

Omadacycline vs. Moxifloxacin for Community-Acquired Pneumonia: A Real-World Retrospective Comparative Effectiveness and Safety Study

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Abstract

Background

This retrospective study aimed to compare the real-world clinical effectiveness and safety of omadacycline versus moxifloxacin in treating adult patients with CAP.

Methods

This single-center, retrospective cohort study was conducted at the First Affiliated Hospital of Guangxi University of Science and Technology. A total of 348 adult inpatients diagnosed with CAP between June 2022 and December 2024 were enrolled and divided into an Omadacycline group (n = 170) and a Moxifloxacin group (n = 178). The primary outcome was early clinical response (ECR), assessed 72–120 hours after treatment initiation. Secondary outcomes included overall clinical response rate, bacterial eradication rate, changes in inflammatory biomarkers, and adverse events..

Results

Baseline characteristics were comparable between the two groups. The ECR success rate was 92.9% (158/170) in the Omadacycline group and 91.0% (162/178) in the Moxifloxacin group (absolute risk difference: 1.9%, 95% CI: -4.1% to 7.9%; $p = 0.508$), demonstrating the non-inferior efficacy of omadacycline. Overall clinical response (92.9% vs. 91.0%, $p = 0.508$) and bacterial eradication rates (88.2% vs. 86.8%, $p = 0.776$) were also similar. Both groups showed significant and comparable improvements in inflammatory markers and pneumonia severity scores post-treatment. However, the overall incidence of adverse events was significantly lower in the Omadacycline group (15.3% vs. 30.3%, $p < 0.001$), primarily due to a lower incidence of gastrointestinal adverse reactions (5.9% vs. 20.8%, $p < 0.001$).

Conclusion

In this real-world study, omadacycline demonstrated non-inferior clinical effectiveness compared to moxifloxacin for treating CAP, with a significantly more favorable safety profile, particularly regarding gastrointestinal tolerability. These findings support omadacycline as an effective and safer alternative for CAP, especially for patients with concerns regarding fluoroquinolone-associated risks.

1. Introduction

Community-acquired pneumonia (CAP) remains a leading global cause of infectious disease mortality, posing a persistent challenge to public health systems [1]. The estimated annual incidence of CAP in adults ranges from 1 to 10 per 1,000, with in-hospital mortality reaching 5% to 15% [2, 3]. Appropriate

initial empirical antibiotic therapy is a critical determinant of improved clinical outcomes, necessitating agents with broad-spectrum antibacterial activity and a reliable safety profile [4].

Respiratory fluoroquinolones, represented by moxifloxacin, have long been a cornerstone of CAP treatment. They exert a rapid bactericidal effect by inhibiting bacterial DNA gyrase and topoisomerase IV [5, 6]. However, their clinical utility is increasingly constrained by significant safety concerns. The U.S. Food and Drug Administration (FDA) has issued black box warnings highlighting the potential for disabling and potentially permanent adverse reactions, including tendinitis, tendon rupture, peripheral neuropathy, and central nervous system effects [7]. Furthermore, contemporary epidemiological studies have associated fluoroquinolone use with an increased risk of serious cardiovascular events, such as aortic aneurysm and dissection, as well as QT interval prolongation [8, 9].

In this context, omadacycline, a novel aminomethylcycline antibiotic, has emerged as a promising therapeutic alternative. Omadacycline binds with high affinity to the bacterial ribosome 30S subunit, inhibiting protein synthesis [10]. This unique mechanism, coupled with its broad-spectrum activity against common and atypical CAP pathogens (*Streptococcus pneumoniae*, *Chlamydia pneumoniae*), and the convenience of once-daily intravenous-to-oral transition, offers significant practical advantages [11, 12]. Furthermore, its primary adverse effects are typically mild-to-moderate gastrointestinal reactions, and it avoids the severe, class-specific adverse reactions associated with fluoroquinolones [13]. The pivotal phase III OPTIC trial established the non-inferior efficacy of omadacycline compared to moxifloxacin for community-acquired bacterial pneumonia within a rigorous randomized controlled trial (RCT) framework [14]. Subsequent integrated analyses have further corroborated its clinical efficacy [15, 16].

