BIOPACE TRIAL PRELIMINARY RESULTS

Biventricular Pacing for Atrio-ventricular Block to Prevent Cardiac Desynchronization

BioPace Trial Investigators and Coordinators

DISCLOSURE

St. Jude Medical : consultant

BOARDS AND COMMITEES

Steering Committee

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Investigators

Trial Statistician

- Mueller H.H. – Munich, Germany

Sponsor

- St. Jude Medical

Data Management

- Coordinating Center for Clinical Trials (KKS) – Marburg, Germany

Clinical trials.gov identifier:

- NCT00187278

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BACKGROUND

- **Atrio-Ventricular Block (AVB) is a common disease currently treated with Right Ventricular (RV) pacing.**

- **However numerous trials (DAVID, MOST...) have shown that RV pacing may have deleterious long-term effects on Left Ventricular (LV) function and clinical outcome.**

AIM OF STUDY

To investigate whether biventricular (BiV) pacing prevents the deleterious consequences of right ventricular (RV) pacing in patients with a standard indication for permanent ventricular pacing

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STUDY DESIGN

- International, multicenter
- Parallel group design
- Randomization (RV / BiV) prior to implant
- Blinded endpoint assessment

STUDY CENTERS

STUDY PURPOSE AND ENDPOINT

PURPOSE

- BiV pacing is superior to RV pacing in patients with AVB who require permanent ventricular pacing

PRIMARY ENDPOINT

- Combination of time-to-death or first hospitalization due to Heart Failure (HF)

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STUDY PURPOSE AND ENDPOINTS

SECONDARY ENDPOINTS

- Death due to cardiovascular causes
- Functional capacity (6-minute walk test) and Quality of Life (Minnesota Questionnaire) 12 months after implantation.
- Echo core laboratory results
  - Left ventricular end diastolic and end systolic diameters
  - Left ventricular ejection fraction
  - Left atrial dimensions
  - Amount of mitral and tricuspid regurgitation
- Adverse events related to
  - Implantation procedure
  - Left ventricular lead (successful implantation of the SJM LV lead)
  - All leads

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INCLUSION CRITERIA

- **Indication for implantation of a ventricular pacemaker according to guidelines and an anticipated need for frequent ventricular pacing**
  - **Permanent 3rd degree AV-block or**
  - **Intermittent 3rd degree AV-block in combination with 1st degree AV-block with a PR-interval ≥ 220 ms or**
  - **2nd degree AV-block in combination with 1st degree AV-block with a PR-interval ≥ 220 ms or**
  - **1st degree AV-block with a PR-interval ≥ 220 ms and indication for ventricular pacing or**
  - **Chronic atrial fibrillation with a spontaneous ventricular rate at rest ≤ 60/min**
- **Any left ventricular ejection fraction (LVEF) as measured by echocardiography**

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EXCLUSION CRITERIA

- Implanted ventricular pacing device
- Status 1 for heart transplantation
- Evidence of acute left ventricular dysfunction and high probability for its reversibility (e.g. acute myocarditis, tachy-cardiomyopathy)
- Implanted prosthetic tricuspid valve
- Severe musculoskeletal disorder(s)
- Age below 18 years
- Life expectancy of less than 6 months

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STATISTICAL ANALYSIS

- Two-sided stratified logrank test
- Type I error level: α = 5%
- Power: 1–β = 80%
- Detectable difference: Hazard Ratio = 0.8
- Intention-to-treat analysis
- Adjusted for differences in gender, age and AF
- 635 events required
- Maximum loss to follow-up: 15%
- 1800 subjects needed
- Pre-specified analysis stratified by LVEF

