

TCTAP, 2024. April 26

5:43 PM ~ 5:51 PM (8min)

Presentation Room 1

All About New Data of Antithrombotics

Long-term DOAC Management of AF and Stable CAD : Expectation on the EPIC-CAD Trial After the AFIRE Trial

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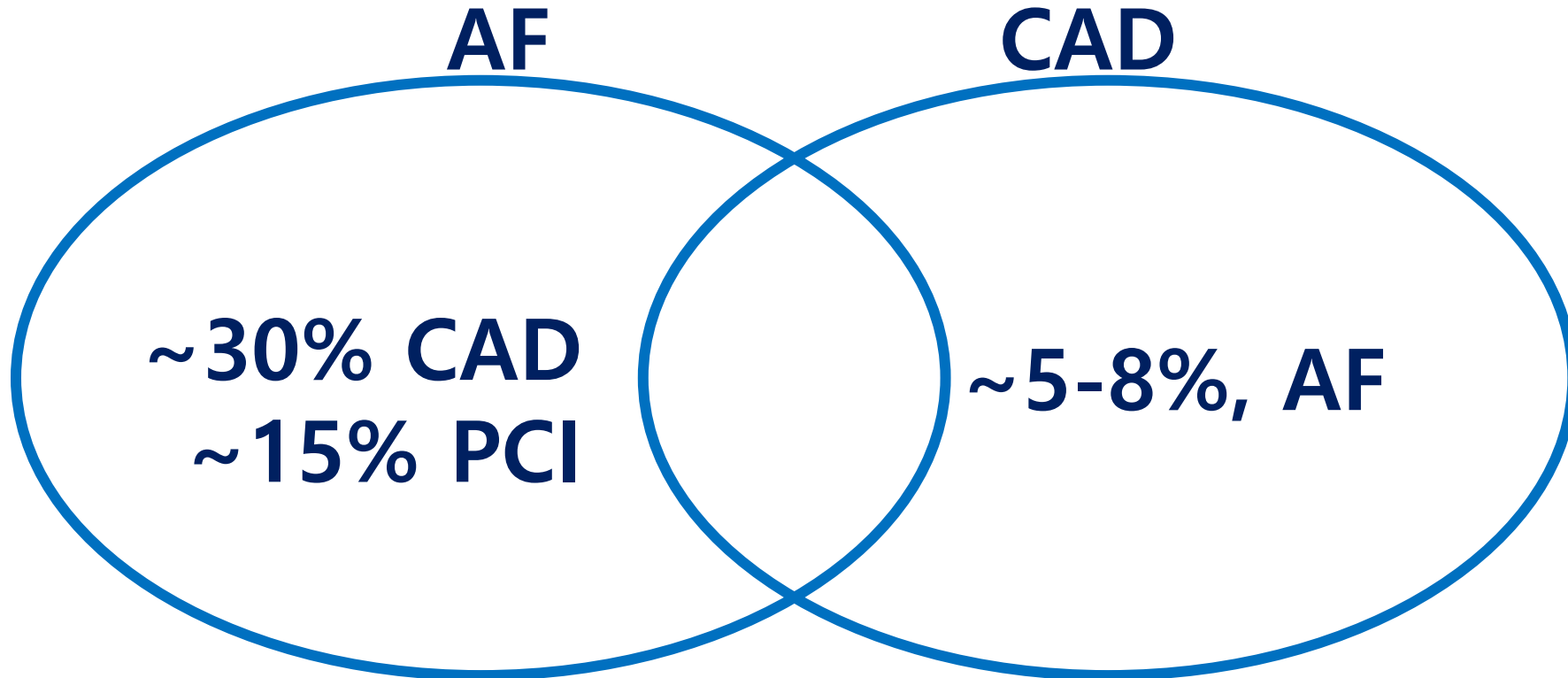
Disclosure

Research fund from Daiichi-Sankyo (Tokyo, Japan)
and Daewoong Pharmaceutical Co., Ltd (Seoul, Korea)

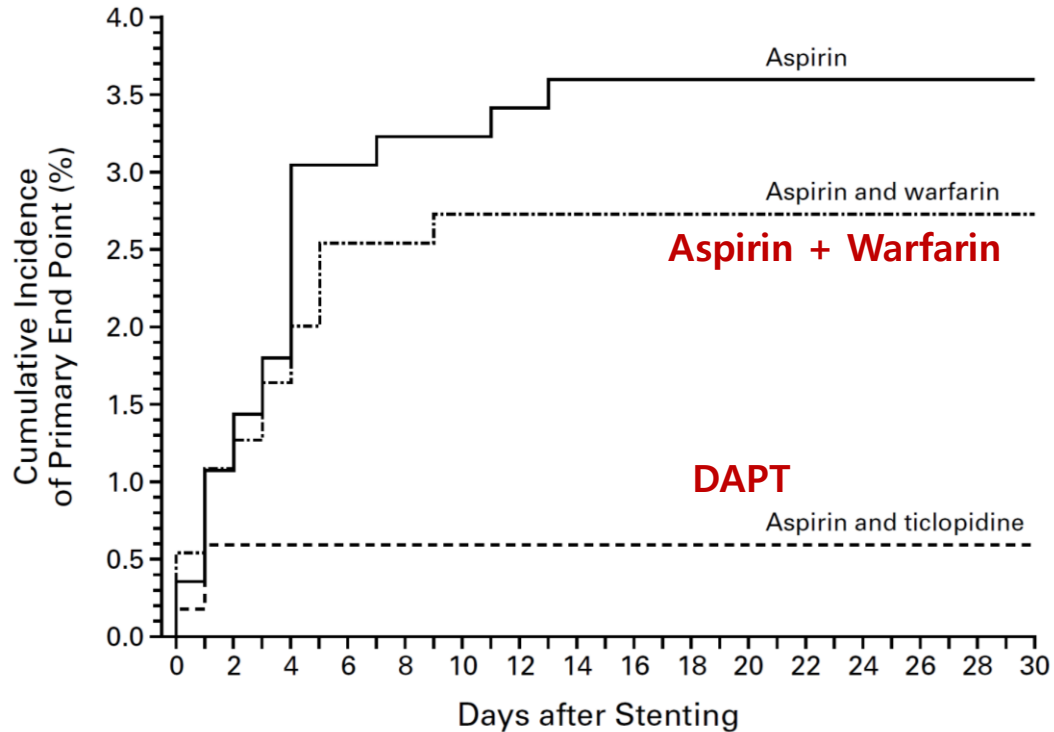
Contents : Patients with AF and CAD (ACS, PCI, CAD)

- 1. Overview on antithrombotic management, in AF and CAD**
- 2. Early after PCI, from triple to dual anti-thromb. Rx
(WOEST, PIONEER, RE-DUAL, ENTRUST to AUGUSTUS)**
- 3. Late after PCI, from dual anti-thromb. to single OAC alone
(OAC trial, AFIRE, EPIC-CAD)**
- 4. Introduction to EPIC-CAD and its clinical implications**

**CAD is present in 20-30% of pts w AF, half of them, requiring PCI.
The incidence of AF in patients with ACS: 10% to 21%**



