Main Arena III, Wednesday, Oct. 14
Plenary Session XX. Late-Breaking Clinical Trials 3: Co-sponsored by JAMA

#3 LBCT- PANDA III

A Prospective Randomized Trial of Two Sirolimus-Eluting Bioresorbable-Polymer-Based Metallic Stents With Varying Elution and Absorption Kinetics

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On behalf of PANDA III Investigators

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11:42 AM-11:52 AM, Wednesday, October 14th, 2015
San Francisco, CA, USA

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Disclosure Statement of Financial Interest

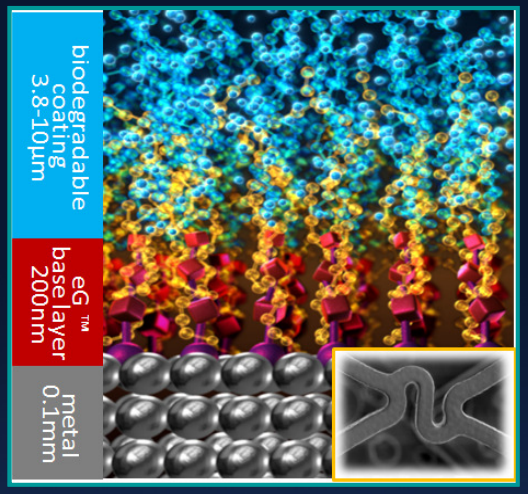
- The study was funded by a research grant from SinoMed (Tianjin, China)
- I, (Bo Xu) have no relevant conflicts of interest to disclose

Background

- Whether the rate of drug elution and polymer absorption affects clinical outcomes of biodegradable polymer-based drug-eluting stents (DES) is unknown.
- The PLGA polymer-based **BuMA** sirolimus-eluting stent (SES) has a unique design incorporating an electro-grafting (eG™) base layer between the polymer and stent strut, securing adhesion of the PLGA coating. Sirolimus is 100% eluted within 30 days, and the PLGA polymer is completely absorbed within 3 months.
- In contrast, the PLA polymer-based **Excel** SES elutes sirolimus completely within 180 days, and the PLA polymer is completely absorbed within 6-9 months.
- Both DES elute sirolimus from a stainless steel platform, isolating major differences to the polymer and elution kinetics.

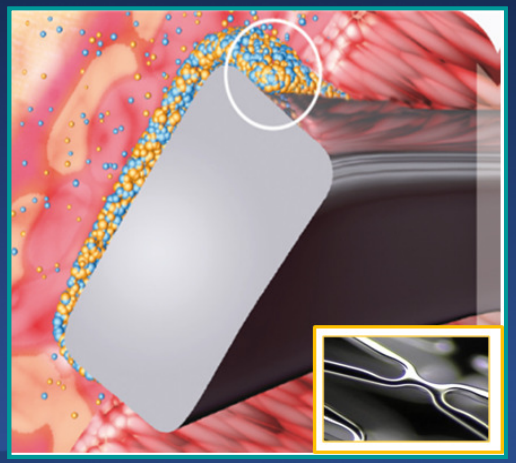
BuMA

SinoMed, Tianjin, China



Excel

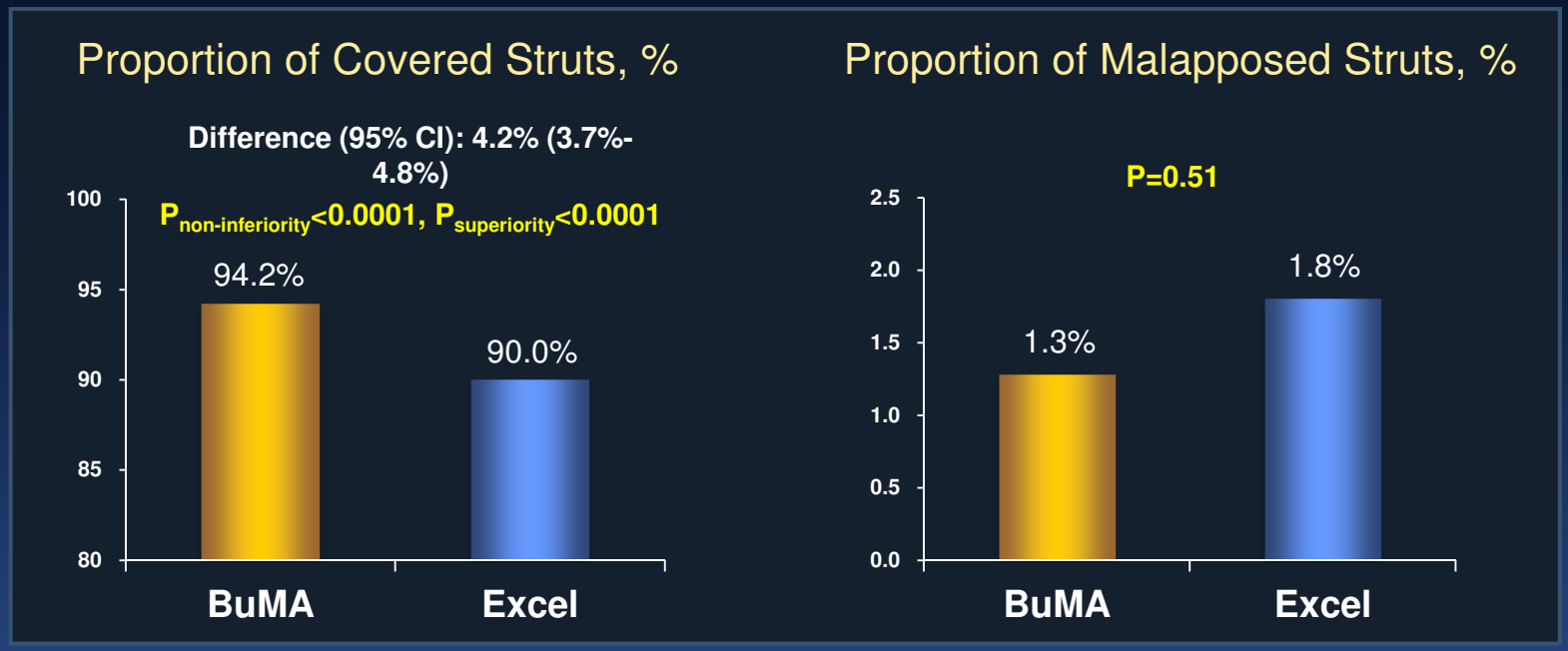
JWMS, Weihai, China



BuMA-OCT Trial

80 patients were randomly assigned to receive either BuMA (n=40) or Excel (n=40) SES

Primary Endpoint: Stent strut coverage evaluated with OCT at 3 months



The randomized BuMA-OCT trial demonstrated that the BuMA SES was superior to the Excel SES in stent strut coverage at 3-month follow-up

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Qian J et al, *EuroIntervention* 2014;10:806-814.

