

Antithrombotic and Antiplatelet Choice in Complex PCI: Updated Issues in 2019 - 2020

Duk-Woo Park, MD, PhD

Department of Cardiology, Ulsan College of Medicine,
Asan Medical Center

Disclosure

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

To Improve PCI Outcomes in Complex CAD

PCI procedure and equipment

- Thin-strut durable and bioabsorbable polymer-based DES
- Improved PCI guide wires, delivery systems and adjunct devices
- Expert techniques and devices to recanalize CTOs, manage bifurcations, calcium, etc.
- Advanced hemodynamic support options: transaxial forward flow pumps, ECMO
- Transradial artery access
- Approaches to prevent contrast nephropathy
- Superior catheterization labs: Better imaging, reduced radiation exposure

PCI guidance (pre- and post-procedure)

- Physiologic lesion assessment (iFR, FFR)
- Intravascular imaging (IVUS, OCT, NIRS)
- Goal of complete revascularization (anatomic, ischemic)

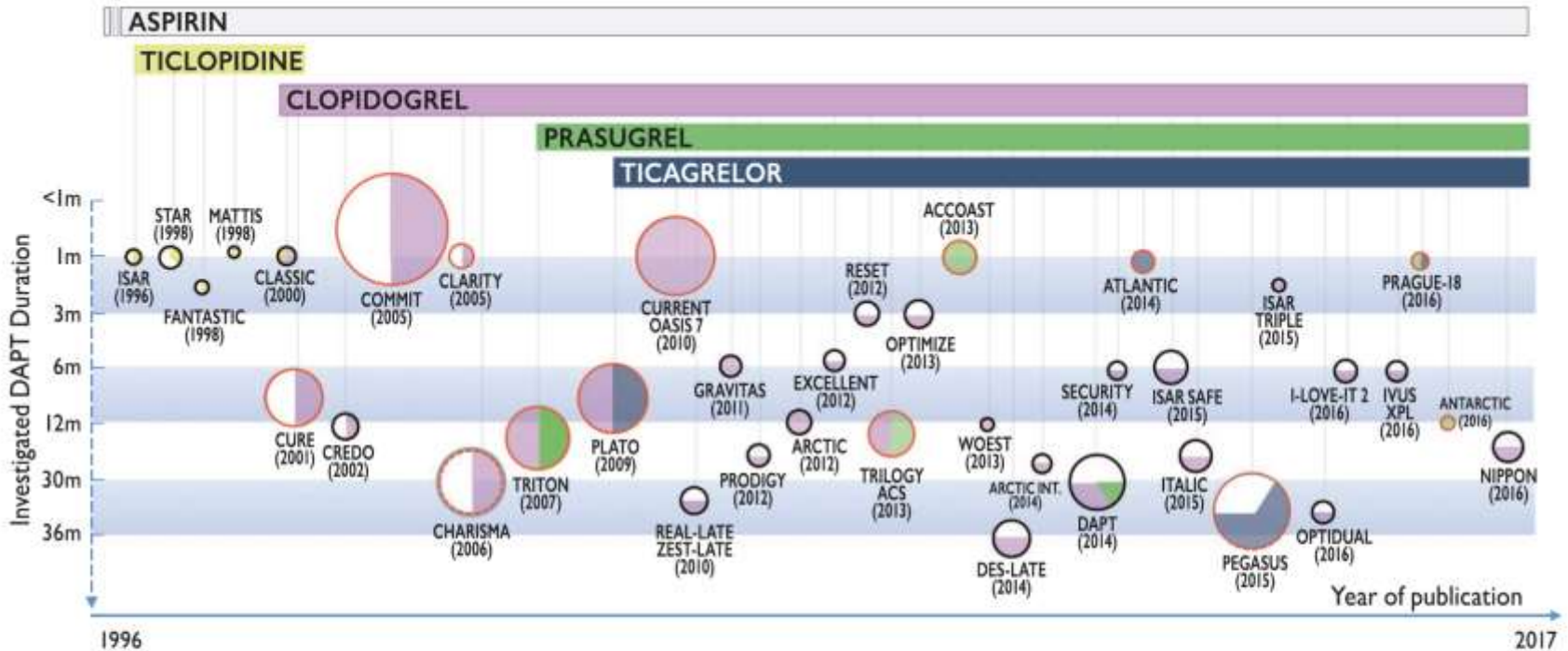
Adjunctive pharmacotherapy

- Procedural anticoagulation: Bivalirudin
- Potent P2Y12 inhibitors: Oral (prasugrel, ticagrelor), intravenous (cangrelor)
- Appropriate DAPT duration after PCI: Abbreviated vs. extended
- Foundational role of GDMT: statins, PCSK9i, beta-blockers, ACEI/ARB, etc.

Patient selection and pre-procedural planning

- Use of risk scores: SS, SSII, NERS I and II, others
- PCI planning tools: CTA and CT-FFR

