#AHA22

Long Term Follow-Up of Aspirin vs. Clopidogrel Monotherapy in the Chronic Maintenance Period After PCI with DES : The Host-Exam Extended Study

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Disclosures

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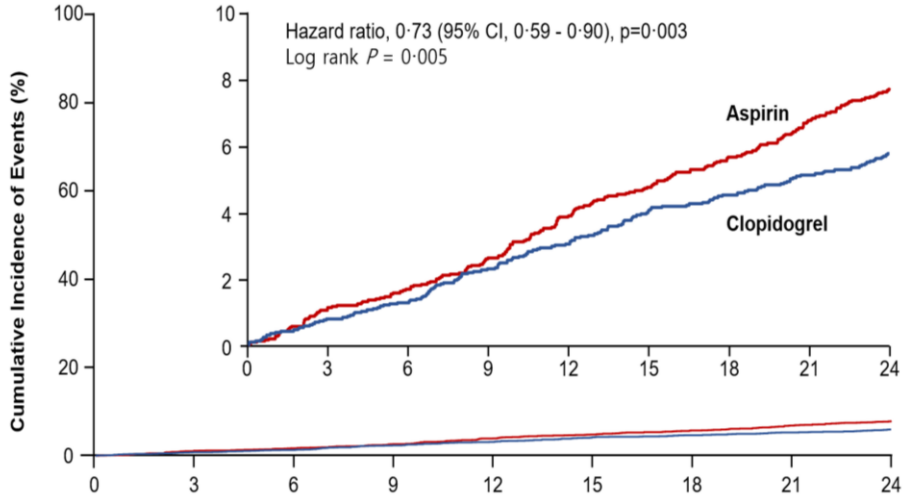
Background

- Post-percutaneous coronary intervention (PCI), guidelines recommend indefinite maintenance of single antiplatelet therapy after the initial 6- to 12-months of dual antiplatelet therapy (DAPT).
- ***Aspirin*** is the most widely used antiplatelet agent (LOE 1A), and ***Clopidogrel*** is recommended as recommended as an alternative strategy.
- The **HOST-EXAM trial** reported superiority of Clopidogrel over Aspirin monotherapy during a 2-year follow-up in stable CAD pts who were event-free under DAPT for 12month after PCI with DES.



BK Koo, J Kang, KW Park,,,, HS Kim.

Lancet 2021

Background

- However, the **higher mortality** in the clopidogrel arm (which did not yield statistical significance) confused interpretation of the results.
- To clarify the confusing mortality issue, and given that antiplatelet monotherapy is prescribed ***lifelong for secondary prevention***, a ***long-term follow-up study*** is is warranted.
- Therefore, a ***post-trial extended follow-up study*** was designed to compare the long-term outcomes between clopidogrel and aspirin monotherapy.

BK Koo, J Kang, KW Park,,,,,, HS Kim.

Lancet 2021

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	Clopidogrel (n=2710)	Aspirin (n=2728)	Hazard ratio (95% CI)*	p value
Primary composite endpoint†	152 (5·7%)	207 (7·7%)	0·73 (0·59–0·90)	0·003
Thrombotic composite endpoint‡	99 (3·7%)	146 (5·5%)	0·68 (0·52–0·87)	0·003
Any bleeding (BARC type ≥2)§	61 (2·3%)	87 (3·3%)	0·70 (0·51–0·98)	0·036
All-cause death¶	51 (1·9%)	36 (1·3%)	1·43 (0·93–2·19)	0·101
Cardiac death	19 (0·7%)	14 (0·5%)	1·37 (0·69–2·73)	0·374
Non-cardiac death	32 (1·2%)	22 (0·8%)	1·47 (0·85–2·52)	0·167
Non-fatal myocardial infarction	18 (0·7%)	28 (1·0%)	0·65 (0·36–1·17)	0·150
Stroke	18 (0·7%)	43 (1·6%)	0·42 (0·24–0·73)	0·002
Ischaemic stroke	14 (0·5%)	26 (1·0%)	0·54 (0·28–1·04)	0·064
Haemorrhagic stroke	4 (0·2%)	17 (0·6%)	0·24 (0·08–0·70)	0·010
Readmission due to ACS	66 (2·5%)	109 (4·1%)	0·61 (0·45–0·82)	0·001
Major bleeding (BARC type ≥3)	33 (1·2%)	53 (2·0%)	0·63 (0·41–0·97)	0·035
Any revascularisation	56 (2·1%)	69 (2·6%)	0·82 (0·57–1·16)	0·261
Target lesion revascularisation	24 (0·9%)	36 (1·4%)	0·67 (0·40–1·12)	0·130
Target vessel revascularisation	37 (1·4%)	48 (1·8%)	0·78 (0·50–1·19)	0·245
Definite or probable stent thrombosis	10 (0·4%)	16 (0·6%)	0·63 (0·29–1·39)	0·251
Any minor gastrointestinal complications	272 (10·2%)	320 (11·9%)	0·85 (0·72–1·00)	0·048

