STOPDAPT-2 Total Cohort:

Pooled Results from Two Randomized Controlled Trials of Clopidogrel Monotherapy After 1-Month DAPT Following PCI, and Subgroup Analyses by ACS Presentation, HBR, and Complex PCI

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On behalf of the STOPDAPT-2 and STOPDAPT-2 ACS investigators.

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Disclosure Statement of Financial Interest

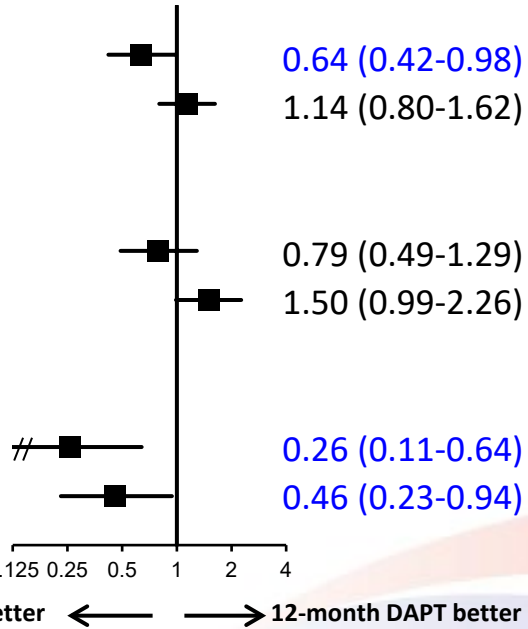
I, [Yuki Obayashi, and Ko Yamamoto] DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Faculty disclosure information can be found on the app

Background and Objective (1)

- Both STOPDAPT-2[1)] and STOPDAPT-2 ACS[2)] trials were underpowered based on the actual event rates.

	N of event/Total (incidence %)				HR (95%CI)	Post-hoc actual stat. power*
	1-month DAPT		12-month DAPT			
Primary endpoint						
STOPDAPT-2 (N=3009)	35/1500	(2.37%)	55/1509	(3.72%)	0.64 (0.42-0.98)	77%
STOPDAPT-2 ACS (N=4136)	65/2058	(3.20%)	58/2078	(2.83%)	1.14 (0.80-1.62)	78%
Major secondary CV endpoint						
STOPDAPT-2	29/1500	(1.96%)	37/1509	(2.55%)	0.79 (0.49-1.29)	60%
STOPDAPT-2 ACS	56/2058	(2.76%)	38/2078	(1.86%)	1.50 (0.99-2.26)	60%
Major secondary bleeding endpoint						
STOPDAPT-2	6/1500	(0.41%)	23/1509	(1.54%)	0.26 (0.11-0.64)	89%
STOPDAPT-2 ACS	11/2058	(0.54%)	24/2078	(1.17%)	0.46 (0.23-0.94)	60%



1) Watanabe et al. JAMA. 2019;321(24):2414-2427.
2) Watanabe et al. Presented at ESC Congress 2021

Background and Objective (2)

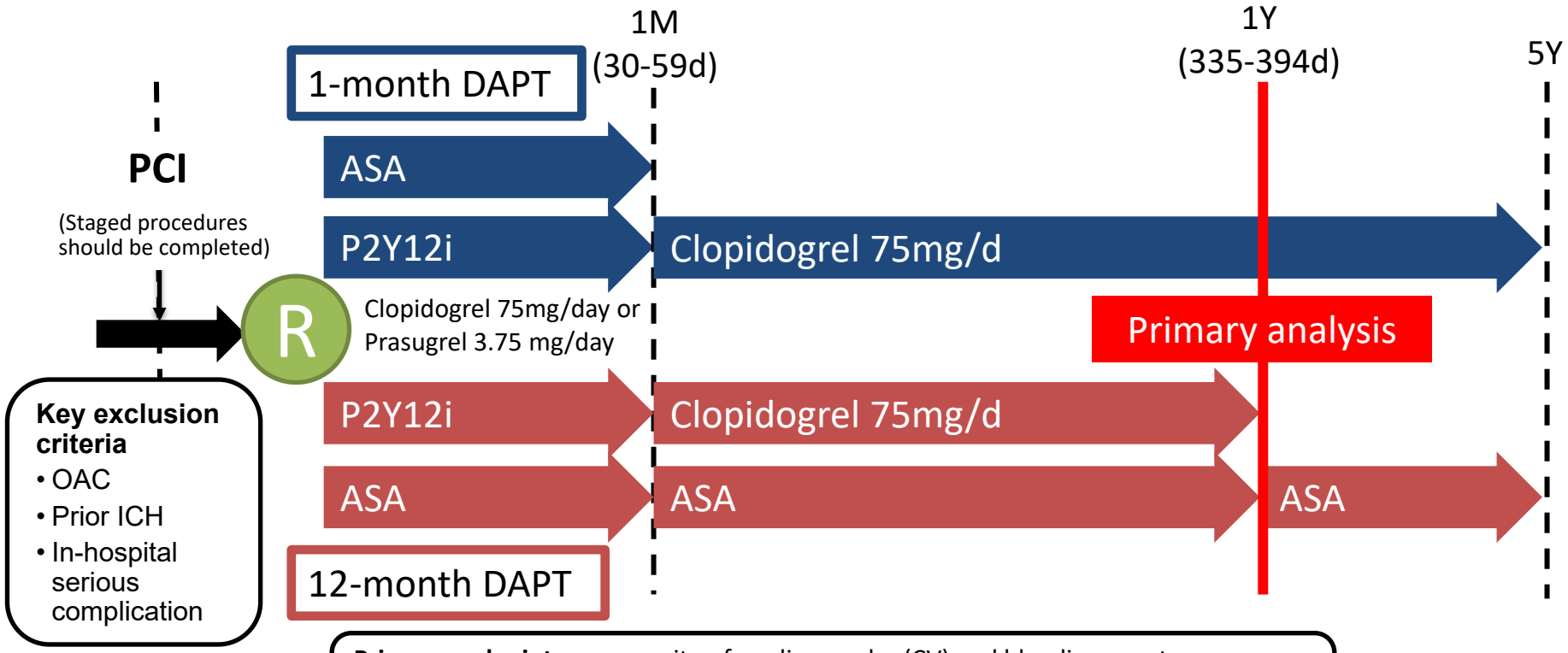
- Moreover, ACS presentation, high bleeding risk (HBR) and complex PCI are often taken into consideration in adopting shorter or longer DAPT durations in real clinical practice.

