Pragmatic Antithrombotic Strategies According to Temporal Ischemic and Bleeding Risk: TAILORED-CHIP Trial

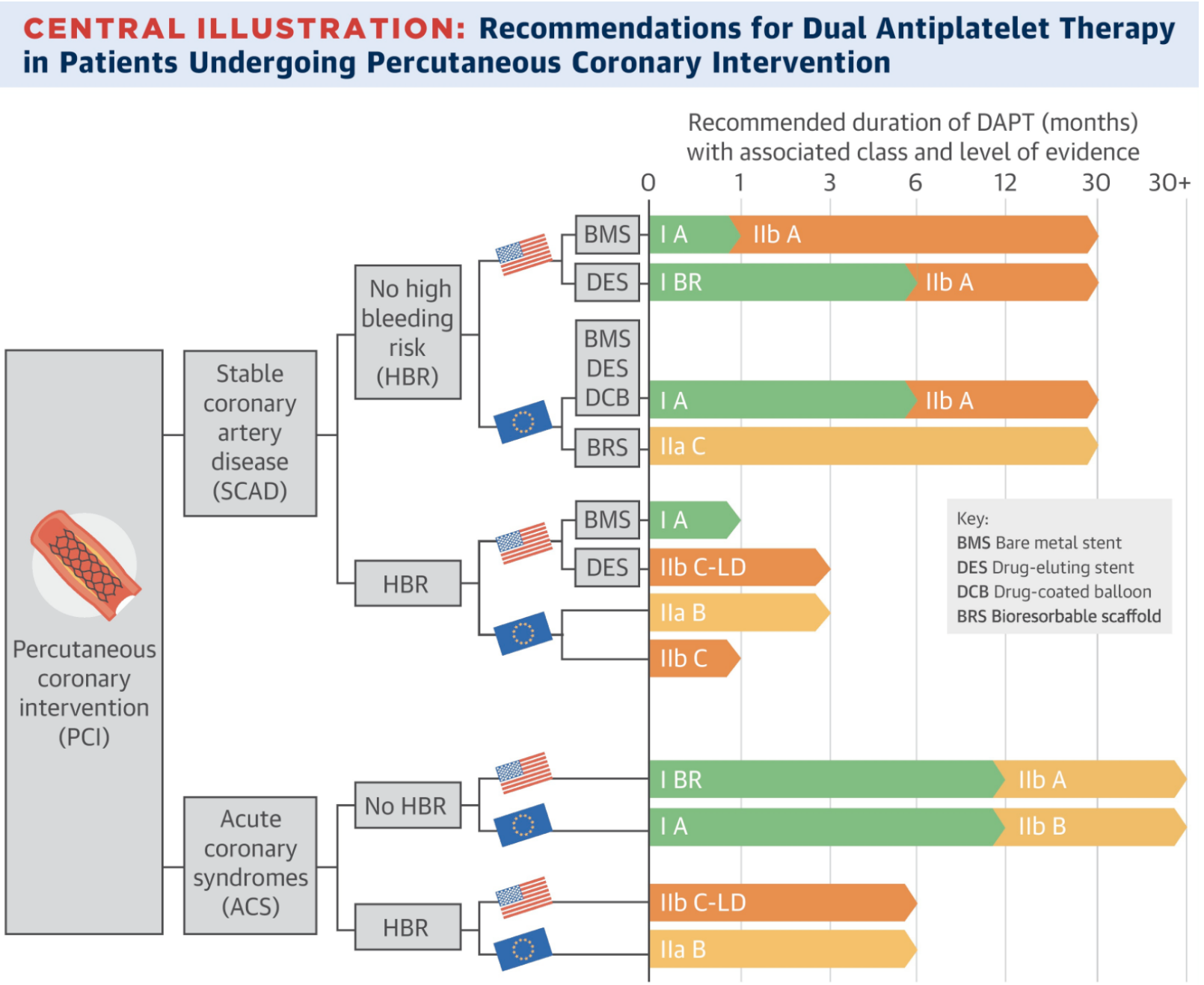
Duk-Woo Park, MD

Asan Medical Center, Ulsan University College of Medicine,
Seoul, Korea

Disclosure

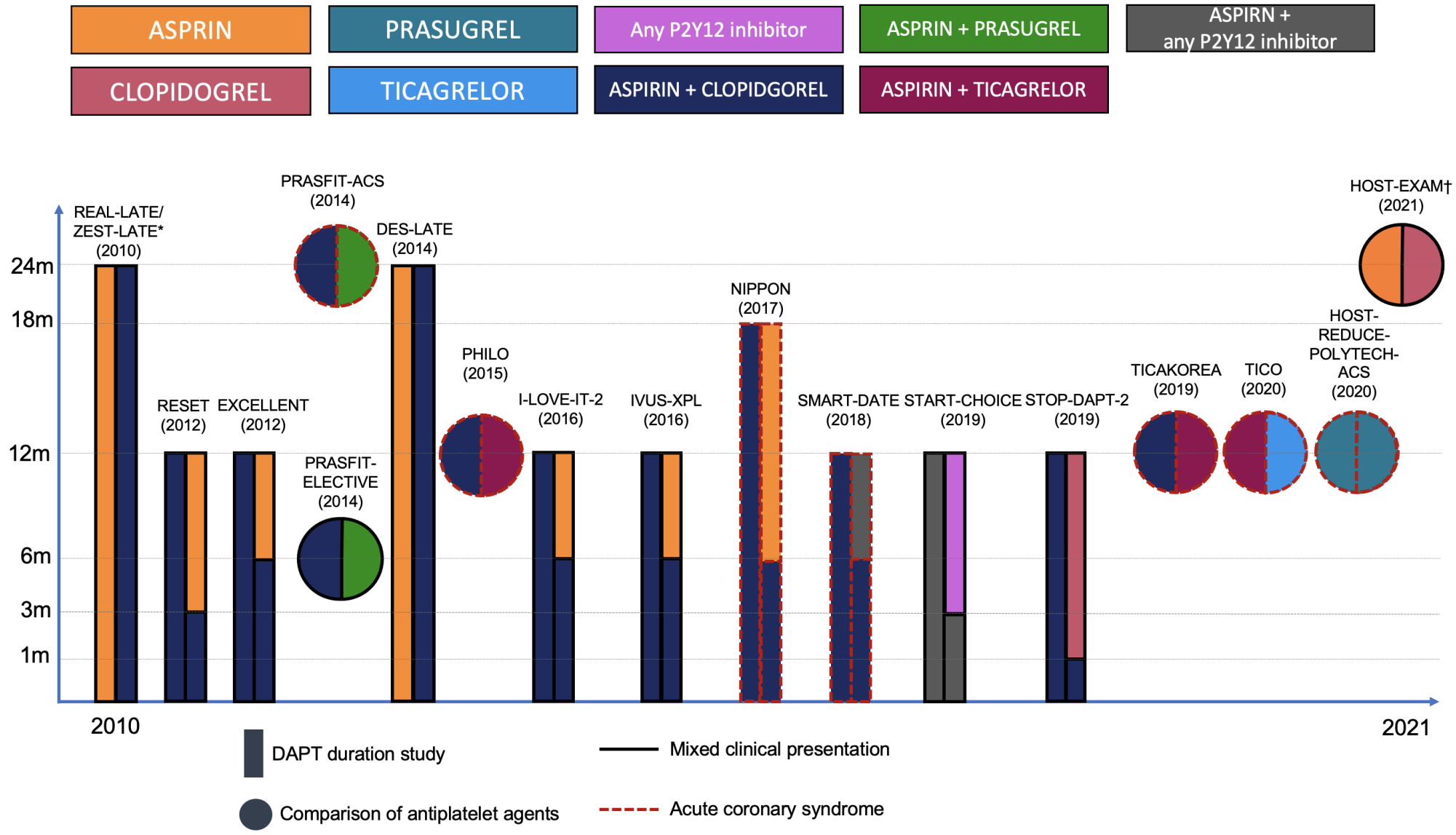
- Institutional grant/research funding to CardioVascular Research Foundation (CVRF, Korea) and/or Asan Medical Center from Abbott, Boston Scientific, Medtronics, Daiichi-Sankyo, Edwards Lifescience, HK InnoN, Daewoong Pharm, and ChongKunDang Pharm.

