ESC Heart & Brain Workshop

Workshop 3:

Anticoagulants and antiplatelet drugs

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Supported by Bayer, Bristol-Myers Squibb and Pfizer Alliance, Boehringer Ingelheim, Daiichi Sankyo Europe GmbH and Medtronic in the form of educational grants. The scientific programme has not been influenced in any way by its sponsors.

ESC Council Stroke

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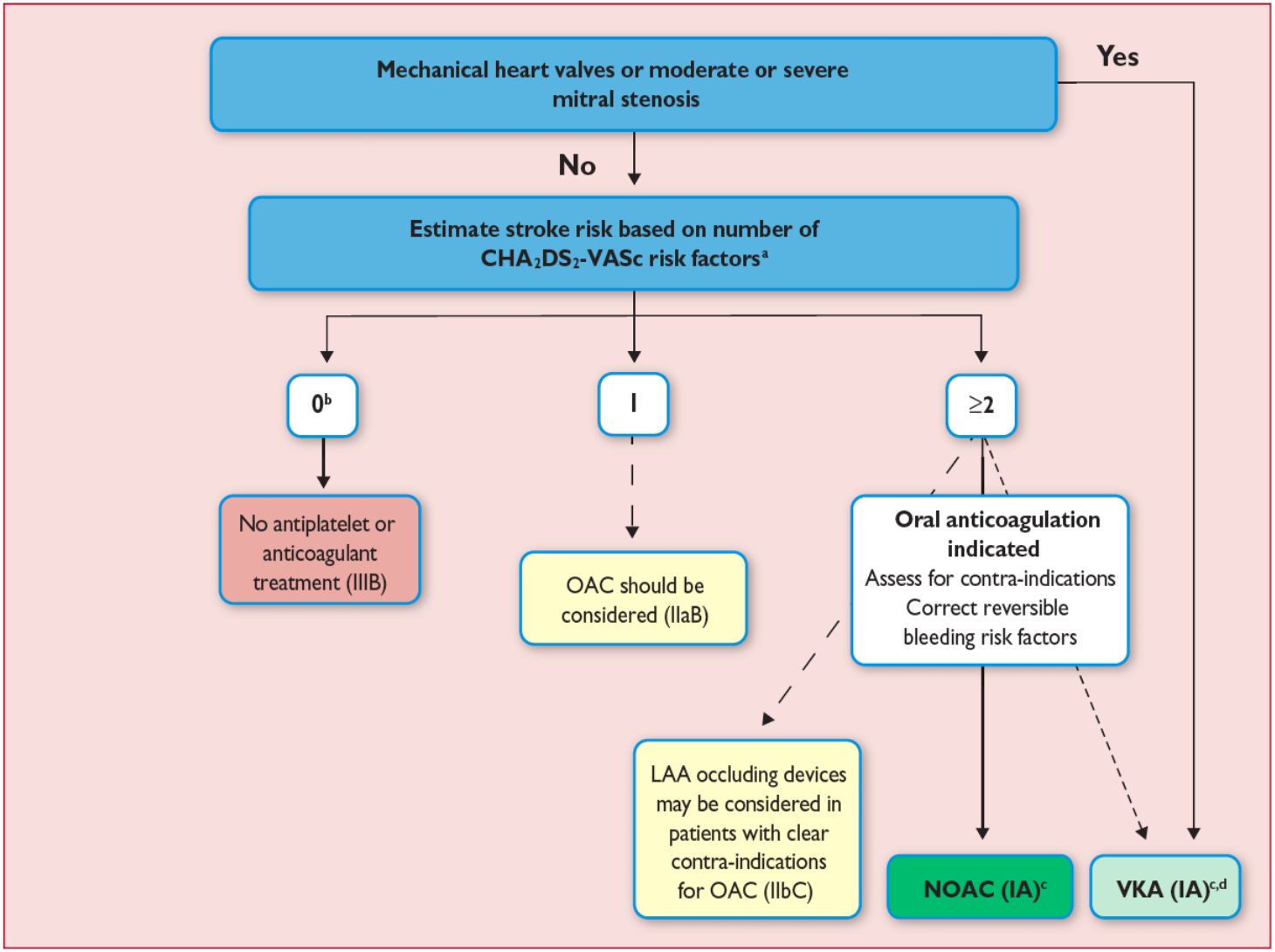
Case 1

