TAVI WITH ATRIAL FIBRILLATION: WHICH ANTITHROMBOTIC REGIMEN?

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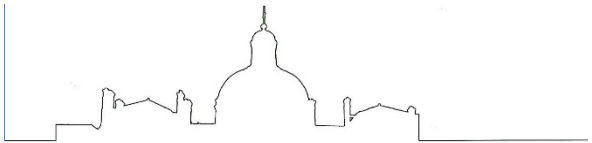

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European Heart Journal (2016) **37**, 2893–2962
doi:10.1093/eurheartj/ehw210

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Vitamin K antagonist therapy (INR 2.0–3.0 or higher) is recommended for stroke prevention in AF patients with moderate-to-severe mitral stenosis or mechanical heart valves.	I	B
NOACs (apixaban, dabigatran, edoxaban, and rivaroxaban) are not recommended in patients with mechanical heart valves (Level of evidence B) or moderate-to-severe mitral stenosis (Level of evidence C).	III (harm)	B

TAVI?

European Heart Journal (2012) **33**, 2451–2496
doi:10.1093/eurheartj/ehs109

ESC/EACTS GUIDELINES

Guidelines on the management of valvular heart disease (version 2012)

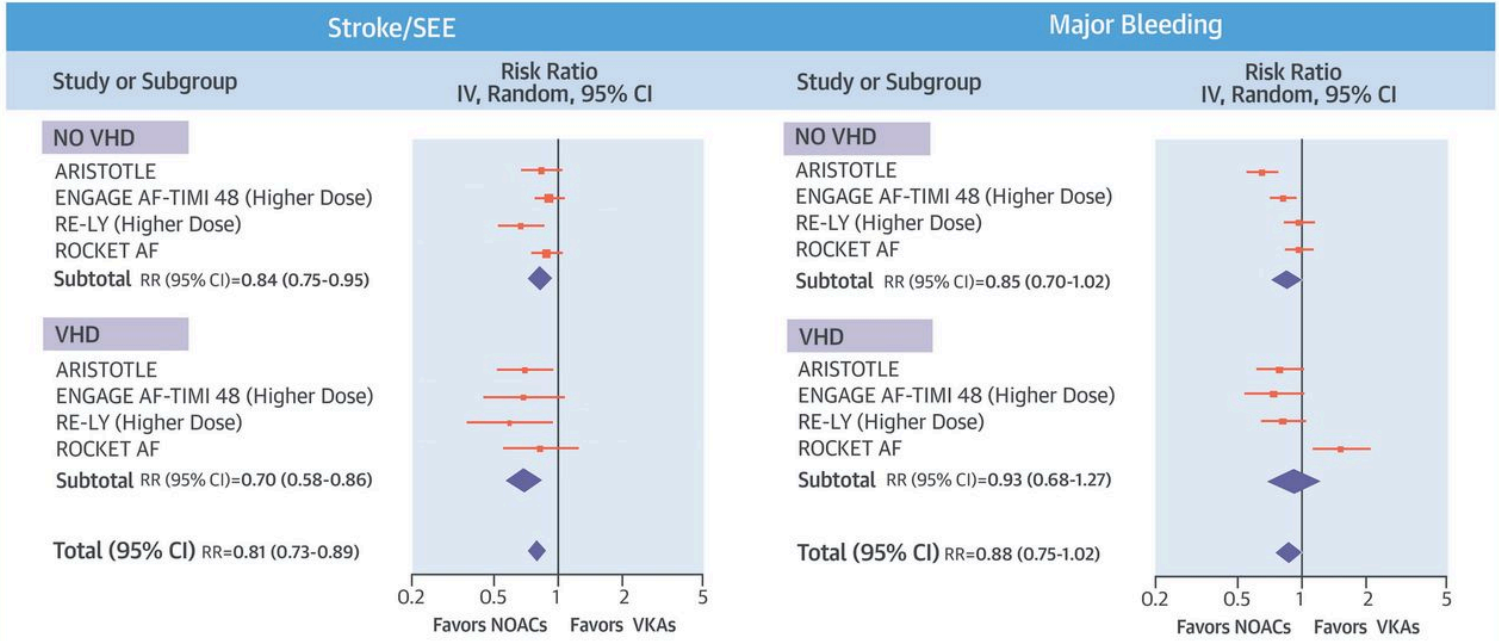
Oral anticoagulation is recommended lifelong for patients with bioprostheses who have other indications for anticoagulation.[d]	I	C	

TAVI?

