Boston Scientific

CLINICAL SUMMARY

CONTAK RENEWAL 3 AVT

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

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 materials. As we work through the transition, we will continue to offer doctors and their patients technologically advanced and high quality medical devices and therapies.

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CLINICAL STUDY - CONTAK RENEWAL 3 AVT

CLINICAL STUDY POPULATIONS

The CONTAK RENEWAL 3 AVT trial, a prospective clinical study, was conducted using the CONTAK RENEWAL 3 AVT CRT-D system in patients with a history of atrial tachyarrhythmias (AT) and with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction (EF ≤35%), and QRS duration ≥ 120 ms.

SUMMARY

Boston Scientific conducted the CONTAK RENEWAL 3 AVT study, which demonstrated the safety and effectiveness of the CONTAK RENEWAL 3 AVT device.

Safety

The adverse event rate was well within acceptable limits. The lower one-sided confidence bound was 79.8%, which met the primary safety endpoint of greater than 70%. The safety performance of the CONTAK RENEWAL 3 AVT system compares favorably with the safety performance observed with other commercially available CRT-D devices.

Effectiveness

The atrial shock therapy conversion rate for CONTAK RENEWAL 3 AVT was compared to the conversion rate associated with conventional pharmacological options and other commercially available devices in converting AF using shock and met the pre-specified performance criteria of greater than 60%. AF can be safely and effectively terminated with atrial shocks in patients with heart failure. Additionally, the CONTAK RENEWAL 3 AVT device is effective at discriminating atrial arrhythmias from all other rhythms.

A secondary safety endpoint with the objective to confirm that BiV trigger does not induce ventricular arrhythmias was also met. The study results indicate that the BiV trigger feature is safe and not proarrhythmic.

ADVERSE EVENTS SUMMARY

Table 1. Adverse Events

		Complications		Observations	
Adverse Event	**Number Of Events (Number of Patients)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**
Total Adverse Events	204 (97)	27.4 (46)	6.7 (62)	44.0 (74)	15.4 (142)
Defib Lead Related Events					
Oversensing - Defibrillation lead	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
EASYTRAK 2 Lead Related Events					
Dislodgment - Elevated threshold - LV	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Dislodgment - Extracardiac stimulation - LV	3 (3)	1.8 (3)	0.3 (3)	0.0 (0)	0.0 (0)
Dislodgment - Multiple signs - LV	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Dislodgment - Unable to capture - LV	4 (4)	2.4 (4)	0.4 (4)	0.0 (0)	0.0 (0)
Elevated threshold - LV	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Extracardiac stimulation - LV	26 (19)	0.6 (1)	0.1 (1)	10.7 (18)	2.7 (25)
Unable to capture - LV	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
EASYTRAK Lead Related Events					
Dislodgment - Extracardiac stimulation - LV	2 (2)	1.2 (2)	0.2 (2)	0.0 (0)	0.0 (0)

Table 1. Adverse Events

		Complications		Observations	
Adverse Event	**Number Of Events (Number of Patients)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**
Elevated threshold - LV	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Extracardiac stimulation - LV	2 (2)	0.6 (1)	0.1 (1)	0.6 (1)	0.1 (1)
PG Related Events					
Elevated DFT - Defibrillation	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Inappropriate tachy therapy - Noise	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Inappropriate tachy therapy - SVT	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Infection (> 30 days post-implant)	2 (2)	1.2 (2)	0.2 (2)	0.0 (0)	0.0 (0)
Other - PG system	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Pacemaker-mediated tachycardia (PMT)	16 (14)	0.0 (0)	0.0 (0)	8.3 (14)	1.7 (16)
Programmer / Software error code	9 (9)	0.0 (0)	0.0 (0)	5.4 (9)	1.0 (9)
Psychological effect due to device therapy	3 (3)	0.0 (0)	0.0 (0)	1.8 (3)	0.3 (3)
Undersensing - RA	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
RA Lead Related Events					
Elevated threshold - RA	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)

