infection for testing antibiotics that utilize free time above MIC as the pharmacokinetic (PK) driver to predict efficacy. We further established the mouse model for antibiotic testing by defining the in vivo efficacy of ciprofloxacin (CIP), an antibiotic that uses the free area under the curve over MIC (f/AUC/MIC).

Methods Lower genital tract infection with N. gonorrhoeae using in vivo methods for two days, after which increasing oral doses of CIP (or controls) were administered (n = 10–20 mice/group) and infection was quantified for 8 days. Plasma drug levels from uninfected mice were measured after administration of similar doses of CIP, and PK parameters (modeled using WinNonlin software) were correlated with observed efficacy.

Results Single oral doses ranging from 5 to 60 mg/kg CIP showed significant activity against strain FA1090, with the highest doses (15, 30, and 60 mg/kg) clearing 100% of infections within 8 days; these correspond to predicted f/AUC/MICs of 66–264. The 60 mg/kg dose cleared infection in all mice within 48 h, which we defined previously as the endpoint in the model that best correlates with in vivo exposures required for successful CRO/CFX treatment regimens.

Conclusion The gonorrhea mouse model shows a dose-dependent response for CIP against a CIP-resistant strain with a dose of 60 mg/kg required to clear infection in 48 hrs. PK modeling suggests that achieving exposures necessary for effective treatment of CIPR strains (mic ≥ 1 μg/ml) would be challenging. These data that establish PK/PD correlations for CIP - with a f/AUC/MIC driver - further strengthens the usefulness of this mouse model to test novel antimicrobial compounds against gonorrhea.

Disclosure No significant relationships.

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GENTAMICIN SUSCEPTIBILITY TO NEISSERIA GONORRHOEAE IN MALAWI AFTER TWENTY-FIVE YEARS OF SUSTAINED USE

Background Gentamicin has been used exclusively for the treatment of Neisseria gonorrhoeae (GC) in Malawi, since 1993. Previous gentamicin susceptibility testing in 1993, 1996 and 2019, showed ≥95% susceptibility by both agar dilution and E-test. However, clinical cure rates 1–2 weeks following treatment, have been in the 90% range. We are in the process of repeating this assessment to inform treatment guidelines.

Methods We are enrolling HIV-infected men presenting with acute urethritis at the sexually transmitted infections (STI) clinic at Bwaila District Hospital in Lilongwe, Malawi. All participants provide urethral swabs for STI etiologic testing, and are treated syndromically per Malawian standard of care, with gentamicin 240 mg IM, doxycycline 100 mg, BID for 7 days, and metronidazole 2g single dose. Patients are seen one week post-treatment for repeat clinical exam and GC culture. All specimens with a positive GC culture are tested locally for gentamicin susceptibility via E-test. E-test inhibition with ranges from 0-4, 4-16, and ≥16 are categorized as high, moderate, and low susceptibility, respectively. Clinical cure is determined by genital examination.

Results 42 men with gonococcal urethritis have been enrolled to date. Baseline gentamicin E-test results: high susceptibility: 0-1: 21%; 1-2: 60%; 2-4: 19%; moderate or low susceptibility ≥4: 0%. 37/42 men (88%) returned for follow-up. 4/37 (11%) were culture positive for GC, including 2 (5%) symptomatic men. 3/4 (75%) of the week one E-test results were in the high susceptibility range, and 1/4 (25%) was in the low susceptibility range (≥16).
Conclusion Based on our E-test results, all of the baseline GC isolates appear to be susceptible to gentamicin. However, at one-week follow-up, ~11% continued to be infected with GC. Determining if these are treatment failures, re-infections or new infections is a challenge. Laboratory comparisons of matched isolates are planned to help categorize these concerning results. Study enrollment continues.

Disclosure No significant relationships.