COVANCE

Motif BioSciences

Protocol No.: ICL-24-ABSSSI2

A Phase 3, randomized double-blind, multicenter study to evaluate the safety and efficacy of intravenous iclaprim versus vancomycin in the treatment of acute bacterial skin and skin structure infections suspected or confirmed to be due to Gram-positive pathogens. (REVIVE-2)

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STATISTICAL ANALYSIS PLAN

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APPROVALS

The undersigned agree that all required reviews of this document are complete, and approve this Statistical Analysis Plan as final. Programming of the tables, figures and listings based upon the specifications within this document can proceed.

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VERSION HISTORY

Version Number	Version Date	Summary and rational of change(s)
Final 1.0	17-Aug-2016	
Amendment 1.0	12-Jan-2017	Section 2.3 (Sample Size and Power) • Revised power assumption related to TOC visit. Section 3.2 (Secondary Efficacy Endpoints) • The order of PP population and mCE population was changed. •Two definitions of "Persistent Infection" and "Recurrent Infection" were added when defining clinical failure. Section 5 (Analysis Population) • The order of PP population and mCE population was changed. Section 6.2 (Handling of Dropouts or Missing Data) • Added mITT efficacy analyses for primary endpoint, while patients who do not have an adequate assessment at the appropriate visit assumed as non-responders. Section 7.2 (Patient Disposition and Data Sets Analysed) • The order of PP population and mCE population was changed. Section 7.4 (Demographics and Other Baseline Characteristics) • The order of PP population and mCE population was changed. • Added two demographic variables, diabetes (present or absent) and geographic region (US vs ex-US). Section 7.7 (Measurements of Treatment Compliance and Exposure) • Clarify the treatment is started in the AM and completed in the PM when patients are administered with iclaprim q12h for 5 to 14 days. Section 7.8.2.2 (Time to Resolution of Signs and Symptoms of ABSSSI) • The order of PP population and mCE population was changed. Section 7.8.3 (Exploratory Analysis) • For primary endpoint, added exploratory analysis for ITT population with ≥50%, ≥75%, and ≥90% reduction in lesion size at ETP compared from baseline. • For the secondary endpoint of resolution or near resolution of ABSSSI at EOT and TOC, added exploratory analysis for ITT population with at least 50% and at least 75% reduction in lesion size at both EOT and TOC compared from baseline. • If it is concluded that Iclaprim is non-inferior to Vancomycin (i.e., the lower bound of two-sided 95% confidence interval of group difference in early clinical response is greater than -0.1), it may be concluded that Iclaprim is superior to Vancomycin if the entire 95% confidence interval is >0. Superiority may also be

Version Number	Version Date	Summary and rational of change(s)
		concluded for resolution of ABSSSI at TOC in a similar manner. Section 7.8.4 (Subgroup Analysis) • Added two demographic variables for subgroup analysis: diabetes (present or absent) and geographic region (US vs ex-US). Section 7.9.1 (Adverse Events) • Added another summary of TEAEs by diabetes (present or absent). • Added the definition of SAE. Section 7.9.2 (Laboratory Evaluations) • Parameter of CRP was updated from category of haematology to chemistry. Section 7.10 (Interim Analysis) • Clarified analysis for the primary endpoint under blinded interim data was using at least 20% reduction in lesion size at ETP when compared to baseline visit. Section 7.10.2 (Laboratory Evaluations) • Add another kind of shift table between baseline and post-baseline change, only applied for liver enzyme and renal function tests.
Amendment 1.0	15–Feb-2017	Table 1 Summary of Assessments was deleted. Same information is given in the text and it is a copy from protocol.
		Section 4 (Pharmacokinetics/ Pharmacodynamics Variables) • Deleted "After the study is complete, the database locked, and the data unblinded, patients randomized to iclaprim will have their samples assayed."
		Section 5 (Analysis Population) • Added details to Per Protocol population definition. • Table 1 reformatted to separate protocol deviation types that would exclude a patient from some visits and visits from deviation types that excludes a patient from all visits. • Deleted Type I A and Type III antiarrhythmic drugs from list of prohibited medications that would exclude a patient from per protocol analysis. • Added mITT subpopulation, strep-enriched mITT for exploratory analysis. • Added PP population for EMA analysis.
		Section 5.6.1 Important Protocol Deviations Leading to Exclusion from the mPP Analysis. • This section was deleted because it provides some

Version Number	Version Date	Summary and rational of change(s)
		information as in PP population.
		Section 6.1 (Time Points and Visit Widows) • Baseline for microbiology analysis was added.
		7.4 (Demographic and Other Baseline Characteristics) • Blood culture at baseline was defined; • Geographic region subgroups were revised
		7.9.2 (Secondary Efficacy Analysis) • Added *S. pyogenes*-enriched mITT population and PP population for EMA to repeat the primary efficacy analysis.
		7.9.2.1 (Resolution or Near Resolution of ABSSSI) • Added *S. pyogenes*-enriched mITT at TOC to the analysis
		7.9.2.2 (Signs and Symptoms of ABSSSI) • Descriptive summary statistics for signs and symptoms will be limited to baseline display only.
		7.9.2.3 (Bacteriological response) • By-pathogen and by-patient bacteriological outcome section were moved from Section 3 to this section. • Added more description of analyses. • Added summary of MIC frequency and interpretation.
		7.10.1 (Adverse Events) • Treatment-emergent adverse event definition was clarified.
Amendment 2.0	10–Mar-2017	6.1 (Time Points and Visit Windows) • Added definition of baseline for microbiology data.
		6.2 (Handling of Dropouts or Missing Data) • Deleted general principle for imputing dates and clarified the imputing details refer to mockup.
		7.6 (Prior and Concomitant Medications) • Added the definition of prior medication.
		7.9.2.2 (Signs and Symptoms of ABSSSI) • Clarified patients are free of specific signs or symptoms at baseline should be out of that time-to-event analysis.

Version Number	Version Date	Summary and rational of change(s)
		7.9.3 (Exploratory Analysis) • Revised the definition for one exploratory analysis and added another exploratory analysis.
		7.10.1 (Adverse Events) • Treatment-emergent adverse event definition was clarified.
	11 July 2017	7.9.3.1 (Exploratory Analysis Excluding Lesion Size Criteria) • New section to describe analysis excluding the criteria for lesion size reduction for the following exploratory analyses: – Resolution or near resolution of ABSSSI – Clinical outcome – By-pathogen bacteriological response – By-patient bacteriological response
		7.4 (Demographic and Other Baseline Characteristics) • Age is obtained from IXRS rather than derived. • Defined Gram-positive pathogen groups. • Defined categories of severe infection.
		7.9.2.1 (Resolution or Near Resolution of ABSSSI) • Add categories of cure criteria in each analysis
		7.2.9.2 (Signs and Symptoms of ABSSSI) • Add categories of intensity to each sign and symptom.
		7.9.4 (Subgroup Analysis) • Add categories of severe infection.
		7.10.1 (Adverse Events) • Add summary of SAE > 1%
		7.10.2 (Laboratory Evaluations) • Add grade 0 (<= ULN) Add description of urinalysis categorical summary
	21 July 2017	7.9.3.1 (Exploratory Analysis Excluding Lesion Size Criteria) • Revised definition of persistent and recurrent infection • Clarified definition of unplanned significant procudures (throughout the SAP)

TABLE OF CONTENTS

APPROVALS **2**

VERSION HISTORY **3**

GLOSSARY OF ABBREVIATIONS **9**

1 SOURCE DOCUMENTS **11**

2 PROTOCOL DETAILS **11**

2.1 Study Objectives **11**

2.2 Overall Study Design **11**

2.3 Sample Size and Power **12**

3 EFFICACY AND SAFETY VARIABLES **14**

3.1 Primary Efficacy Endpoint **14**

3.2 Secondary Efficacy Endpoints **14**

3.3 Safety Variables **15**

4 PHARMACOKINETIC/PHARMACODYNAMIC VARIABLES **15**

5 ANALYSIS POPULATIONS **15**

5.1 Safety Population **15**

5.2 Intent-to-treat (ITT) population **15**

5.3 Microbiological intent-to-treat (mITT) population **15**

5.4 Per Protocol (PP) Population **16**

5.4.1 Important Protocol Deviations Leading to Exclusion from the PP Analysis 16

5.5 Modified clinically evaluable (mCE) population **18**

5.6 PP microbiological evaluable (mPP) population **18**

5.7 *S. pyogenes*-enriched mITT (*S. pyogenes* mITT) population **18**

5.8 PP population for EMA sensitivity analysis **18**

6 DATA HANDLING **18**

6.1 Time Points and Visit Windows **18**

6.2 Handling of Dropouts or Missing Data **19**

7 STATISTICAL METHODS **19**

7.1 General Principles **19**

7.2 Patient Disposition and Data Sets Analyzed **20**

7.3 Protocol Deviations **20**

7.4 Demographics and Other Baseline Characteristics **20**

7.5 Medical History **21**

7.6 Prior and Concomitant Medications **21**

7.7 Significant Procedures **22**

7.8 Measurements of Treatment Compliance and Exposure **22**

7.9 Efficacy 22
7.9.1 Primary Efficacy Analysis 22
7.9.2 Secondary Efficacy Analysis 22
7.9.3 Exploratory Analysis 24
7.9.4 Subgroup Analysis 26
7.10 Safety 27
7.10.1 Adverse Events 27
7.10.2 Laboratory Evaluations 28
7.10.3 Vital Signs 29
7.10.4 Electrocardiograms 29
7.10.5 Physical Examination 30
7.11 Interim Analysis 30
8 REFERENCES 30
9 APPENDICES 31
Appendix A – Prohibited Medicines 31
Appendix B – Schedule of Events 32
Appendix C – Table, Figure and Listing Shells 34

TABLES:
Table 1: Important Protocol Deviations Leading to Exclusion from the PP population 17
Table 2: Laboratory Evaluations 28

FIGURES:
Figure 1: Study Design 13

GLOSSARY OF ABBREVIATIONS

Abbreviation	Term
ABSSSI	acute bacterial skin and skin structure infection
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
ASO	anti-streptolysin O
AST	aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BUN	blood urea nitrogen
CBC	complete blood count
CCLS	Covance Central Laboratory Services
CI	confidence interval
CO_2	carbon dioxide
CPK	creatine phosphokinase
CrCL	creatinine clearance
CRF	case report form
CRP	C-reactive protein
CTMS	Clinical Trial Management System
CV	Conventional units for laboratory results
ECG	Electrocardiogram
eCRF	electronic case report form
EOT	End of Therapy
EMA	European Medicines Agency
ETP	early timepoint
GGT	gamma glutamyl transferase
hCG	beta-human chorionic gonadotropin
ITT	intent-to-treat
IXRS	Interactive Phone and Web Response System
LDH	lactate dehydrogenase
LFT	Liver Function Test
LFU	Late Follow-Up
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume
MedDRA	Medical Dictionary for Regulatory Activities
MIC	minimum inhibitory concentration
MRSA	Methicillin-resistant Staphylococcus aureus
MSSA	Methicillin-sensitive Staphylococcus aureus
mCE	Modified clinically evaluable population
mITT	microbiological intent-to-treat
mPP	Per-protocol microbiologically evaluable population
N	analysis population

Abbreviation	Term
NI	non-inferiority
PK	pharmacokinetic
PP	Per-protocol population
PT	Preferred Term
Q12h	every 12 hours
QTc	QT interval corrected for heart rate
QTcB	QTc corrected according to Bazett
QTcF	QTc corrected according to Fridericia
RBC	red blood cell
SAE	serious adverse event
SCr	serum creatinine
SD	standard deviation
SI Units	International System of Units
SOC	system organ class (MedDRA classification)
TEAE	treatment-emergent adverse event
TFLs	Tables, Figures and Listings
TOC	Test of Cure
UA	Urinalysis
WBC	white blood cells

1 SOURCE DOCUMENTS

The Statistical Analysis Plan (SAP) was written based on the following documentation:

Document	Date	Version
Protocol	21 Oct 2015	Final 1.0
Protocol Amendment 1	3 Dec 2015	Amendment 1.0
eCRF	3 Feb 2016	Production 3.0

2 PROTOCOL DETAILS

2.1 Study Objectives

Primary Objective:

The primary objective of this study is to demonstrate that iclaprim is non-inferior to vancomycin in achieving a ≥ 20% reduction in lesion size at 48 to 72 hours (early timepoint, ETP) compared to baseline in all randomized patients (intent-to-treat, ITT).

Secondary Objectives:

The secondary objectives of this study are to demonstrate non-inferiority of iclaprim compared to vancomycin in the ITT, microbiological ITT (mITT), modified clinically evaluable (mCE), per protocol (PP), and microbiological PP (mPP) populations for the following:

1. Resolution or near resolution of acute bacterial skin and skin structure infection (ABSSSI) (clinical cure, defined by a ≥ 90% reduction in lesion size from the size at baseline, no increase in lesion size since ETP, and no requirement for additional antibiotics [except aztreonam and metronidazole] or unplanned significant surgical procedures [excluding procedures that reflect failure of antimicrobial therapy] after ETP other than bedside wound care) at Test of Cure (TOC) visit (7 to14 days after the end of treatment);
2. Resolution or near resolution (≥ 90%) of ABSSSI at End of Therapy (EOT);
3. Resolution or near resolution (≥ 90%) of ABSSSI at EOT and TOC among patients with severe infection at baseline defined by meeting one or more of the following criteria:
    a. fulfilled the published definition for systemic inflammatory response syndrome (SIRS) by having ≥ 2 of the following findings: body temperature > 38°C or < 36°C, heart rate > 90 bpm, respiration rate >20 breaths/minute, and WBC > 12000/mm^3 or < 4000/mm^3 or > 10% bands;
    b. Evaluated as having severe tenderness or severe erythema at the infection site; or
    c. Positive blood cultures at baseline.
4. Time to resolution of systemic and local signs and symptoms of ABSSSI.

Additional secondary objectives are to:

5. Assess microbiological outcome in the mITT, mCE, and mPP populations at EOT and TOC;
6. Establish the pharmacokinetic (PK) profile for iclaprim using population pharmacokinetics; and
7. Establish the safety profile of iclaprim in patients with ABSSSI.

2.2 Overall Study Design

This is a multicenter, randomized, double-blind study of the efficacy and safety of iclaprim compared to vancomycin. Patients will receive either iclaprim or vancomycin for 5 to 14 days, which comprises the range of total treatment duration. Patients will be evaluated daily up to ETP, then every 48 to 72 hours through the end of treatment. If the last dose of study drug falls on a day when an evaluation was not

planned, an additional evaluation visit will need to be performed on that day (i.e. All EOT evaluations should be performed on the last day [+2 days] of drug dose). Patients will also be evaluated at the TOC visit (7 to 14 days post-EOT) for both efficacy and safety, and will have a Late Follow-Up (LFU) phone call (28 to 32 days post-first dose) for safety only. Note, however, that patients with high liver function tests (LFTs) and unresolved adverse events (AEs) at TOC must be seen in person for an additional visit at LFU. The total duration of participation in the study for each patient is 29 to 33 days.

After completing screening procedures, including obtaining cultures from a clinical specimen prior to antibacterial therapy, a total of 600 patients (300 per treatment group) will be randomized (1:1) to receive either: (1) iclaprim 80 mg every 12 hours or (2) vancomycin 15 mg/kg. The duration of treatment for both groups will be 5 days (minimum duration) to 14 days (maximum duration). Assignment to study drug will be performed using a central randomization system. Approximately 80 active centers will be recruited.

Figure 1 displays a diagram of the study design.

The investigators, clinical study personnel, sponsor, and the patients will remain blinded with respect to the study drug treatment allocation. The unblinded pharmacist or his/her designee will be responsible for preparation of infusions. To account for the variable vancomycin dosing intervals, normal saline dummy infusions will be used to maintain the blind for patients who require a vancomycin dosing frequency other than every 12 hours (Q12h).

Concomitant antibiotics aztreonam and metronidazole used in compliance with their respective prescribing information are allowed at the discretion of the investigator during the study drug phase.

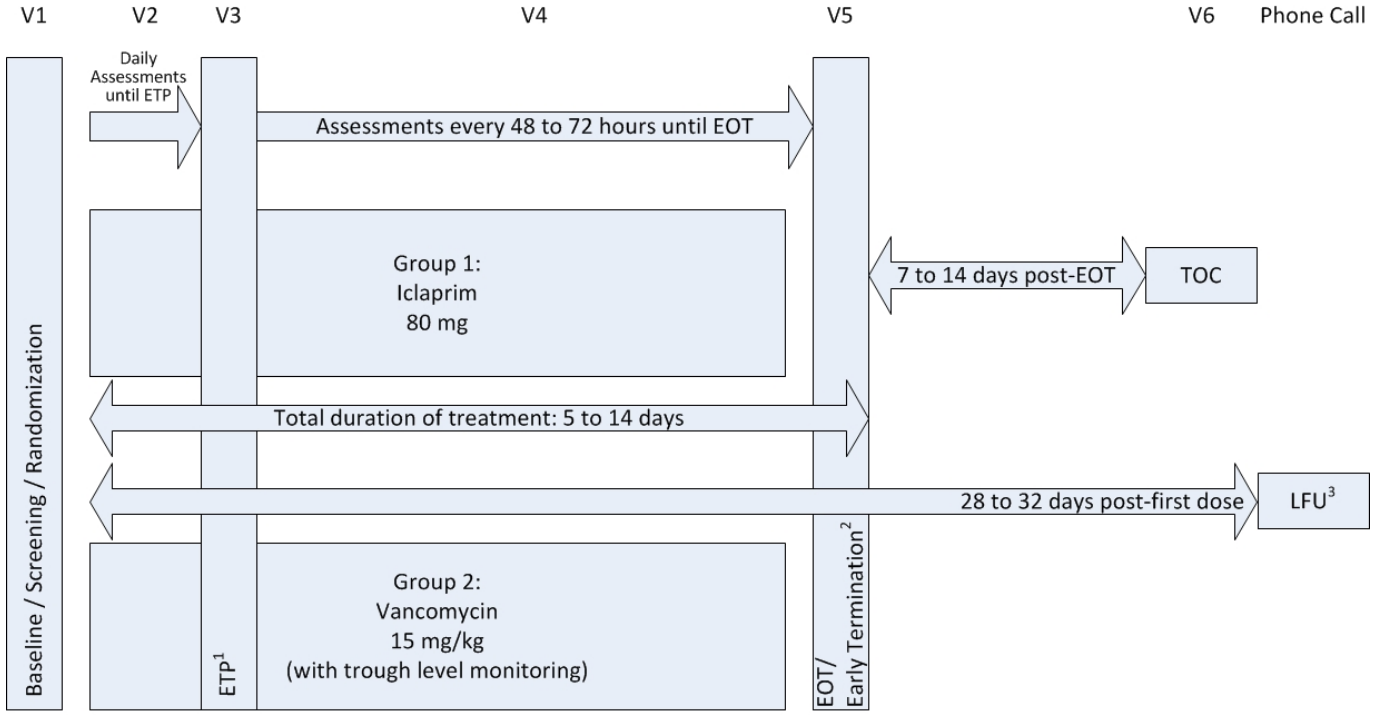
Systemic antibiotics (other than aztreonam and metronidazole) or topical antibiotics at the site of the ABSSSI under investigation, steroids >20 mg/day prednisolone or equivalent; and Type I A and Type III-antiarrhythmic drugs are prohibited.

2.3 Sample Size and Power

For non-inferiority (NI) testing with a 1-sided alpha of 0.025, assuming a 75% early clinical response rate in each group and a 10% NI bound delta, a sample size of 295 ITT patients per treatment group is required for 80% power. In addition, using similar methods of NI testing with a 1-sided alpha of 0.025, assuming a 90% clinical response rate at TOC in vancomycin and iclaprim group and a 10% NI bound delta, a sample size of 300 patients in the ITT population per treatment group is required for 98% power.

A total of 600 patients (approximately 300 per treatment group) will be randomized (1:1) for this study.

Figure 1: Study Design



Note: A window of +/- 2 hours is acceptable for infusion of study medication.
1. ETP assessment is 48 to 72 hours post-first dose
2. If the last dose of study drug falls on a day when an evaluation was not planned, an additional evaluation visit will need to be performed on that day (ie. All EOT evaluations should be performed on the last day [+/- 2 days] of drug dose).
3. If duration of therapy is 14 days, LFU may overlap with TOC. In this case, all LFU evaluations may take place at the TOC visit.
V*n*=Visit *n*; ETP=Early Time Point; EOT=End of Therapy; TOC=Test of Cure; LFU=Late Follow-up

3 EFFICACY AND SAFETY VARIABLES

3.1 Primary Efficacy Endpoint

The primary efficacy endpoint is the proportion of randomized patients who achieve an early clinical response (defined as reduction in the lesion size ≥ 20% compared to baseline) at 48 to 72 hours (ETP) and will be evaluated in ITT population.

3.2 Secondary Efficacy Endpoints

The primary efficacy endpoint will be repeated in mITT, PP, mCE and mPP populations.

The secondary endpoints are:

1. Resolution or near resolution of ABSSSI (i.e., Clinical Cure, defined by a ≥ 90% reduction in lesion size from baseline, no increase in lesion size since ETP, and no requirement for additional antibiotics [except aztreonam and metronidazole] or unplanned significant surgical procedures [excluding procedures that reflect failure of antimicrobial therapy] after ETP other than bedside wound care) at TOC for iclaprim (80 mg q12h) compared with vancomycin (weight-based dose) for ITT, mITT, PP, mCE, and mPP populations
2. Resolution or near resolution (≥ 90%) of ABSSSI at EOT for ITT, mITT, PP, mCE, and mPP populations
3. Resolution or near resolution (≥ 90%) of ABSSSI at EOT and TOC among patients with severe infection at baseline for ITT, mITT, mCE, PP, and mPP populations
4. Time to resolution of signs and symptoms of ABSSSI from start of treatment for ITT, mITT, PP, mCE, and mPP populations
5. Patient-level bacteriological response rate at EOT and TOC for mITT, mCE, and mPP populations
6. Pathogen-level bacteriological response rate at EOT and TOC for mITT, mCE, and mPP populations

The clinical outcome will be evaluated at EOT and TOC (7 to 14 days post-EOT) programmatically for ITT, PP and mPP populations, and categorized as cure, failure, or indeterminate defined as follows:

- Cure: defined by a ≥ 90% reduction in lesion size from baseline, no increase in lesion size since ETP, and no requirement for additional antibiotics (except aztreonam and metronidazole) or unplanned significant surgical procedures (excluding procedures that reflect failure of antimicrobial therapy);
- Failure: reduction in lesion size that is < 20% for ETP and < 90% for EOT and TOC compared to baseline, death related to the infection, persisting or recurrent infection, need for unplanned surgical procedure (i.e., procedures that reflect failure of antimicrobial therapy), or administration of rescue antibiotic therapy for the index infection before or at assessed visits or recurrence of index infection;
- Indeterminate: data inadequate for assessment of efficacy (there are no post-baseline local or systemic signs and symptoms data available to make this assessment [e.g., patient lost to follow up] after < 2 days of treatment or < 4 doses and no EOT evaluation), lost to follow-up prior to ETP, withdrawal of consent, receipt of effective antibiotic therapy for a cause other than the index infection before assessed visits, or death not attributed to the index ABSSSI or complication of ABSSSI.

Note: If a patient starts an antibiotic for an infection other than the primary ABSSSI at EOT visit date, they will still be included as clinical cure or clinical failure dependent on the size of the lesion at EOT. The same rule will be applied to the evaluation of clinical outcome at TOC visit.

The definition of "Persistent Infection" and "Recurrent infection" when defining clinical failure are listed as follows:

(1) Persistent infection occurs if a patient receives additional antibiotics for treatment of primary ABSSSI (except aztreonam and metronidazole) at EOT compared to baseline. The same rule applies when evaluating clinical failure at TOC visit.

(2) Recurrent infection occurs if a patient does not receive additional antibiotics (except aztreonam and metronidazole) at EOT and receives additional antibiotics (except aztreonam and metronidazole) at TOC for treatment of primary ABSSSI.

3.3 Safety Variables

Safety endpoints are AEs, serious adverse events (SAEs), electrocardiogram (ECG) results, liver function tests, hematology, coagulation, serum chemistry including creatinine and creatinine clearance, urinalysis (UA), vital signs, and physical examinations.

4 PHARMACOKINETIC/PHARMACODYNAMIC VARIABLES

Pharmacokinetic samples will be obtained from patients on 3 occasions: following the first dose of study medication, at ETP, and at EOT.

Iclaprim plasma concentrations will be used to determine population PK parameters with a non-linear mixed effect model. The potential influence of clinical characteristics (age, size, sex, hepatic function, renal function, concomitant medications, etc.) on PK parameters will be evaluated. Further details will be provided in a separate population PK analysis plan.

5 ANALYSIS POPULATIONS

The ITT population will be the primary population for analysis of primary endpoint. Microbiological response will be evaluated for mITT, mCE and mPP populations. All other efficacy analyses will be performed for each of the ITT, mITT, PP, mCE and mPP populations. All safety analysis will be performed in the Safety population. Enrolled patients are those who signed the inform consent form.

5.1 Safety Population

All patients who receive any study drug during the trial will be included in the Safety population. It is the primary population for safety analyses. Patients will be analyzed according to the treatment they receive.

5.2 Intent-to-treat (ITT) population

All randomized patients will be included in the ITT population. It is the primary population for efficacy analyses. Patients will be analyzed in the treatment group to which they are randomized.

5.3 Microbiological intent-to-treat (mITT) population

All randomized patients who have a Gram-positive baseline bacteria pathogen identified as the cause of ABSSSI will be included in mITT population.

