Training course:
All About Clinical Trials

What's Next – Upcoming and ongoing clinical trials:

ACS / Antithrombotics

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Declaration of Conflict of Interest

The existence of potential conflicts of interest does not necessarily indicate a bias. However it is our ethical obligation to inform organisers and participants so that they are made aware of any relationship that might cause unintentional bias. A potential conflict of interest may arise from various relationships, past or present, such as employment, consultancy, investments and stock ownerships, funding for research, family relationship etc.

□ **I have no potential conflict of interest to report**

X I have the following potential conflict(s) of interest to report

Type of affiliation / financial interest	**Name of commercial company**
Receipt of grants/research supports:	No
Receipt of honoraria or consultation fees:	Boehringer Ingelheim, Daiichi Sankyo, AstraZeneca, Pfizer, Apontis
Participation in a company sponsored speaker's bureau:	Amgen, AstraZeneca, Berlin Chemie, Bristol Myers Squibb, Boehringer Ingelheim, Daiichi Sankyo, Merck Sharp Dohme, Novartis, Pfizer
Stock shareholder:	No
Spouse/partner:	No
Other support (please specify):	No

Add-on antithrombotics, aspirin replacement and aspirin-free strategies in cardiovascular disease and cardioembolic stroke prevention

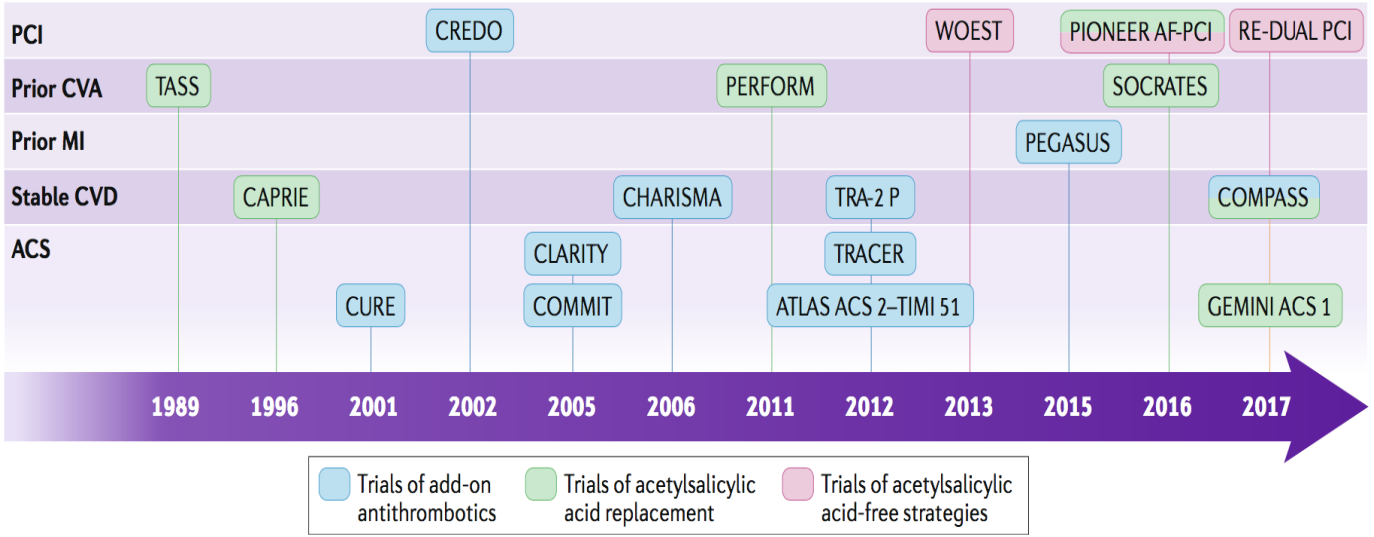
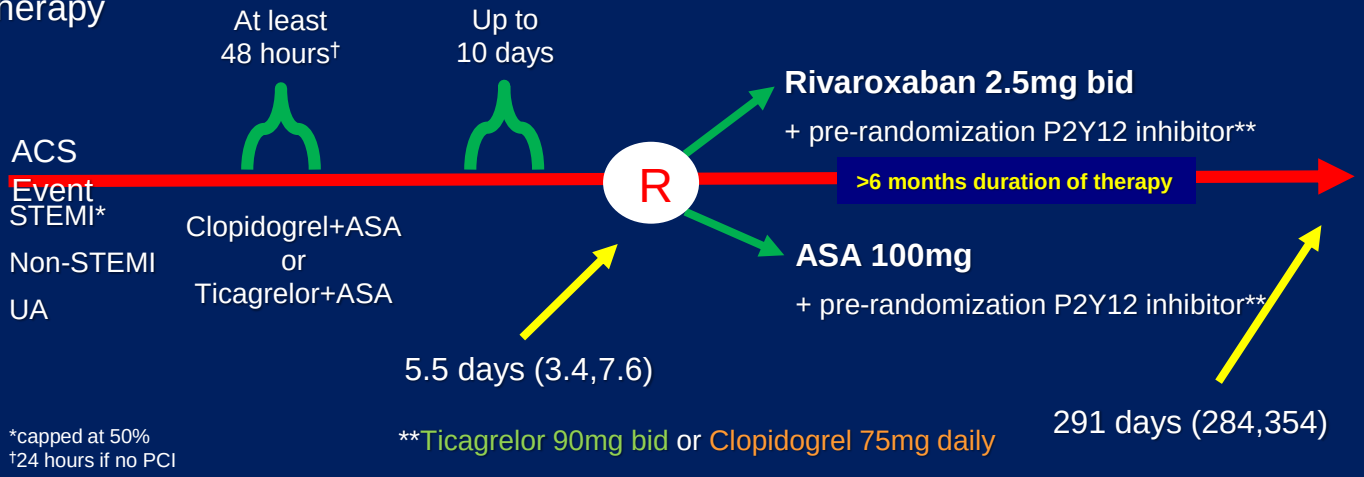


Fig. 2 | **Trials of antithrombotic approaches in cardiovascular diseases.** A timeline of studies investigating

Nat Rev Cardiol. 2018;15:480-496

GEMINI ACS-1: Protocol Outline

3037 patients randomized after having been started on DAPT
Adherence to P2Y12 therapy 95% during study period, 6.5% switched P2Y12 therapy

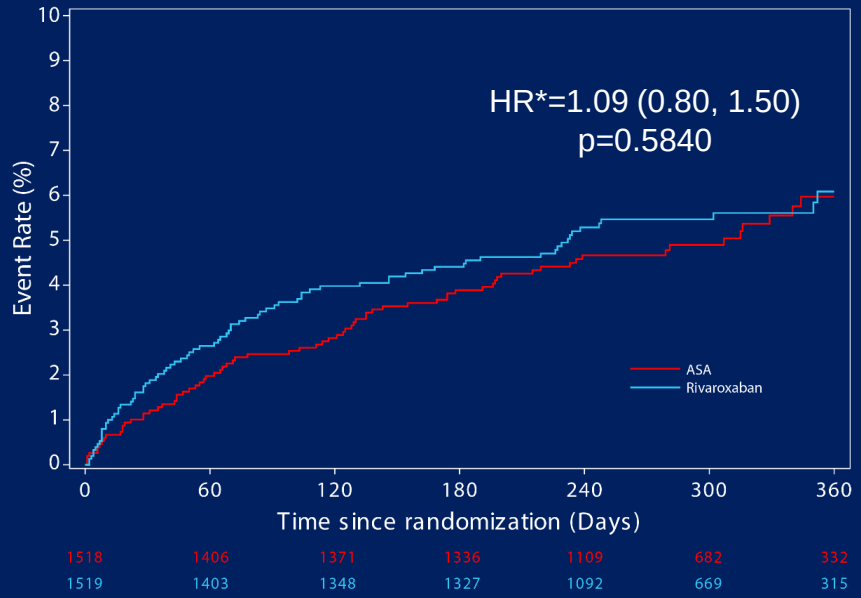


*capped at 50%
†24 hours if no PCI

**Ticagrelor 90mg bid or Clopidogrel 75mg daily

Primary Endpoint: TIMI Non-CABG Clinically Significant Bleeding

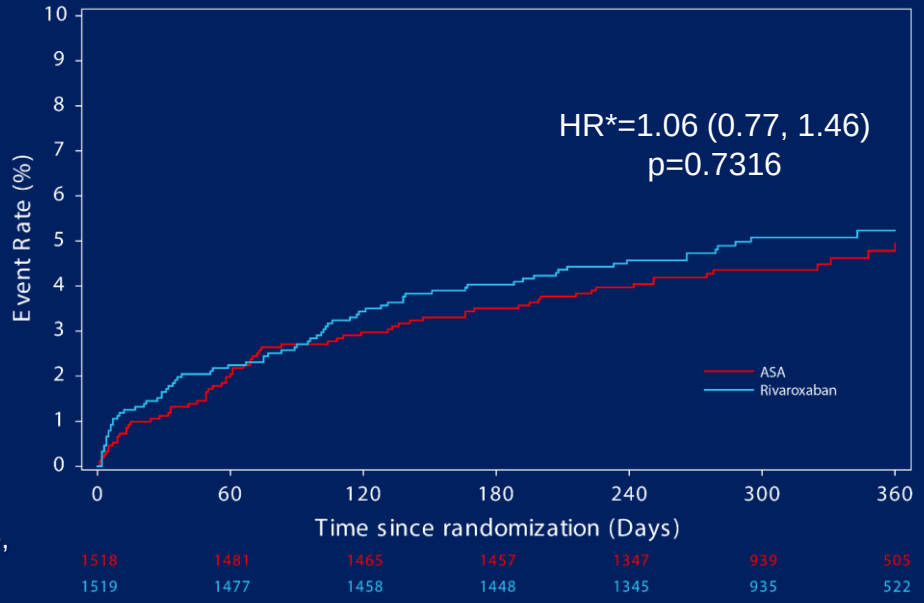
TIMI non-CABG clinically significant bleeding:
non-CABG major, minor,
or requiring medical attention



*Hazard Ratio (95%CI)

Exploratory Composite Ischemic Endpoint

Exploratory composite ischemic endpoint: cardiovascular death, MI, stroke, or definite stent thrombosis.

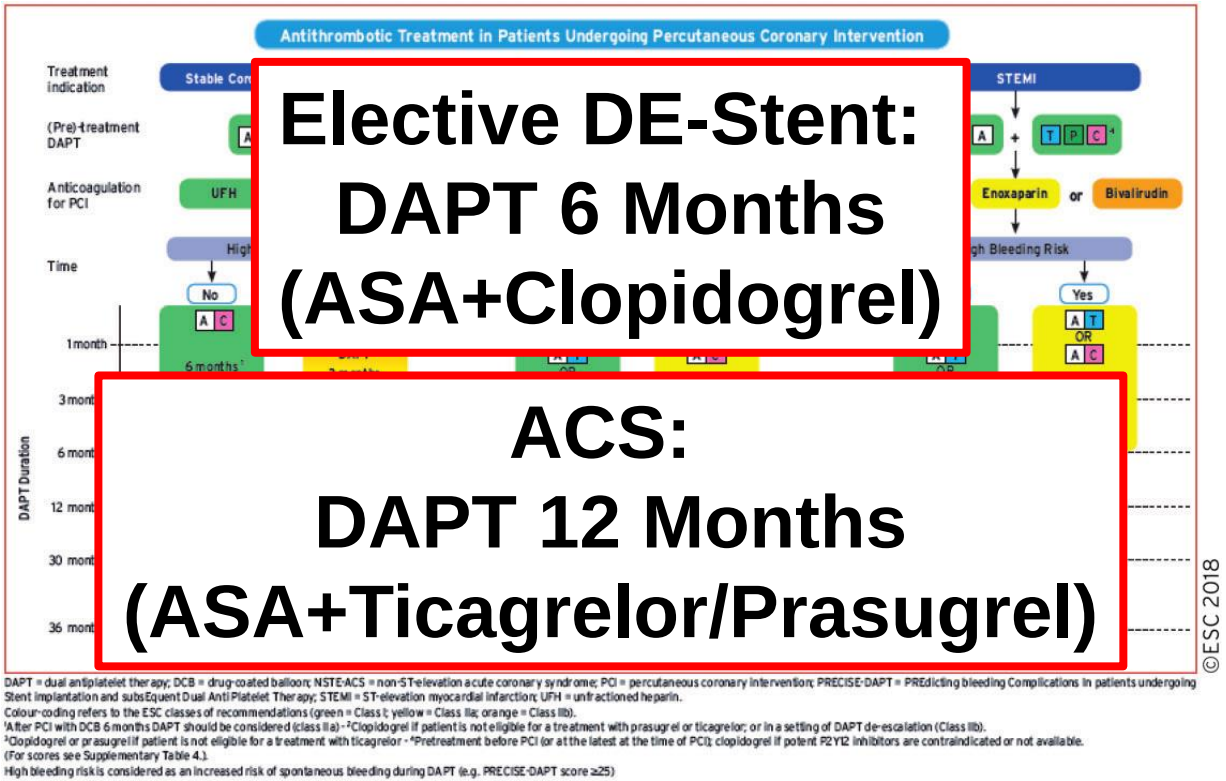


*Hazard Ratio (95%CI)

Do we need Aspirin during/after ACS? Is Xa better?

- **GEMINI ACS-2 will be an outcome trial – to test**
  - **Aspirin (100mg) vs Rivaroxaban (2.5mg bid) in pts with ACS**
  - **On top of a P2Y12 inhibitor**
  - **Primary triple endpoint: CV death, MI, stroke**
  - **N=22,000**

Antithrombotic Therapy after PCI: ESC/EACTS 2018 Guidelines Myocardial Revascularization

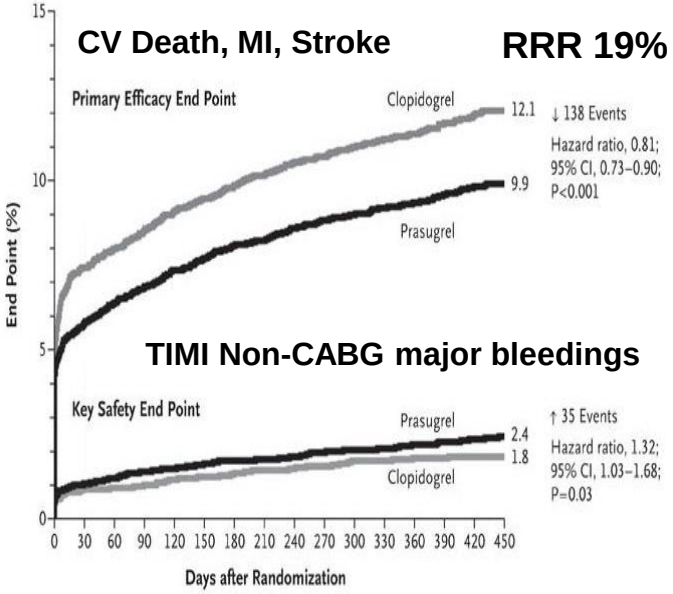


DAPT = dual antiplatelet therapy; DCB = drug-coated balloon; NSTE-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; STEMI = ST-elevation myocardial infarction; UFH = unfractionated heparin.
Colour-coding refers to the ESC classes of recommendations (green = Class I; yellow = Class IIa; orange = Class IIb).
[1]After PCI with DCB 6 months DAPT should be considered (class IIa) - [2]Clopidogrel if patient is not eligible for a treatment with prasugrel or ticagrelor; or in a setting of DAPT de-escalation (Class IIb).
[3]Clopidogrel or prasugrel if patient is not eligible for a treatment with ticagrelor - [4]Pretreatment before PCI (or at the latest at the time of PCI); clopidogrel if potent P2Y12 inhibitors are contraindicated or not available.
(For scores see Supplementary Table 4.).
High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score ≥25)

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

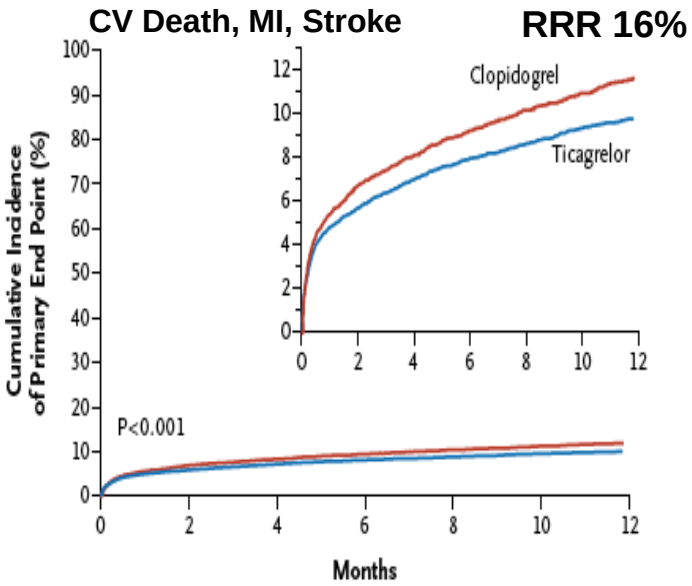
Prasugrel vs Clopidogrel in ACS: TRITON-TIMI 38
Ticagrelor vs Clopidogrel in ACS: PLATO

