Pharmacotherapy After TAVR:

Antiplatelet or Anticoagulation Therapy

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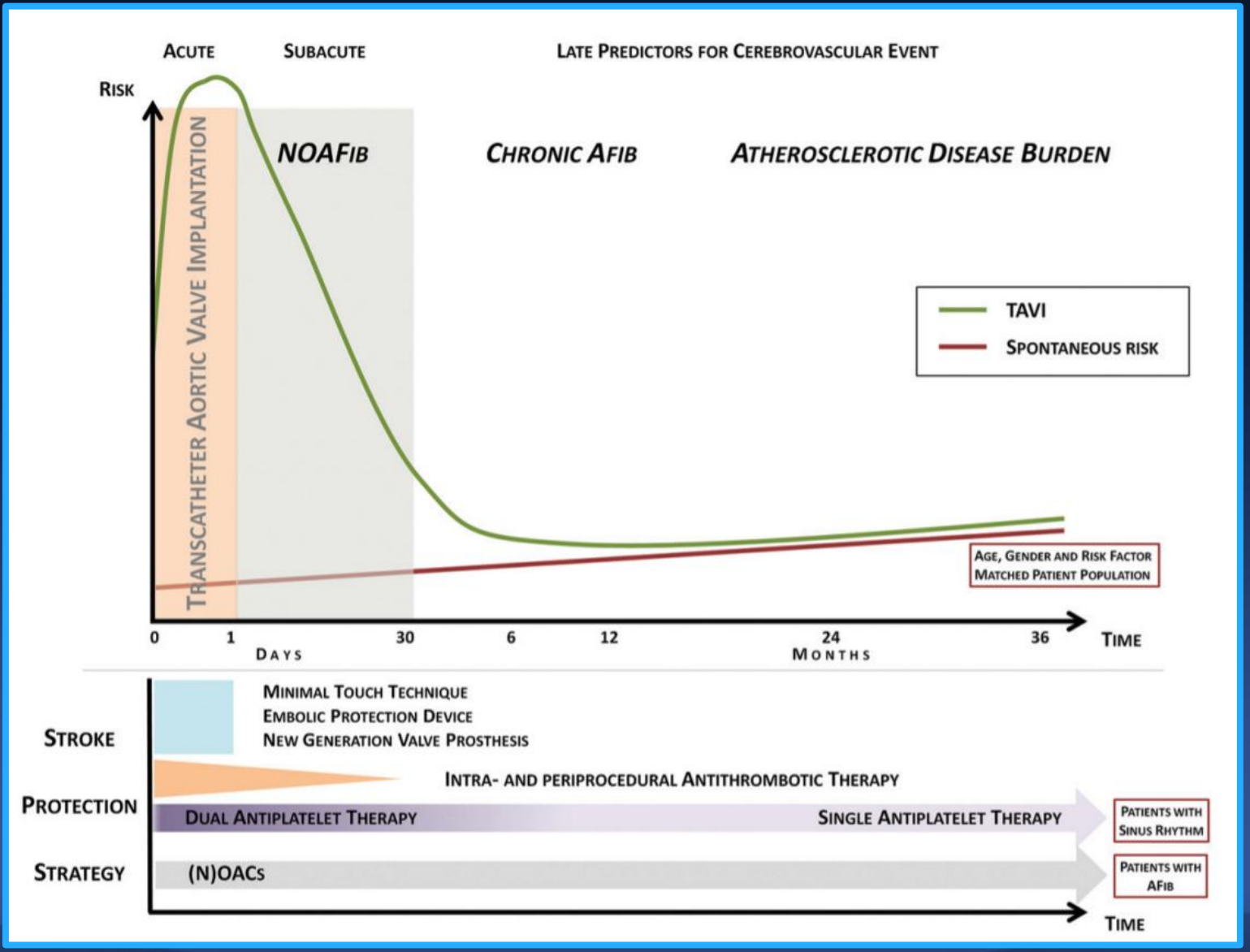
Conflict of Interest Statement

I have nothing to disclose.

Timing of CVA After TAVR



Stortecky et al. Circulation 2012;126:2921-4

2017 AHA/ACC Guideline for Post-TAVR Antithrombotics

- Anticoagulation with VKA to achieve an INR of 2.5 may be reasonable in patients at low risk of bleeding for at least 3 mo.

IIb	B-NR

- Clopidogrel 75 mg the first 6 mo after TAVR may be reasonable in addition to lifelong aspirin 75-100 mg daily.

IIb	C

Nishimura RA et al., J Am Coll Cardiol;70:252-289.

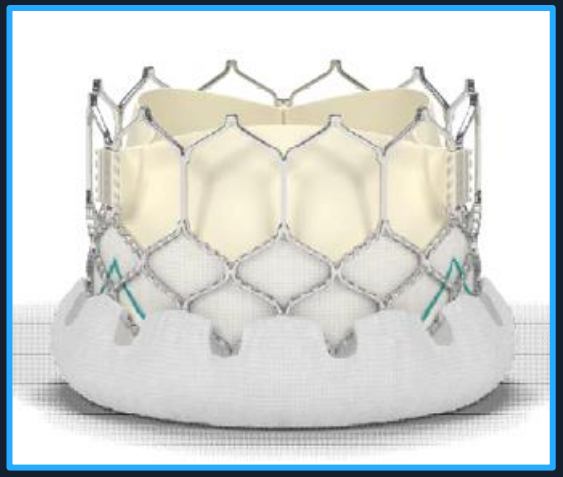
2017 ESC Guideline for Post-TAVR Antithrombotics

- Oral anticoagulation is recommended lifelong for patients with surgical or transcatheter implanted bioprostheses who have other indications for anticoagulation — **I** **C**
- DAPT should be considered for the first 3-6 months after TAVR, followed by lifelong SAPT in patients who do not need OAC for other reasons. — **IIa** **C**
- SAPT may be considered after TAVR in the case of high bleeding risk. — **IIb** **C**

Baumgartner H et al., Eur Heart J. 2017;38:2739-2791.

Why DAPT Post-TAVR?

