How Long is Enough for DAPT following LM Stenting

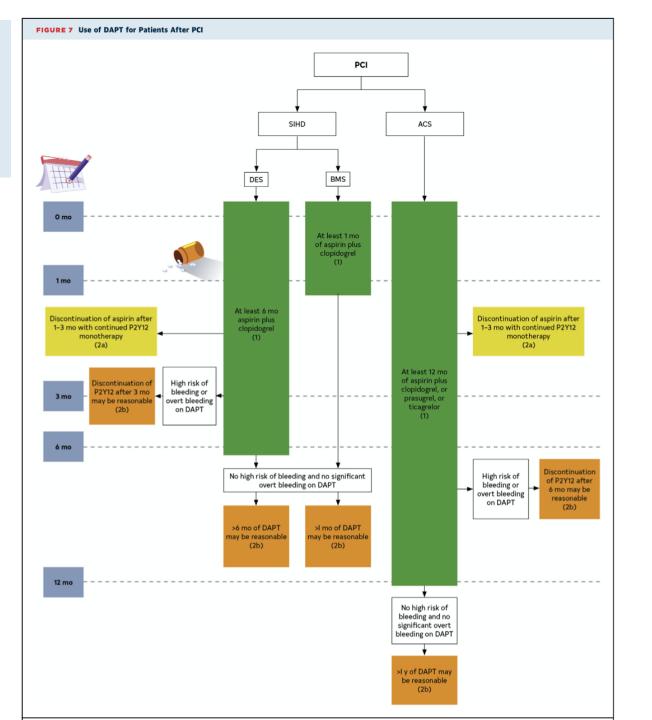
Jung-Cheng Hsu M.D.

Far Eastern Memorial Hospital, Taiwan (ROC)

CLINICAL PRACTICE GUIDELINE: FULL TEXT

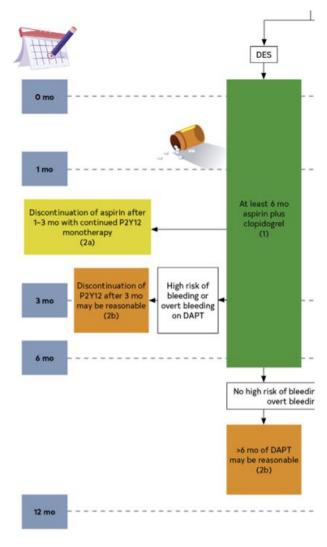
2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization

Lawton JS, Tamis-Holland JE, Bangalore S, et al. J Am Coll Cardiol. 2022;79:e21-e129.



Duration of Anti-PLT therapy

- Clinical Presentation: ACS vs SIHD (SCAD)
- Stent types: DES vs BMS (time of endothelialization)
 - current DES vs earlier DES
- Short DAPT: monotherapy with P2Y12i (2a) or Aspirin (2b)
 - HBR (high bleeding risk) patients:ARC-HBR/Precise-DAPT score
- Prolonged (extended) DAPT (2b)
 - Lesion complexity, patient factors: DAPT score



minimum duration of 6 months of DAPT after DES, emphasized the need to individualize therapy on the basis of ischemic and bleeding risk

Treatment Dilemmas between Bleeding Risk and Ischemic Risk

- Prior major bleeding
- Anemia

Event Risk (%)

- Clinical significant bleeding
- Socioeconomic factors

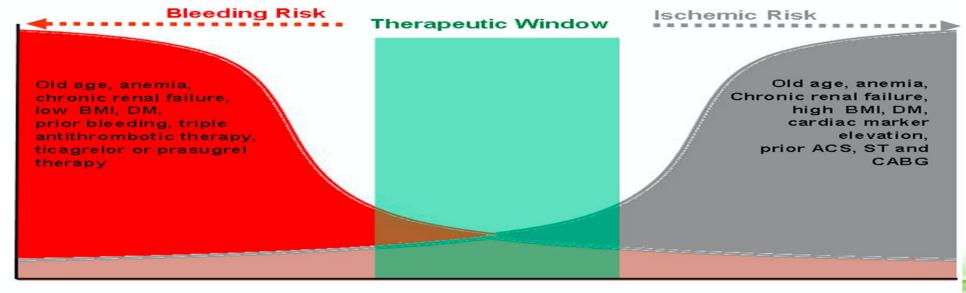
(insurance, financial hardship of current medication)

- Need for oral anticoagulation
- Side effects of Potent P2Y₁₂ inhibitors
 (e.g. dyspnea in ticagrelor)
- Presumed high bleeding risk

Escalation Prolonged DAPT

Short DAPT De-escalation

- Prior stent thrombosis on adequate antiplatelet therapy
- Stenting of the last remaining patent coronary artery
- ≥ 3stents implanted
- Bifurcation with two stents implanted
- Total stent length > 60mm
- Treatment of chronic total occlusion



P2Y₁₂ Receptor Reactivity

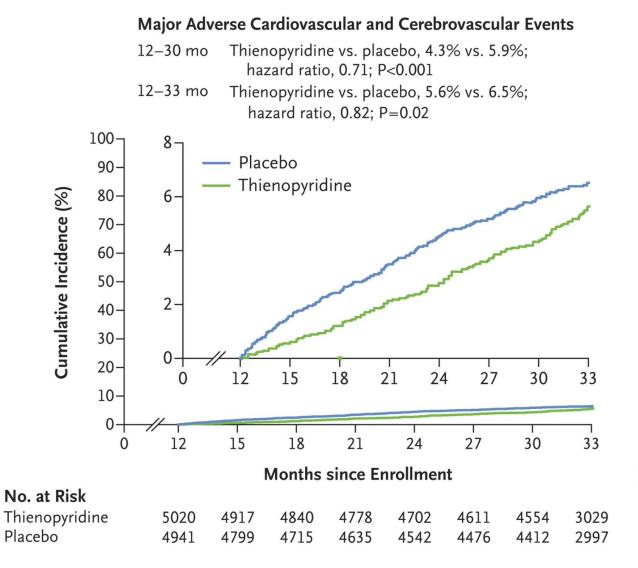
The Dual Antiplatelet Therapy (DAPT) study

Large RCT to address the issue of prolonged DAPT (30 m/o vs 12m/o) Exclude MACCE/bleeding events within 1st year after DES