DAPT Guidelines Are Mainly Based on; (1) ACS vs. Stable, (2) HBR



Capodanno, D. et al. J Am Coll Cardiol. 2018;72(23PA):2915-31.

Several Key RCTs in Asia



OS Kwon and DW Park. JACC: Asia 2022;2:1–18

East-Asian Paradox

Clinical characteristics of East-Asians compared with Caucasians

High bleeding risk

↑Hemorrhagic stroke

↑GI bleeding

Low ischemic risk

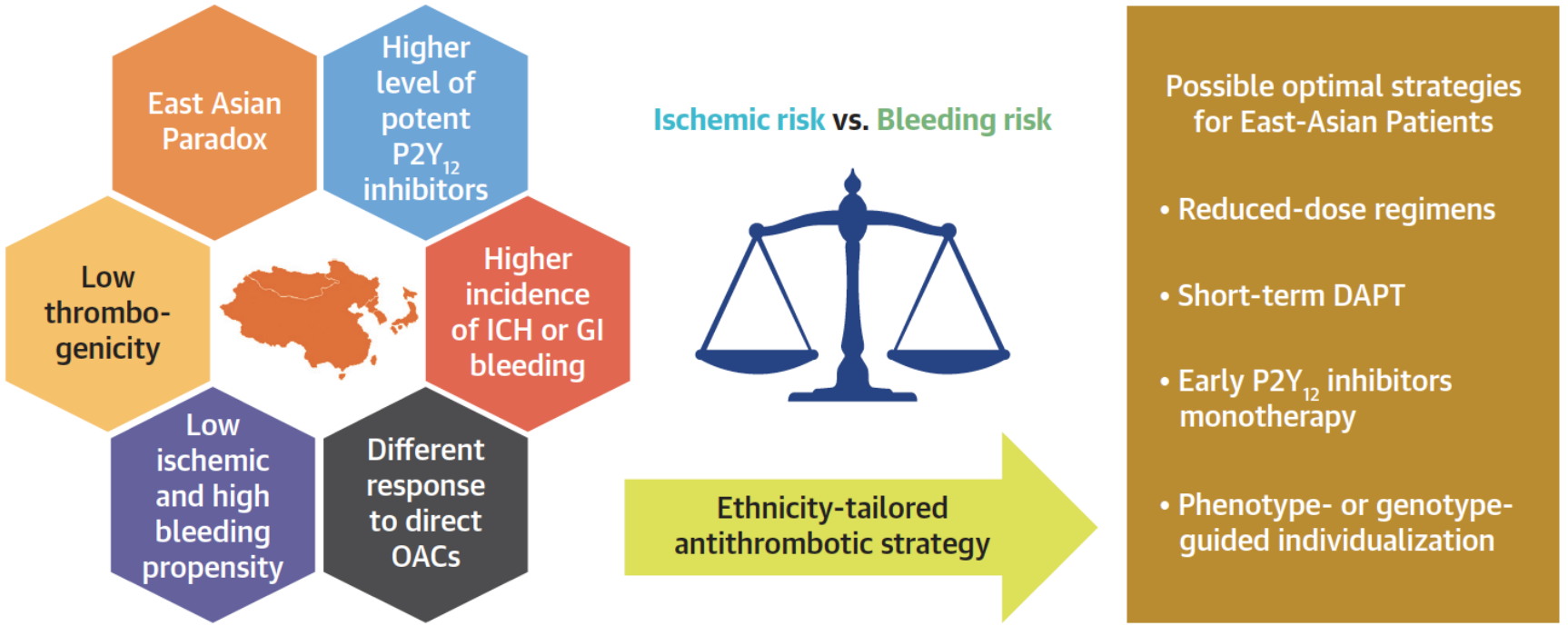
↓CV death, MI, and Stent thrombosis

Plausible mechanism of East-Asian Paradox

- **Unique demographics**
  (Low body weight, different comorbidities and disease patterns)
- **Different response to P2Y12 inhibitors**
  (↑ prasugrel, ticagrelor, and ↓ clopidogrel)
- **Low ischemic risk**
  ↓ Intrinsic thrombogenicity
  (Inflammation, coagulation activity)
  Genetic predisposition
  (↓ Prothrombin G20210A, Factor V Leiden)
- **High bleeding risk**
  ↑ Intracranial atherosclerosis
  ↑ Helicobacter pylori infection
  ↑ CYP polymorphism

OS Kwon and DW Park. JACC: Asia 2022;2:1–18

CENTRAL ILLUSTRATION **Unique Characteristics of East Asian Patients and Updates to Optimal Antithrombotic Strategies**



Kwon, O. et al. JACC: Asia. 2022;2(1):1-18.