A Gram-positive bacteria pathogen is identified as the cause of ABSSSI if the Gram-positive pathogen is identified from the lesion sample, and is subsequently confirmed by Covance Central Laboratory Services (CCLS).

5.4 Per Protocol (PP) Population

The PP population will consist of all patients in the ITT population who receive at least 80% of their planned doses and provide adequate data for assessment for each of the following time points: ETP, EOT, and TOC. This population excludes patients with Gram-negative bloodstream infections at baseline who are discontinued in order to treat the Gram-negative pathogen.

The data are considered adequate for inclusion in the PP population when the assessment of lesion size and clinical signs and symptoms are both performed at corresponding time point. To be included in the PP population, a patient must not have important protocol deviations.

5.4.1 Important Protocol Deviations Leading to Exclusion from the PP Analysis

Only those important protocol deviations considered to have a major effect on efficacy will lead to complete exclusion of the patient from the PP population. For the purposes of this study, the following criteria (Table 1) have been identified as important protocol deviations leading to exclusion from the PP population as it is considered that the occurrences of any of these criteria might have an important influence on the primary efficacy endpoint.

The majority of the important protocol deviations leading to exclusion from the PP population will be determined programmatically from the data. Those criteria which require clinical or medical monitoring interpretation will be reviewed prior to database lock, following discussion with the medical monitor and Sponsor.

Table 1: Important Protocol Deviations Leading to Exclusion from the PP population

Type	**Important Protocol Deviations Leading to Exclusion from the PP population**	**Method of Identification**
Discontinuation of study drug	Patients with Gram-negative bloodstream infections who are discontinued in order to treat the Gram-negative pathogen.	**Programmatic** check on blood culture results and patient disposition status. **Manual** review will be performed for identifying patients who discontinue the study drug.
Noncompliance	Received less than 80% of the planned study drug.	**Programmatic** check based on the exposure and drug accountability data. **Manual** review will be performed for identifying patients who miss the study drug.
Errors in Treatment Allocation	Patients that receive a wrong treatment at 1 or more study visits due to packaging or dispensing errors	**Programmatic** check based on unblinded IXRS database after the study is unblinded. The check will be done by comparing the package number that IXRS had assigned to the patient against the package number actually used.
Clinical Trial Management System (CTMS)	Covance Clinical will provide the list of protocol deviations based on the clinical monitoring	**Manual** review: This list will be reviewed and the important protocol deviations that will lead to exclusion from the PP population will be identified.
Type	**Important Protocol Deviations Leading to Exclusion at Affected Visits**	**Method of Identification**
Missing the required clinical evaluation	No adequate data at ETP, EOT and TOC	**Programmatic** check the missing assessment of lesion size, and the signs and symptoms at time points ETP, EOT and TOC
Prohibited medications	Systemic antibiotics (other than aztreonam and metronidazole) or topical antibiotics at the site of the ABSSSI under investigation, and steroids >20 mg/day prednisolone or equivalent (See Appendix A).	**Manual** review: List of preceding and concomitant medications will be reviewed by the study physician for potential prohibited medications occurring during the study up to and including TOC.

All important protocol deviations leading to exclusion from the PP population occurring during the study will be reviewed and approved by the Sponsor prior to database lock and unblinding. Should additional important protocol deviations leading to exclusion from the PP population, not anticipated at the time of preparing this SAP, be identified during the study (and prior to unblinding), they will be documented in a SAP amendment and included in all relevant protocol deviation reviews and approvals.

If a patient is one or more visits, the rule to determine if they are included in Per-protocol population for different time-point is summarized in the table below. For overall analysis, such as demographic summary, patients are included in the overall Per-protocol population if they are included in PP analysis at any visit.

ETP visit	EOT visit	TOC visit	Per-protocol Assessment
Missing	Missing or not missing	Missing or not missing	Patient is excluded from all visits even if EOT or TOC are not missing because lesion size difference from ETP cannot be determined.
Not missing	Missing	Missing	Evaluable at ETP only.
Not missing	Missing	Not missing	Evaluable at ETP and TOC, excluded from EOT.
Not missing	Not missing	Missing	Evaluable at ETP and EOT, excluded from TOC.
Missing	Missing	Missing	Non-evaluable at all visits

When analyzing efficacy endpoints, the following two rules will be applied to determine the clinical outcome for Per-protocol analysis:

1. If a rescue antibiotic is taken at a visit for clinical failure in ITT analysis, then the patient is still included for Per-protocol analysis at that timepoint and the outcome of failure is carried forward to subsequent visits and the patient is included at each of those visits for PP population.

2 If antibiotic is taken for a cause other than the index infection before assessed visits, the clinical outcome for this patient is Indeterminate for ITT population; however, this patient is excluded from PP population at that visit and subsequent visits.

5.5 Modified clinically evaluable (mCE) population

The mCE population will consist of all patients excluded from the PP population only because they have received prohibited concomitant or preceding antibiotics therapy active against Gram-positive pathogens.

5.6 PP microbiological evaluable (mPP) population

All mITT patients who receive at least 80% of their planned doses and provide adequate data for assessment for each of the following time points: ETP, EOT, and TOC.

5.7 *S. pyogenes*-enriched mITT (*S. pyogenes* mITT) population

S. pyogenes mITT include all mITT patients and patients who have infection site culture negative and ASO titer positive for *S. pyogenes* at baseline or TOC.

5.8 PP population for EMA sensitivity analysis

All PP patients without excluding any results at visits because of missing results at ETP.

6 DATA HANDLING

6.1 Time Points and Visit Windows

All analyses will use the nominal study visit as defined in the Study Schedule and eCRF. The study visit designations throughout tables and listings are listed as Baseline, Visit 2 (0-24 HRS), VISIT 2 (25-48 HRS), VISIT 2 (49-72 HRS), ETP, EOT, TOC, every 48 to 72 hours until EOT for Visit 4 and LFU. For microbiology data, baseline is defined within ±24 hours for first study treatment.

Study Visit in Protocol	Visit designations in tables and listings
Baseline/Screening/Visit 1 or Visit 2 (0-24 HRS)	Baseline
Visit 1	Visit 1
Daily until ETP for Visit 2	Visit 2.1, Visit 2.2 and Visit 2.3
ETP for Visit 3	ETP
Every 48 to 72 hours until EOT for Visit 4	Visit 4.1, Visit 4.2, Visit 4.3 and Visit 4.4
EOT for Visit 5	EOT
TOC for Visit 6	TOC
LFU phone call	LFU

6.2 Handling of Dropouts or Missing Data

For all ITT and mITT efficacy analyses, including the analysis of the primary endpoint, patients who do not have an adequate assessment at the appropriate visit will be assumed to be non-responders.

The safety evaluations will be performed on observed data only. Missing data will not be imputed for safety analyses except following rules to determine onset or stop dates of AEs or concomitant medications (see Section 1.4 in Appendix C – Table, Figure and Listing Shells for more details).

The imputed dates will not be listed. Study day relative to the first dose of treatment associated with missing or partial dates will not be displayed in AE listings.

The imputed dates of a medication will only be used to determine whether that medication will be classified as prior medication or concomitant medication.

7 STATISTICAL METHODS

7.1 General Principles

All data processing, summarization and analyses will be performed using Hosted SAS Environment / Version 9.3 (or later) of the SAS® (SAS Institute, Cary, NC) statistical software package.

Unless specified otherwise, data will be displayed using the following treatment group labels, in the order presented:

- Iclaprim
- Vancomycin
- Total (if applicable)

All data collected will be presented in listings by treatment group, country, center, patient, and visit (where applicable), unless otherwise specified.

Data will be presented in summary tables by treatment group, assessment and visit (where applicable). The category “Missing” will be presented if the number missing is greater than zero for at least one treatment group.

Descriptive summary statistics for continuous variables will include the number of observations (N), mean, standard deviation (SD), median and range.

Descriptive summary statistics for categorical variables will include frequency counts and percentages. Unless stated otherwise in the table shells, the denominator for percentage calculations will be the number of patients in the analysis population.

Dates will be displayed as DDMMMYYYY.

All significance tests will use a significance level of 5% for two-sided tests and a significance level of 2.5% for one-sided tests.

7.2 Patient Disposition and Data Sets Analyzed

Patient disposition will be listed and summarized by treatment group and overall, and will include the number and percentage of patients:

- enrolled;
- randomized (ITT population);
- treated (Safety populations);
- other study populations (mITT, PP, mCE, mPP, *S. pyogenes* mITT, safety).

In addition, the number and percentage of patients who complete the study, who discontinue from study early, including a breakdown of the primary reasons for discontinuation, will be presented for ITT and Safety populations. The number and percentage of patients who complete the treatment will be analyzed in a similar manner.

A summary of patient enrollment by country and center will also be provided by treatment group and overall for the ITT population.

The number of patients who complete study or complete each visit of ETP, TOC and TOC will be analyzed by treatment groups and study populations.

7.3 Protocol Deviations

All important protocol deviations leading to exclusion from the PP population (see Section 5.4.1) will be listed and summarized by treatment group for the ITT and mITT populations.

The deviations will be identified before data are unblinded.

7.4 Demographics and Other Baseline Characteristics

Demographic and baseline characteristics will be listed and summarized by treatment group and overall for ITT, mITT, PP, mCE, mPP and safety populations. Standard descriptive statistics will be presented for the continuous variables of:

- age (years obtained from IXRS)
- weight (kg);
- height (cm);
- body mass index (BMI; kg/m^2) calculated as ($weight/height^2$) where weight is in kilograms and height is in meters;
- lesion size (cm^2)

The total counts and percentages of patients will be presented for the categorical variables of:

- age group (grouped as 18-39 years, 40-64 years, and 65 years and older);
- sex;
- race;
- ethnicity;

- creatinine clearance (CrCL) in mL/min (grouped as ≥ 90, 60-89, 30-59, 15-29, and < 15 or hemodialysis);
- lesion type (major cutaneous abscess, cellulitis/erysipelas, and wound infection);
- Receipt of prior antibiotics (obtained from IXRS as Yes, No);
- Blood culture at baseline (positive, if anaerobic or aerobic blood culture has pathogen; negative, if culture taken and organism isolated but there is no pathogen or no organism was isolated)
- Gram-positive pathogen in infection site (multiple ABSSSI Gram-positive pathogen only, single Gram-positive pathogen only, single or multiple ABSSSI Gram-positive pathogens and Gram-negative pathogens) ;
- Methicillin-resistant *Staphylococcus aureus* (MRSA) vs Methicillin-sensitive *Staphylococcus aureus* (MSSA);
- Infection site pathogen (multiple pathogens vs single pathogen);
- *Streptococcus pyogenes* determined from ASO and either blood or infection site culture results from baseline (ASO positive only (> 330 IU/mL), culture positive only, ASO positive and culture positive, ASO negative (<= 330 IU/mL) and culture negative).
- severe infection (met the criteria of SIRS, has severe tenderness or severe erythema, has positive blood culture at baseline), defined in Section 2.1
- diabetes (yes – if patient have medical history for diabetes, or baseline glucose > 200 mg/dL, or concomitant medications of either insulin or oral hypoglycemic; or no – no medical history for diabetes, baseline glucose <= 200 mg/dL, no concomitant medications of either insulin or oral hypoglycemic.)
- geographic region (US, Europe, Latin America).

Other baseline measurements, such as type of culture specimen / culture result, lesion type, blood culture by visit, baseline pathogens, vital signs, ECG, and laboratory evaluations, will be summarized by treatment group with the post-baseline measurements.

7.5 Medical History

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 18.1 (or a later version if updated during the study). All medical history will be listed, and the number and percentage of patients with any medical history will be summarized for ITT population by system organ class (SOC) and preferred term (PT) for each treatment group and overall.

7.6 Prior and Concomitant Medications

Medications received prior to or concomitantly with treatment will be coded by Covance using the WHO Drug Dictionary, Version WHODRUG Enhanced 201509, DDEB2 (or a later version if updated during the study), Anatomical Therapeutic Chemical (ATC) Classification codes.

Prior medications are those taken prior to the first dose date of treatment and within the preceding 30 days of the Informed Consent.

Concomitant medications are those with a start date on or after the first dose date of treatment, or those with a start date before the first dose date of treatment and a stop date on or after the first dose date of treatment, or with a start date before the first dose date of treatment and are reported as ongoing.

If a medication cannot be classified as “prior” or “concomitant” after applying imputation rules for missing/incomplete dates, it will be classified as concomitant.

The number and percentage of patients using each medication will be displayed together with the number and percentage of patients using at least one medication within each therapeutic class (ATC-Level 2), chemical subgroup (ATC-Level 4), and generic term.

Separate summaries will be presented for prior medications, concomitant medication excluding antibiotics, and concomitant antibiotic medications for ITT population. A patient listing of all prior and concomitant medications will be provided for ITT population.

7.7 Significant Procedures

The number and percentage of patients receiving any significant procedures, such as debridement or incision and drainage will be displayed by study visits and treatment groups for ITT population.

7.8 Measurements of Treatment Compliance and Exposure

Percentage compliance is calculated as:

100 * actual number of doses received / planned number of doses.

For example, patients are administered iclaprim q12h for 5 to 14 days, so the planned number of doses is 2 times the number of days in treatment period if the treatment is started in the AM. If a patient was treated for < 5 days, the planned number of dosing days will be considered as 5 days. If a patient was treated for > 5 days, the planned number of dosing days is the actual number of days dosed. Missed doses will not be included in the actual number of doses for the compliance calculation.

The number and percentage of compliant patients will be presented for the Safety population, where compliant is defined as percentage compliance greater ≥ 80.0%. The category of percentage compliance < 80.0% will also be presented. The treatment compliance will be tabulated with three categories with number and percentage of patients: < 80%, 80% to 100%, >100%.

The total treatment duration is defined as: Date of last dose – Date of first dose + 1 if treatment is started in the AM and completed in the PM. Treatment duration (days) will be summarized using descriptive statistics (n, mean, SD, median, minimum, and maximum) by treatment group for the Safety population.

7.9 Efficacy

7.9.1 Primary Efficacy Analysis

The primary efficacy analysis will be the NI (at significance level 0.025) of iclaprim (group 1) to vancomycin (group 2) for the proportion of ITT patients with a ≥20% reduction in lesion size at ETP compared to baseline. The NI bound will be 10%. Let P1 be the proportion for iclaprim and P2 be the proportion for vancomycin. Equivalently, if the lower bound of the two-sided 95% confidence interval (CI) for P1 – P2 is greater than -0.100 based on the Z test with unpooled variance estimate, NI will be concluded.

7.9.2 Secondary Efficacy Analysis

The primary NI efficacy analysis will be repeated in the mITT, mCE, PP, mPP populations, *S. pyogenes* enriched mITT population and PP population for EMA.

The secondary endpoints are resolution or near resolution of ABSSSI (i.e., clinical cure) at TOC for iclaprim compared with vancomycin, resolution or near resolution (≥90%) of ABSSSI at EOT, resolution or near resolution (≥90%) of ABSSSI at EOT and TOC among patients with severe infection at baseline,

time to resolution of signs and symptoms of ABSSSI, by-patient bacteriological response rate at EOT and TOC, and by-pathogen bacteriological response rate at EOT and TOC.

7.9.2.1 Resolution or Near Resolution of ABSSSI

For resolution or near resolution of ABSSSI at TOC, the NI test described in Section 7.9.1 will be used to demonstrate the non-inferiority of iclaprim to vancomycin in the ITT population EMA primary endpoint. The same NI test will be repeated for mITT, mCE, PP, mPP and *S. pyogenes* enriched mITT population at TOC. All above tests will then be repeated for resolution or near resolution of ABSSSI at EOT. Additionally, the number and percentage of patients in each cure criteria will be displayed.

The NI test will be performed for resolution or near resolution of ABSSSI at TOC as well as EOT among patients with severe infection at baseline in ITT population, and repeated for mITT, PP populations.

A summary of clinical outcome, including the number and percent of patients with cure, failure and indeterminate outcomes at EOT and at TOC will be produced for the ITT, mITT, PP, and mPP.

7.9.2.2 Signs and Symptoms of ABSSSI

Baseline signs (tender to palpitations, erythema, edema, purulent drainage/discharge, fluctuance, induration, ulceration, and necrotic tissue) and baseline symptoms (localized pain, swelling, chills, and fever) will be summarized by intensity (none, mild, moderate and severe) using descriptive statistics.

Time (in days) to resolution of each of the signs and symptoms of ABSSSI is defined as: first date with no specified sign/symptom of ABSSSI recorded on eCRF post treatment – date of first dose + 1. For patients who are not free of the specified sign/ symptom until the end of study, the last day recorded available sign/symptom on eCRF will be used as the censoring day. For patients free of any specific signs or symptoms at baseline (i.e. “none” of results for sign/symptom), please exclude these patients when analyzing time to resolution of that specific sign or symptom.

For each of the signs and symptoms, the hazard ratio of iclaprim vs vancomycin will be estimated in a Cox proportional hazard model for time to resolution of the specified sign/symptom, with the treatment group as the only covariate. The Kaplan-Meier (KM) method will be applied to estimate the distribution of the resolution time of each signs or symptom for each treatment group. The 95% CI of the hazard ratio will also be reported. This Cox regression will be performed in the ITT, mITT, PP populations.

7.9.2.3 Bacteriological response

Bacteriological response will be assessed at the patient level and at the microbiological level on the basis of results of the cultures, the susceptibilities of identified organisms, and the clinical outcome of the patient for the mITT, mCE and mPP populations.

For each assessment (ETP, EOT, and TOC), the by-pathogen bacteriological response for each causative organism identified at baseline will be defined as follows:

- Eradication: baseline causative organism cannot be isolated from any culture(s) at the assessment.
- Presumed eradication: The patient is a clinical cure at the assessment, and there is no appropriate material for culture from the original site of infection.
- Persistence: The baseline causative pathogen (based on susceptibility profile or molecular typing) is isolated at the assessment.
- Presumed persistence: The patient is a clinical failure at the assessment, and no appropriate material is available for culture from the original site of ABSSSI.
- Indeterminate: Clinical response was Indeterminate at the assessment and no appropriate material is available for culture from the original site of ABSSSI.

- Superinfection: A pathogen is isolated at the assessment that is different from the baseline causative pathogen.
- Recurrent infection: A pathogen is isolated only after the EOT visit that is different from the baseline pathogen(s).

By-pathogen bacteriological response categories will be summarized in a frequency table for each causative baseline pathogen per treatment group.

The by-patient bacteriological response will be determined according to the following definitions:

- Eradication: All baseline Gram-positive causative organism(s) have a response of Eradication.
- Presumed eradication: All baseline Gram-positive causative organism(s) have a response of Presumed Eradication or a combination of responses of Eradication and Presumed Eradication.
- Persistence: All or some baseline Gram-positive causative organism(s) have a response of Persistence or a combination of responses of Persistence and Presumed Persistence.
- Presumed persistence: All or some baseline Gram-positive causative organism(s) have a response of Presumed Persistence.
- Indeterminate: All baseline causative organism(s) have a response of Indeterminate.
- Superinfection: Any patient classified as a clinical failure who has a pathogen isolated during therapy that is different from the baseline causative pathogen.
- Recurrent infection: Any patient classified as a clinical failure who has a pathogen isolated after the EOT visit only, that is different from the baseline pathogen(s).

The by-patient bacteriological response will be determined by ordering the pathogen outcome for the patient by medical importance: persistence, presumed persistence, superinfection, recurrent infection, presumed eradication, and eradication. Patient bacteriological outcome is determined by the pathogen outcome of higher importance. For the combined rate of eradication or presumed eradication, 95% CI will be calculated per treatment group and for the difference as specified for the primary endpoint analysis, and number and percentages for all underlying by-patient bacteriological response categories will be tabulated.

Minimum inhibitory concentrations (MIC) will be summarized using EUCAST and CSLI methods for vancomycin and iclaprim antibiotics for mITT population. The number and corresponding percentage for interpretation of the MIC result will be summarized for three categories: susceptible, Intermediate or resistance.

7.9.3 Exploratory Analysis

- Mortality rate within 28 days of first dose of treatment will be summarized overall and by treatment group for the ITT population.
- For early clinical response of ABSSSI, the NI test described for the primary endpoint analysis will be used to evaluate the proportion of ITT patients with a ≥ 50%, ≥ 75%, and ≥ 90% reduction in lesion size at ETP compared to baseline.
- For improvement of ABSSSI at EOT and TOC, the NI test described for the primary endpoint analysis will be used to evaluate the proportion of ITT patients with a ≥ 50% and ≥ 75% reduction in lesion size at EOT and TOC.

7.9.3.1 Exploratory Analysis Excluding Lesion Size Criteria

The criteria for lesion size reduction will be excluded for the following exploratory analyses.

1. Resolution or near resolution of ABSSSI excluding both criteria for lesion size reduction (≥ 90% reduction in lesion size from baseline and no increase in lesion size since ETP) at TOC for ITT, mITT, mCE and PP populations.
2. Resolution or near resolution of ABSSSI excluding both criteria for lesion size reduction (≥ 90% reduction in lesion size from baseline and no increase in lesion size since ETP) at EOT for ITT populations.
3. Resolution or near resolution of ABSSSI excluding both criteria for lesion size reduction (≥ 90% reduction in lesion size from baseline and no increase in lesion size since ETP) at TOC among patients with severe infection at baseline for ITT and PP population.
4. Resolution or near resolution of ABSSSI excluding both criteria for lesion size reduction (≥ 90% reduction in lesion size from baseline and no increase in lesion size since ETP) at TOC by subgroups for ITT and PP population.
5. Resolution or near resolution of ABSSSI excluding the criteria for no increase in lesion size since ETP at TOC for ITT population.
6. Clinical outcome excluding both criteria for lesion size reduction (≥ 90% reduction in lesion size from baseline and no increase in lesion size since ETP) will be evaluated at EOT and TOC programmatically for ITT and PP populations and categorized as cure, failure or indeterminate as follows:
   - Cure: defined by no requirement for additional antibiotics for treatment of primary ABSSSI (except aztreonam and metronidazole) or unplanned significant surgical procedures (excluding procedures that reflect failure of antimicrobial therapy);
   - Failure: death related to the infection, persisting or recurrent infection, need for unplanned significant surgical procedure (i.e., procedures that reflect failure of antimicrobial therapy), administration of rescue antibiotic therapy for the index infection before or at assessed visits;
   - Indeterminate: data inadequate for assessment of efficacy (there are no post-baseline local or systemic signs and symptoms data available to make this assessment [e.g., patient lost to follow up] after < 2 days of treatment or < 4 doses and no EOT evaluation), withdrawal of consent, receipt of effective antibiotic therapy for a cause other than the index infection before assessed visits, or death not attributed to the index ABSSSI or complication of ABSSSI.

   Note: If a patient starts an antibiotic for an infection other than the primary ABSSSI at EOT visit date, they will still be included as clinical cure or clinical failure. The same rule will be applied to the evaluation of clinical outcome at TOC visit.

   – Persistent infection occurs if a patient receives additional antibiotics for treatment of primary ABSSSI (except aztreonam and metronidazole) at EOT compared to baseline. The same rule applies when evaluating clinical failure at TOC visit.

   – Recurrent infection occurs if a patient does not receive additional antibiotics (except aztreonam and metronidazole) at EOT and receives additional antibiotics (except aztreonam and metronidazole) at TOC for treatment of primary ABSSSI.

7. Pathogen-level bacteriological response rate at TOC for mITT and mPP populations, where presumed eradication and presumed persistence will be defined without the lesion size criteria for the clinical cure and clinical failure.
8. Patient-level bacteriological response rate at EOT for mITT and mCE populations and TOC for mITT and mPP populations, where superinfection and recurrent infection will be defined without the lesion size criteria for clinical failure.
9. Patient-level combined bacteriological response rate at EOT for mCE population and TOC for mITT and mPP populations.

- If it is concluded that Iclaprim is non-inferior to Vancomycin (i.e., the lower bound of two-sided 95% confidence interval of group difference in early clinical response is greater than -0.1), it may be concluded that Iclaprim is superior to Vancomycin if the entire 95% confidence interval is >0. Superiority may also be concluded for resolution of ABSSSI at TOC in a similar manner.

7.9.4 Subgroup Analysis

The primary endpoint, the proportion of patients with a ≥20% reduction in lesion size at ETP compared to baseline and the key secondary endpoint, proportion of patients with a clinical cure at TOC, will be presented for ITT and PP populations.

- age group (grouped as 18-39 years, 40-64 years, and 65 years and older);
- sex;
- race (white vs non-white);
- creatinine clearance (CrCL) in mL/min (grouped as ≥ 90, 60-89, 30-59, 15-29, and < 15 or hemodialysis);
- blood culture at baseline (positive, if anaerobic or aerobic blood culture has pathogen; negative, if culture taken and organism isolated but there is no pathogen or no organism was isolated)
- MRSA vs MSSA;
- multiple pathogens vs single pathogen;
- *Streptococcus pyogenes* determined from ASO and either blood or infection site culture results from baseline (ASO positive only, culture positive only, ASO positive and culture positive, ASO negative and culture negative).
- diabetes (yes – if patient have medical history for diabetes, or baseline glucose > 200 mg/dL, or concomitant medications of either insulin or oral hypoglycemic; or no – no medical history for diabetes, baseline glucose ≤ 200 mg/dL, no concomitant medications of either insulin or oral hypoglycemic.)
- severe infection (met the criteria of SIRS, has severe tenderness or severe erythema, has positive blood culture at baseline), defined in Section 2.1;
- geographic region (US, Europe and Latin America).

The difference in the proportions of the two treatment groups and 95% CI will be calculated for each subgroup, and forest plots will be used to display these intervals graphically.