Is A.Fib in a TAVI patient, a valvular A.Fib?

- Valvular A.Fib is A.Fib in patients with a mechanical prosthesis *or* moderate-to-severe mitral stenosis
- Patients with biological heart valves or valve repair have been included in some trials on non-valvular A.Fib
- There is no prospective data on A.Fib in TAVI patients

CENTRAL ILLUSTRATION: SSEE and Major Bleeding in Patients Without and With VHD, Treated With Higher-Dose NOACs or Warfarin



Renda, G. et al. J Am Coll Cardiol. 2017;69(11):1363-71.

EHRA update on NOAC use

Table 1 Valvular indications and contraindications for NOAC therapy in AF patients

	Eligible	Contra-indicated
Mechanical prosthetic valve		✓
Moderate to severe mitral stenosis (usually of rheumatic origin)		✓
Mild to moderate other native valvular disease	✓	
Severe aortic stenosis	✓ Limited data. Most will undergo intervention	
Bioprosthetic valve[a]	✓ (except for the first 3 months post-operatively)	
Mitral va		
PTAV ar		
Hypertr		

✓
(but no prospective data; may require combination with single or double antiplatelets: consider bleeding risk)

PTAV, percutaneous transluminal aortic valvuloplasty; TAVI, transcatheter aortic valve implantation.
[a]American guidelines do not recommend NOAC in patients with biological heart valves or after valve repair.[8]

Europace (2015) 17, 1467–1507

2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

JACC

I	C-LD

See Online Data Supplements 3 and 4.

Anticoagulation is indicated in patients with AF and a CHA_2DS_2-VASc score of 2 or greater with native aortic valve disease, tricuspid valve disease, or MR (36–38).

IIa	C-LD

See Online Data Supplements 3 and 4.

It is reasonable to use a DOAC as an alternative to a VKA in patients with AF and native aortic valve disease, tricuspid valve disease, or MR and a CHA_2DS_2-VASc score of 2 or greater (35–38).

AF and TAVI?

ANTITHROMBOTICS AFTER TAVR

	ACC/AHA/STS[1]	ESC[2]	ACCP[3]	CCS[4]
Post-procedural	Aspirin 81mg indefinitely	ASA or clopidogrel indefinitely	ASA (75-100mg/d)	ASA
	Clopidogrel 75mg for up to 6 mo	ASA and clopidogrel early after TAVI	Clopidogrel up to 3 months	Clopidogrel 1 to 3 months
	If OAC is indicated, it is reasonable to continue low dose ASA; no other AP therapy should be avoided	If VKA indicated, no AP therapy		OAC - adjunctive APT is controversial and triple therapy should be avoided

NON - STANDARDIZED

1. *Holmes DR Jr et al. J Thorac Cardiovasc Surg 2012;144:e29-84 and Nishimura RA et al JACC 2017;70-252-89; ; 2. Vahanian A et al. Eur HeartJ 2012;33:2451-96; 3. Whitlock RP et al. Chest 2012;141:e576S-e600S;* Can J Cardiol 2012:520-8

