Update Antithrombotika bei Atherosklerose

Prof. Dr. Jan Steffel

Stv. Klinikdirektor, Klinik für Kardiologie

Leitender Arzt Rhythmologie

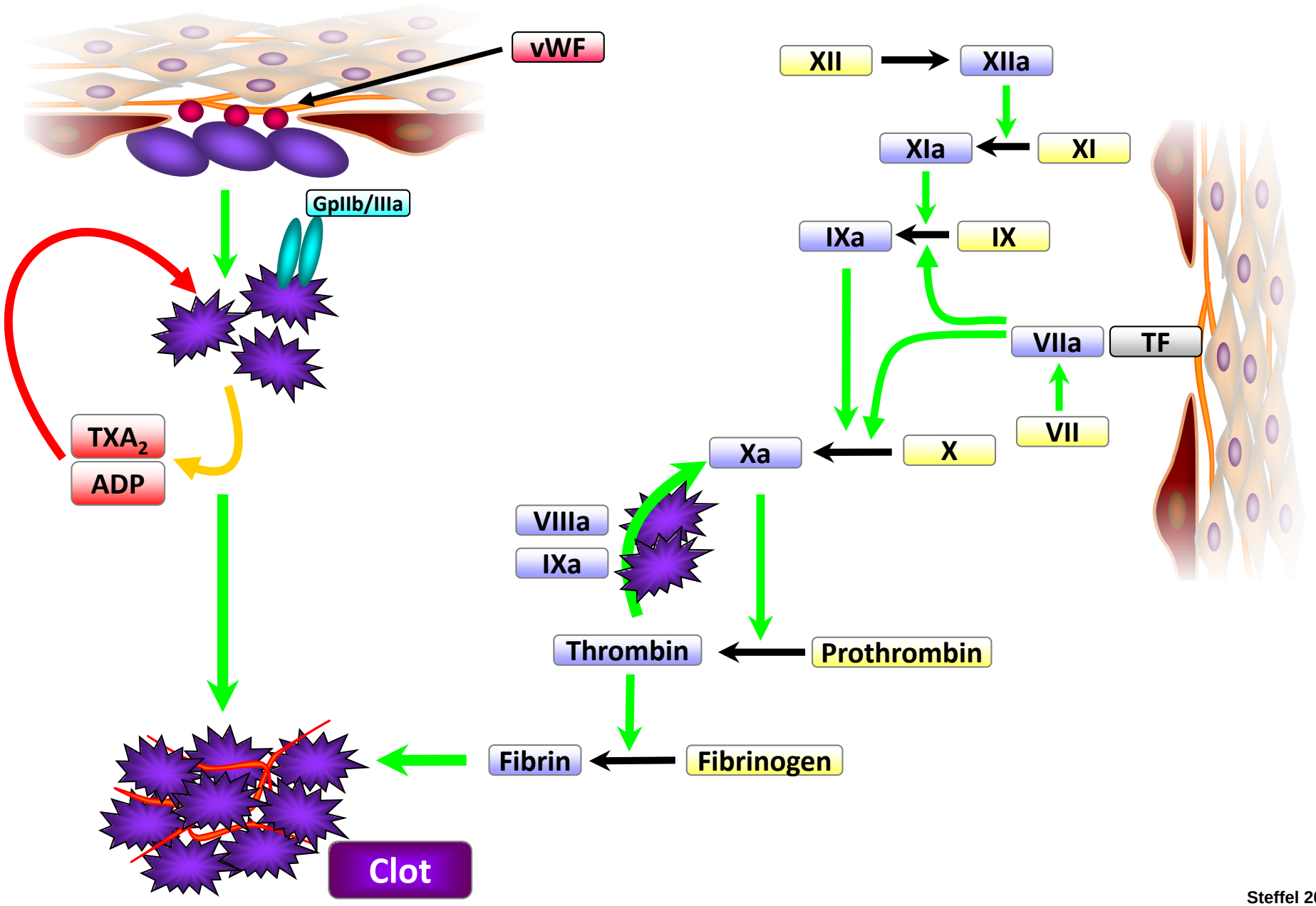
Universitätsspital Zürich

Chair, EHRA Education Committee

Disclosures

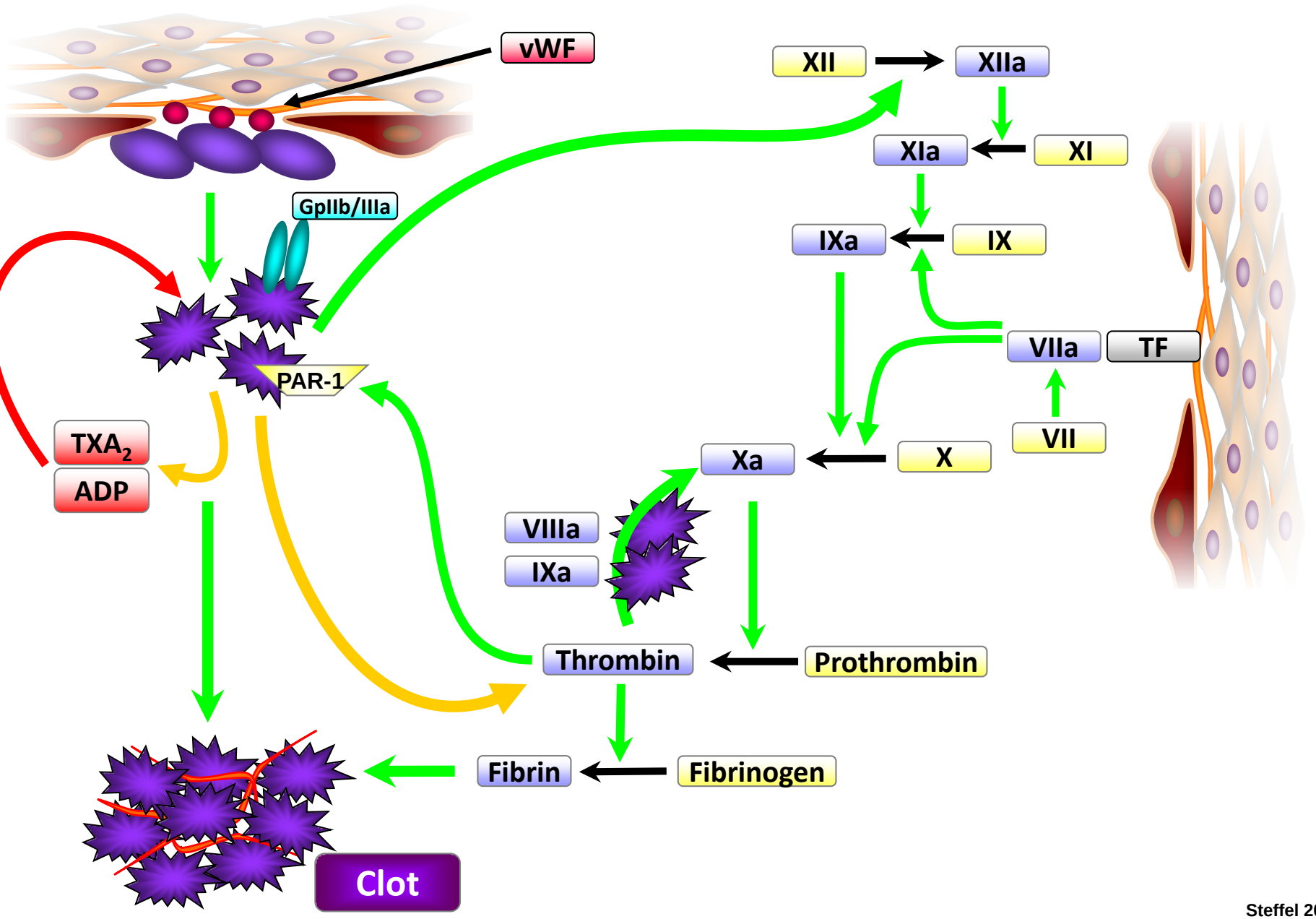
- Consulting / Speaker: Abbott, Amgen, Astra Zeneca, AtriCure, Bayer, Biosense Webster, Biotronik, BMS, Boehringer Ingelheim, Boston Scientific, Daiichi-Sankyo, Medscape, Medtronic, MSD, Novartis, Pfizer, Sanofi-Aventis, WebMD, Zoll
- Grants (through institution): Bayer, Biotronik, Boston Scientific, Daiichi-Sankyo, Medtronic, Abbott
- Ownership CorXL

(Patho-)physiology of Thrombus Formation



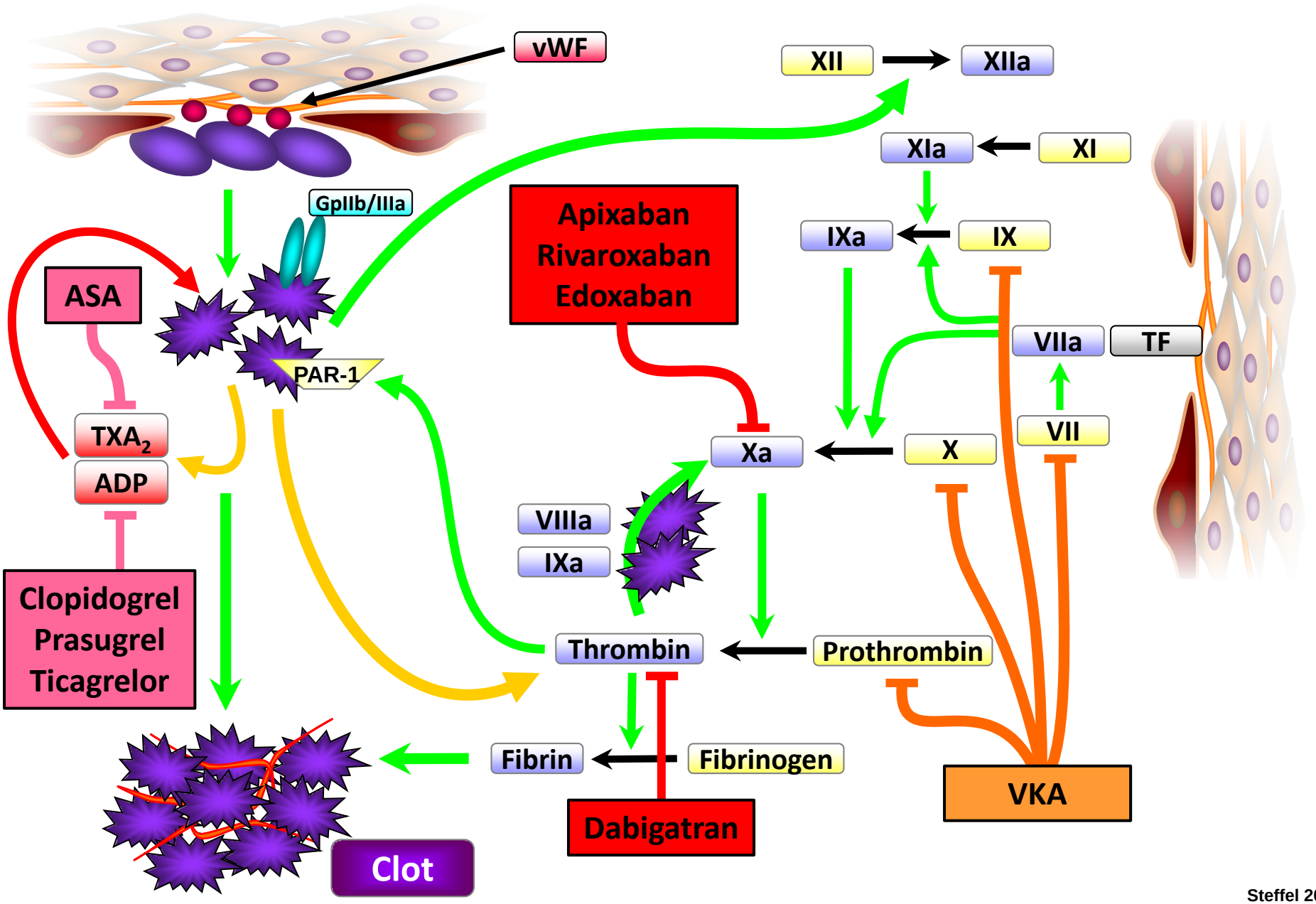
Steffel 2013

(Patho-)physiology of Thrombus Formation



Steffel 2013

(Patho-)physiology of Thrombus Formation

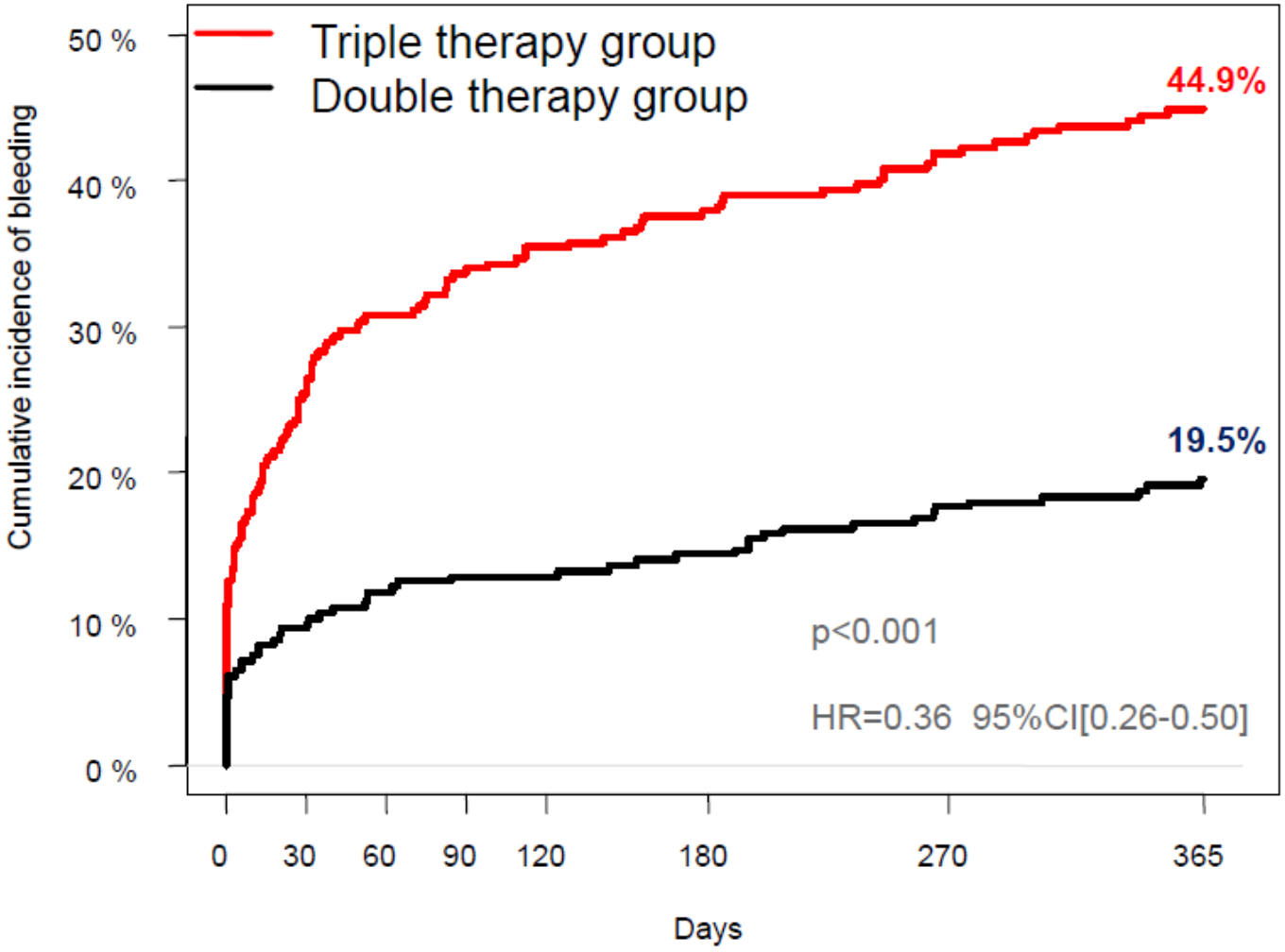


Steffel 2013

Zwei Situationen für Patienten mit Chronischem Coronarsyndrom (CCS)

