ACTION Study Group
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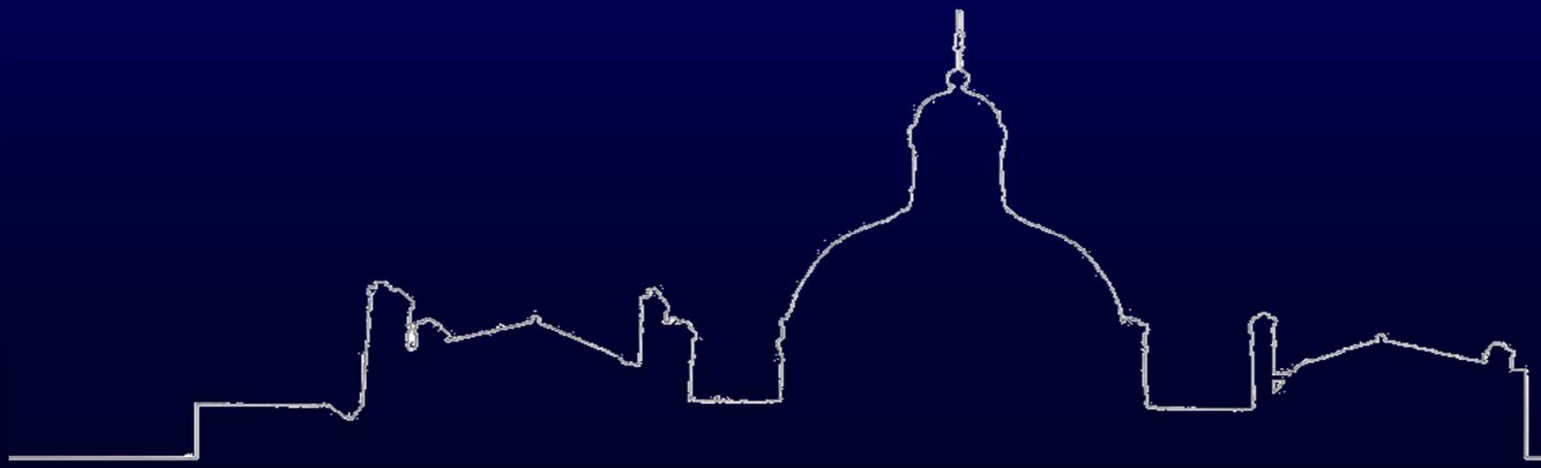
Advancing patient care with NOACs in other cardiac interventions

Gilles Montalescot



www.action-cœur.org

Disclosures

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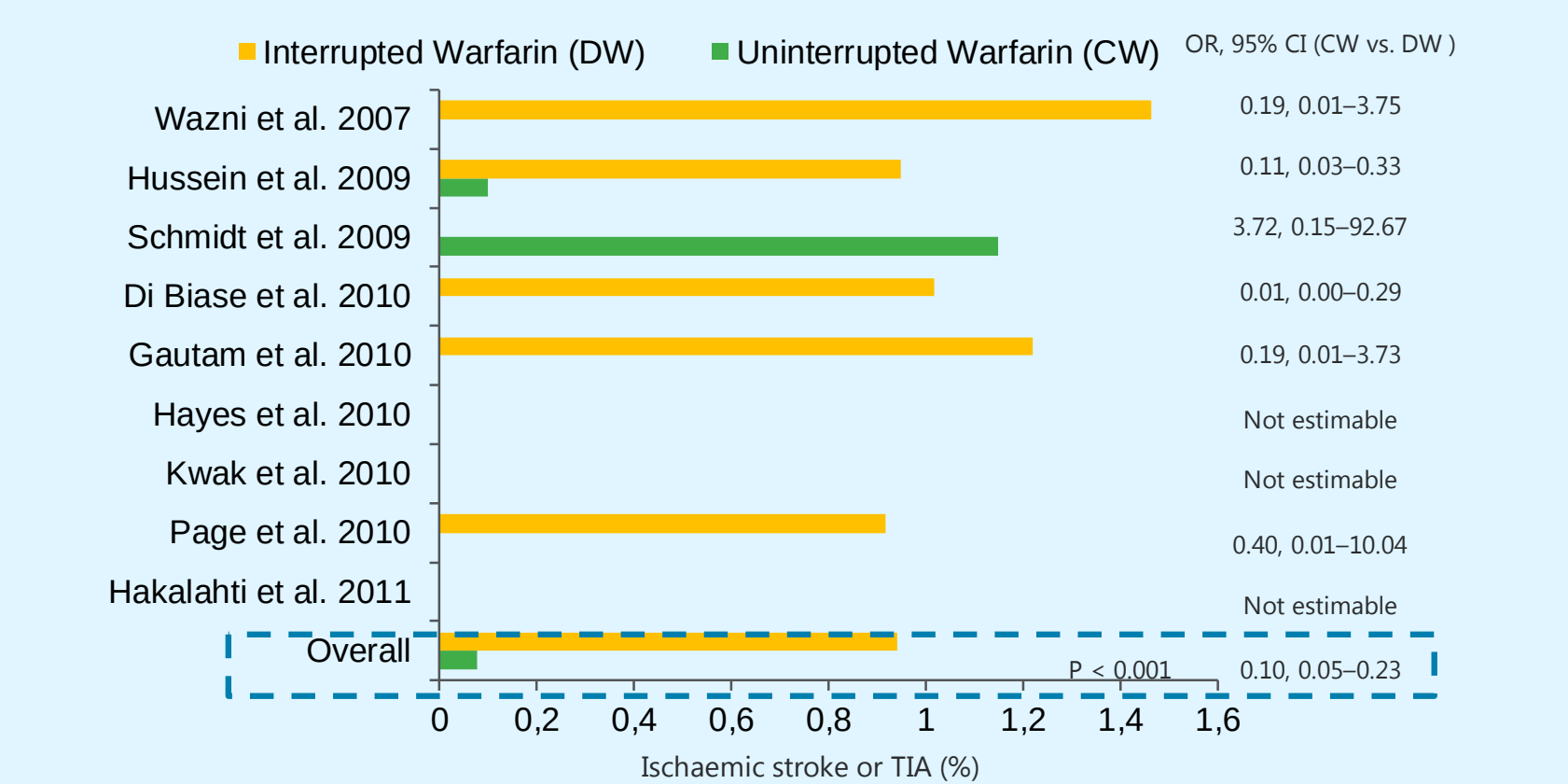
Abbott, American College of Cardiology Foundation, Actelion, Amgen, AstraZeneca, Axis-Santé, Bayer, Beth Israel Deaconess Medical, Boehringer Ingelheim, Boston-Scientific, Brigham Women's Hospital, Bristol-Myers Squibb, China heart House, Daiichi-Sankyo, Elsevier, Europa, Fédération Française de Cardiologie, ICAN, Idorsia, Lead-Up, Medtronic, Menarini, MSD, NovoNordisk, Partners, Pfizer, Quantum Genomics, Sanofi, Servier and WebMD.

NOACs and AF ablation

NOAC, non-vitamin K antagonist oral anticoagulant.

Stroke/TIA risk when anticoagulation is interrupted in patients undergoing ablation: Meta-analysis[1]



CW, continuous warfarin; DW, discontinuous warfarin; OR, odds ratio.

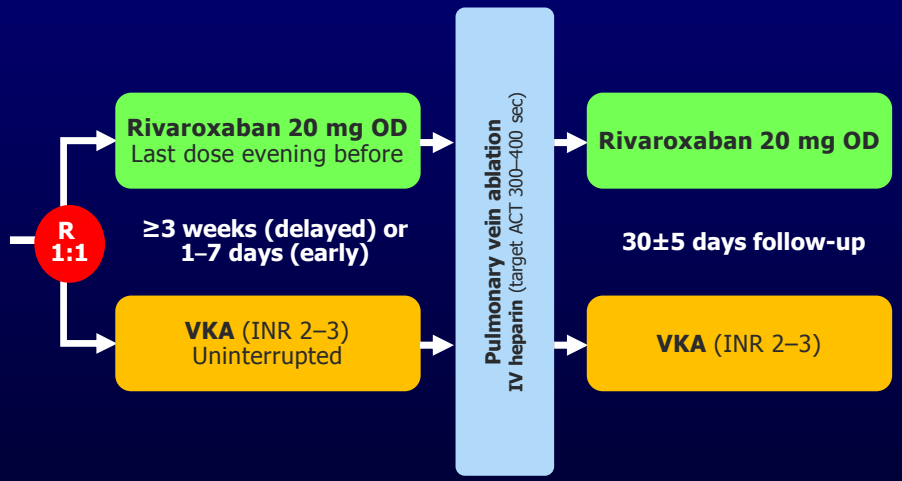
Santangeli P, Di Biase L, et al. Circ Arrhythm Electrophysiol 2012;5:302–11.

CI, confidence interval; CW, continuous wafarin; DW, discontinuous wafarin; OR, odds ratio.

1. Santangeli P, et al. Circ Arrhythm Electrophysiol 2012;5:302–11.

VENTURE-AF: Rivaroxaban vs VKA in AF ablation[1]

- Patients with paroxysmal or persistent NVAF, scheduled for pulmonary vein ablation
- 248 patients randomised
  - Mean age 59.6±10.2 years
  - Mean CHA_2DS_2-VASc score 1.6±1.3



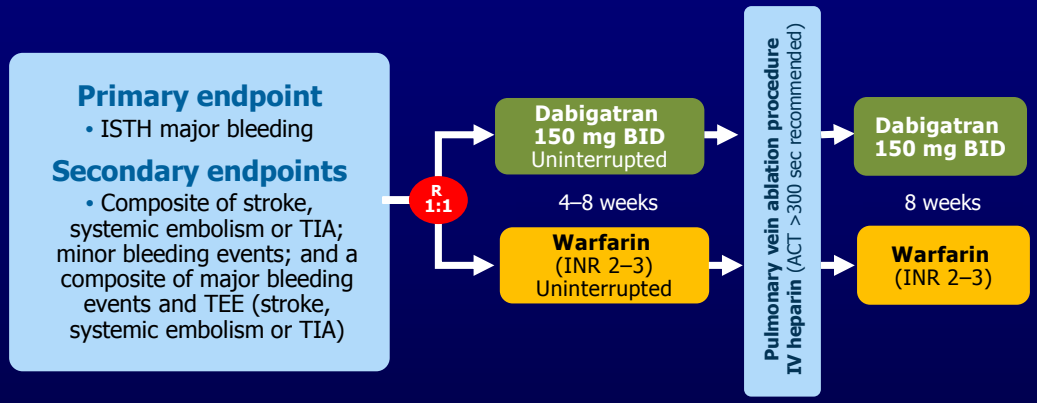
Number of events	Rivaroxaban (n=124)	VKA (n=124)
Primary outcome (post-procedure major bleeding)		
Major bleed	0	1
Secondary outcomes		
Thromboembolic event	0	2
Any bleeding events	21	18

