FDA Approves Omadacycline for CABP and ABSSSI

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This new-generation tetracycline carries less risk for bacterial drug resistance than older tetracyclines and fewer adverse effects than quinolones.

On October 2, 2018, the U.S. FDA approved omadacycline (Nuzyra) for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP).

Omadacycline is a new-generation tetracycline, dosed once daily in both oral and intravenous forms, that was designed to subvert common tetracycline resistance mechanisms, including efflux and ribosomal protection. Among gram-positive bacteria, it exhibits excellent in vitro activity against methicillin-susceptible and methicillin-resistant Staphylococcus aureus (MIC₉₀, 0.5 mg/L), vancomycin-susceptible and vancomycin-resistant enterococci (MIC₉₀, 0.5 mg/L), penicillin-susceptible and penicillin-resistant Streptococcus pneumoniae (MIC₉₀, 0.12 mg/L), and beta-hemolytic and viridans streptococci (MIC₉₀, 0.12 mg/L). Among gram-negative bacteria, activity is excellent against Haemophilus influenzae (MIC₉₀, 2.0 mg/L), and Escherichia coli (MIC₉₀, 2.0 mg/L). However, activity in vitro is less reliable against other gram-negatives and activity is generally poor against the “MP3” group (Morganella, Providencia, Proteus, and Pseudomonas spp.), with MIC₉₀ ≥32 mg/L. Consistent with the tetracycline class, activity against atypical pathogens (e.g., Legionella, Mycoplasma) is excellent. Among anaerobes, activity is less reliable against gram-negatives (e.g. Bacteroides) than gram-positives (Clostridium, Peptostreptococcus).

In three phase 3 studies (OASIS-1 and OASIS-2 for ABSSSI, OPTIC for CABP) totaling about 2000 subjects, omadacycline met all primary and secondary efficacy outcomes designated by the FDA and the European Medicines Agency. The comparator was linezolid in OASIS and moxifloxacin in OPTIC. Intravenous dosing of omadacycline is 100 mg every 12 hours for 2 doses, then 100 mg every 24 hours for the remainder of the course. Oral dosing is 450 mg every 24 hours for the first 2 days, followed by 300 mg daily.

COMMENT

Omadacycline will be an interesting option in treating ABSSSI and CABP. Its approval comes on the heels of the approval of eravacycline, a similar molecule also derived from minocycline (NEJM JW Infect Dis Nov 2018 and http://www.fda.gov). However, despite their similar structures and overlapping spectrum of activities, eravacycline's approval in complicated intra-abdominal infections is complementary to that of omadacycline. Despite omadacycline's anticipated higher cost than generic quinolones (commonly used to treat CABP), quinolones have more potential adverse effects, including C. difficile infection, tendon rupture, QT prolongation, and effects on glucose homeostasis. Whereas older-generation tetracyclines have been used frequently in low-risk CABP patients to avoid these adverse events, their use in higher-risk patients is limited by concerns for bacterial drug resistance, which omadacycline overcomes. Real-world pharmaco-economic analyses will be important in defining use of omadacycline; it is expected to become available in the first quarter of 2019.