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Antimicrobial activity of ceftobiprole versus other currently marketed cephalosporins and beta-lactams when tested against contemporary Gram-positive and -negative organisms collected from Europe (2015)

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Background: Ceftobiprole (active form of the prodrug ceftobiprole medocaril) is a fifth-generation cephalosporin with an expanded spectrum and potent activity against Gram-positive and -negative bacteria. Ceftobiprole medocaril is approved in various European countries for the treatment of hospital-acquired pneumonia, excluding ventilator-associated pneumonia, and community-acquired pneumonia in adults. Ceftobiprole is active *in vitro* against methicillin-resistant staphylococci including *Staphylococcus aureus* (MRSA) and multidrug-resistant *Streptococcus pneumoniae*. It is generally β-lactamase stable with activity against *Enterobacteriaceae* and *Pseudomonas aeruginosa*.

Material/methods: A total of 12,240 clinically relevant isolates (one per patient episode) were collected from patients at 37 medical centres in Europe (34), Turkey (2), and Israel (1) in 2015. Isolates were from multiple infection sites, including bloodstream, respiratory, skin and soft tissue, urinary tract, and others. Ceftobiprole, comparators, and quality-control organisms were susceptibility tested according to Clinical and Laboratory Standards Institute guidelines using broth microdilution panels. EUCAST (2016) interpretive criteria were applied.

Results: Ceftobiprole and ceftaroline were highly active when tested against 2,588 *S. aureus* isolates (22.4% methicillin-resistant). Against MRSA isolates, the percentage of susceptibility to ceftobiprole ($MIC_{50/90}$, 2/2 mg/L; [96.5% susceptible]) was higher than for ceftaroline ($MIC_{50/90}$, 1/2 mg/L; [86.2% susceptible]). All MRSA isolates were susceptible to linezolid and vancomycin. Potent activity was also demonstrated against coagulase-negative staphylococci by ceftobiprole ($MIC_{50/90}$, 0.5/2 mg/L) and ceftaroline ($MIC_{50/90}$, 0.25/1 mg/L). Ceftobiprole demonstrated good potency against *E. faecalis* ($MIC_{50/90}$ values of 0.5/2 mg/L), while ceftaroline was 4-fold less active against these strains with MIC_{50} and MIC_{90} values of 2 and 8 mg/L, respectively. All isolates were susceptible to daptomycin and

tigecycline. Ceftobiprole, ceftaroline, and ampicillin displayed limited activity against *E. faecium* isolates (MIC_{50}, >4 mg/L) regardless of vancomycin susceptibility. Of the β-lactam agents tested, ceftobiprole (99.3% susceptible), ceftaroline (99.9% susceptible) and imipenem (100.0% susceptible) were the most active against *S. pneumoniae*. A high degree of potency was shown by ceftobiprole against viridans group streptococci ($MIC_{50/90}$, 0.06/0.25 mg/L) and β-haemolytic streptococci ($MIC_{90,}$ 0.03 mg/L). For *Enterobacteriaceae*, 73.8% of isolates tested were susceptible to ceftobiprole, which was similar to the rates for cefepime (78.2%), ceftazidime (74.2%) and ceftriaxone (73.3%) and greater than ceftaroline (66.1%). Ceftobiprole and ceftaroline inhibited 70.4% and 20.0% of *P. aeruginosa* at ≤4 mg/L, respectively, while cefepime and ceftazidime exhibited 82.6% and 77.0% susceptibility. Ceftobiprole inhibited all *Haemophilus influenzae* and *Moraxella catarrhalis* isolates at ≤0.5 mg/L while ceftaroline inhibited all isolates at ≤0.25 mg/L.

Conclusions: Ceftobiprole was active *in vitro* against a broad range of clinically relevant Gram-positive and Gram-negative bacterial isolates from Europe, Turkey, and Israel. Ceftobiprole *in vitro* offers potency and spectrum advantages when compared to currently marketed cephalosporins and other β-lactams.