History of DAPT



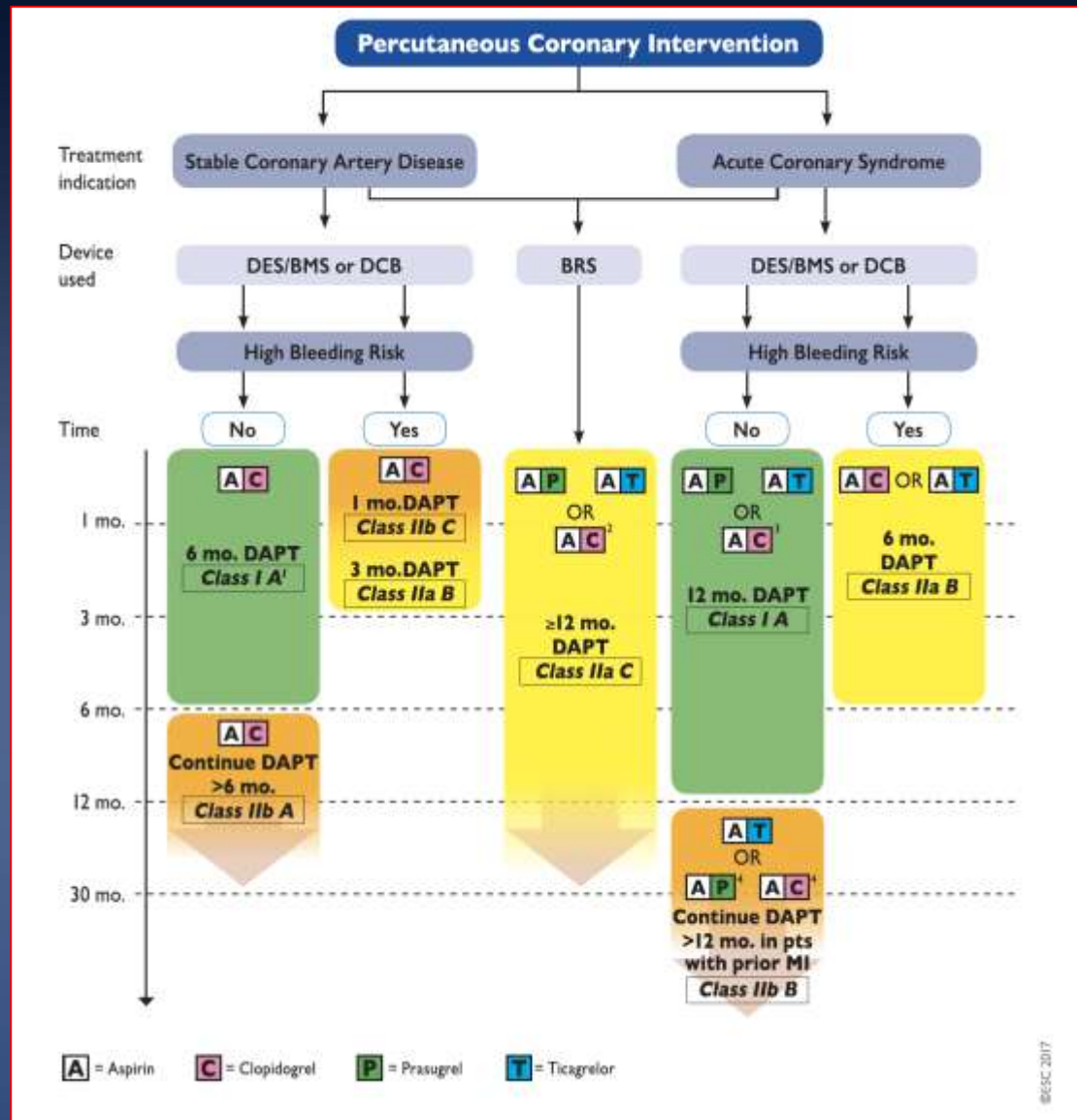
Size of the circles denotes sample size

Perimeter of the circles denotes type of investigated population



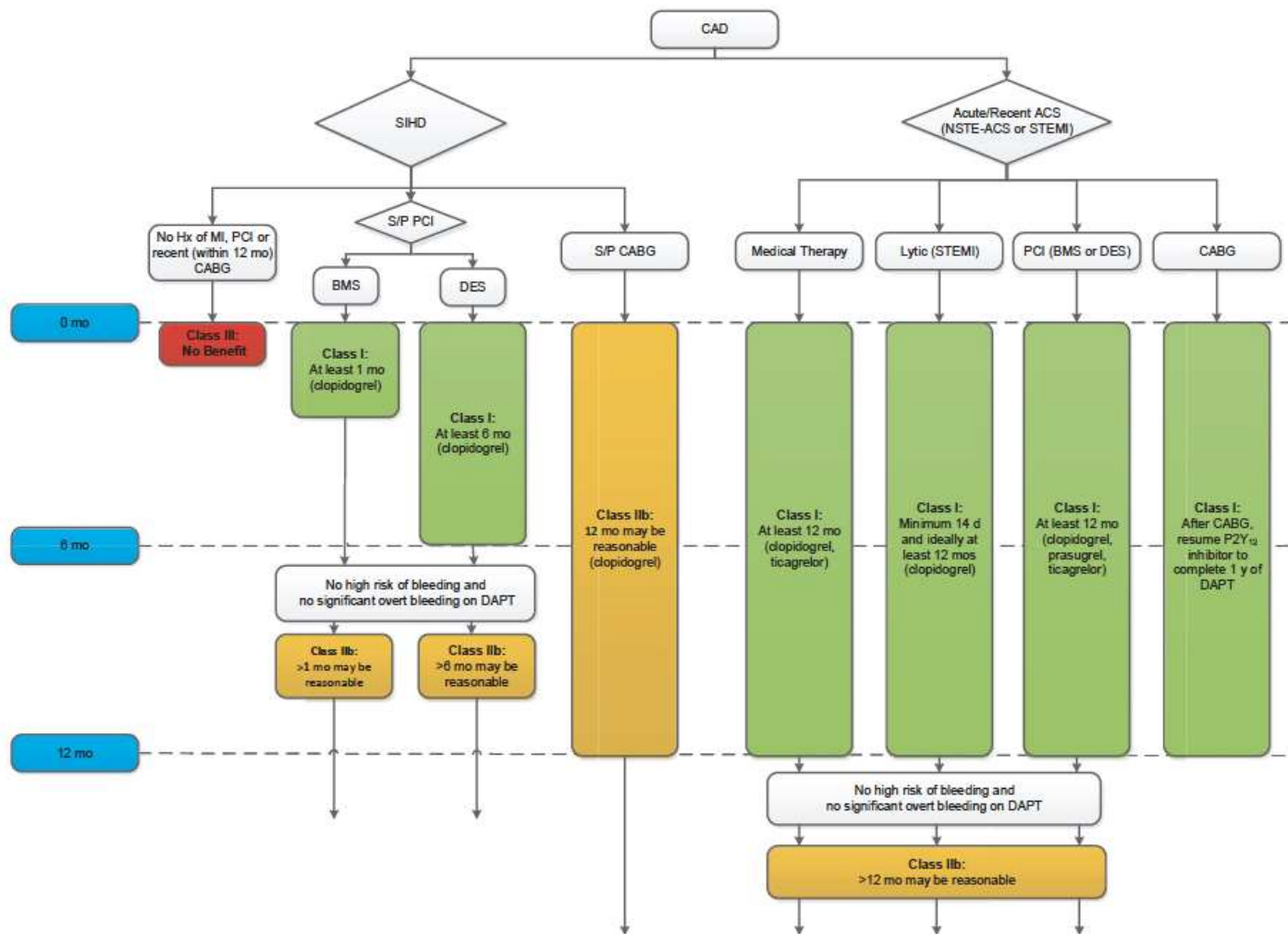
- Mixed clinical presentation at the time of stent implantation
- Acute coronary syndrome at presentation
- DAPT initiated in patients with prior myocardial infarction
- DAPT for primary prevention

Simple DAPT Guideline, 2017 ESC



Simple DAPT Guideline, 2016 ACC/AHA

FIGURE 1 Master Treatment Algorithm for Duration of P2Y₁₂ Inhibitor Therapy in Patients With CAD Treated With DAPT



However, Real-World Practice Is Not Simple

TABLE 4

Clinical and Procedural Factors Associated with Increased Ischemic Risk/Thrombosis) or Increased Bleeding Risk

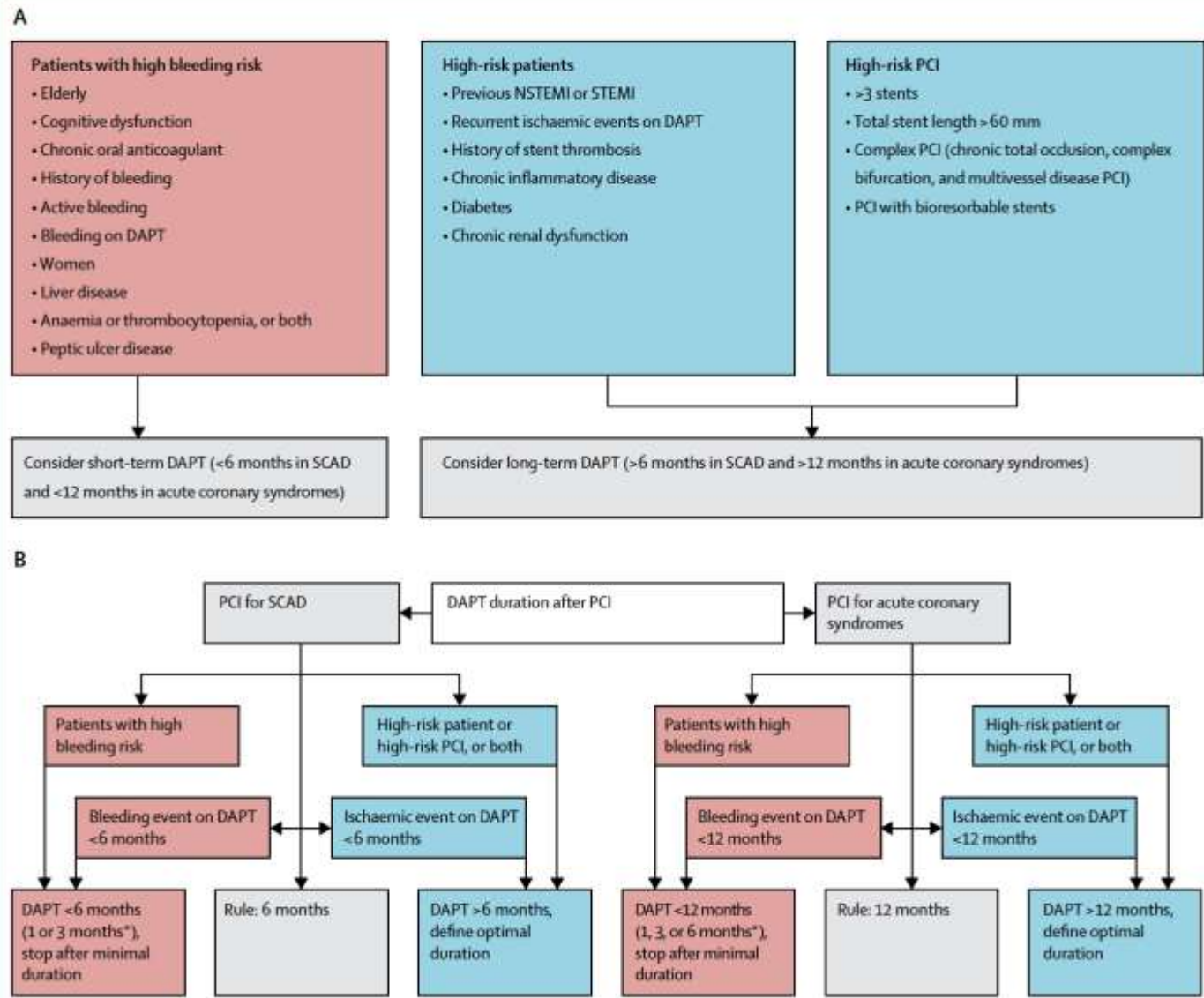
Increased Ischemic Risk/Risk of Stent Thrombosis (may favor longer-duration DAPT)

