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Atrial Fibrillation and ACS/PCI: Chains of RCTs up to AUGUSTUS - Enough Evidence or More?

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ATRIAL FIBRILLATION AND PCI

Stent thrombosis and coronary events

↓

High shear stress platelet-rich thrombi

↓

Antiplatelet therapy

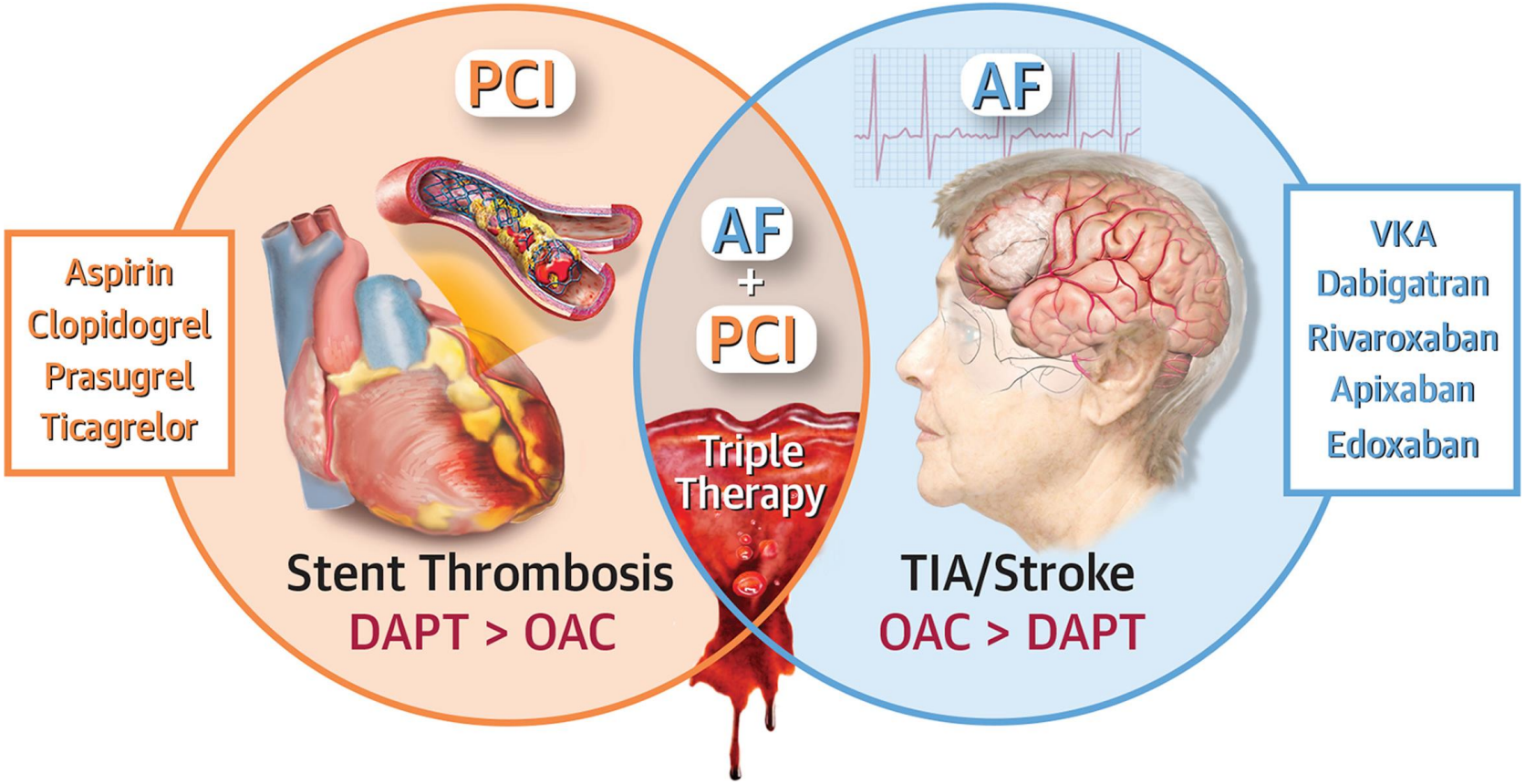
Stroke, TIA and systemic embolism

↓

Low shear stress, less platelet-dependent thrombi

↓

Anticoagulation therapy



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Capodanno D, Angiolillo DJ. JACC Cardiovasc Interv. 2017;10:1086-1088

BLEEDING AFTER INITIATION OF ANTITHROMBOTIC DRUGS

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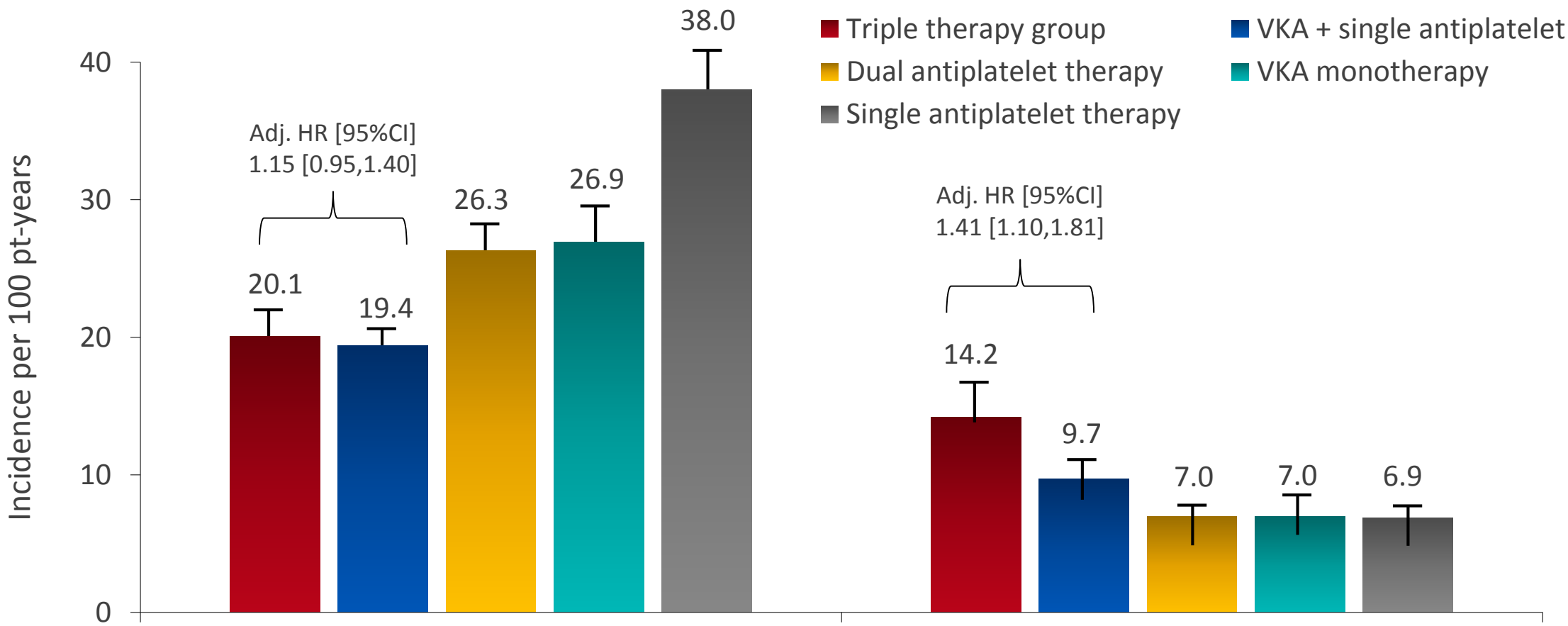

