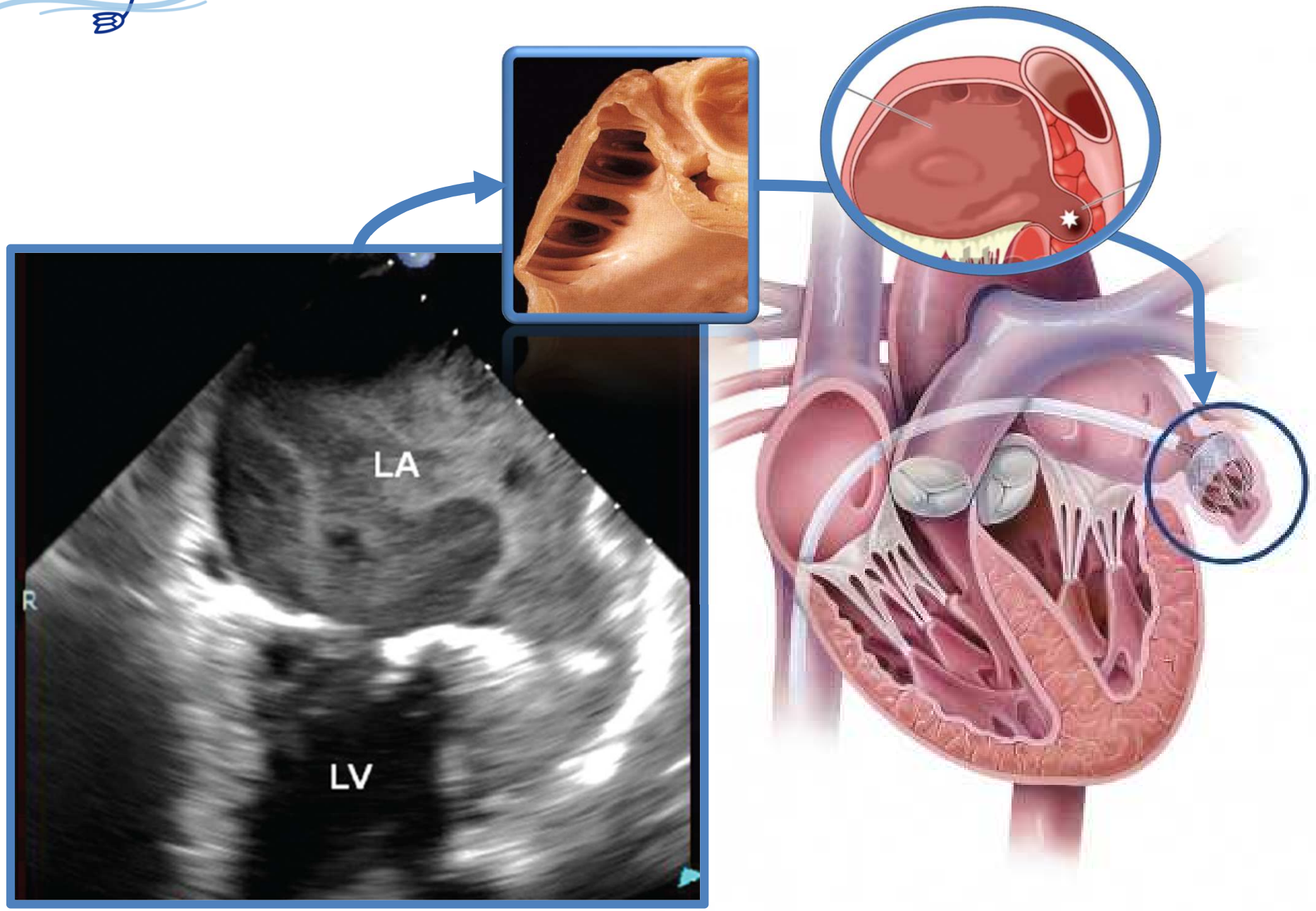
Adrift

Assessment of Dual antiplatelet therapy versus Rivaroxaban In atrial Fibrillation patients Treated with left atrial appendage closure

