Real World Use of BES in Korea:

From HOST-BIOLIMUS registry

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"It's better to deal with something _good_* you know than with something new you don't know _very well_*."

* modified

Biolimus-A9™ Eluting Stent
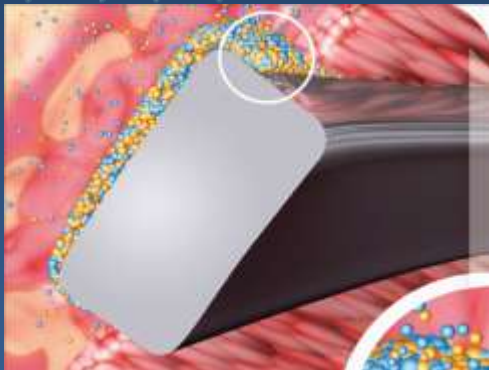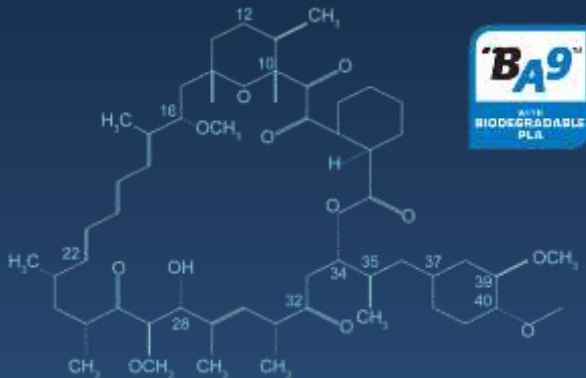
- Biolimus is a semi-synthetic sirolimus analogue with **10x higher lipophilicity** and similar potency as sirolimus.

- Biolimus is immersed at a concentration of 15.6 μg/mm into a biodegradable polymer, polylactic acid, and applied solely to **the abluminal stent surface** by a fully automated process.

- Biolimus is co-released with polylactic acid and completely desolves into carbon dioxide and water after **a 6-9 months period.**

- The stainless steel stent platform has a strut thickness of 120 μm with a quadrature link design.

COMPARE II trial in Europe

- Open-label, prospective, randomized, controlled, non-inferiority trial
- Total N= 2,707 (4025 lesions)
- **BES 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

A Primary endpoint

— Biolimus-eluting stent
— Everolimus-eluting stent

Log-rank p=0.725
P non-inferiority <0.0001

Log-rank p=0.7249

Number at risk
Biolimus-eluting stent: 1795 1755 1745 1736 1728 1721 1708 1703 1698 1696 1695 1692 1689 1689
Everolimus-eluting stent: 912 892 885 883 881 879 877 876 874 870 868 865 863 860

COMPARE II - Kaplan-Meier survival curves - Cumulative events target vessel revascularisation (All)
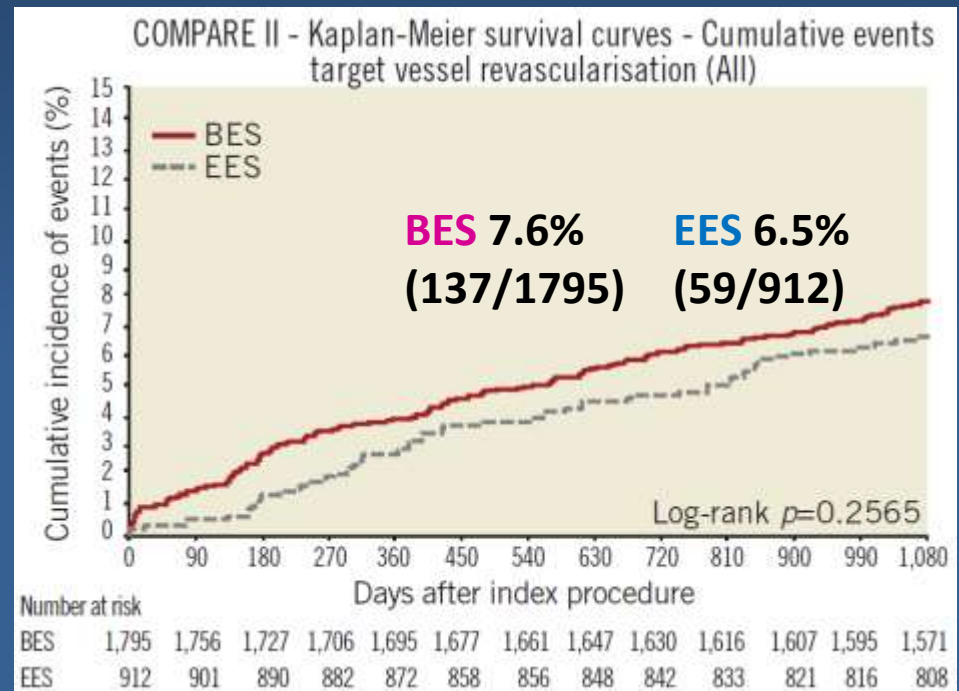
— BES
--- EES

BES 7.6% **EES 6.5%**
(137/1795) **(59/912)**

Log-rank p=0.2565

Days after index procedure

Number at risk
BES: 1,795 1,756 1,727 1,706 1,695 1,677 1,661 1,647 1,630 1,616 1,607 1,595 1,571
EES: 912 901 890 882 872 858 856 848 842 833 821 816 808

Smits PC et al. Lancet. 2013

Vlachojannis GJ, et al. Eurointervention 2015

NEXT trial in Japan

- Multicenter, randomized, non-inferiority trial
- Total N= 3,235 (4069 lesions)   (mostly stable angina)
- **BES 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=0.8

