

In This Edition

- 9th Annual Scientific Meeting
- New Investigator and Nursing Research Awards Presented
- 2005 HFSA Research Fellowship Awards Announced
- Developments in Gene and Cell Therapy Presented to Clinicians
- Heart Failure Disease Management Programs Discussed from Varying Perspectives
- Benefits and Cost-Effectiveness of Population Screening
- Symposium Looks at Clinical Trials for Devices
- 2006 HFSA Comprehensive Heart Failure Guideline
- Patient Education Modules Complete
- The Jury Acquits the Stethoscope in Court Session
- Remodeling and Disease Management among the Topics Discussed in the Recent and Late Breaking Clinical Trial Session
- Debates on Nesiritide and Registries Spark Lively Exchanges

Heart Failure Society News

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9th Annual Scientific Meeting

HFSA president Gary S. Francis welcomed attendees to HFSA's 9th Annual Scientific Meeting, September 18-21, 2005, at the Boca Raton Resort & Club, Boca Raton, FL. The Society is becoming recognized as the "voice of heart failure," Dr. Francis said, and it is involved in many initiatives, including more involvement with governmental agencies. HFSA research fellowships have been an outstanding success and are helping the Society meet one of its primary goals – that of training young people to become academic researchers in heart failure. The Nursing Committee has completed a series of patient education modules, and new guidelines on heart failure are scheduled for on-line publication concurrently with Heart Failure Awareness Week in February, 2006.



President Gary S. Francis opens 9th Annual Scientific Meeting

Dr. Francis also announced a \$10,000 HFSA donation to support medical teams working on hurricane recovery in New Orleans. He also extended his thanks and appreciation to Drs. Stephen Gottlieb and Douglas Mann (2005 Scientific Meeting Co-chairs) and the program committee for putting together a superb program which features sessions of interest for the diverse group of attendees at this scientific meeting.

Opening Session Focuses on Ethical Dilemmas in Research

Recent controversies about medical research, cardiac devices and conflicts of

continued on page 2

New Investigator and Nursing Research Awards Presented

Five finalists were selected from the abstract submissions received to present their research in three HFSA award sessions at the 2005 annual scientific meeting: Jay N. Cohn New Investigator Award in Basic Science, Jay N. Cohn New Investigator Award and the Nursing Research Award.

The Judges all commented on the difficulty of selecting winners based on the high quality of the work submitted for these award competitions. Winners are chosen based on scientific merit, manner of presentation, and the effectiveness of the discussion.

All finalists receive a cash prize and complimentary registration for the annual meeting. The Jay N. Cohn New Investigator awards are supported by an educational grant from Novartis Corporation.

The 2005 top awards were as follows:

Jay N. Cohn New Investigator Award: Basic Science

- An Interferon Independent Innate Defense Mechanism Against Virus Infection with the Cardiac Myocyte: A Role for gp130 Signaling
Toshitaka Yajima, UCSD, San Diego, CA

Jay N. Cohn New Investigator Award: Clinical/Physiology

- Transcriptional Regulation in the Failing Human Heart: Genomic Analysis Validates Murine Models and Suggests Unanticipated Role of FOX Factors
Thomas P. Cappola, University of Pennsylvania, Philadelphia, PA

Nursing Research Award

- Depressive Symptoms are Associated with Self-Reported but Not Objective Sleep Characteristics in Patients With Stable Heart Failure
Nancy S. Redeker, University of Medicine and Dentistry, Newark, NJ

Opening Session Focuses on Ethical Dilemmas in Research

continued from page 1

interest provided the backdrop for opening session of the 2005 Annual Scientific Meeting, a critical look at ethical issues in medical research. A medical ethicist; an expert in healthcare law; and an editor at a well respected major medical journal participated in the session moderated by Jay N. Cohn, Minneapolis, MN, and Marvin A. Konstam, Boston, MA.

