Activity of cefepime-taniborbactam (formerly cefepime/VNRX-5133) and comparators against NDM-producing *Enterobacterales* from a regional outbreak

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Introduction

NDM is a metallo-β-lactamase able to hydrolyze most β-lactams and is not inhibited by the new β-lactamase inhibitors (avibactam, vaborbactam and relebactem). NDM-producing *Enterobacterales* are often resistant also to other antimicrobial classes with a shortage of effective therapies. Taniborbactam (formerly VNRX-5133), is a novel broad spectrum bicyclic boronate β-lactamase inhibitor active against both serine and metallo-β-lactamases (including NDM) currently used in combination with cefepime.

The aim of this study was to evaluate the *in vitro* activity of cefepime-taniborbactam and comparator antibiotics against a collection of NDM-producing *Enterobacterales*.

Collection	TGC	AMI	FEP	FTB	CZA	P/T4	C/T	LEVO
MIC50	0.5	>64	>32	0.5	>32	>128	>32	>4
MIC90	1	>64	>32	4	>32	>128	>32	>4

Table 1. MIC_{50} and MIC_{90} of collected isolates. MIC values are expressed in mg/L.

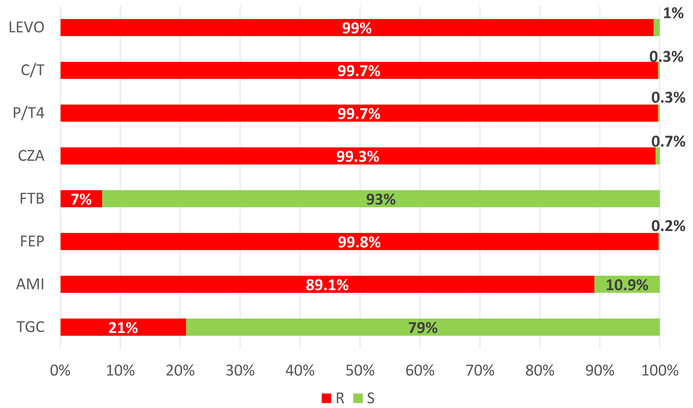

Figure 1 Percentage of susceptibility (S) and resistance (R) for NDM-producing strains.

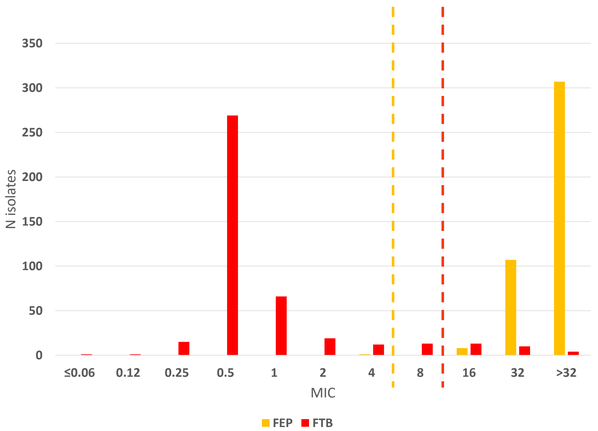

Figure 2. MIC distribution of cefepime and cefepime/taniborbactam.

Materials and methods

Bacterial strains. Clinical isolates of NDM-producing *Enterobacterales* were collected from a large outbreak in the Tuscany region (Italy) started in 2019 and still ongoing.

Susceptibility testing. MICs of cefepime with taniborbactam fixed at 4 mg/L and comparator antibiotics were measured by broth microdilution using lyophilized custom plates (Sensititre, Thermo Fisher Scientific, USA) and results were interpreted according to the EUCAST Clinical Breakpoints (v11.0, 2021). A provisional susceptibility breakpoint of ≤ 8 mg/L was applied for cefepime-taniborbactam.

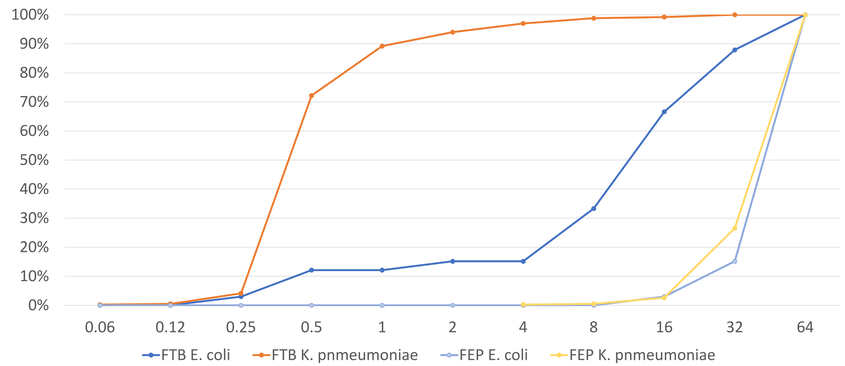

Figure 3. Inhibitory activity of cefepime and cefepime/taniborbactam on *E. coli* and *K. pneumoniae.*

Results

- 423 non-duplicate isolates of NDM-producing *Enterobacterales* (389 *Klebsiella pneumoniae*, 33 *Escherichia coli* and 1 *Enterobacter cloacae*) were tested.
- Compared to other antibiotics cefepime/taniborbactam showed the lowest values of MIC_{50} and MIC_{90} (0.5 mg/L and 4 mg/L respectively) (Table 1).
- Cefepime/taniborbactam restored cefepime susceptibility in 396/423 (93%) isolates (**Figure 1** and **Figure 2**) and this was the highest provisional susceptibility value compared to amikacin (10.9%S), ceftazidime/avibactam (0.7%S), piperacillin/tazobactam (0.3%S), ceftolozane/tazobactam (0.3%S), levofloxacin (1.0%S) and tigecycline (79%S, interpreted with *E. coli* breakpoints)
- Most NDM-producing *E. coli* isolates (22/33; 66%) had cefepime/taniborbactam MICs >8 mg/L (with 11 having an MIC of 16 mg/L) compared to a lower proportion of NDM-producing *K. pneumoniae* (5/389; 1.3%) (**Figure 3**).

Conclusions

Taniborbactam was able to restore the activity of cefepime for the majority of NDM-producing *Enterobacterales* and could represent a valuable alternative to current available antimicrobial treatments.

Acknowledgements

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LEVO: levofloxacin; C/T: ceftolozane/tazobactam; P/T4: piperacillin/tazobactam; CZA: ceftazidime/avibactam; FTB: cefepime/taniborbactam; FEP: cefepime; AMI: amikacin; *TGC: tigecycline (interpreted with EUCAST clinical breakpoints for *E. coli*).