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Lamberts M et al. Circulation. 2012;126:1185-1193

TRIALS OF VKA: WOEST AND ISAR-TRIPLE

WOEST

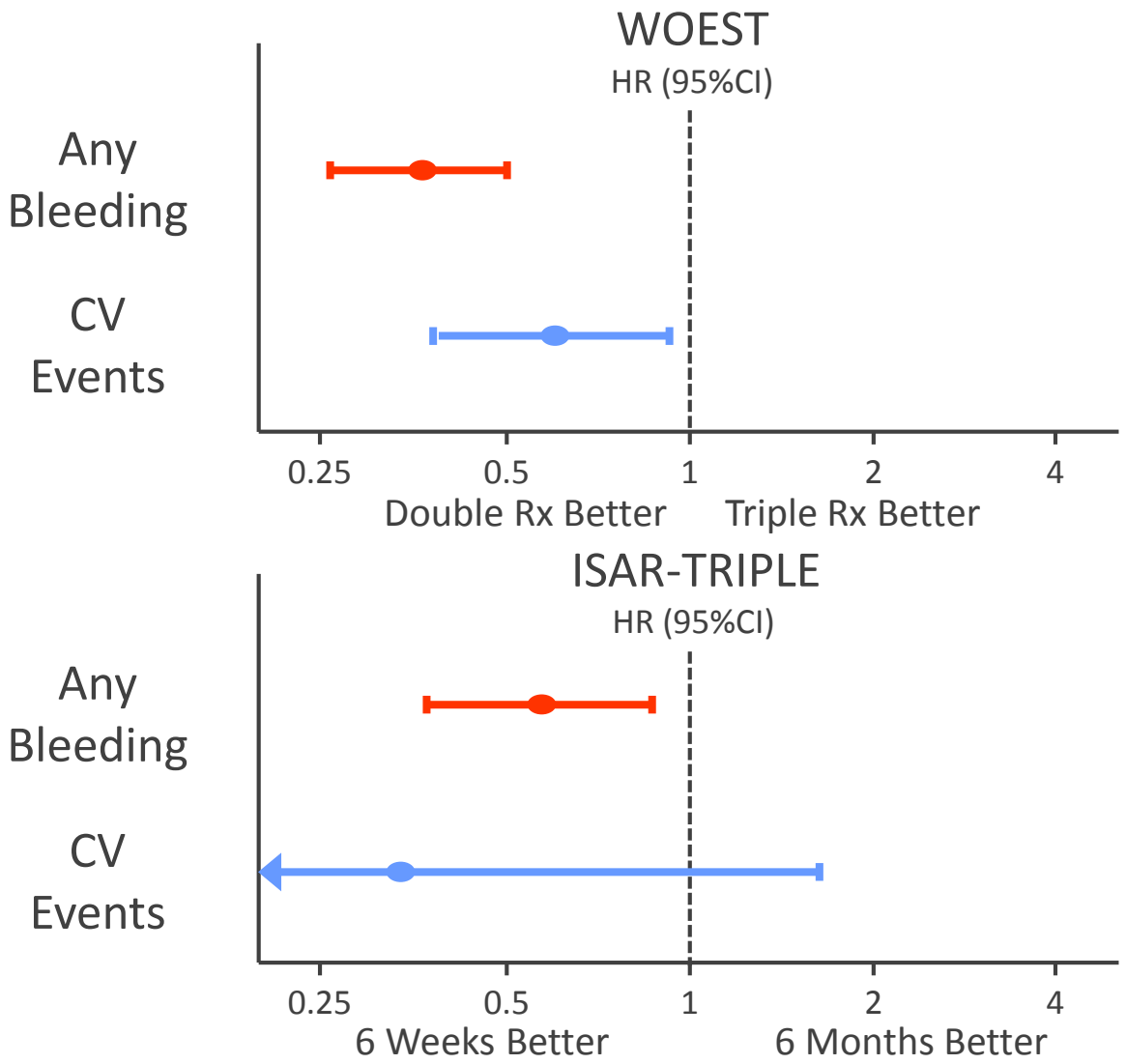
573 low-risk pts receiving warfarin undergoing PCI randomized to clopidogrel alone (DAT) vs. clopidogrel plus aspirin (TAT)

1-year primary endpoint

ISAR-TRIPLE

614 low-risk pts receiving warfarin and aspirin undergoing PCI randomized to 6 weeks vs. 6 months of clopidogrel