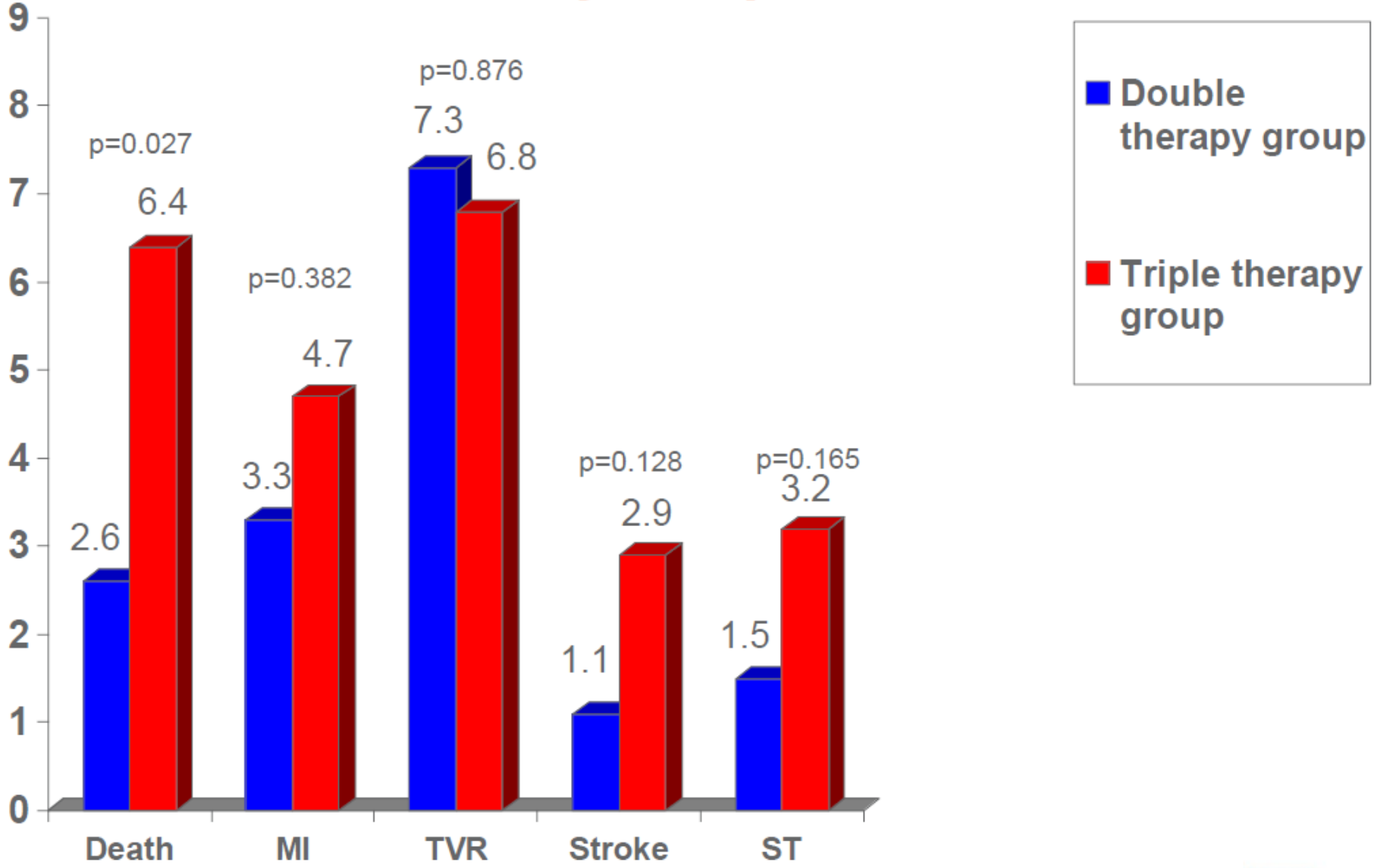
- Patient hat Vorhofflimmern
- Patient hat kein Vorhofflimmern

Primary Endpoint: Total number of bleeding events (TIMI criteria)



ZIEKENHUIS ST ANTONIUS

Secondary Endpoint

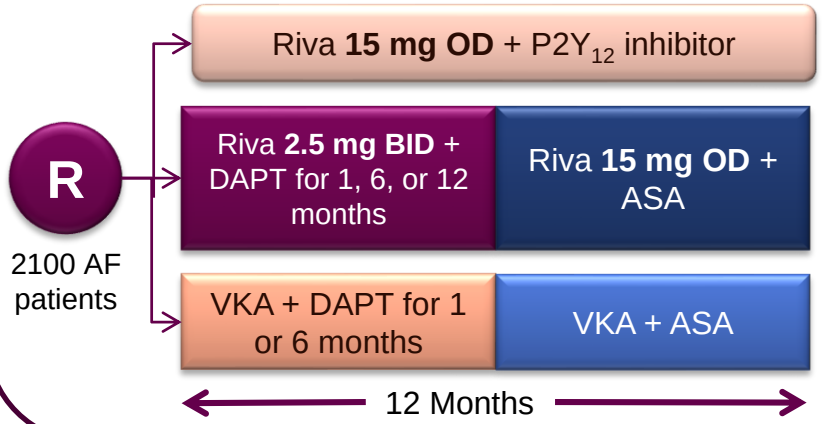


MI=any myocardial infarction; TVR= target vessel revascularisation (PCI + CABG); ST= stent thrombosis

NOAC AF-PCI clinical studies

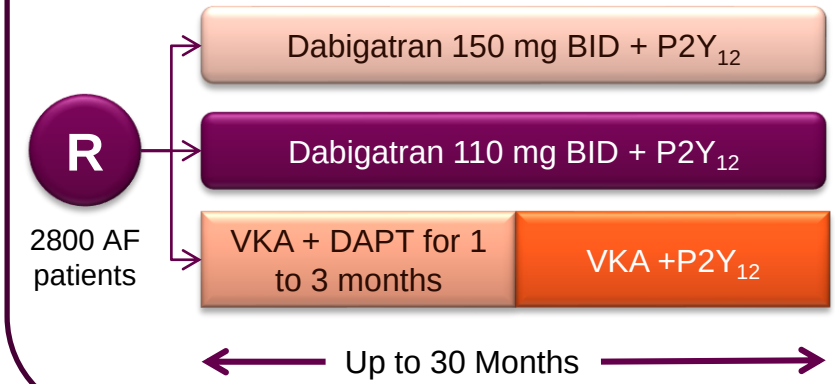
Pioneer AF-PCI - Rivaroxaban[1]

Primary endpoint: TIMI major, minor bleeding or bleeding requiring medical attention (for 12 mo)



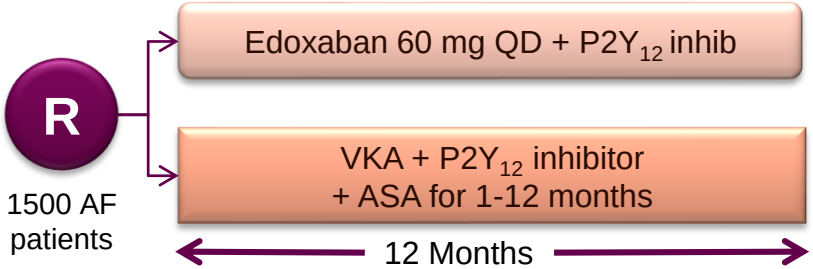
RE-DUAL AF-PCI - Dabigatran[2]

Primary endpoint: Time to first major or clinically relevant non-major bleeding event (ISTH)



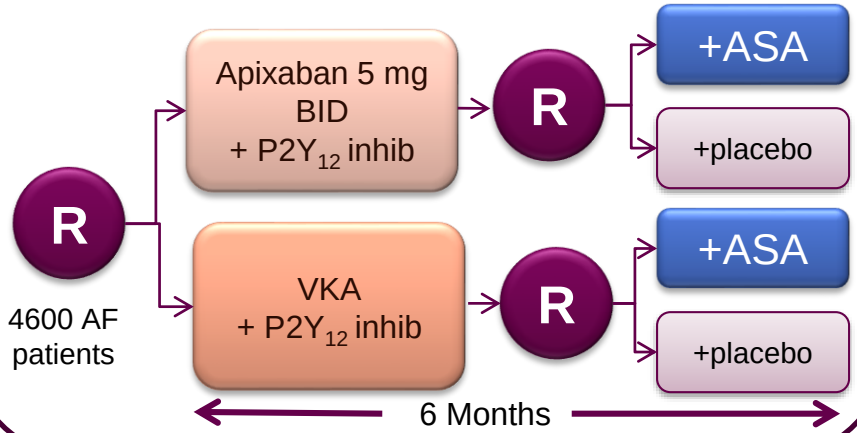
ENTRUST AF-PCI - Edoxaban[3]

Primary endpoint: ISTH Major and clinically relevant non-major bleeding.



AUGUSTUS AF-PCI - Apixaban[4]

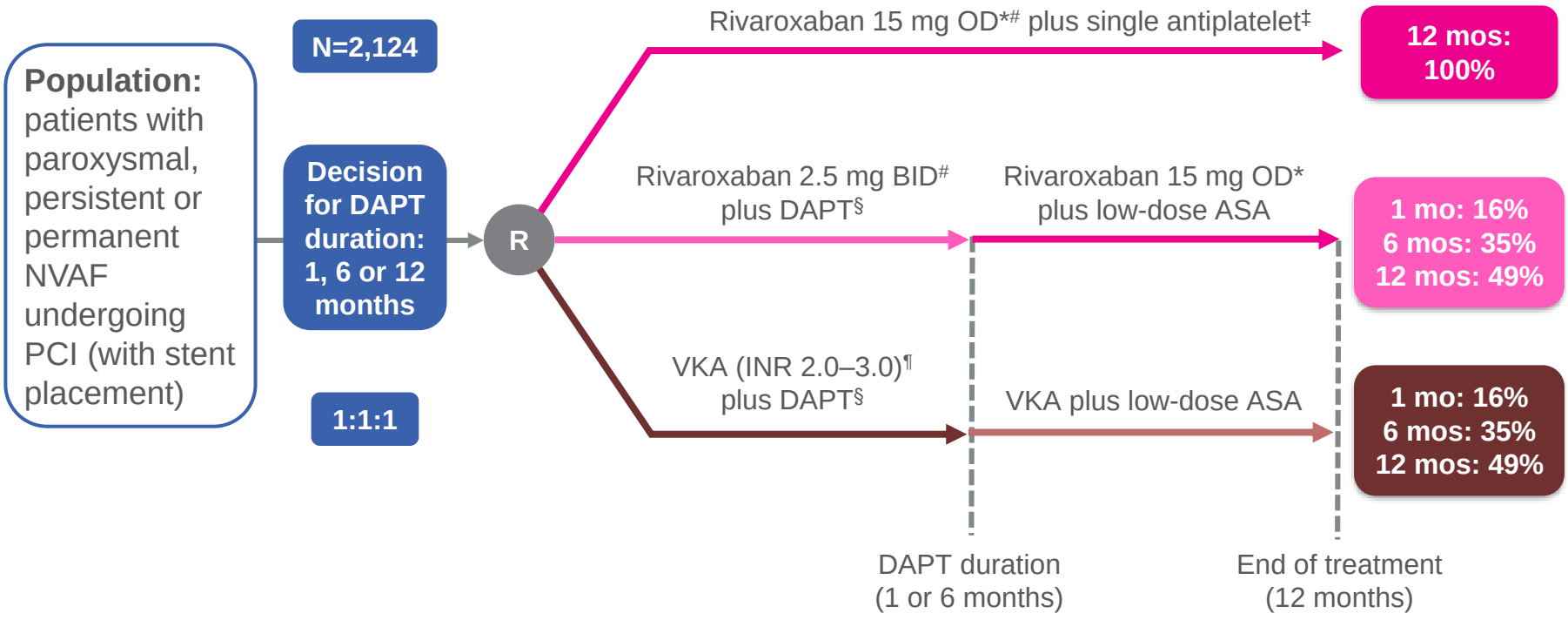
Primary endpoint: Major/clinically relevant bleeding (for 6 months)



1. Gibson et al. NEJM 2016. 2. Cannon et al. NEJM 2017. 3. ClinicalTrials.gov. NCT02866175 4. ClinicalTrials.gov. NCT02415400.

PIONEER-AF – AF patients undergoing PCI

Design: An open-label, randomized, controlled phase IIIb safety study



*CrCl 30–49 ml/min: 10 mg OD; #first dose 72–96 hours after sheath removal; ‡clopidogrel (75 mg daily) (alternative use of prasugrel or ticagrelor allowed, but capped at 15%); §ASA (75–100 mg daily) plus clopidogrel (75 mg daily) (alternative use of prasugrel or ticagrelor allowed, but capped at 15%); ¶first dose 12–72 hours after sheath removal

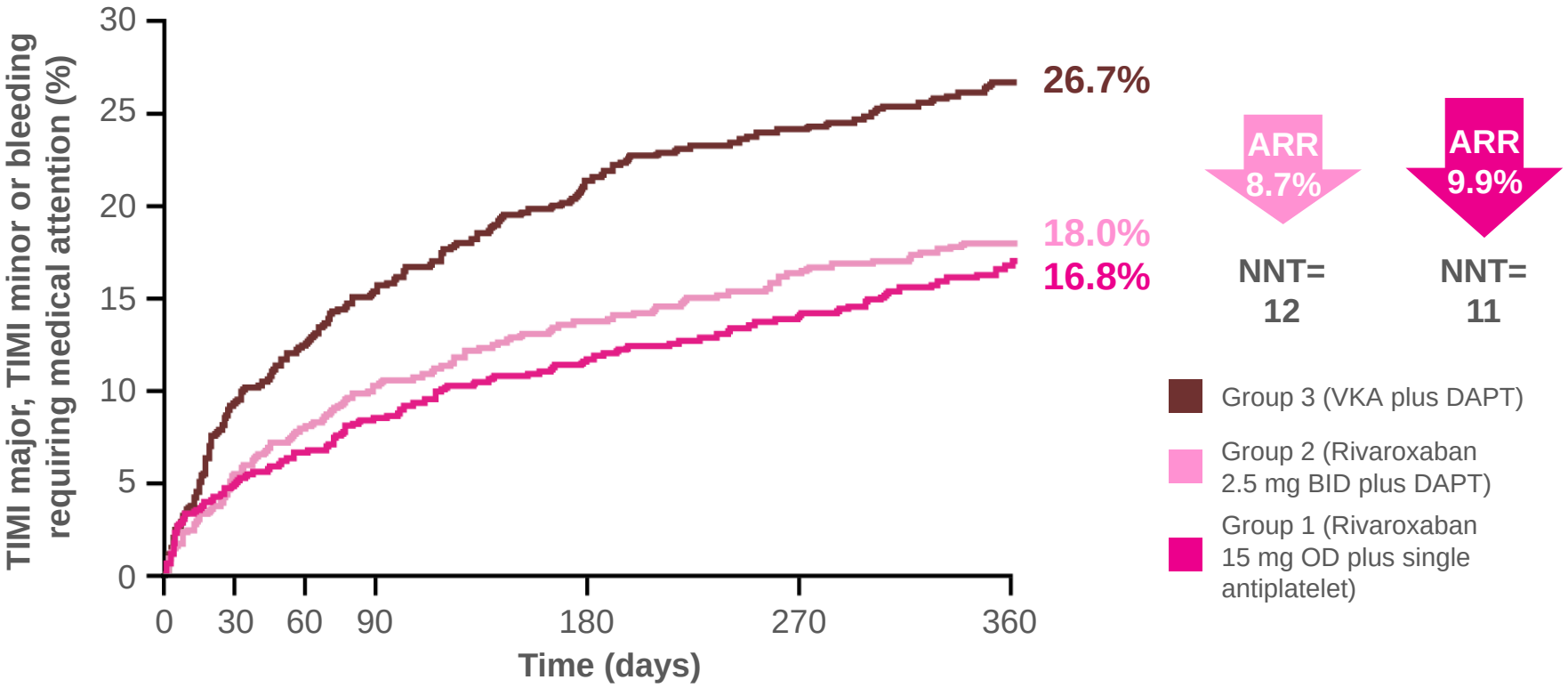
1. Janssen Scientific Affairs, LLC. 2016. https://clinicaltrials.gov/ct2/show/NCT01830543 [accessed 10 Oct 2016];
2. Gibson CM *et al*, *Am Heart J* 2015;169:472–478e5; 3. Gibson CM et al, *New Engl J Med* 2016; doi: 10.1056/NEJMoa1611594

