Strategies for ABSSSI Management in Adults:

Harnessing Tetracyclines through an Interdisciplinary Approach

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Faculty Disclosures

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Learning Objectives

- Correlate the increase of acute bacterial skin and skin structure infection (ABSSSI) with increased morbidity, mortality, length of hospital stay, and overall costs
- Explain the mechanisms of action of tetracycline-class antibacterials and describe their spectrum of activity against common pathogens associated with ABSSSI
- Examine current trends in antibiotic resistance relevant to ABSSSI, including the prevalence of resistant strains and how tetracyclines compare to other antibiotic classes

ABSSSI = acute bacterial skin and skin structure infection;

Update on ABSSSI: **Current State of Treatments and Why a Superhero Team Is Needed**

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Identifying the Enemy: ABSSSI

- **SSTI** (Skin and Soft Tissue Infections)
  - All chronic and acute,
  - All complicated and uncomplicated skin infections
  - No minimal size

- **ABSSSI** – Acute Bacterial Skin and Skin Structure Infections
  - FDA-derived definition for skin infection for clinical trials
  - Limited to 3 main types of common acute skin infections
    - Cellulitis/ Erysipelas
    - Major Cutaneous Abscess
    - Wound Infection
  - Lesion areas of ≥ 75cm^2 in size

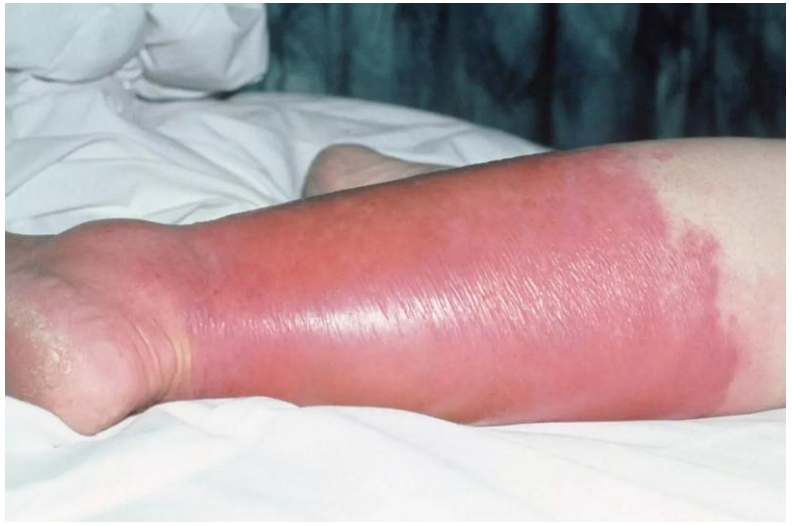
TABLE 1 Classification of skin and soft-tissue infections according to different criteria

	Uncomplicated uSSTI	Complicated cSSTI	ABSSSI
Involvement	>Superficial	Deep	Varies according to infection
Hospital admission	No	Yes	Yes
Surgery requirement/drainage	No/minimal	Yes	Yes for wound infections or abscesses
Extension	Limited	Extended	>75 cm^2
Progression	No	Yes	Yes
Clinical presentation	Mild	Severe	Severe

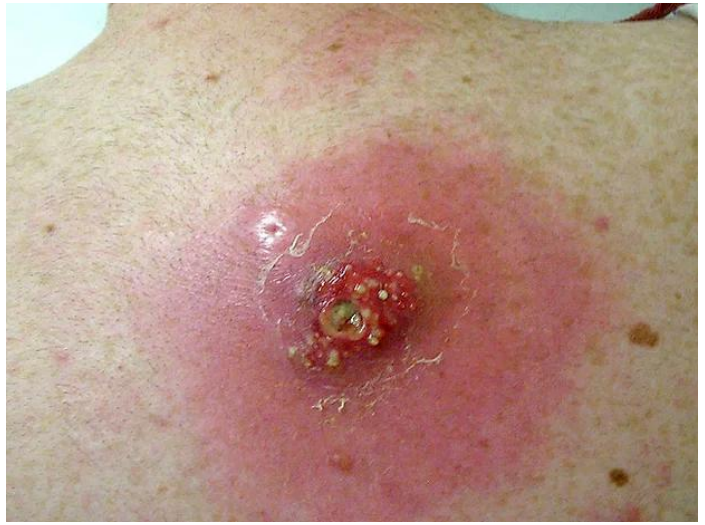
Abbreviations: ABSSSI, Acute Bacterial Skin and Skin Structure Infections; cSSTI, complicated Skin and Soft Tissue Infections; uSSTI, uncomplicated Skin and Soft Tissue Infections.

Miller GM, et al. *Clin Infect Dis.* 2014;58(Suppl 1):S4-S9. Bouza E, et al. *JEADV Clin Pract*. 2022;1(3):165-175.

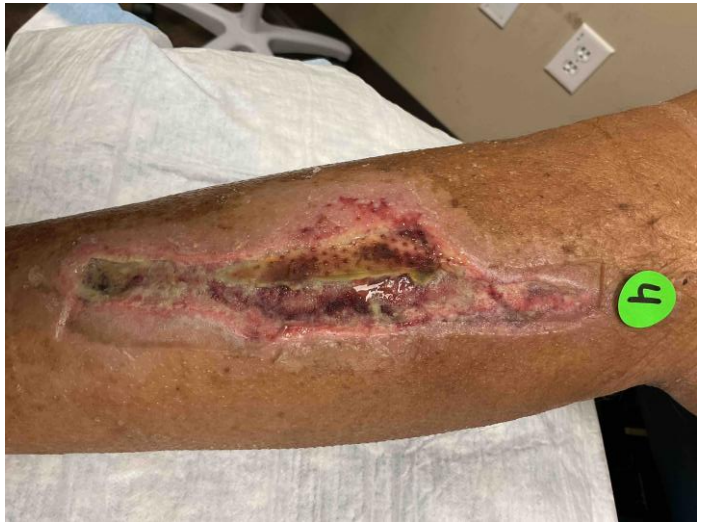
Identifying the Enemy: ABSSSI



Cellulitis/ Erysipelas



Major Cutaneous Abscess



Wound Infection

Common ABSSSI Pathogens

- *Staph aureus* (most common)[1]
  - MRSA (~20% of all *Staph aureus* isolates) depending on region[2]
- *Streptococcus pyogenes* and other beta hemolytic *Strep*
- *Enterococcus faecalis*
- Other Gram-negative bacteria – less common

Prevalence of MRSA in various regions based on surveillance programs.

Region	*S. aureus* (N)	MSSA (%)	MRSA (%)	Testing period	Reference
US	43,331	53.6	**46.4**	2011–2014	57
Canada	2539	80.2	**19.8**	2010–2012	58
Europe	40,414	82.6	**17.4**	2013	59
China	6656	51.1	**48.9**	2004–2011	60
Asia	4117	47.5	**52.5**	2004–2006	61
Asia Pacific	1971	38.1	**61.9**	2012	62
Latin America	1066	41.7	**58.3**	2012	63
Middle East/North Africa	NR	NR	**42.1**	Before 2014	25

MRSA, methicillin-resistant *Staphylococcus aureus;* MSSA, methicillin-sensitive *Staphylococcus aureus;* NR, not reported.

How to Choose Empirical Therapy

- Guided by pathogens most likely to appear
  - MRSA coverage against the most locally prevalent MRSA strains
- Clinical presentation
- History
- Physical exam
- Efficacy of empiric treatment should be assessed 48-72 hrs after initiation of treatment

Bouza E, et al. *JEADV Clin Pract*. 2022;1(3):165-175. Pulido-Cejudo A, et al. *Ther Adv Infect Dis*. 2017;4(5):143-161.

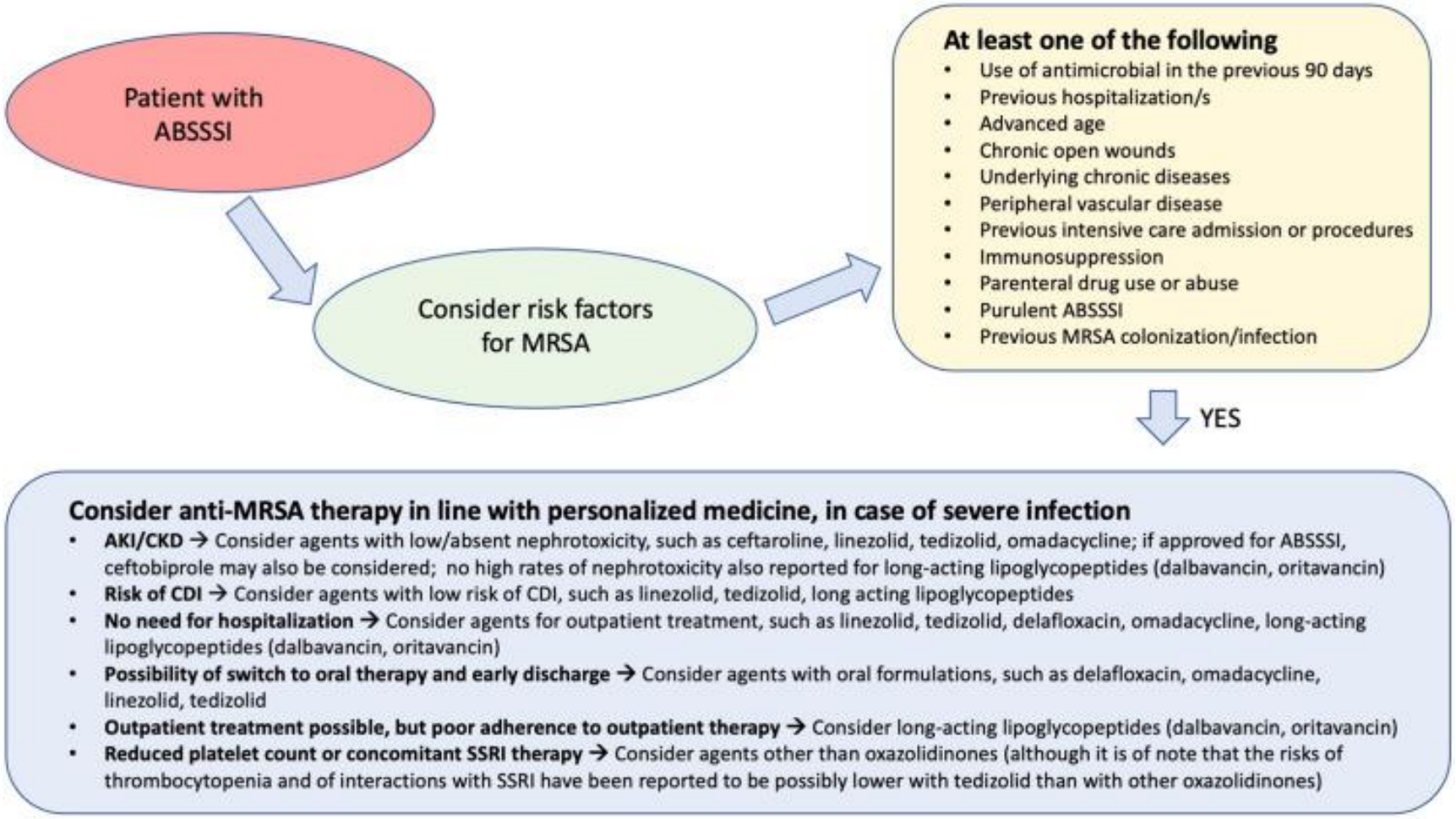
ABSSSI: A Significant Healthcare Burden

- More than 21 million outpatient SSTI visits per yr (2010-2020)[1]
- More than 4.1 million cases of SSTI treated in the ED (2022) [2]
- More than $2 billion in aggregate ED healthcare costs per yr (2022)[2]
- Up to 34% of hospitalized ABSSSI patients previously failed initial outpatient antibiotic treatments[3]

SSTI = skin and soft tissue infection.