9-month primary endpoint



Bhatt DL. J Am Coll Cardiol. 2015;65:1630-2

RIVAROXABAN FOR AF-PCI

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PIONEER AF

2,124 AF pts with PCI

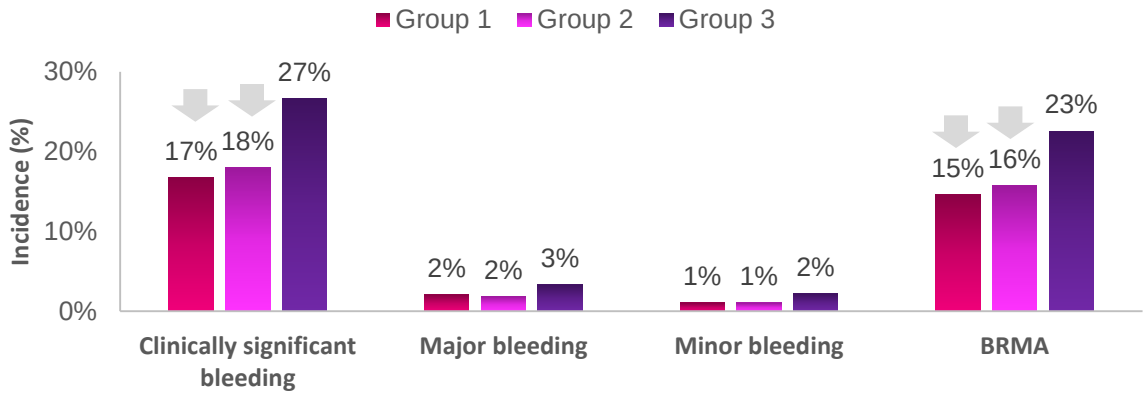
1:1:1

Group 1	Group 2	Group 3
Riva 15 mg 12 months	**Riva 2.5 mg** 1, 6 or 12 months, then Riva 15 mg	**VKA** 12 months
P2Y$_{12}$ inhib 12 months	**P2Y$_{12}$ inhib** 1, 6 or 12 months	**P2Y$_{12}$ inhib** 1, 6 or 12 months
	Aspirin 12 months	**Aspirin** 12 months

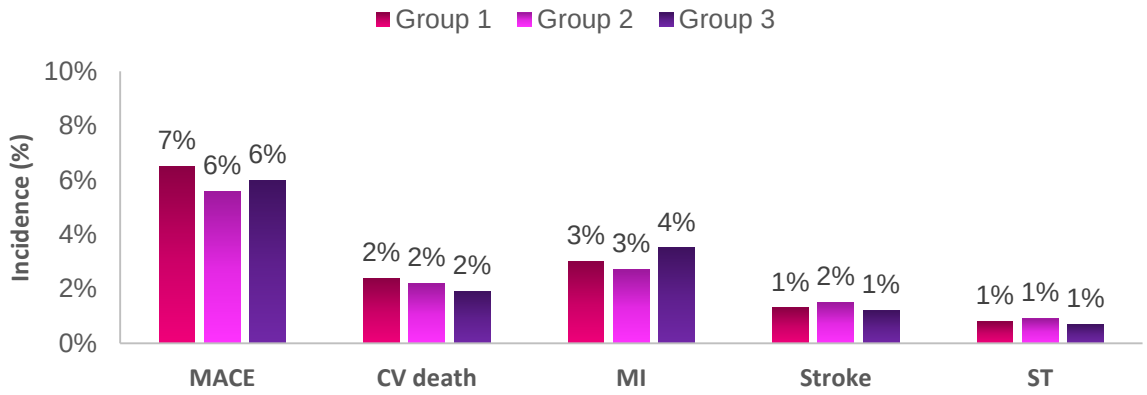
Primary endpoint

Clinically significant bleeding at 12 months

SAFETY ENDPOINTS



EFFICACY ENDPOINTS



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Gibson CM, et al. N Engl J Med. 2016;375:2423-2434

DABIGATRAN FOR AF-PCI

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RE-DUAL PCI

2,725 AF pts with PCI

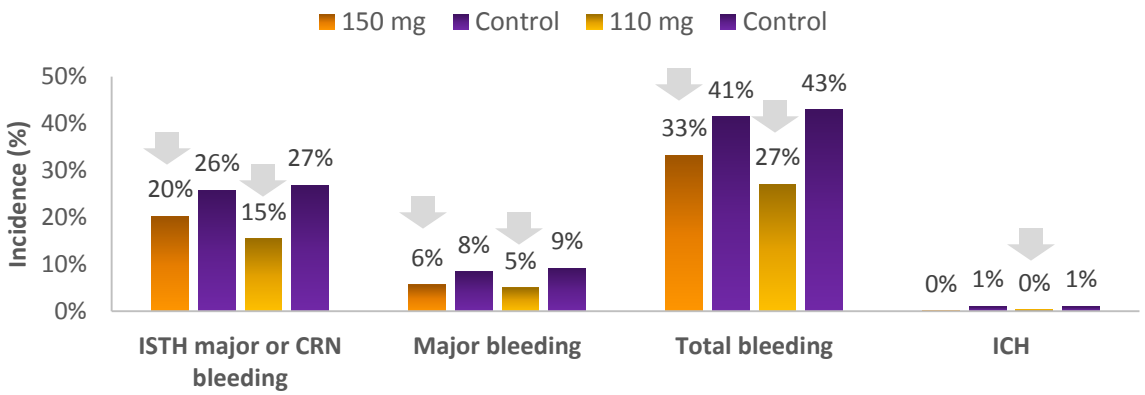
1:1:1

Group 1	Group 2	Group 3
Dabi 150 mg 12 months	**Dabi 110 mg** 12 months	**VKA** 12 months
P2Y$_{12}$ inhib 12 months	**P2Y$_{12}$ inhib** 12 months	**P2Y$_{12}$ inhib** 12 months
		Aspirin 1 to 3 months

