mg in 26 healthy subjects [7]. Systemic exposure parameters of omadacycline increased with increasing dose but were less than dose proportional (ie, 71–96% of expected C_{max} and 24-hour AUC [$AUC_{0–24}$] values). The plasma exposure of the 450 mg oral omadacycline dose on day 1 (mean C_{max} 0.87 μg/mL; $AUC_{0–24}$ 8.98 μg × hour/mL) was similar to that of the 300 mg oral dose on day 5 (mean C_{max} 0.81 × μg/mL; $AUC_{0–24}$ 9.27 μg hour/mL). Nausea was reported in 16.7% of subjects with the 600 mg dose and in 7.7% of subjects with the 300 mg and 450 mg doses. This study supported an oral loading-dose strategy for omadacycline (eg, 450 mg once-daily oral for 1–2 days followed by an oral maintenance dose of 300 mg once daily), in clinical situations where high initial systemic exposure is desired, or to eliminate the need to start with IV therapy [7]. This strategy was assessed in the phase III clinical trial of oral-only omadacycline in the treatment of ABSSSI (ClinicalTrials.gov identifier NCT02877927).

Single- and multiple-dose pharmacokinetics of IV omadacycline were studied in 41 healthy adults [13]. Single IV doses (25–600 mg) increased the $AUC_{0–24}$ from 0.9 to 24.9 μg × hour/mL in a dose-dependent manner. Over the same dose range, C_{max} ranged from 0.3 to 4.5 μg/mL. Mean elimination $t_{1/2}$ and volume of distribution ranged from 17 to 21 hours and 333 to 640 L, respectively. In the second phase of this study, 2 groups of 10 healthy adult subjects received omadacycline 200 mg as a 30-minute IV infusion once daily for 7 days. Mean $AUC_{0–24}$ values observed on day 7 (range, 17.4–18.0 μg × hour/mL) were 50% higher compared with day 1 (range, 11.2–12.2 μg × hour/mL). Mean C_{max} on day 1 (range, 2.8–3.0 μg/mL) also

increased by day 7 (range, 3.4–3.6 µg/mL). This study supported an IV loading dose regimen for omadacycline of 200 mg (100 mg every 12 hours for 2 doses followed by 100 mg once daily), which was evaluated in phase III studies of IV-to-oral omadacycline for the treatment of ABSSSI (ClinicalTrials.gov identifier NCT02378480) and CABP (ClinicalTrials.gov identifier NCT02531438).

Distribution

The mean apparent steady-state volume of distribution of omadacycline in humans following IV administration ranges from 168 to 286 L [8, 13–15]. Mean (± standard deviation [SD]) plasma protein binding of omadacycline in humans is 21.3% ± 9.7% [16]. Omadacycline is weakly bound to plasma proteins in other species including monkey (21.2% ± 7.3%), rat (26.1% ± 12.1%), and mouse (15.3% ± 5.3%) [16]. In contrast to other tetracyclines (71–93% protein bound) [17, 18], the degree of protein binding was independent of omadacycline concentration and was similar across the range of plasma concentrations tested in vitro (0.01–10 µg/mL).

Following IV administration of ^{14}C-omadacycline in rats, radioactivity was rapidly and widely distributed into most tissue types [9]. Tissue concentrations exceeded blood concentrations in skin, lungs, and kidneys after oral or IV single-dose administration. Highest tissue-to-blood ratios were observed in bone minerals, liver, spleen, salivary gland, and Harderian gland; lowest tissue-to-blood ratios were observed in the brain and spinal cord, eyes, fat, and seminal vesicles.

Administration of omadacycline 100 mg (30-minute IV infusion) in 41 healthy subjects produced drug concentrations that were higher in epithelial lining fluid (ELF) and alveolar cells (AC) than simultaneous total and unbound plasma concentrations throughout the 24-hour period after 5 doses [8]. Ratios of ELF and AC to unbound plasma concentrations for omadacycline based on the mean AUC_{0-24} values were 1.84 and 32.2, respectively. The pattern and time course of omadacycline concentrations (all matrixes) were similar to those observed with tigecycline (Figure 2) [8, 19]. However, the magnitude of plasma, ELF, and AC concentrations for omadacycline was greater than for tigecycline.

