

## Keeping gonorrhoea treatable and lowering antimicrobial resistance selection: findings from a prospective clinical study

Dr Leong Hoe Nam, reviewing Klausner JD, *et al. Clin Infect Dis*, published online 7 Aug 2020.

*Prospective clinical study findings indicate that resistance-guidance gonorrhoea treatment with 500 mg, oral, single-dose ciprofloxacin is effective and reduces antimicrobial resistance*

Antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* is a public health issue with the implications of treatment failure, disease complications and transmission of AMR strains (1, 2). The US Centers for Disease Control and Protection recommend treatment with ceftriaxone 250 mg plus azithromycin 1 g delivered as intramuscular (i.m.) injection (3), however, an oral therapy would be more advantageous allowing partner treatment and in a non-clinical setting (4). Ciprofloxacin 500 mg, oral single-dose therapy is an effective treatment for susceptible *N. gonorrhoeae* infections (5, 6), but a single point mutation in the gyrase A gene (*gyrA*) can make ciprofloxacin ineffective against *N. gonorrhoeae* (7).

In a US-based, multisite, prospective study, Klausner *et al.* assessed the efficacy of 500 mg, oral, single-dose ciprofloxacin in treating *N. gonorrhoeae* wild-type *gyrA* serine 91 infections. Of the participants enrolled (N=211), mostly men (92.5%) who had sex with men (68.9%), 106 had culture-positive infections with wild-type *gyrA* serine 91 *N. gonorrhoeae* genotype, as determined by a laboratory-developed polymerase chain reaction (PCR) assay. Wild-type *gyrA* serine 91 *N. gonorrhoeae* genotype infected individuals treated with ciprofloxacin had 100% microbiological cure regardless of anatomic site of infection in the per-protocol population and 91.7% in the intent-to-treat analysis. This prospective study provides strong evidence that *gyrA* serine 91 *N. gonorrhoeae* reliably predicts outcomes in individuals treated with ciprofloxacin.

### Comment

*GyrA* serine 91 *N. gonorrhoeae* PCR assay-guided ciprofloxacin therapy has many advantages including the ability to predict positive treatment outcomes with ciprofloxacin, which may contribute to slower emergence of antibiotic-resistant gonococcal strains.

Treatment of *N. gonorrhoeae* infection with oral ciprofloxacin also has medical and public health benefits including the possibility of reducing overall treatment costs and need for i.m. injections (8), the ability to treat partners, having a non-clinical treatment setting, and still offering a well-tolerated, inexpensive antibiotic that may reduce gonorrhoea re-infections (9). This prospective study supports widespread introduction and scale-up of *gyrA* serine 91 genotyping in *N. gonorrhoeae* infections as a way to guide gonorrhoea treatment, and deserves large-scale verification. The study findings clearly illustrate the important principle of using antibiotics appropriately to target susceptible pathogens.

## References

1. Whiley DM, Jennison A, Pearson J, *et al.* Genetic characterisation of *Neisseria gonorrhoeae* resistant to both ceftriaxone and azithromycin. *Lancet Infect Dis* 2018; **18**: 717–18.
2. Allen VG, Mitterni L, Seah C, *et al.* *Neisseria gonorrhoeae* treatment failure and susceptibility to cefixime in Toronto, Canada. *JAMA* 2013; **309**: 163–70.
3. Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep* 2015; **64**: 1–137.
4. Steiner KC, Davila V, Kent CK, *et al.* Field-delivered therapy increases treatment for chlamydia and gonorrhea. *Am J Public Health* 2003; **93**: 882–4.
5. Fifer H, Saunders J, Soni S, *et al.* 2018 UK national guideline for the management of infection with *Neisseria gonorrhoeae*. *Int J STD AIDS* 2020; **31**: 4–15.
6. Allan-Blitz LT, Hemarajata P, Humphries RM, *et al.* Ciprofloxacin may be efficacious in treating wild-type gyrase A genotype *Neisseria gonorrhoeae* infections. *Sex Transm Dis* 2018; **45**: e18.
7. Siedner MJ, Pandori M, Castro L, *et al.* Real-time PCR assay for detection of quinolone-resistant *Neisseria gonorrhoeae* in urine samples. *J Clin Microbiol* 2007; **45**: 1250–4.
8. Wynn A, Klausner JD. Addressing *Neisseria gonorrhoeae* treatment resistance with the DNA gyrase A assay: an economic study, United States. *Sex Transm Dis* 2020; **47**: 111–13.
9. Golden MR, Whittington WL, Handsfield HH, *et al.* Effect of expedited treatment of sex partners on recurrent or persistent gonorrhea or chlamydial infection. *N Engl J Med* 2005; **352**: 676–85.