

SHORT DUAL ANTITHROMBOTIC THERAPY AFTER PCI IN PATIENTS WITH ATRIAL FIBRILLATION: OPTIMA-AF TRIAL

 Scientific
Sessions

 OPTIMA-AF

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#AHA25

CONFLICT OF INTEREST

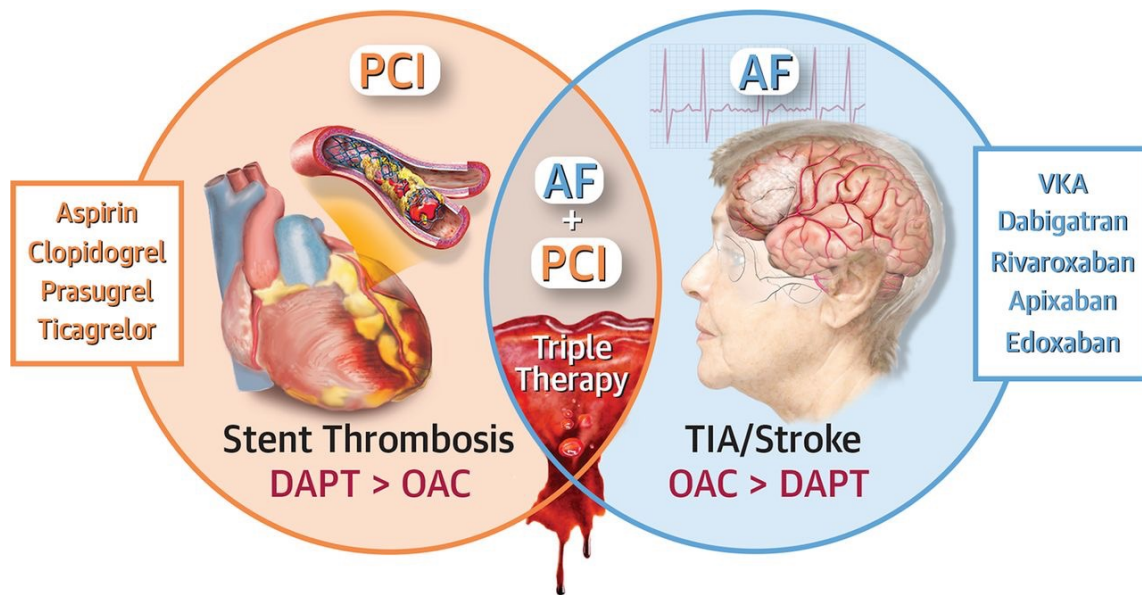
Yohei Sotomi received research funding from Abbott Medical Japan, Abiomed, Boston Scientific, Bristol Myers Squibb, Johnson & Johnson, Kaneka, Nipro, and Terumo; and personal fees from Abbott Medical Japan, Bayer, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Daiichi Sankyo, Kaneka, Nipro, Terumo, Pfizer, and Shockwave.

KKz received research funding from Abbott Medical Japan; and personal fees from Abbott Medical Japan, Boston Scientific, Medtronic, Shockwave Medical, Otsuka, Daiichi Sankyo, Amgen, Novartis, Boehringer Ingelheim, Bayer, Mochida, and Novo Nordisk. GN received research funding from Abbott Medical Japan; and personal fees from OrbusNeich, Abbott Medical Japan, Boston Scientific, and Daiichi Sankyo. YM received research funding from Abbott Medical Japan, Boston Scientific, Terumo, Edwards Lifesciences, Boehringer Ingelheim, and Pfizer; and personal fees from Abbott Medical Japan, Daiichi Sankyo, Boston Scientific, Terumo, Edwards Lifesciences, Boehringer Ingelheim, Bayer, and Pfizer. KA received personal fees from Abbott Medical Japan, Japan Lifeline, Medtronic, Biotronik, and Novartis. JA received personal fees from Abbott Medical Japan, Medtronic, AstraZeneca, Boehringer Ingelheim, Pfizer, Bristol Myers Squibb, and Bayer. KT received personal fees from Abbott Medical Japan, Biotronik, Daiichi Sankyo, Boehringer Ingelheim, Boston Scientific, Bayer, Pfizer, Bristol Myers Squibb, Kaneka, Terumo, OrbusNeich, Fukuda Denshi, and Medtronic. TM received personal fees from OrbusNeich, Abbott Medical Japan, Boston Scientific, Daiichi Sankyo, Medtronic, Novartis, Shockwave Medical, and Terumo. YI received personal fees from Abbott Medical Japan, Medtronic, and Kaneka. TI received personal fees from Kaneka, Nipro, and Boston Scientific. SS received personal fees from Abbott Medical Japan, Daiichi Sankyo, Boehringer Ingelheim, Bayer, and Pfizer. TW received personal fees from Abbott Medical Japan, Boston Scientific, CathWorks, Kaneka, Medtronic, OrbusNeich, Philips, Shockwave Medical, Siemens, Terumo, Amgen, Boehringer Ingelheim, Daiichi Sankyo, Kyowa Kirin, Pfizer, and Viatrix. TN received personal fees from Abbott Medical Japan, Medtronic, and Boston Scientific. AK received personal fees from Abbott Medical Japan. NO received personal fees from Abbott Medical Japan, Boston Scientific, Terumo, Kaneka, Medtronic, OrbusNeich, Nipro, Edwards Lifesciences, and Abiomed. YT received research funding from Abbott Medical Japan, Kaneka, and Nihon Medi-Physics. AO received personal fees from Terumo, Abbott Medical Japan, Boston Scientific, Daiichi Sankyo, and Nipro. SH received research funding from Abbott Medical Japan, Otsuka, Sumitomo Pharma, Toa Eiyo, Mochida, and Boehringer Ingelheim; and personal fees from Boehringer Ingelheim, Alnylam, MSD, AstraZeneca, Astellas, Amgen, Otsuka, Kyowa Kirin, Kowa, Sanofi, Sanwa Kagaku Kenkyusho, Daiichi Sankyo, Toa Eiyo, Nippon Shinyaku, Nipro, Nihon Medi-Physics, Novartis, Novo Nordisk, Bayer, Pfizer, Bristol Myers Squibb, Mallinckrodt, and Janssen. YSa received research funding from Abbott Medical Japan, Medtronic, Boston Scientific, Terumo, and Edwards Lifesciences; and personal fees from Edwards Lifesciences and Medtronic. The other authors have no conflicts of interest to declare.

