

Activity of ceftobiprole against methicillin-resistant *Staphylococcus aureus* including strains with reduced susceptibility to daptomycin, linezolid, and vancomycin

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Objective: To evaluate the activity of ceftobiprole (BPR) against methicillin-resistant *Staphylococcus aureus* (MRSA) with decreased susceptibility (S) to daptomycin (DAP), linezolid (LZD), vancomycin (VAN). Ceftobiprole medocaril is an anti-MRSA, broad-spectrum cephalosporin active against Gram-negative pathogens including *Pseudomonas aeruginosa*. It has been studied in hospitalized community-acquired bacterial pneumonia, hospital-acquired bacterial pneumonia, and acute bacterial skin and skin structure infections. **Methods:** A total of 216 MRSA were tested against BPR and comparator agents by CLSI reference broth microdilution methods. The collection consisted of 21 molecularly characterized LZD non-S isolates, 32 phenotypically characterized DAP non-S isolates, 32 hVISA, 12 VISA and 10 VRSA (from the NARSA collection). In addition, a panel of SCCmec types (SCCmec type I [21 isolates], SCCmec type II [22], SCCmec type III [22], SCCmec type IV [44]) were evaluated. Interpretive criteria applied were those published in CLSI and EUCAST documents. **Results:** BPR was highly potent against this selected collection of SA (MIC_{50/90}, 1/2 mg/L). The MIC₉₀ for BPR was 2 mg/L against the LZD non-S, DAP non-S, VISA and hVISA subsets and 1 mg/L against the VRSA strains. There was one VAN non-S isolate (VAN MIC, 4 mg/L) in the DAP non-S group. All isolates in the LZD non-S subset were S to DAP and VAN. The MIC_{50/90} value for BPR was 2/4, 1/2, 2/2, and 1/1 mg/L against SCCmec type I, II, III, and IV, respectively. The rank order of BPR activity was SCCmecIV>SCCmecII>SCCmecIII>SCCmecI. A total of 43 SCCmecIV isolates had a BPR MIC value of 1 mg/L with one strain at 0.5 mg/L. SCCmec type II strains exhibited the broadest BPR MIC range from 0.25-2 mg/L. SCCmec type I strains had the highest MIC values with 6 strains exhibiting a BPR MIC value of 4 and 15 strains at 2 mg/L. Three of the isolates with MIC values at 4 mg/L were from Venezuela, two from Italy, and one from Chile. **Conclusions:** BPR demonstrated potent activity against SA including subsets of isolates with reduced susceptibility to DAP, LZD and VAN. The activity of BPR against these resistant phenotypes indicates that it may have clinical utility in treatment of infections caused by MDR SA, and across strains from various SCCmec types.

Organism (No.)	cumulative % inhibited at ceftobiprole MIC (mg/L) of:						MIC _{50/90}
	≤0.12	0.25	0.5	1	2	4	
<i>Staphylococcus aureus</i> (216)	0.5	4.5	14.5	53.8	97.2	100.0	1/2
LZD-non-susceptible (21)	--	4.5	22.7	63.6	100.0	--	1/2
DAP-non-susceptible (32)	--	12.5	50.0	81.3	100.0	--	0.5/2
SCCmec type I (21)	--	--	--	--	71.4	100.0	2/4
SCCmec type II (22)	--	4.5	9.1	54.5	100.0	--	1/2
SCCmec type III (22)	--	--	--	4.5	100.0	--	2/2
SCCmec type IV (44)	--	--	2.3	100.0	--	--	1/1