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

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•Background:

Carbapenems represent the most potent and broad-spectrum β-lactams and are minimally affected by most β-lactamase enzymes, However, all carbapenems currently in use including meropenem and ertapenem, are parenterally administered. Tebipenem pivoxil hydrobromide (TBPM-PI-HBr) is a new broad-spectrum orally-administered antibiotic, from the carbapenem subgroup of β-lactam antibiotics. It is the only oral carbapenem and could be an alternative to intravenous injection carbapenem antibiotic therapy. This study aimed to evaluate the in vitro activity of tebipenem, a novel oral carbapenem, against recent gram-positive clinical isolates from cancer patients
ointment.

•Material and Methods:

We tested 300-gram positive isolates are recently isolated (2019-2021) from our cancer patients, collected from blood cultures against tebipenem and comparators. Clinical and Laboratory Standards Institute (CLSI) approved broth microdilution method was used with appropriate ATCC controls. MIC50, MIC90, MIC ranges and percent of susceptibility calculations were made using FDA breakpoints when available. There is no tebipenem susceptibility breakpoint for gram positive isolates currently.

Table (1): MIC90 and MICs range of Tebipenem and comparators against 300-gram positive isolates from cancer patients

organisms	Tebipenem		Meropenem		Cefepime		Levofloxacin		Vancomycin		Daptomycin		Linezolid	
	MIC_{90}	Range	MIC_{90}	Range	MIC_{90}	Range	MIC_{90}	Range	MIC_{90}	Range	MIC_{90}	Range	MIC_{90}	Range
Bacillus sp. N= 20	0.06	<0.004 to 0.25	8	0.03 to 8	>32	4 to >32	0.125	0.06 to 0.25	1	0.06 to 2	8	0.125 to 16	4	0.25 to 4
Corynebacterium sp. N= 20	0.125	0.008 to 1	0.5	0.03 to 8	>32	0.5 to >32	16	0.06 to 32	0.5	0.06 to 2	0.5	0.06 to 2	0.5	0.06 to 2
E. faecalis (VSE) N = 35	1	<0.004 to 4	>16	0.125 to >16	>32	1 to >32	>32	0.5 to >32	1	0.25 to 2	4	0.5 to 4	4	0.5 to 4
E. faecium (VSE) N = 35	>4	0.125 to >4	>16	2 to >16	>32	32 to >32	>32	1 to >32	1	0.06 to 2	4	1 to 8	2	1 to 4
E. faecium (VRE) N = 20	>4	4 to >4	>16	16 to >16	>32	>32	>32	32 to >32	>32	32 to >32	4	1 to 8	2	1 to 4
Micrococcus sp. N = 20	0.008	<0.004 to 0.015	0.125	<0.015 to 0.125	0.125	<0.03 to 0.125	2	0.25 to 16	0.25	0.06 to 0.25	0.25	0.06 to 0.5	1	0.25 to 1
Staphylococcus aureus (MSSA) N=40	0.03	0.008 to 0.06	0.125	0.03 to 0.25	4	1 to 16	8	0.06 to 16	1	0.5 to 2	1	0.06 to 2	2	1 to 2
Staphylococcus lugdunensis N=10	0.25	0.03 to 0.5	0.25	0.06 to 0.25	16	2 to 32	0.25	0.125 to 0.5	0.5	0.25 to 1	0.5	0.125 to 0.5	0.5	0.5 to 1
Beta-hemolytic streptococcus N=20	0.015	<0.004 to 0.125	0.06	<0.015 to 0.125	0.25	0.06 to 4	1	0.06 to 1	0.25	0.06 to 0.5	0.5	0.125 to 1	2	0.125 to 2
Streptococcus pneumonie (PS) N=15	0.015	<0.004 to 0.015	0.125	<0.015 to 0.125	0.5	0.06 to 0.5	1	0.06 to 2	0.06	<0.03 to 0.06	0.25	0.06 to 0.5	0.5	0.125 to 1
Streptococcus pneumonie (PR) N=15	0.06	<0.004 to 0.125	1	0.06 to 4	4	0.125 to 8	16	0.5 to 32	0.125	<0.03 to 0.25	0.5	0.125 to 0.5	0.5	0.25 to 1
Viridans group Streptococci N=25	0.06	<0.004 to 0.125	1	<0.015 to 1	4	<0.03 to 16	4	0.125 to 4	0.5	<0.03 to 1	1	0.06 to 1	1	0.125 to 2
Rothia/Stomatococcus N=20	0.125	0.008 to 0.125	0.25	0.03 to 0.5	4	0.06 to 2	2	0.06 to 4	1	0.125 to 1	0.5	0.06 to 1	1	0.25 to 1
Rhodococcus equi N= 5	NA	0.25 to 0.5	NA	0.5 to 1	NA	4 to>32	NA	0.5 to 1	NA	0.25 to 0.5	NA	0.125 to 0.25	NA	0.5 to 1

Best MIC_{90} results | Best MICs Range

Results:

MIC90 and range of tebipenem and comparators are shown in table (1). Tebipenem gave the lowest MIC90 and MICs range against most gram-positive isolates including Bacillus species, Corynebacterium species, Enterococcus faecalis, Micrococcus species, MSSA S. aureus, Staphylococcus lugdunensis, Beta-hemolytic streptococcus, Streptococcus pneumonie, Viridans group streptococci, and Rothia species. The comparative potency of tebipenem vs meropenem as a carbapenem in this study showed that, tebipenem MICs were generally lower at least by 2-4-fold.

Summary and Conclusions:

Our data demonstrate that oral tebipenem has promising activity against clinically significant bacterial pathogens isolated from cancer patients and it has compatible activity to that of meropenem as carbapenems in this study. Further clinical evaluation for oral carbapenem treatment of bacterial infections is warranted