Changing Priorities in Clinical Trials

There is more than a perception that clinical research is in crisis, said Art Caplan, Pittsburgh, PA, in his talk, "Is it Time to Shift Clinical Trials from Efficacy to Effectiveness?" Caplan, the Emmanuel and Robert Hart Professor of Bioethics, Chair of the Department of Medical Ethics, and Director of the Center for Bioethics at the University of Pennsylvania, noted that the pharmaceutical and device industries and governmental regulatory agencies have been embroiled in questions about suppressing data and conflicts of interest. The pharmaceutical industry now has a lower public rating than managed care and the oil industry. "You have to really work to get there," he said.



Putting an end to pharmaceutical marketing and cutting the financial ties between industry and academia are neither realistic nor desirable solutions, said Caplan "These discussions are masking discussions about harder and deeper questions" about the goals of clinical trials.

There is a need to move away from the current gold standard of using randomized, placebo controlled trials to study the efficacy of a particular treatment. Such trials use carefully screened patient populations who are closely monitored and do not necessarily reflect the realities of the everyday practice of medicine. It's time to design trials to demonstrate effectiveness in the real world with diverse patient populations. There is a need for comparative trials to show a new treatment is better – not just better than a placebo. Such emphasis will divert



Drs. Arthur Kaplan and Marvin Konstam at the Opening Session

investment from "me-too" and "copycat" drugs to more productive agents.

Finally, there is a need to rethink the question of how much a patient will risk in return for increased quality of life. The model of "mega trials" and "blockbuster drugs" is going to go away. It's time to move clinical research into the 21st century, Caplan said in closing.

How Market and Regulatory Incentives Shape Clinical Research

We want to believe that medical research is driven by intellectual curiosity and that changes in the practice of medicine are shaped by the results of basic clinical research, said M. Gregg Bloche, Baltimore, MD, a physician, law professor at Georgetown University, visiting fellow at the Brookings Institution, and professor at the Bloomberg School of Public Health at Johns Hopkins University. We also want to believe that conflicts of interest with industry can be actively managed through mandated disclosure and preserving the right to publish. However, Dr. Bloche described the way in which marketing and regulatory considerations inevitably influence trial design.

Dr. Bloche also criticized the FDA's role as a "passive umpire" and the willingness of academic medicine to collaborate with industry "research geared to commercial needs."

He proposed a number of solutions to the excessive impact of commercial interests on medical research and education, including a sliding scale of patent protection based on the degree of innovation, conditional regulatory approval based on follow-up research, measures to promote comparative research and research on orphan drugs, an end to industry-sponsored CME courses, and limits on prepublication review of papers by commercial sponsors.

What Ethical Dilemmas Can Journals Confront?

Christine Laine, Philadelphia, PA, senior deputy editor, *Annals of Internal Medicine* and Clinical Associate Professor of Medicine at Jefferson College of Medicine, addressed the question of what journal editors can do to overcome ethical problems in clinical research.

"Readers want to know and need to know who did what when reading a study," Dr. Laine said. The practice of "gift" authorship should be ended. Ghost authors should be disclosed. "Don't put your name on work whose validity you aren't prepared to defend," said Dr. Laine, citing the example of a physician listed as an author on a paper, who later admitted that he never saw the data and only offered advice on the industry-authored paper.



Christine Laine, MD, MPH

Laine said conflicts of interest are pervasive. They can be financial, professional, or personal, among others. "We can not pretend these conflicts are not there." Journals should ask specifically about potential conflicts and disclose them.

Future Annual Scientific Meeting Dates

2006: September 10-13, Seattle, WA

2007: September 16-19, Washington, DC

2008: September 21-24, Toronto, ONT CA

2009: September 13-16, Boston, MA

2010: September 12-15, San Diego, CA

2005 HFSA Research Fellowship Awards Announced

In 2003 the HFSA established a research fellowship award program to help develop clinical investigators in the field of heart failure. The fellowship program is open to all individuals who hold a doctoral degree in medicine, osteopathy or nursing. For detailed information please visit the hfsa.org web site.

