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Table of Content

1. Introduction

The aim of this document is to provide detailed instructions on all mandatory descriptive and inferential statistical analyses for the Clinical Investigation Report.

The text contains verbatim excerpts from the CIP. Such excerpts are italicized with grey background; e.g.

This study is designed as post market clinical follow-up study to identify and evaluate residual risks associated with the use of the Ilivia ICD family and the Plexa ICD lead that are unveiled…

The main aspects and the design of the clinical investigation are presented in chapters 2 to 4.

General statistical procedures are summarized in chapter 5. Those methods are used in case there is no other instruction within this document.

Definitions of the specific dates, e.g. effective randomization and termination are presented in chapter 0.

Specific analysis sets are defined in chapter 7.

General data for the complete study are handled in chapter 8. Data related to the Ilivia group and for the Plexa group are handled separately in the subsequent chapters.

Thereby the following statistical considerations are specified:

- Definition of the analysis set for the following analyzes, e.g. excluding patients without any measured or imputed data for this endpoint.
- Definition of the endpoint(s) to be analyzed including references to the source data, e.g. CRF sheet and item.
- Treatment of missing and spurious data for evaluation of the above endpoint(s).
- Exclusion of particular information from the evaluation of the above endpoint(s) in addition to the exclusion of patients from the analysis set.
- Descriptive analyses including tables and figures
- Statistical alternative hypothesis/hypotheses (HA) to analyze the above endpoint(s).
- Statistical tests intended to analyze the above hypothesis/hypotheses.

All variables are defined in tables using the following columns:

Data file	Name of a data file exported from the CDMS with one data row per unique identifier (e.g. patient specific "patient_display_ID_full"). Additionally, a new data file ("data_SAR") is generated by merging all relevant data from the original CDMS data files and generating derived variables (e.g. BMI from weight and height or date of first AE episode)
Descriptive	Information whether data has to be presented with descriptive methods as defined in the following sub-chapter ("Yes") or data needed for generating of derived variables only ("No")
Variable name	Original name of a variable in the CDMS data file or name of a derived variables (indicated with a suffix "_SAR");
Variable label	Variable label which might be shortened ("…") if remaining clear; note that original labels from the CDMS data will be used for generating the Statistical Analysis Report unless a new label is defined in this document ("NEW")
Variable level	Nominal, ordinal, scale (metric, continuous), or date
Nominal values	Values might be shortened ("…") if remaining clear; note that original values from CDMS data will be used for generating the Statistical Analysis Report unless new nominal values are defined in this document ("NEW"); for numeric data this information is not applicable (n.a.)

Data file, unique identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values

2. Objectives

CIP chapter 7.1 Objectives

This study is designed as post market clinical follow-up study to identify and evaluate residual risks associated with the use of the Ilivia ICD family and the Plexa ICD lead that are unveiled or remained even after risk analysis, risk mitigation and successful conformity assessment. Furthermore, the study aims at providing additional data, as required by regulatory authorities.

3. Investigational Device

CIP chapter 4.7. Definition of the investigational Devices

4.7.1 Ilivia ICD family

The Ilivia/Intica/Inlexa ICD family includes the following devices:

- *Ilivia 7 VR-T, VR-T DX, DR-T and HF-T QP*
- *Intica 7 VR-T, VR-T DX, DR-T and HF-T QP*
- *Intica 5 VR-T, VR-T DX, DR-T*
- *Inlexa 7 VR-T, VR-T DX, DR-T and HF-T QP*

4.7.7 Plexa ICD lead

4. Design

CIP chapter 8. Design of the Clinical Investigation

*The study is designed as a multicenter, international, non-randomized, open-label and prospective study including two subgroups: **group A** with the Ilivia ICD family and **group B** with the Plexa right ventricular ICD lead. Patients can be enrolled into both groups, if they receive both study devices, see below for more details.*

Group A

Ilivia ICD family

Enrollment:

In group A, a total of 105 patients will be enrolled. With an expected drop-out rate of 10% a minimum number of 94 patients will be included in the analysis set. In total, 26 patients should receive a single chamber ICD, 26 patients a dual chamber ICD and 53 patients a triple chamber ICD (CRT-D).

Group B

Plexa ICD lead

Enrollment:

In group B, a total number of 185 patients will be enrolled. With an expected drop-out rate of 10% a mimimum number of 166 patients will be included in the analysis set.

Tab. 4: Required visit windows (1 month is defined as 30 days)

	Window	Days post-implant
Pre-hospital discharge or wound check	+ 10 days	0 to 10
3 months post-implant	± 30 days	61 to 121
6 months post-implant	± 30 days	151 to 211

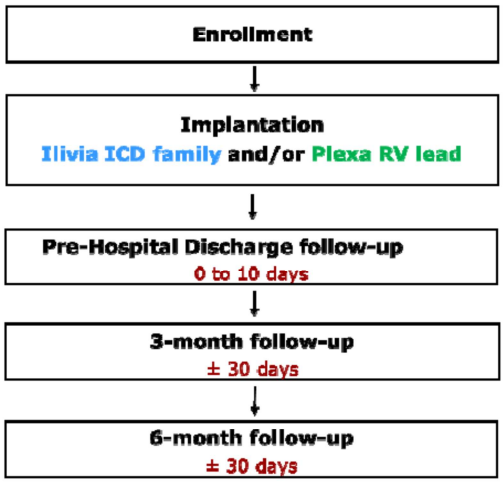

Fig. 4: Follow-up scheme of group A (Ilivia ICD family) and group B (Plexa ICD lead)

Fig. 5: Overlap of both study groups. Patients implanted with an ICD device of the Ilivia family and a Plexa ICD lead can belong to both groups A and B

5. General Statistical Procedures

5.1. Descriptive analyses

CIP chapter 11.1 Statistical design, methods and analytical procedures

For continuous variables descriptive statistics (mean, standard deviation, minimum, 1. quartile, median, 3. quartile and maximum) will be calculated. For nominal variables absolute numbers and relative frequencies based on the non-missing data will be determined. ~~Ordinal data are described by the 1. quartile, median, and 3. quartile as well as the absolute numbers and relative frequencies based on the non-missing data of each category~~

Ordinal data are described by the absolute numbers and relative frequencies based on the non-missing data of each category and by the 1.quartile, median and 3. quartile, when appropriate.
For illustration, see the following standard tables based on dummy data.

Nominal - dichotomous

Variable label	Category	Missing data	Non-missing data	Absolute frequency	Relative frequency [%]
Sex	Female	1	9	5	55.6
History of AF	Yes	2	8	4	50.0

Nominal – more than two categories

NYHA class, all patients	Absolute frequency	Relative frequency [%]
NYHA I	5	62.5
NYHA II	1	12.5
NYHA III	1	12.5
NYHA IV	1	12.5
Sum	8	100.0

NYHA class, all patients; N total =10; N missing = 2

Scale / metric

Variable	N non-missing	N missing	Mean	SD	Min	Lower quartile	Median	Upper quartile	Max
Age [years]	7	3	51.7	15.0	25.0	40.0	57.0	60.0	70.0
Height [cm]	8	2	177.3	14.4	150.0	170.0	179.0	187.5	195.0
Weight [kg]	7	3	77.1	14.5	55.0	69.0	77.0	90.0	99.0

Ordinal

Variable	N non-missing	N missing	Min	Lower quartile	Median	Upper quartile	Max
NYHA class	8	2	1.0	1.0	1.0	2.5	4.0
Patient self assessment	8	2	1.0	1.0	1.0	2.0	3.0

5.2. Inferential analyses

CIP chapter 11.1 Statistical design, method and analytical procedures

For both primary hypotheses exact binomial tests are carried out. All endpoints are analysed per-protocol (PP), whereby the analysis sets are defined for each hypothesis separately.

5.3. Significance level

CIP chapter 11.3 Level of significance and the power of the study

The 2-sided level of significance is alpha = 2.5% for each alternative hypothesis (1-sided 1.25% significance level). Thus, the 2-sided significance level of the global hypothesis of 5% (1-sided 2.5% significance level) is maintained

5.4. Missing Data

CIP chapter 11.11 Handling of missing, unused and spurious data

Missing or spurious data will not be imputed.

Spurious data, which were not clarified by the query process before CDMS closure, are indicated. If appropriate, descriptive and inferential analyses are performed both with and without such data.

5.5. Exclusion of data from confirmatory data analysis

CIP chapter 11.12 Exclusion of data from the confirmatory data analysis

If the patient has atrial fibrillation during the device based measurements, the P-wave amplitude and the atrial threshold are not included in the analysis. Protocol deviations in regard to the follow-up schedule will not result in an exclusion of data in the analysis but will be subject to query management.

If the patient has atrial fibrillation during the device based measurements, data are classified as „not measurable: no p-wave visible" in the CRFs.

5.6. Subgroups

CIP chapter 11.9 Specification of subgroups

Results of the Ilivia ICD family and the Plexa ICD lead are analysed separately. No further subgroup analysis is planned.

5.7. Interim analyses

CIP chapter 11.6 Provision of an Interim analysis

In the BIO|MASTER.Ilivia Family / Plexa study no interim analysis is planned to accept the primary alternative hypothesis, e.g. like in a group-sequential design. However, in case of a significant discrepancy of the enrollment periods between both groups, the first group may be analyzed prior to the overall final analysis. This kind of preliminary analysis would not bias the analysis of the other group, as the hypotheses of both groups are analyzed independently. The preliminary analysis of one group (after completion of data collection for this group) would not constitute a multiple interim testing and therefore does not necessitate further statistical adjustment.

Additionally, specific data will be provided to the Australian competent authorities based on a database-freeze planned Q4 2016. This kind of preliminary analysis would not bias the further data because no investigator except the Coordination Investigator will be informed about the results. Except for safety reasons, no instruction for the further conductance of the clinical investigations will be made based on the preliminary analysis.

During the course of the study, some data may be entered in the CDMS with the signature of the investigator missing. Such data are excluded from the analysis. The following tables define which record status values are considered confirmed or not confirmed.

Variable name	Nominal vales	Variable name	Nominal vales
record_status_text	Record complete Record contains errors Open query Answered query	record_status	1 3 1149 1150

Datasets not confirmed by the investigator

Variable name	Nominal vales	Variable name	Nominal vales
record_status_text	Investigator signed Monitor approved Record Clean Field Monitor approved	record_status	1047 1051 1052 1082

Datasets confirmed by the investigator[1]

5.8. Software

All analyses will be carried out using validated software, e.g. SAS version 9.4 or upgrades.

[1] Note that all data can be changed based on query management before CDMS closure.

6. Specific Study Dates

6.1. Enrollment date

CIP chapter 8.8.5 Point of enrollment and study termination

The point of enrollment is defined as the date of signature of the informed consent form by the patient. Study related procedures, documentation and collection/following of adverse events will start from this day on.

Data file, unique identifier patient_display_id_full	Variable name	Variable label	Variable level	Nominal values
enrollment	dmicdtc	Patient: Date of IC signature	date	n.a.

6.2. Implantation Date

Data file, unique identifier patient_display_id_full	Variable name	Variable label	Variable level	Nominal values
implantation_general_data	imp_visdate	Date of implantation of Ilivia and Plexa	date	n.a.

6.3. Termination Date

CIP chapter 8.8.5 Point of enrollment and study termination

The point of study termination is defined as date of 6-month follow-up for patients with regular study termination. For a non-regular study termination, the following rules apply:

- *If none of the investigational devices could successfully be implanted, date of study termination should be the date of the last unsuccessful implantation attempt.*
- *In case of replacement or repositioning of the Plexa ICD lead in patients of Group B date of study termination should be date of revision.*
- *In case of withdrawal of a patient's consent, date of study termination should be the date of withdrawal of consent.*
- *In case of patient death, the date of study termination should be the date of the patient's death.*
- *If patient is lost to follow-up, date of termination should be the date of last contact of the physician to the patient.*
- *If patient is defined as drop-out patient for any other reason, date of study termination should be the date of latest medical information of the patient (e.g. follow-up, IEGM).*

Ilivia Termination Date

Data file, identifier patient_display_id_full	Variable name	Variable label	Variable level	Nominal values
study_termination	end_visdate	Date of study termination	date	n.a.
study_termination	end_group_term	Was group participation in one of the groups already terminated before the overall termination date?	nominal	No Yes, group A terminated Yes, group B terminated
study_termination	end_group_term_date	Date of group specific termination	date	n.a.
data_SAR	enddate_Ilivia_SAR[2]	Date of Ilivia study termination	date	n.a.

Plexa Termination Date

Data file, identifier patient_display_id_full	Variable name	Variable label	Variable level	Nominal values
data_SAR	enddate_Plexa_SAR[3]	Date of Plexa study termination	date	n.a.

7. Analysis Sets

7.1. Full Analysis Set

Data file, identifier patient_display_id_full	Variable name	Variable label	Variable level	Nominal values
enrollment	DMSUBIC	Patient has provided written informed consent	nominal	Yes /No
data_SAR	analysis_set_full_SAR[4]	Full analysis set	nominal	Yes / No

[2] IF end_group_term = Yes, group A terminated
THEN enddate_Ilivia_SAR = end_group_term_date
ELSE enddate_Ilivia_SAR = end_visdate

[3] IF end_group_term = Yes, group B terminated
THEN enddate_Plexa_SAR = end_group_term_date
ELSE enddate_Plexa_SAR = end_visdate

[4] IF DMSUBIC = Yes
THEN analysis_set_full_SAR = Yes
ELSE analysis_set_full_SAR = No

7.2. Ilivia Analysis Set

The analysis set Ilivia consists of all patients in group A and in group AB, who met all in- and exclusion criteria. Patients who did not come in contact with any Ilivia device are not included in the analysis set.

