

S. aureus, a primary pathogen, is capable of biofilm production allowing organism persistence in harsh environments, offering antimicrobial protection” Barber et al (2015).

Reference:

Barber, K.E., Smith, J.R., Ireland, C.E., Boles, B.R., Rose, W.E. and Rybak, M.J. (2015) Evaluation of Ceftaroline Alone and in Combination Against Biofilm-producing Methicillin-resistant *Staphylococcus aureus* (MRSA) with Reduced Susceptibility to daptomycin and vancomycin in an In Vitro Pharmacokinetic/Pharmacodynamic Model. *Antimicrobial Agents and Chemotherapy*. May 18th. .

Abstract:

BACKGROUND: Annually, medical-device infections are associated with over 250,000 catheter-associated blood stream infections (CLABSI) with up to 25% mortality. *S. aureus*, a primary pathogen, is capable of biofilm production allowing organism persistence in harsh environments, offering antimicrobial protection. With *S. aureus* isolates with reduced susceptibility to current agents increasing, ceftaroline (CPT), offers a therapeutic alternative. Therefore, we evaluated whether CPT would have a role against biofilm-producing MRSA including those with decreased susceptibilities to alternative agents.

METHODS: We investigated CPT activity alone or combined with daptomycin (DAP) or rifampin (RIF) against 3 clinical biofilm-producing MRSA strains in an in vitro biofilm PK/PD model. Simulated antimicrobial regimens were as follows: CPT 600mg q8h (fC_{max} 17.0 mg/L, t_{1/2} 2.66h), DAP 12mg/kg/d (fC_{max} 14.7 mg/L, t_{1/2} 8h) and RIF 450mg q12h (fC_{max} 3.5 mg/L, t_{1/2} 3.4h), CPT plus DAP, and CPT plus RIF. Samples were obtained and plated for colony counts. Differences in log₁₀ CFU/cm² were evaluated by analysis of variance with Tukey’s post hoc test.

RESULTS: Strains were CPT and vancomycin susceptible and DAP non-susceptible (DNS). CPT displayed activity throughout the experiment. DAP demonstrated initial activity with regrowth at 24 hours in all strains. RIF was comparable to drug free control and little benefit observed when combined with CPT. CPT plus DAP displayed potent activity with an average log₁₀ CFU/cm² reduction of 3.33±1.01 from baseline.

CONCLUSION: CPT demonstrated activity against biofilm-producing DNS MRSA. CPT plus DAP displayed therapeutic enhancement over monotherapy providing a potential option for difficult to treat medical-device infections.

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