Metabolism

Omadacycline does not undergo significant metabolism in humans [10]. Two inactive metabolites were recovered in rats, accounting for <15% of an administered dose of omadacycline [9]. No measurable metabolites were identified in microsomal and hepatocyte incubation studies [10].

Elimination

Omadacycline is primarily excreted unchanged in feces and secondarily excreted in urine. Systemic clearance of omadacycline in healthy subjects is 10 L/hour (range, 8.8–11.8 L/hour) [8, 13–15]. The elimination $t_{1/2}$ of omadacycline is 16–17 hours (range, 11–25 hours) [6–8, 13–15]. Renal clearance accounts for 30% of systemic clearance [14]. A mass-balance study (involving 6 healthy male subjects) collected serial plasma, urine, and fecal samples for 7 days after a single 300 mg oral dose of
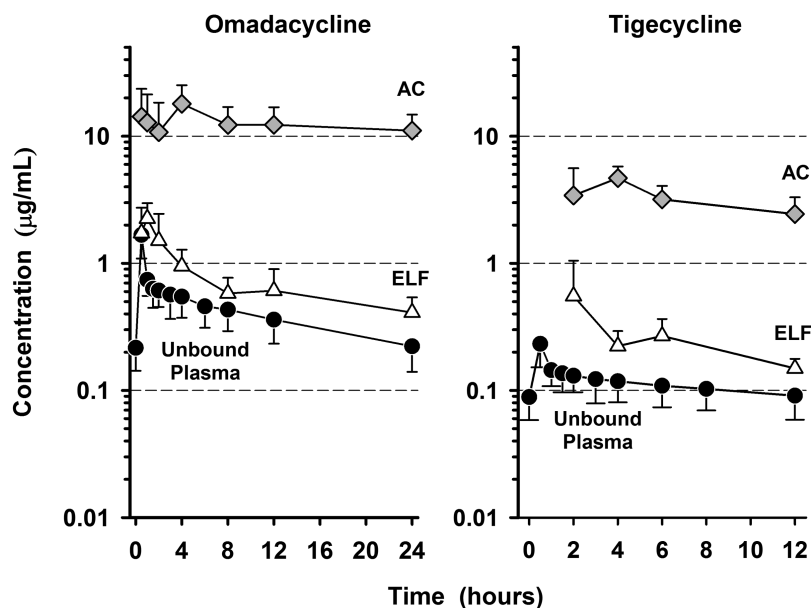

Figure 2. Mean (± standard deviation) concentration-versus-time profiles of omadacycline (left) and tigecycline (right). Key: Unbound plasma (closed circles), epithelial lining fluid (open triangles), and alveolar cells (closed diamonds) after the last intravenous dose. Data on the *y*-axis are on the log scale. Adapted by authors from Gotfried et al, with permission. Copyright © American Society for Microbiology [8]. Abbreviations: AC, alveolar cells; ELF, epithelial lining fluid.

[14]C-omadacycline, administered under fasting conditions [10]: 81.1% of total radioactivity administered was excreted in feces; 14.4% was excreted in urine as unchanged omadacycline and C-4 epimer [10]. The C-4 epimer of omadacycline was observed in all body fluids and represents tetracycline impurity [10]. The mean (± SD) fraction excreted in urine (fe) of the 100 mg dose of IV omadacycline was 27.0% ± 3.49% [14]. In contrast, fe values were 10.8–12.7% after multiple oral doses of 300 mg in healthy subjects [15].

Special Populations

Renal Impairment

No clinically meaningful changes in AUC or C_{max} were observed following administration of a single 100 mg IV dose of omadacycline to subjects with end-stage renal disease (ESRD) on stable hemodialysis, compared with matched healthy control subjects [14]. Pharmacokinetic parameters following omadacycline administered either before or after hemodialysis (10–20-day washout period between doses) in subjects with ESRD were not statistically significantly different than parameters observed in healthy control subjects. The mean fraction of dose recovered in dialysate was only 7.89% (7.89 mg) in subjects with ESRD undergoing 4-hour hemodialysis. No dose adjustments are necessary for omadacycline in patients with impaired renal function or in patients receiving hemodialysis [1].