BP-BES
DP-EES

Death or Myocardial Infarction

Log-rank P=0.7

BP-BES
DP-EES

Days after PCI

Natsuaki M, et al. J Am Coll Cardiol 2013:16:181-90
Natsuaki M, et al. Circ Cadiovasc Interv 2016, in press
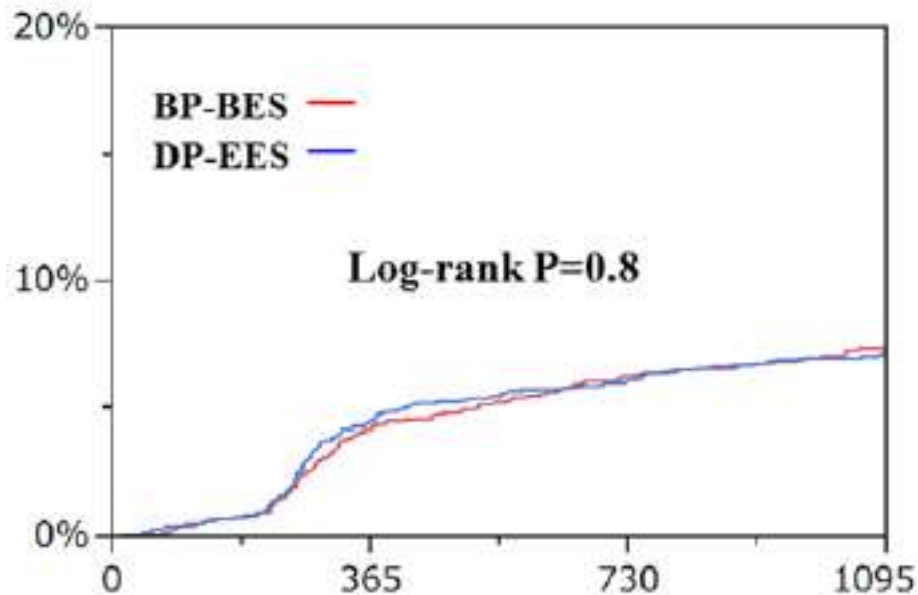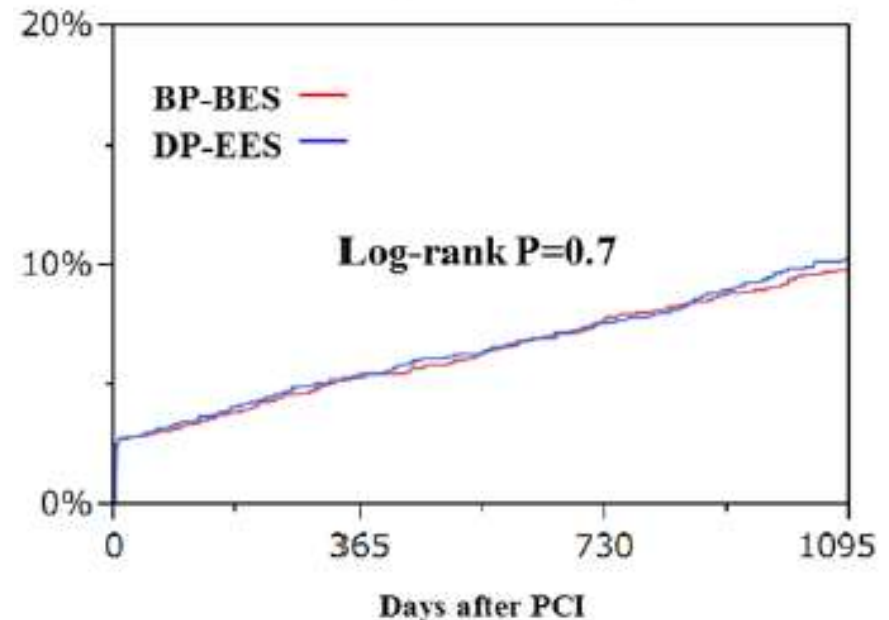
HOST-Biolimus registry

- To assess clinical outcomes in Korean patients treated with biolimus-eluting stent in a *real world, all-comers*

▪ **Inclusion criteria**

: **All-comer registry** of BIOLIMUS-eluting stents

(stable angina, acute coronary syndrome, silent ischemia….)

→ Presence of more than 1 of the following

- Luminal stenosis > 50%

- No limitation for number of lesion/vessel, and vessel length

Active Participants of HOST-Biolimus-3000 Korea registry

- Nation-wide registry, from 24 institutions of South Korea
- Number of patients = 3007 (2010.3~2014.11.)

Enrollment summary, HOST-Biolimus-3000 Korea Registry
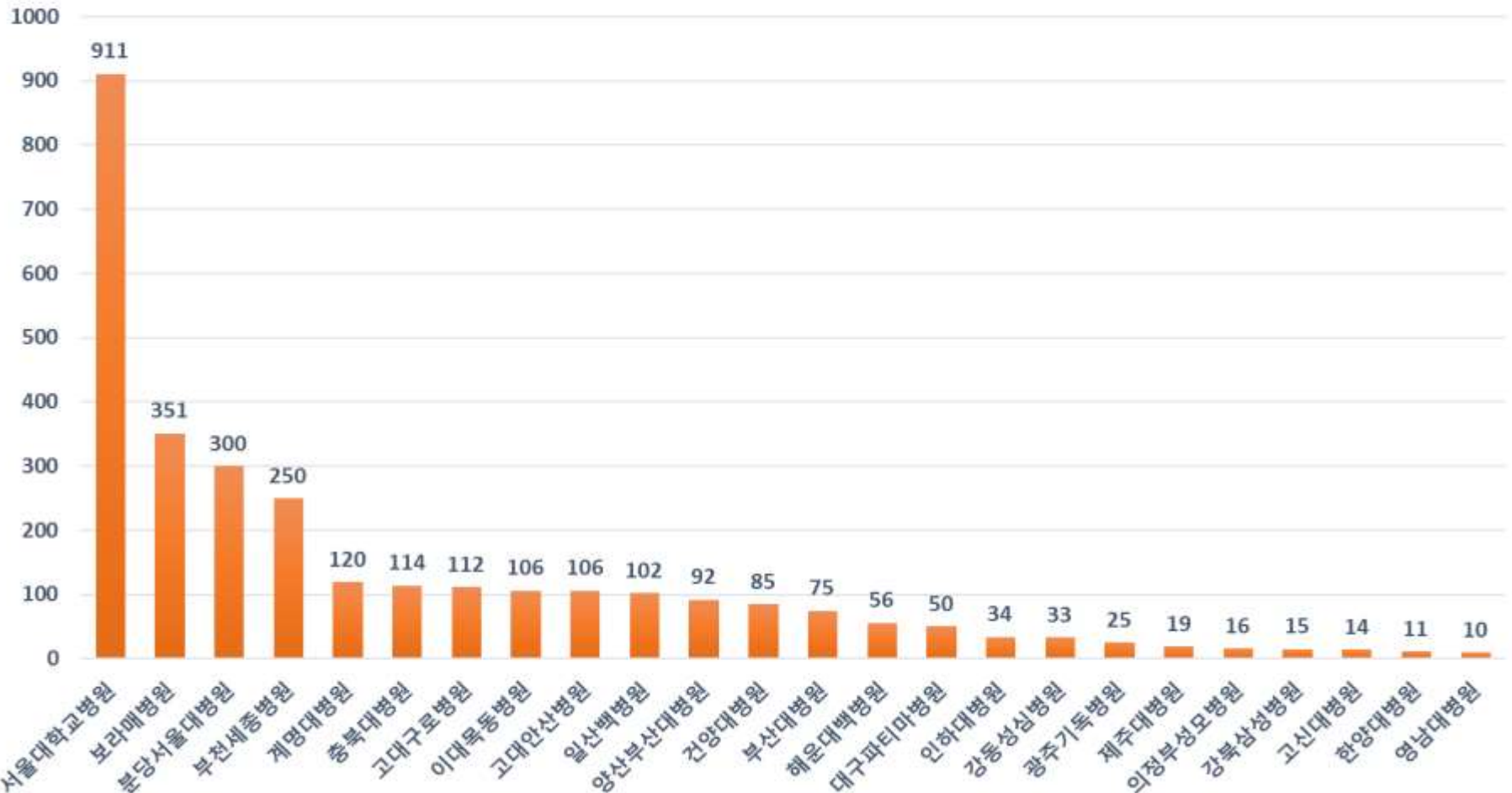
Biodegradable polymer BES vs. Durable polymer EES

