SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name:	Cardiac Resynchronization Therapy Defibrillator (CRT-D) System
Device Trade Name:	St. Jude Medical Epic™ HF and Atlas® + HF Cardiac Resynchronization Therapy Defibrillator (CRT-D) including the Epic™ HF Model V-337 and V-338 and the Atlas® + HF Model V-340 and V-343
Applicant's Name and Address:	St. Jude Medical Cardiac Rhythm Management Division 15900 Valley View Court Sylmar, CA 91342
Date(s) of Panel Recommendation:	None
Premarket Approval Application Number:	P030054/S10
Date of Notice of Approval to Applicant:	NOV 18 2005

The Epic HF V-338 and Atlas + HF V-340 were originally approved on June 30, 2004 under PMA P030054. The Epic HF V-337 and Atlas + FH V-343 were approved on November 17, 2004 under PMA P030054/S1. The sponsor has submitted the current supplement to further expand the indications for use statement. The clinical data to support the expanded indication, i.e., to maintain synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic (permanent) atrial fibrillation and have NYHA Class II or III heart failure, are provided in this summary and were the basis for the approval of the Frontier™ Biventricular Pacing System reviewed under P030035. The pre-clinical test results were presented in the original PMA application and subsequent supplement as mentioned above. The summary of P030054 can also be found on the FDA CDRH Internet Home Page located at http://www.fda.gov/cdrh/pmapage.html.

II. Indications for Use

The St. Jude Medical the Epic™ and Atlas®+ HF CRT-D Systems are intended to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias.

In patients indicated for an ICD, the Epic™ and Atlas®+ HF CRT-D Systems are also intended:

- to provide a reduction of the symptoms of moderate to severe heart failure (NYHA Functional Class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy (as defined in the clinical trials section) and have a left ventricular ejection fraction less than or equal to 35% and a prolonged QRS duration
- to maintain synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic (permanent) atrial fibrillation and have NYHA Class II or III heart failure.

III. Contraindications

Contraindications for use of the Epic HF and Atlas + HF Systems include ventricular tachyarrhythmias resulting from transient or correctable factors such as drug toxicity, electrolyte imbalance, or acute myocardial infarction.

IV. Warnings and Precautions

Please refer to the specific device labeling for a list of warnings and precautions.

V. System Description

The St. Jude Medical Epic HF and Atlas + HF dual chamber implantable cardioverter defibrillator (ICD) systems are multi-programmable, implantable cardioverter defibrillators with biventricular pacing for cardiac resynchronization therapy (CRT) that monitor and regulate a patient's heart rate by providing ventricular tachyarrhythmia therapy and single- or dual-chamber bradycardia pacing with rate adaptive response (DDD(R)). The devices have five port headers (3 IS-1 Ports, 2 DF-1 Ports).

The devices are supported on the Model 3510 programmer platform with Model 3307, version 4.5m (or higher) programmer software.

Please refer to the physician User's Manual specific to the device being implanted.

VI. Alternative Practices or Procedures

The present established therapies for the treatment of patients with chronic atrial fibrillation include pharmacological therapy, cardioversion or right ventricular/biventricular pacing therapy post AV nodal ablation. The present established treatment of heart failure patients include pharmacological therapy, heart transplantation, other legally marketed CRT pacemakers (CRT-P) or CRT defibrillators (CRT-D) or other surgical procedures.

VII. Marketing History

The Epic HF and Atlas + HF family of pulse generators are currently distributed commercially in and outside the United States. Specifically, the Epic HF and Atlas + HF pulse generators are market approved in the US, European Community, Eastern Europe, Canada, Australia, Latin America, and Asia.

VIII. Adverse Events

The safety data presented in this section includes data from two St. Jude Medical biventricular pacing clinical studies. One study was the Resynchronization for HemodYnamic Treatment for Heart Failure Management (RHYTHM ICD) clinical investigation and the second was the Post AV Node Ablation Evaluation (PAVE) study. The data summarized in this section reflects the information presented and reviewed in this supplement. The data sets are updates from the referenced trials which continued beyond the dates of approval of the applications referenced below.

The PAVE study (approved under PMA P030035 on May 13, 2004) showed that the St. Jude Medical Frontier biventricular pacing system was safe and effective for "maintaining synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic atrial fibrillation and have NYHA Class II or III heart failure". The RHYTHM ICD study (approved under PMA P030054 on June 30, 2004) showed that the St. Jude Medical Epic HF and Atlas + HF cardiac resynchronization therapy defibrillator systems were safe and effective for providing ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias and providing a reduction of the symptoms of moderate to severe heart failure (NYHA Functional Class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy, and have a left ventricular ejection fraction less than or equal to 35% and a prolonged QRS duration.

Potential Adverse Events

Potential adverse events (in alphabetical order) associated with the Epic HF and Atlas + HF CRT-Ds, include, but are not limited to the following:

- Acceleration of arrhythmias (caused by device)
- Air embolism
- Allergic reaction
- Bleeding
- Cardiac tamponade
- Chronic nerve damage
- Death
- Erosion
- Exacerbation of heart failure
- Excessive fibrotic tissue growth
- Extracardiac stimulation (phrenic nerve, diaphragm, chest wall)
- Extrusion
- Fluid accumulation
- Formation of hematomas or cysts
- Inappropriate shocks
- Infection
- Keloid formation
- Lead abrasion and discontinuity
- Lead migration/ dislodgement
- Myocardial damage
- Pneumothorax
- Shunting current or insulating myocardium during defibrillation with internal or external paddles
- Potential mortality due to inability to defibrillate or pace
- Thromboemboli
- Venous occlusion
- Venous or cardiac perforation.

Patients susceptible to frequent shocks despite antiarrhythmic medical management may develop psychological intolerance to an ICD system that may include the following:

- Dependency
- Depression
- Fear of premature battery depletion
- Fear of shocking while conscious
- Fear that shocking capability may be lost
- Imagined shocking (phantom shock).

Deaths

RHYTHM ICD Study

Twenty-two (22) patients enrolled in the RHYTHM ICD clinical investigation were withdrawn from the study due to death. Three (3) of the deaths occurred in patients with an unsuccessful implant, 2 deaths occurred between the implant and the Baseline visit, 8 deaths occurred between Baseline and the 6-month visit and 9 deaths occurred after the 6-month visit. Five (5) of the 22 deaths were considered to be *peri-operative mortalities* (i.e., occurred ≤ 30 days post-implant). There were no deaths classified as related to the pulse generator or lead system. Three (3) of the twenty-two (22) deaths were in patients with an unsuccessful Epic HF System implantation although none of these deaths was attributed to the attempted implantations. A summary of the Events Committee death classifications is shown in Table 1 below.

TABLE 1: RHYTHM ICD DEATHS

Primary Cause	CRT OFF	CRT ON	N/A*	Total
Cardiac-Arrhythmic	0	0	0	0
Cardiac-Nonarrhythmic	1	2	4	7
Cardiac-Unknown	0	1	0	1
Non-Cardiac	3	8	1	12
Unknown	0	2	0	2
Total	**4**	**13**	**5**	**22**

**Death occurred in patients who did not have a successful Epic HF system implant (unrelated to the implant procedure) or death occurred before their Baseline visit and randomization.*

PAVE Study

Forty seven (47) deaths occurred throughout the study in the investigational groups. A summary of the death classification is shown in Table 2 below.

TABLE 2: PAVE DEATHS

Primary Cause	BV (N=151)	LV (N=53)	Roll-in (N=56)	Total (N=260)
Cardiac: Arrhythmic	1	2	0	**3**
Cardiac: Other	6	3	2	**11**
Cardiac: Unknown	2	0	0	**2**
Non-Cardiac	5	6	5	**16**
Unknown	7	4	3	**14**
Total	**21**	**15**	**10**	**46***

* One additional patient was consented, but died prior to any study related procedure.

Observed Adverse Events

RHYTHM ICD Study

The RHYTHM ICD study was a prospective, multicenter, randomized, double-blind, controlled clinical investigation designed to assess the safety and efficacy of the Epic HF ICD system in patients who were indicated for implantable cardioverter defibrillation therapy with New York Heart Association Class III/IV heart failure and a prolonged QRS duration.

Adverse events were classified as complications or observations based on the following definitions:

- ***Complications*** are defined as adverse events that require invasive intervention (e.g. lead dislodgement requiring repositioning).
- ***Observations*** are defined as adverse events that can be managed without invasive intervention (e.g., oversensing or loss of pacing capture, which is then remedied by reprogramming of the pulse generator).

