JOURNAL CLUB

EDOXABAN VERSUS VITAMIN K ANTAGONIST FOR ATRIAL FIBRILLATION AFTER TAVR

2022.02.23

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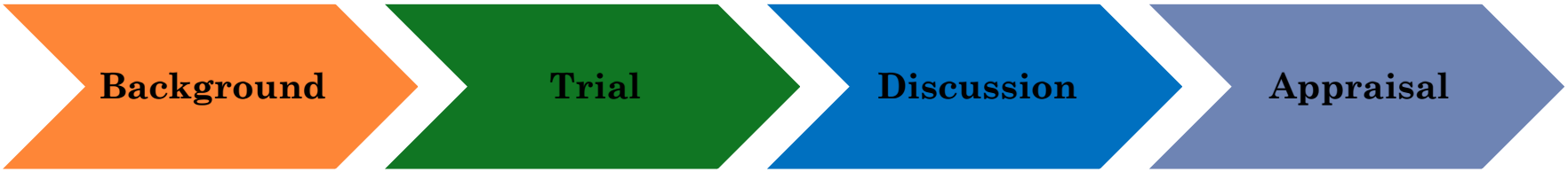
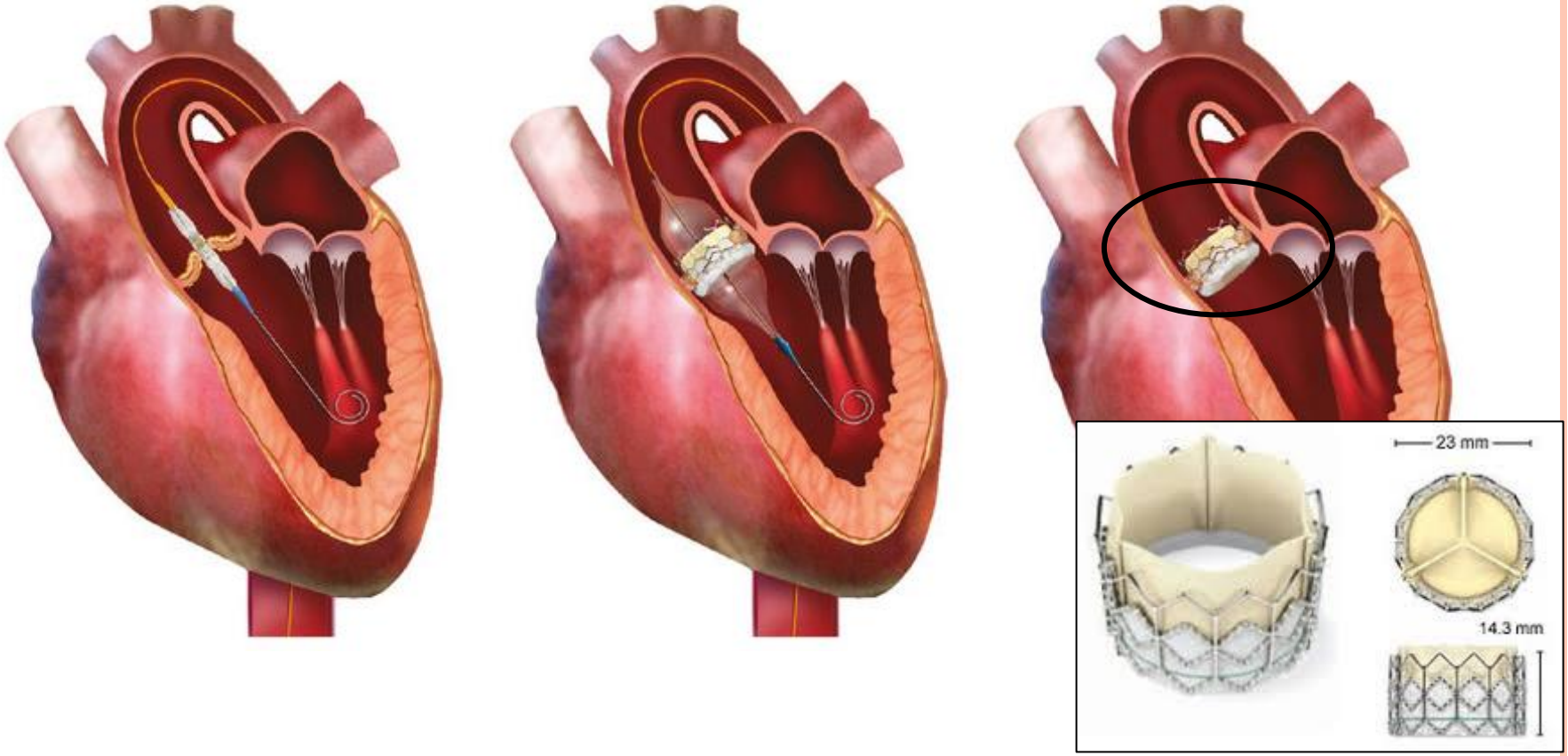
OUTLINE



Background → Trial → Discussion → Appraisal

INTRODUCTION

- **TAVR** (**T**ranscatheter **A**ortic-**V**alve **R**eplacement)
  - ✓ 又稱**TAVI** (Transcatheter Aortic-Valve Implantation)

