STOPDAPT-2 Total cohort

Clopidogrel Monotherapy after Short-term DAPT

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Disclosures

Name of Author : Takeshi Kimura

ABBOTT Vascular, and Boston Scientific.

Why we chose clopidogrel monotherapy after DAPT in the STOPDAPT-2 ?

In Japan, we have adopted an upfront de-escalation strategy after coronary DES implantation, using clopidogrel or reduced-dose prasugrel as a component of DAPT.

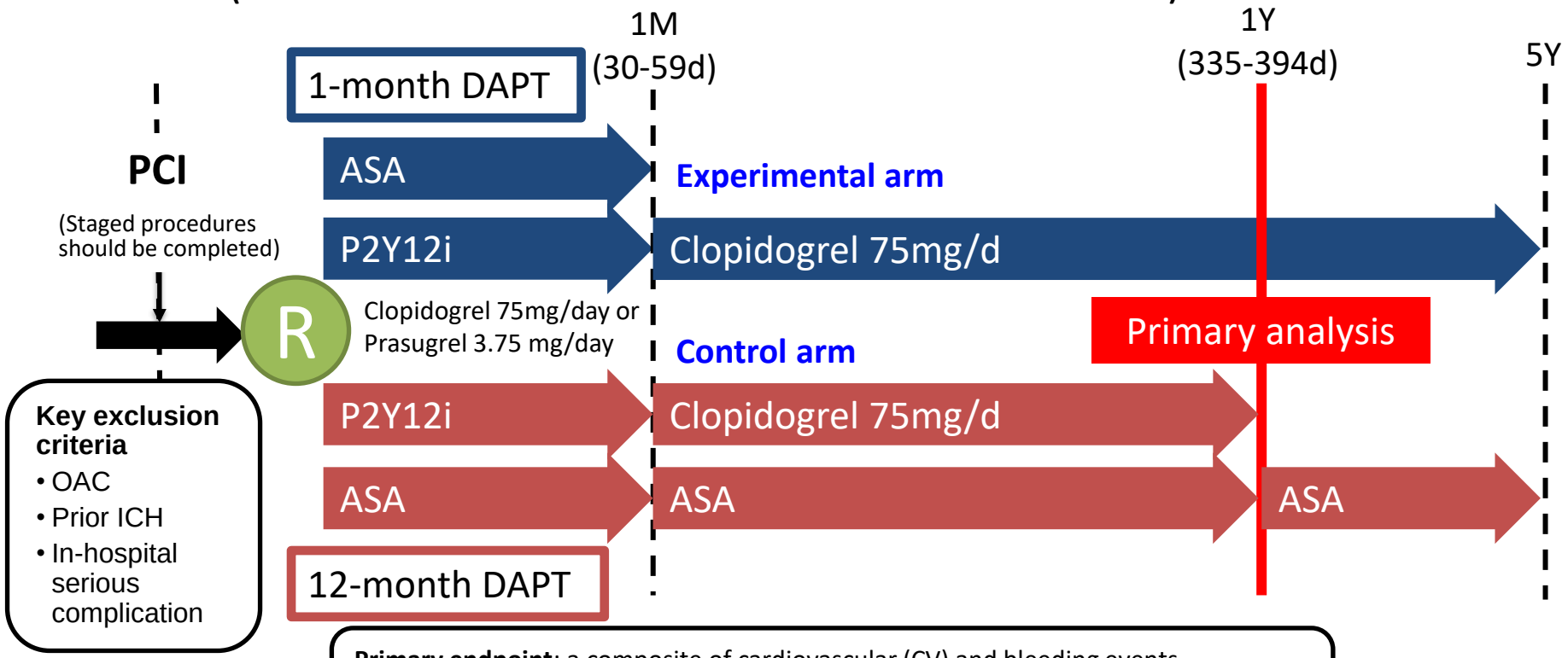
Accordingly, we should choose an antiplatelet monotherapy after short-term DAPT, that is different from ticagrelor monotherapy currently used outside Japan.

Therefore, we should conduct our own clinical trials to establish the optimal antiplatelet monotherapy following short-term DAPT after coronary DES implantation in Japan.

