CONGRESO PARAGUAYO DE CARDIOLOGIA

SIMPOSIO SOLACI

Procedimientos intervencionistas percutáneos en el 2015. Puesta al dia.

MARCO ANTONIO PERIN

Hospital I. Albert Einstein
Sao Paulo, Brasil

Futuro da Cardiologia Intervencionista

- Intervenções Coronárias:
- Balão Farmacológico
- Stents Farmacológicos de 2ª geração

  Stents bioabsorvíveis

- Intervenções estruturais:

  Estenose Aórtica

  Insuf. Mitral

  Leak paravalvar

  Defeitos congênitos

  Denervação renal

Cardiologia Intervencionista

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  Defeitos congênitos
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BALÃO FARMACOLÓGICO

QUANDO E COMO UTILIZAR

MARCO ANTONIO PERIN
HIAE; HSM;H9J

BALÃO FARMACOLÓGICO
MECANISMO DE AÇÃO

- Nos ultimos anos , o balão farmacológico surgiu como uma alternativa no tratamento da reestenose intrastent
- Balões farmacológicos são balões convêncionais recobertos com uma droga anti-proliferativa de liberação local (lesão)
- Após a expansão do balão, a droga é liberada na parede do vaso atingindo uma concentração mínima para reduzir a proliferação de celulas muscular lisa, reduzindo assim a reestenose

BALÃO FARMACOLÓGICO

COMO UTILIZAR

1. PRE-DILATATION

- Required for all lesions, prior to DCB procedure
- Standard PTA 1 mm less than reference vessel diameter (RVD)
- Balloon length should not be greater than the planned DCB length

2. ATHERECTOMY

- Recommended in severely calcified lesions

3. DRUG-COATED BALLOON

- DCB diameter:RVD = 1:1; length 1 cm beyond lesion on both ends
- Inflation time ≥ **1 minute**
- Inflation pressure < RBP as required to reach full DCB expansion

BALÃO FARMACOLÓGICO

QUANDO UTILIZAR

- REESTENOSE INTRASTENT
- VASOS DE PEQUENO DIAMETRO
- LESÕES DE BIFURCAÇÃO
- AREAS DE DIFICIL TRATAMENTO (Ca+ ; tortuosidade)

Conduta na Reestenose Intrastent

- STENTS CONVECIONAIS (BMS)
- STENTS FARMACOLÓGICOS (DES)

- **Balão**
- **Balão Farmacológico**
- **Stent Farmacológico**

BMS-ISR: DCB vs Angioplasty

PACCOCATH ISR: Study Design

52 Patients with single in-stent restenosis in a coronary artery with a diameter stenosis of ≥ 70%, < 25mm length, and vessel diameter of 2.5 mm to 3.5 mm; stable or unstable angina or a positive functional study.

Randomized. Double-Blind. Parallel.

29% female, mean age 64 years, mean follow-up: 12 months

Paclitaxel-Eluting Balloon Catheter (3 µg paclitaxel/mm^2)
n=26

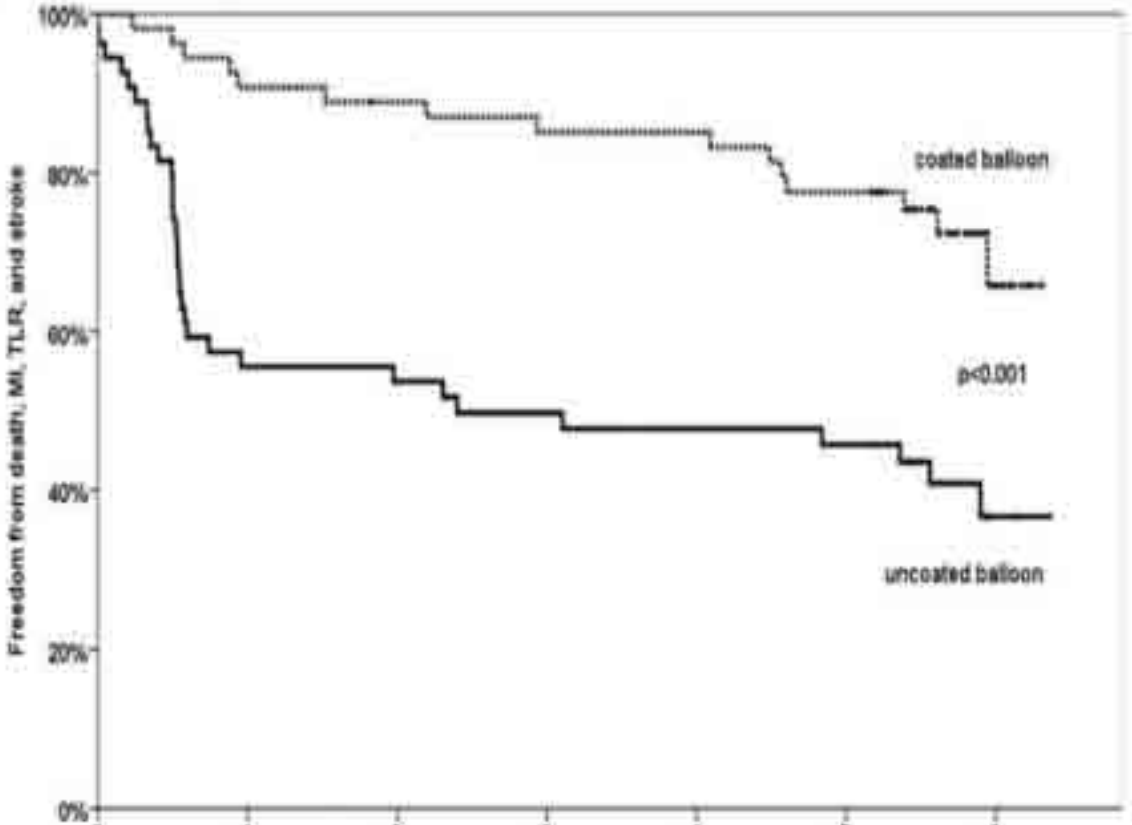
Non-Eluting Balloon Catheter
(same balloon design without drug)
n=26

- Primary Endpoint: Angiographic late lumen loss at 6 months
- Secondary Endpoint: Rates of restenosis; major adverse cardiac events (MACE)

Scheller et al. *N Engl J Med* 2006

PACCOCATH ISR : 5-year Results

Death, myocardial infarction, TLR and Stroke



No. at risk							
Uncoated balloon	54	31	30	27	26	25	22
Coated balloon	54	49	48	46	46	42	39

Scheller et al. *JACC Cardiovasc Interv* 2012

BMS-ISR: DCB vs DES

PEPCAD II ISR Study: Study Design

131 patients ≥ 18 years eligible for coronary revascularization for instent restenosis by means of PCI

R

SeQuent™ Please	Taxus
Drug Eluting Balloon Catheter	Drug Eluting Stent
n=66	n=65

6 month, 1 and 3 year follow-ups

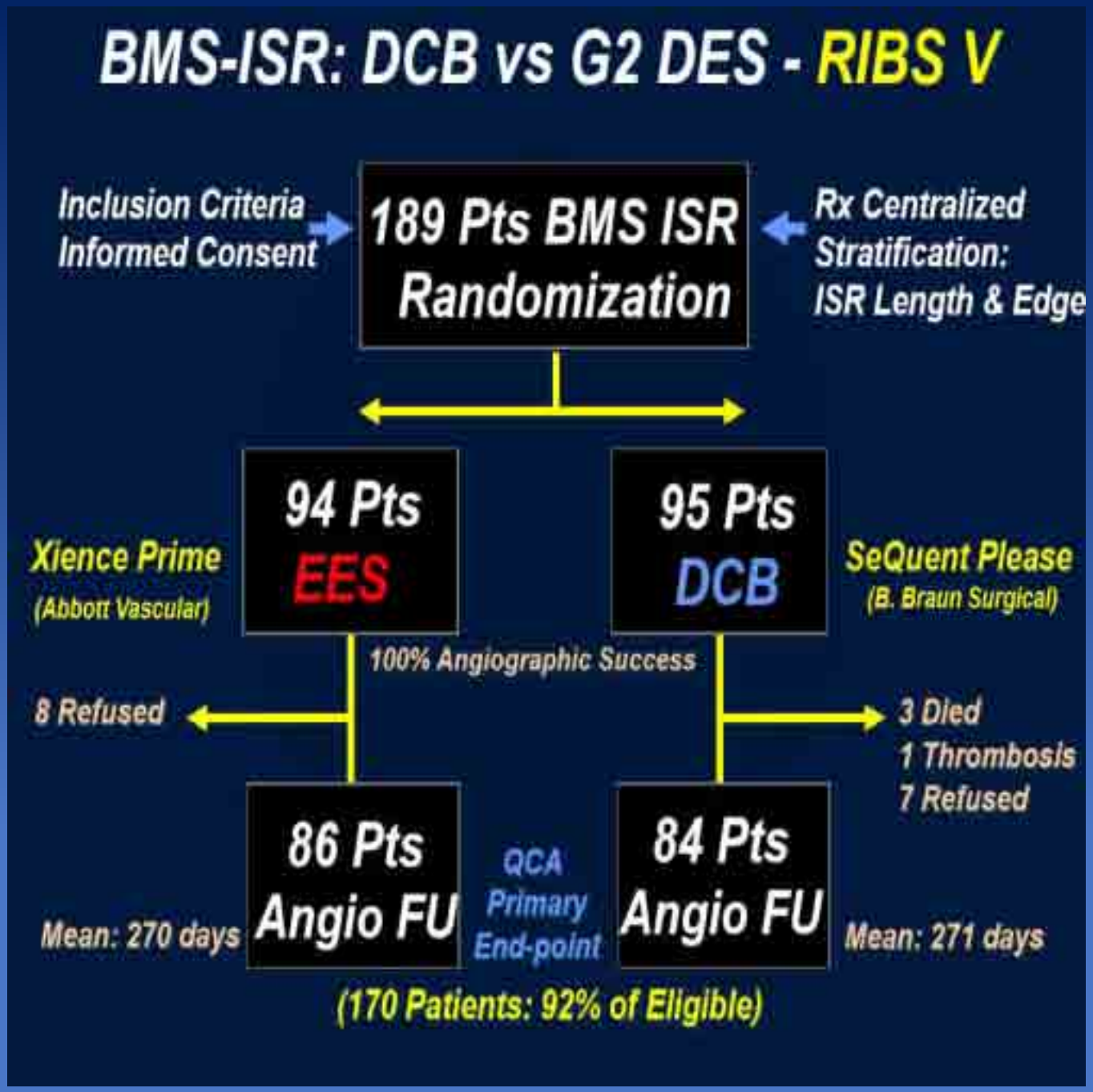
- Primary Endpoint: 6 month late lumen loss
- Secondary Endpoint: Procedural success (≤30% stenosis), 6 month binary restenosis, 6 month MACE, MACE at 1 and 3 years

Unverdorben et al. *Circulation* 2009

BMS-ISR: DCB vs DES

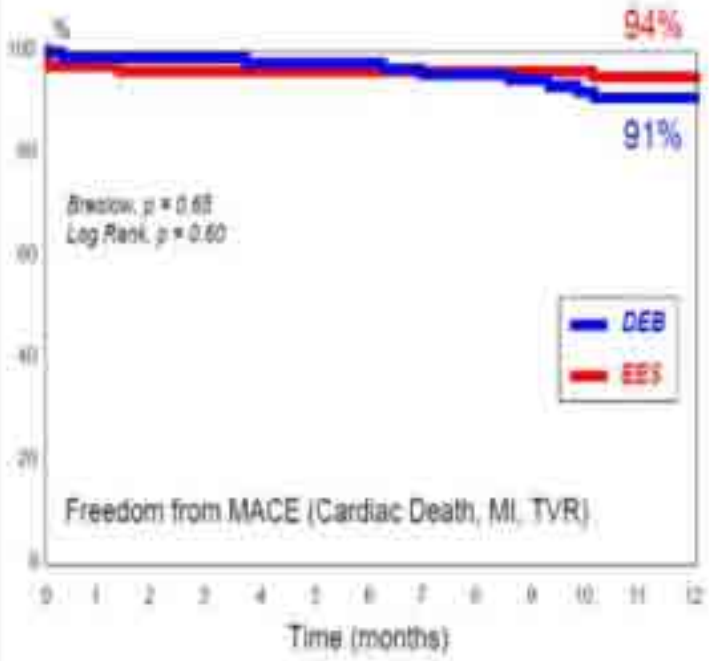
PEPCAD II ISR Study: Results

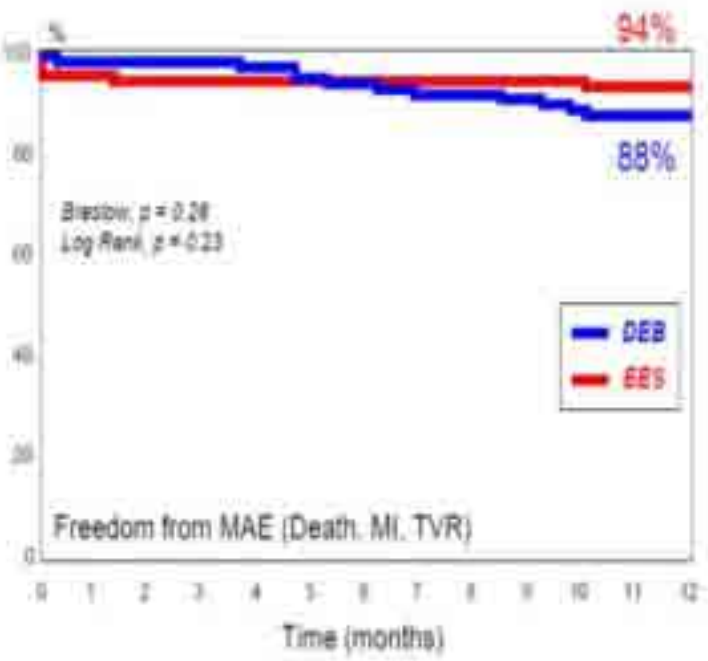
In comparing modalities with different acute gain, late loss is not a valid endpoint


BMS-ISR: DCB vs G2 DES - RIBS V
Inclusion Criteria
Informed Consent
189 Pts BMS ISR
Randomization
Rx Centralized
Stratification:
ISR Length & Edge
94 Pts
EES
95 Pts
DCB
Xience Prime
(Abbott Vascular)
SeQuent Please
(B. Braun Surgical)
100% Angiographic Success
8 Refused
3 Died
1 Thrombosis
7 Refused
86 Pts
Angio FU
QCA
Primary
End-point
84 Pts
Angio FU
Mean: 270 days
Mean: 271 days
(170 Patients: 92% of Eligible)

BMS-ISR: DCB vs G2 DES - RIBS V

Clinical outcomes at 12 months





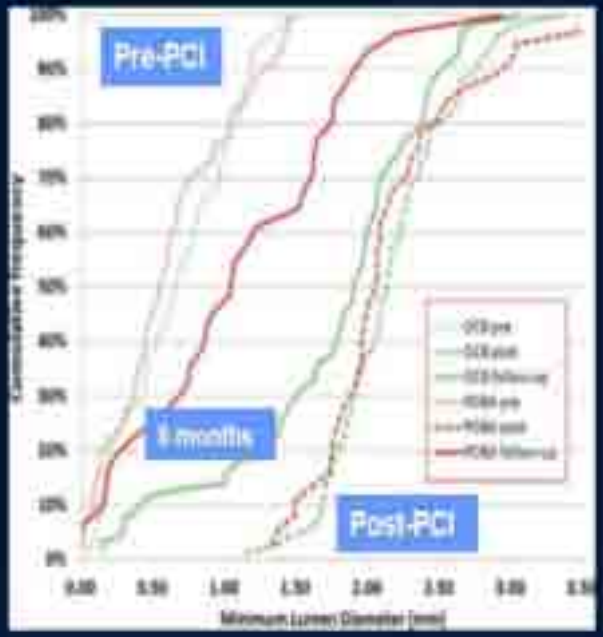
DES-ISR: DCB v Angioplasty

PEPCAD-DES: Primary Results

95/110 patients with angiographic follow-up

Late Loss (mm)

Min. Lumen Diameter (mm)



Rittger et al. *A Am Coll Cardiol* 2012

DES-ISR: DCB v DES v Angioplasty

Design

DESIGN:
Prospective, randomized, active controlled, multicenter clinical trial

INCLUSION CRITERIA:
1. Stenosis > 50% in "limus"-eluting DES
2. Symptoms/signs of ischemia

EXCLUSION CRITERIA:
1. Lesion in left main stem
2. Acute STEMI
3. Cardiogenic shock

SPONSOR: Deutsches Herzzentrum

402 patients with DES-restenosis enrolled between August 2009 and October 2011 in 3 centers in Germany

- Paclitaxel-eluting balloon (SeQuent) (N=137)
- Paclitaxel-eluting stent (Taxus) (N=131)
- Balloon angioplasty alone (N=134)

Angiographic follow-up at 6-8 months in 84.1% (N=338)

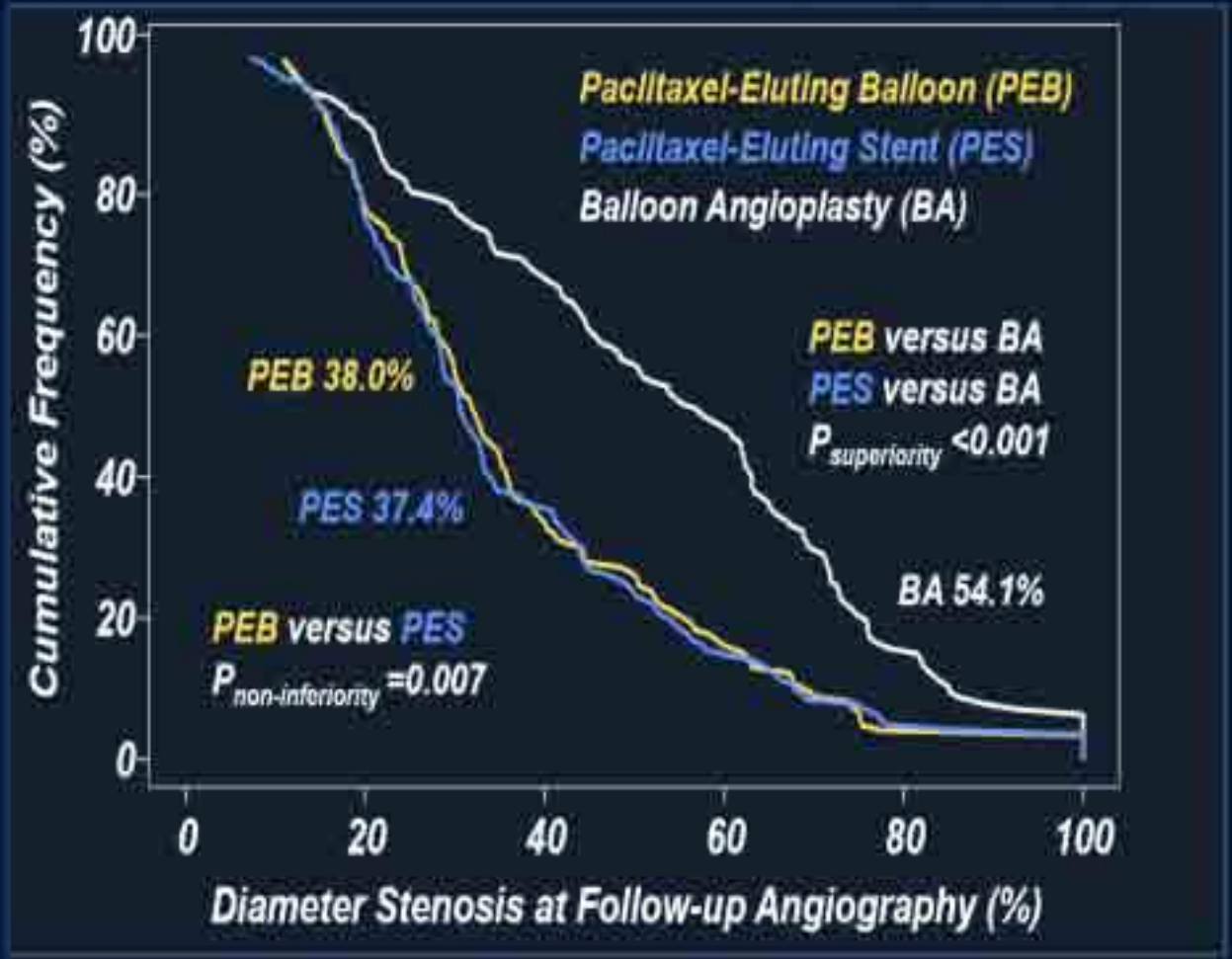
Clinical follow-up at 12 months in 97.5% (N=392)

No significant differences across groups

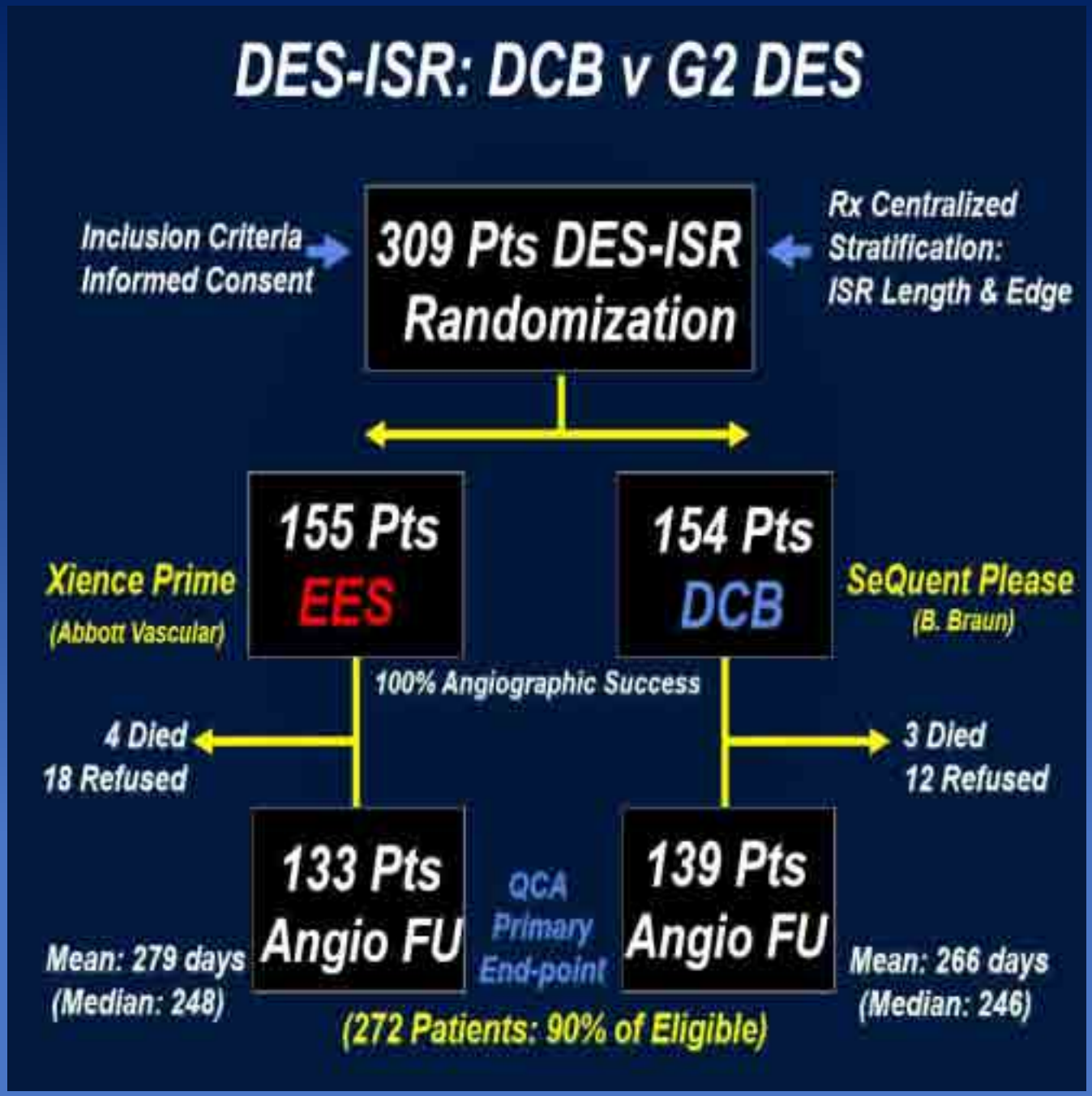
ISAR-DESIRE 3: Intracoronary Stenting and Angiographic Results: Drug Eluting Stents for In-Stent Restenosis: 3 Treatment Approaches; Byrne et al. Lancet 2013

DES-ISR: DCB v DES v Angioplasty

Diameter Stenosis at Follow-up Angiography

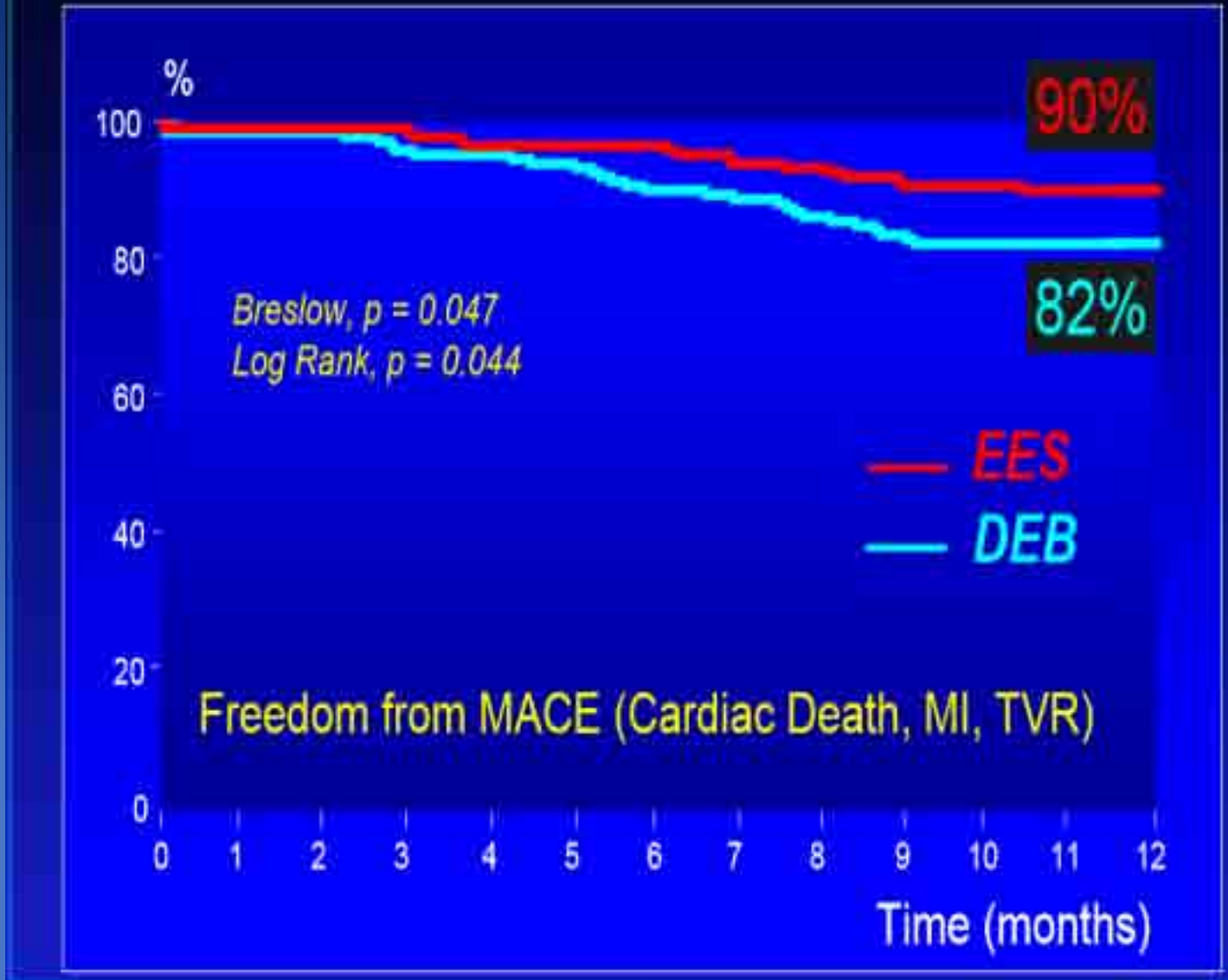


ISAR-DESIRE 3: Intracoronary Stenting and Angiographic Results: Drug Eluting Stents for In-Stent Restenosis: 3 Treatment Approaches; Byrne et al. Lancet 2013


DES-ISR: DCB v G2 DES
Inclusion Criteria
Informed Consent
309 Pts DES-ISR
Randomization
Rx Centralized
Stratification:
ISR Length & Edge
155 Pts
EES
Xience Prime
(Abbott Vascular)
154 Pts
DCB
SeQuent Please
(B. Braun)
100% Angiographic Success
4 Died
18 Refused
3 Died
12 Refused
133 Pts
Angio FU
QCA
Primary
End-point
139 Pts
Angio FU
Mean: 279 days
(Median: 248)
Mean: 266 days
(Median: 246)
(272 Patients: 90% of Eligible)

Clinical Follow-up:

1 Year FU 309 P (100%); FU Time 360±35 days



Clinical Follow-up:

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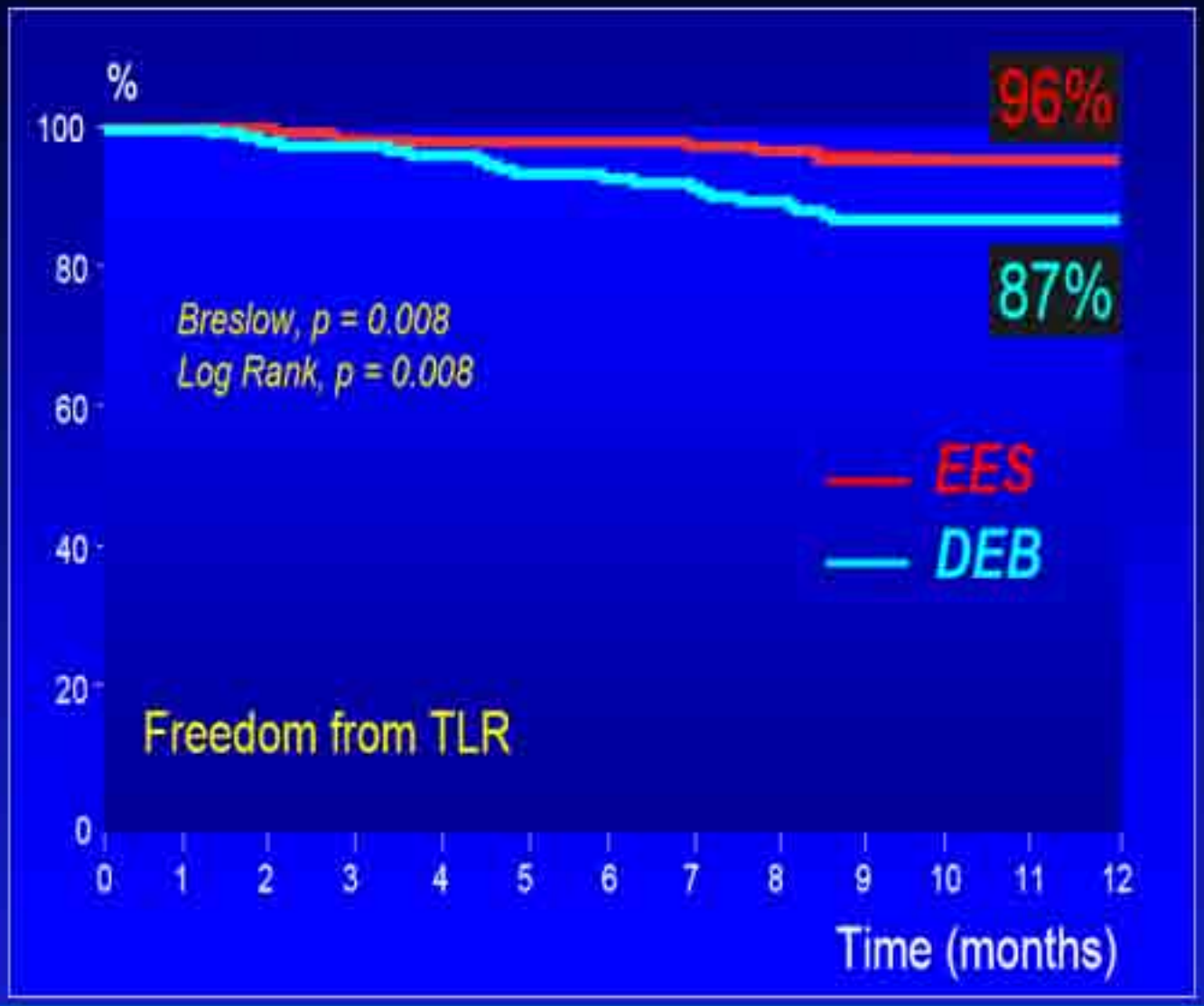
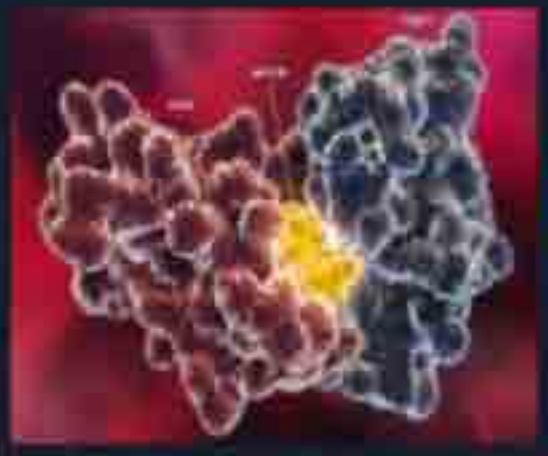
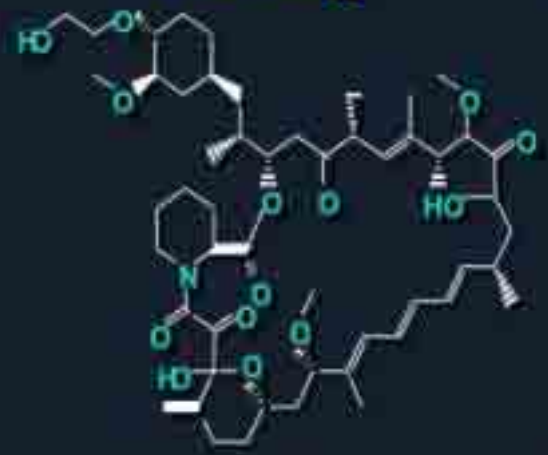


In-stent Restenosis in 2015: DCB vs DES

1. *Both angioplasty with DCB and repeat stenting with DES are safe and effective treatments for the management of BMS-ISR and DES-ISR*
2. *By obviating the need for additional stent implantation, DCB therapy may be the preferred treatment option*
3. *Future studies should explore the role of OCT tissue characterization to guide treatment decision between DCB and DES*

Second Generation DES

	Drug	Polymer	Stent
Resolute	 Zotarolimus	 BioLinx copolymer	 Driver
Xience V*	 Everolimus	 VDF + HFP copolymer	 Vision

Final Three-Year Outcome of a Randomized Trial Comparing Second Generation Drug-eluting Stents Using Either Biodegradable Polymer or Durable Polymer

The NOBORI Biolimus-Eluting versus XIENCE/PROMUS Everolimus-eluting Stent Trial (NEXT)

Masahiro Natsuaki, MD

Kyoto University Graduate School of Medicine, Saiseikai Fukuoka General Hospital

Ken Kozuma, MD; Takeshi Morimoto, MD, MPH; Kazushige Kadota, MD; Toshiya Muramatsu, MD, Yoshihisa Nakagawa, MD, Takashi Akasaka, MD; Keiichi Igarashi, MD; Kengo Tanabe, MD; Yoshihiro Morino, MD; Tetsuya Ishikawa, MD; Hideo Nishikawa, MD; Masaki Awata, MD; Masaharu Akao, MD; Hisayuki Okada, MD; Yoshiki Takatsu, MD; Nobuhiko Ogata, MD; Kazuo Kimura, MD; Kazushi Urasawa, MD; Yasuhiro Tarutani, MD; Nobuo Shiode, MD; and Takeshi Kimura, MD

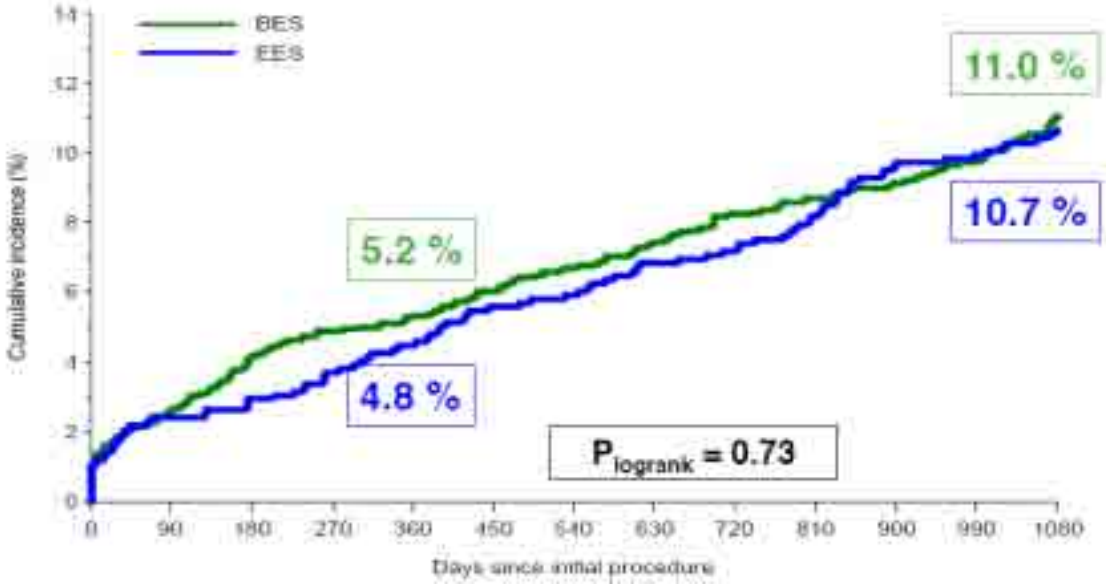
On behalf of the NEXT Investigators

Background

The advantage of coronary stent using biodegradable polymer could emerge beyond 1-year after stent implantation, when polymer has been fully degraded.

However, there are only a few randomized controlled trials other than the NEXT reporting the clinical outcomes beyond 1-year after biodegradable polymer biolimus-eluting stent (BP-BES) implantation as compared with durable polymer everolimus-eluting stent (DP-EES) implantation.

Therefore, we report the clinical outcomes of BP-BES compared with DP-EES through 3-year and beyond 1-year after stent implantation in the largest ever reported prospective multicenter randomized open label trial.



Smits P. EuroPCR 2014.

***COMPARE II** Cardiac death, myocardial infarction and TVR at 3-year*

NEXT Trial

Multicenter, randomized, non-inferiority trial comparing BP-BES with DP-EES

3235 patients scheduled for PCI using drug-eluting stent

No Exclusion Criteria (All-comer Design)

Randomization 1:1

Nobori BP-BES (N=1617)

Xience/Promus DP-EES (N=1618)

Enrollment from 98 Japanese centers between May and October, 2011

BP-BES (N=1576)
<1035 days follow-up: N=41

3-Year Clinical Follow-up (N=3158; 97.6%)

DP-EES (N=1582)
<1035 days follow-up: N=36

<Primary Endpoint>

Efficacy: Target lesion revascularization at 1-year

Safety: Death or Myocardial Infarction at 3-year

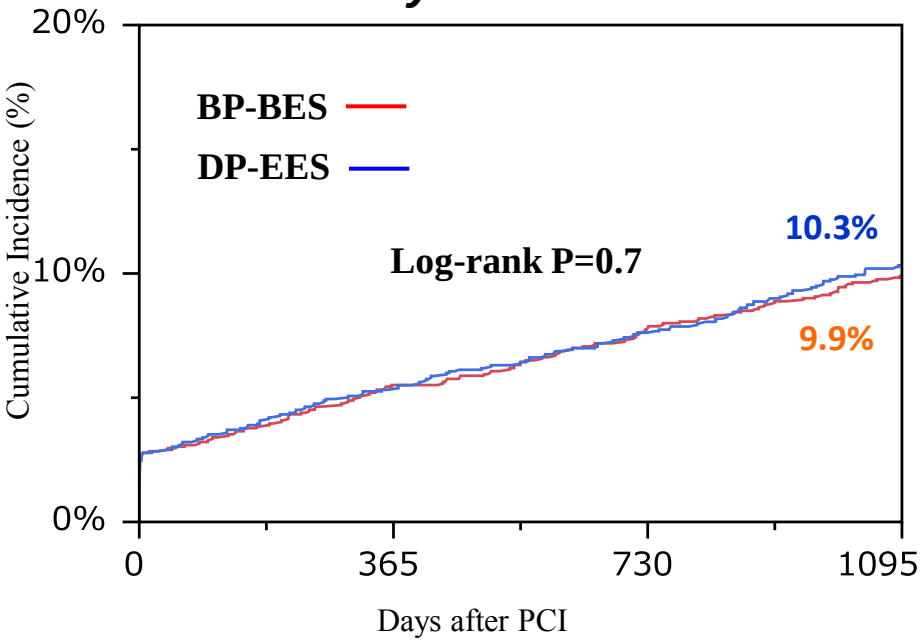
<Power Calculation>

3000 patients would yield 91% power to detect non-inferiority with the non-inferiority margin of 4.3% (True rate 12.2%)

Cumulative 3-year Incidence

Primary Safety Endpoint

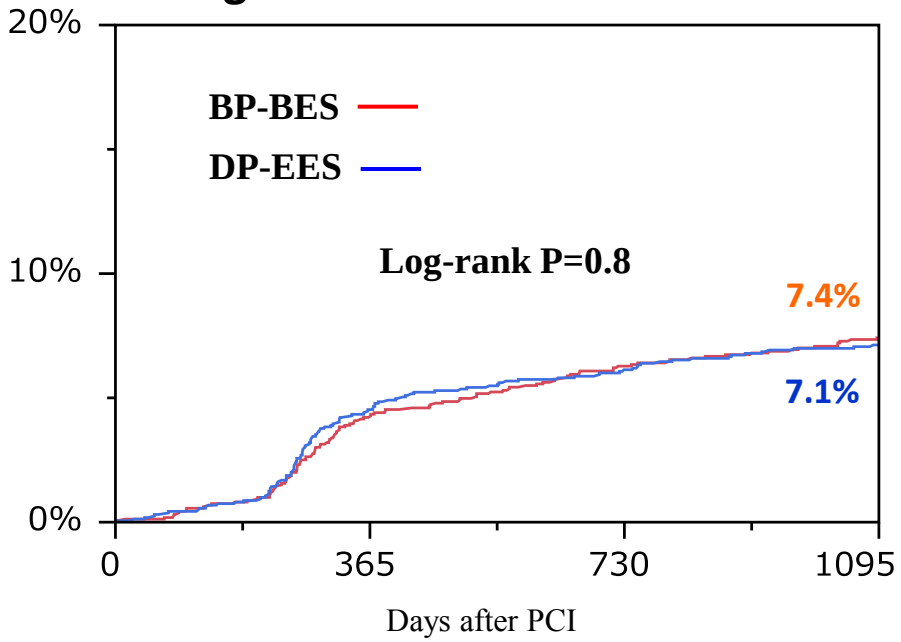
Death or Myocardial Infarction



Interval	0 day	365 days	730 days	1095 days
BP-BES group				
N of patients with at least 1 event		89	126	159
N of patients at risk	1617	1524	1478	1416
Cumulative Incidence		5.5%	7.8%	9.9%
DP-EES group				
N of patients with at least 1 event		87	124	166
N of patients at risk	1618	1529	1482	1413
Cumulative Incidence		5.4%	7.7%	10.3%

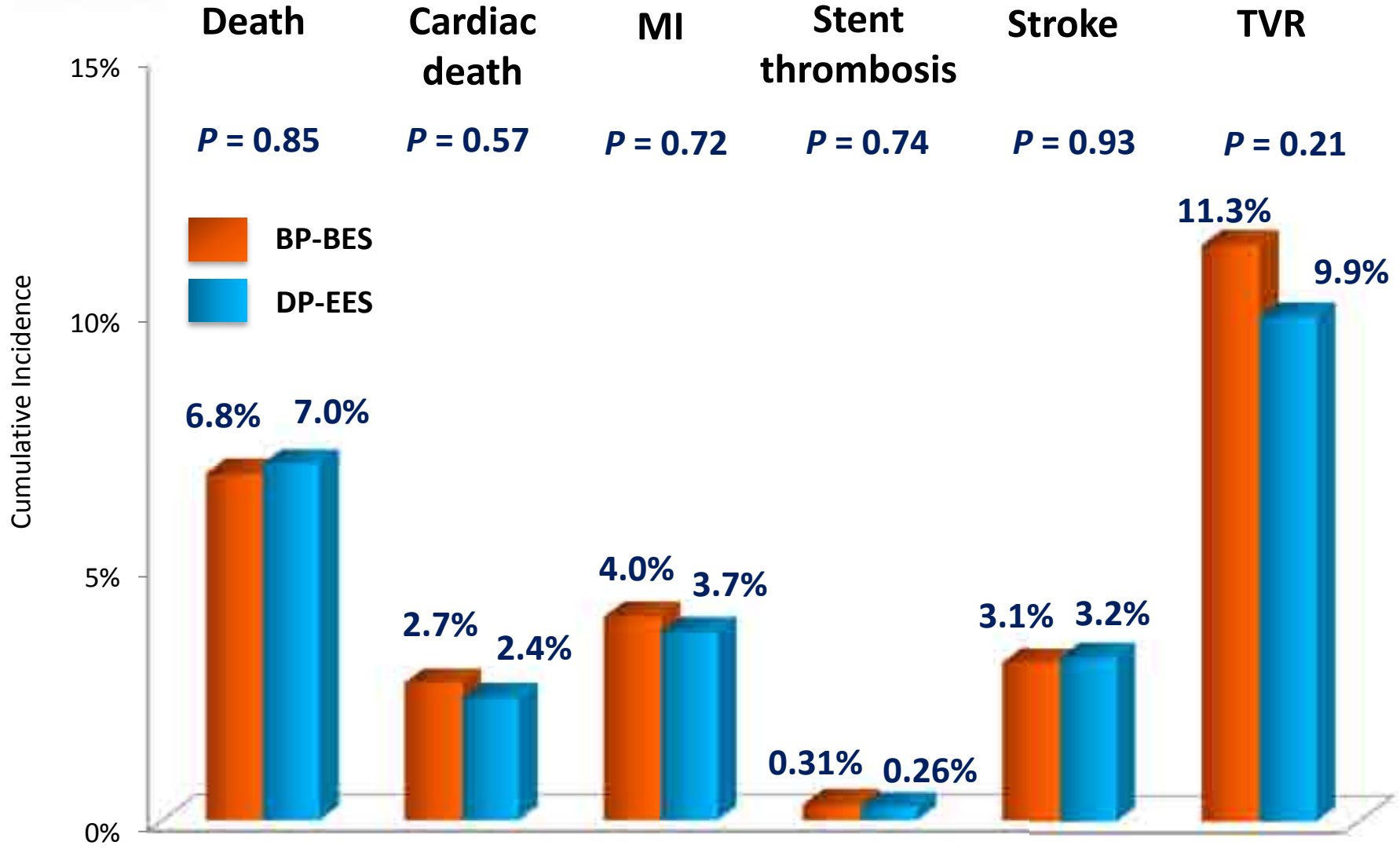
Primary Efficacy Endpoint

Target Lesion Revascularization



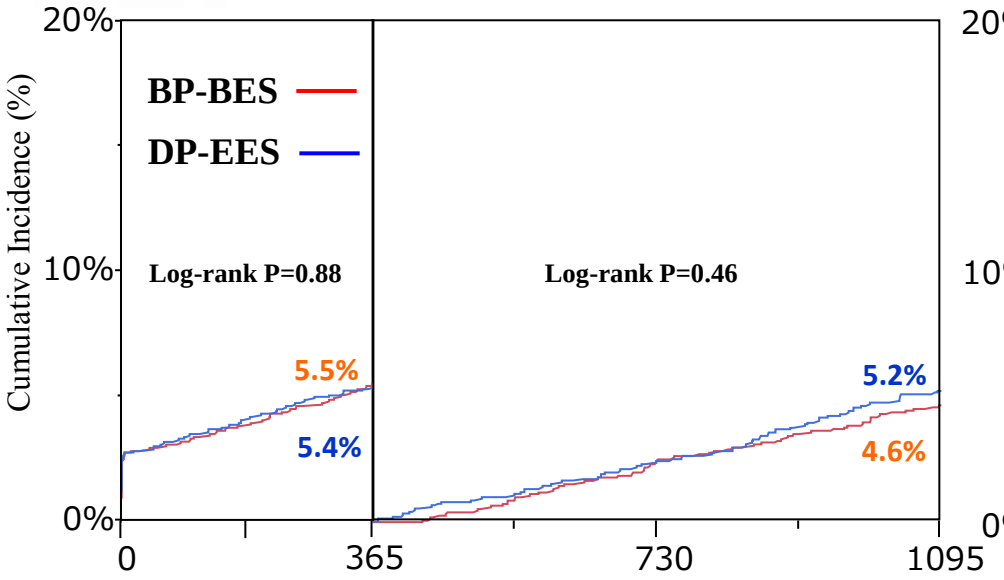
Interval	0 day	365 days	730 days	1095 days
BP-BES group				
N of patients with at least 1 event		68	99	116
N of patients at risk	1617	1506	1432	1353
Cumulative Incidence		4.3%	6.3%	7.4%
DP-EES group				
N of patients with at least 1 event		72	97	112
N of patients at risk	1618	1506	1440	1359
Cumulative Incidence		4.5%	6.1%	7.1%

Clinical Outcomes at 3-Year

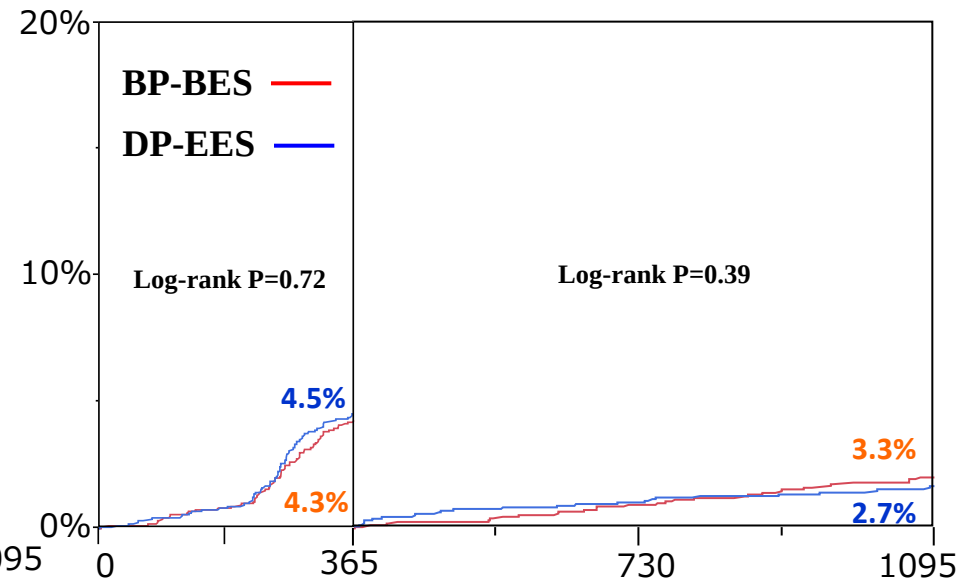


Landmark Analysis at 1-year

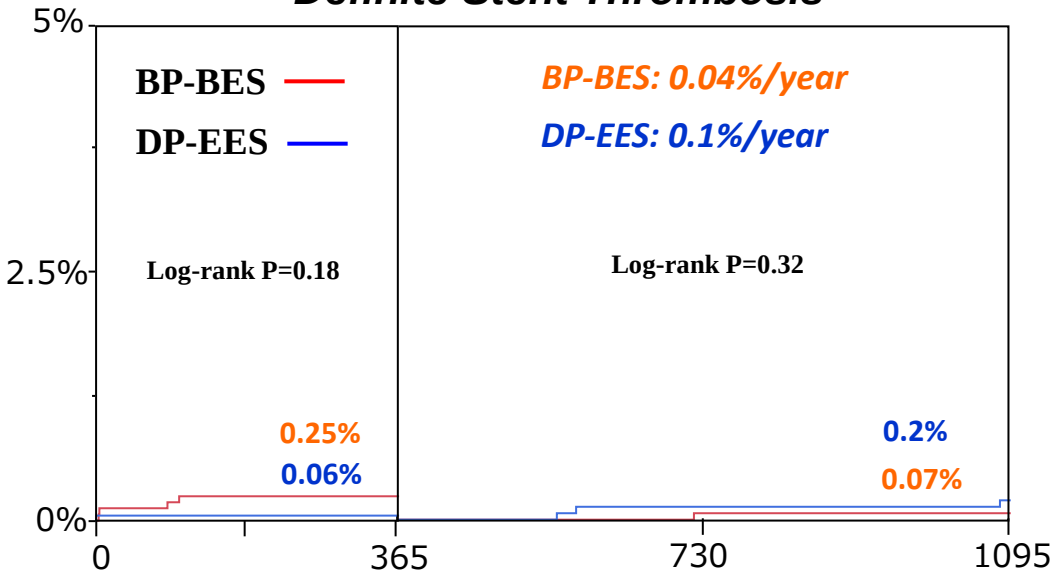
Primary Safety Endpoint
Death or Myocardial Infarction



Primary Efficacy Endpoint
Target Lesion Revascularization



Definite Stent Thrombosis



Conclusions

- *The safety and efficacy outcomes of BP-BES remained comparable to those of DP-EES through 3-year and beyond 1-year after stent implantation.*
- *There was no apparent signal suggesting either improvement or impairment of clinical outcomes with BP-BES compared with DP-EES.*
- *Longer-term follow-up is mandatory to fully understand whether BP-BES could provide any long-term benefit over DP-EES.*

Bioresorbable Scaffolds

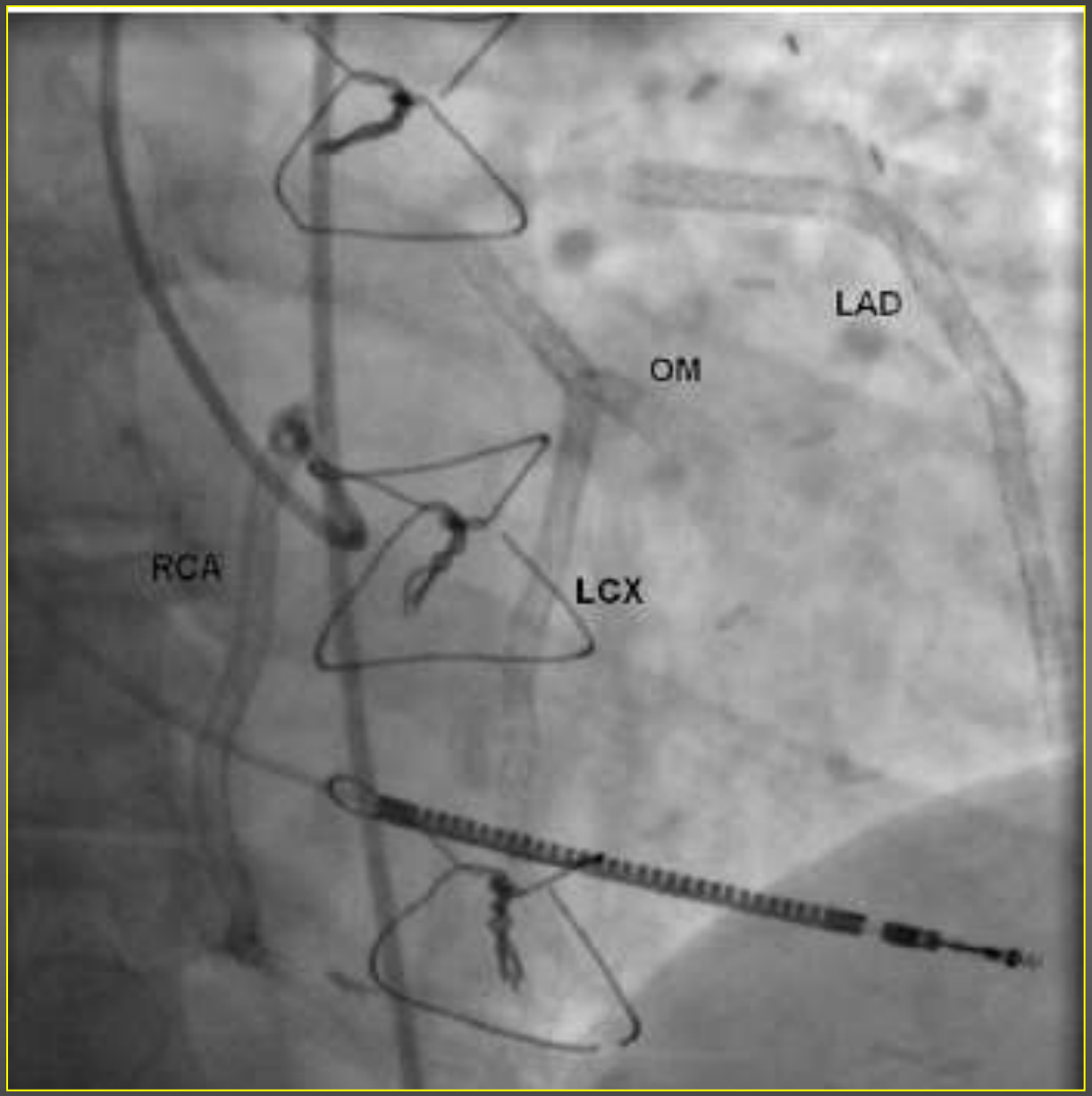
Igaki-Tamai		PLLA
Abbott Absorb		PLLA Everolimus
Elixir DESolve		PPLLA based Novolimus
REVA REsolve		Tyrosine- Policarbonate Sirolimus
Biotronik Dreams		Magnesium Sirolimus
Amaranth		PLLA resin

Racional e Potenciais Benefícios dos Stents Bioabsorvíveis

- Revascularizar o vaso como o stent metálico e ser naturalmente reabsorvido pelo organismo.
- Restaurar a vasomotricidade
- Reduzir o estímulo a inflamação crônica: consequentemente a necessidade de uso prolongado de terapia anti-agregante dupla.
- Facilitar revascularizações futuras
- Compatibilidade com exames não-invasivos.

