Asundexian inferior to apixaban for stroke prevention in atrial fibrillation: Study

September 2 2024

Credit: Anna Shvets from Pexels

Asundexian 50 mg daily was inferior to apixaban for stroke and systemic embolism prevention in high-risk patients with atrial fibrillation (AF), according to late-breaking research presented in a Hot Line session Sept.

1 at ESC Congress 2024.

"AF can lead to thromboembolic events, such as stroke, which carry a high risk of permanent disability and death. The availability of direct-acting oral anticoagulants (DOACs) has improved stroke prevention over vitamin K antagonists, but even with DOACs, many patients are not anticoagulated due to their anticipated bleeding risk or the occurrence of actual bleeding events.

"Asundexian, an inhibitor of activated factor XI (XIa), is a new oral anticoagulant that reduced bleeding risk compared with the DOAC, apixaban, in a phase II trial.

"We conducted the phase III OCEANIC-AF trial to test whether asundexian could prevent stroke and systemic embolism to the same extent as apixaban; however, asundexian was found to be inferior," explained Principal Investigator, Professor Manesh Patel from the Duke University Medical Center, Durham, U.S.

OCEANIC-AF was a double-blind randomized trial conducted in patients with AF with a high stroke risk (CHA2DS2-VASc score ≥3 if male or ≥4 if female, or ≥2 if male or ≥3 if female with additional risk factors). Patients were randomized (1:1) to asundexian 50 mg once daily or standard dosing with apixaban (5 mg or 2.5 mg twice daily based on dose-reduction criteria).

The primary efficacy objective was to demonstrate that asundexian was at least non-inferior to apixaban for prevention of stroke or systemic embolism. The primary safety objective was to demonstrate that asundexian was superior to apixaban with fewer events of major bleeding (as defined by the International Society on Thrombosis and Hemostasis).

In total, 14,830 patients were randomized from more than 1,000 sites in more than 35 countries. In November 2023, the independent data monitoring committee recommended that the trial be stopped early. In the randomized population, the mean age was 73.9 years and 35% were women. The mean CHA2DS2-VASc score was 4.3 (standard deviation 1.3) and 17% had previous oral anticoagulation use of 6 weeks or less.

After a median follow-up of 160 days, the occurrence of stroke or systemic embolism was higher in those receiving asundexian (1.3%) compared with apixaban (0.4%), and asundexian was considered to be inferior (hazard ratio [HR] 3.79; 95% confidence interval [CI] 2.46–5.83).

Cardiovascular death occurred in 0.6% in each group (HR 1.09; 95% CI 0.72–1.64). All-cause mortality occurred in 0.8% of patients receiving asundexian compared with 1.0% receiving apixaban (HR 0.84; 95% CI 0.60–1.19).

Major bleeding was lower with asundexian vs. apixaban (0.2% vs. 0.7%; HR 0.32; 95% CI 0.18–0.55). Lower rates were also observed for the composite of major or clinically relevant non-major bleeding with asundexian compared with apixaban (1.1% vs. 2.6%; HR 0.44; 95% CI 0.34–0.57).

Discussing the key learnings from the trial, Professor Patel said, "Our results show that the dose of asundexian tested was inferior for stroke or systemic embolism compared with apixaban. We could speculate that near-total factor XIa suppression may be needed to prevent thrombus formation.

"We also noted a lower-than-expected rate of stroke or systemic embolism in the apixaban group, which may reflect prior use of oral anticoagulants and improved medical therapy. Finally, we were able to

demonstrate lower bleeding rates with asundexian, which has to be put into context with the stroke findings.

"There remains a need for better antithrombotic therapy for AF with lower bleeding risk than current DOACs."

Provided by European Society of Cardiology