The effect of new $P2Y_{12}$ inhibitor on clinical outcomes in AMI patients using Korean Registry of Regional Cardiocerebrovascular center for Acute Myocardial Infarction (KRAMI)

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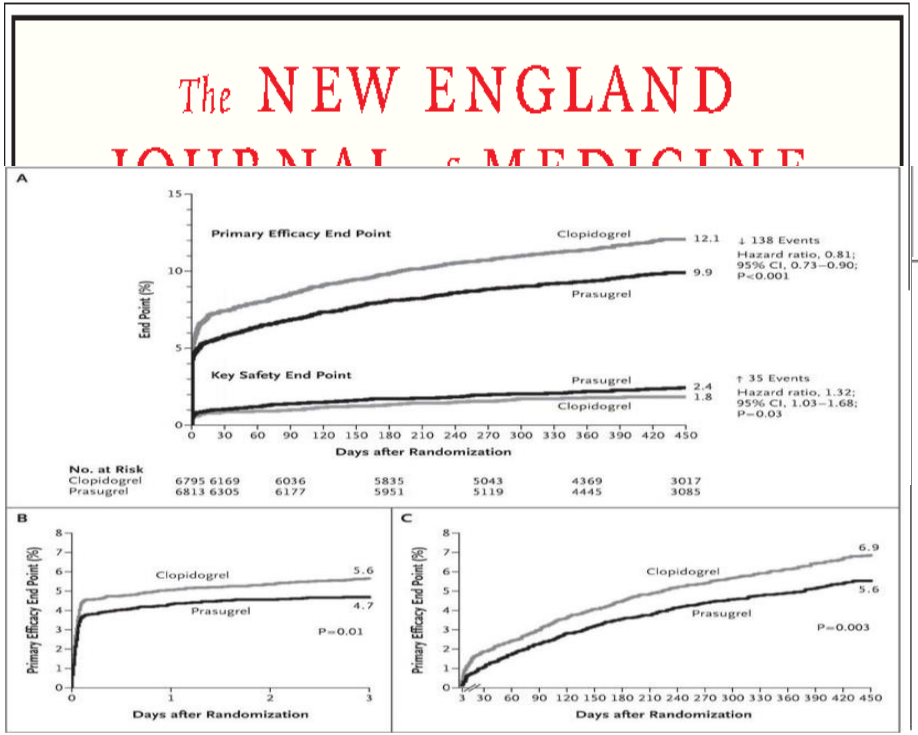
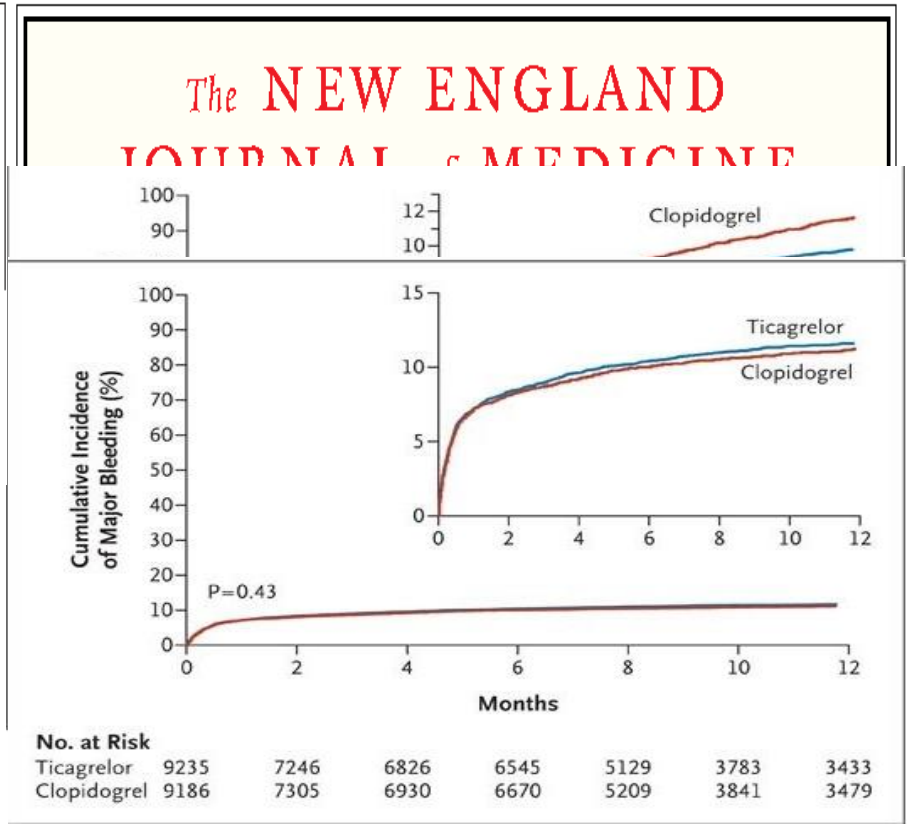
Comparing for Clopidogrel vs New $P2Y_{12}$



N Engl J Med 2007;357:2001-15.