Data file, identifier patient_display_id_full	Variable name	Variable label	Variable level	Nominal values
enrollment	DMSUBIC	Patient has provided written informed consent	nominal	Yes /No
enrollment	TIINCL01 TIINCL02 TIINCL03 TIINCL04 TIINCL05 TIINCL06	Inclusion criteria […]	nominal	Yes /No
enrollment	TIEXCL01 TIEXCL02 TIEXCL03 TIEXCL04 TIEXCL05 TIEXCL06 TIEXCL07	Exclusion criteria […]	nominal	Yes /No
implantation_general_data	imp_group	Patient Group		Device of the Ilivia family (group A) Plexa right ventricular lead (group B) Both Ilivia and Plexa (group AB)
study_termination	end_early_a	Reason for early study termination	nominal	Implantation of Ilivia ICD family was planned but not performed (patient did not come in contact with the investigational device) […]
study_termination	end_early_ab	Reason for early study termination	nominal	Implantation of Ilivia ICD family and Plexa lead were planned but not performed (patient did not come in contact with the investigational devices) […]
data_SAR	analysis_set_Ilivia_SAR[5]	Analysis set Ilivia	nominal	Yes / No

A list of all patients with early drop-out with patient ID, patient group and reason for early study termination will be provided.

[5] IF DMSUBIC = Yes AND
TIINCL01 = Yes AND TIINCL02 = Yes AND TIINCL03 = Yes AND
TIINCL04 = Yes AND TIINCL05 = Yes AND TIINCL06 = Yes AND
TIEXCL01 = No AND TIEXCL02 = No AND TIEXCL03 = No AND
TIEXCL04 = No AND TIEXCL05 = No AND TIEXCL06 = No AND TIEXCL07 = No AND
(imp_group = … (group A) OR imp_group = … (group AB)) AND
end_early_a ≠ Implantation of Ilivia ICD family was planned but not performed … AND
end_early_ab ≠ Implantation of Ilivia ICD family and Plexa lead were planned but not performed …
THEN analysis_set_Ilivia_SAR = Yes
ELSE analysis_set_Ilivia_SAR = No

7.3. Plexa Analysis Set

Similar to the definition of the Ilivia analysis set (see chapter 7.2), the Plexa analysis set consists of all patients in group B and in group AB, who met all in- and exclusion criteria. Patients who did not come in contact with any Plexa lead are not included in the analysis set.

Data file, identifier patient_display_id_full	Variable name	Variable label	Variable level	Nominal values
enrollment	DMSUBIC	Patient has provided written informed consent	nominal	Yes /No
enrollment	TIINCL01 TIINCL02 TIINCL03 TIINCL04 TIINCL05 TIINCL06	Inclusion criteria […]	nominal	Yes /No
enrollment	TIEXCL01 TIEXCL02 TIEXCL03 TIEXCL04 TIEXCL05 TIEXCL06 TIEXCL07	Exclusion criteria […]	nominal	Yes /No
implantation_general_data	imp_group	Patient Group		Device of the Ilivia family (group A) Plexa right ventricular lead (group B) Both Ilivia and Plexa (group AB)
study_termination	end_early_b	Reason for early study termination	nominal	Implantation of Plexa lead was planned but not performed (patient did not come in contact with the investigational device) […]
study_termination	end_early_ab	Reason for early study termination	nominal	Implantation of Ilivia ICD family and Plexa lead were planned but not performed (patient did not come in contact with the investigational devices) […]
data_SAR	analysis_set_Plexa_SAR[6]	Analysis set Plexa	nominal	Yes / No

[6] IF DMSUBIC = Yes AND
TIINCL01 = Yes AND TIINCL02 = Yes AND TIINCL03 =Yes AND
TIINCL04 = Yes AND TIINCL05 = Yes AND TIINCL06 =Yes AND
TIEXCL01 = No AND TIEXCL02 = No AND TIEXCL03 =No AND
TIEXCL04 = No AND TIEXCL05 = No AND TIEXCL06 = No AND TIEXCL07 = No AND
(imp_group = … (group B) OR imp_group = … (group AB)) AND
end_early_b ≠ Implantation of Plexa lead was planned but not performed … AND
end_early_ab ≠ Implantation of Ilivia ICD family and Plexa lead were planned but not performed …
THEN analysis_set_Plexa_SAR = Yes
ELSE analysis_set_Plexa_SAR = No

8. General data

8.1. Analysis set

All analyses are performed for the full analysis set[7].

8.2. Variables

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_general_data	Yes	imp_group	Patient Group	nominal	Device of the Ilivia family (group A) Plexa right ventricular lead (group B) Both Ilivia and Plexa (group AB)

Baseline / Demographics

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
baseline	Yes	bas_age	Age	scale	n.a.
baseline	Yes	bas_weight	Weight [kg]	scale	n.a.
baseline	Yes	bas_height	Height [cm]	scale	n.a.
baseline	Yes	bas_bmi	BMI [kg/m2]	scale	n.a.
baseline	Yes	bas_sex	Gender	nominal	Male Female

The total study duration will be calculated as the total sum of all patients' time between informed consent and termination. If a patient's study participation is terminated earlier for one of the study arms A or B, the later termination date will be used for this patient.

This total study duration will be used to calculate the mortality in deaths per 100 patient-years.

Additionally:

- Number of all patients, that signed the informed consent
- Number of patients in the full analysis set, in the Ilivia analysis set (A) and in the Plexa analysis set (B), and number of patients in both the Ilivia and the Plexa analysis set (AB)
- Number of regular terminations (altogether and per group)
- Number of patients with early study termination (split by reason for early termination, altogether and per group)

8.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

8.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

8.5. Descriptive Analyses

See general definitions in chapter 5.1.

[7] analysis_set_full_SAR = Yes

8.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

9. Baseline Data: Ilivia

9.1. Analysis set

All analyses are performed for the Ilivia analysis set[8].

9.2. Variables

Baseline / Demographics

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
baseline	Yes	bas_age	Age	scale	n.a.
baseline	Yes	bas_weight	Weight [kg]	scale	n.a.
baseline	Yes	bas_height	Height [cm]	scale	n.a.
baseline	Yes	bas_bmi	BMI [kg/m2]	scale	n.a.
baseline	Yes	bas_sex	Gender	scale	Male / Female

Baseline / Indications

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
baseline	Yes	bas_heart_disease	Underlying heart disease	nominal	Ischemic Non-ischemic
baseline	Yes	bas_indication	ICD indication	nominal	Primary prevention Secondary prevention
baseline	Yes	bas_pacing_dependent	Pacemaker-dependency	nominal	Yes / No
baseline	Yes	bas_hf	heart failure	nominal	Yes / No
baseline	Yes	bas_lbbb	Left BBB	nominal	Yes / No
baseline	Yes	bas_rbbb	Right BBB	nominal	Yes / No
baseline	Yes	bas_nyha	heart failure status	nominal[9]	NYHA I NYHA II NYHA III NYHA IV
baseline	Yes	bas_atrial_rhythm	Current Atrial rhythm	nominal	[…] sinus rhythm Sinus bradycardia Sinus Tachycardia Atrial Fibrillation Atrial Flutter Other SVT
baseline	Yes	bas_avblock	AV block	nominal	None I° II° III°
baseline	Yes	bas_af_type	History of atrial fibrillation (according to ESC guidelines)	nominal	Paroxysmal (usually ≤ 48h) Persistent (> 7 days […] Long-standing persistent […] Permanent (accepted)

[8] analysis_set_Ilivia_SAR = Yes
[9] No conversion to ordinal data planned e.g. to calculate Median and inter-quartile range

					None
baseline	Yes	bas_qrs	QRS Duration [ms]	scale	n.a.
baseline	No	bas_rr_interval	Mean RR-interval	scale	n.a.
baseline	No	bas_heart_rate	mean heart rate	scale	n.a.
baseline	Yes	bas_heart_rate_SAR[10]	mean heart rate [bpm]	scale	n.a.
baseline	Yes	bas_lvef	LVEF [%]	scale	n.a.

Baseline / Diseases

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
baseline	Yes	bas_comorb_01	Hypertension […]	nominal	Yes /No
baseline	Yes	bas_comorb_02	History of TIA / Stroke	nominal	Yes /No
baseline	Yes	bas_comorb_03	Peripheral vascular disease	nominal	Yes /No
baseline	Yes	bas_comorb_04	Asthma or other […]	nominal	Yes /No
baseline	Yes	bas_comorb_05	[…] (COPD)	nominal	Yes /No
baseline	Yes	bas_comorb_06	Renal dysfunction	nominal	Yes /No
baseline	Yes	bas_comorb_07	Sleep apnoea	nominal	Yes /No
baseline	Yes	bas_comorb_08	Liver disease	nominal	Yes /No
baseline	Yes	bas_comorb_09	Diabetes mellitus	nominal	Yes /No
baseline	Yes	bas_comorb_10	Anemia	nominal	Yes /No
baseline	Yes	bas_comorb_11	Cancer	nominal	Yes /No

Baseline / Medication

Baseline medication is reported only, whereby "Other" medications, and medication names, are not reported.

Data file including rows for each medication per patient per date	Descriptive	Variable name	Variable label	Variable level	Nominal values
cm_embedded_log	No	CMBLFL	Baseline medication	nominal	Yes / No
cm_embedded_log	No	CMCLAS	Medication class		ACE inhibitors Angiotensin receptor blocker Aldosterone blocker Betablocker (excluding sotalol) Calcium channel blocker Digoxin Statins Diuretics Anticoagulation Antiplatelets Antiarrhythmics Other

[10] IF bas_heart_rate ≠ missing THEN bas_heart_rate_SAR = bas_heart_rate
ELSE IF bas_rr_interval ≠ missing THEN bas_heart_rate_SAR = 60000 / bas_rr_interval

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
data_SAR	Yes	med01_SAR[11]	ACE inhibitors	nominal	Yes /No
data_SAR	Yes	med02_SAR[12]	Angiotensin receptor blocker	nominal	Yes /No
data_SAR	Yes	med03_SAR[13]	Aldosterone blocker	nominal	Yes /No
data_SAR	Yes	med04_SAR[14]	Betablocker (excluding sotalol)	nominal	Yes /No
data_SAR	Yes	med05_SAR[15]	Calcium channel blocker	nominal	Yes /No
data_SAR	Yes	med06_SAR[16]	Digoxin	nominal	Yes /No
data_SAR	Yes	med07_SAR[17]	Statins	nominal	Yes /No
data_SAR	Yes	med08_SAR[18]	Diuretics	nominal	Yes /No
data_SAR	Yes	med09_SAR[19]	Anticoagulation	nominal	Yes /No
data_SAR	Yes	med10_SAR[20]	Antiplatelets	nominal	Yes /No
data_SAR	Yes	med11_SAR[21]	Antiarrhythmics	nominal	Yes /No
data_SAR	Yes	med01_02_SAR[22]	ACE inhibitors OR Angiotensin receptor blocker	nominal	Yes /No

9.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

9.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

9.5. Descriptive Analyses

See general definitions in chapter 5.1.

9.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

[11] IF CMBLFL = Yes AND any CMCLAS = ACE inhibitors THEN med01_SAR= Yes ELSE med01_SAR = No
[12] IF CMBLFL = Yes AND any CMCLAS = Angiotensin receptor ... THEN med02_SAR= Yes ELSE med02_SAR = No
[13] IF CMBLFL = Yes AND any CMCLAS = Aldosterone blocker THEN med03_SAR= Yes ELSE med03_SAR = No
[14] IF CMBLFL = Yes AND any CMCLAS = Betablocker ... THEN med04_SAR= Yes ELSE med04_SAR = No
[15] IF CMBLFL = Yes AND any CMCLAS = Calcium channel blocker THEN med05_SAR= Yes ELSE med05_SAR = No
[16] IF CMBLFL = Yes AND any CMCLAS = Digoxin THEN med06_SAR= Yes ELSE med06_SAR = No
[17] IF CMBLFL = Yes AND any CMCLAS = Statins THEN med07_SAR= Yes ELSE med07_SAR = No
[18] IF CMBLFL = Yes AND any CMCLAS = Diuretics THEN med08_SAR= Yes ELSE med08_SAR = No
[19] IF CMBLFL = Yes AND any CMCLAS = Anticoagulation THEN med09_SAR= Yes ELSE med09_SAR = No
[20] IF CMBLFL = Yes AND any CMCLAS = Antiplatelets THEN med10_SAR= Yes ELSE med10_SAR = No
[21] IF CMBLFL = Yes AND any CMCLAS = Antiarrhythmics THEN med11_SAR= Yes ELSE med11_SAR = No
[22] IF CMBLFL = Yes AND any CMCLAS = ACE inhibitors OR any CMCLAS = Angiotensin receptor ... THEN med01_02_SAR= Yes ELSE med01_02_SAR = No

10. Implantation Data: Ilivia

10.1. Analysis set

All analyses are performed for the Ilivia analysis set[23].

10.2. Variables

Implantation / ICD/CRTD

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_ general_data	Yes	imp_category	Study implantation	nominal	De novo CRT-D / ICD implantation Upgrade from pacemaker […] Upgrade from ICD […] Exchange of ICD / CRT-D […]
implantation_ general_data	Yes	imp_site	Implantation site	nominal	left / right
implantation_ general_data	Yes	imp_dev_ type_other	Device type	nominal	Single chamber ICD Dual Chamber ICD CRT-D
implantation_ general_data	Yes	imp_dev	Device model	nominal	Ilivia 7 […]
implantation_ general_data	Yes	imp_dev_type	Device type	nominal	VR-T […]
implantation_ general_data	Yes	imp_connector	Connector type for RV lead	nominal	DF-1 / DF4

Implantation / Leads

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_ general_data	No	imp_rv_model	RV lead model	Nominal	Plexa S […]
data_SAR	Yes	imp_rv_model_ SAR[24]	RV lead model	Nominal	Plexa Other

[23] analysis_set_Ilivia_SAR = Yes

[24] IF imp_rv_model = Plexa S OR Plexa SD OR Plexa DF-1 S OR Plexa DF-1 SD or Plexa DF-1 S DX
THEN imp_rv_model_SAR = Plexa
ELSE imp_rv_model_SAR = other

Implantation Analyzer Data / RA

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label NEW prefix added to all labels "Implantation analyzer data, RA: "	Variable level	Nominal values
implantation_analyzer_data	Yes	imp_ana_ra_amp	Sensing amplitude [mV]	scale	n.a.
implantation_analyzer_data	Yes	imp_ana_ra_imp	Pacing impedance [Ω]	scale	n.a.
implantation_analyzer_data	Yes	imp_ana_ra_thresh	Pacing threshold [V] at Pulse width 0.4 ms	scale	n.a.
implantation_analyzer_data	No	imp_ana_ra_thresh2	Pacing threshold [V]	scale	n.a.
implantation_analyzer_data	No	imp_ana_ra_pulse	at Pulse width [ms]	scale	n.a.
data_SAR	Yes	imp_ana_ra_thresh_05[25]	Pacing threshold [V] at Pulse width 0.5 ms	scale	n.a.