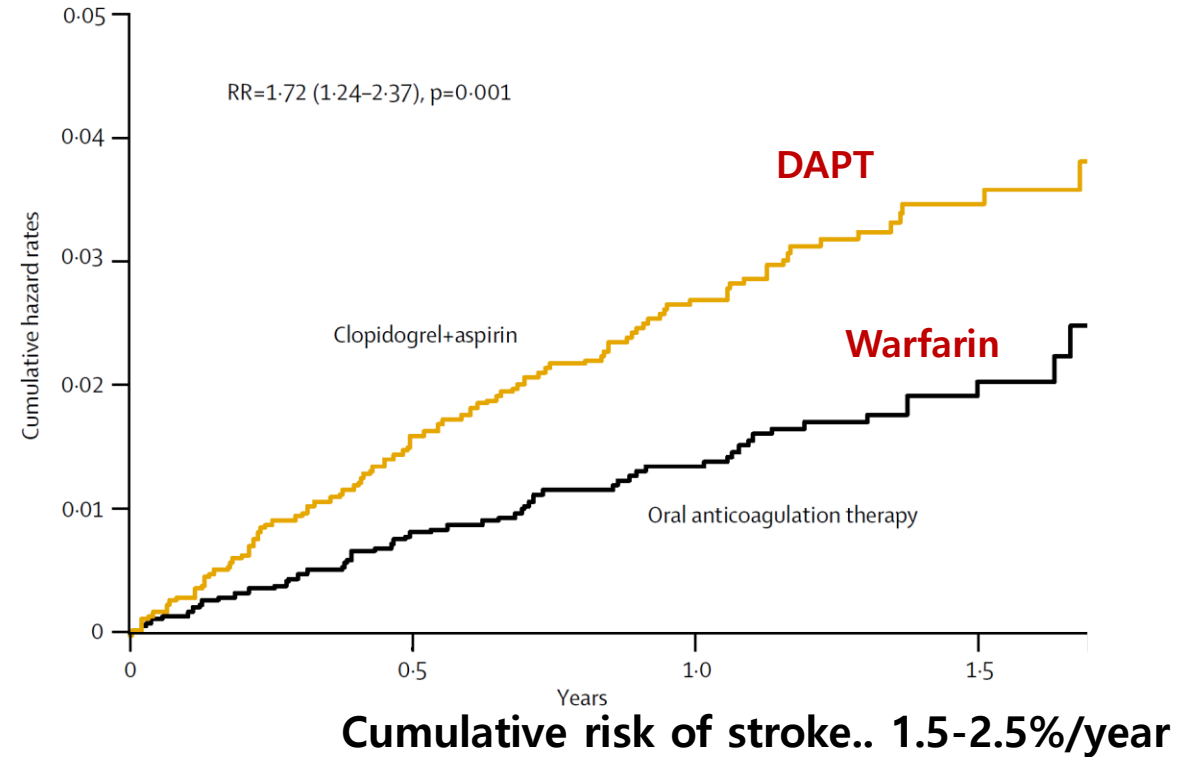
ANTITHROMBOTIC-DRUG REGIMENS AFTER PCI



DAPT >> OAC

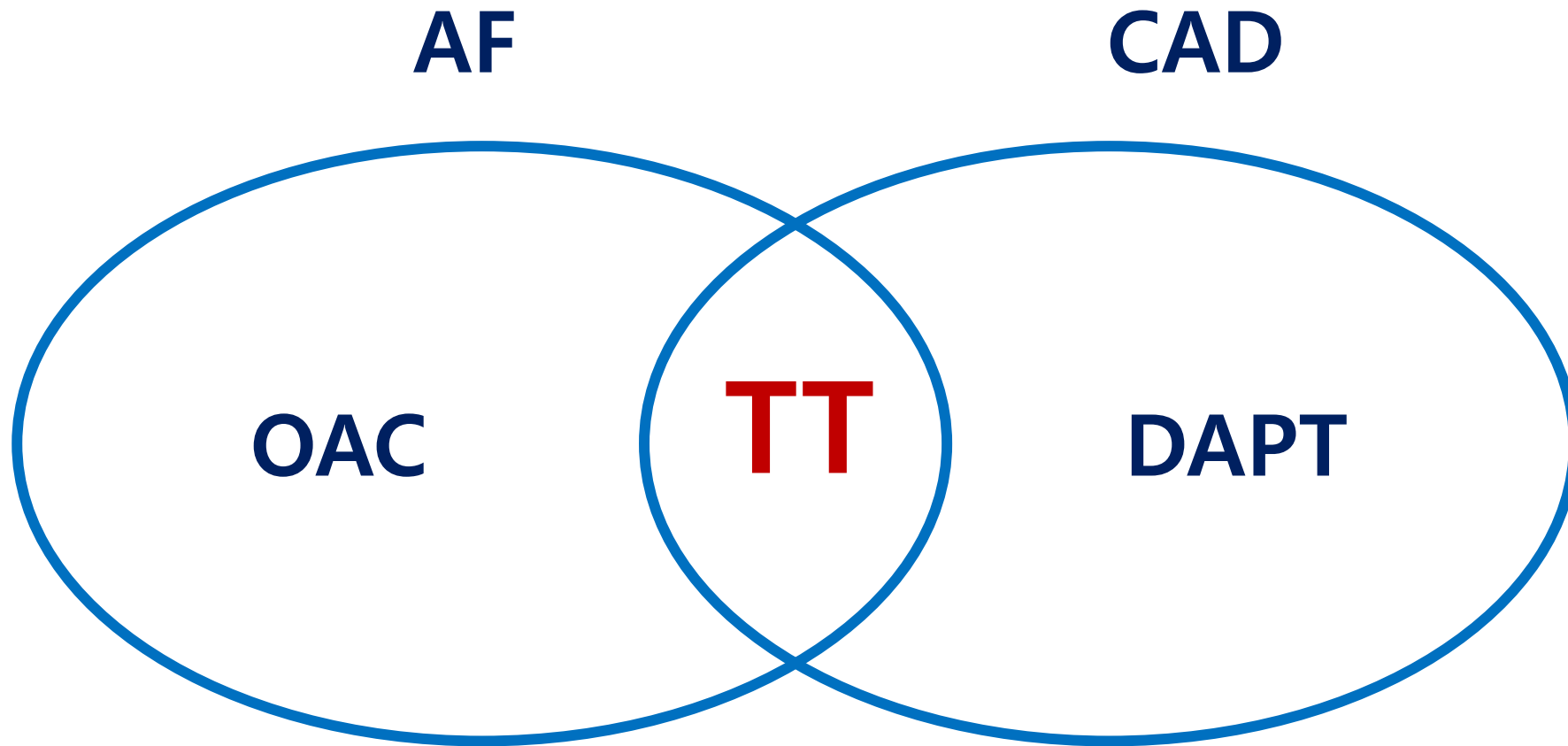
N Engl J Med 1998;339:1665-71

DAPT vs oral anticoagulation for AF : DAPT is not enough



DAPT << OAC

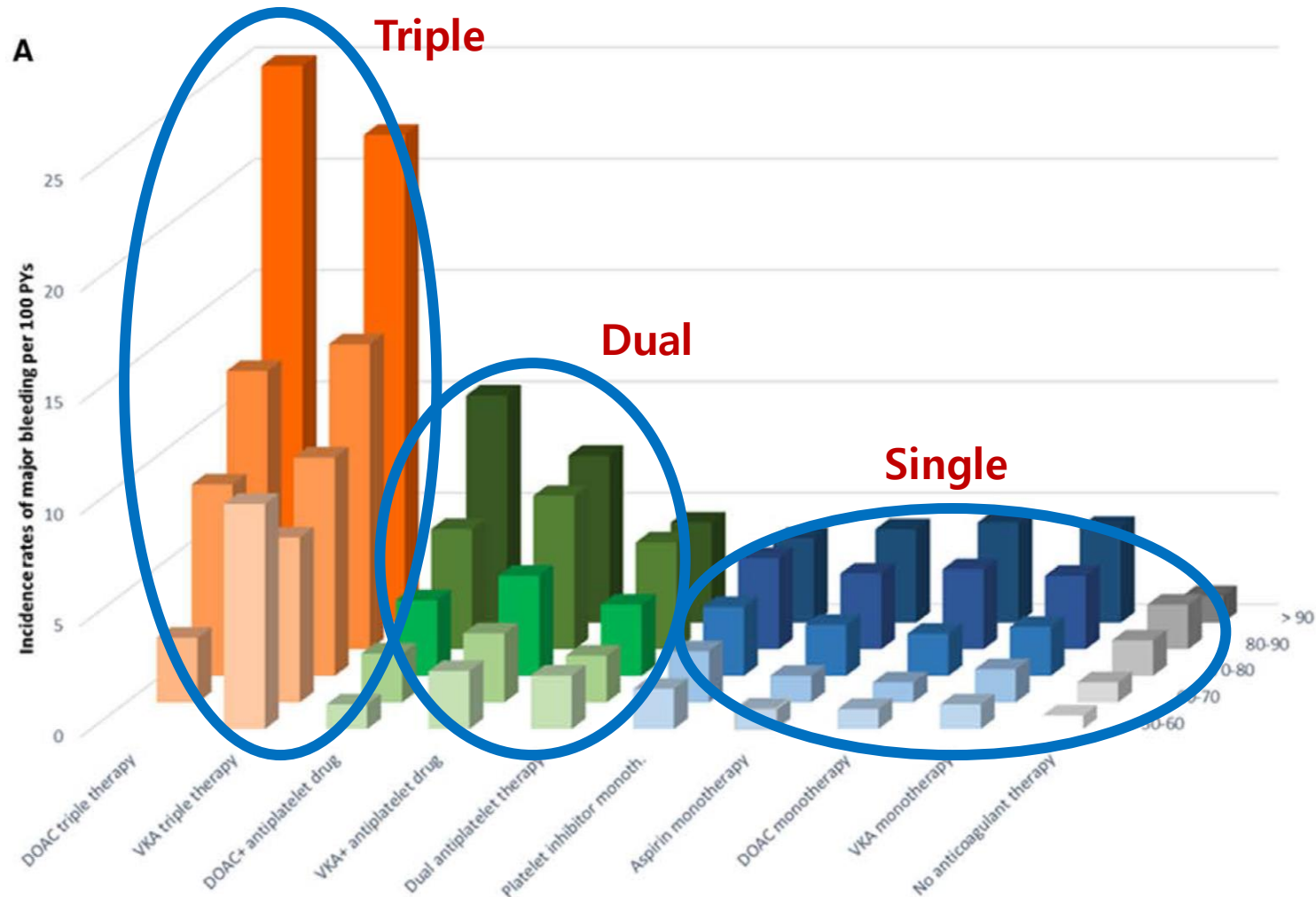
Lancet 2006; 367: 1903-12



TT: triple therapy (OAC+DAPT)