N Engl J Med 2009;361:1045-57.

Comparing for Clopidogrel vs New $P2Y_{12}$

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Ischemic Heart Disease

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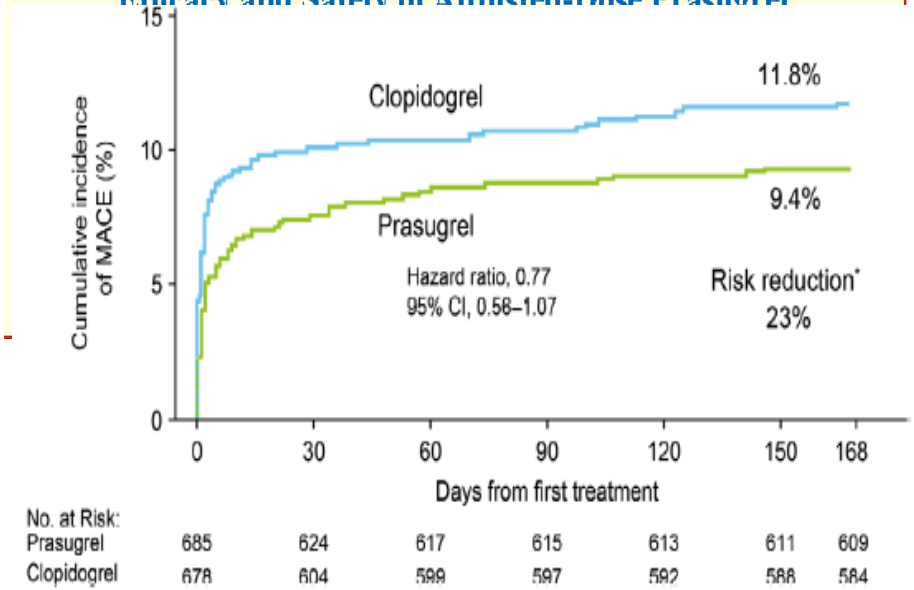

Circ J 2014; 78:1684 – 1692.

Circ J 2018; **82:** 747–756
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ORIGINAL ARTICLE
Ischemic Heart Disease

Table 3. Ticagrelor: Efficacy and Safety Outcomes of AMI After Propensity Score Matching

	Clopidogrel (n=19,112)	Ticagrelor (n=2,389)	Adjusted HR (95% CI)
Primary efficacy endpoint (all-cause mortality/AMI/stroke)	3,097 (16.2)	254 (10.6)	0.779 (0.684–0.887)
All-cause mortality	1,322 (6.9)	53 (2.2)	0.407 (0.308–0.536)
AMI	1,726 (9.0)	180 (7.5)	0.984 (0.807–1.199)
Stroke	564 (2.9)	42 (1.7)	0.745 (0.542–1.023)
Ischemic stroke	508 (2.7)	37 (1.5)	0.684 (0.457–1.023)
Primary safety endpoint (ICH/major GI bleeding)	779 (4.1)	76 (3.2)	0.731 (0.522–1.026)
ICH	81 (0.4)	7 (0.3)	0.943 (0.429–2.072)
Major GI bleeding	712 (3.7)	70 (2.9)	0.955 (0.752–1.214)

Circ J 2018; 82: 747 – 756

Comparing for Clopidogrel vs New $P2Y_{12}$

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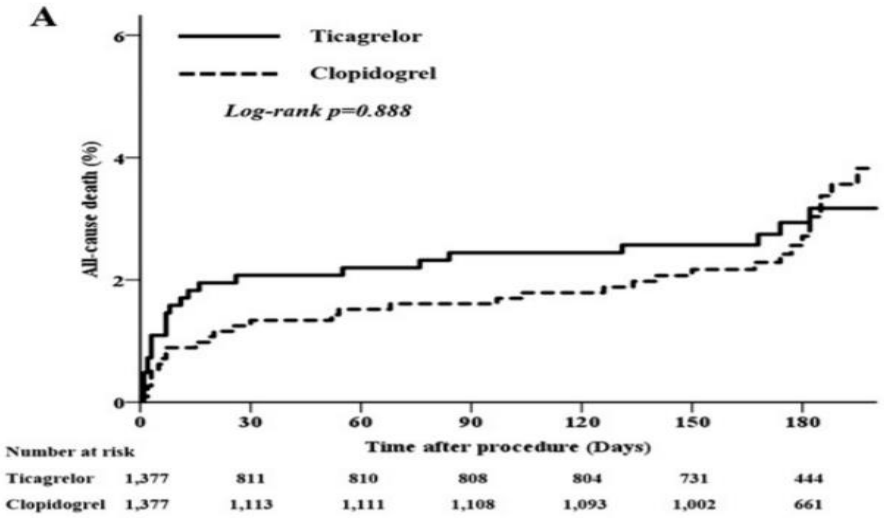