- 73 year old female
- Paroxysmal AF diagnosed 3 months ago
- Mild carotid plaques
- Aspirin 100 mg OD
- CrCl 65 ml/min
- CHA_2DS_2-VASc = 2, HAS-BLED = 2 (1)

Case 1

- 73 year old female
- Paroxysmal AF diagnosed 3 months ago
- Mild carotid plaques
- Arterial hypertension, BP 165/90 mmHg
- Aspirin 100 mg OD
- CrCl 65 ml/min
- CHA_2DS_2-VASc = 3, HAS-BLED = 3 (2)

ESC Guidelines on Atrial Fibrillation 2016



AF = atrial fibrillation; LAA = left atrial appendage; NOAC = non-vitamin K antagonist oral anticoagulant; OAC = oral anticoagulation; VKA = vitamin K antagonist.
[a]Congestive heart failure, Hypertension, Age ≥75 years (2 points), Diabetes, prior Sstroke/TIA/embolus (2 points), Vascular disease, age 65–74 years, female Sex.
[b]Includes women without other stroke risk factors.
[c]IIaB for women with only one additional stroke risk factor.
[d]IB for patients with mechanical heart valves or mitral stenosis.

Kirchhof et al., Eur Heart J. 2016;37:2893-2962

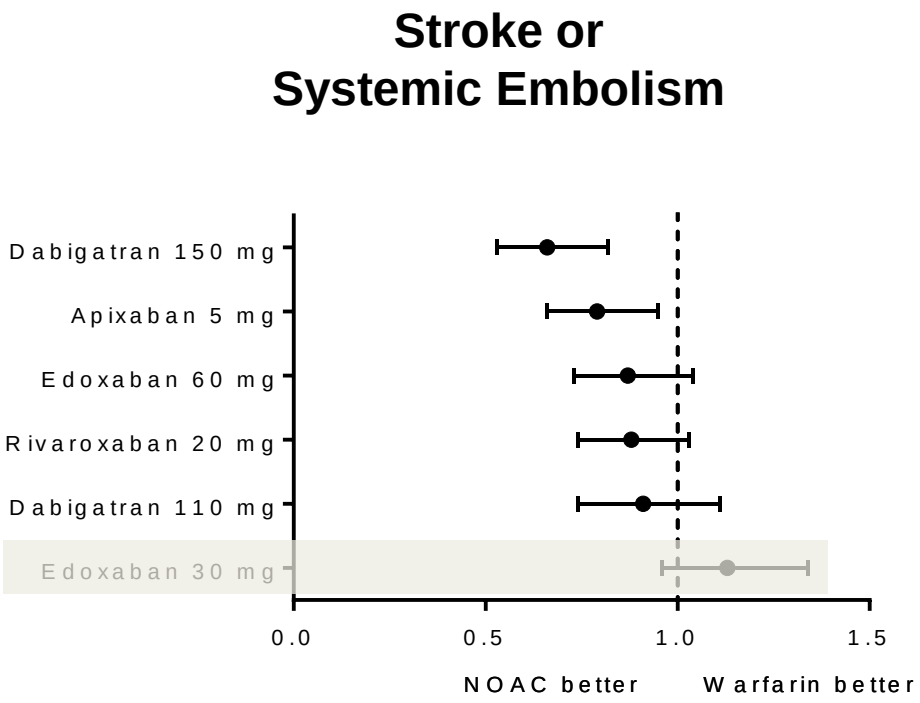
ESC Guidelines on Atrial Fibrillation 2016

