A PHASE II, RANDOMISED, STUDY IN ADULT SUBJECTS
DOES HIGH-LEVEL AZITHROMYCIN RESISTANCE
EMERGE FROM LOW-LEVEL RESISTANCE IN NEISSERIA
GONORRHOEAE?

005.4

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. gon-
rhoeae (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 0.12–32 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 iso-
lates from Scotland isolated in 2014. A phylogeny was con-
bstructed 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 0.25–1.0 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.

005.3

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 triazaacenaphy-
lene 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 gon-
rhorrhea, a prior culture or nucleic acid amplification test
(NAAT) positive for GC, a urethral Gram stain with intracel-
lar 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 rando-
mised 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 (diar-
rhoea, flatulence, abdominal pain and nausea) with the major-
ity 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 with-
drawal 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.

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005.5

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

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.