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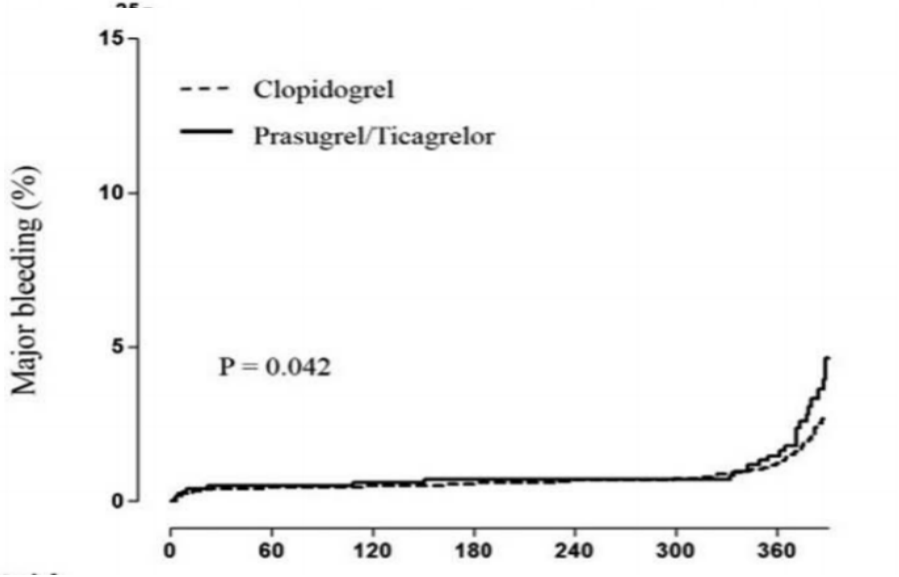
Observational Study

Medicine



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Comparing for Clopidogrel vs New $P2Y_{12}$

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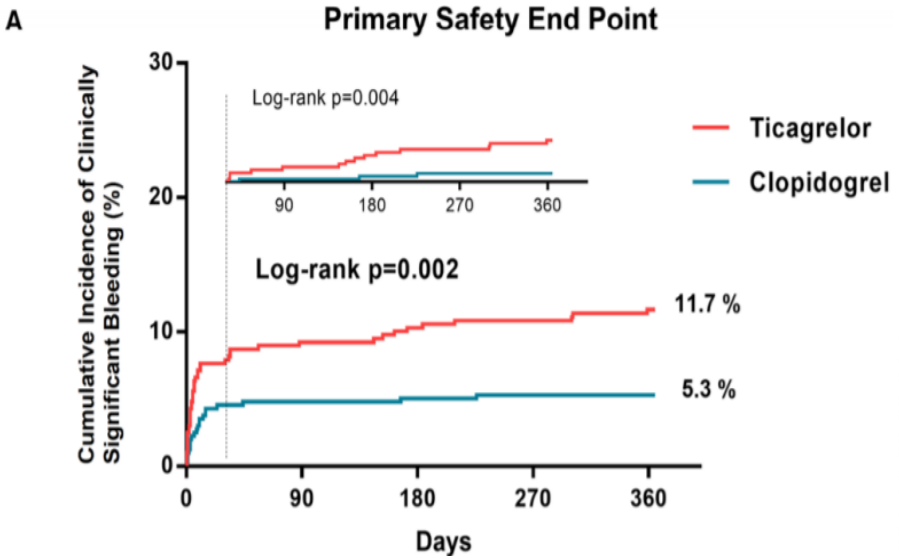
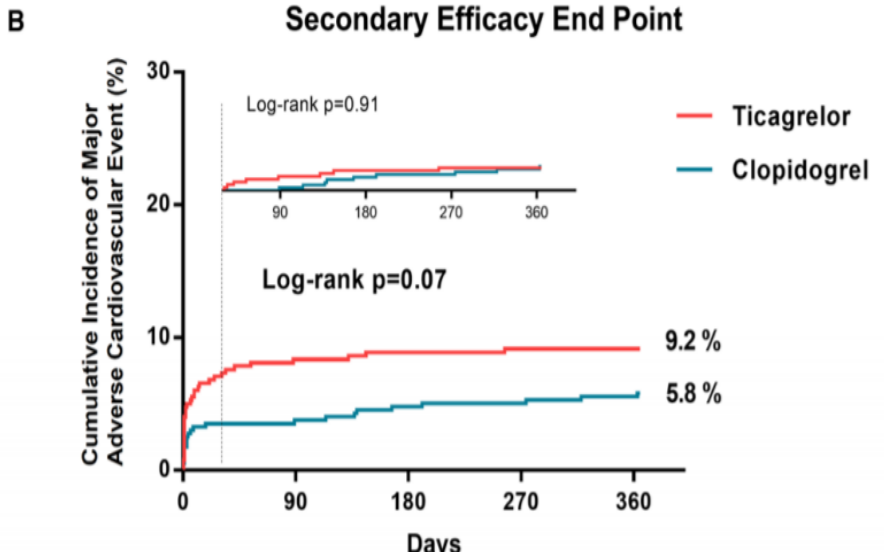