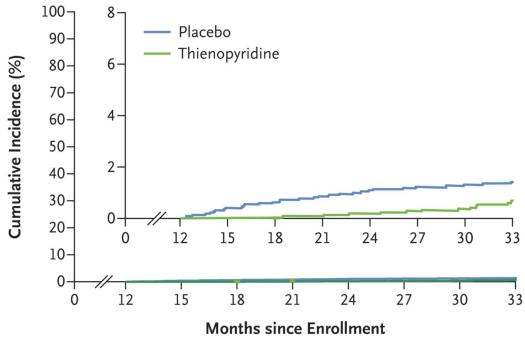
Table 2. Stent Thrombosis and Major Adverse Cardiovascular and Cerebrovascular Events.*					
Outcome	Continued Thienopyridine (N = 5020)	Placebo (N = 4941)	Hazard Ratio, Thienopyridine vs. Placebo (95% CI)†	P Value†	
	no. of patients (%)			
Stent thrombosis‡	19 (0.4)	65 (1.4)	0.29 (0.17–0.48)	< 0.001	
Definite	15 (0.3)	58 (1.2)	0.26 (0.14-0.45)	< 0.001	
Probable	5 (0.1)	7 (0.1)	0.71 (0.22–2.23)	0.55	
Major adverse cardiovascular and cerebrovascular events(211 (4.3)	285 (5.9)	0.71 (0.59–0.85)	<0.001	
Death	98 (2.0)	74 (1.5)	1.36 (1.00–1.85)	0.05	
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66–1.52)	0.98	
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28-3.39)	0.98	
Noncardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32-3.78)	0.002	
Myocardial infarction	99 (2.1)	198 (4.1)	0.47 (0.37-0.61)	<0.001	
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51-1.25)	0.32	
Ischemic	24 (0.5)	34 (0.7)	0.68 (0.40-1.17)	0.16	
Hemorrhagic	13 (0.3)	9 (0.2)	1.20 (0.50–2.91)	0.68	
Type uncertain	0	1 (<0.1)	_	0.32	

3275 (65.2)	3230 (65.4)
1745 (34.8)	1711 (34.6)
2345 (46.7)	2358 (47.7)
1350 (26.9)	1316 (26.6)
642 (12.8)	622 (12.6)
577 (11.5)	541 (10.9)
106 (2.1)	104 (2.1)
1.30±0.55	1.29±0.54
1.11±0.33	1.12±0.34
1.47±0.75	1.45±0.75
2341 (46.6)	2293 (46.4)
2679 (53.4)	2648 (53.6)
27.70±16.77	27.43±17.02
6396/6586 (97.1)	6204/6407 (96.8)
55/6586 (0.8)	55/6407 (0.9)
2715/6586 (41.2)	2586/6407 (40.4)
2153/6586 (32.7)	2057/6407 (32.1)
1473/6586 (22.4)	1506/6407 (23.5)
154/6586 (2.3)	173/6407 (2.7)
36/6586 (0.5)	30/6407 (0.5)
2754/6335 (43.5)	2643/6137 (43.1)
	2345 (46.7) 1350 (26.9) 642 (12.8) 577 (11.5) 106 (2.1) 1.30±0.55 1.11±0.33 1.47±0.75 2341 (46.6) 2679 (53.4) 27.70±16.77 6396/6586 (97.1) 55/6586 (0.8) 2715/6586 (41.2) 2153/6586 (22.4) 154/6586 (2.3) 36/6586 (0.5)

Prolonged DAPT decreased MACCE/ST



Stent Thrombosis 12–30 mo Thienopyridine vs. placebo, 0.4% vs. 1.4%; hazard ratio, 0.29; P<0.001 12–33 mo Thienopyridine vs. placebo, 0.7% vs. 1.4%; hazard ratio, 0.45; P<0.001



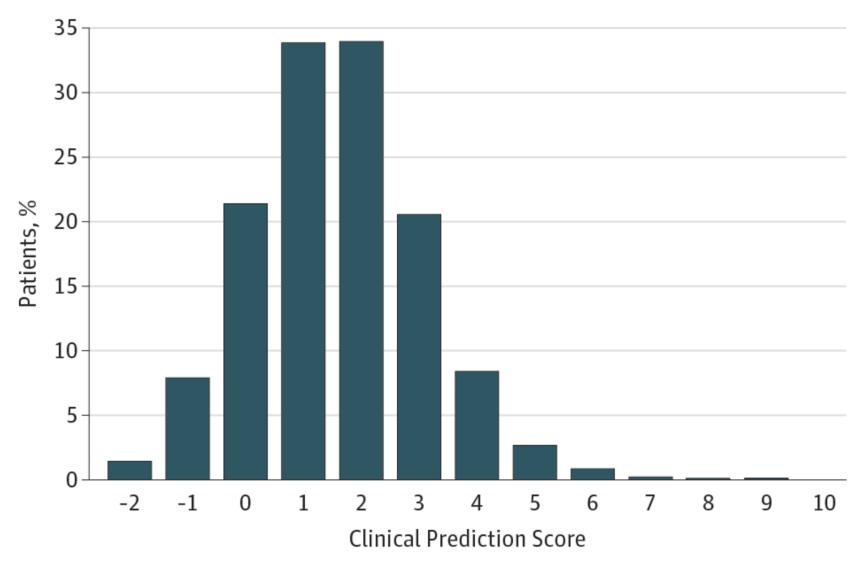
No. at Risk Thienopyridine Placebo

Prolonged DAPT increased Bleeding (trade-off)

Table 3. Bleeding End Point during Month 12 to Month 30.*					
Bleeding Complications	Continued Thienopyridine (N = 4710)	Placebo (N = 4649)	Difference	Two-Sided P Value for Difference	
	percentage points (95% CI)				
GUSTO severe or moderate†	119 (2.5)	73 (1.6)	1.0 (0.4 to 1.5)	0.001	
Severe	38 (0.8)	26 (0.6)	0.2 (-0.1 to 0.6)	0.15	
Moderate	81 (1.7)	48 (1.0)	0.7 (0.2 to 1.2)	0.004	
BARC type 2, 3, or 5	263 (5.6)	137 (2.9)	2.6 (1.8 to 3.5)	<0.001	
Type 2	145 (3.1)	72 (1.5)	1.5 (0.9 to 2.1)	<0.001	
Type 3	122 (2.6)	68 (1.5)	1.1 (0.6 to 1.7)	<0.001	
Type 5	7 (0.1)	4 (0.1)	0.1 (-0.1 to 0.2)	0.38	

DAPT score

Clinical Prediction Score	
Variable	Points
Age, y	
≥75	-2
65-<75	-1
<65	0
Cigarette smoking	1
Diabetes mellitus	1
MI at presentation	1
Prior PCI or prior MI	1
Paclitaxel-eluting stent	1
Stent diameter <3 mm	1
CHF or LVEF <30%	2
Vein graft stent	2
Total score range: -2 t	o 10



Yeh RW, Secemsky EA, Kereiakes DJ, et al. Development and Validation of a Prediction Rule for Benefit and Harm of Dual Antiplatelet Therapy Beyond 1 Year After Percutaneous Coronary Intervention. *JAMA*.2016;315(16):1735–1749. doi:10.1001/jama.2016.3775

