One-Year Outcome of HOST-BIOLIMUS-3000 Korea registry

interim analysis

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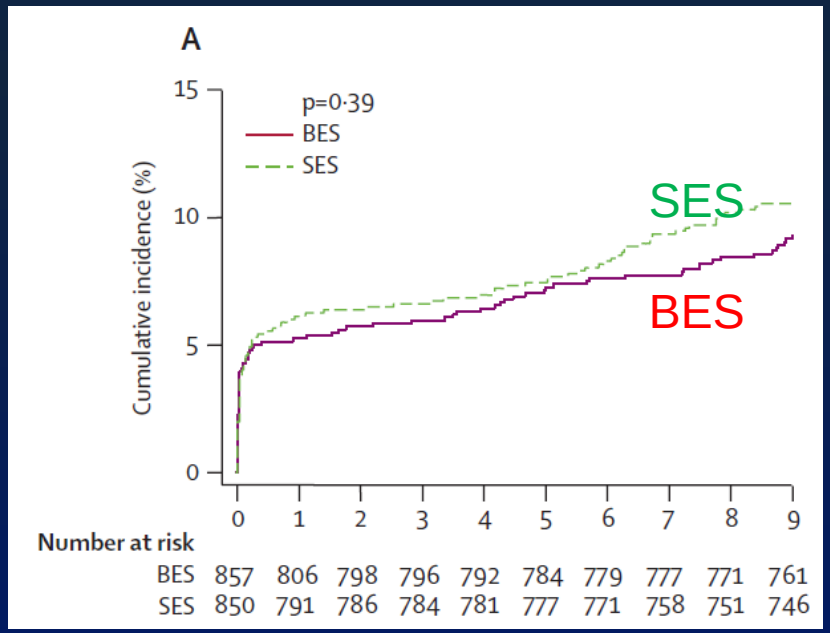
Part I.

Previous RCTs regarding Biolimus Eluting Stents

LEADERS trial in Europe

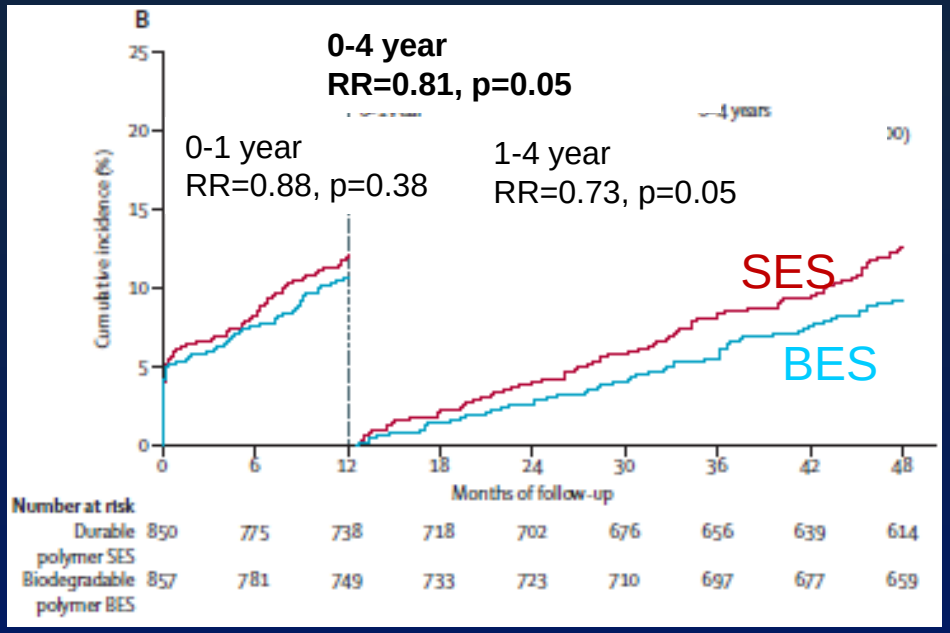
- Multicenter, assessor-blind, non-inferiority study
- Total N= 1,707 (2472 lesions)
- **BES (Biomatrix Flex) versus SES (Cypher)**
- Primary Efficacy end point: Cardiac death + MI + clinically-driven TVR at 9 months and at 4 years

At 9 months



BES (N=857) → 45 events (5.3%)
SES (N=850) → 52 events (6.1%)

At 4 years

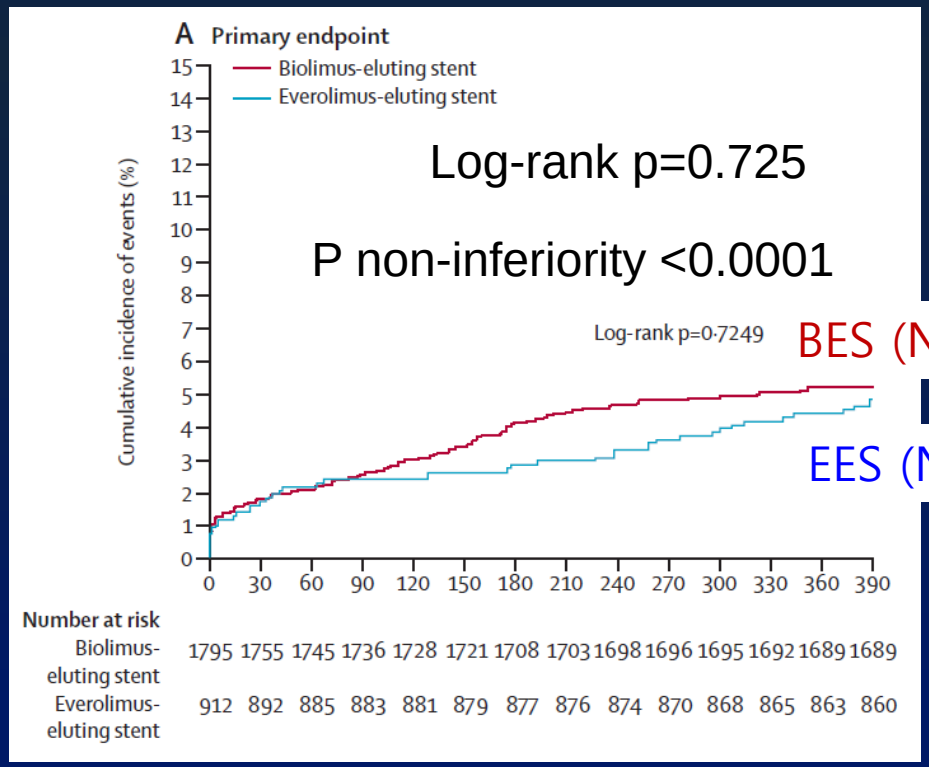


→ 160 events (19%)
→ 192 events (23%)

P Juni et al. Lancet. 2008/2011

COMPARE II trial in Europe

- Open-label, prospective, randomized, controlled, non-inferiority trial
- Total N= 2,707 (4025 lesions)
  (exclusion criteria :age >18YO, life expectancy > 5Y, ref.VD 2.0-4.0mm)
- **BES (Nobori) versus EES (Xience V or Promus)**
- **Primary end point:** composite of safety(cardiac death and non-fatal MI) and efficacy (clinically indicated TVR) at 12 months



BES (N=1795) → 93 events (5.2%)

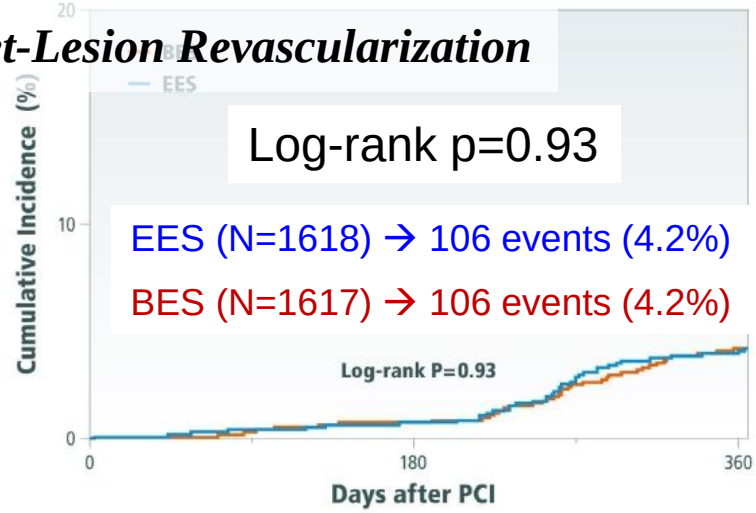
EES (N=912) → 44 events (4.8%)

Smits PC et al. Lancet. 2013

NEXT trial in Japan

- Multicenter, randomized, non-inferiority trial
- Total N= 3,235 (4069 lesions) (mostly stable angina)
- **BES (Nobori) versus EES (Xience V or Promus)**
- Primary Efficacy end point: Any TLR at 1 year
  Primary Safety end point: Death or Myocardial infarction at 3 years

Target-Lesion Revascularization



Log-rank p=0.93

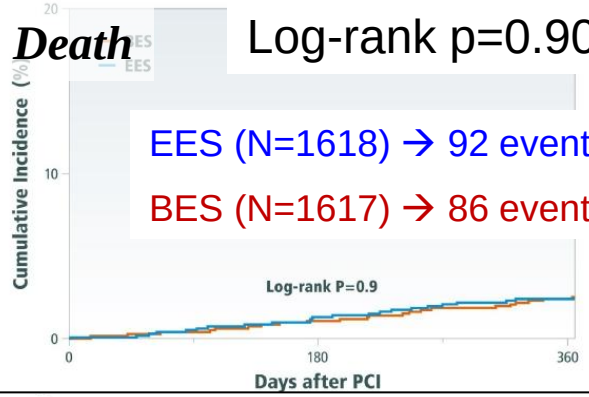
EES (N=1618) → 106 events (4.2%)