ETIOLOGY OF THROMBOEMBOLIC EVENTS AFTER TAVI

Antiplatelet Hypothesis

To obviate stent-mediated risk of platelet-related thrombosis/embolization

=> Use of DAPT

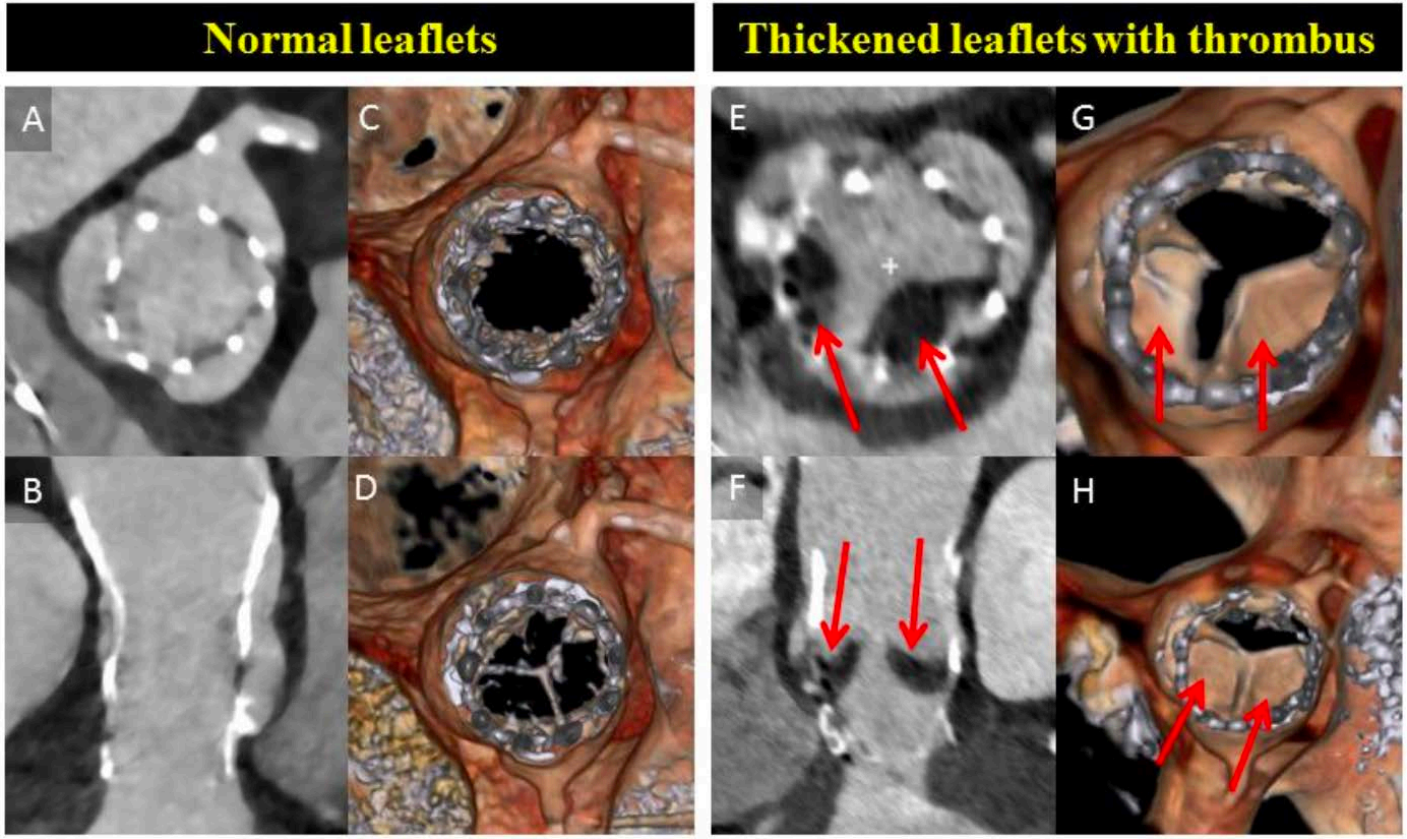
Antithrombin Hypothesis

To prevent thrombin-based thrombus formation during the first 3 months after implantation

=> Use of OAC

A clearer mechanistic understanding of the pathobiology of thromboembolic events during and after TAVI will provide a translatable foundation for optimal therapies

VALVE THROMBOSIS



EDITORIAL COMMENT

JACC VOL. 68, NO. 6, 2016
AUGUST 9, 2016:600–2

Cerebral Embolism

A Silent Iatrogenic Complication of TAVR That Needs Voiced Consideration*

Olivier Barthélémy, MD, Jean Philippe Collet, MD, PhD, Gilles Montalescot, MD, PhD

