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Gyrase A serine 91 genotyping predicts ciprofloxacin treatment outcome of gonorrhea

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BACKGROUND

- *Neisseria (N). gonorrhoeae* infections are rapidly increasing and among the most common co-infections in HIV-infected patients
- Novel treatment strategies are urgently needed in order to slow the continued emergence of antimicrobial resistance
- One promising strategy is the use of resistance-guided therapy
- We developed an assay to predict the susceptibility of *N. gonorrhoeae* to ciprofloxacin based on the gyrase A (*gyrA*) serine 91 codon



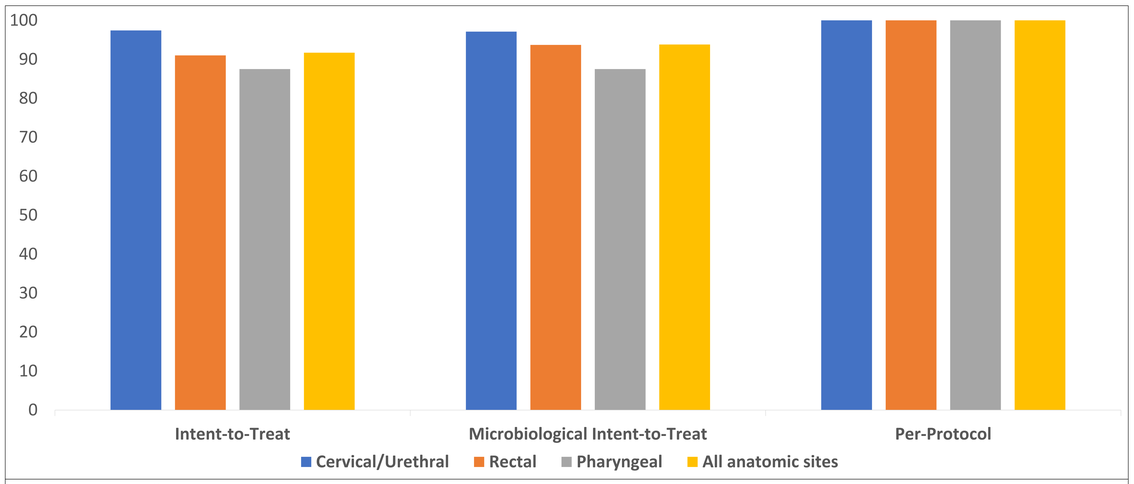
METHODS

- We conducted a large multi-site prospective clinical study of the efficacy of a single oral dose of ciprofloxacin 500mg in patients with culture-positive gonorrhea
- We recruited and enrolled study participants from 8 STD clinics across the U.S.
- We determined *N. gonorrhoeae gyrA* serine 91 wild type status using a previously Clinical Laboratory Improvement Act-verified laboratory-developed polymerase chain reaction (PCR) assay with high – resolution melt analysis
- We report outcomes in participants who were *N. gonorrhoeae* culture positive for *gyrA* serine 91 wild type infection at enrollment and had culture assessment 5-10 days after treatment
- We also report treatment outcomes in cases with non-wild type *gyrA* serine 91 *N. gonorrhoeae* infections at enrollment

Resistance-guided treatment of *N. gonorrhoeae* infections with single dose oral ciprofloxacin was highly efficacious

In this clinical study, 100% (95% one-sided confidence interval 97.5-100%) of 117 infections among 106 evaluable subjects were successfully treated using single dose oral ciprofloxacin

Figure: Microbiologic cure percentages by anatomic site and study population



Intent-to-treat: All subjects with culture-positive *N. gonorrhoeae* infection at enrollment
Microbiological Intent-to-Treat: Only subjects with *gyrA* serine 91 wild type *N. gonorrhoeae* culture-positive result at enrollment
Per-Protocol: Subjects from the microbiological intent-to-treat population with a follow-up culture result collected within the protocol-specific window (5-10 days after enrollment) and who did not receive any additional antibiotics

RESULTS

- Among 106 patients with 117 infections across 8 clinics, the frequency of microbiological cure was 100% (95% one-sided confidence interval 97.5-100%)
- The cure frequency did not vary by anatomic site of infection, sex or age of the study participant
- Two cases with mutated gyrase A *N. gonorrhoeae* infection failed therapy (0% cure)

Table: Characteristics of the per-protocol study population

Characteristics	N	%
Age, years (mean, SD)	28.1	7.9
Male	98	92.5%
Sexual orientation		
Heterosexual / straight	16	15.1%
Homosexual / gay / lesbian	73	68.9%
Bisexual	14	13.2%
Other/refused to answer	3	2.8%
Race/Cultural Origin		
American Indian/Alaskan Native	2	1.9%
Asian	7	6.6%
Hawaiian/Pacific Islander	1	0.9%
African American/Black	29	27.4%
White	57	53.8%
Multiracial	5	4.7%
Other/Unknown	5	4.7%

CONCLUSIONS

- Resistance-guided treatment of *N. gonorrhoeae* infections with single dose oral ciprofloxacin was highly efficacious
- *GyrA* serine 91 *N. gonorrhoeae* genotyping was highly predictive of clinical outcomes in patients with gonorrhea treated with ciprofloxacin
- In settings where the majority of gonococcal infections are ciprofloxacin susceptible, the use of resistance- guided therapy has substantial medical and public health benefits

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