Pharmacologie médicale

Bordeaux PharmacoEpi
CIC Bordeaux CIC1401

Comparative effectiveness and medical cost of dabigatran *versus* vitamin K antagonists from ENGEL 2: A French nationwide cohort of 100,000 patients with non-valvular atrial fibrillation

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

[1] Bordeaux PharmacoEpi, INSERM CIC1401, University of Bordeaux, Bordeaux, France – [2] ESSEC, Cergy-Pontoise, France – [3] CHU, Dijon, France – [4] CHU, Rouen, France – [5] INSERM U1219, Bordeaux, France – [6] Hôpital Nord, Saint-Etienne, France

Background

- Dabigatran (Pradaxa®), rivaroxaban (Xarelto®), and apixaban (Eliquis®), direct oral anticoagulants (DOAC), had better benefit-risk than vitamin K antagonists (VKA) for non-valvular atrial fibrillation (NVAF) in clinical trials.
- French health authorities have questioned the generalization of these results in current practice, where physicians, patients, drug prescription and use may not be the same as those of the clinical trials.

Disclosure statement

This study was supported by an unconditional grant from Boehringer Ingelheim France. It was designed, conducted, and analysed independently by the Bordeaux PharmacoEpi of the Bordeaux University. It was overseen by independent experts.

Objectives

The aim of the ENGEL 2 study was to compare effectiveness, risk and medical costs of dabigatran *versus* VKA for NVAF in real-life setting.

Methods

Study design

Cohort study in the SNDS nationwide French claims database including all new users of anticoagulant for NVAF in 2013, with three-year history and one-year follow-up in the database.

Data source

The SNDS database contains individual pseudonymised information on:

- Gender, date of birth, area of residence, date of death;
- Long-term disease (LTD) registration with associated ICD-10 codes for full insurance coverage (with start and end dates);
- Outpatient reimbursed healthcare expenditures with codes, cost, date of event and date of prescription, prescriber and professional caregiver information;
- 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 date and duration of hospitalisation, medical procedures, cost coding system (diagnosis related group, DRG).

NVAF population

Patients with long-term disease registration, hospitalisation or procedure for atrial fibrillation without valvular disease history, and nor other probable indication using three-year database history.

Outcomes: during anticoagulant exposure (on treatment)

- Clinical events: hospital admission with main diagnosis of
  - Clinically relevant bleeding (CRB)
  - Arterial thrombotic event (ATE)
  - Acute coronary syndrome (ACS)
- Death (all-cause)
- Composite criterion: first event among CRB, ATE, ACS or death.

Data analysis

- 1:1 matched analysis on gender, age, high-dimensional propensity score* (hdPS), and date of 1st drug dispensing.
- Hazard ratios (HR) of outcomes during drug exposure using Cox proportional hazard risk model (death, composite) or Fine and Gray model (other outcomes).
- Medical costs estimated in euros (€) according to the collective perspective for the same period using DRG for hospitalisations and claims reimbursement for outpatient healthcare resources.

* Probability to be treated by dabigatran *versus* VKA using a logistic regression model with 500 variables including gender, age, stroke risk factors, bleeding risk factors

Results

Populations

- Of 371,539 new users of dabigatran, rivaroxaban, or VKA in 2013, 103,101 were included in the NVAF population: **27,060 dabigatran**, 31,388 rivaroxaban, and **44,653 VKA**.
- Patient characteristics showed differences between groups, and were normalized after matching (Table 1).
- For dabigatran *versus* VKA, **20,489 patients were matched** per arm.

Table 1. Main patient characteristics in all and matched NVAF populations: dabigatran versus VKA

	All patients		Matched patients		Standardized difference (%) Dabigatran *versus* VKA		
	Dabigatran n = 27,060	VKA n = 44,653	Dabigatran n = 20,489	VKA n = 20,489	Crude	Adjusted	Matched
Male, %	56.4	51.2	54.5	54.5	-10.4	0.1	0.0
Age (in years), mean (± SD)	73.2 (11.8)	77.9 (11.1)	75.3 (10.7)	75.4 (10.7)	-40.8	-1.3	-0.2
Risk factors, %							
Hypertension	39.4	53.3	43.2	44.0	-28.2	0.3	-1.7
Diabetes mellitus	20.3	26.2	21.7	22.9	-14.1	-0.4	-3.0
Vascular disease history	12.2	21.6	14.2	14.4	-25.4	0.6	-0.7
Congestive heart failure	16.2	30.7	19.3	19.9	-34.7	0.7	-1.4
Stroke or TIA history	11.4	15.0	12.9	12.9	-10.8	2.0	0.0
Abnormal renal function	3.3	16.6	4.3	4.8	-43.5	-1.6	-2.4
Abnormal liver function	1.5	3.1	1.7	1.8	-7.4	0.0	-0.2
CHA_2DS_2-VASc score ≥ 2	77.3	89.5	83.2	83.5	-33.1	4.9	-0.9
HAS-BLED score ≥ 3	26.5	45.0	31.5	31.5	-39.3	3.8	-0.2

Results

Effectiveness of dabigatran *versus* VKA

The risk of all outcomes (ATE, CRB, ACS, death, and composite) was significantly lower with dabigatran than VKA, with 29% less events for the composite of all events (HR: 0.71, 95%CI [0.66 to 0.76]) (Figure 1).