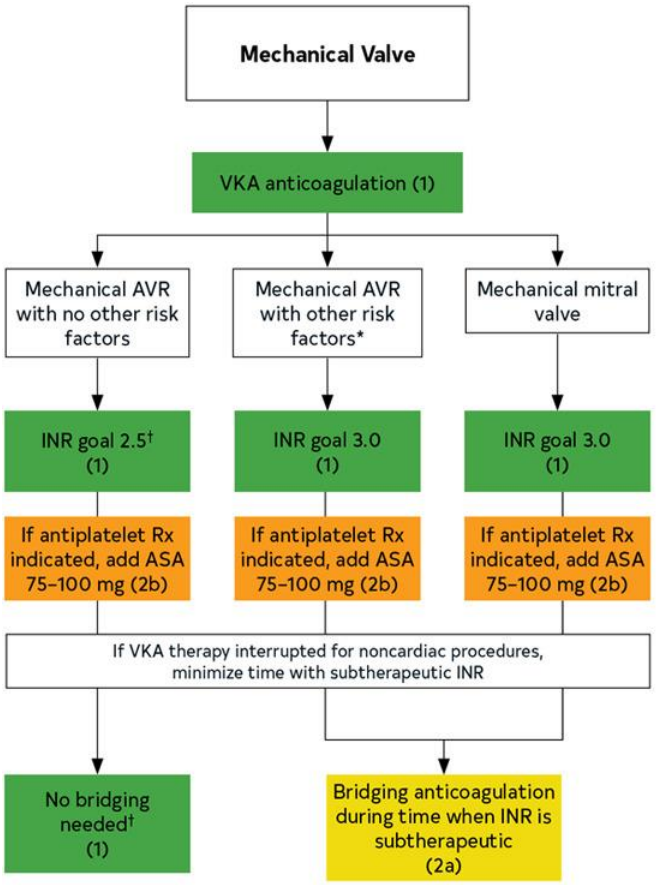


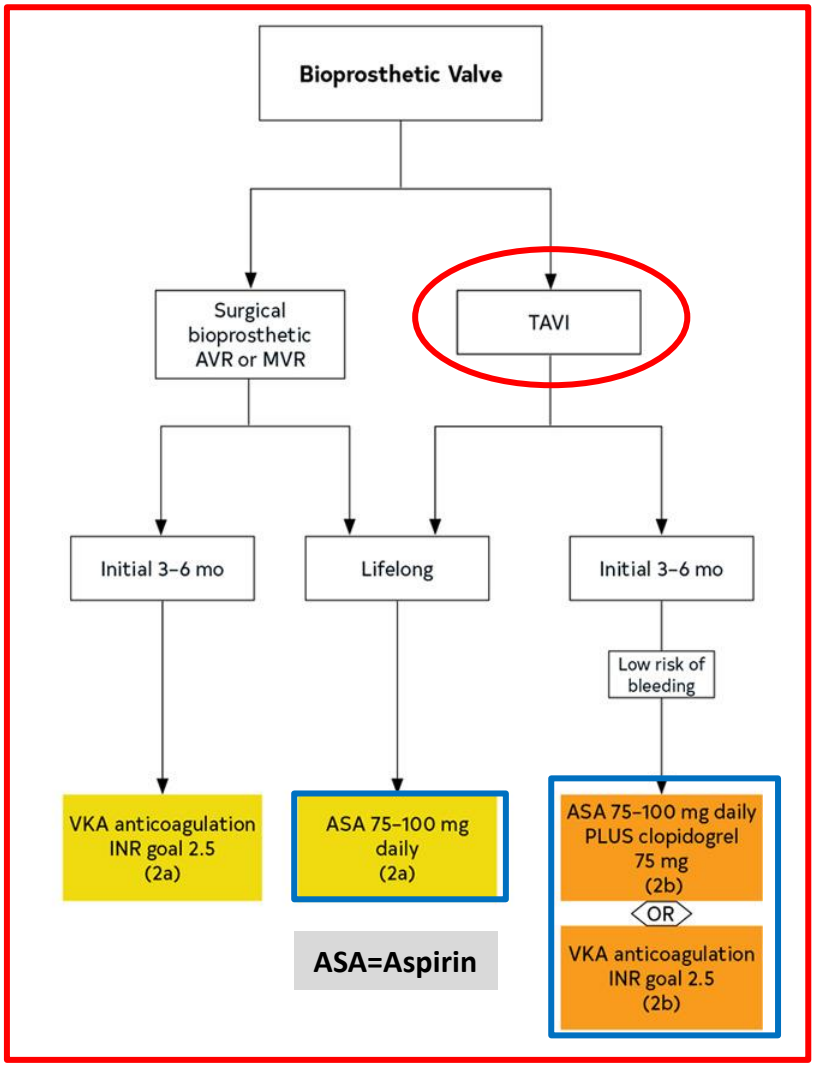
COMPLICATIONS OF TAVI

- Mortality
- **Thrombotic events**
  - ✓ Cerebrovascular events
  - ✓ Atrial fibrillation
  - ✓ Valve thrombosis
  - ✓ Myocardial infarction
- Acute kidney injury
- **Bleeding Events**
- Prosthetic valve endocarditis

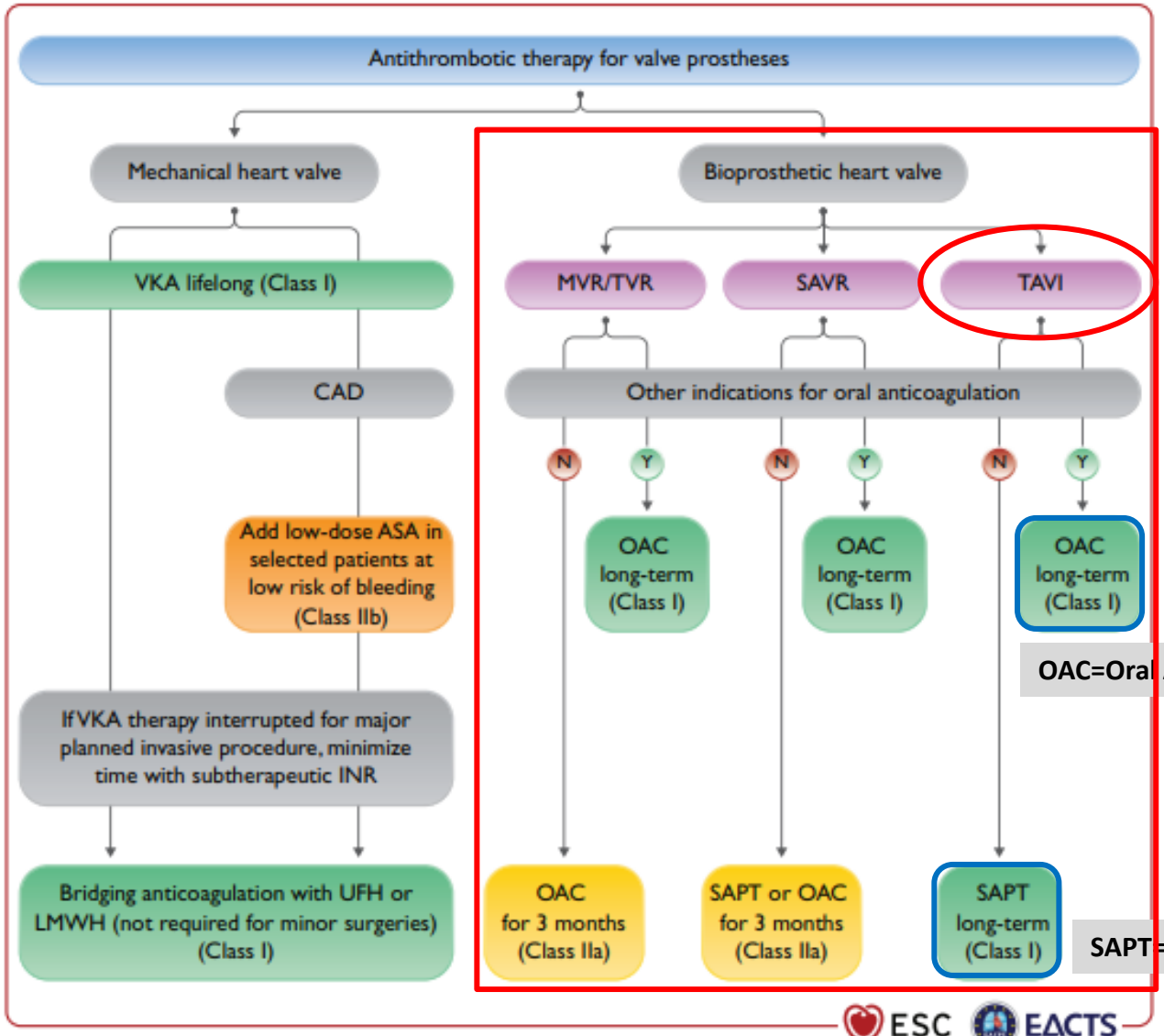
2020 ACC/AHA GUIDELINE

- **Antithrombotic therapy for prosthetic valves**





2021 ESC GUIDELINE



OAC=Oral Anticoagulation

SAPT=Single Antiplatelet Therapy

2020 JCS GUIDELINE

Table 47. Antithrombotic Therapy for Prosthetic Valve Patients

Recommendations	COR	LOE
Mechanical valve		
Oral anticoagulat therapy with warfarin is recommended lifelong for all patients Target INR of warfarin control • Aortic position: INR 2.0–2.5 • Aortic position and thrombotic risks: INR 2.0–3.0 • Mitral position: INR 2.0–3.0	I	B
Warfarin control of INR 2.5–3.5 is reasonable for patients with thrombotic event despite adequate anticoagulation therapy	IIa	C
Aspirin combination therapy may be considered for patients with thrombotic event despite adequate anticoagulation therapy	IIb	C
Single aspirin therapy is contraindicated	III	B
DOAC usage is contraindicated	III	B
Bioprosthetic valve		
Anticoagulation therapy with warfarin control of INR 2.0–2.5 is reasonable for the first 3 months after surgery	IIa	B
DAPT (aspirin 75–100 mg+clopidogrel 75 mg) is reasonable for the first 6 months after TAVI, followed by lifelong single antiplatelet therapy (aspirin or clopidogrel)	IIa	C