PIONEER AF-PCI

PIONEER AF – Safety outcomes

Rivaroxaban 15 mg OD plus single antiplatelet vs VKA plus DAPT: HR=0.59; (95% CI 0.47–0.76); *p*<0.001

Rivaroxaban 2.5 mg BID plus DAPT vs VKA plus DAPT: HR=0.63 (95% CI 0.50–0.80); *p*<0.001



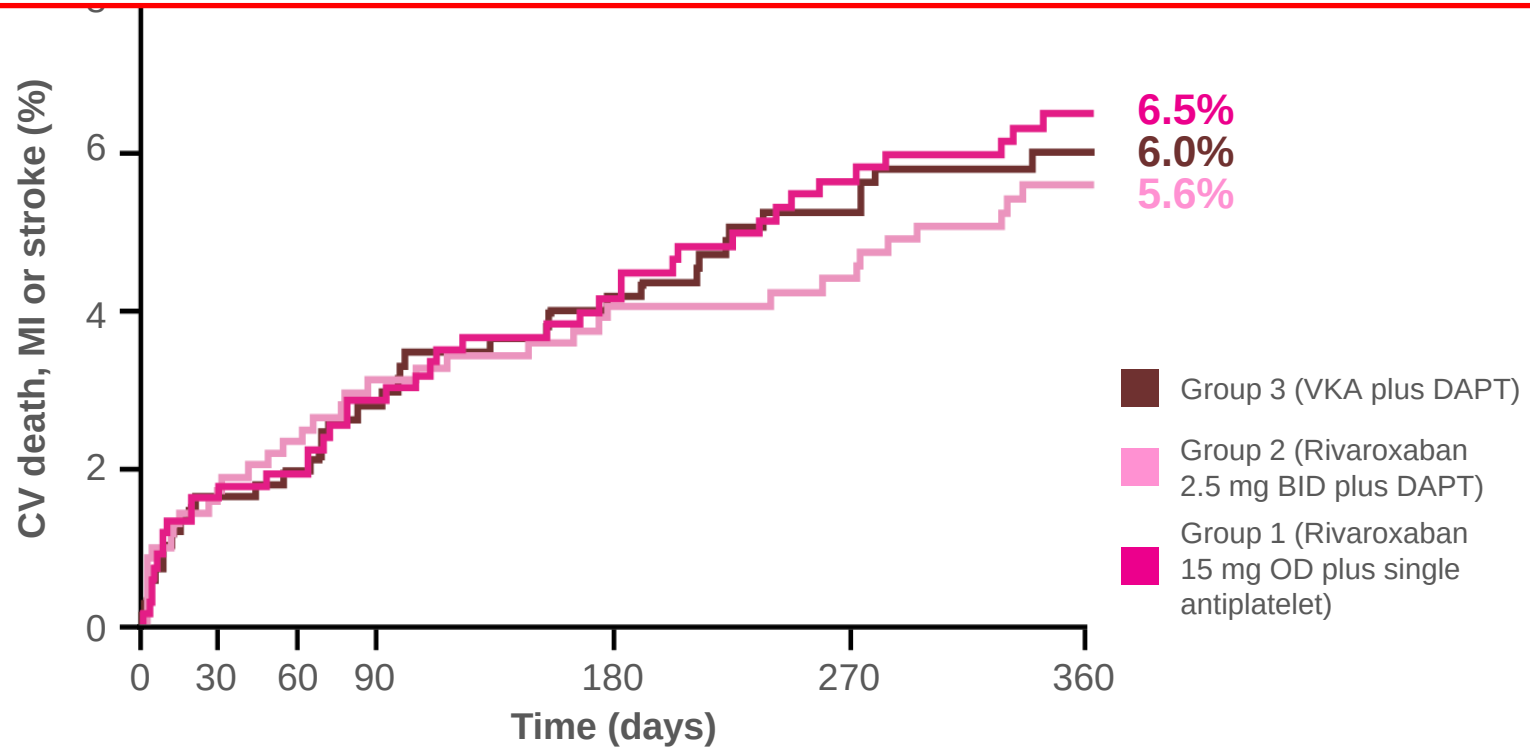
Gibson CM et al, *New Engl J Med* 2016; doi: 10.1056/NEJMoa1611594

PIONEER AF – Efficacy outcomes

Rivaroxaban 15 mg OD plus single antiplatelet vs VKA plus DAPT: HR=1.08; (95% CI 0.69–1.68); *p*=0.750

Rivaroxaban 2.5 mg BID plus DAPT vs VKA plus DAPT: HR=0.93 (95% CI 0.59–1.48); *p*=0.765

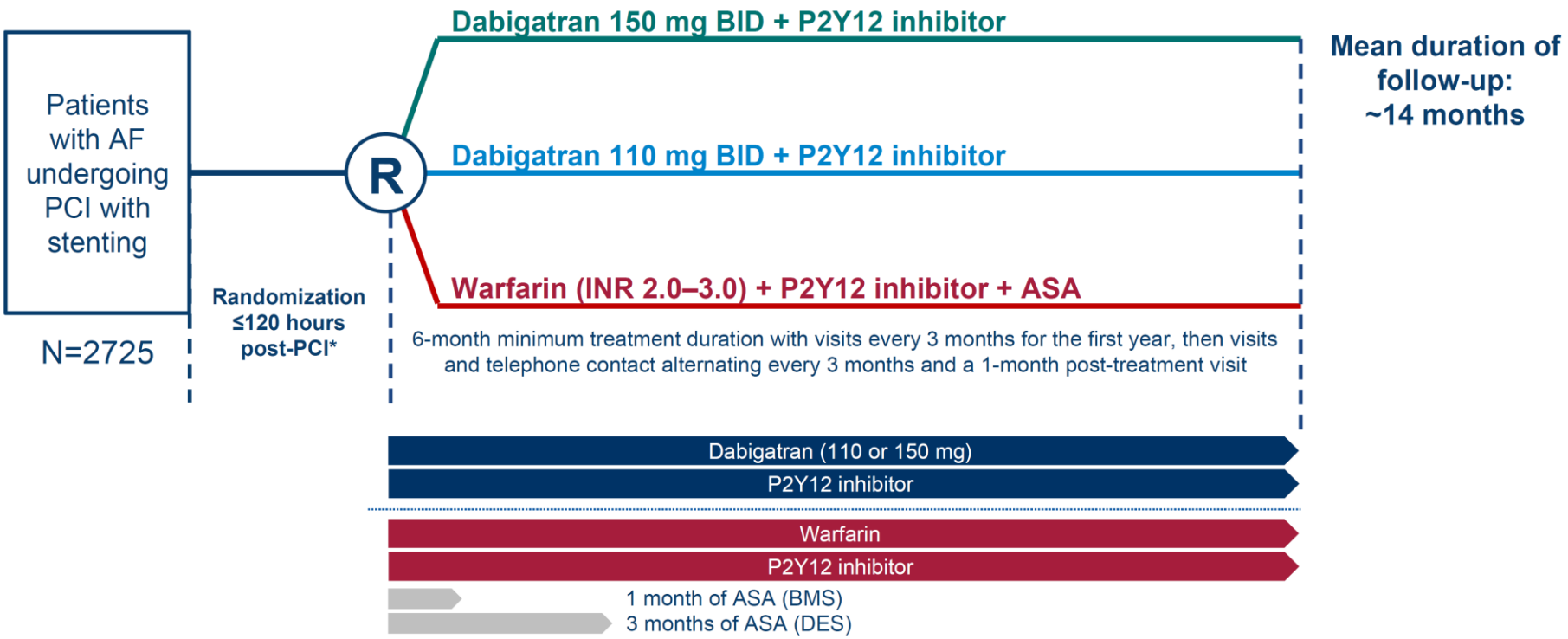
BUT: Not powered for efficacy



*Trial not powered to definitively demonstrate either superiority or non-inferiority for efficacy endpoints

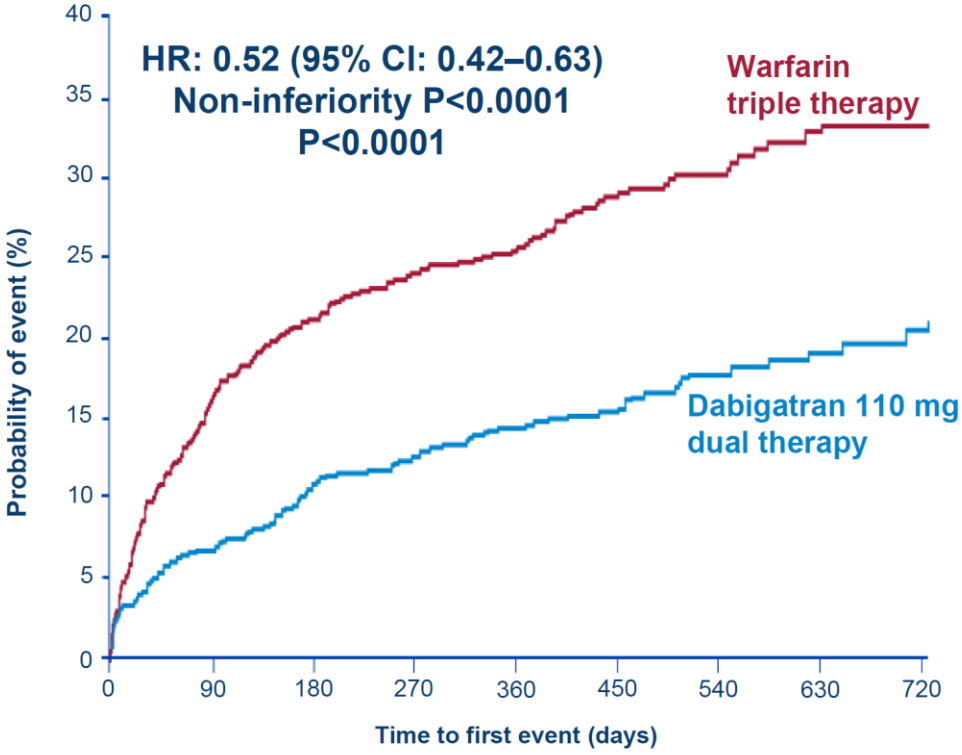
Gibson CM et al, *New Engl J Med* 2016; doi: 10.1056/NEJMoa1611594