- Therefore, we sought to evaluate the safety and efficacy of clopidogrel monotherapy after 1-month DAPT relative to 12-month DAPT in the STOPDAPT-2 Total Cohort (the pooled population of the STOPDAPT-2 and the STOPDAPT-2 ACS) with an increased power, and to explore the treatment-by-subgroup interaction for ACS, HBR, and complex PCI.

STOPDAPT-2 Total cohort

STOPDAPT-2 and STOPDAPT-2 ACS

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



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

Acknowledgement

104 participating centers
(Top 10 enrollers)

Teine Keijinkai Hospital
Megumino Hospital
Hokko Memorial Hospital
Hirosaki University Hospital
Iwate Medical University Hospital
Nakadori General Hospital
Sendai Kousei Hospital
Sendai Cardiovascular Center
Tohoku Medical and Pharmaceutical University Hospital
Nihonkai General Hospital
Hoshi General Hospital
Jichi Medical University Hospital
Mito Saiseikai General Hospital
Kawaguchi Cardiovascular and Respiratory Hospital
Mashiko Hospital
Ageo Central General Hospital
Mitsui Memorial Hospital
Toranomon Hospital
Juntendo University Hospital
Edogawa Hospital
Showa University Koto Toyosu Hospital
Tokyo Women's Medical University Hospital
Tokyo General Hospital
Juntendo University Nerima Hospital
Kawakita General Hospital
Sakakibara Heart Institute
Tokyo Metropolitan Tama Medical Center
Minamino Cardiovascular Hospital
Higashiyamato Hospital
St.Marianna University School of Medicine Hospital
Yokohama Rosai Hospital
Showa University Fujigaoka Hospital
Saiseikai Yokohamashi Tobu Hospital
Yokohama City University Medical Center
Fujisawa City Hospital
Kitasato University Hospital
Hiratsuka Kyosai Hospital
Tokai University Hospital
Kimitsu Central Hospital
Kanazawa Cardiovascular Hospital
University of Fukui Hospital
Municipal Tsuruga Hospital
University of Yamanashi Hospital
Gifu Prefectural General Medical Center
Ogaki Municipal Hospital
Juntendo University Shizuoka Hospital
Shizuoka General Hospital
Shizuoka Saiseikai General Hospital
Nagoya Daini Red Cross Hospital
Handa City Hospital
Tosei General Hospital
Ichinomiyanishi Hospital
Yokkaichi Hazu Medical Center
Matsusaka Central General Hospital
Nabari City Hospital
Otsu Red Cross Hospital
Hikone Municipal Hospital
Kyoto University Hospital
Uji Tokushukai Hospital
Kyoto Medical Center
Mitsubishi Kyoto Hospital
Kitano Hospital
Osaka Red Cross Hospital
Osaka General Medical Center
National Cerebral and Cardiovascular Center
Kindai University Hospital
Mimihara General Hospital
Bell Land General Hospital
Kobe City Medical Center General Hospital
Tsukazaki Hospital
Kindai University Nara Hospital
Tenri Hospital
Japanese Red Cross Wakayama Medical Center
Wakayama Medical University Hospital
Okayama Medical Center
Shimane University Hospital
Japanese Red Cross Okayama Hospital
Kurashiki Central Hospital
Hiroshima University Hospital
Hiroshima Prefectural Hospital
Iwakuni Medical Center
Tokuyama Central Hospital
Shimonoseki City Hospital
Tokushima University Hospital
Tokushima Red Cross Hospital
Kagawa Prefectural Central Hospital
Ehime Prefectural Central Hospital
Matsuyama Red Cross Hospital
Chikamori Hospital
Kokura Memorial Hospital
Hospital of University of Occupational and Environmental Health Japan
Saiseikai Fukuoka General Hospital
Iizuka Hospital
Fukuoka Tokushukai Hospital
Saga University Hospital
Kumamoto University Hospital
Saiseikai Kumamoto Hospital
Japanese Red Cross Kumamoto Hospital
Hitoyoshi Medical Center
Miyazaki Prefectural Nobeoka Hospital
Ibusuki Medical Center
Izumi Regional Medical Center
Urasoe General Hospital
Nakagami Hospital

