Is OAC alone OK after 1 year in stented patients with AF?: Lessons from OAC-ALONE and registry data

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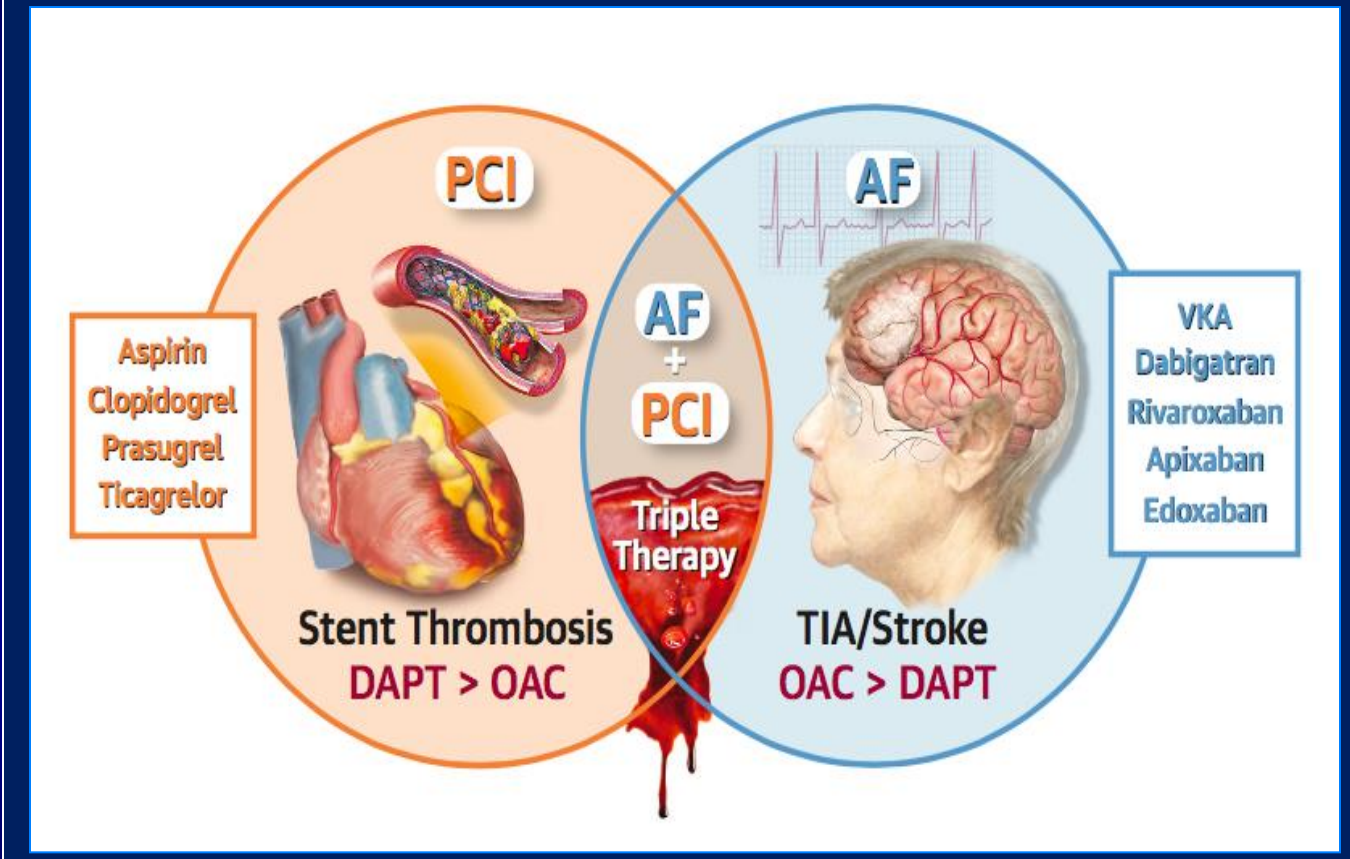
Atrial Fibrillation and PCI: Key Concepts



Stent thrombosis and coronary events

↓

High shear stress platelet-rich thrombi

↓

Antiplatelet therapy

Stroke, TIA and systemic embolism

↓

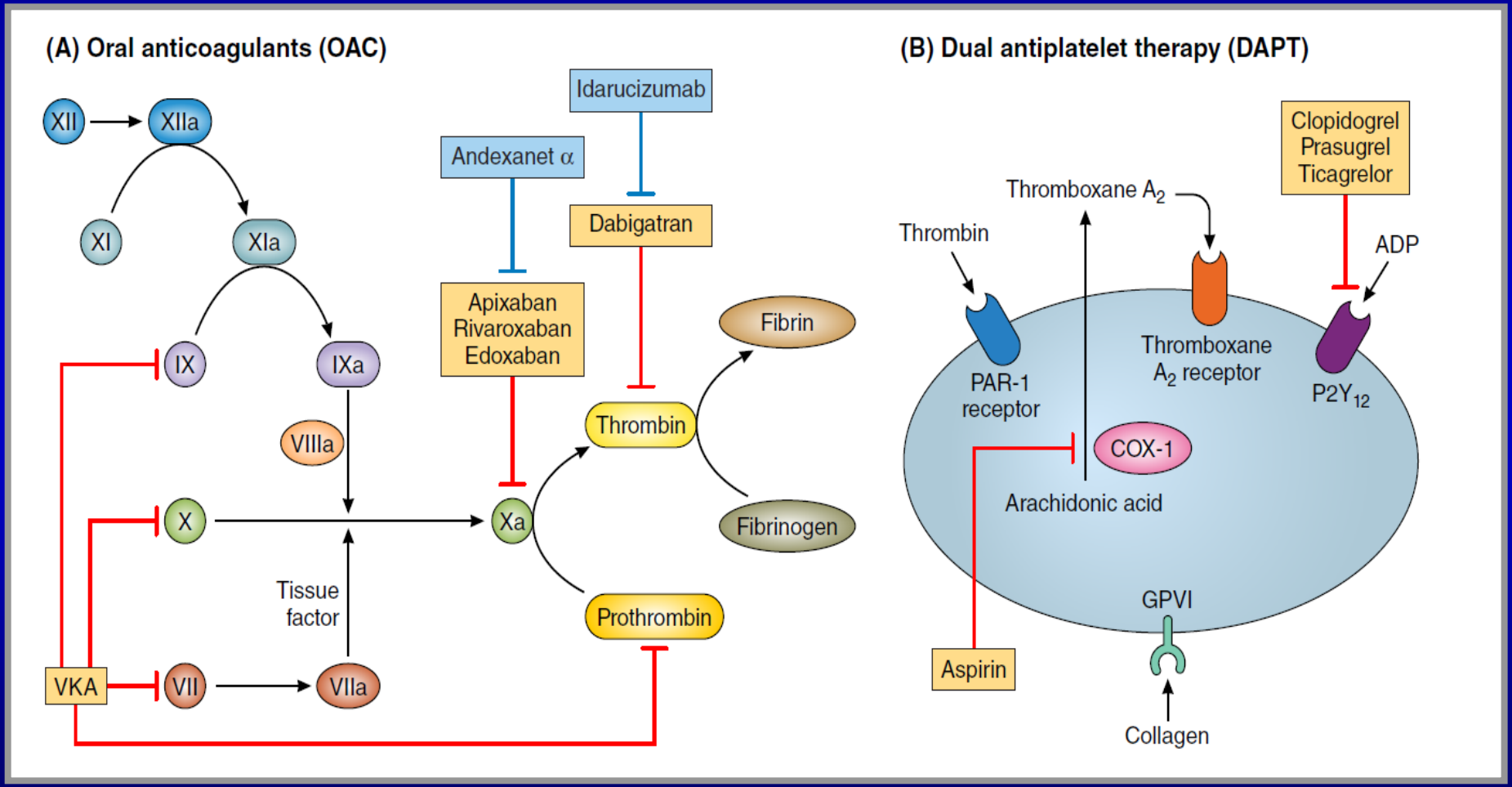
Low shear stress, less platelet-dependent thrombi

↓

Anticoagulation therapy

Capodanno D, Angiolillo DJ. JACC Cardiovasc Interv. 2017;10:1086-1088

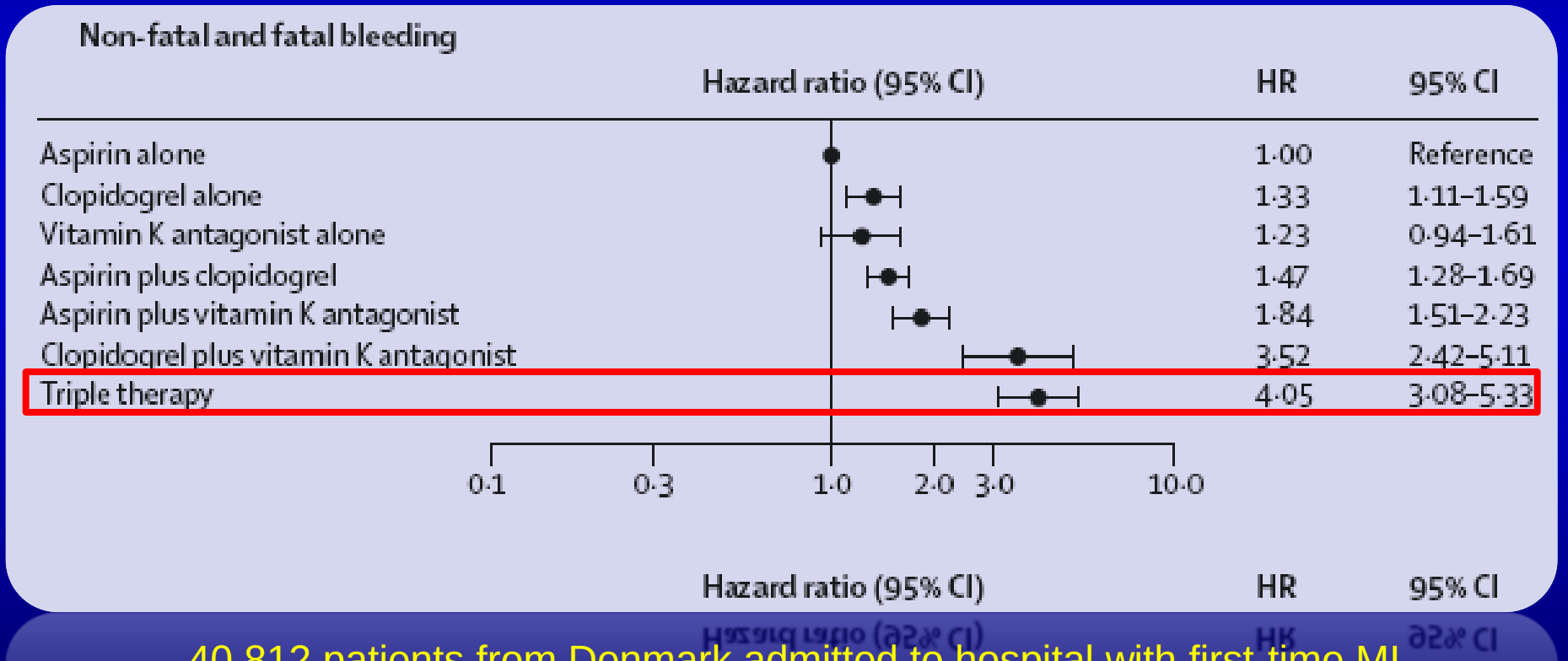
The Challenge: Discerning the choice of antithrombotic therapy



Angiolillo DJ et al. Circ Cardiovasc Interv. 2016

Triple therapy is associated with increased bleeding

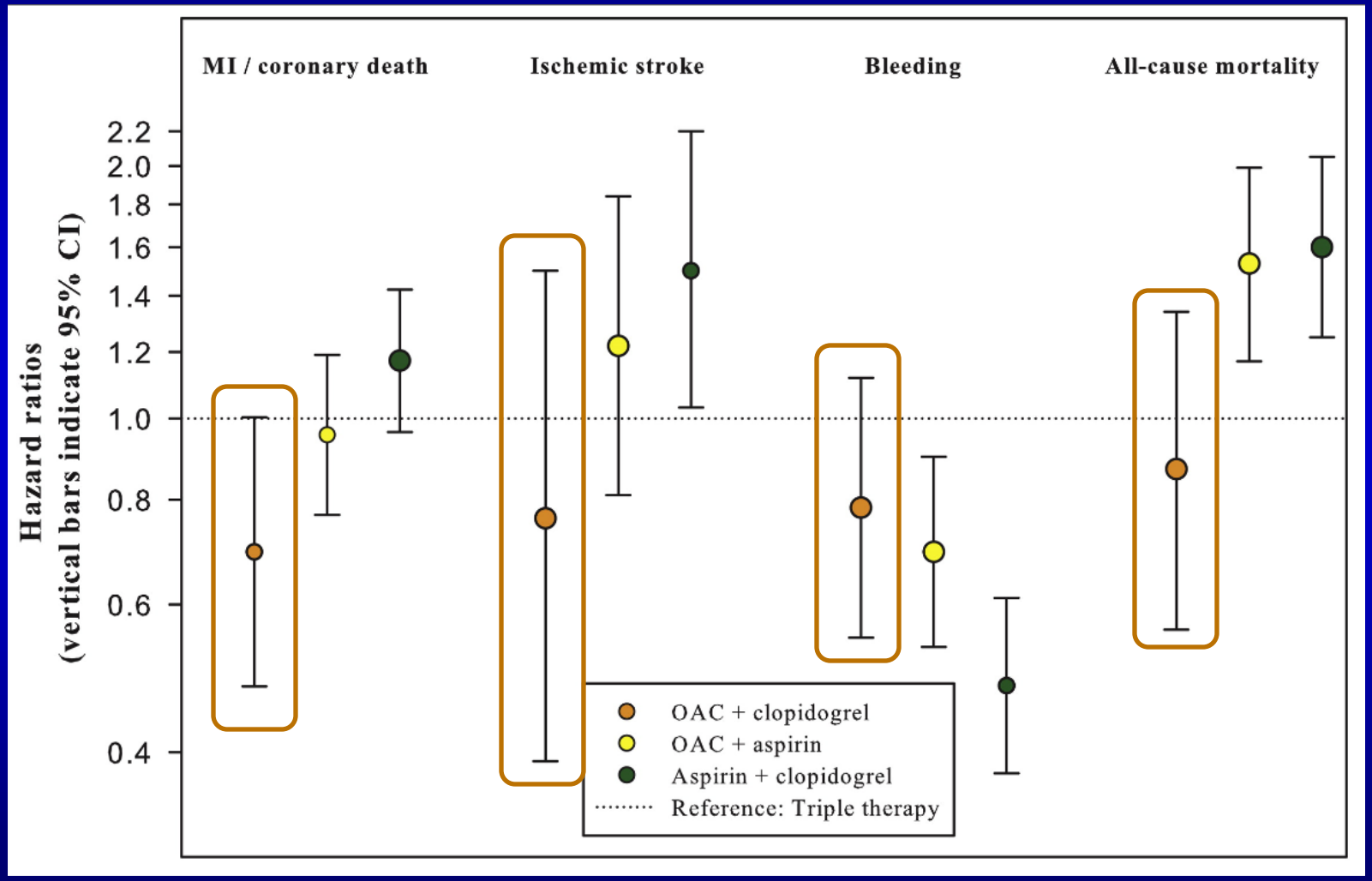
Bleeding risk in PCI patients (n=40,812) with AMI treated with different combination of aspirin, clopidogrel and VKA