INR, international normalised ratio; IV, intravenous; NVAF, non-valvular atrial fibrillation; OD, once daily; R, randomisation; SmPC, summary of product characteristics; VKA, vitamin K antagonist. Please refer to the SmPC for further information.[2]

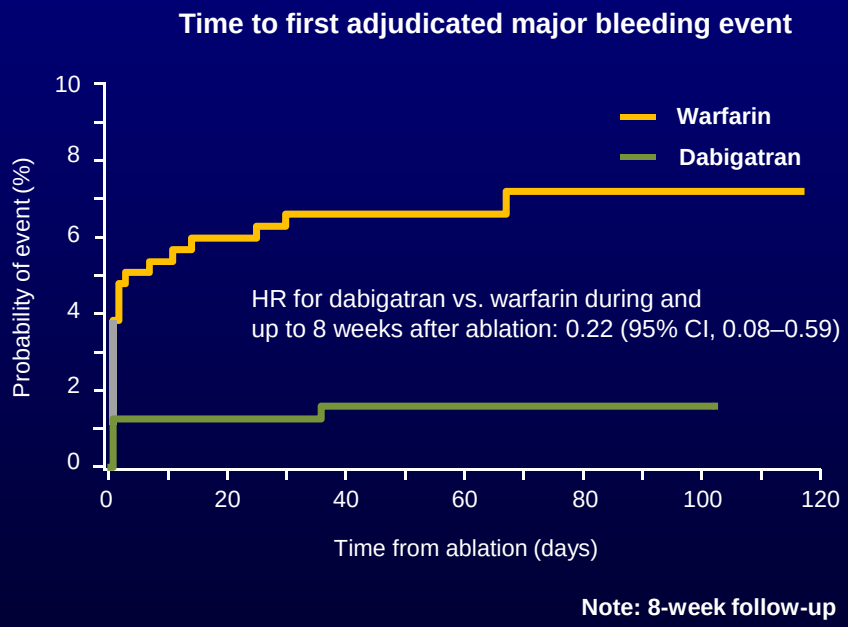
1. Cappato R, et al. Eur Heart J 2015;36:1805–11;
2. Rivaroxaban SmPC. Available at: http://www.ema.europa.eu.

RE-CIRCUIT: Dabigatran vs warfarin in AF ablation[1]

- Patients with paroxysmal (~68%) or persistent NVAF, scheduled for first pulmonary vein ablation (n=635)
  - Time in therapeutic range (INR 2–3) was 66% in the warfarin arm
  - Mean CHA_2DS_2-VASc score was 2 and mean age was 59 years, in both arms



	Dabigatran	Warfarin
Tamponade	1 event	6 events
Groin haematoma	0 events	8 events
Minor bleeding	18.6%	17.0%
Prolonged hospitalisation	3.8%	6.5%

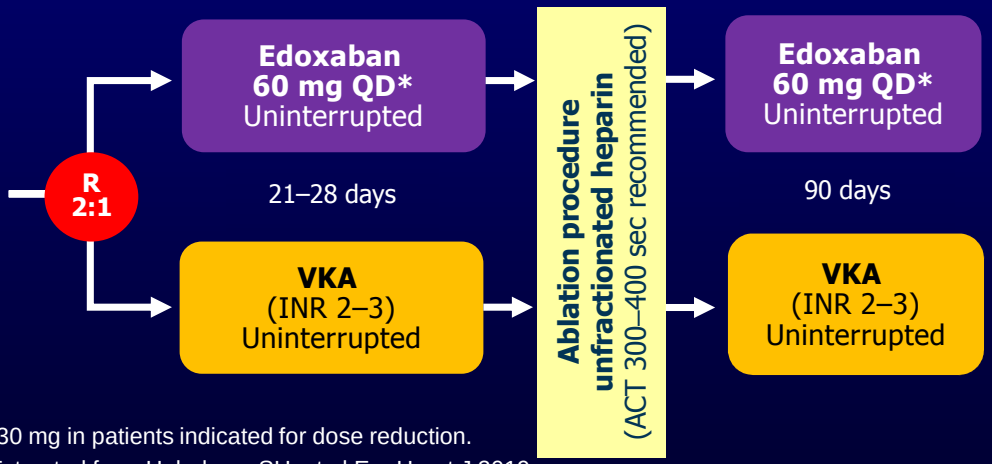


ACT, activated clotting time; BID, twice daily; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis; TEE, transesophageal echocardiography.
Please refer to the SmPC for further information.[2]

1. Calkins H, et al. New Engl J Med 2017;376:1627–36;
2. Dabigatran SmPC. Available at: http://www.ema.europa.eu.

ELIMINATE-AF: Edoxaban vs VKA for AF ablation[1]

- Patients with paroxysmal, persistent or long-standing persistent NVAF, scheduled for first or repeated catheter ablation
- 614 patients randomised
  - Median age 60.5 (Q1–Q3: 53–67) years
  - CHA_2DS_2-VASc scores ≥2=50.2%; 1=27.0%; 0=22.8%
  - 533 patients received study drug and underwent catheter ablation
  - 177 underwent brain MRI to assess silent cerebral infarcts



*30 mg in patients indicated for dose reduction.
Extracted from Hohnloser SH, et al.Eur Heart J 2019.

Primary endpoint (composite of death, stroke, or ISTH-defined major bleeding post-ablation) in the PP and the mITT population

	Edoxaban	VKA	HR (95% CI)
PP population post-ablation[a]	**N=316**	**N=101**	
Primary endpoint events, n (%)	1 (0.3)	2 (2.0)	0.16 (0.02–1.73)
mITT population peri- and post-ablation[b]	**n=375**	**n=178**	
Primary endpoint events, n (%)	10 (2.7)	3 (1.7)	1.60 (0.44–5.78)

[a]From the end of catheter ablation to day 90/end of treatment;
[b]From the start of catheter ablation to day 90/ end of treatment.

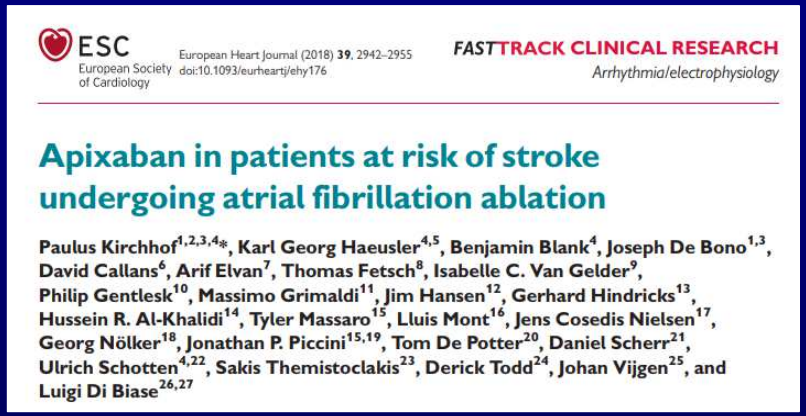
- Rates of acute cerebral microemboli were similar (13.8% vs 9.6%) after catheter ablation under edoxaban compared with VKA (MRI sub-analysis)

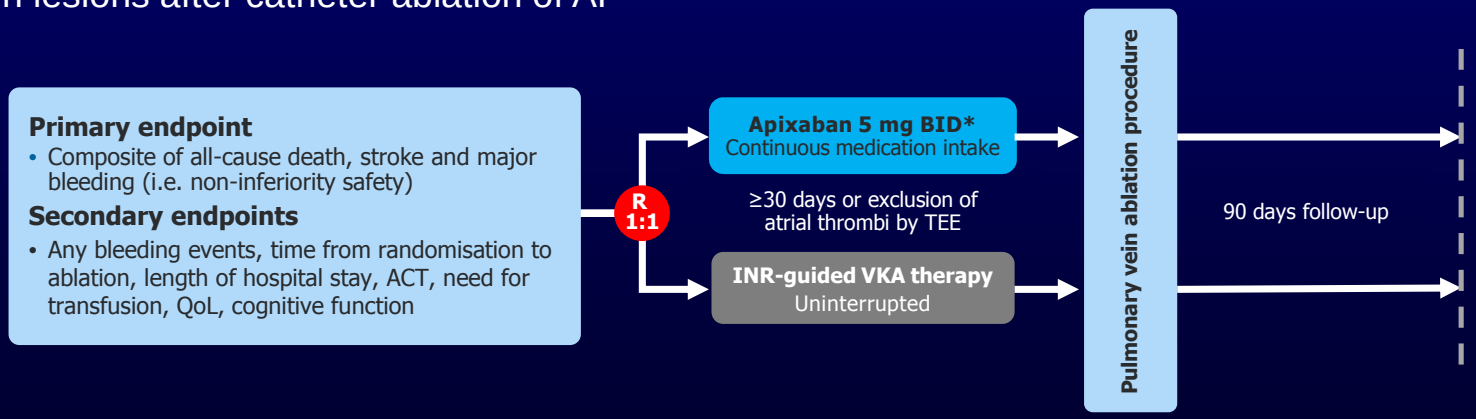
mITT, modified intent-to-treat; MRI, magnetic resonance imaging; PP, per-protocol; Q, quartile; QD, once daily.
Please refer to the SmPC for further information.[2]

1. Hohnloser SH et al. Eur Heart J. 2019; doi:10.1093/eurheartj/ehz190;
2. Edoxaban SmPC. Available at: http://www.ema.europa.eu.

AXAFA: Apixaban vs VKA in AF ablation[1]

- Open, blinded endpoint non-inferiority study
- Patients with AF scheduled for pulmonary vein ablation and $CHADS_2$ ≥1
  - Median time in the therapeutic range (INR ≥2) was 84% in the warfarin arm
  - Mean CHA_2DS_2-VASc score was 2.4 and median age 64 years, in both arms
- In a subset of patients, MRI analyses performed to explore clinically silent brain lesions after catheter ablation of AF



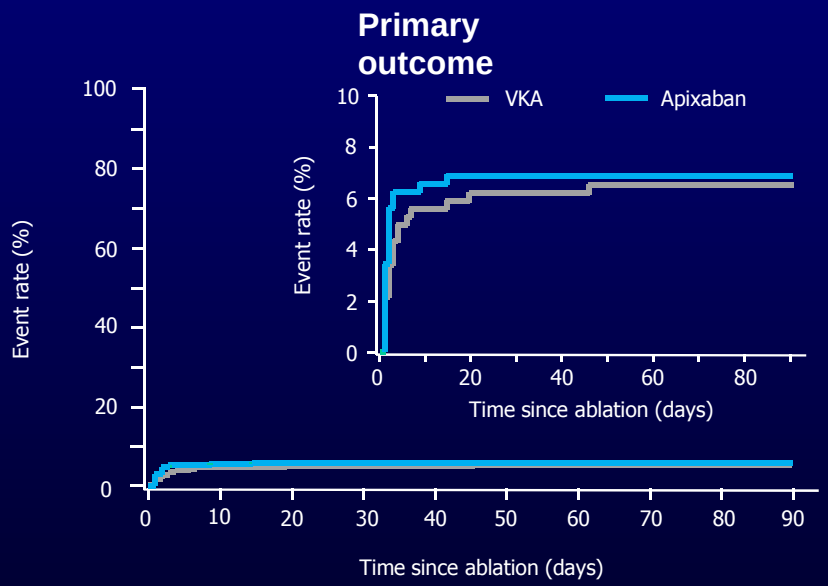


*2.5 mg BID if ≥2 of the following criteria: age ≥80 years, weight ≤60 kg or serum creatinine ≥1.5 mg/dL (133 µmol/L). QoL, quality of life.
Please refer to the SmPC for further information.[2]