DAPT=Dual Antiplatelet Therapy

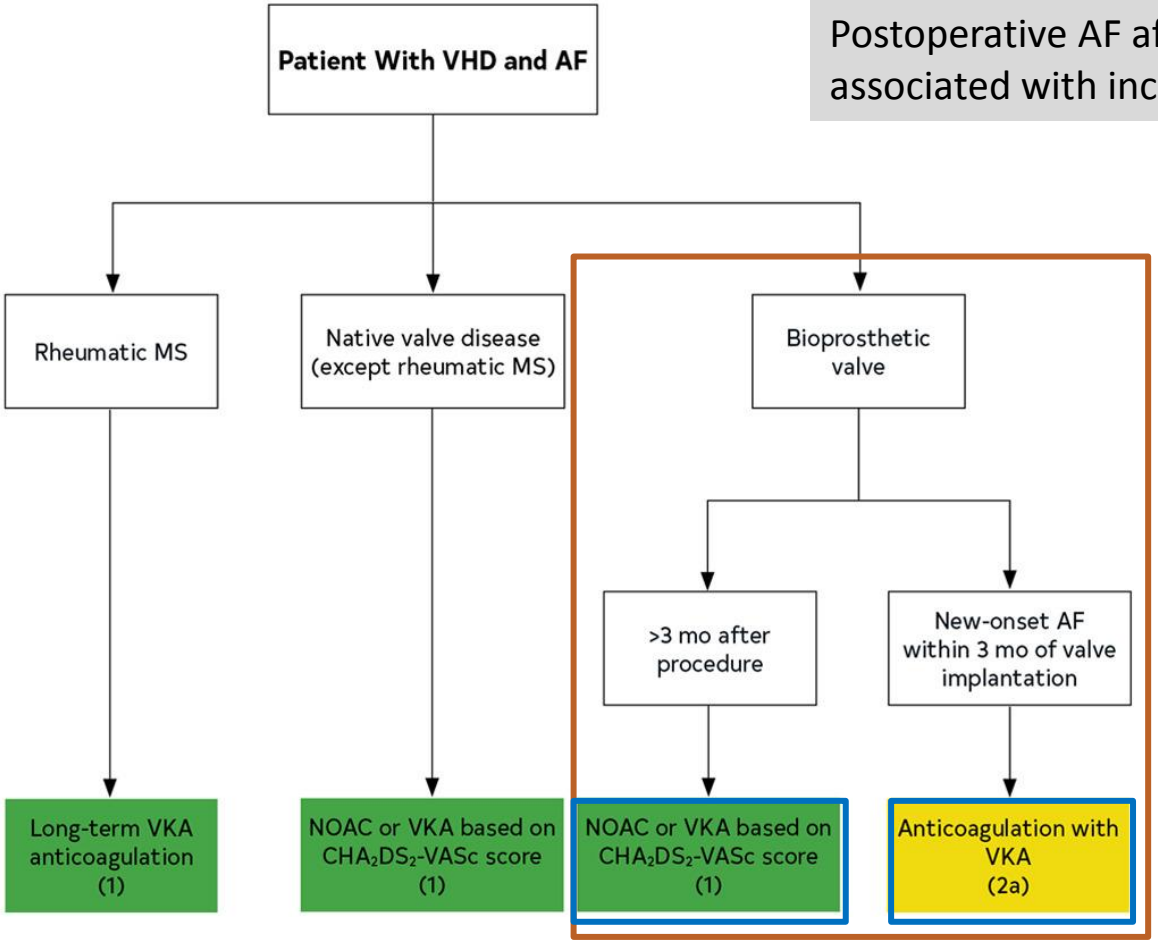
TAVI GUIDELINE

2020 ACC/AHA	2021 ESC	2020 JCS
● 終身Aspirin 75-100 mg QD ●低出血險者：可考慮使用DAPT 3-6個月或Warfarin (INR 2.5)至少3個月	OAC適應症 ●有：終身 OAC ●無：終身 SAPT	使用DAPT 6個月後，終身使用SAPT

OAC=Oral Anticoagulation
SAPT=Single Antiplatelet Therapy
DAPT=Dual Antiplatelet Therapy
(Aspirin 75-100mg + Clopidogrel 75mg)

2020 ACC/AHA GUIDELINE

- **Anticoagulation for AF in Patients With VHD**



Postoperative AF after VHD intervention is associated with increased stroke and mortality rates.

CHA_2DS_2-VASc score ≥ 2

Q&A

- 有一位病患在做完TAVI之後，出現了A-Fib的症狀，在抗凝血劑的選擇上是否會建議優先使用Edoxaban取代Warfarin以達到更好的效果呢?

Edoxaban

Warfarin

Background | **Trial** | Discussion | Appraisal

ENVISAGE-TAVI AF trial

CLINICAL TRIAL

ENVISAGE-TAVI AF trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Edoxaban versus Vitamin K Antagonist for Atrial Fibrillation after TAVR

N.M. Van Mieghem, M. Unverdorben, C. Hengstenberg, H. Möllmann, R. Mehran, D. López-Otero, L. Nombela-Franco, R. Moreno, P. Nordbeck, H. Thiele, I. Lang, J.L. Zamorano, F. Shawl, M. Yamamoto, Y. Watanabe, K. Hayashida, R. Hambrecht, F. Meincke, P. Vranckx, J. Jin, E. Boersma, J. Rodés-Cabau, P. Ohlmann, P. Capranzano, H.-S. Kim, T. Pilgrim, R. Anderson, U. Baber, A. Duggal, P. Laeis, H. Lanz, C. Chen, M. Valgimigli, R. Veltkamp, S. Saito, and G.D. Dangas, for the ENVISAGE-TAVI AF Investigators*

N Engl J Med 2021;385:2150-60.

DOI: 10.1056/NEJMoa2111016

August 28, 2021

STUDY DESIGN

P patient	Adult with either prevalent or incident atrial fibrillation lasting more than 30 seconds after successful TAVR
I intervention	Edoxaban 60mg QD
C comparison	Vitamin K Antagonist (target INR= 2.0-3.0)
O outcome	Efficacy and Safety

- A multinational, multicenter, **prospective, randomized, open-label, adjudicator-masked, Non-inferior** trial

PATIENTS – INCLUSION CRITERIA

- 18 years of age or older
- **Indication for chronic oral anticoagulant**
  - ✓ **Pre-existing AF**
  - ✓ **New onset AF** (e.g., >30 seconds documented by ECG)
- After **successful TAVR** for severe aortic stenosis

✓ Correct positioning of a transcatheter bioprosthetic heart valve into the proper anatomical location

✓ Presence of all 3 conditions post TAVR
- Peak transvalvular velocity <3.0 m/s
- Mean aortic valve gradient < 20mmHg
- Aortic valve regurgitation of 2 or less

✓ No clinically overt stroke

✓ No uncontrolled bleeding

	輕微	中期	嚴重
主動脈瓣血流速（公尺/秒）	小於3.0	3.0～4.0	大於4.0
主動脈瓣壓差（mmHg）	小於20	20～40	大於40

PATIENTS – EXCLUSION CRITERIA

- **Conditions with a high risk of bleeding**

Concomitant conditions and therapies

- Clinically overt stroke within the last 90 days before TAVR
- Any scheduled drug or device-based therapy during the treatment period that would eliminate the need for chronic OAC
- Valve replacement for native aortic valve insufficiency
- Any scheduled or unscheduled catheter-based interventional procedure during the index TAVR
- Subjects with mechanical heart valves
- Mitral valve stenosis, Grade III to IV/IV (moderate to severe/severe)
- Active infective endocarditis
- Major surgery within 30 days prior to randomization
- Elective percutaneous coronary intervention within 7 days prior to randomization
- ST-elevation myocardial infarction within 30 days prior to randomization (non-ST-elevation myocardial infarction is not excluded)
- End-stage renal disease with CrCl <15 mL/min or on dialysis at randomization
- Severe hepatic impairment or hepatic disease associated with coagulopathy (e.g., acute or chronic active hepatitis or cirrhosis, Child Pugh B and C [significant functional compromise and decompensated disease, respectively)
- Uncontrolled severe hypertension defined as blood pressure that repeatedly measures 170/100 mm Hg despite medical intervention
- Respiratory failure requiring mechanical ventilation at time of randomization
- Critically ill or hemodynamically unstable subjects at the time of randomization (i.e., cardiogenic shock, acute heart failure, including the requirement for pharmacologic treatment, or mechanical support to assist circulation)
- Active malignancy (requiring chemotherapy, radiation, or surgery at the time of randomization) except for adequately treated nonmelanoma skin cancer or other noninvasive or in situ neoplasms (e.g., cervical cancer in situ that has been successfully treated)