TRITON



Wiviott et al., N Engl J Med 2007;357:2001-15

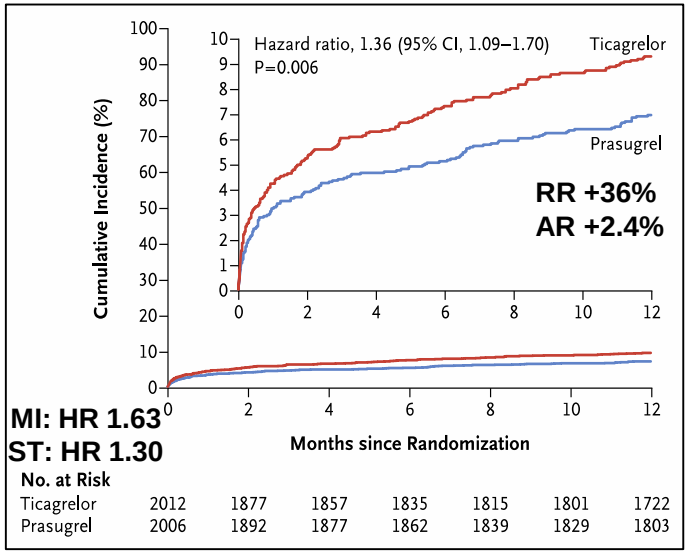
PLATO



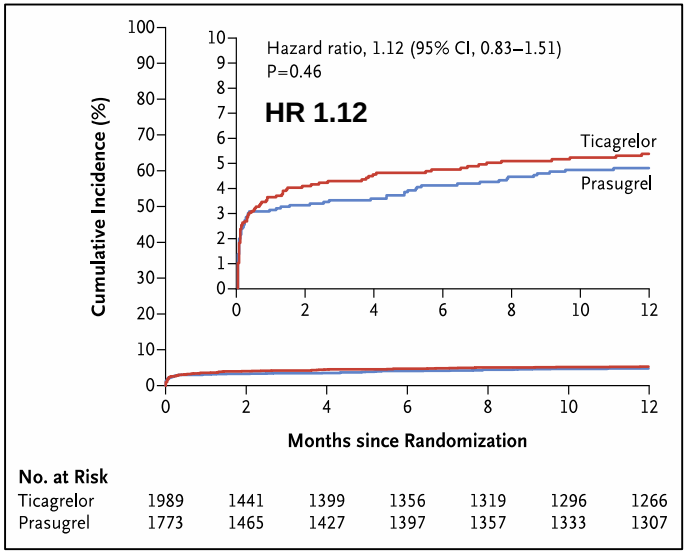
Wallentin et al., N Engl J Med 2009;361:1045-57.

Ticagrelor or Prasugrel in ACS: ISAR-REACT-5

Death, MI, Stroke



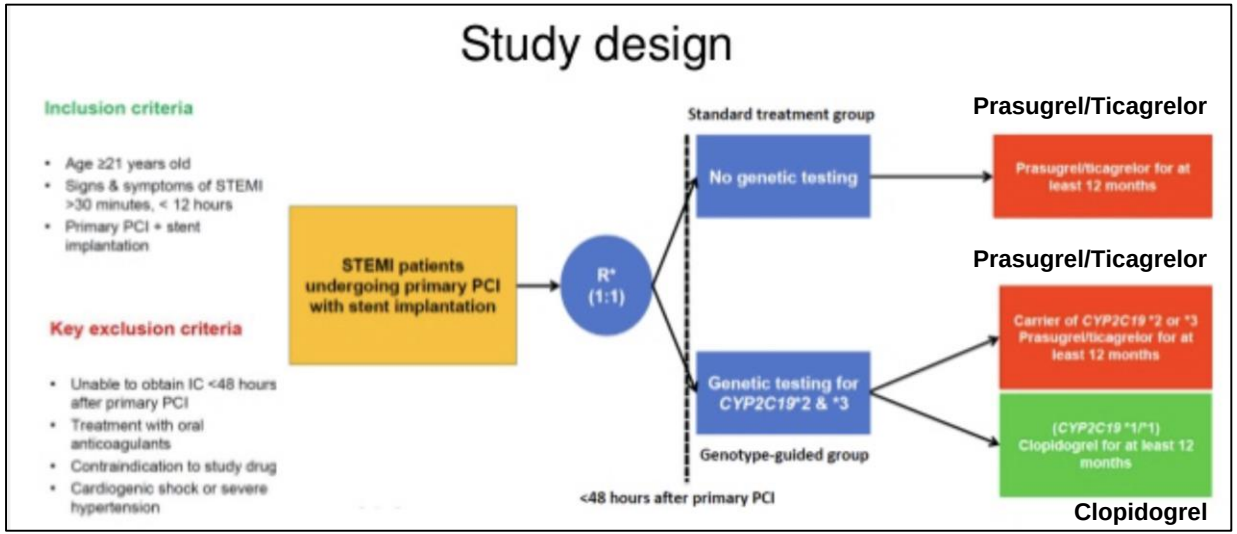
Major Bleeding



- **N=4.018 with ACS (41% STEMI, 46% NSTEMI, 13% UA), 100% invasive management**
- **Rx Ticagrelor 90 mg BID vs. Prasugrel 10 mg BID, plus standard Tx inkl. ASA, FU 1 year**

Schüpke et al., N Engl J Med. 2019;381:1524-1534

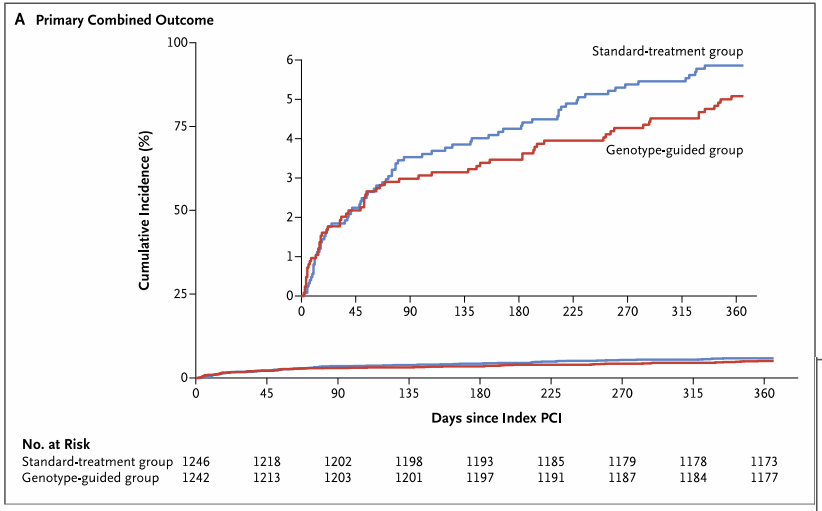
DAPT in STEMI stratified by *CYP2C19* Genetic Testing: POPular Genetics



N=2.488 patients

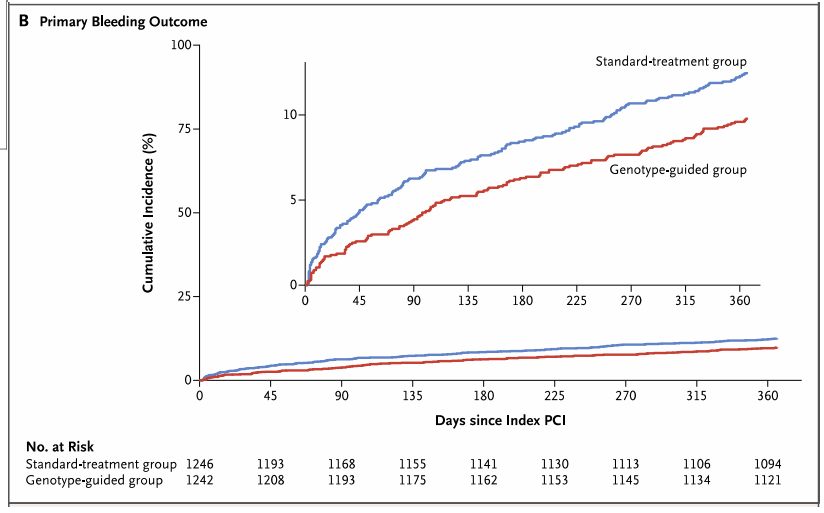
Claassens et al., N Engl J Med. 2019;381:1621-1631

DAPT in STEMI stratified by *CYP2C19* Genetic Testing: POPular Genetics



Death from any cause, MI, definite stent thrombosis, stroke, or major bleeding

PLATO major or minor bleeding



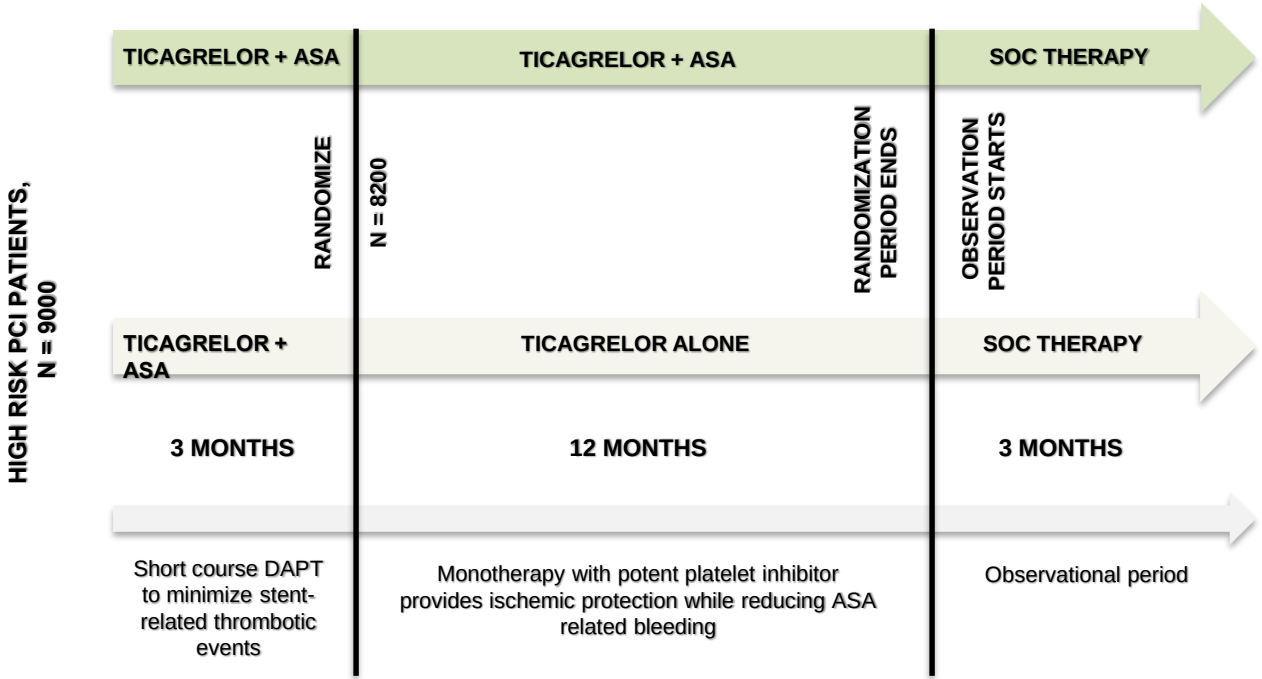
Combined ischemic outcomes: =

Major bleeding: =

Claassens et al., N Engl J Med. 2019;381:1621-1631

TWILIGHT (Monotherapy with Ticagrelor vs DAPT)

Study Flow

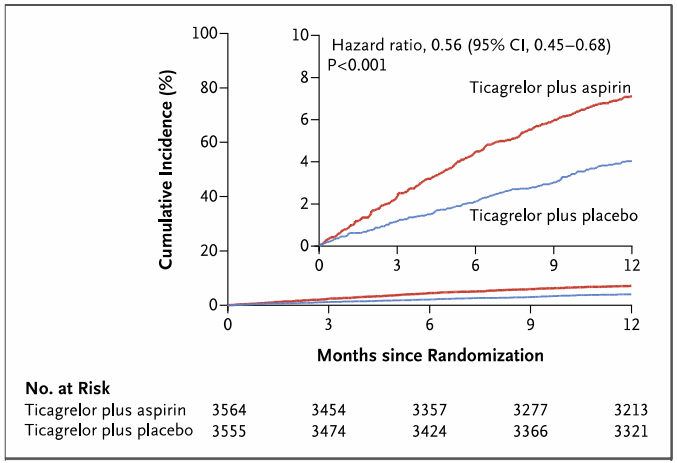


Endpoint ascertainment for primary bleeding and secondary ischemic endpoints

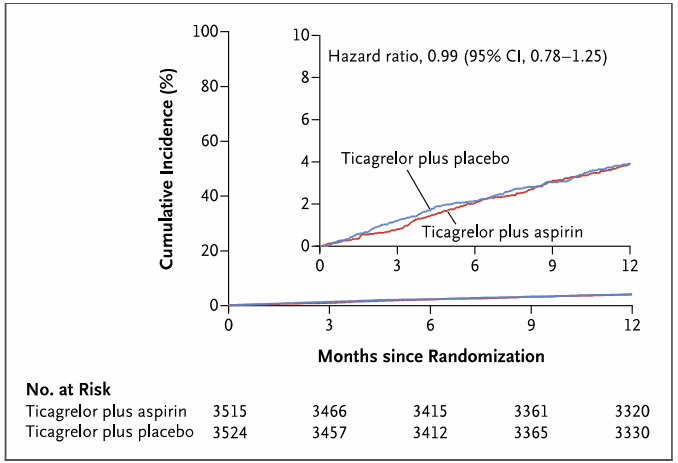
Baber et al., Am Heart J 2016;182:125-134

TWILIGHT (Monotherapy with Ticagrelor vs DAPT)

BARC 2,3,5 Bleeding



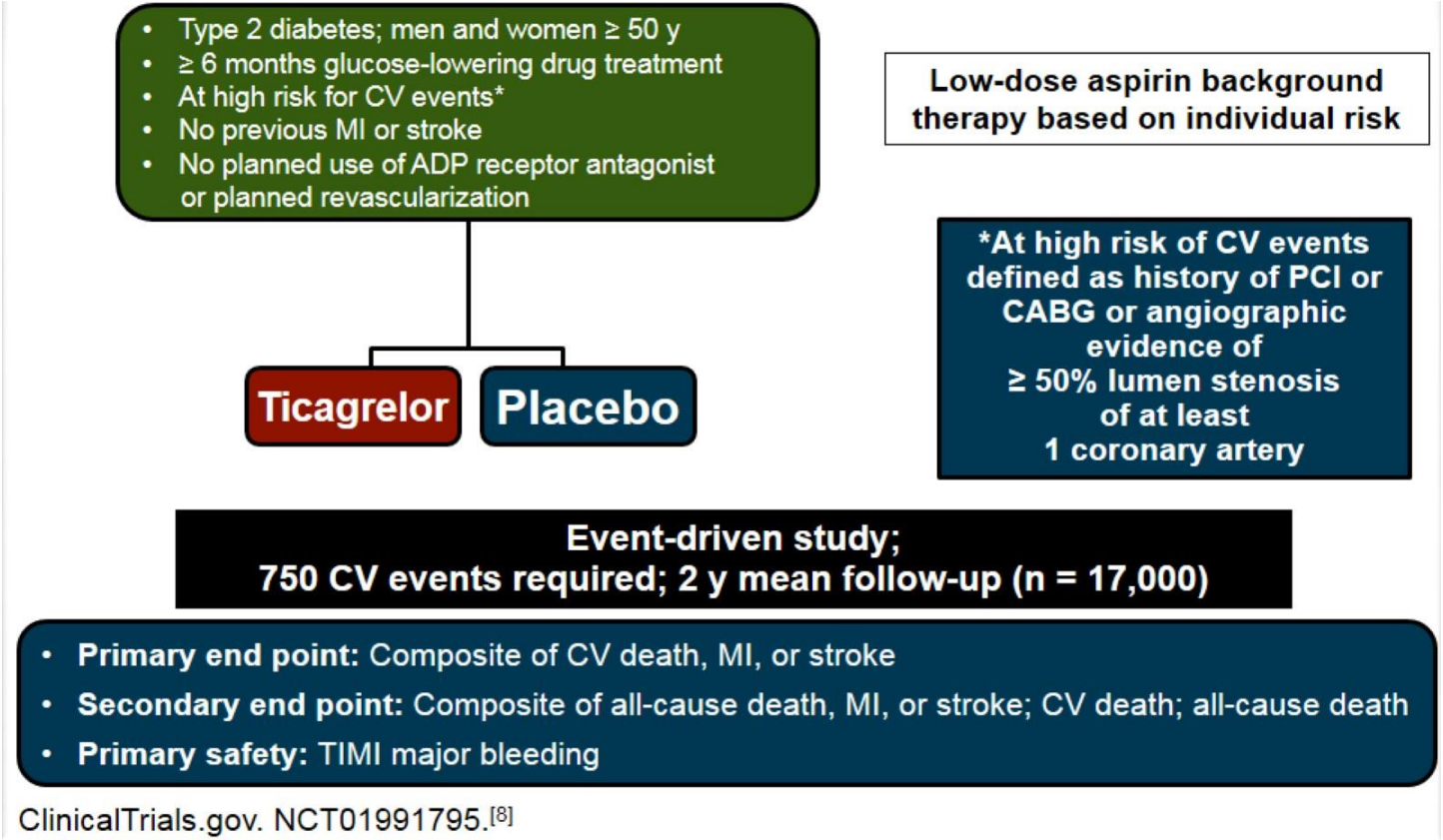
Death, MI, stroke



- **N=9.006, 7.119 Rx after 3 months, 65% ACS (30% NSTEMI), 35% elective high-risk PCI**