: Long-term clinical outcomes

All-comer registries for contemporary DESs platforms

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HOST-Biolimus-3000 Korea Registry

Enrolled patients = 3007		
Biomatrix	**Biomatrix Flex**	**Nobori**
1253 (41.7%)	754 (25.1%)	1000 (33.3%)

1-year = 2873 (95.5%)

2-year = 2376 (79.0%)		
Biomatrix	**Biomatrix Flex**	**Nobori**
1105 (46.5%)	413 (17.4%)	858 (36.1%)

<u>3-year = 1912 (63.6%)</u>		
Biomatrix	**Biomatrix Flex**	**Nobori**
1005 (52.6%)	**145 (7.6%)**	**762 (39.9%)**
Overall angiographic follow-up = 799 (41.8%)		
Dedicated 9-mo. Angiographic f/u = 436 (22.8%)		

HOST-Excellent-Prime Registry

Enrolled patients = 2076
Excellent Prime
2076

1-year = 2061 (99.3%)

2-year = 2023 (97.4%)

<u>3-year = 1940 (93.4%)</u>
Overall angiographic f/u = 546 (28.1%)
Dedicated 13-mo. angiographic f/u = 197 (10.2%)
Allocated stent = 1739 (89.6%)

Preliminary, Data upto 2016 Apr

Baseline characteristics for study population

	BES (N= 1,912)	EES (N= 1,940)	P-value
Demographics			
Age (years)	64.0 ± 10.9	64.0 ± 10.7	0.864
Male gender	1332 (69.7%)	1377 (71.0%)	0.372
BMI (kg/m^2)	24.1 ± 6.7	24.6 ± 11.4	0.104
Coexisting conditions			
Diabetes	636 (33.3%)	704 (36.3%)	0.049
Hypertension	1134 (59.3%)	1145 (59.0%)	0.855
Dyslipidemia (+ statin user)	1295 (67.7%)	1204 (62.1%)	<0.001
Peripheral artery disease	37 (1.9%)	39 (2.0%)	0.867
Chronic kidney disease	68 (3.6%)	103 (5.3%)	0.008
Risk factors			
Prev. PCI	253 (13.2%)	295 (15.2%)	0.080
Prev. CABG	31 (1.6%)	39 (2.0%)	0.366
Prev. MI	88 (4.6%)	121 (6.2%)	0.025
Prev. CHF	39 (2.0%)	72 (3.7%)	0.002
Prev. CVA	144 (7.5%)	171 (8.8%)	0.146
FHx. of coronary disease	114 (6.0%)	100 (5.2%)	0.274
LV EF (%)	59.3 ± 10.9	56.7 ± 11.3	<0.001

Baseline characteristics for study population

	BES (N= 1,912)	EES (N= 1,940)	P-value
Clinical indication of PCI			
Silent ischemia	49 (2.6%)	150 (7.8%)	
Stable angina	709 (37.5%)	517 (26.8%)	
Unstable angina	545 (28.8%)	589 (30.5%)	
NSTEMI	297 (15.7%)	370 (19.2%)	
STEMI	293 (15.5%)	302 (15.7%)	
AMI	590 (30.9%)	672 (34.6%)	0.012
Complexity of CAD			
Disease extent			<0.001
1VD	834 (43.8%)	701 (36.3%)	
2VD	609 (32.0%)	654 (33.9%)	
3VD	461 (24.2%)	574 (29.8%)	
Number of treated lesion	1.4 ± 0.7	1.4 ± 0.7	0.054
Lesion characteristics			
ISR as target lesion	81 (4.2%)	169 (8.7%)	<0.001
Bifurcation	632 (33.1%)	631 (32.5%)	0.727
Thrombotic lesion	244 (12.8%)	195 (10.1%)	0.008
Long lesion (≥28mm)	666 (34.8%)	1199 (61.8%)	<0.001
Small vessel (≤2.75mm)	406 (21.2%)	518 (26.7%)	<0.001
Lt. main disease	94 (4.9%)	143 (7.4%)	0.002

Baseline characteristics for study population

	BES (N= 1,912)	EES (N= 1,940)	P-value
Procedural characteristics			
Multi-vessel PCI	554 (29.0%)	609 (31.4%)	0.102
IVUS-guided procedure	710 (37.1%)	844 (43.5%)	**<0.001**
Cardiogenic shock	2 (0.1%)	12 (0.6%)	**0.013**
Dissection	8 (0.4%)	7 (0.4%)	0.802
Vascular access site bleeding	2 (0.1%)	4 (0.2%)	0.687
Retroperitoneal bleeding	0 (0%)	1 (0.1%)	1.000
Medication at discharge			
Aspirin	1886 (98.6%)	1895 (97.7%)	**0.027**
Clopidogrel	1880 (98.3%)	1889 (97.4%)	**0.041**
Beta-blockers	1289 (67.4%)	1363 (70.3%)	0.057
ACE inhibitors	684 (35.8%)	609 (31.4%)	**0.004**
ARBs	539 (28.2%)	729 (37.6%)	**<0.001**
Statins	1683 (88.0%)	1695 (87.4%)	0.538
Calcium antagonists	441 (23.1%)	401 (20.7%)	0.072

3-year clinical outcomes in whole population

TLF (Target Lesion Failure)

Biolimus registry
Excellent prime registry

Hazard ratio for BES 0.86
(95% CI 0.67-1.11, p=0.256)

EES 6.6%
(128/1940)