TABLE 1 Stroke Rates in TAVR Studies

		Event	TAVR	Control*	p Value
PARTNER Inoperable (1)	30 days	All stroke/TIA	6.7	1.7	0.03
		Major stroke	5.0	1.1	0.06
	1 year	All stroke/TIA	10.6	4.5	0.04
		Major stroke	7.8	3.9	0.18
PARTNER High-Risk (2)	30 days	All stroke/TIA	5.5	2.4	0.04
		Major stroke	3.8	2.1	0.20
	1 year	All stroke/TIA	8.3	4.3	0.04
		Major stroke	5.1	2.4	0.07
U.S. CoreValve Pivotal (3)	30 days	Stroke	4.9	6.2	0.46
		Major stroke	3.9	3.1	0.55
	1 year	Stroke	8.8	12.6	0.10
		Major stroke	5.8	7.0	0.59
PARTNER 2 (4)	30 days	Neurologic event	6.4	6.5	0.94
		Disabling stroke	3.2	4.3	0.20
	1 year	Neurologic event	10.1	9.7	0.76
		Disabling stroke	5.0	5.8	0.46

PATIENTS CHARACTERISTICS

- 1/3→ coronary stent PCI
- 1/3 → secondary prevention for stroke
- 2/5 → permanent AF or NOAF

- 30%→ Antiplatelet Therapy
- 50% → Oral Anticoagulation
- 25% → OAC + APT

LATE BLEEDING AND MORTALITY AFTER TAVI

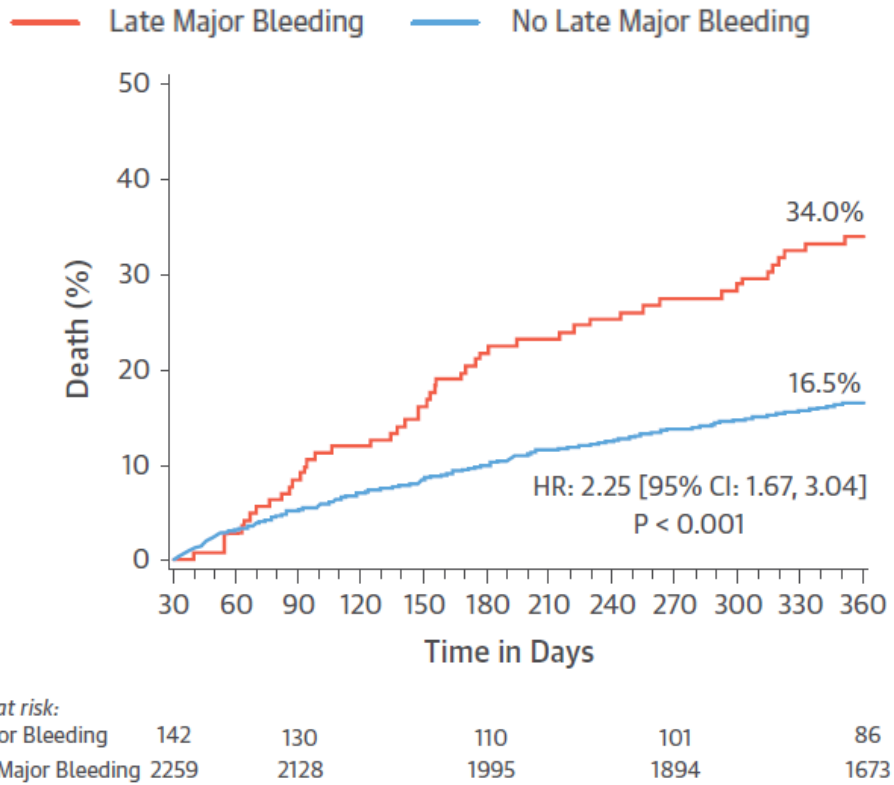
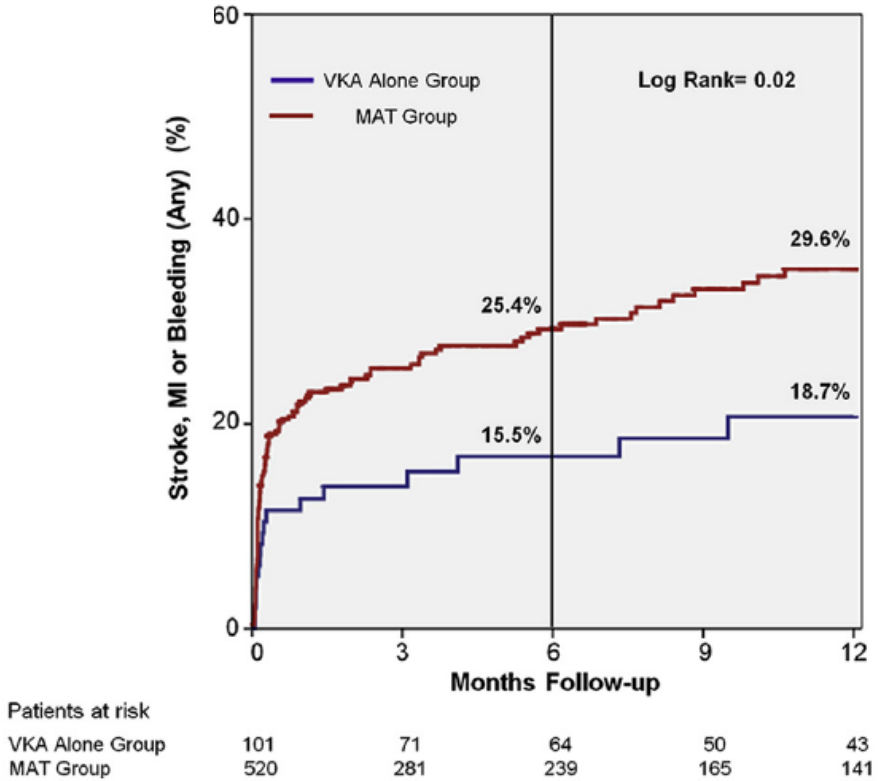


