Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for A Phase III, Randomized, Multicenter, Open-Label Study in Adolescent and Adult Participants Comparing the Efficacy and Safety of Gepotidacin to Ceftriaxone Plus Azithromycin in the Treatment of Uncomplicated Urogenital Gonorrhea Caused by *Neisseria gonorrhoeae*
Compound Number	:	GSK2140944
Effective Date	:	13 Oct 2023

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol BTZ116577.
- This RAP is intended to describe the full analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for study BTZ116577.

Revision Chronology:	
Version	Date
Original	05 Oct 2022
Amendment No. 1	16 Mar 2023

Updates include:
• Minor formatting and typographical updates.
• Alignment with changes in Protocol Amendment 2:
  ○ Increased the total number of enrolled participants from approximately 600 to approximately 620 (Section 2.3).
  ○ Primary analysis population (Micro ITT) updated with ceftriaxone susceptibility evaluated using EUCAST breakpoints (Section 4).
• Clarified primary and secondary efficacy estimands variable/endpoint attribute to state that for microbiological success participant must not receive other systemic antimicrobials prior to the TOC assessment (Section 2.2.1).
• Clarified text on declaration of superiority (Section 2.4).
• Clarified that all Microbiologically Evaluable analysis populations include the condition that actual treatment is the same as randomized (Section 4).
• Added Micro-ITT CLSI Analysis Population (Section 4) for the sensitivity analysis for the primary analysis including isolates identified as resistant by EUCAST but susceptible by CLSI (Section 7.1.6.2).
• Removed references to Lu K., Guo H. Multiple imputation analysis of Miettinen-Nurminen interval for difference in proportions, Pharmaceutical Statistics. 2021;1–13 as this method will not be used (Section 7.1.6.1, Section 7.1.6.2 and Section 11).
• Updated confidence interval methods for pooled estimates (after using Rubin's rules) to Wald-type confidence intervals for both the multiple-imputation and tipping point sensitivity analyses (Section 7.1.6.2).
• Clarified that there will be no multiplicity adjustment or formal hypothesis testing of secondary or exploratory endpoints, but that confidence intervals may be included for descriptive purposes (Section 7.2.6 and Section 7.3.3).
• Added Adverse Reactions analyses (Section 8.5).
• Clarified efficacy analyses for Benefit/Risk (Section 10).
• Clarification on "Out of stability" isolates for the Keepers file (Section 12.4.2).
• Clarification on the calculation of MIC_{50} and MIC_{90} (Section 12.4.2).
• Removed imputation rules for laboratory parameter character values (Section 12.4.3).
• Removal of laboratory values not relevant to this study (Section 12.7).
• Added note regarding All Analyses Complete (AAC) (Section 12.9.3).	

Amendment No. 2	13 Oct 2023
Updates Include: • Minor formatting and typographical updates throughout. • Added a note for clarification that "systemic antimicrobials before the TOC Visit" in the intercurrent event strategy for the efficacy estimands in Table refers to "other systemic antimicrobials" i.e., excluding the investigational product (Section 2.2.1). • For the Micro-ITT population, ceftriaxone susceptibility determination has been changed to CLSI from EUCAST guidelines in order to meet regulatory submission requirements (Section 4). Additionally:	

  - Micro-ITT CLSI population amended to Micro-ITT EU population (Section 4).
  - References to EUCAST in primary analysis updated to CLSI (Section 7.1).
  - Sensitivity analysis for the primary analysis changed from being based on Micro-ITT CLSI to Micro-ITT EU population (Section 7.1.6.2) and corresponding text relating to determination of ceftriaxone susceptibility by disk diffusion (CLSI guidelines) added.
  - Provision added for the reproduction of any summaries or listings using populations based on CLSI guidelines to be repeated on the equivalent population but using EUCAST guidelines for the determination of ceftriaxone susceptibility (Section 4 and Section 7).
- Added clarification that the Micro-ITT population will be used for Study Population summaries as well as Efficacy summaries (Section 4).
- Added clarification that for participants with more than 1 NG isolate recovered at baseline from the same body site, all of the isolates must be susceptible to ceftriaxone for that participant to be included in the Micro-ITT populations (Section 4).
- Added clarification on the handling of out of stability NG negative samples at the TOC visit for the purposes of Microbiologically Evaluable populations (Section 4).
- Added clarification that final determination of population inclusion will be performed after final data extraction and that two pre-specified criteria for ME populations will be applied on unblinded data (Section 4).
- Added clarification that the Micro-ITT CAPA population may be defined, and corresponding supplementary analysis be conducted, if one or more sites/investigators had a CAPA that stipulates that a supplementary analysis should be conducted, as agreed by a GSK multidisciplinary team (Section 4 and Section 7.1.6.3).
- Summary of randomized versus actual pooled strata added (Section 5.4.1).
- Clarified that any medication or vaccine that the participant is receiving within 6 months prior to the Baseline Visit or receives during the study will be recorded (Section 6.1.3).
- Added instructions on how to handle estimation of risk differences and CIs when 100% (or 0%) success rates are observed in both treatment arms (Section 7).
- Updated denominator for bacterial eradication rate equation to correctly reflect the population of interest (Section 7.1.2).
- Clarified that the overall test for homogeneity will use the combined pooled strata levels (Section 7.1.6.1).
- Added summaries for further granularity of reasons for microbiological failure and on the use of systemic antibiotics (Section 7.1.6.1).
- Clarified that 'randomized' treatment group will be used in the multiple imputation sensitivity analysis logistic regression model (Section 7.1.6.2).
- Added instructions on the handling of dominant pathogens in the multiple imputation analysis and updated text on MIC grouping for clarity (Section 7.1.6.2).
- Added provision for repeating MI and tipping point sensitivity analyses, if data warrant, with all missing microbiological response data imputed, irrespective of the reason for missingness (Section 7.1.6.2).
- Clarified that for the tipping point sensitivity analysis, CIs will be displayed for the risk difference but not for the proportion of successes within each treatment arm as not required (Section 7.1.6.2).
- Added provision for repeating MI and tipping point analyses with a higher number of imputations, should results be considered sensitive to the random number seed and/or number of imputations (Section 7.1.6.2).
- Added instructions for handling MI / tipping point analyses in situations where between imputation variance is zero (Section 7.1.6.2).
- Added provision for additional sensitivity analyses if data warrant repeating the primary analysis (Micro-ITT) and Micro-ITT EU sensitivity analyses but excluding participants whose ceftriaxone

susceptibility was determined by disk diffusion (Section 7.1.6.2).

- Added analyses of phenotypes and genotypes within subgroups (Section 7.1.6.5).
- Clarified that some summaries will be presented at the isolate level, so that participants with multiple isolates may enter a descriptive summary more than once. However, when point estimates and confidence intervals are presented, results will be presented at the participant-level (Section 7.1.6.5).
- Updated disk diffusion summary statistics to include median and standard deviation but not include the mode and add that results will not be displayed if <10 isolates (Section 7.3.1.2).
- Added that the relatedness of pre- and post-baseline isolates (e.g., as it relates to 4-fold increases and/or microbiological failures) will be described in a stand-alone report, if needed (Section 7.3.1.3).
- Added that analyses of reduction in susceptibility may be repeated for study treatments by phenotypic and genotypic subgroups (Section 7.3.1.3).
- Clarified that the relatedness of pre- and post-baseline isolates (e.g., as it relates to 4-fold increases and/or microbiological failures) will be described in a stand-alone report, if needed (Section 7.3.1.3).
- Updated NAAT FU analyses (Pharyngeal NG and Urogenital Mgen) of microbiological response to be unadjusted since it is anticipated that there will be insufficient observations to adequately perform an adjusted analysis (Section 7.3.1.5).
- Added clarification that both CLSI and EUCAST versions of the Micro Review Aid will be created (Section 7.3.1.6).
- Added non-serious drug-related AEs to AE types to be summarised (Section 8.1)
- Added Cockroft-Gault formula for determination of renal impairment by baseline CrCL (Section 8.3).
- Clarified that Adverse Reactions will be reported in the regulatory submission but are not required as part of the CSR (Section 8.5).
- Updated Benefit-Risk analysis to additionally include incidence of any AE (Section 10).
- Updated references (Section 11).
- Added data-handling instructions relating to extra NAAT specimens i.e., where both urine and swab specimen are taken for the central laboratory urogenital NAAT at the same visit/timepoint (Section 12.4.2).
- Added further clarification on the Keepers file process (Section 12.4.2).
- Added clarification on the determination and handling of Out-of-Stability samples (Section 12.4.2).
- Updated instructions on handling laboratory values with non-detectable levels reported in the data base (Section 12.4.3).
- Updated output numbering, titles and programming notes in list of data displays as required and included additional summaries added in this RAP update (Appendix 9, Section 12.9).

2. SUMMARY OF KEY PROTOCOL INFORMATION

This Phase III study (BTZ116577) aims to evaluate the efficacy and safety of oral gepotidacin compared to intramuscular (IM) ceftriaxone plus oral azithromycin, a currently recommended treatment regimen, for the treatment of uncomplicated urogenital gonorrhea (GC) caused by *Neisseria gonorrhoeae* (NG).

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes to the planned statistical analyses specified in protocol amendment 3 (GSK Document Number: TMF-16433266, Dated 10 Aug 2023). Additional analysis sets to those described in the protocol are given in Section 4.

2.2. Study Objective(s) and Estimand(s) / Endpoint(s)

Objectives	Endpoints
Primary	**Primary**
To evaluate the efficacy of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin to treat participants with uncomplicated urogenital gonorrhea caused by *Neisseria gonorrhoeae* (NG)	Culture-confirmed bacterial eradication of NG from the urogenital body site (i.e., microbiological success) at the TOC (Day 4 to 8) Visit
Secondary	**Secondary**
To evaluate the efficacy of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin to treat participants with rectal gonorrhea caused by NG	Culture-confirmed bacterial eradication of NG from the rectal body site (i.e., microbiological success) at the TOC (Day 4 to 8) Visit
To evaluate the efficacy of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin to treat participants with pharyngeal gonorrhea caused by NG	Culture-confirmed bacterial eradication of NG from the pharyngeal body site (i.e., microbiological success) at the TOC (Day 4 to 8) Visit
To evaluate the safety and tolerability of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin	Treatment-emergent adverse events (AEs) and serious AEs (SAEs) and change from baseline results for clinical laboratory tests and vital sign measurements
Exploratory	**Exploratory**
To assess the clearance or persistence of NG nucleic acid (by nucleic acid amplification test [NAAT] assay) from urogenital specimens for oral gepotidacin compared to IM ceftriaxone plus oral azithromycin	Urogenital NG NAAT results at the TOC (Day 4 to 8) Visit
To assess the clearance or persistence of NG nucleic acid (NAAT assay) from pharyngeal specimens for oral gepotidacin compared to IM ceftriaxone plus oral azithromycin	Pharyngeal NG NAAT results at the TOC (Day 4 to 8) and Follow-up (Day 14 to 21) Visits, where only participants who did not receive other systemic antimicrobials at or after the TOC (Day 4 to 8) Visit will be evaluated at the Follow-up Visit
To assess the clearance or persistence of NG nucleic acid (NAAT assay) from rectal specimens for oral gepotidacin compared to IM ceftriaxone plus oral azithromycin	Rectal NG NAAT results at the TOC (Day 4 to 8) Visit
To assess the clearance or persistence of *Mycoplasma genitalium* (Mgen) nucleic acid (by NAAT assay) from urogenital specimens for oral gepotidacin compared to IM ceftriaxone plus oral azithromycin	Urogenital Mgen NAAT results at the Follow-up (Day 14 to 21) Visit, where only participants who did not receive other systemic antimicrobials at or after the TOC (Day 4 to 8) Visit will be evaluated
To evaluate the microbiological characteristics and antimicrobial susceptibility profile of NG from urogenital, pharyngeal, or rectal specimens	Gram stain (urogenital specimens only), bacterial culture, and in vitro susceptibility test results from urogenital, pharyngeal, or rectal specimens at the Baseline (Day 1), TOC (Day 4 to 8), and Follow-up (Day 14 to 21), as data permits

2.2.1. Estimands

The primary clinical question of interest is: What is the treatment effect on the culture-confirmed bacterial eradication of NG from the urogenital body site (i.e., microbiological success) at the TOC (Day 4 to 8) Visit after treatment with oral gepotidacin compared to IM ceftriaxone plus oral azithromycin in participants with uncomplicated urogenital gonorrhea and have confirmed NG isolated from baseline culture of their urogenital specimen, regardless of treatment discontinuation for any reason.

Prespecified estimands with related attributes are presented in Table 1 for the primary and secondary objectives.

Table 1 Estimands

Estimand Category	Estimand				
	Variable/Endpoint	**Population**	**Treatment Condition**	**Summary Measure**	**Intercurrent Event Strategy**
Primary Objective: To evaluate the efficacy of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin to treat participants with uncomplicated urogenital gonorrhea caused by NG					
Primary	Microbiological success: Participants with culture confirmed bacterial eradication of NG from the urogenital body site (i.e., urogenital microbiological success) at the TOC (Day 4 to 8) Visit without the participant receiving other systemic antimicrobials prior to the TOC assessment. Refer to Table 2 for further details on the endpoint definition, including the missing data strategy for participants who do not return for the TOC Visit	Participants with uncomplicated urogenital gonorrhea caused by culture confirmed NG	Gepotidacin 2×3000 mg versus Ceftriaxone 500 mg plus azithromycin 1 g, regardless of adherence	Difference in proportions (microbiological success rate in the gepotidacin treatment group - ceftriaxone plus azithromycin treatment group)	Participants who receive systemic antimicrobials before the TOC Visit will be considered microbiological failures (composite strategy) For study treatment discontinuation, the data will be analyzed as collected (treatment policy strategy)

Estimand Category	Estimand				
	Variable/Endpoint	**Population**	**Treatment Condition**	**Summary Measure**	**Intercurrent Event Strategy**
Secondary Objective: To evaluate the efficacy of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin to treat participants with rectal gonorrhea caused by NG in the Micro ITT Population					
Secondary	Participants with culture-confirmed bacterial eradication of NG from the rectal body site (i.e., rectal microbiological success) at the TOC (Day 4 to 8) Visit without the participant receiving other systemic antimicrobials prior to the TOC assessment. Refer to Table 2 for further details on the endpoint definition, including missing data strategy for participants who do not return for the TOC Visit	Participants with uncomplicated urogenital and rectal gonorrhea caused by culture-confirmed NG	Gepotidacin 2×3000 mg versus Ceftriaxone 500 mg plus azithromycin 1 g, regardless of adherence	Difference in proportions (microbiological success rate in the gepotidacin treatment group - ceftriaxone plus azithromycin treatment group)	Participants who receive systemic antimicrobials before the TOC Visit will be considered microbiological failures (composite strategy) For study treatment discontinuation, the data will be analyzed as collected (treatment policy strategy)

Estimand Category	Estimand				
	Variable/Endpoint	**Population**	**Treatment Condition**	**Summary Measure**	**Intercurrent Event Strategy**
Secondary Objective: To evaluate the efficacy of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin to treat participants with pharyngeal gonorrhea caused by NG					
Secondary	Participants with culture-confirmed bacterial eradication of NG from the pharyngeal body site (i.e., pharyngeal microbiological success) at the TOC (Day 4 to 8) Visit without the participant receiving other systemic antimicrobials prior to the TOC assessment. Refer to Table 2 for further details on the endpoint definition, including the missing data strategy for participants who do not return for the TOC Visit	Participants with uncomplicated urogenital and pharyngeal gonorrhea caused by culture-confirmed NG	Gepotidacin 2×3000 mg versus Ceftriaxone 500 mg plus azithromycin 1 g, regardless of adherence	Difference in proportions (microbiological success rate in the gepotidacin treatment group - ceftriaxone plus azithromycin treatment group)	Participants who receive systemic antimicrobials before the TOC Visit will be considered microbiological failures (composite strategy) For study treatment discontinuation, the data will be analyzed as collected (treatment policy strategy)

Estimand Category	Estimand				
	Variable/Endpoint	**Population**	**Treatment Condition**	**Summary Measure**	**Intercurrent Event Strategy**
Secondary Objective: To evaluate the safety and tolerability of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin					
Secondary (Safety)	Treatment-emergent AEs and serious AEs and change from baseline results for clinical laboratory tests and vital sign measurements	Participants with uncomplicated urogenital gonorrhea	Gepotidacin 2×3000 mg versus Ceftriaxone 500 mg plus azithromycin 1 g, regardless of adherence	The proportions for treatment-emergent AEs and serious AEs will be produced for each arm **separately**. The means for change from baseline results (clinical laboratory results and vital sign measurements) will be produced for each arm **separately**.	For study treatment discontinuation, the data will be analyzed as collected (treatment policy strategy)

1. AE=adverse events; NG=*Neisseria gonorrhoeae*; TOC=Test-of-Cure. Note that “systemic antimicrobials before the TOC Visit” refers to "other systemic antimicrobials” i.e., excluding the investigational product (see Table 2).

Rationale for estimands:

The rationale for a treatment policy intercurrent event strategy of study treatment discontinuation is that interest lies in the treatment effect irrespective of whether the full course of treatment was taken or not, this is reflective of how patients may be treated in clinical practice.

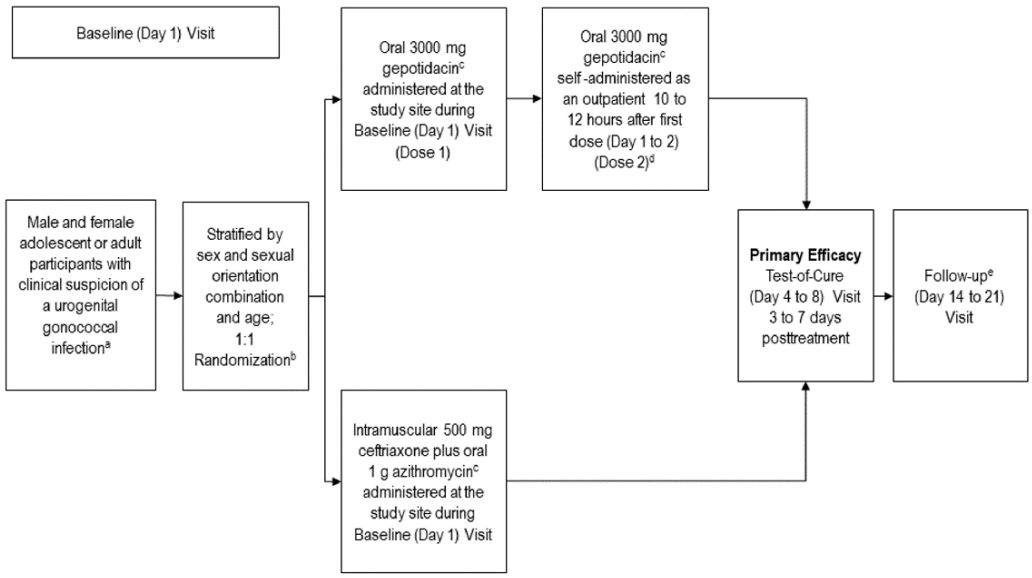
The rationale for using a composite strategy for the intercurrent event of antimicrobial use is because usage could affect bacterial culture response; thus, a conservative approach has been adopted and if a participant receives systemic antimicrobials before the TOC Visit, the participant will be assumed to be a microbiological failure. Note: The intercurrent event of antimicrobial use is not applicable for the safety estimands.

2.3. Study Design

Overview of Study Design and Key Features

The study design schematic is shown in Figure 1.

Figure 1 Study Design Schematic



a. Refer to Inclusion Criterion #2 in protocol amendment 3 for details regarding urogenital gonococcal infection eligibility requirements.
b. Stratification will be performed before randomization to ensure that treatment groups are balanced with regard to sex, sexual orientation and age.
c. Study treatment will be administered under open-label conditions. All doses of oral study treatment should always be taken after food consumption and with water.
d. Participants randomly assigned to gepotidacin will self-administer their second dose (3000 mg) as an outpatient 10 to 12 hours after the first dose; however, for participants who weigh <50 kg or have moderate renal impairment, the second dose should be taken approximately 12 hours after the first dose.
e. Participants will return to the study site anytime from Day 14 to 21 for a Follow-up Visit. The investigator and/or study site staff should make every effort to ensure a participant returns for this visit. If it is determined that a participant is unable to return to the study site, the Follow-up Visit assessments may be completed via telephone, with the exception of assessments requiring sample collection for laboratory testing.

Overview of Study Design and Key Features	

Design Features	• Phase III, randomized, multicenter, open-label (sponsor-blinded), comparator-controlled, noninferiority study
	• The study duration is approximately 21 days with 3 planned study visits:
	  • Baseline (Day 1) Visit
	  • TOC (Day 4 to 8) Visit
	  • Follow-up (Day 14 to 21) Visit
	• The study will screen and randomize approximately 620 participants to obtain approximately 400 participants with culture-confirmed urogenital gonorrhea in the Micro-ITT Population, for an estimated total of 200 participants per treatment group in the Micro-ITT Population. Enrollment will continue until the target number of participants in the Micro-ITT Population has been reached.

Dosing	• Participants will receive 1 of the following study treatments:
	  • Gepotidacin: 3000 mg administered orally at the study site during the Baseline (Day 1) Visit followed by self-administration of a second oral 3000-mg dose as an outpatient 10 to 12 hours after the first dose.
	  • Ceftriaxone plus azithromycin: A single IM 500-mg dose of ceftriaxone plus a single oral 1-g dose of azithromycin administered at the study site during the Baseline (Day 1) Visit.

Time & Events	• Refer to Appendix 1: Schedule of Activities
Treatment Assignment	• Participants will be stratified by sex and sexual orientation (men who have sex with men [MSM], men who have sex with women [MSW], or female) and age (<18 years, ≥18 to 65 years, or >65 years). The MSM category will include MSM and bisexual males (i.e., male participants who have sex with both males and females) and participants ≥12 years will be included in the study. Eligible participants will be randomly assigned in a 1:1 ratio to receive 1 of the study treatments (gepotidacin or ceftriaxone plus azithromycin) with dosing as described above.
Interim Analysis	• No interim analyses are planned for this study.

2.4. Statistical Hypotheses /Statistical Analyses

The study is designed to demonstrate that gepotidacin administered orally is noninferior compared to ceftriaxone plus azithromycin on the primary efficacy endpoint of culture-confirmed eradication of NG from the urogenital body site (i.e., microbiological success) at the TOC visit.

The following are null and alternative hypotheses for the primary analysis of the microbiological success rate at the prespecified noninferiority margin of -10%:

H_0: Microbiological success rate of gepotidacin – Microbiological success rate of ceftriaxone plus azithromycin ≤ -10.0%

H_1: Microbiological success rate of gepotidacin – Microbiological success rate of ceftriaxone plus azithromycin > -10.0%

Gepotidacin will be declared noninferior to treatment with ceftriaxone plus azithromycin if the lower limit of the 2-sided 95% confidence interval (CI) for the difference between the microbiological success rate of gepotidacin and ceftriaxone plus azithromycin at the TOC visit is above -10.0%.

If noninferiority is declared between gepotidacin and ceftriaxone plus azithromycin, then superiority will be tested using the following null and alternative hypothesis:

H_0: Microbiological success rate of gepotidacin – Microbiological success rate of ceftriaxone plus azithromycin ≤ 0%

H_1: Microbiological success rate of gepotidacin – Microbiological success rate of ceftriaxone plus azithromycin > 0%

Superiority of gepotidacin will be declared if the lower end of the 2-sided 95% CI is above 0%. Testing for superiority using 2.5% level of significance will occur if noninferiority is achieved and one-sided p-value will be calculated.

The difference in microbiological success rate between the 2 treatment groups and the corresponding CI will be computed using the Miettinen and Nurminen (MN) method (Miettinen, 1985) stratified by sex and sexual orientation (men who have sex with men [MSM], men who have sex with women [MSW], or female) combination. In the event that any participants are mis-stratified, for the primary efficacy analysis, the actual sex and sexual orientation collected in eCRF will be used to create actual pooled stratification. A sensitivity analysis of the primary efficacy analysis will also be conducted from the pooled stratification as randomized (Section 7.1.6.2).

3. PLANNED ANALYSES

3.1. Interim Analyses

No formal interim analyses are planned.