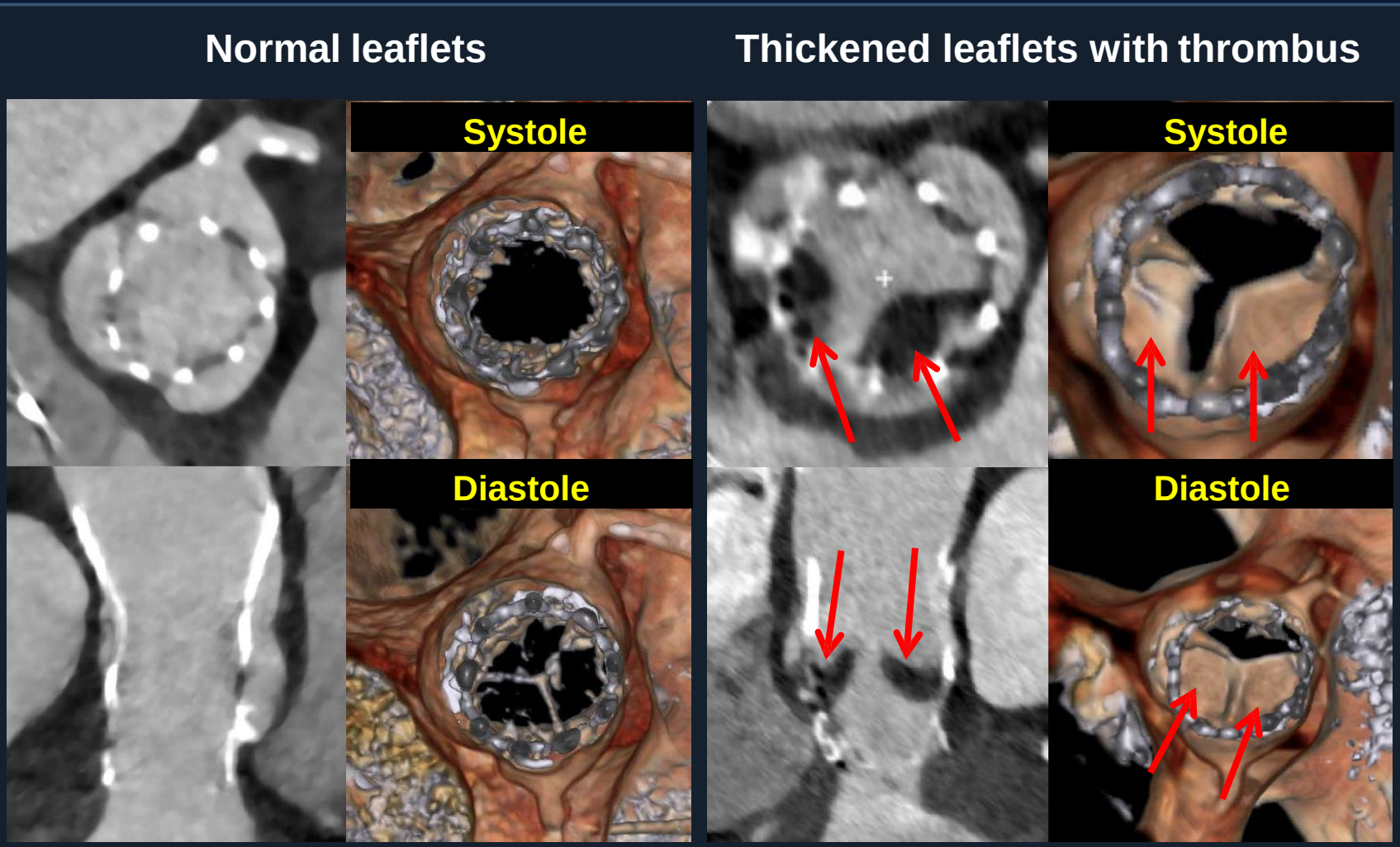
- Decision based on Consensus
  "It's like a stent" treat like
  Coronary or Peripheral stent



- Protocol of RCT

  PARTNER I: *DAPT* for 6 months
  PARTNER II: *Aspirin* indefinitely
  Clopidogrel at least 1 month
  PARTNER III: *DAPT* at least 1 month
  Evolut R low risk trial: *DAPT* at least 1 months
  followed by *aspirin* through 1 year

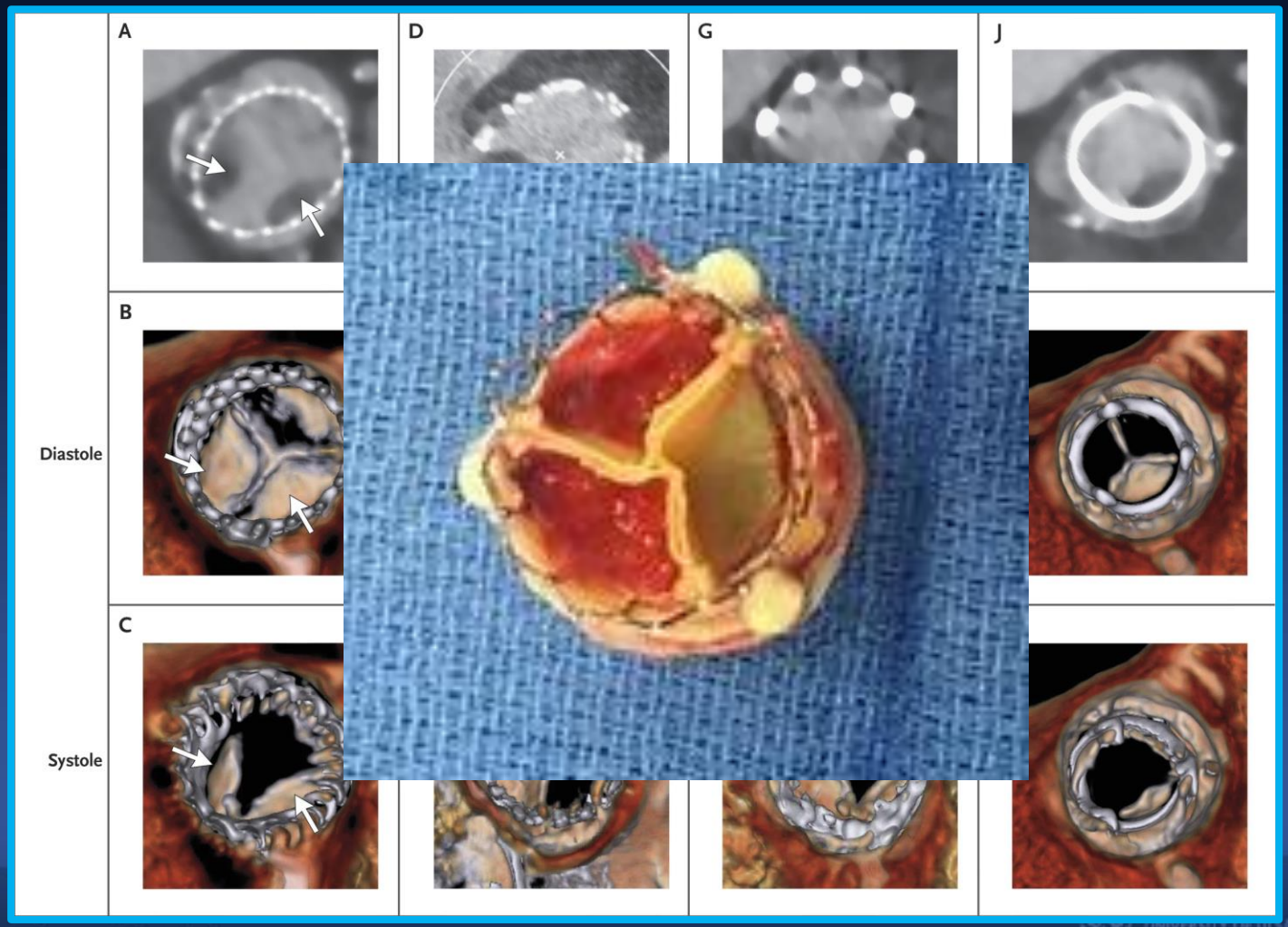
Valve Thrombosis



Makkar RR et al. N Engl J Med 2015;373:2015-2024

Subclinical Leaflet Thrombosis

Evidence of Reduced Leaflet Motion in Multiple Prosthesis Types



Makkar RR et al. N Engl J Med 2015;373:2015-2024

Subclinical leaflet thrombosis

Potential clinical consequences:

- Progression to clinical valve thrombosis
- Stroke
- Impaired hemodynamic performance
- Reduced durability of bioprosthetic aortic valves

…or Just an innocent bystander?