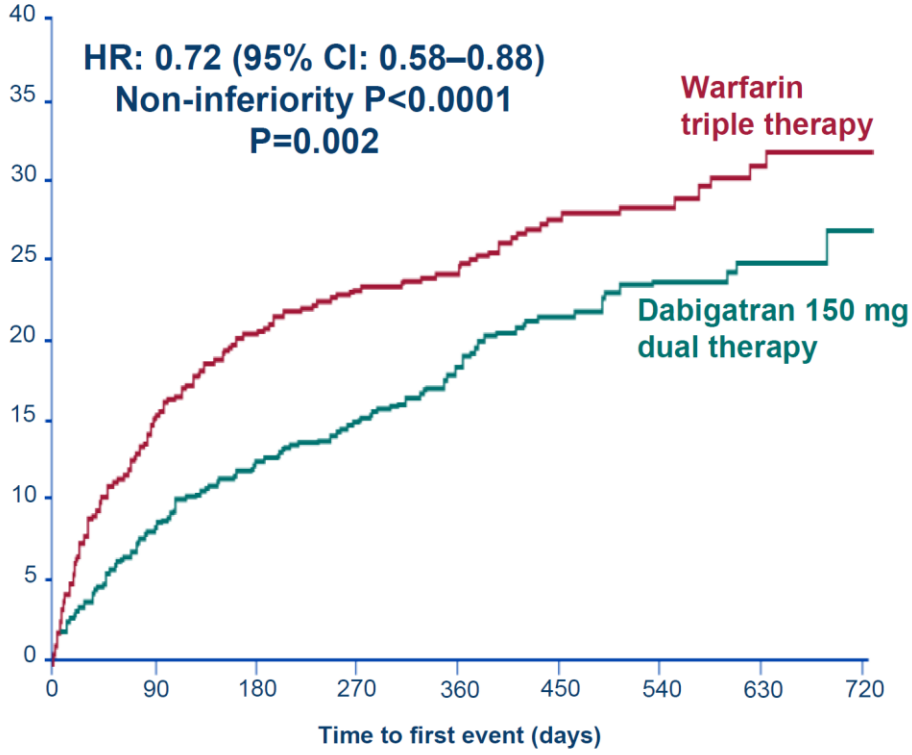
RE-DUAL PCI



Cannon et al., NEJM 2017

RE-DUAL PCI

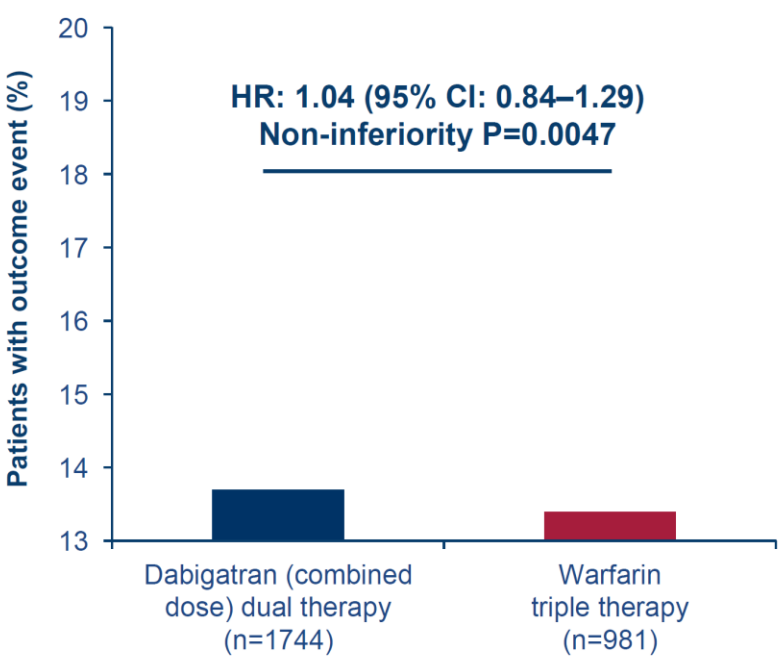


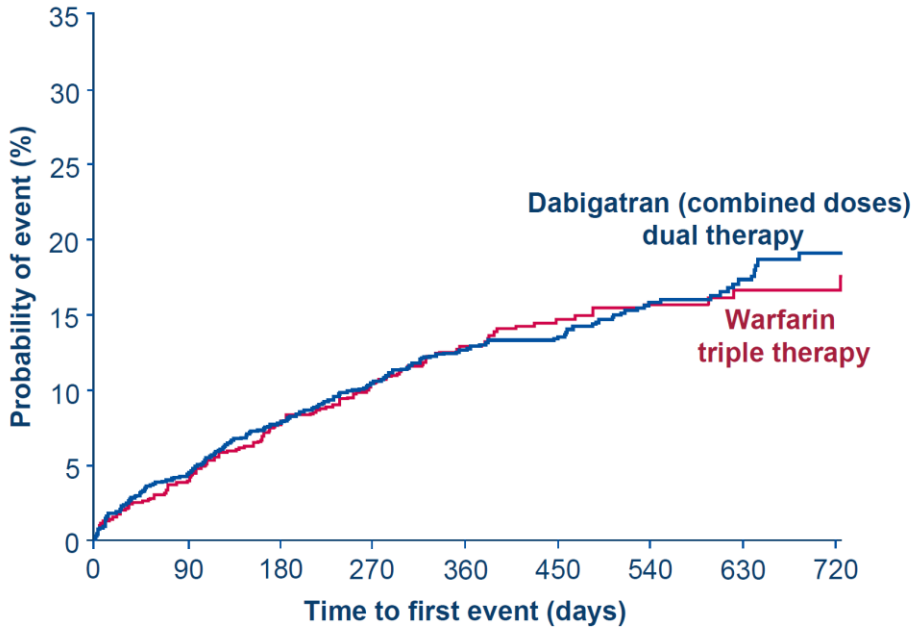


Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event

Cannon et al., NEJM 2017

RE-DUAL PCI





Time to death or thromboembolic event, or unplanned revascularization

Cannon et al., NEJM 2017

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation

Renato D. Lopes, M.D., Ph.D., Gretchen Heizer, M.S., Ronald Aronson, M.D., Amit N. Vora, M.D., M.P.H., Tyler Massaro, Ph.D., Roxana Mehran, M.D., Shaun G. Goodman, M.D., Stephan Windecker, M.D., Harald Darius, M.D., Jia Li, Ph.D., Oleg Averkov, M.D., Ph.D., M. Cecilia Bahit, M.D., Otavio Berwanger, M.D., Ph.D., Andrzej Budaj, M.D., Ph.D., Ziad Hijazi, M.D., Ph.D., Alexander Parkhomenko, M.D., Ph.D., Peter Sinnaeve, M.D., Ph.D., Robert F. Storey, M.D., Holger Thiele, M.D., Dragos Vinereanu, M.D., Ph.D., Christopher B. Granger, M.D., and John H. Alexander, M.D., M.H.S., for the AUGUSTUS Investigators*

Trial Design

INCLUSION
- Atrial fibrillation (prior, persistent, >6 hr)
  - Physician decision for OAC
- Acute coronary syndrome or PCI
  - Planned $P2Y_{12}$ inhibitor for ≥6 months

Randomize
n=4600
patients

EXCLUSION
- Contraindication to DAPT
- Other reason for VKA (prosthetic valve, moderate / severe mitral stenosis)

Apixaban 5 mg BID
Apixaban 2.5 mg BID in selected patients

Open Label

VKA
(INR 2–3)

Aspirin for all on the day of ACS or PCI
Aspirin versus placebo after randomization

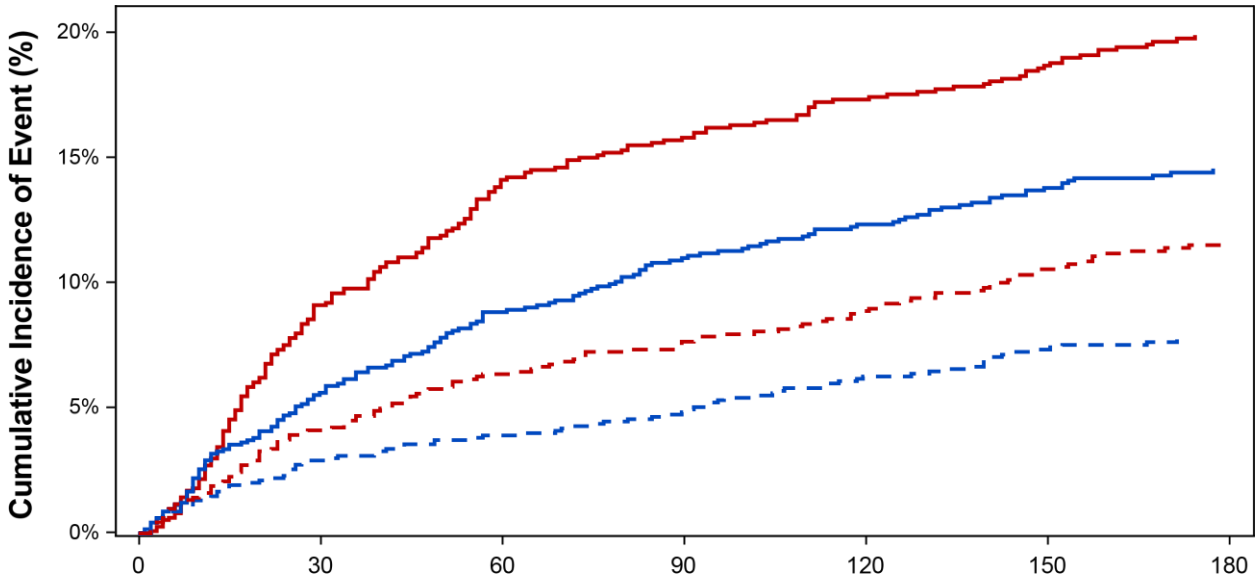
Aspirin — *Double Blind* — **Placebo**

Aspirin — *Double Blind* — **Placebo**

Primary outcome: ISTH major / CRNM bleeding
Secondary outcome(s): death / hospitalization, death / ischemic events

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

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 + DAPT (18.7%)

Apixaban + DAPT (13.8%)

VKA + P2Y12i (10.9%)

Apixaban + P2Y12i (7.3%)

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

Lopes et al., NEJM 2019

Ischemic Outcomes
Apixaban vs. VKA

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 al., NEJM 2019

Ischemic Outcomes
DAPT vs. P2Y12 inhibitor

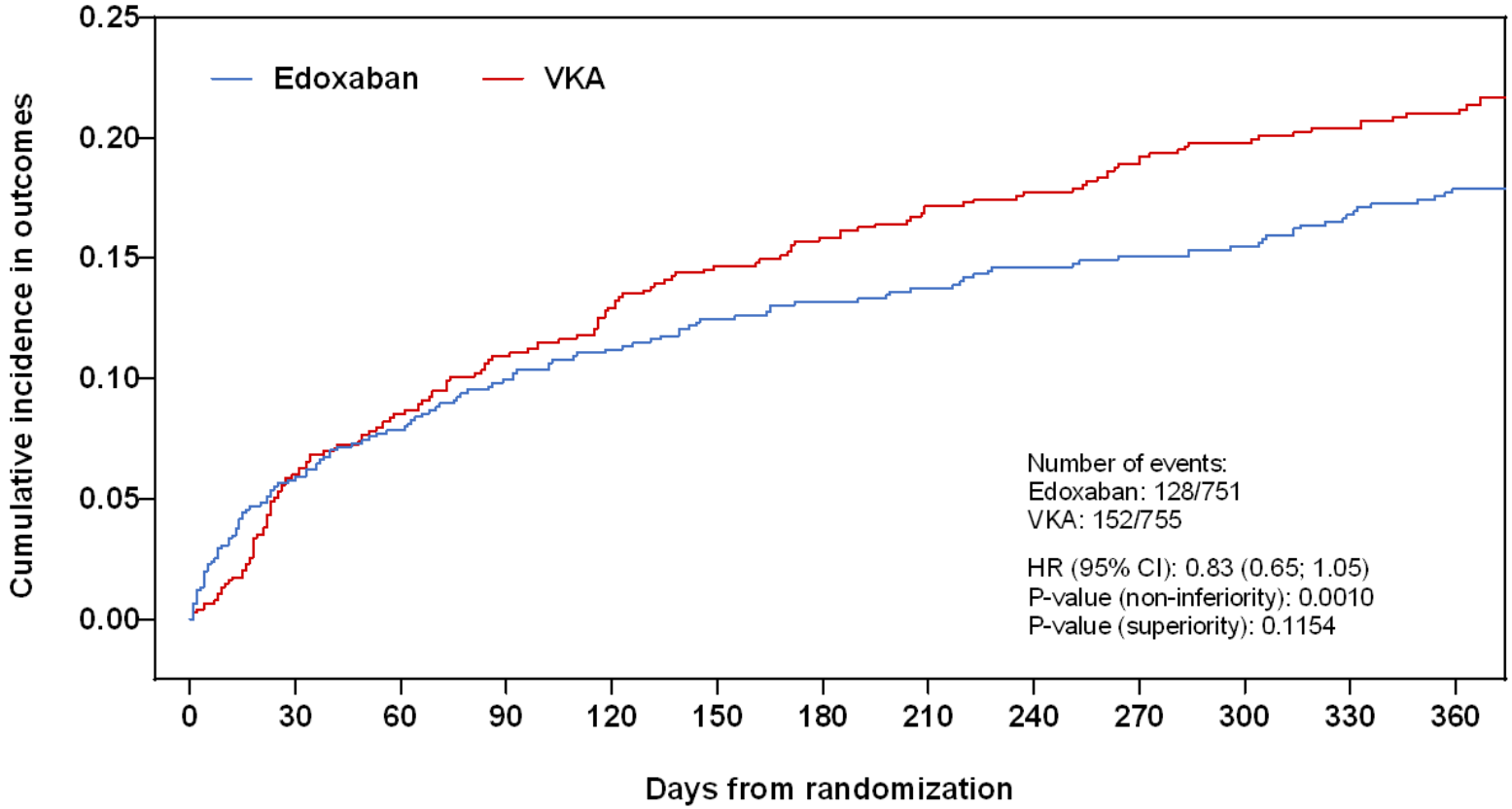
Endpoint	DAPT (N=2307)	P2Y12i (N=2307)	HR (95% CI)
Death / Ischemic Events (%)	6.5	7.3	0.89 (0.71–1.11)
Death (%)	3.1	3.4	0.91 (0.66–1.26)
CV Death (%)	2.3	2.5	0.92 (0.63–1.33)
Stroke (%)	0.9	0.8	1.06 (0.56–1.98)
Myocardial Infarction (%)	2.9	3.6	0.81 (0.59–1.12)
Definite or Probable Stent Thrombosis (%)	0.5	0.9	0.52 (0.25–1.08)
Urgent Revascularization (%)	1.6	2.0	0.79 (0.51–1.21)
Hospitalization (%)	25.4	23.4	1.10 (0.98–1.24)

Lopes et al., NEJM 2019

Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial

Pascal Vranckx, Marco Valgimigli, Lars Eckardt, Jan Tijssen, Thorsten Lewalter, Giuseppe Gargiulo, Valerii Batushkin, Gianluca Campo, Zoreslava Lysak, Igor Vakaliuk, Krzysztof Milewski, Petra Laeis, Paul-Egbert Reimitz, Rüdiger Smolnik, Wolfgang Zierhut, Andreas Goette

ENTRUST-AF PCI – Primary Endpoint (ITT)



Number at risk:

EDOXABAN	751	688	665	646	629	618	609	600	590	584	575	565	506
VKA	755	678	648	625	603	588	578	568	561	552	543	538	485

Vranckx et al., Lancet 2019

NOAC AF PCI – Meta analysis

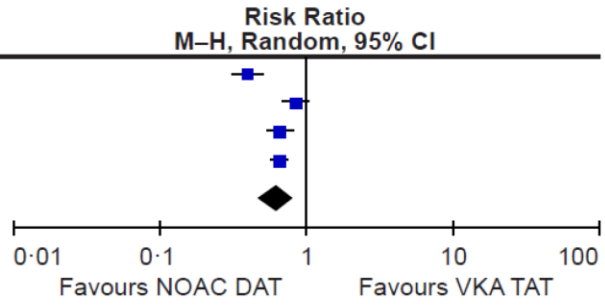
Figure S3: Research in context: Forest plots for safety and efficacy outcomes.

ISTH Major or Clinically Relevant Non-Major Bleeding

Study or Subgroup	NOAC DAT Events	NOAC DAT Total	VKA TAT Events	VKA TAT Total	Weight	Risk Ratio M–H, Random, 95% CI
AUGUSTUS	84	1143	210	1123	23·7%	0·39 (0·31, 0·50)
ENTRUST AF-PCI	128	751	152	755	24·7%	0·85 (0·68, 1·05)
PIONEER AF-PCI	117	696	178	697	24·8%	0·66 (0·53, 0·81)
RE-DUAL PCI	305	1744	264	981	26·8%	0·65 (0·56, 0·75)
Total (95% CI)		**4334**		**3556**	**100·0%**	**0·62 (0·47, 0·81)**
Total events	634		804			

Heterogeneity: $Tau^2 = 0·07$; $Chi^2 = 22·84$, df = 3 (P <0·0001); $I^2 = 87\%$

Test for overall effect: Z = 3·47 (P = 0·0005)

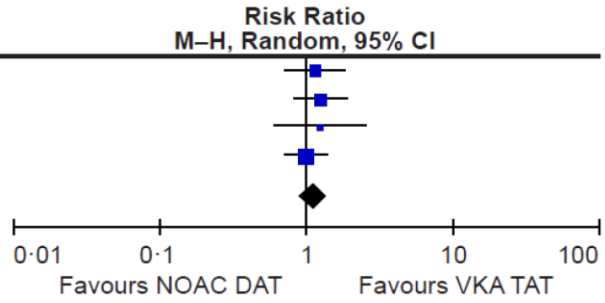


All-Cause Death

Study or Subgroup	NOAC DAT Events	NOAC DAT Total	VKA TAT Events	VKA TAT Total	Weight	Risk Ratio M–H, Random, 95% CI
AUGUSTUS	39	1153	34	1154	23·4%	1·15 (0·73, 1·81)
ENTRUST AF-PCI	46	751	37	755	27·1%	1·25 (0·82, 1·90)
PIONEER AF-PCI	16	694	13	695	9·2%	1·23 (0·60, 2·54)
RE-DUAL PCI	85	1744	48	981	40·3%	1·00 (0·71, 1·41)
Total (95% CI)		**4342**		**3585**	**100·0%**	**1·12 (0·90, 1·39)**
Total events	186		132			

Heterogeneity: $Tau^2 = 0·00$; $Chi^2 = 0·78$, df = 3 (P = 0·85); $I^2 = 0\%$

Test for overall effect: Z = 0·99 (P = 0·32)



