Endothelial Progenitor Capture Technology and Beyond

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DES Rollercoaster

"Despite the implantation of millions of drug

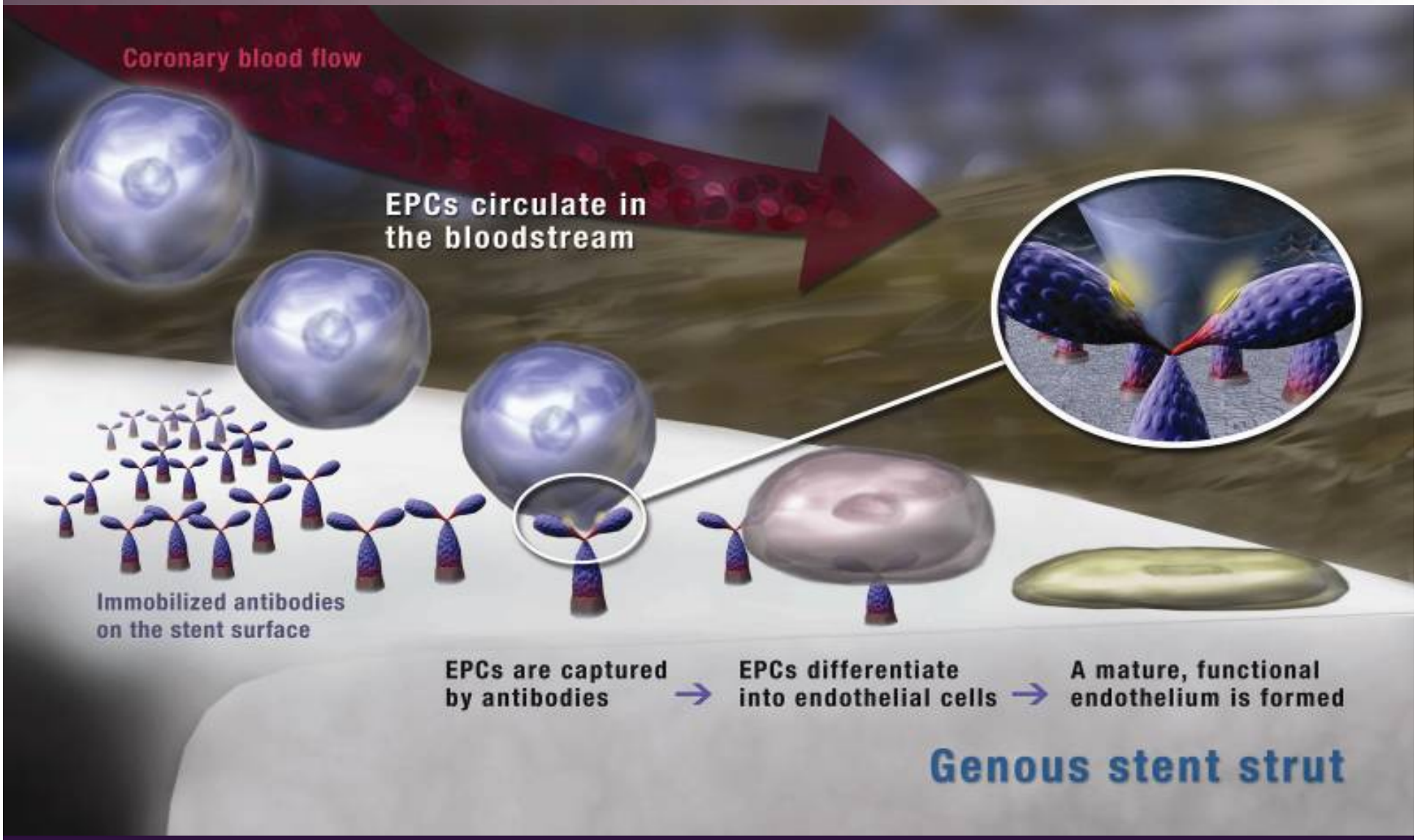
We Need Better Technologies!

remains uncertain about their long-term safety."