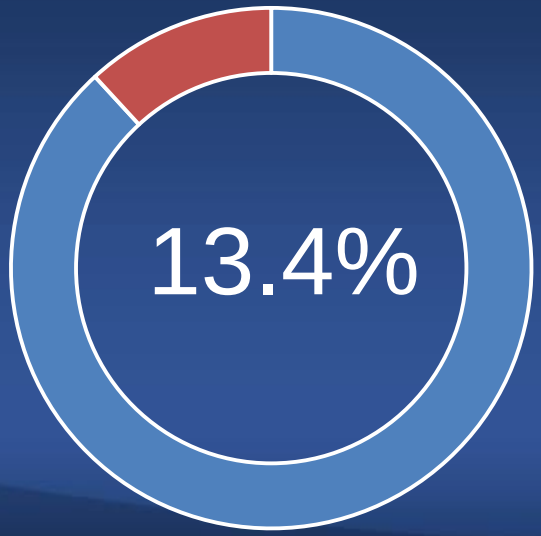
Prevalence of reduced leaflet motion

657 patients underwent CTs in the **RESOLVE registry** Cedars-Sinai Medical Center, LA

274 patients underwent CTs in the **SAVORY registry** Rigshospitalet, Copenhagen

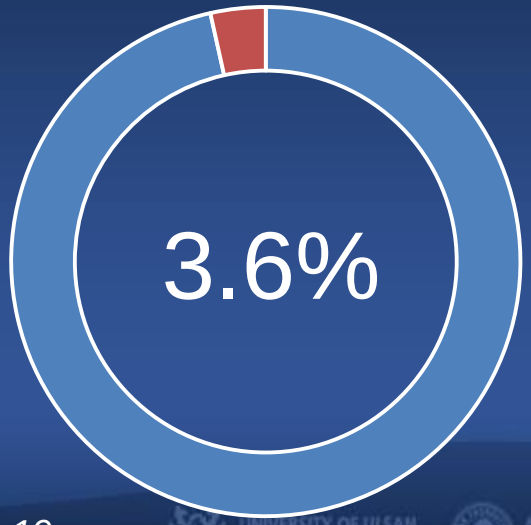
Reduced leaflet motion 106 (11.9%) patients

TAVR (N=752)



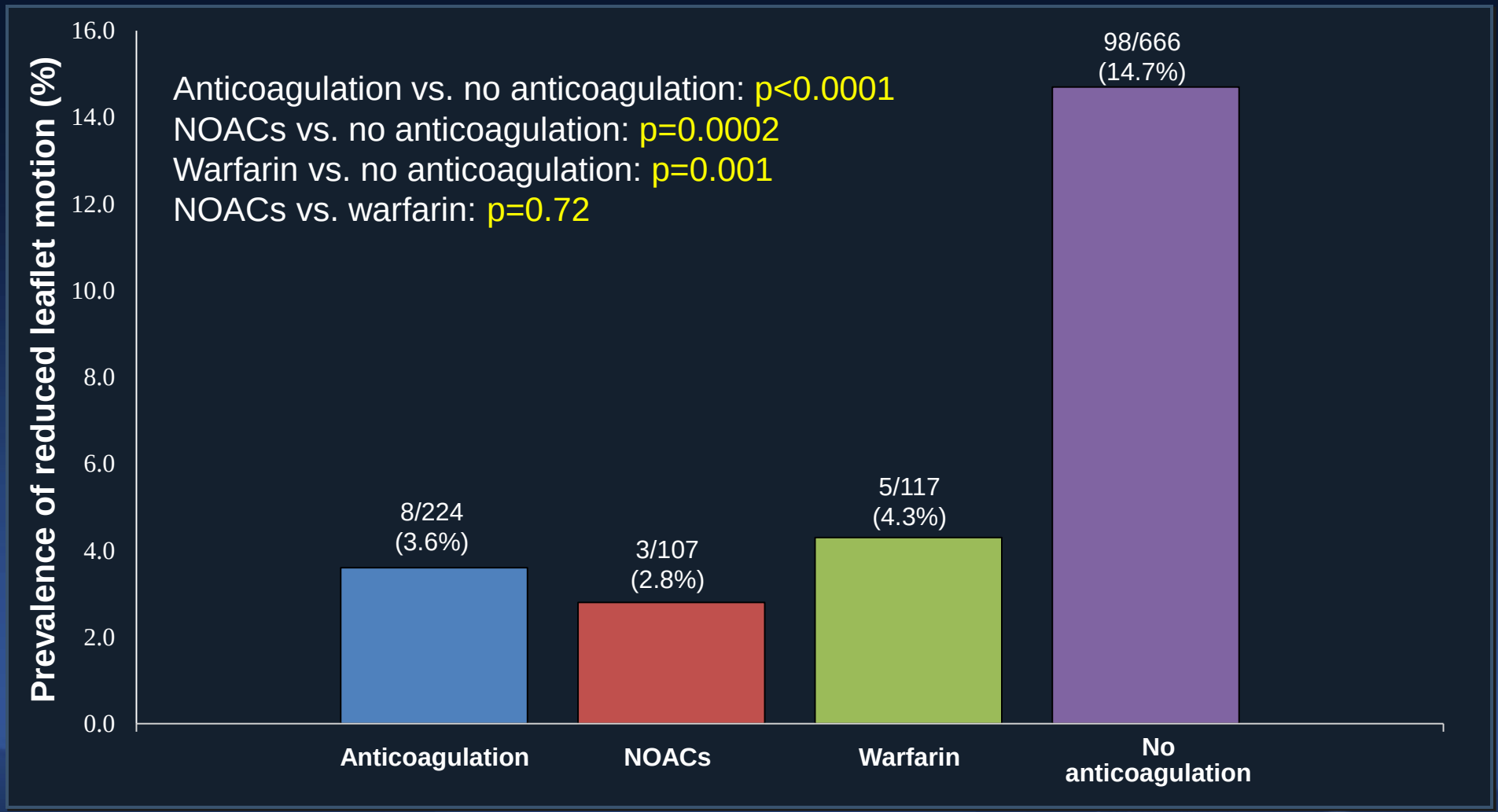
P=0.001

SAVR (N=138)



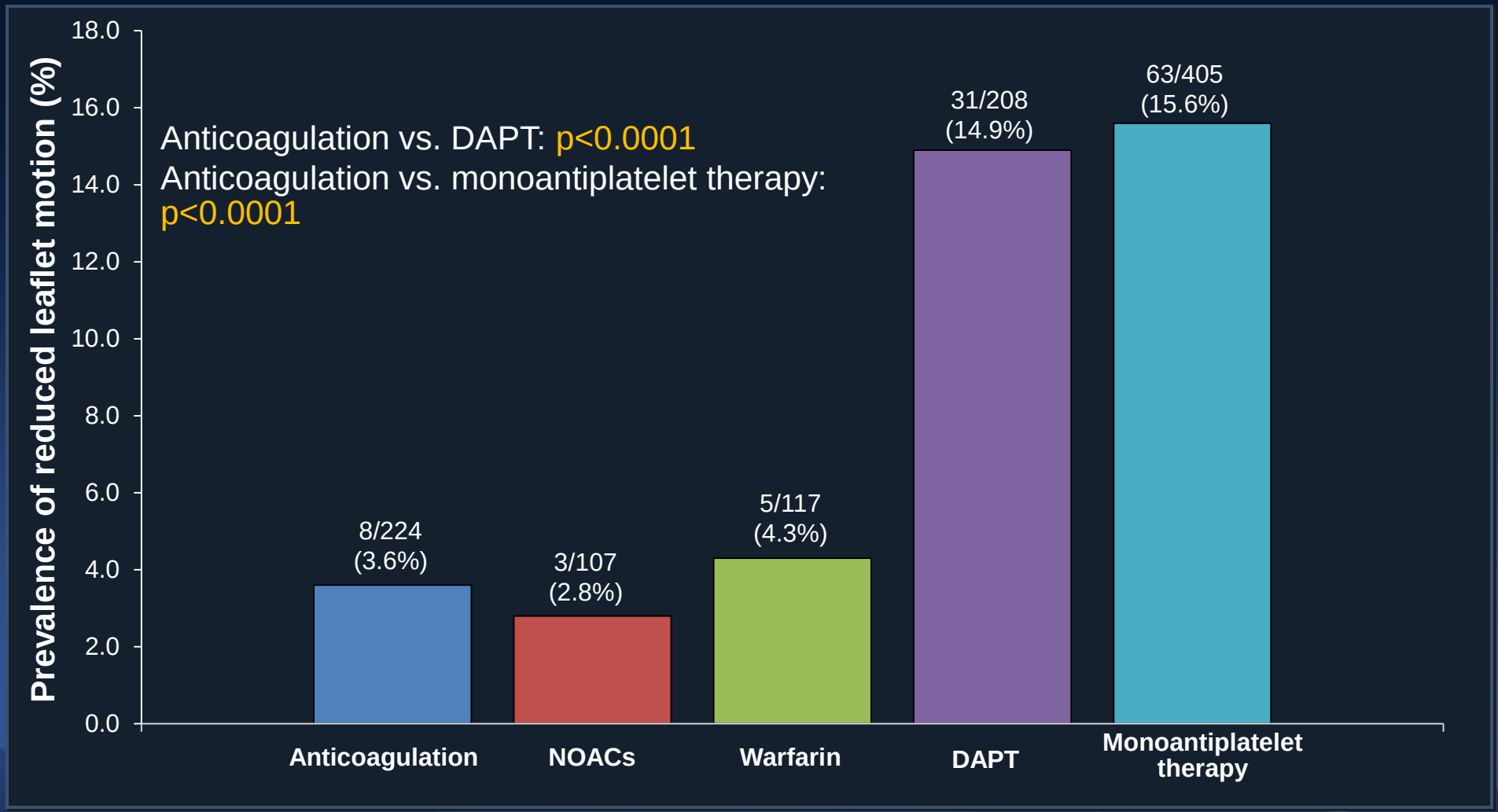
Chakravarty T, et al. Lancet. 2017 Mar 19.