Given the unique ischemic and bleeding propensity of East Asian patients, the so-called East Asian paradox, ethnically tailored antithrombotic strategies are warranted.
DAPT = dual antiplatelet therapy; GI = gastrointestinal; ICH = intracranial hemorrhage; OAC = oral anticoagulation.

OS Kwon and DW Park. JACC: Asia 2022;2:1–18

Pragmatic Antithrombotic Strategies

TABLE 4 Pragmatic Antithrombotic Strategies for East Asian Patients According to Bleeding and Ischemic Risk

	Default Approach		High Bleeding Risk		
Clinical Situations	**DAPT Duration**	**Antiplatelet Agents**	**DAPT Duration**	**Antiplatelet Agents**	**After DAPT Duration**
Stable angina	3-6 mo	Aspirin + clopidogrel	1-3 mo	Aspirin + clopidogrel	Clopidogrel
Acute coronary syndrome	6-12 mo	Aspirin + prasugrel 3.75 or 5mg (or reduced-dose ticagrelor)	3-6 mo	Aspirin + clopidogrel	Clopidogrel
Requiring oral anticoagulation	1 wk[a]	Aspirin + clopidogrel + DOAC and then,	Until discharge (1 to 2 d)	Aspirin + clopidogrel + DOAC and then,	DOAC alone after double therapy
		clopidogrel + DOAC up to 12 mo		clopidogrel + DOAC up to 3-6 mo	
CHIP (or high ischemic risk)	6-12 mo	Aspirin + (reduced-dose) potent $P2Y_{12}$ inhibitors			Continue DAPT or potent $P2Y_{12}$ inhibitors monotherapy

OS Kwon and DW Park. JACC: Asia 2022;2:1–18

Novel Trend of Pragmatic Anti-thrombotic Strategy After High-Risk PCI
: Escalation and De-escalation

High Ischemic Risk: Need for Escalation

High-risk Patient

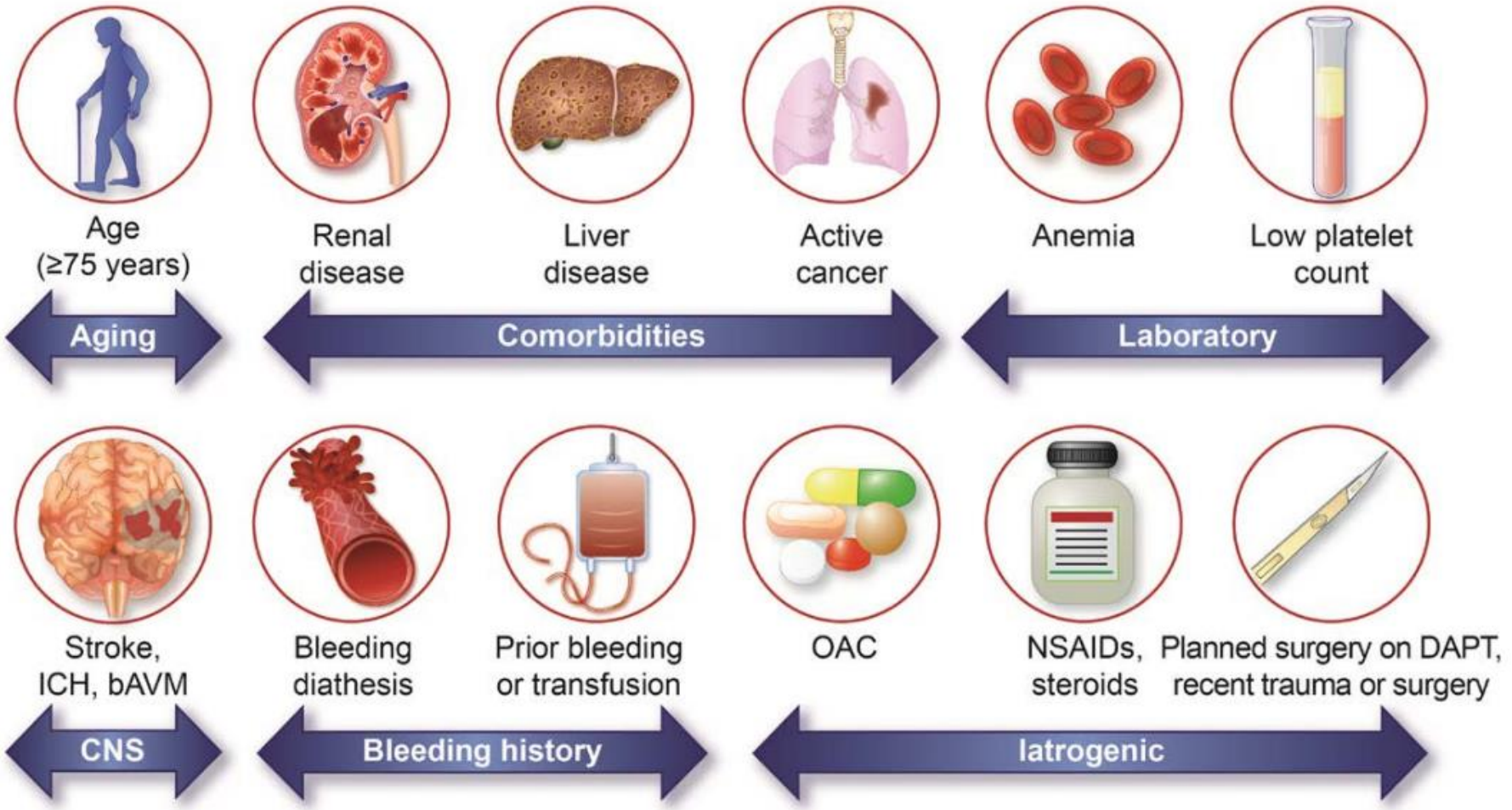
- Previous NSTEMI or STEMI
- Recurrent ischemic event on DAPT
- History of stent thrombosis
- Chronic inflammatory disease
- Diabetes
- Chronic renal dysfunction

High-risk PCI

- Complex PCI: Left main, CTO, complex bifurcation, multivessel PCI, severe calcification, diffuse long
- >3 Stents
- Total stent length >60 mm

Lancet 2017;390:810-20.