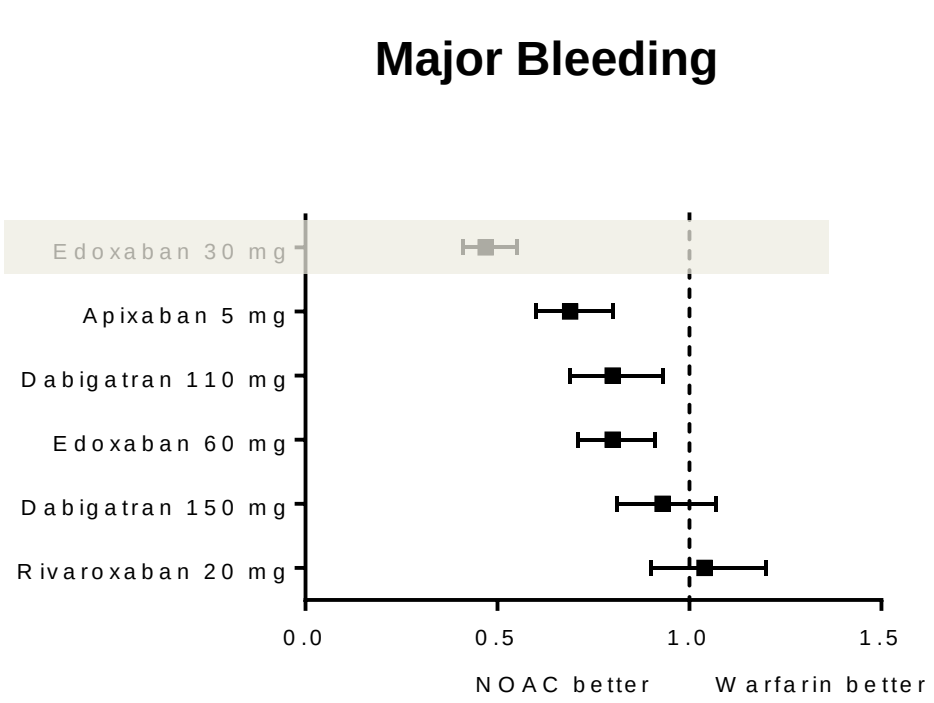
Recommendations for stroke prevention in patients with atrial fibrillation

Oral anticoagulation therapy to prevent thromboembolism is recommended for all male AF patients with a CHA_2DS_2-VASc score of 2 or more.	I	A
Oral anticoagulation therapy to prevent thromboembolism is recommended in all female AF patients with a CHA_2DS_2-VASc score of 3 or more.	I	A
CHA_2DS_2-VASc score of 1, considering individual characteristics and patient preferences.	IIa	B
Oral anticoagulation therapy to prevent thromboembolism should be considered in female AF patients with a CHA_2DS_2-VASc score of 2, considering individual characteristics and patient preferences.	IIa	B
Vitamin K antagonist therapy (INR 2.0–3.0 or higher) is recommended for stroke prevention in AF patients with moderate-to-severe mitral stenosis or mechanical heart valves.	I	B
When oral anticoagulation is initiated in a patient with AF who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a Vitamin K antagonist.	I	A
When patients are treated with a vitamin K antagonist, time in therapeutic range (TTR) should be kept as high as possible and closely monitored.	I	A
AF patients already on treatment with a vitamin K antagonist may be considered for NOAC treatment if TTR is not well controlled despite good adherence, or if patient preference without contra-indications to NOAC (e.g. prosthetic valve).	IIb	A
recommended for stroke prevention.	(harm)	
Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.	III (harm)	A
NOACs (apixaban, dabigatran, edoxaban, and rivaroxaban) are not recommended in patients with mechanical heart valves (Level of evidence B) or moderate-to-severe mitral stenosis (Level of evidence C).	III (harm)	B C

Kirchhof et al., Eur Heart J. 2016;37:2893-2962

Phase 3 RCTs comparing NOAC vs Warfarin in AF: Comparison of Effect on Stroke and Bleeding