A pacing threshold must always consist of amplitude and duration (pulse width). It is not reasonable to report one without the other.

Here, the CIP requires using 0.4 ms, but it can be expected that other pulse durations were used because different analyzer devices which are being used in the investigational centers have different standard settings.

In the SAP version 1.0 it has been defined that it will be tested during blind review whether a meaningful number of measurements were performed with another pulse duration than 0.4 ms.

This test showed that, in fact, in a meaningful number of threshold measurements, 0.5 ms has been used, but only single or no other values. The same was found for other analyzer threshold measurements at the implantation (RV, LV).

Therefore**, thresholds of analyzer measurements will be reported for 0.4 and 0.5 ms pulse duration**. Measurements at other pulse duration (if any) will be discarded.

[25] IF imp_ana_ra_pulse =0.5 THEN imp_ana_ra_thresh_05 = imp_ana_ra_thresh2

Implantation Analyzer Data / RA / Not-measured

Data file, identifier patient_ display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_ analyzer_ data	No	imp_ana_ra_ amp_no	-	nominal	Not measurable: P-wave visible but […] Not measurable: No P-wave visible Not done
data_SAR	Yes	imp_ana_ra_ amp_no_SAR[26]	Implantation analyzer data, RA: Sensing amplitude	nominal	Not measurable: P-wave visible but […]Measured
implantation_ analyzer_ data	No	imp_ana_ra_ imp_no	-	nominal	Above range Below range Not measurable: no overdrive pacing Not done
data_SAR	Yes	imp_ana_ra_ imp_no_SAR[27]	Implantation analyzer data, RA: Pacing impedance	nominal	Out of range Measured
implantation_ analyzer_ data	No	imp_ana_ra_ thresh_no	-	nominal	Not measured at 0.4 ms No capture with maximum output […] Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_ana_ra_ thresh_no_SAR [28]	Implantation analyzer data, RA: Pacing threshold	nominal	No capture with maximum output […] Measured

[26] IF imp_ana_ra_amp_no = Not measurable: P-wave visible but …
THEN imp_ana_ra_amp_no_SAR = imp_ana_ra_amp_no
ELSE IF imp_ana_ra_amp ≠ missing
THEN imp_ana_ra_amp_no_SAR = Measured

[27] IF imp_ana_ra_imp_no = Above range OR imp_ana_ra_imp_no = Below range
THEN imp_ana_ra_imp_no_SAR = Out of range
ELSE IF imp_ana_ra_imp ≠ missing THEN imp_ana_ra_imp_no_SAR = Measured

[28] IF imp_ana_ra_thresh_no = No capture … THEN imp_ana_ra_thresh_no_SAR = imp_ana_ra_thresh_no
ELSE IF imp_ana_ra_thresh ≠ missing THEN imp_ana_ra_thresh_no_SAR = Measured

Implantation Analyzer Data / RV

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label NEW prefix added to all labels "Implantation analyzer data, RV: "	Variable level	Nominal values
implantation_analyzer_data	Yes	imp_ana_rv_amp	Sensing amplitude [mV]	scale	n.a.
implantation_analyzer_data	Yes	imp_ana_rv_imp	Pacing impedance [Ω]	scale	n.a.
implantation_analyzer_data	Yes	imp_ana_rv_thresh	Pacing threshold [V] at Pulse width 0.4 ms	scale	n.a.
implantation_analyzer_data	No	imp_ana_rv_thresh2	Pacing threshold [V]	scale	n.a.
implantation_analyzer_data	No	imp_ana_rv_pulse	at Pulse width [ms]	scale	n.a.
data_SAR	Yes	imp_ana_rv_thresh05[29]	Pacing threshold [V] at Pulse width 0.5 ms	scale	n.a.

Pacing threshold measurements will be reported for 0.4 and 0.5 ms separately. See the justification above.

Implantation Analyzer Data / RV / Not-measured

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_analyzer_data	No	imp_ana_rv_amp_no	-	nominal	No intrinsic rhythm Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible Not done
data_SAR	Yes	imp_ana_rv_amp_no_SAR[30]	Implantation analyzer data, RV: Sensing amplitude	nominal	Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible Measured
implantation_analyzer_data	No	imp_ana_rv_imp_no	-	nominal	Above range Below range Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_ana_rv_imp_no_SAR[31]	Implantation analyzer data, RV: Pacing impedance	nominal	Out of range Measured
implantation_analyzer_data	No	imp_ana_rv_thresh_no	-	nominal	Not measured at 0.4 ms No capture with maximum output […] Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_ana_rv_thresh_no_SAR[32]	Implantation analyzer data, RV: Pacing threshold	nominal	No capture with maximum output […] Measured

[29] IF imp_ana_rv_pulse =0.5 THEN imp_ana_rv_thresh_05 = imp_ana_rv_thresh2

[30] IF imp_ana_rv_amp_no = Amplitude visible …OR
imp_ana_rv_amp_no = During intrinsic … THEN imp_ana_rv_amp_no_SAR = imp_ana_rv_amp_no
ELSE IF imp_ana_rv_amp ≠ missing THEN imp_ana_rv_amp_no_SAR = Measured

[31] IF imp_ana_rv_imp_no = Above range OR Below range THEN imp_ana_rv_imp_no_SAR = Out of range
ELSE IF imp_ana_rv_imp ≠ missing THEN imp_ana_rv_imp_no_SAR = Measured

Implantation Analyzer Data / LV / 7 Sensing Vectors

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation analyzer data, [specification … to …]: "	Variable level	Nominal values
implantation_analyzer_data	Yes	imp_ana_lv_amp_01	Sensing amplitude [mV]	scale	n.a.

The above analyses are performed for all 7 vector permutations, respectively:

- 01 LV1 tip to LV2 ring
- 02 LV1 tip to ICD
- 03 LV2 ring to LV3 ring
- 04 LV2 ring to ICD
- 05 LV3 ring to LV4 ring
- 06 LV3 ring to ICD
- 07 LV4 ring to ICD

Implantation Analyzer Data / LV / 7 Sensing Vectors / Not-measured

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_analyzer_data	No	imp_ana_lv_svect_no	-	nominal	No intrinsic rhythm Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible Not done
data_SAR	Yes	imp_ana_lv_svect_no_SAR[33]	Implantation analyzer data: Any LV pacing vector	nominal	Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible At least one vector measured

[32] IF imp_ana_rv_thresh_no = No capture … THEN imp_ana_rv_thresh_no_SAR = imp_ana_rv_thresh_no
ELSE IF imp_ana_rv_thresh ≠ missing THEN imp_ana_rv_thresh_no_SAR = Measured

[33] IF imp_ana_lv_svect_no = Amplitude visible but too low to measure
THEN imp_ana_lv_svect_SAR = Amplitude visible but too low to measure
ELSE IF imp_ana_lv_amp_0j_no = During intrinsic rhythm no R-wave visible
THEN imp_ana_lv_svect_no = During intrinsic rhythm no R-wave visible
ELSE IF any j=1-7 imp_ana_lv_amp_0j ≠ missing
THEN imp_ana_lv_svect_SAR = At least one vector measured

Implantation Analyzer Data / LV / 12 Pacing Vectors

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation analyzer data, [specification … to …]: "	Variable level	Nominal values
implantation_analyzer_data	Yes	imp_ana_lv_imp_01	Pacing impedance [Ω]	scale	n.a.
implantation_analyzer_data	No	imp_ana_lv_thresh_01	Pacing threshold [V]	scale	n.a.
implantation_analyzer_data	No	imp_ana_lv_pulse_01	at Pulse width [ms]	scale	n.a.
data_SAR	Yes	imp_ana_lv_thresh_01_04[34]	Pacing threshold [V] at 0.4 ms	scale	n.a.
data_SAR	Yes	imp_ana_lv_thresh_01_05[35]	Pacing threshold [V] at 0.5 ms	scale	n.a.
implantation_analyzer_data	No	imp_ana_lv_pns_amp_01	at pacing amplitude [V]	scale	n.a.
data_SAR	Yes	imp_ana_lv_pns_amp_01_04[36]	Phrenic nerve stimulation threshold [V] at 0.4 ms	scale	n.a.
data_SAR	Yes	imp_ana_lv_pns_amp_01_05[37]	Phrenic nerve stimulation threshold [V] at 0.5 ms	scale	n.a.

Pacing threshold measurements will be reported for 0.4 and 0.5 ms separately. See the justification above.

The above analyses are performed for the following 12 vector permutations, respectively:

- 01 LV1 tip to LV2 ring
- 02 LV1 tip to LV4 ring
- 03 LV1 tip to RV coil
- 04 LV1 tip to ICD
- 05 LV2 ring to LV1 tip
- 06 LV2 ring to LV4 ring
- 07 LV2 ring to RV coil
- 08 LV3 ring to LV2 ring
- 09 LV3 ring to LV4 ring
- 10 LV3 ring to RV coil
- 11 LV4 ring to LV2 ring
- 12 LV4 ring to RV coil

[34] IF imp_ana_lv_pulse_01 =0.4 THEN imp_ana_lv_thresh_01_04 = imp_ana_lv_thresh_01
[35] IF imp_ana_lv_pulse_01 =0.5 THEN imp_ana_lv_thresh_01_05 = imp_ana_lv_thresh_01
[36] IF imp_ana_lv_pulse_01 = 0.4 THEN imp_ana_lv_pns_amp_01_04 = imp_ana_lv_pns_amp_01
[37] IF imp_ana_lv_pulse_01 = 0.5 THEN imp_ana_lv_pns_amp_01_05 = imp_ana_lv_pns_amp_01

Implantation Analyzer Data / LV /12 Pacing Vectors / Not-measured

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation analyzer data, [specification … to …]: "	Variable level	Nominal values
implantation_analyzer_data	No	imp_ana_lv_imp_01_no	-	nominal	Above range Below range Not done
data_SAR	Yes	imp_ana_lv_imp_01_no_SAR[38]	Implantation analyzer data, LV1 tip to LV2 ring: Pacing impedance	nominal	Out of range Measured
implantation_analyzer_data	Yes	imp_ana_lv_thresh_01_no	no capture with maximum output possible	nominal	True / False
implantation_analyzer_data	Yes	imp_ana_lv_pns_01	Phrenic nerve stimulation detected	nominal	Yes / No

The above analyzes are performed for all 12 vector permutations, respectively.

[38] IF imp_ana_lv_imp_01_no = Above range OR Below range THEN imp_ana_lv_imp_01_no_SAR = Out of range
ELSE IF imp_ana_lv_imp_01 ≠ missing THEN imp_ana_lv_imp_01_no_SAR = Measured

Implantation Device Data / RA

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation device data, RA:"	Variable level	Nominal values
implantation_ device_data	Yes	imp_ra_amp	Sensing amplitude [mV]	metric	n.a.
implantation_ device_data	Yes	imp_ra_imp	Pacing impedance [Ω]	scale	n.a.
implantation_ device_data	Yes	imp_ra_thresh	Pacing threshold [V] at Pulse width 0.4 ms	scale	n.a.

The CIP requires using 0.4 ms pulse width for all RA and RV threshold measurements. However, in the SAP version 1.0 it has been defined that it will be tested during blind review whether a meaningful number of measurements were performed with another pulse duration than 0.4 ms. This test showed that very few or no threshold measurements used other values than 0.4 ms at RA and RV measurements.

Therefore**, thresholds of device measurements will be reported for 0.4 ms pulse duration** only and measurements at other pulse duration will be discarded.

Implantation Device Data / RA / Not-measured

Data file, identifier patient_ display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_ device_data	No	imp_ra_ amp_no	-	nominal	Not measurable: P-wave visible but […] Not measurable: No P-wave visible Not done
data_SAR	Yes	imp_ra_ amp_no_SAR[39]	Implantation device data, RA: Sensing amplitude	nominal	Not measurable: P-wave visible but Measured
implantation_ device_data	No	imp_ra_ imp_no	-	nominal	Out of range >3000 Out of range <200 Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_ra_ imp_no_SAR[40]	Implantation device data, RA: Pacing impedance	nominal	Out of range Measured
implantation_ device_data	No	imp_ra_ thresh_no	-	nominal	Not measured at 0 .4 ms No capture with 7.5V possible Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_ra_ thresh_no_SAR [41]	Implantation device data, RA: Pacing threshold	nominal	No capture with 7.5V possible Measured

[39] IF imp_ra_amp_no = Not measurable: P-wave visible but …THEN imp_ra_amp_no_SAR = imp_ra_amp_no
ELSE IF imp_ra_amp ≠ missing THEN imp_ra_amp_no_SAR = Measured

[40] IF imp_ra_imp_no = Out of range >3000 OR Out of range <200
THEN imp_ra_imp_no_SAR = Out of range
ELSE IF imp_ra_imp ≠ missing THEN imp_ra_imp_no_SAR = Measured

[41] IF imp_ra_thresh_no = No capture … THEN imp_ra_thresh_no_SAR= imp_ra_thresh_no
ELSE IF imp_ra_thresh ≠ missing THEN imp_ra_thresh_no_SAR= Measured

Implantation Device Data / RV

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation device data, RV: "	Variable level	Nominal values
implantation_ device_data	Yes	imp_rv_amp	Sensing amplitude [mV]	scale	n.a.
implantation_ device_data	Yes	imp_rv_imp	Pacing impedance [Ω]	scale	n.a.
implantation_ device_data	Yes	imp_rv_thresh	Pacing threshold [V] at Pulse width 0.4 ms	scale	n.a.
implantation_ device_data	Yes	imp_rv_shock	Painless shock impedance [Ω]	scale	n.a.

