

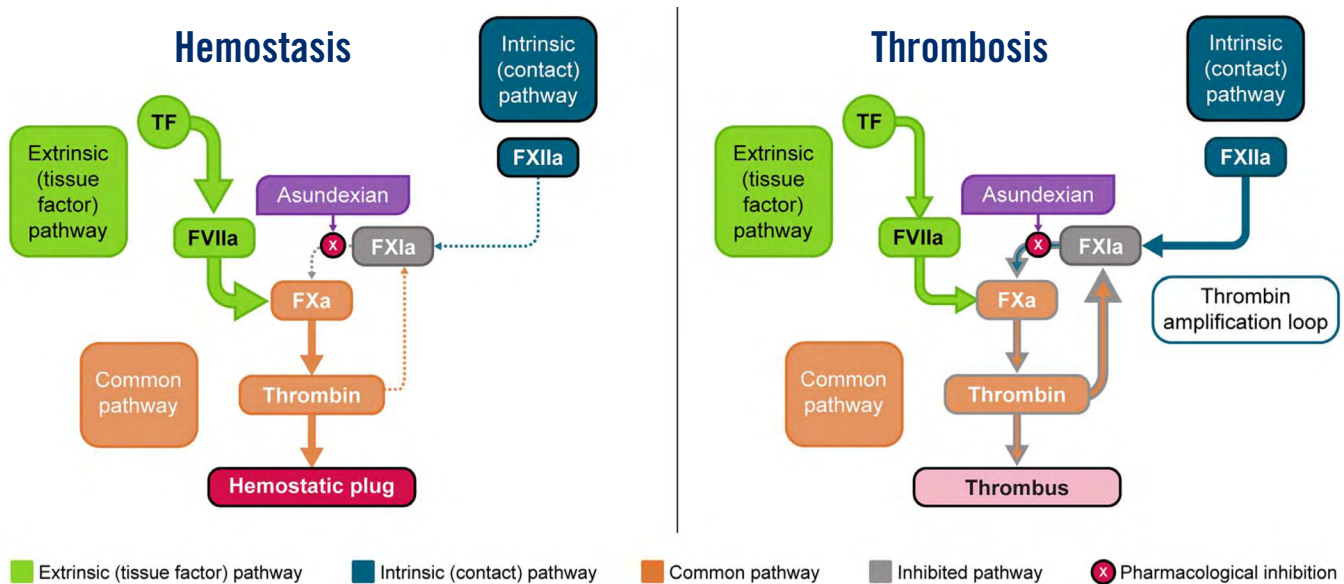


Rethinking

# SECONDARY STROKE PREVENTION: The Emerging Role of **FACTOR XI INHIBITION**

## RAPID RECAP

### The Role of FXI/XIa in Hemostasis and Thrombosis<sup>1,2</sup>



- Inhibition of FXI/XIa attenuates thrombin amplification and pathologic clot propagation<sup>1,2</sup>

## Oral FXIa Inhibitors in Clinical Trials for Stroke

- Asundexian is an orally administered small-molecule FXIa inhibitor and is currently being evaluated in the Phase 3 OCEANIC-STROKE clinical trial<sup>2,3</sup>
  - Asundexian reduced the occurrence of ischemic stroke by 26% compared to placebo in OCEANIC-STROKE
  - Efficacy was not impacted by age, sex, stroke severity, or index event
  - No increase in ISTH major bleeding between the placebo and treated groups
- Milvexian is an orally administered small-molecule FXIa inhibitor and is currently being evaluated in the Phase 3 LIBREXIA-STROKE clinical trial<sup>4,5</sup>
  - Phase 2 studies in ~2,300 participants showed no significant increase in major bleeding over placebo with or without antiplatelets
  - Efficacy and safety data of milvexian from the Phase 3 trials LIBREXIA-STROKE and LIBREXIA-AF are eagerly anticipated



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### Practical and Implementation Considerations

#### Which stroke subtypes stand to benefit the most?<sup>2,3,6</sup>

- OCEANIC-STROKE showed that efficacy was not impacted by stroke severity; subtype; or patient age, sex, or index event

#### Should FXI/XIa inhibitors be used as add-on or replacement for current therapies? Is there an optimal combination?<sup>2,3,6</sup>

- Current evidence **ONLY** supports FXIa inhibitors as add-on therapy for secondary stroke prevention
- Clinical trials **ONLY** examined FXI/XIa when added to antiplatelet therapy, and not independently

#### What is the optimal duration of treatment with FXI/XIa inhibitors?<sup>2,3,6</sup>

- So far there has been no loss of efficacy or safety of asundexian for over 780 days

#### How should patients taking FXI/XIa inhibitors be monitored? Can procedures be performed while on this treatment?<sup>2,3,6</sup>

- Monitoring schedule might be comparable to direct oral anticoagulants, and reversal strategies are unlikely to be needed
- Likely to be safe for procedures based on evidence in other clinical trials for other clinical indications

### Key Takeaways

- Current therapies to reduce risk of stroke after non-cardioembolic ischemic stroke or TIA are limited
- FXIa inhibition has the potential to block the thrombosis that leads to stroke without impacting hemorrhage risk
- Asundexian is now proven as an adjunct to antiplatelet therapy for secondary stroke prevention
  - Other indications for FXI/FXIa inhibition are under study



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### References

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