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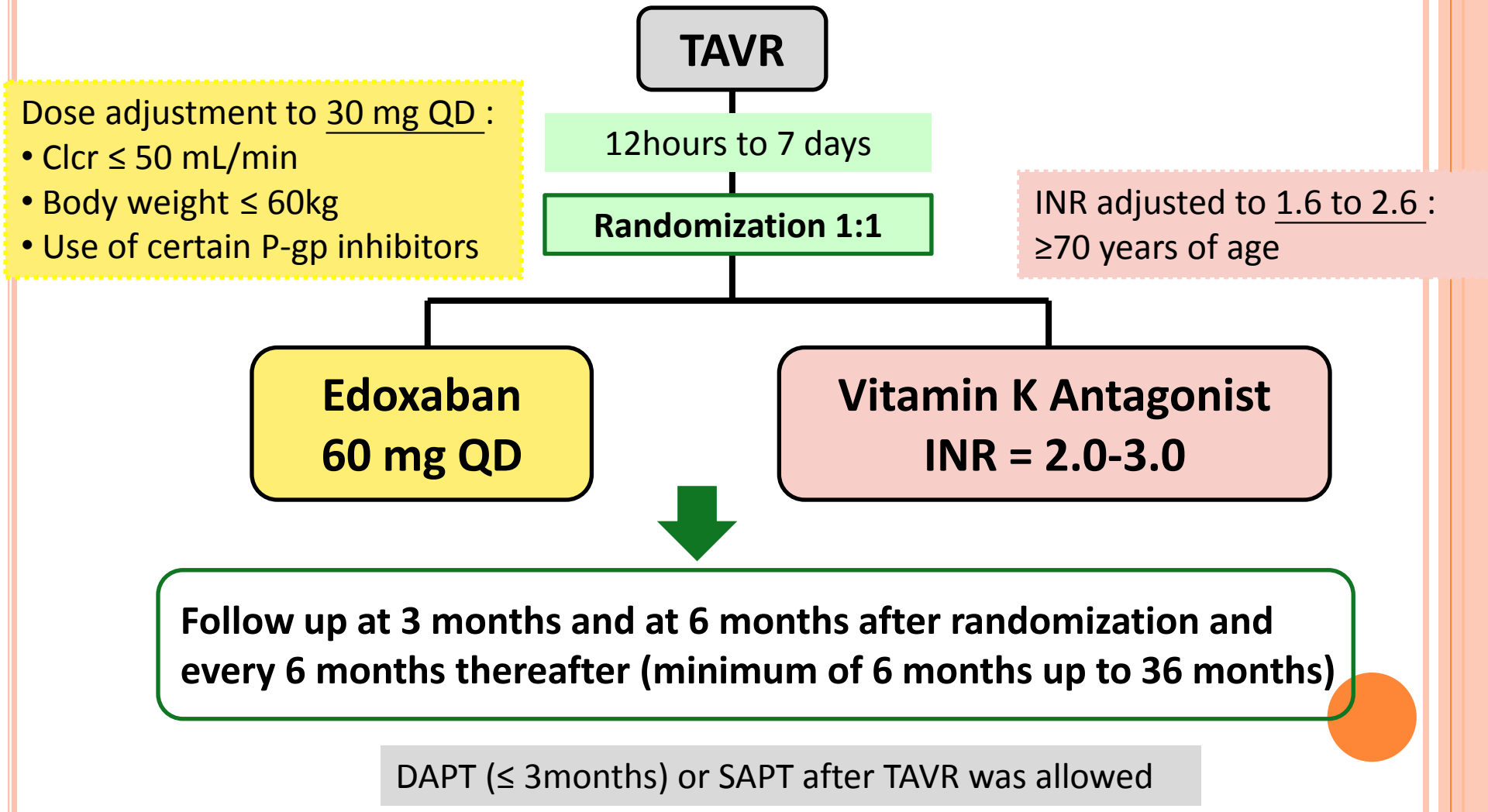
STUDY PROCEDURES



OUTCOME ASSESSMENT

- **Primary efficacy outcome**
  - ✓ **Net Adverse Clinical Events**

    (all-cause death, myocardial infarction, ischemic stroke, systemic thromboembolic event, valve thrombosis, and ISTH-defined major bleeding)
- **Primary safety outcome**
  - ✓ **ISTH-defined major bleeding**

ISTH (International Society on Thrombosis and Haemostasis) Go to:

Major: fatal bleeding, and/or symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome, and/or bleeding causing a fall in hemoglobin levels of 1.24 mmol/L (20 g/L or greater) or more, or leading to a transfusion of 2 U or more of whole blood or red cells.

Minor: all reported bleedings not classified as major.

OUTCOME ASSESSMENT

BARC (Bleeding Academic Research Consortium)

Go to:

Type 1: bleeding that is not actionable and does not cause the patient to seek an unscheduled performance of studies, hospitalization, or treatment by a health care professional; it may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a health care professional.

Type 2: any overt, actionable sign of hemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for type 3, type 4, or type 5 but does meet at least one of the following criteria: requiring nonsurgical, medical intervention by a health care professional; leading to hospitalization or increased level of care; or prompting evaluation.

Type 3a: overt bleeding plus a hemoglobin drop of 3 to 5 g/dL* (provided the hemoglobin drop is related to bleed); any transfusion with overt bleeding.

Type 3b: overt bleeding plus a hemoglobin drop of 5 g/dL (provided the hemoglobin drop is related to bleed); cardiac tamponade; bleeding requiring surgical intervention for control (excluding dental, nasal, skin, and hemorrhoid); bleeding requiring intravenous vasoactive agents.

Type 3c: intracranial hemorrhage (does not include microbleeds or hemorrhagic transformation, does include intraspinal); subcategories confirmed by autopsy or imaging, or lumbar puncture; intraocular bleed compromising vision.

Type 4: coronary artery bypass grafting-related bleeding; perioperative intracranial bleeding within 48 hours; reoperation after closure of sternotomy for the purpose of controlling bleeding; transfusion of 5 U of whole blood or packed red blood cells within a 48-hour period; chest tube output 2 L within a 24-hour period.

Type 5a: probable fatal bleeding; no autopsy or imaging confirmation but clinically suspicious.

Type 5b: definite fatal bleeding; overt bleeding or autopsy, or imaging confirmation.

