Potential new treatment for pulmonary arterial hypertension enters clinical trials

Following an initial pilot study carried out in December 2010, GeNO LLC, an advanced development-stage technology company, has announced the launch of the PHiano Study. This is a Phase II, dose-escalation trial for the treatment of pulmonary hypertension in patients with pulmonary arterial hypertension (PAH) and pulmonary hypertension secondary to idiopathic pulmonary fibrosis (PH-IPF) using inhaled NITROSYL™ nitric oxide (NO).

Pulmonary hypertension secondary to idiopathic pulmonary fibrosis is characterized by progressive fibrosis in the lungs and carries a median survival time from diagnosis of 2–5 years, with a 5-year survival rate of just 20%. PAH is rare and progressive with survival rates rarely exceeding 5 years. At present, no medications are approved for the treatment of these disorders.

The current trial will investigate the safety and efficacy of various doses of inhaled NO, up to a maximum of 80 ppm, delivered for up to 150 min with GeNO’s stand-alone NITROSYL system. The primary objective of the PHiano Study is to define the clinically effective dose parameters (minimum and maximum effective dose) of inhaled NITROSYL NO compared with placebo. The study will also be used to assess the safety and tolerability of inhaled NO within the study population.

Conducted across multiple clinical sites in the USA, the trial is expected to enrol up to 75 patients with WHO Group 1 PAH and WHO Group 3 PH-IPF currently undergoing right heart catheterization. NO will be delivered to patients from GeNO’s stand-alone gas cylinder. Premixed NO is stored in the cylinder as nitrogen dioxide in air. Immediately prior to inhalation the gas flows through a cartridge containing ascorbic acid, which generates NO.

GeNO hope that the results from this Phase II trial will enable them to design a Phase II/III trial for chronic ambulatory administration of NO. David Fine, Founder and President of GeNO LLC, hopes that “the combined results from this current Phase II study and planned Phase II/III chronic study will help to define responses in both populations and further guide Phase III development”.

GeNO Vice President Robert F Roscigno points out that while the two conditions being studied are different the trial will focus on the common element, pulmonary hypertension, which is a determinant of survival in both disorders. Discussing the aims of PHiano he adds, “Our Phase II program will assess whether NO improves pulmonary hypertension in both populations, whether there are safety concerns in either group that are unique to that condition or shared by both, and whether the profile of effect is common.”

The next planned stage of study is scheduled for launch late in 2011 and will see GeNO testing their Ambulatory NITROSYL System, a hand-held unit with a disposable liquid source, that should provide up to 4 days of continuous supply of inhaled NO for chronic use.

Breakfast may be the most important meal of the day for reducing high blood pressure

Research from the Beth Israel Deaconess Medical Center and the Veterans Affairs Boston Healthcare System, Boston, MA, USA, presented at the recent American Heart Association’s Scientific Session in Atlanta, GA, USA, has shown that eating a bowl of whole-grain cereal for breakfast could reduce the risk of developing high blood pressure by 20%.

The research team collected data from 13,368 male doctors who took part in the Physicians’ Heart Study I. At the outset in 1982 none of the men had high blood pressure, but over 16 years of follow-up 7267 of the doctors developed hypertension. Hypertension and its related conditions, such as heart disease and stroke, is the leading cause of death in the USA. The group, lead by Jinesh Kochar, analyzed the data obtained from the male doctors to see if any correlation could be identified between high blood pressure and lifestyle data that were also collected. They found that men who ate whole grain cereal at least once a week reduced their risk of hypertension by 8% compared with men who ate no cereal. Eating cereal two to six times a week reduced hypertension risk by 16% whereas eating cereal seven or more times a week reduced the risk by as much as 20%.

Kochar’s team adjusted their findings to allow for other factors that may have influenced the doctors’ risk of developing hypertension, such as smoking history, weight, alcohol intake and physical activity. Following these adjustments, they still found a significant reduction in hypertension risk associated with whole grain cereal intake; approximately 12% for those eating two to six serving a week and 19% for those eating seven or more servings.

Director of the Prevention Research Center at Yale University School of Medicine, David L Katz, commented: “There has long been evidence that whole grain intake can lower blood pressure fairly acutely, and it is associated with lower blood pressure over time. [Whole grains] contain vitamins and minerals that relax blood vessels as well as soluble fiber, which helps lower blood sugar, lipid and insulin levels and in turn lowers blood pressure.” He adds that while there are lots of benefits associated with consuming more whole grains, part of the reason for the observed effects may be that whole-grain cereal is replacing a breakfast that would have adverse effects on hypertension risk. “… it may be as much what a bowl of cereal knocks out of one’s diet, as what it puts in, that helps lower blood pressure and enhance health”.


Antibody shows promising results in hypertension study

DiaMedica announces antihypertensive results with its monoclonal GSK3β-blocking antibody DM-204.

