Statistical Analysis Plan (SAP)

SPECTRUM: A Prospective Observational Registry Study to Characterise Normal Conditions of Use, Dosing and Safety Following Administration of Vernakalant IV Sterile Concentrate

Post-Authorisation Safety Study (PASS)

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ABBREVIATIONS

AA	Antiarrhythmics
ACS	Acute coronary syndrome
AE	Adverse Event
AF	Atrial Fibrillation
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System.
BP	Blood Pressure
bpm	Beats per Minute
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence interval
CRO	Clinical Research Organisation
EC	Ethics Committee
ECV	Electrical Cardioversion
eCRF	Electronic Case Report Form
eGFR	Estimated Glomerular Filtration Rate
EMA	European Medicines Agency
ESC	European Society of Cardiology
EU	European Union
GFR	Glomerular Filtration Rate
HLT	High Level Term
HOI	Health Outcome of Interest
ICD	Implantable cardioverter-defibrillator
IV	Intravenous
LVEF	Left Ventricular Ejection Fraction
MDRD	Modification of Diet and Renal Disease
MedDRA	Medical Dictionary for Regulatory Activities
MI	Myocardial Infarction
NSAE	Non-serious Adverse Experience
NYHA	New York Heart Association
PASS	Post-Authorisation Safety Study
PSUR	Periodic Safety Update Report
PT	Preferred Term
SADR	Serious Adverse Reaction
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
Scr	Serum creatinine
SmPC	Summary of Product Characteristics

SMQ	Standardized MedDRA Query
SQQ	Site Qualification Questionnaire
SRC	Safety Review Committee
SOC	System Organ Class
TB	Total Bilirubin
ULN	Upper limit of normal
VT	Ventricular Tachycardia

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1. OVERVIEW OF STUDY DESIGN

This is an observational single-exposure cohort PASS (no study intervention or mandated procedures) of patients administered vernakalant intravenous (IV) within clinical sites across European Union (EU) member countries. Participating countries include Denmark, Sweden, Germany, Austria, Spain and Finland. Patients enrolled in the study received vernakalant IV at the discretion of their physicians and were followed for 24 hours after the last vernakalant IV infusion or until discharge/end of medical encounter, whichever occurred first, for health outcomes of interest (HOIs) and serious adverse events (SAEs). No follow-up visits or examinations, laboratory tests, or procedures are mandated as part of this study.

2 OBJECTIVES

2.1 Primary Objectives

The primary objectives of the study are to:

1. Estimate the incidence of the following medically significant HOIs reported during treatment and during the first 24 hours after last infusion of vernakalant IV or until discharge/end of medical encounter, whichever occurs earlier: significant hypotension, significant ventricular arrhythmia (sustained ventricular tachycardia (VT), Torsades de Pointes, ventricular fibrillation), significant atrial flutter, and significant bradycardia.

2. In order to investigate the potential risk of overdose and medication error, describe vernakalant IV administration/dosing by summarising patient body weight, total dose with each intravenous (IV) infusion, and length of time for each IV infusion.

3. To evaluate the effectiveness of the risk minimisation activities by:

- Describing the appropriateness of selection of patients for treatment with vernakalant IV, monitoring of patients during and after vernakalant IV administration, and use of anti-arrhythmics before and after vernakalant IV, as consistent with the label and risk minimisation activities (health provider educational card).
- Monitoring for the occurrence and incidence SAEs and HOIs to review with the EU Regulatory Agency with respect to risk minimisation activities.

2.2 Secondary Objectives

The secondary objectives of the study are to:

1. Summarise the count and rate of all SAEs for HOIs that may not meet the definitions of medically significant HOIs, as well as all other SAEs reported during treatment and during the first 24 hours after the last infusion of vernakalant IV or until discharge/end of medical encounter, whichever occurs earlier.

2. Characterise patients administered vernakalant IV in terms of patient demographics, medical history, and presenting conditions. Specific conditions to be summarised include:

- Heart failure, New York Heart Association (NYHA) functional class
- Prolonged QT, severe bradycardia, sinus node dysfunction, second or third degree heart block, clinically meaningful valvular stenosis, hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy, constrictive pericarditis
- History of hyperthyroidism
- Severe aortic stenosis, low systolic blood pressure (BP)
- Recent acute coronary syndrome (including myocardial infarction [MI])
- Presence of pacemaker/year of implantation
- Hepatic impairment

3. Document the administration of concomitant treatment modalities to restore or maintain sinus rhythm during the hospitalisation/medical encounter (e.g., oral or IV anti-arrhythmics, electrical cardioversion, ablation, Maze procedure).

4. Describe the rate of successful cardioversion to sinus rhythm for at least one minute within 90 minutes of start of first vernakalant IV administration and time (in hours) from vernakalant infusion until discharge/end of medical encounter.

3 STUDY OUTCOMES AND DEFINITIONS

3.1 Health Outcomes of Interest (HOI)

3.1.1 Significant Hypotension

Significant hypotension is defined as symptomatic hypotension with systolic BP <90 mmHg, requiring treatment with vasopressors.

3.1.2 Significant Ventricular Arrhythmia

Significant ventricular arrhythmia is defined as

- Sustained ventricular tachycardia (VT) with a ventricular heart rate > 120 beats per minute with duration > 30 seconds or VT that required intervention with either electrical shock or anti-arrhythmic drugs, or
- Torsade de Pointes with a duration of >10 seconds, or
- Ventricular fibrillation of any duration.

3.1.3 Significant Atrial Flutter

Significant atrial flutter is defined as atrial flutter with 1:1 atrioventricular conduction of >10 seconds duration and a ventricular rate of >200 beats per minute (bpm).

3.1.4 Significant Bradycardia

Significant bradycardia is defined as bradycardia requiring electrical pacing (temporary or permanent) or any other SAEs involving bradycardia.

It is anticipated that rates of HOIs may be somewhat higher in this real-world study setting compared to rates observed in the vernakalant clinical trial program due to the selective patient entry criteria of these randomized clinical trials. Likewise, comparisons to the published literature are not planned and would prove difficult due to differences in case definitions for each specific HOI and variability of reported follow-up periods from administration of a given study drug or intervention to time of the event. However, the frequency of HOIs will be carefully monitored by the Sponsor, the Contract Research Organisation (CRO), and the independent Safety Review Committee (SRC) throughout the duration of the study.

3.2 Safety Outcomes

3.2.1 Adverse Events (AEs)

AE is defined as any untoward medical occurrence in a patient administered a pharmaceutical product at any dose that does not necessarily have a causal relationship with vernakalant IV treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of the medicinal product, whether or not considered related to the pharmaceutical product. This definition includes intercurrent illnesses or injuries and exacerbation of pre-existing conditions.

If the onset of an event occurred before the patient entered the study (e.g., any pre-planned hospitalisation or non-emergency routine visits for a pre-existing condition), the condition or pre-existing condition would not be considered an AE unless it worsened following medicinal product use or hospitalisation was prolonged due to a worsening of the pre-existing condition.

A pre-existing condition is a clinical condition (including a condition being treated) which is diagnosed prior to use of a Cardiome product or protocol-specified intervention, and which is documented as part of the patient's medical history (e.g., pre-planned hospitalisation or a routine visit for the pre-existing condition). Any worsening of a pre-existing condition temporally associated with the use of a Cardiome product is by definition an adverse event.

3.2.2 Serious Adverse Events (SAE)

An SAE is defined as an AE which is fatal or life threatening, results in persistent or significant disability, requires inpatient hospitalisation, prolongation of existing inpatient hospitalisation, or is a congenital anomaly, cancer, the result of an overdose or is another important medical event. Other important medical events that may not result in death, may not be life-threatening, or may not require hospitalisation may be considered a SAE when based upon appropriate medical judgment, they may jeopardise the patient or subject and may require medical or surgical interventions to prevent one of the other outcomes listed previously.

Specifically, the SRC is responsible for (1) review of individual patient listings of SAE reports and aggregated data in data tables and study result reports; (2) periodic assessment of subject accrual rate and study status; (3) evaluation on an ad hoc basis of any urgent safety issue identified by the Sponsor, CRO or the SRC, and (4) documentation and communication in writing of all SRC activities to Sponsor. Source documentation routinely collected for the study

which may include ECG tracings corresponding to arrhythmic events if performed as part of standard of care is also provided to the SRC for review of individual HOIs and SAEs.

3.2.3 Non-Serious Adverse Events

AEs which do not meet the above criteria are defined as **non-serious adverse experiences (NSAE)**. For regulatory reporting requirements in the European Union, SAEs and NSAEs that are at least possibly drug related are defined as serious adverse reactions (SADR) and non-serious adverse reactions, respectively.

3.3 Effectiveness Outcome: Conversion to Sinus Rhythm

Effectiveness of vernakalant IV will be assessed as a secondary endpoint, defined as the proportion of patients who are converted to sinus rhythm for at least one minute within 90 minutes of start of first vernakalant IV administration. Additionally, the proportion who are converted to sinus rhythm regardless of timing will be reported. (Refer to Section 4.3 for description of further effectiveness subgroup analyses per Summary of Product Characteristics (SmPC)).

3.4 Derived Variable Definitions

The following derived/calculated values will be used:

- Age at enrolment = [(date of informed consent – date of birth) + 1]/365.25, or self-reported age if date of birth is not available.
- BMI = Weight (Kg)/Height $(m)^2$. English standard units should be converted to international or metric units.
- (S)AE or HOI onset in days and time (in hours or minutes) following vernakalant IV infusion = date/time of onset or (S)AE-date – date/time of start of first infusion.
- Duration or period = (stop time – start time). Note there are key durations that include, but are not limited to, duration of vernakalant IV infusions and duration of HOI and SAE.
- Vernakalant IV dose per body weight = vernakalant IV dose (mg) / body weight (kg).
- Duration of time to conversion to sinus rhythm = (date/time of conversion to sinus rhythm – date/time of start of first infusion).
- Percentage of weight-based dosing recommendation per label (%) = (Vernakalant IV dose [mg/kg] / Recommended vernakalant IV dose [mg/kg]) * 100. Range from 0% to above 100%, with 100% indicating that dose is equal to recommended dose, calculated per first or second infusion. Patients with cumulative doses greater than the maximum recommended dose will be noted (overall and for first and second infusion, separately).
- Duration of current AF in hours = (Vernakalant administration date/time - AF onset date/time).

- Time since first AF diagnosis = (Start date of Vernakalant IV administration - Date of first AF diagnosis).
- Rate of conversion to sinus rhythm for at least one minute within 90 minutes of start of first vernakalant IV administration = (Number of relevant patients converted to sinus rhythm for at least one minute within 90 minutes of start of first vernakalant IV administration) / (Total number of relevant patients administered vernakalant IV). Rate of conversion can be evaluated based on different types of patients, e.g. all patients receiving vernakalant IV or all such patients with other restrictions.
- Elevated liver enzymes (inclusive of possible abnormal liver function or liver injury) = an increase above upper limit of normal (ULN) for alanine aminotransferase (ALT), aspartate aminotransferase (AST), or total bilirubin (TB) or conjugated bilirubin. [1,2]
- Total hospital length of stay (hours) = (Date/time of discharge or release of facility – Date/time of hospital admission).
- Modification of Diet and Renal Disease (MDRD) estimated Glomerular Filtration Rate (GFR) (mL/min per 1.73 m^2) = 186 x (Serum creatinine [Scr])$^{-1.154}$ x (Age)$^{-0.203}$ x (0.742 if female) x (1.210 if Black). [2]
- Time between Current and Previous Study Enrolment = (Informed consent date of current enrolment – Informed consent date of previous study enrolment).

4 GENERAL CONSIDERATIONS FOR ANALYSIS

4.1 Sample Size and Power Calculations

Patients may be enrolled in the study more than once in association with multiple administrations of vernakalant IV. The study targeted 2,000 patients, per administration of vernakalant IV, across participating EU countries. The target sample size was selected in order to have adequate statistical precision as expressed by a two-sided, 95% confidence limit around the expected incidence rate for each HOI for sample sizes of 500, 1,000 1,500, and 2,000 patients. The incidence of each HOI during the first 24 hours post-vernakalant IV administration among patients randomised to receive vernakalant IV in the pooled phase II/III clinical trial database (n=889, including the AVRO Study [3]) ranged from 0% to 0.22% for each HOI.

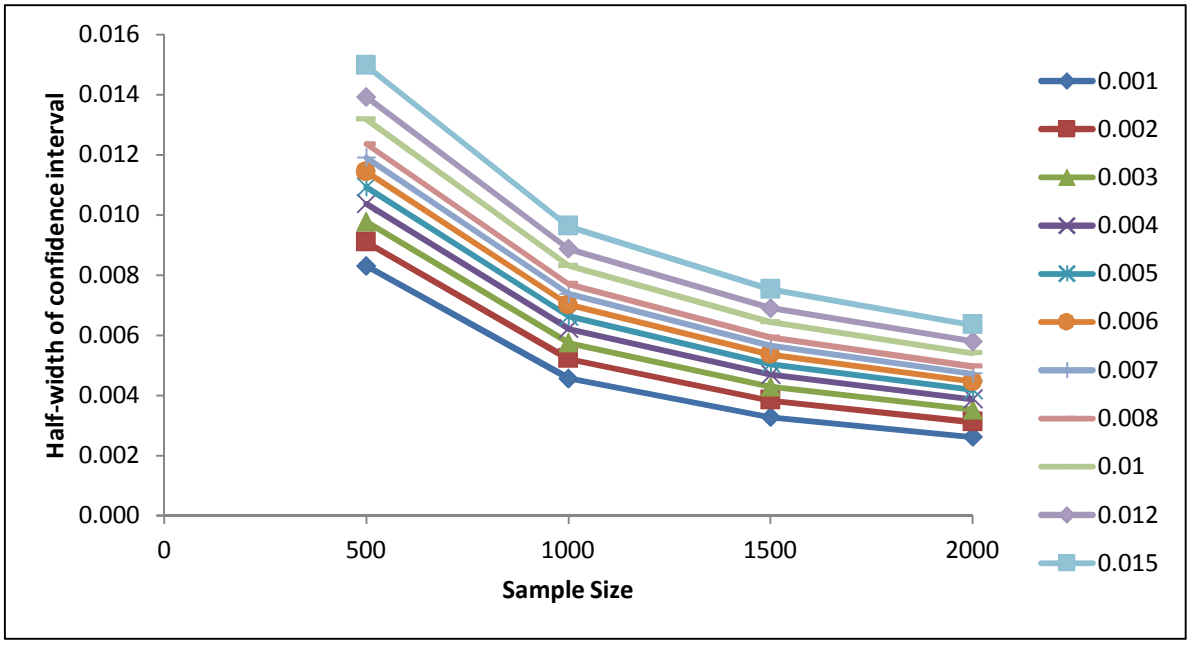
Table A shows the margins of error, defined as the distance from the expected proportion to the upper limit of the confidence interval (CI) as shown in the table, and confidence limits of the two-sided 95% confidence intervals with sample size of 500, 1,000, 1,500, and 2,000, respectively. For example, if the expected proportion of significant hypotension is 0.003 and the sample size is 1,500, the margin of error is 0.004, and the lower and upper bounds of the two-sided 95% confidence interval will be 0.001 and 0.007, respectively. The calculation of the confidence intervals was performed using the Clopper-Pearson exact method [3] and PASS software (2008, Kaysville, Utah).

Table A Margins of error and confidence limits of the two-sided 95% confidence intervals for one sample proportion with various sample sizes.

Since the confidence interval is not symmetric around the expected proportion of patients with events, the precision is the distance from the expected proportion to the upper limit of the confidence interval as shown in this table.

