Summit TCT Asia Pacific 2009

The OrbusNeich GENOUS EPC-Capture Stent Clinical Trial Program
HEALING and TRIAS

Margo Klomp MD

On behalf of

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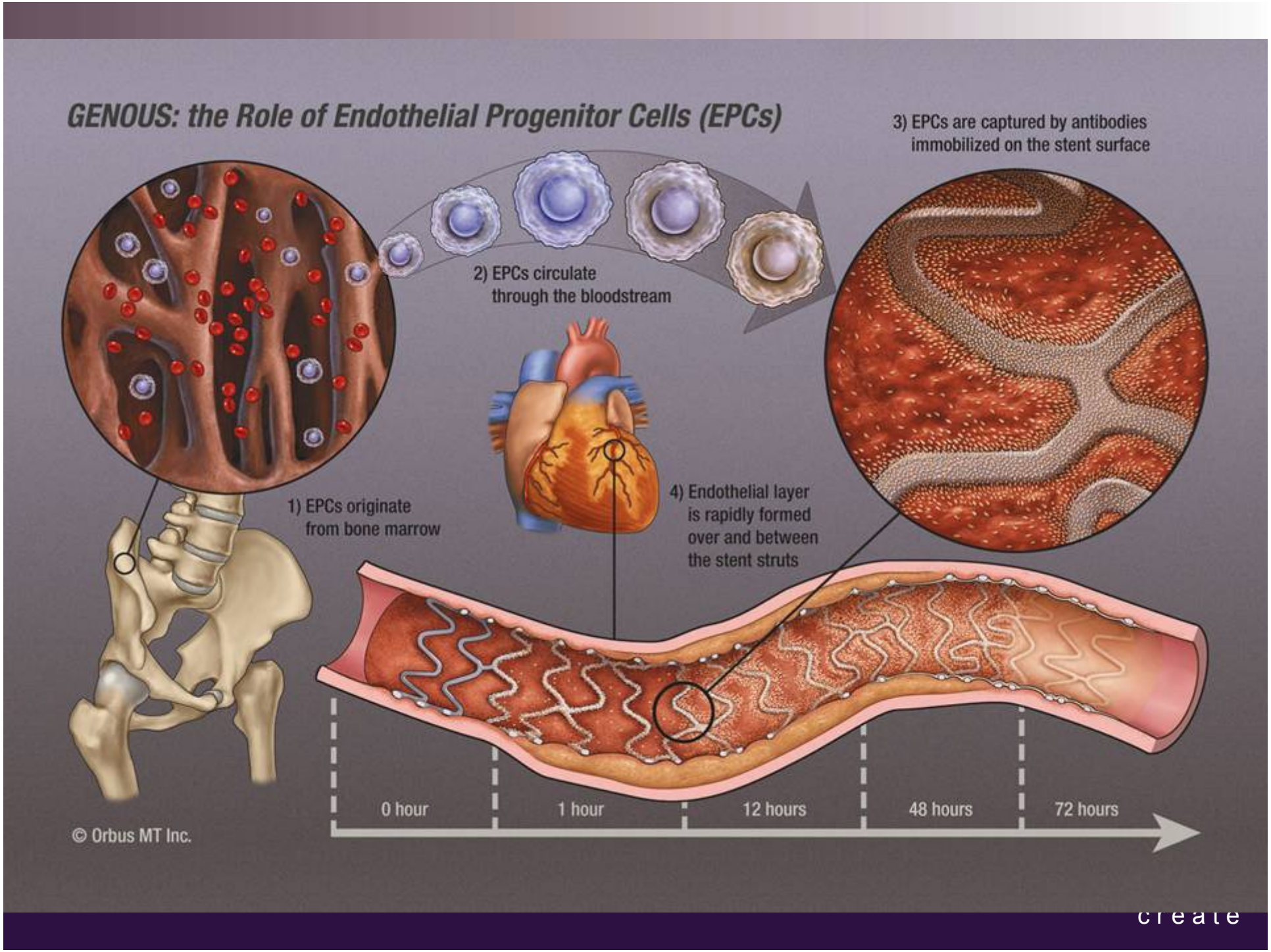
Academic Medical Center
University of Amsterdam
The Netherlands