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Objective

We sought to determine in an "all-comers" population whether the BuMA SES is non-inferior or superior to the Excel SES for the primary endpoint of 1-year target lesion failure (TLF), the composite of cardiac death, target vessel myocardial infarction, or ischemia driven target lesion revascularization.

PANDA III (N=2,350)

Prospective, multicenter, randomized controlled trial. No lesion/vessel limitations.

Inclusion:

- Age ≥18 years
- Symptomatic CAD or silent ischemia, or ACS, and qualifies for PCI
- ≥1 coronary artery stenosis of ≥50% with visually estimated RVD ≥2.5 mm and ≤4.0 mm

Exclusion:

- Known allergy to contrast and/or device or study meds (PLA, PLGA, sirolimus, aspirin, clopidogrel, stainless steel, cobalt chromium alloy, etc.)
- Planned surgery within 6 months after the index procedure
- Participation in another investigational clinical trial that has not reached its primary endpoint

1:1 Randomization

BuMA (N=1,175)
Diameter: 2.5, 2.75, 3.0, 3.25, 3.5, 4.0mm
Length: 10, 15, 20, 25, 30, 35 mm

Excel (N=1,175)
Diameter: 2.5, 2.75, 3.0, 3.5, 4.0 mm
Length: 14, 18, 24, 28, 33, 36 mm

Primary Endpoint

1-year target lesion failure (TLF; cardiac death, TV-MI, or ID-TLR), powered for sequential non-inferiority and superiority testing

Statistical Assumptions

Primary Endpoint: Target Lesion Failure at 1 Year

For non-inferiority testing:

- Expected 1-year TLF in both groups = 8.3%
- Non-inferiority margin = 3.5%
- One-sided type I error = 0.025

2,232 patients randomized in a 1:1 ratio would yield at least 85% power to detect non-inferiority

Considering anticipated loss to follow-up of 5%, a total of 2,350 patients would need to be enrolled

For superiority testing:

- Expected 1-year TLF in Excel group = 8.3%, BuMA group = 5.3%
- One-sided type I error = 0.025

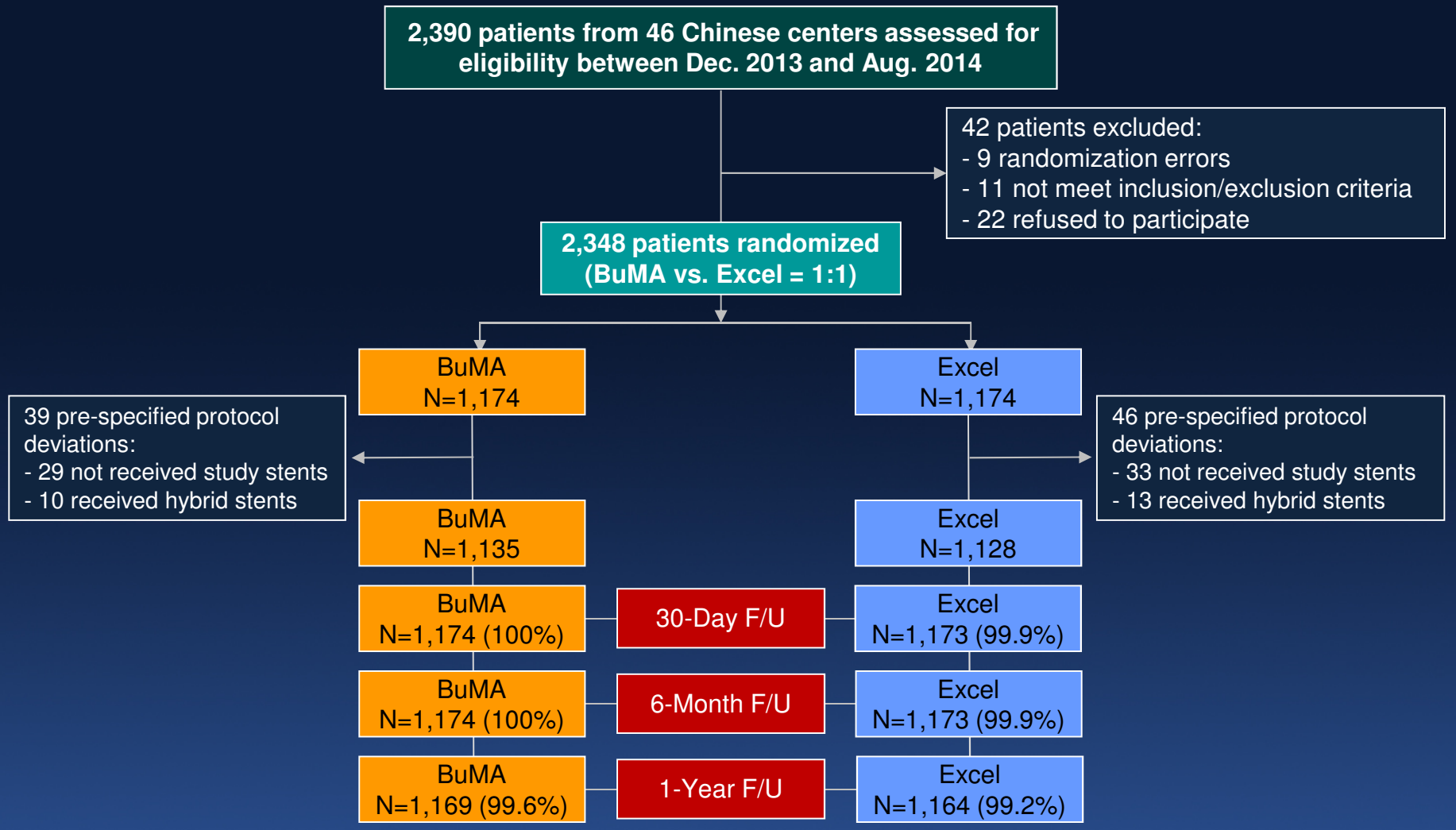
2,232 patients randomized in a 1:1 ratio would yield at least 80% power to detect superiority of BuMA over Excel

Considering anticipated loss to follow-up of 5%, a total of 2,350 patients would need to be enrolled