Study Objective

- To compare the long-term efficacy and safety between Aspirin and Clopidogrel monotherapy in stable coronary artery disease patients who received PCI with a DES.

The HOST-EXAM Extended study

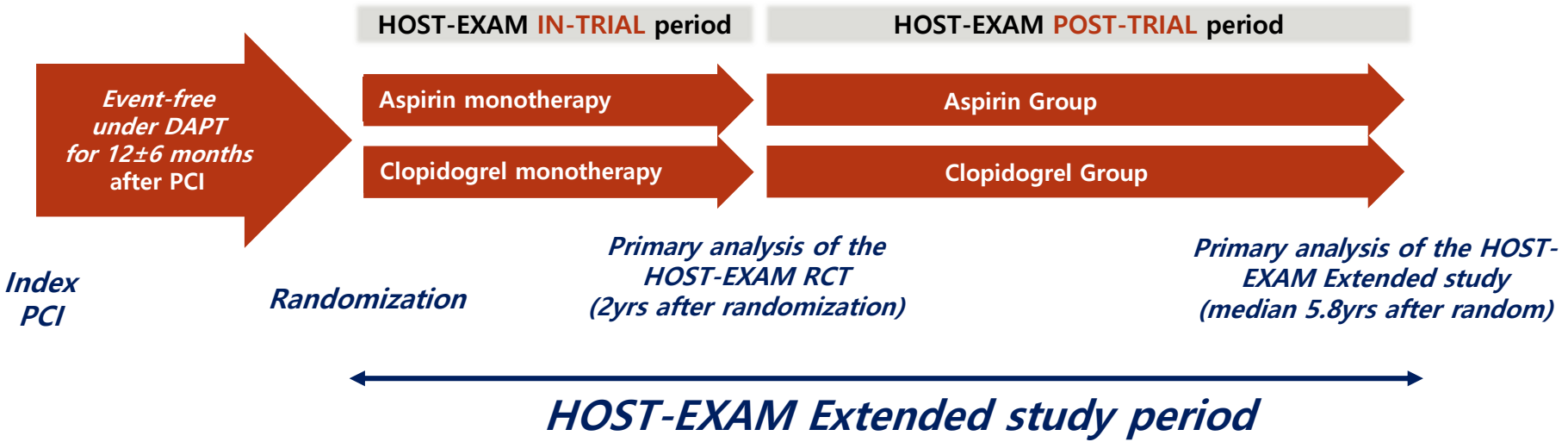
H*armonizing* **O***ptimal* **S***trategy for* **T***reatment of coronary artery diseases*

*- **EX**tended **A**ntiplatelet **M**onotherapy - **Extended** follow-up*

- Open label follow-up study after the initial 2-year follow-up of the HOST-EXAM trial
- During the extended follow-up (median 5.8 yrs), the single antiplatelet agent was determined by the treating physician with no mandatory designation.

Study Design and Patient Population

- 5,530 eligible patients screened, from 37 centers in Korea



Clinical events and final clinical status ascertained at March, 2022.
The vital status of all patients coss-checked via the National Health Insurance Service system.