Mehran et al., N Engl J Med 2019;381:2032-42

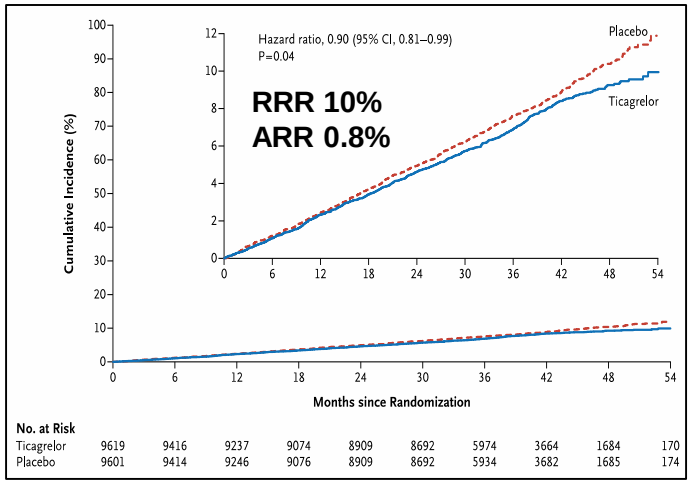
THEMIS: A Study Comparing Cardiovascular Effects of Ticagrelor Versus Placebo in Patients with Type 2 Diabetes and Stable Coronary Artery Disease



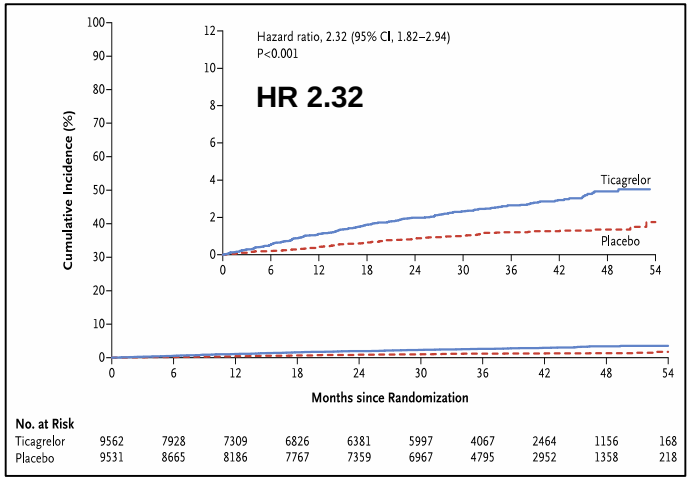
ClinicalTrials.gov. NCT01991795.[8]

DAPT with Ticagrelor in Stable CAD and Diabetes: THEMIS

CV Death, MI, stroke



Major Bleeding



MI ↓, stroke ↓, CV death =, revasc. =, MALE ↓

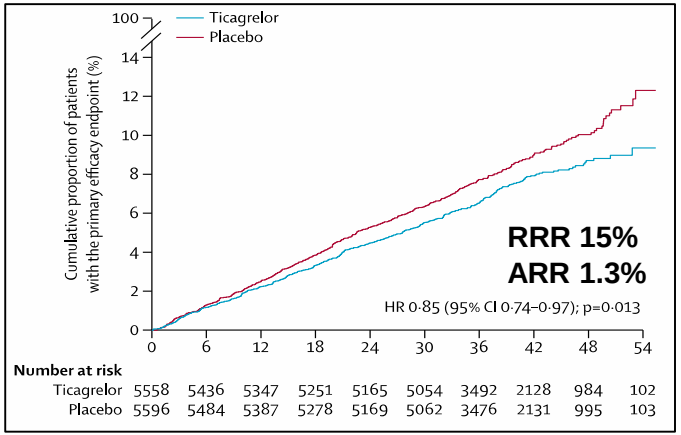
ICB ↑, fatal bleeding =

- **N=19.220, stable CAD and type-2 diabetes, > 50 y, no MI/stroke, mean age 66 y, 80% revascularization**
- **Rx Ticagrelor (90 mg BID → 60 mg BID plus ASA or Placebo plus ASA, 3.3 y follow-up**

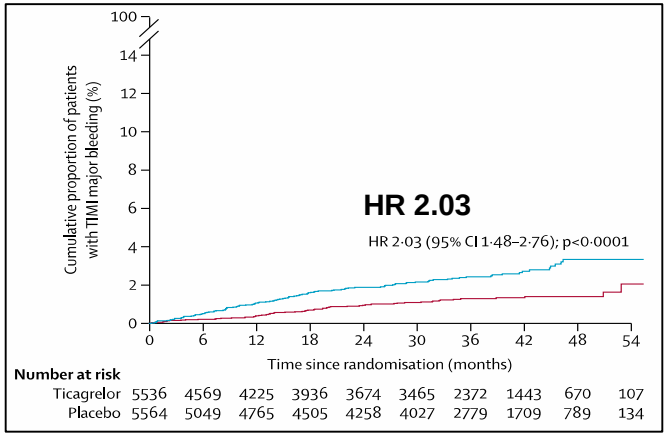
Steg et al., N Engl J Med. 2019;381:1309-1320

DAPT with Ticagrelor in Stable CAD and Diabetes: THEMIS-PCI

CV Death, MI, stroke



Major Bleeding



CV mortality =

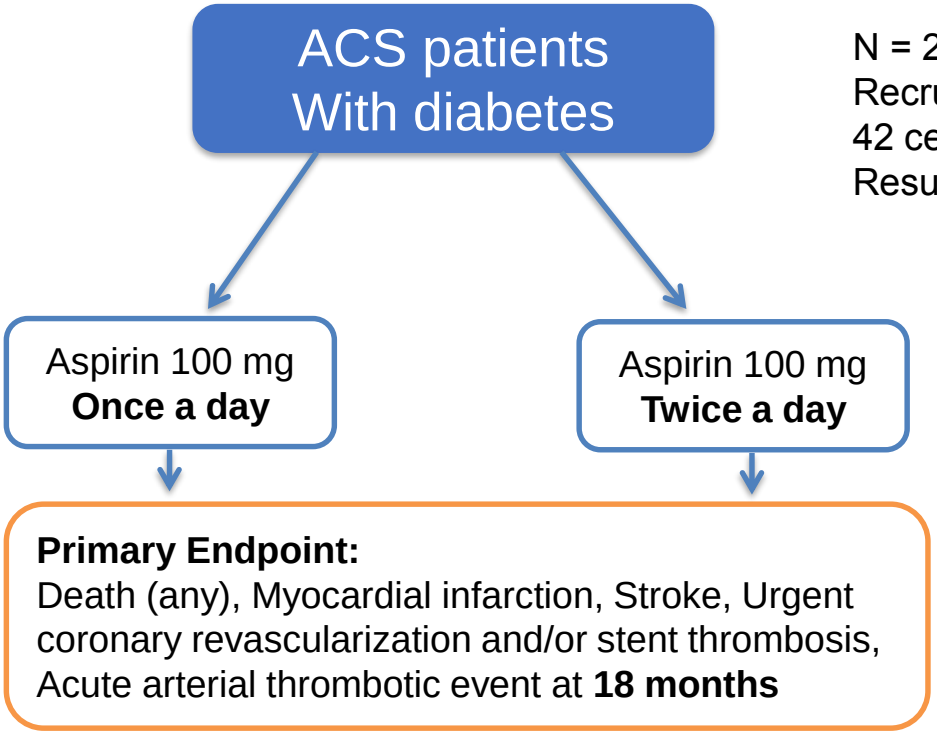
ICB =, fatal bleeding =

Net benefit ↑: irreversible events 9.3% vs. 11.0%, RRR 15%, ARR 1.7%

- **N=11.154, subgroup with previous PCI, stable CAD, type-2 diabetes, 58% of study population**
- **Rx Ticagrelor (90 mg BID → 60 mg BID plus ASA or Placebo plus ASA, 3.3 y follow-up**

Bhatt et al., Lancet. 2019;394:1169-1180

Aspirin Twice a Day in Patients With Diabetes and Acute Coronary Syndrome: ANDAMAN



N = 2.574
Recruiting
42 centers in France
Results in 2020

ClinicalTrials.gov.NCT02520921

MAnagement of high bleeding risk patients post bioresorbable polymer coated STEnt implantation with an abbReviated versus prolonged DAPTregimen – MASTER DAPT

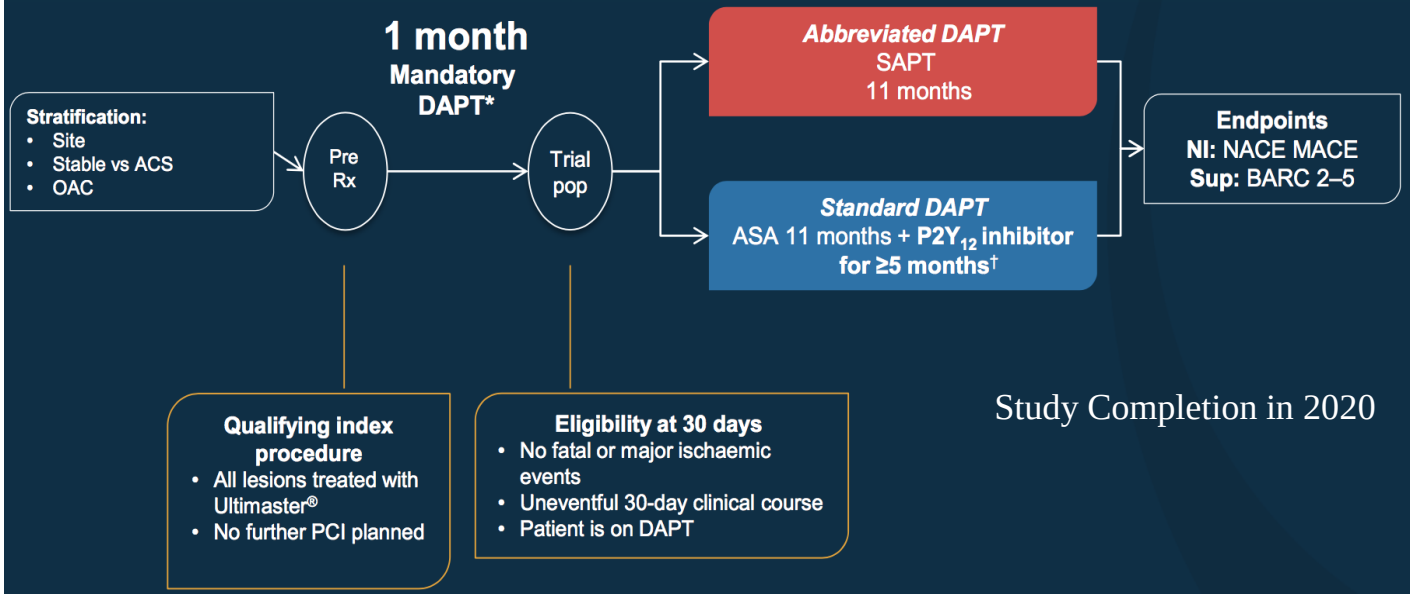
MASTER-DAPT is an investigator-initiated, multi-center, randomized clinical trial in **high bleeding risk (HBR) patients after PCI (**with a bioresorbable polymer coated sirolimus-eluting stent) comparing short vs longer DAPT.

3 Primary endpoints:

1) **Net adverse clinical endpoints (NACE)** defined as a composite of all-cause death, myocardial infarction, stroke and bleeding events defined as BARC 3 or 5
2) **Major adverse cardiac and cerebral events** (MACCE) defined as a composite of all-cause death, myocardial infarction and stroke
3) **Major or clinically relevant non-major bleeding** (MCB) defined as a composite of type 2, 3 and 5 BARC bleeding events

MASTER DAPT
Study design and key features

4300 HBR patients, 130 international sites



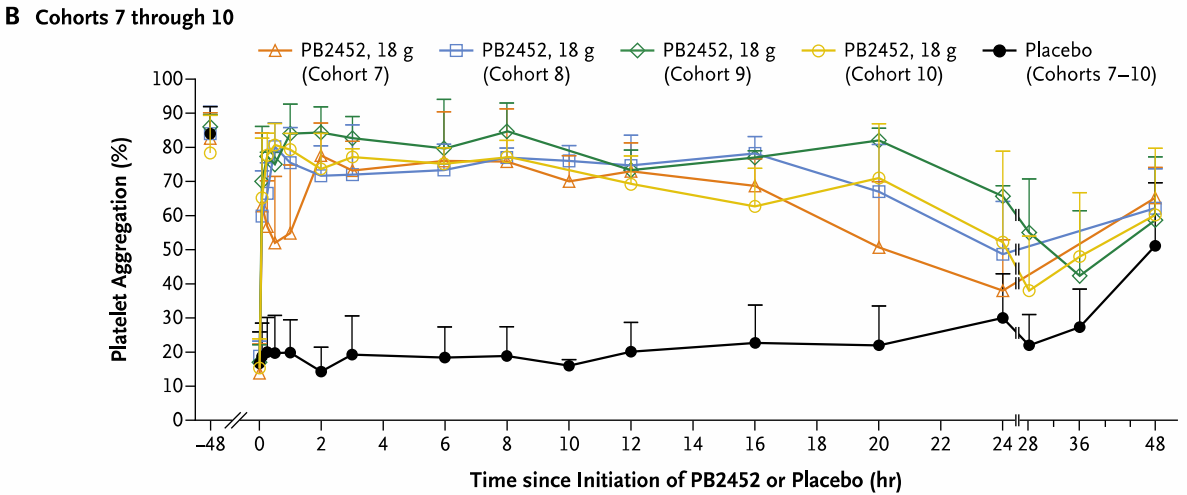
Study Completion in 2020

*DAPT duration is counted from the day of last implanted stent; staging has to be pre-specified at the time of screening and cannot be planned later than 2 months after index PCI;

†OAC pts can stop DAPT 2 months after confirmed randomization.

BARC, Bleeding Academic Research Consortium.

Antibody-Based Ticagrelor Reversal Agent

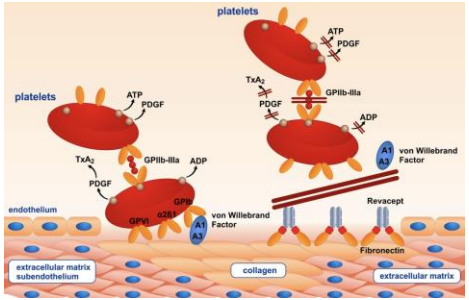


P Values at Time Point:	5 Min	0.25 Hr	0.5 Hr	1 Hr	2 Hr	3 Hr	6 Hr	8 Hr	10 Hr	12 Hr	16 Hr	20 Hr
Cohort 7	0.04	0.04	0.13	0.04	0.40	0.02	0.02	0.02	0.15	0.02	0.02	0.22
Cohort 8	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.15	0.02	0.02	0.02
Cohort 10	0.04	0.02	0.02	0.02	0.02	0.02	0.02	0.02	NA	0.02	0.02	0.02

64 healthy volunteers

Bhatt et al., N Engl J Med. 2019;380:1825-1833

Antithrombotic targets that may preserve hemostasis in cardiovascular disease prevention



Target: Glycoprotein VI (GPVI) is a key platelet receptor which mediates plaque-induced platelet activation.