1. Vella V, et al. *Open Forum Infect Dis*. 2024;11(6):ofae267. 2. Estrada S, et al. *Drugs Real World Outcomes*. 2020;7(Suppl 1):6-12. 3. AHRQ Data Tools. Content last reviewed April 2025. Agency for Healthcare Research and Quality, Rockville, MD. https://www.ahrq.gov/data/data-tools/index.html

ABSSSI Management Recommendations



Giacobbe DR, et al. *Infect Drug Resist*. 2022;15:2137-2157.

ABSSSI Management Complicated by Comorbidities

- ABSSSI – frequent cause of morbidity in both hospital and community settings
  - CA-MRSA prevalence has increased significantly in past decade as the most frequent pathogen; tends to be more virulent than HA-MRSA
    - CA-MRSA tends to occur in younger patients with little to no risk factors
    - HA-MRSA tends to colonize in elderly patients with prior exposure to healthcare facilities
- The alphabet soup of comorbidities complicates treatment options
  - CKD, ARF, NIDDM, IDDM, CAD, HTN, CHF, PAD, etc.…
  - ….but also, obesity, venous insufficiency, trauma, immunosuppression, lymphedema
- Complicated comorbidities require adjustments of antibiotics and treatment plans in order not to interfere with patients' current medications or exacerbate other medical conditions

We need a HERO – or at the very least, treatment options that are effective, empiric, have broad spectrum activity and cover the most common ABSSSI pathogens

Bouza E, et al. *JEADV Clin Pract*. 2022;1(3):165-175.

Large RCT Evaluating Agents with Anti-MRSA Activity for the Treatment of ABSSSI or SSTI*

Study, Year [Ref]	Primary Endpoint and Study Population	Intervention Comparator	Results Regarding Primary Endpoint/s in the Primary Study Population/s	Difference (95% CI)	Information on MRSA Subgroups
Boucher et al., 2014[34] (Pooled results from 2 RCT)	Early clinical response in the intention-to-treat population	*Study arms* Dalbavancin Vancomycin (with possible switch to oral linezolid)	*Early clinical response* 525/659 (79.7%) 521/653 (79.8%)	*Early clinical response* -0.1% (−4.5 to 4.2) (ref)	Investigator-assessed clinical response in patients with MRSA infection was 97.3% (72/74) in the dalbavancin arm and 98.0% (49/50) in the vancomycin arm
Breedt et al, 2005[35]	Clinical success in the clinically evaluable and in the clinically modified intention-to-treat populations	*Study arms (CE)* Tigecycline Vancomycin plus aztreonam *Study arms (c-mITT)* Tigecycline Vancomycin plus aztreonam	*Clinical success (CE)* 200/223 (89.7%) 201/213 (94.4%) *Clinical success (c-mITT)* 220/261 (84.3%) 225/259 (86.9%)	*Clinical success (CE)* -4.7% (−10.2 to 0.8) (ref) *Clinical success (c-mITT)* -2.6% (−9.0 to 3.8) (ref)	Microbiological response in patients with MRSA infection was 83.3% (5/6) in the tigecycline arm and 83.3% (5/6) in the vancomycin plus aztreonam arm
Corey et al., 2010[38]	Clinical cure in the clinically evaluable and the modified intention-to-treat populations	*Study arms (CE)* Ceftaroline Vancomycin plus aztreonam *Study arms (MITT)* Ceftaroline Vancomycin plus aztreonam	*Clinical cure (CE)* 288/316 (91.1%) 280/300 (93.3%) *Clinical cure (MITT)* 304/351 (86.6%) 297/347 (85.6%)	*Clinical cure (CE)* -2.2% (−6.6 to 2.1) (ref) *Clinical cure (MITT)* 1.0% (−4.2 to 6.2) (ref)	Clinical cure in patients with MRSA infection was 95.1% (78/82) in the ceftaroline arm and 95.2% (59/62) in the vancomycin plus aztreonam arm
Corey et al. 2014[37]	Early clinical response in the modified intention-to-treat population	*Study arms* Oritavancin Vancomycin	*Early clinical response* 391/475 (82.3%) 378/479 (78.9%)	*Early clinical response* 3.4% (−1.6 to 8.4) (ref)	Early clinical response in patients with MRSA infection was 80.8% (84/104) in the oritavancin arm and 80.0% (80/100) in the vancomycin arm

Giacobbe DR, et al. *Infect Drug Resist*. 2022;15:2137-2157.

Large RCT Evaluating Agents with Anti-MRSA Activity for the Treatment of ABSSSI or SSTI*

Study, Year [Ref]	Primary Endpoint and Study Population	Intervention Comparator	Results Regarding Primary Endpoint/s in the Primary Study Population/s	Difference (95% CI)	Information on MRSA Subgroups
Corey et al., 2015[36]	Early clinical response in the modified intention-to-treat population	*Study arms* Oritavancin Vancomycin	*Early clinical response* 403/503 (80.1%) 416/502 (82.9%)	*Early clinical response* -2.7% (−7.5 to 2.0) (ref)	Early clinical response in patients with MRSA infection was 82.0% (82/100) in the oritavancin arm and 81.2% (82/101) in the vancomycin arm
Daum et al., 2017[29]	Clinical cure in the intention-to-treat populations (patients with skin abscesses after incision and drainage of the abscess)	*Study arms (ITT)* Clindamycin TMP-SMX Placebo	*Clinical cure (ITT)* 221/266 (83.1%) 215/263 (81.7%) 177/257 (68.9%)	*Clinical cure (ITT)* 14.2% (6.4 to 22.0) 12.9% (5.0 to 20.8) (ref)	Clinical cure in patients with MRSA infection in the intention-to-treat population was 81.7% (116/142) in the clindamycin arm, 84.6% (110/130) in the TMP/SMX arm, and 62.9% (73/116) in the placebo arm.
Dryden et al., 2016[39]	Clinical cure in the clinically evaluable and the modified intention-to-treat populations	*Study arms (CE)* Ceftaroline Vancomycin plus aztreonam *Study arms (MITT)* Ceftaroline Vancomycin plus aztreonam	*Clinical cure (CE)* 342/395 (86.6%) 180/211 (85.3%) *Clinical cure (MITT)* 396/506 (78.3%) 202/255 (79.2%)	*Clinical cure (CE)* 1.3% (−4.3 to 7.5) (ref) *Clinical cure (MITT)* -0.9% (−6.9 to 5.4) (ref)	Favorable clinical response in patients with MRSA infection was 84.0% (21/25) in the ceftaroline arm and 80.0% (12/15) in the vancomycin plus aztreonam arm
Itani et al., 2010[42]	Clinical outcome in the per protocol population	*Study arms* Linezolid Vancomycin	*Clinical success* 191/227 (84.1%) 167/209 (79.9%)	*Clinical success* 4.2% (−3 to 11.5) (ref)	All enrolled patients had MRSA infection
Jauregui et al., 2005[43]	Clinical success in the intention-to-treat population	*Study arms* Dalbavancin Linezolid	*Clinical success* NA (88.9%) NA (91.2%)	*Clinical success* -2.3% (−7.3 to NA) (ref)	MRSA was isolated from 51% (181/358) of cultures in the dalbavancin arm and from 51% (97/192) of cultures in the linezolid arm MRSA eradication was registered in 91% of patients with MRSA infection in the dalbavancin arm and in 89% of patients with MRSA infection in the linezolid arm

Large RCT Evaluating Agents with Anti-MRSA Activity for the Treatment of ABSSSI or SSTI*

Study, Year [Ref]	Primary Endpoint and Study Population	Intervention Comparator	Results Regarding Primary Endpoint/s in the Primary Study Population/s	Difference (95% CI)	Information on MRSA Subgroups
Kauf et al., 2015[44]	Infection-related length of stay	*Study arms* Daptomycin Vancomycin	*Infection-related LOS* 91.5 hours (SD 57.8) 93.2 hours (SD 60.8)	*Infection-related LOS* Rate ratio 1.0 (0.8–1.2) (ref)	Infection-related length of stay in patients with MRSA infection was 98.5 h (SD 67.0) in the daptomycin arm and 85.9 h (SD 51.8) in the vancomycin arm
Lv et al., 2019[45]	Early clinical response in the intention-to-treat population	*Study arms* Tedizolid Linezolid	*Early clinical response* 226/300 (75.3%) 238/298 (79.9%)	*Early clinical response* -4.6% (−11.2 to 2.2) (ref)	Clinical success in patients with MRSA infection was 72.4% (21/29) in the tedizolid arm and 62.5% (20/32) in the linezolid arm
Miller et al., 2015[30]	Clinical cure in the clinically evaluable and intention-to-treat populations of patients with uncomplicated skin infections	*Study arms (CE)* Clindamycin TMP-SMX *Study arms (ITT)* Clindamycin TMP-SMX	*Clinical cure (CE)* 212/237 (89.5%) 202/229 (88.2%) *Clinical cure (ITT)* 212/264 (80.3%) 202/260 (77.7%)	*Clinical cure (CE)* (ref) -1.2 (-7.6 to 5.1) *Clinical cure (ITT)* (ref) -2.6 (-10.2 to 4.9)	MRSA was isolated from 31.8% (84/264) of cultures in the clindamycin arm and from 31.9% (83/260) of cultures in the TMP-SMX arm
Moran et al., 2014[46]	Early clinical response in the intention-to-treat population	*Study arms* Tedizolid Linezolid	*Early clinical response* 283/332 (85.2%) 276/334 (82.6%)	*Early clinical response* 2.6% (−3 to 8.2) (ref)	Early clinical response in patients with MRSA infection was 83% (44/53) in the tedizolid arm and 79% (44/56) in the linezolid arm
Noel et al., 2008[48]	Clinical cure in the clinically evaluable and in the intention-to-treat populations	*Study arms (CE)* Ceftobiprole Vancomycin *Study arms (ITT)* Ceftobiprole Vancomycin	*Clinical cure (CE)* 263/282 (93.3%) 259/277 (93.5%) *Clinical cure (ITT)* 309/397 (77.8%) 300/387 (77.5%)	*Clinical cure (CE)* -0.2% (−4.4 to 3.9) (ref) *Clinical cure (ITT)* 0.3% (−5.5 to 6.1) (ref)	Clinical cure in patients with MRSA infection was 91.8% (56/61) in the ceftobiprole arm and 90.0% (54/60) in the vancomycin arm

The Superhero Team Approach to Vanquishing ABSSSI

- Primary care
- Emergency med
- Hospitalist
- Infectious Disease
- Endocrinology
- Radiology