High Bleeding Risk: Need for De-Escalation



Philip Urban, et al. Circulation. 2019;140:240–261.

Contemporary
Escalation and De-Escalation Strategies

- Potency of P2Y12 inhibitor
- Omission of Aspirin
- Duration of DAPT

ESCALATION: More Potent (High ischemic risk)

Trial	Study Population	Intervention	Control	Primary outcome	Follow-up duration	Result
THEMIS-PCI (2019)	Stable angina with diabetes Previous PCI	Ticagrelor (SD → LD) + ASA	Ticagrelor	A composite of CV death, MI, or stroke	3.3 years	Intervention: 7.3% Control: 8.6% HR 0.85 (0.74-0.97) Major Bleeding Intervention: 2.0% Control: 1.1% HR 2.03 (1.48-2.76)
COMPASS-PCI (2020)	Stable angina Previous PCI Previous MI, MVD	2.5mg Rivaroxaban bid + ASA	ASA	A composite of CV death, MI, or stroke	3 years	Intervention: 4.0% Control: 5.5% HR 0.74 (0.61-0.88) Major Bleeding Intervention: 3.3% Control 2.0% HR 1.72 (1.34-2.21)
HOST-EXAM (2021)	PCI after 6-18 months	Clopidogrel monotherapy	ASA monotherapy	A composite of all-cause death, MI, stroke, ACS, BARC 3, or 5 bleeding	2 years	Intervention: 5.7% Control: 7.7% HR 0.73 (0.59-0.90)

ESCALATION: More Potent and Longer DAPT (High ischemic risk)

Trial	Study Population	Intervention	Control	Primary outcome	Follow-up duration	Result
PEGASUS-TIMI 54 (2015)	Prior MI (1~3 year) + High ischemic risk feature	1) Ticagrelor 90mg bid + ASA 2) Ticagrelor 60mg bid + ASA	ASA monotherapy	A composite of CV death, MI, or stroke	33 months	1) Ticagrelor 90mg: 7.85% 2) Ticagrelor 60mg: 7.77% 3) ASA only: 9.04% 1) Vs 3): HR 0.85 (0.75-0.96) 2) vs 3): HR 0.84 (0.74-0.95)
				TIMI major bleeding		1) Ticagrelor 90mg: 2.60% 2) Ticagrelor 60mg: 2.30% 3) ASA only: 1.06% 1) vs 3) HR 2.69 (1.96-3.70) 2) vs 3) HR 2.32 (1.68-3.21)

DE-ESCALATION: SHORT DAPT (High-Risk Patients)

Trial	Study Population	Intervention	Control	Primary outcome	Follow-up duration	Result
GLOBAL LEADER (2018)	Stable CAD (53%) ACS (47%)	Ticagrelor monotherapy after 1 month	Clopidogrel (stable CAD) or ticagrelor (ACS) + ASA for 12 months	A composite of all-cause death, or MI	24 months	Intervention: 3.81% Control: 4.37% HR 0.78 (0.75-1.01)
SMART-DATE (2018)	ACS (100%)	6M DAPT, then 6M ASA monotherapy	≥ 12M DAPT	A composite of all-cause death, MI, or stroke	18 months	Intervention: 4.7% Control: 4.2% Non-inferiority P 0.03 MI risk Intervention: 1.8% Control: 0.8% HR 2.41 (1.15-5.05)
SMART CHOICE (2019)	Stable CAD (42%) ACS (58%)	Any P2Y12i monotherapy after 3 month	Any P2Y12i + ASA	A composite of all-cause death, MI or stroke	12 months	Intervention: 2.9% Control: 2.5% Non-inferiority P 0.007
STOPDAPT-2 (2019)	Stable CAD(62%) ACS (38%)	Clopidogrel monotherapy after 1 month	Clopidogrel + ASA	A composite of cv death, MI, ST, stroke or TIMI major or minor bleeding	12 months	Intervention: 2.36% Control: 3.70% Non-inferiority P <0.001 Superiority P 0.04
TWILIGHT (2019)	Stable CAD (35%) ACS (65%)	Ticagrelor monotherapy after 3 month	Ticagrelor + ASA	BARC 2, 3, or 5 bleeding	15 months	Intervention: 4.0% Control: 7.1% HR 0.56 (0.45-0.68)
TICO (2020)	ACS (100%)	Ticagrelor monotherapy after 3 month	Ticagrelor + ASA	A composite of TIMI major bleeding, death, MI, ST, stroke, or TVR	12 months	Intervention: 3.9% Control: 5.9% HR 0.66 (0.48-0.92)

DE-ESCALATION: SHORT DAPT (HBR Patients)

Trial	Study Population	Intervention	Control	Primary outcome	Follow-up duration	Result
MASTER DAPT (2021)	High Bleeding Risk Stable CAD (52%) ACS (48%)	No OAC: 1M DAPT OAC: 1M DAPT, then 5M SAPT	No OAC: 6M DAPT, 6M SAPT OAC: 3M DAPT, 9M SAPT	A composite of all-cause death, MI, stroke or major bleeding	12 months	Intervention: 7.5% Control 7.7% HR 0.97 (0.78-1.20) Non-inferiority P <0.001
SENIOR (2018)	Old age ≥ 75 y/o Stable CAD (55%) ACS (45%)	1M DAPT (Stable CAD) 6M DAPT (ACS) DES patients	1M DAPT (Stable CAD) 6M DAPT (ACS) BMS patients	A composite of all-cause death, MI, ID-TLR, or stroke	12 months	Intervention: 12% Control: 16% HR 0.71 (0.52-0.94)
ONYX ONE (2020)	High Bleeding Risk Stable CAD (46%) ACS (54%)	1M DAPT DES patients	1M DAPT PF-DCS patients	A composite of CV death, MI or ST	12 months	Intervention: 17.1% Control: 16.9% Non-inferiority P 0.01
AUGUTUS (2019)	NOAC (Apixaban) ACS (100%)	NOAC + DAPT For 6M	NOAC + P2Y12 For 6M	Major or clinically relevant nonmajor bleeding	6 Months	Intervention: 16.1% Control: 9.0% HR 1.89 (1.59-2.24)

DE-ESCALATION: Less Potent (All-Comer Setting)

