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

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Disclosure statement

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- 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 **$CHAD_2DS_2$-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
  - **$CHAD_2DS_2$-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

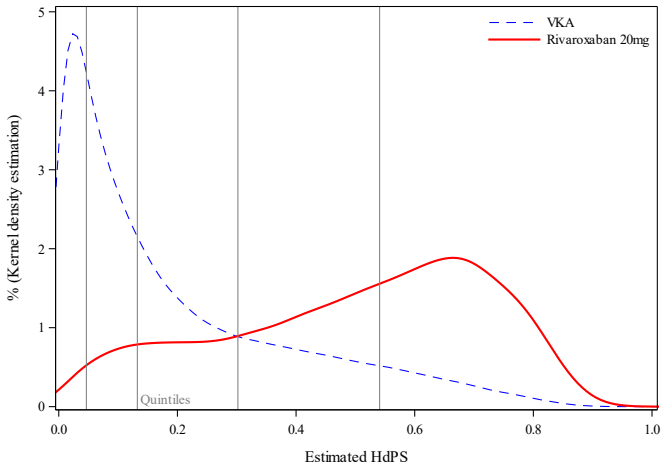
- **86,517** new users of rivaroxaban or VKA for NVAF in 2013 in France
  - 20,465 rivaroxaban 20mg
  - 12,800 rivaroxaban 15mg
  - 53,252 VKA

- **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)

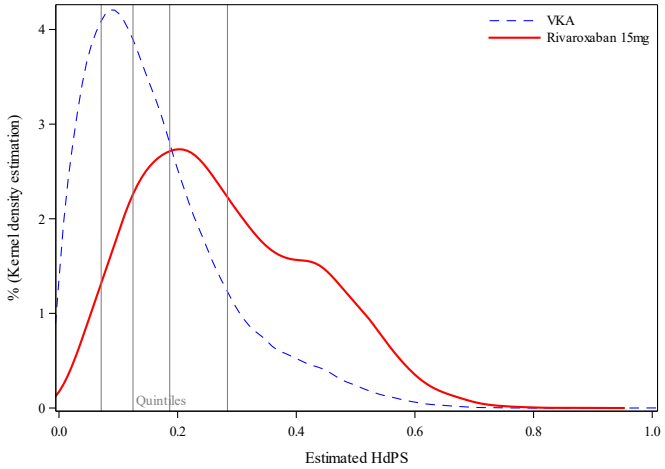
hdPS distributions (1)

All patients

Rivaroxaban 20mg *vs* VKA



Rivaroxaban 15mg *vs* VKA

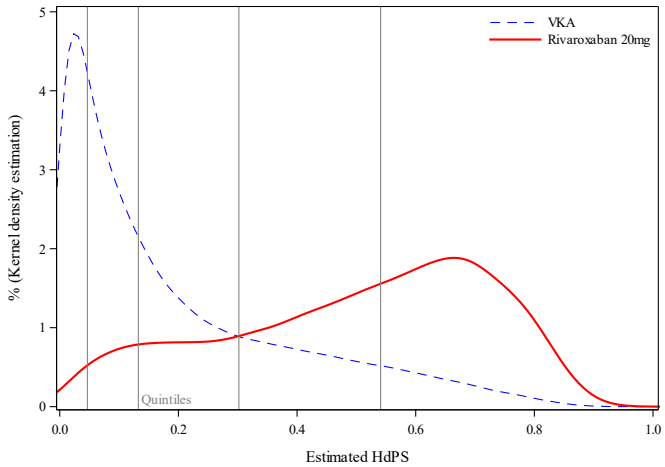


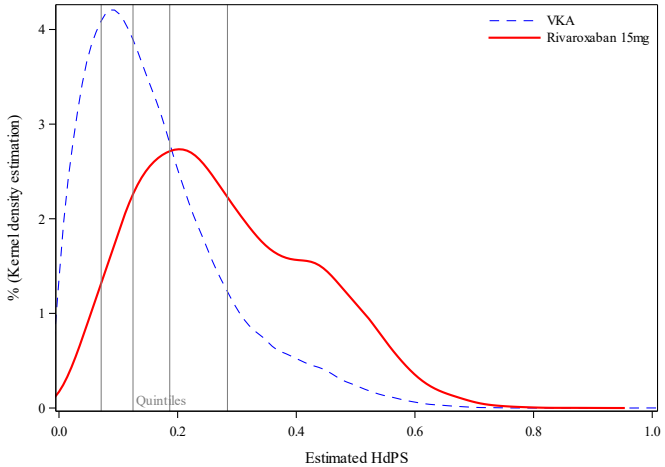
hdPS distributions (2)

