RECOVERY: A Randomized Trial of a Bioabsorbable Polymer-Based Metallic DES With a Luminal CD34+ Antibody Coating vs. a Polymer-Free Metallic DES in Patients With Coronary Artery Disease

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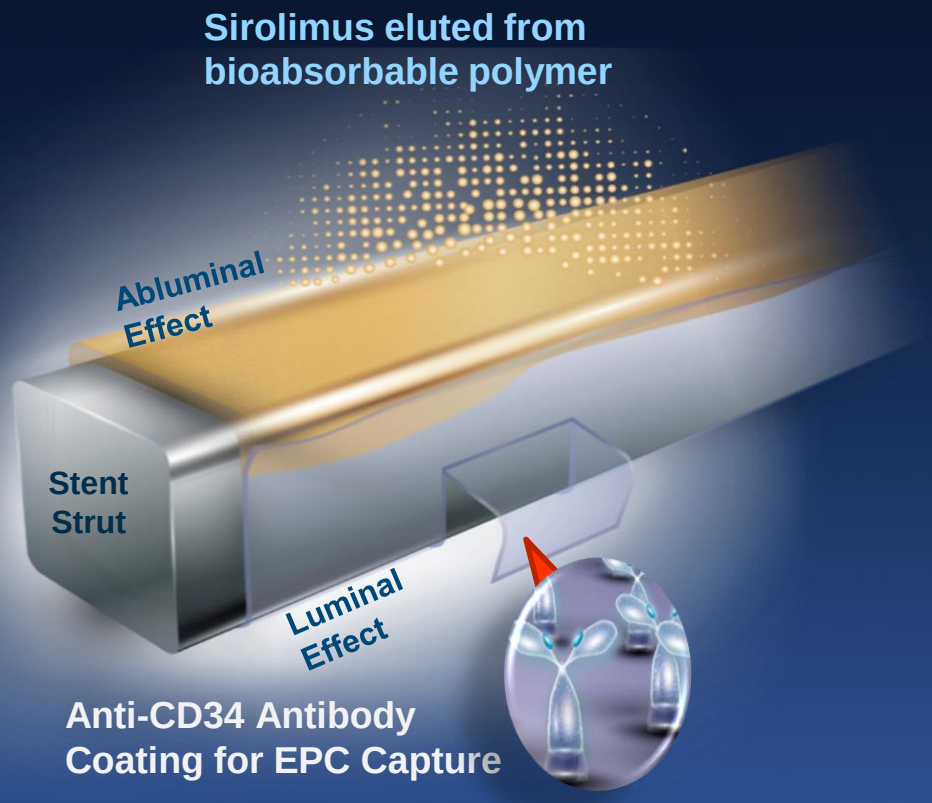
Disclosure Statement of Financial Interest

- The study was funded by a research grant from OrbusNeich Medical Company
- I, (Ling Tao) have no relevant conflicts of interest to disclose

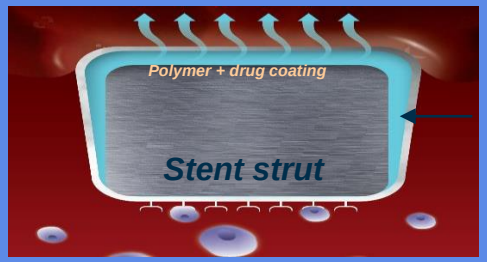
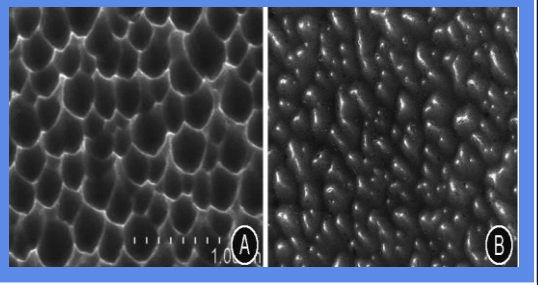
Combo Bio-Engineered Sirolimus-Eluting Stent

COMBO stent is more than just a drug-eluting stent – it is a combination of traditional DES components with an addition of a biological therapy

UNIQUE	**Biological**	Anti-CD34 antibody coating induces functional endothelial layer
TRADITIONAL	**Drug**	Pharmaceutical agent reduces neointimal hyperplasia
	Polymer	Bioabsorbable polymer transports and delivers drug in an abluminal direction
	Stent Platform	Robust stent design with improved deliverability to easily treat workhorse cases



Combo Stent vs. PE-SES Stent

Technical Parameters	Combo	Nano
		
Stent material	316L stainless steel	316L stainless steel
Surface modification	Biological-Anti CD34 antibody coating	Abluminal nanoporous surface
Polymer	Bioabsorbable, degrades within **90 days**	Polymer-free
Drug	Sirolimus, elutes within **30 days**	Sirolimus, release 80% in **30 days**
Drug dosage	1.5μg/mm^2	2.2ug/mm^2

Stent Sizes	Combo	Nano
Stent diameter	2.5, 2.75, 3.0, 3.5, 4.0 mm	2.5, 2.75, 3.0, 3.5, 4.0 mm
Stent length	9, 13, 15, 18, 23, 28, 33, 38 mm	12, 15, 18, 21, 24, 29, 36 mm

Objectives

We sought to evaluate the safety and effectiveness of the combined sirolimus-eluting CD34 antibody coated Combo stent in a randomized trial designed to enable its approval by the China Food and Drug Administration.

