

Original Article

The large-scale placebo-controlled beta-blocker studies in systolic heart failure revisited: results from CIBIS-II, COPERNICUS and SENIORS-SHF compared with stratified subsets from MERIT-HF

1. J. Wikstrand^{1,*},
2. H. Wedel²,
3. D. Castagno³,
4. J. J. V. McMurray^{4,*}

Article first published online: 24 OCT 2013

DOI: 10.1111/joim.12141

© 2013 The Association for the Publication of the Journal of Internal Medicine

Issue



Journal of Internal Medicine

[Early View \(Online Version of Record published before inclusion in an issue\)](http://journal/10.1111/(ISSN)1365-2796/earlyview)
[\(/journal/10.1111/\(ISSN\)1365-2796/earlyview\)](http://journal/10.1111/(ISSN)1365-2796/earlyview)

Additional Information

How to Cite

Wikstrand J, Wedel H, Castagno D, McMurray JJV Gothenburg University; Nordic School of Public Health, Gothenburg, Sweden; University of Turin, Turin, Italy; University of Glasgow, Glasgow, UK. The large-scale placebo-controlled beta-blocker studies in systolic heart failure revisited: results from CIBIS-II, COPERNICUS and SENIORS-SHF compared with stratified subsets from MERIT-HF. *J Intern Med* 2013; doi:[10.1111/joim.12141](https://doi.org/10.1111/joim.12141) (<http://dx.doi.org/10.1111/joim.12141>).

Author Information

- 1 Wallenberg Laboratory for Cardiovascular Research, Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden
- 2 Nordic School of Public Health, Gothenburg, Sweden
- 3 Division of Cardiology, Department of Medical Sciences, University of Turin, Turin, Italy
- 4 BHF Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow, UK

* *Correspondence:* Dr John Wikstrand, Wallenberg Laboratory for Cardiovascular Research, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden.

(e-mail: john.wikstrand@wlab.gu.se (<mailto:john.wikstrand@wlab.gu.se>)).

and

Professor John McMurray, BHF Cardiovascular Research Centre, 126 University Place, Glasgow, G12 8TA, UK.

(e-mail: john.mcmurray@glasgow.ac.uk

(<mailto:john.mcmurray@glasgow.ac.uk>))

Publication History

1. Article first published online: 24 OCT 2013
2. Accepted manuscript online: 1 OCT 2013 01:00AM EST

- Abstract
- [Article \(/doi/10.1111/joim.12141/full\)](https://doi.org/10.1111/joim.12141/full)
- [References \(/doi/10.1111/joim.12141/references\)](https://doi.org/10.1111/joim.12141/references)
- [Cited By \(/doi/10.1111/joim.12141/citedby\)](https://doi.org/10.1111/joim.12141/citedby)

[View Full Article \(HTML\) \(/doi/10.1111/joim.12141/full\)](https://doi.org/10.1111/joim.12141/full) [Get PDF \(266K\) \(/doi/10.1111/joim.12141/pdf\)](https://doi.org/10.1111/joim.12141/pdf)

Keywords:

beta-blockers; clinical trials; heart failure

Abstract

Aims

The four pivotal beta-blocker trials in heart failure (HF) had different inclusion criteria, making comparison difficult without patient stratifying. The aim of this study was to compare, in similar patients, the effects of bisoprolol, metoprolol controlled release/extended release (CR/XL), carvedilol and nebivolol on (i) total mortality, (ii) all-cause mortality or hospitalization due to cardiovascular causes (time to first event), (iii) all-cause mortality or hospitalization because of HF and (iv) tolerability, defined as discontinuation of randomized treatment.

Methods

We compared stratified (s) subsets in MERIT-HF with patients in CIBIS-II [New York Heart Association (NYHA) class III/IV and ejection fraction (EF) $\leq 35\%$] and COPERNICUS (NYHA III/IV and EF $< 25\%$) and in patients with systolic HF in SENIORS-SHF (age ≥ 70 years and EF $\leq 35\%$).

Results

The annual mortality rates in the placebo and beta-blocker arms were: (i) CIBIS-II ($n = 2647$), 13.2% vs. 8.8% (relative risk reduction 34%, 95% CI: 19–46, $P < 0.0001$) and MERIT-HF $_s$ ($n = 2002$), 14.8% vs. 8.6% (relative risk reduction 42%, 95% CI: 24–56, $P < 0.0001$); (ii) COPERNICUS ($n = 2289$), 19.7% vs. 12.8% (relative risk reduction 35%, 95% CI: 19–48, $P = 0.0014$) and MERIT-HF $_s$ ($n = 795$), 19.1% vs. 11.7% (relative risk reduction 39%; 95% CI: 11–58, $P = 0.0086$); (iii) SENIORS-SHF ($n = 1359$), 11.3% vs. 9.7% (relative risk reduction 16%, NS) and MERIT-HF $_s$ ($n = 985$), 14.8% vs. 10.1% (relative risk reduction 32%, 95% CI: 2–53, $P = 0.038$). The effects on the other outcomes assessed were similar. Analyses indicated fewer discontinuations from randomized treatment on beta-blockers compared with placebo in COPERNICUS and the MERIT-HF $_s$ subsets.

Conclusion

The efficacy and tolerability of bisoprolol, carvedilol and metoprolol CR/XL are similar in patients with systolic HF, irrespective of NYHA class or ejection fraction. Nebivolol is less effective and not better tolerated.

[View Full Article \(HTML\) \(/doi/10.1111/joim.12141/full\)](#) [Get PDF \(266K\) \(/doi/10.1111/joim.12141/pdf\)](#)

More content like this

Find more content:

- [like this article \(/advanced/search/results?articleDoi=10.1111/joim.12141&scope=allContent&start=1&resultsPerPage=20\)](/advanced/search/results?articleDoi=10.1111/joim.12141&scope=allContent&start=1&resultsPerPage=20)

Find more content written by:

- [J. Wikstrand \(/advanced/search/results?searchRowCriteria\[0\].queryString="\]. Wikstrand"&searchRowCriteria\[0\].fieldName=author&start=1&resultsPerPage=20\)](/advanced/search/results?searchRowCriteria[0].queryString=)
- [H. Wedel \(/advanced/search/results?searchRowCriteria\[0\].queryString="H. Wedel"&searchRowCriteria\[0\].fieldName=author&start=1&resultsPerPage=20\)](/advanced/search/results?searchRowCriteria[0].queryString=)
- [D. Castagno \(/advanced/search/results?searchRowCriteria\[0\].queryString="D. Castagno"&searchRowCriteria\[0\].fieldName=author&start=1&resultsPerPage=20\)](/advanced/search/results?searchRowCriteria[0].queryString=)
- [J. J. V. McMurray \(/advanced/search/results?searchRowCriteria\[0\].queryString="\]. J. V. McMurray"&searchRowCriteria\[0\].fieldName=author&start=1&resultsPerPage=20\)](/advanced/search/results?searchRowCriteria[0].queryString=)
- [All Authors \(/advanced/search/results?searchRowCriteria\[0\].queryString="\]. Wikstrand" "H. Wedel" "D. Castagno" "\]. J. V. McMurray"&searchRowCriteria\[0\].fieldName=author&start=1&resultsPerPage=20\)](/advanced/search/results?searchRowCriteria[0].queryString=)