

# Clinical trials of resynchronization (CRT) - defibrillators (ICD) for prevention of sudden death in heart failure

TrialResults-center [www.trialresultscenter.org](http://www.trialresultscenter.org)

## 1 cardiac resynchronization therapy

Trial	Treatments	Patients	Trials design and methods
<b>CRT vs no CRT</b>			
<b>MUSTIC-SR , 2001</b> n=58/58 follow-up: 3 months	CRT Medtronic/ELA medical versus CRT off	patients with severe heart failure (New York Heart Association class III) due to chronic left ventricular systolic dysfunction, with normal sinus rhythm and a duration of the QRS interval of more than 150 msec	Cross over Single blind
<b>MIRACLE , 2002</b> n=228/225 follow-up: 6 months	CRT Medtronic versus CRT off	patients with moderate-to-severe symptoms of heart failure associated with an ejection fraction of 35 percent or less and a QRS interval of 130 msec	Parallel groups Double blind
<b>PATH-CHF , 2002</b> n=NA follow-up: 1 month	CRT versus no CRT	patients with heart failure and ventricular conduction delay	Parallel groups open
<b>MUSTIC AF , 2002</b> n=43/43 follow-up: 3 months	CRT Medtronic/ELA medical versus CRT off	patients with NYHA class III left ventricular systolic dysfunction, chronic atrial fibrillation, slow ventricular rate necessitating permanent ventricular pacing, and a wide QRS complex (paced width $\geq 200$ ms)	Cross over Single blind
<b>CARE-HF , 2005</b> n=409/404 follow-up: 29.4 months	CRT medtronic versus no CRT	patients with NYHA class III or IV heart failure due to left ventricular systolic dysfunction and cardiac dyssynchrony	parallel group open
<b>RD-CHF , 2003</b> n=NA follow-up:	CRT versus no CRT	patients with advanced heart failure	Parallel groups
<b>COMPANION (CRT vs MT) , 2004</b> n=617/308 follow-up: 16 months	CRT guidant versus no CRT, optimized medical therapy	patients with advanced heart failure (NYHA III or IV) due to ischemic and non-ischemic cardiomyopathy with EF $\leq 35\%$ and QRS duration $> 120$ ms	Parallel groups open
<b>Garrigue , 2002</b> n=NA follow-up:	CRT versus no CRT	patients with chronic atrial fibrillation, severe heart failure and QRS prolongation of $\geq 140$ ms	Parallel groups single blind
<b>CRT with triple site ventricular stimulation vs conventional cardiac resynchronization</b>			
<b>NCT00887237 ongoing</b> n=NA follow-up:	CRT with triple site ventricular stimulation versus Conventional cardiac resynchronization	patients with NYHA Class III/IV heart failure	Parallel groups open

## References

### MUSTIC-SR, 2001:

Cazeau S, Leclercq C, Lavergne T, Walker S, Varma C, Linde C, Garrigue S, Kappenberger L, Haywood GA, Santini M, Bailleul C, Daubert JC Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med* 2001;344:873-80 [[11259720](#)]

Duncan A, Wait D, Gibson D, Daubert JC Left ventricular remodelling and haemodynamic effects of multisite biventricular pacing in patients with left ventricular systolic dysfunction and activation disturbances in sinus rhythm: sub-study of the MUSTIC (Multisite Stimulation in Cardiomyopathies) trial. *Eur Heart J* 2003;24:430-41 [[12633545](#)]

### MIRACLE, 2002:

Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, Kocovic DZ, Packer M, Clavell AL, Hayes DL, Ellestad M, Trupp RJ, Underwood J, Pickering F, Truex C, McAtee P, Messenger J Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002;346:1845-53 [[12063368](#)]

Barold H. Preliminary clinical review of Medtronic InSync MIRACLE PMA (Report) <http://www.fda.gov/cdrh/pdf/p010015.html>. (26 September 2005).