GPVI	Revacept	Dimeric GPVI-Fc that blocks vascular collagen at sites of plaque or vascular erosion and collagen-induced platelet activation	Inhibits platelet thrombus formation at sites of vascular injury in preclinical models; no effect on bleeding time	II	NCT01645306 (REF. 113)

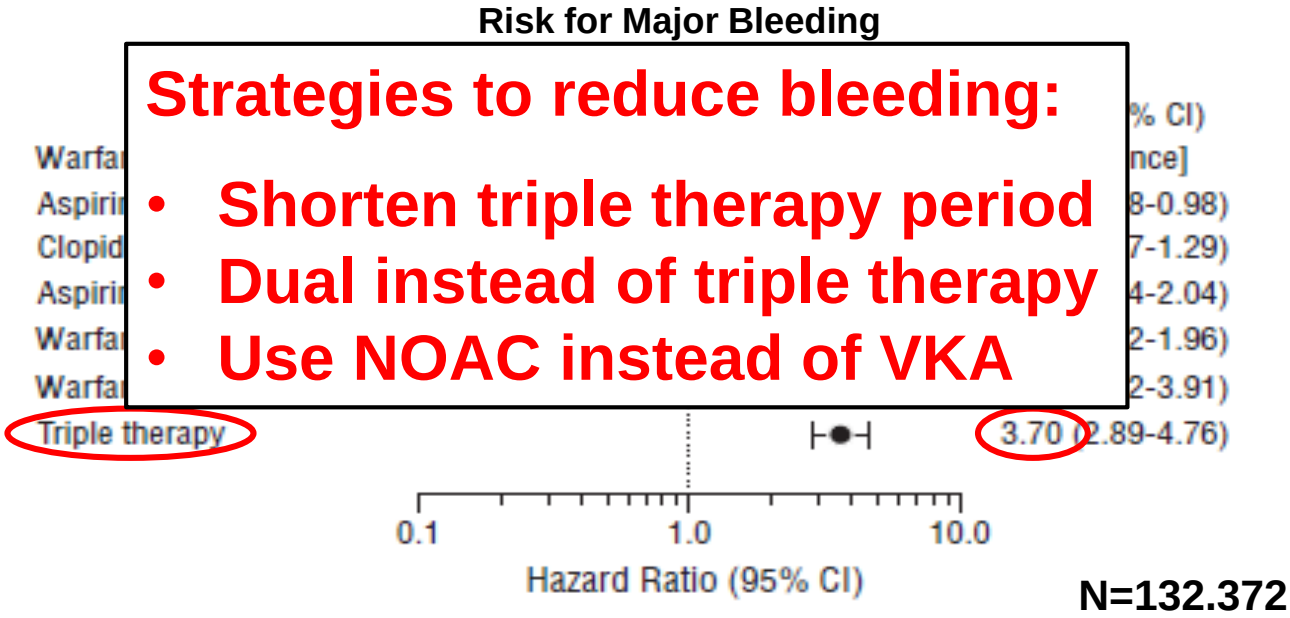
Agent:

- ***Revacept* (IV)** binds to its ligand (collagen) on atherosclerotic plaques **preventing circulating platelets from binding to collagen exposed by the injured plaque**. All this is achieved without affecting systemic hemostasis.
- **Ongoing phase II trials** in patients with **stable coronary artery disease undergoing PCI** and in patients with **symptomatic carotid stenosis.**

Nat Rev Cardiol. 2018;15:181-191

Anticoagulation and Platelet Inhibition in Patients with AF and PCI: Bleeding Risk

Stent + AF = Triple Therapy ?



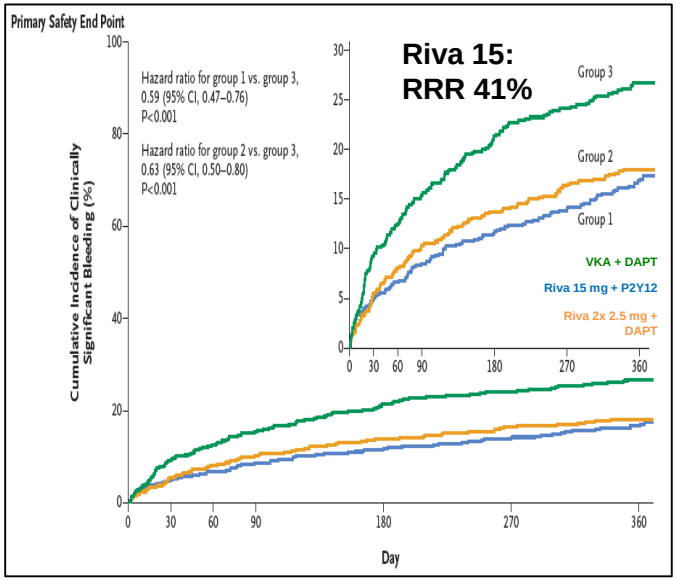
N=132.372

Hansen et al., Arch Intern Med. 2010;170:1433-1441

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

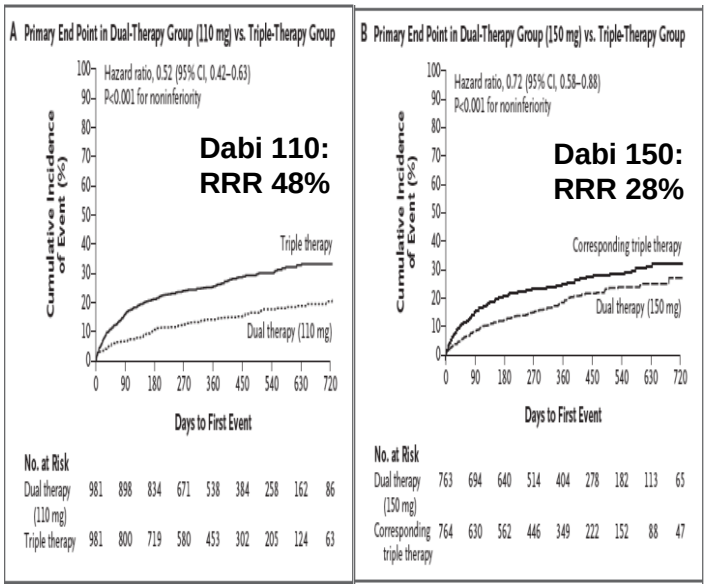
PIONEER AF-PCI, N=2.124

(Dual with Riva 15 OD vs. Triple with Riva 2.5 BID vs. Triple with VKA)



RE-DUAL PCI, N=2.725

(Dual with Dabi 150 BID vs. Dual with Dabi 110 BID vs. Triple with VKA)

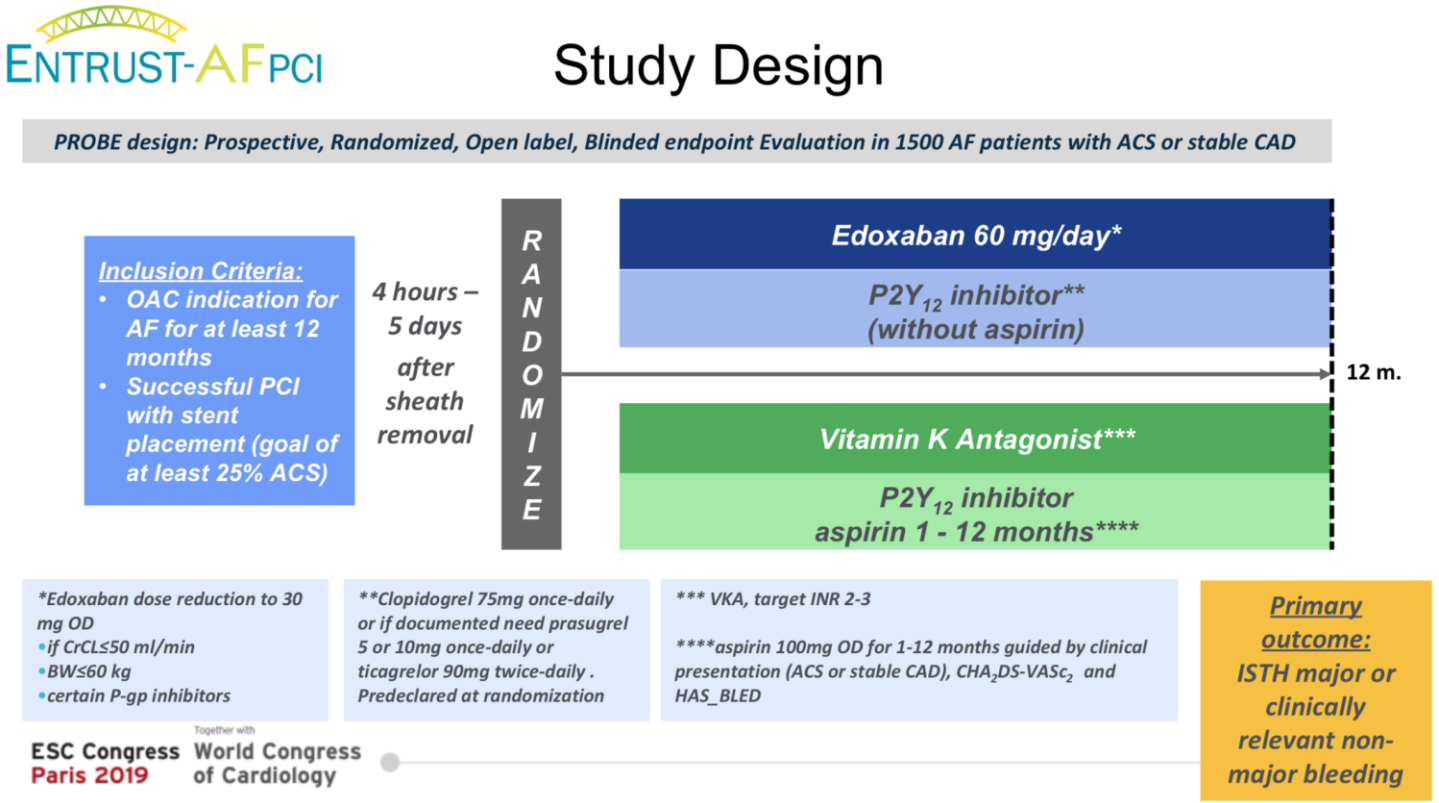


Bleeding ↓↓; Ischemic events = (But: low statistical power)

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

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

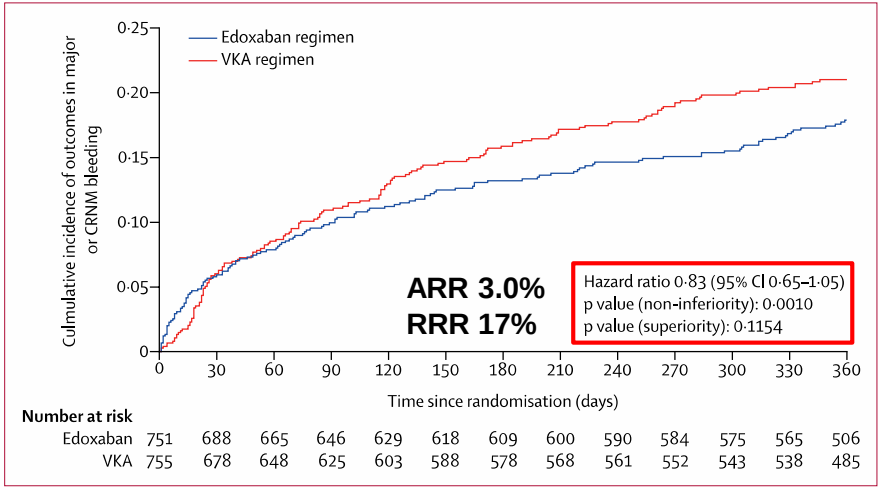
Anticoagulation and Platelet Inhibition in Patients with AF and PCI: ENTRUST-AF PCI

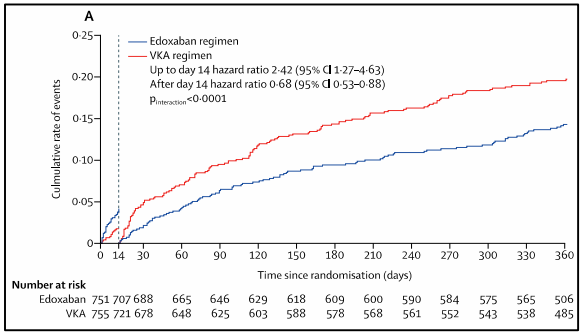


Goette et al., Presented at ESC Congress 2019, Paris, France

Anticoagulation and Platelet Inhibition in Patients with AF and PCI: ENTRUST-AF PCI

Major or CRNM bleeding

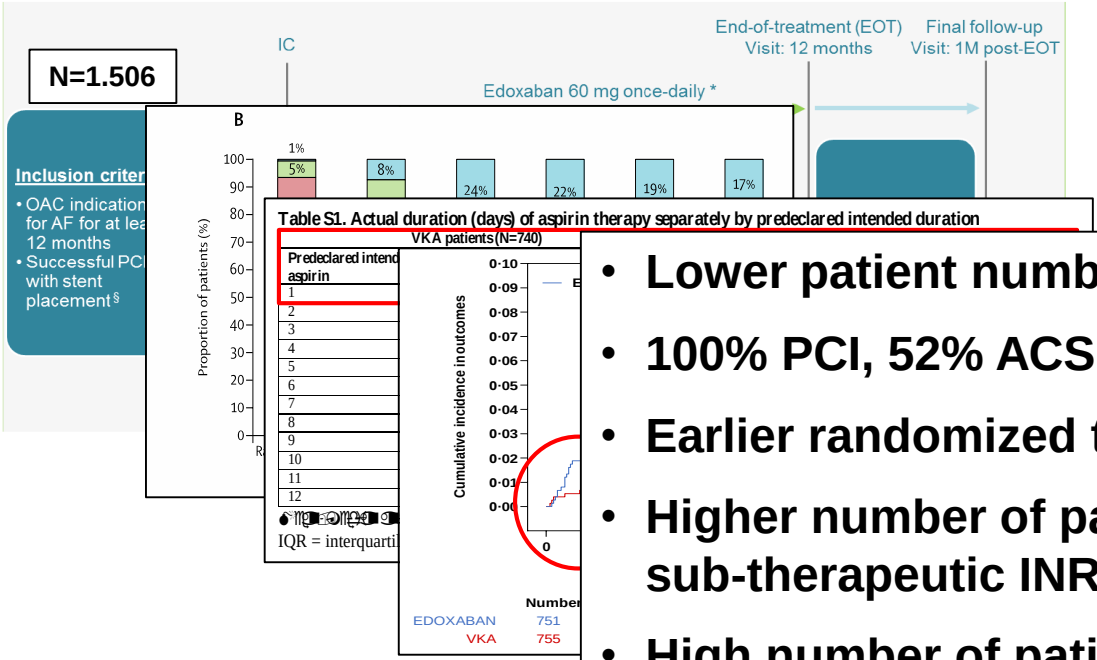




- **N=1.506, AF and PCI with stent**
- **Rx median 45h post PCI**
- **52% ACS, 93% Clopidogrel, 7% Ticagrelor**
- **50% ASA 1 month**

Vranckx et al., Lancet. 2019;394:1335-1343

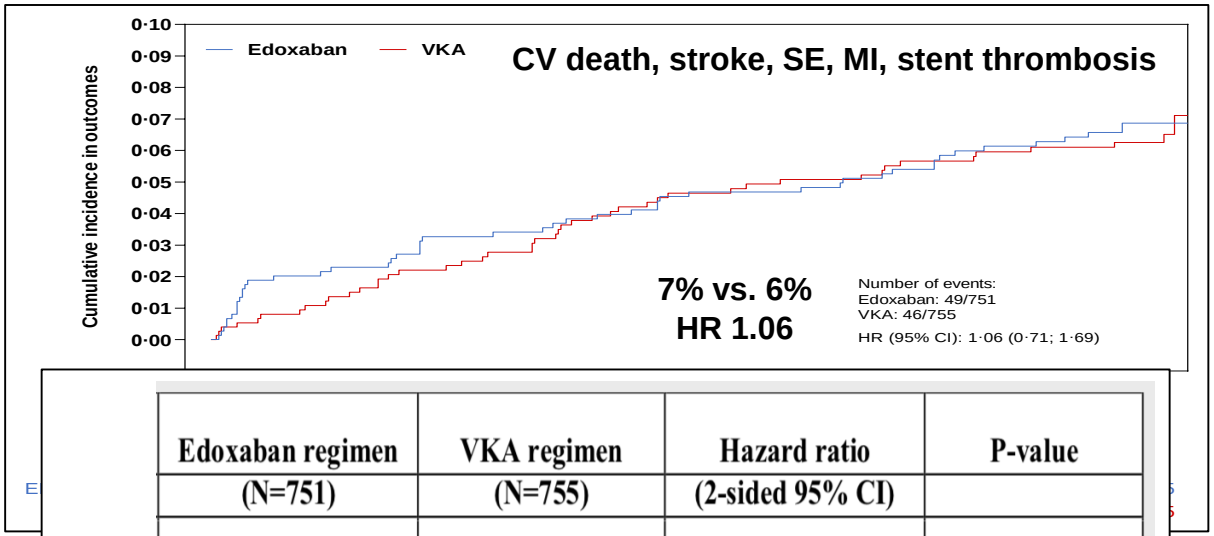
ENTRUST-AF PCI: Why “only“ Non-Inferiority and not Superiority?