Trial	Study Population	Intervention	Control	Primary outcome	Follow-up duration	Result
TALOS-AMI (2021)	AMI (100%)	1M Ticagrelor + ASA 11M Clopidogrel + ASA	12M Ticagrelor + ASA	A composite of CV death, MI, stroker, or BARC 2,3, or 5 bleeding	12 months	Intervention: 4.6% Control: 8.2% HR 0.55 (0.40-0.76) Non-inferiority P <0.001 Superiority P 0.0001
HOST-REDUCE-POLYTECH-ACS (2021)	ACS (100%)	SD prasugrel +ASA for 1 month, then LD prasugrel + ASA for 11 months	SD prasugrel + ASA for 12 months	A composite of all-cause death, MI, ST, RR, stroke, BACR 2,3, or 5 bleeding	12 months	Intervention: 7.2% Control: 10.1% HR 0.70 (0.52-0.92)
AFIRE (2019)	NOAC (Rivaroxaban) PCI or CABG after 1 year	NOAC only	NOAC + SAPT	A composite of stroke, systemic embolism, MI, UAP, or all-cause death	36 Months	Intervention: 4.14% Control: 5.75% HR 0.72 (0.55-0.95)

“Story About Temporal Antithrombotic Tuning”

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Management of Antithrombotic Therapy after Acute Coronary Syndromes

Fatima Rodriguez, M.D., M.P.H., and Robert A. Harrington, M.D.

From the Division of Cardiovascular Medicine, Department of Medicine, and the Stanford Cardiovascular Institute (F.R., R.A.H.), Stanford University, Palo Alto, CA. Address reprint requests to Dr. Harrington at the Department of Medicine, Stanford University, 300 Pasteur Dr., S102, MC:5110, Stanford, CA 94305, or at robert.harrington@stanford.edu.

N Engl J Med 2021;384:452-60.
DOI: 10.1056/NEJMra1607714

BECAUSE OF RAPIDLY CHANGING GUIDELINES IN RESPONSE TO MULTIPLE clinical trials of new therapies, the management of antithrombotic agents for patients after an acute coronary syndrome is becoming increasingly complex. Patients and clinicians must make treatment decisions by weighing the antithrombotic benefits of antiplatelet agents and the anti-ischemic benefits of anticoagulant agents against the risk of bleeding, including severe, life-threatening bleeding. Treatment decisions should be individualized by incorporating additional variables in this risk–benefit assessment, including but not limited to demographic characteristics of the patient, examination findings, laboratory testing, and imaging, as well as the patient's values and preferences.

The pathobiology of acute coronary syndromes is characterized by disruption of coronary atherosclerotic plaque through fissure, erosion, or rupture, resulting in activation of platelets and the coagulation system; the clinical result is myocardial ischemia or infarction, depending on the extent of coronary-artery occlusion.[1,2] Acute coronary syndromes are initially categorized on the basis of the 12-lead electrocardiogram (ECG), with patients separated into two treatme pathways: one for patients with ST-segment elevation (STE) and one for pat without persistent STE. This initial ECG-guided risk stratification drive treatment decisions during hospitalization and is also important for prog

N Engl J Med 2021;384:452-60.

Story About Temporal Antithrombotic Tuning

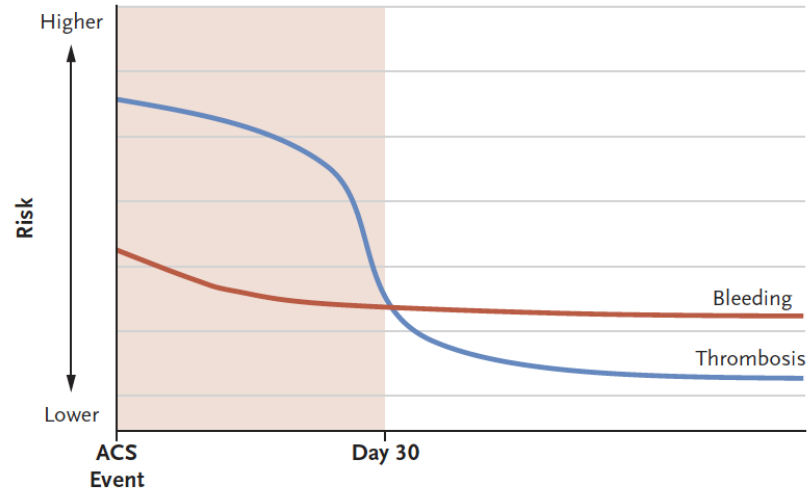


Figure 1. Risks of Thrombosis and Bleeding after an Acute Coronary Syndrome (ACS).

In the first 30 days after an ACS event, the benefits of intensive antithrombotic therapy generally outweigh the increased risk of bleeding. However, this benefit dissipates with additional time after the ACS event, favoring a therapeutic approach that considers the risks of both bleeding and thrombosis.

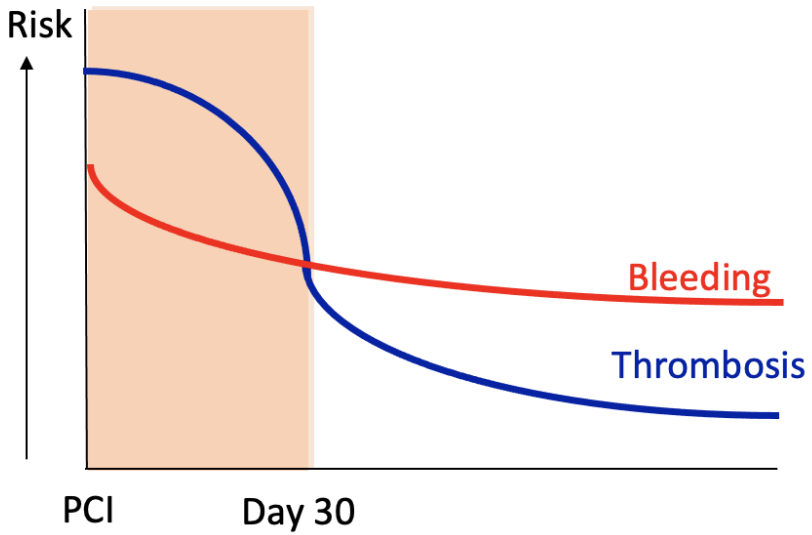
Table 2. Suggested Approaches to Antithrombotic Treatment after an ACS Event.*