Maesurements at other pulse widths than 0.4 ms will be discarded (see above).

Implantation Device Data / RV / Not-measured

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_device_data	No	imp_rv_amp_no	-	nominal	No intrinsic rhythm Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible Not done
data_SAR	Yes	imp_rv_amp_no_SAR[42]	Implantation device data, RV: Sensing amplitude	nominal	Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible Measured
implantation_device_data	No	imp_rv_imp_no	-	nominal	Out of range >3000 Out of range <200 Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_rv_imp_no_SAR[43]	Implantation device data, RV: Pacing impedance	nominal	Out of range Measured
implantation_device_data	No	imp_rv_thresh_no	-	nominal	Not measured at 0 .4 ms No capture with 7.5V possible Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_rv_thresh_no_SAR[44]	Implantation device data, RV: Pacing threshold	nominal	No capture with 7.5V possible Measured
implantation_device_data	No	imp_rv_shock_no	-		Out of range >150 Out of range <25 Not done
data_SAR	Yes	imp_rv_shock_no_SAR[45]	Implantation device data, RV: Painless shock impedance	nominal	Out of range Measured

[42] IF imp_rv_amp_no = Amplitude visible … OR
imp_rv_amp_no = During intrinsic … THEN imp_rv_amp_no_SAR = imp_rv_amp_no
ELSE IF imp_rv_amp ≠ missing THEN imp_rv_amp_no_SAR = Measured

[43] IF imp_rv_imp_no = Out of range >3000 OR
imp_rv_imp_no = Out of range <200 THEN imp_rv_imp_no_SAR = Out of range
ELSE IF imp_rv_imp ≠ missing THEN imp_rv_imp_no_SAR = Measured

[44] IF imp_rv_thresh_no = No capture … THEN imp_rv_thresh_no_SAR = imp_rv_thresh_no
ELSE IF imp_rv_thresh ≠ missing THEN imp_rv_thresh_no_SAR = Measured

[45] IF imp_rv_shock_no = Out of range >150 OR
imp_rv_shock_no = Out of range <25 THEN imp_rv_shock_no_SAR = Out of range
ELSE IF imp_rv_shock ≠ missing THEN imp_rv_shock_no_SAR = Measured

Implantation Device Data / LV / 7 Sensing Vectors

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation device data, [specification … to …]"	Variable level	Nominal values
implantation_device_data	Yes	imp_lv_amp_01	Sensing amplitude [mV]	scale	n.a.

The above analyses are performed for all 7 vector permutations, respectively:

- 01 LV1 tip to LV2 ring
- 02 LV1 tip to ICD
- 03 LV2 ring to LV3 ring
- 04 LV2 ring to ICD
- 05 LV3 ring to LV4 ring
- 06 LV3 ring to ICD
- 07 LV4 ring to ICD

Implantation Device Data / LV / 7 Sensing Vectors / Not-measured

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_device_data	No	imp_lv_svect_no	-	nominal	No intrinsic rhythm Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible Not done
data_SAR	Yes	imp_lv_svect_SAR[46]	Implantation device data, any LV pacing vector: Sensing amplitude	nominal	Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible At least one vector measured

[46] IF imp_lv_amp__no = Amplitude visible but too low to measure
THEN imp_lv_svect_SAR = Amplitude visible but too low to measure
ELSE IF imp_lv_amp__no = During intrinsic rhythm no R-wave visible
THEN imp_lv_svect_SAR = During intrinsic rhythm no R-wave visible
ELSE IF any j=1-7 imp_lv_amp_0j ≠ missing
THEN imp_lv_svect_SAR = At least one vector measured

Implantation Device Data / LV / Programmed Pacing Vectors

Final programmed pacing vectors are handled in the multipole_pacing CRFs.

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation device data, first LV pacing vector: "	Variable level	Nominal values
implantation_device_data	Yes	imp_lv_first_imp	Pacing impedance [Ω]	scale	n.a.
implantation_device_data	No	imp_lv_first_thresh	Pacing threshold [V]	scale	n.a.
implantation_device_data	No	imp_lv_first_pulse	at Pulse width [ms]	scale	n.a.
data_SAR	Yes	imp_lv_first_thresh_04[47]	Pacing threshold [V] at Pulse width 0.4 ms	scale	n.a.

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation device data, second LV pacing vector: "	Variable level	Nominal values
implantation_device_data	Yes	imp_lv_sec_imp	Pacing impedance [Ω]	scale	n.a.
implantation_device_data	No	imp_lv_sec_thresh	Pacing threshold [V]	scale	n.a.
implantation_device_data	No	imp_lv_sec_pulse	at Pulse width [ms]	scale	n.a.
data_SAR	Yes	imp_lv_sec_thresh_04[48]	Pacing threshold [V] at Pulse width 0.4 ms	scale	n.a.

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation device data, second LV pacing vector: "	Variable level	Nominal values
implantation_device_data	No	imp_lv_first_pvect	Programmed first LV pacing vector	nominal	[…]
implantation_device_data	No	imp_lv_sec_pvect	Programmed second LV pacing vector	nominal	[…]
data_SAR	Yes	imp_lv_first_sec_pvect_SAR[49]	Programmed first and second LV pacing vector	nominal	#

There are 132 possible vector combinations. All vector combinations used in the study have to be reported in the SAR, whereby the most frequent vector combination has to be reported in the CIR, only.

The CIP suggests using 0.4 ms pulse width for all LV threshold measurements, but other values were permitted. In the SAP version 1.0 it has been defined that it will be tested during blind review whether a meaningful number of measurements were performed with another pulse duration than 0.4 ms.

This test showed that very few or no LV threshold measurements used other values than 0.4 ms at implantation.

Therefore**, thresholds of device measurements will be reported for 0.4 ms pulse duration** only and measurements at other pulse duration will be discarded.

[47] IF imp_lv_first_pulse = 0.4, THEN imp_lv_first_thresh_04 = imp_lv_first_thresh
[48] IF imp_lv_sec_pulse = 0.4, THEN imp_lv_sec_thresh_04 = imp_lv_sec_thresh
[49] imp_lv_first_sec_pvect_SAR = combination of imp_lv_first_pvect and imp_lv_sec_pvect per patient

Implantation Device Data / LV / Programmed Pacing Vectors / Not-measured

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_device_data	No	imp_lv_first_imp_no	-	nominal	Out of range >3000 Out of range <200 Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_lv_first_imp_no_SAR[50]	Implantation device data, first LV pacing vector: Pacing impedance	nominal	Out of range Measured
implantation_device_data	No	imp_lv_first_thresh_no	-	nominal	No capture with 7.5V possible Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_lv_first_thresh_no_SAR[51]	Implantation device data, first LV pacing vector: Pacing threshold	nominal	No capture with 7.5V possible Measured

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_device_data	No	imp_lv_sec_imp_no	-	nominal	Out of range >3000 Out of range <200 Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_lv_sec_imp_no_SAR[52]	Implantation device data, second LV pacing vector: Pacing impedance	nominal	Out of range Measured
implantation_device_data	No	imp_lv_sec_thresh_no	-	nominal	No capture with 7.5V possible Not measurable: no overpacing possible Not done
data_SAR	Yes	imp_lv_sec_thresh_no_SAR[53]	Implantation device data, second LV pacing vector: Pacing threshold	nominal	No capture with 7.5V possible Measured

[50] IF imp_lv_first_imp_no = Out of range >3000 OR imp_lv_first_imp_no = Out of range <200 THEN imp_lv_first_imp_no_SAR = Out of range
ELSE IF imp_lv_first_imp ≠ missing THEN imp_lv_first_imp_no_SAR = Measured

[51] IF imp_lv_first_thresh_no = No capture … THEN imp_lv_first_thresh_no_SAR = imp_lv_first_thresh_no
ELSE IF imp_lv_first_thresh ≠ missing THEN imp_lv_first_thresh_no_SAR = Measured

[52] IF imp_lv_sec_imp_no = Out of range >3000 OR imp_lv_sec_imp_no = Out of range <200 THEN imp_lv_sec_imp_no_SAR = Out of range
ELSE IF imp_lv_sec_imp ≠ missing THEN imp_lv_sec_imp_no_SAR = Measured

[53] IF imp_lv_sec_thresh_no = No capture … THEN imp_lv_sec_thresh_no_SAR = imp_lv_first_thresh_no
ELSE IF imp_lv_sec_thresh ≠ missing THEN imp_lv_sec_thresh_no_SAR = Measured

Implantation Device Data / LV / Programmed Delay

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Implantation device data: "	Variable level	Nominal values
implantation_device_data	No	imp_order_rvlv	Pacing order	nominal	RV first LV first
implantation_device_data	Yes, for the above groups "RV first" and "LV first"	imp_lvlv_delay	LV-LV delay [ms]	scale	n.a.
implantation_device_data	Yes, for the above groups "RV first" and "LV first"	imp_rvlv_delay	RV-LV delay [ms]	scale	n.a.

10.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

10.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

10.5. Descriptive Analyses

See general definitions in chapter 5.1.

10.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

11. PHD Data: Ilivia

11.1. Analysis set

All analyses are performed for the Ilivia analysis set[54].

11.2. Variables

PHD / General data

Data file, identifier patient_display_id_full	Descri ptive	Variable name	Variable label, NEW prefix added to all labels "PHD data:"	Variable level	Nominal values
phd_general_data	No	phd_visdate	Date of follow-up	date	n.a.
phd_general_data	Yes	phd_not_done	visit not performed	nominal	True / False

The following variables are analyzed as defined for the Ilivia analysis set, as described in chapter 10.2 device data.

PHD Device Data / RA

PHD Device Data / RA / Not-measured

PHD Device Data / RV

PHD Device Data / RV / Not-measured

PHD Device Data / LV / 7 Sensing Vectors

PHD Device Data / LV / 7 Sensing Vectors / Not-measured

PHD Device Data / LV / Programmed Pacing Vectors

PHD Device Data / LV / Programmed Pacing Vectors / Not-measured

Note: all variable names have the prefix "phd_" instead of "imp_".

For the programmed first and second LV pacing vector here the pacing threshold should have been measured at pulse width 0.4 ms (phd_lv_first_thresh_04 and phd_lv_sec_thresh_04, "Pacing threshold [V] at Pulse width 0.4 ms").

As threshold measurements at other pulse durations than 0.4 will be discarded (see 10.2), the variables "Pacing threshold [V]" (phd_lv_first_thresh and phd_lv_sec_thresh) and "at Pulse width [ms]" (phd_lv_first_pulse and phd_lv_sec_pulse) are not needed for analysis.

However, phd_lv_first_thresh_no and phd_lv_first_thresh_no have the additional option "Not measured at 0.4 ms".

[54] analysis_set_Ilivia_SAR = Yes

PHD / Device Data / LV / Vector Change

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "PHD data: "	Variable level	Nominal values
phd_device_data	Yes	phd_lv_change	Has any of the LV vectors been changed since implant	nominal	No Yes, first LV vector Yes, second LV vector Yes, both vectors
phd_device_data	Yes	phd_lv_change_reason	Primary reason for change	nominal	Phrenic nerve stimulation High LV pacing threshold PNS and high threshold better safety margin […] CRT optimization […] Other
phd_device_data	Reporting for each patient if the above variable = other	phd_lv_change_reason_co	[NEW] PHD data: Comments related to Primary reason for change	text	...
phd_device_data	Yes	phd_lv_change_pns	Phrenic nerve stimulation or high pacing threshold could successfully be resolved	nominal	Yes / No
phd_device_data	Yes	phd_lv_change_pns_outcome	[New] Actions to resolve PNS	nominal	LV lead deactivated Surgical repositioning No action taken Other
phd_device_data	Reporting for each patient if the above variable = other	phd_lv_change_pns_co	[NEW] PHD data: Comments related to actions to resolve PNS	text	...

PHD Device Data / LV Programmed Delay

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "PHD data: "	Variable level	Nominal values
phd_device_data	Yes	phd_lvlv_reprog	LV-LV delay reprogrammed since implant	nominal	Yes / No
phd_device_data	Yes	phd_rvlv_reprog	RV-LV delay reprogrammed since implant	nominal	Yes / No
phd_device_data	Yes	phd_order_reprog	Pacing order reprogrammed since implant	nominal	Yes / No
phd_device_data	No	phd_order_rvlv	Pacing order	nominal	RV first LV first
phd_device_data	Yes, for the above groups "RV first" and "LV first"	phd_lvlv_delay	LV-LV delay [ms]	scale	n.a.
phd_device_data	Yes, for the above groups "RV first" and "LV first"	phd_rvlv_delay	RV-LV delay [ms]	scale	n.a.

PHD Device Data / CRT / Atrial burden

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "PHD data: "	Variable level	Nominal values
phd_device_data	Yes	phd_crt	CRT pacing [%]	scale	n.a.
phd_device_data	Yes	phd_aburden	Atrial burden [%]	scale	n.a.

11.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

11.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

11.5. Descriptive Analyses

See general definitions in chapter 5.1.

11.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

12. Multipole Pacing Data: Ilivia

12.1. Analysis set

All analyses are performed for the Ilivia analysis set[55].

12.2. Variables

Multipole Pacing / General Information

Data file, identifier patient_ display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Multipole pacing data: "	Variable level	Nominal values
Multipole_ pacing	No	mpp_visdate	Date of MPP programming	date	n.a.
Multipole_ pacing	Yes	mpp_visit	Final programming of MPP has been done	nominal	At implant At Pre-hospital discharge Not done Other
Multipole_ pacing	Reporting for each patient if the above variable = other	mpp_visit_co	[NEW] Multipole pacing data: Comments related to final programming	text	...
phd_device_data	Yes	phd_lv_first_pvect_no	no LV pacing programmed	nominal	True / False
phd_device_data	Yes	phd_lv_sec_pvect_no	no second vector programmed, MPP inactive	nominal	True / False
fu_3_month_device_data	Yes	fu3_lv_first_pvect_no	no LV pacing programmed	nominal	True / False
fu_3_month_device_data	Yes	fu3_lv_sec_pvect_no	no second vector programmed, MPP inactive	nominal	True / False
fu_6_month_device_data	Yes	fu6_lv_first_pvect_no	no LV pacing programmed	nominal	True / False
fu_6_month_device_data	Yes	fu6_lv_sec_pvect_no	no second vector programmed, MPP inactive	nominal	True / False

A list of all patients with True for one of the "no LV pacing / second vector programmed" variables, together with general comments for the respective follow-up, will be presented.