The recipients of the 2005 HFSA Research Fellows awards are:

- A double-blind randomized, placebo-controlled single-center study to assess the impact of statins on the autonomic nervous system and cardiac structure/function in non-ischemic heart failure
PI: **Tamara Horwich, MD** (UCLA; sponsor: Gregg Fonarow, MD)
- Effects of chronic sildenafil citrate therapy on exercise tolerance, hemodynamics and serum proteomic profiles in patients with HF
PI: Gregory Lewis, MD (Massachusetts General; sponsor: Marc Semigran, MD)
- HMG CoA reductase inhibition and inflammation, oxidative stress and vascular stiffness in heart failure
PI: **Sunil Matiwala, MD** (Boston University; sponsor: Wilson Colucci, MD)
- Beta-adrenergic receptor kinase expression in HF patients treated with cardiac resynchronization therapy
PI: **Amit Mittal, MD** (Thomas Jefferson University; Sponsor: Walter Koch, PhD)

This program has been made possible through the generous contributions of AstraZeneca, GlaxoSmithKline, The Guidant Foundation, Medtronic Inc. and Scios Inc.

Heart Failure Society
of America

2006 HFSA RESEARCH FELLOWSHIPS

The purpose of the research fellowship is to develop clinician-investigators in the field of heart failure.

Eligibility

The full-year fellowship is designed for individuals seeking specialty education and research training in the area of heart failure. Strong preference will be given to research involving patients or patient-derived materials. Candidates who have a doctoral degree in medicine, osteopathy, or nursing may apply.

Applications available on-line November, 2005
2006 Research Fellowship Application
Receipt Deadline: Monday, February 6, 2006

www.hfsa.org

Developments in Gene and Cell Therapy Presented to Clinicians

Developments in gene and cell therapy and possible applications to clinical practice were discussed in the Fundamentals of Basic Science for Clinicians session moderated by Arthur M. Feldman, Philadelphia, PA, and Douglas L. Mann, Houston, TX.

Gene Therapy: From New Vectors to State-of-the-Art Applications

The promise of gene therapy lost some of its luster in the wake of a patient death and complications in other patients, but the promise remains, said Kirk U Knowlton, San Diego, CA. Currently, there are more than 1000 clinical trials involving human gene therapy underway. Seventy percent are cancer-related.

Dr. Knowlton reviewed the advantages and challenges involved in using non-viral and viral vectors for gene therapy as well as novel vectors for gene therapy. The ideal vector would be easily administered, give a high level of gene expression once in the tissue of interest, and be non-toxic. Viral vectors are very efficient, but there have been problems with immunogenicity, cytotoxicity, and malignancy. Adeno-associated viruses have been the most promising vector for transferring genes of interest in cardiology, Dr. Knowlton said.

Cell Therapy: Basic Potential Applications

W. Robb MacLellan, Los Angeles, CA, reviewed research on cell transplantation to treat heart failure using skeletal myoblasts and adult and embryonic stem cells. Transplantation of myoblasts

has resulted in improved left ventricular function post-MI in human clinical studies. However, skeletal myoblasts do not differentiate into cardiac myocytes, and do not couple electrically with myocytes, exposing patients to the risk of arrhythmias. Studies show that the use of myoblasts is feasible, but long-term efficacy data are needed.

Clinical trials have also been conducted using adult stem cells, but have not shown advantages over the use of myoblasts. Additionally, it takes more time to prepare stem cells. " Dr. MacLellan acknowledged that the optimal dose, timing, and delivery method for cell therapy remain unsolved.

Model Organisms to Study Heart Failure

Howard A. Rockman, Durham, NC, reported on the use of mice, zebra fish, and even drosophila (fruit flies) to identify novel and modifier genes and to validate candidate genes involved in cardiomyopathy. Flies have a far less complex genome than humans, and cardiac function can not be measured in their small, one-chambered heart, said Dr. Rockman. However, fly strains with defective delta-sarcoglycan genes have been developed and used to study cardiomyopathy.

