Pharmacokinetics and Pharmacodynamics of IONIS-FXI$_{Rx}$, an Antisense Inhibitor of Factor XI, in Patients with End-Stage Renal Disease on Hemodialysis

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

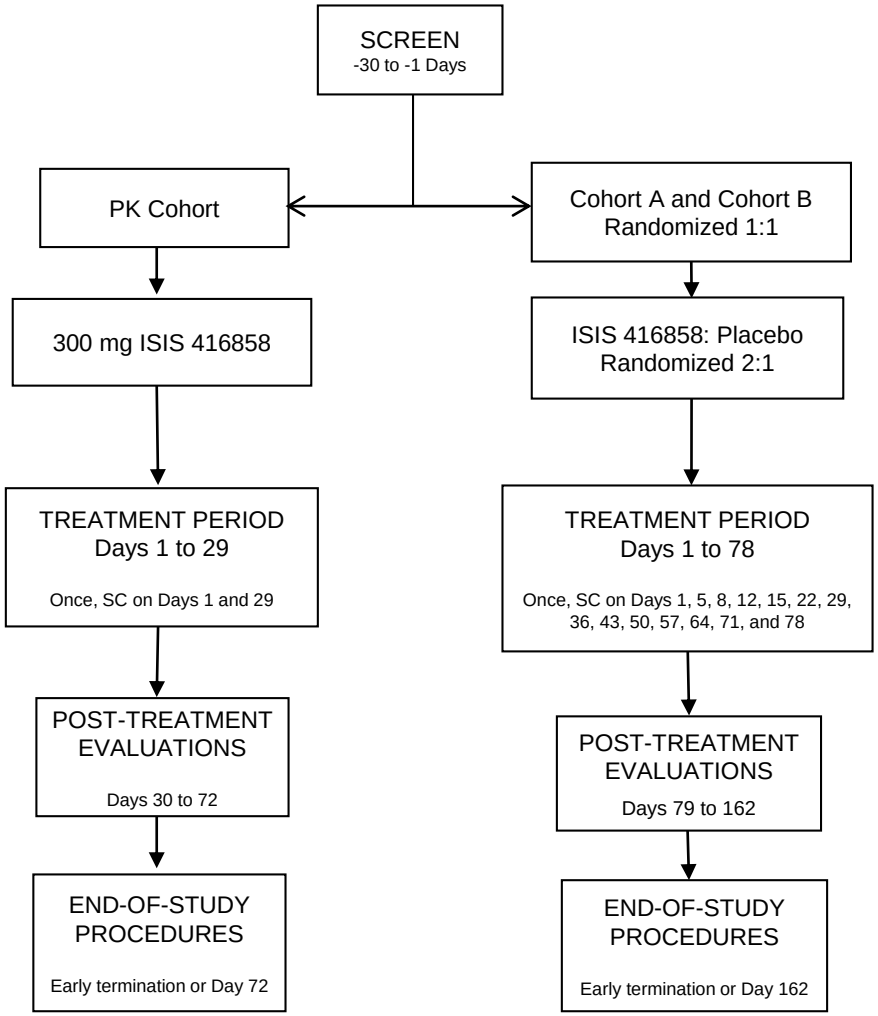
Hamilton Health Sciences
McMaster University HEALTH SCIENCES

Methods

A total of 49 ESRD patients were enrolled:

6 participants receiving chronic in-center hemodialysis (HD) to receive an open-label single-dose of 300 mg IONIS-FXI_{Rx} either 5 minutes before or 10 minutes after HD

43 participants in a double-blind design to one of two multiple-dose regimens (200 mg or 300 mg) IONIS-FXI_{Rx} or placebo for 12 weeks with 12 weeks of additional follow up. In the double-blind portion, IONIS-FXI_{Rx} was administered subcutaneously ~10 minutes after HD


SCREEN
-30 to -1 Days
PK Cohort
Cohort A and Cohort B
Randomized 1:1
300 mg ISIS 416858
ISIS 416858: Placebo
Randomized 2:1
TREATMENT PERIOD
Days 1 to 29
Once, SC on Days 1 and 29
TREATMENT PERIOD
Days 1 to 78
Once, SC on Days 1, 5, 8, 12, 15, 22, 29, 36, 43, 50, 57, 64, 71, and 78
POST-TREATMENT EVALUATIONS
Days 30 to 72
POST-TREATMENT EVALUATIONS
Days 79 to 162
END-OF-STUDY PROCEDURES
Early termination or Day 72
END-OF-STUDY PROCEDURES
Early termination or Day 162

Conclusions

This study demonstrated that:

1) *Hemodialysis had no effect on IONIS-FXI$_{Rx}$ pharmacokinetics*
2) *IONIS-FXI$_{Rx}$ was well tolerated and produced sustained, and dose-dependent reductions in FXI antigen and activity*
3) *IONIS-FXI$_{Rx}$ reduced severe dialysis circuit clotting events beyond standard heparin use.*
4) *These data support further evaluation of IONIS-FXI$_{Rx}$ as a potentially safe, effective antithrombotic therapy in ESRD patients on hemodialysis*