- Lower patient number in the trial (statist. power)
- 100% PCI, 52% ACS, no conservative therapy
- Earlier randomized treatment after PCI
- Higher number of patients in the triple group with sub-therapeutic INR at the beginning of the trial
- High number of patients in the triple group with cessation of ASA treatment early after 1 month
- Early increae of ischemic events with likely additional anti-thrombotic treatment

Vranckx et al., Lancet. 2019;394:1335-1343

Anticoagulation and Platelet Inhibition in Patients with AF and PCI: ENTRUST-AF PCI



	Edoxaban regimen (N=751)	VKA regimen (N=755)	Hazard ratio (2-sided 95% CI)	P-value
	29 (3·90)	23 (3·00)		
MI	4·27	3·41	1·26 (0·729; 2·169)	P=0·4106
	8 (1·10)	6 (0·80)		
ST	1·16	0·88	1·32 (0·463; 3·791)	P=0·6008

Vranckx et al., Lancet. 2019;394:1335-1343

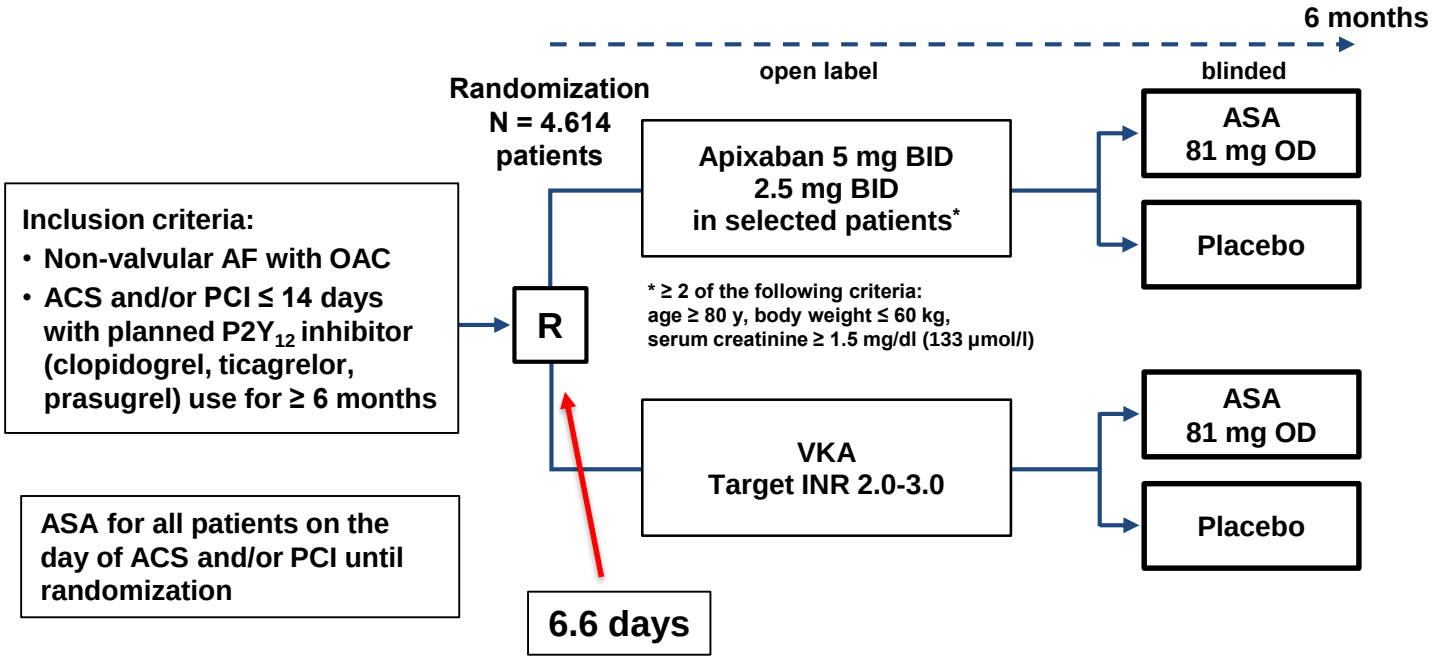
Atrial Fibrillation and PCI – Dual vs Triple Therapy

PIONEER AF-PCI, RE-DUAL PCI, ENTRUST AF-PCI tested:

Dual Therapy with NOAC + SAPT
vs
Triple Therapy with VKA + DAPT

Effects mediated by NOAC instead of VKA
or
mediated by stopping ASA?

Apixaban versus VKA in Patients with AF and ACS and/or PCI: AUGUSTUS



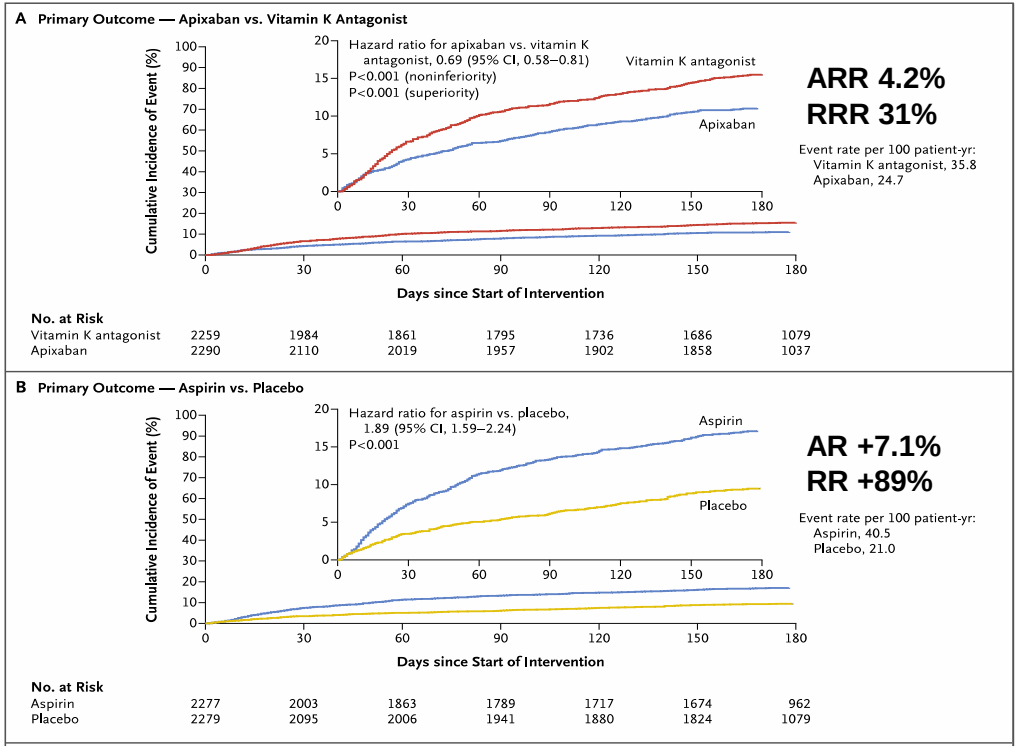
- Primary endpoint: Major or clinically relevant non-major bleeding (within 6 months)
- Secondary endpoint: Death, MI, stroke, stent thrombosis, urgent revascularization, re-hospitalization

Lopes et al., N Engl J Med. 2019;380:1509-1524

Apixaban versus VKA in Patients with AF and ACS and/or PCI: AUGUSTUS

Major or CRNM bleeding

N=4.614
100% AF
61% ACS
93% Clopidogrel
6% Ticagrelor
1% Prasugrel



Major bleedings: Apixaban/VKA: ARR 1.6%, RRR 36%; ASA/Placebo: AR +1.8%, RR +70%

Lopes et al., N Engl J Med. 2019;380:1509-1524

Apixaban versus VKA in Patients with AF and ACS and/or PCI: AUGUSTUS

Secondary Ischemic Endpoint

Outcome	Apixaban	VKA	Hazard Ratio (95% CI)	P Value for Superiority
Anticoagulation-regimen comparison				
Death or ischemic event‡				
No. of patients with event/total no. (%)	154/2306 (6.7)	163/2308 (7.1)	—	—
Event rate per 100 patient-yr	14.3	15.3	0.93 (0.75–1.16)	NS

Stroke

MI

Stent thromb.

Revasc.

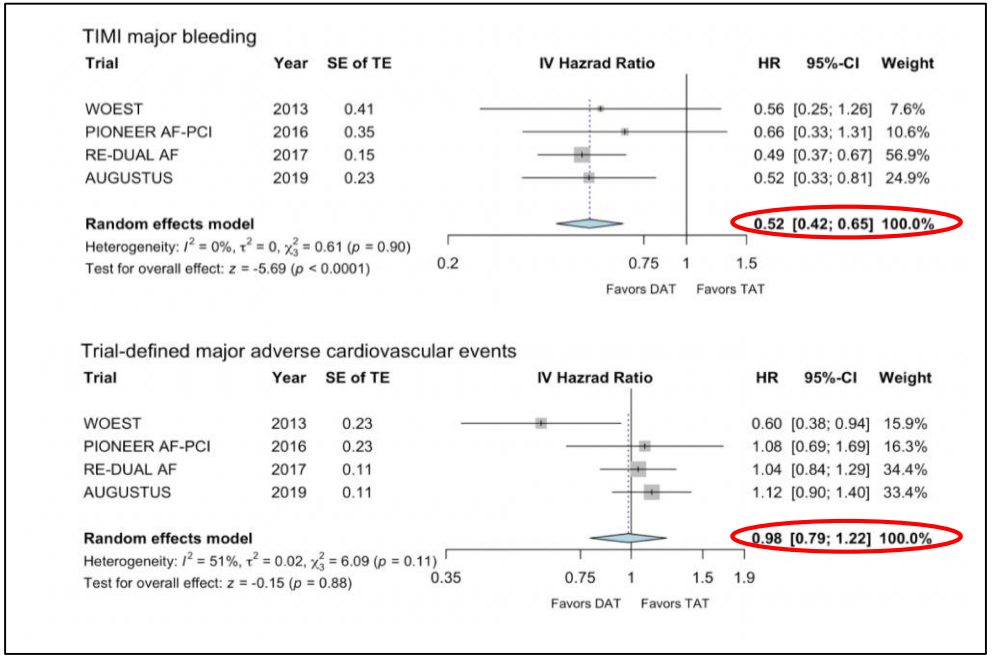
Efficacy outcomes	Apixaban	VKA		ASA	Placebo	Ratio (95% CI)
No. of patients in analysis	2306	2308		2307	2307	
Stroke						
No. of patients with event (%)	13 (0.6)	26 (1.1)	—	20 (0.9)	19 (0.8)	—
Event rate per 100 patient-yr	1.2	2.4	0.50 (0.26–0.97)	1.8	1.7	1.06 (0.56–1.98)
Myocardial infarction						
No. of patients with event (%)	72 (3.1)	80 (3.5)	—	68 (2.9)	84 (3.6)	—
Event rate per 100 patient-yr	6.6	7.4	0.89 (0.65–1.23)	6.3	7.8	0.81 (0.59–1.12)
ARC definite or probable stent thrombosis						
No. of patients with event (%)	14 (0.6)	18 (0.8)	—	11(0.5)	21 (0.9)	—
Event rate per 100 patient-yr	1.3	1.6	0.77 (0.38–1.56)	1.0	1.9	0.52 (0.25–1.08)
Urgent revascularization						
No. of patients with event (%)	40 (1.7)	44 (1.9)	—	37 (1.6)	47 (2.0)	—
Event rate per 100 patient-yr	3.7	4.1	0.90 (0.59–1.38)	3.4	4.3	0.79 (0.51–1.21)

Lopes et al., N Engl J Med. 2019;380:1509-1524

Atrial Fibrillation and PCI – Dual vs Triple Therapy: Meta-Analysis

Major Bleeding

Trial-defined MACE



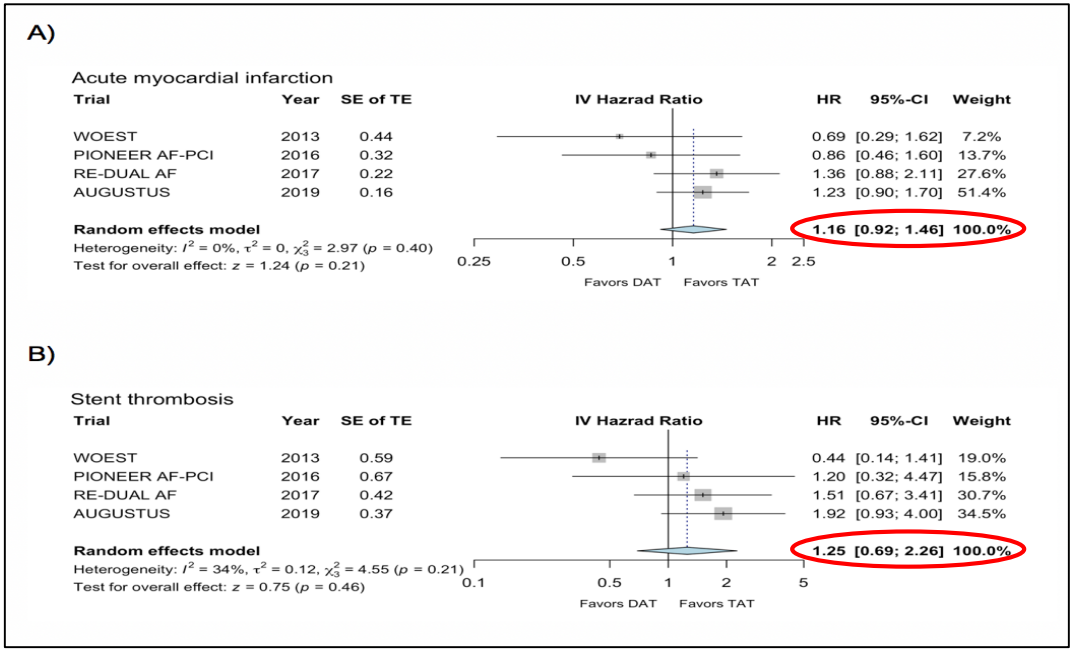
Meta-Analysis: WOEST, PIONEER AF-PCI, RE-DUAL PCI, AUGUSTUS; N=9.317

Haller et al., Eur Heart J Cardiovasc Pharmacother. 2019;5:226-236

Atrial Fibrillation and PCI – Dual vs Triple Therapy: Meta-Analysis

Myocardial infarction

Stent thrombosis

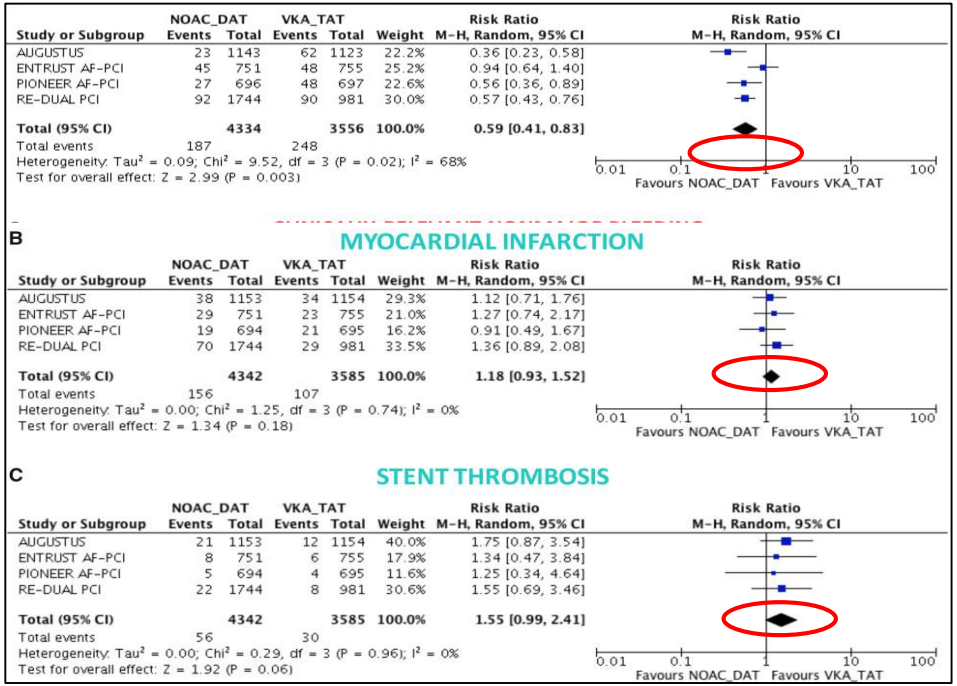


Meta-Analysis: WOEST, PIONEER AF-PCI, RE-DUAL PCI, AUGUSTUS; N=9.317

Haller et al., Eur Heart J Cardiovasc Pharmacother. 2019;5:226-236

Atrial Fibrillation and PCI – Dual vs Triple Therapy: Meta-Analysis

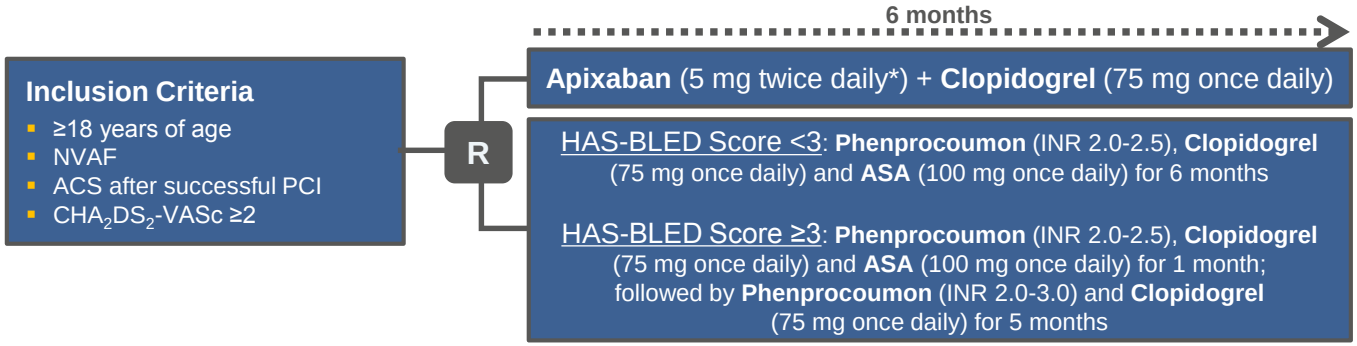
NOAK DAT vs. VKA TAT



Meta-Analysis: PIONEER AF-PCI, RE-DUAL PCI, AUGUSTUS, ENTRUST-AF PCI; N=10.234

Gargiulo et al., Eur Heart J. 2019;40:3757-3767

Apixaban versus VKA in NVAF Patients with ACS After PCI: APPROACH-ACS



Select Exclusion Criteria

- Severe renal insufficiency (CrCl <30 mL/min)
- History of TIMI major bleeding according to TIMI and/or type ≥3b BARC criteria in the last 6 months