Table 1. Adverse Events

		Complications		Observations	
Adverse Event	**Number Of Events (Number of Patients)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**
Oversensing - RA	4 (3)	0.0 (0)	0.0 (0)	1.8 (3)	0.4 (4)
Undersensing - RA	5 (3)	0.0 (0)	0.0 (0)	1.8 (3)	0.5 (5)
RV Lead Related Events					
Elevated threshold - RV	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Extracardiac stimulation - RV	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Oversensing - RV	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Subtotal Device Related Events	91 (59)	10.1 (17)	2.0 (18)	29.2 (49)	7.9 (73)
Procedure Related Events					
Adverse reaction - General	7 (7)	2.4 (4)	0.4 (4)	1.8 (3)	0.3 (3)
Adverse reaction - Hypotension	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Adverse reaction - Respiratory	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Coronary venous dissection	3 (3)	0.6 (1)	0.1 (1)	1.2 (2)	0.2 (2)
Elevated DFT - Defibrillation	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Hematoma - Pocket (<=30 days post-implant)	8 (8)	0.0 (0)	0.0 (0)	4.8 (8)	0.9 (8)

Table 1. Adverse Events

		Complications		Observations	
Adverse Event	**Number Of Events (Number of Patients)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**
Inadvertent VT/ VF	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Other - PG system - Procedure	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Physical trauma	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Post-surgical infection (<= 30 days post-implant)	5 (5)	2.4 (4)	0.4 (4)	0.6 (1)	0.1 (1)
Post-surgical pocket hemorrhage	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Post-surgical wound discomfort	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.2 (2)
Subtotal Procedure Related Events	32 (24)	6.0 (10)	1.2 (11)	8.9 (15)	2.3 (21)
Cardiovascular - HF Related Events					
Dehydration - Heart failure	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Dyspnea - Heart failure	6 (6)	3.0 (5)	0.5 (5)	0.6 (1)	0.1 (1)
Fatigue - Heart failure	2 (2)	0.6 (1)	0.1 (1)	0.6 (1)	0.1 (1)
Heart failure symptoms	10 (9)	3.0 (5)	0.7 (6)	2.4 (4)	0.4 (4)
Heart failure symptoms - Unspecified	3 (3)	1.8 (3)	0.3 (3)	0.0 (0)	0.0 (0)
Hypotension - Heart failure	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.2 (2)

Table 1. Adverse Events

		Complications		Observations	
Adverse Event	**Number Of Events (Number of Patients)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**
Renal insufficiency - Heart failure	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Weight gain - Heart failure	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Cardiovascular - Non-HF Related Events					
Atrial fibrillation (AF)	3 (3)	0.6 (1)	0.1 (1)	1.2 (2)	0.2 (2)
Atrial flutter	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Cerebrovascular accident (CVA)	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.2 (2)
Chest pain - Ischemic	3 (3)	0.6 (1)	0.1 (1)	1.2 (2)	0.2 (2)
Chest pain - Other	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Chronotropic incompetence	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.2 (2)
Dizziness	2 (2)	0.0 (0)	0.0 (0)	1.2 (2)	0.2 (2)
Fatigue	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Hypertension	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Hypotension	3 (3)	0.6 (1)	0.1 (1)	1.2 (2)	0.2 (2)
Mitral regurgitation	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Mitral stenosis	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Multiple symptoms	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)

Table 1. Adverse Events

		Complications		Observations	
Adverse Event	**Number Of Events (Number of Patients)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**	**% of Patients (N Patients)**	**N Events/100 Device Months (N Events)**
Nonsustained ventricular tachycardia (NSVT)	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Other SVT (AVRT, AVNRT, EAT etc.)	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Pulseless electrical activity (PEA)	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Sinus tachycardia	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Syncope	1 (1)	0.0 (0)	0.0 (0)	0.6 (1)	0.1 (1)
Ventricular fibrillation (VF)	1 (1)	0.6 (1)	0.1 (1)	0.0 (0)	0.0 (0)
Ventricular tachycardia (VT)	4 (4)	0.0 (0)	0.0 (0)	2.4 (4)	0.4 (4)
Subtotal Cardiovascular Related Events	**58 (42)**	**10.7 (18)**	**2.8 (26)**	**16.7 (28)**	**3.5 (32)**
Total Non-cardiovascular Related Events	**23 (21)**	**4.2 (7)**	**0.8 (7)**	**8.3 (14)**	**1.7 (16)**

