Doxycycline and Sitafloxacin Combination Therapy for Treating Highly Resistant *Mycoplasma genitalium*

Authors:
Durukan D [1,2], Doyle M[2], Murray G[3,4], Bodiyabadu K[4], Vodstrcil L[1,2], Chow EPF[1,2], Jensen JS[5], Fairley CK[1,2], Aguirre I[2], Bradshaw CS[1,2]

[1] Monash University, Clayton, Victoria, Australia
[2] Melbourne Sexual Health Centre, Alfred Health, Carlton, Victoria, Australia
[3] Royal Children's Hospital, Parkville, Victoria, Australia
[4] The Royal Women's Hospital, Parkville, Victoria, Australia
[5] Statens Serum Institut, Copenhagen S, Denmark

Background:
M.genitalium with dual-class resistance to macrolides and fluoroquinolones has been rising globally and resulting in infections that do not respond to moxifloxacin and pristinamycin-based regimens. Limited treatment options exist for patients who have treatment-resistant infections. Since August 2017, we have treated these patients with a combination of doxycycline and sitafloxacin, which shows synergy in vitro for quinolone-susceptible *M. genitalium* strains but has not been evaluated for quinolone-resistant strains. We provide early data on the efficacy and tolerability of this regimen.

Methods The study took place at Melbourne Sexual Health Centre between August 2017 and April 2019. Patients who failed prior regimens with moxifloxacin and pristinamycin were offered a combination of doxycycline (100mg twice/day) and sitafloxacin (100mg twice/day) for 7 days. Some patients received a course of doxycycline monotherapy prior to combination therapy to reduce bacterial load. Test of cure was performed at 14-28 days following completion of antimicrobials. Adherence, tolerability, and reinfection risk was assessed using an electronic template.

Results
Sixteen patients were given combination therapy, twelve provided a test of cure and were subsequently included in the study. All men (10/12) had urethral infections and the two women had cervicovaginal infections. Combination therapy achieved cure in 11 of 12 cases (91.7%; 95% CI 64.9%–98.5%) and cured cases had complete symptom resolution. Adherence to the regimen was >95% and side effects were mild and resolved spontaneously. Sanger sequencing revealed single nucleotide polymorphisms for *parC* (S83I, n=11) and for *gyrA* (M95I n=3) prior to receiving combination therapy.

Conclusion
Doxycycline and sitafloxacin combination therapy was well tolerated and cured 11/12 infections that had failed prior regimens with moxifloxacin and pristinamycin. The regimen was acceptable to clinicians and is now used as our third-line regimen.

Disclosure of Interest Statement:
None to declare