Park DW, et al. Circulation (2019);140:1-13

Comparing for Clopidogrel vs New $P2Y_{12}$

Table 3. Secondary Efficacy End Point and Its Components at 12 Months

End Point, n (%)*	Ticagrelor (N=400)	Clopidogrel (N=400)	Hazard Ratio for Ticagrelor Group (95% CI)	*P* Value†
Major adverse cardiovascular event				
Composite of cardiovascular death, myocardial infarction, or stroke	36 (9.2)	23 (5.8)	1.62 (0.96–2.74)	0.07
Post hoc: composite of cardiovascular death, spontaneous myocardial infarction, or stroke	21 (5.4)	17 (4.3)	1.27 (0.67–2.40)	0.47
Other secondary efficacy end points				
Composite of all-cause death, myocardial infarction or stroke	37 (9.4)	27 (6.8)	1.42 (0.86–2.33)	0.17
All-cause death	16 (4.1)	10 (2.5)	1.65 (0.75–3.63)	0.22
Cardiovascular death	15 (3.8)	6 (1.5)	2.61 (1.01–6.72)	0.05
Noncardiovascular death	1 (0.3)	4 (1.0)	0.26 (0.03–2.31)	0.23
Myocardial infarction type	20 (5.1)	16 (4.0)	1.28 (0.66–2.47)	0.46
Periprocedural	16 (4.0)	7 (1.7)	2.30 (0.95–5.60)	0.07
Spontaneous	4 (1.1)	9 (2.3)	0.45 (0.14–1.47)	0.19
Stroke	6 (1.6)	5 (1.3)	1.25 (0.38–4.09)	0.72

Park DW, et al. Circulation (2019);140:1-13

The Purpose of our Study

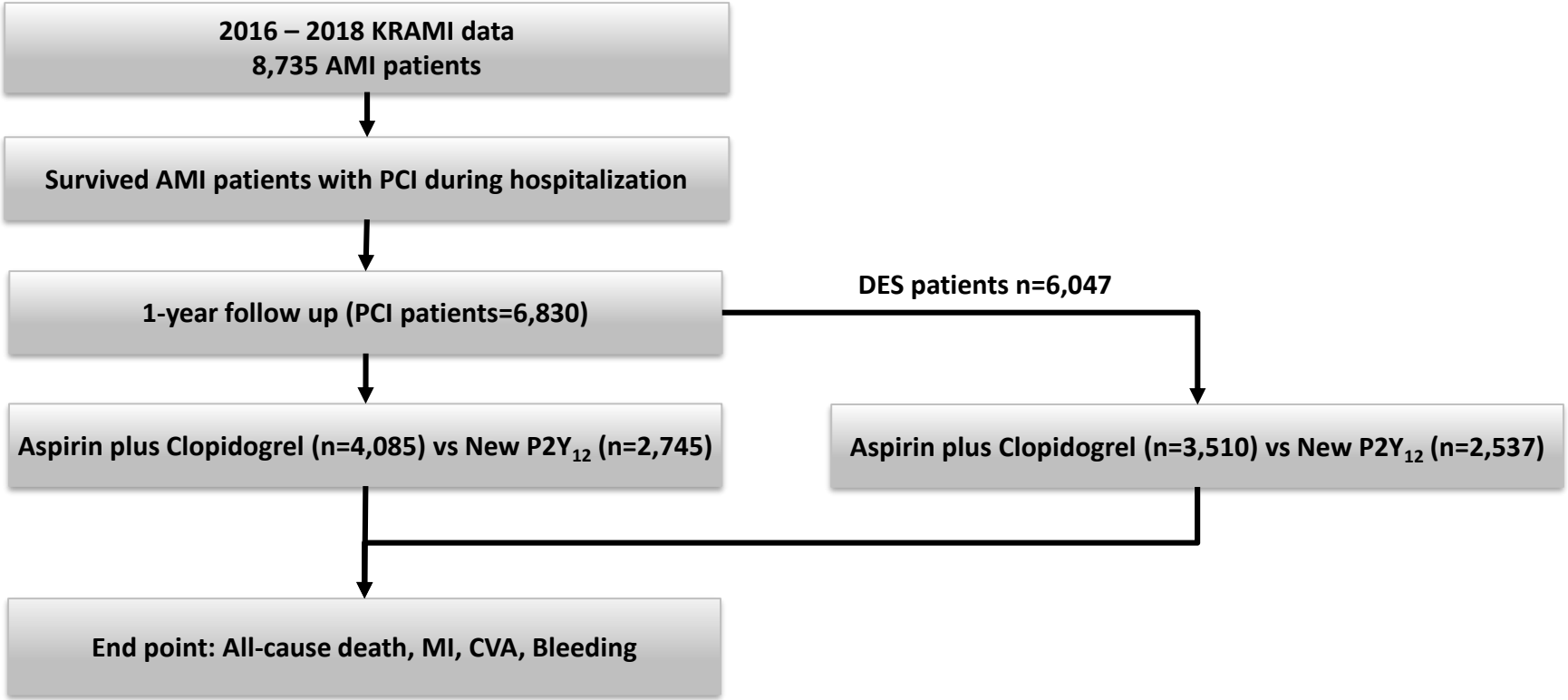
- We sought to compare 1-year clinical outcomes of aspirin plus clopidogrel versus aspirin plus ticagrelor or prasugrel using Korean Registry of Regional Cardiocerebrovascular center for Acute Myocardial Infarction (KRAMI).