Hepatic Impairment

No clinically meaningful changes in dose-normalized AUC or C_{max} were observed following administration of a single 50 or 100 mg IV dose (study period 1) and a single 150 or 300 mg oral dose (study period 2) of omadacycline in subjects with mild, moderate, or severe hepatic impairment (Child–Turcotte–Pugh class A, B, or C) compared with matched healthy control subjects [2, 20]. No dose adjustments are necessary for omadacycline in patients with hepatic impairment [1].

Age and Sex

The effect of age and sex on omadacycline pharmacokinetics was evaluated in healthy subjects receiving a single 200 mg oral dose [21]. Young (aged 33–43 years) and elderly (aged 65–73 years) female subjects exhibited greater systemic exposure (mean $AUC_{0-\infty}$ 13.57 and 16.12 µg × hour/mL, respectively) than young and elderly male subjects (mean $AUC_{0-\infty}$ 9.33 and 9.99 µg × hour/mL, respectively). The ratio of geometric means (90% confidence intervals [CI]) for sex was 0.64 (0.52–0.80; P = .001), whereas age had no major effect on systemic exposure (ratio of geometric means 1.13 [0.91–1.41; P = .246]). The effect of sex was also evaluated in a study following administration of a single oral or IV dose of omadacycline in 24 young male or female healthy subjects [21]. After a 200 mg oral dose of omadacycline, systemic exposure was similar ($AUC_{0-\infty}$

ratio [90% CI] for male to female subjects was 1.02 [0.69–1.50; P = .934]). The geometric means of the elimination $t_{1/2}$ were 17.2 and 11.4 hours for male and female subjects, respectively. Following a 100 mg IV dose of omadacycline, compared with male subjects, female subjects displayed a higher $AUC_{0-\infty}$ (10.95 vs 8.48 × µg h/mL) and more variability (18.4% vs 4.9%). Although the $AUC_{0-\infty}$ ratio for male to female subjects was 0.77, the 90% CI (0.67–0.89) was within the criteria of similarity. No dose adjustments are necessary for omadacycline on the basis of sex or age [1].

Drug Interactions

In vitro and in vivo data suggest a low potential for clinically significant drug–drug interactions with omadacycline [9, 10]. Omadacycline at clinically relevant concentrations (IC_{50} values >100 µM) has little or no inhibition of the cytochrome P450 (CYP) isoforms CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A4/5 in human liver microsomes in vitro [10]. Omadacycline (≤100 µM) showed slight or no potential for in vitro induction of CYP1A1, CYP1A2, CYP1B1, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2J2, CYP3A4, CYP3A5, or UDP-glucuronosyltransferase (UGT) 1A1 in human hepatocytes [10].

Omadacycline did not inhibit the following transporters in vitro at clinically relevant concentrations: organic anion transporter (OAT)1, OAT3, OAT polypeptide transporter (OATP) 1B1, OATP1B3, organic cation transporter 2 (OCT2), multidrug resistance-associated protein 2 (MRP2), P-glycoprotein (P-gp) or breast cancer resistance protein (BCRP) [9]. Higher concentrations (25 µM) of omadacycline moderately (20–32%) inhibit OAT1. Omadacycline was not found to induce P-gp or MRP2. Omadacycline was not a substrate for BCRP or MRP2 but is likely a substrate of P-gp.

