Angioplasty Summit
TCTAP 2011
OrbusNeich Lunch Symposium

Clinical Applications for the Pro-Healing Stent Use of Endothelial Progenitor Cell Capture Stent in Patients with ST-segment Elevation Myocardial Infarction

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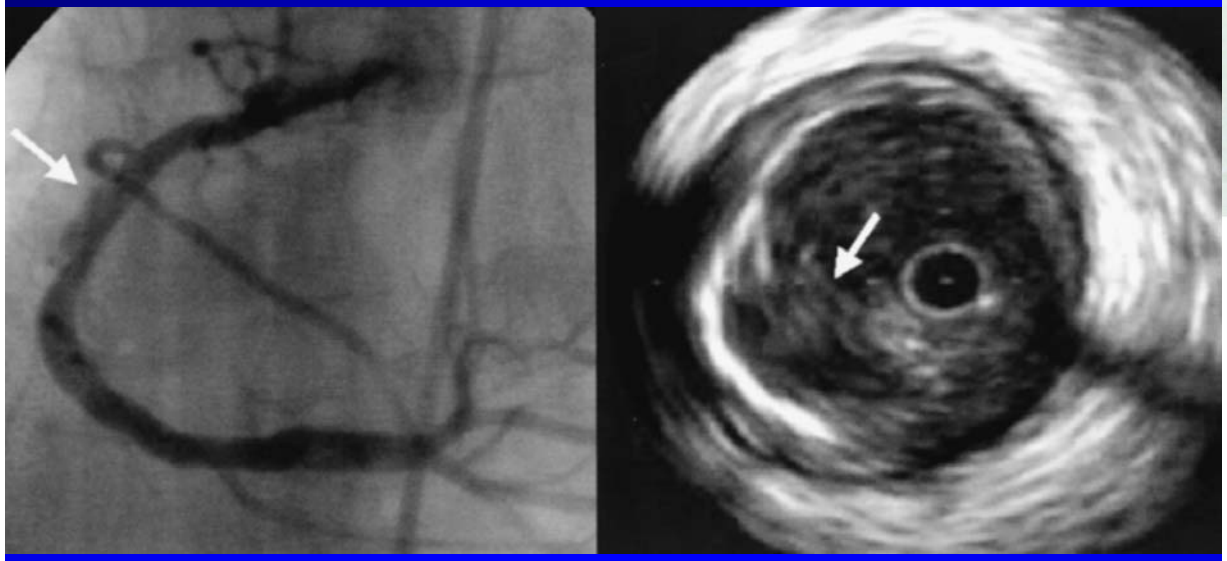
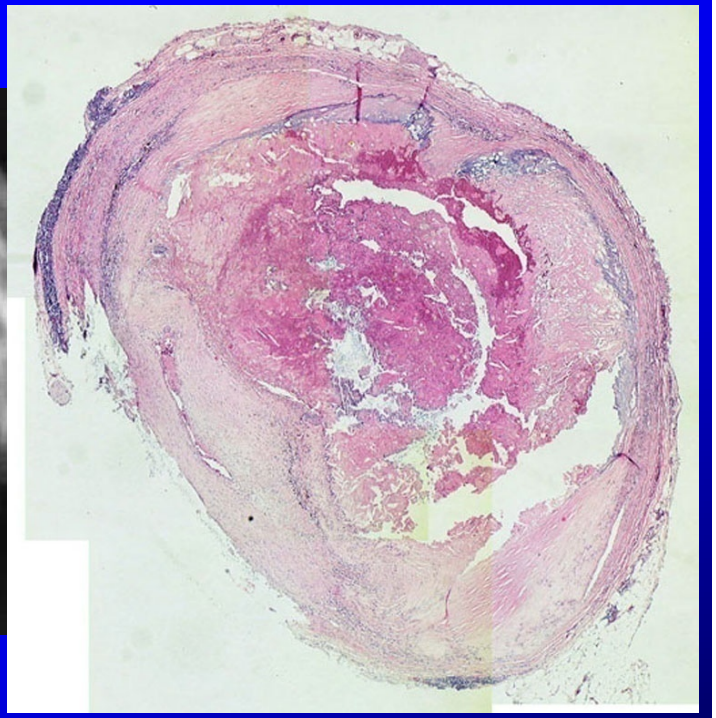
AMI: Disrupted Endothelium with Overlying Thrombus

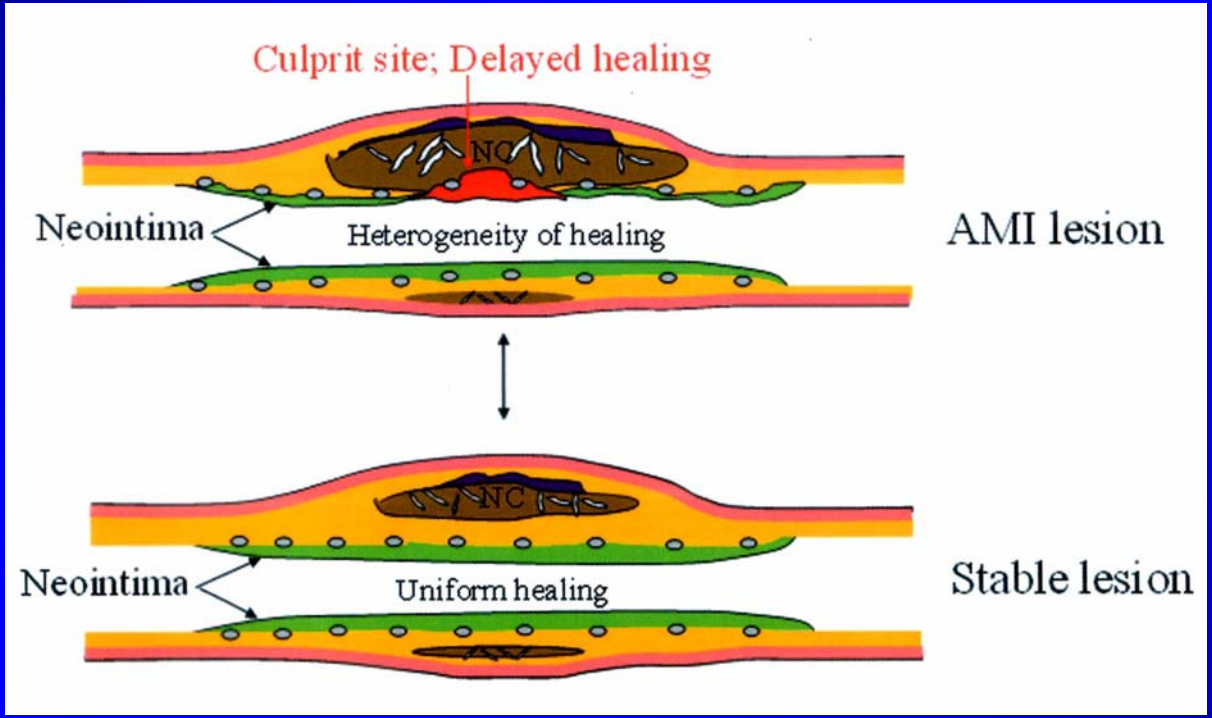




- Thinned fibrous cap, rich lipid core
- Marked inflammation
- Less atherosclerotic burden