3.2. Final Analyses

The final planned primary analyses will be performed after the completion of the following sequential steps:

1. All participants have completed the study as defined in the protocol at the FU visit.
2. All protocol deviations captured and categorized, and analysis populations defined.
3. All final database cleaning and data lock activities completed by data management.
4. All criteria for the unblinding of participant randomization codes have been achieved.
5. All randomization codes have been distributed per standard operating procedures.
6. All access to unblinded data prior to the final DBF will be restricted in accordance with the Master Blinding Plan.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened Population	• All participants who were screened for eligibility.	• Study Population
Intent-to-Treat (ITT) Population	• All participants randomly assigned to study treatment. • Participants will be analyzed according to their randomized treatment arm	• Study Population • Efficacy
Microbiological ITT (Micro-ITT) Population	• All participants randomly assigned to study treatment who receive at least 1 dose of study treatment and have confirmed NG isolated that is ceftriaxone-susceptible (based on CLSI breakpoints) from baseline culture of their urogenital specimen. • Participants will be analyzed according to their randomized study treatment arm. • This is the primary analysis population.	• Study Population • Efficacy
Microbiological ITT FDA (Micro-ITT FDA) Population	• All participants randomly assigned to study treatment who receive at least 1 dose of study treatment and have confirmed NG isolated that is ceftriaxone-susceptible (based on CLSI breakpoints) from baseline culture of their urogenital specimen plus participants who have missing susceptibility and NG isolated at the local laboratory, identified using a recognized method. • Participants will be analyzed according to their randomized study treatment arm.	• Study Population

Population	Definition / Criteria	Analyses Evaluated
Microbiological ITT EU (Micro-ITT EU) Population	• All participants who meet the definition of the Micro-ITT population and any participants randomly assigned to study treatment who receive at least 1 dose of study treatment and have confirmed NG isolated that is ceftriaxone-susceptible (based on EUCAST breakpoints) from baseline culture of their urogenital specimen. • Participants will be analyzed according to their randomized study treatment arm.	• Efficacy
Micro-ITT Rectal Population	• Participants who meet the definition of the Micro-ITT Population and have confirmed NG isolated that is ceftriaxone susceptible from baseline culture of their rectal specimen. • Participants will be analyzed according to their randomized study treatment.	• Efficacy
Micro-ITT Pharyngeal Population	• Participants who meet the definition of the Micro-ITT Population and have confirmed NG isolated that is ceftriaxone susceptible from baseline culture of their pharyngeal specimen. • Participants will be analyzed according to their randomized study treatment.	• Efficacy
Microbiologically Evaluable (ME) Population	• Participants who meet the definition of the Micro-ITT Population and follow important components of the study (i.e., (1) receive all planned doses as randomized and actual treatment is the same as randomized, (2) have a urogenital specimen collected at the TOC Visit, with available culture results, (3) have not taken any other systemic antibiotic prior to TOC, unless it was taken for the current infection, and (4) have no major deviation that prevents evaluation of efficacy). • Participants will be analyzed according to their randomized treatment arm.	• Efficacy
Microbiologically Evaluable (ME) Rectal Population	• Participants who meet the definition of the Micro-ITT Rectal Population and follow important components of the study (i.e., (1) receive all planned doses as randomized and actual treatment is the same as randomized, (2) have a Rectal specimen collected at the TOC Visit, with available culture results, (3) have not taken any other systemic antibiotic prior to TOC, unless it was taken for the current infection, and (4) have no major deviation that prevents evaluation of efficacy). • Participants will be analyzed according to their randomized treatment arm.	• Efficacy
Microbiologically Evaluable (ME) Pharyngeal Population	• Participants who meet the definition of the Micro-ITT Pharyngeal Population and follow important components of the study (i.e., (1) receive all planned doses as randomized and actual treatment is the same as randomized, (2) have a Pharyngeal	• Efficacy

Population	Definition / Criteria	Analyses Evaluated
	specimen collected at the TOC Visit, with available culture results, (3) have not taken any other systemic antibiotic prior to TOC, unless it was taken for the current infection, and (4) have no major deviation that prevents evaluation of efficacy). • Participants will be analyzed according to their randomized treatment arm.	
ME NAAT TOC Population	• Participants who meet the definition of the Micro-ITT and follow important components of the study and were NG NAAT positive at baseline (i.e., (1) receive all planned doses as randomized and actual treatment is the same as randomized, (2) have a Urogenital NAAT specimen collected at the TOC Visit, with available NAAT results, (3) have not taken any other systemic antibiotic prior to TOC, unless it was taken for the current infection, and (4) have no major deviation that prevents evaluation of efficacy). • Participants will be analyzed according to their randomized treatment arm.	• Efficacy
ME NAAT TOC Rectal Population	• Participants who meet the definition of the Micro-ITT Rectal Population and follow important components of the study and were NG NAAT positive for Rectal specimen at baseline (i.e., (1) receive all planned doses as randomized and actual treatment is the same as randomized, (2) have a Rectal NAAT specimen collected at the TOC Visit, with available NAAT results, (3) have not taken any other systemic antibiotic prior to TOC, unless it was taken for the current infection, and (4) have no major deviation that prevents evaluation of efficacy). • Participants will be analyzed according to their randomized treatment arm.	• Efficacy
ME NAAT TOC Pharyngeal Population	• Participants who meet the definition of the Micro-ITT Pharyngeal Population and follow important components of the study and were NG NAAT positive for Pharyngeal specimen at baseline (i.e., (1) receive all planned doses as randomized and actual treatment is the same as randomized, (2) have a Pharyngeal NAAT specimen collected at the TOC Visit, with available NAAT results, (3) have not taken any other systemic antibiotic prior to TOC, unless it was taken for the current infection, and (4) have no major deviation that prevents evaluation of efficacy). • Participants will be analyzed according to their randomized treatment arm.	• Efficacy
ME NAAT FU Mgen Population	• Participants who meet the definition of the Micro-ITT and follow important components of the study and were Mgen (urogenital) NAAT positive at baseline (i.e., (1) receive all planned doses as randomized and actual treatment is the same as randomized, (2) have Mgen (urogenital) NAAT specimen collected at	• Efficacy

Population	Definition / Criteria	Analyses Evaluated
	the FU Visit, with available NAAT results, (3) have not taken any other systemic antibiotic prior to FU, unless it was taken for the current infection, and (4) have no major deviation that prevents evaluation of efficacy). • Participants will be analyzed according to their randomized treatment arm.	
ME NAAT FU Pharyngeal Population	• Participants who meet the definition of the Micro-ITT Pharyngeal Population and follow important components of the study and were NG (pharyngeal) NAAT positive at baseline and TOC (i.e., (1) receive all planned doses as randomized and actual treatment is the same as randomized, (2) have a NG (pharyngeal) NAAT specimen collected at the FU Visit, with available NAAT results, (3) have not taken any other systemic antibiotic prior to FU, unless it was taken for the current infection, and (4) have no major deviation that prevents evaluation of efficacy). • Participants will be analyzed according to their randomized treatment arm.	• Efficacy
Safety Population	• All participants who receive at least 1 dose of study treatment. • Participants will be analyzed according to their actual treatment received	• Safety

1. NAAT = Nucleic Acid Amplification Test.
2. Refer to Appendix 9: List of Data Displays.
3. Note:
   - The Micro-ITT populations are based on culture confirmed NG isolates at the central laboratory. Ceftriaxone susceptibility will be evaluated by applying CLSI MIC breakpoints to results from ceftriaxone agar dilution testing (or EUCAST MIC breakpoints in the case of the Micro-ITT EU population). If an agar dilution value is not available for ceftriaxone, CLSI disk diffusion breakpoints will be applied to results from ceftriaxone disk diffusion testing for the Micro-ITT populations (including Micro-ITT EU). The ceftriaxone MIC breakpoints for *N. gonorrhoeae* currently differ between CLSI and EUCAST, if isolates are identified with different interpretations applying the EUCAST breakpoints as compared to CLSI, any populations/subjects/isolates impacted by the difference in breakpoints will be described in the text as narratives and additional sensitivity analyses for the primary endpoint may be performed (Section 7.1.6.2). Further, any summaries and listings presented on CLSI-based populations may be repeated on EUCAST-based equivalent populations, as required (see Section 7).
   - The term “ME Population” is used to refer to all ME Populations and the term “NAAT Population” is used to refer to all NAAT populations.
   - Micro-ITT FDA population will be used for listings only and not summaries.
   - If more than 1 NG isolate is recovered at baseline from the same participant and body site, all of the isolates must be susceptible to ceftriaxone for the participant to be included in the corresponding Micro-ITT populations.
   - If a participant has an out-of-stability urogenital sample at the TOC visit which is NG negative then that participant is not considered as having ‘available culture results’ for the purposes of ME Population criterion 2: “have a urogenital specimen collected at the TOC Visit, with available culture results”. The same rule will be applied to the other ME populations for the corresponding body sites.

Inclusion into the ITT and Safety Population will be determined programmatically from eCRF data.

Inclusion criteria for the Micro-ITT/Micro-ITT Rectal/Micro-ITT Pharyngeal, ME Populations, and NAAT Populations will be determined programmatically and through manual review conducted by the Sponsor. The Sponsor will be blinded to treatment assignment and may review the data concurrent with conduct of the study. Final determination of population inclusion will be performed after final extraction and prior to unblinding. Exclusion from ME Populations related to receipt of incorrect study drug and related to receipt of other systemic antimicrobials not for the current infection (see e.g., ME Population criteria 1 and 3) will be determined programmatically on unblinded data using the prespecified criteria in Section 4.

In the event that one or more investigators/sites receive a corrective and preventative action (CAPA) that stipulates a supplementary analysis should be conducted excluding them as agreed by a multidisciplinary GSK team prior to unblinding, a supplementary analysis will be performed. A flag will be included to identify subjects enrolled by those investigators/sites. This will enable further subpopulations to be defined for the primary analysis population (Micro-ITT). These sub populations (micro-ITT [CAPA]) may be defined which will consist of all subjects in the micro-ITT population excluding subjects from those investigative sites (e.g., micro-ITT (CAPA)).

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management or participant assessment) will be summarized and listed. In addition, important deviations which result in exclusion from analysis populations will be listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan, entitled Study Deviation Rules Document.

- Data will be reviewed prior to unblinding and locking the database to define all analysis populations, and thus ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorized in the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of important protocol deviations.

A separate listing of all inclusion/exclusion criteria deviations will also be provided. This listing will be based on data as recorded on the inclusion/exclusion page of the electronic case report form (eCRF).

5. CONSIDERATIONS FOR DATA ANALYSIS AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions	
Data Displays for Reporting	
Description	**Order in TFL**
Gepotidacin 2x 3000 mg	1
Ceftriaxone 500 mg plus azithromycin 1 g	2

Note: Total across treatment groups will be presented for study population, safety, and selected microbiology displays.

Whilst the scientific formatting requirements for bacterial nomenclature is for genus and species names to be italicized, with first letter of genus upper case, and rest of the genus and species name in lower case, system limitations have resulted in the lack of italicization in TFL outputs.

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value (or randomization date for participants who are randomized but did not receive treatment), including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline. Unless otherwise stated, if baseline data is missing, then change from baseline calculations will not be performed and will be set to missing.

5.3. Multicenter Studies

In this multicenter global study, enrollment will be presented by investigative site, country, and region for descriptive summaries. Data from all sites will be combined for statistical analyses; analyses will not be adjusted by site.

5.4. Examination of Covariates, Other Strata and Subgroups

In the case of a difference between the stratification assigned at the time of randomization and the data collected in the eCRF:

- subgroups will be summarized based on the actual subgroup to which the participant belongs,
- covariate adjustment will be based on the actual strata for primary analysis.

5.4.1. Strata and Other Covariates

The list of covariates and other strata may be used in descriptive summaries and statistical analyses, some of which may also be used for subgroup analyses. Additional covariates and other strata of clinical interest may also be considered.

- If the number of participants is small within a category of a covariate or strata, then the covariate/strata categories may be further refined prior to unblinding the trial.
- If the category cannot be refined further, then the covariate may be included as a continuous measure.

Participants will be randomized to a treatment arm using stratification by sex and sexual orientation (men who have sex with men [MSM], men who have sex with women [MSW], or female) and age (<18 years, ≥18 to 65 years, or >65 years). The MSM category will include MSM and bisexual males (i.e., male participants who have sex with both males and females).

Summaries of participants for whom the randomized and actual strata differ, quantifying the number of participants whose strata differ between the primary analysis (adjusting for actual pooled strata) and the relevant sensitivity analysis (adjusting for pooled strata as randomized, Section 7.1.6.2) will be provided.

Randomized Stratification Factor	**Randomized Stratification Level**
Age Category	<18 years
	≥18 to 65 years
	>65 years
Sex and Sexual Orientation	Men who have sex with men (and females) (MSM)
	Men who have sex with women (MSW)
	Female

The stratification combinations are as follows:

Randomized Stratification Value	Randomized Stratification Description
1	<18 years, MSM
2	<18 years, MSW
3	<18 years, Female
4	≥18 to 65 years, MSM
5	≥18 to 65 years, MSW
6	≥18 to 65 years, Female
7	>65 years, MSM
8	>65 years, MSW
9	>65 years, Female

For primary analysis, stratification values (after combining the three age strata) are defined as follows:

Stratification Value	Stratification Description
1	MSM
2	MSW
3	Female

Other covariates considered in statistical analyses (for logistic regression used in multiple imputation):

Covariates
Randomized treatment
Sex and sexual orientation (MSM, MSW, or female)
Interaction term between treatment and MIC (gepotidacin or ceftriaxone plus azithromycin) for randomized treatment
Site (Sites with <10 participants in the Micro-ITT Population may be combined prior to unblinding)

5.4.2. Examination of Subgroups

Subgroup analyses will be performed using the following categories for the efficacy analyses. Treatment group differences will be displayed for subgroups with ≥10 participants across both treatment groups. Additional subgroups of clinical interest may also be considered. If the number of participants is small within a subgroup, then the subgroup categories may be refined prior to unblinding the trial.

Subgroup	Categories
Age category	<18 years, ≥18 to 65 years, or >65 years
Sex and sexual orientation	Male (MSM, MSW), or Female
Stratification combinations	as defined in Section 5.4.1 (for above mentioned age and sex and sexual orientation categories)
Ethnicity	Hispanic, not Hispanic
Race	White, Black or African American, Asian, American Indian or Alaskan Native, Native Hawaiian or other Pacific Islander, Multiple
Region	Americas (United States and Mexico), Europe: (Germany, Spain, and United Kingdom), Asia-Pacific: Australia
Country	United States, Mexico, Germany, Spain, United Kingdom and Australia
FDA Region	United States regions: • Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont • South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia • Midwest: Ohio, Michigan, Indiana, Illinois, Wisconsin, Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas • West: Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming • Pacific: Alaska, Hawaii (Not applicable)
Baseline BMI Category	•<25 kg/m2 •≥25-<30 kg/m2 •≥30 kg/m2
Phenotypic and genotypic subcategories	as defined in Section 7.1.6.5
Number of sexual partners	1-5, 6-10, 11-15, greater than 15 (for primary endpoint only)
Recreational drug use	Yes, No (for primary endpoint only)
Co-infections	With or without co-infection with *Chlamydia trachomatis* and/or *Mycoplasma genitalium* (for primary endpoint only)
Multiple Body Sites	With or without infections at multiple body sites (for primary endpoint only)
Renal impairment	Creatinine clearance <30 mL/min, ≥30 to 59 mL/min, ≥60 to 89 mL/min, ≥90 mL/min (for primary endpoint only)
HIV Status	HIV positive, HIV negative (for primary endpoint only)

The following subgroups will be explored for the safety analyses:

Subgroup	Categories
Age category	<18 years, ≥18 to 64 years, ≥65 to 74 years, ≥ 75 years
Sex	Male or Female
Race	White, Black or African American, Asian, American Indian or Alaskan Native, Native Hawaiian or other Pacific Islander, Multiple
Region	Americas (United States and Mexico), Europe: (Germany, Spain, and United Kingdom), Asia-Pacific: Australia
Renal impairment	Creatinine clearance <30 mL/min, ≥30 to 59 mL/min, ≥60 to 89 mL/min, ≥90 mL/min
HIV Status	HIV positive, HIV negative

If the number of participants is small (i.e., <10 participants) within a subgroup, then the subgroup categories may be refined prior to unblinding the trial.

5.5. Multiple Comparisons and Multiplicity

The primary comparison of interest is the comparison between oral gepotidacin to IM ceftriaxone plus oral azithromycin for the primary endpoint of urogenital microbiological success in the Micro-ITT population. This analysis will be adjusted for stratification factors at randomization that are defined in Section 5.4.1. The issue of multiple comparisons in the primary analysis will be addressed via a hierarchical testing strategy (Fixed-Sequence Method, FDA 2022), that is, the noninferiority of gepotidacin to treatment with ceftriaxone plus azithromycin must first be achieved before subsequently testing for superiority as described in Section 2.4. The statistical analyses of all other efficacy endpoints will be descriptive in nature, and therefore, will not be subject to multiplicity adjustments.

5.6. Analysis Visits

Due to participants potentially returning outside the protocol scheduled visit window, analysis visit windows will be defined for by-visit summaries and analysis purposes as illustrated in the table below. Data not reported by-visit, including adverse events and concomitant medications, will not employ analysis visits. Analysis visit labels will be assigned to each post-baseline record (including records from unscheduled and early termination visits) based on the corresponding study day (relative to first study treatment or randomization if not treated). For post-baseline records collected outside the analysis visit window, a blank analysis visit label will be assigned. For example, a record collected at study Day 11 will not be utilized in any analyses conducted at the TOC or FU scheduled visit. Descriptive summaries that are shown for “any assessment post baseline” e.g., maximum/minimum/ worst case post baseline, will use all assessments irrespective of whether they fall in an analysis visit window. There are no scheduled FU assessments for Urogenital (except Mgen participants) or rectal body site, but it is possible that any unscheduled assessment or a late TOC fall into this FU window and in that case FU visit will not be presented in summaries but in listings it will be included.

Scheduled Post-baseline Visit	Protocol Window	Target Day	Analysis Visit Window (Days)
Test-of-Cure	4 to 8	6	4 to 10
Follow-up	14 to 21	18	13 to 24

If multiple records exist within the same analysis visit window, then the record occurring closest to the target day will be utilized in all analyses and analysis population determinations. If multiple records are equally close to the target day, then the later record will be utilized. If multiple records occur on the same day and time is not collected, then the record with the larger Study Data Tabulation Model (SDTM) record sequence number will be utilized in all analyses. All protocol scheduled assessments (including unscheduled and early termination visits) will be presented in subject listings. Both the nominal and analysis visit will be presented in listings.

5.7. Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the appendices:

Section	Component
12.1	Appendix 1: Schedule of Activities
12.2	Appendix 2: Study Phases and Treatment Emergent Adverse Events
12.3	Appendix 3: Data Display Standards & Handling Conventions
12.4	Appendix 4: Derived and Transformed Data
12.5	Appendix 5: Reporting Standards for Missing Data
12.6	Appendix 6: Values of Potential Clinical Importance
12.7	Appendix 7: Division of Microbiology and Infectious Diseases Toxicity Tables for Adverse Event Assessment
12.8	Appendix 8: Abbreviations & Trademarks
12.9	Appendix 9: List of Data Displays

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the ITT population and the primary analysis population (Micro-ITT), unless otherwise specified.

Study population analyses including analyses of participant's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Baseline disease characteristics including baseline NG recovery rate (including body site of recovery), substance use, and past and current medical conditions will be summarized. Baseline ECG results will be provided in listings. Social sexual history will be summarized and provided in listings.

Details of the planned displays are presented in Appendix 9.

6.1.1. Disposition and Withdrawals

A summary of the number of participants included in each of the analysis populations defined in Section 4 will be provided. A listing and summary of participants excluded from each analysis population will be provided.

The number and percentage of participants enrolled by country and site will be summarized for each treatment group and overall for the ITT Population.

Participant disposition will be tabulated for each study treatment and for all participants combined with the number and percentage of participants who complete the study, prematurely withdraw, and the reason for study withdrawal for ITT and Micro-ITT Populations. A listing of the reasons for study withdrawal will be provided. A separate listing of the reasons for treatment discontinuation will also be provided.

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently randomized. Participants who are screen failures are not allowed to be rescreened for the same infection episode; however, participants who were screen failures for an earlier infection episode may be newly screened for a second infection episode ≥4 weeks later and participate in the study if they meet all the inclusion and exclusion criteria. Any participant who was originally a screen failure, but is then enrolled after a new screening, will be counted once as a screen failure (for the earlier episode) and once as enrolled (for the second episode). Summary and listing of reasons for screen failures will be produced.

6.1.2. Demographic and Baseline Disease Characteristics

Demographic characteristics such as age, sex, race, ethnicity, childbearing potential, height, weight, and body mass index (BMI) will be summarized and tabulated by treatment and for all participants in ITT and Micro-ITT Populations. Descriptive statistics will be presented for age, height, weight, and BMI. Frequency counts and percentages will be presented for age category (<18 years, ≥18 to 65 years, >65 years as well as 12-

17, 18-64, 65-84, ≥85), sex, ethnicity, renal impairment category and childbearing potential. Age is computed as integer part of (First Dose Date - JUN30 of Collected Birth Year + 1)/365.25; when first dose date is missing, the informed consent date is used. Individual participant demographics (including baseline renal impairment) will be presented in listings.

Race and racial combinations will be summarized and listed as reported using the five high level categories (American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White, Multiple). In addition, the nine standard race categories collected on the Integrated Data Standards Library (IDSL) eCRF along with categories for mixed race will be summarized and listed. Baseline renal impairment will be summarized and included in a listing.

Baseline disease characteristics will be summarized including pre-treatment NG, CT, and Mgen NAAT assay results and presence of white blood cells (WBCs), epithelial cells and bacteria in urogenital bacteriological specimens evaluated by Gram stain. Separately, the overall recovery rate of NG by culture will be summarized by specimen source (urogenital, pharyngeal, and rectal), sex and sexual orientation, and age. The concordance of presumptive diagnosis of NG at baseline visit and NAAT test on samples collected from baseline visit with central lab identification will be summarized, respectively. Data will be listed and summarized using frequency counts and percentages. Serology including HIV, Hepatitis B, and Hepatitis C will also be summarized.

Substance use such as smoking history, cigarettes per day, alcohol consumption, alcohol weekly use, caffeine consumption, and average caffeinated servings per day will also be summarized in ITT and Micro-ITT Populations and listed.

Social sexual history at baseline will be summarized for ITT and Micro-ITT Populations and will be listed. Social sexual history at the TOC visit, since last visit will also be listed separately.

6.1.3. Prior and Concomitant Medications

Any medication or vaccine (including over the counter or prescription medicines, vitamins, and/or herbal supplements) that the participant is receiving within 6 months prior to the Baseline Visit or receives during the study will be recorded. Prior and concomitant medications will be coded using GSK Drug coding dictionary, summarized, and listed using generic term, verbatim text, and indication. Separate summaries of prior and concomitant medications will show the number and percentage of participants in the ITT and Micro-ITT Populations taking each prior and concomitant medications and corresponding Anatomical Therapeutic Chemical (ATC) classification Level 1 information. The number and percentage of participants with prior and concomitant antibiotic medications will be presented. The summary of prior medications will include a separate summary of prior antibiotic medications. The summary of concomitant medications will display separate summaries for systemic concomitant medications, non-systemic concomitant medications, systemic antibiotics taken for the disease under study, systemic antibiotics taken for another disease/condition and prohibited (non-antibiotic) medications. Prohibited concomitant medications are listed in Protocol Appendix 9.

A concomitant medication is considered systemic if the route is oral, subcutaneous, intramuscular, intravenous, or rectal.

All prior and concomitant medications, as well as prior and concomitant antibiotic medications for NG, will be provided in separate listings. Listing of Concomitant Antibiotic Therapies for *Chlamydia trachomatis* or *Mycoplasma genitalium* after TOC Visit also will be provided.

6.1.4. Medical History and Current Medical Conditions

Past (medical history) and current medical conditions will be summarized and displayed by the number and percentage of participants for each body system for ITT and Micro-ITT Populations. They will also be displayed in the listings.

6.1.5. Treatment Exposure

All eligible participants will be randomized to receive two doses of gepotidacin (the first dose administered at the investigational site and the second dose self-administered up to 12 hours later) or a single dose of ceftriaxone plus azithromycin administered at the investigational site. Therefore, exposure duration will not be calculated in this study. A listing of treatment exposure will be provided. A separate listing for gepotidacin compliance will be provided.

7. EFFICACY ANALYSES

Note: For any analyses of binary outcomes discussed in this section for which a risk difference will be estimated, if 100% (or 0%) success rates are observed in both treatment arms then a constant of 1E-10 will be added to each zero cell in the resultant contingency table to overcome software limitations and enable determination of the risk difference and two-sided 95% CI.

The ceftriaxone MIC breakpoints for *N. gonorrhoeae* currently differ between CLSI and EUCAST, if isolates are identified with different interpretations applying the EUCAST breakpoints as compared to CLSI, then any summaries or listings on CLSI-based populations may be repeated on corresponding EUCAST-based populations.

7.1. Primary Efficacy Analyses

The primary clinical question of interest is: What is the treatment effect on the culture-confirmed bacterial eradication of NG from the urogenital body site (i.e., microbiological success) at the TOC (Day 4 to 8) Visit after treatment with oral gepotidacin compared to IM ceftriaxone plus oral azithromycin in participants with uncomplicated urogenital gonorrhea and have confirmed NG isolated from baseline culture of their urogenital specimen, regardless of treatment discontinuation for any reason. For clarification this population are also required to be ceftriaxone susceptible. Further details on the primary estimand are given in Section 2.2.

7.1.1. Endpoint / Variables

The primary efficacy endpoint is culture-confirmed bacterial eradication of NG from the urogenital body site (i.e., microbiological success) at the TOC visit.

- Only those participants who have central laboratory confirmed NG from culture of their baseline bacteriology specimen will be evaluated for microbiological outcome and response. Ceftriaxone susceptibility will be evaluated by applying CLSI MIC breakpoints to results from ceftriaxone agar dilution testing. If an agar dilution value is not available for ceftriaxone, CLSI disk diffusion breakpoints will be applied to results from ceftriaxone disk diffusion testing. The microbiological outcome and response to study treatment will be determined by prespecified programmed algorithm for each participant (see Table 2).
- The microbiological outcome is determined by comparing the baseline culture results to the respective culture results at the TOC visit. The corresponding microbiological response (success or failure) “by participant” is then assigned. The criteria of microbiological participant level outcome and response is shown in Table 2.
- Participant level microbiological success refers to participants who have been deemed a “microbiological success” based on their microbiological response. All other participants are deemed “microbiological failures” for participant level microbiological response.