Rivaroxaban 20mg *vs* VKA

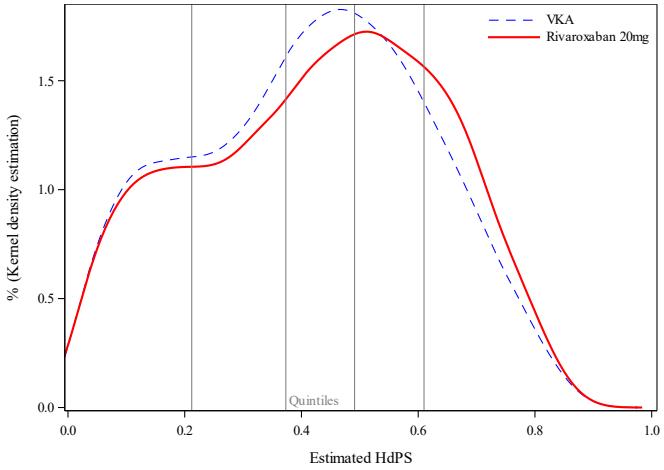
Rivaroxaban 15mg *vs* VKA

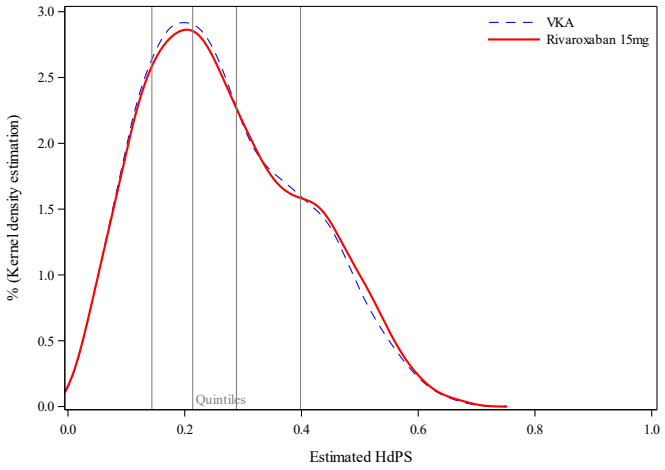
All patients





Matched patients

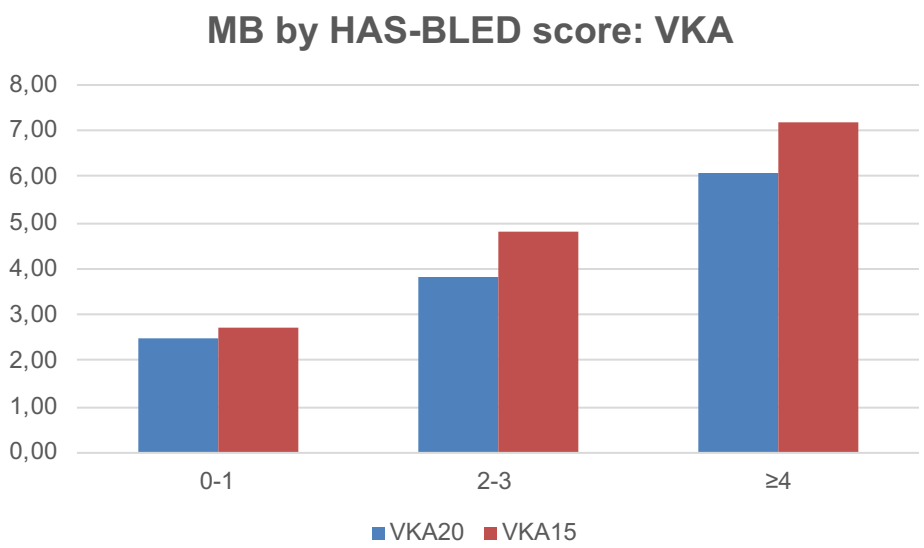


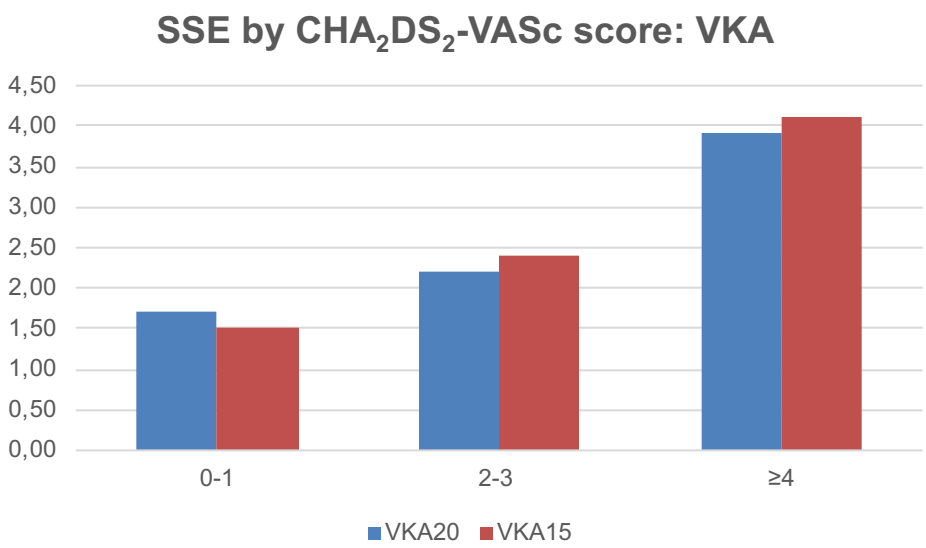


Baseline patient characteristics

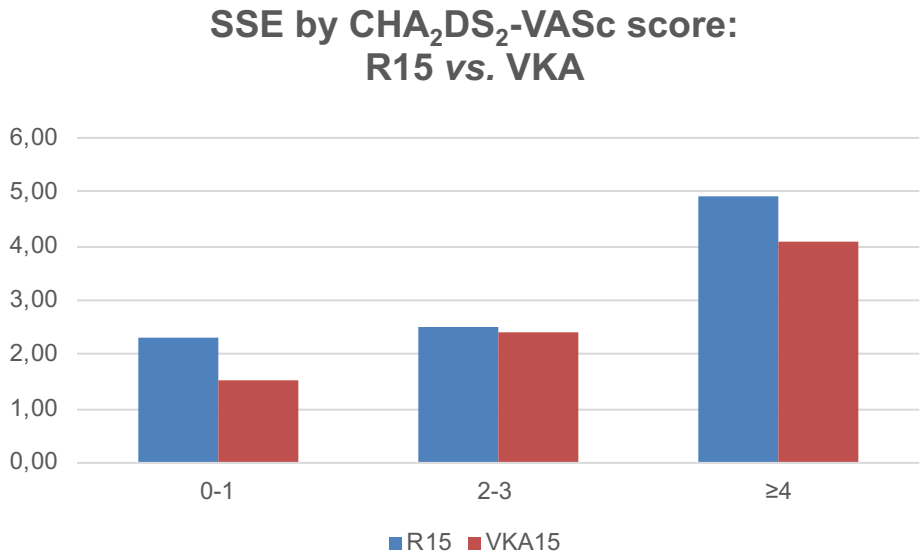
	Matched populations			
	Rivaroxaban 20mg n = 15,680	VKA n = 15,680	Rivaroxaban 15mg n = 12,018	VKA n = 12,018
Male, %	61.9	61.9	47.3	47.3
Age, mean (± SD)	71.3 (10.1)	71.3 (10.1)	80.4 (8.6)	80.4 (8.6)
Risk factors, %				
Hypertension	38.2	39.3	47.1	47.9
Diabetes mellitus	22.8	23.6	21.7	21.9
Congestive heart failure	15.2	15.4	24.8	24.6
Vascular disease history	13.5	14.1	17.7	18.0
Stroke or transient ischemic attack history	11.0	11.3	11.5	11.9
Abnormal renal function	2.8	3.3	8.0	8.6
Abnormal liver function	1.5	1.6	1.6	1.7
CHA_2DS_2-VASc score				
0-1	24.1	24.1	6.8	6.5
2	24.2	23.0	16.1	15.6
3	23.2	23.0	27.5	27.4
≥ 4	28.4	29.9	49.6	50.5
HAS-BLED score				
0-1	36.5	34.8	21.9	20.3
2-3	58.2	60.0	68.3	69.8
> 3	5.2	5.1	9.8	9.9