Impact of Anticoagulation on Prevalence of Reduced Leaflet Motion



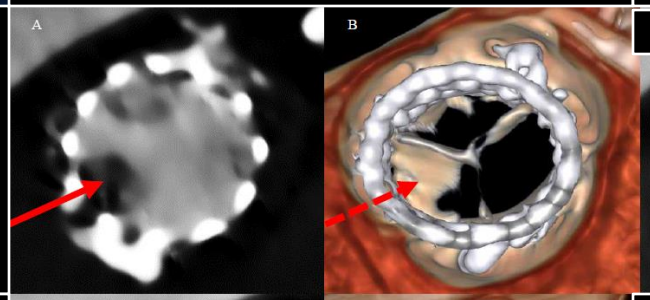
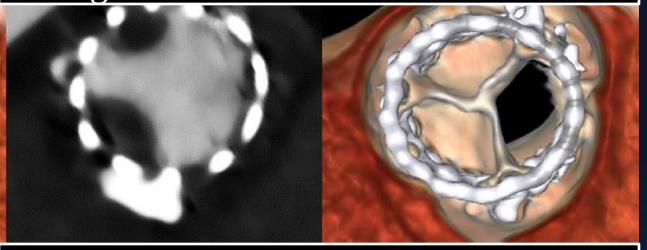
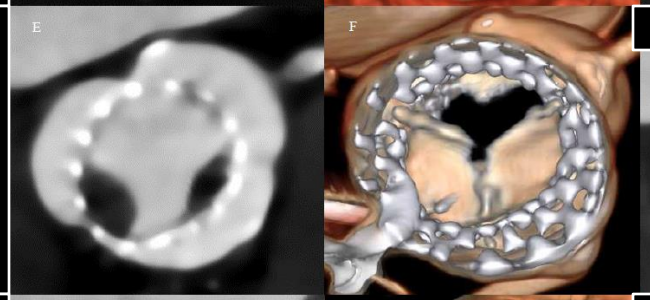
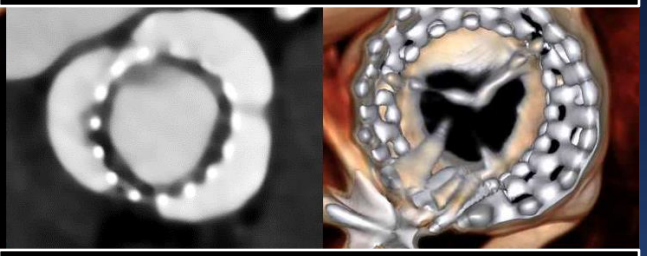
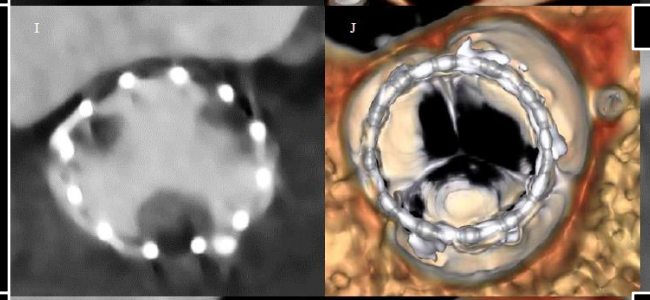
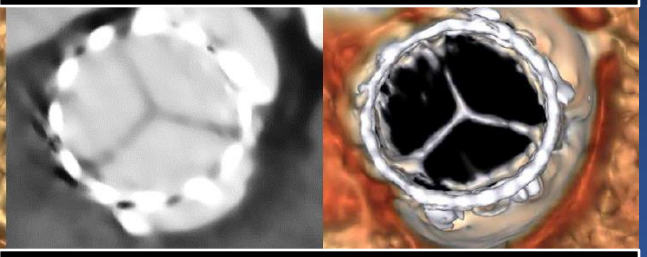
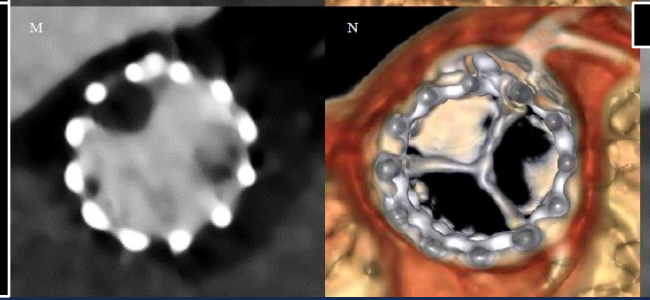
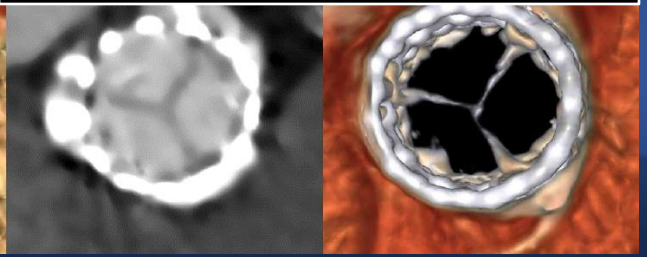
Chakravarty T, et al. Lancet. 2017 Mar 19.