Maisel W et al., NEJM 2007

create

EPC Capture Technology



Genous Clinical Programs

- Healing II clinical trial
- eHealing clinical registry
- Naples Trial
- Trias Pilot Clinical Trial

HEALING II
clinical registry

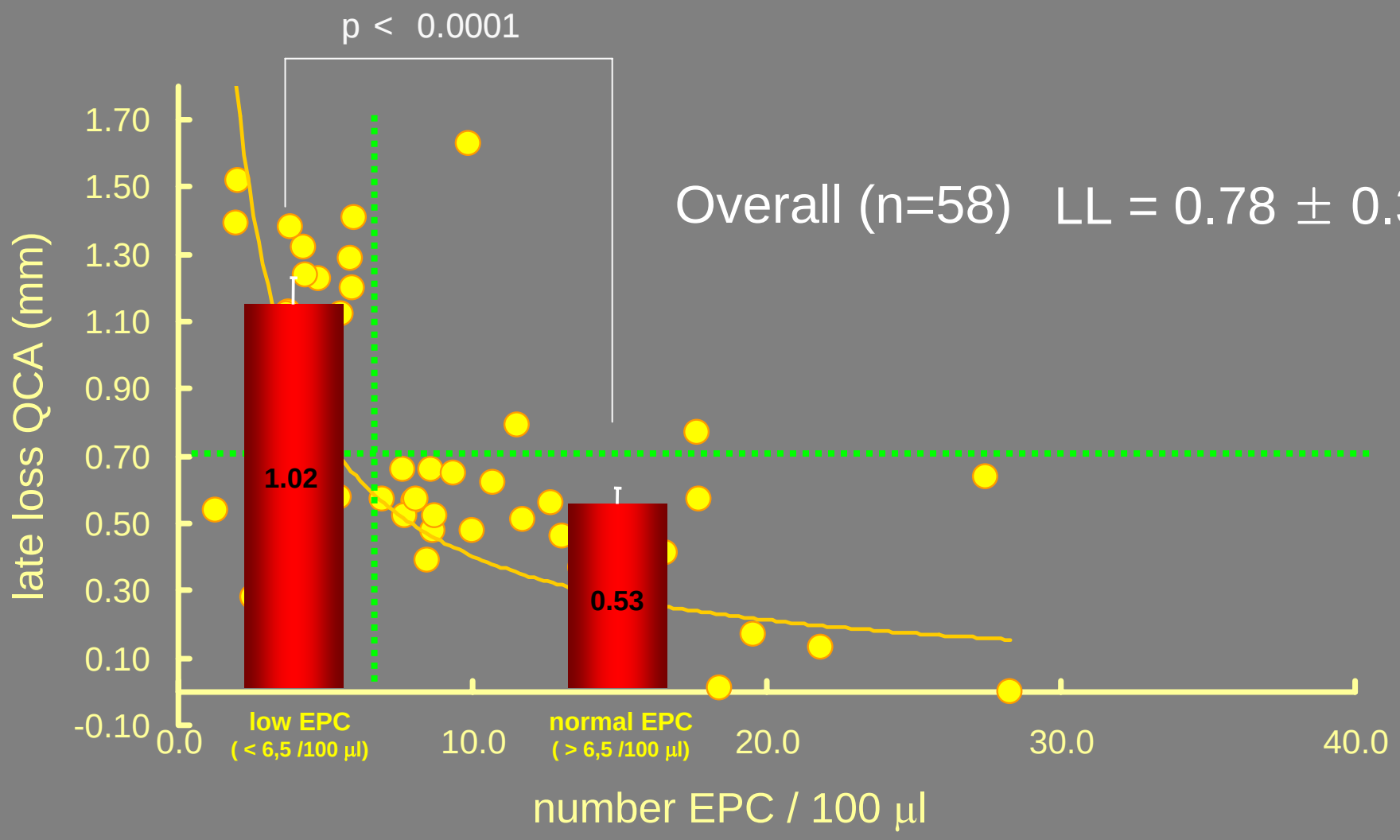
HEALING II – Trial Design

HEALING II study design:

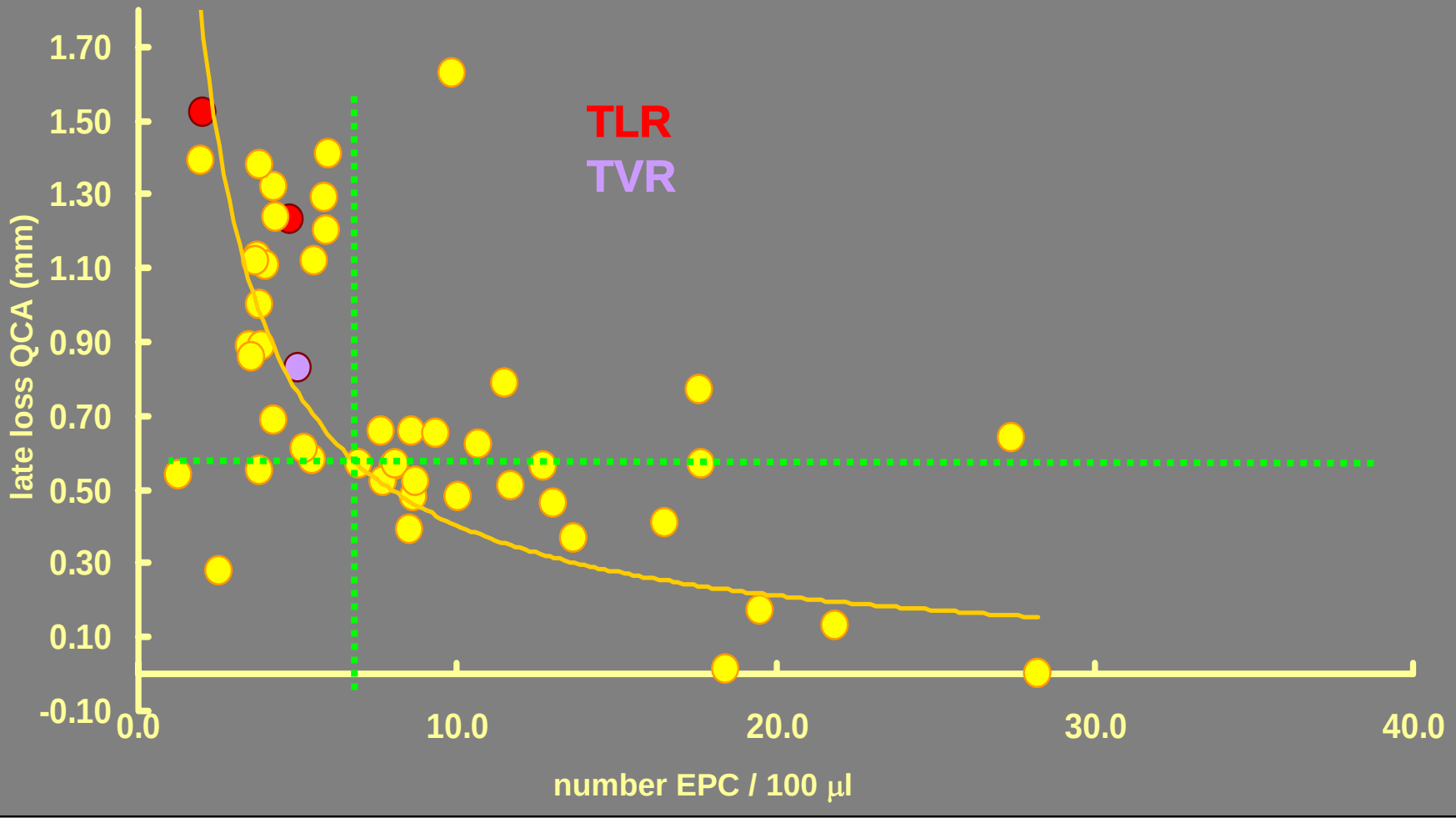
- Multi-centered, prospective, non-randomized trial
- 63 patients; 10 invited centers (NL, B, G)

- Objective:
  - Demonstrate the safety and efficacy of an EPC coated R stent™ stent (OrbusNeich)
- Indication:
  - De novo & non-stented restenotic lesions in native coronary arteries with reference vessels 2.5-3.5 mm
- Follow-up:
  - Quantitative coronary angiography and IVUS analysis at 6 (and 18) months
  - Clinical follow-up 6, 9 and 18 months