BES 5.7%
(109/1912)

3-year clinical outcomes in whole population

POCO (Patient-Oriented Clinical Outcome)

Biolimus registry
Excellent prime registry

EES 13.8%
(267/1940)

BES 13.2%
(252/1912)

Hazard ratio for BES 0.96
(95% CI 0.81-1.14, p=0.637)
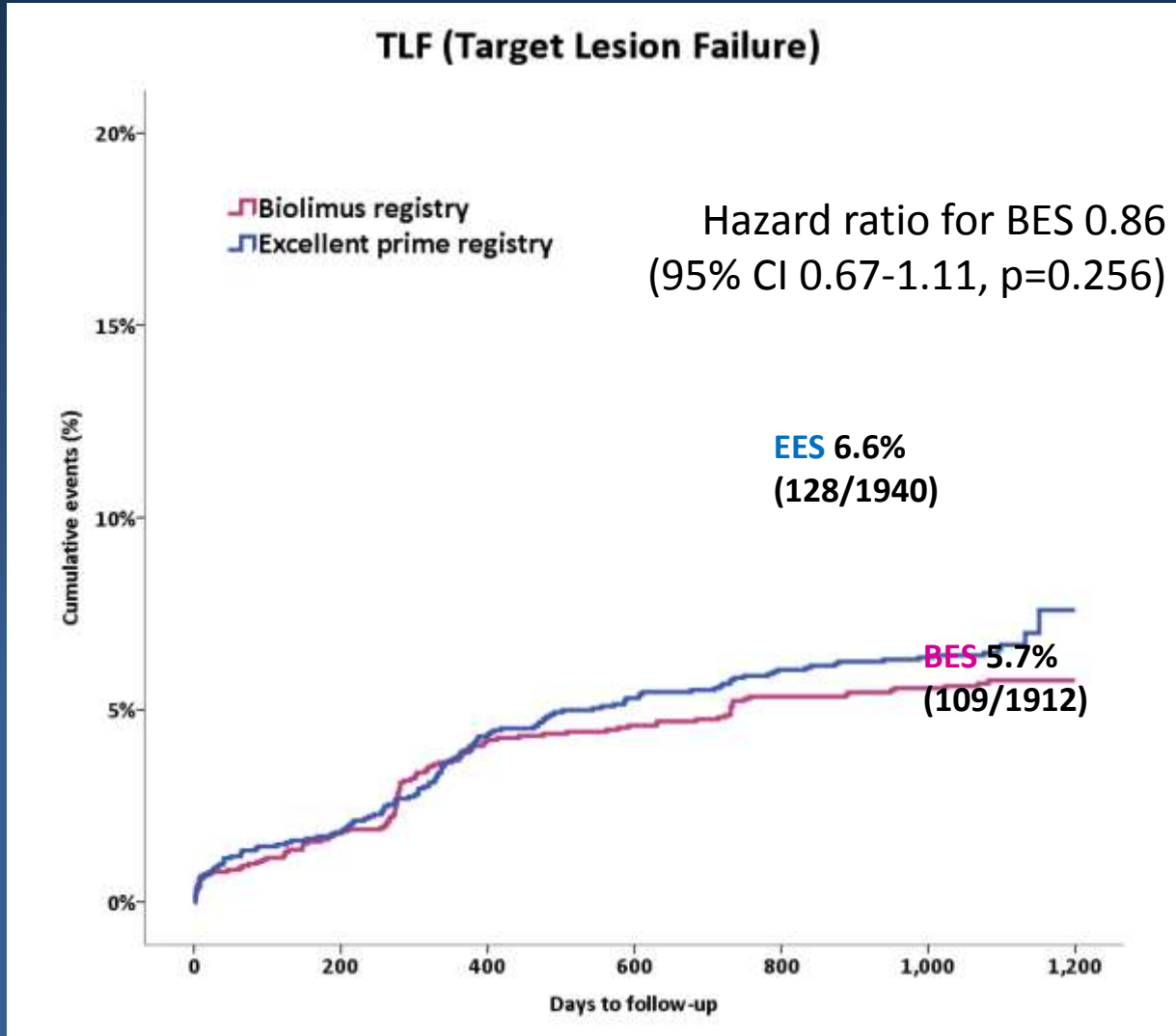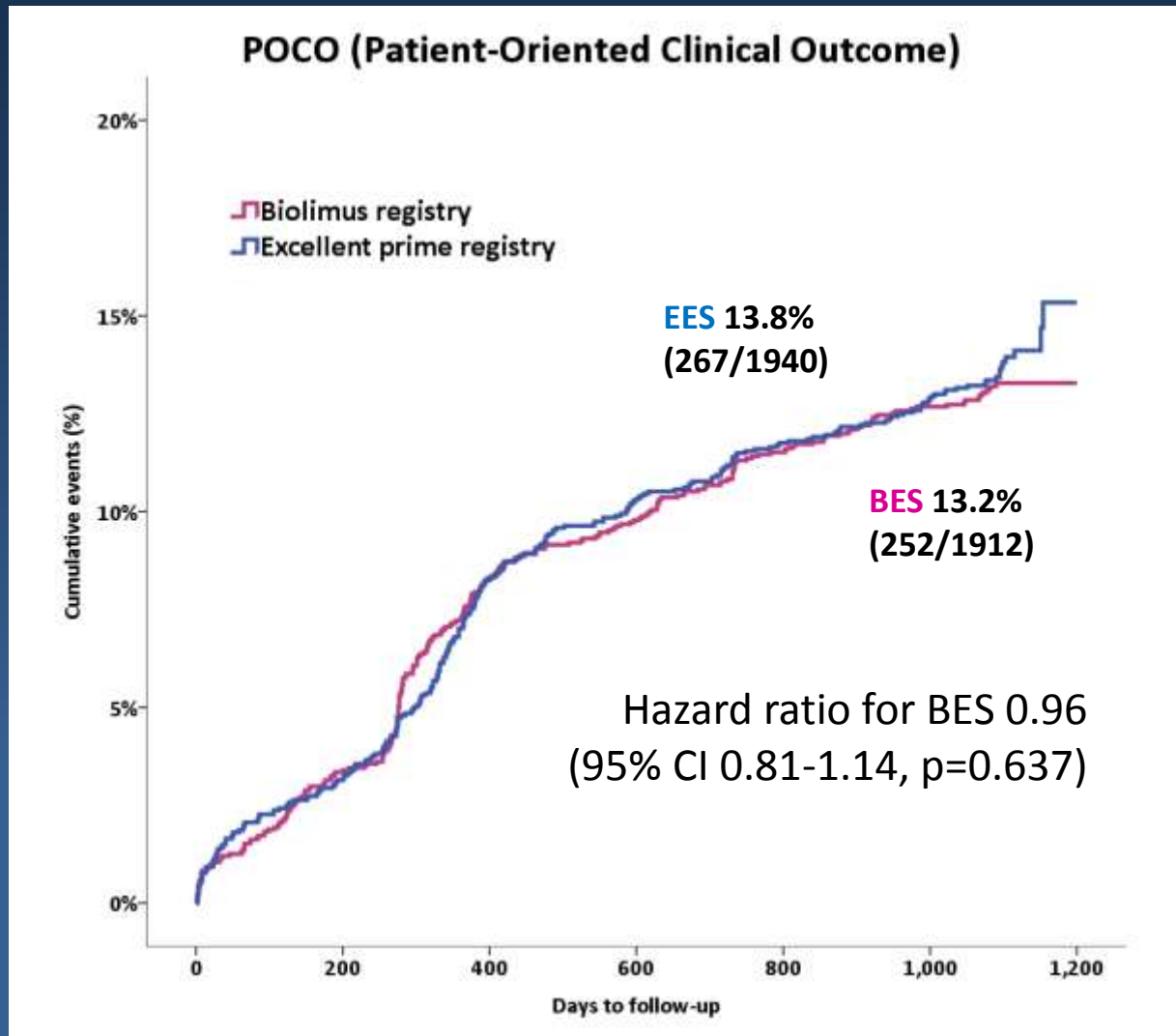
Clinical outcome

