Pulmonary Hypertension: Encourage clinical research and innovation

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Therapy of PH: Development of PAH Drugs

![Image of a timeline chart showing the development of PAH drugs from 1990 to 2015, with key trials and medications listed such as Epoprostenol, Bosentan, Beraprost-US, and pivotal studies like ARIES-1/2, PHIRST, SERAPHIN, and more.]

**FIGURE 1** Time-course of completed randomised controlled trials (RCTs) in pulmonary arterial hypertension (PAH) (n=41) according to treatment strategy. SSC: systemic sclerosis; IPAH: idiopathic PAH. Reproduced and modified from [70] with permission.

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Galie et al. ERJ 2019.
Therapy of PH

A lot has been done but it is still a long way to go...
Encourage clinical research and innovation

- Clinical trials in PH subtypes other than PAH
- Patient-relevant treatment outcome goals: Quality of Life
- Non-invasive diagnostic tests
- Artificial intelligence & machine learning
- International Collaborations
PH in the world

[Map showing prevalence of PH in different regions of the world, with pie charts indicating the proportions of different causes of PH.]
Clinical trials in PH subtypes other than PAH: Inhaled Treprostinil bei PH-ILD

Figure 2. Mean Change from Baseline in Peak 6-Minute Walk Distance through Week 16.

Shown are mean (±SEM) changes from baseline (dashed line) in peak 6-minute walk distance over the 16-week trial period. The data shown are for patients with available data (observed) as well as for the results of two analysis methods used to account for missing data. The values shown at each data point indicate the number of patients assessed at that time point. The primary analysis used mixed-model repeat-measurement (MMRM) methods, with the assumption that missing data were missing at random.

The model included the change from baseline to peak 6-minute walk distance as the dependent variable, with treatment, week, and treatment-by-week interaction as fixed effects, and the baseline 6-minute walk distance as a covariate. A sensitivity analysis for the primary end point was performed with the use of a multiple imputation approach with a multivariate normal imputation model using the Markov chain Monte Carlo (MCMC) method. The imputation model included treatment group, all scheduled visits, patient’s sex, and patient’s age at randomization. The confidence intervals have not been adjusted for multiplicity and cannot be used to infer definitive treatment effects.
Patient-relevant treatment outcome goals: Quality of Life
Non-invasive diagnostic tests
Artificial intelligence & machine learning

Figure 4. Layers of artificial intelligence approaches applied to medical imaging.

Figure 6. Demonstration of a quantitative CT (QCT) approach (adaptive multiple features method), acquired using PASS software. Different lung parenchymal disease patterns are identified and highlighted. Blue, emphysema/low attenuation pattern. Yellow, fibrotic changes. Pink, ground glass change.
International Collaborations

- Pulmonary Hemodynamics during Exercise – Research Network (PEX-NET)
- ERS Clinical Research Collaboration: investigating the clinical relevance of pulmonary hemodynamics during exercise
- Established in 2017
- 39 expert centers participating from 15 countries (EU, CH, GB, US, BRA, AUS)
- More than 1500 patients included so far
- Data analysis ongoing for retrospective registry
- Recruitment ongoing for prospective registry

Kovacs et al. ERJ 2017.