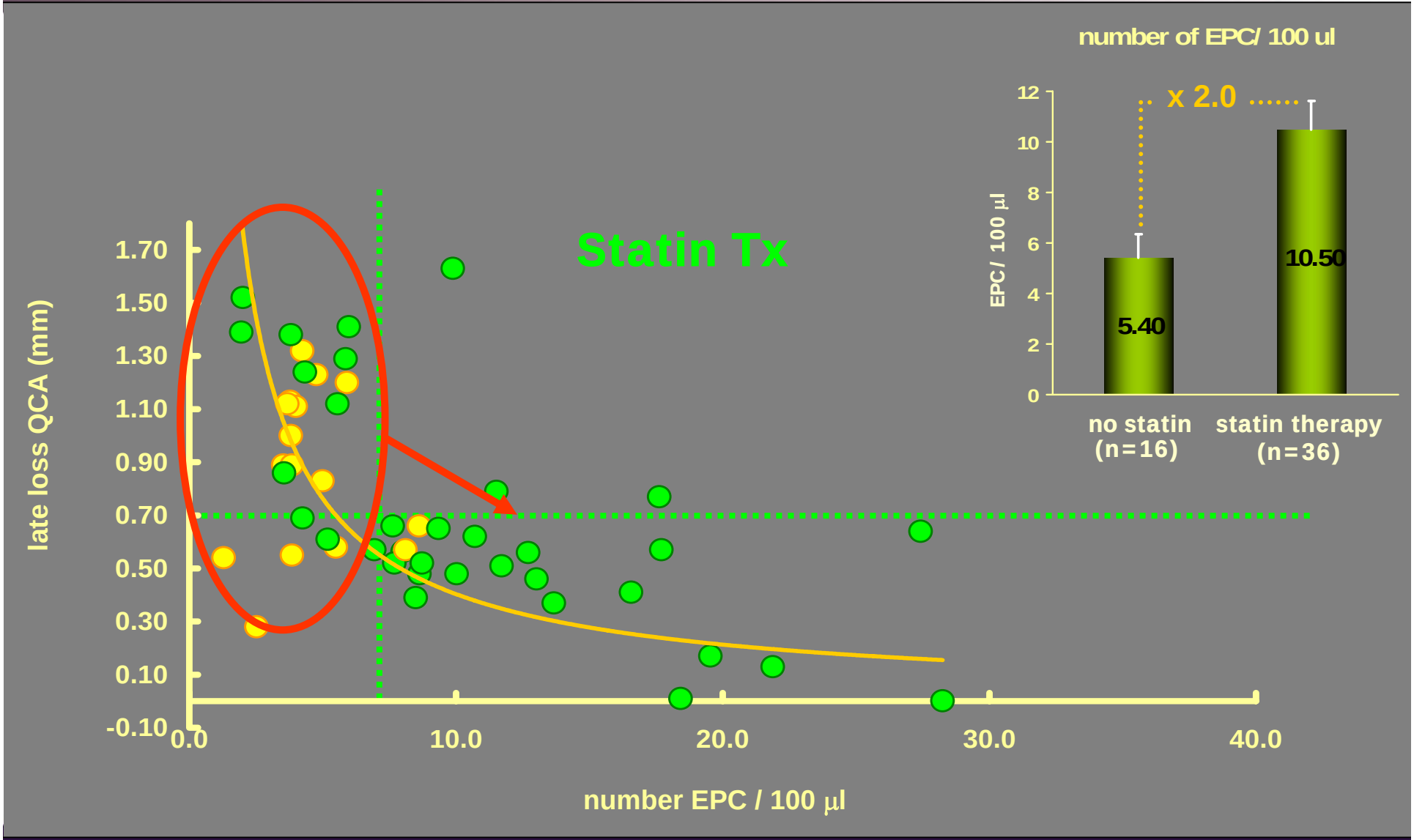
Correlation Late Luminal Loss and Circulating EPC Titer at 6 Months FU



Correlation Late Luminal Loss and Circulating EPC Titer at 6 Months FU



Correlation Between Late Luminal Loss and Circulating EPC Titer at 6 Months FU



HEALING II Clinical Events and EPCs

GenOus

Major Adverse Cardiac Events
9 months*

	H2 overall (n=63)	Low EPC (n=25)	Normal EPC (n=27)
Cardiac Death	1.6 %	0.0 %	0.0 %
MI	0.0 %	0.0 %	0.0 %
CABG	0.0 %	0.0 %	0.0 %
TLR (Clinically Driven)	6.3 %	8.0 %	0.0 %
MACE	7.9 %	8.0 %	0.0 %