40,812 patients from Denmark admitted to hospital with first-time MI

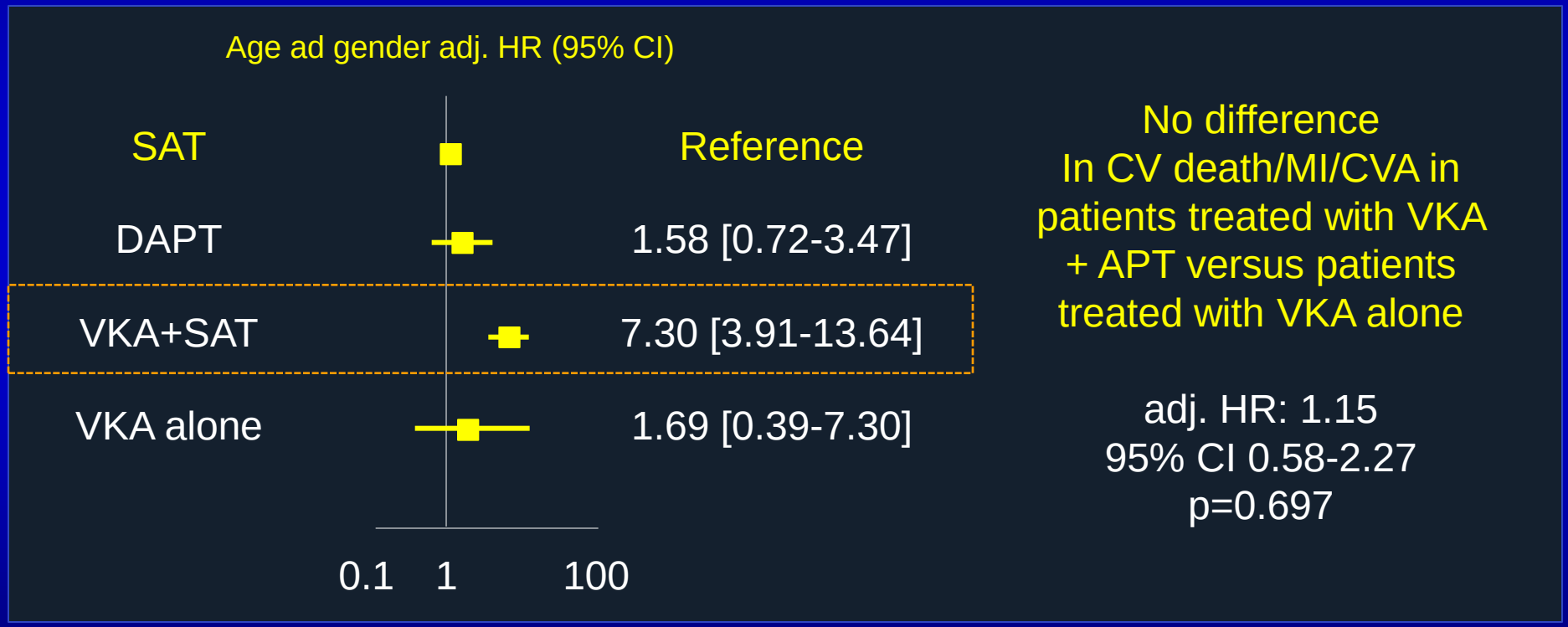
Sorensen R, et al. Lancet. 2009;374:1967-74

Benefit and Safety With Triple Therapy Versus Dual Therapies



Lamberts et al. JACC 2013; 62: 981 - 989

Aspirin might be no longer needed after 12 months in AF patients with stable CAD on VKA



CORONOR – 4,184 patients on oral anticoagulation with stable (>12 mo) CAD

Hamon M, et al. J Am Coll Cardiol 2014;64:1430–6

Less bleeding with VKA monotherapy than VKA plus single antiplatelet therapy without difference in ischemic events among stabilized ACS patients (after 1 year) having AF

Antiplatelet Therapy for Stable Coronary Artery Disease in Atrial Fibrillation Patients Taking an Oral Anticoagulant

A Nationwide Cohort Study

Morten Lamberts, MD, PhD; Gunnar H. Gislason, MD, PhD; Gregory Y.H. Lip, MD; Jens Flensted Lassen, MD, PhD; Jonas Bjerring Olesen, MD, PhD; Anders P. Mikkelsen, MB; Rikke Sørensen, MD, PhD; Lars Køber, MD, DMSc; Christian Torp-Pedersen, MD, DMSc; Morten Lock Hansen, MD, PhD

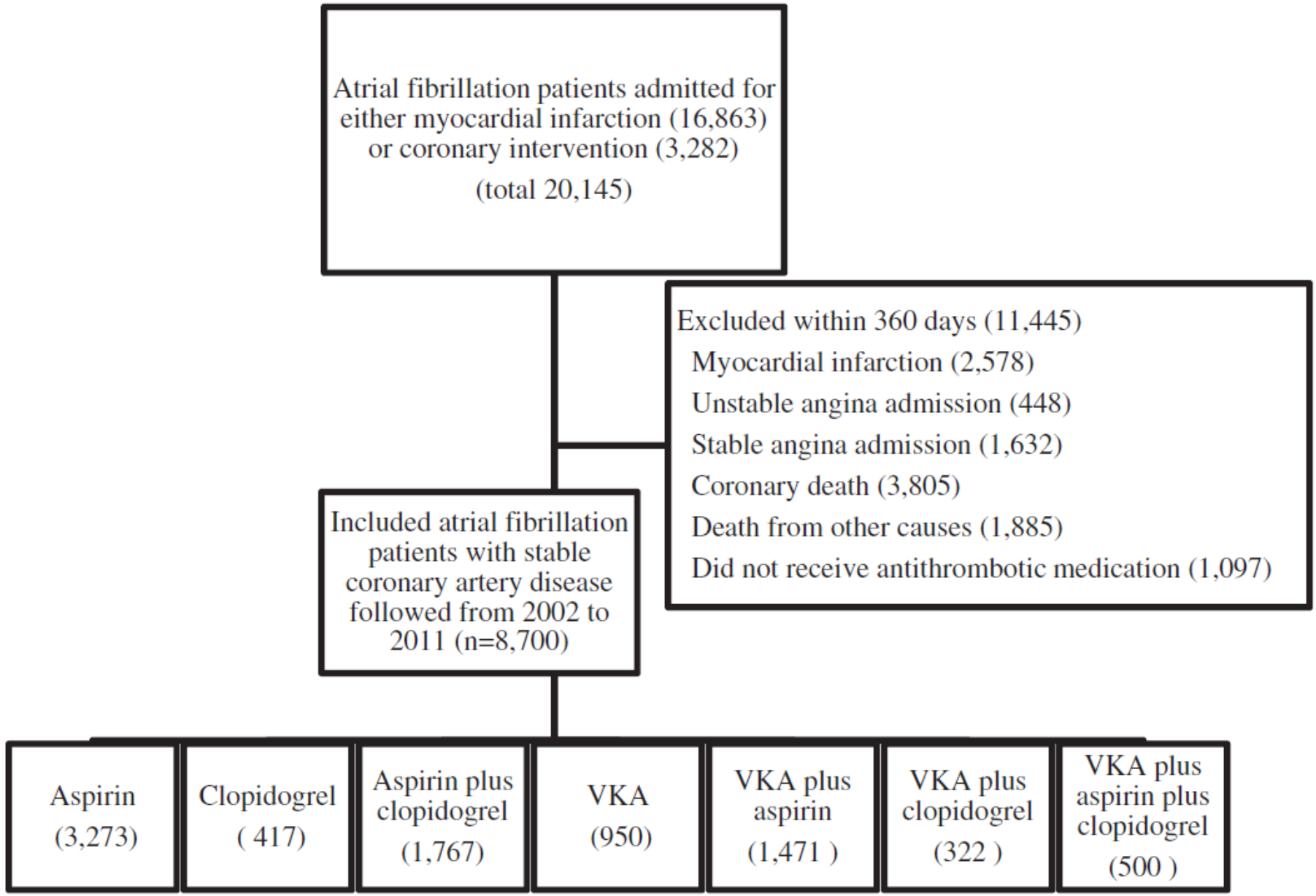
Background—The optimal long-term antithrombotic treatment of patients with coexisting atrial fibrillation and stable coronary artery disease is unresolved, and commonly, a single antiplatelet agent is added to oral anticoagulation. We investigated the effectiveness and safety of adding antiplatelet therapy to vitamin K antagonist (VKA) in atrial fibrillation patents with stable coronary artery disease.

Methods and Results—Atrial fibrillation patients with stable coronary artery disease (defined as 12 months from an acute coronary event) between 2002 and 2011 were identified. The subsequent risk of cardiovascular events and serious bleeding events (those that required hospitalization) was examined with adjusted Cox regression models according to ongoing antithrombotic therapy. A total of 8700 patients were included (mean age, 74.2 years; 38% women). During a mean follow-up of 3.3 years, crude incidence rates were 7.2, 3.8, and 4.0 events per 100 person-years for myocardial infarction/coronary death, thromboembolism, and serious bleeding, respectively. Relative to VKA monotherapy, the risk of myocardial infarction/coronary death was similar for VKA plus aspirin (hazard ratio, 1.12 [95% confidence interval, 0.94–1.34]) and VKA plus clopidogrel (hazard ratio, 1.53 [95% confidence interval, 0.93–2.52]). The risk of thromboembolism was comparable in all regimens that included VKA, whereas the risk of bleeding increased when aspirin (hazard ratio, 1.50 [95% confidence interval, 1.23–1.82]) or clopidogrel (hazard ratio, 1.84 [95% confidence interval, 1.11–3.06]) was added to VKA.

Conclusions—In atrial fibrillation patients with stable coronary artery disease, the addition of antiplatelet therapy to VKA therapy is not associated with a reduction in risk of recurrent coronary events or thromboembolism, whereas risk of bleeding is increased significantly. The common practice of adding antiplatelet therapy to oral VKA anticoagulation in patients with atrial fibrillation and stable coronary artery disease warrants reassessment. (***Circulation*. 2014;129:1577-1585.**)

Lamberts M et al. Circulation 2014;129:1577-1585.

Overview of study population



Patient Characteristics at Inclusion According to Antithrombotic Treatment

	Not Including VKA			Including VKA			
Characteristics	Aspirin (n=3273)	Clopidogrel (n=417)	Aspirin Plus Clopidogrel (n=1767)	VKA (n=950)	VKA Plus Aspirin (n=1471)	VKA Plus Clopidogrel (n=322)	VKA Plus Aspirin Plus Clopidogrel (n=500)
Female	1494 (46)	161 (39)	659 (37)	360 (38)	460 (31)	96 (30)	101 (20)
Age, y, mean (SD)	76.1 (10.9)	73.4 (10.9)	73.0 (10.8)	73.2 (10.0)	73.6 (9.0)	72.6 (8.1)	71.0 (8.4)
Previous MI	2858 (87)	279 (67)	1159 (66)	804 (85)	1104 (75)	141 (44)	211 (42)
With PCI performed*	259 (9)	83 (30)	495 (43)	57 (79)	170 (15)	77 (55)	108 (51)
With stent implantation*	210 (7)	73 (26)	424 (37)	44 (5)	134 (12)	70 (50)	96 (45)
Previous PCI without MI	415 (13)	138 (33)	608 (34)	146 (15)	367 (25)	181 (56)	289 (58)
With stent implantation*	288 (69)	124 (90)	561 (92)	112 (77)	255 (69)	168 (93)	272 (94)
CHA_2DS_2-VASc score							
Low (0)†	24 (1)	10 (2)	28 (2)	7 (1)	12 (1)	0 (0)	6 (1)
Intermediate (1)	130 (4)	34 (8)	120 (7)	42 (4)	62 (4)	19 (6)	38 (8)
High (≥2)	3119 (95)	373 (89)	1619 (92)	901 (95)	1397 (95)	303 (94)	456 (91)
HAS-BLED score							
Low (0–1)	900 (28)	102 (24)	506 (29)	237 (25)	315 (21)	55 (17)	106 (21)
Intermediate (2)	1325 (40)	163 (39)	677 (38)	380 (40)	658 (45)	135 (42)	218 (44)
High (≥3)	1048 (32)	152 (37)	584 (33)	333 (35)	498 (34)	132 (41)	176 (35)
% stented patients	**15%**	**47%**	**55%**	**16%**	**26%**	**73%**	**74%**

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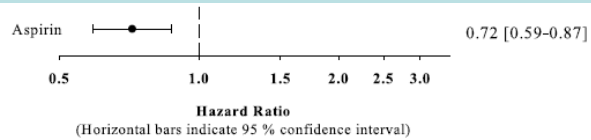
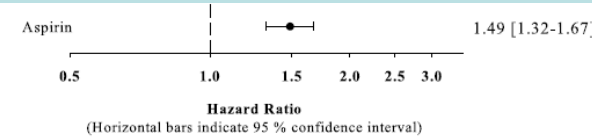
Risk of MI/coronary death(A), thromboembolism(B), bleeding(C) and all-cause death(D)

1) Additional antiplatelet agent on top of VKA has no benefit in reducing ischemic events, not to mention increased bleeding
2) Antiplatelet monotherapy increases all-cause death

➔ Monotherapy with VKA may be the best choice in patients with AF and stable CAD including PCI-treated ones after I year.





