

TOPIC: An Update on Investigational Agents
TIME: June 22nd 10:15-11:15
CHAIR: Adaani Frost,
DISCUSSANTS: Fernando Torres, M.D.; Zeenat Safdar, MD.; Traci Stewart R.N.

This session is designed to provide overviews of the following areas:

New Concepts:

Pulmonary arterial hypertension (PAH) is a proliferative process involving pulmonary arteries. The intracellular signaling mechanisms are being targeted as therapies in PAH, these include imatinib and sunitinib. Gene therapy that may prove to be a potential therapy for PAH will be discussed. In one protocol autologous or patient's own blood cells are harvested, grown and then infused back through a catheter in an attempt to treat PAH. Recently another potential agent that restores mitochondrial function was identified. These new and exciting therapies will be discussed in detail to increase our understanding of emerging therapies.

New Studies:

TRIUMPH: This is a trial studying the efficacy and safety of using inhaled treprostinil for the treatment of Pulmonary Arterial Hypertension. The patients in the study were on baseline therapy of bosentan or sildenafil. The preliminary data has been presented at ATS 2008 showing improvement of 6MWD, but changes in the secondary endpoints did not achieve statistical significance.

EARLY: This is a trial studying the efficacy and safety of using bosentan for the treatment of Pulmonary Arterial Hypertension in patients who have mild PHTN NYHA functional class II. This is the first trial dedicated to this population. The results were presented at ACCP 2007 showing a trend towards improvement in 6 MWD at 6 months and statistically significant improvement on secondary end points including time to clinical worsening. Hemodynamic data was also presented and had statistically significant improvement.

COMPASS 3: This is a multicenter trial studying the effects of goal directed therapy on cardiac MRI parameters. This is a study where patients are placed on bosentan to achieve a certain therapeutic goal and if at 4 months they have not reached it, sildenafil will be added. Hemodynamics, Biomarkers, echocardiography, and cardiac MRI imaging will be recorded at baseline and 4 months, and at 7 months imaging will be repeated. This study is still enrolling patients.

ARIES 3: The purpose of this study is to assess the safety of ambrisentan (Letairis) in patients on no therapy or already on sildenafil (Revatio) therapy. In addition, it is studying the safety of ambrisentan in subgroups of people with PH not previously studied before, such as those with underlying HIV, congenital heart defects, lung diseases (pulmonary fibrosis or COPD), or chronic thromboembolic disease. This trial is closed to enrollment and may serve to guide further research with PH therapies in these subgroups of people with PH.

COMPASS 2: This trial is ongoing and is assessing the effects of bosentan (Tracleer) and sildenafil (Revatio) compared to sildenafil (Revatio) treatment alone. Sildenafil must be started for 12 weeks prior to starting this study. Most PH trials have been short term trials, however, this is a long term study comparing changes in six minute walk distance and time to hospitalization, worsening symptoms, and survival related to PAH.

FREEDOM: This trial compares the effectiveness of oral treprostinil (Remodulin) vs. placebo in patients with PAH. This is done by looking at changes in six minute walk distance and time to clinical worsening. There are 2 parts to this trial. The first part is 16 weeks and makes the comparison in patients that are also taking sildenafil (Revatio) and/or bosentan (Tracleer) or ambrisentan (Letairis). This part is closed to enrollment. The second part is a 12 week trial that looks at people recently diagnosed with PH and is comparing oral treprostinil (Remodulin) to placebo without other PH specific medications.