STOPDAPT-2 and STOPDAPT-2 ACS

Prospective multicenter open-label randomized trial comparing 1-month versus 12-month DAPT after CoCr-EES implantation

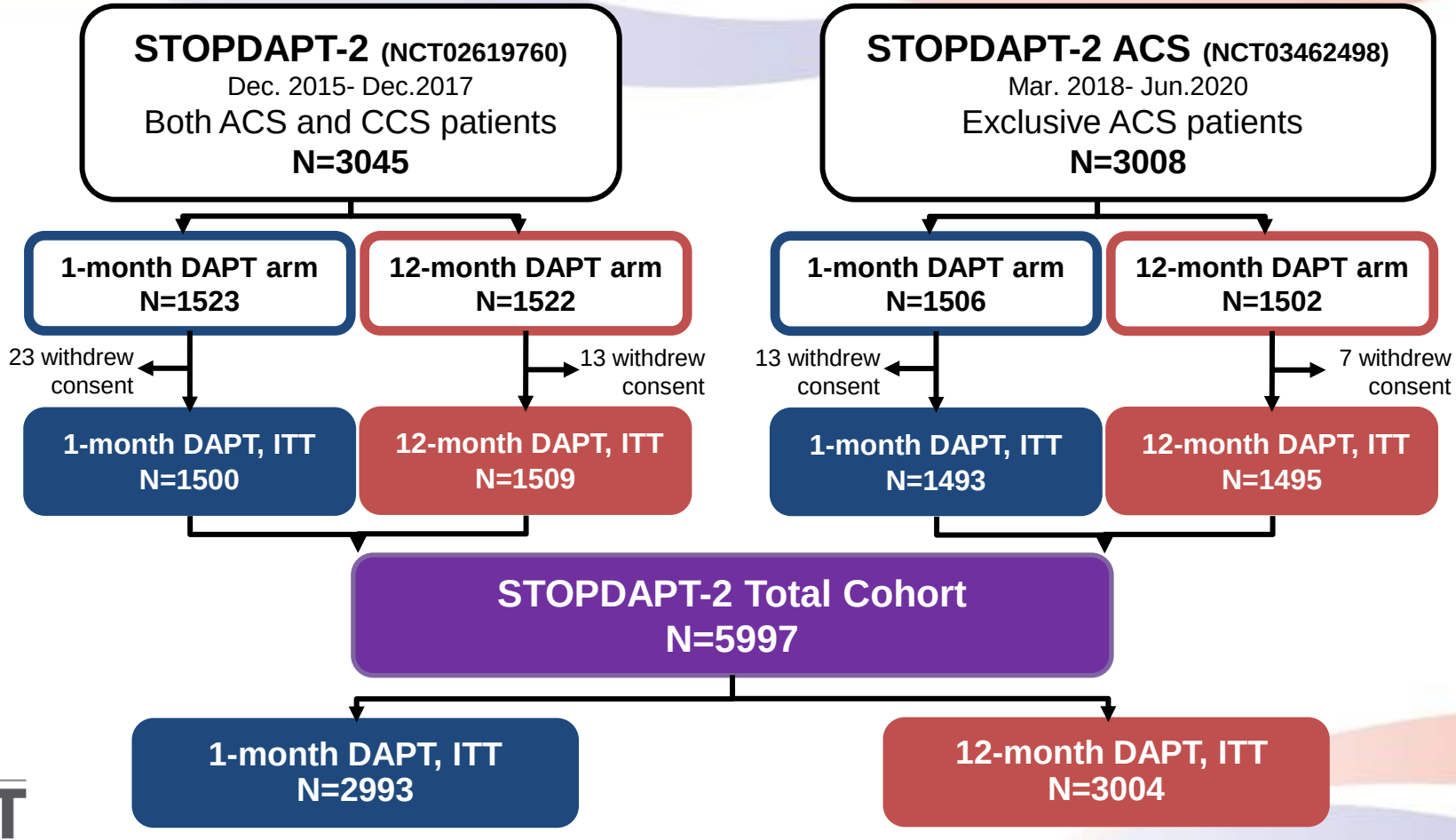
(Enrollment December 2015-October 2017 and March 2018-June 2020)