Time after ACS Event	Default Strategy	Patients with High Ischemic Risk	Patients with High Bleeding Risk	Patients with Concomitant Atrial Fibrillation†
≤1 mo	Aspirin and newer-generation $P2Y_{12}$ inhibitor	Aspirin and newer-generation $P2Y_{12}$ inhibitor	Aspirin and newer-generation $P2Y_{12}$ inhibitor	Aspirin, clopidogrel, and DOAC‡
>1 mo to 12 mo	Aspirin and newer-generation $P2Y_{12}$ inhibitor	Aspirin and newer-generation $P2Y_{12}$ inhibitor	Any $P2Y_{12}$ inhibitor alone	Clopidogrel and DOAC
>12 mo	Any $P2Y_{12}$ inhibitor alone	Aspirin and newer-generation $P2Y_{12}$ inhibitor, or switch to aspirin and low-dose rivaroxaban	Any $P2Y_{12}$ inhibitor or aspirin	DOAC

N Engl J Med 2021;384:452-60.

Pragmatic Antithrombotic Strategies According to Temporal Bleeding and Ischemic Risk

Rationale



Adapted from N Engl J Med 2021;384:452-60

Proposed strategy

Standard guideline-directed DAPT

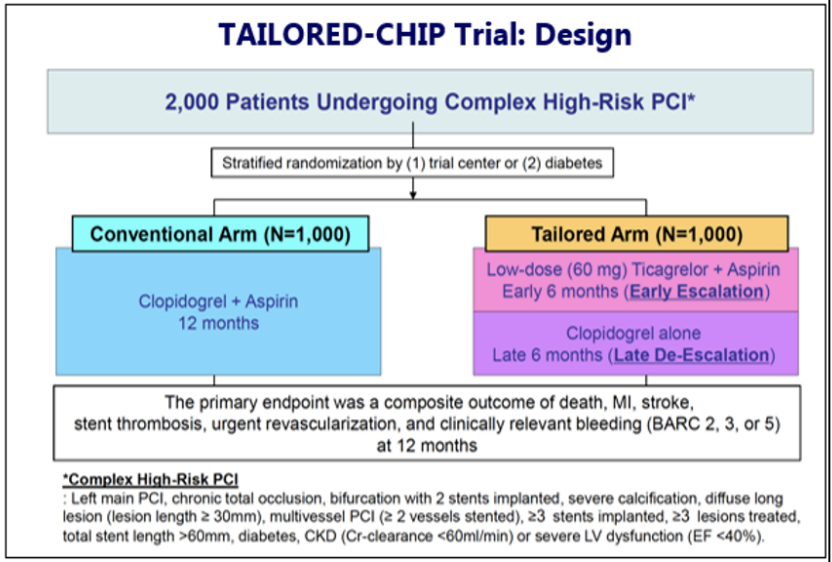
Versus

DAPT escalation with potent P2Y12 inhibitors

DAPT de-escalation
- PFT-guided
- Genotype-guided
- Non-guided

Aspirin or P2Y12 inhibitor monotherapy

Related ongoing trial



OS Kwon and DW Park. JACC: Asia 2022;2:1–18

Complex CHIP Population : TAILORED-CHIP Trial

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Find Studies | About Studies | Submit Studies | Resources | About Site

Home > Search Results > Study Record Detail

Save this study

Trial record **1 of 7** for: tailored chip

Previous Study | Return to List | Next Study

TAILored Versus COnventional AntithRombotic StratEgy IntenDed for Complex HIgh-Risk PCI (TAILORED-CHIP)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03465644

Recruitment Status : Recruiting
First Posted : March 14, 2018
Last Update Posted : March 5, 2019

See Contacts and Locations

Sponsor:
Duk-Woo Park, MD

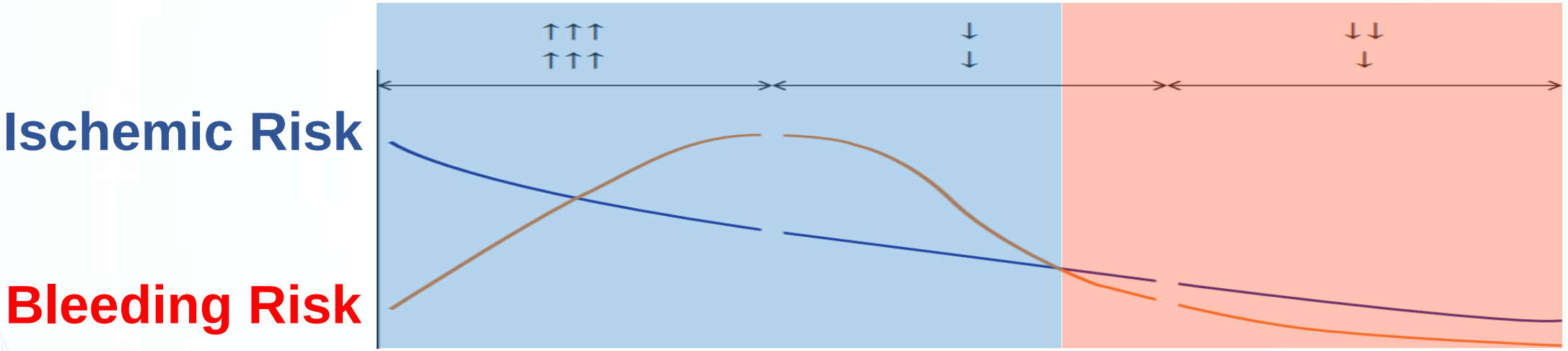
Collaborator:
CardioVascular Research Foundation, Korea

Information provided by (Responsible Party):
Duk-Woo Park, MD, Asan Medical Center

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

TAILORED-CHIP Trial:
Study Hypothesis

Complex High-risk PCI (CHIP Patients)