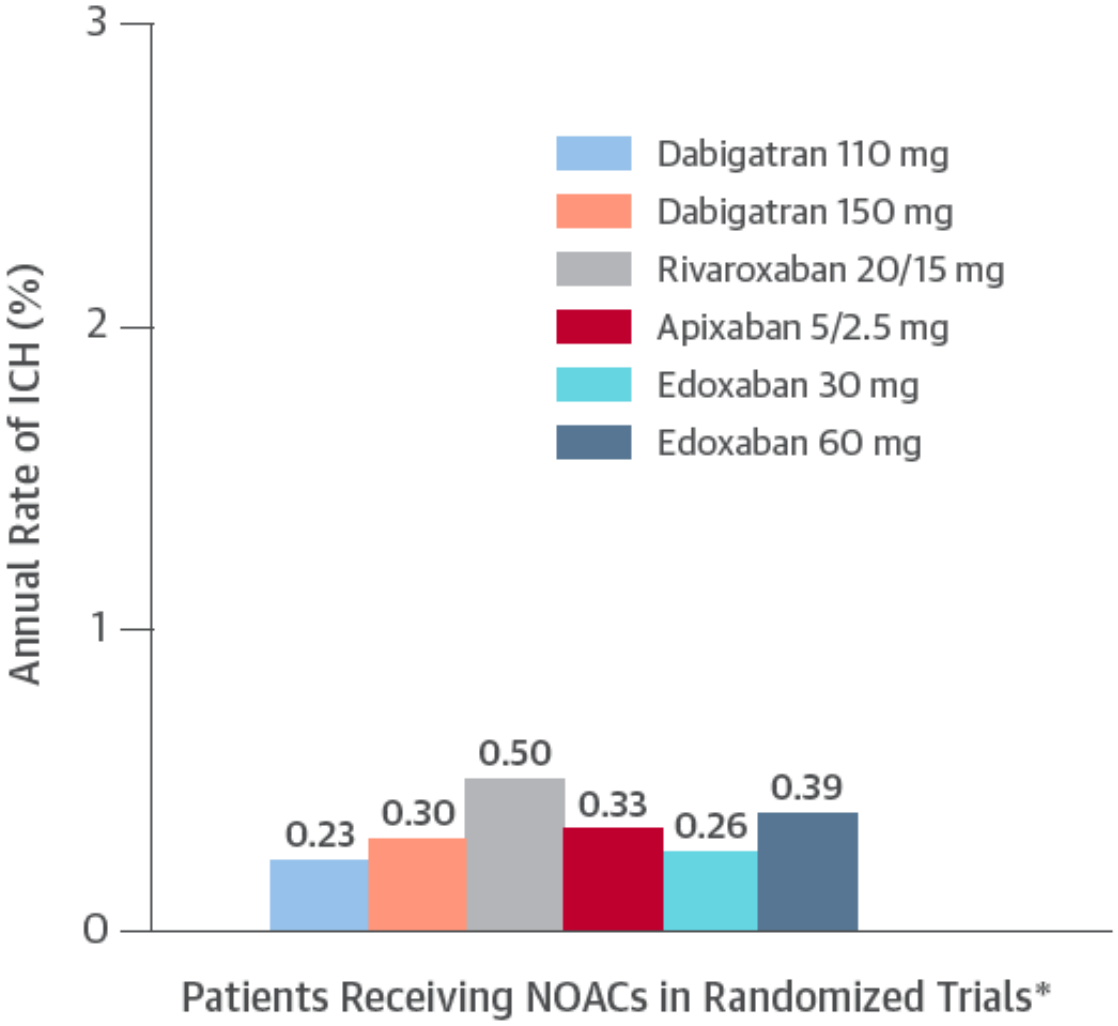




No head to head comparisons

Modified from Schulman, Thromb Haemost. 2014;111:575-82

Risk of Intracranial Bleeding in NOAC RCTs in Patients with Atrial Fibrillation



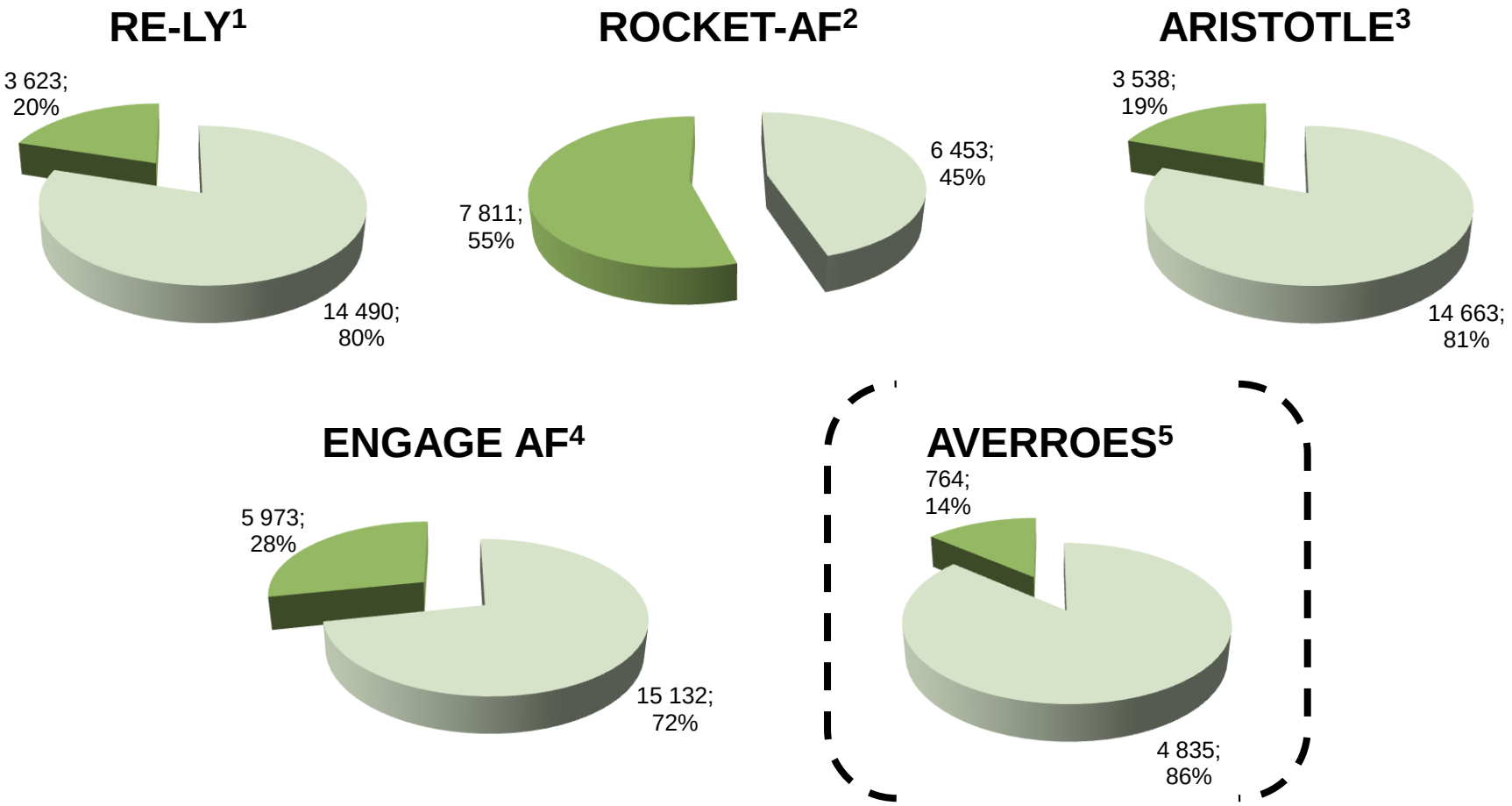
No head to head comparisons

Chao et al., J Am Coll Cardiol 2015;65:635–42

Case 2

- 73 year old female
- S/P mild ischemic stroke 2 weeks ago
- Diagnosis of paroxysmal AF at follow-up visit (3 day Holter ECG)
- Arterial hypertension, well-controlled
- Stable coronary artery disease with S/P stenting 2 years ago
- Aspirin 100 mg OD
- CrCl 65 ml/min
- CHA_2DS_2-VASc = 6, HAS-BLED = 3 (2)