Primary endpoint: a composite of cardiovascular (CV) and bleeding events
Major secondary CV endpoint: a composite of CV death, MI, definite ST, or any stroke
Major secondary bleeding endpoint: TIMI major/minor bleeding

STOPDAPT-2 Total cohort

STOPDAPT-2 Total Cohort



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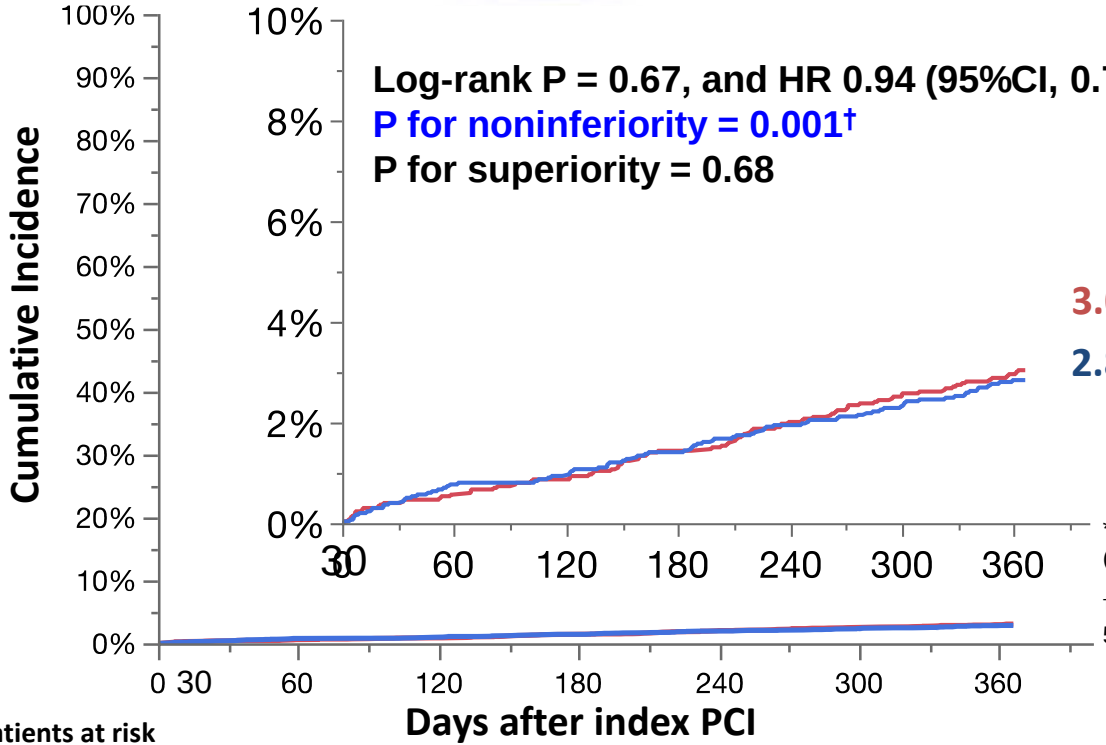
STOPDAPT-2 Total cohort

STOPDAPT-2 Total Cohort

Primary Endpoint

CV death/MI/ST/Stroke/TIMI major/minor bleeding



*Adjusted by ACS and study (STOPDAPT-2 vs. STOPDAPT-2 ACS).

†Non-inferiority margin: 50% on the hazard ratio scale

Number of patients at risk

12-month DAPT	3004	2991	2970	2959	2941	2922	2902	2327
1-month DAPT	2993	2980	2956	2946	2928	2905	2885	2357

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Circ Cardiovasc Interv 2022.