DUAL RISK AFTER PCI IN PATIENT WITH AF

The combination of antiplatelet and anticoagulation therapy increases bleeding

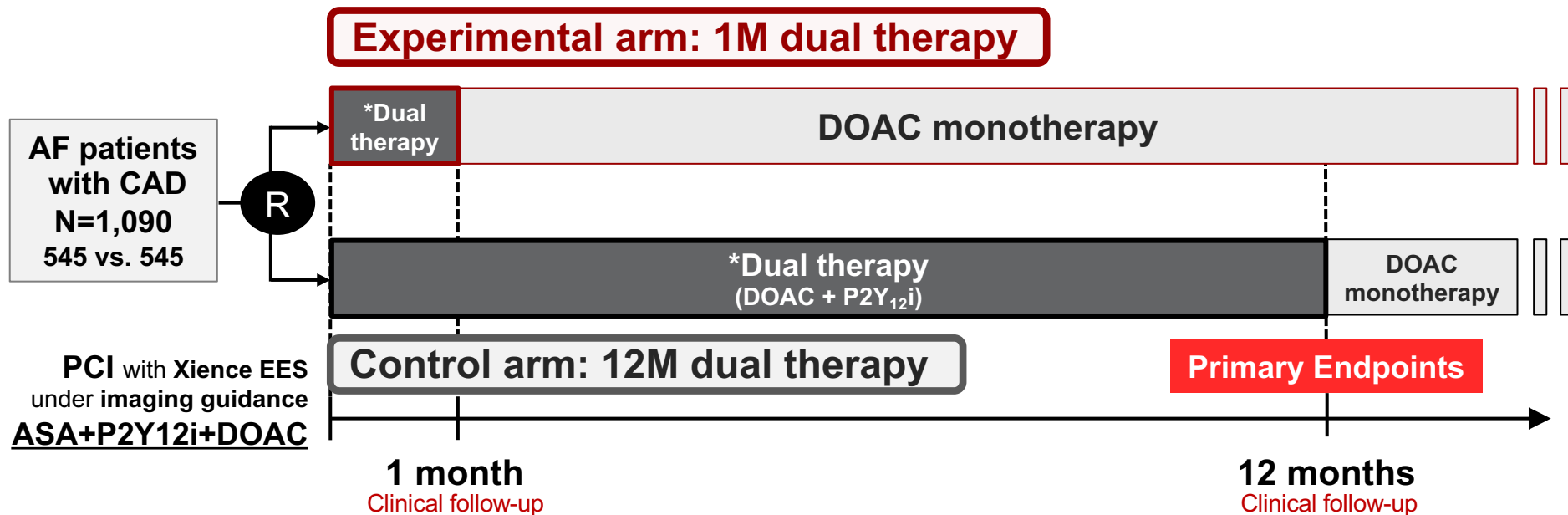
- Patients with AF undergoing PCI are at increased risk of bleeding due to the concomitant use of oral anticoagulants and antiplatelets; thus, minimizing the duration of dual use is desirable.
- The optimal antithrombotic regimen within one year after PCI for this population has not been fully investigated.



STUDY DESIGN AND AIM



A prospective, investigator-initiated, nationwide, multicenter, open-label, blinded-endpoint, active-control, randomized, noninferiority-superiority hybrid trial



This trial aims to assess **the safety and efficacy of a 1-month dual antithrombotic therapy** in patients with AF undergoing PCI with contemporary DES, **Xience everolimus-eluting stents**.

* Add-on aspirin is permitted up to 1 month in cases where an attending physician considers more appropriate (e.g. CYP2C19 polymorphism, etc.).

KEY INCLUSION / EXCLUSION CRITERIA



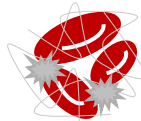
Key Inclusion criteria

- Patients with AF and a CHADS₂ score ≥ 1 , having an indication for PCI of native coronary lesions.
- Adjunctive oral anticoagulation treatment with DOAC is planned to continue after PCI.
- Presentation with stable angina, unstable angina, or silent myocardial ischemia.
- Appropriate for PCI treatment as judged by the operator or heart team.
- Age ≥ 20 years.
- Signed informed consent obtained prior to PCI.
- The patient understands and accepts clinical follow-up.

Key Exclusion criteria

- Non-compliance expected with antithrombotic therapy of study regimen
- Planned staged PCI procedure scheduled more than 2 weeks (+14 days allowable) after the index PCI.
- Presentation with ST-elevation or non-ST-elevation myocardial infarction.
- Active bleeding / cardiogenic shock at the time of enrolment.
- Reference vessel diameter < 2.25 mm or > 5.75 mm. PCI for bypass graft vessels.
- PCI within the previous 6 months for a lesion other than the index lesion.
- Life expectancy < 1 year.
- Severe renal insufficiency (creatinine clearance < 15 mL/min or on dialysis).

