Durable Polymer versus Biodegradable Polymer Drug-Eluting Stents after percutaneous coronary intervention in patients with Acute Coronary Syndrome

: The HOST-Reduce-Polytech-ACS trial

Session of Late Breaking Trial Session IV

Co-sponsored by European Heart Journal

TCT Congress 2020

Hyo-Soo Kim, MD/PhD
Cardiovascular Center,
Seoul National University Hospital, Korea

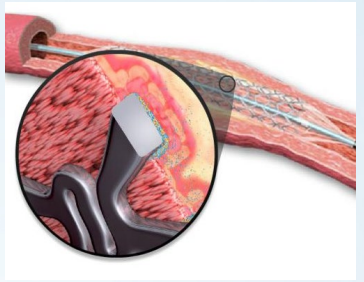
Disclosures

- *The* **HOST-Reduce-Polytech-ACS trial,**
  - *is an investigator-initiated, randomized, open-label, multicenter trial sponsored by Seoul National University Hospital*

- *The* **HOST-Reduce-Polytech-ACS trial** *has received research funds from,*
  - *Daiichi Sankyo*
  - *Boston Scientific*
  - *Terumo*
  - *Biotronik*
  - *Qualitech Korea Ltd.*
  - *Dio*

Background

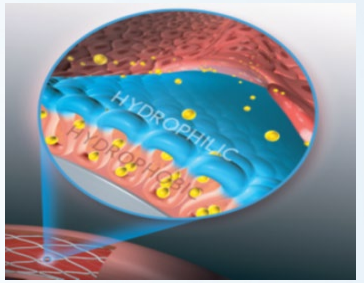
- Drug-eluting stents (DES) have significantly improved outcomes of PCI.
- However, the polymers used in the 1st generation DES were blamed as the cause of a *chronic inflammatory response* that leads to stent oriented adverse clinical outcomes, i.e. stent thrombosis.



- Strategies to mitigate this adverse effect was,

  1) ***Development of 'biocompatible durable polymers'***

  : Applied in the contemporary DES, Durable-Polymer-DES (**DP-DES**)



  2) ***Development of a 'biodegradable polymer' which dissolves with time***

  : Seems more attractive in the biologic aspect

  : Applied in the recent DES, Biodegradable-Polymer-DES (**BP-DES**)

- The comparison of the two polymer technologies in patients with acute coronary syndrome (who have ***a heightened risk of thrombosis and delayed vascular healing after PCI***) has not been previously performed in a large scale randomized trial.

Objective

- **The HOST-Reduce-Polytech-ACS trial**
  - ***H****armonizing* ***O****ptimal* ***S****trategy for* ***T****reatment of coronary artery diseases*
  - – Comparison of ***R****eduction of prasugrel or* ***P****olymer technology in* ***ACS*** *patients*

- To investigate the efficacy and safety of a ***Biodegradable Polymer DES*** *Versus* ***Durable Polymer DES*** in patients with ***ACS*** undergoing PCI.

Working Hypothesis

For PCI in ACS patients,

Durable Polymer DES will be non-inferior to the ***Biodegradable Polymer DES***, with respect to Patient Oriented Composite Outcomes (POCO)

Endpoint and Sample size Calculation

HOST REDUCE POLYTECH ACS

- **Endpoints**
  - ***Primary endpoint*: *POCO*** (Patient Oriented Composite outcome) at 12 months
    - *A composite of All-cause death, nonfatal MI, Stent thrombosis and any Repeat revascularization*
  - ***Key Secondary endpoints*: *DOCO*** (Device oriented composite Outcome) at 12 months
    - *A composite of Cardiac death, Target Vessel MI, Target Lesion Revascularization*

- **Sample Size Calculation**
  - Assumed a 1-year POCO rate in the DP-DES group: 6.0%
  - Assumed a 1-year POCO rate in the BP-DES group: 6.0%
  - Type I error: 0.025, Power: 81%
  - Non-inferiority Margin: 2.0%
  - Estimated withdrawal rate: 5%

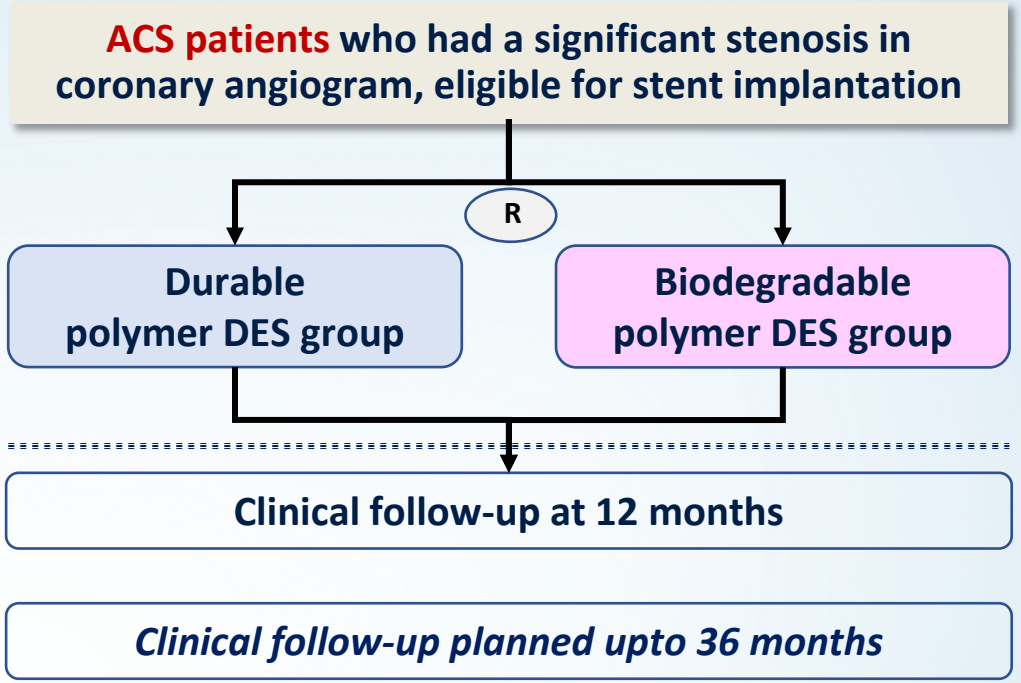
A sample size of 3,384 patients was needed to prove non-inferiority in terms of the primary endpoint