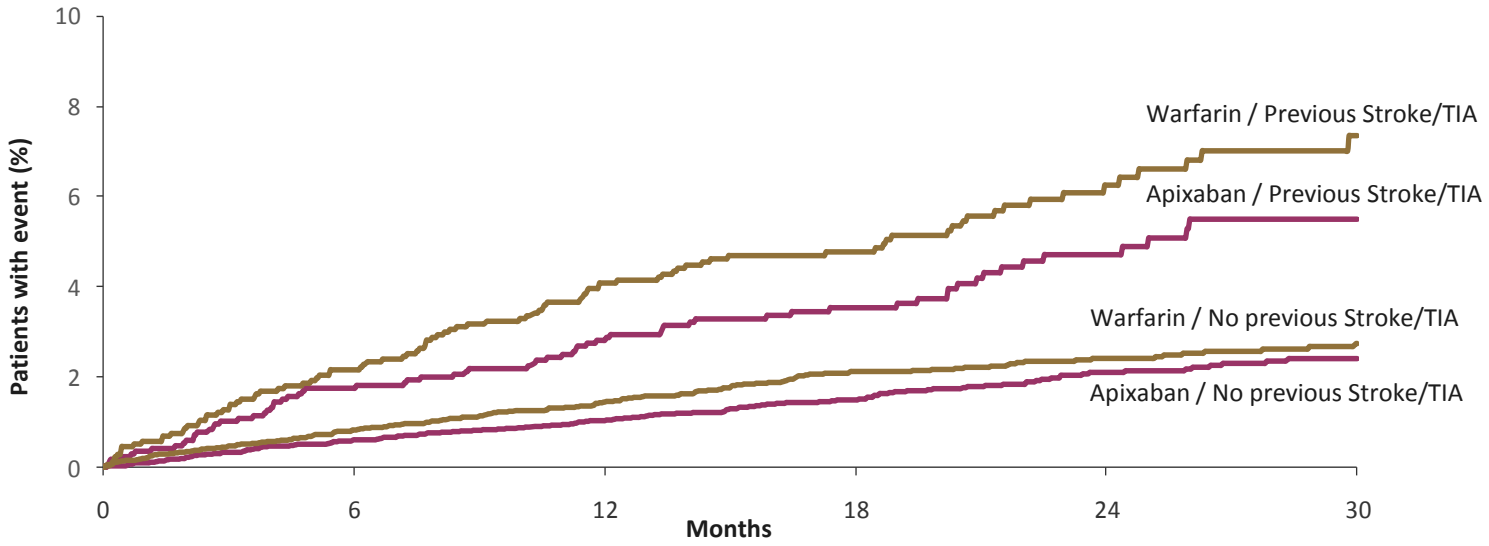
Representation of patients with previous stroke in the Phase 3 RCTs comparing NOAC vs Warfarin in AF



1. Connolly et al. N Engl J Med 2011;364:806-17 ; 2. Patel et al. New Engl J Med 2011;365:883-91;
3 . Granger et al. New Engl J Med 2011;365:981-92; 4. Giugliano et al. N Engl J Med 2013;369:2093-104;
5. Connolly et al. N Engl J Med 2011;364:806-17;

ARISTOTLE: Subgroup analysis of patients with or without previous stroke

Stroke or Systemic Embolism



Treatment	Previous stroke/TIA	Number patients (n)					
Apixaban	Yes	1694	1604	1547	1066	560	263
Warfarin	Yes	1742	1643	1564	1092	554	263
Apixaban	No	7426	7122	6893	4985	2904	1491
Warfarin	No	7339	6977	6737	4880	2851	1505