Increased ischemic risk

- Advanced age
- ACS presentation
- Multiple prior MIs
- Extensive CAD
- Diabetes mellitus
- CKD

Increased risk of stent thrombosis

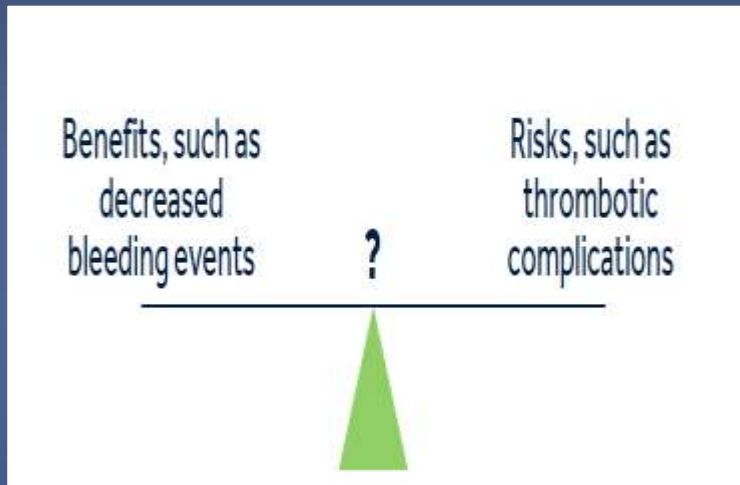
- ACS presentation
- Diabetes mellitus
- Left ventricular ejection fraction <40%
- First-generation drug-eluting stent
- Stent undersizing
- Stent underdeployment
- Small stent diameter
- Greater stent length
- Bifurcation stents
- In-stent restenosis



Good or Bad Leverage

Ischemic & Bleeding Leverage Is More Complex in Real-World Setting

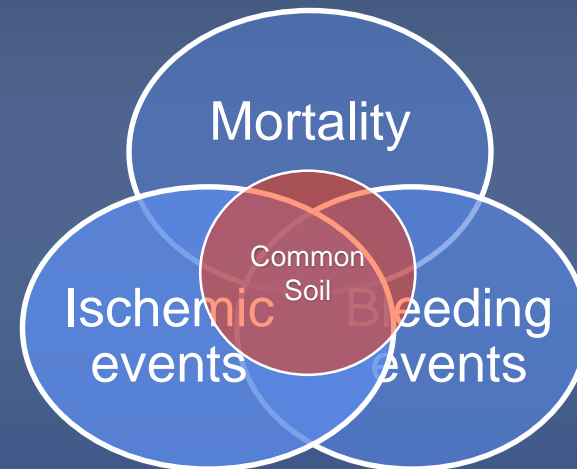
Theory



“Good Leverage”

Reality

Clustering effect



“Bad Leverage”

Theory – One Spaghetti



**Sweet and Sour and Smoky: Rachael's Red
Onion and Smoked Bacon Spaghetti with
Cherry Peppers**

Reality – More than 100 Recipe of Spaghetti



Spaghetti Bolognese | The Cozy Apron
thecozyapron.com



One Pot Turkey Spaghetti...
sixsistersstuff.com



Instant Pot Spaghetti (...)
spicichofealthy.com



Garlic Lovers' Spaghetti...
gimmesomeoven.com

관련 검색어

spaghetti noodle >

cream spaghetti >

pasta spaghetti >



Instant Pot Homemade ...
30daysofkickbut.com



Instant Pot Spaghetti Recipe - ...
cookingclassy.com



Spaghetti With Cheese And Pea...
tasty.co



BEST One Pot Spaghetti...
fisherathome.com



Spaghetti with Meatballs in Marinara Sauce - TODAY.com
today.com



All-in-One Spaghetti Recipe - Southern Living
southernliving.com



Spaghetti Pomodoro with H...
yellowblissroad.com



Ultimate Cheesy Baked Spaghe...
smotherndessert.com



Best Garlic Spaghetti Recipe - How To Make Garlic S...
delish.com



Saucy Spaghetti Sauce - Hearty Smarty
hearty-smarty.com



Pasta Pomodoro Recipe | Bon Appetit
bonappetit.com



Spaghetti in Tomato sauce | Spaghetti Recipe | Red ...
youtube.com



Homemade Spaghetti Sauce - T...
tastesbetterfromscratch.com



One-Pot Spaghetti and ...
skillettaste.com



Red Wine Spaghetti With Pancetta Recipe - NY...
cooking.nytimes.com



Kid-Friendly Spaghetti ...
kikuna.com



Instant Pot Spaghetti and ...
eatinyourtasty.com



Instant Pot Spaghetti and ...
simplyhappyfamily.com



Instant Pot Spaghetti with Marin...
totallyvegan.net



Homemade Venison Spaghetti Sauce - Deer ...
deerrecipesonline.com



Instant Pot Spaghetti - The Ski...
thekoreyishdsh.com



One-Pot Creamy Spaghetti Recipe - Pillsbury.com
pillsbury.com

Recent RCTs for Antithrombotic Recipe in High-Risk (Ischemic or Bleeding) PCI Patients

- Aspirin omission, Ticagrelor mono: TWILIGHT, GLOBAL-LEADERS
- Short DAPT, Clopidogrel mono: SMART-CHOICE, STOPDAPT-2
- HBR patients: ONYX-ONE, LEADERS-FREE
- PCI & AF: PIONEER-AF, REDUAL, AUGUSTUS, ENTRUST-AF
- PCI & Stable CAD/DM: COMPASS, THEMIS
- PCI & TAVR: GALILEO, GALILEO 4-D
- **Finally, Headache, Headache, Headache....**

Optimal Antiplatelet Therapy

“Ethnic Difference”

Can One Size Really Fit All?