KORAF (KOREan patients with Atrial Fibrillation) VKA treatment & INR control in KOREA

- **Approximately 40% of the Korean AF patients treated with VKA maintained the range of INR from 2.0 to 3.0.**

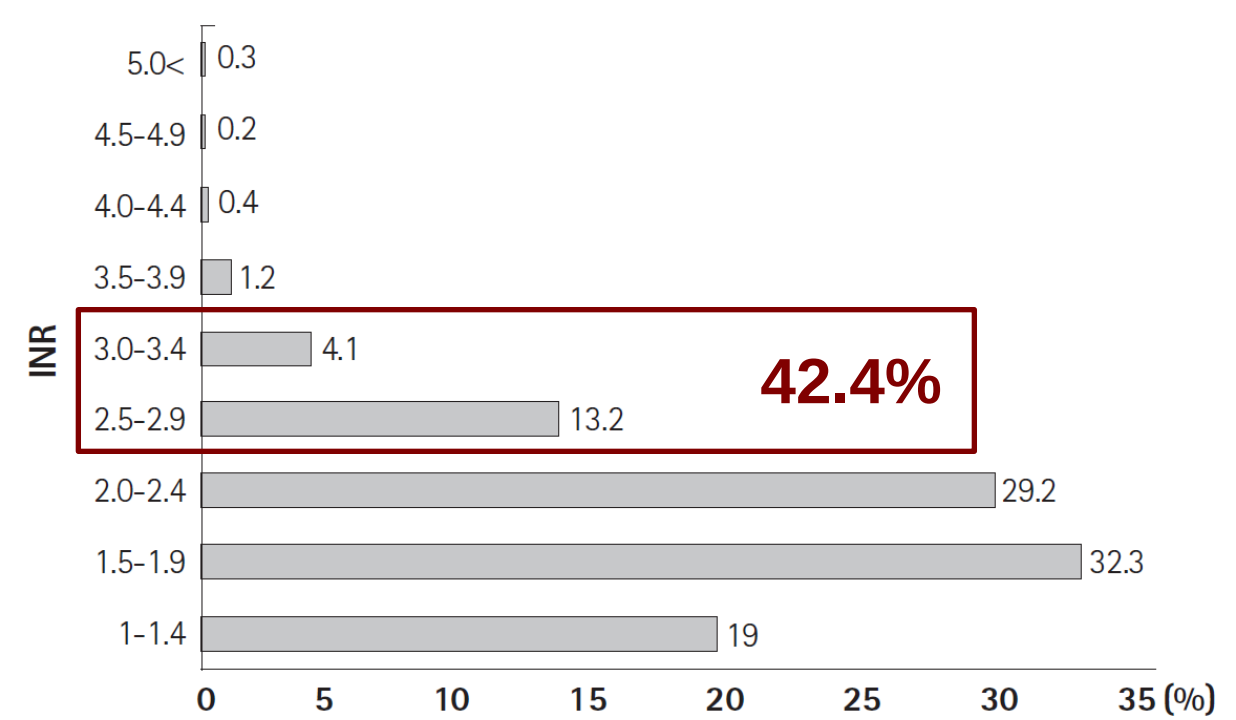


Fig. 4. Proportion of INR level in patient with AF who taken oral anticoagulants. The proportion of individuals achieving an optimal INR level (2-3) was only 42.4%. INR: international normalized ratio, AF: atrial fibrillation.

Shin HW et al. *Korean Circ J* 2012;42:113-117

ARISTOTLE trial
Country distribution of percentage of TTR of INR 2.0-3.0

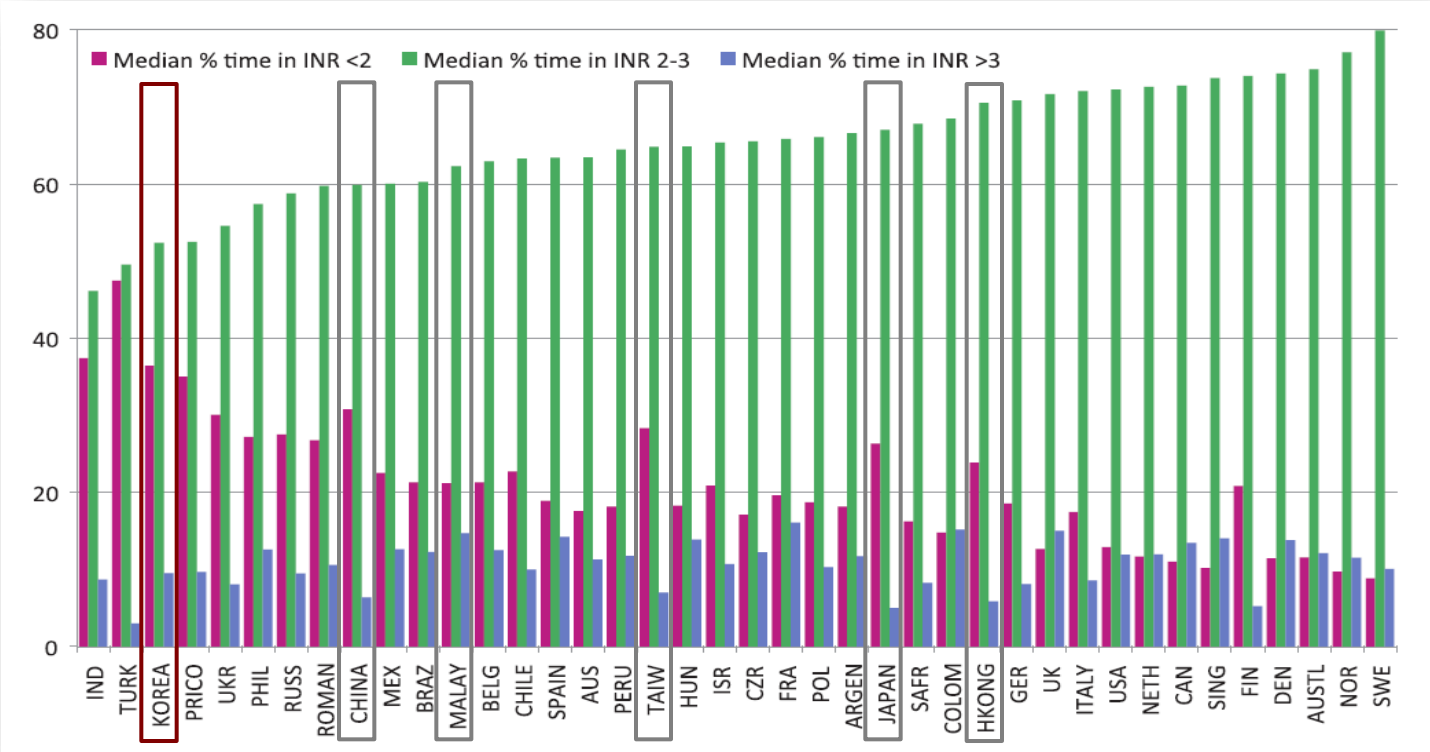
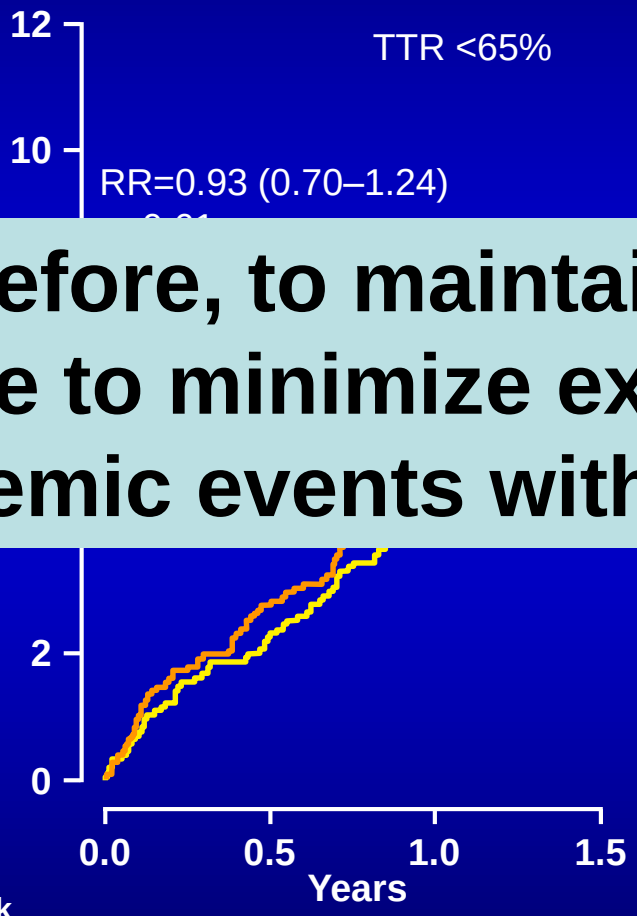


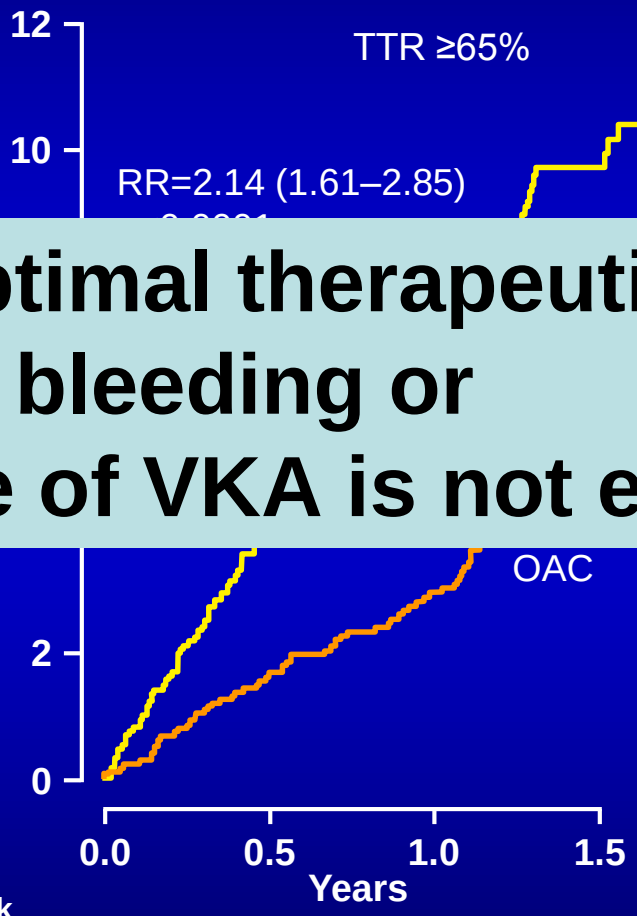
Figure 1. Country distribution of percentage of time in therapeutic range (TTR) of 2.0 to 3.0, percentage of time above treatment range (>3.0), and percentage of time below treatment range (<2.0) in the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial. ARGEN indicates Argentina; AUS, Austria; AUSTL, Australia; BELG, Belgium; BRAZ, Brazil; CAN, Canada; COLOM, Colombia; CZR, Czech Republic; DEN, Denmark; FIN, Finland; FRA, France; GER, Germany; HKONG, Hong Kong; HUN, Hungary; IND, India; INR, international normalized ratio; ISR, Israel; MALAY, Malaysia; MEX, Mexico; NETH, Netherlands; NOR, Norway; PHIL, Phillipines; POL, Poland; PRICO, Puerto Rico; ROMAN, Romania; RUSS, Russia; SAFR, South Africa; SING, Singapore; SWE, Sweden; TAIW, Taiwan; TURK, Turkey; and UKR, Ukraine.

Wallentin L et al., *Circulation.* 2013;127:2166-2176.

Defining the need for chronic OAC: Importance of Compliance

Poorly controlled warfarin patients

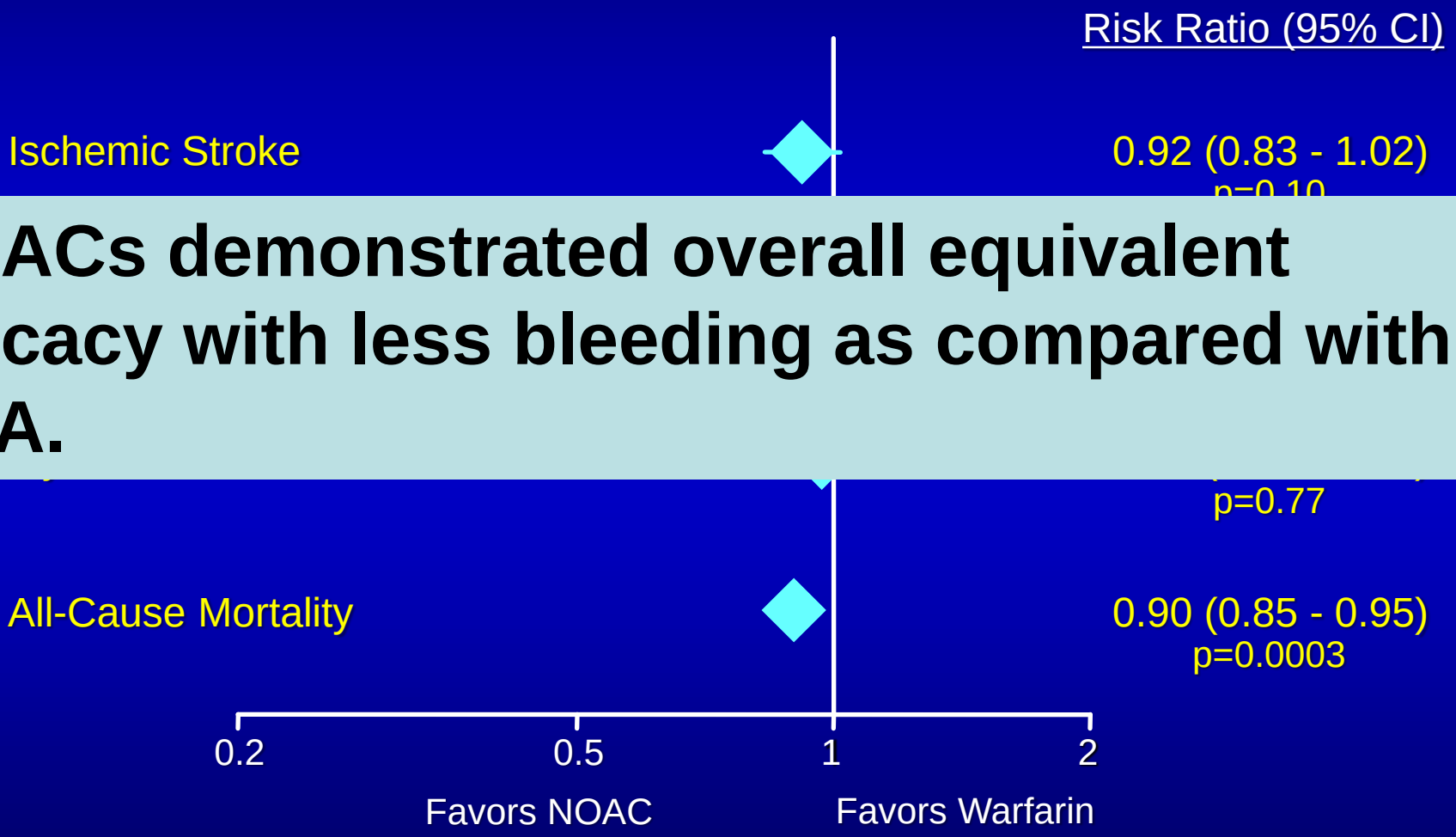




Therefore, to maintain the optimal therapeutic range to minimize excessive bleeding or ischemic events with the use of VKA is not easy.

Connolly SJ, et al. Circulation 2008; 118: 2029-2037.

Novel Oral Anticoagulants in AF



NOACs demonstrated overall equivalent efficacy with less bleeding as compared with VKA.