Study Endpoints

- **Primary Endpoint: POCO (Patient Oriented Composite outcome)**
  - All-cause death, nonfatal myocardial infarction, stroke, readmission due to and major bleeding complications (defined as BARC type ≥3 bleeding)
- **Key Secondary Endpoints**
  - **Thrombotic composite endpoint**
    - Cardiac death, nonfatal myocardial infarction, ischemic stroke, readmission to ACS and stent thrombosis (definite & probable)
  - **Bleeding endpoint**
    - BARC type ≥2 bleeding

Study Organization

Principle Investigator

Hyo-Soo Kim

Steering Committee

Hyo-Soo Kim Bon Kwon Koo

Eun-Seok Shin Jung-Kyu Han

Clinical event adjudication committee

Woo Jin Jang Ki-Hyun Jeon

Publication Committee

Hyo-Soo Kim Bon Kwon Koo

Eun-Seok Shin Seung-Woon Rha

Jang-Whan Bae Kyung Woo Park

Jung-Kyu Han Jeehoon Kang

Primary Statistician

Jeehoon Kang

Data coordination and management

National University Hospital

Medical Research Collaborating Center of Seoul

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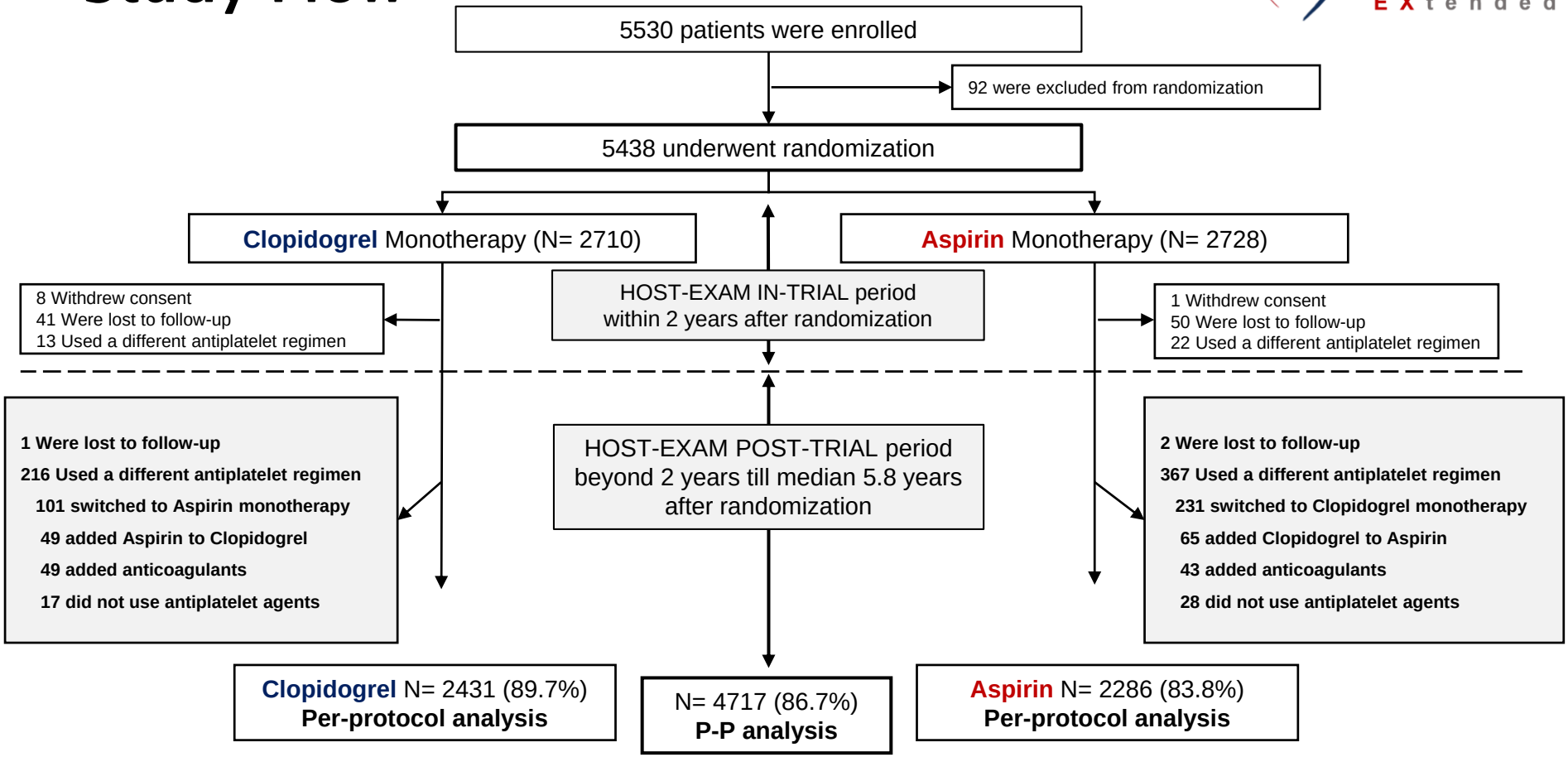
Study Flow