Methods

- From KRAMI database, patients over 18 years old who were diagnosed as acute myocardial infarction were selected.

- We included patients who received aspirin plus clopidogrel, aspirin plus new $P2Y_{12}$ inhibitors (ticagrelor or prasugrel) at discharge and we excluded in-hospital mortality.

The Study Flow



Baseline Characteristics of the Patients

	Overall data			PSM data		
	Aspirin + Clopidgrel (n =4,085)	**Aspirin + New $P2Y_{12}$ (n = 2,745)**	**p-value**	**Aspirin + Clopidgrel (n = 2,082)**	**Aspirin + New $P2Y_{12}$ (n = 2,082)**	**p-value**
Age	**67.56 ± 12.55**	**59.97 ± 11.59**	**<.0001**	**62.55 ± 12.47**	**62.46 ± 11.20**	**0.807**
Sex (=male)	**2,893 (70.8)**	**2,317 (84.4)**	**<.0001**	**1,659 (79.7)**	**1,685 (80.9)**	**0.311**
BMI	24.01 ± 14.79	24.66 ± 5.35	**0.027**	24.56 ± 16.03	24.48 ± 5.79	**0.826**
Insurance Type			**0.000**			**0.550**
Medical insurance	3,787 (92.7)	2,603 (94.8)		1,969 (94.6)	1,954 (93.9)	
Medical care	275 (6.7)	122 (4.4)		101 (4.9)	112 (5.4)	
No insurance	22 (0.5)	19 (0.7)		12 (0.6)	16 (0.8)	
Education			**0.000**			**0.990**
Elementary school	1,183 (29.0)	430 (15.7)		398 (19.1)	395 (19.0)	
Middle school	600 (14.7)	379 (13.8)		295 (14.2)	305 (14.6)	
High school	1,260 (30.9)	1,074 (39.1)		774 (37.2)	772 (37.1)	
University	753 (18.4)	687 (25.0)		474 (22.8)	471 (22.6)	
Graduate school	103 (2.5)	94 (3.4)		76 (3.7)	70 (3.4)	
Unknown	184 (4.5)	81 (3.0)		65 (3.1)	69 (3.3)	
Living Type (=single)	792 (19.4)	457 (16.6)	**0.004**	339 (16.3)	347 (16.7)	**0.738**
Current Smoking			**<.0001**			**0.668**
No	1,825 (44.7)	867 (31.6)		760 (36.5)	739 (35.5)	
Yes	1,303 (31.9)	1,371 (49.9)		903 (43.4)	903 (43.4)	
Stop	957 (23.4)	507 (18.5)		419 (20.1)	440 (21.1)	