Hong MK et al Circulation 2004; 110: 928-933

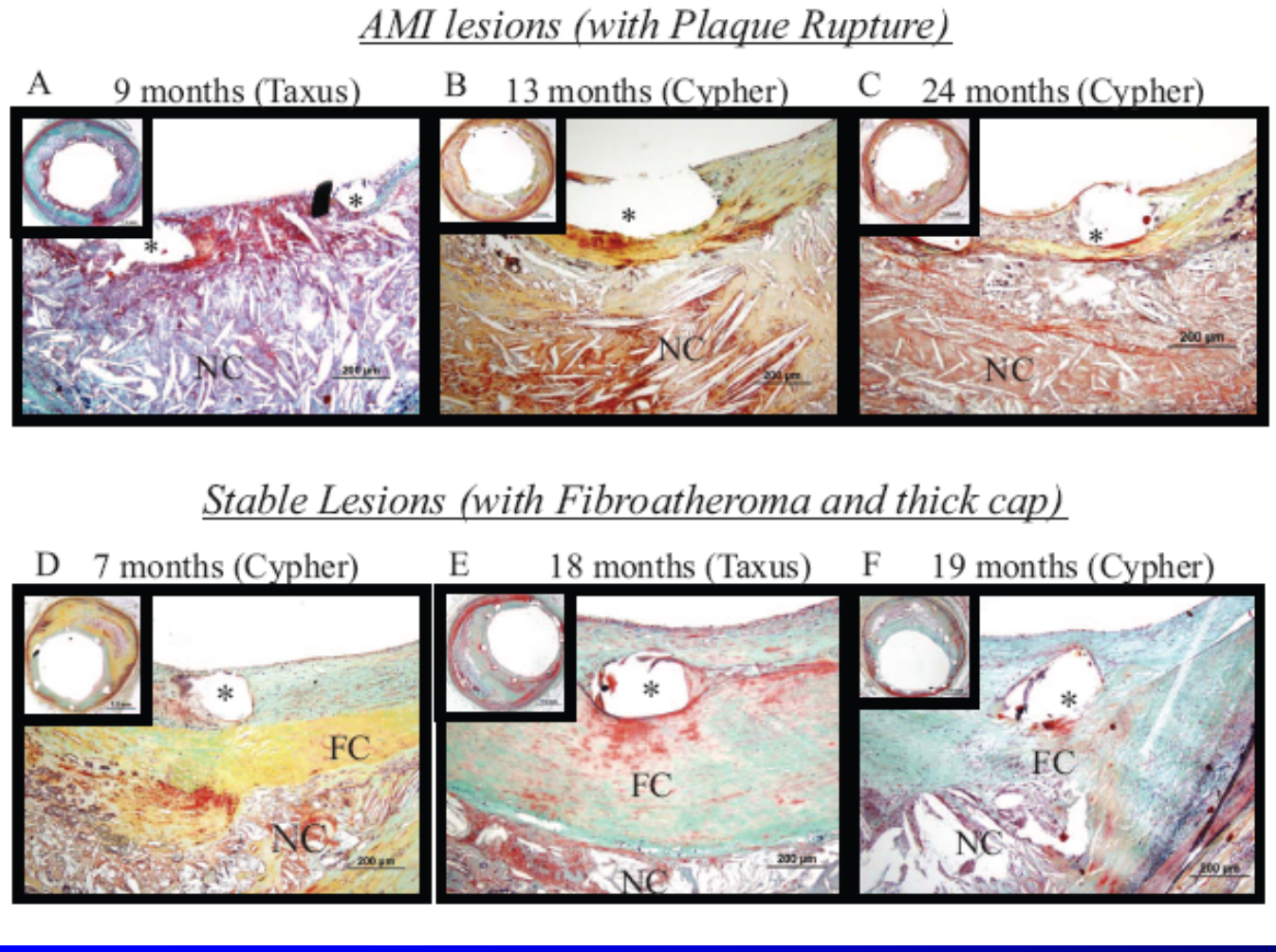
Delayed Healing of DES in AMI



- Greater delayed arterial healing (evidenced by greater fibrin deposition and incomplete strut coverage) at culprit sites compared with non-culprit sites within the AMI lesions (heterogeneity of healing)
- Stable lesions showed similar arterial healing between culprit and non-culprit sites

Nakazawa G et al Circulation 2008; 118: 1138-1145

Delayed Healing of DES in AMI: Autopsy Study



Nakazawa G et al Circulation 2008; 118: 1138-1145

Comparison of Underlying Plaque Morphology Between Pts with AMI versus Stable Angina

	CS in Patients With AMI (n=17)	CS in Patients With Stable Angina (n=18)	*P*
EEL, mm^2	19.4±7.1	14.6±4.8	0.027
Stent area, mm^{2*}	7.3 (5.7–9.3)	5.7 (5.1–8.0)	0.08
Plaque area, mm^2	11.2±4.5	8.1±3.6	0.029
Plaque area, %	57±7	54±8	0.18
NC area, mm^{2*}	2.6 (1.8–4.4)	1.0 (0.6–1.4)	<0.0001
Fibrous cap thickness, μm	55±24	286±118	<0.0001
NC arc, °*	180 (180–270)	90 (90–180)	<0.0001
NC area, %	32±11	16±9	<0.0001
Longitudinal NC length, mm	16.2±8.3	10.0±4.9	0.01
Longitudinal rupture site length, mm*	6.3 (2.9–8.6)	0 (0, 0)	<0.0001
Struts penetrating NC, %*	30 (15–39)	0 (0–0)	<0.0001

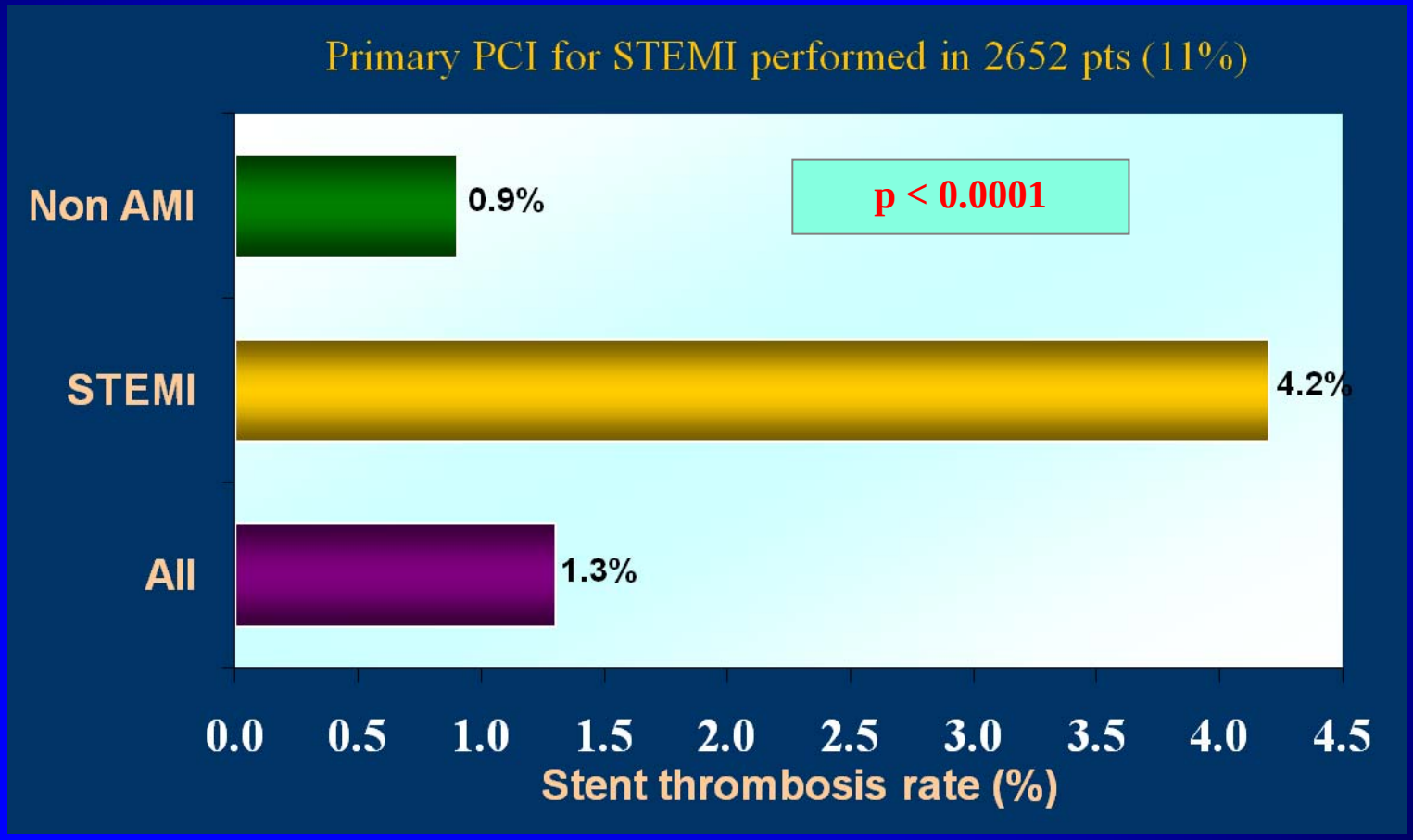
EEL indicates external elastic lamina; NC, necrotic core.
*Expressed as median (IQR).