Primary Outcome

- Combined endpoint of moderate or major bleeding complications during the initial hospitalization and follow-up (BARC type ≥2 bleeding)

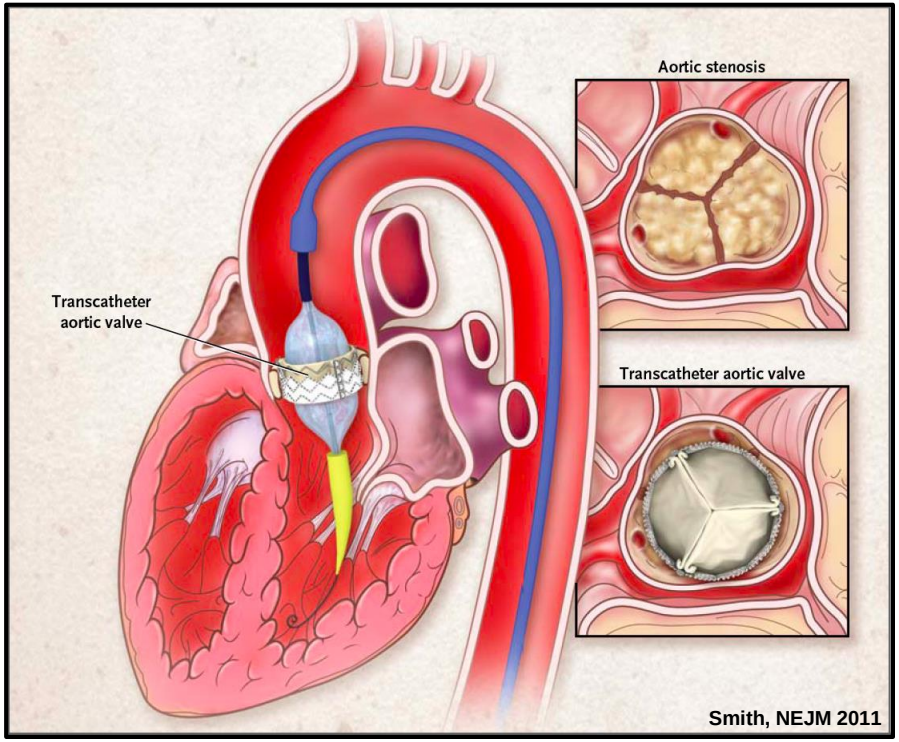
Key Secondary Outcome

- Combined event of death, myocardial infarction, definite stent thrombosis, stroke/other systemic thromboembolism
- Major bleeding (BARC >3b)

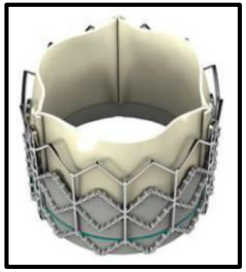
*Reduced dosing of 2.5 mg twice daily depending on age, renal function and body weight.

Klinikum der Universitaet Muenchen. Apixaban vs. phenprocoumon in patients with ACS and AF: APPROACH-ACS-AF (APPROACH). Available from: https://clinicaltrials.gov/ct2/show/NCT02789917. NLM Identifier: NCT02789917. Accessed on February 09, 2017.

TAVI Procedure for Aortic Stenosis

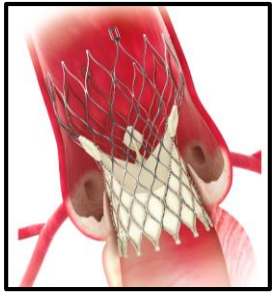


Balloon-expandable



Leon, NEJM 2010

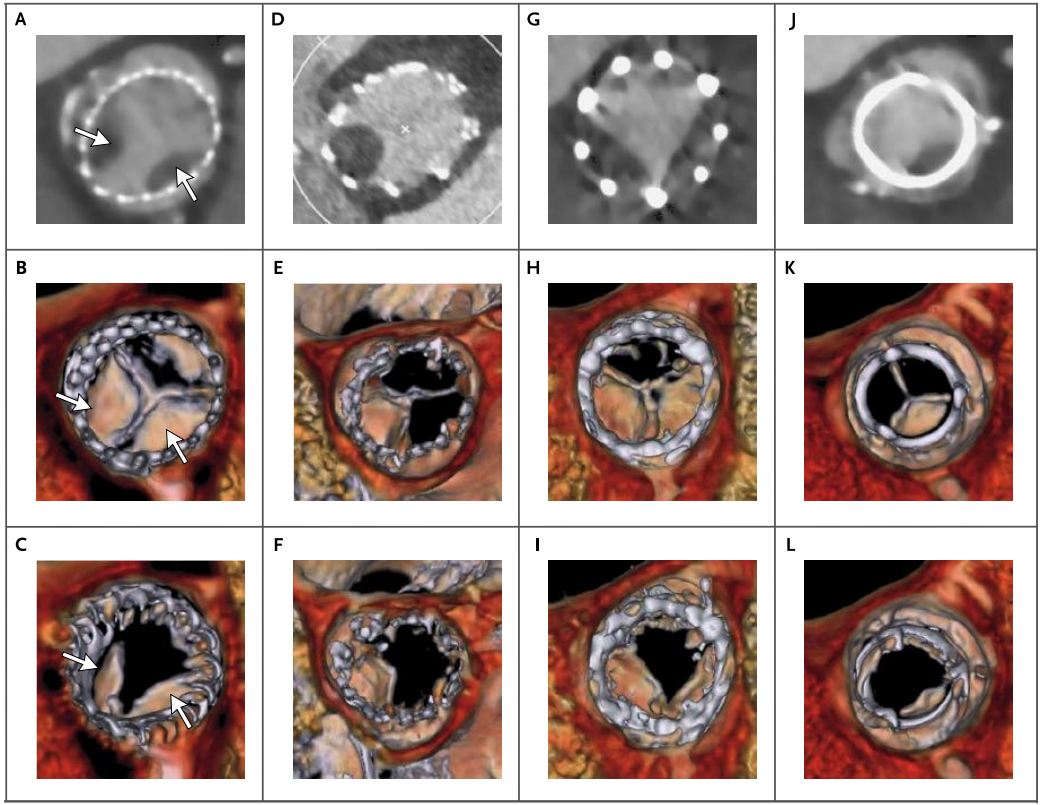
Self-expanding



Adams, NEJM 2014

Smith et al., N Engl J Med. 2011;364:2187-2198; Leon et al., N Engl J Med. 2010;363:1597-1607 (Suppl); Adams et al., N Engl J Med. 2014;370:1790-1798 (Suppl)

Subclinical Leaflet Thrombosis in Bio-AVR



Makkar et al., N Engl J Med. 2015;373:2015-2024.

Subclinical Leaflet Thrombosis in Bio-AVR

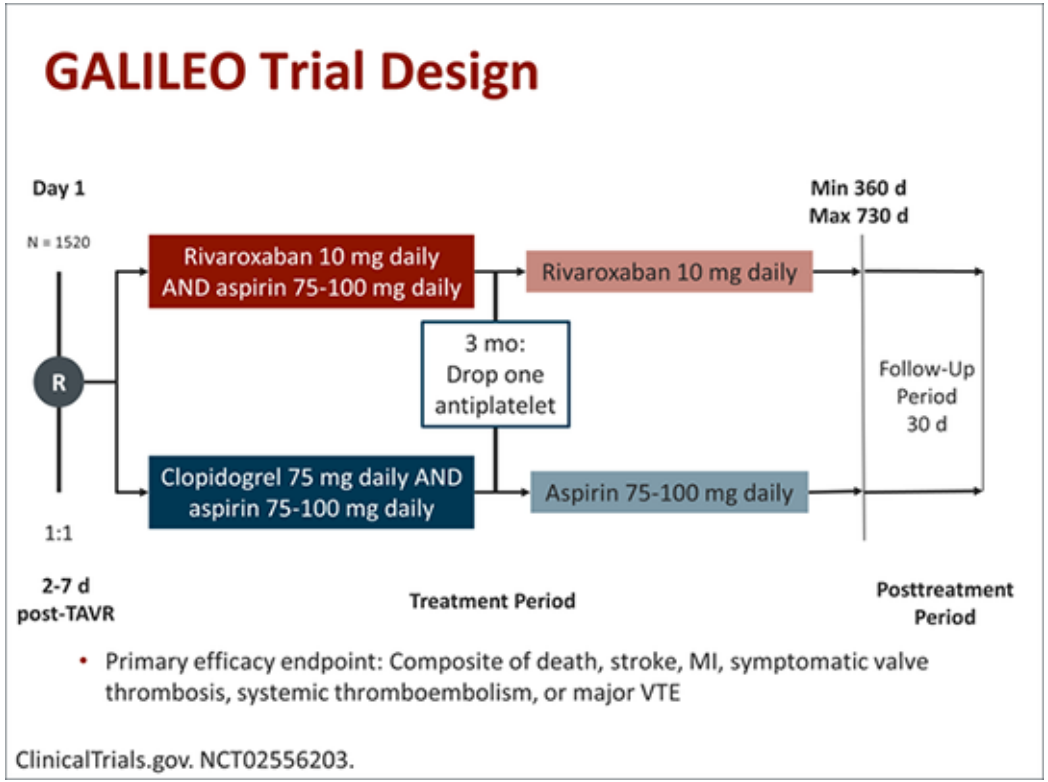
Antithrombotic Strategies in TAVI

- Problem: subclinical leaflet thrombosis post AVR
- OAC with VKA recommended for 3 months post Bio-AVR
- Stroke and bleeding risk high within first 30 days post TAVI
- Standard treatment DAPT 3-6 months

Do we need more intensive OAC with less bleeding?

Makkar et al., N Engl J Med 2015;373:2015-24.

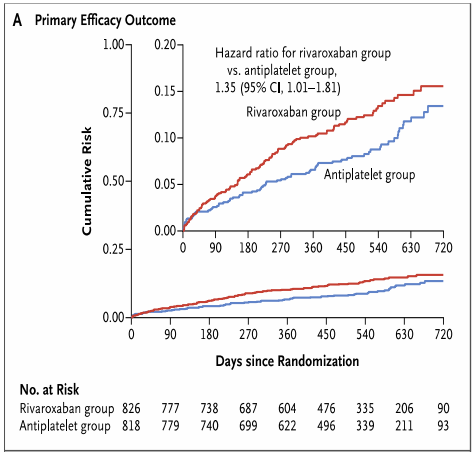
NOAC plus ASA vs DAPT post TAVI: GALILEO



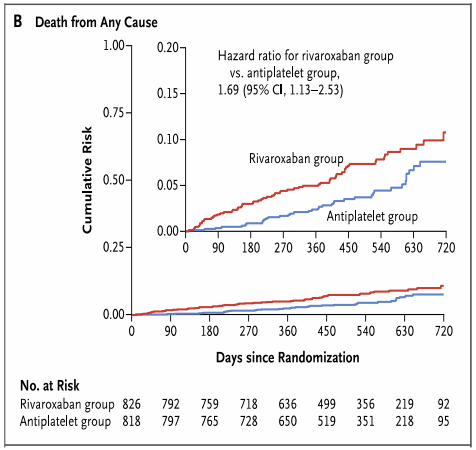
Dangas et al., N Engl J Med. 2019; DOI: 10.1056/NEJMoa1911425

NOAC plus ASA vs DAPT post TAVI: GALILEO

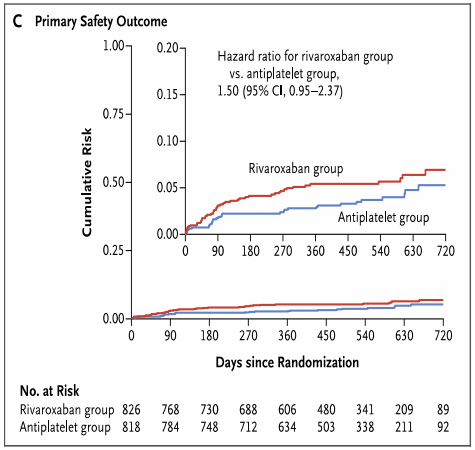
Death, stroke, MI, sympt. valve thrombosis, PE, DVT, SE



All-cause death

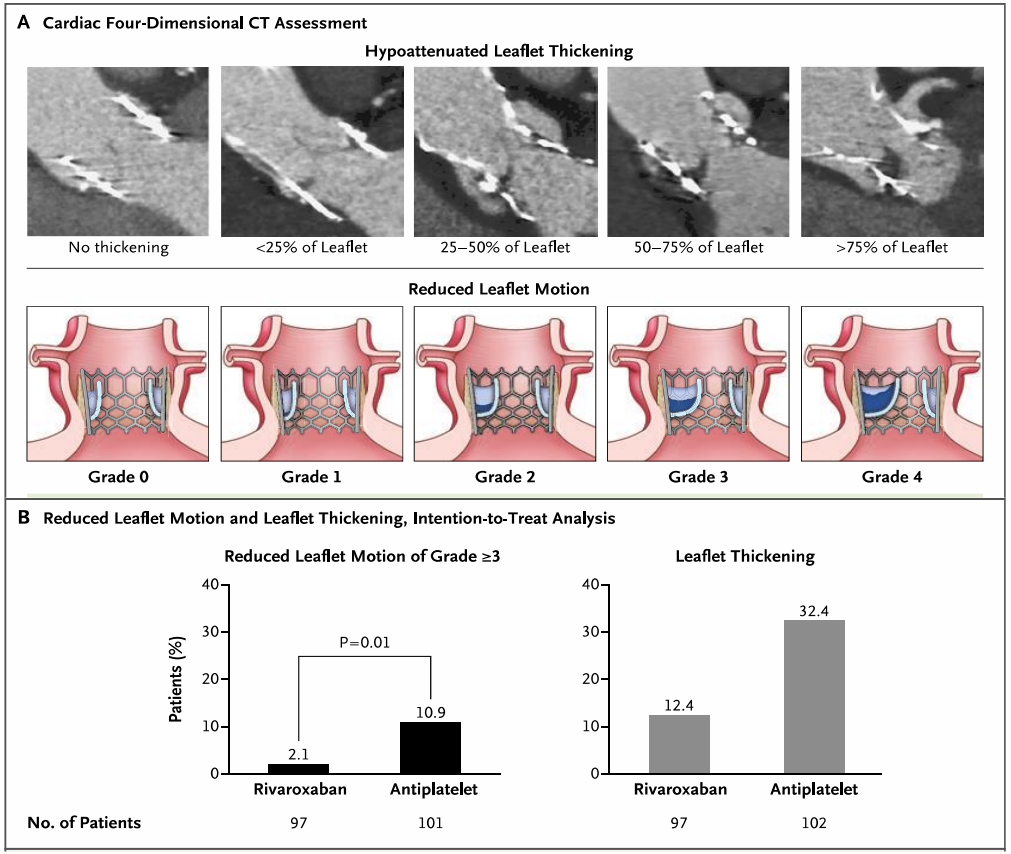


VARC life-threatening, disabling, or major bleeding



Dangas et al., N Engl J Med. 2019; DOI: 10.1056/NEJMoa1911425

NOAC plus ASA vs DAPT post TAVI: GALILEO-4D

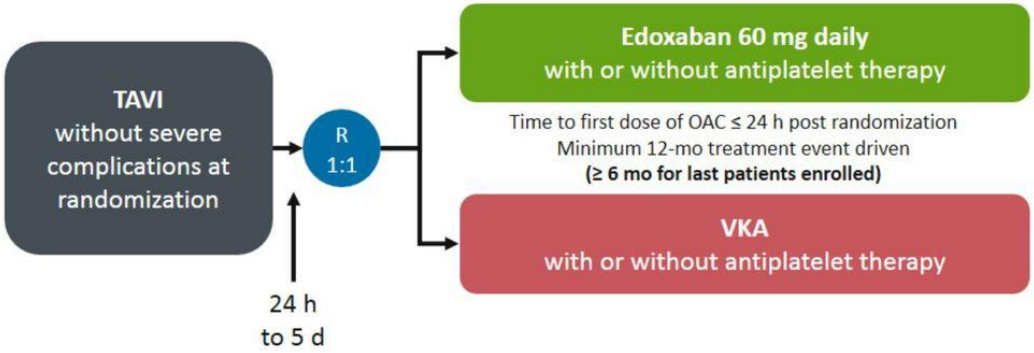


De Backer et al., N Engl J Med. 2019; DOI: 10.1056/NEJMoa1911426

ENVISAGE TAVI AF

ENVISAGE TAVI AF -- Study Design

Prospective, randomized, open-label, blinded evaluation of edoxaban vs VKA in approximately 1400 patients with AF indicated for chronic OAC after successful TAVI (~2500 patient-y)