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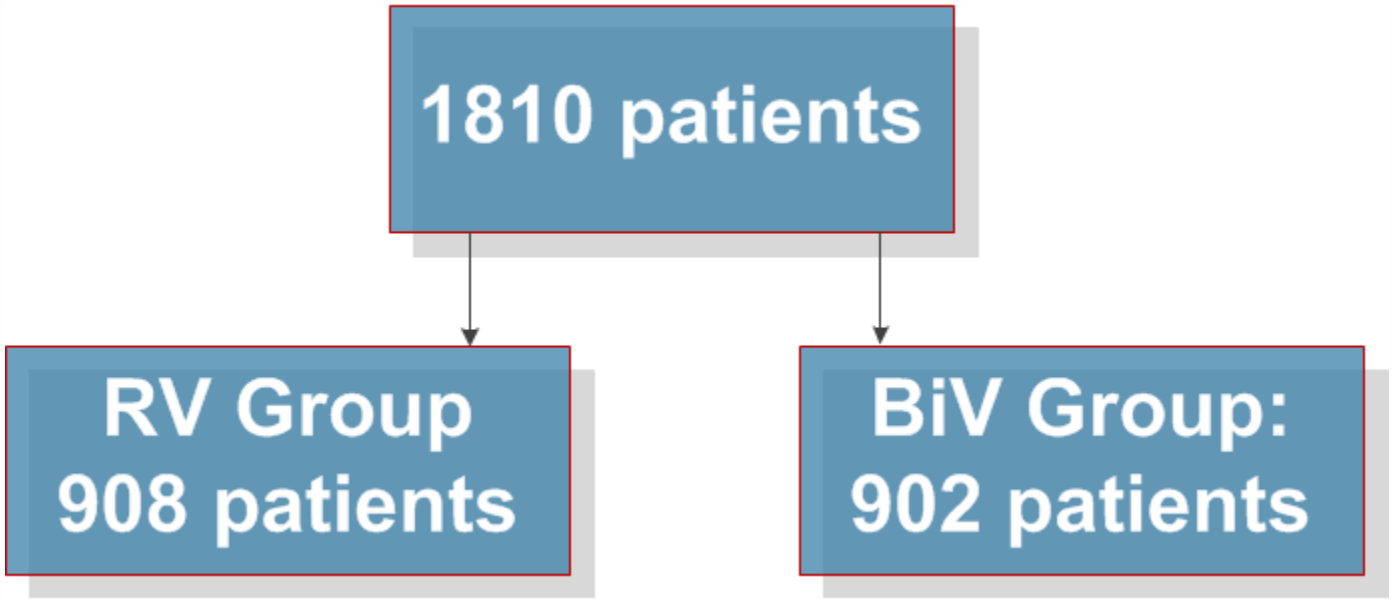
STUDY FLOW CHART

Enrollment period from May 2003 to September 2007



Mean FU: 5.6 years

689 combined events (439 Deaths + 250 HF Hospitalizations)

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BASELINE PARAMETERS

	TOTAL 1810	RV 908 (50.2%)	BiV 902 (49.8%)	p
• Age [year]	73.5±9.2	73.3±9.3	73.8±9.0	0.27
• Men	68.3%	67.4%	69.2%	0.42
• % Ventricular pacing at 1 month	88.2	86.3	90.1	0.07
• LVEF [%]	55.4±12.2	55.5±12.4	55.3±12.1	0.95
• QRS Duration [ms]	118.4±30.5	118.8±30.3	118.1±30.8	0.61
• Underlying Cardiac Disease	63.1%	63.0%	63.3%	0.92
• Atrial Fibrillation	24.9%	24.8%	24.9%	0.96
• LBBB	17.2%	18.3%	16.6%	0.39

