Large clinical trial finds pirfenidone may help lung function in IPF patients

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A large, well-controlled, multi-national clinical trial program has demonstrated the effectiveness and safety of what may become the first FDA-approved medicine for idiopathic pulmonary fibrosis, or IPF.

In a Phase III clinical study program called "CAPACITY," investigators discovered that the oral anti-fibrotic and anti-inflammatory agent, pirfenidone, could slow the deterioration of lung capacity in patients suffering from IPF.

The researchers presented their findings on Sunday, May 17, at the American Thoracic Society's 105th International Conference in San Diego.

The CAPACITY trial consisted of two multi-national, randomized, double-blind, placebo-controlled Phase III trials (CAPACITY 1 and CAPACITY 2) designed to evaluate the safety and efficacy of pirfenidone in IPF patients with mild to moderate impairment in lung function. The primary endpoint of change in percent predicted forced vital capacity (FVC) at week 72 was met with statistical significance in CAPACITY 2 (p=0.001), along with the secondary endpoints of categorical change in FVC and progression-free survival (PFS), defined as time to either death, a 10-percent decrease in FVC or a 15-percent decrease in DLCO (diffusing capacity of the lung for carbon monoxide). The primary endpoint was not met in CAPACITY 1 (p=0.501), but evidence of a pirfenidone treatment effect on the primary endpoint was observed at several periods in that trial. Importantly, greater than 80 percent of patients in the trials completed treatment and greater than 90 percent completed the study.

An exploratory analysis of pooled data from both trials revealed that treatment with pirfenidone resulted in a 30-percent relative reduction in the percentage of patients who experienced an absolute decline in percent predicted FVC of at least 10 percent. This magnitude of decline is considered clinically meaningful, as a 10-percent decline in percent predicted FVC has been shown in multiple studies to be an independent predictor of mortality in patients with IPF. Exploratory analyses of pooled data from the two CAPACITY studies also demonstrated a statistically significant treatment effect on the primary endpoint of change in percent-predicted FVC at week 72, progression-free survival time and change in six-minute walk test distance.

"While it was disappointing that the primary endpoint was not met in CAPACITY 1, important consistencies between the two CAPACITY studies were observed in the overall treatment effect of pirfenidone," said Paul Noble, M.D., co-chair of the CAPACITY program and professor of medicine and chief of Pulmonary, Allergy and Critical Care Medicine at Duke University Medical Center. "The treatment effect observed in the CAPACITY studies was generally consistent with that observed in the Phase III study in IPF patients conducted by Shionogi in Japan. Collectively, these three studies give us a very good sense of the impact that pirfenidone has on the progression of IPF over at least one year."

According to the National Heart, Lung, and Blood Institute, about 200,000 Americans have idiopathic pulmonary fibrosis, a condition that scars tissue deep in the lungs. Most patients are diagnosed with the disease in their 50s and 60s, and many people live only three to five years after being diagnosed. There are no approved medications in the United States or Europe to treat the disease. Pirfenidone is approved in Japan for the treatment of IPF.

A total of 779 patients were enrolled in the CAPACITY trials at 110 sites in 11 countries. The mean age of participants was 66. To be eligible for the study, patients had to have a definitive diagnosis made by high-resolution CT scan or by biopsy, and a FVC ? 50 percent of predicted values and a DLCO ? 35 percent of predicted value.

Dr. Roland du Bois, M.D., professor of medicine at National Jewish Health, in Denver, Colo., and CAPACITY co-chair, concurred that these studies were very encouraging for IPF sufferers and added that "the safety and tolerability of pirfenidone was reassuring. The principal side effects experienced by patients in the studies were gastrointestinal discomfort and photo-sensitivity, both of which were manageable in the majority of patients."

The CAPACITY trials follow a Phase III clinical study conducted in Japan that was reported at the American Thoracic Society's 2008 International Conference in Toronto. That trial, which demonstrated the ability of pirfenidone to reduce the decline of lung capacity and improve progression-free survival, served as the basis for the Japanese regulatory authorities' approval of the medicine for the treatment of IPF in Japan.

Dr. du Bois concluded, "When taken in the context of the urgent unmet medical need for new medicines to treat IPF patients, the collective efficacy and safety data from the two CAPACITY studies, corroborated by a similar study in Japan, make a case for the use of pirfenidone in this disease setting."

InterMune, Inc., the developer of the medication, is preparing a New Drug Application (NDA) for pirfenidone for the treatment of IPF, which it expects to submit to the FDA in the summer of 2009, to be followed by a Marketing Authorization Application (MAA), which will be submitted to the European Medicines Agency (EMEA) around the end of 2009. Meanwhile, all patients in the study have been offered pirfenidone as part of an open-label, long-term safety study called RECAP.

Source: American Thoracic Society (news : web)