

Minocycline activity tested against *Acinetobacter baumannii*, *Burkholderia cepacia* species complex, *Stenotrophomonas maltophilia*, and select Enterobacteriaceae isolates from a European surveillance programme (2013)

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Objective: *Acinetobacter* spp. are frequently multidrug-resistant (MDR) and treatment of infections is problematic due to a limited number of therapeutic options. Recently, an intravenous formulation of minocycline (MINO) was reintroduced in the United States (USA) as it is one of the few treatments with USA-FDA approval to treat *Acinetobacter* infections. This study evaluated the contemporary activity of MINO against contemporary *Acinetobacter baumannii* and other Gram-negative (GN) bacilli collected at European centres during 2013.

Methods: Over 1000 clinical isolates from 48 medical centers in 22 countries were evaluated. Isolates included *A. baumannii* (389), *Stenotrophomonas maltophilia* (154), *Burkholderia cepacia* spp. complex (3), and Enterobacteriaceae (500). Only one isolate per infected patient episode was included and local identifications were confirmed by the monitoring laboratory using biochemical methods, Vitek 2, and MALDI-TOF. Susceptibility (S) testing was performed following CLSI methods and quality control guidelines. Interpretations were based on EUCAST guidelines, where available. CLSI interpretive criteria were applied when EUCAST criteria were not available. MDR were classified based on published recommendations (Magiorakos et. al.).

Results: Based on the definition of non-susceptible to ≥ 1 agent in ≥ 3 antimicrobial categories, 92.8% of *A. baumannii* and 14.6% of Enterobacteriaceae were MDR. MINO was the most active "tetracycline" against *A. baumannii* with a MIC₅₀ of 4 mg/L (58.6% S; doxycycline [DOXI], 35.2% S, tetracycline [TETRA], 14.9% S). S to colistin was 94.1%. S to gentamicin/amikacin/levofloxacin was 18.8/17.3/8.2%, respectively. A total of 55.4% of MDR *A. baumannii* were S to MINO, 30.2% for DOXI, and 8.9% for TETRA. For *S. maltophilia*, 98.7% of isolates were S to MINO (MIC₉₀, 1 mg/L), 94.8% to DOXI (MIC₉₀, 4mg/L), and only 4.5% to TETRA (MIC₉₀, 32mg/L). MINO MICs for the three *Burkholderia cepacia* spp. complex isolates ranged from 2-4 mg/L (DOXI, 4->8 µg/mL; TETRA, 4->32 µg/mL), the latter often used as a class surrogate. MINO was the most active "tetracycline" tested against the Enterobacteriaceae. The MIC₉₀s for MINO/DOXI/TETRA were 8/>8/>32 mg/L, respectively. A total of 85.6% of Enterobacteriaceae were S to MINO, 76.6% to DOXI, and 66.4% to TETRA. For the MDR Enterobacteriaceae, S to MINO/DOXI/TETRA were 49.3/41.1/32.9%, respectively. MIC₅₀ values for MINO for *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. ranged from 1-2 mg/L (MIC₉₀, >8mg/L except *Citrobacter* spp. [4mg/L]).

Conclusions: Tetracyclines differ in their activity to GN organisms. MINO was the most active "tetracycline" tested against *A. baumannii*, *S. maltophilia*, and Enterobacteriaceae isolates collected from patients across Europe during 2013.

Cumulative % inhibited at minocycline MIC (mg/L) of:

Organism (No.)	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8	MIC ₅₀	MIC ₉₀
<i>Acinetobacter baumannii</i> (389)	0.5	1.8	5.4	10.0	17.0	23.9	32.4	42.4	58.6	77.6	100.0	4	>8
MDR (361)	0.0	0.0	1.4	4.7	10.5	18.0	27.2	38.0	55.4	75.9	100.0	4	>8
<i>Burkholderia cepacia</i> species complex (3)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	33.3	100.0	4	..
<i>Stenotrophomonas maltophilia</i> (154)	0.0	0.0	0.6	14.9	49.4	78.6	92.2	97.4	98.7	100.0	..	0.5	1
Enterobacteriaceae (500)	0.0	0.0	0.0	0.0	2.4	18.2	40.0	68.2	85.6	91.6	100.0	2	8
MDR (73)	0.0	0.0	0.0	0.0	0.0	0.0	11.0	21.9	49.3	71.2	100.0	8	>8