ISHLT2022 Roving Reporters – Reports from Pulmonary Vascular Disease (PAH & CTEPH) (PVD)

- **Wednesday, 27 April, 2022**
  - Featured Abstract 1: Impact of Sex on Outcome After Pulmonary Endarterectomy (PEA) for Chronic Thromboembolic Pulmonary Hypertension (CTEPH)
  - SYMPOSIUM SESSION 05: Controversial Debates in Pulmonary Hypertension
  - ORAL SESSION 12: Bench to Bedside: CTEPH and PAH
  - ORAL SESSION 19: Risky Business in Pulmonary Hypertension
- **Thursday, 28 April, 2022**
  - SYMPOSIUM SESSION 33: Between a Rock and a Hard Place: Pulmonary Vascular Disease and Solid Organ Transplantation
  - ORAL SESSION 22: Philip K. Caves Award Candidate Presentations
- **Friday, 29 April, 2022**
  - SUNRISE 11: Rookies and Sages: The International Pulmonary Hypertension Challenge
  - SYMPOSIUM SESSION 47: Updates in Pulmonary Arterial Hypertension (PAH) Research: What is On the Horizon?
- **Saturday, 30 April, 2022**
  - SYMPOSIUM SESSION 71: Transformative Care: Literature Year in Review

Thank you to all of our ISHLT2022 Roving Reporters.

ADVANCED HEART FAILURE AND TRANSPLANTATION (AHFTX)

Anju Bhardwaj, MD, University of Texas / McGovern Medical School / Memorial Hermann Hospital, Houston, TX, USA
Rachna Kataria, MD, Massachusetts General Hospital, Boston, MA, USA
Brian Wayda, MD, Stanford University School of Medicine, Stanford, CA, USA

ADVANCED LUNG FAILURE AND TRANSPLANTATION (ALFTX)

Prangthip Charoenpong, MD, MPH, LSU Health Science Center Shreveport, Shreveport, LA, USA
Grant Turner, MD, MHA, UCLA, Los Angeles, CA, USA

MECHANICAL CIRCULATORY SUPPORT (MCS)

David Bearl, MD, MA, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN, USA
Varinder Randhawa, MD, PhD, Cleveland Clinic / University of Toronto, Toronto, ON, Canada

PULMONARY VASCULAR DISEASE (PVD)

Nicholas Kolaitis, MD, MAS, UCSF, San Francisco, CA, USA

Featured Abstract 1 at Plenary Session 1: Impact of Sex on Outcome After Pulmonary Endarterectomy (PEA) for Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Presenter: ***Justin C.y. Chan, MD****, University Health Network, Toronto, ON Canada*

The Opening Plenary session started off the meeting, and pulmonary vascular disease was the first abstract reported at ISHLT 2022! In this presentation **Justin Chan, MD**, (University Health Network, Toronto, ON Canada), reported on sex differences in outcomes of patients undergoing pulmonary endarterectomy (PEA) for a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH).

Dr. Chan's report consisted of a retrospective study of 401 patients who underwent PEA at the University Health Network in Toronto, Canada. They compared the 203 female patients to the 198 male patients and assessed the outcomes of survival, functional class, and need for post-operative vasodilator therapy. Interestingly, there were sex differences in clinical outcomes, with female patients having less improvement in the pulmonary vascular resistance (final pulmonary vascular resistance after PEA, 437 Dynes·s·cm^{-5} vs 324 Dynes·s·cm^{-5}in males, $p<0.01$). Survival was similar at 10 years, but female patients had a worse functional class, increased symptom burden, and increased need for vasodilator therapy. In addition to their clinical outcomes assessment, there were five patients who underwent single cell RNA sequencing (3 males and 2 females), with an overexpression of TGF- β1 in endothelial cells in females.

In a robust discussion following the abstract presentation, **David Jenkins, FRCS**,(Papworth Hospital, Cambridge UK) asked Dr. Chan to postulate on why female patients fared poorly as compared to their male counterparts. Ultimately, it was felt that female patients were more susceptible to having segmental and subsegmental disease, and less central disease, potentially explaining the decreased response to PEA surgery.

VIEW FULL ABSTRACT

– Summary by Nicholas Kolaitis, MD, MAS

SESSION 05: Controversial Debates in Pulmonary Hypertension

The first **symposium** in the pulmonary vascular disease interdisciplinary network was a series of three controversial debates related to pulmonary hypertension.