Study Design and Patient population

HOST REDUCE POLYTECH ACS

- 3,429 eligible patients with ACS screened
- From 35 centers in Korea
- Enrollment period: Sep 2014 to Dec 2018

Inclusion Criteria
a) Subject must be ≥ 19 years b) Subject must have a clinical diagnosis of ACS and a culprit lesion in a native coronary artery eligible for stent implantation c) Subject must have clinical diagnosis of acute coronary syndrome d) Subject must provide a written informed consent
Exclusion Criteria
a) Known hypersensitivity or contraindication to key medications b) Patients with active pathologic bleeding c) Female of childbearing potential, unless a recent pregnancy test is negative d) History of bleeding diathesis, known coagulopathy e) Non-cardiac co-morbid conditions are present with life expectancy <1 year



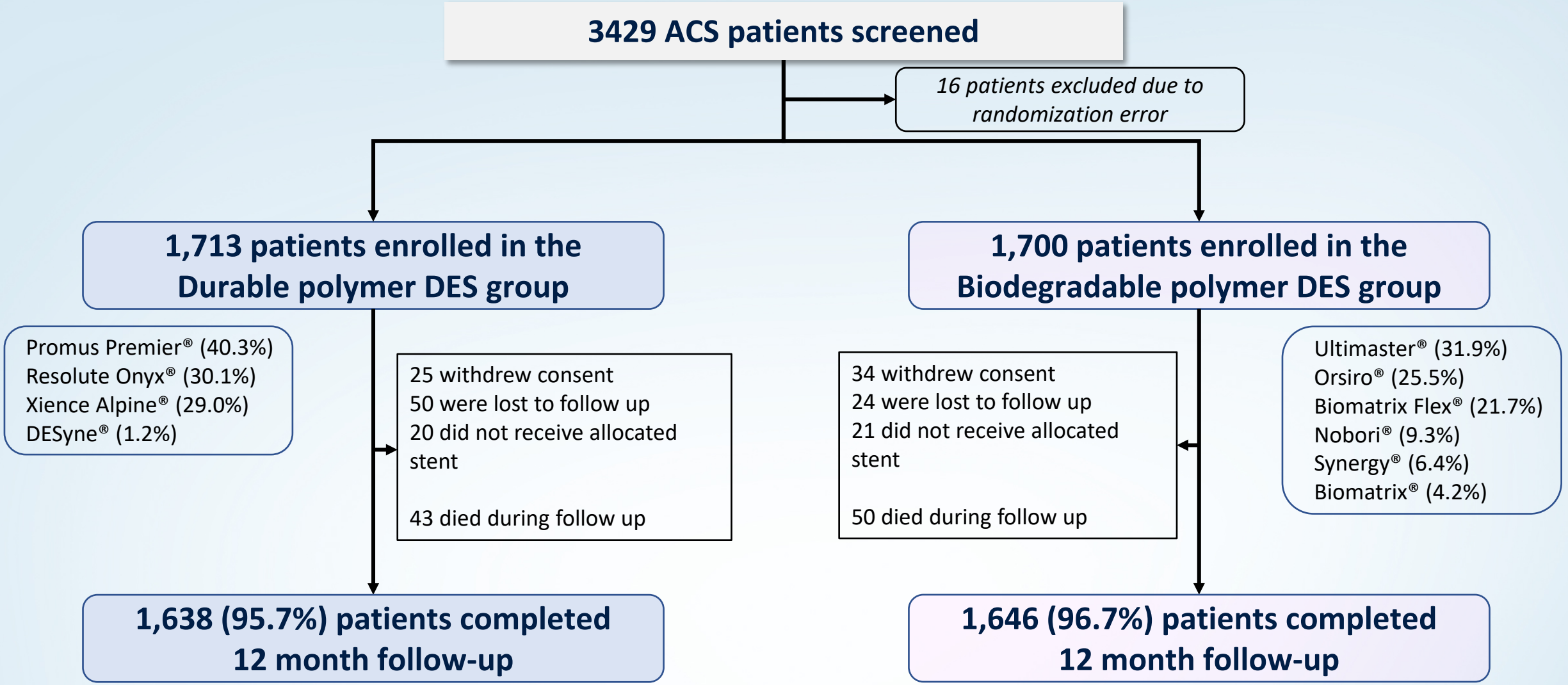
Randomization and Data collection

- ***Randomization***
  - Eligible patients were centrally randomized, via a web-based randomization sequence (MRCC IWRS System) developed by the Medical Research Collaborating Center (Seoul, South Korea).
  - No blocking or stratification methods were applied.

- ***Data collection and management***
  - Data collected by a web-based electronic case report form (eCRF)
  - All clinical events were adjudicated by an independent event adjudication committee, who were unaware of the treatment allocations.

- ***Role of funding source***
  - The funders of this study had no role in study design, collection of data and data analysis, or writing of the manuscript.

