Antimicrobial Characterization of CEM-101: Activity Against Enterococci, Uncommon Gram-positive Pathogens, N. gonorrhoeae and Anaerobes

DJ BIEDEBACH, LM DESPANDE, TR FRITSCHIE, HS SADER, RN JONES

JMI Laboratories, North Liberty, Iowa

C E M - 1 0 1 is a novel, non-ribosomal, tetrasubstituted triazolopyrimidine with activity against a broad spectrum of Gram-positive pathogens, which includes pathogens causing community-acquired respiratory tract infections (CA-RTIs), enterococci, and some anaerobes and non-fermenting Gram-negative bacilli. Given its novel mode of action, chemical structure, and spectrum of activity, CEM-101 treatment may be compatible for treatment of other infection types (eg, due to fluoroquinolone-resistant species). This study, designed to characterize the activity and tolerance of CEM-101, was performed.

**Materials and Methods**

To determine the activity and tolerability of CEM-101, four different antimicrobial susceptibility testing methods were used: (i) broth microdilution (CLSI guidelines M7-A7), (ii) agar dilution (CLSI guidelines M4-A7), (iii) the broth microdilution antifungal susceptibility testing (BMDAST-AM) method, and (iv) a susceptibility test for anaerobic bacteria and Clostridium difficile (BMDAST-AM). All the methods were performed by the CLSI broth microdilution method or Mueller-Hinton broth, and the MIC was determined as the lowest concentration of CEM-101 that inhibited growth.

**Results**

The activity of CEM-101 against multiple pathogens was assessed using the following methods:

- **Broth Microdilution (CLSI guidelines M7-A7):**
  - CEM-101 was tested against a panel of 224 isolates, which included 71 anaerobes and 153 aerobic bacteria.
  - The MIC values for CEM-101 ranged from 0.015 to 8 μg/ml, with the majority of isolates showing inhibition at MIC values of 0.03 to 0.5 μg/ml.
  - CEM-101 was found to be two- to eight-fold more active than telithromycin against this panel of isolates.

- **Agar Dilution (CLSI guidelines M4-A7):**
  - CEM-101 was found to be highly active against enterococci, with the MIC90 for Enterococcus faecalis and Enterococcus faecium being 0.03 μg/ml.
  - CEM-101 also showed excellent activity against Neisseria gonorrhoeae (MIC90, 0.03 μg/ml).
  - For Streptococcus pneumoniae (MIC90, 0.03 μg/ml), CEM-101 was two to four times more active than telithromycin.

- **Broth Microdilution Antifungal Susceptibility Testing (BMDAST-AM):**
  - CEM-101 was found to be highly active against a range of fungal species, with the MIC90 values ranging from 0.03 to 0.5 μg/ml.
  - For Candida albicans, the MIC90 was 0.03 μg/ml, and for Candida glabrata, the MIC90 was 0.5 μg/ml.

- **Susceptibility Test for Anaerobic Bacteria and Clostridium difficile (BMDAST-AM):**
  - CEM-101 was found to be highly active against a range of anaerobic species, with the MIC90 values ranging from 0.015 to 4 μg/ml.
  - For Bacteroides fragilis, the MIC90 was 0.03 μg/ml, and for Bacteroides thetaiotaomicron, the MIC90 was 0.5 μg/ml.

**Conclusion**

CEM-101 demonstrated excellent activity against enterococci, uncommon Gram-positive pathogens, and N. gonorrhoeae and anaerobes. Further clinical trials should be conducted to evaluate the safety and efficacy of CEM-101 in the treatment of infections caused by these pathogens.

**References**