STUDY DESIGN

This clinical investigation was a 170 patient prospective, multi-center, single-arm study at 38 centers in the United States. One hundred sixty eight (168) patients underwent a procedure to receive the CONTAK RENEWAL 3 AVT or

CONTAK RENEWAL 3 AVT HE device and the EASYTRAK/EASYTRAK 2 pace/sense lead. Patients underwent an evaluation of the investigational system at implant, pre-discharge, one month, three months, and quarterly thereafter. Patients were programmed to a biventricular pacing mode during the three-month study period post-implant. The programmed atrial and ventricular tachyarrhythmia device therapy was left to the discretion of the investigator.

Evaluation of the EASYTRAK 2 lead, consisting of measurement of left ventricular pacing thresholds, left ventricular lead impedances, and left ventricular R-wave amplitudes, was performed at each scheduled visit.

Inclusion Criteria

Patients enrolled in the study were required to meet the following inclusion criteria:

- Meet all device indications and contraindications. (LVEF and QRS must be documented within 90 days prior to enrollment. NYHA must be documented at time of enrollment.)
- 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.
- Prescribed to stable optimal pharmacological therapy for heart failure as defined below:
  - Beta Blockers: All patients must be prescribed to beta blockers for 90 days prior to enrollment, and on a stable dose (e.g., no greater than a 50% increase or decrease in dosage) for the 30 days prior to enrollment unless the patient is not indicated, is contraindicated, is intolerant, or has developed a recent ICD indication that necessitates ICD therapy concurrent with the optimization of beta blocker therapy. The choice of selective or non-selective beta-blocker use is left to the investigator's discretion.
  - Angiotensin Converting Enzyme (ACE) Inhibitors: All patients must be prescribed to stable ACE inhibitor therapy for 30 days or angiotensin receptor blocker (ARB) unless the patient is not indicated, contraindicated, is intolerant, or has developed a recent ICD indication that necessitates ICD therapy concurrent with the optimization of ACE inhibitor therapy.
- Creatinine < 2.5 mg/dL obtained no more than two weeks prior to enrollment

- Age 18 or above, or of legal age to give informed consent specific to state and national law
- Geographically stable residents who are available for follow-up
- Able to provide documented[1] evidence of one or more episodes of AF/AT within 12 months of implantation

NOTE: *Boston Scientific recommends anticoagulation therapy per physician discretion.*

Exclusion Criteria

Patients were excluded from the investigation if they met any of the following criteria:

- Have a preexisting non-Guidant left ventricular lead
- Have a preexisting unipolar pacemaker that will not be explanted/abandoned
- Documented life expectancy of less than six months or expected to undergo heart transplant within the next six months
- Have an atrial tachyarrhythmia that is permanent (i.e., does not terminate spontaneously and cannot be terminated with medical intervention) within 180 days prior to enrollment
- Have a known hypersensitivity to a 0.7 mg dose of dexamethasone acetate
- Have surgically uncorrected primary valvular heart disease
- Currently requiring hemo-dialysis
- Have had a myocardial infarct, unstable angina, percutaneous coronary intervention, or coronary artery bypass graft during the preceding 30 days prior to enrollment
- Have hypertrophic obstructive cardiomyopathy or infiltrative cardiomyopathy (e.g., amyloidosis, sarcoidosis)

1. Source documentation includes but is not limited to one or more of the following: 12-lead ECG, telemetered rhythm strips, Holter and event monitor recordings, physician reports, and/or medical records/progress notes.