TABLE 5 Independent Predictors of 30-Day to 1-Year Mortality

Predictor	Adjusted HR (95% CI)	p Value
Major stroke within 1 yr	5.44 (3.33-8.90)	<0.0001
Major late bleeding*	3.83 (2.62-5.61)	<0.0001
AF/atrial flutter†	2.03 (1.60-2.58)	<0.0001
Moderate to severe PVL†	1.70 (1.27-2.27)	0.0004
Hemodynamic support use (CPB or IABP)	1.63 (1.10-2.39)	0.01
Renal insufficiency (creatinine ≥2 mg/dl)	1.61 (1.23-2.10)	0.0006
Severe pulmonary hypertension	1.40 (1.11-1.77)	0.005
Liver disease	1.78 (1.00-3.19)	0.051
Moderate to severe MR†	1.30 (1.00-1.70)	0.051
Platelet count at baseline	1.00 (1.00-1.00)	0.02
AV mean gradient at baseline	0.99 (0.98-0.99)	0.002
Dual-antiplatelet therapy†	0.76 (0.60-0.98)	0.03

Généreux et al. JACC 2014; 64: 2605-15

COMBINED ANTITHROMBOTIC THERAPIES



Stroke: 5% *vs*. 5.2% (NS)
MACE: 13.9% *vs*. 16.3% (NS)

MB: 14.9% *vs*. 24.4% (p=0.04)

Abdul-Jawad Altisent et al. JACC Cardiovasc Inter 2016

POST-TAVI ANTITHROMBOTICS

Need for OAT (50%)

Concomitant CAD*

Yes

Dual therapy

O + C or A

OAC Monotherapy

O

No

OAC Monotherapy

O

No need for OAT (50%)

DAPT A and C

and/or

SAPT A or C

TAVI

4 weeks

6 months

12 months

O Oral anticoagulation (VKA or NOACs)