Anticoagulation vs. Antiplatelets on Reduced Leaflet Motion

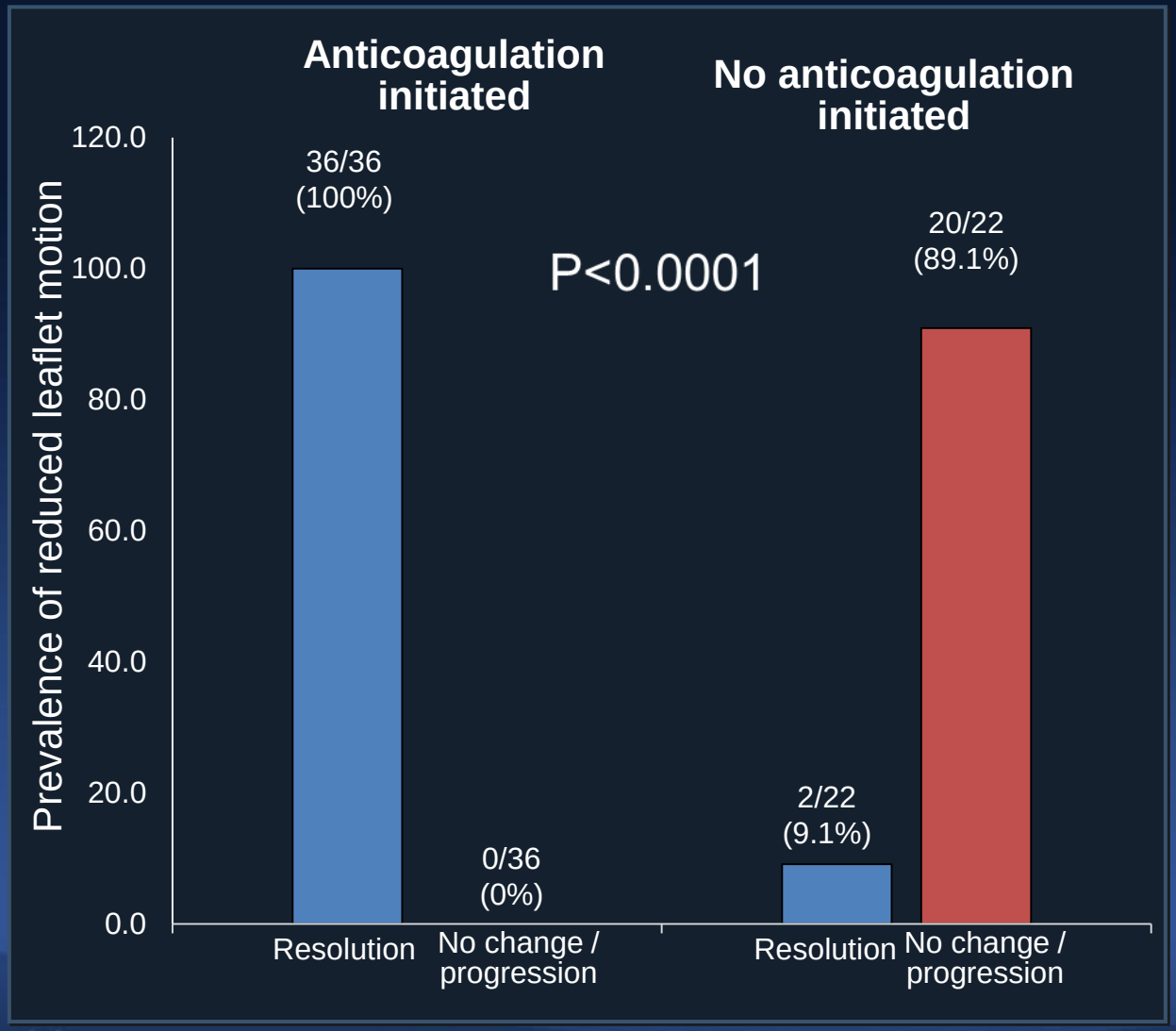


Chakravarty T, et al. Lancet. 2017 Mar 19.

Anticoagulation vs. DAPT

	Index CT	Follow-up CT
DAPT continued after index CT		Progression of reduced leaflet motion 
Warfarin initiated after index CT		Resolution of reduced leaflet motion 
Rivaroxaban initiated after index CT		Resolution of reduced leaflet motion 
Apixaban initiated after index CT		Resolution of reduced leaflet motion 

Impact of initiation of anticoagulation on reduced leaflet motion



- Resolution in 36 out of 36 patients treated with anticoagulation (NOACs, n=12; warfarin, n=24)
- Persistence or progression in 20 out of 22 patients not treated with anticoagulation

Chakravarty T, et al. Lancet. 2017 Mar 19.

Clinical Impact of Leaflet Thrombosis

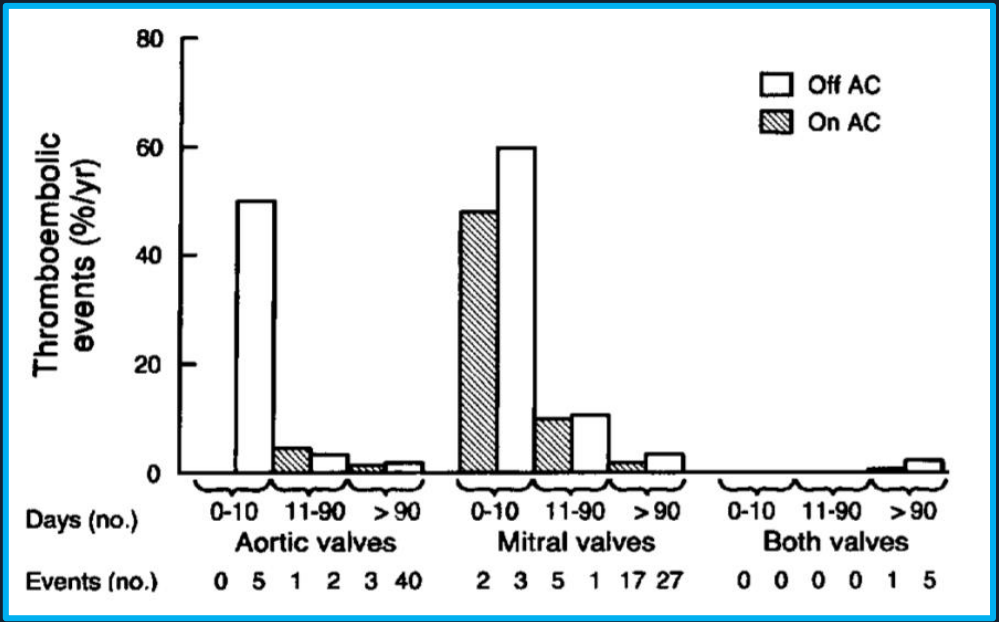
Only non-procedural events (>72 hours post-TAVR/SAVR) included

	Normal leaflet motion (N=784)		Reduced leaflet motion (N=106)			
Non-procedural events	n/N(%)	Rate per 100 person-years	n/N(%)	Rate per 100 person-years	HR (95% CI)	P value
Death	34/784 (4.3%)	2.91	4/106 (3·8%)	2.66	0.96 (0.34-2.72)	0.94
MI	4/784 (0.5%)	0.34	1/106 (0·9%)	0.67	1.91 (0.21-17.08)	0.56
Stroke/TIAs	20/784 (2.6%)	1.75	8/106 (7·6%)	5.71	3.30 (1.45-7.50)	0.004
All stroke	15/784 (1.9%)	1.31	4/106 (3·8%)	2.75	2.14 (0.71-6.44)	0.18
Ischemic stroke	14/784 (1.8%)	1.22	4/106 (3·8%)	2.75	2.29 (0.75-6.97)	0.14
TIAs	7/784 (0.9%)	0.60	5/106 (4·7%)	3.48	5.89 (1.87-18.60)	0.002

Chakravarty T, et al. Lancet. 2017 Mar 19.

