Trombocythämning och antikoagulation i initialskedet efter akut koronart syndrom och efter elektiv PCI

Vad säger riktlinjerna?

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Conflicts of Interest

AstraZeneca: Institutional research grants, lecture fees, Adv board
Bayer: lecture fees, Adv board
Boehringer Ingelheim: Adv board
Bristol Myers Squibb/Pfizer: Institutional research grants
GlaxoSmithKline: Institutional research grants
Coala Life: Adv board
Clinical Endpoint Committee member for GlaxoSmithKline, Bristol Myers Squibb, AstraZeneca, Merck and Roche

Introduktion

- Dubbel trombocythämning utgör en etablerad strategi vid akut koronart syndrom
- Ticagrelor (eller prasugrel) rekommenderas före clopidogrel
- Behandlin åna
  blödnings
- Balans mellan risk för blödning och risk för ischemisk händelse
- Drygt 20% av patienter med AKS har även förmaksflimmer och indikation för antikoagulantia och många får trippelbehandling
- Kunskapen kring trippelbehandling är fortfarande bristfällig

Akut koronart syndrom/ Stenttrombos

Ischemisk stroke

Dubbel trombocythämning

Oralt antikoagulantia

Allvarlig blödning

Figure 77. Trend in the use of P2Y12 receptor blockers at discharge in STEMI patients, < 80 years, 2011–2017.

About 90 % of patients today receive ticagrelor.

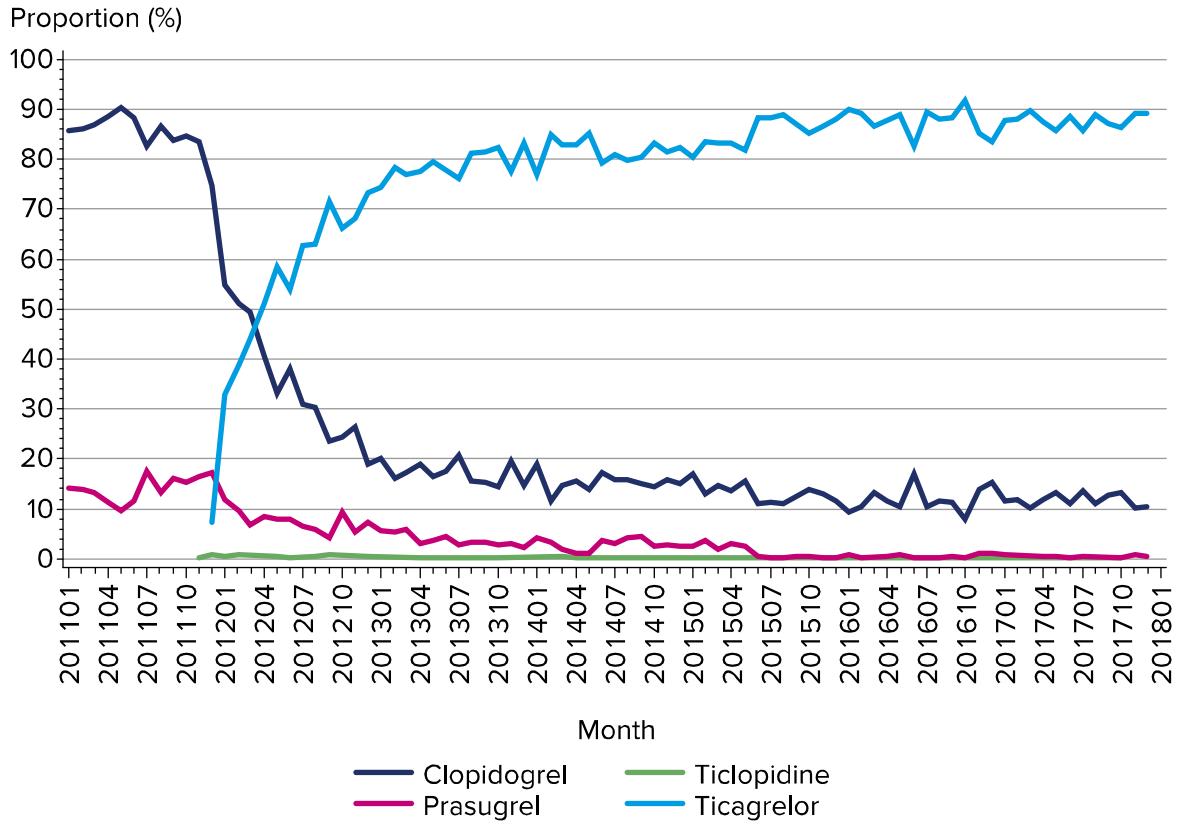
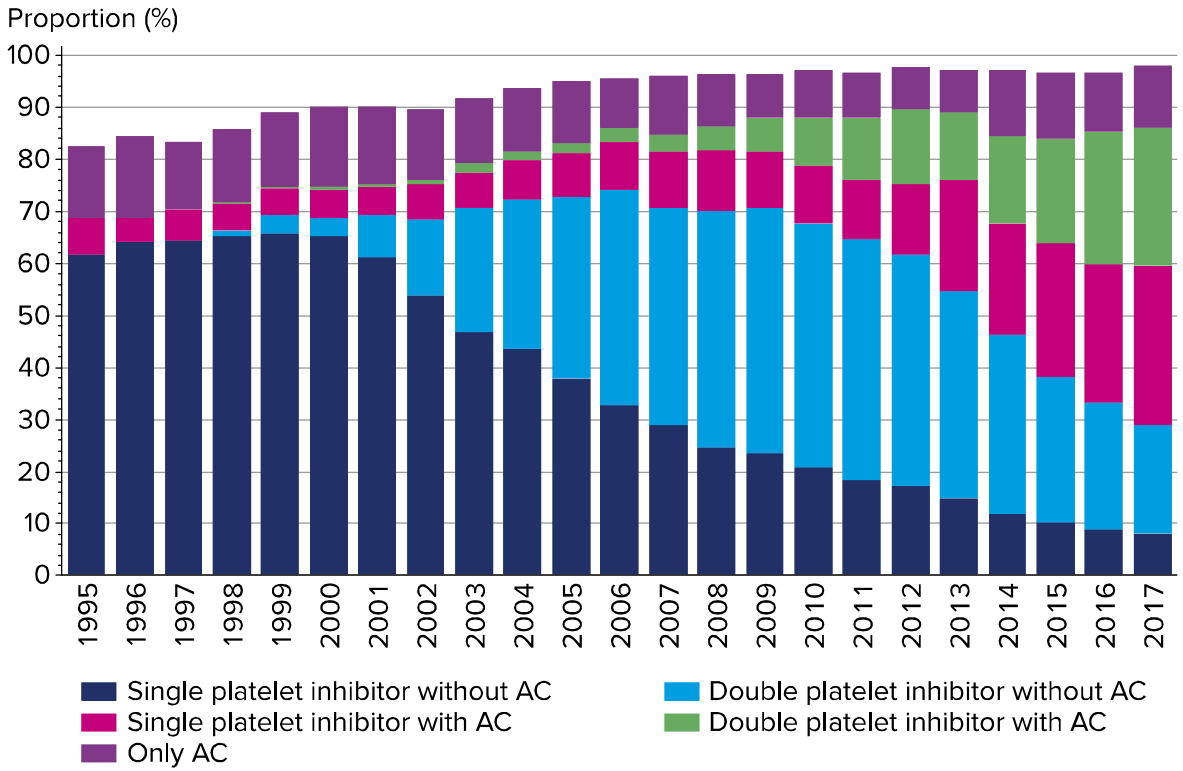
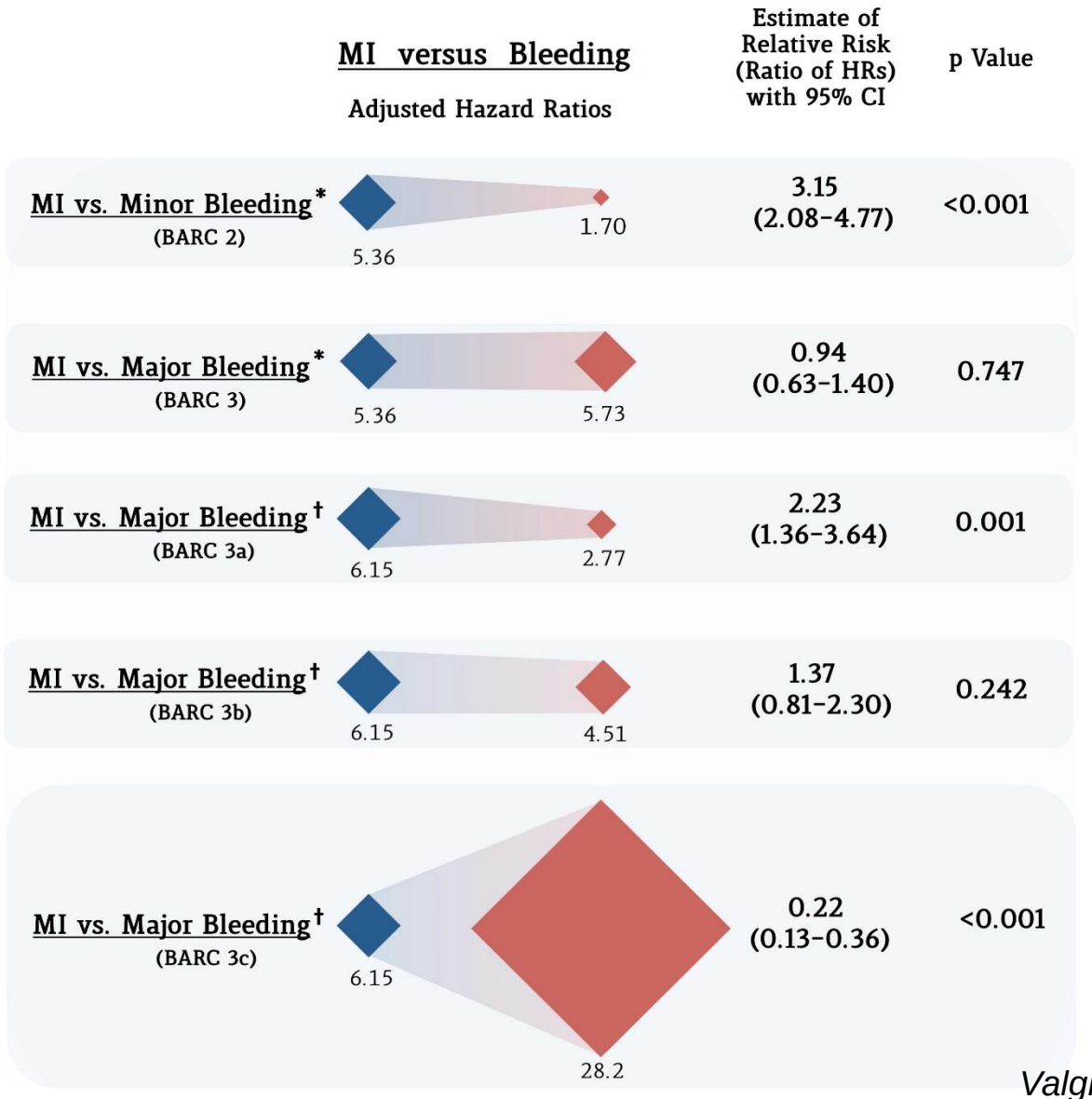


Figure 75. Trend of antithrombotic treatment at discharge in MI patients with AF, discharged alive, all ages, 1995–2017.

There has been a rapid improvement with more MI patients with AF receiving anticoagulation (AC) at discharge.



Differential impact on mortality of MI vs bleeding



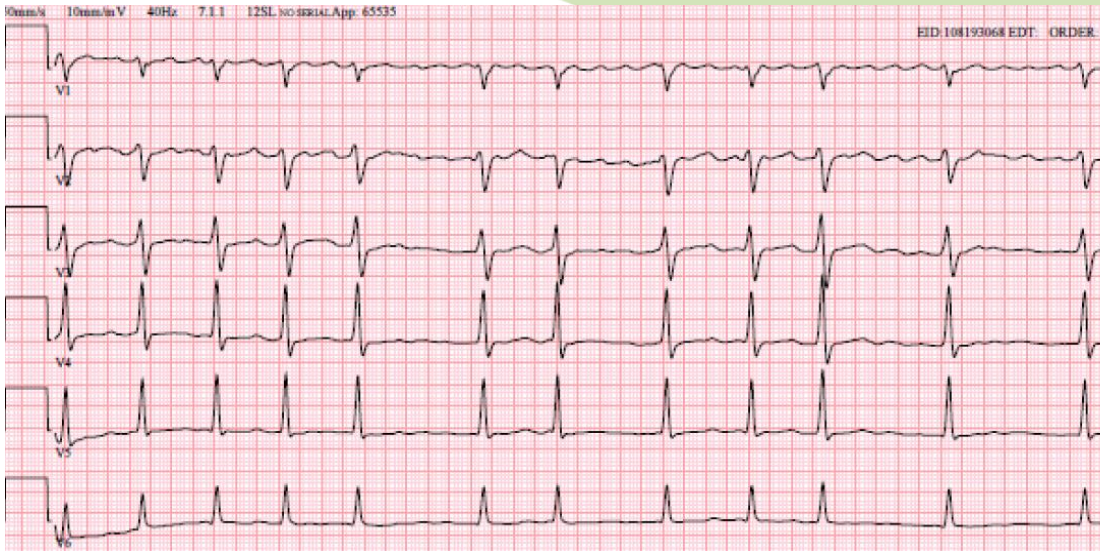
Valgimigli M et al Eur Heart J 2017;38(11):804-810

Gunnar

En 80-årig man med gikt, hypertoni och ett kroniskt förmaksflimmer (Eliquis 5 mg x2) inkommer till Akuten med akuta bröstsmärtor som strålar ut mot vänster arm. Ankomst EKG visar ….. och inga ST-höjningar. Pat blir smärtfri efter Morfin och Nitrospray och patienten läggs in på HIA. Du vill starta behandling med ASA och en P2Y12-hämmare i laddningsdos och planerar för angio nästa dag.

Frågor:

- Vilka trombocythämmare väljer du?
- Bör man sätta ut Eliquis innan angio?
- Hur länge bör du fortsätta med trippelbehanding efter PCI?
- Vilken trombocythämmare sätter du ut först?