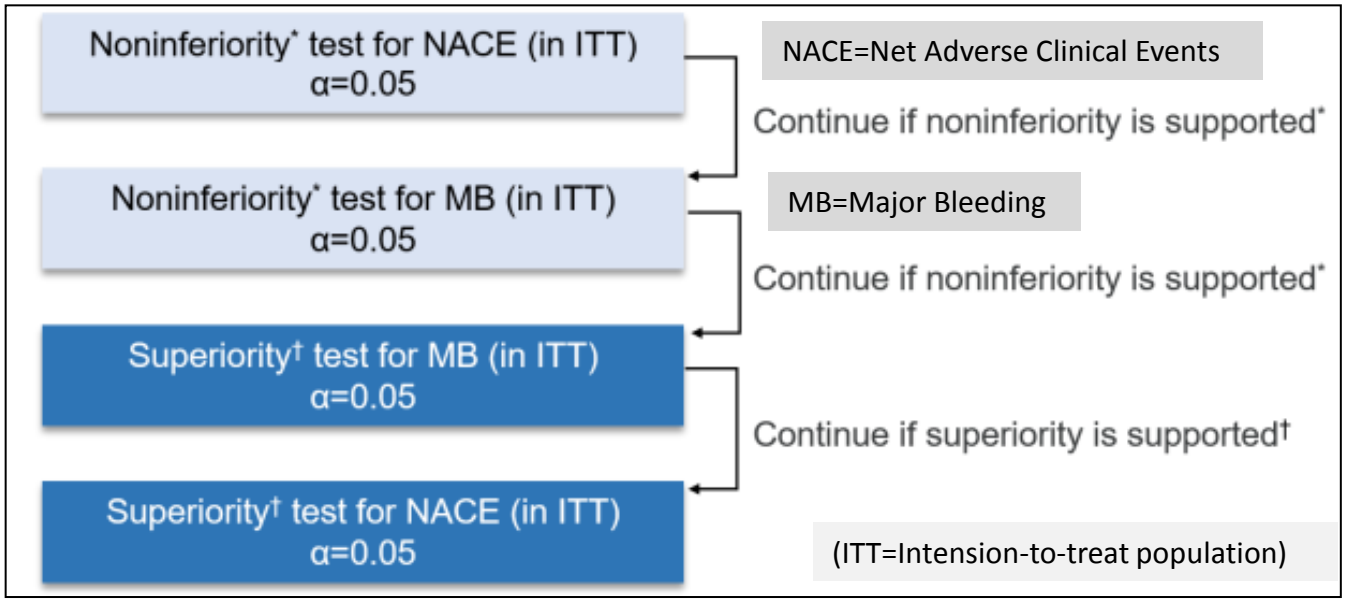
STATISTICAL ANALYSIS

- **320 net adverse clinical events** would need to occur in approximately **1400 patients**
  - ✓ Noninferiority of edoxaban vs. VKAs with **80% power** and a **two-sided significance level of 0.05**

- **Intention-to-treat analysis**

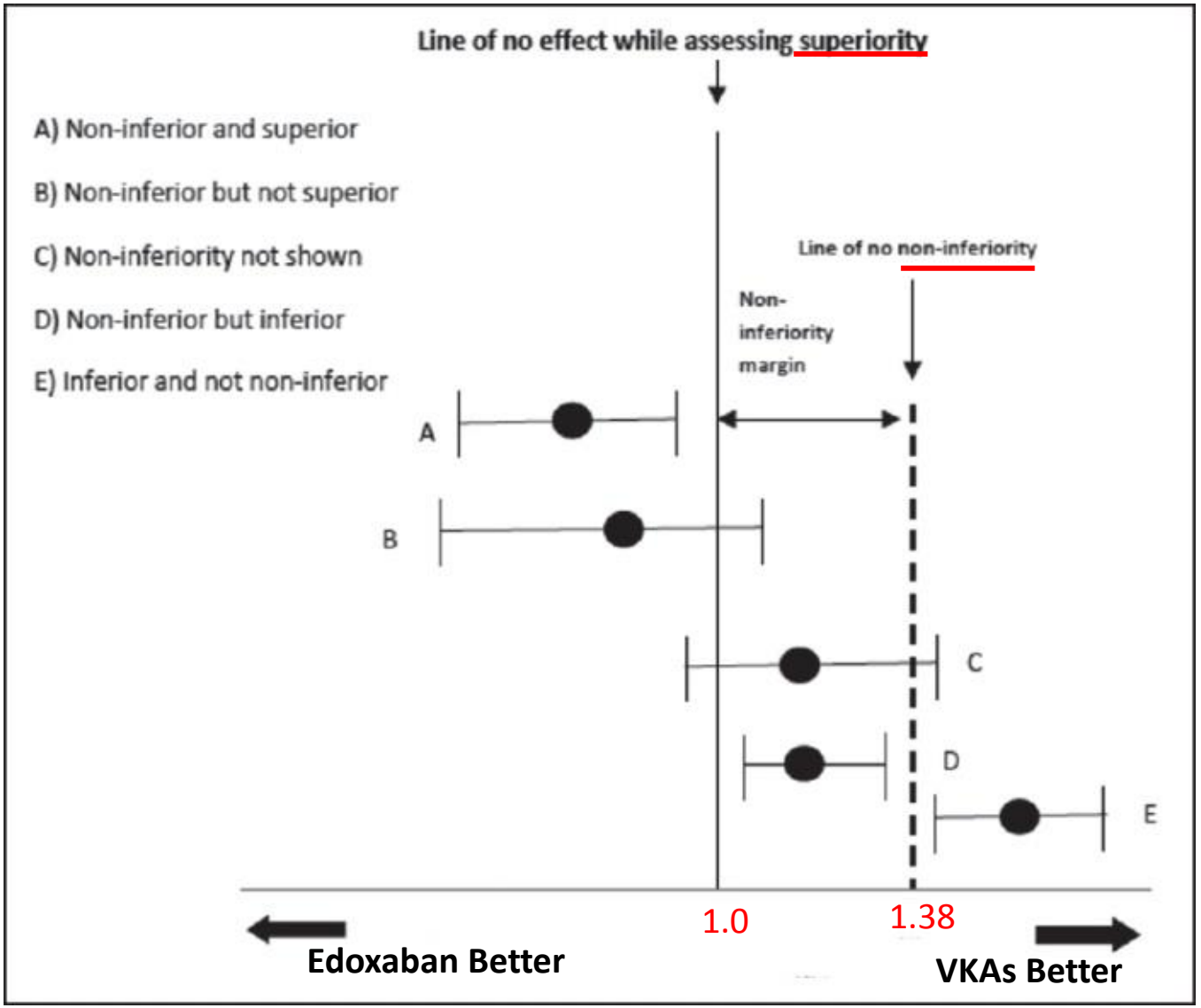
STATISTICAL ANALYSIS

- Four-step testing strategy (Edoxaban vs. VKAs)