Male

57 years

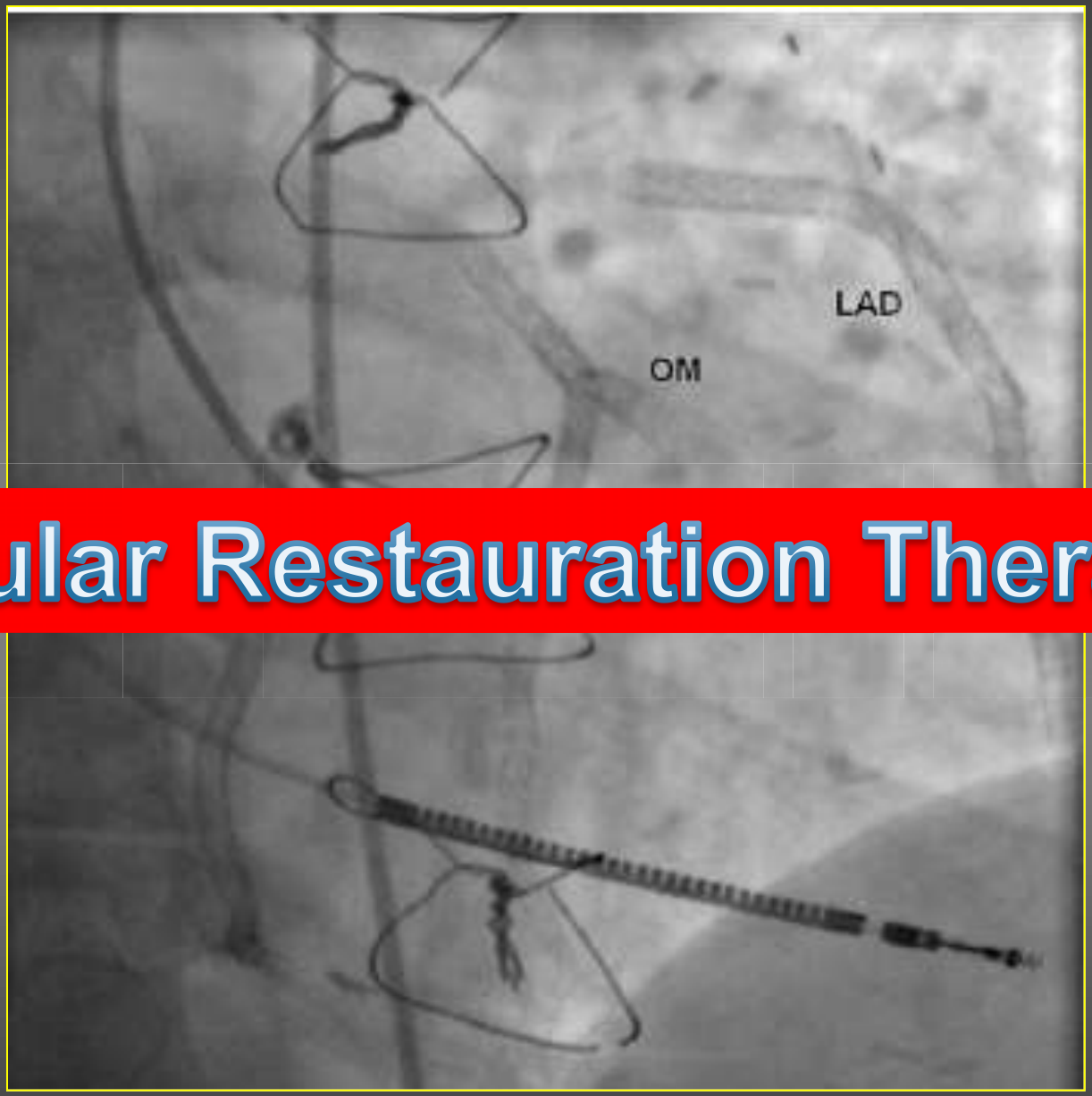


Khouzam, RN, et al. *J Am Coll Cardiol.* 2010;56;1605

Male

57 years

...

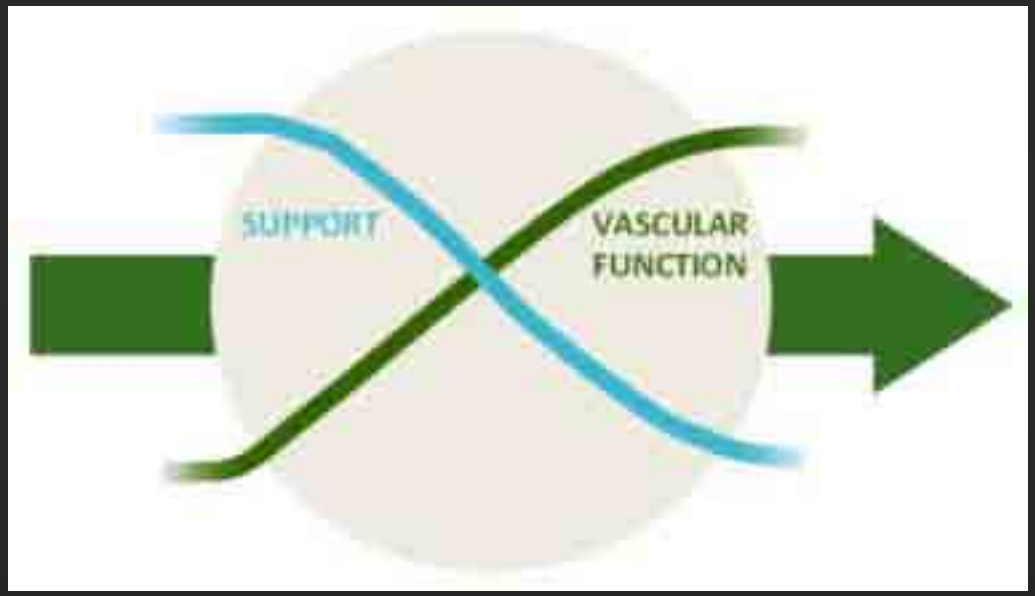


Vascular Restauration Therapy

Khouzam, RN, et al. *J Am Coll Cardiol.* 2010;56;1605

Mechanical Conditioning: A Key Component of VRT

Gradual disappearance of supportive structure



Vessel recovers the ability to respond to physiologic stimuli

Shear stress, pulsatility & cyclic strain

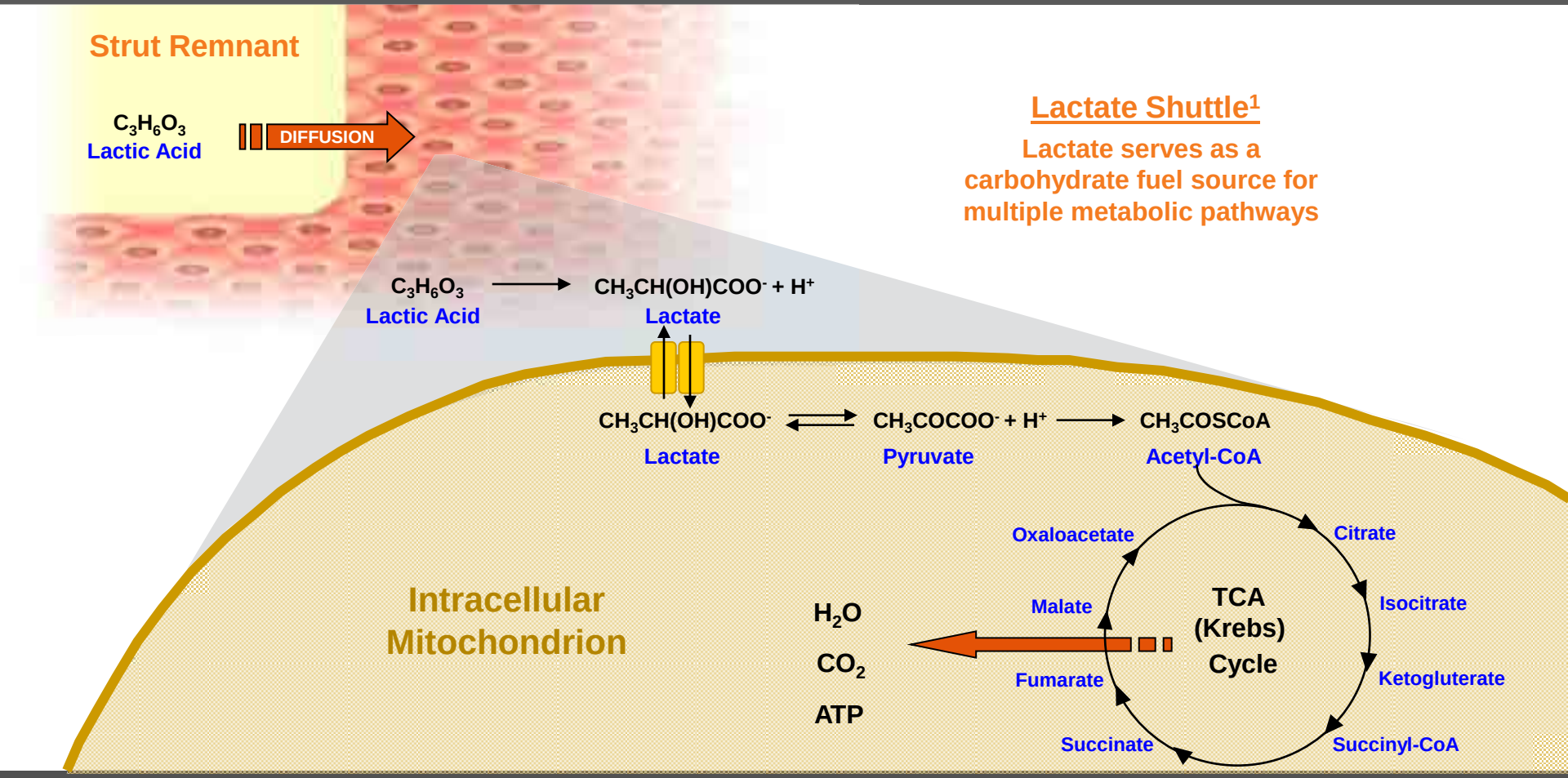
Tissue adaptation*

Structure and functionality*

Tissues in the body require physiologic stress to maintain normal structure and function

*** Histology images are from porcine animal models, Cohort A device.**
Serruys PW et al. *Eur Heart J*. 2012;33:16-25b

Polylactide Degradation & Lactate Metabolism

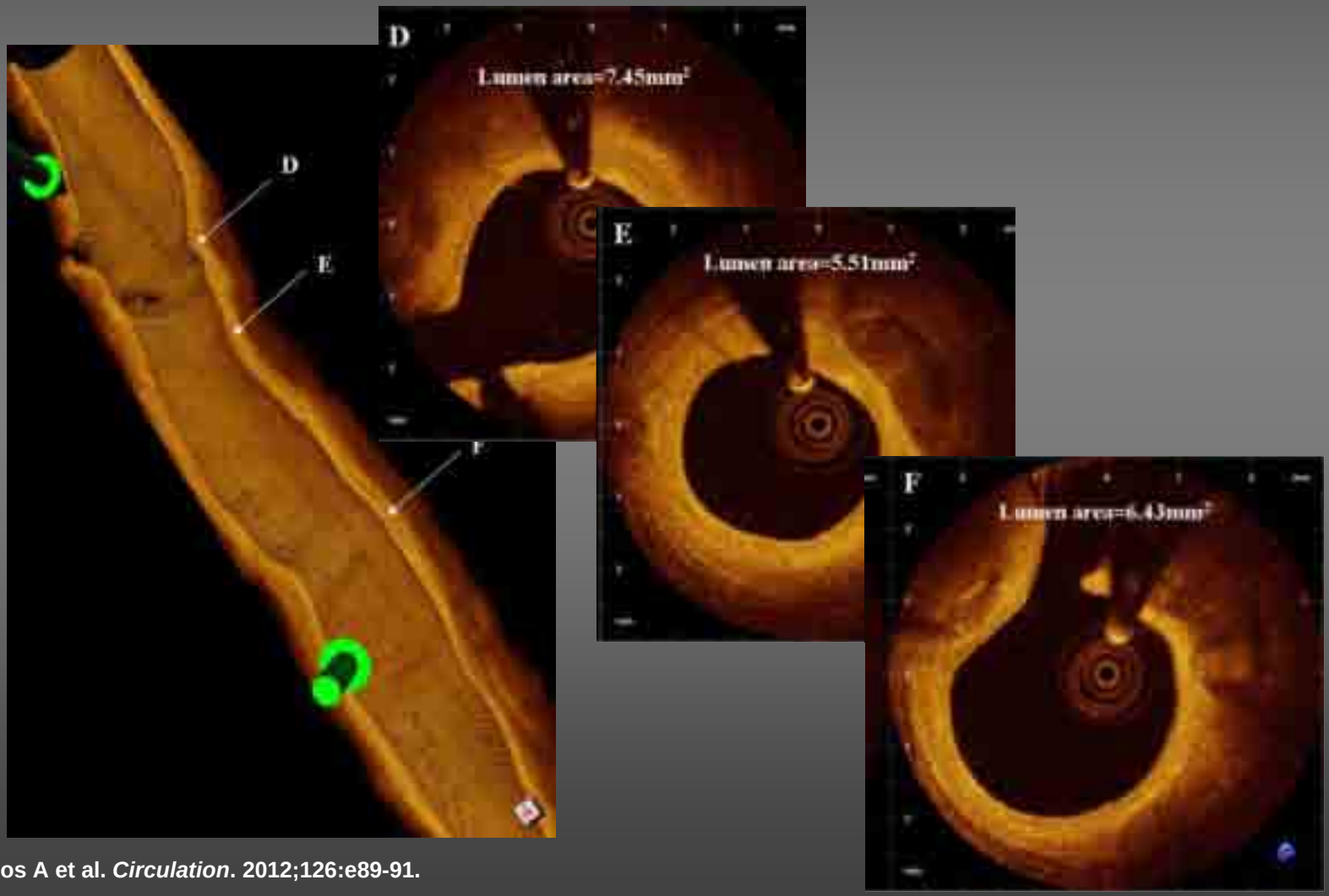


Lactate Shuttle[1]

Lactate serves as a carbohydrate fuel source for multiple metabolic pathways

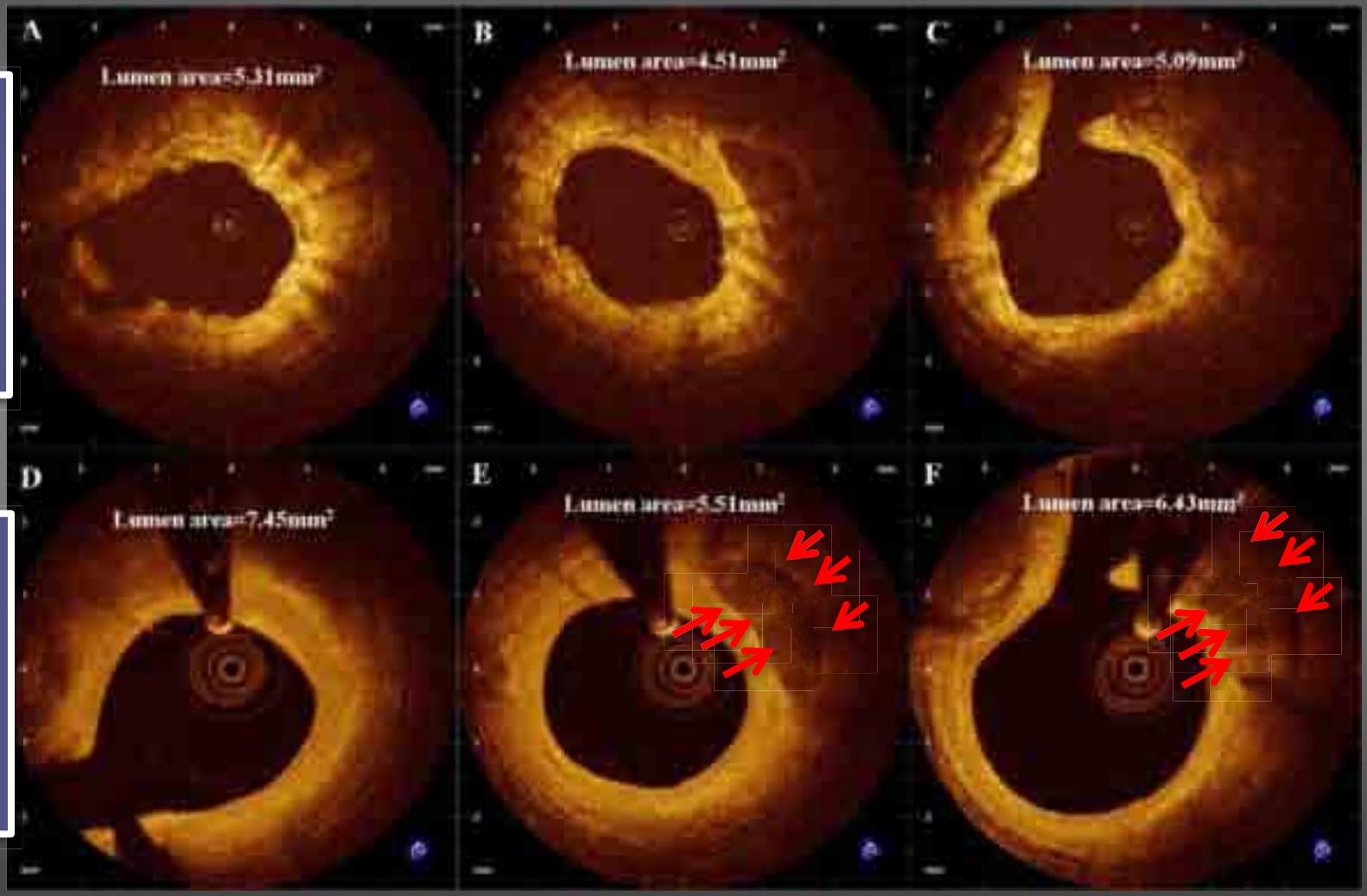
1. Philp, A., et.al. *J. Exp. Biol*. 2005; 208: 4561-4575.

Healing From the Outside:
Could Scaffold Implantation Seal and Protect the Underlying Plaque?



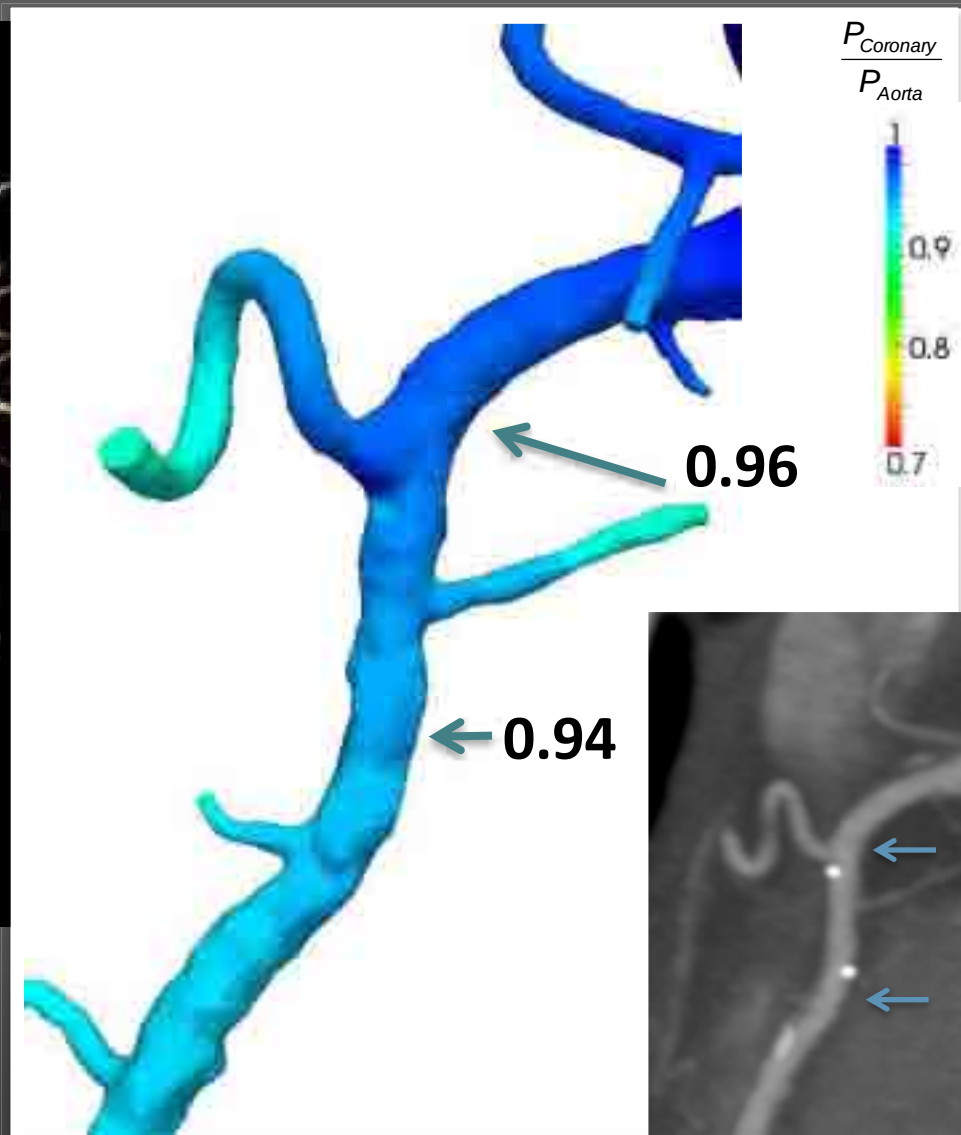
Karanasos A et al. *Circulation*. 2012;126:e89-91.

At 60 Months a Smooth Rheologically-Favorable Surface is Created



Serruys PW et al. The Science Behind the Dream; TCT 2012.

Non-invasive assessment of FFR at 5 years showed persistence of the normalization of coronary flow dynamics



Bioresorbable Scaffolds

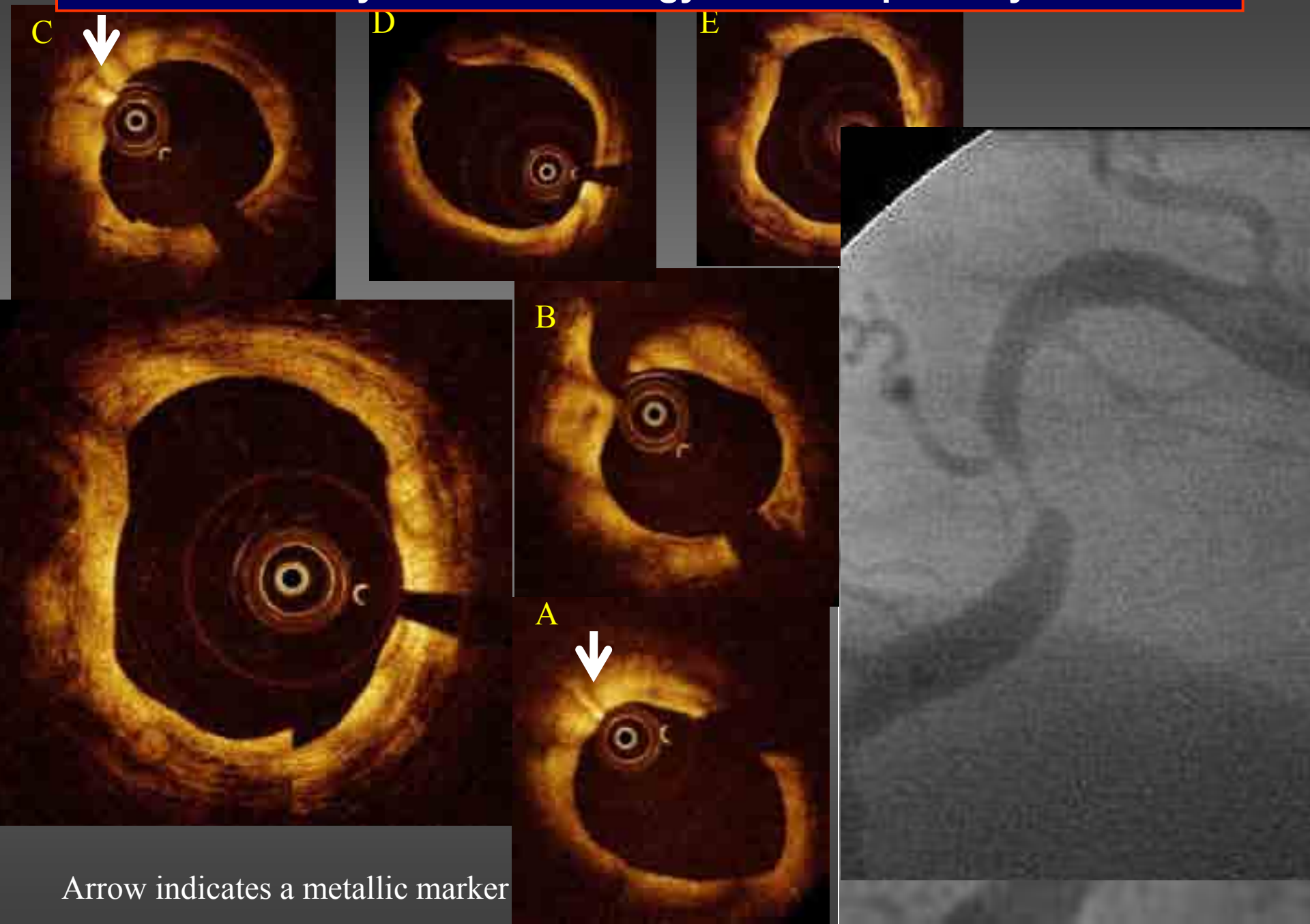
Igaki-Tamai		PLLA
Abbott Absorb		PLLA Everolimus
Elixir DESolve		PPLLA based Novolimus
REVA REsolve		Tyrosine- Policarbonate Sirolimus
Biotronik Dreams		Magnesium Sirolimus
Amaranth		PLLA resin

Bioresorbable Scaffolds

Igaki-Tamai

PLLA

The safety of this technology remains up to 10 years.



Arrow indicates a metallic marker

Bioresorbable Scaffolds

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Biotronik Dreams		Magnesium Sirolimus
Amaranth		PLLA resin

Bioresorbable Scaffolds

BVS (Abbott)

PLLA

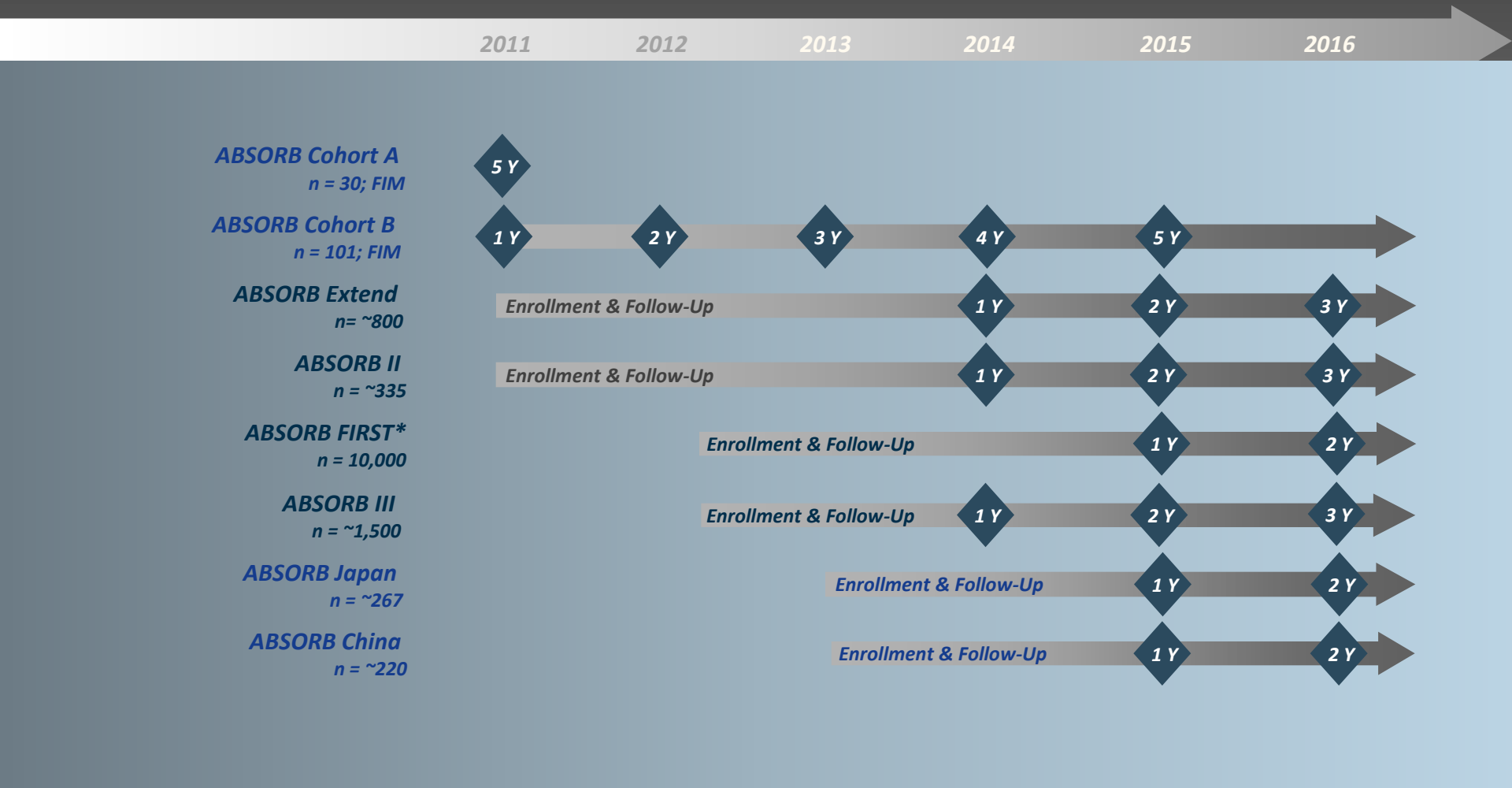
Everolimus-Eluting Bioresorbable Vascular Scaffold

ML VISION Delivery System	Bioresorbable Device Platform	Bioresorbable Coating	Everolimus
• Seven generations of MULTI-LINK success • World-class deliverability	• Polylactide (PLLA) • Naturally resorbed, fully metabolized	• Polylactide (PDLLA) coating • Fully biodegradable	• Similar dose and release rate to XIENCE V




All illustrations are artists' renditions

The ABSORB Clinical Trial Program



Total Pts Studied	*n=~599*	*n~800*	*n~5,474*	*n~13,253*	*n~13,253*	*n~13,253*

Note: Sample sizes reflect Absorb patients only.

