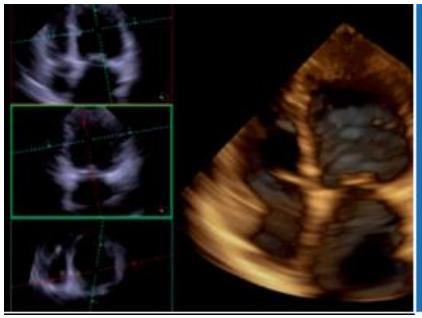


EuroValve

April 26-27, 2018

NH, Palermo, Sicily, ITALY

Overview on ongoing randomized clinical trials in TAVI **?**

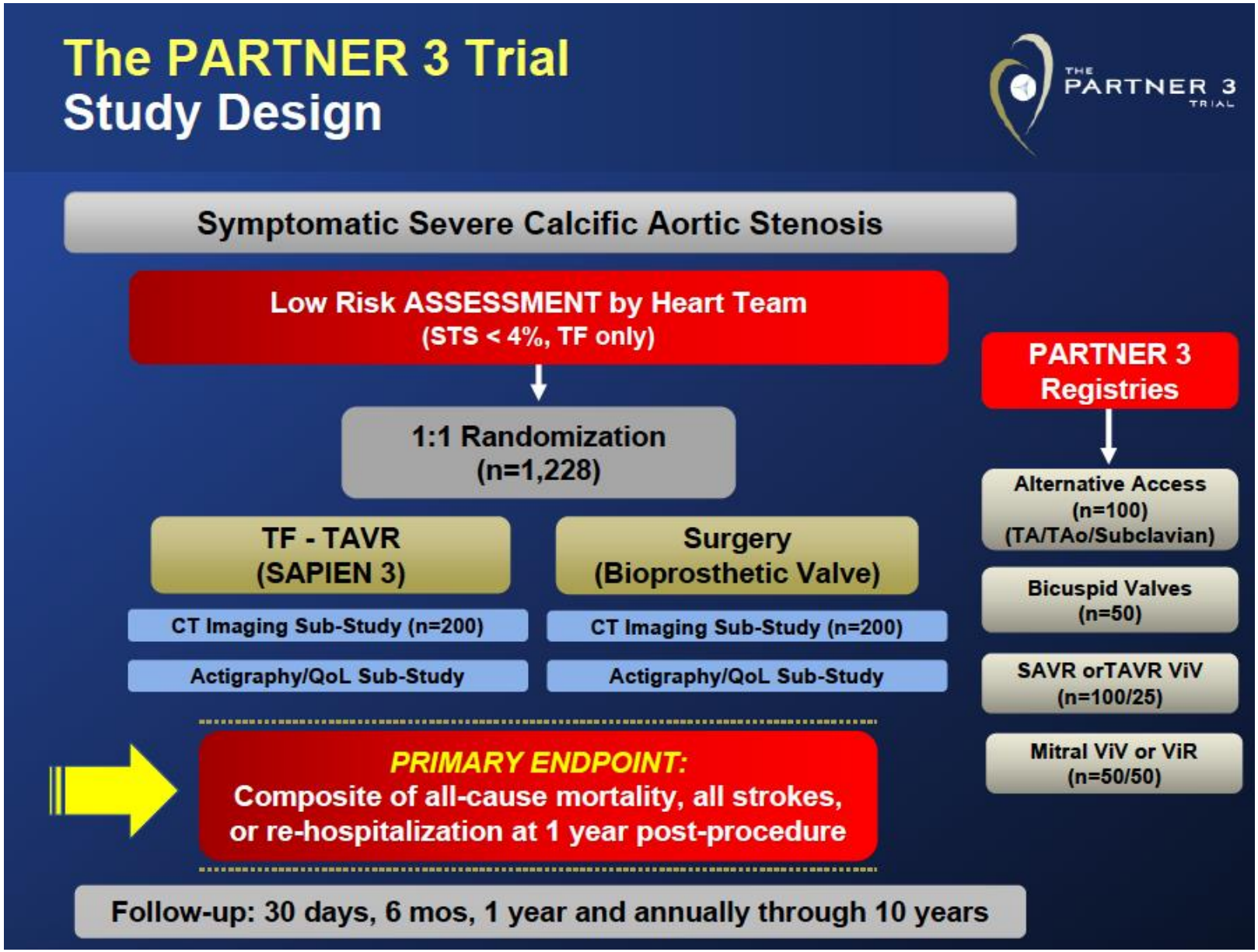
Massimo Mancone

"Sapienza" Università di Roma

Policlinico Umberto I

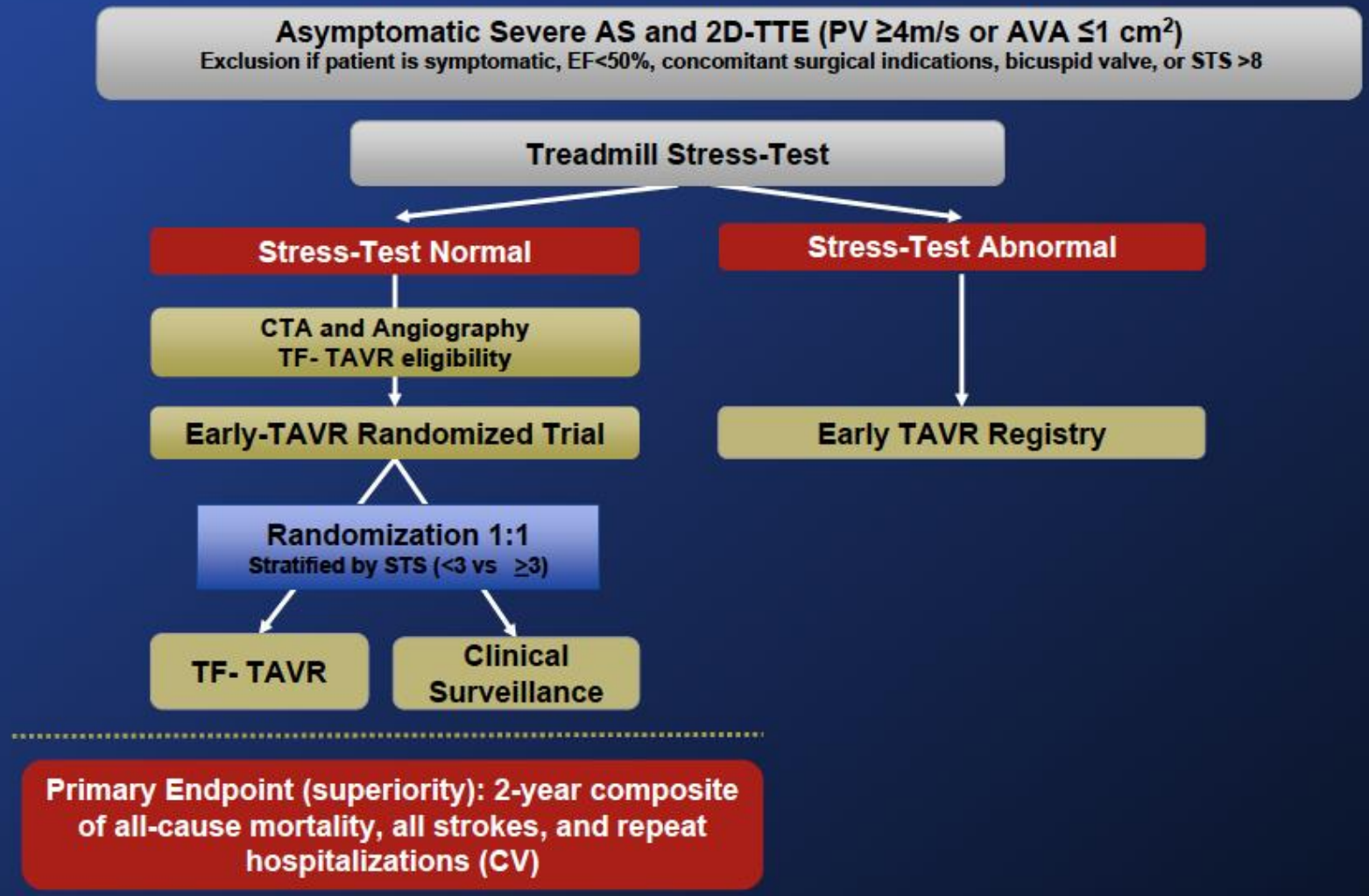
Cardiologia Interventistica

- **Expanding TAVR Clinical Indications**


The PARTNER 3 Trial
Study Design
THE PARTNER 3 TRIAL
Symptomatic Severe Calcific Aortic Stenosis
Low Risk ASSESSMENT by Heart Team
(STS < 4%, TF only)
1:1 Randomization
(n=1,228)
TF - TAVR
(SAPIEN 3)
Surgery
(Bioprosthetic Valve)
CT Imaging Sub-Study (n=200)
CT Imaging Sub-Study (n=200)
Actigraphy/QoL Sub-Study
Actigraphy/QoL Sub-Study
PRIMARY ENDPOINT:
Composite of all-cause mortality, all strokes, or re-hospitalization at 1 year post-procedure
Follow-up: 30 days, 6 mos, 1 year and annually through 10 years
PARTNER 3 Registries
Alternative Access
(n=100)
(TA/TAo/Subclavian)
Bicuspid Valves
(n=50)
SAVR orTAVR ViV
(n=100/25)
Mitral ViV or ViR
(n=50/50)