At >30 days, AMI culprit sites had : (1) Less neointimal thickness (median, 0.04mm vs 0.11mm), (2) Greater fibrin deposition (63±28% vs 36%±27%), (3) Inflammation (35% vs 17%) and (4) Higher prevalence of uncovered struts (49% vs 9%)

Nakazawa G et al Circulation 2008; 118: 1138-1145

The Spanish ESTROFA Registry

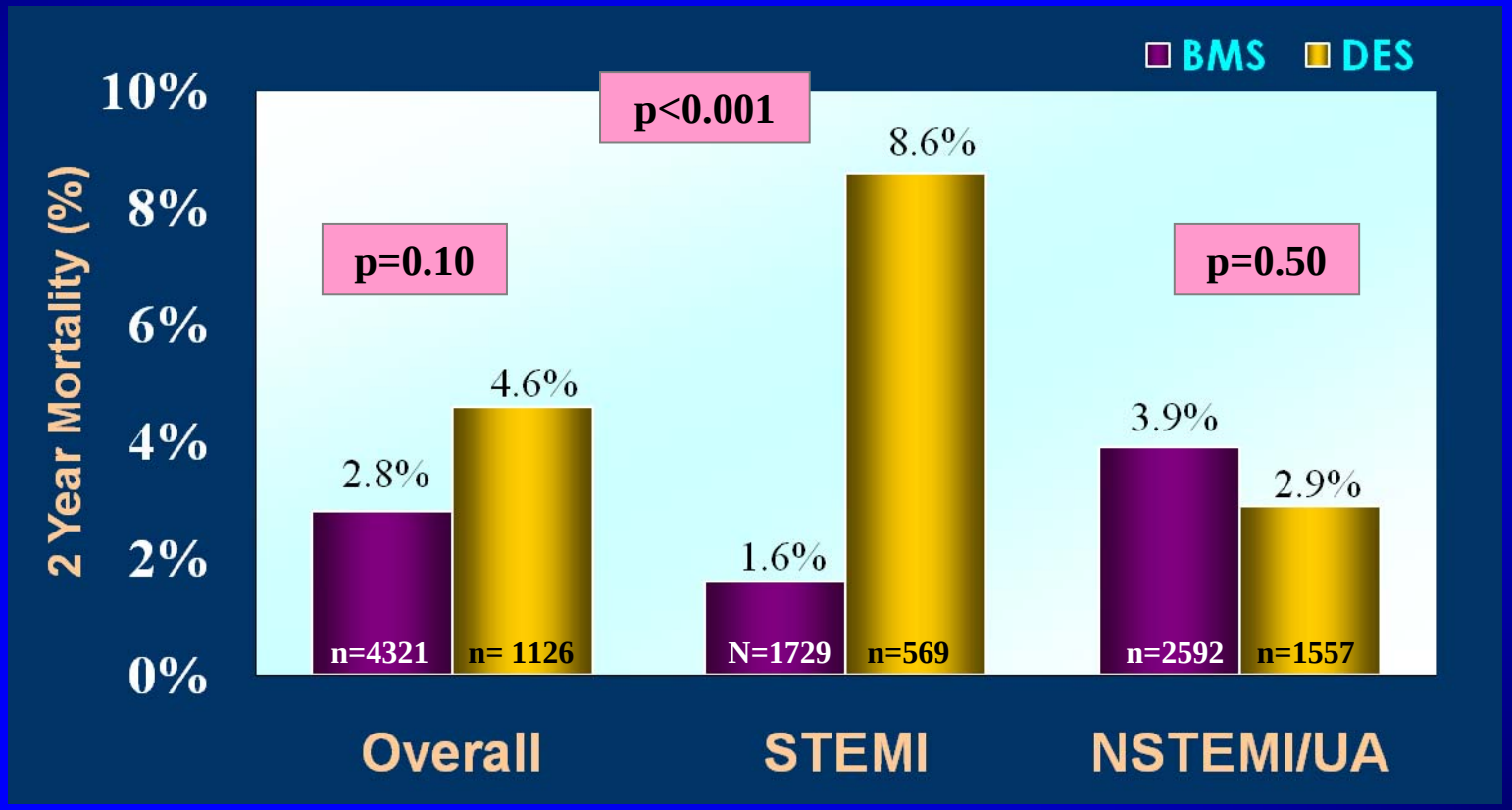
23,500 pts treated w/DES at 20 Spanish hospitals from 2002-06;
63% PES, 37% SES, Dual antiplatelet Rx for 8 ± 3 months.
1.3% ST rate at median FU 22 (11, 32) mos ; 2.0% ST at 3 yrs



de la Torre Hernandez JM et al JACC 2008; 51: 986-90

DES vs BMS in AMI: GRACE Registry

Landmark analysis in 569 pts treated with DES, 1729 pts treated with BMS for STEMI between 2004-2006



Steg G e al Euro Hear J 2009; 30: 321-329

European Heart Journal (2009) **30**, 321–329
doi:10.1093/eurheartj/ehn604

CLINICAL RESEARCH
Acute coronary syndrome

Mortality following placement of drug-eluting and bare-metal stents for ST-segment elevation acute myocardial infarction in the Global Registry of Acute Coronary Events

Ph. Gabriel Steg[1]*, Keith A.A. Fox[2], Kim A. Eagle[3], Mark Furman[4], Frans Van de Werf[5], Gilles Montalescot[6], Shaun G. Goodman[7], Álvaro Avezum[8], Wei Huang[4], and Joel M. Gore[4] for the Global Registry of Acute Coronary Events (GRACE) Investigators

The observation of increased late mortality with DES vs. BMS suggests that DES should probably be avoided in STEMI, until more long-term data become available.

Received 17 July 2008; revised 25 October 2008; accepted 16 December 2008; online publish-ahead-of-print 15 January 2009

Aims To assess mortality after drug-eluting stent (DES) or bare-metal stent (BMS) for ST-segment elevation myocardial infarction (STEMI).

Methods and results In this multinational registry, 5093 STEMI patients received a stent: 1313 (26%) a DES and 3780 (74%) only BMS. Groups differed in baseline characteristics, type, or timing of percutaneous coronary intervention, with a higher baseline risk for patients receiving BMS. Two-year follow-up was available in 55 and 60% of the eligible BMS and DES patients, respectively. Unadjusted mortality was lower during hospitalization, similar for the first 6 months after discharge, and higher from 6 months to 2 years, for DES patients compared with that of BMS patients. Overall, unadjusted 2-year mortality was 5.3 vs. 3.9% for BMS vs. DES patients ($P = 0.04$). In propensity- and risk-adjusted survival analyses (Cox model), post-discharge mortality was not different up to 6 months ($P = 0.21$) or 1 year ($P = 0.34$). Late post-discharge mortality was higher in DES patients from 6 months to 2 years (HR 4.90, $P = 0.01$) or from 1 to 2 years (HR 7.06, $P = 0.02$). Similar results were observed when factoring in hospital mortality.

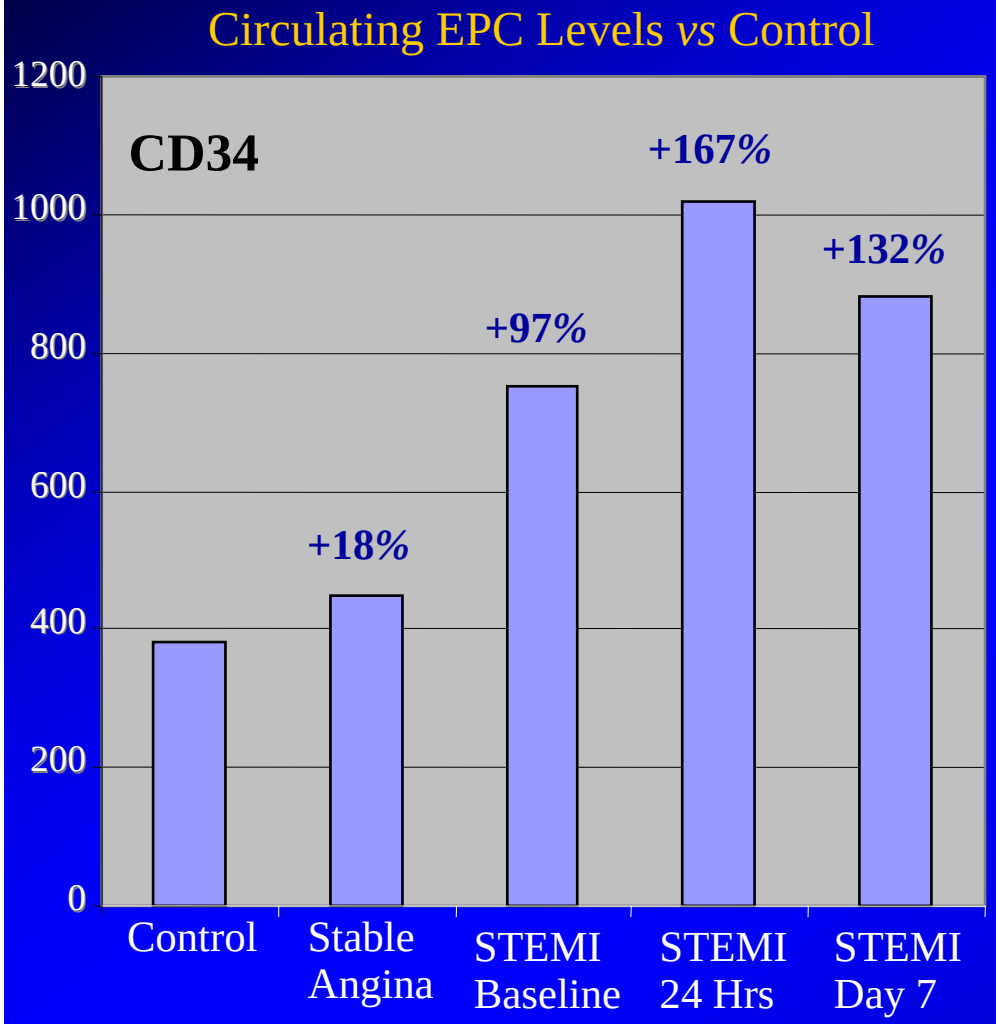
Conclusion The observation of increased late mortality with DES vs. BMS suggests that DES should probably be avoided in STEMI, until more long-term data become available.