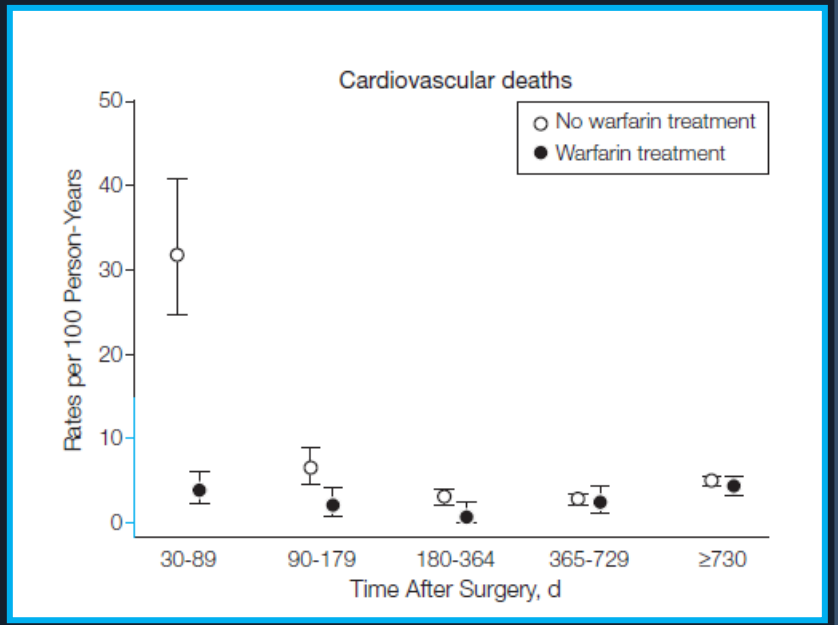
Experience of Bioprosthetic Surgical Valve

Incidence of Thrombotic Events



J Am Coll Cardio11995;25:1111-9

Effect of Warfarin



Merie C. et al. JAMA 2012

2017 AHA/ACC Guideline for Post-TAVR Antithrombotics

➢ Anticoagulation with VKA to achieve an INR of 2.5 may be reasonable in patients at low risk of bleeding for at least 3 mo.	IIb	B-NR
➢ Clopidogrel 75 mg the first 6 mo after TAVR may be reasonable in addition to lifelong aspirin 75-100 mg daily.	IIb	C

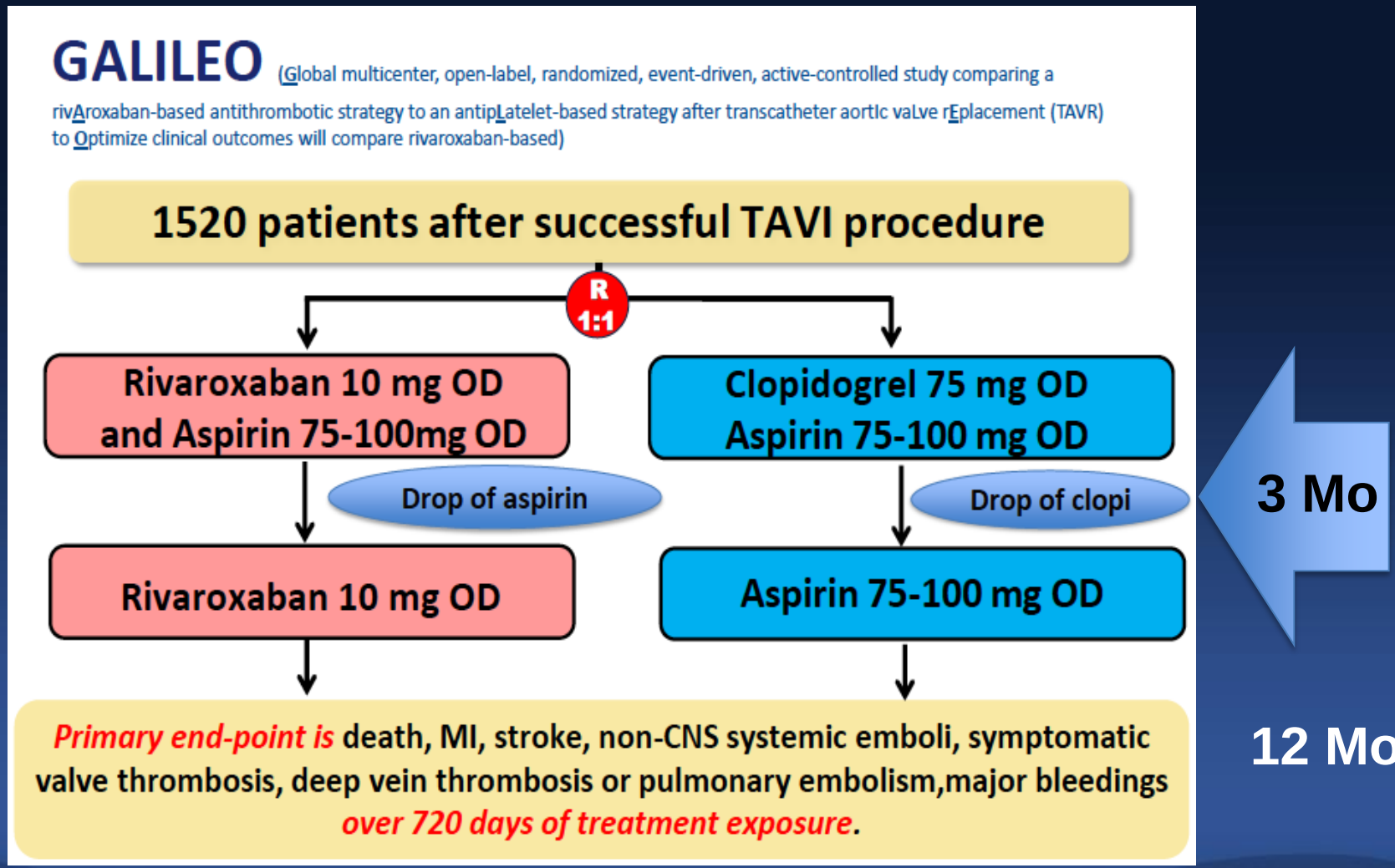
Nishimura RA et al., J Am Coll Cardiol;70:252-289.

Current Landscape of Adjunctive Pharmacotherapy Clinical Trials for TAVR

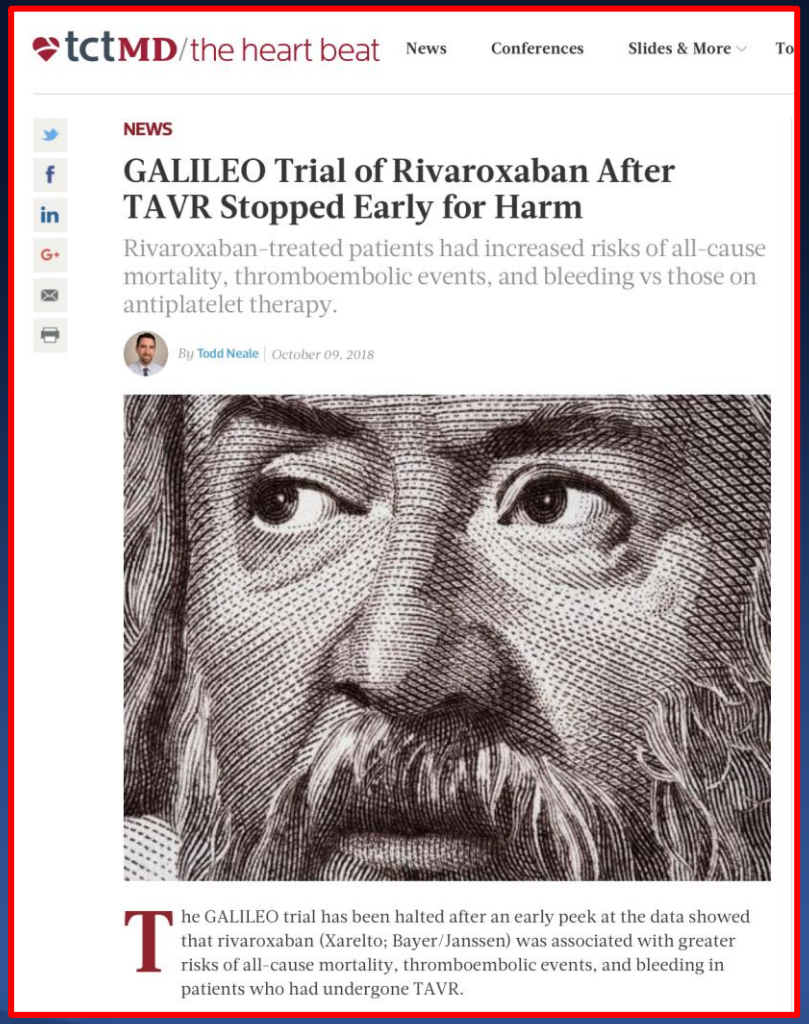
	Patients with no indication for OAT	Patients with indication for OAT
Studies of antiplatelet strategies	ARTE	AVATAR
	POPular TAVI	POPular TAVI
	CLOE	CLOE
Studies comparing antiplatelet and anticoagulant strategies	AUREA	
	GALILEO (Rivaroxaban)	
	ATLANTIS (Apixaban)	
	ADAPT-TAVR (Endoxaban)	
Studies comparing anticoagulant strategies		ATLANTIS (Apixaban)
		ENVISAGE-TAVI AF (Endoxaban)