Primary Endpoint: MACE at 30 days – 0%
Stent Thrombosis – 0%

*** 9 month window: +/- 1 month, no additional events reported from 6 month follow up**

e-HEALING Registry
Interim Analysis

Post Marketing Surveillance Registry of the Genous Bio-engineered R stent

e-HEALING Clinical Registry

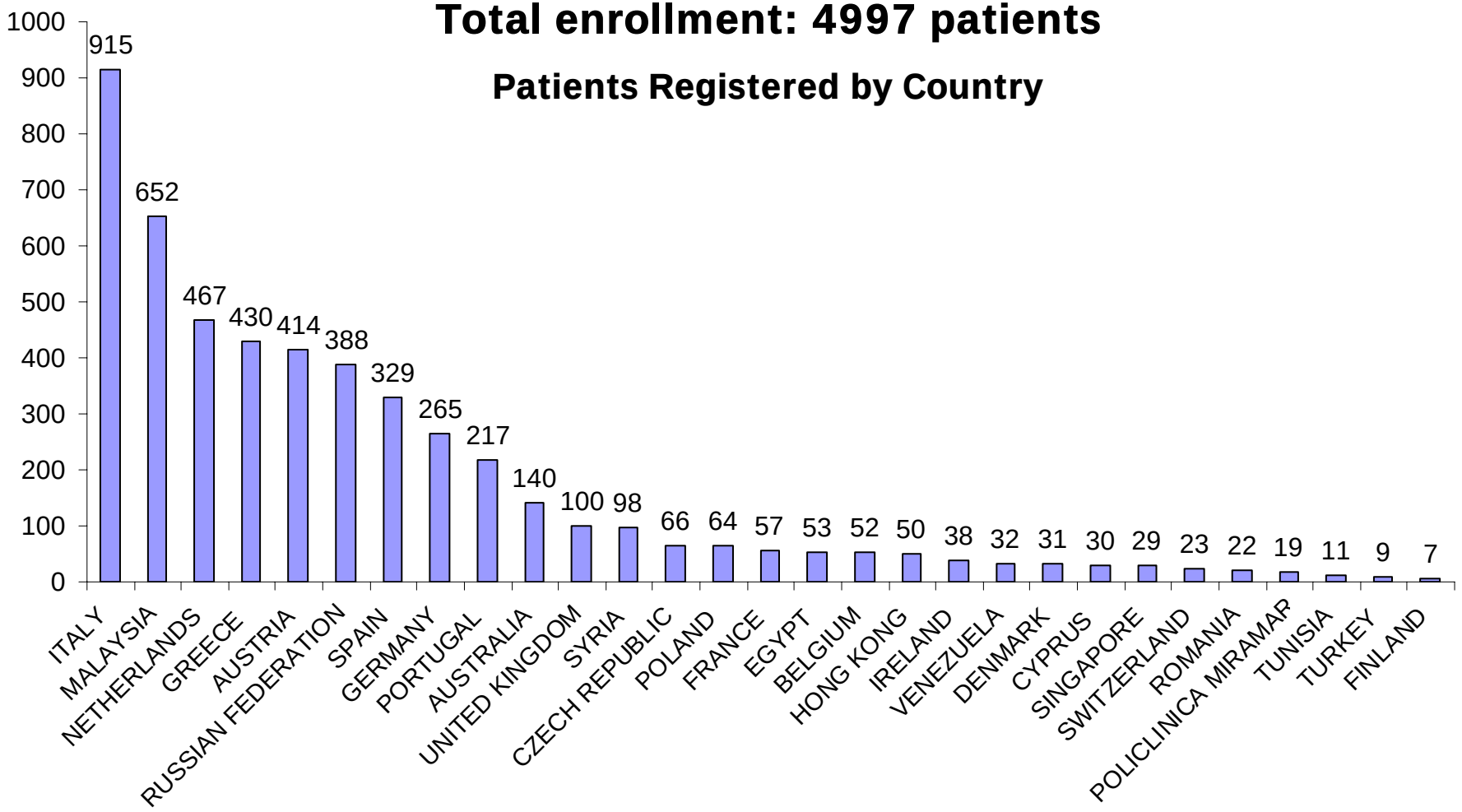
Overview

- Principal Investigators: Prof. Silber and Dr. de Winter
- Multi-center (120 sites), worldwide, prospective registry of patients treated with a Genous Bio-engineered R stent in accordance with the Instructions for Use
- 5000 patients
- Recommendation of at least two weeks statin treatment prior to the procedure and one month clopidogrel post-procedure
- Follow-up: 1, 6, and 12 month clinical follow-up
- Primary outcome: Target Vessel Failure at 12 months

Status - Enrollment complete


EUROPE
Austria 8
Belgium 3
Cyprus 2
Denmark 2
France 8
Germany 11
Greece 6
Ireland 1
Italy 26
Netherlands 5
Portugal 3
Spain 8
Switzerland 1
United Kingdom 9
Czech Republic 5
Finland 1
Hungary 2
Poland 2
Romania 1
Russian Federation 5
MIDDLE EAST
Egypt 6
Lebanon 1
Saudi Arabia 1
Syria 3
Turkey 3
LATIN AMERICA
Venezuela 1
NORTH AFRICA
Tunisia 2
ASIA PACIFIC
Australia 6
Hong Kong 1
Malaysia 9
Singapore 2
144 SITES
eHEALING

e-HEALING


Total enrollment: 4997 patients
Patients Registered by Country
1000
900
800
700
600
500
400
300
200
100
0
915
652
467
430
414
388
329
265
217
140
100
98
66
64
57
53
52
50
38
32
31
30
29
23
22
19
11
9
7
ITALY
MALAYSIA
NETHERLANDS
GREECE
AUSTRIA
RUSSIAN FEDERATION
SPAIN
GERMANY
PORTUGAL
AUSTRALIA
UNITED KINGDOM
SYRIA
CZECH REPUBLIC
POLAND
FRANCE
EGYPT
BELGIUM
HONG KONG
IRELAND
VENEZUELA
DENMARK
CYPRUS
SINGAPORE
SWITZERLAND
ROMANIA
POLICLINICA MIRAMAR
TUNISIA
TURKEY
FINLAND