- Have a mechanical tricuspid heart valve
- Enrolled in any concurrent study, without Guidant written approval, that may confound the results of this study
- A Cerebral Vascular Event/ Transient Ischemic Attack within 12 months of implantation
- During the four weeks prior to implantation, a patient experiences an episode of AF ≥ 48 hours in duration and was not anticoagulated at an adequate therapeutic level for the 4 weeks prior to enrollment with an INR = 2.0-3.0 at enrollment

  NOTE: *If above criteria is not met or adequate documentation on anticoagulation does not exist, then the patient may be included if a routine transesophageal echocardiogram (TEE) is negative for intracavitary "smoke" or thrombus at the time of implant.*

- Women who are pregnant or plan to become pregnant

  NOTE: *Women of childbearing potential must have a negative pregnancy test within 7 days of enrollment.*

Follow-up schedule

Enrollment	Initial assessment of patient eligibility; patient history
Implant	Implant of investigational device and acute device testing
Routine Follow-up	Routine evaluation of device function and patient condition at pre-discharge, one-month, three-month
Quarterly Visits	After the 3-month follow-up patients were seen for routine evaluation of device function and patient condition

Endpoints

The CONTAK RENEWAL 3 AVT clinical study consisted of:

Primary Endpoints

- Safety Endpoint: System Complication-Free Rate

Objective: To show that the CONTAK RENEWAL 3 AVT system functions safely

- Effectiveness Endpoint: Atrial Fibrillation Shock Conversion Rate

  Objective: To demonstrate the effective termination of induced episodes of atrial fibrillation by cardioversion

- Effectiveness Endpoint: Appropriate Detection and Classification of Atrial Arrhythmias

  Objective: To correctly detect and classify atrial arrhythmias (AF and/or SVT) from all other rhythms

Secondary Endpoints

- Safety Endpoint: Ventricular Fibrillation (VF) Detection Time

  Objective: To confirm normal ICD sensing and detection in the presence of atrial therapies

- Safety Endpoint: Percent Biventricular (BiV) Pacing

  Objective: To confirm CRT pacing is delivered in the presence of atrial therapies

- Safety Endpoint: Rate of Inappropriate Response to BiV Trigger Feature

  Objective: To confirm BiV Trigger does not induce ventricular arrhythmias

- Safety Endpoint: EASYTRAK 2 Lead Complication-Free Rate

  Objective: To show that the EASYTRAK 2 lead functions safely

Note that during the course of the CONTAK RENEWAL 3 AVT trial, the EASYTRAK 2 Coronary Venous pace/sense lead was established as safe and effective in a separate clinical study and was approved for commercial distribution (*P010012/S024, 8/6/04*). Refer to the commercially available EASYTRAK 2 Coronary Venous pace/sense lead labeling for clinical safety and performance characteristics.