PRIMARY ENDPOINTS AND ANALYSIS



Primary efficacy endpoint

A composite of death or thromboembolic events (myocardial infarction, definite stent thrombosis, stroke, or systemic embolism) at 365 days



Primary safety endpoint

Bleeding (ISTH major or clinically relevant nonmajor bleeding) at 365 days

Noninferiority-Superiority hybrid design

The following three hypotheses were tested step by step using a fixed-sequence procedure to account for multiplicity, controlling the familywise type I error rate at a one-sided α of 0.05.

1. **Non-inferiority** of the primary efficacy endpoint
2. **Superiority** of the primary safety endpoint
3. **Superiority** of the primary efficacy endpoint



If the current hypothesis is met, proceed to the next; otherwise, stop.

SAMPLE SIZE CALCULATION

Primary driver: Non-inferiority test for the primary efficacy endpoint

- $\alpha = 0.05$ (one-sided)
- Power = 85%, 1:1 randomization
- Expected event rate: **10%**
- Non-inferiority margin: **5%**

➔ **n = 1,036**

With 5% attrition → Total = **1,090 patients**

Power for superiority of the primary safety endpoint

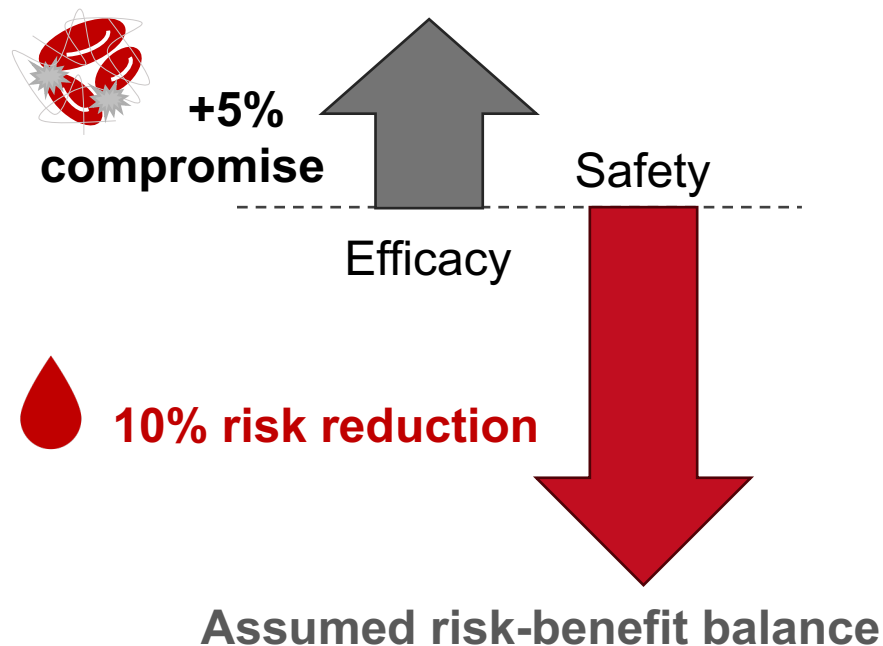
Based on the same sample size (n = 1,036)

Fisher's exact test for superiority of the primary safety endpoint

- Control: **25%**, Experimental :**15%**
- $\alpha = 0.10$ (two-sided)

➔ Resulting power: 99.2%

The noninferiority margin of +5% absolute risk difference was prespecified by the Steering Committee as a clinically justified boundary that balances a modest reduction in efficacy against the expected safety benefit of approximately 10% absolute risk reduction in bleeding (25% to 15%).

