

# HEART OF THE MATTER

## Obsessing on Atrial Fib

The recent Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation (RECORD AF) provides further data to belie our obsession with obtaining or maintaining normal sinus rhythm in patients with intermittent or paroxysmal AF (J. Am. Coll. Cardiol. 2011;58:493-501).

Registry studies fail to provide the randomized data that we demand in control trials, but can often yield data about real-world therapy. This registry, which included 5,604 patients from around the world and whose authors were either consultants or employees of Sanofi-Aventis, the makers of dronedarone, confirms much of what has already been said on the issue. There is little or no benefit associated with the rhythm control therapy compared to a heart rate strategy when examined in this community-based unselected population.

Because patients in this study were not randomized to a particular therapy, participating doctors could use either strategy. Unfortunately, patients in the rate control arm were older and more often had AF, heart failure, and valvular heart disease at baseline. Despite this imbalance, the heart rate strategy was as good as rhythm control. Both groups experienced an 18% incidence of adverse clinical events that were determined by the clinical characteristics of the patient and not the therapeutic strategy used or heart rate achieved. Success was measured by the presence of normal sinus rhythm in the rhythm-controlled patients or a heart rate of less than 80 bpm in the rate-controlled patients at 1 year follow-up, which was achieved in 60% and 47%, respectively. If the heart rate target was below 85 bpm, the success was achieved in 60% vs. 52%, respectively. These observations are consistent with previous studies comparing rhythm and rate control strategies.

This obsession with the maintenance of normal sinus rhythm in patients with AF has spawned a whole industry associated with the technology and application of catheter ablation, atrial defibrillation, left atrial occlusive devices, and the continued development of anti-arrhythmic drugs. All of these interventions have achieved some success but have been associated with significant drug and device adverse events.

The most recently approved anti-arrhythmic drug, dronedarone (Multaq), has been extensively studied in AF. Three major clinical trials have examined the drug in paroxysmal, persistent, and permanent AF. The most recent trial, Permanent Atrial Fibrillation Outcome Study Using Dronedarone (PALLAS), compared dronedarone to placebo in 3,000 patients with permanent AF and who also had a number of comorbidities, including symptomatic heart failure and a decrease

in ejection fraction, but excluded New York Heart Association class III heart failure. Only an electrophysiologist is able to make the distinction between these two clinical heart failure settings. The study was prematurely stopped because of a significant increase in cardiovascular events, including mortality (CARDIOLOGY NEWS, August 2011, p. 5).

Dronedarone was approved in 2009 for patients with paroxysmal and persistent AF and atrial flutter by the Food and Drug Administration based on the ATHENA trial, which reported a decrease in recurrent AF in patients treated with the drug. In addition, dronedarone decreased the combined cardiovascular end point of mortality and rehospitalization, achieved mostly by a decrease in rehospitalization. However, its approval included a boxed warning

that it is "contraindicated in patients with NYHA Class IV heart failure or NYHA Class II-III heart failure with a recent decompensation requiring hospitalization," because of the increased risks observed in the previous Trial with Dronedarone in Moderate to Severe CHF Evaluating Morbidity Decrease (ANDROMEDA). That trial, which included mostly patients with NYHA class III-IV, was stopped prematurely because of the increase in heart failure mortality.

Dr. Stuart Connolly, the co-primary investigator of PALLAS, emphasized the difference between ATHENA, which randomized patients with nonpermanent AF, and PALLAS, which randomized patients with permanent AF. He thought that it was "reasonable" for patients with nonpermanent AF to continue with dronedarone, because "they will still benefit from it in terms of reduced CV hospitalization."

