O318
2-hour Oral Session
Updates in bloodstream infection epidemiology and management

A pooled analysis of clinical cure and mortality with ceftobiprole medocaril versus comparators in staphylococcal bacteraemia in complicated skin infections, and community- and hospital-acquired pneumonia

Jordi Rello*[1], Galia Rahav[2], Thomas Scheeren[3], Mikael Saulay[4], Marc Engelhardt[5], Tobias Welte[6]

[1]*Ciberes, Universitat Autonoma de Barcelona, Barcelona, Spain*

[2]*The Chaim Sheba Medical Center, Infectious Disease Unit, Ramat-Gan, Israel*

[3]*University Medical Center Groningen, Groningen, Netherlands*

[4]*Icon Plc, Allschwil, Switzerland*

[5]*Basilea Pharmaceutica International Ltd, Basel, Switzerland*

[6]*Medizinische Hochschule Hannover, Klinik Für Pneumologie, Medizinische Hochschule Hannover, Abteilung Für Pneumologie, Hannover, Germany*

Background: Ceftobiprole medocaril, the prodrug of the active moiety ceftobiprole, is an intravenous cephalosporin, approved for the treatment of community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP), excluding ventilator-associated pneumonia (VAP). Ceftobiprole exhibits bactericidal activity against Gram-negative and Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA). Studies in animal models of *S. aureus* endocarditis show superior efficacy of ceftobiprole over vancomycin, linezolid and daptomycin,[1] supporting a potential role for ceftobiprole in the treatment of staphylococcal bacteraemia.

Material/methods: A post-hoc pooled analysis was performed from four double-blind, randomized, phase 3 studies:[2,3,4,5] two studies in complicated skin and soft tissue infections (cSSTI study 1: ceftobiprole 500 mg b.i.d. [N=397] vs vancomycin [N=387];[2] cSSTI study 2: ceftobiprole 500 mg t.i.d. [N=547] vs vancomycin/ceftazidime [N=281][3]); one study in CAP (ceftobiprole 500 mg t.i.d. [N=314] vs ceftriaxone ± linezolid [N=324][4]); and one study in HAP including VAP (ceftobiprole 500 mg t.i.d. [N=391] vs linezolid/ceftazidime [N=390][5]). Clinical cure rates at the test-of-cure (TOC) visit (primary endpoint) and 30-day all-cause mortality (ACM) were analysed.

Results: Of the 3031 patients in the studies, 95 had staphylococcal bacteraemia and 51 had *S. aureus* bacteraemia. The prevalence of staphylococcal bacteraemia was 3.2% (25/784) in cSSTI study 1 and 2.4% (20/828) in study 2, 0.2% (1/638) in the CAP study, and 4.7% (27/571) in non-VAP patients and 10.5% (22/210) in VAP patients from the HAP study. The prevalence of *S. aureus* bacteraemia was 1.7% (13/784) in cSSTI study 1 and 1.3% (11/828) in study 2, 0.2% (1/638) in the CAP study, and 2.6% (15/571) in non-VAP patients and 5.2% (11/210) in VAP patients in the HAP study. Pooled clinical cure rates and 30-day ACM are reported below (Table). Forty-three patients in the ceftobiprole group and 48 in the comparator group had MRSA pneumonia (3 and 8 patients, respectively, had MRSA bacteraemia). Clinical cure rates were 41.9% vs 43.8%, and 30-day ACM was 20.9% vs 31.3% for ceftobiprole vs comparators. For pneumonia patients with MRSA bacteraemia, 30-day ACM was 0% (0/3; ceftobiprole) and 25% (2/8; comparator).

Conclusions: In this post-hoc analysis of patients with staphylococcal bacteraemia in the context of complicated skin or pulmonary infections, clinical responses with ceftobiprole were similar to those for standard-of-care comparators, with a trend towards lower 30-day all-cause mortality with ceftobiprole. These data support further clinical evaluation of ceftobiprole in staphylococcal bacteraemia.

	Ceftobiprole, n/N (%)	**Comparator, n/N (%)**	**Difference,[a] % (95% CI)**
Clinical cure at TOC			
Any staphylococcal bacteraemia	22/45 (48.9)	22/50 (44.0)	4.9 (–15.2, 25.0)
Coagulase-negative staphylococci	10/22 (45.5)	10/22 (45.5)	0 (–29.4, 29.4)
S. aureus	12/23 (52.2)	12/28 (42.9)	9.3 (–18.1, 36.8)
MSSA	4/9 (44.4)	7/15 (46.7)	–2.2 (–43.4, 38.9)
MRSA	5/9 (55.6)	2/9 (22.2)	33.3 (–9.0, 75.7)
30-day ACM			
Any staphylococcal bacteraemia	4/45 (8.9)	8/50 (16.0)	–7.1 (–20.2, 6.0)
Coagulase-negative staphylococci	1/22 (4.5)	2/22 (9.1)	–4.5 (–19.4, 10.3)
S. aureus	3/23 (13.0)	6/28 (21.4)	–8.4 (–28.9, 12.1)
MSSA	1/9 (11.1)	2/15 (13.3)	–2.2 (–29.0, 24.6)
MRSA	0/9 (0.0)	2/9 (22.2)	–22.2 (–49.4, 4.9)

[a]Ceftobiprole minus comparator. ACM, all-cause mortality; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus.*

[1]Tattevin et al. Antimicrob Agents Chemother 2010;54:610-3; [2]Noel et al. Antimicrob Agents Chemother 2008;52:37-44; [3]Noel et al. Clin Infect Dis 2008;46;647-55; [4]Nicholson et al. Int J Antimicrob Agents 2012;39:240-6; [5]Awad et al. Clin Infect Dis 2014;59:51-61.