1. Kirchhof P, et al. Eur Heart J 2018; 39:2942–55;
2. Apixaban SmPC. Available at: http://www.ema.europa.eu.

AXAFA: Primary outcome[1]

- Difference in primary outcome (composite of all-cause death, stroke or major bleeding) rate
  - -0.38% (90% CI -4.0%, 3.3%); non-inferiority *p*=0.0002
  - Apixaban was also non-inferior to VKA among all randomized patients as assessed by Cox proportional hazards model comparison between treatment groups using a relative non-inferiority margin of 1.44 (HR=0.88, 90% CI 0.55, 1.41; *p*=0.042)



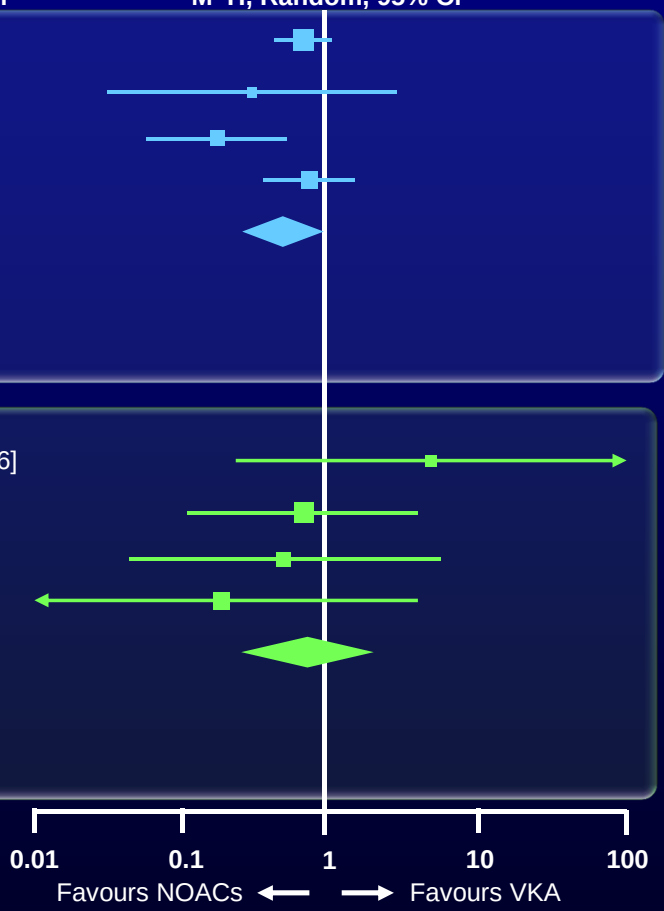
	Apixaban	VKA
Patients with primary endpoint n (%)	22/318 (6.9%), non-inferiority *p*=0.0002	23/315 (7.3%)
Death	1 (0.3%)	1 (0.3%)
Stroke or TIA	2 (0.6%)	0
Intracranial haemorrhage	0	1 (0.3%, fatal)
TIMI major bleeding	1 (0.3%)	3 (1%)
ISTH major bleeding	10 (3.1%)	14 (4.4%)
Tamponade	2 (0.6%)	5 (1.6%)

TIMI, thrombolysis in myocardial infarction.
Please refer to the SmPC for further information.[2]

1. Kirchhof P, et al. Eur Heart J 2018; 39:2942–55;
2. Apixaban SmPC. Available at: http://www.ema.europa.eu.

Meta-analysis: Uninterrupted NOAC vs uninterrupted VKA[1]

		NOACs		VKA				
	Study or subgroupz	Events	Total	Events	Total	Weight M–H	Risk ratio Random, 95% CI	Risk ratio M–H, Random, 95% CI
Major bleeding	AXAFA	31	318	42	315	41.4%	0.73 [0.47, 1.13]	
	Kuwahara et al.	1	100	3	100	6.5%	0.33 [0.04, 3.15]	
	RE-CIRCUIT	4	317	21	318	20.5%	0.19 [0.07, 0.55]	
	VENTURE-AF	13	123	16	121	31.6%	0.80 [0.40, 1.59]	
	Total (95% CI)		858		854	100.0%	0.54 [0.29, 1.00]	
	Total events	49		82				
	Heterogeneity. Tau^2 =0.19; Chi^2 = 6.27, df=3 (*P*=0.10); I^2 = 52%							
	Test for overall effect: Z=1.95 (*P*=0.05)							
Thromboembolic events	AXAFA	2	318	0	315	6.2%	4.95 [0.24, 102.76]	
	Kuwahara et al.	2	100	3	100	37.1%	0.67 [0.11, 3.90]	
	RE-CIRCUIT	1	317	2	318	24.7%	0.50 [0.05, 5.50]	
	VENTURE-AF	0	114	2	107	31.9%	0.19 [0.01, 3.87]	
	Total (95% CI)		849		840	100.0%	0.74 [0.26, 2.11]	
	Total events	5		7				
	Heterogeneity. Chi^2 =2.41; df=3 (*P*=0.49); I^2 =0%							
	Test for overall effect: Z=0.56 (*P*=0.57)							



There are no head-to-head studies comparing the NOACs; direct comparisons cannot be made between individual NOACs based on these data

Mean CHA_2DS_2-VASc score: AXAFA 2.4; Kuwahara 2.2; RE-CIRCUIT 2.1; VENTURE-AF 1.6.

M-H, Mantel-Haenszel.

Please refer to the SmPC for further information.[2–4]

1. Romero J, et al. Europace 2018; 20:1612–20; 2. Dabigatran SmPC; 3. Rivaroxaban SmPC; 4. Apixaban SmPC.

All SmPCs available at: http://www.ema.europa.eu.

Recommendations for anticoagulation post ablation: 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus[1]

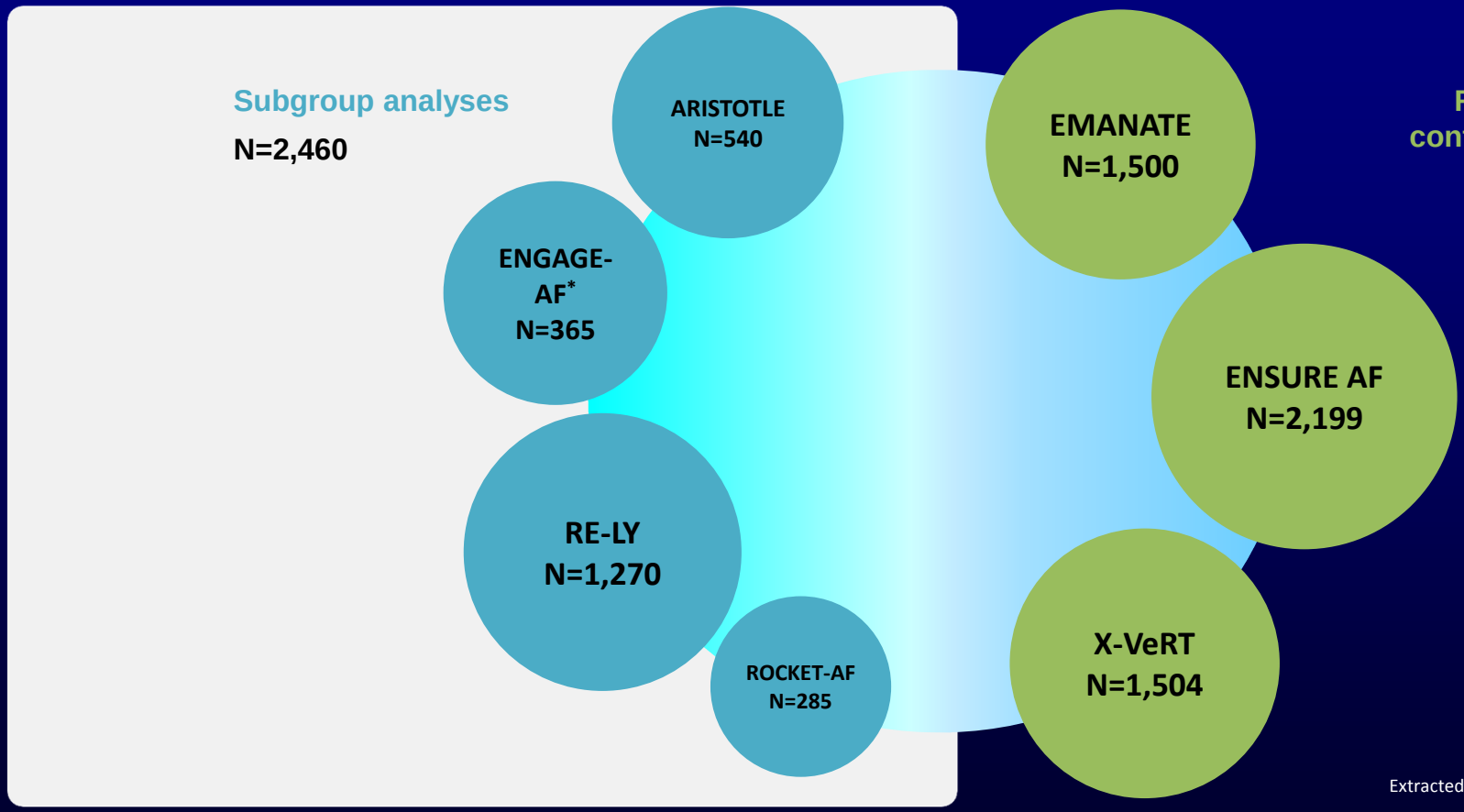
Postablation	In patients who are not therapeutically anticoagulated prior to catheter ablation of AF and in whom warfarin will be used for anticoagulation postablation, low molecular weight heparin or intravenous heparin should be used as a bridge for initiation of systemic anticoagulation with warfarin following AF ablation.*	I	C-EO	
	Systemic anticoagulation with warfarin* or a NOAC is recommended for at least 2 months postcatheter ablation of AF.	I	C-EO	1,2
	Adherence to AF anticoagulation guidelines is recommended for patients who have undergone an AF ablation procedure, regardless of the apparent success or failure of the procedure.	I	C-EO	
	Decisions regarding continuation of systemic anticoagulation more than 2 months post ablation should be based on the patient's stroke risk profile and not on the perceived success or failure of the ablation procedure.	I	C-EO	5,6
	In patients who have not been anticoagulated prior to catheter ablation of AF or in whom anticoagulation with a NOAC or warfarin has been interrupted prior to ablation, administration of a NOAC 3 to 5 hours after achievement of hemostasis is reasonable postablation.	IIa	C-EO	
	Patients in whom discontinuation of anticoagulation is being considered based on patient values and preferences should consider undergoing continuous or frequent ECG monitoring to screen for AF recurrence.	IIb	C-EO	

*Time in therapeutic range (TTR) should be >65–70% on warfarin.
APHRS, Asia Pacific Heart Rhythm Society; ECAS, European Cardiac Arrhythmia Society; ECG, echocardiogram; EHRA, European Heart Rhythm Association; HRS, Heart Rhythm Society; SOLAECE, Latin American Society of Cardiac Stimulation and Electrophysiology.