Although there are surely some patients in whom AF causes significant symptoms that warrant aggressive therapy, the vast majority of patients, as indicated in RECORD AF, tolerate AF quite well. Much of the quest for rhythm control is related to the need to prevent systemic emboli and the requirement for anticoagulation therapy using vitamin K derivatives. The development of new antithrombotic drugs and factor Xa inhibitors now provides a safer and more effective alternative. It is time to relax our obsessive approach to atrial fibrillation therapy and become more realistic about our long-term goals for its therapy. ■

DR. GOLDSTEIN, *medical editor of CARDIOLOGY NEWS, is professor of medicine at Wayne State University and division head emeritus of cardiovascular medicine at Henry Ford Hospital, both in Detroit. He is on data safety monitoring committees for the National Institutes of Health and several pharmaceutical companies.*



SIDNEY GOLDSTEIN, M.D.

## Cardiology News

President, IMNG Alan J. Imhoff

**Editor in Chief** Mary Jo M. Dales

**Executive Editors** Denise Fulton, Kathy Scarbeck

**Managing Editor** Catherine Hackett

**Senior Editors** Christina Chase, Kathryn DeMott, Jeff Evans, Lori Buckner Farmer, Keith Haglund, Gina L. Henderson, Sally Koch Kubetin, Teresa Lassman, Mark S. Lesney, Jane Salodof MacNeil, Renée Matthews, Catherine Cooper Nellist, Amy Pfeiffer, Terry Rudd, Leanne Sullivan, Elizabeth Wood

**Editorial Production Manager** Carol Nicotera-Ward

**Associate Editors** Felicia Rosenblatt Black, Therese Borden, Lorinda Bullock, Jay C. Cherniak, Stephen Cimino, Richard Franki, Virginia Ingram-Wells, Jane Locastro, January W. Payne

**Reporters** *Chicago:* Patrice Wendling; *Denver:* Bruce Jancin; *Germany:* Jennie Smith; *Miami:* Damian McNamara; *Mid-Atlantic:* Michele G. Sullivan; *New England:* Diana Mahoney; *New York:* Mary Ellen Schneider; *Philadelphia:* Mitchel L. Zoler; *San Diego:* Doug Brunk; *San Francisco:* Sherry Boschert, Robert Finn; *Washington:* Alicia Ault, Frances Correa, Elizabeth Mechatie, Naseem S. Miller, Heidi Splete, Miriam E. Tucker, Kerri Wachter

**Multimedia Producer** Nick Piegari

**Contributing Writers** Christine Kilgore, Mary Ann Moon

**Multimedia Intern** Nancy Pham

**Project Manager** Susan D. Hite

**Assignments Manager** Megan Evans

**Editorial Offices** 5635 Fishers Lane, Suite 6000, Rockville, MD 20852, 877-524-9335, [cardiologynews@elsevier.com](mailto:cardiologynews@elsevier.com)

**Address Changes** Fax change of address (with old mailing label) to 973-290-8245 or e-mail change to [subs@elsevier.com](mailto:subs@elsevier.com)

**Director of Information Technology** Doug Sullivan

**Senior Systems Administrators** Lee J. Unger

**Systems Administrator/Application Support** Peter Ayinde

**Executive Director, Operations** Jim Chicca

**Director, Production/Manufacturing** Yvonne Evans Struss

**Production Manager** Judi Sheffer

**Production Specialists** Maria Aquino, Anthony Draper, Rebecca Siebodnik

**Creative Director** Louise A. Koenig

**Design Supervisor** Elizabeth Byrne Lobdell

**Senior Designers** Sarah L.G. Breeden, Yenling Liu

**Designer** Lisa M. Marfori

**Photo Editor** Catherine Harrell

**Web Production Engineer** Jon Li

**Web Production Specialist** Jennifer Calhoun

**Sales Director, IMNG** Mark E. Altier, 973-290-8220, [m.altier@elsevier.com](mailto:m.altier@elsevier.com)

**National Account Manager** Courtney Leonard, 973-290-8223, [c.leonard@elsevier.com](mailto:c.leonard@elsevier.com)

**Advertising Offices** 60 Columbia Rd., Bldg. B, 2<sup>nd</sup> fl., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250

**Classified Sales Manager, IMNG** Robert Zwick, 973-290-8226, fax 973-290-8250, [r.zwick@elsevier.com](mailto:r.zwick@elsevier.com)