ESC Guidelines on DAPT 2017

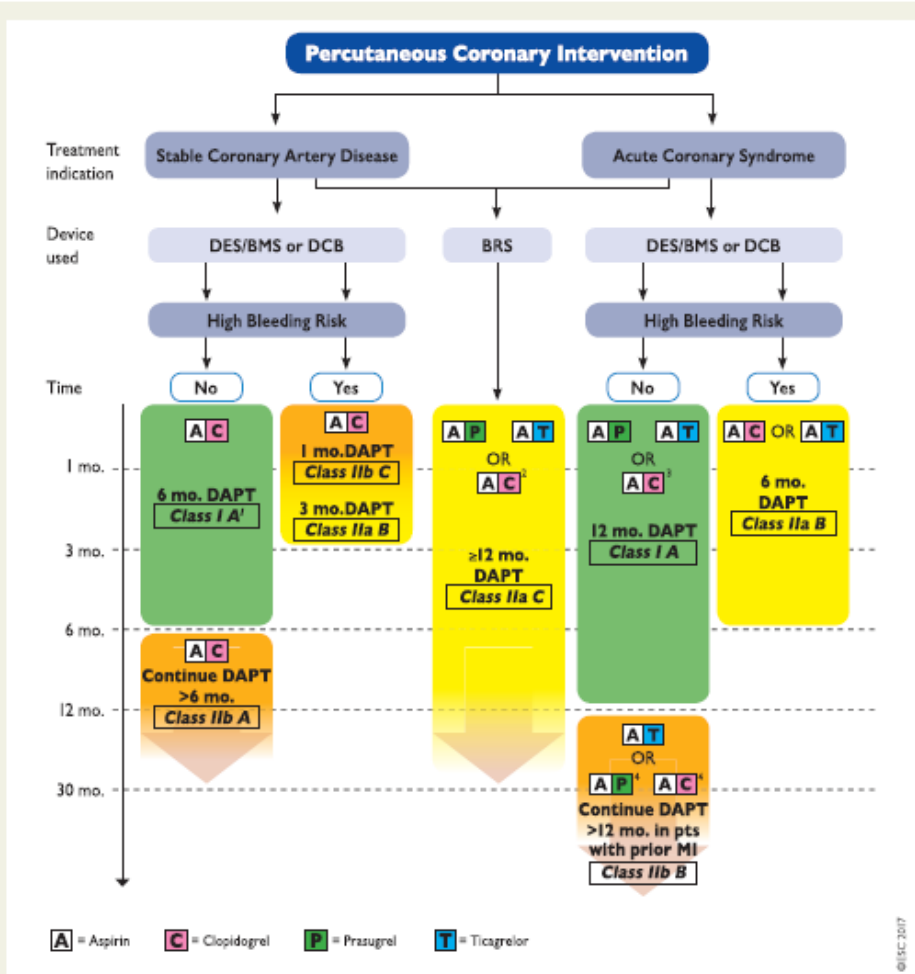


Figure 4 Algorithm for dual antiplatelet therapy (DAPT) in patients treated with percutaneous coronary intervention. ACS = acute coronary syndrome; BMS = bare-metal stent; BRS = bioresorbable vascular scaffold; CABG = coronary artery bypass graft surgery; DCB = drug-coated balloon; DES: drug-eluting stent; PCI = percutaneous coronary intervention; Stable CAD = stable coronary artery disease.
High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score ≥25).
Colour-coding refers to the ESC Classes of Recommendations (green = Class I; yellow = IIa; orange = Class IIb).
Treatments presented within the same line are sorted in alphabetic order, no preferential recommendation unless clearly stated otherwise.
[1]: After PCI with DCB 6 months. DAPT should be considered (Class IIa B).
[2]: If patient presents with Stable CAD or, in case of ACS, is not eligible for a treatment with prasugrel or ticagrelor.
[3]: If patient is not eligible for a treatment with prasugrel or ticagrelor.
[4]: If patient is not eligible for a treatment with ticagrelor.

ESC European Society of Cardiology

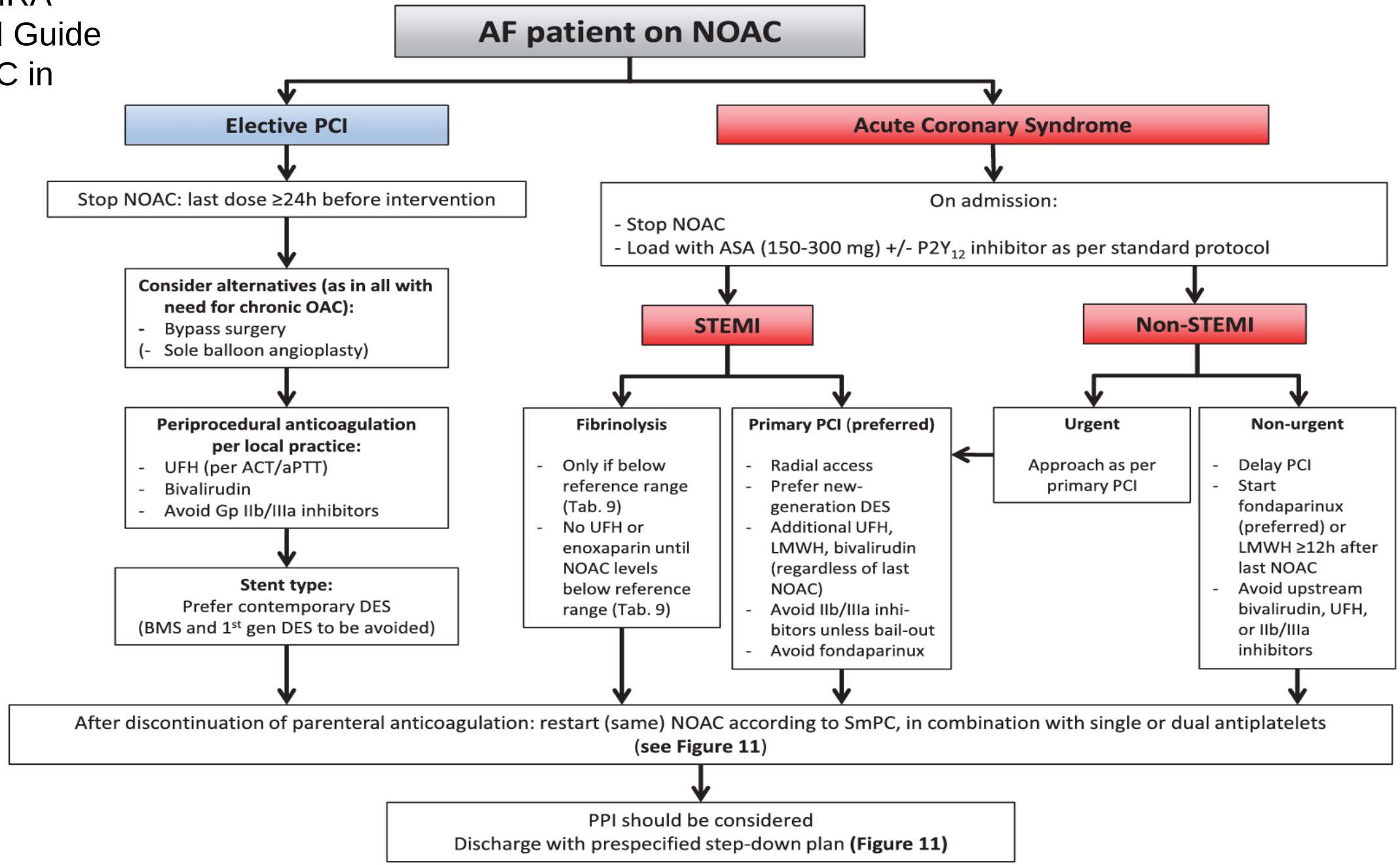
European Heart Journal (2018) **39**, 1330–1393
doi:10.1093/eurheartj/ehy136

SPECIAL ARTICLE

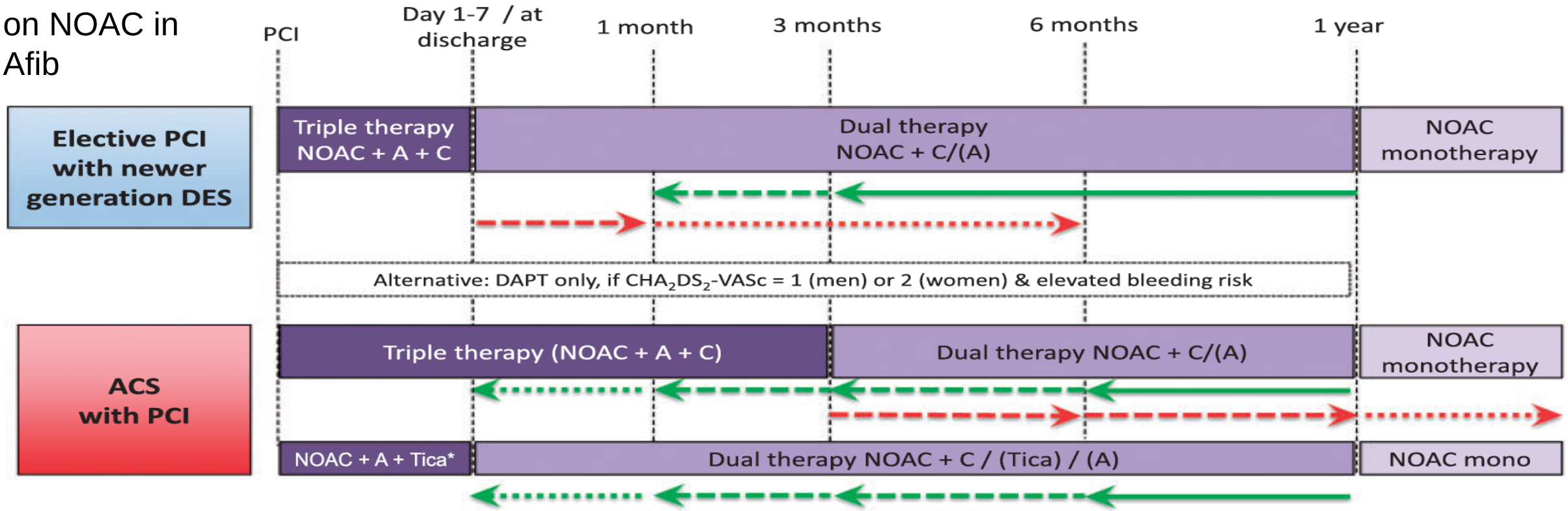
The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

Jan Steffel[1]*, Peter Verhamme[2], Tatjana S. Potpara[3], Pierre Albaladejo[4], Matthias Antz[5], Lien Desteghe[6], Karl Georg Haeusler[7], Jonas Oldgren[8], Holger Reinecke[9], Vanessa Roldan-Schilling[10], Nigel Rowell[11], Peter Sinnaeve[2], Ronan Collins[12], A. John Camm[13], and Hein Heidbüchel[6,14]

2018 EHRA Practical Guide on NOAC in Afib



2018 EHRA Practical Guide on NOAC in Afib



Factors to shorten combination therapy

- (Uncorrectable) high bleeding risk
- Low atherothrombotic risk (by REACH or SYNTAX score if elective; GRACE ≥140 if ACS)

Factors to lengthen combination therapy

- First-generation DES
- High atherothrombotic risk (scores as above ; stenting of the left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis etc.) and low bleeding risk

Antitrombotisk strategi för långtidsbehandling

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Trials of dual vs triple therapy with NOAC or VKA after PCI for stable CAD or ACS, or medically managed ACS, in patients with AF

	PIONEER AF-PCI[1]	RE-DUAL PCI[2]	AUGUSTUS[3]	ENTRUST-AF PCI[4]
Trial size and design	N=2,124; multicentre, randomised, open-label	N=2,725; multicentre, randomised, open-label	N=4,614; multicentre, randomised, open-label	N=~1,500; multicentre, randomised, open-label (EU + Asia)
Formal hypothesis testing	**Primary endpoint Safety (bleeding); not powered for efficacy (ischaemic endpoints)**			
Eligibility	AF, PCI + stent for ACS or stable CAD	NVAF; PCI + stent for ACS or stable CAD	NVAF, ACS and/or PCI	AF, PCI + stent for ACS or stable CAD
Enrolment window	Within 72 hours of sheath removal	Within 120 hours of stent placement	Within 14 days of index event	Between 4 hours and 5 days after sheath removal
NOAC vs VKA comparison	Yes, riva 2.5mg BID vs VKA	No	Yes	No
Approved SPAF dose	No; 2.5 mg BID and 15 mg OD*	Yes	Yes	Yes
DAPT duration	1, 6 or 12 months (investigator discretion)	1 (BMS) or 3 (DES) months	6 months	1 to 12 months (investigator discretion)

*15 mg OD: approved dose only for the prevention of stroke and systemic embolism in patients with AF and moderate (CrCl 30–49 ml/min) or severe (CrCl 15–29 ml/min) renal impairment[6].

1. Gibson CM, et al. N Engl J Med 2016;375:2423–34
2. Cannon CP, et al. N Engl J Med 2017;377:1513–24
3. Lopes RD, et al. N Engl J Med 2019;380:1509–24
4. Vranckx P, et al. Am Heart J 2018;196:105–12

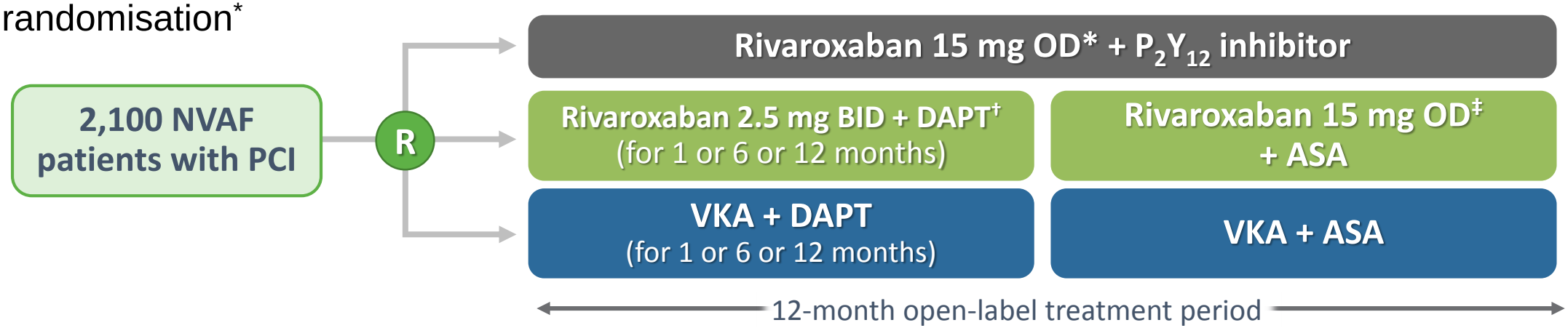
PIONEER AF-PCI: Rivaroxaban dual/triple vs VKA triple in AF patients undergoing PCI

Primary objective:

- To assess the safety of two rivaroxaban treatment strategies versus a dose-adjusted VKA treatment strategy in NVAF patients undergoing PCI with stenting.

Primary endpoint:

- The percentage of subjects experiencing clinically significant bleeding 12 months post-randomisation*

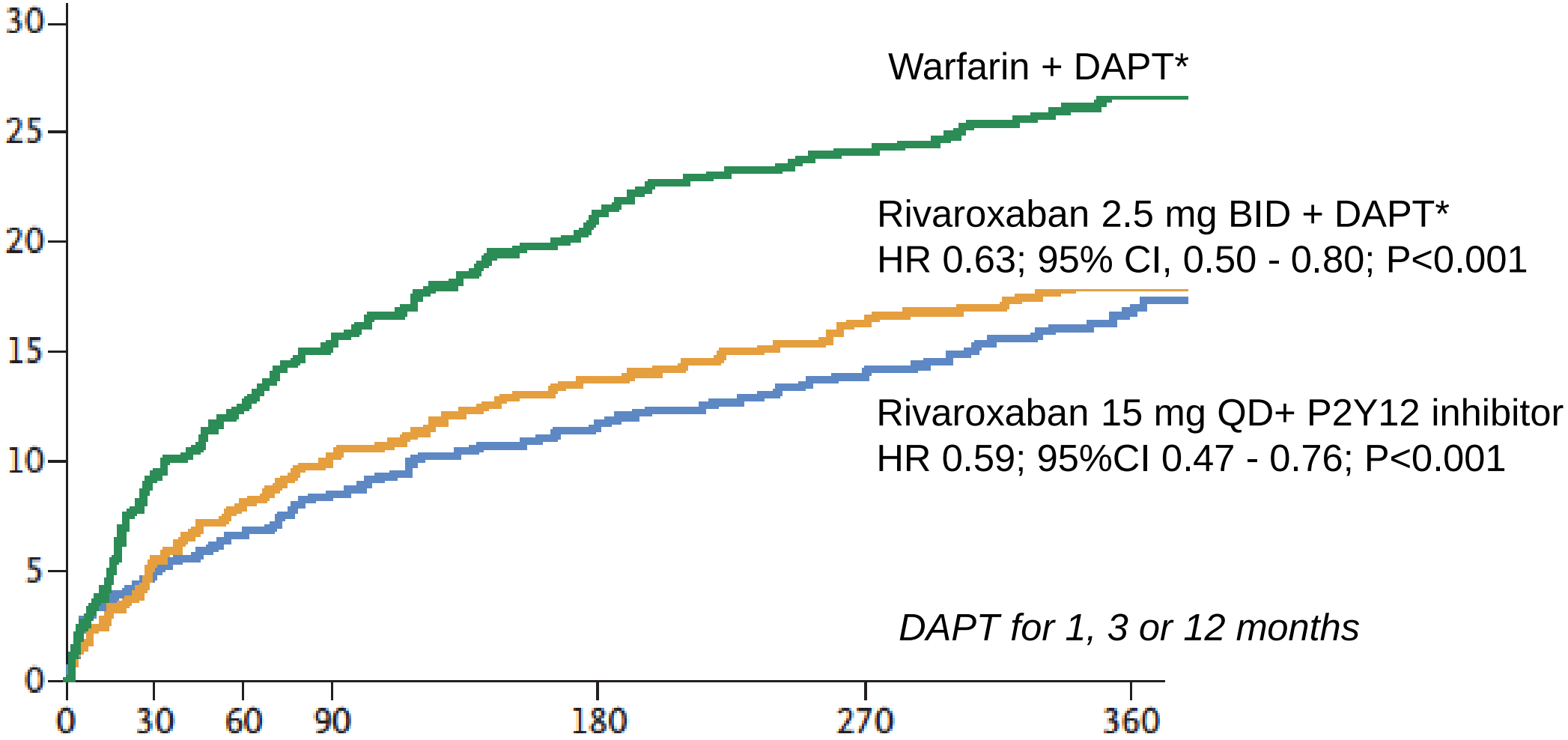


*Either TIMI major bleeding, minor bleeding or bleeding requiring medical attention events; †P_2Y_{12} inhibitor plus ASA; ‡Rivaroxaban 10 mg OD if CrCl 30–50 mL/min