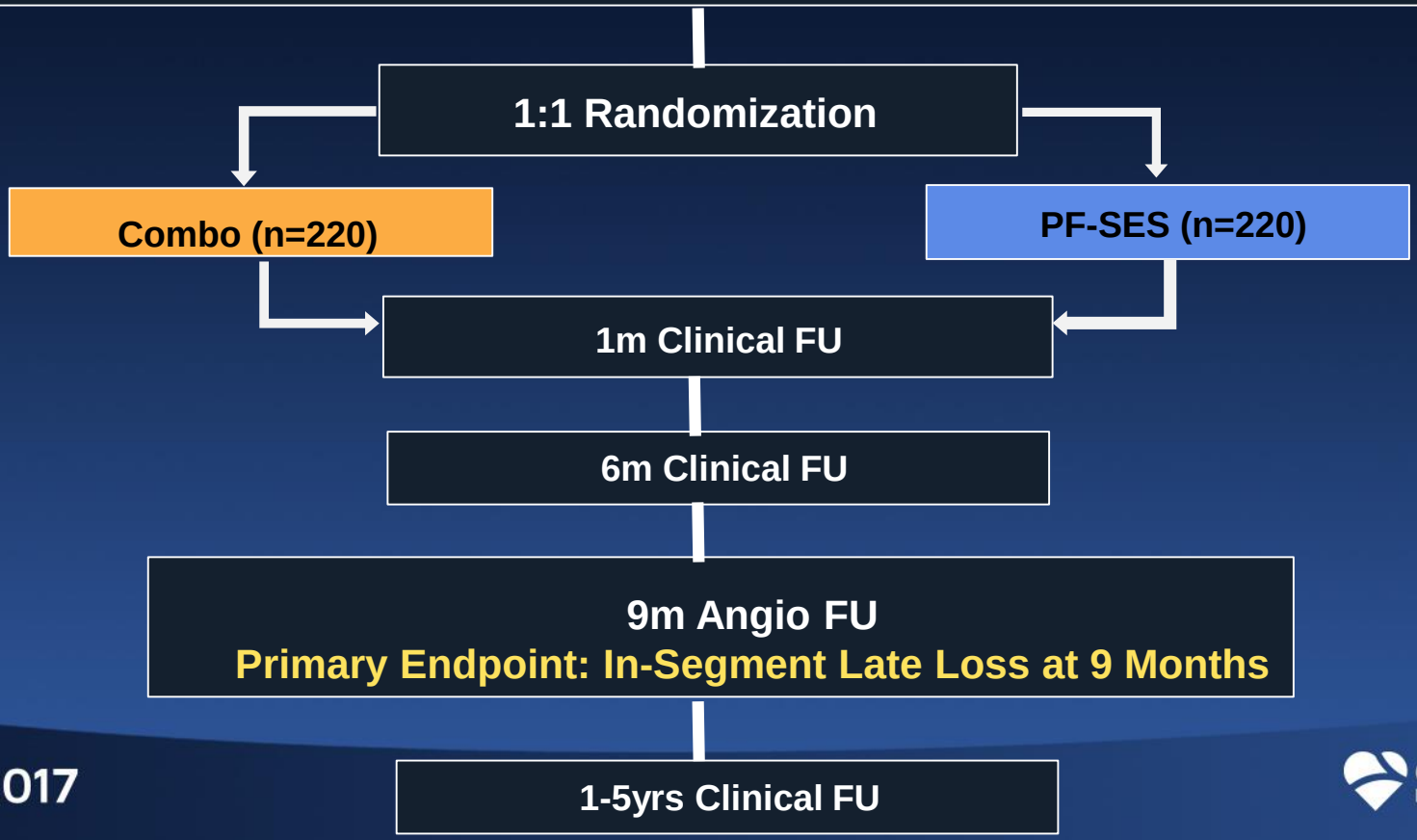
Study Design (N =440)

Major Inclusion Criteria:

- Clinical evidence of asymptomatic or symptomatic heart disease, stable or unstable angina, old myocardial infarction
- De novo lesions of native coronary arteries (number ≤2)
- Target lesion located in one or two different vessels; the number of target lesions in one vessels =1
- Target vessel diameter: 2.5 to 4.0 mm; target lesion length ≤ 32mm, which can be covered by one combo stent with length 38mm or one Nano stent with length 36mm
- Target lesion diameter stenosis ≥ 70%
- Each target lesion is permitted to implant only one stent at most, except bailout stent

Major Exclusion Criteria:

- AMI within one week
- Chronic total occlusion lesion (TIMI 0 flow), Left main disease, Ostial lesion, and/or triple-vessel lesion that might require treatment, bifurcation lesions with a side branch diameter ≥2.5mm or graft lesions
- Heavily calcified or tortuous lesions cannot be successfully pre-dilated, lesions not suitable for stent delivery and deployment
- In-stent restenosis; Thrombotic lesion
- Received any other stent in the past six months



Endpoints

Primary Endpoint

- In-segment late loss at 9 months

Secondary Endpoints

- Device, lesion and clinical success rates
- The device-oriented target lesion failure defined as a composite of cardiac death, target vessel myocardial infarction and ischemia-driven target lesion revascularization at 30 days, 6 months, 12 months and annually up to 5 years follow-up
- The patient-oriented composite endpoint, which includes all-cause death, all myocardial infarction, or any revascularization at 30 days, 6 months, 12 months and annually up to 5 years follow-up
- In-stent late loss at 9 months post-procedure
- In-stent and In-segment binary restenosis rates at 9 months post-procedure
- In-stent and In-segment minimal lumen diameter at 9 months post-procedure
- Definite and probable stent thrombosis in acute, sub-acute, late and very late period per Academic Research Consortium definition criteria