EARLY TAVR Trial
Study Flow

THE PARTNER 3 TRIAL



TAVR UNLOAD Trial

Study Design

(600 patients, 1:1 Randomized)

TAVR UNLOAD Trial

International Multicenter Randomized

Heart Failure
LVEF < 50%
NYHA ≥ 2
Optimal HF therapy (OHFT)
Moderate AS

R

TAVR + OHFT

OHFT Alone

Follow-up:
1 month
6 months
1 year

Clinical endpoints
Symptoms
Echo
QoL

Primary Endpoint
Hierarchical occurrence of:
- **All-cause death**
- **Disabling stroke**
- **Hospitalizations for HF, aortic valve disease**
- **Change in KCCQ**

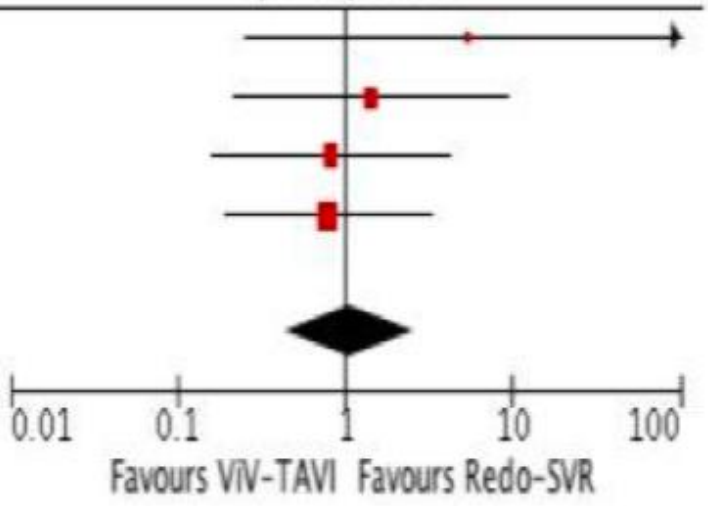
Reduced AFTERLOAD
Improved LV systolic and diastolic function

Metanalysis of Transcatheter Valve-in-Valve Implantation Versus Redo Aortic Valve Surgery for Bioprosthetic Aortic Valve Dysfunction

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Erlebach 2015	1.6887	1.5619	8.5%	5.41 [0.25, 115.58]
Grubitzsc 2016	0.3629	0.9584	22.5%	1.44 [0.22, 9.41]
Silaschi 2016	-0.1942	0.8362	29.5%	0.82 [0.16, 4.24]
Spaziano 2017	-0.2364	0.7221	39.6%	0.79 [0.19, 3.25]
Total (95% CI)			**100.0%**	**1.08 [0.44, 2.62]**

Heterogeneity: $Chi^2 = 1.45$, $df = 3$ ($P = 0.69$); $I^2 = 0\%$

Test for overall effect: $Z = 0.16$ ($P = 0.87$)



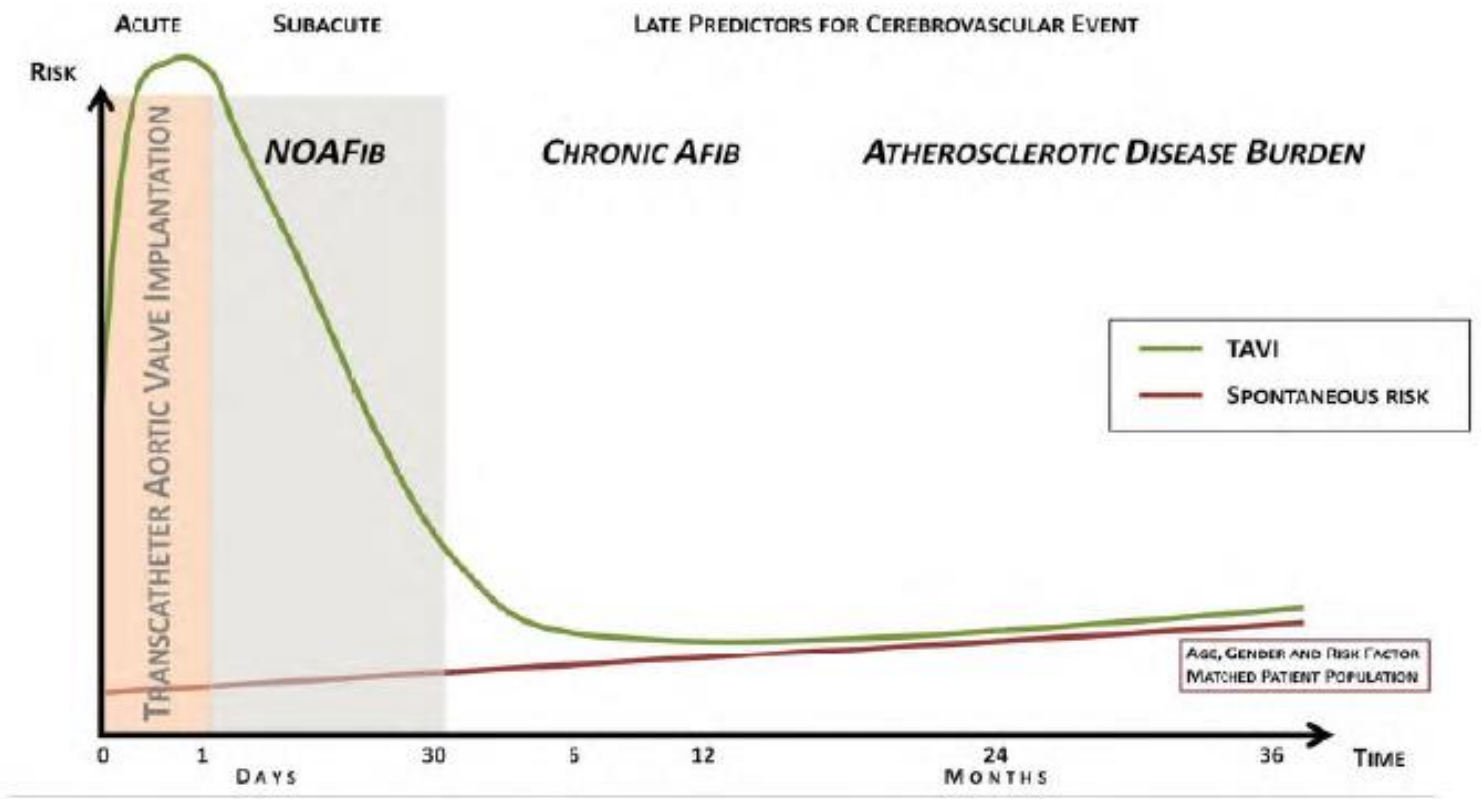
This meta-analysis of nonrandomized studies with modest number of patients suggested that ViV-TAVI had similar 30-day survival compared with redo-SAVR for aortic BPV dysfunction.