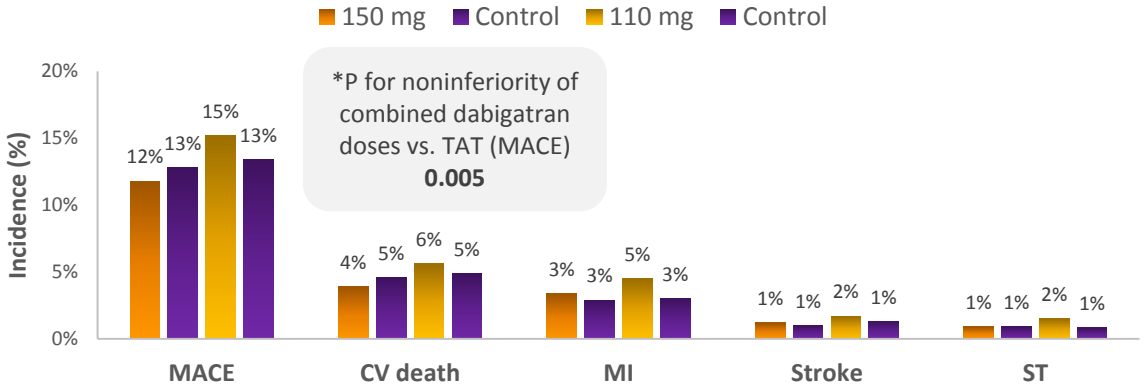
Primary endpoint

Major or CRNM bleeding at 12 months

SAFETY ENDPOINTS



EFFICACY ENDPOINT



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

META-ANALYSIS OF DOUBLE VS. TRIPLE THERAPY

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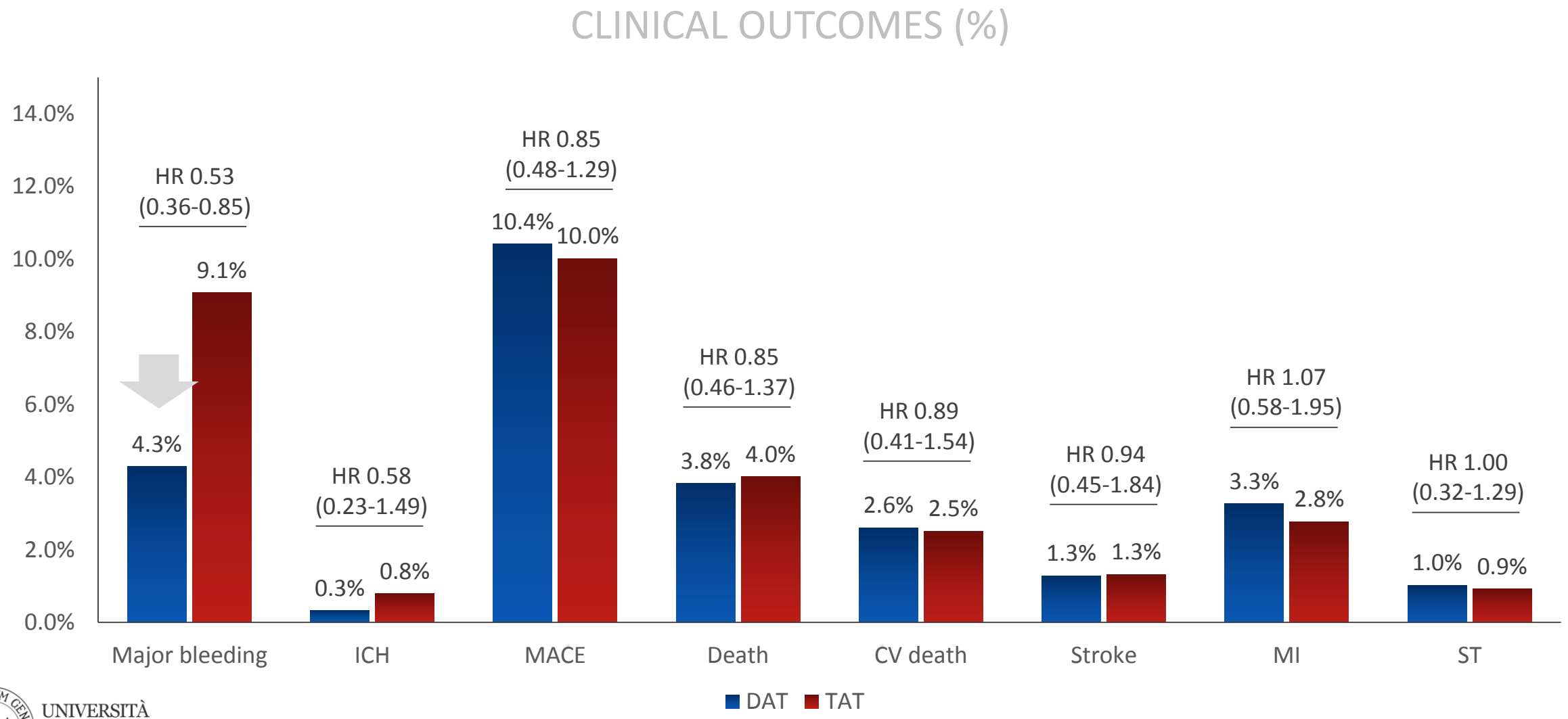

Golwala HB, et al. Eur Heart J. 2018;39:1726-1735

ISCHEMIC EVENTS: IS THE EVIDENCE CONCLUSIVE?

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Study parameters	
Incidence in the TAT group*	10.0%
Meaningful reduction with DAT	20%
Alpha	0.05
Beta	0.2
Power	0.8
Sample size required**	**6,426**

*As reported in the Golwala HB, et al. study-level meta-analysis; **ClinCalc.com

WOEST
N=573

PIONEER-AF PCI
N=2,124

RE-DUAL PCI
N=2,725

Meta-analysis
N=5,317

APIXABAN FOR AF-PCI NEW!

AUGUSTUS

4,614 AF pts with ACS or PCI

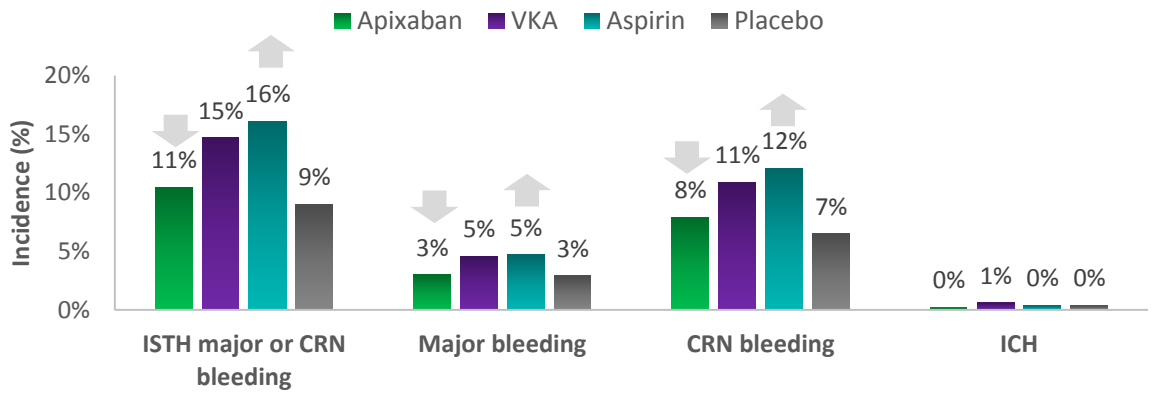
at a mean of 1 week

Apixaban 5 mg 6 months	**VKA** 6 months
P2Y$_{12}$ inhibitor 6 months	**P2Y$_{12}$ inhibitor** 6 months
Aspirin 6 months	**Placebo** 6 months
Aspirin 6 months	**Placebo** 6 months

