# RESISTANCE-GUIDED COMBINATION THERAPY FOR MYCOPLASMA GENITALIUM

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**Background:**
Mycoplasma genitalium (MG) is challenging to cure. While resistance-guided sequential monotherapy (doxycycline followed by azithromycin for macrolide-susceptible infections or moxifloxacin for macrolide-resistant infections) increased cure to 95.4%(95%CI;89.7-98.0) for macrolide-susceptible and 92.0%(95%CI;88.1-94.6) for macrolide-resistant infections, selection of resistance and rising antimicrobial resistance remains a concern. In an effort to further increase cure and reduce *de novo* resistance, we evaluated the efficacy and tolerability of combination therapy with doxycycline+azithromycin or doxycycline+moxifloxacin.

**Methods:**
We conducted a prospective evaluation of patients treated with resistance-guided combination therapy at Melbourne Sexual Health Centre between August 2019 and December 2020. All patients received doxycycline for 7 days followed by either combination doxycycline+azithromycin (1g day 1, 500mg daily for 3 days) for macrolide-susceptible infections or combination doxycycline+moxifloxacin (400mg daily for 7 days) for macrolide-resistant infections. Adherence and adverse effects were recorded at test of cure, which was recommended 14-28 days after completing antimicrobials. Sequencing was performed to determine the prevalence of *parC* mutations in macrolide-resistant infections.

**Results:**
Of 101 patients treated with doxycycline+azithromycin, 93 were cured (92.1% [95%CI:85.0-96.5%]). Of 247 patients treated with doxycycline+moxifloxacin, 210 were cured (85.0% [95%CI: 80.0-89.2%]). Sequencing was available for 119 (48%) of the doxycycline+moxifloxacin group; *parC* S83 mutations were detected in 26%. Doxycycline+moxifloxacin cured 97.6 % (91.5-99.7%) of cases without and 32.2% (16.7-5.1%) of cases with *parC* S83 mutations. Almost half of patients (46% and 44%, respectively) reported adverse effects, predominantly mild gastro-intestinal.

**Conclusion:**
Combination doxycycline+azithromycin was not more effective than sequential monotherapy. Overall combination doxycycline+moxifloxacin achieved 85% cure in macrolide-resistant infections, where the prevalence of S83 mutations was 26%.

Absence of *parC* S83 mutations was associated with 98% cure for doxycycline+moxifloxacin. High levels of quinolone resistance has significantly impacted on the efficacy of moxifloxacin and this was not improved with combination therapy. Adverse effects were common.

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