A clinical study evaluated the potential for drug–drug interactions of verapamil (a known P-gp inhibitor) and omadacycline (Hunt, T: Personal Communication: A phase I, open-label, 3-period, single-sequence study to evaluate the effect of verapamil extended release and a light meal on the pharmacokinetics, safety, and tolerability of omadacycline in healthy adult subjects. Protocol PTK0796-DDI-17106, 2018). A single oral dose of omadacycline 300 mg was administered with and without a single oral dose of extended-release 240 mg verapamil in healthy adults. Verapamil increased the geometric means of $AUC_{0-\infty}$ and C_{max} of omadacycline by 25% and 14%, respectively. T_{max} and elimination $t_{1/2}$ of omadacycline were essentially the same during both study phases, suggesting that absorption and elimination rates of omadacycline were unaffected. The increase of systemic exposure was likely due to a 25% increase in oral bioavailability (from 34.5% to 43%) in the presence of a P-gp inhibitor. This study suggests that P-gp-mediated drug–drug interactions primarily impact the oral administration of omadacycline and are likely to have minimal clinical significance.

Although drug interactions studies of the concomitant administration of omadacycline and warfarin have not been conducted, the tetracycline class has been shown to depress plasma prothrombin activity. Patients may require an adjustment in their anticoagulation dosage and should have a suitable anticoagulation test (eg, prothrombin time and/or International Normalized Ratio) monitored if omadacycline is administered with warfarin [1].

PHARMACODYNAMICS

Tetracyclines have demonstrated time-dependent antimicrobial activity and modest postantibiotic effect (PAE) against selected pathogens [17, 18]. The pharmacokinetic–pharmacodynamic parameter that usually correlates with these characteristics has been the 24-hour unbound AUC/minimum inhibitory concentration ratio ($f\text{AUC}_{0-24}$/MIC). Tetracycline pharmacodynamics have been poorly studied, and limited data have been published regarding the optimal $f\text{AUC}_{0-24}$/MIC ratios for tetracycline, doxycycline, and minocycline [17, 18]. Tigecycline, a glycylcycline derivative, has been more extensively investigated than other compounds, including studies of dose fractionation, pharmacodynamic target attainment, and clinical efficacy and toxicity, in healthy subjects and infected patients [17, 22].

The PAE of omadacycline varied with pathogen being tested, ranging from 1.4 hours for *Escherichia coli* to 3.3 hours for *Streptococcus pneumoniae* [23]. For *Staphylococcus aureus*, the PAEs of omadacycline were 2.6 hours and 2.2 hours for methicillin-sensitive and methicillin-resistant isolates, respectively. PAEs for omadacycline were similar to tigecycline except for enterococci, where the PAE of tigecycline was slightly longer (3.8–4.4 hours) compared with omadacycline (2.0–2.1 hours).

Studies have been conducted in neutropenic and normal murine thigh and lung infection models to identify and characterize the pharmacokinetic–pharmacodynamic indices required for optimal in vivo efficacy of omadacycline [24, 25]. A study evaluated the efficacy and magnitude of pharmacokinetic–pharmacodynamic parameters in neutropenic and normal murine thigh infection models and 21 bacterial strains with an in vitro MIC range of 0.03–2 µg/mL [25]. The $f\text{AUC}_{0-24}$/MIC ratio had the best coefficient of determination ($r^2 = 0.81–0.85$)

to in vivo efficacy against strains of *S. pneumoniae*, *S. aureus*, *E. coli*, and *Klebsiella pneumoniae*. The magnitude of $f\text{AUC}_{0-24}$/MIC required for a static effect ranged from 14.9 to 38.0 (mean 25.7) for 12 isolates of *S. pneumoniae* and 21.6 to 25.0 (mean 23.0) for 4 isolates of *E. coli*. A slightly higher magnitude of $f\text{AUC}_{0-24}$/MIC was required for a static effect against 5 isolates of *S. aureus* (mean 53.5; range, 37.8–81.0) and 1 isolate of *K. pneumoniae* (mean 59.4). The presence of neutrophils enhanced the in vivo efficacy of omadacycline by over 6-fold for 1 strain of *S. pneumoniae* and by approximately 2-fold for 1 strain of *K. pneumoniae*. A subsequent pharmacodynamics study with the neutropenic murine thigh infection model demonstrated in vivo potency against 10 diverse strains of *S. aureus* [26]. The magnitude of AUC_{0-24}/MIC ratio associated with static effect and 1-$\log_{10}$ kill averaged 23.7 (range, 13.8–51.1) and 78.1 (range, 32.2–302.5), respectively. Overall, omadacycline was slightly more potent than tigecycline in both neutropenic and normal murine thigh infection models.

