

# Temocillin susceptibility testing with Vitek2® system and E-test®

## Are these methods reliable to determine temocillin MIC ?

Contact: Julie Descy  
Clinical Microbiology  
CHU, B-23, Sart-Tilman, 4000 Liège, BELGIUM  
Phone: (32)4 366 24 39 - Fax: (32)4 366 24 40  
Email: julie.descy@chuliege.be

Julie Descy<sup>1</sup>, Clotilde Visée<sup>2</sup>, Frédéric Fripiat<sup>2</sup>, Cécile Meex<sup>1</sup>, Nathalie Layios<sup>3</sup>, Françoise Van Bambeke<sup>4</sup>, Pierrette Melin<sup>1</sup>  
<sup>1</sup>CHU of Liège; Clinical Microbiology - <sup>2</sup>CHU of Liège; Infectious Diseases - <sup>3</sup>CHU of Liège; Intensive Care - <sup>4</sup>Université catholique de Louvain; Louvain Drug Research Institute



### INTRODUCTION

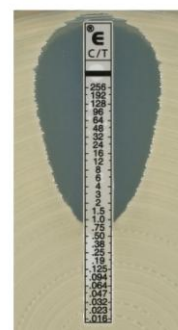
- The use of temocillin (TEM) is increasing in serious infections caused by *Enterobacteriaceae*, including extended-spectrum  $\beta$ -lactamases (ESBL), as an alternative to carbapenems (1-5).
- Therefore, accuracy of *in vitro* minimal inhibitory concentration (MIC) values is of high importance in an era of antibiotic stewardship based on PK/PD.

### OBJECTIVE

- To perform and compare two antimicrobial susceptibility testing (AST) methods used routinely in many laboratories:
  - Vitek2®, bioMérieux France
  - E-test®, bioMérieux France
 for determination of TEM MICs with a reference broth microdilution (BMD) method.
- To evaluate which method is reliable to determine TEM MICs.

### MATERIALS AND METHODS

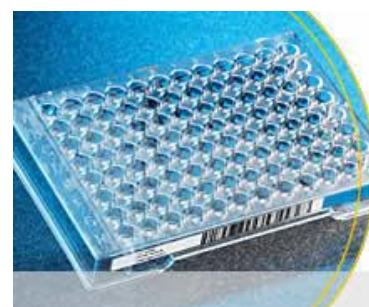
- 100 isolates of *Enterobacteriaceae* were collected from respiratory samples isolated from ICU patients.
- MICs of temocillin were determined in parallel by 3 methods:
  - E-test® (Biomérieux, France) (A)
  - Vitek2® (Biomérieux, France) (B)
  - BMD, following CLSI recommendations (C)



(A)



(B)



(C)

- Since no EUCAST or CLSI breakpoint guidelines exist at this time, susceptibility to temocillin was determined according to breakpoints provided by BSAC (British Society for Antimicrobial Chemotherapy) (6) (S: MIC  $\leq$  8 mg/L; R: MIC > 8 mg/L).
- Evaluation of **categorical agreement (CA)**, **essential agreement (EA)**, **very major errors (VME)** and **major errors (ME)**, as defined in Cumitech 31A (7).
- The production of ESBL or carbapenemase was screened according to the antibiotic susceptibility profile.
  - ESBL expression was confirmed by the double-disc synergy test.
  - Carbapenemase production was established by a colorimetric test detecting the carbapenem hydrolysis or using an immunochromatographic assay.

### RESULTS

- 100 *Enterobacteriaceae* isolates were collected:
  - Klebsiella pneumoniae* (KP) (34%), *Escherichia coli* (EC) (23%), *Serratia* spp. (18%), others (25%).
- 35 were ESBL-producers; 13 were carbapenemase-producers.
- 41 isolates were resistant to temocillin (MIC > 8 mg/L) according to BMD method (Table1).