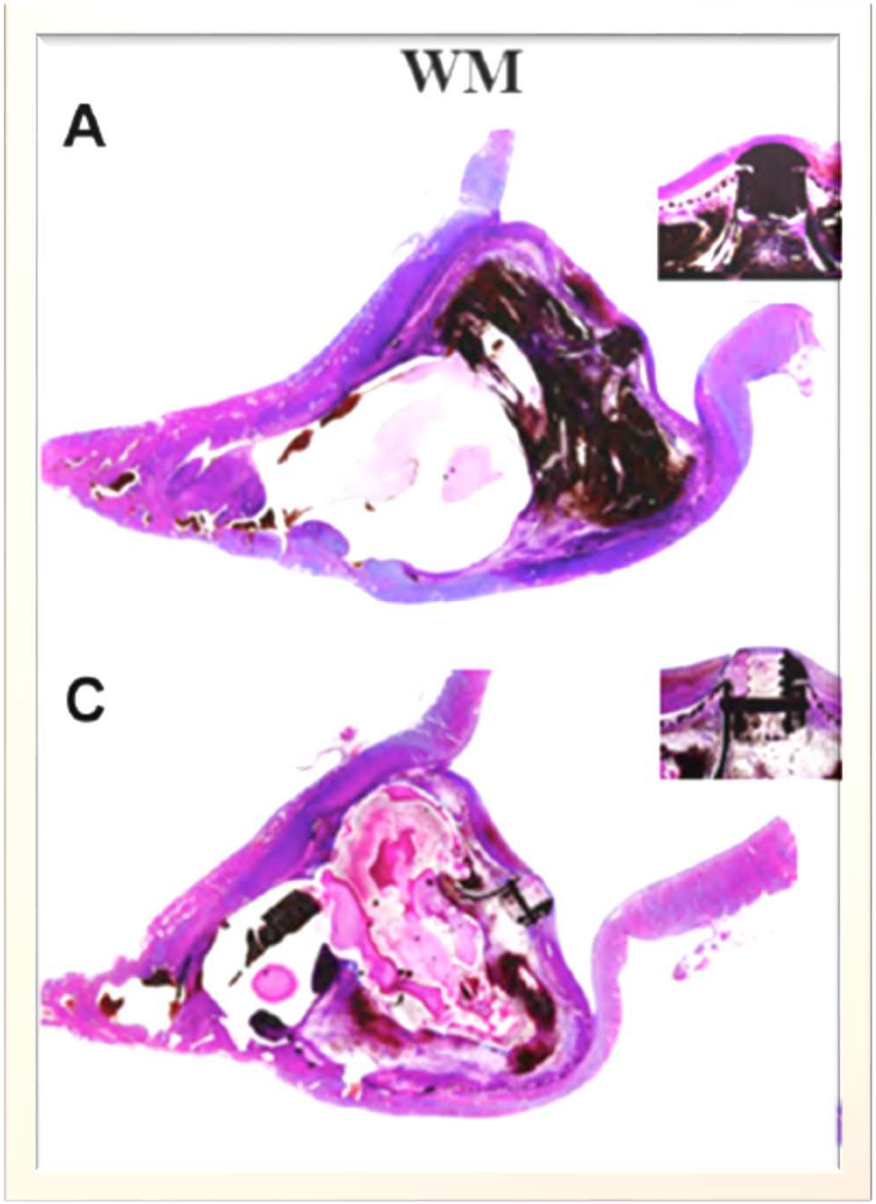
ADRIFT investigators

DOI public at www.action-coeur.org

ACTION
www.action-coeur.org

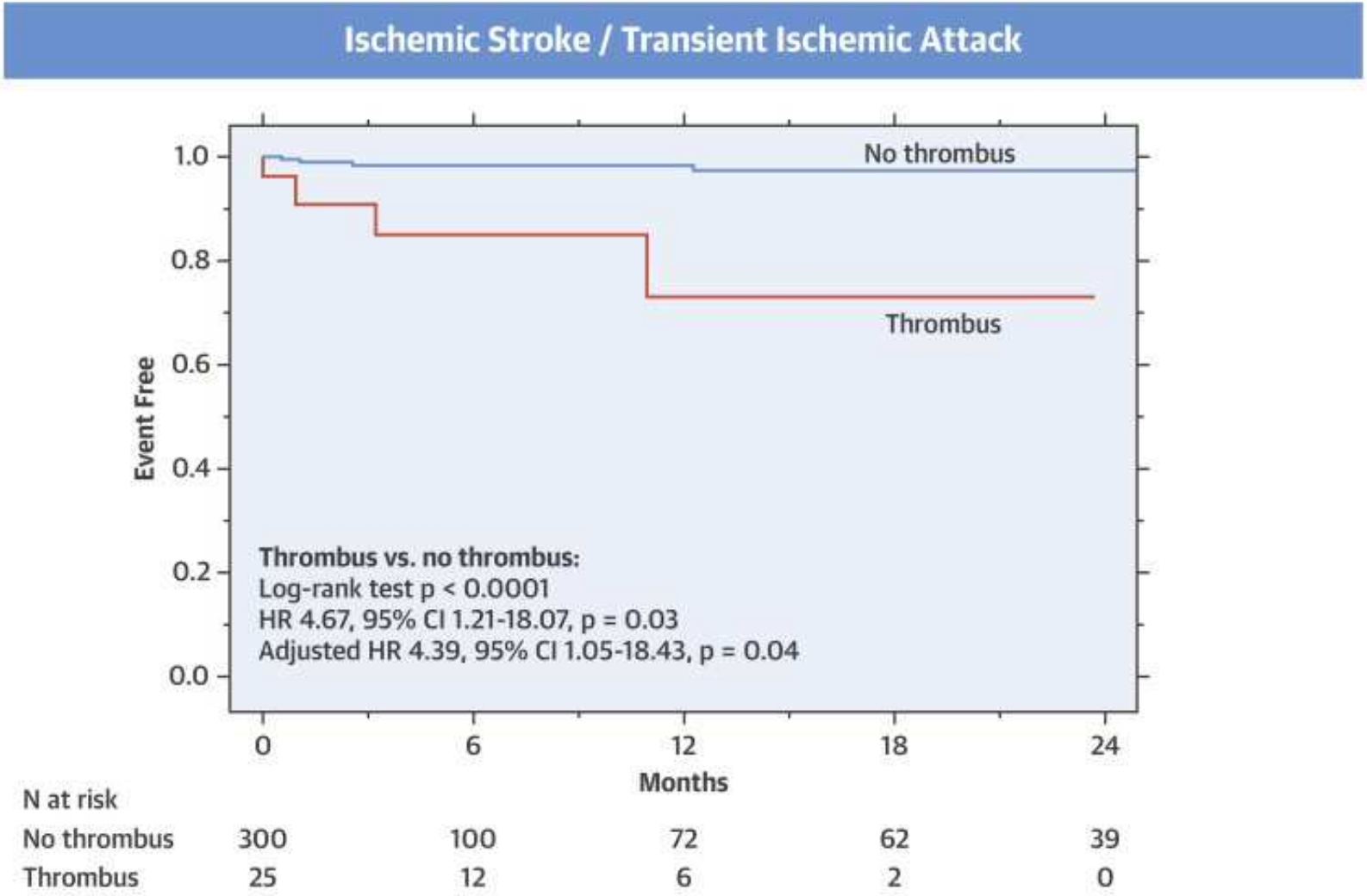

LA
R
LV

Healing: 30 days to 3 months



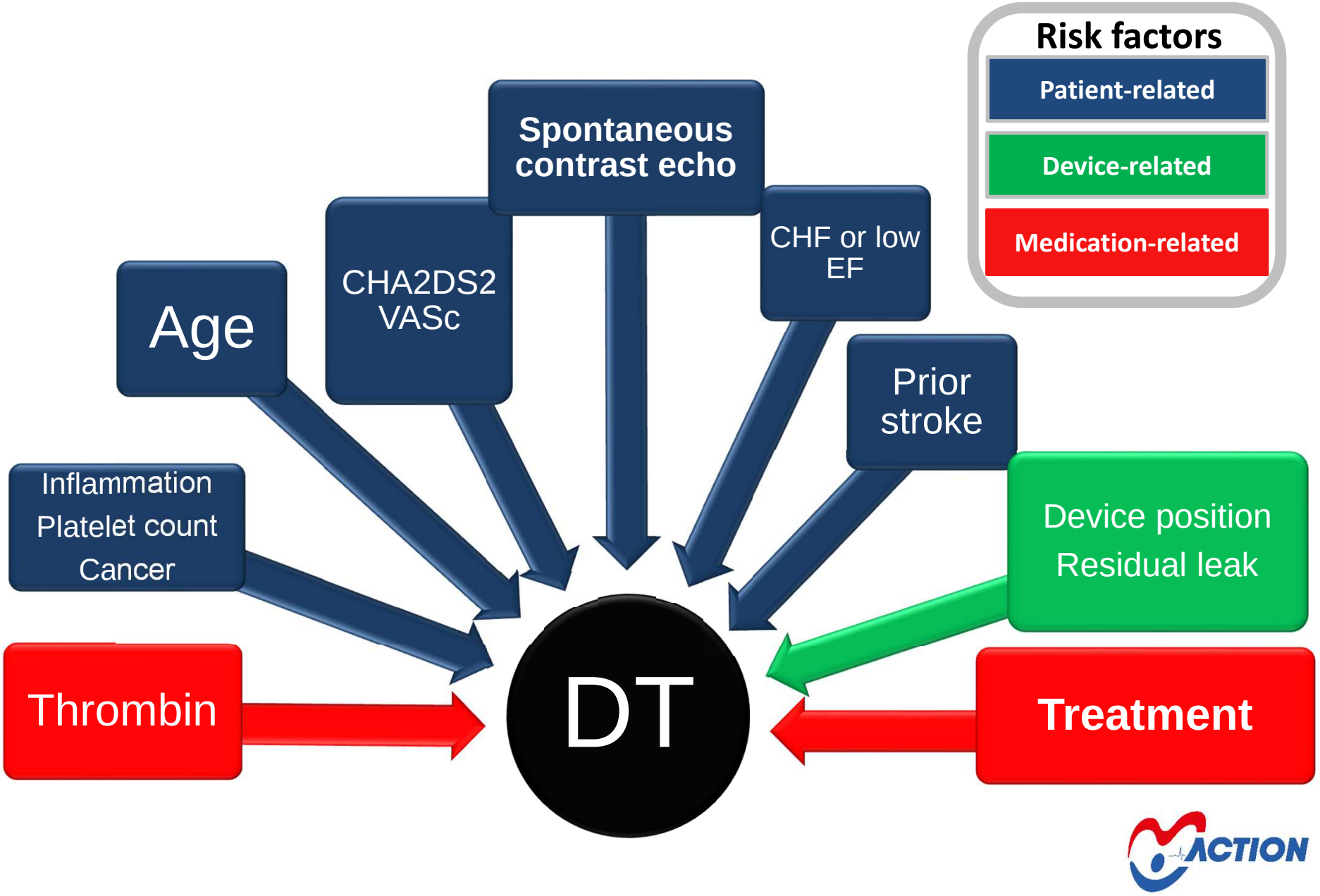
Kar et al. JACC Intv 2014;7:801-9