Table 2. Myocardial Infarction or Stent Thrombosis Prediction Model and Moderate or Severe Bleeding Prediction Model

	Predictors of Myocardial Infarction or Stent Thrombosis ^b		arction Predictors of Moderate or S Bleeding ^c	
Predictors of Events ^a	HR (95% CI)	P Value	HR (95% CI)	P Value
Continued thienopyridine vs placebo	0.52 (0.42-0.65)	<.001	1.66 (1.26-2.19)	<.001
Myocardial infarction at presentation	1.65 (1.31-2.07)	<.001		
Prior PCI or prior myocardial infarction	1.79 (1.43-2.23)	<.001		
History of CHF or LVEF <30%	1.88 (1.35-2.62)	<.001		
Vein graft stent	1.75 (1.13-2.73)	.01		
Stent diameter <3 mm	1.61 (1.30-1.99)	<.001		
Paclitaxel-eluting stent	1.57 (1.26-1.97)	<.001		
Cigarette smoking	1.40 (1.11-1.76)	.01		
Diabetes mellitus	1.38 (1.10-1.72)	.01		
Age, per 10 y			1.54 (1.34-1.78)	<.001
Peripheral arterial disease	1.49 (1.05-2.13)	.03	2.16 (1.46-3.20)	<.001
Hypertension	1.37 (1.03-1.82)	.03	1.45 (1.00-2.11)	.05
Renal insufficiency/failure	1.55 (1.03-2.32)	.04	1.66 (1.04-2.66)	.03

Observed outcomes stratified by DAPT score

Major Adverse Cardiovascular and Cerebrovascular Events ^b				Risk difference (%)			
Score							
-2 to 0	1373	1356	99 (3.7)	52 (3.9)	47 (3.5)	0.40 (-1.06 to 1.86)	.02
1	1501	1501	110 (3.8)	50 (3.4)	60 (4.1)	-0.65 (-2.04 to 0.75)	
2	1525	1486	137 (4.7)	51 (3.4)	86 (6.0)	-2.54 (-4.10 to -0.98)	
≥3	1463	1443	221 (7.9)	91 (6.4)	130 (9.3)	-2.95 (-4.97 to -0.92)	_

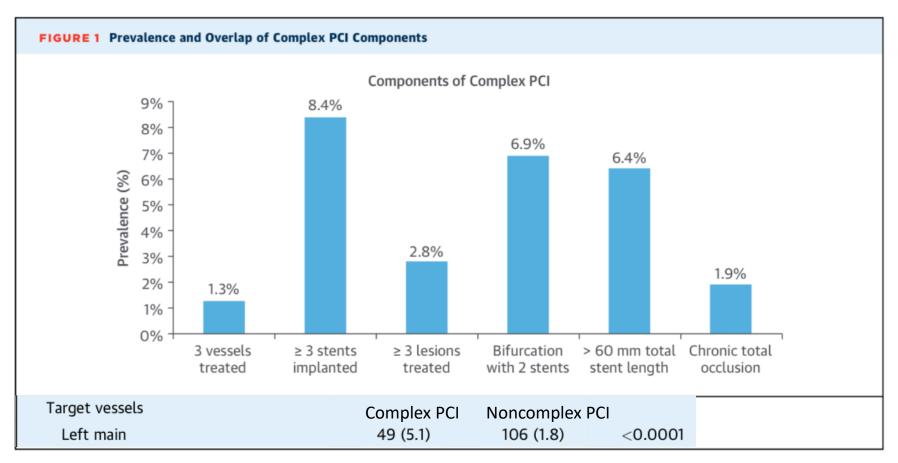
Moderate or S	Severe Bleed ^c			Risk difference (%)			
Score							
-2 to 0	1373	1356	72 (2.7)	49 (3.7)	23 (1.7) 1.97 (0.71 to 3.23)	.04	
1	1501	1501	51 (1.8)	34 (2.3)	17 (1.2) 1.17 (0.20 to 2.14)		
2	1525	1486	45 (1.5)	28 (1.9)	17 (1.2) 0.69 (-0.22 to 1.60)	
≥3	1463	1443	47 (1.7)	24 (1.7)	23 (1.7) 0.03 (-0.95 to 1.01)	

Prolonged DAPT maybe more beneficial in high DAPT score (≥ 2)

Yeh RW, Secemsky EA, Kereiakes DJ, et al. Development and Validation of a Prediction Rule for Benefit and Harm of Dual Antiplatelet Therapy Beyond 1 Year After Percutaneous Coronary Intervention. *JAMA*.2016;315(16):1735–1749. doi:10.1001/jama.2016.3775

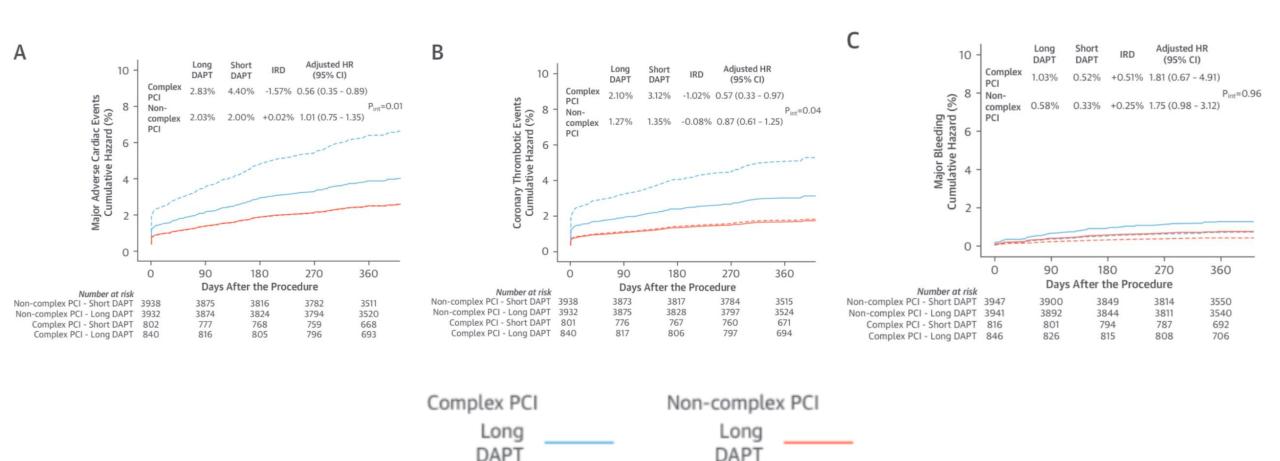
Efficacy and Safety of DAPT after Complex PCI

 Complex PCI: 3 vessels treated, ≥ 3 stents, ≥ 3 lesions, Bifurcation with 2 stents, > 60mm total stent length, CTO



Long DAPT better than Short DAPT in Complex PCI (NOT in Noncomplex PCI)

Short



Giustino, G. et al. J Am Coll Cardiol. 2016;68(17):1851-64.