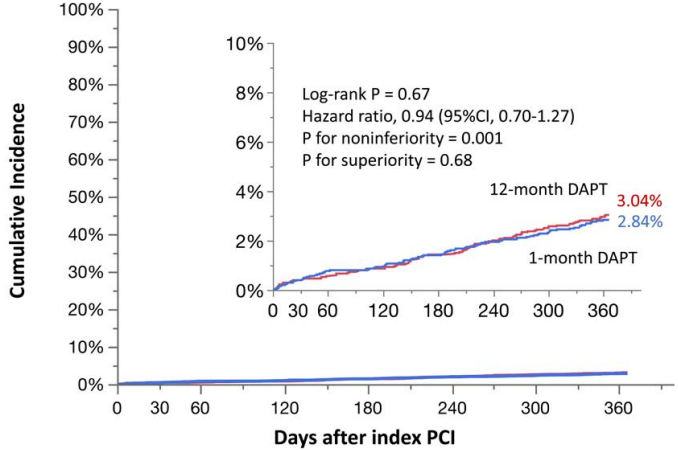
STOPDAPT-2 Total Cohort

Major Secondary Endpoints

Cardiovascular Endpoint

CV death/MI/ST/Stroke

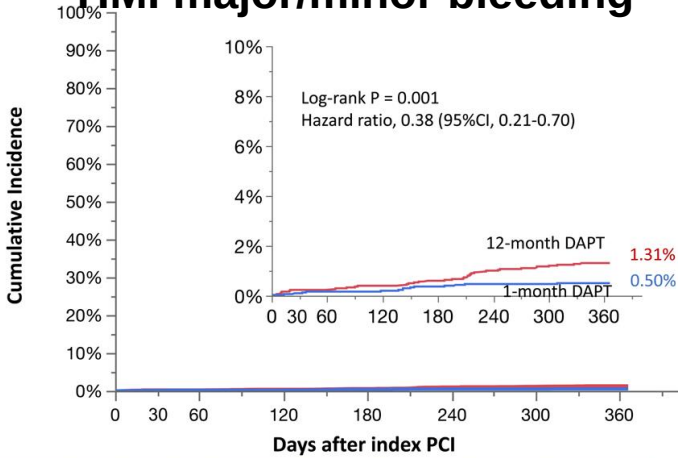
A



1-month DAPT	0	30	60	120	180	240	300	365
Number of patients with event		13	23	29	42	58	70	84
Number of patients at risk	2993	2980	2956	2946	2928	2905	2885	2357
Cumulative incidence (%)		0.43	0.77	0.97	1.41	1.95	2.35	2.84
12-month DAPT	**0**	**30**	**60**	**120**	**180**	**240**	**300**	**365**
Number of patients with event		12	18	26	43	60	77	90
Number of patients at risk	3004	2991	2970	2959	2941	2922	2902	2327
Cumulative incidence (%)		0.40	0.60	0.87	1.44	2.01	2.58	3.04

Major Bleeding Endpoint

TIMI major/minor bleeding



1-month DAPT	0	30	60	120	180	240	300	365
Number of patients with event		3	5	6	11	14	14	15
Number of patients at risk	2993	2985	2970	2965	2955	2941	2927	2400
Cumulative incidence (%)		0.10	0.17	0.20	0.37	0.47	0.47	0.50
12-month DAPT	**0**	**30**	**60**	**120**	**180**	**240**	**300**	**365**
Number of patients with event		7	8	12	18	30	36	39
Number of patients at risk	3004	2995	2977	2968	2957	2941	2929	2360
Cumulative incidence (%)		0.23	0.27	0.40	0.60	1.01	1.21	1.31

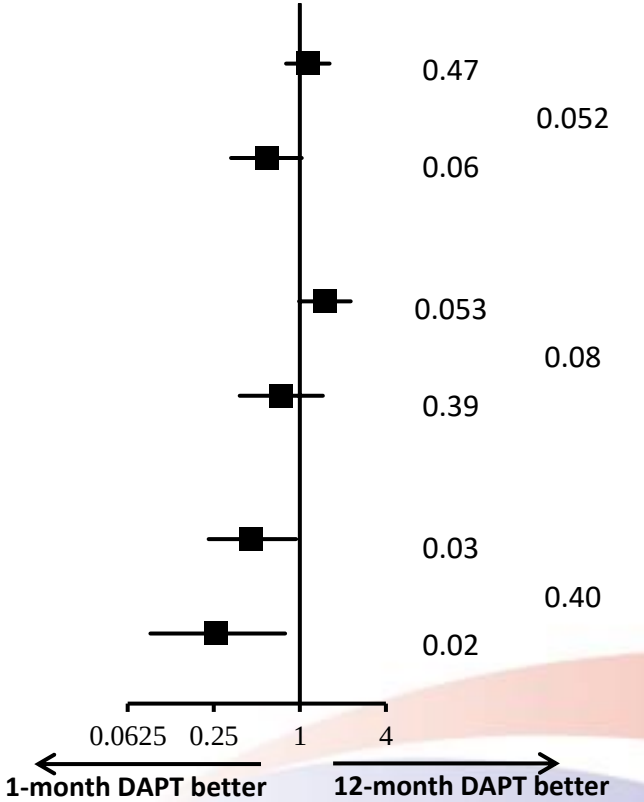
Clopidogrel monotherapy after 1-month DAPT compared to 12-month DAPT with aspirin and clopidogrel:

Significant reduction in major bleeding without increase in CV events!!

Obayashi Y, et al. Circ cardiovasc Interv. 2022.

ACS/CCS Subgroup Analysis

	1-year incidence (N with event/subtotal N) 1-month DAPT (N=2993)	12-month DAPT (N=3004)	Absolute difference (95%CI)	Hazard Ratio (95%CI)	P value	P interaction
Primary Endpoint						
ACS	3.20% 65/2058	2.83% 58/2078	0.40% (-0.68% to 1.42%)	1.14 (0.80-1.62)	0.47	0.052
CCS	2.05% 19/935	3.49% 32/926	-1.44% (-2.95% to 0.07%)	0.59 (0.33-1.03)	0.06	
Major Secondary Cardiovascular Endpoint						
ACS	2.76% 56/2058	1.86% 38/2078	0.90% (-0.02% to 1.82%)	1.50 (0.99-2.27)	0.053	0.08
CCS	1.62% 15/935	2.21% 20/926	-0.59% (-1.85% to 0.67%)	0.74 (0.38-1.45)	0.39	
Major Secondary Bleeding Endpoint						
ACS	0.54% 11/2058	1.17% 24/2078	-0.63% (-1.20% to -0.06%)	0.46 (0.23-0.94)	0.03	0.40
CCS	0.43% 4/935	1.63% 15/926	-1.20% (-2.13% to -0.27%)	0.26 (0.09-0.79)	0.02	



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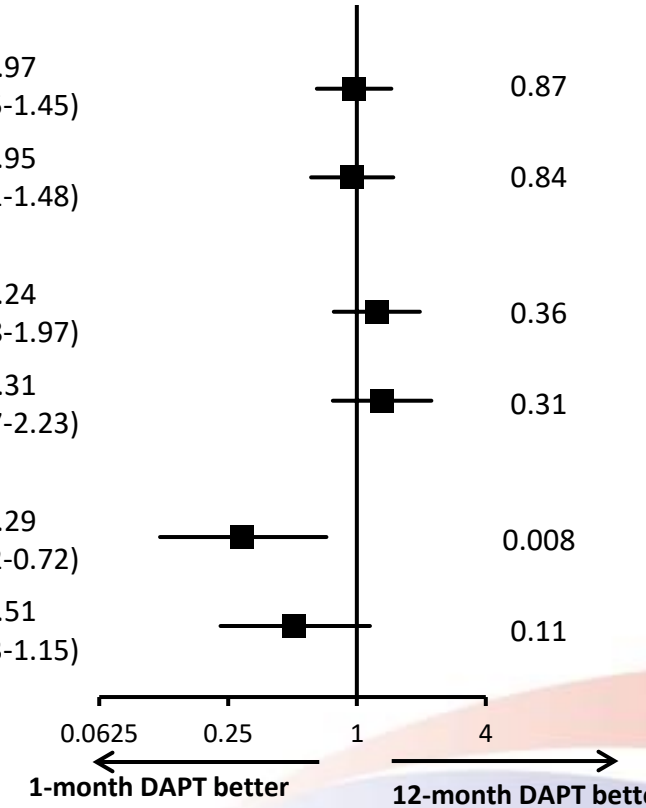
STOPDAPT-2 Total cohort