Study Organization

Principal Investigator	Runlin Gao, MD
Co-Principal Investigator	Bo Xu, MBBS
Clinical Events Committee	Shaoping Nie, MD (Chair); Li Xu, MD; Xin Qi, MD; Jun Guo, MD; Peng Qu, MD
Angiographic Core Lab	CCRF, Beijing, China
Statistical Analysis	
Data Management	R&G, Beijing, China
Data Monitoring	
Sponsor	SinoMed, Tianjin, China

Patient Flow and Follow-up



Intention-to-Treat (ITT): 2,348 subjects (BuMA: 1,174 and Excel: 1,174)
Per-Treatment-Evaluable (PTE*): 2,263 subjects (BuMA: 1,135 and Excel: 1,128)

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

Top 20 Enrollers

Site PI	Hospital, City	Patients Enrolled	Site PI	Hospital, City	Patients Enrolled
Yuejin Yang	Fu Wai Hospital, National Center for Cardiovascular Diseases, Beijing	434	Chun Xiao	Huizhou No. 3 People's Hospital	63
Xuebin Cao	Chinese PLA 252 Hospital, Baoding	124	Xinhu Lu	Shijiazhuang No.1 People's Hospital	61
Lei Qin	Kaifeng Central Hospital, Kaifeng	120	Fuyuan Liu	Xiangyang No.1 People's Hospital	60
Yi Li	Yunnan St. John's Hospital, Kunming	108	He Hang	Xiangtan Central Hospital, Xiangtan	60
Zhanquan Li	Liaoning Provincial People's Hospital, Shenyang	108	Xi Su	Wuhan Asia Heart Hospital, Wuhan	60
Xueqi Li	Fourth Affiliated Hospital of Haerbin Medical University, Haerbin	96	Bin Liu	The 2nd Hospital of Jilin University, Changchun	57
Hailong Lin	Dalian Municipal Central Hospital Affillated	92	Qingmin Wei	Xingtai People's Hospital, Xingtai	52
Yong Guo	Dazhou Central Hospital, Dazhou	84	Jianjun Peng	Beijing Shijitan Hospital, Beijing	50
Yitong Ma	The First Affiliated Hospital of Xinjiang Medical University	81	Hao Zhang	North Hospital, Baotou	47
Jian'an Wang	Affiliated 2nd Hospital of Zhejiang University School of Medicine, Hangzhou	68	Kefei Dou	Qingdao Fu Wai Hospital, Qingdao	44

Baseline Patient Characteristics (1)

	BuMA (N=1174)	Excel (N=1174)	P-Value
Age, years	60.8 ± 10.6	61.5 ± 10.6	0.11
Male	70.5%	70.7%	0.93
Body Mass Index, kg/m^2	24.9 ± 3.4	24.9 ± 3.3	1.00
Diabetes Mellitus	23.4%	25.1%	0.34
Insulin-requiring	5.9%	7.3%	0.16
Hypertension	61.7%	61.6%	0.97
Hyperlipidemia	31.4%	31.0%	0.86
Family History of CAD	5.3%	4.7%	0.51
Smoking History			0.39
Current Smoker	37.2%	37.7%	
Ex-smoker	11.9%	13.6%	
None	50.9%	48.7%	

Baseline Patient Characteristics (2)

	BuMA (N=1174)	Excel (N=1174)	P-Value
Prior Stroke	11.0%	11.8%	0.52
Peripheral Arterial Disease	3.1%	3.0%	0.90
Prior PCI	10.4%	13.6%	0.02
Prior CABG	0.3%	0.3%	1.00
STEMI	14.5%	16.4%	0.21
NSTEMI	16.7%	14.8%	0.21
Unstable Angina	49.2%	52.2%	0.15
Stable Angina	15.5%	14.0%	0.29
Silent Ischemia	4.1%	2.6%	0.05
LVEF, %	59.2 ± 9.1	59.4 ± 8.8	0.56

Baseline Lesion Characteristics

	BuMA (N=1174, L=1605)	Excel (N=1174, L=1572)	P-Value
Baseline SYNTAX Score	15.6 ± 9.4	15.9 ± 9.6	0.45
Target Vessel Location			
LM	1.3%	1.5%	0.60
LAD	45.4%	45.7%	0.89
LCX/Ramus	21.3%	20.6%	0.63
RCA	32.0%	32.3%	0.89
Number of Target Lesions per Patient	1.37 ± 0.62	1.34 ± 0.58	0.40
ACC/AHA Class B2/C Lesions	82.6%	82.4%	0.90
Bifurcation Lesion	34.3%	35.5%	0.49
Ostial Lesion	3.7%	4.3%	0.35
Total Occlusion	13.1%	13.9%	0.52
Severely Tortuous or Angulated Lesion	1.3%	1.1%	0.56
Moderate to Heavy Calcification	5.4%	5.0%	0.67

Procedural Information

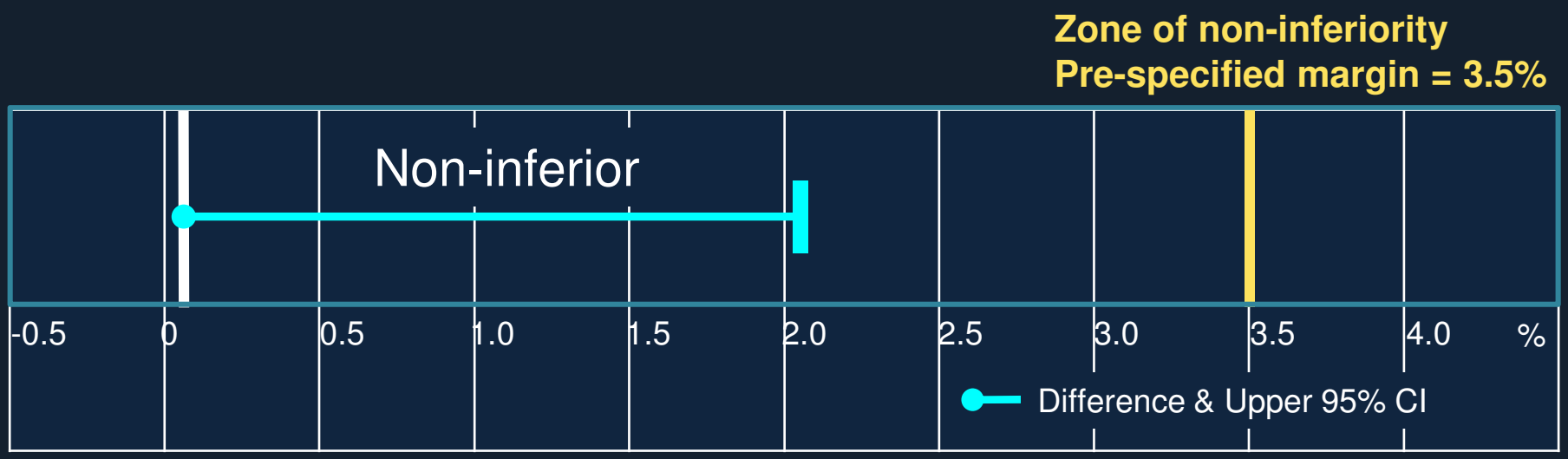
	BuMA (N=1174, L=1605)	Excel (N=1174, L=1572)	P-Value
Transradial Approach	95.2%	95.7%	0.62
Balloon Pre-dilatation	89.2%	90.5%	0.20
Stents per Patient	1.74 ± 0.96	1.70 ± 0.90	0.34
Stents per Lesion	1.27 ± 0.54	1.27 ± 0.52	0.97
Stent Diameter, mm	3.03 ± 0.43	3.02 ± 0.42	0.55
Total Stent Length per Patient, mm	42.6 ± 26.6	42.0 ± 25.4	0.60
Total Stent Length per Lesion, mm	31.2 ± 17.8	31.4 ± 17.0	0.71
Post-dilatation	52.9%	50.1%	0.11
Post-procedural TIMI 3 Flow	98.8%	98.6%	0.59