A ASA 75–100 mg daily

C Clopidogrel 75 mg daily

* Recent ACS or coronary stenting (<6 months)

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PROPOSED ALGORTIHM

Need for OAT (70%)

Concomitant CAD*

Yes

Dual therapy

O C or A

OAC Monotherapy

O

No

OAC Monotherapy

O

No need for OAT (30%)

OAC Monotherapy

O

TAVI

4 weeks

6 months

12 months

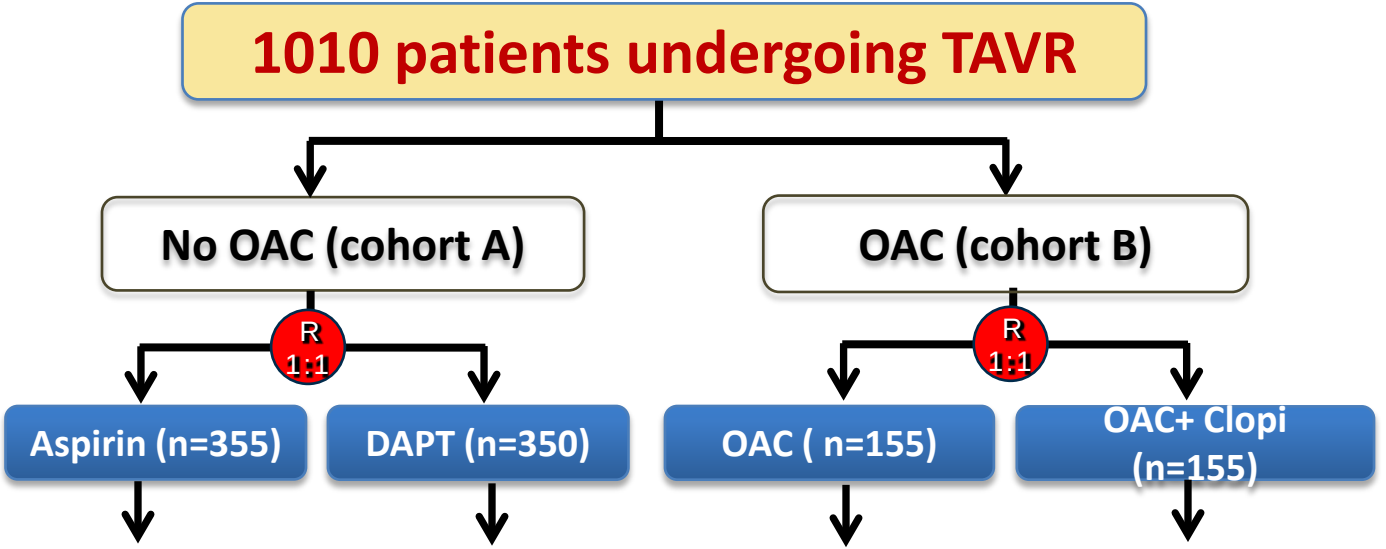
O Oral anticoagulation (VKA or NOACs)

