Société Française de Cardiologie

Effectiveness and safety of standard and reduced doses of dabigatran versus rivaroxaban in non-valvular atrial fibrillation: a cohort study in the French nationwide claims database SNDS

P. Blin[1], Y. Cottin[2], C. Dureau-Pournin[1], A. Abouelfath[1], R. Lassalle[1], J. Bénichou[3,4], G. de Pouvourville[5], P. Mismetti[6], C. Droz-Perroteau[1], N. Moore[1,4]

[1]Bordeaux PharmacoEpi, INSERM CIC1401, Université de Bordeaux, Bordeaux – [2]CHU, Dijon – [3]CHU, Rouen – [4]INSERM U1219, Bordeaux – [5]ESSEC, Cergy-Pontoise – [6]CHU, Saint-Etienne

- **Background:** Dabigatran and rivaroxaban showed better benefit-risk than VKA for stroke prevention in non-valvular atrial fibrillation (NVAF), but no randomized trial compared dabigatran versus rivaroxaban
- **Objectives:** To compare 2-year risk of major benefit-risk outcomes between new users of dabigatran and rivaroxaban (standard and reduced doses) for NVAF during drug exposure, i.e. “on treatment”
- **Method:**
  - **Cohort study**: All new users of dabigatran or rivaroxaban in 2013 (3-year history, as well as no other DOAC or VKA) for NVAF identified and followed for 2 years in the SNDS (*Système National des Données de Santé)* database
  - **Outcomes**:
    - Hospitalisation with primary diagnosis for clinically relevant bleeding (CRB), major bleeding, stroke and systemic embolism (SSE), and acute coronary syndrome (ACS)
    - Death (all-cause)
    - Composite criterion: First event among CRB, SSE, ACS, or death
- **Statistical analysis:** Dabigatran versus rivaroxaban according to the dose
  - 1:1 matched analysis on gender, age, date of first anticoagulant dispensing, and high-dimensional propensity score (hdPS)*
  - Hazard ratios (HR) [95% confidence interval (CI)] of outcomes during drug exposure, using Cox proportional hazard risk model (death, composite) or Fine and Gray model (other outcomes) for crude, hdPS adjusted with all patients and matched analyses

* Probability to be treated by dabigatran versus rivaroxaban (standard or reduced doses) using a logistic regression model with 500 variables including gender, age, stroke and bleeding risk factors

Société Française de Cardiologie

- **Populations:**
  - 56,403 new users of dabigatran and rivaroxaban for NVAF in 2013
    - 8,290 matched patients per arm for standard doses comparison
    - 7,639 matched patients per arm for reduced doses comparison
  - Patient characteristics and hdPS distribution showed differences between groups which were dramatically reduced after matching (**Table 1, Figure 1**). For both comparisons, standardized differences after matching were < 10% for all variables, even < 2% for most variables (**Figure 2**)

Table 1. Main patient characteristics in all and matched NVAF populations

	Standard dose				Reduced dose			
	All patients		Matched patients		All patients		Matched patients	
	Dabigatran n = 10,847	Rivaroxaban n = 18,829	Dabigatran n = 8,290	Rivaroxaban n = 8,290	Dabigatran n = 15,532	Rivaroxaban n = 11,195	Dabigatran n = 7,639	Rivaroxaban n = 7,639
Male, %	68.3	69.7	69.7	69.7	48.5	46.6	46.4	46.4
Age, mean (± SD)	65.3 (10.2)	69.0 (11.1)	66.9 (8.8)	66.9 (8.8)	78.5 (9.5)	79.9 (9.3)	80.4 (7.5)	80.4 (7.6)
Risk factors, %								
Hypertension	31.0	33.0	29.0	29.4	45.3	44.2	43.1	44.0
Diabetes mellitus	19.9	19.8	19.3	19.6	20.5	20.3	19.4	19.8
Vascular disease history	11.1	11.0	8.9	8.9	19.6	20.5	14.0	14.9
Congestive heart failure	8.9	11.1	9.8	9.8	14.4	16.1	18.4	19.4
Stroke or TIA history	8.4	9.2	7.9	7.8	13.3	11.2	11.2	11.5
Abnormal renal function	1.3	2.1	1.2	1.1	4.6	6.9	4.9	5.0
Abnormal liver function	1.2	1.2	0.9	1.1	1.6	1.6	1.5	1.5
CHA_2DS_2-VASc score ≥ 2	57.1	67.4	59.3	58.5	92.3	91.0	94.0	93.9
HAS-BLED score ≥ 3	15.7	20.0	15.4	15.8	35.2	33.9	34.8	33.2