Table 3 lists the observations and complications reported from the RHYTHM ICD clinical trial. A total of 107 adverse events were reported in 73 patients, of which 31 were complications and 76 were observations.

TABLE 3: RHYTHM ICD STUDY OBSERVED ADVERSE EVENTS

Event Description	# of Patients with AEs* (n = 205)	% of Patients with AEs	#AEs	AE/pt-years (n=231.95 years)
Complications (total)	**22**	**10.7%**	**31**	**0.134**
Coronary Sinus Perforation/Dissection	2	1.0%	2	0.009
Diaphragmatic/Phrenic Nerve Stimulation	3	1.5%	3	0.013
Lead Dislodgement or Migration	9	4.4%	10	0.043
Bleeding/Hematoma**	6	2.9%	6	0.026
Blood Clot/Thrombosis	1	0.5%	1	0.004
High Defibrillation/Cardioversion Requirements	2	1.0%	2	0.009
Infection	2	1.0%	2	0.009
Noise on EGM Post Shock (Non-SJM RV lead)	1	0.5%	1	0.004
Pneumothorax	2	1.0%	2	0.009
Retained Foreign Body (surgical sponge)	1	0.5%	1	0.004
Elevated Pacing Threshold – LV Lead	1	0.5%	1	0.004

TABLE 3: RHYTHM ICD STUDY OBSERVED ADVERSE EVENTS (CONTINUED)

Event Description	# of Patients with AEs* (n = 205)	% of Patients with AEs	#AEs	AE/pt-years (n=231.95 years)
Observations (total)	**59**	**28.8%**	**76**	**0.328**
Asystolic Episode during LV Lead Placement	1	0.5%	1	0.004
Bleeding/Hematoma**	10	4.9%	10	0.043
Blood Clot/Thrombosis	2	1.0%	2	0.009
Coronary Sinus Perforation/Dissection	6	2.9%	6	0.026
Diaphragmatic/Phrenic Nerve Stimulation – LV Lead	14	6.8%	14	0.060
Diaphragmatic/Phrenic Nerve Stimulation – RV Lead	2	1.0%	2	0.009
Elevated Pacing Thresholds – LV Lead	12	5.9%	12	0.052
Elevated Pacing Thresholds – RV Lead	2	1.0%	2	0.009
Heart Block at Implant	2	1.0%	2	0.009
High Defibrillation/Cardioversion Requirements	1	0.5%	1	0.004
Hypotension Requiring Ventilatory Support	1	0.5%	1	0.004
Inappropriate Therapy for SVT	11	5.4%	14	0.060
Infection	4	2.0%	4	0.017
Possible Pulmonary Embolism	1	0.5%	1	0.004
T-Wave Sensing	2	1.0%	3	0.013
Lead Insulation Damage-RA Lead	1	0.5%	1	0.004

**Some patients experienced more than one observation and/or complication and therefore the # of patients is less than the # of events.*
*** Fifteen (15) of the 16 patients with bleeding/hematoma related adverse events were on active anticoagulation therapy.*

An Other Reported Event is defined as any other clinical event that was reported by the investigator, which is not an Adverse Event as defined above. Table 4 contains a summary of all Other Reported Events, along with a brief description of each.

TABLE 4: RHYTHM ICD STUDY OTHER REPORTED EVENTS

Event Description	# of Patients	# of Events	Comments
Atrial arrhythmias observed	7	8	Atrial arrhythmias noted on electrograms that did not result in therapy delivery.
Bacteremia	2	2	Chronically diagnosed Gram positive bacteremia, unrelated to implant procedure, treated with antibiotics
Cardiopulmonary/ respiratory arrest	1	1	Syncopal episode leading to brief respiratory arrest probably due to vagal response while retching with spontaneous resolution following re-hydration.
Chest pain/tightness	3	3	ER visit for chest pain associated with pleurisy (1 pt); Chest pain associated with leaking thoracic aneurysm (1 pt); Chest pain managed medically (1 pt).
CNS related disorders	4	4	Seizure in 2 patients with history of seizure disorder and changes in mental status in 2 patients (secondary to dementia in 1 pt. and wife withheld medication for 1 pt.).
Fatigue/Shortness of breath	1	1	Shortness of breath/fatigue reported on a clinic visit possibly secondary to resolving pneumonia.
Hemoptysis	1	1	Blood noted in sputum; lung biopsy performed; no further events reported.
Inflammatory response/swelling/ elevated WBCs	3	3	General clinical symptoms evaluated and treated medically; no further sequelae reported.
Elective surgery	4	4	Left hydrocelectomy; cholecystectomy; hernia repair; percutaneous transluminal coronary angioplasty.
Inappropriate mode switches	9	12	Ten events were resolved with device re-programming.
Nausea/Vomiting/ Diarrhea/Abdominal pain or bloating	6	6	GI symptoms treated medically with no further sequelae.
Nose bleed	1	1	Resulted from elevated INR while on coumadin therapy; dose adjustment and no further sequelae.
Occasional Far-R sensing noted on electrogram	2	2	Did not result in mode switching or other inappropriate device behavior; devices re-programmed.
Occasional Crosstalk noted on electrogram	1	1	Resolved with device reprogramming.
Pacing sensation	3	4	Symptoms possibly associated with pacing felt in chest. 1 pt. required re-programming.

TABLE 4: RHYTHM ICD STUDY OTHER REPORTED EVENTS (CONTINUED)

Event Description	# of Patients	# of Events	Comments
Pain not related to procedure	2	2	Pain not associated with the device implant procedure: 1 pt was R/O ischemia and discharged and 1 pt diagnosed with gangrene of leg.
Pericardial effusion/Pericarditis	2	2	Treated medically with NSAIDs; no further sequelae.
Placement of LV epicardial leads	1	1	During LV lead revision, endocardial lead removed and not able to recannulate. Epicardial leads placed with no further sequelae.
Post-operative pain at incision site	2	3	Post surgical incisional pain treated with analgesics; no further sequelae reported.
PVC resulting in shortened AV delay	1	1	Device reprogrammed.
Renal insufficiency/Elevated BUN and creatinine	1	1	Acute renal failure secondary to bilateral renal artery stenosis; treated medically with no further sequelae reported.
Respiratory related events	8	11	Reports of pneumonia, cough, bronchitis, cold, or wheezing treated medically; no further sequelae.
Shocks delivered for SVT/Afib in ventricular fibrillation zone	6	7	Therapy delivery appropriate: device performed as programmed (SVT discrimination not available to be programmed in Fib zone).
Shocks for MTD/MTF during SVT episode	2	2	Therapy delivery appropriate: device and features performed as Programmed. 1 pt. was re-programmed and 1 pt. prescribed amiodarone therapy.
Sinus bradycardia observed	4	4	2 pts. resolved by device reprogramming pacing rate; 2 pts did not require reprogramming.
Stroke/TIA	2	2	TIA in setting of continuous AF at 3 mos. post-op in 1 pt.; Mid-cerebral artery CVA in 1 pt.
Syncope/Pre-syncope/Dizziness/ Vasovagal/ Hypotension	5	5	General clinical symptoms treated medically with IV fluids post-op (2pts.) and at rest (3pts.); no further sequelae reported.
Replacement of RA lead during initial implant procedure	1	1	Replacement of RA lead due to helix extension mechanism failure during initial implant procedure.
VT below rate cut off of device	1	1	Cardioversion performed and device reprogrammed.
VF episode requiring multiple external shocks prior to Epic HF system implant	1	1	Ventricular fibrillation episode that occurred in the EP lab during initial implant procedure and reported as possibly associated with hypokalemia.

TABLE 4: RHYTHM ICD STUDY OTHER REPORTED EVENTS (CONTINUED)

Event Description	# of Patients	# of Events	Comments
Occasional noise/EMI/ noted on electrogram	2	3	Noise observed on atrial channel of stored electrogram was not reproduced in clinic; device re-programming was not required.
TOTAL	**68***	**100**	

** Some patients experienced more than one event, and therefore the number of patients is less than the number of events*

PAVE Study

The PAVE study was a prospective, randomized, controlled, multi-center clinical trial comparing the safety and effectiveness results for patients receiving the Frontier™ Model 5508 pulse generator and the Aescula™ 1055K Left Heart Lead to those receiving legally marketed right ventricular pulse generators and standard leads following an AV nodal ablation for chronic atrial fibrillation (AF). The purpose of this investigation was to study the benefit of biventricular pacing over traditional RV pacing for those patients electing to undergo AV nodal ablation for treatment of chronic atrial fibrillation.