Trial flow


3429 ACS patients screened
16 patients excluded due to randomization error
1,713 patients enrolled in the Durable polymer DES group
1,700 patients enrolled in the Biodegradable polymer DES group
Promus Premier® (40.3%)
Resolute Onyx® (30.1%)
Xience Alpine® (29.0%)
DESyne® (1.2%)
25 withdrew consent
50 were lost to follow up
20 did not receive allocated stent
43 died during follow up
34 withdrew consent
24 were lost to follow up
21 did not receive allocated stent
50 died during follow up
Ultimaster® (31.9%)
Orsiro® (25.5%)
Biomatrix Flex® (21.7%)
Nobori® (9.3%)
Synergy® (6.4%)
Biomatrix® (4.2%)
1,638 (95.7%) patients completed 12 month follow-up
1,646 (96.7%) patients completed 12 month follow-up

Baseline Clinical Profiles

	Durable polymer DES (N=1,713)	Biodegradable polymer DES (N=1,700)
Age, years	63.0±11.1	63.1±11.1
Male	1,351 (78.9%)	1,337 (78.6%)
Body mass index, kg/m^2	24.9±3.1	25.0±3.2
Hypertension	1,092 (63.7%)	1,147 (67.5%)
Diabetes	789 (46.1%)	747 (43.9%)
Dyslipidemia	1,280 (74.7%)	1,247 (73.4%)
Chronic kidney disease	79 (4.6%)	65 (3.8%)
Peripheral vessel disease	24 (1.4%)	25 (1.5%)
Prior myocardial infarction	67 (3.9%)	70 (4.1%)
Prior stroke	92 (5.4%)	110 (6.5%)
LVEF, %	58.5±10.4	58.7±10.4
Presentations		
- STEMI	233 (13.6%)	214 (12.6%)
- NSTEMI	448 (26.2%)	412 (24.2%)
- Unstable angina	1,031 (60.2%)	1,074 (63.2%)

Baseline Lesion Profiles

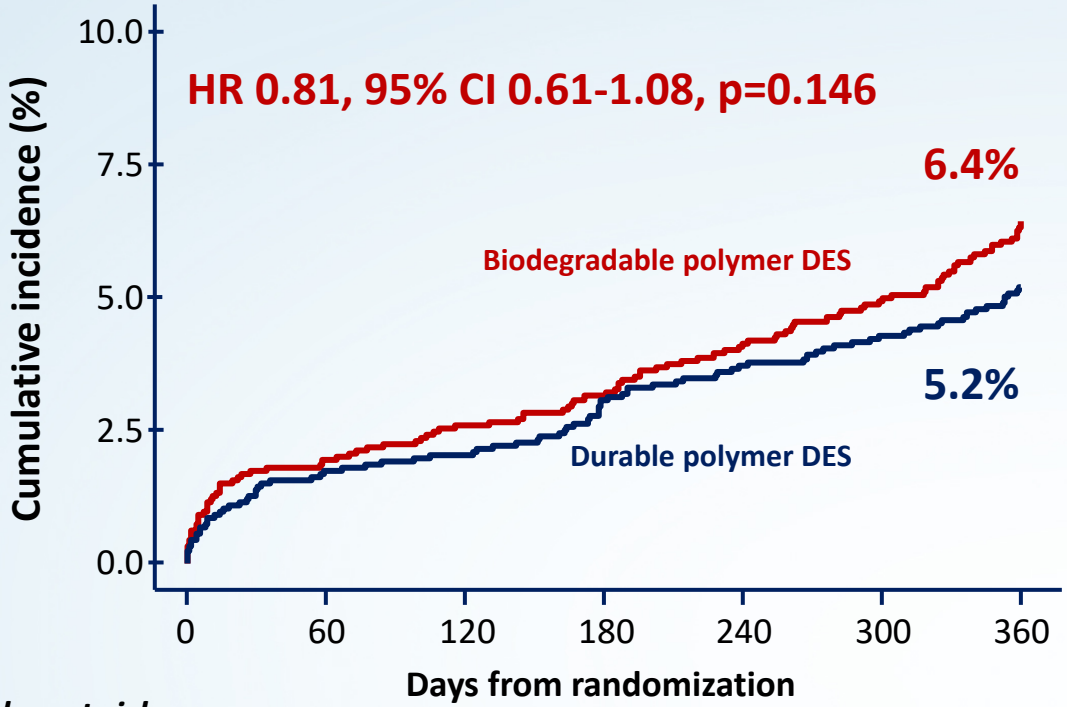
	Durable polymer DES (N=1,713)	Biodegradable polymer DES (N=1,700)
Multivessel disease	925/1,703 (54.3%)	920/1,689 (54.5%)
Culprit lesion		
- Left main	62/1679 (3.7%)	58/1,669 (3.5%)
- Left anterior descending artery	837/1679 (49.9%)	8451,669 (50.6%)
- Left circumflex artery	307/1679 (18.3%)	3081,669 (18.5%)
- Right coronary artery	473/1679 (28.2%)	4581,669 (27.4%)
Multi-lesion intervention	512/1,687 (30.3%)	512/1,674 (30.6%)
Lesion complexity		
- Heavy calcification	317/2,353 (13.5%)	344/2,329 (14.8%)
- Bifurcation lesion	422/2,351 (17.9%)	438/2,326 (18.8%)
- Thrombotic lesion	204/2,353 (8.7%)	208/2,328 (8.9%)
- Type B2/C lesion	1,165/2,351 (49.6%)	1,215/2,328 (52.2%)
- ISR lesion	56/2,353 (2.4%)	42/2,328 (1.8%)
IVUS use	706/2,360 (29.9%)	752/2,339 (32.2%)
Treated lesion number per person	1.4±0.7	1.4±0.7
Stent number per person	1.7±1.0	1.7±1.1
Total stent length, mm	41.7±30.2	42.9±31.9

Primary outcome (POCO at 1 year)