### PATH-CHF, 2002:

Auricchio A, Stellbrink C, Sack S, Block M, Vogt J, Bakker P, Huth C, Schndube F, Wolfhard U, Bcker D, Krahnfeld O, Kirkels H Long-term clinical effect of hemodynamically optimized cardiac resynchronization therapy in patients with heart failure and ventricular conduction delay. *J Am Coll Cardiol* 2002;39:2026-33 [[12084604](#)]

### MUSTIC AF, 2002:

Leclercq C, Walker S, Linde C, Clementy J, Marshall AJ, Ritter P, Djiane P, Mabo P, Levy T, Gadler F, Bailleul C, Daubert JC Comparative effects of permanent biventricular and right-univentricular pacing in heart failure patients with chronic atrial fibrillation. *Eur Heart J* 2002;23:1780-7 [[12419298](#)]

### CARE-HF, 2005:

Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005;352:1539-49 [[15753115](#)]

### RD-CHF, 2003:

Leclercq C, Cazeau S, Lellouche D, et al Upgrading from right ventricular pacing to biventricular pacing in previously paced patients with advanced heart failure: a randomized controlled study [the RD-CHF Trial] [Abstract] European Society of Cardiology Congress, Vienna, Austria, 30 August-3 September 2003

### COMPANION (CRT vs MT), 2004:

Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, DiCarlo L, DeMets D, White BG, DeVries DW, Feldman AM Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med* 2004;350:2140-50 [[15152059](#)]

Proestel S. Preliminary clinical review of COMPANION PMA (Report).pj <http://www.fda.gov/ohrms/dockets/ac/04/briefing/>. . . (26 September 2005).

### Garrigue, 2002:

Garrigue S, Bordachar P, Reuter S, Jas P, Kobeissi A, Gaggini G, Hassaguere M, Clementy J Comparison of permanent left ventricular and biventricular pacing in patients with heart failure and chronic atrial fibrillation: prospective haemodynamic study. *Heart* 2002;87:529-34 [[12010933](#)]

### NCT00887237, :

## 2 Combined CRT + ICD

Trial	Treatments	Patients	Trials design and methods
<b>Combined CRT + ICD vs no CRT</b>			
<b>RethinQ , 2007</b> [NCT00132977] n=85/85 follow-up: 6 months	cardiac-resynchronization therapy ICD+CRT versus no cardiac-resynchronization therapy	patients with standard indication for an implantable cardioverter-defibrillator, NYHA 3, EF<35% , QRS<130ms, and evidence of mechanical dyssynchrony	Parallel groups open USA

continued...

Trial	Treatments	Patients	Trials design and methods
<b>Combined CRT + ICD vs no CRT no ICD</b>			
<b>AMIOVIRT , 2003</b> n=51/52 follow-up: 24 months	ICD versus amiodarone as medical therapy	patients with non ischemic cardiomyopathy with EF <=0.35 and Nonsustained ventricular tachycardia	Parallel groups open
<b>COMPANION (CRT+ICD vs MT) , 2004</b> n=595/308 follow-up: 16 months	ICD+CRT versus no ICT no CRT, optimized medical therapy	patients with advanced heart failure (NYHA III or IV) due to ischemic and non-ischemic cardiomyopathy with EF <=0.35 and QRS duration >120 ms	Parallel groups open
<b>Combined CRT + ICD vs CRT</b>			
<b>COMPANION (CRT+ICD vs CRT) , 2004</b> n=595/617 follow-up: 16 months	ICD+CRT versus CRT	patients with advanced heart failure (NYHA III or IV) due to ischemic and non-ischemic cardiomyopathy with EF <=0.35 and QRS duration >120 ms	Parallel groups open
<b>Combined CRT + ICD vs ICD alone</b>			
<b>MIRACLE-ICD-II , 2004</b> n=85/101 follow-up: 6 months	ICD+CRT (and optimalmedical treatment) versus ICD (optimalmedical treatment)	NYHA class II heart failure patients on optimal medical therapy with a left ventricular (LV) ejection fraction <=35% , a QRS >=130 ms, and a class I indication for an ICD	Parallel groups double blind
<b>MIRACLE-ICD-I , 2003</b> n=187/182 follow-up: 6 months	ICD+CRT (plus optimal medical treatment) versus ICD (plus optimal medical treatment)	patients with NYHA class III or IV congestive HF despite appropriate medical management	Parallel groups double blind
<b>CONTAK-CD , 2003</b> n=245/245 follow-up: 4.7 months	ICD+CRT versus ICD (no CRT)	patients with symptomatic heart failure, intraventricular conduction delay, and malignant ventricular tachyarrhythmias	Parallel groups open

