Table of Contents

Guest Editor for this issue:

R. James White, MD, PhD
Assistant Professor of Medicine,
Pharmacology & Physiology
Division of Pulmonary and
Critical Care Medicine
University of Rochester
Rochester, New York

Publisher
Pulmonary Hypertension Association
Carl Hicks, *Board Chair*
Rino Aldrighetti, *President*
Sherrie Borden, *Vice President, Medical and Patient Education*

Publishing Staff
Managing Editor
Deborah L. McBride
McBride Strategic Services
mcbridedeb@aol.com
Design Director
Michael McClain

PHA Office
Pulmonary Hypertension Association
801 Roeder Road., Ste 400
Silver Spring, MD 20910
301-565-3004, 301-565-3994 (fax)
www.PHAssociation.org

Advances in Pulmonary Hypertension is circulated to cardiologists, pulmonologists, rheumatologists and other selected physicians by the Pulmonary Hypertension Association. The contents of the articles are independently determined by the Editor and the Editorial Advisory Board.

Cover Image
A new day is dawning in the treatment of pulmonary arterial hypertension as new therapeutic approaches become available. These advancements are captured visually in Max Hayslette's painting "Tuscan Sunrise." Copyright © Grand Image, Ltd.

Guest Editor's Memo

A New Day for PAH

When the editorial board first considered an issue devoted to recent clinical trial results, clinicians had 6 FDA approved drugs to treat pulmonary arterial hypertension (PAH). We now have 7, and it seems conceivable that we might have an 8th before the end of 2009. With collaborative, international efforts, the pace of progress has quickened in the last 5 years, and indeed, a "New Day is Dawning" on treatment options for our patients.

In this issue, Bob Schilz and I wanted to provide an authoritative update on recent clinical trials and to highlight therapies that have "graduated" from bench science to bedside investigation. An author on the pivotal epoprostenol report, David Langleben has a long perspective and remains committed to bench research on mechanisms of vascular dysfunction in PAH. His article highlights Phases I and II trial data that have been reported only in abstract form at international meetings in the last 2 years. He also invites readers to consider an important question about whether our current therapies address fundamental disease mechanisms. I think readers will especially appreciate the figure illustrating how cicletanine, riociguat, and phospho-diesterase inhibitors are related in the nitric oxide-cyclic GMP signaling pathway.

Murali Chakinala's information-packed article summarizes key data from recently published or presented combination trials including PACES (adding sildenafil), TRIUMPH (adding inhaled treprostinil), and PHIRST (adding tadalafil). A useful table in the paper shows trends in the baseline characteristics of patients over the last decade, and his thoughtful analysis on endpoints highlights the limitations of our current approach in drug development and invites us to "Raise the bar" for future investigations.

(continued on bottom of page 39)

Editor's Memo

Starting with this issue of *Advances in Pulmonary Hypertension*, I am delighted to assume the editor-in-chief position. I am extremely grateful to Ron Oudiz for his productive tenure and his guidance through the process of creating and producing a quality journal. The feedback we have received during Ron's time in charge has been almost uniformly glowing, a testament to his calm leadership. I will do my best to maintain the quality of the journal and provide similar (although possibly less calm) guidance.

The mission of *Advances* has always been to provide, for practicing physicians, cutting edge updates on all aspects of pulmonary hypertension (PH). The journal has, we hope, been accessible and understandable to the diverse readers, including nurses, pharmacists, internists, rheumatologists, pulmonologists, and cardiologists. We have, thus, avoided including primary, original research papers or articles with too narrow a focus.

The overall tenor of *Advances* will continue, unchanged under my editorship. However, I am excited to introduce several new features that we believe will enhance the variety and accessibility of the journal. These 4 new sections will debut in the Summer 2009 issue:

Article Reviews (Section Editors: Drs Todd Bull and Francisco Soto): Brief summaries of recently published papers related to pulmonary vascular disease.

Pulmonary Hypertension Resource Network Corner (Section Editor: Glenna Traiger, RN, MSN): Topics of particular interest to allied health personnel involved in PH, such as nutrition, insurance issues, etc…

Ask the Expert (Section Editor: Dr Myung Park) We will solicit questions related to any

(continued on bottom of page 5)

Advances in Pulmonary Hypertension Author Guidelines 2009

Scope of Manuscripts

Advances in Pulmonary Hypertension considers the following types of manuscripts for publication:

- Reviews that summarize and synthesize peer-reviewed literature to date on relevant topics in a scholarly fashion and format
- Letters to the Editor
- Clinical Case Studies

Manuscript Submission

Authors are required to submit their manuscripts in an electronic format, preferably by email to the Editor-in-Chief, Richard Channick, MD, rchannick@ucsd.edu. Please provide manuscripts in a word processing program. Images should be submitted electronically as well.

All material reproduced from previously published, copyrighted material should contain a full credit line acknowledging the original source. Authors are responsible for obtaining permission to reproduce such material.

Contact Information: List all authors, including mailing address, titles and affiliations, phone, fax, and email. Please note corresponding author.

Peer Review and Editing: Manuscripts will be peer reviewed. Accepted manuscripts will be edited for clarity, spelling, punctuation, grammar, and consistency with American Medical Association (AMA) style.

Manuscript Preparation

Length: Full-length manuscripts should not exceed 4,000 words, including references. Please limit the reference list to 50 citations. Manuscripts should be accompanied by figures and/or tables. Generally, 4 to 5 figures and 2 to 3 tables are preferred for each manuscript. Please include a brief description to accompany these items, as well as a key for all abbreviated words.

Spacing: One space after commas and periods. Manuscripts should be double spaced. Manuscripts should not contain an abstract but an introduction is recommended.

References: All submissions should include numbered references that are referred to in the text by superscripts and that conform to AMA style. Example: Lewczuk J, Piszko P, Jagas J, et al. Prognostic factors in medically treated patients with chronic pulmonary embolism. *Chest.* 2001;119:818-823.

Copyright: Manuscripts and accompanying material are accepted for exclusive publication in *Advances in Pulmonary Hypertension*. None of the contents may be reproduced without permission of the Pulmonary Hypertension Association. To request permission, please contact Donica Merhazion, PHA Associate Director of Medical Services, 240-485-0744 or Donica@phassociation.org

Editor's Memo

(continued from page 2)

aspect of pulmonary vascular disease. The questions will be addressed by an assigned expert and the answers published, as space allows. (*See page 48 for details on how to be involved with this new section*.)

Clinical Trials Update (Section Editors: Drs Fernando Torres and Deborah Levine): A rundown of ongoing clinical trials, top line results, and planned trials.

In this current issue of *Advances*, Drs Jim White and Bob Schilz have tackled the area of new therapeutics. Although we already have several effective pulmonary arterial hypertension (PAH) therapies, the field of PAH treatment continues to move forward rapidly. New therapeutic targets and new ways to give existing therapies are being studied. With more therapies on the market, however, the feasibility and ethics of randomized controlled trials has changed. These important issues have been addressed in a Roundtable discussion that I hope you will find as lively as I did!

Richard N. Channick, MD
Editor-in-Chief