Statistical Assumptions

Primary Endpoint: In-Segment Late Loss at 9 Months

Non-inferiority testing:

- One-sided alpha=0.025
- Randomization ration is 1:1
- The mean of in-segment late loss at 9 months post-procedure is assumed to be 0.39 mm for Combo stent
- The mean of in-segment late loss at 9 months post-procedure is assumed to be 0.37 mm for Nano stent
- The pooled standard deviation is assumed to be 0.45mm
- Non-inferiority margin is 0.16 mm

A sample size of 326 subjects (163 subjects per study arm) will provide approximately 80% power. Assuming a 25% loss to angiographic follow-up, approximately 436 subjects (218 subjects per study arm) will be required.

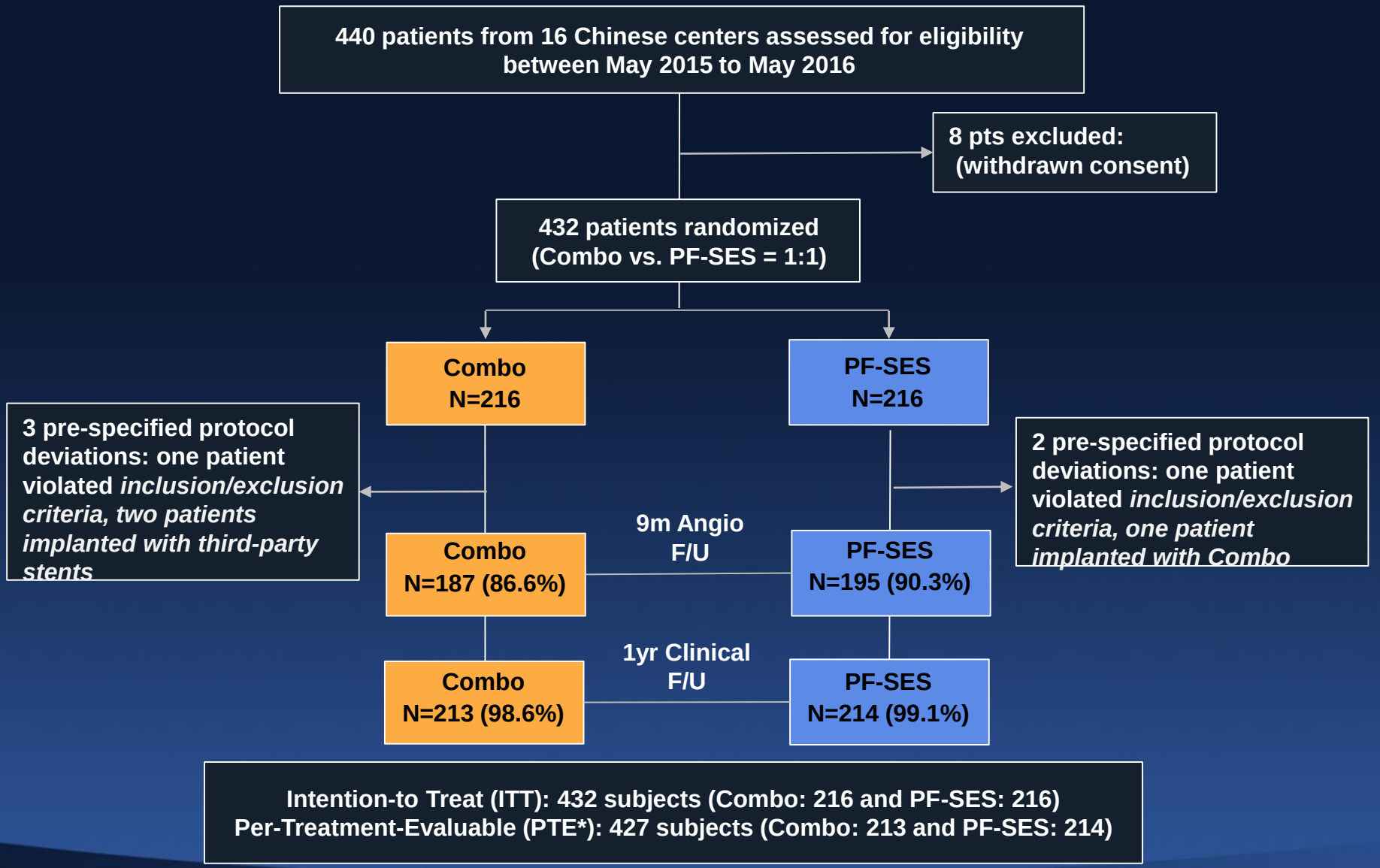
Program Organization

Principal Investigator	Ling Tao, MD
Co-Principal Investigator	Bo Xu, MBBS
Clinical Events Committee	ShuYang Zhang, MD, LiJun Kuo, MD, Jian Liu, MD
Angiographic Core Lab	CCRF, Beijing, China
Data Monitoring	
Data Management	
Statistical Analysis	Wei Li, Medical Research & Biometrics Center of National Center for Cardiovascular Disease, Beijing, China.
Sponsor	OrbusNeich Medical (Shenzhen), Co. Ltd.