Adverse events were classified as complications or observations based on the following definitions:

- ***Complication:*** Any adverse event resulting in an injury or an invasive intervention (e.g., lead repositioning after lead dislodgement) which would not have occurred in the absence of the implanted device and/or system components.
- ***Observation:*** Any adverse event that is not associated with injury to the patient or an invasive intervention, but which is associated with the system under investigation, or the programming thereof.

Table 5 lists the observations and complications reported from the PAVE clinical trial. A total of 169 adverse events were reported for this study. The adverse events reported were classified as 56 Complications and 113 Observations.

TABLE 5: PAVE STUDY OBSERVED ADVERSE EVENTS[1]

Events	BV, LV and Roll-in (N = 259)[2]			
	# of Events	# of Patients	% of Patients	Events / Device-Months[3]
Complications	**56**	**48**	**18.5**	**0.0094**
Acute LV Lead Dislodgement	11	11	4.2	0.0019
Acute RV Lead Dislodgement	3	2	0.8	0.0005
Arrhythmia – VT at Implant	1	1	0.4	0.0002
Cardiac Tamponade at Implant	1	1	0.4	0.0002
CS Dissection at Implant	7	7	2.7	0.0012
CS Perforation at Implant	3	3	1.2	0.0005
Diaphragmatic Stimulation	6	6	2.3	0.0010
High LV Pacing Threshold at Implant, Later System Revised	9	8	3.1	0.0015
LV Lead Dislodgment during Ablation Procedure	1	1	0.4	0.0002
LV Lead Loss of Capture	4	4	1.5	0.0007
Oversensing	1	1	0.4	0.0002
Pectoral Stimulation	1	1	0.4	0.0002
Pneumothorax at Implant	3	3	1.2	0.0005
Pulmonary Edema post Ablation	1	1	0.4	0.0002
RV Insulation Failure	2	2	0.8	0.0003
RV Lead Fracture	1	1	0.4	0.0002
RV Perforation	1	1	0.4	0.0002
Observations	**113**	**83**	**32.0**	**0.0191**
Acute LV Lead Dislodgment (minor)	2	2	0.8	0.0003
Arrhythmia – Torsades	1	1	0.4	0.0002
CS Dissection at Implant	3	3	1.2	0.0005
Device Site Discomfort	1	1	0.4	0.0002
Diaphragmatic Stimulation	22	20	7.7	0.0037
Discomfort - Chest	1	1	0.4	0.0002
Dyspnea on Exertion	2	2	0.8	0.0003
Fatigue	7	7	2.7	0.0012
Hematoma at Implant	8	8	3.1	0.0013
High LV Threshold at Implant	7	7	2.7	0.0012

TABLE 5: PAVE STUDY OBSERVED ADVERSE EVENTS (CONTINUED)[1]

Events	BV, LV and Roll-in (N = 259)[2]			
	# of Events	# of Patients	% of Patients	Events / Device-Months[3]
High LV Pacing Threshold	15	15	5.8	0.0025
Hypotension	1	1	0.4	0.0002
Infection	5	5	1.9	0.0008
LV Loss of Capture	3	3	1.2	0.0005
LV Lead Undersensing	1	1	0.4	0.0002
Noise on IEGM	1	1	0.4	0.0002
Oversensing	3	3	1.2	0.0005
Palpitation	1	1	0.4	0.0002
Pectoral Stimulation	17	15	5.8	0.0029
Pneumothorax	1	1	0.4	0.0002
RV Back-up Pacing due to PVCs	1	1	0.4	0.0002
RV Loss of Capture	1	1	0.4	0.0002
Stuck Stylet	1	1	0.4	0.0002
Syncope	1	1	0.4	0.0002
Telemetry Error	3	2	0.8	0.0005
Thrombosis	2	2	0.8	0.0003
Transient Ischemic Attack	1	1	0.4	0.0002
VVI Backup	1	1	0.4	0.0002

[1] Each patient may have more than one complication or observation in more than one category.
[2] System-related complications and observations based on total number of attempted implants (N = 259), Procedure-related complications based on total number of procedures (N = 260).
[3] Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in BV, LV and Roll-in groups. The cumulative duration in months in these groups was 5,927 (5,928 for procedure related complication calculation).

An Other Reported Event is defined as any other clinical event that was reported by the investigator, which was not caused by, or associated with the study device.

Table 6 contains a summary of all Other Reported Events.

TABLE 6: PAVE STUDY OTHER REPORTED EVENTS

Event	BV (n=151)	LV (n=53)	Roll-in (n=56)
Arrhythmia – NSVT	0	3	0
Cardiovascular – Non-Study	25	3	9
Dyspnea	3	1	3
Fatigue	2	0	0
Lead Dislodgment during CABG Procedure	0	1	0
Lead Dislodgement during Valve Surgery	0	1	0
Non-cardiovascular	66	19	17
Palpitations	1	0	1
Pre-Syncope	10	0	2
Pulmonary Diseases	7	2	1
Renal Insufficiency	1	0	0
Surgery – Unrelated	0	0	1
Syncope	8	0	2
Thromboembolic Events	4	0	2
Ventricular Arrhythmia	5	3	0
Worsening Heart Failure	34	17	10
Total Events	**166**	**50**	**48**
Total Patients	**73**	**30**	**23**

IX. Summary of Pre-Clinical Studies

The St. Jude Medical Epic HF and Atlas + HF devices (P030054) are legally marketed. The device systems were previously tested via nonclinical laboratory testing including bench testing, biocompatibility evaluation, electromagnetic compatibility, sterilization, packaging, shelf life testing and animal study. Device design and system compatibility involved verification and validation of each system. The test results were previously found acceptable.

X. Summary of Clinical Investigations

The data summarized in this section reflects the information presented and reviewed in this supplement. The data sets are updates from the referenced trials which continued beyond the dates of approval of the applications P030054 (RHYTHM ICD) and P030035 (PAVE).

RHYTHM ICD Clinical Investigation

The RHYTHM ICD study was a prospective, multicenter, randomized, double-blind, controlled clinical investigation designed to assess the safety and efficacy of the Epic HF ICD system in patients who were indicated for implantable cardioverter defibrillation therapy with New York Heart Association Classification of III or IV and a prolonged QRS duration. The products being evaluated were the Epic HF V-338 ICD and the Aescula and QuickSite LV leads. The objective of this clinical study was to verify the safety and efficacy of the Epic HF ICD (Model V-338) system in an ICD indicated patient population with advanced heart failure (NYHA Classification III or IV) and prolonged QRS duration.

Study Inclusion and Exclusion criteria are listed below:

Inclusion Criteria

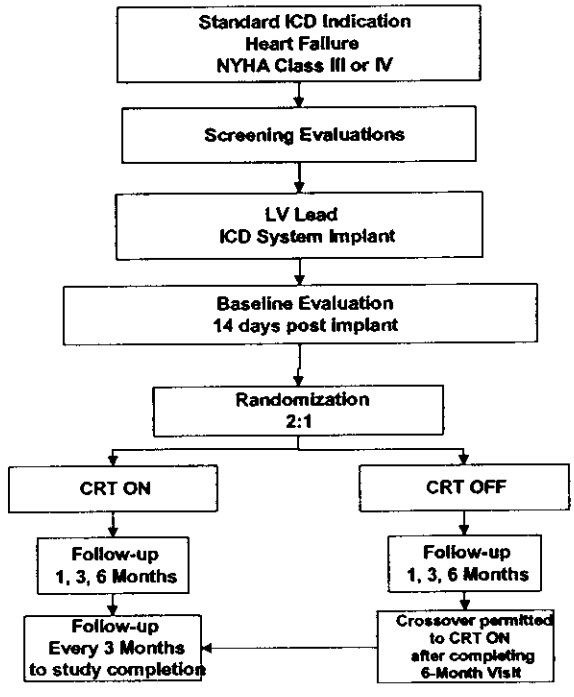
1. Approved indication for implantation of an ICD for treatment of a life-threatening ventricular tachyarrhythmia(s).
2. Symptomatic, advanced heart failure (ischemic or non-ischemic) not due to reversible causes, diagnosed for at least 6-months.
3. New York Heart Association (NYHA) Classification of III or IV, despite receiving a minimum of 90 days of appropriate pharmacological therapy.
4. Receive optimal pharmacological therapy for CHF (including angiotensin converting enzyme inhibitor and beta blocker, as tolerated) which has been stable during the 30 days prior to enrollment.
5. Left ventricular ejection fraction (LVEF) ≤ 35%.
6. Ventricular conduction delay manifested as a QRS duration ≥150 msec.
7. Ability to complete cardiopulmonary exercise stress testing and 6-Minute hall walk test, with the only limiting factor(s) being fatigue and/or shortness of breath.
8. Ability to independently comprehend and complete a quality of life questionnaire (Minnesota Living with Heart Failure).
9. Ability to provide informed consent for study participation and be willing and able to comply with the prescribed follow-up tests and schedule of evaluations.

