PROFID EHRA

Nikolaos Dagres

Charité – DHZC, International Chief Investigator PROFID EHRA trial

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 847999

PROFID PROJECT: BACKGROUND AND CONSORTIUM

- Current strategy for primary prevention ICD implantation after myocardial infarction insufficient
- PROFID objective: Improve strategy of primary prevention ICD implantation

Project Coordinator:
Charité - Universitätsmedizin Berlin
(Gerhard Hindricks & Nikolaos Dagres)
Project start:
1st January 2020

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: BACKGROUND

ESC European Society of Cardiology
European Heart Journal (2022) 43, 3997–4126
https://doi.org/10.1093/eurheartj/ehac262

ESC GUIDELINES

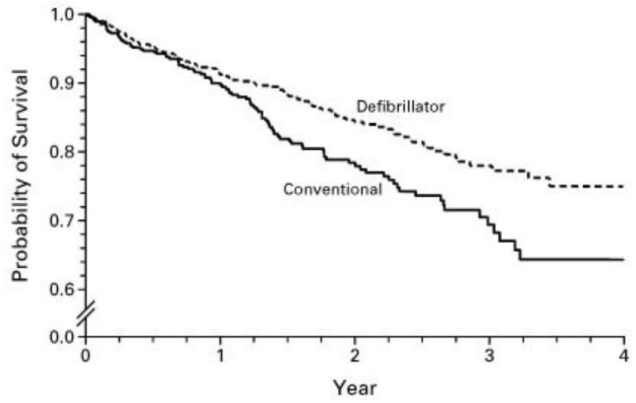
2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

ICD therapy is recommended in patients with CAD, symptomatic heart failure (NYHA class II–III), and LVEF ≤35% despite ≥3 months of OMT.[354,356]	I	A
ICD therapy should be considered in patients with CAD, NYHA class I, and LVEF ≤30% despite ≥3 months of OMT.[354]	IIa	B
ICD implantation should be considered in patients with CAD, LVEF ≤40% despite ≥3 months of OMT, and NSVT, if they are inducible for SMVT by PES.[355]	IIa	B

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: BACKGROUND

MADIT-II

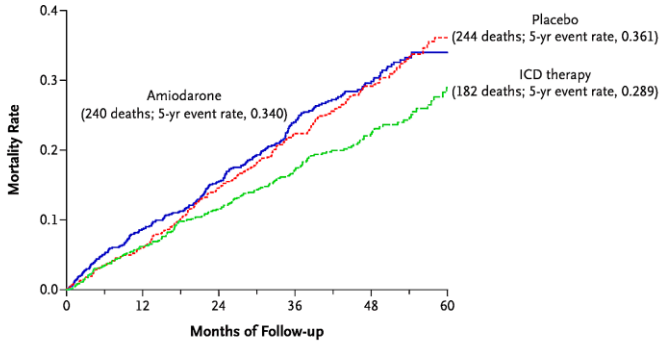


No. at Risk					
Defibrillator	742	503 (0.91)	274 (0.84)	110 (0.78)	9
Conventional	490	329 (0.90)	170 (0.78)	65 (0.69)	3

Moss A et al. N Engl J Med. **2002**

SCD-HeFT

	Hazard Ratio (97.5% CI)	P Value
Amiodarone vs. placebo	1.06 (0.86–1.30)	0.53
ICD therapy vs. placebo	0.77 (0.62–0.96)	0.007



No. at Risk						
Amiodarone	845	772	715	484	280	97
Placebo	847	797	724	505	304	89
ICD therapy	829	778	733	501	304	103

Bardy G et al, N Engl J Med. **2005**

Publicly funded under Horizon 2020 program, no. 847999

Limitations of left ventricular ejection fraction

Reduced LVEF is risk marker for:

- Total mortality
- Cardiac mortality
- Sudden cardiac death

=> Non-specific risk marker for sudden and non-sudden cardiac death

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: BACKGROUND

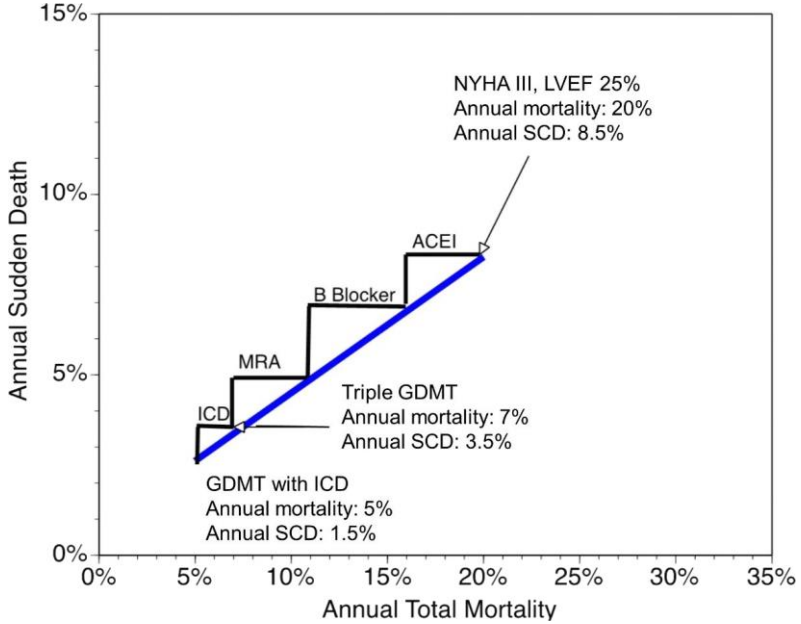
- **Changes in treatment in the last 25 years**
  - Beta blockers
  - Mineralocorticoid antagonists
  - ARNI
  - SGLT2 inhibitors
  - Statins
  - Primary recanalization
  - Cardiac resynchronization therapy
  - …

Most of these reduce not only mortality but ***specifically sudden cardiac death***

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: BACKGROUND

- **Changes in treatment and impact on SCD events**

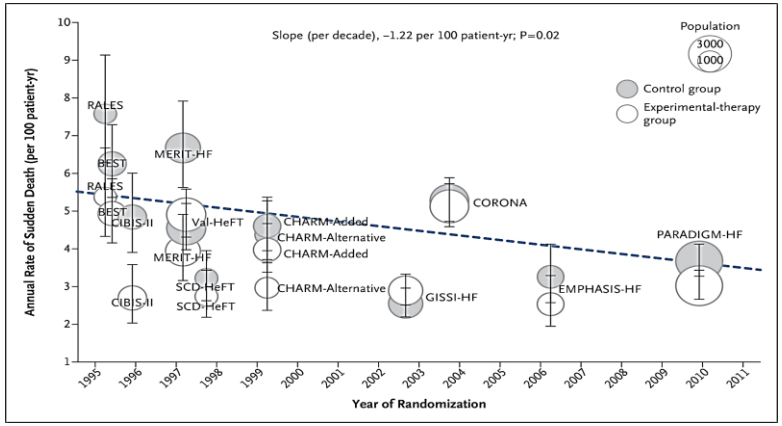


Merchant FM, Levy WC, Kramer DB.
J Am Heart Assoc. **2020**; 9:e015139.

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: RATIONALE

- **Reduced SCD risk** over the last two decades.
- Decreased annual shock rate.



Shen L et al. N Engl J Med **2017**;377:41-51

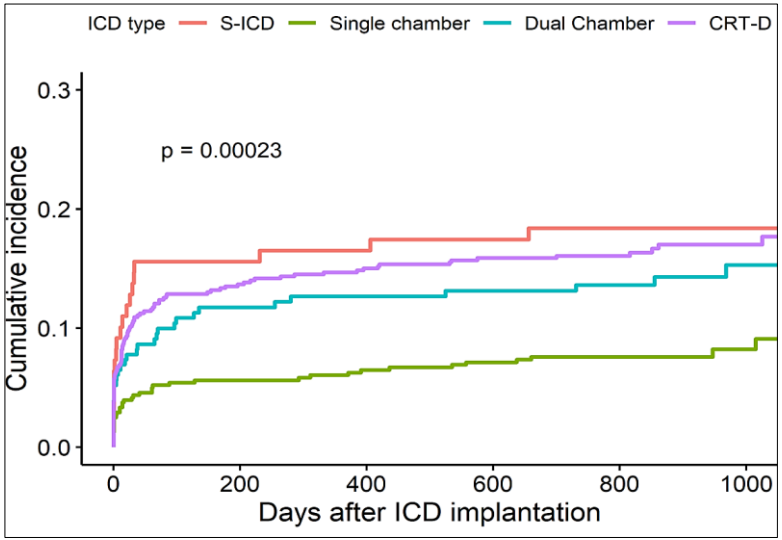
Trial	Year	Average duration (mo)	Average annual rate of appropriate shock, %
MADIT II	2002	24	17
SCD-HeFT	2005	45.5	5
PREPARE	2008	12	5.4
MADIT-RIT	2012	16	3
ICD Registry	2014	20	1

