



JACC

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Journal of the American College of Cardiology


Volume 71, Issue 4, January 2018
DOI: 10.1016/j.jacc.2017.11.041


 [PDF Article](#)


[Download](#)

Biomarker-Guided Versus Guideline-Based Treatment of Patients With Heart Failure Results From BIOSTAT-CHF

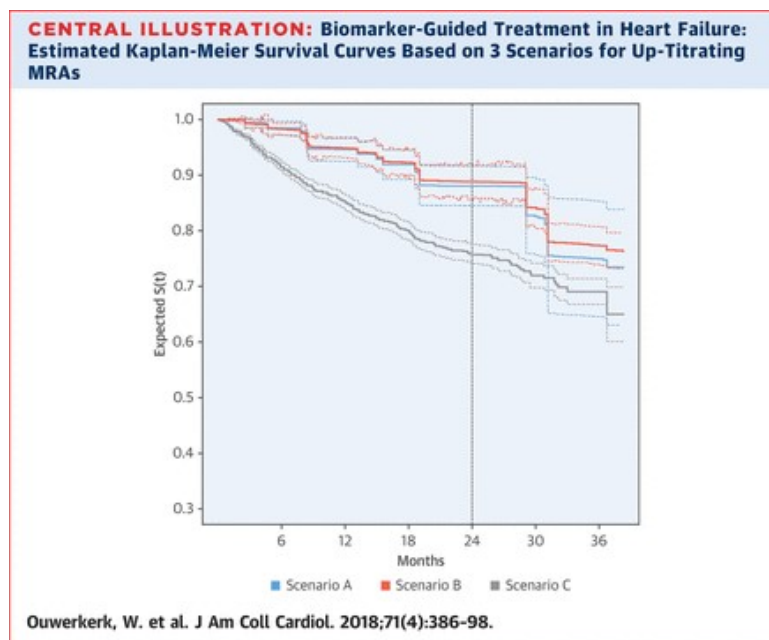
Wouter Ouwerkerk, Aeilko H. Zwinderman, Leong L. Ng, Biniyam Demissei, Hans L. Hillege, Faiez Zannad, Dirk J. van Veldhuisen, Nilesh J. Samani, Piotr Ponikowski, Marco Metra, Jozine M. ter Maaten, Chim C. Lang, Pim van der Harst, Gerasimos Filippatos, Kenneth Dickstein, John G. Cleland, Stefan D. Anker and Adriaan A. Voors

 This article requires a subscription or purchase to view the full text. If you are a subscriber or member, click the login link or the subscribe link in the top menu above to access this article.

 [Add to Cart \(\\$35\)](#)

 [Author + information](#)

Central Illustration



[Download figure](#) | [Open in new tab](#) | [Download powerpoint](#)

Abstract

Background Heart failure guidelines recommend up-titration of angiotensin-converting enzyme (ACE) inhibitor/angiotensin receptor blockers (ARBs), beta-blockers, and mineralocorticoid receptor antagonists (MRAs) to doses used in randomized clinical trials, but these recommended doses are often not reached. Up-titration may, however, not be necessary in all patients.

Objectives This study sought to establish the role of blood biomarkers to determine which patients should or should not be up-titrated.

Methods Clinical outcomes of 2,516 patients with worsening heart failure from the BIOSTAT-CHF (BIOlogy Study to Tailored Treatment in Chronic Heart Failure) were compared between 3 theoretical treatment scenarios: scenario A, in which all patients are up-titrated to >50% of recommended doses; scenario B, in which patients are up-titrated according to a biomarker-based treatment selection model; and scenario C, in which no patient is up-titrated to >50% of recommended doses. The study conducted multivariable Cox regression using 161 biomarkers and their interaction with treatment, weighted for treatment-indication bias to estimate the expected number of deaths or heart failure hospitalizations at 24 months for all 3 scenarios.

Results Estimated death or hospitalization rates in 1,802 patients with available (bio)markers were 16%, 16%, and 26%, respectively, in the ACE inhibitor/ARB up-titration scenarios A, B, and C. Similar rates for beta-blocker and MRA up-titration scenarios A, B, and C were 23%, 19%, and 24%, and 12%, 11%, and 24%, respectively. If up-titration was successful in all patients, an estimated 9.8, 1.3, and 12.3 events per 100 treated patients could be prevented at 24 months by ACE inhibitor/ARB, beta-blocker, and MRA therapy, respectively. Similar numbers were 9.9, 4.7, and 13.1 if up-titration treatment decision was based on a biomarker-based treatment selection model.

Conclusions Up-titrating patients with heart failure based on biomarker values might have resulted in fewer deaths or hospitalizations compared with a hypothetical scenario in which all patients were successfully up-titrated.