5530 patients were enrolled
92 were excluded from randomization
5438 underwent randomization
Clopidogrel Monotherapy (N= 2710)
Aspirin Monotherapy (N= 2728)
8 Withdrew consent
41 Were lost to follow-up
13 Used a different antiplatelet regimen
HOST-EXAM IN-TRIAL period
within 2 years after randomization
1 Withdrew consent
50 Were lost to follow-up
22 Used a different antiplatelet regimen
1 Were lost to follow-up
216 Used a different antiplatelet regimen
101 switched to Aspirin monotherapy
49 added Aspirin to Clopidogrel
49 added anticoagulants
17 did not use antiplatelet agents
HOST-EXAM POST-TRIAL period
beyond 2 years till median 5.8 years
after randomization
2 Were lost to follow-up
367 Used a different antiplatelet regimen
231 switched to Clopidogrel monotherapy
65 added Clopidogrel to Aspirin
43 added anticoagulants
28 did not use antiplatelet agents
Clopidogrel N= 2431 (89.7%)
Per-protocol analysis
N= 4717 (86.7%)
P-P analysis
Aspirin N= 2286 (83.8%)
Per-protocol analysis

Baseline Profiles (1/2)

		Clopidogrel (N = 2431)	Aspirin (N = 2286)
Demographics	Age (years)	63.3 ± 10.8	63.3 ± 10.7
	Body Mass Index (kg/m^2)	24.9 ± 3.1	24.8 ± 3.4
	Male	1807 (74.3%)	1723 (75.4%)
Comorbidities	Diabetes mellitus	818 (33.6%)	775 (33.9%)
	IDDM	48 (2.0%)	51 (2.2%)
	Hypertension	1493 (61.4%)	1402 (61.3%)
	Dyslipidemia	1690 (69.5%)	1613 (70.6%)
	Current smoker	479 (19.7%)	500 (21.9%)
	Chronic kidney disease	314 (12.9%)	273 (11.9%)
	Previous MI	406 (16.7%)	362 (15.8%)
	Previous CVA	103 (4.2%)	110 (4.8%)
Clinical Indication of PCI	Silent ischemia	52 (2.1%)	61 (2.7%)
	Stable angina	620 (25.5%)	593 (26.0%)
	Unstable angina	871 (35.8%)	773 (33.8%)
	NSTEMI	471 (19.4%)	454 (19.9%)
	STEMI	417 (17.2%)	404 (17.7%)

Baseline Profiles (2/2)

		Clopidogrel (N = 2431)	Aspirin (N = 2286)
Angiographic data per patient	1-vessel disease	1229 (50.6%)	1140 (49.9%)
	2-vessel disease	763 (31.4%)	716 (31.3%)
	3-vessel disease	439 (18.1%)	428 (18.7%)
	Left main disease	127 (5.2%)	112 (4.9%)
	PCI for bifurcation lesion	261 (10.7%)	232 (10.2%)
	2-stenting for bifurcation PCI	39 (1.6%)	33 (1.4%)
	PCI for CTO lesion	235 (9.3%)	223 (9.8%)
	Number of treated lesions	1.32 ± 0.59	1.30 ± 0.57
	Total length of implanted stents	36.3 ± 24.3	35.3 ± 23.2
	Total number of implanted stents	1.5 ± 0.8	1.5 ± 0.8
Concurrent medication	ACE inhibitors / ARBs	1224 (50.3%)	1092 (47.8%)
	Beta blockers	1217 (50.1%)	1138 (49.8%)
	Nitrates	234 (9.6%)	195 (8.5%)
	Statins	2057 (84.6%)	1932 (84.5%)
	Proton pump inhibitors	251 (10.3%)	266 (11.6%)