Lesion Complexity and Outcomes of Extended Dual Antiplatelet Therapy After Percutaneous Coronary Intervention

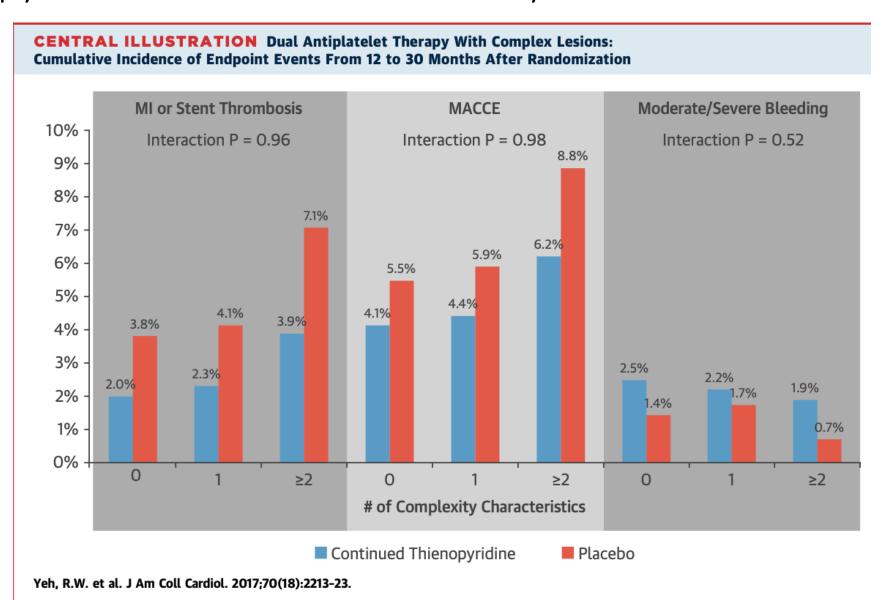
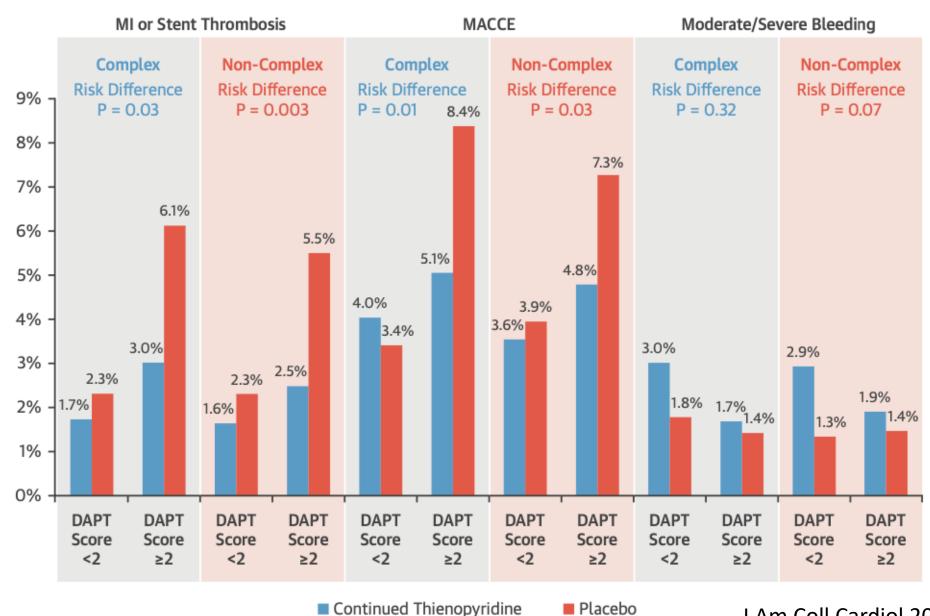


FIGURE 3 Cumulative Incidence of Endpoint Events From 12 to 30 Months After Randomization, Stratified by Treatment Arm, Anatomical Complexity, and DAPT Score

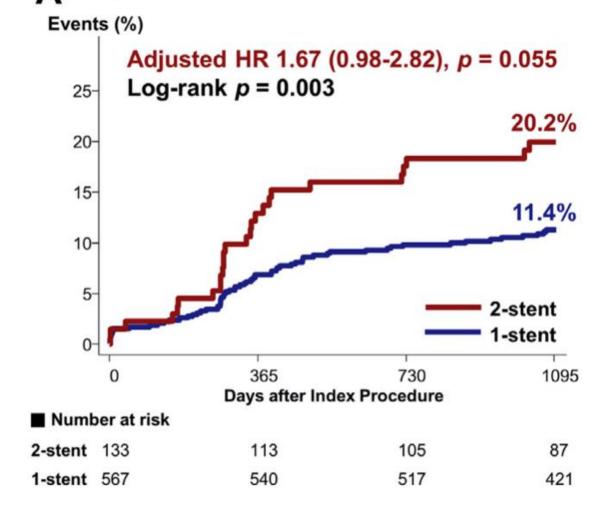


Dual Antiplatelet Therapy Duration Determines Outcome After 2- But Not 1-Stent Strategy in Left Main Bifurcation Percutaneous Coronary Intervention

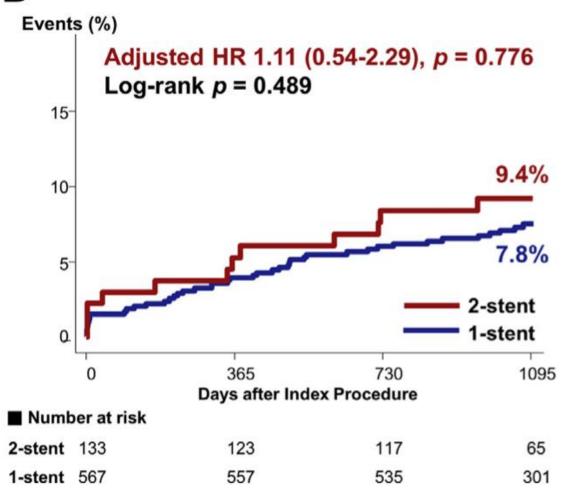
	Grand-I	DES Registry : N	lew-generation D	ES Sub-cohort		
	Korean Na	tionwide Multicente	r Pooled Registry of	Drug-Eluting Stent	s	
Registry	HOST-BIOLIMUS- Korea-3000	EXCELLENT- PRIME	EXCELLENT Prospective cohort	HOST-RESOLINTE	RESOLUTE-Korea	
Period	2010.3 - 2014.11	2010.12 - 2012.8	2008.4 - 2010.5	2011.10 - 2014.7	2009.1 - 2010.6	
Stent type	BP-BES	DP-EES-Prime	DP-EES	DP-ZES-RI	DP-ZES-R	
Patients	3007	2076	3078	3004	2007	
Lesions	4070	2899	4176	4099	2801	
1Y f/u loss	23 (0.8%)	1 (0.05%)	15 (0.5%)	9 (0.3%)	6 (0.3%)	
2Y f/u loss	32 (1.1%)	2 (0.1%)	15 (0.5%)	10 (0.3%)	8 (0.4%)	
3Y f/u loss	37 (1.2%)	2 (0.1%)	15 (0.5%)	13 (0.4%)	8 (0.4%)	
Bifurcation	1284 (42.7%)	923 (44.5%)	995 (32.3%)	1348 (44.9%)	789 (39.3%)	
						