[55] analysis_set_Ilivia_SAR = Yes

Multipole Pacing / LV / Programmed Sensing Vector

Data file, identifier patient_ display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Multipole pacing data: "	Variable level	Nominal values
Multipole_ pacing	Yes	mpp_lv_svect	Permanent programmed sensing vector	nominal	LV1 tip to LV2 ring […]
Multipole_ pacing	Yes	mpp_lv_svect_ reason	Main reason for vector choice	nominal	Highest amplitude […] Best signal quality Most appropriate […] Standard use of vector Other
Multipole_ pacing	Reporting for each patient if the above variable = other	mpp_lv_svect_ reason_co	[NEW] Multipole pacing data: Comments related to reason for vector choice	text	…

Multipole Pacing / LV / Programmed Pacing Vectors

Data file, identifier patient_ display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Multipole pacing data, first LV pacing vector: "	Variable level	Nominal values
Multipole_ pacing	Yes	mpp_lv_ first_pvect	Programmed first LV pacing vector	nominal	LV1 tip to LV2 ring […]
Multipole_ pacing	Yes	mpp_lv_ first_reason	Main reason for vector choice	nominal	According to clinical routine Lowest available threshold To prevent phrenic nerve stimulation Best anatomical position Best available threshold […] According to recommended […] Other
Multipole_ pacing	Reporting for each pt. if the above variable = other	mpp_lv_ first_reason_co	[NEW] Multipole pacing data: Comments related to programmed first vector	text	...

Data file, identifier patient_ display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "Multipole pacing data, second LV pacing vector: "	Variable level	Nominal values
Multipole_ pacing	Yes	mpp_lv_ sec_pvect	Programmed second LV pacing vector	nominal	[…]
Multipole_ pacing	Yes	mpp_lv_ sec_reason	Main reason for vector choice	nominal	According to clinical routine Lowest available threshold To prevent phrenic nerve stimulation Best anatomical position Best available threshold […] According to recommended […] Other
Multipole_ pacing	Reporting for each pt. if the above variable = other	mpp_lv_ sec_reason_co	[NEW] Multipole pacing data: Comments related to programmed second vector	text	...
data_SAR	Yes	mpp_lv_first_sec_pvect_SAR[56]	Programmed first and second LV pacing vector	nominal	#

A large number of combinations of vector pairs for MPP is possible. Only the most frequent combinations will be reported.
Combinations of two vectors for MPP in which only the designation as "first" and "second" are exchanged will be reported as one.

[56] mpp_lv_first_sec_pvect_SAR = combination of mpp_lv_first_pvect and mpp_lv_sec_pvect per patient

Multipole Pacing / LV / 12 Pacing Vectors

Data file, identifier patient_ display_id_full	Des crip tive	Variable name	Variable label, NEW prefix added to all labels "Multipole pacing data, [specification … to …]: "	Variable level	Nomin al values
Multipole_ pacing	Yes	mpp_lv_imp_01	Pacing impedance [Ω]	scale	n.a.
Multipole_ pacing	No	mpp_lv_thresh_01	Pacing threshold [V]	scale	n.a.
Multipole_ pacing	No	mpp_lv_pulse_01	at Pulse width [ms]	scale	n.a.
data_SAR	Yes	mpp_lv_thresh_01_04[57]	Pacing threshold [V] at 0.4 ms	scale	n.a.
data_SAR	Yes	mpp_lv_thresh_01_15[58]	Pacing threshold [V] at 1.0 or 1.5 ms	scale	n.a.
Multipole_ pacing	Yes	mpp_lv_pns_amp_01	Phrenic nerve stimulation at pacing amplitude [V]	scale	n.a.

A pacing threshold must always consist of amplitude and duration (pulse width). It is not reasonable to report one without the other.

Here, the CIP does not suggest a specific pulse duration.

In the SAP version 1.0 it has been defined that it will be tested during blind review whether a meaningful number of measurements were performed with another pulse duration than 0.4 ms.

This test showed that most threshold measurements were done with 0.4 ms, but a number were done with 1.0 or 1.5 ms. These will be reported additionally to those at 0.4 ms, because long pulse durations indicate that the threshold was high at shorter pulse durations.

Thresholds of 1.0 and 1.5 ms duration will be summarized because the thresholds at these durations are similar.

The above analyses are performed for the following 12 vector permutations, respectively:

- 01 LV1 tip to LV2 ring
- 02 LV1 tip to LV4 ring
- 03 LV1 tip to RV coil
- 04 LV1 tip to ICD
- 05 LV2 ring to LV1 tip
- 06 LV2 ring to LV4 ring
- 07 LV2 ring to RV coil
- 08 LV3 ring to LV2 ring
- 09 LV3 ring to LV4 ring
- 10 LV3 ring to RV coil
- 11 LV4 ring to LV2 ring
- 12 LV4 ring to RV coil

[57] IF mpp_lv_pulse_01 = 0.4, THEN mpp_lv_thresh_01_04 = mpp_lv_thresh_01
[58] IF mpp_lv_pulse_01 = 1.0 OR 1.5, THEN mpp_lv_thresh_01_15 = mpp_lv_thresh_01

Multipole Pacing / LV / 12 Pacing Vectors / Not-measured

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels	Variable level	Nominal values
Multipole_pacing	No	mpp_lv_imp_01_no	-	nominal	Out of range > 3000 out of range < 200 Not done
data_SAR	Yes	mpp_lv_imp_01_no SAR[59]	Multipole pacing data, LV1 tip to LV2 ring: Pacing impedance	nominal	Out of range Measured
Multipole pacing	No	mpp_lv_thresh_01_no	-	nominal	True / False
data_SAR	Yes	mpp_lv_thresh_01_no_SAR[60]	Multipole pacing data, LV1 tip to LV2 ring: Pacing threshold	nominal	No capture with 7.5 V possible Measured
Multipole_pacing	Yes	mpp_lv_pns_01	Phrenic nerve stimulation detected	nominal	Yes / No

The above analyzes are performed for all 12 vector permutations, respectively.

Multipole Pacing / LV / Programmed Delay

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all "Multipole pacing data: "	Variable level	Nominal values
Multipole_pacing	Yes	mpp_lvlv_delay_reason	NEW: Main reason for choice of delay LV-LV	nominal	According to recommended […] Standard setting used Best hemodynamic response […] Other
Multipole_pacing	Yes	mpp_rvlv_delay_reason	NEW: Main reason for choice of delay RV-LV	nominal	According to recommended […] Standard setting used Best hemodynamic response […] Other
Multipole_pacing	Yes	mpp_order_rvlv	Pacing order	nominal	RV first LV first
Multipole_pacing	Yes, for the above groups "RV first" and "LV first""	mpp_lvlv_delay	LV-LV delay [ms]	scale	n.a.
Multipole_pacing	Yes, for the above groups "RV first" and "LV first"	mpp_rvlv_delay	RV-LV delay [ms]	scale	n.a.

[59] IF mpp_lv_imp_01_no = … > 3000 OR
mpp_lv_imp_01_no = …< 200 THEN mpp_lv_imp_01_no_SAR = Out of range
ELSE IF mpp_lv_imp_01 ≠ missing THEN mpp_lv_imp_01_no_SAR = Measured

[60] IF mpp_lv_thresh_01_no = True THEN mpp_lv_thres_01_no_SAR= No capture …
ELSE IF mpp_lv_thresh_01 ≠ missing THEN mpp_lv_thres_01_no_SAR = Measured

Multipole Pacing / LV /Handling Evaluation

Data file, identifier patient_ display_id_full	Des cript ive	Variable name	Variable label, NEW prefix added to all "Multipole pacing data: "	Variable level	Nominal values
Multipole_ pacing	Yes	mpp_handling_activation	Activation of MPP	nominal	Very easy.... Easy.... Moderate.... Moderate-difficult... Difficult
Multipole_ pacing	Yes	mpp_handling_navigation	Navigation to MPP programming from the parameter page	nominal	
Multipole_ pacing	Yes	mpp_handling_lvlv	Programming of LV-LV delay	nominal	
Multipole_ pacing	Yes	mpp_handling_rvlv	Programming of RV-LV delay	nominal	
Multipole_ pacing	Yes	mpp_handling_overall	Overall handling of MPP programmer interface	nominal	
data_SAR	Yes	mpp_handling_activation_ SAR[61]	Activation of MPP	ordinal	1/2/3/4/5
data_SAR	Yes	mpp_handling_navigation_ SAR[62]	Navigation to MPP programming from the parameter page	ordinal	
data_SAR	Yes	mpp_handling_lvlv_ SAR[63]	Programming of LV-LV delay	ordinal	
data_SAR	Yes	mpp_handling_rvlv_ SAR[64]	Programming of RV-LV delay	ordinal	
data_SAR	Yes	mpp_handling_overall_ SAR[65]	Overall handling of MPP programmer interface	ordinal	

[61] IF mpp_handling_activation = Very easy.... THEN mpp_handling_activation = 1
ELSE IF mpp_handling_activation = Easy.... THEN mpp_handling_activation = 2
ELSE IF mpp_handling_activation = Moderate.... THEN mpp_handling_activation = 3
ELSE IF mpp_handling_activation = Moderate-difficult... THEN mpp_handling_activation = 4
ELSE IF mpp_handling_activation = Difficult THEN mpp_handling_activation = 5

[62] see above
[63] see above
[64] see above
[65] see above

Multipole Pacing / LV / Handling Information

Data file, identifier patient_ display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all "Multipole pacing data: "	Variable level	Nominal values
Multipole_ pacing	Yes	mpp_time_program	At which point in time would you program MPP in a regular CRT-D patient (independent from study set-up)	nominal	After implantation Prior to 6 -month FU At 6 -month FU After 6 -month FU Not at all Other
Multipole_ pacing	Yes	mpp_pat_program	In which patients would you programm MPP ? (independent from study participation)	nominal	Responder to conventional CRT Non-responder to conventional CRT All CRT patients
Multipole_ pacing	Yes	mpp_info_sufficient	Did you measure several available vectors during implantation via external analyzer to ensure that sufficient vectors are available due to lead positioning ?	nominal	Yes / No
Multipole_ pacing		mpp_info_sufficient	Was the information sufficient to find suitable vectors for programming later ?	nominal	Yes / No
Multipole_ pacing	Yes	mpp_vect_suitable	Were suitable vectors available for final programming ?	nominal	Yes / No

12.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

12.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

12.5. Descriptive Analyses

See general definitions in chapter 5.1.

12.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

13. Three-month Follow-up Data: Ilivia

13.1. Analysis set

All analyses are performed for the Ilivia analysis set[66].

13.2. Variables

3mFU General data

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "3mFU data: "	Variable level	Nominal values
fu_3_month_general_data	No	fu3_visdate	Date of 3-month follow-up	date	n.a.
fu_3_month_general_data	Yes	fu3_not_done	visit not performed	nominal	True / False
fu_3_month_general_data	Yes	fu3_interim	Did another follow-up occur since Pre-hospital discharge	nominal	Yes / No
fu_3_month_general_data	Yes	fu3_interim_reason	NEW: Reason for another FU	nominal	Home Monitoring alert Medical symptoms Other

The following variables are analyzed as defined for the Ilivia analysis set, as described in chapter 11.2.

3mFU Device Data / RA

3mFU Device Data / RA / Not-measured

3mFU Device Data / RV

3mFU Device Data / RV / Not-measured

3mFU Device Data / LV / Programmed Pacing Vectors

3mFU Device Data / LV / Programmed Pacing Vectors / Not-measured

3mFU Device Data / LV / Vector Change

3mFU Device Data / LV / Programmed Delay

3mFU Device Data / CRT / Atrial burden

3mFU Device Data / LV / Programmed Sensing Vector

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "3m FU data: "	Variable level	Nominal values
fu_3_month_device_data	Yes	fu3_lv_svect	Permanent programmed sensing vector	nominal	[…]
fu_3_month_device_data	Yes	fu3_lv_amp	Sensing amplitude [mV]	scale	n.a.