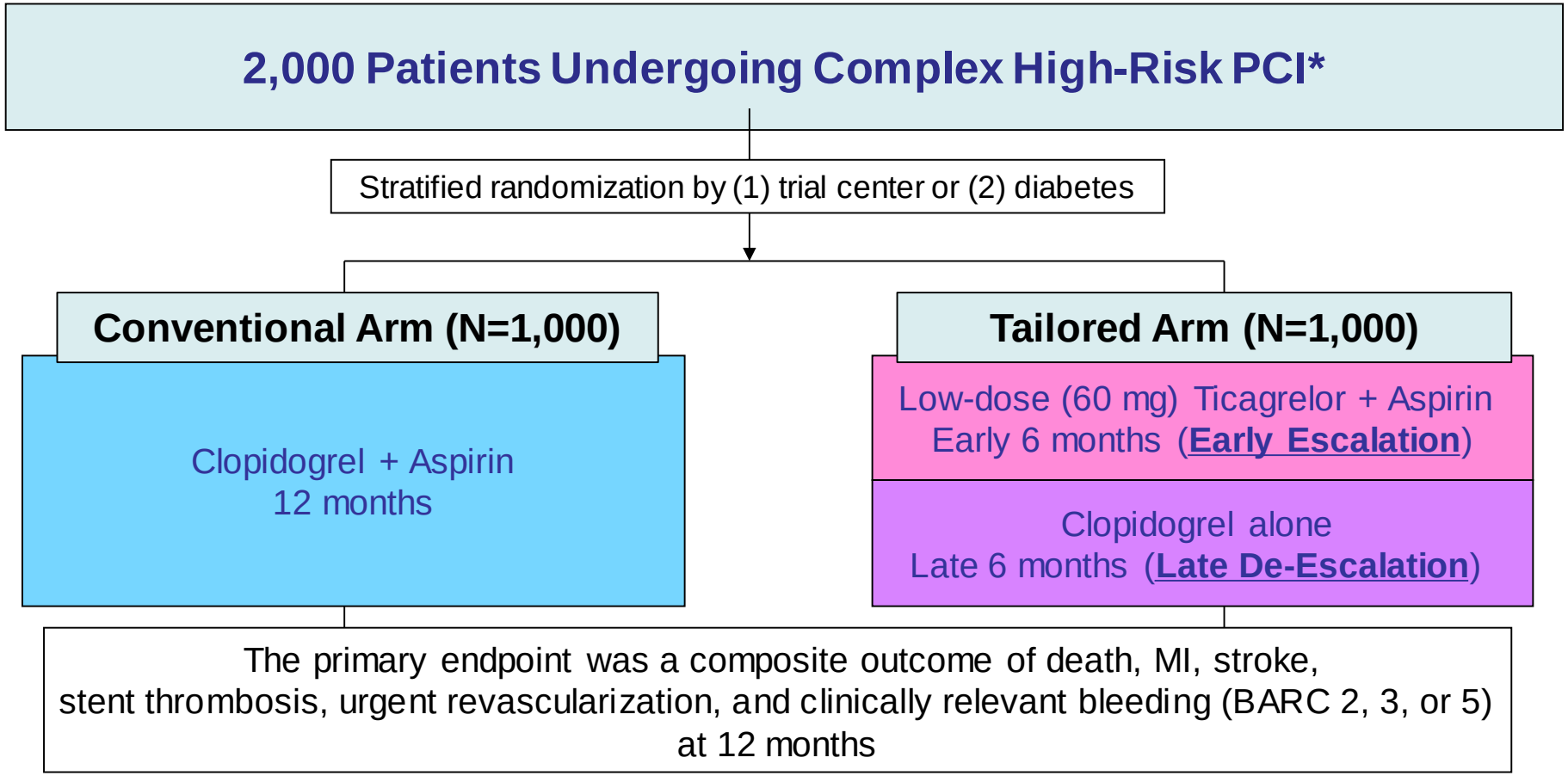


More Potent Strategy
For Early Ischemic Risk
"Low-dose Ticagrelor + ASA"

Less Potent Strategy
For Late Bleeding Risk
"Clopidogrel Only"

TAILored versus C***O***nventional Antith***R***ombotic Strat***E***gy
Inten***D***ed for ***C***omplex ***HI***gh-Risk ***P***CI

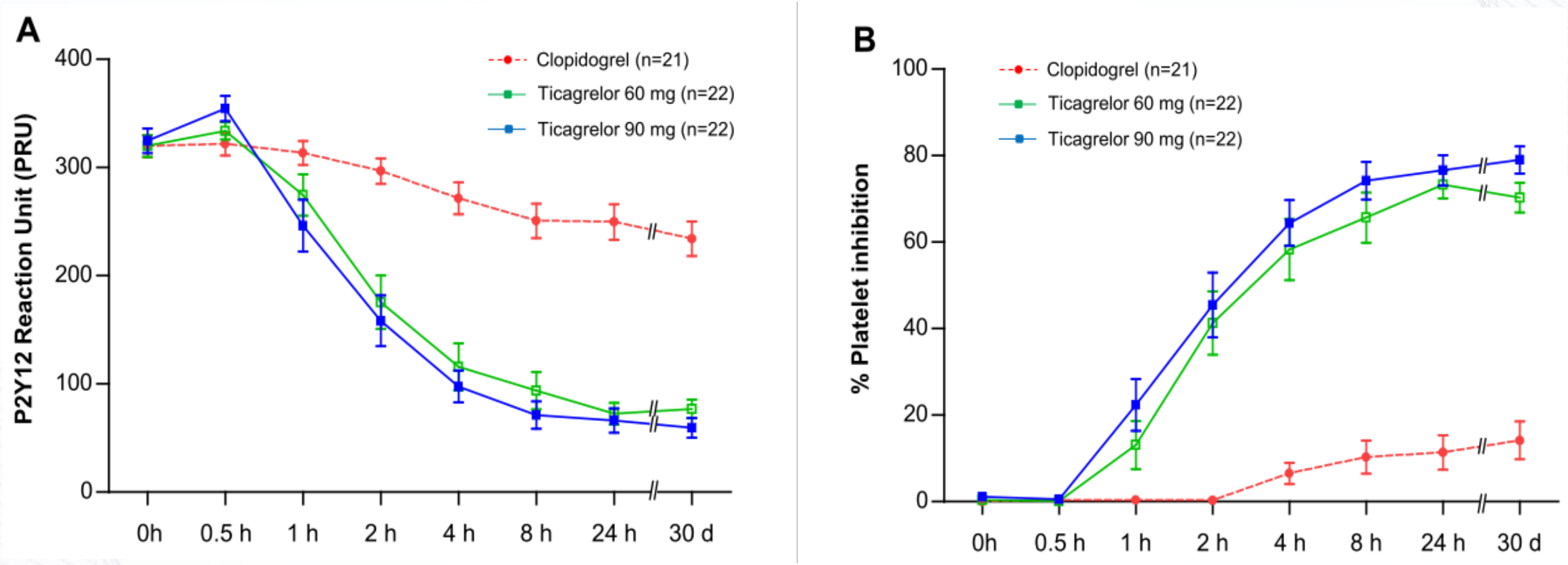
TAILORED-CHIP Trial



***Complex High-Risk PCI**

: Left main PCI, chronic total occlusion, bifurcation requiring two-stent technique, severe calcification, diffuse long lesion (lesion length ≥ 30mm), multivessel PCI (≥ 2 vessels requiring stent implantation), ≥3 requiring stents implantation, ≥3 lesions will be treated, predicted total stent length for revascularization >60mm, diabetes, CKD (Cr-clearance <60ml/min) or severe LV dysfunction (EF <40%).

