

and ciprofloxacin were determined using Etest or agar dilution method.

**Results** For AZD0914, the MIC range, modal MIC, MIC<sub>50</sub> and MIC<sub>90</sub> was ≤0.002–0.25 mg/L, 0.125 mg/L, 0.064 mg/L and 0.125 mg/L, respectively. The MIC values were substantially lower than those of the fluoroquinolone ciprofloxacin and most other antimicrobials examined. No cross-resistance with any other examined antimicrobial was observed.

**Conclusion** The *in vitro* susceptibility to the novel spiropyrimidinetrione AZD0914 among 873 contemporary clinical isolates from 21 European countries was high and no cross-resistance to antimicrobials currently or previously used for gonorrhoea treatment was indicated. Additional studies investigating the *in vitro* and *in vivo* induction and mechanisms of AZD0914 resistance in gonococci, pharmacokinetics/pharmacodynamics in modelling/simulations and in humans, and performance in randomised controlled gonorrhoea treatment trials, are essential.

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### 006.3 HOST-DIRECTED THERAPEUTICS AS ADJUNCTIVE THERAPY FOR ANTIBIOTIC-RESISTANT *NEISSERIA GONORRHOEAE*

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**Background** Due to the emergence of antibiotic resistance, novel therapies such as host-directed therapeutics (HDT) are being explored as adjunctive therapies against *Neisseria gonorrhoeae* (Gc). Inhibitors of histone deacetylases (HDACi) are HDTs that restore the balance between host histone acetylases and HDAC, the latter of which are induced by pathogens to enhance infection. We recently reported that sulforaphane (SFN), a natural HDACi, induced effectors with anti-Gc activity in tissue culture cells and reduced colonisation of female mice. Here we tested SFN against the multidrug-resistant strain HO41 and its potential to increase the susceptibility of this strain to antibiotics.

**Methods** ME180 cervical epithelial cells were treated with 40 or 80 μM SFN or no SFN for 24 h. Cell culture supernatants were then incubated with HO41; in some experiments, sub-lethal concentrations of ciprofloxacin (CIP) or cefixime (CFX) were added to the supernatants. The number of viable Gc recovered after a 4-hour incubation was determined by quantitative culture.

**Results** Supernatants from cervical cells treated with 40 or 80 μM SFN reduced the survival of strain HO41 to 53% and 20%, respectively, relative to recovery from supernatants from untreated cells. Addition of sub-inhibitory concentrations of CIP or CFX to supernatants from SFN-treated (40 μM) cells resulted in a dose-dependent reduction in survival, with 4 μg/ml CIP resulting in 27% survival. Two and 4 μg/ml doses of CFX resulted in 13% and 7% survival, respectively. Addition of 1, 2 and 4 μg/ml of CFX to supernatants from cells treated with 80 μM SFN reduced survival to 15%, 8% and 1%, respectively.

**Conclusion** The susceptibility of strain HO41 to CIP or CFX is enhanced when tested in tissue culture media containing SFN-induced host effectors. These findings suggest that a combination of HDACi and antibiotics may be an effective adjunct therapy against antibiotic-resistant Gc.

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### 006.4 AZITHROMYCIN VERSUS DOXYCYCLINE FOR UROGENITAL CHLAMYDIA: A RANDOMISED CLINICAL TRIAL IN FEMALES AND MALES IN YOUTH CORRECTIONAL FACILITIES

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**Background** Urogenital *Chlamydia trachomatis* infection (“chlamydia”) remains highly prevalent and causes significant reproductive morbidity. Earlier randomised chlamydia treatment trials comparing azithromycin 1g versus a 7-day regimen of doxycycline 100mg twice daily reported high cure rates, but used less sensitive diagnostics and results may have been confounded by chlamydia re-exposure or doxycycline nonadherence. Recent studies have raised concern about azithromycin efficacy for chlamydia.

**Methods** We conducted a randomised trial comparing azithromycin versus doxycycline for chlamydia in males and females in youth correctional facilities (YCFs) to evaluate for noninferiority of azithromycin compared to doxycycline. Treatment was directly observed and participants had no furloughs from the YCF throughout the study. The primary endpoint was treatment failure at 28 days after treatment initiation, determined by nucleic acid amplification test results, sexual history, and *C. trachomatis* OmpA genotyping.

**Results** Of 567 participants enrolled, 284 were randomised to azithromycin and 283 to doxycycline. There were 155 participants in each treatment arm comprising the per protocol population: 65% male and 35% female. No treatment failures occurred in the doxycycline arm. In the azithromycin arm, five treatment failures occurred (3.2%; 95% CI: 0.4–7.4%): four were males (3.9%; 95% CI: 1.1–9.7%) and one female (1.9%; 95% CI: 0.0–10.1%). The observed failure rate difference in the treatments was 3.2%, with a 90% upper CI of 5.9%, exceeding the predetermined 5% cutoff for establishing azithromycin noninferiority.

**Conclusion** Doxycycline had a 100% cure rate for chlamydia. Noninferiority of azithromycin to doxycycline was not established in this study, although azithromycin treatment failures occurred infrequently and the high azithromycin cure rate was consistent with earlier chlamydia treatment trials. Because of possible chlamydia treatment failures when azithromycin is used, further surveillance is needed and doxycycline might be considered for persons with suspected chlamydia treatment failure following azithromycin treatment.

**Disclosure of interest statement** Nothing to Declare.