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Efficacy and safety of vernakalant for cardioversion of recent-onset atrial fibrillation in real-world clinical practice: the SPECTRUM post-approval safety study

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Background: Vernakalant is an antiarrhythmic agent designed for pharmacological conversion of recent onset of atrial fibrillation (AF) with combined action on cardiac potassium and sodium currents mainly concentrated in the atria.

Purpose: SPECTRUM was a post-authorisation safety study of vernakalant, conducted to collect information about real-life conditions of use and appropriate dosing, and to quantify possible medically significant risks associated with the use of vernakalant in real-world clinical practice.

Methods: This prospective and retrospective registry was conducted from Sep 2011 to Apr 2018 in 53 hospitals in EU countries including Austria, Denmark, Finland, Germany, Spain and Sweden. A total of 1,778 patients with 2,009 episodes of recent-onset AF received vernakalant and were followed up for 24 hours after the last infusion or until hospital discharge/end of medical encounter to obtain information on medically significant health outcomes of interest (HOIs, defined as significant hypotension, significant ventricular arrhythmia, significant atrial flutter, significant bradycardia), and serious adverse events (SAEs).

Results: In more than 99% of treatments, vernakalant was used in accordance to the labelled indication for conversion of AF for non-surgery (94.7%) or post-cardiac surgery patients (5.2%). Vernakalant was administered in the emergency department in 64.2% of cases, with a median stay of 7.5 hours and successfully converted 70.2% (95% CI: 68.1–72.2) of patients in the effectiveness analysis population with a median time to conversion of 11 minutes (95% CI: 8.0–27.0). A total of 19 HOIs were reported in 17 patients (0.8%, 95% CI: 0.5– .4%) with individual HOIs ranging from <0.1% to 0.7% suggesting these HOIs are uncommon. Significant bradycardia was the most common HOI observed in 15 patients (0.8%, 95% CI: 0.4–1.2%), with all events occurring within the first two hours (0.8%, 95% CI: 0.4–1.2%). The incidence of significant hypotension was 0.1% (2/2,009), significant atrial flutter (with 1:1 conduction) was 0.1% (2/2,009), and significant ventricular arrhythmia (sustained ventricular tachycardia) was <0.1% (1/2,009). A total of 28 SAEs, including all HOIs, were observed (1.3%, 95% CI: 0.8–1.9%); all patients fully recovered, except one who recovered with sequelae after an SAE of pericardial effusion definitely not related to vernakalant. There were no cases of torsades de pointes, ventricular fibrillation, or deaths reported in the SPECTRUM study.

Conclusion(s): SPECTRUM is, to our knowledge, the largest drug registry conducted on the cardioversion of recent onset AF. The cumulative data from 2,009 vernakalant treatment episodes demonstrate an incidence of HOIs and SAEs similar or lower to what has been reported in earlier vernakalant IV clinical trials. The observed conversion rate was higher than reported in pivotal trials supporting vernakalant's efficacy and allowing early discharge.