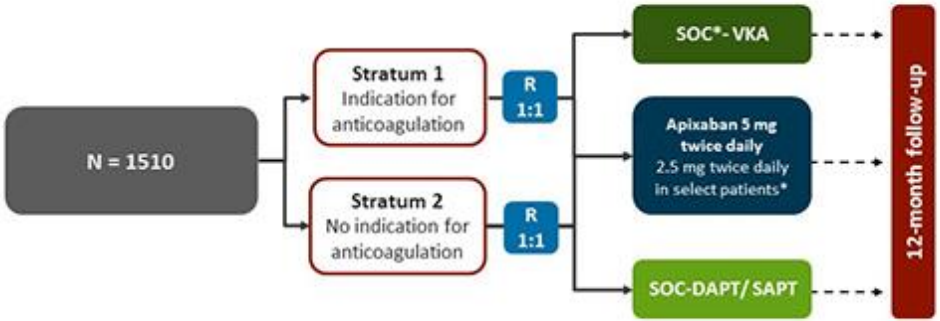


clinicaltrials.gov: NCT02943785; Van Mieghem NM, et al. *Am Heart J.* (Submitted)

ATLANTIS

ATLANTIS Trial: Apixaban vs Standard of Care

Apixaban in Patients Who Underwent a Clinically Successful TAVI Procedure

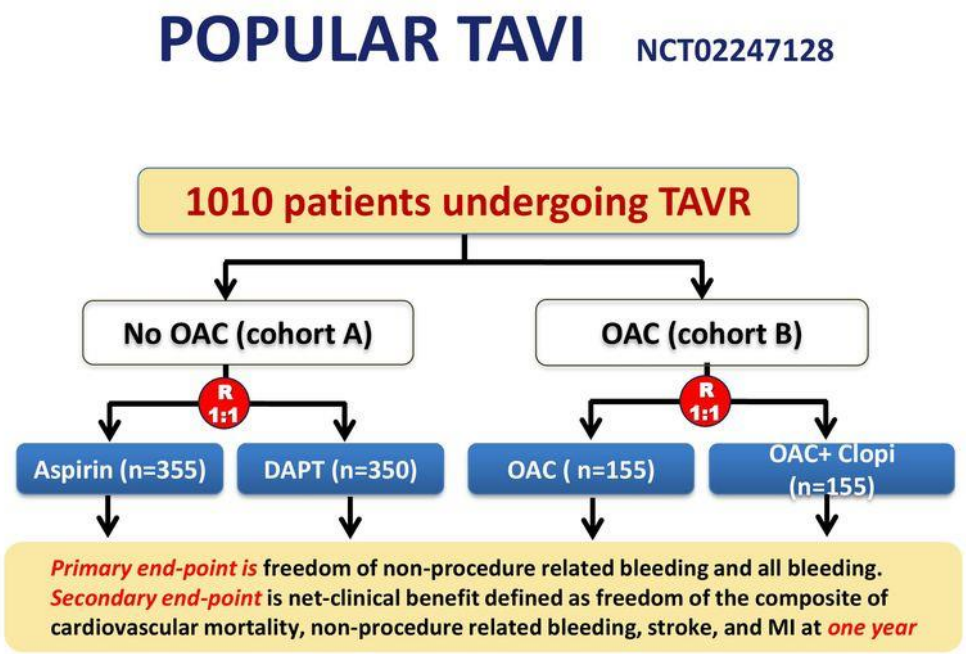


Primary endpoint: Composite of death, MI, stroke/TIA/systemic emboli, intracardiac or bioprosthesis thrombus, episode of DVT/PE, major bleeding, over 6 months of follow-up

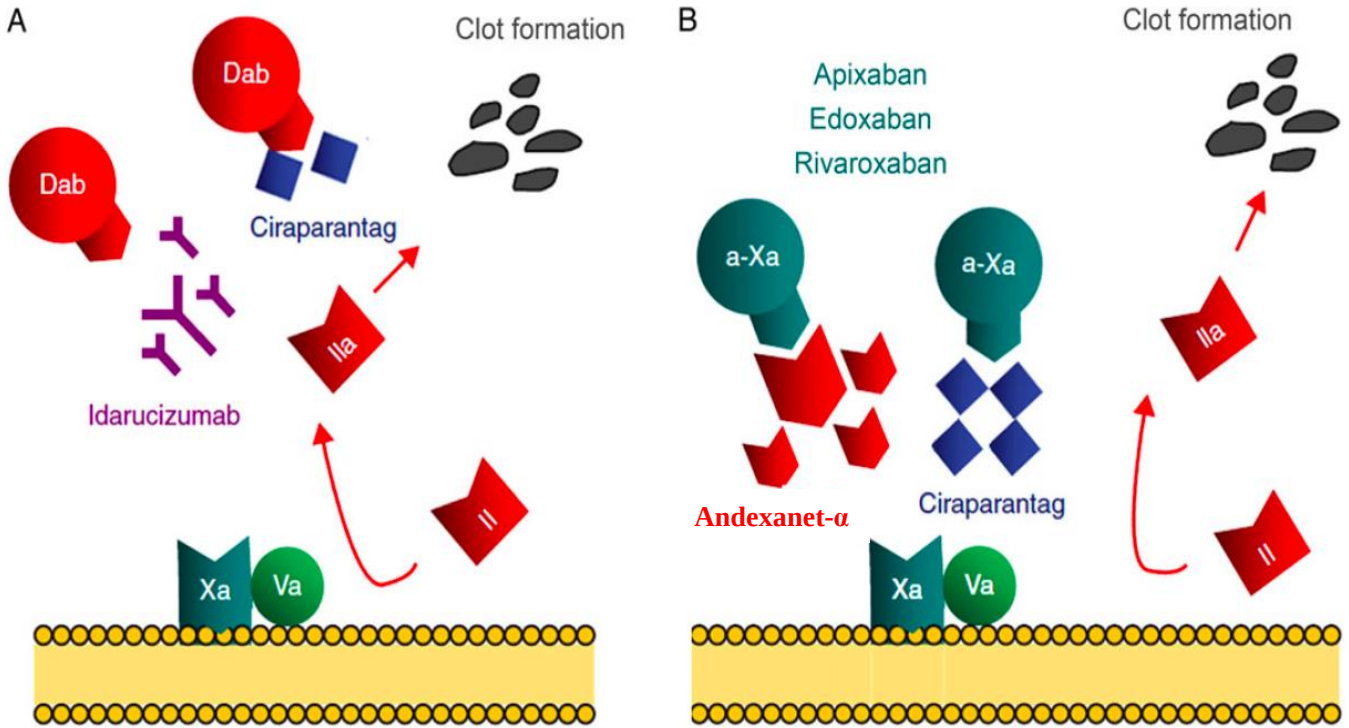
*2.5 mg twice daily if CrCl 15 to 29mL/min or if 2 of the following criteria: age ≥ 80, weight ≤ 60 kg, or Cr ≥ 1.5 mg/dL (133 µmol).

ClinicalTrials.gov. NCT02664649.

POPular TAVI



NOAC Antidotes and Reversal Agents – Mechanisms



Niessner et al., Eur Heart J. 2017;38:1710-1716

NOAC Antidotes and Reversal Agents – Studies

	Idarucizumab	Andexanet	Ciraparantag (PER977)
Target	Dabigatran	Oral direct factor Xa-inhibitors, low-molecular-weight heparins and fondaparinux	Oral direct factor Xa and IIa inhibitors, low-molecular-weight heparins, un-fractionated heparin and fondaparinux
Structure	Humanized Fab fragment	Human rFXa variant	Synthetic small molecule
Immediate onset of reversal (<10 min)	Yes	Yes	Yes
Duration of effect	(12 to) 24 h	2 h	24 h
Re-administration possible	Yes, after 24 h	Unknown	Currently tested (NCT02207257)
Tested in healthy volunteers	Yes (NCT020287809)	Yes	Yes (NCT01826266, NCT02207257)
Elderly	Yes	Yes (NCT022207725)	No
Renally impaired	Yes	No	No

RE-VERSE AD
Full study cohort published
Idarucizumab approved (EMA & FDA)

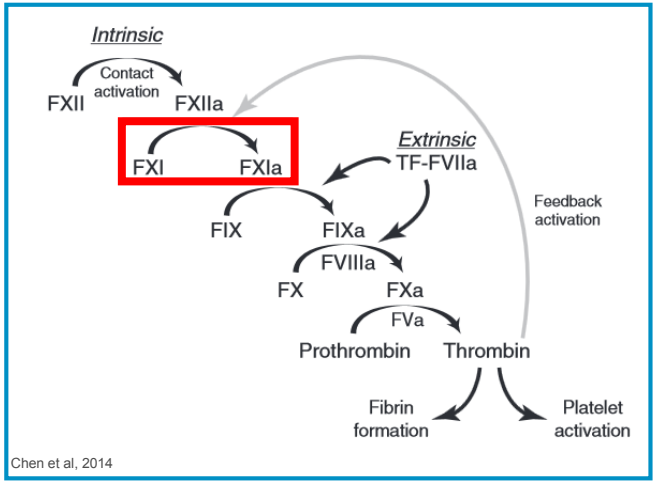
ANNEXA-4
Full study cohort published
Andexanet approved by FDA and EMA (conditional marketing authorization)

Phase 2 Study enrolling

Niessner et al., Eur Heart J. 2017;38:1710-1716

Rationale for FXI(a) as innovative drug target

- FXI activation occurs by contact activation and during the amplification phase after formation of small amounts of thrombin
- FXIa contributes to clot formation, clot stabilisation and amplification of clot growth
- FXIa triggers thrombosis, but has a minor role for hemostasis

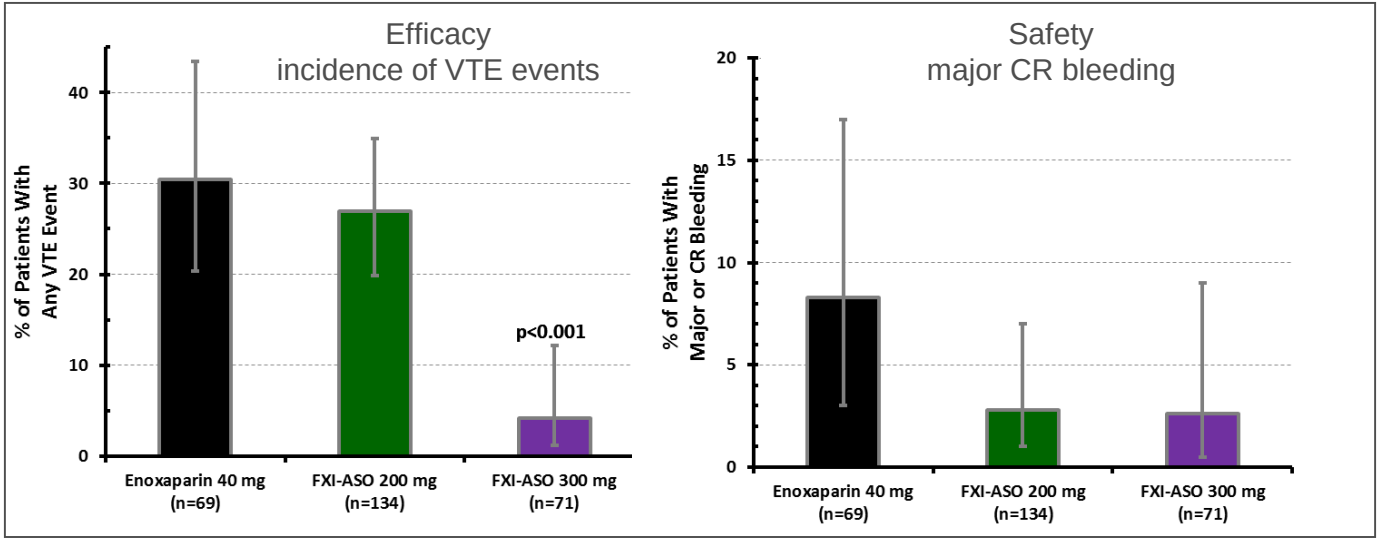


Chen et al, 2014

Hypothesis: inhibition of FXI(a) has the potential for anti-thrombotic effect without increased bleeding

Phase 2a data using FXI-ASO
(antisense oligonucleotide)

Open-label, randomized, study comparing 200 or 300 mg FXI-ASO vs LMWH in ~300 knee replacement surgery patients



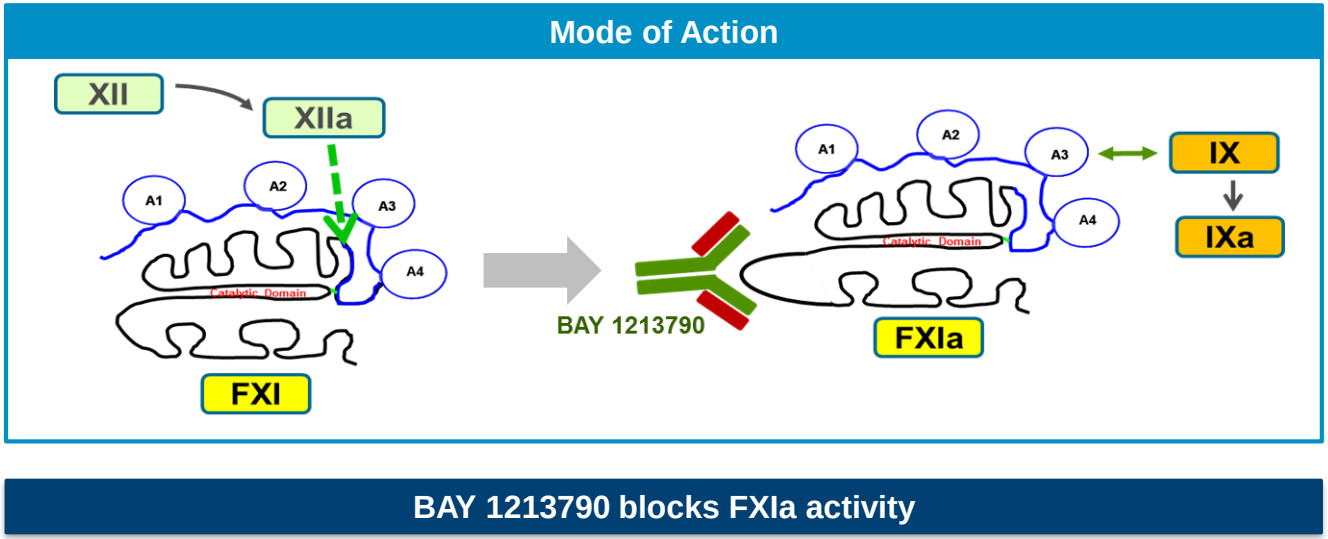
Proof of concept for the inhibition of factor XI in humans available

N Engl J Med (2015); 372 (3): 232-240

Mode of Action of the FXIa antibody

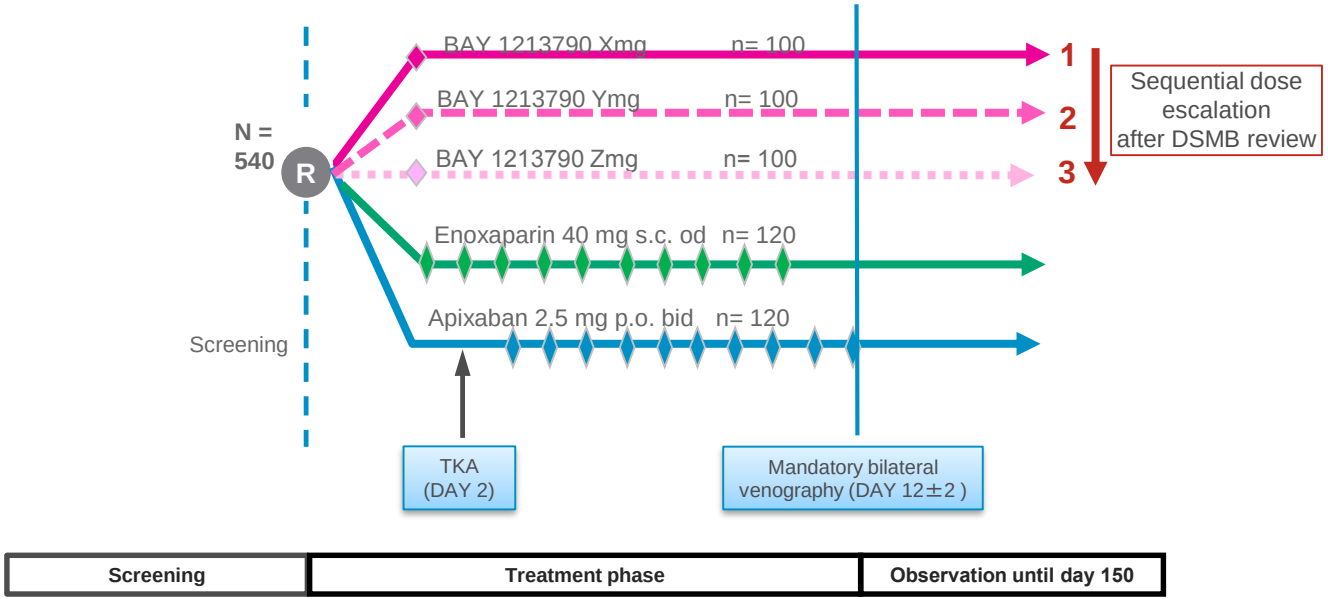
FXIa antibody BAY 1213790

- Fully human IgG1 antibody
- Binds to activated FXI and blocks FXIa activity by addressing the catalytic domain