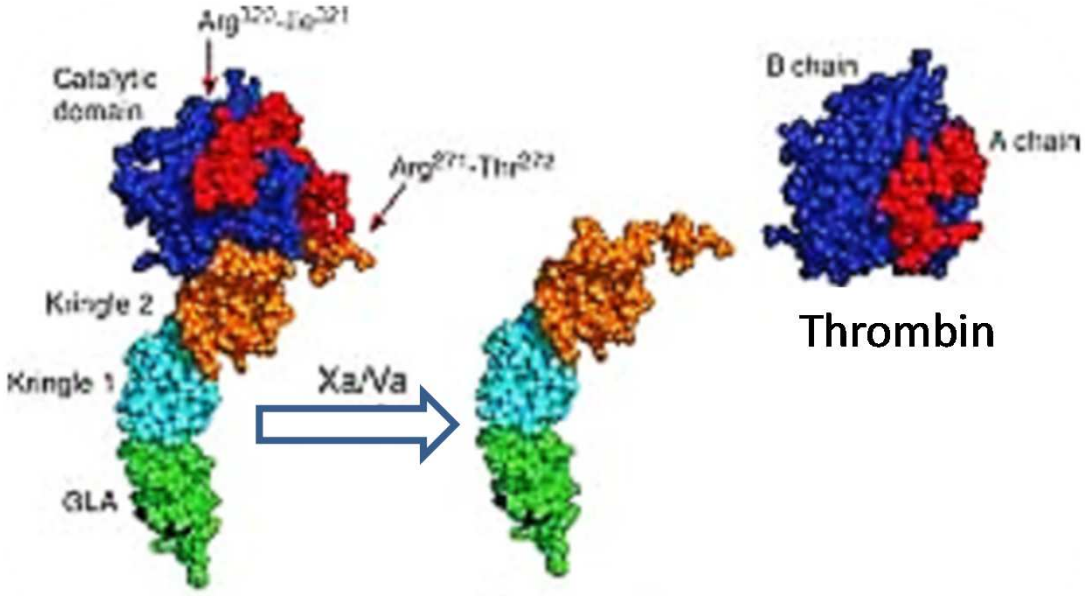
CENTRAL ILLUSTRATION: Kaplan-Meier Cumulative Event-Free Curves of Ischemic Strokes and Transient Ischemic Attacks With and Without Thrombus on the Device



Fauchier, L. et al. J Am Coll Cardiol. 2018;71(14):1528-36.