The first debate was whether invasive hemodynamics were essential for the risk stratification of patients with pulmonary arterial hypertension (PAH). In this debate, **Sophia Airhart, MD**, (Providence Heart and Vascular Institute, Portland, OR USA), made the argument that patients with pulmonary hypertension need the gold standard measurement of pulmonary pressures, an invasive right heart catheterization when doing risk assessments. Her argument focused on how clinician gestalt does not adequately discriminate risk in patients with pulmonary arterial hypertension (PAH). Further, she argued that the various risk prediction algorithms in PAH utilize invasive hemodynamics in their assessment.

In rebuttal, **Marc A. Simon, MD**, (UCSF Medical Center, San Francisco, CA USA) argued that the use of various imaging modalities, including echocardiogram and cardiac magnetic resonance imaging, provide sufficient evidence to discriminate risk, and that we should be more judicious in whom we put through a right heart catheterization. At the end of the debate the audience in the room sided with the need for invasive hemodynamics in risk assessment.

The second debate was focused on whether patients with interstitial lung disease associated pulmonary arterial hypertension (ILD-PH) should be treated with approved PAH therapies. This classic debate in pulmonary hypertension was given renewed vigor this year given the results of a clinical trial (INCREASE trial) assessing the use of inhaled treprostinil in patients with ILD-PH (Waxman et al. *NEJM* 2021).

The debate started off with a vigorous defense of the use of vasodilators in PH-ILD by **Colin Church, MD, PhD**, (Golden Jubilee Hospital, Glasgow, Scotland UK) who argued that the results of the INCREASE trial, which showed improvements in 6MWD, BNP, and time to clinical worsening, justified the use of inhaled treprostinil in select patients with PH-ILD.

On the converse side, **Helen Whitford, MBBS, FRACP**, (Alfred Hospital, Melbourne, Australia) argued that patients with PH-ILD should not be treated with inhaled treprostinil because there was no long-term outcome data, there is no mortality data, and that the outcome of improvement in 6MWD was modest for a drug with a high burden of use. Further, she cautioned against the use of vasodilators in the population given that it may push back listing for transplantation, and then patients will be sicker at the time of transplantation. At the end of the debate the audience was mostly split, with a slight increase in votes for the use of vasodilators in patients with PH-ILD.

The final debate was on whether patients with symptomatic chronic thromboembolic disease (CTED) should be treated with pulmonary endarterectomy (PEA) or balloon pulmonary angioplasty. In the pro-treatment group, **David Jenkins, FRCS**, (Papworth Hospital, Cambridge, UK) argued in favor of surgery given that CTED can be associated with exercise intolerance,

progression to CTEPH, and that patients with CTED can have a significant burden of disease. He displayed the specimens of various CTEPH and CTED patients after PEA and challenged his opponent to pick out those with CTED and not CTEPH.

In opposition was **Isabelle Opitz, MD**, (University Hospital Zurich, Zurich, Switzerland), who argued that the lack of randomized controlled trial data warranted caution, and that PEA for CTED surgery often results in only mild improvements in 6MWD amongst patients with a fairly low symptom burden. As such, these patients should not undergo major cardiac surgery. At the end of the debate, the audience agreed that CTED should be treated.

– Summary by Nicholas Kolaitis, MD, MAS

DEBATE: Invasive Hemodynamics are Essential for Risk Stratification in PAH (PRO)
Sophia Airhart, MD, Providence Heart and Vascular Institute, Portland, OR USA

DEBATE: Invasive Hemodynamics are Essential for Risk Stratification in PAH (CON)
Marc A. Simon, MD, UCSF Medical Center, San Francisco, CA USA

DEBATE: PH Due to Interstitial Lung Disease (ILD) Should Be Treated with PAH Approved Therapies (PRO)
Colin Church, PhD, Golden Jubilee Hospital, Glasgow UK

DEBATE: PH Due to Interstitial Lung Disease (ILD) Should Be Treated with PAH Approved Therapies (CON)
Helen M. Whitford, MBBS, FRACP, Alfred Hospital, Melbourne, Australia

DEBATE: Symptomatic Chronic Thromboembolic Disease (CTED) Should Be Treated with PEA or BPA (PRO)
David P. Jenkins, FRCS, Papworth Hospital, Cambridge UK

DEBATE: Symptomatic Chronic Thromboembolic Disease (CTED) Should Be Treated with PEA or BPA (CON)
Isabelle Opitz, MD, University Hospital Zurich, Zurich, Switzerland

VIEW SESSION DETAILS

SESSION 12: Bench to Bedside: CTEPH and PAH

The first oral session was focused on translating research from the bench to the bedside in the pulmonary vascular disease space.