## References

### RethinQ, 2007:

Beshai JF, Grimm RA, Nagueh SF, Baker JH 2nd, Beau SL, Greenberg SM, Pires LA, Tchou PJ Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med 2007;357:2461-71 [[17986493](#)]

### AMIOVIRT, 2003:

Strickberger SA, Hummel JD, Bartlett TG, Frumin HI, Schuger CD, Beau SL, Bitar C, Morady F Amiodarone versus implantable cardioverter-defibrillator: randomized trial in patients with nonischemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia-AMIOVIRT. J Am Coll Cardiol 2003;41:1707-12 [[12767651](#)]

### COMPANION (CRT+ICD vs MT), 2004:

Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, DiCarlo L, DeMets D, White BG, DeVries DW, Feldman AM Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med 2004;350:2140-50 [[15152059](#)]

### COMPANION (CRT+ICD vs CRT), 2004:

Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, DiCarlo L, DeMets D, White BG, DeVries DW, Feldman AM Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med 2004;350:2140-50 [[15152059](#)]

### MIRACLE-ICD-II, 2004:

Abraham WT, Young JB, Len AR, Adler S, Bank AJ, Hall SA, Lieberman R, Liem LB, O'Connell JB, Schroeder JS, Wheelan KR Effects of cardiac resynchronization on disease progression in patients with left ventricular systolic dysfunction, an indication for an implantable cardioverter-defibrillator, and mildly symptomatic chronic heart failure. *Circulation* 2004;110:2864-8 [[15505095](#)]

**MIRACLE-ICD-I, 2003:**

Young JB, Abraham WT, Smith AL, Leon AR, Lieberman R, Wilkoff B, Canby RC, Schroeder JS, Liem LB, Hall S, Wheelan K Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. *JAMA* 2003;289:2685-94 [[12771115](#)]

**CONTAK-CD , 2003:**

Higgins SL, Hummel JD, Niazi IK, Giudici MC, Worley SJ, Saxon LA, Boehmer JP, Higginbotham MB, De Marco T, Foster E, Yong PG Cardiac resynchronization therapy for the treatment of heart failure in patients with intraventricular conduction delay and malignant ventricular tachyarrhythmias. *J Am Coll Cardiol* 2003;42:1454-9 [[14563591](#)]

### 3 Implantable cardioverter defibrillator therapy

Trial	Treatments	Patients	Trials design and methods
<b>ICD vs no ICD</b>			
<b>MADIT , 1996</b> n=95/101 follow-up: 27 months	ICD versus anti arrhythmic drugs as conventional therapy	65279;patients with MI >=3 wk before entry and EF <=0.35 and 65279;Asymptomatic unsustained VT unrelated to an acute MI with inducible VT not suppressed after iv procainamide	Parallel groups open
<b>MADIT-II , 2002</b> n=742/490 follow-up: 20 months	implantable cardiac defibrillator versus no ICD, optimized medical therapy	patients with a prior myocardial infarction and EF<=0.30	Parallel groups open
<b>CAT , 2002</b> n=50/54 follow-up: 66 months	ICD versus no iCD, conventional therapy	patients with recent onset nonischemic cardiomyopathy withEF <=0.30	Parallel groups open
<b>DEFINITE , 2004</b> n=229/229 follow-up: 29 months	ICD versus no ICD, standard medical therapy	patients with non ischemic cardiomyopathy with EF <0.36 and Nonsustained ventricular tachycardia or frequent premature ventricular complexes	Parallel groups open
<b>SCD-HeFT (ICD vs placebo) , 2005</b> [NCT00000609] n=829/847 follow-up: 45.5 months	ICD versus optimized medical therapy	patients with ischemic and nonischemic cardiomyopathy withEF<=0.35	Parallel groups open
<b>CABG-patch , 1997</b> [NCT00000540] n=446/454 follow-up: 32 months	ICD versus control	65279;patients undergoing CABG with EF <=0.35 and Abnormal signal-averaged electrocardiogram	Parallel groups open
<b>DINAMIT , 2004</b> n=332/342 follow-up: 30 months	implantable cardioverter defibrillator versus no ICD, optimized medical therapy	patients within 640 days of myocardial infarct ischemic with EF<=0.35 and cardiac autonomic modulation (depressed heart rate variability or increased mean 24-hour heart rate)	Parallel groups open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>MUSIT , 1999</b> n=351/353 follow-up: median 39 months	ICD or drugs as indicated by electrophysiologic testing versus no antiarrhythmic therapy	patients with ischemic cardiomyopathy with EF<=0.40 and 65279;Inducible, sustained ventricular tachyarrhythmias	Parallel groups open
<b>SCD-HeFT (ICD vs amiodarone) , 2005</b> [NCT00000609] n=829/845 follow-up: 45.5 months	ICD versus optimized medical therapy with amiodarone	patients with ischemic and nonischemic cardiomyopathy with EF<=0.35	Parallel groups open