		Bifurcation T	reated by New-ge N = 5,339	eneration DES		
4,639 were excluded : Non-LM bifurcation						
Left Main Bifurcation N = 700						
		1-stent str N = 56		nt strategy N = 133		

Rhee TM, Park KW, Kim CH, et al. J Am Coll Cardiol Intv 2018;11:2453–63

▲ Target lesion failure

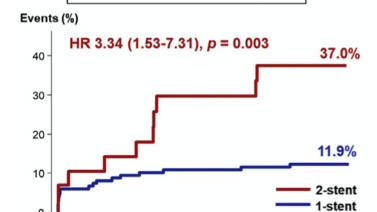


B Thrombotic adverse cardiovascular event

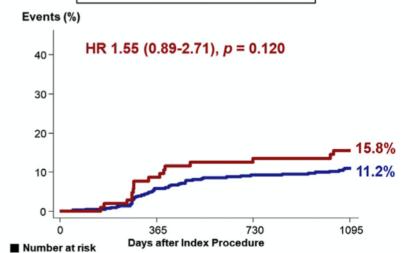


A Target lesion failure

DAPT interruption < 1-year



DAPT maintenance ≥ 1-year



B Thrombotic adverse cardiovascular event

Days after Index Procedure

730

16

127

1095

14

100

2-stent 104

1-stent 420

365

18

130

■ Number at risk

2-stent 29

1-stent 147

DAPT interruption < 1-year

Events (%) HR 2.78 (1.25-6.19), p = 0.01234.8% 30 20 12.8% 10 2-stent 1-stent 365 730 1095 **Days after Index Procedure** Number at risk **2-stent** 29 20 18 1-stent 147 130 124 63

DAPT maintenance ≥ 1-year

410

89

390

73

321

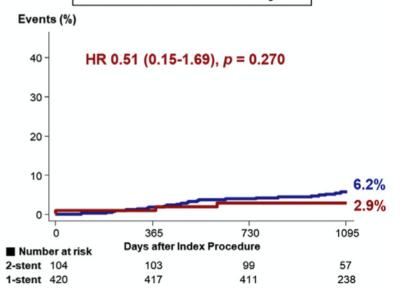
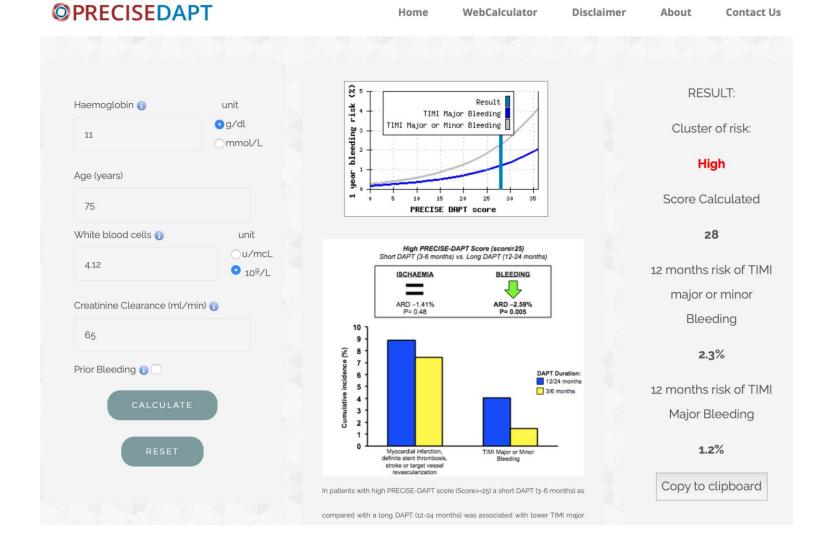


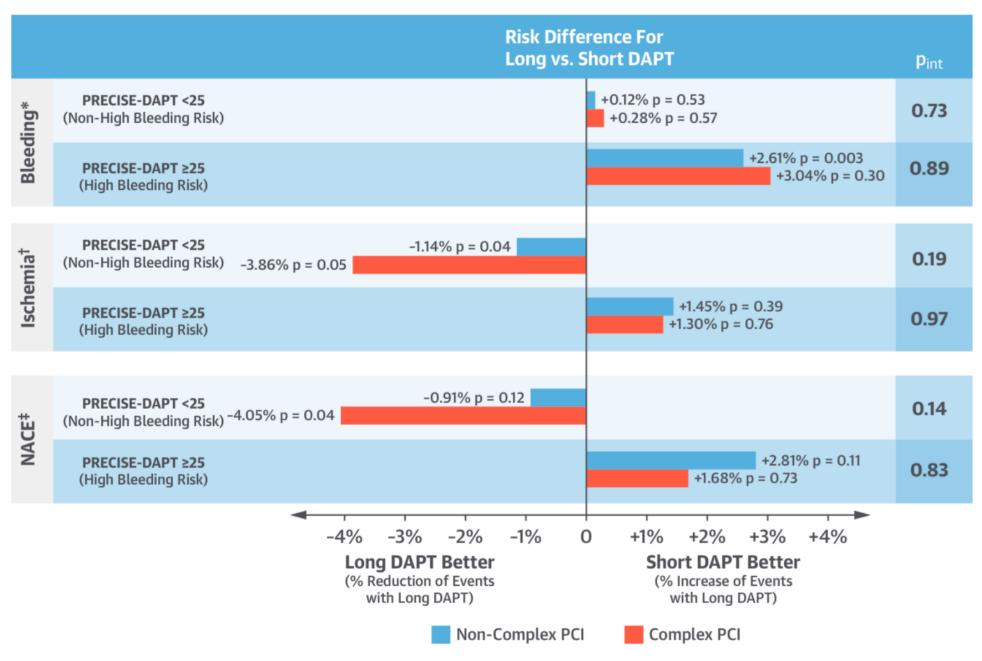
TABLE 5 Independent Predictors of Target Lesion Failure						
	Hazard Ratio	95% CI	p Value			
1-stent group						
LV dysfunction (EF <40%)	2.339	1.172-4.667	0.016			
Acute myocardial infarction	2.309	1.361-3.916	0.002			
3-vessel disease	1.993	1.194-3.325	0.008			
2-stent group						
Peripheral vascular disease	5.591	1.230-25.414	0.026			
Lesion at in-stent restenosis	3.811	0.980-14.813	0.053			
DAPT interruption before 1 yr	3.810	1.564-9.282	0.003			
LV dysfunction (EF <40%)	3.257	1.201-8.835	0.020			
Total number of implanted stents (per 1 ↑)	1.444	1.136-1.836	0.003			