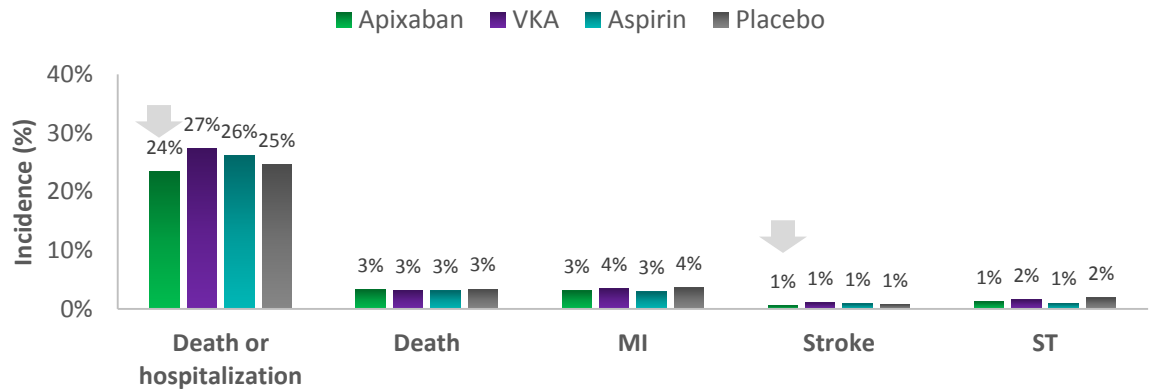
Primary endpoint

Major or CRNM bleeding at 6 months

SAFETY ENDPOINTS



EFFICACY ENDPOINTS



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Lopes RD, et al. N Engl J Med. 2019; Epub ahead of print

APIXABAN FOR AF-PCI NEW!

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AUGUSTUS

4,614 AF pts with ACS or PCI

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Apixaban 5 mg 6 months	**VKA** 6 months
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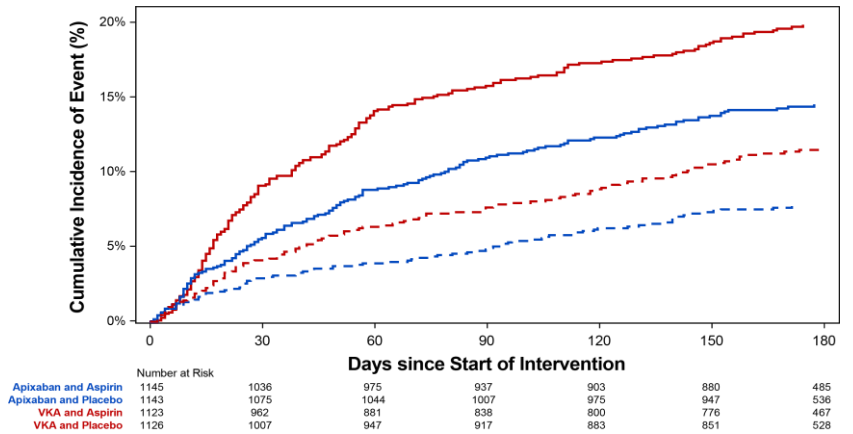
Aspirin 6 months	**Placebo** 6 months

Primary endpoint

Major or CRNM bleeding at 6 months

ISTH MAJOR OR CRNM BLEEDING



VKA + Aspirin (18.7%)

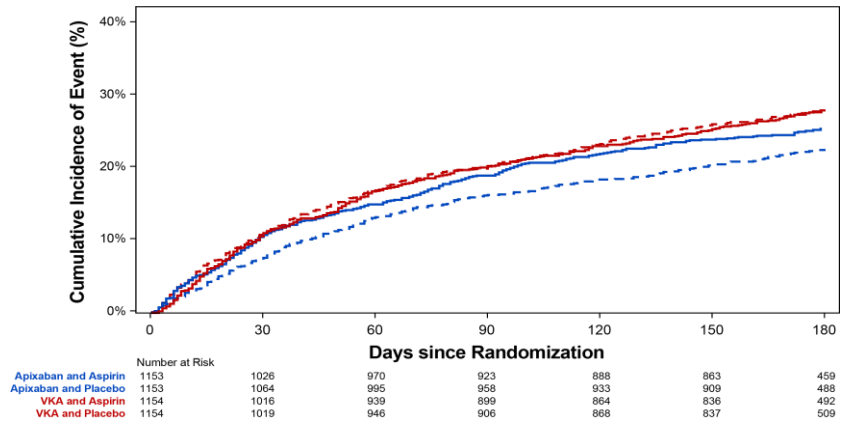
Apixaban + Aspirin (13.8%)

VKA + Placebo (10.9%)

Apixaban + Placebo (7.3%)

Apixaban + Placebo vs. VKA + Aspirin: 11.4% absolute risk reduction (**NNT=9**)

DEATH OR REHOSPITALIZATION



VKA + Aspirin (27.5%)
VKA + Placebo (27.3%)
Apixaban + Aspirin (24.9%)
Apixaban + Placebo (22.0%)

Apixaban + Placebo vs. VKA + Aspirin: 5.5% absolute risk reduction (**NNT=18**)

Lopes RD, et al. N Engl J Med. 2019; Epub ahead of print

EDOXABAN FOR AF-PCI

ENTRUST AF PCI

1,500 AF pts with PCI

4h-5d after PCI

Edoxaban 60 mg 12 months	**VKA** 12 months
$P2Y_{12}$ inhibitor 12 months	**$P2Y_{12}$ inhibitor** 12 months
	Aspirin 1 to 12 months

Primary endpoint

Major or CRNM bleeding at 12 months

The first patient in The ENTRUST-AF PCI trial was enrolled in Hospital La Paz, Madrid, Spain, on February 24, 2017. End of enrollment is projected for March 2018.