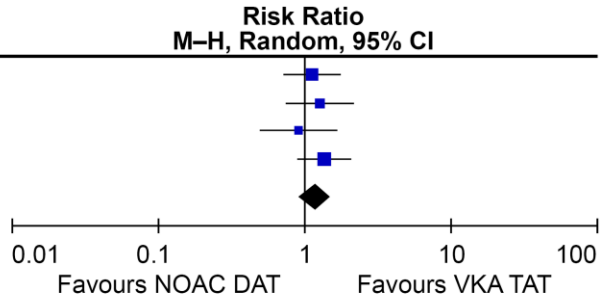
Vranckx et al., Lancet 2019 (Supplement)

NOAC AF PCI – Meta analysis

Myocardial Infarction

Study or Subgroup	NOAC DAT Events	Total	VKA TAT Events	Total	Weight	Risk Ratio M–H, Random, 95% CI
AUGUSTUS	38	1153	34	1154	29.3%	1.12 (0.71, 1.76)
ENTRUST AF-PCI	29	751	23	755	21.0%	1.27 (0.74, 2.17)
PIONEER AF-PCI	19	694	21	695	16.2%	0.91 (0.49, 1.67)
RE-DUAL PCI	70	1744	29	981	33.5%	1.36 (0.89, 2.08)
Total (95% CI)		**4342**		**3585**	**100.0%**	**1.18 (0.93, 1.52)**
Total events	156		107			

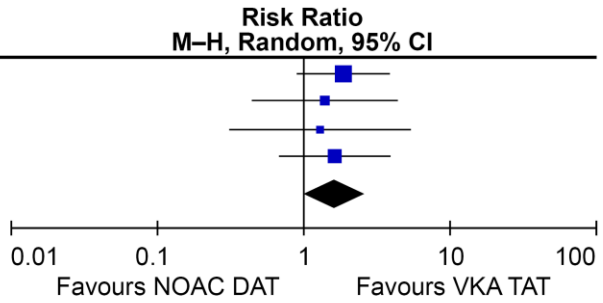
Heterogeneity: Tau² = 0.00; Chi² = 1.25, df = 3 (P = 0.74); I² = 0%
Test for overall effect: Z = 1.34 (P = 0.18)



Stent Thrombosis

Study or Subgroup	NOAC DAT Events	Total	VKA TAT Events	Total	Weight	Risk Ratio M–H, Random, 95% CI
AUGUSTUS	21	1153	12	1154	40.0%	1.75 (0.87, 3.54)
ENTRUST AF-PCI	8	751	6	755	17.9%	1.34 (0.47, 3.84)
PIONEER AF-PCI	5	694	4	695	11.6%	1.25 (0.34, 4.64)
RE-DUAL PCI	22	1744	8	981	30.6%	1.55 (0.69, 3.46)
Total (95% CI)		**4342**		**3585**	**100.0%**	**1.55 (0.99, 2.41)**
Total events	56		30			

Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 3 (P = 0.96); I² = 0%
Test for overall effect: Z = 1.92 (P = 0.06)



Vranckx et al., Lancet 2019 (Supplement)

ESC European Society of Cardiology

European Heart Journal (2018) **00**, 1–64
doi:10.1093/eurheartj/ehy136

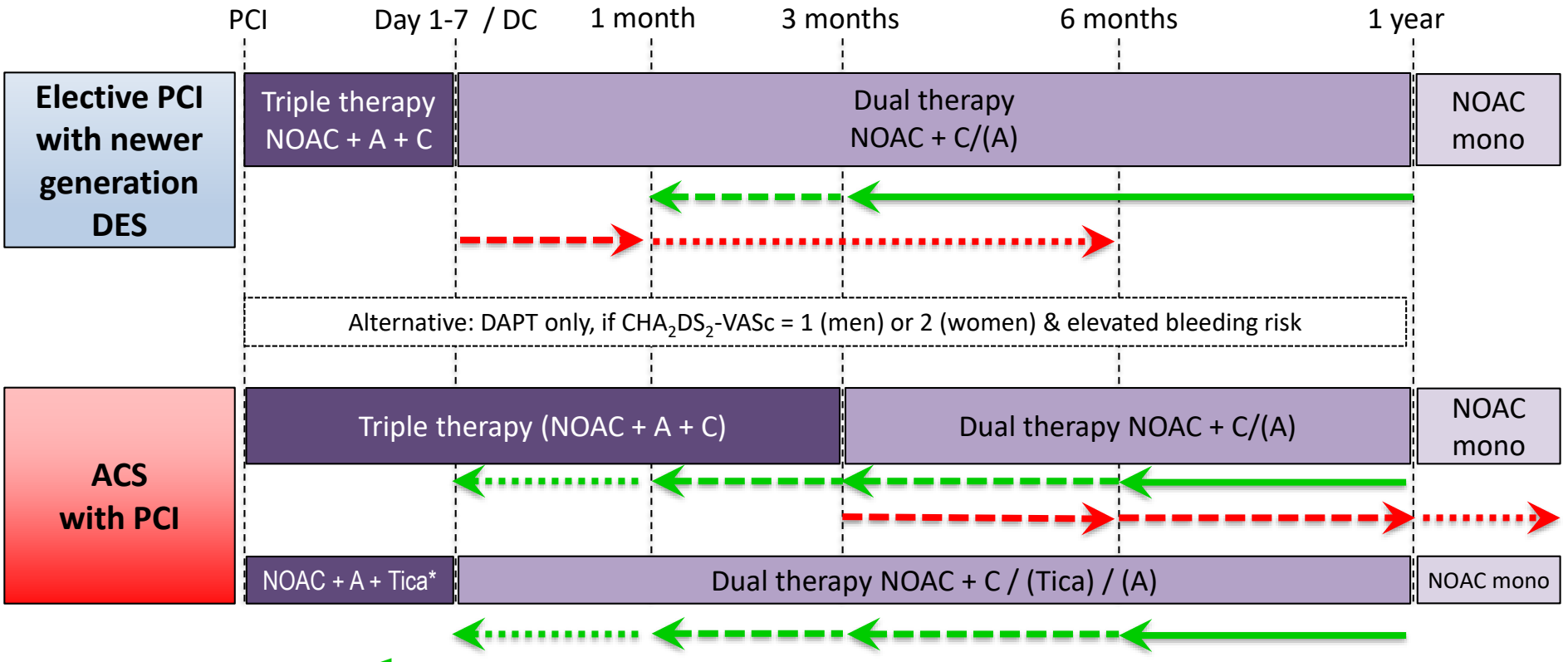
SPECIAL ARTICLE

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[2], Peter Sinnaeve[2], Ronan Collins[12], A. John Camm[13], and Hein Heidbüchel[6,14]

www.NOACforAF.eu

Anticoagulation post PCI / ACS (+ NOAC)



Factors to shorten combination therapy

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

Steffel et al., EHRA Practical Guide, European Heart Journal 2018

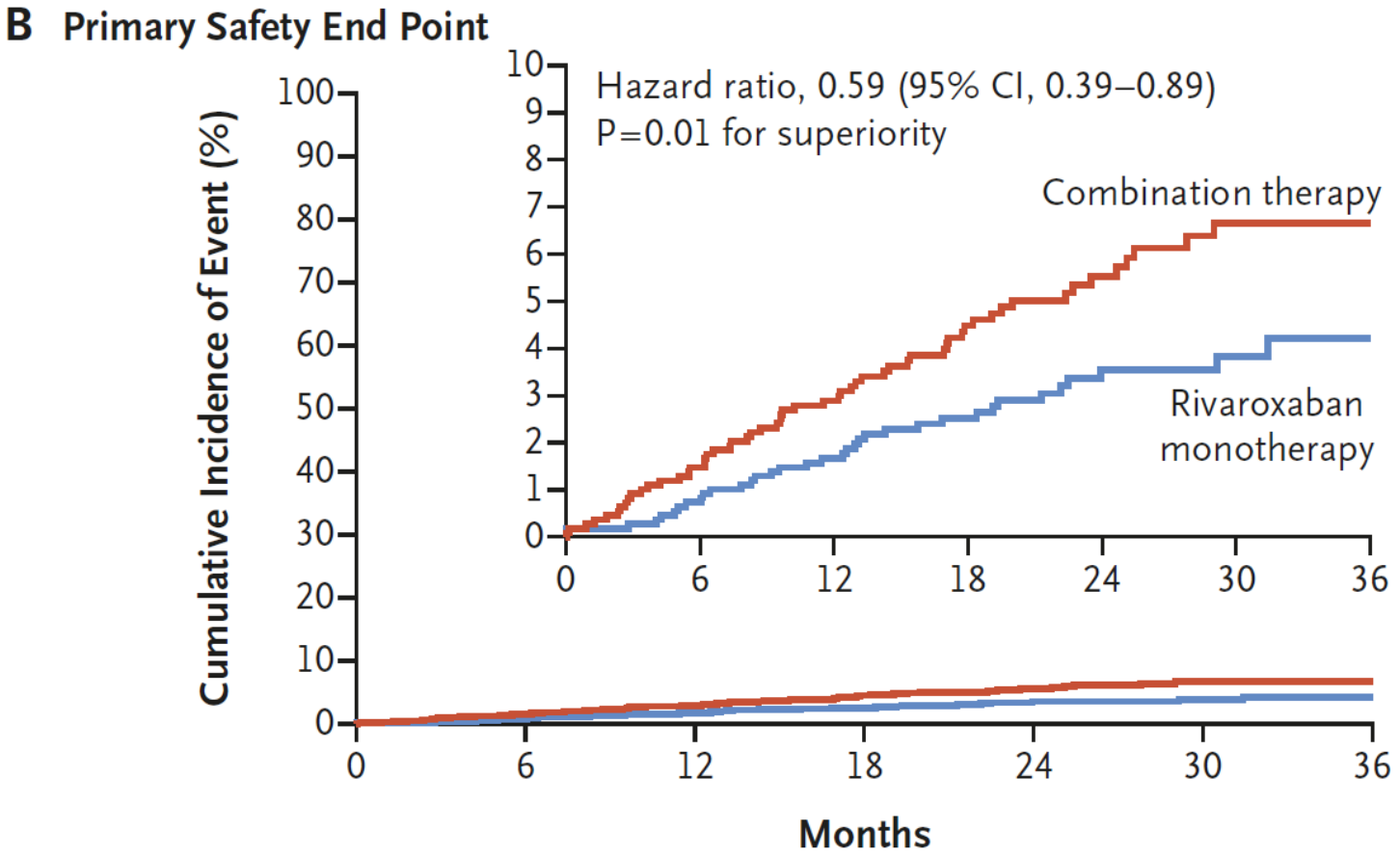
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease

Satoshi Yasuda, M.D., Ph.D., Koichi Kaikita, M.D., Ph.D., Masaharu Akao, M.D., Ph.D., Junya Ako, M.D., Ph.D., Tetsuya Matoba, M.D., Ph.D., Masato Nakamura, M.D., Ph.D., Katsumi Miyauchi, M.D., Ph.D., Nobuhisa Hagiwara, M.D., Ph.D., Kazuo Kimura, M.D., Ph.D., Atsushi Hirayama, M.D., Ph.D., Kunihiko Matsui, M.D., M.P.H., and Hisao Ogawa, M.D., Ph.D., for the AFIRE Investigators*

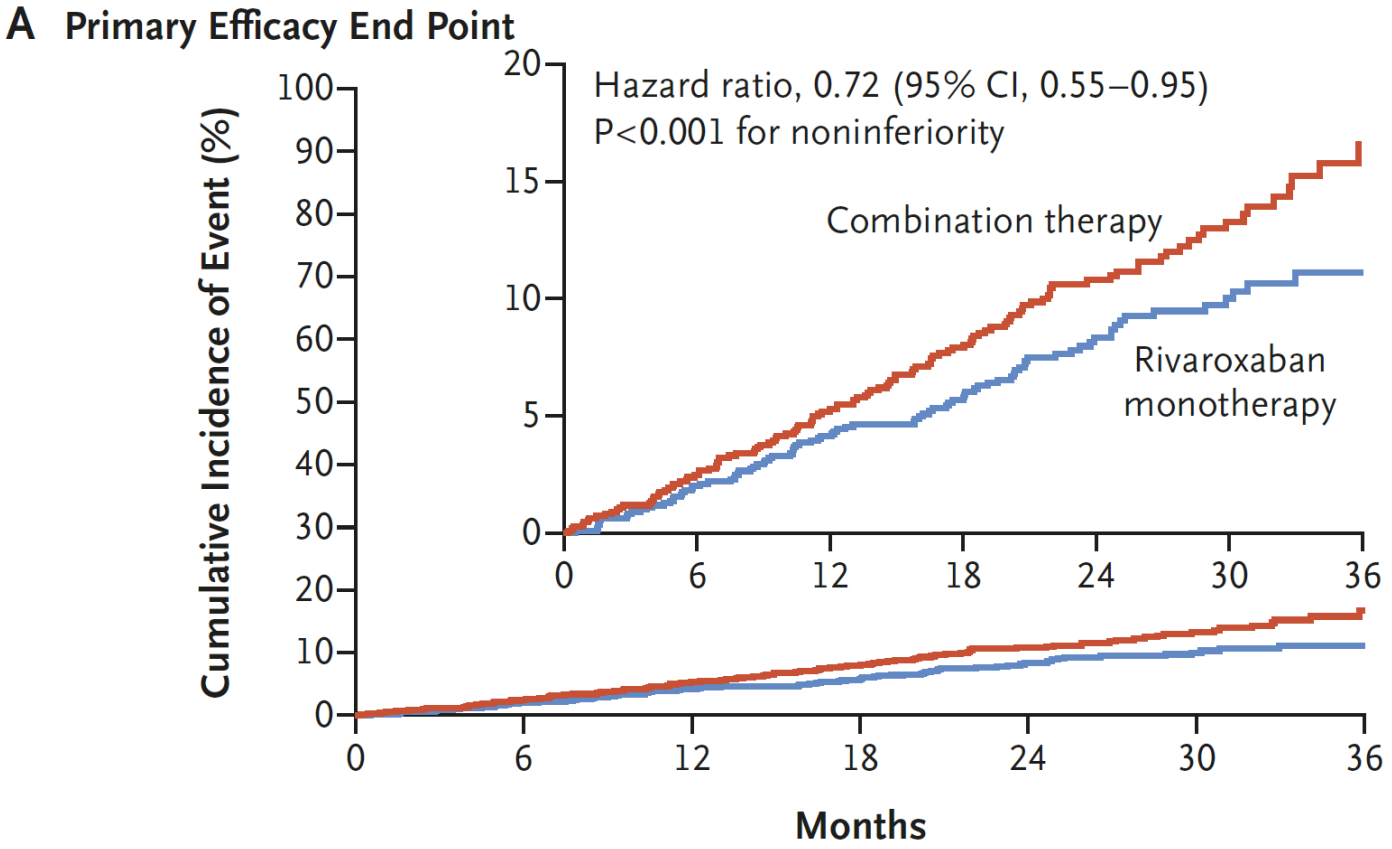
NOAC Monotherapy 1 year post ACS / PCI?



No. at Risk							
Combination therapy	1099	1055	962	750	506	294	80
Rivaroxaban monotherapy	1099	1074	994	786	526	312	89

Yasuda et al., NEJM 2019

NOAC Monotherapy 1 year post ACS / PCI?