1. Calkins H, et al. Heart Rhythm 2017;14:e275–e444.

NOACs and cardioversion

Evidence of use of different NOACs in cardioversion



Extracted from Mahaffey K, et al. 2018.[1]

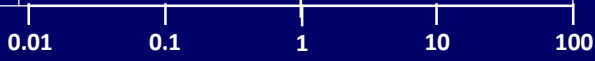
*Electrical cardioversion only.

1. Mahaffey K, et al. Eur Heart J 2018;39:2972–4.

Cardioversion in prior φ III NOAC trials: Meta analysis[1]

Stroke/SE

	NOACs		VKAs			
Study or subgroup	Events	Total	Events	Total	Weight	Risk ratio M–H, Random, 95% CI
RE-LY	7	1319	4	664	52.7%	**0.88** (0.26–3.00)
ROCKET-AF	2	138	1	132	13.9%	**1.91** (0.18–20.85)
ARISTOTLE	0	331	0	412		Not estimable
ENGAGE AF-TIMI 48	2	251	0	114	8.6%	**2.28** (0.11–47.15)



Major bleeding

	NOACs		VKAs			
Study or subgroup	Events	Total	Events	Total	Weight	Risk ratio M–H, Random, 95% CI
RE-LY	15	1319	4	664	48.8%	**1.89** (0.63–5.67)
ROCKET-AF	0	138	2	132	6.4%	**0.19** (0.01–3.95)
ARISTOTLE	1	331	1	142	7.7%	**1.24** (0.08–19.82)
ENGAGE AF-TIMI 48	0	251	0	114		Not estimable

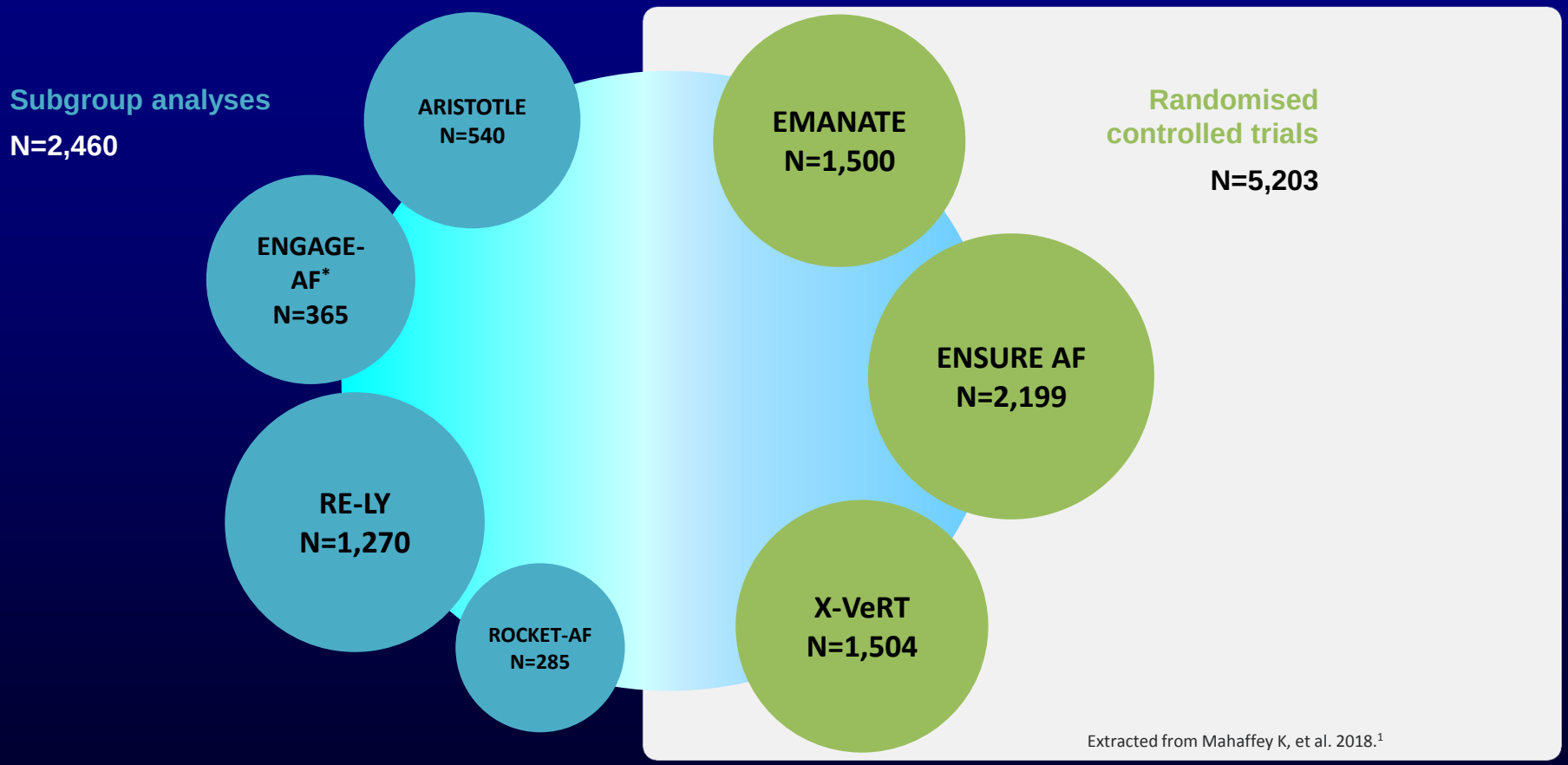
There are no head-to-head studies comparing the NOACs; direct comparisons cannot be made between individual NOACs based on these data

Extracted from Renda G, et al. Am J Med 2016;129:1117–23.e2.

Please refer to the SmPC for further information.[2–5]
SE, systemic embolism.

1. Renda G, et al. Am J Med 2016;129:1117–23.e2; 2. Dabigatran SmPC; 3. Rivaroxaban SmPC; 4. Apixaban SmPC; 5. Edoxaban SmPC. All SmPCs available at: http://www.ema.europa.eu.

Evidence of use of different NOACs in cardioversion

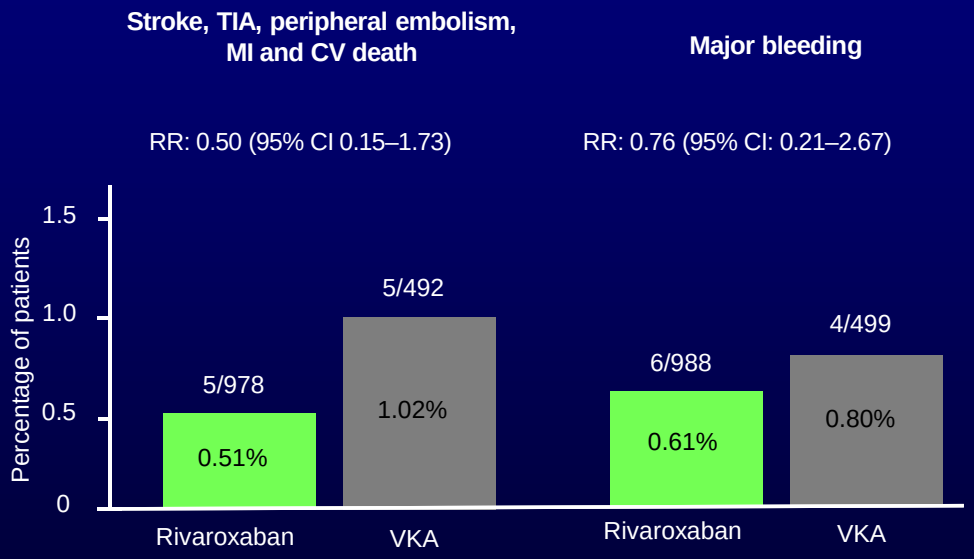


*Electrical cardioversion only.

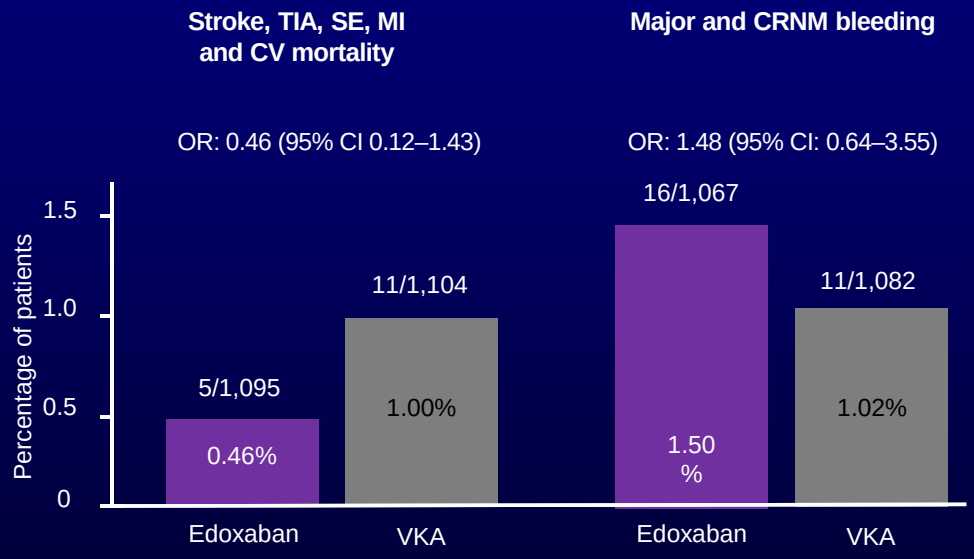
1. Mahaffey K, et al. Eur Heart J 2018;39:2972–4.