A ASA 75–100 mg daily

C Clopidogrel 75 mg daily

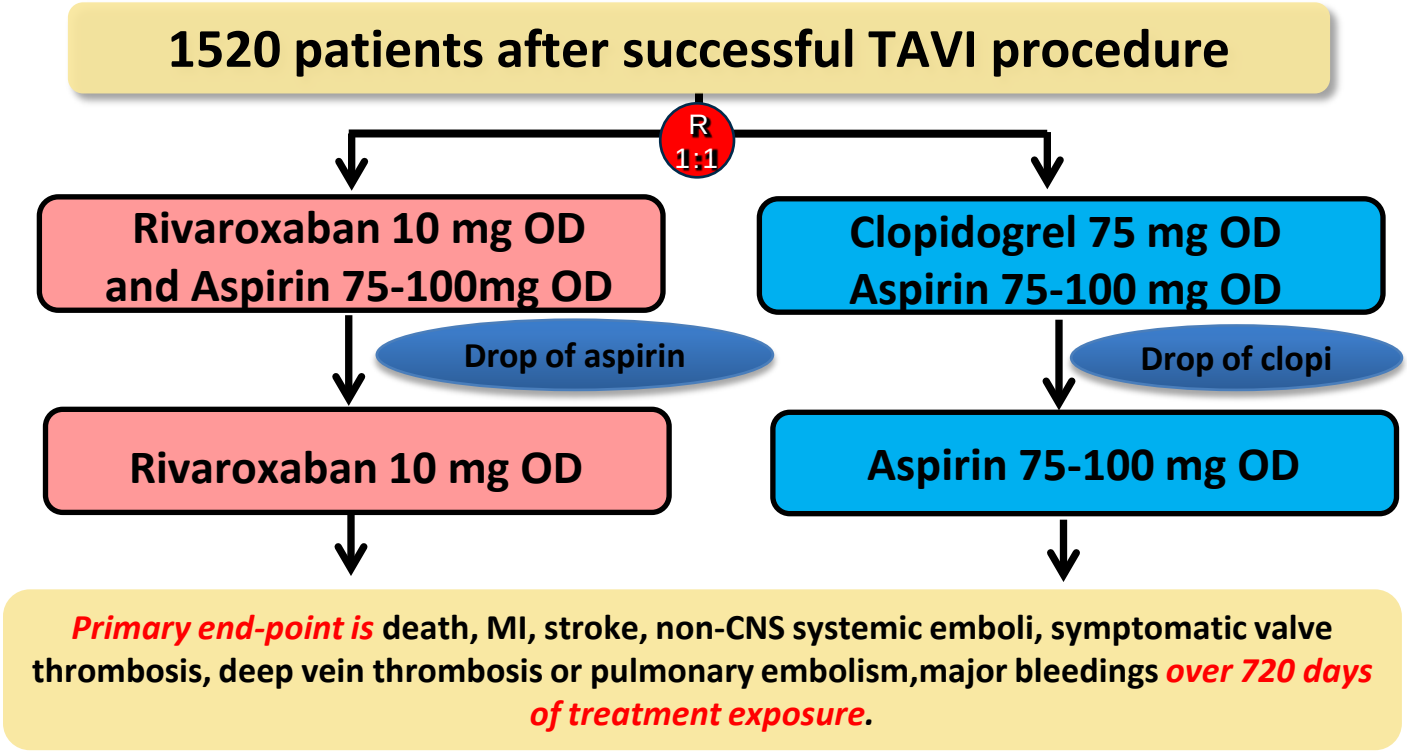
* Recent ACS or coronary stenting (<6 months)

POPULAR TAVI NCT02247128



Primary end-point is **freedom of non-procedure related bleeding and all bleeding.**
Secondary end-point **is net-clinical benefit defined as freedom of the composite of cardiovascular mortality, non-procedure related bleeding, stroke, and MI at** ***one year***