in propensity score-matched population

Propensity score matching for 1:1 matched population

Distribution of propensity score in matched population

Biolimus-3000 Korea registry (**BES**)   Excellent Prime registry (**EES**)

1912	3-year follow-up completed	**1940**
⬇		⬇
1683	Study population for per-protocol analysis	**1739**
⬇		⬇
1301 (68.0%)	1:1 propensity score matched population	**1301 (67.1%)**
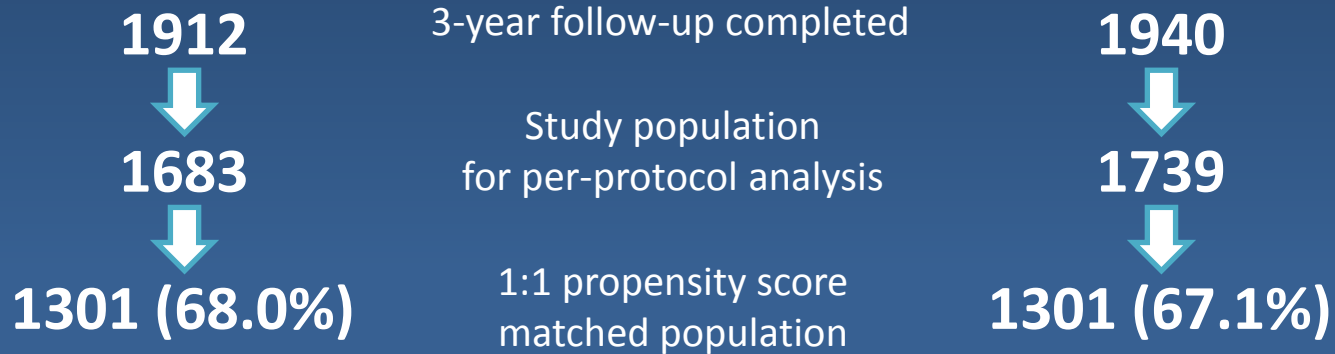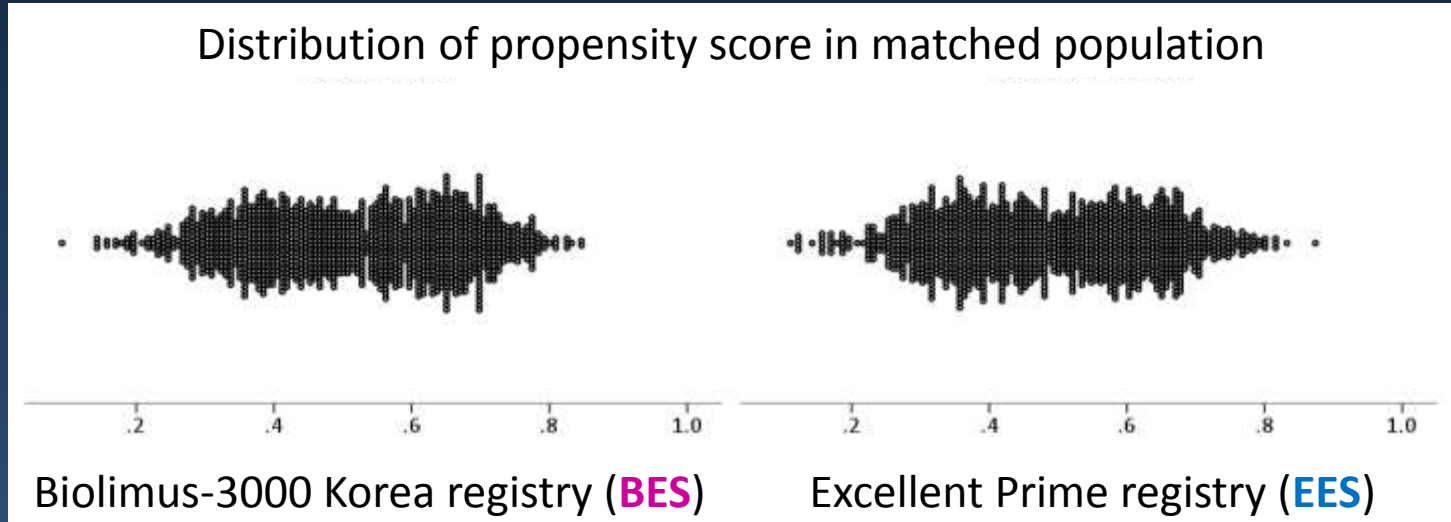
* Variables for logistic regression to calculate propensity score;
gender, age, hypertension, diabetes mellitus, current smoker, dyslipidemia(±statin), chronic renal failure, severe left ventricular dysfunction (LVEF<30%), value of serum creatinine, history of previous coronary intervention or bypass surgery / MI / CHF, burden of coronary disease (number of involved vessels, Lt. main disease, in-stent restenosis as target lesion, bifurcation lesion, long lesion (≥28mm), small vessel (diameter <2.75mm), presence of thrombus), use of GP IIb/IIIa inhibitor, off-label usage of BES, multi-lesion PCI, clinical indication for PCI (AMI)

