A Randomized Clinical Trial of Andexanet Alfa in Acute Intracranial Hemorrhage in Patients Receiving an Oral Factor Xa Inhibitor (ANNEXA)

Principal Investigator:	PD Dr. med. Georg Kägi
Status:	ongoing, recruiting
Project Start:	2021
Project End:	2022
Trial Design /Class:	international, multicentre, prospective, randomized, open-label trial, Category: A
Number of Patient:	900
Centers:	Switzerland, Denmark, Finland, Sweden, Norway, Czech Republic, Greece, Poland, Spain, Italy, UK, Israel, Estonia, Latvia, Lithuania, Austria, Belgium, France, Germany, Netherlands, Portugal (132 Sites)
Sponsor/Partner:	Portola Pharmaceuticals
Funding:	Industry Sponsor - Portola Pharmaceuticals

Summary:

ANNEXA is a randomized, multicenter clinical trial designed to determine the efficacy and safety of andexanet compared to usual care in patients presenting with acute intracerebral hemorrhage within 6 hours of symptom onset (from the baseline scan) and within 15 hours of taking an oral FXa inhibitor (from randomization). The study will use a prospective, randomized, open-label design, as it is unfeasible to blind the Investigator to the treatment assignment given the many potential therapeutic options available under usual care treatment. The primary efficacy outcome will be adjudicated by a blinded Endpoint Adjudication Committee (EAC). To support the adjudication of hemostatic efficacy, a blinded Imaging Core Laboratory will review all available scans.

Objectives:

Primary Efficacy Objective
To evaluate the effect of andexanet versus usual care on the rate of effective hemostasis.

Secondary Efficacy Objective
To evaluate the effect of andexanet versus usual care on anti-fXa activity.
To evaluate the effect of andexanet versus usual care on neurologic function.

Additional Efficacy Objectives
To evaluate the effect of andexanet versus usual care on thrombin generation.
To assess the relationship between anti-fXa activity and the achievement of hemostatic efficacy.
To evaluate the occurrence and outcome of extracranial bleeding.
To evaluate the effect of andexanet versus usual care on health-related quality of life.

Safety Objectives
To evaluate the occurrence of thrombotic events (TEs) at 30 days.
To evaluate in-hospital and 30-day mortality (all-cause, cardiovascular, and bleeding).
To evaluate the occurrence of invasive intracranial procedures post-randomization.
To evaluate the length of initial hospitalization for primary bleeding event.
To evaluate the rate of re-hospitalization.
To evaluate adverse events (AEs) and vital signs.
To evaluate the immunogenicity of andexanet.