Steg G e al Euro Hear J 2009; 30: 321-329

National University Health System

GENOUS™ Stent In Acute Myocardial Infarction At The National University Hospital

Circulating EPCs in AMI

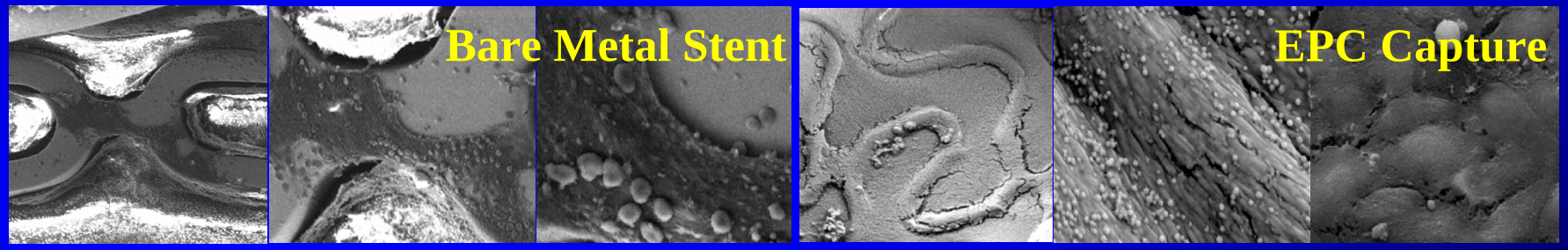


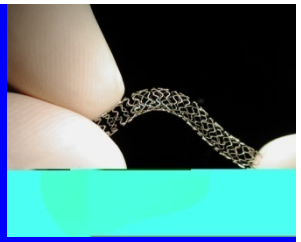
- Endogenous Granulocyte-Colony Stimulating Factor ***(G-CSF)*** and Vascular Endothelial Growth Factor ***(VEGF)*** are significantly increased in acute phase of MI, and are directly correlated to circulating *CD34+* levels
- Independent predictors of increasing levels of circulating CD34+ after AMI
  - patients treated with statins *($p<0.01$)*
  - patients treated by P-PCI *($p=0.048$)*
- Associated with improvement in LV function and reduction in infarct size

Wojakowski W , Leone AM et al Eur Heart J 2005; Leone AM et al Int J Cardiol 2005; Massa M et al Blood 2005; Shintani S et al Circ 2001; Numaguchi Y et al Circ 2006

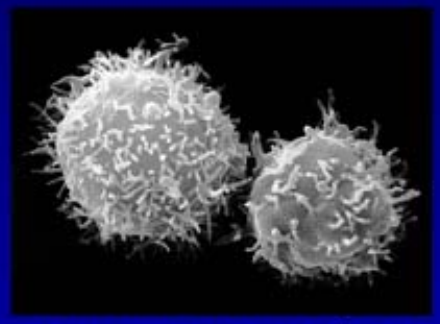
Objective

- We hypothesized that the use of the EPC Capture (GENOUS ™) stent may result in more rapid healing process by maximising the effects of mobilised EPCs on injured vessel surface, and lead to better clinical outcomes in patients with ST-segment myocardial infarction (STEMI)



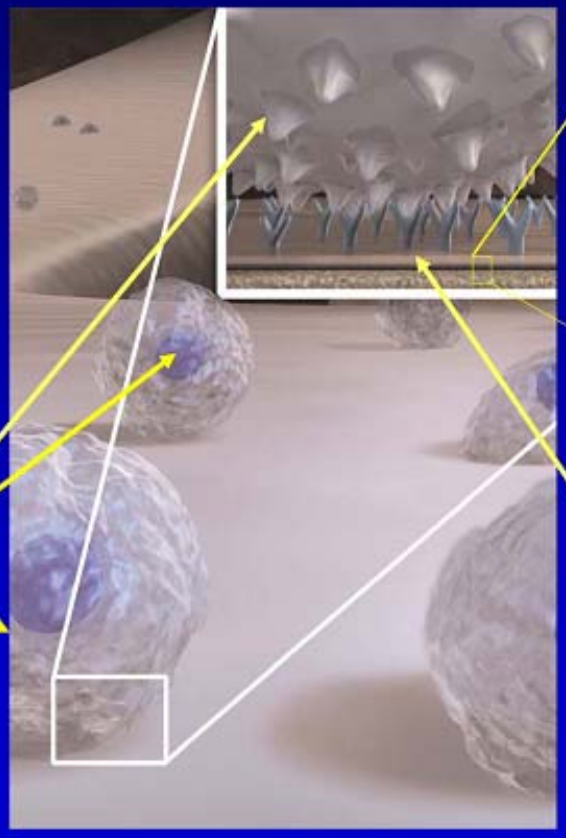


GENOUS™ Stent:
EPC Capture Coating Technology



Human progenitor cell with CD34 Cell Surface Antigen

Captured EPC on Surface using bond Antibodies



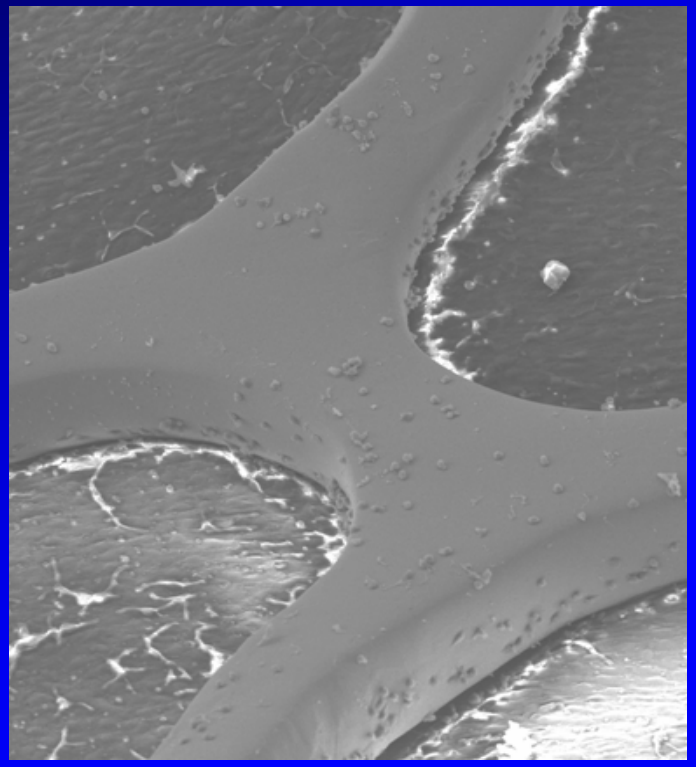
Intermediate Layer

Stent Adhering Bottom Layer

Stent Surface

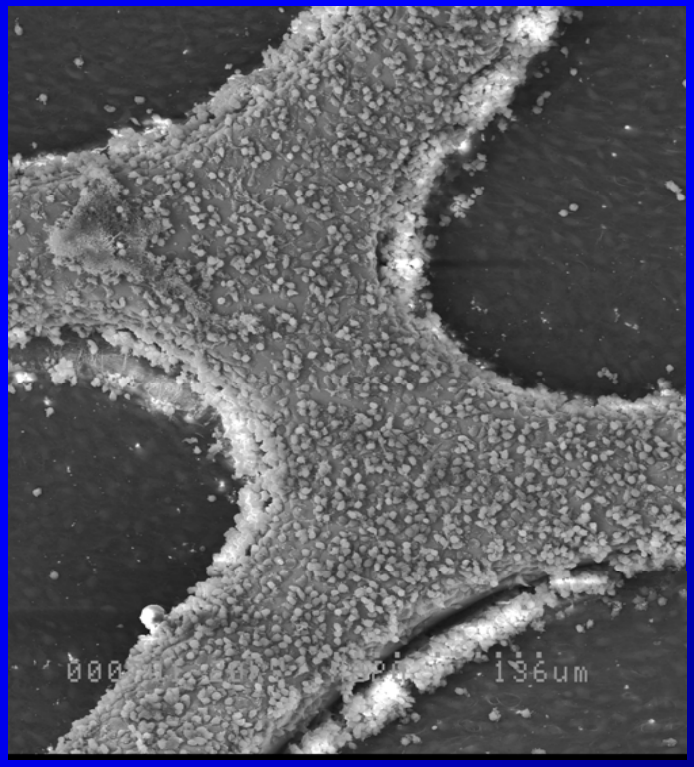
CD34 Antibody Layer

In vivo: Electron Microscopy
1-Hr Post Porcine Coronary Artery Implantation



BMS at 50X

Sparsely littered with platelets and fibrin



GENOUS at 50X

Greater than 70% cell coverage

Thursday, August 5, 2004 | THE STRAITS TIMES

TECH & SCIENCE

1st in Asia: 'Antibodies' stent for NUH

Already tried out in Europe, the stent is coated with antibodies instead of drugs to form a protective lining on artery wall

metal stent inserted end up with extensive scar tissue at the point where the device sits, as inserting it destroys the protective lining on the sel walls, and induces them to form a new protective lining.