Nevertheless, a critical gap persists between evidence from highly controlled clinical trials and the needs of real-world clinical decision-making. RCTs, such as the OPTIC study, often employ strict inclusion and exclusion criteria, potentially excluding patients with significant comorbidities, polypharmacy, or frailty who are commonly encountered in daily practice [14]. Consequently, the generalizability of these findings to broader, more diverse patient populations remains uncertain. Notably, there is a paucity of direct comparative data on the safety profiles of omadacycline and moxifloxacin outside the controlled RCT environment [13, 17, 18]. High-quality real-world evidence (RWE) addressing this specific safety comparison is needed

To address this evidence gap, we conducted a retrospective cohort study to systematically compare the clinical efficacy and safety profiles of omadacycline and moxifloxacin in treating CAP patients within a real-world clinical setting. Our findings aim to provide clinicians with evidence-based data on the efficacy-safety balance when selecting empirical treatment for CAP.

2. Materials and Methods

2.1. Study Design

This was a single-center, retrospective cohort study. The study was executed in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Review Committee of the First Affiliated Hospital of Guangxi University of Science and Technology (Approval No.: 2025-LC158). The requirement for informed consent was waived due to the retrospective nature of the study. All patient data were de-identified to protect privacy.

2.2. Study Participants

Data were extracted from the electronic medical record system of the First Affiliated Hospital of Guangxi University of Science and Technology. A total of 348 patients hospitalized with a diagnosis of CAP between June 2022 and December 2024 were included.

Inclusion Criteria

☐ Age ≥ 18 years; ☐ Diagnosis of CAP meeting the 2019 ATS/IDSA Joint Guidelines criteria (presence of corresponding clinical symptoms and confirmation of pulmonary infiltrates on chest imaging) [19]; ☐ Receipt of omadacycline or moxifloxacin as the primary initial or sequential anti-infective regimen for a duration of ≥ 72 hours.

Exclusion Criteria

☐ Hospital stay < 48 hours or severely incomplete clinical data; ☐ Use of other potent antibiotics targeting Gram-positive or -negative bacteria within 48 hours prior to admission; ☐ Co-existing active pulmonary tuberculosis, lung tumor, or immunodeficiency diseases (e.g., HIV infection, long-term immunosuppressant use); ☐ Pregnancy or lactation; ☐ Documented history of allergy to tetracyclines or fluoroquinolones.

Grouping: Based on the initial primary treatment agent, patients were divided into two groups: the Omadacycline group (n = 170) and the Moxifloxacin group (n = 178).

2.3. Therapeutic Intervention

All patients received standard supportive care for CAP as clinically indicated.

Omadacycline Group

Patients received intravenous (IV) omadacycline (Nuzail®[®], Zhejiang Hisun Pharmaceutical Co., Ltd.) with a loading dose of 100 mg twice on Day 1, followed by 100 mg once daily. Upon clinical improvement, treatment was switched to oral omadacycline tablets (Nuzail®[®], Jiangsu XuanTai Pharmaceutical Co., Ltd.) at 300 mg once daily.

Moxifloxacin Group

Patients received IV moxifloxacin hydrochloride (Yangtze River Pharmaceutical Group Co., Ltd.) at 400 mg once daily. Upon clinical improvement, treatment was switched to oral moxifloxacin tablets (CSPC

Ouyi Pharmaceutical Co., Ltd.) at 400 mg once daily.

The total treatment duration for both groups ranged from 7 to 14 days, as determined by the attending physician based on clinical response and guidelines.

2.4.Outcome Measures

2.4.1.Primary outcome

The primary endpoint was **Early Clinical Response (ECR)**, assessed 72 to 120 hours after the first dose. Clinical success was defined as meeting all the following criteria: 1) Survival; 2) No receipt of rescue antibacterial therapy for CAP; 3) Improvement in at least two of four baseline CAP core symptoms (cough, sputum production, pleuritic chest pain, dyspnea), with no worsening in any symptom [15]. Failure to meet any of these criteria was considered early clinical failure.