Sample Size	**N=500**		**N=1,000**		**N=1,500**		**N=2,000**	
Expected Prop.	Margin of Error	Lower and Upper Limit	Margin of Error	Lower and Upper Limit	Margin of Error	Lower and Upper Limit	Margin of Error	Lower and Upper Limit
0.001	0.008	0.000, 0.009	0.005	0.000, 0.006	0.003	0.000, 0.004	0.003	0.000, 0.004
0.002	0.009	0.000, 0.011	0.005	0.000, 0.007	0.004	0.000, 0.006	0.003	0.001, 0.005
0.003	0.010	0.000, 0.013	0.006	0.001, 0.009	0.004	0.001, 0.007	0.004	0.001, 0.007
0.004	0.010	0.000, 0.014	0.006	0.001, 0.010	0.005	0.001, 0.009	0.004	0.002, 0.008
0.005	0.011	0.001, 0.016	0.007	0.002, 0.012	0.005	0.002, 0.010	0.004	0.002, 0.009
0.006	0.011	0.001, 0.017	0.007	0.002, 0.013	0.005	0.003, 0.011	0.004	0.003, 0.010
0.007	0.012	0.002, 0.019	0.007	0.003, 0.014	0.006	0.003, 0.013	0.005	0.004, 0.012
0.008	0.012	0.002, 0.020	0.008	0.003, 0.016	0.006	0.004, 0.014	0.005	0.005, 0.013
0.010	0.013	0.003, 0.023	0.008	0.005, 0.018	0.006	0.006, 0.016	0.005	0.006, 0.015
0.012	0.014	0.004, 0.026	0.009	0.006, 0.021	0.007	0.007, 0.019	0.006	0.008, 0.018
0.015	0.015	0.006, 0.030	0.010	0.008, 0.025	0.008	0.009, 0.023	0.006	0.010, 0.021

Figure A **Plot of precision and margin of error at various levels of expected proportion of patients with events.**



Footnote: Margin of error (half-width of confidence interval) is defined as the distance between the expected proportion (point estimate) and upper bound of the two-sided 95% confidence limit as the confidence interval is not symmetric.

4.2 Analysis Populations

All screened patients will be included in summary of patient disposition with additional summary of their demographic characteristics. All enrolled patients who meet the eligibility criteria, sign the informed consent form, and are administered vernakalant IV will be included in the analysis population set, regardless of their disposition status. If a patient's consent is withdrawn prior to completing follow-up period, all data already collected as part of the study will be retained for analysis unless country-specific ethics committee (EC) requirements prohibit this or the patient requests otherwise. In addition, patients who discontinue from the study prior to receiving vernakalant administration will not be included in the overall analysis population. All the summaries will be presented on the overall analysis population set unless otherwise stated.

Patients may be enrolled in the study more than once in association with multiple administrations of vernakalant IV. Patients with multiple enrolments are included in the analysis population, and the number of previous study enrolments is provided in the study analysis. All study analyses presented in the study tables, listings, and figures of this report treat each patient's subsequent administrations of vernakalant IV as occurring independently.

Effectiveness analysis population is defined as all patients from overall analysis population defined above EXCEPT those who receive ECV or IV Class I/III AA for cardioversion within 90 minutes of start of the first vernakalant IV administration. But for analysis of the effectiveness of

vernakalant IV, e.g., rate of conversion, both analysis population and effectiveness population may be used.

4.3 Subgroup Analysis

The tables relating to patient selection (i.e., demographics, presenting conditions, and medical history) and vernakalant dosing and administration will be repeated for each country. Country-specific tables will include:

- **Table 1.2** Use of Pre-Infusion Checklist Prior to Vernakalant IV
- **Table 1.3** Receipt of Healthcare Provider (HCP) Educational Card, by Site
- **Table 4.1** Patient Demographics
- **Table 5** Other Baseline Presenting Conditions and Medical History
- **Table 9.1** Vernakalant IV Administration and Dosing (Overall)
- **Table 9.2** Vernakalant IV Administration and Dosing (Prospective Patients)
- **Table 9.3** Vernakalant IV Administration and Dosing (Retrospective Patients)
- **Table 10** Patient Age and Therapeutic Indication for Use in Accordance with the Vernakalant IV Summary of Product Characteristics
- **Table 11** Contraindications for Use in Accordance with the Vernakalant IV Summary of Product Characteristics

Rates of HOIs will not be reported by country or other specified subgroups as individual events are expected to be rare, and stratification of event rates will yield statistically unstable results.

Secondary analysis of rates of HOIs may be conducted for subgroups of patients with certain medical characteristics if the sample size is sufficient to allow for reasonably precise point estimates of HOI incidence (in general, 500 patients or more). Regardless, a description of each patient with an SAE or HOI will be given in narrative form.

A pre-specified secondary analysis of the effectiveness of vernakalant will be restricted to a subgroup of patients who receive vernakalant IV in accordance with the Summary of Product Characteristics (SmPC). Specifically, the following patients will be **excluded** from the pre-specified subgroup analysis:

- Patients not administered vernakalant IV in accordance to SmPC in terms of adult indication (age < 18 years of age), therapeutic indication (indication other than conversion of atrial fibrillation), duration of atrial fibrillation (atrial fibrillation > 7 days for non-surgery patients and > 3 days for post-cardiac surgery patients).

- Patients with at least one of the following contraindications: baseline systolic blood pressure < 100 mmHg, MI/ACS past 30 days, severe aortic stenosis, severe bradycardia in absence of pacemaker, prolonged QT at baseline (uncorrected > 440 msec) in absence of pacemaker, sinus node dysfunction in absence of pacemaker, 2nd or 3rd degree heart

block in absence of pacemaker, heart failure NYHA functional class III or IV, use of class I or class III intravenous anti-arrhythmics within 4 hours before, or within 4 hours after, the start of first vernakalant infusion).

In addition, the effectiveness of vernakalant will be evaluated by the indication of use for which vernakalant IV was prescribed (i.e., conversion of atrial fibrillation for non-surgery patient and conversion of atrial fibrillation for post-cardiac surgery patients).

4.4 Handling Withdrawals and Missing Data

There will be no imputation of missing data. Data will be presented and summarised as it was recorded. Reasonable attempts should be made by the treating physician and/or site personnel to limit the amount of missing data. The proportion of missing data is expected to be low for this study, especially with regard to the details of administration of vernakalant IV and concomitant therapies, collected laboratory values, and occurrence of HOIs during the brief, in-hospital follow-up period. Reasonable attempts will be made to limit the amount of missing medical history and presenting condition data to ensure that important information is captured. Prospective supplemental data collection of study-specific data elements, such as patient's weight, heart failure NYHA functional class, vernakalant administration and patient monitoring is expected to limit missing data.

4.5 Analysis Software and Coding

SAS® version 9.2 or later will be used for all analyses and data summary tables. All AE and SAE verbatim terms will be coded using MedDRA (version 14.0). Medications will be coded using WHO-DD, Format C (01Mar2011) and the Anatomical Therapeutic Chemical (ATC) Classification System. For the purposes of this study, medications sotalol and sotalol hydrochloride will be re-classified for consistency with the Vaughan Williams Classification of Antiarrhythmic Drugs listed in the Section 5.9 [5]. Thus study programmers will manually reclassify sotalol from the assigned ATC code of C07AA (Beta Blocking Agents, Non-Selective) to the ATC code C01BD (Antiarrhythmics, Class III) in the analysis datasets.

5 STATISTICAL ANALYSIS

Categorical variables (e.g., gender) will be summarised by the number and percentage (%) of patients. For the pre-specified HOIs, both stratified (based on enrolment method, i.e. prospective or retrospective) and unstratified (i.e. overall) cumulative incidences will be reported, and corresponding 95% confidence intervals will be displayed for each such specific HOI. Unless otherwise specified, the 95% confidence intervals around the proportions will be calculated using exact methods described by Clopper and Pearson [3].

Continuous variables (e.g., age) will be summarised using descriptive statistics (number of non-missing values, mean, standard deviation, median, Q1 and Q3, minimum and maximum values).

Some continuous variables will be described using categorizations to provide additional detailed information regarding vernakalant IV administration. For instance, percentage of weight-based dosing recommendation may be described using the following categories: < 70%, 70% to < 85%,

85% to < 95%, 95% to 105%, > 105% to 110%, > 110% and the duration of infusion will be reported in categories such as: < 7 minutes, 7 minutes to < 9 minutes, 9 minutes to 11 minutes, >11 minutes to 13 minutes, > 13 minutes. The categorizations will be based on the empirical data and may be adjusted.

Key results will be presented overall and by patient enrolment method (i.e. prospective or retrospective). Any changes to the analysis over the course of the study will be described in Statistical Analysis Plan (SAP) addendums or amendments. Ad hoc analyses (by country, site, or other) will be performed as requested by the sponsor.

5.1 Patient Disposition, Enrolment, and Demographics

5.1.1 Patient Disposition

NOTE: Patients may be enrolled in the study more than once in association with multiple treatment episodes of vernakalant IV. The study protocol does not prohibit multiple enrolments for a single patient. Patients receive a new, unique study ID at each new vernakalant treatment episode. **Note: the vernakalant treatment episode as referenced does not pertain to each infusion of vernakalant, as one treatment episode may involve multiple vernakalant infusions.** A summary of patients with multiple treatment episodes included in the analysis population set and the number of previous treatment episodes, if any, will be provided in the patient disposition table. All study tables and listings will treat each patient's subsequent administrations of vernakalant IV as occurring independently. For each patient with multiple treatment episodes, information regarding each episode including dates of informed consent, will be listed (**Listing 6**). Each patient's cumulative profile of SAEs (including HOIs) and contraindications by treatment episode will also be listed (**Listings 7-8**).

Patient disposition, per administration of vernakalant IV, will be summarised, as follows (**Table 2, Figure 1**):

- Total number of patients screened from site enrolment log (**Figure 1** only) and reasons for non-participation listed below, if available
    - No Informed Consent (Patient/Guardian unable to and/or refusal to give consent)
    - Patient not approached prior to vernakalant administration
    - Patient enrolled in an investigational drug or device clinical trial in the past 30 days prior to vernakalant administration
- Total number of patients enrolled in the registry
    - Total number of patients discontinued from the study due to conversion to sinus rhythm before vernakalant administration
- Total number of patients in the analysis population. All enrolled patients who meet the eligibility criteria and sign the informed consent form and are administered vernakalant IV are included in the analysis population. Patients discontinued from the study due to conversion to sinus rhythm before vernakalant administration or, based on patient request or ethic committee requirements, withdrawal of patient consent, will not be included in the analysis set.

- Total number of patients with single and multiple vernakalant treatment episodes in the analysis population
- For patients with multiple treatment episodes of vernakalant IV, number of previous treatment episodes
- Total number of patients who completed the study and reasons for discontinuation. Note: For the interim analyses, patients displayed as "not complete" will include patients who do not have a complete End of Study case report form at the time of data extraction for the interim report.
- Number of patients excluded from analysis population either due to spontaneous conversion to sinus rhythm or withdrawal of patient consent

5.1.2 Patient Enrolment

An overview of enrolled patients since previous report and total patients enrolled will be reported for each country (**Table 3**).

5.1.3 Patient Demographics

The following demographics characteristics will be summarised for enrolled patients in the analysis set (**Table 4.1**):

- Gender (male, female)
- Age (years) at Informed Consent date
- Race or ethnicity as recorded in the medical record, if available (White, Black, Hispanic, Asian, other). Note: Patients may have more than one race recorded.
- Body weight (Note: Patient weights were either obtained from medical record or were prospectively collected after administration of vernakalant IV in a supplemental data collection tool for prospectively enrolled patients.)
- Method of measurement for weights (direct measurement, patient-reported, estimated from health professional, unknown, recorded after vernakalant IV administration)
- Reason patient weight not measured prior to vernakalant IV administration (patient bed-bound, weighing equipment unavailable or broken, unknown, other)
- Body mass index (BMI)

Gender and age will also be summarised for screened patients and for screened but not enrolled patients (**Table 4.2**):

5.2 Hospital Characteristics and Medical Encounter

The following hospital characteristics and medical encounter will be summarised at the patient level (**Table 1.1**):

- Hospital type (Public hospital, private hospital, university hospital, regional/community hospital, other) from Site Qualification Questionnaire (SQQ).

- Hospital size (large, small). Hospital size based on number of beds. Large hospitals defined as 300 or more beds; small hospitals defined as fewer than 300 beds. Number of beds based on direct hospital and site contact.
- Hospital admission (emergency, planned admission, transfer from another facility).
- Department in which vernakalant IV was administered (Intensive Care Unit (ICU), Coronary Care Unit (CCU), Post-Surgical ICU, Emergency Department, Operating Room/Surgical, Cardiac Procedure Room, General Medical Ward, Other).
- Total hospital length of stay (hours) and length of stay by department in which vernakalant IV was administered. Note: total hospital length of stay may be converted to days.

5.3 Receipt and Use of Risk Minimisation Tools

Data regarding use and receipt of Pre-Infusion Checklist and HCP Educational Card (resulting from Pharmacovigilance Risk Assessment Committee [PRAC] feedback) were collected starting on August 9, 2014. **Table 1.2** includes information on whether the Pre-Infusion Checklist was used prior to vernakalant IV administration, and **Table 1.3** includes information on whether the site investigator and/or co-investigator received and read the HCP Educational Card.

5.4 Primary Objective # 1: Incidence of HOIs

Based on the primary objective #1, the incidence of HOIs reported from the start of first infusion through the first 24 hours following the last infusion of vernakalant IV or until discharge/end of medical encounter (whichever occurs earlier) will be calculated as the number of patients who have at least one specific pre-specified event starting from the beginning of the study period, divided by total number of patients enrolled and treated with vernakalant, multiplied by 100. The incidence of HOIs as designated by the investigator is summarised by method of enrolment (overall, prospective and retrospective) in **Table 8.1.1** to **Table 8.1.3** and the incidence of HOIs as designated by the SRC by method of enrolment (overall, prospective and retrospective) are displayed in **Table 8.2.1** to **Table 8.2.3**. The incidence of HOIs as designated by either the investigator or the SRC by method of enrolment (overall, prospective and retrospective) is displayed in **Table 8.3.1 to 8.3.3.** Patients with more than one HOI will be counted once in the numerator. Patients with more than one HOI event (either more than one HOI within the same HOI type, or multiple HOI types) will be identified in the report, along with a footnote in the Table 8 series.

Results from the SRC review, including the SRC's classification of the event and whether the event qualifies as a study-defined HOI, are included in some of the HOI and SAE tables and listings (**Listings 1a, 2a, 7**, and **8**). A listing of all SAEs and HOIs, both defined by the investigator and by the SRC, is shown in **Listing A**.

Definitions for HOIs (significant hypotension, significant ventricular arrhythmia, significant atrial flutter, and significant bradycardia) are provided in Section 3.1. For the HOI significant bradycardia, the incidence of bradycardia requiring electrical pacing (temporary or permanent) and the incidence of patients experiencing any other SAEs involving bradycardia (but not

requiring temporary or permanent pacing) will be reported both separately and combined. A study definition of SAEs involving bradycardia is conservatively added to the investigator assessment based on a list of MedDRA terms that would be considered to be SAEs involving bradycardia (**Appendix 2**). Therefore "investigator assessment" includes bradycardia HOIs designated as such per the investigator and/or study definition. MedDRA code version 14.0 used to identify SAEs are consistent with clinical development program.

For patients who receive one infusion during a treatment episode, the follow-up period for HOIs is from the start of this infusion through the first 24 hours, or until discharge/end of medical encounter, whichever occurs earlier.

For patients who receive more than one infusion during a treatment episode, the follow-up period for HOIs is from the start of the first infusion through the first 24 hours following the start of the last infusion, or until discharge/end of medical encounter, whichever occurs earlier.

Because HOIs are expected to be rare events, Clopper Pearson (Exact) confidence intervals will be constructed around the point estimate of the incidence for each HOI. [3] Numbers and rates of HOIs will also be presented according to time intervals since start of first vernakalant infusion, i.e., 0 to less than 2 hours, 2 to less than 4 hours, and 4 hours to a maximum of 24 hours.

The primary analysis for HOI incidence is the 0-2 hour post infusion time point. Given the lower expected sample size, vernakalant's mode of action and the non-interventional nature of the study design, the 2-4 hour and 4-24 hour post infusion time points are considered secondary and tertiary analyses, respectively.

The HOI incidence for each time interval will be calculated as follows.

For each time interval, the numerator will be the number of patients with at least one HOI with an onset date and time in the time interval occurring among patients enrolled and treated with vernakalant. The denominator will be the number of patients enrolled and treated with vernakalant.

For the 0-<2 hour time internal, the number of patients with at least one HOI with an onset date and time in the 0-2 hour interval (interval is from start date and time of vernakalant administration to 1:59:59 following start date and time of vernakalant administration) divided by the number of patients enrolled and treated with vernakalant.

For the 2-<4 hour time interval, the number of patients with at least HOI with an onset date and time in the 2-<4 hour interval (interval is from 2:00:00 following start date and time of vernakalant administration to 3:59:59 following start date and time of vernakalant administration) divided by the number of patients enrolled and treated with vernakalant.