** n= 10.000 f/u at 1 year. 1.000 patients f/u at 3 years, 1.000 patients at 2-4 years*

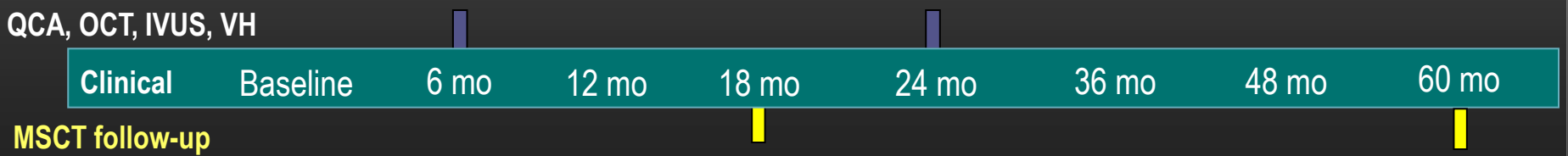
ABSORB Cohort A

Completed

Principal Investigators:

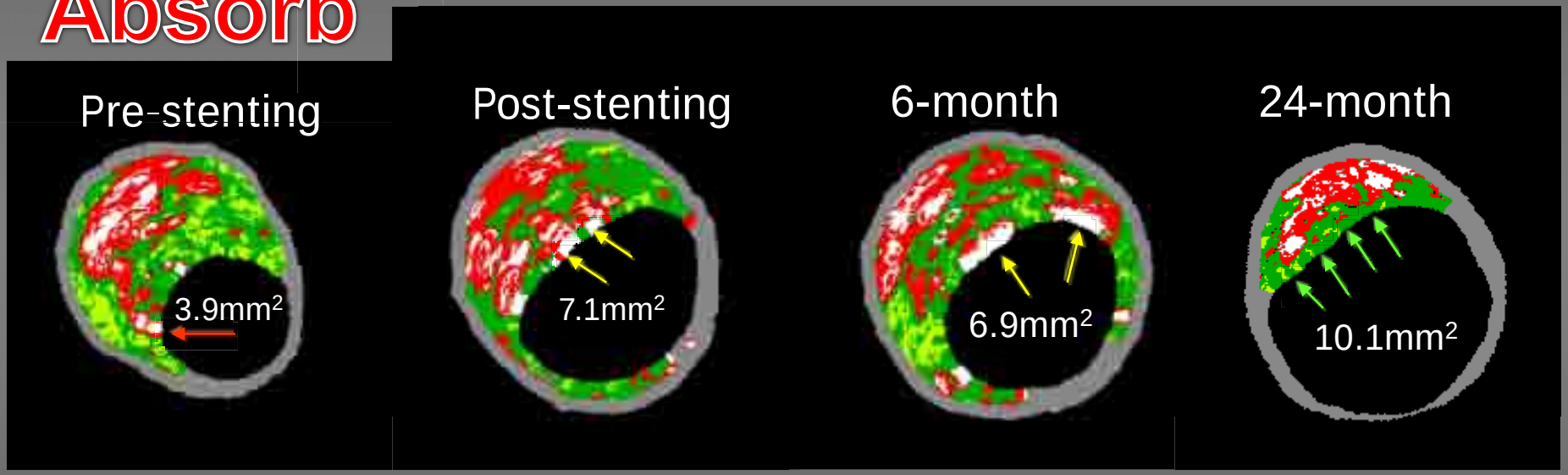
Patrick Serruys, John Ormiston

- Prospective, open label, single arm study.
- 30 patients enrolled at 4 sites
- Device sizes: 3.0 x 12 mm; 3.0 x 18 mm in two patients
- Treatment: single *de novo* lesion
- Follow-up schedule:



ABSORB BVS is neither approved nor available for sale in the U.S.

IVUS – VH after Absorb implantation (FIM)

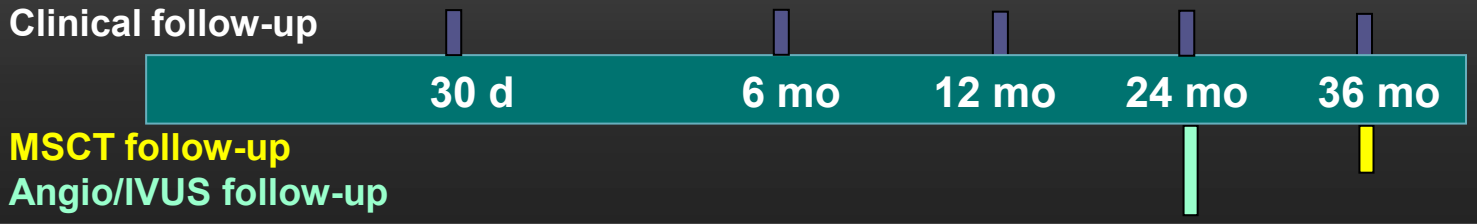


ABSORB II

Therapy Differentiation: RECRUITING

- Prospective, multi-centered, single blind, randomized (2:1 ABSORB BVS: XIENCE PRIME) study in Europe and New Zealand

- Co-Primary Endpoints:
  - Minimum lumen diameter (MLD) at 2 years post-nitrate minus MLD post-procedure post-nitrate by QCA (non-inferiority, reflex to superiority)
- Device sizes: Scaffold diameters: 2.5, 3.0 mm
  Scaffold lengths: 18, 28 mm
- Treatment: Up to two *de novo* lesions; $D_{max} \geq 2.25$ and ≤ 3.3 mm; lesion length ≤ 48 mm



ABSORB BVS is neither approved nor available for sale in the U.S.

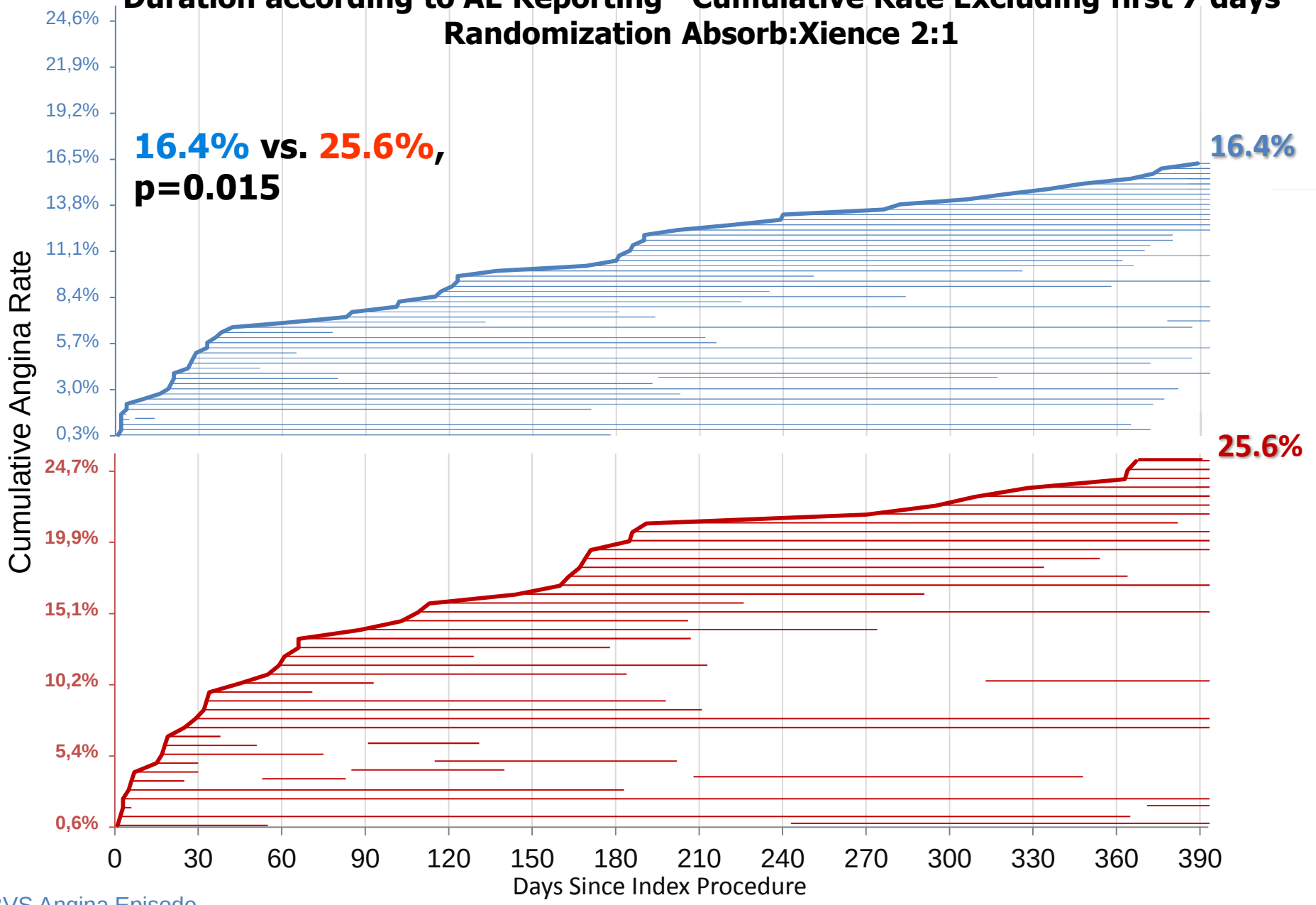
Clinical Outcomes

Cumulative incidence in percentage	Absorb 335 pts	Xience 166 pts	*p* value
Composite of cardiac death, target vessel MI and clinically indicated target lesion revascularization (TLF, DoCE)	**4.8 %**	**3.0 %**	**0.35**
Cardiac death	0 %	0 %	1.00
Target vessel MI	4.2 %	1.2 %	0.07
Clinically indicated TLR	1.2 %	1.8 %	0.69
All TLR	1.2 %	1.8 %	0.69
Composite of all death, all MI and all revascularization (PoCE)	**7.3 %**	**9.1 %**	**0.47**
All death	0 %	0.6 %	0.33
All MI	4.5 %	1.2 %	0.06
All revascularization	3.6 %	7.3 %	0.08

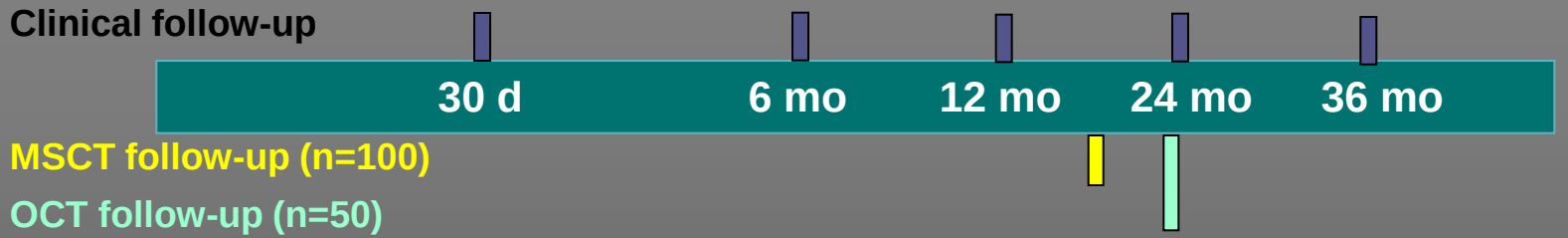
Definite scaffold/stent thrombosis

Cumulative incidence in percentage	Absorb 335 pts	Xience 166 pts	*p* value
Definite scaffold/stent thrombosis			
Acute (0-1 day)	0.3 (1pt)	0.0	NS
Sub-acute (2–30 days)	0.3 (1pt)	0.0	NS
Late (31–365 days)	0.0	0.0	NS
Probable scaffold/stent thrombosis			
Acute (0-1 day)	0.0	0.0	NS
Sub-acute (2–30 days)	0.0	0.0	NS
Late (31–365 days)	0.3 (1pt)	0.0	NS

Time to the First Occurrence of Angina(Worsening or Recurrent) and its Duration according to AE Reporting– Cumulative Rate Excluding first 7 days Randomization Absorb:Xience 2:1



ABSORB EXTEND
Non-Randomized, Single-Arm, Continued Access Trial

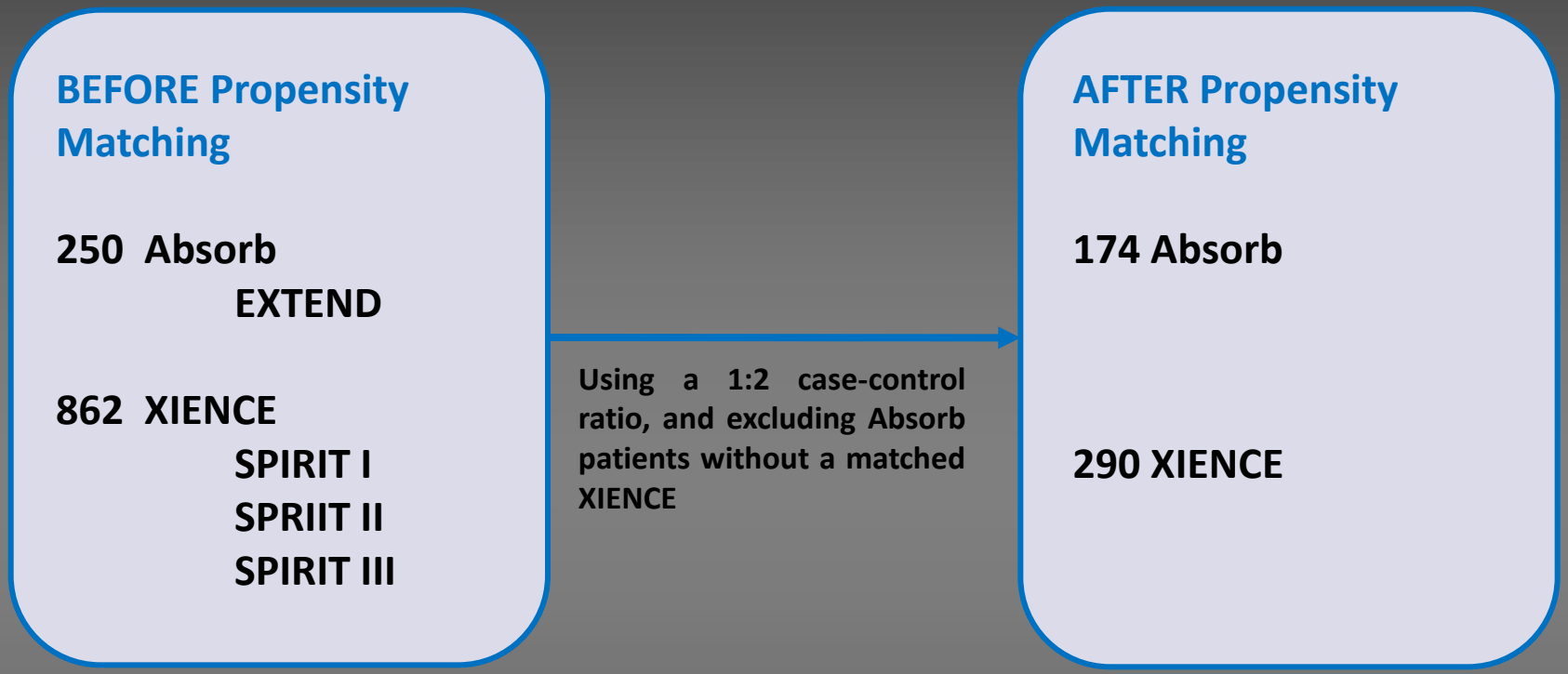


Study Objective:	Continued Access trial. FPI*: Jan 11, 2010
Endpoints:	No hypothesis-testing, typical PCI clinical endpoints
Treatment:	Up to 2 *de novo* lesions in different epicardial vessels Planned overlapping allowed in lesions >22 and ≤ 28 mm
Device Sizes:	Scaffold diameters: 2.5, 3.0 mm Scaffold lengths: 18, 28 mm

*FPI: First Patient In

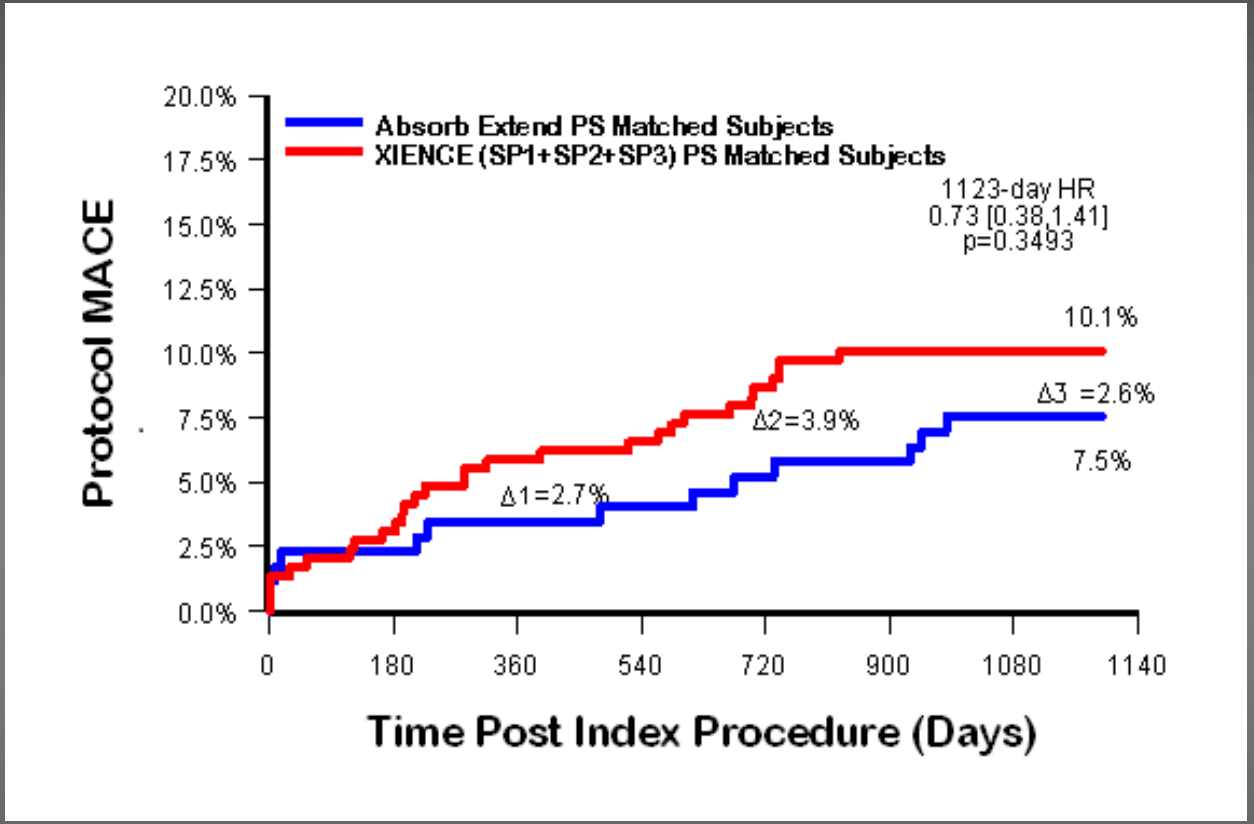
ABSORB BVS is neither approved nor available for sale in the U.S.

Propensity Score Matched Analysis



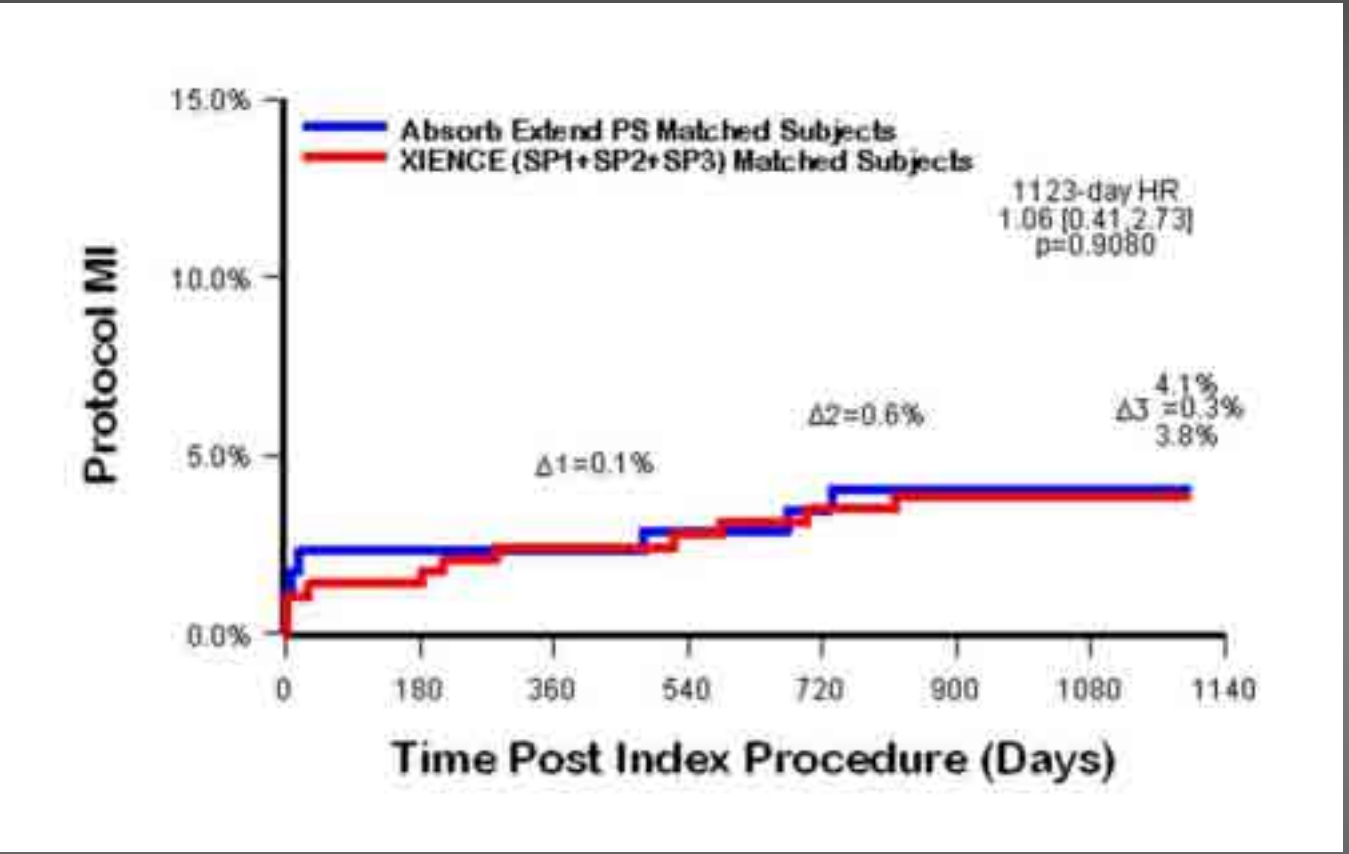
- Unadjusted data showed statistical differences in patient characteristics of prior MI, unstable angina, dyslipidemia, hypertension, and familial history of CAD, multiple vessel disease and all lesion characteristics except for percentage of LCX/Ramus treated.
- Adjusted data showed that the above baseline characteristics were no longer significantly different, indicating an effective PSA.