HOST REDUCE POLYTECH ACS

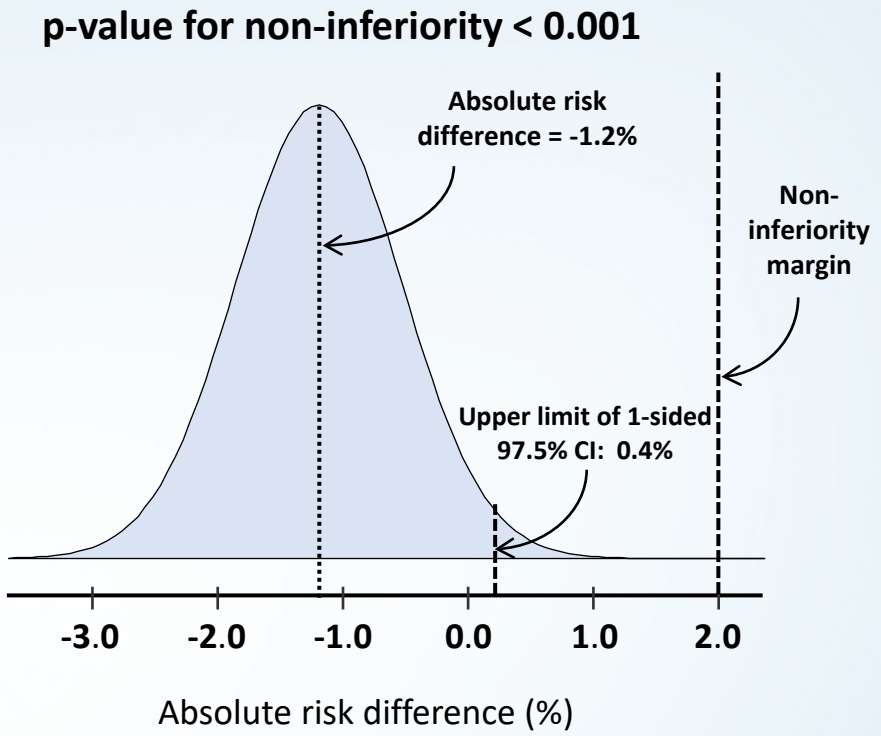
ACS patients who had a significant stenosis in coronary angiogram, eligible for stent implantation

- **Durable polymer DES group**
- **Biodegradable polymer DES group**



Number at risk

BP-DES	1700	1634	1617	1607	1593	1576	1555
DP-DES	1713	1651	1643	1629	1612	1600	1578



POCO: [All-cause death, nonfatal MI, Stent thrombosis and any repeat revascularization] at 1 year

** Event rates are based on Kaplan Meier estimates*

Key Secondary outcomes (DOCO at 1 year)

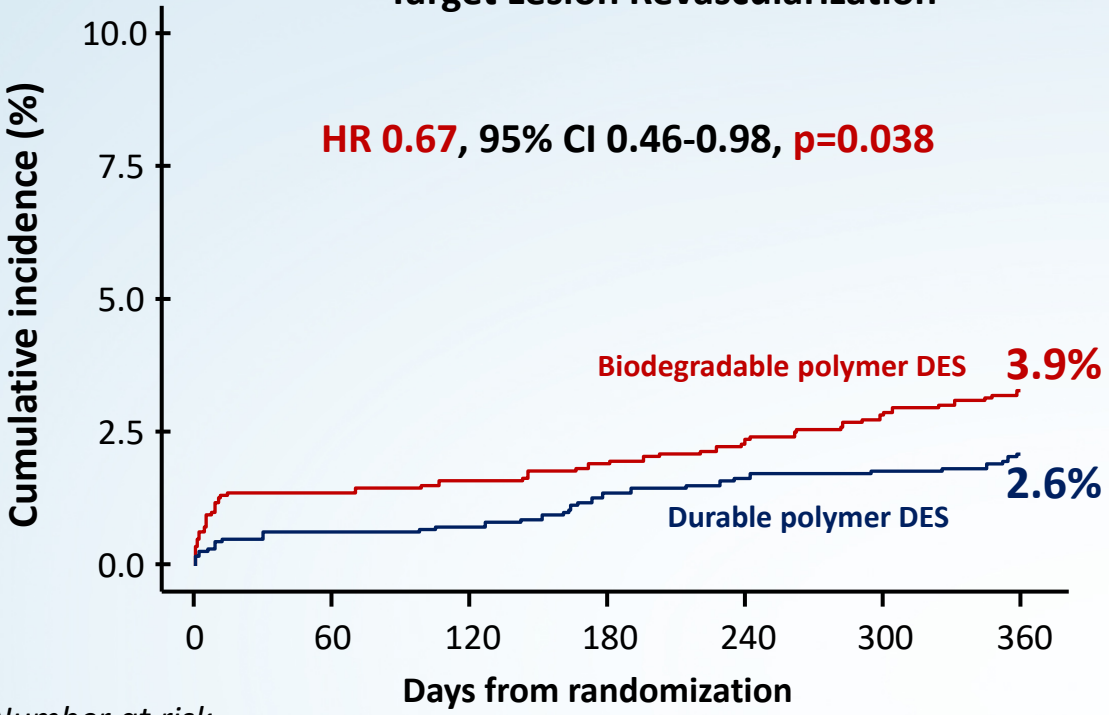
HOST REDUCE POLYTECH ACS

- ***DOCO***:

Cardiac death,

Target vessel MI, or

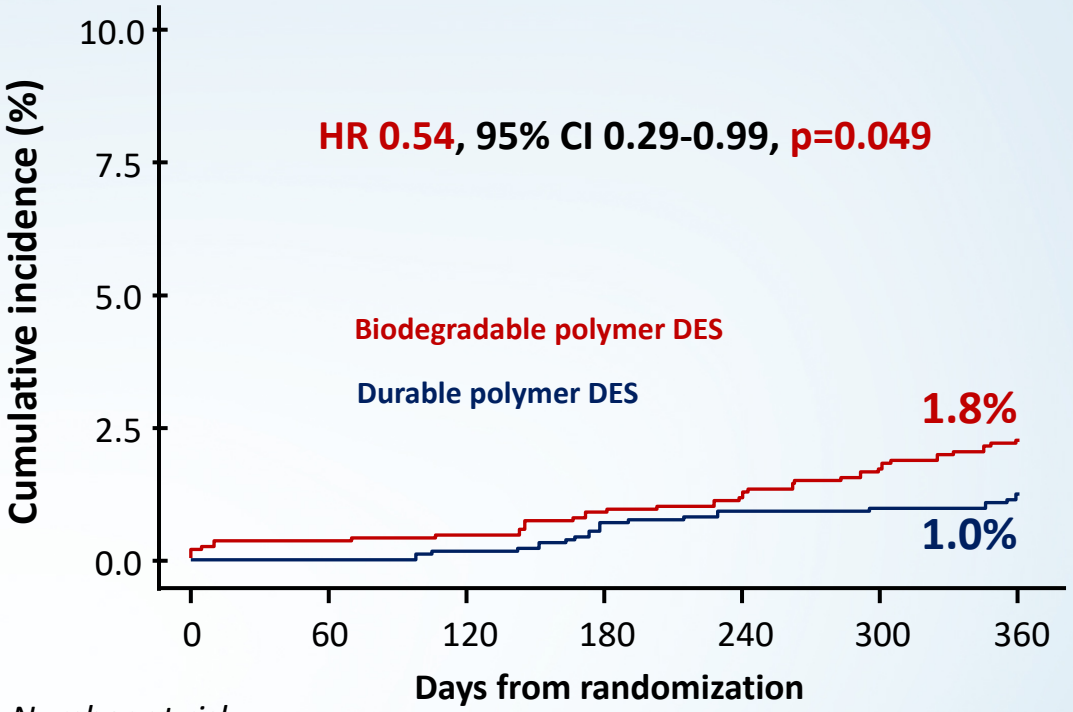
Target Lesion Revascularization



Number at risk

BP-DES	1700	1635	1623	1614	1607	1595	1581
DP-DES	1713	1662	1655	1641	1627	1620	1604

Target lesion revascularization



Number at risk

BP-DES	1700	1635	1621	1612	1603	1590	1574
DP-DES	1713	1661	1653	1639	1625	1618	1602

** Event rates are based on Kaplan Meier estimates*

Clinical outcomes at 1 year

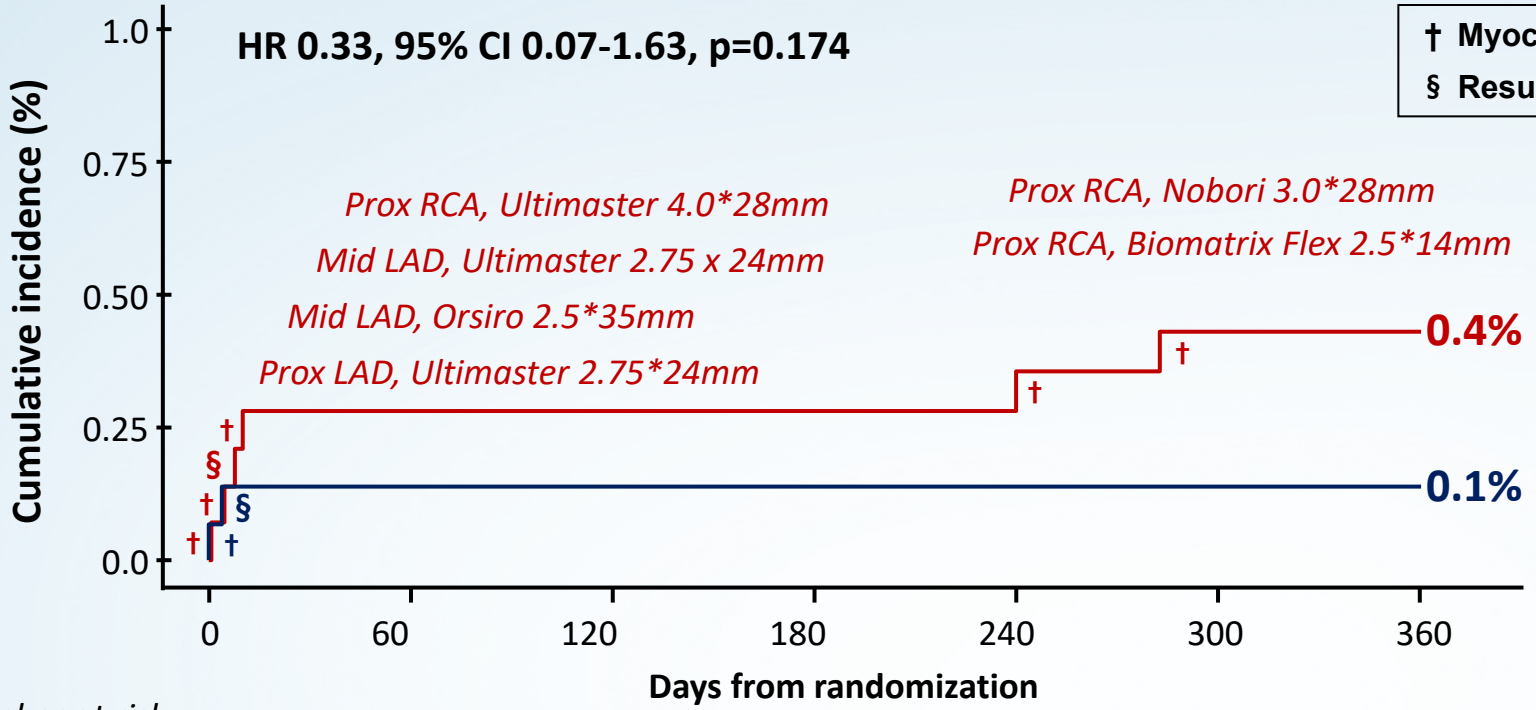
** Event rates are based on Kaplan Meier estimates*

