Background Resistance in Neisseria gonorrhoeae to all therapeutic antimicrobials for gonorrhoea has emerged. Novel antimicrobials for treatment are imperative and the first-in-class spiropropymidinetrione zoliflodacin appears promising. Zoliflodacin could be introduced in dual antimicrobial therapies to prevent the emergence and/ or spread of resistance. We investigated the in vitro activity and induction/selection of resistance to zoliflodacin alone and in combination with six novel, currently or previously used therapeutic antimicrobials against N. gonorrhoeae.

Methods The international gonococcal reference strains examined were WHO F (wild-type), and WHO O, WHO V, and WHO X (strains with different AMR profiles). Zoliflodacin was evaluated alone or in combination with ceftriaxone, spectinomycin, gentamicin, tetracycline, cethromycin, and sitafloxacin in checkerboard assays, time-kill curve analysis, and induction/selection of resistance studies.

Results Zoliflodacin alone or in combination with all six antimicrobials showed rapid rates of in vitro bacterial killing against all examined strains in time-kill studies. Tetracycline or cethromycin combined with zoliflodacin decreased the rate of zoliflodacin growth inhibition, while ceftriaxone or gentamicin increased the rate of cell killing. The frequency of induced/selected zoliflodacin resistance mutations was low for zoliflodacin and further reduced for all antimicrobial combinations. All resistant mutants contained the GyrB mutations D429N, K450T or K450N, resulting in zoliflodacin MICs of 0.5 mg/L consistent with previous results.

Conclusion Zoliflodacin, alone or in combination with STI therapeutic antimicrobials has a rapid and high in vitro efficacy against gonococci with low resistance emergence. Zoliflodacin remains a promising novel oral therapeutic for gonorrhoea monotherapy and as part of dual antimicrobial therapy with low resistance emergence potential. A phase III clinical trial evaluating efficacy and safety of zoliflodacin for uncomplicated gonorrhoea treatment is planned in 2019.

Disclosure No significant relationships.