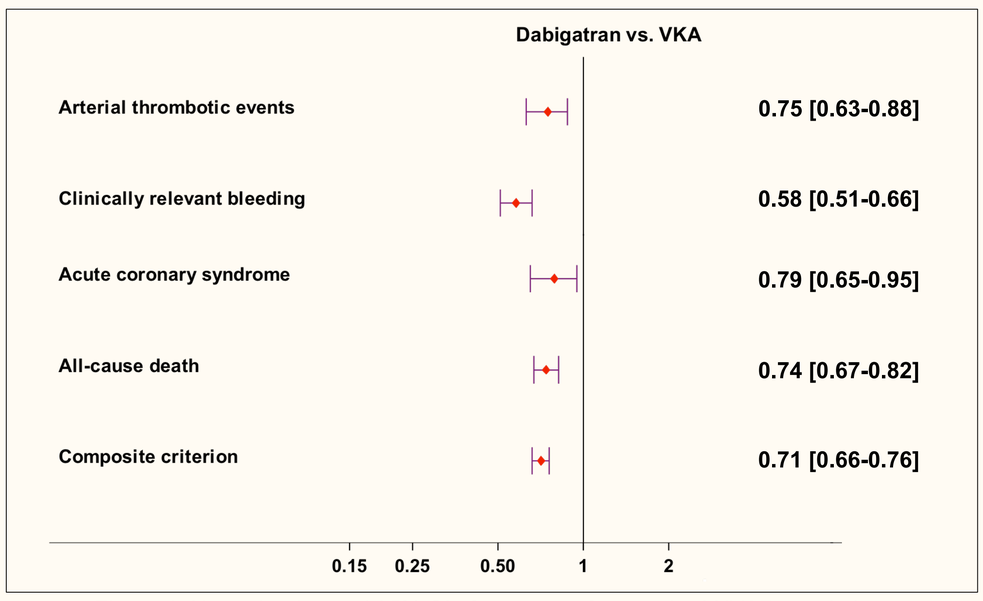

Figure 1. Hazard ratios and 95% CI of outcomes for matched NVAF populations

Medical cost of dabigatran *versus* VKA

The mean medical cost per patient followed during drug exposure was €6,747 for patients treated with dabigatran and €8,009 for those treated with VKA (Table 2, Figure 2):

- The mean cost per patient was higher with dabigatran compared to VKA for AF drugs (€637 *vs* €94);
- The mean cost per patient was lower with dabigatran for the majority of healthcare resources including lab tests (€162 *vs* €384), nursing acts (€450 *vs* 702€), medical visits (€722 *vs* €768), transport (€177 *vs* €247), and cardiovascular hospitalisations (€1,649 *vs* €2,058).

Table 2. Specific AF costs and general healthcare resources costs according to the collective perspective during drug exposure period in dabigatran and VKA matched NVAF populations