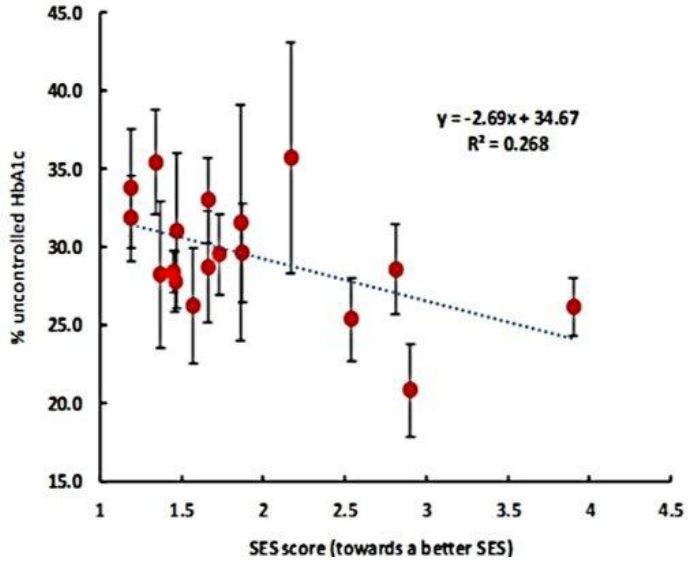
- Podiatry
- Vascular surgery
- General surgery
- Orthopedics

- Nursing
- Pharmacy
- Social work
- Physical therapy
- Occupational therapy
- Microbiology

Risk Factors ⟷ Socioeconomic Status

- Male
- Black, Hispanic, non-White
- Unequal access to care
- Low income
- Under- or uninsured
- Low education level
- Socioeconomically deprived neighborhoods[1]

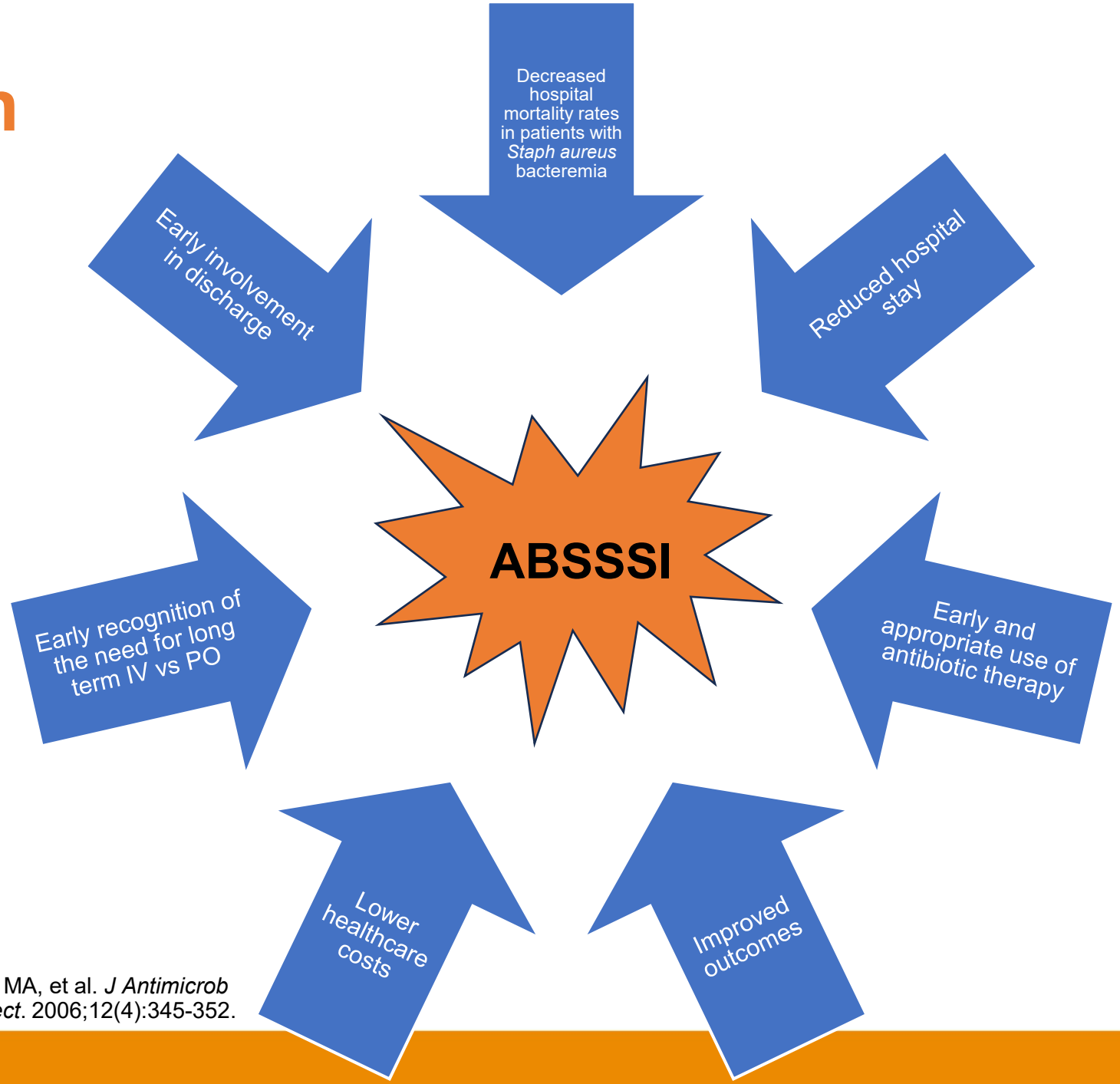
CORRELATION BETWEEN SOCIOECONOMIC STATUS AND PREVALENCE OF UNCONTROLLED HbA1c



- Patients aged 18-54 had higher prevalence of hyperglycemia than older patients
- Hyperglycemia significantly associated with increased total cholesterol: HDL ratio (odds ratio [OR]=1.59, 95% confidence interval [CI]: 1.33–1.90, p<0.001)
- Hyperglycemia significantly associated with coronary artery disease (OR=1.39, 95% CI: 1.16–1.67, p=0.001)
- Neighborhoods with lower socioeconomic status had significantly higher uncontrolled hyperglycemia rates (r=0.52, $R2$=0.27, p=0.03). [2]

1. McDermott K, et al. *Diabetes Care*. 2023;46(1):209-221. 2. Liu L, et al. *Health Equity*. 2020;4(1):525-532.

Early Collaboration
Early Intervention
Better Outcomes



Lahey T, et al. *Medicine (Baltimore)*. 2009;88(5):263-267. Caroline MA, et al. *J Antimicrob Chemother*. 2017;72(3):923-932. Kaech C, et al. *Clin Microbiol Infect*. 2006;12(4):345-352.

Clinical Pearls

- Early collaborative efforts, team approach
- Choose empiric coverage based on MRSA coverage against the most locally prevalent MRSA strains
- History, risk factors need to be accounted for
- Efficacy of empiric treatment should be assessed 48-72 hrs after initiation of treatment

Tetracyclines for ABSSSI – **MOA, Resistance, and Role of Omadacyline**

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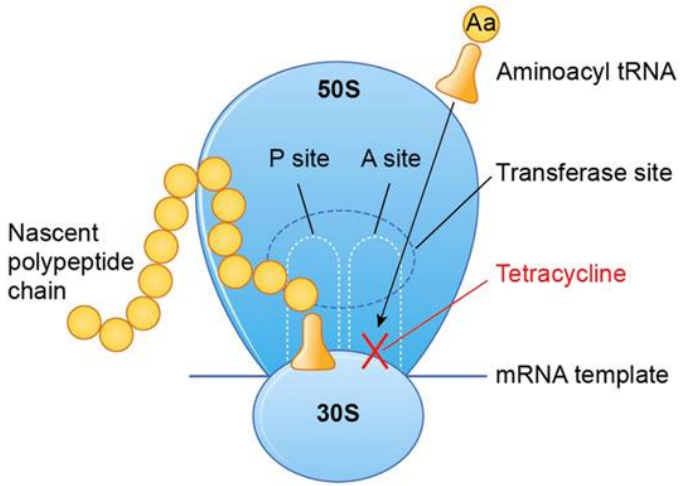
ABSSSI: Definition

- The FDA defines ABSSSI as cellulitis/erysipelas, wound infection, and major cutaneous abscess

Available Tetracyclines and Mechanism of Action

- Tetracycline class antibiotics available to use in humans include demeclocycline, tetracycline, oxytetracycline, minocycline, and doxycycline
  - Synthetic processes have led to development of tetracycline analogs, including tigecycline (glycylcycline), eravacycline (fluorocycline) and omadacycline (aminomethylcycline)



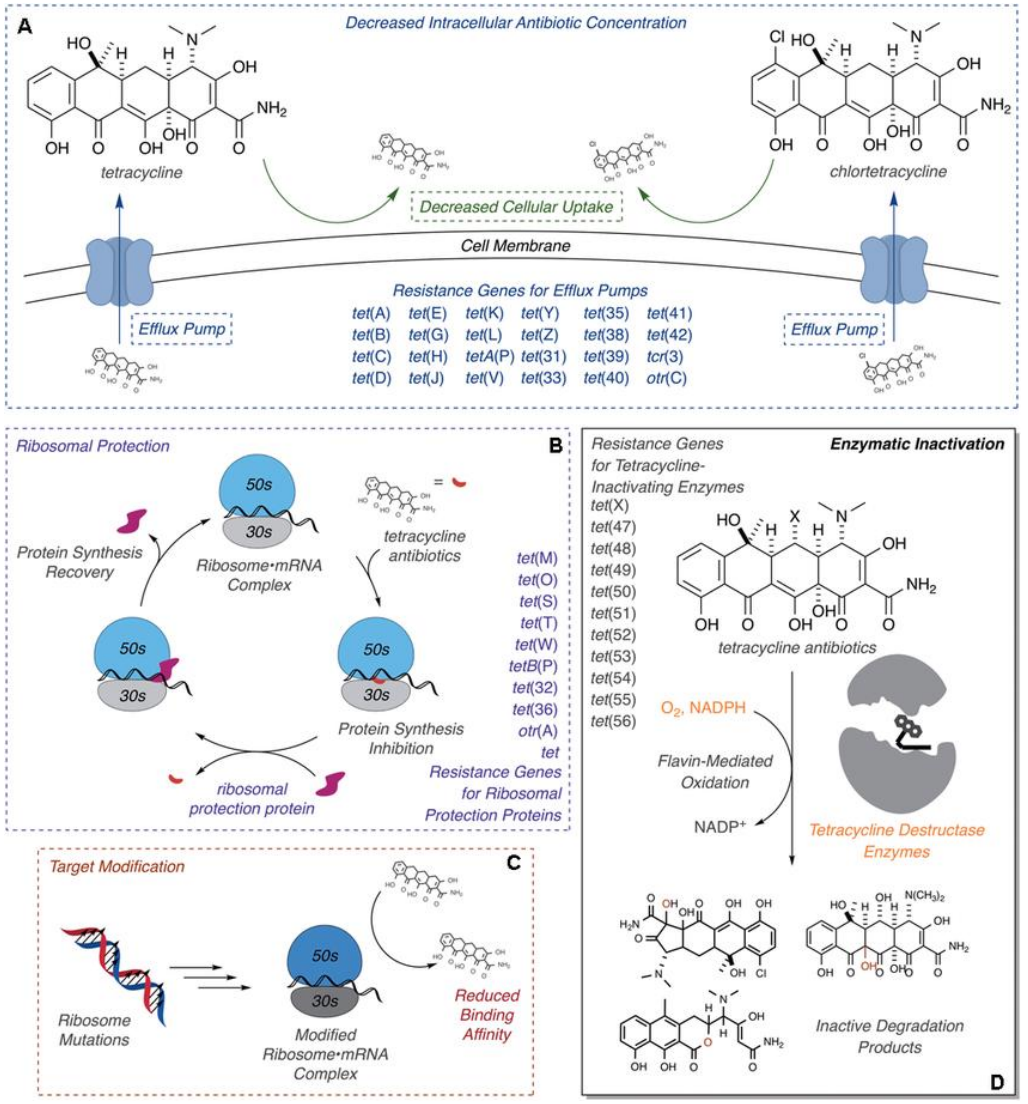
- Act by binding reversibly to the 30s subunits of bacterial ribosomes, and by doing so, inhibit protein synthesis
- Relatively broad spectrum, with activity against aerobic Gram-positives (including *Staphylococcus aureus* and *Streptococcal* spp) and Gram-negatives (including *Haemophilus influenza*, *Escherichia coli* and *Acinetobacter* spp.)
  - Also active against tick-borne and atypical bacteria