Risk of device thrombosis





Thrombus formation in LA

Venous thrombotic events

Arterial thrombotic events

Mortality

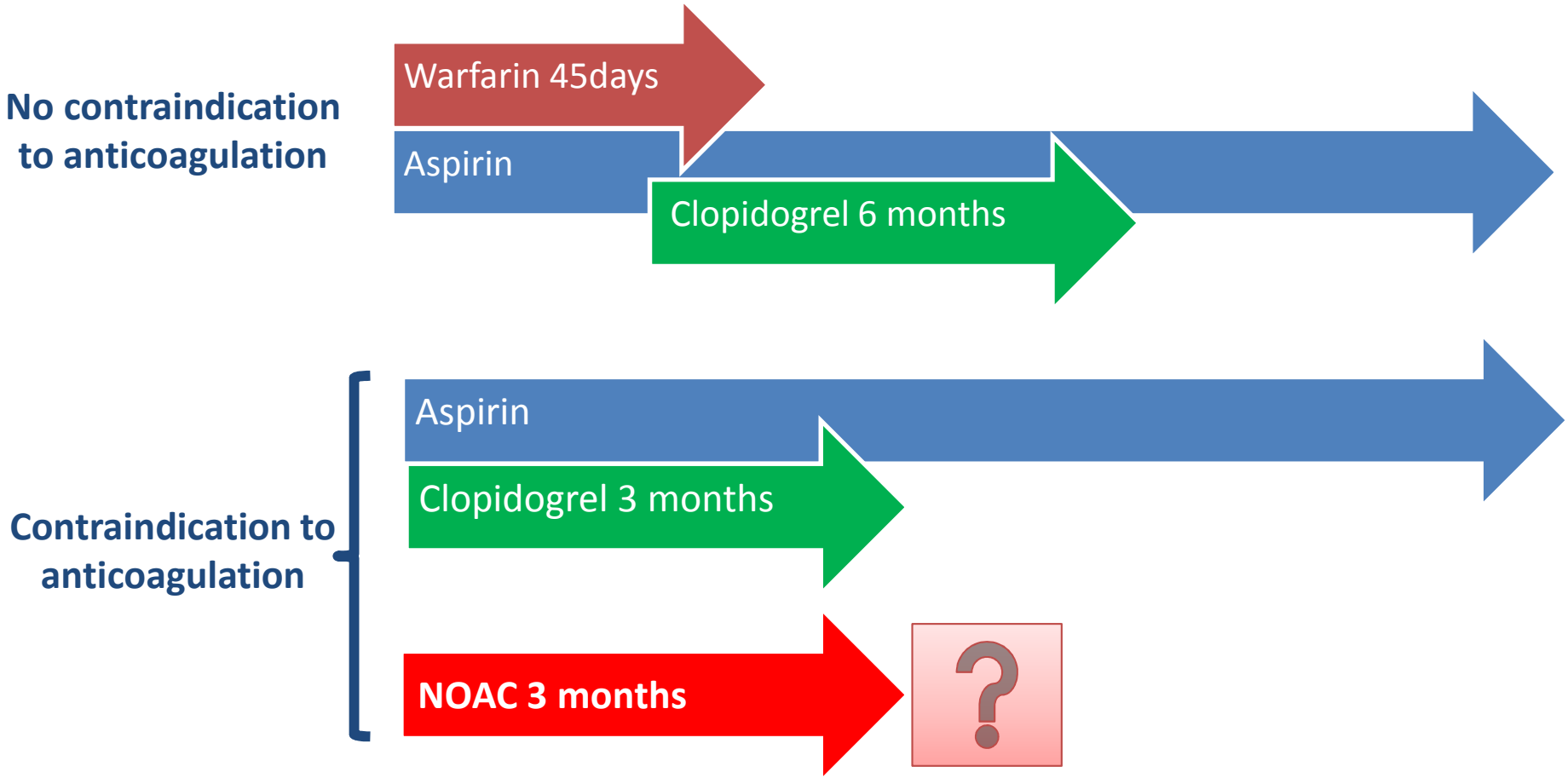
Failure of antithrombotic treatment

Lim HS. Effect of atrial fibrillation on atrial thrombogenesis in humans: impact of rate and rhythm. JACC. 2013;61:852-60

Meus R. Prothrombotic State in Patients With a Left Atrial Appendage Thrombus of Unknown Origin and Cerebrovascular Events. Stroke 2016;47:1872-8.

Kamath GS. Activation of the endogenous coagulation system in patients with atrial flutter: relationship to echocardiographic markers of thromboembolic risk. Cardiol J. 2010;17:390-6.

