

P2442 2016 global assessment of the in vitro activities of ceftaroline and comparator agents against bacterial pathogens frequently causing community-acquired respiratory-tract infections

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Background: Ceftaroline fosamil (CPT), is a cephalosporin approved for treating complicated skin and soft tissue infections (cSSTI) caused by *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA), and other gram-positive and gram-negative pathogens. In 2017 the European Medicines Agency approved a higher CPT dosing regimen (600 mg q8h over 120 min) for the treatment of cSSTIs due to *S. aureus* with a CPT MIC of 2 or 4 mg/L. The availability of this higher dose led to a change in the EUCAST breakpoint for *S. aureus* from S≤1 and R>1 mg/L to S≤1, I=2, and R≥4 mg/L (note: *S. aureus* with CPT MICs of 4 mg/L are rare, but PK/PD analyses suggest they may be treated with the higher CPT dose). This analysis reports the impact of this change on the MIC interpretation of a collection of MRSA from cSSTI collected through the 2015-2016 AWARE program.

Materials/methods: 5,568 MRSA were collected worldwide during 2015 – 2016 from cSSTI. Isolates were collected from in-patients (n=4,546 [medical wards (4,109), ICU (455)]), out-patients (n=670) and other (n=334). MIC values were determined by broth microdilution according to CLSI guidelines.

Results: Percentage susceptible (S), intermediate (I) and resistant (R) by the original and revised ceftaroline breakpoints are shown in the table. Percentage of strains resistant dropped to 1.3% in Asia/South Pacific, 0.1% in LA, and 0% in Europe and MEA.

Organism	n (%S to ceftaroline)				
	Global	Europe	LA	ME/Af	Asia/SP
<i>Haemophilus</i> spp.	338 (92.6)	176 (95.5)	27 (100)	46 (95.7)	89 (83.2)
<i>Moraxella catarrhalis</i>	552 (na)	31 (na)	5 (na)	7 (na)	9 (na)
<i>Staphylococcus aureus</i>	826 (95.6)	468 (97.2)	82 (91.5)	96 (100)	180 (91.1)
PS <i>S. pneumoniae</i>	747 (100)	448 (100)	27 (100)	83 (100)	189 (100)
PNS <i>S. pneumoniae</i>	61 (90.2)	13 (100)	5 (100)	17 (94.1)	26 (80.8)
<i>S. pyogenes</i> (GAS)	98 (100)	71 (100)	5 (100)	11 (100)	11 (100)

%S, % susceptible based on EUCAST breakpoints except GAS (FDA breakpoint); LA, Latin America; ME/Af, Middle East/Africa; SP, South Pacific; *Haemophilus* spp. includes 309 *H. influenzae* and 27 *H. parainfluenzae*; *S. aureus* includes 421 methicillin-resistant- and 405 methicillin-susceptible *S. aureus* PS, penicillin susceptible; PNS, penicillin nonsusceptible; na, no breakpoint available

Conclusions: Revised EUCAST breakpoints for MRSA to include an intermediate category based on high dosage (0.6g x 3 over 2 hours) have decreased the percentage of isolates included in the resistant category, most notably in Latin America and Asia/South Pacific regions, where isolates with

an MIC of 2 mg/L are more prevalent and are now designated in the intermediate category. These findings indicate that the frequency of MRSA resistant to ceftaroline (MIC > 2 mg/L) remains low globally.