So far, of the 16 people in Europe who have had the new device inserted, only one has

biological healing process instead of anti-cancer drugs to kill the excessive muscle cells."

Drug-coated stents have been used for about four years

ternational cardiology conference, organised by the National Healthcare Group's The Heart Institute.

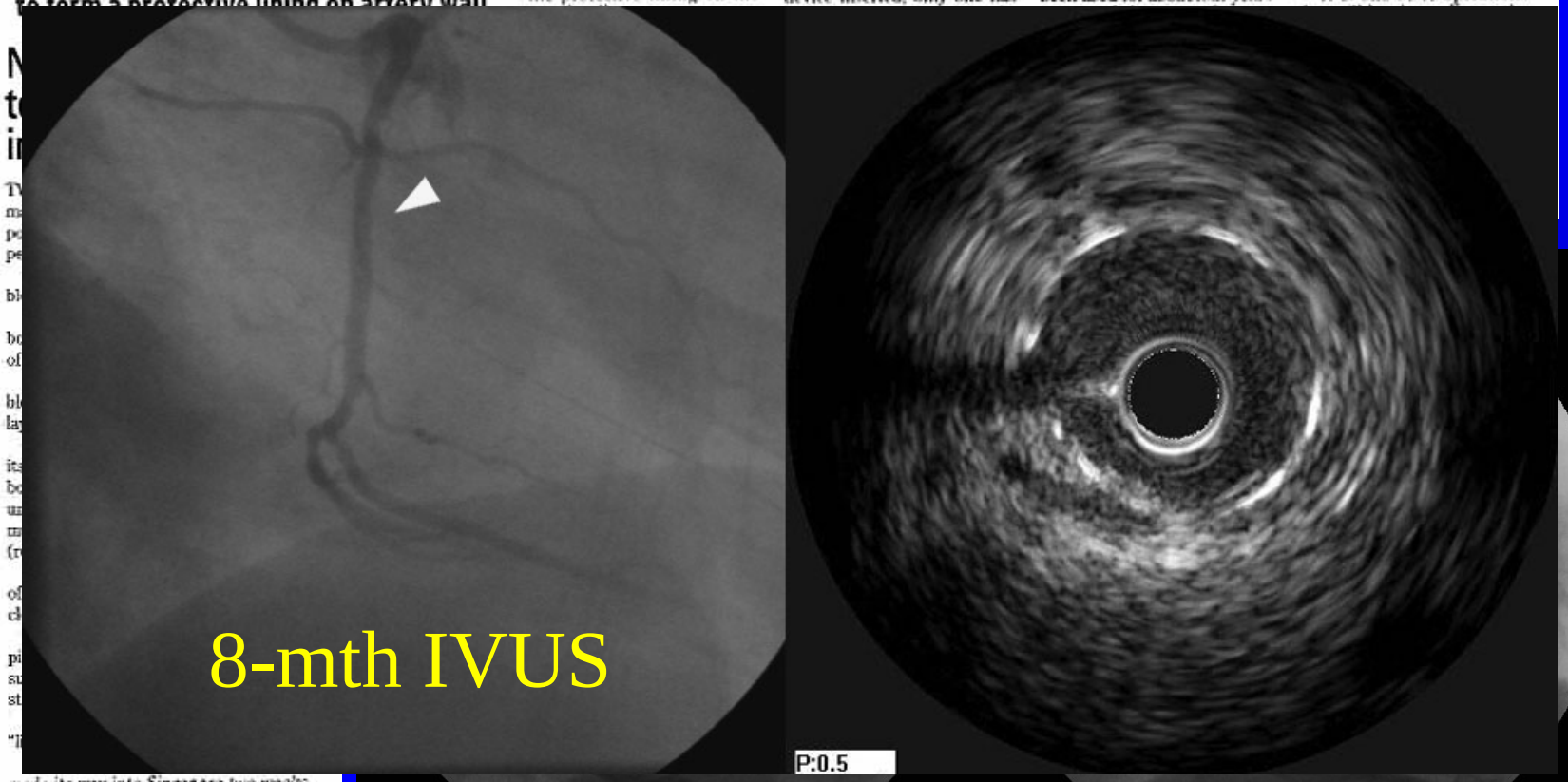
It is one of 11 operations

made its way into Singapore two weeks ago.

The bifurcating stent comes with a short branch, allowing some patients who would otherwise need two stents to make do with just one.

It also lessens the chance of restenosis.

— *Tan Hui Leng*



National University Health System

NUS

Methodology

- Since Jan 2005, all patients with STEMI without cardiogenic shock will receive EPC Capture stent (GENOUS™, OrbusNeich) while undergoing primary PCI
- Primary PCI procedure were performed in standard manner. Thrombectomy, GP IIb/IIIa inhibitor use were at discretion of operator
- All patients received loading dose followed by maintenance dual anti-platelet therapy (aspirin and clopidogrel) for a month
- Simvastatin 20mg therapy commenced immediately after the procedure, and titrated subsequently according to lipid levels

Use of endothelial progenitor cell capture stent (Genous Bio-Engineered R Stent) during primary percutaneous coronary intervention in acute myocardial infarction: Intermediate- to long-term clinical follow-up

Melissa Co, MD,[a] Edgar Tay, MBBS, MRCP,[a] Chi Hang Lee, MBBS, MRCP,[a] Kian Keong Poh, MBBChir, MRCP,[a] Adrian Low, MBBS, MRCP,[a] Jimmy Lim, MBBS, MRCP,[b] Ing Han Lim, MBBS, MRCP,[b] Yean Teng Lim, MBBS, FRCP,[a] and Huay Cheem Tan, MBBS, FRCP[a] *Singapore, Singapore*

	In-hospital n (%)	1 mth n (%)	6 mth n (%)	1 yr n (%)
No. of patients	120 (100%)	120 (100%)	120 (100%)	40 (33%)
Stent thrombosis	1 (0.8%)	2 (1.7%)	2 (1.7%)	2 (1.7%)
MACE	2 (1.7%)	5 (4.2%)	7 (5.8%)	11 (9.2%)
Death	1 (0.8%)	3 (2.4%)	4 (3.3%)	4 (3.3%)
Myocardial infarction	1 (0.8%)	2 (1.5%)	3 (2.5%)	3 (2.5%)
TVR	1 (0.8%)	2 (1.7%)	3 (2.5%)	7 (5.8%)

Dual antiplatelet therapy for 1 mth and statin therapy started immediately after the PCI

M Co, HC Tan et al Am Heart J 2008; 155: 128-32

Endothelial progenitor cell capture stent implantation in patients with ST-segment elevation acute myocardial infarction: one-year follow-up

Yian-Ping Lee[1], MBBS, MRCP; Edgar Tay[1], MBBS, MRCP; Chi Hang Lee[1], MBBS, FACC; Adrian Low[1], MBBS, MRCP; Swee Guan Teo[1], MBBS, MRCP, Kian Keong Poh[1], MBBChir, FACC , Wee-Tiong Yeo[1], MBBS, MRCP; Jimmy Lim[2], MBBS, MRCP; Ing Han Lim[2], MBBS, MRCP; Yean Teng Lim[1], MBBS, FACC; Huay Cheem Tan[1]*, MBBS, FACC

1. National University Hospital, Singapore; 2. Tan Tock Seng Hospital, Singapore

- 321 patients with acute STEMI and underwent primary PCI between Jan 2005 and Apr 2008 were enrolled in this prospective study
- Dual anti-platelet therapy was given for a month
- Clinical follow-up for 1 year

YP Lee, HC Tan et al EuroIntervention 2010; 5: 698-702

Baseline Demographic Characteristics

		Number (n=321)	Percentage (%)
Male		260	81.0
Age (yrs)		55.5±11.6	
Hypertension		159	49.5
Diabetes mellitus		97	30.2
Dyslipidemia		216	67.3
Premature CAD		14	4.4
Smoking history		148	46.1
Intervened Vessel	- LAD	186	57.9
	- LCX	31	9.7
	- RCA	104	32.4

Lesion Characteristics

		Number (n=321)	Percentage (%)
Lesion Classification	- A	6	1.9
	- B1	52	16.2
	- B2	173	53.9
	- C	90	28 .0
Two or more vessel disease		72	22.4
Lesion complexity	Ostial	28	8.8
	Bifurcation	80	25.2
	Calcified	37	11.7
	Thrombotic	220	69.4

Angiographic Characteristics of Lesions

	Baseline	Post-PCI
Diameter Stenosis (%)	93.8 ± 11.5	4.0 ± 3.8
MLD (mm)	0.20 ± 0.42	2.95 ± 0.74
Reference diameter (mm)	3.08 ± 1.76	3.08 ± 0.77
Lesion Length (mm)	18.50 ± 7.96	