BES (N=1617) → 106 events (4.2%)

Interval	0 day	30 days	180 days	240 days	365 days
BES group					
No. of patients with event		2	13	24	67
No. of patients at risk	1617	1607	1579	1556	1491
Cumulative Incidence		0.1%	0.8%	1.5%	4.2%
EES group					
No. of patients with event		2	12	26	66
No. of patients at risk	1618	1612	1578	1556	1497
Cumulative Incidence		0.1%	0.8%	1.6%	4.2%

Death

Log-rank p=0.90

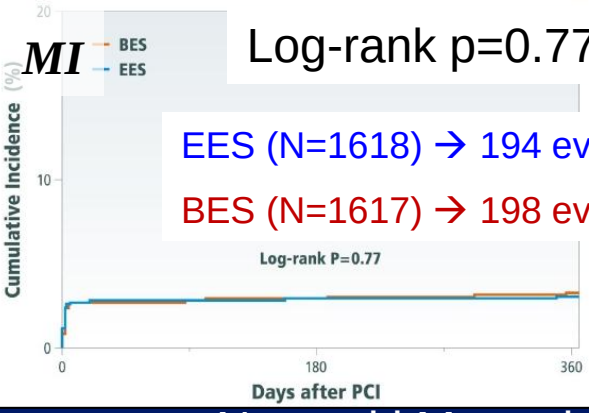


EES (N=1618) → 92 events (2.5%)

BES (N=1617) → 86 events (2.6%)

MI

Log-rank p=0.77



EES (N=1618) → 194 events (3.1%)

BES (N=1617) → 198 events (3.3%)

Natsuaki M. et al. ACC. 2013

How is the BES in the real-world patients?

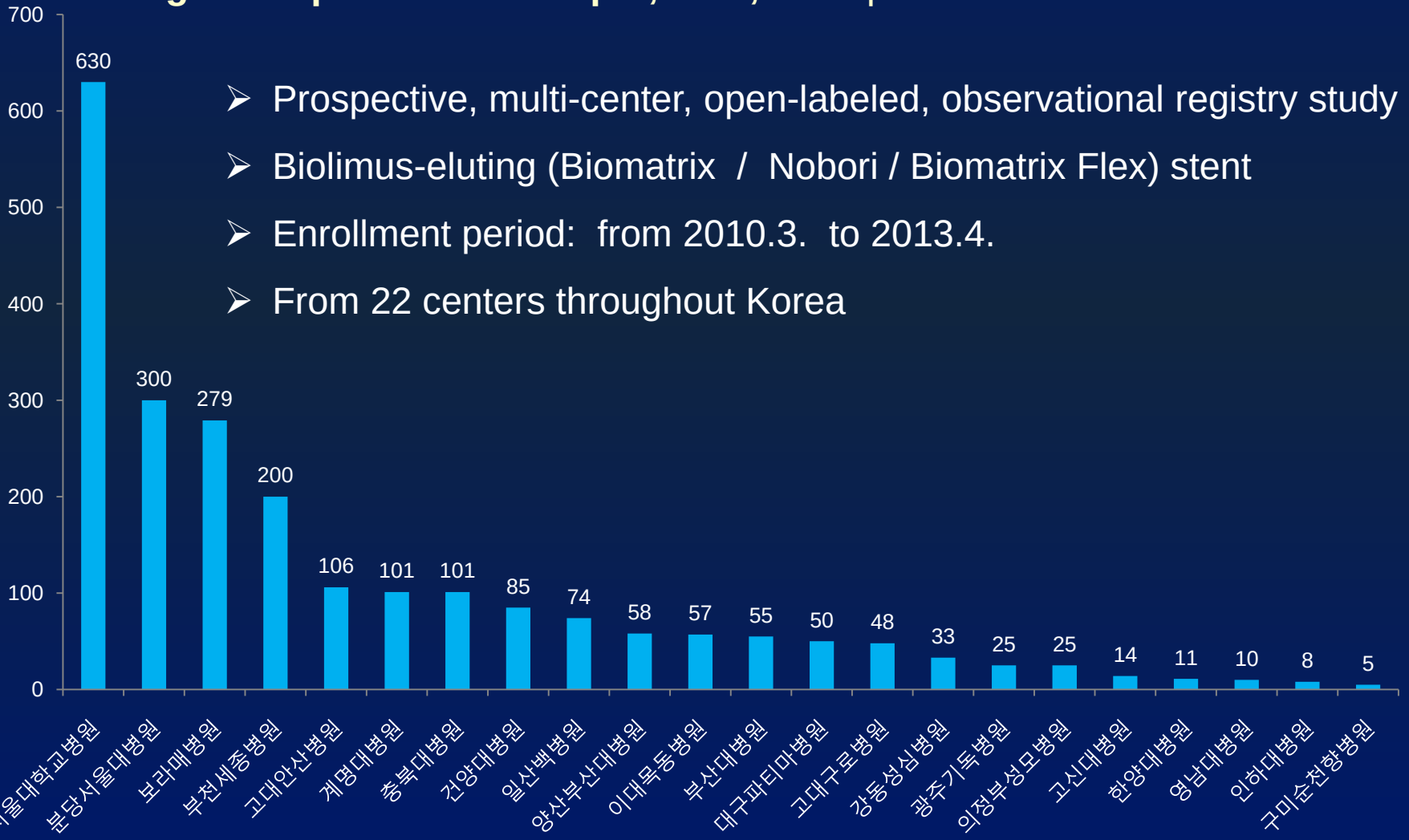
Part II.

Current Status of HOST-BIOLIMUS-3000 Korea registry

HOST =Harmonized Optimal Strategy to Treat CAD

HOST-BIOLIMUS-3000 Korea registry

Target sample size = 3000 pts, Now, 2276 patients from **22** centers



- Prospective, multi-center, open-labeled, observational registry study
- Biolimus-eluting (Biomatrix / Nobori / Biomatrix Flex) stent
- Enrollment period: from 2010.3. to 2013.4.
- From 22 centers throughout Korea

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Enrollment criteria

- **Inclusion criteria**

: Coronary artery disease (stable angina, acute myocardial infarction, silent MI)

→ Presence of more than 1 of the following

- luminal stenosis > 50%
- Number of lesions: no limitation
- Number of vessels: no limitation
- Vessel length: no limitation

- **Exclusion criteria**

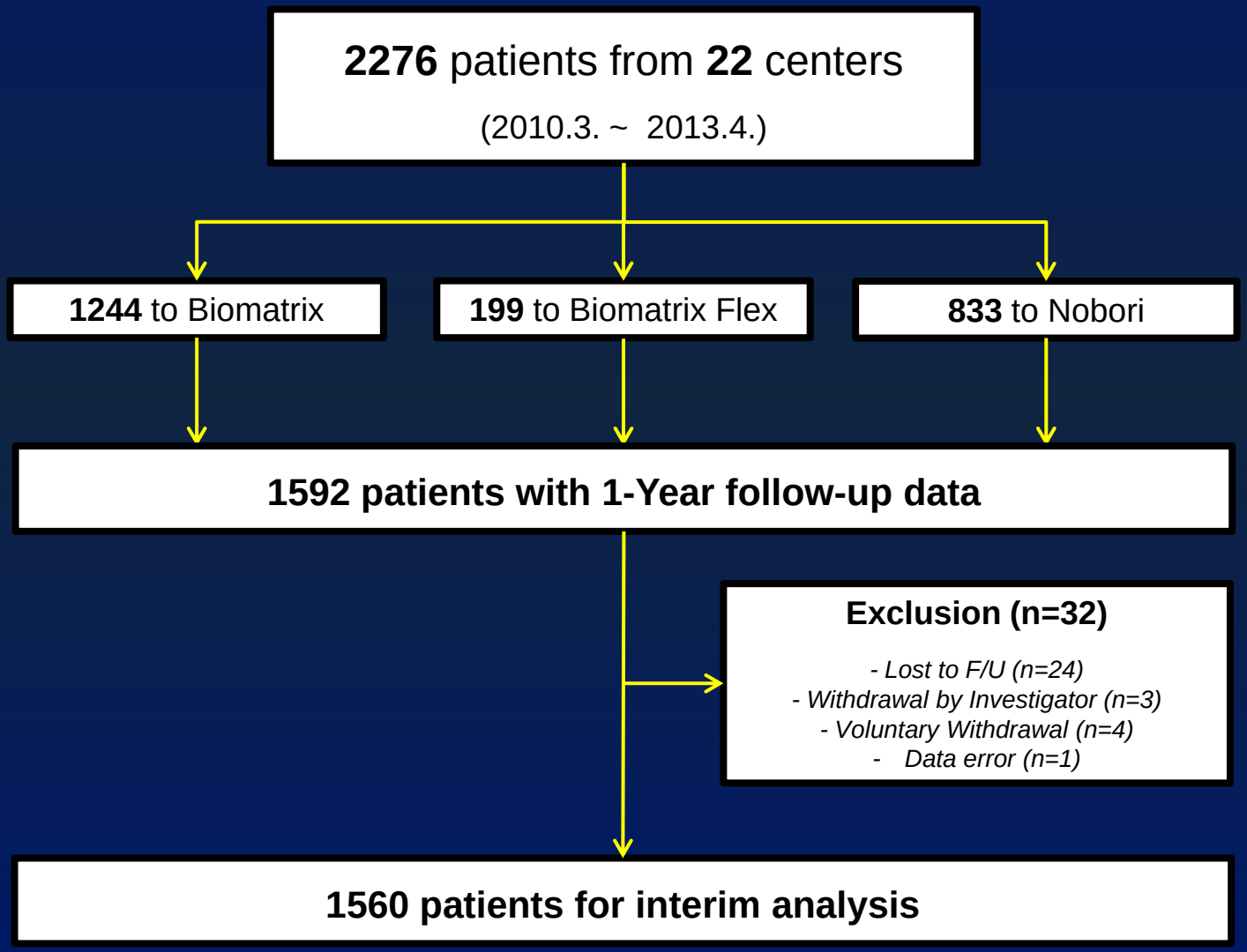
: Alleged drug allergy

(aspirin, clopidogrel, heparin, stainless steel, sirolimus, biolimus, contrast material)

: Pregnancy

: Participants in other clinical trial

Current status of HOST-BIOLIMUS registry



Part III.