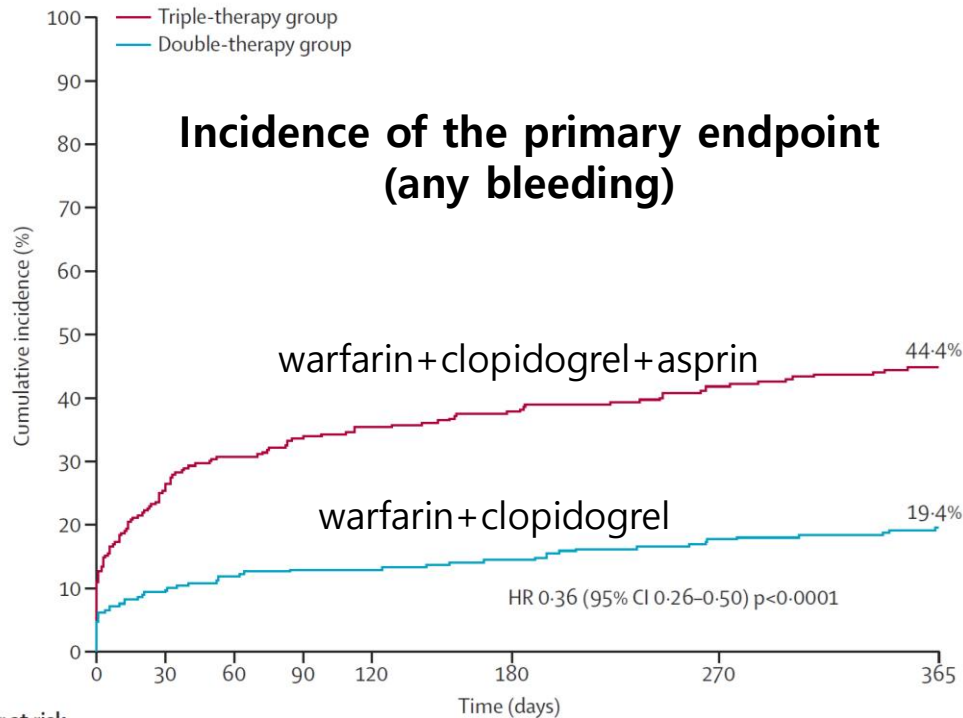
Major Bleeding Rates in Atrial Fibrillation Patients on Single, Dual, or Triple Antithrombotic Therapy

Results From a Nationwide Danish Cohort Study

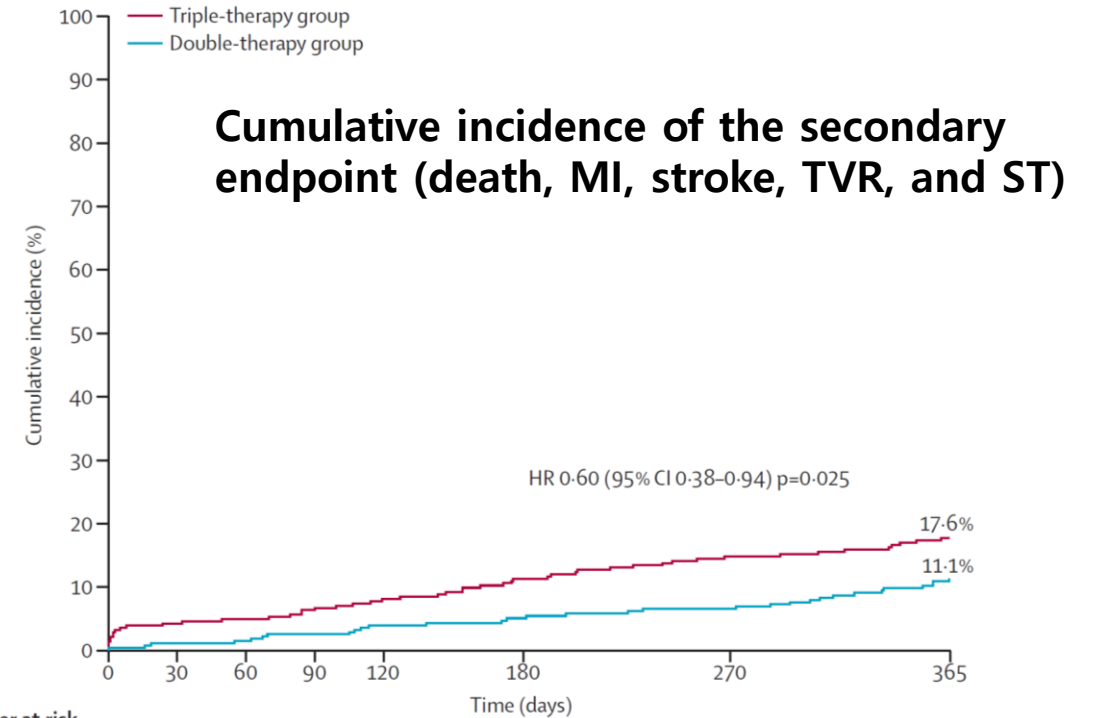


Use of clopidogrel with/without aspirin in pts taking OAC Rx and undergoing PCI: an open-label RCT