Table 2 Microbiological Outcome and Response at the Test-of-Cure Visit

Defining Criteria	Microbiological Outcome	Microbiological Response
Culture-confirmed elimination of baseline pathogen (NG) from a bacteriology sample taken at the TOC visit without the participant receiving other systemic antimicrobials before this visit	Bacterial eradication	Microbiological success
Culture-confirmed persistence of baseline NG pathogen from a bacteriology sample taken at the TOC visit without the participant receiving other systemic antimicrobials before this visit	Bacterial persistence	Microbiological failure
1) A determination of the TOC NG pathogen microbiological outcome cannot be made (e.g., no bacteriological sample taken for culture, sample lost, visit did not occur etc.) 2) The participant received other systemic antimicrobials before the TOC visit	Unable to determine	Microbiological failure

1. TOC=Test-of-Cure.
2. Note: A bacteriological specimen refers to a urogenital specimen obtained for bacteriological culture.
3. Note: If the TOC bacteriological specimen is out of stability and the result is Bacterial eradication, then microbiological outcome will be categorized as 'Unable to determine' and if the TOC bacteriological specimen is out of stability and result is Bacterial persistence then microbiological outcome will be characterized as Bacterial persistence (see Section 12.4.2 for further details).
4. Note: If two different strains of *Neisseria gonorrhoeae* are identified from the baseline urogenital culture sample and at the TOC one is eradicated and the other persists, the participant outcome is Bacterial Persistence and response is Microbiological failure.

7.1.2. Summary Measure

The culture-confirmed bacterial eradication rate (i.e., microbiological success rate) for NG from the urogenital site at the TOC visit will be summarized for the gepotidacin and ceftriaxone plus azithromycin treatment arms. The bacterial eradication rate is calculated as:

$$Rate = \frac{Number\ of\ participants\ with\ urogenital\ microbiological\ success\ at\ TOC\ Visit}{Number\ of\ participants\ from\ the\ population\ of\ interest} \times 100\%$$

The summary measure will be the difference in bacterial eradication rate (i.e., microbiological success rate) between the treatment arms (gepotidacin - ceftriaxone plus azithromycin) at TOC visit. The adjusted estimates of the difference in microbiological success rate for the two treatment groups (gepotidacin – ceftriaxone plus azithromycin) will be calculated and summarized with 2-sided 95% CI based on a stratified analysis using Miettinen and Nurminen (MN) method (see Section 7.1.6.1).

7.1.3. Population of Interest

The primary population of interest is participants with uncomplicated urogenital gonorrhea caused by culture-confirmed NG (*Neisseria gonorrhoeae*). For clarification

this population are also required to be ceftriaxone susceptible. The primary analysis of the primary efficacy endpoint will therefore be performed using the urogenital culture confirmed Micro-ITT Population.

7.1.4. Strategy for Intercurrent Events

There are two kinds of ICE:

- Study treatment discontinuation (due to any reason) – treatment policy strategy (the occurrence of the ICE is considered irrelevant in defining the treatment effect of interest).
- Use of systemic antimicrobials - composite strategy. This intercurrent event is captured through the definitions of microbiological response (see Section 7.1.1) and will be counted as microbiological failures.

If a participant experiences both ICE, then a composite strategy (assigning microbiological response as a failure) will be used from the point that the relevant systemic antimicrobial was taken.

7.1.5. Treatment Condition

Gepotidacin 2×3000 mg versus Ceftriaxone 500 mg plus azithromycin 1 g, regardless of adherence.

7.1.6. Statistical Analyses / Methods

7.1.6.1. Statistical Methodology Specification

The primary efficacy endpoint is culture-confirmed bacterial eradication (microbiological success) of NG from the urogenital body site at the TOC visit.

Microbiological success rate and Exact Clopper-Pearson confidence interval (CI) in each treatment group will be calculated. For the statistical analysis, three strata (subgroups) will be formed according to the combinations of levels of the sex and sexual orientation (MSM, MSW, Female) at baseline. For age strata, due to few participants in <18 years and >65 years age categories, the categories <18 years, ≥18 to 65 years and >65 years will be combined for primary statistical analysis, thereby removing the age effect from the analysis. If a participant is mis-stratified, then the actual pooled strata collected in the eCRF will be used in the analysis instead of the randomized pooled strata, unless specified. The effect of this stratification is to provide statistical control over these potentially important prognostic variables.

The adjusted estimates of the difference in microbiological success rate for the two treatment groups (gepotidacin – ceftriaxone plus azithromycin) will be calculated and summarized with 2-sided 95% CI based on a stratified analysis using Miettinen and Nurminen (MN) method.

The Miettinen-Nurminen (score) confidence limits for the treatment difference [Miettinen, 1985] are computed (SAS PROC FREQ [SAS, 2018] uses iterative computation for this). Stratum based point estimates and variances can be estimated from

these CIs. The MN estimate of the common risk difference and variance is computed by combining the point estimates and variances from the individual pooled strata using MN weights. The estimate uses inverse variance stratum weights to produce MN confidence limits for the stratum risk differences. The mathematics and algorithm of MN method can be found in the SAS procedure guide under "Summary Score Estimate of the Common Risk Difference" [SAS, 2018].

This MN method is the primary estimator of the primary efficacy endpoint and will statistically test the null hypothesis contained in Section 2.4. Gepotidacin will be declared noninferior to treatment with ceftriaxone plus azithromycin if the lower limit of the 2-sided 95% confidence interval (CI) for the difference between the microbiological success rate of gepotidacin and ceftriaxone plus azithromycin at the TOC visit is above -10.0%. Superiority of gepotidacin will be declared if the lower end of the 2-sided 95% CI is above 0%. Testing for superiority using 2.5% level of significance will occur if noninferiority is achieved and one-sided p-value will be calculated.
The number and percentage of participants with culture-confirmed bacterial eradication of NG from the body site will be summarized at the TOC visit by treatment group along with the 95% Exact (Clopper-Pearson) CIs.

Microbiological response and microbiological outcome (success, failure, and reason for failure) of NG at the TOC visit will be summarized. Additional summaries providing further granularity into reasons for microbiological failure, including summaries of participants whose microbiological outcome was unable to determine, and further details on use of systemic antibiotics prior to assessments, differentiating use for the disease under study or for other conditions, may be provided.

Supportive analyses will be performed to enable the assessment of the homogeneity of the treatment difference across analysis strata used in the primary analysis.

The weighted least squares chi-squared statistic of [Fleiss, 1981] will be used to test for one-way homogeneity of the treatment difference across the levels of the strata used for the primary analysis. The overall test for homogeneity will use the combined pooled strata levels. Additional tests for homogeneity of the treatment difference across the levels of each pooled strata will be performed, with each pooled strata considered separately. Following Lui and Kelly [Lui , 2000], ½ will be added to each cell in any stratum (pooled) for which the stratum-specific success rate estimates of either gepotidacin or ceftriaxone plus azithromycin are zero or one, and tests will be one-sided. Tests of homogeneity will be assessed at the one-sided 10% level of significance.

For each stratum, the percent of participants with microbiological successes by treatment group and unadjusted difference in percent between treatment groups with corresponding two-sided 95% CI using MN method will be reported. In addition, the *p*-value from the overall test of homogeneity will be reported.

7.1.6.2. Sensitivity Analyses

Sensitivity analyses will be performed to investigate the robustness of the primary efficacy results for the primary estimand. Treatment group differences will be displayed for subgroups with ≥10 participants across both treatment groups, see Section 5.4.2 for

definition of subgroups. The following sensitivity analyses will be performed in the Micro-ITT Population at the TOC visit.

1) An analysis of microbiological response at TOC unadjusted for the stratification factors. Unadjusted difference in proportions between treatment groups (gepotidacin – ceftriaxone plus azithromycin), and corresponding two-sided 95% CI using MN method (adjusting for treatment only) will be presented.
2) An analysis of microbiological response at TOC adjusted for the stratification factors based on the randomization stratum the participant was randomized to (instead of the actual stratum the participant should be assigned to). Difference in the proportion of microbiological responders between each treatment group adjusted by MN weights (using randomized stratification) will be presented along with two-sided 95% CIs (using MN method adjusting for treatment and pooled strata as randomized).
3) A sensitivity estimator for the primary estimand will be determined by dealing with missing values of the microbiological response at TOC per the following:

    - If the entire visit, bacteriology samples were missed due to COVID-19 then the missing value will be assessed using multiple imputation under a missing at random assumption
    - If the bacteriology sample was taken but a result is not available for the sample for any reason, then the missed value will be assessed using multiple imputation under a missing at random assumption
    - All other missing data will be assumed to be a failure

    The rationale for this strategy is that it may be reasonable to assume that missing data due to either COVID-19 or due to microbiology samples which were taken but not able to be processed will not have been impacted by the treatment the patient received or their response to treatment. Microbiology samples may be missing for reasons due to COVID-19 (e.g., out of stability samples arriving at the local lab due to extended shipping times or lack of couriers to pick up the samples within agreed timeframes). But they may also be missing, for example, due to sample packing or mis-labelling issues at the site. In all cases a missing at random multiple imputation will be performed irrespective of the reason the sample is missing. All other missing data will be considered as a failure (i.e., non-responders), consistent with the primary analysis. Multiple imputations will be implemented with the following steps:

    Step 1: Microbiological response will be imputed by multiple imputation using logistic regression models under a missing at random assumption in the Micro-ITT population. The number of imputations will be 1,000 and SEED= 116577. The variables used in the imputation model will include:

    - Sex and sexual orientation (MSM, MSW, or female)
    - Randomized Treatment group
    - Interaction term between treatment and MIC (gepotidacin or ceftriaxone plus azithromycin) for randomized treatment. If needed, this may be refined prior to unblinding. Note: Baseline pathogen (*N. gonorrhoeae*

isolate) will be determined by GSK Microbiology prior to unblinding and will include separate holistic reviews to:

  - identify dominant isolate for participants with more than one *N. gonorrhoeae* isolate at Baseline. This selection will be completed for all participants with more than one *N. gonorrhoeae* isolate at Baseline in the micro-ITT Population, regardless of missing data and will be based on gepotidacin or ceftriaxone and azithromycin MIC value (and phenotypic profile if required) and will identify the dominant *N. gonorrhoeae* isolate for gepotidacin and for ceftriaxone/azithromycin treatment groups as these may differ. This will be documented prior to unblinding. Post unblinding, the dominant *N. gonorrhoeae* isolate for the randomized treatment will be used and the corresponding Baseline *N. gonorrhoeae* MICs will be used in the analysis.
  - Group MICs (gepotidacin or ceftriaxone and/or azithromycin) by randomized treatment which may be based on Baseline *N. gonorrhoeae* isolate. This will be documented prior to unblinding.

- Site (Sites with <10 participants in the Micro-ITT Population may be combined prior to unblinding)

Any subjects that have a missing value for one or more variables listed above will be excluded from the relevant imputation model(s). While logistic regression will be used for the imputation model, the stratified MN statistic will be used for the analysis of each imputed dataset.

Step 2: Step 1 will produce 1,000 imputed datasets with complete data. For each dataset, participants microbiological response will then be derived using the imputed and non-missing data per Section 7.1.1. We will estimate the proportion of success in each treatment group and its standard error using the sample estimates, and the difference in the proportion of success between the two treatment groups and its standard error using the MN method weighted on actual pooled strata as in the primary efficacy analysis for each imputed dataset separately. All estimated quantities (proportion of success in each treatment group, difference between two groups, and their associated standard errors) will be saved for step 3.
Note: the number of imputations may be increased if required following model checking to ensure results are not sensitive to the random number seed and/or number of imputations.

Step 3: The estimated quantities in Step 2 will be combined across the imputed datasets using Rubin's rules to provide pooled estimates for the success rate in each treatment group and for the difference in the proportion of successes between the two treatment groups. The 95% (Wald) CIs will be calculated for the proportions of successes in each arm as well as for the risk difference between the two treatment groups. Testing for superiority may occur if noninferiority is achieved. A one-sided *p*-value will be calculated.

If there is zero between imputation variance, e.g., if there are no missing data to impute, then the methods described in Step 2 will be applied to a single instance of the complete data set and it will not be necessary to combine estimated quantities in Step 3. Note that if the extent of missing data is considered sufficiently high, this analysis may be repeated with all missing microbiological responses at TOC, i.e. irrespective of the reason for missingness, and assessed using multiple imputation logistic regression. Prior to unblinding a review with GSK Microbiology will determine appropriate groupings of MICs (gepotidacin and ceftriaxone plus azithromycin) for the purposes of this analysis.

4) A tipping point analysis may be performed for the primary endpoint in the Micro-ITT population to assess the impact of failure imputation of missing data on the microbiological response at TOC. The scope of missing data will be consistent with the multiple imputation analyses, specifically, if the entire TOC Visit, microbiology samples were missed due to COVID-19 pandemic, then the missed value will be imputed under the MAR assumption. If the TOC microbiology sample was taken but a result is not available for the sample for any reason, then the missed value will also be imputed under the MAR assumption. All other missing data will be considered as a failure (i.e., non-responders) per the primary analysis. The tipping point analysis will vary assumptions on the proportion of participants achieving success in the two treatment groups. For each combination of assumed success rates in the two treatment groups, the number of additional participants achieving success among subjects with missing microbiological response will be imputed by drawing from a binomial distribution.
    - A grid of paired values will be established, ranging from 0 to 1 in steps of 0.025, establishing the assumed response rates for each treatment group in participants with missing microbiological response.
    - For each pair of assumed response rates corresponding to treatment group, $(\theta^{(i)}_{Gepotidacin}, \theta^{(j)}_{Ceftriaxone\ plus\ azithromycin})$, repeat the following steps 100 times:
        - Sample additional responders among participants with missing responses by drawing from a binomial distribution, using the assumed response rate assigned to each treatment group. Sampling will be completed separately by treatment,

$$r^{a}_{Gepotidacin,} \sim \text{Binomial}\ (n^{miss}_{Gepotidacin}, \theta^{(i)}_{Gepotidacin}),$$

$$r^{a}_{Ceftriaxone\ plus\ azithromycin} \sim \text{Binomial}\ (n^{miss}_{Ceftriaxone\ plus\ azithromycin}, \theta^{(j)}_{Ceftriaxone\ plus\ azithromycin})$$

    - The proportion of success in each treatment group and the difference in the proportion of success between two treatment groups as well as the respective associated standard errors will be computed. Standard error of the risk difference estimate will be calculated using the MN method weighted on actual strata.

- Using Rubin's rules we will combine the estimated quantities (success rate in each treatment group, difference in proportions between two groups, and their standard errors). The calculations for pooled estimates will be implemented using SAS PROC MIANALYZE. 95% (Wald) CIs for the risk difference between the two treatment groups will be presented. The noninferiority conclusion will be drawn if lower limit of the 2-sided 95% confidence interval (CI) is above -10.0%. Testing for superiority may occur if noninferiority is achieved and one-sided *p*-values will be calculated.
- The process described above will be repeated for each pair of assumed response rates, $(\theta^{(i)}_{Gepotidacin}, \theta^{(j)}_{Ceftriaxone\ plus\ azithromycin})$.
    - Visual representations of treatment difference and noninferiority decisions will be produced using a colored heatmap illustrating the gradual change of treatment difference. Colored borders will be used to highlight the microbiological response rates that resulted in noninferiority.

If for a pair of assumed response rates there is zero between imputation variance, e.g., if there are no missing data to impute, then the methods described above for calculating the proportion of successes, risk difference and associated standard errors, will be applied to a single instance of the complete data set and it will not be necessary to combine estimated quantities across imputations. Note also that tipping point analysis may be repeated with a greater number of imputations (if necessary over a smaller, refined grid range), if tipping points are considered to be sensitive to the random number seed and/or number of imputations. Furthermore, if the extent of missing data is considered sufficiently high, tipping point analysis may be repeated, imputing all missing microbiological responses at TOC, irrespective of the reason for missingness, using random draws from a binomial distribution as described above.

5) Primary analysis is based on Micro-ITT population using CLSI breakpoints. The ceftriaxone MIC breakpoints for *N. gonorrhoeae* currently differ between CLSI and EUCAST, if isolates are identified with different interpretations applying the EUCAST breakpoints as compared to CLSI, a sensitivity analysis of primary endpoint will be produced on a population defined based on EUCAST breakpoints (Micro-ITT EU). Ceftriaxone susceptibility will be evaluated by applying EUCAST MIC breakpoints to results from ceftriaxone agar dilution testing. If an agar dilution value is not available for ceftriaxone, CLSI disk diffusion breakpoints will be applied to results from ceftriaxone disk diffusion testing. The number and percentage of participants with culture-confirmed bacterial eradication of NG from the body site will be summarized at the TOC visit by treatment group along with the 95% Exact (Clopper-Pearson) CIs. The adjusted estimates of the difference in microbiological success rate for the two treatment groups (gepotidacin – ceftriaxone plus azithromycin) will be calculated and summarized with 2-sided 95% CI based on a stratified analysis (pooled strata) using Miettinen and Nurminen (MN) method. Non-inferiority and superiority will be tested as stated in Section 2.4.

Note that if data warrant, this analysis may be repeated on the Micro-ITT and Micro-ITT EU populations, but excluding participants whose ceftriaxone susceptibility is determined by disk diffusion.

7.1.6.3. Supplementary Analyses

Supplementary analysis of the primary efficacy endpoint will be performed on the Microbiologically Evaluable (ME) Population with all other details as per Section 7.1.6.1.

In the event that one or more investigators/sites receive a CAPA that stipulates a supplementary analysis should be conducted excluding them as agreed by a multidisciplinary GSK team prior to unblinding, a supplementary analysis will be performed. A flag will be included to identify subjects enrolled by those investigators/sites. This will enable further subpopulations to be defined for the primary analysis population (Micro-ITT). These subpopulations (micro-ITT [CAPA]) may be defined which will consist of all subjects in the micro-ITT population excluding subjects from those investigative sites. The methods described for the primary analysis (Section 7.1.6.1) may then be repeated on the newly defined analysis population(s).

7.1.6.4. Subgroup Analyses

Subgroup analyses will be performed for the microbiological success rate at the TOC visit in Micro ITT and ME population. Microbiological success rate and Exact Clopper-Pearson confidence interval in each treatment group at each level will be calculated. Unadjusted difference in microbiological success rate will be included and summarized with 2-sided 95% CI using MN method (adjustment will not be performed). For each specific subgroup, if there are not enough participants (i.e., <10 participants across treatment groups), treatment difference in microbiological success rate and CI will not be derived. A forest plot showing the results for the subgroup analyses of microbiological success rate will be presented.

See Section 5.4.2 for definition of subgroups.

7.1.6.5. NG Phenotype and Genotype Subgroups

- NG isolated at Baseline will be categorized as listed below. The necessity of these categories will depend on the phenotypes that are recovered. Any present in 10 or more participants across treatment groups will be summarized separately.
- Summaries of participant-level microbiological success, failure, and reasons for failure at the TOC (including phenotypic and genotypic subcategories) overall and by subgroup including by sex and sexual orientation (men who have sex with men [MSM], men who have sex with women [MSW], or female) and age (<18 years, ≥18 to 65 years, or >65 years), geographic region, including country and FDA region) will be presented by phenotypic and genotypic subcategories (Note: FDA region for CLSI summaries only). Phenotypic and genotypic subcategory analysis for subgroups as described above will also be conducted for tables showing microbiology summary and frequency MIC and disk diffusion data. Note: these analyses will be conducted for the urogenital body site and, if required, pharyngeal and rectal body sites.

- *Neisseria gonorrhoeae* (NG) [Clinical & Laboratory Standards Institute (**CLSI) Tables and Listings**]
  - Azithromycin-nonsusceptible NG
  - Ciprofloxacin Intermediate NG
  - Ciprofloxacin-resistant NG
  - Extended spectrum cephalosporin (ESC)-nonsusceptible NG
    - Cefixime-nonsusceptible NG
    - Ceftriaxone-nonsusceptible NG
  - Tetracycline-resistant NG
  - β-lactamase positive NG
  - Susceptible to all tested drugs NG
  - Penicillin/Ciprofloxacin and tetracycline -resistant NG
  - Multidrug-resistant (MDR)[a] NG
  - Extensively drug-resistant[b] (XDR) NG

[a]Multidrug-resistant (MDR) NG: [Resistant or nonsusceptible to at least one of the following CFM, AXO or SPT **plus** resistant or non-susceptible to 2 or more of the following antibiotics (CIP, AZM or PEN)]

[b]Extensively drug-resistant (XDR) NG: [Resistant or nonsusceptible to two or more of the following antibiotics (CFM, AXO or SPT) plus resistant or non-susceptible to all 3 of the following antibiotics (CIP, AZM or PEN)]- if isolate meets XDR criteria MDR flag is not added.

- *Neisseria gonorrhoeae* (NG) [European Committee on Antimicrobial Susceptibility Testing (**EUCAST) Tables and Listings**]
  - Azithromycin[a] (No NG EUCAST Breakpoints)
  - Ciprofloxacin Intermediate NG
  - Ciprofloxacin-resistant NG
  - Extended spectrum cephalosporin (ESC)-resistant NG
    - Cefixime-resistant NG
    - Ceftriaxone-resistant NG
  - Tetracycline-resistant NG
  - β-lactamase positive NG
  - Susceptible to all tested drugs NG
  - Penicillin[b]/Ciprofloxacin and Tetracycline -resistant NG
  - Multidrug-resistant (MDR)[c] NG
  - Extensively drug-resistant[d] (XDR) NG

[a]Given that there are no EUCAST azithromycin breakpoints for NG, EUCAST has provided guidance for defining azithromycin resistance for the definition of the MDR/XDR category. When applying EUCAST guidelines, a NG isolate with an azithromycin MIC of >1 ug/mL is considered resistant for the sole purpose of determining azithromycin resistance for the MDR/XDR definition. However,

azithromycin interpretations are not reported in any BTZ116577 tables, listings or figures that apply EUCAST guidelines.

[b]Given that there are no EUCAST penicillin breakpoints for NG, EUCAST has provided guidance for defining penicillin resistance for the definition of the MDR/XDR category. When applying EUCAST guidelines, a NG isolate with a penicillin MIC of >1 ug/mL or a positive Beta-lactamase test is considered resistant for the sole purpose of determining penicillin resistance for the MDR/XDR definition. However, penicillin interpretations are not reported in any BTZ116577 tables, listings or figures that apply EUCAST guidelines.

[c]Multidrug-resistant (MDR) NG: [Resistant to at least one of the following CIX, CTR or SPE **plus** resistant to 2 or more of the following antibiotics (CIP, AZI or PEN)]

[d]Extensively drug-resistant (XDR) NG: [Resistant to two or more of the following antibiotics (CIX, CTR or SPE) plus resistant to all 3 of the following antibiotics (CIP, AZI or PEN)]- if isolate meets XDR criteria MDR flag is not added.

Subcategories for all significant (n≥10 across treatment groups) drug combinations that comprise MDR/ extensively-drug resistant (XDR) will be analyzed (i.e., tetracycline/ciprofloxacin resistant, penicillin/tetracycline/ciprofloxacin resistant). Note: Some categories may be removed, or new categories added based on final data. Key subcategories with n<10 across treatment groups may be displayed. The Microbiology Team will provide advice on the exact list once data is final and before unblinding.

- The main focus will be ciprofloxacin-resistant, azithromycin-nonsusceptible, ESC-nonsusceptible and MDR NG isolates. These categories will be determined phenotypically based on results from antimicrobial susceptibility testing. Other drug-resistant phenotypes may also be summarized if present in 10 or more participants across treatment groups depending on a final decision from the Microbiology Team. Other drug-resistant phenotypes may include but are not limited to: XDR, ciprofloxacin non-susceptible, or resistance to other drug combinations (i.e., tetracycline/ciprofloxacin, penicillin/tetracycline/ciprofloxacin).
    - A NG isolate will be defined as MDR if it is reported as resistant or nonsusceptible to:
        - At least 1 of the antibiotic classes currently generally recommended for treatment (ESCs [oral and injectable ones are considered separately] and spectinomycin) and
        - ≥2 of the of the following: ciprofloxacin, azithromycin or penicillin
    - A NG isolate will be defined as XDR if it is reported as resistant or nonsusceptible to:
        - ≥2 of the antibiotic classes currently generally recommended for treatment (ESCs [oral and injectable ones are considered separately] and spectinomycin) and
        - All 3 of the following: ciprofloxacin, azithromycin, or penicillin. (Note: if isolate meets XDR criteria MDR flag is not added.)
- All NG isolates will also undergo genetic characterization to test for the presence of various resistance mechanisms (e.g., quinolone-resistant determining region

mutations). Other drug-resistant genotypes may also be summarized if present depending on a final decision from the Microbiology Team.

- Phenotype and genotype results will appear in summary tables, listings, and figures as subsets in blocks. Note that if a participant has multiple NG isolated at baseline, all isolates may be presented separately if applicable for the summary section. For summaries where a point estimate and confidence interval are presented, analyses will be conducted at the participant-level (i.e., participant with multiple isolates at baseline is counted once).
- GSK microbiologists will give the detailed list of applicable phenotypes and genotypes once microbiology data becomes available.