PRECISE-DAPT score

 The PRECISE-DAPT score was calculated based on age, creatinine clearance, hemoglobin, white blood cell count and previous spontaneous bleeding



CENTRAL ILLUSTRATION PRECISE-DAPT Score and Complex Percutaneous Coronary Intervention



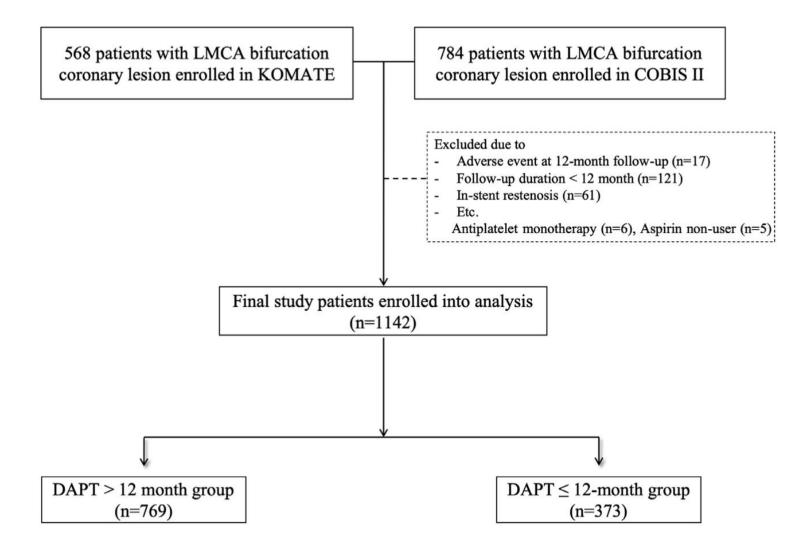
Costa, F. et al. J Am Coll Cardiol. 2019;73(7):741-54.

ARC-High Bleeding Risk (1 major or 2 minor)

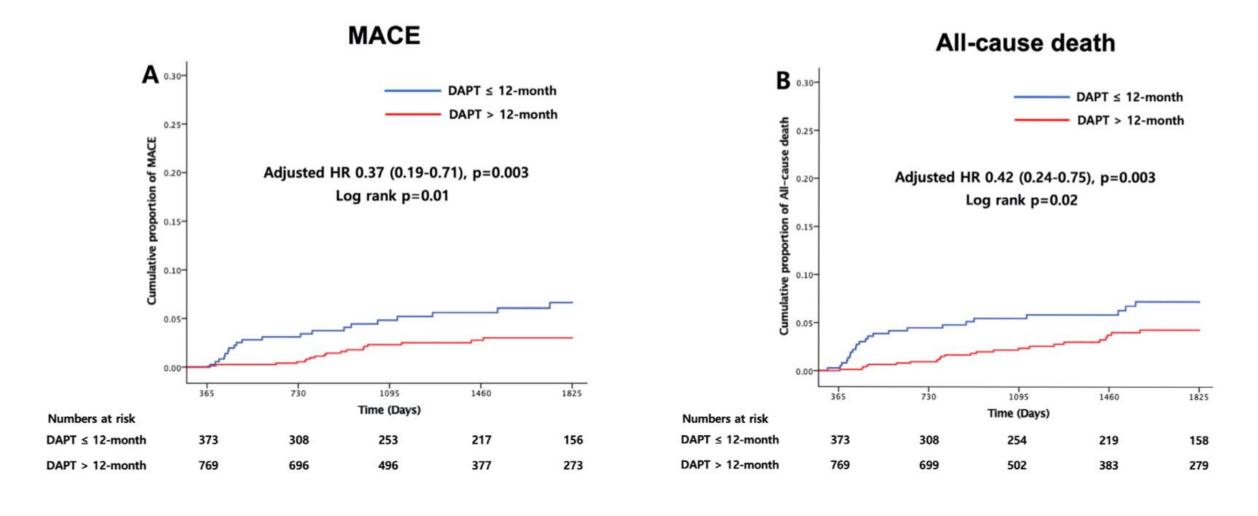
Table 3 Major and minor criteria for hbr at the time of PCI Academic Research Consortium for HBR (High Bleeding Risk)

Major	Minor
	Age ≥75 y
Anticipated use of long-term oral anticoagulation*	
Severe or end-stage CKD (eGFR <30 mL/min)	Moderate CKD (eGFR 30–59 mL/min)
Hemoglobin <11 g/dL	Hemoglobin 11–12.9 g/dL for men and 11–11.9 g/dL for women
Spontaneous bleeding requiring hospitalization or transfusion in the past 6 mo or	Spontaneous bleeding requiring hospitalization or transfusion with-
at any time, if recurrent	in the past 12 mo not meeting the major criterion
Moderate or severe baseline thrombocytopenia \dagger (platelet count <100 $ imes$ 109/L)	
Chronic bleeding diathesis	
Liver cirrhosis with portal hypertension	
	Long-term use of oral NSAIDs or steroids
Active malignancy‡ (excluding nonmelanoma skin cancer) within the past 12 mo	
Previous spontaneous ICH (at any time)Previous traumatic ICH within the past	Any ischemic stroke at any time not meeting the major criterion
12 moPresence of a bAVMModerate or severe ischemic stroke§ within the	
past 6 mo	
Nondeferrable major surgery on DAPT	
Recent major surgery or major trauma within 30 d before PCI	

Long-Term Efficacy of Extended Dual Antiplatelet Therapy After Left Main Coronary Artery Bifurcation Stenting



Long-Term Efficacy of Extended Dual Antiplatelet Therapy After Left Main Coronary Artery Bifurcation Stenting



Long-Term Efficacy of Extended Dual Antiplatelet Therapy After Left Main Coronary Artery Bifurcation Stenting