- **Expanding TAVR Clinical Indications**

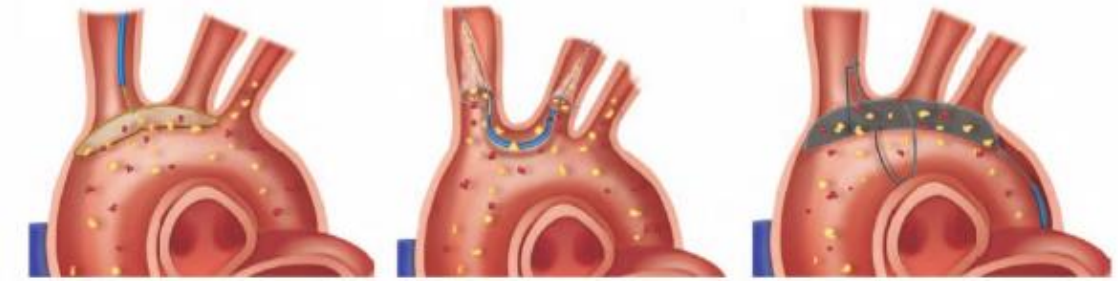
- **TAVI Procedure** – Will cerebral embolic protection become the standard for TAVR in the future?

TAVI AND CEREBROVASCULAR EVENTS

Stortecky, Windecker. *Circulation* 2012;126:2921-4



EMBOLIC PROTECTION DEVICES AND TAVI



Embrella Deflector (Edwards LifeSciences)

Montage 2 Capture Device (Claret Medical)

Triguard Cerebral Deflector (Keystone Heart)

EVIDENCE FROM RANDOMIZED TRIALS

PROTAVI-C

RODÉS-CABAU ET AL JACC CARDIOVASC INTERV. 2014

41 patients

↓ average volume of ischemic lesion

CLEAN-TAVI

HAUSSIG ET AL JAMA 2016

100 patients

↓ frequency of ischemic cerebral lesions

SENTINEL

KAPADIA ET AL JACC 2017

363 patients

No significant reduction of lesion volume on MRI

DEFLECT III TRIAL

LANSKY ET AL EUROPEAN HEART JOURNAL 2015

85 patients

↓ new ischemic brain lesions and neurologic deficits

↑ cognitive function

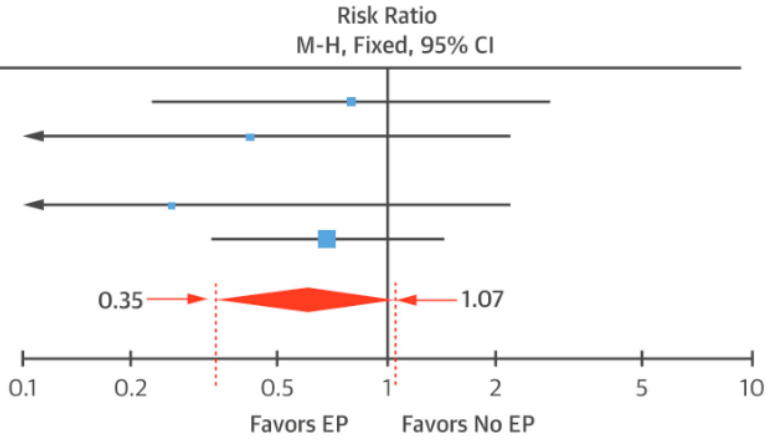
Cerebral Embolic Protection During TAVR

A Clinical Event Meta-Analysis

Study or Subgroup	Embolic Protection Events	Embolic Protection Total	No Embolic Protection Events	No Embolic Protection Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CLEAN-TAVI	4	50	5	50	17.7%	0.80 [0.23, 2.81]
DEFLECT-III	2	46	4	39	15.4%	0.42 [0.08, 2.19]
EMBOL-X	0	14	0	16		Not estimable
MISTRAL-C	1	32	4	33	14.0%	0.26 [0.03, 2.18]
SENTINEL	16	234	11	111	52.9%	0.69 [0.33, 1.44]
Total (95% CI)		**376**		**249**	**100.0%**	**0.61 [0.35, 1.07]**
Total events	23		24			

Heterogeneity: $Chi^2 = 1.10$, df = 3 (P = 0.78); $I^2 = 0\%$

Test for overall effect: Z = 1.73 (P = 0.08)



"In conclusion, the totality of the data suggests that use of EP during TAVR appears to be associated with a nonsignificant trend towards reduction in death or stroke."

JACC VOL. 69, NO. 4, 2017 JANUARY 31, 2017:463–70

- **Expanding TAVR Clinical Indications**

- **TAVI Procedure** – Will cerebral embolic protection become the standard for TAVR in the future?