7.2. Secondary Efficacy Analyses

The secondary clinical questions of interest are: What is the treatment effect on each of the secondary efficacy endpoints after treatment with two doses of gepotidacin 3000 mg, 10-12 hours apart, compared to a single IM 500-mg dose of ceftriaxone plus a single oral 1-g dose of azithromycin in participants with uncomplicated gonorrhea at the body site of interest (rectal/pharyngeal) who have a confirmed NG isolated from baseline culture of their body site (rectal/pharyngeal) specimen. For clarification this population are also required to be ceftriaxone susceptible. Receipt of systemic antimicrobials impacts the endpoint definition. Further details of the estimands for secondary efficacy endpoints are given in Section 2.2. The statistical analyses of all secondary efficacy endpoints will be descriptive in nature, and therefore, will not be subject to multiplicity adjustments.

7.2.1. Endpoint / Variables

- A secondary efficacy endpoint is culture-confirmed bacterial eradication of NG from the rectal body site (i.e., microbiological success) at the TOC visit.
- A secondary efficacy endpoint is culture-confirmed bacterial eradication of NG from the pharyngeal body site (i.e., microbiological success) at the TOC visit.

For definition and derivation, please refer to Section 7.1.1 Endpoint / Variables. The microbiological outcome and response to study treatment (for the rectal and pharyngeal body sites) will be determined for each participant by the same algorithm described in Table 1 Table 2 for the urogenital body site.

7.2.2. Summary Measure

The summary measure for the secondary analyses will be the difference in culture-confirmed bacterial eradication rates for NG between gepotidacin and ceftriaxone plus azithromycin. A similar method to that described in Section 7.1.2 will be used for determining the summary measure for the secondary endpoints, with replacement of urogenital by rectal or pharyngeal, as applicable.

7.2.3. Population of Interest

The secondary population of interest is male and female participants with uncomplicated urogenital and rectal or pharyngeal (depending on the endpoint) gonorrhea caused by *Neisseria gonorrhoeae*. The secondary analyses of the secondary efficacy endpoints will

therefore be performed using the Micro-ITT Rectal Population and the Micro-ITT Pharyngeal Population.

7.2.4. Strategy for Intercurrent Events

For details of the estimand strategy for intercurrent events see Section 2.1 and Section 2.2.1.

7.2.5. Treatment Condition

Gepotidacin 2×3000 mg versus Ceftriaxone 500 mg plus azithromycin 1 g, regardless of adherence.

7.2.6. Statistical Analyses / Methods

7.2.6.1. Statistical Methodology Specification

There will be no multiplicity adjustment for the testing of the secondary endpoints. No formal hypothesis testing will be performed; 95% CIs may be included but only for descriptive purposes. Microbiological response and microbiological outcome for NG from pharyngeal or rectal body sites will be summarized using the Micro-ITT Rectal, Micro-ITT Pharyngeal, ME Rectal and ME Pharyngeal populations for respective body sites. The number and percentage of participants with culture-confirmed bacterial eradication of NG from the rectal body site will be summarized at the TOC visit by treatment group. The corresponding 95% Exact (Clopper-Pearson) CIs will be summarized for each treatment group. The same analysis will also be presented for the pharyngeal body site. The unadjusted difference in microbiological success rate for the two treatments (gepotidacin – ceftriaxone plus azithromycin) will be calculated and summarized along with its 2-sided 95% CI using MN method (adjustment for strata will not be performed).
Participants who do not return for the TOC visit (or have missing data at TOC for any other reason) will be treated as failures. Participants who withdraw from the study prior to TOC will be considered not achieving success for the microbiological response and will be imputed as failures.

7.2.6.2. Subgroup Analyses

Subgroup analysis for rectal or pharyngeal NG body sites will be done for microbiological response at the TOC visit for sex and sexual orientation, age, and ethnicity. Other subgroups (e.g., phenotypic, and genotypic subgroups) defined in Section 5.4.2 will also be analyzed, as appropriate. Continuous data will be summarized using number of subjects, mean, standard deviation, median, minimum and maximum and categorical data will be presented using counts and percentages in subgroup analysis.

Unadjusted difference in microbiological success rate and summarized with 2-sided 95% CI using MN method will be included (adjustment will not be performed). For each specific subgroup, if there are not enough participants (i.e., <10 participants across treatment groups), the corresponding analyses will not be performed.

Analysis/Endpoint Description	Visit	Population	Subgroup
Microbiological Response of Rectal NG	TOC	Micro-ITT Rectal	Sex and Sexual Orientation
	TOC	Micro-ITT Rectal	Age
	TOC	Micro-ITT Rectal	Ethnicity
	TOC	Micro-ITT Rectal	Other subgroup categories defined in Section 5.4.2 & Section 7.1.6.5
	TOC	ME Rectal	Sex and Sexual Orientation
	TOC	ME Rectal	Age
	TOC	ME Rectal	Ethnicity
	TOC	ME Rectal	Other subgroup categories defined in Section 5.4.2 & Section 7.1.6.5
Microbiological Response of Pharyngeal NG	TOC	Micro-ITT Pharyngeal	Sex and Sexual Orientation
	TOC	Micro-ITT Pharyngeal	Age
	TOC	Micro-ITT Pharyngeal	Ethnicity
	TOC	Micro-ITT Pharyngeal	Other subgroup categories defined in Section 5.4.2 & Section 7.1.6.5
	TOC	ME Pharyngeal	Sex and Sexual Orientation
	TOC	ME Pharyngeal	Age
	TOC	ME Pharyngeal	Ethnicity
	TOC	ME Pharyngeal	Other subgroup categories defined in Section 5.4.2 & Section 7.1.6.5

7.3. Exploratory Efficacy Analyses

There will be no multiplicity adjustment for the testing of the exploratory endpoints. No formal hypothesis testing will be performed; 95% CIs may be included but only for descriptive purposes. The details of data displays being presented are in Appendix 9.

7.3.1. Endpoint / Variables/Analysis

7.3.1.1. Gram stain (urogenital only) results at Baseline and TOC visits

- Variables: Gram stain results (WBCs, epithelial cells, and bacteria) from urogenital specimens
- Analysis: The endpoints will be summarized at the Baseline and TOC visits using counts and percentages for ITT Population. A listing of Gram stain results will be provided.

7.3.1.2. In vitro antibacterial susceptibility testing results for NG from urogenital, pharyngeal, or rectal body sites at Baseline, TOC, and FU visits

- Variables: minimum inhibitory concentrations (MICs) and respective interpretations
- Analysis: For antimicrobial susceptibility, results and interpretation from testing for all NG isolates against gepotidacin and other antimicrobials will be summarized by visit, region, country, FDA region, Sex and Sexual Orientation and NG phenotype and genotype subgroups (including phenotypic and genotypic subcategory analysis for subgroups including age, sex and sexual orientation, region, country and FDA region) and antimicrobials tested, for each body site urogenital, rectal and pharyngeal based on respective populations; Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal, ME, ME Rectal and ME Pharyngeal populations (Note: FDA region only for CLSI summaries). For participants with multiple NG isolates from the same body site at the same visit, unique NG isolate(s) will be selected for analysis as described in Appendix 4 ("keepers data"). For summaries, a participant may be counted multiple times if there are multiple unique NG isolates at baseline for the participant. Percent susceptibility (based on interpretations of susceptible, intermediate, resistant, or nonsusceptible) will be summarized where available. Susceptibility interpretations based on Clinical and Laboratory Standards Institute guidelines (CLSI) and EUCAST will be presented separately.
  The overall frequency distribution of minimum inhibitory concentrations (MICs) and the minimum, maximum, 50th percentile (MIC_{50}), and 90th percentile (MIC_{90}) for MIC will be presented. MIC_{50} and MIC_{90} refer to the corresponding antimicrobial concentrations required to inhibit 50% and 90% of the isolates obtained, respectively. MIC_{50} and MIC_{90} will not be reported if less than 10 isolates are obtained. Details of the MIC_{50} and MIC_{90} calculations are presented in Appendix 4. The overall frequency distribution of the disk diffusion zone diameters and the mean, median, standard deviation, minimum and maximum

disk diffusion zone diameters will be presented. The mean, median and standard deviation will not be reported if less than 10 isolates are obtained.
Analyses will be performed to examine the potential relationship between MIC values for the treatment/isolate pairings and microbiological success at the TOC visit. Similar analyses will be performed based on the disk diffusion results. A listing of the susceptibility results as well as a listing of gepotidacin MIC and disk diffusion results including the microbiological outcomes and responses will be provided.

7.3.1.3. Reduction in susceptibility to gepotidacin

- Variables: reduced susceptibility, defined as a post-baseline *N. gonorrhoeae* isolate with a confirmed ≥ 4-fold increase in MIC result when compared with the baseline MIC of the corresponding *N. gonorrhoeae* isolate from the same participant.
- Analysis: Reduction in susceptibility to gepotidacin will be evaluated by comparing the baseline gepotidacin MIC value based on agar dilution with the value obtained post-baseline. Post-baseline isolates from the same participant and body site with a confirmed ≥ 4-fold increase in gepotidacin MIC is considered to have developed a reduction in susceptibility to gepotidacin. The relatedness of pre- and post-baseline isolates (e.g., as it relates to 4-fold increases and/or microbiological failures) will be described in a stand-alone report, if needed. The number and percentage of participants who develop reduction in susceptibility to gepotidacin will be summarized by visit and body site for ITT population. Similar development of resistance analysis will be conducted for the study comparators ceftriaxone and azithromycin. Analysis of reduction in susceptibility may be repeated for study treatments by phenotypic and genotypic subgroups (CLSI and EUCAST).

7.3.1.4. Beta-Lactamase Production

- Variables: Beta-lactamase production (Positive/Negative)
- Analysis: Beta-lactamase production by specimen source (urogenital, pharyngeal, and rectal) will be summarized by visit for Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal Population. A listing for beta-lactamase production will be provided.

7.3.1.5. NAAT outcome and response

- Variables: NAAT outcome and response will be determined by pathogen (NG or Mgen), body site (as applicable), for the TOC and FU visits as follows:
  - Those participants who have NG detected from their baseline NAAT specimen (urogenital, pharyngeal, rectal) will be evaluated for NAAT outcome and response at TOC visit for urogenital, pharyngeal, rectal respectively. For baseline pharyngeal NG confirmed participants, NAAT specimen will be evaluated at follow up visit as well if both the baseline and TOC pharyngeal NAATs were positive. Participants who have Mgen nucleic acid detected from their baseline NAAT specimen will be evaluated for Mgen NAAT outcome and response at follow up visit. The NAAT outcome and

response to study treatment will be determined by prespecified programmed algorithm for each participant (see Table 3).

- The NAAT outcome will be determined by comparing the baseline NAAT result with the respective NAAT result at each subsequent visit. The corresponding NAAT response (success or failure) by participant will then be assigned. The criteria for determining NAAT outcome and response are shown in Table 3 and Table 4.
- Participants who are a NAAT failure at the TOC visit but have not switched to other systemic antimicrobials with activity against NG are evaluable at FU visit (applicable to pharyngeal NG only).
- Participants who received other systemic antimicrobials on or after the TOC visit will be categorized as Unable to determine for NAAT outcome or response at the FU visit.

Table 3 NAAT Outcome and Response at the TOC Visit (NG Only)

Defining Criteria	NAAT Outcome	NAAT Response
Clearance of baseline pathogen nucleic acid from a specimen taken at the TOC visit, without the participant receiving other systemic antimicrobials before this visit	Nucleic acid clearance	NAAT success
Persistence of baseline pathogen nucleic acid from a specimen taken at the TOC visit, without the participant receiving other systemic antimicrobials before this visit	Nucleic acid persistence	NAAT failure[a]
1) A determination of the nucleic acid outcome from a specimen taken at the TOC visit cannot be made (e.g., no sample taken, sample lost, visit did not occur) 2) The participant received other systemic antimicrobials before the TOC visit	Unable to determine	NAAT failure[a]

NAAT=Nucleic Acid Amplification Test; NG=*Neisseria gonorrhoeae*; TOC = Test-of-Cure.
Note: Specimen refers to either a urogenital, pharyngeal, or rectal specimen obtained for NAAT. The NAAT outcomes are determined on a per-pathogen and per-specimen source basis.

a. Participants who are a "NAAT failure" at the TOC visit assessment yet are not switched to other systemic antimicrobials are evaluable at subsequent time points.

Table 4 NAAT Outcome and Response at the FU Visit (Pharyngeal NG and Urogenital Mgen Only)

Defining Criteria	Microbiological Outcome	Microbiological Response
Clearance of baseline pathogen nucleic acid from a specimen taken at the FU visit, without the participant receiving other systemic antimicrobials before this visit	Nucleic acid clearance	NAAT success
Persistence of baseline pathogen nucleic acid from a specimen taken at the FU visit, without the participant receiving other systemic antimicrobials before this visit	Nucleic acid persistence	NAAT failure
A determination of the nucleic acid outcome from a specimen taken at the Follow-up Visit cannot be made (e.g., no sample taken, sample lost, visit did not occur) Note: Any participants who received other systemic antimicrobials before the Follow-up Visit will not be evaluated for NAAT outcome or response at the Follow-up Visit	Unable to determine	NAAT failure

Mgen=*Mycoplasma genitalium*; NAAT=Nucleic Acid Amplification Test; NG=*Neisseria gonorrhoeae*.
Note: Specimen refers to either a urogenital or pharyngeal specimen obtained for NAAT. The NAAT outcomes are determined on a per-pathogen and per-specimen source basis and will only be conducted if either the Baseline (NG or Mgen) and TOC (NG only) NAAT assay showed the presence of nucleic acid for the respective pathogen and specimen.
Note: Participants who are a "NAAT failure" at the TOC visit assessment yet are not switched to other systemic antimicrobials are evaluable at subsequent time points.

- Analyses: NAAT results (outcome and response) will be summarized by visit for each body site as indicated in the table below. Summaries for NAAT outcome at the TOC visit will be based on the 95% Exact (Clopper-Pearson) CIs for each treatment group. For urogenital body site at the TOC visit, the adjusted (adjusting for actual pooled strata of sex and sexual orientation) estimates of the difference in NAAT success rate for the two treatments (gepotidacin – ceftriaxone plus azithromycin) with 2-sided 95% CI using MN method. For the body sites pharyngeal and rectal, unadjusted estimates of difference in NAAT success rate for the two treatments and CIs will be presented. Analyses based on the FU visit (Pharyngeal NG and Urogenital Mgen) will also use this unadjusted approach since it is anticipated that there will be insufficient observations to adequately perform an adjusted analysis. A listing of NAAT results will also be provided. NG phenotype and genotype results will appear in summary tables, listings, and figures. Summary by strata and stratification combinations defined in Section 5.4.1. will also be reported. For each stratum, the percent of participants with NAAT successes by treatment group and unadjusted difference in percent between treatment groups with corresponding two-sided 95% CI using MN method will be reported. Treatment group differences will be displayed for subgroups with ≥10 participants across both treatment groups. The table below outlines planned analyses for NAAT outcome and response:

Analysis/Endpoint Description	Visit	Body site	Population	Subgroup
NAAT outcome and response rate for NG	TOC	Urogenital Rectal Pharyngeal	micro-ITT, micro-ITT Rectal, micro-ITT Pharyngeal	
	TOC	Urogenital Rectal Pharyngeal	micro-ITT, micro-ITT Rectal, micro-ITT Pharyngeal	Subgroup categories defined in Section 5.4.2 Strata and Stratification combination defined in Section 5.4.1
	TOC	Urogenital Rectal Pharyngeal	ME, ME Rectal, ME Pharyngeal	
	TOC	Urogenital Rectal Pharyngeal	ME, ME Rectal, ME Pharyngeal	Subgroup categories defined in Section 5.4.2 Strata and Stratification combination defined in Section 5.4.1
	TOC	Urogenital Rectal Pharyngeal	ME NAAT TOC, ME NAAT TOC Rectal, ME NAAT TOC Pharyngeal	
	TOC	Urogenital Rectal Pharyngeal	ME NAAT TOC, ME NAAT TOC Rectal, ME NAAT TOC Pharyngeal	Subgroup categories defined in Section 5.4.2 Strata and Stratification combination defined in Section 5.4.1

Analysis/Endpoint Description	Visit	Body site	Population	Subgroup
NAAT outcome and response rate for NG	FU	Pharyngeal	micro-ITT Pharyngeal	
	FU	Pharyngeal	ME NAAT FU Pharyngeal	
NAAT outcome and response rate for Mgen	FU	Urogenital	micro-ITT	
	FU	Urogenital	ME NAAT FU Mgen	

7.3.1.6. Additional Microbiology Data

A microbiology database and "Micro Review Aid" (Excel) will be provided for the microbiology reviewer's guide. All pathogen-level and participant-level microbiological outcome/response data, susceptibility tests results, susceptibility phenotypes, and genotype data (where available) will be combined and displayed together (CLSI and EUCAST).

7.3.2. Analysis Population of Interest

For details of the analysis populations used in each exploratory endpoint, see Section 7.3.1.

7.3.3. Statistical Analyses / Methods

There will be no multiplicity adjustment for the testing of the exploratory endpoints. No formal hypothesis testing will be performed; 95% CIs may be included but only for descriptive purposes. For more details of the analysis methods for each exploratory endpoints, see Section 7.3.1.

7.3.3.1. Subgroup Analyses

Subgroup analyses of certain exploratory endpoints will be performed at the relevant visits for the endpoint, which may include Baseline (BL), TOC, and FU. See Section 5.4.2 for definition of subgroups and Section 7.3.1 for subgroup analysis planned for each endpoint. Subgroup analyses for NAAT outcome and response for NG will only be performed if the corresponding subgroup analysis is conducted in the corresponding primary and secondary endpoint analyses. Additional exploratory analyses may be presented as needed.

All subgroup analyses will follow the same layout/content of the overall population for each endpoint. For subgroup analyses, the summary table will be paginated by each level of the subgroup, and only the unadjusted difference in success rate will be presented.

8. SAFETY ANALYSES

The safety analyses will be based on the Safety population, unless otherwise specified.

8.1. Adverse Events Analyses

All AEs will be collected from the start of treatment until the FU visit and all SAEs will be collected from the signing of the informed consent form until the FU visit based on the timepoints specified in Appendix 1. All reported AEs will be coded using Medical Dictionary for Regulatory Activities (MedDRA) and summarized by system organ class (SOC) and preferred term (PT).

A treatment emergent AE (TEAE) is defined as an AE with start date/time after the first dose date/time of the study treatment. If the time part is missing, only dates will be considered. The number and percentage of TEAEs, study treatment-related AEs, non-serious drug-related AEs, SAEs, and AEs leading to study treatment or study withdrawal will be provided. Any AE starting before the first dose date/time will not be included in any summary analyses but will be displayed in the listings. Therefore, only TEAEs will be included in summary tables with all AEs displayed in listings.

The severity of AEs and SAEs will be determined by the investigator according to the US National Institute of Allergy and Infectious Diseases Division of Microbiology and Infectious Diseases (DMID) criteria for adult toxicity assessment, except for serum creatinine adolescent laboratory data, which will be assessed using DMID pediatric toxicity criteria. Adverse event severity is classified as mild (Grade 1), moderate (Grade 2), severe (Grade 3), potentially life-threatening (Grade 4), or resulting in death (Grade 5). Adverse events starting after the first dose of study treatment with a missing severity will be classified as severe. If a participant reports an AE more than once within the same SOC/PT, the AE with the worst-case severity will be used in the corresponding severity summaries.

The relationship to study treatment, as indicated by the investigator, is classified as “not related” or “related”. Adverse events with a missing relationship to study treatment will be regarded as “related” to study treatment. If a participant reports the same AE more than once within an SOC/PT, the AE with the worst-case relationship to study treatment will be used in the corresponding relationship summaries.

Adverse events analyses including the analysis of AEs, SAEs and other significant AEs will be based on GSK Core Data Standards. All AEs, study drug related AEs, SAEs, and AEs leading to discontinuation of study treatment or withdrawal from study will be provided in separate listings. The listings will capture the hierarchical relationship between SOC, PT, and verbatim term.

In summary tables where AEs are presented by SOC, PT, and maximum grade, SOCs will be sorted in descending order of the total incidence then alphabetically, PTs will be sorted in descending order of the total incidence then alphabetically within the SOC.

In addition, a summary of the number and percentage of participants with common AEs, defined as AEs with ≥1% incidence (before rounding) in any treatment group, will be

presented in descending order of total incidence by PT. The incidence of common AEs with relative risk and associated 95% CI (Wald method) will also be summarized in tables and presented graphically by treatment group.

All deaths occurring any time from informed consent through study completions will be listed. Participant-specific details including date of death, cause of death, and whether the death was attributed to a cardiovascular procedure or surgery will be provided.

For completely missing or partial missing AE start date or end date, imputation rules will be applied following Appendix 5. A listing of *Clostridium difficile* laboratory test results will be provided. The details of data displays are presented in Appendix 9.

AE summaries will also be presented for subgroups defined for safety analysis in Section 5.4.2.

8.2. Adverse Events of Special Interest Analyses

Cardiovascular (CV) AEs, gastrointestinal (GI) AEs, *C. difficile* AEs, and AEs related to Acetylcholinesterase Inhibition (AChE-I) as determined by algorithm will be considered AESIs.

8.2.1. *Clostridium difficile* AESI

C. difficile AESIs (PTs *Clostridium difficile* infection and *Clostridium difficile* colitis) will be included in the overall summary of AEs. *C. difficile* laboratory testing results are collected and recorded on distinct eCRF pages, which will be presented in a separate subject listing.

8.2.2. Cardiovascular and Gastrointestinal Adverse Events

Gastrointestinal AESIs are defined as AEs with a gastrointestinal SOC. Cardiovascular AESIs are defined as AEs with PTs that match the terms listed in Appendix 4 (Section 12.4.3).

For cardiovascular and gastrointestinal AESIs, the number and percentage of participants with an event will be summarized by PT and the maximum grade. In addition, the incidence of AEs of gastrointestinal effects and time to the first occurrence will be summarized. Graphical presentation of the cumulative distribution of time to the first gastrointestinal event occurrence will be provided via Kaplan-Meier curve (participants with no occurrence will be regarded as censored at the last day of the study). The details of data displays are presented in Appendix 9.

8.2.3. Acetylcholinesterase-Inhibition Adverse Events

Any reported AE listed in the table in Section 12.4.3 with a start time no later than 12 hours after the last dose administered, as evaluated by the investigator as per the DMID grading criteria provided in in protocol Section 12.5 and Appendix 7, will be included in the programmatic identification of AChE-I related AESI. The list of preferred terms for

programming to be considered due to potential AChE-I is provided in Appendix 4 (Section 12.4.3).

Cumulative grade score of Acetylcholinesterase-Inhibition (AChE-I) will be calculated as the sum of the grade of each reported AE. This enables the number of AEs and the severity of each AE to be considered. The grading scale is defined as

Cumulative Grade:	0	1	2	3	4
Cumulative Grade Score:	0	1 to 3	4 to 6	7 to 10	>=11

For instance, if a participant reports two AEs, one of Grade 1 and the other of Grade 3 their cumulative grade score of 4 would result in cumulative grade 2. This will be calculated for All AChE-I events, non-GI AChE-I events and GI AChE-I events.

Acetylcholinesterase inhibition AESIs will be listed and tabulated by SOC and preferred term and maximum grade. Non-GI AChE-I events will also be summarized. A separate table will summarize the AChE-I AESI by the number of events and unique preferred terms. In addition, time of onset (time from first dose to the onset of first event in hours), duration, and lag time (the time from last dose to the end date/time of the last event for subjects whose end date/time of the last event is after treatment end date/time) of AChE-I event will also be summarized and repeated for non-GI AChE-I and GI AChE-I events. AChE-I events with a start time less than 6 hours after the latest dose administered will also be flagged in listings.

Graphical presentation via stacked bar charts of percentage of subjects in each AChE-I cumulative grade will be produced for All AChE-I events and non-GI AChE-I events separately. In addition, a forest plot of relative risk of AChE-I events between two treatment groups and its 95% Wald CI for each event will also be included. The details of the planned displays are provided in Appendix 9.

8.3. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of chemistry laboratory tests, hematology laboratory tests, urinalysis, and liver function tests will be based on GSK Core Data Standards.

For adults, laboratory abnormalities will be graded according to the modified DMID criteria [DMID, 2007a]. For adolescent participants over 12 years of age and less than 18 years of age, the adult DMID will be applied for all laboratory parameters with the exception of serum creatinine, which will be programmatically graded according to the modified DMID criteria for pediatric participants [DMID, 2007b].

Summaries of change from baseline values over time for clinical chemistry and hematology tests will be provided in separate tables. The frequency of laboratory abnormality events along with the shift from baseline to the worst-case post baseline value will also be provided.

Abnormal liver chemistry results will be summarized by increasing folds above the upper limit of normal (ULN) including tests of interest and thresholds as follows:

- ALT or AST > 3xULN and Total Bilirubin > 2xULN
- ALT or AST > 3xULN and ALP < 2xULN and Total Bilirubin ≥ 2xULN
- ALT or AST > 3xULN and Total Bilirubin > 1.5xULN
- ALT or AST > 3xULN and INR > 1.5xULN
- (ALT/ALT ULN)/(ALP/ALP ULN)) > 5 and ALT > 3xULN *
- ALT or AST ≥ 20xULN
- ALT or AST ≥ 10xULN
- ALT or AST ≥ 8xULN
- ALT or AST ≥ 5xULN
- ALT or AST ≥ 3xULN
- ALT ≥ 20xULN
- ALT ≥ 10xULN
- ALT ≥ 8xULN
- ALT ≥ 5xULN
- ALT ≥ 3xULN
- AST ≥ 20xULN
- AST ≥ 10xULN
- AST ≥ 8xULN
- AST ≥ 5xULN
- AST ≥ 3xULN
- Total Bilirubin > 2xULN
- Total Bilirubin > 1.5xULN

*: sign of hepatocellular injury, ALT and ALP values must occur on the same day.

