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Senior Inspector Medical Technology
Health and Youth Care Inspectorate
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The Netherlands

10 April 2019

Subject: Premature termination of the enrolments in the FRIENDS Study (your ref. VGR2010792)

Dear Sir / Madam,

Thirty-three (33) patients have been included in the FRIENDS study (Eudamed N. CIV-PT-18-08-025366, your ref. VGR2010792), since 27 December 2018. Thirty-two (32) patients were implanted with an active fixation InVicta lead and one (1) patient with a passive fixation InVicta lead, at ten investigational sites in France, Italy, Spain and Portugal.
On March 4, the Sponsor informed the National Competent Authorities, the Ethics Committees, and the Principal Investigators actively involved in the study, about the decision to temporary suspend of the enrolments in the study, following the occurrence of a series of adverse events related to the investigation device, and until a root cause analysis is completed and the advice from the Data Safety Monitoring Board is obtained.

So far, eight (8) serious events (including one continuation of a previous event) have been classified by the investigators (and by the independent Events Adjudicator) as related either to the InVicta active fixation and/or to its implant procedure; these events occurred in six (6) patients, within 9 days from the implant of the investigational device and resulted in lead dislodgment or myocardial injury. These events are expected, but their high incidences triggered the suspension of the enrollments and the beginning of a root cause analysis. All events have been resolved without sequelae, and none resulted in death. Three (3) patients had the InVicta lead repositioned, and three (3) patients had the InVicta lead explanted.
At present, 30 patients remain enrolled in the study. No further adverse events related to the investigational device have been reported, with an average follow up period of 63 days (range 40-102 days).

No active site and no patient enrolled in the Netherlands.

	FRIENDS Study	The Netherlands
Enrolling sites	10	0
Patients enrolled *(InVicta active/passive fixation)*	33 *(32/1)*	0
Patients with SAE related to InVicta device and/or implant procedure *(InVicta active/passive)*	6 *(6/0)*	0
Patients explanted *(InVicta active/passive fixation)*	3 *(3/0)*	0
Patients ongoing in the study *(InVicta active/passive fixation)*	30 *(29/1)*	0

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The Data Safety Monitoring Board met on 4 April 2019, in order to evaluate the accumulated study data and provide recommendations to the Sponsor. The board acknowledged that Sponsor's proactive measures and communication (i.e. suspension of the enrolments and relevant communication on March 4th) were prompt and appropriate, and advised on the next course of action.

Although the technical analysis of the root causes is not yet conclusive and still ongoing, a partial review of the design of the InVicta leads is under consideration by MicroPort CRM.

Consequently and in agreement with the DSMB advices, the Sponsor has decided to:

- Terminate the enrolments of the InVicta active and passive fixation leads;
- Ask the investigators:
  - to perform monthly follow-up visits in clinic, until 6 months post-implant, in order to verity patients' status and electrical parameters of the InVicta lead: pacing threshold and impedance, sensing threshold, and defibrillation impedance (the recommendations for the longer follow-up period will be provided after the next DSMB meeting, in July);
  - to activate the remote monitoring and to perform a remote follow-up in between two consecutive visits in clinic (i.e. two weeks from a visit in clinic, until 6-month visit);
  - to obtain fluoroscopic images or films, in different views, in order to visualize the lead tip and screw deployment, and to exclude dislodgment or myocardial injury, for any patient showing a worsening of the InVicta electrical parameters at follow-up (no cut-off value of the electrical parameters can be pre-defined. This remains at investigator's judgment);
  - to explant the lead, in case a re-intervention is required, following a worsening of the electrical performance and suspicion of lead dislodgment or myocardial injury;
  - to inform the enrolled subjects and collect patients' acknowledgment in writing.

The Sponsor is informing the National Competent Authorities, the ECs, and the Principal Investigators involved in the study.
The Sponsor will continue to ensure the availability of resources to fulfill the obligations from the Clinical Investigation Plan and existing agreements for following up the subjects enrolled in the study.
The Sponsor will promptly inform the other parties of any further relevant information that could arise and any other recommended actions that might be decided.

Sincerely,

Alberto **Borri**/**Brunetto**
Clinical Program Manager

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