Graber EM. *Dermatol Rev*. 2021;2:321-330. Burgos RM, Rodvold KA. *Infect Drug Resist*. 2019;12:1895-1915.

Tetracyclines: Mechanisms of Resistance

- Mechanisms of resistance often due to efflux pumps mediated by genes [including tet(K), tet(L), tet(A), and tet(B)] and ribosomal protection proteins mediated by genes [tet(M), tet(O), and tet(S)]
  - Other mechanisms of tetracycline resistance include drug degradation and mutations in rRNA binding sites

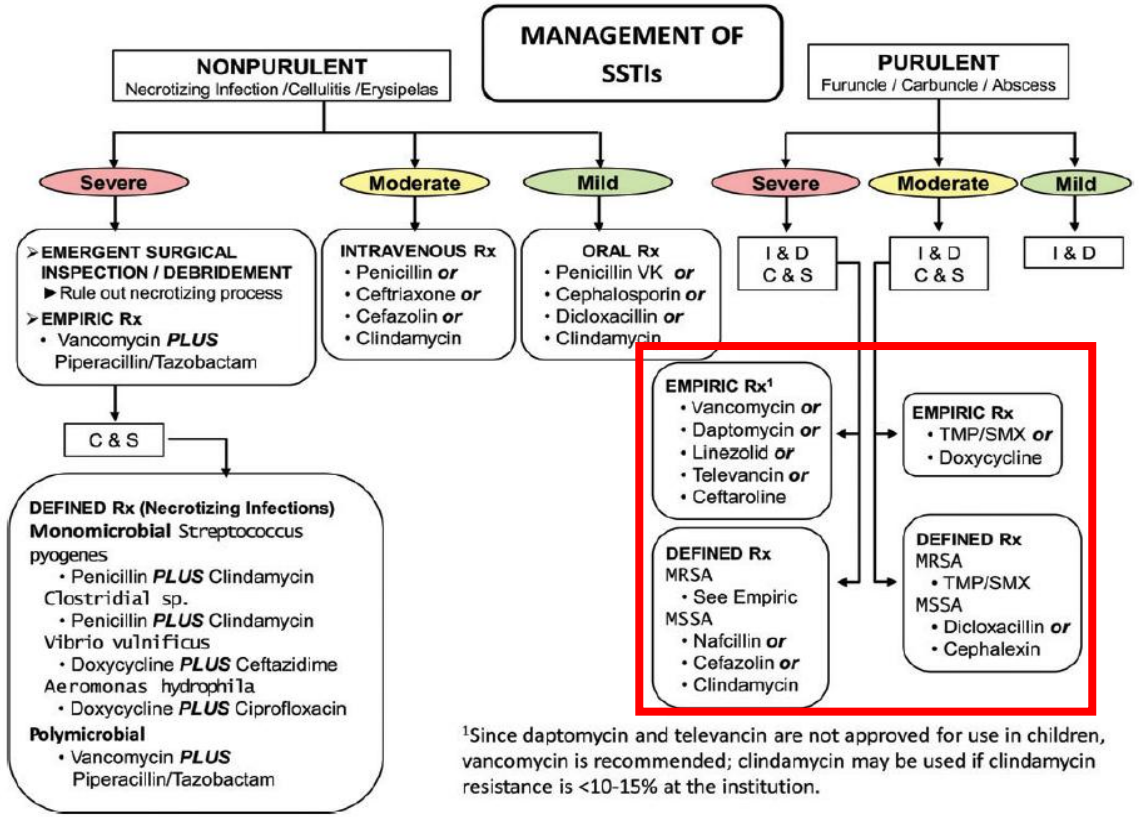
- Newer synthetic tetracycline analogs sometimes retain antibacterial activity even in the presence of these resistance determinants



Burgos RM, Rodvold KA. *Infect Drug Resist*. 2019;12:1895-1915. Markley JL, Wencewicz TA. *Front Microbiol*. 2018;9:1058.

Role of Tetracyclines in ABSSSI

- In IDSA guidelines, doxycycline is one of the recommended antibiotics for empiric treatment of purulent cellulitis and directed treatment of *Staphylococcus aureus* (MSSA and MRSA)



IDSA = Infectious Disease Society of America.
Stevens DL. *Clin Infect Dis*. 2014;59(2):e10-52.

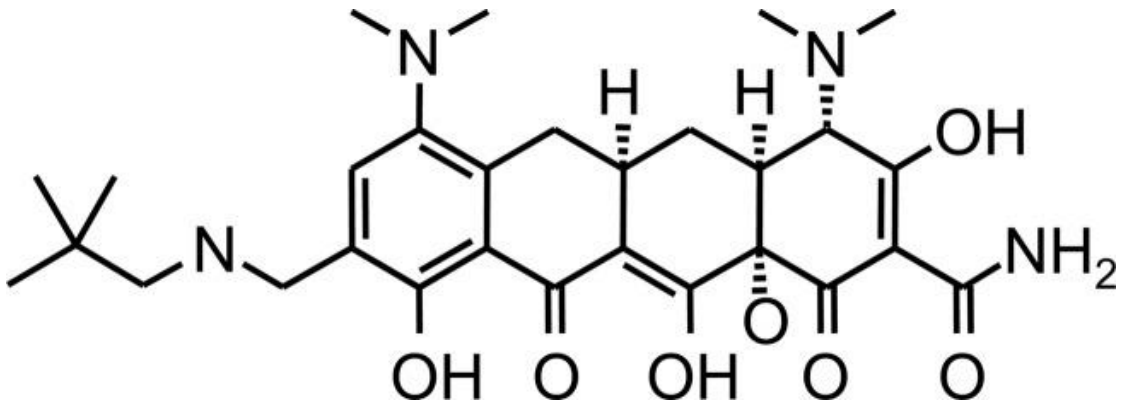
Table 2. Antimicrobial Therapy for Staphylococcal and Streptococcal Skin and Soft Tissue Infections

Disease Entity	Antibiotic	Dosage, Adults	Dosage, Children[a]	Comment
Impetigo[b] (*Staphylococcus* and *Streptococcus*)	Dicloxacillin	250 mg qid po	N/A	N/A
	Cephalexin	250 mg qid po	25–50 mg/kg/d in 3–4 divided doses po	N/A
	Erythromycin	250 mg qid po[c]	40 mg/kg/d in 3–4 divided doses po	Some strains of *Staphylococcus aureus* and *Streptococcus pyogenes* may be resistant.
	Clindamycin	300–400 mg qid po	20 mg/kg/d in 3 divided doses po	N/A
	Amoxicillin-clavulanate	875/125 mg bid po	25 mg/kg/d of the amoxicillin component in 2 divided doses po	N/A
	Retapamulin ointment	Apply to lesions bid	Apply to lesions bid	For patients with limited number of lesions
	Mupirocin ointment	Apply to lesions bid	Apply to lesions bid	For patients with limited number of lesions
MSSA SSTI	Nafcillin or oxacillin	1-2 g every 4 h IV	100–150 mg/kg/d in 4 divided doses	Parental drug of choice; inactive against MRSA
	Cefazolin	1 g every 8 h IV	50 mg/kg/d in 3 divided doses	For penicillin-allergic patients except those with immediate hypersensitivity reactions. More convenient than nafcillin with less bone marrow suppression
	Clindamycin	600 mg every 8 h IV or 300–450 mg qid po	25–40 mg/kg/d in 3 divided doses IV or 25–30 mg/kg/d in 3 divided doses po	Bacteriostatic; potential of cross-resistance and emergence of resistance in erythromycin-resistant strains; inducible resistance in MRSA
	Dicloxacillin	500 mg qid po	25–50 mg/kg/d in 4 divided doses po	Oral agent of choice for methicillin-susceptible strains in adults. Not used much in pediatrics
	Cephalexin	500 mg qid po	25–50 mg/kg/d 4 divided doses po	For penicillin-allergic patients except those with immediate hypersensitivity reactions. The availability of a suspension and requirement for less frequent dosing
	Doxycycline, minocycline	100 mg bid po	Not recommended for age <8 y[d]	Bacteriostatic; limited recent clinical experience
	Trimethoprim-sulfamethoxazole	1–2 double-strength tablets bid po	8–12 mg/kg (based on trimethoprim component) in either 4 divided doses IV or 2 divided doses po	Bactericidal; efficacy poorly documented
MRSA SSTI	Vancomycin	30 mg/kg/d in 2 divided doses IV	40 mg/kg/d in 4 divided doses IV	For penicillin allergic patients; parenteral drug of choice for treatment of infections caused by MRSA
	Linezolid	600 mg every 12 h IV or 600 mg bid po	10 mg/kg every 12 h IV or po for children <12 y	Bacteriostatic; limited clinical experience; no cross-resistance with other antibiotic classes; expensive
	Clindamycin	600 mg every 8 h IV or 300–450 mg qid po	25–40 mg/kg/d in 3 divided doses IV or 30–40 mg/kg/d in 3 divided doses po	Bacteriostatic; potential of cross-resistance and emergence of resistance in erythromycin-resistant strains; inducible resistance in MRSA. Important option for children
	Daptomycin	4 mg/kg every 24 h IV	N/A	Bactericidal; possible myopathy
	Ceftaroline	600 mg bid IV	N/A	Bactericidal
	Doxycycline, minocycline	100 mg bid po	Not recommended for age <8 y[d]	Bacteriostatic; limited recent clinical experience
	Trimethoprim-sulfamethoxazole	1–2 double-strength tablets bid po	8–12 mg/kg/d (based on trimethoprim component) in either 4 divided doses IV or 2 divided doses po	Bactericidal; limited published efficacy data

Stevens DL. *Clin Infect Dis*. 2014;59(2):e10-52.

