Boston Scientific

CLINICAL SUMMARY

# COGENT-4 FIELD FOLLOWING STUDY

**CAUTION:** Federal law (USA) restricts this device to sale by or on the order of a physician trained or experienced in device implant and follow-up procedures.

# ABOUT THIS SUMMARY

Boston Scientific Corporation acquired Guidant Corporation in April 2006. During our transition period, you may see both the Boston Scientific and Guidant names on product and patient material. As we work through the transition, we will continue to offer doctors and their patients technologically advanced and high quality medical devices and therapies.

# COGENT-4 FIELD FOLLOWING STUDY

The COGENT-4 Field Following Study was a prospective, multi-center clinical study designed to evaluate the safety and efficacy of the Boston Scientific COGNIS® and TELIGEN® 100 HE family of implantable cardioverter defibrillators and associated application software. An optional sub-study also evaluated the safety and efficacy of the Reverse Mode Switch (RMS) feature within the TELIGEN 100 HE DR arm and data was collected to evaluate the appropriate function of RMS Mode Switches. A total of 219 patients were enrolled in the study between February 21, 2008 and June 04, 2008.

## PATIENT POPULATION

Of the 219 patients enrolled in the study, 116 were enrolled in the RMS sub-study. The Investigator had the responsibility of screening all potential patients and selecting those who met the study eligibility criteria as described below.

### Inclusion Criteria

- ICD Indication according to normal clinical practice (for those patients receiving a TELIGEN 100 HE)
- CRT-D Indication according to normal clinical practice (for those patients receiving a COGNIS 100 HE)
- Willing and capable of providing informed consent, undergoing a device implant, participating in all testing associated with this clinical investigation at an approved clinical investigational center and at the intervals defined by this protocol
- Geographically stable patients who are available for follow-up at a study center
- Age 18 or above, or of legal age to give informed consent specific to national law

### Exclusion Criteria

- Documented life expectancy of less than six months or expected to undergo heart transplant within the next six months
- Patients currently requiring dialysis
- Women who are pregnant or plan to become pregnant. Method of assessment per physician discretion
- Enrolled in any concurrent study
- Patients implanted with the following leads which will not be abandoned:
  - Atrial or right ventricular unipolar leads
  - Patch defibrillation leads
  - Non-compatible defibrillation leads (e.g. 5/6mm)
- Documented permanent/Complete AV block

- Documented permanent atrial fibrillation (AF)

### Patient Demographics

For the RMS substudy, the average age at implant for all patients was 61.9 ± 11.6 years. 84% of patients were male (n=87) and the documented mean left ventricular ejection fraction was 34.5 ± 13.9%. The majority of substudy patients implanted with a TELIGEN ICD were NYHA classes I and II (40 and 29% respectively). The primary cardiac disease was Ischemic Cardiomyopathy (63% of patient population). Seventy percent of TELIGEN ICD patients had a history of ventricular tachyarrhythmias.

## METHODS

The study was a prospective, multi center clinical evaluation that included an optional, randomized sub-study to evaluate the RMS feature in TELIGEN 100 HE DR devices. All implanted patients were required to be followed at implant, pre-discharge, 1-month and 3-months. The safety and efficacy of the RMS feature in the TELIGEN 100 HE DR device was evaluated by the following endpoints:

- RMS Safety Objective: 1-Month Reverse Mode Switch Related Adverse Event-Free Rate in TELIGEN 100 DR

- RMS Efficacy Objective: Absolute Reduction in Cumulative Vp with RMS ON versus OFF

## RESULTS

### RMS Substudy Objectives

A total of 219 patients were enrolled at 27 international centers of which 216 were successfully implanted and 206 completed their 3 month follow-up. A total of 116 TELIGEN DR patients were included in the RMS Sub-Study. Of these patients, 114 contributed to the 1-Month Reverse Mode Switch Related Adverse Event-Free Rate endpoint. Only three patients were identified as contributing towards the endpoint all prompted by patient symptoms such as fatigue, dizziness, palpitations, demonstrating that the RMS feature can be considered safe (see Table 1 on page 2). These adverse events did not require invasive intervention and the cause of two of these adverse events is unknown and two of the three adverse events were attributed to device sensing. None of these events led to the patient being withdrawn from the study.