QCA and Procedural Results

	BuMA (N=1174, L=1605)	Excel (N=1174, L=1572)	P-Value
Pre-procedural QCA			
RVD, mm	2.75 ± 0.47	2.76 ± 0.45	0.79
MLD, mm	0.70 ± 0.48	0.70 ± 0.48	0.66
DS, %	74.8 ± 16.1	75.0 ± 16.3	0.63
Lesion Length, mm	19.7 ± 12.1	19.8 ± 12.1	0.86
Post-procedural QCA			
MLD, mm			
In-stent	2.55 ± 0.43	2.57 ± 0.40	0.08
In-segment	2.31 ± 0.47	2.32 ± 0.46	0.55
DS, %			
In-stent	8.8 ± 5.9	8.4 ± 5.8	0.05
In-segment	14.5 ± 9.3	14.7 ± 9.9	0.64
Residual SYNTAX Score	4.79 ± 5.88	4.99 ± 5.68	0.40
Device Success	99.8%	99.95%	0.22
Lesion Success	98.8%	98.6%	0.59
Procedure Success	95.1%	94.7%	0.64

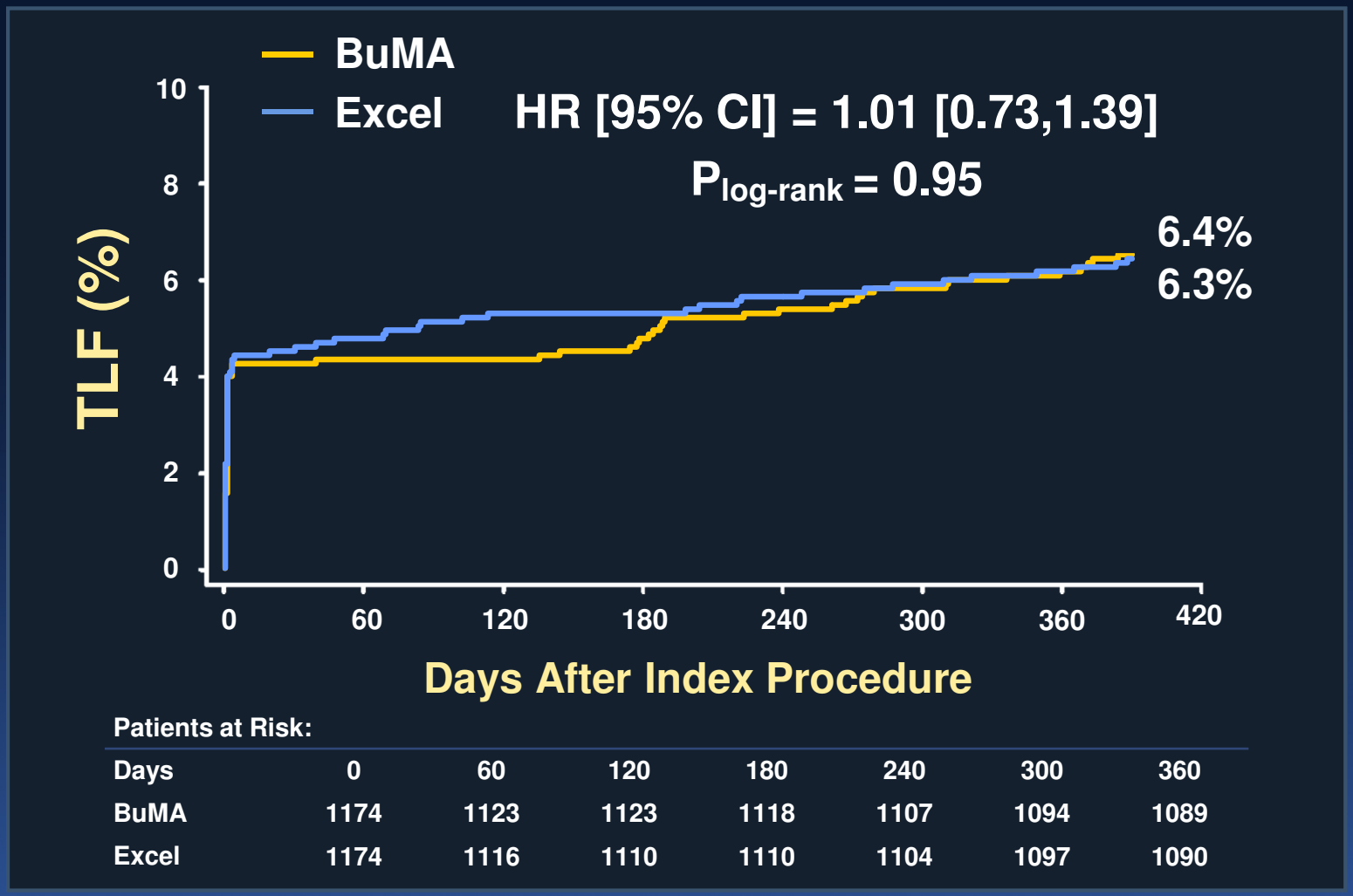
Primary Endpoint:
Target Lesion Failure at 1 Year