Enrollers

Site PI	Hospital, City	Patients Enrolled	Site PI	Hospital, City	Patients Enrolled
Ling Tao	The First Affiliated Hospital of The Fourth Military Medical University, Xian	89	Zhanquan Li	The People Hospital of Liaoning Province, Shenyang	52
Wenhua Lin	TEDA International Cardiovascular Hospital, Tianjin	46	Yin Liu	Tianjin Chest Hospital, Tianjin	43
Hui Li	Daqing Oilfields General Hospital, Daqing	34	Bo Yu	The Second Affiliated Hospital of Harbin Medical University, Harbin	33
Ping Yang	China Japan Union Hospital of Jilin University, Changchun	23	Mian Wang	West China Hospital of Sichuan University, Chengdu	22
Zhiming Yang	The Secondary Affiliated Hospital of Shanxi Medical University, Taiyuan	22	Wen Juan Zhang	Tianjin Medical University General Hospital, Tianjing	18
JunXia Li	The Military General Hospital of Beijing PLA, Beijing	18	Lefeng Wang	Beijing Chao Yang Hospital, Beijing	17
Lixia Yang	Kunming General Hospital of Chengdu Military region, Kunming	14	ShaoLiang Chen	Nanjing First Hospital, Nanjing	6
Dongmei Wang	Bethune International Peace, Shijiazhuang	2	Chunjian Li	First Affiliated Hospital of Nanjing Medical University, Nanjing	1

Patient Flow and Follow-up



*PTE population consisted of subjects who received only study device(s) at the target lesion and who had no pre-specified protocol deviations.

Baseline Patient Characteristics

	Combo (N=216)	PF-SES (N=216)	P-Value
Age, years	58.3±9.6	59.3±8.35	0.26
Male	68.1%	63.4%	0.31
Diabetes Mellitus	19.9%	21.3%	0.72
Hypertension	53.7%	60.2%	0.17
Hyperlipidemia	12.5%	17.1%	0.17
Family History of CAD	12.5%	17.1%	0.17
Current Smoker	44.9%	43.1%	0.59
Prior Stroke	6.5%	7.9%	0.58
Peripheral Arterial Disease	0.9%	0%	0.50
Prior PCI	9.7%	9.3%	0.87
Unstable Angina	86.6%	86.1%	1.00
LVEF, %	60.0±7.5	60.2±8.0	0.75

Baseline Lesion Characteristics

	Combo (N = 216; L =245)	PF-SES (N=216; L = 249)	P-Value
Target Vessel Location			0.37
LAD	51.8%	47%	
LCX/Ramus	19.2%	24.1%	
RCA	29%	28.9%	
Number of Target Lesions per Patient	1.1±0.4	1.2±0.4	0.59
Balloon Pre-dilatation	91.8%	91.6%	0.91
Stents per Patient	1.2±0.4	1.2±0.4	0.45
Stent Diameter, mm	3.18±0.47	3.17±0.49	0.92
Total Stent Length per Patient, mm	27.7±12.1	29.2±12.2	0.19
Total Stent Length per Lesion, mm	24.4±8.0	25.35±8.2	0.21
Post-dilatation	74.3%	72.3%	0.62
Post-procedural TIMI 3 Flow	100%	99.6%	1.00