NOAC trials in patients undergoing cardioversion

X-VERT[1]*



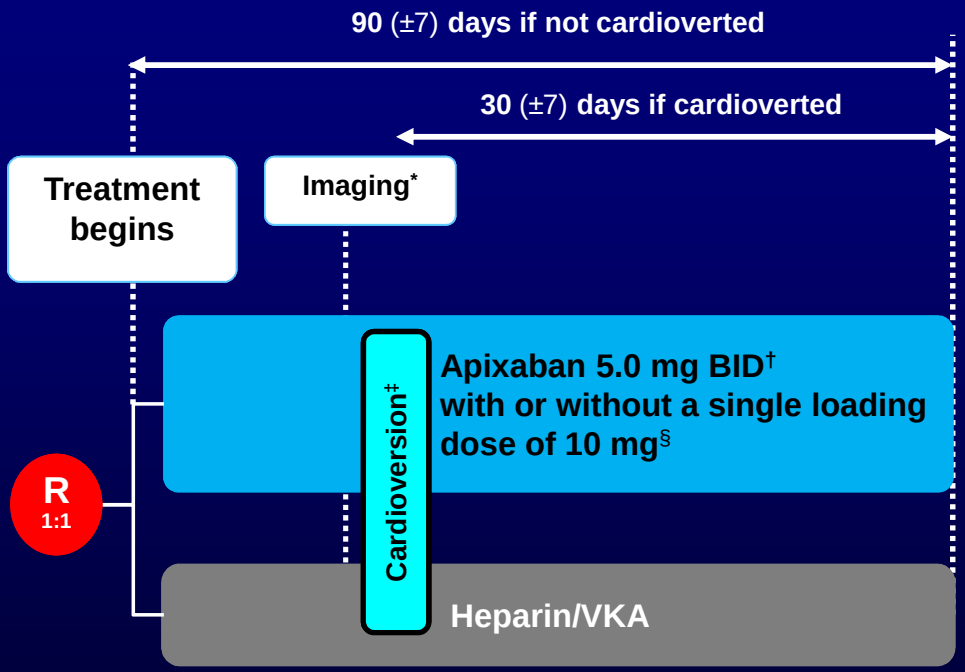
ENSURE-AF[2,3]†



CRNM, clinically relevant non-major; CV, cardiovascular; MI, myocardial infarction; RR, risk ratio.
*Rivaroxaban (n=978) vs VKA (n=492); cardioversion within 5 days or after 3–8 weeks of anticoagulation; 43% anticoagulant-experienced at baseline;
†Edoxaban (n=1,095) vs enoxaparin/VKA (n=1,104); cardioversion within 3 days or after 21–24 days of anticoagulation; 73% anticoagulant-experienced at baseline.
Please refer to the SmPC for further information.[4,5]

1. Cappato R, et al. Eur Heart J 2014;35:3346–55; 2. Goette A, et al. Lancet 2016;388:1995–2003; 3. Lip GHY, et al. Am Heart J 2015;169:597–604; 4. Rivaroxaban SmPC; 5. Edoxaban SmPC. All SmPCs available at: http://www.ema.europa.eu.

EMANATE: Apixaban in patients with AF undergoing cardioversion[1]

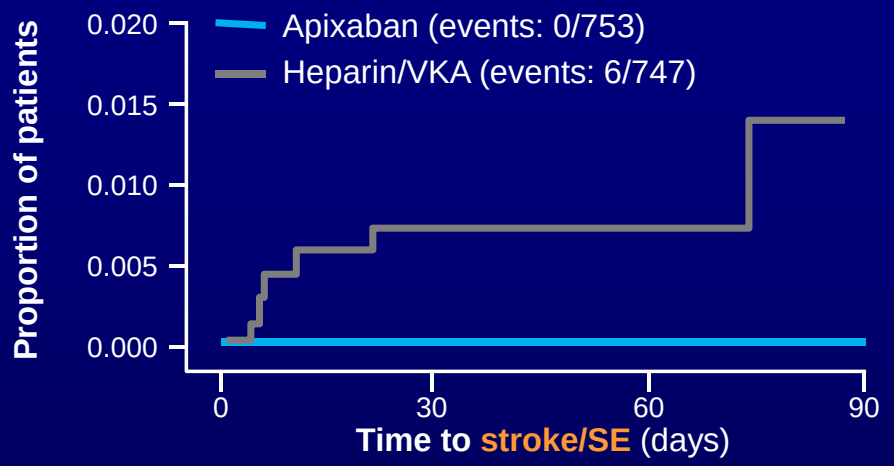


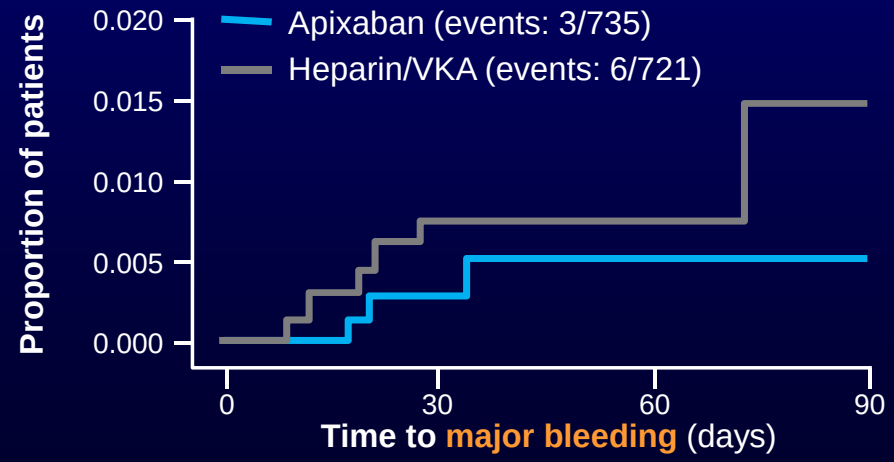
- 78% of subjects with new-onset AF¶
  - Duration of AF was <48 hours in 34%#
- Patients had minimal exposure to anticoagulation prior to cardioversion
  - 62% not anticoagulated prior to randomisation
  - 38% received ≤48 hours' anticoagulation

CT, computerised tomography; TOE, transoesophageal echocardiogram.
*TOE or CT imaging, at the discretion of the investigator; †Dose reduction to 2.5 mg BID in appropriate patients; ‡Local investigators determined the timing and type of cardioversion, within 90 days of randomization; §5 mg if down-titrated in appropriate patients; ¶Diagnosed within 3 months prior to randomisation; #Data on file.
Please refer to the SmPC for further information.[2]

1. Ezekowitz MD, et al. Eur Heart J 2018;39(32):2959–71;
2. Apixaban SmPC. Available at: http://www.ema.europa.eu.

EMANATE: Key efficacy and safety outcomes[1]





Efficacy outcomes

	Apixaban total (n=753)	Apixaban loading dose (n=342)	Heparin/VKA (n=747)
Stroke	**0**	**0**	**6**
Death	**2**	**1**	**1**

Safety outcomes

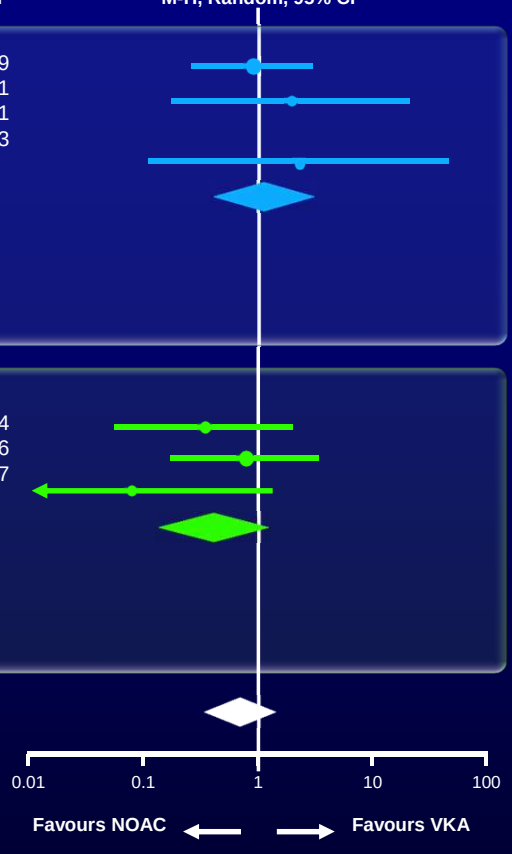
	Apixaban total (n=735)	Apixaban loading dose (n=342)	Heparin/VKA (n=721)
Major bleeds	**3**	**1**	**6**
CRNM bleeds	**11**	**4**	**13**

Please refer to the SmPC for further information.[2]

1. Ezekowitz MD, et al. Eur Heart J 2018;39(32):2959–71;
2. Apixaban SmPC. Available at: http://www.ema.europa.eu.

NOACs vs. VKA for stroke prevention with cardioversion[1]

	Study or subgroup	NOAC Events	NOAC Total	VKA Events	VKA Total	Weight	Risk ratio M–H, Random, 95% CI	Year
RCTs	RE-LY	7	1,319	4	664	36.4%	0.88 (0.26, 3.00)	2009
	ROCKET-AF	2	138	1	132	9.6%	1.91 (0.18, 20.85)	2011
	ARISTOTLE	0	331	0	412		Could not be estimated	2011
	ENGAGE-AF	2	251	0	114	5.9%	2.28 (0.11, 47.15)	2013
	Subtotal (95% CI)		**2,039**		**1,322**	**51.9%**	**1.13 (0.41, 3.16)**	
	Total events	11		5				
	Heterogeneity: Tau²=0.00; Chi²=0.56, df=2 (*p*=0.76); *I*²=0%							
	Test for overall effect: *Z*=0.24 (*p*=0.81)							
Prospective studies	X-VERT	2	1,002	3	502	17.1%	0.33 (0.06, 1.99)	2014
	ENSURE-AF	3	1,095	4	1,104	24.4%	0.76 (0.17, 3.37)	2016
	EMANATE	0	753	6	747	6.6%	0.08 (0.00, 1.35)	2017
	Subtotal (95% CI)		**2,850**		**2,353**	**48.1%**	**0.40 (0.13, 1.24)**	
	Total events	5		13				
	Heterogeneity: Tau²=0.08; Chi²=2.16, df=2 (*p*=0.34); *I*²=7%							
	Test for overall effect: *Z*=1.59 (*p*=0.11)							
	Total (95% CI)		**4,889**		**3,675**	**100.0%**	**0.70 (0.33, 1.46)**	
	Total events	16		18				
	Heterogeneity: Tau²=0.00; Chi²=4.49, df=5 (*p*=0.48); *I*²=0%							
	Test for overall effect: *Z*=0.96 (*p*=0.34)							
	Test for subgroup differences: Chi²=1.78; df=1 (*p*=0.18); *I*²=43.9%							