Interim analysis
To compare three 2nd-generation DES with either Biodegradable or Durable Polymer

- ► BES from HOST-BIOLIMUS registry
- ► EES from EXCELLENT registry
- ► ZES-R from RESOLUTE-KOREA registry

A. Clinical outcome in whole patients
B. Clinical outcome in Propensity score-matched population
C. Stent Thrombosis

HOST =Harmonized Optimal Strategy to Treat CAD

Study population and design to compare three HOST-DES cohorts

BES	EES	ZES-R
(Biolimus-eluting stent) (N=1,560)	**(Xience V/Promus Evorolimus-eluting stent)** (N=3,056)	**(Endeavor Resolute Zotarolimus-eluting stent)** (N=1,998)

Follow-up at 1, 9, and 12 months

Imaging Sub-studies at 8-12 months: Angiography or IVUS

(Scheduled follow-up angiography by local site protocol was allowed beyond 240 days.)

- **Primary outcome: Target lesion failure**
  (cardiac death + MI (not clearly attributed to a non-target vessel), or a clinically indicated TLR)
- **Secondary outcome: POCO**
  (all-cause mortality+ any MI + any revascularization)

HOST =Harmonized Optimal Strategy to Treat CAD

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Part III.

A. Clinical outcome in Whole patients

B. Clinical outcome in Propensity score-matched population

- ► BES from HOST-BIOLIMUS registry
- ► EES from EXCELLENT registry
- ► ZES-R from RESOLUTE-KOREA registry

C. Stent Thrombosis

Baseline Profiles in three HOST-DES cohorts

	BES (N = 1,560)	EES (N=3,056)	ZES-R (N=1998)	P Value for BES versus. EES	P Value for BES versus. ZES-R
Dermographics					
Age (yrs)	**64.2 ± 11.0**	63.9 ± 10.8	63.9 ± 10.9	0.346	0.330
Male	**1108 (71.0%)**	**2053 (67.2%)**	1.336 (68.4%)	0.008	0.091
BMI (kg/m^2)	**24.6 ± 3.2**	25.0 ± 11.7	24.8 ± 3.1	0.861	0.053
Coexisting condition					
Diabetes	**534 (34.7%)**	**1149 (37.6%)**	706 (35.3%)	0.035	0.722
Hypertension	**931 (61.0%)**	**1980 (64.8%)**	1271 (63.6%)	0.004	0.114
Dyslipidemia	**983 (63.8%)**	1850 (61.3%)	**1418 (71.0%)**	0.870	<0.001
PAD	**23 (1.6%)**	47 (1.6%)	33 (1.7%)	0.999	0.892
CKD	**60 (4.0%)**	105 (3.5%)	81 (4.1%)	0.355	0.999
Cardiac risk factors					
Current smokers	**442 (29.4%)**	893 (29.8%)	613 (31.1%)	0.057	0.349
Prev. PCI	**228 (14.8%)**	440 (14.5%)	317 (15.9%)	0.790	0.398
Prev. CABG	**26 (1.7%)**	56 (1.8%)	31 (1.6%)	0.814	0.788
Prev. MI	**89 (5.8%)**	212 (7.0%)	114 (5.7%)	0.130	0.942
Prev. CHF	**31 (2.1%)**	62 (2.1%)	40 (2.0%)	0.999	0.904
Prev. CVA	**125 (8.4%)**	250 (8.3%)	145 (7.3%)	0.999	0.225
FHx. Of CAD	**86 (5.9%)**	171 (5.9%)	92 (4.6%)	0.999	0.102
LVEF	**59.2 ± 11.2**	59.3 ± 11.4	**58.0 ± 11.4**	0.454	<0.001

Baseline Profiles in three HOST-DES cohorts

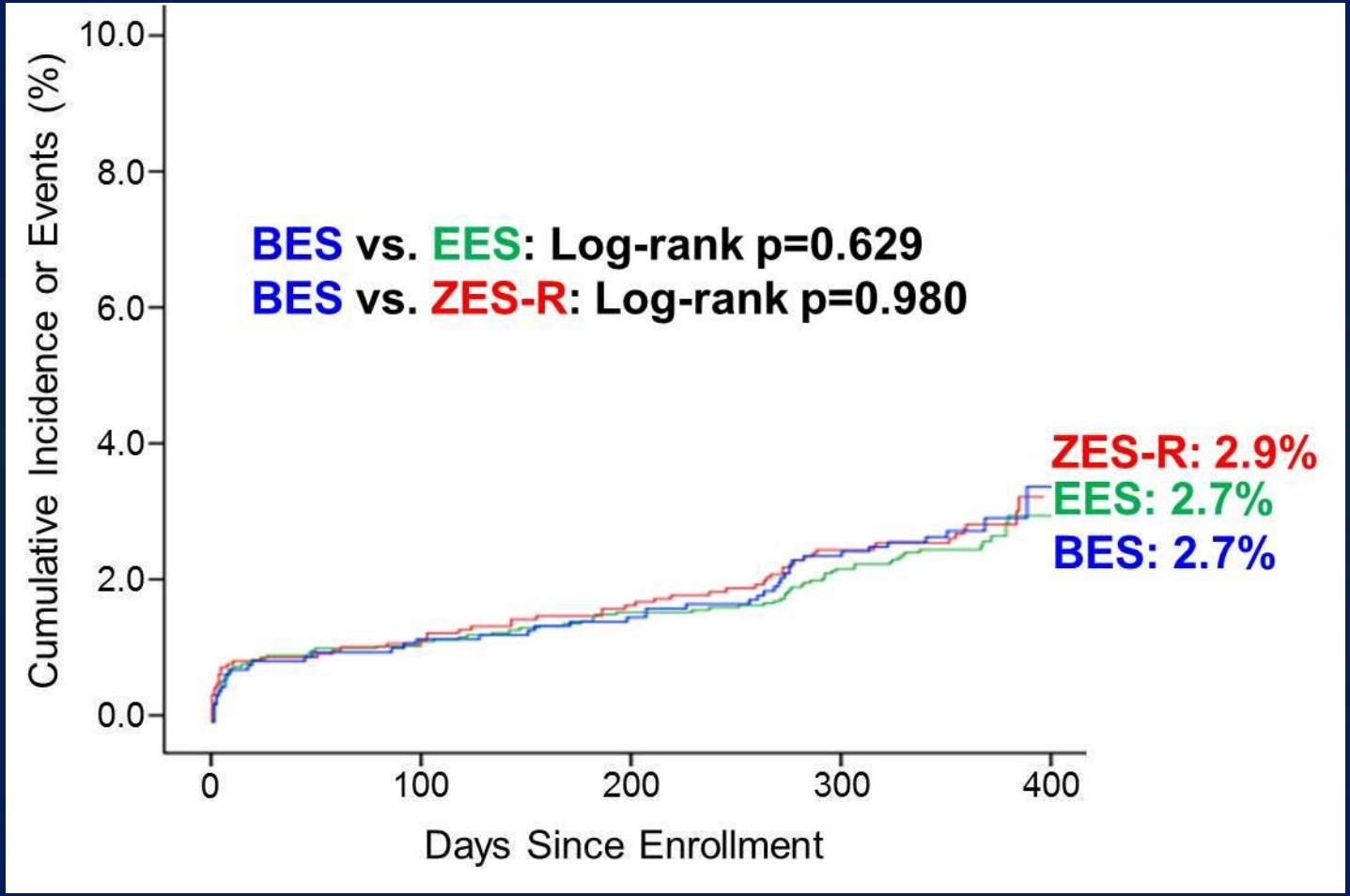
	BES (N = 1,560)	EES (N=3,056)	ZES-R (N=1998)	P Value for BES versus. EES	P Value for BES versus. ZES-R
Clinical indication of PCI					
Stable angina	**564 (36.6%)**	1095 (36.0%)	601 (30.1%)		
Unstable angina	**432 (28.0%)**	1117 (36.8%)	739 (37.0%)		
NSTEMI	**232 (15.0%)**	344 (11.3%)	280 (14.0%)		
STEMI	**248 (16.1%)**	385 (12.7%)	321 (16.1%)		
Silent ischemia	**66 (4.3%)**	97 (3.2%)	57 (2.9%)		
Complexity of CAD					
Disease extent				0.177	0.004
1VD	**686 (44.3%)**	1424 (46.7%)	783 (39.3%)		
2VD	**491 (31.7%)**	923 (30.3%)	674 (33.9%)		
3VD	**370 (23.9%)**	699 (22.9%)	534 (26.8%)		
No of treated lesion	**1.44 ± 0.76**	1.47 ± 0.74	**1.53 ± 0.80**	0.327	0.002
Medication at discharge					
Aspirin	**1539 (99.4%)**	**2969 (98.0%)**	**1960 (98.6%)**	<0.001	0.032
Clopidogrel	**1535 (99.2%)**	2974 (98.2%)	1963 (98.6%)	0.008	0.107
Statin	**1367 (88.4%)**	2613 (86.4%)	1722 (87.2%)	0.062	0.277
ACE inhibitor	**585 (38.1%)**	1113 (37.0%)	730 (37.3%)	0.476	0.673
ARB	**443 (29.0%)**	939 (31.1%)	**623 (32.4%)**	0.142	0.032
BB	**1096 (71.0%)**	**1853 (61.6%)**	**1306 (66.6%)**	<0.001	0.005
CCB	**377 (24.5%)**	**830 (27.5%)**	513 (26.8%)	0.030	0.137