STUDY RESULTS

Patient Accountability

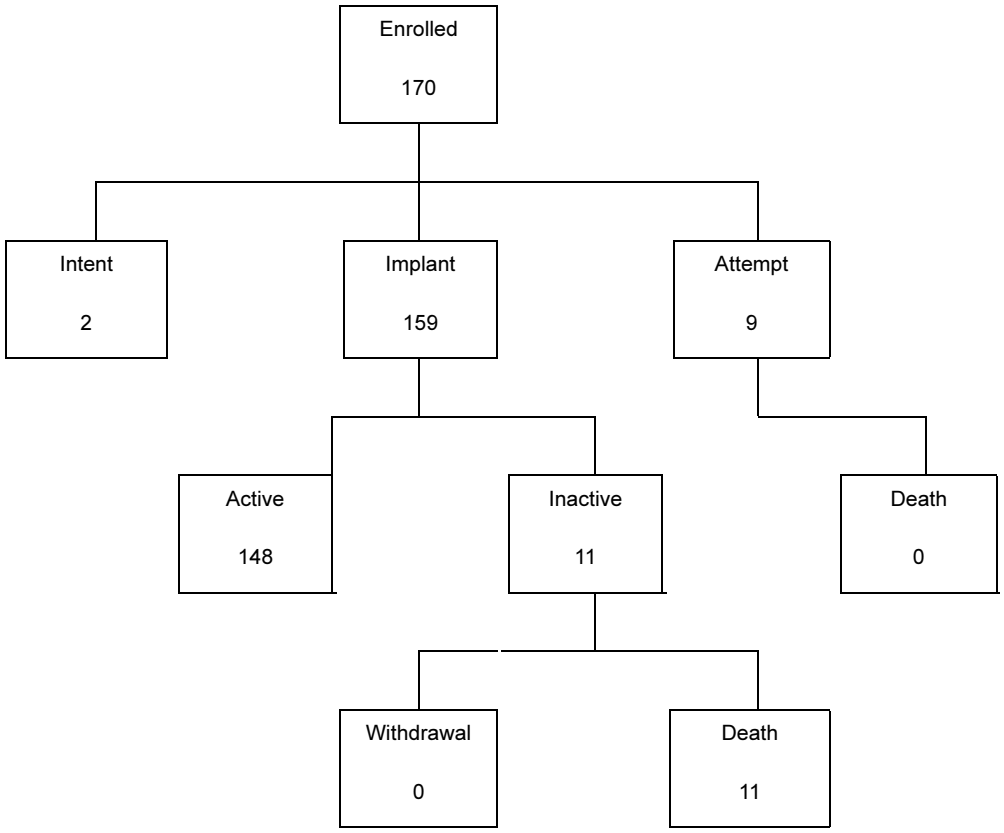

Figure 1 Patient Accountability.

Demographic Data

Table 2. Characteristics of Patient Population

Characteristic	Measurement	Result
Age at Implant (years)	N	168
	Mean ± SD	70.7 ± 10.3
	Range	40.8 - 87.6
Gender [N (%)]	Male	142 (85)
	Female	26 (15)
NYHA Class [N (%)]	III	147 (88)
	IV	21 (12)
LVEF (%)	N	168
	Mean ± SD	22.6 ± 6.4
	Range	10.0 - 35.0
QRS Duration (ms)	N	167
	Mean ± SD	150 ± 25
	Range	120 - 237
Concomitant Medications[a] [N (%)]	ACE Inhibitor or ARB	129 (77)
	Aldosterone Antagonist	59 (35)
	Anticoagulant	150 (90)
	Beta Blocker	111 (66)
	Loop Diuretic	149 (89)
Etiology [N (%)]	Ischemic	131 (78)
	Nonischemic	37 (22)

Characteristic	Measurement	Result
Conduction Disorder [N (%)]	Left Bundle Branch Block	107 (64)
	Nonspecific Intraventricular Delay	34 (20)
	Right Bundle Branch Block	27 (16)
Primary Tachy Arrhythmia [N (%)]	Monomorphic VT (MVT)	44 (26)
	Nonsustained VT with inducible MVT	24 (14)
	Ventricular Fibrillation (VF)	18 (11)
	Inducible VT	9 (5)
	Non-sustained VT	7 (4)
	Ventricular Tachycardia (VT)	3 (2)
	Polymorphic VT (PVT)	2 (1)
	Other	2 (1)
	None[b]	59 (35)
Primary Atrial Arrhythmia [N (%)]	Atrial Fibrillation (AF)	120 (71)
	Atrial Flutter	21 (13)
	Paroxysmal Atrial Fibrillation	10 (6)
	Paroxysmal Atrial Tachycardia (PAT)	10 (6)
	PSVT	5 (3)
	Other	2 (1)

a. Patients may appear more than once.
b. Patients without a primary tachy arrhythmia had the following indications: MADIT II and/or HF.

Primary Endpoints

Primary Safety Endpoint 1: System-Related Complication-Free Rate

The safety of the investigational system was assessed by the system related complication-free rate observed in the period between implant and the three-month follow-up visit in all patients attempted or implanted with a CONTAK RENEWAL 3 AVT system.

The system related complication free rate at three months was 85.1% with a lower 95% confidence bound of 79.8%. These data met the primary safety endpoint – system related complication-free rate of greater than 70% – and demonstrate device safety of the CONTAK RENEWAL 3 AVT system.