7.10 Safety

7.10.1 Adverse Events

All adverse events (AEs) recorded on the eCRF will be coded using the MedDRA dictionary Version 18.1 (or a later version if updated during the study) and classified as either pre-treatment AEs or treatment – emergent AEs (TEAEs) as follows:

- Pre-treatment AEs are events that start prior to the date of first dose of treatment.
- TEAEs are events with start date on or after the date of first dose of treatment (using dates and times as recorded on the medication administration log) through TOC visit, or events with start date prior to the date of first dose of treatment whose severity worsens on or after the date of first dose of treatment. SAEs will be reported through end of study as TEAE.

If any incomplete date/time of AE onset or start of first infusion is not sufficient to exclude that the AE is treatment emergent, then the AE will be considered to be a TEAE.

All AE data will be listed by treatment group with Pre-treatment AEs and TEAEs presented separately. Treatment-emergent status will be flagged in the listing. In addition, corresponding listings of SAEs, AEs leading to discontinuation of treatment and AEs resulting in death will be produced.

The severity of all AEs is recorded as mild, moderate, or severe. If severity is missing for a TEAE, it will be considered severe only in the overall category in the summary tables.

The relationship between an AE and treatment is assessed as related, probably related, probably not related, or not related. A drug-related AE is an AE considered by the investigator as related or probably related to the study drugs, or with unknown/missing relationship to treatment.

Each AE must be assessed and recorded in the eCRF as serious or not serious. Serious AEs must be reported as described in the protocol

An overview table will summarize the number and percentage of patients with at least one of the following TEAEs for Safety population, where patients with more than one TEAE in a particular category are counted only once in that category:

- any TEAE;
- any TEAE by severity (mild, moderate, severe);
- drug-related TEAEs;
- TEAEs leading to discontinuation of the study drug;
- SAEs;
- drug-related SAEs;
- SAEs leading to death.

The number and percentage of patients reporting each TEAE, including TEAE by age (< 65 and ≥ 65), TEAEs by CrCL (≥ 90, 60-89, 30-59, 15, 29, and < 15 or hemodialysis), TEAEs by diabetes (present or absent), TEAEs leading to discontinuation, SAEs, drug related SAEs, and SAEs leading to death, will be summarized for each treatment group and overall, by SOC (sorted alphabetically) and PT (sorted by descending overall total) for Safety population. The analogous summaries will also be given for study drug related TEAEs, all TEAEs by severity and for all SAEs. TEAEs with missing severity will not be included in the counts of patients within a SOC or PT. For counting the number of events, the same rule for multiple events in one category will be applied as specified above. There will also be summaries of the

most common TEAEs (> 5%) and SAEs (> 5%, > 1%) by PT in descending order of frequency in the iclaprim group.

No statistical comparisons of AEs, deaths, AE leading to discontinuation, or SAEs between treatment groups will be performed.

7.10.2 Laboratory Evaluations

Data for the following hematology, blood chemistry, and urinalysis analytes received from central laboratory as well as LFT results (Table 2) recorded in the eCRF will be listed (see Appendix B for the scheduled data collection) and summarized by treatment group and visit. Data received from local laboratories will be listed with the original units. If data for any additional analytes are also received then these will be listed only.

All central laboratory data will be reported in International System of Units (SI Units) and Conventional Units (CV Units). Out-of-reference-range values will be flagged as high (H) or low (L) in the data listings.

Table 2: Laboratory Evaluations

Hematology (CBC)	Chemistry [Fasted] (Chem-20)	Urinalysis (UA)
Hematocrit Hemoglobin MCH MCHC MCV Platelet count Red Blood Cell Count White Blood Cell Count White Blood Cell Differential (% & ABS): Basophils Eosinophils Lymphocytes Monocytes Neutrophils	Albumin ALP ALT AST BUN Chloride Creatinine GGT Glucose LDH Potassium Sodium Magnesium Total Bilirubin Total CO_2 (measured as bicarbonate) Total protein CPK CRP	pH and specific gravity Glucose Ketones Occult blood Proteins Microscopic examination of sediment (including RBCs and WBCs) Bilirubin/Urobilinogen
Source: Protocol Appendix A – Clinical Laboratory Evaluations		

Laboratory test variables will be summarized by treatment group and visit using descriptive statistics (number of patients, mean, SD, minimum, maximum, as well as mean change from baseline, standard error for mean change, minimum, median, and maximum). For each laboratory analyte, the baseline value will be defined as last scheduled or unscheduled value collected prior to the first dose of treatment. The descriptive statistics will be summarized for both SI and CV units.

The number and percentage of patients with values below, within and above the corresponding extended normal range will be tabulated per visit. Shift tables (i.e., cross-tabulations of below the lower limit of the normal range, within the limits of the normal range and above the upper limit of the normal range at baseline versus scheduled visits) will be presented by laboratory test.

In addition, shift tables for 6 liver enzyme tests (AST, ALT, alkaline phosphatase, GGT, total and direct bilirubin) and 3 renal function tests (BUN, creatinine, creatinine clearance) for post-baseline change in grade categories ⩽ ULN, ⩽ 3x ULN, > 3x-5x ULN, > 5x-10x ULN, > 10x-20x ULN, > 20x ULN will be presented. For bilirubin, the category is presented as two categories, < 2x ULN, > 2x ULN. The maximum change through all study will be presented as overall results and results will also be presented by visit.

Urinalysis tests with categorical results will be summarized by frequency patients n each category. All laboratory data, including data obtained from laboratory tests not required by the protocol will not be summarized, but will be listed.

7.10.3 Vital Signs

The following vital signs will be listed and summarized by treatment group and visit (see Appendix B for the scheduled data collection).

- systolic and diastolic blood pressure (mmHg);
- heart rate (bpm);
- respiration rate (breaths/min);
- body temperature (°C).

Vital signs data and changes from baseline in vital signs will be summarized by visit using standard descriptive statistics for the Safety population. The baseline value will be defined as last scheduled or unscheduled value collected prior to the first dose of treatment. Assessments carried out on day of first treatment administration are considered to have taken place before the treatment administration, if the corresponding times have not been recorded. For post-baseline, only data from scheduled visits will be included in the summary tables.

7.10.4 Electrocardiograms

The following quantitative ECG measurements will be taken and read centrally during the study (see Appendix B for the scheduled data collection):

- heart rate (bpm);
- RR interval (msec);
- PR interval (msec);
- QRS interval (msec);
- QT interval (msec);
- Bazett corrected QT (QTcB) interval (msec);
- Fridericia corrected QT (QTcF) interval (msec).

Triplicate ECG measurements will be listed for every ECG measurement, and the median value of the triplicate measurements will be summarized using descriptive statistics.

Based on 12-lead triplicate ECG results as reported on the case report form (CRF) that are read centrally the number and percentage of patients whose median QTcF value is > 500 msec **and/or** is >60 msec

different from the predose baseline value will be provided for every visit. For every visit with ECG measured, the median QTcF and QTcB values will be summarized with descriptive statistics for the following categories:

- > 450 msec;
- > 480 msec;
- > 500 msec;
- increase from baseline > 30 msec;
- increase from baseline > 60 msec.

The central ECG measurements at all pre-planned visits and time points and changes from baseline in ECG will be listed and summarized by treatment group and visit using standard descriptive statistics for the Safety population.

The baseline value will be defined as last scheduled or unscheduled median value collected prior to the first dose of treatment. Assessments carried out on day of first treatment administration are considered to have taken place before the treatment administration, if the corresponding times have not been recorded. For post-baseline, only data from scheduled visits will be included in the summary tables.

7.10.5 Physical Examination

Physical examination results (normal/abnormal) and details of abnormalities will be listed for each patient (see Appendix B for the scheduled data collection).

7.11 Interim Analysis

When 75% of the randomized patients have undergone the 48- to 72-hour (ETP) response assessment, a blinded interim analysis is planned to estimate the percentage of patients in the study who classify as having a reduction in the lesion size ≥20% at the 48- to 72-hour visit compared to baseline. Based on the observed overall percentage, the sample size will be re-estimated as N_1 using z-test with unpooled variance estimate. The new total sample size will be the maximum of 300 and N_1, following Friede T et al (2007). The sponsor may increase the total sample size to attempt to ensure that an adequate number of ITT patients are included in the study. Since the review is blinded and the efficacy analyses will not be reviewed by treatment group, no adjustment of p-values is required. Nevertheless, the sponsor will take steps to minimize the distribution of results to avoid introducing any bias.

8 REFERENCES

1 Friede T, Mitchell C, Müller-Velten R. *Blinded Sample Size Reestimation in Non-Inferiority Trials with Binary Endpoints*. Biometrical Journal. 2007; 49: 903-916.

9 APPENDICES

Appendix A – Prohibited Medicines

The following medications are prohibited:

- Systemic antibiotics (other than aztreonam and metronidazole) or topical antibiotics at the site of the ABSSSI under investigation;
- Steroids >20 mg/day prednisolone or equivalent;
- Type IA and Type III anti-arrhythmic drugs; and
- Local antiseptics.

Appendix B – Schedule of Events

Procedure	**Baseline/ Screening/ Randomization Visit 1** (up to 24 hours prior to first dose)[1]	Daily until ETP **Visit 2**	**ETP** (48 to 72 hours post-first dose) **Visit 3**	Every 48 to 72 hours until EOT **Visit 4**	**EOT**/ Early Termination **Visit 5** (treatment duration: minimum 5 days, maximum 14 days)	**TOC** 7 to 14 days post-EOT **Visit 6**	**LFU** 28 to 32 days post-first dose **Phone Call**[2]
Informed consent	X						
Medical history	X						
Prior medications (preceding 30 days)	X						
Concomitant medications		X	X	X	X	X	
Review of inclusion & exclusion criteria	X						
Complete physical examination[3]	X						
Limited physical examination[4]		X	X	X	X	X	
Assessment of signs & symptoms of ABSSSI with digital photography[5]	X		X		X	X	
Assessment of signs & symptoms of ABSSSI without digital photography[5]		X		X			
Evaluation of adverse events[6]	X	X	X	X	X	X	X
Significant procedures (incision & drainage, debridement, amputation, suture removal, etc.)		X	X	X	X	X	
Creatinine clearance (estimated)	X						
LFT safety	X	X	X		X	X	
C-reactive protein	X		X		X	X	
Hematology[7]	X		X	X	X	X	
Clinical chemistry[7]	X		X	X	X	X	
Urinalysis[7]	X		X	X	X	X	
Serum pregnancy test (females of childbearing potential)[8]	X						
Blood cultures (aerobic/anaerobic)	X[9]	X[10]	X[11]	X[11]			
Study medication administration[12]		X	X	X[13]	X[14]		
Blood sample for PK analysis		X[15]	X[16]		X[16]		
ECG (at each timepoint 3 ECGs at least 1 minute apart will be performed)	X	X[17]	X[18]				
Infection site cultures[19]	X		X		X	X	
ASO antibody titers	X					X	
Draw trough levels[20]				X[21]			
Central randomization	X						
Clinical efficacy assessment					X	X	
Day 28 mortality							X

Abbreviations: ASO = anti-streptolysin O; EOT = End of Therapy; ETP = Early Timepoint; LFT=liver function test; LFU = Late Follow-up; TOC = Test of Cure.
[1] Must be performed during the baseline visit and completed within 24 hours of study entry (first dose of study drug).
[2] Patients with high LFTs and unresolved AEs at TOC will be required to come in for an additional visit at LFU (for LFTs, blood samples will be obtained to document normalization). If duration of therapy

is 14 days, LFU may overlap with TOC. In this case, all LFU evaluations may take place at the TOC visit.

[3] Complete physical examination, including vital signs (includes determination of body temperature), height, weight, and a review by body systems.

[4] Limited physical examination, including vital signs (includes determination of body temperature) and excluding weight and height.

[5] Eight signs (tenderness to palpitation, erythema, edema, purulent drainage/discharge, fluctuance, induration, ulceration, and necrotic tissue) and four symptoms (localized pain, swelling, chills, and fever) of infection will be assessed at each evaluation and graded on a scale of 0 to 3 (0=none, 1=mild, 2=moderate, or 3=severe). The extent of the infection (to include width, length, and depth and diagram of the infection site) will be determined via photography at baseline, ETP, EOT, and TOC only. Photography procedures outlined in protocol Appendix B will be followed. Acetate based planimetric tracing will follow the procedures outlined in Appendix C. (Planimetry measurements are based upon automatic detection of pixels inside of the traced skin infection area. Pixels are converted to calibrated units based on the scanned resolution [e.g., 300 DPI]. Skin infection measurements will be provided in cm^2.). Patients who have a worsening of clinical signs and symptoms of ABSSSI during study medication treatment such that additional or alternative systemic antibacterial therapy is warranted must be withdrawn from study medication.

[6] All adverse events will be recorded throughout the study period, up to and including the LFU phone call.

[7] Hematology comprises a complete blood count (RBC count, WBC count with differential counts, platelet count, hemoglobin, and hematocrit), MCH, MCHC, MCV, and CRP. Clinical chemistry comprises creatinine, BUN, AST, ALT, alkaline phosphatase, total bilirubin, albumin, total protein, glucose, sodium, potassium, chloride, bicarbonate, LDH, GGT, and CPK. Urinalysis comprises determination of pH, specific gravity, presence of blood, glucose, protein, ketones, and bile, and microscopic examination of sediment.

[8] Serum pregnancy test must be obtained immediately prior to randomization. If obtaining the serum pregnancy result would cause a delay in treatment, the patient can be entered on the basis of a negative urine pregnancy test result. The urine pregnancy test must be sensitive to at least 50 mU/mL of beta-hCG, pending results of the serum test. The patient must inform the investigator if she becomes pregnant, and study medication must be withdrawn.

[9] Obtain two sets of blood cultures (aerobic and anaerobic) 10 minutes apart from two separate peripheral sites.

[10] If patient has a blood culture that grows a Gram-negative pathogen from Visit 1 blood cultures, the patient must be withdrawn from study medication and started on the appropriate antibiotics for complicated bacteremia. If patient has signs of bacteremia, obtain two sets of aerobic/anaerobic blood cultures 10 minutes apart that are collected at different sites.

[11] If patient has a blood culture that grows a Gram-negative pathogen from Visit 2 blood cultures, the patient must be withdrawn from study medication and started on the appropriate antibiotics for complicated bacteremia. If patient has a blood culture that grows a Gram-positive pathogen from Visit 1 and/or Visit 2 blood cultures, another 2 sets of blood cultures must be obtained at both Visit 3 and Visit 4. If these are positive, the patient must be withdrawn from study medication and started on the appropriate antibiotics for complicated bacteremia.

[12] A window of +/- 2 hours is acceptable for infusion of study medication. For patients randomized to receive vancomycin, vancomycin dosing will be adjusted based on trough levels to maintain a trough of either 10 to 15 mg/L for patients with an organism whose MIC is ≤1 mg/L or 15 to 20 mg/L for patients with an organism whose MIC is >1 mg/L. Dose adjustments made due to trough monitoring will need to be performed in such a manner as to ensure that the blind is maintained.

[13] If the last dose of study drug falls on a day when an evaluation was not planned, an additional evaluation visit will need to be performed on that day (i.e., all EOT evaluations should be performed on the last day [+2 days] of drug dose).

[14] If clinically indicated (i.e., investigator may decide on a given day that a patient no longer needs treatment. In these cases, medication will not be administered, but all other EOT assessments must be performed.)

[15] On Day 1, before the start of first study medication infusion and within 5 to 15 minutes, 1 to 3 hours, and 5 to 7 (ensure last PK sample is taken prior to next dose) hours after the infusion.

[16] Before the start of study medication infusion at ETP and EOT, and within 5 to 15 minutes, 1 to 3 hours, and 5 to 7 hours (ensure last PK sample is taken prior to next dose) after the ETP and EOT infusions.

[17] On Day 1, before the start of first study medication infusion and within 10 minutes of the end of the first study medication infusion. If the median QTcF value is >500 msec and/or is >60 msec different from the predose baseline value, follow-up ECG tests should be performed every 1 to 2 hours until they are below these threshold values.

[18] At ETP, an ECG should be performed before the start of study medication infusion and within 10 minutes of the end of the study medication infusion.

[19] Prior to randomization, all patients (regardless of the disease type) should have appropriate cultures obtained. Deep culture samples, such as from a biopsy, needle aspiration, surgically obtained specimens, or punch biopsies of an area contiguous to the infected wound should be obtained. Swabs are not acceptable; cultures will be performed locally, where isolates will be retained for transport to a central microbiology laboratory for susceptibility testing according to CLSI-approved methodology. Note that only target pathogens will be sent to the central microbiology laboratory (therefore, contaminants/Gram-negative isolates [from mixed wound infections] in blood cultures do not need to be sent). If the patient is discontinued from the study due to treatment failure, a clinical specimen will be obtained at that time only. Additional clinical specimens will be obtained, if clinically feasible and if the patient has persistent clinical signs or symptoms, at ETP, EOT, and TOC.

[20] For vancomycin patients with a CrCL < 25mL/min, a daily level should be obtained and the unblinded team should monitor and re-dose the patient when that level is below 20 mg/L.

[21] Vancomycin patients with a CrCL ≥25 mL/min should have their vancomycin level checked with the 5th dose due to difficulty interpreting levels checked prior to achieving steady state.

Appendix C – Table, Figure and Listing Shells

The table, figure, and listing shells and corresponding Table of Contents will be created in a separate file.

TABLES, FIGURES, AND LISTINGS SHELLS

A Phase 3, randomized, double-blind, multicenter study to evaluate the safety and efficacy of intravenous iclaprim versus vancomycin in the treatment of acute bacterial skin structure infections suspected or confirmed to be due to Gram-positive pathogens. (REVIVE-2)

TFL Status: Final 1.0
TFL Date: 2016-08-16T22:39:26

Study Drug: iclaprim

Sponsor Reference: Protocol ICL-24-ABSSSI2
Covance Study No: 000000145670

1. INTRODUCTION

The table, figure, and listing (TFL) shells presented in this document are mock-ups and may be subject to minor format modifications once the actual data are used. The data represented in this document are used for example purposes only and do not reflect the actual study data captured. The overall contents in any individual TFL shell will not change, although additional tables may be added if necessary, thus changing the table number scheme. Significant changes will be approved by the responsible Covance Clinical Pharmacology project team member and communicated to the Sponsor.

1.1 General Programming Specifications

All TFLs will follow the following rules:

Papersize will be Letter, with the following margins in Inches:

Landscape			
top	1.5	left	1
bottom	1.73	right	1

Portrait			
Top	1.5	left	1.5
Bottom	1.5	right	1.23

Every TFL will have a footnote containing program location, name, run date and run time (optional), the name of the last person who ran the program, and the status of the output:
Dry run – Draft – Final Draft – Final (others as needed)

Dates will be presented in the format ddMonyyyy
The presentation order of the statistics will be:
Mean, SD, median, minimum, maximum, N. The abbreviations Med, Min, Max may be used, if necessary.
Rules for significant digits in safety data tables are as follows: if the raw value has x decimal places, then the mean and the median will have x+1 decimal places, the standard deviation will have x+2 decimal places.

N will be presented as whole numbers.

Percentages will always be displayed with 1 decimal place. For percentages < 0.1%, <0.1% will be displayed.

1.2 Derived Parameters

Individual derived parameters and appropriate summary statistics will be reported to three significant figures.

1.3 Tables Summarizing Categorical Data

Tables that summarize categorical data will be created per these specifications:

1. If the number of events is zero, data will be presented as “0”.
2. If the categories of a parameter are ordered, all categories between the maximum possible category and the minimum category will be included, even if n=0 for a given category.
3. If the categories are not ordered, only those categories for which there is at least one subject represented will be included.

4. A “missing” category will be included for any parameter for which information is missing. This will ensure that the population size totals are consistent across different parameters.

1.4 Tables for Imputing Onset and Stop Dates of Adverse Events (AEs) and Concomitant Medications

The general principle for imputing dates is as follows:

If an adverse event start date is completely missing or partially missing, then it assumed that the start date occurs at the earliest time on-treatment whenever possible.

If a concomitant medication onset date is completely missing, then the date is not imputed. Otherwise, if the concomitant medication onset date is partially missing, then it is assumed that the start date occurs at the earliest time on-treatment whenever possible.

If a concomitant medication or adverse event stop date is completely missing or partially missing, then the stop date is imputed to maximize the duration of the event or concomitant treatment. It should be noted that imputation of stop dates only applies to concomitant medications that are not ongoing and adverse events that are not ongoing (ie outcome is not resolved).

Scenario		***Imputation rule***
Onset date	***Stop date***	
Partially Missing	Complete	Imputation of onset date: A. If partial date has day and month missing: If year of the partial date < year of the first dose date, assign December 31st to the missing fields. If year of the partial date = year of the first dose date, assign the first dose date to the missing fields.

		If year of the partial date > year of the first dose date, assign January 1st to the missing fields. Note: if first dose date is missing, then use randomization date in the above imputations. B. If partial date has missing day only: If the month and year of the partial date < month and year of the first dose date, assign last day of the onset month to the missing day. If the month and year of the partial date = month and year of the first dose date, assign the day of first dose to the missing day. If the month and year of the partial date > month and year of the first dose date, assign first day of the onset month to the missing day. If the imputed onset date (after A or B above) is after the stop date, the onset date will be imputed to be equal to the stop date.
Complete	Partially Missing	Imputation of stop date (if not reported as ongoing): C. If partial date has day and month missing: If year of partial date < year of the last known alive date (LKAD), assign December 31st to the missing fields. If year of partial date = year of the LKAD, assign the LKAD date to the missing fields If year of partial date > year of the LKAD, the missing day and month will NOT be imputed. D. If partial date has missing day only: If the month and year of the partial data < the month and year of the LKAD, assign the last day of the onset month to the missing day. If the month and year of the partial date = the month and year of the LKAD, assign the LKAD to the missing day. If the month and year > the month and year of the LKAD, the missing day will NOT be imputed. **LKAD is defined as the date of death or the last day recorded on the log form.** If the imputed stop date (after C or D above) is before the onset date, the stop date will be imputed to be equal to the onset date.
Partially Missing	Partially Missing	Impute onset date per A and B above Impute stop date (if not reported as ongoing) per C and D above If imputed onset date > imputed stop date, then set onset date = stop date = minimum of (imputed onset date per A and B, imputed stop date per C and D)

Partially Missing	Completely Missing	Impute onset date per A and B above. Impute stop date (if not reported as ongoing) as the LKAD; see definition above. If imputed onset date > imputed stop date, then set onset date = stop date = minimum of (imputed onset date per A and B, imputed stop date above)
Completely Missing	Partially Missing	**Adverse Events** Impute onset date as the first dose date; if first dose date is missing, then use randomization date If imputed onset date > imputed stop date, then set onset date = stop date = minimum of (imputed onset date above, imputed stop date per C and D) **Concomitant Medications** Do not impute onset date Impute stop date (if not reported as ongoing) per C and D above
Completely Missing	Complete	**Adverse Events** Impute onset date as the first dose date; if first dose date is missing, then use randomization date. If imputed onset date > stop date, then set onset date = (complete) stop date **Concomitant Medications** Do not impute onset date.
Complete	Completely Missing	Impute stop date (if not reported as ongoing) as the LKAD; see definition above. If onset date > imputed stop date, then set stop date = (complete) onset date
Completely	Completely	**Adverse Events**

Missing	Missing	Impute onset date as the first dose date; if first dose date is missing, then use randomization date. Impute stop date (if not reported as ongoing) as the LKAD; see definition above. **Concomitant Medications** Do not impute onset date. Impute stop date (if not reported as ongoing) as the LKAD; see definition above.