One year Clinical Outcomes in three HOST-DES cohorts

	BES	EES	ZES-R	BES vs. EES		BES vs. ZES-R	
	(N = 1,560)	(N=3,056)	(N=1998)	RR	P	RR	P
All-cause death	**33 (2.1%)**	**62 (2.0%)**	**46 (2.3%)**	1.06 (0.70-1.62)	0.773	0.94 (0.60-1.47)	0.784
Cardiac death	**12 (0.8%)**	**37 (1.2%)**	**28 (1.4%)**	0.80 (0.58-1.12)	0.180	0.55 (0.28-1.08)	0.083
Any MI	**15 (1.0%)**	**17 (0.6%)**	**8 (0.4%)**	1.74 (0.87-3.48)	0.118	2.42 (1.02-5.70)	0.044
Target vessel MI	**9 (0.6%)**	**14 (0.5%)**	**5 (0.3%)**	1.27 (0.55-2.94)	0.576	2.34 (0.78-6.98)	0.128
MI due to ST	**4 (0.3%)**	**7 (0.2%)**	**3 (0.2%)**	1.14 (0.34-3.91)	0.830	1.76 (0.39-7.88)	0.460
Any revascularization	**62 (4.0%)**	**161 (5.3%)**	**106 (5.3%)**	0.75 (0.56-1.01)	0.061	0.75 (0.55-1.03)	0.079
Clinically driven revascularization	**46 (2.9%)**	**120 (3.9%)**	**73 (3.7%)**	0.75 (0.54-1.06)	0.105	0.81 (0.56-1.18)	0.266
TLR	**24 (1.5%)**	**40 (1.3%)**	**28 (1.4%)**	1.17 (0.70-1.96)	0.540	1.09 (0.63-1.89)	0.759
CVA	**10 (0.6%)**	**18 (0.6%)**	**12 (0.6%)**	1.10 (0.51-2.37)	0.819	1.07 (0.46-2.49)	0.868
TLF	**42 (2.7%)**	**82 (2.7%)**	**58 (2.9%)**	0.99 (0.82-1.19)	0.884	0.89 (0.60-1.34)	0.584
POCO	**105 (6.7%)**	**225 (7.4%)**	**153 (7.7%)**	0.92 (0.73-1.16)	0.499	0.89 (0.69-1.14)	0.359

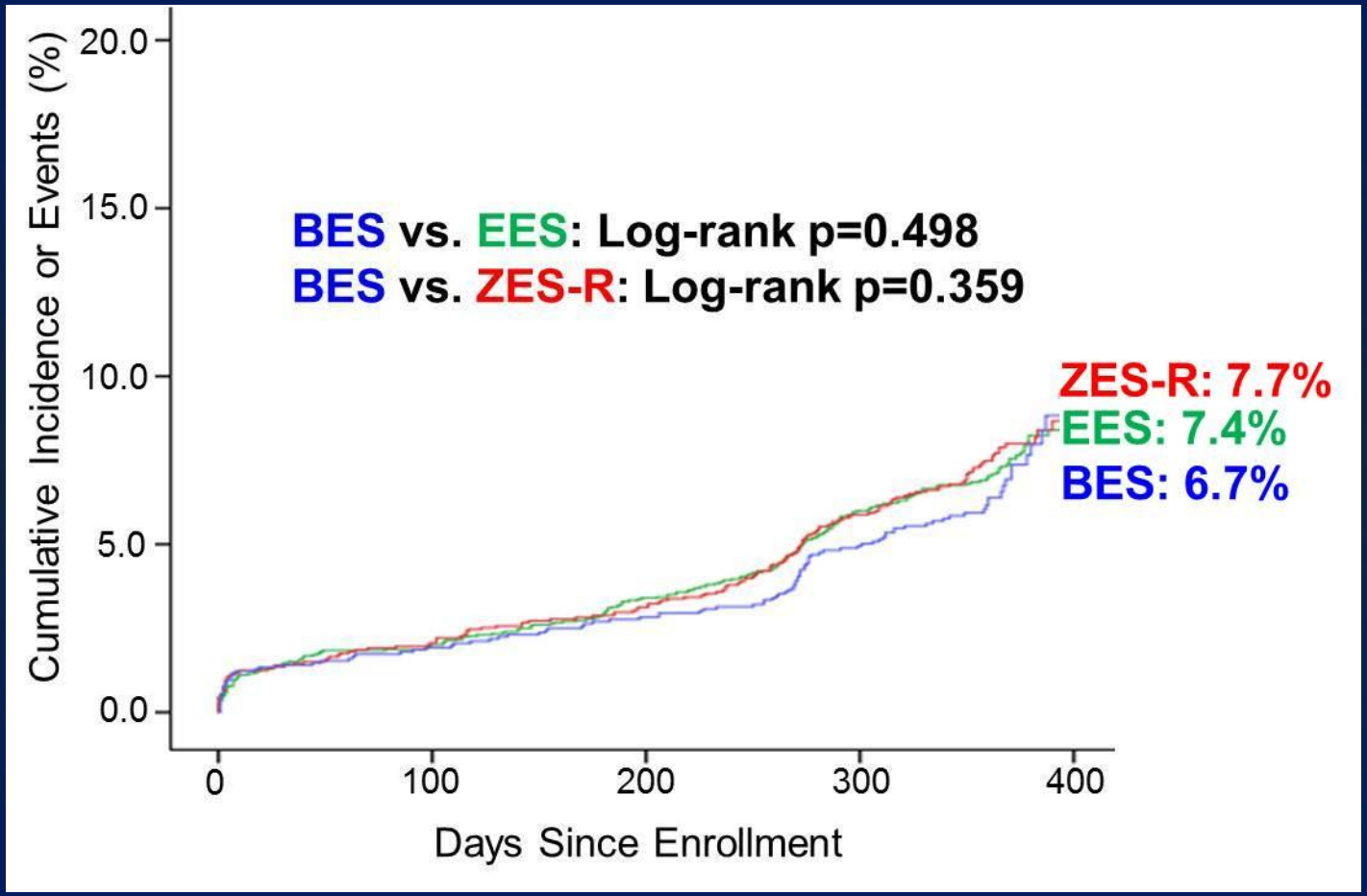
✓ **TLF**: cardiac death + MI (not clearly attributed to a nontarget vessel) + clinically indicated TLR
✓ **POCO**: all-cause mortality+ any MI + any revascularization

Target Lesion Failure at 1y
in three HOST-DES cohorts



No. of patients at risk	0 day	30 days	180 days	270 days	365 days
ZES-R	1,998	1,957	1,928	1,905	1,152
EES	3,056	3,003	2,952	2,928	1,719
BES	1,560	1,543	1,527	1,514	560

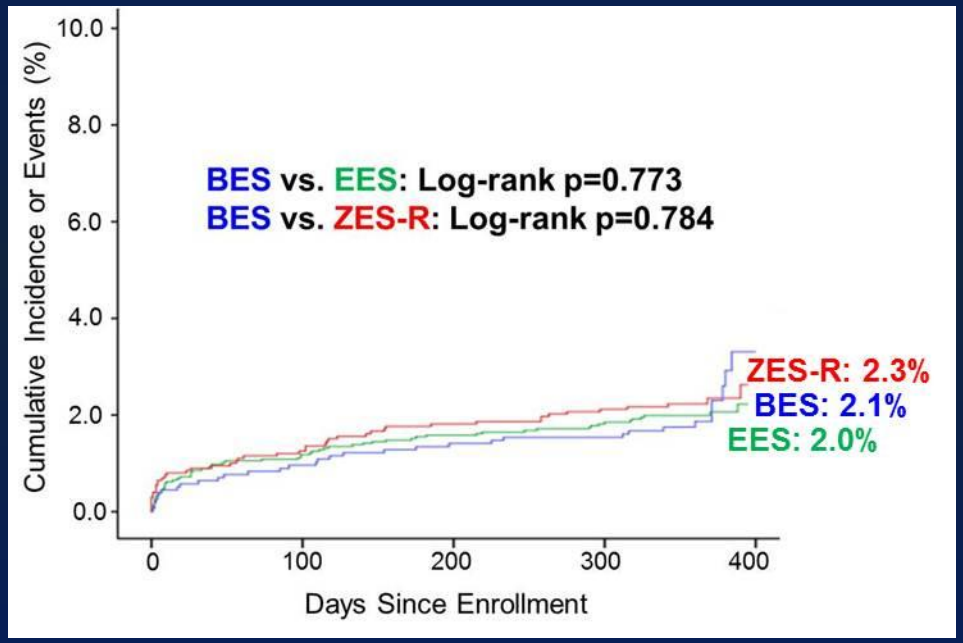
Patient-Oriented Composite Outcome in three HOST-DES cohorts



No. of patients at risk	0 day	30 days	180 days	270 days	365 days
ZES-R	1,998	1,950	1,912	1,866	1,110
EES	3,056	2,996	2,927	2,860	1,654
BES	1,560	1,537	1,514	1,493	552