3-year clinical outcomes in matched population

	BES (N= 1,301)	EES (N= 1,301)	BES vs. EES HR	P-value
Mortality				
All-cause death	79 (6.1%)	98 (7.5%)	0.797 (0.592-1.072)	0.133
Cardiac death	37 (2.8%)	52 (4.0%)	0.698 (0.458-1.066)	0.096
Myocardial infarction (MI)				
Any MI	17 (1.3%)	25 (1.9%)	0.676 (0.365-1.252)	0.213
Target vessel MI	9 (0.7%)	10 (0.8%)	0.894 (0.363-2.201)	0.808
MI due to stent thrombosis	5 (0.4%)	4 (0.3%)	1.246 (0.335-4.639)	0.743
Repeat Revascularization (RR)				
Any RR	112 (8.6%)	108 (8.3%)	1.039 (0.798-1.354)	0.775
Clinically driven RR	93 (7.1%)	84 (6.5%)	1.110 (0.826-1.490)	0.490
Target vessel revascularization (TVR)	67 (5.1%)	66 (5.1%)	1.017 (0.724-1.428)	0.924
Target lesion revascularization (TLR)	50 (3.8%)	49 (3.8%)	1.022 (0.689-1.516)	0.913
TLF	86 (6.6%)	100 (7.7%)	0.854 (0.640-1.140)	0.285
POCO	188 (14.5%)	203 (15.6%)	0.925 (0.758-1.128)	0.439

TLF (target lesion failure); cardiac death + target vessel MI (not clearly attributed to a non-target vessel) + clinically driven TLR
POCO (patient-oriented composite outcome); all-cause mortality + any MI + any RR

Clinically-driven TLR after propensity score matching, BES vs. EES

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After matching

Clinically-driven TLR

Biolimus registry
Excellent prime registry

**Hazard ratio for BES 1.02
(95% CI 0.69-1.52, p=0.913)**

**BES 3.8%
(50/1301)**

**EES 3.8%
(49/1301)**

TLF (Target Lesion Failure)

Biolimus registry
Excellent prime registry

**Hazard ratio for BES 0.85
(95% CI 0.64-1.14, p=0.285)**

**EES 7.7%
(100/1301)**

**BES 6.6%
(86/1301)**
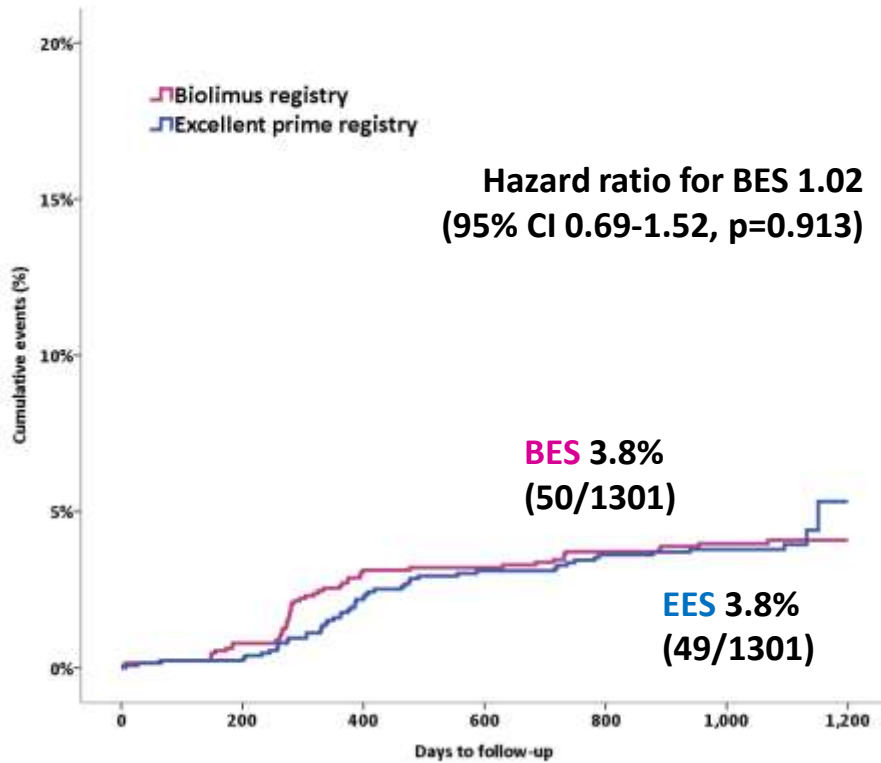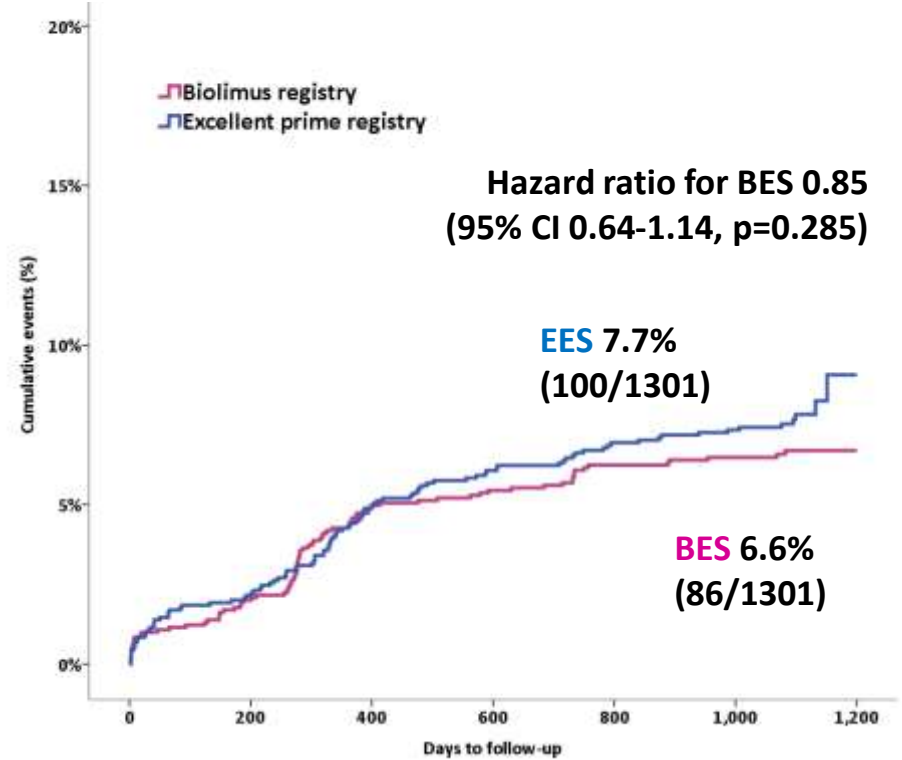
POCO after matching, BES vs. EES

