29th ECCMID Amsterdam, Netherlands 13 – 16 April 2019

The congress of ESCMID

P1197 Susceptibility to ceftolozane-tazobactam among ESBL-producing *Enterobactericeae*: a matter of breakpoints

Laurent Dortet*[1], Sandrine Bernabeu[1], Thierry Naas[1]

[1] UPSud - APHP, Hopital Bicetre, Le Kremlin-Bicetre, France

Background: Ceftolozane/tazobactam is the most potent antipseudomonal cephalosporin and its spectrum of activity includes the most common ESBL-producing *Enterobacteriaceae*. To assess ceftolozane/tazobactam susceptibility EUCAST and CLSI recommend two different breakpoints (≤ 1 mg/L and ≤ 2 mg/l, respectively).

Materials/methods: Ceftolozane-tazobactam, ceftazidime and imipenem MICs were determined using Etest (bioMérieux). 100 well-characterized ESBL-producing *Enterobacteriaceae* were tested (17 TEM-ESBL-, 16 SHV-ESBL-, 1 GES-1-, 5 VEB- and 61 CTX-M-producers). In addition, from June to August 2016, we prospectively tested 100 consecutive clinical ESBL-producing *Enterobacteriaceae* isolates.

Results: From the prospective study, the ESBL producers were isolated from urine (67%), blood culture (12%), wound (6%), bile (6%), pus (3%), pulmonary samples (2%) and other samples (4%). 98 % of the ESBL were of CTX-M type (CTX-M-1, -3, -14, -15, -17, -27, -55, -82, -101, -182) and 2% SHV-12.

Using CLSI breakpoints, the % of isolates susceptible to ceftolozane-tazobactam was significantly higher, in particular in *Klebsiella* spp. and *Enterobacter* spp.

Species	n	% of susceptibility with EUCAST		% of susceptibility with CLSI				
		CAZ	C/T	IMP		CAZ	C/T	I
		≤ 1 mg/L	≤ 1 mg/L	≤ 2 mg/L		≤ 4 mg/L	≤ 2 mg/L	≤ m
Collection strains								
	E. coli	40	12.5%	95.0%	100%		42.5%	9
	Klebsiella spp.	33	6.1%	57.6%	90.9%		18.2%	7 %
	Enterobacter spp., *C. freundii*	23	4.2%	50.0%	95.8%		16.7%	7
	Other	4	66.7%	66.7%	100%		66.7%	1
	All	100	10%	**71.0%**	96.0%		30.0%	**8 %**
Prospective study								
	E. coli	60	11.7%	83.3%	100%		33.3%	9
	Klebsiella spp.	29	0.0%	55.2%	100%		0.0 %	8
	Enterobacter spp., *C. freundii*	11	0.0%	27.3%	100%		0.0 %	4
	All	100	7.0%	**69.0%**	100%		20.0 %	**9 %**

CAZ, ceftazidime; C/T ceftolozane/tazobactam; IMP, imipenem

Conclusions: Despite using both breakpoints the probability of target attainment (determined by Monte-Carlo simulations) was demonstrated to be >90% with 1.5 g ceftolozane/tazobactam every 8h (Xio A.J. et al. 2016), the microbiological categorization is different for ~20% of the ESBL-producers. Accordingly, double-blind trials are mandatory to evaluate the efficacy of ceftolozane-tazobactam for treating infections caused by of ESBL-producing *Enterobacteriaceae*.