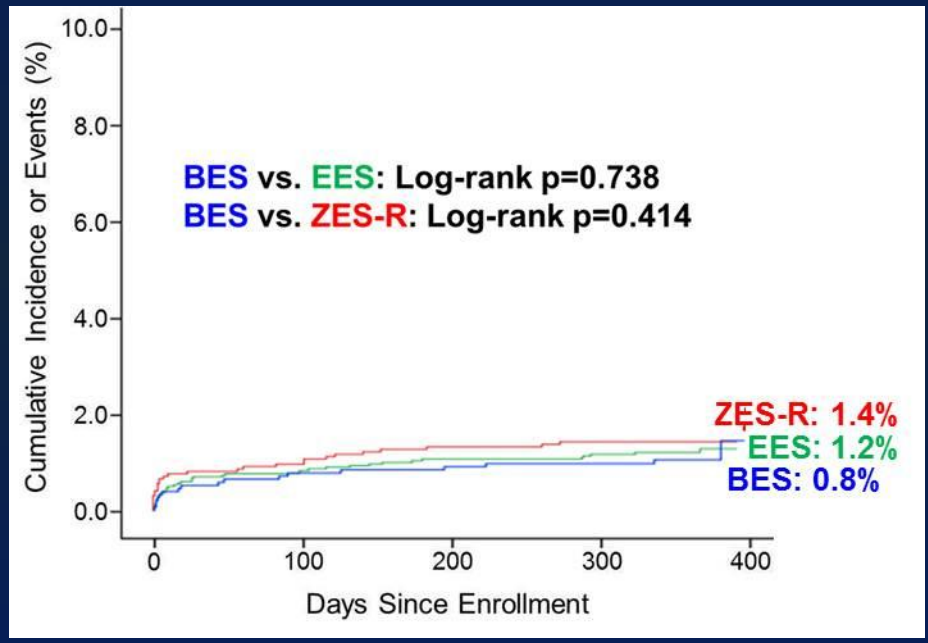
Individual components of TLF and POCO in three HOST-DES cohorts

All-cause death



No. of patients at risk	0	30	180	270	365 (days)
ZES-R	1,998	1,960	1,934	1,920	1,159
EES	3,056	3,012	2,966	2,949	1,745
BES	1,560	1,549	1,535	1,528	568

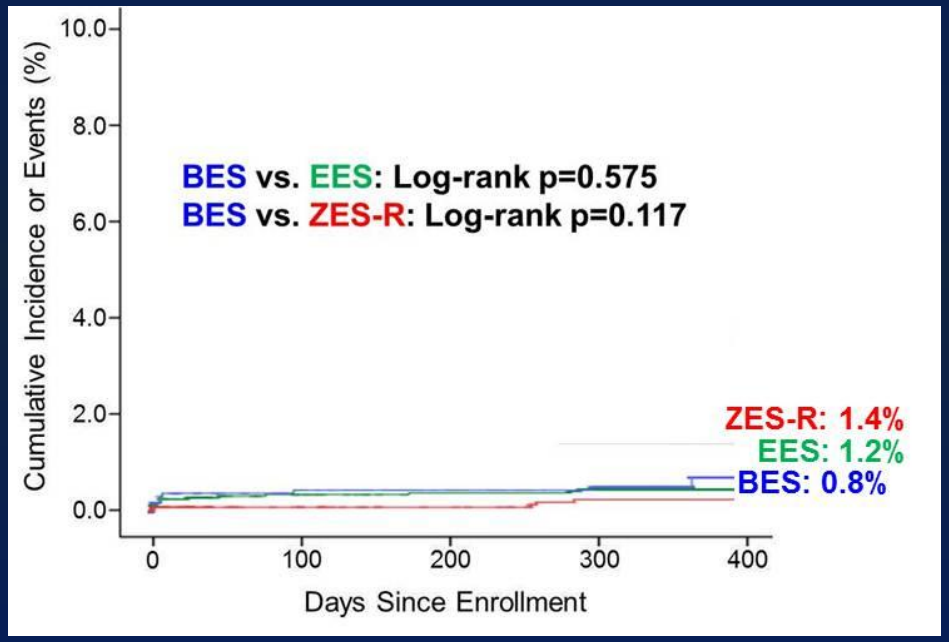
Cardiac death



No. of patients at risk	0	30	180	270	365 (days)
ZES-R	1,998	1,960	1,934	1,920	1,159
EES	3,056	3,012	2,966	2,949	1,745
BES	1,560	1,549	1,535	1,528	568

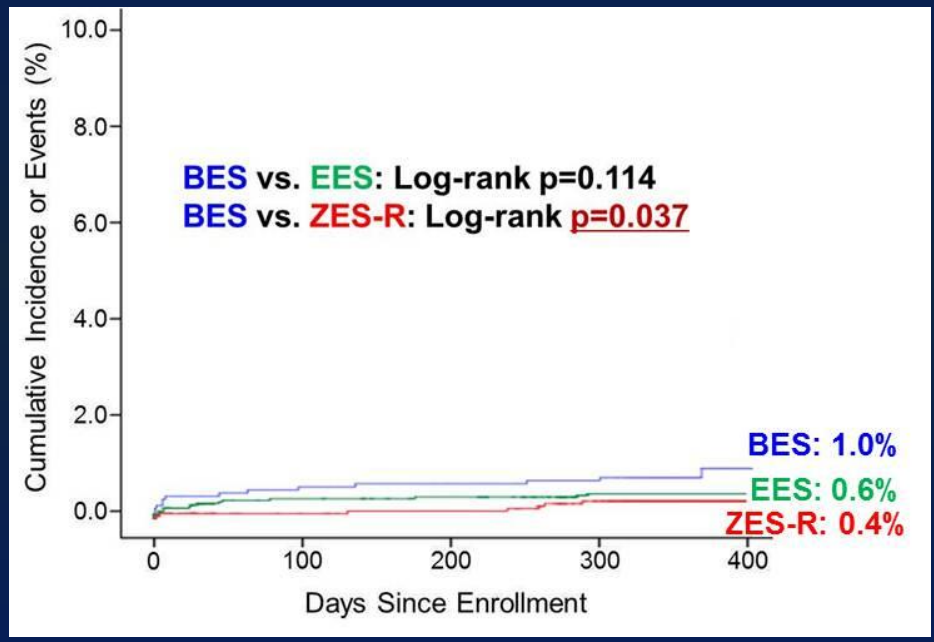
Individual components of TLF and POCO in three HOST-DES cohorts

Any cause MI



No. of patients at risk	0	30	180	270	365 (days)
ZES-R	1,998	1,998	1,933	1,917	1,156
EES	3,056	3,056	2,968	2,953	1,743
BES	1,560	1,560	1,526	1,519	564

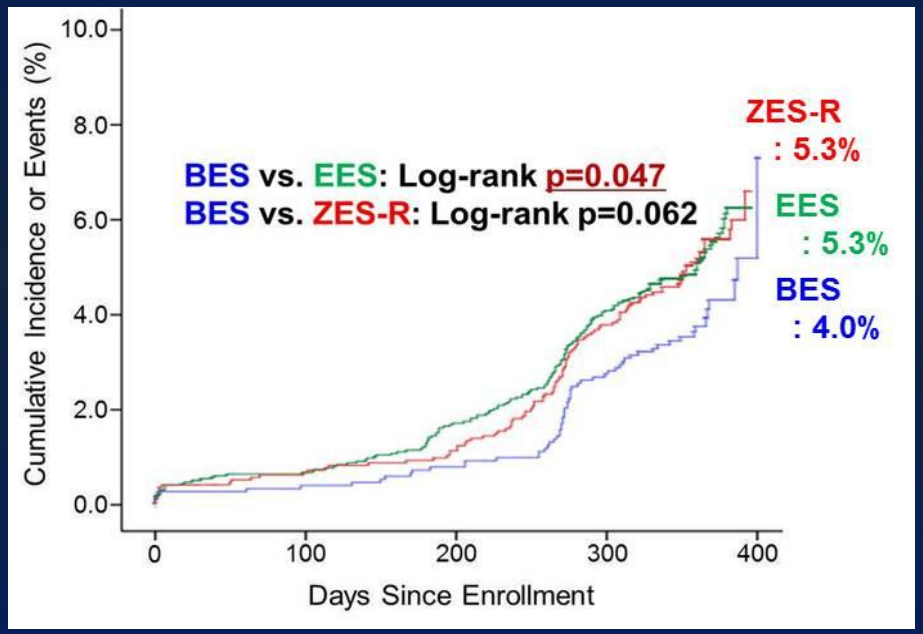
Target vessel MI



No. of patients at risk	0	30	180	270	365 (days)
ZES-R	1,998	1,958	1,931	1,915	1,156
EES	3,056	3,005	2,957	2,941	1,738
BES	1,560	1,543	1,530	1,524	566

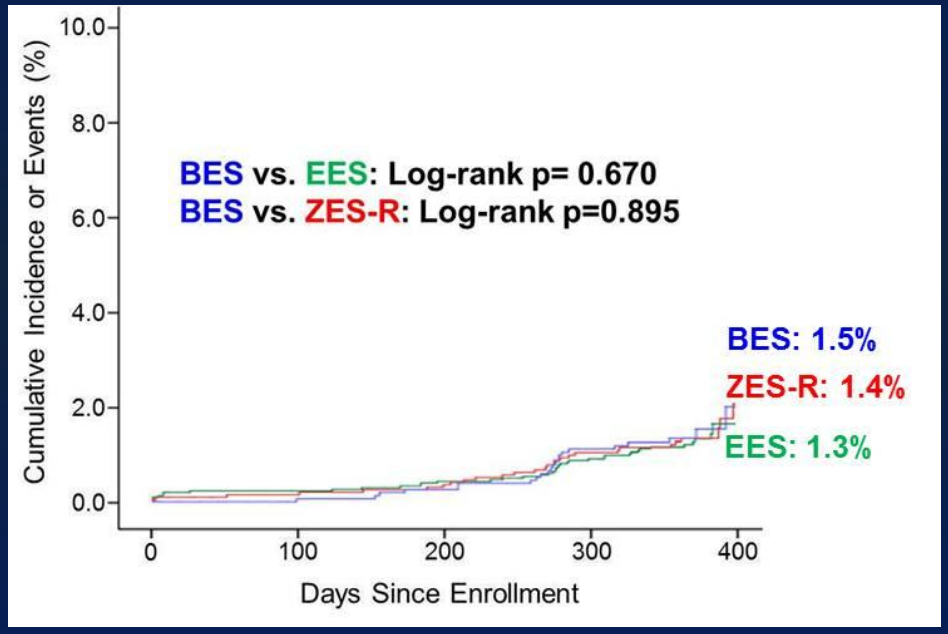
Individual components of TLF and POCO in three HOST-DES cohorts

Any revascularization



No. of patients at risk	0	30	180	270	365 (days)
ZES-R	1,998	1,952	1,916	1,869	1,114
EES	3,056	2,999	2,933	2,866	1,658
BES	1,560	1,545	1,526	1,507	556

TLR



No. of patients at risk	0	30	180	270	365 (days)
ZES-R	1,998	1,958	1,929	1,906	1,154
EES	3,056	3,011	2,971	2,947	1,731
BES	1,560	1,549	1,533	1,520	562

Part III.