GENOUS: the Role of Endothelial Progenitor Cells (EPCs)
3) EPCs are captured by antibodies immobilized on the stent surface
2) EPCs circulate through the bloodstream
1) EPCs originate from bone marrow
4) Endothelial layer is rapidly formed over and between the stent struts
0 hour
1 hour
12 hours
48 hours
72 hours
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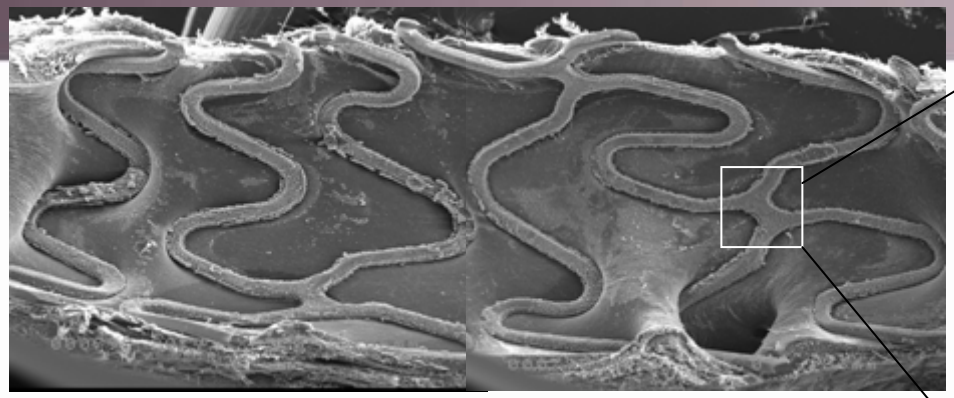
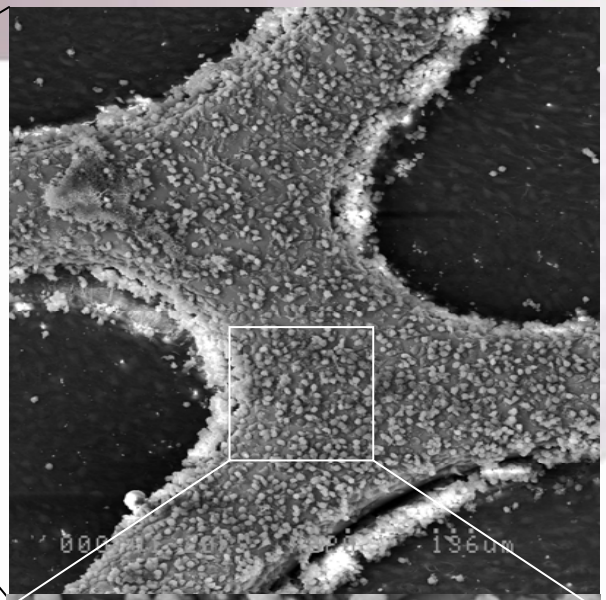
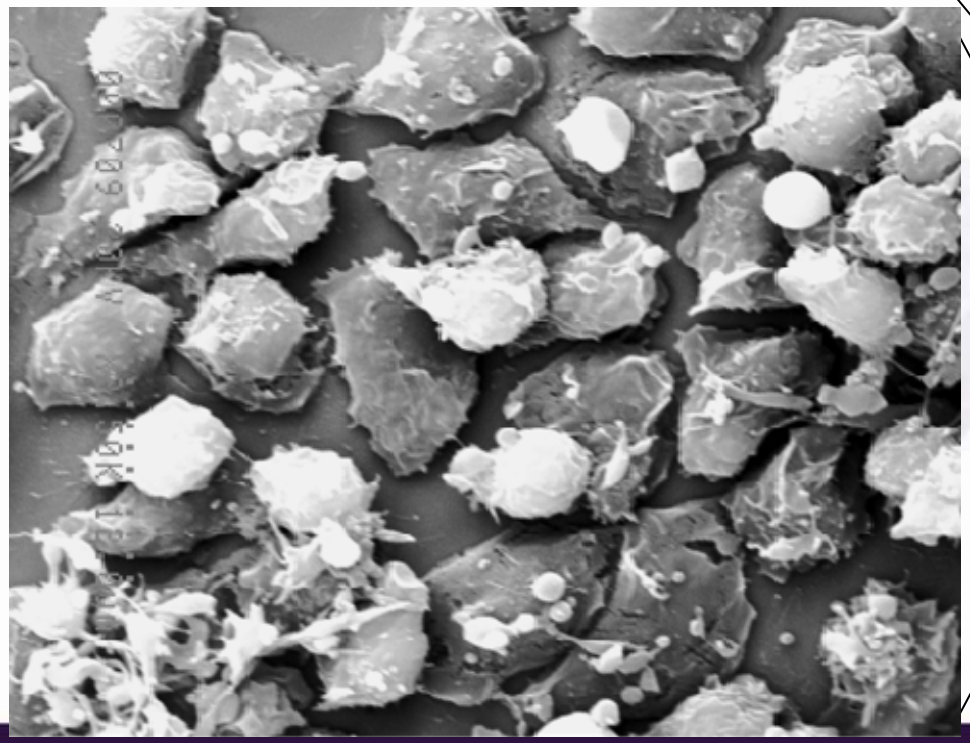
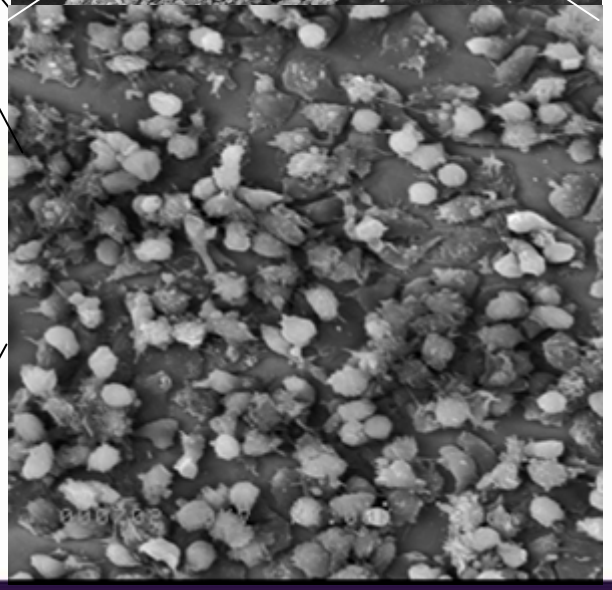
SEM: 1 hour after implantation