WOEST study

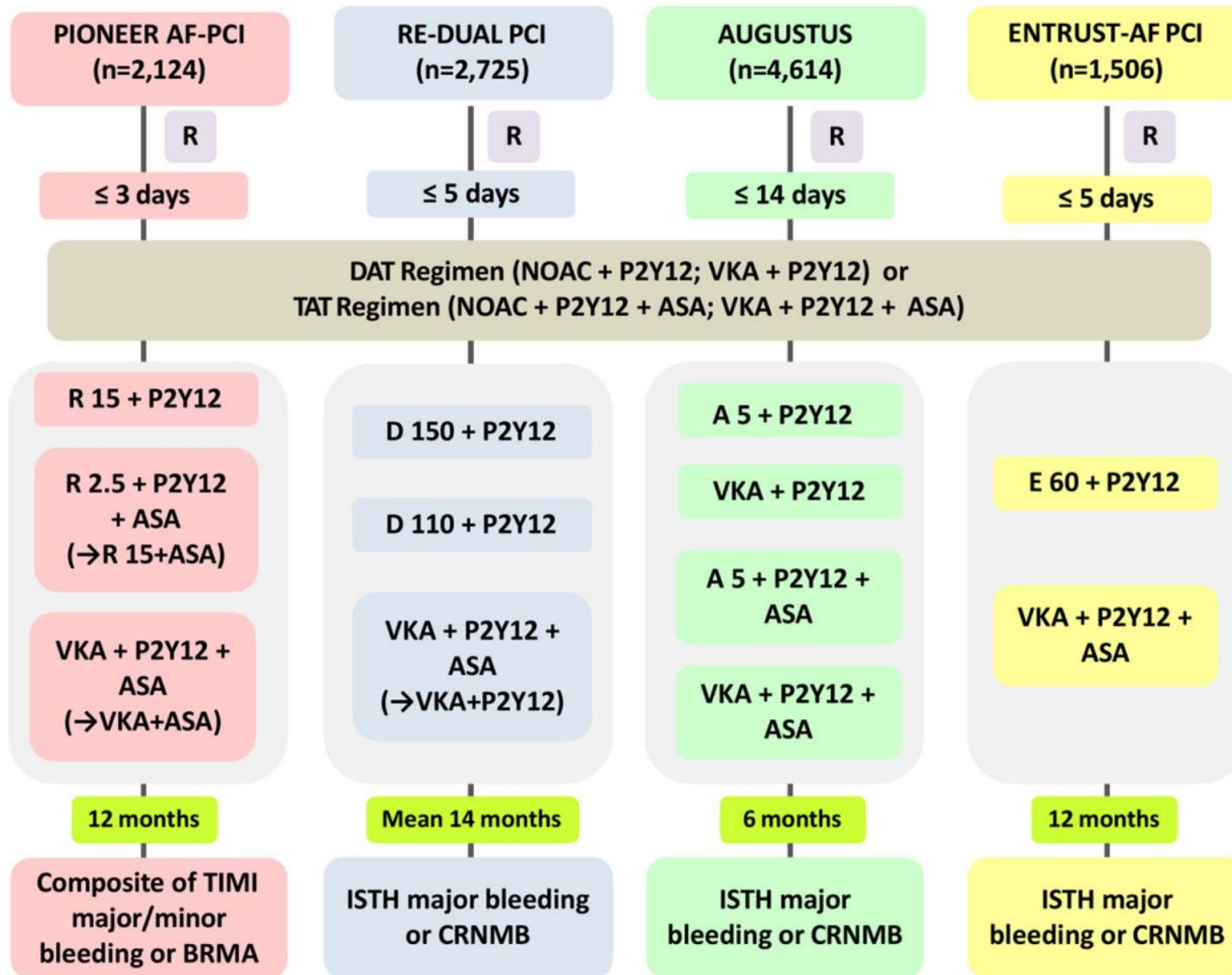


Number at risk	0	30	60	90	120	180	270	365
Triple therapy	284	210	194	186	181	173	159	140
Double therapy	279	253	244	241	241	236	226	208

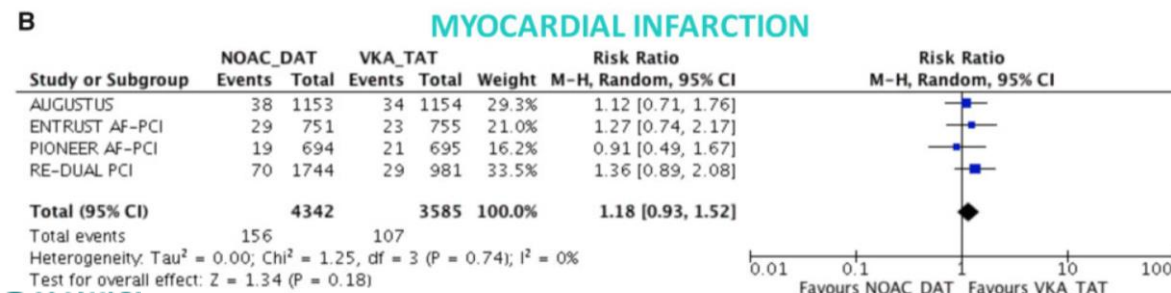
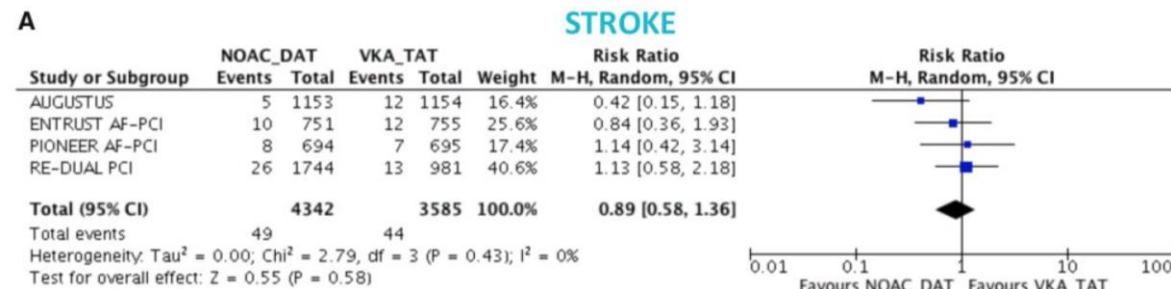
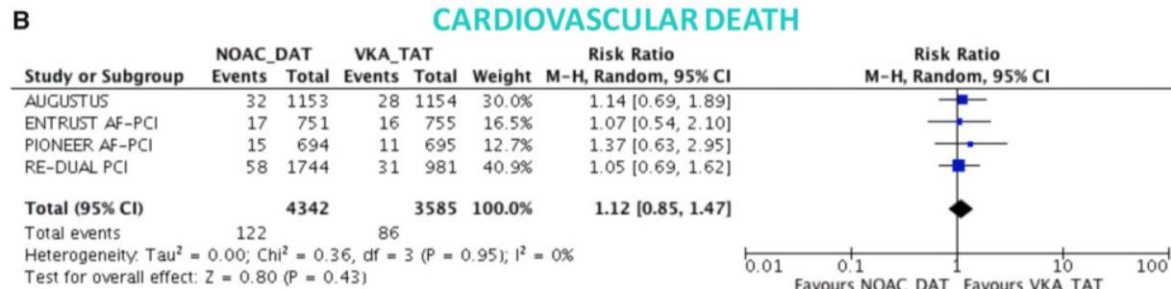
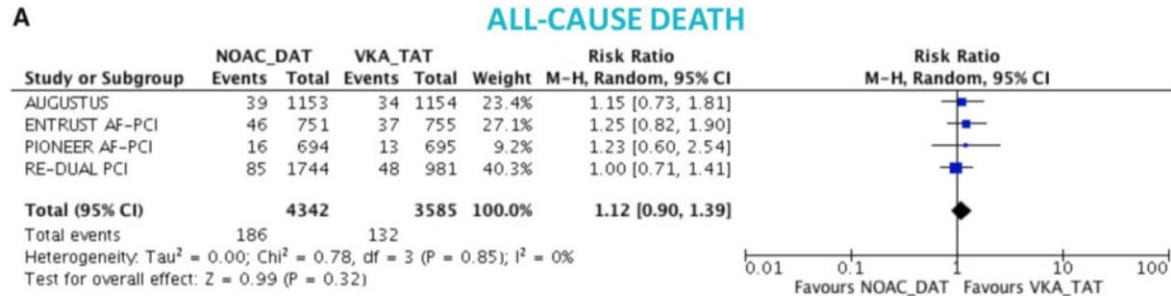


Number at risk	0	30	60	90	120	180	270	365
Triple therapy	284	272	270	266	261	252	242	223
Double therapy	279	276	273	270	266	263	258	234