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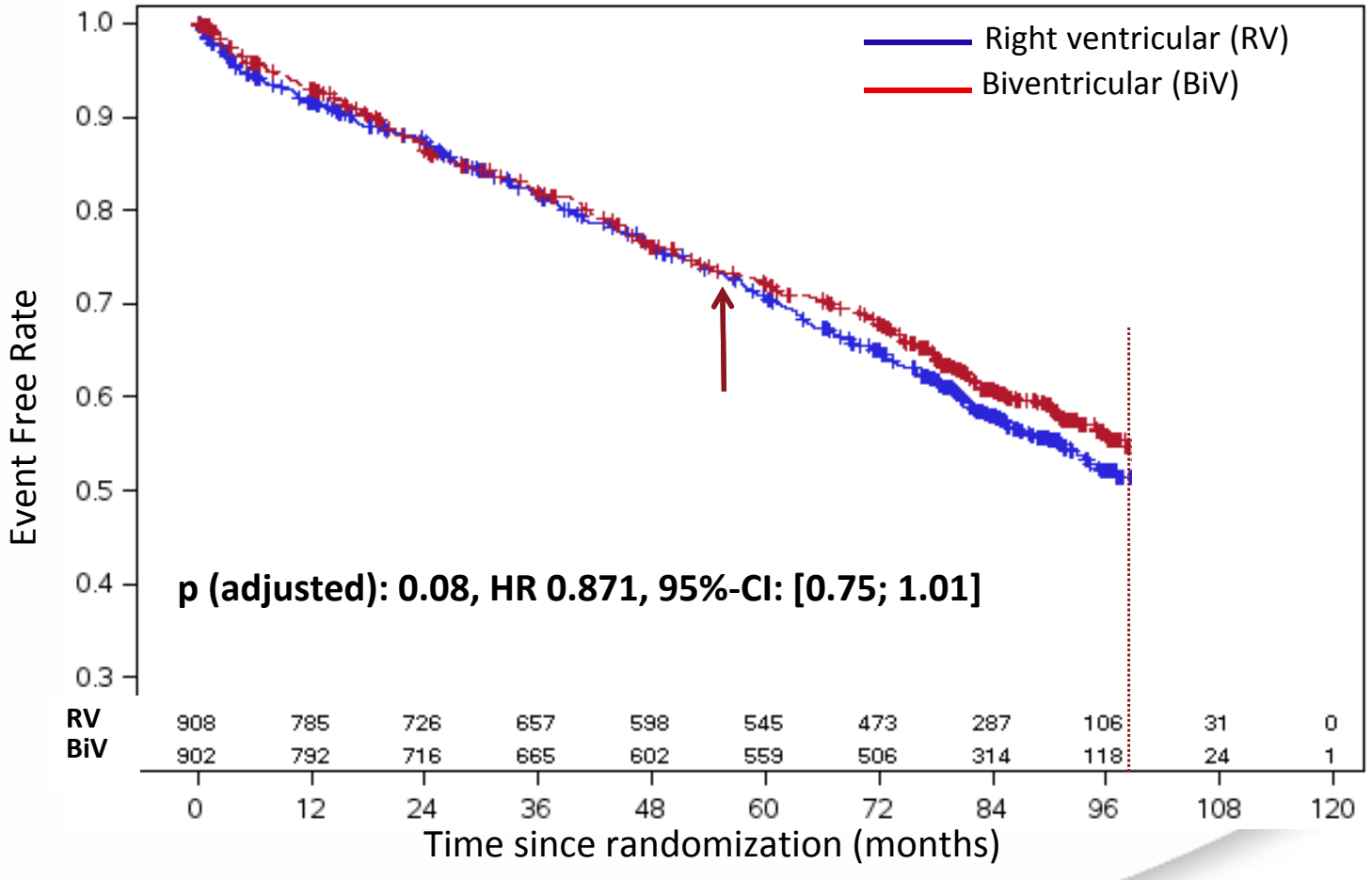
RESULTS