e-HEALING
Patient Demographics as of Feb 21, 2008

Age	62.8 years
Males	78.7%
Diabetics	25.0%
Hypertension	68.3%
Hypercholesterolemia	74.5%
Current Smokers	24.8%
Family History	28.1%
Previous MI	36.7%
Previous PCI	19.1%
Previous CABG	6.2%
Previous Stroke	6.0%

e-HEALING
Ischemia Status as of Feb 21, 2008

Unstable angina	42.3%
Stable angina	43.3%
Silent ischemia	14.4%

e-HEALING
Lesion Characteristics as of Feb 21, 2008

De novo	**97.7%**
Restenotic	**2.3%**

Lesion Classification	
Type A	**15.3%**
Type B1	**35.6%**
Type B2	**29.6%**
Type C	**19.5%**

Lesion Length (mm)	
Mean ± Std Dev	**16.8 ± 8.6**

Reference Vessel (mm)	
Mean ± Std Dev	**3.0 ± 0.4**

Number of stents/patient	**1.5**
Number of lesions/patient	**1.3**

e-HEALING
Deviations to Date as of Feb 21, 2008

Not on statins for at least 2 weeks before procedure	**26.8%**
Patient with diffuse disease or poor flow distal to lesion	**15.3%**
Q wave MI ≤ 3 days	**5.7%**
Non Q wave MI ≤ 3 days	**2.4%**
Previous stent implanted is a drug eluting stent	**3.6%**
Anti-platelet and/or anti-coagulant therapy is contraindicated	**2.0%**
Saphenous vein grafts or unprotected left main coronary artery	**1.8%**
Reference diameter < 2.5 or > 3.75	**7.2%**
Pre procedure thrombus	**10.9%**
Vessel with excessive tortuosity	**1.9%**

e-HEALING

Clinical Events in patients with 6 month follow-up

Interim results as of Feb 21, 2008, n=3193

	30 days	6 months
Cardiac Death	**0.6 %**	**1.3 %**
MI	**1.0 %**	**1.4 %**
Q-wave	0.1 %	0.1 %
Non Q-wave	0.9 %	1.3 %
TLR (Clinically Driven)	**0.2 %**	**2.8 %**
PCI	0.2 %	2.5 %
CABG	0.0 %	0.3 %
MACE	**1.8 %**	**5.5 %**

Acute stent thrombosis	**0.2 %**
Sub-acute stent thrombosis	**0.3 %**
Late stent thrombosis	**0.3 %**

Patients treated before Feb 22, 2007

All events reported before 15 Jan 2008; all events adjudicated by CEC

Worst MACE per patient =cardiac death, MI, CABG, and clinically driven TLR

e-HEALING

Stent thrombosis according to ARC 12 months

Interim results as of Feb 21, 2008

Full population Stent thrombosis (only definite and probable)

Black line:	n=1640	Event Free 30 days: 99.4 %	180 days: 99.3%	365 days: 99.2%
At risk		30 days: 1617 pt	180 days: 1567 pt	365 days: 1405 pt

e-HEALING
Clinical Events in DM patients with 6 m fu

Interim results as of Feb 21, 2008

	6 months
Cardiac Death	**2.6 %**
MI	**1.5 %**
Q-wave	0.2 %
Non Q-wave	1.3 %
TLR (Clinically Driven)	**2.6 %**
PCI	2.4 %
CABG	0.2 %
MACE	**6.7 %**
Acute stent thrombosis	**0.0 %**
Sub-acute stent thrombosis	**0.4 %**
Late stent thrombosis	**1.1 %**

Patients treated before Aug 14, 2006

All events reported before Jan 15, 2008; all events adjudicated by CEC

Worst MACE per patient = cardiac death, MI, CABG, and clinically driven TLR

e-HEALING

Clinical Events in patients w/o statin use with 6 mth fu

Interim results as of Feb 21, 2008

	6 months
Cardiac Death	**2.3 %**
MI	**2.3 %**
Q-wave	0.5 %
Non Q-wave	1.9 %
TLR (Clinically Driven)	**2.3 %**
PCI	2.3 %
CABG	0.0 %
MACE	**6.9 %**
Acute stent thrombosis	**0.0 %**
Sub-acute stent thrombosis	**0.5 %**
Late stent thrombosis	**0.0 %**