Exclusion Criteria

1. Standard bradycardic indication for pacing.
2. History of chronic atrial fibrillation (continuous AF lasting > 1 Month) within 1 year prior to enrollment or have undergone cardioversion for AF in the past month.
3. Ability to walk > 450 meters during the 6-Minute walk test.
4. NYHA Classification of I or II.
5. Contraindication for an emergency thoracotomy.
6. Classification of Status 1 for cardiac transplantation or consideration for transplantation over the next 6-months.
7. Recent myocardial infarction, unstable angina or cardiac revascularization (PTCA or CABG) within 1 month of enrollment.
8. Recent CVA or TIA - within 3 months of enrollment.
9. Severe musculoskeletal disorder(s).
10. Pregnant or a planning for pregnancy in next 6-months.
11. Participating in, or has participated in any clinical investigation within the last 30 days. (the only exception being that of a registry trial)
12. Life expectancy of less than 6-months.
13. Less than 18 years of age.

Figure 1 outlines the study design for the trial. The total time of follow-up from the time of successful implant was 2755 patient months. The average time of follow-up was 15.1 ± 4.1 (range 0.3 to 23.8) patient months.

FIGURE 1: RHYTHM ICD STUDY OVERVIEW



PATIENT POPULATION

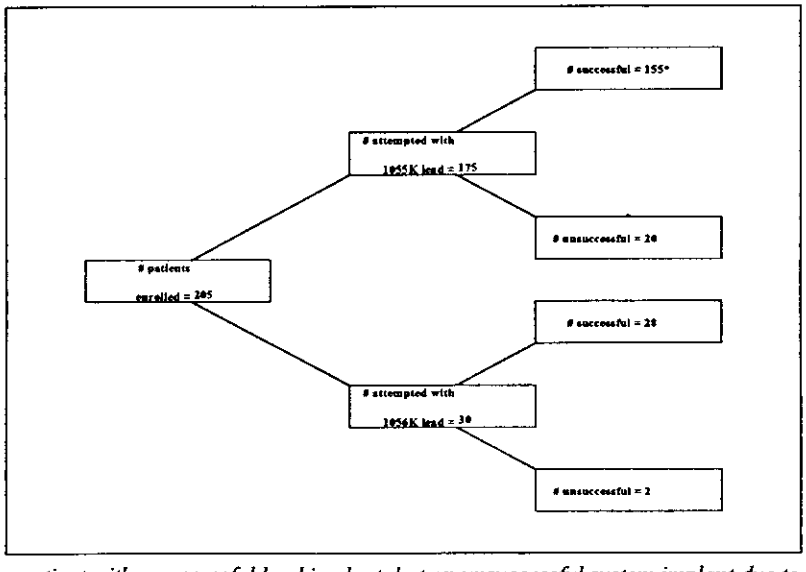
Of the 205 patients enrolled in the RHYTHM ICD study, one hundred and eighty-three (183) lead implant attempts were successful (180 successful on the first attempt and 3 successful on the second attempt). One additional patient had a successful left ventricular lead implant, but had high defibrillation thresholds (DFTs). This patient was withdrawn from the study and received a heart transplant, leaving a total of 182 successful system implants. Table 7 has a breakdown of the reasons for the 23 unsuccessful implants.

TABLE 7: UNSUCCESSFULL IMPLANTS (N=23)

Reason	Number of Patients
LV Lead Related:	
Unable to Cannulate the CS	7
Unable to Obtain Distal Placement	6
Unable to Obtain Stable Lead Position	3
High Pacing Thresholds	3
CS Dissection	3
Other:	
High Defibrillation Threshold	1
TOTAL	**23**

Figure 2 displays the leads used and the number of successful system implants for each category of leads.

FIGURE 2: NUMBER OF PATIENTS ATTEMPTED AND IMPLANTED WITH MODEL 1055K AND 1056K LEADS



**Includes one patient with a successful lead implant, but an unsuccessful system implant due to high defibrillation thresholds*

Patients who were successfully implanted with the Epic HF ICD system had a Baseline visit approximately two weeks after implant, during which the following tests/assessments were performed: Electrical measurements on RA, RV and LV leads, cardiopulmonary exercise (CPET) test, echocardiogram, NYHA class assessment, 6 minute walk test, and Minnesota Living with Heart Failure questionnaire. Of the 182 patients with successful implants, two patients expired and one patient withdrew from the study before the Baseline visit and therefore, 179 patients had a Baseline visit. One additional patient who had a Baseline follow-up visit refused randomization and all the Baseline evaluations except device interrogation and electrical measurements, but remained in the study. Therefore, a total of 178 patients completed the requirements of the Baseline visit.

Table 8 summarizes all the reported data on the 178 patients available for analysis at the Baseline visit, as well as broken down by randomization group.

TABLE 8: SUMMARY OF BASELINE VARIABLES AND COMPARISONS BETWEEN CRT OFF AND CRT ON GROUPS

Demographic variable	Overall group (N = 178)*	CRT OFF (N = 59)	CRT ON (N = 119)	p-value (CRT ON vs. CRT OFF)
NYHA Class, n (%):				0.61
I	3 (1.7%)	2 (3.4%)	1 (0.8%)	
II	10 (5.6%)	4 (6.8%)	6 (5.0%)	
III	154 (86.5%)	50 (84.7%)	104 (87.4%)	
IV	11 (6.2%)	3 (5.1%)	8 (6.7%)	
LV Ejection Fraction (%) - ECHO:				0.07
Mean ± SD	24.8 ± 7.7	23.3 ± 6.4	25.6 ± 8.3	
Range	(9, 48)	(11, 43)	(9, 48)	
QRS Duration (ms):				0.40
Mean ± SD	168 ± 15	167 ± 15	169 ± 16	
Range	(120, 210)	(130, 200)	(120, 210)	
LVEDD (mm):				0.88
Mean ± SD	66.2 ± 8.8	66.0 ± 9.4	66.2 ± 8.5	
Range	(47.7, 85.9)	(50.1, 84.2)	(47.7, 85.9)	
LVESD (mm):				0.93
Mean ± SD	57.0 ± 9.87	56.9 ± 10.5	57.1 ± 9.4	
Range	(37.1, 78.2)	(37.9, 78.2)	(37.1, 76.2)	
Quality of Life Score:				0.53
Mean ± SD	48 ± 24	46 ± 24	48 ± 24	
Range	(0, 103)	(4, 100)	(0, 103)	
Six-Minute Walk (meters):				0.30
Mean ± SD	280 ± 99	291 ± 89	275 ± 103	
Range	(31, 561)	(31, 480)	(37, 561)	

** Of the 182 patients that had successful system implants, two patients expired and one patient withdrew from the study before their Baseline visit; one additional patient refused randomization and all Baseline evaluations, except device interrogation and electrical measurements, and therefore, is not included.*