For 4-24 hour time interval, the number of patients with at least one HOI with an onset date and time in the 4-24 hour interval (interval is from 4:00:00 following start date and time of vernakalant administration to 24:00:00 following start date and time of vernakalant administration) divided by the number of patients enrolled and treated with vernakalant

Characteristics of patients with HOIs, which may include prior medical history, presenting conditions, medication use, dosing/administration of vernakalant IV, concomitant therapies, and assessment of relatedness as provided by the investigator will be summarised as a narrative in the listing of individual HOI events in study reports. Case narratives will be provided in **Listing 1b** and **Listing 2b** for each HOI and SAE regardless of the relationship to vernakalant and will describe patients with more than one HOI event reported. Listings will be by-event (i.e., patient with multiple events will be repeated for each event type) and will contain the patient's case narrative for each event type.

5.5 Primary Objective #2: Administration of Vernakalant Consistent with Weight-Based Dosing and Patient Monitoring

Based on Primary Objective #2, distributions of patient body weight, number of infusions, total dose administered with each IV infusion and administration duration stratified by body weight (<113 kg and ≥113 kg) will be summarised (**Table 9**). Body weight and details of dosing and administration (indication, number of infusions, dose in mg and mg/kg, percentage of weight-based dosing recommendations, duration, whether stopped prematurely, and the reasons for stopping) will be presented separately for each body weight group.

Percentage of weight-based dosing recommendation per label will be calculated as actual vernakalant IV dose divided by the recommended vernakalant IV dose, multiplied by 100. The measure will range from greater than 0% to above 100%, with 100% indicating that dose is equal to recommended dose, calculated per first or second infusion. The recommended vernakalant administration dose is weight-based. If patient's body weight is < 113 kg, total dose for initial and second infusions should be 3 mg/kg and 2 mg/kg, respectively, over a 10 minute period. If the patient is ≥113 kg, total dose for initial and second infusions should be 339 mg and 226 mg, respectively, over a 10 minute period. For example, a patient weighing less than 113 kg receiving one infusion of vernakalant at a dose of 2.5 mg/kg would have a percentage of weight-based dosing recommendation per label of 83.3% (recommended dose is 3 mg/kg). A patients weighing greater than 113 kg who received an initial infusion of vernakalant at a dose of 350 mg would have a value of 103.2% (recommended dose is not to exceed 339 mg).

For exploratory analysis, listings of patients with vernakalant IV stopped prematurely, those whose first infusion was shorter than 9 minutes and those whose second infusion was shorter than 9 minutes, (**Listing 5a, 5b,** and **5c,** respectively) will be produced. The listing will include the following data elements: patient ID, age, gender, weight, country, number of infusions, dose (in mg and mg/kg), percentage of weight-based dose recommendation, duration (minutes). Dose, percentage of weight-based dosing recommendation, and duration will be reported for the first infusion and second infusion, if applicable.

For **Listing 5a**, the reason for premature stopping of vernakalant (e.g., successful cardioversion, non-serious adverse event, other verbatim responses) will also be included. Patients with early termination of vernakalant IV will be included in **Table 9** as a separate subgroup if the total number of patients with vernakalant stopped prematurely reaches a minimum of 10% of patients, otherwise patients with reported early termination of the infusion will be included in the overall analysis population presented in **Table 9** with appropriate description in report text and table footnotes.

Additionally, data on patient's body weight in kg (x-axis) and total dose in mg (y-axis) for first infusion and second infusion, if applicable, will be presented graphically. Given the large number of overlapping data points, a jittered scatterplot may be used (**Figure 2**).

Monitoring of patients during and after vernakalant IV administration by number of infusions include (**Table 14a, 14b**):

- Frequency and duration of blood pressure monitoring
- Blood pressure monitoring by healthcare provider (nurse, physician, other)
- Continuous monitoring of cardiac rhythm (yes, no)
- Cardiac rhythm monitoring by healthcare provider (nurse, physician, other)

5.6 Primary Objective #3: Evaluate Effectiveness of Risk Minimisation Activities

The receipt and use/read of effective risk minimisation activities will be summarised [addressed in Section 5.3]. To explore the effectiveness of the risk minimisation activities, assessment of physician behaviour in terms of compliance with key aspects of the SmPC including the use of the pre-infusion checklist and health provider education card will be described for the following parameters among enrolled patients in the registry:

- Appropriate patient selection for treatment with vernakalant IV (adherence to recommended indications and contraindications) [addressed in Sections 5.5 and 5.8]
- Administration and weight-based dosing of vernakalant IV, including patient monitoring during and after infusion [addressed in Section 5.5]
- Use of anti-arrhythmics before and after vernakalant IV [addressed in Section 5.9]
- Monitoring for the occurrence and incidence of serious adverse events (SAEs) and HOIs [addressed in Sections 5.4 and 5.7]

5.7 Secondary Objective #1: Counts and Rates of Serious Adverse Events (SAEs)

Per Secondary Objective #1, tables with counts and cumulative incidence of SAEs (including HOIs) will be provided and summarised by MedDRA system organ class (SOC), high level term (HLT), and preferred term (PT), and also stratified by outcome (recovered, recovered with sequelae, and not recovered) (**Tables 16.1a.1** to **16.1a.3**), fatal or non-fatal (**Tables 16.1b.1** to **16.1b.3**), and relationship to the study drug (definitely related, probably related, possibly related, probably not related, definitely not related) (**Tables 16.1c.1** to **16.1c.3**). Incidence is calculated as the number of patients who have a SAE starting during the study period, divided by the total number of patients in the analysis population set, times 100.

Characteristics of patients with SAEs, which may include medical history, presenting conditions, medication use, dosing/administration of vernakalant IV, and concomitant therapies, will be summarised in the narrative in a listing of individual SAEs in study reports (**Listing 2b**). Site-reported case narratives and clinical narrative from the medical monitor will be provided for each

SAE. Listings will be by event (i.e., patient with multiple events will be repeated for each event type) and will contain the patient's case narrative for each event.

5.8 Secondary Objective #2: Characterise Patients Administered Vernakalant IV by Medical History, Presenting Conditions and Other Baseline Characteristics

Pertaining to Secondary Objective #2 and Primary Objective #3, the number and percentage of patients greater than18 years of age (adults) and patients administered vernakalant for recent onset atrial fibrillation (≤ 7 days duration for non-surgical atrial fibrillation and≤ 3 days duration for post-cardiac surgery atrial fibrillation) in accordance with the vernakalant Summary of Product Characteristics (SmPC) will be described (**Table 10**).

In addition, the number and percentage of patients with a reported contraindication for use as specified in the vernakalant IV SmPC will be described (**Table 11**). Specifically, the description will include the following conditions:

- Patients with systolic blood pressure <100 mm Hg
- Acute coronary syndrome (including myocardial infarction) within the last 30 days
- Patients with prolonged QT at baseline (uncorrected > 440 msec) in absence of pacemaker
- Severe aortic stenosis
- Severe bradycardia in the absence of a pacemaker
- Sinus node dysfunction in the absence of a pacemaker
- Heart block (second or third degree) in the absence of a pacemaker
- Patients with heart failure NYHA functional class III or NYHA functional class IV
- Use of class I or class III intravenous anti-arrhythmics within four hours prior to or after the start of vernakalant administration other presenting conditions and medical history at baseline will be summarised.

The following presenting conditions and medical history information will be reported in term of number and percentage (**Table 5**):

Presenting Conditions:

- Systolic blood pressure (mm Hg) as recorded most immediately prior to initial vernakalant infusion
- Diastolic blood pressure (mm Hg) as recorded most immediately prior to initial vernakalant infusion
- Heart rate (beats per minute) as recorded most immediately prior to initial vernakalant infusion)
- New York Heart Association (NYHA) functional class at hospital presentation (0, I, II, III, IV)

- History of heart failure (yes, no, unknown) and among these patients who had NYHA heart failure class III or IV at hospital presentation
- Previously documented left ventricular ejection fraction (LVEF, ≤30%, >30 – ≤50%, >50%, Not Available). LVEF information will be reported as recorded in the electronic case report form (eCRF) from either (1) the baseline echocardiogram (performed during the index hospitalization, but prior to vernakalant administration), if available, or (2) the baseline medical history CRF, which records previously documented LVEF for patients with a reported history of heart failure. If data are available in both forms, the data with the most recent associated date will be included. Otherwise patients will be classified as LVEF > 35% or "not available". The "not available" classification includes patients with no LVEF information on either the medical history or echocardiogram data collection forms. Additional details regarding LVEF (%), such as range of LVEF, may be reported, if available.
- Clinically meaningful valvular stenosis, as per physician assessment (yes, no, unknown), and among these patients who have a history of valve replacement and had heart valve surgery during index hospitalisation
- Cardiomyopathy (yes, no, unknown, and whether hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy or other)
- Constrictive pericarditis (yes, no, unknown)
- Advanced hepatic impairment (yes, no, unknown)
- Elevated liver enzymes (inclusive of possible abnormal liver function or liver injury), defined as an increase above ULN for alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TB) or conjugated bilirubin based on recommended algorithms to define abnormal liver function and liver injury in the literature [1,2]. Patients must have at least one laboratory value available for ALT, AST, TB or conjugated bilirubin to be eligible to determine if liver enzymes are elevated for this calculation.
- Estimated GFR calculated by abbreviated MDRD. MDRD will be calculated for patients with available race information [1].

Medical History:

- Pacemaker implantation
- Implantable cardioverter-defibrillator (ICD)
- History valve replacement
- History of vascular surgery
- History of left atrial clot
- History of left ventricular hypertrophy
- History of hypertension
- History of angina

- History of stroke
- History of diabetes
- History of hyperlipidaemia
- Current smoking status
- History of hyperthyroidism
- History of rheumatic heart disease

In addition, a summary of atrial fibrillation disease history and current episode will be presented separately to further characterise the population (**Table 6**). The following information will be described:

- Duration of current AF (hours). Duration of current AF is defined as date/time of vernakalant IV administration minus date/time of current AF episode onset and will be expressed both as a continuous variable and as a categorical variable (<3, 3-24, 24-48, 48-168, >168 hours).
- Time since first AF diagnosis (days)
- Lone atrial fibrillation (yes, no, unknown)
- Type of AF (first diagnosed, paroxysmal, persistent, long-standing persistent, permanent, post-operative, unknown/ not assessed) [4]
- Symptoms of AF, including shortness of breath, palpitation/irregular heartbeat, chest pain/angina, dizziness/light-headedness, syncope/ near syncope, other (yes, no unknown/not assessed. Note: "unknown/not assessed" is not available for "other").

Lastly, selected concomitant medications will be presented for patients receiving vernakalant as shown in the example **Table 7**. The frequency for selected concomitant medications will be reported for the following time periods: within 24 hours prior to hospitalization or medical encounter; during hospitalization or medical encounter but prior to vernakalant administration; during hospitalization or medical encounter but subsequent to vernakalant administration; and any time within 24 hours prior to or during hospitalization or medical encounter. For each time interval, the denominator will be the total number of patients enrolled and treated with vernakalant. Additional concomitant medications may be included in Table 7 for specific medications or classes that are reported in a minimum of 5% of patients after the minimum enrolment of 100 patients has been reached. Note: Concomitant medications will be coded using the WHO-DD, Format C (01Mar2011) and the ATC Classification System. However, for the purposes of this study, medications sotalol and sotalol hydrochloride will be re-classified for consistency with the Vaughan Williams Classification of Antiarrhythmic Drugs listed in the next section [5]. Thus study programmers will manually reclassify sotalol from the assigned ATC code of C07AA (Beta Blocking Agents, Non-Selective) to the ATC code C01BD (Antiarrhythmics, Class III) in the analysis datasets.

5.9 Secondary Objective #3: Concomitant Therapies to Restore Sinus Rhythm including Anti-Arrhythmic Medication, Electrical Cardioversion, Ablation, and Maze Procedures

Corresponding to Secondary Objective #3, tables will summarise the frequency of concomitant therapies (pharmacological cardioversion, electrical cardioversion, and surgical treatment) to restore sinus rhythm for atrial fibrillation during the medical encounter. Each patient may receive multiple pharmacological and electrical cardioversion treatments (episodes) and tables will summarise patient- and episode-level data.

Summary of the use of intravenous and oral pharmacological cardioversion before, concurrent with, and/or after vernakalant IV includes (**Table 12a, 12b**):

- Administration of other anti-arrhythmic agents for pharmacologic cardioversion (yes, no) (per patient)
- Number of anti-arrhythmic administrations (total episodes)
- Rhythm disorder type for pharmacological cardioversion (atrial fibrillation, atrial flutter, ventricular tachycardia, ventricular fibrillation, other) (per episode)
- Class of anti-arrhythmics (IA, IB, IC, II, III, IV) (per episode)
- Specific intravenous or oral anti-arrhythmic drugs (e.g., Flecainide, Propafenone, Amiodarone, Ibutilide), by class (per episode)

Note: Anti-arrhythmic class will be derived for each pharmacological cardioversion for each drug field based on ATC classification and the following clinical guidelines [6,8,9] Note: for the purposes of this study, sotalol and sotalol hydrochloride will be re-classified from beta blocking agents to antiarrhythmics, Class III for consistency with the Vaughan Williams Classification of Antiarrhythmic [5]. Study programmers will manually reclassify sotalol from the assigned ATC code of C07AA (Beta Blocking Agents, Non-Selective) to the ATC code C01BD (Antiarrhythmics, Class III) in the analysis datasets.

Vaughn Williams Class	Examples of Anti-Arrhythmic Drugs
IA	Disopyramide Procainamide Quinidine
IB	Lidocaine Mexiletine
IC	Flecainide Propafenone
II	Beta blockers (e.g., propranolol)
III	Amiodarone Bretylium Dofetilide Dronedarone Ibutilide Sotalol

Vaughn Williams Class	Examples of Anti-Arrhythmic Drugs
IV	Nondihydropyridine calcium channel antagonists (verapamil and diltiazem)
Other AA/Class V	Adenosine

Characteristics of conditions and classification of treatments will be summarized based on number of patients who received other IV or ORAL Anti-Arrhythmic agents respectively and number of episodes within corresponding timeframes (**Table 12a, 12b**).

Summary of the use of electrical cardioversion before, within 90 minutes from the start of the first vernakalant IV infusion, and at any time after the start of the first vernakalant IV infusion includes (**Table 13a**):

- Electrical cardioversion used to restore sinus rhythm (yes, no) (per patient)
- Total number of electrical cardioversion episodes (all patients)
- Successful restoration of sinus rhythm (yes, no) (per episode)
- Type of electrical cardioversion for all rhythm disorders (atrial fibrillation, atrial flutter, ventricular tachycardia, ventricular fibrillation) and type of defibrillator. Number of patients receiving electrical cardioversion for each rhythm disorder will be presented.

Surgical procedures (**Table 13b)**, including such procedures as ablation and maze, will be stratified by whether they were administered prior to the first vernakalant infusion and subsequent to the start of the first vernakalant infusion.

Concomitant therapies (**Table 7**) will be stratified by the timing of administration relative to vernakalant IV administration (prior, concurrent, or subsequent), based on the start and stop date/time of the concomitant treatment and administration.

5.10 Secondary Objective #4: Rate of Conversion to Sinus Rhythm

For patients in the analysis population set and the effectiveness analysis population set, the rate of successful conversion to sinus rhythm for at least one minute within 90 minutes from the start of first vernakalant IV administration (Secondary Objective 4) will be expressed as the proportion of patients with successful conversion, together with the associated 95% confidence interval. (**Table 15a**). The rate of successful conversion to sinus rhythm without time restriction will also be expressed as the proportion of patients with successful conversion, together with the associated 95% confidence interval. The time (in minutes) from start of vernakalant infusion to conversion to sinus rhythm among those patients who converted will be summarised using appropriate measures of dispersion and central tendency (means, medians, ranges, Q1-Q3 ranges, and standard deviations) **(Figure 3)**. As defined in Section 4.3, a pre-specified secondary analysis of the effectiveness of vernakalant will be restricted to a subgroup of patients who receive vernakalant IV in accordance with the SmPC (i.e., adult indication, therapeutic indication for AF, duration of AD $\leq$ 7 days for non-surgery patients and $\leq$ 3 days for post-cardiac surgery patients, and no contraindications) (**Table 15b**). Rates of successful conversion will also be

tabulated for all patients by non-surgery and post-cardiac surgery indications, respectively (**Table 15c, 15d**).