No significant interactions for stroke or bleeding endpoints including ICH

Easton et al., Lancet Neurol 2012;11:503–11

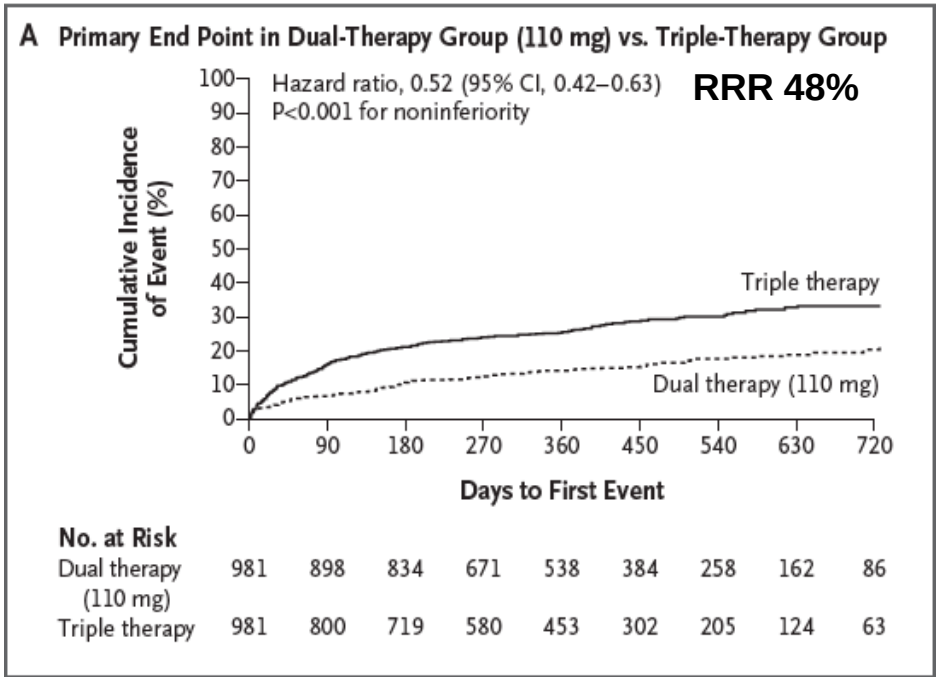
Case 3

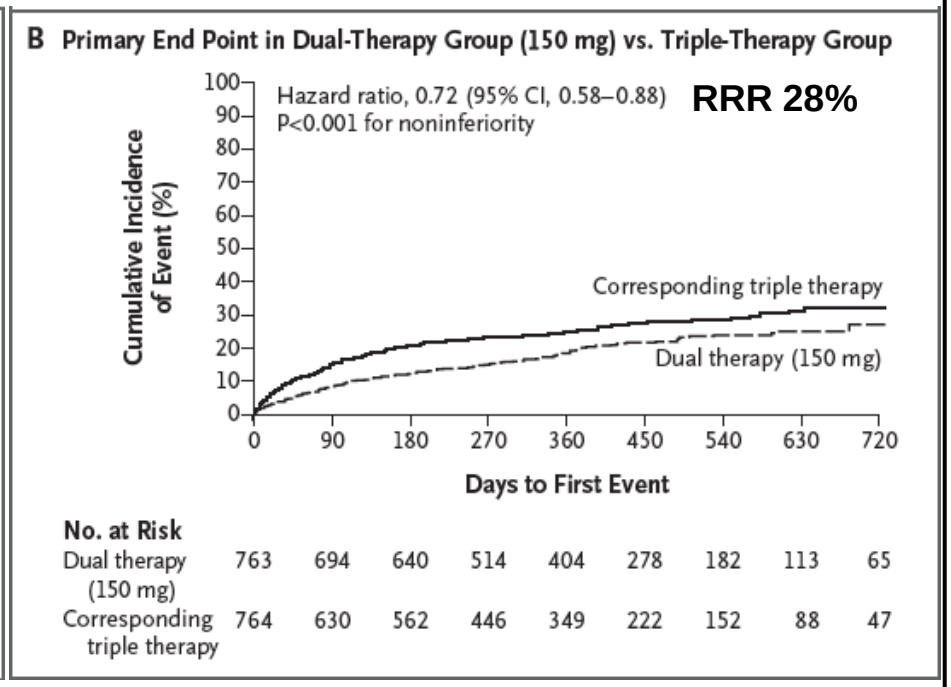
- 73 year old female
- S/P mild ischemic stroke 3 months ago
- Paroxysmal AF, currently normal sinus rhythm
- Arterial hypertension, well-controlled
- Now acute coronary syndrome (NSTEMI), PCI of LAD with 2 DES
- Dabigatran 150 mg BID
- CrCl 65 ml/min
- CHA_2DS_2-VASc = 6, HAS-BLED = 3