Sabbag A et al. Heart Rhythm **2015**;12:2426–33

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: RATIONALE

Complication rates of ICD therapy remain substantial



van Barreveld M, et al.
J Am Heart Assoc. 2021;10(7):e018063.

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: RATIONALE

- Existing data is outdated and does not represent current therapies.
- New evidence is necessary to define future strategy for primary prevention ICD implantation.
- A novel randomized, adequately powered assessment of the role of the defibrillator under contemporary optimal medical therapy is imperative.
- EHRA and ESC strong supporters (PROFID EHRA trial) to close the evidence gap

EHRA European Heart Rhythm Association

ESC European Society of Cardiology

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: OBJECTIVES

Study population:

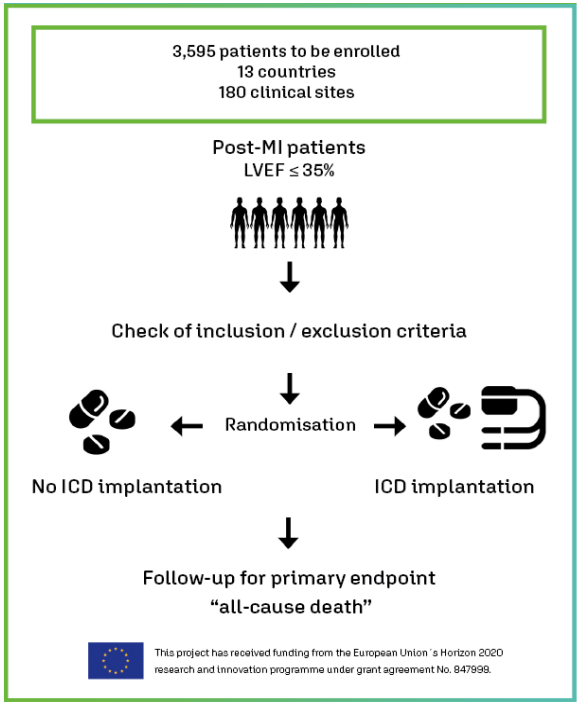
3,595 post-MI patients with symptomatic heart failure and reduced LVEF ≤35%.

