In Vitro Activity of Tebipenem Against Clinically Significant Gram-Negative Bacteria Isolated from Patients with Cancer

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Background:

Gram negative (GN) bacterial infections are on the rise in patients with cancer (PWC) and frequently require extended hospital stays that may lead to a major increase in healthcare cost. This study aimed to evaluate the in vitro activity of a novel oral carbapenem, a tebipenem against recent gram-negative clinical isolates from our cancer patients.

Material and Methods:

All 301 clinical isolates (2019-2021) from our cancer patients including 68 Extended Spectrum Beta-Lactamase (ESBL) isolates from blood cultures were tested against tebipenem and comparators. Clinical and laboratory Standards Institute (CLSI) approved broth microdilution method was used. Appropriate ATCC controls were included. MIC_{50}, MIC_{90}, MIC ranges and percent of susceptibility calculations were made using FDA breakpoints when available. The tebipenem provisional susceptibility breakpoint for most *Enterobacterales* is ≤ 0.125 mg/L.

Results:

Tebipenem and comparators antibiotics susceptibility percentage (S: %), and MIC_{90} are shown in table below. Tebipenem demonstrated highly potent activity against most of *Enterobacterales* isolates including *Citrobacter species, Enterobacter cloacae, Escherichia coli including ESBL isolates, Klebsiella pneumonie, Proteus mirabilis and Serratia* species *with 100%* susceptibility, while it was 97%, and 95% for ESBL *Klebsiella pneumonie and Enterobacter aerogenes respectively*. MIC_{90} ranged from 0.06 – 0.25 mg/L for all tested *Enterobacterales*. At a provisional breakpoint of 0.125 mg/L, the susceptibilities, MICs and ranges were comparable to meropenem, and ertapenem

Comparative study between Tebipenem and comparators MIC90 (mg/L.) and Susceptibility (%) results against Enterobacterales Isolated from Patients with Cancer

Organisms	Tebipenem MIC_{90} (S: %)	Ertapenem MIC_{90} (S: %)	Meropenem MIC_{90} (S: %)	TMP/SMX MIC_{90} (S: %)	Levofloxacin MIC_{90} (S: %)	Amikacin MIC_{90} (S: %)	Cefepime MIC_{90} (S: %)
Citrobacter spp. (N= 15)	0.06 (100)	0.5 (93)	0.03 (100)	8/152 (87)	8 (87)	2 (100)	4 (87)
Enterobacter aerogenes (N=21)	0.06 (95)	0.25 (90)	0.06 (95)	0.25/1.2 (95)	0.06 (95)	2 (95)	0.5 (95)
Enterobacter cloacae (N=30)	0.125 (100)	1 (87)	0.06 (100)	>32/608 (77)	0.25 (93)	2 (100)	32 (77)
ESBL Escherichia coli (N=33)	0.03 (100)	0.5 (100)	0.06 (100)	>32/608 (42)	>32 (18)	8 (100)	>32 (27)
Non-ESBL Escherichia coli (N=32)	0.015 (100)	0.06 (100)	0.015 (100)	>32/608 (56)	32 (47)	4 (100)	2 (90)
Klebsiella oxytoca (N=30)	0.03 (100)	0.125 (100)	0.06 (100)	>32/608 (80)	1 (90)	2 (100)	32 (73)
ESBL Klebsiella pneumonie (N=35)	0.125 (97)	0.25 (100)	0.125 (100)	>32/608 (11)	16 (43)	4 (100)	>32 (11)
Non-ESBL Klebsiella pneumonie (N=35)	0.015 (100)	0.03 (100)	0.03 (100)	>32/608 (86)	1 (94)	1 (100)	0.125 (100)
Proteus mirabilis (N=20)	0.125 (100)	0.06 (100)	0.06 (100)	>32/608 (55)	8 (80)	64 (65)	1 (90)
Serratia species (N=20)	0.125 (100)	0.125 (100)	0.06 (100)	2/38 (100)	0.125 (100)	4 (100)	0.125 (100)

Summary and Conclusions:

Our data demonstrate that oral tebipenem has promising activity against clinically significant bacterial pathogens isolated from cancer patients and it has similar activity to that of other tested carbapenems such as meropenem and ertapenem. Further clinical evaluation for oral carbapenem treatment of bacterial infections is warranted.