Effectiveness and safety of standard and reduced doses of rivaroxaban compared to vitamin K antagonists, according to stroke and bleeding risk score in non-valvular atrial fibrillation, from a hdPS matched cohort within the SNDS French nationwide claims database

N. Moore\textsuperscript{1,2}, P. Blin\textsuperscript{1}, L. Fauchier\textsuperscript{3}, F. Sacher\textsuperscript{4}, J. Dallongeville\textsuperscript{5}, C. Dureau-Pournin\textsuperscript{1}, R. Lassalle\textsuperscript{1}, M-A. Bernard\textsuperscript{1}, C. Droz-Perroteau\textsuperscript{1}

\textsuperscript{1}Bordeaux PharmacoEpi, INSERM CIC1401, Université de Bordeaux, Bordeaux, France - \textsuperscript{2}INSERM U1219, Bordeaux, France - \textsuperscript{3}CHU, Tours, France - \textsuperscript{4}LIRYC, CHU, Pessac, France - \textsuperscript{5}Institut Pasteur, Lille, France

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Disclosure statement

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• Designed, conducted and analysed independently by the Bordeaux PharmacoEpi platform of Bordeaux University
• Supervised by a scientific committee who received expert fees from Bayer AG
Background

• In **clinical trials**, direct oral anticoagulants (DOAC) had generally similar effectiveness on stroke and systemic embolism to vitamin K antagonists (VKA) in non-valvular atrial fibrillation (NVAF), but better safety with fewer major bleeding, especially intracranial, and fewer deaths.

• In **real-life setting**, these results were confirmed for drugs overall, and for standard and reduced doses of rivaroxaban or dabigatran.

• However, results according to **CHAD2DS2-VASc** and **HAS-BLEB risk scores** are sparse.
Objectives

• To compare **2-year risk** of outcomes
  - **Effectiveness**: stroke and systemic embolism (SSE)
  - **Safety**: major bleeding (MB)

• Between **new rivaroxaban or VKA users for NVAF**
  - Rivaroxaban 20mg (standard dose) *versus* VKA
  - Rivaroxaban 15mg (dose recommended for patients with moderate or severe renal failure) *versus* VKA

• In **real-life setting** according to
  - CHAD$_2$DS$_2$-VASc score
  - HAS-BLEB score
Method (1)

• **Cohort study**
  - In the 66 million persons French nationwide claims database (SNDS, *Système National des Données de Santé*)
  - New users of rivaroxaban 20mg, 15mg or VKA for NVAF in 2013
  - With 3-year history and 2-year follow-up

• **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 (3-year history)
Method (2)

• Outcomes (on treatment)
  – **SSE**: 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
  – **MB**: hospital admission with one of the following main diagnosis of
    ✓ Haemorrhagic stroke (linked or associated diagnosis also considered)
    ✓ Other critical organ or site bleeding
    ✓ Other bleeding with a transfusion during hospital stay, or resulting in death
Method (3)

- **Data analysis**
  - 1:1 matched analysis on gender, age (± 1 year), date of first anticoagulant dispensing (± 14 days), and logit of high-dimensional propensity score (hdPS)* (± 0.2 SD)
  - 2-year cumulative incidence of outcomes using cumulative incidence function
  - **Comparison of risk** using Fine and Gray model

*Probability 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
Results: Populations

- **86,517** new users of rivaroxaban or VKA for NVAF in 2013 in France
  - 20,465 rivaroxaban 20mg
  - 12,800 rivaroxaban 15mg
  - 53,252 VKA

- **Matched populations**
  - 15,680 per arm for rivaroxaban 20mg *versus* VKA (77% of rivaroxaban 20mg group)
  - 12,018 per arm for rivaroxaban 15mg *versus* VKA (94% of rivaroxaban 15mg group)
hdPS distributions (1)

Rivaroxaban 20mg vs VKA

All patients

Rivaroxaban 15mg vs VKA
hdPS distributions (2)

Rivaroxaban 20mg vs VKA

Rivaroxaban 15mg vs VKA

All patients

Matched patients
### Baseline patient characteristics

<table>
<thead>
<tr>
<th>Matched populations</th>
<th>Rivaroxaban 20mg n = 15,680</th>
<th>VKA n = 15,680</th>
<th>Rivaroxaban 15mg n = 12,018</th>
<th>VKA n = 12,018</th>
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<td>61.9</td>
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<td>Age, mean (± SD)</td>
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<td>71.3 (10.1)</td>
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<td>80.4 (8.6)</td>
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Events by score

MB by HAS-BLED score: VKA

SSE by CHA₂DS₂-VASc score: VKA
Stroke and systemic embolism

SSE by CHA$_2$DS$_2$-VASc score: R15 vs. VKA

SSE by CHA$_2$DS$_2$-VASc score: R20 vs. VKA
Major bleeding

MB by HAS-BLED score: R15 vs. VKA

MB by HAS-BLED score: R20 vs. VKA
Discussion / Conclusion

This nationwide cohort study of new rivaroxaban or VKA users for NVAF shows:

• Different rivaroxaban 20mg or 15mg and VKA prescription patterns in France, but similar population characteristics after hdPS matching

• Increasing incidence of SSE and MB with increasing risk scores

• No statistical difference in effectiveness of rivaroxaban compared to VKA at either dose

• Clear benefit of rivaroxaban for safety, in the high-risk of bleeding patients given reduced dose rivaroxaban
Thank you

nicholas.moore@u-bordeaux.fr

Bordeaux PharmacoEpi - http://www.pharmacoepi.eu
Plateforme de recherche en Pharmaco-épidémiologie
CIC Bordeaux CIC1401
INSERM - Université de BORDEAUX - CHU de Bordeaux - Adera
Bâtiment Le Tondu - case 41 - 146 rue Léo Saignat - 33076 Bordeaux Cedex
Acc. +33 (0)5 57 57 46 75 – Fax +33 (0)5 57 57 47 40