Before matching

POCO (Patient-Oriented Clinical Outcome)

EES 13.8%
(267/1940)

BES 13.2%
(252/1912)

Hazard ratio for BES 0.96
(95% CI 0.81-1.14, p=0.637)

After matching

POCO (Patient-Oriented Clinical Outcome)

EES 15.6%
(203/1301)

BES 14.5%
(188/1301)

Hazard ratio for BES 0.93
(95% CI 0.76-1.13, p=0.439)
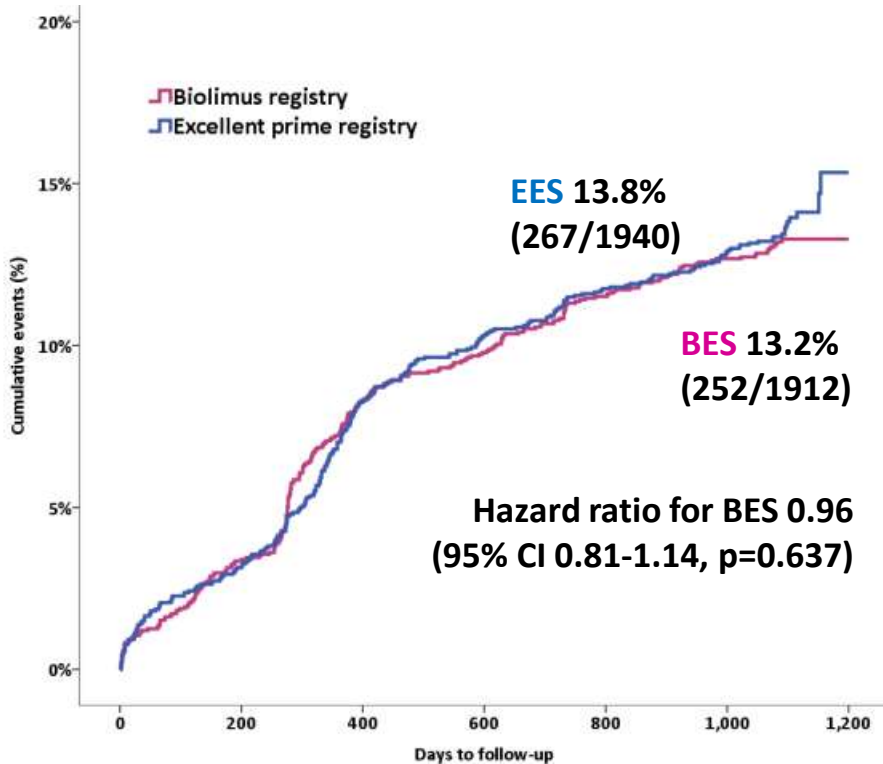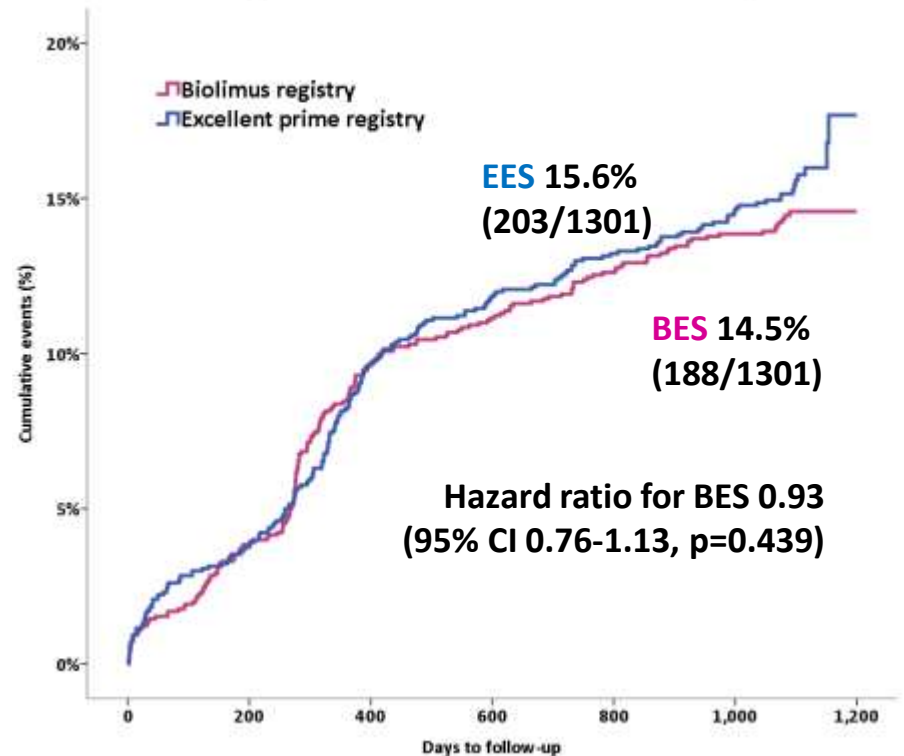
Subgroup analysis for TLF at 3-year follow-up