In addition, graphical summary of liver function test as described below will be presented.

- Scatterplot of maximum post-baseline ALT against baseline ALT by treatment group
- Scatterplot of maximum total bilirubin value post baseline against maximum post-baseline ALT by treatment group
- Participant profiles of ALT, AST, ALP and total bilirubin

If liver events are reported in the study, listings of liver event assessment, liver biopsy details and liver imaging details will be provided. Urinalysis dipstick results will be summarized using categorical statistics. Clinical chemistry and hematology test results with toxicity grade 3 or higher will be listed in separate listings. Urinalysis data will be listed.

Renal impairment will be evaluated by baseline creatinine clearance (CrCL) using the Cockcroft and Gault formula (1976)

$$CrCl\ (mL/min) = \frac{\big((140 - Age) \times Weight\big)}{72 \times Scr} \times c$$

where:

- Scr is serum creatinine in (mg/dL),
- Age is in years (actual at baseline).
- $Weight$ is in kg (at baseline),
- And where c = 1 for males and c = 0.85 for females.

Severity of renal impairment will be categorized based on CrCL at baseline (rounded to the nearest integer):

- Normal (≥90 mL/min)
- Mild impairment (≥60 to 89 mL/min)
- Moderate impairment (≥30 to 59 mL/min)
- Severe impairment (<30 mL/min)

The details of data displays are presented in Appendix 9.

8.4. Vital Signs and ECG

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on GSK Core Data Standards, unless otherwise specified. Summary tables will be provided for vital signs change from baseline values, and worst post-baseline vital signs results relative to baseline results. Participants with missing baseline values are assumed to have within range baseline values.

The arithmetic mean of the three recorded ECG measurements will be employed in all data summaries and participant listings. ECG measurements at baseline will be recorded, including heart rate, PR interval, QRS duration, QT interval, QRS axis and RR interval. When not entered directly on eCRF, corrected QT intervals will be calculated by Bazett's formula:

$$\text{QTcB (msec)} = \frac{QT}{\sqrt{\text{RR}/1000}}$$

and by Fridericia's formula:

$$\text{QTcF (msec)} = \frac{QT}{\sqrt[3]{RR/1000}}$$

depending on the availability of other measurements. ECGs may be collected after start of treatment, when medically warranted. In such cases, change from baseline in measurements will be derived.

Listings will be provided for baseline abnormal ECG findings, ECG values of potential clinical importance, and vital sign values of potential clinical importance. Details of the ECG values or vital signs of potential clinical importance are provided in Appendix 6 The details of data displays are presented in Appendix 9.

8.5. Classification and analysis of safety signals

As per GSK Guidance document (VQD-REF-019393), "Adverse reactions" (ARs) are undesirable effects, reasonably associated with use of a product that may occur as part of the pharmacological action of the product or may be unpredictable in its occurrence."

Determining which AEs should be considered ARs is a two-step process:

1) Identification of potential ARs using quantitative methodology,
2) Qualitative evaluation of the potential ARs to determine if there is sufficient evidence of a causal association with the product (gepotidacin) to support inclusion in the label.

This section details the quantitative screening methods to identify potential ARs and key data displays that support quantitative identification of potential ARs and qualitative causality assessments. ARs will be reported separately from the CSR within the regulatory submission to support the safety profile of Gepotidacin.

8.5.1. Multiplicity Adjustment

As screening for potential ARs is intended as an aid to medical judgment rather than to be used for decision making, no adjustment for multiplicity will be applied.

8.5.2. Quantitative Screening for Identification of Potential ARs

Frequentist approach to screen for potential ARs will be used. Specifically, the Crowe method [Crowe B, et al, 2013] will be applied for initial screening of the large number of adverse events to generate a "short list" of potential ARs. This method is based on three measures:

- Absolute incidence rate (%) in control arm (ceftriaxone plus azithromycin),
- Estimate of treatment effect (Relative Risk [RR]) relative to active control arm (ceftriaxone plus azithromycin),
- An estimate of variability around the treatment effect (95% CI for RR).

High Level Terms (HLTs) will be used to group adverse events and the screening for potential ARs will be conducted at HLT level. Quantitative screening criteria for potential ARs endorsed by the Safety Review Team (SRT) are displayed in the following table:

Criterion	Absolute Incidence in ceftriaxone plus oral azithromycin	HLT RR (Gepotidacin vs ceftriaxone plus azithromycin)	95% CI for HLT RR*
1	No conditions	No conditions	Lower CI > 1
2	≥5%	≥1.25	No conditions
3	<5%	≥1.50	No conditions

*95% CI for RRs determined using Wald method.

For each criterion, it is necessary to have all the features described in the column headings in order for the event to be considered to have achieved that particular criterion. Events may meet more than one criterion. Events that meet at least one of the criteria are shortlisted as a potential AR.

Based on 310 participants being exposed to Gepotidacin, there is a 90% chance of observing at least one particular adverse event if the true incidence rate of that adverse event is not below 0.75%. When the active control arm has zero events, the estimate of relative risk (RR) would be undefined and therefore cannot be evaluated using the quantitative screening criteria given above. The screening criteria in this case will be based on the minimum number of subjects with the event of interest in gepotidacin arm (vs 0 in ceftriaxone plus azithromycin arm). At least 3 participants with the AE of interest must be observed in the gepotidacin arm in order to be included in the "short list" of potential ARs.
A summary table of treatment emergent adverse events by SOC, HLTs and PTs with incidence (%) for each treatment group, RR and the associated 95% CI will be generated. An additional table will be produced displaying only the adverse events meeting the pre-specified quantitative screening criteria.

The incidence of treatment emergent AEs at HLT level for each treatment group with relative risk (95% CI) will also be presented graphically. In addition to potential ARs identified using the screening criteria shown above, AESIs (specified in Section 8.2 will be automatically included in the "short list" of potential ARs.

ARs listed in the Development Core Safety Information (DCSI) for gepotidacin will be re-assessed using data from this study to determine whether they should be carried forward as ARs based on the current supporting data.

Extra care has been taken when considering labelled/known ARs, such as fungal infections and hepatobiliary disorders, for the active comparators, ceftriaxone and azithromycin. It is not known whether the investigational product, gepotidacin, may also cause the event known to be associated with the active comparator, and therefore quantitative criteria may not be met if the incidence of these ARs are similar for the investigational product, gepotidacin.

The following AEs will automatically be included in the "short list" of potential ARs for further qualitative evaluation:

- QT Prolongation: It is a very rare serious event that has been observed in early phase gepotidacin studies and therefore needs further evaluation. It is identified using HLT "ECG investigations".
- Serious and severe adverse events: The incidence of serious and severe AEs is expected to be very low, and the qualitative assessment will be applied directly to these events without going through the quantitative screening process.
- Fungal infections: It is a known AR for ceftriaxone plus azithromycin. It is identified using HLT "Fungal infections".
- Hepatobiliary disorders: It is a known AR for ceftriaxone plus azithromycin. It is identified using HLT "Hepatic and hepatobiliary disorders".

8.5.3. Qualitative Causality Assessment

After identification of potential ARs using the quantitative method, qualitative evaluation of the potential ARs in the "short list" will be performed to determine if there is sufficient evidence of causal association with gepotidacin. The following data displays will be produced for each AE in the "short list" of potential ARs to support the qualitative causality assessments.

- Summary of treatment emergent adverse events by SOC, HLT and PTs by subgroups (Consistency check between subgroups: Actual Age Category, Sex, Race, Renal Impairment Evaluated by Baseline CrCL, Geographic Region and HIV Status)
- Incidence rate of treatment emergent AEs according to different attributes by treatment group (Consistency check in AE attribute: AEs related to study treatment, AEs leading to permanent discontinuation of study treatment, AE leading to dose reduction, AE leading to dose interruption/delay, SAEs related to study treatment, Fatal SAEs, and Fatal SAEs related to study treatment)
- Summary of treatment emergent AEs by HLT and Maximum Grade (Consistency check in AE attribute)
- Summary of Cumulative Incidence of Treatment Emergent Adverse Events (HLTs) by Time to First Occurrence (Temporal association)
- Heatmap of RR for treatment emergent AE HLTs that meet the screening criteria by SOC (Consistency check in AE attribute: AEs, Drug-related AEs, SAEs, AEs leading to discontinuation of study treatment, and Grade 3 or Higher AEs)
- Kaplan Meier Curve for Treatment Emergent Potential AR Event by Treatment (Temporal association)

Additional data displays may be generated as needed to assist with further qualitative assessment of the potential ARs once the safety data is reviewed. The generated data displays may be useful in evaluating the likelihood of a causal association and the strength of causality by assessing the following factors:

- Consistency across pre-defined subgroups,
- Consistency according to clinically relevant attributes,
- Temporal association.

9. ADDITIONAL ANALYSES DUE TO THE COVID-19 PANDEMIC

9.1. Study Population

9.1.1. Participant Disposition

A summary of recruitment by country and site, relative to COVID-19 pandemic measures will be produced. For details on the determination of phases of the COVID-19 pandemic measures see Appendix 2. A country level listing of the dates of the COVID-19 Pandemic measures will be produced.

9.1.2. Protocol Deviations

An optional participant listing of significant protocol deviations related to COVID-19 may be produced, however, these deviations will already be captured in the listing of all significant protocol deviations. Visits and assessments missed due to the COVID-19 pandemic, together with visits conducted remotely, will be summarized in both a table and listed by participant.

9.2. Safety

COVID-19 assessments and symptom assessments for participants with COVID-19 AEs will be listed, which will include the clinical outcome of any COVID-19 AE.

10. BENEFIT/RISK

Forest plots showing the treatment effect and confidence intervals related to benefits and risks of treatment with gepotidacin will be created. Benefits will be represented by risk differences and corresponding confidence intervals from the following analyses based on the Micro-ITT analysis population:

- Microbiological outcome and response rate of urogenital Gonorrhea at the TOC Visit (primary analysis),
- NAAT outcome and response rate of urogenital Gonorrhea at the TOC Visit (exploratory analysis).

For these analyses, risk differences and 95% confidence intervals will be determined using the methods described in Section 7.1.6.1 and Section 7.3.1.5, respectively. Additionally, relative risks and corresponding 95% confidence intervals will be displayed for the following safety endpoints: incidence of AEs, SAEs and, separately, CV, GI, *C. difficile*, and AChE-I AESIs using the Safety analysis population. Confidence intervals for relative risks will be determined using the asymptotic Wald method.

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FDA (2022), Multiple Endpoints in Clinical Trials Guidance for Industry

12. APPENDICES

12.1. Appendix 1: Schedule of Activities

12.1.1. Protocol Defined Schedule of Events

Table 5 Schedule of Activities

Visit[a]	Baseline		TOC[b]	Follow-up[c]	Early Withdrawal
Study Day	1		4 to 8	14 to 21	NA
Procedure	**Predose**	**Postdose**	**NA**	**NA**	**NA**
Written informed consent/assent	X				
IRT – Screening module	X				
Inclusion and exclusion criteria	X				
Participant demography	X				
Participant social and sexual history[d]	X				
Medical/surgical history	X				
Diagnosis of presumptive uncomplicated urogenital gonorrhea	X				
Bacteriology samples[e]	X		X	X	X
NAAT assay samples[f]	X		X	X	X
Physical examination (including height and weight at Baseline only)[g]	X		X		
12-lead electrocardiogram[h]	X				
Vital sign measurements[i]	X		X		
Hematology, chemistry, and urinalysis	X		X		
Serology (hepatitis B and C and HIV)[j]	X				
Urine pregnancy test[k]	X[k]		X		X
Drug and alcohol screen	X				
IRT – Randomization module	X				
Administer oral gepotidacin[l]		X[l]			
Administer IM ceftriaxone plus oral azithromycin[m]		X[m]			
Sexual history since last visit[d]			X	X	X
Serious adverse events[n]	X	X	X	X	X
Adverse events[o]		X	X	X	X
Concomitant medication review	X	X	X	X	X
Schedule TOC and Follow-up Visits	X[p,q]		X[q]	X[p]	
Treatment for CT and/or Mgen infection[r]			X	X	X
Genetic sample[s]	X				

CT=*Chlamydia trachomatis*; HIV=human immunodeficiency virus; IM=intramuscular; Mgen=*Mycoplasma genitalium*; NA=not applicable; NAAT=nucleic acid amplification test; TOC=Test-of-Cure.

a. For all study visits, to minimize the amount of time that participants spend at the clinic, eConsent may be utilized and remote collection of study-related data may be obtained as described in the Study Reference Manual. Thus, some visit data may be collected through a combination of telemedicine and on-site visits. Collection of information via telemedicine will be performed only where local regulations permit.
b. TOC (Day 4 to 8) Visit: Participants will be instructed to return to the study site within 3 to 7 days after study treatment administration. This visit may occur earlier if participants experience an adverse event.
c. Participants will be instructed to return to the study site from Day 14 to 21 for a Follow-up Visit. The investigator and/or study site staff should make every effort to ensure the participant returns for this visit. If the participant is unable to return to the study site, the visit assessments may be completed via telephone, with the exception of assessments requiring sample collection for laboratory testing.
d. Refer to the Study Reference Manual for information to collect for social and sexual history.
e. See Table 6 for collection of bacteriology samples. Also refer to the laboratory manual.
f. See Table 6 for collection of NAAT assay samples. Also refer to the laboratory manual.
g. A complete physical examination will be performed at the Baseline Visit and a gonorrhea-focused examination will be performed at the TOC Visit (see Protocol Section 9.4.1). Height and weight will only be measured and recorded at the Baseline Visit (before dosing).
h. See Protocol Section 6.2 for electrocardiogram exclusion criterion for participants aged ≥12 to <18 years. For additional details see Protocol Section 8.1.2 and Section 9.4.3.
i. Take measurement of temperature, blood pressure, and pulse rate. See Protocol Section 9.4.2.
j. If serology testing was performed within 3 months prior to the first dose of study treatment and results were positive, testing at Baseline is not required. If testing was performed within 3 months and any result was negative, testing at Baseline is required.
k. For women of childbearing potential, a negative urine pregnancy test is sufficient for eligibility. See Protocol appendix 6 for Baseline urine test sensitivity requirements and associated contraception requirements.
l. During the Baseline Visit, participants randomly assigned to gepotidacin will receive their first oral dose (3000 mg) at the study site. Participants will self-administer their second dose (3000 mg) as an outpatient 10 to 12 hours after the first dose; however, for participants who weigh <50 kg or have moderate renal impairment, the second dose should be taken approximately 12 hours after the first dose). See Protocol Section 7.1. Each dose should be taken after food consumption and with water to assist with tolerability. Participants will be contacted to confirm that they took their second gepotidacin dose. See Protocol Section 7.6.
m. During the Baseline Visit, participants randomly assigned to ceftriaxone plus azithromycin will receive a single IM dose of ceftriaxone (500 mg) plus a single oral dose of azithromycin (1 g). See Protocol Section 7.1. Azithromycin should be taken after food consumption and with water.
n. Record serious adverse events from the time of consent/assent in order to fulfill international regulatory requirements.
o. Record adverse events from the time of the first dose of study treatment.
p. Confirm return day/time for the TOC and Follow-up Visits.
q. Previsit reminder: Study site staff will contact the participant 24±4 hours before the respectively scheduled Baseline (if applicable), TOC, or Follow-up Visit.
r. Participants who tested positive for CT and/or Mgen per NAAT results at the Baseline Visit should be treated per local standard of care at or after the TOC Visit or at the Follow-up Visit (if treatment has not already been initiated), as required, after all study procedures at the visit have been completed.
s. Collect sample only if the participant has a signed consent/assent specific for this purpose. The Baseline Visit is the recommended time to collect the sample; however, it can be collected at any time during the study.

Table 6 Collection of Bacteriological Microbiological Specimens

Visit	Baseline	TOC[a]	Follow-up	Early Withdrawal
Study Day	1	4 to 8	14 to 21	NA
Collection Type Anatomical Site[b] – Organism	**Predose**	**NA**	**NA**	**NA**
Bacteriology sample collection[b]				
Urogenital – NG[c]	X	X		X
Pharyngeal – NG[d]	X	X	X[e]	X
Rectal – NG[d]	X	X		X
NAAT assay sample collection[f]				
Urogenital – NG and CT[g]	X	X[h]		X
Urogenital – Mgen[g]	X		X[i]	X
Pharyngeal – NG and CT[j]	X	X	X[k]	X
Rectal – NG and CT[j]	X	X		X

NA=not applicable; NG=*Neisseria gonorrhoeae*; TOC=Test-of-Cure.

CT=*Chlamydia trachomatis*; Mgen=*Mycoplasma genitalium*; NA=not applicable; NAAT=nucleic acid amplification test; NG=*Neisseria gonorrhoeae*; TOC=Test-of-Cure.

a. Any participant that withdraws before TOC should have all bacteriology and NAAT assay collections performed as indicated at the TOC Visit.

b. Multiple swab specimens and types may need to be obtained from each anatomical site; refer to the laboratory manual.

c. Collect a pretreatment urogenital swab specimen from all participants for Gram stain (males and females), bacterial culture, and in vitro susceptibility testing at Baseline. At TOC, a urogenital swab specimen will be collected for Gram stain, bacterial culture, and in vitro susceptibility testing. Note: All urogenital swab specimens will be processed for Gram stain testing following inoculation of the culture plates.

d. Pretreatment rectal and pharyngeal swab specimens for bacterial culture and in vitro susceptibility testing will be obtained from participants who are willing to provide such specimens, regardless of known exposure. At TOC, swab specimens will be collected from pharyngeal and/or rectal sites that were collected at Baseline for bacterial culture and in vitro susceptibility testing. Note: None of the rectal or pharyngeal swab specimens will be processed for Gram stain testing.

e. At Follow-up, pharyngeal swab specimens will be obtained for bacterial culture and in vitro susceptibility testing from participants who had a positive NAAT assay for pharyngeal NG at both Baseline and TOC. Results from the NAAT assay will be available to the study sites by the Follow-up Visit.

f. See the laboratory manual for local versus central laboratory details and the number and type of specimens to collect.

g. Pretreatment baseline urogenital specimens will be obtained from all participants for detection of NG, Mgen, and CT by NAAT. At Baseline, while detection of NG and CT by NAAT may be performed using the same urogenital sample, 2 separate samples must be obtained (1 for the local laboratory and 1 for the central laboratory).

h. Urogenital specimens will be obtained from all participants for detection of NG and CT by NAAT at the TOC Visit.

i. At Follow-up, a urogenital specimen will be collected for the detection of Mgen only by NAAT from participants who had a positive NAAT assay for Mgen at Baseline. Results from the NAAT assay will be available to the study sites by the Follow-up Visit.

j. Pretreatment baseline pharyngeal and rectal specimens for detection of NG and CT by NAAT will be obtained from participants who are willing to provide such specimens, regardless of known exposure. At TOC, a specimen will be collected from pharyngeal and/or rectal sites that were collected at Baseline.

k. At Follow-up, a pharyngeal specimen will be collected for detection of NG and CT by NAAT from participants whose NAAT assay had the presence of nucleic acid for NG at both Baseline and TOC. NAAT assay results will be available to the study sites by the Follow-up Visit.

Table 7 BTZ116577 NAAT Overview by Body Site and Organism

Body site	Organism	Baseline Visit			TOC Visit		F/U Visit	
		Local Lab	Central Lab		Central Lab		Central Lab	
			Real Time	Batch	Real Time	Batch	Real Time	Batch
Urogenital	NG/CT	X	X		X			
	MGen			X				X[b]
Pharyngeal[a]	NG/CT		X		X		X[c]	
Rectal[a]	NG/CT		X		X			

NG = *N. gonorrhoeae;* CT = *C. trachomatis;* MGen = *M. genitalium;* RT = real time (processed upon arrival); F/U=Follow-up.

a. Optional (upon patient consent)

b. Only if positive NAAT at baseline visit. MG NAATs will be run weekly by the central lab, so that baseline and results are back to the site in time for F/U.

c. Only if positive NG NAAT at baseline and TOC visit. Sites will have baseline and TOC pharyngeal NAAT results back by F/U

Note: Only central laboratory NAAT results will be used in the exploratory analysis, local lab NAAT is conducted to guide therapy at the TOC visit (*Chlamydia trachomatis*)

12.2. Appendix 2: Study Phases and Treatment Emergent Adverse Events

12.2.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to the start and end date of study treatment.

Study Phase	Definition
Pre-Treatment	Date/Time < Study Treatment Start Date/Time
On-Treatment	Study Treatment Start Date and Time < Date and Time ≤ Study Treatment Stop Date and Time
Post-Treatment	Date and Time > Study Treatment Stop Date and Time

12.2.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication started prior to the first dose date (or randomized date if first dose date is missing)
Concomitant	If medication ended after the first dose date or is ongoing regardless of the start date (or randomized date if first dose date is missing)

NOTES:

- Please refer to Appendix 5: for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.
- If a single medication taken on the same date as the first dose date, time will be used to determine if it's prior or concomitant. If time is missing, it will be considered concomitant.

12.2.1.2. Phases of COVID-19 Pandemic Measures

Pandemic measures began in different countries at different times. A dataset containing the date when COVID-19 pandemic measures began, as determined by the GSK country Issue Management Teams will be used to determine the start date of pandemic measures within each country. A copy of this dataset will be taken at the time of DBF.

12.2.1. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date/time is on or after treatment start date/time. That is, study treatment start date/time ≤ AE start date/time. If time is missing, only date will be compared.

NOTES:

- All doses of study treatments administered within 24 hours.

12.3. Appendix 3: Data Display Standards & Handling Conventions

12.3.1. Reporting Process

Software
• The currently supported versions of SAS software will be used.
Analysis Datasets
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.0) • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.
Generation of RTF Files
• RTF files will be generated for all reporting efforts described in the RAP.

12.3.2. Reporting Standards

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
• Do not include participant level listings in the main body of the GSK Clinical Study Report. All participant level listings should be located in the modular appendices as ICH or non-ICH listings

Formats
• GSK IDSL Statistical Principles (5.03, 6.06.3, & 6.09) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. • For efficacy outputs, both summaries and Statistical analysis outputs percentages will be presented with 1 dp. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time

• Reporting for tables, figures and formal statistical analyses:
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the participant's listings.

Unscheduled Visits	
• Unscheduled visits and Early withdrawal visits may be included in summary tables and/or figures as described in Section 5.6 on Analysis Visits and analyses such as “all post baseline”, “worst case post baseline”, and “max post baseline” etc. All unscheduled visits and Early Withdrawal visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principles 7.01 to 7.13.	

12.4. Appendix 4: Derived and Transformed Data

12.4.1. General

Multiple Measurements at One Analysis Time Point
• Analysis visits will be created based on visit windows as described in Section 5.6. All assessments (including unscheduled and early termination visits) will be presented in participant listings. The arithmetic mean of the three recorded ECG measurements will be employed as described in Section 8.4. • Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from Study Treatment Start Date (or Randomization Date if not dosed):
  • Ref Date = Missing→ Study Day = Missing
  • Ref Date < Study Treatment Start Date → Study Day = Ref Date – First Dose Date
  • Ref Date ≥ Study Treatment Start Date → Study Day = Ref Date – (First Dose Date) + 1

12.4.2. Efficacy

Microbiology Procedures

• Microbiology data will be received from below sources
  • Local laboratory
  • Central laboratory
  • 3rd party laboratory
<u>Local laboratory procedures:</u>
  • A local laboratory will be utilized for processing of the specimen for Gram stain (urogenital specimen only), NG culture, and shipment of the presumptive NG isolates to the central laboratory. Presumptive identification of NG is based on the following: (1) growth of typical appearing colonies on a selective medium such as Thayer-Martin at 35 °C to 36.5 °C in 5% CO_2, (2) a positive oxidase test, and (3) the observation of gram-negative diplococci in stained smears.

- Gram stain results (WBCs, epithelial cells, and bacteria) from urogenital specimens only will be reported as follows:

	Observed	Report Terminology
WBCs per 100x field	0 <1 1-9 10-25 >25	No cells seen Rare or occasional Few Moderate Many
Epithelial cells per 100x field	0 <1 1-9 10-25 >25	No cells seen Rare or occasional Few Moderate Many
Bacteria per 1000x field (oil immersion)	0 <1 1-5 6-30 >30	No organisms seen Rare or occasional Few Moderate Many

Central laboratory procedures:

- The central laboratory will conduct confirmatory identification of NG isolates, susceptibility testing (agar dilution will be conducted at a 3rd party laboratory) and storage.
    - All isolates received by the central laboratory will be identified to genus and species by matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) and stored. If MALDI-TOF MS is not available, isolate identification will be performed based on colony morphology and Gram stain characteristics and the use of routine microbiology laboratory identification procedures.
    - Various methodologies may be used to identify each isolate to genus and species. If an isolate is not identified to genus and species by the first methodology used, a second attempt may be made to identify the isolate to genus and species using an alternate methodology.
        - If the isolate is still not identified to genus and species after using at least two methodologies, the best identification available will be reported e.g. *Pseudomonas* species.
- Susceptibility testing, as outlined below will be performed on all NG isolates from all body sites including duplicate isolates recovered from the same participant:
    - MIC testing will be conducted on all NG isolates as follows:
        - Agar dilution: ranges for the antimicrobial agents to be tested are shown below. Isolates displaying MIC results higher than the last concentration tested for any given agent (i.e., off-scale high) will be re-tested at the end of the trial using a higher dilution range in an attempt to get on-scale values for all isolates; however, the highest concentration will be set at 512 µg/mL for tetracycline and spectinomycin, at 16 µg/mL for ceftriaxone and cefixime, and at 256 µg/mL for all remaining drugs.
            a. Gepotidacin (0.06 – 32 µg/mL)
            b. Ceftriaxone (0.002 – 0.5 µg/mL)
            c. Ciprofloxacin (0.0005 – 32 µg/mL)
            d. Azithromycin (0.03 – 16 µg/mL)
            e. Cefixime (0.002 – 0.5 µg/mL)
            f. Penicillin (0.06 – 16 µg/mL)

g. Tetracycline (0.12 – 64 µg/mL)
h. Spectinomycin (4 – 256 µg/mL)
i. Gentamicin (1 – 32 µg/mL)

- Gradient diffusion results will also be generated for all NG isolates for susceptibility to gepotidacin only.