5.11 Interim and Final Analysis and Reporting

Interim and final reports [6] will be submitted to the Committee for Medicinal Products for Human Use (CHMP) in accordance with the vernakalant Periodic Safety Update Report (PSUR) schedule, beginning with the 18-month, 24-month reports and then annually thereafter until study completion. The interim and final analyses will address each of the study's primary and secondary objectives and will include descriptive summaries of:

- Patient disposition and enrolment
- Patient characteristics (medical history, presenting conditions, and AF disease history)
- Hospital characteristics and medical encounter
- Details of vernakalant IV administration, dosing, and monitoring
- Administration of concomitant treatment modalities
- Frequencies and incidences of HOIs and SAEs following administration. Two-sided 95% confidence intervals around rates of HOIs will be computed. Line listings of all HOIs and SAEs as well as narratives will be required for interim reports.
- Effectiveness (rate of successful cardioversion)
- Country-specific tables, as described in Section 4.3 Subgroup Analysis, will be included in the Appendix of the interim and final reports.

All interim reports will clearly indicate the total number of patients included, and any additional information included in the data extraction used for the report.

In addition, the final study report will summarise the frequency of non-serious AEs. A table of NSAEs will display numbers and the cumulative incidence of all AEs and will be included for the final report (**Table 17**). The final study report is expected to be prepared after the registry is completed (currently planned for 2016). The timing of the interim and final analysis may be adjusted based on actual site recruitment and data accrual rates.

Full explanation of study methods, status of study site and patient enrolment, results, and discussion and interpretation will be included with interim and final study reports.

In addition, the following reporting conventions will be applied: All percentages will be carried out to one decimal place. Mean, median, Q1, Q3, minimum, and maximum will be carried out one decimal place further than the manner in which the data is reported. The standard deviation will be carried out 2 decimal places farther than the manner in which the data is reported. Standard rounding rules at the last decimal place apply. When appropriate, additional information will be provided in the specifications.

6 REFERENCES

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APPENDIX 1. TABLES, FIGURES, AND LISTINGS

Table 1.1 Hospital Characteristics and Medical Encounter by Patient

Characteristic	Analysis Set (N = xxx)	Prospective Patients (N = xxx)	Retrospective Patients (N = xxx)
Hospital type			
n	xxx	xxx	xxx
Public hospital	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Private hospital	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
University hospital	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Regional/community hospital	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Hospital size[1]			
n	xxx	xxx	xxx
Large	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Small	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Hospital admission			
n	xxx	xxx	xxx
Emergency	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Planned admission	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Transfer from another facility	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Department vernakalant IV administered			
n	xxx	xxx	xxx
Intensive care unit (ICU)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Coronary care unit (CCU)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Post-surgical ICU	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Emergency department	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Operating room/surgical	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cardiac procedure room	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
General medical ward	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Total Hospital Length of Stay (hours)			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1; Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Length of stay <24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of stay >24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Characteristic	Analysis Set (N = xxx)	Prospective Patients (N = xxx)	Retrospective Patients (N = xxx)
Missing	xx	xx	xx
Length of Stay by department vernakalant IV administered[2]			
Intensive care unit (ICU)			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1; Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Length of stay <24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of stay >24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Coronary care unit (CCU)			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1; Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Length of stay <24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of stay >24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Post-surgical ICU			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1; Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Length of stay <24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of stay >24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Emergency department			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1; Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Length of stay <24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of stay >24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Operating room/surgical			
n	xxx	xxx	xxx

Characteristic	Analysis Set (N = xxx)	Prospective Patients (N = xxx)	Retrospective Patients (N = xxx)
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1; Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Length of stay <24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of stay >24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Cardiac procedure room			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1; Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Length of stay <24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of stay >24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
General medical ward			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1; Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Length of stay <24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of stay >24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Other			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1; Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Length of stay <24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of stay >24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1] Hospital size based on number of beds. Large hospitals defined as 300 or more beds; small hospitals defined as fewer than 300 beds.

Table 1.2 Use of Pre-Infusion Checklist Prior to Vernakalant IV Administration

Characteristic	Analysis Set (N = xxx)[1]	Prospective Patients (N = xxx)[1]	Retrospective Patients (N = xxx)[1]
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Don't know	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.
[1] Patients with available data on usage of Pre-infusion Checklist. For prospective patients data collection regarding the Pre-infusion Checklist was initiated on August 9, 2014.

Table 1.3 Receipt of Healthcare Provider (HCP) Educational Card, by Site

Characteristic	Number of Unique Sites in Analysis Set (N=xx)[1]
Investigator and/or co-investigator received the HCP Educational Card[2]	
n	xxx
Yes	xx (xx.x%)
No	xx (xx.x%)
Don't know	xx (xx.x%)
Missing	xx
Investigator and/or co-investigator read the HCP Educational Card[2]	
n	xxx
Yes	xx (xx.x%)
No	xx (xx.x%)
Don't know	xx (xx.x%)
Missing	xx
Reason the HCP Educational Card was not read[3]	
n	xxx
Did not receive it	xx (xx.x%)
Too busy	xx (xx.x%)
Didn't think it was important	xx (xx.x%)
Already know about Brinavess	xx (xx.x%)
Missing	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1] Sites with available data on whether the HCP card was received and/or read. Data regarding the HCP card was initiated on August 9, 2014.

[2] Also known as the Appropriate Use of Brinavess™ card

[3] Includes those who answered "No" to Investigator and/or co-investigator read the HCP Education Card.

Programming note: for this table external data will be used. If "Missing" is not applicable please remove all "Missing" rows.

Table 2 Enrolled Patient Disposition

	Analysis Set (N=xxx)	Prospective Patients (N=xxx)	Retrospective Patients (N=xxx)
Total patient enrolments in the study (includes patients with single or multiple episodes)	xx	xx	xx
Unique patients included in the analysis population set[1]	xx	xx	xx
Patients with single inclusion in the analysis population set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patients with multiple inclusions in the analysis population set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total number of patients with multiple treatment episodes			
n[2]	xx	xx	xx
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
≥5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patients included in the effectiveness analysis population set[3,4]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patients who completed study[4]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patients who did not complete the study[4,5]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patients who discontinued study[4]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reasons for discontinuation[4]			
n	xx	xx	xx
Withdrawal of patient consent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1]Analysis population set is defined as all treatment episodes among enrolled patients who meet the eligibility criteria and sign the informed consent form and are administered vernakalant IV.
[2]Number of patients with multiple enrolments in SPECTRUM.
[3]Effectiveness analysis population set is defined as all treatment episodes among patients from the analysis population set except for those treatment episodes in which patients receive another therapy for cardioversion within 90 minutes of start of the first vernakalant IV administration (i.e. electrical or pharmacologic cardioversion).

[4]Includes patients with single or multiple enrolments.
[5]Patients who discontinued the study for any reason or who did not have a complete end of study form as of the time of data extraction for interim reports.

Table 3 Overview of Enrolled Patients in the Analysis Set by Enrolment Period and Country

Country	Analysis Set (N = xxx)	Prospective Patients (N = xxx)	Retrospective Patients (N = xxx)
Country 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Country 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Country 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc.			

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

Table 4.1 Patient Demographics, All Enrolled Patients

Characteristic	Analysis Set (N = xxx)	Prospective Patients (N = xxx)	Retrospective Patients (N = xxx)
Age (years)			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Missing	xx	xx	xx
Gender			
n	xxx	xxx	xxx
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Race[1]			
n	xxx	xxx	xxx
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Black	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hispanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Body weight (kg)[2]			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Missing	xx	xx	xx
Source of weight measurement as recorded in medical record			
n	xx	xx	xx
Direct measurement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patient-reported	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Estimated by Health Professional	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown method of ascertainment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Body weight collected after vernakalant administration (kg)[2]			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Missing	xx	xx	xx
Reason patient's weight not collected prior to vernakalant IV administration[3]			

Characteristic	Analysis Set (N = xxx)	Prospective Patients (N = xxx)	Retrospective Patients (N = xxx)
n	xx	xx	xx
Patient bed-bound	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Weighing equipment unavailable or broken	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
BMI			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Missing	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1]Patients may select more than one race category.

[2]Patient weights were either obtained from medical record or were prospectively collected after administration of vernakalant.

[3]Number of patients (n) includes patients whose weights were not recorded in the medical record.

Table 4.2 Patient Demographics, Screened Patients

Characteristic	Screened Patients (N = xxx)	Screened but Not Enrolled Patients (N = xxx)
Age (years)		
n	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x
Missing	xx	xx
Gender		
n	xxx	xxx
Male	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

Table 5 Other Baseline Presenting Conditions and Medical History

Characteristic	Analysis Set (N=xxx)	Prospective Patients (N=xxx)	Retrospective Patients (N=xxx)
Systolic blood pressure (mm Hg) as recorded most immediately prior to initial vernakalant infusion)[1]			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Missing	xx	xx	xx
Diastolic blood pressure (mm Hg) as recorded most immediately prior to initial vernakalant infusion[1]			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Missing	xx	xx	xx
Heart rate (beats per minute) as recorded most immediately prior to initial vernakalant infusion)[1]			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Missing	xx	xx	xx
NYHA heart failure functional class at presentation[2]			
n	xxx	xxx	xxx
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
I	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
II	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
III	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
IV	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of heart failure[2]			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
NYHA heart failure class III or IV at Presentation[3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Characteristic	Analysis Set (N=xxx)	Prospective Patients (N=xxx)	Retrospective Patients (N=xxx)
Missing	xx	xx	xx
Previously documented left ventricular ejection fraction [4]			
n	xxx	xxx	xxx
≤30 %	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
>30 -≤ 50%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
>50%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not available	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Clinically meaningful valvular stenosis			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
History of valve replacement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Heart valve surgery during index hospitalisation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
History of valve replacement and heart valve surgery during index hospitalisation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Cardiomyopathy			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Specify type, if yes			
n	xx	xx	xx
Hypertrophic obstructive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Restrictive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Constrictive pericarditis			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Advanced hepatic impairment[5]			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx

Characteristic	Analysis Set (N=xxx)	Prospective Patients (N=xxx)	Retrospective Patients (N=xxx)
Elevated liver enzymes[6]			
n	xxx	xxx	xxx
Elevated	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not elevated	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Estimated GFR using MDRD[7]			
n	xxx	xxx	xxx
Mean (SD)	xx (xx)	xx (xx)	xx (xx)
Median	xx	xx	xx
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
GRF <30mL/min/1.73 m2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
GRF ≥30mL/min/1.73 m2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Pacemaker implanted			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Implantable cardioverter-defibrillator (ICD)			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of valve replacement			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of vascular surgery			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of left atrial clot			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx

Characteristic	Analysis Set (N=xxx)	Prospective Patients (N=xxx)	Retrospective Patients (N=xxx)
History of left ventricular hypertrophy			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of hypertension			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of angina			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of stroke			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of diabetes			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of hyperlipidaemia			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Current Smoker			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of hyperthyroidism			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Characteristic	Analysis Set (N=xxx)	Prospective Patients (N=xxx)	Retrospective Patients (N=xxx)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
History of rheumatic heart disease			
n	xxx	xxx	xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1] As recorded on the Baseline (Personal Data, Physical Measurements and Vital Signs) Case Report Form (CRF).

[2] NYHA heart failure functional class at presentation is physician's assessment of patient's status at the time of the index hospitalization or medical encounter prior to administration of vernakalant IV. History of heart failure as recorded in the baseline medical history CRF. These values may differ.

[3] Number of patients with NYHA heart failure class III or IV (as assigned by physicians at presentation) among those with heart failure recorded in the baseline medical history CRF.

[4] Left ventricular ejection fraction (LVEF) reported as recorded in the baseline echocardiogram CRF, if available or the baseline medical history CRF for patients with reported history of heart failure, if available. If data are available in both forms, the data with the most recent associated date was included. The "not available" classification includes patients with no LVEF information on either the medical history or echocardiogram data collection forms.

[5] Advanced hepatic impairment is physician-reported based on question, "Does the patient currently have any of the following presenting conditions: advanced hepatic impairment (yes, no, unknown)."

[6]Elevated liver enzymes (inclusive of possible abnormal liver function or liver injury), defined as an increase above upper limit of normal (ULN) for alanine aminotransferase, aspartate aminotransferase, or total or conjugated bilirubin based on recommended algorithms to classify abnormal liver function and liver injury in the literature. Patients must have at least one laboratory value available for alanine aminotransferase, aspartate aminotransferase, total bilirubin or conjugated bilirubin to be included.

[7] Estimated Glomerular Filtration Rate (eGFR) will be calculated using Modification of Diet in Renal Disease (MDRD) for patients with available race information.

Table 6 Atrial Fibrillation (AF) Disease History and Current Episode

Characteristic	Analysis Set (N=xx)	Prospective Patients (N=xx)	Retrospective Patients (N=xx)
Duration of current AF (hours)[1]			
n	xx	xx	xx
Mean (SD)	xx (xx)	xx (xx)	xx (xx)
Median	xx	xx	xx
Q1, Q3	xx,xx	xx,xx	xx,xx
Min, Max	xx,xx	xx,xx	xx,xx
Missing	xx	xx	xx
Duration of current AF (hours, categorical)[1]			
n	xx	xx	xx
<3 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3-24 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
24-48 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
48-168 hours (7 days)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
≥168 hours (7 days)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Time since first AF diagnosis (days)[2]			
n	xx	xx	xx
Mean (SD)	xx (xx)	xx (xx)	xx (xx)
Median	xx	xx	xx
Q1, Q3	xx,xx	xx,xx	xx,xx
Min, Max	xx,xx	xx,xx	xx,xx
Missing	xx	xx	xx
Lone AF			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Type of AF[3,4]			
n	xx	xx	xx
First diagnosed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Paroxysmal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Persistent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Long-standing persistent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Permanent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Post-operative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown/Not Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
AF symptoms			
Shortness of breath			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Characteristic	Analysis Set (N=xx)	Prospective Patients (N=xx)	Retrospective Patients (N=xx)
Unknown/not assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Palpitation/irregular heartbeat			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown/not assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Chest pain/angina			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown/not assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Dizziness/light-headedness			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown/not assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Syncope/near syncope			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown/not assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Other			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1] Duration of current AF episode is between AF onset date/time and start of vernakalant IV administration.

[2] Time since first AF diagnosis is between date of first AF diagnosis and start date of Vernakalant IV administration.

[3] Percentage may add up to more than 100% due to multiple selections

[4] Type of AF based on categories specified in the 2010 European Society of Cardiology (ESC) guidelines.

Table 7.1 Selected Concomitant Medications (Analysis Set)

Concomitant Medications[19]	Within 24 hour prior to hospitalisation or medical encounter admission[15] (N=xxx)	During hospitalisation or medical encounter but prior to vernakalant administration[15, 16, 17] (N= xxx)	During hospitalisation or medical encounter but subsequent to vernakalant administration[15, 16, 17] (N=xxx)	Any time within 24 hours prior to or during hospitalisation or medical encounter[15, 16, 18] (N=xxx)
Rhythm Control / Rate Control				
Antiarrhythmics, class Ia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Antiarrhythmics, class Ib	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Antiarrhythmics, class Ic[1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Antiarrhythmics, class III[2,3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other antiarrhythmics, class I and III	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Beta blocking agents, selective[4]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Beta blocking agents, non-selective[4]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Selective calcium channel blockers with direct cardiac effects[5]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Digitalis glycosides[6]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Anti-thrombotic				
Platelet aggregation inhibitors excl. Heparin[7]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vitamin K antagonists[8]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Heparin group[9]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Proteinase inhibitors	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Direct thrombin inhibitors	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Concomitant Medications[19]	**Within 24 hour prior to hospitalisation or medical encounter admission**[15] **(N=xxx)**	**During hospitalisation or medical encounter but prior to vernakalant administration**[15, 16, 17] **(N= xxx)**	**During hospitalisation or medical encounter but subsequent to vernakalant administration**[15, 16, 17] **(N=xxx)**	**Any time within 24 hours prior to or during hospitalisation or medical encounter**[15, 16, 18] **(N=xxx)**
Other anti-thrombotic agents	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other Medications				
Angiotensin II antagonists, plain[10]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Angiotensin II antagonists and diuretics[11]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ACE inhibitors, plain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Aldosterone antagonists	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Benzodiazepine derivatives[12]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blood glucose lowering drugs, excluding insulins	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Diuretics	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
HMG CoA reductase inhibitors[13]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Insulins and analogues	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Organic nitrates[14]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other general anesthetics	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Potassium	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Proton pump inhibitors	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Selective calcium channel blockers with mainly vascular effects	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Thyroid hormones	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1]Vaughn Williams Class Ic antiarrhythmic includes flecainide and propafenone.
[2]Vaughn Williams Class III antiarrhythmic includes amiodarone, dofetilide, and dronedarone.
[3]Includes sotalol
[4]Includes beta-blockers for both AF and non-AF indications.
[5]Includes diltiazem and verapamil.
[6]Includes digitalis/digoxin for AF and non-AF indications.
[7]Includes aspirin, clopidogrel and phosphodiesterase inhibitor.
[8]Includes oral anticoagulant.
[9]Includes heparin and low-molecular weight heparin.
[10]Includes angiotensin-receptor blocker (ARB).
[11]A combination of ARB.
[12]Includes hypnotic and sedative.
[13]Includes lipid-lowering drug.
[14]Includes long-acting nitrates.
[15]For each time interval, the denominator will be the total number of patients enrolled and treated with vernakalant.
[16]For hospitalisations that exceed 7 days in duration, concomitant medication collected during medical encounter for up to 7 days following the last infusion of vernakalant.
[17]Retrospective patients may have missing vernakalant administration date/time
[18]Counts and frequency of medication use as reported by patient.
[19]Concomitant medications are grouped by ATC classes and are mutually exclusive.