Propensity Score Matched: MACE through 36 Months



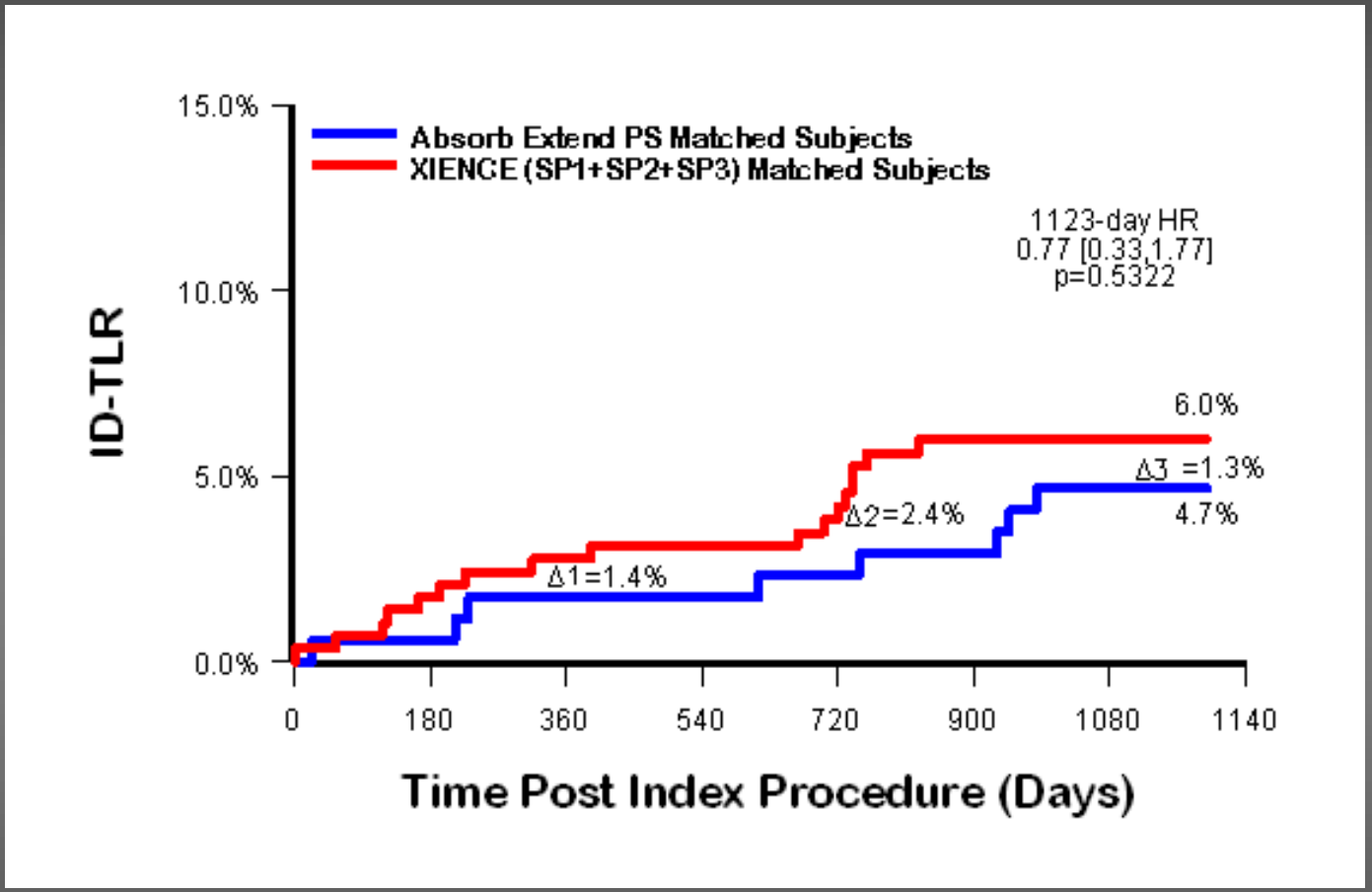
	0	37	194	393	758	1123
ABSORB EXTEND at Risk	174	169	169	166	161	157
XIENCE V (SPI,II,III) at Risk	290	285	279	271	255	252

Propensity Score Matched: MI through 36 Months



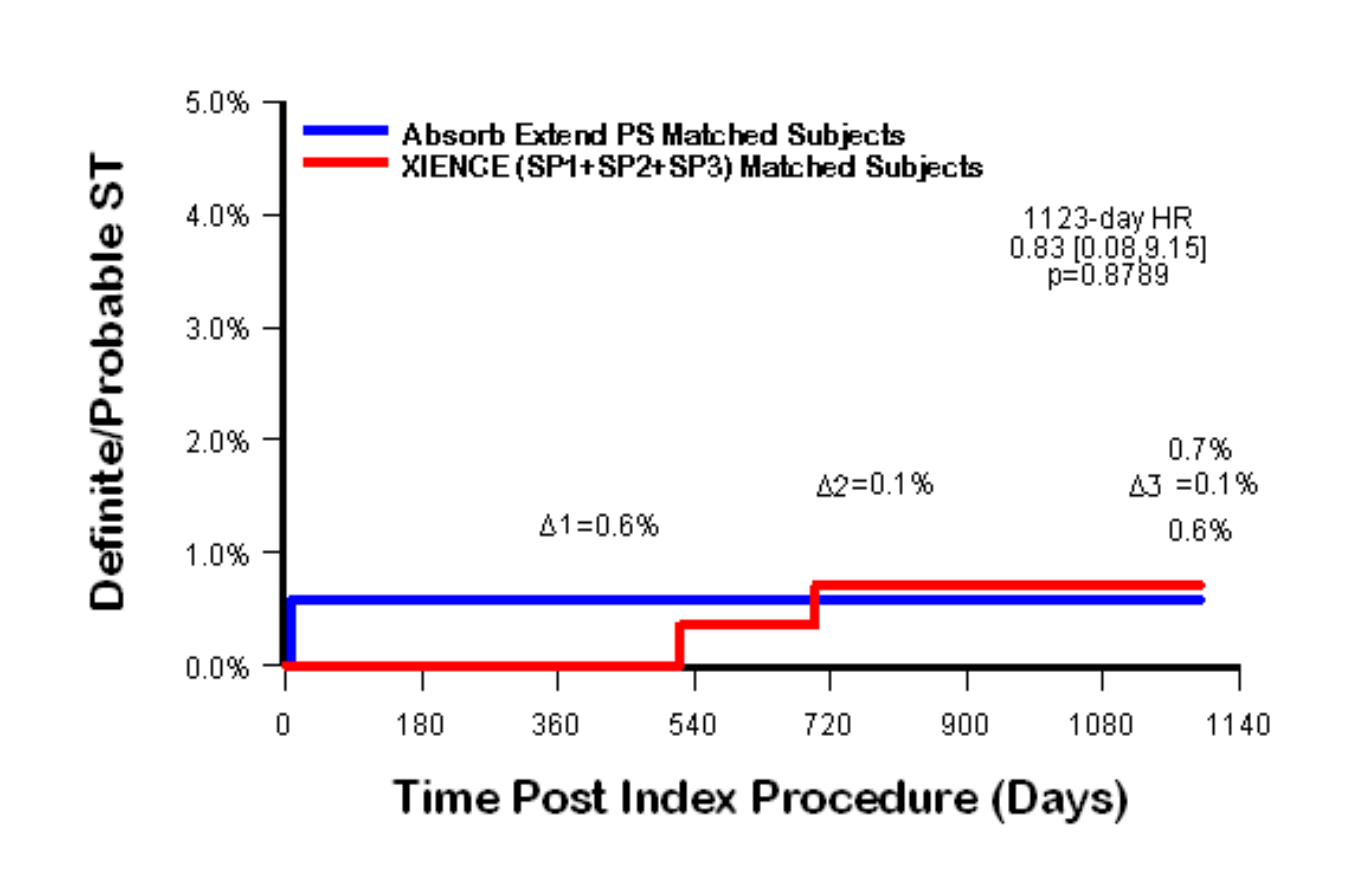
	0	37	194	393	758	1123
ABSORB EXTEND at Risk	174	169	169	168	164	163
XIENCE V (SPI,II,III) at Risk	290	286	285	279	269	266

Propensity Score Matched: ID-TLR through 36 Months



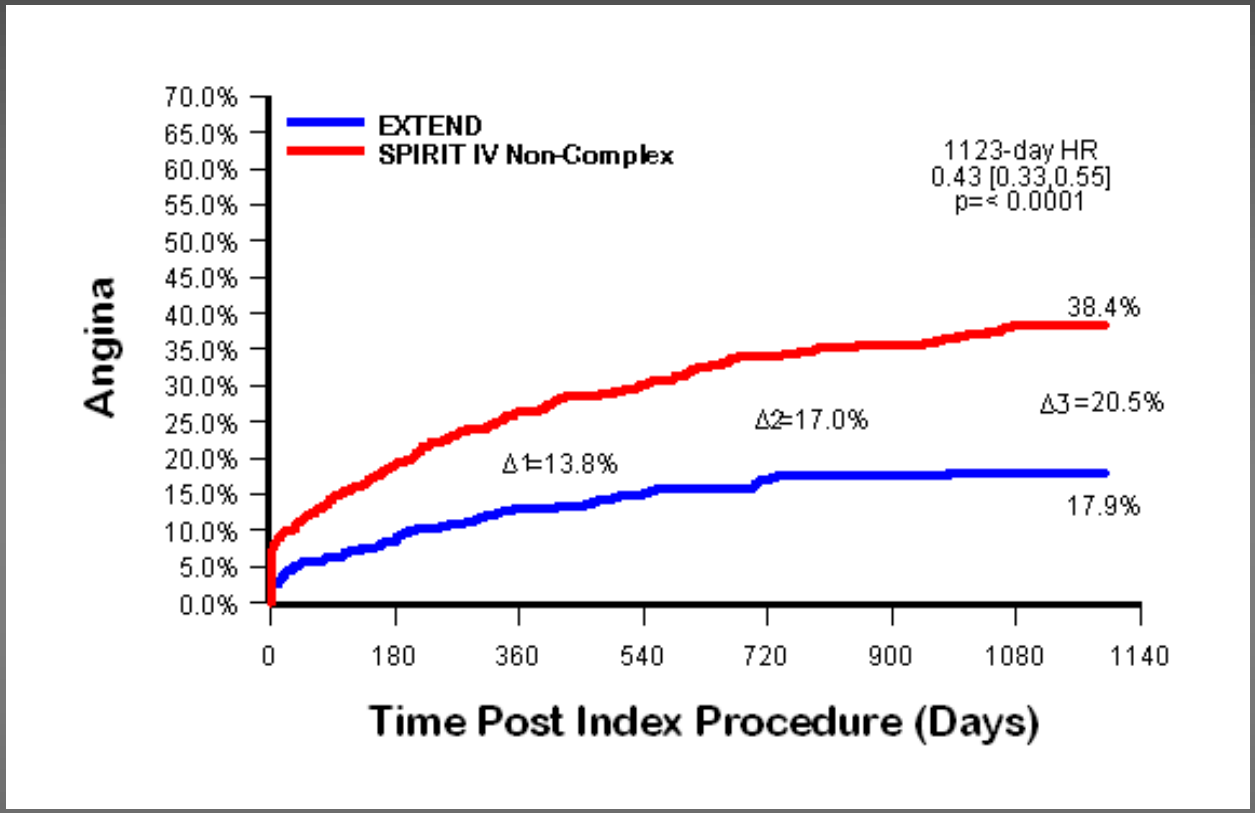
	0	37	194	393	758	1123
ABSORB EXTEND at Risk	174	172	172	169	166	161
XIENCE V (SPI,II,III) at Risk	290	289	284	278	264	260

Propensity Score Matched: ST (def/prob) through 36 Months



	0	37	194	393	758	1123
ABSORB EXTEND at Risk	174	172	172	171	170	168
XIENCE V (SPI,II,III) at Risk	290	290	290	286	277	275

Angina KM Curve Through 3 Years
PS-Matched ABSORB EXTEND and SPIRIT IV Populations*



	0	37	194	393	758	1123
Absorb Extend* *	483	459	437	370	258	111
	1.7%	5.0%	9.5%	13.0%	17.4%	17.9%
SPIV**	483	430	382	340	299	276
	4.6%	11.0%	19.5%	26.8%	34.4%	38.4%
Difference	2.9%	6.0%	10.0%	13.8%	17.0%	20.5%

ABSORB Japan

Prospective, randomized, active control, single-blind, non-inferiority, multi-center Japanese study

Inclusion: Patients with up to 2 *de novo* target lesions in separate native coronary arteries
Lesion length ≤ 24 mm, D_{max} ≥ 2.5 mm to ≤ 3.75 mm, %DS ≥50% to <100%

Randomized 2:1

400

Absorb
Tx. with single study device
266

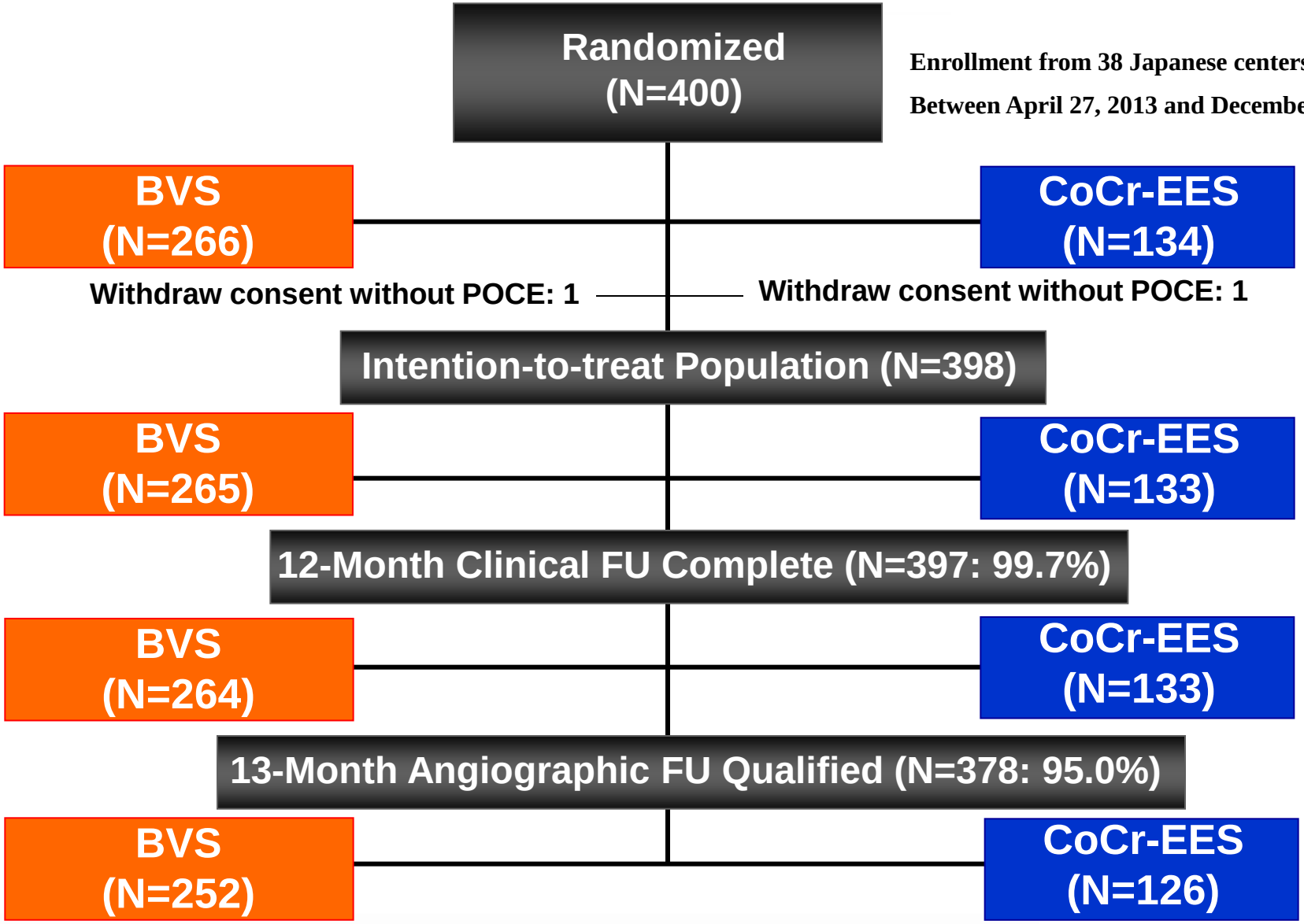
Xience
Tx. with single study device
134

<u>Primary Clinical Endpoint</u>: Target Lesion Failure (TLF): Cardiac death, TV-MI, ID-TLR at 12 months

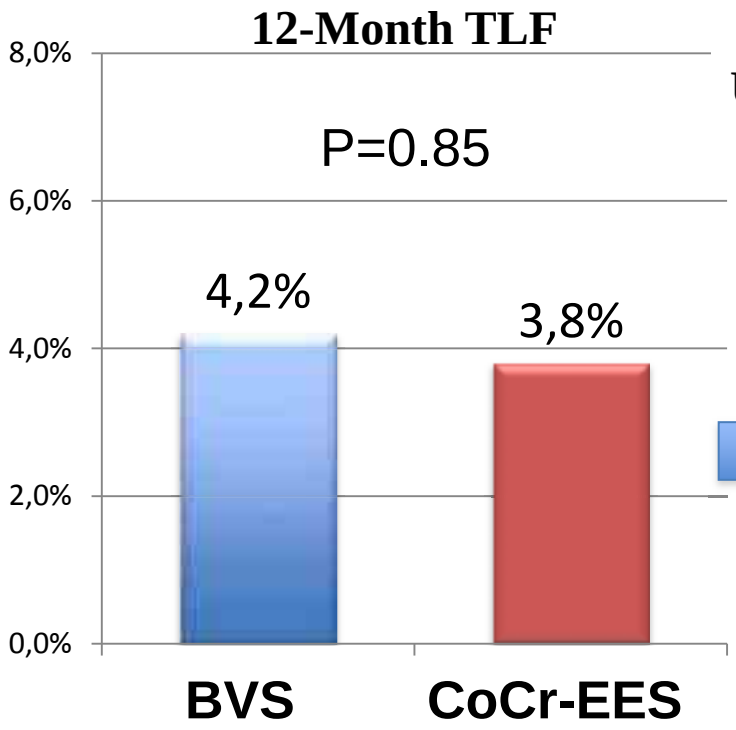
<u>Major Secondary Angiographic Endpoint</u>: In-segment Late Lumen Loss at 13 months

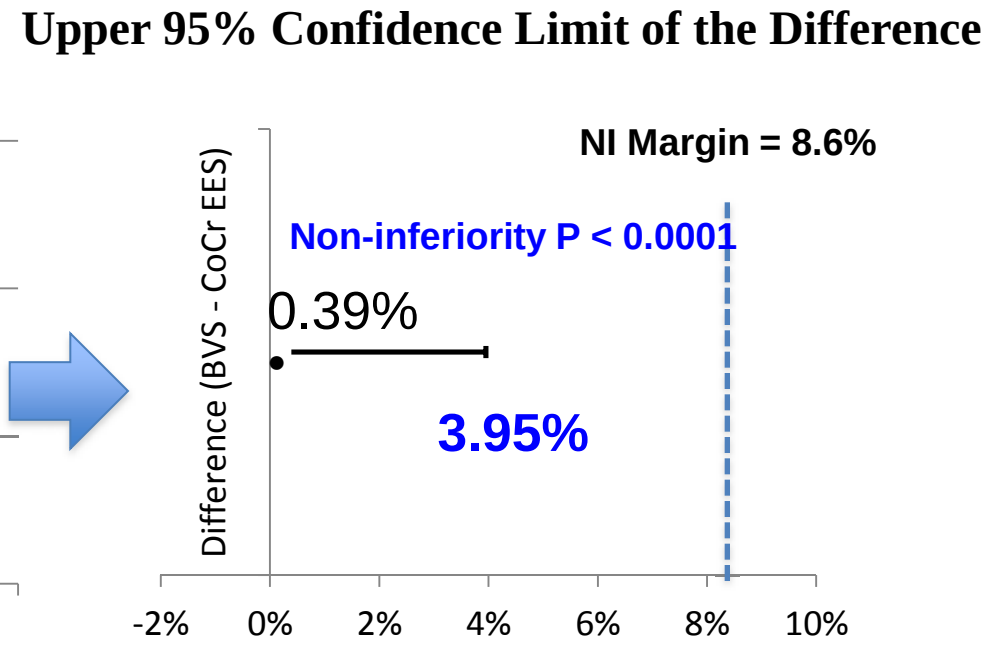
ABSORB Japan

Patient Flow Chart



Primary Endpoint:
12-Month TLF (through 393 days)

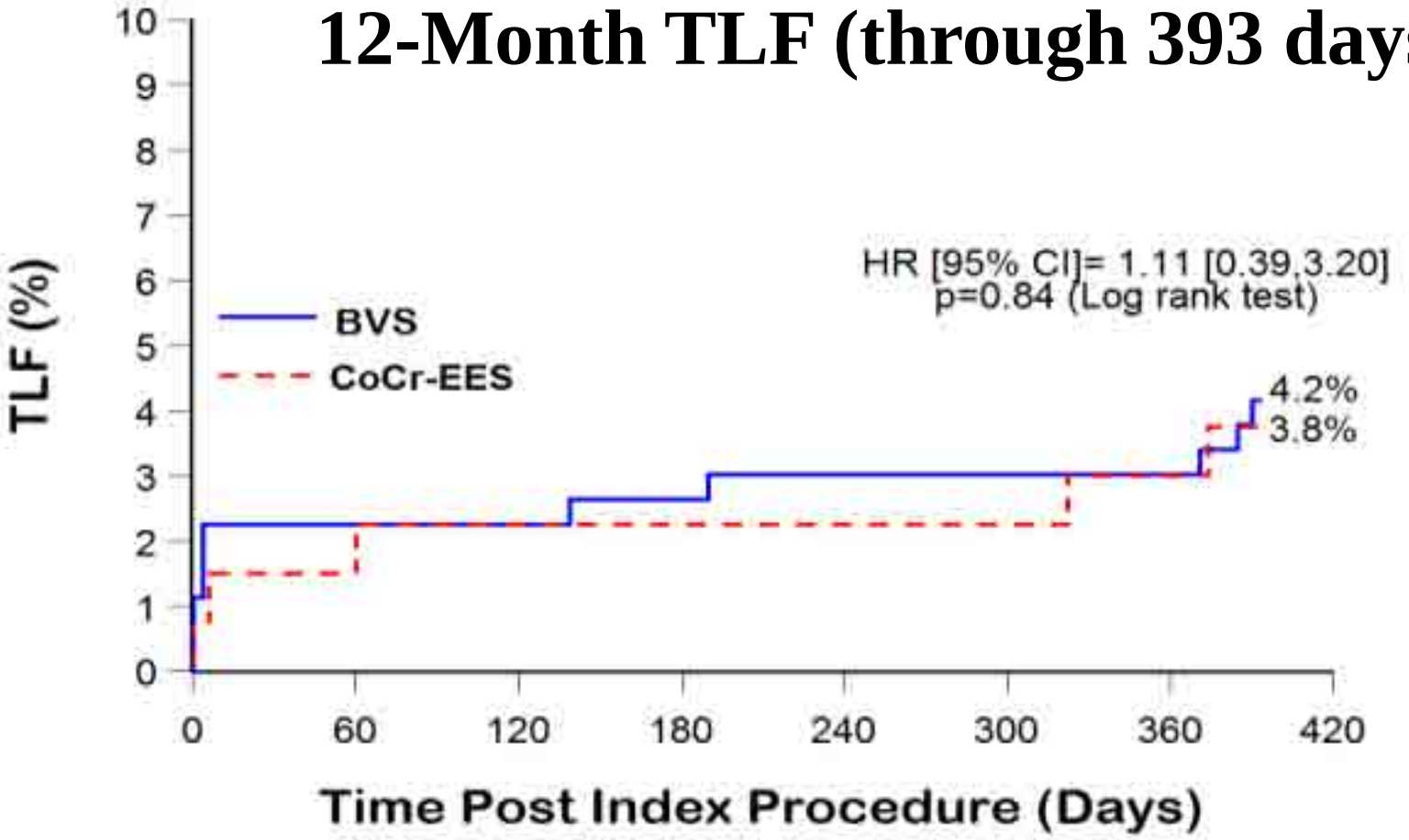




The one-sided upper 95% confidence limit for the 0.39% observed difference in event rates was 3.95%, suggesting that any absolute difference between the 2 devices is likely to be small.

Likelihood score method by Farrington and Manning

Primary Endpoint:
12-Month TLF (through 393 days)

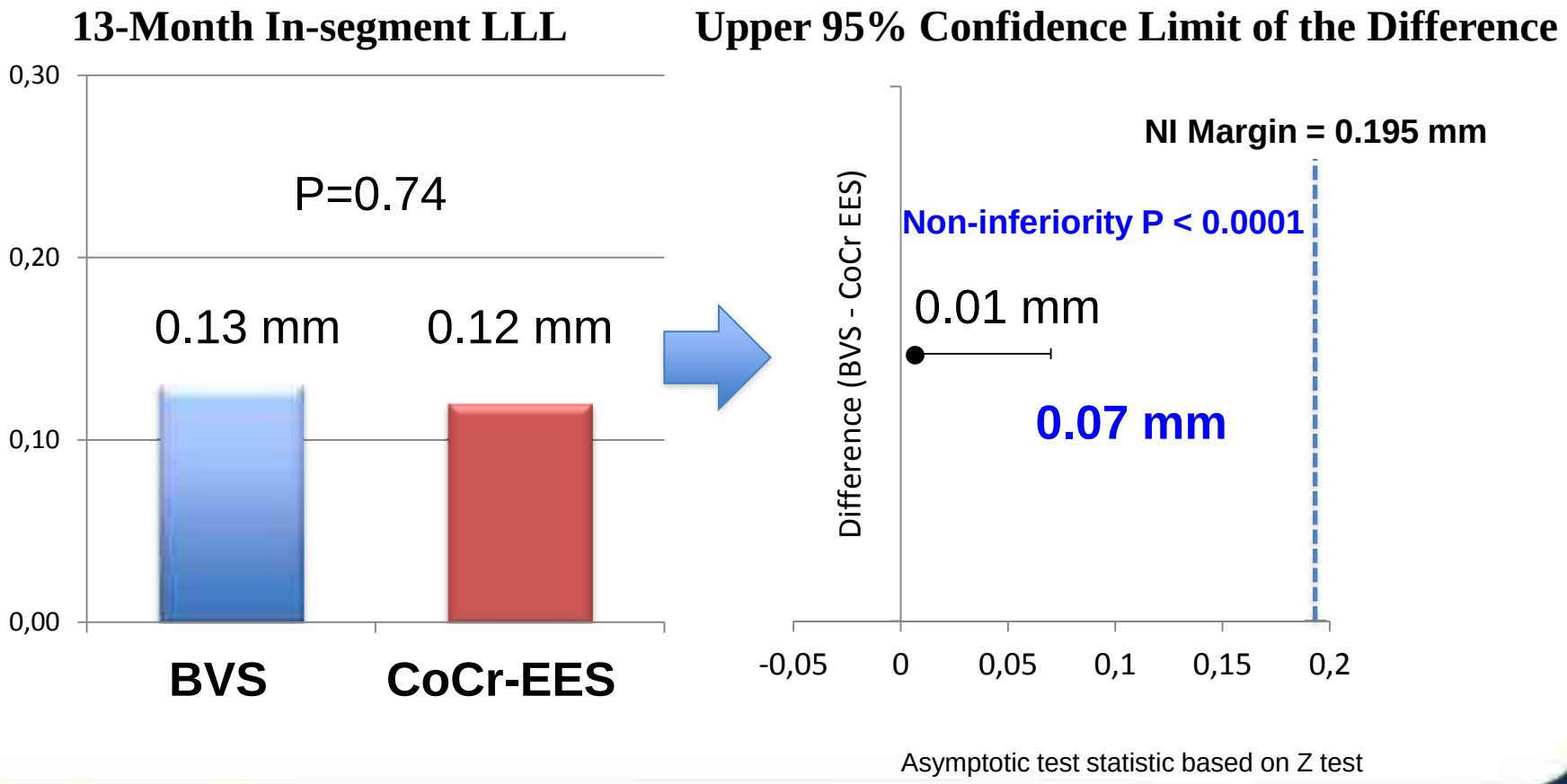


	0 days	37 days	208 days	393 days
BVS at Risk	266	259	256	251
CoCr-EES at Risk	134	131	130	128

12-Month Clinical Outcomes (~393-Day)

	BVS (N=266)	CoCr-EES (N=134)	P-value
TLF (CD/TV-MI/ID-TLR)	4.2% (11/265)	3.8% (5/133)	0.85
- Cardiac Death	**0.0% (0/265)**	**0.0% (0/133)**	**1.00**
- Target Vessel MI	**3.4% (9/265)**	**2.3% (3/133)**	**0.76**
- Ischemia driven-TLR	**2.6% (7/265)**	**2.3% (3/133)**	**1.00**

Major Secondary Angiographic Endpoint: 13-Month In-Segment LLL



Asymptotic test statistic based on Z test

Bioresorbable Scaffolds

Igaki-Tamai		PLLA
Abbott Absorb		PLLA Everolimus
Elixir DESolve		PPLLA based Novolimus
REVA REsolve		Tyrosine- Policarbonate Sirolimus
Biotronik Dreams		Magnesium Sirolimus
Amaranth		PLLA resin

Which patients?

Conclusões

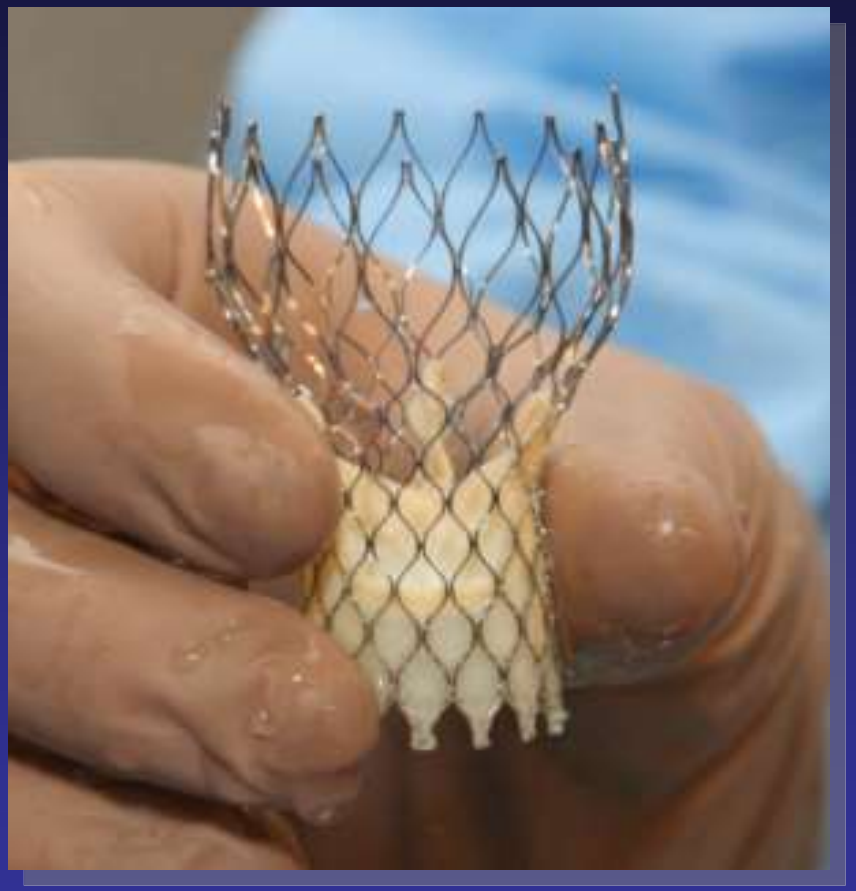
- Uma nova era na cardiologia intervencionista começou....
- Algumas limitações parecem ter sido contornadas (força radial, retração elástica aguda e crônica, retauração da vasomotricidade) .
- Estudos randomizados com maior número de pacientes serão necessários para determinarmos o real benefício destes novos dispositivos

Futuro da Cardiologia Intervencionista

- Intervenções Coronárias:
  - Stents bioabsorvíveis
- Intervenções estruturais:
  - Estenose Aórtica
  - Insuf. Mitral
  - Leak paravalvar
  - Defeitos congênitos
  - Endovascular
  - Denervação renal

Percutaneous Aortic Valve Replacement

Cribier-Edwards Prosthesis



CoreValve Prosthesis

Critérios (segurança / eficácia)

- **Doença em Valva Aortica nativa -** (protese biológica)
- **EAo severa com area valvar ≤ 0,8 cm^2**
- **Anel valvar ≥ 19 e ≤ 29 mm** (18 -30 mm)
- **Junção sino tubular ≤ 43 mm e coronárias >10mm de altura**

Idade ≥ 80 a

EuroScore logístico ≥ 15% ou STS score > 8

Idade ≥ 65 a

1 ou +

Cirrose hepática
Insuf. Pulmonar
Cirurgia cardica prévia
Torax ostil
Falencia de VD
Doença do tecido conectivo , etç

Risco Intermediário
STS score entre 4 e 8

Protocolo TAVI

- Seleção de casos baseada em:

  História clínica

  Comorbidades

  Medidas anatômicas não invasivas (características anatômicas e morfológicas): Seleção do tamanho adequado da prótese. Eco e Tomo

  Medidas invasivas - Cinecoronariografia

  EuroScore/STS

Preparo para o procedimento

- Escolha da prótese apropriada baseada nos critérios anatômicos.
- Dose de ataque de clopidogrel e aspirina. Clopidogrel por 6 meses.
- Profilaxia anti-microbiana periprocedimento. (cefalosporina)
- Passagem de eletrodo de marcapasso temporário.