A. Clinical outcome in Whole patients

B. Clinical outcome in Propensity score-matched population

- ► BES from HOST-BIOLIMUS registry
- ► EES from EXCELLENT registry
- ► ZES-R from RESOLUTE-KOREA registry

C. Stent Thrombosis

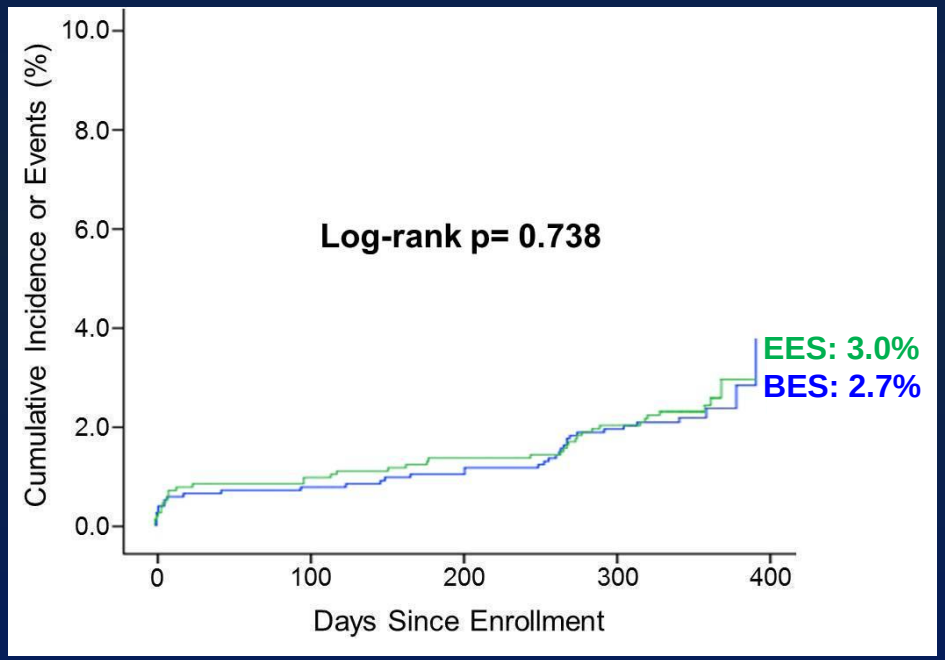
HOST =Harmonized Optimal Strategy to Treat CAD

Propensity score-matched group analysis

BES *versus* EES

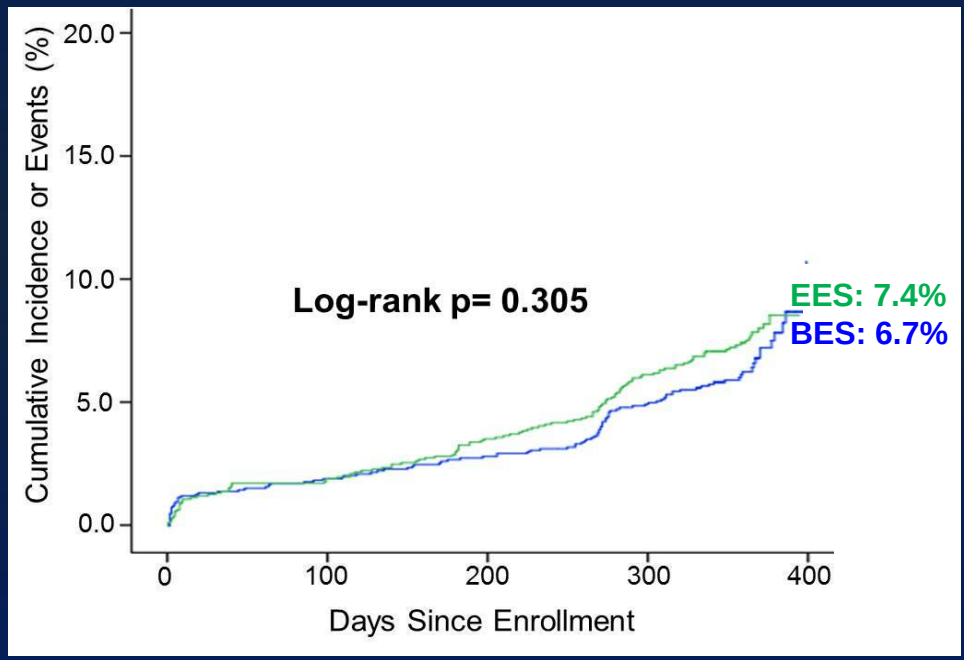
1:1 matching with 1560:1560 patients

Target lesion failure



No. of patients at risk	0	30	180	270	365 (days)
EES	1,560	1,540	1,514	1,503	884
BES	1,560	1,543	1,527	1,514	560

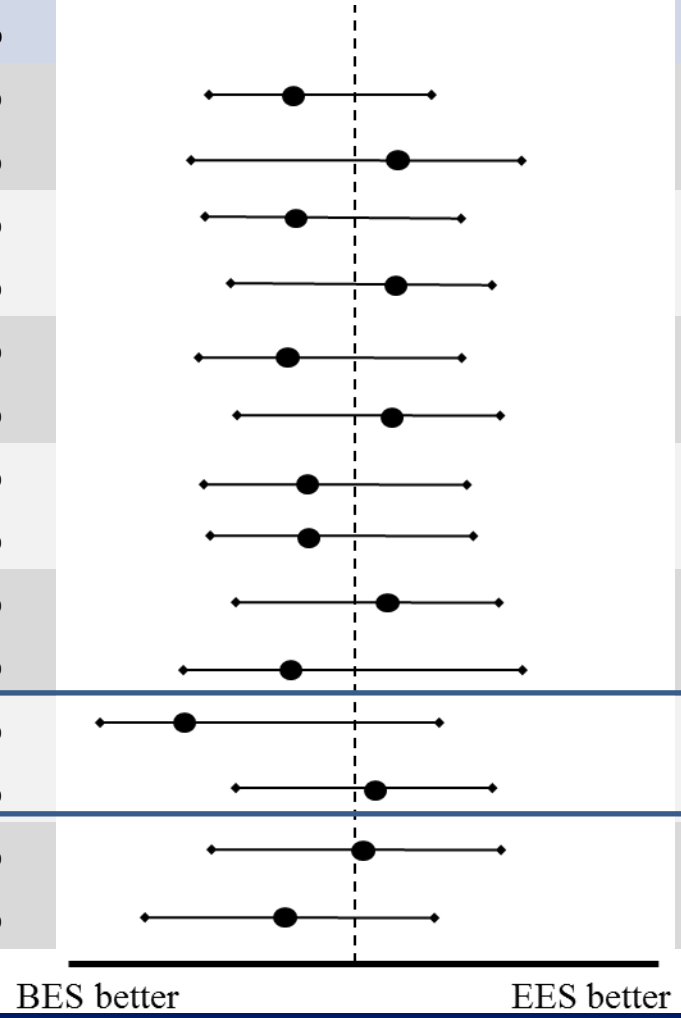
POCO



No. of patients at risk	0	30	180	270	365 (days)
EES	1,560	1,536	1,499	1,464	844
BES	1,560	1,537	1,514	1,493	552

Propensity score-matched group analysis
BES *versus* EES
Subgroup analysis for TLF at 1y

	BES	EES	HR (95% CI)	Interaction P value
All patients	**2.4%**	**2.5%**	**0.93 (0.59-1.46)**	
Age over 60	2.6%	2.9%	0.86 (0.50-1.45)	0.631
Age under 60	1.9%	1.7%	1.15 (0.47-2.83)	
Male gender	2.1%	2.3%	0.87 (0.46-1.64)	0.563
Female gender	3.1%	2.7%	1.15 (0.58-2.28)	
Diabetes	3.0%	3.5%	0.84 (0.44-1.61)	0.546
No diabetes	2.1%	1.8%	1.14 (0.60-2.22)	
Dyslipidemia	2.7%	2.9%	0.92 (0.47-1.81)	0.404
No dyslipidemia	2.1%	2.2%	0.93 (0.49-1.76)	
Hypertension	3.0%	2.7%	1.11 (0.67-1.86)	0.641
No hypertension	1.5%	1.7%	0.78 (0.27-2.26)	
STEMI	1.2%	4.4%	0.27 (0.06-1.11)	0.064
Other indication	2.6%	2.4%	1.06 (0.65-1.72)	
Multi lesion PCI	4.0%	3.8%	1.04 (0.56-1.92)	0.621
Single lesion PCI	1.5%	1.8%	0.83 (0.42-1.65)	