[66] analysis_set_Ilivia_SAR = Yes

3mFU Device Data / LV / Programmed Sensing Vector / Not-measured

Data file, identifier patient_ display_id_full	Des crip tive	Variable name	Variable label	Varia ble level	Nominal values
fu_3_month_ device_data	No	fu3_lv_ amp_no	-	nomi nal	No intrinsic rhythm Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible Not done
data_SAR	Yes	fu3_lv_ amp_no_SAR[67]	Implantation device data, any LV pacing vector: Sensing amplitude	nomi nal	Amplitude visible but too low to measure During intrinsic rhythm no R-wave visible Measured

3mFU Device Data / RA /System performance

Data file, identifier patient_display_id_full	Descri ptive	Variable name	Variable label, NEW prefix added to all labels "3mFU data: "	Variable level	Nominal values
fu_3_month_ device_data	No	fu3_perf_ra_sens	Adequate RA sensing	nominal	Yes / No
fu_3_month_ devoice_data	Yes	fu3_perf_ra_sens_ reason	Reason for inadequate RA sensing	nominal	Oversensing Undersensing Other
fu_3_month_ device_data	Yes	fu3_perf_ra_pac	Adequate RA pacing	nominal	Yes / No
fu_3_month_ device_data	Yes	fu3_perf_ra_pac_ reason	Reason for inadequate RA pacing	nominal	Non-capture No output Other
fu_3_month_ device_data	Yes	fu3_perf_ra_pac_ nocap	NEW: Reason for non-capture RA		medical […] technical

3mFU Device Data / RV/ System performance

Data file, identifier patient_display_id_full	Descri ptive	Variable name	Variable label, NEW prefix added to all labels "3mFU data: "	Variable level	Nominal values
fu_3_month_ device_data	No	fu3_perf_rv_sens	Adequate RV sensing	nominal	Yes / No
fu_3_month_ devoice_data	Yes	fu3_perf_rv_sens_ reason	Reason for inadequate RV sensing	nominal	Oversensing Undersensing Other
fu_3_month_ device_data	Yes	fu3_perf_rv_pac	Adequate RV pacing	nominal	Yes / No
fu_3_month_ device_data	Yes	fu3_perf_rv_pac_ reason	Reason for inadequate RV pacing	nominal	Non-capture No output Other
fu_3_month_ device_data	Yes	fu3_perf_rv_pac_ nocap	NEW: Reason for non-capture RV		medical […] technical

[67] IF fu3_lv_amp_no = Amplitude visible … OR
fu3_lv_amp_no = During intrinsic rhythm… THEN fu3_lv_amp_no_SAR = fu3_lv_amp_no
ELSE IF fu3_lv_amp ≠ missing THEN fu3_lv_amp_no_SAR = Measured

3mFU Device Data / LV /System performance

Data file, identifier patient_display_id_full	Descri ptive	Variable name	Variable label, NEW prefix added to all labels "3mFU data: "	Variable level	Nominal values
fu_3_month_ device_data	No	fu3_perf_lv_sens	Adequate LV sensing	nominal	Yes / No
fu_3_month_ devoice_data	Yes	fu3_perf_lv_sens_ reason	Reason for inadequate LV sensing	nominal	Oversensing Undersensing Other
fu_3_month_ device_data	Yes	fu3_perf_lv_pac	Adequate LV pacing	nominal	Yes / No
fu_3_month_ device_data	Yes	fu3_perf_lv_pac_ reason	Reason for inadequate LV pacing	nominal	Non-capture No output Other
fu_3_month_ device_data	Yes	fu3_perf_lv_pac_ nocap	NEW: Reason for non-capture LV		medical […] technical

13.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

13.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

13.5. Descriptive Analyses

See general definitions in chapter 5.1.

13.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

14. Six-month Follow-up Data: Ilivia

14.1. Analysis set

All analyses are performed for the Ilivia analysis set[68].

14.2. Variables

6mFU / General data

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "6mFU data: "	Variable level	Nominal values
fu_6_month_general_data	No	fu6_visdate	Date of 6-month follow-up	date	n.a.
fu_6_month_general_data	Yes	fu6_not_done	visit not performed	nominal	True / False
fu_6_month_general_data	Yes	fu6_interim	Did another follow-up occur since 3-month Follow-up	nominal	Yes / No
fu_6_month_general_data	Yes	fu6_interim_reason	NEW: Reason for another FU	nominal	Home Monitoring alert Medical symptoms Other

6mFU / General Data / Heart Failure

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "6mFU data: "	Variable level	Nominal values
fu_6_month_general_data	No	fu6_hf	Heart failure	nominal	Yes / No
fu_6_month_general_data	Yes	fu6_nyha	Heart failure status	nominal	NYHA I NYHA II NYHA III NYHA IV
fu_6_month_general_data	Yes	fu6_responder	Responder to CRT-D therapy	nominal	Yes / No

[68] analysis_set_Ilivia_SAR = Yes

The following variables are analyzed as defined for the Ilivia analysis set, as described in chapter 13.2.

6mFU Device Data / RA
6mFU Device Data / RA / Not-measured
6mFU Device Data / RV
6mFU Device Data / RV / Not-measured
6mFU Device Data / LV / Programmed Sensing Vector
6mFU Device Data / LV / Programmed Sensing Vector / Not-measured
6mFU Device Data / LV / Programmed Pacing Vectors
6mFU Device Data / LV / Programmed Pacing Vectors / Not-measured
6mFU Device Data / LV / Vector Change
6mFU Device Data / LV / Programmed Delay
6mFU Device Data / CRT / Atrial burden

14.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

14.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

14.5. Descriptive Analyses

See general definitions in chapter 5.1.

14.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

15. MRI Data: Ilivia

15.1. Analysis set

All analyses are performed for the Ilivia analysis set[69].

3mFU General Data / MRI

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "3mFU data: "	Variable level	Nominal values
fu_3_month_general_data	Yes	fu3_mri	Routine MRI scan performed since previous follow-up	nominal	Yes / No
fu_3_month_general_data	Yes	fu3_mri_autodetect	MRI AutoDetect feature used or attempted to be used	nominal	Yes / No

6mFU General Data / MRI

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "6mFU data: "	Variable level	Nominal values
fu_6_month_general_data	Yes	fu6_mri	Routine MRI scan performed since previous follow-up	nominal	Yes / No
fu_6_month_general_data	Yes	fu6_mri_autodetect	MRI AutoDetect feature used or attempted to be used	nominal	Yes / No

MRI AutoDetect

Data file, list of MRI events, identifier record_ID	Report all events without any statistics	Variable name	Variable label	Variable level	Nominal values
mri_autodetect	Yes	patient_display_id_full	Patient Display ID	nominal	…
mri_autodetect	Yes	mri_visdate	(Planned) date of MRI scan	nominal	Yes / No
mri_autodetect	Yes	mri_successful	MRI AutoDetect could be successfully programmed	nominal	Yes / No
mri_autodetect	Yes	mri_test_mode	Was the "MRI Test Mode" used to test the effect of programming the patient to MRI mode?	nominal	Yes / No
mri_autodetect	Yes	mri_deactivation_hm	Was deactivation of MRI mode checked via Home Monitoring the day after the scan	nominal	Yes / No
mri_autodetect	Yes	mri_ae_dd	Were any Adverse Events/ Device deficiencies detected in regard to the MRI procedure or activation of MRI AutoDetect?	nominal	Yes / No

15.2. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

[69] analysis_set_Ilivia_SAR = Yes

15.3. Exclusion of Particular Information

See general definitions in chapter 5.5.

15.4. Descriptive Analyses

See general definitions in chapter 5.1.

15.5. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

16. Primary Endpoint 1 Ilivia: SADE-free Rate

16.1. Analysis set

CIP chapter 11.1. Statistical design, methods and analytical procedures

All endpoints are analysed per-protocol (PP), whereby the analysis sets are defined for each hypothesis separately.

CIP chapter 8.1 General considerations

Tab. 4: Required visit windows (1 month is defined as 30 days)

	Window	Days post-implant
3 months post-implant	± 30 days	61 to 121

All analyses are performed for a subset of the Ilivia analysis set. To avoid an over-estimation of the SADE-free rate, patients with premature study termination less or equal 60 days after implantation are excluded from the analysis set if no primary endpoint occurred.

16.2. Variables

CIP chapter 8.3.1.1 Group A: Ilivia family related SADE-free rate through 3 months

*The parameter of interest "Ilivia$_{SADE\ free}$" is the device related SADE-d free rate per patient, which will be calculated by Ilivia$_{SADE\ free}$ = [1 - number of patients with one or more ICD related SADEs (SADE-dI$_{Ilivia}$)until 3-month follow-up divided by all patients in the analysis set] * 100%. SADEs will be adjudicated by an internal adjudication board, whereby the seriousness and device relatedness will be re-examined. If any amply documented external physical influence (e.g. accident, sport, twiddling) or medical AE caused the SADE, it does not contribute to this endpoint. SADEs that occur later than the 3-months follow-up do not contribute to this endpoint.*

In patients without 3 month FU, and in patients with a date of the 3-month Follow-Up outside the required visit window from 61 to 121 days post-implant, all SADEs until and including 121 days after implantation can contribute to the endpoint (if they fulfil the requirements for an endpoint).

Data file, list of AE evaluations, identifier parent_record_ID	Descr iptive	Variable name	Variable label	Variable level	Nominal values
ae_evaluation_form_1	No	endpoint_ilivia → endpoint_ilivia1	relevant for the primary endpoint (Ilivia family related SADE-free rate)	nominal	Yes / No
ae_evaluation_form_1	No	AESTDT	Onset date	date	n.a.
ae_evaluation_form_2	No	endpoint_ilivia → endpoint_ilivia2	relevant for the primary endpoint (Ilivia family related SADE-free rate)	nominal	Yes / No
ae_evaluation_form_2	No	AESTDT	Onset date	date	n.a.

There are two evaluation CRFs. An AE is defined as endpoint relevant when both evaluations came to this result. All divergent evaluations have to be reported[70].

Data file, identifier patient_display_id_full	Descr iptive	Variable name	Variable label	Variable level	Nominal values
implantation_general_ data	No	imp_visdate	Date of implantation	date	n.a.
data_SAR	No	enddate_Ilivia_SAR	Date of Ilivia study termination	date	n.a.
data_SAR	No	date_1stIliviaSADE_SAR[71]	Date of 1st primary Ilivia-related SADE	dummy	No
data_SAR	No	Ilivia_primEP_analysis_set_SAR[72]	Analysis set Ilivia primary endpoint	nominal	Yes /No
data_SAR	Yes	Ilivia_primEP_SAR[73]	Ilivia-related SADE(s)	nominal	Yes /No

[70] Report any endpoint_ilivia1 ≠ endpoint_ilivia2

[71] date_1stIliviaSADE_SAR = minimum AESTDT with
endpoint_ilivia1 = Yes AND
endpoint_ilivia2 = Yes
per patient_display_id_full

[72] IF analysis_set_Ilivia_SAR = Yes AND
date_1stIliviaSADE_SAR - imp_visdate ≤ 60days OR enddate_Ilivia_SAR – imp_visdate ≥ 61 days
THEN Ilivia_primEP_analysis_set_SAR = Yes
ELSE Ilivia_primEP_analysis_set_SAR = No

[73] IF analysis_set_Ilivia_SAR = Yes AND
date_1stIliviaSADE_SAR ≠ missing AND
{[fu3_visdate ≠ missing AND fu3_visdate is compliant AND_date_1st_IliviaSADE_SAR ≤ fu3_visdate] OR
[fu3_visdate ≠ missing AND fu3_visdate is not compliant
AND date_1st_IliviaSADE_SAR – imp_visdate ≤ 121 days] OR
[fu3_visdate = missing AND date_1stIliviaSADE_SAR – imp_visdate ≤ 121days] }
THEN Ilivia_primEP_SAR = Yes
ELSE Ilivia_primEP_SAR = No

16.3. Treatment of Missing and Spurious Data

To avoid an over-estimation of the SADE-free rate, patients with premature study termination less or equal 60 days after implantation and without any primary endpoint are excluded from the analysis set.

16.4. Exclusion of Particular Information

All SADEs that occurred later than the 3M-FU, or more than 121 days after implantation, if 3M-FU was outside the required visit window, are not considered.

16.5. Descriptive Analyses

Absolute and relative frequencies and additionally the two-sided 97.5% CI are presented.

16.6. Hypotheses & Statistical Tests

CIP chapter 8.3.1.1 Group A: Ilivia family related SADE-free rate through 3 months

Null hypothesis: $H_{0\_Ilivia}: Ilivia_{SADE\_free} \leq 90\%$

Alternative hypothesis: $H_{A\_Ilivia}: Ilivia_{SADE\_free} > 90\%$

CIP chapter 11.1. Statistical design, methods and analytical procedures

For both primary hypotheses exact binomial tests are carried out.

CIP chapter 11.2. Sample size

A correction for multiple testing is considered by adjusting the significance level.

CIP chapter 11.3. Level of significance and the power of the study

The 2-sided level of significance is alpha = 2.5% for each alternative hypothesis (1-sided 1.25% significance level)

A one–sided exact binomial test is carried out for the significance level 1.25%. Additionally, a two-sided 97.5% confidence interval for an exact binomial test is calculated.

16.7. Alternative analysis (as suggested by the study objective)

In the definition of the hypothesis, it is stated that endpoints are analyzed if they occur before the 3-months FU (see above, 16.2). However, in section 7 the CIP states that safety through 3 months is the primary study objective.

7.1.1 Primary Objectives

7.1.1.1 Group A: Ilivia family related safety through 3 months

This objective of the clinical investigation is to confirm the clinical safety of the Ilivia ICD family by the analysis of the Ilivia related SADEs ***within 3 months after implantation****.*

A way to analyse the data that is more closely oriented at the study objective than the method described above is a Kaplan-Meyer analysis. The Kaplan-Meyer estimated rate at 91 days represents the best estimate of the target variable.
All patients of the Ilivia analysis set will be included until the time of a first event or censoring due to study discontinuation.

17. Secondary EP 1 Ilivia: Vent. Arrhythmia Conversion Rate

17.1. Analysis set

CIP chapter 8.3.2.1.1 Percentage of patients with successful fast ventricular arrhythmia conversion by ATP one-shot at 6-month follow-up

This endpoint examines the percentage of patients with successful conversion of ventricular arrhythmia detected in the VF zone by ATP one-shot of all patients with such episodes.

All analyses are performed for patients from the Ilivia analysis set with ventricular arrhythmia episodes detected in the VF zone.

17.2. Variables

CIP chapter 8.3.2.1.1 Percentage of patients with successful fast ventricular arrhythmia conversion by ATP one-shot at 6-month follow-up

This endpoint examines the percentage of patients with successful conversion of ventricular arrhythmia detected in the VF zone by ATP one-shot of all patients with such episodes. Events will only be included in the analysis of this endpoint if

1) the arrhythmia was detected in the VF detection zone, and

2) if it was classified as true ventricular tachyarrhythmia by the investigator, and

3) if ATP one-shot was delivered with the recommended programming (8 pulses with 88% R-S1).

The period under observation starts with the implantation and lasts until the 6-month follow-up. The parameter of interest Conversion $_{R\text{-}S1\ 88\%}$ is defined as following:
*Conversion $_{R\text{-}S1\ 88\%}$ = (Number of patients with at least one successful conversion / Number of patients with events as defined here) * 100%.*

Thereby, a patient is considered to have experienced successful conversion if at least one episode detected in the VF zone in that patient was converted by ATP one-shot therapies at the recommended programming, i.e ATP one-shot was beneficial and shock delivery could be avoided.

It is possible that ATP one-shot is programmed but not delivered, if the device classifies the rhythm instable. This endpoint will only investigate episodes with delivered ATP one-shot therapy.