	Durable polymer DES (N=1,713)	Biodegradable polymer DES (N=1,700)	Hazard ratio (95% CI)	p-value
Primary endpoint				
- POCO	87 (5.2%)	106 (6.4%)	0.81 (0.61-1.08)	0.146
Key Secondary endpoint				
- DOCO	44 (2.6%)	65 (3.9%)	0.67 (0.46-0.98)	0.038
Other Secondary endpoints				
- All-cause death	43 (2.6%)	50 (3.0%)	0.85 (0.57-1.28)	0.433
- Cardiac death	27 (1.6%)	38 (2.3%)	0.70 (0.43-1.15)	0.160
- Non-fatal MI	10 (0.6%)	13 (0.8%)	0.76 (0.33-1.73)	0.513
- Target vessel MI	5 (0.3%)	8 (0.5%)	0.62 (0.20-1.89)	0.617
- Stent thrombosis	2 (0.1%)	6 (0.3%)	0.33 (0.07-1.63)	0.174
- Repeat revascularization	48 (2.9%)	58 (3.6%)	0.82 (0.56-1.20)	0.298
- TLR	16 (1.0%)	29 (1.8%)	0.54 (0.29-0.99)	0.049
- Non-TLR	36 (2.1%)	34 (2.0%)	1.04 (0.65-1.67)	0.856

POCO: (all-cause death, non-fatal MI, stent thrombosis, repeat revascularization) at 1 year
DOCO: (Cardiac death, target vessel MI, target lesion revascularization) at 1 year

Stent Thrombosis

- Stent thrombosis (definite and probable) at 12 months
  - Two patients (0.1%) in the DP-DES group and six patients (0.4%) in the BP-DES group



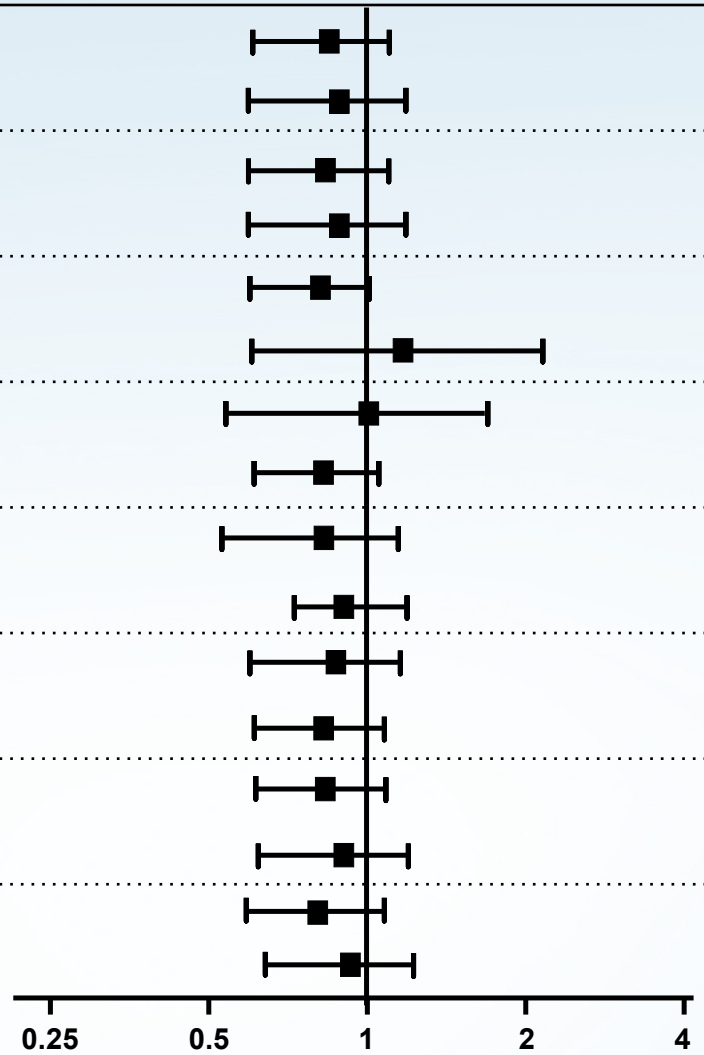
Number at risk

BP-DES	1700	1635	1626	1622	1617	1609	1601
DP-DES	1713	1661	1656	1646	1638	1632	1618

Subgroup analysis

HOST REDUCE POLYTECH ACS

		DP-DES (events/patients)	BP-DES (events/patients)	HR (95% CI)	P value	Int. P-value
Age (years)	< 65	35/946	40/927	0.85 (0.65-1.13)	0.260	0.945
	≥ 65	52/767	66/777	0.87 (0.62-1.20)	0.385	
Diabetes	No	28/924	43/953	0.82 (0.62-1.10)	0.191	0.758
	Yes	59/789	31/552	0.88 (0.65-1.20)	0.421	
Chronic Kidney Disease	No	67/1634	94/1635	0.80 (0.64-1.01)	0.056	0.203
	Yes	20/79	12/65	1.22 (0.66-2.27)	0.522	
Clinical Diagnosis	STEMI	20/233	20/214	1.00 (0.58-1.70)	0.991	0.541
	NSTE-ACS	67/1479	86/1486	0.83 (0.66-1.05)	0.115	
Multi-lesion Intervention	No	54/1175	58/1162	0.83 (0.57-1.20)	0.319	0.605
	Yes	31/512	43/512	0.93 (0.69-1.26)	0.391	
Multi-vessel disease	No	61/925	72/920	0.87 (0.62-1.22)	0.414	0.977
	Yes	26/778	33/769	0.86 (0.66-1.14)	0.297	
Total Stent length	< 40 mm	47/1018	44/986	0.86 (0.64-1.14)	0.283	0.784
	≥ 40 mm	38/594	53/638	0.91 (0.66-1.26)	0.563	
Stent number	1 stent	43/1018	44/986	0.83 (0.62-1.11)	0.636	0.605
	≥ 2 stents	42/669	57/688	0.93 (0.68-1.26)	0.563	