2.4.2.Secondary outcomes

Bacterial Eradication Rate

For patients with positive pre-treatment microbiological results, post-treatment cultures were evaluated. Eradication rate (%) = (Number eradicated) / (Number eradicated + Number not eradicated) × 100%.

Changes in Inflammatory Markers and Body Temperature

White blood cell count (WBC), C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), neutrophil count (NEUT), and axillary body temperature were measured pre-treatment, on Day 3, and at the end of treatment.

Disease Severity Scores

The Pneumonia Severity Index (PSI) and SMART-COP scores were compared before and after treatment [20].

Pathogen Distribution

Pre-treatment pathogens identified via culture or serology were recorded.

Incidence of Adverse Events (AEs)

All drug-related or potentially drug-related AEs occurring during treatment and within 7 days after completion were recorded. Overall AE incidence (%) = (Number of patients with at least one AE) / Total number of patients × 100%.

2.5.Statistical Analysis

All statistical analyses were performed using SPSS software version 27.0.1. Normally distributed continuous variables are presented as mean $\pm$ standard deviation (SD) and were compared using the independent samples t-test. Non-normally distributed data are presented as median (interquartile range) and compared using the Mann-Whitney U test. Categorical variables are presented as frequency (percentage) and were compared using the Chi-square test or Fisher's exact test. All statistical tests were two-sided, with $p < 0.05$ considered statistically significant.

3. Results

3.1. Baseline Characteristics of the Patients

A total of 348 eligible CAP patients were included (Omadacycline, $n = 170$; Moxifloxacin, $n = 178$). As shown in Table 1, baseline characteristics, including age, gender, BMI, comorbidities, CURB-65 score, and pathogen distribution, were well-balanced between the two groups (all $p > 0.05$).

Table 1
Baseline Demographic and Clinical Characteristics of the Study Population

Characteristic	The Omadacycline Group (n = 170)	The Moxifloxacin Group (n = 178)	P value
Gender (Male)	102 (60.0%)	107 (60.1%)	0.983
Age (years, Mean $\pm$ SD)	66.4 $\pm$ 7.4	65.8 $\pm$ 6.0	0.346
Age > 65 years	113 (66.5%)	125 (70.2%)	0.451
BMI (kg/m ² , Mean $\pm$ SD)	23.3 $\pm$ 2.8	23.6 $\pm$ 3.0	0.289
Treatment Duration (days, Mean $\pm$ SD)	10.7 $\pm$ 1.9	10.5 $\pm$ 1.9	0.455
Pathogen Distribution			
<i>Streptococcus pneumoniae</i>	29 (17.1%)	34 (19.1%)	0.621
<i>Haemophilus influenzae</i>	19 (11.2%)	23 (12.9%)	0.617
<i>Klebsiella pneumoniae</i>	17 (10.0%)	18 (10.1%)	0.972
<i>Atypical Pathogens*</i>	20 (11.8%)	16 (9.0%)	0.395
<i>Other/Mixed Infection</i>	18 (10.6%)	20 (11.2%)	0.846
<i>Not Detected</i>	67 (39.4%)	67 (37.6%)	0.734
Comorbidities			
<i>Chronic Pulmonary Disease</i>	49 (28.8%)	57 (32.0%)	0.517
<i>Diabetes Mellitus</i>	44 (25.9%)	50 (28.1%)	0.643
<i>Hypertension</i>	78 (45.9%)	87 (48.9%)	0.576
<i>Cardiovascular Disease</i>	36 (21.2%)	41 (23.0%)	0.677
CURB-65 Score			
Low Risk (0–1 points)	109 (64.1%)	110 (61.8%)	0.654
<i>Intermediate Risk (2 points)</i>	44 (25.9%)	50 (28.1%)	0.643
<i>High Risk ($\geq$ 3 points)</i>	17 (10.0%)	18 (10.1%)	0.972
<i>Note: *Atypical pathogens include Mycoplasma pneumoniae, Chlamydophila pneumoniae, and Legionella species.</i>			

3.2.Early Clinical Response

In the treatment population, the ECR success rate was 92.9% (158/170) in the Omadacycline group and 91.0% (162/178) in the Moxifloxacin group. The difference was not statistically significant (absolute risk difference: 1.9%, 95% CI: -4.1% to 7.9%; p = 0.508) (Table 2).

