ceftriaxone with other antibiotics leads to faster clearance. TOC for pharyngeal Ng 7 days after treatment may be too soon.

Support: This study was funded by Excellence Scholarship Program (Beasiswa Unggulan), Ministry of Research, Technology and Higher Education, Republic of Indonesia and Public Health Service of Amsterdam, the Netherlands

005.3 A PHASE II, RANDOMISED, STUDY IN ADULT SUBJECTS EVALUATING THE EFFICACY, SAFETY, AND TOLERABILITY OF SINGLE DOSES OF GEPOTIDACIN (GSK2140944) FOR TREATMENT OF UNCOMPLICATED UROGENITAL GONORRHOEA

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10.1136/sextrans-2017-053264.26

Introduction Gonorrhoea is currently the second most common bacterial sexually transmitted infection and represents a serious public health threat. The increasing antimicrobial resistance in *Neisseria gonorrhoeae* (GC) to currently available therapies is driving an urgent need for new novel agents. Gepotidacin (GEP) is a novel, first in class triazaacenaphthylene antibacterial which inhibits bacterial DNA replication. This multicenter (11 US and 1 UK) trial evaluated GEP as a single oral dose in men and women.

Methods Patients with signs and symptoms of urogenital gonorrhoea, a prior culture or nucleic acid amplification test (NAAT) positive for GC, a urethral Gram stain with intracellular diplococci, or who had sexual contact with an individual diagnosed with gonorrhoea in the past 14 days were eligible for enrollment. Participants were randomised 1:1 to receive either 1.5g or 3g GEP orally. The primary efficacy endpoint was culture confirmed microbiological eradication at test-of-cure (TOC) visit 3–7 days post dose.

Results 106 patients (101 men and 5 women) were randomised and 105 received treatment. Baseline GC isolates were identified in 69 (65%) urogenital, 3 (3%) pharyngeal, and 4 (4%) rectal specimens. Microbiological success was achieved by 97% and 95% of subjects with urogenital GC in the 1.5g and 3g treatment groups, respectively. Isolates from 2 subjects developed resistance to GEP between baseline and TOC. The most common GEP-related AEs were gastrointestinal (diarrhoea, flatulence, abdominal pain and nausea) with the majority being mild or moderate in intensity. Treatment-related AEs of moderate intensity occurred with a higher incidence in the 3g treatment group than the 1.5g treatment group (15% and 10%, respectively). There were no AEs that led to study withdrawal and no SAEs were reported.

Conclusions Both the GEP 1.5g and 3g single doses eradicated urogenital GC with microbiological success rates of 29/30 (97%) and 37/39 (95%), respectively. The data support further development of GEP in this indication.

Support: This study was supported by GSK (BTZ116576; NCT02294682). This project was funded in whole or in part with Federal funds from the Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority (BARDA), under agreement # HHSO100201300011C

005.4 DOES HIGH-LEVEL AZITHROMYCIN RESISTANCE EMERGE FROM LOW-LEVEL RESISTANCE IN *NEISSERIA GONORRHOEA*?

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10.1136/sextrans-2017-053264.27

Introduction High-level azithromycin (Azi) resistance (HL-AziR) threatens gonorrhoea dual therapy (ceftriaxone 500 mg and Azi 1g) as it renders Azi ineffective. Between November 2014–2016, 58 cases of HL-AziR (MIC >256 mg/L) *N. gonorrhoeae* (NG) were detected in England. Whole genome sequencing (WGS) revealed that most HL-AziR isolates were from a single clade (NG-MAST ST9768) with an A2059G mutation in 3/4 or all 4 alleles of the 23S rRNA gene. Lower-level AziR (MICs 1.0–32 mg/L) is commonly associated with a C2611T 23S rRNA gene mutation and *mtrR* promoter mutations. We performed WGS of ST9768 isolates with Azi susceptibility (MICs).

Methods WGS was performed on 7 non-HL-AziR ST9768 isolates from Scotland isolated in 2014. A phylogeny was constructed using the maximum likelihood algorithm based on whole genome variants. Genetic resistance determinants were analysed by mapping the WGS short reads to the 23S rRNA gene.

Results All ST9768 isolates with Azi MICs of 0.12–1.0 mg/L were part of the same WGS clade as the ST9768 HL-AziR isolates. One susceptible isolate (MIC 0.12 mg/L) had 0/4 mutated (A2059G) 23S rRNA alleles, five susceptible isolates (MICs 0.25 mg/L) had 1/4 mutated alleles and one low-level resistant isolate (MIC 1.0 mg/L) had 2/4 mutated alleles. No isolates carried the C2611T mutation.

Conclusion This is the first report of the A2059G mutation in NG isolates with Azi MICs of 0.25–1.0 mg/L. The phylogeny suggested that the HL-AziR ST9768 isolates are descendants of the low-level AziR isolates, which are in turn, descendants of the susceptible isolates. We hypothesise that azithromycin exposure provided selection pressure for one or two mutated copies of the 23S rRNA gene to recombine with wild-type copies, leading to 3 to 4 mutated copies in HL-AziR isolates. Greater understanding of the prevalent mechanisms of lower level AziR is required as HL-AziR could emerge in isolates with A2059 mutations and eliminate the effectiveness of dual therapy.

005.5 WHAT ROLE DOES IMPORTATION PLAY IN THE SPREAD OF ANTIMICROBIAL RESISTANT *NEISSERIA GONORRHOEA* IN THE UK? ASSOCIATIONS BETWEEN ANTIMICROBIAL RESISTANT STRAINS AND RECENT SEX ABROAD

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10.1136/sextrans-2017-053264.28

Introduction People living in Britain who have sex abroad are more likely to report sexual behaviour that puts them at greater risk of acquiring STIs, including *Neisseria gonorrhoeae*