Anticoagulation for Stroke Prevention In patients with Recent Episodes of perioperative Atrial Fibrillation after noncardiac surgery (ASPIRE-AF)

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Background

- Patients with perioperative AF have an increased risk of stroke and death in the first month after surgery
- The benefits of oral anticoagulation seen in patients with non-operative AF suggests oral anticoagulation may also be beneficial in patients with perioperative AF
- It is unclear whether the stroke mechanisms are the same in patients with perioperative AF compared to those with non-operative AF
- Postoperative patients have an increased risk of bleeding; the benefit-risk balance of anticoagulation in this patient population is unknown
- Oral anticoagulation in high-risk postoperative patients may help to prevent other thrombotic events

Anticoagulation for Perioperative AF

- Only 20-30% of patients with perioperative AF after noncardiac surgery are anticoagulated
- Therefore, it cannot be considered standard of care in this patient population
- Guidelines acknowledge that it is unclear whether and how long patients with perioperative AF should be anticoagulated
- A randomized controlled trial (RCT) is therefore needed to assess the efficacy and safety of oral anticoagulation in patients with perioperative AF after noncardiac surgery
    - Before initiating a large endpoint trial, we need a pilot study to assess the feasibility of such a trial

Trial Design

- 100 patients with perioperative AF after noncardiac surgery that are in sinus rhythm at the time of randomization
- Prospective, randomized, open-label clinical trial with blinded outcome assessment (PROBE design)
- Randomized 1:1 to non-vitamin K oral anticoagulant (NOAC) or no anticoagulation
- 24 month follow-up period

Intervention

For the **non-vitamin K oral anticoagulation arm**, any of the following treatments are possible:

- Edoxaban 60mg daily
  Dose reduction to 30mg if specified criteria are present
- Apixaban 5mg twice daily
  Dose reduction to 2.5mg if specified criteria are present
- Dabigatran 110mg twice daily
- Rivaroxaban 20mg daily
  Dose reduction to 15 mg daily if creatinine clearance is 30-50 ml/min

For the **no anticoagulation arm**, patients are not allowed to receive oral anticoagulation (unless the patient develops a clear indication for oral anticoagulation during follow-up)

Patient Population

Inclusion Criteria:

1. Noncardiac surgery with at least an overnight hospital admission after surgery in the last 35 days
2. ≥1 episode of clinically significant perioperative AF
3. Sinus rhythm at the time of randomization
4. Any of the following high-risk criteria:
    - Age ≥55 years and having either known cardiovascular disease, recent major vascular surgery, or CHA_2DS_2VASc score ≥3, or
    - Age ≥65 and CHA_2DS_2VASc score ≥2, or
    - Age ≥75 years

Patient Population

Exclusion Criteria:

1. History of documented AF prior to noncardiac surgery
2. Need for long-term systemic anticoagulation
3. Ongoing need for long-term dual antiplatelet treatment
4. Contraindication to oral anticoagulation
5. Severe renal insufficiency (eGFR <30 ml/min)
6. Acute stroke in the past 3 months
7. Underwent cardiac surgery in the past 3 months
8. History of intracranial, intraocular, or spinal bleeding
9. Hemorrhagic disorder or bleeding diathesis
10. Expected to be non-compliant
11. Known life expectancy <1 year due to concomitant disease;
12. Women of childbearing potential
13. Previously enrolled in the trial

Outcomes

Primary Outcome:

To assess the feasibility of an RCT of NOACs vs. no anticoagulation in patients with perioperative AF after noncardiac surgery and additional stroke risk factors.

Secondary Outcomes

To collect preliminary information on the effects of NOACs on the incidence of:

1. Non-hemorrhagic stroke or systemic embolism
2. All-cause mortality
3. Vascular mortality
4. Myocardial infarction
5. Symptomatic venous thromboembolism
6. Hospitalization for congestive heart failure

Outcomes Continued

Tertiary Outcome:

To collect preliminary information on the effects of NOACs on the change in Montreal Cognitive Assessment scores.

Main Safety Outcomes

To collect preliminary information on the effects of NOACs on:

1. A composite of life-threatening, major, and critical organ bleeding
2. Major bleeding according to the ISTH criteria
3. Hemorrhagic stroke

Although we do not expect oral anticoagulation with a NOAC will affect the incidence of non-operative AF, the incidence of non-operative AF in the overall study population is a pre-specified endpoint of this trial

Follow-Up

- Clinic visits will occur at 1-month and 6 months after randomization, then every 6 months thereafter (to a maximum of 24 months)
- Telephone visits will occur at 3 months, then every 6 months thereafter (to a maximum of 24 months)
- Study ends when the last patient enrolled (n=100) has been treated for 3 months
- Montreal Cognitive Assessments to be completed at baseline, 12 months and study end