	Dabigatran n = 20,489		VKA n = 20,489	
	Mean (± SD)	[p25%; p75%]	Mean (± SD)	[p25%; p75%]
Specific AF* costs (in €) per patient				
Total specific cost	1683.4 (2461.9)	[398.5; 1610.0]	1494.1 (2755.6)	[298.5; 1256.2]
AF* drugs	637.2 (406.0)	[237.7; 1031.0]	94.4 (69.8)	[39.9; 138.2]
Specific medical consultations and visits	129.3 (112.5)	[46.0; 184.0]	156.4 (128.3)	[66.0; 217.0]
Specific lab tests	27.2 (51.8)	[3.8; 32.2]	243.3 (241.6)	[84.3; 329.8]
Specific hospitalisations	862.3 (2365.5)	[0.0; 626.1]	948.8 (2675.2)	[0.0; 0.0]
Specific transport	27.3 (101.4)	[0.0; 0.0]	51.2 (241.5)	[0.0; 0.0]
Overall costs (in €) per patient				
Total medical cost **	6747.4 (7475.8)	[1943.2; 8986.3]	8008.7 (9315.9)	[1995.7; 10613.4]
Cardiovascular hospitalisations	1649.1 (3817.3)	[0.0; 1637.3]	2057.8 (4769.7)	[0.0; 2033.5]
Non-cardiovascular hospitalisations	1464.8 (3830.2)	[0.0; 787.2]	1997.5 (4904.1)	[0.0; 1387.7]
Cardiovascular and antidiabetic drugs	922.4 (657.0)	[332.6; 1364.8]	444.6 (425.0)	[163.1; 583.9]
Medical consultations, visits and technical acts	721.6 (938.7)	[200.0; 894.3]	767.9 (984.5)	[232.0; 917.8]
Nursing acts	449.7 (1789.3)	[0.0; 73.8]	702.3 (1967.9)	[23.1; 365.7]
Non-cardiovascular and non-antidiabetic drugs	426.0 (1189.3)	[58.0; 460.0]	516.3 (1742.1)	[77.5; 517.1]
Products and services	330.3 (972.9)	[0.0; 181.2]	404.5 (1153.2)	[0.0; 261.3]
Other medical healthcare resources	193.7 (579.0)	[0.0; 80.0]	188.3 (556.1)	[0.0; 80.0]
Transport	176.9 (698.8)	[0.0; 128.9]	246.5 (878.4)	[0.0; 194.6]
Lab tests	161.9 (211.8)	[38.9; 209.0]	383.6 (337.4)	[171.5; 503.0]
Physiotherapy acts	150.9 (502.9)	[0.0; 0.0]	183.3 (558.8)	[0.0; 73.3]
Public hospital external consultations and acts	108.2 (213.2)	[0.0; 140.9]	132.8 (232.8)	[0.0; 178.2]
Assistances, pensions and disability allowances	139.4 (1016.1)	[0.0; 0.0]	143.7 (1030.2)	[0.0; 0.0]
Daily allowances	100.3 (1035.3)	[0.0; 0.0]	114.2 (940.9)	[0.0; 0.0]
Other non-medical healthcare resources	4.4 (241.0)	[0.0; 0.0]	4.1 (163.1)	[0.0; 0.0]

* Atrial fibrillation; ** Cost of all healthcare expenditures, except "Assistance, pensions and disability allowances", "Daily allowances" and "Other non-medical healthcare resources"

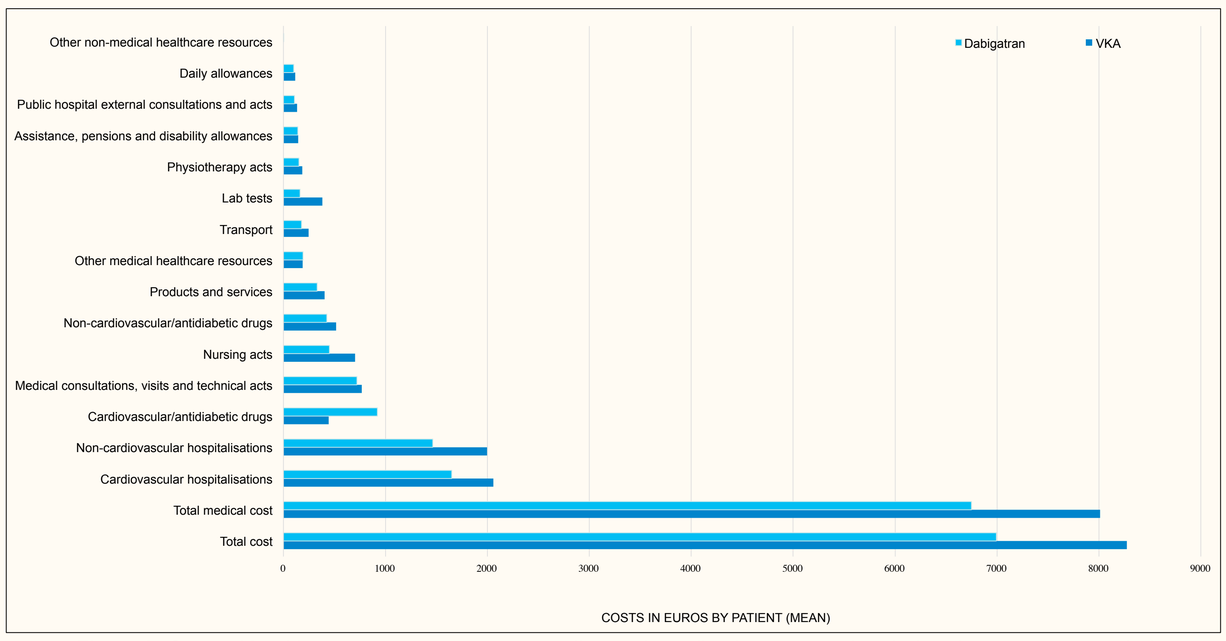

Figure 2. General healthcare resources costs according to the collective perspective during drug exposure period in dabigatran and VKA matched NVAF populations

Conclusions

- **Different dabigatran and VKA prescription patterns, but similar populations after matching.**
- **All clinical results for studied outcomes in favour of dabigatran.**
- **Dabigatran for NVAF is cost-saving due to its better benefit-risk in real-life setting with a 16% lower medical cost for the collective perspective.**

ISPOR 20th Annual European Congress, 4-8 November 2017, Glasgow, Scotland