BuMA (N = 1169) 6.4%	Excel (N = 1164) 6.4%	Difference: 0.06% Upper 2-sided 95% CI: 2.04%	Non-inferiority P value = 0.0003



Primary Non-inferiority Endpoint Met

Target Lesion Failure

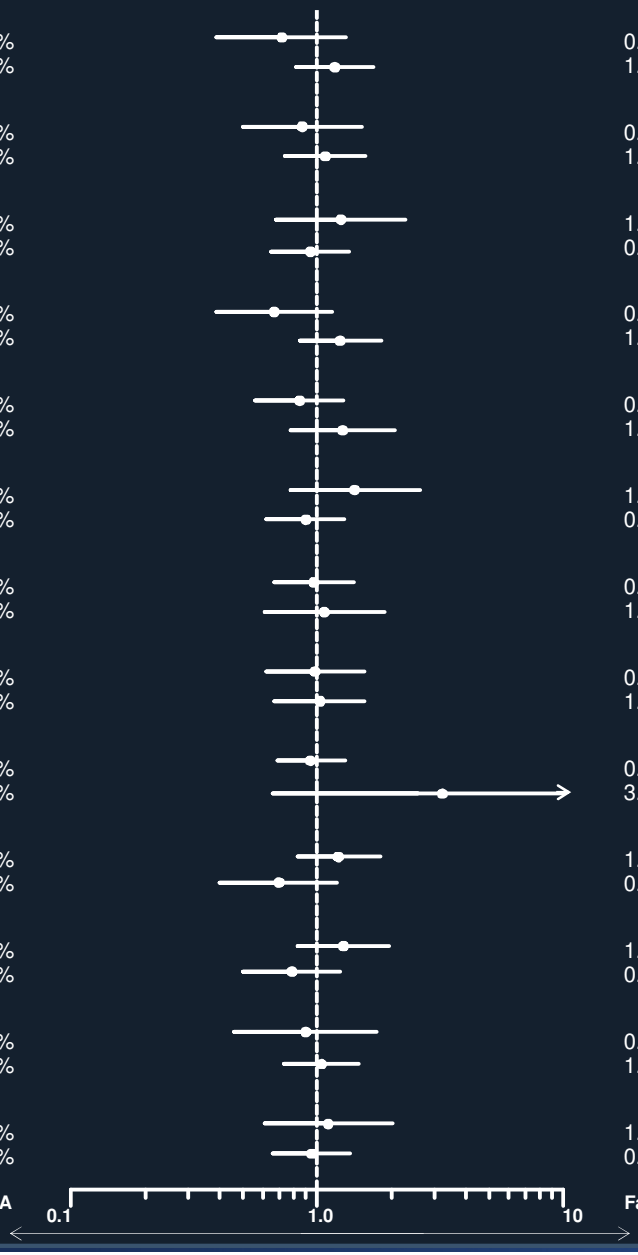


Patients at Risk:

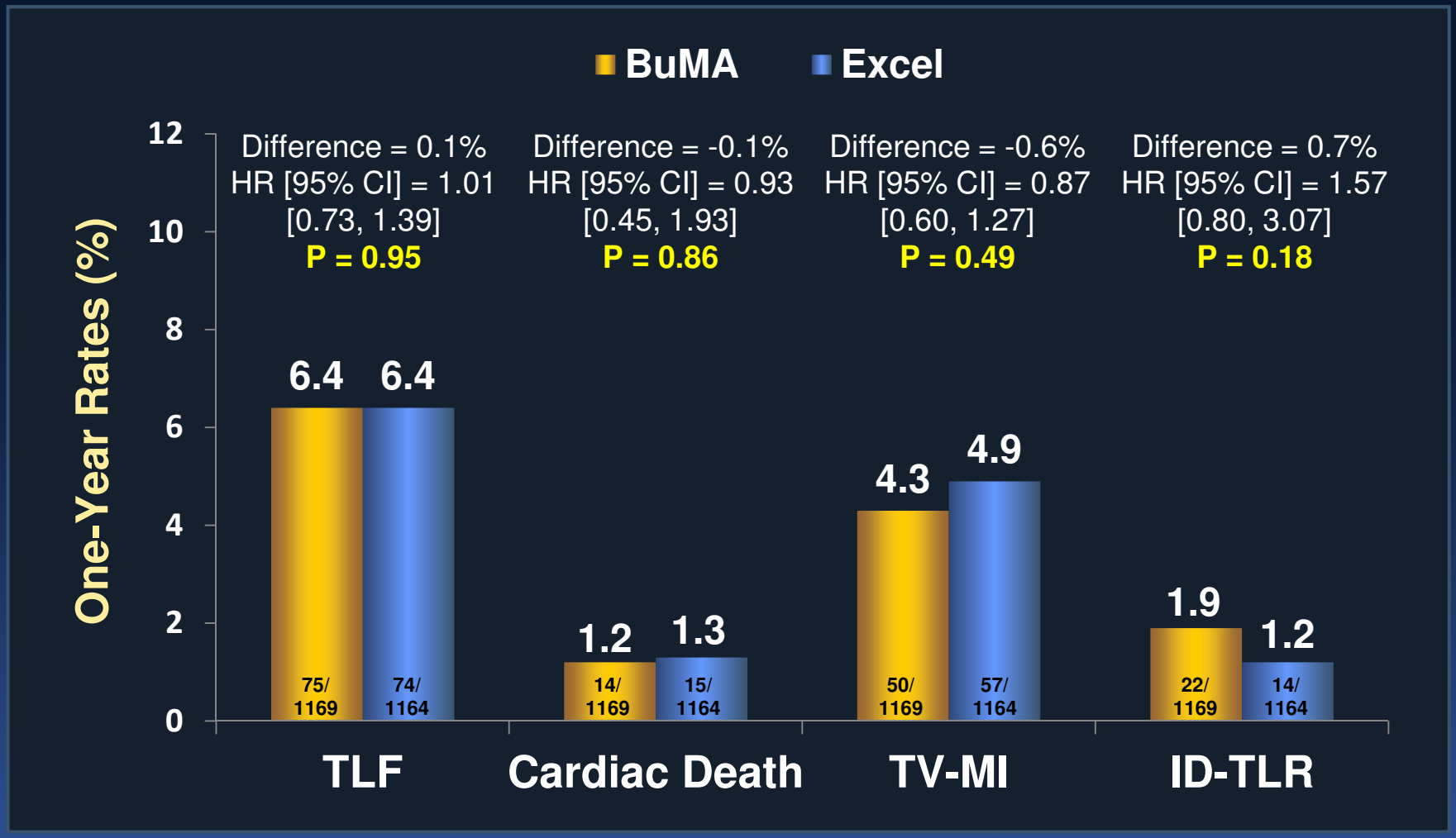
Days	0	60	120	180	240	300	360
BuMA	1174	1123	1123	1118	1107	1094	1089
Excel	1174	1116	1110	1110	1104	1097	1090