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

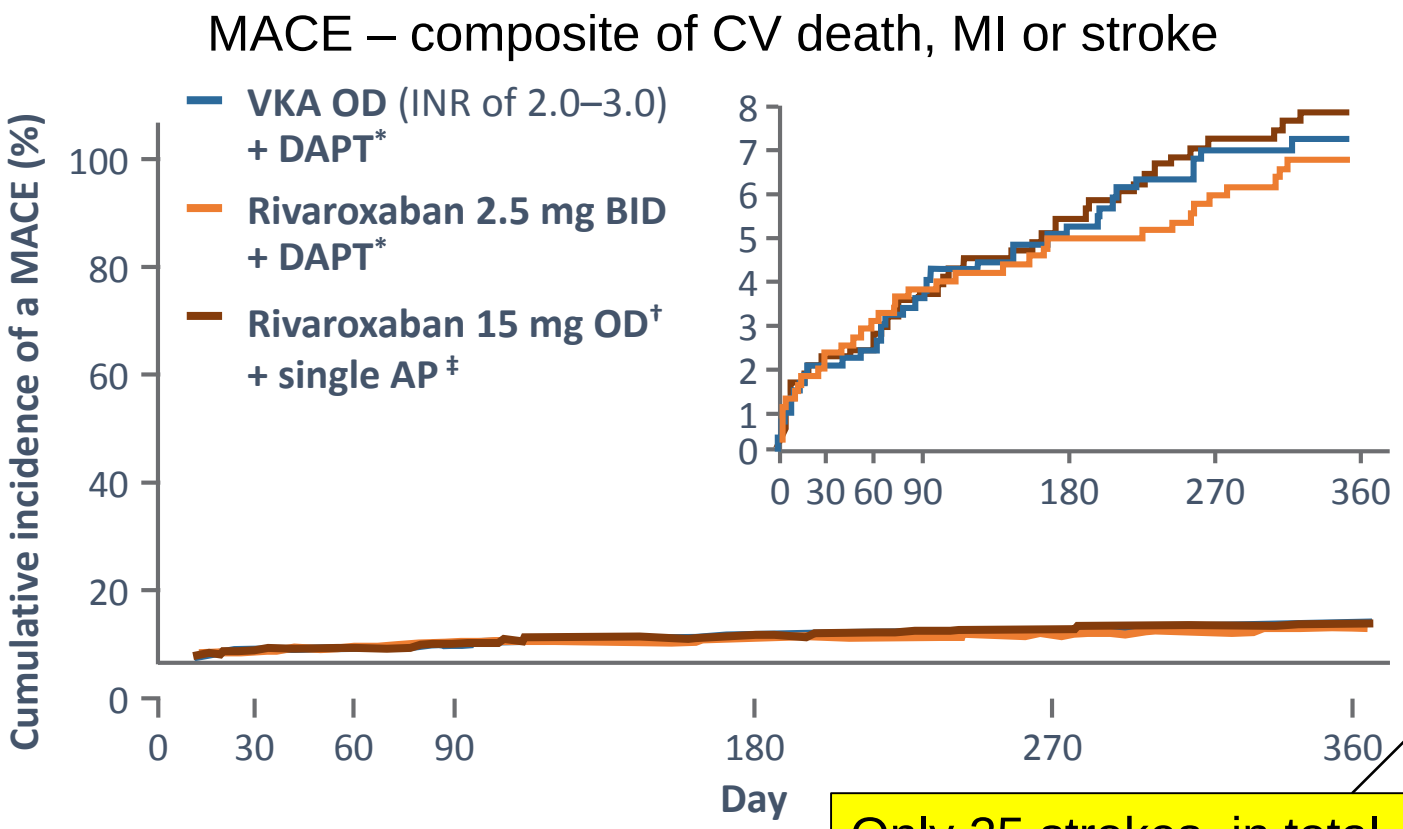
PIONEER AF study - Clinically significant bleedings

(Composite of major or minor bleeding according to TIMI criteria or bleeding requiring medical attention)



Gibson, et al. NEJM 2016;375:2423-34

PIONEER AF-PCI: Ischemic/thromboembolic outcomes



Secondary endpoint	Rivaroxaban 15 mg OD vs warfarin		Rivaroxaban 2.5 mg BID vs warfarin	
	HR (95% CI)	p value	HR (95% CI)	p value
MACE	1.08 (0.69–1.68)	0.75	0.93 (0.59–1.48)	0.76
Death from CV cause	1.29 (0.59–2.80)	0.52	1.19 (0.54–2.62)	0.66
MI	0.86 (0.46–1.59)	0.62	0.75 (0.40–1.42)	0.37
Stroke	1.07 (0.39–2.96)	0.89	1.36 (0.52–3.58)	0.53
Stent thrombosis	1.20 (0.32–4.45)	0.79	1.44 (0.40–5.09)	0.57

Only 25 strokes, in total.
ROCKET-AF >00 strokes

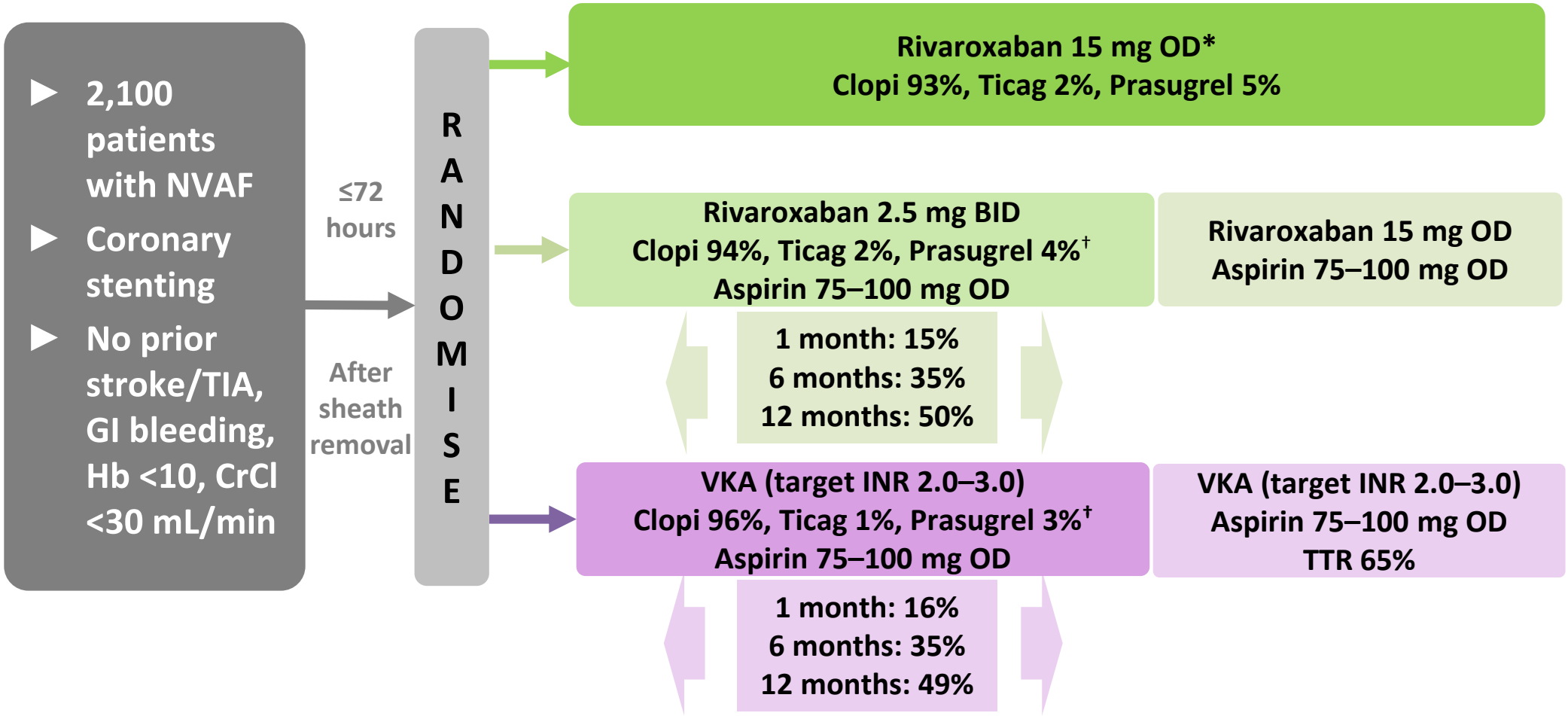
The dose of 15 mg OD rivaroxaban used in this study differs from the recommendations for the management of NVAF in the SmPC.

*DAPT was with low-dose ASA (75–100 mg/day) and clopidogrel 75 mg OD, or ticagrelor 90 mg BID, or prasugrel 10 mg OD in ≤15% of patients; †A dose of 10 mg was used in patients with a CrCl of 30–50 mL/min; ‡Or ticagrelor 90 mg BID or prasugrel 10 mg OD in ≤15% of patients.

MACE, major adverse cardiovascular events; MI, myocardial infarction.

1Gibson CM, et al. *N Engl J Med* 2016;375:2423–2434;

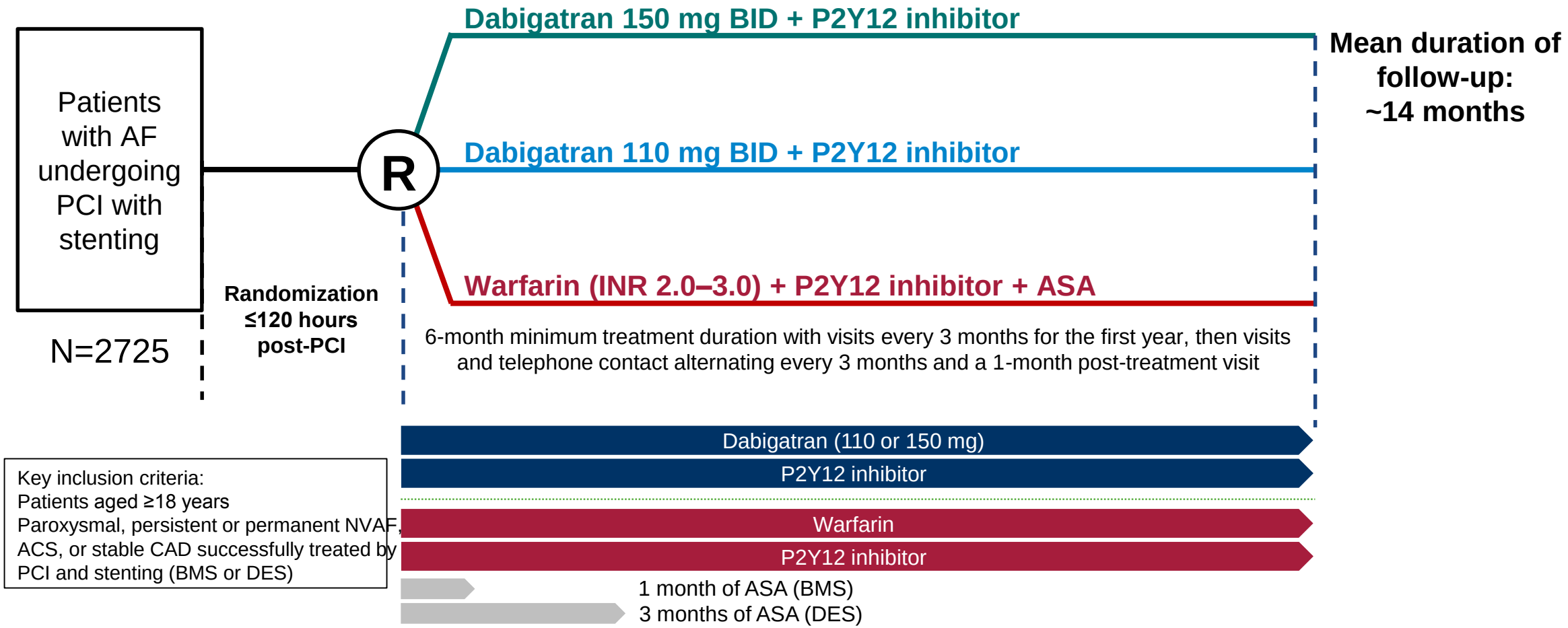
PIONEER AF-PCI: Pre-randomisation choice of duration of DAPT and P2Y12i



*Rivaroxaban dosed at 10 mg OD in patients with CrCl of 30 to <50 mL/min. †Alternative $P2Y_{12}$ inhibitors: 10 mg OD prasugrel or 90 mg BID ticagrelor.

Gibson et al. *Circulation* 2017;135:323-333

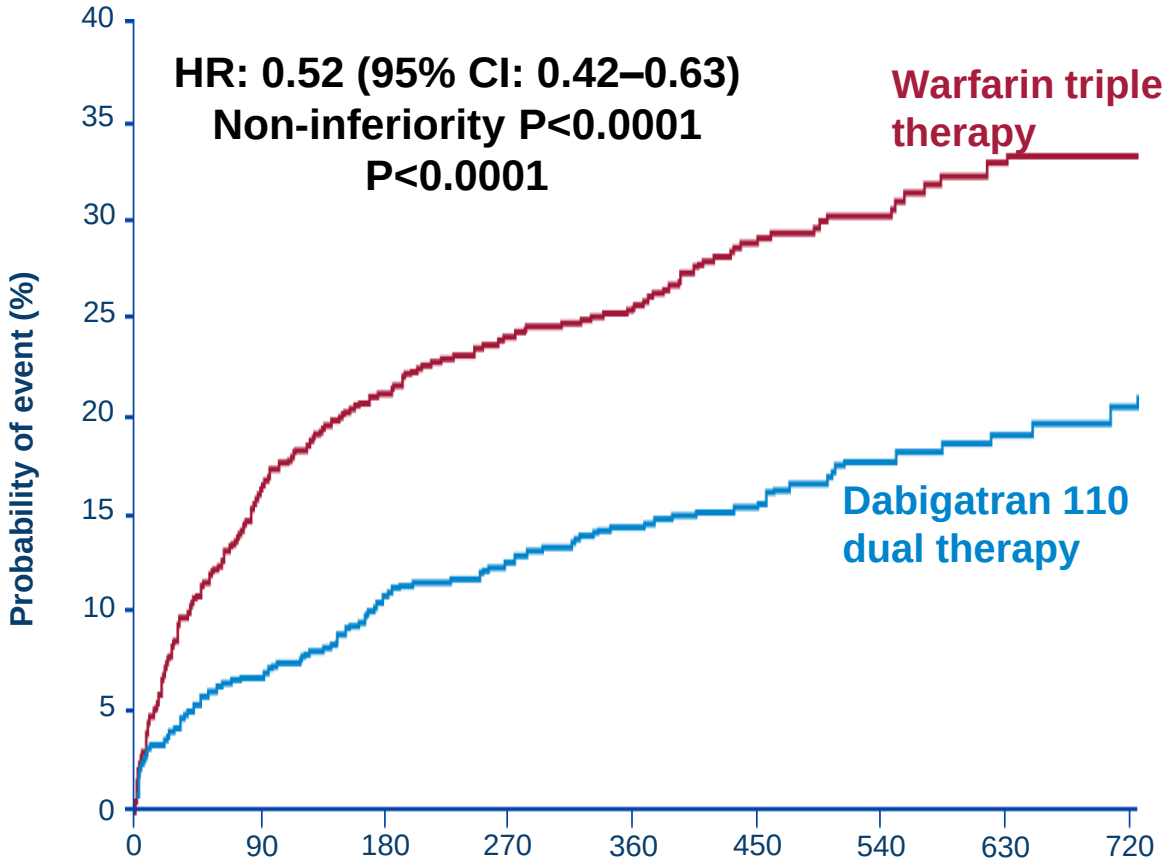
RE-DUAL PCI: Dabigatran dual therapy vs warfarin triple therapy

