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# *In vitro* Activity of Omadacycline and Comparator Antibiotics against *Clostridioides difficile*

**Andrew Skinner MD[1,2]**, Laurica Petrella BS[1], Adam Cheknis BA[1], Stuart Johnson MD[1,2]

[1]Edward Hines, Jr. VA Hospital, Hines, IL; [2]Loyola University Medical Center, Maywood, IL

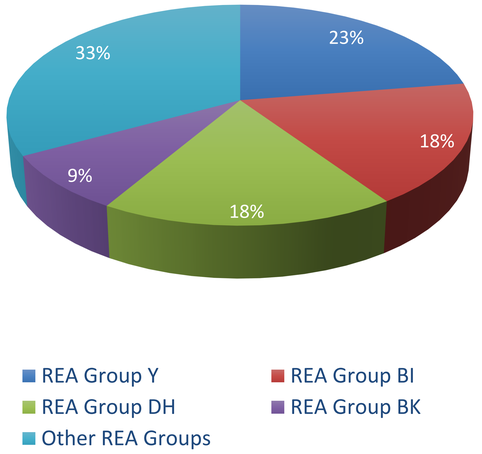
## Background

- Omadacycline was approved for the treatment of community acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI) in 2018.
- Previous studies demonstrate that omadacycline has *in vitro* activity against *Clostridioides difficile.*
- Antibiotic activity towards *C. difficile* may influence risk of *C. difficile* infection for that antibiotic.
- We determined the *in vitro* activity of omadacycline and of comparator antimicrobials used for the approved indications, CABP and ABSSSI, towards a contemporary and clinically relevant collection of *C. difficile* isolates.

## Methods

- Antimicrobial susceptibility testing was performed by agar dilution on 200 clinical *C. difficile* isolates collected from 2014 – 2021.
- Isolates were selected based on the most prevalent restriction endonuclease analysis (REA) groups locally and nationally.
- Omadacycline (OMC) was compared to 8 standard of care antimicrobials for CABP and ABSSSI: amoxicillin-clavulanate (AMC), azithromycin (AZ), ceftriaxone (CRO), clindamycin (CLI), doxycycline (DOX), linezolid (LZD), moxifloxacin (MXF), and trimethoprim-sulfamethoxazole (SXT).

### *C. difficile* Isolate Selection




| | Geometric mean MIC (µg/ml) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| REA group | OMC | AMC | AZ | CRO | CLI | DOX | LZD | MXF | SXT |
| All Isolates (200) | 0.07 | 0.72 | 10.63 | 47.18 | 7.36 | 0.062 | 1.99 | 2.04 | 9.32 |
| REA Y (45) | 0.08 | 0.66 | 2.94 | 36.20 | 4.06 | 0.05 | 1.82 | 1.34 | 9.33 |
| REA DH (36) | 0.07 | 0.89 | 5.99 | 60.41 | 5.55 | 0.04 | 1.82 | 1.31 | 17.28 |
| REA BI (36) | 0.06 | 1.04 | 335.20 | 80.63 | 32.00 | 0.04 | 2.20 | 13.20 | 5.66 |
| REA BK (17) | 0.09 | 0.44 | 8.68 | 46.19 | 8.33 | 0.7 | 2.55 | 1.33 | 8.33 |
| Other REA (66) | 0.08 | 0.64 | 5.60 | 37.07 | 5.60 | 0.06 | 1.96 | 1.38 | 8.98 |

| | | MIC (µg/ml) | | | Resistant Isolates | |
|---|---|---|---|---|---|---|
| Antimicrobial Agent | Breakpoint[a] | $MIC_{50}$ | $MIC_{90}$ | Range | R[c] | HR[d] |
| Omadacycline | - | 0.0625 | 0.125 | 0.031 - 0.25 | - | - |
| Amoxicillin/Clavulanate | ≥16/8 | 1/0.5 | 1/0.5 | 0.25/0.125 – 2/1 | 0 (0%) | - |
| Azithromycin | - | 4 | 512 | 1 - >512 | - | 50 (25%) |
| Ceftriaxone | ≥64 | 64 | 128 | 8 - 512 | 104 (52%) | - |
| Clindamycin | ≥8 | 4 | 128 | 0.5 - >512 | 73 (37%) | 34 (17%) |
| Doxycycline | ≥16[b] | 0.0625 | 0.0625 | 0.031 – 16 | 1 (<1%) | - |
| Linezolid | - | 2 | 2 | 1 – 16 | - | - |
| Moxifloxacin | ≥8 | 1 | 16 | 0.5 – 128 | 34 (17%) | 4 (2%) |
| Trimethoprim/sulfamethoxazole | - | 8/152 | 16/304 | 1/19 – 32/608 | - | - |

a. MIC Breakpoint established per CLSI m100
b. Breakpoint for tetracycline substituted for doxycycline
c. R, Resistant - Organisms as defined as isolates with MIC greater than established CLSI breakpoint
d. HR, Highly Resistant - Organisms with MIC ≥64 µg/ml for azithromycin, clindamycin, and moxifloxacin
Antibiotic Abbreviations: OMC – Omadacycline, AMC – Amoxicillin/Clavulanate, AZ – Azithromycin, CRO – Ceftriaxone, CLI – Clindamycin, DOX – Doxycycline, LZD – Linezolid, MXF – Moxifloxacin, SXT – Trimethoprim/Sulfamethoxazole

## Results

- The geometric mean MIC of OMC was 0.07 µg/ml and the MIC50 and MIC90 were 0.0625 µg/ml and 0.125 µg/ml, respectively.
- The majority of REA BI (RT027) isolates were resistant to CLI (77.7%, 28/36) and CRO (83.3%, 30/36), but susceptible to OMC
- The CLI geometric mean MIC for REA BI was elevated when compared to all other REA group strains (32 µg/ml and 5.33 µg/ml, respectively, p<0.005).
- REA BI (RT027) had an elevated AZ and MXF geometric MIC (335.2 and 17.3 µg/ml, respectively).
- REA DH (RT106) isolates had a higher trimethoprim-sulfamethoxazole geometric MIC compared to all other REA group strains (17.28 µg/ml and 8.14 µg/ml, respectively p<0.001).
- Nearly half of REA BK (RT078/126) isolates (47%) had a DOX MIC ≥2 µg/ml which did not correspond with an elevated OMC MIC for the same isolates.

## Conclusion

- Omadacycline demonstrated consistently low MICs against *C. difficile* when compared to other approved antimicrobials for CABP and ABSSSI.
- Omadacycline may reduce the risk of developing a C. difficile infection and requires further study.

## Disclosures

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