East-Asian Paradox

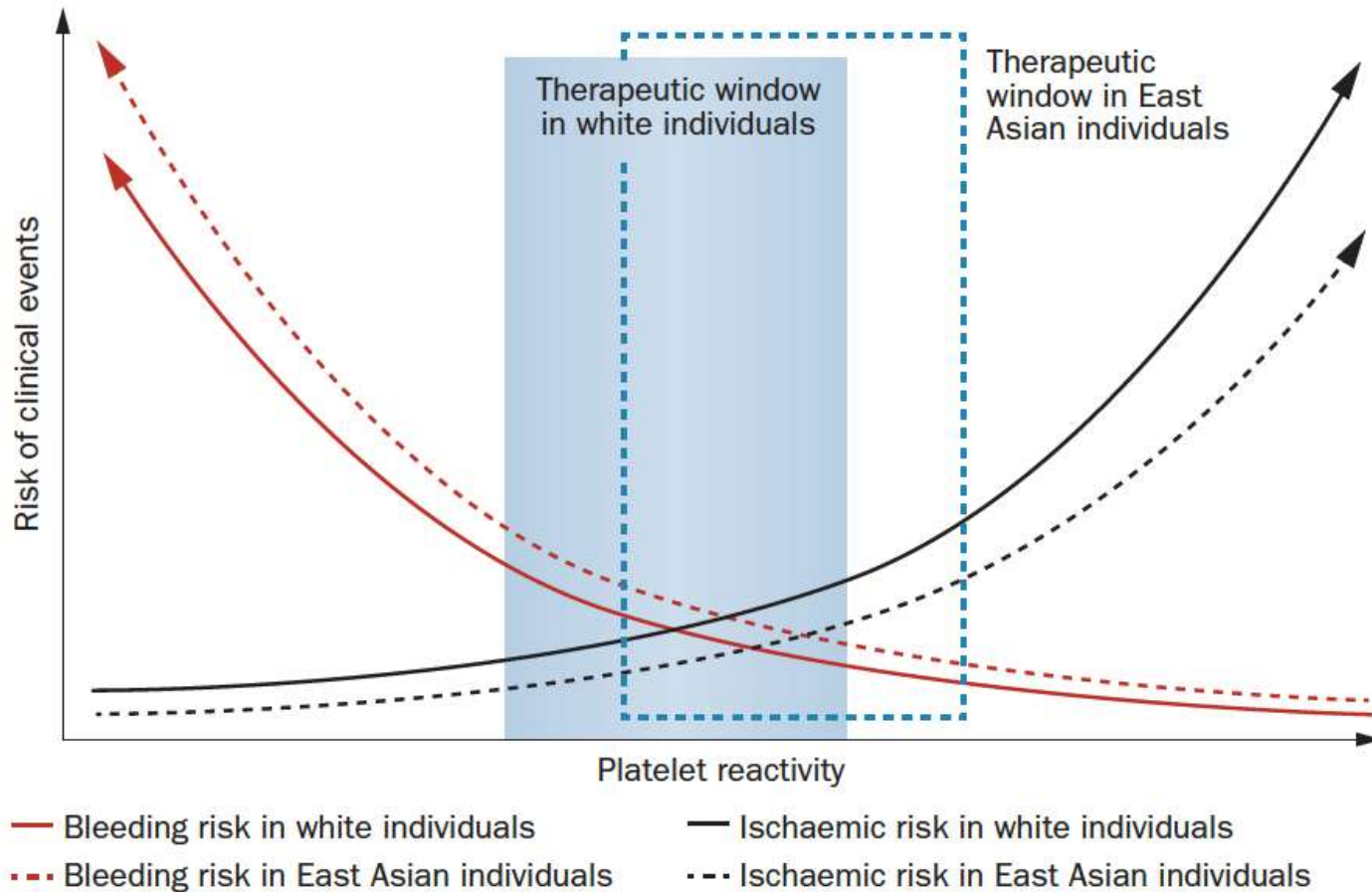


Figure 2 | Postulated differences in the optimal 'therapeutic window' of platelet reactivity between white and East Asian populations.

Different Ethnicity: TICA KOREA Trial

Circulation

ORIGINAL RESEARCH ARTICLE

Clinically Significant Bleeding With Ticagrelor Versus Clopidogrel in Korean Patients With Acute Coronary Syndromes Intended for Invasive Management

A Randomized Clinical Trial

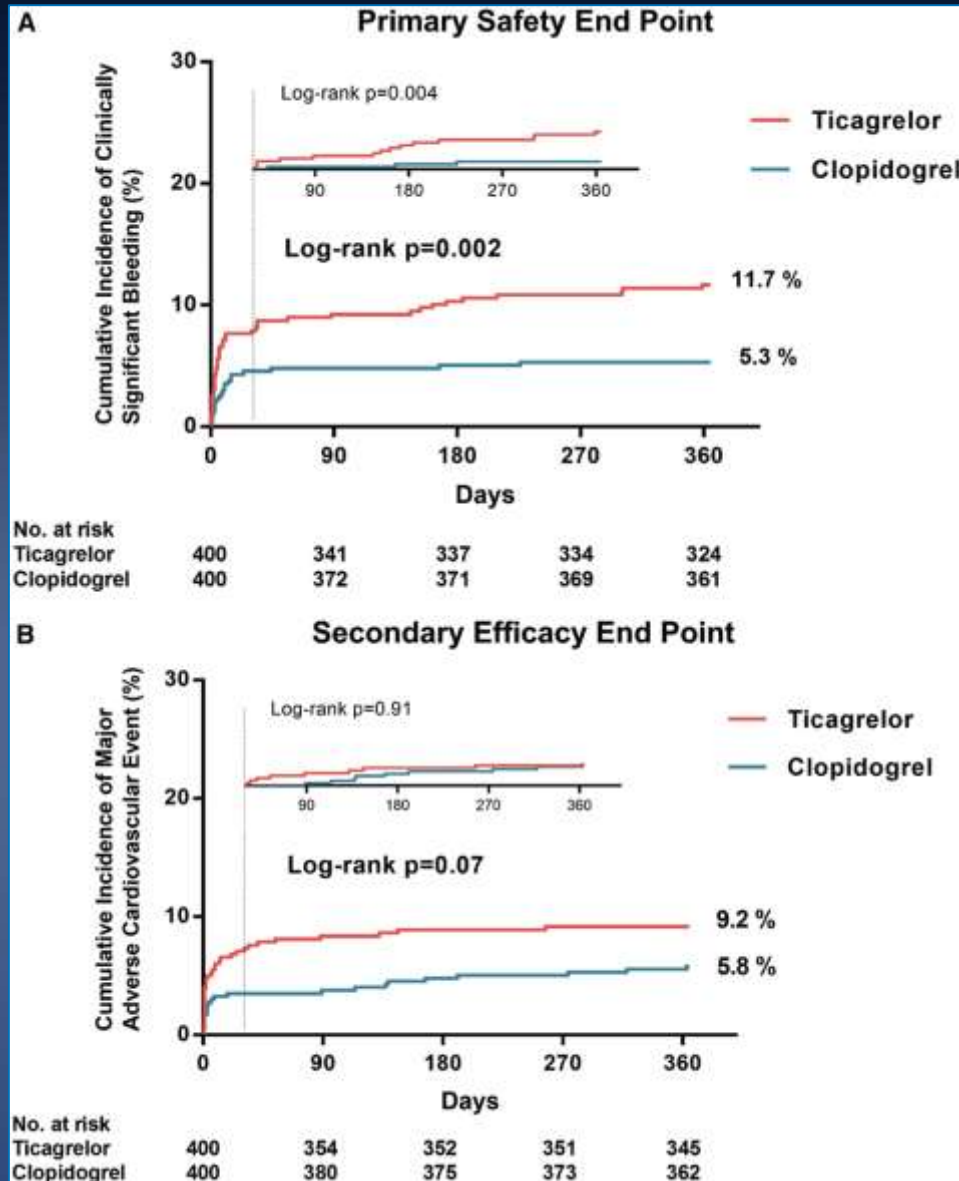
BACKGROUND: Owing to the differential propensity for bleeding and ischemic events with response to antiplatelet therapy, the safety and effectiveness of potent P2Y12 inhibitor ticagrelor in East Asian populations remain uncertain.

METHODS: In this multicenter trial, 800 Korean patients hospitalized for acute coronary syndromes with or without ST elevation and intended for invasive management were randomly assigned to receive, in a 1:1 ratio, ticagrelor (180 mg loading dose, 90 mg twice daily thereafter) or clopidogrel (600 mg loading dose, 75 mg daily thereafter). The primary safety outcome was clinically significant bleeding (a composite of major bleeding or minor bleeding according to PLATO (Platelet Inhibition and Patient Outcomes) criteria at 12 months.

