DRAFT

PVRI
Pulmonary Vascular Research Institute

13th Annual World Congress on PVD
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Scientific Programme

ADAPTATION TO HIGH ALTITUDE – MORE THAN EXPECTED

Target Audience: Basic, translational and clinical researchers and clinicians (adult and paediatrics) interested in the physiological adaptation of the pulmonary circulation to hypoxia, as well as the development of pulmonary vascular diseases.

Objectives: At the conclusion of this session, the participant will be able to:

- Understand the hypoxic response of the pulmonary circulation
- Recognize the role of ROS in the pulmonary circulation and their contribution to PAH progression
- Describe the clinical consequences of living in high altitude

This session will focus on hypoxic pulmonary vasoconstriction. Speakers will discuss the history of this common clinical finding and its relevance to human disease, provide important insight into the implications for inhabitants of high altitude and convey current understanding of the underlying molecular mechanisms that promote this clinical response.

Title

- Historical discovery of HPV and its physiological and pathophysiological importance
- Redox signaling in pulmonary circulation: from HPV to pulmonary hypertension
- Reactive oxygen species, flavonoids and the role of vitamin D deficiency in PH
- Mitochondria and oxygen sensing in pulmonary circulation
- Adaptation to high altitude
- Genetic adaptation to high altitude

BEST ABSTRACTS PRESENTATION FROM OUR TRAINEES

SYSTEMIC DISORDERS IN PAH

Target Audience : Basic, translational and clinical researchers and clinicians (adult and paediatrics) interested in the systemic nature and manifestations of pulmonary hypertension.

Objectives: At the conclusion of this session, the participant will be able to:

- Understand the manifestations pulmonary hypertension outside of the lungs
- Recognize the changing epidemiology of PAH, including the increasing prevalence comorbidities in PAH patients

PAH is increasingly recognized as a systemic disease. Insulin resistance, metabolic syndrome and skeletal muscle finding have all been recently described. This session will discuss how PAH may manifest as a systemic disease, the organ-specific findings, the potential impact of these findings and also highlight novel comorbidities in PAH.

Title

- Skeletal muscle molecular disorders in PAH and consequences on exercise intolerance
- Systemic manifestation in COPD-PH
- PVDOMICS
- Novel comorbidities in PAH patients

PRO AND CON DEBATE: TOP ISSUES AND CONTROVERSIES IN DIFFERENT GROUPS OF PH

Target Audience: Basic, translational and clinical researchers and clinicians (adult and paediatrics) interested in pulmonary vascular diseases occurring in the setting of left heart diseases, respiratory diseases and chronic thromboembolism.

Objectives: At the conclusion of this session, the participant will be able to:

- Recognize the similarities and differences in disease pathophysiology and phenotype between PAH and other types of pulmonary hypertension
- Understand current controversies regarding the pathophysiology PH of other etiologies (WHO groups 2–5)
- Acknowledge the urgent need for medical therapies in most types of pulmonary hypertension

A number of controversies exist regarding the pathophysiology, natural history, diagnosis, and treatment of in PH of other etiologies (WHO groups 2–5). In addition, limited progress has been made towards specific therapies for WHO groups 2-5. This session will address controversies, uncertainties and future Research in these groups of PH in pros and cons debate fashion.

Title

- Pulmonary vascular remodeling is an important driver of COPD (PRO)
- Pulmonary vascular remodeling is a consequence of COPD (CON)
- Targeting Metabolic syndrome is a strategy to treat PH associated with Left Heart Disease/ HFpEF (PRO)
- Targeting Metabolic syndrome is not a sufficient strategy to treat PH associated with Left Heart Disease/ HFpEF (CON)
- Defective angiogenesis is a major contributor of CTEPH (PRO)
- Defective angiogenesis is not a major contributor of CTEPH (CON)

EPIGENETICS - FROM RV FAILURE TO PULMONARY CIRCULATION: ANY THERAPEUTIC VALUES?

Target Audience: Basic, translational and clinical researchers and clinicians (adult and paediatrics) interested in pulmonary vascular disease and right heart failure.

Objectives: At the conclusion of this session, the participant will be able to:

- Understand of the role of epigenetic in pulmonary hypertension and the associated RV dysfunction
- Acknowledge the clinical impact of epigenetics in PAH
- Realize the challenges and opportunities in targeting epigenetics in future clinical trials

This session will address whether epigenetic therapies may play a prominent role in the future management of PH. Broad cellular, molecular and pre-clinical evidence suggests that epigenetic events are central to progression of PH. The study of this level of gene control has blossomed over the last years and is a critical link to our understanding of the PH and right heart failure.

