

ANDEXXA Phase IV Trial Stopped Early after Achieving Criteria on Hemostatic Efficacy

ANNEXA-I, a post-marketing Phase IV trial to assess the efficacy and safety of Andexxa (andexanet alfa) in patients on oral FXa inhibitor treatment experiencing an intracranial hemorrhage will be stopped early, AstraZeneca, the drug's manufacturer, announced June 5.

The decision was based on achieving prespecified stopping criteria of superior hemostatic efficacy, the ability to limit the expansion of a potentially life-threatening bleed in the brain compared with usual care. (ClinicalTrials.gov. May 17, 2023; <https://bit.ly/3Nb7VbB>.)

The recommendation to stop the trial was made by the independent Data and Safety Monitoring Board following a planned interim assessment of efficacy after 450 patients had been randomized and followed for one month, which showed Andexxa's reversal benefits earlier in the study than anticipated. The primary endpoint was the rate of effective hemostasis following treatment with Andexxa compared with usual care, including four-factor prothrombin complex concentrate (4F-PCC), the company said in a news release.

"We are pleased that the study has met its efficacy endpoint at the planned interim analysis, showing improved control of bleeding with targeted anticoagulation reversal, compared to usual care," said Stuart J. Connolly, MD, a senior scientist at the Population Health Research Institute and a professor emeritus at McMaster University in Hamilton, Ontario. "We look forward to sharing the full efficacy and safety results after further analysis, with the hope that the data will pave the way for further guidance on the treatment of potentially life-threatening bleeds."

Mene Pangalos, the executive vice president for BioPharmaceuticals R&D at AstraZeneca, said in the news release that millions of people worldwide depend on FXa inhibitors to prevent harmful blood clots from forming, but these agents also carry a small but significant risk of increasing the likelihood that an acute major bleed could occur. "We are proud to offer the first and only approved treatment to specifically reverse FXa inhibitor activity and help achieve hemostasis, providing an effective and reliable treatment when immediate care is required," he said.

Andexxa is designed to rapidly reverse the anticoagulation effects of direct oral FXa inhibitors due to life-threatening or uncontrolled bleeding, AstraZeneca said in the news release. The treatment has been granted accelerated approval in the United States, and it is conditionally approved in the European Union, Switzerland, and the United Kingdom as Ondexxya for adults treated with FXa inhibitors apixaban and rivaroxaban. It is also approved in Japan as Ondexxya for the FXa inhibitors apixaban, rivaroxaban, and edoxaban. Use of Andexxa is supported by more than 15 national and international guidelines across multiple disciplines. (Find complete references on AstraZeneca's website: <https://bit.ly/43K8BuU>.)

AstraZeneca will initiate closure of ANNEXA-I and proceed with regulatory filings in the United States and the European Union to convert to full-label approval. The full efficacy and safety results will be submitted for presentation at a forthcoming medical meeting and publication.

Andexxa is a recombinant protein designed to bind to FXa inhibitors and rapidly reverse their anticoagulant effect, AstraZeneca said. (Full prescribing information at <https://bit.ly/42oUNVu>.) It is a modified form of the human FXa molecule, an enzyme that helps blood clot. Andexxa works by acting as a decoy for oral and injectable FXa inhibitors, which target and bind to FXa, allowing them to exert their anticoagulant effect. When it is given through an intravenous infusion to a patient with FXa inhibitor-related bleeding, it binds with high affinity to the FXa inhibitor, prevents it from inhibiting the activity of FXa, and reverses the anticoagulant effects of the inhibitor.

Cardiovascular, Renal and Metabolism (CVRM), part of BioPharmaceuticals, forms one of AstraZeneca's three disease areas. By following the science to understand more clearly the underlying links between the heart, kidneys, and pancreas, AstraZeneca said it is investing in a portfolio of medicines for organ protection and improving outcomes by slowing disease progression, reducing risks and tackling co-morbidities. The company said its ambition is to modify or halt the natural course of CVRM diseases and potentially regenerate organs and restore function by continuing to deliver transformative science that improves treatment practices and CV health for patients worldwide.

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialization of prescription medicines in oncology, rare diseases, and biopharmaceuticals, including cardiovascular, renal and metabolism, and respiratory and immunology. Based in Cambridge, UK, AstraZeneca operates in more than 100 countries and its medicines are used by millions of patients worldwide. Learn more at astrazeneca-us.com or follow the company on Twitter [@AstraZenecaUS](https://twitter.com/AstraZenecaUS).