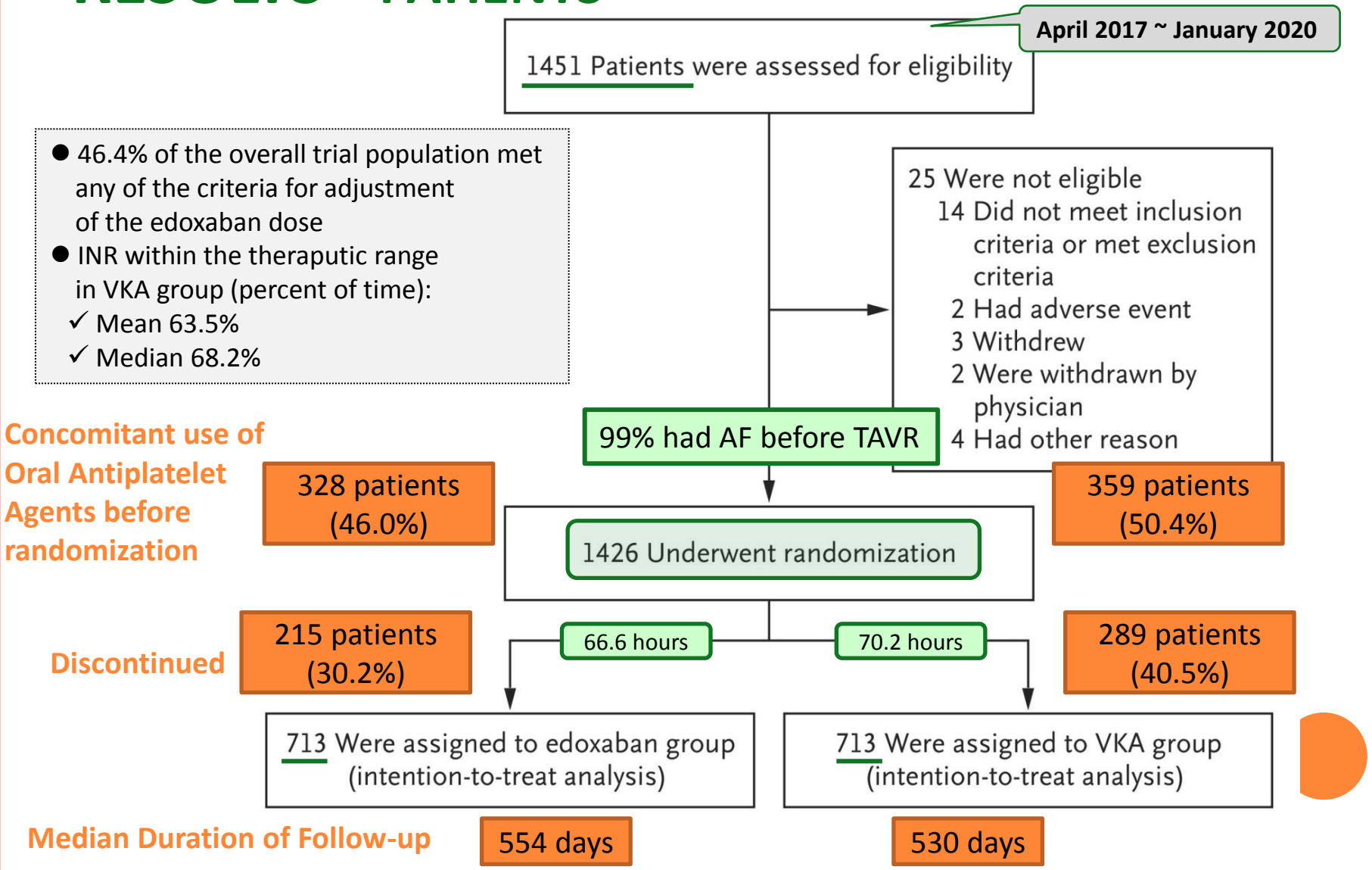


- ✓ **Noninferiority** will be accepted if the upper boundary of the 2-sided 95% CI of the Hazard Ratio falls below 1.38
- ✓ **Superiority** will be accepted if the upper boundary of the 2-sided 95% CI of the Hazard Ratio falls below 1.00

STATISTICAL ANALYSIS



RESULTS - PATIENTS



- 46.4% of the overall trial population met any of the criteria for adjustment of the edoxaban dose
- INR within the theraputic range in VKA group (percent of time):
  - ✓ Mean 63.5%
  - ✓ Median 68.2%

RESULTS - PATIENTS

The baseline characteristics of the patients were similar across groups

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline (Intention-to-Treat Population).*

Characteristic	Edoxaban (N=713)	Vitamin K Antagonist (N=713)
Age — yr	82.1±5.4	82.1±5.5
Female sex — no. (%)	347 (48.7)	331 (46.4)
Race — no. (%)†		
Asian	92 (12.9)	89 (12.5)
White	593 (83.2)	594 (83.3)
Other	28 (3.9)	30 (4.2)
Weight — kg	74.6±17.9	76.0±17.3
Body-mass index‡	27.5±5.7	27.9±5.4
Creatinine clearance by Cockcroft–Gault formula — ml/min	57.9±24.0	58.6±24.3
Hypertension — no. (%)	647 (90.7)	657 (92.1)
Diabetes mellitus — no. (%)	270 (37.9)	257 (36.0)
Congestive heart failure — no. (%)	591 (82.9)	619 (86.8)
NYHA class III or IV	314 (44.0)	328 (46.0)
Mitral-valve disease — no. (%)	57 (8.0)	60 (8.4)
History of stroke or TIA — no. (%)	123 (17.3)	116 (16.3)
History of coronary artery disease — no. (%)	293 (41.1)	297 (41.7)
Previous CABG	67 (9.4)	60 (8.4)
Previous PCI	176 (24.7)	192 (26.9)
PCI performed within 30 days before TAVR	34 (4.8)	28 (3.9)
Previous myocardial infarction	97 (13.6)	101 (14.2)
Incident (new onset) atrial fibrillation — no. (%)	7 (1.0)	8 (1.1)

RESULTS - PATIENTS

Table 1. (Continued.)

CHA_2DS_2-VASc score

CHA_2DS_2VASc score

Risk factor		Score	總分	中風機率(%年)	建議用藥
Diabetes mellitus	糖尿病	1	3	3.2%	Rivaroxaban, Apixaban
Stroke/TIA/thromboembolism	中風/短暫性腦缺血發作/血栓栓塞	2	4	4.0%	
Vascular diseases	血管疾病	1	5	6.7%	
Age 65–74	年齡 65–74	1	6	9.8%	
Sex category (female sex)	女性	1	7	9.6%	
Maximum score		9	8	6.7%	
			9	15.2%	

Scoring on the risk model of the Society of Thoracic Surgeons (STS) uses an algorithm that is based on the presence of coexisting illnesses in order to predict 30-day operative mortality. The STS score equals the predicted mortality expressed as a percentage.

OAC: 口服抗凝血藥物

Reference: 2014 AHA/ACC/HRS Atrial Fibrillation Guideline

Indication for dose adjustment — no. (%)††	330 (46.3)	331 (46.4)
Valve type — no. (%)‡‡		
Any balloon-expandable valve	342 (48.0)	335 (47.0)
Intraannular self-expanding valve	46 (6.5)	49 (6.9)
Supraannular self-expanding valve	325 (45.6)	328 (46.0)

RESULTS - EFFICACY AND SAFETY OUTCOMES

Table 2. Efficacy and Safety Outcomes (Intention-to-Treat Population).*

Outcome	Edoxaban (N=713)	Vitamin K Antagonist (N=713)	Hazard Ratio (95% CI)	
	no. of patients (rate per 100 person-yr)			
Primary efficacy outcome: net adverse clinical events†	170 (17.3)	157 (16.5)	1.05 (0.85–1.31)‡	P=0.01
Primary safety outcome: major bleeding§	98 (9.7)	68 (7.0)	1.40 (1.03–1.91)¶	P=0.93

NI

O
X

Noninferiority for NACE had shown.

Noninferiority for MB had not shown.

- **More patients in the edoxaban group than in the VKA group had major gastrointestinal bleeding [56(5.4) vs 27(2.7); HR=2.03(1.28-3.22)]**
- One case of major gastrointestinal bleeding was fatal in the edoxaban group

The four-step testing failed at this step;
hence, formal testing for superiority was not performed.

RESULTS - EFFICACY AND SAFETY OUTCOMES

	Secondary outcomes			
v	Death from any cause	85 (7.8)	93 (9.1)	0.86 (0.64–1.15)
	Death from cardiovascular causes	49 (4.5)	46 (4.5)	1.00 (0.67–1.50)
v	Ischemic stroke	22 (2.1)	28 (2.8)	0.75 (0.43–1.30)
v	Myocardial infarction	12 (1.1)	7 (0.7)	1.65 (0.65–4.14)
v	Systemic thromboembolic event	2 (0.2)	3 (0.3)	Not calculated
v	Valve thrombosis§	0	0	Not calculated
	Any stroke	29 (2.7)	35 (3.5)	0.78 (0.48–1.28)
	Major adverse cardiac or cerebrovascular event‖	86 (8.2)	80 (8.1)	1.02 (0.76–1.39)
	Major adverse cardiac event**	61 (5.7)	53 (5.2)	1.10 (0.76–1.58)
v	Fatal bleeding§	11 (1.0)	10 (1.0)	Not calculated
v	Life-threatening bleeding	17 (1.6)	19 (1.9)	Not calculated
v	Intracranial hemorrhage	16 (1.5)	21 (2.1)	0.72 (0.38–1.39)
	Clinically relevant nonmajor bleeding§	164 (18.2)	142 (16.4)	1.13 (0.90–1.14)