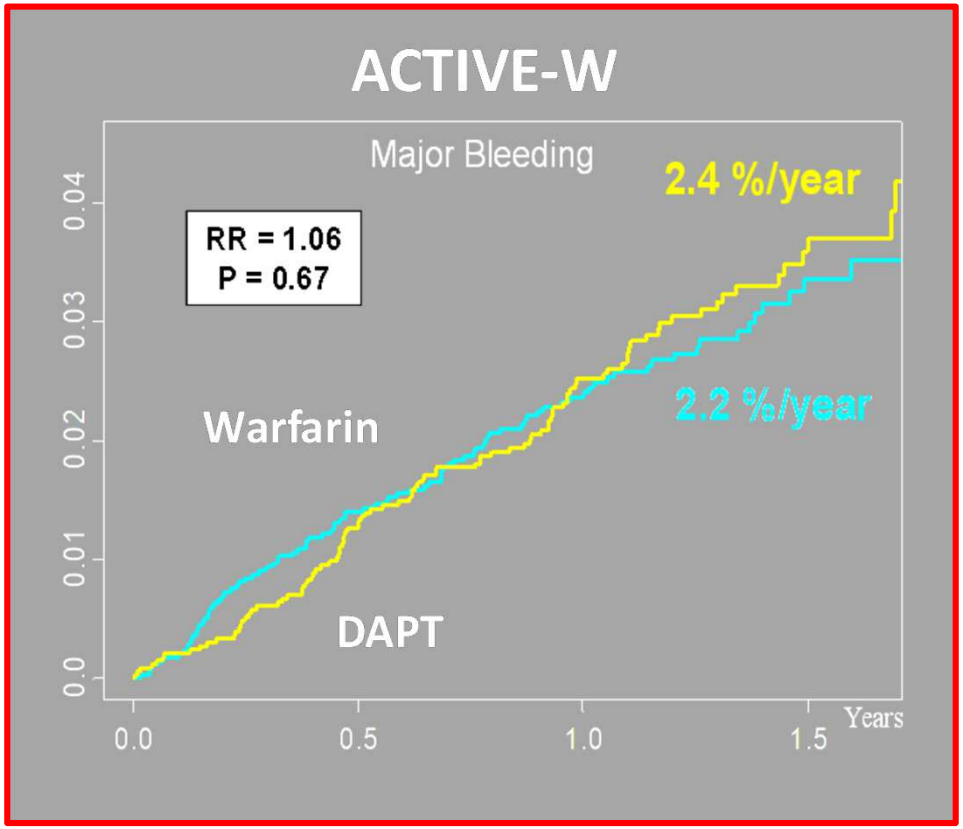
Post-LAAC antithrombotic treatment



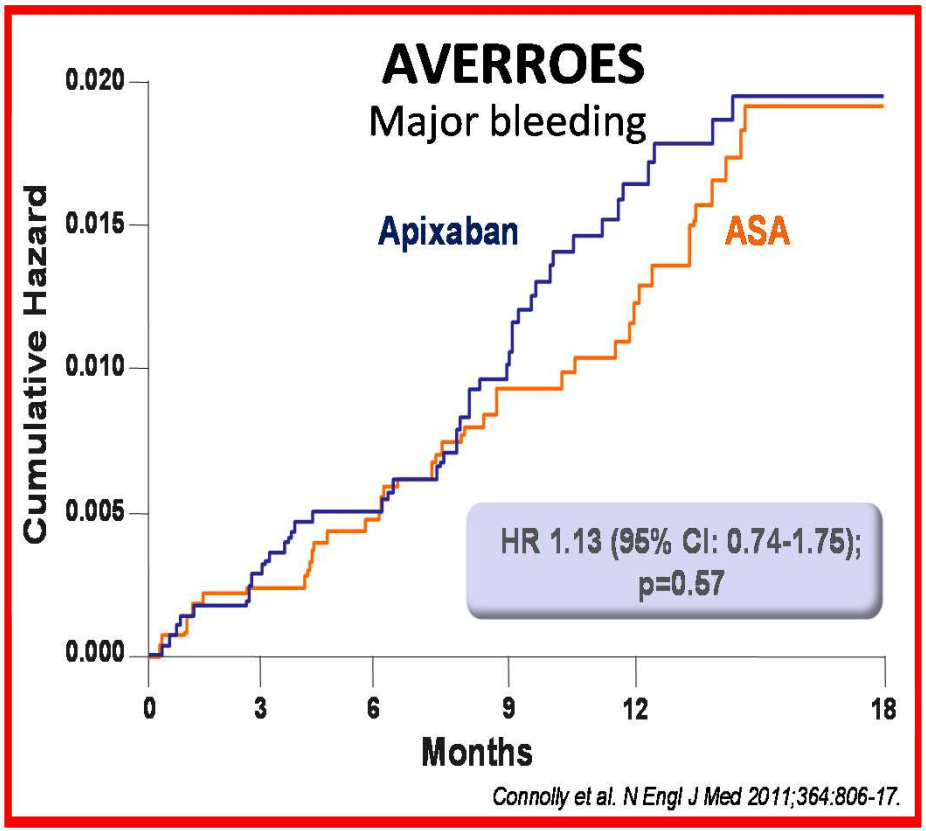
Holmes et al . JACC 2014;64:1-12

Safety

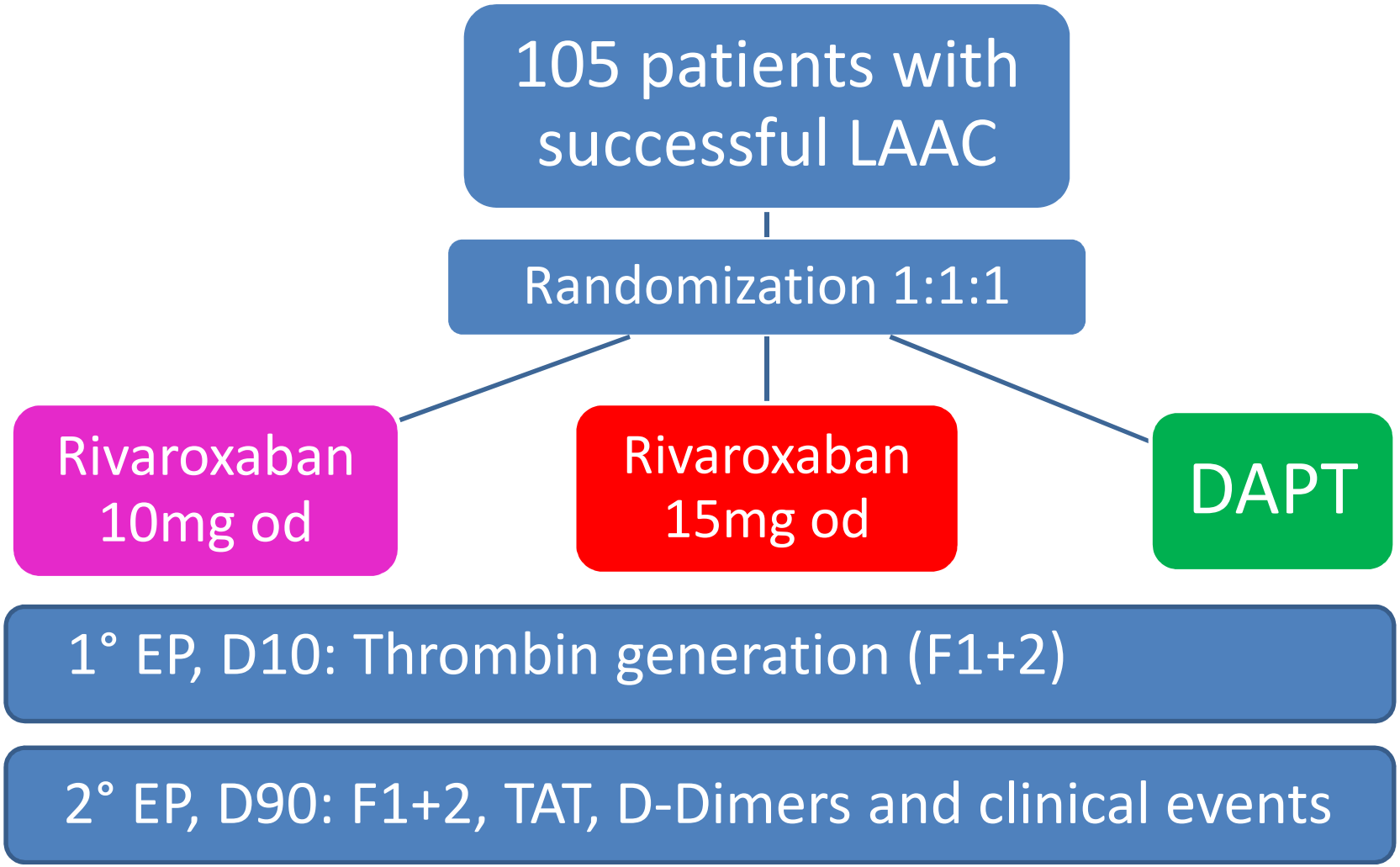
DAPT vs. warfarin



SAPT vs. NOAC



Study Design



Central randomization: CleanWeb® software (Telemedicine Technologies SAS) in a 1:1:1 allocation to rivaroxaban 10 mg (R^{10}); rivaroxaban 15mg (R^{15}); DAPT with aspirin 75mg and clopidogrel 75mg.

Objectives

- **Thrombin generation** (F1+2) at **Day 10**, 2-4 hours after drug intake, on platelet poor plasma (Primary EP)
- Thrombin-antithrombin complex, D-Dimers, vWf, PAI-1, Prothrombin time, Rivaroxaban anti-Xa activity, at Day 10 and Day 90 (secondary EP)
- **Clinical endpoints at Day 90**: death, MI, Stroke, peripheral embolism, major or clinically significant bleeding and, device thrombosis