No. at Risk							
Combination therapy	1108	1057	962	754	499	292	80
Rivaroxaban monotherapy	1107	1071	984	774	518	309	89

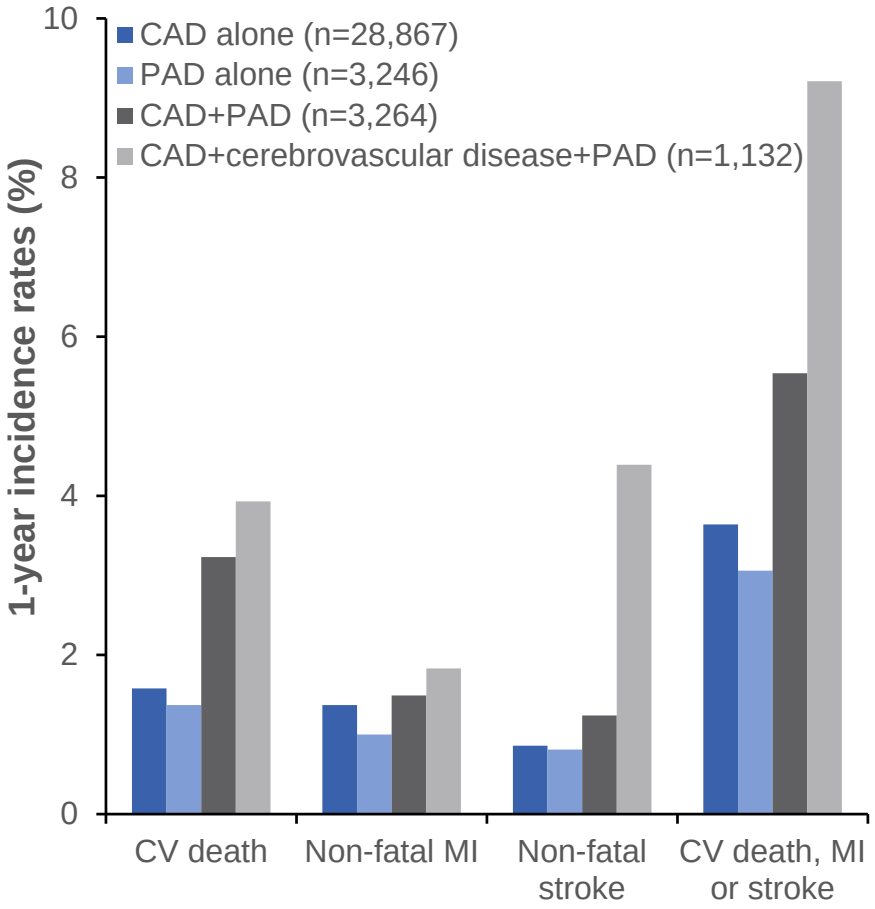
Yasuda et al., NEJM 2019

Zwei Situationen für Patienten mit Chronischem Coronarsyndrom (CCS)

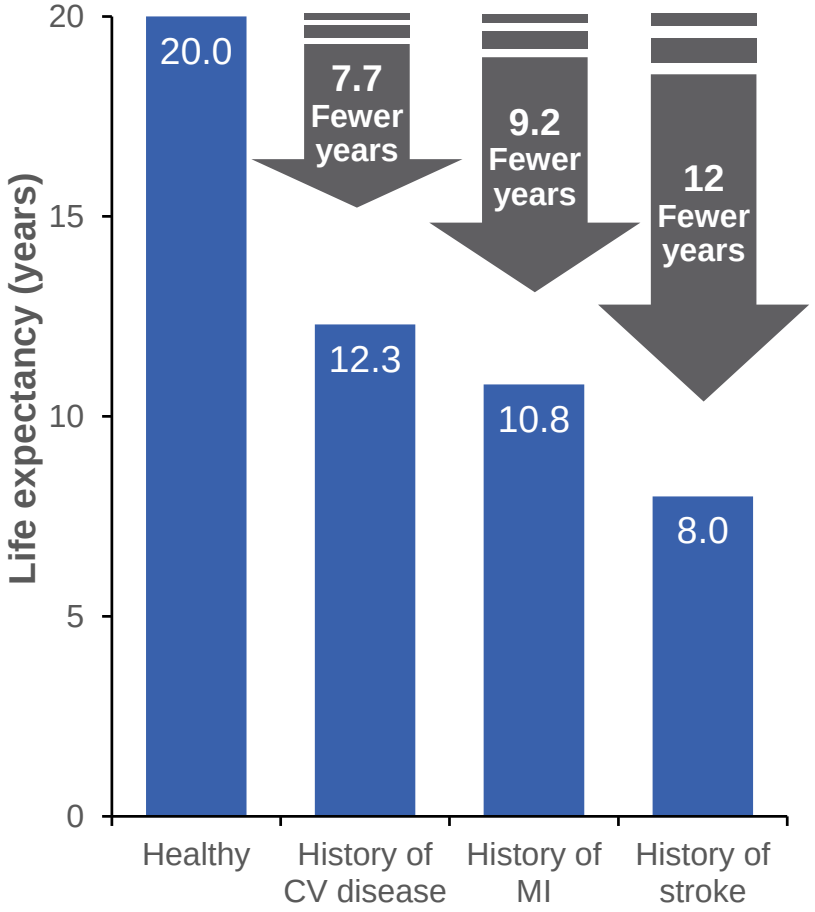
- Patient hat Vorhofflimmern
- Patient hat kein Vorhofflimmern

Lebenserwartung von Patienten mit “stabiler” atherosklerotischer Erkrankung

- 1-year outcomes in patients with atherosclerotic disease[1]

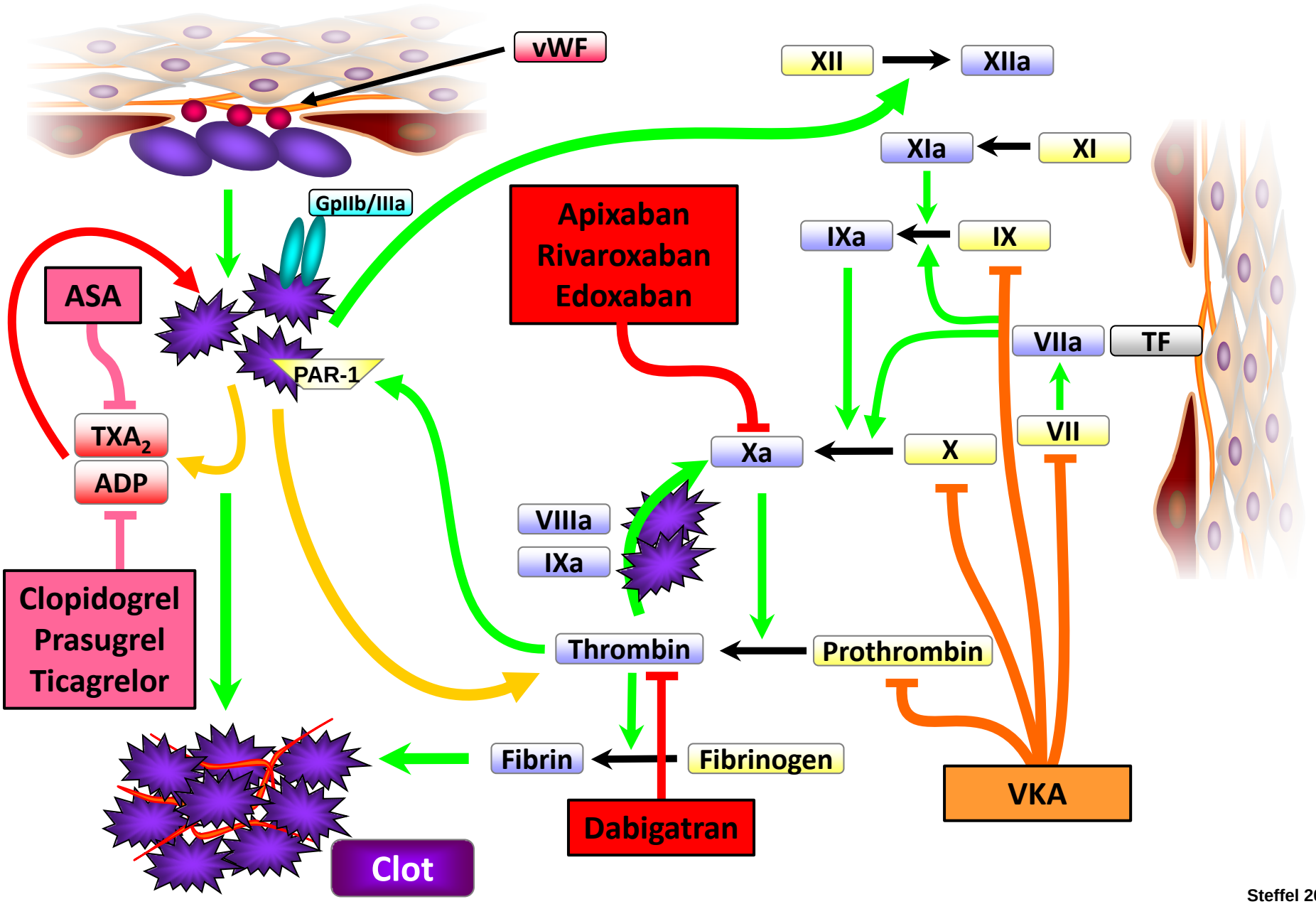


- Life expectancy in patients aged 60 years ± atherosclerosis[2]



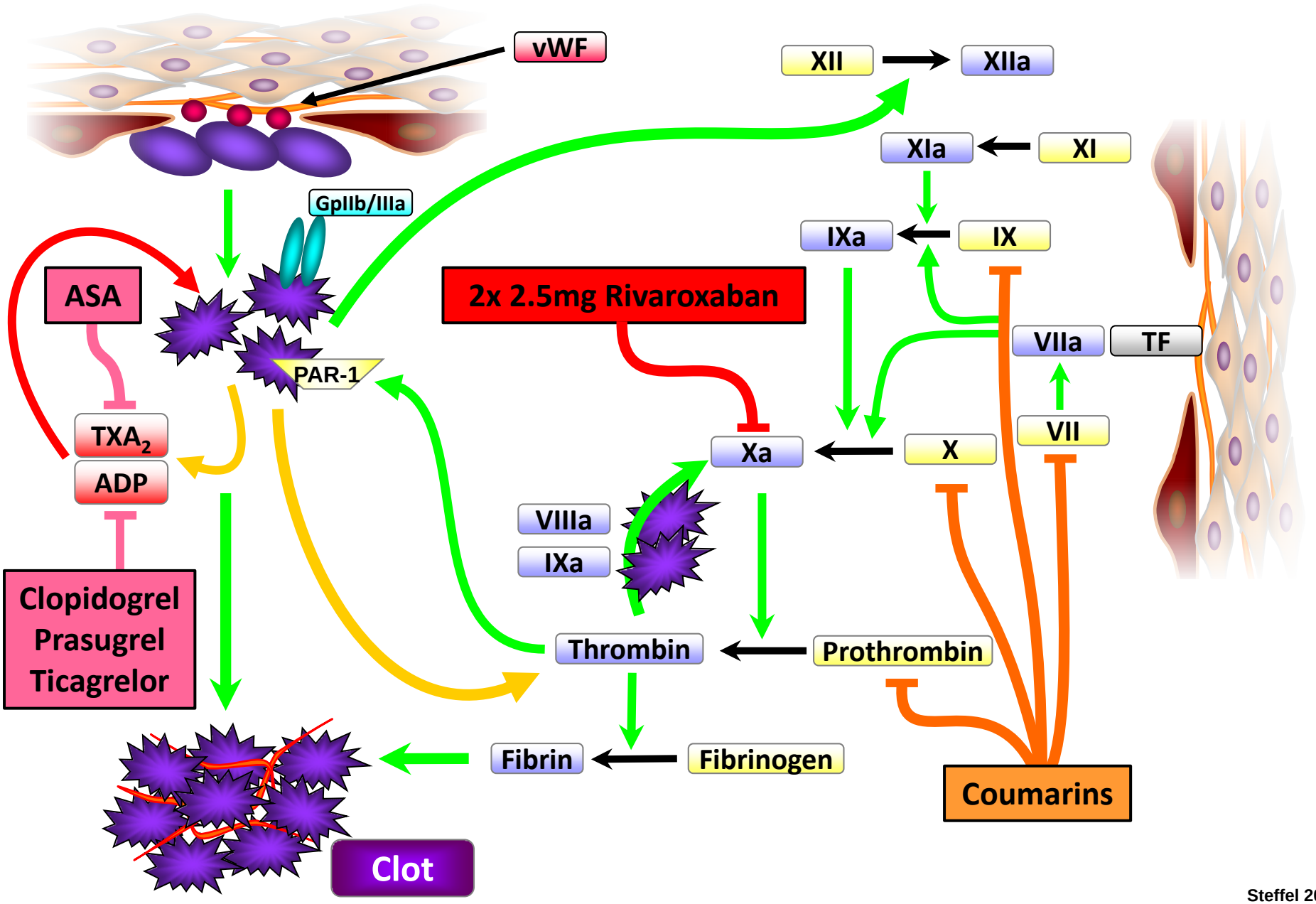
1. Steg P *et al*. *JAMA* 2007;297:1197–1206; 2. Peeters A *et al. Eur Heart J* 2002;23:458–466

(Patho-)physiology of Thrombus Formation



Steffel 2013

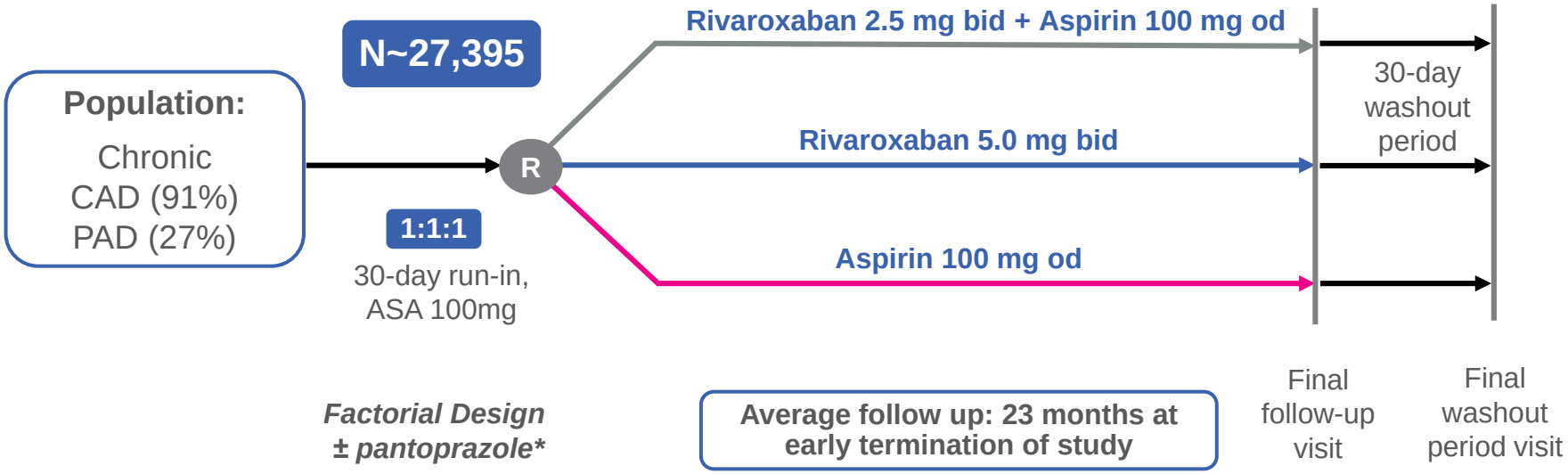
(Patho-)physiology of Thrombus Formation