Template of Table 7.1 will be applied to the following two tables.

Table 7.2 Selected Concomitant Medications (Prospective Patients)

Table 7.3 Selected Concomitant Medications (Retrospective Patients)

Table 8.1.1 Incidence of Health Outcomes of Interest (HOI) by Time since Start of First Infusion (Analysis Set) – Investigator Assessment

	Time Since First Vernakalant Infusion											
	0 - < 2 hours from start of first infusion (N=xxx)[1]			2- < 4 hours from start of first infusion (N=xxx)[1]			4- 24 hours from start of first infusion (N=xxx)[1]			Overall (N=xxx)		
HOI	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**
Any HOI	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Hypotension[3]	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Ventricular Arrhythmia	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Sustained Ventricular Tachycardia	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Torsades de Pointes	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Ventricular Fibrillation	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Atrial Flutter	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Bradycardia[3, 4]	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Bradycardia Requiring	xx	x.x	xx	xx	x.x	xx	xx	x.x	xx	xx	x.x	xx

	Time Since First Vernakalant Infusion											
	0 - < 2 hours from start of first infusion (N=xxx)[1]			2- < 4 hours from start of first infusion (N=xxx)[1]			4- 24 hours from start of first infusion (N=xxx)[1]			Overall (N=xxx)		
HOI	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**
Electrical Pacing		(x.xx – x.xx)			(x.xx – x.xx)			(x.xx – x.xx)			(x.xx – x.xx)	
SAE involving Bradycardia[5]	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx

[1]For each time interval, the numerator will be the number of patients with at least one HOI with an onset date and time in the time interval occurring to any patients enrolled and treated with vernakalant. The denominator will be the total number of patients enrolled and treated.

[2]Incidence (95% confidence intervals) calculated as the number of patients who have a specific pre-specified event starting during the study period, divided by the total number of patients enrolled, multiplied by 100.

[3]According to the investigator, xx events were reported to include both bradycardia and hypotension. Therefore, each event was counted individually in both the hypotension and bradycardia SAE subtotals and in total number of events.

[4] Significant bradycardia defined as combination of bradycardia requiring electrical pacing (temporary or permanent) or any other serious adverse event reports involving bradycardia.

[5]SAE involving bradycardia but not requiring electrical pacing. A study definition of SAEs involving bradycardia is conservatively added to the investigator assessment based on a list of MedDRA terms that would be considered to be SAEs involving bradycardia (SAP - Appendix 2).

Template of Table 8.1.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively. Please also note: footnote 3 is for one retrospectively patient and therefore does not apply to Table 8.1.2 , and for Table 8.1.2 all subsequent footnote number(s) and footnote indicator(s) should be adjusted accordingly.

Table 8.1.2 Incidence of Health Outcomes of Interest (HOI) by Time since Start of First Infusion (Prospective Patients) – Investigator Assessment

Table 8.1.3 Incidence of Health Outcomes of Interest (HOI) by Time since Start of First Infusion (Retrospective Patients) – Investigator Assessment

Table 8.2.1 Incidence of Health Outcomes of Interest (HOI) by Time since Start of First Infusion (Analysis Set) – SRC Classification

	Time Since First Vernakalant Infusion											
	0 - < 2 hours from start of first infusion (N=xxx)[1]			2- < 4 hours from start of first infusion (N=xxx)[1]			4- 24 hours from start of first infusion (N=xxx)[1]			Overall (N=xxx)		
HOI	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**
Any HOI	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Hypotension[3]	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Ventricular Arrhythmia	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Sustained Ventricular Tachycardia	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Torsades de Pointes	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Ventricular Fibrillation	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Atrial Flutter	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Bradycardia[3, 4]	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx

[1]For each time interval, the numerator will be the number of patients with at least one HOI with an onset date and time in the time interval occurring to any patients enrolled and treated with vernakalant. The denominator will be the total number of patients enrolled and treated with vernakalant.

[2]Incidence (95% confidence intervals) calculated as the number of patients who have a specific pre-specified event starting during the study period, divided by the total number of patients enrolled, multiplied by 100.

[3]xx SAEs were reported to include both bradycardia and hypotension. The xx bradycardia events and xx of the three hypotension events were individually considered HOIs by the SRC. Therefore, each HOI was counted individually in both the hypotension and bradycardia HOI subtotals and in total number of events.

[4]Significant bradycardia defined as combination of bradycardia requiring electrical pacing (temporary or permanent) or any other serious adverse event reports involving bradycardia.

Template of Table 8.2.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively. Please also note: footnote 3 is for one retrospectively patient and therefore does not apply to Table 8.2.2, and for Table 8.2.2 all subsequent footnote number(s) and footnote indicator(s) should be adjusted accordingly.

Table 8.2.2 Incidence of Health Outcomes of Interest (HOI) by Time since Start of First Infusion (Prospective Patients) – SRC Classification

Table 8.2.3 Incidence of Health Outcomes of Interest (HOI) by Time since Start of First Infusion (Retrospective Patients) – SRC Classification

Table 8.3.1 Incidence of Health Outcomes of Interest (HOI) by Time since Start of First Infusion (Analysis Set) – Investigator or SRC Assessment

	Time Since First Vernakalant Infusion											
	0 - < 2 hours from start of first infusion (N=xxx)[1]			2- < 4 hours from start of first infusion (N=xxx)[1]			4- 24 hours from start of first infusion (N=xxx)[1]			Overall (N=xxx)		
HOI	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**
Any HOI	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Hypotension [3]	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Ventricular Arrhythmia[4]	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Sustained Ventricular Tachycardia	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Torsades de Pointes	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Ventricular Fibrillation	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Atrial Flutter	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
Significant Bradycardia [3, 5, 6]	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx

	Time Since First Vernakalant Infusion											
	0 - < 2 hours from start of first infusion (N=xxx)[1]			2- < 4 hours from start of first infusion (N=xxx)[1]			4- 24 hours from start of first infusion (N=xxx)[1]			Overall (N=xxx)		
HOI	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**
Bradycardia Requiring Electrical Pacing	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx
SAE involving Bradycardia	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx	xx	x.x (x.xx – x.xx)	xx

[1]For each time interval, the numerator will be the number of patients with at least one HOI with an onset date and time in the time interval occurring to any patients enrolled and treated with vernakalant. The denominator will be the total number of patients enrolled and treated.

[2]Incidence (95% confidence intervals) calculated as the number of patients who have a specific pre-specified event starting during the study period, divided by the total number of patients enrolled, multiplied by 100.

[3]According to either the investigator or the SRC, xx SAEs were reported to include both bradycardia and hypotension. Therefore, each event was counted individually in both the hypotension and bradycardia SAE subtotals and in total number of events.

[4] The event "ventricular tachycardia" (verbatim term) was classified as a different HOI by the investigator (significant ventricular arrhythmia) and by the SRC (significant atrial flutter). Both classifications are presented in this table but they count only as one event in the Any HOI total.

[5] Subtypes are not applicable to "significant bradycardia" HOIs assessed by the SRC.

[6] Significant bradycardia defined as combination of bradycardia requiring electrical pacing (temporary or permanent) or any other serious adverse event reports involving bradycardia.

Template of Table 8.3.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively. Please also note: footnote 3 is for one retrospectively patient and therefore does not apply to Table 8.3.2, and for Table 8.3.2 all subsequent footnote number(s) and footnote indicator(s) should be adjusted accordingly.

Table 8.3.2 Incidence of Health Outcomes of Interest (HOI) by Time since Start of First Infusion (Prospective Patients) – Investigator or SRC Assessment

Table 8.3.3 Incidence of Health Outcomes of Interest (HOI) by Time since Start of First Infusion (Retrospective Patients) – Investigator or SRC Assessment

Table 9.1 Vernakalant IV Administration and Dosing (Analysis Set)

Vernakalant IV Administration	Body weight <113 kg (N=xxx)	Body weight ≥113 kg (N=xxx)	Overall[2] (N=xxx)
Indication			
n	xx	xx	xx
Conversion of AF for non-surgery patient	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Conversion of AF for post-cardiac surgery patient	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Free Response 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Free Response 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Number of vernakalant IV infusions			
n	xx	xx	xx
1 infusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 infusions	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Greater than 2 infusions	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Dose (in milligrams)			
First Infusion			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
Second Infusion (if applicable)			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
Dose (in milligrams per kilogram)			
First Infusion			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
Second Infusion (if applicable)			
n	xx	xx	xx

Vernakalant IV Administration	Body weight <113 kg (N=xxx)	Body weight ≥113 kg (N=xxx)	Overall[2] (N=xxx)
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
Percentage of weight-based dosing recommendation (%)[1]			
First Infusion			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
First Infusion (categorical)			
n	xx	xx	xx
< 70%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
70% to < 85%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
85% to < 95%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
95% to 105%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
> 105% to 110%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
> 110 %	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Second Infusion (if applicable)			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
Second Infusion (if applicable, categorical)			
n	xx	xx	xx
< 70%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
70% to < 85%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
85% to < 95%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
95% to 105%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
> 105 to 110%	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
> 110 %	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Duration of infusion (minutes)			
First infusion			
n	xx	xx	xx

Vernakalant IV Administration	Body weight <113 kg (N=xxx)	Body weight ≥113 kg (N=xxx)	Overall[2] (N=xxx)
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
First infusion (categorical)			
n	xx	xx	xx
< 7 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
7 - < 9 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
9 - 11 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
> 11 - 13 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
> 13 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Second infusion (if applicable)			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x	xx.x
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
Second infusion (if applicable, categorical)			
n	xx	xx	xx
< 7 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
7 - < 9 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
9 - 11 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
> 11 -13 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
> 13 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Vernakalant IV stopped prematurely			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Reason for Vernakalant IV stopped prematurely			
n	xx	xx	xx
SAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other[3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

Vernakalant administration dose is weight-based per label. If patient's body weight is < 113 kg, total dose for initial and second infusions should be 3 mg/kg and 2 mg/kg, respectively, over a 10 minute period. If the patient is ≥113 kg, total dose for initial and second infusions should be 339 mg and 226 mg, respectively, over a 10 minute period.

[1]Percentage of weight-based dosing recommendations (%) = (Vernakalant IV dose [mg/kg] / Recommended dose [mg/kg])*100

[2]Totals in the overall column may be higher than the sum of the totals in the previous two columns due to the inclusion of patients with missing body weights.

[3]Reasons listed for the Other category are displayed in Listing 5a.

Template of Table 9.1 will be applied to the following two tables.

Table 9.2 Vernakalant IV Administration and Dosing (Prospective Patients)

Table 9.3 Vernakalant IV Administration and Dosing (Retrospective Patients)

Table 10 Patient Age and Therapeutic Indication for Use in Accordance with the Vernakalant IV Summary of Product Characteristics (SmPC)

Criteria	Analysis Set (N=xx)	Prospective Patients (N=xx)	Retrospective Patients (N=xx)
Patient Age ≥ 18			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Therapeutic Indication[1]			
Recent onset atrial fibrillation for non-surgery patients	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Duration of current AF episode (hours)			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
Duration of current AF episode (hours, categorical)			
n	xx	xx	xx
<48 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
48-168 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
>168 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Recent onset atrial fibrillation for post-cardiac surgery patients	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Duration of current AF episode (hours)			
n	xx	xx	xx
Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Median	xx	xx	xx
Q1, Q3	xx, xx	xx, xx	xx, xx
Min, Max	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx
Duration of current AF episode (hours, categorical)			
n	xx	xx	xx
≤72 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
>72 hours	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Other indication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1]For non-surgery patients: atrial fibrillation ≤ 7 days duration; for post-cardiac surgery patients: atrial fibrillation ≤ 3 days duration.

Table 11 Contraindication for Use in Accordance with Vernakalant Summary of Product Characteristics (SmPC)

Chracteristics	Prospective Patients (N=xxx)	Retrospective Patients (N=xxx)	Analysis Set (N=xxx)
Baseline systolic blood pressure < 100 mmHg (as recorded most immediately prior to initial vernakalant infusion)[1]			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
MI or ACS past 30 days[2]			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe aortic stenosis[2]			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe bradycardia in absence of pacemaker[2]			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Prolonged QT at baseline (uncorrected > 440 msec) in absence of pacemake[3]			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sinus node dysfunction in absence of pacemaker[3]			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Heart block (2nd of 3rd degree) in absence of pacemaker [3]			

Chracteristics	Prospective Patients (N=xxx)	Retrospective Patients (N=xxx)	Analysis Set (N=xxx)
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Heart failure NYHA functional class III or IV[1]			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Use of class I or class III intravenous anti-arrhythmics within four hours prior to the start of vernakalant administration or four hours subsequent to the start of vernakalant administration[4]			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patients with at least one contraindication			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing/Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.
[1]As recorded on the Baseline (Personal Data, Physical Measurements, Vital Signs and Cardiac Info) Case Report Form (CRF)
[2]As recorded on the Baseline (Conditions, Presenting Conditions) CRF.
[3]As recorded on the Baseline (Conditions, Presenting Conditions) or ECG CRF.
[4]As recorded on the Pharmacologic Cardioversion or Concomitant Medication CRF. Class I or class III anti-arrythmics use with missing drug start date/time, vernakalant administration date/time, or route classified as unknown.

Table 12a.1 Frequency of Pharmacological Cardioversion Using Intravenous Anti-Arrhythmics to Restore Sinus Rhythm by Timing in Relation to Vernakalant IV Administration (Analysis Set)

Characteristic	Within 4 hours prior to the start of first vernakalant infusion [1, 2]	Within 4 hours subsequent to the start of first vernakalant infusion [1, 2]	Within 90 minutes subsequent to the start of first vernakalant infusion [1, 2]	Any time during the hospitalisation/medical encounter (but not within 4 hours prior or subsequent to the start of first vernakalant infusion) [1, 2]	Ov
Administration of Other Intravenous Anti-Arrhythmic Agents for Pharmacologic Cardioversion (per patient)					
n	xx	xx	xx	xx	
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Missing	xx	xx	xx	xx	
Number of IV AA Administrations (episodes)	xx	xx	xx	xx	
Type of Rhythm Disorder, if Yes[3]					
n	xx	xx	xx	xx	
Atrial fibrillation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Atrial flutter	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Ventricular tachycardia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Ventricular fibrillation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Missing	xx	xx	xx	xx	
Class of Anti-arrhythmic[3,4]					
n	xx	xx	xx	xx	
IA	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
IB	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
IC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
II	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
III	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
IV	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Other AA/Class V	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Missing	xx	xx	xx	xx	
Intravenous Anti-arrhythmics [3] (Class I & III)					
n	xx	xx	xx	xx	
Class I					
Flecainide	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
<Other class I medications, if used>					

Characteristic	Within 4 hours prior to the start of first vernakalant infusion [1, 2]	Within 4 hours subsequent to the start of first vernakalant infusion [1, 2]	Within 90 minutes subsequent to the start of first vernakalant infusion [1, 2]	Any time during the hospitalisation/medical encounter (but not within 4 hours prior or subsequent to the start of first vernakalant infusion) [1, 2]	Ov
Class III					
Amiodarone	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Ibutilide	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Sotalol	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
< Other class III medications, if used >	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (
Missing	xx	xx	xx	xx	

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1] Includes patients administered IV anti-arryhthmic agents for pharmacological cardioversion during the specified time during the hospitalisation/medical encounter. First column includes administration within 4 hours prior to the start of first vernakalant infusion. Second column includes administration within 4 hours subsequent to the start of first vernakalant infusion. Third column includes administration NOT within 4 hours prior and/or subsequent to the start of first vernakalant infusion.

[2] Retrospective patients may have missing vernakalant administration date/time.

[3] Percentages based on number of IV AA administrations

[4] Based on the ATC classification, except for sotalol. For the purposes of this study, study programmers manually re-classifiedsotalol from ATC code C07AA (Beta Blocking Agents, Non-Selective) to ATC Code C01BD (Antiarrhythmics, Class III) in the analysis datasets as consistent with the Vaughan Williams Classification of Antiarrhythmic Drugs detailed in the SAP.