In a pre-recorded talk entitled "***Distinct Endothelial Cell Populations Characterize the Pulmonary Endarterectomy Specimen in Chronic Thromboembolic Pulmonary Hypertension***," **H.S. Jeffrey Man, MD, PhD**, (University of Toronto, Toronto, ON Canada) reported on the use of human pulmonary endarterectomy (PEA) specimens in five patients with chronic thromboembolic pulmonary hypertension (CTEPH). In this study, the authors performed single-cell RNA sequencing in five CTEPH patients and three controls. They performed a cluster analysis of transcriptional profiles and determined that four of the twenty clusters displayed markers of endothelial cell phenotypes in the organized thrombotic material. The composition of the endothelial cell clusters was different between CTEPH and control, with CTEPH clusters having increased expression of TGFβ1 and P-selectin.

In a live talk entitled "***Left Ventricular Diastolic Dysfunction in Chronic Thromboembolic Pulmonary Hypertension***," **Dorothée Brunet, MD, MSc**, (Marie Lannelongue Hospital, Le Plessis Robinson, France) reported on a pig model of CTEPH. In this study, six piglets underwent weekly embolization of the right lower lobe with a tissue glue, and were compared to six sham-operated animals. The authors assessed left ventricular diastolic function and left ventricular fibrosis at six weeks, showing that there was increased end-diastolic pressure, increased ventricular stiffness, and an increased fibrosis score in the left ventricle of the CTEPH piglets. They also looked at echocardiograms in 102 human patients before and after PEA, finding mild LV diastolic dysfunction in CTEPH patients after PEA.

In a live talk entitled "***Balloon Pulmonary Angioplasty Results in Anatomically Operable CTEPH Patients***," **Justin Issard, MD, MSc**, (Marie Lannelongue Hospital, Le Plessis Robinson, France) reported on a retrospective review of CTEPH patients treated with balloon pulmonary angioplasty (BPA) in patients with CTEPH. Notably, they had 36 patients with proximal disease who could not undergo PEA surgery, either due to comorbidities (27 of 36) or due to patient refusal (9 of 36). Patients that couldn't undergo PEA due to co-morbidities did improve in functional class and hemodynamics after PEA, however, those who refused surgery did not improve in functional class or in hemodynamics. To the knowledge of the audience, this was the first report on BPA for proximal disease in CTEPH.

In his live talk entitled "***Pirfenidon Prevents Experimental Flow-Associated PAH by Suppression of the NLRP3 Inflammasome***," **Emmanouil Mavrogiannis, BSc**, (University Medical Center Groningen, Groningen, Netherlands) reported on the use of pirfenidone in a rat model for neointimal PAH induced by monocrotaline and aortocaval shunt. The authors noted that high levels of IL-1β and IL-18 are seen in animal models of PAH, and hypothesized that using pirfenidone may suppress inflammasome activation and led to less vascular disease. The rats who were exposed to pirfenidone had decreased inflammasome activation. In addition, rats treated with pirfenidone

had reduced mean pulmonary artery pressures.

In a live talk entitled "***Impact of Initial Therapeutic Strategy on Long-Term Outcomes in Pulmonary Arterial Hypertension: An Analysis of the PHSANZ Registry***," **Katherine Kearney, MBBS**, (St Vincents Hospital, Darlinghurst, Australia) reported on the impact of monotherapy and early double combination therapy using the PHSANZ registry. They defined early combination therapy as the use of two or more PAH-specific vasodilators within three months of therapy. There was no difference in transplant-free survival amongst the two groups, however, 6MWD improved greater in the combination therapy group.

VIEW SESSION DETAILS

– Summary by Nicholas Kolaitis, MD, MAS

SESSION 19: Risky Business in Pulmonary Hypertension

This oral session was focused on risk stratification in pulmonary arterial hypertension (PAH). Given that many of the presenters were unable to present in person, the moderators **Mardi Gomberg-Maitland, MD, MSc**, (GW Heart and Vascular Institute, Washington, DC USA) and **Marc Simon, MD**, (UCSF Medical Center, San Francisco, CA USA) took on a key role, and led a robust discussion on the various abstracts.