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Vranckx P, et al. Am Heart J. 2018 Feb;196:105-112

CHOICE OF ORAL ANTICOAGULANT

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Recommendation	COR	LOE
In patients with non-valvular AF requiring anticoagulation and antiplatelet treatment, a NOAC should be preferred over VKAs.[1,2,3]	IIa	A

[1] Dans AL, et al. Concomitant use of antiplatelet therapy with dabigatran or warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial. Circulation 2013;127:634–640.

[2] Kopin D, et al. Percutaneous coronary intervention and antiplatelet therapy in patients with atrial fibrillation receiving apixaban or warfarin: Insights from the ARISTOTLE trial. Am Heart J 2018;197:133–141.

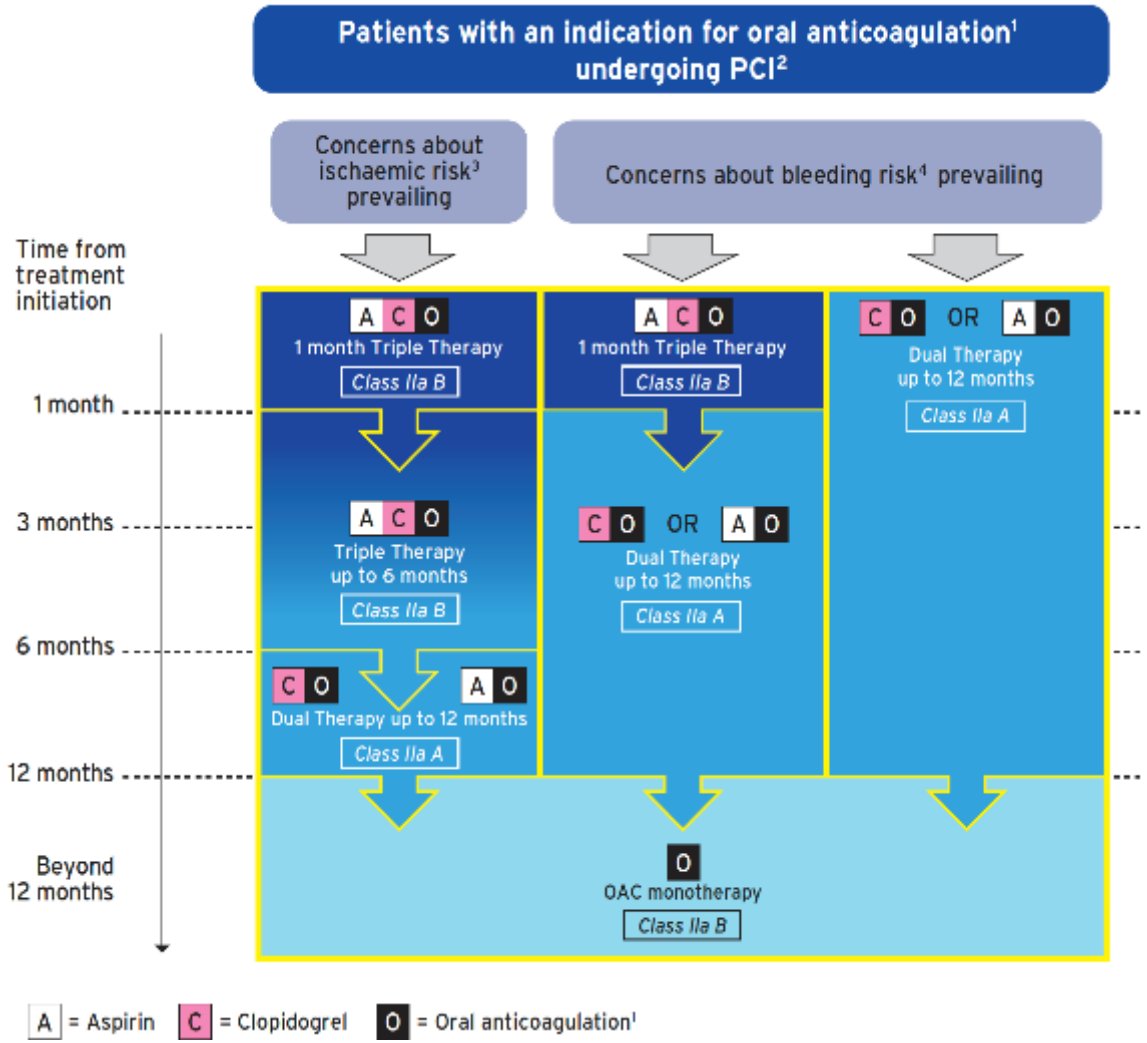
[3] Ruff CT, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: A meta-analysis of randomised trials. Lancet 2014;383:955–962.

Recommendation	COR	LOE
When a NOAC is used in combination with aspirin and/or clopidogrel, the lowest approved dose effective for stroke prevention tested in AF trials should be considered.	IIa	C
When rivaroxaban is used in combination with aspirin and/or clopidogrel, rivaroxaban 15 mg q.d. may be used instead of rivaroxaban 20 mg q.d	IIb	B
When dabigatran is used in combination with aspirin or clopidogrel, a dose of 150 mg b.i.d. may be preferred over a dose of 110 mg b.i.d.	IIb	B

Apixaban 5 mg b.i.d. or apixaban 2.5 mg b.i.d. if at least two of the following: age ≥80 years, body weight ≤60 kg, or serum creatinine level ≥1.5 mg/dL (133 mmol/ L); dabigatran 110 mg or 150 mg b.i.d.; and edoxaban 60 mg q.d. or edoxaban 30 mg q.d. if any of the following: creatinine clearance of 30–50 mL/min; body weight ≤60 kg; concomitant use of verapamil, quinidine, or dronedarone; and rivaroxaban 20 mg q.d. or rivaroxaban 15 mg q.d. if creatinine clearance 30–49 mL/min.