Table 3. System Related Complications

Complication	Number of Events	Number of Patients	Complication Free Rate	Lower One-Sided 95% Confidence Bound
LV Lead	10	10	94.0	90.1
EASYTRAK 2 Lead	8	8	95.2	91.6
EASYTRAK Lead	2	2	98.8	96.3
PG	4	4	97.6	94.6
Procedure	12	11	93.5	89.4
Total	**26**	**25**	**85.1**	**79.8**

An additional analysis using the Kaplan-Meier method was performed with results demonstrating a 3-month event free rate of 85.7% with a lower confidence bound of 81.1%. This bound is similar to that resulting from the straight rate and is still above the acceptance criterion.

Figure demonstrates the time to first system related complication using a Kaplan-Meier analysis; details are provided in Table 4.

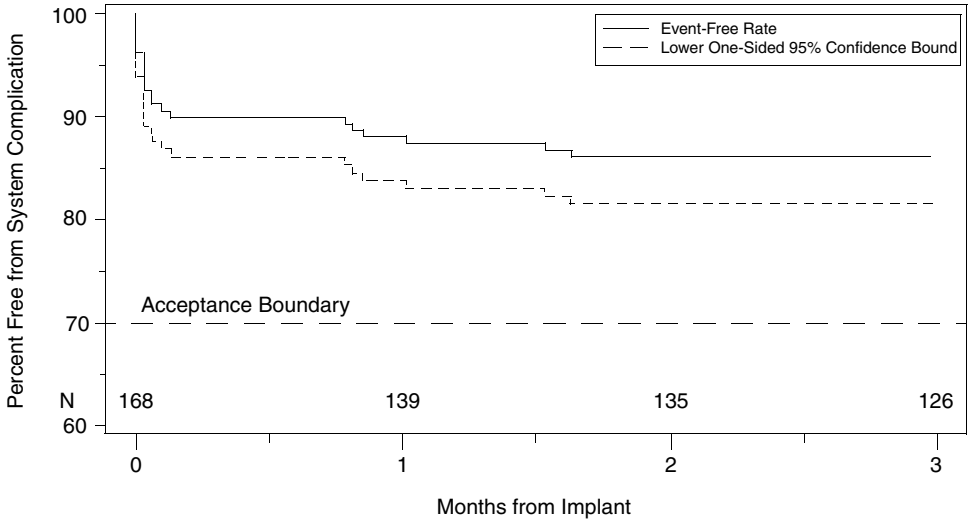

Figure 2. Time to System Related Complication.

Table 4. Details for Time to System Related Complication

	Start of Interval (Months from Implant)			
Statistic	**0**	**1**	**2**	**3**
Number at Risk at Start of Interval	167	139	134	125
Number of Events in Interval	19	4	0	0
Cumulative Number of Events	19	23	23	23
Number Censored in Interval	9	1	9	125
Cumulative Number Censored	9	10	19	144
% Freedom from Event	100.0	88.2	85.7	85.7
Lower One-Sided 95% Confidence Limit	100.0	84.0	81.1	81.1

Primary Effectiveness Endpoint 1: AF Shock Conversion Rate

AF Shock Conversion Rate was calculated from induced and spontaneous episodes classified as AF that received verifiable shock therapy and compared to conversion rates for conventional pharmacological options and other commercially available devices.

A total of 152 AF episodes had verifiable conversion data of which 138 were successfully converted, for an AF Shock Conversion Rate of 90.8%. The CONTAK RENEWAL 3 AVT AF Shock Conversion Rate met the pre-specified and agreed upon performance criteria of greater than 60% ($p<0.001$). An additional generalized estimating equations (GEE) analysis to account for the correlation due to multiple episodes per patient produced an adjusted rate of 91.3% with a 95% confidence interval of (85.2, 95.0). Table 5 contains details of AF Shock Conversion Rate, First Shock Conversion Rate and Clinical Conversion Rate (defined as sinus rhythm two minutes post shock, induced episodes only) for all AF episodes. Separate device conversion efficacies are also shown for induced and spontaneous AF episodes.