Key Words

ACE inhibitor/ARB beta-blocker biomarkers MRA treatment decision

Footnotes

This work was supported by a grant from the European Commission (FP7-242209-BIOSTAT-CHF; EudraCT 2010-020808-29). Dr. Metra has received consulting honoraria from Amgen, Bayer, Novartis, and Servier; and speaker fees from Abbott Vascular, Bayer, and ResMed. Dr. Lang has received consultancy fees and/or research grants from Amgen, AstraZeneca, MSD, Novartis, and Servier. Dr. van der Harst has received a research grant from Abbott. Dr. Filippatos has received fees and/or research grants from Novartis, Bayer, Cardioventis, Vifor, Servier, Alere, and Abbott. Dr. Dickstein has received honoraria and/or research support from Medtronic, Boston Scientific, St. Jude Medical, Biotronik, Sorin, Merck, Novartis, Amgen, Boehringer Ingelheim, AstraZeneca, Pfizer, Bayer, GlaxoSmithKline, Roche, Sanofi, Abbott, Otsuka, Leo, Servier, and Bristol-Myers Squibb. Dr. Cleland has received grant support from Amgen, Novartis, and Stealth Biopharmaceuticals; and honoraria from Servier. Dr. Anker has received grants from Vifor and Abbott Vascular; and consulting fees from Vifor, Bayer, Boehringer Ingelheim, Brahms, Cardioventis, Janssen, Novartis, Relypsa, Servier, Stealth Peptides, and ZS Pharma. Dr. Voors has received consultancy fees and/or research grants from Alere, Amgen, Bayer, Boehringer Ingelheim, Cardio3Biosciences, Celladon, GlaxoSmithKline, Merck/MSD, Novartis, Servier, Stealth Peptides, Singulex, Sphingotec, Trevena, Vifor, and ZS Pharma. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Listen to this manuscript's audio summary by JACC Editor-in-Chief Dr. Valentin Fuster.


Received October 24, 2017.


Revision received November 5, 2017.

Accepted November 7, 2017.

2018 American College of Cardiology Foundation

[View Full Text](#)

 This article requires a subscription or purchase to view the full text. If you are a subscriber or member, click Login or the Subscribe link (top menu above) to access this article.

 Add to Cart (\$35)

[Login](#)

[Previous](#)


[Next](#)

[Back to top](#)

Toolbox

 [Print PDF](#)

 [Email](#)

 [Share](#)


 [\(X\) Citation](#)

 [Alerts](#)

 [Permissions](#)

 [Metrics](#)



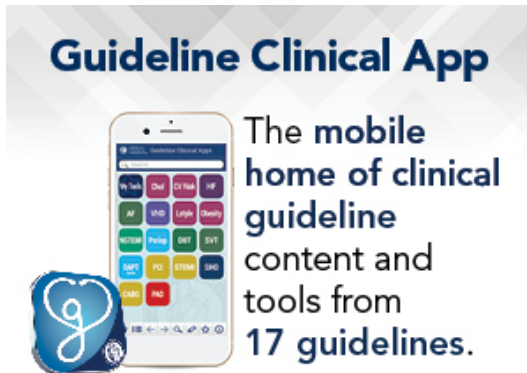
 Add to Cart (\$35)

Audio Summary

[Subscribe to Podcast](#)

[Download MP3](#)

Advertisement



Similar Articles

[Can Biomarker Panels Predict Response to Pharmacotherapy in Heart Failure?](#)

Richard W. Troughton, Christopher M.A. Frampton

[Beta-Blocker Therapy After Myocardial Infarction: More Questions Than Answers](#)

Viviany R. Taqueti, Patrick T. O’Gara

[TCTAP A-017 Timing of Beta-blocker Initiation in Myocardial Infarction Patients](#)

Jae Min Kim, Jong Shin Woo, et al

We recommend

[The Ongoing Evolution of Optimal Clinical Endpoints for Heart Failure Trials](#)

Henry Krum et al., JACC: Heart Failure

[Adherence Tradeoff to Multiple Preventive Therapies and All-Cause Mortality After Acute Myocardial Infarction](#)

Maarit J. Korhonen et al., Journal of the American College of Cardiology

[A hard look at angiotensin receptor blockers in heart failure](#)

Christian N. Gring, Journal of the American College of Cardiology

[Beta-blockers and angiotensin-converting enzyme inhibitors/receptor blockers prescriptions after hospital discharge for heart failure are associated with decreased mortality in Alberta, Canada](#)

David Johnson, Journal of the American College of Cardiology

[Up to 80 percent of heart failure patients denied therapy to reduce hospitalization and early death](#)

European Society of Cardiology, ScienceDaily

[Combination therapy for heart failure does not reduce risk of CV death or rehospitalization](#)

American Medical Association (AMA), ScienceDaily

[Serum creatinine elevation after renin-angiotensin system blockade and long term cardiorenal risks: cohort study](#)

Morten Schmidt et al., The BMJ

[Cardiotoxic effects of anthracycline-based therapy: what is the evidence and what are the potential harms?](#)

Bennett E Levis et al., The Lancet Oncology

Powered by

Advertisement

A banner advertisement for Mendeley Funding. On the left, there is a small logo with three stylized figures and the text "Mendeley Funding". To the right of the logo is a photograph of two men in a laboratory setting; one man has a beard and is wearing a lab coat, while the other is partially visible. On the right side of the banner, the text "Connect to a world of research funding" is displayed in a large, white, sans-serif font. Below this text, there is a white rectangular button with the text "Find the right opportunity" in a smaller, blue, sans-serif font.

Mendeley Funding

Connect to a world of research funding

Find the right opportunity

JACC

[Home](#)

[Topics](#)

[CME/MOC](#)

[Author Instructions](#)

[Submit Your Manuscript](#)

[JACC Journals Best of 2016](#)



JACC Journals

[JACC: Basic to Translational Science](#)

[JACC: Cardiovascular Imaging](#)

[JACC: Cardiovascular Interventions](#)

[JACC: Clinical Electrophysiology](#)

[JACC: Heart Failure](#)

General Information

[About the Journals](#)

[Subscribe](#)

[eTable of Content Alerts](#)

[Reprints/Permissions](#)

[Operating Policies](#)

[Contact Us](#)

[Help](#)

[Conditions of Use](#)

[Privacy Policy](#)

American College of Cardiology

[ACC.org](#)

[Image and Slide Gallery](#)

[CardioSmart](#)

[Cardiology Career Network](#)

[Cardiology](#)

[Cardiology: Interventions](#)

© 2018 JACC: Journal of the American College of Cardiology

Powered by  HighWire