Subgroup Analyses of 1-Year TLF

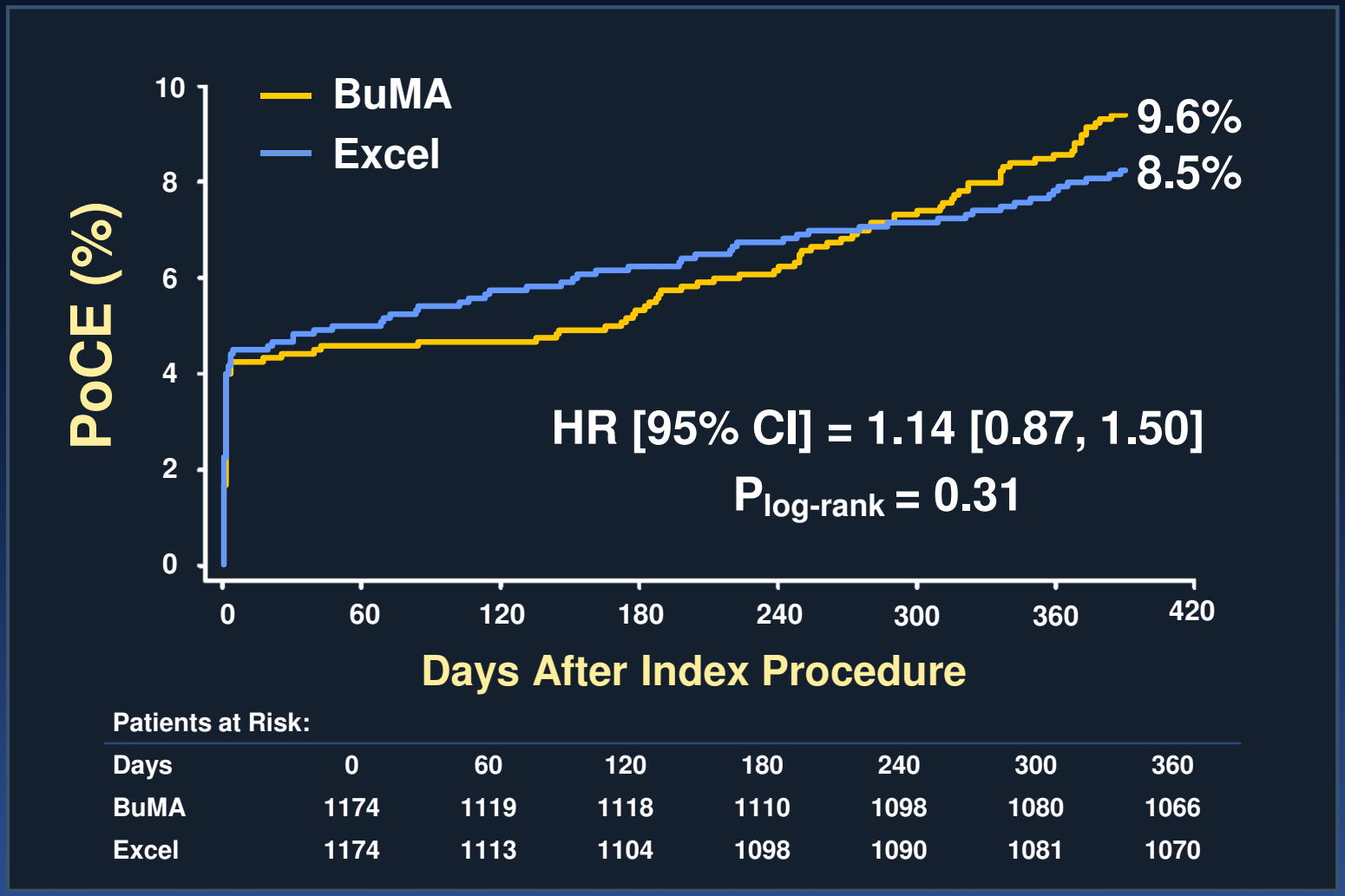
	Target Lesion Failure, %		Relative Risk (95% CI)	P-Value for Interaction
	BuMA, N=1169	Excel, N=1164		
Age				
<61 years	3.3%	4.5%	0.72 (0.39-1.31)	0.17
≥61 years	9.3%	7.9%	1.18 (0.82-1.69)	
Sex				
Female	6.4%	7.3%	0.87 (0.50-1.52)	0.54
Male	6.4%	6.0%	1.08 (0.74-1.57)	
Diabetes				
Present	7.7%	6.1%	1.25 (0.68-2.29)	0.43
Absent	6.0%	6.4%	0.94 (0.65-1.35)	
AMI				
Present	5.5%	8.3%	0.67 (0.39-1.15)	0.07
Absent	6.8%	5.5%	1.24 (0.85-1.82)	
Number of target lesions				
1	4.9%	5.8%	0.85 (0.56-1.28)	0.21
≥2	9.9%	7.8%	1.27 (0.78-2.07)	
SYNTAX Score				
<14	4.4%	3.1%	1.42 (0.78-2.61)	0.20
≥14	8.3%	9.2%	0.90 (0.62-1.29)	
Reference vessel diameter				
<2.71 mm	7.9%	8.1%	0.97 (0.67-1.41)	0.77
≥2.71 mm	4.6%	4.3%	1.07 (0.61-1.87)	
Lesion length				
<16.4 mm	6.6%	6.7%	0.98 (0.62-1.56)	0.89
≥16.4 mm	6.3%	6.2%	1.03 (0.67-1.56)	
ACC/AHA lesion class				
B2/C	6.7%	7.1%	0.94 (0.69-1.30)	0.14
A/B1	4.2%	1.3%	3.23 (0.66-15.7)	
LAD lesion				
Yes	8.0%	6.6%	1.22 (0.83-1.80)	0.10
No	4.2%	6.1%	0.70 (0.40-1.20)	
Bifurcation lesion				
Yes	8.8%	6.8%	1.28 (0.83-1.97)	0.13
No	4.7%	6.0%	0.79 (0.50-1.24)	
Total occlusion				
Yes	7.4%	8.3%	0.90 (0.46-1.74)	0.69
No	6.2%	5.9%	1.04 (0.73-1.48)	
Total stent length per patient				
<35 mm	4.0%	3.6%	1.11 (0.61-2.02)	0.65
≥35 mm	8.5%	9.0%	0.95 (0.66-1.36)	