Clinical Outcomes

▪ *Primary Endpoint*

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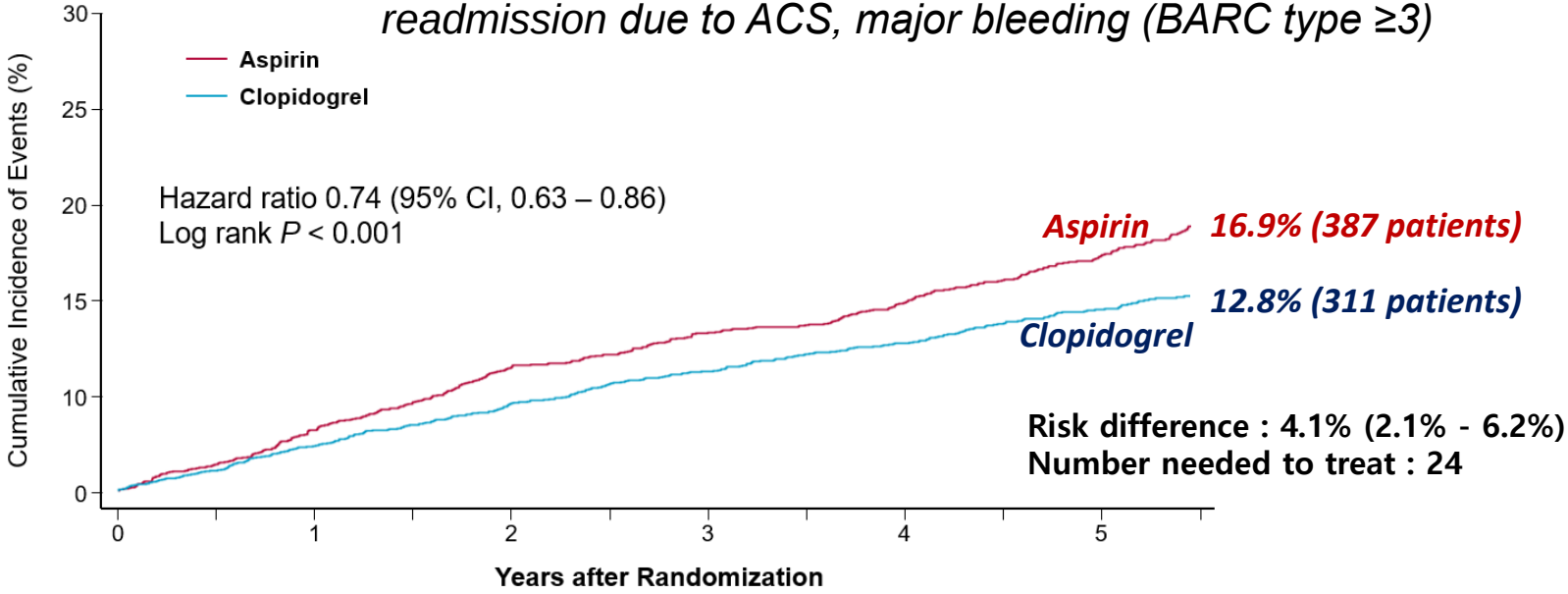
Primary endpoint: *All-cause death, nonfatal MI, stroke, readmission due to ACS, major bleeding (BARC type ≥3)*



Number at Risk

Aspirin	2286	2189	2086	2014	1777	1287	1007
Clopidogrel	2431	2355	2280	2214	1964	1462	1181

