

PHA Scientific Sessions Provide a Great Window Into Treatment Breakthroughs While Inspiring Physicians and Patients Alike



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This roundtable discussion, reviewing the proceedings from the Pulmonary Hypertension Association's Eighth International PH Conference and Scientific Sessions in Houston in 2008, was moderated by Karen Fagan, MD, Chief, Division of Pulmonary and Critical Care Medicine, University of South Alabama, Mobile, Alabama. It included Todd Bull, MD, Associate Professor of Medicine, Division of Pulmonary Sciences and Critical Care Medicine, University of Colorado Health Sciences Center, Aurora, Colorado; Ivan F. McMurtry, PhD, Professor, Department of Pharmacology, University of South Alabama School of Medicine, Mobile, Alabama; and Omar A. Minai, MD, Staff Physician in the Department of Pulmonary, Allergy, and Critical Care Medicine and the Lung Transplant Center at the Cleveland Clinic, Cleveland, Ohio.

Dr Fagan: The first thing I wanted to do is to thank you for attending the Scientific Sessions. As you know, 2008 was the third Scientific Sessions that were held in conjunction with the PHA (Pulmonary Hypertension Association) International Conference meeting. The ultimate goal of the Sessions was to provide the medical professionals who volunteer their time during the medically led sessions and the patient and family oriented sessions an opportunity to hear state-of-the-art scientific speakers, and interact with their peers before they're put to work in the International Conference. I am a little biased because I chaired the 2008 Scientific Sessions committee; I think it went well.

I think we were successful in bringing together a diverse crowd and I'd like to hear what your impression was of what you heard and enjoyed about the meeting.

Dr Minai: The PHA International Conference provides a great opportunity for physicians to hear lectures on cutting edge research, to network with other physicians who may be doing similar work, and to discuss ideas that later blossom into novel studies. To me this is a unique meeting in that it is the only one in our field

that brings patients and physicians together. This experience serves to "humanize" the disease for professionals who focus on basic science research and don't have the opportunity to meet patients. In addition, this meeting provides a unique opportunity to the greater pulmonary hypertension (PH) community to recognize the achievements and breakthroughs in this field and to recognize and honor people who give of their precious time and other resources to the cause of PH. The meeting allows us to truly see the breadth of the true impact of PH on patients, their caregivers, and families.

Dr Bull: The Scientific Sessions have become a part of the Conference that I enjoy thoroughly. The first meeting I attended was one of the earlier forays into this and I think it has progressed beautifully to date. The most recent Scientific Session was fantastic and

built beautifully on the previous sessions. A key strength is bringing speakers outside the PH community to the meeting to talk about new ideas and directions to consider in PH. For those of us in the PH community, we have a general understanding of what everyone's working on and of course are excited to hear about new directions they're taking with their own work. But, this meeting allows the opportunity to stimulate new thoughts and new directions.

This year I particularly enjoyed the pharmacogenomics discussion. Where the field of pharmacogenomics has arisen from was fascinating not just from a historical perspective but also where we may take it in the years to come. It really tied in well to some of the work that Ray Benza has been working on, and where we'd like to take this from a PH standpoint. Quite frankly it transcends more than just PH and the Dick Weinshilboum approach was great. I also really enjoyed Hunter Champion's talk on the molecular basis of right ventricular (RV) dysfunction.

Dr Minai: Hunter Champion's talk about the molecular basis of RV dysfunction really stood out to me. Even though PH is a disease of the pulmonary vasculature,



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the real cause of most morbidity and mortality in our patients is RV (dys)function. I thought Hunter did a great job of delivering the message while making it understandable and interesting to the general audience which included not only basic scientists but clinicians and patients as well.

Dr Fagan: I also thought that the pharmacogenomics talk by Dr Weinshilboum was great. He was able to show how pharmacogenomics doesn't just have the promise of impacting therapy in a wide range of diseases, he actually showed concrete examples of the role of this technology in patient care today. I don't know how far into the future we are until we have this type of personalized medicine in PH, but it certainly raised the hope that maybe through pharmacogenomics we'll understand a little bit more about which patients should be on which initial therapies and which patients may not respond even to combination treatments. I think that the hopefulness and the potential promise of this line of investigation is totally exciting.