RESULTS: At 12 months, the incidence of clinically significant bleeding was significantly higher in the ticagrelor group than in the clopidogrel group (11.7% [45/400] vs 5.3% [21/400]; hazard ratio [HR], 2.26; 95% confidence interval [CI], 1.34 to 3.79; $P=0.002$). The incidences of major bleeding (7.5% [29/400] vs 4.1% [16/400], $P=0.04$) and fatal bleeding (1% [4/400] vs 0%, $P=0.04$) were also higher in the ticagrelor group. The incidence of death from cardiovascular causes, myocardial infarction, or

Duk-Woo Park, MD*
Osung Kwon, MD*
Jae-Sik Jang, MD
Sung-Cheol Yun, PhD
Hanbit Park, MD
Do-Yoon Kang, MD
Jung-Min Ahn, MD
Pil Hyung Lee, MD
Seung-Whan Lee, MD
Seong-Wook Park, MD
Si Wan Choi, MD
Sang-Gon Lee, MD
Hyuck-Jun Yoon, MD
Taehoon Ahn, MD
Moo Hyun Kim, MD
Deuk Young Nah, MD
Sung Yun Lee, MD
Jei Keon Chae, MD
Seung-Jung Park, MD
On behalf of the
TICA KOREA Investigators

Different Ethnicity: TICA KOREA Trial



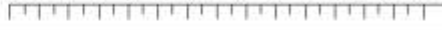
Park DW, Park SJ et al. Circulation. 2019;140

Different Scoring System

Table 3 Risk scores validated for dual antiplatelet therapy duration decision-making

| | PRECISE-DAPT score ¹⁸ | DAPT score ¹⁵ |
|-----------------------------------|----------------------------------|------------------------------------|
| Time of use | At the time of coronary stenting | After 12 months of uneventful DAPT |
| DAPT duration strategies assessed | Short DAPT (3–6 months) vs. | Standard DAPT (12 months) vs. |

**Optimal Antithrombotic Strategy in Elderly, East-Asian Women With High DAPT Score Receiving Complex Distal LM PCI?
==> Headache, Headache, Headache...**

| | Points  | Vein graft stent | +2 pt |
|-----------------------------------|---|---|-------|
| Score range | 0 to 100 points | –2 to 10 points | |
| Decision making cut-off suggested | Score ≥ 25 → Short DAPT Score < 25 → Standard/long DAPT | Score ≥ 2 → Long DAPT Score < 2 → Standard DAPT | |
| Calculator | www.precisedaptscore.com | www.daptstudy.org | |

©ESC 2017

Optimal Antithrombotic in Complex PCI Patients

- Diverse clinical and anatomic situations
- Different drugs
- Different DES
- Different ethnicity
- Different scoring system

One-Size Pill Doesn't Fit All Diverse Situations



One Recipe for Complex PCI : TWILIGHT Trial



Ticagrelor **W**ith **A**sprin or **A**Lone **I**n **H**i**G**H-Risk Patients After Coronary **I**n**T**ervention

Roxana Mehran, MD

@Drroxmehr

on behalf of the TWILIGHT Investigators

Icahn School of Medicine at Mount Sinai, New York, NY



ClinicalTrials.gov Number: NCT02270242



TWILIGHT Inclusion Criteria

Patients undergoing successful PCI with at least 1 locally-approved DES whom the treating clinician intended to discharge on ticagrelor plus aspirin were enrolled in the study

Clinical criteria

Age ≥ 65 years

Female gender

Troponin positive ACS

Established vascular disease (previous MI, documented PAD or CAD/PAD revasc)

DM treated with medications or insulin

CKD (eGFR < 60 ml/min/1.73m² or CrCl < 60 ml/min)

Angiographic criteria

Multivessel CAD

Target lesion requiring total stent length > 30 mm

Thrombotic target lesion

Bifurcation lesion(s) with Medina X, 1, 1 classification requiring ≥ 2 stents

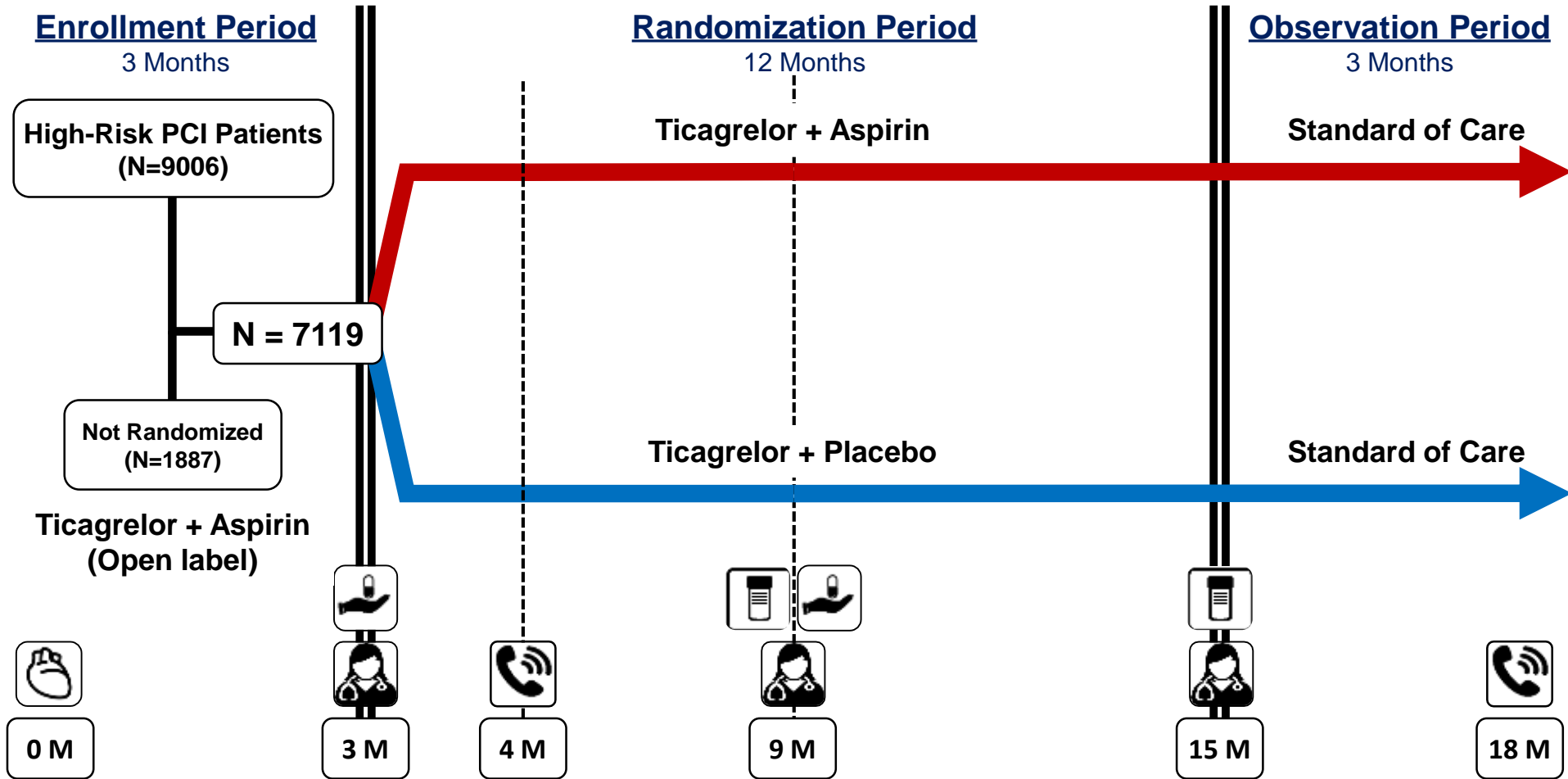
Left main ($\geq 50\%$) or proximal LAD ($\geq 70\%$) lesions

Calcified target lesion(s) requiring atherectomy

Trial inclusion required the presence of at least 1 additional clinical ***and*** angiographic feature associated with a high risk of ischemic or bleeding events.

