**Introduction**

- Direct oral anticoagulants (DOAC), dabigatran and rivaroxaban, had an effectiveness on stroke and systemic embolism (SSE) prevention in atrial fibrillation similar to vitamin K antagonists (VKA), but with better safety, with less major bleeding (MB) especially intracranial hemorrhage [1, 2]. However, the results correlation with the CHADS2-VASc and HAS-BLED scores is not known.

- To compare the 2-year risk of SSE and MB in new users of rivaroxaban 20mg versus VKA for NVAF in 2013, with three-year history and two-year follow-up or until death in the database.

- Study design: Cohort study in the SNDS (Système National des Données de Santé) nationwide French claims database including all new users of rivaroxaban 20mg or VKA for NVAF in 2013, with three-year history and two-year follow-up or until death in the database.

- Data source: The SNDS database contains individual pseudonymised information from 66 million persons on:
  - Gender, date of birth, area of residence, date of death;
  - Chronic disease registration (affection de longue durée, ALD) with associated ICD-10 codes for full insurance coverage (with start and end dates);
  - Outpatient reimbursed healthcare expenditures: visits, medical procedures, lab tests, drugs …;
  - Hospital discharge summaries with ICD-10 codes for diagnosis (primary, linked and associated diagnoses) for all private and public medical, obstetric and surgery hospitalisations, with the dates and duration of hospitalisation, medical procedures.

- NVAF population: Patients with chronic disease registration, hospitalisation or procedure for atrial fibrillation without rheumatic valve disease or valve replacement, and no other probable indication using three-year database history.

**Objectives**

- Outcomes: during anticoagulant exposure period (on treatment)
  - For this re-analysis, studied clinical outcomes were the following:
    - Stroke and systemic embolism, defined as a hospital admission with one of the following main diagnosis of:
      - Ischemic or undefined stroke;
      - Other systemic arterial embolism or surgical procedure for systemic arterial embolism;
      - Major bleeding, defined as a hospital admission with one of the following main diagnosis of:
        - Haemorrhagic stroke (link to matched diagnosis also considered);
        - Other critical organ or site bleeding;
        - Other bleeding with a transfusion during hospital stay, or resulting in death.

- Data analysis:
  - 1:1 matched analysis on gender, age (+1 year), day of the first drug dispensing (+14 days), duration and log of high-dimensional propensity score (hDPS) [2, 3.5];
  - 2-year cumulative incidence of outcomes using cumulative incidence function;
  - Hazard ratios (HR) (95% confidence interval (CI)) of outcomes during first prescribed anticoagulant exposure using Fine and Gray model.

*Prohibited to be treated by rivaroxaban 20mg or 15mg versus VKA using a logistic regression model with 500 variables including gender, age, stroke risk factors, bleeding risk factors, hospital and non-hospital costs.

**Methods**

**Results**

**Table 1. Baseline patient characteristics in matched NVAF populations**

<table>
<thead>
<tr>
<th>Rivaroxaban (n=15,680)</th>
<th>VKA (n=15,680)</th>
<th>Rivaroxaban (n=12,018)</th>
<th>VKA (n=12,018)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>61.9</td>
<td>61.9</td>
<td>47.3</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>71.3 (10.1)</td>
<td>71.3 (10.1)</td>
<td>80.4 (8.6)</td>
</tr>
<tr>
<td>Risk factors, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>38.2</td>
<td>39.3</td>
<td>47.1</td>
</tr>
<tr>
<td>Diabeticism</td>
<td>23.8</td>
<td>23.6</td>
<td>21.7</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>15.2</td>
<td>15.4</td>
<td>24.8</td>
</tr>
<tr>
<td>Vascular disease history</td>
<td>13.5</td>
<td>14.1</td>
<td>17.7</td>
</tr>
<tr>
<td>Stroke or transient ischemic attack history</td>
<td>11.0</td>
<td>11.3</td>
<td>11.5</td>
</tr>
<tr>
<td>Abnormal renal function</td>
<td>2.6</td>
<td>3.3</td>
<td>8.0</td>
</tr>
<tr>
<td>Abnormal liver function</td>
<td>1.5</td>
<td>1.6</td>
<td>1.6</td>
</tr>
</tbody>
</table>

**The two-year cumulative incidences of SSE and MB according to the stroke and bleeding risk scores for matched patients are presented in Tables 2 and 3.**

**Discussion**

- **EFFECTIVENESS AND SAFETY OF STANDARD AND REDUCED DOSAGE RIVAROXABAN COMPARED TO VITAMIN K ANTAGONISTS IN PATIENTS AT HIGH RISK OF BLEEDING OR STROKE**

- **Conclusions**
  - Different rivaroxaban 20mg or 15mg and VKA prescription patterns, but similar population characteristics after hDPS matching.
  - Increasing risk scores for stroke and systemic embolism and major bleeding are associated with increasing incidence of events.
  - No statistical difference in effectiveness of rivaroxaban compared to VKA at either dose.
  - Clear benefit of rivaroxaban for safety, which increases with increasing risk in the high-risk of bleeding patients given reduced dose rivaroxaban.