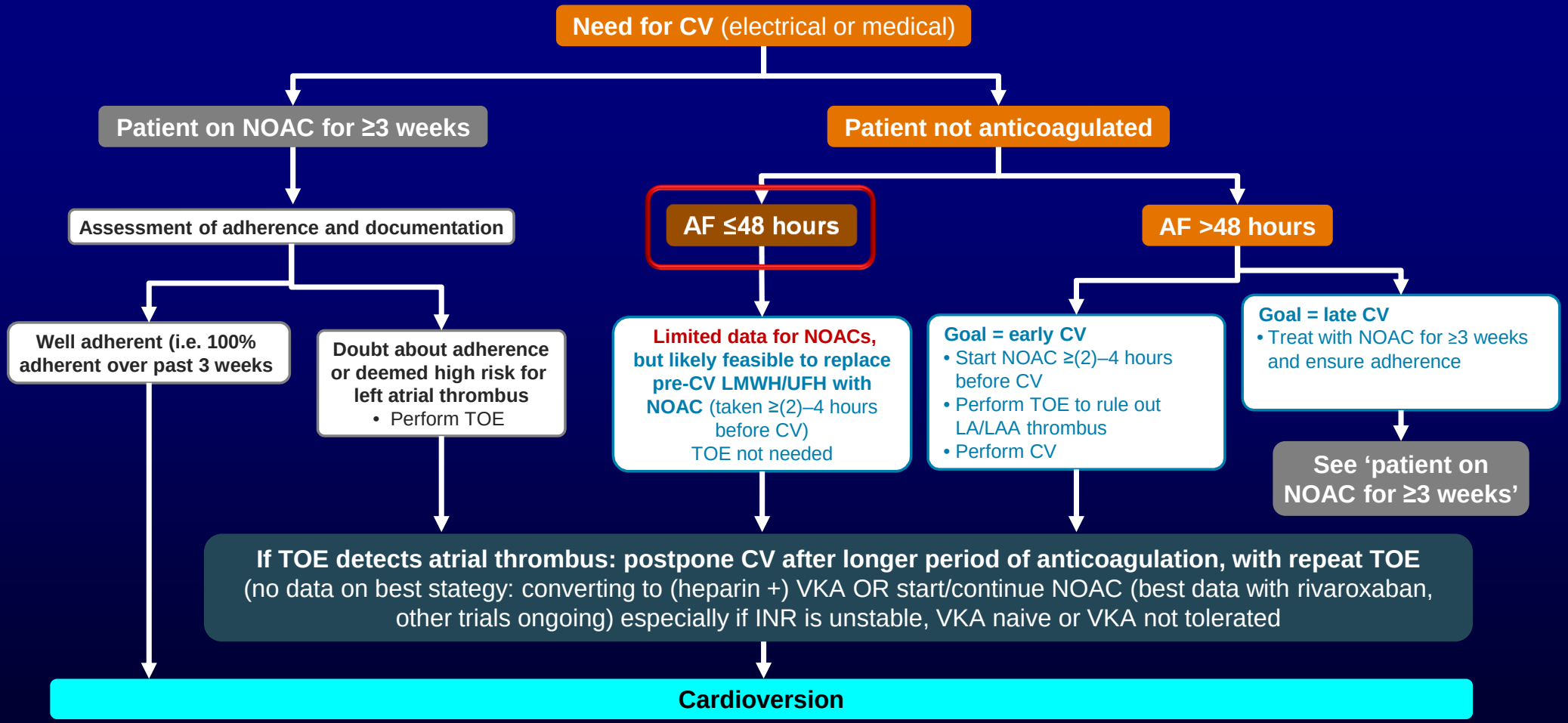
Forest plot describing the risk ratio and 95% CI of stroke/SE with use of NOACs vs VKA.

Head-to-head trials do not exist and direct comparisons between agents cannot be made. This analysis compared NOACs with warfarin in observational and randomised studies

Please refer to the SmPC for further information.[2–5]

1. Brunetti ND, et al. J Thromb Thrombolysis 2018;45:550–6;
2. Dabigatran SmPC; 3. Rivaroxaban SmPC; 4. Apixaban SmPC;
5. Edoxaban SmPC. All SmPCs available at: http://www.ema.europa.eu.

EHRA Practical NOAC Guide 2018 for cardioversion[1]



CV, cardioversion; LA, left atrium; LAA, left atrial appendage; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.

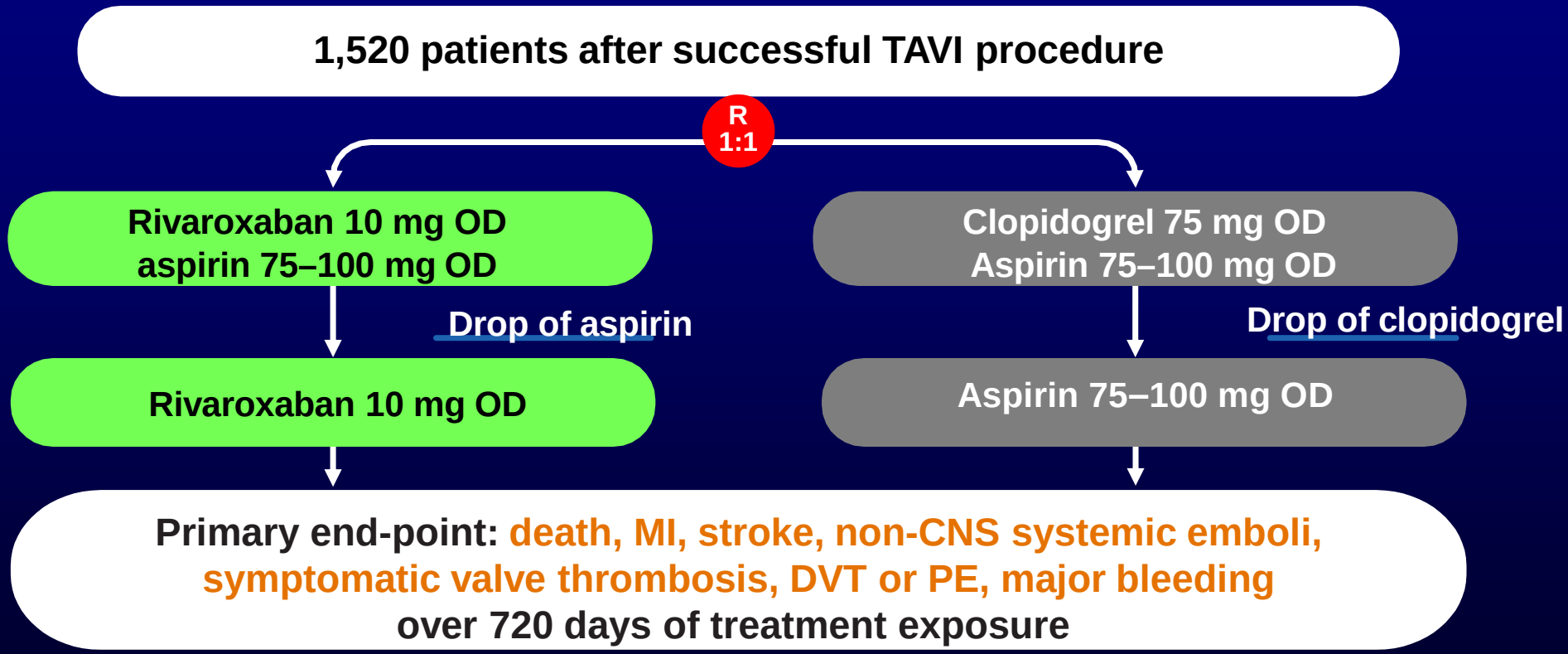
1. Steffel J, et al. Eur Heart J 2018;39:1330–93.

NOACs and TAVI

TAVI, trans-aortic valve implantation.

GALILEO

Global multicenter, open-label, randomized, event-driven, active-controlled 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 (TAVR) to **O**ptimize clinical outcomes will compare rivaroxaban-based[1]

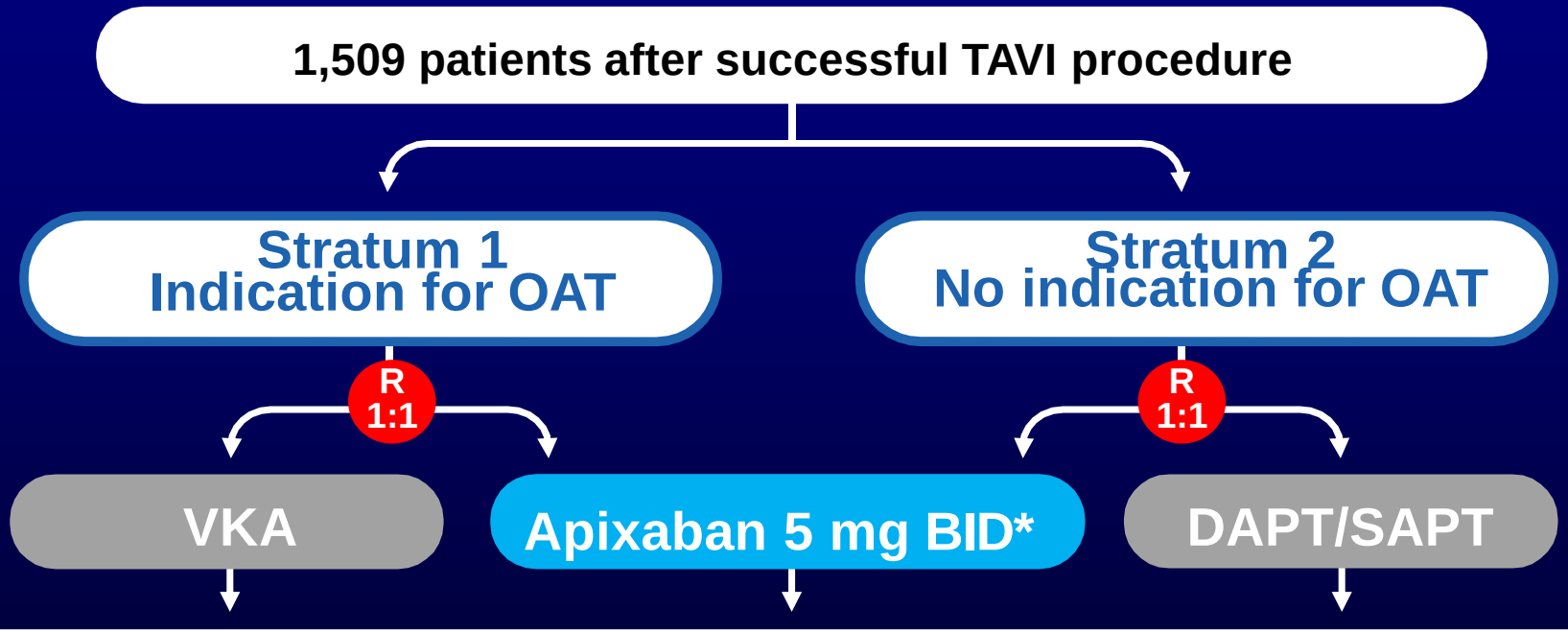


Please refer to the SmPC for further information.[2]
CNS, central nervous system; DVT, deep vein thrombosis; PE, pulmonary embolism.

1. NCT02556203. Available at: https://clinicaltrials.gov/ct2/show/NCT02556203. Accessed July 2019;
2. Rivaroxaban SmPC. Available at: http://www.ema.europa.eu.

ATLANTIS

Anti-Thrombotic Strategy to Lower All cardiovascular and Neurologic Ischemic and Hemorrhagic Events after Trans-Aortic Valve Implantation for Aortic Stenosis)[1]



Primary end-point: composite of death, MI, stroke, systemic emboli, intracardiac or bioprosthesis thrombosis, episode of DVT or PE, major bleeding over 1 year follow-up.

*2.5mg bid if creatinine clearance 15–29 mL/min or if two of the following criteria: age ≥80 years, weight ≤60k or creatinine ≥1.5 mg/dL (133 µMol).