Inoperable PARTNER Cohort
Primary Endpoint: All-Cause Mortality

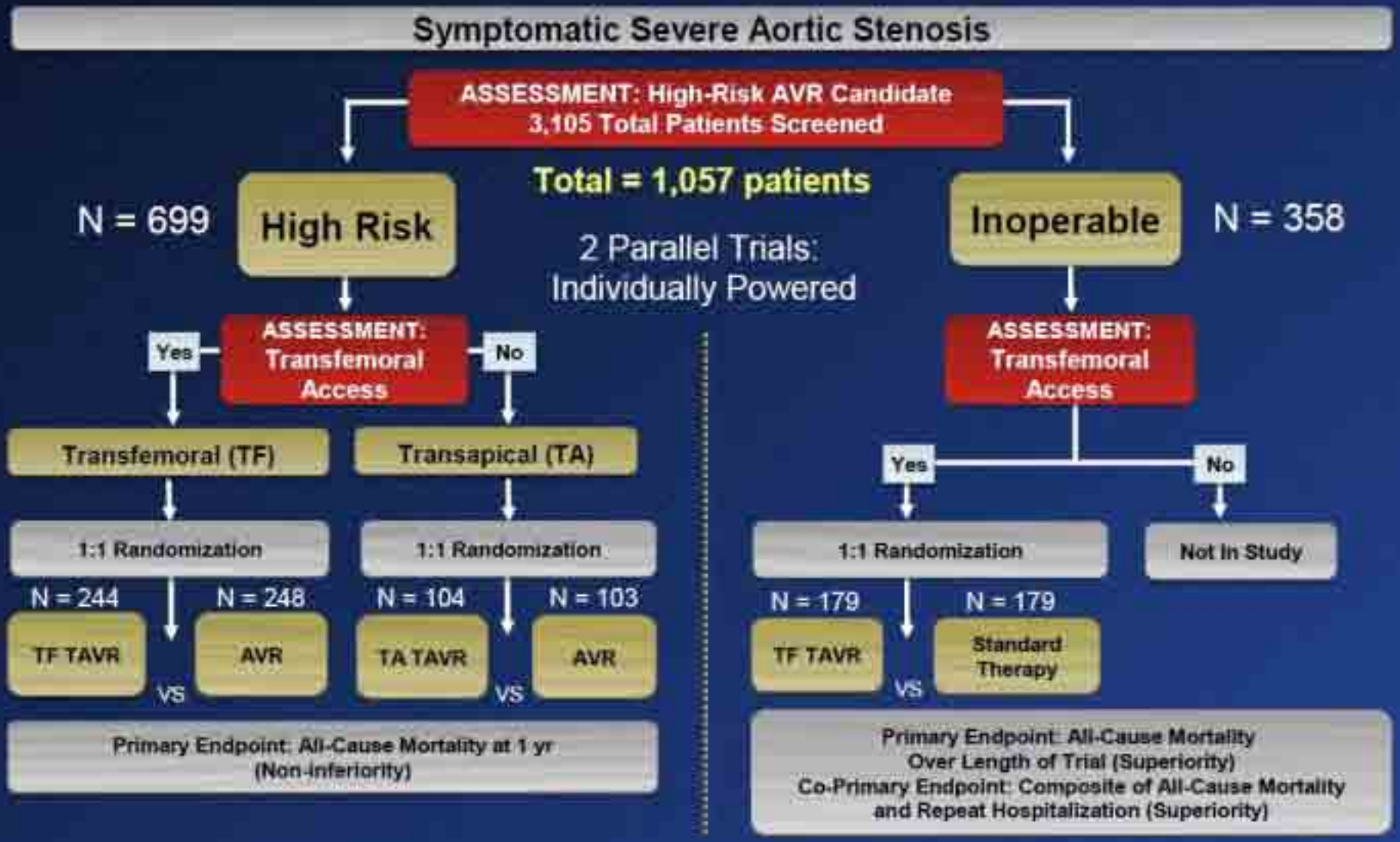
The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

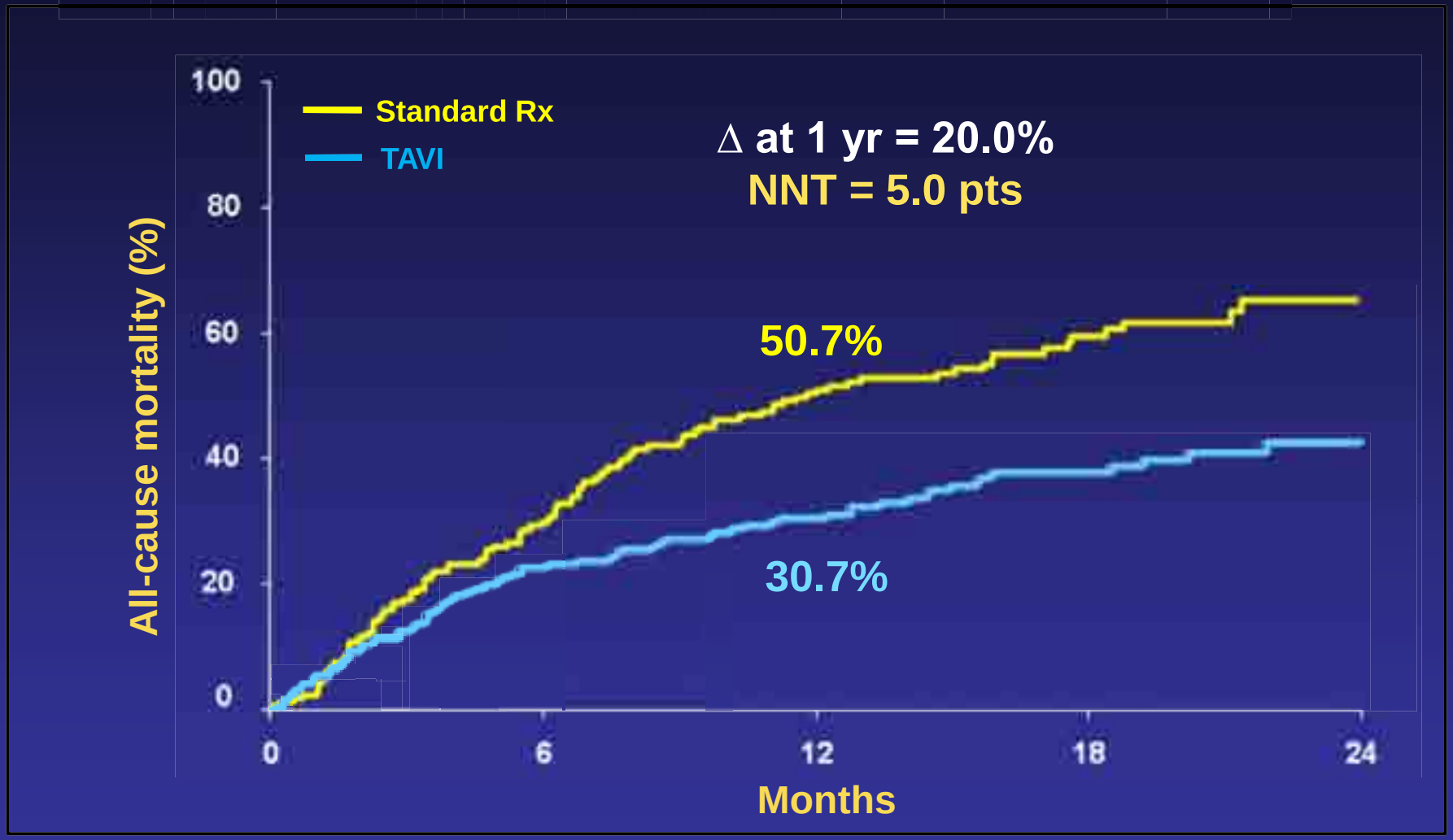
Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela C. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

Numbers at Risk					
TAVI	179	138	122	67	26
Standard Rx	179	121	83	41	12

PARTNER Study Design



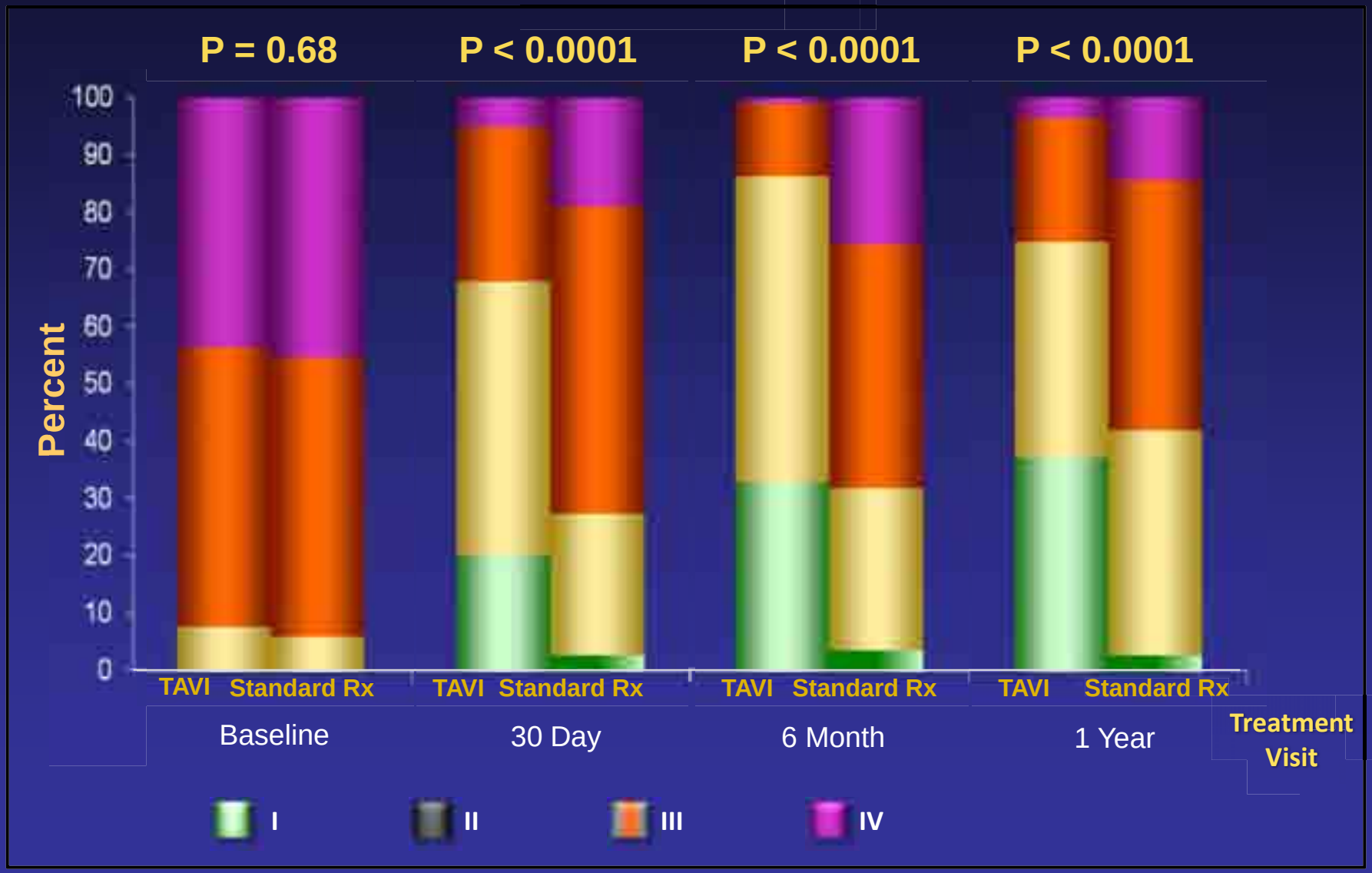
1ry Endpt - All Cause Mortality



Numbers at Risk					
TAVI	179	138	122	67	26
Standard Rx	179	121	83	41	12

NYHA Class Over Time

Survivors



Study Flow


Randomized = 699 patients
Transfemoral
n = 492
TF = 492
TA = 207
Transapical
n = 207
TAVR (244)
AVR (248)
TAVR (104)
AVR (103)
30 Days (236)
Dead = 8
Withdrawal = 0
30 Days (223)
Dead = 15
Withdrawal = 10
30 Days (100)
Dead = 4
Withdrawal = 0
30 Days (92)
Dead = 7
Withdrawal = 4
1 Year (189)
Dead = 46
Withdrawal = 1
1 Year (168)
Dead = 47
Withdrawal = 8
1 Year (73)
Dead = 26
Withdrawal = 0
LTFU = 1
1 Year (68)
Dead = 20
Withdrawal = 3
LTFU = 1

All-Cause Mortality
Transfemoral (N=492)

No. at Risk					
TAVR	244	215	188	119	59
AVR	248	180	168	109	56

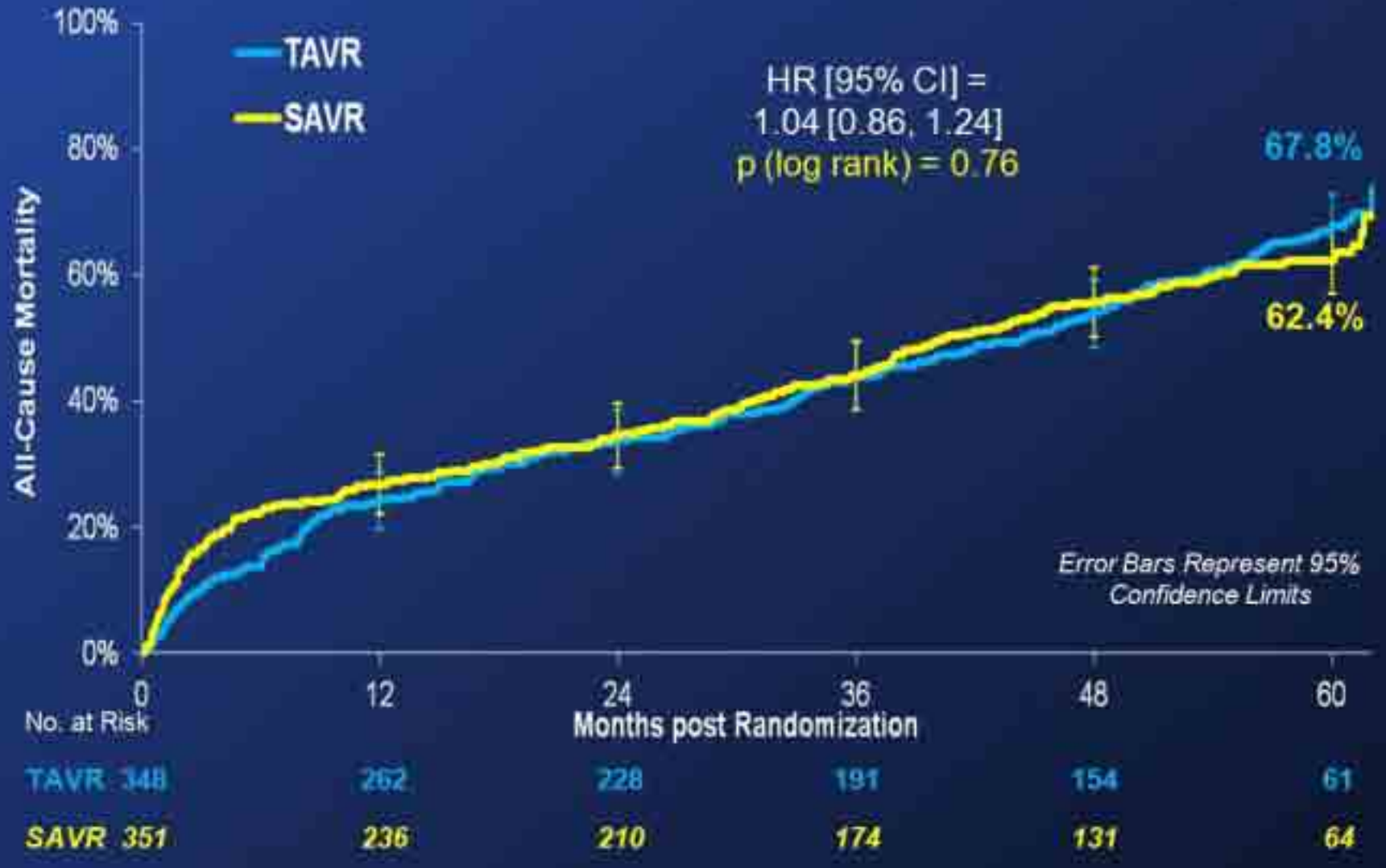
Five-Year Outcomes after Randomization to Transcatheter or Surgical Aortic Valve Replacement: Final Results of The PARTNER 1 Trial

Michael J. Mack, MD
on behalf of The PARTNER Trial Investigators

ACC 2015 | San Diego | March 15, 2015

All-Cause Mortality (ITT)

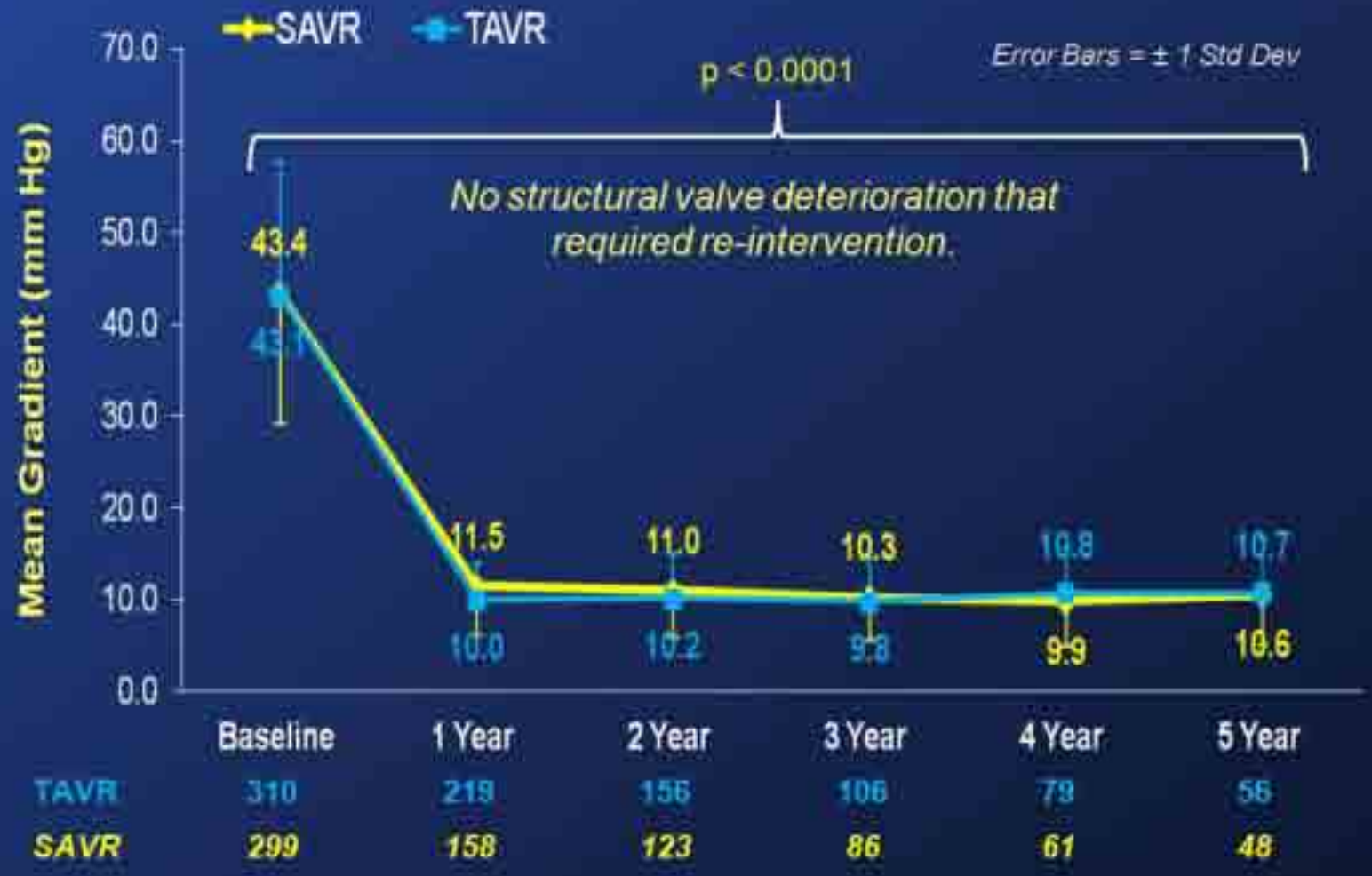
All Patients



Cardiovascular Mortality (ITT)

All Patients

Aortic Valve Mean Gradient

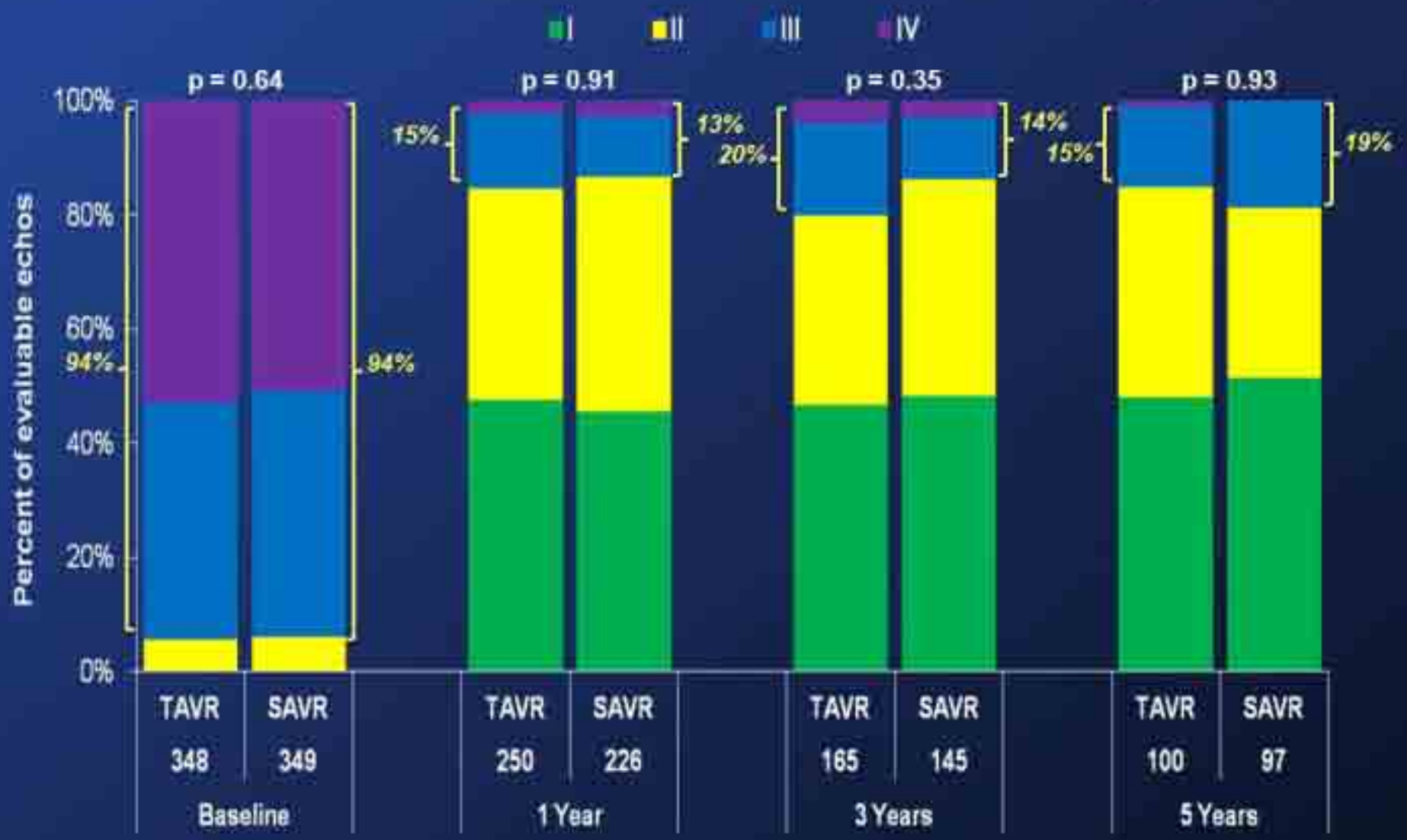


All Stroke (ITT)

All Patients

NYHA Over Time (ITT)

Survivors



Summary

- At five years in The PARTNER 1A Trial of high surgical risk patients with severe aortic stenosis randomized to TAVR or SAVR there was no significant difference in:
  - All-Cause and Cardiovascular Mortality
  - Strokes
  - NYHA Class
  - Rehospitalization
  - Valve Hemodynamics
- No structural valve deterioration requiring re-intervention in TAVR patients.
- The presence of ≥ mild paravalvular leak is associated with decreased survival.