Coordinating center

Research Institute for Production Development

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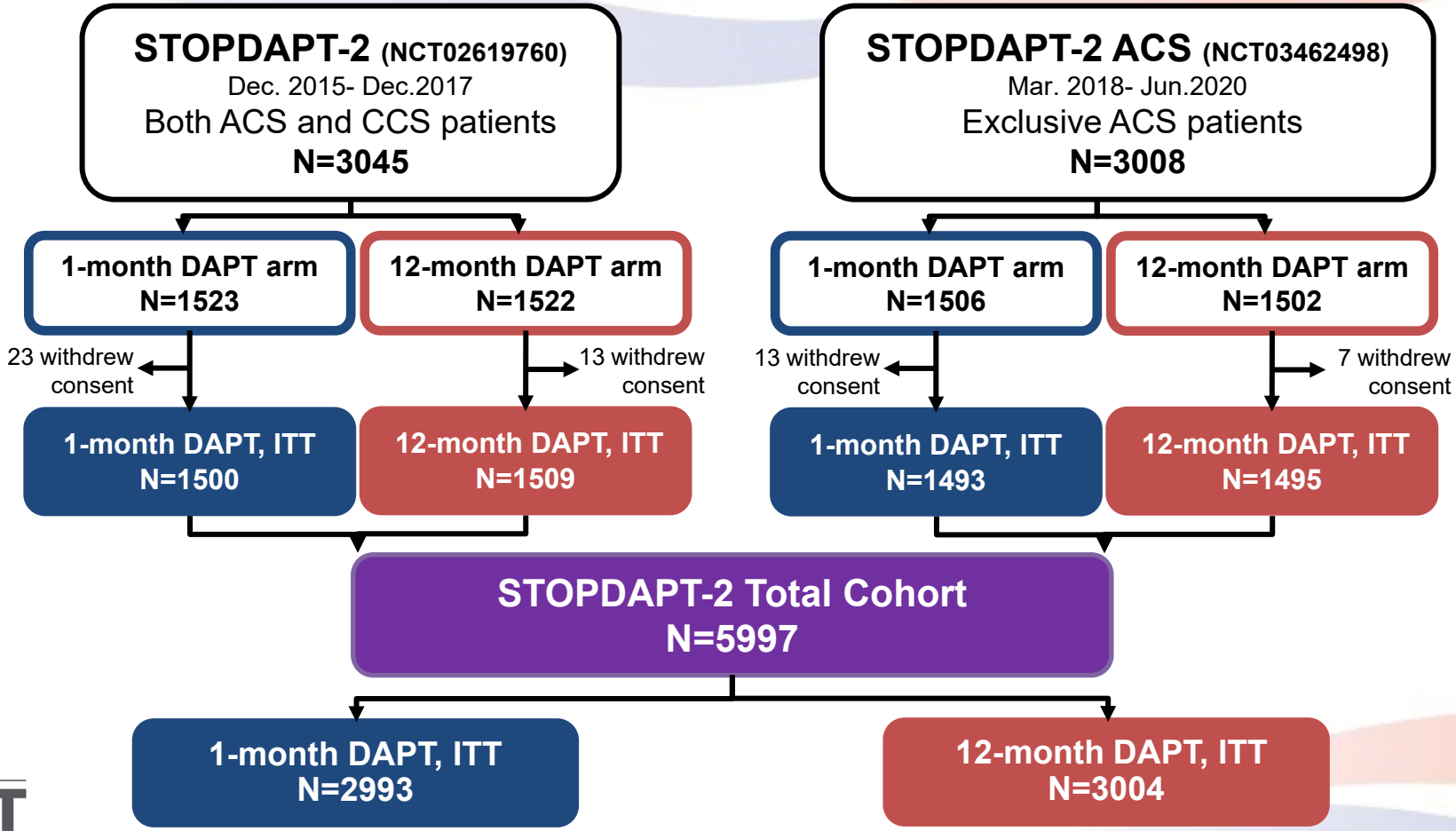
STOPDAPT-2 Total cohort

Study Flow



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STOPDAPT-2 Total cohort

Key baseline characteristics

	1-month DAPT N=2993	12-month DAPT N=3004
Age, years	67.7±11.4	67.9±11.4
Male	79%	78%
ACS	69%	69%
Prior MI	10%	9%
Prior stroke	5%	6%
Diabetes	34%	34%
Severe CKD	5%	5%
Staged procedure	12%	14%
Radial approach	88%	88%
No of target lesions	1.26±0.58	1.29±0.61
Two or more target vessels	17%	19%
IVUS or OCT	97%	98%
Clopidogrel	57%	58%
Prasugrel (3.75mg/day)	43%	42%
Statin/High intensity statin	93%/25%	93%/25%
PPI	86%	87%

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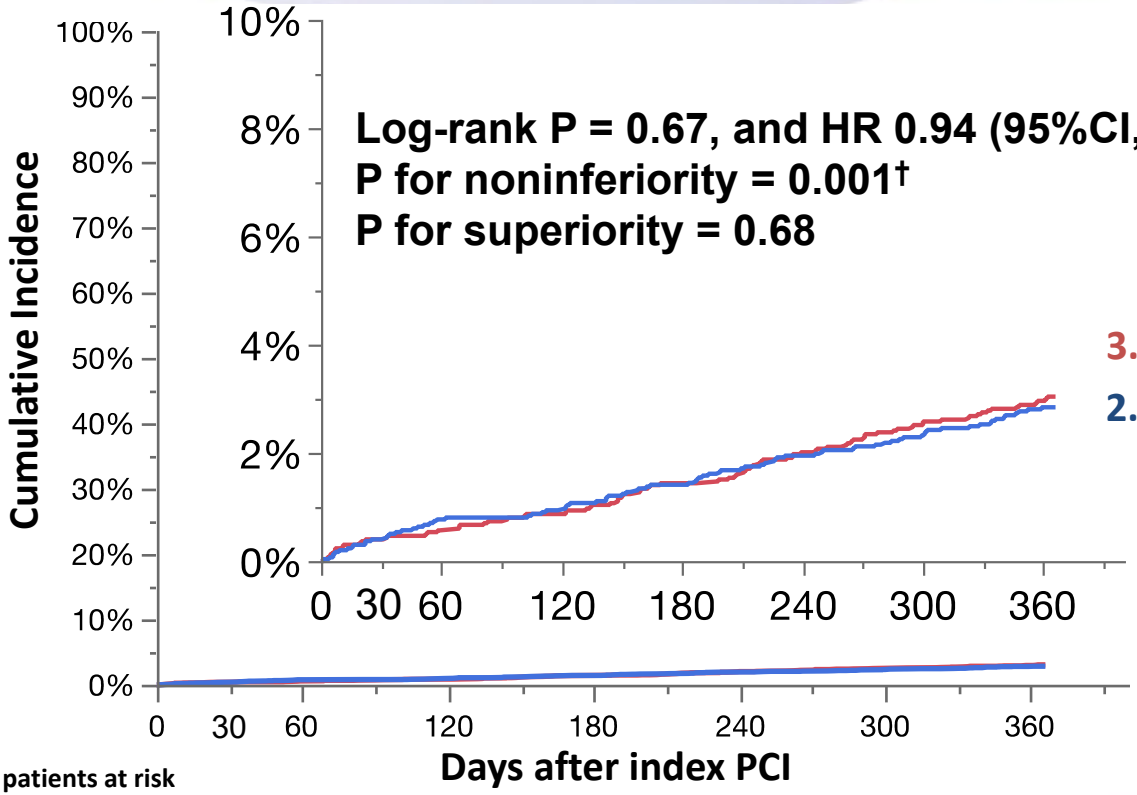
Primary Endpoint