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Clinical Outcomes

- *Landmark analysis of the Primary Endpoint*

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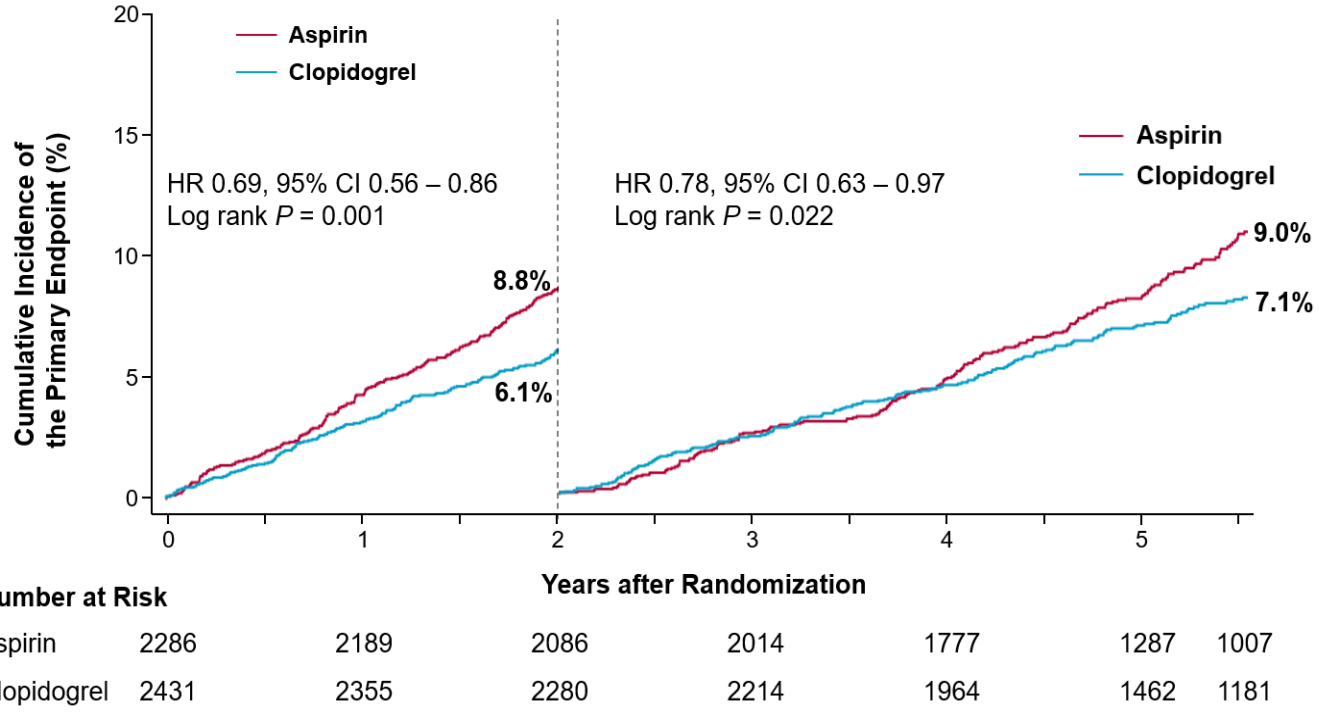
Consistent beneficial effects
both
in the In-trial period
and post-trial period



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Clinical Outcomes ▪ *Secondary Endpoints*

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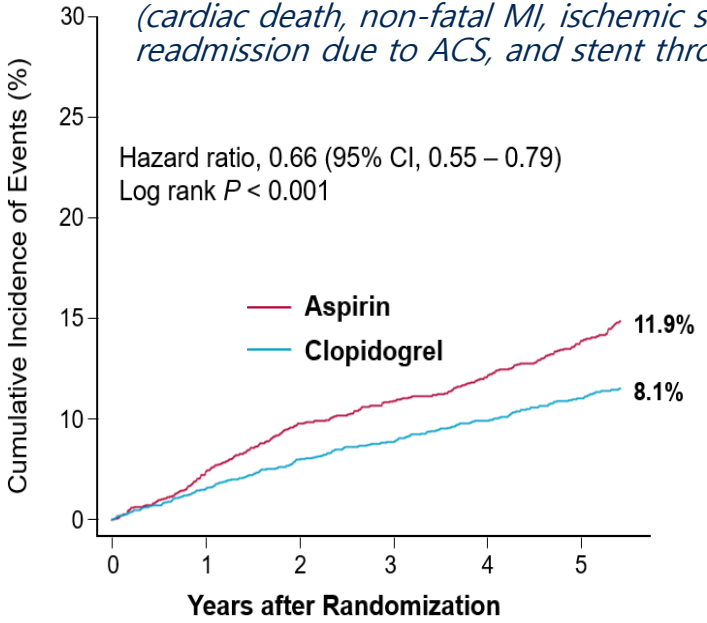
Thrombotic composite outcome