Patients treated before Aug 14, 2006

All events reported before Jan 15, 2008; all events adjudicated by CEC

Worst MACE per patient = cardiac death, MI, CABG, and clinically driven TLR

e-HEALING

Clinical Events in TIMI 0/1 patients with 6 mth fu

Interim results as of Feb 21, 2008

	6 months
Cardiac Death	**2.1 %**
MI	**0.9 %**
Q-wave	0.3 %
Non Q-wave	0.6 %
TLR (Clinically Driven)	**2.1 %**
PCI	2.1 %
CABG	0.0 %
MACE	**5.0 %**
Acute stent thrombosis	**0.0 %**
Sub-acute stent thrombosis	**0.9 %**
Late stent thrombosis	**0.3 %**

Patients treated before Aug 14, 2006

All events reported before Jan 15, 2008; all events adjudicated by CEC

Worst MACE per patient = cardiac death, MI, CABG, and clinically driven TLR

e-HEALING

Clinical Events in patients with 12 month follow-up

Interim results as of Feb 21, 2008, n=1640

	30 days	6 months	12 months
Cardiac Death	**0.6 %**	**1.5 %**	**2.1%**
MI	**1.2 %**	**1.6 %**	**1.8%**
Q-wave	0.1 %	0.2 %	0.2%
Non Q-wave	1.0 %	1.4 %	1.5%
TLR (Clinically Driven)	**0 %**	**2.8 %**	**5.4%**
PCI	0.1 %	2.6 %	5.1%
CABG	0.0 %	0.2 %	0.4%
MACE	**1.9 %**	**5.9 %**	**9.3%**

Acute stent thrombosis	**0.0 %**
Sub-acute stent thrombosis	**0.5 %**
Late stent thrombosis	**0.5 %**

Patients treated before Aug 14, 2006

All events reported before Jan 15, 2008; all events adjudicated by CEC

Worst MACE per patient = cardiac death, MI, CABG, and clinically driven TLR

Non-Hierarchal Comparison

Registry	Product	12 Months		
		TLR	MACE	Stent thrombosis
e- HEALING *	Genous	5.4%	9.3%	1.0%
ARRIVE 1[1]	Taxus	5.4%	8.3%	2.1%
MILESTONE II	Taxus	5.5%	8.7%	2.6%

*Interim results of 1,640 patients treated before Aug 14, 2006 / All events reported before 15 Jan 2008; all events adjudicated by CEC

[1] N= 2,458 12 month follow-up on a total of 2,585 patients / http://www.bostonscientific.com (Taxus Express 2 Clinical Programs)

[2] N= 3,303 12 month follow-up on a total of 3,303 patients / http://www.bostonscientific.com (Taxus Express 2 Clinical Programs)

Conclusions

- The interim data from the e-HEALING Registry demonstrate that the Genous Bio-engineered R stent is safe and effective.

- The 1.6% MACE and 0.4% SAT rates at 30 days in 2,175 patients are low and are comparable to Cypher and Taxus registry data.

- The 5.5% MACE and 0.8% ST rates at 6 months in 3,193 patients are comparable to Cypher and Taxus registry data.

- The 5.4% TLR and 9.3% MACE rates at 12 months in the first 1,640 patients are low and comparable to Taxus registry data, and the 1.0% thrombosis rate at 1 year is superior to data reported with DES use.

Naples Clinical Trial

Objective

To evaluate the outcome of patients undergoing PCI with Genous implant and patients undergoing DES (SES or PES) implant

Design

- Single center trial – (Università degli Studi di Napoli - Federico II)
- PI: F. Piscione
- 195 consecutive patients underwent PCI with either Genous or DES (SES or PES) implantations in the period May – July 2006.
- Dual anti-platelet therapy for 1 month post-Genous implant and 9 months post DES implant.
- Clinical follow-up (average FU 10.1 ± 3.2 months).
- Follow-up major adverse clinical events (MACE): cardiac death, MI, target vessel re-PTCA, CABG.