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

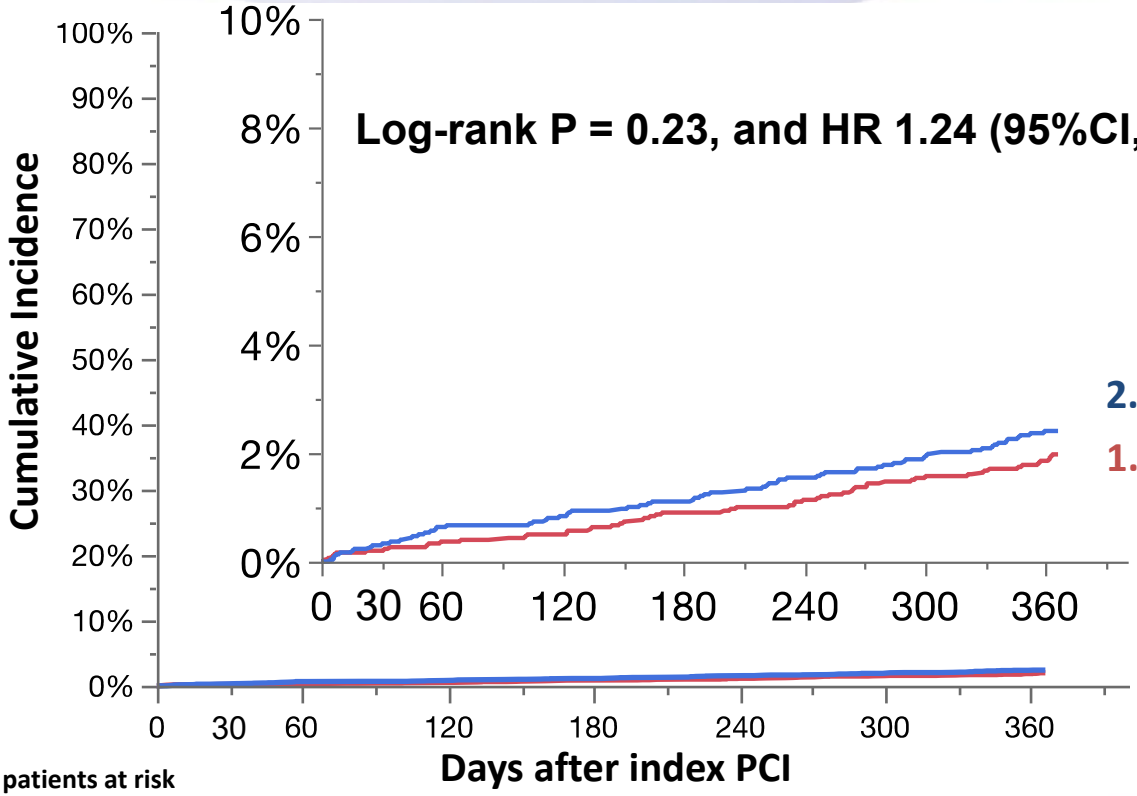
Number of patients at risk

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

STOPDAPT-2 Total cohort

Major Secondary CV Endpoint

CV death/MI/ST/Stroke



Log-rank P = 0.23, and HR 1.24 (95%CI, 0.88–1.75)*

2.40% 1-month DAPT

1.97% 12-month DAPT

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

Number of patients at risk

12-month DAPT	3004	2997	2977	2970	2957	2947	2930	2352
1-month DAPT	2993	2983	2960	2950	2937	2917	2897	2369

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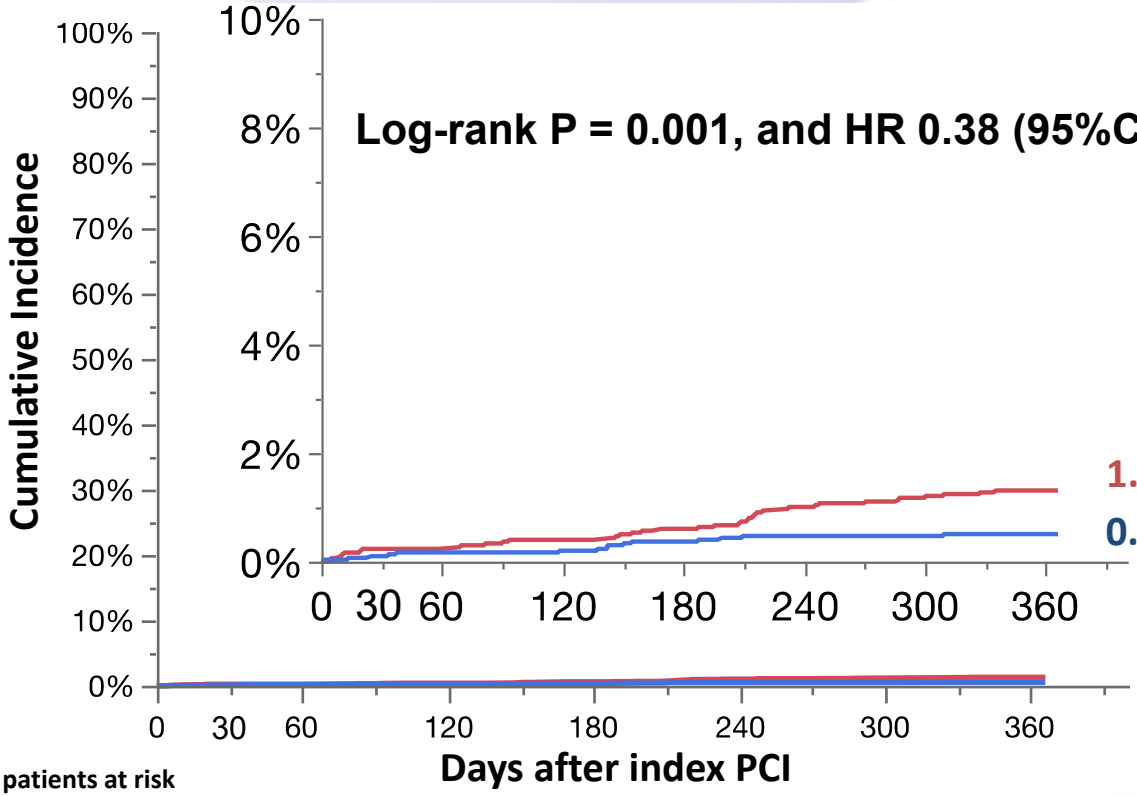
STOPDAPT-2 Total cohort