In a live talk entitled "***Imaging of Improved Right Ventricular Coupling, Risk Status and Survival in Pulmonary Arterial Hypertension***," **Roberto Badagliacca, MD, PhD**, (Sapienza University of Rome, Rome, Italy) described the benefit of using the ratio of TAPSE/PASP in risk stratification. The authors assessed 677 patients retrospectively and noted an increase in TAPSE/PASP ratio as pulmonary vascular resistance decreased in patients with pulmonary arterial hypertension (PAH). Lower risk patients by REVEAL or ERS/ESC were more likely to have a TAPSE/PASP ⩾ 0.35 mm/mmHg than those at intermediate or high risk scores.

In a pre-recorded talk entitled "***Risk Assessment in Pulmonary Arterial Hypertension (PAH): Insights from the Inspire Study with LIQ861***," **Sandeep Sahay, MD**, (Houston Methodist Hospital, Houston, TX USA) reported on the impact of dry powder treprostinil (LIQ861) in risk stratification. In this Phase 3, open-label study, patients who went on LIQ861 were either transitioned from Tyvaso to LIQ861 or were prostacyclin naïve. At baseline, 51% of patients met two or three low risk variables by the French non-invasive criteria. By month eight there were 76% of patients who met two or three low risk criteria. The primary driver of improvement was in the prostacyclin naïve patients.

In a pre-recorded talk entitled "***Clinical Variables in Predicting Survival and Hospitalization for Pulmonary Arterial Hypertension Using Harmonized Data***," **Zilu Liu**, PhD student at The Ohio State University, Columbus, OH USA, harmonized data from seven adult PAH trials: GRIPHON, SERAPHIN, EARLY, COMPASS-2, COMPASS-3, MAESTRO and TRANSIT-1. They then conducted a Cox proportional hazard analysis to study the association between time to death at 30 days and the pulmonary artery pulsatility index (PAPi) and the aortic pulsatility index (API). PAPi was associated with death at 30 days (HR 0.84, 95%CI: 0.73-0.96). In an exciting moment after the presentation, **Ray Benza, MD**, (The Ohio State University, Columbus, OH USA) told the audience that Zilu Liu had successfully defended her PhD thesis that morning back in Ohio, and was now Dr. Liu. **Congratulations, Dr. Liu!**

In a pre-recorded talk entitled "***Atrial Fibrillation- A Risk Factor for In-Hospital Mortality of Patient with Pulmonary Hypertension***," **Sandra Chaparro, MD**, (MCVI Baptist Health South, Miami, FL USA) reported on the association between atrial fibrillation and adverse outcomes in PAH using a retrospective analysis of the National Inpatient Sample data. The authors found that patients hospitalized with PAH and atrial fibrillation were at an increased risk of mortality, had longer hospital lengths of stay, and had higher costs per hospitalization than when hospitalized without atrial fibrillation.

In a live talk entitled "***Risk Stratification in Patients with Pulmonary Arterial Hypertension and Candidates for Lung or Heart-Lung Transplantation***," **Laurent Savale, MD, PhD**, (CHU Bicêtre, Le Kremlin Bicetre, France) reported on a retrospective application of the ERS/ESC risk stratification using the invasive French and COMPERA methods, as well as the REVEAL Lite score to patients with PAH who underwent lung transplantation or heart-lung transplantation. They reported 106 patients with PAH who were listed for transplant. Patients who were high risk by the various risk assessment methods suffered from increased mortality after transplant, arguing for earlier listing in these patients.

The final talk of the session was pre-recorded by **Georg Hansmann, MD, PhD**, (Hannover Medical School, Hannover, Germany). This talk, entitled "***Validation of the New Pediatric Pulmonary Hypertension Risk Score by Cardiac Magnetic Resonance Imaging and Speckle Tracking Echocardiography. The European Pediatric Pulmonary Vascular Disease Network (EPPVDN)***," explored the validation of a new pulmonary hypertension risk score in pediatric patients using cardiac MRI and speckle tracking echocardiogram, through the European Pediatric Pulmonary Vascular Disease Network (EPPVDN). The authors demonstrated correlations between cardiac MRI and echo parameters with the EPPVDN risk score.