Omadacycline – First-in-Class Aminomethylcycline

- Broad spectrum activity against Gram-positive aerobes, Gram-negative aerobes, anaerobes, and atypical bacteria
  - Lacks activity against *Proteus* spp., *Providencia* spp., *Pseudomonas* spp., *Morganella* spp., and *Eikenella corrodens*
- Retains activity against bacteria expressing the 2 most common tetracycline resistance mechanisms (bacterial ribosomal protection proteins and efflux pumps)
- Available both IV and PO and indicated for treatment of acute bacterial skin and skin structure infections (ABSSSI), as well as community-acquired pneumonia)



Macone AB, et al. *Antimicrob Agents Chemother*. 2014;58(2):1127-1135.

Omadacycline Dosing

TABLE 1 Omadacycline dosing recommendations[a]

Indication	Loading dose options	Maintenance dose
Acute bacterial skin and skin structure infections	IV[b]: Day 1, 200 mg once OR 100 mg twice	IV: 100 mg daily
	Oral: Days 1 and 2, 450 mg daily	Oral: 300 mg daily
Community-acquired bacterial pneumonia	IV: Day 1, 200 mg once or 100 mg twice	IV: 100 mg daily
	Oral: Day 1, 300 mg twice	Oral: 300 mg daily

[a]From reference 1.
[b]IV, intravenous.

- Recommended treatment duration for omadacycline for both indications is 7-14 days

Nuzyra, package insert, 10/2018; File, TM, *Antimicrob Agents Chemother.* 2025;69(2)

Omadacycline Activity Compared to Other Tetracyclines

- Enhanced activity against Gram-positives and Gram-negatives
  - Particularly important and relevant for ABSSSI with regard to *Streptococcus* spp.

- Good anaerobic activity (similar to tigecycline)

Biddell MR. *Pharmacotherapy.* 2021;41(11):915-931.

Omadacycline Injection and Oral Products

FDA Identified Breakpoints for Omadacycline

For Acute Bacterial Skin and Skin Structure Infections (ABSSSI)

	Minimum Inhibitory Concentrations (mcg/mL)			Disk Diffusion (zone diameters in mm)		
Pathogen	**S**	**I**	**R**	**S**	**I**	**R**
Enterobacteriaceae [a,†]	≤4	8	≥ 16	≥18	16-17	≤15
Staphylococcus aureus **(including methicillin-resistant isolates)**	≤ 0.5	1.0	≥ 2.0	≥ 21	19-20	≤18
Staphylococcus lugdunensis	≤ 0.12	0.25	≥0.5	≥ 29	26-28	≤25
Enterococcus faecalis	≤ 0.25	0.5	≥ 1.0	≥18	16-17	≤15
Streptococcus anginosus **group** [b]	≤ 0.12	0.25	≥ 0.5	≥ 24	18-23	≤17
Streptococcus pyogenes	≤ 0.12	0.25	≥ 0.5	≥19	16-18	≤15

S = Susceptible; I = Intermediate; R = Resistant

† Omadacycline is not active *in vitro* against *Morganella* spp., *Proteus* spp., and *Providencia* spp.

[a] *Klebsiella pneumoniae* and *Enterobacter cloacae* only

[b] *Streptococcus anginosus* group includes *S. anginosus*, *S. intermedius*, and *S. constellatus*

U.S. FDA. Updated June 6, 2022. Accessed Oct. 27, 2025. https://www.fda.gov/drugs/development-resources/omadacycline-injection-and-oral-products

Broad Spectrum of Omadacycline: Maintained Over Time

Omadacycline susceptibility against indicated organism groups from the United States stratified by year of surveillance.

Organism	% Susceptible (no. tested) 2019	2020	2021	2022	2023	2019-2023
Staphylococcus aureus	98.3 [b] 96.6 [c,d] (1,623)	96.8 [b] 95.5 [c,d] (1,666)	98.7 [b] 97.3 [c,d] (1,673)	98.7 [b] 96.5 [c,d] (1,672)	98.7 [b] 97.5 [c,d] (1,341)	98.2 [b] 96.6 [c,d] (7,975)
MSSA	99.1 [c,d] (939)	99.0 [c,d] (939)	99.3 [c,d] (1,061)	99.2 [c,d] (983)	98.2 [c,d] (798)	99.2 [c,d] (4,720)
MRSA	98.5 [b] (684)	93.3 [b] (727)	96.7 [b] (612)	97.0 [b] (689)	97.4 [b] (543)	96.1 [b] (3,255)
Staphylococcus lugdunensis	100.0 [b] (26)	96.9 [b] (32)	100.0 [b] (32)	100.0 [b] (34)	100.0 [b] (24)	99.3 [b] (148)
Streptococcus anginosus group	100.0 [b] (16)	90.0 [b] (33)	100.0 [b] (31)	100.0 [b] (42)	100.0 [b] (31)	98.0 [b] (153)
Streptococcus pneumoniae	99.8 [c] (422)	99.7 [c] (321)	100.0 [c] (322)	100.0 [c] (306)	100.0 [c] (358)	99.9 [c] (1,729)
Penicillin-R oral (MIC ≥2 mg/L; CLSI)	100.0 [c] (43)	100.0 [c] (33)	100.0 [c] (35)	100.0 [c] (31)	100.0 [c] (51)	100.0 [c] (193)
Erythromycin (macrolide)-resistant (CLSI)	99.5 [c] (197)	100.0 [c] (142)	100.0 [c] (148)	100.0 [c] (135)	100.0 [c] (153)	99.9 [c] (775)
Tetracycline-resistant (CLSI)	98.9 [c] (91)	100.0 [c] (62)	100.0 [c] (66)	100.0 [c] (63)	100.0 [c] (61)	99.7 [c] (343)
Streptococcus pyogenes	99.2 [b] (123)	100.0 [b] (126)	100.0 [b] (80)	98.6 [b] (71)	99.2 [b] (120)	99.4 [c] (520)
Erythromycin (macrolide)-resistant (CLSI)	96.3 [b] (27)	100.0 [b] (27)	100.0 [b] (32)	100.0 [b] (29)	94.4 [b] (18)	98.5 [c] (133)
Tetracycline-resistant (CLSI)	96.7 [b] (30)	100.0 [b] (28)	100.0 [b] (35)	97.6 [b] (42)	96.3 [b] (27)	98.1 [c] (162)
Enterococcus faecalis	100.0 [b] (229)	100.0 [b] (226)	100.0 [b] (266)	100.0 [b] (270)	99.5 [b] (221)	99.9 [c] (1,212)
Vancomycin-resistant (MIC ≥32 mg/L; CLSI)	100.0 [b] (7)	100.0 [b] (7)	85.7 [b] (5)	100.0 [b] (5)	100.0 [b] (6)	100.0 [c] (30)
Haemophilus influenzae	100.0 [c] (304)	99.6 [c] (230)	100.0 [c] (184)	100.0 [c] (223)	100.0 [c] (270)	99.9 [c] (1,211)
Haemophilus parainfluenzae	95.8 [c] (24)	100.0 [c] (25)	92.6 [c] (27)	93.3 [c] (30)	97.1 [c] (35)	95.7 [c] (141)
Enterobacter cloacae species complex	93.6 [b] (218)	90.0 [b] (229)	87.8 [b] (238)	94.7 [b] (246)	96.4 [b] (220)	92.4 [b] (1,151)
Klebsiella pneumoniae	93.2 [b,c] (511)	92.8 [b,c] (566)	87.6 [b,c] (467)	92.8 [b,c] (512)	95.5 [b,c] (528)	92.4 [b,c] (2,584)
ESBL phenotype (CLSI)	80.9 [b,c] (89)	80.8 [b,c] (99)	73.6 [b,c] (91)	82.3 [b,c] (96)	88.2 [b,c] (110)	81.4 [b,c] (485)
Carbapenem-resistant (CLSI)	77.8 [b,c] (9)	100.0 [b,c] (13)	70.6 [b,c] (17)	100.0 [b,c] (5)	100.0 [b,c] (6)	86.0 [b,c] (50)

Abbreviations: ESBL, extended-spectrum β-lactamase MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*.

[a] FDA breakpoint interpretive criteria (2024) applied for omadacycline

[b] Using ABSSSI breakpoints.

[c] Using CABP breakpoints.

[d] US FDA breakpoints published for MSSA (methicillin-susceptible *S. aureus*) isolates were applied to all *Staphylococcus aureus* isolates.

Huband MD. *Diagn Microbiol Infect Dis.* 2025;3.

Comparative *in vitro* Activity of Omadacycline vs *S. aureus*

Organism/organism group (no. isolates tested) antimicrobial agent	CLSI or FDA [a] %S	%R	MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC Range (mg/L)
***Staphylococcus aureus* (7,975)**					
Omadacycline	98.2 [b] 96.6 [e,f]	0.3 1.8	0.12	0.12	≤0.015 to 2
Doxycycline	98.2	0.1	≤0.06	0.5	≤0.06 to >8
Minocycline (6,352)	98.3	1.0	0.06	0.12	≤0.03 to >8
Tetracycline	93.7	5.3	≤0.5	1	≤0.5 to >8
Tigecycline	>99.9		0.06	0.12	≤0.015 to 1
Oxacillin	59.2	40.8	0.5	>2	≤0.06 to >2
Ceftaroline	98.1 [f]	0.0	0.25	1	≤0.06 to 4
Levofloxacin	69.1	30.6	0.25	>4	≤0.03 to >4
Erythromycin	45.5	49.9	4	>8	≤0.06 to >8
Clindamycin	87.4	12.3	0.06	>2	≤0.03 to >2
Linezolid	100.0	0.0	1	2	≤0.12 to 4
Daptomycin	99.9		0.25	0.5	≤0.12 to 2
Vancomycin	100.0	0.0	0.5	1	≤0.12 to 2
Gentamicin	97.7	2.0	≤1	≤1	≤1 to >8
Trimethoprim-sulfamethoxazole	97.1	2.9	≤0.5	≤0.5	≤0.5 to >16

Organism/organism group (no. isolates tested) antimicrobial agent	CLSI or FDA [a] %S	%R	MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC Range (mg/L)
MRSA (3,255)					
Omadacycline	96.1 [b] 92.9 [e,f]	0.5 3.9	0.12	0.25	≤0.015 to 2
Doxycycline	96.9	0.2	≤0.06	1	≤0.06 to >8
Minocycline (2,571)	96.8	1.7	0.06	0.25	≤0.03 to >8
Tetracycline	90.4	8.5	≤0.5	4	≤0.5 to >8
Tigecycline	>99.9		0.06	0.12	≤0.015 to 1
Oxacillin	0.0	100.0	>2	>2	>2 to >2
Ceftaroline	95.3 [f]	0.0	0.5	1	0.12 to 4
Levofloxacin	36.2	63.4	4	>4	0.06 to >4
Erythromycin	16.3	80.8	>8	>8	≤0.06 to >8
Clindamycin	75.2	24.5	0.06	>2	≤0.03 to >2
Linezolid	100.0	0.0	1	2	≤0.12 to 4
Daptomycin	99.9		0.25	0.5	≤0.12 to 2
Vancomycin	100.0	0.0	0.5	1	0.25 to 2
Gentamicin	96.5	3.2	≤1	≤1	≤1 to >8
Trimethoprim-sulfamethoxazole	93.7	6.3	≤0.5	≤0.5	≤0.5 to >16

Organism/organism group (no. isolates tested) antimicrobial agent	CLSI or FDA [a] %S	%R	MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC Range (mg/L)
***S. aureus* tetracycline-resistant (422)**					
Omadacycline	92.9 [b] 87.9 [e,f]	2.8 7.1	2	>8	0.06 to >8
Doxycycline	66.1	2.1	>8	>8	>8 to >8
Minocycline (357)	68.9	17.9	0.12	0.25	0.03 to 1
Tetracycline	0.0	100.0	>2	>2	0.12 to >2
Tigecycline	99.8		0.5	1	≤0.06 to 4
Oxacillin	34.6	65.4	4	>4	0.06 to >4
Ceftaroline	93.1 [f]	0.0	>8	>8	≤0.06 to >8
Levofloxacin	41.5	58.3	0.06	>2	≤0.03 to >2
Erythromycin	24.2	71.5	1	2	≤0.12 to 4
Clindamycin	58.1	41.7	0.25	0.5	≤0.12 to 1
Linezolid	100.0	0.0	0.5	1	0.25 to 2
Daptomycin	100.0		≤1	≤1	≤1 to >8
Vancomycin	100.0	0.0	≤0.5	8	≤0.5 to >16
Gentamicin	91.9	7.8	0.12	0.5	≤0.015 to 2
Trimethoprim-sulfamethoxazole	86.5	13.5	4	8	0.5 to >8

Huband MD. *Diagn Microbiol Infect Dis.* 2025;3.