**Table 1. RMS Adverse Event-Free Rate**

| Patients contributing to endpoint | Patients Free of RMS Related Adverse Event | Lower one-sided 95% confidence limit | P-value |
|---|---|---|---|
| 114 | 111 / 114 (97.4%) | 93.3% | <0.01 |

As the sub-study safety objective evaluated the RMS adverse event-free rate between implant and 1-month in which all patients had RMS ON, an additional summary is presented in Table 2 on page 2 to display the number of reported events that occurred once a patient was randomized to RMS ON or OFF (i.e., between the 1-month and 3-month visits).

**Table 2. AEs Occurring between 1-Month and 3-Month Visits**

| | Randomized to RMS ON at 1-Month (N=53) | | Randomized to RMS OFF at 1-Month (N=53) | |
|---|---|---|---|---|
| Adverse Event | Events | Patients (% of Patients) | Events | Patients (% of Patients) |
| PG Related Events | 6 | 6 (11%) | 22 | 17 (32%) |
| RA Lead Related Events | 6 | 5 (9%) | 7 | 5 (9%) |

**Table 2. AEs Occurring between 1-Month and 3-Month Visits** (continued)

| | Randomized to RMS ON at 1-Month (N=53) | | Randomized to RMS OFF at 1-Month (N=53) | |
|---|---|---|---|---|
| **Adverse Event** | **Events** | **Patients (% of Patients)** | **Events** | **Patients (% of Patients)** |
| Procedure Related Events | 4 | 4 (8%) | 2 | 2 (4%) |
| Cardiovascular Related Events | 10 | 10 (19%) | 5 | 4 (8%) |
| Non-Cardiovascular Related Events | 0 | 0 (0%) | 3 | 2 (4%) |
| Total Adverse Events | 26 | 19 (36%) | 39 | 23 (43%) |

Of the 116 patients enrolled in the RMS safety endpoint, 103 were included in the intention-to-treat evaluation of efficacy where patients were randomized to either ON or OFF at the 1 Month Follow Up using a 1:1 randomization (51 were randomized to RMS OFF and 52 to RMS ON). The percentage of right ventricular pacing (RVp) was then evaluated at the 3-month follow-up and compared in a parallel design. At the 3 Month follow-up, RVp in the RMS OFF arm was 18.7% versus 5.2% in the RMS ON arm, an absolute difference of 13.5%. There was a significant reduction in RVp between the OFF and ON arms (P=0.01), however it was not possible to demonstrate a significant difference based on the endpoint requirement of an absolute reduction of at least 10% between arms (see Table 3 on page 3).

**Table 3. RMS Efficacy-Intention-to-Treat**

| RMS ON | | RMS OFF | | | | |
|---|---|---|---|---|---|---|
| **N** | **Mean** | **N** | **Mean** | **Difference** | **Lower one-sided 95% confidence limit** | **P-value** |
| 52 | 5.2% | 51 | 18.7% | 13.5% | 4.8% | 0.25 |

## Appropriate Function of RMS Mode Switches

A total of 395 stored RMS episodes were collected as ancillary data and retrospectively evaluated for appropriate function (see Table 4 on page 3). For all episodes AAI(R) pacing was appropriate at the programmed LRL and backup VVI pacing support was appropriate at LRL minus 15 bpm. In addition, consistent ventricular activity was documented for all episodes and the VVI backup pacing was appropriately maintained within the range of 30 bpm to 60 bpm, depending on programming. Since the timing of VVI back-up pacing was always appropriate it means that there were no ventricular pauses longer than 2 seconds documented in any of the 395 RMS episodes. Finally, the transition from AAI(R)/VVI to DDD(R) was always according to pre-defined criteria and no ventricular pauses longer than 2 seconds were observed for any AAI(R)/VVI to DDD (R) transition. Based on this information it was considered that appropriate functioning of the algorithm had been demonstrated for 100% of stored episodes.

**Table 4. Reverse Mode Switch Episodes**

| Type | Frequency |
|---|---|
| Patients with TELIGEN 100 HE DR | 120 |
| Patients with RMS On at Implant, Pre-Discharge, or 1 Month | 115 |
| Patients with an RMS Episode | 78 |
| RMS Episodes Stored | 395 |
| Appropriate RMS Episodes | 395 |

## CONCLUSION

RMS was demonstrated to be considered safe as only three patients were identified as contributing towards the safety endpoint. While it was not possible to show the endpoint-defined difference of >10% reduction in RV pacing using an intention-to-treat population, efficacy was demonstrated by the significant reduction in total percentage of RV pacing at 3 months between patients with RMS ON (5.2%) versus OFF (18.7%; p=0.01).

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358487-012 EN US 06/10