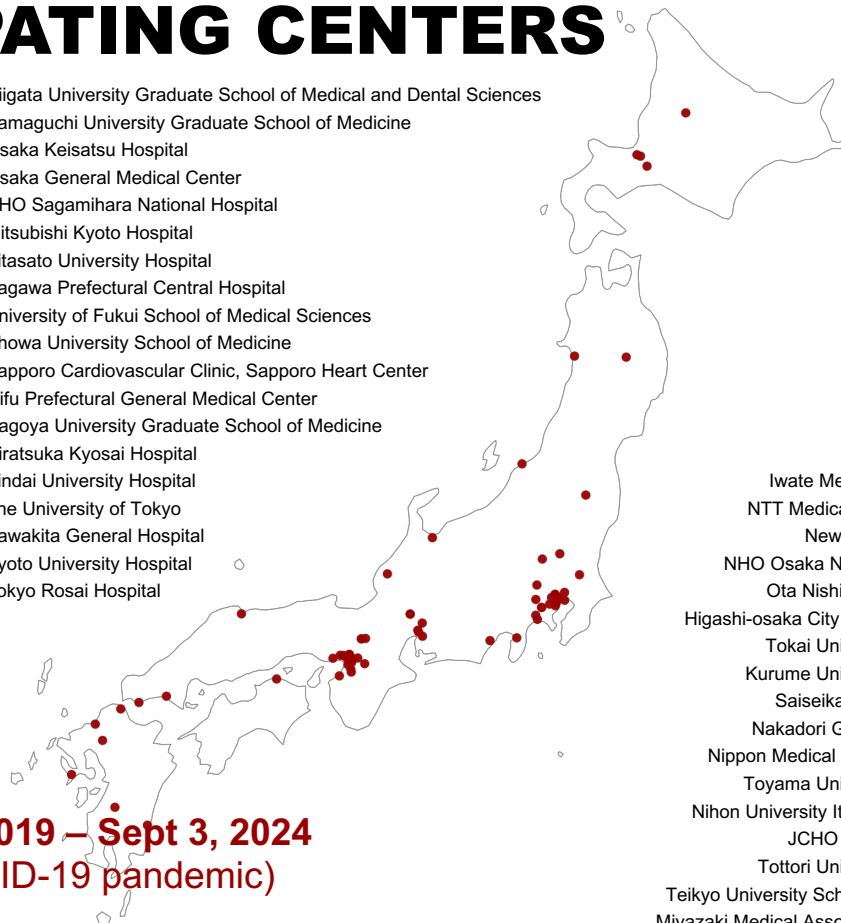


PARTICIPATING CENTERS



The University of Osaka Hospital
Minamino Cardiovascular Hospital
Kokura Memorial Hospital
Rinku General Medical Center
Megumino Hospital
Tenri Hospital
Japanese Red Cross Otsu Hospital
JCHO Hitoyoshi Medical Center
St. Luke's International Hospital
The Cardiovascular Institute
Mitsui Memorial Hospital
Kindai University Nara Hospital
Gifu Heart Center
Yao Municipal Hospital
JCHO Hoshigaoka Medical Center
Osaka Rosai Hospital
Japanese Red Cross Ashikaga Hospital
Tsuchiura Kyodo General Hospital
Kasugai Municipal Hospital

Niigata University Graduate School of Medical and Dental Sciences
Yamaguchi University Graduate School of Medicine
Osaka Keisatsu Hospital
Osaka General Medical Center
NHO Sagami National Hospital
Mitsubishi Kyoto Hospital
Kitasato University Hospital
Kagawa Prefectural Central Hospital
University of Fukui School of Medical Sciences
Showa University School of Medicine
Sapporo Cardiovascular Clinic, Sapporo Heart Center
Gifu Prefectural General Medical Center
Nagoya University Graduate School of Medicine
Hiratsuka Kyosai Hospital
Kindai University Hospital
The University of Tokyo
Kawakita General Hospital
Kyoto University Hospital
Tokyo Rosai Hospital



Principal Investigator

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- Ken Kozuma

CEC/DSMB

- Takahiro Imanaka
- Yasutsugu Shiono
- Kenichi Fujii

Steering committee

- Junya Ako
- Kenji Ando
- Kengo Tanabe
- Yoshiharu Higuchi
- Yoshihiro Morino
- Yohei Sotomi
- Gaku Nakazawa
- Takashi Muramatsu

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NHO Osaka National Hospital
Ota Nishinouchi Hospital
Higashi-osaka City Medical Center
Tokai University Hospital
Kurume University Hospital
Saiseikai Senri Hospital
Nakadori General Hospital
Nippon Medical School Hospital
Toyama University Hospital
Nihon University Itabashi Hospital
JCHO Osaka Hospital
Tottori University Hospital
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Miyazaki Medical Association Hospital
Juntendo University Shizuoka Hospital
Hyogo Prefectural Nishinomiya Hospital

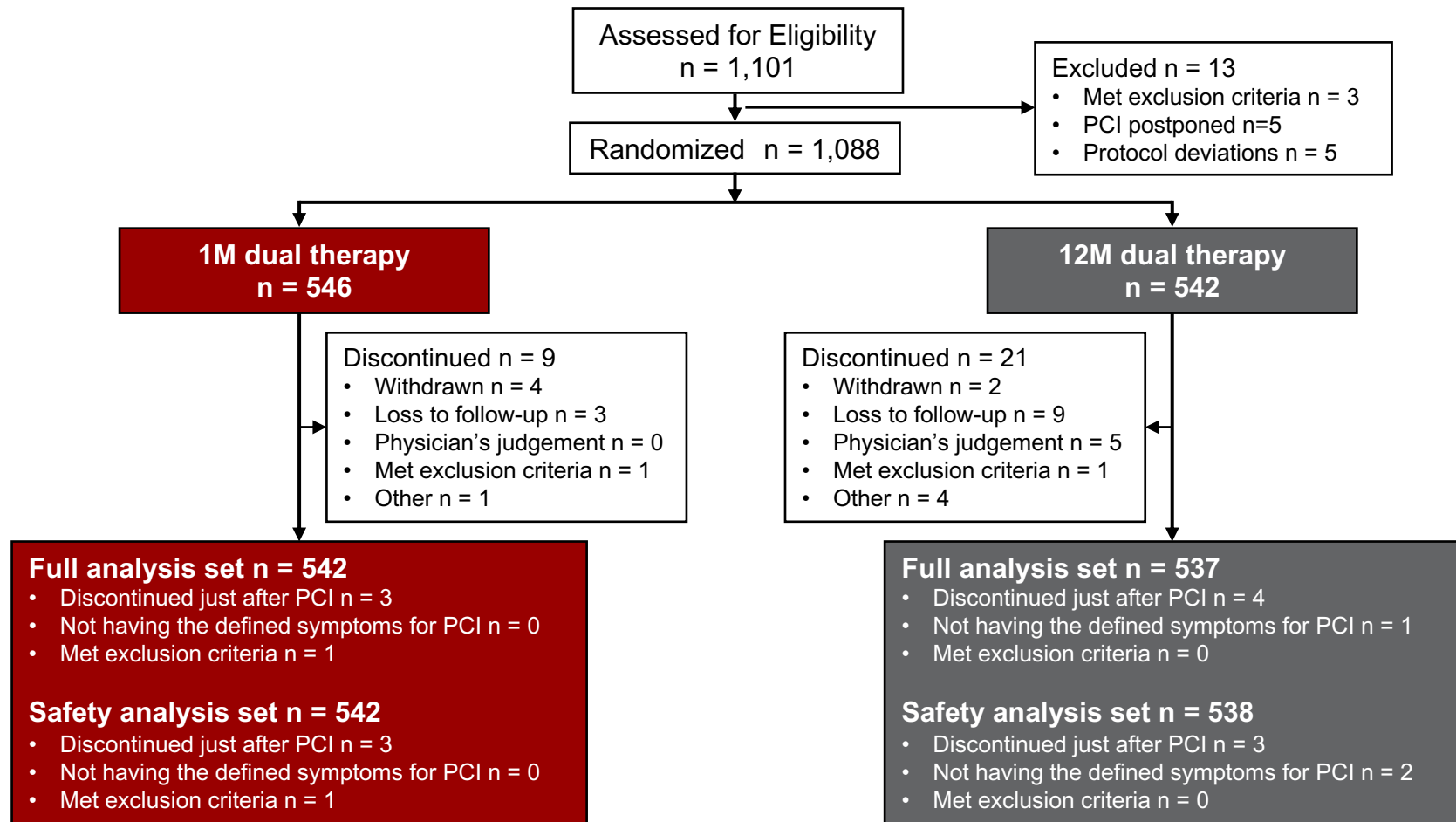
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St. Marianna University School of Medicine
NHO Osaka Minami Medical Center
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Kobe City Medical Center General Hospital
Sakurabashi Watanabe Advanced Healthcare Hospital
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Asahikawa-Kosei General Hospital
Fujita Health University Hospital
Saiseikai Fukuoka General Hospital
Tokyo Bay Urayasu Ichikawa Medical Center
Osaka Metropolitan University Graduate School of Medicine
Shizuoka City Shizuoka Hospital
National Cerebral and Cardiovascular Center
Nagasaki University Hospital
Dokkyo Medical University Hospital
Sapporo Higashi Tokushukai Hospital