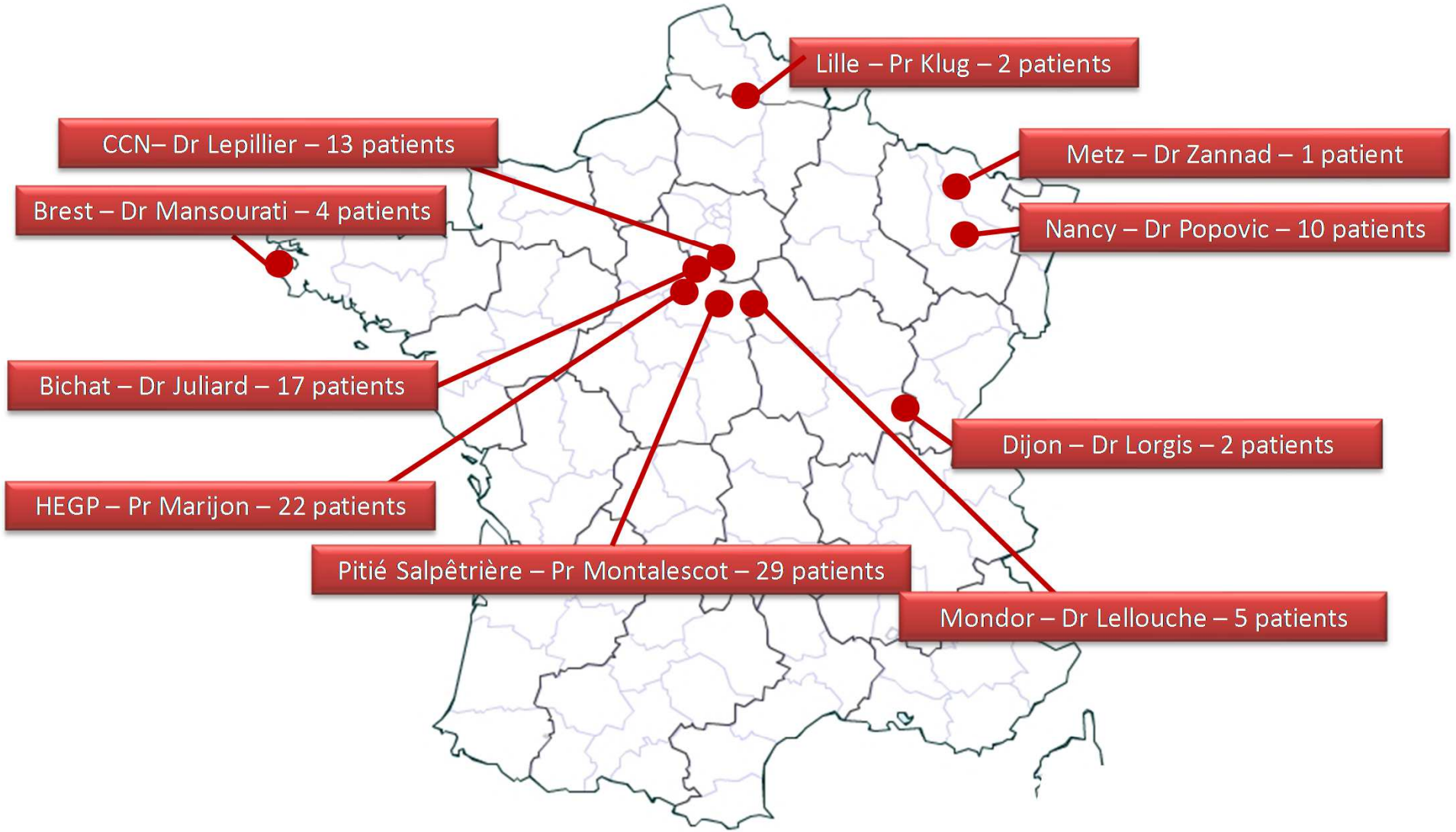
Statistical analyses

- Main analysis on the per-protocol population
- Complementary ITT and as-treated analyses were performed as sensitivity analyses
- Global comparisons among the 3 groups used Kruskall-Wallis non-parametric test
- Then *a priori* defined comparisons between each dose of Rivaroxaban and DAPT were performed using Wilcoxon test or using Chi-square or Fisher's exact test for binary variables
- Nominal p values <0.05 and < 0.016 (Bonferroni's adjustment) were considered significant for global study and Rivaroxaban *vs.* DAPT comparisons, respectively

Study organization

- **Academic Coordinating Center**: ACTION, Institute of Cardiology–Pitié-Salpêtrière, Paris
- **Academic Sponsor**: AP-HP, Paris
- **Academic Global Trial Operations**: ACTION, URC-Lariboisière, Paris
- **Funding**: Bayer and ACTION
- **Investigation sites** : 10 French Intervention Centers
- **Blinded Central Lab for biological** measurements
- **Blinded Central Imaging Lab** for echo and CT scans
- **Blinded Clinical Event Committee** for adjudication