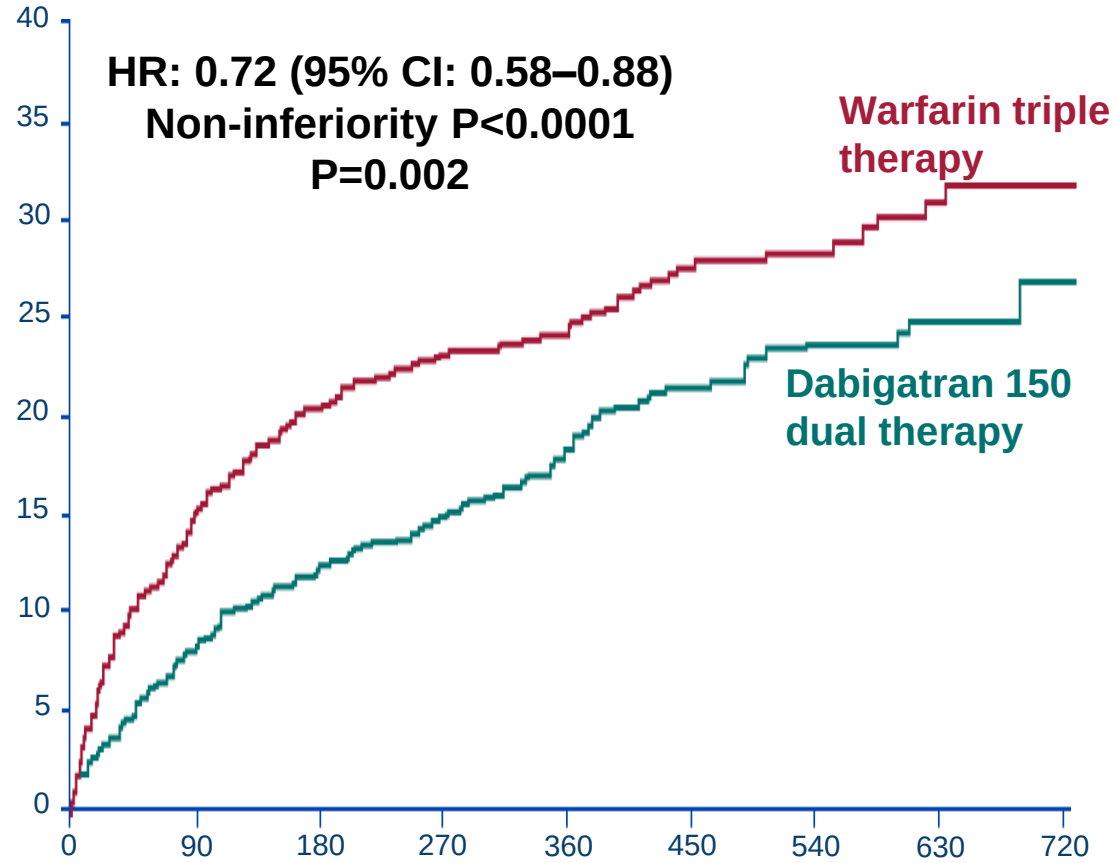


- Patients aged <80 yr (<70 yr in Japan) were randomized to dabigatran 110 or 150 dual therapy, or warfarin triple therapy.
- Patients aged ≥80 yr in the United States were randomized to dabigatran 110 or 150 dual therapy, or warfarin triple therapy in a 1:1:1 ratio.
- Patients aged ≥80 yr in other countries (≥70 yr in Japan) were randomized to dabigatran 110 dual therapy or warfarin triple therapy in a 1:1 ratio.

- ACS, acute coronary syndrome; AF, atrial fibrillation; ASA, acetylsalicylic acid; BID, twice daily; BMS, bare-metal stent; CAD, coronary artery disease; DES, drug-eluting stent; INR, international normalized ratio; NVAF, non-valvular atrial fibrillation; PCI, percutaneous coronary intervention; PROBE, prospective, randomized, open, blinded endpoint. Cannon et al. Clin Cardiol. 2016;39(10):555-564.

RE-DUAL PCI: ISTH major or clinically relevant non-major (CRNM) bleeding event



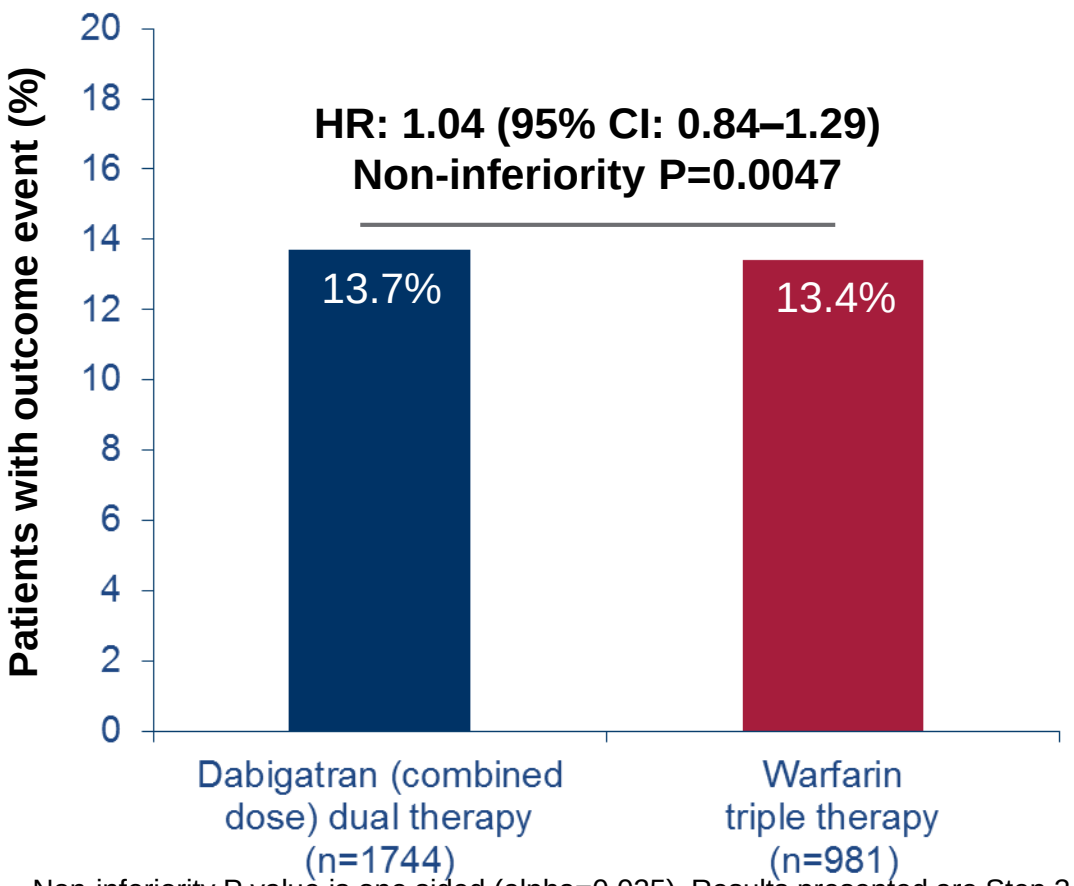


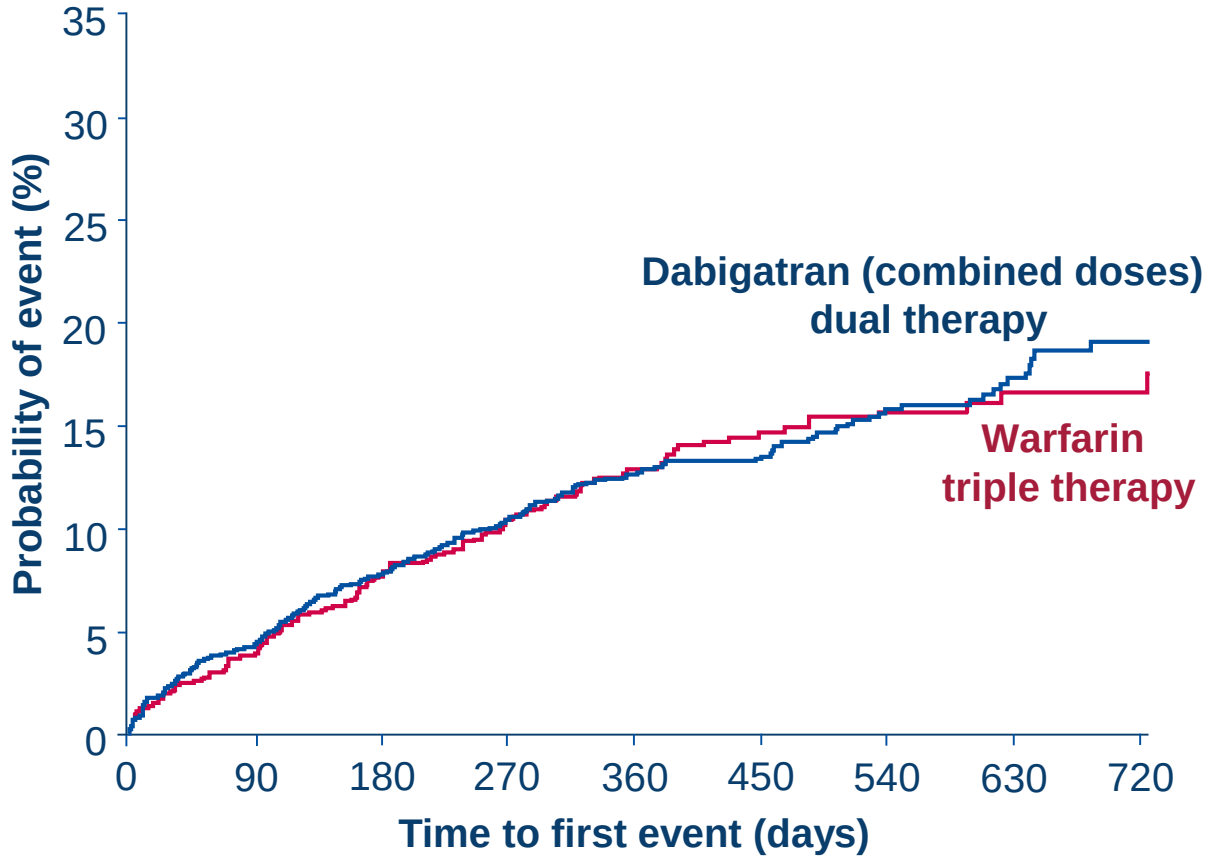
Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 dual therapy vs warfarin triple therapy comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 years old in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 dual therapy vs warfarin triple therapy comparison, an unstratified model is used; elderly patients outside the United States are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05).

CI, confidence interval; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis.

Cannon et al. NEJM. 2017;377(16):1513-1524.

RE-DUAL PCI: Composite of death, MI, stroke, SE, or unplanned revasc.





Non-inferiority P value is one sided (alpha=0.025). Results presented are Step 3 of hierarchical testing procedure, testing non-inferiority of dabigatran dual therapy (combined doses) to warfarin triple therapy in death or thromboembolic event and unplanned revascularization. CI, confidence interval; HR, hazard ratio.

Cannon, et al. NEJM. 2017;377(16):1513-1524

RE-DUAL PCI trial: Individual ischemic/thromboembolic endpoints

	Dabigatran 110 mg dual therapy (n=981) n (%)	Warfarin triple therapy (n=981) n (%)	D110 DT vs warfarin TT HR (95% CI)	D110 DT vs warfarin TT P value	Dabigatran 150 mg dual therapy (n=763) n (%)	Warfarin triple therapy (n=764) n (%)	D150 DT vs warfarin TT HR (95% CI)	D150 DT vs warfarin TT P value
All-cause death	55 (5.6)	48 (4.9)	1.12 (0.76–1.65)	0.56	30 (3.9)	35 (4.6)	0.83 (0.51–1.34)	0.44
Stroke	17 (1.7)	13 (1.3)	1.30 (0.63–2.67)	0.48	9 (1.2)	8 (1.0)	1.09 (0.42–2.83)	0.85
Unplanned revascularization	76 (7.7)	69 (7.0)	1.09 (0.79–1.51)	0.61	51 (6.7)	52 (6.8)	0.96 (0.65–1.41)	0.83
Myocardial infarction	44 (4.5)	29 (3.0)	1.51 (0.94–2.41)	0.09	26 (3.4)	22 (2.9)	1.16 (0.66–2.04)	0.61
Stent thrombosis	15 (1.5)	8 (0.8)	1.86 (0.79–4.40)	0.15	7 (0.9)	7 (0.9)	0.99 (0.35–2.81)	0.98

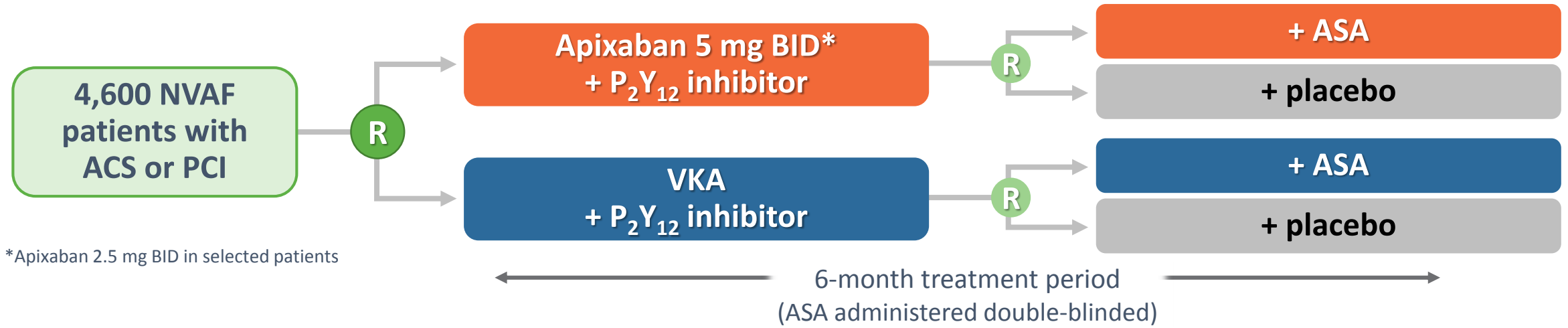
Very limited number of strokes, but both dabigatran doses according to SmPC (already evaluated in RE-LY)

Cannon, et al. NEJM. 2017;377(16):1513-1524

AUGUSTUS: Apixaban vs VKA and ASA vs placebo, in addition to P2Y12 inhibition, in patients with AF and ACS and/or PCI

Primary endpoint:

