In Vitro Synergy/Antagonism of the Pleuromutilin BC-3781 with Selected Antibiotics Against Gram-Positive and Gram-Negative Bacteria

In a study conducted at Nabriva Therapeutics AG, Vienna, Austria, and Micromyx, Kalamazoo, MI, USA, S. Paukner and colleagues investigated the in vitro activity of BC-3781, a pleuromutilin antibiotic, against Gram-positive and Gram-negative bacteria. The study assessed the antibiotic's activity in combination with various other agents, including amikacin, ceftriaxone, levofloxacin, and piperacillin/tazobactam.

### Methods

**Background:** The study was designed to evaluate the potential synergy or antagonism of BC-3781 when combined with other antibiotics, focusing on its activity against Gram-positive and Gram-negative bacteria. Synergy was assessed using the fractional inhibitory concentration index (FICI), where an FICI of 0.5-1 indicated synergy, >1-2 was considered indifferent, and >2-4 was interpreted as antagonism.

**Results:**

- **S. pneumoniae:** BC-3781 showed good activity against S. pneumoniae with all isolates inhibited at MICs of 0.12-0.5 mg/L, irrespective of resistance to penicillin/β-lactams or macrolides (Table 1).
- **Mean FICIs were close to 1, indicating an indifferent/additive effect for BC-3781 and the tested antibiotics for all strains except one where a mean FICI of 0.43 indicated synergy.** Individual FICI values >0.5 were observed for single strain/drug combinations, whereas a trend towards synergy was noted with aminoglycosides with at least one isolated having at least one FICI >0.5 (Figure 3).

**No antagonism was observed for any antibiotic tested with BC-3781.**

**Enterbacteriaceae and P. aeruginosa:** MICs of <0.12 mg/L confirmed the lack of activity of BC-3781 against Enterobacteriaceae and P. aeruginosa (Table 1).

**Conclusion:** When BC-3781 was combined with other agents, the effect was largely indifferent/additive with the exception of a trend towards synergy observed across evaluated isolates of S. aureus when BC-3781 was combined with chloramphenicol. Some exceptions were also observed for single strain/antibiotic combinations when single FICI values were close to or below 0.5. BC-3781 was confirmed not to have any antagonistic effect on the activity of combination agents against Gram-positive or Gram-negative pathogens, including those with important resistance phenotypes (e.g., MRSA and ESBL).

**The results of this study suggest no potential issue for combination therapy with BC-3781 when Gram-negative coverage is unnecessary.**

### References