Heterogeneity p=NS for all outcomes

Ruff CT, et al. Lancet 2014;383:955-962

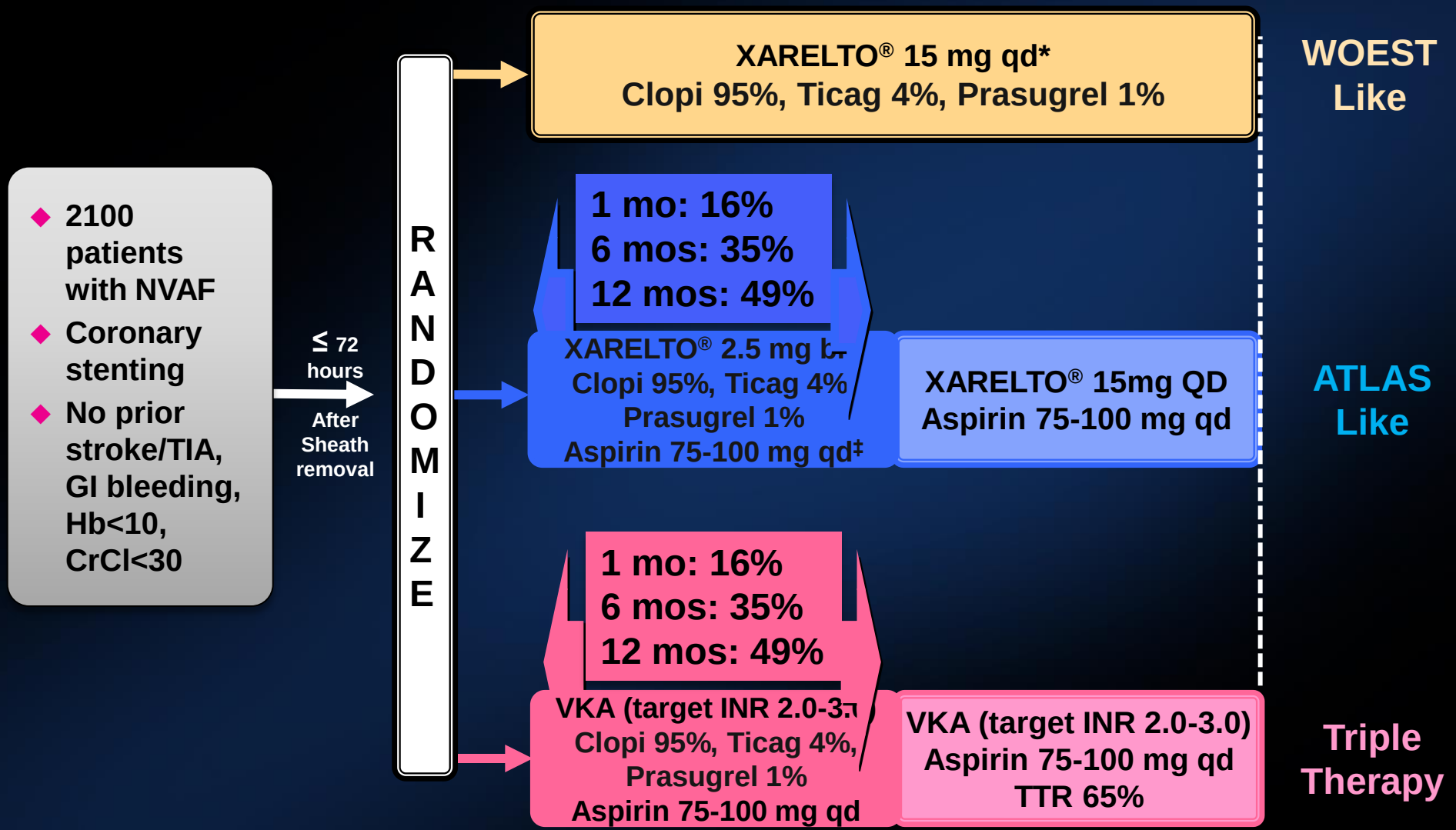
Ongoing trials of NOACs in AF patients undergoing PCI

	PIONEER AF-PCI	REDUAL-PCI	AUGUSTUS	ENTRUST AF-PCI
NOAC	Rivaroxaban	Dabigatran	Apixaban	Edoxaban
Clinicaltrials.gov identifier	NCT01830543	NCT02164864	NCT02415400	NCT02866175
Trial status	Enrollment completed	Enrolling	Enrolling	Planning
Study type	Open-label, randomized	Open-label, randomized	Open-label (apixaban vs warfarin) and blinded (aspirin vs placebo), randomized	Open-label, randomized
Patients	2169 patients with AF who undergo a PCI with stenting	2500 patients with AF undergoing PCI with stenting (elective or post ACS)	4600 patients with AF undergoing PCI with stenting or an ACS	1500 patients with AF after successful PCI with stenting (elective or post ACS)

AHA 2016	ESC 2017
NOAC wins Double therapy wins	NOAC wins Double therapy wins

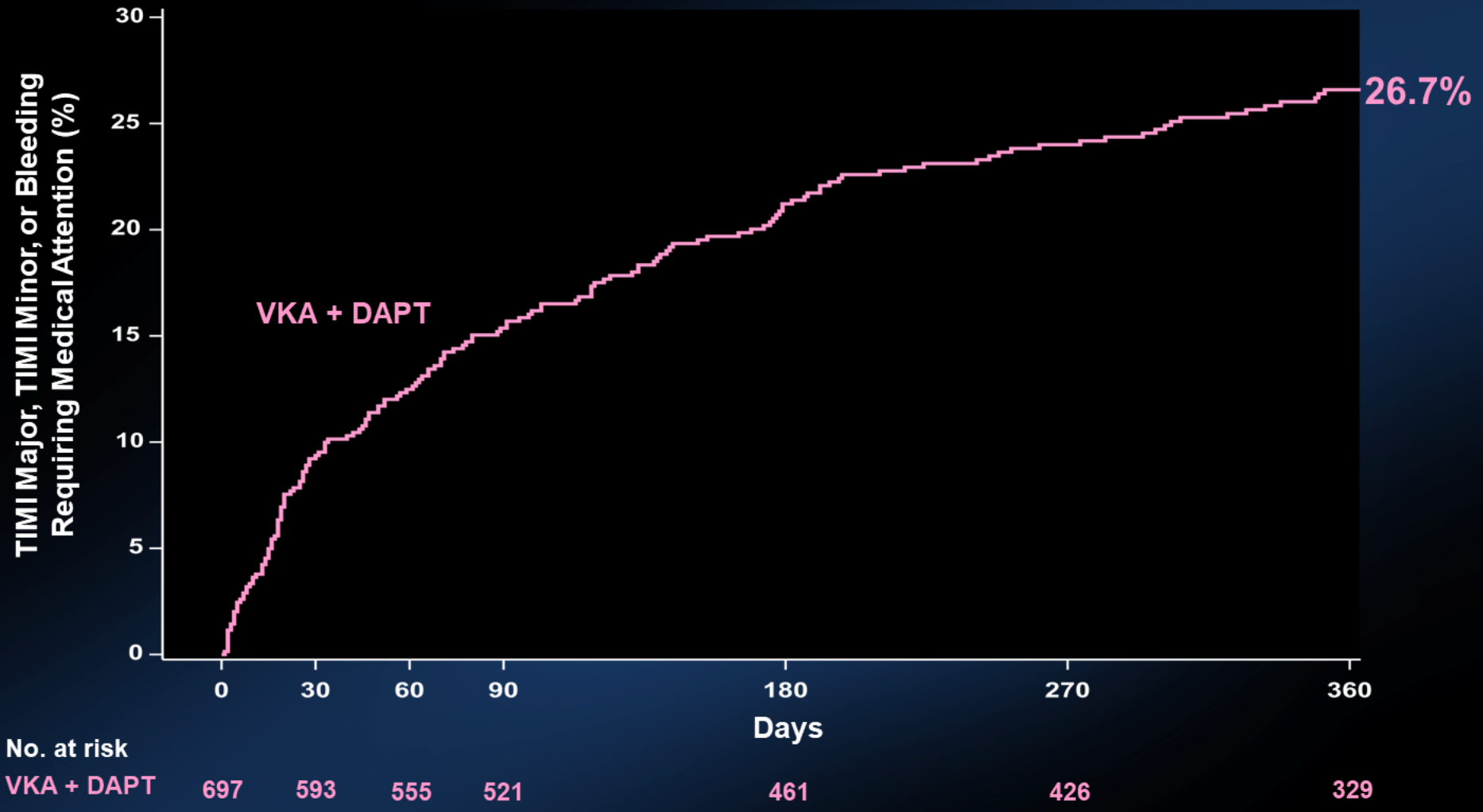
Angiolillo DJ et al. Circ Cardiovasc Interv. 2016

Pre-Randomization Choice of Duration of DAPT & Thienopyridine: PIONEER AF-PCI



Gibson et al. AHA 2016

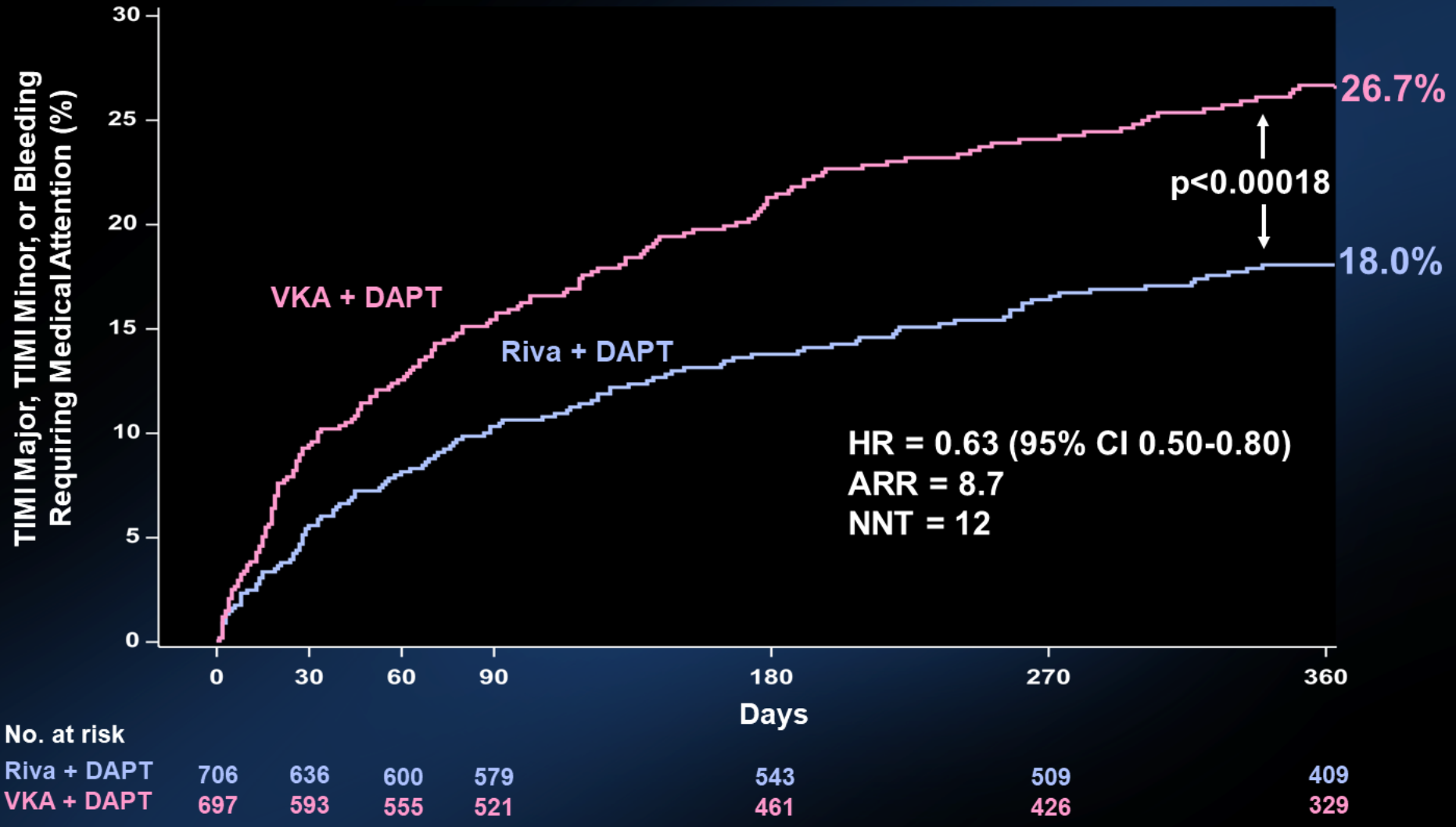
Kaplan-Meier Estimates of First Occurrence of Clinically Significant Bleeding Events



Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Clinically significant bleeding is the composite of TIMI major, TIMI minor, and BRMA.
Hazard ratios as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.

Gibson et al. AHA 2016

Kaplan-Meier Estimates of First Occurrence of Clinically Significant Bleeding Events



No. at risk							
Riva + DAPT	706	636	600	579	543	509	409
VKA + DAPT	697	593	555	521	461	426	329

Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
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Gibson et al. AHA 2016

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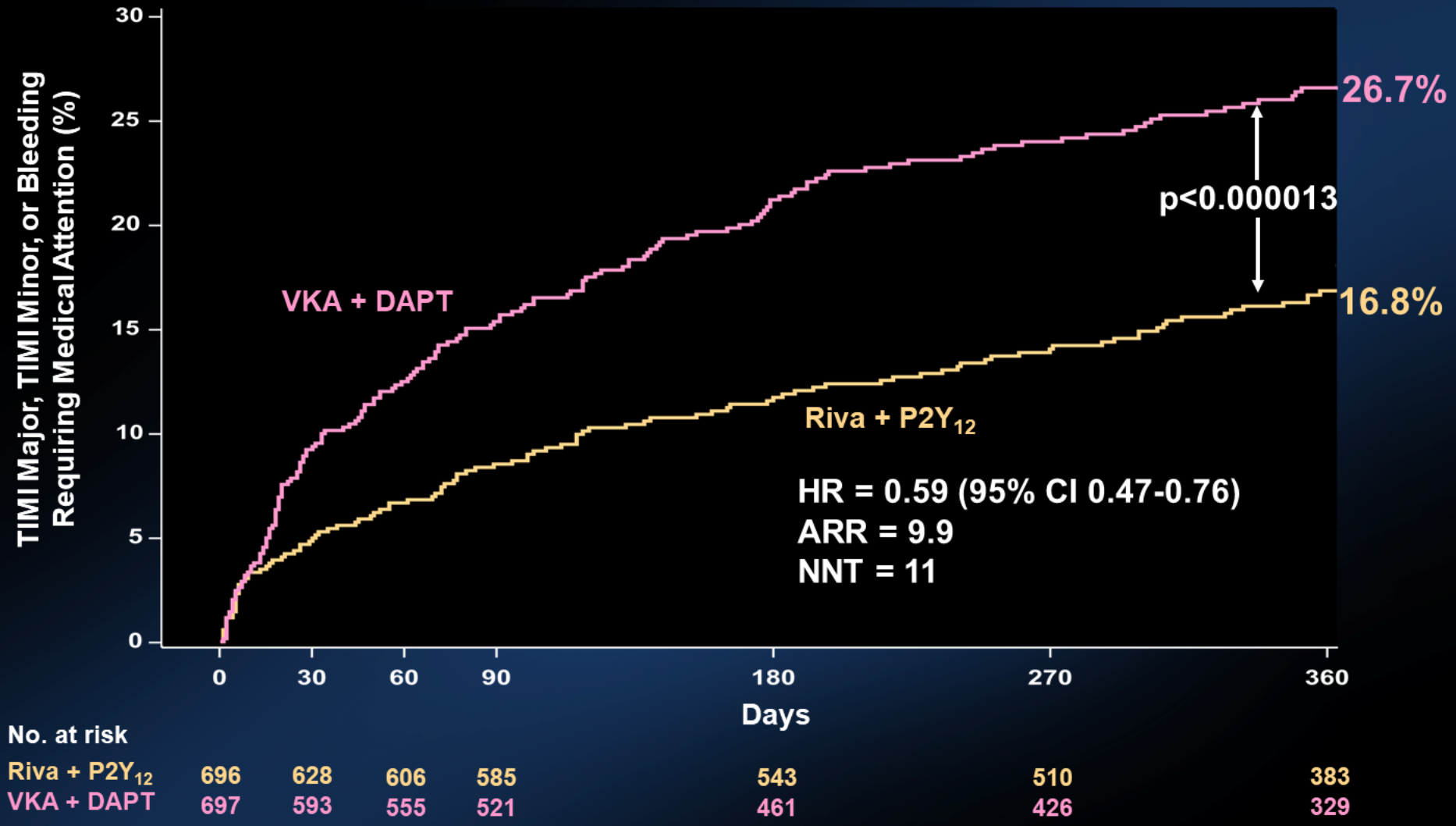