Table 2
Early Clinical Response

Early Clinical Response	The Omadacycline Group n(%)	The Moxifloxacin Group n(%)	Absolute Risk Difference (95% CI)	P value
Clinical Success	158 (92.9%)	162 (91.0%)	1.9% (-4.1% ~ 7.9%)	0.508
Clinical Failure/Indeterminate	12 (7.1%)	16 (9.0%)	-	-

3.3. Post-Treatment Assessment of Clinical Efficacy

At the end of treatment, the overall clinical response rate was 92.9% (158/170) in the Omadacycline group and 91.0% (162/178) in the Moxifloxacin group (p = 0.508) (Table 3).

Table 3
Post-Treatment Clinical Efficacy

Group	No.	Cure	Marked Improvement	Improvement	Failure	Overall Response Rate
The Omadacycline Group	170	97 (57.1%)	44 (25.9%)	17 (10.0%)	12 (7.1%)	158 (92.9%)
The Moxifloxacin Group	178	98 (55.1%)	48 (27.0%)	16 (9.0%)	16 (9.0%)	162 (91.0%)
P value						0.508

3.4. Bacterial Eradication Rate

Among patients with positive pre-treatment cultures (Omadacycline, n = 85; Moxifloxacin, n = 91), the bacterial eradication rate was 88.2% (75/85) in the Omadacycline group and 86.8% (79/91) in the Moxifloxacin group (p = 0.776) (Table 4).

Table 4
Bacterial Eradication Rates

Group	No.*	Eradicated	Not Eradicated	Indeterminate	Eradication Rate (%)
The Omadacycline Group	85	75 (88.2%)	8 (9.4%)	2 (2.4%)	88.2%
The Moxifloxacin Group	91	79 (86.8%)	10 (11.0%)	2 (2.2%)	86.8%
P value	0.776				
*Note: Number of patients with identified pathogens (excluding those with Other/Mixed Infection or Not Detected).					

3.5.Changes in Inflammatory Markers

Pre-treatment levels of body temperature and inflammatory markers were similar between groups. By Day 3 and at the end of treatment, all markers showed significant decreases from baseline within each group ($p < 0.01$). However, the magnitude of reduction at any time point was not significantly different between the two groups (all $p > 0.05$) (Table 5).

Table 5
Body Temperature and Inflammatory Markers Over Time

Parameter	Time Point	The Omadacycline Group (n = 170)	The Moxifloxacin Group (n = 178)	P value
Body Temp (°C)	Pre-treatment	39.02 ± 0.56	38.97 ± 0.38	0.531
	Day 3 of Treatment	37.06 ± 0.33	37.10 ± 0.27	0.329
	End of Treatment	36.70 ± 0.16	36.73 ± 0.14	0.227
WBC (×10 ⁹ /L)	Pre-treatment	13.80 ± 2.22	13.94 ± 2.25	0.553
	Day 3 of Treatment	8.92 ± 2.31	9.29 ± 2.57	0.230
	End of Treatment	7.40 ± 1.61	7.51 ± 1.69	0.517
CRP (mg/L)	Pre-treatment	85.73 ± 23.51	87.13 ± 23.59	0.644
	Day 3 of Treatment	31.63 ± 9.01	32.26 ± 9.46	0.072
	End of Treatment	8.50 ± 3.50	8.41 ± 3.36	0.872
PCT (ng/mL)	Pre-treatment	2.97 ± 1.64	3.10 ± 1.67	0.645
	Day 3 of Treatment	0.75 ± 0.39	0.72 ± 0.40	0.426
	End of Treatment	0.14 ± 0.07	0.15 ± 0.08	0.056
NEUT (×10 ⁹ /L)	Pre-treatment	8.46 ± 1.70	8.16 ± 1.59	0.119
	Day 3 of Treatment	5.16 ± 1.28	5.00 ± 1.28	0.239
	End of Treatment	4.00 ± 0.84	3.85 ± 0.77	0.349
IL-6 (pg/mL)	Pre-treatment	13.60 ± 1.90	13.50 ± 2.10	0.693
	Day 3 of Treatment	5.47 ± 1.84	5.26 ± 1.86	0.321
	End of Treatment	3.08 ± 1.18	3.15 ± 1.30	0.603

3.6.Comparison of Disease Severity Scores

Pre-treatment PSI and SMART-COP scores were comparable between groups. Post-treatment, both scores decreased significantly from baseline within each group (both $p < 0.001$), with no significant differences in the degree of reduction between groups (all $p > 0.05$) (Table 6).