Favors Durable polymer DES ← → Favors Biodegradable polymer DES

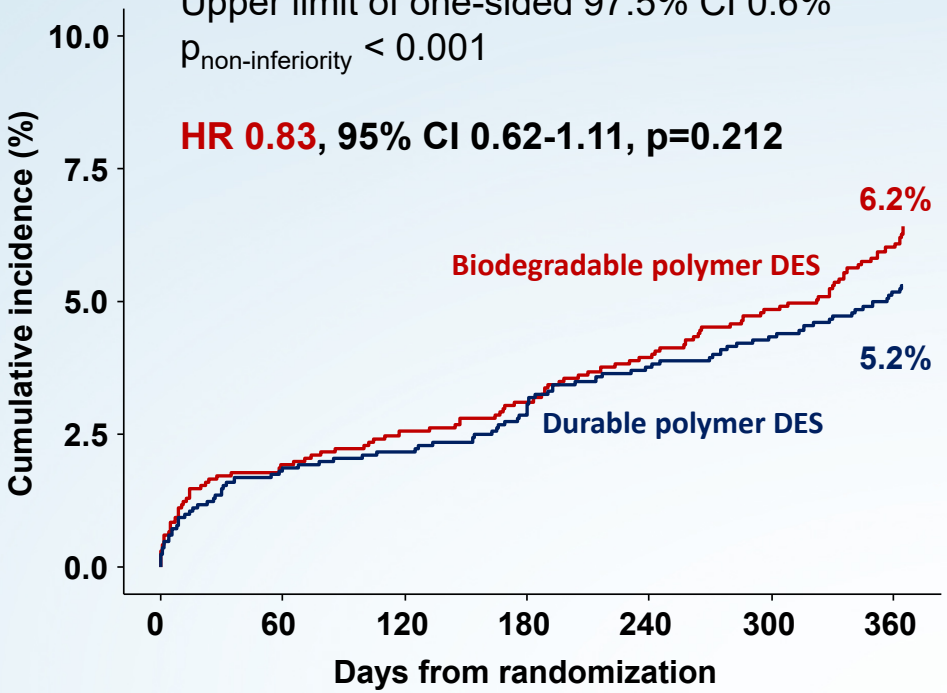
Per Protocol analysis

HOST REDUCE POLYTECH ACS

Primary outcome (POCO)

Absolute risk difference -1.0%
Upper limit of one-sided 97.5% CI 0.6%
$p_{non\text{-}inferiority} < 0.001$

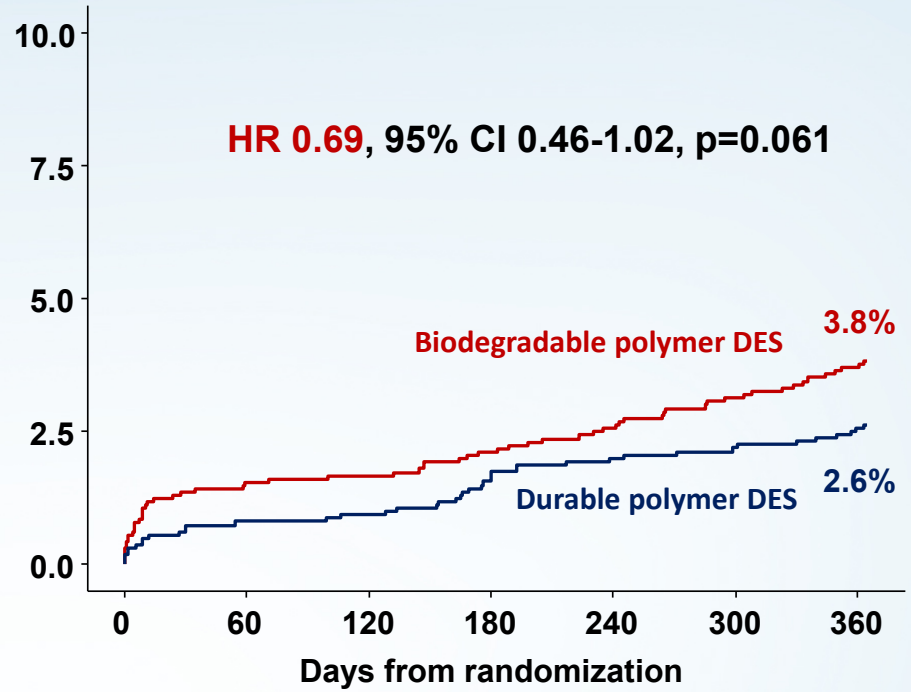
HR 0.83, 95% CI 0.62-1.11, p=0.212



Number at risk							
BP-DES	1627	1596	1586	1577	1564	1550	1532
DP-DES	1622	1593	1587	1576	1562	1553	1540

Key secondary outcome (DOCO)

HR 0.69, 95% CI 0.46-1.02, p=0.061



Number at risk							
BP-DES	1627	1597	1592	1584	1577	1568	1557
DP-DES	1622	1604	1599	1588	1577	1573	1566

POCO: [All-cause death, nonfatal MI, Stent thrombosis and any repeat revascularization] at 1 year
** Event rates are based on Kaplan Meier estimates*