One-Year TLF and Components



Patient-oriented Composite Endpoint*

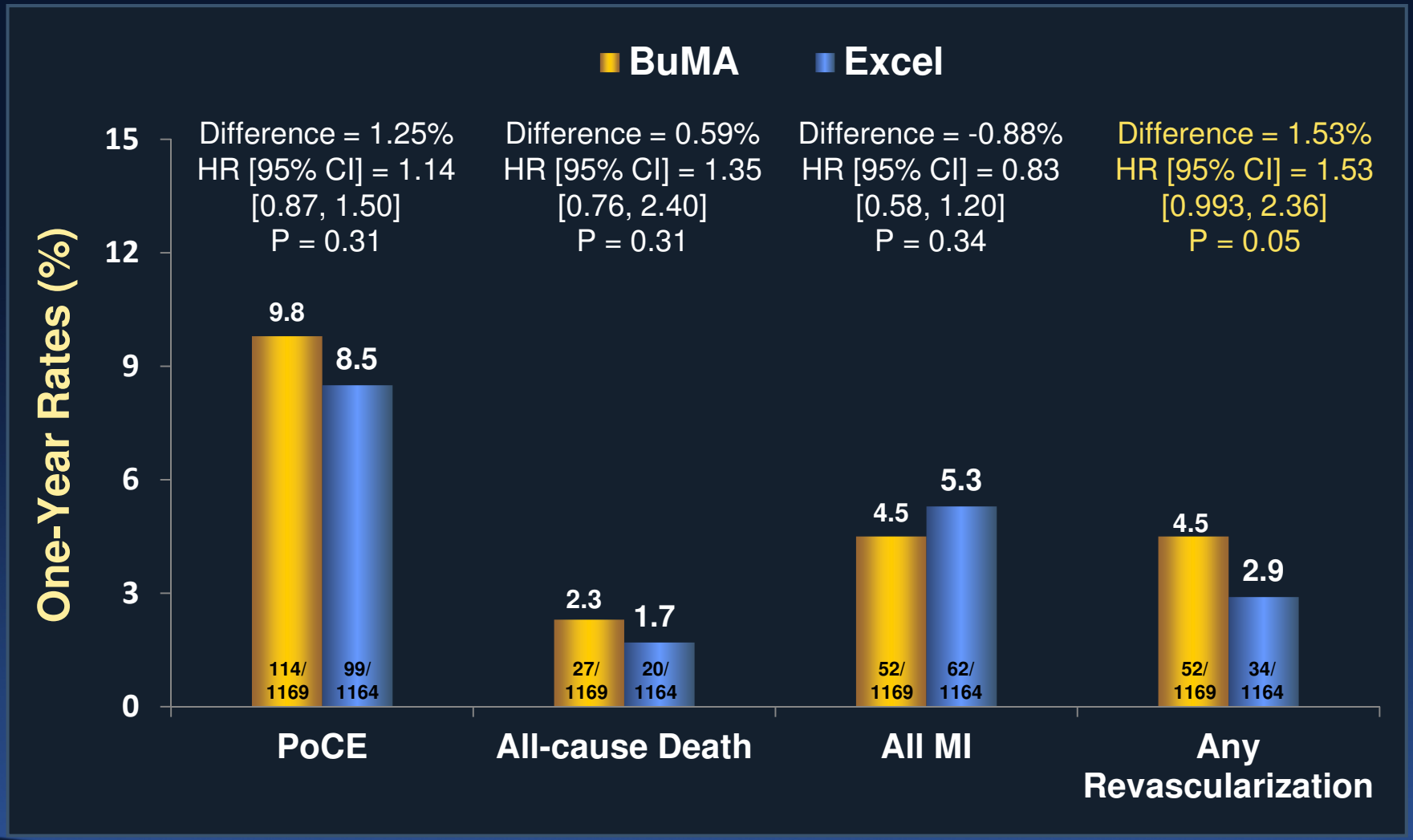


Patients at Risk:

Days	0	60	120	180	240	300	360
BuMA	1174	1119	1118	1110	1098	1080	1066
Excel	1174	1113	1104	1098	1090	1081	1070

*Death, MI, or any revascularization

One-Year PoCE and Components



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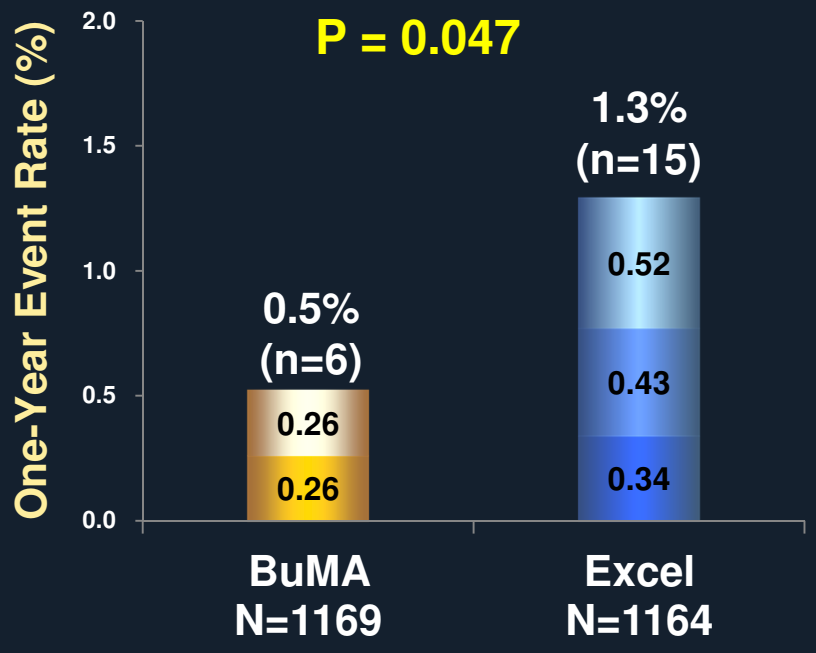
One-Year Definite/Probable Stent Thrombosis