The session represented a new approach to bridging the gap between science and practice and was very well received by the audience.

Heart Failure Disease Management Programs Discussed from Varying Perspectives

The benefits of disease management programs, quality issues, and cost effectiveness were among the topics discussed in a symposium moderated by Kathleen A. Dracup, San Francisco, CA, and Mary N. Walsh, Indianapolis, IN.

Quality Issues

Disease management programs in heart failure reduce hospital admissions and mortality, said Edward P. Havranek, Denver, CO. They may also reduce cost and improve patient quality of life. There is a growing consensus and momentum for heart failure disease management programs, he said.

The elements involved in a successful disease management program include established relationships with trained nurses, including remote access; patient education; and coordinated care. The inclusion of a heart failure specialist and a sophisticated IT infrastructure can also be valuable factors.

"Why shouldn't disease management be available for everyone," Dr. Havranek asked in closing.

Cost Effectiveness

Gregory L. Freeman, San Antonio, TX, took issue with the prevailing wisdom supporting disease management programs. A study involving 53,000 health-related encounters and 18-month follow-up

showed that disease management alone had no impact on heart failure-related hospitalization, Dr. Freeman said. Although disease management helped patients feel a little better, it did not save money.

More work is needed to make disease management cost effective, said Dr. Freeman. Patients who need disease management are the sickest. The best approach is to tailor disease management to the severity of the disease.

Benefits of Disease Management

Nancy Houston-Miller, Stanford, CA, stressed that disease management programs for heart failure resulted in improved survival and reduced hospitalization and that the programs were either cost saving or cost neutral.

However, she said the outcomes of disease management programs were dependent on factors such as population characteristics, age, co-morbidities, the methods of intervention used in a particular program and the intensity of the intervention. The ability to influence physicians to prescribe and titrate the appropriate drugs and to influence emergency room referral practices also impacted disease management programs. The impact of psycho-social factors, such as depression and social support systems, is not clear at this time.

There are many unanswered questions about what makes some disease management programs successful than others. However, programs tailored to individual patient circumstances appear to be more successful and cost-effective.



Doug Mann and Steve Gottlieb challenging a speaker during a scientific session.

What Does the Future Hold for Disease Management?

John C. Pilotte, Baltimore, MD, a research analyst with the Centers for Medicare and Medicaid Services (CMS), spoke on the demonstration disease management programs underway or under development at institutions across the country. Chronically ill patients with diabetes, heart failure, and chronic obstructive pulmonary disease account for the majority of patients enrolled in these programs. It is clear from these programs that "we need to have incentives to provide the right care at the right time and in the right place," Pilotte said.

Benefits and Cost-Effectiveness of Population Screening

The rationale and strategies for cost-effective population screening for heart failure and cardiac dysfunction were the subjects of a symposium held on the final day of the 2005 Annual Scientific Meeting. Thomas S. Rector, Minneapolis, MN, and W.H. Wilson Tang, Cleveland, OH, moderated the session. Thomas Jue-Fuu Wang, Boston, MA; Paul A. Heidenreich, Palo Alto, CA; William S. Weintraub, Atlanta, GA; and Jay N. Cohn, Minneapolis, MN, presented.

Although the speakers agreed that screening can improve outcomes, cost-effectiveness was seen as a barrier. Prevalence is critical to deciding whom to screen, said Dr. Heidenreich. In a

population with a prevalence of at least one percent, a screening strategy using echocardiography and BNP is cost-effective, he said. The question is which populations to screen. Should it be people with ischemic heart disease, hypertension, or diabetes?

Dr. Wang agreed that echocardiography is a definitive test, but costly. In a population with low prevalence, a test with high specificity is needed to minimize false positives, he said.