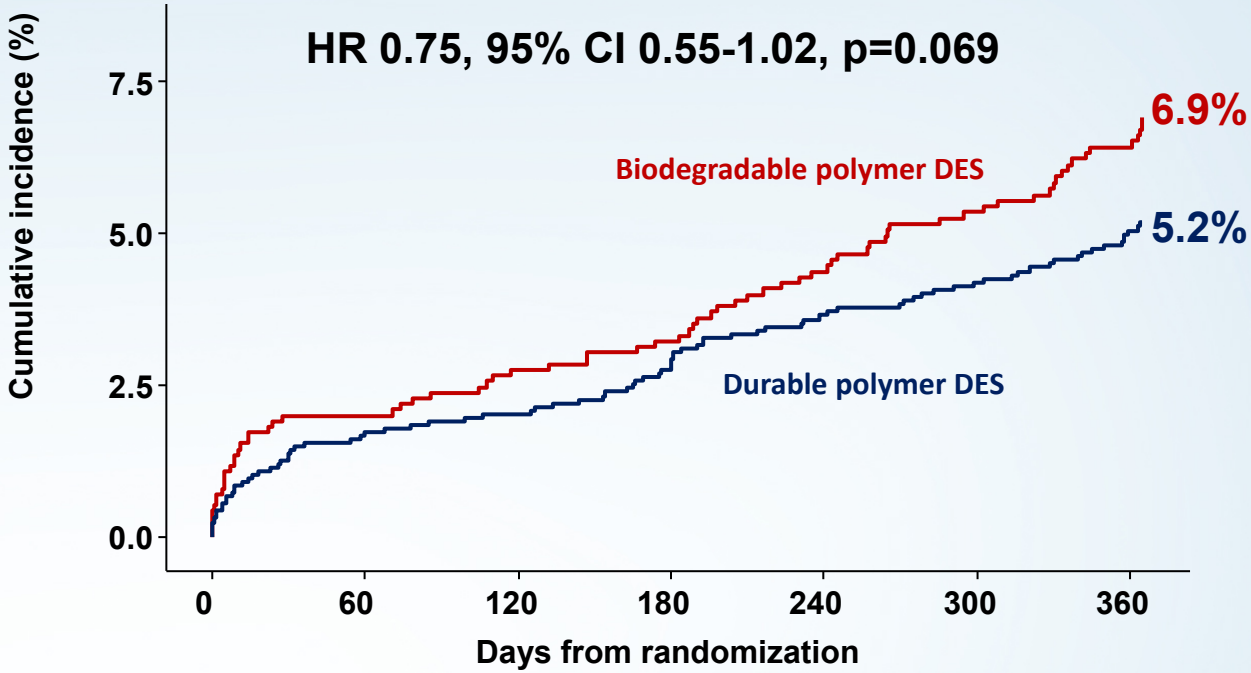
Post hoc analysis

HOST REDUCE POLYTECH ACS

- **Post hoc analysis of Thin Strut stents**
  - *Thick- strut stents are associated with greater thrombogenicity, slower endothelialization rate, and an increased risk of neointimal hyperplasia.*
  - *Excluding Biomatrix, B-Flex, and Nobori (120μm)*

- ***DP-DES group***
  - Promus Premier®, Resolute Onyx®, Xience Alpine®, DESyne®
- ***BP-DES group***
  - Ultimaster®, Orsiro®, Synergy®

Primary outcome (POCO)



Number at risk

BP-DES	1088	1041	1028	1022	1010	999	988
DP-DES	1710	1648	1640	1626	1609	1597	1575

POCO: [All-cause death, nonfatal MI, Stent thrombosis and any repeat revascularization] at 1 year

** Event rates are based on Kaplan Meier estimates*

Limitations (HOST-Reduce-Polytech-ACS RCT)

- ✓ Only the polymer technique was randomized, and therefore various stents with various profiles were included in each group.
- ✓ This study was not double blinded, investigators were acknowledged which arm the patient was enrolled.
- ✓ Our study lacks power to detect differences in the risk of rare device oriented ischemic endpoints, such as non-fatal MI and stent thrombosis.
- ✓ A 12-month follow-up period may be short in determining the clinical outcomes depending on polymer technology
- ✓ *(We plan to continue follow-up to 3 years post-PCI to detect differences in late events).*

Conclusion (**HOST-Reduce-Polytech-ACS** RCT)

- In ACS patients

  who had a significant coronary stenosis and are eligible for stent implantation,

  - Durable polymer DES was non-inferior to Biodegradable polymer DES, in terms of 1-year POCO (patient oriented composite outcomes).
  - Regarding DOCO (device oriented composite outcomes), we observed a sign of higher clinical events in the Biodegradable than Durable polymer DES.
  - Further follow-up is needed to assess the effect of polymer technology on the late (>1 year post PCI) clinical outcomes.

Thank you for your kind attention

We thank our co-investigators

Of the HOST-Reduce-Polytech-ACS RCT

Dr Jay Young Rhew, Presbyterian medical center
Dr. Kook Jin Chun Pusan National University Yangsan Hospital
Dr. Young-Hyo Lim, Hanyang University Seoul Hospital
Dr. Jung Min Bong, Hanlim General Hospital
Dr. Jang-Whan Bae, Chungbuk National University
Dr. Bong Ki Lee, Kangwon National University
Dr. Seok-Yeon Kim, Seoul Medical Center
Dr. Keun-Ho Park, Chosun Medical Center
Dr. Seung-Woon Rha, Korea University Guro Hospital
Dr. Won-Yong Shin, Soonchunhyang University Cheonan Hospital
Dr. Hong-Seok Lim, Ajou University Medical Center
Dr. Kyungil Park, Dong-A University Hospital
Dr. Yun-Kyeong Cho, Keimyung University Dongsan Medical Center
Dr. Soon Jun Hong, Korea University Anam Hospital
Dr. Sanghyun Kim, Seoul Boramae Hospital
Dr. Sang-Ho Jo, Hallym University Sacred Heart Hospital
Dr. Yong Hoon Kim, Kangwon National University

Dr. Won Kim, Kyung Hee University Medical Center
Dr. Sung Yun Lee, Ilsan Paik Hospital
Dr. Young Dae Kim, Dong-A University Hospital
Dr. Seok Kyu Oh, Wonkwang University Hospital
Dr. Jung Hee Lee, Yeungnam University Hospital
Dr. Dong-Bin Kim, Bucheon ST. Mary's Hospital
Dr. In-Ho Chae, Seoul National University Bundang Hospital
Dr. Keon-Woong Moon, ST. Vincent's Hospital
Dr. Hyun Woong Park, Gyeongsang National University Hospital
Dr. Ki-Bum Won, Ulsan University Hospital
Dr. Dong Woon Jeon, National Health Insurance Service Ilsan Hospital
Dr. Gyu-Rok Han, Kangdong Sacred Heart Hospital
Dr. Si Wan Choi, Chungnam National University Hospital
Dr. Jae Kean Ryu, Daegu Catholic University Medical Center
Dr. Myung Ho Jeong, Chonnam University Hospital
Dr. Kwang Soo Cha, Pusan National University Hospital
Dr. Namho Lee, Kangnam Sacred Heart Hospital