- Time to first occurrence of major/CRNM bleeding over the first 6 months

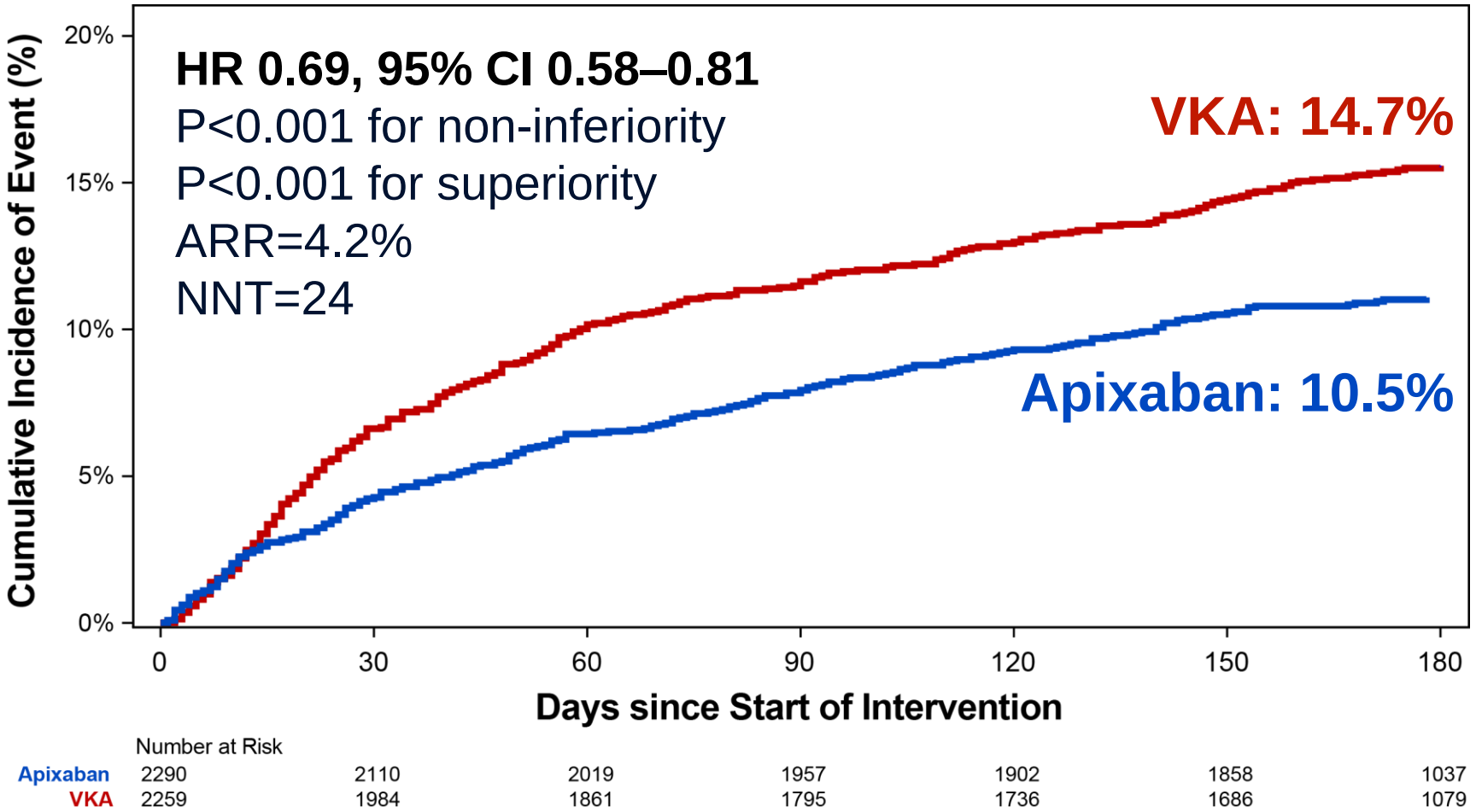


*Apixaban 2.5 mg BID in selected patients

Lopes, et al. Am Heart J 2018; 200: 17-23

ISTH Major / CRNM Bleeding Apixaban vs VKA

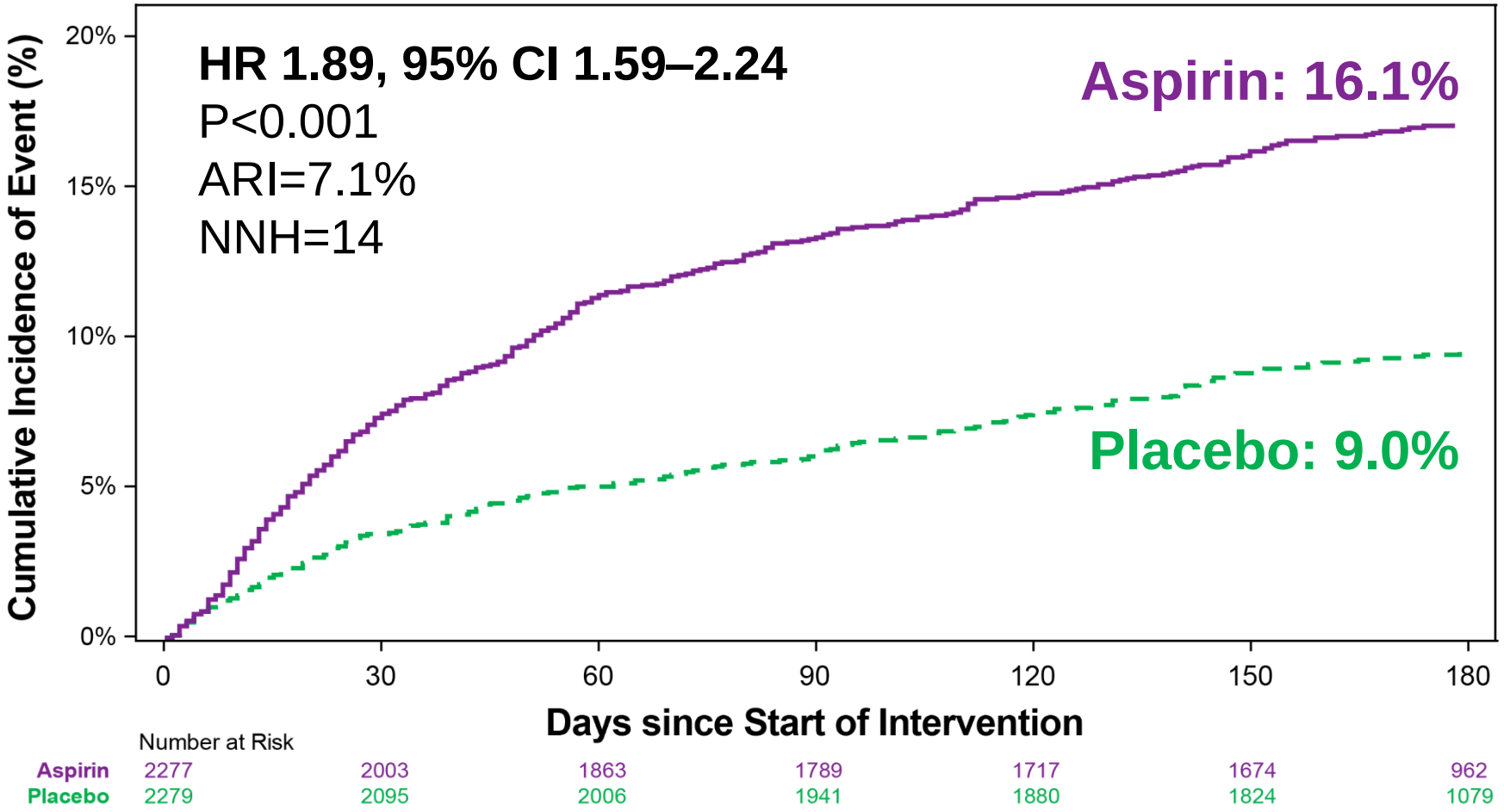
in addition to P2Y12 and ASA or placebo



ARR: absolute risk reduction
NNT: number needed to treat

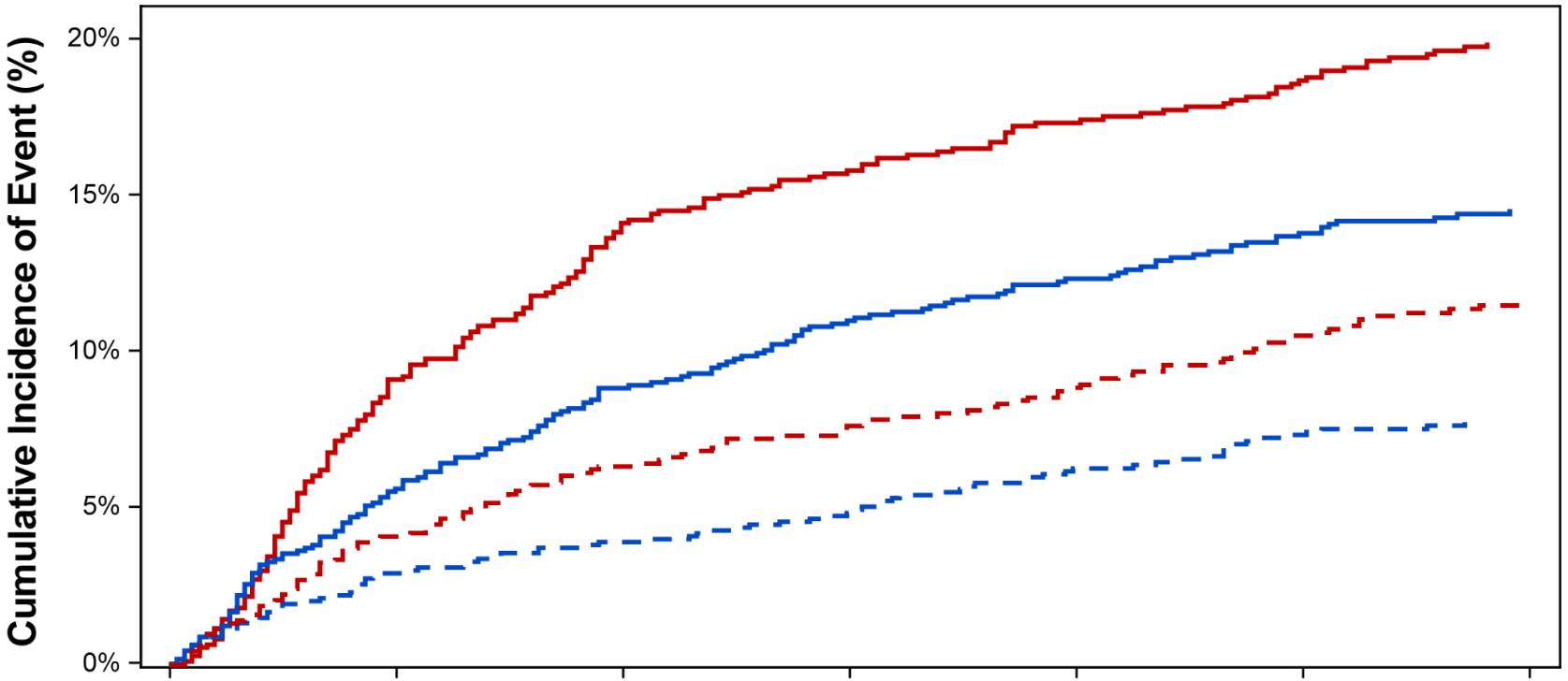
ISTH Major / CRNM Bleeding Aspirin vs. Placebo

in addition to P2Y12 and Apixaban or VKA



ARI: absolute risk increase
NNH: number needed to harm

ISTH Major / CRNM Bleeding



Number at Risk							
Apixaban and Aspirin	1145	1036	975	937	903	880	485
Apixaban and Placebo	1143	1075	1044	1007	975	947	536
VKA and Aspirin	1123	962	881	838	800	776	467
VKA and Placebo	1126	1007	947	917	883	851	528

VKA + Aspirin (18.7%)

Apixaban + Aspirin (13.8%)

VKA + Placebo (10.9%)

Apixaban + Placebo (7.3%)

In addition to P2Y12 inhibition:
Apixaban + Placebo vs. VKA + Aspirin:
11.4% absolute risk reduction (NNT=9)

Lopes, et al. NEJM2019

Ischemic Outcomes
Apixaban vs. VKA, on top of P2Y12i w/wo aspirin

Endpoint	Apixaban (N=2306)	VKA (N=2308)	HR (95% CI)
Death / Ischemic Events (%)	6.7	7.1	0.93 (0.75–1.16)
Death (%)	3.3	3.2	1.03 (0.75–1.42)
CV Death (%)	2.5	2.3	1.05 (0.72–1.52)
Stroke (%)	**0.6**	**1.1**	**0.50 (0.26–0.97)**
Myocardial Infarction (%)	3.1	3.5	0.89 (0.65–1.23)
Definite or Probable Stent Thrombosis (%)	0.6	0.8	0.77 (0.38–1.56)
Urgent Revascularization (%)	1.7	1.9	0.90 (0.59–1.38)
Hospitalization (%)	**22.5**	**26.3**	**0.83 (0.74–0.93)**

Lopes, et

Very limited number of strokes, but apixaban according to SmPC (already evaluated in ARISTOTLE)

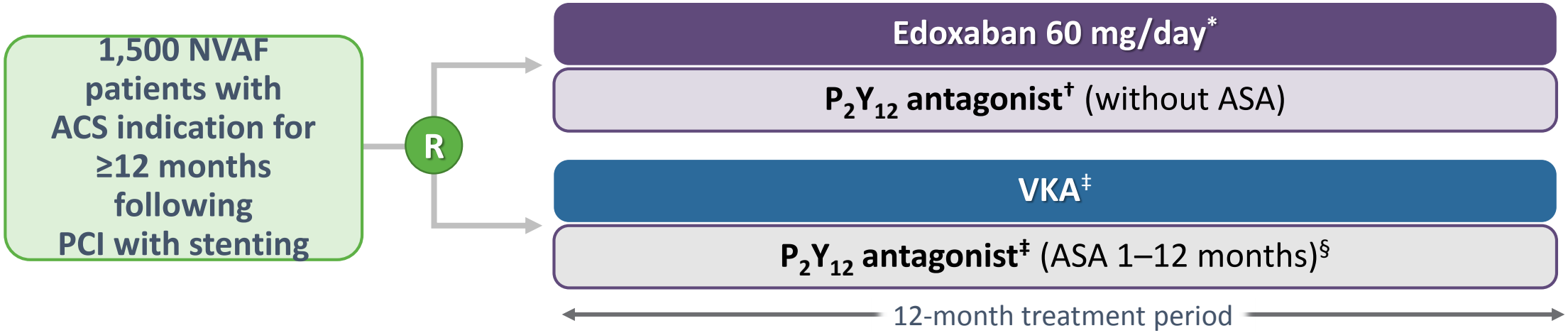
ENTRUST AF-PCI: Edoxaban vs VKA in NVAF patients undergoing PCI

Primary objectives:

- To evaluate the safety and the efficacy of an edoxaban-based antithrombotic regimen vs a VKA-based anti-thrombotic regimen in subjects with AF following PCI with stent placement

Primary endpoint:

- Major/clinically relevant bleeding (for 12 months)



Edoxaban according to SmPC (already evaluated in ENGAGE-AF)

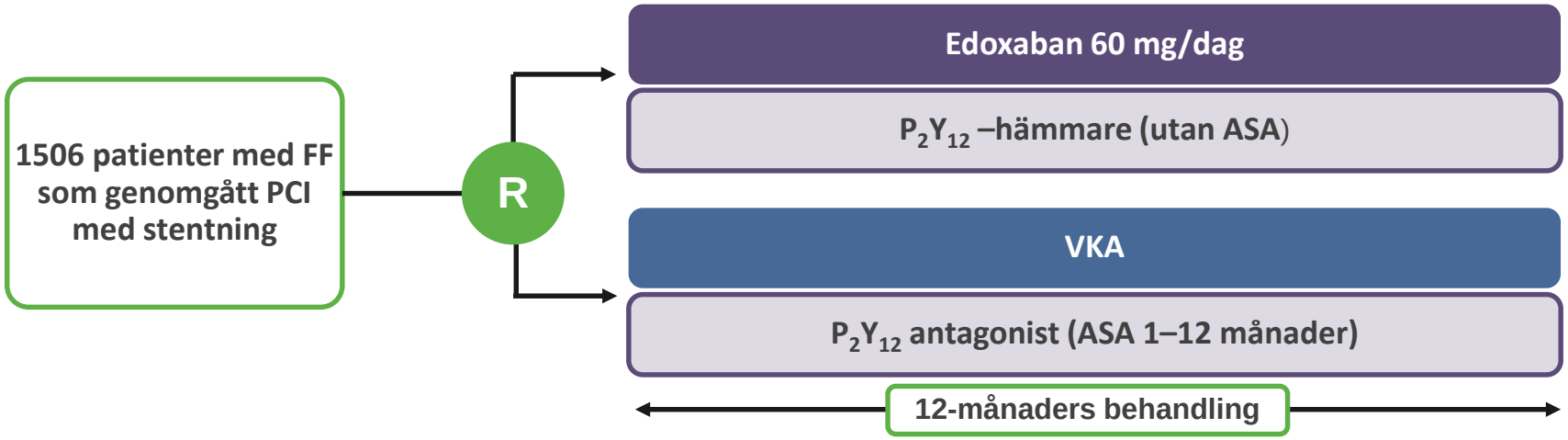
*Edoxaban dose reduced to 30 mg OD if CrCl ≤50 mL/min, body weight ≤60 kg or the patient is on certain P-gp inhibitors;
†Clopidogrel 75mg OD or if documented need prasugrel 5 or 10 mg OD or ticagrelor 90 mg BID. Predeclared at randomisation;
‡VKA predefined by country, target INR 2.0–3.0; § ASA 100 mg OD for 1–12 months guided by clinical presentation (ACS or stable CAD), CHA_2DS_2-VASc and HAS-BLE

1. ENTRUST AF-PCI, NCT02866175. Available at: www.clinicaltrials.gov.

ENTRUST AF-PCI (edoxaban)

Primärt syfte: Att utvärdera säkerhet och effekt för en antitrombotisk behandlingsregim med edoxaban vs VKA hos patienter med icke-valvulärt förmaksflimmer som genomgått PCI med stentning.