		BES	EES		HR (95% CI)	Interaction p-value
All patients		86 (6.6%)	100 (7.7%)		0.85 (0.64-1.14)	
Hypertension	Yes	58 (7.4%)	67 (8.4%)		0.86 (0.60-1.24)	0.327
	No	28 (5.5%)	33 (6.5%)		0.83 (0.49-1.39)	
Dyslipidemia (±statins)	Yes	53 (6.2%)	57 (6.7%)		0.92 (0.63-1.36)	0.324
	No	33 (7.4%)	43 (9.6%)		0.75 (0.47-1.21)	
Current smoker	Yes	19 (5.1%)	19 (5.1%)		0.99 (0.52-1.01)	0.325
	No	67 (7.2%)	81 (8.7%)		0.82 (0.58-1.14)	
AMI (<72hr)	Yes	37 (8.9%)	31 (8.1%)		1.10 (0.67-1.82)	0.297
	No	49 (5.5%)	69 (7.5%)		0.72 (0.50-1.06)	
IVUS-guided PCI	Yes	37 (7.5%)	54 (9.9%)		0.74 (0.48-1.15)	0.381
	No	49 (6.0%)	46 (6.1%)		0.99 (0.65-1.50)	
ISR as target lesion	Yes	5 (7.4%)	8 (12.3%)		0.57 (0.18-1.83)	0.320
	No	81 (6.6%)	92 (7.4%)		0.87 (0.64-1.19)	
Bifurcation as target lesion	Yes	37 (8.0%)	46 (9.3%)		0.85 (0.54-1.33)	0.350
	No	49 (5.9%)	54 (6.7%)		0.87 (0.58-1.29)	
Lesion length (≥28mm)	Yes	48 (8.1%)	64 (9.3%)		0.87 (0.59-1.28)	0.452
	No	38 (5.3%)	36 (5.9%)		0.90 (0.57-1.45)	
Vessel diameter (<2.75mm)	Yes	32 (10.2%)	43 (12.1%)		0.82 (0.51-1.34)	0.411
	No	54 (5.5%)	57 (6.0%)		0.90 (0.62-1.32)	
Thrombotic lesion	Yes	7 (4.6%)	9 (6.7%)		0.68 (0.24-1.87)	0.334
	No	79 (6.9%)	91 (7.8%)		0.87 (0.64-1.19)	
Multiple target vessel	Yes	39 (9.4%)	30 (7.4%)		1.30 (0.79-2.14)	0.317
	No	47 (5.3%)	70 (7.8%)		0.66 (0.45-0.97)	
Lt. main disease	Yes	13 (18.1%)	13 (13.7%)		1.39 (0.60-3.21)	0.404
	No	73 (5.9%)	87 (7.2%)		0.81 (0.59-1.12)	
Off-label indication	Yes	85 (7.1%)	91 (7.6%)		0.94 (0.69-1.27)	0.330
	No	1 (0.9%)	9 (8.7%)		0.10 (0.01-0.77)	

0.1   1   10

Favor for BES   Favor for EES

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★	★	**Definite ST, Death**
☆	☆	**Probable ST, Death**
▲	▲	**Definite ST, Myocardial infarction**
△	△	**Probable ST, Myocardial infarction**
●	●	**Definite ST, Revascularization**
○	○	**Probable ST, Revascularization**

Definite or Probable Stent Thrombosis

Hazard ratio for BES 1.38
(95% CI 0.63-3.01, p=0.416)

BES 0.8%
(15/1912)

EES 0.6%
(11/1940)

Biolimus registry
Excellent prime registry

Cumulative events (%)

2.0%
1.5%
1.0%
0.5%
0.0%

Days to follow-up

0   200   400   600   800   1,000   1,200
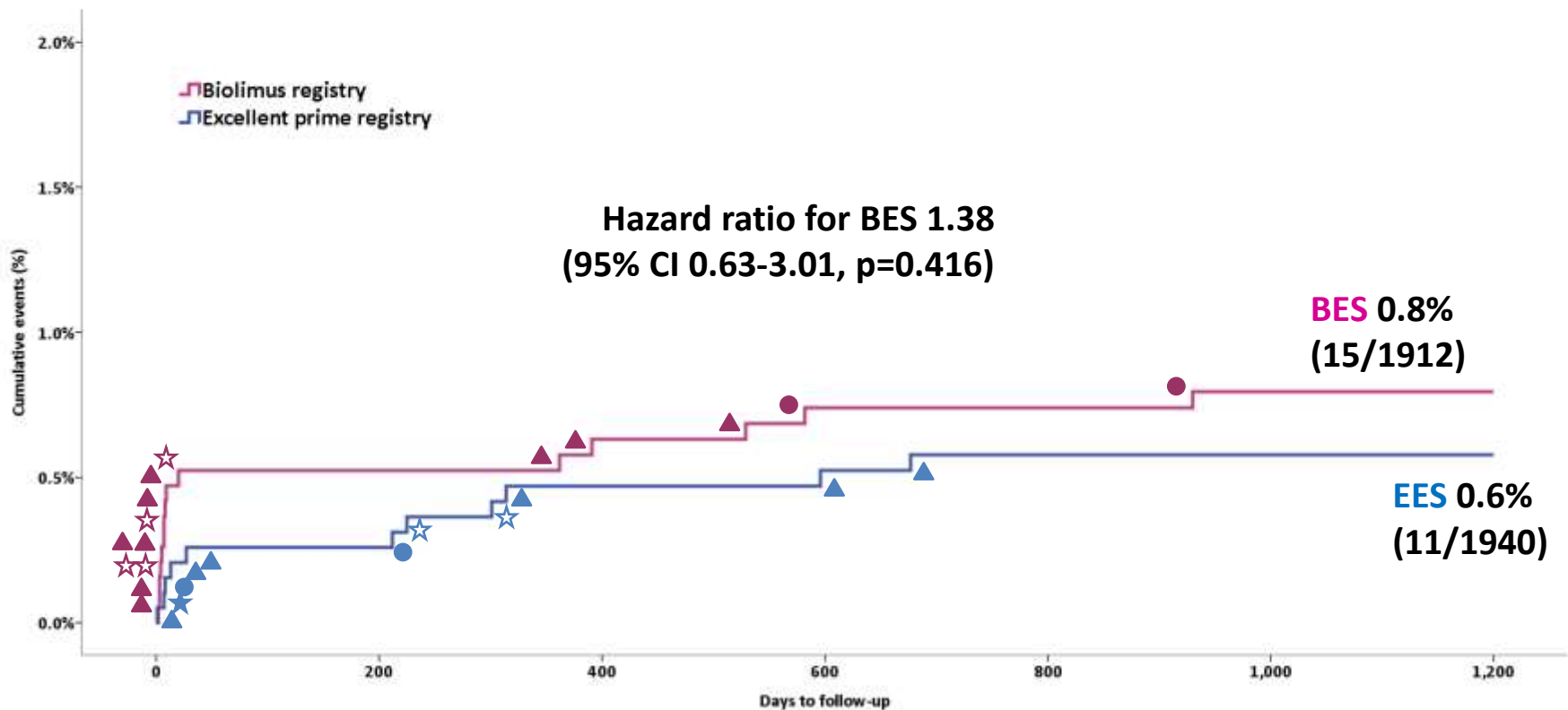
Conclusion

1. The HOST-Biolimus registry showed the performance of the bioabsorbable polymer technology based BES in a 'real-world' cohort of Korean patients.

2. Biomatrix® stent demonstrated excellent acute and long-term performance in complex lesion subsets.

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

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

Ewha Womans University Mokdong Hospital

Thank you for your attention!!!