TWILIGHT

Study Design



Patient Characteristics

Baseline Demographics

| Variable | Tica + Placebo (N = 3555) | Tica + Aspirin (N = 3564) |
|-------------------------------|------------------------------|------------------------------|
| Age, years [Mean ± SD] | 65.2 ± 10.3 | 65.1 ± 10.4 |
| Age, years [Mean ± SD] | 65.2 ± 10.3 | 65.1 ± 10.4 |
| Diabetes Mellitus | 37.1% | 36.5% |
| Insulin requiring | 9.4% | 10.5% |
| Chronic Kidney Disease | 16.8% | 16.8% |
| Anemia | 19.8% | 19.1% |
| ACS presentation | 64.0% | 65.7% |
| Previous MI | 28.7% | 28.6% |
| Previous PCI | 42.3% | 42.0% |
| Previous CABG | 10.2% | 9.8% |
| Previous major bleed | 0.9% | 0.9% |

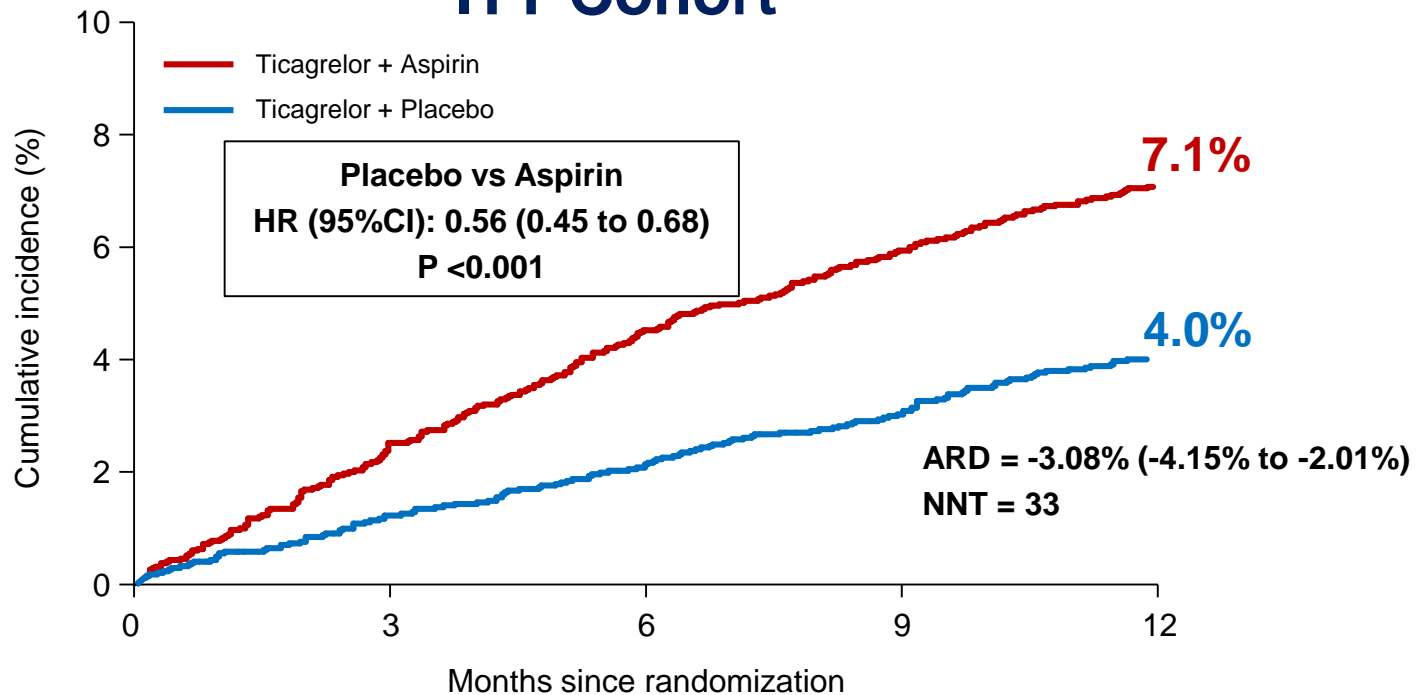
Patient Characteristics

Baseline Procedural Details

| Variable | Tica + Placebo (N = 3555) | Tica + Aspirin (N = 3564) |
|---------------------------------------|------------------------------|------------------------------|
| Radial access | 73.1% | 72.6% |
| Multivessel CAD | 63.9% | 61.6% |
| Lesion morphology | | |
| Thrombus | 10.4% | 10.7% |
| Calcification, moderate/severe | 14.0% | 13.7% |
| Any bifurcation | 12.2% | 12.1% |
| Total stent length | 40.1 ± 24.2 | 39.7 ± 24.3 |
| Calcification, moderate/severe | 14.0% | 13.7% |
| Any bifurcation | 12.2% | 12.1% |
| Chronic total occlusion | 6.2% | 6.3% |
| Total stent length | 40.1 ± 24.2 | 39.7 ± 24.3 |

Primary Endpoint: BARC 2, 3 or 5 Bleeding

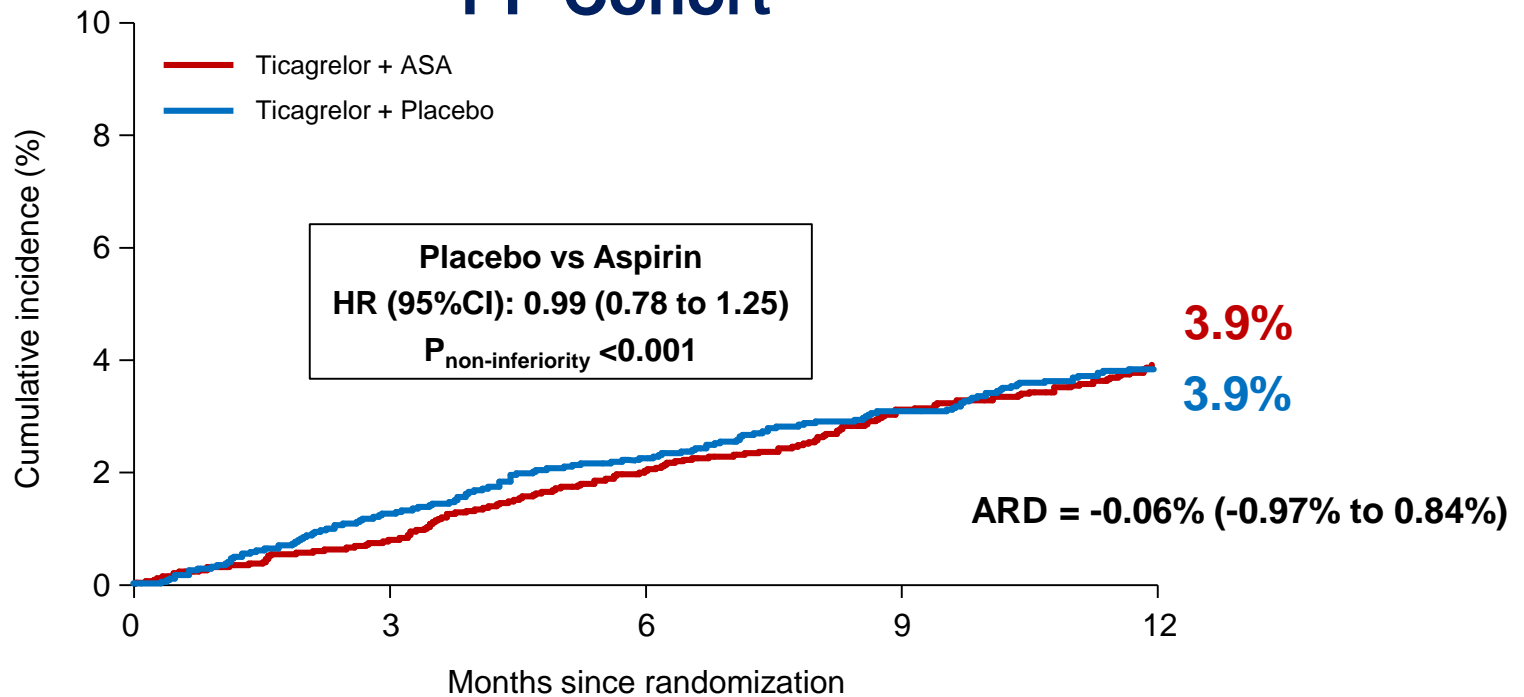
ITT Cohort



| | No. at risk | 0 | 3 | 6 | 9 | 12 |
|----------------------|-------------|------|------|------|------|----|
| Ticagrelor + Aspirin | 3564 | 3454 | 3357 | 3277 | 3213 | |
| Ticagrelor + Placebo | 3555 | 3474 | 3424 | 3366 | 3321 | |

Key Secondary Endpoint: Death, MI or Stroke

PP Cohort



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

One Recipe for Complex PCI : 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 COntventional AntithRombotic StratEgy IntenDed for Complex High-Risk PCI (TAILORED-CHIP)

ClinicalTrials.gov Identifier: NCT03465644

 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.