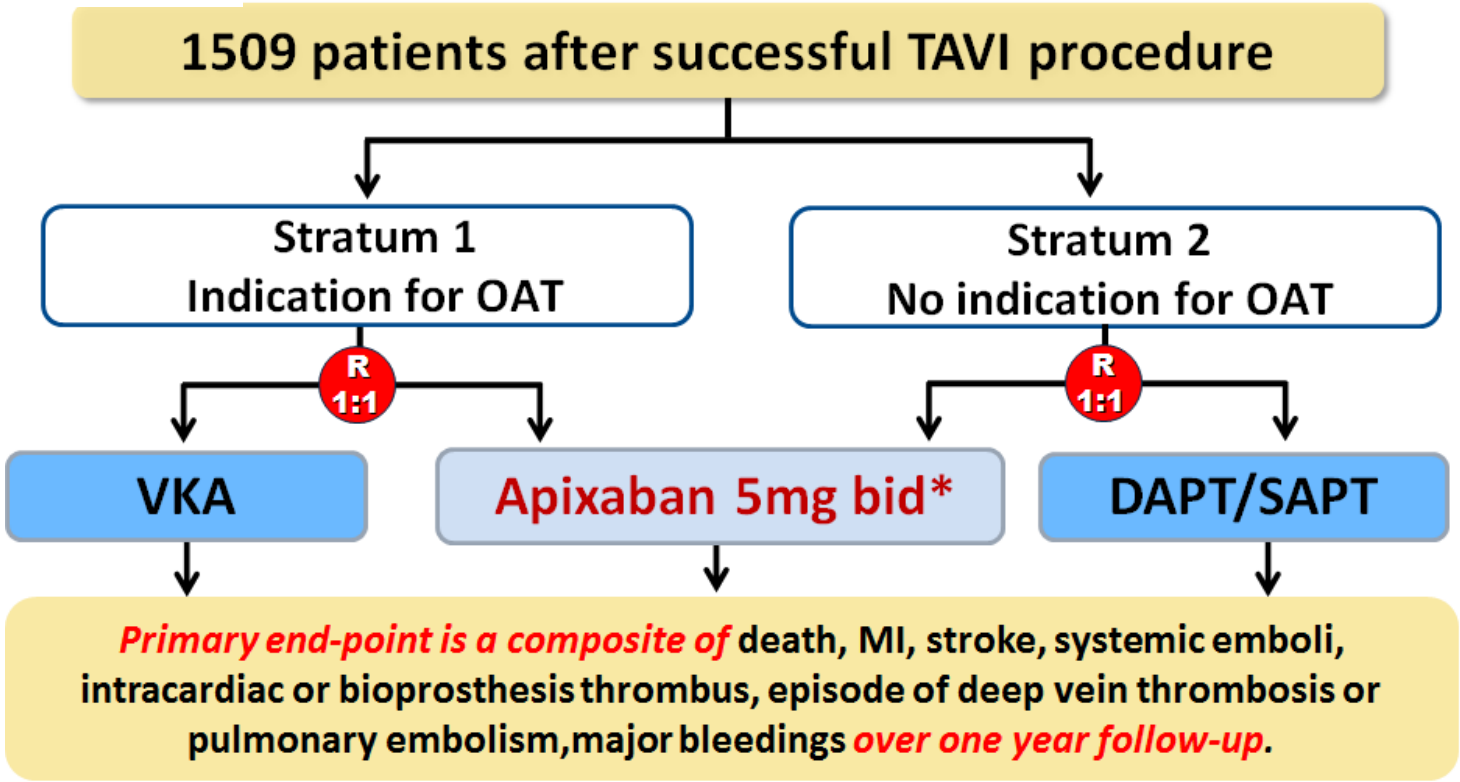
GALILEO NCT02556203



Primary end-point is **death, MI, stroke, non-CNS systemic emboli, symptomatic valve thrombosis, deep vein thrombosis or pulmonary embolism,major bleedings** ***over 720 days of treatment exposure*****.**

Atlantis

Anti-**T**hrombotic Strategy to **L**ower **A**ll cardiovascular and **N**eurologic Ischemic and Hemorrhagic Events after **T**rans-Aortic Valve **I**mplantation for Aortic **S**tenosis



*2.5mg bid if creatinine clearance 15-29mL/min or if two of the following criteria: age≥80 years, weight≤60kg or creatinine≥1,5mg/dL (133µMol).

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Specific issues with NOACs in TAVI/AFib patients

- Drug-drug interactions increasing the levels of NOACs: protease inhibitors, cyclosporine, ketoconazole, dronedarone, amiodarone, verapamil…
- Drug-drug interactions lowering the levels of NOACs: Carbamazepine, Phenobarbital, rifampicin, erythromycin, …
- Renal function

Conclusions

- Stroke is a frequent (~10% at 1 yr) and deadly event after TAVI
- A.Fib (known or unknown) is a major contributor
- Except for a definite contra-indication (i.e. ICH) anticoagulation is always required in TAVI patients with A.Fib
- No prospective data but NOAC in A.Fib/TAVI (± ASA) appears as an acceptable option, while waiting for the ongoing RCTs. Otherwise VKA still an option.

Slides available at **www.action-coeur.org**