Enrollment: Oct 7, 2019 – Sept 3, 2024
(overlapping the COVID-19 pandemic)

75 sites in Japan

Funding: Abbott Medical Japan

STUDY FLOWCHART



PATIENTS' BACKGROUND

	1M dual therapy 542 patients, 737 lesions	12M dual therapy 537 patients, 716 lesions
Age, yr	75.4 (8.1)	74.9 (8.8)
Male sex	80.8%	77.5%
BMI, kg/m ²	24.2 (3.9)	24.4 (3.8)
Diabetes	38.4%	40.2%
Hypertension	86.9%	85.5%
Dyslipidemia	70.5%	73.0%
History of cerebral infarction	13.1%	11.4%
CrCl, mL/min	56 [43, 74]	57 [43, 75]
CHA ₂ DS ₂ -VASc score	4 [3, 5]	4 [3, 5]
Chronic coronary syndrome	94.1%	94.6%
Acute coronary syndrome	5.9%	5.4%
OCT/IVUS use	99.5%	99.7%
Complex PCI	23.1%	23.5%

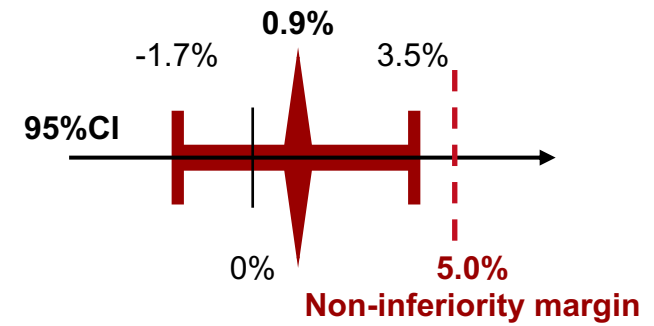
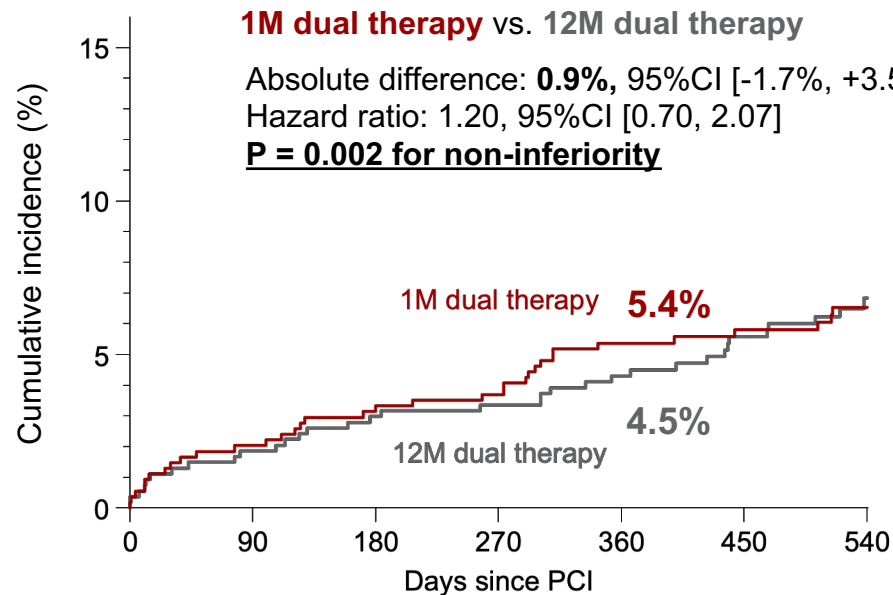
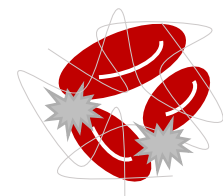
MEDICATION AT HOSPITAL DISCHARGE

	1M dual therapy 542 patients, 737 lesions	12M dual therapy 537 patients, 716 lesions
Type of antiplatelet agents		
Clopidogrel	48.5%	48.1%
Prasugrel	50.4%	50.9%
Aspirin	4.4%	5.4%
Others	0.6%	0.2%
Type of direct oral anticoagulants		
Dabigatran	4.2%	4.1%
Rivaroxaban	23.2%	22.2%
Apixaban	26.2%	26.5%
Edoxaban	46.3%	47.2%

HYPOTHESIS 1

NON-INFERIORITY OF THE PRIMARY EFFICACY ENDPOINT

A composite of death or thromboembolic events (myocardial infarction, definite stent thrombosis, stroke, or systemic embolism) at 365 days.