Capodanno D, Leon MB. EuroIntervention 2016;12:Y1-Y5

GALILEO Trial



GALILEO Stopped, Oct 2018



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GALILEO Trial of Rivaroxaban After TAVR Stopped Early for Harm

Rivaroxaban-treated patients had increased risks of all-cause mortality, thromboembolic events, and bleeding vs those on antiplatelet therapy.

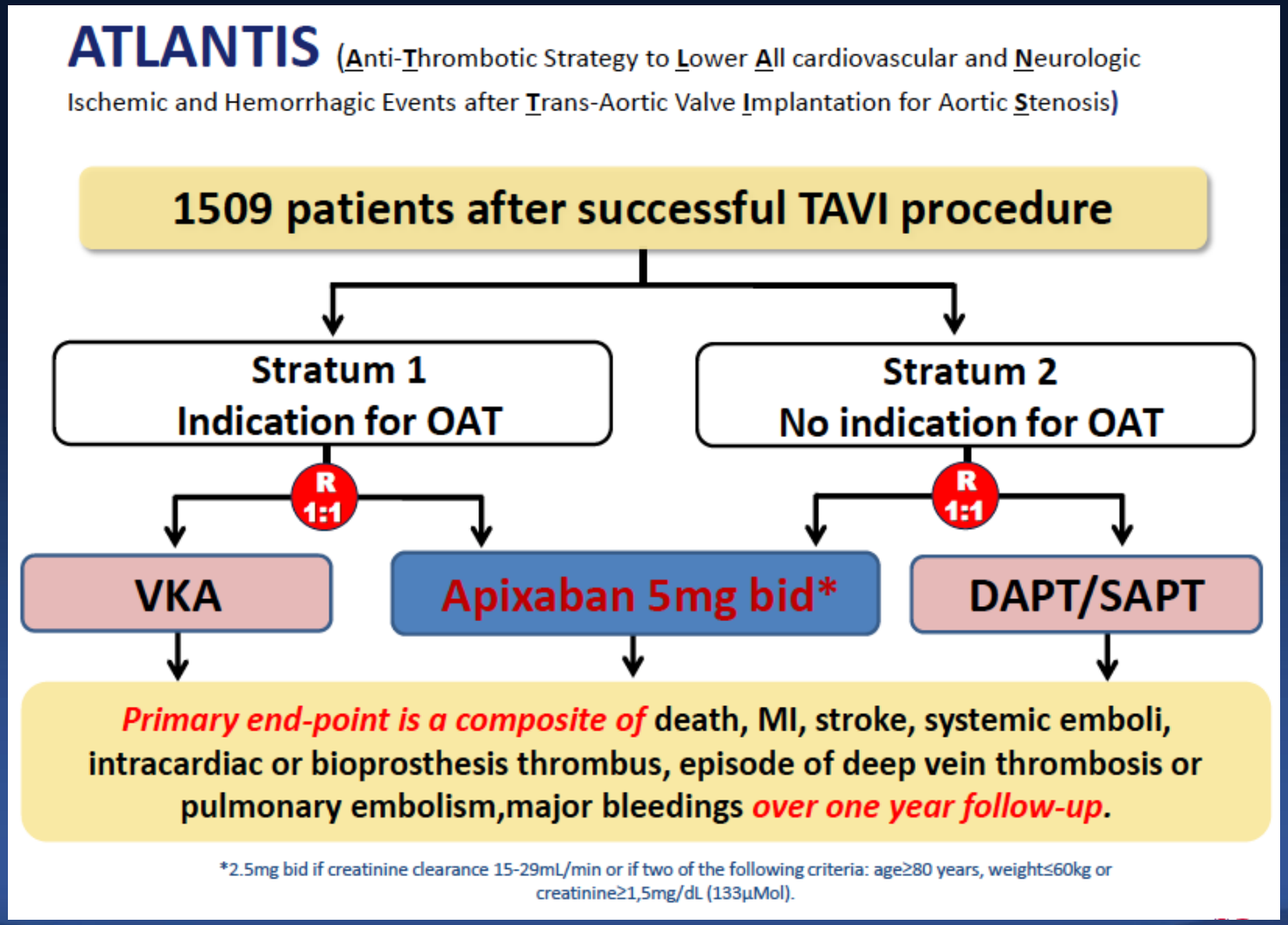
By Todd Neale | October 09, 2018

The GALILEO trial has been halted after an early peek at the data showed that rivaroxaban (Xarelto; Bayer/Janssen) was associated with greater risks of all-cause mortality, thromboembolic events, and bleeding in patients who had undergone TAVR.

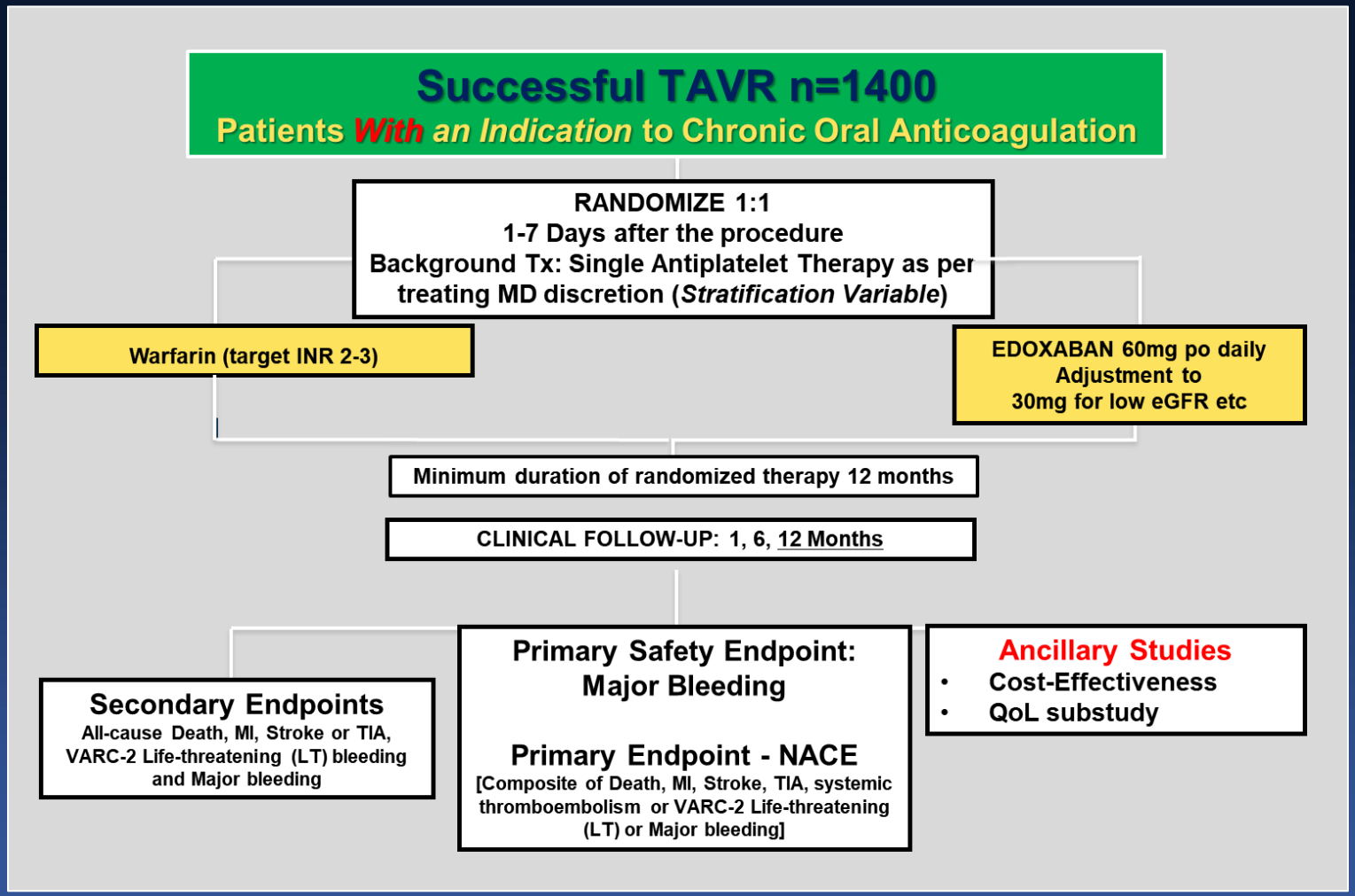
	Rivaroxaban	Antiplatelet
First thromboembolic events	11.4%	8.8%
Death	6.8%	3.3%
Primary bleeding	4.2%	2.4%