- MIC results will be reported according to Clinical and Laboratory Standards Institute (CLSI) guidelines. CCI [redacted] The concentration (in micrograms per milliliter) and the interpretation code (S=susceptible, I=intermediate, R=resistant, NS=nonsusceptible) will be reported for the minimum inhibitory concentration (MIC) values. Where no CLSI or EUCAST interpretation is available, only the MIC will be reported.
- Gradient Diffusion MICs and Interpretation
  - Being a fully quantitative MIC method, gradient diffusion enables the laboratory to report the exact MIC value together with the interpretive category. Gradient diffusion strips generate MIC values from a continuous scale and can give results in-between conventional two-fold dilutions i.e. half dilutions. A gradient diffusion MIC value which falls between standard two-fold dilutions must be rounded up to the next upper two-fold value before categorization. Example: Benzylpenicillin MIC (ug/mL) breakpoints for *Streptococcus pneumoniae*
    - S: <=0.06
    - I: 0.12-1
    - R: 2
  - A gradient diffusion MIC of 1 ug/mL is reported as intermediate (I) while 1.5 is rounded up to 2 ug/mL and the category reported as resistant (R).
  - When growth occurs along the entire strip i.e. no inhibition ellipse is seen, report the MIC as ≥ the highest value on the MIC scale. When the inhibition ellipse is below the strip (does not intersect the strip), report the MIC < the lowest value on the MIC scale.
- MIC Reporting Concentrations
  - When serial two-fold dilution MICs are being prepared and tested, the actual dilution scheme is, e.g.: 16, 8, 4, 2, 1, 0.5, 0.25, 0.125, 0.0625, 0.03125, 0.015625, 0.0078125 ug/ml, etc.
  - For convenience only, it was decided to use the following values for reporting purpose (reporting format):16, 8, 4, 2, 1, 0.5, 0.25, 0.12, 0.06, 0.03, 0.015, 0.008, 0.004, 0.002 ug/mL, etc. The values that appear in the tables are equivalent to the actual values tested, e.g., 0.12 ug/mL = 0.125 ug/mL; 0.015 ug/mL = 0.015625 ug/mL.
  - Any values contain '<', '<=', '>=', '>' will be counted in its separate categories. However, when calculating the minimum, maximum, MIC_{50}, MIC_{90}, a small amount will be added or subtracted in order to impute the corresponding numeric value for calculation. For example,
    - '<0.06' will be imputed as 0.06-0.001;
    - '>256' will be imputed as 256+0.001.
    - '>=32' will be imputed as 32.
  - But for reporting, they will still be presented in original format if they happen to be those summary statistics.

- Disk diffusion will be conducted on all NG isolates as follows:

Compound	Organisms
Gepotidacin[a]	All NG isolates
Ceftriaxone	All NG isolates
Azithromycin	All NG isolates
[a] Two manufacturers (Becton Dickinson and MAST)	

- Disk diffusion results will be reported according to approved microbiology standards (e.g. CLSI or EUCAST, note that there are currently no EUCAST disk diffusion interpretive criteria for *N. gonorrhoeae*). The zone size will be recorded and reported in millimeters along with the interpretation code (S=susceptible, I=intermediate, R=resistant, NS=nonsusceptible) for disk diffusion results. Where no interpretation is available, only zone diameters will be recorded.
- Urogenital, pharyngeal, and rectal specimens for NAAT will be collected from all participants at designated visits (refer to Table 6) and processed as outlined below at the central laboratory:
    - Detection of NG and CT (Positive or Negative)
    - Detection of Mgen and five macrolide resistance markers (Detected or Not Detected)
    - Detection of ciprofloxacin resistance markers in NG (Detected or Not Detected)
    - Detection of gepotidacin resistance markers in NG (Detected or Not Detected)
- Testing for Beta-lactamase production will be performed on all NG isolates. Results will be reported as β-lactamase positive or β-lactamase negative.
- Susceptibility data will be included in PPD GCL data transfers to PPD clinical and therefore available for PPD Biostatistics and PPD clinical programing for inclusion in analysis database.
- The data from two or more *N. gonorrhoeae* isolates reported from the same patient from the same body site at the same visit will be reviewed by the study microbiologist and the algorithm in the 'keepers data" process below applied to determine if the isolates are the same or different strains (see microbiological "Keepers" process below).

Microbiological Data Procedures

- JMI isolate genotype data is derived from isolate whole genome sequencing and other genomic assays as requested by GSK and will be performed by JMI when a minimum of 20 isolates are available but not more frequent on a monthly basis (testing may be conducted more frequently near the end of the study). Genotype data therefore will be available no sooner than 1-2 months after isolate receipt.
- JMI isolate genotypic data will be sent to PPD GCL and included in PPD GCL data transfers to PPD clinical and therefore available for PPD Biostatistics and PPD clinical programming for inclusion in analysis database.

Keepers Process

Scenario #1: Keepers

- All cases will be identified within the central laboratory dataset where two or more pathogens of the same genus and species have been identified for the same participant at the same visit from the same body site. An excel file containing a list of these pathogens and the associated MIC results for each isolate will be provided to the study microbiologist. (Note: There may be instances where the comment "Out of stability" appears for an isolate. It will be isolate number 2. If the time to receipt of the isolate is markedly longer than the 1st isolate, select the 1st isolate that tested closer to the visit date to maintain in the analysis set.) The microbiologist will review the list and determine if the isolates are the same or different strains of the identified pathogen based on a predefined algorithm:
- If there is a ≥4-fold difference in MIC to three or more antibiotic classes, then the applicable isolates will be considered different strains and each of the applicable different isolates will be used in the analysis regardless of susceptibility interpretations (Note: agar dilution MIC will be used in this analysis, not the gradient diffusion MIC).
- If two or more NG isolates from the same visit and same sample type and there is a ≥4-fold difference in MIC to two antibiotic classes, and if at least one isolate has different breakpoint interpretations to both antibiotic classes (e.g. susceptible and resistant or non-susceptible), the applicable isolates will be considered different strains and each of the applicable different isolates will be analyzed.
- NOTE: In certain instances, should there be two or more NG that DO NOT have a ≥4-fold difference in MIC to two antibiotic classes but at least one isolate has a different breakpoint interpretation (e.g. susceptible and resistant) for an antimicrobial of epidemiological or study importance [i.e. ceftriaxone, cefixime, azithromycin, gepotidacin (presumptive breakpoints applied)], the applicable isolates will be considered different strains and each of the applicable NG isolates will be analyzed.
- In some cases, molecular results may be used to determine if two or more *N. gonorrhoeae* isolates are the same or different strains.
    - If none of the criteria for determining the isolates as different are met, only one isolate will be kept for analysis based on a pre-defined algorithm.
    - The microbiologist will add a flag to the list to indicate which of the duplicate records to keep (flag = >0; e.g. 1, 2). All records with this flag will be kept in the SDTM/ADaM datasets, and those records that are deemed to be duplicates (flag = 0) will be removed from the final analyses.
    - Isolates other than *Neisseria gonorrhoeae* will receive a 'Keepers' designation of 'NA' to signify that the Keepers process does not apply for isolates other than *Neisseria gonorrhoeae*.
    - Should an NG isolate be recovered from post-baseline visits of participants with more than one NG recovered from the baseline visit, each baseline NG will be presented alongside participant-level microbiological outcome. The relatedness of pre- and post-baseline isolates as it relates to microbiological failure will be described in a stand-alone report.

Phenotype and Genotype Subcategory Flagging

- A summary for the number of participants for each distinct phenotype and genotype isolated at Baseline by body site will be produced for the microbiologist.
- The microbiologist will review that summary to flag those phenotype and genotype subcategories to be reported in the TLFs.

Fold Change

- Fold change will be used to describe how much the MIC for gepotidacin changes between Baseline Visit and subsequent visits). Fold change analysis will also be conducted for study comparators azithromycin and ceftriaxone.
- Fold change will be calculated (in doubling dilutions) as the ratio of the MIC at the subsequent visit to the MIC at the Baseline Visit. However, ratio of 1 will be reported as 0-fold. Ratio less than 1 will be reported in reciprocal with negative sign (e.g. ratio of 0.5 will be reported as -2-fold). Below are some examples:

Baseline MIC (mcg/mL)	Post-baseline MIC (mcg/mL)	Fold-change
1	1	0-fold
1	2	2-fold
1	4	4-fold
1	8	8-fold
1	16	16-fold
1	0.5	- 2-fold
1	0.25	- 4-fold
1	>32	>/=64-fold
1	>/=32	>/=32-fold
1	<0.125	>/= - 16-fold
1	</=0.125	>/= - 8-fold

MIC_{50} and MIC_{90}

- MIC_{50} and MIC_{90} refer to the corresponding concentrations required to inhibit 50% and 90% of the strains tested, respectively. The MIC_{50} is the dilution which includes the 50th percentile (similar for MIC_{90}). The 50^{th} and 90^{th} percentiles will be determined by tabulation of the cumulative percentage of MICs: the MIC_{50} is the first value for which the cumulative percentage is >=50% and the MIC_{90} is the first value for which the cumulative percentage is >=90%. They will only be reported if sample size is larger or equal to 10 (otherwise reported as 'NC').
- MIC ranges to be tested in this protocol (in ug/mL):

Gepotidacin Gradient Strip	<0.015; 0.015, 0.03; 0.06; 0.12; 0.25; 0.5; 1; 2; 4; 8; 16; 32; 64; 128; >=256
Gepotidacin (JMI)	<=0.06; 0.12; 0.25; 0.5; 1; 2; 4; 8; 16; 32; >32; 64; 128; 256; >256
Ceftriaxone (JMI)	<=0.002; 0.004; 0.008; 0.015; 0.03; 0.06; 0.12; 0.25; 0.5; >0.5; 1; 2; 4; 8; 16; >16
Cefixime (JMI)	<=0.002; 0.004; 0.008; 0.015; 0.03; 0.06; 0.12; 0.25; 0.5; >0.5; 1; 2; 4; 8; 16; >16
Azithromycin (JMI)	<=0.03; 0.06; 0.12; 0.25; 0.5; 1; 2; 4; 8; 16; >16; 32; 64; 128; 256; >256
Ciprofloxacin (JMI)	<=0.0005; 0.001; 0.002; 0.004; 0.008; 0.015; 0.03; 0.06; 0.12; 0.25; 0.5; 1; 2; 4; 8; 16; 32; >32; 64; 128; 256; >256
Penicillin (JMI)	<=0.06; 0.12; 0.25; 0.5; 1; 2; 4; 8; 16; >16; 32; 64; 128; 256; >256
Tetracycline (JMI)	<=0.12; 0.25; 0.5; 1; 2; 4; 8; 16; 32; 64; >64; 128; 256; 512; >512
Spectinomycin (JMI)	<=4; 8; 16; 32; 64; 128; 256; >256; 512; >512
Gentamicin (JMI)	<=1; 2; 4; 8; 16; 32; >32; 64; 128; 256; >256

Susceptibility Interpretations

- Susceptibility interpretations will be calculated and reported by the central laboratory and will be based on the CLSI M100 and EUCAST guidelines in effect at that time the bacterial isolate is tested.
- Since CLSI or EUCAST breakpoints for certain drug/bug combinations can change in new yearly editions of the guidelines, as GSK and/or the central laboratory become aware of relevant breakpoint changes, the central laboratory will identify any reports which would qualify as needing a change in interpretation (e.g., a MIC value that was originally reported as susceptible, and would now be considered resistant based on the new breakpoint) and will issue amended reports.
- The final clinical database will report interpretations according to the most recent CLSI M100 and EUCAST interpretations regardless of what the breakpoints were at the time the isolate was initially tested.
- A NG isolate will be defined as MDR if it is reported as resistant (or nonsusceptible for drugs without a resistant breakpoint) to:
    - At least 1 of the antibiotic classes currently generally recommended for treatment (ESCs [oral and injectable ones are considered separately] and spectinomycin) and ≥2 of the following: penicillin, ciprofloxacin, or azithromycin
- A NG isolate will be defined as extensively-drug resistant (XDR) if it is reported as resistant) (or nonsusceptible for drugs without a resistant breakpoint) to:
    - ≥2 of the antibiotic classes currently generally recommended for treatment (ESCs [oral and injectable ones are considered separately] and spectinomycin) and
    - All 3 of the following: penicillin, ciprofloxacin, and azithromycin (Note: if isolate meets XDR criteria, MDR flag is not added)
- CCI [redacted]

Molecular Testing

- All *N. gonorrhoeae* isolates will be submitted to a 3rd party laboratory for whole genome sequencing and screened for mutations in the quinolone-resistance determinant region (QRDR) of *gyrA,* and *gyrB* (encodes for DNA gyrase), and *parC* and *parE* (encodes for topoisomerase IV) genes.
- All isolates will also be subjected to molecular typing by multilocus sequence typing (MLST) and *N. gonorrhoeae* multiantigen sequence typing (NG-MAST) to determine clonality.
- Additional molecular analysis for antibiotic resistance markers will be conducted on a subset of NG isolates based on strain specific susceptibility profiles and may include, but is not limited to:
    - Beta-lactams
        - Penicillinase genes (TEM-1)
        - *mtrCDE* and *mtrR* multidrug efflux pumps (Pen/tet/Mac/ceph R isolates)
        - *penA* and *ponA* (penicillin binding protein mutations)
        - *penB* (porins that effect influx of penicillins, cephalosporins and tetracycline)
    - Fluoroquinolone resistance
        - Expression of NorM
    - Macrolide resistance
        - macAB and repressor gene promoter and/or coding sequences
        - 23S rRNA (peptidyltransferase loop of domain V)
        - MLSb genes (rRNA methylases)
    - Tetracycline resistance
        - rpsJ (ribosomal protein S10)
        - TetM (ribosomal protection protein)
    - Spectinomycin resistance
        - rpsE (30S ribosomal protein S5)

Extra NAAT Specimens

Note: Sites are instructed to take one urogenital NAAT specimen for the central laboratory analysis per patient at any study visit. There may be instances where sites sampled both a urogenital aliquot (urine) and a urogenital swab specimen for the central laboratory urogenital NAAT at the same visit/timepoint. If both aliquot and swab records are available but the result for one of them is missing or cannot be determined, the record with the available result will be kept in the analysis.

Data handling in instances where results are available for both specimen types will be as outlined below.

a. Male patients:

1. If both the aliquot (preferred specimen for male) and the swab is NG negative, report the aliquot negative result and omit the swab negative result.

2. If both the aliquot and the swab are NG positive, report the aliquot positive result and omit the swab positive result.

3. If one of the specimens is negative and the other positive, report the positive, regardless of the specimen type. (This would apply to any visit, for example, if at baseline the aliquot was reported as positive but at test of cure the aliquot was negative but the swab was positive, the positive swab result would be reported at TOC and the aliquot at baseline.)

b. Female patients:

1. If both the aliquot and the swab (preferred specimen for females) is negative, report the swab negative result and omit the aliquot negative result.

2. If both the aliquot and the swab is positive, report the swab positive result and omit the aliquot positive result.

3. If one of the specimens is negative and the other positive, report the positive, regardless of the specimen type. (This would apply to any visit, for example, if at baseline the swab was reported as positive but at test of cure the swab was negative but the aliquot was positive, the positive aliquot result would be reported at TOC and the swab at baseline.)

Identifying Out-of-Stability samples

If the culture procedure at the local laboratory date/time is >24 hours after the culture specimen collection date/time at the site, then the sample is out-of-stability:

1. If NG has been isolated in that sample, then the sample can be used as any others to derive populations and microbiological responses/outcomes and will be identified as 'Out of stability – NG Pos'.
2. If NG has not been isolated in that sample, then it is not possible to determine if NG is truly absent or if it did not survive. Such results cannot be used to derive populations and microbiological responses/outcomes and will be identified as 'Out of stability – NG Neg'. Corresponding TOC outcomes and responses will be unable to determine (failure).

If missing or partial date/time information prevents determination of whether a sample is out-of-stability or not, it will be considered as out-of-stability.

12.4.3. Safety

Adverse Events
AEs of Special Interest (AESI)
• *Clostridium difficile* events • Cardiovascular events • Gastrointestinal events • Acetylcholinesterase inhibition events

List of Cardiovascular AESIs Preferred Terms	
Pulmonary oil microembolism	Atrioventricular node dispersion
Peripheral revascularization	Cardiac arrest
Supraventricular extrasystoles	Holiday heart syndrome
Rebound tachycardia	Anomalous atrioventricular excitation
Cardio-respiratory arrest neonatal	Bundle branch block
Atrial conduction time prolongation	Adams-Stokes syndrome
Cardiac death	Atrioventricular dissociation
Paroxysmal arrhythmia	Atrial flutter
Cardiac flutter	Prosthetic cardiac valve thrombosis
Neonatal sinus bradycardia	Heart valve incompetence
Neonatal bradyarrhythmia	Cardiac valve disease
Sinus bradycardia	Metastatic pulmonary embolism
Bradycardia foetal	Renal revascularisation surgery
Junctional ectopic tachycardia	Angina unstable
Ventricular fibrillation	Ventricular extrasystoles
Accessory cardiac pathway	Lenegre's disease
Sinoatrial block	Atrioventricular block
Pulseless electrical activity	Nodal arrhythmia
Ventricular parasystole	Rhythm idioventricular
Paroxysmal atrioventricular block	Nonreassuring foetal heart rate pattern
Ogden syndrome	Ventricular asystole
Nodal rhythm	Defect conduction intraventricular
Bundle branch block left	Atrial fibrillation
Heart valve stenosis	Tachycardia foetal
Acute myocardial infarction	Atrioventricular block first degree
ECG signs of myocardial infarction	Foetal arrhythmia
Embolism arterial	Neonatal tachycardia
Pulmonary embolism	Carcinoid heart disease
Central bradycardia	Cardiac valve replacement complication
Sinus arrest	Degenerative multivalvular disease
Cardiac fibrillation	Cardiac valve sclerosis
Trifascicular block	Cardiac valve abscess
Ventricular tachycardia	Newborn persistent pulmonary hypertension
Accelerated idioventricular rhythm	Deep vein thrombosis postoperative
Bundle branch block bilateral	Carotid revascularization
Bundle branch block right	Transmyocardial revascularization
Bezold-Jarisch reflex	Ventricular tachyarrhythmia
Chronotropic incompetence	Tachycardia
Arrhythmia neonatal	Torsade de pointes
Inherited cardiac conduction disorder	Lown-Ganong-Levine syndrome
Baseline foetal heart rate variability disorder	Conduction disorder
Ventricular flutter	Congenital supraventricular tachycardia
Lambl's excrescences	Pacemaker generated arrhythmia
Periprocedural myocardial infarction	Wolff-Parkinson-White syndrome
Congenital pulmonary hypertension	Long QT syndrome
Portopulmonary hypertension	Parasystole
Deep vein thrombosis	Cardiac arrest neonatal
Revascularisation procedure	Neonatal sinus tachycardia
Cardiac failure congestive	Foetal tachyarrhythmia
Atrioventricular node dysfunction	Cerebrovascular disorder
Ventricular pre-excitation	Pulmonary arterial hypertension
Supraventricular tachyarrhythmia	Post procedural pulmonary embolism
Arrhythmia	Pulmonary microemboli

Cerebral revascularization	Supraventricular tachycardia
Timothy syndrome	Sinusoidal foetal heart rate pattern
Heart alternation	Bradyarrhythmia
Reperfusion arrhythmia	Tachycardia paroxysmal
Foetal heart rate disorder	Sinus tachycardia
Atrial parasystole	Wandering pacemaker
Atrial tachycardia	Withdrawal arrhythmia
Bifascicular block	Foetal heart rate acceleration abnormality
Atrioventricular block complete	Pacemaker syndrome
Sudden cardiac death	Structural valve deterioration
Sinus node dysfunction	Cardiac valve thickening
Sudden death	Post procedural myocardial infarction
Cardio-respiratory arrest	Pulmonary hypertension
Arrhythmia supraventricular	Obstetrical pulmonary embolism
Neonatal tachyarrhythmia	Heart block congenital
Bradycardia	Atrioventricular block second degree
Congenital heart valve incompetence	Extrasystoles
Cardiac valve rupture	Brugada syndrome
Heart valve calcification	Wolff-Parkinson-White syndrome congenital
Cardiac valve discolouration	BRASH syndrome
Cardiac valve vegetation	Ventricular arrhythmia
Congenital heart valve disorder	Foetal heart rate deceleration abnormality
Myocardial infarction	Long QT syndrome congenital
Silent myocardial infarction	Agonal rhythm
Septic pulmonary embolism	Frederick's syndrome
Coronary revascularization	Bradycardia neonatal
Atrioventricular conduction time shortened	Shone complex
Sinus arrhythmia	Transient ischaemic attack
Tachyarrhythmia	Cerebrovascular accident
Postural orthostatic tachycardia syndrome	

List of Acetylcholinesterase Inhibition AESIs Preferred Terms

Abdominal discomfort	Generalised non-convulsive epilepsy
Abdominal pain	Generalised tonic-clonic seizure
Abdominal pain lower	Heart rate decreased
Abdominal pain upper	Hyperhidrosis
Abdominal symptom	Hyperkinesia
Abdominal tenderness	Hypocalcaemic seizure
Asthma	Hypoglycaemic seizure
Atonic seizures	Hyponatraemic seizure
Atypical benign partial epilepsy	Idiopathic generalised epilepsy
Autonomic seizure	Idiopathic partial epilepsy
Bradyarrhythmia	Irregular breathing
Bradycardia	Lacrimation increased
Bronchial hyperreactivity	Lafora's myoclonic epilepsy
Bronchospasm	Lennox-Gastaut syndrome
Clonic convulsion	Myoclonic epilepsy
Cold sweat	Nausea
Convulsions local	Night sweats
Convulsive threshold lowered	Partial seizures
Defaecation urgency	Partial seizures with secondary generalisation
Diarrhoea	Petit mal epilepsy
Drooling	Psychomotor hyperactivity
Dyspnoea	Retching
Dyspnoea at rest	Salivary hypersecretion
Dyspnoea exertional	Seizure
Epigastric discomfort	Seizure cluster
Epilepsy	Simple partial seizures
Epilepsy with myoclonic-atonic seizures	Status asthmaticus
Faeces soft	Status epilepticus
Febrile convulsion	Sweat gland disorder
Febrile infection-related epilepsy syndrome	Syncope
Flatulence	
Focal dyscognitive seizures	Tonic clonic movements
Frequent bowel movements	Tonic convulsion
Frontal lobe epilepsy	Unilateral bronchospasm
Gastrointestinal disorder	Vomiting
Gastrointestinal pain	Vomiting projectile
Gastrointestinal tract irritation	Wheezing

Adverse Events with Missing Relationship or Missing Serious Indicator

- If the relationship to study treatment is missing for a treatment-emergent AE (TEAE), then the TEAE will be considered related to the study treatment.
- If the serious indicator "Was event serious?" is missing, the AE will be considered as SAE.
- Adverse events with missing relationship or missing serious indicator will be presented as it is in listings but will be treated as related AEs or SAEs in summary tables.

Laboratory Parameters

If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the data base, where the numeric value is missing, but typically a character value starting with '<=', '>=', '>', '<' (or indicated as less than x or greater than x in the comment field) or is present, the number of significant digits (i.e. decimal places) in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value.

Laboratory Parameters
1. Example 1: 2 significant digits = '<= x' becomes x – 0.01 (Note: also applies to '<x') 2. Example 2: 1 significant digit = '>= x' becomes x + 0.1 (Note: also applies to '>x') 3. Example 3: 0 significant digits = '<=x' becomes x – 1 (Note: also applies to '>x')

12.5. Appendix 5: Reporting Standards for Missing Data

12.5.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study treatment completion is defined as if the participant has taken all doses of the study treatment and completed the TOC Visit. Participants who discontinue study treatment will not be considered withdrawn from the study and should attend the TOC and Follow-up Visits as applicable. • Participant study completion (i.e., as specified in the protocol) is defined as if the participant has completed all study visits including the Follow-up Visit. • Withdrawn participants will not be replaced in the study. • All available data from participants who were withdrawn from the study will be listed and data will be included in summary tables and figures as described in Section 5.6 on Analysis Visits.

12.5.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: o These data will be indicated by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Primary and Secondary Efficacy	• Participants who do not return for the TOC visit will be treated as failures. • Participants who withdraw from the study prior to TOC will be considered not achieving success for the microbiological response. Microbiological outcome for these participants will be imputed as failures. • Any participant in whom a determination of the baseline pathogen microbiological outcome cannot be made at TOC (e.g., no bacteriological sample taken for culture, sample lost, sample plated out of stability, etc.) will be considered as failures.
Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

12.5.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 2 o Missing Start Time: Midnight 0:00:00 will be used for AEs with missing start time to determine if it's AChE-I.