No. at risk							
Riva + P2Y$_{12}$	696	628	606	585	543	510	383
VKA + DAPT	697	593	555	521	461	426	329

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Gibson et al. AHA 2016

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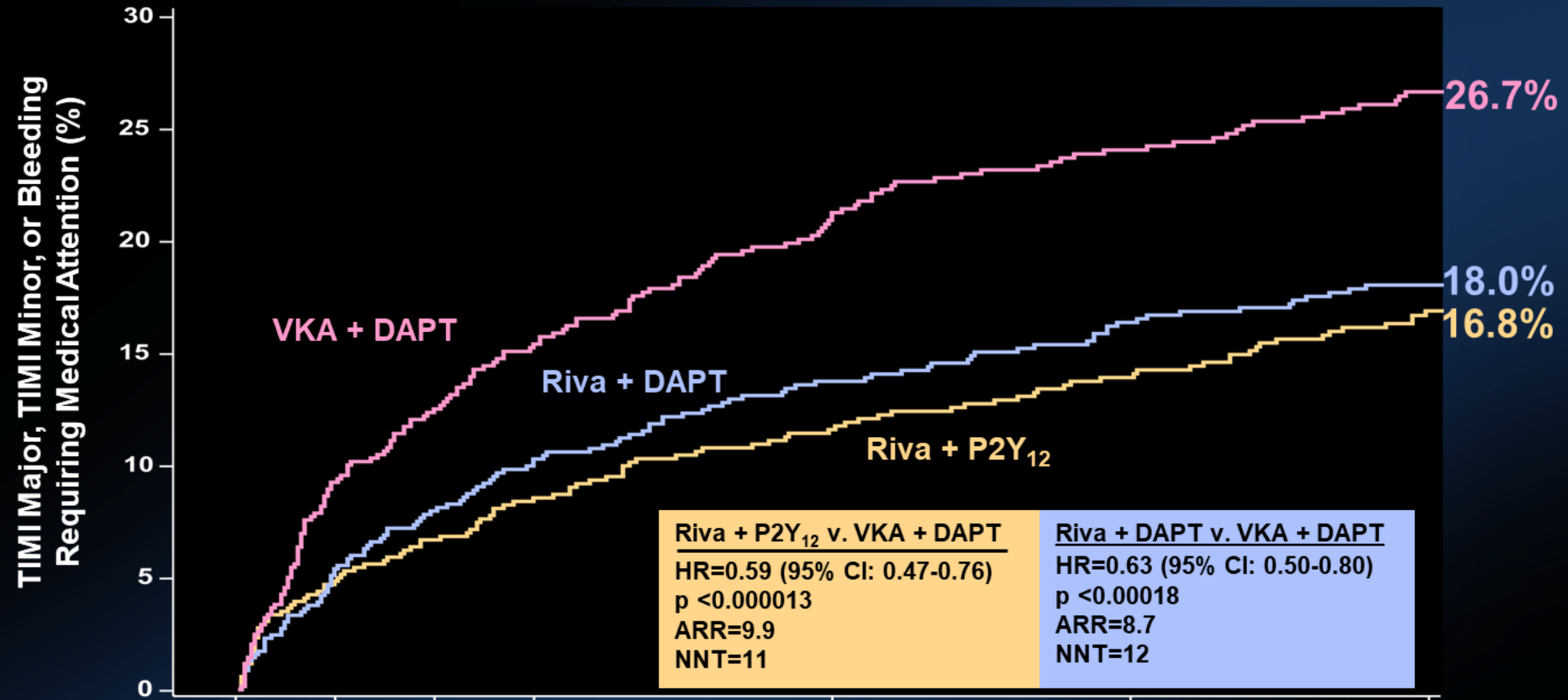

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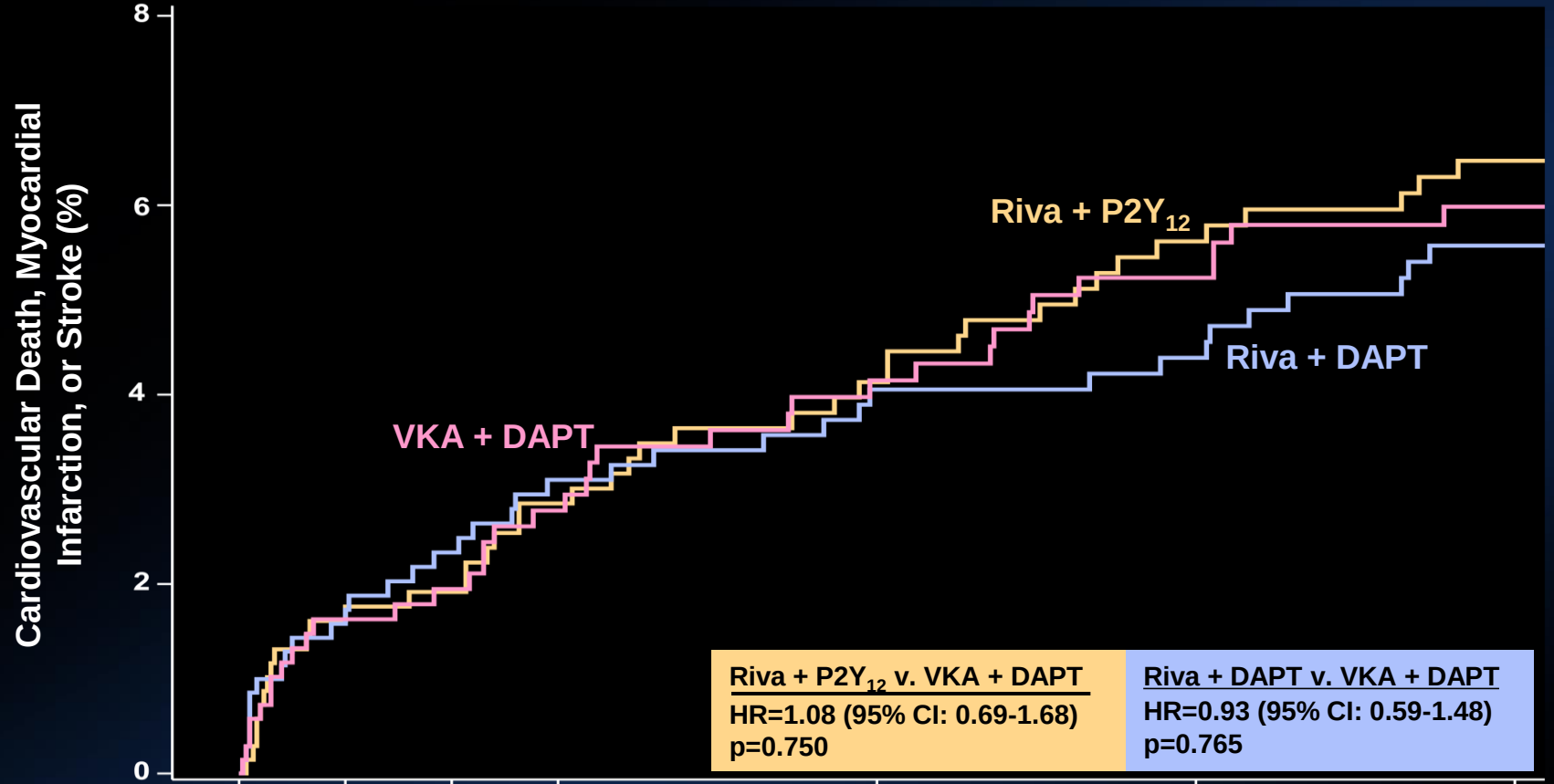
VKA + DAPT	697	593	555	521	461	426	329

Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Clinically significant bleeding is the composite of TIMI major, TIMI minor, and BRMA.
Hazard ratios as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.

Gibson et al. AHA 2016

Kaplan-Meier Estimates of First Occurrence of CV Death, MI or Stroke



No. at risk							
Riva + P2Y$_{12}$	694	648	633	621	590	562	430
Riva + DAPT	704	662	640	628	596	570	457
VKA + DAPT	695	635	607	579	543	514	408

Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Composite of adverse CV events is composite of CV death, MI, and stroke.
Hazard ratios as compared to VKA group are based on the (stratified, only for the Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Log-Rank P-values as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/115 mg QD comparing VKA) two-sided log rank test.
6 Subjects were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines

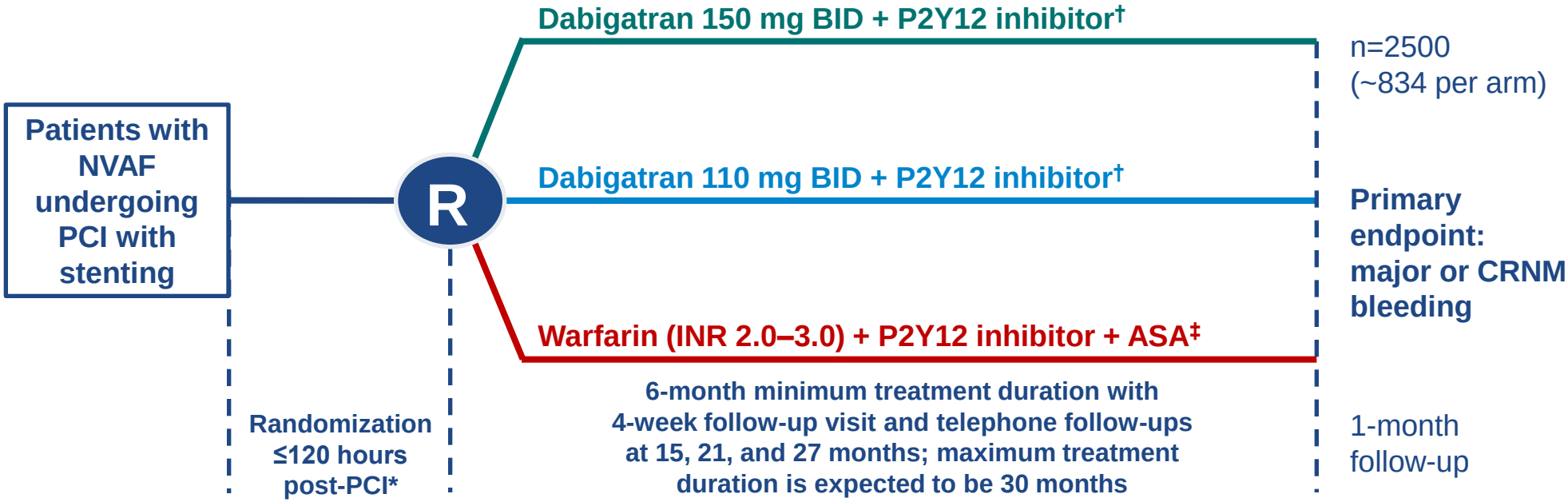
Gibson et al. AHA 2016

CONCLUSION

Among stented AF participants, administration of either rivaroxaban 15 mg daily plus $P2Y_{12}$ monotherapy for one year or rivaroxaban 2.5 mg BID plus 1, 6, or 12 months of DAPT reduced the risk of clinically significant bleeding as compared with standard of care VKA plus 1, 6, or 12 months of DAPT and yielded comparable efficacy with broad confidence intervals

Gibson et al. AHA 2016

RE-DUAL PCI™ tests the hypothesis of non-inferiority in safety of dual antithrombotic therapy with VKA



Estimated completion March 2017

Click here to see the RE-DUAL PCI key inclusion/exclusion criteria

***Study drug should be administered 6 hours after sheath removal and no later than ≤120 hrs post-PCI (≤72 hrs is preferable). †Dabigatran arms: ASA discontinued at randomization. ‡Warfarin arm: ASA discontinued 1 month after bare metal stent or 3 months after drug-eluting stent.**

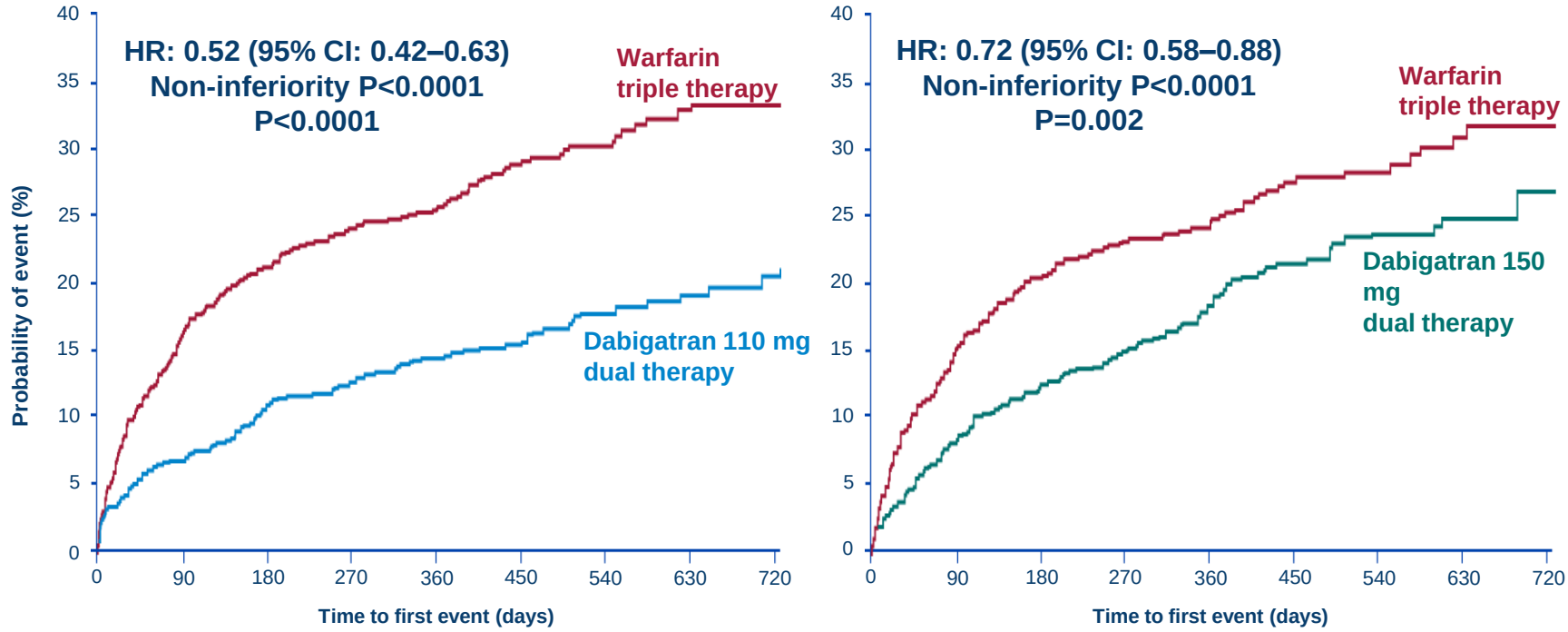
ASA, acetylsalicylic acid; CRNM, clinically-relevant non-major; PCI, percutaneous coronary intervention; R, randomization.