2. TABLE OF CONTENTS

	Introduction -	1
	Table of Contents -	8
Table 14.1.1	Overall Summary of Study Populations - Enrolled Patients	14
Table 14.1.2.1	Summary of Study Completion - ITT Population	16
Table 14.1.2.2	Summary of Study Completion - Safety Population	17
Table 14.1.2.3	Summary of Treatment Completion - ITT Population	18
Table 14.1.2.4	Summary of Treatment Completion - Safety Population	19
Table 14.1.3	Study Sample Sizes by Country and Center - Enrolled Patients	20
Table 14.1.4	Number of Patients Assessed at Visits with Efficacy Assessment - All Randomized Patients	21
Table 14.1.5.1	Summary of Major Protocol Violations/Deviations - ITT Population	22
Table 14.1.5.2	Summary of Major Protocol Violations/Deviations - mITT Population	22
Table 14.1.6	Summary of Patients Validity - All Randomized Patients	23
Table 14.1.7.1	Summary of Demography - ITT Population	25
Table 14.1.7.2	Summary of Demography - mITT Population	26
Table 14.1.7.3	Summary of Demography - PP Population	26
Table 14.1.7.4	Summary of Demography - mPP Population	27
Table 14.1.7.5	Summary of Demography - mCE Population	27
Table 14.1.7.6	Summary of Demography - Safety Population	27
Table 14.1.8.1	Baseline Disease Characteristics - ITT Population	28
Table 14.1.8.2	Baseline Disease Characteristics - mITT Population	29
Table 14.1.8.3	Baseline Disease Characteristics - PP Population	29
Table 14.1.8.4	Baseline Disease Characteristics - mPP Population	29
Table 14.1.8.5	Baseline Disease Characteristics - mCE Population	29
Table 14.1.8.6	Baseline Disease Characteristics - Safety Population	29
Table 14.1.9	Summary of Medical History - ITT Population	30
Table 14.1.10.1	Prior Medications - ITT Population	31
Table 14.1.10.2	Concomitant Medication Excluding Antibiotics - ITT Population	32
Table 14.1.10.3	Concomitant Antibiotic Medication - ITT Population	33
Table 14.1.10.4	Summary of Significant Procedures by Visit - ITT Population	34
Table 14.1.11.1.1	Clinical Signs and Symptoms of ABSSSI by Visit: Tender to Palpitation - ITT Population	35
Table 14.1.11.1.2	Clinical Signs and Symptoms of ABSSSI by Visit: Tender to Palpitation - PP Population	35
Table 14.1.11.1.3	Clinical Signs and Symptoms of ABSSSI by Visit: Tender to Palpitation - mCE Population	35
Table 14.1.11.2.1	Clinical Signs and Symptoms of ABSSSI by Visit: Erythema - ITT Population	35
Table 14.1.11.2.2	Clinical Signs and Symptoms of ABSSSI by Visit: Erythema - PP Population	35
Table 14.1.11.2.3	Clinical Signs and Symptoms of ABSSSI by Visit: Erythema - mCE Population	35
Table 14.1.11.3.1	Clinical Signs and Symptoms of ABSSSI by Visit: Edema - ITT Population	36

Table 14.1.11.3.2 Clinical Signs and Symptoms of ABSSSI by Visit: Edema - PP Population 36
Table 14.1.11.3.3 Clinical Signs and Symptoms of ABSSSI by Visit: Edema - mCE Population 36
Table 14.1.11.4.1 Clinical Signs and Symptoms of ABSSSI by Visit: Purulent Drainage/Discharge - ITT Population 36
Table 14.1.11.4.2 Clinical Signs and Symptoms of ABSSSI by Visit: Purulent Drainage/Discharge - PP Population 36
Table 14.1.11.4.3 Clinical Signs and Symptoms of ABSSSI by Visit: Purulent Drainage/Discharge - mCE Population 36
Table 14.1.11.5.1 Clinical Signs and Symptoms of ABSSSI by Visit: Fluctuance - ITT Population 36
Table 14.1.11.5.2 Clinical Signs and Symptoms of ABSSSI by Visit: Fluctuance - PP Population 36
Table 14.1.11.5.3 Clinical Signs and Symptoms of ABSSSI by Visit: Fluctuance - mCE Population 36
Table 14.1.11.6.1 Clinical Signs and Symptoms of ABSSSI by Visit: Induration - ITT Population 36
Table 14.1.11.6.2 Clinical Signs and Symptoms of ABSSSI by Visit: Induration - PP Population 36
Table 14.1.11.6.3 Clinical Signs and Symptoms of ABSSSI by Visit: Induration - mCE Population 36
Table 14.1.11.7.1 Clinical Signs and Symptoms of ABSSSI by Visit: Ulceration - ITT Population 36
Table 14.1.11.7.2 Clinical Signs and Symptoms of ABSSSI by Visit: Ulceration - PP Population 36
Table 14.1.11.7.3 Clinical Signs and Symptoms of ABSSSI by Visit: Ulceration - mCE Population 36
Table 14.1.11.8.1 Clinical Signs and Symptoms of ABSSSI by Visit: Necrotic Tissue - ITT Population 36
Table 14.1.11.8.2 Clinical Signs and Symptoms of ABSSSI by Visit: Necrotic Tissue - PP Population 36
Table 14.1.11.8.3 Clinical Signs and Symptoms of ABSSSI by Visit: Necrotic Tissue - mCE Population 36
Table 14.1.11.9.1 Clinical Signs and Symptoms of ABSSSI by Visit: Localized Pain - ITT Population 36
Table 14.1.11.9.2 Clinical Signs and Symptoms of ABSSSI by Visit: Localized Pain - PP Population 36
Table 14.1.11.9.3 Clinical Signs and Symptoms of ABSSSI by Visit: Localized Pain - mCE Population 36
Table 14.1.11.10.1 Clinical Signs and Symptoms of ABSSSI by Visit: Swelling - ITT Population 37
Table 14.1.11.10.2 Clinical Signs and Symptoms of ABSSSI by Visit: Swelling - PP Population 37
Table 14.1.11.10.3 Clinical Signs and Symptoms of ABSSSI by Visit: Swelling - mCE Population 37
Table 14.1.11.11.1 Clinical Signs and Symptoms of ABSSSI by Visit: Chills - ITT Population 37
Table 14.1.11.11.2 Clinical Signs and Symptoms of ABSSSI by Visit: Chills - PP Population 37
Table 14.1.11.11.3 Clinical Signs and Symptoms of ABSSSI by Visit: Chills - mCE Population 37
Table 14.1.11.12.1 Clinical Signs and Symptoms of ABSSSI by Visit: Fever - ITT Population 37
Table 14.1.11.12.2 Clinical Signs and Symptoms of ABSSSI by Visit: Fever - PP Population 37
Table 14.1.11.12.3 Clinical Signs and Symptoms of ABSSSI by Visit: Fever - mCE Population 37
Table 14.1.12.1 Type of Culture Specimen and Culture Results by Visit - ITT Population 38
Table 14.1.12.2 Summary of Culture Specimen for Lesion Type by Visit - ITT Population 39
Table 14.1.12.3 Microbiological Assessment of Primary Infection Site - Gram Stain - ITT Population 40
Table 14.1.12.4 Blood Culture Results by Visit - ITT Population 41
Table 14.1.12.5 Gram-positive Pathogens Occurring in Patients at Baseline - ITT Population 42
Table 14.1.12.6 Frequency Distribution of MIC by Baseline Pathogen - ITT Population 43
Table 14.1.13.1 Summary of Treatment Compliance - ITT Population 44
Table 14.1.13.2 Summary of Treatment Exposure: Duration in Days - Safety Population 45
Table 14.2.1 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP - ITT Population 46
Table 14.2.2.1 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP - mITT Population 46
Table 14.2.2.2 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP - mCE Population 47
Table 14.2.2.3 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP - PP Population 47

Table 14.2.2.4 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP - mPP Population 47
Table 14.2.3.1 Resolution or Near Resolution of ABSSSI at TOC - ITT Population 48
Table 14.2.3.2 Resolution or Near Resolution of ABSSSI at TOC - mITT Population 48
Table 14.2.3.3 Resolution or Near Resolution of ABSSSI at TOC - mCE Population 49
Table 14.2.3.4 Resolution or Near Resolution of ABSSSI at TOC - PP Population 49
Table 14.2.3.5 Resolution or Near Resolution of ABSSSI at TOC - mPP Population 49
Table 14.2.4.1 Resolution or Near Resolution of ABSSSI at EOT - ITT Population 49
Table 14.2.4.2 Resolution or Near Resolution of ABSSSI at EOT - mITT Population 50
Table 14.2.4.3 Resolution or Near Resolution of ABSSSI at EOT - mCE Population 50
Table 14.2.4.4 Resolution or Near Resolution of ABSSSI at EOT - PP Population 50
Table 14.2.4.5 Resolution or Near Resolution of ABSSSI at EOT - mPP Population 50
Table 14.2.5.1 Summary of Clinical Response at EOT and TOC - PP Population 51
Table 14.2.5.2 Summary of Clinical Response at EOT and TOC - mPP Population 51
Table 14.2.6.1 Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline - ITT Population 52
Table 14.2.6.2 Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline - mITT Population 52
Table 14.2.6.3 Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline - mCE Population 53
Table 14.2.6.4 Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline - PP Population 53
Table 14.2.6.5 Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline - mPP Population 53
Table 14.2.7.1 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - ITT Population 53
Table 14.2.7.2 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - mITT Population 54
Table 14.2.7.3 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - mCE Population 54
Table 14.2.7.4 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - PP Population 54
Table 14.2.7.5 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - mPP Population 54
Table 14.2.8.1 Time to Resolution of Signs and Symptoms of ABSSSI - ITT Population 55
Table 14.2.8.2 Time to Resolution of Signs and Symptoms of ABSSSI - mITT Population 55
Table 14.2.8.3 Time to Resolution of Signs and Symptoms of ABSSSI - mCE Population 56
Table 14.2.8.4 Time to Resolution of Signs and Symptoms of ABSSSI - PP Population 56
Table 14.2.8.5 Time to Resolution of Signs and Symptoms of ABSSSI - mPP Population 56
Table 14.2.9.1 Percent of Resolution of Signs and Symptoms of ABSSSI - ITT Population 57
Table 14.2.9.2 Percent of Resolution of Signs and Symptoms of ABSSSI - mITT Population 57
Table 14.2.9.3 Percent of Resolution of Signs and Symptoms of ABSSSI - mCE Population 57
Table 14.2.9.4 Percent of Resolution of Signs and Symptoms of ABSSSI - PP Population 58
Table 14.2.9.5 Percent of Resolution of Signs and Symptoms of ABSSSI - mPP Population 58
Table 14.2.10.1.1 By Patient Bacteriological Response Rate at EOT - mITT Population 59
Table 14.2.10.1.2 By Patient Combined Bacteriological Response Rate at EOT - mITT Population 60
Table 14.2.10.2.1 By Patient Bacteriological Response Rate at EOT - mCE Population 59
Table 14.2.10.2.2 By Patient Combined Bacteriological Response Rate at EOT - mCE Population 60
Table 14.2.10.3.1 By Patient Bacteriological Response Rate at EOT - mPP Population 59
Table 14.2.10.3.2 By Patient Combined Bacteriological Response Rate at EOT - mPP Population 60
Table 14.2.11.1.1 By Patient Bacteriological Response Rate at TOC - mITT Population 59
Table 14.2.11.1.2 By Patient Combined Bacteriological Response Rate at TOC - mITT Population 60

Table 14.2.11.2.1 By Patient Bacteriological Response Rate at TOC - mCE Population 59
Table 14.2.11.2.2 By Patient Combined Bacteriological Response Rate at TOC - mCE Population 61
Table 14.2.11.3.1 By Patient Bacteriological Response Rate at TOC - mPP Population 59
Table 14.2.11.3.2 By Patient Combined Bacteriological Response Rate at TOC - mPP Population 61
Table 14.2.12.1 By Pathogen Bacteriological Response Rate at EOT - mITT Population 62
Table 14.2.12.2 By Pathogen Bacteriological Response Rate at EOT - mCE Population 62
Table 14.2.12.3 By Pathogen Bacteriological Response Rate at EOT - mPP Population 62
Table 14.2.13.1 By Pathogen Bacteriological Response Rate at TOC - mITT Population 62
Table 14.2.13.2 By Pathogen Bacteriological Response Rate at TOC - mCE Population 62
Table 14.2.13.3 By Pathogen Bacteriological Response Rate at TOC - mPP Population 62
Table 14.2.14 Mortality Rate within 28 Days of First Dose of Treatment - ITT Population 63
Table 14.2.15.1 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP by Subgroups - ITT Population 64
Table 14.2.15.2 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP by Subgroups - PP Population 65
Table 14.2.16.1 Resolution or Near Resolution of ABSSSI at TOC by Subgroups - ITT Population 65
Table 14.2.16.2 Resolution or Near Resolution of ABSSSI at TOC by Subgroups - PP Population 66
Table 14.3.1.1 Overall Summary of Treatment-emergent Adverse Events (TEAEs) - Safety Population 67
Table 14.3.1.2 Summary of Treatment-emergent Adverse Events (TEAEs) by MedDRA System Organ Class and Preferred Term - Safety Population 69
Table 14.3.1.3 Summary of Treatment-emergent Adverse Events (TEAEs) by Maximum Severity, MedDRA System Organ Class and Preferred Term - Safety Population 71
Table 14.3.1.4 Summary of Study Drug-Related Treatment-emergent Adverse Events (TEAEs) by System Organ Class and Preferred Term - Safety Population 70
Table 14.3.1.5 Summary of Treatment-emergent Adverse Events (TEAEs) Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term - Safety Population 70
Table 14.3.1.6 Summary of Treatment-emergent Adverse Events (TEAEs) by Age Group, MedDRA System Organ Class and Preferred Term - Safety Population 73
Table 14.3.1.7 Summary of Treatment-emergent Adverse Events (TEAEs) by Creatinine Clearance, MedDRA System Organ Class and Preferred Term - Safety Population 74
Table 14.3.1.8 Summary of Treatment-emergent Adverse Events (TEAEs) with Frequency > 5% by MedDRA Preferred Term - Safety Population 76
Table 14.3.1.9 Summary of Serious Adverse Events (SAEs) by MedDRA System Organ Class and Preferred Term - Safety Population 70
Table 14.3.1.10 Summary of Study Drug-related Serious Adverse Events (SAEs) by MedDRA System Organ Class and Preferred Term - Safety Population 70
Table 14.3.1.11 Summary of Serious Adverse Events (SAEs) Leading to Death by MedDRA System Organ Class and Preferred Term - Safety Population 70
Table 14.3.1.12 Summary of Serious Adverse Events (SAEs) with Frequency > 5% by MedDRA Preferred Term - Safety Population 75
Table 14.3.2.1 Listing of Treatment-emergent Adverse Events (TEAEs) Leading to Discontinuation of Study Drug - Safety Population 77
Table 14.3.2.2 Listing of Serious Adverse Events (SAEs) - Safety Population 78
Table 14.3.2.3 Listing of Serious Adverse Events (SAEs) Leading to Death - Safety Population 79
Table 14.3.4.1 Summary of Laboratory Test Results and Change from Baseline by Visit: Hematology - Safety Population 80
Table 14.3.4.2 Summary of Laboratory Test Results and Change from Baseline by Visit: Chemistry including Creatinine Clearance - Safety Population 81
Table 14.3.4.3 Summary of Laboratory Test Results and Change from Baseline by Visit: Urinalysis - Safety Population 81
Table 14.3.4.4 Shift Table of Laboratory Test Results: Hematology - Safety Population 82
Table 14.3.4.5 Shift Table of Laboratory Test Results: Chemistry including Creatinine Clearance - Safety Population 82
Table 14.3.4.6 Shift Table of Laboratory Test Results: Urinalysis - Safety Population 83
Table 14.3.4.7 Liver Function Test - CTCAE Toxicity Grade - Safety Population 84
Table 14.3.4.8 Laboratory Abnormality - Safety Population 86

Table 14.3.5.1 Summary of Vital Signs - Body Temperature (°C) - Safety Population 87
Table 14.3.5.2 Summary of Vital Signs - Heart Rate (bmp) - Safety Population 88
Table 14.3.5.3 Summary of Vital Signs - Respiratory Rate (breaths/min) - Safety Population 88
Table 14.3.5.4 Summary of Vital Signs - Systolic Blood Pressure (mmHg) - Safety Population 88
Table 14.3.5.5 Summary of Vital Signs - Diastolic Blood Pressure (mmHg) - Safety Population 88
Table 14.3.6.1 Summary of ECG Measurements by Visit - heart rate - Safety Population 89
Table 14.3.6.2 Summary of ECG Measurements by Visit - RR interval - Safety Population 90
Table 14.3.6.3 Summary of ECG Measurements by Visit - PR Interval - Safety Population 90
Table 14.3.6.4 Summary of ECG Measurements by Visit - QRS Interval - Safety Population 90
Table 14.3.6.5 Summary of ECG Measurements by Visit - QT Interval - Safety Population 90
Table 14.3.6.6 Summary of ECG Measurements by Visit - QTcB Interval - Safety Population 90
Table 14.3.6.7 Summary of ECG Measurements by Visit - QTcF Interval - Safety Population 90
Table 14.3.6.8 Summary of ECG Interpretations by Visit - Safety Population 91
Table 14.3.6.9 Summary of Marked QT/QTc Prolongation by Visit - Safety Population 92
Table 14.3.6.10 Summary of ECG QTc Interval Prolongation Evaluated Using Median QTcB, by Visit - Safety Population 93
Table 14.3.6.11 Summary of ECG QTc Interval Prolongation Evaluated Using Median QTcF, by Visit - Safety Population 94
Figure 14.2.1.1 Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI - ITT Population 95
Figure 14.2.1.2 Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI - mITT Population 96
Figure 14.2.1.3 Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI - mCE Population 96
Figure 14.2.1.4 Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI - PP Population 96
Figure 14.2.1.5 Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI - mPP Population 96
Figure 14.2.2.1 Forest Plots for Subgroup Analysis of the Difference in Early Clinical Response Rate at ETP between Iclaprim and Vancomycin group - ITT Population 97
Figure 14.2.2.2 Forest Plots for Subgroup Analysis of the Difference in Early Clinical Response Rate at ETP between Iclaprim and Vancomycin group - PP Population 98
Figure 14.2.3.1 Forest Plots for Subgroup Analysis of the Difference in Clinical Cure Rate at TOC between Iclaprim and Vancomycin group - ITT Population 98
Figure 14.2.3.2 Forest Plots for Subgroup Analysis of the Difference in Clinical Cure Rate at TOC between Iclaprim and Vancomycin group - PP Population 98
Listing 16.2.1.1 Patients Enrolled - Enrolled Patients 99
Listing 16.2.1.2 Patients Disposition - ITT Population 100
Listing 16.2.1.3 End of Treatment - ITT Population 101
Listing 16.2.2.1 Inclusion and Exclusion Criteria - All enrolled Patients 102
Listing 16.2.2.2 Protocol Deviations - ITT Population 103
Listing 16.2.3 Study Population - ITT Population 104
Listing 16.2.4.1 Demographics - ITT Population 105
Listing 16.2.4.2 Baseline Characteristics - ITT Population 106
Listing 16.2.4.3 Medical History - ITT Population 107
Listing 16.2.4.4 Prior and Concomitant Medication - ITT Population 108
Listing 16.2.5.1 Study Drug Administration - Safety Population 109
Listing 16.2.5.2 Overall Compliance - Safety Population 110
Listing 16.2.5.3 Population Pharmacokinetic - Safety Population 111
Listing 16.2.6.1 Blood Culture Results - ITT Population 112

Listing 16.2.6.2 Signs and Symptoms of ABSSSI - ITT Population ... 113
Listing 16.2.6.3 Clinical Efficacy Assessment - ITT Population ... 114
Listing 16.2.6.4.1 Microbiological Assessment - Patient Level - ITT Population ... 115
Listing 16.2.6.4.2 Microbiological Assessment - Pathogen Level - ITT Population ... 116
Listing 16.2.6.5 Microbiological Assessment of Primary Infection Site - Gram Stain Results - ITT Population ... 117
Listing 16.2.6.6 Significant Surgical Procedures - ITT Population ... 118
Listing 16.2.6.7 Death - ITT Population ... 119
Listing 16.2.6.8.1 Unblinding - ITT Population ... 120
Listing 16.2.6.8.2 Unblinding Dose - ITT Population ... 121
Listing 16.2.7 Adverse Events - Safety Population ... 122
Listing 16.2.8.1 Laboratory Findings in Local Labs at Baseline - Hematology - Safety Population ... 123
Listing 16.2.8.2 Laboratory Findings in Local Labs at Baseline - Chemistry - Safety Population ... 124
Listing 16.2.8.3 Laboratory Findings in Local Labs at Baseline - Urinalysis - Safety Population ... 125
Listing 16.2.8.4 Laboratory Findings in Central Labs by Visit - Hematology - Safety Population ... 126
Listing 16.2.8.5 Laboratory Findings in Central Labs by Visit - Chemistry - Safety Population ... 127
Listing 16.2.8.6 Laboratory Findings in Central Labs by Visit - Urinalysis - Safety Population ... 128
Listing 16.2.9 Vital Signs - Safety Population ... 129
Listing 16.2.10.1 ECG Results - Safety Population ... 130
Listing 16.2.10.2 ECG Assessment - Safety Population ... 131
Listing 16.2.11 Physical Examination Results - Safety Population ... 132

Table 14.1.1
Overall Summary of Study Populations
Enrolled Patients

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients Enrolled			xxx
Patients Randomized [a]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients Treated	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ITT Population [b]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Microbiological ITT (mITT) Population [c]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Per Protocol (PP) Population [d]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
PP Microbiologically Evaluable (mPP) population [e]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Modified Clinically Evaluable (mCE) Population [f]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Safety Population [g]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Completed Study [h]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

[a] The denominator for percentage in each treatment group is the number of total patients randomized.
[b] The ITT Population consists of all randomized patients, analysed according to treatment a patient was randomized to. The percentage is based on patients randomized in each treatment group.
[c] The mITT Population consists of all randomized patients who had a Gram+ baseline bacterial pathogen identified as the cause of ABSSSI, analysed according to treatment randomized to. The percentage is based on patients randomized in each treatment group.
[d] The PP Population consists of all randomized patients who received at least 80% of their planned doses and have adequate assessment for each of the following timepoints: ETP, EOT and TOC, analysed according to treatment received at Visit 1. The percentage is based on patients randomized in each treatment group.
[e] The mPP Population consists of mITT patients who received at least 80% of their planned doses and had adequate assessment for each of the following timepoints: ETP, EOT and TOC, analysed according to treatment received at Visit 1. The percentage is based on patients randomized in each treatment group.
[f] The mCE Population consists of PP and all patients who may have been excluded from PP due to receipt of prohibited medications, including concomitant antibiotics or high dose steroids. The percentage is based on patients randomized in each treatment group.
[g] The Safety Population consists of all patients who received any study drug during the trial, analysed according to treatment received at Visit 1. The percentage is based on patients randomized in each treatment group.

[h] The percentage is calculated from all enrolled patients who signed inform consent in each treatment group.
Programming Notes:
Enrolled = informed consent. Counts for enrolled patients will only be presented in the total column.
Program Name: Date Generated: Page x of y

Table 14.1.2.1
Summary of Study Completion
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients who completed study	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Primary reason for early discontinuation of study			
Adverse Event	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Pregnancy	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Death	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Lost To Follow-up	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Non-Compliance With Study Drug	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Investigator Decision	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Protocol Violation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Study Terminated By Sponsor	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Screen Failure	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Withdrew Consent	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Other	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Gram-positive bacteremia	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Gram-negative bacteremia	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Note: Percentages of patients with each primary reason calculated based on the number of patients not completing the study; all other percentages are calculated based on the ITT Population within each treatment group.

Programming Notes:

Obtain reasons for early discontinuation from CRF.

Program Name: Date Generated: Page x of y

Repeat for the following displays:

```
Table 14.1.2.2 Summary of Study Completion - Safety Population
  Add:
    Footnote: Note: Percentages of patients with each primary reason calculated based on the number of patients not completing the
study; all other percentages are calculated based on the Safety Population within each treatment group.
  Delete:
    Footnote: Note: Percentages of patients with each primary reason calculated based on the number of patients not completing the
study; all other percentages are calculated based on the ITT Population within each treatment group.
```

Table 14.1.2.3
Summary of Treatment Completion
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients who discontinued treatment	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Primary reason for discontinuation of treatment:			
Adverse Event	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Investigator Decision	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Pregnancy	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Protocol Deviation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Withdrew Consent	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Lost to Follow-Up	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Sponsor Decision	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Unblinding	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Lack of Efficacy	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Screen Failure	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Death	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Other	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Note: Percentages of patients with each primary reason calculated based on the number of patients not completing the study; all other percentages are calculated based on the ITT Population within each treatment group.

Programming Notes:

Obtain reasons for early discontinuation from CRF.

Program Name: Date Generated: Page x of y

Repeat for the following displays:

```
Table 14.1.2.4 Summary of Treatment Completion - Safety Population
  Add:
    Footnote: Note: Percentages of patients with each primary reason calculated based on the number of patients not completing the
study; all other percentages are calculated based on the Safety Population within each treatment group.
  Delete:
    Footnote: Note: Percentages of patients with each primary reason calculated based on the number of patients not completing the
study; all other percentages are calculated based on the ITT Population within each treatment group.
```

Table 14.1.3
Study Sample Sizes by Country and Center
Enrolled Patients

Region	Country	Center	Number of Patients enrolled	Treatment group	Randomized	Valid for ITT	Valid for mITT	Valid for PP	Valid for mPP	Valid for mCE	Valid for Safety
Overall			xx	Total	xx	xx	xx	xx	xx	xx	xx
				Iclaprim	xx	xx	xx	xx	xx	xx	xx
				Vancomycin	xx	xx	xx	xx	xx	xx	xx
North America	xxxxxxxxxxx	Xxxxxx	xx	Total	xx	xx	xx	xx	xx	xx	xx
				Iclaprim	xx	xx	xx	xx	xx	xx	xx
				Vancomycin	xx	xx	xx	xx	xx	xx	xx
	xxxxxxxxxxx	Xxxxxx	xx	Total	xx	xx	xx	xx	xx	xx	xx
				Iclaprim	xx	xx	xx	xx	xx	xx	xx
				Vancomycin	xx	xx	xx	xx	xx	xx	xx
Europe	xxxxxxxxxxx	Xxxxxx	xx	Total	xx	xx	xx	xx	xx	xx	xx
				Iclaprim	xx	xx	xx	xx	xx	xx	xx
				Vancomycin	xx	xx	xx	xx	xx	xx	xx
	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .

Program Name: Date Generated:
Page x of y

Table 14.1.4
Number of Patients Assessed at Visits with Efficacy Assessment
All Randomized Patients

Analysis Population	Treatment group	N	Number completed study	Number completed ETP	Number completed EOT	Number completed TOC	Number of Discontinuation of treatment
ITT	Total	xx	xx	xx	xx	xx	xx
	Iclaprim	xx	xx	xx	xx	xx	xx
	Vancomycin	xx	xx	xx	xx	xx	xx
mITT	Total	xx	xx	xx	xx	xx	xx
	Iclaprim	xx	xx	xx	xx	xx	xx
	Vancomycin	xx	xx	xx	xx	xx	xx
PP	Total	xx	xx	xx	xx	xx	xx
	Iclaprim	xx	xx	xx	xx	xx	xx
	Vancomycin	xx	xx	xx	xx	xx	xx
mPP	Total	xx	xx	xx	xx	xx	xx
	Iclaprim	xx	xx	xx	xx	xx	xx
	Vancomycin	xx	xx	xx	xx	xx	xx
mCE	Total	xx	xx	xx	xx	xx	xx
	Iclaprim	xx	xx	xx	xx	xx	xx
	Vancomycin	xx	xx	xx	xx	xx	xx
Safety	Total	xx	xx	xx	xx	xx	xx
	Iclaprim	xx	xx	xx	xx	xx	xx
	Vancomycin	xx	xx	xx	xx	xx	xx

Program Name: Date Generated:
Page x of y

Table 14.1.5.1
Summary of Major Protocol Violations/Deviations
ITT Population

Protocol Violation	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Subjects with at Least 1 Major Protocol Violation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Major Protocol Violation 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
etc			

The violations/deviations were identified prior to data unblinding.
Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.1.5.2 Summary of Major Protocol Violations/Deviations - mITT Population

Table 14.1.6
Summary of Patients Validity
All Randomized Patients

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients valid for ITT analysis (Randomized Patients)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients valid for Safety analysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients valid for mITT analysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients valid for PP analysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients valid for mPP analysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients valid for mCE analysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Excluded from Safety analysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Never took study drug	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Excluded from mITT analysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Non-Gram-positive pathogen at baseline	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ASO titer positive for *S. pyogenes*	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Excluded from PP analysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Non-compliance with study drug	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No efficacy data for any ETP evaluation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No efficacy data for any EOT evaluation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No efficacy data for any TOC evaluation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

<repeat for each population defined in SAP>

Note: Patients in ITT and mITT are grouped according to the randomized treatment group. Patients in PP, mPP, mCE and safety populations are analysed as treated.
Programming Notes:

The values of categorical variables are sorted in coded order. Multiple reasons for exclusion from the analysis are possible. All data sets defined in the SAP are to be included in the table. Display reason(s) for exclusion from the population as defined in SAP.

Program Name: Date Generated: Page x of y

Table 14.1.7.1
Summary of Demography
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Age (Years) [a]			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.xx (xx.xx)
Median	xx.x	xx.x	xx.x
Min,Max	xxx, xxx	xxx, xxx	xxx, xxx
Age Categories (years) n (%)			
n	xxx	xxx	xxx
18-39	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
40-64	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
65+	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Sex, n (%)			
n	xxx	xxx	xxx
Male	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Female	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Race, n (%)			
n	xxx	xxx	xxx
American Indian or Alaska Native	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Asian	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Black or African American	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
White	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Other	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Multi-racial	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Ethnicity, n (%)			
n	xxx	xxx	xxx
Hispanic or Latino	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No Hispanic or Latino	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Not Reported	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

	Unknown	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Weight	(kg)			
	n	xxx	xxx	xxx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.xx (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min,Max	xxx, xxx	xxx, xxx	xxx, xxx
Height	(m)			
	n	xxx	xxx	xxx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.xx (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min,Max	xxx, xxx	xxx, xxx	xxx, xxx
BMI	(kg/m2)			
	n	xxx	xxx	xxx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.xx (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min,Max	xxx, xxx	xxx, xxx	xxx, xxx

Note: Denominators for percentages are based on the number of patients with non-missing data in each treatment group for the relevant variable.
[a] Age is calculated as (calendar months from birth to informed consent - I(day of informed consent < day of birth))/12, and will be reported as whole years.

Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.1.7.2 Summary of Demography - mITT Population

Table 14.1.7.3 Summary of Demography - PP Population

Table 14.1.7.4 Summary of Demography - mPP Population

Table 14.1.7.5 Summary of Demography - mCE Population

Table 14.1.7.6 Summary of Demography - Safety Population

Table 14.1.8.1
Baseline Disease Characteristics
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Lesion Type			
Major Cutaneous Abscess, n (%)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Cellulitis/ Erysipelas, n (%)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Wound Infection, n(%)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Lesion Size at Baseline (cm^2)			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.xx (xx.xx)
Median	xx.x	xx.x	xx.x
Min,Max	xxx, xxx	xxx, xxx	xxx, xxx
Receipt of Prior Antibiotics (based on IVRS)			
Yes	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Blood Culture at Baseline			
Positive	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Negative	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
CrCL (mL/min)			
N	xxx	xxx	xxx
>=90	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
60-89	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
30-59	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
15-29	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<15 or hemodialysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Any Severe Infection[a]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Gram-positive Pathogen	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Gram-positive PLUS Gram-negative Pathogen	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

MRSA	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
MSSA	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Multiple Pathogens	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Single Pathogen	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Only *S. pyogenes* by ASO Titer and Blood Culture at baseline			
ASO positive only	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Culture positive only	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ASO and Culture both positive	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ASO and Culture both negative	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

CrCL=Creatinine Clearance, MRSA=Methicillin-resistant Staphylococcus aureus, MSSA=Methicillin-sensitive Staphylococcus aureus
Note: Denominators for percentages are based on the number of patients with non-missing data in each treatment group for the relevant variable.
[a] Severe infection is defined as meeting one or more of the following criteria:
a. fulfilled the published definition for systemic inflammatory response syndrome (SIRS) by having >=2 of the following findings: body temperature >38°C or <36°C, heart rate >90 bpm, respiration rate >20 breaths/minute, and WBC >12000/mm3 or <4000/mm3 or >10% bands;
b. Evaluated as having severe tenderness or severe erythema at the infection site; and
c. Positive blood cultures at baseline
Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.1.8.2 Baseline Disease Characteristics - mITT Population

Table 14.1.8.3 Baseline Disease Characteristics - PP Population

Table 14.1.8.4 Baseline Disease Characteristics - mPP Population

Table 14.1.8.5 Baseline Disease Characteristics - mCE Population

Table 14.1.8.6 Baseline Disease Characteristics - Safety Population

Table 14.1.9
Summary of Medical History
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients with Any Medical History?			
No	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Yes	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Medical History			
System Organ Class 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 3	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 4	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
System Organ Class 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 3	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 4	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

The denominator for percentages is the number of patients in the ITT Population for each treatment group.

Note: This table contains counts of patients. If a patient had more than one medical history within a preferred term, the patient is counted only once within a preferred term. If a patient had more than one medical history within a system organ class, the patient is counted once for each preferred term and once for the system organ class.
Note: MedDRA Version 18.1 used for coding.

Program Name: Date Generated: Page x of y

Table 14.1.10.1
Prior Medications
ITT Population

ATC CLASS (ATC Level 2) SUBCLASS (ATC Level 4)/ GENERIC TERM	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Number(%) of patients with at least one medication	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ANY MEDICATION CLASS	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Any medication	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ATC Class Term	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 1/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 2/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 3/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 4/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<continue other ATC class and subclass>			

Note: Patients in ITT are grouped according to the randomized treatment group.
Prior medications are those taken prior to the first dose date of treatment and within the preceding 30 days of the Informed Consent.
Programming Notes:
Includes antibiotics started prior to first dose of study drug.
Program Name: Date Generated: Page x of y

Table 14.1.10.2
Concomitant Medication Excluding Antibiotics
ITT Population

ATC CLASS (ATC Level 2) SUBCLASS (ATC Level 4)/ GENERIC TERM	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Number(%) of patients with at least one medication	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ANY MEDICATION CLASS	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Any medication	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ATC Class Term	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 1/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 2/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 3/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 4/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<continue other ATC class and subclass>			

Note: Patients in ITT are grouped according to the randomized treatment group.
Note: Concomitant medications are those with a start date on or after the first dose date of treatment, or those with a start date before the first dose date of treatment and a stop date on or after the first dose date of treatment.
Program Name: Date Generated: Page x of y

Table 14.1.10.3
Concomitant Antibiotic Medication
ITT Population

ATC CLASS (ATC Level 2) SUBCLASS (ATC Level 4)/ GENERIC TERM	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Number(%) of patients with at least one medication	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ANY MEDICATION CLASS	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Any medication	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ATC Class Term	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 1/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 2/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 3/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBCLASS 4/ GENERIC TERM	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<continue other ATC class and subclass>			

Note: Patients in ITT are grouped according to the randomized treatment group.
Note: Concomitant antibiotics are selected from medications that are checked as antibiotic in the CRF
Program Name: Date Generated: Page x of y

Table 14.1.10.4
Summary of Significant Procedures by Visit
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Number (%) of patients receiving any significant procedures at Visit 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Debridement	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Incision and drainage	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Other	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...			
<Repeat for all visits with significant procedures performed>			

Note: Patients in ITT are grouped according to the randomized treatment group.
Program Name: Date Generated: Page x of y

Table 14.1.11.1.1
Clinical Signs and Symptoms of ABSSSI by Visit: Tender to Palpitation
ITT Population

Tender to Palpitation	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Baseline			
None	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Mild	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Moderate	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Severe	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Visit 2			
None	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Mild	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Moderate	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Severe	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

< Repeat for all visits where signs and symptoms were assessed >

Program Name: Date Generated: Page x of y

Repeat for the following displays:

Table 14.1.11.1.2 Clinical Signs and Symptoms of ABSSSI by Visit: Tender to Palpitation - PP Population

Table 14.1.11.1.3 Clinical Signs and Symptoms of ABSSSI by Visit: Tender to Palpitation - mCE Population

Table 14.1.11.2.1 Clinical Signs and Symptoms of ABSSSI by Visit: Erythema - ITT Population

Table 14.1.11.2.2 Clinical Signs and Symptoms of ABSSSI by Visit: Erythema - PP Population

Table 14.1.11.2.3 Clinical Signs and Symptoms of ABSSSI by Visit: Erythema - mCE Population

Table 14.1.11.3.1	Clinical Signs and Symptoms of ABSSSI by Visit: Edema - ITT Population
Table 14.1.11.3.2	Clinical Signs and Symptoms of ABSSSI by Visit: Edema - PP Population
Table 14.1.11.3.3	Clinical Signs and Symptoms of ABSSSI by Visit: Edema - mCE Population
Table 14.1.11.4.1	Clinical Signs and Symptoms of ABSSSI by Visit: Purulent Drainage/Discharge - ITT Population
Table 14.1.11.4.2	Clinical Signs and Symptoms of ABSSSI by Visit: Purulent Drainage/Discharge - PP Population
Table 14.1.11.4.3	Clinical Signs and Symptoms of ABSSSI by Visit: Purulent Drainage/Discharge - mCE Population
Table 14.1.11.5.1	Clinical Signs and Symptoms of ABSSSI by Visit: Fluctuance - ITT Population
Table 14.1.11.5.2	Clinical Signs and Symptoms of ABSSSI by Visit: Fluctuance - PP Population
Table 14.1.11.5.3	Clinical Signs and Symptoms of ABSSSI by Visit: Fluctuance - mCE Population
Table 14.1.11.6.1	Clinical Signs and Symptoms of ABSSSI by Visit: Induration - ITT Population
Table 14.1.11.6.2	Clinical Signs and Symptoms of ABSSSI by Visit: Induration - PP Population
Table 14.1.11.6.3	Clinical Signs and Symptoms of ABSSSI by Visit: Induration - mCE Population
Table 14.1.11.7.1	Clinical Signs and Symptoms of ABSSSI by Visit: Ulceration - ITT Population
Table 14.1.11.7.2	Clinical Signs and Symptoms of ABSSSI by Visit: Ulceration - PP Population
Table 14.1.11.7.3	Clinical Signs and Symptoms of ABSSSI by Visit: Ulceration - mCE Population
Table 14.1.11.8.1	Clinical Signs and Symptoms of ABSSSI by Visit: Necrotic Tissue - ITT Population
Table 14.1.11.8.2	Clinical Signs and Symptoms of ABSSSI by Visit: Necrotic Tissue - PP Population
Table 14.1.11.8.3	Clinical Signs and Symptoms of ABSSSI by Visit: Necrotic Tissue - mCE Population
Table 14.1.11.9.1	Clinical Signs and Symptoms of ABSSSI by Visit: Localized Pain - ITT Population
Table 14.1.11.9.2	Clinical Signs and Symptoms of ABSSSI by Visit: Localized Pain - PP Population
Table 14.1.11.9.3	Clinical Signs and Symptoms of ABSSSI by Visit: Localized Pain - mCE Population

Table 14.1.11.10.1 Clinical Signs and Symptoms of ABSSSI by Visit: Swelling - ITT Population

Table 14.1.11.10.2 Clinical Signs and Symptoms of ABSSSI by Visit: Swelling - PP Population

Table 14.1.11.10.3 Clinical Signs and Symptoms of ABSSSI by Visit: Swelling - mCE Population

Table 14.1.11.11.1 Clinical Signs and Symptoms of ABSSSI by Visit: Chills - ITT Population

Table 14.1.11.11.2 Clinical Signs and Symptoms of ABSSSI by Visit: Chills - PP Population

Table 14.1.11.11.3 Clinical Signs and Symptoms of ABSSSI by Visit: Chills - mCE Population

Table 14.1.11.12.1 Clinical Signs and Symptoms of ABSSSI by Visit: Fever - ITT Population

Table 14.1.11.12.2 Clinical Signs and Symptoms of ABSSSI by Visit: Fever - PP Population

Table 14.1.11.12.3 Clinical Signs and Symptoms of ABSSSI by Visit: Fever - mCE Population

Table 14.1.12.1
Type of Culture Specimen and Culture Results by Visit
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Baseline			
Was a specimen obtained for the culture?			
Yes	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Specimen type			
Aerobic blood culture	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Anaerobic blood culture	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Infection site culture	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Was culture performed?			
Yes	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Did the culture grow an organism?			
Yes	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Was the organism a pathogen?			
Yes	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
< Repeat for all visits where culture was performed >			

Program Name: Date Generated: Page x of y

Table 14.1.12.2
Summary of Culture Specimen for Lesion Type by Visit
ITT Population

Lesion Type Specimen Type Genus Species	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Baseline			
Major Cutaneous Abscess	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Aerobic Blood Culture	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Genus1 Species1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Genus1 Species2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...			
Anaerobic Blood Culture	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Genus1 Species1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...			
Infection Site Culture	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Genus1 Species1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...			
Missing	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Cellulitis/Erysipelas	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Aerobic Blood Culture	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Genus1 Species1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...			
...			
Wound Infection	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...			

< Repeat for all visits where culture was performed >

Program Name: Date Generated: Page x of y

Table 14.1.12.3
Microbiological Assessment of Primary Infection Site - Gram Stain
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Method of Collection			
Needle aspirate	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Biopsy	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Tissue/fluid/pus surgically obtained in operating room	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Tissue/fluid/pus obtained during during bedside procedure	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Gram Stain, n (%)			
Gram Stain Not Done	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
No Bacteria	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Gram-positive cocci (clusters)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Gram-positive cocci (chains)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Gram-negative cocci	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Gram-positive bacilli	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Gram-negative bacilli	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Program Name: Date Generated: Page x of y

Table 14.1.12.4
Blood Culture Results by Visit
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Baseline			
Blood Cultures, n (%)			
Positive	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Negative	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing Data/Not Done	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Visit 2			
...			
< Repeat for all visits where culture was performed >			

Program Name: Date Generated: Page x of y

Table 14.1.12.5
Gram-positive Pathogens Occurring in Patients at Baseline
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Pathogen			
Pathogen 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Pathogen 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
…			

<Continue for other identified pathogens>

Note: Patients may have more than one pathogens.
Program Name: Date Generated: Page x of y

Table 14.1.12.6
Frequency Distribution of MIC by Baseline Pathogen
ITT Population

Treatment Group: *treatment 1*

Pathogen 1

	Frequency of MIC (mcg/mL) (n, %, Cumulative %)												
Test [a]	0.0625	0.125	0.25	0.5	1.0	2.0	4.0	8.0	16.0	32.0	64.0	MIC50	MIC90
AMP, N=xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx.x	xx.x
	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x		
	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x		
...													

<Continue for other antibiotics tested>

<Continue for other pathogens identified at baseline>

N = number of isolates; MIC = Minimum Inhibitory Concentration; MIC50 = MIC at which 50% of isolates tested are inhibited; MIC90 = MIC at which 90% of isolates tested are inhibited.

[a] Antibiotics Tested: AMP=Ampicillin, ….
[b] MIC50 and MIC90 values are only reported when >=10 isolates were tested.

Program Name: Date Generated: Page x of y

Table 14.1.13.1
Summary of Treatment Compliance
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Compliance (%)			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.xx (xx.xx)
Median	xx.x	xx.x	xx.x
Min	xx.x	xx.x	xx.x
Max	xx.x	xx.x	xx.x
Range	xxx, xxx	xxx, xxx	xxx, xxx
Overall Compliance			
n	xxx	xxx	xxx
<80.0%	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
80.0% to 100.0%	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
>100.0%	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Note: Percentage compliance is calculated as (number of doses received / number of doses scheduled)*100%. Compliance is defined as percentage compliance at least 80.0%.

Program Name: Date Generated: Page x of y

Table 14.1.13.2
Summary of Treatment Exposure: Duration in Days
Safety Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Duration (days)		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min	xx.x	xx.x
Max	xx.x	xx.x
Range	xx.x, xx.x	xx.x, xx.x

The denominator for percentages is the number of patients with non-missing data in the Safety Population for each treatment group.
Note: Duration of exposure calculated as (date of last dose – date of first dose) + 1.

Program Name: Date Generated: Page x of y

Table 14.2.1
Proportions of Patients with a >=20% Reduction in Lesion Size at ETP
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	% Difference (Iclaprim - Vancomycin)
Early Clinical Response [a]	xxx (xx.x)	xxx (xx.x)	xx.x
95% CI [b]	(x.xx , x.xx)	(x.xx , x.xx)	(x.xx , x.xx)
p-value [c]			x.xxx

[a] Early Clinical Response is defined as >=20% reduction in lesion size at ETP.
[b] The two-sided 95% CI is based on the exact binomial CI for the proportions of the 2 groups, and is based on the z-test with unpooled variance estimate for the difference in the 2 proportions. If the lower bound of 95% CI is greater than -0.10, NI is concluded.
[c] p-value is for the NI test with significance level of 0.025.
The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.2.2.1 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP - mITT Population
Add:
The denominator for percentages is the number of patients with non-missing data in the mITT Population for each treatment group.

Delete:
The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.2.2 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP - mCE Population
Add:
The denominator for percentages is the number of patients with non-missing data in the mCE Population for each treatment group.

Delete:
The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.2.3 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP - PP Population
Add:
The denominator for percentages is the number of patients with non-missing data in the PP Population for each treatment group.

Delete:
The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.2.4 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP - mPP Population
Add:
The denominator for percentages is the number of patients with non-missing data in the mPP Population for each treatment group.

Delete:
The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.3.1
Resolution or Near Resolution of ABSSSI at TOC
ITT Population

	Iclaprim (N = xxx) n (%)	**Vancomycin (N = xxx) n (%)**	**% Difference (Iclaprim - Vancomycin)**
Clinical cure rate	xxx (xx.x)	xxx (xx.x)	xx.x
95% CI [a]	(x.xx , x.xx)	(x.xx , x.xx)	(x.xx , x.xx)
p-value [b]			x.xxx

[a] The two-sided 95% CI is based on the exact binomial CI for the proportions of the 2 groups, and is based on the z-test with unpooled variance estimate for the difference in the 2 proportions. If the lower bound of 95% CI is greater than -0.10, NI is concluded.
[b] p-value is for the NI test with significance level of 0.025.
The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.2.3.2 Resolution or Near Resolution of ABSSSI at TOC - mITT Population
Add:
Footnote: The denominator for percentages is the number of patients with non-missing data in the mITT Population for each treatment group.

Delete:
Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

```
Table 14.2.3.3 Resolution or Near Resolution of ABSSSI at TOC - mCE Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mCE Population for each treatment
group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment
group.


Table 14.2.3.4 Resolution or Near Resolution of ABSSSI at TOC - PP Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the PP Population for each treatment
group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment
group.


Table 14.2.3.5 Resolution or Near Resolution of ABSSSI at TOC - mPP Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mPP Population for each treatment
group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment
group.


Table 14.2.4.1 Resolution or Near Resolution of ABSSSI at EOT - ITT Population
```

Table 14.2.4.2 Resolution or Near Resolution of ABSSSI at EOT - mITT Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mITT Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.4.3 Resolution or Near Resolution of ABSSSI at EOT - mCE Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mCE Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.4.4 Resolution or Near Resolution of ABSSSI at EOT - PP Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the PP Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.4.5 Resolution or Near Resolution of ABSSSI at EOT - mPP Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mPP Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.5.1
Summary of Clinical Response at EOT and TOC
PP Population

Clinical Response	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
EOT		
n [a]		
Cure	xxx (xx.x)	xxx (xx.x)
Failure	xxx (xx.x)	xxx (xx.x)
Indeterminate	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)
TOC		
n [a]		
Cure	xxx (xx.x)	xxx (xx.x)
Failure	xxx (xx.x)	xxx (xx.x)
Indeterminate	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)

[a] Number of patients who completed the visit at the corresponding time point.
Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.2.5.2 Summary of Clinical Response at EOT and TOC - mPP Population

Table 14.2.6.1
Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	% Difference (Iclaprim - Vancomycin)
Patients with severe infection, n	xxx	xxx	
Clinical cure	xxx (xx.x)	xxx (xx.x)	xx.x
95% CI [a]	(x.xx , x.xx)	(x.xx , x.xx)	(x.xx , x.xx)
p-value [b]			x.xxx

[a] The two-sided 95% CI is based on the exact binomial CI for the proportions of the 2 groups, and is based on the z-test with unpooled variance estimate for the difference in the 2 proportions. If the lower bound of 95% CI is greater than -0.10, NI is concluded.
[b] p-value is for the NI test with significance level of 0.025.
The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.2.6.2 Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline - mITT Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mITT Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.6.3 Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline - mCE Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mCE Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.6.4 Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline - PP Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the PP Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.6.5 Resolution or Near Resolution of ABSSSI at TOC among Patients with Severe Infection at Baseline - mPP Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mPP Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.7.1 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - ITT Population

Table 14.2.7.2 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - mITT Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mITT Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.7.3 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - mCE Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mCE Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.7.4 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - PP Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the PP Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.7.5 Resolution or Near Resolution of ABSSSI at EOT among Patients with Severe Infection at Baseline - mPP Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mPP Population for each treatment group.

  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.8.1
Time to Resolution of Signs and Symptoms of ABSSSI
ITT Population

Tender to Palpitation	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Number of Patients with Events	xxx (xx.x)	xxx (xx.x)
Number of Patients Censored	xxx (xx.x)	xxx (xx.x)
Time to event (days)		
Median [a]	xx.x	xx.x
95% CI for Median [a]	(xx.xx , xx.xx)	(xx.xx , xx.xx)
25% and 75% (Percentiles)	xx.x, xx.x	xx.x, xx.x
Range [b]	xx.x, xx.x	xx.x, xx.x
P-value (Log-Rank Test)		x.xxx
Unadjusted Hazard Ratio [c]		x.xx
95% CI		[x.xxx, x.xxx]

<Repeat for other signs and symptoms of ABSSSI>

Time to resolution of signs and symptoms of ABSSSI is defined as: first date with no signs and symptoms of ABSSSI (in log form) post treatment – date of first dose + 1.
Note: Denominators for percentages are based on the number of patients in the ITT Population
[a] Kaplan-Meier estimates.
[b] Including censored observations.
[c] Hazard ratio is estimated using Cox's Proportional Hazards Model for Iclaprim versus Vancomycin, and the confidence interval is based on inverting the Wald test. If the upper bound of 95% CI is less than 1.10, NI is concluded. The p-value is based on one-sided Wald test with significant level of 0.025.
Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.2.8.2 Time to Resolution of Signs and Symptoms of ABSSSI - mITT Population
Add:
Note: Denominators for percentages are based on the number of patients in the mITT Population
Delete:
Note: Denominators for percentages are based on the number of patients in the ITT Population

```
Table 14.2.8.3 Time to Resolution of Signs and Symptoms of ABSSSI - mCE Population
  Add:
Note: Denominators for percentages are based on the number of patients in the mCE Population
  Delete:
Note: Denominators for percentages are based on the number of patients in the ITT Population

Table 14.2.8.4 Time to Resolution of Signs and Symptoms of ABSSSI - PP Population
  Add:
Note: Denominators for percentages are based on the number of patients in the PP Population
  Delete:
Note: Denominators for percentages are based on the number of patients in the ITT Population

Table 14.2.8.5 Time to Resolution of Signs and Symptoms of ABSSSI - mPP Population
  Add:
Note: Denominators for percentages are based on the number of patients in the mPP Population
  Delete:
Note: Denominators for percentages are based on the number of patients in the ITT Population
```

Table 14.2.9.1
Percent of Resolution of Signs and Symptoms of ABSSSI
ITT Population

% of Resolution of Tender to Palpitation	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
ETP		
...		
<Continue for other visits with the assessment>		
<Repeat for other signs and symptoms of ABSSSI>		

n is the number of patients with non-missing data in the ITT Population for each treatment group.
Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.2.9.2 Percent of Resolution of Signs and Symptoms of ABSSSI - mITT Population
  Add:
    Footnote: n is the number of patients with non-missing data in the mITT Population for each treatment group.
  Delete:
    Footnote: n is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.9.3 Percent of Resolution of Signs and Symptoms of ABSSSI - mCE Population
  Add:
    Footnote: n is the number of patients with non-missing data in the mCE Population for each treatment group.
  Delete:
    Footnote: n is the number of patients with non-missing data in the ITT Population for each treatment group.

```
Table 14.2.9.4 Percent of Resolution of Signs and Symptoms of ABSSSI - PP Population
  Add:
    Footnote:  n is the number of patients with non-missing data in the PP Population for each treatment group.
  Delete:
    Footnote:  n is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.9.5 Percent of Resolution of Signs and Symptoms of ABSSSI - mPP Population
  Add:
    Footnote:  n is the number of patients with non-missing data in the mPP Population for each treatment group.
  Delete:
    Footnote:  n is the number of patients with non-missing data in the ITT Population for each treatment group.
```

Table 14.2.10.1.1
By Patient Bacteriological Response Rate at EOT
mITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Number of Patients with Gram-positive Pathogen response assessment	xxx	xxx
Bacteriological Response		
Eradication	xxx (xx.x)	xxx (xx.x)
Presumed Eradication	xxx (xx.x)	xxx (xx.x)
Persistence	xxx (xx.x)	xxx (xx.x)
Presumed Persistence	xxx (xx.x)	xxx (xx.x)
Indeterminate	xxx (xx.x)	xxx (xx.x)
Superinfection	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)

Program Name: Date Generated: Page x of y

Repeat for the following displays:

Table 14.2.10.2.1 By Patient Bacteriological Response Rate at EOT - mCE Population

Table 14.2.10.3.1 By Patient Bacteriological Response Rate at EOT - mPP Population

Table 14.2.11.1.1 By Patient Bacteriological Response Rate at TOC - mITT Population

Table 14.2.11.2.1 By Patient Bacteriological Response Rate at TOC - mCE Population

Table 14.2.11.3.1 By Patient Bacteriological Response Rate at TOC - mPP Population

Table 14.2.10.1.2
By Patient Combined Bacteriological Response Rate at EOT
mITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	% Difference (Iclaprim - Vancomycin)
Eradication/Presumed Eradication	xxx (xx.x)	xxx (xx.x)	xx.x
95% CI [a]	(xx.xx , xx.xx)	(xx.xx , xx.xx)	

The denominator for percentages is the number of patients with non-missing data in the mITT Population for each treatment group.
Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.2.10.2.2 By Patient Combined Bacteriological Response Rate at EOT - mCE Population
Add:
Footnote: The denominator for percentages is the number of patients with non-missing data in the mCE Population for each treatment group.
Delete:
Footnote: The denominator for percentages is the number of patients with non-missing data in the mITT Population for each treatment group.

