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# КОНГРЕС НА РЕСПИРАТОРНА МЕДИЦИНА НА РЕПУБЛИКА МАКЕДОНИЈА

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# ABSTRACT BOOK

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# CLINICAL TRIALS IN PULMONARY ARTERIAL HYPERTENSION: WHAT DO THEY REVEAL TO US?

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Pulmonary arterial hypertension (PAH) is a rare disease (prevalence of 12-25 per million) of the pulmonary vasculature that leads to right ventricular dysfunction, right ventricular failure, and premature death.

Phenotyping PAH requires a differential diagnosis with Pulmonary Hypertension (PH) secondary to cardiac, respiratory and thrombo-embolic conditions, especially in aging patients with comorbidities. PAH targeted therapies are ineffective or even deleterious in PH due to cardiac or respiratory conditions. PAH targeted therapies are palliative, thus with a clinically relevant effect size difficult to demonstrate, and furthermore, they are very expensive. Therefore, even more than for other diseases, drug development in PAH needs rigorous methodology trials of biologically plausible disease modifiers.

In this paper we aimed to provide an overview of both the current state of end-points and trial design.

The most widely used primary end point for PAH trials, change in 6-minute walk distance (6MWD) from baseline, has substantial limitations. Experts have noted that it may be more meaningful to use primary end points that measure "clinical worsening" rather than 6MWD, thus shifting a paradigm towards, not only a better demonstration of efficacy and safety as new agents emerge on the market, rather to providing important information on long term benefits.

In conclusion, progress in the treatment of PAH is unlikely to occur through further refinement of trial designs, even though a reasonable consensus on the definition of "time to clinical worsening" (TTCW) is still needed. Event driven trials produce more meaningful results, but may exhaust the PAH community and delay innovation. The PAH community may wish to switch away from development of treatments that are only incremental improvements and focus on a better understanding of the disease. This can be achieved by rigorously designed phase II trials.