HBR Subgroup Analysis

	1-year incidence (N with event/subtotal N)				P value	P interaction
	1-month DAPT (N=2993)	12-month DAPT (N=3004)	Absolute difference (95%CI)	Hazard Ratio (95%CI)		
Primary Endpoint						
HBR	5.01% (45/912)	5.14% (50/981)	-0.13% (-2.13% to 1.87%)	0.97 (0.65-1.45)	0.87	0.95
Non-HBR	1.90% (39/2081)	2.02% (40/2023)	-0.12% (-0.98% to 0.74%)	0.95 (0.61-1.48)	0.84	
Major Secondary Cardiovascular Endpoint						
HBR	4.35% (39/912)	3.52% (34/981)	0.83% (-0.93% to 2.59%)	1.24 (0.78-1.97)	0.36	0.90
Non-HBR	1.56% (32/2081)	1.22% (24/2023)	0.34% (-0.38% to 1.06%)	1.31 (0.77-2.23)	0.31	
Major Secondary Bleeding Endpoint						
HBR	0.66% (6/912)	2.27% (22/981)	-1.61% (-2.69% to -0.53%)	0.29 (0.12-0.72)	0.008	0.36
Non-HBR	0.43% (9/2081)	0.85% (17/2023)	-0.42% (-0.90% to 0.06%)	0.51 (0.23-1.15)	0.11	



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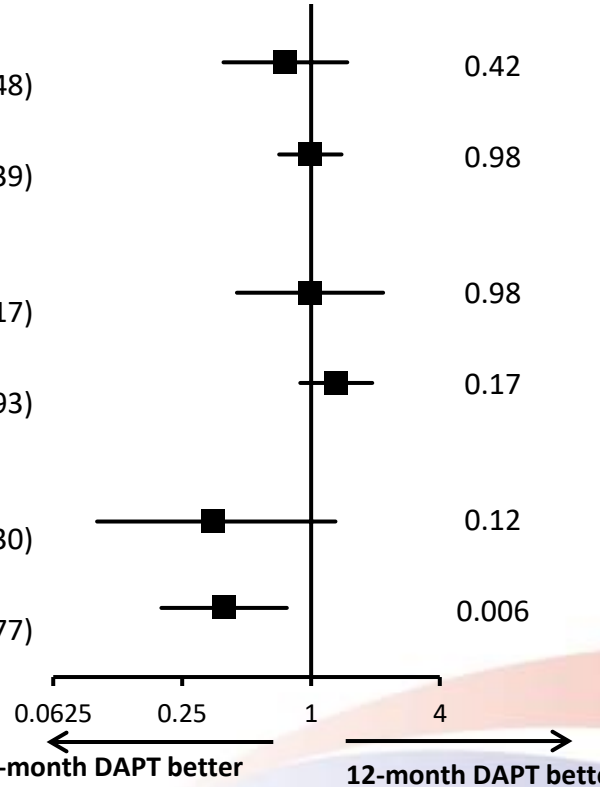
STOPDAPT-2 Total cohort

Complex PCI Subgroup Analysis

	1-year incidence (N with event/subtotal N)				P value	P interaction
	1-month DAPT (N=2993)	12-month DAPT (N=3004)	Absolute difference (95%CI)	Hazard Ratio (95%CI)		
Primary Endpoint						
Complex PCI	3.15% (15/481)	4.07% (21/518)	-0.92% (-3.24% to 1.40%)	0.76 (0.39-1.48)	0.42	0.48
Non-complex PCI	2.78% (69/2512)	2.82% (69/2486)	-0.04% (-0.97% to 0.89%)	0.99 (0.71-1.39)	0.98	
Major Secondary Cardiovascular Endpoint						
Complex PCI	2.53% (12/481)	2.52% (13/518)	0.01% (-1.94% to 1.96%)	0.99 (0.45-2.17)	0.98	0.53
Non-complex PCI	2.38% (59/2512)	1.86% (45/2486)	0.52% (-0.29% to 1.33%)	1.31 (0.89-1.93)	0.17	
Major Secondary Bleeding Endpoint						
Complex PCI	0.63% (3/481)	1.75% (9/518)	-1.12% (-2.46% to 0.22%)	0.35 (0.10-1.30)	0.12	0.90
Non-complex PCI	0.48% (12/2512)	1.22% (30/2486)	-0.74% (-1.25% to -0.23%)	0.39 (0.20-0.77)	0.006	



