FOOD AND DRUG ADMINISTRATION (FDA)
Center for Biologics Evaluation and Research (CBER)
77th Meeting of the Cellular, Tissue, and Gene Therapies Advisory Committee (CTGTAC)
November 21, 2024

Committee Discussion Questions

1. Primary efficacy endpoint in ANNEXA-I was met, with largest treatment affect from among the 3 endpoint components consisting of the change in the hematoma volume at 12 hours. Other clinically meaningful outcomes (e.g., neurologic status at 24 hours and overall mortality) were not different between the two arms; mRS at Day 30 was worse in the andexanet arm. *Discuss whether the treatment effect on the study's primary efficacy endpoint constitutes a clinical benefit to patients.*

    - *Does an effect on hematoma volume change at 12 hours alone constitute clinical benefit?*
    - *Should neurologic status at 24 hours, mRS at Day 30, and overall mortality be incorporated into the assessment of benefit of andexanet?*
    - *Does anti-FXa reduction have a role in the assessment of the benefit of andexanet?*

2. ANNEXA-I demonstrated an increased incidence of thrombosis (14.6% versus 6.9%) and thrombosis-related deaths at Day 30 (2.5% versus 0.9%) in the andexanet arm compared to the usual care. *Are the serious risks of Andexanet as demonstrated in ANNEXA-I acceptable in the indicated population and in the context of the clinical efficacy demonstrated in ANNEXA-I?*