VIEW SESSION DETAILS

– Summary by Nicholas Kolaitis, MD, MAS

SESSION 33: Between a Rock and a Hard Place: Pulmonary Vascular Disease and Solid Organ Transplantation

In this very exciting **symposium**, the Pulmonary Vascular Disease Interdisciplinary Network explored the complex challenges related to solid-organ transplantation in patients with pulmonary vascular disease. The session was a true interdisciplinary experience, with the speakers representing three different continents, and three different subspecialties (pulmonary, cardiology, surgery).

In the first talk, ***Take a Deep Breath: Pulmonary Hypertension and Lung Transplantation***, **Nicholas Kolaitis, MD**, University of California San Francisco in San Francisco, CA USA, explored the complexities of lung transplantation in patients with pulmonary arterial hypertension (PAH). This included a discussion of how the lung allocation score impacts allocation for patients with PAH in the United States, the new referral and listing criteria based on the 2021 ISHLT Consensus Document on the Selection of Lung Transplant Recipients (Leard et al. JHLT 2021), and a discussion of the perioperative risk that patients with PAH face, including primary graft dysfunction and left ventricular dysfunction.

The next talk, ***Getting to the "Heart" of the Matter: PH and Heart Transplantation***, given by **Peter Bergin, MBBS, FRACP**, of Alfred Hospital in Melbourne, Australia, was a hemodynamic tour de force. There was a robust discussion of the hemodynamics necessary to successful pursue heart transplantation including a conversation of how to do a vasodilator challenge in this population. Further discussion included the importance of the transpulmonary gradient, as well as how right heart failure can accompany left heart failure. Finally, there was in important point that PDE5i do not work in late right heart failure for patients on mechanical circulatory support.

The last of the live talks, ***Gut Feeling: Pulmonary Hypertension and Liver Transplantation***, given by **Sonja Bartolome, MD**, of the University of Texas Southwestern Medical Center in Dallas, TX USA, described the complexities of liver transplantation in patients with portopulmonary hypertension. The focus of the discussion was on hemodynamic cutoffs necessary to pursue safe liver transplantation, given the increased risk of hemodynamic collapse in the surgery. In general, recommendations were to try and achieve a mean pulmonary artery pressure <35 mmHg via vasodilator therapy. However, there was a very interesting discussion in the audience, sparked by Dr. Bartolome, about how we should approach patients with a mPAP >35 mmHg who only have a mild elevation in the pulmonary vascular resistance.

The last talk of the session, ***More is Better: Pulmonary Hypertension and Multi-Organ Transplantation***, was given by **Thirugnanasambandan Sunder, MD**, of Apollo Hospitals in Chennai, India. In this talk. Dr. Sunder provided a thorough literature review on the complexities of various types of multi-organ transplantation. The end of the talk was a special treat as he described the current state of organ transplantation in India, with a focus on the work Apollo hospitals is doing, including a thorough description of a patient with situs inversus who required a combined heart

and lung transplantation.

VIEW SESSION DETAILS

– Summary by Nicholas Kolaitis, MD, MAS

SESSION 22: Philip K. Caves Award Candidate Presentations

The field of pulmonary vascular disease was well represented in the **Philip K. Caves Award Session**, as there were two talks related to pulmonary arterial hypertension.

The first of the pulmonary vascular disease talks, ***Transcriptomic Analysis of Right Ventricular Adaptation and Failure in a Novel Ovine Model of Pulmonary Hypertension***, by **Rei Ukita, PhD**, of Vanderbilt University Medical Center in Nashville, TN USA, described a novel sheep animal model of PAH. In this model, the investigators performed pulmonary artery banding on sheep over multiple weeks. These sheep then developed right ventricular failure and were placed onto mechanical circulatory support, to elucidate the impact on salvage mechanical circulatory support on gene expression. Investigators described the impact of this model on four sheep, three that underwent mechanical circulatory support for 3-6 hours, and one that died before they could be initiated on mechanical circulatory support. The authors then did RNAseq and identified differential expression of 358 genes between the pre-PAH and post-PAH tissues, with higher myosin, motilin, TGF-B, and BMPR2. They then assess the sheep that died due to the maladapted right ventricle before salvage mechanical circulatory support, and found that this sheep had reduced expression of metabolic genes and in genes responsible for fatty acid oxidation.