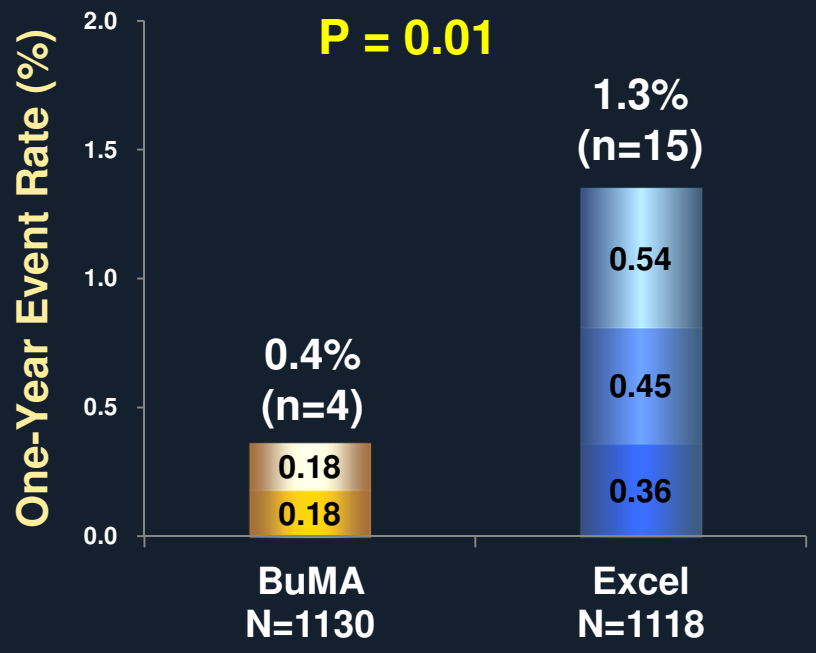
ITT

- Acute ST (0-1 day) n=3
- Subacute ST (2-30 days) n=0
- Late ST (31-365 days) n=3
- Acute ST (0-1 day) n=4
- Subacute ST (2-30 days) n=5
- Late ST (31-365 days) n=6



PTE

- Acute ST (0-1 day) n=2
- Subacute ST (2-30 days) n=0
- Late ST (31-365 days) n=2
- Acute ST (0-1 day) n=4
- Subacute ST (2-30 days) n=5
- Late ST (31-365 days) n=6



Limitations

- Some element of selective enrollment and selection bias cannot be ruled out
- Low proportion of enrolled pts with stable CAD
- The study was not powered adequately to evaluate low frequency safety endpoints such as stent thrombosis
- The modified ARC definition of peri-procedural MI may overestimate the occurrence of TV-MI
- Longer-term follow-up is required

Conclusions

- In the multicenter randomized PANDA III trial, the BuMA SES was non-inferior to the Excel SES for the primary endpoint of TLF at 1 year
- The PLGA polymer-based BuMA (with eG™ base layer) SES was associated with a lower incidence of stent thrombosis compared to the PLA polymer-based Excel SES, consistent with the previous findings of enhanced strut coverage with this device

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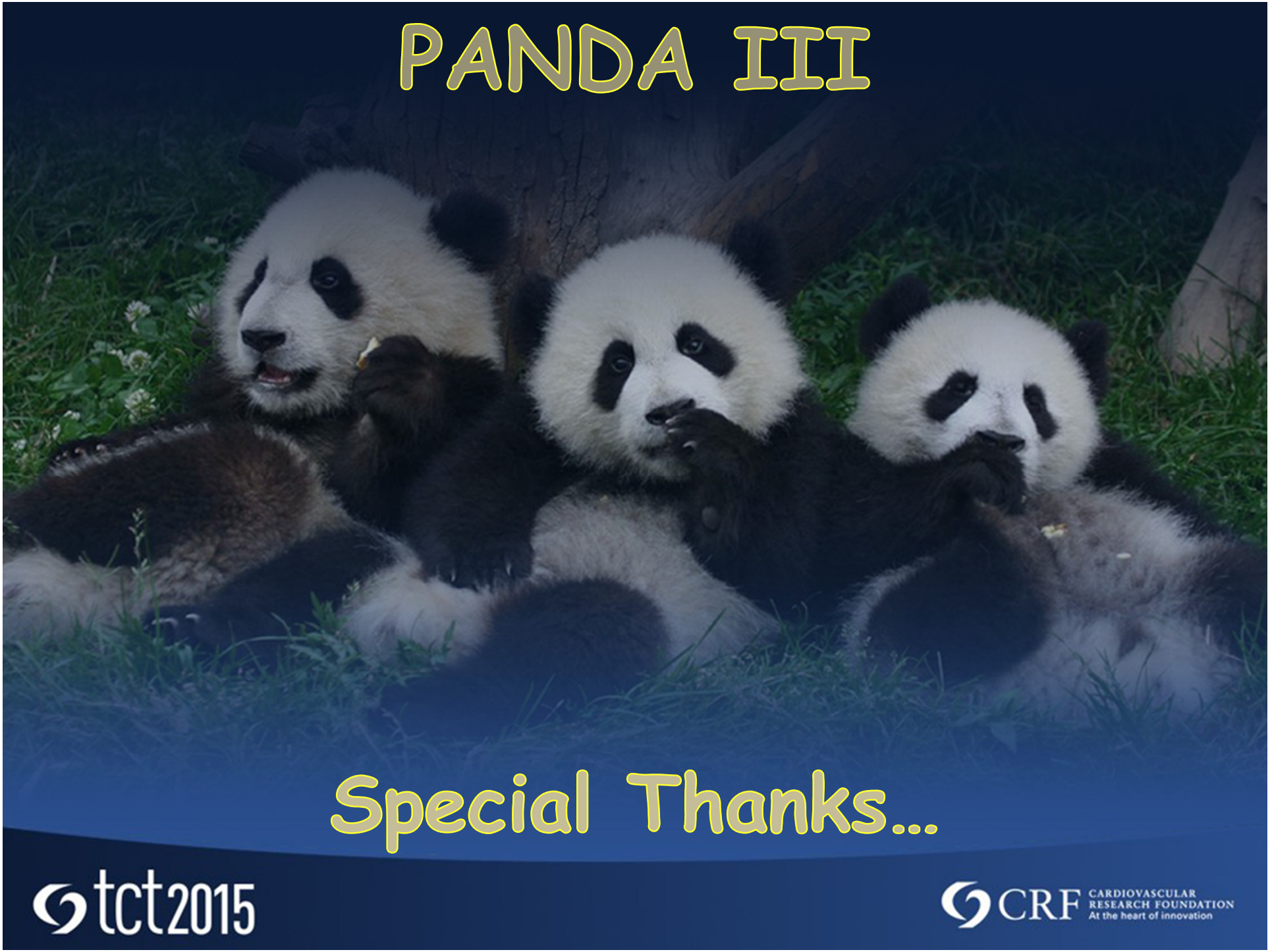

Special Thanks…

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