MORTALITY/HF HOSPITALIZATION

1810 patients / LVEF 55.4±12.2%



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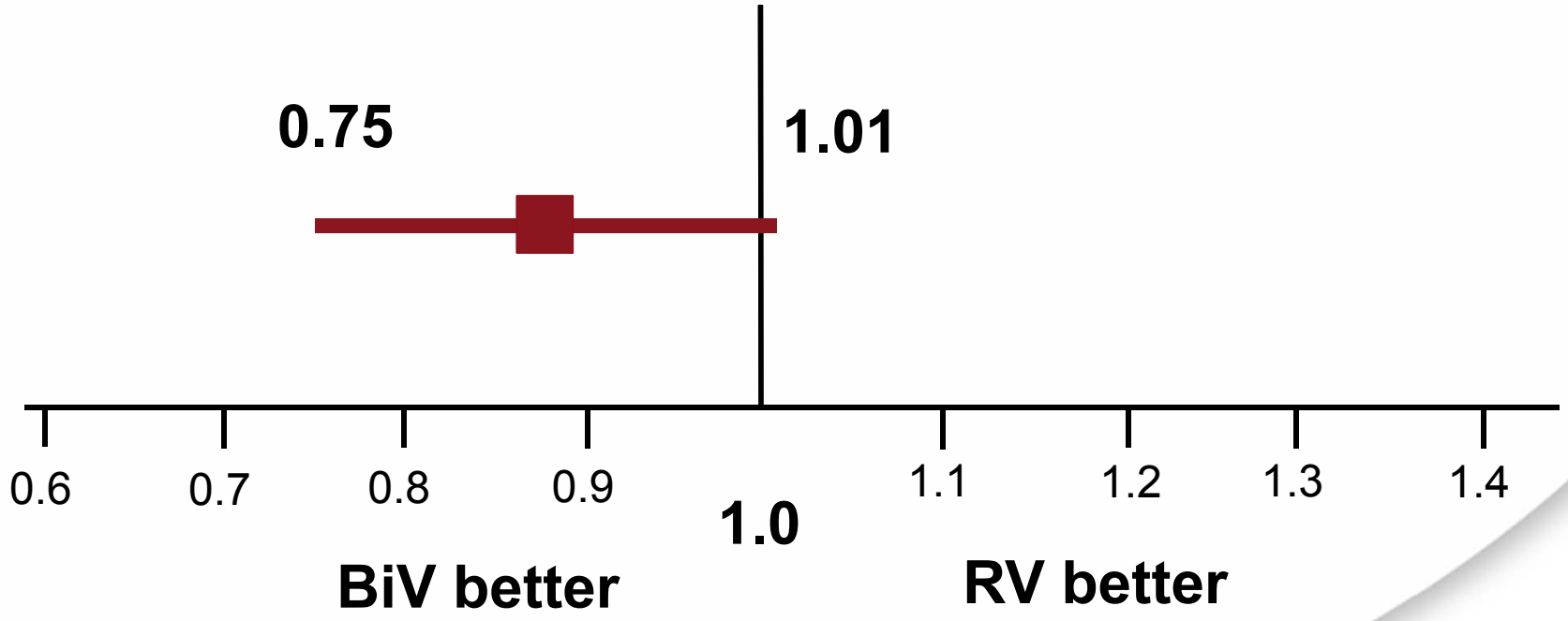
MORTALITY/HF HOSPITALIZATION

HR 0.87, 95%-CI: [0.75; 1.01]

p = 0.08



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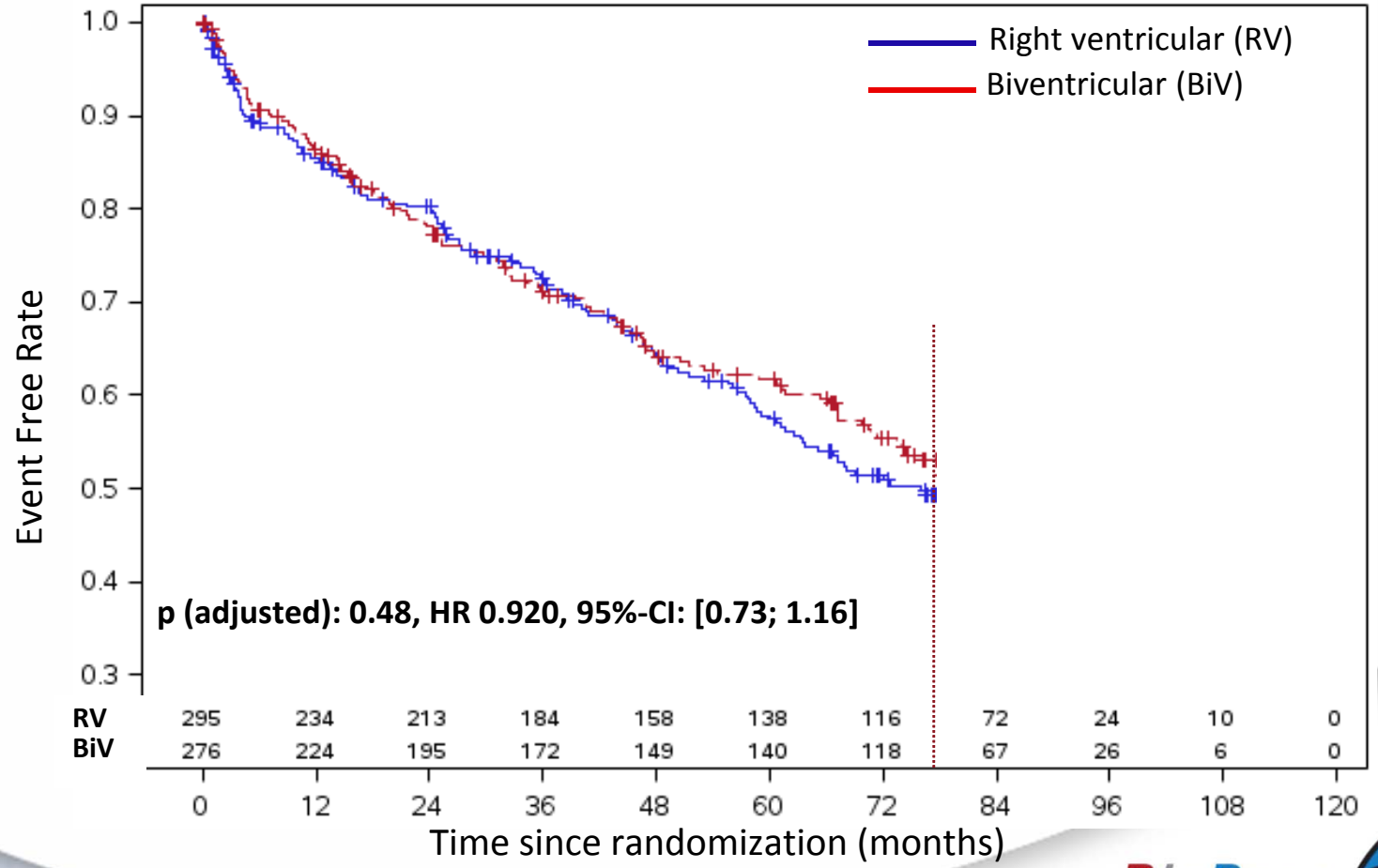
MORTALITY/HF HOSPITALIZATION (LVEF≤50%)