Table 14.2.10.3.2 By Patient Combined Bacteriological Response Rate at EOT - mPP Population
Add:
Footnote: The denominator for percentages is the number of patients with non-missing data in the mPP Population for each treatment group.
Delete:
Footnote: The denominator for percentages is the number of patients with non-missing data in the mITT Population for each treatment group.

Table 14.2.11.1.2 By Patient Combined Bacteriological Response Rate at TOC - mITT Population

```
Table 14.2.11.2.2      By Patient Combined Bacteriological Response Rate at TOC - mCE Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mCE Population for each treatment
group.
  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mITT Population for each
treatment group.

Table 14.2.11.3.2      By Patient Combined Bacteriological Response Rate at TOC - mPP Population
  Add:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mPP Population for each treatment
group.
  Delete:
    Footnote: The denominator for percentages is the number of patients with non-missing data in the mITT Population for each
treatment group.
```

Table 14.2.12.1
By Pathogen Bacteriological Response Rate at EOT
mITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Pathogen 1		
Eradication	xxx (xx.x)	xxx (xx.x)
Presumed Eradication	xxx (xx.x)	xxx (xx.x)
Persistence	xxx (xx.x)	xxx (xx.x)
Presumed Persistence	xxx (xx.x)	xxx (xx.x)
Indeterminate	xxx (xx.x)	xxx (xx.x)
Superinfection	xxx (xx.x)	xxx (xx.x)
Missing	xxx (xx.x)	xxx (xx.x)
Pathogen 2		
...		

<Continue for all pathogens identified>

Program Name: Date Generated: Page x of y

Repeat for the following displays:

Table 14.2.12.2 By Pathogen Bacteriological Response Rate at EOT - mCE Population

Table 14.2.12.3 By Pathogen Bacteriological Response Rate at EOT - mPP Population

Table 14.2.13.1 By Pathogen Bacteriological Response Rate at TOC - mITT Population

Table 14.2.13.2 By Pathogen Bacteriological Response Rate at TOC - mCE Population

Table 14.2.13.3 By Pathogen Bacteriological Response Rate at TOC - mPP Population

Table 14.2.14
Mortality Rate within 28 Days of First Dose of Treatment
ITT Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients Who Died within 28 Days of First Dose of Treatment	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

The denominator for percentages is the number of patients with non-missing date of first dose.
Program Name: Date Generated: Page x of y

Table 14.2.15.1
Proportions of Patients with a >=20% Reduction in Lesion Size at ETP by Subgroups
ITT Population

	Total (N = xxx)	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	% Difference[a] (95% CI[b])
Age Group				
18-39	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
40-64	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
65+	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Sex				
Male	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Female	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Race				
White	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Non-white	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Cr Clearance (mL/min)				
>=90	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
60-89	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
30-59	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
15-29	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
<15 or hemodialysis	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Positive Blood Culture at Baseline	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
MRSA	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
MSSA	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Multiple pathogens	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Single pathogen	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Patients with *S. pyogenes*				

ASO+ only	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Culture+ only	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Both ASO+ and Culture+	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Both ASO- and Culture-	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
Patients with severe infection				
Yes	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)
No	xxx	xxx (xx.x)	xxx (xx.x)	xx.x (x.xx, x.xx)

MRSA=Methicillin-resistant *Staphylococcus aureus*, MSSA=Methicillin-sensitive *Staphylococcus aureus*.
[a] The difference is defined as the % of iclaprim - % of vancomycin.
[b] The two-sided 95% CI is based on the exact binomial CI for the proportions of the 2 groups, and is based on the z-test with unpooled variance estimate for the difference in the 2 proportions.
The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.2.15.2 Proportions of Patients with a >=20% Reduction in Lesion Size at ETP by Subgroups - PP Population
Add:
Footnote: The denominator for percentages is the number of patients with non-missing data in the PP Population for each treatment group.

Delete:
Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.2.16.1 Resolution or Near Resolution of ABSSSI at TOC by Subgroups - ITT Population

Table 14.2.16.2 Resolution or Near Resolution of ABSSSI at TOC by Subgroups - PP Population

Add:

Footnote: The denominator for percentages is the number of patients with non-missing data in the PP Population for each treatment group.

Delete:

Footnote: The denominator for percentages is the number of patients with non-missing data in the ITT Population for each treatment group.

Table 14.3.1.1
Overall Summary of Treatment-emergent Adverse Events (TEAEs)
Safety Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients with Any TEAEs [a]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Any TEAEs			
Patients with Mild TEAEs	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Moderate TEAEs	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Severe TEAEs	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Missing Severity	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Study Drug Related TEAEs [b]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with TEAE Leading to Discontinuation of Study Drug	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Serious Adverse Events (SAEs)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Study Drug Related SAEs [b]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with SAE Leading to Death	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with Study Drug Related SAE Leading to Death	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with a SAE Leading to Study Drug Discontinuation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Patients with a SAE Leading to Discontinuation from Study	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

The denominator for percentages is the number of patients in the Safety Population
[a] TEAEs are defined as events with start date on or after the date of first dose of study drug through the end of study, or events with start date prior to the date of first dose of treatment whose severity worsens on or after the date of first dose of treatment through the end of study. Note that study drug exposure is 5-14 days.
[b] Included are AEs considered probably related or related to study drug and AEs with unknown or missing relationship to study drug.

Program Name: Date Generated: Page x of y

Table 14.3.1.2
Summary of Treatment-emergent Adverse Events (TEAEs) by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients with Any TEAEs	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
System Organ Class 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 3	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
.. etc.			
System Organ Class 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 3	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
.. etc.			

The denominator for percentages is the number of patients in the Safety Population
Note: This table contains counts of patients. If a patient experienced more than one episode of an adverse event, the patient is counted only once within a preferred term. If a patient experienced more than one adverse event within a system organ class, the patient is counted once for each preferred term and once for the system organ class.
Programming Notes:
SOC will be sorted alphabetically and PT will be sorted by descending overall total.
Program Name: Date Generated: Page x of y

Repeat for the following displays:

Table 14.3.1.4 Summary of Study Drug-Related Treatment-emergent Adverse Events (TEAEs) by System Organ Class and Preferred Term - Safety Population
  Add:
    Footnote: Note: Included are AEs considered related or probably related to study drug and AEs with unknown or missing relationship to study drug.
Note: This table contains counts of patients. If a patient experienced more than one episode of an adverse event, the patient is counted only once within a preferred term and for the episode with the maximum severity. If a patient experienced more than one adverse event within a system organ class, the patient is counted once for each preferred term and once for the system organ class.

  Delete:
    Footnote: Note: This table contains counts of patients. If a patient experienced more than one episode of an adverse event, the patient is counted only once within a preferred term. If a patient experienced more than one adverse event within a system organ class, the patient is counted once for each preferred term and once for the system organ class.

Table 14.3.1.5 Summary of Treatment-emergent Adverse Events (TEAEs) Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term - Safety Population

Table 14.3.1.9 Summary of Serious Adverse Events (SAEs) by MedDRA System Organ Class and Preferred Term - Safety Population

Table 14.3.1.10 Summary of Study Drug-related Serious Adverse Events (SAEs) by MedDRA System Organ Class and Preferred Term - Safety Population

Table 14.3.1.11 Summary of Serious Adverse Events (SAEs) Leading to Death by MedDRA System Organ Class and Preferred Term - Safety Population

Table 14.3.1.3
Summary of Treatment-emergent Adverse Events (TEAEs) by Maximum Severity, MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term Maximum Severity	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients with Any TEAEs	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Mild	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Moderate	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Severe	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing Severity	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
System Organ Class 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Mild	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Moderate	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Severe	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing Severity	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Mild	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Moderate	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Severe	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing Severity	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Mild	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Moderate	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Severe	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Missing Severity	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
etc	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

The denominator for percentages is the number of patients in the Safety Population
Note: This table contains counts of patients. If a patient experienced more than one episode of an adverse event, the patient is counted only once within a preferred term and for the episode that is most related to the study drug. If a patient experienced more than one adverse event within a system organ class, the patient is counted once for each preferred term and once for the system organ class.
Programming Notes:
SOC will be sorted alphabetically and PT will be sorted by descending overall total.
Program Name: Date Generated: Page x of y

Table 14.3.1.6
Summary of Treatment-emergent Adverse Events (TEAEs) by Age Group, MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term Age Group	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients with Any TEAEs	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Age 18-64	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Age 65+	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
System Organ Class 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Age 18-64	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Age 65+	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Age 18-64	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Age 65+	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Age 18-64	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Age 65+	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
etc	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

The denominator for percentages is the number of patients in the Safety Population
Note: This table contains counts of patients. If a patient experienced more than one episode of an adverse event, the patient is counted only once within a preferred term. If a patient experienced more than one adverse event within a system organ class, the patient is counted once for each preferred term and once for the system organ class.
Programming Notes:
SOC will be sorted alphabetically and PT will be sorted by descending overall total.
Program Name: Date Generated: Page x of y

Table 14.3.1.7
Summary of Treatment-emergent Adverse Events (TEAEs) by Creatinine Clearance, MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term CrCL(mL/min)	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients with Any TEAEs	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
>= 90	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
60-89	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
30-59	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
15-29	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<15	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Hemodialysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
System Organ Class 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
>= 90	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
60-89	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
30-59	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
15-29	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<15	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Hemodialysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Overall	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
>= 90	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
60-89	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
30-59	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
15-29	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<15	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Hemodialysis	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
etc	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

The denominator for percentages is the number of patients in the Safety Population
Note: This table contains counts of patients. If a patient experienced more than one episode of an adverse event, the patient is counted only once within a preferred term. If a patient experienced more than one adverse event within a system organ class, the patient is counted once for each preferred term and once for the system organ class.
Programming Notes:
SOC will be sorted alphabetically and PT will be sorted by descending overall total.
Program Name: Date Generated: Page x of y
Repeat for the following displays:
Table 14.3.1.12 Summary of Serious Adverse Events (SAEs) with Frequency > 5% by MedDRA Preferred Term - Safety Population

Table 14.3.1.8
Summary of Treatment-emergent Adverse Events (TEAEs) with Frequency > 5% by MedDRA Preferred Term
Safety Population

Preferred Term	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)	Total (N = xxx) n (%)
Patients with Any TEAEs of Frequency >10%	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Preferred Term 3	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
... etc.			

The denominator for percentages is the number of patients in the Safety Population PT is sorted in descending order of frequency in the iclaprim group

Note: This table contains counts of patients. If a patient experienced more than one episode of an adverse event, the patient is counted only once within a preferred term. If a patient experienced more than one adverse event within a system organ class, the patient is counted once for each preferred term and once for the system organ class.

Programming Notes:

SOC will be sorted alphabetically and PT will be sorted by descending overall total.

Program Name: Date Generated: Page x of y

Table 14.3.2.1
Listing of Treatment-emergent Adverse Events (TEAEs) Leading to Discontinuation of Study Drug
Safety Population

Treatment: T*reatment 1*

Center	Patient	AE No.	System Organ Class/ Preferred Term/ Verbatim [a]	Onset Date (day)[b]/ End Date (day)[b]/ Duration (days)	TEAE/ Severity	Relationship to Study Drug/ADR?	Treatment required?/ Action Taken[c]	Outcome	SAE?
Xxxxxx	xxx	xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxx	DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx	Yes/ Mild	Not related/ No	Yes/ No	Completely recovered	No
		xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxx	DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx	No/ Moderate	Probably not related/ No	No/ Discontinued	Death	Yes
xxxxxx	xxx	xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxx	DDMMMYYYY (xx)/ Ongoing	Yes/ Severe	Probably related/ Yes Related/ Yes	Yes/ Interrupted	Ongoing Recovered to stability	Yes No

[a] Coded using MedDRA Dictionary (Version 18.1)
[b] Relative to the day of first dose of study treatment.
[c] Action Taken: No =xxx; Stop = xxxxxx xxxx; Disc = xxxx xxxxxxxxxx; Remedy = xxxx xxxxxxx xxxxxxx.
Programming Notes:
Sort by treatment group, subject, AE start date, end date, and preferred term.
Program Name: Date Generated: Page x of y

Table 14.3.2.2
Listing of Serious Adverse Events (SAEs)
Safety Population

Treatment: *Treatment 1*

Center	Patient	AE No.	System Organ Class/ Preferred Term/ Verbatim [a]	Onset Date (day)[b]/ End Date (day)[b]/ Duration (days)	TEAE/ Severity	Relationship to Study Drug/ADR?	Treatment required?/ Action Taken[c]	Outcome	SAE Type [d]
Xxxxxx	xxx	xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxx	DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx	Yes/ Mild	Not related/ No	Yes/ No	Completely recovered	LT
		xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxx	DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx	No/ Moderate	Probably not related/ No	No/ Discontinued	Death	Death
xxxxxx	xxx	xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxx	DDMMMYYYY (xx)/ Ongoing	Yes/ Severe	Probably related/ Yes Related/ Yes	Yes/ Interrupted	Ongoing Recovered to stability	PD Hosp Other

[a] Coded using MedDRA Dictionary (Version 18.1)
[b] Relative to the day of first dose of study treatment.
[c] Action Taken: No =xxx; Stop = xxxxxx xxxx; Disc = xxxx xxxxxxxxxx; Remedy = xxxx xxxxxxx xxxxxxx.
[d] SAE Type: LT = Life-threatening; PD = Permanently Disabling; Hosp = Hospitalization/prolonged hospitalization; C = Congenital anomaly; CC = Current condition.
Programming Notes:
Sort by treatment group, subject, AE start date, end date, and preferred term.
Program Name: Date Generated: Page x of y

Table 14.3.2.3
Listing of Serious Adverse Events (SAEs) Leading to Death
Safety Population

Treatment: *Treatment 1*

Center	Patient	AE No.	System Organ Class/ Preferred Term/ Verbatim [a]	Onset Date (day)[b]/ End Date (day)[b]/ Duration (days)	TEAE/ Severity	Relationship to Study Drug/ADR?	Treatment required?/ Action Taken[c]	Date of Death (days)[a]	Cause of Death
Xxxxxx	xxx	xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxx	DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx	Yes/ Mild	Not related/ No	Yes/ No	DDMMMYYYY (xx)	Xxxxx
		xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxx	DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx	No/ Moderate	Probably not related/ No	No/ Discontinued	DDMMMYYYY (xx)	Xxxxx
xxxxxx	xxx	xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxx						

[a] Coded using MedDRA Dictionary (Version 18.1)
[b] Relative to the day of first dose of study treatment.
[c] Action Taken: No =xxx; Stop = xxxxxx xxxx; Disc = xxxx xxxxxxxxxx; Remedy = xxxx xxxxxxx xxxxxxx.
Programming Notes:
Sort by treatment group, subject, AE start date, end date, and preferred term.
Program Name: Date Generated: Page x of y

Table 14.3.4.1
Summary of Laboratory Test Results and Change from Baseline by Visit: Hematology
Safety Population

Hematocrit (%)

Study Visit	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
<Visit> Pre-dose		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
Change from Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
<Visit> Post-dose		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
Change from Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x

[Continue for remaining post-baseline time points]

Note: This table only presents central lab (CCLS) results for patients with non-missing data at baseline and the time point of interest.
Note: Low = below lower limit of normal range, Normal = within normal limits, High = above upper limit of normal range.
Programming Notes:
Repeat the table for other continuous Hematology variables. See SAP for variable list.
Note: Only the tests with continuous values will be summarized.
Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.3.4.2 Summary of Laboratory Test Results and Change from Baseline by Visit: Chemistry including Creatinine Clearance - Safety Population
Add:
Note to Programmer: Repeat the table for other continuous Chemistry including Creatinine Clearance variables. See SAP for variable list.
Delete:
Note to Programmer: Repeat the table for other continuous Hematology variables. See SAP for variable list.

Table 14.3.4.3 Summary of Laboratory Test Results and Change from Baseline by Visit: Urinalysis - Safety Population
Add:
Note to Programmer: Repeat the table for other continuous Urinalysis variables. See SAP for variable list.
Delete:
Note to Programmer: Repeat the table for other continuous Hematology variables. See SAP for variable list.

Table 14.3.4.4
Shift Table of Laboratory Test Results: Hematology
Safety Population

	Iclaprim (N = xxx)				Vancomycin (N = xxx)			
	Baseline				Baseline			
Hematocrit (%)	L	N	H	Tot	L	N	H	Tot
<Visit>								
Low (L)	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Normal (N)	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
High (H)	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Total (Tot)	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
<Visit>								
Low (L)	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Normal (N)	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
High (H)	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Total (Tot)	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

<Continue for all visits>

Note: This table only presents results for patients with non-missing data at baseline and the time point of interest.
Note: Low = below lower limit of normal range, Normal = within normal limits, High = above upper limit of normal range.
Programming Notes:
Repeat the table for other Hematology variables. See SAP for variable list.
Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.3.4.5 Shift Table of Laboratory Test Results: Chemistry including Creatinine Clearance - Safety Population
Add:
Note to Programmer: Repeat the table for other Chemistry including Creatinine Clearance variables. See SAP for variable list.
Note to Programmer: Use categories negative, positive, missing.
Delete:
Note to Programmer: Repeat the table for other Hematology variables. See SAP for variable list.

```
Table 14.3.4.6 Shift Table of Laboratory Test Results: Urinalysis - Safety Population
  Add:
    Note to Programmer: Repeat the table for other Urinalysis variables. See SAP for variable list.
  Delete:
    Note to Programmer: Repeat the table for other Hematology variables. See SAP for variable list.
```

Table 14.3.4.7
Liver Function Test - CTCAE Toxicity Grade
Safety Population

Laboratory Test (Unit)	Grade Criteria	Worst CTCAE Grade	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Baseline				
Number (%) of Patients			xxx (xx.x)	xxx (xx.x)
ALP (U/L)	1.25-2.5x ULN	Grade 1	xxx (xx.x)	xxx (xx.x)
	2.6-5.0x ULN	Grade 2	xxx (xx.x)	xxx (xx.x)
	5.1-10.0x ULN	Grade 3	xxx (xx.x)	xxx (xx.x)
	>10.0x ULN	Grade 4	xxx (xx.x)	xxx (xx.x)
		Grade 1-4	xxx (xx.x)	xxx (xx.x)
ALT (U/L)	1.25-2.5x ULN	Grade 1	xxx (xx.x)	xxx (xx.x)
	2.6-5.0x ULN	Grade 2	xxx (xx.x)	xxx (xx.x)
	5.1-10.0x ULN	Grade 3	xxx (xx.x)	xxx (xx.x)
	>10.0x ULN	Grade 4	xxx (xx.x)	xxx (xx.x)
		Grade 1-4	xxx (xx.x)	xxx (xx.x)
AST (U/L)	1.25-2.5x ULN	Grade 1	xxx (xx.x)	xxx (xx.x)
	2.6-5.0x ULN	Grade 2	xxx (xx.x)	xxx (xx.x)
	5.1-10.0x ULN	Grade 3	xxx (xx.x)	xxx (xx.x)
	>10.0x ULN	Grade 4	xxx (xx.x)	xxx (xx.x)
		Grade 1-4	xxx (xx.x)	xxx (xx.x)
Total bilirubin (mg/dL)	1.1-1.5x ULN	Grade 1	xxx (xx.x)	xxx (xx.x)
	1.6-2.5x ULN	Grade 2	xxx (xx.x)	xxx (xx.x)
	2.6-5.0x ULN	Grade 3	xxx (xx.x)	xxx (xx.x)
	>5.0x ULN	Grade 4	xxx (xx.x)	xxx (xx.x)
		Grade 1-4	xxx (xx.x)	xxx (xx.x)
[Continue for remaining post-baseline time points]				

ALP=alkaline phosphatase, ALT=alanine aminotransferase, AST=aspartate aminotransferase.
The percentages are based on patients with at least one laboratory value for that specific lab test at the corresponding visit.
Program Name: Date Generated: Page x of y

Table 14.3.4.8
Laboratory Abnormality
Safety Population

Laboratory Variable	Iclaprim (N = xxx) Baseline num/denom (%)	Vancomycin (N = xxx) Baseline num/denom (%)
Visit 2		
Laboratory category 1	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)
Parameter 1	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)
Parameter 2	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)
Parameter 3	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)
……	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)
Laboratory category 2	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)
Parameter 1	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)
Parameter 2	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)
Parameter 3	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)
……	xxx/xxx (xx.x%)	xxx/xxx (xx.x%)

<Continue with additional category and analysts and for remaining post-baseline visits>

CNS=clinically not significant, CS=clinically significant.
Note: The denominator (denom) represents the number of patients at baseline with normal or abnormal CNS laboratory assessment who also had at least one valid laboratory value after start of treatment. Patients with missing or abnormal CS values at baseline are not included in the denominator.
Note: The numerator (num) represents the number of patients with at least one abnormal CS laboratory assessment after the start of treatment who had a normal or abnormal CNS laboratory assessment at baseline.
Note: Unscheduled visits were also considered in the summary.
Program Name: Date Generated: Page x of y

Table 14.3.5.1
Summary of Vital Signs - Body Temperature (°C)
Safety Population

Study Visit	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
<Visit> Pre-dose		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
Change from Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
<Visit> Post-dose		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
Change from Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x

[Continue for remaining post-baseline time points]

Baseline values are defined as the last non-missing scheduled or unscheduled values collected prior to first dose of study drug.
Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.3.5.2 Summary of Vital Signs - Heart Rate (bmp) - Safety Population
  Delete:
    Footnote: Baseline values are defined as the last non-missing scheduled or unscheduled values collected prior to first dose of study drug.

Table 14.3.5.3 Summary of Vital Signs - Respiratory Rate (breaths/min) - Safety Population
  Delete:
    Footnote: Baseline values are defined as the last non-missing scheduled or unscheduled values collected prior to first dose of study drug.

Table 14.3.5.4 Summary of Vital Signs - Systolic Blood Pressure (mmHg) - Safety Population
  Delete:
    Footnote: Baseline values are defined as the last non-missing scheduled or unscheduled values collected prior to first dose of study drug.

Table 14.3.5.5 Summary of Vital Signs - Diastolic Blood Pressure (mmHg) - Safety Population
  Delete:
    Footnote: Baseline values are defined as the last non-missing scheduled or unscheduled values collected prior to first dose of study drug.