Baseline Characteristics of the Patients

	Overall data			PSM data		
	Aspirin + Clopidgrel (n =4,085)	Aspirin + New $P2Y_{12}$ (n = 2,745)	p-value	Aspirin + Clopidgrel (n = 2,082)	Aspirin + New $P2Y_{12}$ (n = 2,082)	p-value
Comorbid diseases						
STEMI/NSTEMI			**<.0001**			**0.901**
STEMI	**2,841 (69.5)**	**1,321 (48.1)**		**1,173 (56.3)**	**1,169 (56.1)**	
NSTEMI	**1,244 (30.5)**	**1,424 (51.9)**		**909 (43.7)**	**913 (43.9)**	
HTN	**2,217 (54.3)**	**1,191 (43.4)**	**<.0001**	**973 (46.7)**	**967 (46.4)**	**0.852**
Dyslipidemia	**526 (12.9)**	**323 (11.8)**	**0.173**	**284 (13.6)**	**255 (12.2)**	**0.181**
DM	**106 (2.6)**	**20 (0.7)**	**<.0001**	**23 (1.1)**	**20 (1.0)**	**0.646**
Prior MI	423 (10.4)	207 (7.5)	**<.0001**	160 (7.7)	173 (8.3)	**0.458**
Prior PCI	613 (15.0)	300 (10.9)	**<.0001**	252 (12.1)	252 (12.1)	**1.000**
Prior CABG	38 (0.9)	7 (0.3)	**0.001**	9 (0.4)	7 (0.3)	**1.000**
Prior CVA	**359 (8.8)**	**102 (3.7)**	**<.0001**	**92 (4.4)**	**95 (4.6)**	**1.000**
Peripheral vascular diseases	33 (0.8)	11 (0.4)	**0.039**	9 (0.4)	9 (0.4)	**1.000**
Discharge medications						
Cilostazol	158 (3.9)	21 (0.8)	**<.0001**	23 (1.1)	21 (1.0)	**0.762**
Ca-channel Blocker	477 (11.7)	164 (6.0)	**<.0001**	141 (6.8)	150 (7.2)	**0.584**
Beta-Blocker	3,390 (83.0)	2,320 (84.5)	**0.094**	1,732 (83.2)	1,745 (83.8)	**0.587**
ACE Inhibitor	1,479 (36.2)	952 (34.7)	**0.197**	739 (35.5)	741 (35.6)	**0.948**
ARB	1,584 (38.8)	1,146 (41.7)	**0.014**	853 (41.0)	850 (40.8)	**0.925**
Stain	3,850 (94.2)	2,633 (95.9)	**0.002**	1,998 (96.0)	1,990 (95.6)	**0.538**
Warfarin	75 (1.8)	18 (0.7)	**<.0001**	20 (1.0)	18 (0.9)	**0.745**
New oral anticoagulant	173 (4.2)	18 (0.7)	**<.0001**	19 (0.9)	18 (0.9)	**0.869**
Insulin	148 (3.6)	65 (2.4)	**0.003**	53 (2.5)	58 (2.8)	**0.631**
PPI	2,371 (58.0)	1,271 (46.3)	**<.0001**	1,027 (49.3)	1,049 (50.4)	**0.495**

In-hospital Clinical Event

	Aspirin + Clopidgrel (n = 4,085)	Aspirin + New $P2Y_{12}$ (n = 2,745)	Odds Ratio (95% CI)	p-value
In-hospital arrest	58 (1.4)	38 (1.4)	0.989 (0.641-1.524)	0.958
In-hospital CVA	27 (0.7)	4 (0.1)	0.286 (0.097-0.843)	0.023
In-hospital bleeding	198 (4.8)	37 (1.3)	0.334 (0.231-0.481)	<.001