ClinicalTrials.gov: NCT02164864; Cannon C et al. Clin Cardiol 2016

RE-DUAL PCI™
Study in NVAF patients undergoing PCI

Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event

RE-DUAL PCI
Study in NVAF patients undergoing PCI



Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 mg vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 mg vs warfarin comparison, an unstratified model is used, elderly patients outside the USA are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05)

Additional individual thromboembolic endpoints

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	Dabigatran 110 mg dual therapy (n=981) n (%)	Warfarin triple therapy (n=981) n (%)	D110 DT vs warfarin TT HR (95% CI)	D110 DT vs warfarin TT P value	Dabigatran 150 mg dual therapy (n=763) n (%)	Warfarin triple therapy (n=764) n (%)	D150 DT vs warfarin TT HR (95% CI)	D150 DT vs warfarin TT P value
All-cause death	55 (5.6)	48 (4.9)	1.12 (0.76–1.65)	0.56	30 (3.9)	35 (4.6)	0.83 (0.51–1.34)	0.44
Stroke	17 (1.7)	13 (1.3)	1.30 (0.63–2.67)	0.48	9 (1.2)	8 (1.0)	1.09 (0.42–2.83)	0.85
Unplanned revascularization	76 (7.7)	69 (7.0)	1.09 (0.79–1.51)	0.61	51 (6.7)	52 (6.8)	0.96 (0.65–1.41)	0.83
MI	44 (4.5)	29 (3.0)	1.51 (0.94–2.41)	0.09	26 (3.4)	22 (2.9)	1.16 (0.66–2.04)	0.61
Stent thrombosis	15 (1.5)	8 (0.8)	1.86 (0.79–4.40)	0.15	7 (0.9)	7 (0.9)	0.99 (0.35–2.81)	0.98

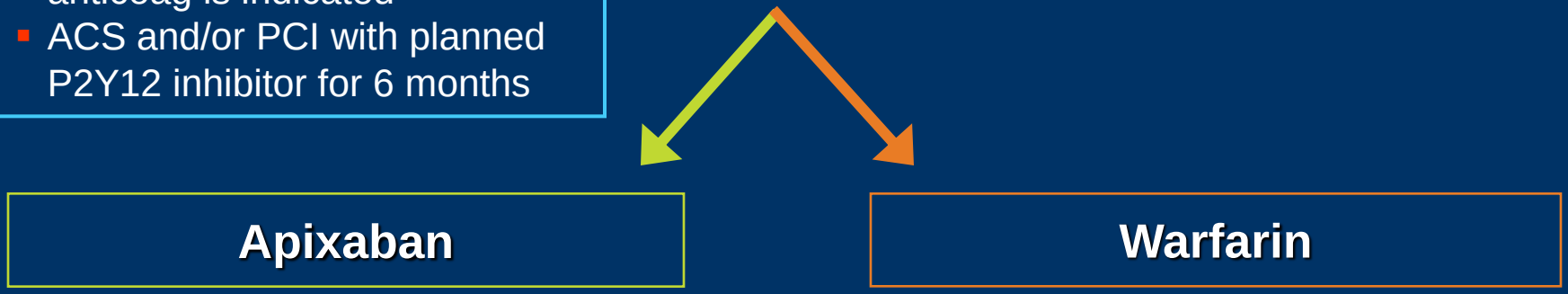
Results presented are times to event. Stent thrombosis is time to definite stent thrombosis

Apixaban Versus Warfarin in Patients with AF and ACS or PCI: The AUGUSTUS Trial

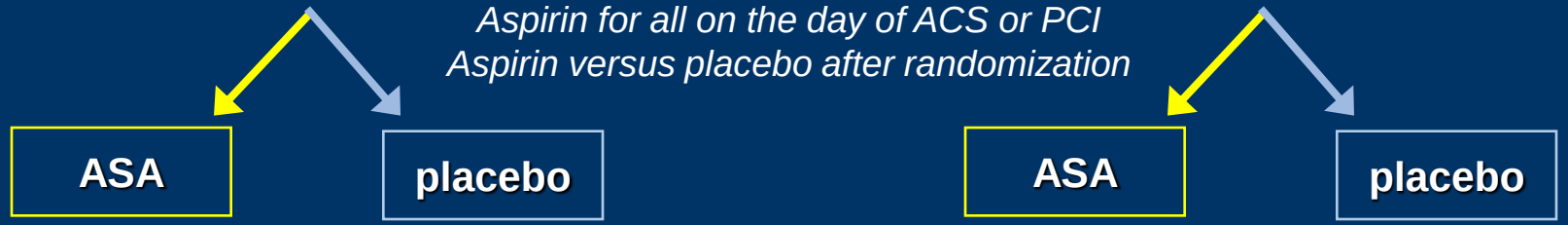
Inclusion
- AF (prior, persistent, or >6 hrs duration)
- Physician decision that oral anticoag is indicated
- ACS and/or PCI with planned P2Y12 inhibitor for 6 months

Randomize
n =4,600
Patients

Exclusion
- Contraindication to DAPT
- Other reason for warfarin (prosthetic valve, mod/sev MS)



P2Y12 inhibitor for all patients x 6 months
Aspirin for all on the day of ACS or PCI
Aspirin versus placebo after randomization



Primary outcome: major/clinically relevant bleeding (through 6 months)

Secondary objective: Death, MI, stroke, stent thrombosis

Current expert consensus on antithrombotic therapy in patients with AF plus PCI setting

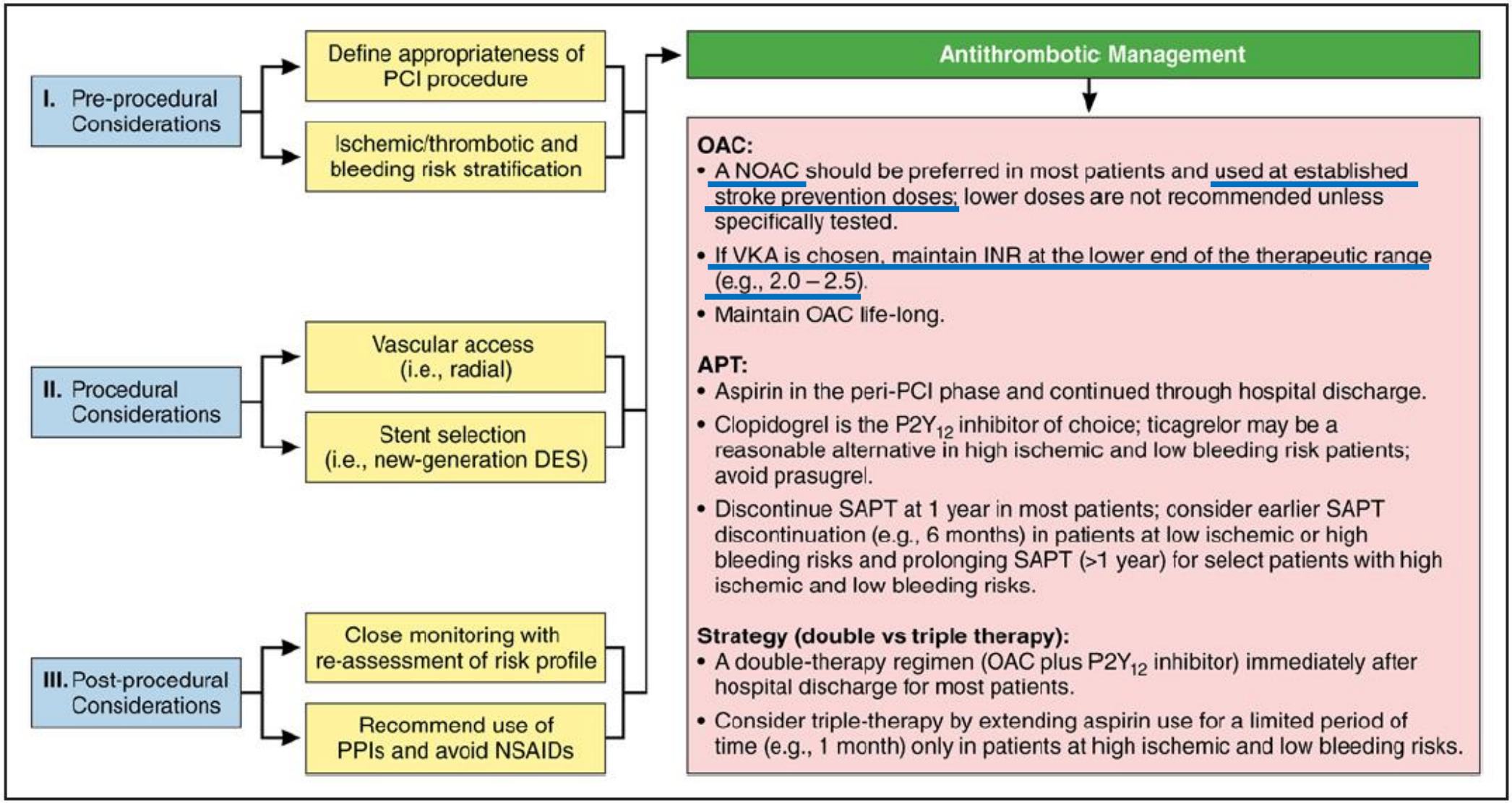
HALLYM UNIVERSITY MEDICAL CENTER
KANGNAM SACRED HEART HOSPITAL

Summary of Key Changes Between 2016 and 2018 Expert Consensus on Antithrombotic Management on Patients With AF Undergoing PCI

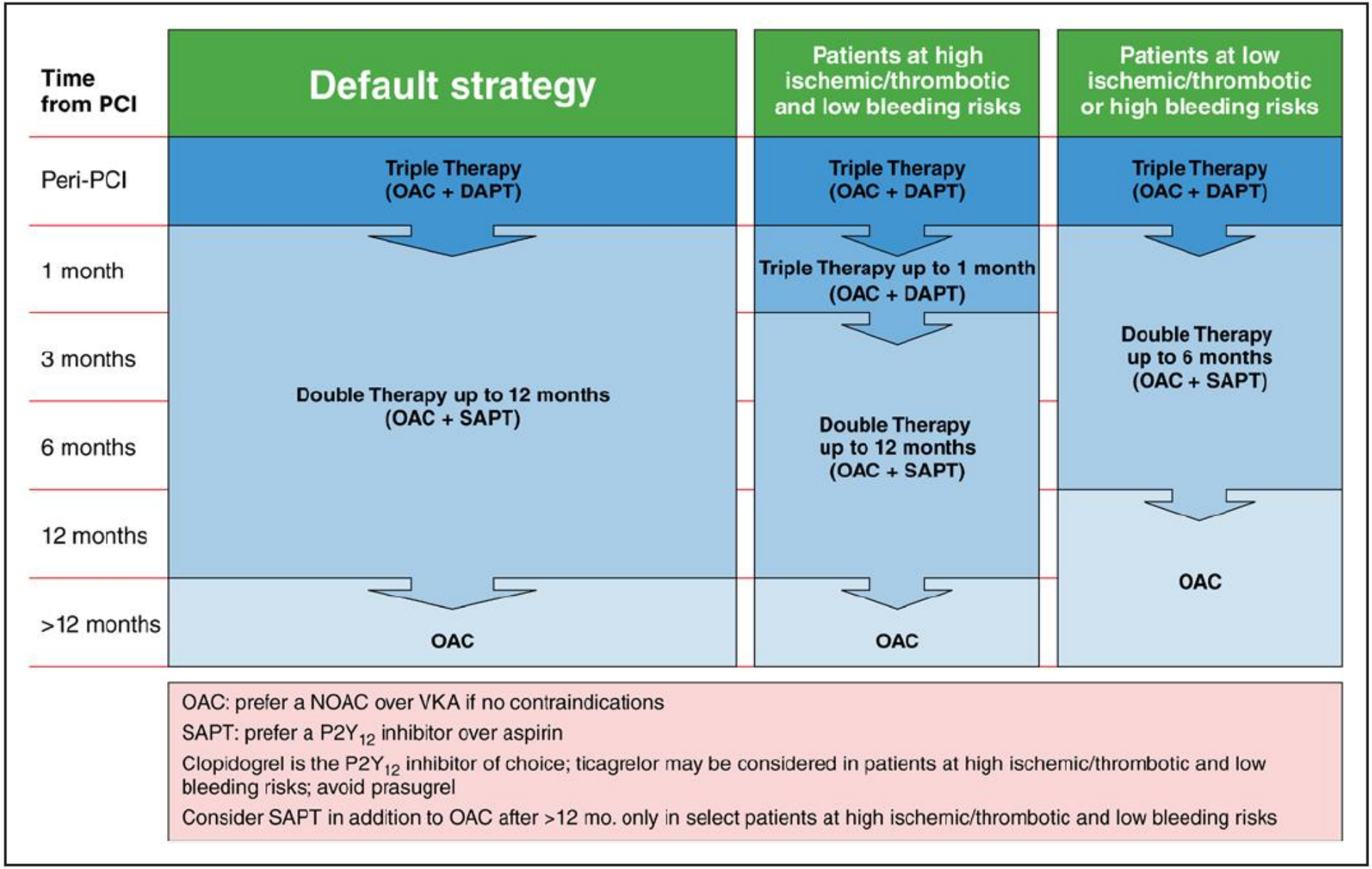
	2016 Expert Consensus	2018 Expert Consensus Update
Choice of anticoagulant	Both VKAs and NOACs may be considered, with choice of agent at the discretion of the treating physician and taking into consideration patient preference	An NOAC (rather than a VKA) should generally be preferred in most patients unless contraindicated
Choice of $P2Y_{12}$ inhibitor	Clopidogrel is the $P2Y_{12}$ inhibitor of choice; avoid prasugrel or ticagrelor	Clopidogrel is the $P2Y_{12}$ inhibitor of choice; ticagrelor may represent a reasonable treatment option in patients at high ischemic/thrombotic and low bleeding risks; avoid prasugrel
Strategy (double vs triple therapy)	DAPT in adjunct to OAC (ie, triple therapy) should not extend to a full 12 mo; consider SAPT (preferably clopidogrel and dropping aspirin) in adjunct to OAC (ie, double therapy) as early as possible (0 to 6 mo after stenting), depending on the ischemic/thrombotic and bleeding risk profiles	A double-therapy regimen (OAC plus $P2Y_{12}$ inhibitor) immediately after hospital discharge should be considered for most patients, whereas extending the use of aspirin beyond hospital discharge (ie, triple therapy) should be considered only for patients at high ischemic/thrombotic and low bleeding risks and for a limited period of time (eg, 1 mo)