Template of Table 12a.1 will be applied to the following two tables. Please note: for Table 12a.2, footnote 2 does NOT apply , and all subsequent footnote numbers should be adjusted correspondingly.

Table 12a.2 Frequency of Pharmacological Cardioversion Using Intravenous Anti-Arrhythmics to Restore Sinus Rhythm by Timing in Relation to Vernakalant IV Administration (Prospective Patients)

Table 12a.3 Frequency of Pharmacological Cardioversion Using Intravenous Anti-Arrhythmics to Restore Sinus Rhythm by Timing in Relation to Vernakalant IV Administration (Retrospective Patients)

Table 12b.1 Frequency of Pharmacological Cardioversion Using Oral Anti-Arrhythmics to Restore Sinus Rhythm by Timing in Relation to Vernakalant IV Administration (Analysis Set)

Characteristic	Prior to the start of first vernakalant infusion [1, 2]	Subsequent to the start of first vernakalant infusion [1, 2]	Overall [1]
Administration of Oral Anti-Arrhythmic Agents for Pharmacologic Cardioversion[3] (per patient)			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Number of Oral Anti-arrhythmic Administrations (episodes)	xx	xx	xx
Type of Rhythm Disorder, if Yes [4]			
n	xx	xx	xx
Atrial fibrillation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Atrial flutter	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ventricular tachycardia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ventricular fibrillation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Class of Anti-arrhythmic [4,5]			
n	xx	xx	xx
IA	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
IB	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
IC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
II	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
III	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
IV	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other AA/Class V	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Oral Anti-arrhythmics [4] (Class I)			
n	xx	xx	xx
Flecainide	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Propafenone	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
<other class I medications, if available>	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1] Includes all patients administered oral anti-arryhthmic agents for pharmacological cardioversion at any time during the hospitalisation/medical encounter.

[2] Retrospective patients may have missing vernakalant administration date/time.
[3] The category of oral anti-arrhythmics includes pre-treatment in preparation for electrical cardioversion as well as administration as standalone therapy for cardioversion.
[4] Percentages based on number of oral AA administrations
[5] Based on the ATC classification, except for sotalol. For the purposes of this study, study programmers manually re-classified sotalol from ATC code C07AA (Beta Blocking Agents, Non-Selective) to ATC Code C01BD (Antiarrhythmics, Class III) in the analysis datasets as consistent with the Vaughan Williams Classification of Antiarrhythmic Drugs detailed in the SAP.

Template of Table 12b.1 will be applied to the following two tables. Please note: for Table 12b.2, footnote 2 does NOT apply , and all subsequent footnote numbers should be adjusted correspondingly.

Table 12b.2 Frequency of Pharmacological Cardioversion Using Oral Anti-Arrhythmics to Restore Sinus Rhythm by Timing in Relation to Vernakalant IV Administration (Prospective Patients)

Table 12b.3 Frequency of Pharmacological Cardioversion Using Oral Anti-Arrhythmics to Restore Sinus Rhythm by Timing in Relation to Vernakalant IV Administration (Retrospective Patients)

Table 13a.1 Frequency of Electrical Cardioversion to Restore Sinus Rhythm by Timing in Relation to Vernakalant IV Administration (Analysis Set)

Characteristic	Prior to the start of first vernakalant infusion [1]	Within 90 minutes subsequent to the first vernakalant infusion [1]	Subsequent to the start of first vernakalant infusion [1]	Overall[2]
Electrical Cardioversion				
Electrical Cardioversion Used to Restore Sinus Rhythm (per patient)				
n	xx	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx	xx
Successful Restoration of Sinus Rhythm (per episode)				
n	xx	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx	xx
Number of Shocks Needed for Successful Conversion (per episode)				
n	xx	xx	xx	xx
Mean (SD)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Median	xx	xx	xx	xx
Q1, Q3	xx,xx	xx,xx	xx,xx	xx,xx
Min, Max	xx,xx	xx,xx	xx,xx	xx,xx
Missing	xx	xx	xx	xx
Type of Arrhythmia[3]				
n	xx	xx	xx	xx
Atrial fibrillation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Atrial flutter	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ventricular tachycardia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ventricular fibrillation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx	xx
Type of Electrical Cardioversion [3]				
n	xx	xx	xx	xx
External	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Transvenous	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Transesophageal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx	xx

Characteristic	Prior to the start of first vernakalant infusion [1]	Within 90 minutes subsequent to the first vernakalant infusion [1]	Subsequent to the start of first vernakalant infusion [1]	Overall[2]
Type of defibrillator [3]				
n	xx	xx	xx	xx
Biphasic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Monophasic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx	xx

NOTE: Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted. An EC episode represents a period of EC administration which may be composed on one or multiple shocks.

[1] Retrospective patients may have missing vernakalant administration date/time.
[2] Includes patients with missing electrical cardioversion or timing responses.
[3] Frequency and percentages reported by episode.

Template of Table 13a.1 will be applied to the following two tables. Please note: for Table 13a.2, footnote 1 does NOT apply , and all subsequent footnote numbers should be adjusted correspondingly.

Table 13a.2 Frequency of Electrical Cardioversion to Restore Sinus Rhythm by Timing in Relation to Vernakalant IV Administration (Prospective Patients)

Table 13a.3 Frequency of Electrical Cardioversion to Restore Sinus Rhythm by Timing in Relation to Vernakalant IV Administration (Retrospective Patients)

Table 13b.1 Surgical Procedures at Index Hospitalization by Timing Relation to Vernakalant IV Administration (Analysis Set)

Characteristic	Prior to the start of first vernakalant infusion [1]	Subsequent to the start of first vernakalant infusion [1]	Overall [2]
Any Surgical Procedure (per patient)			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Surgical Procedure [3]			
n	xx	xx	xx
Radiofrequency ablation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Catheter ablation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ablation of AV node with pacemaker	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
High-intensity focused ultra sound ablation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cryoablation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Maze	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Percutaneous intervention (PCI), Angioplasty, or Stent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Heart valve surgery	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Atherectomy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Bypass surgery	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cardiomyoplasy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Heart transplant	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Transmyocardial revascularization (TMR)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pacemaker implantation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Left atrial appendage exclusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ICD implantation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other not specified	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.
[1] Retrospective patients may have missing vernakalant administration date/time.
[2]Includes patients with missing electrical cardioversion, surgical dates, or timing responses.
[3]Frequency and percentages reported by episode.

Template of Table 13b.1 will be applied to the following two tables. Please note: for Table 13b.2 footnote 1 does NOT apply , and all subsequent footnote numbers should be adjusted correspondingly.

Table 13b.2 Surgical Procedures at Index Hospitalization by Timing Relation to Vernakalant IV Administration (Prospective Patients)

Table 13b.3 Surgical Procedures at Index Hospitalization by Timing Relation to Vernakalant IV Administration (Retrospective Patients)

Table 14a.1 Blood Pressure and Cardiac Rhythm Monitoring among Patients Administered Only One Vernakalant IV Infusion (Analysis Set)

	Overall (N = XXX) Time Period		
	During first infusion of vernakalant IV	**During the 15 min. immediately following the completion of the infusion**	**From 15 min. to 2 hours following completion the infusion**
BP monitoring during specified time period			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Frequency of BP monitoring (time interval between BP measurements in minutes)[1,2]			
n	xx[2]	xx[2]	xx[2]
Mean (SD)	xx (xx)	xx (xx)	xx (xx)
Median	xx	xx	xx
Q1, Q3	xx,xx	xx,xx	xx,xx
Min, Max	xx,xx	xx,xx	xx,xx
Missing	xx	xx	xx
BP monitoring performed by healthcare provider[3]			
n	xx	xx	xx
Nurse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physician	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Cardiac rhythm continuous monitoring during specified time period			
n	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx
Cardiac rhythm monitoring performed by healthcare provider[3]			
n	xx	xx	xx
Nurse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physician	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1] Excludes patients for which sites reported verbatim frequencies other than intervals (in minutes) between measurements for all periods during vernakalant infusion through 2 hours following infusion.
[2] The CRF did not specifically capture continuous BP monitoring which occurs at programmed fixed intervals during and after the infusion. In these cases the same fixed BP interval could have been reported throughout the different time periods.
[3] May add up to more than 100% due to multiple applicable rows.

Template of Table 14a.1 will be applied to the following two tables.

Table 14a.2 Blood Pressure and Cardiac Rhythm Monitoring among Patients Administered Only One Vernakalant IV Infusion (Prospective Patients)

Table 14a.3 Blood Pressure and Cardiac Rhythm Monitoring among Patients Administered Only One Vernakalant IV Infusion (Retrospective Patients)

Table 14b.1 Blood Pressure and Cardiac Rhythm Monitoring among Patients Administered Two Vernakalant IV Infusions (within Single Episode of Treatment) (Analysis Set)

	Overall (N = XXX) Time Period				
	During first infusion of vernakalant IV	**During the time between the first and second infusion of vernakalant IV**	**During the second infusion of vernakalant IV**	**During the 15 min. immediately following the completion of the last vernakalant infusion**	**From 15 min. to 2 hours following completion of the last vernakalant IV infusion**
BP monitoring during specified time period					
n	xx	xx	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx	xx	xx
Frequency of BP monitoring (time interval between measurements in minutes)[1,2]					
n	xx[2]	xx[2]	xx[2]	xx[2]	xx[2]
Mean (SD)	xx (xx)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Median	xx	xx	xx	xx	xx
Q1, Q3	xx,xx	xx,xx	xx,xx	xx,xx	xx,xx
Min, Max	xx,xx	xx,xx	xx,xx	xx,xx	xx,xx
Missing	xx	xx	xx	xx	xx
BP monitoring performed by healthcare provider(s)[3]					
n	xx	xx	xx	xx	xx
Nurse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physician					
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx	xx	xx
Continuous cardiac rhythm monitoring during specified time period					
n	xx	xx	xx	xx	xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx	xx	xx
Cardiac rhythm monitoring performed by healthcare provider(s)[3]					
n	xx	xx	xx	xx	xx

	Overall (N = XXX) Time Period				
	During first infusion of vernakalant IV	**During the time between the first and second infusion of vernakalant IV**	**During the second infusion of vernakalant IV**	**During the 15 min. immediately following the completion of the last vernakalant infusion**	**From 15 min. to 2 hours following completion of the last vernakalant IV infusion**
Nurse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physican					
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx	xx	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1] Excludes patients for which sites reported verbatim frequencies other than intervals (in minutes) between measurements for all periods during vernakalant infusion through 2 hours following infusion.

[2] The CRF did not specifically capture continuous BP monitoring which occurs at programmed fixed intervals during and after the infusion. In these cases the same fixed BP interval could have been reported throughout the different time periods.

[3] May add up to more than 100% due to multiple applicable rows.

Template of Table 14b.1 will be applied to the following two tables.

Table 14b.2 Blood Pressure and Cardiac Rhythm Monitoring among Patients Administered Two Vernakalant IV Infusions (within Single Episode of Treatment) (Prospective Patients)

Table 14b.3 Blood Pressure and Cardiac Rhythm Monitoring among Patients Administered Two Vernakalant IV Infusions (within Single Episode of Treatment) (Retrospective Patients)

Table 15a Proportion of Patients Converted to Sinus Rhythm and Time to Conversion Following Vernakalant Infusion

Characteristic	Overall			Prospective Patients			Retrospective Patients		
Conversion to sinus rhythm for at least 1 minute within 90 minutes from start of first infusion within the effectiveness analysis population [2]									
n	xx			xx			xx		
Yes, n (% [95% CI]) [2]	xx (xx.x [xx.x, xx.x])			xx (xx.x [xx.x, xx.x])			xx (xx.x [xx.x, xx.x])		
Time to conversion (minutes) from start of first infusion (among patients with conversion to sinus rhythm for at least 1 minute within 90 minutes from start of first infusion within the effectiveness analysis population)	**All responders**	**Responders (receiving 1 infusion)**	**Responders (receiving 2 infusions)** [1]	**All responders**	**Responders (receiving 1 infusion)**	**Responders (receiving 2 infusions)** [1]	**All responders**	**Responders (receiving 1 infusion)**	**Responders (receiving 2 infusions)** [1]
n	xx	xx	xx	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x

Q1, Q3	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
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx	xx	xx	xx	xx	xx	xx
Conversion to sinus rhythm for at least 1 minute within 90 minutes from start of first infusion among all patients receiving vernakalant excluding those who received ECV or IV Class I/III AA within 90 minutes of vernakalant administration [3]									
n	xx			xx			xx		
Yes, n (% [95% CI]) [3]	xx (xx.x [xx.x, xx.x])			xx (xx.x [xx.x, xx.x])			xx (xx.x [xx.x, xx.x])		
Time to conversion (minutes) from start of first infusion (among patients with conversion to sinus rhythm for at least 1 minute within 90 minutes from start of first infusion among all patients receiving vernakalant	**All responders**	**Responders (receiving 1 infusion)**	**Responders (receiving 2 infusions)** [1]	**All responders**	**Responders (receiving 1 infusion)**	**Responders (receiving 2 infusions)** [1]	**All responders**	**Responders (receiving 1 infusion)**	**Responders (receiving 2 infusions)** [1]

excluding those who received ECV or IV Class I/III AA within 90 minutes of vernakalant administration)									
n	xx	xx	xx	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	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
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx	xx	xx	xx	xx	xx	xx
Conversion to sinus rhythm for at least 1 minute within 90 minutes from start of first infusion among all patients receiving vernakalant excluding those who received ECV or oral propafenone/flecainide or IV Class I/III AA within 90 minutes of vernakalant administration [4]									
n	xx			xx			xx		
Yes, n (% [95% CI]) [4]	xx (xx.x [xx.x, xx.x])			xx (xx.x [xx.x, xx.x])			xx (xx.x [xx.x, xx.x])		

Time to conversion (minutes) from start of first infusion (among patients with conversion to sinus rhythm for at least 1 minute within 90 minutes from start of first infusion among all patients receiving vernakalant excluding those who received ECV or oral propafenone/flecainide or IV Class I/III AA within 90 minutes of vernakalant administration)	**All responders**	**Responders (receiving 1 infusion)**	**Responders (receiving 2 infusions)[1]**	**All responders**	**Responders (receiving 1 infusion)**	**Responders (receiving 2 infusions)[1]**	**All responders**	**Responders (receiving 1 infusion)**	**Responders (receiving 2 infusions)[1]**
n	xx	xx	xx	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	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
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx	xx	xx	xx	xx	xx	xx

Note: Total n for each variable includes non-missing observations. Percentages, where applicable, are calculated with non-missing observations in denominator unless otherwise noted.

[1] Includes patients who receive more than 1 infusion within a single treatment episode.

[2] Rate of conversion (%) is calculated as: (number of patients who have conversion to sinus rhythm for at least one minute with 90 minutes after first vernakalant infusion within effectiveness analysis population) / (total number of patients within effectiveness analysis population) x 100.

[3] Rate of conversion (%) is calculated as: (number of patients who, within 90 minutes after first vernakalant infusion, have conversion to sinus rhythm for at least one minte but have no ECV or IV Class I/III AA within overall analysis population) / (total number of patients within overall analysis population).

[4] Rate of conversion (%) is calculated as: (number of patients who, within 90 minutes after first vernakalant infusion, have conversion to sinus rhythm for at least one minte but have no ECV, oral propafenone/flecainide or IV Class I/III AA within overall analysis population) / (total number of patients within overall analysis population).

Template of Table 15a will be applied to the following three tables.

Table 15b Proportion of Patients Converted to Sinus Rhythm and Time to Conversion Following Vernakalant Infusion (SmPC Subgroup Analysis)

Table 15c Proportion of Patients Converted to Sinus Rhythm and Time to Conversion Following Vernakalant Infusion (Non-Surgery Patients)

Table 15d Proportion of Patients Converted to Sinus Rhythm and Time to Conversion Following Vernakalant Infusion (Post-Cardiac Surgery Patients)

Table 16.1a.1 Serious Adverse Events (System Organ Class and Preferred Term) by Outcome (Analysis Set) – Investigator Assessment

	Analysis Set (N=xxx) Outcome							
	Recovered		Recovered with Sequelae		Not Recovered		Overall	
System Organ Class/ High Level Term/ Preferred Term	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n
Any SAE	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
SOC 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
HLT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
SOC 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
HLT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx

Note: SAE events include reported HOIs that are mapped to specific MedDRA terms.
[1] Cumulative incidence calculated as the number of patients who have SAE starting during the study period, divided by the total number of patients enrolled, multiplied by 100.