NI

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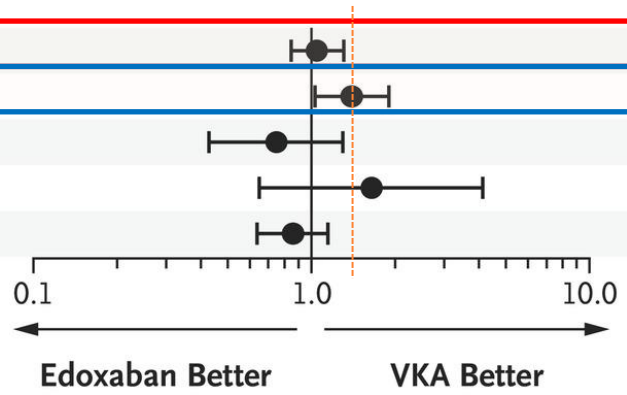
RESULTS - EFFICACY AND SAFETY OUTCOMES

Cox proportional-hazards regression model

Event	Edoxaban	VKA
	rate per 100 person-yr (no. of patients/total no.)	
Net adverse clinical events	17.3 (170/713)	16.5 (157/713)
Major bleeding	9.7 (98/713)	7.0 (68/713)
Ischemic stroke	2.1 (22/713)	2.8 (28/713)
Myocardial infarction	1.1 (12/713)	0.7 (7/713)
Death from any cause	7.8 (85/713)	9.1 (93/713)



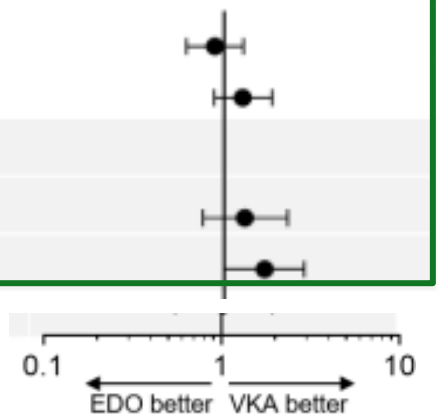
(Treatment group, transcatheter aortic-valve replacement procedure undergone with stenting, and indication for dose adjustment as covariates)

	Inferiority	Noninferiority	Superiority
Net adverse clinical events		O	X
Major bleeding	O	X	
Ischemic stroke		O	X
Myocardial infraction		X	X
Death from any cause		O	X

RESULTS - EFFICACY AND SAFETY OUTCOMES

Figure S6. Hazard Ratio of Clinical Events by Dose Adjustment Subgroups (Intention-to-Treat)

Endpoint	Event rate, %/yr (No. of patients/Total no.) Edoxaban	VKA	Hazard ratio (95% CI)
NACE			
D/A Yes	18.38 (80/330)	20.55 (84/331)	
D/A No	16.38 (90/383)	13.45 (73/382)	
Major bleeding*			
D/A Yes	9.74 (44/330)	7.91 (33/331)	
D/A No	9.65 (54/383)	6.28 (35/382)	



No significant difference had shown.

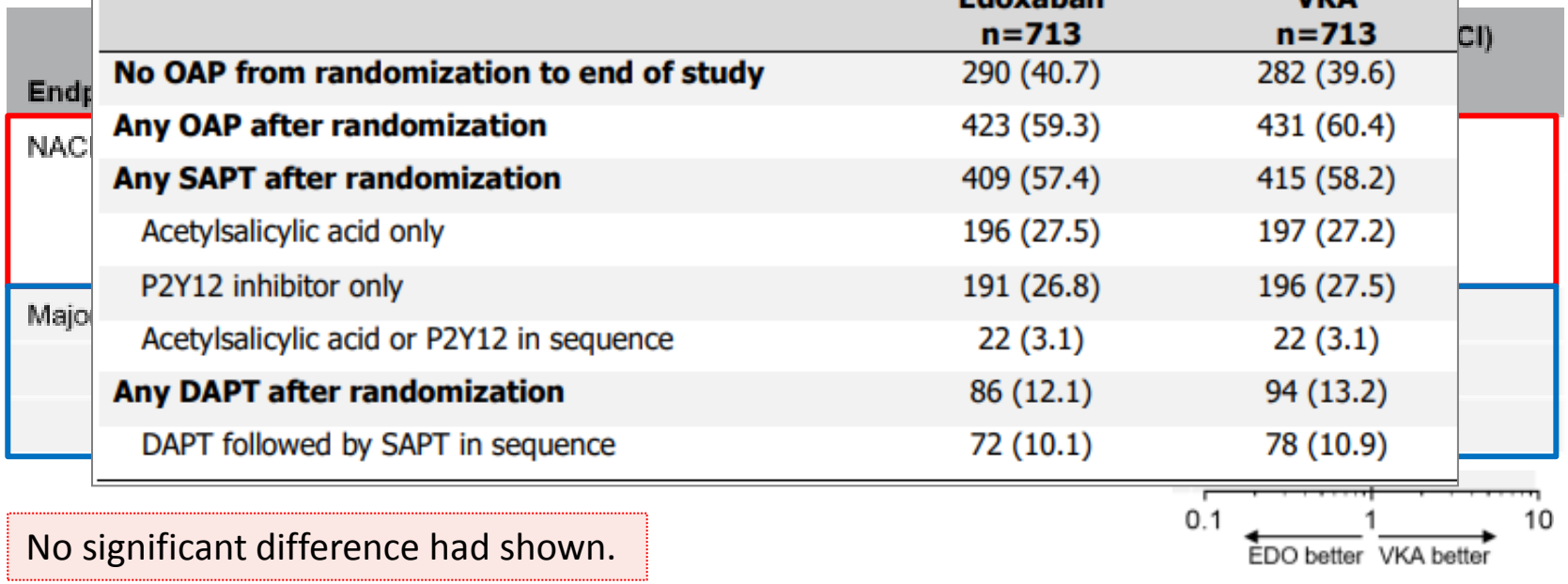
- 84.7% met the CrCl ≤50 mL/min indication
- 42.2% met the body weight ≤60 kg indication
- 6.5% met the P-gp inhibitor indication
- 30.3% met more than 1 indication

RESULTS - EFFICACY AND SAFETY OUTCOMES

Figure S10. Hazard Ratio of Clinical Events by Specified Antiplatelet Therapy (Intention-to-Treat)

Table S6. Concomitant Use of Oral Antiplatelet Drugs Throughout the Trial Period

	Edoxaban n=713	VKA n=713
No OAP from randomization to end of study	290 (40.7)	282 (39.6)
Any OAP after randomization	423 (59.3)	431 (60.4)
Any SAPT after randomization	409 (57.4)	415 (58.2)
Acetylsalicylic acid only	196 (27.5)	197 (27.2)
P2Y12 inhibitor only	191 (26.8)	196 (27.5)
Acetylsalicylic acid or P2Y12 in sequence	22 (3.1)	22 (3.1)
Any DAPT after randomization	86 (12.1)	94 (13.2)
DAPT followed by SAPT in sequence	72 (10.1)	78 (10.9)



No significant difference had shown.

