In vitro activity of eravacycline against cefiderocol-resistant ESBL/NDM-producing Enterobacterales: a preliminary series

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KEYWORDS
Eravacycline; Cefiderocol resistance; NDM-producing Enterobacterales; Multidrug-resistant bacteria.

INTRODUCTION

Infections caused by carbapenemase-producing Enterobacterales, represent a major therapeutic challenge. Among them, NDM-type metallo-β-lactamases limit treatment options. Cefiderocol has emerged as one of the main therapeutic alternatives.

Eravacycline a novel fluorocycline approved for complicated intra-abdominal infections, has demonstrated potent in vitro activity against carbapenemase-producing Enterobacterales, including KPC, NDM, and OXA-48 producing isolates. However, its clinical use should be interpreted in light of infection source, drug exposure, absence of a urinary indication, and the limited availability of outcome data in infections caused by cefiderocol-resistant NDM-producing organisms.

OBJECTIVES

To evaluate the in vitro activity of eravacycline against cefiderocol-resistant ESBL/NDM-producing Enterobacterales and to describe tetracycline-associated resistance determinants detected by whole-genome sequencing.

MATERIALS AND METHODS

The MIC of eravacycline was determined using gradient diffusion (Etest, bioMérieux, France), and cefiderocol MIC was determined using a commercial broth microdilution system (UMIC, Bruker, USA), in nine ESBL-and-NDM- producing Enterobacterales isolates (six *Escherichia coli* and three *Klebsiella pneumoniae*). Four isolates were recovered from urine, four from rectal surveillance swabs and one from prosthetic tissue. Isolates were sequenced by Oxford Nanopore Technologies.

RESULTS

All nine ESBL/NDM-producing Enterobacterales isolates showed low eravacycline MICs according to the interpretive criteria applied in this study, while all were classified as cefiderocol-resistant. Genomic analysis identified multiple tetracycline-associated resistance determinants, including efflux systems or related components (acrAB-tolC, oqxAB, KpnEF, tet(A), tet(B)), transporters (emrKY), and regulatory genes (marA, evgAS). Despite the presence of these determinants, no phenotypic reduction in eravacycline activity was observed in this isolate set.

	MICROORGANISM		CEFIDEROCOL	ERAVACYCLINE
1	URINE	*K. PNEUMONIAE*	4	1
2	URINE	*E. COLI*	4	0,094
3	URINE	*E. COLI*	4	0,25
4	URINE	*K. PNEUMONIAE*	16	1-1,5
5	PROSTHETIC	*E. COLI*	8	0,19
6	SURVEILLANCE SWAB	*E. COLI*	4	0,38
7	SURVEILLANCE SWAB	*E. COLI*	4	0,5
8	SURVEILLANCE SWAB	*K. PNEUMONIAE*	8	0,75
9	SURVEILLANCE SWAB	*E. COLI*	4	0,38
% IN VITRO ACTIVITY			0%	100%

CONCLUSIONS

- Eravacycline showed high in vitro activity against ESBL/NDM-producing Enterobacterales with cefiderocol resistance.
- The presence of tetracycline resistance genes was not associated with reduced susceptibility to eravacycline, suggesting its ability to overcome classical resistance mechanisms.
- These findings are clinically relevant as a hypothesis-generating observation in difficult-to-treat NDM-producing Enterobacterales.