Major Secondary Bleeding Endpoint

TIMI major/minor bleeding



Log-rank P = 0.001, and HR 0.38 (95%CI, 0.21–0.70)*

1.31% 12-month DAPT

0.50% 1-month DAPT

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

Number of patients at risk

12-month DAPT	3004	2995	2977	2968	2957	2941	2929	2360
1-month DAPT	2993	2985	2970	2965	2955	2941	2927	2400

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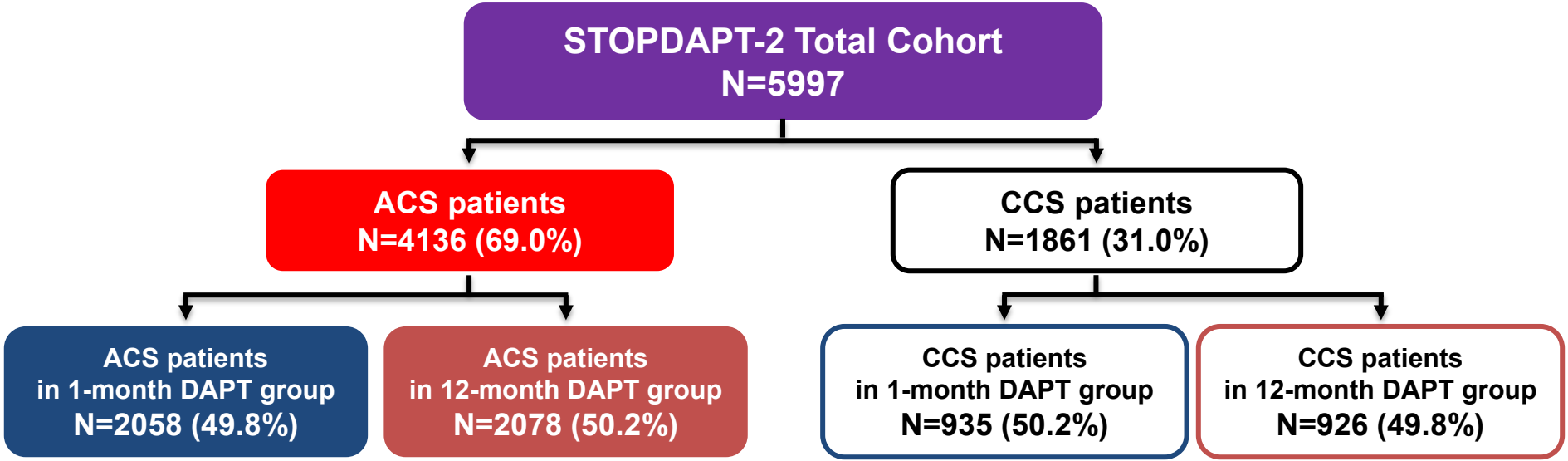
Subgroup analysis #1:

Acute Coronary Syndrome and Chronic Coronary Syndrome



STOPDAPT-2 Total cohort

Key baseline characteristics

	ACS N=4136	CCS N=1861	P value
Age, years	66.8±11.9	69.9±9.8	<0.001
Male	79%	77%	0.01
Prior MI	6%	18%	<0.001
Prior stroke	5%	7%	<0.001
Diabetes	30%	43%	<0.001
Severe CKD	3%	7%	<0.001
Emergency procedure	82%	2%	<0.001
Staged procedure	14%	10%	<0.001
Radial approach	89%	85%	<0.001
No of target lesions	1.27±0.59	1.28±0.60	0.82
Two or more target vessels	18%	18%	0.74
IVUS or OCT	97%	98%	0.04
Clopidogrel/Prasugrel (3.75mg/day)	53%/47%	68%/32%	<0.001/<0.001
β-blocker	59%	37%	<0.001
ACE-I or ARB	76%	56%	<0.001
Statin/High intensity statin	97%/34%	84%/4%	<0.001
PPI	92%	73%	<0.001

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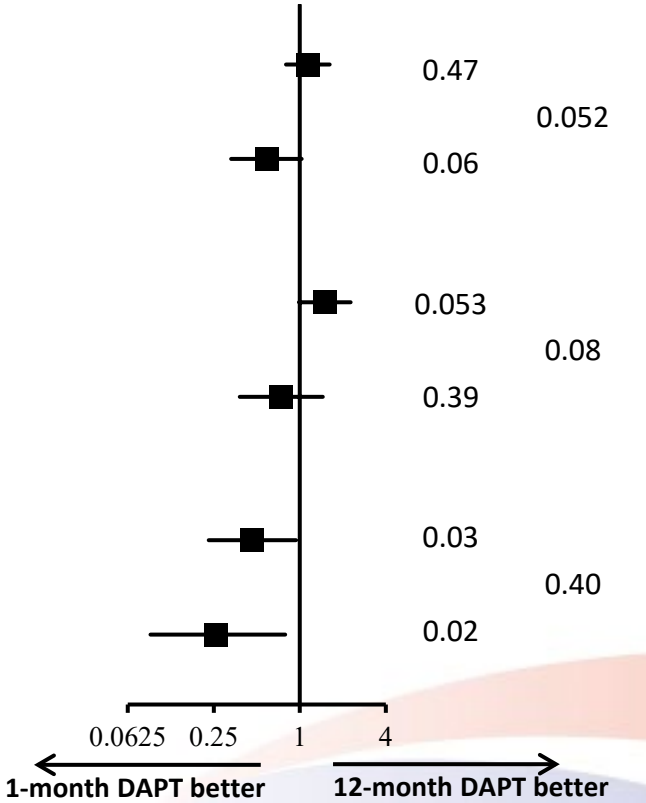
STOPDAPT-2 Total cohort

