Intercostal Susceptibility Testing for Ceftaroline, a Novel MRSA-Active Cephalosporin: Selecting Potent Surrogate β-Lactams to Predict CPT Activity Against Clinically Significant Cocci

Abstract

Background: Ceftaroline (CPT), the active form of CPT, is a broad-spectrum cephalosporin with unique high affinity for binding to bacterial peptidyltransferase (PBP2a) responsible for meropenem resistance among staphylococci and aerobic Gram-negative organisms. Laboratory studies have shown that ceftaroline is active against vancomycin-resistant Enterococcus faecalis (VREF) and methicillin-resistant Staphylococcus aureus (MRSA), but direct testing of CPT is not utilized in routine susceptibility testing (ST) panels. The current study compared ceftaroline activity against an expanded panel of Gram-positive and Gram-negative bacteria to identify promising surrogate agents.

Methods: The susceptibility of 5,364 isolates from major collections of awake subjects was assessed using CLSI broth microdilution methods. The MIC breakpoints for both ceftaroline and the surrogate agents were determined using a panel of well-characterized strains and existing susceptibility testing results generated by commercial systems. For each pathogen, susceptible and resistant strains selected on the basis of CLSI category (MIC) were tested against each β-lactam agent.

Results: Among β-lactams, ceftaroline was ≤5% less active as compared to candidates evaluated for potential ST surrogate. Specifically, the best surrogate candidates were imipenem for ceftaroline against Gram-negative pathogens and oxacillin for Gram-positive strains. For MRSA, the use of oxacillin and/or clindamycin was preferable.

Conclusions: These results suggest that imipenem and oxacillin are the best surrogate agents for predicting ceftaroline activity against Gram-negative and Gram-positive bacteria, respectively.

Keywords: Ceftaroline, surrogate agents, susceptibility testing, Gram-negative, Gram-positive

References


Results

Table 1: Susceptibility of Surrogate Candidates to Ceftaroline (Cef) Against Clinical Isolates

- For Gram-positive organisms, the use of oxacillin and/or clindamycin was preferable.
- For MRSA, the use of oxacillin and/or clindamycin was preferable.

Conclusions

- These results suggest that imipenem and oxacillin are the best surrogate agents for predicting ceftaroline activity against Gram-negative and Gram-positive bacteria, respectively.

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