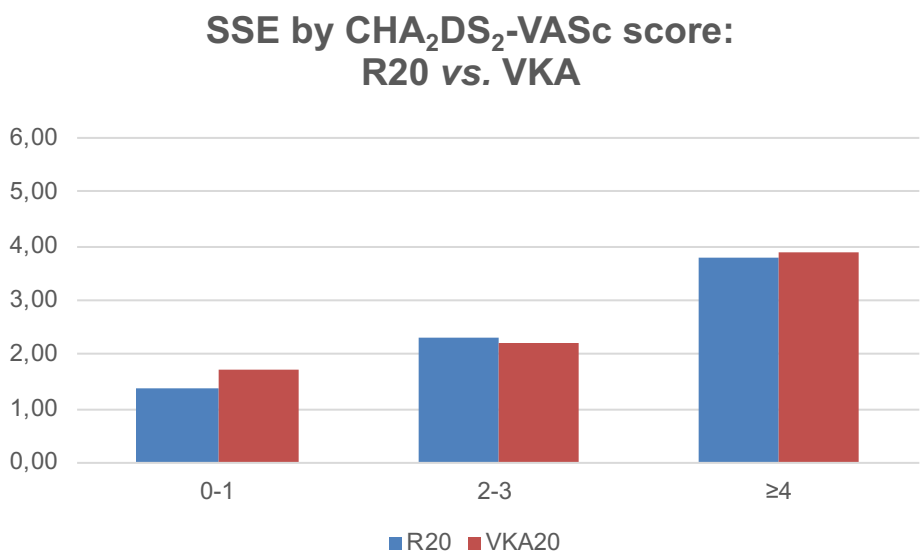
Events by score



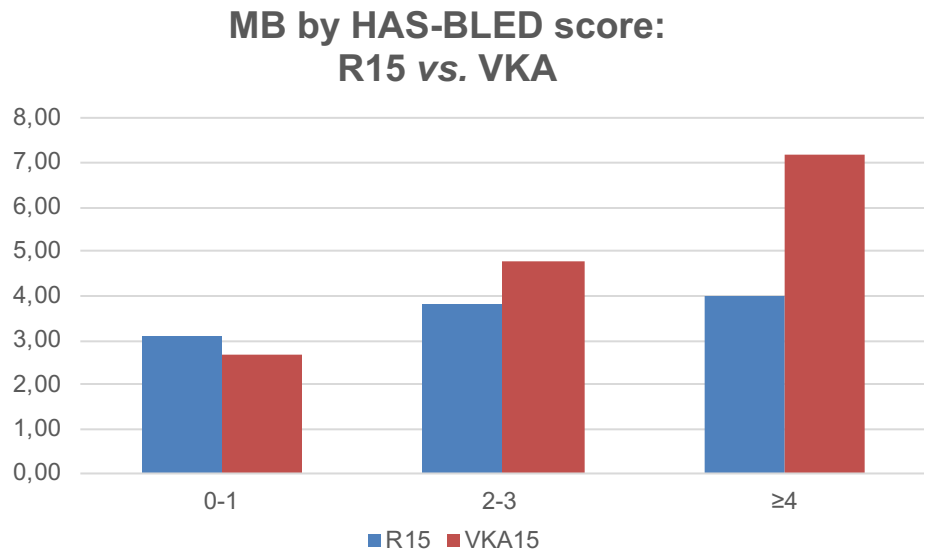


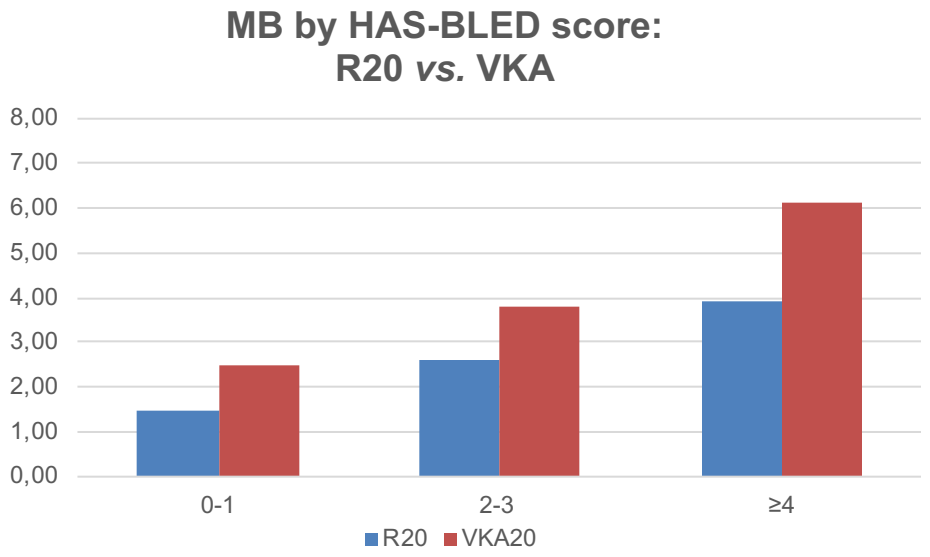
Stroke and systemic embolism





Major bleeding





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

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