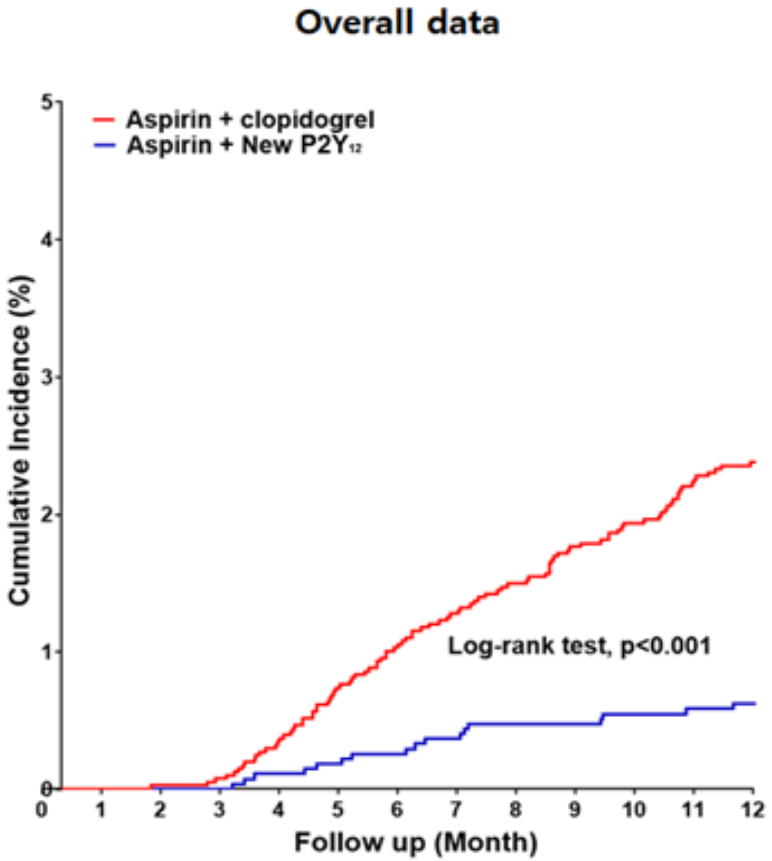
3-month event follow-up data

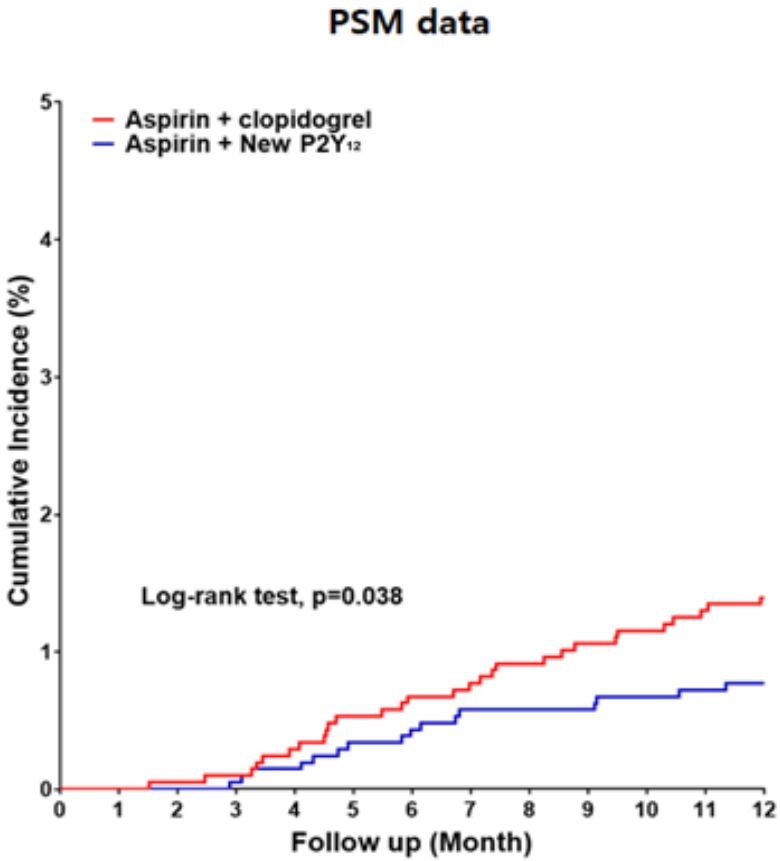
3-month event		Aspirin + Clopidgrel (n = 4,085)	Aspirin + New $P2Y_{12}$ (n = 2,745)	HR (95% CI)	P-value
Overall data	All-cause death	6 (0.15)	1 (0.04)	0.575 (0.054 ~ 6.116)	0.647
	MI	11 (0.27)	4 (0.15)	1.172 (0.318 ~ 4.315)	0.812
	CVA	9 (0.22)	6 (0.22)	1.446 (0.452 ~ 4.631)	0.535
	MACE (Death, MI, CVA)	25 (0.61)	11 (0.40)	1.157 (0.532 ~ 2.518)	0.713
	Bleeding	9 (0.22)	8 (0.29)	1.258 (0.434 ~ 3.646)	0.673
		Aspirin + Clopidgrel (n = 2,082)	Aspirin + New $P2Y_{12}$ (n = 2,082)	HR (95% CI)	p-value
PSM data	All-cause death	2 (0.1)	1 (0.0)	0.500 (0.045 ~ 5.512)	0.571
	MI	3 (0.1)	3 (0.1)	1.000 (0.202 ~ 4.955)	1.000
	CVA	2 (0.1)	5 (0.2)	2.501 (0.485 ~ 12.892)	0.273
	MACE (Death, MI, CVA)	7 (0.34)	9 (0.43)	1.286 (0.479 ~ 3.452)	0.618
	Bleeding	4 (0.2)	7 (0.3)	1.751 (0.512 ~ 5.980)	0.372