Adrift



ACTION

Results

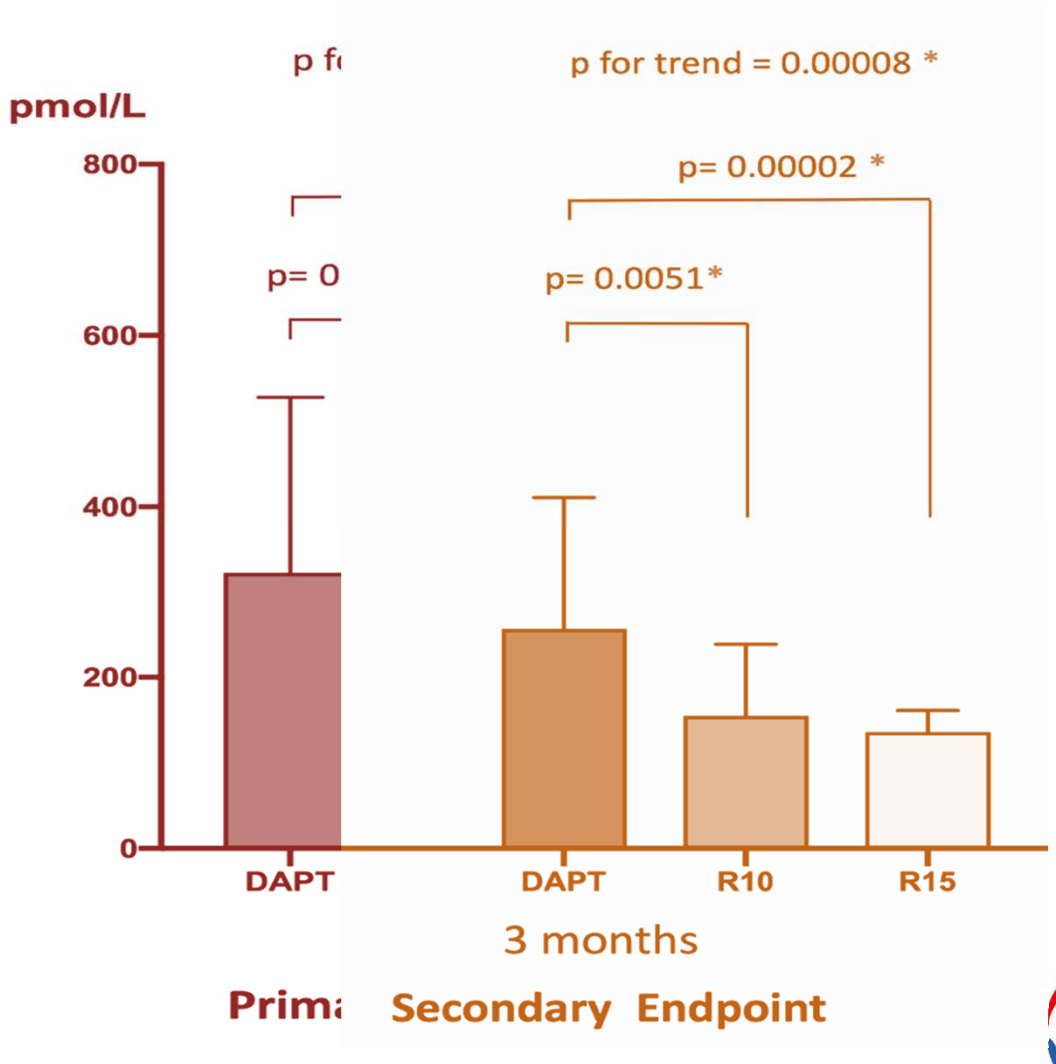
Baseline characteristics

	Rivaroxaban 10 mg n=37	Rivaroxaban 15 mg n=34	DAPT n=33
Male gender	20 (54%)	22 (65%)	23 (70%)
Age (years)	78 ± 8	78 ± 9	76 ± 8
Heart Failure	6 (16%)	7 (21%)	6 (18%)
$CHADS_2$-VASc Score	**4.6 ± 1.3**	**4.7 ± 1.5**	**4.5 ± 1.5**
HAS-BLED Score	**3.8 ± 1.1**	**3.7 ± 1.0**	**3.5 ± 0.8**
Previous Stroke (any)	**15 (41%)**	**20 (59%)**	**15 (45%)**
- **Hemorrhagic**	8 (22%)	4 (12%)	7 (21%)
- **Ischemic**	4 (11%)	11 (32%)	5 (15%)
- **Hemorrhagic and Ischemic**	1 (3%)	4 (12%)	3 (9%)
- **Unknown**	2 (5%)	1 (3%)	0 (0%)
Previous TIA	2 (5%)	4 (12%)	4 (12%)
Permanent contraindication to	**33 (89%)**	**30 (88%)**	**27 (82%)**

Procedural characteristics

	Rivaroxaban 10 mg n=37	Rivaroxaban 15 mg n=34	DAPT n=33
Indication for LAAC *(several possible)*			
Previous major ISTH bleeding	**26 (70%)**	**22 (65%)**	**22 (67%)**
High risk of fall	8 (22%)	5 (15%)	2 (6%)
Labile INRs	3 (8%)	2 (6%)	0 (0%)
Known hemostasis disorder	0 (0%)	0 (0%)	2 (6%)
Stroke recurrence despite adequate anticoagulation	1 (3%)	3 (9%)	3 (9%)
Lack of compliance with anticoagulation therapy	1 (3%)	1 (3%)	0 (0%)
Other contraindication to chronic anticoagulation	0 (0%)	1 (3%)	4 (12%)
Left atrial diameter (mm)	**55 ± 18**	**43 ± 13**	**44 ± 14**
Type of LAAC device			
Watchman	12 (32%)	12 (35%)	12 (36%)
Amulet	25 (68%)	22 (65%)	21 (64%)
Procedure related complication (any)	**3 (8%)**	**2 (6%)**	**2 (6%)**
Groin hematoma	2 (5%)	1 (3%)	1 (3%)
Blood transfusion and groin hematoma	0 (0%)	0 (0%)	1 (3%)
Pseudoaneurysm	0 (0%)	1 (3%)	0 (0%)
Transfusion	1 (3%)	0 (0%)	0 (0%)

Primary Endpoint
Prothrombin fragments 1+2 @ Day_{10}



Biological endpoints @ day 10

	Rivaroxaban 10 mg (n=37)	Rivaroxaban 15 mg (n=34)	DAPT (n=33)	p value
TAT (ng/mL)	**3.3** (2.7-4.0)	**3.6** (3.1-5.7)	**4.2** (3.0-7.2)	0.096
D-Dimers (ng/mL)	**1006** (796-1306)	**1162** (688-1451)	**1213** (949-1472)	0.286
VWF Ag (%)	**207** (176-295)	**208** (156-273)	**221** (178-265)	0.982
PAI-1 (UI/mL)	**17** (10-24)	**15** (10-25)	**14** (9-21)	0.312

