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O0496 The differential in vitro effects of single and multidrug treatment against Mycobacterium avium

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Background: *Mycobacterium avium* cause difficult to treat opportunistic infections in humans. New antibiotic treatment regimens are urgently needed. Therefore, we aim to explore new multi-drug treatment regimes against *M. avium*.

Materials/methods: The minimum inhibitory concentration (MIC) of rifampicin, clarithromycin, clofazimine and ethambutol against the *M. avium* reference strain was determined by broth microdilution according to CLSI guidelines. To study the relative contributions of rifampicin, clarithromycin, clofazimine and ethambutol alone and in combinations to mycobacterial killing, we performed time-kill assays against *M. avium* ATCC 700898 in Middlebrook 7H9 broth. All drugs were tested at concentrations of 2 times MIC.

Results: The single drugs at concentrations equal to 2 times MIC proved to be bacteriostatic. Killing was enhanced with the addition of a second drug and was most pronounced for the three-drug combination that included clarithromycin. Strongest killing was achieved by the rifampicin, ethambutol, and clarithromycin combination, which is the current recommended treatment regimen. A greater than 2-log was also seen for three-drug combinations in which clofazimine replaced either rifampicin or ethambutol.

Conclusions: Current regimen is the most effective of all three-drug regimens in the current study, but clofazimine might be a reasonable replacement for either rifampicin or ethambutol in terms of killing capacity. The potential of all these regimens to suppress the emerging of macrolide resistance after prolonged exposure (28 days) is currently being investigated.

Time-kill assay *M. avium* ATCC 700898 vs rifampicin, clofazimine, clarithromycin and ethambutol.