Data file, list of episodes, identifier recoerd_ID	Descriptive	Variable name	Variable label	Variable level	Nominal values
tachyarrhythmia_episode	No	patient_display_id_full	Patient Display ID	nominal	n.a.
tachyarrhythmia_episode	No	tac_detect_zone	Detection zone	nominal	nsVT / nsT SVT VT1 **/** VT2 VF
tachyarrhythmia_episode	No	tac_assessment	Episode assessment	nominal	non-sustained VT / VF sustained VT / VF SVT / oversensing / other
tachyarrhythmia_episode	No	tac_vf_atp_prog	ATP one-shot programming	nominal	8 pulses with RS1 88% Other programming
tachyarrhythmia_episode	No	tac_vf_first_therapy	First therapy attempt	nominal	ATP one-shot Shock
tachyarrhythmia_episode	Yes #	tac_vf_atp_success	ATP one-shot successfully terminated the episode	nominal	Yes / No
dummy	Yes	relevant_secEP_Ilivia_SAR[74]	Episode relevant for secondary endpoint Ilivia	nominal	Yes / No

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
data_SAR	Yes	Ilivia_secEP_analysis_set_SAR[75]	Analysis set Ilivia secondary endpoint	nominal	Yes /No
data_SAR	Yes	Ilivia_secEP_SAR[76]	Any successful ATP (secondary endpoint Ilivia)	nominal	Yes /No

Beyond the number of patients with endpoint relevant episodes, also the number of episodes, in which ATP-one-shot was delivered (as defined "relevant" in the footnote below) and thereof the number of episodes in which ATP-one-shot was successful (#), will also be reported.

[74] IF tac_detect_zone = VF AND
(tac_assessment = sustained VT / VF OR
tac_assessment = non-sustained VT / VF) AND
tac_vf_atp_prog = 8 pulses with RS1 88% AND
tac_vf_first_therapy = ATP one-shot
THEN relevant_secEP_Ilivia_SAR = Yes
ELSE relevant_secEP_Ilivia_SAR = No

[75] IF any relevant_secEP_Ilivia_SAR = Yes per patient_display_id_full
THEN Ilivia_secEP_analysis_set_SAR = Yes
ELSE Ilivia_secEP_analysis_set_SAR = No

[76] IF Ilivia_secEP_analysis_set_SAR = Yes AND
any tac_vf_atp_success = Yes (regarding the relevant episodes) per patient_display_id_full
THEN Ilivia_secEP_SAR = Yes
ELSE Ilivia_secEP_SAR = No

17.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

17.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

17.5. Descriptive Analyses

See general definitions in chapter 5.1.

17.6. Hypotheses & Statistical Tests

CIP chapter 8.3.2.1.1 Percentage of patients with successful fast ventricular arrhythmia conversion by ATP one-shot at 6-month follow-up

No hypotheses are pre-specified for this endpoint due to the low expected number of episodes.

A two-sided 95% confidence interval for an exact binomial test is calculated.

18. Baseline Data: Plexa

18.1. Analysis Set

All analyses are performed for the Plexa analysis set[77].

18.2. Variables

Baseline / Demographics

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
baseline	Yes	bas_age	Age	scale	n.a.
baseline	Yes	bas_weight	Weight [kg]	scale	n.a.
baseline	Yes	bas_height	Height [cm]	scale	n.a.
baseline	Yes	bas_bmi	BMI [kg/m2]	scale	n.a.
baseline	Yes	bas_sex	Gender	nominal	Male / Female

Baseline / Indications

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
baseline	Yes	bas_heart_disease	Underlying heart disease	nominal	Ischemic Non-ischemic
baseline	Yes	bas_indication	ICD indication	nominal	Primary prevention Secondary prevention
baseline	Yes	bas_pacing_dependent	Pacemaker-dependency	nominal	Yes / No
baseline	Yes	bas_hf	heart failure	nominal	Yes / No
baseline	Yes	bas_lbbb	Left BBB	nominal	Yes / No
baseline	Yes	bas_rbbb	Right BBB	nominal	Yes / No
baseline	Yes	bas_nyha	heart failure status	nominal[78]	NYHA I ; NYHA II NYHA III ; NYHA IV
baseline	Yes	bas_atrial_rhythm	Current Atrial rhythm	nominal	[…] sinus rhythm Sinus bradycardia Sinus Tachycardia Atrial Fibrillation Atrial Flutter ; Other SVT
baseline	Yes	bas_avblock	AV block	nominal	None ; I° ; II° ; III°
baseline	Yes	bas_af_type	History of atrial fibrillation (according to ESC guidelines)	nominal	Paroxysmal (usually ≤ 4 8h) Persistent (> 7 days […] Long-standing persistent […] Permanent (accepted) None
baseline	Yes	bas_qrs	QRS Duration [ms]	scale	n.a.
baseline	No	bas_rr_interval	Mean RR-interval	scale	n.a.
baseline	No	bas_heart_rate	mean heart rate	scale	n.a.
baseline	Yes	bas_heart_rate_SAR[79]	mean heart rate [bpm]	scale	n.a.
baseline	Yes	bas_lvef	LVEF [%]	scale	n.a.

[77] analysis_set_Plexa_SAR = Yes
[78] No conversion to ordinal data planned e.g. to calculate Median and inter-quartile range
[79] IF bas_heart_rate ≠ missing THEN bas_heart_rate_SAR = bas_heart_rate
ELSE IF bas_rr_interval ≠ missing THEN bas_heart_rate_SAR = 60000 / bas_rr_interval

Baseline / Diseases

Data file, identifier patient_display_id_full	Descrip tive	Variable name	Variable label	Variable level	Nominal values
baseline	Yes	bas_comorb_01	Hypertension […]	nominal	Yes /No
baseline	Yes	bas_comorb_02	History of TIA / Stroke	nominal	Yes /No
baseline	Yes	bas_comorb_03	Peripheral vascular disease	nominal	Yes /No
baseline	Yes	bas_comorb_04	Asthma or other […]	nominal	Yes /No
baseline	Yes	bas_comorb_05	[…] (COPD)	nominal	Yes /No
baseline	Yes	bas_comorb_06	Renal dysfunction	nominal	Yes /No
baseline	Yes	bas_comorb_07	Sleep apnoea	nominal	Yes /No
baseline	Yes	bas_comorb_08	Liver disease	nominal	Yes /No
baseline	Yes	bas_comorb_09	Diabetes mellitus	nominal	Yes /No
baseline	Yes	bas_comorb_10	Anemia	nominal	Yes /No
baseline	Yes	bas_comorb_11	Cancer	nominal	Yes /No

Baseline / Medication

Baseline medication is reported only, whereby "Other" medications, and medication names, are not reported.

Data file including rows for each medication per patient per date	Descrip tive	Variable name	Variable label	Variable level	Nominal values
cm_embedded_log	No	CMBLFL	Baseline medication	nominal	Yes / No
cm_embedded_log	No	CMCLAS	Medication class		ACE inhibitors Angiotensin receptor blocker Aldosterone blocker Betablocker (excluding sotalol) Calcium channel blocker Digoxin Statins Diuretics Anticoagulation Antiplatelets Antiarrhythmics Other

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
data_SAR	Yes	med01_SAR[80]	ACE inhibitors	nominal	Yes /No
data_SAR	Yes	med02_SAR[81]	Angiotensin receptor blocker	nominal	Yes /No
data_SAR	Yes	med03_SAR[82]	Aldosterone blocker	nominal	Yes /No
data_SAR	Yes	med04_SAR[83]	Betablocker (excluding sotalol)	nominal	Yes /No
data_SAR	Yes	med05_SAR[84]	Calcium channel blocker	nominal	Yes /No
data_SAR	Yes	med06_SAR[85]	Digoxin	nominal	Yes /No
data_SAR	Yes	med07_SAR[86]	Statins	nominal	Yes /No
data_SAR	Yes	med08_SAR[87]	Diuretics	nominal	Yes /No
data_SAR	Yes	med09_SAR[88]	Anticoagulation	nominal	Yes /No
data_SAR	Yes	med10_SAR[89]	Antiplatelets	nominal	Yes /No
data_SAR	Yes	med11_SAR[90]	Antiarrhythmics	nominal	Yes /No
data_SAR	Yes	med01_02_SAR[91]	ACE inhibitors OR Angiotensin receptor blocker	nominal	Yes /No

18.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

18.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

18.5. Descriptive Analyses

See general definitions in chapter 5.1.

18.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

[80] IF CMBLFL = Yes AND any CMCLAS = ACE inhibitors THEN med01_SAR= Yes ELSE med01_SAR = No
[81] IF CMBLFL = Yes AND any CMCLAS = Angiotensin receptor ... THEN med02_SAR= Yes ELSE med02_SAR = No
[82] IF CMBLFL = Yes AND any CMCLAS = Aldosterone blocker THEN med03_SAR= Yes ELSE med03_SAR = No
[83] IF CMBLFL = Yes AND any CMCLAS = Betablocker ... THEN med04_SAR= Yes ELSE med04_SAR = No
[84] IF CMBLFL = Yes AND any CMCLAS = Calcium channel blocker THEN med05_SAR= Yes ELSE med05_SAR = No
[85] IF CMBLFL = Yes AND any CMCLAS = Digoxin THEN med06_SAR= Yes ELSE med06_SAR = No
[86] IF CMBLFL = Yes AND any CMCLAS = Statins THEN med07_SAR= Yes ELSE med07_SAR = No
[87] IF CMBLFL = Yes AND any CMCLAS = Diuretics THEN med08_SAR= Yes ELSE med08_SAR = No
[88] IF CMBLFL = Yes AND any CMCLAS = Anticoagulation THEN med09_SAR= Yes ELSE med09_SAR = No
[89] IF CMBLFL = Yes AND any CMCLAS = Antiplatelets THEN med10_SAR= Yes ELSE med10_SAR = No
[90] IF CMBLFL = Yes AND any CMCLAS = Antiarrhythmics THEN med11_SAR= Yes ELSE med11_SAR = No
[91] IF CMBLFL = Yes AND any CMCLAS = ACE inhibitors OR any CMCLAS = Angiotensin receptor ... THEN med01_01_SAR= Yes ELSE med01_02_SAR = No

19. Implantation Data: Plexa

19.1. Analysis set

All analyses are performed for the Plexa analysis set[92].

19.2. Variables

General Data

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label	Variable level	Nominal values
implantation_ general_data	Yes	imp_rv_model	RV lead model	Nominal	Plexa S Plexa SD Plexa DF-1 S Plexa DF-1 SD Plexa DF-1 S DX […]
implantation_ general_data	Yes	imp_rv_promri	Pro MRI lead	Nominal	Yes / No
implantation_ general_data	Yes	imp_rv_length	lead length	Nominal	60 65 75 60 / 16 65 / 16 65 / 18 75 / 18 65 / 15 65 / 17

The following variables are analyzed as defined for the Ilivia analysis set, as described in chapter 10.2:

Analyzer Data / RA (only Plexa DF-1 S DX)

Analyzer Data / RA / Not-measured (only Plexa DF-1 S DX)

Device Data / RA (only Plexa DF-1 S DX)

Device Data / RA / Not-measured (only Plexa DF-1 S DX)

Analyzer Data / RV

Analyzer Data / RV / Not-measured

Device Data / RV

Device Data / RV / Not-measured

RV measurements will be reported for all Plexa leads, and for Plexa leads with DF4 connectors. Only few leads with DF-1 connector have been implanted, therefore a comparison of the new DF4 connector with historical data may be more reasonable.

[92] analysis_set_Plexa_SAR = Yes

Handling

Data file, identifier patient_display_id_ful	Descriptive	Variable name	Variable label	Variable level	Nominal values
plexa_handling	Yes	plx_insertion_site	Insertion site	nominal	L. Subclavian L. Cephalic L. Axillaris R. Subclavian R. Cephalic R. Axillaris
plexa_handling	Yes	plx_imp_technique	Implantation technique	nominal	Vein puncture Cutdown
plexa_handling	Yes	plx_tip_position	Lead tip position	nominal	RV apex Septal RVOT HIS-bundle Other
plexa_handling	Yes	plx_time	Incision to suture time [min]	scale	n.a.
plexa_handling	Yes	plx_insertion_assessment	Lead Insertion Assessment	nominal	Very easy Easy Moderately difficult Difficult
plexa_handling	Yes	plx_nb_turns	Number of turns needed to extend the screw	scale	

Handling / Evaluation

Data file, identifier patient_display_id_ful	Descriptive	Variable name	Variable label	Variable level	Nominal values
plexa_handling	Yes	plx_tracking	Tracking from deployment to target area	nominal	Excellent Good Average Fair Poor
plexa_handling	Yes	plx_flexibility	Flexibility	nominal	
plexa_handling	Yes	plx_pushability	Pushability	nominal	
plexa_handling	Yes	plx_ability_position	Ability to position the lead in the RV	nominal	
plexa_handling	Yes	plx_ability_extend	Ability to extend the screw	nominal	
plexa_handling	Yes	plx_ability_visualize	Ability to visualize the extended screw	nominal	
plexa_handling	Yes	plx_ability_fixate	Ability to fixate the lead tip	nominal	
plexa_handling	Yes	plx_radiopacity	Radiopacity in final position	nominal	

19.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

19.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

19.5. Descriptive Analyses

See general definitions in chapter 5.1.

19.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

20. PHD Data: Plexa

20.1. Analysis set

All analyses are performed for the Plexa analysis set[93].

20.2. Variables

PHD / General data

Data file, identifier patient_display_id_full	Descri ptive	Variable name	Variable label	Variable level	Nominal values
phd_general_data	No	phd_visdate	[NEW] Date of PHD	date	n.a.
phd_general_data	Yes	phd_not_done	[NEW] PHD: visit not performed	nominal	True / False

The following variables are analyzed as defined for the Ilivia analysis set, as described in chapter 11.2.

PHD Device Data / RA (only Plexa DF-1 S DX)

PHD Device Data / RA / Not-measured (only Plexa DF-1 S DX)

PHD Device Data / RV

PHD Device Data / RV / Not-measured

RV measurements will be reported for all Plexa leads, and for Plexa leads with DF4 connectors (see 19.2).