Template of Table 16.1a.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively.

Table 16.1a.2 Serious Adverse Events (System Organ Class and Preferred Term) by Outcome (Prospective Patients) – Investigator Assessment

Table 16.1a.3 Serious Adverse Events (System Organ Class and Preferred Term) by Outcome (Retrospective Patients) – Investigator Assessment

Note: According to investigator, two events were reported to include both bradycardia and hypotentsion. Therefore, each event was counted individually in both the hypotension and bradycardia SAE subtotals and in total number of events. Please add this fact as a footnote for Tables 16.1a.1 and 16.1a.2 (since that was a prospective patient).

Table 16.1b.1 Serious Adverse Events (System Organ Class and Preferred Term) by Fatality (Analysis Set) – Investigator Assessment

	Analysis Set (N=xxx) Fatality					
	Fatal Events		Non-Fatal Events		Overall	
System Organ Class/ High Level Term/ Preferred Term	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n
Any SAE	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
SOC 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
HLT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
SOC 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
HLT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx

Note: SAE events include reported HOIs that are mapped to specific MedDRA terms.

[1]Cumulative incidence calculated as the number of patients who have a SAE starting during the study period, divide by the total number of patients enrolled, multiplied by 100.

Template of Table 16.1b.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively.

Table 16.1b.2 Serious Adverse Events (System Organ Class and Preferred Term) by Fatality (Prospective Patients) – Investigator Assessment

Table 16.1b.3 Serious Adverse Events (System Organ Class and Preferred Term) by Fatality (Retrospective Patients) – Investigator Assessment

Note: According to investigator, two events were reported to include both bradycardia and hypotentsion. Therefore, each event was counted individually in both the hypotension and bradycardia SAE subtotals and in total number of events. Please add this fact as a footnote for Tables 16.1b.1 and 16.1b.2 (since that was a prospective patient).

Table 16.1c.1 Serious Adverse Events (System Organ Class and Preferred Term) by Relationship to Vernakalant IV (Analysis Set) – Investigator Assessment

	Analysis Set (N=xxx) Relationship to Vernakalant IV											
	Definitely Related		Probably Related		Possibly Related		Probably Not Related		Defnitely Not Related		Overall	
	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n
Any SAE	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
SOC 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
HLT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
SOC 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
HLT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx

Note: SAE events include reported HOIs that are mapped to specific MedDRA terms.
[1]Cumulative incidence calculated as the number of patients who have a SAE starting during the study period, divide by the total number of patients enrolled, multiplied by 100.

Template of Table 16.1c.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively.

Table 16.1c.2 Serious Adverse Events (System Organ Class and Preferred Term) by Relationship to Vernakalant IV (Prospective Patients) – Investigator Assessment

Table 16.1c.3 Serious Adverse Events (System Organ Class and Preferred Term) by Relationship to Vernakalant IV (Retrospective Patients) –Investigator Assessment

Note: According to investigator, two events were reported to include both bradycardia and hpotentsion. Therefore, each event was counted individually in both the hypotension and bradycardia SAE subtotals and in total number of events. Please add this fact as a footnote for Tables 16.1c.1 and 16.1c.2 (since that was a prospective patient).

Table 16.2a.1 Serious Adverse Events by Outcome (Analysis Set) – SRC Classification

	Analysis Set (N=xxx) Outcome							
	Recovered		**Recovered with Sequelae**		**Not Recovered**		**Overall**	
Verbatim Term	**Patients n (Cumulative Incidence[1])**	**Events n**	**Patients n (Cumulative Incidence[1])**	**Events n**	**Patients n (Cumulative Incidence[1])**	**Events n**	**Patients n (Cumulative Incidence[1])**	**Events n**
Any SAE	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
Verbatim Event Name 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
Verbatim Event Name 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx

[1]Cumulative incidence calculated as the number of patients who have a SAE starting during the study period, divide by the total number of patients enrolled, multiplied by 100.

Template of Table 16.2a.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively.

Table 16.2a.2 Serious Adverse Events by Outcome (Prospective Patients) – SRC Classification

Table 16.2a.3 Serious Adverse Events by Outcome (Retrospective Patients) – SRC Classification

Table 16.2b.1 Serious Adverse Events by Fatality (Analysis Set) – SRC Classification

	Analysis Set (N=xxx) Fatality Status					
	Fatal Events		Non-Fatal Events		Overall	
Verbatim Term	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n
Any SAE	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
Verbatim Event Name 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
Verbatim Event Name 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx

[1]Cumulative incidence calculated as the number of patients who have a SAE starting during the study period, divide by the total number of patients enrolled, multiplied by 100.

Template of Table 16.2b.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively.

Table 16.2b.2 Serious Adverse Events by Fatality (Prospective Patients) – SRC Classification

Table 16.2b.3 Serious Adverse Events by Fatality (Retrospective Patients) – SRC Classification

Table 16.2c.1 Serious Adverse Events by Relationship to Vernakalant IV (Analysis Set) – SRC Classification

	Analysis Set (N=xxx) Relationship to Vernakalant IV											
	Definitely Related		**Probably Related**		**Possibly Related**		**Probably Not Related**		**Definitely Not Related**		**Overall**	
Verbatim	**Patients n (Cumulative Incidence[1])**	**Events n**	**Patients n (Cumulative Incidence[1])**	**Events n**	**Patients n (Cumulative Incidence[1])**	**Events n**	**Patients n (Cumulative Incidence[1])**	**Events n**	**Patients n (Cumulative Incidence[1])**	**Events n**	**Patients n (Cumulative Incidence[1])**	**Events n**
Any SAE	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
Verbatim Event Name 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
Verbatim Event Name 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx

[1]Cumulative incidence calculated as the number of patients who have a SAE starting during the study period, divide by the total number of patients enrolled, multiplied by 100.

Template of Table 16.2c.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively.

Table 16.2c.2 Serious Adverse Events by Relationship to Vernakalant IV (Prospective Patients) – SRC Classification

Table 16.2c.3 Serious Adverse Events by Relationship to Vernakalant IV (Retrospective Patients) – SRC Classification

Table 16.3.1 Incidence of Bradycardia Events of Special Interest by Time since Start of First Infusion – Investigator Assessment (Analysis Set)

	Time Since First Vernakalant Infusion											
	0 - < 2 hours from start of first infusion (N=xxx)			2- < 4 hours from start of first infusion (N=xxx)			4- 24 hours from start of first infusion (N=xxx)			Overall (N=xxx)		
Bradycardia Event	**Patients n**	**Incidence (95% CI)[1]**	**Events n**	**Patients n**	**Incidence (95% CI)[1]**	**Events n**	**Patients n**	**Incidence (95% CI)[1]**	**Events n**	**Patients n**	**Incidence (95% CI)[2]**	**Events n**
Bradycardia following conversion due to vernakalant IV administration [2]	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx
Bradycardia following pharmacological cardioversion [3]	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx
Bradycardia following electrical cardioversion [4]	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx
Bradycardia Associated with Hypotension [5]	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx	xx	x.x (x.x – x.x)	xx

[1]Cumulative incidence calculated as the number of patients who have a specific pre-specified event starting during the study period, divided by the total number of patients enrolled, multiplied by 100.
[2]Includes all bradycardia SAEs which occurred after the date and time of conversion due to vernakalant IV administration.
[3]Includes all bradycardia SAEs which occurred after the date and time of pharmacological cardioversion.
[4]Includes all bradycardia SAEs which occurred after the stop date and time of the last shock of electrical cardioversion administration.
[5]Includes all bradycardia SAEs which occurred with hypotension during the same episode.

Template of Table 16.3.1 will be applied to the following two tables.

Table 16.3.2 Incidence of Bradycardia Events of Special Interest by Time since Start of First Infusion – Investigator Assessment (Prospective Patients)

Table 16.3.3 Incidence of Bradycardia Events of Special Interest by Time since Start of First Infusion – Investigator Assessment (Retrospective Patients)

Table 17.1 Non-Serious Adverse Events by System Organ Class (SOC) and Preferred Term (PT) (Final Report) – Analysis Set

	Time Since First Vernakalant Infusion							
	0 - < 2 hours from start of first infusion (N=xxx)[1]		2- < 4 hours from start of first infusion (N=xxx)[1]		4- 24 hours from start of first infusion (N=xxx)[1]		Overall (N=xxx)	
	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n	Patients n (Cumulative Incidence[1])	Events n
Any NSAE	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
SOC 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
HLT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
SOC 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
HLT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 1	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx
PT 2	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx	xx (x.x%)	xx

[1]Cumulative incidence calculated as the number of patients who have a specific pre-specified event starting during the study period, divide by the total number of patients enrolled, multiplied by 100.

Template of Table 17.1 will be applied to the following two tables. Please make sure in the header "Analysis Set" is changed to "Prospective Patients" and "Retrospective Patients", respectively.

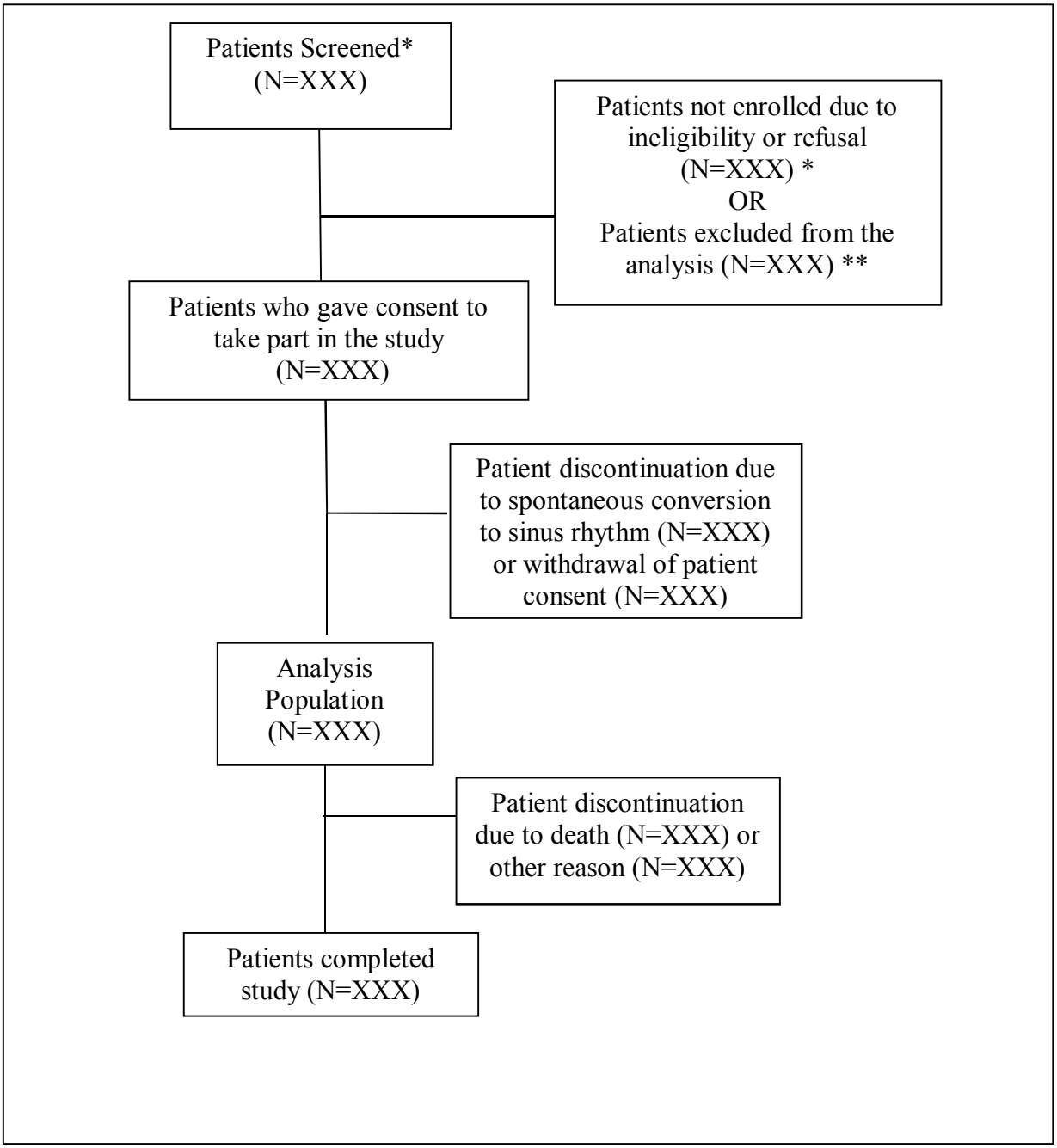
Table 17.2 Non-Serious Adverse Events by System Organ Class (SOC) andPreferred Term (PT) (Final Report) – Prospective Patients

Table 17.3 Non-Serious Adverse Events by System Organ Class (SOC) and Preferred Term (PT) (Final Report) – Retrospective Patients

Table 18 Number of Patients with Missing Information for Selected Critical Fields

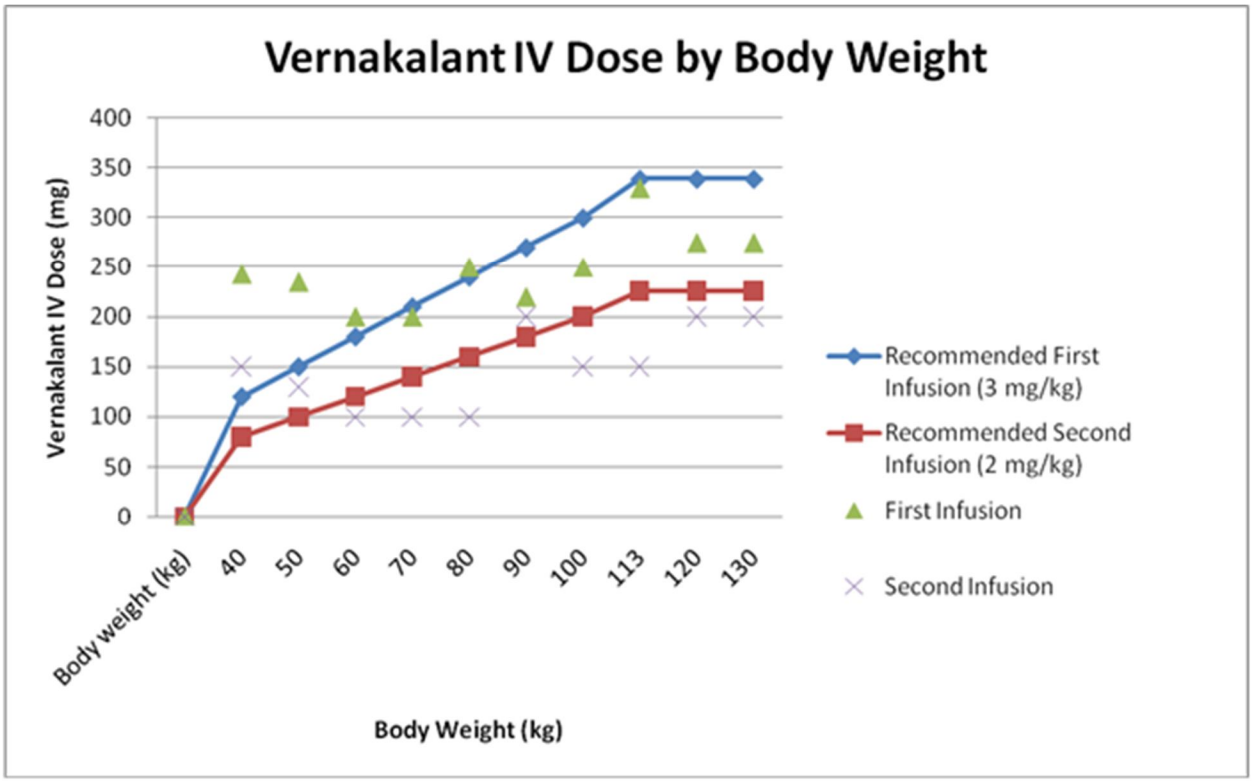
Critical Field	Prospective Patients (N=xxx)	Retrospective Patients (N=xxx)	Analysis Set (N=xxx)
Height	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
NYHA Heart Failure Class	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Smoking Status	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stop Time (for each infusion)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Time to Cardioversion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Duration and/or Frequency of Blood Pressure Measurement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
During Each Infusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
During 15-Minute Post-Infusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Up to Two Hours up to Post-Infusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type of Health Provider of Blood Pressure Measurement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type and/or Duration of Cardiac Rhythm Monitoring	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
During Each Infusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Up to Two Hours up to Post-Infusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type of Health Provider of Cardiac Rhythm Monitoring	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Figure 1 Patient Disposition Flow Chart



*Data source for number of patients screened and number of patients enrolled due to ineligibility or refusal data is study screening log.