Angiolillo D et al. Circulation 2018;138:527-536

Pragmatic algorhithm for the patients with AF + PCI



Strategy according to time schedule post-PCI



Messages from the randomized, OAC-ALONE study

Oral Anticoagulation With vs Without Single Antiplatelet Therapy in Patients With Atrial Fibrillation Beyond One Year After Coronary Stent Implantation

Yukiko Nakano, Satoshi Shizuta, Akihiro Komasa, Takeshi Morimoto, Hisaki Masuda, Hiroki Shiomi, Kentaro Nakai, Satoru Suwa, Takeshi Aoyama, Mamoru Takahashi, Yuko Onishi, Toshiaki Mano, Mitsuo Matsuda, Makoto Motooka, Hirofumi Tomita, Moriaki Inoko, Takatoshi Wakeyama, Nobuhisa Hagiwara, Masaharu Akao, Kenji Ando, Yutaka Furukawa, Yoshihisa Nakagawa, Kazushige Kadota, Kazuya Kawai, and Takeshi Kimura:

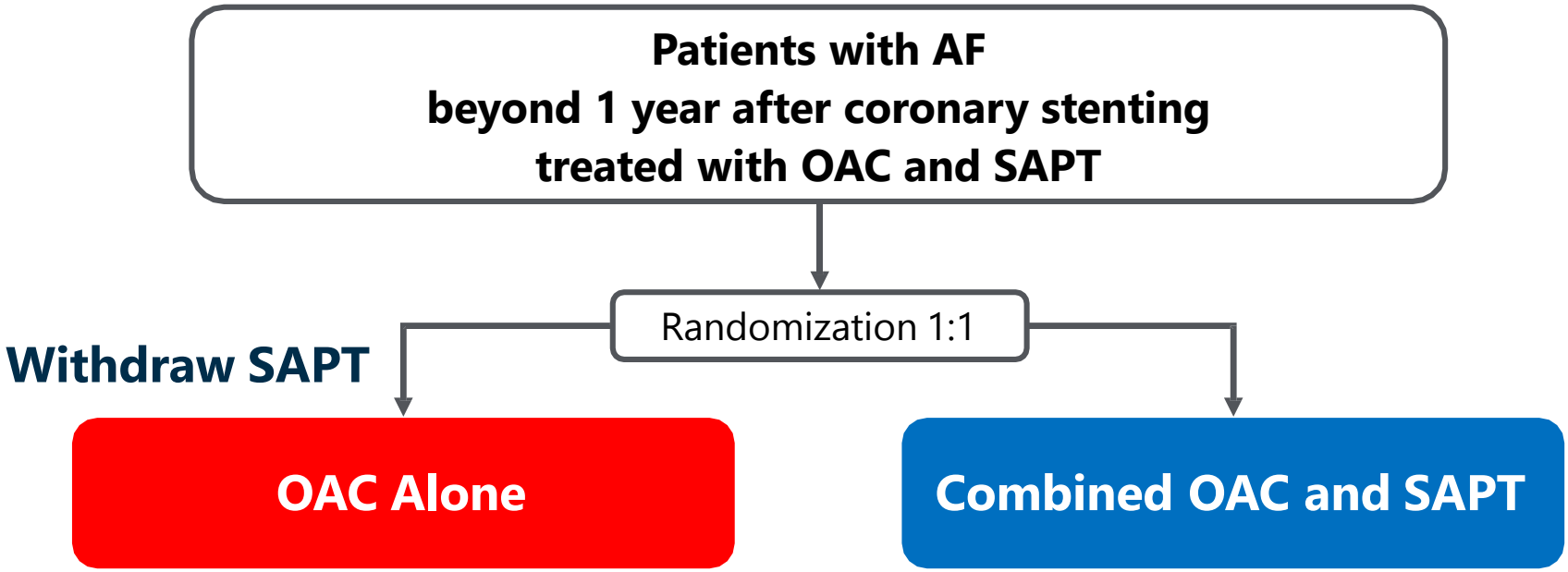
On behalf of the OAC-ALONE Study Investigators

Aim

To evaluate non-inferiority of OAC alone to a combination of OAC and single APT (SAPT) in AF patients beyond 1 year after coronary stenting

Study Design

Prospective, multicenter, open-label, randomized, non-inferiority trial



Key Inclusion Criteria

- AF beyond 1 year after coronary stenting
- Treated with OAC and SAPT

Key Exclusion Criteria

- PCI within 12 months prior to enrollment
- History of stent thrombosis

Antithrombotic Therapy

➢ Warfarin

Predefined target INR range was **2.0-3.0 (<70 years) and 1.6-2.6 (≥70 years)** based on the Japanese guidelines.

➢ DOAC

Dabigatran (150/110 mg twice daily), **Rivaroxaban** (15/10 mg once daily), **Apixaban** (5/2.5 mg twice daily), or **Edoxaban** (60/30 mg once daily)

➢ SAPT

Aspirin (81-324 mg/day) or **Clopidogrel** (75 mg/day)

Endpoints

- **Primary Endpoint:**

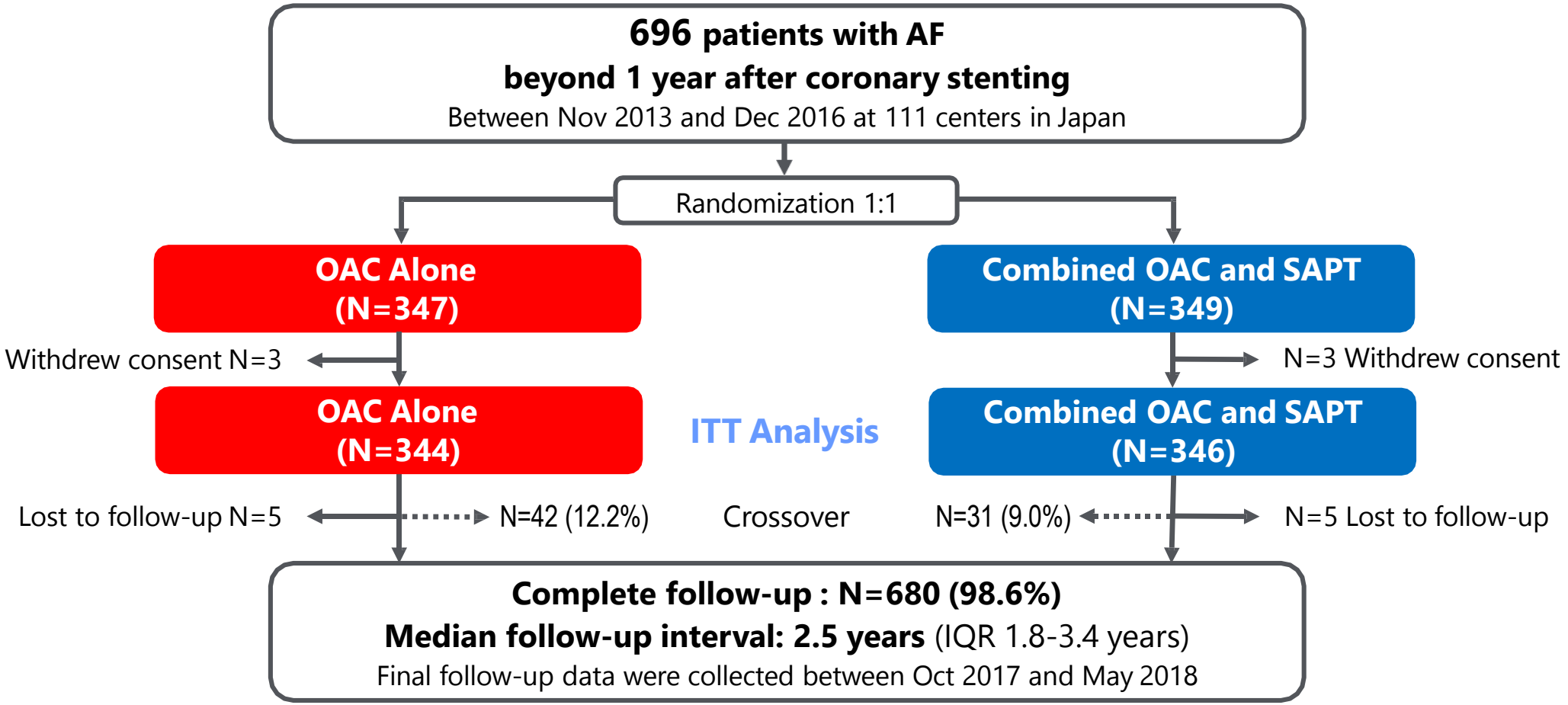
  All-Cause Death, MI, Stroke, or Systemic Embolism (SE)

- **Major Secondary Endpoint:**

  Primary Endpoint or ISTH Major Bleeding

ISTH : International Society on Thrombosis and Haemostasis

Study Flow Chart



Baseline Patient Characteristics

	OAC Alone	Combined OAC and SAPT	P value
No. of Patients	344	346	
Age (years)	74.9 ± 0.4	75.2 ± 0.4	0.61
Male sex	85%	85%	0.85
Diabetes mellitus	44%	40%	0.25
Heart failure	41%	44%	0.43
Prior MI	38%	40%	0.57
Prior stroke	16%	14%	0.50
$CHADS_2$ score	2.6 ± 1.2	2.5 ± 1.2	0.51
CHA_2DS_2-VASc score	4.6 ± 1.4	4.6 ± 1.4	0.82
HAS-BLED score ≥3	44%	45%	0.75
Drug-eluting stent use	72%	71%	0.74
Years from the last PCI	4.4 (1.8-7.7)	4.6 (2.4-7.4)	0.49

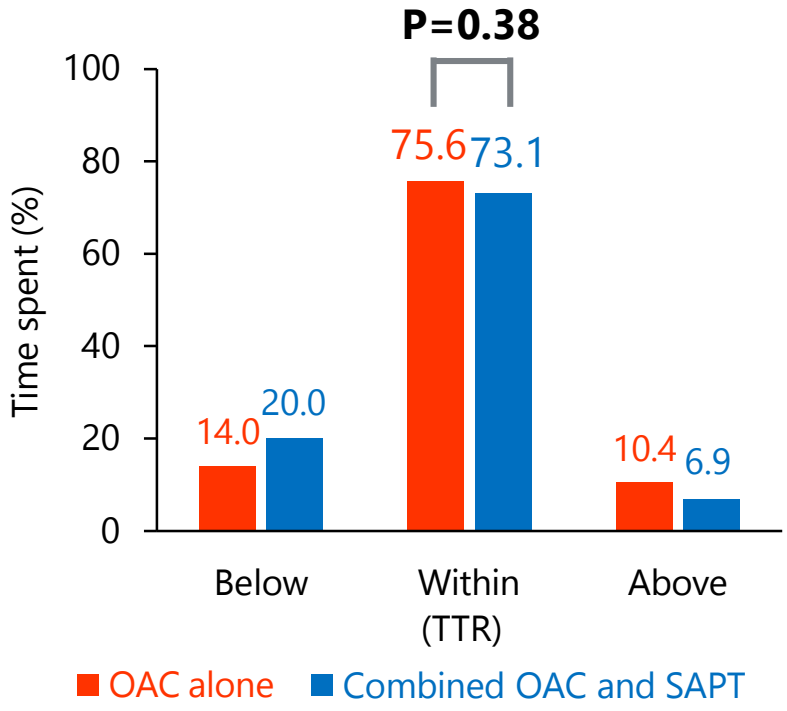
Baseline Medications

	OAC Alone	Combined OAC and SAPT	P value
No. of Patients	344	346	
Warfarin	74%	76%	0.51
DOACs	26%	24%	0.51
Dabigatran	6%	6%	
Rivaroxaban	7%	5%	
Apixaban	9%	11%	
Edoxaban	3%	2%	
Aspirin	85%	86%	0.72
Clopidogrel	15%	14%	0.64
Statins	78%	80%	0.49
Beta-blockers	64%	68%	0.27
ACE-I/ARB	66%	68%	0.59

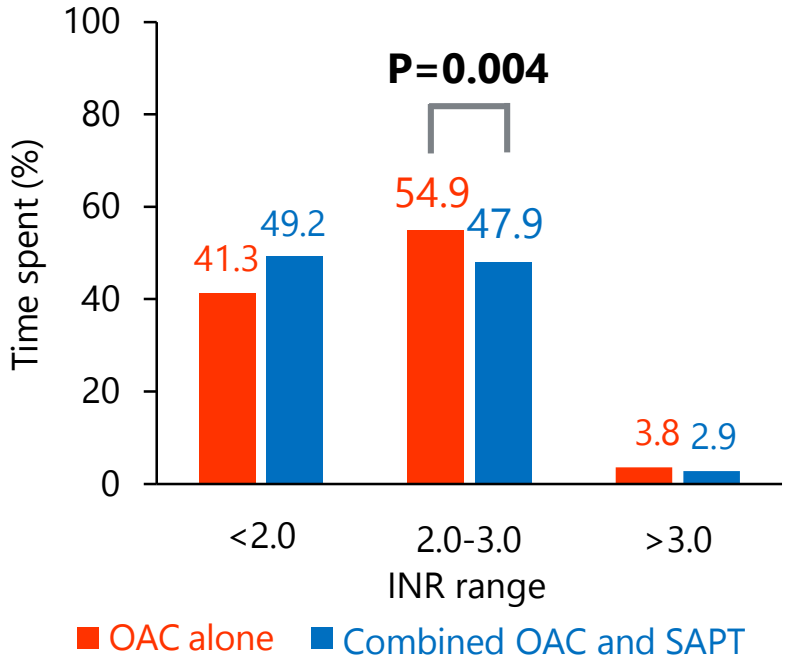
Time in Therapeutic Range (TTR)

TTR was available in 93.6% of warfarin-treated patients

Predefined target INR range:
2.0-3.0 (<70 y) and 1.6-2.6 (≥70 y)