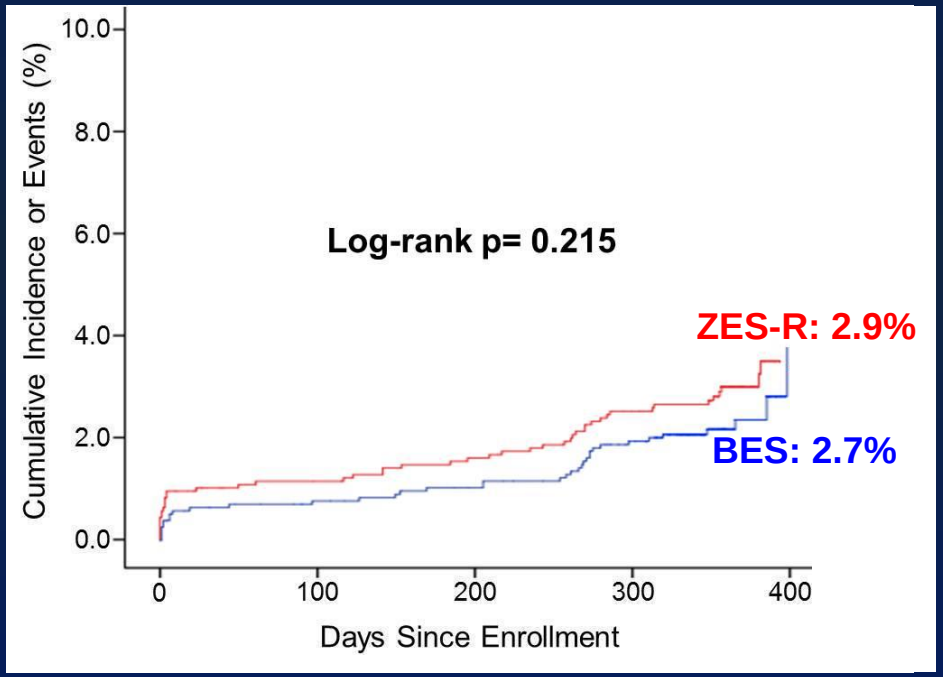


Propensity score-matched group analysis

BES *versus* ZES-R

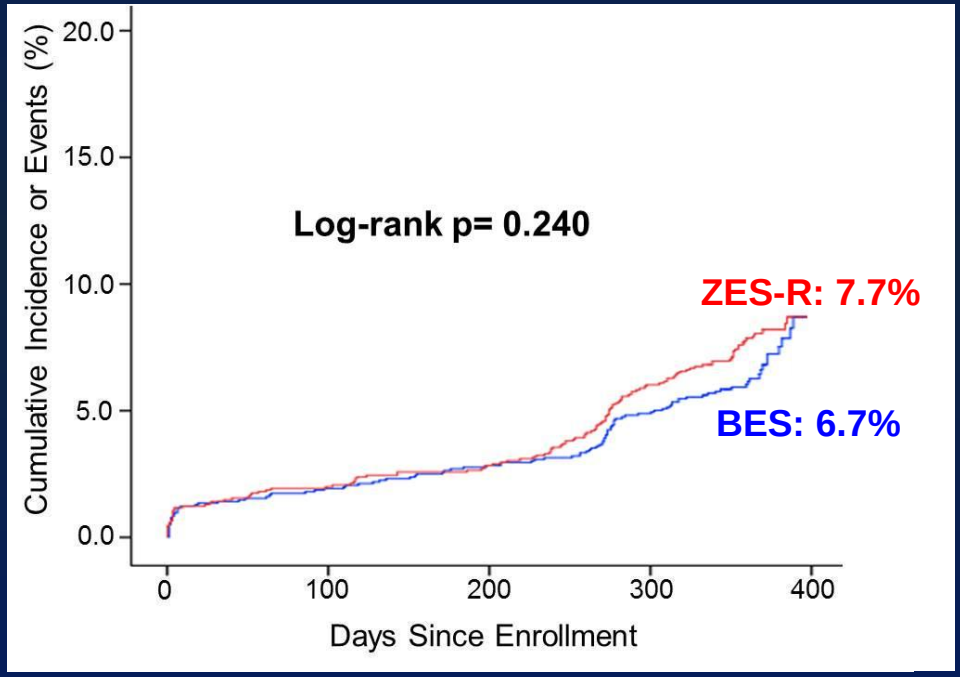
1:1 matching with 1560:1560 patients

Target lesion failure



No. of patients at risk	0	30	180	270	365 (days)
ZES-R	1,560	1,530	1,511	1,492	904
BES	1,560	1,543	1,527	1,514	560

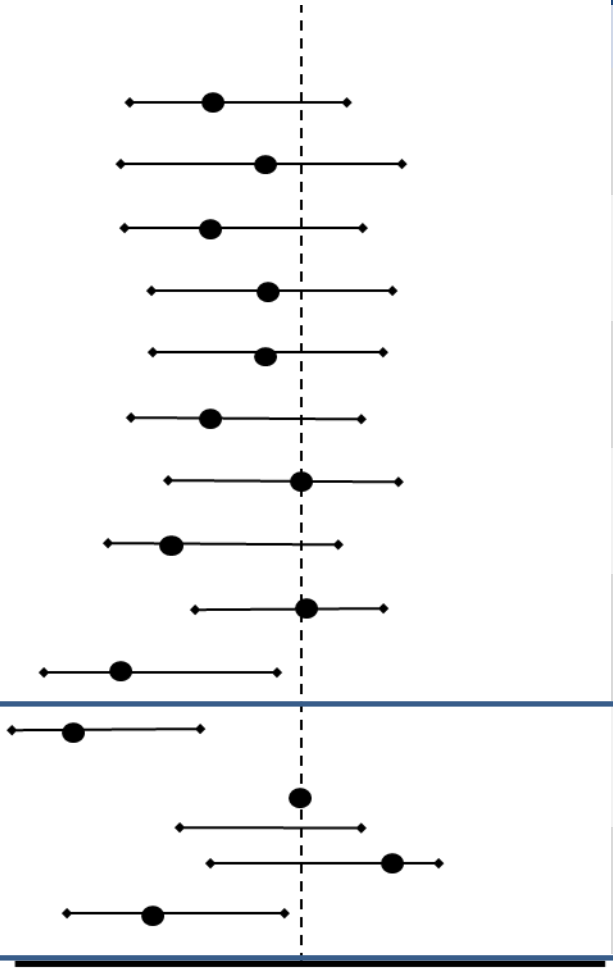
POCO



No. of patients at risk	0	30	180	270	365 (days)
ZES-R	1,560	1,526	1,502	1,463	867
BES	1,560	1,537	1,514	1,493	552

Propensity score-matched group analysis
BES *versus* ZES-R
Subgroup analysis for TLF at 1y

	BES	ZES-R	HR (95% CI)	Interaction P value
All patients	**2.4%**	**3.0%**		
Age over 60	2.6%	3.5%	0.70 (0.42-1.17)	0.681
Age under 60	1.9%	2.1%	0.91 (0.39-2.11)	
Male gender	2.1%	2.9%	0.69 (0.40-1.21)	0.466
Female gender	3.1%	3.2%	0.92 (0.45-1.89)	
Diabetes	3.0%	3.1%	0.91 (0.46-1.81)	0.463
No diabetes	2.1%	2.9%	0.69 (0.39-1.22)	
Dyslipidemia	2.7%	2.7%	1.00 (0.52-1.92)	0.384
No dyslipidemia	2.1%	3.4%	0.58 (0.32-1.07)	
Hypertension	3.0%	3.0%	1.02 (0.61-1.72)	0.110
No hypertension	1.5%	3.1%	0.42 (0.18-0.98)	
STEMI	1.2%	6.1%	0.19 (0.05-0.67)	0.012
Other indication	2.6%	2.5%	1.00 (0.61-1.63)	
Multi lesion PCI	4.0%	3.0%	1.30 (0.71-2.38)	0.026
Single lesion PCI	1.5%	3.0%	0.49 (0.26-0.93)	



Part III.

A. Clinical outcome in Whole patients
B. Clinical outcome in Propensity score-matched population

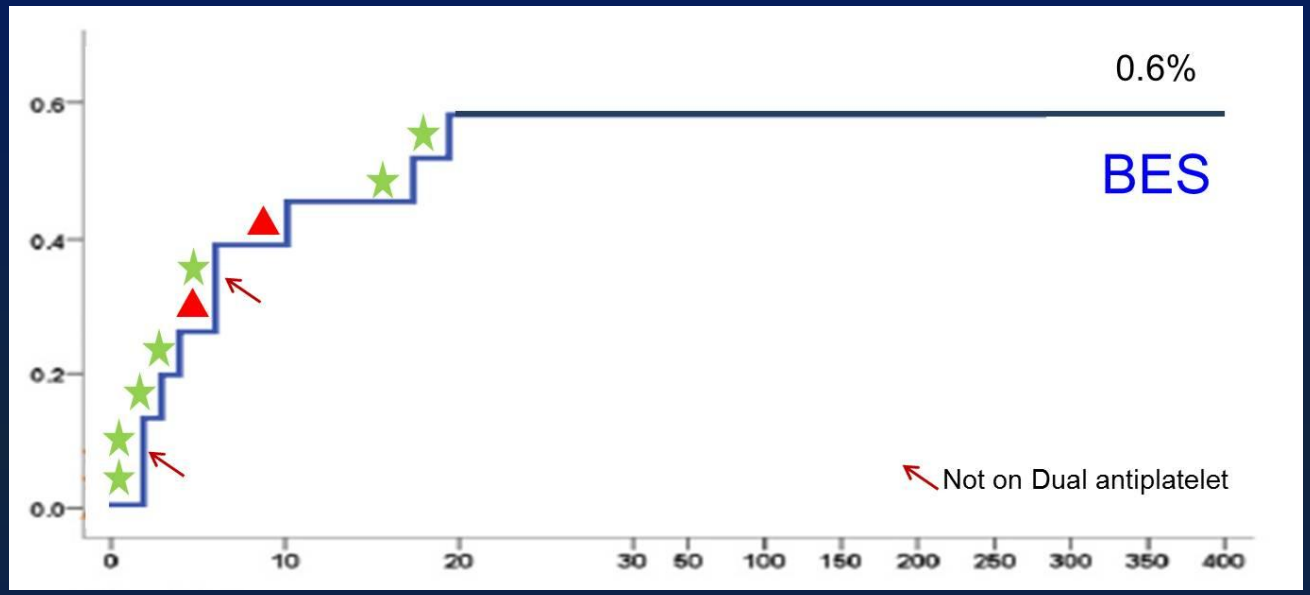
- ► BES from HOST-BIOLIMUS registry
- ► EES from EXCELLENT registry
- ► ZES-R from RESOLUTE-KOREA registry