The second PVD-related talk in this session was pre-recorded and assessed ***Sex Differences in Endothelial-to-Mesenchymal Transition in Chronic Thromboembolic Pulmonary Hypertension***. This was presented by **Usman Asghar, MD**, of Toronto General Hospital Respiratory Institute in Toronto, ON Canada. As previously noted in the opening plenary, the Toronto group demonstrated sex differences in CTEPH outcomes. Dr. Asghar assessed endarterectomy specimens from ten male and ten female patients. These were stained for markers of endothelial-to-mesenchymal transition (endothelin-1, TGF-ß1, vimentin, and alpha smooth muscle actin). Female patients had higher total expression of vimentin and TGF- ß1. Segmental sections from female patients also had higher expression of vimentin, TGF- ß1, ET-A and alpha smooth muscle actin than male segmental sections. Taken together, the authors argued that the endothelial-to-mesenchymal transition markers may explain some of the poorer outcomes they found in female patients with CTEPH.

Additionally, congratulations to **Aditi Nayak, MD**, of Emory University in Atlanta, GA USA for winning the Caves award. Her presentation on the application of machine learning to the ISHLT Mechanically Assisted Circulatory Support database identified novel pathophysiological phenotypes of right heart failure—you can **read the abstract here**.

VIEW SESSION DETAILS

– Summary by Nicholas Kolaitis, MD, MAS

SUNRISE 11: Rookies and Sages: The International Pulmonary Hypertension Challenge

Friday morning started off with a **special Sunrise Session**, the international pulmonary hypertension challenge. In this session, early career members presented complex cases, and they were followed by an interesting discussion from renowned experts.

In the first case, **Julie Wacker, MD**, of University Hospital of Geneva in Switzerland, described a complex case of a 13 year old male who had echo evidence of PH and a PVR of 4.3 wood units on right heart catheterization. CT angiogram showed a large portocaval shunt, and liver biopsy returned with hypoplasia of the intrahepatic portal venous branches. **Erika Rosenzweig, MD**, of Columbia University Medical Center in New York, NY USA, led the discussion, commenting on the challenges we face in diagnosis. In particular, she made the point that idiopathic pulmonary arterial hypertension (PAH) is a diagnosis of exclusion. Dr. Rosenzweig reminded us of the necessity of abdominal imaging in the workup of PAH. In this case the patient had portopulmonary hypertension from a congential portocaval shunt, which responded to ligation and vasodilator therapy. We were also reminded by Dr. Rosenzweig that we need to monitor portal pressures with temporary balloon occlusion before ligation of the portocaval shunt.

In the next case, **Julien Guihaire, MD, PhD**, of Marie Lannelongue Hospital in Paris, described a complex case of a 57-year-old female who had chronic thromboembolic pulmonary hypertension resulting from antiphospholipid syndrome. The patient underwent pulmonary endarterectomy, but still had a PVR of 9.8 wood units, which persisted despite the addition of riociguat. This was followed by six sessions of balloon pulmonary angioplasty, finally leading to an improvement in the PVR to < 5 wood units. **Joanna Pepke-Zaba, MD**, of Royal Papworth Hospital, in Cambridge, UK, then proceeded to discuss the International CTEPH Association's new Global CTEPH Registry, and the outcomes in the registry, reminding us that with multimodal management we can achieve excellent survival, and improved functional class.

Following these two cases there was a pre-recorded case from **Sandeep Sahay, MD**, of Houston Methodist Hospital in Houston, TX USA, about telehealth and remote monitoring in patients with pulmonary arterial hypertension. He discussed a 43-year-old female with HIV-PAH who developed COVID-19 in July 2020, requiring oxygen at discharge. Unfortunately, she had persistent dyspnea, and a worsening of the echocardiogram. Repeat RHC was not allowed because of being persistently COVID-19 positive. The patient was then empirically started on parenteral prostacyclin. The case led to a nice discussion of risk assessment in PAH by **Raymond Benza, MD**, of The Ohio State University in Columbus, OH USA, where he highlighted the benefits and pitfalls of using telemedicine to treat and monitor disease progression in patients with PAH. He also introduced the concept of virtual physical exams through a remote device that captures respiratory and heart sounds, new apps which allow for a home six minute walk test, a home ultrasound, and a home BNP kit.

The final case was presented by **Nichole Sisserson, MMS, PA-C**, of the Inova Advanced Lung

Disease and Transplant Program, USA), and described as case of COVID-19 in a 49-year-old male with pulmonary arterial hypertension. The patient was unable to tolerate PO due to the infection so was switched to IV prostacyclin. Discussant **John Granton, MD**, of the University of Toronto, then described the complexities of managing COVID-19 in patients with pulmonary vascular disease including the options for treatment.