Primärt utfallsmått: Allvarlig/kliniskt relevant blödning



Ref. Anpassad från Vranckx. P. Am Heart J. 2018 Feb;196:105-112

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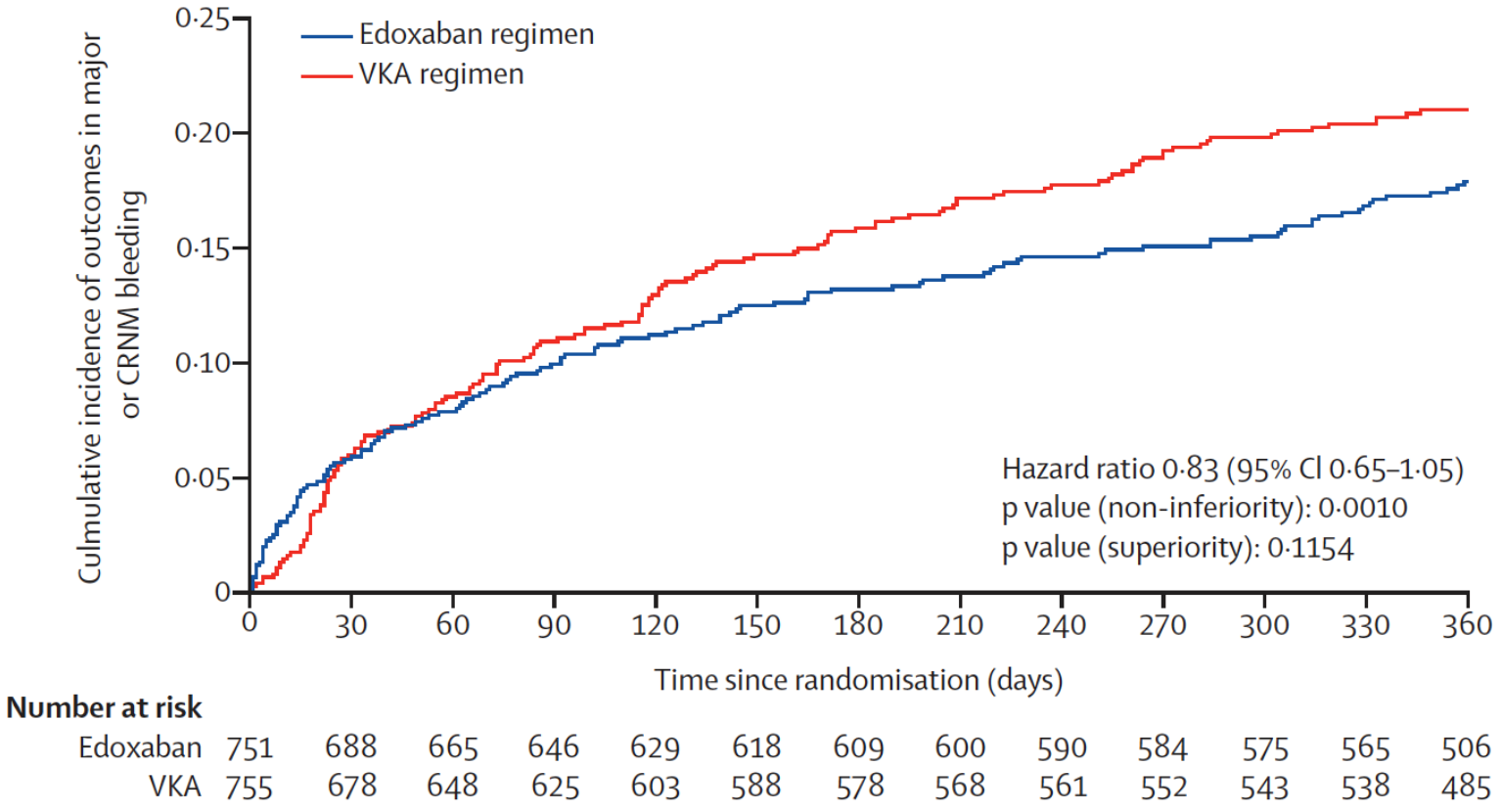
ENTRUST AF-PCI

Primärt utfallsmått: ISTH allvarlig eller kliniskt relevant icke-allvarlig blödning



Vranckx. P. *Lancet*. Sept 2019

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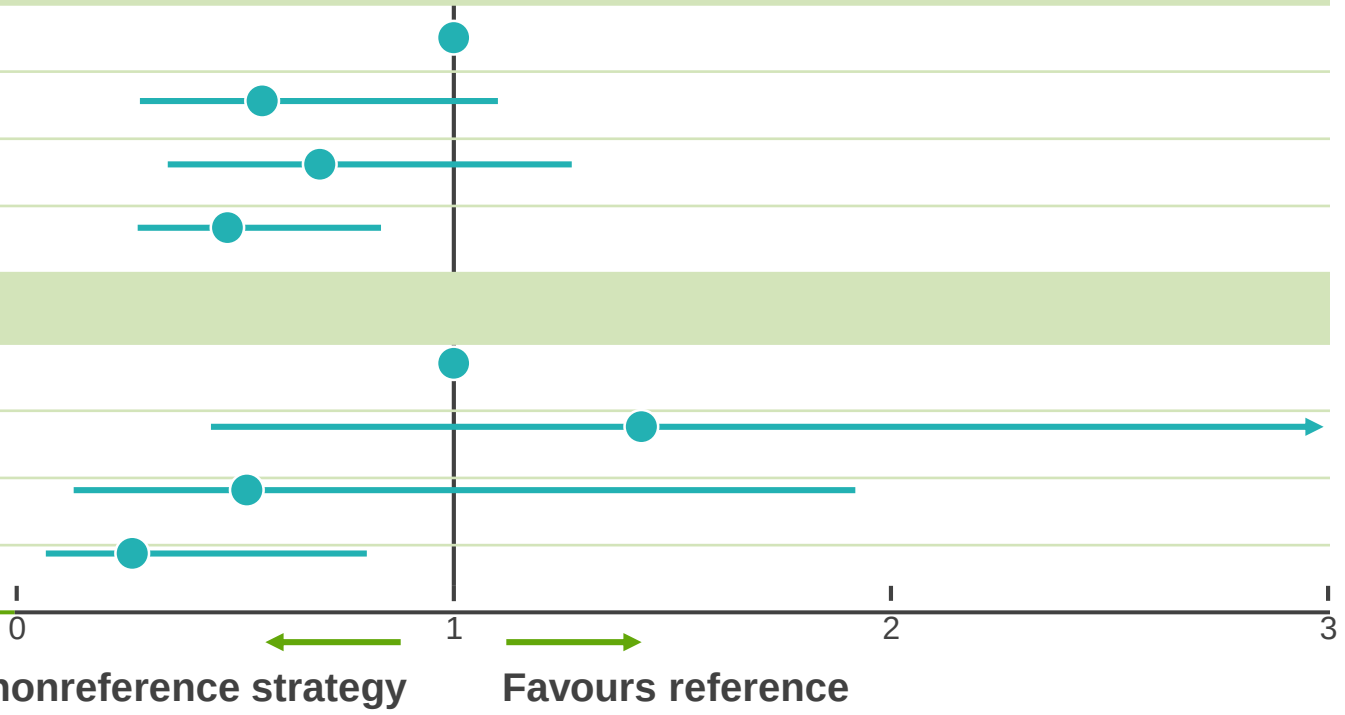
Safety outcomes with four antithrombotic strategies: Network meta-analysis of RCTs

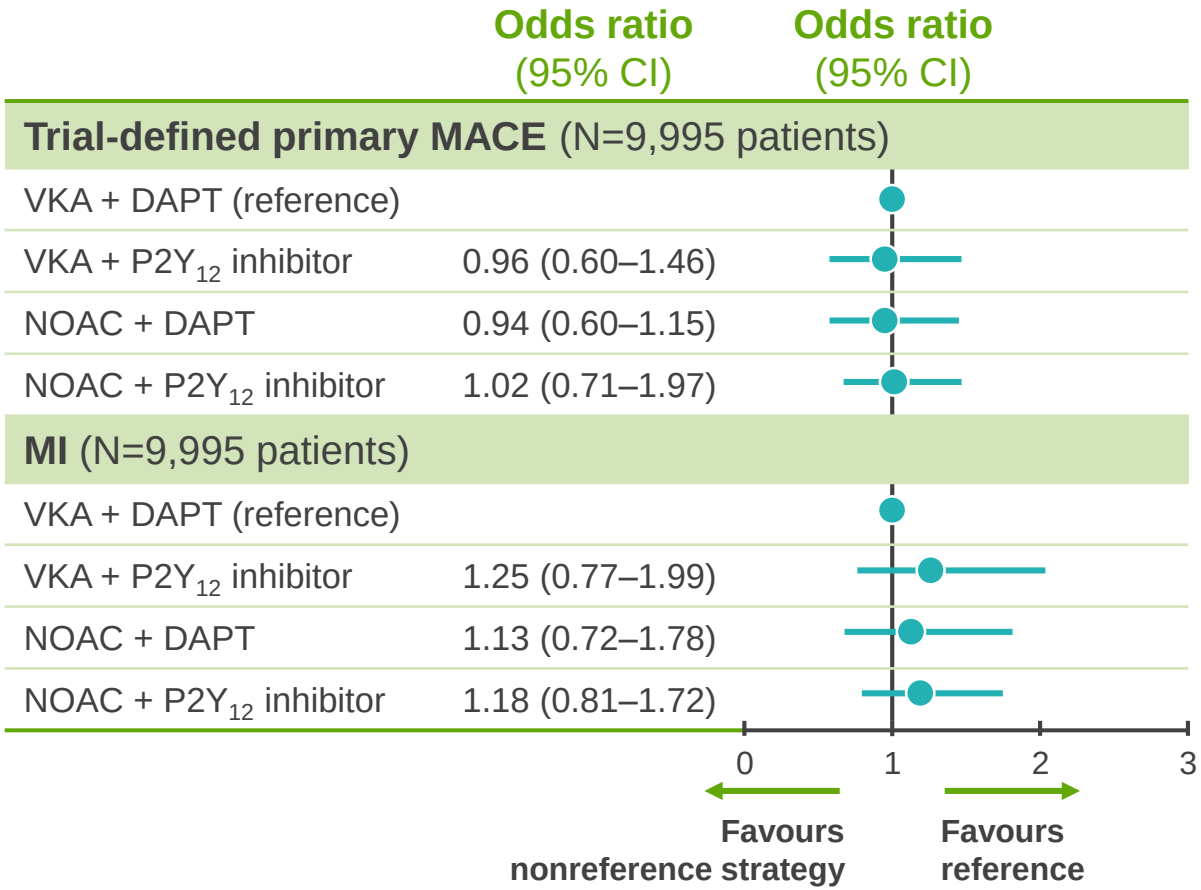
	Odds ratio (95% CI)	**Odds ratio** (95% CI)
TIMI major bleeding (N=9,924 patients)		
VKA + DAPT (reference)		
VKA + $P2Y_{12}$ inhibitor	0.58 (0.31–1.08)	
NOAC + DAPT	0.70 (0.38–1.23)	
NOAC + $P2Y_{12}$ inhibitor	0.49 (0.30–0.82)	
ICH (N=9,924 patients)		
VKA + DAPT (reference)		
VKA + $P2Y_{12}$ inhibitor	1.44 (0.40–5.22)	
NOAC + DAPT	0.54 (0.15–1.92)	
NOAC + $P2Y_{12}$ inhibitor	0.26 (0.08–0.79)	

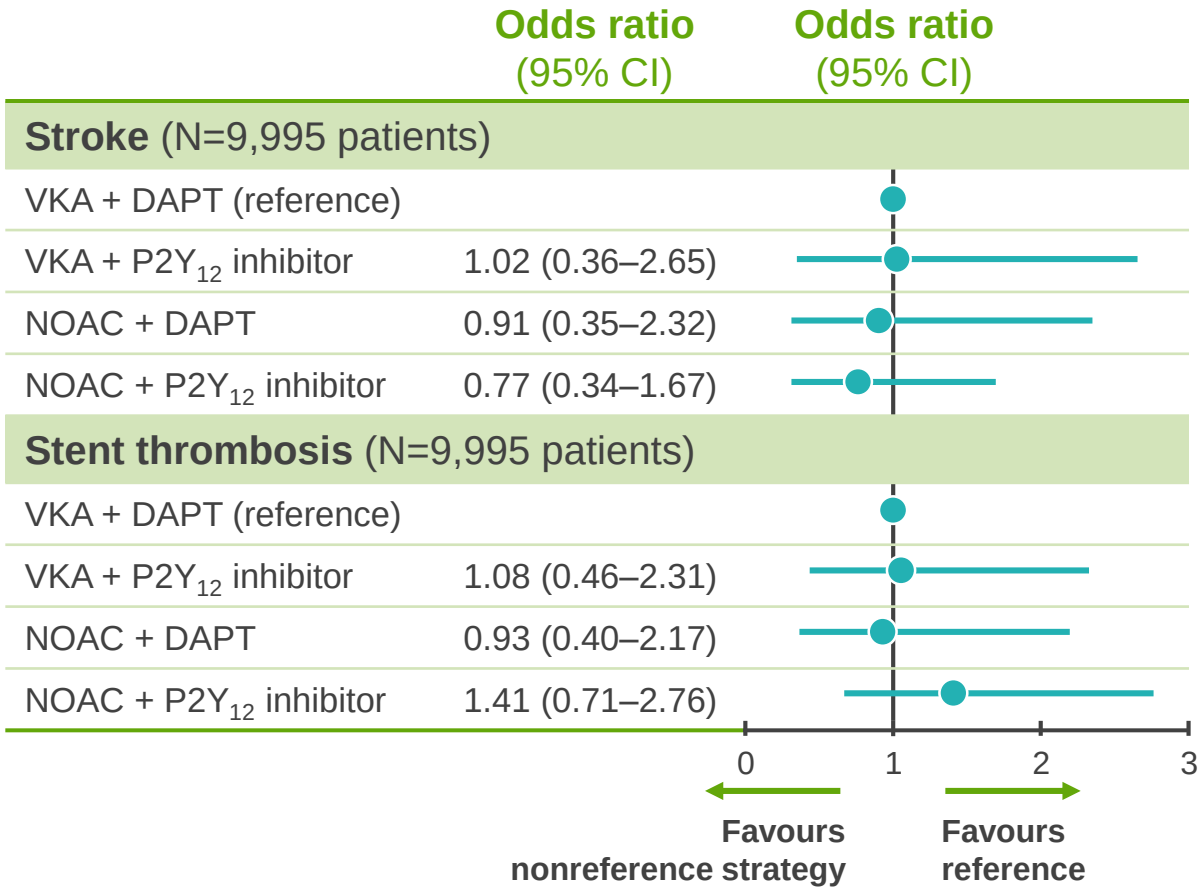


NOAC plus $P2Y_{12}$ inhibitor was associated with significantly less bleeding compared with VKA plus DAPT

Lopes RD, et al. JAMA Cardiol 2019. doi:10.1001/jamacardio.2019.1880.