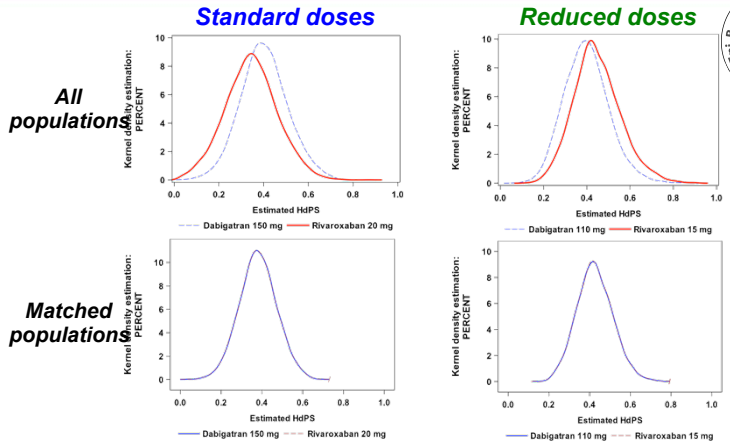


Figure 1. hdPS distribution in all and matched populations

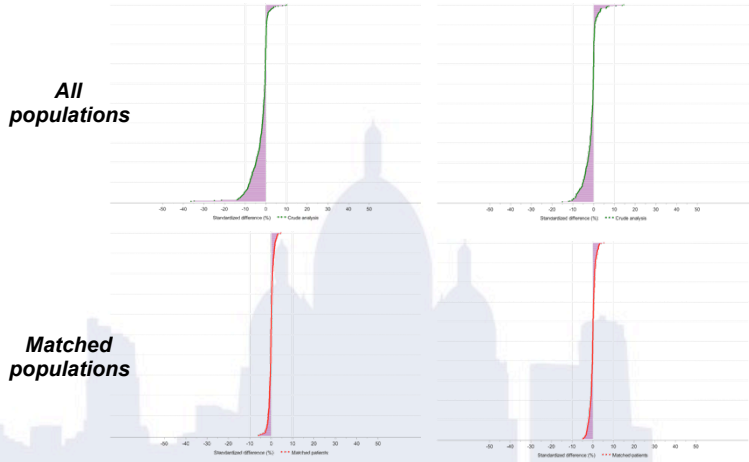
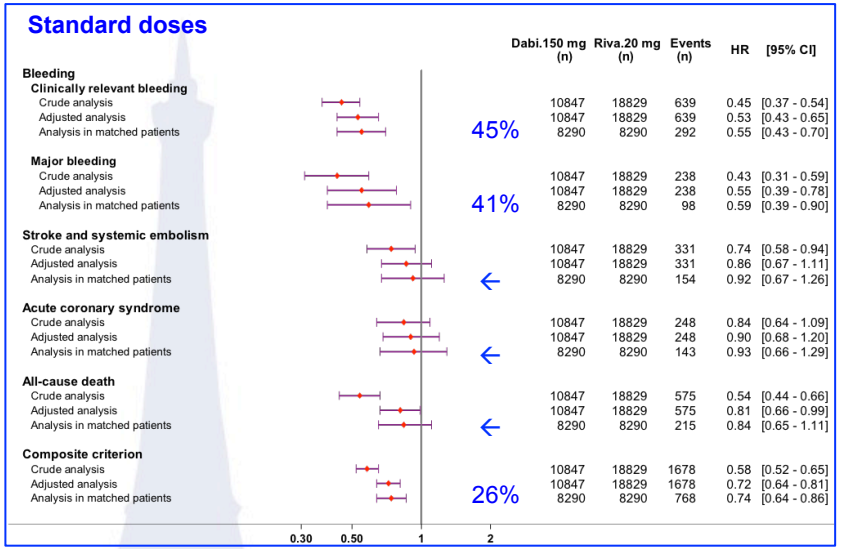


Figure 2. Standardized differences for all and matched populations

- **Benefit-risk: Figure 3**



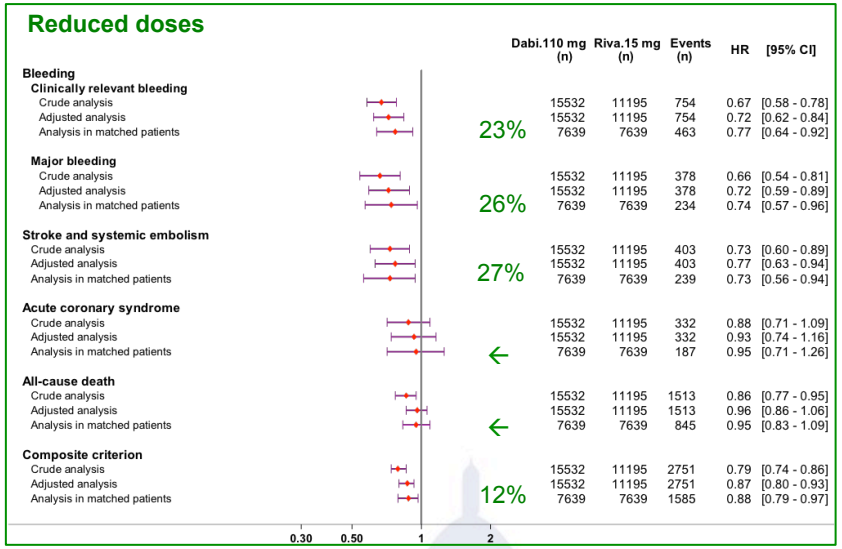


Figure 3. Hazard ratios and 95% CI of outcomes

- **Conclusions:** This nationwide cohort study of new dabigatran or rivaroxaban users for NVAF shows in real-life
  - Some differences of prescription patterns between dabigatran and rivaroxaban according to doses in France
  - No difference of effectiveness between two DOAC standard dose but a safer bleeding risk for dabigatran
  - Better effectiveness and bleeding risk of dabigatran than rivaroxaban for reduced dose
  - An overall benefit-risk profile in favour of dabigatran for both doses
  - When compared within similar patients in hdPS matched groups, as well as for all patients and adjusted analysis