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

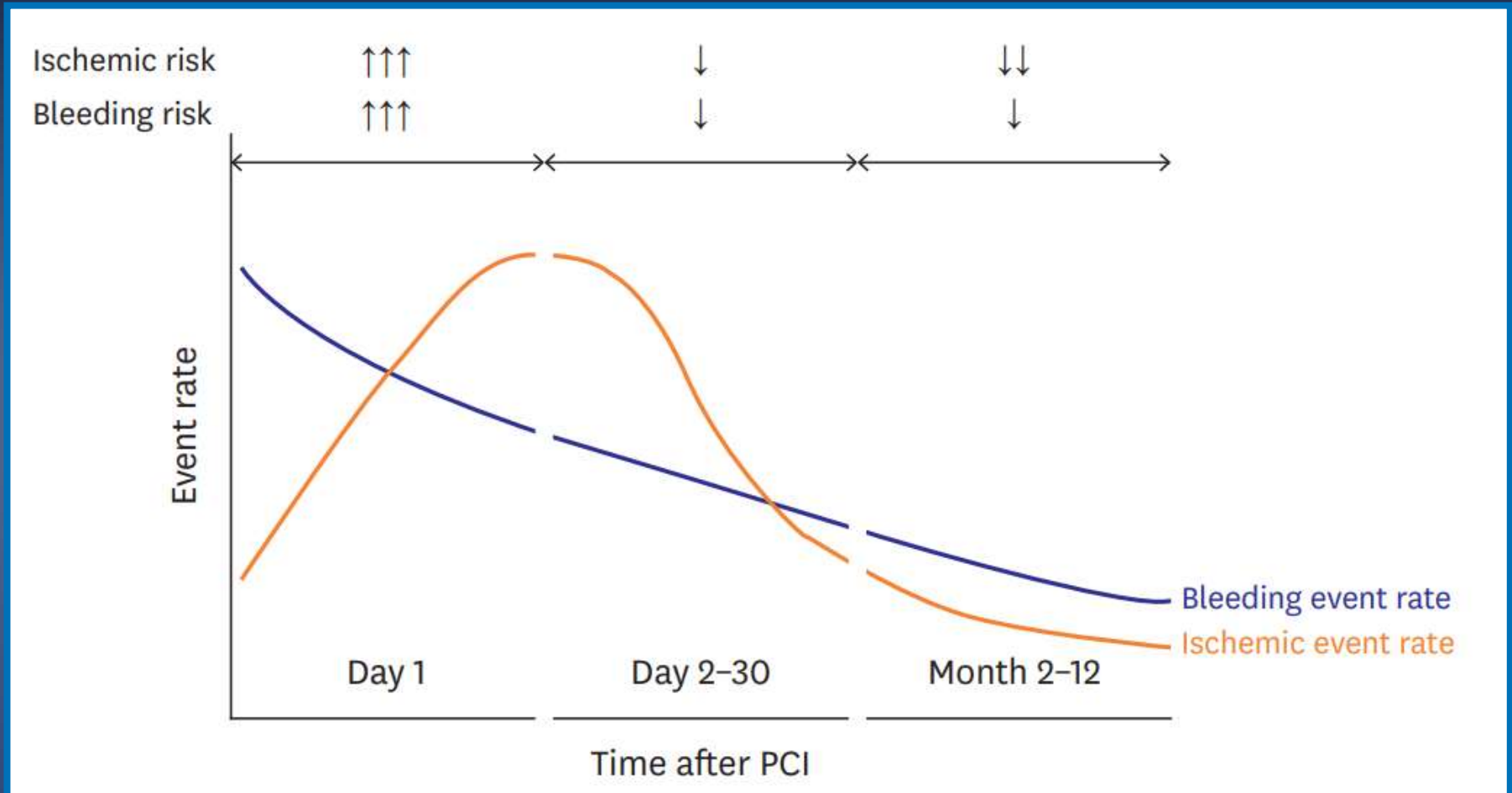
No Results Posted

Disclaimer

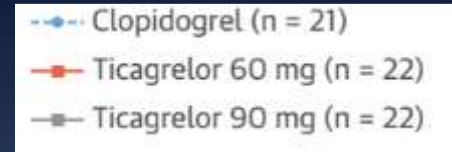
 How to Read a Study Record

Timing of Ischemic vs. Bleeding Risks Is Different after PCI

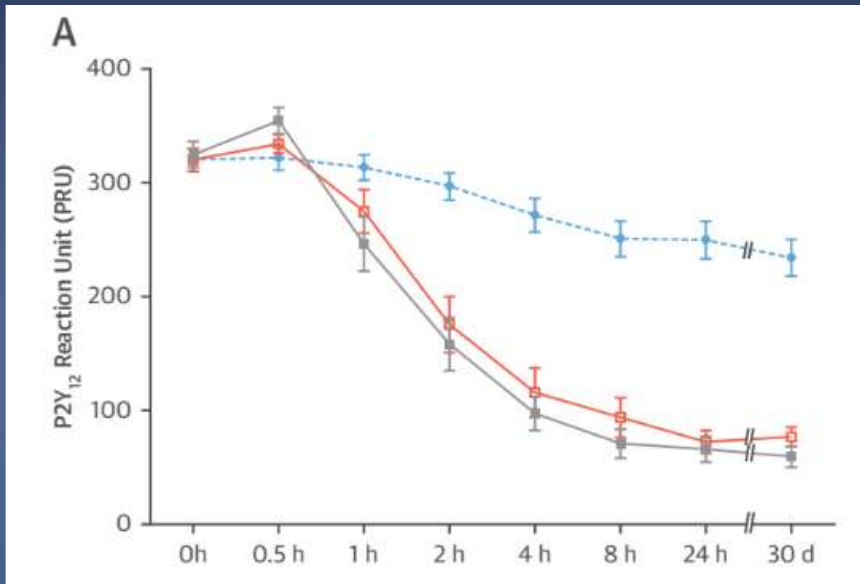
Concept of TAILORED-CHIP Trial



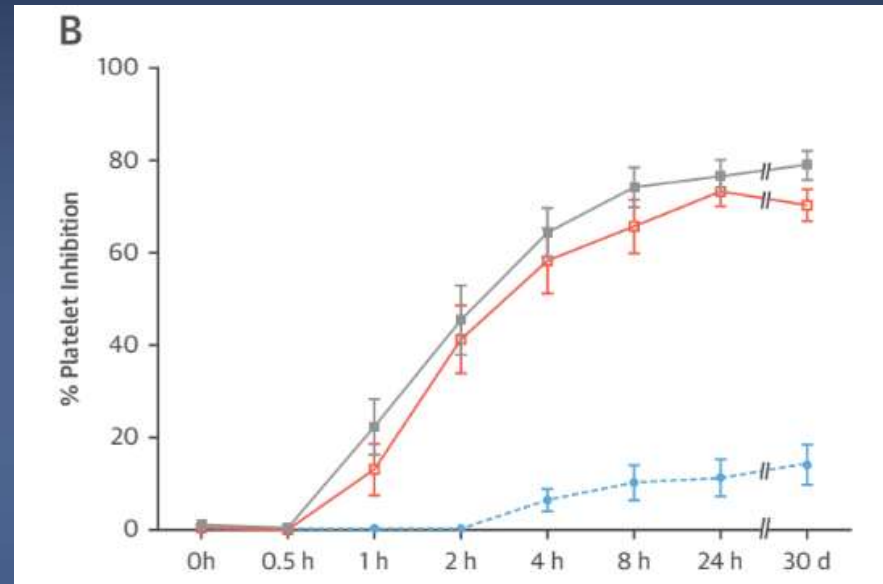
Potency of Low-Dose Ticagrelor: OPTIMA trial



P2Y12 reaction unit (PRU)