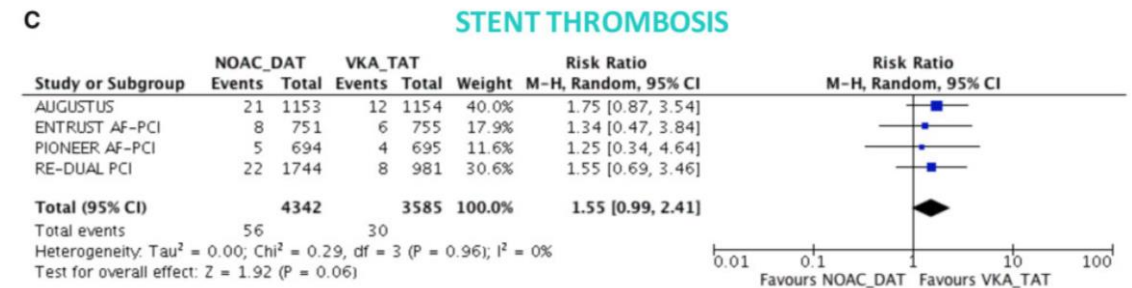
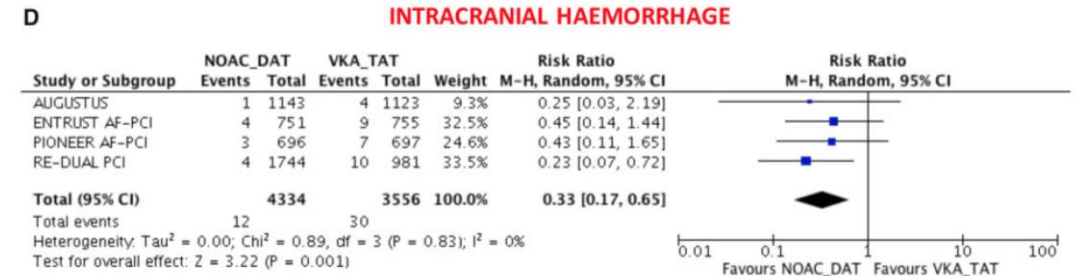
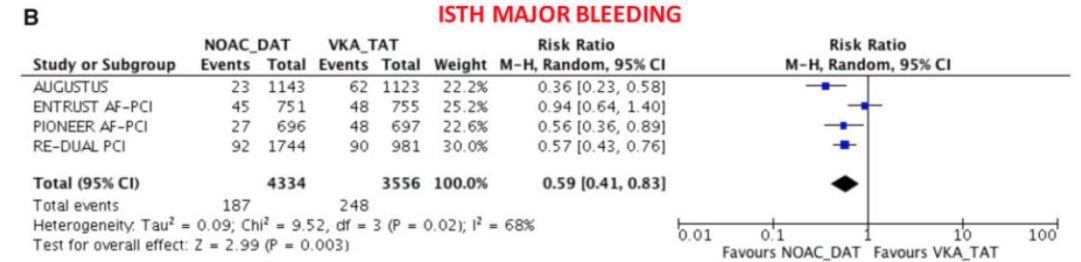
Use of clopiogrel without aspirin was associated with a significant reduction in bleeding complications and no increase in the rate of thrombotic events.



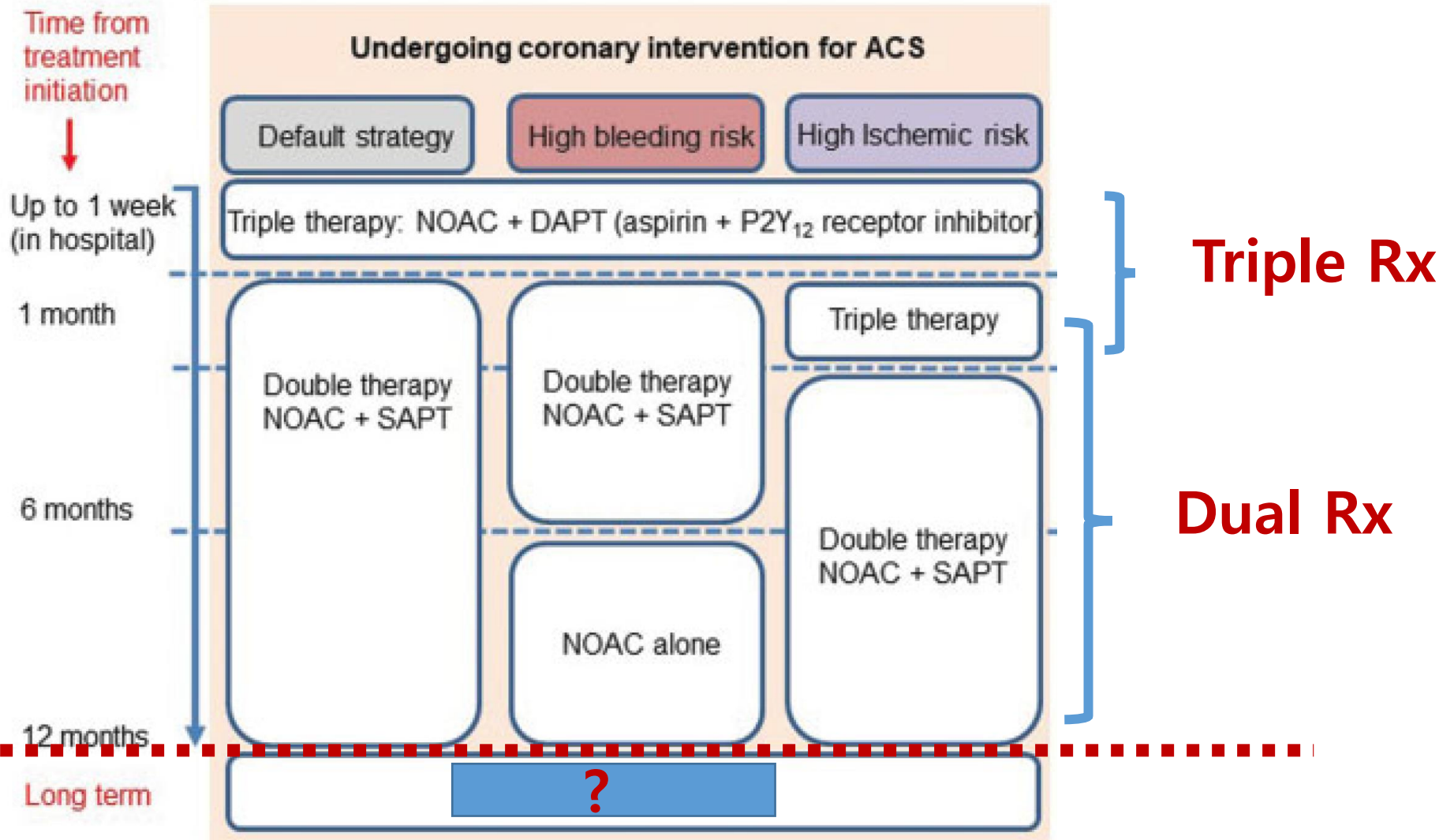
Safety/efficacy outcomes of double vs. triple antithrombotic Rx in pts w AF following PCI meta-analysis of the 4 trials



