

**P1847 *In vitro* activity of BWC0977 (a novel bacterial topoisomerase inhibitor) and comparators against recent clinical and molecularly characterized *Enterobacteriaceae* and non-fermenter isolates from the United States and Europe**

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**Background:** BWC0977 represents a new broad-spectrum bacterial topoisomerase inhibitor with potent *in vitro* activity against susceptible and resistant (R) Enterobacteriaceae and non-fermenter isolates, including fluoroquinolone-R (FQ-R), aminoglycoside-R, extended-spectrum  $\beta$ -lactamase (ESBL)-phenotype, carbapenem-R Enterobacteriaceae (CRE), multidrug-R (MDR), and metallo- $\beta$ -lactamase (MBL)-producing strains. In this study, we tested BWC0977, ciprofloxacin (CIP), levofloxacin (LEV), ceftazidime (CAZ), and meropenem against 1,237 recent (2017) Enterobacteriaceae and non-fermenter isolates and 309 molecularly characterized Enterobacteriaceae and non-fermenter isolates from the United States (USA) and Europe (EUR).

**Materials/methods:** A total of 1,237 non-duplicate bacterial isolates were collected from 106 medical centers in the USA (50.4%) and EUR (49.6%) during 2017 according to a common surveillance design. Among the isolates tested, 24.9% were from bloodstream infections, 21.7% from skin and skin structure infections, 20.4% from pneumonia in hospitalized patients, 26.7% from urinary tract infections, 4.9% from intra-abdominal infections, and 1.4% from other infection types. Additionally, 309 molecularly characterized Enterobacteriaceae and non-fermenter isolates (2001-2017) expressing various bacterial resistance mechanisms were tested. All isolates were tested by CLSI reference broth microdilution.

**Results:** BWC0977 (MIC<sub>50/90</sub>, 0.25/0.5 mg/L) was the most potent topoisomerase inhibitor tested against Enterobacteriaceae isolates from the USA and EUR compared to CIP (MIC<sub>50/90</sub>,  $\leq$ 0.06/4 mg/L) and LEV (MIC<sub>50/90</sub>,  $\leq$ 0.06/4 mg/L) (Table). BWC0977 was very active against FQ-R, ESBL-phenotype, and CRE isolates with MIC<sub>50/90</sub> values of 0.5-1/4-8 mg/L compared to CIP (MIC<sub>50/90</sub>, 32/ $\geq$ 128 mg/L) and LEV (MIC<sub>50/90</sub>, 16/64-128 mg/L). BWC0977 was highly active against non-fermenter isolates, including *Acinetobacter baumannii* (MIC<sub>50/90</sub>, 0.25/0.5 mg/L) and *Pseudomonas aeruginosa* (MIC<sub>50/90</sub>, 0.5/2 mg/L), whereas reduced susceptibility was noted for CIP (2/ $>$ 128 mg/L and 0.12/4 mg/L, respectively) and LEV (1/64 mg/L and 0.5/16 mg/L, respectively).

**Conclusions:** BWC0977 demonstrated potent *in vitro* activity against recent clinical and molecularly characterized Enterobacteriaceae and non-fermenter isolates, including FQ-R, ESBL-phenotype, CRE, MDR, and MBL containing strains. BWC0977 was the most potent topoisomerase inhibitor tested and retained activity against FQ-R Enterobacteriaceae, *A. baumannii*, and *P. aeruginosa* isolates. Additional studies are needed to demonstrate the utility of BWC0977 in difficult-to-treat resistant Gram-negative infections.

Organism (no. tested)	MIC <sub>50/90</sub> (mg/L)			
	BWC0977	CIP	LEV	CAZ
FQ-R Enterobacteriaceae (97)	0.5/8	32/128	16/64	8/>32
ESBL Enterobacteriaceae and CRE (100)	1/4	32/>128	16/128	>32/>32
Enterobacteriaceae (1,033)	0.25/0.5	≤0.06/4	≤0.06/4	0.25/32
<i>Citrobacter freundii</i> species complex (103)	0.25/1	≤0.06/0.5	≤0.06/0.5	0.5/>32
<i>Enterobacter cloacae</i> species complex (107)	0.25/2	≤0.06/2	≤0.06/2	0.5/>32
<i>Escherichia coli</i> (102)	0.12/0.5	≤0.06/64	≤0.06/16	0.25/8
<i>Klebsiella oxytoca</i> (104)	0.12/0.5	≤0.06/≤0.06	≤0.06/≤0.06	0.12/0.5
<i>K. pneumoniae</i> (103)	0.25/2	≤0.06/64	≤0.06/8	0.25/>32
<i>Morganella morganii</i> (101)	0.12/0.25	≤0.06/8	≤0.06/8	0.25/4
<i>Proteus mirabilis</i> (103)	0.12/0.5	≤0.06/32	0.12/32	0.06/0.12
<i>Serratia marcescens</i> (103)	0.25/1	≤0.06/0.5	0.12/1	0.25/0.5
<i>Acinetobacter baumannii</i> (103)	0.25/0.5	2/>128	1/64	16/>32
FQ-R <i>A. baumannii</i> (11)	0.5/1	>128/>128	32/64	>32/>32
<i>Pseudomonas aeruginosa</i> (101)	0.5/2	0.12/4	0.5/16	2/16
FQ-R <i>P. aeruginosa</i> (11)	0.25/1	16/32	16/64	2/4

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