Table 14.3.6.1
Summary of ECG Measurements by Visit - heart rate
Safety Population

heart rate (bpm)

Study Visit	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
<Visit> Pre-dose		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
Change from Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
<Visit> Post-dose		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x
Change from Baseline		
n	xxx	xxx
Mean (SD)	xx.xx (x.xxx)	xx.xx (x.xxx)
Median	xx.x	xx.x
Min,Max	xx.x, xx.x	xx.x, xx.x

[Continue for remaining post-baseline time points]

Program Name: Date Generated: Page x of y

Repeat for the following displays:
Table 14.3.6.2 Summary of ECG Measurements by Visit - RR interval - Safety Population

Table 14.3.6.3 Summary of ECG Measurements by Visit - PR Interval - Safety Population

Table 14.3.6.4 Summary of ECG Measurements by Visit - QRS Interval - Safety Population

Table 14.3.6.5 Summary of ECG Measurements by Visit - QT Interval - Safety Population

Table 14.3.6.6 Summary of ECG Measurements by Visit - QTcB Interval - Safety Population

Table 14.3.6.7 Summary of ECG Measurements by Visit - QTcF Interval - Safety Population

Table 14.3.6.8
Summary of ECG Interpretations by Visit
Safety Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Baseline		
..N	xxx	xxx
Normal (N)	xxx (xx.x)	xxx (xx.x)
Abnormal Not Clinical Significant (ANCS)	xxx (xx.x)	xxx (xx.x)
Abnormal Clinical Significant (ACS)	xxx (xx.x)	xxx (xx.x)
<Visit>		
..N	xxx	xxx
Normal (N)	xxx (xx.x)	xxx (xx.x)
Abnormal Not Clinical Significant (ANCS)	xxx (xx.x)	xxx (xx.x)
Abnormal Clinical Significant (ACS)	xxx (xx.x)	xxx (xx.x)
< Repeat for all visits where ECG performed >		

The denominator for percentages is the number of patients with non-missing data in the Safety Population for each treatment group.
Note: N: Normal; ANCS: Abnormal, Not Clinically Significant; ACS: Abnormal, Clinically Significant
Program Name: Date Generated: Page x of y

Table 14.3.6.9
Summary of Marked QT/QTc Prolongation by Visit
Safety Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Baseline		
..n	xxx	xxx
Any marked QT/QTc prolongation	xxx (xx.x)	xxx (xx.x)
Visit 2		
..n	xxx	xxx
Any marked QT/QTc prolongation	xxx (xx.x)	xxx (xx.x)
ETP		
..n	xxx	xxx
Any marked QT/QTc prolongation	xxx (xx.x)	xxx (xx.x)

The marked QT/QTc prolongation is defined as median QTcF value >500 msec and/or >60 msec different from the pre-dose baseline value.
Program Name: Date Generated: Page x of y

Table 14.3.6.10
Summary of ECG QTc Interval Prolongation Evaluated Using Median QTcB, by Visit
Safety Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Baseline		
..n	xxx	xxx
Value > 450 ms	xxx (xx.x)	xxx (xx.x)
Value > 480 ms	xxx (xx.x)	xxx (xx.x)
Value > 500 ms	xxx (xx.x)	xxx (xx.x)
Visit 2		
..n	xxx	xxx
Value > 450 ms	xxx (xx.x)	xxx (xx.x)
Value > 480 ms	xxx (xx.x)	xxx (xx.x)
Value > 500 ms	xxx (xx.x)	xxx (xx.x)
Increase > 30 ms from baseline	xxx (xx.x)	xxx (xx.x)
Increase > 60 ms from baseline	xxx (xx.x)	xxx (xx.x)
ETP		
n		
Value > 450 ms	xxx (xx.x)	xxx (xx.x)
Value > 480 ms	xxx (xx.x)	xxx (xx.x)
Value > 500 ms	xxx (xx.x)	xxx (xx.x)
Increase > 30 ms from baseline	xxx (xx.x)	xxx (xx.x)
Increase > 60 ms from baseline	xxx (xx.x)	xxx (xx.x)

Program Name: Date Generated: Page x of y

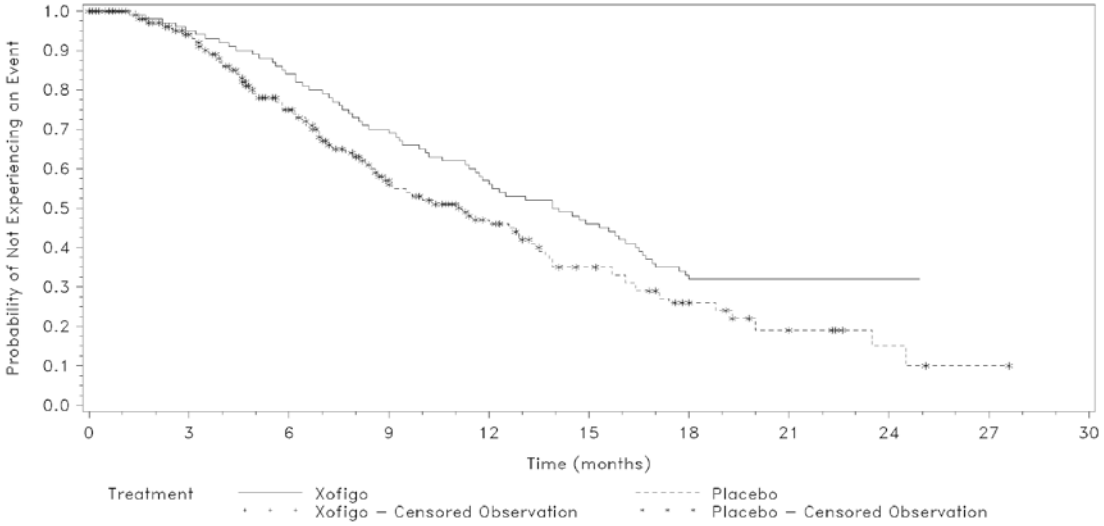
Table 14.3.6.11
Summary of ECG QTc Interval Prolongation Evaluated Using Median QTcF, by Visit
Safety Population

	Iclaprim (N = xxx) n (%)	Vancomycin (N = xxx) n (%)
Baseline		
..n	xxx	xxx
Value > 450 ms	xxx (xx.x)	xxx (xx.x)
Value > 480 ms	xxx (xx.x)	xxx (xx.x)
Value > 500 ms	xxx (xx.x)	xxx (xx.x)
Visit 2		
..n	xxx	xxx
Value > 450 ms	xxx (xx.x)	xxx (xx.x)
Value > 480 ms	xxx (xx.x)	xxx (xx.x)
Value > 500 ms	xxx (xx.x)	xxx (xx.x)
Increase > 30 ms from baseline	xxx (xx.x)	xxx (xx.x)
Increase > 60 ms from baseline	xxx (xx.x)	xxx (xx.x)
ETP		
n		
Value > 450 ms	xxx (xx.x)	xxx (xx.x)
Value > 480 ms	xxx (xx.x)	xxx (xx.x)
Value > 500 ms	xxx (xx.x)	xxx (xx.x)
Increase > 30 ms from baseline	xxx (xx.x)	xxx (xx.x)
Increase > 60 ms from baseline	xxx (xx.x)	xxx (xx.x)

Program Name: Date Generated: Page x of y

Figure 14.2.1.1
Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI
ITT Population

Tender to Palpitation



Number of subjects remaining under observation

Xofigo	541	450	329	207	115	69	28	14	3	0	0
Placebo	268	218	145	86	48	28	15	7	3	1	0

Programming Notes:
The y-axis will be ticked at every 0.1, and x-axis will be ticked at every 2 days. The y-axis label will be "Probability of Resolution of Tender to Palpitation", and x-axis label will be "Days Since First Dose". The two lines will represent "iclaprim" and "vancomycin" using solid line and dashed line respectively.
<Continue for other signs and symptoms of ABSSSI>

```
Program Name:                          Date Generated:                                    Page x of y
Repeat for the following displays:
```

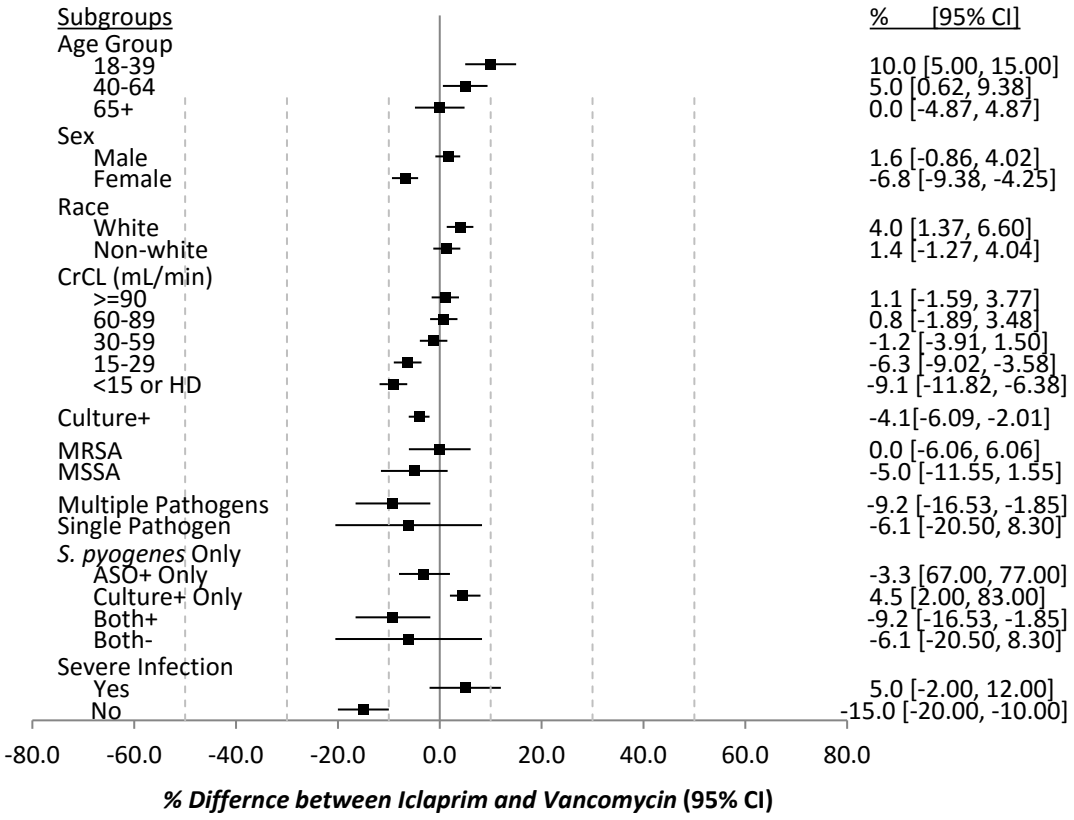
Figure 14.2.1.2 Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI - mITT Population
Add:
Note to Programmer: The y-axis will be ticked at every 0.1, and x-axis will be ticked at every 2 days. The y-axis label will be "Probability of Resolution of ", and x-axis label will be "Days Since First Dose". The two lines will represent "iclaprim" and "vancomycin" using solid line and dashed line respectively.
Delete:
Note to Programmer: The y-axis will be ticked at every 0.1, and x-axis will be ticked at every 2 days. The y-axis label will be "Probability of Resolution of Tender to Palpitation", and x-axis label will be "Days Since First Dose". The two lines will represent "iclaprim" and "vancomycin" using solid line and dashed line respectively.

Figure 14.2.1.3 Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI - mCE Population
Add:
Note to Programmer: The y-axis will be ticked at every 0.1, and x-axis will be ticked at every 2 days. The y-axis label will be "Probability of Resolution of ", and x-axis label will be "Days Since First Dose". The two lines will represent "iclaprim" and "vancomycin" using solid line and dashed line respectively.
Delete:
Note to Programmer: The y-axis will be ticked at every 0.1, and x-axis will be ticked at every 2 days. The y-axis label will be "Probability of Resolution of Tender to Palpitation", and x-axis label will be "Days Since First Dose". The two lines will represent "iclaprim" and "vancomycin" using solid line and dashed line respectively.

Figure 14.2.1.4 Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI - PP Population
Add:
Note to Programmer: The y-axis will be ticked at every 0.1, and x-axis will be ticked at every 2 days. The y-axis label will be "Probability of Resolution of ", and x-axis label will be "Days Since First Dose". The two lines will represent "iclaprim" and "vancomycin" using solid line and dashed line respectively.
Delete:
Note to Programmer: The y-axis will be ticked at every 0.1, and x-axis will be ticked at every 2 days. The y-axis label will be "Probability of Resolution of Tender to Palpitation", and x-axis label will be "Days Since First Dose". The two lines will represent "iclaprim" and "vancomycin" using solid line and dashed line respectively.

Figure 14.2.1.5 Kaplan-Meier Curves for Time to Resolution of Each Sign/Symptom of ABSSSI - mPP Population

Figure 14.2.2.1
Forest Plots for Subgroup Analysis of the Difference in Early Clinical Response Rate at ETP between Iclaprim and Vancomycin group
ITT Population



MRSA=Methicillin-resistant Staphylococcus aureus, MSSA=Methicillin-sensitive Staphylococcus aureus

Program Name: Date Generated: Page x of y
Repeat for the following displays:
Figure 14.2.2.2 Forest Plots for Subgroup Analysis of the Difference in Early Clinical Response Rate at ETP between Iclaprim and Vancomycin group - PP Population
Delete:
Footnote: MRSA=Methicillin-resistant Staphylococcus aureus, MSSA=Methicillin-sensitive Staphylococcus aureus

Figure 14.2.3.1 Forest Plots for Subgroup Analysis of the Difference in Clinical Cure Rate at TOC between Iclaprim and Vancomycin group - ITT Population
Delete:
Footnote: MRSA=Methicillin-resistant Staphylococcus aureus, MSSA=Methicillin-sensitive Staphylococcus aureus

Figure 14.2.3.2 Forest Plots for Subgroup Analysis of the Difference in Clinical Cure Rate at TOC between Iclaprim and Vancomycin group - PP Population
Delete:
Footnote: MRSA=Methicillin-resistant Staphylococcus aureus, MSSA=Methicillin-sensitive Staphylococcus aureus

Listing 16.2.1.1
Patients Enrolled
Enrolled Patients

Treatment: *Treatment 1*

Center	Patient	Date of Informed Consent	Primary Reason for Screen Failure
Xxxxxx	xxx	DDMMMYYYY	*Reason 1*
Xxxxxx	xxx	DDMMMYYYY	*Reason 2*
xxxxxx	xxx	DDMMMYYYY	

Programming Notes:
Repeat for all treatments. Sort by treatment, center and patient

Program Name: Date Generated: Page x of y

Listing 16.2.1.2
Patients Disposition
ITT Population

Treatment: *Treatment 1*

Center	Patient	Completed Study	Date of Discontinuation or Completion (Day)[a]	Primary Reason for Discontinuation/ Other, specify	If AE, Specify AE No.	If Protocol Violation, Specify	Gram-positive bacteremia?
xxxxxx	xxx	No	DDMMMYYYY (xx)	*Reason 1/*			Yes
Xxxxxx	xxx	No	DDMMMYYYY (xx)	*Other/ xxxxxxx*			No
xxxxxx	xxx	Yes	DDMMMYYYY (xx)				

[a] Relative to date of first dose of study treatment

Programming Notes:
Repeat for all treatments. Sort by treatment, center and patient
Variable "Completed Study"=Yes comes from 1st option of "Subject Status" on page "Disposition"

Program Name: Date Generated: Page x of y

Listing 16.2.1.3
End of Treatment
ITT Population

Treatment: *Treatment 1*

Center	Patient	Discontinuation of treatment?	Primary Reason for Discontinuation/ Other, specify	If AE, Specify AE No.	Date of First Dose (Day)[a]/ Date of Last Dose (Day)[a]	FU phone call agreed by Patient?
xxxxxx	xxx	Yes	*Reason 1/*		DDMMMYYYY (1)/ DDMMMYYYY (xx)	Yes
Xxxxxx	xxx	Yes	*Other/ xxxxxxx*		DDMMMYYYY (1)/ DDMMMYYYY (xx)	No
xxxxxx	xxx	No			DDMMMYYYY (1)/ DDMMMYYYY (xx)	Yes

LFU=Last Follow-up Visit.
[a] Relative to date of first dose of study treatment
Programming Notes:
Repeat for all treatments. Sort by center and patient
Program Name: Date Generated: Page x of y

Listing 16.2.2.1
Inclusion and Exclusion Criteria
All enrolled Patients

Treatment: *Treatment 1*

Center	Patient	Overall eligibility met?	If no, category of criterion	Identifier
Xxxxxx	xxx	Yes		
Xxxxxx	xxx	No	Inclusion	5, 6
xxxxxx	xxx	No	Exclusion	2, 3

Refer to Protocol for full descriptions of the Inclusion and Exclusion Criteria.
[a] Relative to the day of first dose of study treatment

Programming Notes:
Repeat for all treatments. Sort by treatment, center and patient

Program Name: Date Generated: Page x of y

Listing 16.2.2.2
Protocol Deviations
ITT Population

Treatment: *Treatment 1*

Center	Patient	Any Deviations?	Date	Deviation Category	Details of Deviation
xxxxxx	xxx	Yes	DDMMMYYYY	xxxxxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxx
		No			

Note: Deviations were identified and categorized prior to unblinding. Patients may have more than one violation leading to exclusion from ITT Population

Programming Notes:
Repeat for all treatments. Sort by treatment, center and patient

Program Name: Date Generated: Page x of y

Listing 16.2.3
Study Population
ITT Population

Treatment: T*reatment 1*

Center	Patient	Completed Treatment	Completed Study	ITT	mITT	PP	mPP	mCE	Safety
xxxxxx	xxx	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
		No	No	No	No	No	No	No	No

Programming Notes:
Repeat for all treatments. Sort by treatment, center and patient

Program Name: Date Generated: Page x of y

Listing 16.2.4.1
Demographics
ITT Population

Treatment: *Treatment 1*

Center	Patient	Date of Birth	Age (Years)	Sex	Race/ Other, specify	Ethnicity
xxxxxx	xxx	DDMMMYYYY	xx	Male	*Race1*	Ethnicity1
xxxxxx	xxx	DDMMMYYYY	xx	Female	*Race2* *Other/ xxxxx*	Ethnicity2

Programming Notes:
Repeat for all treatments. Sort by treatment, center and patient

Program Name: Date Generated: Page x of y

Listing 16.2.4.2
Baseline Characteristics
ITT Population

Treatment: *Treatment 1*

Center	Patient	Lesion Type	Gram-positive pathogen?	CrCL (mL/min)	Date of Randomization (Day)[a]	Randomization Number
xxxxxx	xxx	Wound infection	Yes		DDMMMYYYY (xx)	xxxxx

See SAP for definition of severe infection at baseline.
[a] Relative to the day of first dose of study treatment
Programming Notes:
Repeat for all treatments. Sort by treatment, center and patient
Program Name: Date Generated: Page x of y

Listing 16.2.4.3
Medical History
ITT Population

Treatment: *Treatment 1*

Center	Patient	System Organ Code (SOC)/ Preferred Term[a]	Verbatim	Start Date (Day[b])/ Stop Date (Day[b])	Ongoing?
xxxxxx	xxx	xxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxxxxx	xxxxxxxxxxxxxxx	DDMMMYYYY (xx)/ DDMMMYYYY (xx)	No
xxxxxx	xxx	xxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxxxxx	xxxxxxxxxxxxxxxx	DDMMMYYYY (xx)/	Yes
xxxxxx	xxx	None			

[a] MedDRA Dictionary (Version 18.1) was used for coding.
[b] Relative to the day of first dose of study treatment
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient, SOC and preferred term.
Program Name: Date Generated: Page x of y

Listing 16.2.4.4
Prior and Concomitant Medication
ITT Population

Treatment: *Treatment 1*

Center	Patient	CM No.	Therapeutic Class Chemical Subgroup Generic Term [a]	Prior/ Concomitant	Dose/Unit/ Frequency/ Route	Antibiotic?	Reason or Indication/ Other, specify	Start Date (day)[b]/ Stop Date (day)[b]/ Duration (days)
xx	xxx	xx	xxxxxxxxxx xxxxxxxxxxxxxx (xxxxxxxxxxxx)	Yes/ No	xx/units/ xx/ xx	Yes	xxxxxxxxxx/	DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx
xx	xxx	xx	xxxxxxxxxx xxxxxxxxxxxxxx (xxxxxxxxxxxx)	Yes/ Yes	xx/units/ xx/ xx	No	*Other/* *xxxxxxxxx*	DDMMMYYYY (xx)/ Ongoing
xx	xxx		None					

[a] WHO Drug Dictionary (Version WHODRUG Enhanced 201509, DDEB2) was used for coding.
[b] Relative to date of first dose of study treatment
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient, start date and drug class.
Program Name: Date Generated: Page x of y

Listing 16.2.5.1
Study Drug Administration
Safety Population

Treatment: *Treatment 1*

Center	Patient	Dose No.	Start Date Time (day)[a]/ Stop Date Time (day)[a]	Full dose infused?	If no, explain	Volume infused (mL)	Inpatient or Outpatient?
xxxxxx	xxx	xxx	DDMMMYYYY:HHMM (xx)/ DDMMMYYYY:HHMM (xx)	Yes		xxx	Inpatient
		xxx	DDMMMYYYY:HHMM (xx)/ DDMMMYYYY:HHMM (xx)	Yes		xxx	Outpatient

[a] Relative to date of first dose of study treatment
Programming Notes:
Repeat for all treatments. Sort by treatment, center and patient
Program Name: Date Generated: Page x of y

Listing 16.2.5.2
Overall Compliance
Safety Population

Treatment: *Treatment 1*

Center	Patient	Visit	Actual number of doses received	Planned number of doses	Total Compliance (%)	Duration of Exposure (days)
xxxxxx	xxx	ETP EOT TOC	xx	xx	xx.x	xx

...

% compliance for each patient is calculated as 100*Actual number of doses received / Planned number of doses

Programming Notes:

Repeat for all treatments. Sort by treatment, center and patient

Program Name: Date Generated: Page x of y

Listing 16.2.5.3
Population Pharmacokinetic
Safety Population

Treatment: *Treatment 1*

Center	Patient	Visit	PK Time Point	Was Sample Collected?	Date and Time of Collectin (Day)[a]
xxxxxx	xxx				DDMMMYYYY:HHMM (xx)

[a] Relative to the day of first dose of study treatment

Programming Notes:

Repeat for all treatments. Sort by treatment, center, patient and visit.

Program Name: Date Generated: Page x of y

Listing 16.2.6.1
Blood Culture Results
ITT Population

Treatment: *Treatment 1*

Center	Patient	Visit	Was a specimen obtained?/ If no, specify	Specimen No.	Specimen Type	Was culture performed?	If no, reason/ Other, specify	Did the culture grow an organism?	Accession No.	Was the organism a pathogen?	Pathogen Genus/ Species	Culture Agent	MIC Panel result (mg/mL)/ Interpre-tation
xxxxxx	xxx	Baseline	Yes	xxx	Aerobic blood	Yes		Yes	xx	Yes	xxxxxx/ xxxx	xxxxx	1/ Intermediate
		Visit 2	No/ *xxxxxx*										
		ETP				No	*Other/ xxxxx*						
		EOT											
. . .													

Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.
Program Name: Date Generated: Page x of y

Listing 16.2.6.2
Signs and Symptoms of ABSSSI
ITT Population

Treatment: *Treatment 1*

Center	Patient	Visit	Date of Assessment (day)[a]	TEN	ERY	EDE	PUR	FLUC	IND	ULC	NEC	LOC	SWL	CHL	FEV
xxxxxx	xxx	Baseline	DDMMMYYYY (xx)												
		Visit 2	DDMMMYYYY (xx)												
		ETP	DDMMMYYYY (xx)												
		Visit 4	DDMMMYYYY (xx)												
		EOT	DDMMMYYYY (xx)												
		TOC	DDMMMYYYY (xx)												

. . .

TEN=Tender to palpitation, ERY=Erythema, EDE=Edema, PUR=Purulent drainage/ discharge, FLUC=Fluctuance, IND=Induration, ULC=Ulceration, NEC=Necrotic tissue, LOC=Localized pain, SWL=Swelling, CHL=Chills, FEV=Fever.
[a] Relative to the day of first dose of study treatment
Programming Notes:
Repeat for all treatments. Sort by treatment, center and patient
Program Name: Date Generated: Page x of y

Listing 16.2.6.3
Clinical Efficacy Assessment
ITT Population

Treatment: *Treatment 1*

Center	Patient	Visit	Date of Assessment (day) [a]	Total lesion size (cm^2)	Change of lesion size from baseline	>=20% reduction in lesion size at ETP	>=90% reduction in lesion size at TOC	Clinical outcome at TOC
xxxxxx	xxx	Baseline	DDMMMYYYY (xx)	xx.x		NA	NA	NA
		ETP	DDMMMYYYY (xx)	xx.x	xx.x	Yes	NA	NA
		EOT	DDMMMYYYY (xx)	xx.x	xx.x	NA	NA	NA
		TOC	DDMMMYYYY (xx)	xx.x	xx.x	NA	Yes	Cure

...

[a] Relative to the day of first dose of study treatment

Programming Notes:

Programming notes: Repeat for all treatments. Sort by treatment, center, patient and visit.

Program Name: Date Generated: Page x of y

Listing 16.2.6.4.1
Microbiological Assessment - Patient Level
ITT Population

Treatment: *Treatment 1*

Center	Patient	Visit	Bacteriological Response
xxxxxx	xxx	ETP	xxxxxxx
		EOT	xxxxxxx
		TOC	xxxxxxx
xxxxxx	xxx	ETP	xxxxxxx
		EOT	xxxxxxx
		TOC	xxxxxxx

Programming Notes:
Programming notes: Repeat for all treatments. Sort by treatment, center, patient and visit.

Program Name: Date Generated: Page x of y

Listing 16.2.6.4.2
Microbiological Assessment - Pathogen Level
ITT Population

Treatment: T*reatment 1*

Center	Patient	Visit	Pathogen	Bacteriological Response
xxxxxx	xxx	ETP	*pathogen 1*	xxxxxx
			pathogen 2	xxxxxx
			...	
		EOT	*pathogen 1*	xxxxxx
			pathogen 2	xxxxxx
			...	
		TOC	*pathogen 1*	xxxxxx
			pathogen 2	xxxxxx
			...	
xxxxxx	xxx	...		

Programming Notes:
Programming notes: Repeat for all treatments. Sort by treatment, center, patient and visit.

Program Name: Date Generated: Page x of y

Listing 16.2.6.5
Microbiological Assessment of Primary Infection Site - Gram Stain Results
ITT Population

Treatment: *Treatment 1*

Center	Patient	Specimen No.	Date of Collection (day)[a]	Method of Collection	Result of Gram Stain
xxxxxx	xxx	xx	DDMMMYYYY (xx)	xxxxxxx	xxxxxx
					xxxxxx
			DDMMMYYYY (xx)	xxxxxxx	xxxxxx
					xxxxxx
			DDMMMYYYY (xx)	xxxxxxx	Not Done
...					