Hypertension affects nearly a third of American adults and is a leading risk factor for cardiovascular disease and stroke. At present only 20% of hypertension patients adequately control their blood pressure and patients often require a combination of antihypertensive drugs to treat their high blood pressure.

DiaMedica is a biopharmaceutical company focused on developing novel therapeutic products to improve the lives of people living with Type 1 and Type 2 diabetes. Their leading drug, DM-199, has been shown to significantly improve glucose metabolism and protect proliferative beta cells.

Their new results are from a preclinical study, which was carried out in a range of animal models of hypertension. They found that DM-204 significantly lowered systolic blood pressure in all of the animals studied by an average of 15 mmHg (p < 0.05) and was able to maintain this reduction over the course of the study.

The DM-240 antibody works by blocking the activity of glycogen synthase kinase 3 beta (GSK3β), a key cell signaling enzyme that is implicated in several diseases, including diabetes and some cancers. Since approximately 70% of Type 2 diabetes patients also suffer from hypertension, a therapy that can improve both hypertension and diabetes could be beneficial to a large patient group.

The next stage of research is to investigate whether these preclinical results can be reproduced in a clinical setting. If the clinical phases produce favorable results then Rick Pauls, President and CEO of DiaMedica,
believes that “DM-240 has the potential to replace the current standard of care for treating hypertension patients”. This could still be many years away as the drug still needs to undergo development through all clinical phases and achieve approval; however, Pauls is optimistic, adding that the “results of the present study further demonstrate the exceptional potential of DM-240 that is also being tested for diabetes and other indications”.


Afternoon naps could aid blood pressure management

New research from Allegheny College, Pennsylvania, PA, USA, suggests that taking a nap during the day could have cardiovascular benefits.

Numerous characteristics of modern society, such as long work schedules, shift work, increased anxiety and increased television viewing at night, have had an impact on nocturnal sleep. Today the average sleep duration is nearly 2 h shorter than it was 50 years ago. Researchers believe that this reduction in sleep could have an impact on long-term health; for example, reduced sleep time has been linked to an increased risk of hypertension and cardiovascular problems.

Ryan Brindle and Sarah Conklin, from Allegheny College, created a study to examine how daytime sleep might influence cardiovascular recovery after a mental stress test carried out in the laboratory. They studied a total of 85 university students, split into two groups; one of which was allowed a 60-min time period during the day in which they could nap. Students in the second group were not permitted to sleep during the day. All participants completed a questionnaire to assess sleep quality and also underwent cardiovascular reactivity tasks consisting of mental subtracting exercises. Throughout the course of the experiment the students’ blood pressure and pulse rates were measured at regular intervals.

“...daytime sleep may offer cardiovascular benefit by accelerating cardiovascular recovery following mental stressors.”

Blood pressure and pulse rates were observed to rise in both groups between baseline and stress. However, during the recovery phase students who had been allowed to nap had significantly lower average blood pressure readings. These results demonstrate that sleeping for between 45 and 60 min during the day can lead to better blood pressure recovery following mental stress.

Brindle and Conklin conclude: “Our findings suggest that daytime sleep may offer cardiovascular benefit by accelerating cardiovascular recovery following mental stressors.” They acknowledge that further research will be necessary in order to “explore the mechanism by which daytime sleep is linked with cardiovascular health and to evaluate daytime sleep as a recuperative and protective practice, especially for individuals with known cardiovascular disease risk and those with suboptimal sleep quality”.


ACE inhibitor combination implicated in kidney failure

New research from the University of Alberta and the University of Calgary, Canada, suggests that elderly patients who are prescribed combination angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) have an increased risk of kidney failure.

In the past, randomized controlled trials have indicated that combination ACE inhibitor–ARB is associated with an increased risk of kidney failure, but since these trials may over- or under-estimate the risk of adverse events the Canadian researchers of the present study carried out an investigation to determine the safety of ACE inhibitor–ARB combination therapy in a clinical setting.

The researchers studied a total of 32,312 patients aged 65 years and older in Alberta, Canada. All of the patients were routinely prescribed an ACE inhibitor and/or an ARB and patients receiving both drugs were compared with patients who received only one. The results showed that patients taking the combination therapy had a higher risk of adverse events, including higher creatinine levels, end-stage kidney disease and death.

Interestingly, the researchers also found that less than a seventh of elderly people who were prescribed the combination therapy had either of the conditions for which the therapy has been proven
beneficial in clinical trials. Most patients were also observed to stop taking the combination therapy within 3 months; something the researchers think might result development of low blood pressure in these patients.

The group conclude: “Our most striking findings were that combination therapy was commonly prescribed for patients who did not have the trial-proven indications and that it was frequently stopped after only a few months, even when hyperkalemia or renal dysfunction did not occur.”