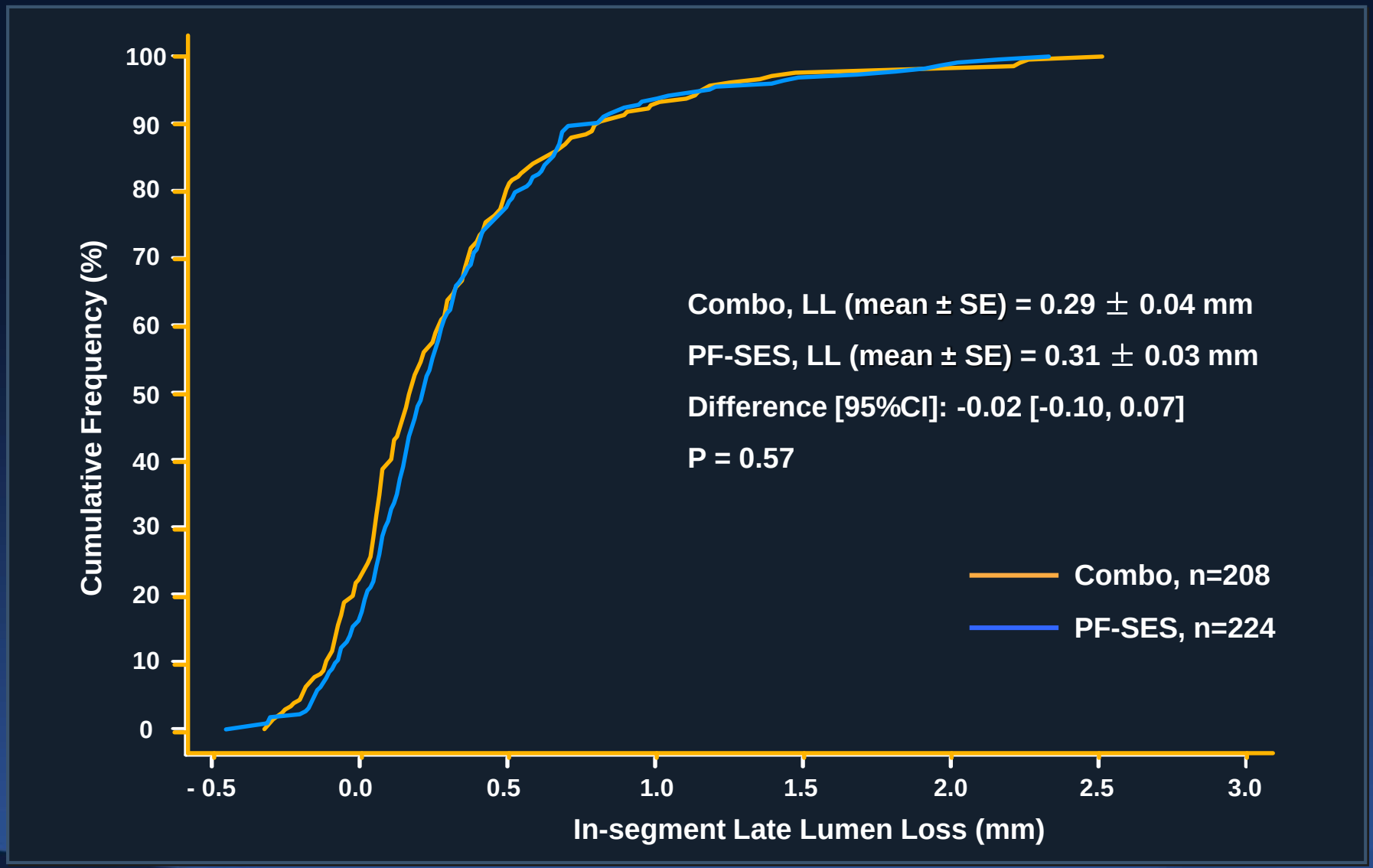
QCA and Procedural Results

	Combo (N = 216; L =245)	PF-SES (N=216; L =249)	P-Value
Pre-procedural QCA			
RVD, mm	2.89±0.52	2.89±0.50	0.87
MLD, mm	0.94±0.38	0.92±0.44	0.62
DS, %	67.7±11.6	68.4±13.4	0.53
Lesion Length, mm	16.3±7.24	17.1±7.73	0.23
Post-procedural QCA			
MLD, mm			
In-stent	2.76±0.44	2.71±0.45	0.21
In-segment	2.49±0.50	2.46±0.51	0.50
DS, %			
In-stent	6.3±5.8	7.0±5.7	0.15
In-segment	12.4±8.9	13.1±9.1	0.40
Device Success, %	99.6	99.2	1.00
Lesion Success, %	100	99.2	0.50
Clinical Success, %	97.2	94.4	0.14

Angiographic Results at 9 Months

	Combo (N = 187; L =208)	PF-SES (N=195; L = 224)	P-Value
Reference Vessel Diameter, mm	2.74±0.49	2.71±0.45	0.66
Minimum Lumen Diameter, mm			
In-Stent	2.37±0.57	2.33±0.51	0.53
In-Segment	2.20±0.57	2.15±0.51	0.37
Diameter Stenosis, %			
In-Stent	15.4±15.9	16.1±15.2	0.67
In-Segment	19.2±16.8	20.2±15.9	0.55
Binary Restenosis Rate, %			
In-Stent	5.8	4.5	0.54
In-Segment	7.2	5.4	0.43
Late Loss, mm (mean ± SD)			
In-Stent	0.39±0.45	0.38±0.43	0.88
In-Segment	0.29±0.46	0.31±0.44	0.57