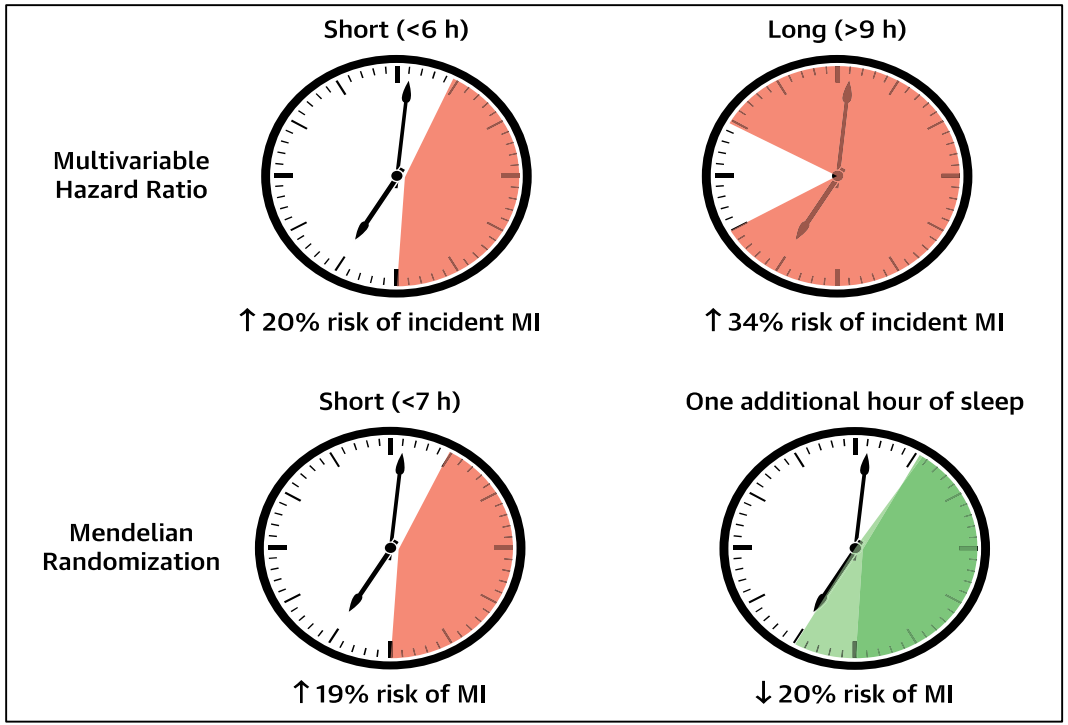


A1-A1: Apple domain 1-4 of FXI

Study 17664 Design – FOXTROT Study

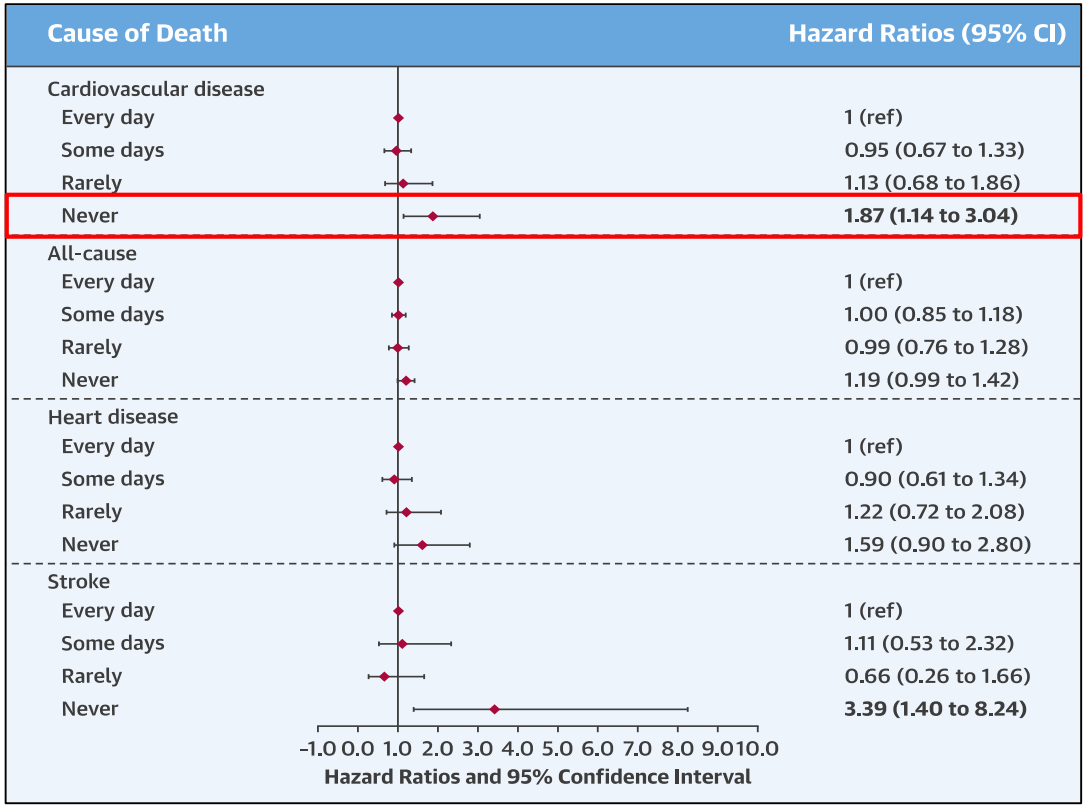


Sleep Duration and Risk of Myocardial Infarction: UK Biobank Analysis



Daghlas et al., J Am Coll Cardiol. 2019;74:1304-1314

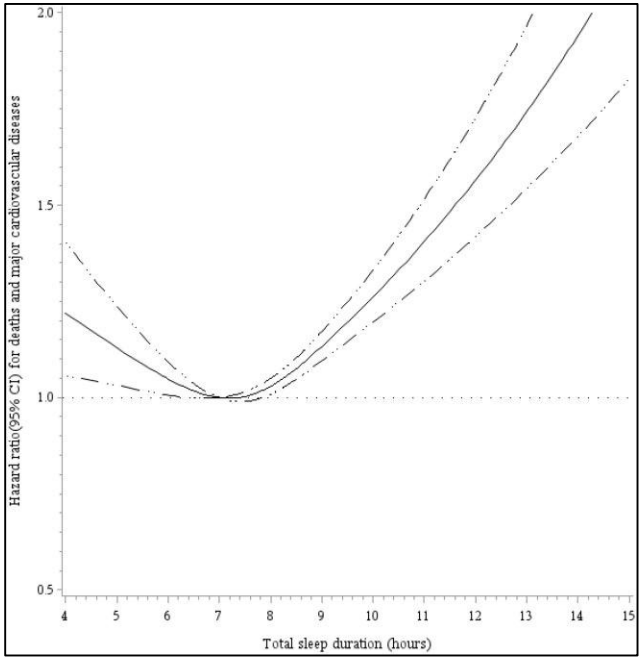
Skipping Breakfast and Cardiovascular Mortality: NHANES III



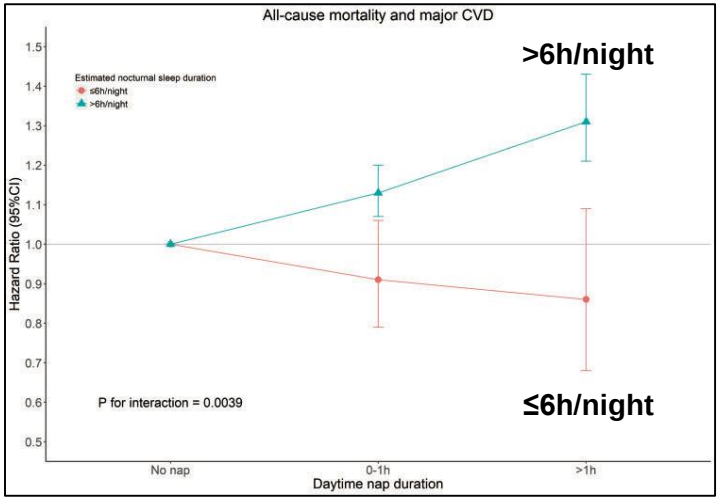
Rong et al., J Am Coll Cardiol. 2019;73:2025-2032

Sleep Duration, Napping and Risk of Death and Cardiovascular Diseases: PURE

Total Sleep Duration



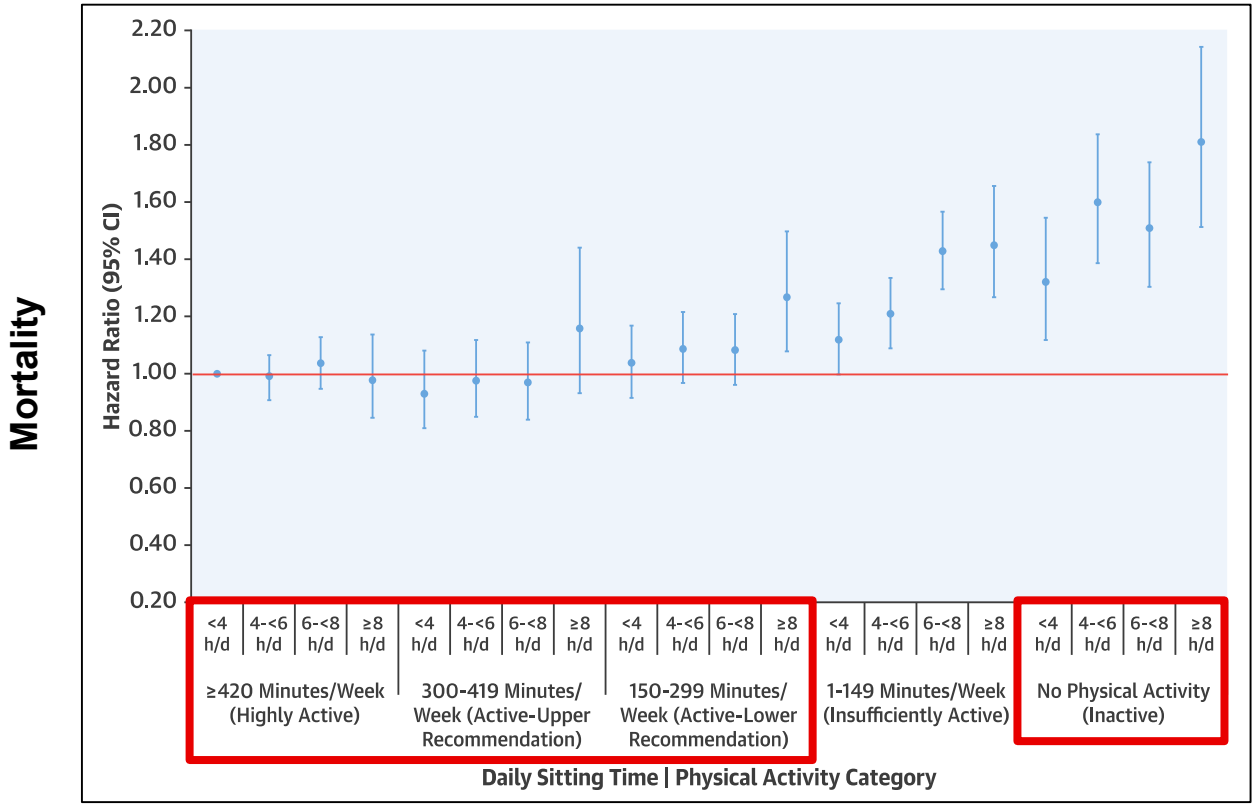
Daytime Nap Duration



No Nap **0-1 h** **>1 h**

Wang et al., Eur Heart J. 2019;40:1620-1629

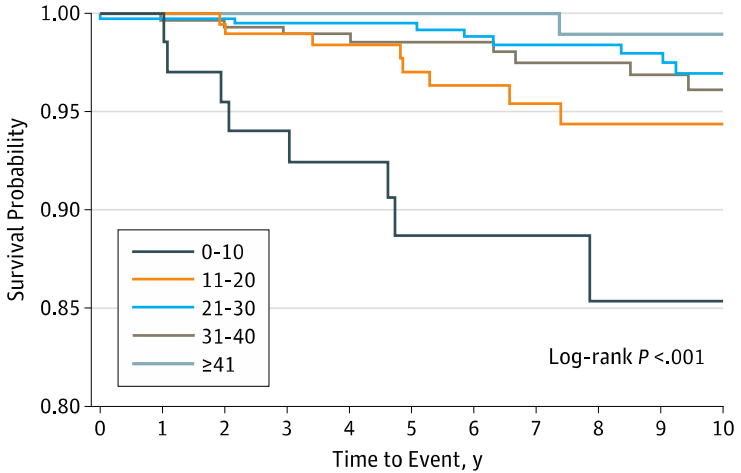
Daily Sitting Time and Mortality: 45 and Up Study



Stamatakis et al., J Am Coll Cardiol. 2019;73:2062-2072

Push-ups and Cardiovascular Events: Indiana Firefighters

Figure. Kaplan-Meier Curves for the Cumulative Risk of Cardiovascular Disease Outcome in 5 Push-up Categories



>10

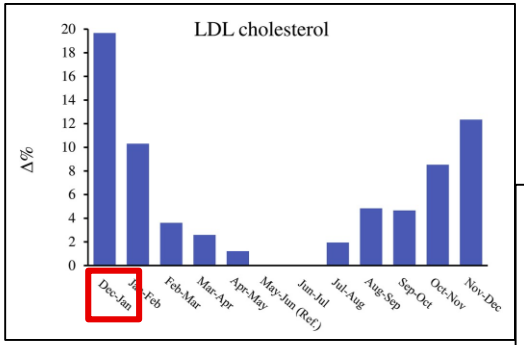
≤10

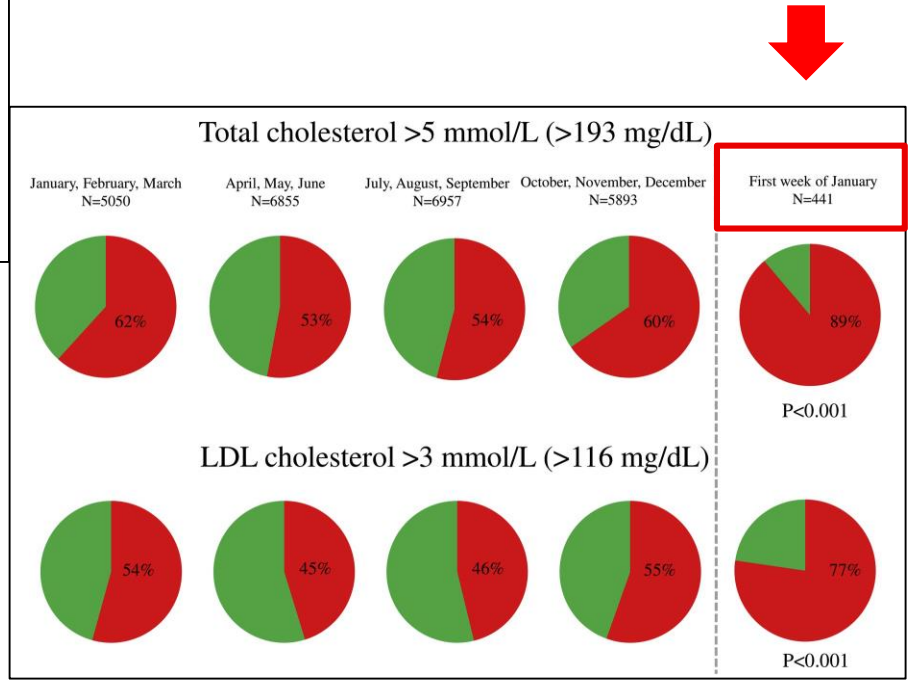
No. at risk

0-10	75	68	63	60	53	39	32	28	26	23	17
11-20	200	200	186	184	172	139	118	96	89	78	63
21-30	389	386	382	375	368	310	275	238	227	202	155
31-40	285	283	276	271	267	232	208	179	169	148	120
≥41	155	153	151	149	147	129	112	99	92	86	63

Yang et al., JAMA Network Open. 2019;2:e188341

Hypercholesterolemia after Christmas





Vedel-Krogh et al., Atherosclerosis. 2019;281:121-127

Thank you for your attention!

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Cardiovascular
Pharmacotherapy