– Summary by Nicholas Kolaitis, MD, MAS

Case Study: Is This Really Idiopathic Pulmonary Arterial Hypertension?
Julie Wacker, MD, University Hospital of Geneva, Geneva, Switzerland

Expert Discussant
Erika B. Rosenzweig, MD, Columbia University Medical Center, New York, NY USA

Case Study: BPA for Residual Pulmonary Hypertension Post PEA for CTEPH
Julien Guihaire, MD, PhD, Marie Lannelongue Hospital, Le Plessis-Robinson, France

Expert Discussant
Joanna Pepke-Zaba, MD, Royal Papworth Hospital, Cambridge UK

Case Study: Telehealth and Remote Monitoring in Pulmonary Arterial Hypertension
Sandeep Sahay, MD, Houston Methodist Hospital, Houston, TX USA

Expert Discussant
Raymond L. Benza, MD, The Ohio State University, Columbus, OH USA

Cast Study: Pulmonary Arterial Hypertension and COVID-19
Nichole Sisserson, MMS, PA-C, Inova Advanced Lung Disease and Transplant Program, Falls Church, VA USA

Expert Discussant
John Granton, MD, University of Toronto, Toronto, ON Canada

VIEW SESSION DETAILS

SESSION 47: Updates in Pulmonary Arterial Hypertension (PAH) Research: What is On the Horizon?

The **final pulmonary vascular disease interdisciplinary network symposium** of the meeting was a wonderful look into the future of care for patients with pulmonary arterial hypertension.

The session started with two talks describing the impact of pulmonary hypertension at the extremes of life (in pediatric patients and in geriatric patients). Rolf Berger, MD, PhD, of University Medical Center in Gronigen, Netherlands, took on the complexities of caring for pulmonary hypertension in the pediatric population in his session. He described the unique nature of PH in infants and children, and how it differs from adults. He then described a Dutch cohort of around 3,000 pediatric patients with PAH, demonstrating that the minority had progressive disease. There was also a nice discussion of the pathogenesis of pulmonary hypertension in the context of bronchopulmonary dysplasia. **Hassan Alnuaimat, MD**, of the University of Florida in Gainesville, FL USA, took on the complexities of caring for elderly patients with pulmonary hypertension. He described age-related changes in hemodynamics, and compared various parameters in registries stratified by age. There was also a nice discussion of how older patients may not be able to tolerate as aggressive therapy as younger patients.

The talks then turned to novel imaging approaches in pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension (CTEPH). **Micheal McInnis, MD**, of Toronto General Hospital in Toronto, ON Canada described the novel tools to better assess pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension, including dual energy CT iodine maps, the use of a C-arm CT of the pulmonary arteries, and digital subtraction angiography in the diagnosis of CTEPH.

Maurice Beghetti, MD, of HUG, Children's University Hospital in Geneva, Switzerland then described the management of pulmonary arterial hypertension in children, and the surgical techniques used to make pulmonary to systemic shunts (Potts shunt). He also described the potential benefits of the shunt to decrease right ventricular afterload to improve RV-PA coupling and outcomes after the shunt. Dr. Beghetti then went on to describe the high risks associated with percutaneous Potts shunts. Finally, there was discussion of the optimal timing of Potts shunts, stating that it should be done before the patient has severe RV dysfunction.

The session then turned to clinical trials, and started off with **Jean-Luc Vachiery, MD**, of Erasme University Hospital in Brussels, who advocated for better clinical trial design with more clinically important outcomes. He described the review and recommendations from the 6th World Symposium on Pulmonary Hypertension. The paradigm shift of moving towards event driven trials, the use of patient reported outcomes in clinical trials, and the potential benefits of an adaptive study design.

Finally, the session ended with **Bradley Maron, MD**, of Brigham and Women's Hospital in Boston,

MA USA, who gave an overview of the novel treatment pathways in pulmonary arterial hypertension with a description of the current pipeline in PAH. There was a special focus on sotatercept, which aims to rebalance activin/GDF versus BMP signaling and a thorough description of the Phase 2 results. There was also a nice discussion of the phase 1 results of Bromodomain Containing Protein-4, and the potential of NEDD9, which is a mediator of platelet-endothelial adhesion.