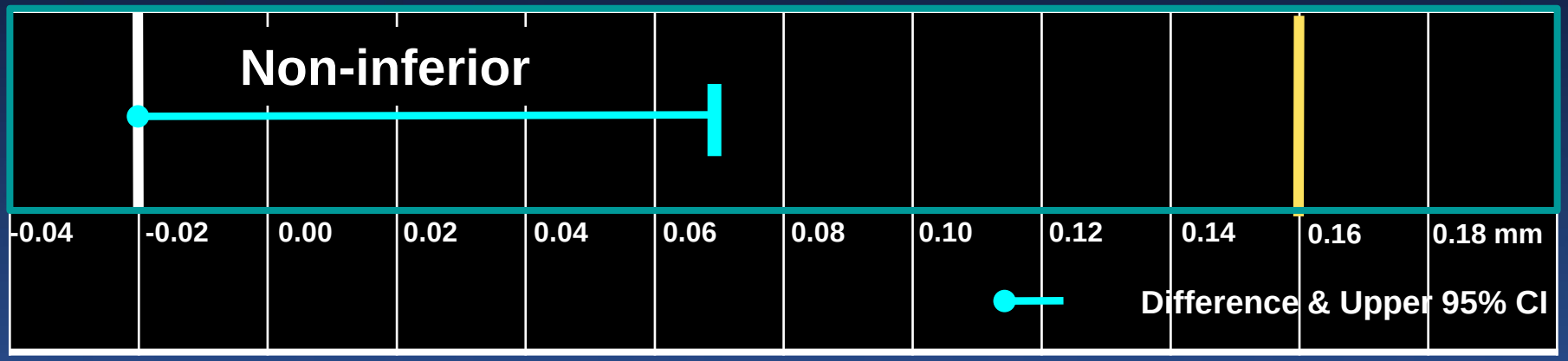
Cumulative Frequency of In-Segment LL



Primary Endpoint: In-Segment Late Loss at 9 Months

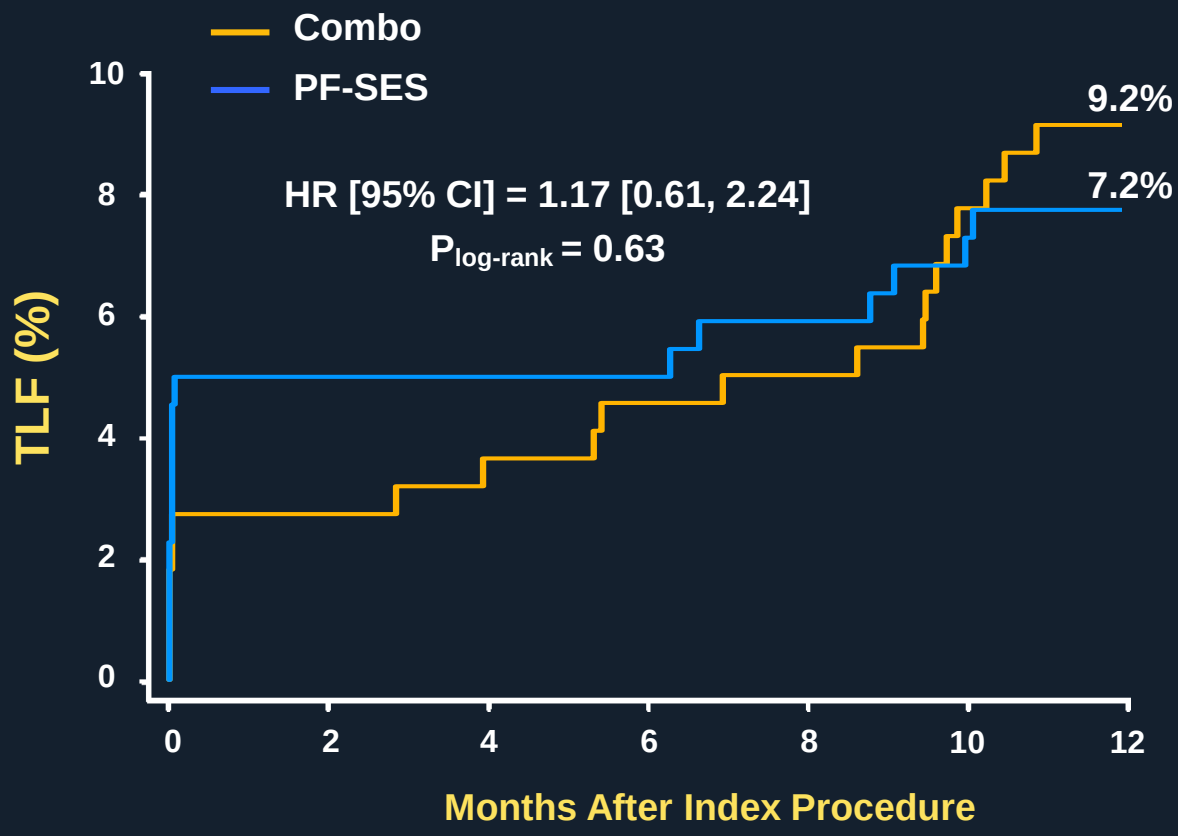
Combo (N = 208) mean ± SD 0.29 ± 0.04	PF-SES (N = 224) mean ± SD 0.31 ± 0.03	Difference : -0.02mm Upper 2-sided 95% CI: 0.07 mm	Noninferiority P =0.0001