- **TAVR Adjunct Pharmacology Customized Patient-Based Therapy.**

TAVR Adjunct Pharmacology
Customized Patient-Based Therapy

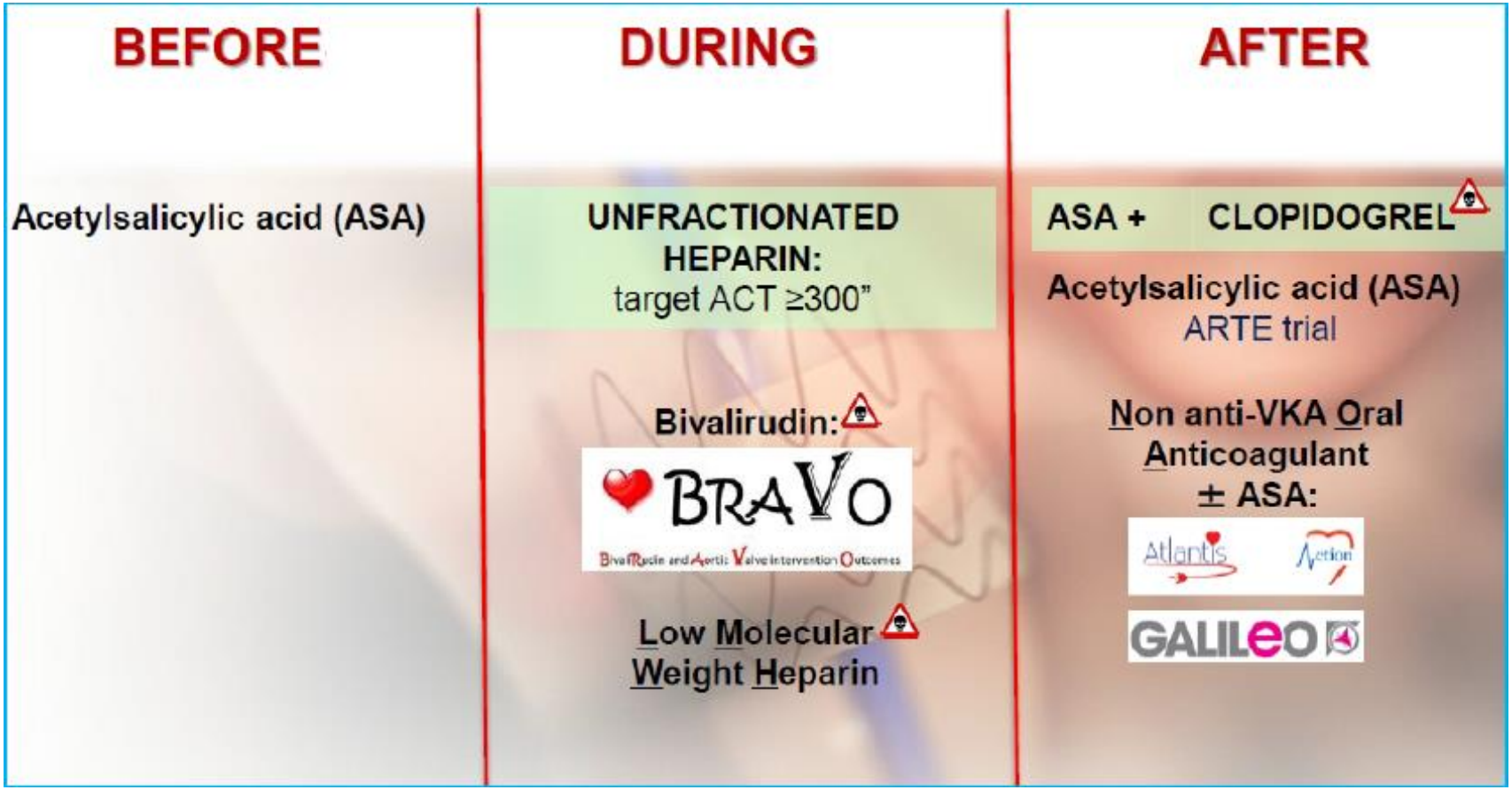


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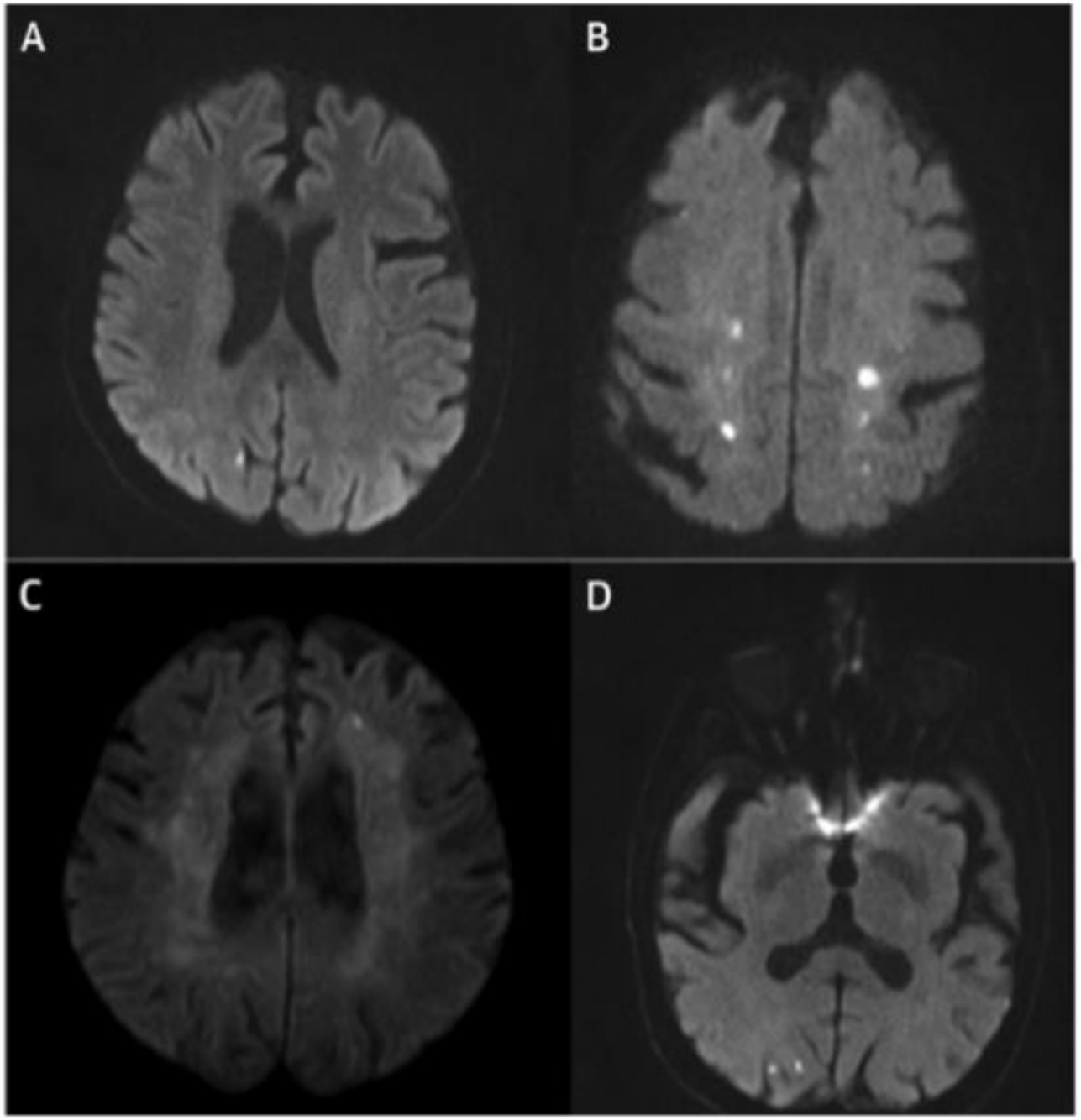
FIGURE 2 MRI Showing Location of New Cerebral Emboli in 4 Patients Without Clinical Stroke or TIA



Bivalirudin
in Transcat
The Randomize

George D. Dangas, MD, PhI
Ulrich Schäfer, MD,‖ Nicola
Stephan Windecker, MD,††
Peter Boekstegers, MD,‖‖ A
Anita W. Asgar, MD,††† An
Hans Ulrich Hink, MD,¶¶¶
Ilknur Lechthaler,‡‡‡‡ Debr
Christian Hengstenberg, M

8 Did not receive bivalir
6 Did not undergo TA

1 Day 30 visit <23 days
1 Lost to follow-up <23
1 Withdrew consent but
allowed data use prior t
withdrawal
2 Physician decision
2 Due to study criteria
2 Other reason

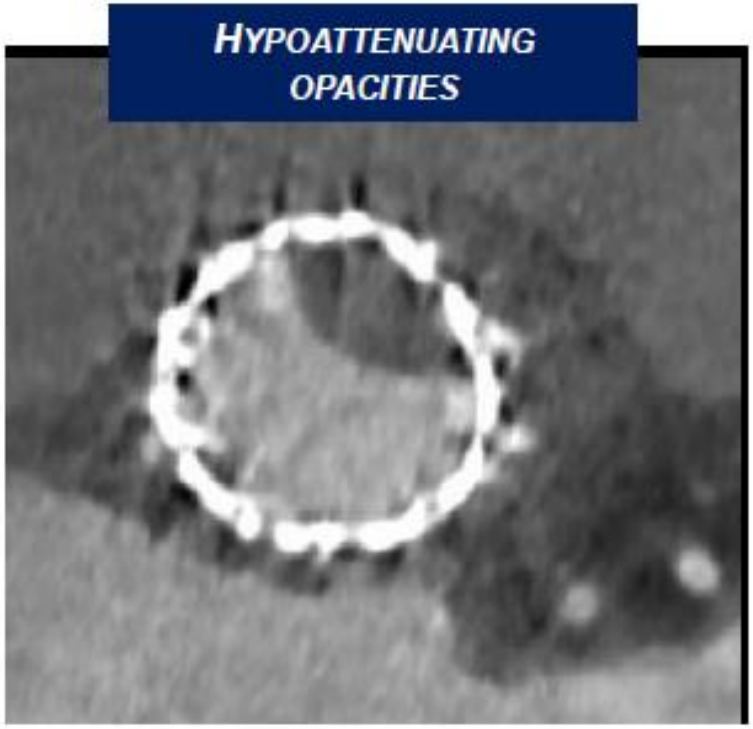
n . The 48-
or heparin.

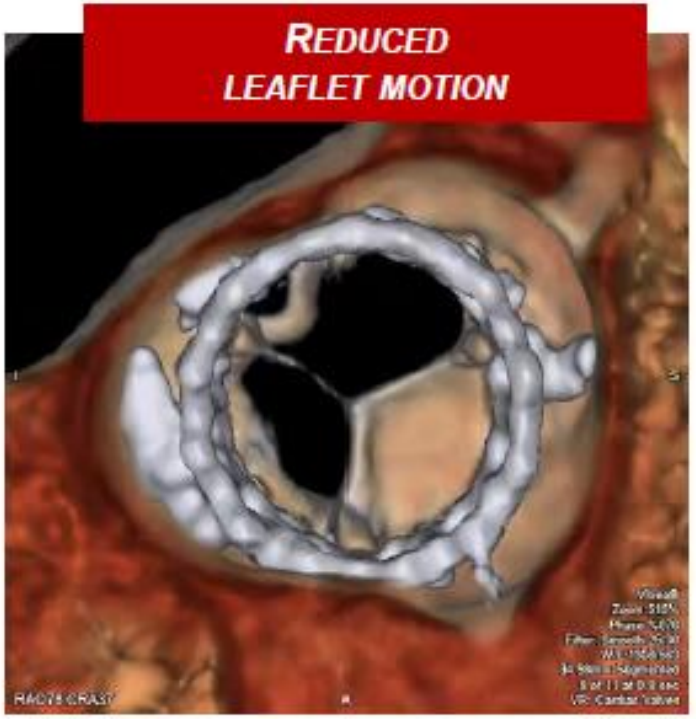
10.4%
9.0%
30
30
278
269
15.6%
14.4%
30
30
270
261