Neumann FJ, et al. Eur Heart J. 2019;40:87-165

POST-PROCEDURAL CONSIDERATIONS



Patient type #1

Ischemic risk

Prior ST on DAPT, stenting of the last remaining patent coronary artery, diffuse MVD (especially in diabetic patients), CKD (CrCl <60 mL/min), at least 3 stents implanted, at least 3 lesions treated, bifurcation with 2 stents implanted, total stent length >60 mm, treatment of a CTO, history of STEMI

→ **Bleeding risk**

Patient type #2

Bleeding risk

Short life expectancy, ongoing malignancy, poor expected adherence, poor mental status, end-stage renal failure, advanced age, prior major bleeding or prior hemorrhagic stroke, chronic alcohol abuse, anemia, clinically significant bleeding on dual antithrombotic therapy

→ **Ischemic risk**

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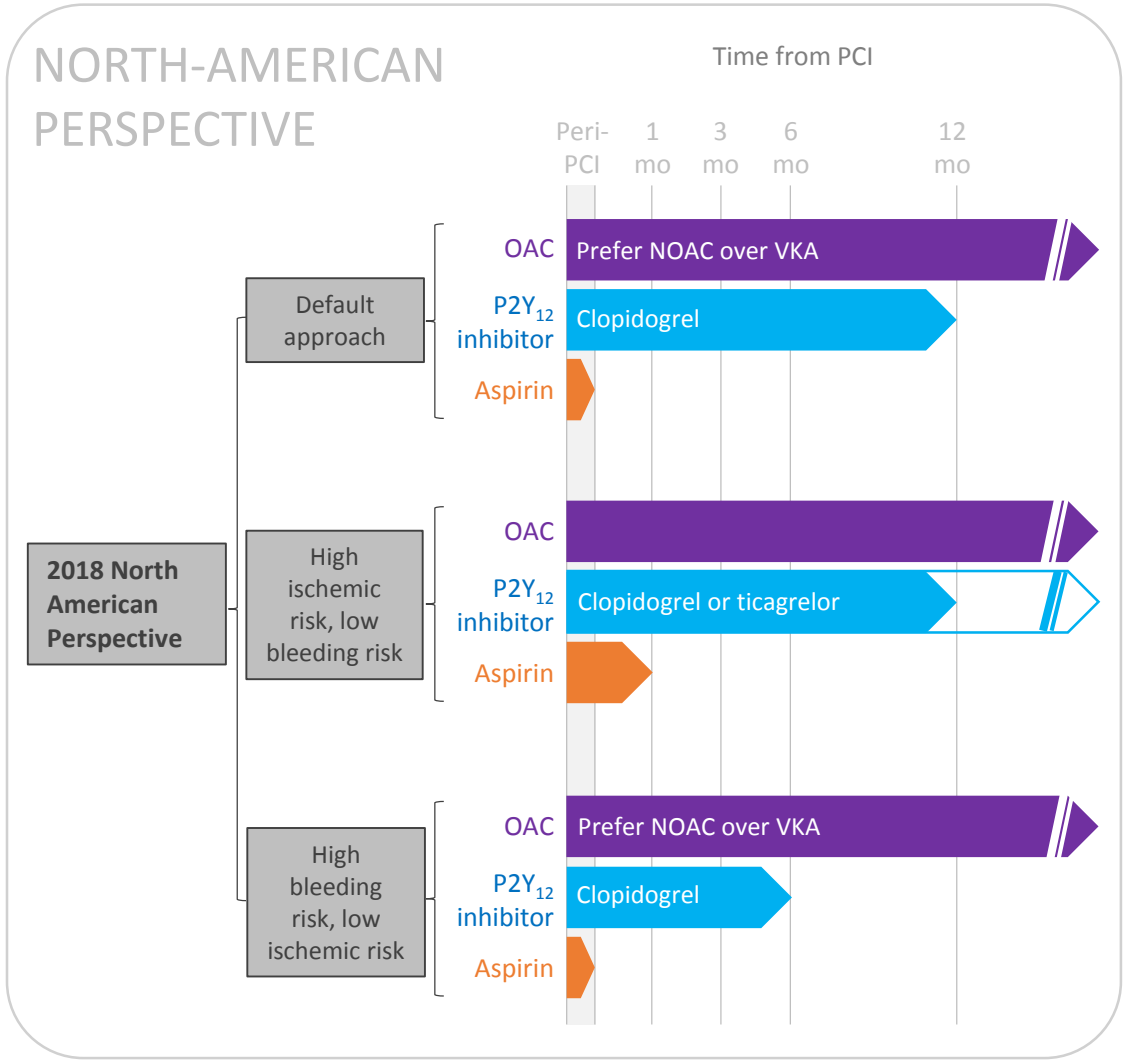
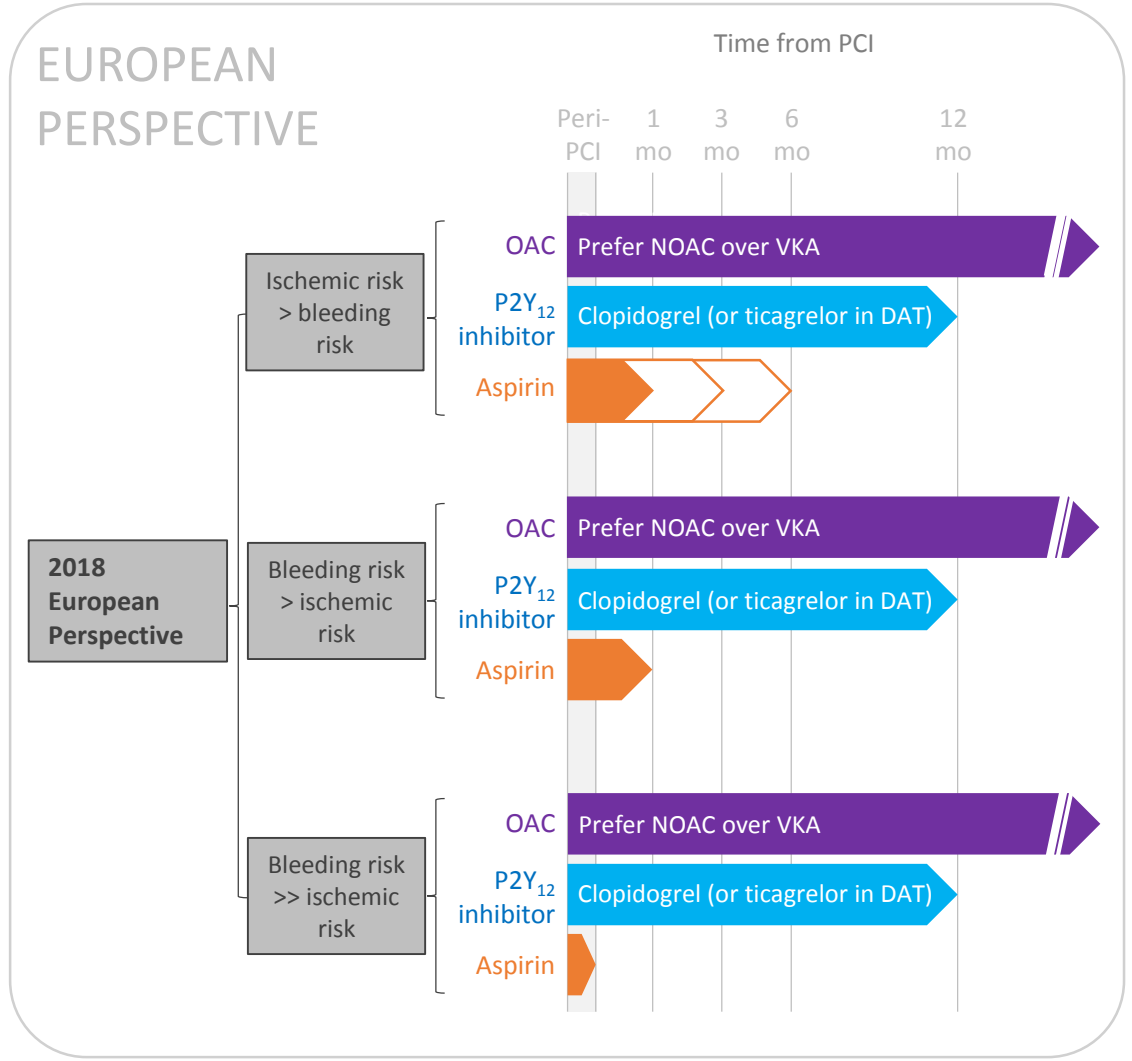
Neumann FJ, et al. Eur Heart J. 2019;40:87-165