Title

- LnRNAs and cardiovascular diseases
- 10 years of miRNAs research in PAH: any therapeutic values?
- Methylation acetylation disorders in PAH
- Methylation and miRNAs in RV failure

METABOLIC DISORDERS: TOMORROWS HEART FAILURE AND PAH THERAPEUTIC TARGETS ?

Target Audience: Basic, translational and clinical researchers and clinicians (adult and paediatrics) interested in pulmonary vascular disease and right heart failure.

Objectives: At the conclusion of this session, the participant will be able to:

- Discuss the novel findings in metabolic disorders associated with PAH
- Understand the impact of metabolic theory of PAH in the clinical setting
- Recognize the promising potential of metabolomics in disease assessment and management
- Acknowledge the recent advances in targeting metabolic alterations in PAH

The association and possible causative role of aberrant metabolism in PAH and Heart Failure has only recently come to the foreground. Recent evidence suggests that modulating cardiac energy metabolism by reducing fatty acid oxidation and/or increasing glucose oxidation represents a promising approach to the treatment of patients with Heart Failure. This session will update you on the rationale and evidence base of metabolic modulators, in the management of patients with PAH and Heart Failure.

Title

- Pkm2 and heart failure: what can we learn from that?
- AMPK and PAH
- Selenoprotein P and mitochondrial dysfunction in PAH
- Metabolic alterations and Volatolomic
- Metabolic modulators and PAH clinical trials: from DCA to Ranolazine

PROGENITOR CELLS IN PH: GOOD, BAD AND REFORMABLE

Target Audience : Basic, translational and clinical researchers and clinicians (adult and pediatrics) interested in pulmonary vascular disease and right heart failure

Objectives: At the conclusion of this session, the participant will be able to:

- Highlight the role of circulating and resident progenitor cells in PA vascular remodeling
- Understand the role of exosome in PAH

Accumulating evidence indicates that the mobilization and recruitment of circulating or tissue-resident progenitor cells can participate in pulmonary vascular remodeling. This session will update the progress in progenitor cell study related to the development of PH, and discuss the controversial issues that regard the origins, frequency, and impact of the progenitors in the disease pathogenesis and treatment.

Title

- PW1 positive cells in PAH
- Pericytes in PAH
- Circulating progenitors contribute to pulmonary vascular remodeling
- Resident progenitors contribute to pulmonary vascular remodeling
- Exosomes – Outlook for Future Cell-Free PH Therapy?

FROM PRECLINICAL STUDIES TO DRUG APPROVAL IN PAH: A LONG UNPAVED ROAD

Target Audience: Basic, translational and clinical researchers, as well as clinicians (adult and pediatrics) interested in drug development for pulmonary hypertension.

Objectives: At the conclusion of this session, the participant will be able to:

- Learn about pitfalls in translational research in order to minimize the gap from bench to bedside.
- Acknowledge the challenges of prioritizing drug development amongst potential novel therapeutic targets.
- Understand that available therapies and the changing demographics of PAH mandate changes in study design for future trials

PAH presently has no cure and there is an active search for new compounds, repurposed drugs and other novel therapies to provide transformative care for patients with PAH. This session will combine experts in regulatory drug approval, translational scientists and experts in clinical trial design to fully discuss the challenges and opportunities to bringing new therapies to patients with PAH in a safe yet timely manner.

Title

- The industry overview of clinical development for novel targets in PAH: considerations and expectations before initiating early-stage clinical programs
- Repurposing drugs for an orphan disease: opportunities and pitfalls
- The landscape of clinical trials has changed in PAH: stakeholders are raising the bar
- Choosing the best of the best: How do we select the most promising drugs for trials in human pulmonary hypertension?
- Future clinical trials in PAH: what innovative strategies will be needed to succeed?

NEW DEFINITIONS AND INTERPRETATIONS OF HAEMODYNAMIC DATA

Target Audience: Basic, translational and clinical researchers, as well as clinicians (adult and paediatrics) interested in the diagnostic methods and the hemodynamic definition of pulmonary hypertension.

Objectives: At the conclusion of this session, the participant will be able to:

- Acknowledge how normality, abnormality and disease state are defined in general as in terms of pulmonary hemodynamics.
- Recognize the challenges and the opportunities associated with the newly proposed definition for pulmonary hypertension.
- Understand the state-of-art methods to obtain reliable hemodynamic measures and their impacts on patients' management.