TABLE 8: SUMMARY OF BASELINE VARIABLES AND COMPARISONS BETWEEN CRT OFF AND CRT ON GROUPS

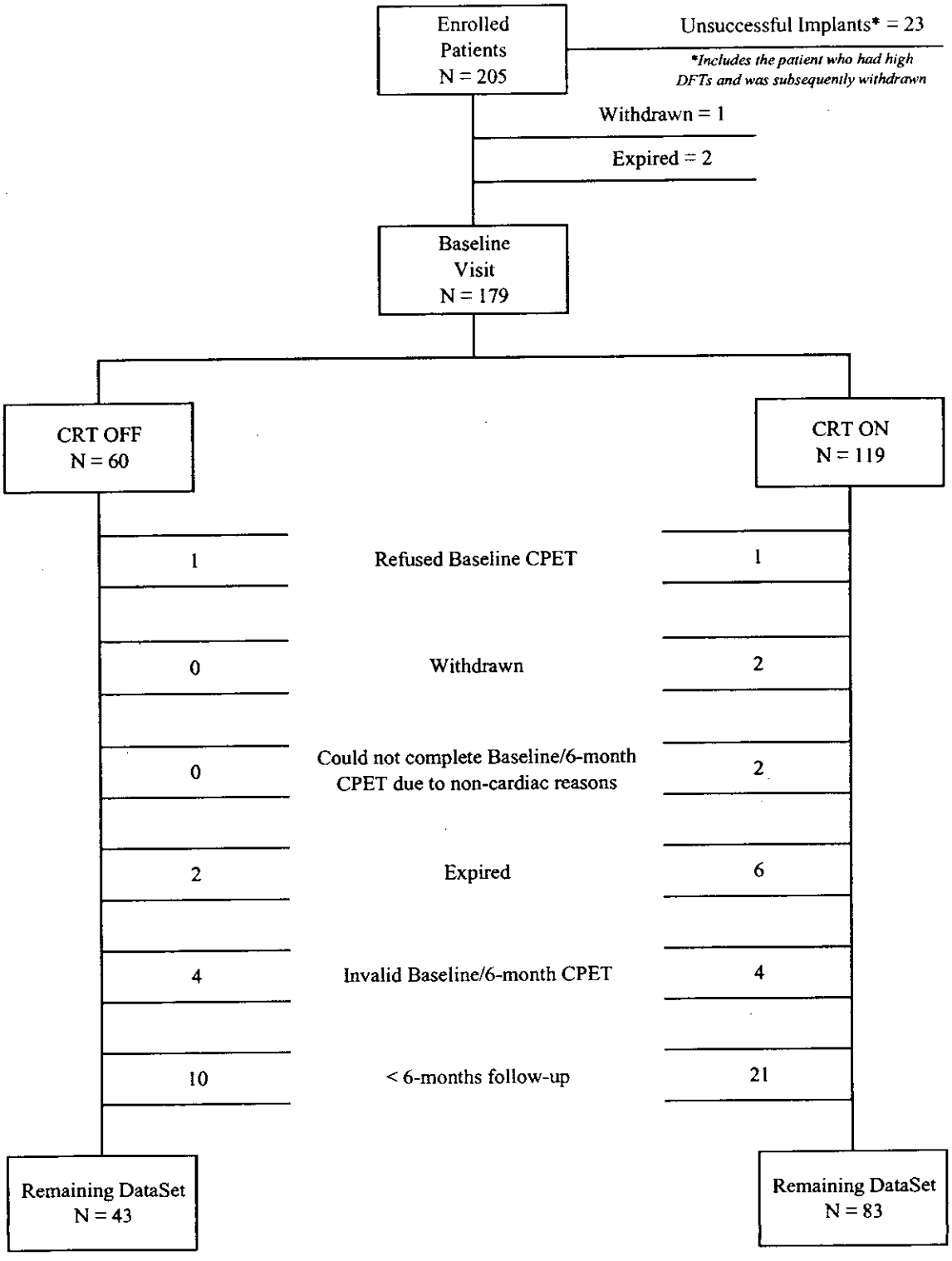
Demographic variable	**Overall group (N = 178)***	**CRT OFF (N = 59)**	**CRT ON (N = 119)**	**p-value (CRT ON vs. CRT OFF)**
Cardiopulmonary Exercise Test:				
Peak VO_2 (ml/kg/min):				
Mean ± SD	11.3 ± 3.3	12.3 ± 3.5	10.8 ± 3.0	0.006
Range	(4.3, 26.9)	(6.0, 23.1)	(4.3, 26.9)	
Exercise Time (minutes):				
Mean ± SD	8.3 ± 3.3	8.9 ± 3.6	8.0 ± 3.2	0.08
Range	(0.7, 19.8)	(2.3, 19.8)	(0.7, 16.5)	
Baseline Medications, n (%):				
ACE Inhibitors/Substitutes	129 (72.5%)	44 (74.6%)	85 (71.4%)	0.79
Beta Blockers	147 (82.6%)	52 (88.1%)	95 (79.8%)	0.24
Angiotensin Receptor Blockers	34 (19.1%)	10 (16.9%)	24 (20.2%)	0.76
Diuretics	157 (88.2%)	54 (91.5%)	103 (86.6%)	0.47
Positive Inotropics/Glycoside	112 (62.9%)	39 (66.1%)	73 (61.3%)	0.65
Nitrates	62 (34.8%)	23 (39.0%)	39 (32.8%)	0.51
Anti-Coagulants and Anti-Platelets	150 (84.3%)	48 (81.4%)	102 (85.7%)	0.59
Calcium Channel Blockers	20 (11.2%)	9 (15.3%)	11 (9.2%)	0.35
Anti-Arrhythmics	42 (23.6%)	13 (22.0%)	29 (24.4%)	0.87

** Of the 182 patients that had successful system implants, two patients expired and one patient withdrew from the study before their Baseline visit; one additional patient refused randomization and all Baseline evaluations, except device interrogation and electrical measurements, and therefore, is not included.*

8

Figure 3 outlines the patient population for the effectiveness analysis.

FIGURE 3: ANALYZABLE PATIENT GROUP FOR PRIMARY RESYNCHRONIZATION EFFECTIVENESS ANALYSIS



Primary Objectives and Results

1. *LV Lead-Related Complications (at 6 Months)*

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Aescula lead-related complications through six months will not be less than 75%.

Results: One hundred and fifty-five (155) patients who had a successful 1055K LV lead implant were analyzed for this endpoint. A total of 11 patients experienced 13 1055K LV lead related complications. The survival from 1055K lead related complications at 6-months was calculated as 92.8% with a 95% lower confidence bound of 89.4%. Objective met.

2. *Epic HF System-Related Complications (at 6 Months)*

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Epic HF system-related complications through six months will not be less than 70%.

Results: One hundred and eighty-two (182) patients who had a successful Epic HF system implant with either the Aescula or QuickSite LV lead were analyzed for this endpoint. A total of 14 patients experienced 18 Epic HF system-related complications. The survival from system-related complications at 6-months was calculated as 92.8% with a 95% lower confidence bound of 89.7%. Objective met.

3. *Defibrillation System Effectiveness: VF Detection/Redetection Times*

Objective: The upper bound of the one-sided 95% confidence interval of the median VF detection time will be less than 3.4 seconds. The upper bound of the one-sided 95% confidence interval of the median VF redetection time will be less than 1.9 seconds.

Results: Detection and redetection times for induced VF episodes (including Ventricular Fibrillation, Polymorphic Tachycardia, and Ventricular Flutter) during biventricular pacing were included in the analysis. Detection and redetection times were calculated for each episode from the stored electrograms or rhythm strip from an external recorder. A total of 440 episodes in 172 patients were analyzed for detection times, and 90 episodes in 55 patients were analyzed for redetection times. The 95% upper confidence bound for the mean detection time was 3.11 seconds and that for the redetection time was 1.61 seconds.
Objective met.

4. *Cardiac Resynchronization Therapy Efficacy* (Peak VO_2)

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: In the intention-to-treat analysis, patients who crossed over from the CRT OFF group to the CRT ON group during the study were analyzed according to the original treatment group they belonged to. Table 9 contains a summary of the improvement in peak VO_2 values in the two treatment groups for this analysis. The average improvement in the CRT ON group over the CRT OFF group was approximately 1.9 ml/kg/min. The p-value for this analysis was 0.001. Objective met.

TABLE 9: IMPROVEMENT IN PEAK VO_2 VALUES (ML/KG/MIN) INTENTION-TO-TREAT ANALYSIS (N = 126)

	CRT OFF Mean ± SD (N = 43)	**CRT ON Mean ± SD (N = 83)**
Baseline	12.8 ± 3.7	11.2 ± 3.0
6-months	11.4 ± 5.6	11.7 ± 3.2
Change	-1.41 ± 4.6	0.52 ± 2.5

In the per-protocol analysis, patients who crossed over from the CRT OFF group to the CRT ON group during the study were analyzed according to the new treatment group they belonged to. Of the 126 patients who were part of the peak VO_2 endpoint analysis, two patients crossed over from the CRT OFF group to the CRT ON group due to symptoms attributed to worsening heart failure before their 6-month follow up visit. Table 10 displays a summary of the improvement in the two groups for this analysis. The CRT ON group showed an average improvement of approximately 2.0 ml/kg/min over the CRT OFF group. The p-value for this analysis was 0.001. Objective met.

TABLE 10: IMPROVEMENT IN PEAK VO_2 VALUES (ML/KG/MIN) PER-PROTOCOL ANALYSIS (N = 126)

	CRT OFF	**CRT ON**
N	41	85
Mean ± SD	-1.47 ± 4.7	0.52 ± 2.5

Secondary Objectives and Results

1. *Improvement in NYHA Class at 6-months Over Baseline*

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: Table 11 shows the average change in NYHA Class from Baseline to 6-months for each group.