C. Stent Thrombosis

Stent Thrombosis in three HOST-DES cohorts

	BES (N=1,650)	EES (N=3,056)	ZES-R (N=1,998)	P Value for BES versus. EES	P Value for BES versus. ZES-R
Definite	2 (0.1%)	6 (0.2%)	3 (0.2%)	1.000	1.000
Acute (0-1day)	0 (0%)	3 (0.1%)	1 (0.1%)	0.555	1.000
Subacute (2-30 days)	2 (0.1%)	2 (0.1%)	1 (0.1%)	0.608	0.585
Late (31-365days)	0 (0%)	1 (<0.1%)	1 (0.1%)	1.000	1.000
Probable	7 (0.4%)	12 (0.4%)	5 (0.3%)	0.810	0.387
Acute (0-1 day)	2 (0.1%)	1 (<0.1%)	3 (0.2%)	1.000	0.636
Subacute (2-30 days)	5 (0.3%)	10 (0.3%)	2 (0.1%)	0.793	0.149
Late (31-360 days)	0 (0%)	1 (<0.1%)	0 (0%)	1.000	-
ST Definite or probable	9 (0.6%)	18 (0.6%)	7 (0.4%)	1.000	0.326
Duration of DAPT					
9 months	1394 (94.1%)	2638 (93.2%)	1702 (93.2%)		
1 yr	1079 (73.6%)	2277 (84.8%)	1463 (84.7%)		

Cumulative Incidence of ST in three HOST-DES cohorts



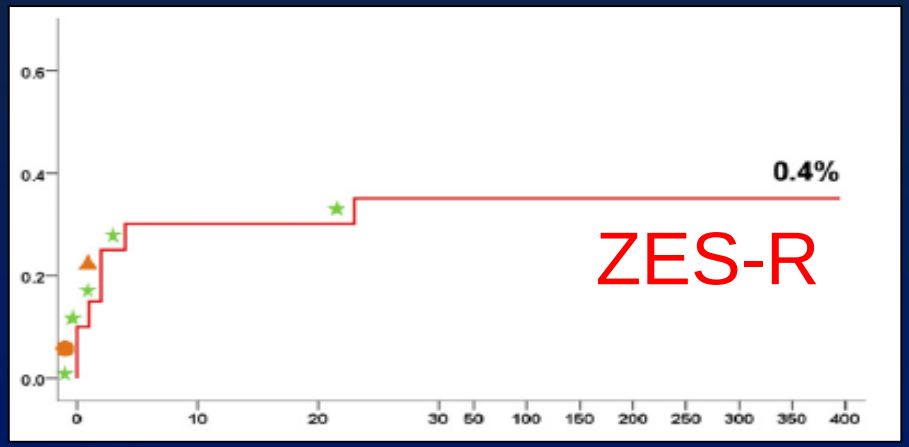
Definite Stent Thrombosis

- Cardiac Death
- Myocardial Infarction
- Target lesion revascularization

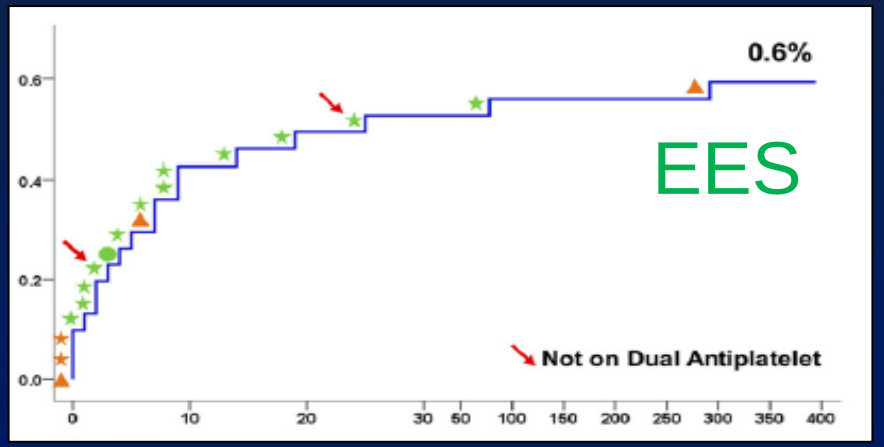
Probable Stent Thrombosis

- Cardiac Death
- Myocardial Infarction
- Target lesion revascularization

Cardiac Death

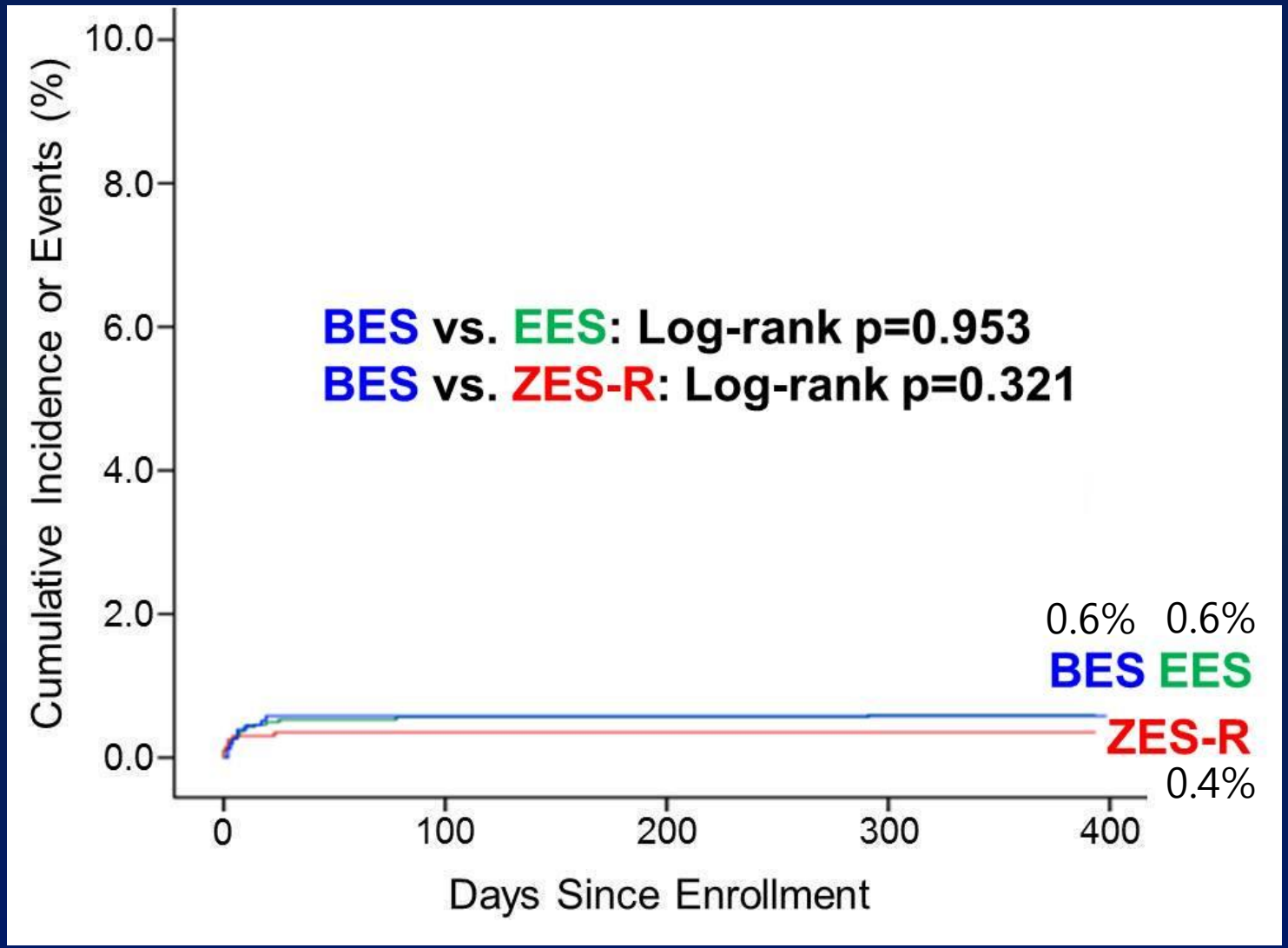


Park et al. JACC 2013



Park et al. JACC 2013

Cumulative Incidence of ST in three HOST-DES cohorts



Part IV.

Future Plan

HOST-BIOLIMUS-3000-KOREA registry

HOST =Harmonized Optimal Strategy to Treat CAD

HOST-BIOLIMUS-3000-KOREA registry

A. Completion of enrollment

: end of 2013

B. Clinical data of 1, 2, 3 years

C. Angiographic substudy

: 50% of cohort

: 9 months angiography follow-up

HOST-Biolimus-3000-Korea
Participating Centers

Seoul National University Hospital

Seoul National University Bundang Hospital

Seoul National University Boramae Hospital

Sejong Heart Institute, Sejong General Hospital

Korea University Ansan Hospital

Keimyung University Hospital

Chungbuk National University Hospital

Konyang University Hospital

Ilsan Baek Hospital

Korea University Guro-Hospital

Yangsan Pusan National University Hospital

Ewha Womans University Mokdong Hospital

Pusan National University Hospital

Daegu Fatima Hospital

Gangdong Sungshim Hospital

Kwangju Christian hospital

The Catholic University of Korea Uijeongbu St. Mary's Hospital

Kosin University Hospital

Hanyang University Hospital

Youngnam University Hospital

Inha University Hospital

Soon-chun-hyang University Hoapital, Gumi

Jeju University Hospital