Element	Reporting Detail
	○ Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case date the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • Adverse events with entirely missing or unknown start dates will be assumed to be on-treatment and also treatment emergent for reporting purposes.
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month • The recorded partial date will be displayed in listings.

12.6. Appendix 6: Values of Potential Clinical Importance

12.6.1. ECG

ECG Parameter	Units	Potential Clinically Important Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		>450
Absolute PR Interval	msec	< 110	> 220
Absolute QRS Interval	msec	< 75	> 110

NOTES:

1. Represent further subdivisions of ECG values for analysis.

12.6.2. Vital Signs

Vital Sign Parameter (Absolute)	Units	Potentially Clinically Important Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	< 85	> 160
Diastolic Blood Pressure	mmHg	< 45	> 100
Heart Rate	bpm	< 40	> 110

12.7. Appendix 7: Division of Microbiology and Infectious Diseases Toxicity Tables for Adverse Event Assessment

12.7.1. Laboratory Values

12.7.1.1. Adults

For adults, laboratory abnormalities will be graded according to the modified US National institute of Allergy and Infectious Diseases Division of Microbiology and Infectious Diseases (DMID) criteria [DMID, 2007a]. Laboratory results are converted to SI units.

HEMATOLOGY				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Hemoglobin	9.5 to 10.5 gm/dL	8.0 to 9.4 gm/dL	6.5 to 7.9 gm/dL	<6.5 gm/dL
Absolute Neutrophil Count	1000 to 1500 /mm^3	750 to 999 /mm^3`	500 to 749 /mm^3	<500 /mm^3
Platelets	75,000 to 99,999 /mm^3	50,000 to 74,999 /mm^3	20,000 to 49,999 /mm^3	<20,000 /mm^3
White Blood Cells	11,000 to 13,000 /mm^3	13,001 to 15,000 /mm^3	15,001 to 30,000 /mm^3	>30,000 or <1000 /mm^3
% Polymorphonuclear Leukocytes + Band Cells	>80%	90 to 95%	>95%	N/A

N/A=not applicable; ULN=upper limit of normal.

CHEMISTRIES				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Hyponatremia	130 to 135 mEq/L	123 to 129 mEq/L	116 to 122 mEq/L	<116 mEq/L or abnormal sodium *with* mental status changes or seizures
Hypernatremia	146 to 150 mEq/L	151 to 157 mEq/L	158 to 165 mEq/L	>165 mEq/L or abnormal sodium *with* mental status changes or seizures
Hypokalemia	3.0 to 3.4 mEq/L	2.5 to 2.9 mEq/L	2.0 to 2.4 mEq/L or intensive replacement therapy of hospitalization required	<2.0 mEq/L or abnormal potassium *with* paresis, ileus, or life-threatening arrhythmia
Hyperkalemia	5.6 to 6.0 mEq/L	6.1 to 6.5 mEq/L	6.6 to 7.0 mEq/L	>7.0 mEq/L or abnormal potassium *with* life-threatening arrhythmia
Hypoglycemia	55 to 64 mg/dL	40 to 54 mg/dL	30 to 39 mg/dL	<30 mg/dL or abnormal glucose *with* mental status changes or coma
Hyperglycemia (nonfasting and no prior diabetes)	116 to 160 mg/dL	161 to 250 mg/dL	251 to 500 mg/dL	>500 mg/dL or abnormal glucose *with* ketoacidosis or seizures
Hypocalcemia (corrected for albumin)	8.4 to 7.8 mg/dL	7.7 to 7.0 mg/dL	6.9 to 6.1 mg/dL	<6.1 mg/dL or abnormal calcium *with* life-threatening arrhythmia or tetany
Hypercalcemia (corrected for albumin)	10.6 to 11.5 mg/dL	11.6 to 12.5 mg/dL	12.6 to 13.5 mg/dL	>13.5 mg/dL or abnormal calcium *with* life-threatening arrhythmia
Hypomagnesemia	1.4 to 1.2 mEq/L	1.1 to 0.9 mEq/L	0.8 to 0.6 mEq/L	<0.6 mEq/L or abnormal magnesium *with* life-threatening arrhythmia
Hyperbilirubinemia (when accompanied by any increase in other liver function test)	1.1 to <1.25 × ULN	1.25 to <1.5 × ULN	1.5 to 1.75 × ULN	>1.75 × ULN
Hyperbilirubinemia (when other liver function tests are	1.1 to <1.5 × ULN	1.5 to <2.0 × ULN	2.0 to 3.0 × ULN	>3.0 × ULN

CHEMISTRIES				
in the normal range)				
Blood urea nitrogen	1.25 to 2.5 × ULN	2.6 to 5 × ULN	5.1 to 10 × ULN	>10 × ULN
Creatinine	1.1 to 1.5 × ULN	1.6 to 3.0 × ULN	3.1 to 6.0 × ULN	>6 × ULN or dialysis required

Rx=therapy; ULN=upper limit of normal.

CHEMISTRIES				
ENZYMES				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Aspartate aminotransferase (AST)	1.1 to <2.0 × ULN	2.0 to <3.0 × ULN	3.0 to 8.0 × ULN	>8.0 × ULN
Alanine aminotransferase (ALT)	1.1 to <2.0 × ULN	2.0 to <3.0 × ULN	3.0 to 8.0 × ULN	>8.0 × ULN
Alkaline Phosphatase	1.1 to <2.0 × ULN	2.0 to <3.0 × ULN	3.0 to 8.0 × ULN	>8.0 × ULN

ULN=upper limit of normal.

URINALYSIS				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Proteinuria	1+ or 200 mg to 1 gm loss/day	2 to 3+ or 1 to 2 gm loss/day	4+ or 2 to 3.5 gm loss/day	Nephrotic syndrome or >3.5 gm loss/day
Hematuria	Microscopic only <10 RBC/hpf	Gross, no clots >10 RBC/hpf	Gross, with or without clots, or red blood cells casts	Obstructive or required transfusion

HPF=high powered field; RBC=red blood cells.

12.7.1.2. Adolescent Participants

For adolescent participants over 12 years of age and less than 18 years of age, the adult DMID will be applied for all parameters with the exception of serum creatinine which will be graded programmatically according to the modified DMID pediatric toxicity criteria [DMID, 2007b]. Laboratory results are converted to SI units.

CHEMISTRIES				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Creatinine	1.0 to 1.7 x ULN	1.8 to 2.4 x ULN	2.5 to 3.5 x ULN	>3.5 x ULN

ULN=upper limit of normal.

12.8. Appendix 8: Abbreviations & Trademarks

12.8.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AR	Adverse Reaction
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
CDISC	Clinical Data Interchange Standards Consortium
CFU	Colony-Forming Units
CI	Confidence Interval
CLSI	Clinical and Laboratory Standards Institute
CT	*Chlamydia trachomatis*
DBF	Database Freeze
DBR	Database Release
DMID	Division of Microbiology and Infectious Diseases
DP	Decimal Places
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FDA	Food and Drug Administration
GSK	GlaxoSmithKline
HDL	Headline TFL
ICE	Intercurrent Event
ICH	International Conference on Harmonization
IDSL	Integrated Data Standards Library
ITT	Intent-To-Treat
LLN	Lower Limit of Normal
MALDI-TOF MS	Matrix assisted laser desorption ionization-time of flight mass spectrometry
Mgen	*Mycoplasma genitalium*
MIC	Minimum Inhibitory Concentration
MN	Miettinen and Nurminen
NAAT	Nucleic Acid Amplification Test
NG	*Neisseria gonorrhoeae*
RAP	Reporting and Analysis Plan
SAC	Statistical Analysis Complete
SAE	Serious AE
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SOC	System Organ Class
SRM	Study Reference Manual

Abbreviation	Description
TEAE	Treatment-emergent AE
TFL	Table/Figure/Listing
TOC	Test-of-Cure
ULN	Upper Limit of Normal
WBC	White Blood Cell

12.8.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
GSKDrug

Trademarks not owned by the GlaxoSmithKline Group of Companies
MedDRA
SAS
WHODrug

12.9. Appendix 9: List of Data Displays

12.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.101 to 1.502	1.101 to 1.102
Efficacy	2.101 to 2.340	2.101 to 2.202
Safety	3.101 to 3.506	3.101 to 3.403
Section	**Listings**	
ICH Listings	101 to 1303	

12.9.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in each tables, listings, and figures shells.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

12.9.3. Deliverables

Delivery	Description
DS	During Study
SAC	Final Statistical Analysis Complete

NOTE:

- A blinded dry run will be performed during the study (DS).
- For outputs presented by phenotypic/genotypic subcategories or MIC susceptibility by drugs sort according to the alphabetic order of the categories/drugs.
- Some TFLs designated as being for SAC deliverable may be provided at All Analyses Complete (i.e. all output to support the writing of the CSR and disclosures). The final list of TFLs to be provided at SAC and AAC will be documented outside of the RAP.

12.9.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Participant Disposition					
1.101.	Intent-to-Treat	ES1	Summary of Participant Disposition		DS, SAC
1.102.	Micro-ITT	ES1	Summary of Participant Disposition		DS, SAC
1.103.	Intent-to-Treat	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment		DS, SAC
1.104.	Micro-ITT	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment		DS, HDL, SAC
1.105.	Intent-to-Treat	NS1	Summary of Number of Participants Enrolled by Region, Country, and Site ID		DS, SAC
1.106.	Screened	ES6	Summary of Screen Status and Reasons for Screening Failures		DS, SAC
1.107.	Screened	SP1	Summary of Study Populations		DS, HDL, SAC
1.108.	Intent-to-Treat	SP2	Summary of Exclusions from Study Population		DS, SAC
Protocol Deviation					
1.201.	Intent-to-Treat	DV1	Summary of Important Protocol Deviations		DS, SAC
Demographic and Baseline Characteristics					
1.301.	Intent-to-Treat	DM1	Summary of Demographic Characteristics		DS, SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.302.	Micro-ITT	DM1	Summary of Demographic Characteristics		DS, HDL, SAC
1.303.	Intent-to-Treat	DM6	Summary of Race and Racial Combinations		DS, SAC
1.304.	Intent-to-Treat	DM11	Summary of Age Ranges		DS, SAC
1.305.	Intent-to-Treat	POP_T1	Summary of Disease Characteristics and Renal Impairment at Baseline	Summarized by body site.	DS, SAC
1.306.	Intent-to-Treat	MH4	Concordance of Local and Central Laboratory Culture Identification of NG at Baseline Visit	Numbers are determined using the local and central laboratory identification results from NG culture. By body site	DS, SAC
1.307.	Intent-to-Treat	MH4	Concordance of Central Laboratory Culture Identification and Central Laboratory NAAT NG Test Result at Baseline Visit	Numbers are determined using the central lab NAAT and central lab culture results for NG only. By body site.	DS, SAC
1.308.	Intent-to-Treat	POP_T2	Summary of Recovery Rate for NG at Baseline Visit by Culture (CLSI)	Number/Rates are determined using the central laboratory identification for NG; summarized by sex and sexual orientation, body site and age Overall and by phenotypic/genotypic subcategory	DS, SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.309.	Intent-to-Treat	POP_T2	Summary of Recovery Rate for NG at Baseline Visit by Culture (EUCAST)	Number/Rates are determined using the central laboratory identification for NG; summarized by sex and sexual orientation, body site and age Overall and by phenotypic/genotypic subcategory	DS, SAC
1.310.	Intent-to-Treat	MH1	Summary of Past and Current Medical Conditions		DS, SAC
1.311.	Micro-ITT	MH1	Summary of Past and Current Medical Conditions		DS, SAC
1.312.	Intent-to-Treat	LB1	Summary of Serology Results		DS, SAC
1.313.	Micro-ITT	LB1	Summary of Serology Results		DS, SAC
1.314.	Intent-to-Treat	SU1	Summary of Substance Use		DS, SAC
1.315.	Micro ITT	SU1	Summary of Substance Use		DS, SAC
1.316.	Intent-to-Treat	POP_T3	Summary of Social Sexual History at Baseline	Includes recreational drug use, number of sexual partners	DS, SAC
1.317.	Micro ITT	POP_T3	Summary of Social Sexual History at Baseline	Includes recreational drug use, number of sexual partners	DS, HDL, SAC
Prior and Concomitant Medications					
1.401	Intent-to-Treat	CM1	Summary of Prior Medications	Subset this table by prior antibiotics and prior medications	DS, SAC
1.402	Micro-ITT	CM1	Summary of Prior Medications	Subset this table by prior antibiotics and prior medications	

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.403	Intent-to-Treat	CM1	Summary of Concomitant Medications	Subset this table: display separate summaries for systemic concomitant medications, non-systemic concomitant medications, systemic antibiotics taken for the disease under study, systemic antibiotics taken for another disease/condition and prohibited (non-antibiotic) medications	DS, SAC
1.404	Micro-ITT	CM1	Summary of Concomitant Medications	Subset this table: display separate summaries for systemic concomitant medications, non-systemic concomitant medications, systemic antibiotics taken for the disease under study, systemic antibiotics taken for another disease/condition and prohibited (non-antibiotic) medications	DS, SAC
1.405	Micro-ITT	-	Summary of Participants Mis-stratified or Randomized Pooled Strata is Not Equal to Actual Pooled Strata		DS, SAC
Others					
1.501	Intent-to-Treat	NS1	Summary of Number of Participants Enrolled by Country and Site ID Relative to COVID-19 Pandemic Measure		DS, SAC
1.502	Intent-to-Treat	PAN4	Summary of COVID-19 Pandemic Visit Impacts		DS, SAC

12.9.5. Study Population Figures

Study Population: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.101	Intent-to-Treat	PKPL1P	Bar Plot of NG Isolates Recovered at Baseline	Categorized by body site	DS, SAC
1.102	Intent-to-Treat	PKPL1P	Bar Plot of Social Sexual History at Baseline	Categorized sexual orientation, recreational drug use, and # of sexual partners	DS, SAC

12.9.6. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Microbiological Response					
2.101.	Micro-ITT	EFF_T1	Analysis of Microbiological Outcome and Response Rate of Urogenital Gonorrhea at the TOC Visit	Only for urogenital site and NG	DS, HDL, SAC
2.102.	Micro-ITT	EFF_T1	Treatment by Strata Tests of Homogeneity for Percent of Participants with Microbiological Success of Urogenital Gonorrhea at the TOC Visit		DS, SAC
2.103.	ME	EFF_T1	Summary of Microbiological Outcome and Response of Urogenital Gonorrhea at the TOC Visit	Only for urogenital site and NG	DS, HDL, SAC
2.104.	Micro-ITT	EFF_T1	Sensitivity Analysis of Microbiological Outcome and Response of Urogenital Gonorrhea at the TOC Visit with Multiple Imputation		DS, SAC
2.105.	Micro-ITT	EFF_T2	Sensitivity Analysis of Microbiological Outcome and Response of Urogenital Gonorrhea at the TOC Visit with Tipping Point Analysis		DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.106.	Micro-ITT (CAPA)	EFF_T1	Supplementary Analysis of Microbiological Outcome and Response at the TOC Visit (Excluding Sites with CAPA Exclusion Requirements)	This will be produced for the primary analysis population subset to exclude Sites with CAPA Exclusion Requirements	DS, SAC
2.107.	Micro-ITT	EFF_T1	Summary of Microbiological Outcome and Response of Urogenital Gonorrhea at the TOC Visit by Actual Strata	For urogenital site and NG in the Actual strata (age/sex and sexual orientation/age*sex and sexual orientation)	DS, SAC
2.108.	ME	EFF_T1	Summary of Microbiological Outcome and Response of Urogenital Gonorrhea at the TOC Visit by Actual Strata	For urogenital site and NG in the Actual strata (age/sex and sexual orientation/age*sex and sexual orientation)	DS, SAC
2.109.	Micro-ITT	EFF_T1	Summary of Microbiological Outcome and Response of Urogenital Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups -CLSI)	For urogenital site and NG in the other strata specified in RAP, including Sex and Sexual Orientation. Include phenotypic and genotypic subcategory analysis for subgroups including age, sex and sexual orientation, region, country and FDA region	DS, SAC
2.110.	ME	EFF_T1	Summary of Microbiological Outcome and Response of Urogenital Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups -CLSI)	For urogenital site and NG in the other strata specified in RAP, including Sex and Sexual Orientation. Include phenotypic and genotypic subcategory analysis for subgroups including age, sex and sexual orientation, region, country and FDA region	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.111	Micro-ITT	EFF_T1	Summary of Microbiological Outcome and Response of Urogenital Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups – EUCAST)	For urogenital site and NG in the other strata specified in RAP, including Sex and Sexual Orientation. Include phenotypic and genotypic subcategory analysis for subgroups including age, sex and sexual orientation, region, country	DS, SAC
2.112	ME	EFF_T1	Summary of Microbiological Outcome and Response of Urogenital Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups - EUCAST)	For urogenital site and NG in the other strata specified in RAP, including Sex and Sexual Orientation. Include phenotypic and genotypic subcategory analysis for subgroups including age, sex and sexual orientation, region, country and FDA region	DS, SAC
2.113	Micro-ITT EU	EFF_T1	Sensitivity Analysis of Microbiological Outcome and Response Rate of Urogenital Gonorrhea at the TOC Visit Using EUCAST Breakpoints	Only for urogenital site and NG. Conditional output: if the Micro-ITT EUCAST population is the same as the Micro-ITT population then this output does not need to be produced.	DS, SAC
2.201.	Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response of Pharyngeal and Rectal Gonorrhea at the TOC Visit	Only for pharyngeal and rectal body site and NG	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.202.	ME Rectal, ME Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response of Pharyngeal and Rectal Gonorrhea at the TOC Visit	Only for pharyngeal and rectal body site and NG	DS, SAC
2.203.	Micro-ITT Rectal	EFF_T1	Summary of Microbiological Outcome and Response of Rectal Gonorrhea at the TOC Visit by Actual Strata	Only for rectal body site and NG for Actual strata (sex and sexual orientation, age)	DS, SAC
2.204.	ME Rectal	EFF_T1	Summary of Microbiological Outcome and Response of Rectal Gonorrhea at the TOC Visit by Actual Strata	Only for rectal body site and NG for Actual strata (sex and sexual orientation, age)	DS, SAC
2.205.	Micro-ITT Rectal	EFF_T1	Summary of Microbiological Outcome and Response of Rectal Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups - CLSI)	Only for rectal body site and NG in the other strata specified in RAP	DS, SAC
2.206.	ME Rectal	EFF_T1	Summary of Microbiological Outcome and Response of Rectal Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups - CLSI)	Only for rectal body site and NG in the other strata specified in RAP	DS, SAC
2.207.	Micro-ITT Rectal	EFF_T1	Summary of Microbiological Outcome and Response of Rectal Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups - EUCAST)	Only for rectal body site and NG in the other strata specified in RAP	DS, SAC
2.208.	ME Rectal	EFF_T1	Summary of Microbiological Outcome and Response of Rectal Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups - EUCAST)	Only for rectal body site and NG in the other strata specified in RAP	DS, SAC
2.209.	Micro-ITT Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response of Pharyngeal Gonorrhea at the TOC Visit by Actual Strata	Only for pharyngeal body site and NG for Actual Strata (sex and sexual orientation, age)	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.210.	ME Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response of Pharyngeal Gonorrhea at the TOC Visit by Actual Strata	Only for pharyngeal body site and NG for Actual Strata (sex and sexual orientation, age)	DS, SAC
2.211.	Micro-ITT Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response of Pharyngeal Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups - CLSI)	Only for pharyngeal body site and NG in the other strata specified in RAP	DS, SAC
2.212.	ME Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response of Pharyngeal Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups - CLSI)	Only for pharyngeal body site and NG in the other strata specified in RAP	DS, SAC
2.213.	Micro-ITT Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response of Pharyngeal Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups - EUCAST)	Only for pharyngeal body site and NG in the other strata specified in RAP	DS, SAC
2.214.	ME Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response of Pharyngeal Gonorrhea at the TOC Visit by Other Subgroups (Phenotypic Subgroups - EUCAST)	Only for pharyngeal body site and NG in the other strata specified in RAP	DS, SAC
2.215.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response for NG at TOC Visit by Body Site	Include all body sites urogenital, rectal, pharyngeal	DS, SAC
2.216.	ME, ME Rectal, ME Pharyngeal	EFF_T1	Summary of Microbiological Outcome and Response for NG at TOC Visit by Body Site	Include all body sites urogenital, rectal, pharyngeal	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Bacteriology Assessments and Microbiological Outcome and Response					
2.30 101	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit (CLSI)	By body site.	DS, SAC
2.30 102	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Geographic Location (CLSI)	By body site and region By body site and country By body site and United States region By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 103	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Sex and Sexual Orientation (CLSI)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 104	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Phenotypic/Genotypic Subgroups (CLSI)	By body site and phenotype/genotype	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.30 201	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit (CLSI)	By body site.	DS, SAC
2.30 202	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Geographic Location (CLSI)	By body site and region By body site and country By body site and United States region By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 203	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Sex and Sexual Orientation (CLSI)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 204	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Phenotypic/Genotypic Subgroups (CLSI)	By body site and phenotype/genotype	DS, SAC
2.30 301	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit (EUCAST)	By body site.	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.30 302	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Geographic Location (EUCAST)	By body site and region By body site and country By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 303	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Sex and Sexual Orientation (EUCAST)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 304	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Phenotypic/Genotypic Subgroups (EUCAST)	By body site and phenotype/genotype	DS, SAC
2.30 401	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit (EUCAST)	By body site.	DS, SAC
2.30 402	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Geographic Location (EUCAST)	By body site and region By body site and country By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.30 403	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Sex and Sexual Orientation (EUCAST)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 404	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of MICs and Susceptibility Results against NG by Visit and Phenotypic/Genotypic Subgroups (EUCAST)	By body site and phenotype/genotype	DS, SAC
2.30 501	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit (CLSI)	By body site.	DS, SAC
2.30 502	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Geographic Location (CLSI)	By body site and region By body site and country By body site and United States region By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 503	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Sex and Sexual Orientation (CLSI)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.30 504	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Phenotypic/Genotypic Subgroups (CLSI)	By body site and phenotype/genotype	DS, SAC
2.30 601	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit (CLSI)	By body site.	DS, SAC
2.30 602	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Geographic Location (CLSI)	By body site and region By body site and country By body site and United States region By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 603	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Sex and Sexual Orientation (CLSI)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 604	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Phenotypic/Genotypic Subgroups (CLSI)	By body site and phenotype/genotype	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.30 701	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit (EUCAST)	By body site.	DS, SAC
2.30 702	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Geographic Location (EUCAST)	By body site and region By body site and country By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 703	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Sex and Sexual Orientation (EUCAST)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 704	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Phenotypic/Genotypic Subgroups (EUCAST)	By body site and phenotype/genotype	DS, SAC
2.30 801	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit (EUCAST)	By body site.	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.30 802	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Geographic Location (EUCAST)	By body site and region By body site and country By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 803	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Sex and Sexual Orientation (EUCAST)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 804	ME, ME Rectal, ME Pharyngeal	EFF_T3	Summary of Disk Diffusion Results and Susceptibility against NG by Visit and Phenotypic/Genotypic Subgroups (EUCAST)	By body site and phenotype/genotype	DS, SAC
2.30 901	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug (CLSI)	By body site.	DS, SAC
2.30 902	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Geographic Location (CLSI)	By body site and region By body site and country By body site and United States region By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.30 903	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Sex and Sexual Orientation (CLSI)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.30 904	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Phenotypic/Genotypic Subgroups (CLSI)	By body site and phenotype/genotype	DS, SAC
2.31 001	ME, ME Rectal, ME Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug (CLSI)	By body site.	DS, SAC
2.31 002	ME, ME Rectal, ME Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Geographic Location (CLSI)	By body site and region By body site and country By body site and United States region By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 003	ME, ME Rectal, ME Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Sex and Sexual Orientation (CLSI)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.31 004	ME, ME Rectal, ME Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Phenotypic/Genotypic Subgroups (CLSI)	By body site and phenotype/genotype	DS, SAC
2.31 101	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug (EUCAST)	By body site.	DS, SAC
2.31 102	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Geographic Location (EUCAST)	By body site and region By body site and country By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 103	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Sex and Sexual Orientation (EUCAST)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 104	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Phenotypic/Genotypic Subgroups (EUCAST)	By body site and phenotype/genotype	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.31 201	ME, ME Rectal, ME Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug (EUCAST)	By body site.	DS, SAC
2.31 202	ME, ME Rectal, ME Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Geographic Location (EUCAST)	By body site and region By body site and country By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 203	ME, ME Rectal, ME Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Sex and Sexual Orientation (EUCAST)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 204	ME, ME Rectal, ME Pharyngeal	EFF_T4	Distribution of MIC Results against NG by Drug and Phenotypic/Genotypic Subgroups (EUCAST)	By body site and phenotype/genotype	DS, SAC
2.31 301	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug (CLSI)	By body site.	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.31 302	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Geographic Location (CLSI)	By body site and region By body site and country By body site and United States region By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 303	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Sex and Sexual Orientation (CLSI)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 304	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Phenotypic/Genotypic Subgroups (CLSI)	By body site and phenotype/genotype	DS, SAC
2.31 401	ME, ME Rectal, ME Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug (CLSI)	By body site.	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.31 402	ME, ME Rectal, ME Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Geographic Location (CLSI)	By body site and region By body site and country By body site and United States region By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 403	ME, ME Rectal, ME Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Sex and Sexual Orientation (CLSI)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 404	ME, ME Rectal, ME Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Phenotypic/Genotypic Subgroups (CLSI)	By body site and phenotype/genotype	DS, SAC
2.31 501	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug (EUCAST)	By body site.	DS, SAC
2.31 502	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Geographic Location (EUCAST)	By body site and region By body site and country By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.31 503	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Sex and Sexual Orientation (EUCAST)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 504	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Phenotypic/Genotypic Subgroups (EUCAST)	By body site and phenotype/genotype	DS, SAC
2.31 601	ME, ME Rectal, ME Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug (EUCAST)	By body site.	DS, SAC
2.31 602	ME, ME Rectal, ME Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Geographic Location (EUCAST)	By body site and region By body site and country By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC
2.31 603	ME, ME Rectal, ME Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Sex and Sexual Orientation (EUCAST)	By body site and sex and sexual orientation By phenotype/genotype within each subgroup (for urogenital site only)	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.31 604	ME, ME Rectal, ME Pharyngeal	EFF_T5	Distribution of Disk Diffusion Results against NG by Drug and Phenotypic/Genotypic Subgroups (EUCAST)	By body site and phenotype/genotype	DS, SAC
2.317.	Intent-to-Treat	EFF_T6	Summary of Reduction in Susceptibility with >= 4-fold Increase in MIC by Drug for *Neisseria gonorrhoeae*	By body site.	DS, HDL, SAC
2.318.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T7	Summary of Microbiological Success at TOC Visit by MIC Result (CLSI) against NG at Baseline	By MIC result for Gepotidacin, Azithromycin, and Ceftriaxone By phenotypic/genotypic subcategories	DS, SAC
2.319.	ME, ME Rectal, ME Pharyngeal	EFF_T7	Summary of Microbiological Success at TOC Visit by MIC Result (CLSI) against NG at Baseline	By MIC result for Gepotidacin, Azithromycin, and Ceftriaxone	DS, SAC
2.320.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T7	Summary of Microbiological Success at TOC Visit by MIC Result (EUCAST) against NG at Baseline	By MIC result for Gepotidacin, Azithromycin, and Ceftriaxone By phenotypic/genotypic subcategories	DS, SAC
2.321.	ME, ME Rectal, ME Pharyngeal	EFF_T7	Summary of Microbiological Success at TOC Visit by MIC Result (EUCAST) against NG at Baseline	By MIC result for Gepotidacin, Azithromycin, and Ceftriaxone By phenotypic/genotypic subcategories	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.322.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T8	Summary of Microbiological Success at TOC Visit by Disk Diffusion Result against NG at Baseline		DS, SAC
2.323.	ME, ME Rectal, ME Pharyngeal	EFF_T8	Summary of Microbiological Success at TOC Visit by Disk Diffusion Result against NG at Baseline		DS, SAC
2.324.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T8	Summary of Microbiological Success at TOC Visit by Susceptibility Interpretation (based on CLSI MIC) against NG at Baseline		DS, SAC
2.325.	ME, ME Rectal, ME Pharyngeal	EFF_T8	Summary of Microbiological Success at TOC Visit by Susceptibility Interpretation (based on CLSI MIC) against NG at Baseline		DS, SAC
2.326.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T8	Summary of Microbiological Success at TOC Visit by Susceptibility Interpretation (based on EUCAST MIC) against NG at Baseline		DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.327.	ME, ME Rectal, ME Pharyngeal	EFF_T8	Summary of Microbiological Success at TOC Visit by Susceptibility Interpretation (based on EUCAST MIC) against NG at Baseline		DS, SAC
2.328.	Intent-to-Treat	EFF_T9	Summary of Gram Stain Results by Visit		DS, SAC
2.329.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for NG at TOC Visit	By body site	DS, SAC
2.330.	ME, ME Rectal, ME Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for NG at TOC Visit	By body site	DS, SAC
2.331.	ME NAAT TOC, ME NAAT TOC Rectal, ME NAAT TOC Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for NG at TOC Visit	By body site	DS, SAC
2.332.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for NG at TOC Visit by Actual Strata and Other Subgroups (Phenotypic Subgroups - CLSI)	By body site Actual strata (age/sex and sexual orientation/age*sex and sexual orientation) and other relevant subgroups defined in Section 5.4.2	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.333.	ME, ME Rectal, ME Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for NG at TOC Visit by Actual Strata and Other Subgroups (Phenotypic Subgroups - CLSI)	By body site Actual strata (age/sex and sexual orientation/age*sex and sexual orientation) and other relevant subgroups defined in Section 5.4.2	DS, SAC
2.334.	ME NAAT TOC, ME NAAT TOC Rectal, ME NAAT TOC Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for NG at TOC Visit by Actual Strata and Other Subgroups (Phenotypic Subgroups - CLSI)	By body site Actual strata (age/sex and sexual orientation/age*sex and sexual orientation) and other relevant subgroups defined in Section 5.4.2	DS, SAC
2.335.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for NG at TOC Visit by Actual Strata and Other Subgroups (Phenotypic Subgroups - EUCAST)	By body site Actual strata (age/sex and sexual orientation/age*sex and sexual orientation) and other relevant subgroups defined in Section 5.4.2	DS, SAC
2.336.	ME, ME Rectal, ME Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for NG at TOC Visit by Actual Strata and Other Subgroups (Phenotypic Subgroups - EUCAST)	By body site Actual strata (age/sex and sexual orientation/age*sex and sexual orientation) and other relevant subgroups defined in Section 5.4.2	DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.337.	ME NAAT TOC, ME NAAT TOC Rectal, ME NAAT TOC Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for NG at TOC Visit by Actual Strata and Other Subgroups (Phenotypic Subgroups - EUCAST)	By body site Actual strata (age/sex and sexual orientation/age*sex and sexual orientation) and other relevant subgroups defined in Section 5.4.2	DS, SAC
2.338.	Micro-ITT, Micro-ITT Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for Pharyngeal NG and Urogenital Mgen at FU Visit		DS, SAC
2.339.	ME NAAT FU Mgen, ME NAAT FU Pharyngeal	EFF_T1	Summary of NAAT Outcome and Response for Pharyngeal NG and Urogenital Mgen at FU Visit		DS, SAC
2.340.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	EFF_T10	Summary of NG Beta-Lactamase Production by Visit		DS, SAC
2.341.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal		Summary of Missing Data by visit for subjects with Unable to Determine Microbiological outcomes at TOC		DS, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.342.	Micro-ITT		Summary of Non-Study Systemic Antibiotic Use During Study Participation		DS, SAC
2.343.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal		Summary of Baseline Pathogen Resistance (CLSI)		DS, SAC
2.344.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal		Summary of Baseline Pathogen Resistance (EUCAST)		DS, SAC
2.345.	Intent-to-Treat	EFF_T6	Summary of Reduction in Susceptibility to Study Treatment by Phenotypic/Genotypic Subgroups (CLSI)	By body site and phenotypic/genotypic subgroup.	DS, SAC
2.346.	Intent-to-Treat	EFF_T6	Summary of Reduction in Susceptibility to Study Treatment by Phenotypic/Genotypic Subgroups (EUCAST)	By body site and phenotypic/genotypic subgroup.	DS, SAC