meta-analysis of the 4 trials

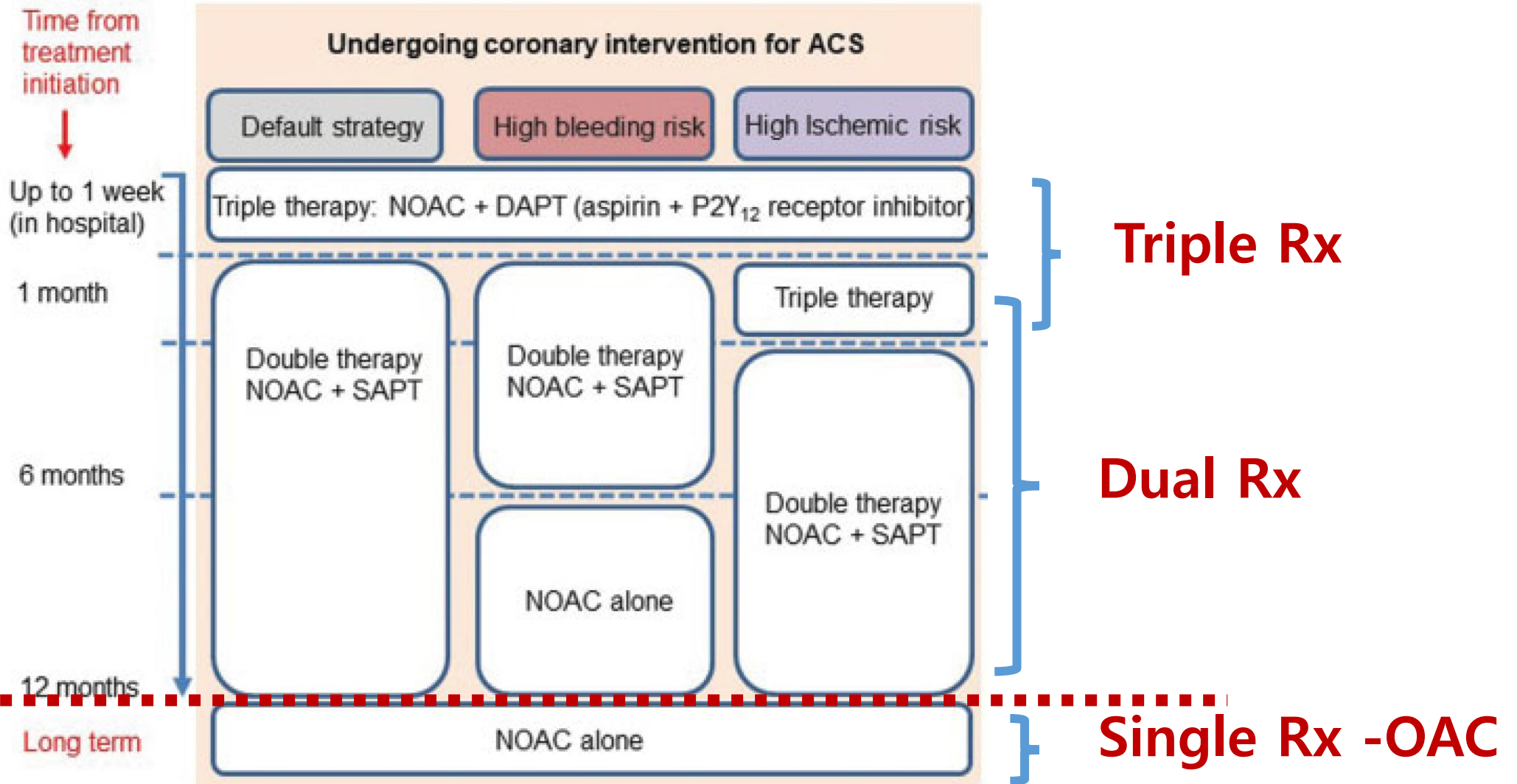


Management of patients requiring OAC undergoing PCI



WOEST,
PIONEER AF-PCI,
RE-DUAL PCI,
AUGUSTUS,
ENTRUST-AF PCI

Management of patients requiring OAC undergoing PCI



WOEST,
PIONEER AF-PCI,
RE-DUAL PCI,
AUGUSTUS,
ENTRUST-AF PCI

OAC ALONE
AFIRE
EPIC-CAD

EPIC-CAD trial

the Edoxaban versus Edoxaban with AntiPlatelet Agent in Patients with Atrial Fibrillation and Chronic Stable Coronary Artery Disease

Aims:

To determine whether edoxaban monotherapy (vs. dual edoxaban+SAPT) can reduce the net adverse clinical events compared to combination therapy in AF patients with high thromboembolic risk and stable CAD

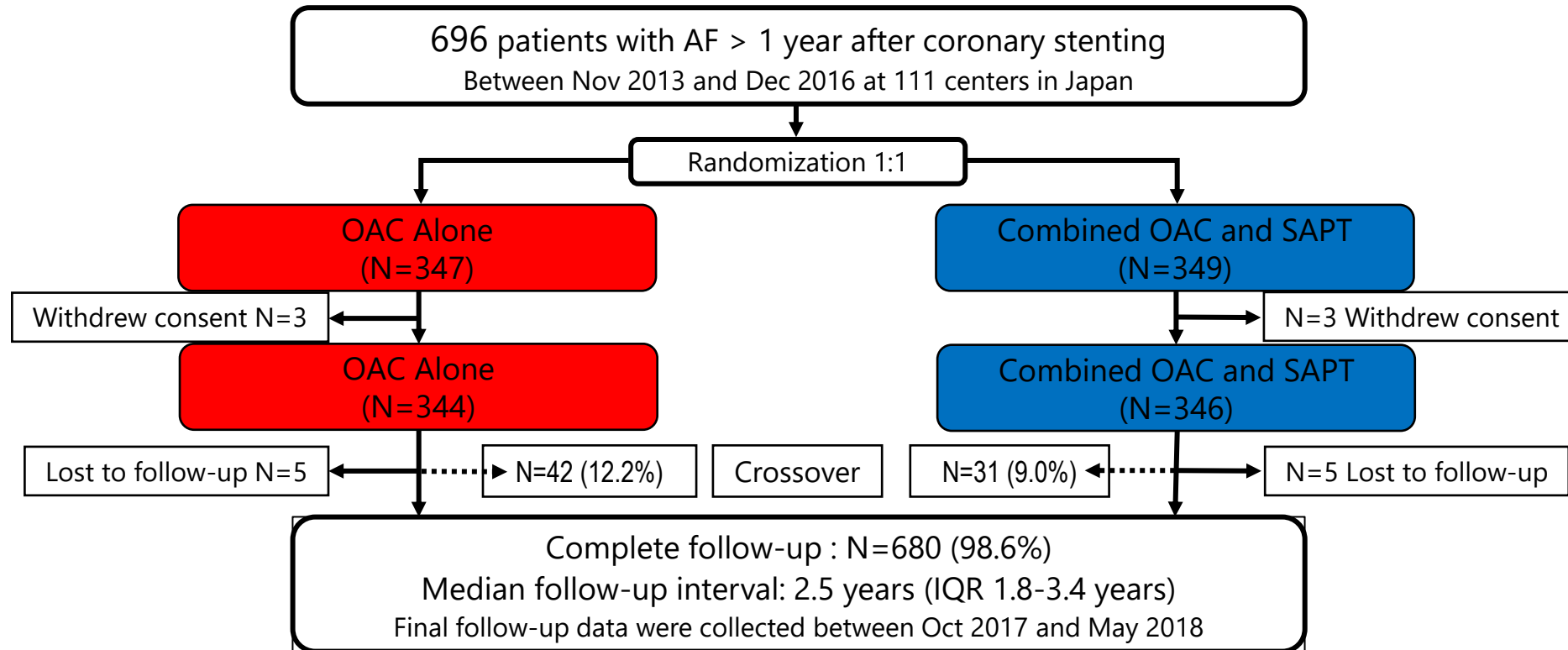
Design:

Multicenter, randomized, open-label, superiority trial

OAC-ALONE trial

(Optimizing Antithrombotic Care in Patients With AF and Coronary Stent)

Prospective, multicenter, open-label, noninferiority trial comparing OAC vs OAC+SAPT
Prim. End=death, MI, stroke/SE (analyzed for non-inferiority)
Seonc. End=composite of Prim. End point or ISTH major bleeding



The enrollment was too slow and the study was prematurely terminated before reaching the target population, and the results are inconclusive.