Efficacy outcomes with four antithrombotic strategies: Network meta-analysis of RCTs

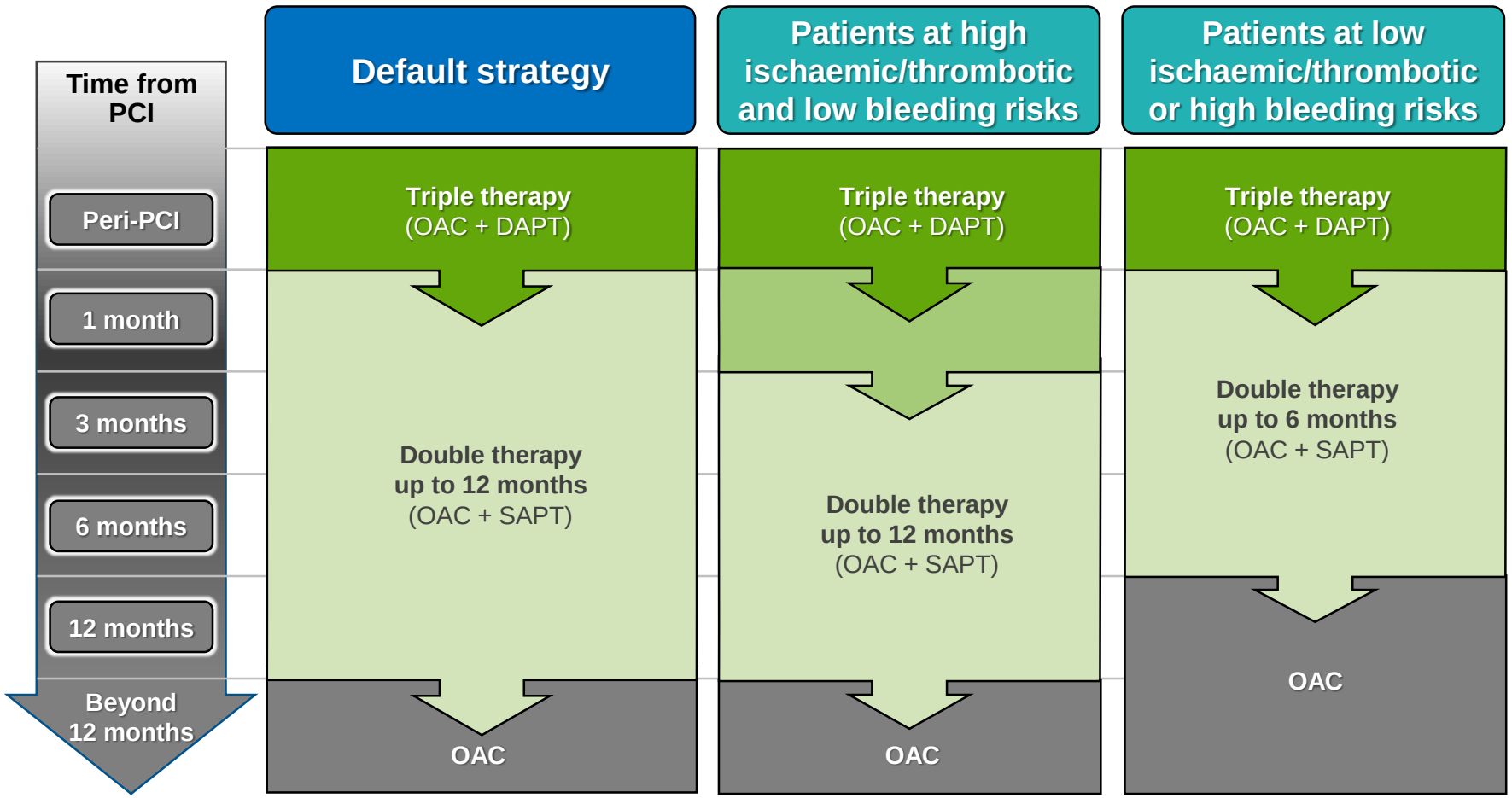




MACE outcomes were comparable between all four treatment strategies
There were no significant differences for stroke, MI and stent thrombosis between strategies

Lopes RD, et al. JAMA Cardiol 2019. doi:10.1001/jamacardio.2019.1880.

2018 North American expert consensus document



'A **double therapy** approach (OAC + $P2Y_{12}$ inhibitor) should represent the **default strategy** for most patients…'

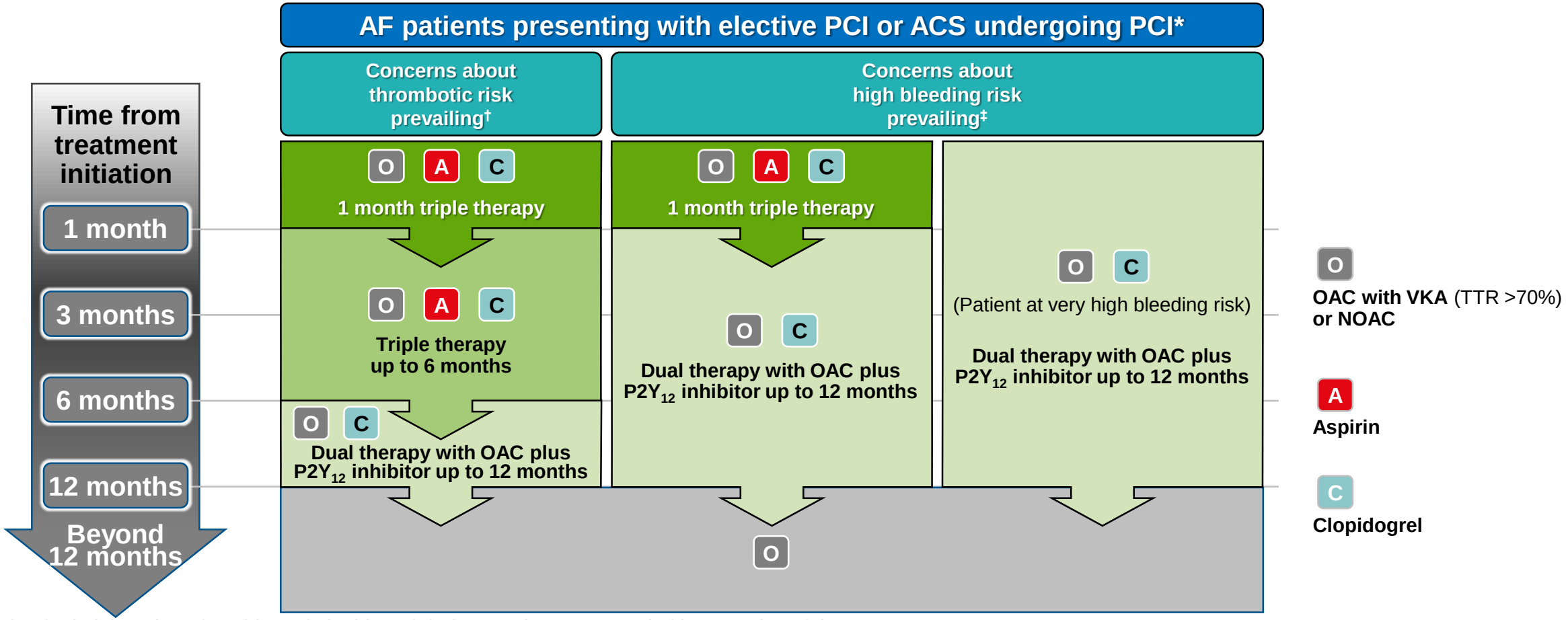
'A NOAC (rather than VKA) should generally be preferred...'

'If ticagrelor is chosen as the $P2Y_{12}$ agent, concomitant aspirin should not be given (i.e. avoid triple therapy), as was done in the RE-DUAL PCI trial'

The preferred OAC is a NOAC over VKA if there are no contraindications; the preferred SAPT is a $P2Y_{12}$ inhibitor over aspirin. Clopidogrel is the $P2Y_{12}$ inhibitor of choice; ticagrelor may be considered in patients at high ischaemic/thrombotic and low bleeding risks; avoid prasugrel. Consider SAPT in addition to OAC after >12 months only in select patients at high ischaemic/thrombotic and low bleeding risk.

Angiolillo DJ, et al. Circulation 2018;138:527–36.

ESC 2018 Joint European consensus, endorsed by the Asia Pacific Heart Rhythm Society



*Periprocedural administration of aspirin and clopidogrel during PCI is recommended irrespective of the treatment strategy; as dual therapy, potent $P2Y_{12}$ inhibitors (ticagrelor) may be combined with dabigatran;

†High atherothrombotic risk (for elective PCI, use SYNTAX score; for ACS, Grace score >140; stenting of the left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis, etc) and low bleeding risk;

‡Bleeding risk can be estimated using the HAS-BLED score; correct modifiable bleeding risk factors.

ESC, European Society of Cardiology; TTR, time in therapeutic range.

Lip GYH, et al. Europace 2019;21:192–3.

2019 ESC Guidelines för Chronic coronary disease

Antithrombotic therapy in post-PCI patients with AF or another indication for OAC	
In patients who are eligible for a NOAC, it is recommended that a NOAC (apixaban 5 mg b.i.d., dabigatran 150 mg b.i.d., edoxaban 60 mg o.d., or rivaroxaban 20 mg o.d.) is used in preference to a VKA in combination with antiplatelet therapy.	I
When rivaroxaban is used and concerns about high bleeding risk prevail over concerns about stent thrombosis or ischaemic stroke, rivaroxaban 15 mg o.d. should be considered in preference to rivaroxaban 20 mg o.d. for the duration of concomitant single or dual antiplatelet therapy.	IIa
When dabigatran is used and concerns about high bleeding risk prevail over concerns about stent thrombosis or ischaemic stroke, dabigatran 110 mg b.i.d. should be considered in preference to dabigatran 150 mg b.i.d. for the duration of concomitant single or dual antiplatelet therapy	IIa

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2019 ESC Guidelines for Chronic coronary disease

Antithrombotic therapy in post-PCI patients with AF or another indication for OAC	
In patients who are eligible for a NOAC, it is recommended that a NOAC (apixaban 5 mg b.i.d., dabigatran 150 mg b.i.d., edoxaban 60 mg o.d., or rivaroxaban 20 mg o.d.) is used in preference to a VKA in combination with antiplatelet therapy.	I
After uncomplicated PCI, early cessation (≤1 week) of aspirin, and continuation of dual therapy with OAC and clopidogrel, should be considered if the risk of stent thrombosis is low or if concerns about bleeding risk prevail over concerns about risk of stent thrombosis, irrespective of the type of stent used.	IIa
Triple therapy with aspirin, clopidogrel, and an OAC for ≥1 month should be considered when the risk of stent thrombosis outweighs the bleeding risk, with the total duration (≤6 months) decided upon according to the assessment of these risks and clearly specified at hospital discharge.	IIa
Dual therapy with an OAC and either ticagrelor or prasugrel may be considered as an alternative to triple therapy with an OAC, aspirin, and clopidogrel in patients with a moderate or high risk of stent thrombosis, irrespective of the type of stent used.	IIb

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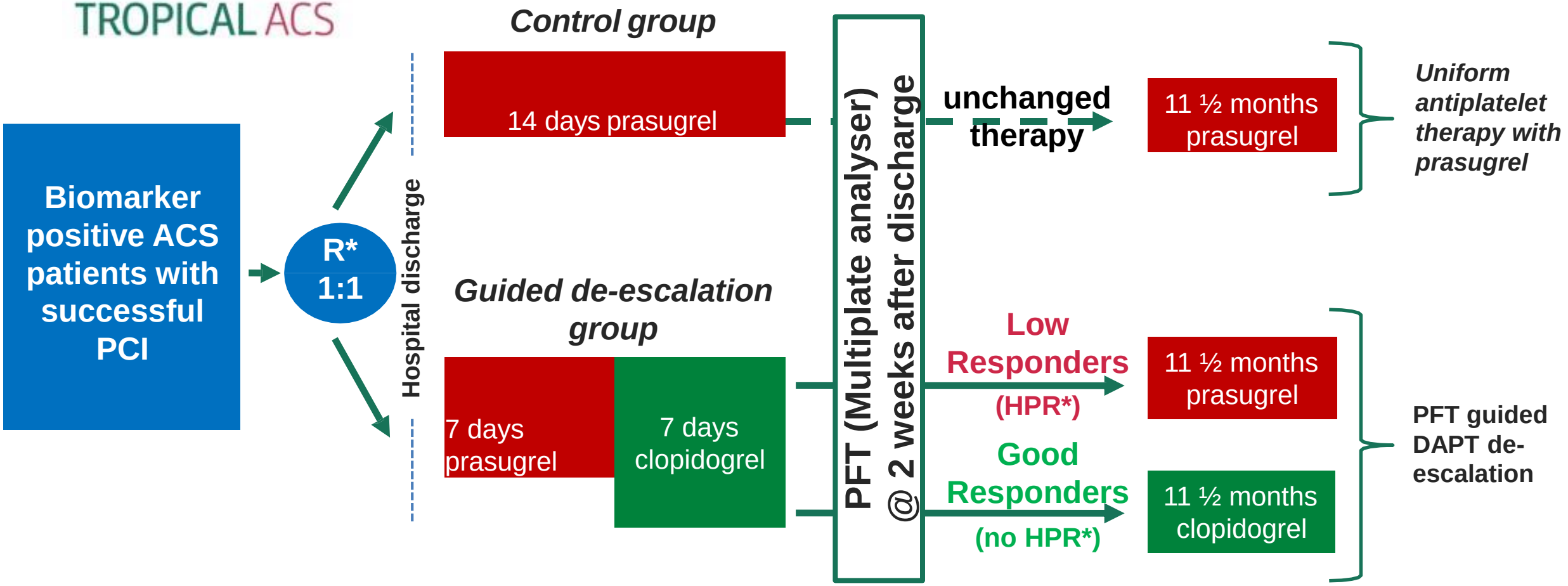
Framtidens trombocythämning

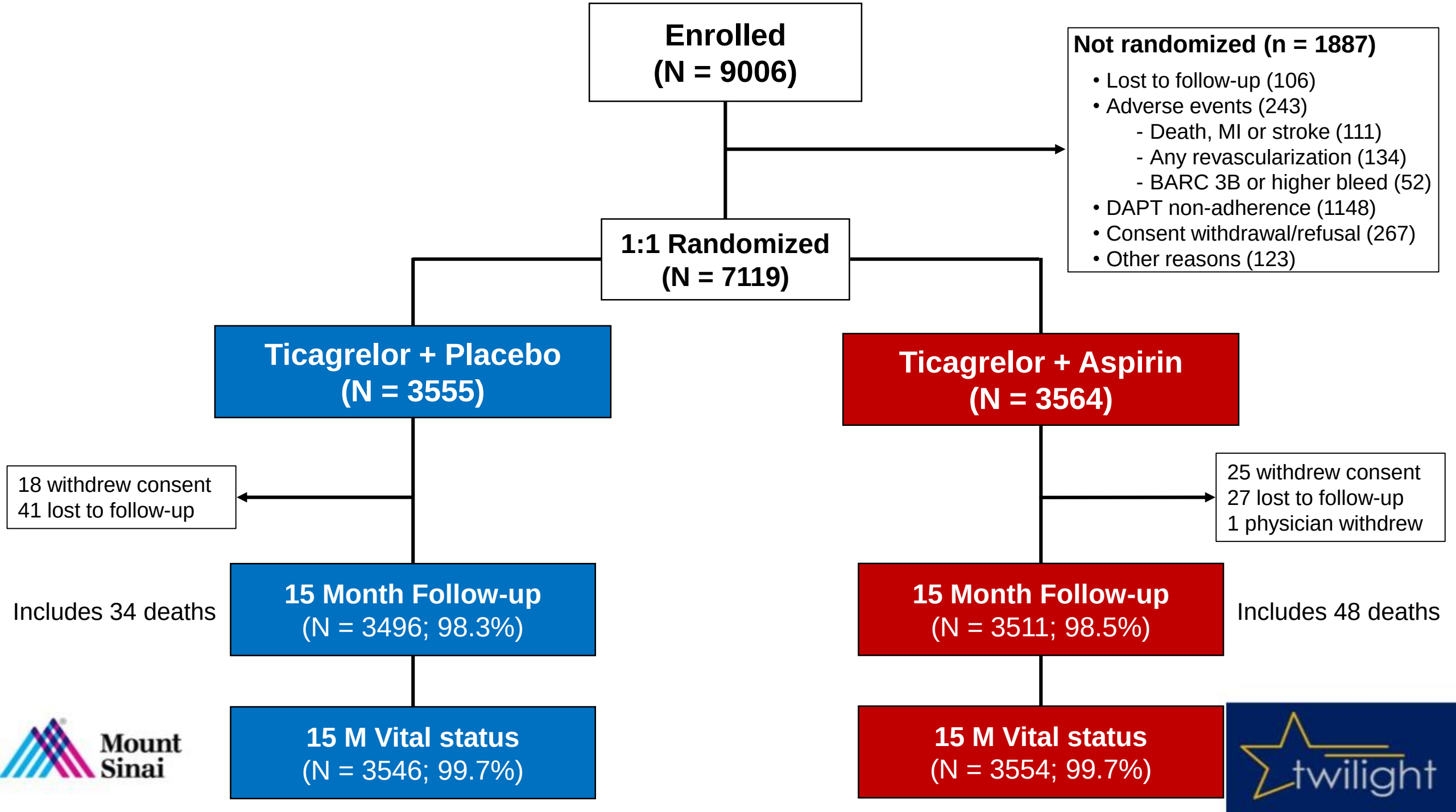
- Nedgradering (de-escalation) från Ticagrelor/prasugrel till clopidogrel efter den första (TROPICAL ACS – NEJM 2017)?
- Övergång till SAPT efter initial DAPT (Global Leaders)?
- Twilight-studien (ASA bort NEJM 2019)?