Subclinical Leaflet Thrombosis in Bioprosthetic Valves

Makkar RR et al. *N Engl J Med* 2015

- *Incidence: 17 of 132 patients (13%)*
- *Reduced incidence with oral anticoagulation (0% vs 29%, p=0.04)*
  Restoration of leaflet motion in all 11 patients who received oral anticoagulation
- *Higher incidence of stroke/TIA in patients with leaflet motion abnormality (18% vs 1%, p=0.007)*

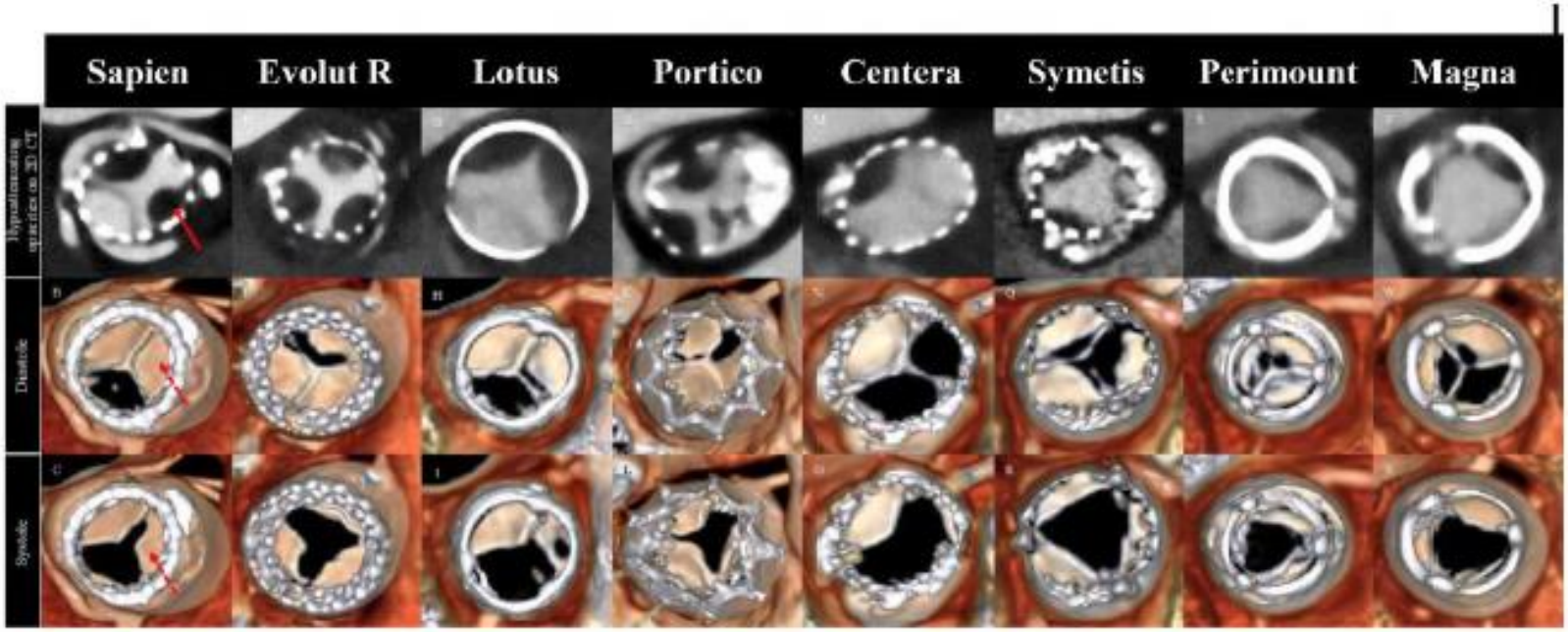




Subclinical Leaflet Thrombosis in Bioprosthetic Valves

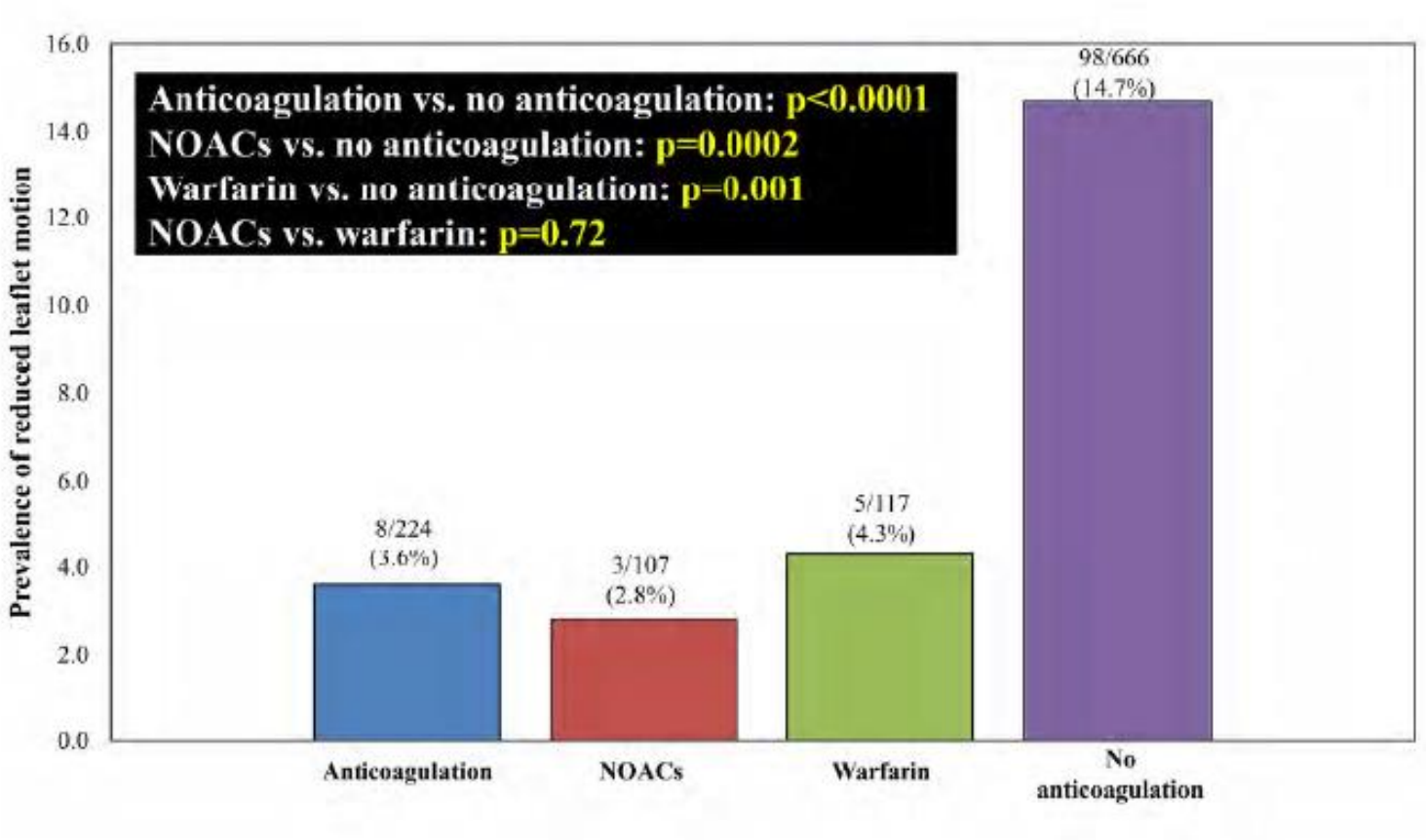
Chakravarty et al. Lancet 2017

- *890 patients with interpretable CT scans were included (RESOLVE registry, n=626; SAVOR Registry, n=264)*
- *Incidence: 12%: 4% after SAVR and 13% after TAVR (p<0.001)*