(cardiac death, non-fatal MI, ischemic stroke, readmission due to ACS, and stent thrombosis)

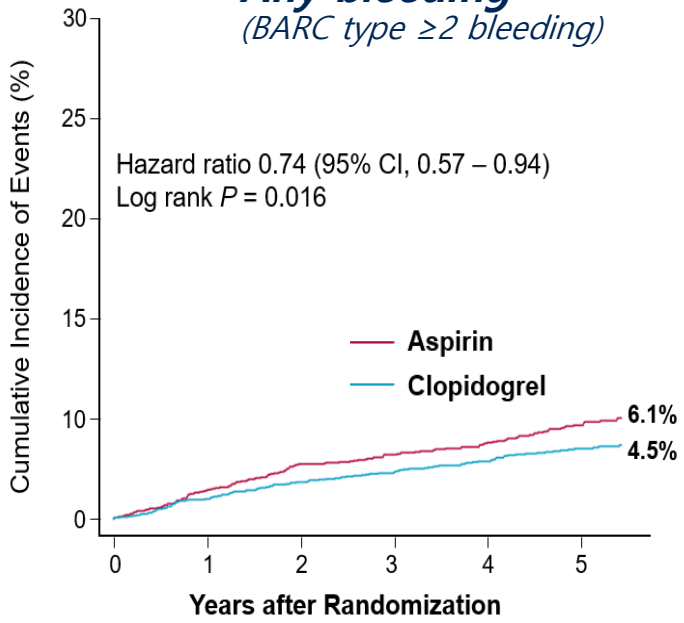


Number at Risk

Aspirin	2286	2120	1819	1040
Clopidogrel	2431	2304	1992	1202

Any bleeding

(BARC type ≥2 bleeding)



Number at Risk

Aspirin	2286	2175	1888	1104
Clopidogrel	2431	2323	2028	1238

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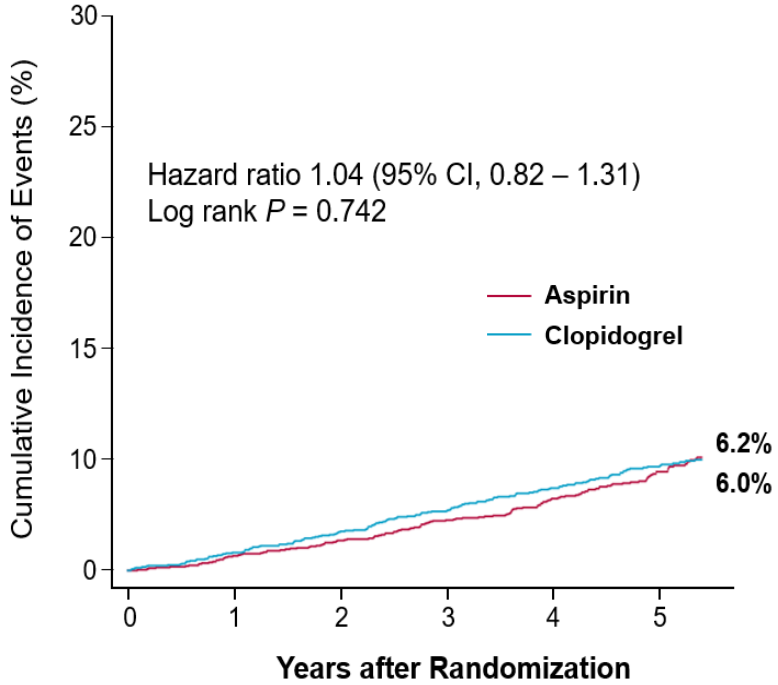
Clinical Outcomes