571 patients / LVEF 41.2±8.8%



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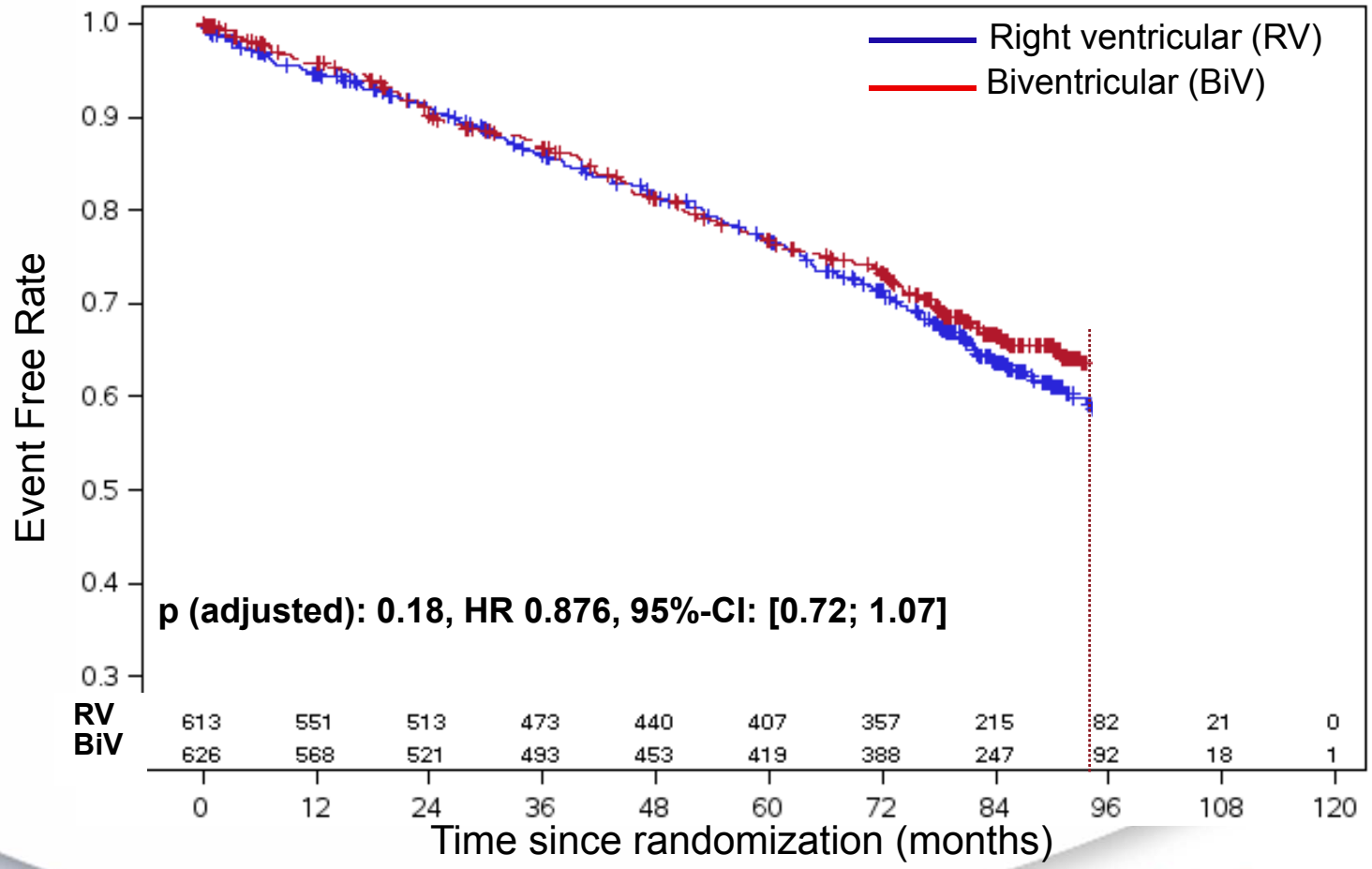
MORTALITY/HF HOSPITALIZATION (LVEF>50%)