No. of Patients (censored)

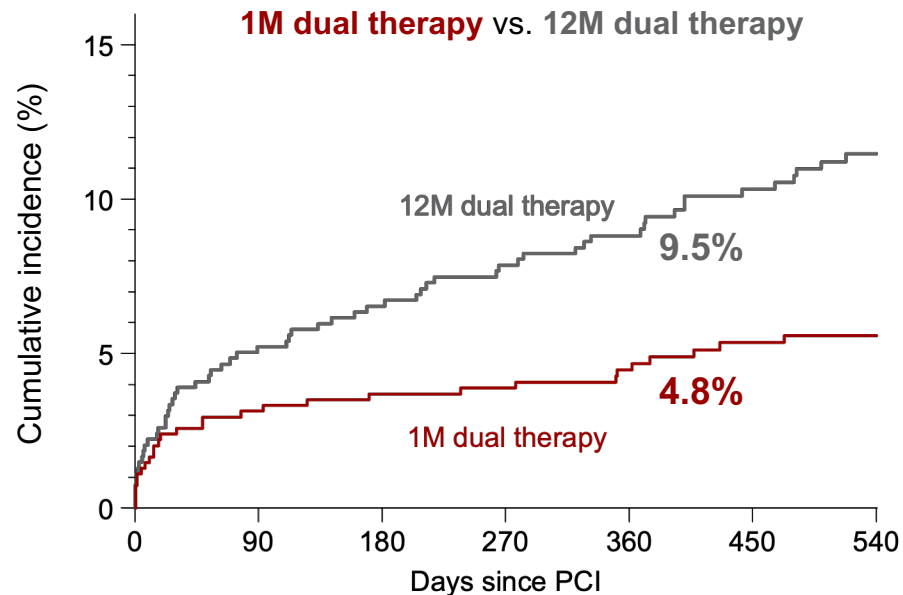
1M dual therapy	542(0)	531(1)	524(1)	520(3)	475(39)	423(89)	247(508)
12M dual therapy	537(0)	528(0)	521(1)	516(4)	477(38)	438(71)	258(503)



HYPOTHESIS 2

SUPERIORITY OF THE PRIMARY SAFETY ENDPOINT

Bleeding (ISTH major or clinically relevant nonmajor bleeding) at 365 days



Absolute difference: -4.7% 95%CI [-7.8%, -1.6%]
Hazard ratio: 0.50, 95%CI [0.31, 0.80]
P = 0.004 for superiority

No. of Patients (censored)

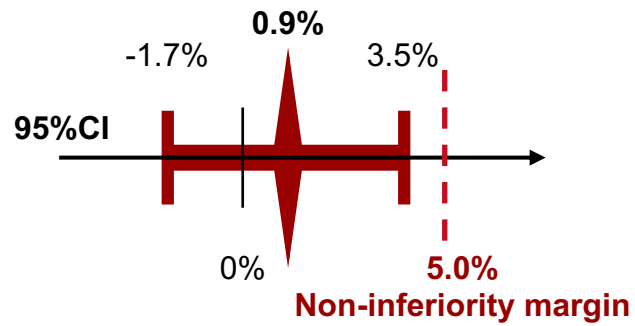
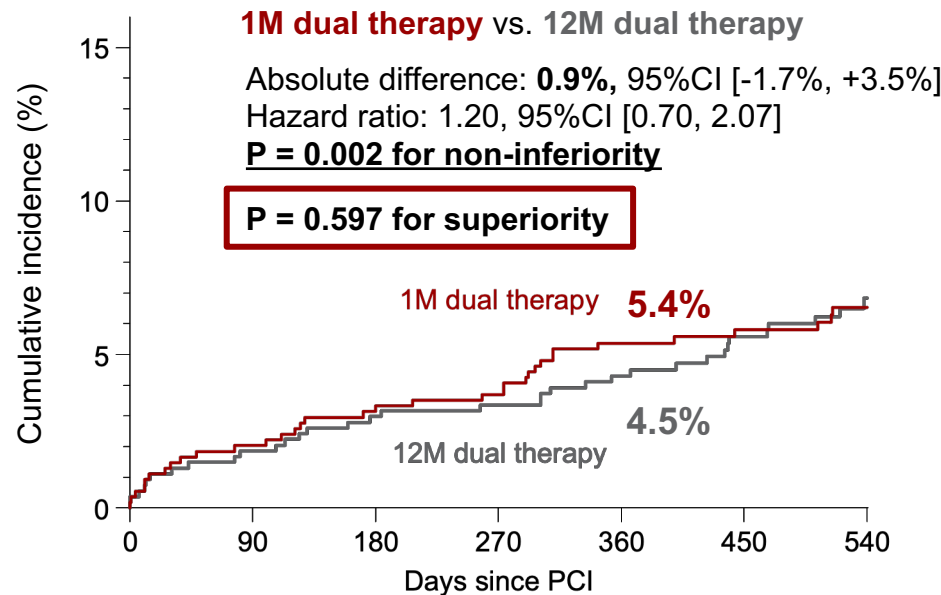
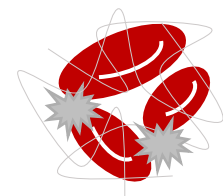
1M dual therapy	542(0)	522(4)	515(8)	511(11)	466(53)	411(104)	240(513)
12M dual therapy	537(0)	507(3)	498(5)	486(10)	445(46)	407(77)	236(478)



HYPOTHESIS 3

SUPERIORITY OF THE PRIMARY EFFICACY ENDPOINT

A composite of death or thromboembolic events (myocardial infarction, definite stent thrombosis, stroke, or systemic embolism) at 365 days.