STEMI and NSTEMI

Under contemporary optimal medical treatment (OMT) for at least 3 months

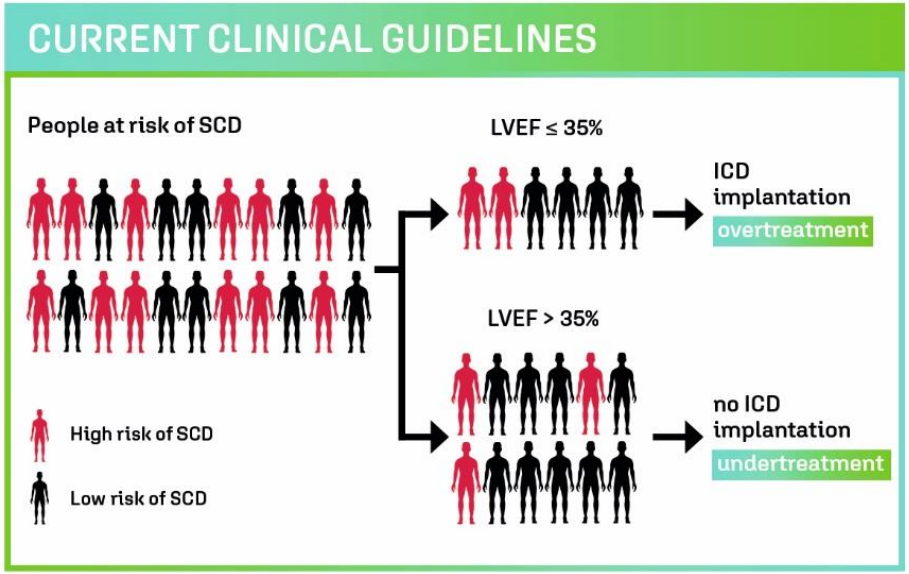
Randomization in OMT+ ICD vs. OMT

Primary endpoint: total mortality



Publicly funded under Horizon 2020 program, no. 847999

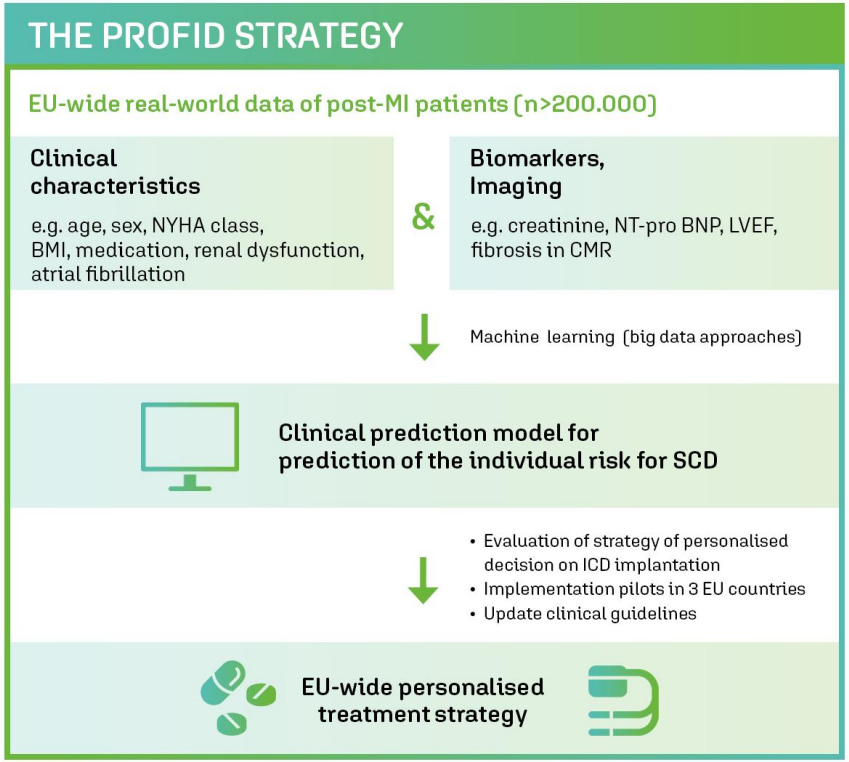
Original PROFID plan



Most devices that are currently implanted will never be needed.

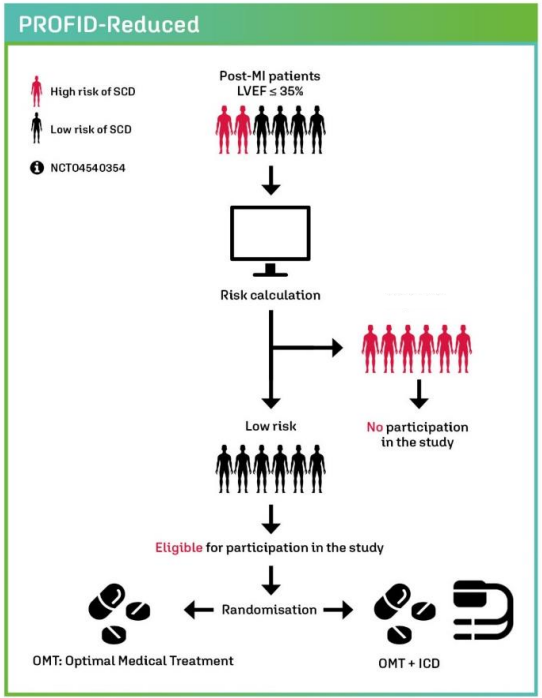
Most patients at true individual risk are not protected.