Dr Bull: I agree, and I think all of us tell the patient after we complete their evaluation, we will pick a therapy. A patient will ask, "Is this going to work?" And our answer is, "We're going to have to wait and see." And we can look at the odds and tell you what we think is going to happen. Of course at this juncture really honestly we don't know. We've all had patients who have significant improvements with a phosphodiesterase inhibitor, for example, and others it does not seem to touch. There's got to be something to that. We're just not smart enough yet to know who will benefit from what drug up front. In the future, pharmacogenomics may give us some insight. It is my experience that when I consider therapy, especially oral therapy, that my recommendations are more based on toxicity than efficacy, ie, this treatment potentially could cause this problem as opposed to this, may really help. Pharmacogenomics may help in both areas to identify persons with expected benefit as well as persons with higher likelihood of toxicity.

Dr Minai: Karen and Todd, I completely agree. When we look at clinical trials of oral medications in PH, we find that several medications have very similar overall efficacy in a cluster of patients and we tend to focus on the mean or average response rate. However, within each study population there are patients who respond extremely well, ie, much better than average and those that don't respond at all to the same medication. Currently, we lack a reliable method of identifying these subgroups with any degree of accuracy. The patient who responds poorly to one medication may respond very well to another medication. Pharmacogenomics holds the promise of helping us match the patient with the right drug up front. That would be a great benefit to physicians in choosing therapy and to patients in this rapidly progressing disease.

Dr Fagan: To be able to sit in the clinic with a patient and to have on a piece of paper an assessment about what they're most likely to respond to is a powerful thought. It might limit the "wait and see" period after starting a treatment to see if it has any effect. It also might limit the possibility of losing ground.

Dr McMurtry: Not only was Dr Weinshilboum's talk on pharmacogenomics up to date and educational; it was also very entertaining. He is a personable and skillful lecturer, and anyone who gets the chance to hear him speak should definitely do so.

Dr Fagan: I also thought Dale Able's lecture on metabolic determinants of a cardiac myocyte performance was really intriguing. His work has illuminated the mechanisms of cardiac dysfunction associated with the metabolic syndrome. I was really impressed with his ability to make the incredible complex metabolic signaling pathways approachable to clinicians and to people who are nonmetabolic researchers. It really reminded me that our patients have comorbidities that they're bringing to the table as well. So it's not just what their genes are, it's not just whether they have scleroderma or whether they've got congenital heart disease, but they bring all sorts of other things to the table that can directly impact their overall health and PH treatment. Obviously one of those are

people who have metabolic syndrome related to obesity. There are several articles that are beginning to look more carefully at the effects of metabolism on cardiac performance. It certainly spurred me to think about RV performance in a different way.

Dr Minai: Several studies have established a clear link between the metabolic syndrome and cardiovascular disease. Despite recent studies, this link remains tantalizingly close but as yet unproven in PH. Studies looking at the association between PH and obesity and sleep apnea have reported mixed results. This is an area that requires further study.

Dr Bull: We tend to hone in on the pulmonary vascular bed and the RV response to pressure overload but our patients live in the real world and have all the diseases of the real world and how these things interact in a more sophisticated manner is important to consider. So I thought that was a great lecture as well.

Dr Fagan: The meeting gave us a chance to also look at clinical and translational research opportunities. I know that you, Todd, participated in some research at these scientific sessions and I was hoping you could tell us how you did it, some of the difficulties in doing research away from your own primary site and what you thought about how the meeting contributes to your research.

Dr Bull: This is actually my second time doing research at the PHA conference. In Minneapolis I was working on the same project. It is only possible through the generosity of PHA and most importantly, the patients who attend the PHA meeting. My current work is looking at gene expression profiling and peripheral blood cells and people with PH. My hypothesis is that we can gain information about PH by looking at immune-related cells from the blood. Part of the difficulty has always been that the lung tissue, where PH is manifest, is not readily accessible in our patients. So we need to find surrogate tissue to examine. We're looking at the blood cells as a surrogate marker of the disease and have had some success using this approach. This success has been in large part due to the PHA conference research. Greg Elliot really started



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performing research at the PHA conference at the very first meeting at Stone Mountain in Georgia. He realized then that in this rare disease a meeting where patients from all over the world come together would be a great opportunity to learn more about the disease and hopefully help improve how we diagnose and treat PH. In a one-day period at the PHA meeting, I can get a year's worth of samples; it would take us that long to collect the same amount in our clinic and we have a pretty busy clinic. For my work, we obtain a blood sample, isolate the peripheral blood mononuclear cell component, and then look at gene expression. One factor is that after we draw the blood, we need to arrange to have a laboratory nearby available to us.