– Summary by Nicholas Kolaitis, MD, MAS

Pulmonary Hypertension at the Extremes of Life (Pediatric)
Rolf Berger, MD, PhD, University Medical Center, Groningen, Netherlands

Pulmonary Hypertension at the Extremes of Life (Geriatric)
Hassan Alnuaimat, MD, University of Florida, Gainesville, FL USA

Novel Imaging Approaches in PAH and CTEPH
Micheal McInnis, MD, Toronto General Hospital, Toronto, ON Canada

Pulmonary to Systemic Shunts in PAH: Who, When, and How
Maurice Beghetti, MD, HUG, Children's University Hospital, Geneva, Switzerland

What the Future of Clinical Trials in PAH Should Be: Trial End Points, Design, and Treatment Strategies
Jean-Luc Vachiery, MD, Erasme University Hospital, Brussels, Belgium

Novel Treatment Pathways in PAH: What's in the Pipeline?
Bradley Maron, MD, Brigham and Women's Hospital, Boston, MA USA

VIEW SESSION DETAILS

SESSION 71: Transformative Care: Literature Year in Review

The **literature year in review** was very exciting for pulmonary vascular disease because of the results of three very exciting trials in pulmonary hypertension. **Edith Boyes, APN**, from Amita Health in Chicago, IL USA, presented, and **Christopher King, MD, FACP, FCCP**, of Inova Fairfax Hospital in Falls Church, VA USA discussed the three pivotal trials that resulted in the pulmonary vascular world since we last met in Orlando in 2019.

The first discussion centered on the results of the INCREASE Trial, which was a 16-week trial of inhaled prostacyclin (Treprostinil) in patients with WHO Group 3 pulmonary hypertension due to interstitial lung disease. Patients were randomized to either placebo or drug, and the outcome was six-minute walk distance. This was the first positive trial in WHO Group 3 PH! Patients had a 31-meter improvement in six-minute walk distance at 16 weeks with an improvement in NT-proBNP and time to clinical worsening.

The next trial discussed was the PULSAR Trial, which was a Phase 2, 24-week trial of sotatercept in patients with WHO Group 1 PAH. Sotatercept is a ligand trap that aims to rebalance activin/GDF versus BMP signaling. In the PULSAR study there was an improvement in pulmonary vascular resistance, six-minute walk distance, and NT-proBNP. This trial is very exciting for the future of PAH. While not discussed in this ISHLT session, the open label extension was recently presented at the American Thoracic Society meeting, and the drug was very well tolerated in the open label extension. Further, patients who crossed over from placebo to sotatercept caught up in terms of reduction in pulmonary vascular resistance!

The final trial discussed was the TRITON trial, which was a Phase 3 trial of upfront dual combination therapy with macitentan and tadalafil versus upfront combination triple therapy with selexipag, macitentan, and tadalafil. The trail did not show any improvement in pulmonary vascular resistance, six-minute walk distance, or NT-proBNP. However, there was a trend towards a reduced risk for disease progression. The discussion was interesting, centering on clinical trial design and implications for treatment.

– Summary by Nicholas Kolaitis, MD, MAS

Highlights of Advanced Heart Disease and Cardiac Transplantation
Asvin Ganapathi, MD, The Ohio State University Wexner Medical Center, Columbus, OH USA

Expert Discussant in Advanced Heart Disease and Cardiac Transplantation
Hermann Reichenspurner, MD, PhD, University Heart Centre Hamburg, Hamburg, Germany

Highlights of Advanced Lung Disease and Lung Transplantation
Erin Lowery, MD, University of Wisconsin-Madison, Madison, WI USA

Expert Discussant in Advanced Lung Disease and Transplantation
Allan R. Glanville, MBBS, MD, FRACP, St. Vincent's Hospital, Sydney, Australia

Highlights of Mechanical Circulatory Support
Jamila Kremer, MD, University Hospital Heidelberg, Heidelberg, Germany

Expert Discussant in Mechanical Circulatory Support
Stephan M. Ensminger, MD, DPhil, University of Lubeck, Lubeck, Germany

Highlights of Pulmonary Vascular Disease (PAH & CTEPH)
Edith Boyes, APN, Amita Health, Chicago, IL USA

Expert Discussant in Pulmonary Vascular Disease (PAH & CTEPH)
Christopher King, MD, FACP, FCCP, Inova Fairfax Hospital, Falls Church, VA USA

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