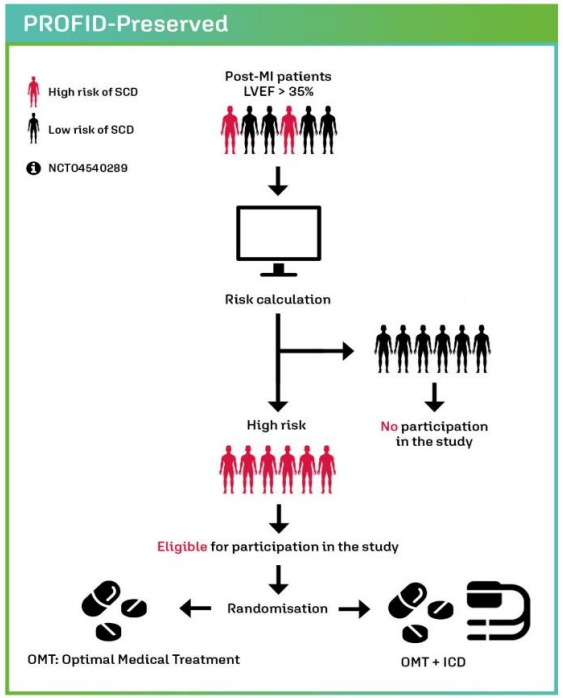
Publicly funded under Horizon 2020 program, no. 847999



Publicly funded under Horizon 2020 program, no. 847999

PROFID clinical trial programme: Original plan

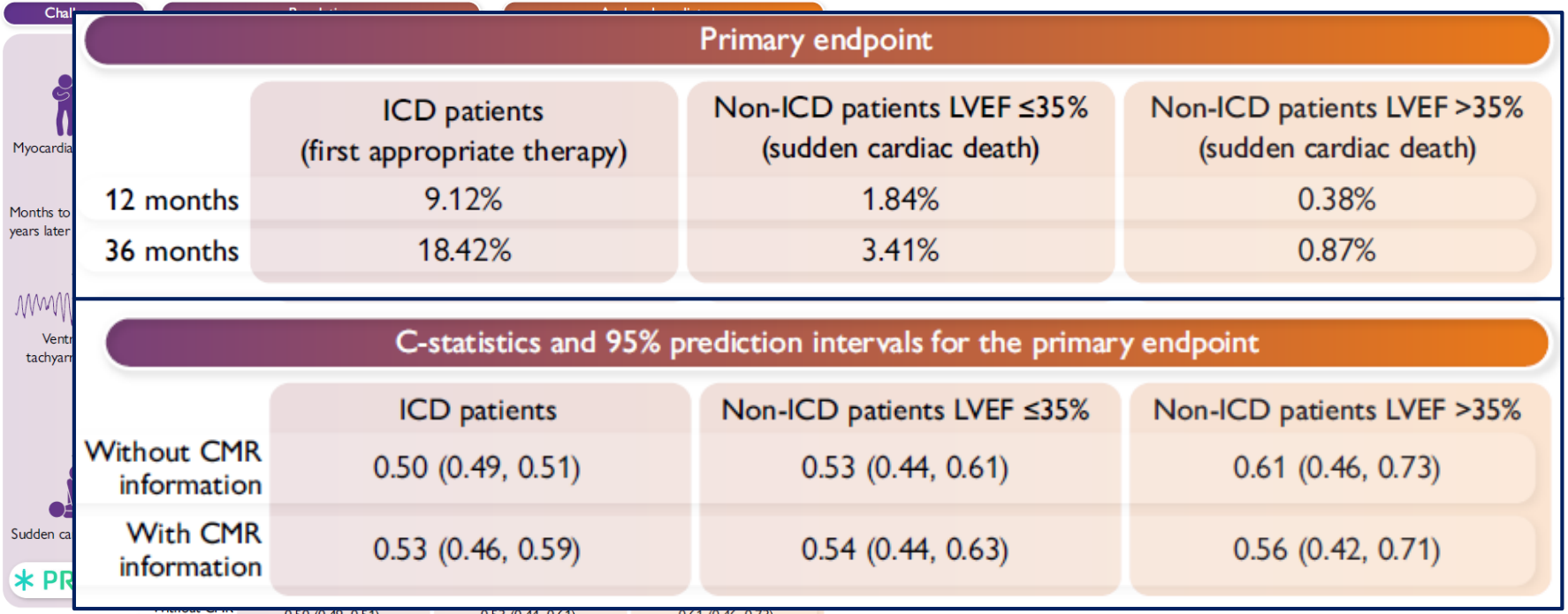




Publicly funded under Horizon 2020 program, no. 847999

Can we identify those at risk?