**Classified Sales Representative** Andrea LaMonica 800-381-0569, fax 914-381-0573, [a.lamonica@elsevier.com](mailto:a.lamonica@elsevier.com)

**Reprints/Eprints** Contact Wright's Media 877-652-5295

**Sr. Program Manager, Customized Programs** Malika Wicks

**Audience Development Manager** Barbara Cavallaro, 973-290-8253, [b.cavallaro@elsevier.com](mailto:b.cavallaro@elsevier.com)

**Program/Marketing Manager** Jennifer Eckert

**Business Controller** Dennis Quirk

**Adv. Services Manager** Joan Friedman

**Credit Supervisor** Patricia H. Ramsey

**Manager, Administration/Conventions** Lynne Kalish

**Receptionist** Linda Wilson

**Accounts Payable Coordinator** Daniela Silva

CARDIOLOGY NEWS is an independent newspaper that provides the practicing specialist with timely and relevant news and commentary about clinical developments in the field and about the impact of health care policy on the specialty and the physician's practice.

The ideas and opinions expressed in CARDIOLOGY NEWS do not necessarily reflect those of the Publisher. International Medical News Group, LLC, an Elsevier company, will not assume responsibility for damages, loss, or claims of any kind arising from or related to the information contained in this publication, including any claims related to the products, drugs, or services mentioned herein.

POSTMASTER Send changes of address (with old mailing label) to CARDIOLOGY NEWS Circulation, 60 Columbia Rd., Bldg. B, 2<sup>nd</sup> fl., Morristown, NJ 07960.

CARDIOLOGY NEWS (ISSN 1544-8800) is published monthly by International Medical News Group, LLC, an Elsevier company, 60 Columbia Rd., Bldg. B, 2<sup>nd</sup> fl., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250. Subscription price is \$114.00 per year.



©Copyright 2011, by Elsevier Inc.

INTERNATIONAL MEDICAL NEWS GROUP



## EDITORIAL ADVISORY BOARD

**SIDNEY GOLDSTEIN, M.D.**, Wayne State University, Detroit;

*Medical Editor*

**ERIC R. BATES, M.D.**, University of Michigan, Ann Arbor

**GEORGE BELLER, M.D.**, University of Virginia, Charlottesville

**ROBERT M. CALIFF, M.D.**, Duke University, Durham, N.C.

**PRAKASH C. DEEDWANIA, M.D.**, University of California, San Francisco, Fresno

**JOHN FLACK, M.D.**, Wayne State University, Detroit

**ANTONIO M. GOTTO JR., M.D.**, Cornell University, New York

**DAVID L. HAYES, M.D.**, Mayo Clinic, Rochester, Minn.

**DAVID R. HOLMES JR., M.D.**, Mayo Clinic, Rochester, Minn.

**BARRY M. MASSIE, M.D.**, University of California, San Francisco

**CHRISTOPHER M. O'CONNOR, M.D.**, Duke University, Durham, N.C.

**GEORGE J. PHILIPIDES, M.D.**, Boston University

**ILEANA L. PIÑA, M.D.**, Case Western Reserve University, Cleveland

**OTELIO RANDALL, M.D.**, Howard University, Washington

**RITA F. REDBERG, M.D.**, University of California, San Francisco

**HOWARD (HANK) ROSMAN, M.D.**, St. John Hospital and Medical Center, Detroit

**THOMAS J. RYAN, M.D.**, Boston University

**HANI N. SABBAB, PH.D.**, Henry Ford Hospital, Detroit

**LESLIE ANNE SAXON, M.D.**, University of Southern California, Los Angeles

**DAVID H. SPODICK, M.D.**, University of Massachusetts, Worcester

**RICHARD M. STEINGART, M.D.**, Memorial Sloan Kettering Cancer Center, New York

**PAUL D. THOMPSON, M.D.**, Hartford (Conn.) Hospital

**CHRISTOPHER J. WHITE, M.D.**, Oschner Clinic Foundation, New Orleans

**ROBERTA WILLIAMS, M.D.**, University of Southern California, Los Angeles