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News Release

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Study Shows Vernakalant Hydrochloride is Effective in Conversion to Normal Heart Rhythm in Atrial Fibrillation Patients Following Cardiac Surgery

ORLANDO, FL – November 7, 2007 – Astellas Pharma US, Inc. today announced that the investigational agent vernakalant hydrochloride increased conversion to normal heart rhythm (sinus rhythm, or SR) in patients with atrial fibrillation (AF) following coronary artery bypass graft (CABG) or valvular surgeries. AF is a potentially serious condition characterized by an irregular heart rhythm and a high heart rate. The study results were presented today at the annual meeting of the American Heart Association.

"Postoperative AF is common after cardiac surgery, occurring in up to 40% of patients and has a significant effect on both the intensive care unit and overall hospital length of stay," said Peter Kowey, MD, William Wikoff Smith Chair in Cardiovascular Research at the Main Line Health System. "This study shows that vernakalant may be an effective treatment option for converting AF to SR following CABG or valvular surgeries."

Study Results

The **A**trial arrhythmia **C**onversion **T**rial or ACT II was a randomized, double-bind, placebo-controlled, parallel-group, multinational, multicenter study evaluating the efficacy and safety of vernakalant among patients who experienced AF or atrial flutter within 24 hours to 7 days after cardiac surgery.

Patients received vernakalant 3 mg/kg (n=107) or placebo (n=54) infused over 10 minutes. After 15 minutes, a second 10 minute infusion of vernakalant 2 mg/kg or placebo was given if AF or atrial flutter was present. The primary efficacy measure was the percentage of patients with treatment-induced conversion of AF/atrial flutter to SR for at least one minute within 90 minutes.

(more)

Patients demonstrating conversion within 90 minutes were categorized as responders. Other efficacy measures included time to conversion of all responders and percentage of AF patients demonstrating conversion to SR within 90 minutes for ≥ one minute.

Following CABG or valvular surgery, a significantly higher percentage of patients with AF/atrial flutter given vernakalant (45 percent) demonstrated conversion to SR within 90 minutes compared to patients given placebo (15 percent), p=.0002. In the subset of patients with AF at baseline, conversion was observed in 47 percent treated with vernakalant compared with 14 percent given placebo, p=.0001. Median time to conversion among vernakalant responders was 12 minutes and SR was maintained for patients with AF/atrial flutter for 24 hours in 60 percent and for seven days in 57 percent. Seventy-five percent of vernakalant responders required only one dose of drug. Vernakalant is not effective in atrial flutter.

The most common adverse events (AEs) in patients given vernakalant were AF (20 percent), nausea (6 percent), constipation (5 percent), weight increase (5 percent) and dyspnea (5 percent). Rates of serious AEs over the entire study were similar with placebo (11 percent) and vernakalant (9 percent). In the first 24 hours, only 2 patients (2 percent) given vernakalant experienced a serious AE (complete AV block and hypotension). There were no deaths or cases of torsade de pointes.

About Atrial Fibrillation

AF is an interruption of the normal sinus rhythm (arrhythmia) of the heart in which the atria, the two uppermost chambers of the heart, beat irregularly and at an extremely rapid rate.[1] During AF, rapid and uncoordinated electrical discharges are generated by the heart's natural pacemaker (sinoatrial node) and other parts of the atria. This causes ineffective contractions of the atria and reduces the ability of the heart to pump blood through the body. Symptoms include dizziness, heart palpitations, weakness, shortness of breath and angina (chest pain).[1] The number of AF patients is expected to triple over the next 50 years due to the increased prevalence of risk factors including hypertension, obesity, diastolic dysfunction, inflammation, diabetes and sleep apnea.[2]

About Astellas

Astellas Pharma US, Inc., located in Deerfield, Illinois, is a U.S. affiliate of Tokyo-based Astellas Pharma Inc. Astellas is a pharmaceutical company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. The organization is committed to becoming a global category leader in focused areas by combining outstanding R&D and marketing capabilities. In the US, Astellas markets products in the areas of Immunology, Urology, Anti-Infectives, Cardiovascular and Dermatology. For more information about Astellas Pharma US, Inc., please visit our website at www.astellas.com/us.

References

1. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation. *Journal of the American College of Cardiology*. 2006;48(4):854-906.

2. Miyasaka Y, Barnes ME, Gersh BJ, et al. *Circulation*. 2006;114:119-125.

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