No. of Patients (censored)

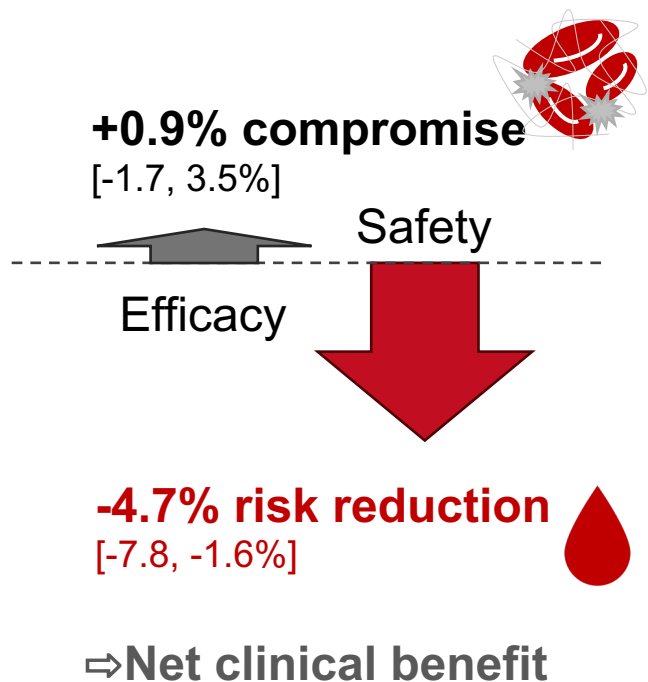
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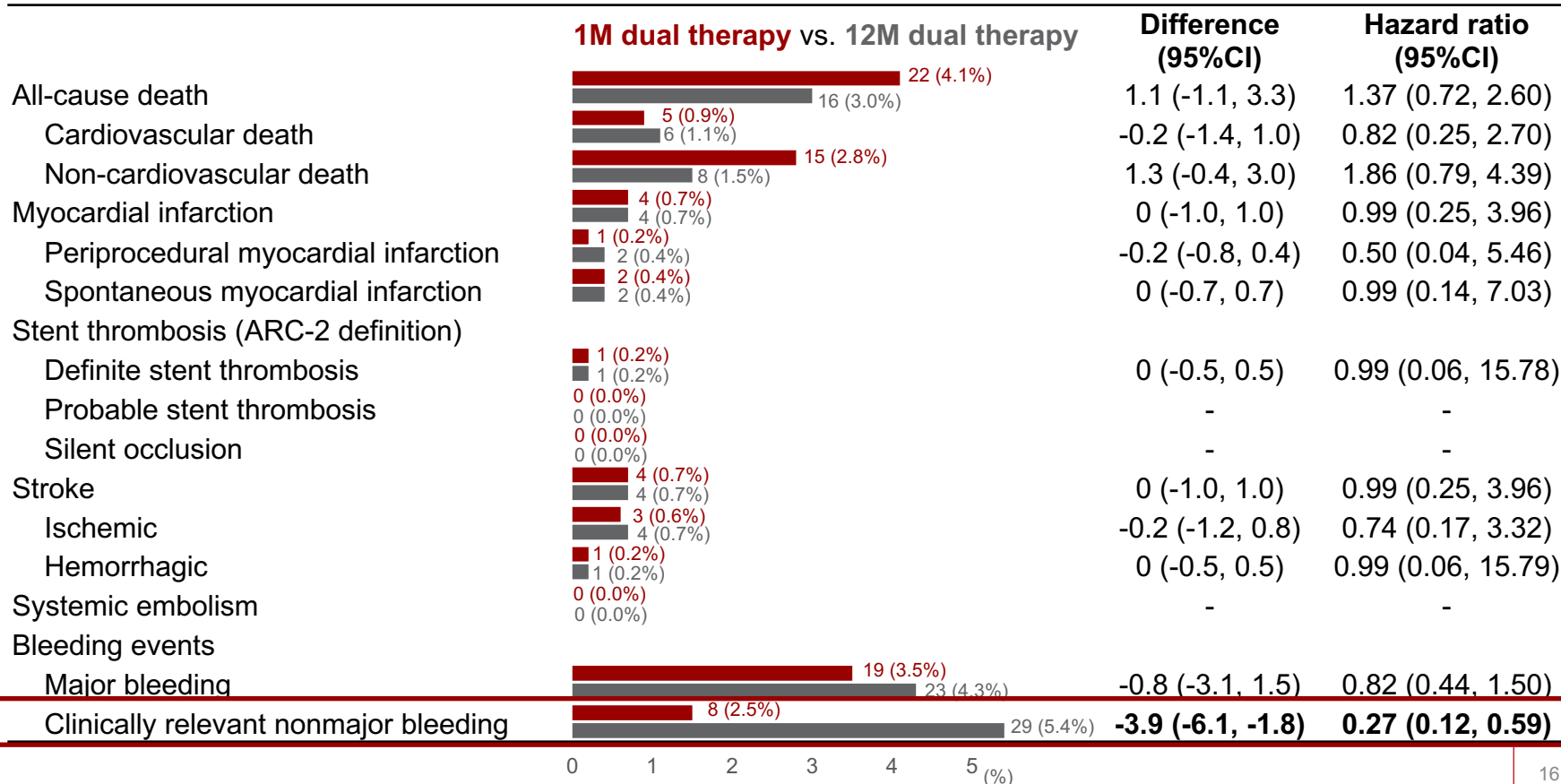
SUMMARY: PRIMARY FINDINGS