Dr. Cohn reviewed the results of a screening program designed to identify cardiovascular risk factors early. Of the approximately 1,000 people screened, 33 percent were found to be at low risk

of cardiovascular disease, 36 percent were at modest risk; and 31 percent at highest risk. "We need to focus on the entire cardiovascular risk profile. Can we intervene earlier to prevent the development of cardiovascular disease," he asked.

Future Heart Failure Awareness Weeks

2006: February 12-18

2007: February 11-17

2008: February 10-16

2009: February 8-14

Symposium Looks at Clinical Trials for Devices

The challenges of designing clinical trials for devices used for heart failure management were the subject of a symposium including panelists from industry, government, and clinical practice. Uri Elkayam, Los Angeles, CA, and Dan Schaber, St. Paul, MN, served as moderators.

Overview

The subject of clinical trial design for devices is a difficult one, said Mariell L. Jessup, Philadelphia, PA. Designing trials for devices presents a different set of regulatory, scientific, and clinical issues than designing trials for drugs, she said.

Drug trials have moved to the concept of using large-scale randomized trials with mortality as an endpoint. Only all-cause mortality can be considered objective and unbiased. With devices, however, it is hard to design a blinded trial, and large-scale trials with mortality as an endpoint are cost prohibitive. When non-randomized trials are considered, even doing a systematic literature search of device trials can be difficult.

Device trials have moved to the concept of using hospitalization as an endpoint. But it is not easy to sort out which hospitalizations are for heart failure. It is also difficult to determine modest effects or unpredictable harm with the use of small-scale trials. Determining which patients can benefit most from devices is another challenge. Devices cannot easily be studied in the sickest patients.

Industry Point of View

Spencer Kubo, St. Paul, MN, Senior Vice President and Global Medical Director of Acorn Cardiovascular, Inc., said that the existing paradigms for clinical trial design do not always fit

devices. We need agreement on endpoints. We need more than mortality and symptom measurement. Survival is an insensitive endpoint for devices designed to slow disease progression. The use of symptoms as an endpoint has some advantages in that functional status can be measured fairly easily in all patients. However, they are hard to measure over the long-term and pose difficulties in an unblinded trial.

Dr. Kubo suggested the use of surrogates, such as LV structure, as endpoints in device trials. Such a surrogate, which could be used to determine whether a device slowed the progression of heart failure, would provide an objective and clinically accepted measure.

Regulatory Point of View

Bram D. Zuckerman, Rockville, MD, Director of the FDA Division of Cardiovascular Device Evaluation, said the device industry has to pay closer attention to clinical trial design. "We hear a lot of reasons from companies why they do not want to randomize," Dr. Zuckerman said. But randomization is the gold standard.

While Dr. Zuckerman agreed that more discussion was needed on optimum endpoints, he also said, "We will not dismiss morbidity and mortality. We also expect long-term follow-up." The issues of bias in unblinded trials and the administration of optimal medical therapy must also be addressed.

Dr. Zuckerman advised companies to ensure that the same protocol and rigorous follow-up standards are used when using data from outside of the U.S. Post-market follow-up will become increasingly important, as will physician training.


2006 HFSA Comprehensive Heart Failure Guideline

The 2006 HFSA Comprehensive Heart Failure Practice Guideline will become available in February, 2006. Its release is scheduled to coincide with Heart Failure Awareness Week, February 12-18. The full text version will be published as an electronic publication in the Journal of Cardiac Failure, and posted on the HFSA website. The executive summary will appear in the 2006 January/February regular issue of the Journal.

As its name suggests, the guideline is comprehensive. It includes an expansion and updating of the 1999 HFSA Guidelines for the Management of Patients with Heart Failure Caused by Left Ventricular Systolic Dysfunction - Pharmacological Approaches. In addition, it has sections on devices, surgical options, prevention, asymptomatic patients with LV dysfunction, heart failure with preserved LVEF, heart failure in special populations, acute heart failure, disease

management, non-pharmacologic management, and health care maintenance in heart failure.