TAT VS. DAT: NORTH-AMERICAN VS. EUROPEAN PERSPECTIVE





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Capodanno D, Angiolillo DJ, et al. Submitted

ANTITHROMBOTIC THERAPY AFTER 1 YEAR FROM PCI

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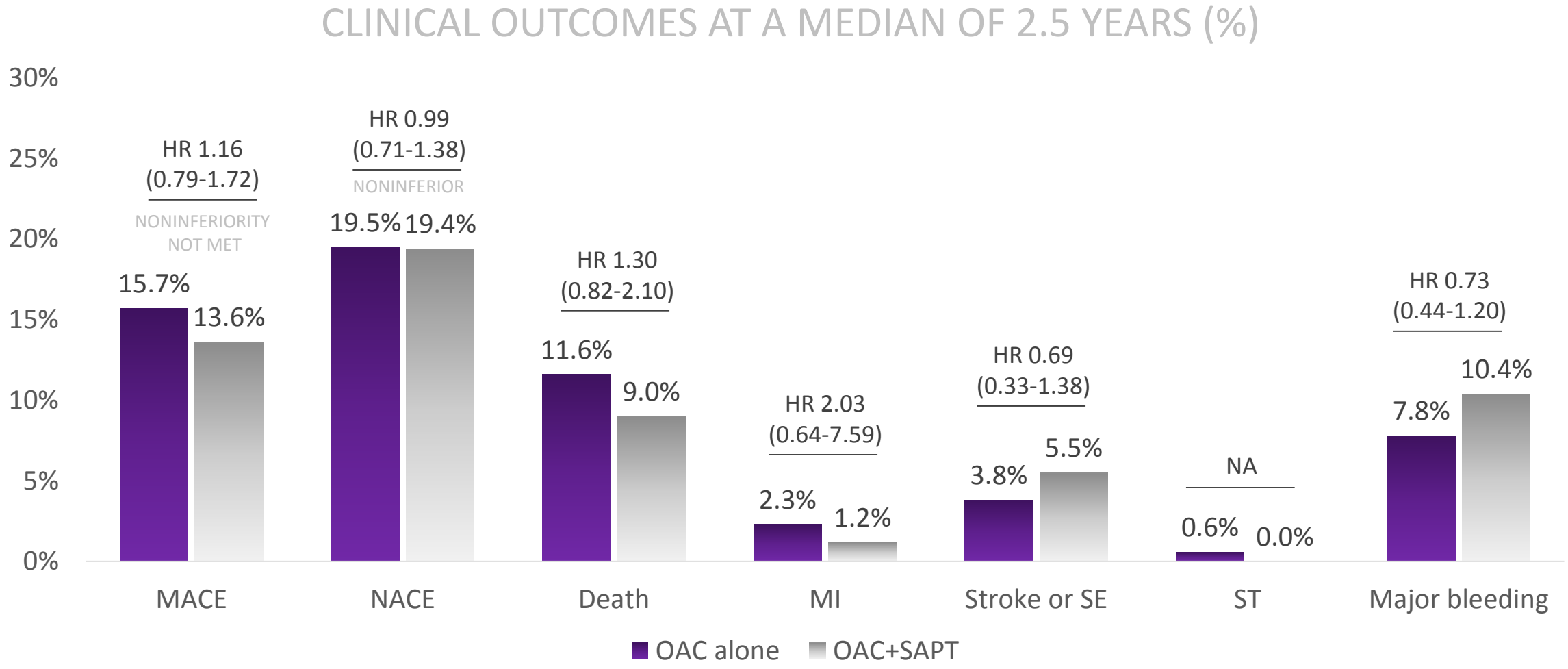

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Matsumura-Nakano Y, et al. Circulation. 2019;139:604-616

DOUBLE OR TRIPLE THERAPY?

- **The current paradigm for AF-PCI is that the association of OAC with DAPT (typically clopidogrel and aspirin) should be as short as possible.**
  - > A North American perspective suggests that TAT should be used in-hospital but soon de-escalated to DAT with OAC and clopidogrel for 6 to 12 months depending on the bleeding risk, followed by OAC alone in most of the cases.
  - > The European perspective suggests that TAT should be stopped at discharge, 1 month or 3 to 6 months depending on considerations surrounding the balance between the individual thrombotic and bleeding profile.
- **The results of the AUGUSTUS and ENTRUST trials will likely impact future recommendations and perhaps provide more synergism between North American and European experts who mostly diverge on duration of TAT.**

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