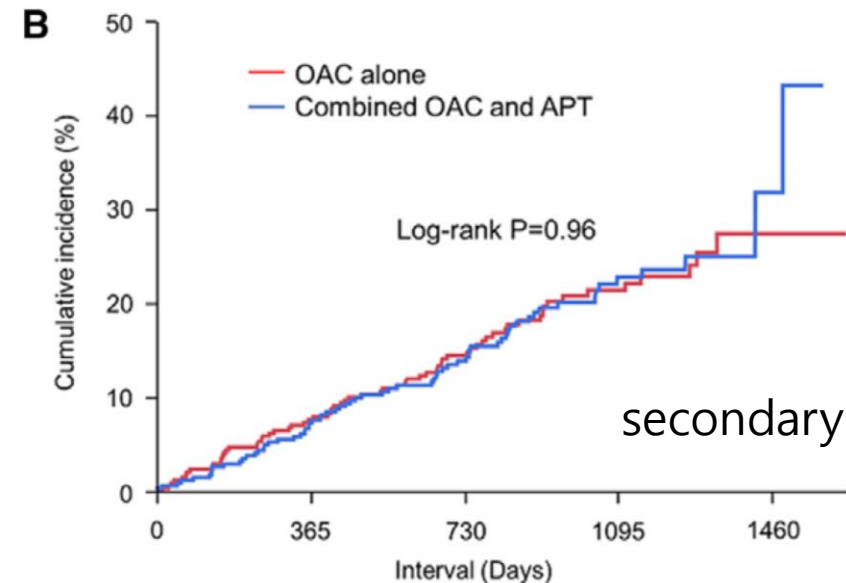
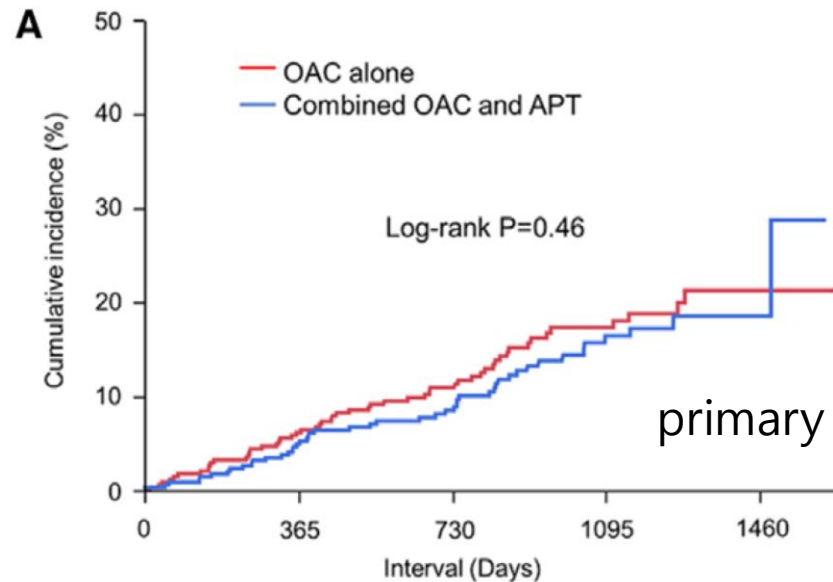
OAC-ALONE Study

Optimizing Antithrombotic Care in pts with AF and PCI

Prospective, multicenter, open-label, noninferiority trial comparing OAC vs OAC+SAPT

Prim. End=death, MI, stroke/SE

Seonc.End=composite of Prim or ISTH major bleeding



CONCLUSIONS: This randomized trial did not establish noninferiority of OAC alone to combined OAC+APT in pts with AF and stable CAD beyond 1 yr after stenting. Because patient enrollment was prematurely terminated, the study was underpowered and inconclusive.

AFIRE trial

(**A**trial **F**ibrillation and **I**schemic Events with **R**ivaroxaban in Patients with Stable CAD)

Prospective, multicenter, open-label, trial comparing rivaroxaban vs rivarox+SAPT
Prim. Efficacy End Point=any death, MI, stroke/SE (non-inferiority)
Prim. Safety End Poin=ISTH major bleeding (superiority)

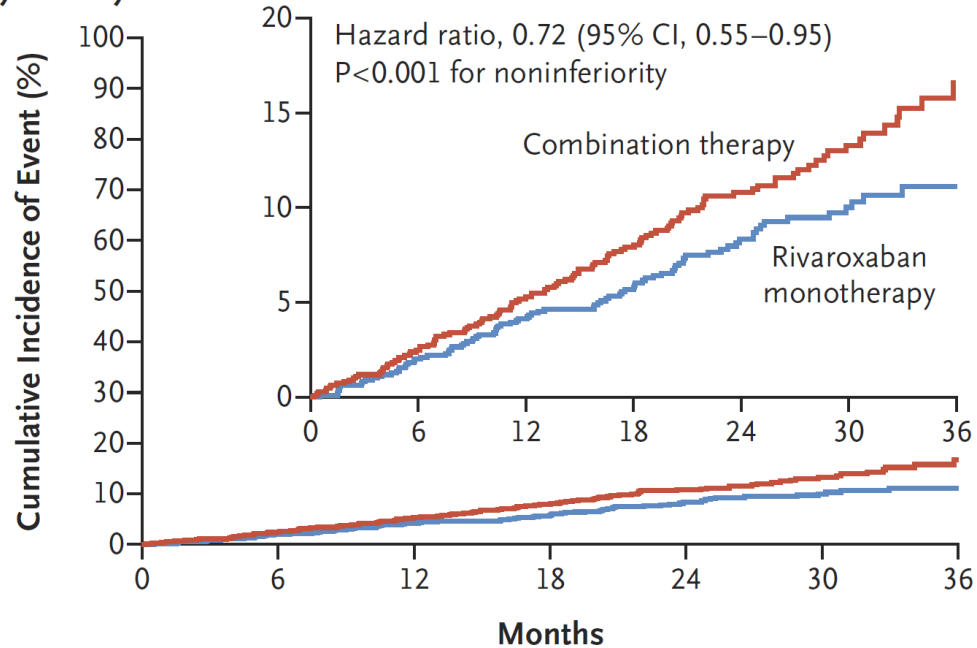
Patients with AF + PCI or CABG > 1yr earlier
Patients with angiographically confirmed CAD
(not requiring revascularization)

- monotherapy with rivaroxaban**
- combination therapy with rivaroxaban+single APT**

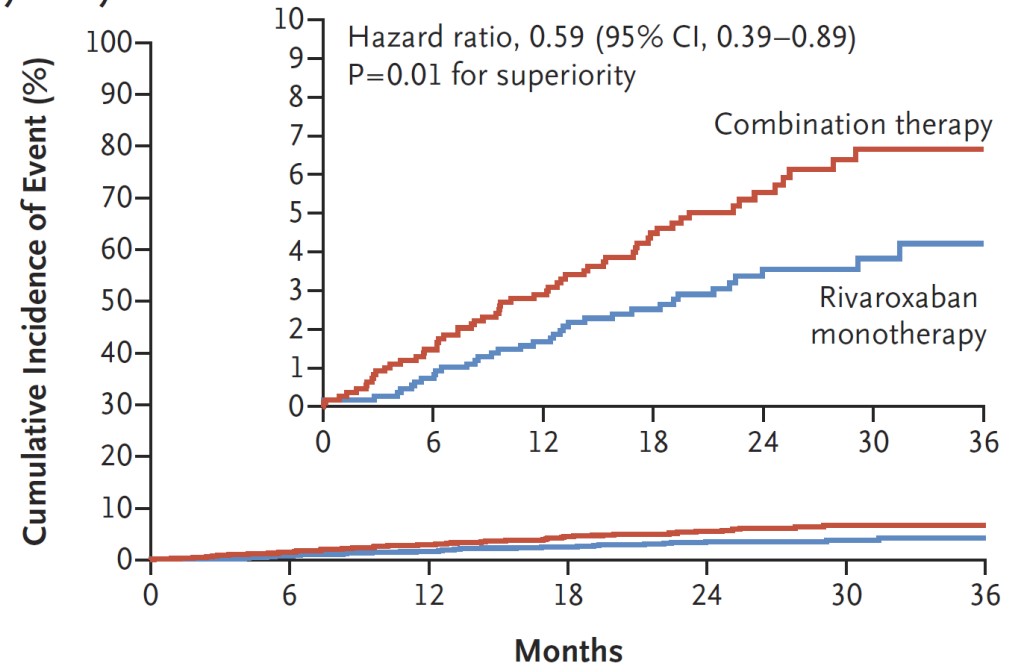
Antithrombotic Therapy for AF with Stable CAD

AFIRE (AF and Ischemic Events with Rivaroxaban in Patients with Stable CAD) trial

A Primary Efficacy End Point



B Primary Safety End Point



CONCLUSIONS

As antithrombotic therapy, rivaroxaban monotherapy was **noninferior** to combination therapy for efficacy and **superior** for safety in patients with AF and stable CAD.