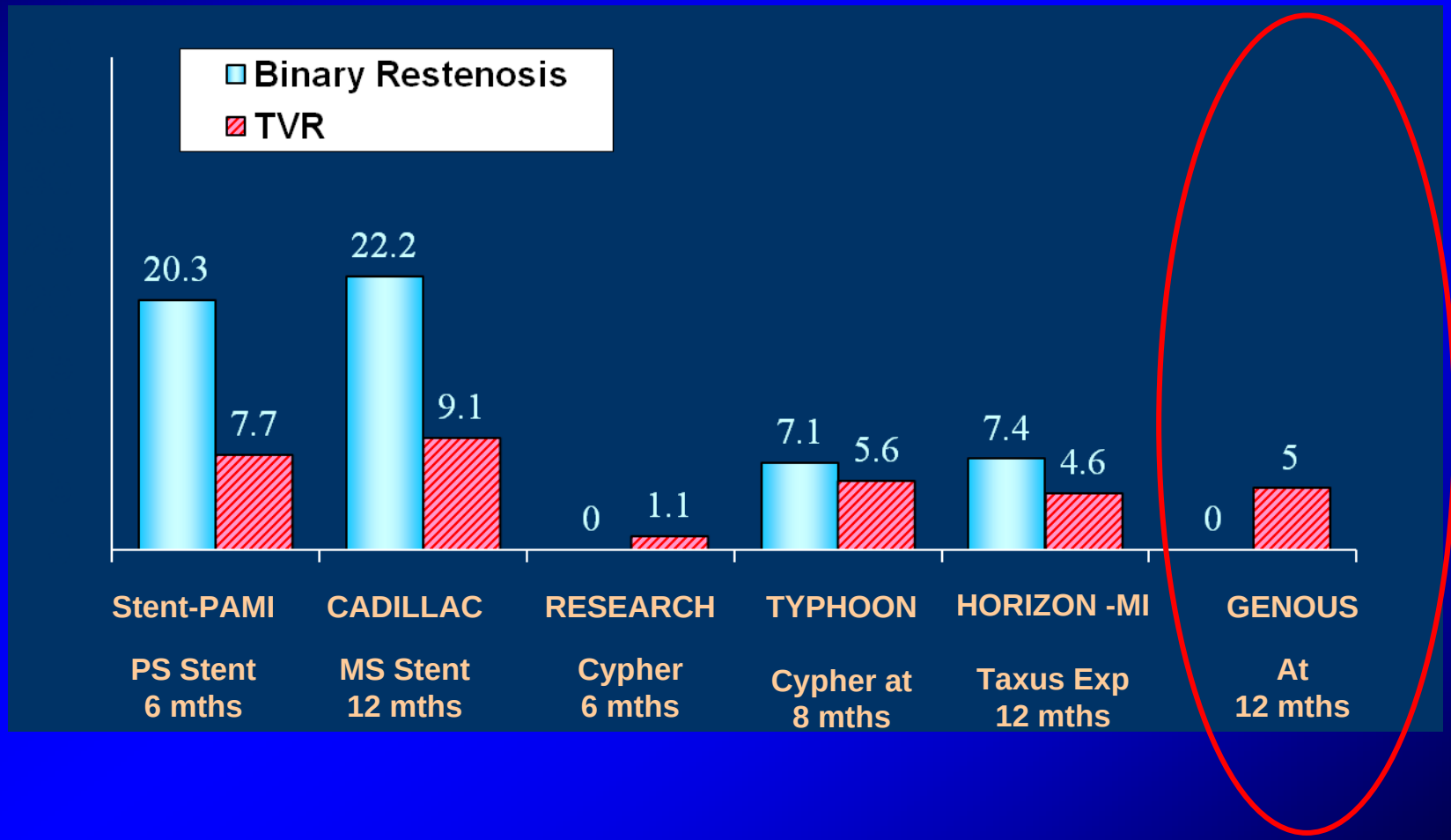
Results: Cumulative Events at 1 Mth, 6 Mth and 1 Year

Event	1-Month N (%)	6-Month N (%)	1-Year N (%)
Number of Patients	321 (100%)	321 (100%)	321 (100%)
Stent thrombosis	3 (0.9%)	3 (0.9%)	3 (0.9%)
MACE	26 (8.1%)	34 (10.6%)	42 (13.1%)
Death	23 (7.2%)	23 (7.2%)	24 (7.5%)
Cardiac Causes	19 (5.9%)	19 (5.9%)	19 (5.9%)
Non-Cardiac Causes	4 (1.2%)	4 (1.2%)	5 (1.6%)
Recurrent Myocardial Infarction	5 (1.6%)	12 (3.7%)	12 (3.7%)
Target vessel revascularization (TVR)	3 (0.9%)	10 (3.1%)	16 (5.0%)
Target lesion revascularization (TLR)	3 (0.9%)	9 (2.8%)	14 (4.4%)

Causes of Death

Total number of deaths	24
Cardiac causes	
Cardiogenic shock/ arrhythmias	15
Myocardial infarction	3
Myocardial rupture	1
Non-cardiac cause	
Sepsis	3
Stroke	1
Liver failure	1

TVR After Primary Stenting in AMI: GENOUS™ vs Others



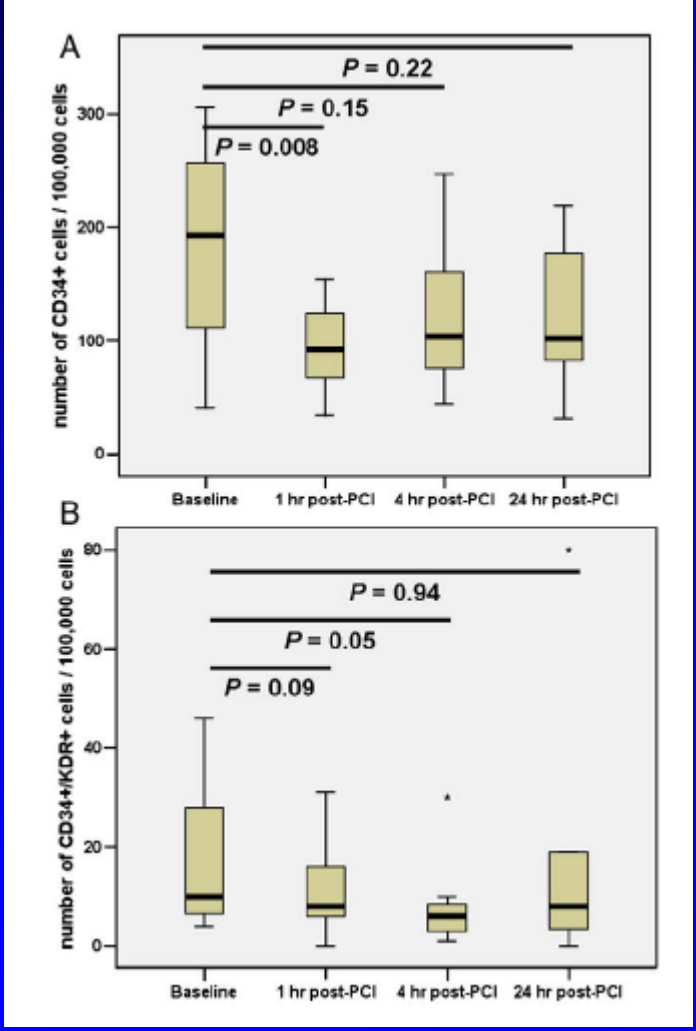
Three-Year FU of Patients with STEMI who Received EPC Capture Stent while undergoing PPCI

- 384 pts who received 465 EPC capture stents (1.2stents/pt)
- 33.1% had diabetes; mean stent length was 21.04±5.6mm and mean stent diameter was 3.0±0.3mm.
- Dual antiplatelet therapy was for 1 mth

	1 Yr	2 Yr	3Yr
Death	25 (6.5%)	26 (6.8%)	27 (7.1%)
MI	14 (3.6%)	16 (4.2%)	18 (4.6%)
TVR	28 (7.2%)	35 (9.1%)	39 (10.2%)
Stent thrombosis	5 (1.3%)	5 (1.3%)	5 (1.3%)
MACE	61(15.9%)	70 (18.2%)	77 (20.1%)

R Sethi et al Submitted to ESC 2011

Time-Dependent Dynamic Mobilisation of Circulating Progenitor Cells During PCI in Diabetics



- 8 diabetics with stable CAD underwent PCI
- After PCI, decrease in CPC from baseline were detected in 7/8 pts.
  Maximal decrease were 47.8% and 53.3% at 1 hr and 4 hr respectively
- Transient dip in CPC early during PCI suggests incorporation of cells into sites of vascular denudation. Absence of subsequent CPC elevation may be associated with poorer outcomes of pts