Table 6
Pneumonia Severity Scores

Group	No. of Cases	PSI Score		SMART-COP Score	
		Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment
The Omadacycline Group	170	87.9 ± 19.3	39.5 ± 16.1*	4.4 ± 1.2	1.0 ± 0.8*
The Moxifloxacin Group	178	84.8 ± 19.0	39.8 ± 15.5*	4.4 ± 1.0	1.1 ± 0.8*
P		0.142	0.186	0.773	0.605
*Note: Compared with pre-treatment within the group, $P < 0.001$					

3.7. Adverse Event

The overall incidence of AEs was significantly lower in the Omadacycline group (15.3%, 26/170) compared to the Moxifloxacin group (30.3%, 54/178; $p < 0.001$). This difference was primarily driven by gastrointestinal reactions (5.9% vs. 20.8%, $p < 0.001$), specifically nausea, vomiting, and diarrhea (Table 7). The incidence of hepatic function abnormalities, rash, and other AEs was comparable between groups. Serious adverse events (SAEs) leading to treatment discontinuation were reported in 2 patients (1.2%) in the Omadacycline group (severe rash, headache) and 5 patients (2.8%) in the Moxifloxacin group (severe diarrhea, severe vomiting, rash, hypertension, and headache), though this difference was not statistically significant ($p = 0.449$).

Table 7
Adverse Events

Related Adverse Event	The Omadacycline Group (n = 170)	The Moxifloxacin Group (n = 178)	P value
Any AE	26 (15.3%)	54 (30.3%)	< 0.001
Gastrointestinal Reactions	10 (5.9%)	37 (20.8%)	< 0.001
Nausea	3 (1.8%)	13 (7.3%)	0.014
Vomiting	2 (1.2%)	9 (5.1%)	0.039
Diarrhea	2 (1.2%)	15 (8.4%)	0.002
Constipation	1 (0.6%)	0 (0.0%)	0.116
Hepatic Function Abnormalities	6 (3.5%)	3 (1.7%)	0.328
ALT Elevation	3 (1.8%)	2 (1.1%)	0.679
AST Elevation	3 (1.8%)	1 (0.6%)	0.362
Skin Reactions	1 (0.6%)	2 (1.1%)	1.000
Rash	1 (0.6%)	2 (1.1%)	1.000
Other	9 (5.3%)	12 (6.7%)	0.571
Headache	2 (1.2%)	4 (2.2%)	0.685
Insomnia	1 (0.6%)	3 (1.7%)	0.623
Hypertension	5 (2.9%)	3 (1.7%)	0.494
Injection Site Reaction	1 (0.6%)	2 (1.1%)	1.000
Serious AEs	2 (1.2%)	5 (2.8%)	0.449

4. Discussion

This single-center, retrospective cohort study compared the real-world efficacy and safety of omadacycline versus moxifloxacin for CAP. Our key findings demonstrate that omadacycline has comparable clinical efficacy to moxifloxacin, evidenced by similar rates of early clinical response, overall response, bacterial eradication, and improvements in inflammatory markers and severity scores. Crucially, omadacycline exhibited a significantly superior safety profile, with a substantially lower overall incidence of adverse events, particularly gastrointestinal reactions.

The efficacy results are highly consistent with the findings of the pivotal phase III OPTIC trial [14]. That study established the non-inferior efficacy of omadacycline in a rigorously controlled RCT environment for community-acquired bacterial pneumonia [21]. Our findings extend this equivalence to a broader, real-world patient population that includes those with more comorbidities, thereby supporting the external validity and generalizability of omadacycline's efficacy. The use of Early Clinical Response (ECR) as our primary endpoint, mirroring the OPTIC trial, allows for a direct and compelling comparison. ECR is a clinically relevant indicator that provides immediate value for clinicians assessing the appropriateness of initial empirical therapy [22, 23].