- *Mortality*

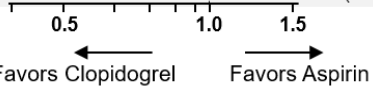


Number at Risk

Aspirin	2286	2244	1971	1165
Clopidogrel	2431	2374	2088	1285

No. of patients	Clopidogrel (N=2431)	Aspirin (N=2286)	P value
Total mortality	150 (6.2%)	136 (6.0%)	0.753
Cardiovascular cause	69 (2.8%)	71 (3.1%)	0.587
Cardiac arrest	21	22	
Heart failure aggravation	5	3	
Cerebrovascular accident	7	3	
Unknown origin of death	36	43	
Non-cardiovascular cause	81 (3.3%)	65 (2.8%)	0.334
Malignancy	34	29	
- Gastrointestinal origin	15	12	
- Respiratory origin	8	11	
- Endocrinology origin	1	1	
- Genitourinary origin	4	3	
- Other	3	2	
- Unknown primary	3	0	
Infectious disease	4	5	
Suicide or Trauma	8	3	
Others	20	16	

	Clopidogrel group (events/patients)	Aspirin group (events/patients)	Hazard Ratio (95% CI)	P value	Interaction P
Age (years)					
≥65	200/1040	232/992	0.80 (0.66-0.96)	0.019	0.176
<65	110/1390	155/1294	0.65 (0.51-0.83)	<0.001	
Sex					
Male	222/1807	287/1723	0.72 (0.60-0.85)	<0.001	0.563
Female	89/624	100/563	0.79 (0.59-1.05)	0.107	
Body Mass Index ≥ 25 kg/m²					
Yes	119/1103	140/976	0.74 (0.58-0.94)	0.014	0.936
No	179/1244	231/1233	0.75 (0.61-0.91)	0.003	
Diabetes Mellitus					
Yes	128/817	165/776	0.71 (0.57-0.90)	0.004	0.764
No	182/1613	222/1510	0.75 (0.62-0.91)	0.004	
Chronic Kidney Disease					
Yes	77/313	95/274	0.67 (0.50-0.90)	0.009	0.614
No	233/2117	292/2012	0.74 (0.62-0.88)	0.001	
Multivessel Disease					
Yes	170/1201	227/1145	0.69 (0.57-0.85)	0.002	0.356
No	140/1229	159/1140	0.80 (0.64-1.00)	0.054	
Acute Myocardial Infarction					
Yes	116/888	143/858	0.77 (0.60-0.98)	0.036	0.756
No	194/1542	244/1428	0.72 (0.59-0.86)	<0.001	
Acute Coronary Syndrome					
Yes	219/1758	274/1631	0.72 (0.61-0.86)	<0.001	0.556
No	91/672	113/655	0.76 (0.58-1.00)	0.053	
Complex PCI					
Yes	60/530	92/499	0.59 (0.43-0.82)	0.002	0.138
No	249/1882	294/1769	0.78 (0.66-0.92)	0.004	
High Bleeding Risk					
Yes	113/461	126/390	0.71 (0.55-0.92)	0.009	0.860
No	161/1616	204/1536	0.74 (0.60-0.90)	0.004	
Proton Pump Inhibitor usage					
Yes	39/251	56/266	0.72 (0.48-1.08)	0.113	0.888
No	272/2180	331/2020	0.74 (0.63-0.87)	<0.001	



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Subgroup Analysis

No significant interaction between the treatment effect on primary endpoints and subgroups

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Conclusion

- In the extended 6 years' follow-up of patients who were event-free under DAPT for 12±6 months after PCI with DES,
  - Clopidogrel monotherapy as compared with Aspirin monotherapy significantly reduced the risk of the composite of all-cause death, nonfatal myocardial infarction, stroke, readmission due to ACS, and BARC type ≥3 bleeding.
  - The beneficial effect of clopidogrel was observed in thrombotic composite endpoints as well as any bleeding endpoint.
  - The mortality risk was similar between the two groups.

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Aspirin vs. Clopidogrel for Chronic Maintenance Monotherapy after Percutaneous Coronary Intervention: the HOST-EXAM Extended Study

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THANK YOU

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