CoreValve US Pivotal Trial

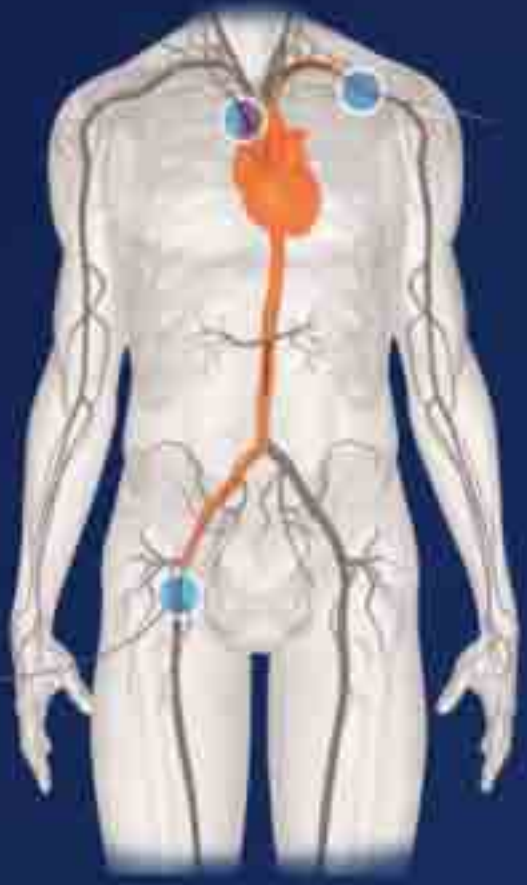
A Randomized Comparison of Self-expanding Transcatheter and Surgical Aortic Valve Replacement in Patients with Severe Aortic Stenosis Deemed at Increased Risk for Surgery
2-Year Outcomes

Michael J Reardon, MD, FACC
On Behalf of the CoreValve US Investigators

Study Device and Access Routes

4 Valve Sizes (23, 26, 29, 31 mm)
(18-29 mm Annular Range)

18F Delivery System



Transfemoral
Subclavian
Direct Aortic

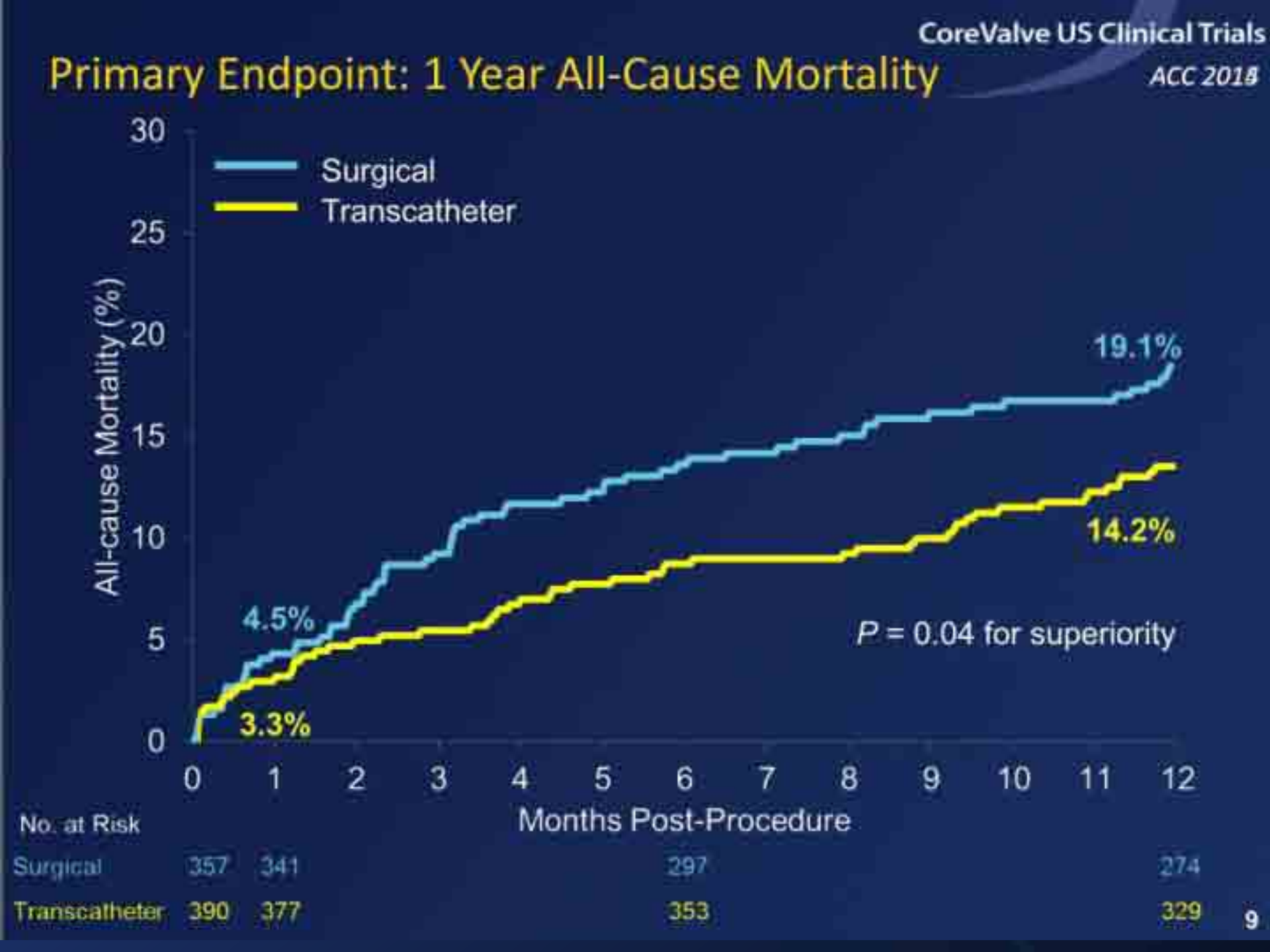
Primary Endpoint

Primary Endpoint: All-cause mortality at 1 year

Non-inferiority Testing: TAVR with the CoreValve bioprosthesis was non-inferior to SAVR for 1 year all-cause mortality with a 7.5% non-inferiority margin

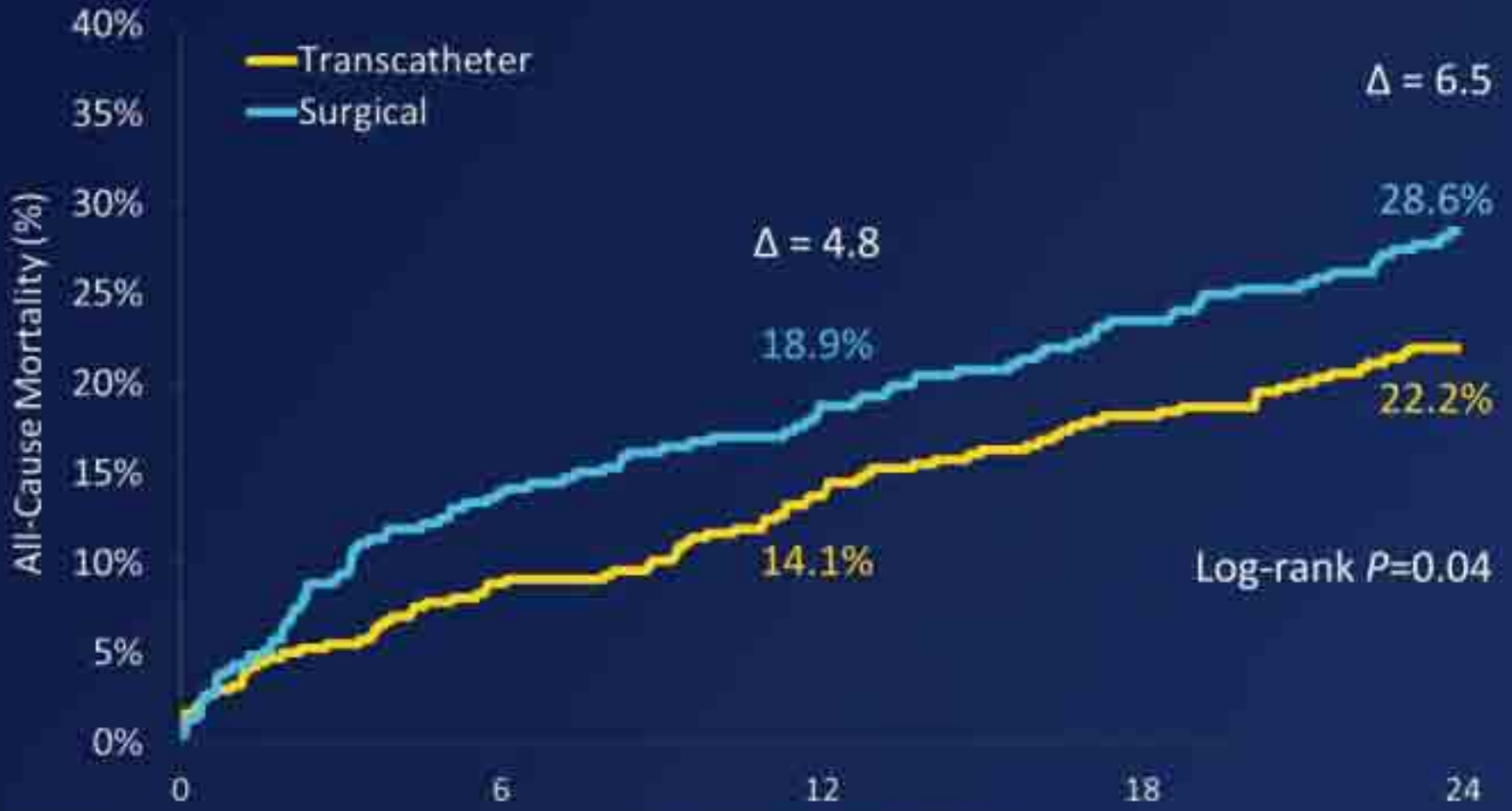
Superiority Testing: If the primary endpoint was met at the 1-sided 0.05 level, a subsequent test for superiority was performed at the 1-sided 0.05 level

Primary Endpoint: 1 Year All-Cause Mortality



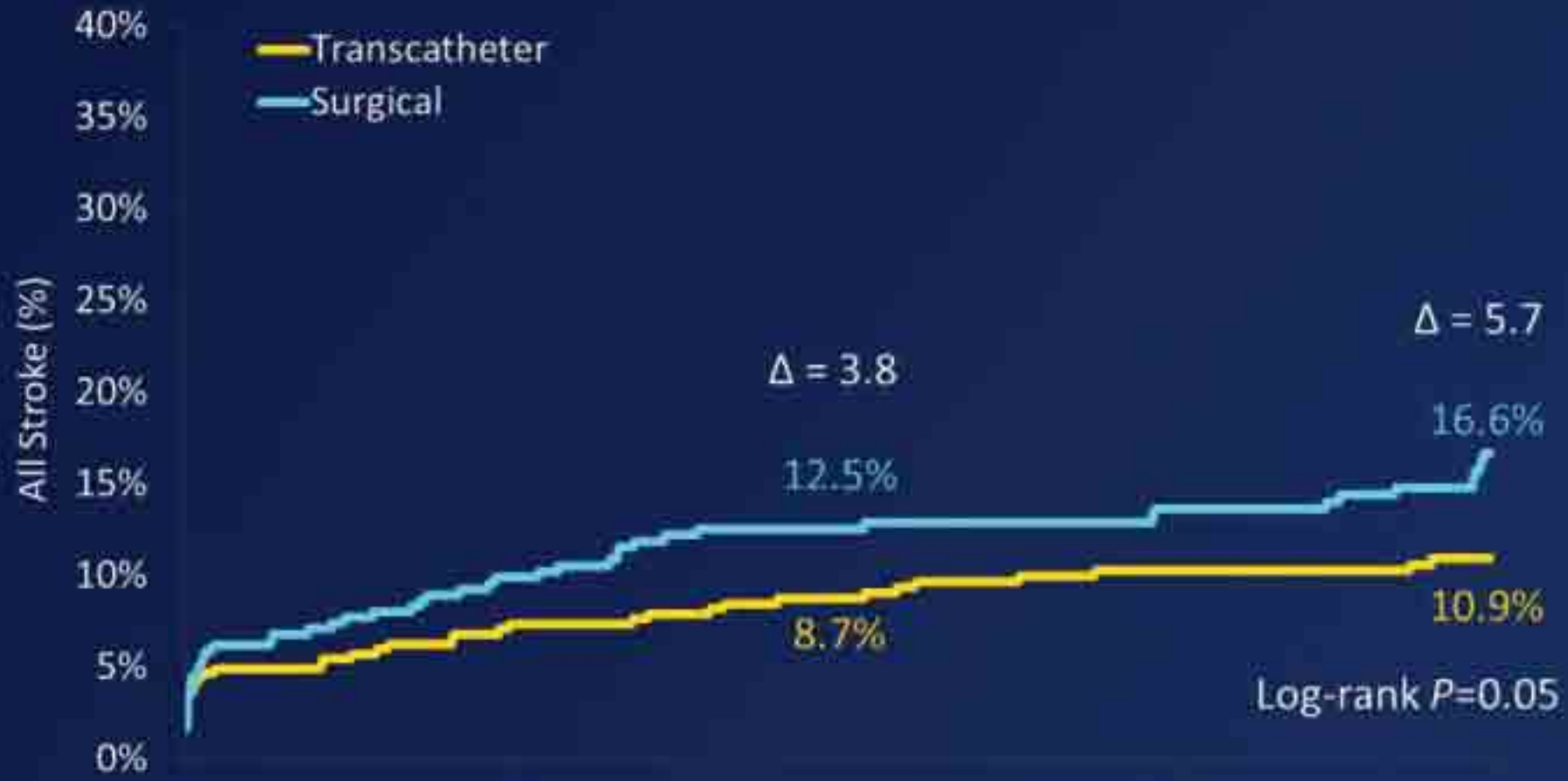
CoreValve US Pivotal Trial
High Risk 2-Year Results

All-Cause Mortality



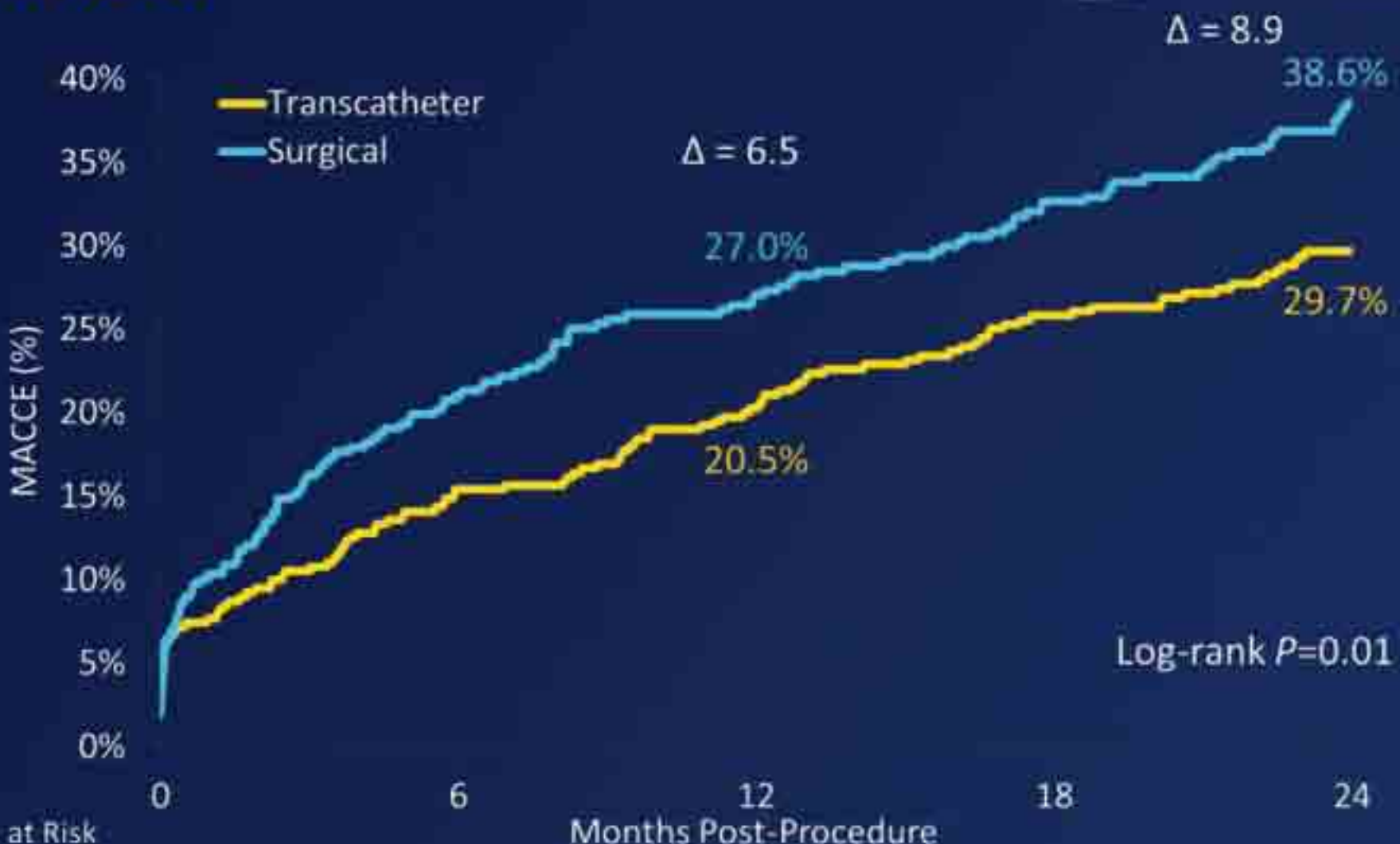
No. at Risk					
Transcatheter	391	378	354	334	219
Surgical	359	343	304	282	191

All Stroke



No. at Risk					
Transcatheter	391	364	335	318	205
Surgical	359	324	281	256	169

MACCE



No. at Risk					
Transcatheter	391	361	329	309	197
Surgical	359	322	280	254	166

All-Cause Mortality STS ≤7%

Conclusions

At 2 years for patients with symptomatic severe AS at increased risk of surgery;

- The superior survival seen at 1 year for TAVR over SAVR is maintained
- All stroke was less with TAVR over SAVR but major stroke showed no difference
- MACCE was significantly less with TAVR over SAVR
- Hemodynamics were superior for TAVR over SAVR at all time points without any structural valve failure
- Post-procedural AR showed a decrease in the TAVR group between 30 days and 1 year and this low level of moderate or severe PVL was maintained at 2 years
- TAVR was favored in every subgroup analysis

Clinical and Echocardiographic Outcomes at 30 Days with the SAPIEN 3 TAVR System in Inoperable, High-Risk and Intermediate-Risk AS Patients

Susheel Kodali, MD
on behalf of The PARTNER Trial Investigators

ACC 2015 | San Diego | March 15, 2015

Evolution of the Edwards Balloon-Expandable Transcatheter Valves

Cribier-Edwards

2002

SAPIEN

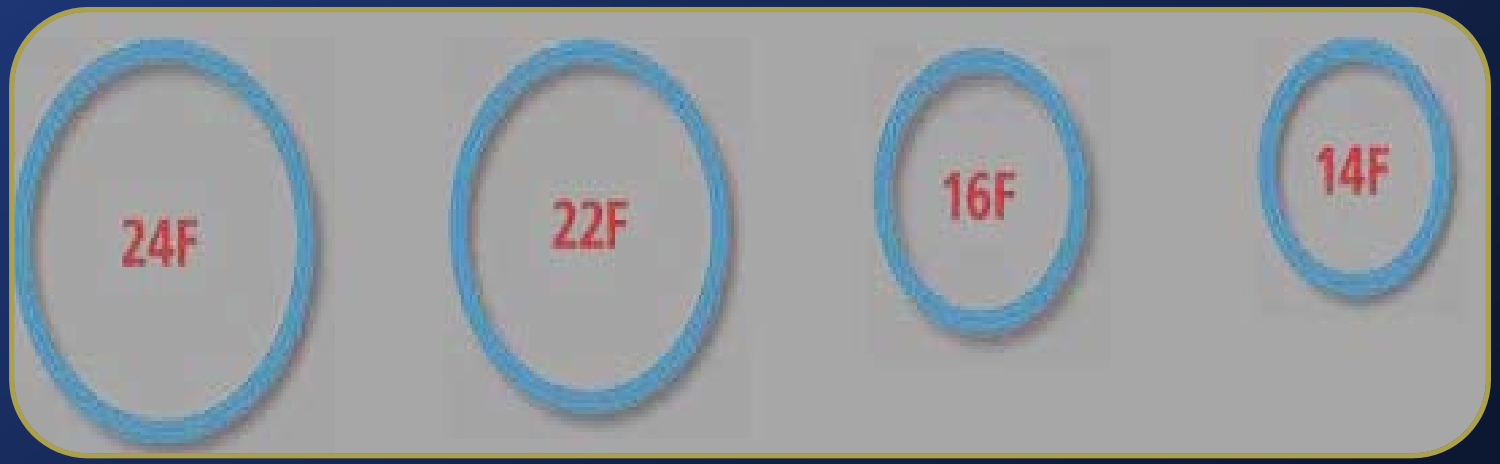
2006

SAPIEN XT

2009

SAPIEN 3

2013



** Sheath compatibility for a 23 mm valve*

The PARTNER II S3 Trial

Purpose

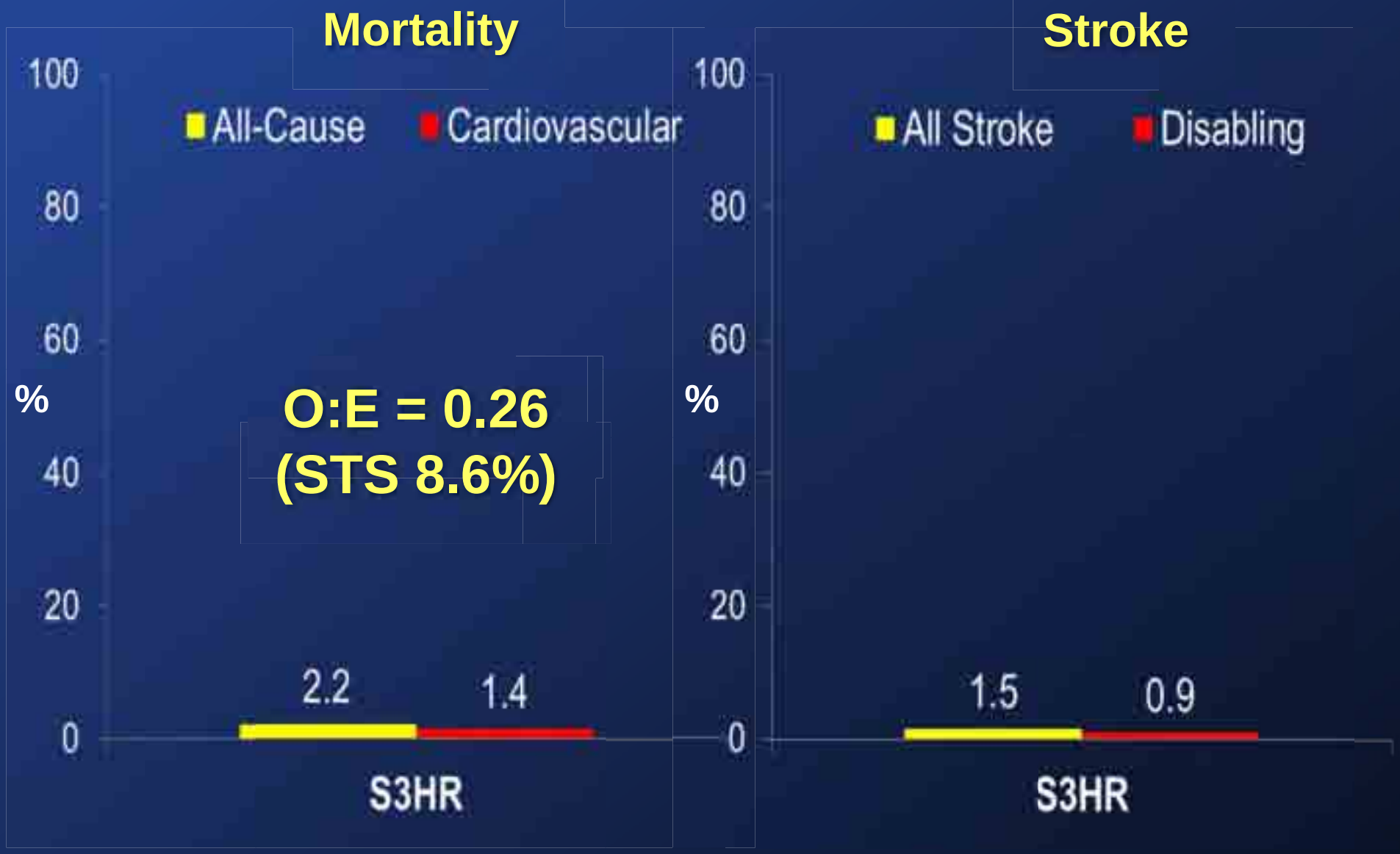
To evaluate the safety and efficacy of the SAPIEN 3 transcatheter heart valve system at 30 days in inoperable, high-risk, and intermediate-risk patients.

Study Flow: S3HR & S3i

30 Day Patient Status

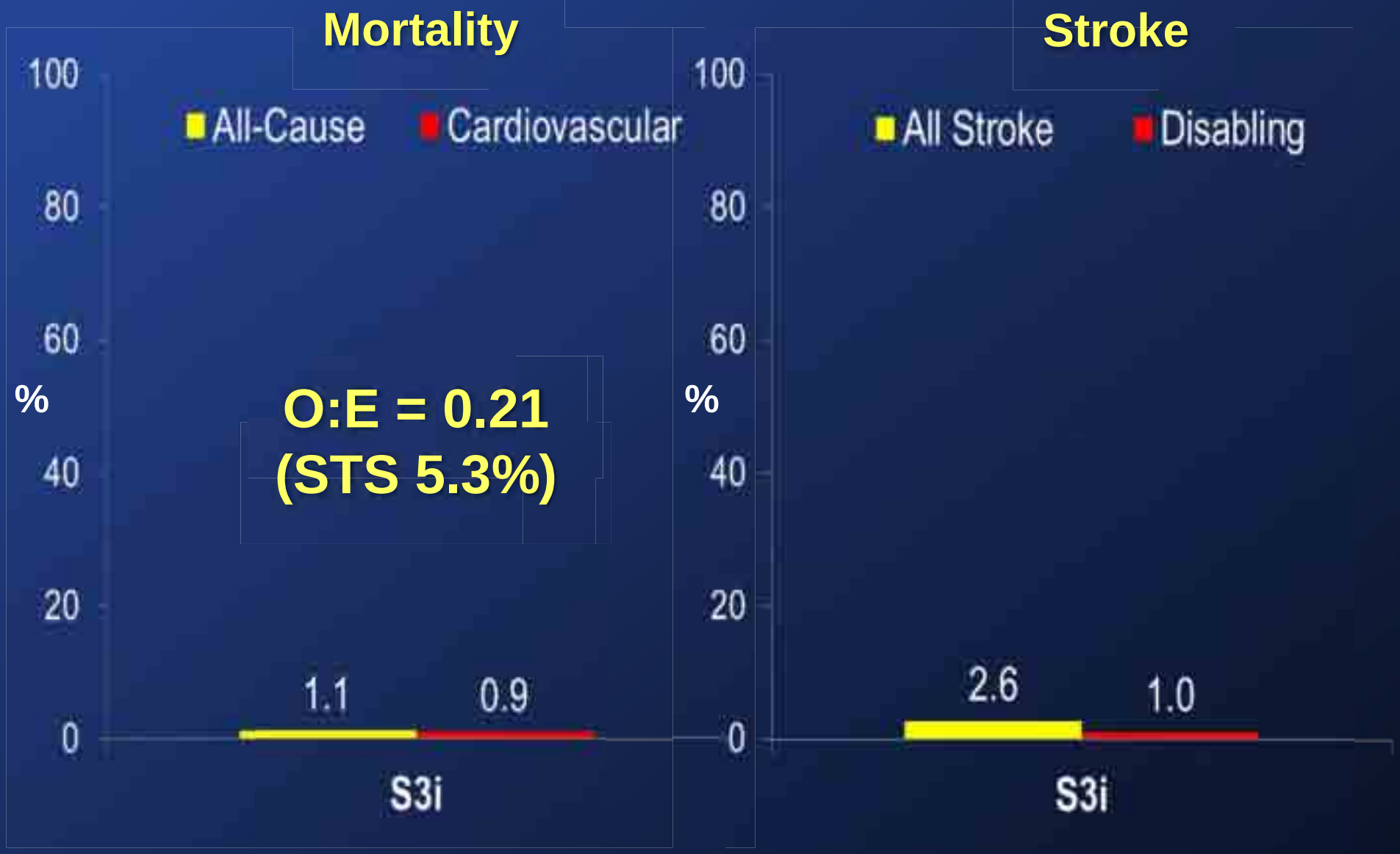
Mortality and Stroke: S3HR

At 30 Days (As Treated Patients)



Mortality and Stroke: S3i

At 30 Days (As Treated Patients)



Mortality: S3HR & S3i

At 30 Days (As Treated Patients)

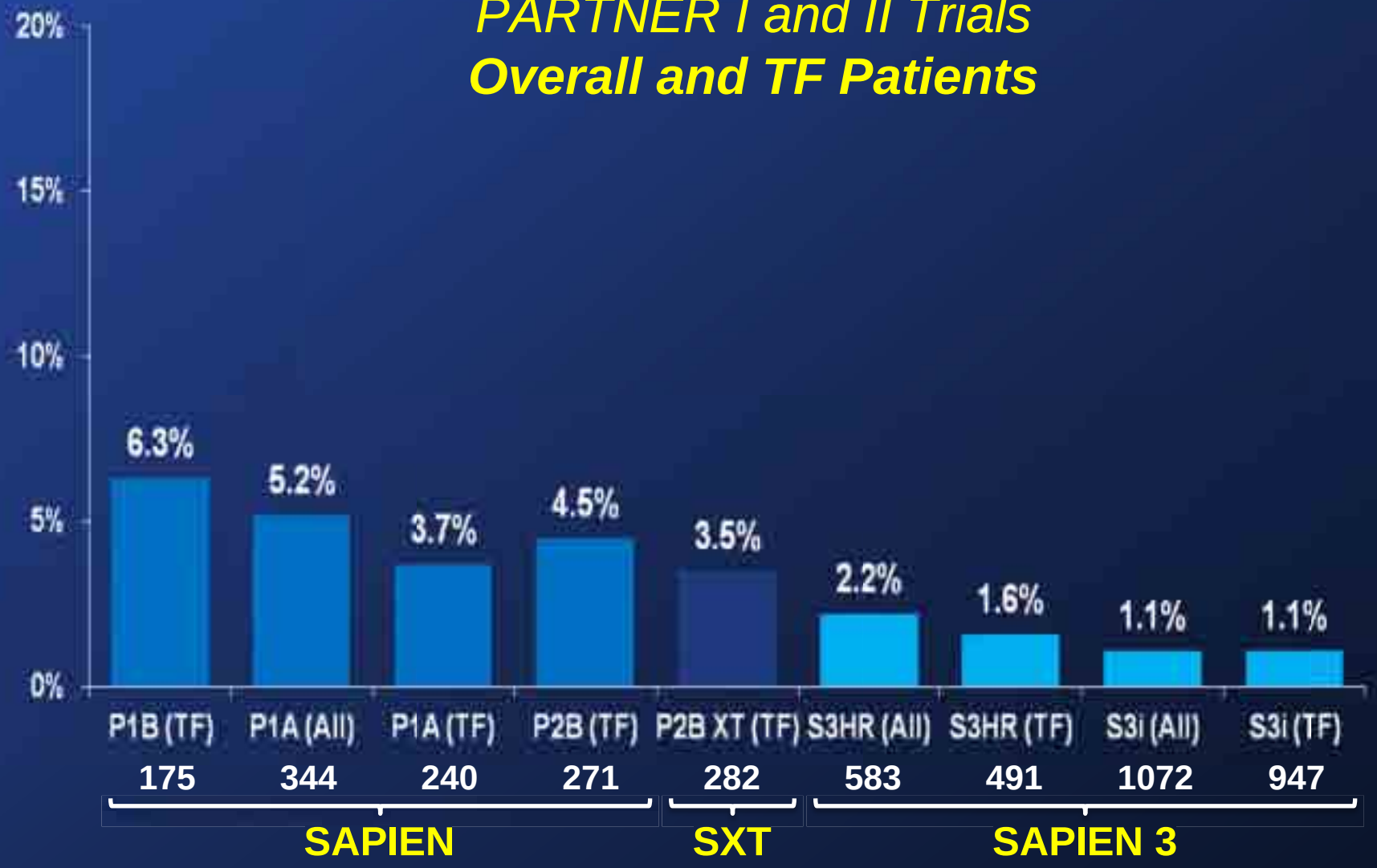
All-Cause Mortality at 30 Days

Edwards SAPIEN Valves (As Treated Patients)