DAPT, dual-antiplatelet therapy; OAT, oral anticoagulant therapy; SAPT, single antiplatelet therapy.

Please refer to the SmPC for further information.[2]

1. Collet JP, et al. Am Heart J. 2018;200:44-50;
2. Apixaban SmPC. Available at: http://www.ema.europa.eu.

NOACs and LAAC

LAAC, left atrial appendage closure.

Left Atrial Appendage Closure

Only a Question of Bleeding!*

Gilles Montalescot, MD, PhD, Paul Guedeney, MD

JACC: CARDIOVASCULAR INTERVENTIONS
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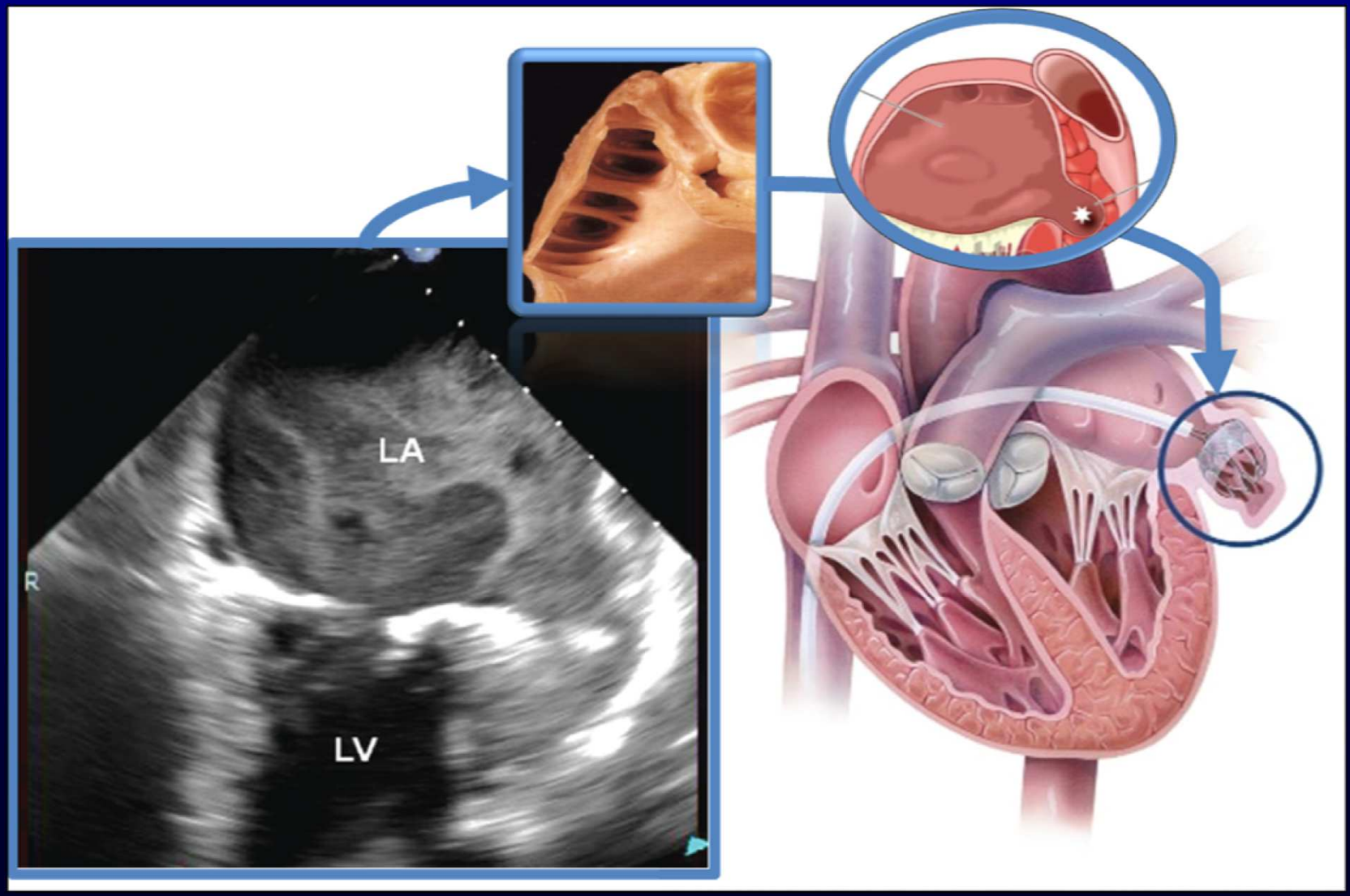
Trials	Estimated sample size	Interventions	Estimated completion date
ADRIFT *NCT03273322*	105	DAPT vs. Low-dose Rivaroxaban after LAAC	Completed
A3ICH *NCT03243175*	300	LAAC + SAPT/DAPT vs. Full-dose Apixaban vs. Optimal care	2020
STROKE-CLOSE *NCT02830152*	750	LAAC (Amulet™) + SAPT/DAPT vs. AOC/DAPT/SAPT	2022
CLOSURE-AF *NCT03463317*	1512	LAAC + DAPT vs. OAC (VKA/NOAC)	2023
ASAP-TOO *NCT02928497*	888	LAAC (Watchman™) + DAPT vs. SAPT/no therapy	2023

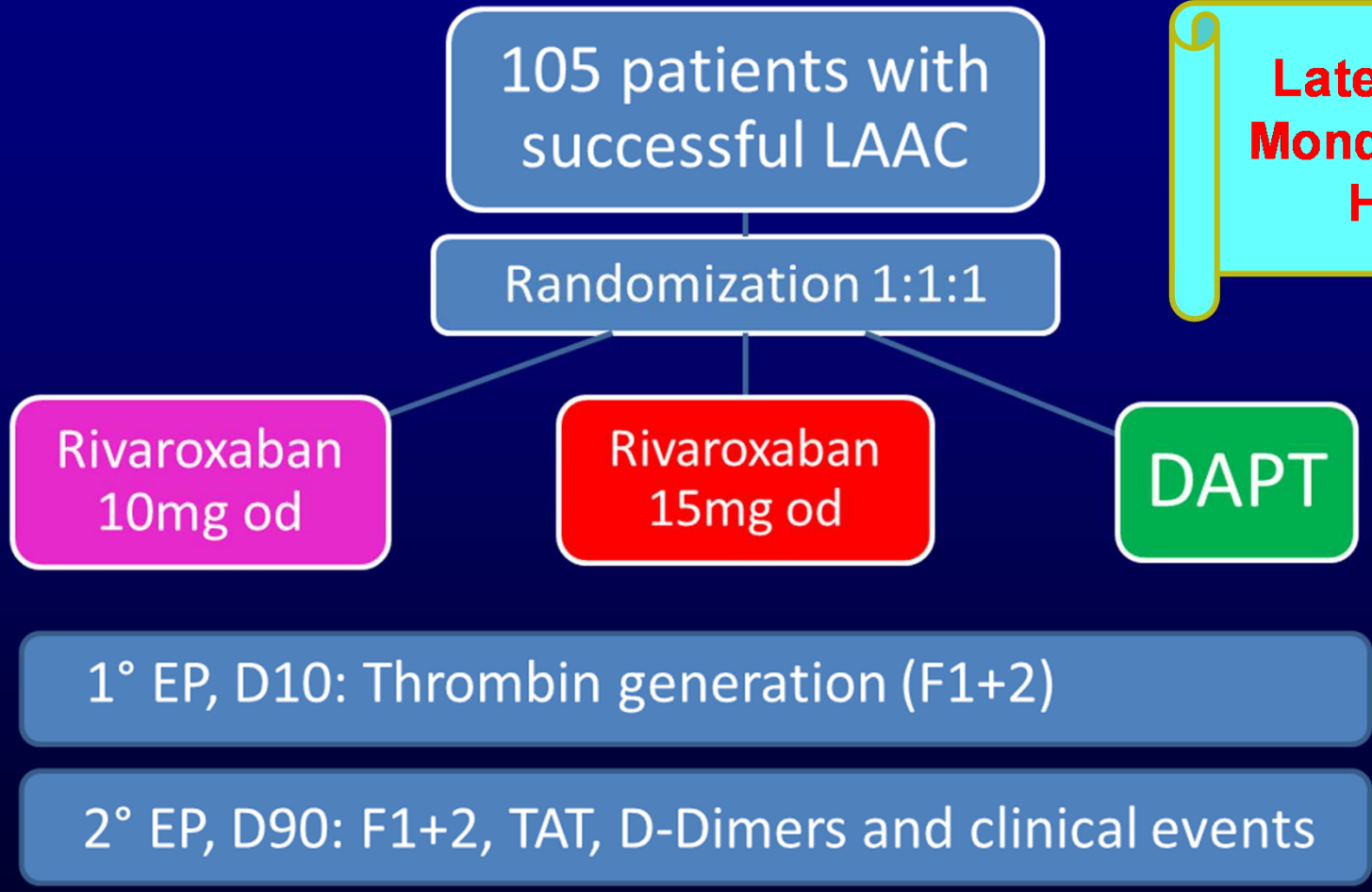
Please refer to the SmPC for further information.[2–5]

1. Montalescot G, Guedeney P. JACC Cardiovasc Interv 2019;12:1077–79;
2. Rivaroxaban SmPC; 3. Apixaban SmPC; 4. Dabigatran SmPC;
5. Edoxaban SmPC. All SmPCs available at: http://www.ema.europa.eu.