Dr Fagan: How do you do that?

Dr Bull: Through networking. At the University of Minnesota I got in touch with the chief of pulmonary who then put me in contact with a principal investigator in a lab that had the materials and equipment that I needed. We had to get IRB approval for these studies at the University of Minnesota. We did the same thing in Houston. As soon as we were done drawing blood at the conference we rushed it over to the university where we processed samples, finishing at about 2 o'clock in the morning. It was an onerous process, but we got great samples that we hope will translate into great data. The next phase is to collect the clinical information from the study subjects.

The most important part of this is really the patients' participation. The patients have really been fantastic; they've lined up at lunchtime, in between their sessions, and are willing to donate blood. It is an amazing thing to see and we are very appreciative of their help.

I think that at this most recent meeting there were at least 6 to 7 groups doing research. There almost wasn't enough room for us all in the research room. I think when we do this again we'll have to get more space. It's been working remarkably well and there's potential to make it even better. Greg Elliot has been the driving force behind this so we owe him a lot.

Dr Fagan: The focus of the PHA in terms of its advocacy for patients includes research. One great thing that I have noticed is that more and more non-clinician researchers are coming to the meeting, especially the Scientific Sessions. Ivan, you gave an excellent review of the current animal models of PH that are used in research. You are also a great example of non-clinicians who attend this meeting, many of whom are seeing patients with PH for the first time. Ivan, perhaps you could share your thoughts about the conference as a PhD scientist who's done PH research for 40 years with limited patient contact.

Dr McMurtry: Attending and participating in the PHA meeting was an incredible experience for me. I've presented results of my research on animal models of PH at numerous scientific meetings over the past 40 years. This was the first time I had PH patients, and their family members, personally thank me for my contributions to their treatment. I actually got a sense of what it must be

like to be a rock star, since I had patients giving me hugs and requesting to have their pictures taken with me! It was a heartwarming and motivating experience, and I would recommend to any PhD scientist working in the field of PH to attend the meeting and experience first hand the appreciation and hope of PH patients.

Dr Fagan: I was very fortunate to see some of the interactions that you had with the patients, Ivan. They really did acknowledge and appreciate your work. It was as meaningful to them as it was for you. It highlights that we really need to encourage non-clinician scientists to come to this conference even more. As a clinician I get a lot of appreciation from my patients all the time. I think people who are not in the clinic but are in the research lab don't get to see the end result from the work they're doing and how much their efforts have impacted on the lives of patients.



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Dr Minai: That is part of PHA's strength that it brings together clinicians and researchers, physicians and patients, physicians from various medical fields including pulmonology, cardiology, and rheumatology for the sole purpose of improving care and outcomes in patients with PH. Since this is the largest PH conference in the world and draws physicians and patients from around the globe, this forum provides a unique opportunity for research that would not be possible at any single center. The PHA is committed to patient advocacy and research and therapeutic advancement in the field of PH and this

conference is a true reflection of that commitment on several levels.

Dr Bull: I think that's a great point. I always leave the PHA meeting inspired. When you come to the PHA and you see the determination and energy, you're reminded about why it is you do what you do, why you've selected this as your career. More people should have this experience

Dr Fagan: I think many of us come to the PHA because we already have not just a professional but a personal commitment to the patients of the organization. We really need to get to our colleagues and say, yes this is a different meeting than you'll ever go to, but it is very worthwhile. Here's the opportunity to see some very high quality state-of-the-art science but these other days you have the chance to interact and see what your work has done for these patients. I think it's important to encourage people to come and see that.

Dr Fagan: I would like to thank you all for your participation in this discussion. It is remarkable to look back and see how far the PH community has come and the Scientific Sessions and International Conference are just a small part of that. I know that the Scientific Sessions will remain an important part of the meeting and am delighted that Dr. Ivan Robbins from Vanderbilt University will be taking the lead role in the Scientific Sessions for 2010. Hopefully we can encourage new participants in the conference in the future. ■