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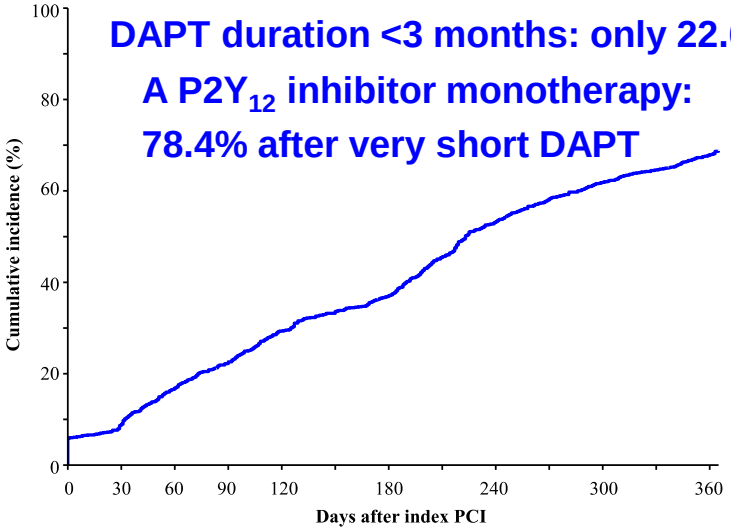
Penetration and CV Outcomes of Very Short DAPT in the OPTIVUS Complex PCI Multivessel Cohort Conducted after Release of the STOPDAPT-2 Trial Results

(March 2019-Apr 2021)

DAPT discontinuation

DAPT duration <3 months: only 22.6%

A $P2Y_{12}$ inhibitor monotherapy: 78.4% after very short DAPT



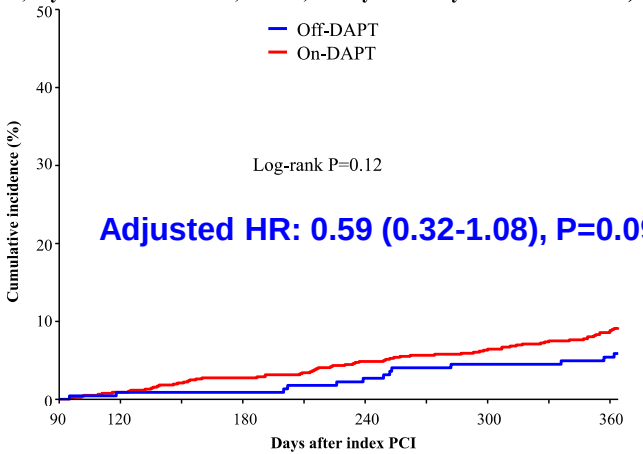
Interval	0	30	60	90	120	180	240	300	365
Number of patients with discontinuation		88	166	222	288	364	522	606	672
Number of patients at risk	982	897	819	764	692	617	459	371	296
Cumulative incidence (%)		9.0	16.9	22.6	29.3	37.1	53.3	61.9	68.8

Primary endpoint

at 3 months

at 3 months

(A composite of death, myocardial infarction, stroke, or any coronary revascularization)



Adjusted HR: 0.59 (0.32-1.08), P=0.09

Interval	90	120	180	240	300	365
Off-DAPT						
Number of patients with event		2	2	6	10	13
Number of patients at risk	222	220	220	217	212	199
Cumulative incidence (%)		0.9	0.9	2.7	4.5	5.9
On-DAPT						
Number of patients with event		7	21	37	48	70
Number of patients at risk	760	753	739	722	710	674
Cumulative incidence (%)		0.9	2.8	4.9	6.3	9.2

Yamamoto K, et al. Circ J. 2023.