SUBCLINICAL LEAFLET THROMBOSIS IN BIOPROSTHETIC VALVES

Chakravarty et al. Lancet 2017



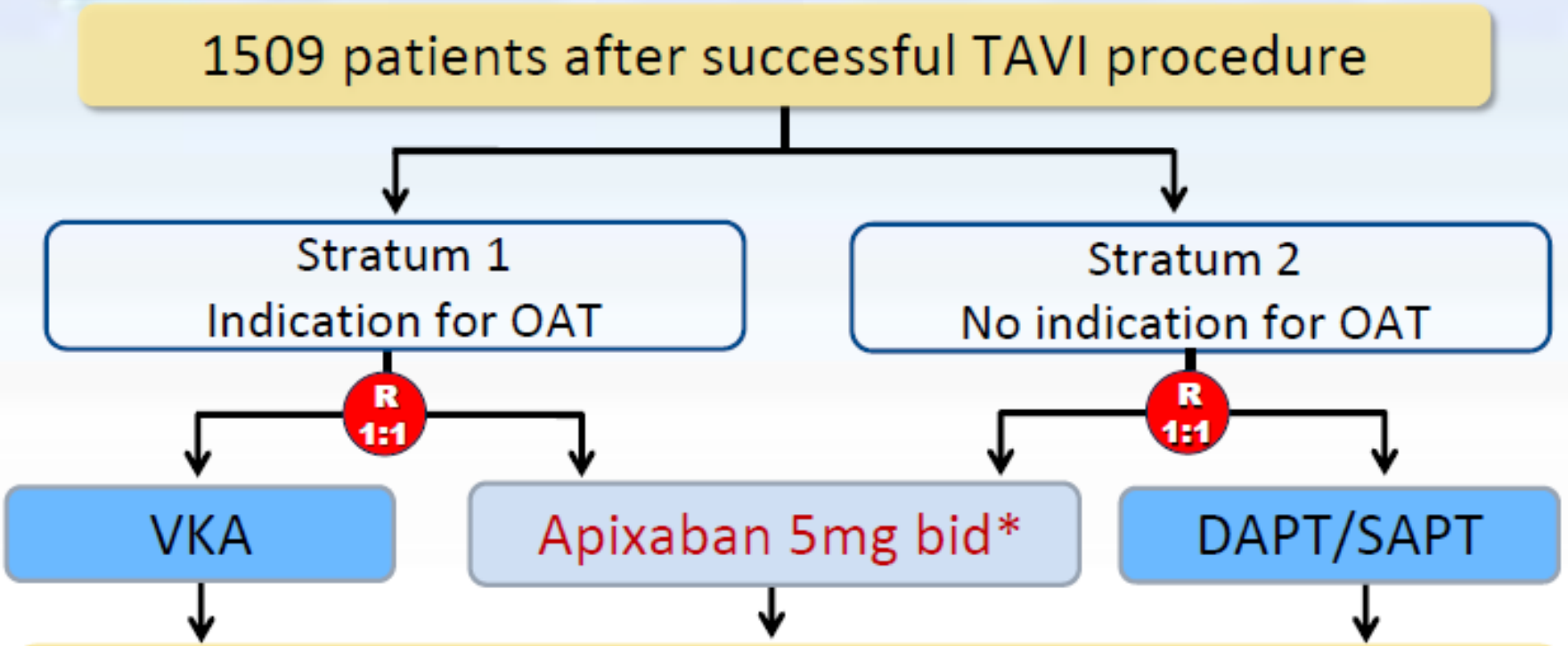
SUBCLINICAL LEAFLET THROMBOSIS IN BIOPROSTHETIC VALVES

Chakravarty et al. *Lancet* 2017

	Normal leaflet motion (N=784)		Reduced leaflet motion (N=106)			
	n/N (%)	Rate per 100 person-years	n/N (%)	Rate per 100 person-years	Hazard ratio (95% CI)	p-value
All events						
Death	34/784 (4.3%)	2.91	4/106 (3.8%)	2.66	0.96 (0.34-2.72)	0.94
Myocardial infarction	4/784 (0.5%)	0.34	1/106 (0.9%)	0.67	1.91 (0.21-17.08)	0.56
Strokes/TIAs	27/784 (3.4%)	2.36	11/106 (10.4%)	7.85	3.27 (1.62-6.59)	0.001
All strokes*	22/784 (2.8%)	1.92	6/106 (5.7%)	4.12	2.13 (0.86-5.25)	0.10
Ischemic strokes	21/784 (2.7%)	1.83	6/106 (5.7%)	4.12	2.23 (0.90-5.53)	0.08
TIAs	7/784 (0.9%)	0.60	6/106 (5.7%)	4.18	7.02 (2.35-20.91)	0.0005

TIA=Transient ischemic attack
* All strokes include hemorrhagic and ischemic strokes

ATLANTIS (Anti-Thrombotic Strategy to Lower All cardiovascular and Neurologic Ischemic and Hemorrhagic Events after Trans-Aortic Valve Implantation for Aortic Stenosis)



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*.

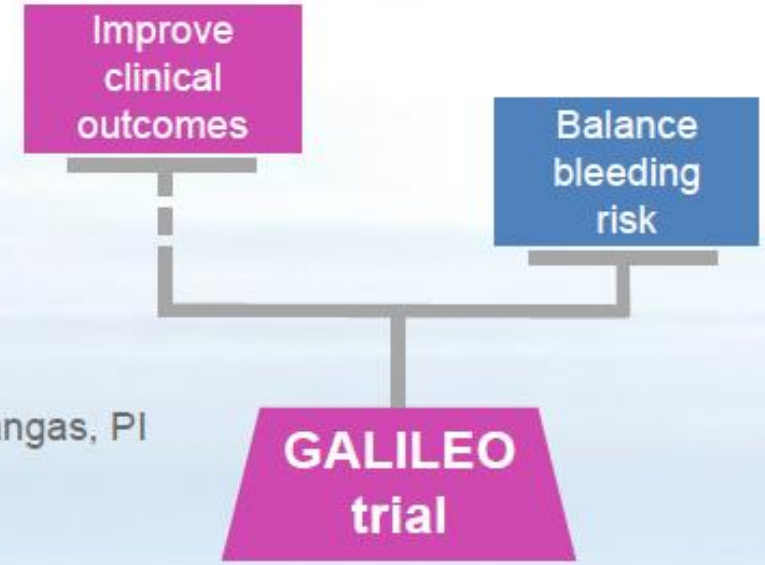
*2.5mg bid if creatinine clearance 15-29mL/min or if two of the following criteria: age≥80 years, weight≤60kg or creatinine≥1,5mg/dL (133µMol).

The GALILEO trial: Study design

Global study comparing a riv**A**roxaban-based antithrombotic strategy to an antip**L**atelet-based strategy after transcatheter aort**I**c va**L**ve r**E**placement to **O**ptimize clinical outcomes

Objective

To assess a rivaroxaban-based anticoagulation regimen following successful TAVR balancing ischaemic and bleeding outcome measures