Table 5. Atrial Fibrillation Shock Conversion

	AF Episodes (N)	Successful Conversions (N)	Conversion Rate
AF Shock Conversion Rate - All AF Episodes	152	138	91%
AF Shock Conversion Rate - Induced	140	127	91%
AF Shock Conversion Rate - Spontaneous	12	11	92%
First Shock Conversion Rate	152	118	78%
Clinical Conversion Rate - Induced	140	121	86%

Primary Effectiveness Endpoint 2: Appropriate Detection and Classification of Atrial Arrhythmias

Appropriate Detection and Classification of Atrial Arrhythmias is measured by sensitivity, defined as the number of atrial arrhythmias identified by the device divided by the total number of documented atrial arrhythmias. Any sustained atrial episode not detected, or incorrectly classified by the device, was counted against this endpoint.

A total of 184 episodes of the 188 induced atrial episodes in 133 patients were appropriately detected and classified resulting in a sensitivity of 97.9%. Three patients had 4 episodes that were not detected as AF/AT due to P-wave undersensing related to the patient's underlying medical condition. The sensitivity of CONTAK RENEWAL 3 AVT met the pre-specified and agreed upon criteria of greater than 83% ($p<0.001$). An additional GEE analysis to account for the correlation due to multiple episodes per patient produced an adjusted sensitivity of 97.8% with a 95% confidence interval of (93.5, 99.2). The

CONTAK RENEWAL 3 AVT device is effective at discriminating atrial arrhythmias from all other rhythms. The Appropriate Detection and Classification endpoint was met.

Secondary Endpoints

Secondary Safety Endpoint: VF Detection Time

VF detection time was evaluated with the typical CRT/ICD features and the addition of the CONTAK RENEWAL 3 AVT atrial features (Atrial Shocks; Atrial ATP; ARC; APP; Post A Therapy APP and ProACt) enabled. Ventricular Fibrillation Detection Time was defined as the interval starting from 250 ms after the last induction artifact (the time of the post induction ventricular refractory period) and ending at the "V-Episode Declared" marker on real-time electrograms. A mean VF detection time was calculated for each patient.

A total of 150 patients had successful VF inductions at implant. The atrial features (Atrial Shocks; Atrial ATP; ARC; APP; Post Atrial APP and ProACt) were required to be programmed ON. Average VF detection time with all features ON was 2.5 ± 0.6 seconds. The CONTAK RENEWAL 3 AVT VF detection time met the pre-specified and agreed upon performance criteria of less than 4.1 seconds based on the CONTAK CD study. The results for VF detection time are shown in Table 6.

Table 6. VF Detection Time

Number of Patients	Mean	SD	p-value[a]
150	2.5	0.6	<0.001

a. P-value determined using a one sample t-test.

Secondary Safety Endpoint: Percent Biventricular Pacing

The safety of CRT therapy provided by the investigational system was assessed by the percent of time a patient is appropriately paced, as recorded by the device counter, at the three-month visit. The appropriateness of CRT delivery was defined by whether the device delivered CRT in accordance with the physician's programming. The objective of this endpoint was to demonstrate that patients receive continuous appropriate pacing from the device during activities of daily living. For each patient, the value for percent of time LV paced as recorded by the device counter was collected at the 3-month follow-up.

As shown in Table 7, the mean percentage of appropriately paced beats during activities of daily living was 95.8 ± 7.1 with a median of 98.0, which meets the prespecified and agreed upon performance criteria of 85%. These data demonstrate device safety of the CONTAK RENEWAL 3 AVT in providing continuous appropriate CRT during activities of daily living.

Table 7. Percent BiV Pacing

Number of Patients	Mean +/- SD	Range	Median	p-value[a]
132	95.8 ± 7.1	33 - 100	98	<0.001

a. P-value calculated from a signed-rank test.