PROFID



Primary endpoint

	ICD patients (first appropriate therapy)	Non-ICD patients LVEF ≤35% (sudden cardiac death)	Non-ICD patients LVEF >35% (sudden cardiac death)
12 months	9.12%	1.84%	0.38%
36 months	18.42%	3.41%	0.87%

C-statistics and 95% prediction intervals for the primary endpoint

	ICD patients	Non-ICD patients LVEF ≤35%	Non-ICD patients LVEF >35%
Without CMR information	0.50 (0.49, 0.51)	0.53 (0.44, 0.61)	0.61 (0.46, 0.73)
With CMR information	0.53 (0.46, 0.59)	0.54 (0.44, 0.63)	0.56 (0.42, 0.71)

Peek N, et al. Eur Heart J 2024;45:4616-26

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: PARTICIPATING COUNTRIES

Country*		National Coordinators	Planned number of sites**
	DE	Prof. Philipp Sommer	85
	ES	Prof. José L. Merino	20
	FR	Prof. Serge Boveda	15
	AT	Prof. Helmut Pürerfellner	10
	NL	Prof. Kevin Vernooy	15
	PL	Prof. Radosław Lenarczyk	8
	HU	Prof. Béla Merkely	7
	DK	Prof. Jens Cosedis Nielsen	6
	BE	Prof. Tom De Potter	5
	CZ	Prof. Miloš Táborský	5
	SE	Prof. Frieder Braunschweig	5
	UK	Prof. Chris P. Gale	5
	IL	Dr. Mahmoud Suleiman	5
	PT	Prof. Dr. Mário Oliveira	5
	BG	Assoc. Prof. Vassil Traykov	5

Chief Investigators

Prof. Gerhard Hindricks **PD Dr. Nikolaos Dagres**

Charité – Universitätsmedizin Berlin
Deutsches Herzzentrum der Charité

* Sorted acc. to the number of planned sites.
** Planned number of sites does not represent a fixed number.

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: STATUS *(NOVEMBER 2025)*

PARTICIPATING SITES

- Sites open for recruitment (OFR): 84
  (including „Recruitment interrupted“)
  - Austria: 9
  - Belgium: 4
  - Czech Republic: 4
  - Denmark: 1
  - France: 11
  - Germany: 35
  - Great Britain: 6
  - Hungary: 1
  - Israel: 1
  - Netherlands: 5
  - Poland: 3
  - Spain: 4
- Total goal: 180

ENROLLMENT STATUS

- Randomized patients: 265
  - Austria: 30
  - Belgium: 5
  - Czech Republic: 72
  - Denmark: 2
  - France: 6
  - Germany: 89
  - Great Britain: 1
  - Hungary: 11
  - Israel: 3
  - Netherlands: 4
  - Poland: 28
  - Spain: 14
- Total randomization goal: 3,595

Publicly funded under Horizon 2020 program, no. 847999

PROFID EHRA TRIAL: CONTACT INFORMATION

PROFID project website

PROFID EHRA trial website

PROFID EHRA trial flyer

Publicly funded under Horizon 2020 program, no. 847999

Conclusions

- Risk for sudden cardiac death has decreased significantly in the last decades, most probably due to advances in medical treatment
- LVEF only moderate predictor of sudden cardiac death
- Accurate prediction of individual risk not feasible with current methods
- Novel randomized assessment of the ICD role imperative

PROFID EHRA TRIAL: FURTHER INFORMATION

CLINICAL RESEARCH ORGANIZATION

CRI – The Clinical Research Institute GmbH – Now part of NAMSA
Rosa-Bavarese-Str. 3
80639 Munich / Germany

www.namsa.com
profid@cri-muc.eu

PROFID HOTLINE: +49 89 990 1649 974

SPONSOR

Charité – Universitätsmedizin Berlin
Charitéplatz 1
10117 Berlin / Germany

info@profid-project.eu

Publicly funded under Horizon 2020 program, no. 847999