Steffel 2013

COMPASS - Design

Objective: To determine the efficacy and safety of rivaroxaban, vascular dose of rivaroxaban plus aspirin or aspirin alone for reducing the risk of MI, stroke and cardiovascular death in CAD or PAD



Antithrombotic investigations* were stopped 1 year ahead of expectations in Feb 2017 due to overwhelming efficacy in the rivaroxaban 2.5mg BID + aspirin arm

*Patients who were not receiving a proton pump inhibitor (PPI) were randomised to pantoprazole or placebo (partial factorial design); the PPI pantoprazole component of the study is continuing; data will be communicated once complete

1. Eikelboom JW *et al. New Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118;
2. Bosch J *et al. Can J Cardiol* 2017;33(8):1027–1035

COMPASS

COMPASS - Inclusion and Exclusion Criteria

Key inclusion criteria*

- PAD
- CAD with ≥1 of:
  - Age ≥65 years
  - Age <65 years plus atherosclerosis in ≥2 vascular beds or ≥2 additional risk factors
    - Current smoker
    - Diabetes mellitus
    - Renal dysfunction (eGFR<60 ml/min)
    - Heart failure
    - Non-lacunar ischemic stroke ≥1 month ago

Key exclusion criteria‡

- Stroke ≤1 month or any haemorrhagic or lacunar stroke
- Severe HF with known ejection fraction <30% or NYHA class III or IV symptoms
- Need for dual antiplatelet therapy, other non-aspirin antiplatelet therapy, or oral anticoagulant therapy
- eGFR <15 ml/min

#Including but not limited to; ‡any other exclusion criteria in conjunction with the local Product Information and any other contraindication listed in the local labelling for rivaroxaban or the comparator have to be considered

www.clinicaltrials.gov/ct2/show/NCT01776424 [accessed 21 Mar 2017];
Bosch J *et al*, *Can J Cardiol* 2017;33:1027–1035

COMPASS

Outcome Measures

Primary efficacy outcome

- Composite of MI, stroke or CV death (=MACE)

Secondary efficacy outcomes

- Composite of major thrombotic events
  - Coronary heart disease death, MI, ischaemic stroke, acute limb ischaemia
  - Cardiovascular death, MI, ischaemic stroke, acute limb ischaemia
- Mortality (all cause)

Primary safety outcome

- ***Modified**** ISTH major bleeding
  - Fatal bleeding, *and/or*
  - Symptomatic bleeding in a critical area or organ, such as intracranial, *or*
  - ***Bleeding into the surgical site requiring re-operation, and/or****
  - ***Bleeding leading to hospitalization****

*Standard ISTH major bleeding definition:

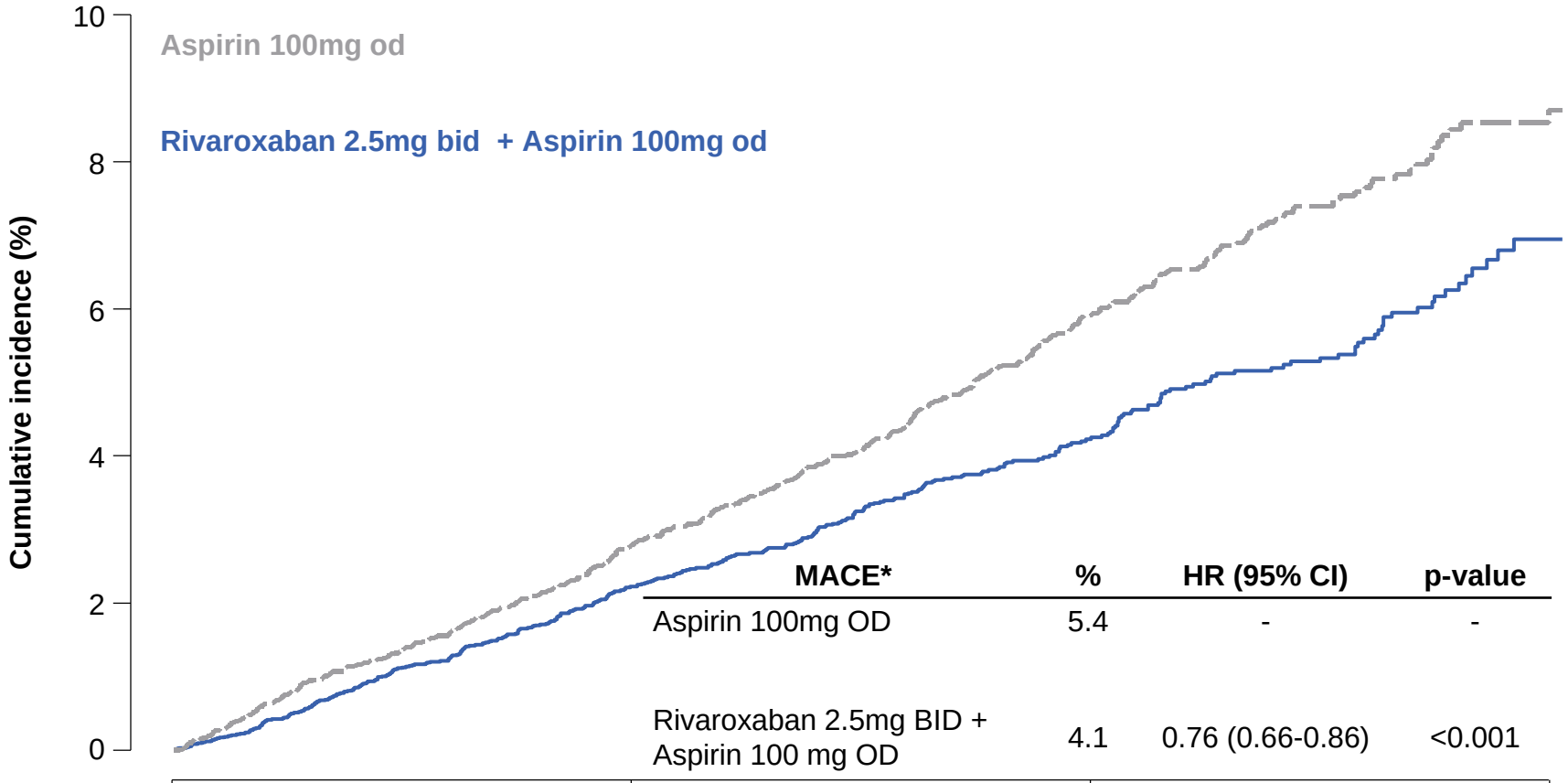
Bleeding causing a drop in haemoglobin level of ≥20 g/l, or leading to transfusion of ≥2 units of whole blood or red cells

Vorzeitiger Abbruch durch das DSMB!

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

COMPASS - Primary Efficacy Outcome



MACE*	%	HR (95% CI)	p-value
Aspirin 100mg OD	5.4	-	-
Rivaroxaban 2.5mg BID + Aspirin 100 mg OD	4.1	0.76 (0.66-0.86)	<0.001

Number at risk				
Aspirin 100mg od	9126	7808	3860	669
Riva 5mg bid	9117	7824	3862	670
Riva 2.5mg bid + Aspirin 100mg od	9152	7904	3912	658

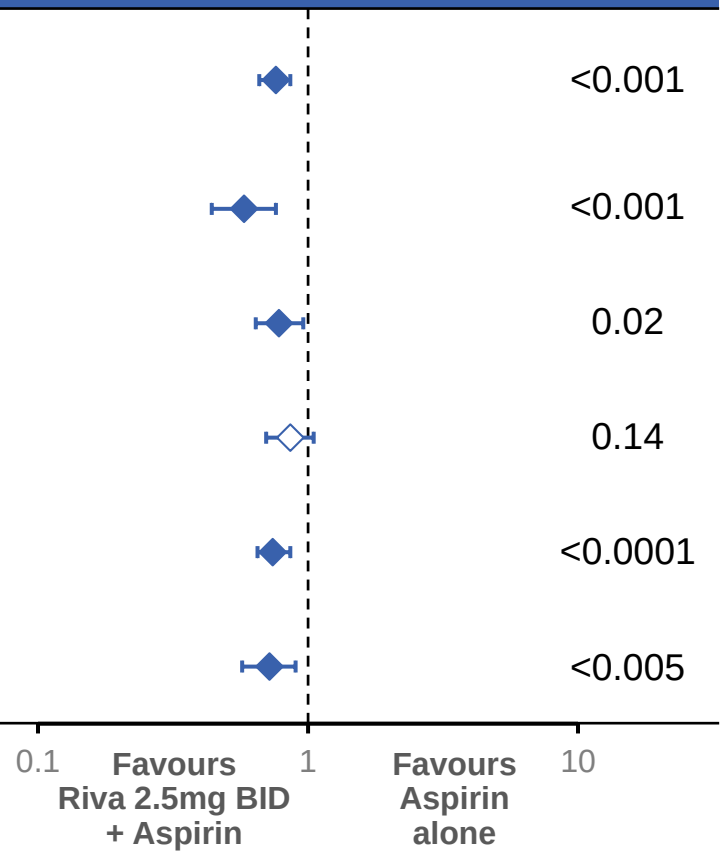
*Rates as at mean follow up of 23 months

Eikelboom JW *et al. N Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

COMPASS – Primary Efficacy Outcome (components)

Primary efficacy: MACE*	Aspirin n (%)	Riva 2.5mg BID + Aspirin n (%)	HR	HR (95% CI)	*p*-value
Overall CAD/PAD	496 (5.4)	379 (4.1)	0.76		<0.001
Stroke	142 (1.6)	83 (0.9)	0.58		<0.001
CV death	203 (2.2)	160 (1.7)	0.78		0.02
MI	205 (2.2)	178 (1.9)	0.86		0.14
CAD	460 (5.6)	347 (4.2)	0.74		<0.0001
PAD	174 (6.9)	126 (5.1)	0.72		<0.005



*Crude incidence over mean follow-up of 23 monthss

Eikelboom JW *et al.* ESC 2017. COMPASS trial: Primary Results. Abstract no. 1154; Available at: http://congress365.escardio.org/; Eikelboom JW *et al. New Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118

COMPASS

Bleeding / Net Clinical Benefit

Crude incidence over mean follow-up of 23 months	Aspirin n (%)	Riva 2.5mg BID + Aspirin n (%)	HR (95% CI)	*p*-value
Primary Safety: Major bleeding	170 (1.9)	288 (3.1)	1.70 (1.40–2.05)	<0.001
Fatal bleeding†	10 (0.1)	15 (0.2)	1.49 (0.67–3.33)	0.32
Non-fatal symptomatic ICH	21 (0.2)	19 (0.2)	1.10 (0.59–2.04)	0.77
Nonfatal, non-ICH, symptomatic bleeding into a critical organ	29 (0.3)	42 (0.5)	1.43 (0.89–2.29)	0.14
Other major bleeding leading to hospitalisation	112 (1.2)	210 (2.3)	1.88 (1.49–2.36)	<0.001
Pre-specified net clinical benefit (CV Death, Stroke, MI, Fatal Bleeding, or Symptomatic Bleeding into a Critical Organ)	534 (5.9)	431 (4.7)	0.80 (0.70–0.91)	<0.001
All cause mortality*	378 (4.1)	313 (3.4)	0.82 (0.71–0.96)	0.01

*Nominally significant because the study was stopped approximately 1 year ahead of schedule due to overwhelming efficacy; threshold for formal significance p=0.0025

1. Eikelboom JW *et al. New Engl J Med* 2017; DOI: 10.1056/NEJMoa1709118;
2. Bosch J *et al. Can J Cardiol.* 2017 Aug;33(8):1027-1035

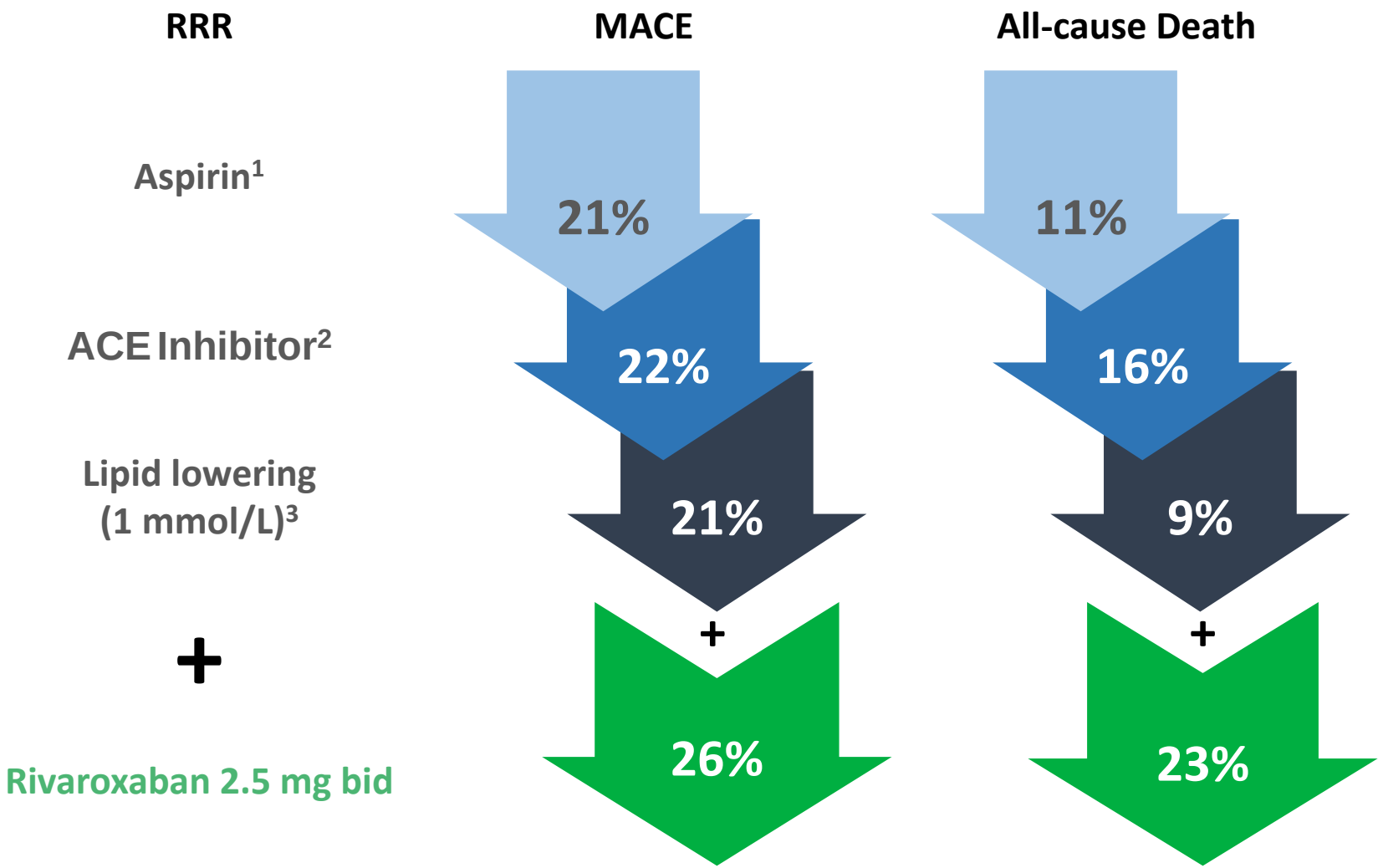
Outcome in PAD Patients

Outcome	Rivaroxaban 2.5 mg bid + aspirin N=2492	Rivaroxaban 5 mg bid N=2474	Aspirin N=2504	Rivaroxaban 2.5 mg bid + aspirin vs. aspirin		Rivaroxaban 5 mg bid vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
MALE	30 (1.2)	35 (1.4)	56 (2.2)	0.54 (0.35–0.84)	0.005	0.63 (0.41–0.96)	0.03
Major amputation	5 (0.2)	8 (0.3)	17 (0.7)	0.30 (0.11–0.80)	0.01	0.46 (0.20–1.08)	0.07