STOPDAPT-3 Trial Exploring Completely Aspirin-free Strategy

＜Entry Criteria＞

1. **PCI with planned exclusive use of CoCr-EES (XIENCE)**
2. **ACS presentation or ARC-HBR**
3. **Eligible for DAPT (Aspirin/$P2Y_{12}$ inhibitor) for 1 month**

No Exclusion Criteria

Informed Consent Before Angiography

Randomization After Angiography, but Before PCI

Loading: Prasugrel 20mg

Loading Aspirin also, if Aspirin naïve

No aspirin Group

3001 Patients

Prasugrel Monotherapy for 1M

1-month DAPT Group

3001 Patients

DAPT (Aspirin and Prasugrel) for 1M

Primary Analysis at 1-Month

Co-primary Bleeding Endpoint ： BARC 3 or 5 bleeding at 1M (Superiority)

Co-primary Cardiovascular Endpoint : CV death/MI/Ischemic Stroke/ST at 1M (Non-inferiority)

Clopidogrel Monotherapy
Between 1M and 12 M

Exploratory Analysis

Aspirin Monotherapy
Between 1M and 12 M

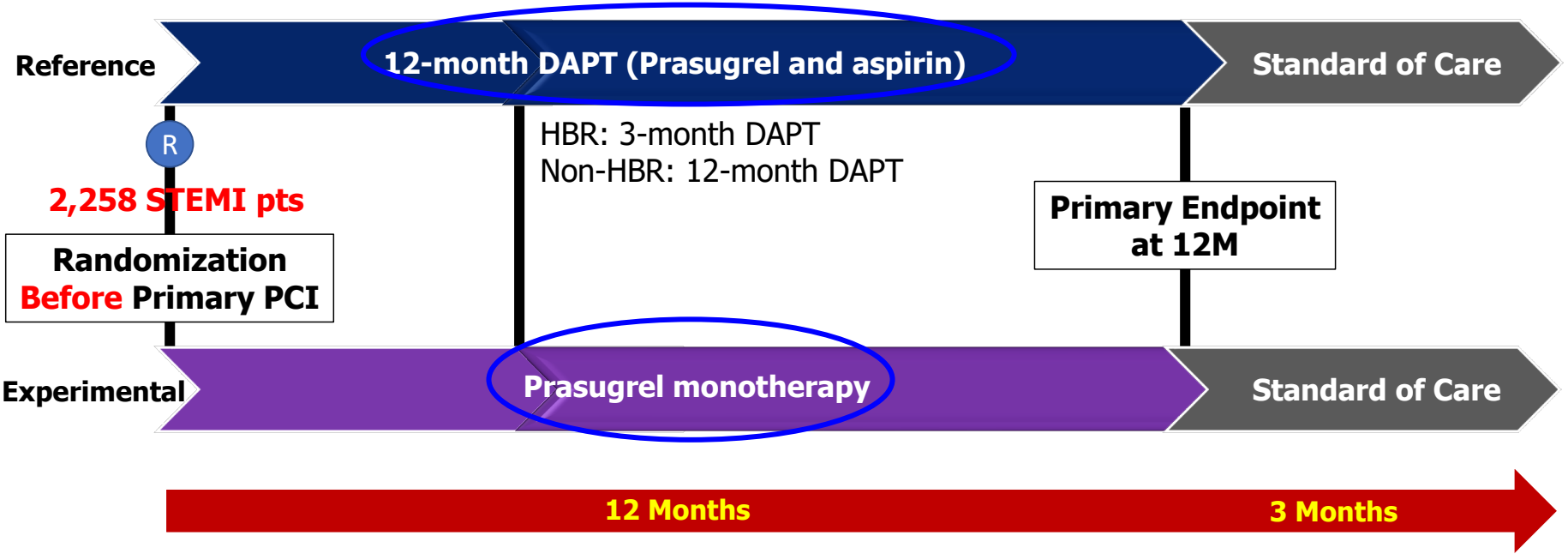
PREMIUM Trial

Multicenter, open-label, randomized controlled trial

PIs: Professor Gaku Nakazawa, Professor Ken Kozuma, Professor Yoshihiro Morino

Primary endpoint: MACE: All-cause death, MI, or stroke at 12 months for Non-inferiority

Major Secondary endpoint: BARC type 3 or 5 bleeding at 12 months for Superiority



Conclusions

Clopidogrel monotherapy after 1-month DAPT compared with 12-month DAPT with aspirin and clopidogrel had a benefit in reducing major bleeding events without significant increase in cardiovascular events in the STOPDAPT 2 Total Cohort.

However, given a numerical increase in cardiovascular events with clopidogrel monotherapy after 1-month DAPT in ACS patients, further studies would be warranted to explore the optimal antiplatelet monotherapy after short-term DAPT in ACS patients.