The most prominent finding of our study is the significantly more favorable safety profile of omadacycline. The overall AE incidence in the moxifloxacin group was double that of the omadacycline group, a difference almost entirely attributable to a higher rate of gastrointestinal reactions (nausea, vomiting, diarrhea). This aligns with the known safety spectrum of omadacycline, where adverse effects are mainly confined to mild-to-moderate gastrointestinal events [24, 25]. In contrast, moxifloxacin carries black box warnings for severe, disabling, and potentially permanent adverse reactions associated with the fluoroquinolone class, in addition to gastrointestinal side effects [7]. Therefore, the better gastrointestinal tolerability of omadacycline, combined with its lack of typical fluoroquinolone-related severe risks, provides a significant safety advantage, particularly for patients requiring extended treatment, the elderly, or those with contraindications to fluoroquinolones. Our real-world data offer valuable corroboration of this benefit.

From clinical and public health perspectives, our findings have important implications. CAP patients, particularly the elderly, often have multiple comorbidities, making them more susceptible to adverse drug reactions [26, 27]. The better tolerability of omadacycline may translate into higher treatment adherence, fewer interruptions, and a reduced need for medical interventions due to AEs [28]. Within the framework of Antimicrobial Stewardship (AMS), promoting agents like omadacycline with comparable efficacy and superior safety can help ensure therapeutic effectiveness while potentially reducing the healthcare burden associated with drug-related AEs and decreasing overall fluoroquinolone use [29]. This study, as a piece of real-world evidence, effectively bridges the gap between pivotal RCT evidence and daily clinical practice [30]. We found that even among complex patients often excluded from RCTs, omadacycline maintains its efficacy and safety advantages, providing clinicians with a strong evidence-based alternative, especially for high-risk patients.

This study has several limitations. First, its retrospective design may introduce residual confounding, despite balanced baseline characteristics. Second, the single-center setting and moderate sample size may limit the generalizability of our findings and the power to detect rare adverse events. Third, symptom severity assessment relied on medical record documentation rather than prospective standardized scales, potentially introducing information bias. Fourth, the sample size was insufficient to detect rare, specific severe adverse reactions. Future large-scale, multicenter prospective studies or pragmatic clinical trials are needed to validate these findings and conduct in-depth health economic evaluations to comprehensively assess omadacycline's role in CAP treatment.

In conclusion, this real-world study demonstrates that omadacycline has comparable efficacy to moxifloxacin in treating CAP, while offering significant advantages in safety, particularly regarding gastrointestinal tolerability. These results provide important evidence on the efficacy-safety balance for clinicians when selecting empirical treatment for CAP, supporting omadacycline as an effective and safer alternative to moxifloxacin, especially for patients concerned about fluoroquinolone-associated risks. Further research with larger sample sizes and including pharmacoeconomic comparisons is warranted to corroborate these findings.

Declarations

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Author Contribution

TL and YQ contributed to conceptualization, study design, data acquisition, data interpretation, and drafting of the manuscript. JT contributed to data acquisition, data curation, and literature investigation. YL contributed to data acquisition, data curation, and statistical analysis. JZ contributed to data acquisition, data curation, and visualization. CY contributed to data acquisition, data curation, and literature investigation. WL contributed to data acquisition, data curation, and methodology. XJ contributed to data acquisition, data curation, and statistical analysis. YML contributed to data acquisition, data curation, and methodology. YM contributed to data acquisition, data curation, and project administration. JQ contributed to data acquisition, data curation, and literature investigation. SH contributed to conceptualization, study design, data interpretation, methodology, project administration, funding acquisition, and manuscript review and editing. SH is the corresponding author. All authors reviewed and approved the final manuscript.

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Everyone who contributed significantly to this study has been listed.

Data Availability

1. The datasets [GENERATED/ANALYZED] for this study can be found in the [figshare] [<https://doi.org/10.6084/m9.figshare.31698838>].

Ethics, Consent to Participate, and Consent to Publish declarations: not applicable.

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