Figure 2.1 Vernakalant IV Dose by Body Weight (Analysis Set)



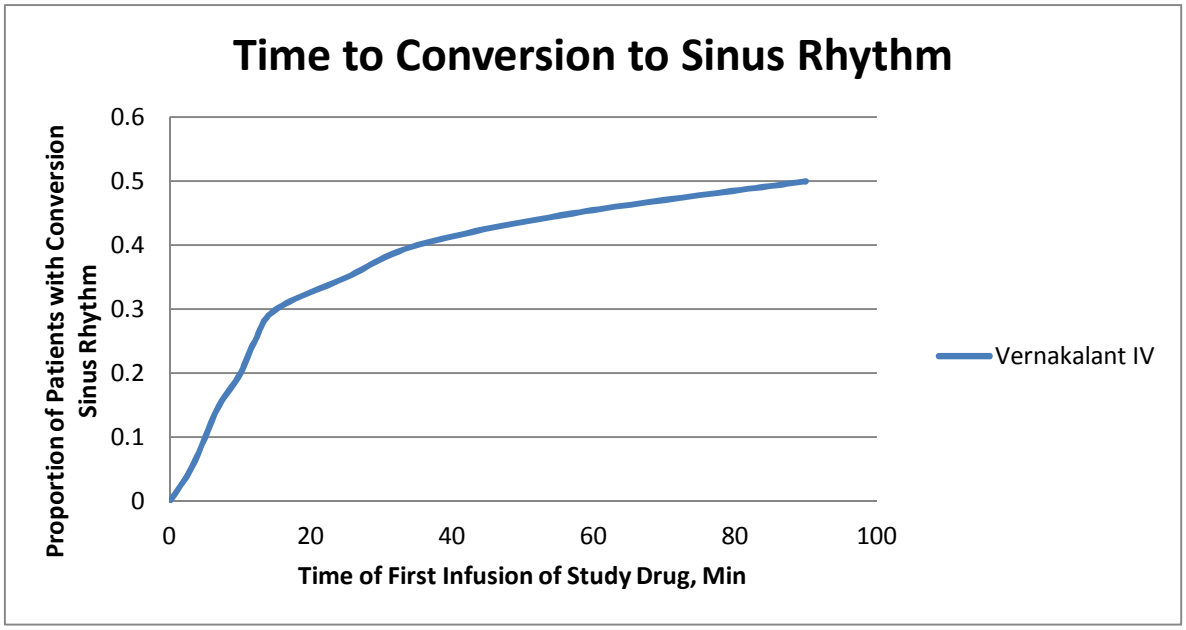
Note: Figure is for illustrative purposes, and is not based on actual data (e.g., weight of zero kg). Actual figure will use jittering to accommodate overlapping data points.

Template of Figure 2.1 will be applied to the following two figures.

Figure 2.2 **Vernakalant IV Dose by Body Weight (Prosective Patients)**

Figure 2.3 **Vernakalant IV Dose by Body Weight (Retrospective Patients)**

Figure 3.1 Time to Conversion to Sinus Rhythm with Vernakalant IV (Analysis Set)



Note: Figure is for illustrative purposes, and is not based actual data
[1]Time to conversion is expressed as the duration between start times of infusion to time of conversion to sinus rhythm for patients receiving one or two infusions.

Template of Figure 3.1 will be applied to the following two figures.

Figure 3.2 Time to Conversion to Sinus Rhythm with Vernakalant IV (Prospective Patients)

Figure 3.3 Time to Conversion to Sinus Rhythm with Vernakalant IV (Retrospective Patients)

Listing A Health Outcomes of Interest (HOIs) and Serious Adverse Events (SAEs) Reported for the Study

Site	Patient ID	Patient Type	Verbatim Event Term	MedDRA PT term	Study-defined HOI[1]	SRC event term	SRC-defined HOI[2]	Contra-Indication	Event occurred since Last Interim Report

[1]Study Defined HOIs are included in Table 8.1 series and the Listing 1 series

[2]SRC-defined HOIs are included in Table 8.2 series

Listing 1a Health Outcomes of Interest (HOI) – Investigator Assessment

Site	Patient ID	Patient Type	Age (yrs)	Gender	Country	Percentage of Weight-Based Dosing Recommendation > 110%		HOI (MedDRA PT Term)	SRC HOI Designation	SRC Adjudication Term	Onset date/ time	Timing in relation to start of first infusion (Min)	
						First Infusion	Second Infusion						
				Male, Female		Yes, No	Yes, No						

Site	Patient ID	Patient Type	Age (yrs)	Gender	Country	Stop date/time	Duration of HOI (hours)	Initial vernakalant IV infusion (Dose 1 in mg/kg)	Second vernakalant IV infusion (Dose 2 in mg/kg)	Contraindica
				Male, Female						

Note: Prior medical history and concomitant therapies deemed to be relevant to the presentation of each HOI will be included in the narrative summaries in Listing 1b.

Listing 1b Health Outcomes of Interest (HOI) Narratives – Investigator Assessment

Site	Patient ID	Patient Type	Site Reported HOI	Investigator Narrative[1]	Medical Monitor Narrative[2]
			Yes/No		

[1] Narrative provided by site as reported in the SAE CRF.
[2]Clinical narrative provided by Medical Monitor.

Listing 2a Serious Adverse Events (SAEs) – Investigator Assessment

Site	Patient ID	Patient Type	Age (yrs)	Gender	Country	Percentage of Weight-Based Dosing Recommendation > 110%		MedDRA Term			SRC HOI Designation	SRC Adjudication Term
						First Infusion	First Infusion	SOC	HLT	PT		
				Male, Female		Yes, No	Yes, No					

Site	Patient ID	Patient Type	Age (yrs)	Gender	Country	Initial vernakalant IV infusion (Dose 1)	Second vernakalant IV infusion (Dose 2)	Onset date/ time	Stop date/ time	Timing (Min) in relation to start of first infusion	Relationship to vernakalant IV	AE outcome	AE result	SRC Adjudication Term
				Male, Female					Y/N					

Note: Prior medical history and concomitant therapies deemed to be relevant to the presentation of each HOI will be included in the narrative summaries in Listing 2b.

Listing 2b Serious Adverse Events (SAEs) Narratives – Investigator Assessment

Site	Patient ID	Patient Type	MedDRA Term			HOI[1]	Investigator Narrative[2]	Medical Monitor Narrative[3]
			SOC	HLT	PT			
						Yes/no		

[1] Indicates whether SAE met definition of HOI (Yes or No)
[2] Narrative provided by site as reported in the SAE CRF.
[3] Clinical narrative provided by Medical Monitor.

Listing 3 Non-Serious Adverse Events (AEs) (Final Report)

Site	Patient ID	Patient Type	Age (yrs)	Gender	Country	Initial vernakalant IV infusion (Dose1)	Second vernakalant IV infusion (Dose 2)	MedDRA Term	Relationship to vernakalant IV	AE outcome	Onset date/ Stop date	Timing in relation to start of first infusion (Min)
				Male, Female				SOC HLT PT	Definitely related, probably related, possibly related, probably not related, definitely not related	Recovered, Recovered w/sequelae, Not recovered		

Site	Patient ID	Patient Type	Age (yrs)	Gender	Country	Contraindication (s)
				Male, Female		

Listing 4 Study Discontinuation

Site	Patient ID	Patient Type	Age (yrs)	Gender	Country	Date/time of discontinuation	Reason for discontinuation
				Male, Female			Withdrawal of patient consent, conversion of sinus rhythm before vernakalant IV administration, , death, other

Listing 5a Vernakalant IV Administration Among Patients with Vernakalant Stopped Prematurely (exploratory)

Site	Patient ID	Patient Type	Age (yrs)	Gender	Weight (kg)	Country	Number of infusions	Dose in mg (1st infusion)	Dose in mg (2nd infusion)	Dose in mg/kg (1st infusion)	Dose in mg/kg (2nd infusion)	Reason vernakalant stopped prematurely
				Male, Female								

Listing 5b Vernakalant IV Administration Among Patients who Infused Shorter than 9 Minutes for First Infusion

Site	Patient ID	Patient Type	Age (yrs)	Gender	Weight (kg)	Country	Number of infusions	Dose in mg	Dose in mg/kg	Percentage of weight-based dosing recommendation	Duration (min)
				Male, Female							

Listing 5c Vernakalant IV Administration Among Patients who Infused Shorter than 9 Minutes for Second Infusion

Site	Patient ID	Patient Type	Age (yrs)	Gender	Weight (kg)	Country	Number of infusions	Dose in mg	Dose in mg/kg	Percentage of weight-based dosing recommendation	Duration (min)
				Male, Female							

Listing 5d Vernakalant IV Administration Among Patients for First Infusion and Second Infusion with Percentage of weight-based dosing recommendation > 105%

Site	Patient ID	Patient Type	Contraindication(s)	SAE	Number of infusions	Dose in mg (1st infusion)	Dose in mg/kg (1st infusion)	Percentage of weight-based dosing recommendation (1st infusion)	Duration (min) (1st infusion)	Dose in mg (2nd infusion)	Dose in mg/kg (2nd infusion)	Percentage of weight-based dosing recommendation (2nd infusion)	D (m in

Listing 6 Enrolment Profile for Patients with Multiple Treatment Episodes in Registry

Patient Label[1]	Current ID Number (Patient ID, Site ID)[1]	Patient Type	Age (yrs)	Gender	Country	Number of Treatment Episode[2]	Informed Consent Dates
				Male, Female			

[1]Patient label is a unique patient identifier for each patient, current ID represents study ID number assigned during current (latest) vernakalant episode.
[2]Treatment Episode may be inclusive of more than 1 vernakalant infusion.
A patient may have patient ID unavailable for certain treatment episode therefore only one record is listed here.

Listing 7 Health Outcomes of Interest (HOI) for Patients with Multiple Treatment Episodes in Registry

Patient Label[1]	Current ID Number (Patient ID, Site ID)[1]	Patient Type	Age (yrs)	Gender	Country	Total Number of Previous Treatment Episodes[2]	Time (days) between Current and Previous Treatment Episode[3]	HOI (MedDRA PT Term)	Onset date/ time	Timing(min) in relation to start of first infusion	Relatedness
				Male, Female							

Patient Label[1]	Current ID Number (Patient ID, Site ID)	Patient Type	Age (yrs)	Gender	Country	Stop date/time	Duration of HOI	Contraindication(s)	SRC HOI Designation	SRC Adjudication Term
				Male, Female					Y/N	

[1]HOIs for each patient ID listed on separate rows. Patient label is a unique patient identifier for each patient, current ID represents study ID number assigned during current treatment episode in which HOI occurred.
[2]Treatment Episode may be inclusive of more than 1 vernakalant infusion.
[3] Based on informed consent dates for each vernakalant treatment episode.

Listing 8 Serious Adverse Events (SAEs) for Patients with Multiple Vernakalant Administrations Enrolled in Registry

Patient Label[1]	Current ID Number (Patient ID, Site ID)[1]	Patient Type	Age (yrs)	Gender	Country	Total Number of Previous Treatment Episode[2]	Time (days) between Current and Previous Treatment Episode [3]	MedDRA Term			Relatedness	AE outcon
								SOC	HLT	PT		
				Male, Female								

Patient Label[1]	Current ID Number (Patient ID, Site ID)[1]	Patient Type	Age (yrs)	Gender	Country	Timing (Min) in relation to start of first infusion	Onset date	Stop date	Contraindication(s)	SRC HOI Designation	SRC Adjudica Term
				Male, Female						Y/N	

[1]SAEs for each patient ID listed on separate rows. Patient label is a unique patient identifier for each patient, current ID represents study ID number assigned during current vernakalant treatment episode in which SAE occurred.
[2]Treatment Episode may be inclusive of more than 1 vernakalant infusion.
[3]Based on informed consent dates for each treatment episode.

Country-Specific Tables

The following tables will be displayed for each country:

- Table 1.2 Use of Pre-Infusion Checklist Prior to Vernakalant IV
- Table 1.3 Receipt of Healthcare Provider (HCP) Educational Card, by Site
- Table 4.1 Patient Demographics
- Table 5 Other Baseline Presenting Conditions and Medical History
- Table 9.1 Vernakalant IV Administration and Dosing (Overall)
- Table 9.2 Vernakalant IV Administration and Dosing (Prospective Patients)
- Table 9.3 Vernakalant IV Administration and Dosing (Retrospective Patients)
- Table 10 Patient Age and Therapeutic Indication for Use in Accordance with the Vernakalant IV Summary of Product Characteristics
- Table 11 Contraindications for Use in Accordance with the Vernakalant IV Summary of Product Characteristics

These country-specific tables will be structured in the same format as the tables for the overall population. The table title will be the original table title plus country name, and the table number for a country-specific table will be like Table x.y, where "Table x" is the number of the original table. For example, if the first country in alphabetical order is Austria, it will be "Table 1.2.1 Use of Pre-Infusion Checklist Prior to Vernakalant IV – Austria".

APPENDIX 2. SERIOUS ADVERSE EVENTS INVOLVING BRADYCARDIA

Serious Adverse Events	MedDRA PT Term	MedDRA PT Numeric Term
Verbatim bradycardia terms:		
Bradycardia	Bradycardia	10006093
Heart rate decreased	Heart rate decreased	10019301
Electrocardiogram RR interval prolonged	Electrocardiogram RR interval prolonged	10067652
Bradyarrhythmia SMQ: (standardized Medical Dictionary for Regulatory Activities [MedDRA] Query)		
Accessory cardiac pathway*	Accessory cardiac pathway	10067618
Adams-Stokes syndrome	Adams-Stokes syndrome	10001115
Agonal rhythm	Agonal rhythm	10054015
Atrial conduction time prolongation	Atrial conduction time prolongation	10064191
Atrioventricular block	Atrioventricular block	10003671
Atrioventricular block complete	Atrioventricular block complete	10003673
Atrioventricular block first degree*	Atrioventricular block first degree	10003674
Atrioventricular block second degree	Atrioventricular block second degree	10003677
Atrioventricular conduction time shortened*	Atrioventricular conduction time shortened	10068180
Atrioventricular dissociation	Atrioventricular dissociation	10069571
Bifascicular block*	Bifascicular block	10057393
Bradyarrhythmia	Bradyarrhythmia	10049765
Brugada syndrome*	Brugada syndrome	10059027
Bundle branch block*	Bundle branch block	10006578

Bundle branch block bilateral*	Bundle branch block bilateral	10006579
Bundle branch block left*	Bundle branch block left	10006580
Bundle branch block right*	Bundle branch block right	10006582
Conduction disorder*	Conduction disorder	10010276
Electrocardiogram delta waves abnormal*	Electrocardiogram delta waves abnormal	10014372
Electrocardiogram PQ interval prolonged*	Electrocardiogram PQ interval prolonged	10053656
Electrocardiogram PR prolongation*	Electrocardiogram PR prolongation	10053657
Electrocardiogram PR shortened*	Electrocardiogram PR shortened	10014374
Electrocardiogram QRS complex prolonged*	Electrocardiogram QRS complex prolonged	10014380
Electrocardiogram QT prolonged*	Electrocardiogram QT prolonged	10014387
Electrocardiogram repolarisation abnormality*	Electrocardiogram repolarisation abnormality	10052464
Lenegre's disease*	Lenegre’s disease	10071710
Long QT syndrome*	Long QT syndrome	10024803
Nodal arrhythmia	Nodal arrhythmia	10029458
Nodal rhythm*	Nodal rhythm	10029470
Sick sinus syndrome	Sick sinus syndrome	10040639
Sinoatrial block*	Sinoatrial block	10040736
Sinus arrest	Sinus arrest	10040738
Sinus arrhythmia	Sinus arrhythmia	10040739
Sinus bradycardia	Sinus bradycardia	10040741
Trifascicular block*	Trifascicular block	10044644
Ventricular asystole	Ventricular asystole	10047284

Ventricular dyssynchrony*	Ventricular dyssynchrony	10071186
Wandering pacemaker*	Wandering pacemaker	10047818
Wolff-Parkinson-White syndrome*	Wolff-Parkinson-White syndrome	10048015
Bradycardia cases coded with the term:		
Cardiac arrest	Cardiac arrest	10007515

*These terms are included in the definition for SAEs involving bradycardia prior to the interim analyses for 2015, and are not included in the definition for SAEs involving bradycardia thereafter.