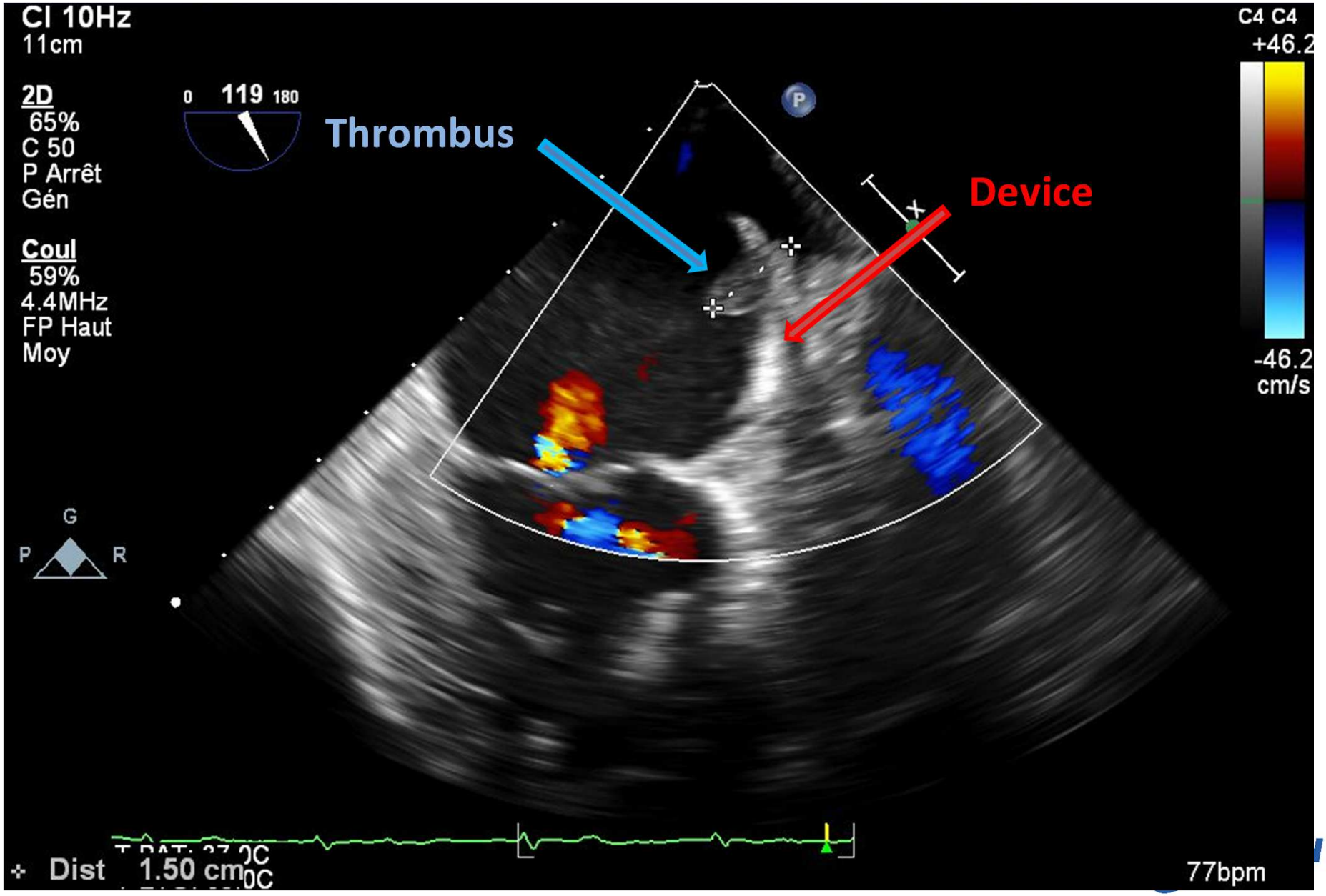
Similar trends @ 3 months

Clinical Endpoints @ 3 months

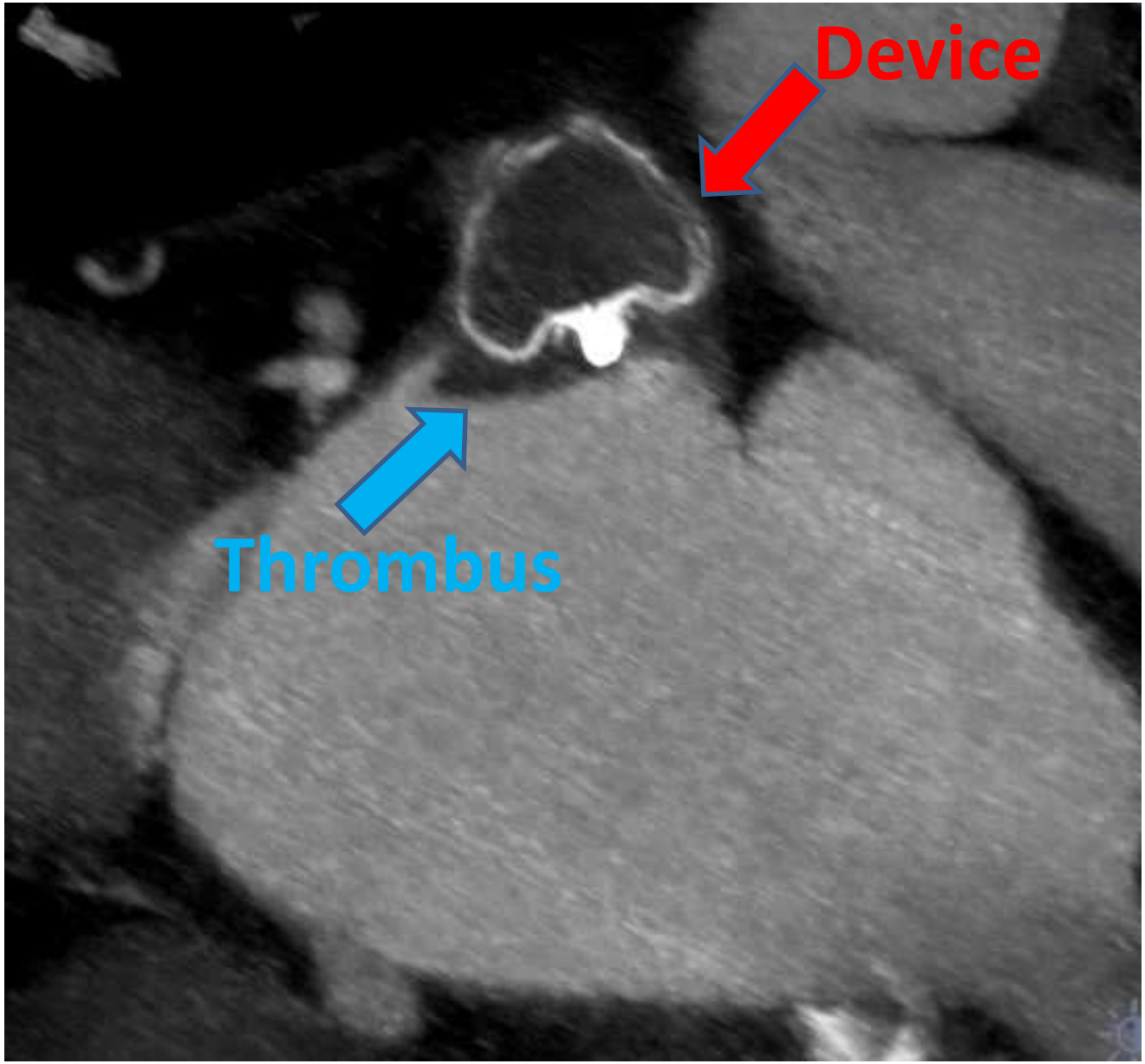
	Rivaroxaban 10mg n=37	Rivaroxaban 15mg n=34	DAPT n=33	p value
Death	0 (0%)	1 (3%)	0 (0%)	NS
Myocardial infarction	1 (3%)	0 (0%)	0 (0%)	NS
Stroke/TIA	1 (3%)	0 (0%)	0 (0%)	NS
Systemic embolism	0 (0%)	0 (0%)	0 (0%)	-
ISTH Major or clinically significant	9 (24%)	4 (11%)	9 (27%)	NS
TIMI Major	2 (5%)	0 (0%)	1 (3%)	NS
TIMI Minor	7 (19%)	4 (12%)	7 (21%)	NS
TIMI Minimal	4 (11%)	8 (23%)	7 (21%)	NS
Net clinical benefit	**9 (24%)**	**5 (15%)**	**9 (27%)**	**NS**

Net clinical benefit: Death, Stroke, Myocardial infarction, Systemic embolism, Major or clinically significant ISTH bleeding

Woman, 79y, Amulet 28, DAPT, @3months



Woman, 69y, Watchman 24, DAPT, @3months



Conclusions

- The combined antithrombotic regimens currently used after LAAC may not be adapted to HBR patients undergoing this procedure
- **A reduced dose of rivaroxaban (monotherapy)** is superior to DAPT in **controlling thrombin generation**
- A reduced dose of rivaroxaban appears **clinically feasible** and deserves further evaluation in large clinical trials.

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