1239 patients / LVEF 61.9±7.0%



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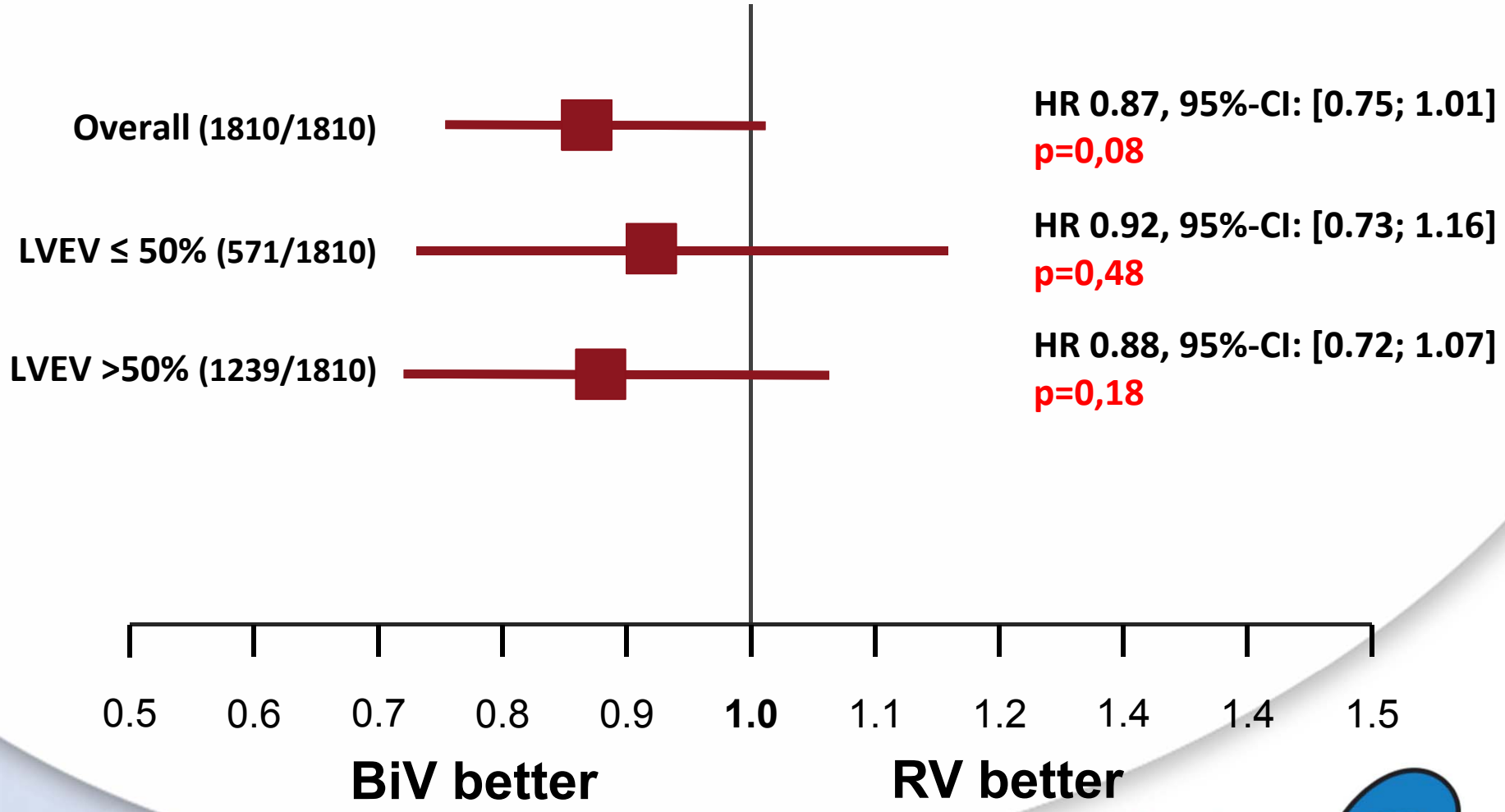
MORTALITY / HF HOSPITALIZATION