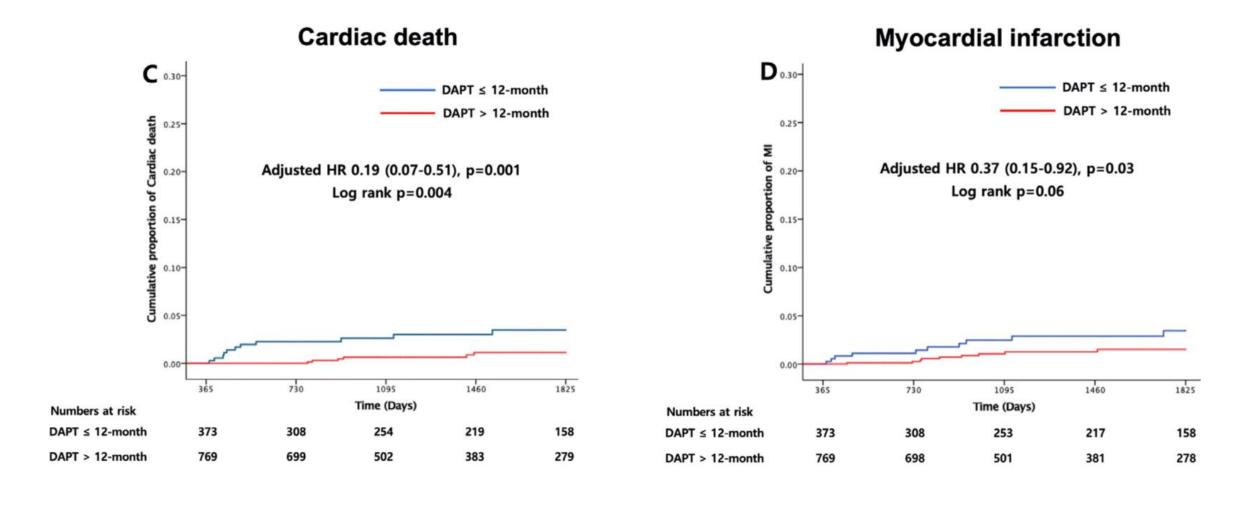
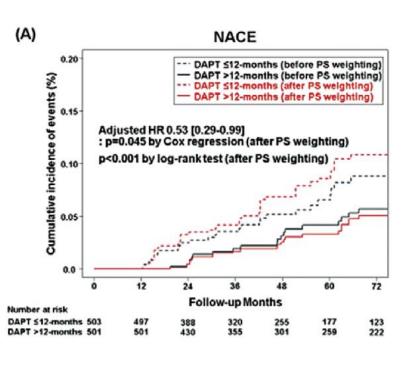


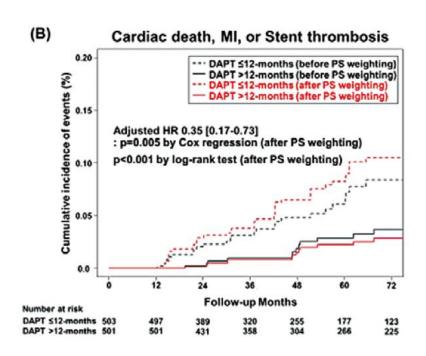
Table 4
Independent predictors of clinical outcomes

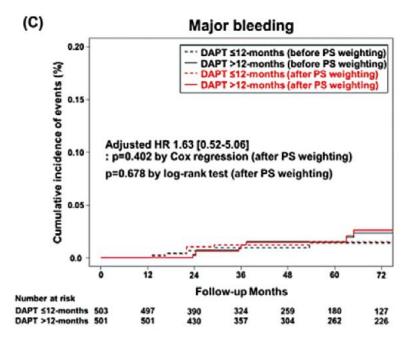
Variable	Univariate ana	alysis	Multivariate an	alysis
	HR (95% CI)	p Value	HR (95% CI)	p Value
Age >75 years	3.5 (1.7-7.2)	0.001	3.58 (1.63-7.87)	0.002
DAPT >12 months	0.43 (0.23-0.81)	0.01	0.34 (0.17-0.67)	0.002
DAPT score ≥2	2.17 (1.08-4.35)	0.03	2.76 (1.33-5.7)	0.01
CKD	6.87 (3.03-15.61)	< 0.0001	6.85 (2.83-16.61)	< 0.0001
2-stent strategy	0.92 (0.43-1.94)	0.82		
Male	1.13 (0.54-2.39)	0.74		
ACS	2.32 (1.17-4.61)	0.02		
Multivessel disease	1.43 (0.71-2.88)	0.32		
DM	1.26 (0.65-2.43)	0.5		
Hypertension	1.29 (0.66-2.53)	0.45		
Previous PCI	1.58 (0.78-3.19)	0.2		
Previous CABG	1.51 (0.36-6.27)	0.57		
IVUS	0.67 (0.36-1.27)	0.22		

Optimal Duration for Dual Antiplatelet Therapy After Left Main Coronary Artery Stenting

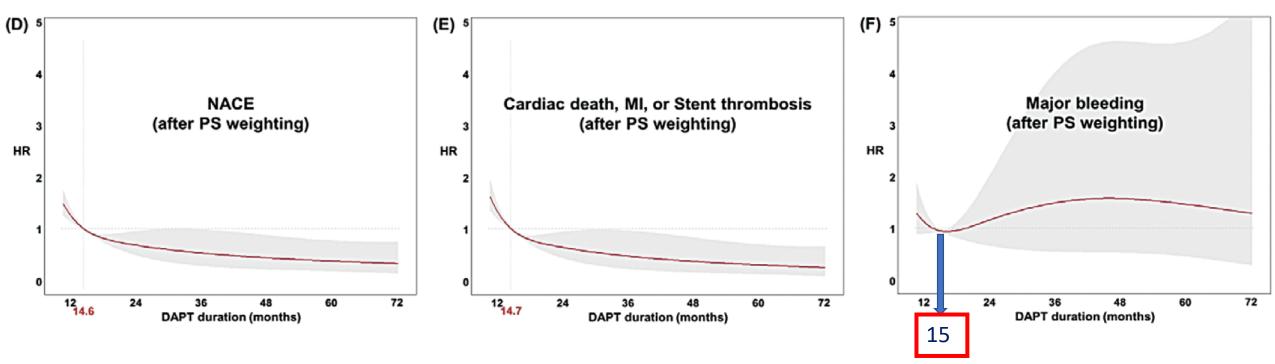
KOMATE (Korean Multicenter Angioplasty Team) registry







Optimal Duration for Dual Antiplatelet Therapy After Left Main Coronary Artery Stenting