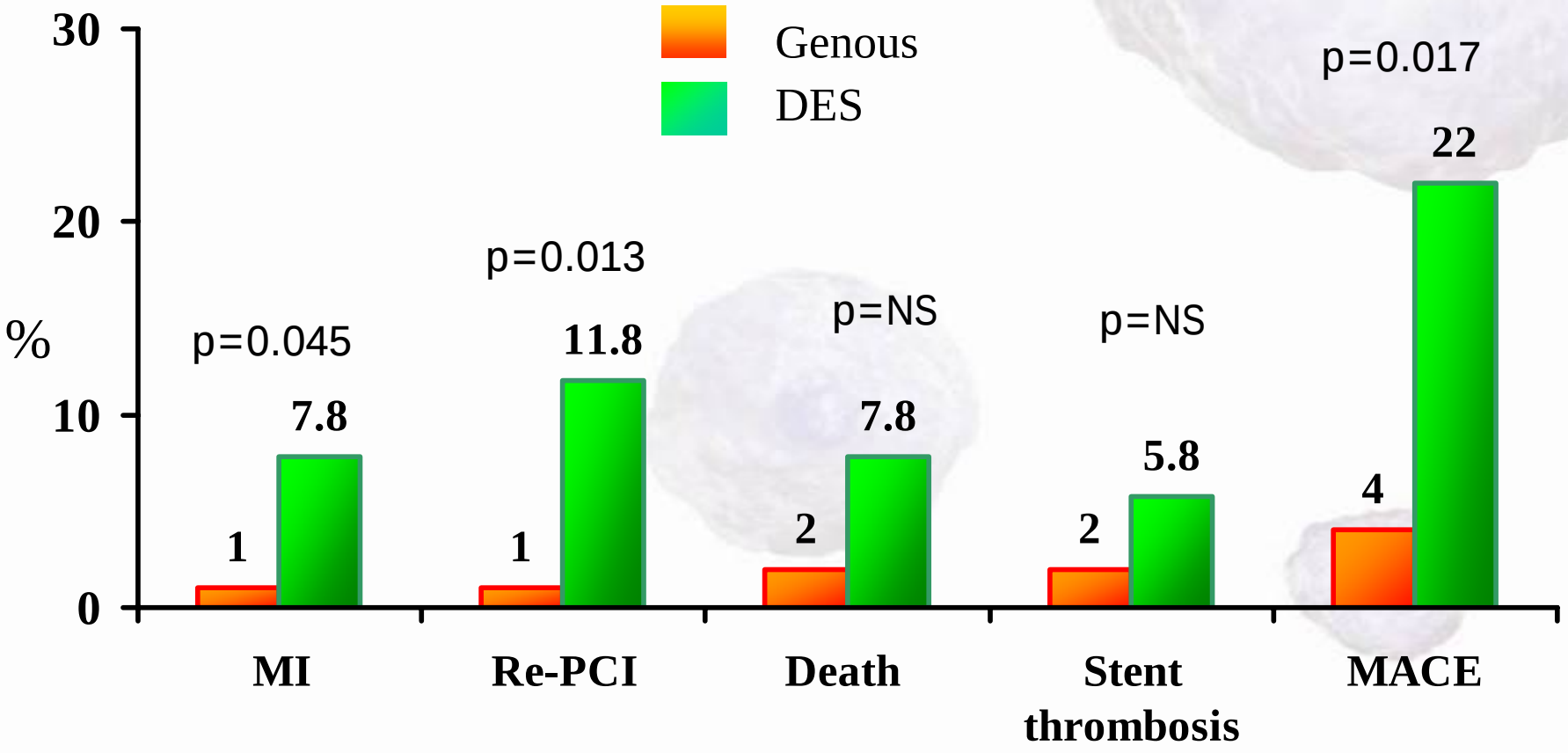
Patient clinical characteristics

	Genous (%) (n=100)	DES (%) (n=95)	p
Age	65.56±10.8	60.11±10.8	0.047
Male	84	67.7	0.048
Hypertension	70	80.6	NS
Diabetes	32	34	NS
Smoke	32.7	50	NS
Dislipidemia	46	63	NS
Familyhistory	38.2	33.4	NS
Pre PTCA	10.9	15.4	NS
Pre CABG	9.1	3.8	NS
Pre EF	45	51	NS

Angiographic characteristics

	Genous	DES	p
LAD (%)	57	43	NS
CX (%)	16.3	26.2	NS
RCA (%)	24.5	26.2	NS
PTCA Multivessel (%)	57	44.6	NS
TIMI grade post	3	3	NS
Multiple stenting (%)	95.4	98.5	NS
Lesion length (mm)	22.67±9	26.9±12	0.049
IIb/IIIa (%)	73	62	NS
Direct stenting (%)	43.8	72.3	0.002

Follow-up MACE (10.1±3.2 months)



Conclusions

- The results indicate that the use of Genous stents in consecutive patients results in a low in-hospital MACE incidence and a favourable 10 month outcome compared with DES in this patient cohort.

HEALING
Clinical Development Program

Underway:

HEALING IIB

- Multi-center, prospective, observational trial designed to assess the safety and effectiveness of the Genous Stent, in conjunction with optimal statin therapy, in patients with *de novo* native coronary artery lesions
- 100 patients
- PI: Patrick Serruys

St. Michael's Hospital

- Single center trial in patients with contra-indications to ASA and/or Clopidogrel