Subgroup analysis #1: ACS/CCS

	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						
ACS[1)]	3.20% 65/2058	2.83% 58/2078	0.37% (-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[1)]	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[1)]	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	



1) Watanabe et al. Presented at ESC Congress 2021

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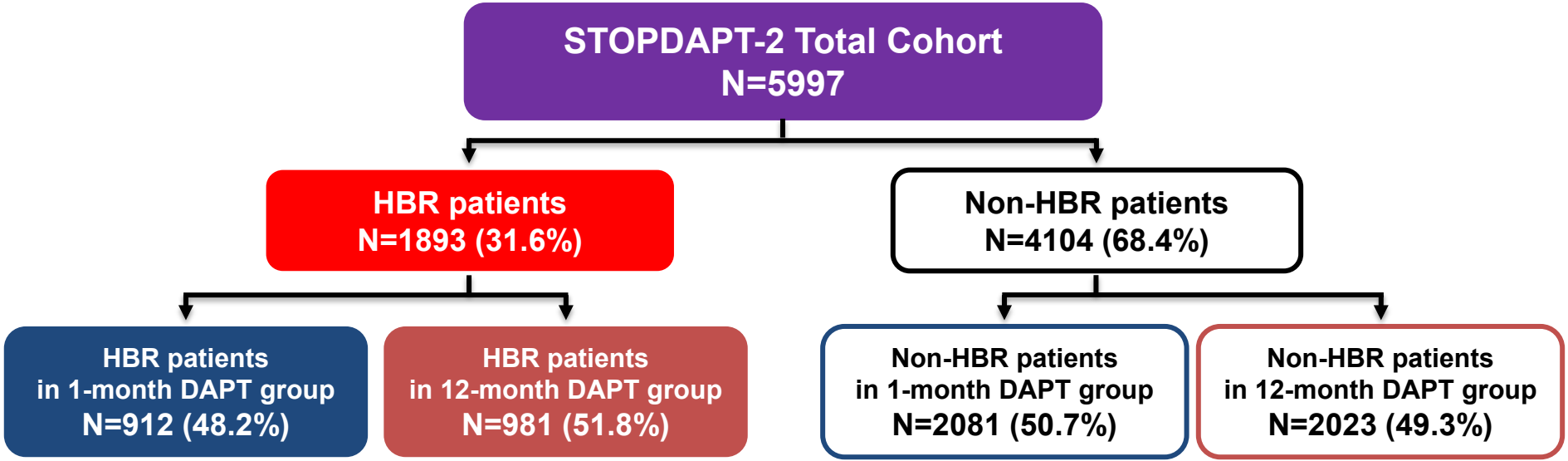
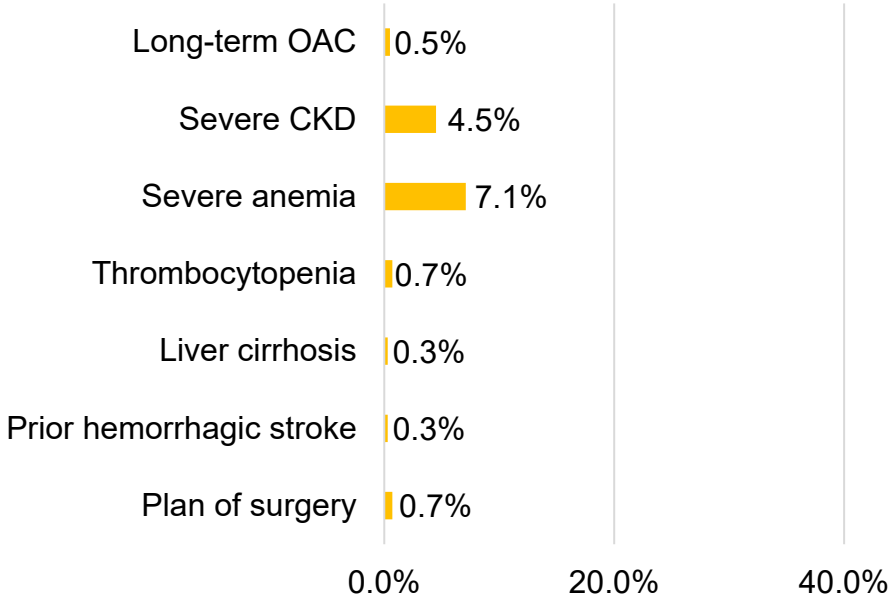
Subgroup analysis #2:
HBR and Non-HBR

