In Vitro Activity of Omadacycline and Comparator Agents Against Periodontal Pathogens

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Background

Omadacycline is a tetracycline class aminomethylcycline antibiotic FDA-approved for the treatment of community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections in adults (IV or oral).[1] Omadacycline has broad spectrum antibacterial activity against Gram-positive and -negative bacteria, including aerobic, anaerobic and atypical bacteria, and has demonstrated immunomodulatory properties.[2] The objective of this study was to evaluate omadacycline activity against common periodontal pathogens. Severe periodontal disease, inflammation of tissues around the teeth, is estimated by the World Health Organization to affect more than a billion people worldwide.[3] In certain cases, antibiotics are prescribed as adjunct therapy to minimize infection and decrease inflammation, with the most common being tetracyclines, metronidazole, fluoroquinolones, amoxicillin, and macrolides.

Methods

Broth microdilution minimum inhibitory concentration (MIC) testing was performed according to CLSI against aerotolerant streptococci and *Actinomyces* spp. that were able to grow in 5% CO_2 atmosphere. Agar dilution was performed according to CLSI for anaerobes. Omadacycline and comparators tetracycline, meropenem, levofloxacin and metronidazole were evaluated against 63 clinical isolates collected from New York, Indiana, Illinois, and California from 2009 to 2018 and 10 ATCC strains. In total, 73 isolates were evaluated across 8 genera: *Streptococcus, Actinomyces, Treponema, Fusobacterium, Parvimonas, Prevotella, Peptostreptococcus,* and *Aggregatibacter*.

Funding and Disclosures: Diane Anastasiou and Alisa Serio: Employees – Paratek Pharmaceuticals, Inc. This work was funded by Paratek Pharmaceuticals, Inc.

Omadacycline demonstrated potent *in vitro* activity against a diverse collection of periodontal disease pathogens

Conclusions

- Omadacycline MIC values ranged from ≤0.03 - 1 µg/mL
- Omadacycline MIC_{50} and MIC_{90} values were similar to meropenem and lower than tetracycline, levofloxacin and metronidazole
- These *in vitro* data, combined with other attributes of omadacycline, including immunomodulatory properties[2], warrant further investigation of omadacycline targeting periodontitis.

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Results

Table 1: *In vitro* activity of omadacycline and comparators against anaerobic periodontal pathogens

Organism	Source or MMX No.	MIC (µg/mL) OMC	TET	MEM	MTZ
Treponema denticola	ATCC 35405	1	1	4	>32
Fusobacterium nucleatum	ATCC 10953	0.12	0.25	≤0.016	≤0.06
	ATCC 25586	0.12	0.12	1	≤0.06
	9887	0.06	0.25	1	≤0.06
	9888	0.25	1	1	0.12
	9889	0.25	0.25	≤0.016	≤0.06
	9890	0.25	0.5	1	0.12
	9891	0.25	1	0.5	0.12
	9892	0.06	0.12	1	≤0.06
	9894	0.06	≤0.06	≤0.016	≤0.06
	9896	0.25	0.5	≤0.016	≤0.06
	9897	0.25	0.5	0.5	≤0.06
	9898	0.12	0.25	1	≤0.06
	9899	0.25	0.5	≤0.016	0.12
	9901	0.25	0.5	0.5	≤0.06
	9902	0.25	0.5	>8	≤0.06
	9903	0.06	0.12	0.5	≤0.06
	9908	0.25	1	1	≤0.06
	9911	0.25	1	2	4
	9912	0.25	0.12	0.5	0.12
	9913	1	2	0.5	0.5
	9914	0.06	0.12	0.5	≤0.06
F. periodenticum	9895	0.12	1	0.5	0.12
Fusobacterium spp.	9893	0.06	0.25	>8	≤0.06
	9906	0.25	1	0.5	≤0.06
	9907	0.06	0.12	≤0.016	0.25
Parvimonas micra	ATCC 33270	≤0.03	0.12	0.5	0.5
	3546	0.12	0.12	0.12	1
Prevotella denticola	3445	0.06	0.25	0.5	0.25
	9976	0.06	0.12	≤0.016	0.12
	10245	0.12	4	0.03	0.12
P. Intermedia	ATCC 15033	0.06	0.12	≤0.016	0.5
	9974	0.06	8	≤0.016	0.25
	3002	≤0.03	≤0.06	≤0.016	0.5
	10247	0.12	0.12	≤0.016	0.25
P. Nigrescens	9978	0.06	0.12	≤0.016	0.12
P. Oralis	ATCC 33269	0.5	0.5	0.5	>32
P. oris	10236	≤0.03	8	0.03	1
Peptostreptococcus micros	3432	0.5	0.5	0.25	>32
	3433	1	0.5	≤0.016	>32
	3434	1	0.5	0.25	>32
	3435	≤0.03	0.12	0.25	0.25
	3436	≤0.03	0.5	0.06	2
Steptococcus gordonii	ATCC 35105	0.5	0.5	0.03	>32
S. constellatus	5673	1	16	0.06	>32
	5674	1	8	0.5	>32
	6190	1	2	0.25	>32
	6665	1	2	≤0.016	>32
Aggregatibacter aphrophilus	ATCC 7901	1	0.5	0.5	8
Actinomyces spp.	9660	1	0.5	0.06	>32
	9665	1	16	0.06	>32
A. turicensis	9662	0.5	4	0.12	16