## References

### **MADIT, 1996:**

Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, Saksena S, Waldo AL, Wilber D, Brown MW, Heo M Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. N Engl J Med 1996;335:1933-40 [[8960472](#)]

### **MADIT-II, 2002:**

Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002;346:877-83 [[11907286](#)]

Goldenberg I, Gillespie J, Moss AJ, Hall WJ, Klein H, McNitt S, Brown MW, Cygankiewicz I, Zareba W Long-term benefit of primary prevention with an implantable cardioverter-defibrillator: an extended 8-year follow-up study of the multicenter automatic defibrillator implantation trial II. Circulation 2010;122:1265-71 [[20837894](#)] [10.1161/CIRCULATION-AHA.110.940148](#)

### **CAT, 2002:**

Bnsch D, Antz M, Boczor S, Volkmer M, Tebbenjohanns J, Seidl K, Block M, Gietzen F, Berger J, Kuck KH Primary prevention of sudden cardiac death in idiopathic dilated cardiomyopathy: the Cardiomyopathy Trial (CAT). Circulation 2002;105:1453-8 [[11914254](#)]

### **DEFINITE, 2004:**

Kadish A, Dyer A, Daubert JP, Quigg R, Estes NA, Anderson KP, Calkins H, Hoch D, Goldberger J, Shalaby A, Sanders WE, Schaechter A, Levine JH Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. N Engl J Med 2004;350:2151-8 [[15152060](#)]

Albert CM, Quigg R, Saba S, Estes NA 3rd, Schaechter A, Subacius H, Howard A, Levine J, Kadish A Sex differences in outcome after implantable cardioverter defibrillator implantation in nonischemic cardiomyopathy. Am Heart J 2008;156:367-72 [[18657670](#)]

### **SCD-HeFT (ICD vs placebo), 2005:**

Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, Troutman C, Anderson J, Johnson G, McNulty SE, Clapp-Channing N, Davidson-Ray LD, Fraulo ES, Fishbein DP, Luceri RM, Ip JH Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005;352:225-37 [[15659722](#)]

### **CABG-patch, 1997:**

Bigger JT Jr Prophylactic use of implanted cardiac defibrillators in patients at high risk for ventricular arrhythmias after coronary-artery bypass graft surgery. Coronary Artery Bypass Graft (CABG) Patch Trial Investigators. N Engl J Med 1997;337:1569-75 [[9371853](#)]

### **DINAMIT, 2004:**

Hohnloser SH, Kuck KH, Dorian P, Roberts RS, Hampton JR, Hatala R, Fain E, Gent M, Connolly SJ Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. N Engl J Med 2004;351:2481-8 [[15590950](#)]

### **MUSIT, 1999:**

Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. N Engl J Med 1999;341:1882-90 [[10601507](#)]

### **SCD-HeFT (ICD vs amiodarone), 2005:**

Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, Troutman C, Anderson J, Johnson G, McNulty SE, Clapp-Channing N, Davidson-Ray LD, Fraulo ES, Fishbein DP, Laceri RM, Ip JH Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005;352:225-37 [[15659722](#)]

Entry terms: catheter ablation

## 4 About TrialResults-center.org

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

TrialResults-center is non-profit and self-funded.