Zone of non-inferiority
Pre-specified margin = 0.16mm



Primary Non-Inferiority Endpoint Met

Target Lesion Failure

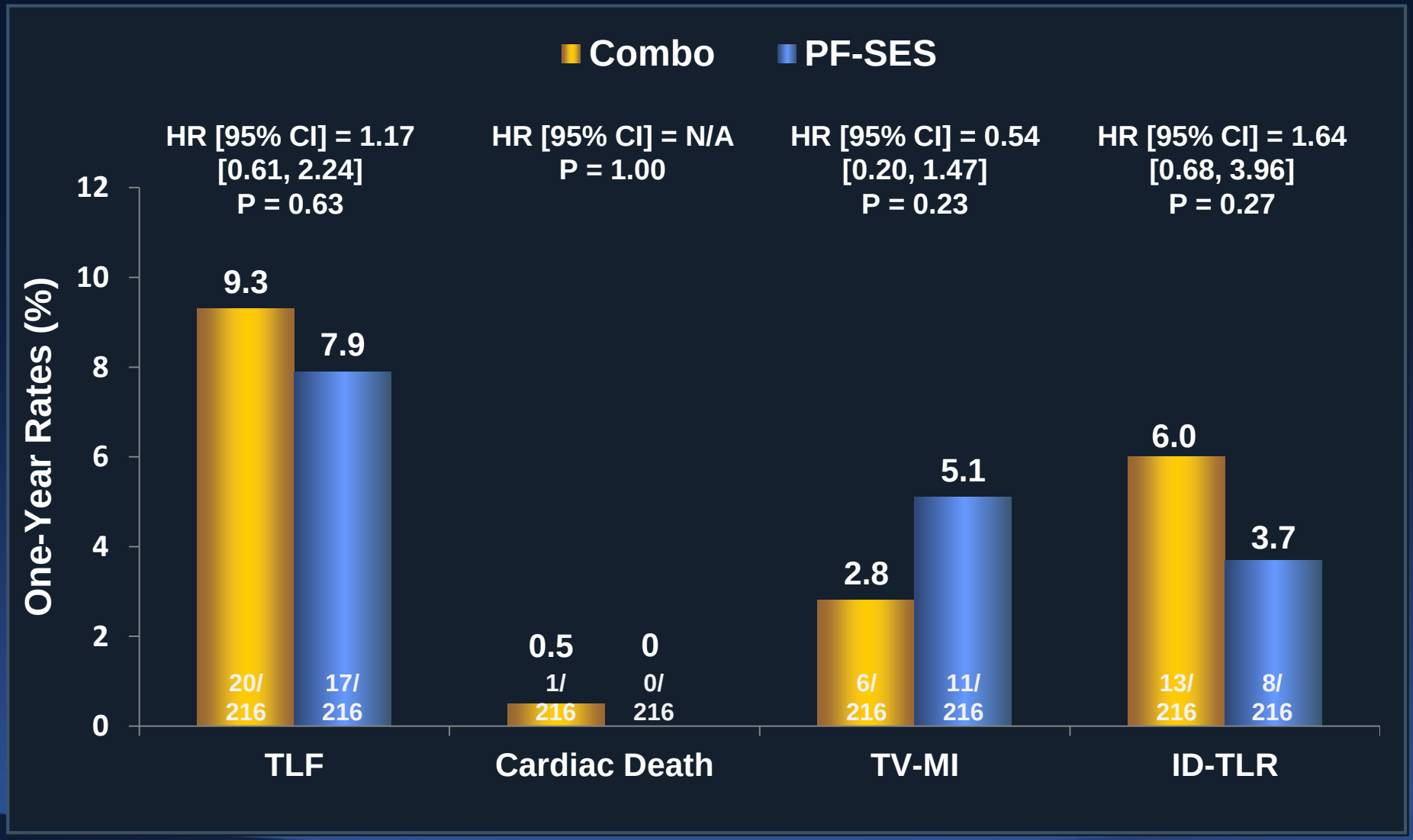


Patients at Risk:

Months	0	2	4	6	8	10	12
Combo	216	210	208	206	205	199	196
PF-SES	216	205	205	205	203	200	199

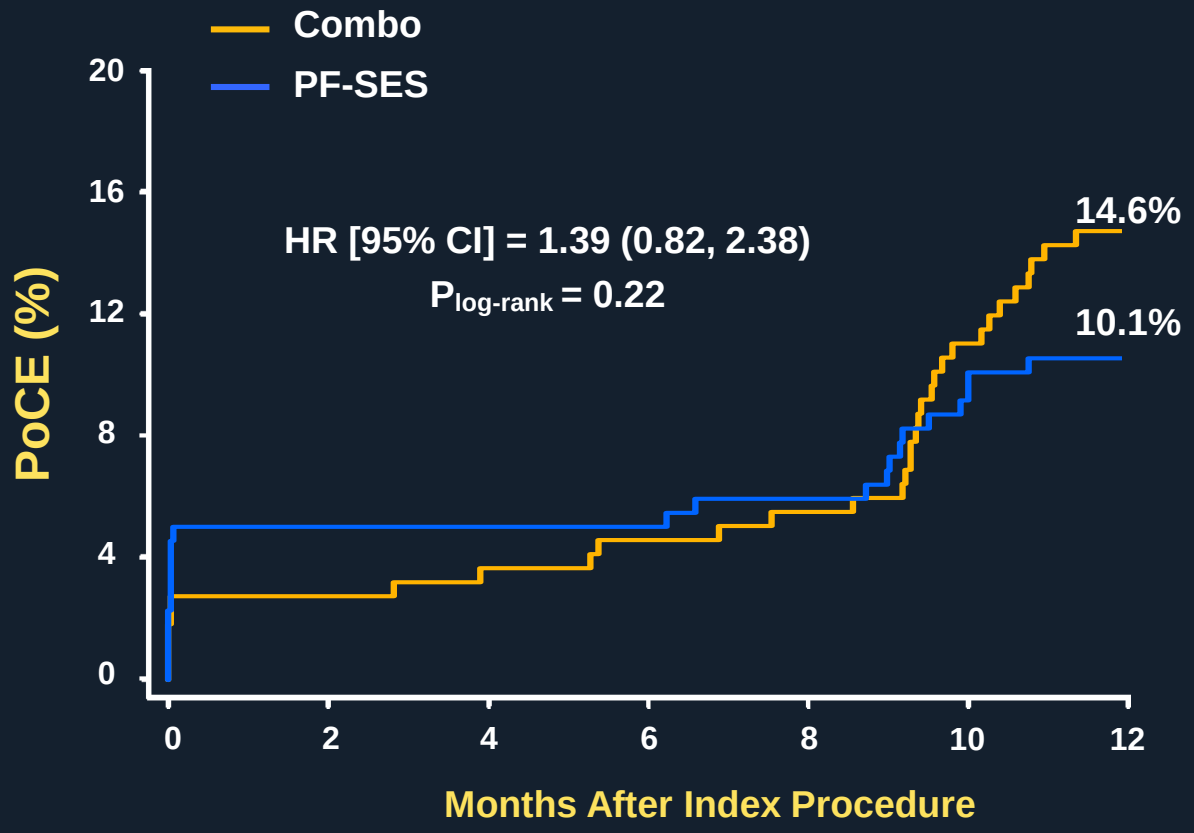
TLF – defined as a composite of cardiac death, target vessel myocardial infarction and ischemia-driven target lesion revascularization

One-Year TLF and Components



TLF – defined as a composite of cardiac death, target vessel myocardial infarction and ischemia-driven target lesion revascularization