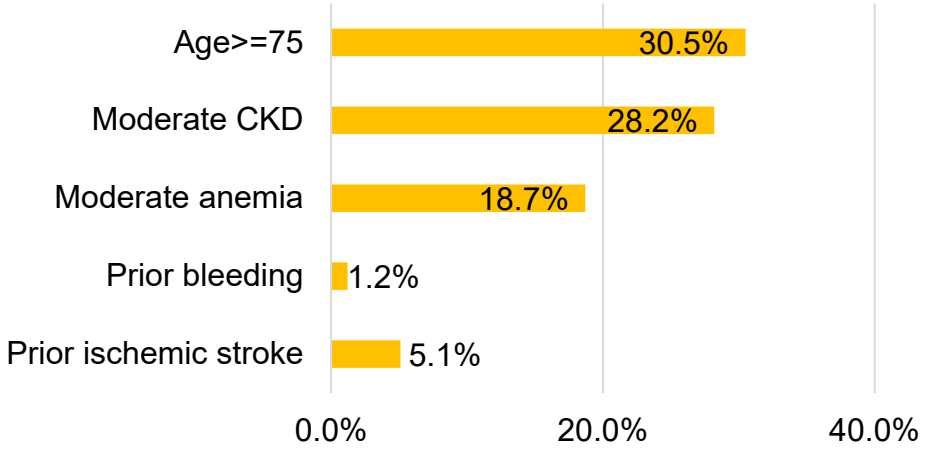


Prevalence of HBR criteria

Major criteria



Minor criteria



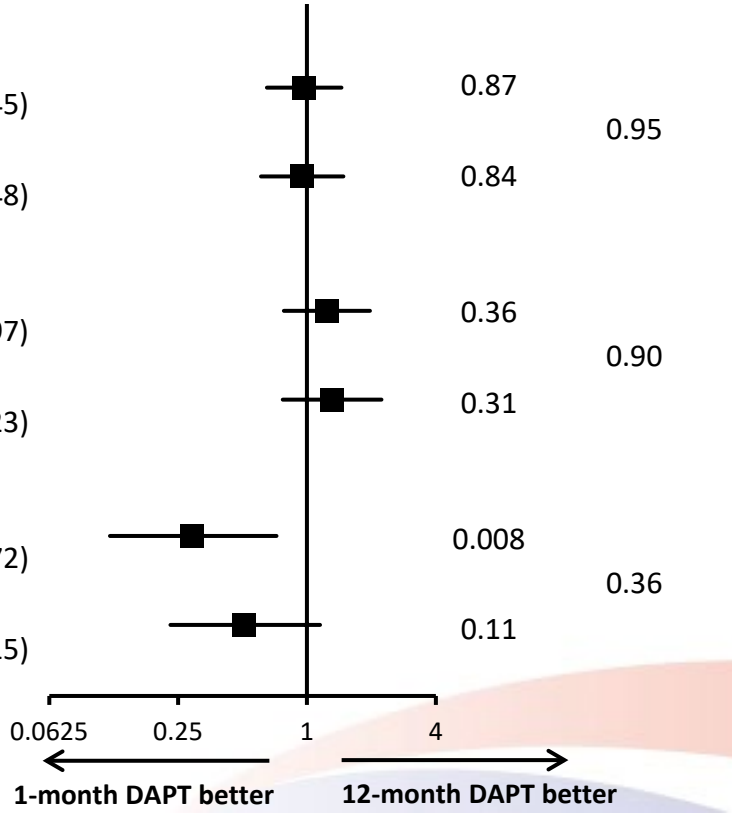
HBR was defined as having at least one major criterion or two minor criteria of ARC-HBR.[1]
We modified the ARC-HBR definitions, because some criteria of ARC-HBR were not exactly captured in this study.

1. Urban et al. Eur Heart J. 2019;40:2632-2653

STOPDAPT-2 Total cohort

Subgroup analysis #2: HBR

	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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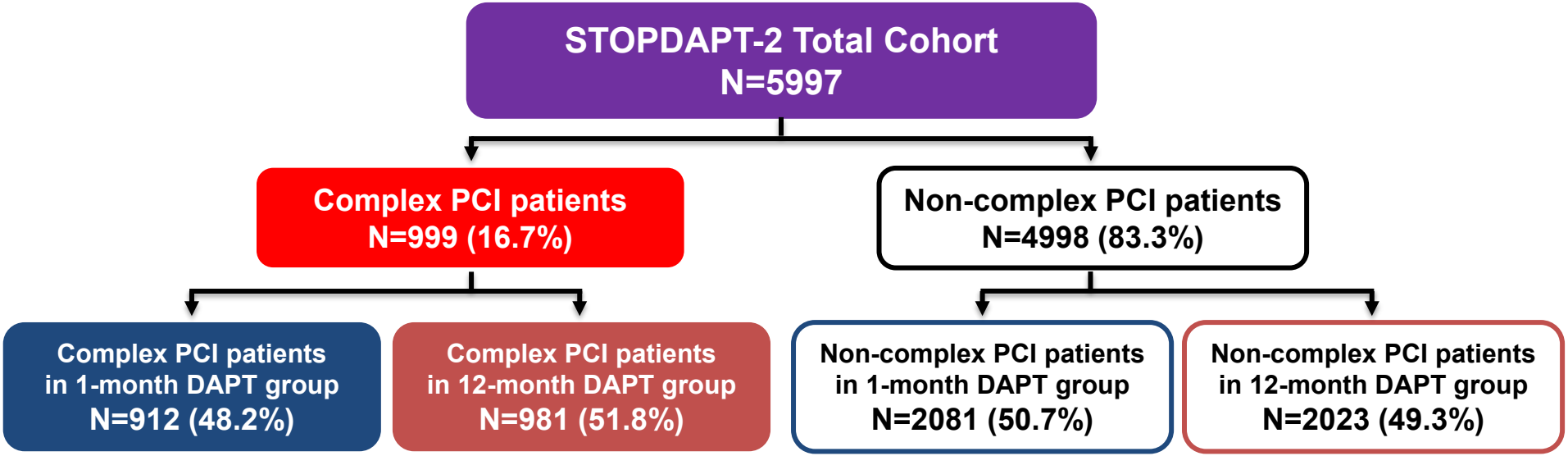
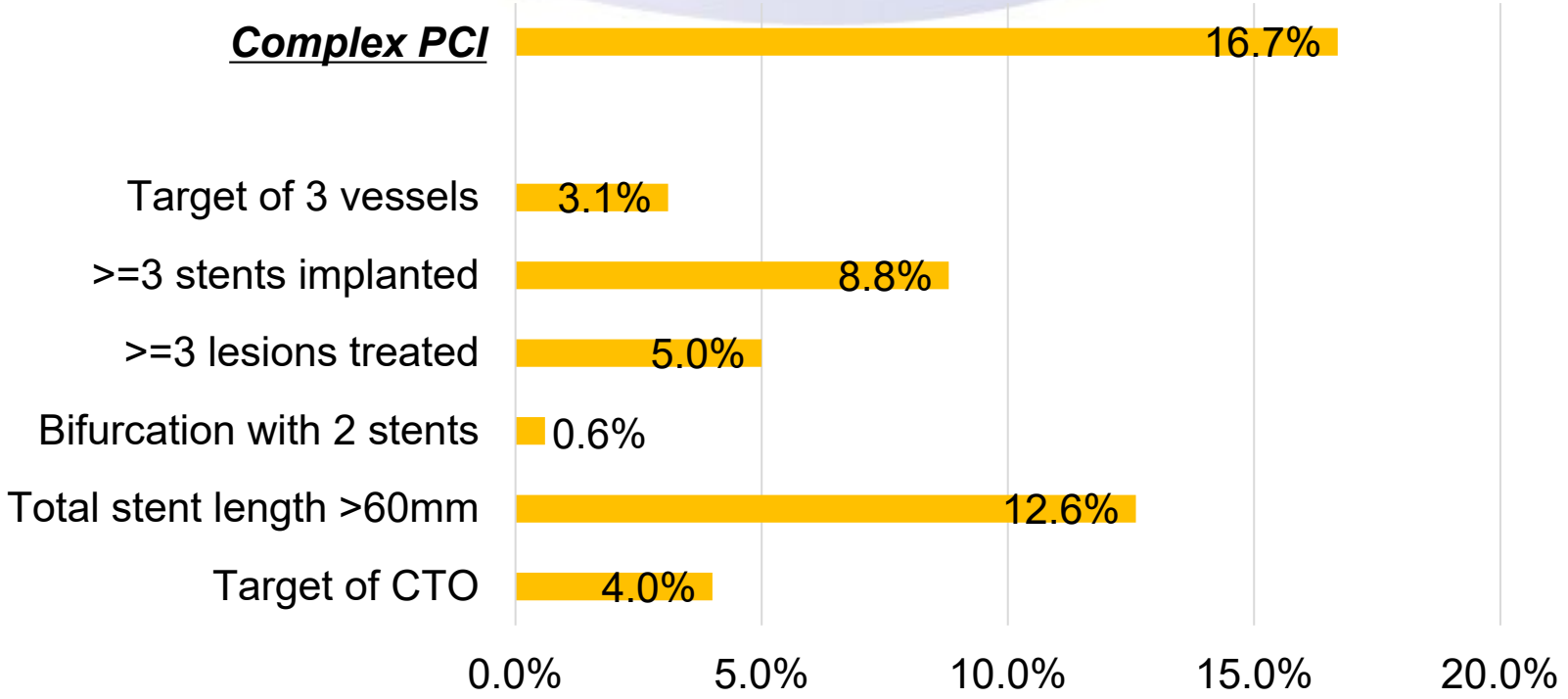
Subgroup analysis #3:
Complex PCI and Non-complex PCI