THE PARTNER TRIAL

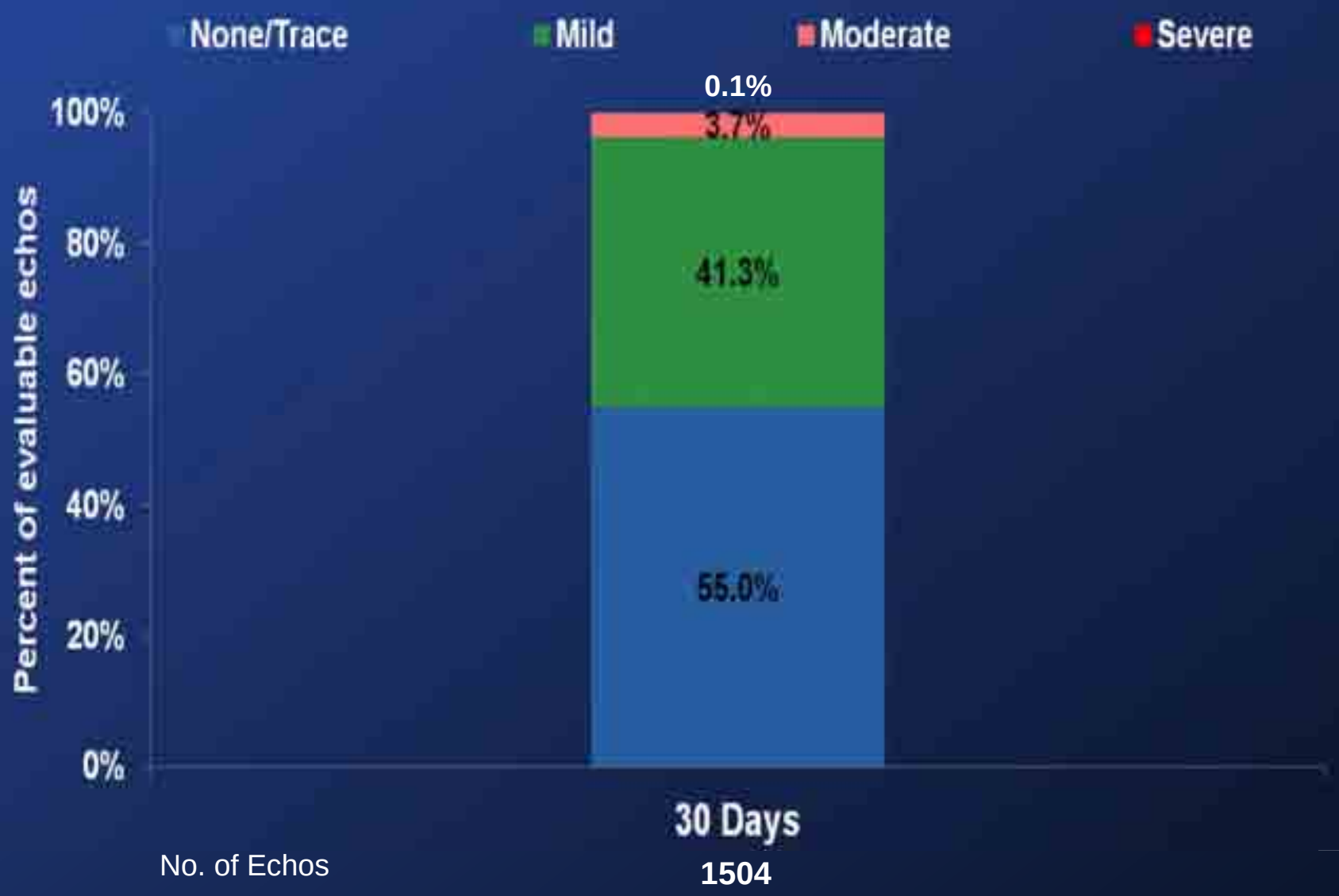
PARTNER I and II Trials

Overall and TF Patients



Paravalvular Leak: S3HR & S3i

(Valve Implant Patients)



Conclusions (1)

- In high-risk and inoperable patients (S3HR), the SAPIEN 3 TAVR system demonstrated low mortality and stroke and excellent clinical outcomes at 30 days:
  - **Mortality:** 2.2% (TF 1.6%, TA/TAo 5.4%)
  - **Disabling Stroke:** 0.9%
- In intermediate-risk patients (S3i), SAPIEN 3 was associated with strikingly low mortality and strokes at 30 days:
  - **Mortality:** 1.1% (TF 1.1%, TA/TAo 1.6%)
  - **Disabling Stroke:** 1.0%

Conclusions (2)

- Other important clinical findings with SAPIEN 3 (both S3HR & S3i) include:
  - **Major vascular complications:** ~5%
  - **Annular rupture:** ~0.2%
  - **Coronary obstruction:** ~0.3%
  - **New pacemakers:** ~10%
- Significant paravalvular regurgitation with SAPIEN 3 (both S3HR & S3i) was rare:
  - **Severe:** 0.1%
  - **Moderate:** 3.7%

New TAVI systems

Before…

Medtronic CoreValve

Edwards Sapien XT

…Today.

Edwards Centera

Boston Sci. Lotus™

HLT

Medtronic Engager

Saint Jude Portico™

Direct Flow

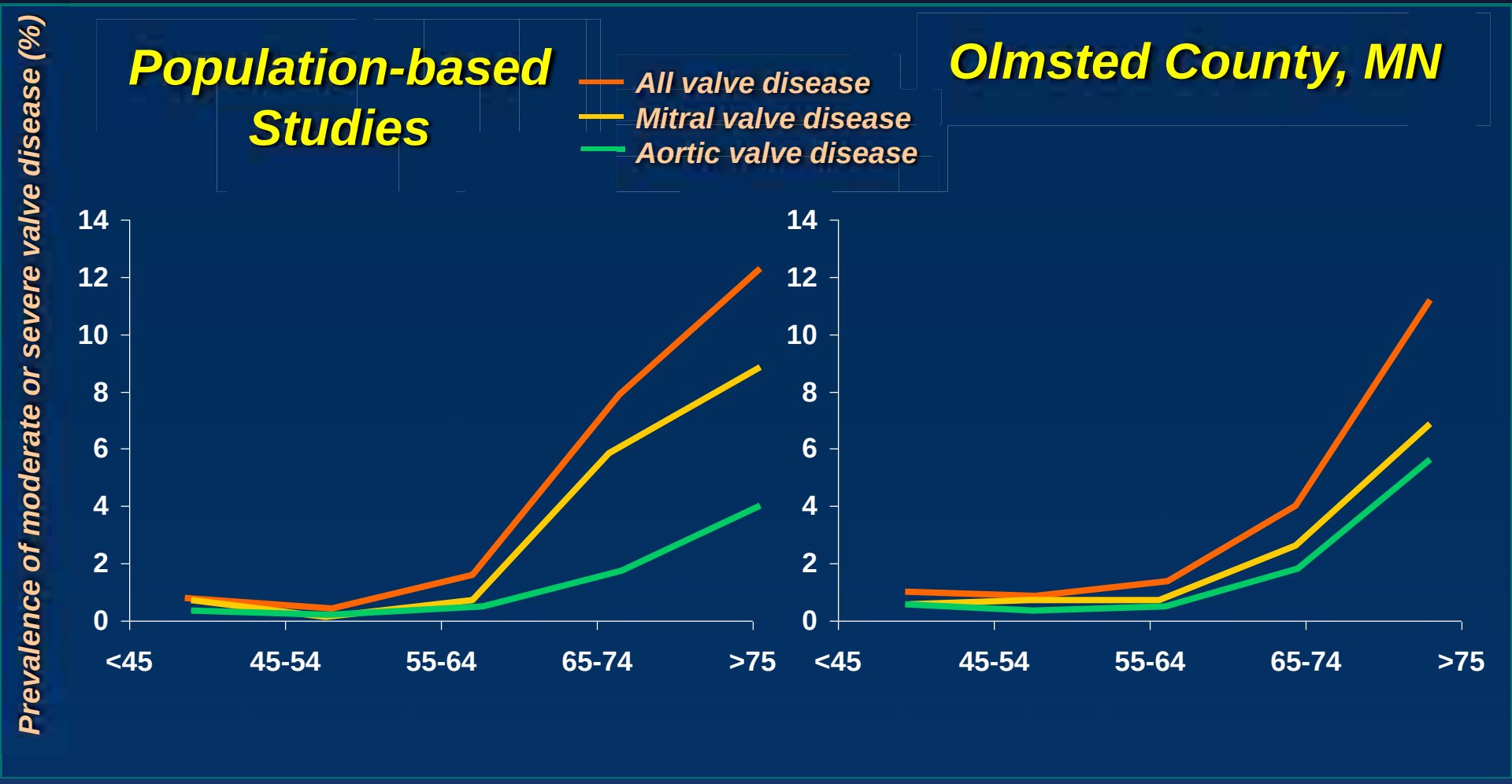
Braile Biom. Inovare

JenaValve

Symetis ACCURATE

MitraClip

Increasing Prevalence of Valvular Heart Disease in the Elderly



Tratamento Percutâneo da Insuficiência Mitral por MITRACLIP

Catheter-Based Mitral Valve Repair

MitraClip® System

Mitral Regurgitation Functional vs. Degenerative

- **Degenerative mitral regurgitation: Primary valve disorder due to mitral valve prolapse spectrum; mechanism of MR typically due to ruptured/elongated chords**

- **Functional mitral regurgitation: Results from distortion of the** mitral valve apparatus secondary to abnormal left ventricular function (CAD or myopathy); Normal leaflet morphology

EVEREST II Randomized Clinical Trial

Study Design

279 Patients enrolled at 37 sites

Significant MR (3+/4+)

Randomized 2:1

Device Group
MitraClip System
N=184

Control Group
Surgical Repair or Replacement
N=95

Echocardiography and Clinical Follow-Up:
Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years

Feldman, T. NEJM 2011

Baseline Demographics & Co-morbidities

Intention to Treat

Patient Demographics	Percutaneous % N=184	Surgery % N=95	P-value
Degenerative MR Etiology	73	73	0.81
Anterior leaflet involvement (prolapse or flail)	31	26	-
Posterior leaflet involvement only (prolapse or flail)	39	45	-
Neither prolapse nor flail (thickened leaflets)	3	2	-
Functional MR Etiology	27	27	0.81
NYHA Functional Class III/IV	51	47	0.61
MR Severity: 3+ to 4+	96	93	0.48
Mean Ejection Fraction (%)	60	61	0.65
Mean LVIDs (cm)	3.7	3.5	0.16

Safety Endpoint: 30 Day MAE

Intention to Treat

30 Day MAE	# (%) Patients experiencing event	
	Percutaneous (N=180)	Surgery (N=94)
Death	2 (1.1%)	2 (2.1%)
Major Stroke	2 (1.1%)	2 (2.1%)
Re-operation of Mitral Valve	0	1 (1.1%)
Urgent / Emergent CV Surgery	4 (2.2%)	4 (4.3%)
Myocardial Infarction	0	0
Renal Failure	1 (0.6%)	0
Deep Wound Infection	0	0
Ventilation > 48 hrs	0	4 (4.3%)
New Onset Permanent Atrial Fib	2 (1.1%)	0
Septicemia	0	0
GI Complication Requiring Surgery	2 (1.1%)	0
Transfusions ≥ 2 units	24 (13.3%)	42 (44.7%)
TOTAL % of Patients with MAE	**15.0%**	**47.9%**

Difference (Percutaneous – Surgery) = -32.9%

p<0.001; (95% CI: -20.7%, -45.0%)

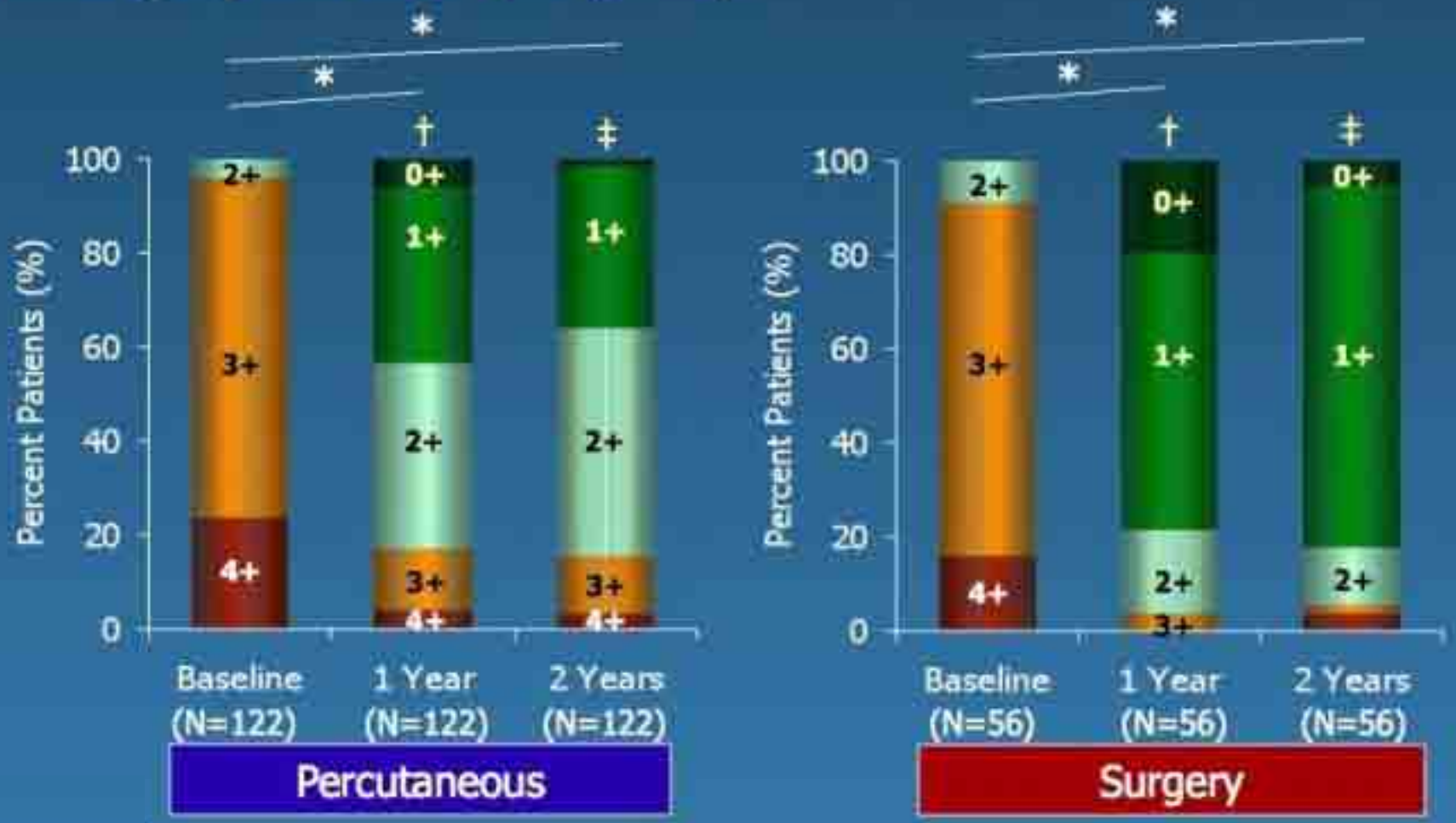
Freedom From Death, Surgery/ Re-operation for Valve Dysfunction or 3+ or 4+ MR

Intention to Treat Analysis

Components of Failure	Percutaneous		Surgery		P-value Percutaneous vs Surgery at 2 years
	1 Year N=181	2 Years N=172	1 Year N=89	2 Years N=83	
Death	11 (6.1%)	19 (11.0%)	5 (5.6%)	9 (10.8%)	>0.999
MV Surgery / Re-operation	37 (20.4%)	38 (22.1%)	2 (2.2%)	3 (3.6%)	<0.001
3+ or 4+ MR *	38 (21.0%)	34 (19.8%)	18 (20.2%)	18 (21.7%)	0.84
Freedom from death, MV surgery / re-operation or 3+ or 4+ MR †	100 (55.2%)	89 (51.7%)	65 (73.0%)	55 (66.3%)	<0.001

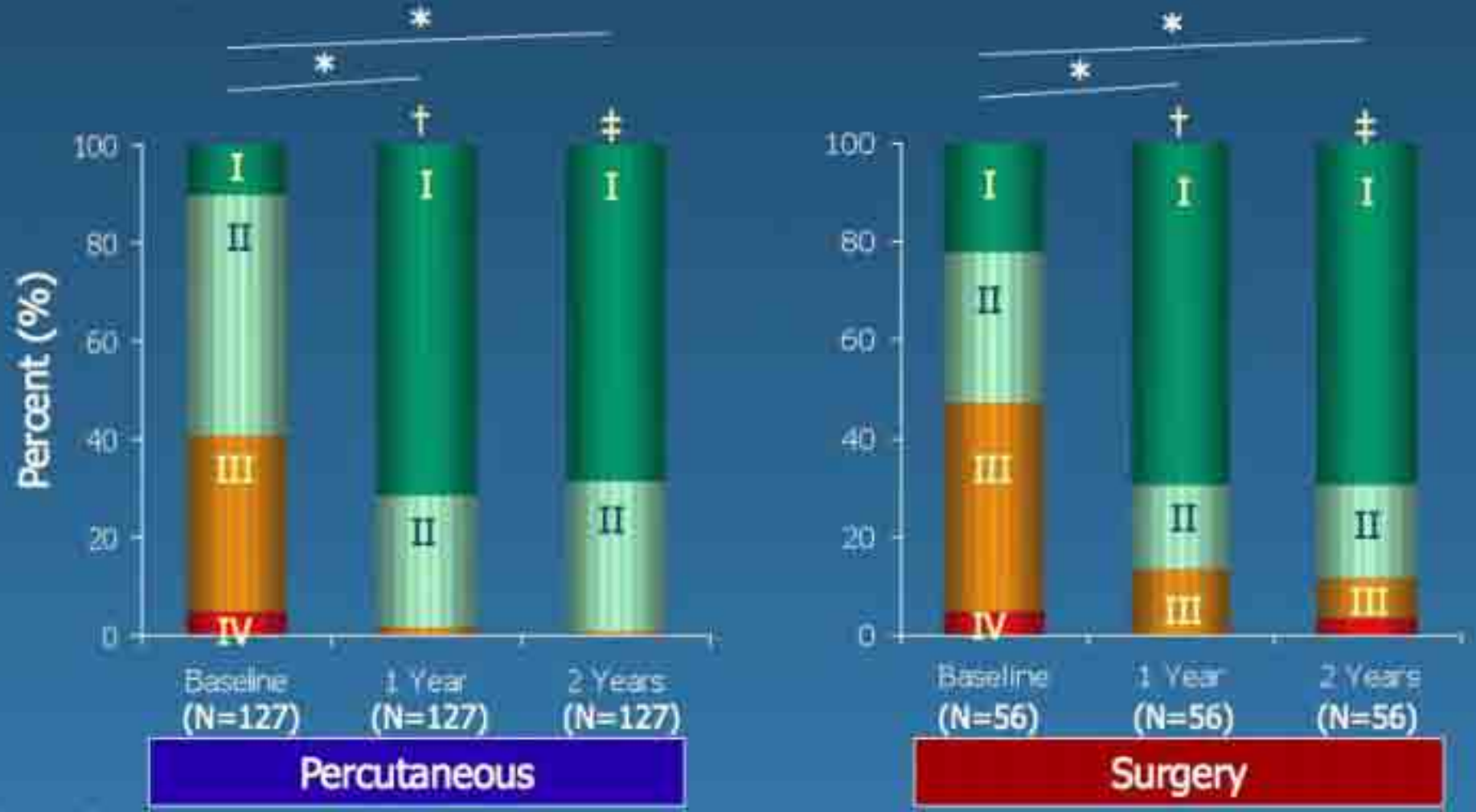
Mitral Regurgitation Grade
Baseline, 1 and 2 Years (matched)
Intention to Treat

* Within group difference (p<0.05)
† Between group difference at 1 year (p<0.05)
‡ Between group difference at 2 year (p<0.05)



NYHA Functional Class
At Baseline, 1 and 2 Years (matched)
Intention to Treat

* Within group difference (p<0.05)
† Between group difference at 1 year (p<0.05)
‡ Between group difference at 2 year (p<0.05)



The NEW ENGLAND JOURNAL of MEDICINE

Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Donald G. Glower, M.D., Saibal Kar, M.D., Michael J. Rinaldi, M.D., Peter S. Fail, M.D., Richard W. Smalling, M.D., Ph.D., Robert Siegel, M.D., Geoffrey A. Rose, M.D., Eric Engeron, M.D., Catalin Loghin, M.D., Alfredo Trento, M.D., Eric R. Skipper, M.D., Tommy Fudge, M.D., George V. Letsou, M.D., Joseph M. Massaro, Ph.D., and Laura Maurl, M.D., for the EVEREST II Investigators*

CONCLUSIONS

Although percutaneous repair was less effective at reducing mitral regurgitation than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical outcomes. (Funded by Abbott Vascular; EVEREST II ClinicalTrials.gov number, NCT00209274.)

Feldman et al. NEJM 2011;364:1395-406

Percutaneous Mitral Valve Edge-to-Edge Repair

Registry data on 628 patients who underwent MitraClip repair for functional or degenerative MR at 25 European centers, 2011-2012.

	Functional (n = 452)	Degenerative (n = 143)	*P* Value
Acute Procedural Success	95.8%	93.7%	.304
In-Hospital Mortality	2.0%	4.9%	.075
1-Year Mortality	15.0%	16.2%	.650
1-Year Rehospitalization for Heart Failure	25.8	12.0	.009

Conclusion: Mitral valve repair with the MitraClip is safe and effective for management of high-risk patients with functional and degenerative MR.

Nickenig G, J Am Coll Cardiol 2014;64:875-884

ACC 2015 LBCT

Outcomes of the Initial Experience with Commercial Transcatheter Mitral Valve Repair in the U.S.

A report from the STS/ACC TVT Registry

Paul Sorajja, MD, Saibal Kar, MD, Amanda Stebbins, Sreekanth Vemulapalli, MD, D. Scott Lim, MD, Vinod Thourani, MD, Michael Mack, MD, David R. Holmes, Jr., MD, Wesley A. Pedersen, MD, and Gorav Ailawadi, MD

Study Population
564 Patients

- Median age (% men)…… 83 yrs (56%)
- NYHA III/IV…… 83.9%
- HF hospitalization prior yr…… 51.8%
- Atrial fibrillation…… 62.6%
- Prior CVA…… 8.7%
- Diabetes…… 25.0%
- Prior CABG 32.4%

24.6%

16.7%

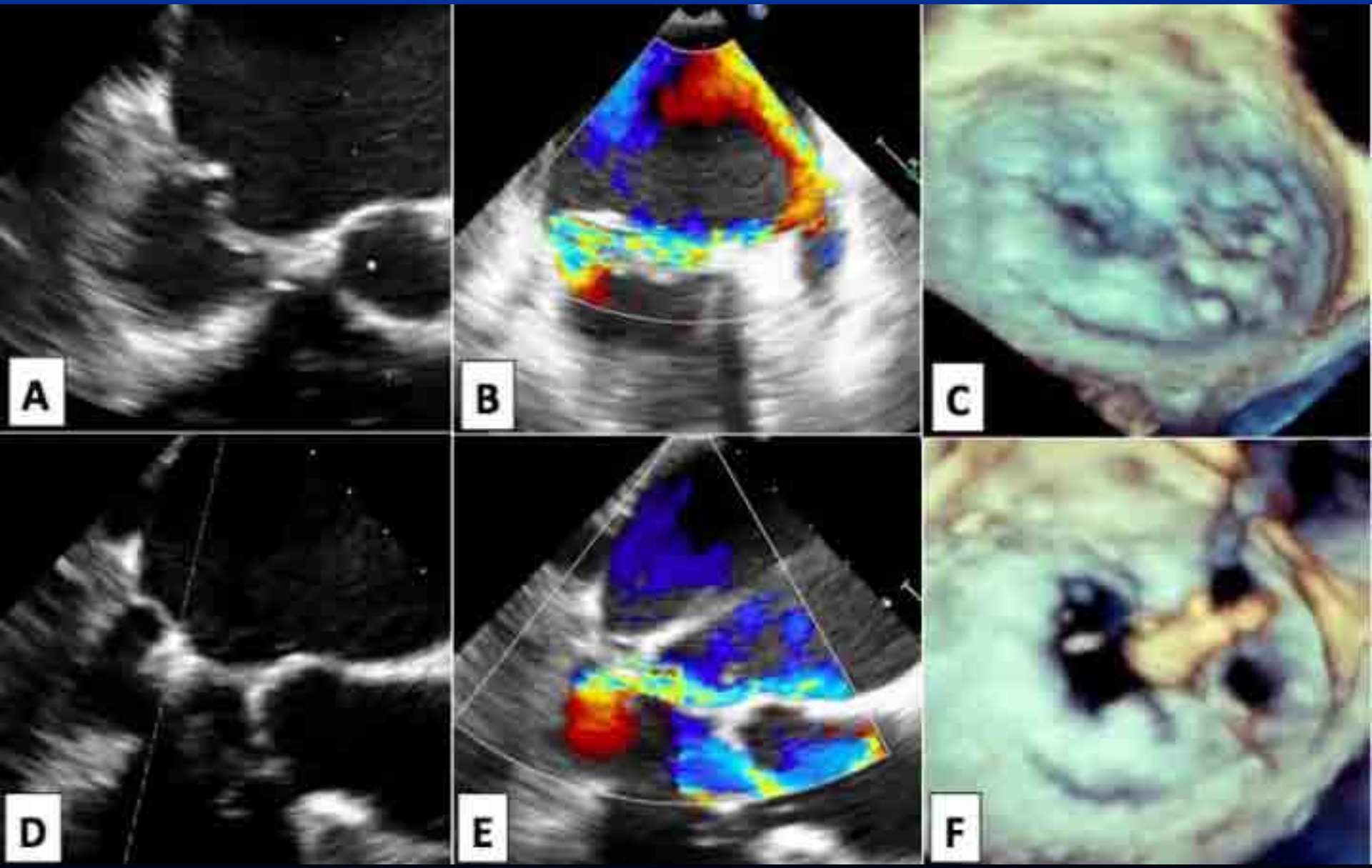
14.7%

7.9% (4.7, 12.2)

10.0% (6.3, 14.5)

Clinical Outcomes

- Procedure success…. 91.8%
- Complications..... 7.8%
- Length-of-stay..... 3 d (1,6 d)
- Home discharge..... 81.9%


A
B
C
D
E
F

Device Landscape 2013
Percutaneous MV Repair

Edge-to-edge
- MitraClip*

Chordal shortening and other
- Cardiosolutions Mitra-Spacer*
- NeoChord
- Valtech VChordal

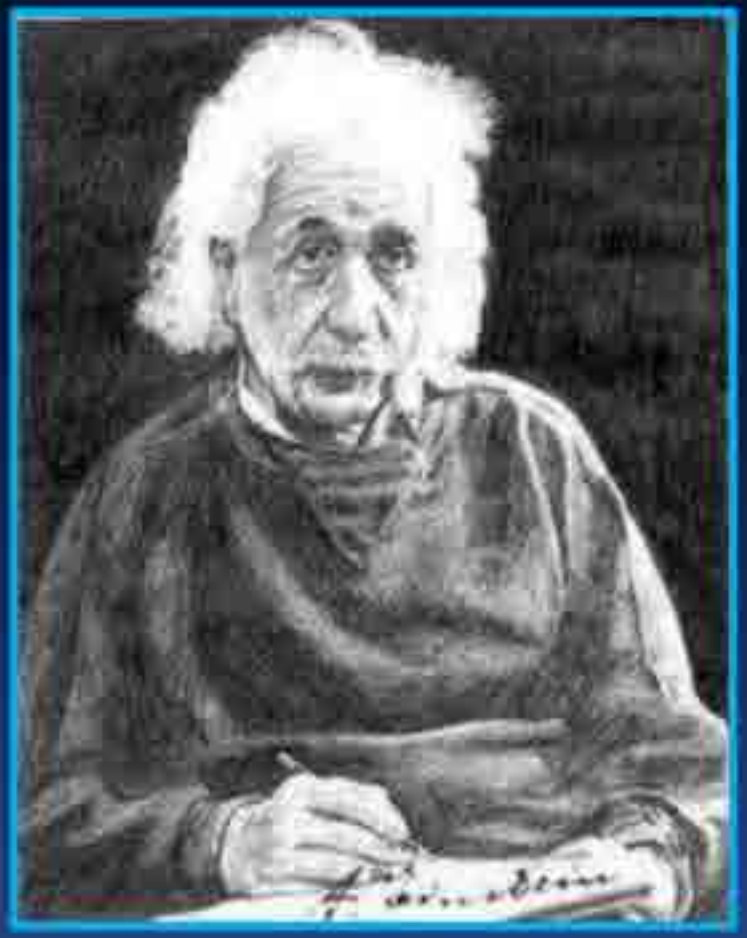
Coronary sinus annuloplasty
- Cardiac Dimensions Carillon*
- Cerclage annuloplasty

MV replacement
- CardiAQ*
- EndoValve
- Tendyme (Lutter)
- Neovasc Tiara
- Edwards Lifesciences
- Valtech Cardiovalve
- ValveXchange

*In patients

Direct annuloplasty
- Mitralign Bident*
- GDS Accucinch*
- Valtech Cardioband*
- Quantum Cor (RF)
- Micardia enCor
- Thermocool

IC Predictions



Albert Einstein
(1879 – 1955)

"I never think of the future - it comes soon enough!"