OMC, omadacycline; TET, tetracycline; MEM, meropenem; MTZ, metronidazole

Table 2: *In vitro* activity of omadacycline and comparators against aerotolerant periodontal pathogens

Organism	Source or MMX No.	MIC (µg/mL) OMC	TET	MEM	LVX
Streptococcus oralis	0350	0.06	32	1	>8
	0356	0.12	>32	0.12	>8
	5804	≤0.03	32	0.016	1
	5806	0.12	32	0.016	2
	5821	≤0.03	16	0.016	1
	5834	0.12	32	>8	2
	5837	≤0.03	0.25	0.12	1
	5839	≤0.03	0.5	0.03	1
	5849	0.06	32	0.03	1
Streptococcus constellatus	4954*	≤0.03	32	0.06	0.5
	5676	≤0.03	16	0.03	0.5
	5677	≤0.03	16	≤0.008	0.5
	6550*	0.06	1	0.016	0.5
	6565*	≤0.03	0.5	0.03	0.5
	6661*	0.06	1	0.016	1
Actinomyces europaeus	9663*	0.12	0.5	0.12	>8
Actinomyces naeslundi	0627*	0.12	2	0.016	2
Actinomyces naeslundii	ATCC 12104*	0.12	0.5	≤0.008	2
Actinomyces odontolyticus	9664	0.06	0.5	0.06	2
Actinomyces turicensis	9666*	0.12	1	0.12	2
Actinomyces viscosus	ATCC 43146	0.06	0.25	≤0.008	1

OMC, omadacycline; TET, tetracycline; MEM, meropenem; LVX, levofloxacin
*, isolates required extended incubation due to growth, read at 48 hr

Table 3: Summary of omadacycline and comparator *in vitro* activity against periodontal pathogens

	MIC (µg/mL) OMC	TET	MEM	LVX[1]	MTZ[2]
Range	≤0.03 - 1	≤0.06 - >32	≤0.016 - >8	0.5 - >8	≤0.06 - >32
MIC_{50}	0.12	0.5	0.12	1	0.25
MIC_{90}	1	16	1	>8	>32

OMC, omadacycline; TET, tetracycline; MEM, meropenem; LVX, levofloxacin; MTZ, metronidazole
[1], LVX evaluated against aerotolerant isolates (N=21)
[2], MTZ evaluated against anaerobic isolates (N=52)

References

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Poster P-1182 presented at the 2025 IDWeek, Atlanta, GA, October 21st, 2025

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