Anand SS *et al.* ESC 2017, Abs 1157; Available at: http://spo.escardio.org/SessionDetails.aspx?eevtid=1220&sessId=22247&subSessId=0;
Anand SS *et al. Lancet* 2017;In Press

COMPASS

Rivaroxaban 2x 2.5mg im Kontext etablierter Therapien bei KHK



1. Antithrombotic Trialists' Collaboration, *BMJ* 2002;324:71–86 2. CTT Collaboration. *Lancet 2015*;385:1397-1405;
3. HOPE Investigators. *N Engl J Med* 2000;342:145-53;

ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–71
doi:10.1093/eurheartj/ehz425

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

A Second Antithrombotic Is Recommended for Selected Patients with Chronic Coronary Syndromes

2019 ESC guidelines for the management of CCS

Recommendations	Class	Evidence level
Adding a **second antithrombotic drug** to aspirin for long-term secondary prevention should be considered in patients with a **high risk of ischaemic events** and without high bleeding risk	IIa	A
Adding a **second antithrombotic drug** to aspirin for long-term secondary prevention may be considered in patients with at least a **moderately increased risk of ischaemic events** and without high bleeding risk	IIb	A

Knuuti J *et al, Eur Heart J* 2019; doi: 10.1093/eurheartj/ehz42

ESC
European Society of Cardiology

European Heart Journal (2019) **00**, 1–69
doi:10.1093/eurheartj/ehz486

ESC GUIDELINES

2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD

The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD)

ESC Guidelines – Diabetes

Recommendations	Class	Evidence level
Prolongation of DAPT beyond 12 months should be considered, for up to 3 years, in patients with DM who have tolerated DAPT without major bleeding complications	IIa	A
The addition of a **second antithrombotic drug** on top of aspirin for long-term secondary prevention should be considered in patients without high bleeding risk	IIa	A

Cosentino et al., EHJ 2019

EMH Special Reports

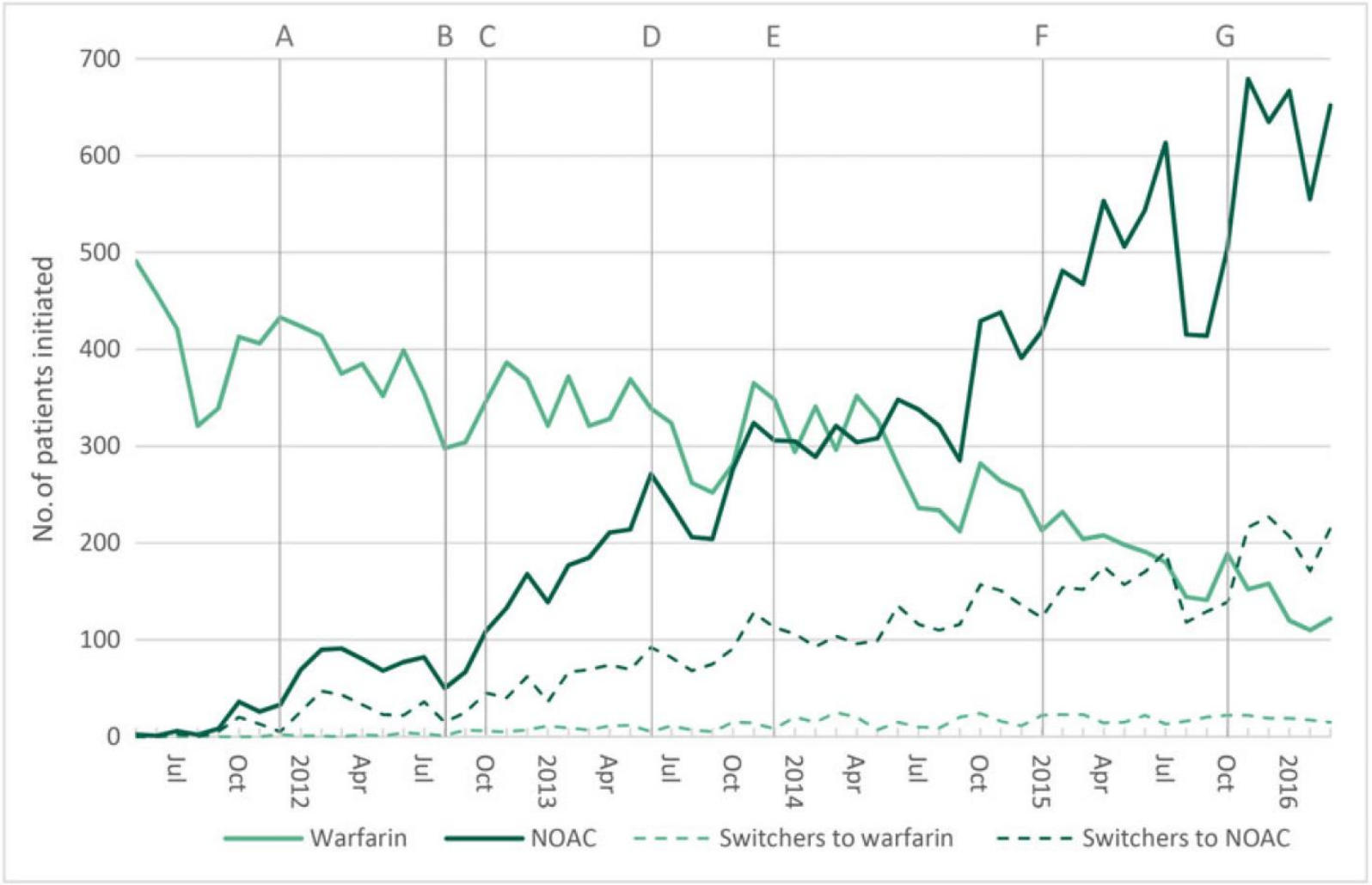
Jan Steffel, Rolf Engelberger, Nils Kucher, François Mach, Lucia Mazzolai, Giovanni Pedrazzini, Hans Rickli, Daniel Staub, Hans Stricker, Marco Valgimigli, Walter A. Wuillemin

Schweizer Expertenbericht zur praktischen Anwendung von Rivaroxaban 2,5 mg plus ASS zur Behandlung von Patienten mit koronarer Herzkrankheit (KHK) und/oder peripherer arterieller Verschlusskrankheit

Wo stehen wir?

10 Jahre nach Einführung der NOACs…

NOAC uptake in Stockholm 2012 – 2016



Komen et al., Br J Clin Pharmacol (2017) 83 642–652

Patient characteristics 2012 vs. 2017

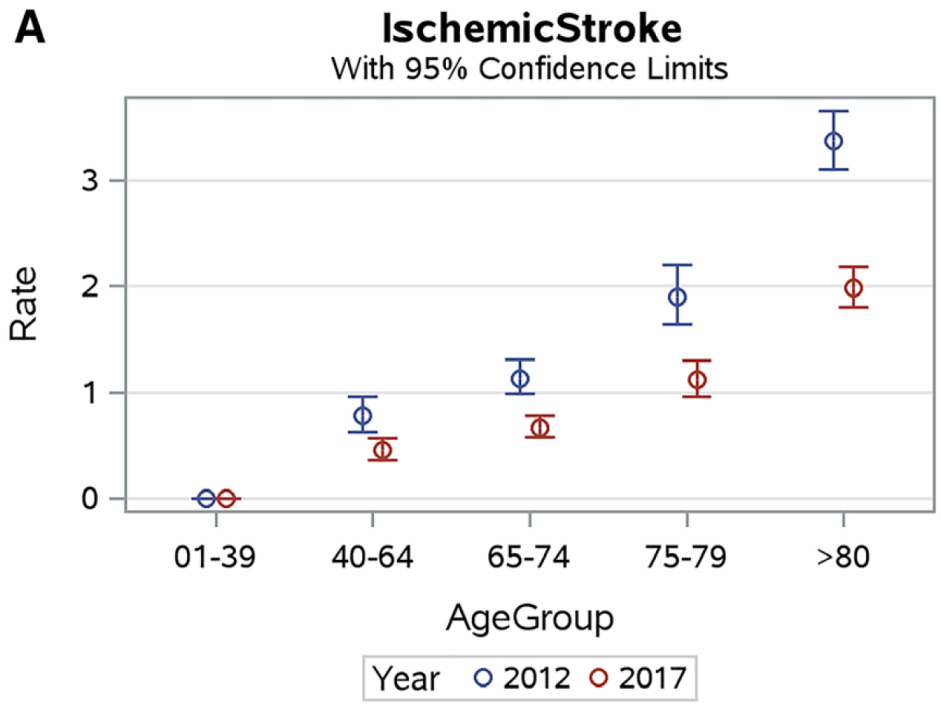
Treatment	2012 (n=41 008)	2017 (n=49 510)
OAC, n (%)	21 152 (51.6)	36 515 (73.8)
0–39 y	61 (10.6)	76 (14.9)
40–64 y	2874 (40.4)	3759 (49.8)
65–74 y	6682 (61.8)	11 701 (81.6)
75–79 y	4002 (65.1)	7031 (84.4)
≥80 y	7533 (46.0)	13 948 (74.3)

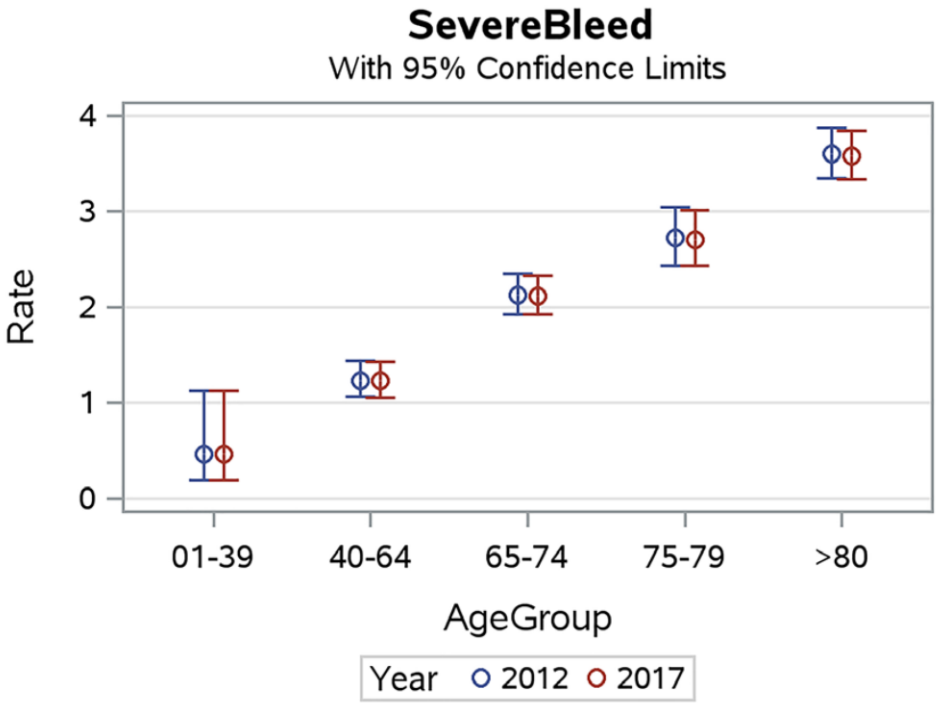
NOAC	178 (0.4)	17 040 (34.4)
Only warfarin	20 974 (51.2)	19 475 (39.3)

Forslund et al., Stroke. 2018;49:2122-2128

Rate of Ischemic stroke 2012 vs 2017

A



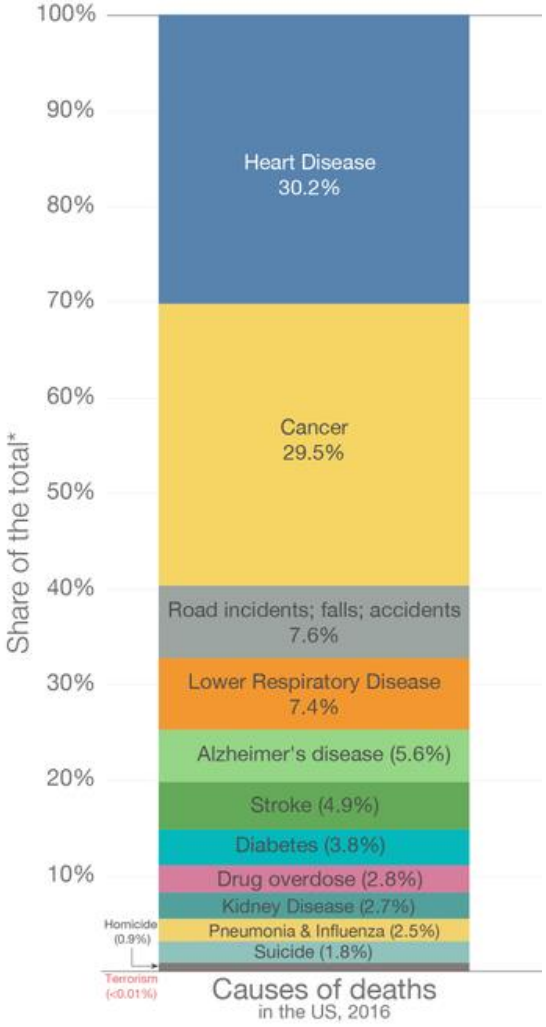


Forslund et al., Stroke. 2018;49:2122-2128

Causes of death in the US

What Americans die from, what they search on Google, and what the media reports on

Our World in Data



*This represents each causes's share of the top ten causes of death in the US plus homicides, drug overdoses and terrorism. Collectively these 13 causes accounted for approximately 88% of deaths in the US in 2016. Full breakdown of causes of death can be found at the CDC's WONDER public health database: https://wonder.cdc.gov/

Based on data from Shen et al (2018) – Death: reality vs. reported. *All data available at: https://owenshen24.github.io/charting-death*
All data refers to 2016.
Not all causes of death are shown: Shown is the data on the ten leading causes of death in the United States plus drug overdoses, homicides and terrorism.
All values are normalized to 100% so they represent their relative share of the top causes, rather than absolute counts (e.g. 'deaths' represents each causes' share of deaths within the 13 categories shown rather than total deaths). The causes of death shown here account for approximately 88% of total deaths in the United States in 2016.

Take Home Message

- NOACs = Standardtherapie zur Schlaganfallsprävention bei VHF
- Individualisierung! Es gibt kein "one size fits all" NOAC.
  → Komplexes Gebiet, aber 'wert zu investieren'…

- Patienten mit KHK und VHF:
  - Hochrisiko für Blutungen
  - Hochrisiko für Schlaganfall / Myokardinfarkt / Tod
  - Triple Therapie: Je kürzer desto besser
  - Optimale Dauer? Unklar → Individuell unterschiedlich…
  - 1 Jahr nach Ereignis: NOAC Monotherapie

- Patienten mit KHK ohne VHF:
  - Chronische KHK! Nicht "stabil"…
  - Rivaroxaban 2x 2.5mg + ASS gute Option (Schlaganfall ↓, Tod ↓)
  - Je höher das Risiko desto höher der Benefit

- Shared decision making – patient engagement / empowerment