1-year event follow-up data

1-year event		Aspirin + Clopidgrel (n = 4,085)	Aspirin + New $P2Y_{12}$ (n = 2,745)	HR (95% CI)	p-value
Overall data	All-cause death	103 (2.52)	17 (0.62)	0.574 (0.355~ 0.983)	0.043
	MI	78 (1.91)	30 (1.09)	0.883 (0.557 ~ 1.401)	0.598
	CVA	21 (0.51)	14 (0.51)	1.767 (0.818 ~ 3.817)	0.147
	MACE (Death, MI, CVA)	195 (4.77)	60 (2.19)	0.790 (0.579 ~ 1.077)	0.1362
	Bleeding	32 (0.78)	16 (0.58)	0.913 (0.467 ~ 1.783)	0.789
		Aspirin + Clopidgrel (n = 2,082)	Aspirin + New $P2Y_{12}$ (n = 2,082)	HR (95% CI)	p-value
PSM data	All-cause death	30 (1.4)	16 (0.8)	0.532 (0.290 ~ 0.976)	0.041
	MI	31 (1.5)	27 (1.3)	0.869 (0.519 ~ 1.456)	0.595
	CVA	4 (0.2)	11 (0.5)	2.754 (0.877 ~ 8.648)	0.083
	MACE (Death, MI, CVA)	64 (3.07)	53 (2.55)	0.827 (0.574 ~ 1.189)	0.304
	Bleeding	13 (0.6)	14 (0.7)	1.078 (0.507 ~ 2.293)	0.845

Cumulative incidence curve of all-cause death according to DAPT





3-month event follow-up data with DES patients

3-month event		Aspirin + Clopidgrel (n = 3,510)	Aspirin + New $P2Y_{12}$ (n = 2,537)	HR (95% CI)	p-value
Overall data	All-cause death	5 (0.1)	1 (0.0)	0.849 (0.075 ~ 9.639)	0.894
	MI	8 (0.2)	3 (0.1)	0.947 (0.208 ~ 4.307)	0.944
	CVA	7 (0.2)	5 (0.2)	1.350 (0.360 ~ 5.072)	0.656
	MACE (Death, MI, CVA)	19 (0.5)	9 (0.4)	1.057 (0.439-2.543)	0.901
	Bleeding	6 (0.2)	8 (0.3)	1.890 (0.588 ~ 6.068)	0.285
		Aspirin + Clopidgrel (n = 1,808)	Aspirin + New $P2Y_{12}$ (n = 1,912)	HR (95% CI)	p-value
PSM data	All-cause death	2 (0.1)	1 (0.1)	0.473 (0.043 ~ 5.212)	0.540
	MI	2 (0.1)	2 (0.1)	0.946 (0.133 ~ 6.713)	0.955
	CVA	1 (0.1)	4 (0.2)	3.785 (0.423 ~ 33.860)	0.233
	MACE (Death, MI, CVA)	5 (0.3)	7 (0.4)	1.324 (0.420-4.173)	0.631
	Bleeding	3 (0.2)	7 (0.4)	2.207 (0.571 ~ 8.534)	0.251

1-year event follow-up data with DES patients

1-year event		Aspirin + Clopidgrel (n = 3,510)	Aspirin + New $P2Y_{12}$ (n = 2,537)	HR (95% CI)	p-value
Overall data	All-cause death	80 (2.3)	14 (0.6)	0.504 (0.274 ~ 0.925)	0.027
	MI	70 (2.0)	25 (1.0)	0.719 (0.436 ~ 1.185)	0.195
	CVA	16 (0.5)	13 (0.5)	1.897 (0.814 ~ 4.419)	0.137
	MACE (Death, MI, CVA)	161 (4.6)	51 (2.0)	0.693 (0.493 ~ 0.974)	0.034
	Bleeding	26 (0.7)	16 (0.6)	0.996 (0.493 ~ 2.012)	0.991
		Aspirin + Clopidgrel (n = 1,808)	Aspirin + New $P2Y_{12}$ (n = 1,912)	HR (95% CI)	p-value
PSM data	All-cause death	26 (1.4)	13 (0.7)	0.471 (0.242 ~ 0.917)	0.026
	MI	29 (1.6)	22 (1.2)	0.715 (0.411 ~ 1.245)	0.235
	CVA	3 (0.2)	10 (0.5)	3.157 (0.869 ~ 11.472)	0.080
	MACE (Death, MI, CVA)	57 (3.2)	44 (2.3)	0.727 (0.491 ~ 0.989)	0.042
	Bleeding	11 (0.6)	14 (0.7)	1.205 (0.547 ~ 2.655)	0.642

Conclusion

- **The new $P2Y_{12}$ inhibitors groups reduced the 1-year all-cause death as compared with aspirin plus clopidogrel groups.**

- **For the DES patients, the new $P2Y_{12}$ inhibitors groups reduced the 1-year all-cause death and MACE(death, MI, CVA) as compared with aspirin plus clopidogrel groups in DES patients.**