Patient-oriented Composite Endpoint

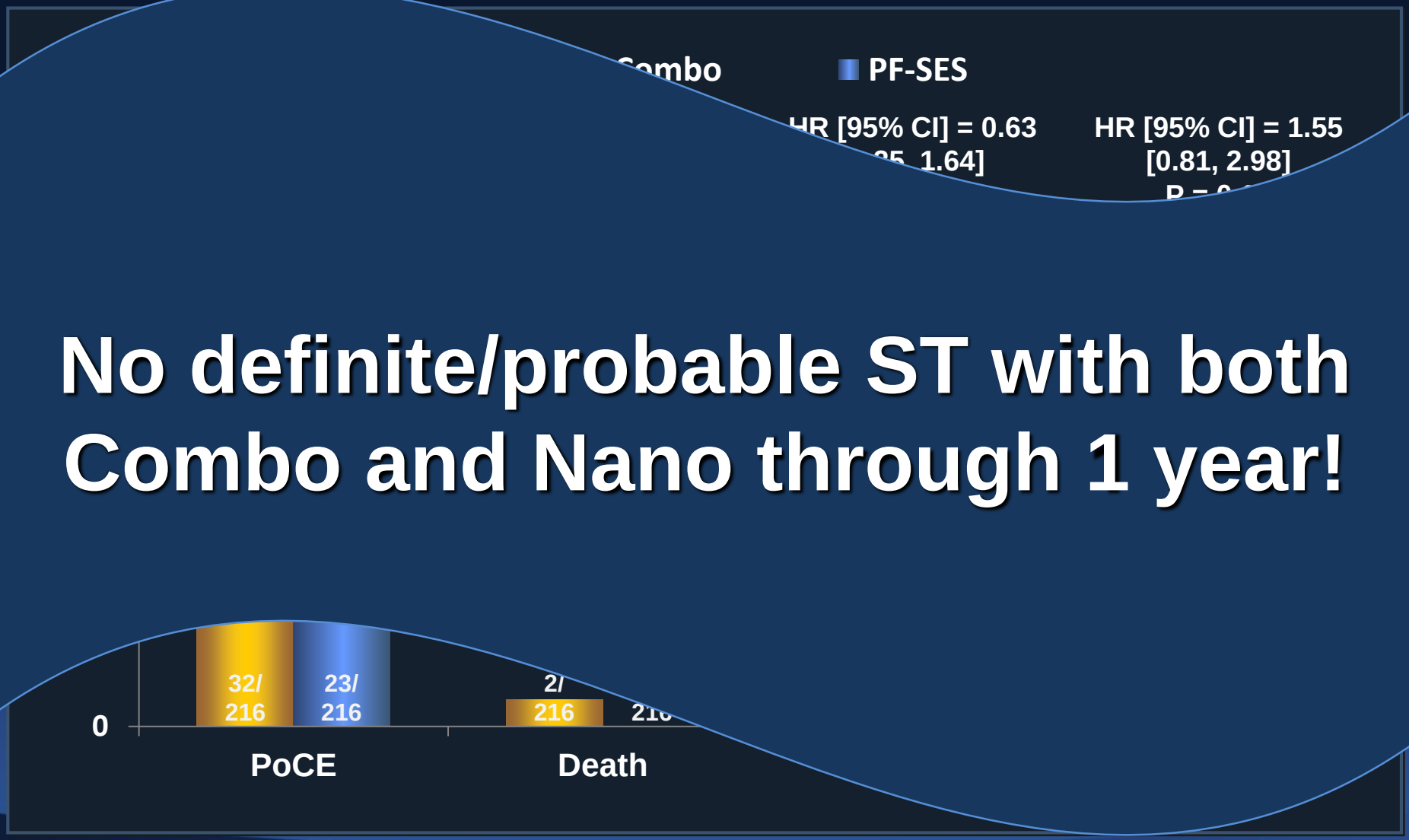


Patients at Risk:

Months	0	2	4	6	8	10	12
Combo	216	210	208	206	204	192	184
PF-SES	216	205	205	205	203	196	193

POCE - includes all-cause death, all MIs, or any revascularization

One-Year PoCE and Components



No definite/probable ST with both Combo and Nano through 1 year!

POCE - includes all-cause death, all MIs, or any revascularization

Conclusions

- The primary endpoint has been met. In the Combo group, in-segment late loss was 0.29 ± 0.46mm, which was non-inferior to that of Nano group with in-segment late loss of 0.31 ± 0.44mm.
- The safety of Combo stent has been confirmed, its efficacy has been proven again with adequate statistical power by angiographic follow-up.
- The clinical outcome of Combo is comparable to Nano with an overall low rate of clinical events in both stent groups
- No ARC definite or probable stent thrombosis was reported for both groups.

Thank You

One-Year Clinical Outcomes

	Combo N=216	PF-SES N=216	P-Value
Target Lesion Failure	9.3%	7.9%	0.61
Patient-oriented Composite Endpoint	14.8%	10.6%	0.19
All-cause Death	0.9%	0%	0.50
Cardiac Death	0.5%	0%	1.00
All MI	3.2%	5.1%	0.33
Target Vessel MI	2.8%	5.1%	0.21
Any Revascularization	10.6%	6.9%	0.17
Ischemia Driven TVR	7.4%	4.2%	0.15
Ischemia Driven TLR	6.0%	3.7%	0.26
Definite/Probable ST	0%	0%	NA

Two death cases:

- A 64 years old female subject was enrolled to the trial on 7 Jan 2016. The patient died in Nov 2016 due to traffic accident. The case was adjudicated as non-cardiac death.

- Another 57 years old male subject was enrolled to the trial in Nov 2015. Patient was admitted due to heart failure on 21 Dec 2015. Patient died due to progressive severe heart failure on 8 March 2016. The case was adjudicated as cardiac death.

  Both cases are non-target vessel related and not associated with the device.