The guideline, under the direction of Kirkwood Adams (Guideline Committee chair 1998-2004) and JoAnn Lindenfeld (Current Chair, Guideline Committee) is the result of work by a dedicated group of individuals committed to bringing forward a document that gives current recommendations for comprehensive care of heart failure patients.



**National
HEART
failure
AWARENESS
Week**

February 12 – 18, 2006

www.abouthf.org

Patient Education Modules Completed

The last two modules designed for patients, their families, and individuals at risk were completed in 2005. All modules have been extremely popular with professionals and patients alike. The modules are available as printed booklets, or they can be downloaded from the abouthf.org website.

The last modules to be completed in the series are Module 9, Advance Care Planning, and Module 11, How to Evaluate Claims of New Heart Failure Treatments and Cures. Both represent challenging topics. Advance care planning is something most people avoid, so this easy-to-read booklet should be extremely valuable. It includes sections on advance care directive, do-not-resuscitate order, living will, palliative care, and other important issues.

With all the information about heart failure treatments bombarding patients and families from television, the internet, and other sources, the module on evaluating claims should prove especially useful.

These modules are not intended to replace regular medical care. Patients should see their doctor or nurse regularly. The information is provided in these modules to help patients work better with their doctor or nurse.

The patient education modules were developed by the HFSA Nursing Committee under the leadership of Debra K. Moser, Lexington, KY. Members of the Nursing Committee who contributed to their development include Nancy M. Albert, Cleveland, OH; Susan Ammon, San Francisco, CA; Susan J. Pressler, Indianapolis, IN; Sandra B. Dunbar, Atlanta, GA; Mariann Piano, Chicago, IL; Barbara J. Riegel, Philadelphia, PA; and Susan Ziesche, Minneapolis, MN.



All materials produced by the HFSA can be viewed on the abouthf.org web site. Individuals can order a complimentary copy online. Multiple copies are available for purchase at a modest cost. Information for ordering and the order form are posted on the abouthf.org web site. Please allow 3-5 weeks for delivery.

The Jury Acquits the Stethoscope in Court Session

In a "trial" notable for its mirth and pointed exchanges, the stethoscope was found not guilty in the Court Is in Session debate on Monday, September 19. The trial marked the first time in three years that the "jury" (session attendees) was able to reach a clear and decisive verdict. Previous trials had been declared mistrials.

Dr. Konstam returned to reprise his role as judge in the case, exchanging his sport coat for black judicial garb. Sanjiv Kaul, Portland, OR, led the prosecution with spirited arguments against the stethoscope, while Mihai Gheorghide, Chicago, IL, assumed the mantle as the chief of the defense team. Howard J. Eisen, Philadelphia, PA, and Alan S. Maisel, San Diego, CA, were called on to testify as expert witnesses for the prosecution, while Gregg C. Fonarow, Los Angeles, CA, and Carl V. Leier, Columbus, OH, served as defense experts.

Although jurors in the end agreed on the continued value of the stethoscope when conducting physical exams, the classic icon of medicine did not escape unscathed.



Judge Marvin A. Konstam presiding over Court is in Session

"The physical exam skills at U.S. medical schools, including those of mentors and teachers, are close to zero," said Dr. Kaul in his opening argument outlining his case for abolishing the stethoscope. He went on to present data from the United Kingdom showing that doctors there had only slightly higher abilities to use a stethoscope to accurately identify heart sounds. "The efficacy of the stethoscope is pathetic," he concluded. He attributed this lack of stethoscope skills in western countries to the lack of exposure to patients with congenital heart defects.

Dr. Gheorghide vigorously defended the stethoscope by stressing the importance of the physical exam in diagnosing heart failure and the role of the stethoscope in

that exam. "Not only is the stethoscope on trial, but also the physical exam." "Heart failure is primarily a bedside diagnosis," he said, quoting from a textbook written by Gary S. Francis. Use of a stethoscope without tests is preferable to doing tests without a stethoscope in the diagnosis and management of heart failure.