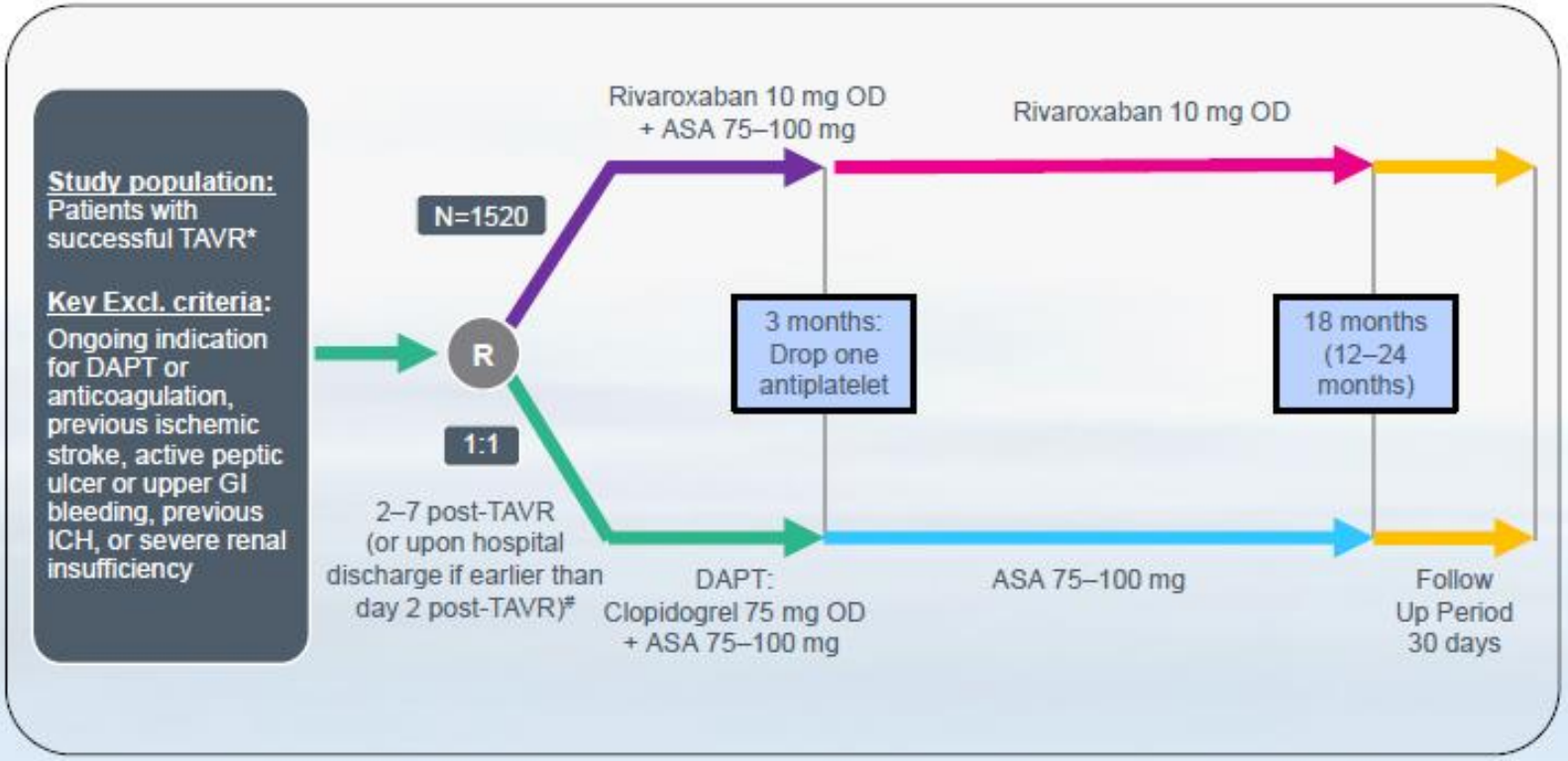


- Stephan Windecker, PI, George Dangas, PI
- Roxana Mehran, Marco Valgimigli
- Pascal Vranckx, Robert Welsh

PI=Principal investigator; TAVR=Transcatheter aortic valve replacement.
www.ClinicalTrials.gov Identifier: NCT02556203.

GALILEO TRIAL

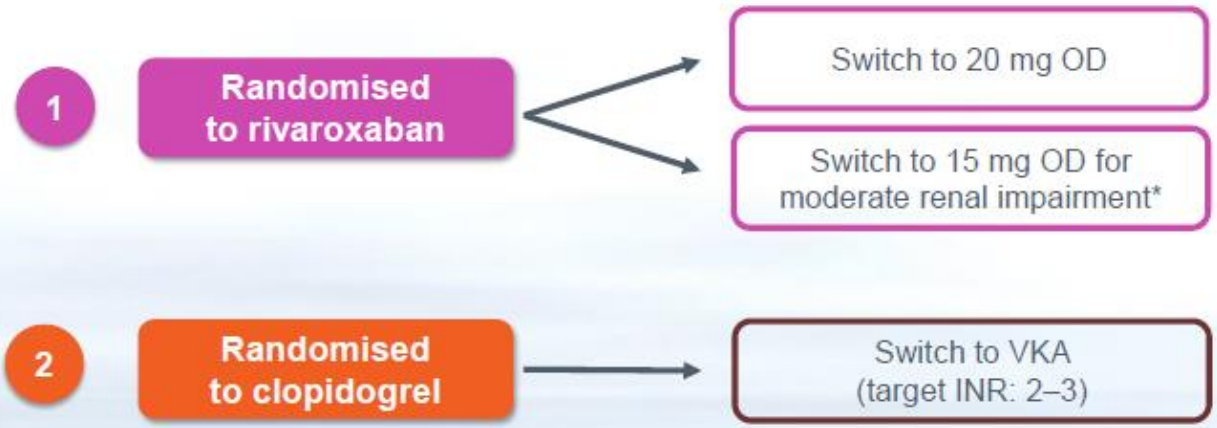
Design overview



*~110 sites in Europe & North America (15 countries); # Majority of patients will be on DAPT after TAVR gastric protection recommended throughout study.
ASA=Acetylsalicylic acid; DAPT=Dual antiplatelet therapy; GI=Gastrointestinal; ICH=Intracranial haemorrhage; OD=Once daily; TAVR=Transcatheter aortic valve replacement.
www.ClinicalTrials.gov Identifier: NCT02556203.

Treatment after new onset of AF (NOAF)

15% of patients develop NOAF after randomisation



- Follow-up until end of study
  - Included in primary efficacy analysis (ITT)
  - Censoring in secondary analysis

* i.e. CrCl=30–49 mL/min.
CrCl=Creatinine clearance; INR=International normalised ratio; ITT=Intention to treat; NOAF=New onset atrial fibrillation; OD=Once daily; VKA=Vitamin K antagonist.
Unpublished data.

- **Expanding TAVR Clinical Indications**
- **TAVI Procedure** – Will cerebral embolic protection become the standard for TAVR in the future?
- **TAVR Adjunct Pharmacology Customized Patient-Based Therapy.**
- **Discharge:** The “minimalist” TAVR procedure strategy has become imbedded as a preferred treatment approach in the majority of patients!time

3M TAVR Study Design

To evaluate the efficacy, feasibility, and safety of next day discharge home in patients undergoing balloon-expandable transfemoral TAVR utilizing the Vancouver 3M Clinical Pathway

Patients undergoing elective Transfemoral TAVR

↓

Considered at *increased surgical risk* by the Heart Team

↓

Vancouver 3M Clinical Pathway (n = 411)
Meet all anatomical, functional, and peri-procedural exclusion criteria

↓

Primary Outcomes: 1) All cause mortality or stroke at 30 days
2) The proportion of patients discharged the next day

↓

Secondary Outcomes: 1) Readmission within 30 days
2) Greater than mild PAR at 30 days
3) New permanent pacemaker at 30 days
4) Major vascular complications, bleed, or repeat valve procedure at 30 days
5) Conversion to GA/Intubation
6) KCCQ and SF 12 at 2 weeks, 30 days, and 1 year
7) All cause mortality and stroke at 1 year

Vancouver TAVR Clinical Pathway

Minimalist Peri-Procedure Approach

Facilitated Post-Procedure Recovery

Criteria-Driven Discharge

PATIENT JOURNEY

Procedure Room
Cath Lab or Hybrid OR

Access and Closure
Percutaneous

Equipment
Peripheral IV
Radial artery monitoring
No urinary catheter
No PA catheter
Temporary Pacemaker removed in procedure room

Anesthesia
Local anesthesia with no or minimal procedural sedation

Echocardiogram
TTE peri or post procedure

Monitoring
Vital Signs: Q15 x4, Q30 x2
ECG, eGFR, CBC on admission and POD1
Removal of all remaining lines < 2 hours

Facilitated Recovery
Bedrest x 4 hours
Nurse-led mobilization
Hydration, nutrition, elimination

Communication
Multidisciplinary communication to maintain pathway
Patient and family education
Implementation of pre-procedure discharge plan

Monitoring
Review of TTE
Absence of:
- new persistent conduction delay
- vascular access complications
- laboratory contraindications

Facilitated Recovery
Return to baseline mobilization
Absence of elimination issues
Return to baseline hydration