Patients with oral antiplatelet therapy **showed significant difference(VKA better).**

Background → Trial → **Discussion** → Appraisal

CONCLUSION

- **ENVISAGE-TAVI AF** trial involving patients **who had an indication for oral anticoagulation for atrial fibrillation after successful TAVR**

EFFICACY

- **Edoxaban was noninferior to vitamin K antagonists for the composite primary outcome of adverse clinical events**

SAFETY

- **Edoxaban was associated with a higher risk of major bleeding than vitamin K antagonists**
- Subtherapeutic INR values and a higher incidence of drug discontinuation in the vitamin K antagonist group may have affected the bleeding outcomes

LIMITATIONS

- **Our trial results apply only to patients with atrial fibrillation, intermediate operative risk, and symptomatic aortic stenosis, and the trial involved a population of older adults who were undergoing TAVR**
- The coronavirus disease 2019 pandemic affected the outpatient clinic follow-up routine and may have resulted in **underassessment of laboratory data and mild-to-moderate clinical events**
- The outcomes of death and trial-drug discontinuation may have been competing risks in relation to the outcomes we studied, and we **did not perform competing-risk analyses**
- Formal testing for superiority was not performed
- Lack of a plan for adjustment of confidence intervals

DISCUSSION

- **ENGAGE AF-TIMI 48** (2013)
  - ✓ Patients with atrial fibrillation who were at moderate-to-high thromboembolic risk

→ Edoxaban were noninferior to warfarin in the prevention of stroke or systemic embolism and had lower rates of bleeding and death from cardiovascular causes

- **POPular TAVI** (2020)
  - ✓ Clopidogrel in addition to oral anticoagulation after TAVR in patients with an indication for oral anticoagulation

→ Combination regimen showed more bleeding and had no clinical benefits

- **GALILEO** (2020)
  - ✓ Intermediate-dose rivaroxaban in patients without an indication for oral anticoagulation but who were receiving antiplatelet therapy

→ Increased risks of major bleeding and death

DISCUSSION

- Mean age = 82.1 years
- Concomitent use of antiplatelet drugs

Major bleeding*			
OAP Yes	11.85 (54/328)	7.26 (36/359)	
OAP No	7.92 (44/385)	6.68 (32/354)	

Background → Trial → Discussion → **Appraisal**

CASP RCT checklist

SECTION A:

IS THE BASIC STUDY DESIGN VALID FOR A RANDOMISED CONTROLLED TRIAL?

1. Did the study address a clearly focused research question?

   ☑ Yes ☐ No ☐ Can't tell

P patient	Adult with either prevalent or incident atrial fibrillation lasting more than 30 seconds after successful TAVR
I intervention	Edoxaban 60mg QD
C comparison	Vitamin K Antagonist (target INR= 2.0-3.0)
O outcome	Efficacy and Safety

2. Was the assignment of participants to interventions randomised?

   ☑ Yes ☐ No ☐ Can't tell

- Patients were **randomly assigned in a 1:1 ratio** to receive edoxaban or a vitamin K antagonist.

3. Were all participants who entered the study accounted for at its conclusion?

   ☑ Yes ☐ No ☐ Can't tell

- **Intention-to-treat** analysis
- **The modified ITT population comprised all randomized patients receiving ≥1 dose of the study drug**

SECTION B:

WAS THE STUDY METHODOLOGICALLY SOUND?

4. Were the participants/ investigators/people analyzing outcome 'blind'?

   ☐ Yes ☑ No ☐ Can't tell

- **Open-label trial**
- **Adjudicator-masked trial**
- Most data analyses were performed by a clinical research organization (Covance), whose members were unaware of the trial-group assignments.

5. Were the study groups similar at the start of the randomised controlled trial?

   ☑ Yes ☐ No ☐ Can't tell

- **The demographic and clinical characteristics of the patients at baseline were similar in the two trial groups (Table 1)**

6. Apart from the experimental intervention, did each study group receive the same level of care (that is, were they treated equally)?

   ☑ Yes ☐ No ☐ Can't tell

Table S6. Concomitant Use of Oral Antiplatelet Drugs Throughout the Trial Period

	Edoxaban n=713	VKA n=713
No OAP from randomization to end of study	290 (40.7)	282 (39.6)
Any OAP after randomization	423 (59.3)	431 (60.4)
Any SAPT after randomization	409 (57.4)	415 (58.2)
Acetylsalicylic acid only	196 (27.5)	197 (27.2)
P2Y12 inhibitor only	191 (26.8)	196 (27.5)
Acetylsalicylic acid or P2Y12 in sequence	22 (3.1)	22 (3.1)
Any DAPT after randomization	86 (12.1)	94 (13.2)
DAPT followed by SAPT in sequence	72 (10.1)	78 (10.9)

- **Similar incidences of administration of PPI (71.7% and 69%)**
- Similar follow-up duration (554 days and 530 days)

SECTION C:

WHAT ARE THE RESULTS?

7. Were the effects of intervention reported comprehensively?

☐ Yes ☑ No ☐ Can't tell

- Because of the hierarchical design of our statistical analysis, the failure to show noninferiority for major bleeding **precluded formal testing for superiority of edoxaban**.

8. Was the precision of the estimate of the intervention or treatment effect reported?

☑ Yes ☐ No ☐ Can't tell

- 320 net adverse clinical events would need to occur in approximately 1400 patients : Noninferiority of edoxaban vs. VKAs with **80% power** and a **two-sided significance level of 0.05**
- Noninferiority will be accepted if the upper boundary of the 2-sided 95% CI of the Hazard Ratio falls below 1.38
- Superiority will be accepted if the upper boundary of the 2-sided 95% CI of the Hazard Ratio falls below 1.00

9. Do the benefits of the experimental intervention outweigh the harms and costs?

☐ Yes ☑ No ☐ Can't tell

Benefits	Noninferiority of primary efficacy outcome
Harms	Higher risk of major bleeding

Section D:

Will the results help locally?

10. Can the results be applied to your local population/in your context?

☑ Yes ☐ No ☐ Can't tell

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline (Intention-to-Treat Population).*

Characteristic	Edoxaban (N=713)	Vitamin K Antagonist (N=713)
Age — yr	82.1±5.4	82.1±5.5
Female sex — no. (%)	347 (48.7)	331 (46.4)
Race — no. (%)†		
Asian	92 (12.9)	89 (12.5)
White	593 (83.2)	594 (83.3)
Other	28 (3.9)	30 (4.2)

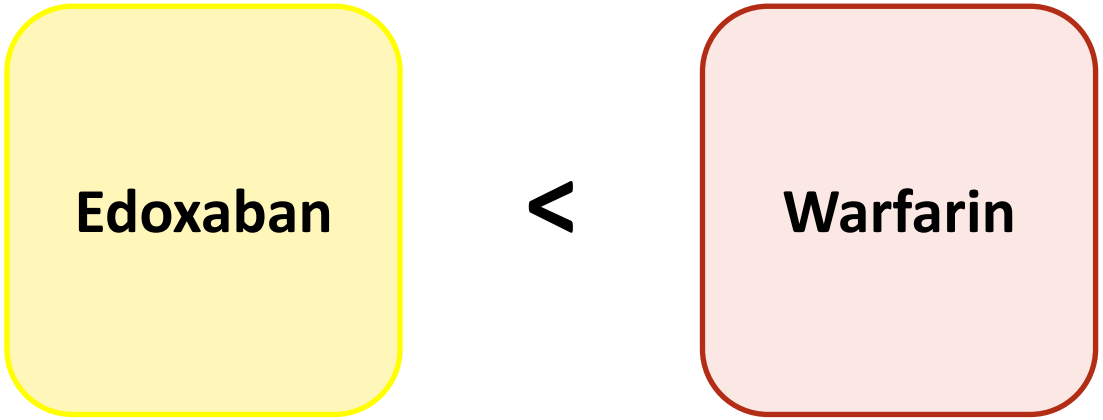
11. Would the experimental intervention provide greater value to the people in your care than any of the existing interventions?

☐ Yes ☑ No ☐ Can't tell

- **Edoxaban was noninferior to vitamin K antagonists for the composite primary outcome of adverse clinical event.**
- **Edoxaban was associated with a higher risk of major bleeding than vitamin K antagonists.**

Q&A

- 有一位病患在做完TAVI之後，出現了A-Fib的症狀，在抗凝血劑的選擇上是否會建議優先使用Edoxaban取代Warfarin以達到更好的效果呢?



Thank You