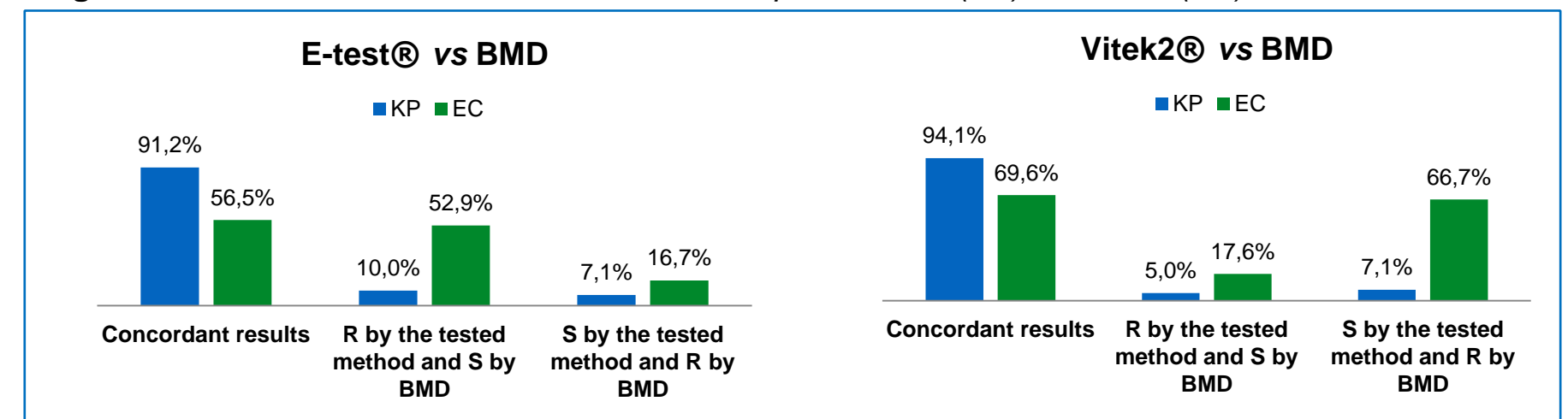
Table1 : Rates of temocilline Resistance (BMD) Table2 : Overall results for agreements, major and very major errors between methods.

	Number of isolates (%)		
	S	R	
<i>K.pneumoniae</i>	34	20	6 (26%)
<i>E.coli</i>	23	17	14 (41%)
<i>Serratia</i> spp.	18	4	14 (78%)
Others	25	18	7 (28%)
Overall	100	59	41

	Essential agreement – EA (should be $\geq$ 90%)	Categorical agreement – CA (should be $\geq$ 90%)	Very Major Errors – VME (should be $\leq$ 3%)	VME with MIC > $\pm$ 1 twofold dilution	Major Errors – ME (should be $\leq$ 3%)	ME with MIC > $\pm$ 1 twofold dilution
E-test® vs BMD	96,0 %	82,0 %	12,2%	0,0%	22,0%	6,8%
Vitek2® vs BMD	95,0%	84,0%	24,4%	7,3%	10,2%	3,4%

- Performances per species were very different as shown in figure 1 for *K.pneumoniae* and *E.coli*

Figure 1 : Concordant and discordant results for *K.pneumoniae* (KP) and *E.coli* (EC) between methods



### CONCLUSION

- Compared to BMD, essential agreements are above 90%, as recommended by Cumitech 31A, for both E-test® and Vitek2®.
- Results for categorical agreement are, for both methods, beyond 90% (not acceptable Cumitech 31A), but this can be explained by BSAC breakpoints (no “intermediate” category).
- When taking the adapted definition of VME and ME with MIC >  $\pm$  1 twofold dilution,
  - Vitek2® still seems to overestimate sensitivity (with VME rate of 7,3%)
  - while E-test® seems to overestimate resistance (with ME rate of 6,8%).
  - Looking at the species level, this is essentially the case for *E.coli*.
- The tested MIC range with Vitek2® is limited ( $\leq$  4 to  $\geq$  32 mg/L).
- When the use of TEM is considered by the clinician, we would recommend to control TEM MIC at least with an E-test®, or, even better, by BMD, especially for *E.coli*.

#### References:

1 Laterre P.-F. and al. JAC 2015; 70: 891–898; 2 Livermore DM, Tulkens PM, JAC. 2009 Feb;63(2):243-245; 3 Gupta ND and al. JAC 2009 Aug;64(2):431-433; 4 Balakrishnan I. and al. JAC. 2011 Nov;66(11):2628-31; 5 De Jongh R. and al. JAC 2008 ; 61, 382–388 ; 6 BSAC. Standing Committee on Susceptibility Testing. Version 14.0, 05-01-2015; 7 Clark, R. B. and al. 2009. Cumitech 31A, Coordinating ed., S. E. Sharp. ASM Press, Washington, DC.