After the World Symposium on Pulmonary Hypertension 2018, many important questions were brought up including the most clinically appropriate definition of pulmonary hypertension, best approaches to measurement of invasive hemodynamics, and definitions of normal. This session will discuss important and controversial new knowledge on hemodynamic interpretation strategies and implications of mild alterations in pulmonary hemodynamics.

Title

- Normal PAP in healthy subjects and beyond
- Elevated PAP already represents end-stage pulmonary vascular disease: time for novel biomarker and imaging technics
- PROs and CONs of the novel definition of PH
- PAWP versus LVEDP: does it really matters?
- PAH with marginal PAWP: a different disease, different phenotype or a misclassification?

EARLY SCREENING IN PATIENTS AT RISK OF PAH: ARE WE DOING ENOUGH? ARE WE DOING TOO MUCH?

Target Audience: Basic, translational and clinical researchers, as well as clinicians (adult and paediatrics) interested in early diagnosis of pulmonary hypertension.

Objectives: At the conclusion of this session, the participant will be able to:

- Understand the limitations of the current screening tools for early diagnosis of PAH.
- Recognize the urgent need for the development of reliable methods for the diagnosis of PAH at a pre-symptomatic stage.
- Acknowledge the limited data supporting the cost-effectiveness of early screening programs for PAH.

There are several groups of patients at elevated risk for development of PAH, yet identification of sub-clinical pulmonary vascular disease remains a major challenge. This session will discuss particular groups at high risk of development of PAH, current approaches to screening in these populations and review current evidence supporting new mechanisms to identify patients at high-risk for PAH or with sub-clinical pulmonary vascular disease.

Title

- Systematic annual screening of all scleroderma patients with PFTs, imaging and circulating biomarkers is cost-effective and mandatory
- Screening in scleroderma should be tailored, primarily focusing on patients at moderate-to-high risk of PAH
- Stress echo/hemodynamics identifies a subgroup of patients with pulmonary vascular disease that should be treated
- Stress echo/hemodynamics most commonly identifies left heart dysfunction and has poor specificity for pulmonary vascular disease
- Screening of Pulmonary Arterial Hypertension in BMPR2 Mutation Carriers

THE CHANGING LANDSCAPE OF TREATMENT ARMATORIUM: IS STANDARD OF CARE IN PULMONARY HYPERTENSION STILL DEBATABLE?

Target Audience: Basic, translational and clinical researchers, as well as clinicians (adult and paediatrics) interested in treatments strategies for pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension

Objectives: At the conclusion of this session, the participant will be able to:

- Acknowledge the strength and limitations of recent PAH clinical trials and whether their results apply to all PAH subtypes.
- Recognize that the treatment algorithm for non-surgical CTPEH patients is rapidly changing.
- Determine which patients are best suitable for balloon pulmonary angioplasty based on data and expertise currently available.

While many improvements have occurred in the management of PAH and chronic thromboembolic pulmonary hypertension (CTEPH) patients, there remain unanswered questions. Two key questions will be addressed in this session using a pro-con format: 1) the role of sequential combination therapy vs. initial combination therapy in PAH and 2) the proper timing and use of balloon pulmonary angioplasty in patients with CTEPH

Title
General overview

- Initial double combination therapy is now standard of care for PAH
- Rapid goal-oriented sequential therapy remains the standard for most non-high-risk PAH patients
- BPA is now the treatment of choice in CTEPH patients with non-surgically accessible disease
- BPA should be reserved for inoperable CTEPH refractory to medical therapy

WHAT HAVE WE LEARNED FROM NATIONAL PH REGISTRIES?

Target Audience: Basic, translational and clinical researchers, as well as clinicians (adult and paediatrics) interested in the epidemiology and risk stratification of pulmonary hypertension.

Objectives: At the conclusion of this session, the participant will be able to:

- Recognize the changing epidemiology of PAH and how it may influence drug development, disease management and patients' outcomes.
- Understand opportunities and methodological pitfalls in analyzing and reporting registry data.
- Acknowledge the complementarity of existing registries and the need for developing and validating registries for non-PAH pulmonary hypertension
- Appreciate the challenges associated with the implementation of registries for specific subpopulations of patients with pulmonary hypertension.

A major focus of research in pulmonary hypertension in the last decade has been on registries to understand pulmonary hypertension phenotypes and natural history. This session will include international experts who will discuss key registries – past and ongoing – in pulmonary vascular disease.

Title

- What have we learned from the existing national PAH registries?
- Registries beyond PAH: what are the existing registries and where are the knowledge gaps
- Pitfalls in interpreting cohort and registry data
- Establishing registries in the developing world
- Paediatric registries.