In vitro Activity of Omadacycline vs *Streptococcus spp.*

Table 2 (*continued*)

Organism/organism group (no. isolates tested) antimicrobial agent	CLSI or FDA [a] %S	%R	MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC Range (mg/L)
***Streptococcus pyogenes* (520)**					
Omadacycline	99.4 [b]	0.0	0.06	0.12	0.03 to 0.25
Doxycycline (397)			0.12	>1	0.06 to >1
Minocycline (397)			0.12	>1	0.03 to >1
Tetracycline	68.7	31.2	0.25	>4	0.12 to >4
Tigecycline	100.0		0.06	0.06	0.015 to 0.12
Ceftaroline	100.0		≤0.008	≤0.008	≤0.008 to 0.03
Levofloxacin	100.0	0.0	0.5	1	0.12 to 2
Erythromycin	71.7	25.6	0.06	>16	0.03 to >16
Clindamycin	92.1	7.1	≤0.25	≤0.25	≤0.25 to >2
Linezolid	100.0		1	2	0.25 to 2
Daptomycin	100.0		≤0.06	≤0.06	≤0.06 to 0.25
Vancomycin	100.0		0.25	0.5	0.12 to 1
Penicillin	100.0		0.015	0.015	≤0.008 to 0.06

Organism/organism group (no. isolates tested) antimicrobial agent	CLSI or FDA [a] %S	%R	MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC Range (mg/L)
***Streptococcus agalactiae* (413)**					
Omadacycline			0.12	0.12	0.03 to 0.5
Doxycycline (330)			>1	>1	0.06 to >1
Minocycline (330)			>1	>1	0.06 to >1
Tetracycline	16.0	83.3	>4	>4	0.12 to >4
Tigecycline	100.0		0.06	0.06	0.03 to 0.12
Ceftaroline	100.0		0.015	0.015	≤0.008 to 0.03
Levofloxacin	99.0	0.7	0.5	1	0.5 to >4
Erythromycin	34.4	65.1	4	>16	≤0.015 to >16
Clindamycin	56.7	41.4	≤0.25	>2	≤0.25 to >2
Linezolid	100.0		1	2	0.5 to 2
Daptomycin	100.0		0.12	0.25	≤0.06 to 0.5
Vancomycin	100.0		0.5	0.5	0.25 to 1
Penicillin	100.0		0.06	0.06	0.03 to 0.12

Huband MD, et al. *Diagn Microbiol Infect Dis*. 2025;111:116711.

Comparative *in vitro* Activity: Omadacycline vs *Enterococcus faecium*

Organism/organism group (no. isolates tested) antimicrobial agent	CLSI or FDA [a]		MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC Range (mg/L)
	%S	%R			
***Enterococcus faecium* (532)**					
Omadacycline			0.06	0.12	≤0.015 to 1
Doxycycline (426)	60.8	9.4	4	8	≤0.03 to 16
Minocycline	52.8	24.4	4	>8	≤0.06 to >8
Tetracycline	26.0	71.6	>16	>16	≤0.12 to >16
Tigecycline			0.06	0.12	≤0.015 to 1
Levofloxacin	15.8	80.5	>4	>4	≤0.03 to >4
Linezolid	99.8	0.2	1	2	≤0.5 to >8
Daptomycin	[d]	1.1	1	2	≤0.06 to >8
Vancomycin	34.8	64.7	>16	>16	0.25 to >16
Ampicillin	18.0	82.0	>16	>16	≤0.12 to >16

Organism/organism group (no. isolates tested) antimicrobial agent	CLSI or FDA [a]		MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC Range (mg/L)
	%S	%R			
***E. faecium* vancomycin-resistant (≥32 mg/L; CLSI) (344)**					
Omadacycline			0.06	0.12	≤0.015 to 1
Doxycycline (276)	56.9	7.6	4	8	≤0.03 to 16
Minocycline	48.8	23.8	8	>8	≤0.06 to >8
Tetracycline	15.5	80.8	>16	>16	≤0.12 to >16
Tigecycline			0.06	0.12	≤0.015 to 0.25
Levofloxacin	0.0	98.5	>4	>4	4 to >4
Linezolid	99.7	0.3	1	2	≤0.5 to >8
Daptomycin	[d]	1.2	1	2	≤0.06 to >8
Vancomycin	0.0	100.0	>16	>16	>16 to >16
Ampicillin	0.6	99.4	>16	>16	4 to >16

Huband MD, et al. *Diagn Microbiol Infect Dis*. 2025;111:116711.

In vitro Activity of Omadacycline vs Gram-Negatives

Organism	Number tested	% Susceptible	MIC50	MIC90
E. coli (EC)	5,798		0.5	1
EC ESBL	1,088		1	2
EC CRE	11		1	4
Enterobacter cloacae	1,151	92.4	2	4
Klebsiella pneumonia (KP)	2,584	92.5	1	4
KP ESBL	485	81.4	2	16
KP CRE	50	86.0	2	8

Omadacycline is the most active oral tetracycline antibiotic – and one of the most active oral antibiotics overall – against GNR, including resistant strains

Huband MD, et al. *Diagn Microbiol Infect Dis*. 2025;111:116711.

Organism/organism group (no. isolates tested) antimicrobial agent	CLSI or FDA [a]		MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC Range (mg/L)
	%S	%R			
***Acinetobacter baumannii-calcoaceticus* species complex (792)**					
Omadacycline			0.25	4	≤0.06 to 32
Doxycycline	80.4	18.7	0.25	>8	≤0.06 to >8
Minocycline (716)	88.4	6.6	0.12	8	≤0.06 to 32
Tetracycline	64.0	30.5	2	>16	≤0.5 to >16
Tigecycline			0.25	2	≤0.06 to >8
Piperacillin-tazobactam	59.9	34.6	8	>128	≤0.06 to >128
Levofloxacin	71.3	26.9	0.25	32	0.03 to >32
Gentamicin	76.4	19.6	1	>16	≤0.12 to >16
Amikacin	86.5	12.9	4	>32	≤0.25 to >32
Cefepime	61.9	29.4	4	>32	0.5 to >32
Imipenem	74.7	24.5	0.25	>8	≤0.12 to >8
Trimethoprim-sulfamethoxazole	75.8	24.2	0.25	>4	≤0.12 to >4

Organism/organism group (no. isolates tested) antimicrobial agent	CLSI or FDA [a]		MIC_{50} (mg/L)	MIC_{90} (mg/L)	MIC Range (mg/L)
	%S	%R			
***A. baumannii-calcoaceticus* species complex (194) carbapenem (imipenem)-resistant**					
Omadacycline			4	8	0.25 to 32
Doxycycline	40.2	59.8	>8	>8	0.12 to >8
Minocycline (172)	59.3	24.4	4	16	≤0.06 to 32
Tetracycline	2.6	91.7	>16	>16	2 to >16
Tigecycline			2	4	0.25 to >8
Piperacillin-tazobactam	0.0	98.5	>128	>128	32 to >128
Levofloxacin	1.0	94.3	16	32	1 to >32
Gentamicin	27.3	63.4	>16	>16	≤0.12 to >16
Amikacin	49.5	48.5	32	>32	≤0.25 to >32
Cefepime	3.6	82.0	>32	>32	8 to >32
Imipenem	0.0	100.0	>8	>8	8 to >8
Trimethoprim-sulfamethoxazole	27.8	72.2	>4	>4	≤0.12 to >4

Huband MD, et al. *Diagn Microbiol Infect Dis*. 2025;111:116711.

Activity of Omadacycline Compared to Other Tetracyclines – Including Tetracycline-Resistant Strains

TABLE 1 *In vitro* activity of omadacycline against tetracycline-resistant and -susceptible bacteria

Organism(s)	Tetracycline resistance gene(s)	No. of isolates	MIC range (μg/ml)[a]		
			Omadacycline	Tetracycline	Doxycycline
Staphylococcus aureus	*tet*(M)	19	0.125–1	32->64	2–16
	tet(K)	5	0.125–0.25	16–32	1–4
		35	≤0.06–0.5	≤0.06–0.25	≤0.06–0.125
Enterococcus faecalis	*tet*(M)	14	0.125–0.5	32–64	4–8
	tet(L)	1	0.25	64	16
	tet(M), *tet*(L)	3	0.5	>64	16
	tet(S)	1	0.25	32	2
		11	0.25–0.5	≤0.06–0.25	≤0.06–0.125
Enterococcus faecium	*tet*(M)	13	0.125–0.5	32–64	2–8
	tet(M), *tet*(L)	2	0.25	>64	8–16
	tet(K)	1	0.12	32	4
	tet(O)	1	0.12	32	4
		8	0.125–0.5	0.125–0.25	≤0.06
Streptococcus pneumoniae	*tet*(M)	22	≤0.06	4–64	2–4
		18	≤0.06–0.25	≤0.06–0.25	≤0.06–0.25
Beta-hemolytic streptococci[b]	*tet*(M)	17	≤0.06–0.5	4–64	2–16
	tet(O)	4	≤0.06–0.25	32–64	8
		26	≤0.06–0.5	≤0.06–0.125	≤0.06
Escherichia coli	*tet*(A)	4	2	64->64	16
		17	0.5–2	0.5–2	0.5–1

[a] Commercial-grade tigecycline was not available at the time of *in vitro* testing.
[b] *S. pyogenes* and *S. agalactiae*.

Macone AB, et al. *Antimicrob Agents Chemother*. 2014;58(2):1127–1135.