Lee LC, Poh KK et al Int J Cardiol 2009

National University Health System

EPC Capture Stent vs BMS: 6-Mth MACE in Diabetics

Outcomes (%)	EPC Capture (n=34)	BMS (n=39)	P value
MACE	3(8.9)	6(15.4)	0.40
Death	1(2.9)	3(7.7)	0.37
AMI	1(2.9)	1(2.6)	0.92
Repeat revascularization	1(2.9)	2 (5.2)	0.64
Acute thrombosis	1(2.9)	0 (0.0)	0.28
Subacute thrombosis	0 (0.0)	1(2.6)	0.28

HC Tan et al ESC 2007 Abstract

Comparison Between EPC Capture Stent and Bare Metal Stent and Drug-Eluting Stent in ST-Segment Elevation Myocardial Infarction

Comparison of EPC Capture Stent vs BMS vs DES

Enrollment period: Jan 2004 and June 2006

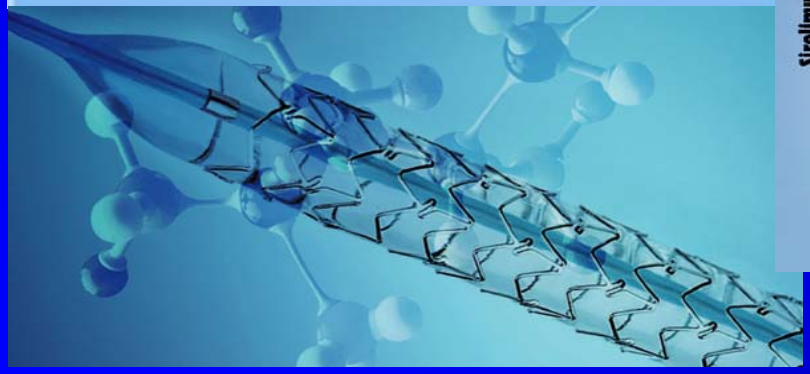
Number of patients	GENOUS™	CURA™	LIBERTE™
N = 366	95	53	218

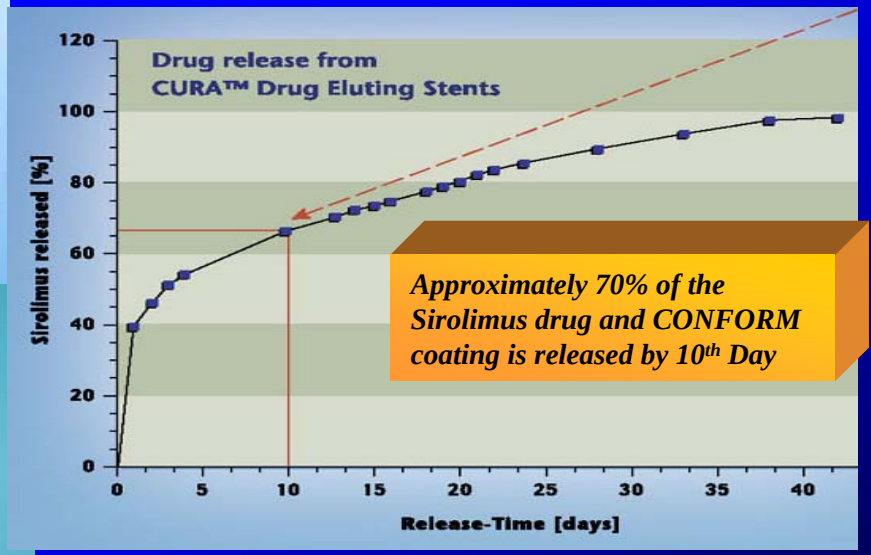
The study endpoints were major adverse cardiac events (MACE) and stent thrombosis

Original Contribution

Sirolimus-Eluting, Bioabsorbable Polymer-Coated Constant Stent (Cura™) in Acute ST-Elevation Myocardial Infarction: A Clinical and Angiographic Study (CURAMI Registry)

Chi-Hang Lee, MBBS, Jimmy Lim, MBBS, Adrian Low, MBBS, Xiao-Ling Zhang, MD, Than-Than Kyaing, MD, Mark Y. Chan, MBBS, Hwee-Bee Wong, MSc, Yean-Teng Lim, MBBS, Huay-Cheem Tan, MBBS