20.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

20.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

20.5. Descriptive Analyses

See general definitions in chapter 5.1.

20.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

[93] analysis_set_Plexa_SAR = Yes

21. Three-month FU Data: Plexa

21.1. Analysis set

All analyses are performed for the Plexa analysis set[94].

21.2. Variables

The following variables are analyzed as defined for the Ilivia analysis set, as described in chapter 13.2.

3mFU General data

3mFU Device Data / RA (only Plexa DF-1 S DX)

3mFU Device Data / RA / Not-measured (only Plexa DF-1 S DX)

3mFU Device Data / RV

3mFU Device Data / RV / Not-measured

RV measurements will be reported for all Plexa leads, and for Plexa leads with DF4 connectors (see 19.2).

3mFU Device Data / RV/ System performance

Data file, identifier patient_display_id_full	Descri ptive	Variable name	Variable label, NEW prefix added to all labels "3mFU data: "	Variable level	Nominal values
fu_3_month_ device_data	Yes	fu3_perf_rv_sens	Adequate RV sensing	nominal	Yes / No
fu_3_month_ devoice_data	Yes	fu3_perf_rv_sens_ reason	Reason for inadequate RV sensing	nominal	Oversensing Undersensing Other
fu_3_month_ device_data	Yes	fu3_perf_rv_pac	Adequate RV pacing	nominal	Yes / No
fu_3_month_ device_data	Yes	fu3_perf_rv_pac_ reason	Reason for inadequate RV pacing	nominal	Non-capture No output Other
fu_3_month_ device_data	Yes	fu3_perf_rv_pac_ nocap	NEW: Reason for non-capture RV	nominal	medical […] technical

21.1. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

21.2. Exclusion of Particular Information

See general definitions in chapter 5.5.

21.3. Descriptive Analyses

See general definitions in chapter 5.1.

21.4. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses. Note, endpoints with respect to appropriate sensing and pacing at the 3m FU are handled in chapters 24 and 25.

[94] analysis_set_Plexa_SAR = Yes

22. Six-month FU Data: Plexa

22.1. Analysis set

All analyses are performed for the Plexa analysis set[95].

22.2. Variables

The following variables are analyzed as defined for the Ilivia analysis set, as described in chapter 14.2.

6mFU General data

6mFU Device Data / RA (only Plexa DF-1 S DX)

6mFU Device Data / RA / Not-measured (only Plexa DF-1 S DX)

6mFU Device Data / RV

6mFU Device Data / RV / Not-measured

RV measurements will be reported for all Plexa leads, and for Plexa leads with DF4 connectors (see 19.2).

22.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

22.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

22.5. Descriptive Analyses

See general definitions in chapter 5.1.

22.6. Hypotheses & Statistical Tests

There are no pre-defined statistical hypotheses.

[95] analysis_set_Plexa_SAR = Yes

23. Primary Endpoint 2: SADE-free Rate Plexa

23.1. Analysis set

All analyses are performed for the Plexa analysis set [96].

CIP chapter 11.1 Statistical design, methods and analytical procedures

All endpoints are analysed per-protocol (PP), whereby the analysis sets are defined for each hypothesis separately.

CIP chapter 8.1 General considerations

Tab. 4: Required visit windows (1 month is defined as 30 days)

	Window	Days post-implant
3 months post-implant	± 30 days	61 to 121

All analyses are performed for a subset of the Plexa analysis set. To avoid an over-estimation of the SADE-free rate, patients with premature study termination less or equal 60 days after implantation are excluded from the analysis set if no primary endpoint occurred.

23.2. Variables

CIP chapter 8.3.1.2 Group B: Plexa related SADE-free rate through 3 months

*The parameter of interest "Plexa$_{SADE\ free}$" is the SADE-free rate per patient, which will be calculated by Plexa $_{SADE\ free}$ = [1 - number of patients with one or more Plexa-related SADEs (SADE-d $_{Plexa}$) until 3-month follow-up divided by all patients in the analysis set] * 100%. SADEs will be adjudicated by an internal adjudication board, whereby the seriousness and device relatedness will be re-examined. If any amply documented external physical influence (e.g. accident, sport, twiddling) or medical AE caused the SADE, it does not contribute to this endpoint. SADEs that occur later than the 3-months follow-up do not contribute to this endpoint.*

In patients without 3M FU and in patients with the 3-months FU outside the CIP defined period, all SADEs until and including 121 days after implantation can contribute to the endpoint (if they fulfil the requirements for an endpoint).

[96] analysis_set_Plexa_SAR = Yes

Data file, list of AE evaluations, identifier parent_record_ID	Descr iptive	Variable name	Variable label	Variable level	Nominal values
ae_evaluation_form_1	No	endpoint_plexa → endpoint_plexa1	relevant for the primary endpoint (Plexa related SADE-free rate)	nominal	Yes / No
ae_evaluation_form_1	No	AESTDT	Onset date	date	n.a.
ae_evaluation_form_2	No	endpoint_plexa → endpoint_plexa2	relevant for the primary endpoint (Plexa related SADE-free rate)	nominal	Yes / No
ae_evaluation_form_2	No	AESTDT	Onset date	date	n.a.

There are two evaluation CRFs. An AE is defined as endpoint relevant when both evaluations came to this result. All divergent evaluations have to be reported[97].

Data file, identifier patient_display_id_full	Descr iptive	Variable name	Variable label	Variable level	Nominal values
implantation_general_ data	Yes	imp_visdate	Date of implantation	date	n.a.
data_SAR	Yes	enddate_Plexa_SAR	Date of Plexa study termination	date	n.a.
data_SAR	No	date_1stPlexaSADE_SAR[98]	Date of 1st primary Plexa-related SADE	dummy	No
data_SAR	No	Plexa_primEP_analysis_set_SAR[99]	Analysis set Plexa primary endpoint	nominal	Yes /No
data_SAR	Yes	Plexa_primEP_SAR[100]	Plexa-related SADE(s)	nominal	Yes /No

[97] Report any endpoint_plexa1 ≠ endpoint_plexa2

[98] date_1stPlexaSADE_SAR = minimum AESTDT with
endpoint_plexa1 = Yes AND
endpoint_plexa2 = Yes
per patient_display_id_full

[99] IF analysis_set_Plexa_SAR = Yes AND
date_1stPlexaSADE_SAR - imp_visdate ≤ 60 days OR enddate_Plexa_SAR - imp_visdate ≥ 61 days
THEN Plexa_primEP_analysis_set_SAR = Yes
ELSE Plexa_primEP_analysis_set_SAR = No

[100] IF analysis_set_Plexa_SAR = Yes AND
date_1stPlexaSADE_SAR ≠ missing AND
{[fu3_visdate ≠ missing AND fu3_visdate is compliant AND date_1stPlexa_SADE_SAR ≤ fu3_visdate] OR
[fu3_visdate ≠ missing AND fu3_visdate is not compliant
AND date_1stPlexaSADE_SAR - imp_visdate ≤ 121 days] OR
[fu3_visdate = missing AND date_1stPlexaSADE_SAR - imp_visdate ≤ 121 days] }
THEN Plexa_primEP_SAR = Yes
ELSE Plexa_primEP_SAR = No

23.3. Treatment of Missing and Spurious Data

To avoid an over-estimation of the SADE-free rate, patients with premature study termination less or equal 60 days after implantation and without any primary endpoint are excluded from the analysis set.

23.4. Exclusion of Particular Information

All SADEs that occurred later than the 3M-FU, or more than 121 days after implantation, if 3M-FU was outside the required visit window, are not considered.

23.5. Descriptive Analyses

Absolute and relative frequencies and additionally the two-sided 97.5% CI are presented.

23.6. Hypotheses & Statistical Tests

CIP chapter 8.3.1.1 Group A: Ilivia family related SADE-free rate through 3 months

Null hypothesis:	H_{0_Plexa} : $Plexa_{SADE\_free} \leq 90\%$
Alternative hypothesis:	H_{A_Plexa} : $Plexa_{SADE\_free} > 90\%$

CIP chapter 11.1. Statistical design, methods and analytical procedures

For both primary hypotheses exact binomial tests are carried out.

CIP chapter 11.2. Sample size

A correction for multiple testing is considered by adjusting the significance level.

CIP chapter 11.3. Level of significance and the power of the study

The 2-sided level of significance is alpha = 2.5% for each alternative hypothesis (1-sided 1.25% significance level)

A one–sided exact binomial test is carried out for the significance level 1.25%. Additionally, a two-sided 97.5% confidence interval for an exact binomial test is calculated.

23.7. Alternative analysis (as suggested by the study objective)

In the definition of the hypothesis, it is stated that endpoints are analyzed if they occurr before the 3-months FU (see above, 23.2). However, in section 7 the CIP states that saftey through 3 months is the primary study objective.

7.1.1 Primary Objectives

…

7.1.1.2 Group B: Plexa related safety through 3 months

This objective of the clinical investigation is to confirm the clinical safety of the Plexa ICD lead by the analysis of the Plexa related SADEs ***within 3 months after implantation****.*

A way to analyse the data that is more closely oriented at the study objective than the method described above is a Kaplan-Meyer analysis. The Kaplan-Meyer estimated rate at 91 days represents the best estimate of the target variable.
All patients of the Plexa analysis set will be included until the time of a first event or censoring due to study discontinuation.

24. Secondary EP: Rate appropriate RV sensing Plexa

24.1. Analysis set

All analyses are performed for the Plexa analysis set[101].

CIP chapter 11.1 Statistical design, methods and analytical procedures

All endpoints are analysed per-protocol (PP), whereby the analysis sets are defined for each hypothesis separately.

CIP chapter 8.3.2.2.1 Rate of appropriate right ventricular sensing at 3-month follow-up

Only the evaluation of the 3-month follow-up is taken into account towards data analysis of this endpoint. Only patients with measurements performed at the 3-month follow-up will be included in this analysis set. Specifically, the percentage of patients with an appropriate RV sensing at the 3-month follow-up will be determined.

All analyses are performed for patients with non-missing RV sensing data at the 3-month follow-up.

24.2. Variables

CIP chapter 8.3.2.2.1 Rate of appropriate right ventricular sensing at 3-month follow-up

*The parameter of interest $Plexa_{Sensing}$ is the rate of patients with appropriate sensing which will be calculated by $Plexa_{Sensing}$ = (Number of patients with appropriate sensing ($Sensing_{app}$) divided by number of patients with sensing measurements performed) * 100%.*

Data file, identifier patient_display_id_full	Descri ptive	Variable name	Variable label, NEW prefix added to all labels "3mFU data: "	Variable level	Nominal values
fu_3_month_ device_data	No	fu3_perf_rv_sens	Adequate RV sensing	nominal	Yes / No

24.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

24.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

24.5. Descriptive Analyses

See general definitions in chapter 5.1.

24.6. Hypotheses & Statistical Tests

Null hypothesis: $H_{0\_Sensing}: Plexa_{Sensing} \leq 93\%$

Alternative hypothesis: $H_{A\_Sensing}: Plexa_{Sensing} > 93\%$

No multiplicity adjustment is performed for the secondary hypotheses. Thus a one–sided exact binomial test is carried out for the significance level 2.5%. Additionally, a two-sided 95% confidence interval for an exact binomial test is calculated.

[101] analysis_set_Plexa_SAR = Yes

25. Secondary EP: Rate appropriate RV pacing Plexa

25.1. Analysis set

All analyses are performed for the Plexa analysis set[102].

CIP chapter 11.1 Statistical design, methods and analytical procedures

All endpoints are analysed per-protocol (PP), whereby the analysis sets are defined for each hypothesis separately.

CIP chapter 8.3.2.2.2 Rate of appropriate right ventricular pacing at 3-month follow-up

Only the evaluation of the 3-month follow-up is taken into account towards data analysis of this endpoint. Only patients with measurements performed at the 3-month follow-up will be included in the endpoint.

All analyses are performed for patients with non-missing RV pacing data at the 3-month follow-up.

25.2. Variables

CIP chapter 8.3.2.2.2 Rate of appropriate right ventricular pacing at 3-month follow-up

*The parameter of interest $Plexa_{Pacing}$ is the rate of patients with appropriate pacing which will be calculated by $Plexa_{Pacing}$ = (Number of patients with appropriate pacing ($Pacing_{app}$) divided by number of patients with pacing measurements performed) * 100%. According to the definitions provided in section 8.5.11, the pacing performance can be "adequate" or "inadequate". If reason for inadequate performance is "No capture", the evaluation will not be considered an endpoint-related event in case the underlying reason is a medical event (e.g. hyperkalaemia, myocardial infarction or drug therapy).*

Data file, identifier patient_display_id_full	Descriptive	Variable name	Variable label, NEW prefix added to all labels "3mFU data: "	Variable level	Nominal values
fu_3_month_device_data	Yes	fu3_perf_rv_pac	Adequate RV pacing	nominal	Yes / No

25.3. Treatment of Missing and Spurious Data

See general definitions in chapter 5.4.

25.4. Exclusion of Particular Information

See general definitions in chapter 5.5.

25.5. Descriptive Analyses

See general definitions in chapter 5.1.

25.6. Hypotheses & Statistical Tests

Null hypothesis: $H_{0\_Pacing}: Plexa_{Pacing} \leq 93\%$

Alternative hypothesis: $H_{A\_Pacing}: Plexa_{Pacing} > 93\%$

No multiplicity adjustment is performed for the secondary hypotheses. Thus a one–sided exact binomial test is carried out for the significance level 2.5%. Additionally, a two-sided 95% confidence interval for an exact binomial test is calculated.

[102] analysis_set_Plexa_SAR = Yes

Abbreviations

ADE	Adverse Device Effect
AE	Adverse Event
AF	Atrial Fibrillation
CDMS	Clinical Data Management System
CI	Confidence Interval
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
CRF	Case Report Form
FU	Follow-up
SADE	Serious Adverse Device Event
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAR	Statistical Analysis Report
SOP	Standard Operating Procedure
SD	Standard Deviation