Percent platelet inhibition



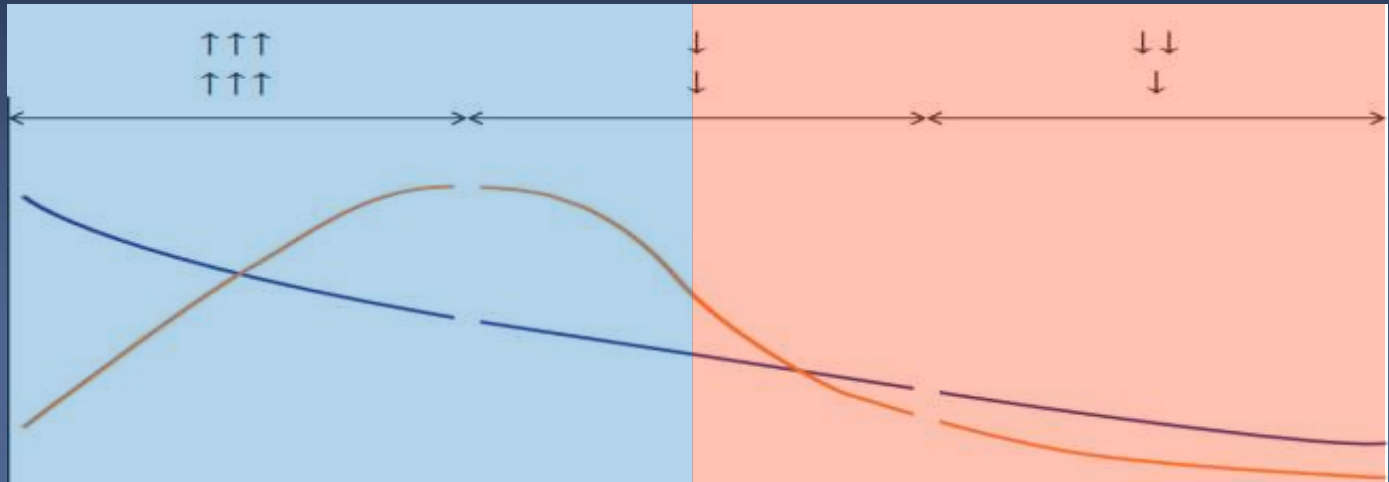
“Low-dose Ticagrelor > Clopidogrel
Low-dose Ticagrelor ≈ Standard-dose ticagrelor”

TAILORED-CHIP Trial Study Hypothesis

Complex High-risk PCI

Ischemic

Bleeding

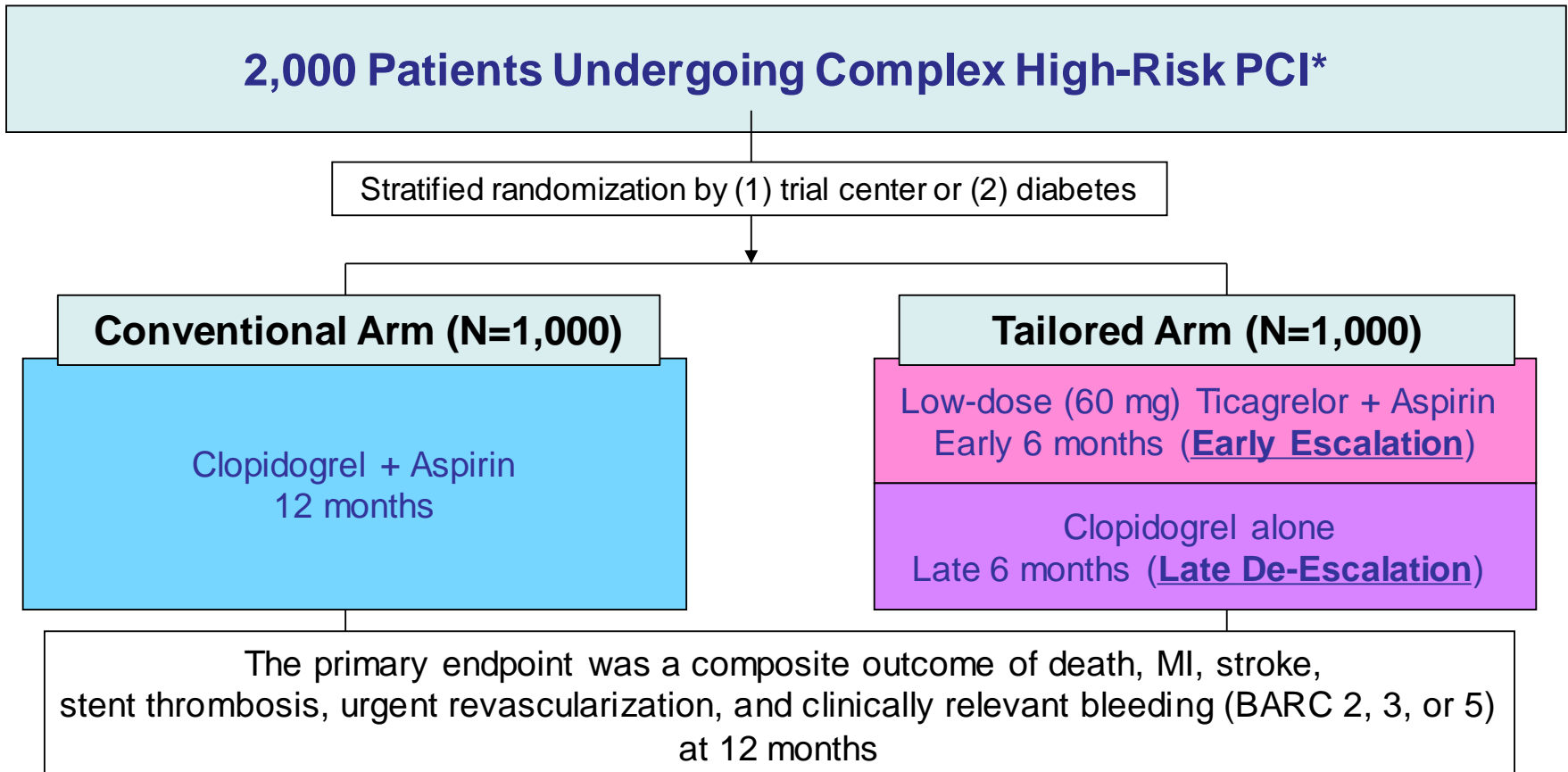


More Potent DAPT
For Ischemic Risk
“Low-dose
Ticagrelor + ASA”

Less Potent DAPT
For Bleeding Risk
“Clopidogrel Only”

**TAILOred versus COnventional AntithRombotic StratEgy
IntenDed for Complex High-Risk PCI**

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 $\geq 30\text{mm}$), multivessel PCI (≥ 2 vessels requiring stent implantation), ≥ 3 requiring stents implantation, ≥ 3 lesions will be treated, predicted total stent length for revascularization $>60\text{mm}$, diabetes, CKD (Cr-clearance $<60\text{ml/min}$) or severe LV dysfunction (EF $<40\%$).

Clinical Perspective of the TAILORED-CHIP

Impact on guideline

| Recommendation | Class | Level | Ref |
|---|-------|-------|-----|
| Complex high-risk PCI | | | |
| Early escalation and late de-escalation DAPT strategy should be considered in patients who underwent complex high-risk PCI. | I | A | |

Tailored Antithrombotic for Complex PCI

How To Do ?

- In the real-world setting, there is no single and simple scenario.
- Antithrombotic strategies for high-ischemic and bleeding risk patients are most challenging issues in the contemporary practice.
- Balancing ischemic and bleeding complications post PCI is an important dilemma for clinicians.

Tailored Antithrombotic for Complex PCI

How To Do ?

- Addressing the clinical imperatives of lowering bleeding while preserving ischemic benefit requires therapeutic strategies that decouple thrombotic from hemorrhagic risk.
- Diverse recipes are available for such complex patients and actively under investigation, which includes
 - P2Y12 monotherapy with aspirin omission
 - Short DAPT with smart DES
 - Escalation and/or de-escalation
 - Tailored and/or combined NOACs