Phase 3 Clinical Trials: OASIS 1 and OASIS 2

- Omadacyline vs linezolid for ABSSSI
  - MITT: primary efficacy population - included all randomized patients without a baseline sole Gram-negative pathogen
  - micro-mITT: all patients in the mITT population who had ≥1 Gram-positive causative pathogen

Table 1. Study Design Characteristics

Characteristic	OASIS-1	OASIS-2
Treatment duration	7–14 days	7–14 days
Omadacycline dosing	100 mg IV q12h for 2 doses, then 100 mg IV q24h for 2 days Optional at >3 days: transition to 300 mg PO q24h[a]	450 mg PO q24h for 2 doses, then 300 mg PO q24h
Linezolid dosing	600 mg IV q12h Optional at >3 days: transition to 600 mg PO q12h	600 mg PO q12h
FDA primary endpoint[b]	ECR at 48–72 h	ECR at 48–72 h
EMA primary endpoint[c]	Investigator-assessed clinical response at PTE	Investigator-assessed clinical response at PTE
Prior antibiotics prohibited	Within 72 h of randomization, any other systemic or topical antibiotic agent potentially effective for ABSSSI	Within 72 h of randomization, any other systemic or topical antibiotic agent potentially effective for ABSSSI[d]
Concomitant antibiotics prohibited	Any other systemic antibiotic against known/suspected ABSSSI pathogens, except in cases of clinical failure Any topical antibacterial agent active against known/suspected ABSSSI pathogen on study infection	Any other systemic antibiotic agent potentially effective for ABSSSI, except in cases of clinical failure Any topical antibacterial agent active against known/suspected ABSSSI pathogen on study infection

Abbreviations: ABSSSI, acute bacterial skin and skin structure infections; ECR, early clinical response; EMA, European Medicines Agency; FDA, Food and Drug Administration; IV, intravenous; OASIS, Omadacycline in Acute Skin and Skin Structure Infections Study; PO, oral; PTE, posttreatment evaluation; q12h, every 12 hours; q24h, every 24 hours.

[a]A transition from the IV to PO study drug was an option if there was evidence of local and systemic improvement (eg, temperature ≤100°F; return of white blood cell count and differential toward normal range, no increase in lesion area compared with baseline, and decrease in extent and intensity of ≥1 inflammatory finding).

[b]ECR was defined as: patient alive, with a reduction in lesion area of ≥20% vs baseline and no receipt of rescue antibacterial therapy.

[c]PTE occurred at 7–14 days after treatment initiation.

[d]A single dose of short-acting non-oxazolidinone antibacterial administered within 72 h prior to randomization was allowed for ≤25% of patients.

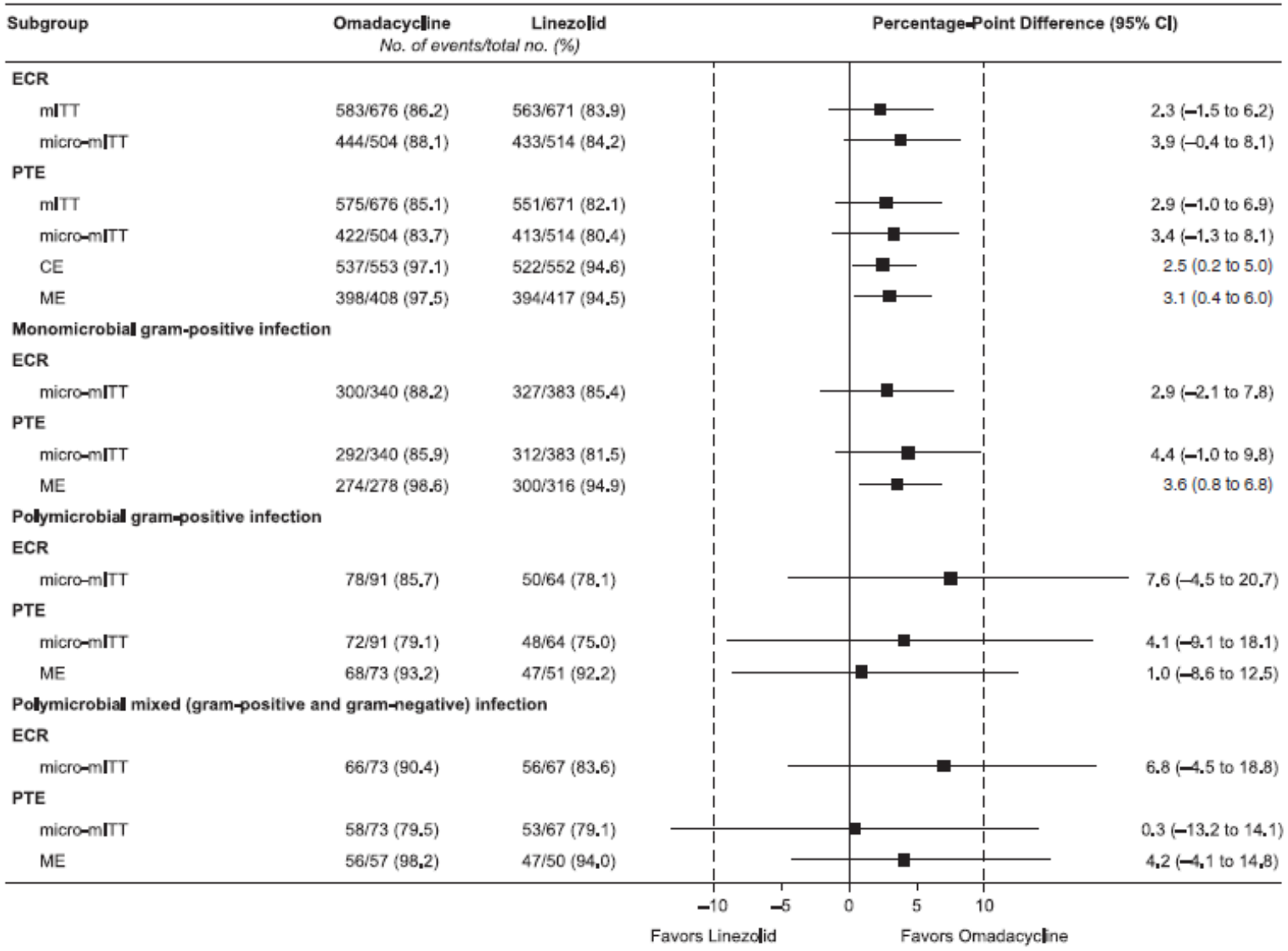
Abrahamian FM, et al. *Clin Infect Dis*. 2019;69(Suppl 1):S23–S32.

Table 2. Demographic and Baseline Characteristics for Patients in the Phase III ABSSSI Studies

Characteristic	OASIS-1 and OASIS-2		
	Omadacycline (n = 691)	Linezolid (n = 689)	All Patients (n = 1380)
Age, years			
Mean (SD)	44.7 (14.2)	45.5 (14.2)	45.1 (14.2)
Min, max	18, 88	18, 90	18, 90
Sex			
Male	445 (64.4)	433 (62.8)	878 (63.6)
Race			
White	621 (89.9)	641 (93.0)	1262 (91.4)
Ethnicity			
Hispanic or Latino	238 (34.4)	247 (35.8)	485 (35.1)
Not Hispanic or Latino	449 (65.0)	440 (63.9)	889 (64.4)
Not reported/unknown	4 (0.6)	2 (0.3)	6 (0.4)
Region			
United States	570 (82.5)	570 (82.7)	1140 (82.6)
Non–United States	121 (17.5)	119 (17.3)	240 (17.4)
European Union[a]	85 (12.3)	88 (12.8)	173 (12.5)
BMI (kg/m^2)[b]			
<25	260 (37.6)	245 (35.6)	505 (36.6)
25–30	221 (32.0)	243 (35.3)	464 (33.6)
>30	210 (30.4)	200 (29.1)	410 (29.7)
Creatinine clearance			
>89 mL/min	603 (87.6)	612 (89.5)	1215 (88.6)
60–89 mL/min	64 (9.3)	51 (7.5)	115 (8.4)
<60 mL/min	21 (3.1)	21 (3.1)	42 (3.1)
Type of primary infection			
N (mITT population)	676	671	1347
Wound infection	312 (46.2)	318 (47.4)	630 (46.8)
Cellulitis/erysipelas	209 (30.9)	202 (30.1)	411 (30.5)
Major abscess	155 (22.9)	151 (22.5)	306 (22.7)
Pathogen[c]			
N (micro-mITT population)	504	514	1018
Gram-positive aerobes	490 (97.2)	497 (96.7)	987 (97.0)
Staphylococcus aureus	376 (74.6)	384 (74.7)	760 (74.7)
MRSA	173 (34.3)	157 (30.5)	330 (32.4)
MSSA	208 (41.3)	232 (45.1)	440 (43.2)
Streptococcus pyogenes	40 (7.9)	34 (6.6)	74 (7.3)
Streptococcus anginosus group[d]	104 (20.6)	82 (16.0)	186 (18.3)
Gram-positive anaerobes	33 (6.5)	32 (6.2)	65 (6.4)
Gram-negative aerobes	52 (10.3)	53 (10.3)	105 (10.3)
Gram-negative anaerobes	28 (5.6)	25 (4.9)	53 (5.2)

Abrahamian FM, et al. *Clin Infect Dis*. 2019;69(Suppl 1):S23–S32.

- ECR: early clinical response (48-72 hrs after rx initiation)
- PTE: posttreatment evaluation (PTE), (7-14 days after last dose)



Subgroup	Omadacycline	Linezolid	Percentage-Point Difference (95% CI)
	No. of events/total no. (%)		
ECR			
mITT	583/676 (86.2)	563/671 (83.9)	2.3 (–1.5 to 6.2)
micro-mITT	444/504 (88.1)	433/514 (84.2)	3.9 (–0.4 to 8.1)
PTE			
mITT	575/676 (85.1)	551/671 (82.1)	2.9 (–1.0 to 6.9)
micro-mITT	422/504 (83.7)	413/514 (80.4)	3.4 (–1.3 to 8.1)
CE	537/553 (97.1)	522/552 (94.6)	2.5 (0.2 to 5.0)
ME	398/408 (97.5)	394/417 (94.5)	3.1 (0.4 to 6.0)
Monomicrobial gram-positive infection			
ECR			
micro-mITT	300/340 (88.2)	327/383 (85.4)	2.9 (–2.1 to 7.8)
PTE			
micro-mITT	292/340 (85.9)	312/383 (81.5)	4.4 (–1.0 to 9.8)
ME	274/278 (98.6)	300/316 (94.9)	3.6 (0.8 to 6.8)
Polymicrobial gram-positive infection			
ECR			
micro-mITT	78/91 (85.7)	50/64 (78.1)	7.6 (–4.5 to 20.7)
PTE			
micro-mITT	72/91 (79.1)	48/64 (75.0)	4.1 (–8.1 to 18.1)
ME	68/73 (93.2)	47/51 (92.2)	1.0 (–8.6 to 12.5)
Polymicrobial mixed (gram-positive and gram-negative) infection			
ECR			
micro-mITT	66/73 (90.4)	56/67 (83.6)	6.8 (–4.5 to 18.8)
PTE			
micro-mITT	58/73 (79.5)	53/67 (79.1)	0.3 (–13.2 to 14.1)
ME	56/57 (98.2)	47/50 (94.0)	4.2 (–4.1 to 14.8)