12.9.7. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.101.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	PKPL1P	Percent of Microbiological Success for NG at the TOC Visit by Baseline Body Site		DS, SAC
2.102.	ME, ME Rectal, ME Pharyngeal	PKPL1P	Percent of Microbiological Success for NG at the TOC Visit by Baseline Body Site		DS, SAC
2.103.	Micro-ITT	EFF_F1	Forest Plot for Microbiological Success Rate Overall and by Subgroup	Categorized sexual orientation, recreational drug use and # of sexual partners	DS, SAC
2.104.	Micro-ITT	EFF_F2	Tipping Point Analysis of Microbiological Response at TOC		DS, SAC
2.105.	Micro-ITT	PKPL1P	Percent of Microbiological Success for Urogenital NG at the TOC Visit by Social Sexual History	Categorized sexual orientation, recreational drug use and # of sexual partners	DS, SAC
2.201.	Micro-ITT, Micro-ITT Rectal, Micro-ITT Pharyngeal	PKPL1P	Percent of NAAT Success for NG at the TOC Visit by Baseline Body Site		DS, SAC

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.202.	ME, ME Rectal, ME Pharyngeal	PKPL1P	Percent of NAAT Success for NG at the TOC Visit by Baseline Body Site		DS, SAC

12.9.8. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events (AEs)					
3.101.	Safety	SAFE_T1	Overall Summary of Adverse Events		DS, HDL, SAC
3.102.	Safety	AE5B	Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Grade		DS, HDL, SAC
3.103.	Safety	AE5B	Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Grade and Subgroup Strata		DS, SAC
3.104.	Safety	AE5B	Summary of Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Grade		DS, SAC
3.105.	Safety	AE3	Summary of Common (>= 1%) Adverse Events by Overall Frequency		DS, SAC
3.106.	Safety	AE3	Summary of Common (>=1%) Adverse Events by Overall Frequency and Relative Risks		DS, SAC
3.107.	Safety	AE3	Summary of Acetylcholinesterase-Inhibition Adverse Events by Overall Frequency and Relative Risks		DS, SAC
3.108.	Safety	AE3	Summary of Common (>= 1%) Adverse Events by Overall Frequency and Subgroup Strata		DS, SAC
3.109.	Safety	AE3	Summary of Common (>= 1%) Non-Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)		DS, SAC
3.110.	Safety	AE13	Summary of Common (>= 1%) Grade 2 to 5 Adverse Events Overall Frequency		DS, SAC
3.111.	Safety	AE5B	Summary of Serious Adverse Events by System Organ Class and Preferred Term and Maximum Grade		DS, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.112.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of participants and Occurrences)		DS, SAC
3.113.	Safety	AE5B	Summary of Serious Adverse Events by System Organ Class and Preferred Term and Maximum Grade and Subgroup Strata		DS, SAC
3.114.	Safety	AE5B	Summary of Drug-Related Serious Adverse Events by System Organ Class and Preferred Term and Maximum Grade		DS, SAC
3.115.	Safety	AE3	Summary of Non-Fatal Serious Adverse Events		DS, SAC
3.116.	Safety	AE3	Summary of Drug-Related Non-Fatal Serious Adverse Events		DS, SAC
3.117.	Safety	AE5B	Summary of Cardiovascular and Gastrointestinal Adverse Events of Special Interest by System Organ Class and Preferred Term and Maximum Grade		DS, SAC
3.118.	Safety	AE5B	Summary of Acetylcholinesterase-Inhibition Adverse Events of Special Interest by System Organ Class and Preferred Term and Maximum Grade		DS, SAC
3.119.	Safety	AE5B	Summary of Acetylcholinesterase-Inhibition Adverse Events of Special Interest by Number of Events and Unique Preferred Terms	a table to summarize the number and % of participants experiencing 1, 2, 3, 4, 5 or more events and 1, 2, 3, 4, >=5 distinct PTs	DS, SAC
3.120.	Safety	AE5B	Summary of Acetylcholinesterase-Inhibition Adverse Events of Special Interest by Number of Events and Unique Preferred Terms and Subgroup Strata		DS, SAC
3.121.	Safety	ESI2B	Summary of Onset, Duration, and Lag Time of Acetylcholinesterase-Inhibition Event	Summary table to present statistics (mean, median, max, min) of time to first event, duration, and lag time since last dose for ACHE-I, non-GI AChE-I, and GI AChE-I events	DS, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.122.	Safety	ESI2B	Summary of Onset, Duration and Lag Time of Acetylcholinesterase-Inhibition Event by Subgroup Strata	Subgroup defined in RAP for safety analysis	DS, SAC
3.123.	Safety	AE5B	Summary of Adverse Events Leading to Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term and Maximum Grade		DS, SAC
3.124.	Safety		Summary of Non-Serious Drug Related Adverse Events by System Organ Class and Preferred Term		DS, SAC
Laboratory					
3.201.	Safety	LB1	Summary of Clinical Chemistry Values Change from Baseline		DS, SAC
3.202.	Safety	LB16	Summary of Emergent Chemistry Laboratory Values by Maximum Grade Increase from Baseline		DS, SAC
3.203.	Safety	LB1	Summary of Hematology Laboratory Values Change from Baseline		DS, SAC
3.204.	Safety	LB16	Summary of Emergent Hematology Laboratory Values by Maximum Grade Increase from Baseline		DS, SAC
3.205.	Safety	UR3	Summary of Urinalysis Dipstick Results		DS, SAC
Vital Signs and Liver Events					
3.301.	Safety	VS1	Summary of Change from Baseline in Vital Signs		DS, SAC
3.302.	Safety	VS7	Summary of Worst-Case Vital Signs Results Relative to Potential Clinical Importance Criteria Post-Baseline Relative to Baseline		DS, SAC
3.303.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting		DS, SAC
3.304.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities		DS, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Family History					
3.401.	Safety	FH1	Summary of Family History of Cardiovascular Risk Factors		DS, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events (Adverse Reactions)					
3.501	Safety	Template Table 1 Incidence rate and group difference by MedDRA classification (Pharma Layout)	Summary of Treatment Emergent Adverse Events by System Organ Class, High Level Term and Preferred Term - Safety		DS, SAC
3.502	Safety	Template Table 1 Incidence rate and group difference by MedDRA classification (Pharma Layout)	Summary of Treatment Emergent Adverse Events by System Organ Class, High Level Term and Preferred Term with High Level Term Meeting the Quantitative Assessment Criteria - Safety		DS, SAC
3.503	Safety	Template Table 1 Incidence rate and group difference by MedDRA classification (Pharma Layout)	Summary of Treatment Emergent Adverse Events by System Organ Class, High Level Term and Preferred Term by Subgroups - Safety		DS, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.504	Safety	Template Table 2 AE13 Incidence rate of AE according to different attributes (by treatment group)	Incidence Rate of Treatment Emergent Adverse Event According to Different Attributes by Treatment Group - Safety		DS, SAC
3.505	Safety	Template Table 3 - AE5A Incidence rate of AE according to severity (by treatment group)	Summary of Treatment Emergent Adverse Events by High Level Term and Maximum Grade - Safety		DS, SAC
3.506	Safety	Template Table 4 AE6 - Incidence rate of AE according to time of first occurrence	Summary of Cumulative Incidence of Treatment Emergent Adverse Events (High Level Terms) by Time to First Occurrence - Safety		DS, SAC

12.9.9. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.101.	Safety	AE10	Plot of Common (>=1%) Adverse Events and Proportion of Participants		DS, SAC
3.102.	Safety	AE11	Cumulative Distribution of Time to First Gastrointestinal Event		DS, SAC
3.103.	Safety	EFF_F3	Stacked Bar Chart of Acetylcholinesterase Inhibition Cumulative Grade	Programming note: Y axis label is "Percentage of Subjects (%)" colors should not use red or blue to avoid misinterpretation with treatment arms. Grade scale is 0 best-case for participant to 4 worst case for participant. Ordering of AChE-I grouping. 1. AChE-I 2. non-GI AChE-I	DS, SAC
3.104.	Safety	EFF_F3	Stacked Bar Chart of non- Gastrointestinal Acetylcholinesterase Inhibition Cumulative Grade		DS, SAC
3.105.	Safety	EFF_F3	Bar Chart of Gastrointestinal Events by Grade in Percentage of Participants over Time		DS, SAC
3.106.	Safety	AE10	Plot of Acetylcholinesterase Inhibition Events Relative Risk		DS, SAC
3.201.	Safety	LIVER14	Plot of Maximum Post-Baseline vs Baseline Alanine Aminotransferase		DS, SAC
3.202.	Safety	LIVER9	Plot of Maximum Total Bilirubin vs Maximum Post Baseline Alanine Aminotransferase		DS, SAC

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.203.	Safety	LB11	Liver Function Tests Participant Profiles		DS, SAC
BENEFIT/RISK					
3.301.	Micro-ITT, Safety	EFF_T4	Forest plot for Benefit/Risk		DS, SAC
Adverse Events (Adverse Reactions)					
3.401	Safety	Template Visual 1 double dot plot	Dot Plot for Treatment Emergent Adverse Events by High Level Term - Safety		DS, SAC
3.402.	Safety	Template Visual 3 Heatmap	Heatmap of Risk Ratios for Treatment Emergent Adverse Event High Level Terms that Meet the Screening Criteria by System Organ Class - Safety		DS, SAC
3.403.	Safety	Template Visual 5 Kaplan Meier curve	Kaplan Meier Curve for Treatment Emergent Potential AR Event by Treatment - Safety		DS, SAC

12.9.10. ICH and Non-ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**ICH/Non-ICH & Programming Notes**	**Deliverable**
Participant Disposition					
101	Intent-to-Treat	ES2	Listing of Reasons for Study Withdrawal	**ICH Listing** Flag participants who also discontinue treatment	DS, SAC
102	Intent-to-Treat	SD2	Listing of Reasons for Study Treatment Discontinuation	**ICH Listing**	DS, SAC
103	Intent-to-Treat	SP3	Listing of Participants Excluded from Any Population	**ICH Listing**	DS, SAC
104	Screened	ES7	Listing of Reasons for Screen Failure	**Non-ICH Listing**	DS, SAC
Protocol Deviations					
201	Intent-to-Treat	DV2	Listing of Important Protocol Deviations	**ICH Listing** Any important deviations related to COVID-19 will be captured here	DS, SAC
202	Intent-to-Treat	IE3	Listing of Participants with Inclusion/Exclusion Criteria Deviations	**ICH Listing**	DS, SAC
Demographic and Baseline Characteristics					
301	Intent-to-Treat	DM2	Listing of Demographic and Baseline Characteristics	**ICH Listing**	DS, SAC
302	Intent-to-Treat	DM9	Listing of Race	**ICH Listing**	DS, SAC
303	Intent-to-Treat	MH2	Listing of Medical Conditions	**ICH Listing**	DS, SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**ICH/Non-ICH & Programming Notes**	**Deliverable**
304	Intent-to-Treat	TA1	Listing of Randomized and Actual Treatments	**Non-ICH Listing**	pre-HDL (post unblinding), SAC
305	Intent-to-Treat	SU2	Listing of Substance Use	**Non-ICH Listing**	DS, SAC
306	Intent-to-Treat	POP_L1	Listing of Social Sexual History at Baseline	**Non-ICH Listing**	DS, SAC
307	Intent-to-Treat	POP_L1	Listing of Social Sexual History at the TOC Visit, Since Last Visit	**Non-ICH Listing**	DS, SAC
Prior and Concomitant Medications					
401	Intent-to-Treat	CM3	Listing of Prior and Concomitant Medications	**Non-ICH Listing** Flag systemic antibiotics with activity against NG, and if before or after TOC or before FU	DS, SAC
402	Intent-to-Treat	CM3	Listing of Concomitant Antibiotic Therapies for Gonorrhea	**Non-ICH Listing**	DS, SAC
403	Intent-to-Treat	CM3	Listing of Concomitant Antibiotic Therapies for *Chlamydia trachomatis* or *Mycoplasma genitalium* after TOC Visit	**Non-ICH Listing**	DS, SAC
Exposure and Treatment Compliance					
501	Intent-to-Treat	EX3	Listing of Exposure Data	**ICH Listing**	SAC
502	Intent-to-Treat	EX3	Listing of Gepotidacin Treatment Compliance	**ICH Listing**	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**ICH/Non-ICH & Programming Notes**	**Deliverable**
Efficacy					
601	Micro-ITT	EFF_L1	Listing of Microbiological Outcome and Response for *Neisseria gonorrhoeae*	**Non-ICH Listing** Include body site	DS, SAC
602	Micro-ITT	EFF_L1	Listing of NAAT Outcomes and Responses	**Non-ICH Listing** Include body site	DS, SAC
603	Intent-to-treat	EFF_L2	Listing of Central Laboratory NAAT Results	**Non-ICH Listing** Include body site	DS, SAC
604	Intent-to-treat	EFF_L3	Listing of Gram Stain Results from Urogenital Specimens	**Non-ICH Listing** Only for urogenital site and NG	DS, SAC
605	Intent-to-treat	EFF_L4	Listing of *Neisseria gonorrhoeae* Culture and Identification	**Non-ICH Listing** By body site	DS, SAC
606	Intent-to-treat	EFF_L4	Listing of *Neisseria gonorrhoeae* Urogenital Culture and Identification (Additional FDA isolates for Micro ITT FDA population)	**Non-ICH Listing**	DS, SAC
607	Intent-to-treat	EFF_L5	Listing of Susceptibility Results, Microbiological Outcome, and Response for *Neisseria gonorrhoeae* (CLSI)	**Non-ICH Listing** Include Body Site and by Drug	DS, SAC
608	Intent-to-treat	EFF_L5	Listing of Susceptibility Results, Microbiological Outcome, and Response for *Neisseria gonorrhoeae* (EUCAST)	**Non-ICH Listing** Include Body Site and by Drug	DS, SAC
609	Intent-to-treat	EFF_L6	Listing of Reduction in Susceptibility (*Neisseria gonorrhoeae*) (CLSI)	**Non-ICH Listing** Include Body Site and by Drug	DS, SAC
610	Intent-to-treat	EFF_L6	Listing of Reduction in Susceptibility (*Neisseria gonorrhoeae*)- (EUCAST)	**Non-ICH Listing** Include Body Site and by Drug	DS, SAC
611	Intent-to-treat	EFF_L7	Listing of Genetic Characterization Results (CLSI)	**Non-ICH Listing** By Body Site	DS, DAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**ICH/Non-ICH & Programming Notes**	**Deliverable**
612	Intent-to-treat	EFF_L7	Listing of Genetic Characterization Results (EUCAST)	**Non-ICH Listing** By Body Site	DS, SAC
613	Micro-ITT	EFF_L8	Listing of Baseline and Post-therapy Results for Microbiological Failures (CLSI)	**Non-ICH Listing** By body site and organism	DS, DAC
614	Micro-ITT	EFF_L8	Listing of Baseline and Post-therapy Results for Microbiological Failures (EUCAST)	**Non-ICH Listing** By body site and organism	DS, SAC
Adverse Events					
701	Safety	AE7	Listing of Participant Numbers for Individual Adverse Events	**ICH Listing**	DS, SAC
702	Safety	AE8CP	Listing of All Adverse Events	**ICH Listing**	DS, SAC
703	Safety	AE2	Listing of Relationship Between System Organ Class, Preferred Term, and Verbatim Text	**Non-ICH Listing**	DS, SAC
Serious and Other Significant Adverse Events					
801	Safety	AE14	Listing of Serious Adverse Events (Fatal and Non-Fatal)	**ICH Listing**	DS, SAC
802	Safety	AE8CP	Listing of Adverse Events of Special Interest	**ICH Listing**	DS, SAC
803	Safety	SAFE_L1	Listing of Deaths	**ICH Listing**	DS, SAC
All Laboratory					
901	Safety	LB5A	Listing of Clinical Chemistry Toxicities of Grade 3 or Higher	**ICH Listing**	DS, SAC
902	Safety	LB5A	Listing of All Clinical Chemistry Data for Participants with Toxicities of Grade 3 or Higher	**ICH Listing**	DS, SAC
903	Safety	LB5A	Listing of Hematology Toxicities of Grade 3 or Higher	**ICH Listing**	DS, SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**ICH/Non-ICH & Programming Notes**	**Deliverable**
904	Safety	LB5A	Listing of Hematology Data for Participants with Toxicities of Grade 3 or Higher	**ICH Listing**	DS, SAC
905	Safety	LB5A	Listing of Serology Results	**ICH Listing**	
906	Safety	UR2A	Listing of Urinalysis Data	**ICH Listing**	DS, SAC
ECG					
1001	Safety	EG5	Listing of All ECG Findings for Participants with an Abnormal Finding	**Non-ICH Listing**	DS, SAC
1002	Safety	EG3	Listing of All ECG Values for Participants with Any Value of Potential Clinical Importance	**Non-ICH Listing**	DS, SAC
Vital Signs					
1101	Safety	VS4	Listing of All Vital Signs for Participants with Potential Clinical Importance Values	**Non-ICH Listing**	DS, SAC
Liver Events and Other Safety Endpoints					
1201	Safety	SAFE_L2	Listing of *Clostridium difficile* Colitis Results	**Non-ICH Listing**	DS, SAC
1202	Safety	SU2	Listing of Alcohol Intake at Onset of Liver Event	**Non-ICH Listing** Conditional Display	DS, SAC
1203	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	**Non-ICH Listing** Conditional Display	DS, SAC
1204	Safety	LIVER7	Listing of Liver Biopsy Details	**Non-ICH Listing** Conditional Display	DS, SAC
1205	Safety	LIVER8	Listing of Liver Imaging Details	**Non-ICH Listing** Conditional Display	DS, SAC
1206	Safety	LIVER15	Liver Stopping Event Profile	**Non-ICH Listing** Conditional Display	DS, SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**ICH/Non-ICH & Programming Notes**	**Deliverable**
1207	Safety	PREG1	Listing of Participants Who Became Pregnant During the Study	**Non-ICH Listing** Conditional Display	DS, SAC
COVID-19					
1301	Intent-to-Treat	PAN5A	Country Level Listing of Start Dates of Waves of COVID-19 Pandemic Measures	**Non-ICH Listing**	DS, SAC
1302	Intent-to-Treat	PAN7	Listing of All Participants with Visits and Assessments Impacted by COVID-19 Pandemic	**Non-ICH Listing**	DS, SAC
1303	Safety	PAN12	Listing of COVID-19 Assessments and Symptom Assessments for Participants with COVID-19 Adverse Events	**Non-ICH Listing**	DS, SAC