The prosecution, however, continued its attack on the stethoscope using humor as well as data. It is hard to hear S3 and S4 heart sounds, said Dr. Maisel. We miss S3 gallop four out of five times, he said. "I always thought of the stethoscope as the only icon we have left," said Dr. Maisel, "pointing out that even dermatologists and pathologists carry one. "I think it needs to go on the shelf. I have mine with my phonograph and record albums" he said. Maisel instead suggested that echo, catheterization, and implantable hemodynamic monitors were better diagnostic tools than the stethoscope.

Although the jurors greatly appreciated the prosecution's arguments, in the end they remained reluctant to vote to abolish use of the stethoscope and delivered a verdict of not guilty.

Remodeling and Disease Management among the Topics Discussed in the Recent and Late Breaking Clinical Trial Session

In what has become a tradition, recent and late breaking clinical trials were discussed on the final morning of the Annual Scientific Meeting. The session moderated by Barry H. Greenberg, San Diego, CA, and Milton Packer, Dallas, TX featured presentations on three trials investigating the impact of drugs on remodeling, a trial studying two types of home monitoring, and a trial of an oral inotrope. For a complete copy of the abstract showing methods and results, see the December 2005 issue of the *Journal of Cardiac Failure*.

REVERT – Metoprolol in Patients with Asymptomatic Systolic Dysfunction

In a presentation on the Metoprolol Reverses LV Remodeling in Patients with Asymptomatic Systolic Dysfunction (REVERT) trial, Wilson S. Colucci, Boston, MA, reported that metoprolol provides a beneficial dose-related effect in reversing left ventricular (LV) remodeling in patients with asymptomatic systolic dysfunction.

The study concluded that metoprolol exerts a beneficial anti-remodeling effect in patients with asymptomatic systolic dysfunction. The positive effects appear dose related, and the study supports the addition of metoprolol to the treatment regimen of these patients.

A-HeFT Sub-Study: Remodeling Effects of Drug Combination

Jay N. Cohn, Minneapolis, MN, reported that a sub-study of A-HeFT (African-American Heart Failure Trial) shows that a fixed-dose combination of isosorbide dinitrate and hydralazine inhibits LV remodeling in self-described African Americans with severe HF already receiving standard heart failure drugs.

The previously reported A-HeFT study itself showed that combination treatment with isosorbide dinitrate and hydralazine significantly reduces mortality and hospitalization and improves quality of life in the study population of 1050 patients.

The study concluded that the beneficial effects of treatment with isosorbide dinitrate and hydralazine on mortality and morbidity in the study population are accompanied by significant reductions in LV chamber diameter, increases in EF, and reductions in BNP consistent with improvements in LV structure and function.



John Teerlink (San Francisco) pleading his case in a scientific session

METEOR Study: Effects of Oral Tolvaptan on LV Dilatation and Function

On behalf of the trial investigators for METEOR (Multicenter, Randomized, Double-Blind, Placebo-Controlled, Efficacy Study of the Effects of Oral Tolvaptan on LV Dilatation and Function in Patients with HF and LV Systolic Dysfunction), James E. Udelson, Boston, MA, presented data showing that oral tolvaptan resulted in no significant improvement or deterioration of LV end diastolic volume index or LVEF in patients with mild-moderate HF and an LVEF < 30% already receiving standard medical therapy.

The objective of the study was to assess the effects of one year of therapy with tolvaptan, a vasopressin receptor antagonist, on measures of remodeling and to assess safety and tolerability of the drug. The on-going, phase III EVEREST trial will provide data on the effects of tolvaptan on HF morbidity and mortality.

Span-CHF II – Two Approaches to Heart Failure Disease Management

Andrew R. Weintraub, Boston, MA, presented the results of the Specialized Primary and Networked Care in Heart Failure (Span-CHF) II trial which compared the addition of automated home monitoring to an effective HF disease management program (Span-CHF I) featuring a multidisciplinary HF team, telephonic patient monitoring, patient education, medication optimization, and medication compliance teaching.

