

P1668 **Outer membrane protein targeting antibiotics (OMPTAs): investigation of the in vitro time-kill kinetics and rate of resistance development by serial passage**

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Background: The OMPTAs are a new class of antibiotics being developed for the treatment of Gram-negative infections belonging to the clinically relevant *ESKAPE* pathogens. Here we investigated the *in vitro* time-kill kinetics and resistance development by serial passage against representative Gram-negative strains.

Materials/methods: Time-kill assays of OMPTAs were determined against WT and clinical isolates of *E. coli*, *P. aeruginosa*, *K. pneumoniae* and *A. baumannii*, at 1, 2 and 4 times MIC, at various time points (0.25, 0.5, 1, 2, 6 and 24 hours). The concentration and time to reach a 3 log₁₀ reduction with no significant re-growth at 24 hours was recorded by measuring viable colonies counts.

Resistance development during serial passage was assessed using a broth 2-fold dilution method in tubes, by transferring cells from tubes showing growth to fresh media containing the antibiotics for up to 21 serial passages or stopped earlier if the MIC breakpoint was reached for 3 consecutive passages.

Results: OMPTAs exhibited a rapid and irreversible 3-log reduction of bacterial counts at 1-2 times the MIC, within 2-6 hours. There were not significant differences between WT and MDR clinical isolates. In serial passage experiments OMPTAs demonstrated a lower propensity to develop resistance compared to reference antibiotics.

Conclusions: OMPTAs display a potent *in vitro* bactericidal activity against representative Gram-negative strains and generally demonstrates a lower rate of resistance development than the standard of care antibiotics.