Final results of the study are expected in the first quarter of 2019 (?) – tctMD

ATLANTIS


ATLANTIS (Anti-Thrombotic Strategy to Lower All cardiovascular and Neurologic Ischemic and Hemorrhagic Events after Trans-Aortic Valve Implantation for Aortic Stenosis)
1509 patients after successful TAVI procedure
Stratum 1
Indication for OAT
Stratum 2
No indication for OAT
R 1:1
R 1:1
VKA
Apixaban 5mg bid*
DAPT/SAPT
Primary end-point is a composite of death, MI, stroke, systemic emboli, intracardiac or bioprosthesis thrombus, episode of deep vein thrombosis or pulmonary embolism,major bleedings over one year follow-up.
*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).

ENVISAGE-TAVI AF



ADAPT-TAVR Trial

Anticoagulant versus Dual Antiplatelet Therapy for Preventing Leaflet Thrombosis and Cerebral Embolization After Transcatheter Aortic Valve Replacement

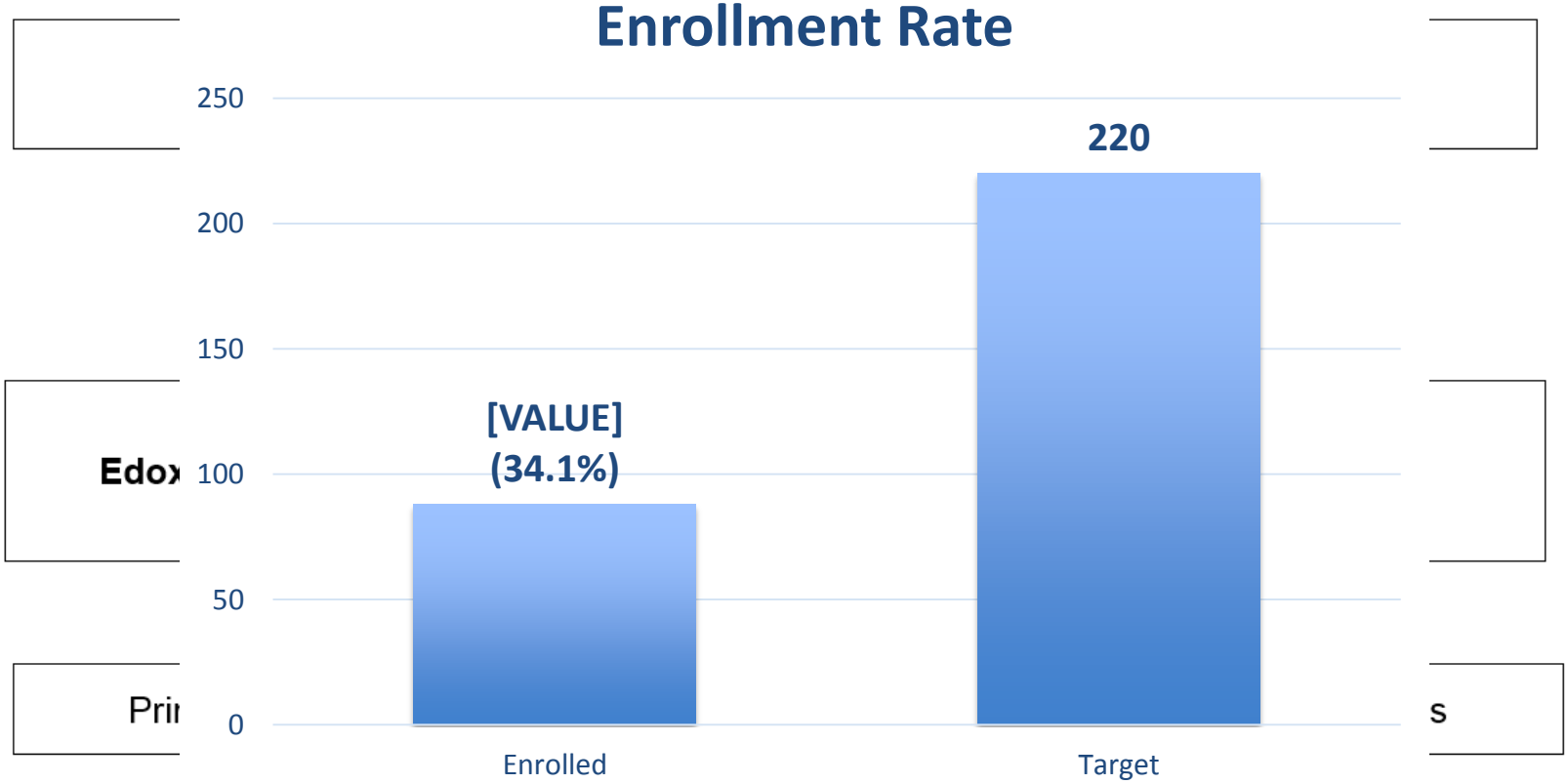
Seung-Jung Park (Trial Chair)
Duk-Woo Park (Trial Co-chair)

Heart Institute, Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

Trial Design: ADAPT-TAVR Trial

Anticoagulant versus ***D***ual ***A***ntiplatelet Therapy for ***P***reventing Leaflet ***T***hrombosis After ***T***ranscatheter ***A***ortic ***V***alve ***R***eplacement

ADAPT-TAVR Trial



*30 mg once daily if moderate or severe renal impairment (creatinine clearance 15 – 50 mL/min), low body weight ≤60kg, or concomitant use of P-glycoprotein inhibitors (cyclosporin, dronedarone, erythromycin, ketoconazole).

Antithrombotic Strategy after TAVR

- TAVR patients have multiple thrombotic- and bleeding-related comorbidities. Thus, it make optimal antiplatelet and anticoagulant management to be complex.
- Currently, optimal antithrombotic strategy following TAVR is still debating.
- Guidelines differ on anticoagulation strategies in TAVR,
  - Without a strong evidence base for their recommendations.
  - Practice variation in the real world is substantially high.
  - Clinical trials on different antithrombotic regimens are ongoing & expanding.