Bayer HealthCare
Bayer Schering Pharma

Riociguat

Riociguat (BAY 63-2521) is an oral agent being investigated in phase III clinical trials as a new approach to treating chronic thromboembolic pulmonary hypertension (CTEPH) and pulmonary arterial hypertension (PAH), two life-threatening types of pulmonary hypertension (PH). Riociguat is the first member of a novel class of therapeutics called soluble guanylate cyclase (sGC) stimulators.[1] It is one of the most advanced product candidates in the Bayer Cardiology pipeline.

Investigating riociguat in CTEPH and PAH

Riociguat showed promising results in phase II trials by significantly improving exercise capacity and hemodynamic parameters such as pulmonary vascular resistance, cardiac output and pulmonary arterial pressure compared to baseline values in patients with CTEPH and PAH. The phase II data also indicate riociguat has a favorable safety profile.[2]

Based on the positive phase II findings, Bayer Schering Pharma has initiated two phase III trials investigating the efficacy, safety and duration of effect of riociguat for the treatment of inoperable CTEPH and PAH.

The phase III program consists of four trials, two per indication (one pivotal trial and one extension trial, respectively):

- **Ch**ronic Thrombo**e**mbolic Pulmonary Hypertension sGC-**S**timulator **T**rial (CHEST)
  The randomized, placebo-controlled pivotal trial CHEST-1 will investigate the efficacy and safety of riociguat in patients with inoperable CTEPH. The primary outcome measure after 16 weeks of treatment will be patient's exercise capacity, measured by the change from baseline in the six-minute walk test (6-MWT). All patients having completed CHEST-1 will be offered to enter the open label extension trial, CHEST-2, after the initial treatment duration of 16 weeks.

- **P**ulmonary **A**rterial Hyper**ten**sion sGC-Stimulator **T**rial (PATENT)
  The randomized, placebo-controlled pivotal trial PATENT-1 will investigate the efficacy and safety of riociguat in patients with PAH. The primary outcome measure after 12 weeks of treatment will be patient's exercise capacity, measured by the change from baseline in the 6-MWT. All patients having completed PATENT-1 will be offered to enter the open label extension trial, PATENT-2, after initial treatment duration of 12 weeks.

The novel science behind riociguat

Riociguat works through the same signaling pathway as the body's own vasodilating substance, nitric oxide (NO). NO relaxes the musculature in the blood-vessel walls, lowers the pulmonary blood pressure and relieves the heart by modulating the activity of the sGC enzyme.

Riociguat has a dual mode of action: it sensitizes sGC to the body's own NO while also directly stimulating sGC independently of NO. This is important because the NO levels in the pulmonary circulation are decreased in patients with PH. With its novel mode of action, riociguat has the potential to overcome a number of limitations of other therapies currently used to treat PH.

Riociguat aims to address areas of high unmet medical need

PH affects people worldwide, and despite improvement in patient care during the last years, there is a concrete need for more efficient therapies. PH encompasses multiple disease subtypes and currently existing treatments are only indicated for PAH, which accounts for only a small portion of the overall PH population. Currently, there are no specific treatments approved to treat CTEPH. In addition to CTEPH and PAH, the new class of sGC stimulators may be feasible for other forms of PH, thus fulfilling a high unmet medical need.

REFERENCES

[1] Ghofrani, Hossein Ardeschir. Presentation: Soluble guanylate cyclase stimulation: an emerging option in pulmonary hypertension therapy. Presentation given at the European Respiratory Society Meeting, October 2008, slide 4.

[2] Ghofrani HA, Hoeper MM, Halank M, Weimann G, Grimminger F. Riociguat treatment in patients with chronic thromboembolic pulmonary hypertension (CTEPH) or pulmonary arterial hypertension (PAH). Poster presentation at: the American Thoracic Society International Conference, 15-20 May 2009, San Diego, California, USA.