The in vivo efficacy of omadacycline was evaluated against 2 isolates of *S. pneumoniae* (1 penicillin-sensitive and 1 penicillin-macrolide resistant) in a neutropenic murine lung infection model [27]. The $f\text{AUC}_{0-24}$/MIC ratio was the pharmacokinetic–pharmacodynamic parameter with the highest coefficient of determination to efficacy ($r^2 = 0.90$). A 1 mg/kg dose resulted in net static effect, whereas a 10 mg/kg dose achieved maximum bacterial kill and a move toward bactericidal activity (2.4–2.7 $\log_{10}$ colony-forming units [CFU] reduction from baseline).

The relationship between pharmacokinetic–pharmacodynamic parameters and in vivo efficacy of omadacycline was confirmed in a neutropenic mouse model of pneumonia [24]. The AUC_{0-24}/MIC ratio for unbound plasma and ELF had the highest correlation with efficacy ($r^2 = 0.74$) against 4 isolates of *S. pneumoniae* (MIC values 0.0315–0.125 µg/mL). Table 2 displays the typical range of plasma $f\text{AUC}_{0-24}$/MIC and ELF AUC_{0-24}/MIC ratios associated with net bacterial stasis and 1-log and 2-log reductions in numbers of CFU from baseline [24]. Corresponding values for plasma $f\text{AUC}_{0-24}$/MIC ratio and ELF AUC_{0-24}/MIC ratio were similar, because the penetration of omadacycline from plasma into ELF approached 100% (range, 72–102%) in mice. In vitro activity of omadacycline was not affected by lung surfactant [28].

Table 2. In Vivo Pharmacodynamics of Omadacycline Against *Streptococcus Pneumoniae* (Murine Lung Infection Model)[a]

Streptococcus pneumoniae Strain (MIC)	Stasis		1-$\log_{10}$ Kill		2-$\log_{10}$ Kill	
	Plasma $f\text{AUC}_{0-24}$/MIC	ELF AUC_{0-24}/MIC	Plasma $f\text{AUC}_{0-24}$/MIC	ELF AUC_{0-24}/MIC	Plasma $f\text{AUC}_{0-24}$/MIC	ELF AUC_{0-24}/MIC
1293, 0.06 µg/mL	19.83	17.80	179.98	200.64	…	…
10813, 0.06 µg/mL	15.79	14.18	19.66	17.61	25.05	23.19
140, 0.125 µg/mL	…	…	6.06	6.00	18.65	17.26
49619, 0.03 µg/mL	…	…	15.21	13.31	56.20	47.27

Abbreviations: AUC_{0-24}/MIC, 24-hour area under the concentration–time curve to MIC ratio; ELF, epithelial lining fluid; $f\text{AUC}_{0-24}$/MIC, 24-hour unbound (*f*) AUC_{0-24} to MIC ratio; MIC, minimum inhibitory concentration.

[a]Adapted by authors from Lepak et al with permission [24].

Omadacycline demonstrated in vivo activity and efficacy in a range of murine models of infection caused by gram-positive, gram-negative, and anaerobic pathogens [2]. Animal models provided preclinical support for the clinical development program of omadacycline in the treatment of ABSSSI and CABP [24–26].

CONCLUSIONS

Omadacycline is a novel aminomethylcycline agent with a pharmacokinetic–pharmacodynamic profile that supports once-daily oral and IV administration. Oral bioavailability of omadacycline is reduced in the presence of food, dairy products, and agents containing divalent and trivalent cations, which necessitates spacing of drug administration. Limited drug metabolism and primary fecal elimination of omadacycline contribute to its low potential for drug–drug interactions, and there is no requirement for dose modification in special populations. This information provides pharmacological understanding of oral and IV dosage regimens of omadacycline, which offer effective treatment and favorable safety profiles for ABSSSI and CABP management.

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