Secondary Safety Endpoint: Rate of Inappropriate Response to BiV Trigger Feature

Biventricular (BiV) Trigger was designed to promote synchronized right and left ventricular contractions by pacing the right and left ventricle immediately after a sensed right ventricular event. The BiV Trigger feature was evaluated in all patients by the investigator at each follow-up visit by reviewing the VT/VF episodes to determine whether any events were associated with a BiV trigger pace. A VT/VF episode was considered associated with BiV Trigger if the first beat of the event onset was immediately preceded by a BiV Trigger pace marker.

The acceptance criterion for this secondary endpoint was defined as a response rate of zero (0). The failure criterion for this endpoint is defined as one or more incidences of inappropriate response.

There were no VT/VF episodes caused by BiV Trigger in the 432 VT/VF episodes from 71 patients reviewed by the investigators. The BiV Trigger feature is safe and is not proarrhythmic.

Ancillary Data Analysis

Concomitant Arrhythmia Testing

To determine the ability of the CONTAK RENEWAL 3 AVT device to discriminate between atrial and ventricular arrhythmias, patients were also induced into AF plus VT/VF. There were 114 successful inductions of AF plus VF/VT at implant. All ventricular episodes were appropriately declared by the device.

The addition of atrial features and therapies (Atrial Shocks; Atrial ATP; ARC; APP; Post A Therapy APP and ProACt) had no affect on the ability of the CONTAK RENEWAL 3 AVT device to successfully detect ventricular fibrillation demonstrating that the CONTAK RENEWAL 3 AVT device is safe and effective in the detection of ventricular fibrillation.

Spontaneous Ventricular Episodes

A total of 1049 spontaneous ventricular episodes were recorded during the clinical investigation in 49 patients. Seventy-five (75) episodes received therapy (ATP and/or shocks). The remainder of spontaneous ventricular episodes were non-sustained. The breakdown of classification of episodes receiving therapy can be found in Table 8.

Table 8. Spontaneous Ventricular Episodes Receiving Therapy

Ventricular Episode Classification	N	%
VF Episodes	4	5.3
VT Episodes	68	90.7
Other	3	4.0
Total	**75**	**100.0**

Of the 4 spontaneous VF episodes, all received shock therapy and were successfully converted with the device, giving a VF shock conversion rate of 100%. VF and VT shock conversion efficacies are shown in Table 9.

Table 9. Spontaneous Episode Shock Conversion Effectiveness

Ventricular Episode Classification	Number of Episodes Receiving Shock Therapy	Number of Successful Conversions	Conversion Rate
VF Episodes	4	4	100%
VT Episodes	24	24	100%

Atrial ATP Conversions of SVT

Successful conversion of an SVT (non-AF) episode is defined by conversion to one of the following: sinus rhythm, sinus tachycardia, or atrial pacing within one-minute post therapy delivery.[1,2]

Forty-one (41) patients experienced 1104 episodes of SVT (8 induced, 1096 spontaneous). Conversion effectiveness at one minute was 65.7% (725/1104). The GEE adjusted rate at one minute was 56.8%.

SVT was terminated with ATP 65.7% of the time.

Expert Ease +

Expert Ease + (EE+) is designed to provide suggested settings for programming the device for CRT in a manual and automatic mode. Expert Ease + evaluates right and left ventricular response to both atrial sensed and atrial paced events to determine suggested settings for the AV Delay, Sensed AV Offset, and Ventricular Pacing Chamber.

This data shows that out of 112 eligible EE+ uses the EE+ recommended AV delay was programmed in the CONTAK RENEWAL 3 AVT device by the physician 88 times (79%). There were no adverse events related to the use of EE+.

1. Guidant. REASSURE AV US Investigational Plan (G040067).
2. Israel, C.W., Ehrlich, J.R., Gronefeld, G., Klesius, A., Lawo, T., Lemke, B., and Hohnloser, S.H. Prevalence, characteristics and clinical implications of regular atrial tachyarrhythmias in patients with atrial fibrillation: insights from a study using a new implantable device, Journal of the American College of Cardiology, Volume 38, Issue 2, August 2001, Pages 355-363.

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