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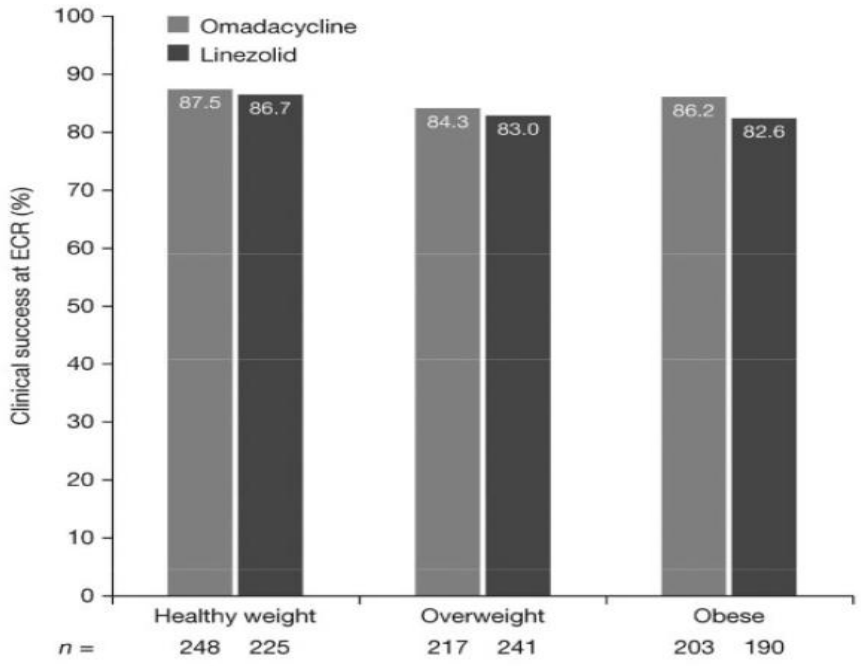
Table 4. Clinical Response by Baseline Pathogen

Pathogen	Omadacycline (n = 504)	Linezolid (n = 514)
Staphylococcus aureus, n	376	384
ECR	332 (88.3)	325 (84.6)
IACR-PTE	312 (83.0)	312 (81.3)
MRSA, n	173	157
ECR	159 (91.9)	139 (88.5)
IACR-PTE	146 (84.4)	128 (81.5)
MSSA, n	208	232
ECR	178 (85.6)	190 (81.9)
IACR-PTE	171 (82.2)	187 (80.6)
Streptococcus pyogenes, n	40	34
ECR	32 (80.0)	30 (88.2)
IACR-PTE	28 (70.0)	25 (73.5)
Staphylococcus lugdunensis, n	11	3
ECR	10 (90.9)	3 (100.0)
IACR-PTE	10 (90.9)	2 (66.7)
Enterococcus faecalis, n	18	25
ECR	16 (88.9)	20 (80.0)
IACR-PTE	17 (94.4)	21 (84.0)
Enterobacter cloacae, n	8	7
ECR	8 (100.0)	6 (85.7)
IACR-PTE	7 (87.5)	7 (100.0)
Klebsiella pneumoniae, n	11	11
ECR	10 (90.9)	9 (81.8)
IACR-PTE	8 (72.7)	6 (54.5)
Streptococcus anginosus group, n[a]	104	82
ECR	93 (89.4)	63 (76.8)
IACR-PTE	84 (80.8)	59 (72.0)

Abrahamian FM, et al. *Clin Infect Dis*. 2019;69(Suppl 1):S23–S32.

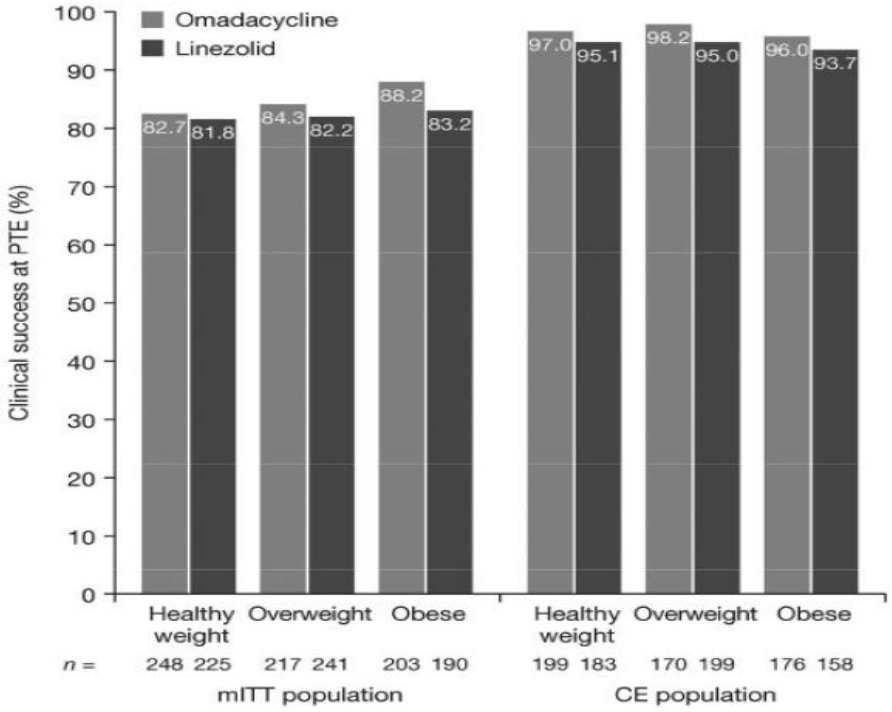
Clinical Response of Fixed-Dose Omadacycline in Obese Patients

Early Clinical Response (ECR)



Clinical success at ECR, mITT population, *n/N* (%)	Omadacycline (*N* = 203)	Linezolid (*N* = 190)
Obese class I	107/123 (87.0)	85/105 (81.0)
Obese class II	39/47 (83.0)	43/47 (91.5)
Obese class III	29/33 (87.9)	29/38 (76.3)

Post-Treatment Evaluation (PTE)



Clinical success at PTE, *n/N* (%)	mITT population		CE population	
	Omadacycline (*N* = 203)	Linezolid (*N* = 190)	Omadacycline (*N* = 176)	Linezolid (*N* = 158)
Obese class I	108/123 (87.8)	83/105 (79.0)	102/105 (97.1)	75/83 (90.4)
Obese class II	43/47 (91.5)	42/47 (89.4)	40/41 (97.6)	41/42 (97.6)
Obese class III	28/33 (84.8)	33/38 (86.8)	27/30 (90.0)	32/33 (97.0)

Pai MP, et al. *J Antimicrob Chemother.* 2021;76:1315-1322.

Omadacycline – Safety Profile

Table 2. Overview of Adverse Events in Phase III Acute Bacterial Skin and Skin Structure Infection and Community-acquired Bacterial Pneumonia Studies (AC3 Pool)

Adverse Event	Omadacycline (n = 1073)	Linezolid (n = 689)	Moxifloxacin (n = 388)
Any TEAE	510 (47.5)	284 (41.2)	188 (48.5)
Drug-related TEAE	236 (22.0)	111 (16.1)	69 (17.8)
Serious TEAE	39 (3.6)	13 (1.9)	26 (6.7)
Drug-related serious TEAE	2 (0.2)	1 (0.1)	2 (0.5)
TEAE leading to death[a]	9 (0.8)	3 (0.4)	4 (1.0)
TEAE leading to premature discontinuation of study drug	33 (3.1)	10 (1.5)	27 (7.0)
TEAE leading to dose interruption of study drug	2 (0.2)	0	0
Serious TEAE leading to premature discontinuation of study drug	16 (1.5)	5 (0.7)	11 (2.8)

Data are presented as No. (%).

Abbreviation: TEAE, treatment-emergent adverse event.

[a]Causes of death by preferred term in the omadacycline group were pleural effusion and metastatic lung cancer, overdose, cerebrovascular accident, aortic aneurysm rupture, septic shock, pneumonia and acute respiratory distress syndrome, cardiogenic shock, cardiorespiratory arrest, acute respiratory failure and multiorgan failure, and acute myocardial infarction; in the linezolid group: cardiac failure, cardiac arrest, and unknown; and in the moxifloxacin group: cardiac failure, acute respiratory failure, lung neoplasm, and pancreatic carcinoma.

Table 3. Most Frequent Treatment-emergent Adverse Events (≥2% for Any Group) in Phase III Acute Bacterial Skin and Skin Structure Infection and Community Acquired Bacterial Pneumonia Studies (AC3 Pool)

Adverse Event	Omadacycline (n = 1073)	Linezolid (n = 689)	Moxifloxacin (n = 388)
Patients with ≥1 TEAE	510 (47.5)	284 (41.2)	188 (48.5)
Gastrointestinal disorders	241 (22.5)	103 (14.9)	70 (18.0)
Nausea	160 (14.9)	60 (8.7)	21 (5.4)
Vomiting	89 (8.3)	27 (3.9)	6 (1.5)
Diarrhea	26 (2.4)	20 (2.9)	31 (8.0)
General disorders and administration-site conditions	70 (6.5)	42 (6.1)	18 (4.6)
Infusion-site extravasation	28 (2.6)	19 (2.8)	0
Infections	132 (12.3)	92 (13.4)	41 (10.6)
Wound infection	30 (2.8)	22 (3.2)	0
Cellulitis	28 (2.6)	24 (3.5)	0
Subcutaneous abscess	23 (2.1)	27 (3.9)	0
Investigations	93 (8.7)	56 (8.1)	46 (11.9)
ALT increased	42 (3.9)	25 (3.6)	18 (4.6)
AST increased	33 (3.1)	24 (3.5)	14 (3.6)
GGT increased	15 (1.4)	8 (1.2)	8 (2.1)
Nervous system disorders	49 (4.6)	32 (4.6)	12 (3.1)
Headache	31 (2.9)	21 (3.0)	5 (1.3)
Psychiatric disorders	23 (2.1)	13 (1.9)	17 (4.4)
Insomnia	14 (1.3)	6 (0.9)	8 (2.1)
Vascular disorders	36 (3.4)	8 (1.2)	16 (4.1)
Hypertension	19 (1.8)	5 (0.7)	11 (2.8)

Data are presented as No. (%). A TEAE was defined as an AE with a start date/time on or after the date/time of the first dose of active study drug. Percentages were based on the number of patients in each treatment group. Patients may have been counted in >1 row.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutamyltransferase; TEAE, treatment-emergent adverse event.

Opal S, et al. *Clin Infect Dis*. 2019;69(Suppl 1):S40-S47.

Summary

- The tetracycline class is an important component in the management of ABSSSI
- Antimicrobial resistance in both Gram-positive and Gram-negative organisms has reduced the activity ─ and the role ─ of many tetracyclines in ABSSSI

- Omadacycline is a broad spectrum oral and IV tetracycline derivative
  - Active against many strains of tetracycline-resistant pathogens
  - Performed well in phase 3 trials for treatment of ABSSSI vs linezolid
  - Good safety profile
  - Important option for treatment of ABSSSI, particularly in populations at high risk for treatment failure and/or with resistant pathogens

Questions?

Thank You