 Authors: maybe 15 m/o of DAPT is the best cut-off time point after LM stenting

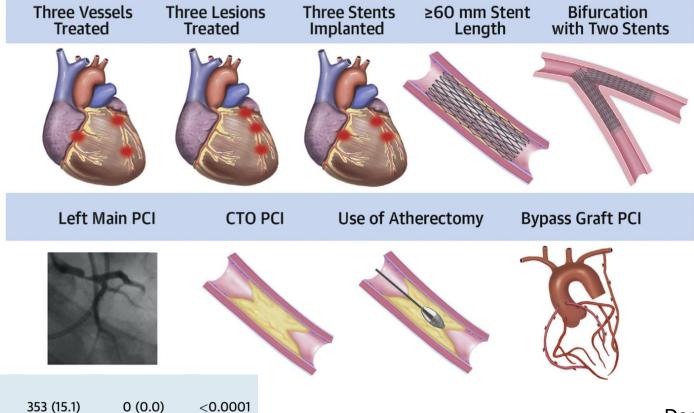
TWILIGHT Complex

Vessel treated Left main

CENTRAL ILLUSTRATION Ticagrelor With or Without Aspirin After Complex Percutaneous Coronary Intervention

Effect of Ticagrelor Monotherapy Versus Ticagrelor Plus Aspirin After 3 Months of DAPT in Patients Who Undergo Complex PCI

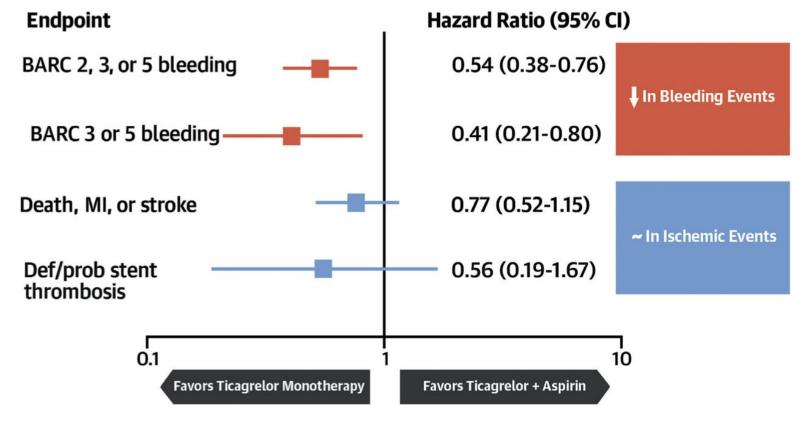
Complex PCI Defined as Any of the Following Characteristics:



Dangas G, et al. J Am Coll Cardiol

A+T 3m/o, then T monotherapy vs A+T 12 m/o

Risk of Adverse Events 12 Months After Randomization in Patients Undergoing Complex PCI



Dangas, G. et al. J Am Coll Cardiol. 2020;75(19):2414-24.

Optimal duration or regimen after LM stenting?

- ACS vs SIHD (SCAD)
- Stent generation: short DAPT outcome trial, OCT substudy (early endothelialization)
- Intra-vascular imaging guidance (IVUS/OCT): stent optimization, atherectomy or plaque modification, POT (proximal optimization therapy) if indicated
- Scoring system: DAPT score, PRECISE-DAPT score
- Lesion/Procedural complexity
- Plaque burden (non-stent segment) ? SYNTAX score ? Un-controlled risk factors (high A1c, LDL, smoking..etc)
- Potent P2Y12i (dosing? Ticagrelor 90mg or 60mg BD, Prasugrel 10mg or 5mg or 3.75mg QD) monotherapy vs DAPT with ASA + clopidogrel?
- De-escalation/ short DAPT (drop off ASA or P2Y12i?) according to the bleeding risk (ARC-HRB or PRECISE-DAPT score) in LM stenting?
- Indication of long-term OAC (triple vs dual? NOAC vs LAA closure)



Table 1. Studies assessing the impact of DAPT duration after PCI of bifurcation lesions.

	Giustino et al ¹⁸	Yeh et al ¹⁹	Jang et al ³²	Rhee et al ³³	Zimarino et al ¹⁰	Kogame et al ²²	Costa et al ²⁰	Dangas et al ²³
Year	2016	2017	2018	2018	2019	2019	2019	2020
Type of study	Pooled analysis from 6 RCTs	Substudy of an RCT	nROS	Pooled analysis from 5 nROS	nROS	Substudy of an RCT	Pooled analysis from RCTs	Substudy of an RCT
Name of the original study	_	DAPT	COBIS II	_	EBC registry	GLOBAL LEADERS	PRECISE-DAPT	TWILIGHT COMPLEX
Study population	n=9,577	n=11,554	n=2,082	n=700	n=5,036	n=15,845	n=14,963	n=2,342
Bifurcation lesions	6.8%	6.2%	100%	100%	100%	15.8%	8%	10.7%
2-stent	100%	100%	26%	19%	10%	20%	100%	100%
DAPT duration Short-term Long-term	3-6 months ≥12 months	12 months 30 months	<12 months ≥12 months	<12 months ≥12 months	<6 months SCAD, <12 months ACS ≥6 months SCAD ≥12 months ACS	1 month (then ticagrelor) 12 months (then aspirin)	3-6 months 12-24 months	3 months 15 months
Follow-up	13 months	30 months	4 years	3 years	18 months	2 years	2 years	18 months
Efficacy endpoint	MACE (cardiac death, MI, or ST)	MI or ST	Death or MI	MACE (cardiac death, MI, or ST)	MACE (cardiac death, MI, or ST)	Death or MI	MI, ST, stroke, TVR	Death, MI, stroke
Safety endpoint	Major bleeding	Moderate/severe bleeding	NA	NA	NA	Major bleeding	Major and minor bleeding	BARC 3 or 5 bleeding
Main findings	Long-term DAPT reduces the risk of MACE in the complex PCI group, increases the risk of major bleeding	Long-term DAPT increases the risk of bleeding and reduces MI or ST, most evident among complex PCI with DAPT score ≥2	After PS matching, the risk of death or MI was lower in the long- vs short-term DAPT group	After PS matching, the risk of MACE in the 2-stent group was lower with long- vs short-term DAPT	Long-term DAPT was associated with a lower risk of MACE	No differences in death or MI. No differences in bleeding risk	Long-term DAPT reduces the risk of ischaemic events in complex PCI only if PRECISE-DAPT score <25.	Long-term DAPT increased the risk of bleeding and is associated with a trend towards a reduction in risk of death, MI or stroke

MACE: major adverse cardiac events; NA: not available; nROS: non-randomised observational study; PS: propensity score; RCT: randomised clinical trial; TVR: target vessel revascularisation