[a] Relative to the day of first dose of study treatment

Programming Notes:

Programming notes: Repeat for all treatments. Sort by treatment, center, patient and visit.

Program Name: Date Generated: Page x of y

Listing 16.2.6.6
Significant Surgical Procedures
ITT Population

Treatment: *Treatment 1*

Center	Patient	Visit	Procedure No.	Significant Procedure	Other, specify	Date performed (day)[a]	Does the need of procedure reflect failure of antimicrobial therapy?
xxxxxx	xxx	Visit 2	xx	Debridement		DDMMMYYYY (xx)	No
		ETP	xx	No procedure			
		Visit 4	xx	...			
		EOT	xx				
		TOC	xx				
xxxxxx	xxx						
. . .							

[a] Relative to the day of first dose of study treatment

Programming Notes:

Programming notes: Repeat for all treatments. Sort by treatment, center, patient and visit.

Program Name: Date Generated: Page x of y

Listing 16.2.6.7
Death
ITT Population

Treatment: *treatment 1*

Center	Patient	Date of final contact (day)[a]	Date of death (day)[a]	Cause of death	Death within 28 days of first dose
xxxxxx	xxx	DDMMMYYYY (xx)	DDMMMYYYY (xx)	xxxxxxx	Yes
xxxxxx	xxx	DDMMMYYYY (xx)	DDMMMYYYY (xx)	xxxxxxx	No

[a] Relative to the day of first dose of study treatment

Program Name: Date Generated: Page x of y

Listing 16.2.6.8.1
Unblinding
ITT Population

Treatment: *treatment 1*

Center	Patient	Date and time of unblinding (day)[a]	Reason of unblinding/ Other, specify	Unblinded by/ Other, specify
xxxxxx	xxx	DDMMMYYYY:HHMM (xx)	*xxxxxxx/* xxxxxx	xxxxxx/ xxxxxxx
xxxxxx	xxx	DDMMMYYYY:HHMM (xx)	*Xxxxxxx/* xxxxxxxx	xxxxxx/ xxxxxxx

[a] Relative to the day of first dose of study treatment

Program Name: Date Generated: Page x of y

Listing 16.2.6.8.2
Unblinding Dose
ITT Population

Treatment: *treatment 1*

Center	Patient	Dose No.	Date and Time prepared (Day)[a]	Dosage prepared (mg)	Reason for dose adjustment
xxxxxx	xxx	xx	DDMMMYYYY:HHMM (xx)	xxx.x	xxxxxxx
		xx	DDMMMYYYY:HHMM (xx)	xxx.x	xxxxxxx
...					

[a] Relative to the day of first dose of study treatment

Program Name: Date Generated: Page x of y

Listing 16.2.7
Adverse Events
Safety Population

Treatment: *Treatment 1*

Center	Patient	AE No.	System Organ Class/ Preferred Term/ Verbatim [a]	Onset Date (day)[b]/ End Date (day)[b]/ Duration (days)	Treatment emergent?/ Severity/ SAE?	Relationship to Study Drug/ ADR?	Treatment required?	Action Taken[c]	Outcome
xxxxxx	xxx	xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxx	DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx	Yes/ Mild	Not related/ No	Yes	xxx	Completely recovered
			xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxx	DDMMMYYYY (xx)/ DDMMMYYYY (xx)/ xx	Moderate	Probably not related/ No	No	xxxx	Death
xxxxxx	xxx	xx	xxxxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxxx/ xxxxxxxxxxxxxx	DDMMMYYYY (xx)/ Ongoing	Severe	Probably related/ Yes	Yes	xxxx	Ongoing
						Related/ Yes	Yes	xxx	Recovered to stability

[a] Coded using MedDRA Dictionary (Version 18.1)
[b] Relative to the day of first dose of study treatment
[c] Action Taken: xxx = xxxxxxx; xxxx = xxxxxx xxxx; xxxx = xxxx xxxxxxxxxx; xxxxx = xxxx xxxxxxx xxxxxxx.
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient, start date and SOC.
Program Name: Date Generated: Page x of y

Listing 16.2.8.1
Laboratory Findings in Local Labs at Baseline - Hematology
Safety Population

Treatment: *Treatment 1*

Center	Patient	Age (years)/ Gender	Test	Visit	Collection Date Time (day) [a]	Result	Units	Normal Range	Out of Range [b]	Clinical Significance [b]
xx	xxx	xx/ Male	Hematocrit	Baseline	DDMMMYYYY HH:MM (xx)	xxx.xxx	xxx	xxx – xxx	H	CS

. . .

[a] Relative to the day of first dose of study treatment
Note: Baseline is defined as the last scheduled or unscheduled value obtained prior to the first dose of treatment
[b] B = Baseline; H = Above upper limit of normal; L = Below lower limit of normal;
* = Unscheduled value, not included in summary tables if post-dose.
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.
Include all Hematology tests (including C-reactive protein and LFT)
Program Name: Date Generated: Page x of y

Listing 16.2.8.2
Laboratory Findings in Local Labs at Baseline - Chemistry
Safety Population

Treatment: *Treatment 1*

Center	Patient	Age (years)/ Gender	Test	Visit	Collection Date Time (day) [a]	Result	Units	Normal Range	Out of Range [b]	Clinical Significance [b]
xx	xxx	xx/ Male	Albumin	Baseline	DDMMMYYYY HH:MM (xx)	xxx.xxx	xxx	xxx – xxx	H	CS

. . .

[a] Relative to the day of first dose of study treatment
Note: Baseline is defined as the last scheduled or unscheduled value obtained prior to the first dose of treatment
[b] B = Baseline; H = Above upper limit of normal; L = Below lower limit of normal;
* = Unscheduled value, not included in summary tables if post-dose.
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.
Include all Clinical Chemistry tests and creatinine clearance
Program Name: Date Generated: Page x of y

Listing 16.2.8.3
Laboratory Findings in Local Labs at Baseline - Urinalysis
Safety Population

Treatment: *Treatment 1*

Center	Patient	Age (years)/ Gender	Test	Visit	Collection Date Time (day) [a]	Result	Units	Normal Range	Out of Range [b]	Clinical Significance [b]
xx	xxx	xx/ Male	pH	Baseline	DDMMMYYYY HH:MM (xx)	xxx.xxx	xxx	xxx – xxx	H	CS

. . .

[a] Relative to the day of first dose of study treatment
Note: Baseline is defined as the last scheduled or unscheduled value obtained prior to the first dose of treatment
[b] B = Baseline; H = Above upper limit of normal; L = Below lower limit of normal;
* = Unscheduled value, not included in summary tables if post-dose.
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.
Include all Urinalysis tests
Program Name: Date Generated: Page x of y

Listing 16.2.8.4
Laboratory Findings in Central Labs by Visit - Hematology
Safety Population

Treatment: *Treatment 1*

Center	Patient	Age (years)/ Gender	Test	Visit	Collection Date Time (day) [a]	Result	SI Units	Normal Range	Out of Range [b]	Clinical Significance [b]
xxxxxx	xxx	xx/ Male	Hematocrit	Baseline	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx - xxx	H	CS
				ETP	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx - xxx	L	NCS
				Visit 4	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx - xxx	L	NCS
				EOT	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx - xxx	L	NCS
				TOC	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx - xxx	L	NCS

. . .

[a] Relative to the day of first dose of study treatment
Note: Baseline is defined as the last scheduled or unscheduled value obtained prior to the first dose of treatment
[b] B = Baseline; H = Above upper limit of normal; L = Below lower limit of normal;
* = Unscheduled value, not included in summary tables if post-dose.
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.
Include all Hematology tests (including C-reactive protein and LFT)
Program Name: Date Generated: Page x of y

Listing 16.2.8.5
Laboratory Findings in Central Labs by Visit - Chemistry
Safety Population

Treatment: *Treatment 1*

Center	Patient	Age (years)/ Gender	Test	Visit	Collection Date Time (day) [a]	Result	SI Units	Normal Range	Out of Range [b]	Clinical Significance [b]
xxxxxx	xxx	xx/ Male	Albumin	Baseline	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	H	CS
				ETP	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	L	NCS
				Visit 4	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	L	NCS
				EOT	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	L	NCS
				TOC	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	L	NCS

. . .

[a] Relative to the day of first dose of study treatment
Note: Baseline is defined as the last scheduled or unscheduled value obtained prior to the first dose of treatment
[b] B = Baseline; H = Above upper limit of normal; L = Below lower limit of normal;
* = Unscheduled value, not included in summary tables if post-dose.
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.
Include all Clinical Chemistry tests
Program Name: Date Generated: Page x of y

Listing 16.2.8.6
Laboratory Findings in Central Labs by Visit - Urinalysis
Safety Population

Treatment: *Treatment 1*

Center	Patient	Age (years)/ Gender	Test	Visit	Collection Date Time (day) [a]	Result	SI Units	Normal Range	Out of Range [b]	Clinical Significance [b]
xxxxxx	xxx	xx/ Male	pH	Baseline	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	H	CS
				ETP	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	L	NCS
				Visit 4	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	L	NCS
				EOT	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	L	NCS
				TOC	DDMMMYYYY:HHMM (xx)	xxx.xxx	xxx	xxx – xxx	L	NCS

. . .

[a] Relative to the day of first dose of study treatment
Note: Baseline is defined as the last scheduled or unscheduled value obtained prior to the first dose of treatment
[b] B = Baseline; H = Above upper limit of normal; L = Below lower limit of normal;
* = Unscheduled value, not included in summary tables if post-dose.
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.
Include all Urinalysis tests
Program Name: Date Generated: Page x of y

Listing 16.2.9
Vital Signs
Safety Population

Treatment: *Treatment 1*

Center	Patient	Visit	Vital Signs	Values
xxxxxx	xxx	Baseline	Systolic BP (mm Hg)	Not Done
			Diastolic BP (mm Hg)	Not Done
			Heart Rate (beat/min)	xx
			Respiration (breaths/min)	xx
			Body Temperature (°C)	xx.x
			Height (cm)	xxx.x
			Weight (kg)	xx.x
			BMI (kg/m^2)	xx.x
<Continue for remaining post-baseline time points>				
xxxxxx	xxx			
...				

Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.

Listing 16.2.10.1
ECG Results
Safety Population

Treatment: *Treatment 1*

Center	Patient	Visit	Assessment Date (day)[a]	ECG Measurements	Units	Values	Interpretation
xxxxxx	xxx	Baseline	DDMMMYYYY (xx)	Median Heart Rate	beats/min	xxx	
				Median RR Interval	msec	Not Done	
				Median PR Interval	msec	xxx	
				Median QRS Duration	msec	xxx	
				Median QT Interval	msec	xxx	
				Median QTcB [b] Interval	msec	xxx	
				Median QTcF [b] Interval	msec	xxx	

<Continue for remaining post-baseline time points>

xxxxxx xxx

...

[a] Relative to the day of first dose of study treatment
[b] QTcB = Bazett corrected QT interval; QTcF = Fridericia corrected QT interval.
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.
Program Name: Date Generated: Page x of y

Listing 16.2.10.2
ECG Assessment
Safety Population

Treatment: *Treatment 1*

Center	Patient	Visit	Assessment Date (day) [a]	Clinical significance [b]	Marked QT/QTc prolongation [c]	Comments
xxxxxx	xxx	Baseline	DDMMMYYYY (xx)	Normal		
				Abnormal, NCS	Yes	xxxxxxxxxxxxxxxx
				Abnormal, CS		xxxxxxxxxxxxxxxx
xxxxxx	xxx			Not Done		

[a] Relative to the day of first dose of study treatment
[b] NCS=not clinically significant, CS=clinically significant.
[c] marked QT/QTc prolongation is defined as median QTcF value >500 msec and/or >60 msec different from the pre-dose baseline value.
Programming Notes:
Repeat for all treatments. Sort by treatment, center, patient and visit.
Program Name: Date Generated: Page x of y

Listing 16.2.11
Physical Examination Results
Safety Population

Treatment: *Treatment 1*

Center	Patient	Visit	Assessment Date (day) [a]	Any PE performed?	Body System	Examined?	Reason for no PE exam/ Other, specify	Overall Results
xxxxxx	xxx	Baseline	DDMMMYYYY (xx)	Yes	Cardiovascular	Yes	*Xxxxxx/*	Abnormal
					Respiratory	No		
					Gastrointestinal	Yes		
					Skin (other than primary site of infection)	Yes		
					Musculoskeletal	Yes		
					Endocrine	Yes		
					Neurological	Yes		
					HEENT	Yes		
					Genitourinary	Yes		
		Visit 2						
		. . .						

[a] Relative to the day of first dose of study treatment

Programming Notes:

Repeat for all treatments. Sort by treatment, center, patient and visit. Only present abnormal body systems. If all body systems are normal at a visit, output "None" in Body System Abnormalities column for the visit.

Program Name: Date Generated: Page x of y

TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145670
Client Protocol No.:	ICL-24-ABSSSI2	**Meaningful Date (*for eTMF only):***	2 October 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan – SAP	**Artifact No:**	01.1.31
Topic :	Pre-unblinding decisions on efficacy analyses		

Description:

This Note to File documents pre-database lock decisions on handling efficacy endpoints with regard to the additional rule in selecting clinical response (Cure, Non-cure) and hard-coding of a patient.

Changes from blinded review of 28 September 2017 are detailed in the attached patient profiles, one for antibiotics of cure patients, one for surgical procedures of cure patients, one for antibiotics of indeterminate/failure patients, and one for surgical procedures of indeterminate/failure patients along with clinical outcome at TOC (without lesion):

- Copy of Motif2_Antibiotics_CLONITOC_Indeterminate_Failure_28Sep2017_PM 28Sep17 dh.xlsx,
- Copy of Motif2_Procedures_CLONITOC_Indterminate_Failure_28Sep2017_PM 28Sep17 dh.xlsx;
- Copy of Motif2_Antibiotics_CLONITOC_Cure_28Sep2017_PM 28Sep17 dh.xlsx.

Columns I to N are those criteria used to derive clinical outcome in the antibiotics spreadsheet.
The clinical outcome has used the most current updated rules from Revive 1 (new added failure rules from Revive 1 NTF).

As a result of the medical review of Copy of Motif2_Antibiotics_CLONITOC_Cure_28Sep2017_PM 28Sep17 dh.xlsx, the criteria for determining efficacy response were refined for programming.

- Cure to Indeterminate: If subject received more than one dose of a short acting (i.e., q12h dosing or less) systemic antibiotic(s) active against Gram-positive pathogens (Appendix F) within the last 7 days, unless there is documented evidence of treatment failure OR demonstrated resistance of Gram-positive pathogens to the prior antibiotic therapy (antibiotics given for surgical prophylqxis are not included in this), the subject should be categorized as non-cure (see exclusion criteria 6 page 34 of the protocol). Given that the antibiotics are given before study drug, they should be categorized as non-cure (indeterminate).

- The above rule is complex to implement in programming so a list of subjects who took more than 1 short acting antibiotics within 7 days of randomization was reviewed by Covance medical monitor who determined the patients that would follow the above rule. We used the list in a spreadsheet format to implement Clinical outcome of seleted subjects in programming ADEFF dataset. This process is similar to hardcoding, and the subjects that are changed to 'Indeterminate' are:

TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145670
Client Protocol No.:	ICL-24-ABSSSI2	**Meaningful Date (*for eTMF only):***	2 October 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan – SAP	**Artifact No:**	01.1.31
Topic :	Pre-unblinding decisions on efficacy analyses		

201001135, 201003009, 201003011, 201008010, 234004002, 236006002, 243006011, 243006012, 243006016, 246002021, 246002024, 246002028, 246003017, 254009001, 254009003.

- Additionally, for the draft topline of 2 October 2017, Covance performed a hard coding for subject 234003001 (the one with indication=Hand lesion which is not the index of infection). Covance medical monitor suggested adding 'secondary' to the Primary_secondary spreadsheet, but the programs on both production and QC side still does not output it to Indeterminate, so Covance programmatically pulled hand-lesion indication in order to output it as Indeterminate. This will be updated to not hardcode for final topline by having the Covance medical monitor update the spread sheet with non-infection indications.

Documents affected:

- SAP: Added condition for the response for Indeterminate: If subject received more than one dose of a short acting (i.e., q12h dosing or less) systemic antibiotic(s) active against Gram-positive pathogens (Appendix F) within the last 7 days, unless there is documented evidence of treatment failure OR demonstrated resistance of Gram-positive pathogens to the prior antibiotic therapy (antibiotics given for surgical prophylqxis are not included in this), the subject should be categorized as non-cure (see exclusion criteria 6 page 34 of the protocol). Given that the antibiotics are given before study drug, they should be categorized as non-cure (indeterminate).
- EDC database: Not affected.
- Analysis dataset specification: ADEFF specification will be updated to reflect the above rule. ADEFF will be affected as stated above.
- TFL: Draft Top-line TFL

- Encl: Spreadsheet for determining Indeterminate and Failure responses: Copy of Motif2_Antibiotics_CLONITOC_Cure_28Sep2017_PM 28Sep17 dh.xlsx.

TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145670
Client Protocol No.:	ICL-24-ABSSSI2	**Meaningful Date (*for eTMF only):***	2 October 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan – SAP	**Artifact No:**	01.1.31
Topic :	Pre-unblinding decisions on efficacy analyses		

Note to File approved by:

Signature — 2 October 2017 (Date)

David Huang, MD, PhD, FACP, FIDSA / Chief Medical Officer
Printed Name/Title

Note to File completed by:

Toyoko Oguri
Typed Name — 2 October 2017 (Date)

Senior Manager, Biostatistics and Statistical Programming
Title

Instructions:

This TMF File Note should only be used to document situations that do not fall under the current CDS procedures for documenting deviations, issues and/or complaints.

The investigator name and site number should match CTMS.

For eTMF studies, when a NTF is written to clarify or support an artifact filed in eTMF, the NTF is uploaded with the same artifact name and meaningful date as the artifact the NTF was written to clarify. In eTMF, if a NTF was written to clarify a process or provide supportive information and is filed at the Trial, Country or Site level, the artifact is filed at the NTF artifact location and the meaningful date is the date of the NTF.

Complete each section. If a section does not apply, write "N/A".

TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145670
Client Protocol No.:	ICL-24-ABSSSI2	**Meaningful Date (*for eTMF only):***	6 October 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan – SAP	**Artifact No:**	01.1.31
Topic :	Post-unblinding decisions on efficacy analyses		

Description:

This Note to File documents post-database lock decisions on programmatically handling efficacy endpoints with regard to (1) the procedure "dressing change" not to be considered a significant surgical procedure, per the protocol; and (2) hard-coding of a patient.

1. Procedures that were checked as significant in EDC (thus picked as Failure of antimicrobial therapy) should have been considered as routine procedure, specifically dressing change. The procedure "DRESSING CHANGE" should not be considered a significant procedure and thus patients with such a procedure should not be considered as Clinical Failure as long as there are no other criteria prohibiting such patients from being a Cure. Such cases were revised programmatically.
2. Failure to Indeterminate : Patient 240006002 – Covance medical expert confirmed that this patient outcome should be Indeterminate. It was recommend to hard code for this subject. This will be applied to all Clinical Outcome parameters including clinical outcome with lesion size.

1) SAP: Add condition to procedure of DRESSING CHANGE as not a significant procedure.
2) EDC database: Not affected.
3) Analysis dataset specification: ADEFF specification will be updated to reflect the above rule.
4) TFL: Final Top-line TFL

5) Encl: none.

TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145670
Client Protocol No.:	ICL-24-ABSSSI2	**Meaningful Date (*for eTMF only):***	6 October 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan – SAP	**Artifact No:**	01.1.31
Topic :	Post-unblinding decisions on efficacy analyses		

Note to File approved by:

Signature — Date: 10/6/2017

David Huang, MD, PhD, FACP, FIDSA / Chief Medical Officer
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Complete each section. If a section does not apply, write "N/A".

TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145670
Client Protocol No.:	ICL-24-ABSSSI2	**Meaningful Date (*for eTMF only):***	6 October 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan – SAP	**Artifact No:**	01.1.31
Topic :	Post-unblinding decisions on efficacy analyses		

Description:

This Note to File documents decisions on programmatically handling efficacy endpoints with regard to (1) the procedure "dressing change" not to be considered a significant surgical procedure, per the protocol; and (2) hard-coding of a patient. These decisions were made after review of patient data in a blinded fashion after the database was locked and randomization codes were applied. The patient data did not have any treatment identifying information.

1. Procedures that were checked as significant in EDC (thus picked as Failure of antimicrobial therapy) should have been considered as routine procedure, specifically dressing change. The procedure "DRESSING CHANGE" should not be considered a significant procedure and thus patients with such a procedure should not be considered as Clinical Failure as long as there are no other criteria prohibiting such patients from being a Cure. Such cases were revised programmatically.
2. Failure to Indeterminate : Patient 240006002 – Covance medical expert confirmed that this patient outcome should be Indeterminate. It was recommend to hard code for this subject. This will be applied to all Clinical Outcome parameters including clinical outcome with lesion size.

1) SAP: Add condition to procedure of DRESSING CHANGE as not a significant procedure.
2) EDC database: Not affected.
3) Analysis dataset specification: ADEFF specification will be updated to reflect the above rule.
4) TFL: Final Top-line TFL

5) Encl: none.

TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145670
Client Protocol No.:	ICL-24-ABSSSI2	**Meaningful Date (*for eTMF only):***	6 October 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan – SAP	**Artifact No:**	01.1.31
Topic :	Post-unblinding decisions on efficacy analyses		

Note to File approved by:

Signature — Date: 10/6/2017

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Instructions:

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Complete each section. If a section does not apply, write "N/A".

TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145416
Client Protocol No.:	ICL-23-ABSSSI1	**Meaningful Date (*for eTMF only):***	2 Dec 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan - SAP	**Artifact No:**	01.1.31
Topic :	Hard coding of mITT population for sensitivity analysis		

Description: This Note to File contains addition of mITT for Sensitivity Analysis population resulting in 3 additional subjects to be included in the original Microbiological intent-to-treat (mITT) population.

The mITT for Sensitivity Analyis consists of patients meeting mITT criteria who had Gram+ baseline pathogen identified in infection site or blood culture.

Subjects 101011133, 101011137 and 137003010 are included in mITT population based on clinical assessment review by Covance medical monitor and sponsor medical expert of blood culture for sensitivity analysis.

USUBJID	Blood_Culture_Visit	Blood_Culture_Baseline_Flag	Infection_Culture1	Infection_Culture2	Conclusion	Motif Comment
ICL-23-ABSSSI1-101011133	VISIT 4.2				questionable	Add
ICL-23-ABSSSI1-101011133	VISIT 4.2					
ICL-23-ABSSSI1-101011137	VISIT 3					Add
ICL-23-ABSSSI1-101011137	VISIT 1	Y				
ICL-23-ABSSSI1-137003010	VISIT 1	Y			consider adding	Add

Note to File approved by:

Signature — December 4, 2017 (Date)

David Huang, MD, PhD, FACP, FIDSA / Chief Medical Officer, Motif BioSciences, Inc
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Note to File completed by:

Toyoko Oguri
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Senior Manager, Biostatistics
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TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145416
Client Protocol No.:	ICL-23-ABSSSI1	**Meaningful Date (*for eTMF only*):**	2 Dec 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan - SAP	**Artifact No:**	01.1.31
Topic :	Hard coding of mITT population for sensitivity analysis		

Note to File completed by:

Toyoko Oguri Toyoko Oguri 4 Dec 2017

Typed Name Date

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Title

TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145416
Client Protocol No.:	ICL-23-ABSSSI1	**Meaningful Date (*for eTMF only):***	8 Dec 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan - SAP	**Artifact No:**	01.1.31
Topic :	Define microbiological Per-Protocol Population and recurrent infection		

Description: This Note to File clarifies the definition of microbiological Per-Protocol population (mPP) population in the protocol and the SAP and the definition of bacteriological response of recurrent infection.

The mPP definition from the protocol and SAP was:

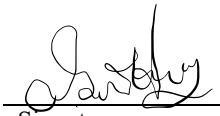
> All mITT patients who receive at least 80% of their planned doses and provide adequate data for assessment for each of the following time points: ETP, EOT, and TOC.

The mPP definition is clarified to include the criteria for the PP population:

> All PP patients who have a Gram-positive baseline bacteria pathogen identified as the cause of ABSSSI.

In addition, the microbiological response definition in the SAP for recurrent infection is clarified to be defined as: A pathogen that is same as the baseline pathogen isolated only after the EOT visit outcome was cure and was either eradication or presumed eradication. This was correctly programmed in the tables as defined.

Note to File approved by:



Signature — December 8, 2017 (Date)

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Note to File completed by:

Toyoko Oguri

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Senior Manager, Biostatistics

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TMF File Note

Client Name:	Motif BioSciences	**Covance Study ID :**	000000145416
Client Protocol No.:	ICL-23-ABSSSI1	**Meaningful Date (*for eTMF only*):**	8 Dec 2017
Investigator Name	NA	**Site No.:**	NA
Artifact Name:	Plan - SAP	**Artifact No:**	01.1.31
Topic :	Define microbiological Per-Protocol Population and recurrent infection		

Description: This Note to File clarifies the definition of microbiological Per-Protocol population (mPP) population in the protocol and the SAP and the definition of bacteriological response of recurrent infection.

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Note to File approved by:

Signature — Date

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Toyoko Oguri — 8 Dec 2017
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