- ✓ 1. **Non-inferiority** of the thrombotic endpoint 
- ✓ 2. **Superiority** of the bleeding endpoint 
- 3. **Superiority** of the thrombotic endpoint 

Observed risk-benefit balance

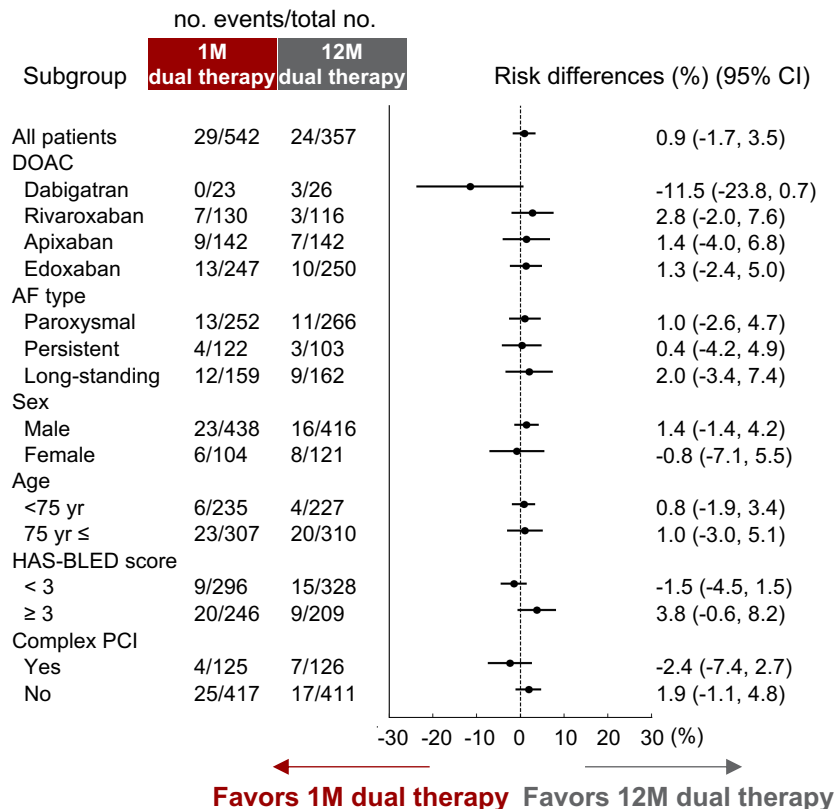


SECONDARY ENDPOINTS

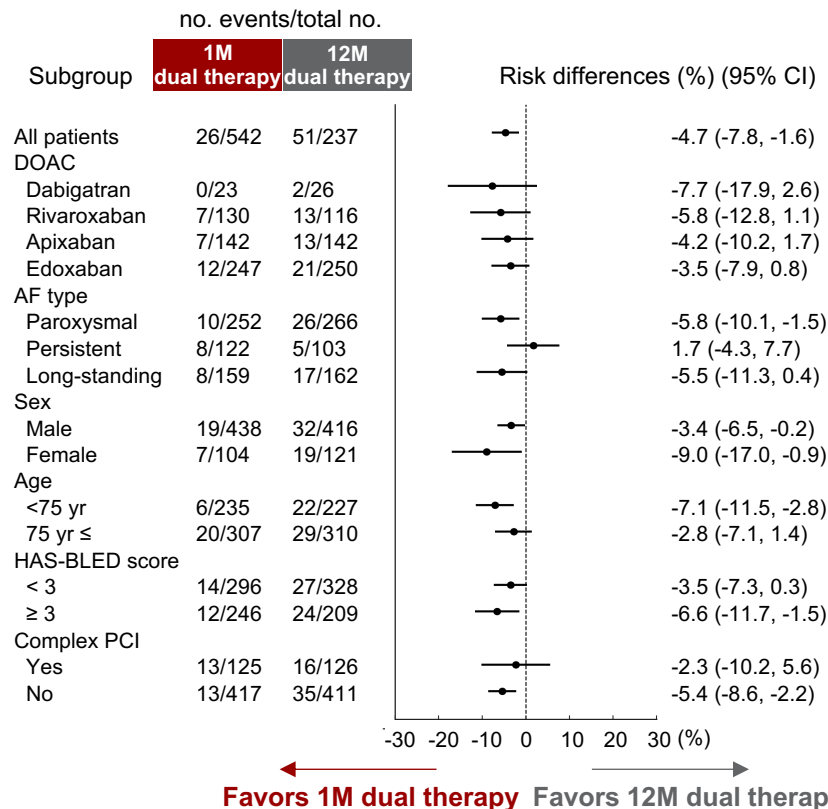


SUBGROUP ANALYSIS

Primary efficacy endpoint (death or thromboembolic events)



Primary safety endpoint (major bleeding or clinically relevant non-major bleeding)



LIMITATIONS

- The open-label design posed a potential risk of reporting and performance bias.
- **Almost all PCI procedures in our trial were performed with intracoronary imaging guidance**, which may limit the generalizability of our findings to angiography-guided PCI.
- Although the trial met the prespecified non-inferiority margin, the observed event rate was substantially lower than expected, making the fixed absolute margin disproportionately large relative to the actual risk. Overall, the clinical profile appears acceptable. However, **the efficacy findings warrant cautious interpretation.**
- Our trial primarily involved **an East Asian population**, which is recognized for having a distinct predisposition to ischemic and bleeding complications compared with Western populations.

CONCLUSION

Among patients with AF and predominantly CCS undergoing PCI, 1M dual antithrombotic therapy followed by DOAC monotherapy was noninferior to 12M therapy for death or thromboembolic events, and superior for major or clinically relevant nonmajor bleeding at 12 months, suggesting an overall favorable net clinical profile.



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