Prevalence of complex PCI criteria



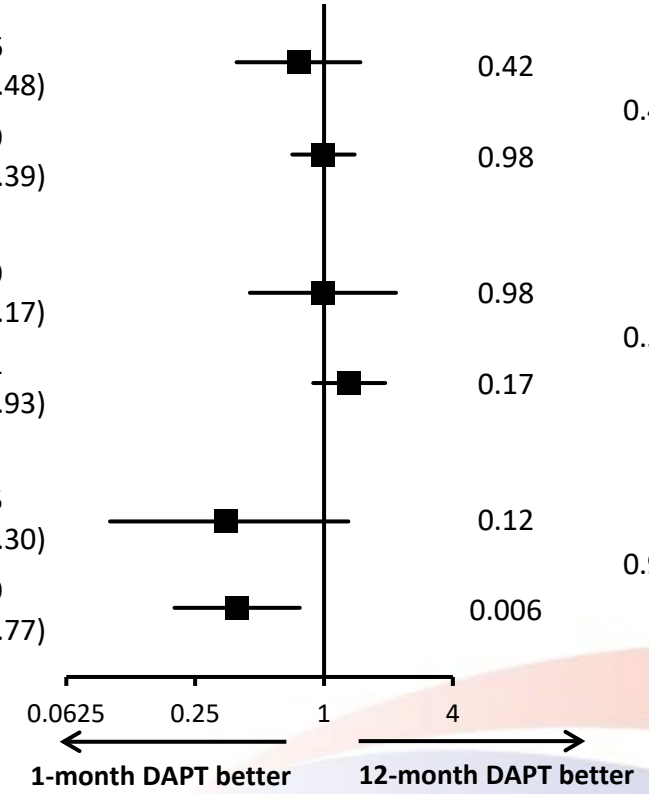
Complex PCI was defined as PCI fulfilled at least one of the followings: 3 vessels treated, >=3 stents implanted, >=3 lesions treated, bifurcation with 2 stents, total stent length >60 mm, or target of CTO.[1]

1. Giustino et al. J Am Coll Cardiol. 2016;68:1851-1864

STOPDAPT-2 Total cohort

Subgroup analysis #3: Complex PCI

	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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Limitations

- The limitations of the individual trials (STOPDAPT-2, and STOPDAPT-2 ACS)
  1. Open-label design
  2. Use of a net clinical benefit for the primary endpoint
  3. Representation of lower risk patients than in the real clinical practice
  4. Randomization at baseline, but not at 1-month when starting the assigned treatment

- Pooled population from 2 trials conducted in different time period.

- Underpowered subgroup analyses.

- Various differences between Japan and US/Europe.
  - The balance of ischemic and bleeding risks
  - Standard antithrombotic regimen after PCI
  - The usage of intracoronary imaging devices at PCI

Conclusions (1)

Total cohort

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.

Subgroup analysis #1: ACS/CCS

The treatment-by-subgroup interaction was not significant for ACS and CCS. 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 antithrombotic strategies in ACS patients.

Conclusions (2)

Subgroup analysis #2, 3: HBR, Complex PCI

The effects of 1-month DAPT relative to 12-month DAPT for cardiovascular and bleeding events were consistent regardless of HBR and complex PCI.

The absolute benefit of 1-month DAPT relative to 12-month DAPT in reducing major bleeding was numerically greater in HBR patients than in non-HBR patients.

Complex PCI might not be an appropriate determinant for DAPT durations after PCI.