The prospective, randomized, multi-center study found that the addition of automated home monitoring to disease management resulted in a relative risk reduction of 72% in HF hospitalization and 63% in all-cardiovascular hospitalizations.

ESSENTIAL: Oral Enoximone in Advanced HF

In his presentation on the Studies of Oral Enoximone Therapy in Advanced Heart Failure (ESSENTIAL) study, Westminster, CO, Eric Eichorn reported that treatment with oral enoximone did not result in significant differences on any of the three pre-specified end points: time to all-cause mortality or cardiovascular hospitalization, distance in the six-minute walk test at six months, or global patient self-assessment at six months. It did show that oral enoximone was safe.



Debates on Nesiritide and Registries Spark Lively Exchanges

Two debates were highlighted at the 2005 Annual Scientific Meeting: (1) the safety and effectiveness of nesiritide and (2) the value of patient registries. Barry M. Massie, San Francisco, CA, and Bertram Pitt, Ann Arbor, MI, served as moderators.

Debate 1: Is Nesiritide Safe and Effective in Acute Heart Failure?

Clyde W. Yancy, Dallas, TX, began the nesiritide debate by arguing that nesiritide does not increase mortality and is safe and effective in the treatment of acute decompensated heart failure. The size of the dose matters. At the doses in use, the change in creatinine does not matter. Nesiritide should be used for on-label indications. We will progress by further study of the data.

Dr. Sackner-Bernstein, Dobbs Ferry, NY argued that Nesiritide remains unproven. He noted that observational data can be misleading and that the benefits of nesiritide are not significantly different than placebo. The hemodynamic benefits observed in preclinical studies were achieved with much higher doses. Yet even low-dose nesiritide can not be considered safe. Nesiritide was approved prematurely.



Chris O'Connor defending his position at the Debate Session

The next step is to withdraw the drug, Dr. Sackner-Bernstein concluded.

The issue regarding safety and efficacy of Nesiritide to some extent will be resolved by the FUSION II study.

Debate 2: Are Registries Really Needed?

The types of patients included in registries are very different from those enrolled in clinical trials and can provide valuable information on the natural history of a disease state, said Christopher M. O'Connor, Durham, NC. "We need registries, because of the inadequacy of randomized clinical trials." Registries can

help answer questions that can not be addressed in trials. We just have to be more careful about the data generated in registries.

Registries collect data to confirm what we already know, argued Milton Packer, Dallas, TX. They result in no new findings and do not change the way we manage patients. Industry sponsors registries to enhance utilization of their products. They collect the data, but what they really care about is whether you use their drug, said Dr. Packer.

It is hard to reach valid conclusions from registries due to measurement bias and the lack of standardization. "The sheer size of some registries makes you think they are important. For example, one registry includes 100,000 people, but what if you make the same mistake 100,000 times," he asked.

Each debater in both debates presented an argument followed by a rebuttal and summary for each position taken.

As with all presentations, the opinions expressed in the debates are those of the presenters and do not necessarily reflect the opinion or position of the HFSA.

Mark Your Calendars

January, 2006:

Registration opens for the 10th Annual Scientific Meeting

Monday, February 6, 2006:

2006 Research Fellowship Application Receipt Deadline

Saturday, February 11, 2006:

Primary Care Symposium, Houston, TX

February 12 – 18, 2006:

Heart Failure Awareness Week

Monday, April 10, 2006:

Abstract Submission Deadline for the 10th Annual Scientific Meeting

Monday, May 8, 2006:

Hyde Park Submission Deadline for the 10th Annual Scientific Meeting

Friday, May 26, 2006:

Late Breaking Clinical Trials Submission Deadline for the 10th Annual Scientific Meeting

September 10 – 13, 2006:

10th Annual Scientific Meeting

Heart Failure Society
of America

10TH ANNUAL SCIENTIFIC MEETING

September 10 - 13, 2006



Washington State Convention & Trade Center
Seattle, Washington

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