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Evaluation of three methodologies for *in vitro* susceptibility testing of Ceftolozane-Tazobacatam (C/T)

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Introduction

Ceftolozane-Tazobactam (C/T) is an effective therapeutic β-lactam/β-lactam-inhibitor combination against multi-drug resistant (MDR) Gram-negative pathogens. C/T carries significant clinical efficacy against *Pseudomonas* pathogens, owning the significant antipseudomonal activity Ceftolozane. Primary clinical indications include complicated urinary tract (cUTI) and complicate intra-abdominal (cIAI) infections. Accurate identification of C/T MICs is imperative to successful and accurate clinical stewardship of this this partnership. Herein, we evaluate the C/T in vitro susceptibility typing by 3 methods

(i) broth microdilution (BMD), used as a reference method
(II) the BMD-based 'ComASP Ceftlozane-Tazobactam panel (Liofilchem®)
(iii) C/T MIC Test Strips (MTS) (Liofilchem®)

Methods

A total of 160 contemporary clinical Enterobacteriaceae were collected and confirmed for the presence of MDR phenotypes. N=119 were confirmed for the presence of $bla_{CTX\text{-}M}$, with the remaining n=41 isolates showing no resistance phenotype.

All test strains (n=160) underwent C/T susceptibility testing by each of the described testing methods on the same day. MICs were read and interpreted following EUCAST guidelines., where Susceptibility (S) ≤1µg/ml.

Essential agreement (EA)= the MICs of two compared methods were +/- 1x 2-log dilution of each other.
Categorical agreement (CA)= Isolate characterised as same S/R by EUCAST breakpoint

Results

The ComASP C/T panel showed significant levels of EA (95.6%) and CA (92.5%) when compared to the BMD reference methodology. In comparison, C/T MTS gave an EA and CA of 92.5% and 92.% respectively, under the same comparison. Interestingly there was little difference across species in the performance of ComASP C/T. When comparing ComASP C/T to BMD, EAs of 95.5% and 95.8% were recorded for *E. coli* and *K. pneumoniae* respectively. The EAs of MTS vs BMD in contract gave large variation, 91.7% (*E. coli*) and 83.3% (*K. pneumoniae).* No significant difference in EA or CA was seen between the methods when comparing $bla_{CTX\text{-}M}$-positive and sensitive strains.

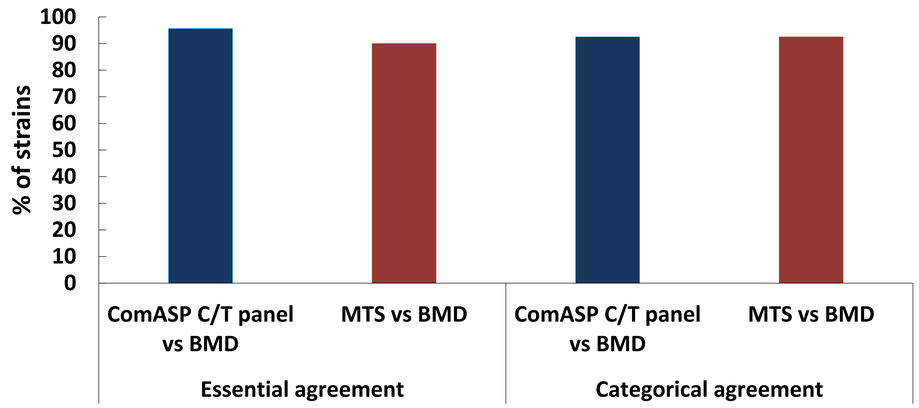

Figure (1): Comparison of ComASP C/T and C/T MTS to BMD Reference method by EA and CA.

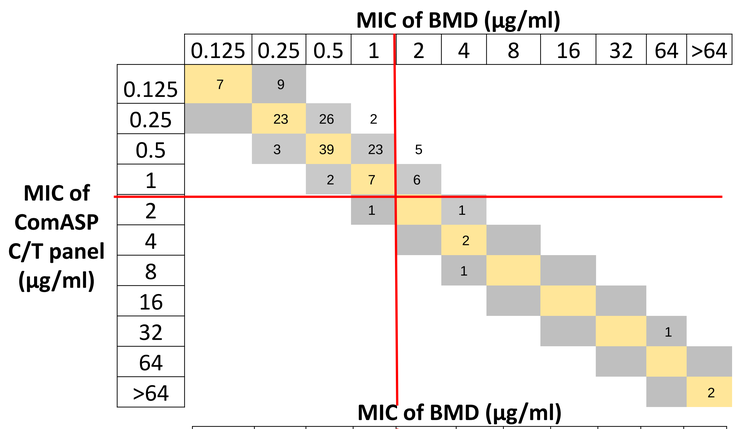

Figure (2): Comparison of ComASP C/T and BMD by MIC (µg/ml). Coloured squares denotes strains of EA.

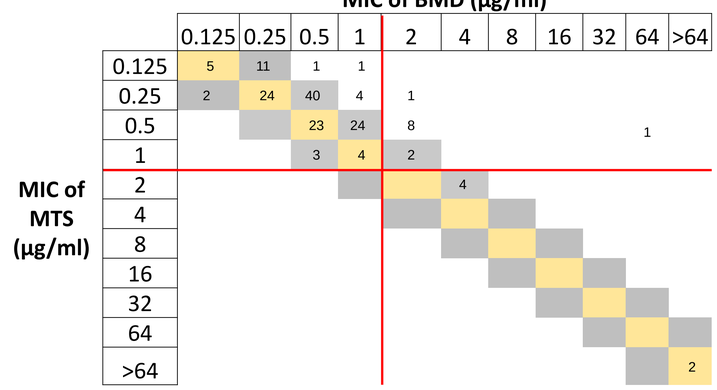

Figure (3): Comparison of C/T MTS and BMD by MIC (µg/ml). Coloured squares denote strains of EA.

Conclusions

- Current pilot data suggests ComASP C/T may represent a viable alternative to the more complex and labour-intensive BMD
- ComASP C/T showed improved correlation to the BMD reference method than MTS (EA of 95.6% vs 92.5%
- Current pilot data suggests similar such correlation in *P. aeruginosa* isolates.

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