TABLE 11: BASELINE AND 6-MONTH NYHA CLASS (N = 126)

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	2.86 ± 0.52	3.01 ± 0.33
6-months	2.58 ± 0.73	2.53 ± 0.69
Change	-0.28 ± 0.63	-0.48 ± 0.65

The CRT ON group shows a statistically significant improvement in NYHA Class over the CRT OFF group. Objective met.

2. *Improvement in Quality of Life at 6-months over baseline*

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: Patient quality of life (QOL) was assessed with the Minnesota Living with Heart Failure questionnaire. A lower score indicates an improvement in quality of life. Table 12 contains a summary of the improvement in Quality of Life in the two groups from baseline to 6 months.

TABLE 12: IMPROVEMENT IN QUALITY OF LIFE SCORE (N = 126)

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	42.0 ± 23	48.3 ± 24
6-months	45.4 ± 31	40.4 ± 22
Change	3.4 ± 31	-7.8 ± 22

The average improvement in the CRT ON group over the CRT OFF group was approximately 11 points. Objective met.

3. *Improvement in Six-Minute Hall Walk at 6-months Over Baseline*

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: Table 13 contains a summary of the improvement in 6-minute walk distance between baseline and 6 months.

TABLE 13: IMPROVEMENT IN 6-MINUTE WALK DISTANCE (METERS) (N = 126)

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	298 ± 94	284 ± 105
6-months	283 ± 150	297 ± 122
Change	-15 ± 142	13 ± 74

The average improvement in the CRT ON group over the CRT OFF group was approximately 28 meters.

4. *Aescula Left Ventricular Lead Performance*

Objective: The lower bound of the one-sided 95% confidence interval of the percent successful implant will not be less than 80%.

Results: Of the175 patients who were attempted with the Aescula 1055K lead, 155 patients, or 87.1% had a successful implant. The 95% lower confidence bound on the percent successful implant was 81.8%. Objective met.

5. *Aescula LV Lead Pacing Capture Threshold at 6-Months*

Objective: The upper bound of the one-sided 95% confidence interval of the LV lead pacing capture threshold is less than 3 V.

Results: The 95% upper confidence limit for the mean LV lead capture threshold at 6 months was 2.33 V. The average pacing capture threshold was 2.1 ± 1.4 V. Objective met.

Additional Data

1. *Biventricular Pacing at 6-months*

The average percentage of biventricular pacing at the 6-month visit in the 83 patients who were in the CRT ON group among the 126 patients in the primary resynchronization cohort was 95% ± 6%, with a range of 70% to 100%.

2. *Echo Data*

Echocardiographic analysis was performed at the baseline and 6-month follow-up visits. The following parameters were evaluated from the echocardiographic analysis: LVEDD, LVESD, LVEF, MR, E/A Wave Point Ratio, and Sphericity Index. Cardiac dyssynchrony (including Pre-Ejection Delay Time and Intraventricular Mechanical Delay) was also evaluated at baseline and 6-Months. Table 14 displays summaries of the improvement in these parameters between baseline and 6-months.

TABLE 14: IMPROVEMENT IN ECHOCARDIOGRAPHY PARAMETERS

Parameter	CRT OFF (N = 40) Mean ± SD	CRT ON (N = 82) Mean ± SD
LVEDD (mm)	-2.4 ± 6.5	-4.3 ± 5.4
LVESD (mm)	-3.0 ± 6.4	-4.6 ± 7.0
LVEDV (ml)	-37 ± 53	-43 ± 69
LVESV (ml)	-36 ± 47	-43 ± 58
LVEF (%)	2.9 ± 6.2	4.3 ± 9.9
MR (grade)	0.10 ± 0.50	-0.06 ± 0.74
E/A Wave Point Ratio	-0.02 ± 1.2	-0.08 ± 0.8
Sphericity Index	0.02 ± 0.1	-0.02 ± 0.1
Pre-Ejection time (ms)	7.3 ± 33	-1.5 ± 52
IVMD (ms)	-6.4 ± 48	-14.5 ± 52
Tei Index	-0.05 ± 0.5	-0.4 ± 0.8
Contraction Interval (ms)	-55 ± 103	-94 ± 124

Patient Discontinuation/Withdrawals

A total of 47 patients participating in the RHYTHM ICD study were withdrawn from the study. Twenty (20) patients (including the 19 patients with unsuccessful LV lead implants and the one patient with an unsuccessful system implant due to high defibrillation thresholds) were withdrawn approximately one month after unsuccessful system implants in accordance with the protocol. Twenty-two (22) patients died and were also withdrawn from the study. Three of the 22 deaths occurred in patients who had

previously unsuccessful implants. In addition to these 20 unsuccessful implants and 22 deaths, 5 additional patients were withdrawn from the study. Table 15 summarizes the reason for these 5 patient withdrawals.

TABLE 15: PATIENT DISCONTINUATIONS/WITHDRAWALS
(Excludes Withdrawals for Deaths and After Unsuccessful Implants)

Reason for Withdrawal	CRT Group	Days after Implant
System Explant	N/A*	1
Heart Transplant	ON	75
Patient Request	ON	28
Patient Request	ON	397
Patient's Family Request	ON	293

** Patient was withdrawn before the Baseline visit and randomization*

PAVE Clinical Investigation

The PAVE study was a prospective, randomized, controlled, multi-center clinical trial conducted at 49 participating sites (44 in the US, 5 in Canada) comparing the safety and effectiveness results for patients receiving the Frontier™ Model 5508 pulse generator and the Aescula™ 1055K Left Heart Lead to those receiving legally marketed right ventricular pulse generators and standard leads following an AV nodal ablation for chronic atrial fibrillation (AF). Chronic AF is defined as persisting without interruption for at least one month.

The purpose of this investigation was to study the benefit of biventricular pacing over traditional RV pacing for those patients electing to undergo AV nodal ablation for treatment of chronic atrial fibrillation. The primary effectiveness objective of the study was to compare exercise performance data, as measured by the 6-minute walk test, for patients with biventricular (BV) pacing versus RV pacing at baseline and 6-months follow-up. Electrical and safety performance data of the Aescula lead as well as the safety performance of the entire implanted pacing system were evaluated as primary safety endpoints. Functional capacity as measured by peak VO_2 and Quality of Life were evaluated as secondary efficacy endpoints.

Patients who satisfied the inclusion and exclusion criteria underwent a baseline evaluation to determine study eligibility. Patient inclusion criteria included:

1. Patients who will undergo complete AV nodal ablation for chronic atrial fibrillation resulting in complete AV Block (chronic atrial fibrillation is defined as persisting without interruption for at least 1 month).
2. Patients who are on a stable medical therapy regimen. Stable medical therapy is defined as either ON or OFF drug therapy for 5 drug half-lives at the time of enrollment. If the eligible candidate is being treated with Amiodarone therapy, the dosage at the time of enrollment must be stable for at least 30 days prior to implant.