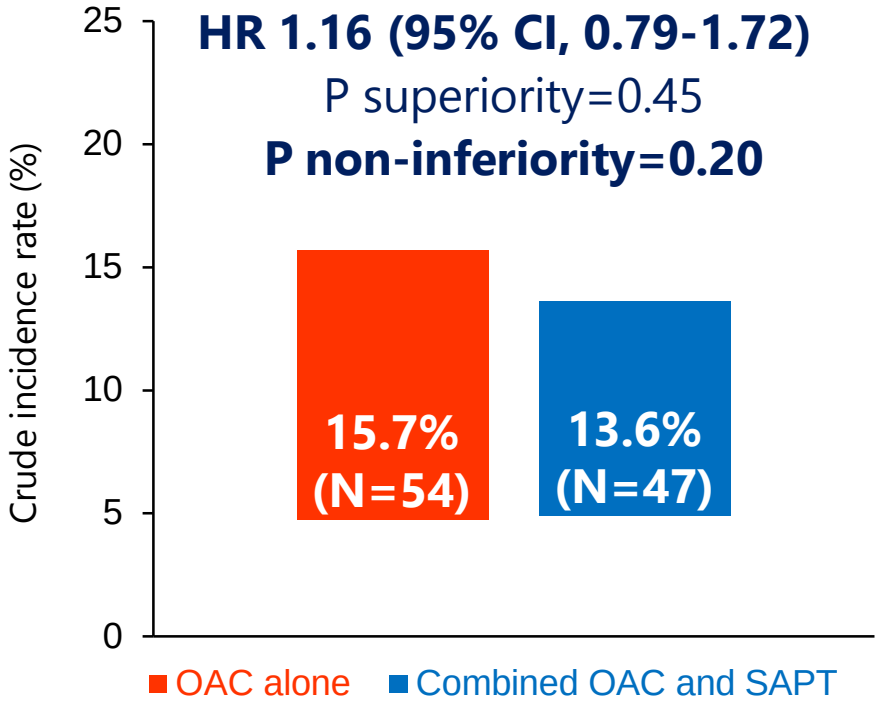


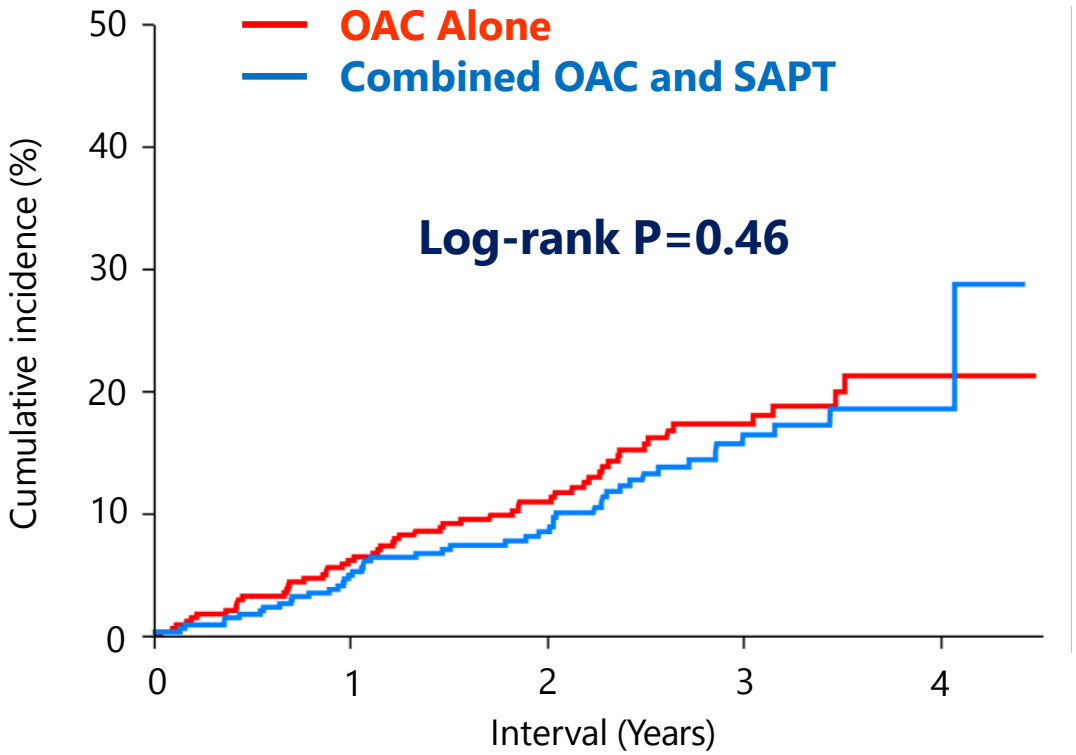
Post hoc target INR range:
2.0-3.0 regardless of age



Primary Endpoint

Death, MI, Stroke, or SE





Primary Endpoint and Individual Components

Outcomes	OAC Alone (N=344)	Combination (N=346)	HR (95% CI)	P value
	N of patients with event (Crude incidence rate)			
Primary endpoint:	**54 (15.7%)**	**47 (13.6%)**	1.16 (0.79-1.72)	0.45*
▪ All-cause death	**40 (11.6%)**	**31 (9.0%)**	1.30 (0.82-2.10)	0.27
Cardiovascular death	**20 (5.8%)**	**17 (4.9%)**	1.18 (0.62-2.28)	0.62
Non-cardiovascular death	**20 (5.8%)**	**14 (4.1%)**	1.45 (0.74-2.94)	0.28
▪ Myocardial infarction	**8 (2.3%)**	**4 (1.2%)**	2.03 (0.64-7.59)	0.23
Stent thrombosis	**2 (0.6%)**	**0 (0.0%)**	NA	0.15
▪ Stroke or Systemic embolism	**13 (3.8%)**	**19 (5.5%)**	0.69 (0.33-1.38)	0.29
Stroke	13 (3.8%)	18 (5.2%)	0.73 (0.35-1.47)	0.38
Systemic embolism	1 (0.3%)	2 (0.6%)	0.94 (0.81-1.09)	0.42

*** P for Non-inferiority = 0.20**

OAC ALONE

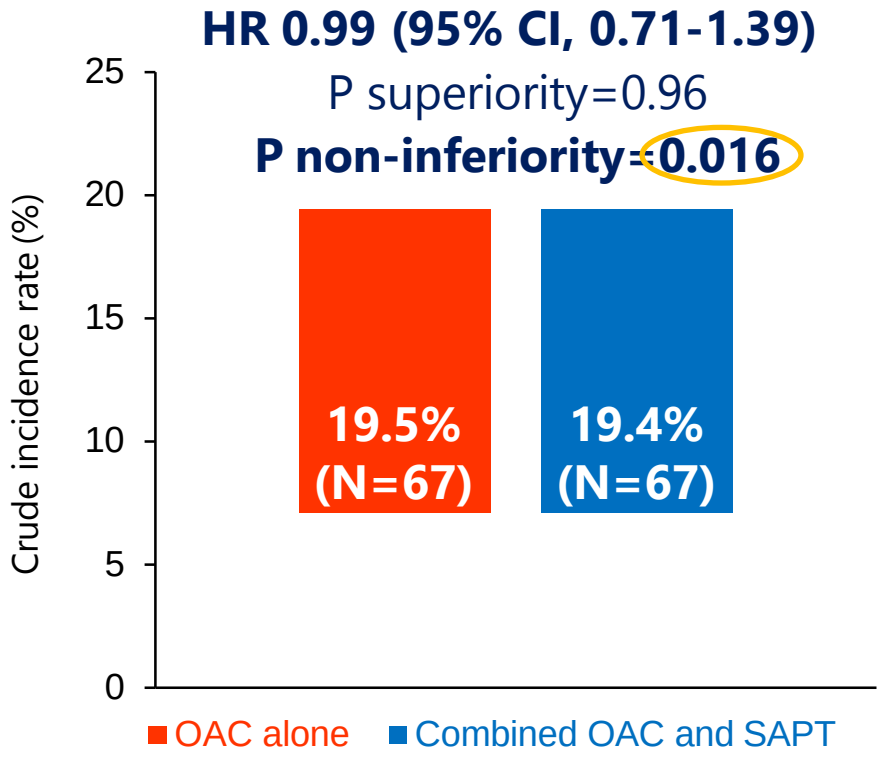
Major Bleeding

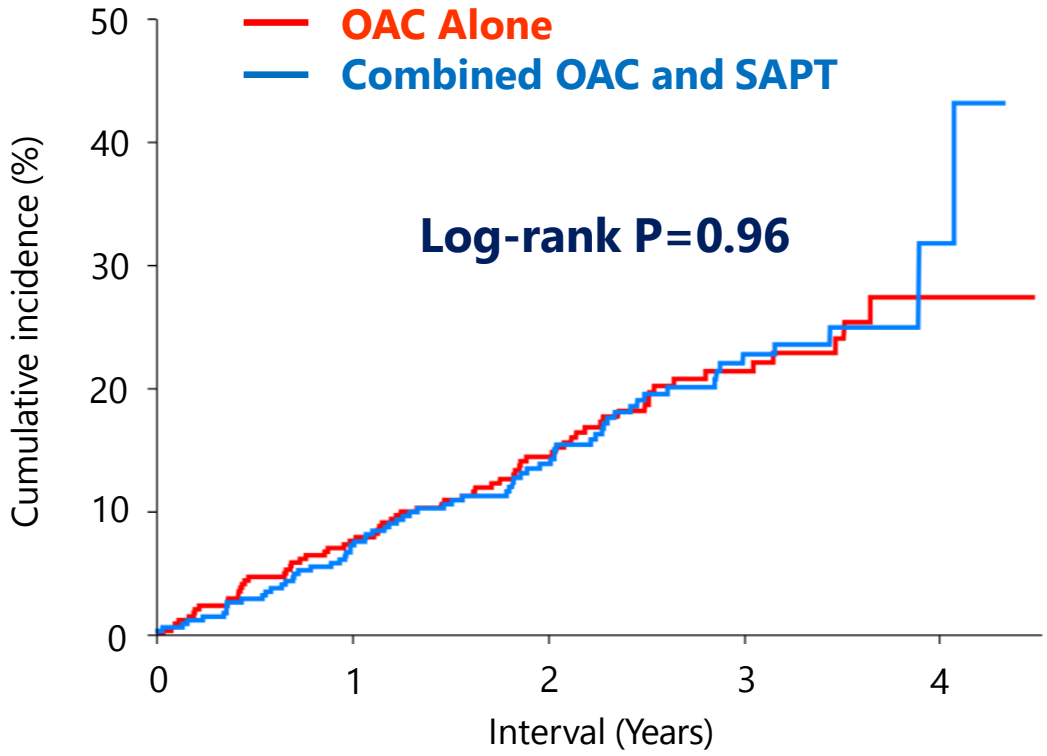
Outcomes	OAC Alone (N=344)	Combination (N=346)	HR (95% CI)	P value
	N of patients with event (Crude incidence rate)			
▪ ISTH major bleeding	**27 (7.8%)**	**36 (10.4%)**	0.73 (0.44-1.20)	0.22
Fatal bleeding	7 (2.0%)	4 (1.2%)	1.77 (0.54-6.77)	0.35
Intracranial bleeding	9 (2.6%)	14 (4.0%)	0.63 (0.26-1.43)	0.27
▪ TIMI major bleeding	**17 (4.9%)**	**29 (8.4%)**	0.57 (0.31-1.03)	0.07

Major Secondary Endpoint

OAC ALONE

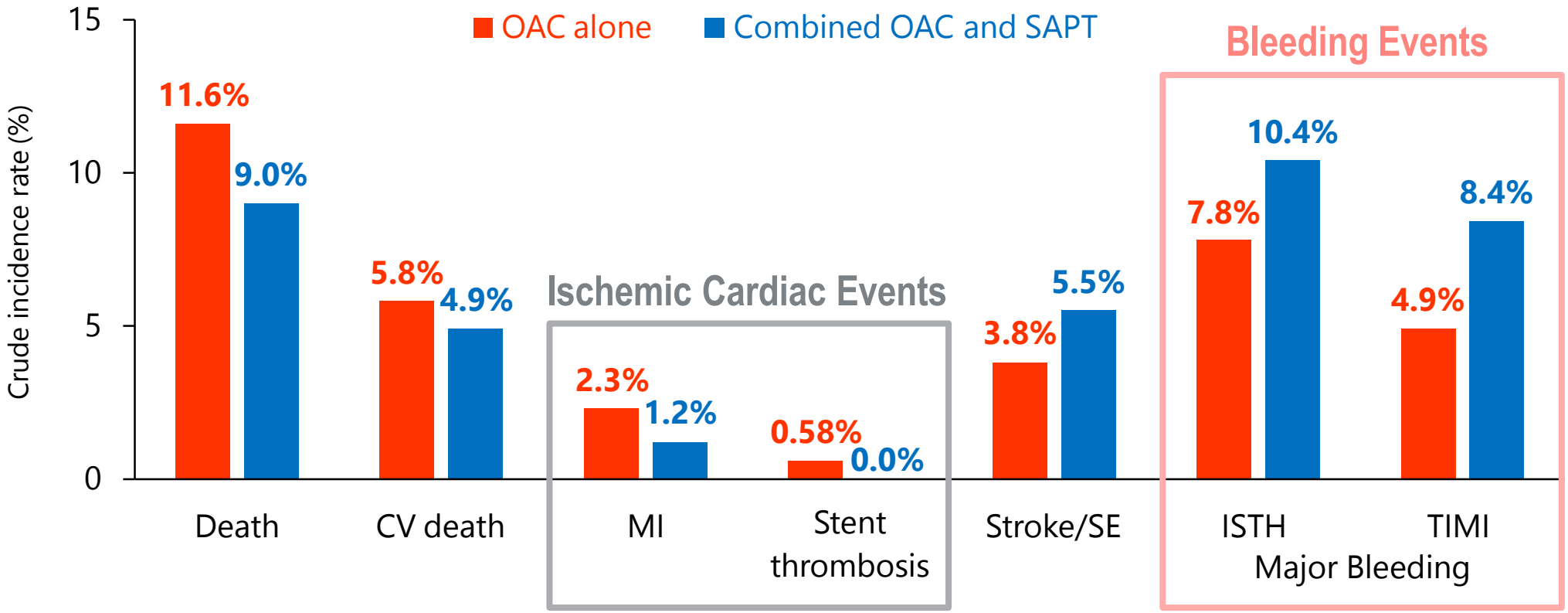
Primary Endpoint (Death/MI/Stroke/SE) or ISTH major bleeding





OAC ALONE

Individual Outcomes



Limitations

- Insufficient sample size
- Relatively large non-inferiority margin of 1.5 on the HR scale
- Open-label study design

  presumably affected the intensity of INR control in warfarin-treated patients

- Heterogeneity in antithrombotic regimen

  OAC : Warfarin or DOAC SA

  PT : Aspirin or Clopidogrel

1) Although there is no difference in INR control in both groups, OAC alone group has disadvantage over OAC+SAPT group in terms of ischemic events.
2) TTR alone may not completely reflects the adequacy of INR control (there might be fluctuations in INR values)
3) In case of AF+PCI setting, there might be difference in optimal INR range in Japanese patients, as compared with those with only AF.

Realistic approach for patients with AF + PCI after 1 year post-PCI (*in my opinion*)

1) For warfarin user → warfarin with modest INR control (INR 1.5-2.5) plus single antiplatelet agent

2) For NOAC alone user with established maximal dose → patient education for drug adherence (esp. twice daily dose-based NOAC)

3) For NOAC user with high thrombotic risk → add single antiplatelet agent with adjustment of NOAC dose if necessary


Thank you for your attention !!!
Nagarkot, Nepal (Nov 2017)