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ADVERSE EVENTS

As treated	TOTAL (N=1774)	RV (N=891) [95% CI]	BiV (N=883) [95% CI]	p
Implant Failure	**7.4%**	**0%** [0.0%; 0.4%]	**14.8%** [11.7%; 16.4%]	**<0.0000 ….**
Infections	**1.6%**	**1.1%**	**2.1%**	**0.10**

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STRENGTHS AND LIMITATIONS

STRENGTHS

- Prospective, international, randomized, single-blind control
- Largest, longest follow-up trial to date
- Percentage of RV and BIV pacing measured
- Effect evaluated according to different baseline LVEF

LIMITATIONS

- Long study duration
- 14.8% initial failed implants in the BiV group

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CONCLUSIONS

- In patients with AVB who need implantation of a permanent pacemaker there is a non statistically significant trend in favor of BiV over RV pacing mode.
- Additional analyses will perhaps identify sub-groups for which BiV confers a clear benefit.

LIST OF INVESTIGATORS

- **Australia:** Nadurata
- **Austria:** Siostrzonek, Grimm, Huber
- **Belgium:** Vrints, Mairesse, Vandekerckhove, Castadot, Zenagui, Stoupel, Deperon, Blommaert
- **Canada:** Paredes, Parker
- **Estonia:** Kolk
- **France:** Poulard, Rey, Dupuis, Etienne, Kacet, Graux, Deharo, Davy, Jauvert, Dennetière, Anselme
- **Germany:** Geller, Liebetrau, Dänschel, Meisel, Sievert, Reinig, Weissmüller, Hindricks, Pfeiffer, Szendey, Brömsen, Schmailzl, Axthelm, Czech, Daub, Sick, Steiner, Oltmanns, Ketteler, Grove, Hahlweg, Sabin, Schmitt, Zahn, Weitkamp, Rub, Perings, Lemke
- **Italy:** Padeletti, Vicentini, Luzzi, Verlato, Di Girolamo, Botto, Toselli, Leonzio, Solimene, Lunati, Vaccari, Carreras
- **Netherlands:** De Voogt, Van den Bos, Saïd, Dijkman, Widdershoven
- **Norway:** Haaland, Helleburst, Lappegard, Gjestvang, Nilsen
- **Poland:** Wilcek, Lewczuk
- **Sweden:** Frykman, Gadler, Kjellman, Aronsson
- **Serbia:** Milasinovic, Angelkov, Perisic, Kovačević
- **Tunisia:** Kachboura
- **UK:** Panthing, Yousef, Paul, Barr, Wright, Haywood

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