Left atrial appendage closure



ADRIFT study design[1]



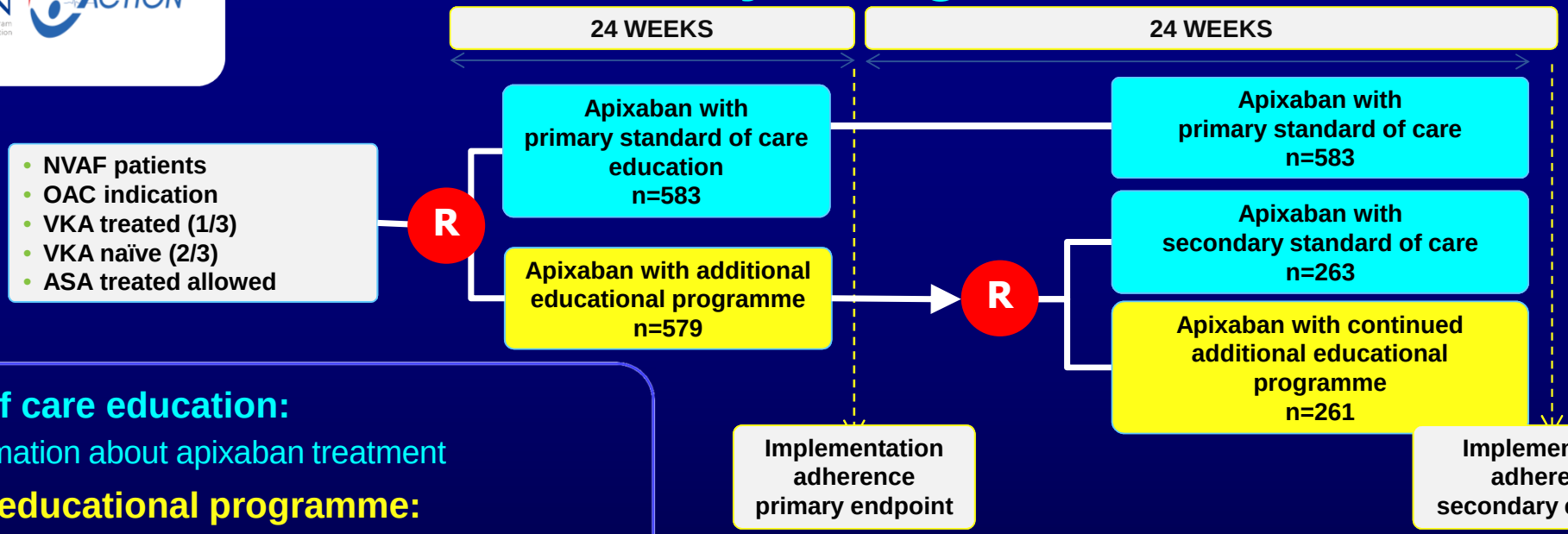
Late Breaking
Monday 8.30am
Helsinki

Please refer to the SmPC for further information.[2]

1. NCT03273322. Available at: https://clinicaltrials.gov/ct2/show/NCT03273322. Accessed July 2019;
2. Rivaroxaban SmPC. Available at: http://www.ema.europa.eu.

Once a patient is on a NOAC, adherence is key to reducing stroke risk

Study design[1]



Standard of care education:

- Usual information about apixaban treatment

Additional educational programme:

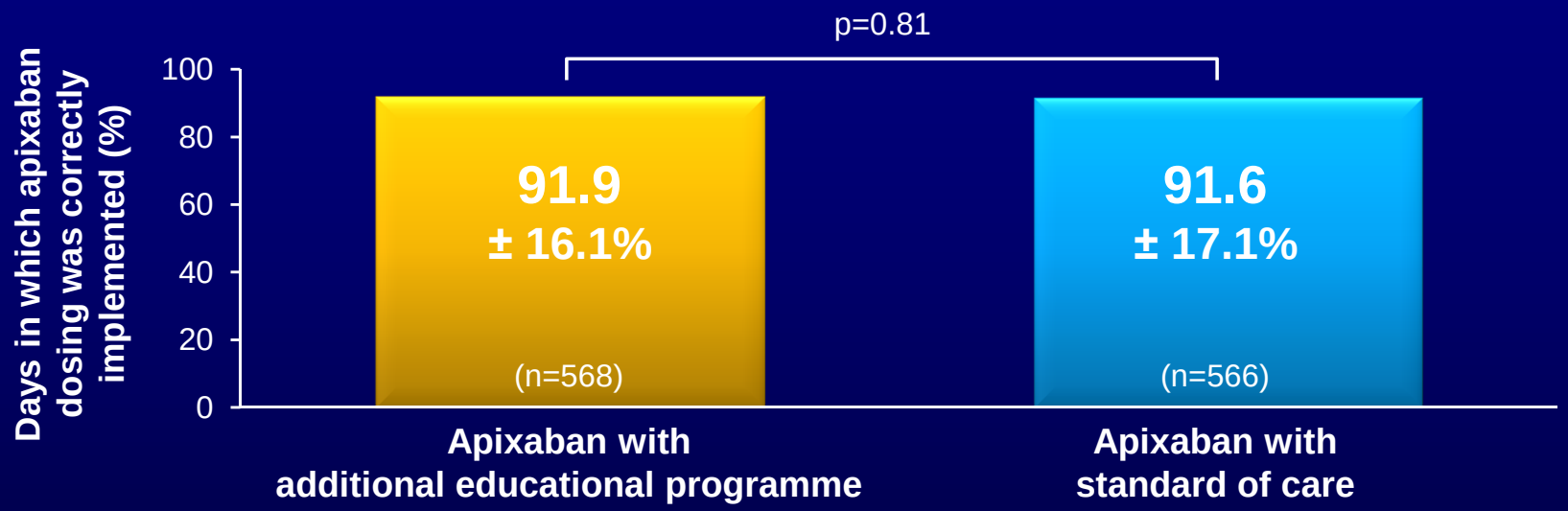
- An additional patient education booklet explaining NVAF and anticoagulant treatment for stroke prevention
- Reminder tools: key ring, SMS alert on mobile phone, or smartphone application
- Access to a virtual clinic organised at country level utilising staff from existing anticoagulant clinics

Adherence was measured via an Electronic Monitoring Device* (adapted to the blister) allowing registration of number and timing of pills intake†

ASA, acetylsalicylic acid; OAC, oral anticoagulant.
*No reminder function on device to enhance implementation.
†The device was operated by inserting commercial blister packs. The device then electronically recorded every time the blister was removed (date and time). It was assumed that a single dose of study medication was administered every time the blister pack was removed.
Implementation adherence defined as treatment taken as prescribed with one or less dose missed within 24 h and no tablet missed on the previous 2 consecutive days.

1. Montalescot G, et al. Am J Cardiovasc Drugs 2019; doi: 10.1007/s40256-019-00356-2.

Implementation adherence at 24 weeks[1] (primary endpoint)



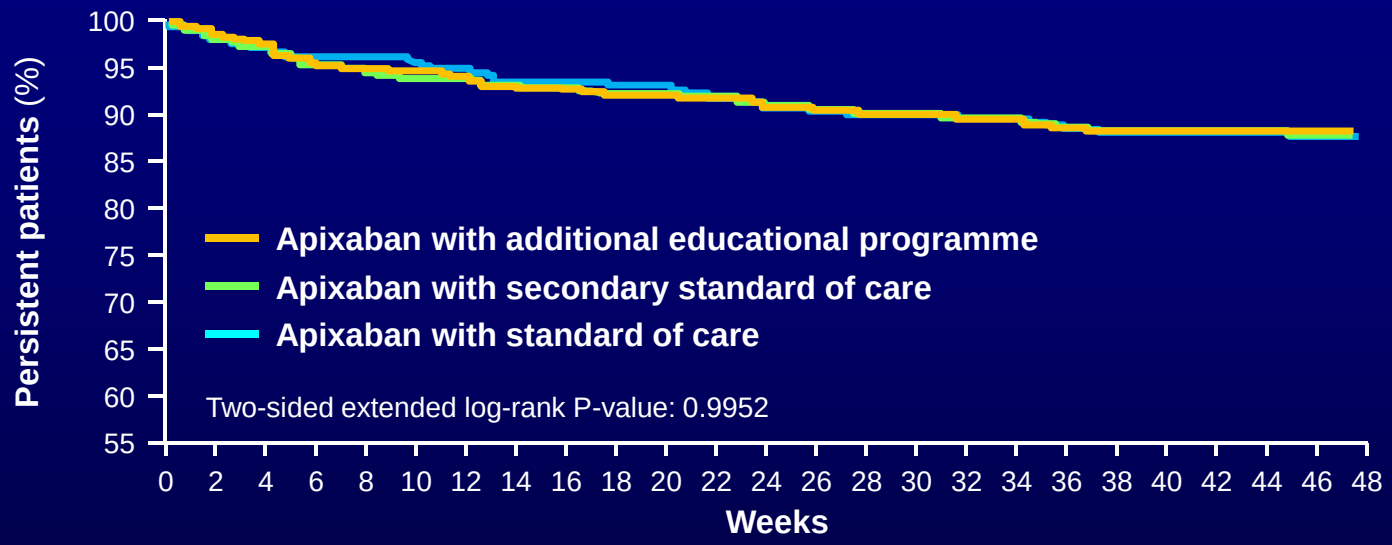
Implementation adherence
Defined as treatment taken as prescribed with one or less dose missed within 24h and no tablet missed on the previous two consecutive days

Implementation adherence at 48 weeks (secondary endpoint; mean ± SD)	
Continued additional educational programme	**90.4 ± 18.0%**
Primary standard of care	**90.1 ± 18.6%**
Secondary standard of care	**89.3 ± 18.1%**
No significant differences between groups at 24 or 48 weeks	

SD, standard deviation.

1. Montalescot G, et al. Am J Cardiovasc Drugs 2019. doi: 10.1007/s40256-019-00356-2.

Persistence over 48 weeks[1] (secondary endpoint)



Persistence

Defined as the length of time between initiation and discontinuation. Study treatment that was withheld for more than 30 consecutive days was considered a permanent discontinuation.

Proportion of patients persistent at 48 weeks	
Continued additional educational programme	**86.1%** (95% CI: 81.3–89.7)
Primary standard of care	**85.2%** (95% CI: 81.5–88.2)
Secondary standard of care	**87.8%** (95% CI: 83.4–91.1)
P>0.5 for all between-group comparisons	

1. Montalescot G, et al. Am J Cardiovasc Drugs 2019. doi: 10.1007/s40256-019-00356-2 + supplement.

Clinical endpoints at week 24[1] (adjudicated)

	Primary standard of care (n=583)		Additional educational programme (n=579)	
	# of Patients n (%)	# of Events	# of Patients n (%)	# of Events
Death	**4** (0.7)	**4**	**4** (0.7)	**4**
Cardiovascular death	**4** (0.7)	**4**	**2** (0.3)	**2**
Stroke, TIA, SE	**1** (0.2)	**1**	**5** (0.9)	**6**
Ischaemic stroke	**1** (0.2)	**1**	0	**0**
Haemorrhagic stroke	0	**0**	**2** (0.3)	**3**
TIA	0	**0**	0	**0**
SE	**0**	**0**	**3** (0.5)	**3**
Myocardial infarction	**2** (0.3)	**2**	**4** (0.7)	**4**
Venous thromboembolism	**0**	**0**	**1** (0.2)*	**1**
Pulmonary embolism	**0**	**0**	**1** (0.2)	**1**
Deep vein thrombosis	**0**	**0**	**1** (0.2)	**1**
Major bleeding (non-fatal) or CRNMB	**7** (1.2)	**7**	**9** (1.6)†	**10**
Major bleeding (non fatal)	**2** (0.3)	**2**	**4** (0.7)	**4**
Clinically relevant non-major bleed	**5** (0.9)	**5**	**5** (0.9)	**5**
Fatal bleeding	0	**0**	**1** (0.2)	**1**

*One patient who had one event of deep vein thrombosis + pulmonary embolism;
†One patient had a major and fatal bleeding.

1. Montalescot G, et al. Am J Cardiovasc Drugs 2019; doi:10.1007/s40256-019-00356-2.

Conclusions

- Careful attention to anticoagulation before, during and after procedures is critical
- Uninterrupted NOAC anticoagulation is recommended for PV ablation
- Cardioversion can be performed on NOACs
- NOAC after successful TAVI?
- NOAC after successful LAAC?
- Adherence can improve outcomes; however, the role or type of education needs to be further studied.