Trial Design



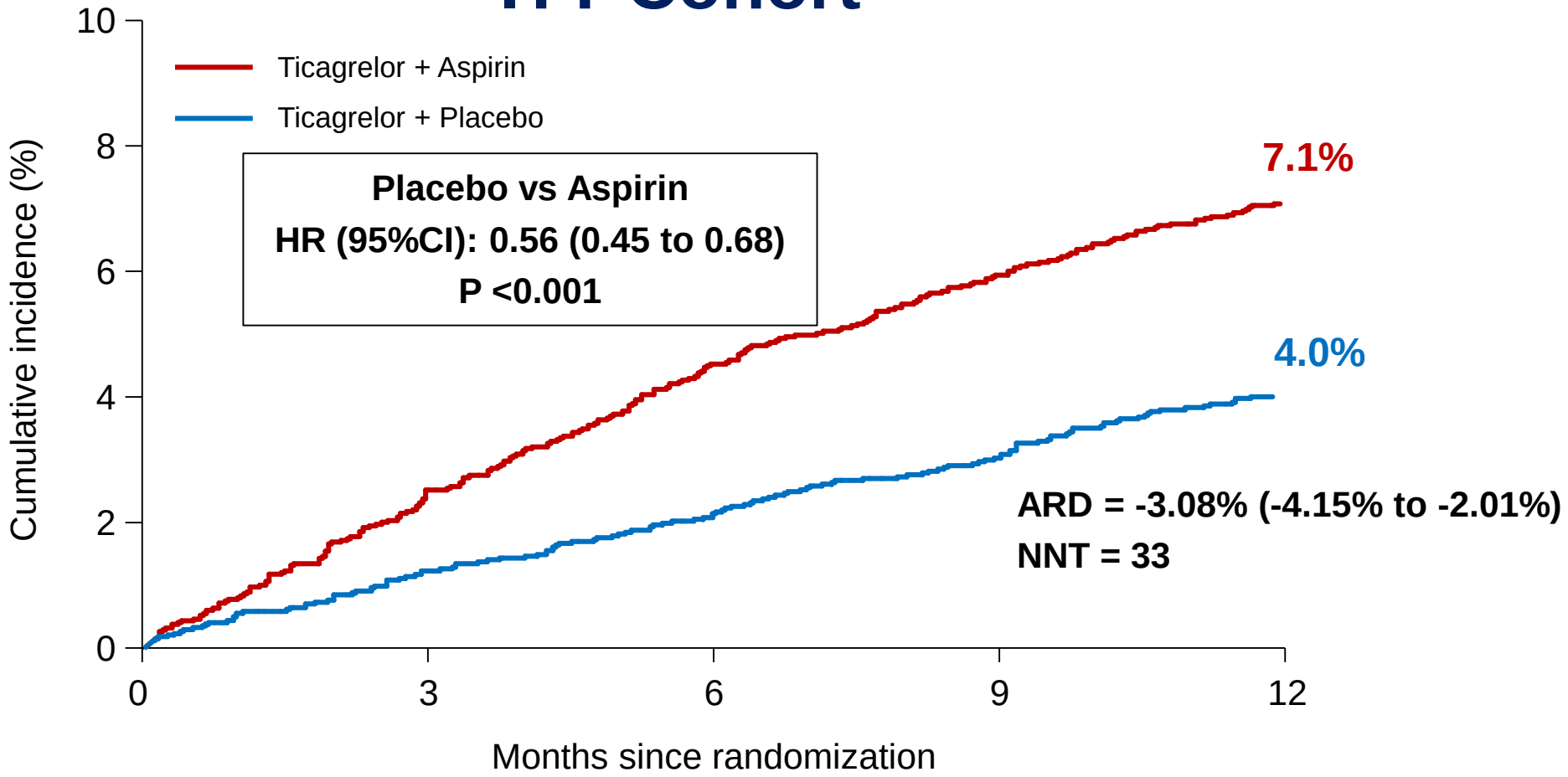
*HPR denotes high platelet reactivity

- For further details on TROPICAL-ACS trial design see: Sibbing et al., Thromb Haemost. 2017;117:188-195 -


Enrolled
(N = 9006)
Not randomized (n = 1887)
• Lost to follow-up (106)
• Adverse events (243)
- Death, MI or stroke (111)
- Any revascularization (134)
- BARC 3B or higher bleed (52)
• DAPT non-adherence (1148)
• Consent withdrawal/refusal (267)
• Other reasons (123)
1:1 Randomized
(N = 7119)
Ticagrelor + Placebo
(N = 3555)
Ticagrelor + Aspirin
(N = 3564)
18 withdrew consent
41 lost to follow-up
25 withdrew consent
27 lost to follow-up
1 physician withdrew
Includes 34 deaths
15 Month Follow-up
(N = 3496; 98.3%)
15 Month Follow-up
(N = 3511; 98.5%)
Includes 48 deaths
15 M Vital status
(N = 3546; 99.7%)
15 M Vital status
(N = 3554; 99.7%)
Mount Sinai
twilight

Primary Endpoint: BARC 2, 3 or 5 Bleeding

ITT Cohort



No. at risk					
Ticagrelor + Aspirin	3564	3454	3357	3277	3213
Ticagrelor + Placebo	3555	3474	3424	3366	3321

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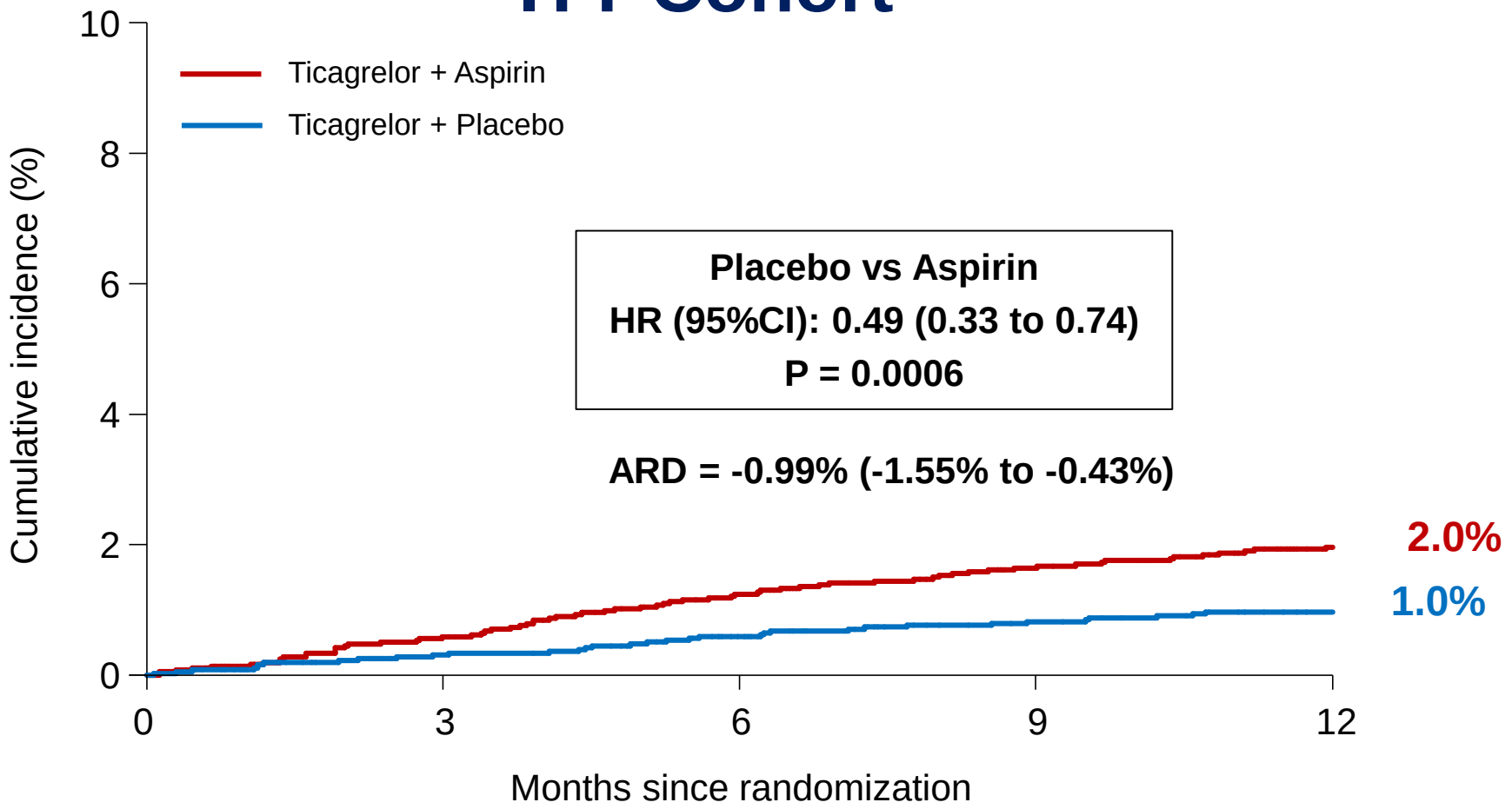
BARC 3 or 5 Bleeding

ITT Cohort



No. at risk					
Ticagrelor + Aspirin	3564	3516	3470	3426	3390
Ticagrelor + Placebo	3555	3504	3475	3440	3423

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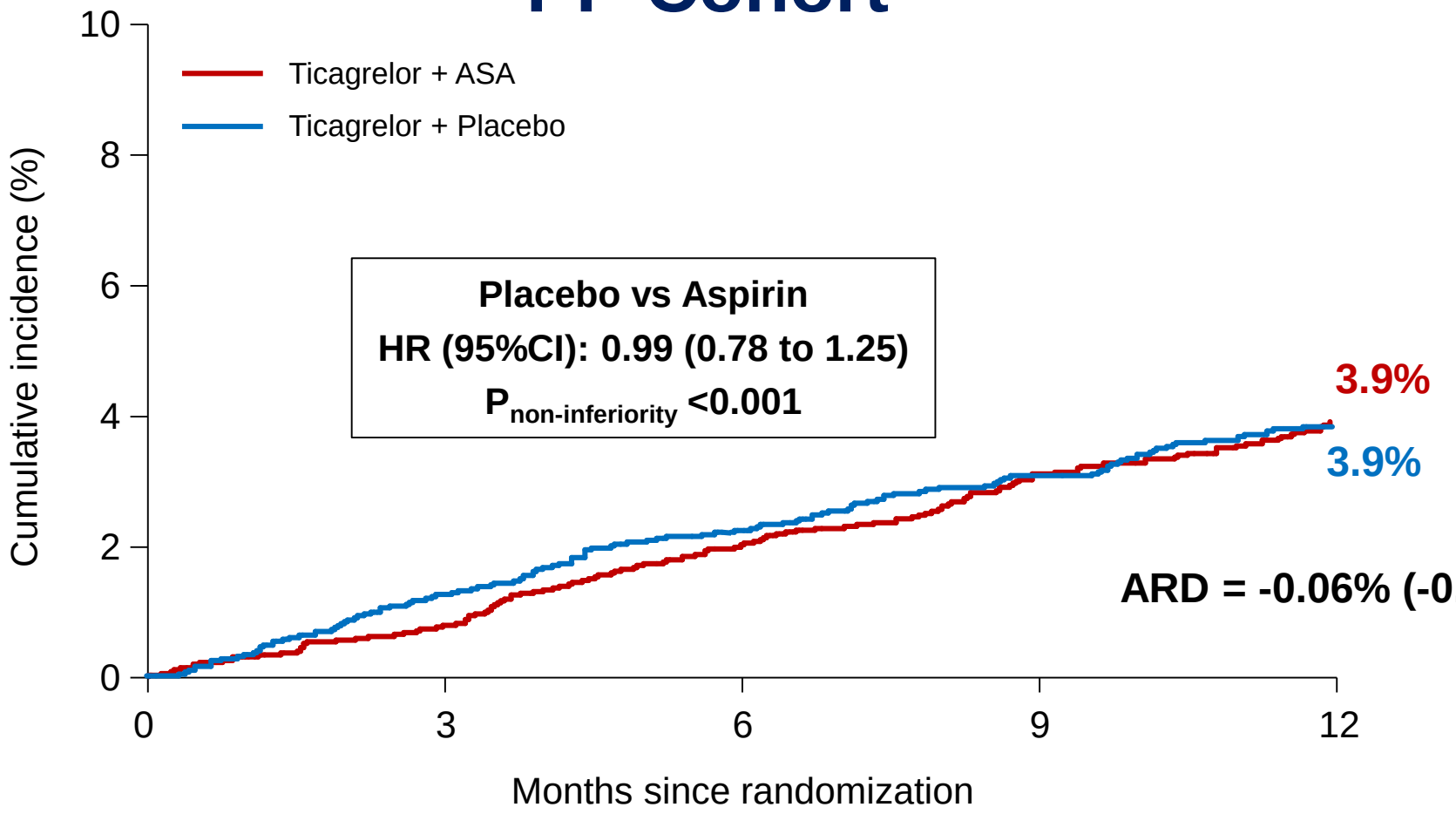
Key Secondary Endpoint: Death, MI or Stroke

PP Cohort



No. at risk					
Ticagrelor + Aspirin	3515	3466	3415	3361	3320
Ticagrelor + Placebo	3524	3457	3412	3365	3330

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twilight

Konklusion

- Dubbel behandling med NOAC + $P2Y_{12}$ hämmare är säkrare än trippelbehandling till patienter med FF och AKS, och den antiischemiska effekten är jämförbar
- Trippelbehandling så kort tid som möjligt
- NOAC dosering godkänd för stroke prevention skall uppmuntras
- Kunskapsluckor:
  - Temporärt uppehåll av NOAC vid PCI?
  - Vilken trombocythämmare är bäst vid dubbel behandling?
  - Optimal tidpunkt för uppehåll av DAPT efter PCI vid AKS eller stabil CAD?
  - Optimal tidpunkt för uppehåll av DAPT vid medicinskt behandlade AKS?