Rationale for Low-Dose Ticagrelor Based on OPTIMA trial



Low-dose Ticagrelor > Clopidogrel

Low-dose Ticagrelor ≈ Standard-dose Ticagrelor

DW Park, SJ Park et al, JACC 2018;71:1594-1595.

Inclusion criteria

- Men or women aged ≥18 years
- Patients undergoing PCI with contemporary newer-generation DES.
- Patients must have at least one of any features of complex high-risk anatomic, procedural and clinical-related factors.

✓Lesion- or procedure-related factors; *Left main* lesion, bifurcation lesion requiring *two stent technique*, *CTO* lesion, severe *calcification*, *diffuse long* lesion (lesion length ≥ at least 30mm), multi-vessel PCI (≥ *2 vessels requiring stent implantation*), ≥*3 requiring stent* implantation, ≥*3 lesions* will be treated, or predicted *total stent length > 60 mm*

Or

✓Clinical factors; *Diabetes, chronic kidney disease* (CrCl <60 mL/min), severe LV dysfunction (*LVEF<40%*)

Exclusion criteria

- ***Enzyme-positive ACS*** *(NSTEMI or STEMI)*
- Contraindication to aspirin or P2Y12 inhibitors (ticagrelor or clopidogrel)
- Cardiogenic shock at index admission
- Patients treated with only BMS or balloon angioplasty during index procedure
- ***Need for chronic oral anticoagulation*** (warfarin or NOAC)
- ***Active bleeding or extreme-risk for major bleeding*** (e.g. active PUD, GI pathology with high risk for bleeding, malignancy with high risk for bleeding)

Study endpoints

Primary

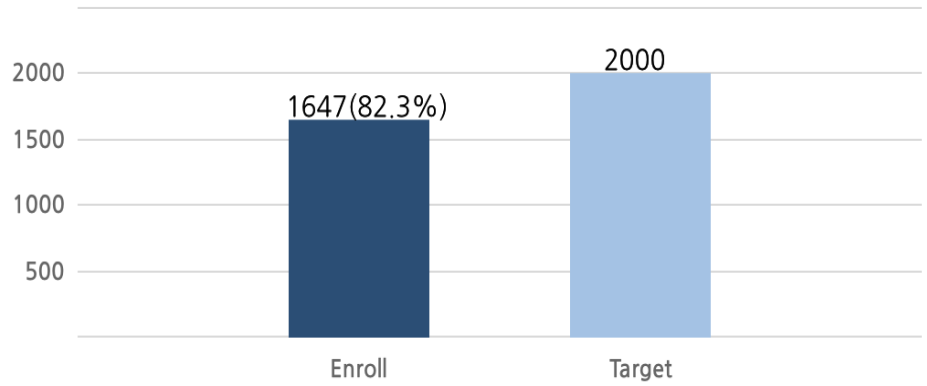
A **net clinical outcome** of all-cause death, MI, stroke, stent thrombosis, urgent revascularization and clinically relevant bleeding (BARC 2,3, or 5) at 12 months post-PCI

Secondary

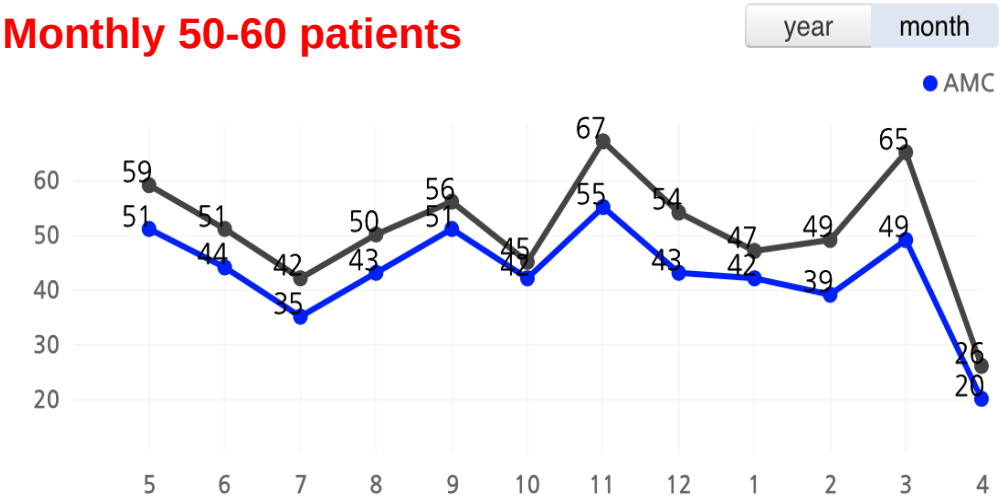
- Each component of primary outcome
- Composite of death (all or CV), MI, stroke, stent thrombosis or urgent revascularization
- Composite of death (all or CV), MI, or stroke
- Composite of death (all or CV) or MI
- Any revascularization
- BARC 3 or 5 bleeding
- Major or minor bleeding according to definition from TIMI
- Major or minor bleeding to definition from ISTH

TAILORED-CHIP Trial Status

Current Enrollment Status (82.3%)



Monthly 50-60 patients



Key Messages

- Optimal antithrombotic strategies are a cornerstone of the management of ACS or PCI and have constantly evolved to balance ischemia and bleeding.
- East Asian patients have reduced anti-ischemic benefits and an increased bleeding risk during antithrombotic therapies compared with Caucasian patients.
- A one-size-fits-all approach is not suited to antithrombotic therapies for East Asians following ACS or PCI.
- A careful assessment of thrombotic risk vs. bleeding risk is thus required via a tailored, potentially dynamic strategy, as well as a treatment plan based on individual risk.