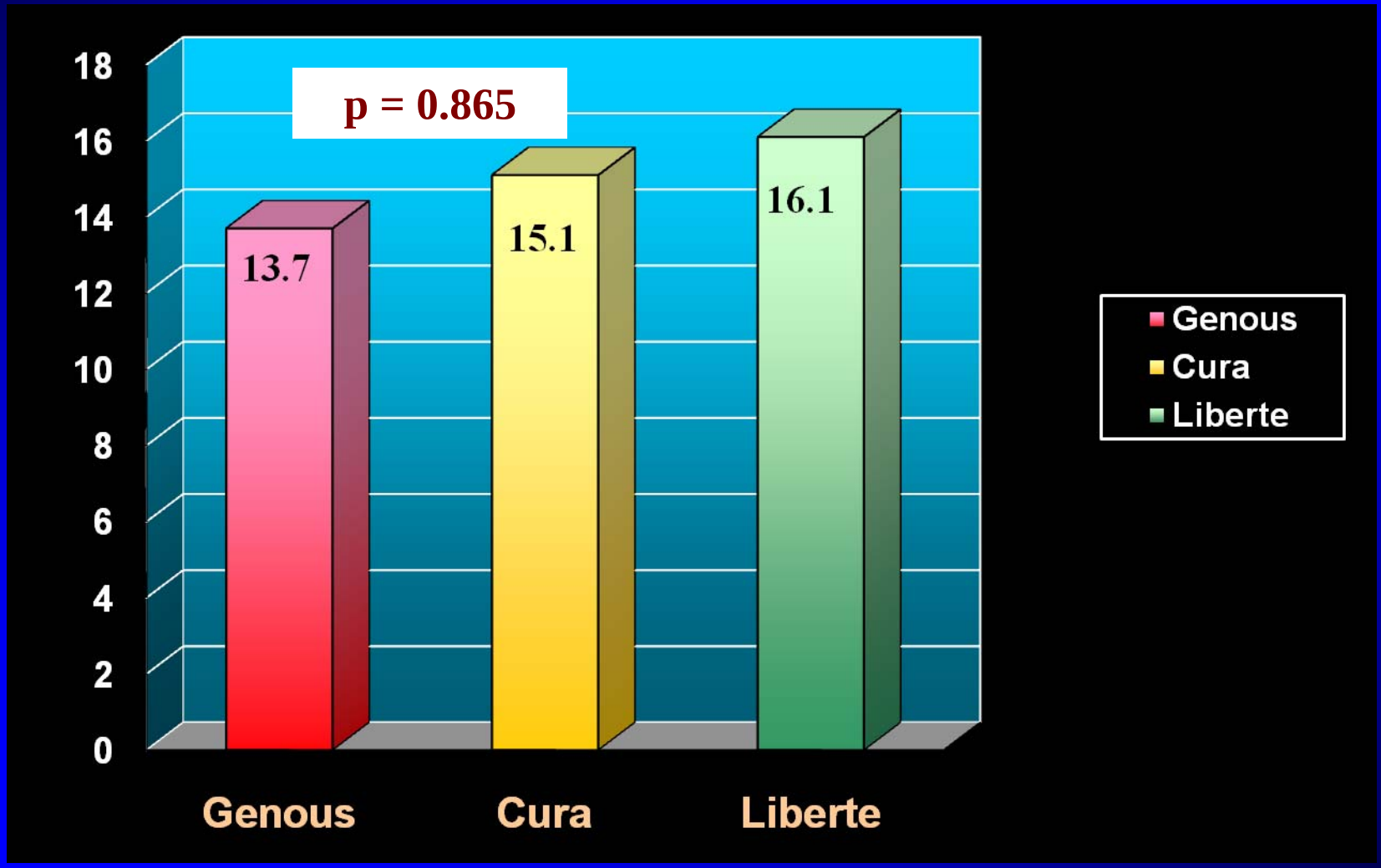


CH Lee et al J Invas Cardiol 2007; 19: 182-185

Baseline Demographic Characteristics

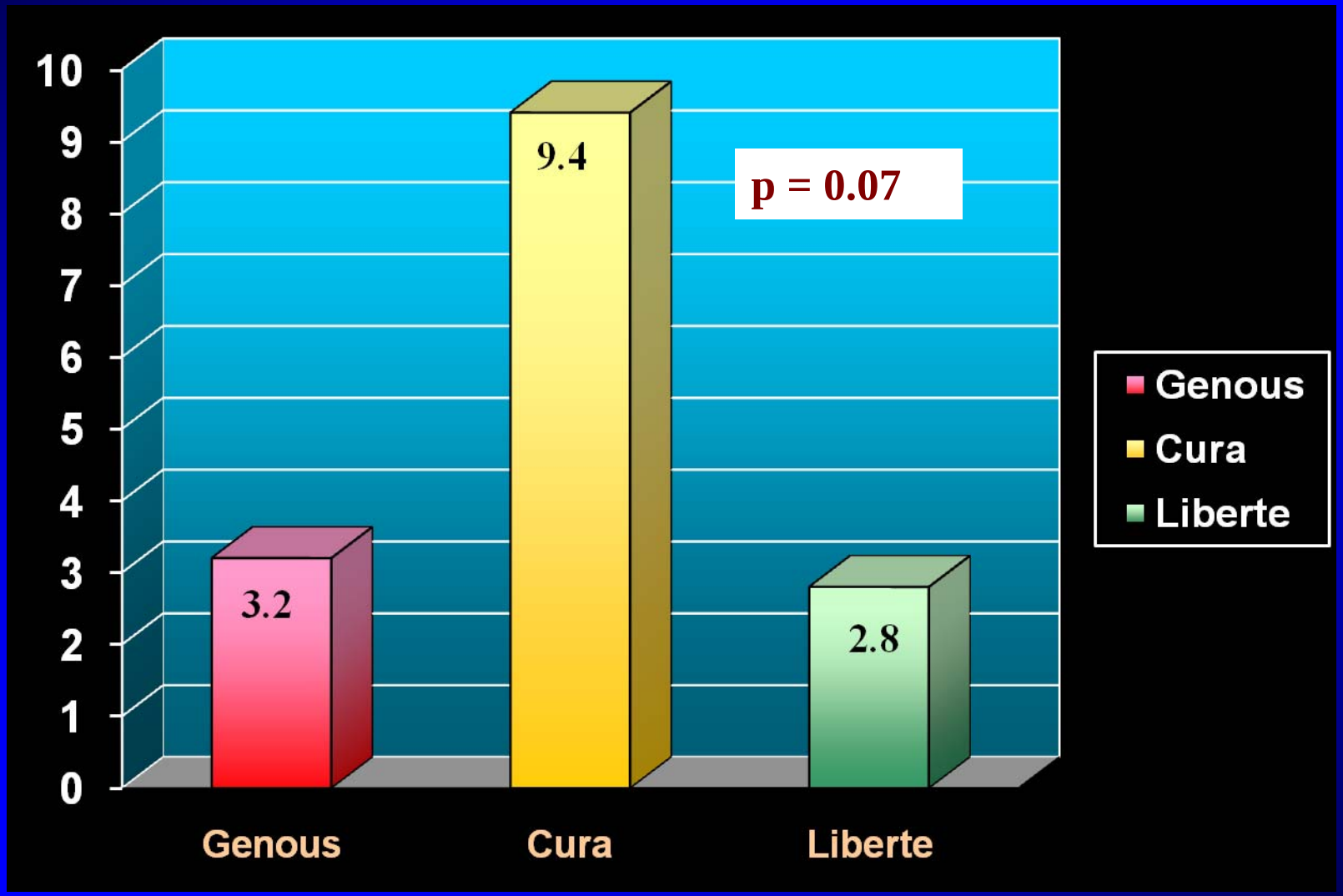
Characteristics	GENOUS (n = 95)	CURA (n = 53)	LIBERTE (n = 218)	P value
Age	53.7±11.3	55.7±10.2	56.8±11.9	0.10
Gender (Male)	86.3%	88.7%	85.3%	0.82
Hypertension	53.7%	49.1%	46.8%	0.53
Diabetes mellitus	33.7%	28.3%	33.5%	0.75
Anemia (Hb<11g/dl)	2.5%	6.1%	2.8%	0.46
Renal Impairment	8.8%	14.6%	10.3%	0.58
LVEF	47.8±10.8%	48.7±11.2%	47.9±12.1%	0.94
Stent length (mm)	20.4±4.8	22.3±5.8	23.1±6.4	0.001
Creatinine Kinase level (U/L)	2388 (119-10732)	1860 (58-8664)	1927 (45-19058)	0.55
Cardiogenic shock	10.5%	3.8%	9.2%	0.36
AHA/ACC B2/C	82.1%	92.3%	92.6%	0.02
Location: LM & proximal LAD	36.8%	43.4%	31.2%	0.21

Results: MACE At 18-Month



CH Lee et al J Invas Cardiol 2007; 19: 182-185

Results: TVR At 18 Months



CH Lee et al J Invas Cardiol 2007; 19: 182-185

Zwolle GENOUS-AMI Program

Safety & Feasibility of Routine use of Genous EPC Capture Stent in All Comers undergoing Primary PCI for STEMI

Interim Results

Baseline *(n=738 All-comers)*		
Age *(yrs)*	62	*(35-81)*
Anterior MI	309	*42%*
Diabetes	81	*11%*
MVD	324	*44%*
Post TIMI-3	687	*93%*

Clinical Outcome *@ 30-days*		
Death*	24	*3.3%*
Re-MI	6	*0.8%*
Stent Thrombosis	8	*1.1%*
(Re)-PCI	42	*5.7%*
MACE	73	*9.9%*

**50% of Deaths were initial survivors of Out-of-Hospital Cardiac Arrest*

e-HEALING Registry: AMI Sub-group Analysis *(n=412)*

A Worldwide Registry (n=5000 @ 144 sites) on Genous EPC Capture Stent

	30 days (%)	6 months (%)	12 months (%)
Cardiac Death	1.7	1.9	2.7
Re-MI	1.0	1.5	1.5
TLR (Clinically Driven)	0.2	2.9	3.9
PCI	0.2	2.7	3.4
CABG	0.0	0.2	0.5
MACE	2.9	6.3	8.1
	Acute	Sub-acute	Late
Stent Thrombosis %	0.0	1.5	0.0

All events adjudicated by CEC
Worst MACE per patient = cardiac death, MI, CABG, and clinically driven TLR

Development of a Novel Prohealing Stent Designed to Deliver Sirolimus From a Biodegradable Abluminal Matrix

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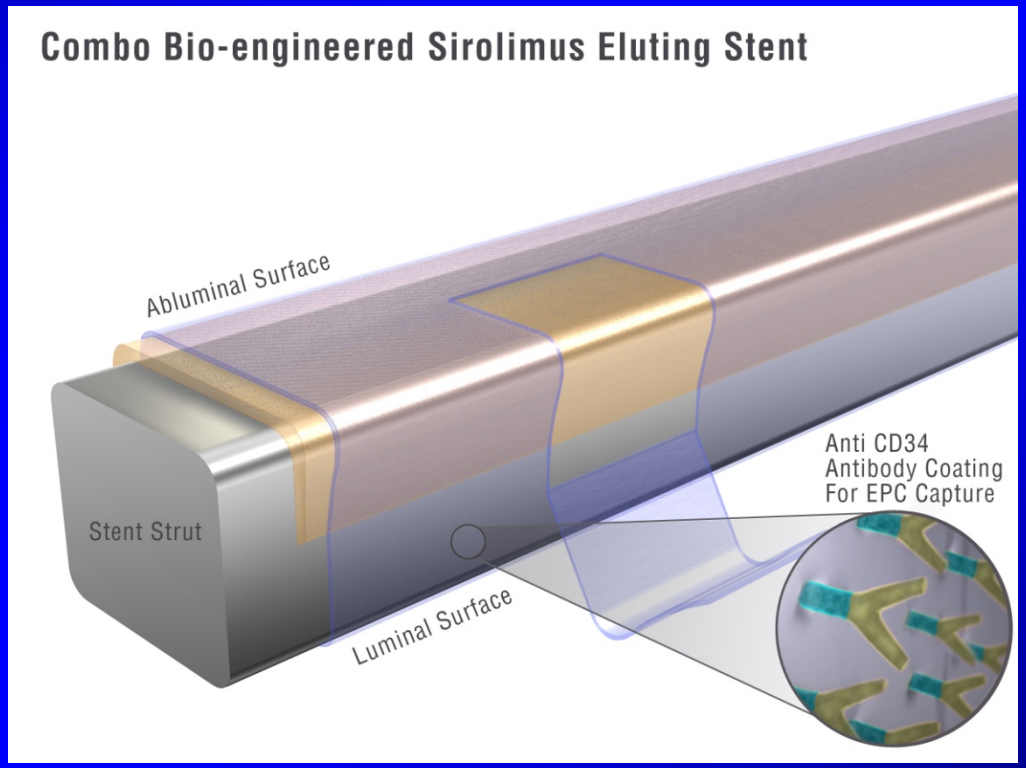

Conclusions

- Pro-healing stents in AMI offers potential in promoting early reendothelialisation and consequent lower rate of stent thrombosis and TVR
- The implantation of EPC Capture (GENOUS™) stent in patients with STEMI during PPCI is safe and effective with low rate of TVR (5.0%) at 12 months
- There is no incidence of late stent thrombosis despite dual antiplatelet duration of one month
- Efficacy and safety findings corroborated by other centre and registry studies