Limitations of OAC alone, AFIRE trials

OAC Alone

1. used warfarin (75%) as OAC (DOAC < 25%)
2. prematurely terminated and the results, inconclusive

AFIRE

NOAC (Rivaroxaban), but low dose 15/10mg

EPIC-CAD, first to use "standard dose", "NOAC" in pts w AF+stable CAD

Summary: AF and CAD

1. AF complicating ACS or PCI (class I, LOE A)
Early discontinuation of aspirin (1-4 wk)
– TT to DT (OAC w P2Y12)
2. AF with chronic CAD (>1yr after PCI) (class I, LOE B-R)
OAC monotherapy, recommended over OAC+SAPT
cf. history of stent thrombosis
3. EPIC-CAD: second RCT for chronic stable CAD pts.
 - first to use standard dose NOAC
 - the results will provide solid scientific evidence
for antithrombotic Tx in AF patients w stable CAD

Expectations on the EPIC-CAD trial after the AFIRE

1. OAC alone(Warf), AFIRE (NOAC, low dose),

EPIC (first to use standard NOAC)

2. OAC monoRx – standard Tx in pts with AF and stable CAD

3. Awareness on AF

...many interv. cardiologists regard AF as a normal variant.

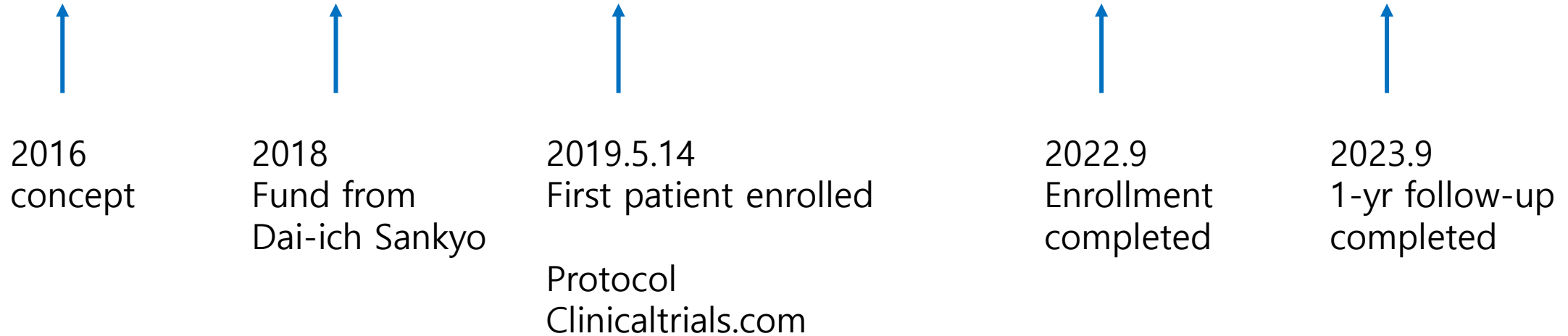
adherence to antiplatelet - many of them still prefer DAPT to NOAC.

low prescription rate of OAC among interv. cardiologists

EPIC-CAD trial

Korean, multicenter, randomized clinical trials
1040 pts from 20 sites
Edoxaban vs edoxaban+single APT

Time-line



Study NCT03718559
Submitted Date: June 18, 2020 (v9)

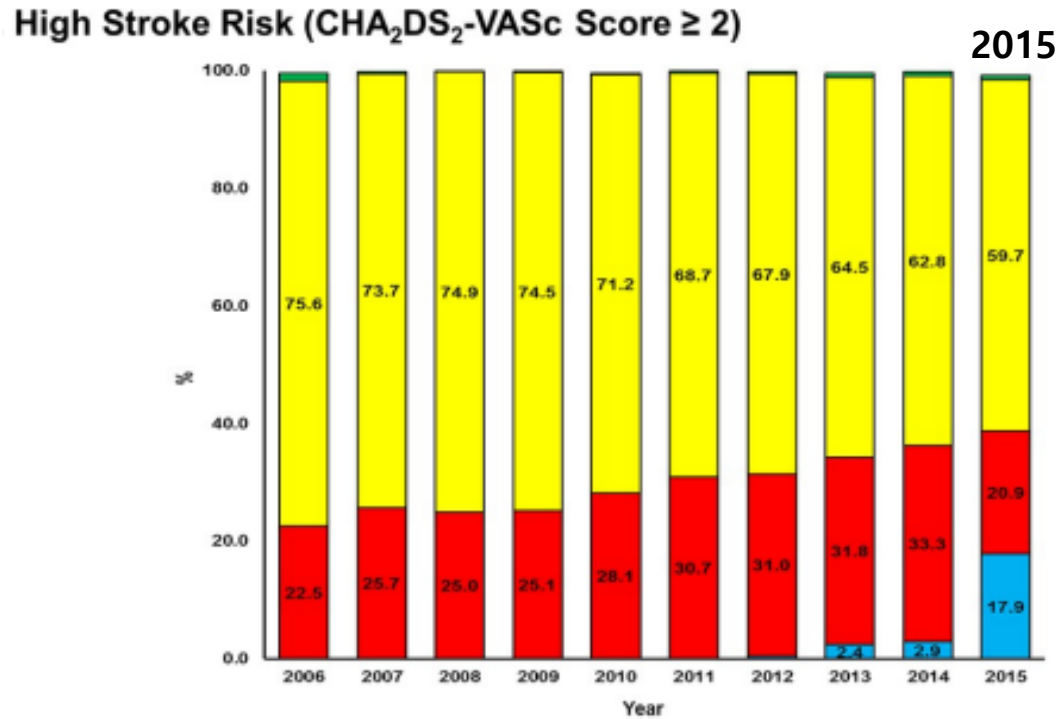
Study Identification

Unique Protocol ID: AMCCVEP2018-01
Brief Title: Edoxaban Versus Edoxaban With antiPlatelet Agent In Patients With Atrial Fibrillation and Chronic Stable Coronary Artery Disease (EPIC-CAD)
Official Title: A Multi-centre, Open-labelled, Randomized Controlled Trial Comparing Two Different Anticoagulation Strategies in High-risk Atrial Fibrillation and Stable Coronary Artery Disease
Secondary IDs:

Study Status

Record Verification: June 2020
Overall Status: Recruiting
Study Start: May 14, 2019
Primary Completion: December 20, 2021 [Anticipated]
Study Completion: June 15, 2022 [Anticipated]
First Submitted: October 23, 2018
First Submitted that Met QC Criteria: October 23, 2018
First Posted: October 24, 2018 [Actual]
Last Update Submitted that Met QC Criteria: June 18, 2020
Last Update Posted: June 18, 2020 [Actual]

Under-utilization of OAC in real practice



The utilization of TAT following PCI among high-stroke risk AF patients steadily increased from 30.3% in 2011 to 65.4% in 2020. However, in 2020, a significant proportion of 29.4% of patients still received DAPT, indicating that many AF patients undergoing PCI did not receive adequate antithrombotic therapy. - the Health Insurance Review & Assessment Service (HIRA-NIS)

PLoS ONE (2019) 14(1): e0209593.

European Journal of Clinical Pharmacology (2023) 79:541–551