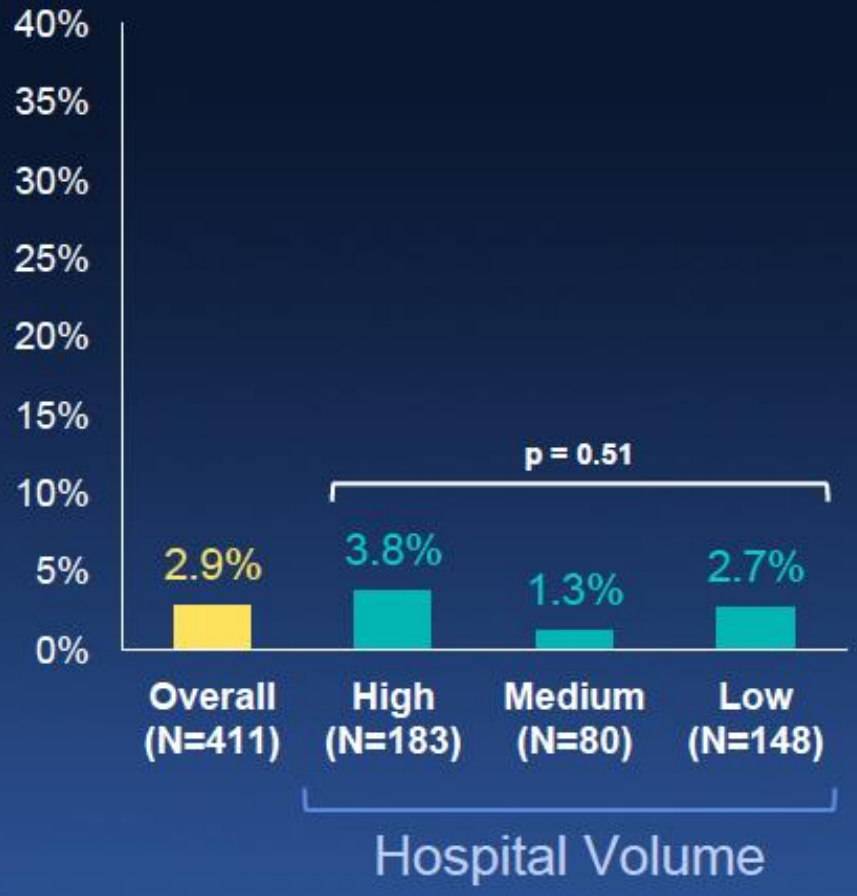
Communication
Multidisciplinary agreement of safety for discharge
Review discharge plan with family
Review follow-up appointments

BC CENTRE FOR
Improved Cardiovascular Health
EVIDENCE FOR CHANGE

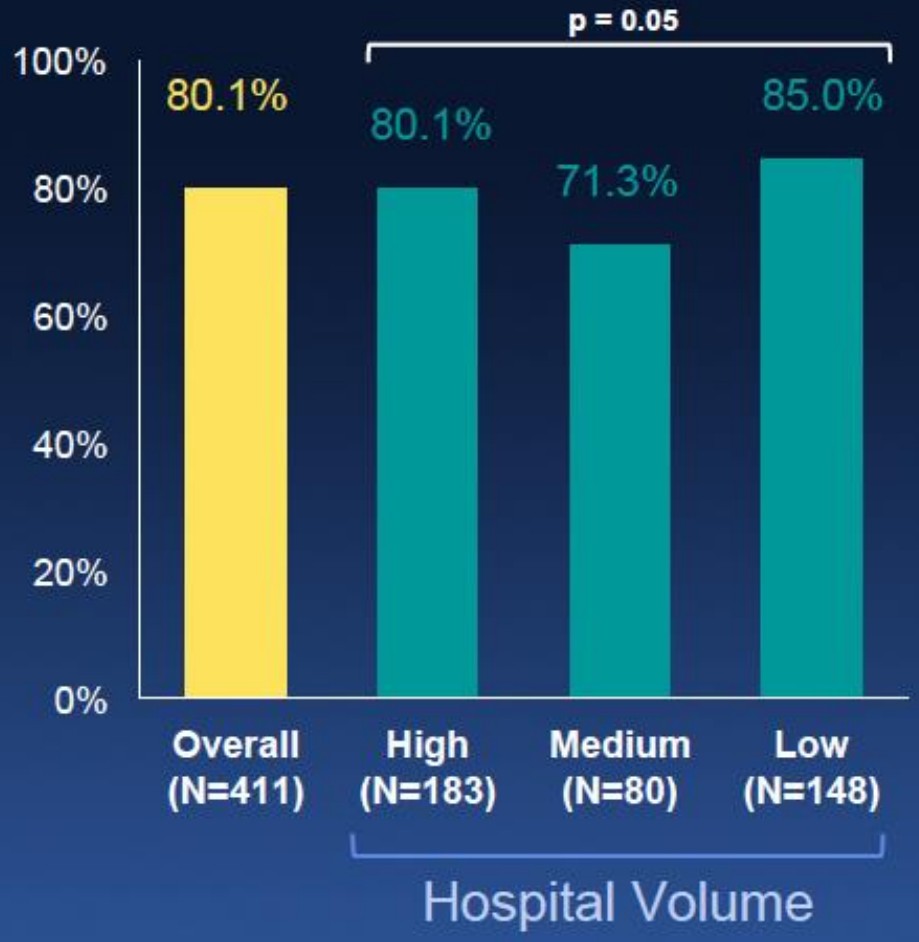
Primary Endpoint

3M TAVR

30-Day Mortality or Stroke



Next Day Discharge



BC CENTRE FOR
Improved Cardiovascular Health
EVIDENCE FOR CHANGE

3M TAVR Outcomes in Perspective

3M TAVR

	3M TAVR (2017) N = 411	GARY TF (2014) N = 2695	STS/TVT Registry (2014) N = 12785	STS/TVT Registry (2015) Conscious Cohort N=1737	PARTNER 2A TAVR (2016) N = 1011	SAPIEN 3i (2016) N = 1077	AQUA (2017) N = 3618 (>200/yr)	Choice (2014) N=241
STS (%)	**4.9**		6.7		5.8	5.2		5.9
Age (yrs)	**84**	81	83	82	82	82	81	81
Median LOS (days)	**1.0**		6.2	6.0	6.0	4.0	14.0	
30-Day Mortality (%)	**1.5**	5.1	4.4	2.9	3.9	1.1	2.4	4.6
30-Day Stroke (%)	**1.5**	1.7	2.2	2.1	6.4	2.7	2.1	4.2
30-Day Cardiac Readmission (%)	**5.7**				6.5	4.6		4.3
30-Day New PPM (%)	**5.7**	25	10.5	15	8.5	10.2		27
> Mild PAR at Discharge (%)	**3.8**	7.3	4.8		3.7	3.8		11.2

NIH U.S. National Library of Medicine

ClinicalTrials.gov

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Home > Search Results

Modify Search | Start Over

149 Studies found for: **TAVI | Recruiting, Not yet recruiting Studies**

Also searched for **Transcatheter aortic valve implantation** and **Transcatheter aortic valve replacement.** See Search Details

Applied Filters: ☑ Recruiting ☑ Not yet recruiting

List | By Topic | On Map | Search Details

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Filters

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Showing: 11-20 of **149** studies 10 studies per page

Show/Hide Columns

Recruitment Status

Clinical Study :

- ☑ Not yet recruiting
- ☑ Recruiting
- ☐ Enrolling by invitation
- ☐ Active, not recruiting
- ☐ Suspended
- ☐ Terminated
- ☐ Completed
- ☐ Withdrawn
- ☐ Unknown status†

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
11	☐	Recruiting	NVT ALLEGRA **TAVI** System TF in Failing Surgical Aortic Bioprosthesis	• **Transcatheter Aortic Valve Implantation**	• Device: **Transcatheter Aortic Valve Implantation (TAVI)**	• Universitäts-Herzzentrum Freiburg-Bad Krozingen Bad Krozingen, Germany • Segeberger Kliniken, Herzzentrum Bad Segeberg, Germany • Immanuel Klinik Bernau Herzzentrum Brandenburg Bernau bei Berlin, Germany • (and 5 more...)
12	☐	Recruiting	Safety and Efficacy Comparison Of Two **TAVI** Systems in a Prospective Randomized Evaluation II	• Aortic Valve Stenosis	• Device: Symetis ACURATE neo™ transfemoral **TAVI** system • Device: Medtronic CoreValve Evolut R **TAVI** System	• Heart Center, Rigshospitalet, University of Copenhagen Copenhagen, Denmark • Oulun University Hospital Oulu, Finland

Thanks