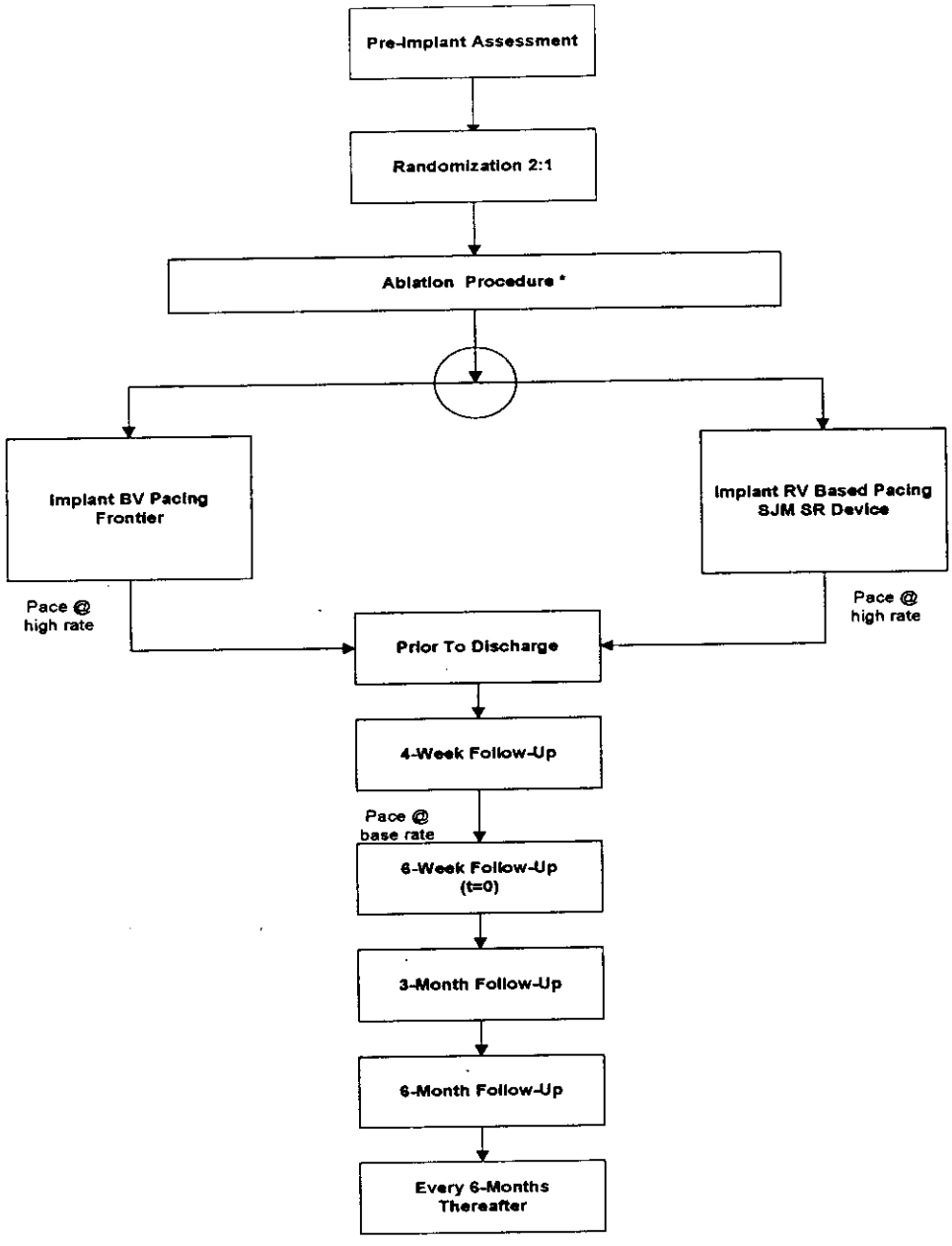
3. Patients who are able and have completed the 6-minute walk test as outlined in this protocol with the only limiting factor(s) being fatigue and/or shortness of breath.
4. Patients who will provide informed consent for study participation and, are willing and able to comply with the prescribed follow-up tests and schedule of evaluations.

Patient exclusion criteria were:

1. Patients who are classified as NYHA class IV.
2. Patients who can walk >450 meters while using the 6-minute walk test.
3. Patients who have an implanted ICD or, are being considered for implantation of an ICD.
4. Patients who are contraindicated for an emergency thoracotomy.
5. Patients who are being considered for cardiac surgery within the next 6 months.
6. Patients with prosthetic valve replacements.
7. Patients with severe musculoskeletal disorder(s).
8. Patients under the age of 18 years.
9. Current or planned pregnancy in the next 6 months.
10. Current participation or participation in the past 30 days in any clinical investigation.
11. Patients with life expectancy less than 6 months.
12. Patients who cannot independently comprehend and complete the Quality of Life (QoL) questionnaire.
13. Patients allergic to dexamethasone sodium phosphate (DSP).

Figure 4 outlines the study design for the trial. Patient cross-over was not allowed in the study and every effort was made to maintain randomized configuration throughout the trial period. The study's cumulative implant duration was 8,979 months with a mean of 24.33 ± 15.22 months (range of 0.13 to 55.95 months).

FIGURE 4: STUDY OVERVIEW

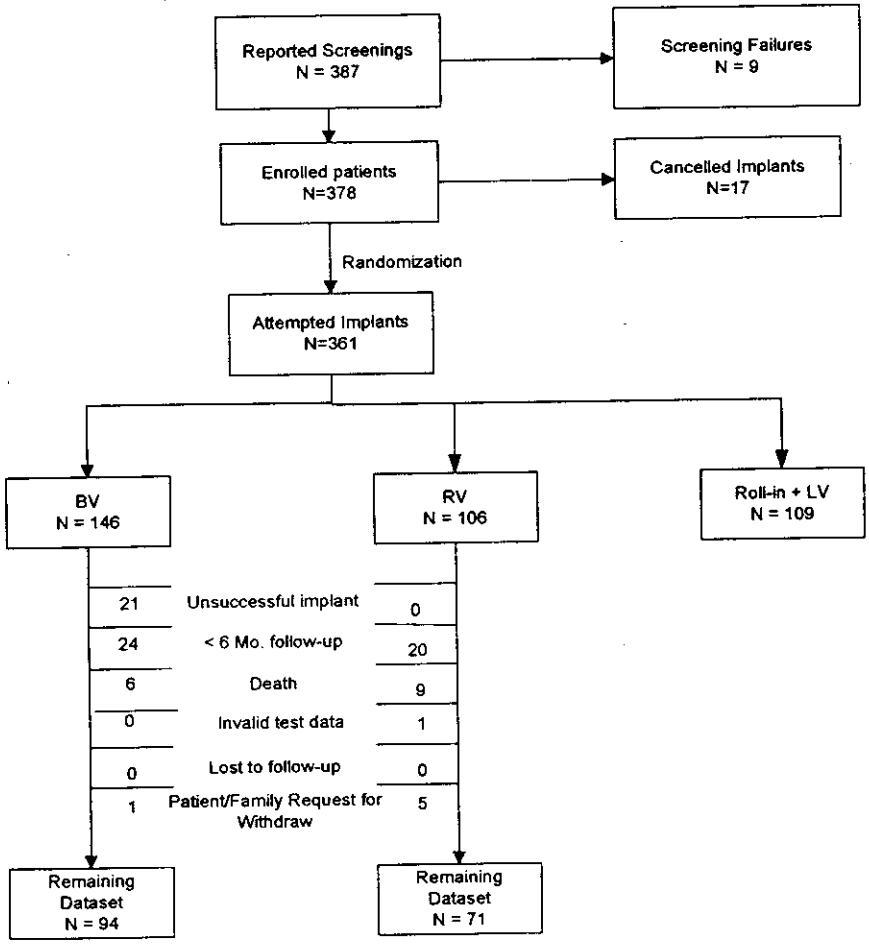


* Implant was allowed per protocol to occur up to 30 days prior to AV node ablation for lead stabilization. In the event this occurred, the base rate of the device was programmed to less than the intrinsic heart rate until the ablation occurred. All timelines were reset when the ablation occurred. It was recommended that all patients be paced at 90 ppm (minimum 80 ppm) post ablation per standard care after AV node ablation.

Patient Population

The overall study population included 369 patients. One hundred and fifty-one (151) patients were randomized to BV and 109 were randomized to RV. In addition, 53 were randomized to LV pacing under a previous revision of the investigational plan. Fifty-six (56) patients were "roll-in" patients (non-randomized) and received the bi-ventricular pacing system (Frontier pulse generator and Aescula lead system). As per the protocol, effectiveness analyses were based on patients randomized to the RV and BV groups only. Safety analyses include all patients with the Frontier pulse generator and the Aescula left heart lead, including LV and Roll-in patients. All patients had permanent pacemaker implant indication following an elective AV nodal ablation for chronic atrial fibrillation. The mean age was 69.30 ± 9.93 years and there were 34.4% female and 65.6% male. Fourteen percent (14%) of the patients had no heart failure or had heart failure and were NYHA Class I, 49% were NYHA Class II, and 37% were NYHA Class III prior to implant. Figure 2 outlines the patient population for the effectiveness analysis.

FIGURE 5: PATIENT POPULATION FOR EFFECTIVENESS ANALYSIS



Primary Objectives and Results

1. Freedom from System-Related Complications through Six Months

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from system-related complications for the BV group will not be less than 70%. A system-related complication was defined as a complication that is caused by a failed pacing system. A pacing system refers to all implanted components, including the pulse generator, leads, and the interaction of these components.

Results: There were 29 system-related complications in 26 patients within six-months follow-up. The freedom from system-related complications is 87.8% with a lower bound of 84.0%. Objective met.

2. Freedom From Pulse Generator-Related Complications Through Six Months

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from pulse generator-related complications for the BV group through six months will not be less than 90%.

Results: There were no pulse generator-related complications through six months. The survival rate is 100% with a lower bound of 98.6%. Objective met.