Anticoagulation and Platelet Inhibition In Patients with AF and PCI: RE-DUAL PCI

N=2.725

Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event



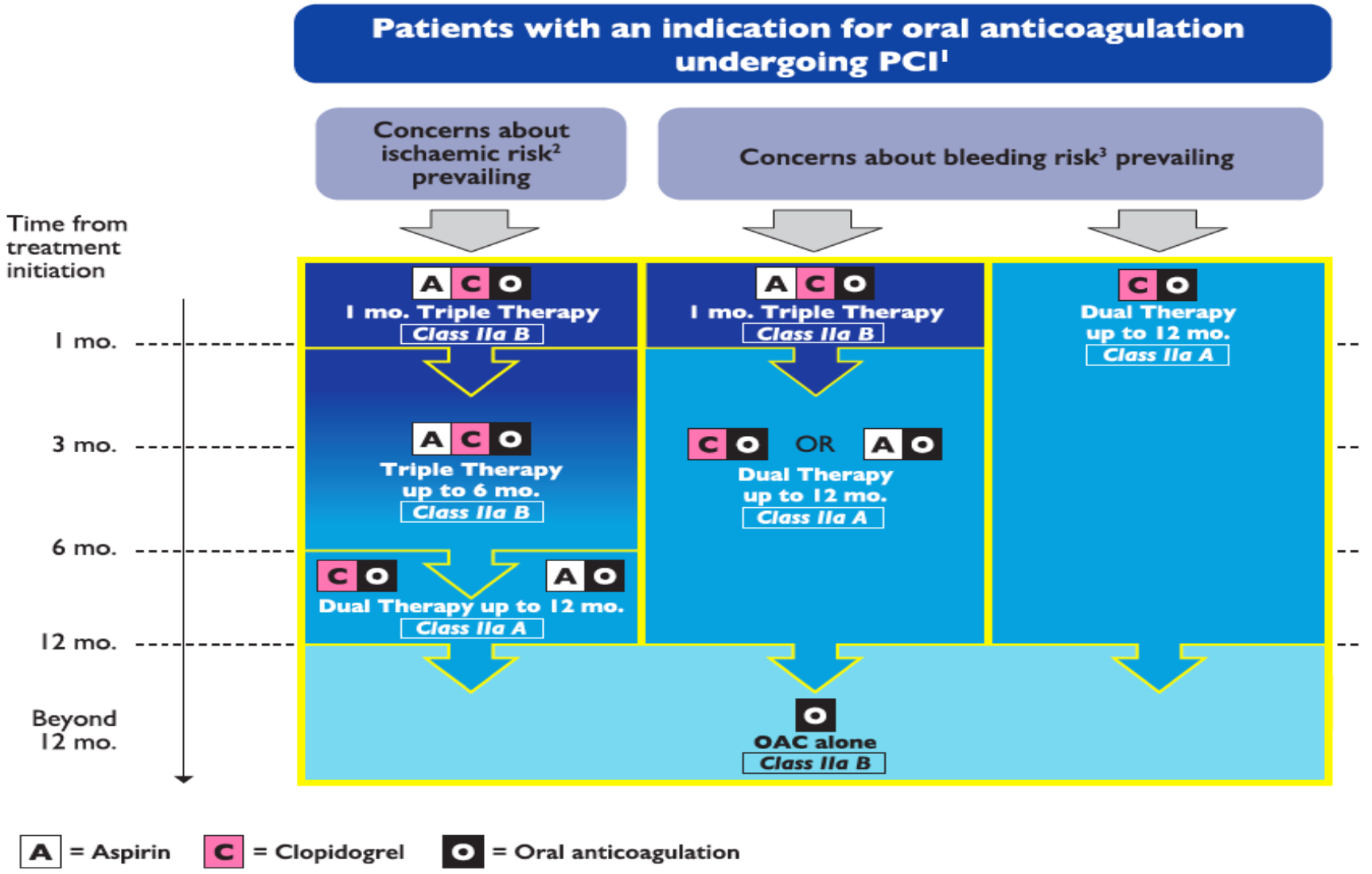


Major bleeding: 5.0% vs 9.2%, HR 0.52* / 5.6% vs 8.4%, HR 0.64*

No significant difference for combined endpoint: death, MI, stroke, SE, unplanned revasc.

Cannon et al., N Engl J Med. 2017;377:1513-1524

ESC Update on DAPT in CAD 2017: AF and PCI



1: Periprocedural administration of aspirin and clopidogrel during PCI is recommended irrespective of the treatment strategy.
2: High ischaemic risk is considered as an acute clinical presentation or anatomical/procedural features which might increase the risk for myocardial infarction.
3: Bleeding risk can be estimated by HAS-BLED or ABC score.

Valgimigli et al., Eur Heart J. 2017; Epub ahead of print

Thank you for your attention!

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