3. Freedom From Aescula™ Lead-Related Complications Through Six Months

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Aescula™ lead-related complication for the BV group through six months will not be less than 75%.

Results: There were 25 Aescula lead-related complications in 24 patients through six-months follow-up. The freedom from Aescula lead-related complications is 88.2% with a lower bound of 84.4%. Objective met.

4. Rate Of Successful Implantation Of The Aescula™ Lead

Objective: The lower bound of the one-sided 95% confidence interval of the successful implantation rate of the Aescula lead for the BV group will not be less than 80%. The succes rate was defined as the proportion of patients who received the complete pacing system.

Results: One hundred and forty-six patients randomized to BV underwent attempted implants. One hundred and twenty-five were successfully implanted. The rate of

successful implant of the Aescula lead for BV group is 86% with a lower bound of 81%. Objective met.

5. Aescula™ Lead Pacing Threshold At Six Months

Objective: The upper bound of the one-sided 95% confidence interval of mean capture threshold will not be greater than 3.0 V for the BV group at six months.

Results: The pacing threshold at six months for the BV group is 2.27 V ± 1.66 V with an upper bound of 2.53 V. Objective met.

6. Exercise Capacity As Measured By Distanced Walked In Six-Minute Walk Test

Objective: The treatment group (BV) shows statistically significant improvement over the control group (RV) at the six months follow-up time.

Results: The treatment group (BV) showed statistically significant improvement over the control group (RV) in distance walked from pre-implant to six months (p = 0.03). The BV group also had a greater percentage of patients showing improvements than the RV group (p = 0.035). Figure 6 illustrates the improvement in the six-minute walk between BV and RV groups. Table 16 outlines the improvement distribution in the six-minute walk between BV and RV groups.

FIGURE 6: IMPROVEMENTS IN SIX-MINUTE WALK DISTANCE IN BV AND RV GROUPS (P = 0.03)

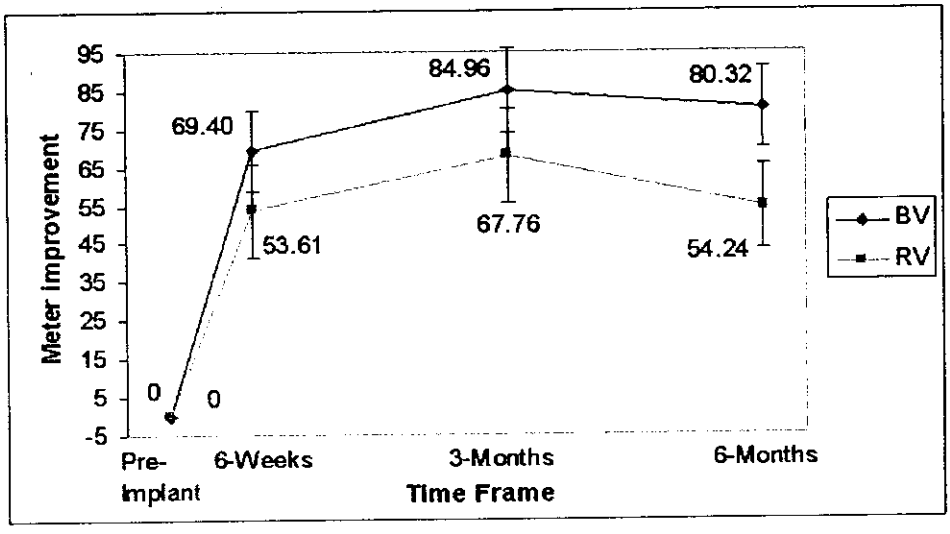


TABLE 16: DISTRIBUTION OF IMPROVEMENT IN BV AND RV GROUP IN SIX-MINUTE WALK (P = 0.035)

	RV (N = 66)	BV (N = 84)
Improved (> 5 m)	46 (69.70%)	69 (82.14%)
No Change (-5 to 5 m)	4 (6.06%)	4 (4.76%)
Worsened (< -5 m)	16 (24.24%)	11 (13.10%)

Secondary Objectives and Results

1. Quality Of Life As Measured By SF-36 Score

Objective: To determine if the BV group shows improvement over the RV group at the six-month follow-up in the health-related quality of life as measured by the SF-36 score.

Results: Using the SF-36 Quality-of-Life questionnaire, a standardized measurement of quality of life, the study found that for the six-week to six-month visit time period, the improvement in SF-36 scales was not different between groups. For the preimplant to six-month visit time period, there was a difference of 4.12 points for the Mental Health component and a difference of 5.16 points for the Physical Function component.

2. Functional Capacity As Measured By Peak Vo_2

Objective: To determine if the BV group shows improvement in functional capacity, as measured by peak VO_2, from the six-week follow-up to the six-month follow-up.

Results: The BV group showed an improvement of 0.86 ml/kg/min in peak VO_2 from six weeks to six months measured during CPX testing. The BV group also had a greater percentage of patients showing improvement in peak VO_2. Figure 7 illustrates the improvement in peak VO_2 in BV and RV groups. Table 17 outlines the distribution of improvement in peak VO_2 between BV and RV groups.

FIGURE 7: IMPROVEMENTS IN PEAK VO_2 IN BV AND RV GROUPS (WITHIN BV GROUP)

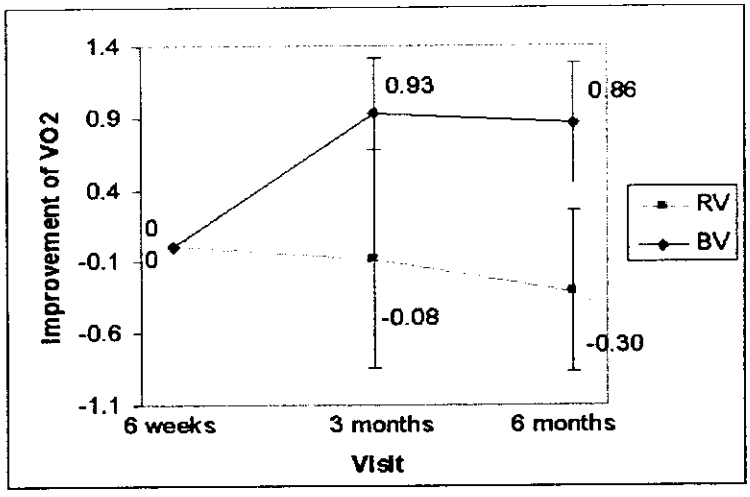


TABLE 17: DISTRIBUTION OF IMPROVEMENTS IN PEAK VO_2 IN BV AND RV GROUPS

Change in Peak VO_2(ml/kg/min)	RV (N = 10)	BV (N = 35)
Improved (> 0.5)	4 (40%)	21 (60.0%)
No Change (-0.5 to 0.5)	0 (0%)	4 (11.4%)
Worsened (<-0.5)	6 (60%)	10 (28.6%)

XI. Conclusions Drawn from the Clinical Study

Patients who have chronic atrial fibrillation may also have an ICD indication and may receive an ICD. This includes patients who have experienced an episode of ventricular tachycardia or ventricular fibrillation (secondary prevention) or meet the criteria for prophylactic ICD therapy (primary prevention). Likewise, patients who have atrial fibrillation may receive a biventricular pacemaker if they have undergone an AV nodal ablation for chronic atrial fibrillation and have NYHA Class II or III heart failure. The PAVE study completed and reviewed under P030035 provided a reasonable assurance that biventricular pacing is safe and effective in post AV nodal ablation patients with NYHA Class II or III heart failure. The addition of ICD back-up therapy does not affect the biventricular pacing performance of the device and ICD therapy is already the standard of care in patients meeting ICD indications who also have atrial fibrillation. As reviewed under P030054, the RHYTHM ICD Study provided a reasonable assurance that St. Jude Medical CRT-D devices were safe and effective in patients with an ICD indication and NYHA Class III or IV heart failure with prolonged QRS durations and LVEF ≤ 35%. The results of the RHYTHM ICD and PAVE Studies together

provide reasonable assurance of safety and effectiveness of the St. Jude Medical Epic HF and Atlas + HF CRT-D systems when used as indicated in accordance with the directions for use.

XII. Panel Recommendation

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH Decision

FDA issued an approval order for P030054/S10 on NOV 18 2005

The sponsor's manufacturing facilities were inspected and determined to be in compliance with the Quality System Regulation (21 CFR Part 820).

XIV. Approval Specifications

Directions for Use:	See labeling.
Hazards to Health from Use of the Device:	See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.
Post-approval Requirements, Restrictions:	See approval order.