Genous Technology

First do no harm, the concept of healing

- **DES inhibit smooth muscle cell growth and intimal hyperplasia, but at the same time endothelialization of the stent struts**

- **Genous endothelial progenitor cell capturing technology, instead of inhibiting cell growth enhances endothelialization.**

Genous Technology

GENOUS clinical trial program		1Y FU
• HEALING FIM	16	√
• HEALING II	63	√
• HEALING IIb	99	√
• e-HEALING	4997	√
• TRIAS Single center	193	√
• TRIAS HR&LR program	2560	

HEALING II

Multi-centered, prospective, non-randomized trial, 63 patients; 10 centers

Enrollment: initiated May 2004; completed October 2004.

Objective: Demonstrate EPC capture stent's safety and efficacy in de novo coronary lesions of native arteries.

Follow-up using quantitative coronary angiography and IVUS analysis at 6 and 18 months.

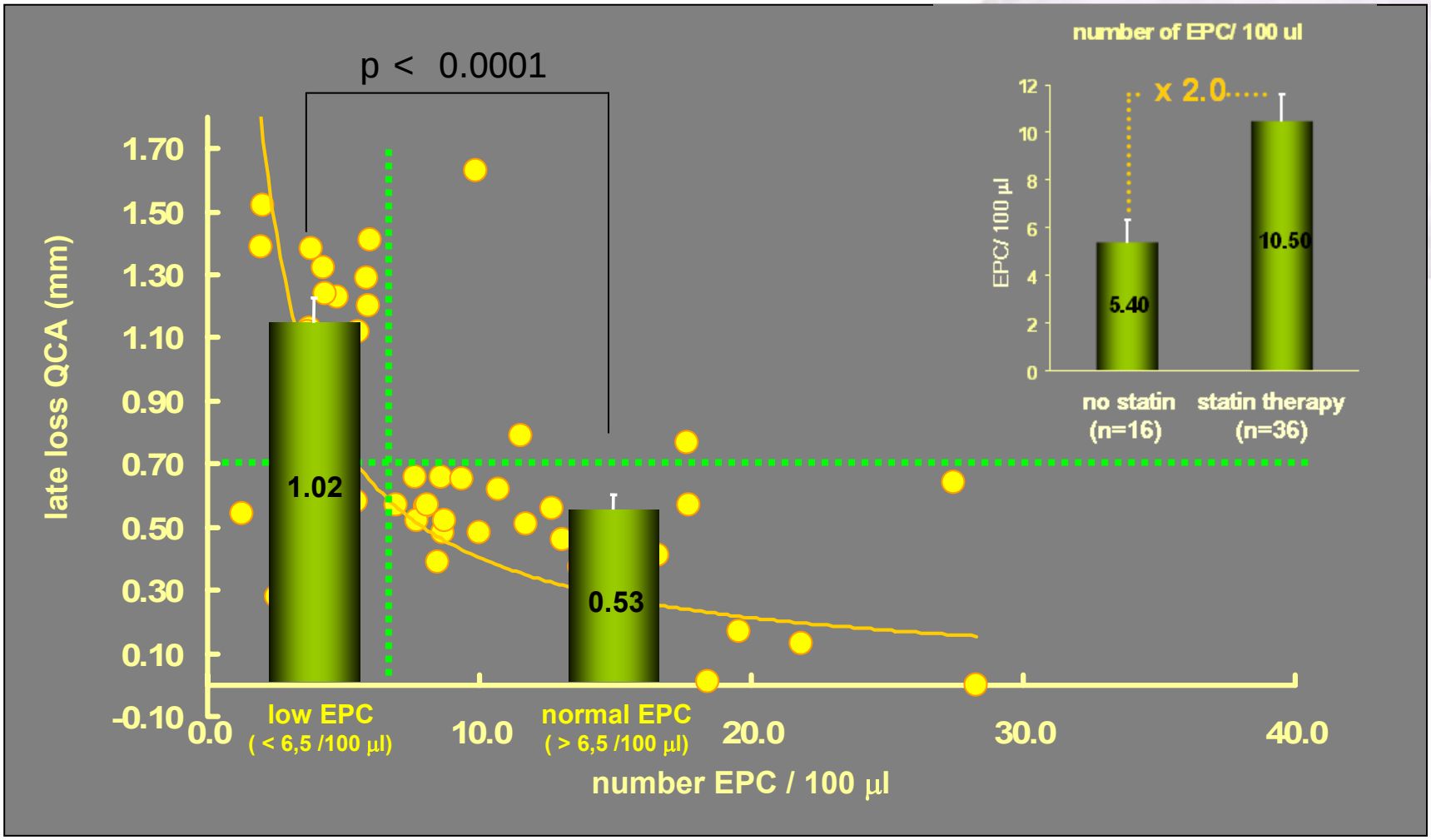
EPC number analysis at 6 months FU.

MACE* at 6 months and 18 months FU was 6.3% and 7.9% respectively.

In-stent LL: 0.78±0.39mm at 6 months and 0.59±0.31mm at 18 months = -24.4%.

*MACE=composite of cardiac death, MI, emergency CABG and ID TLR

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

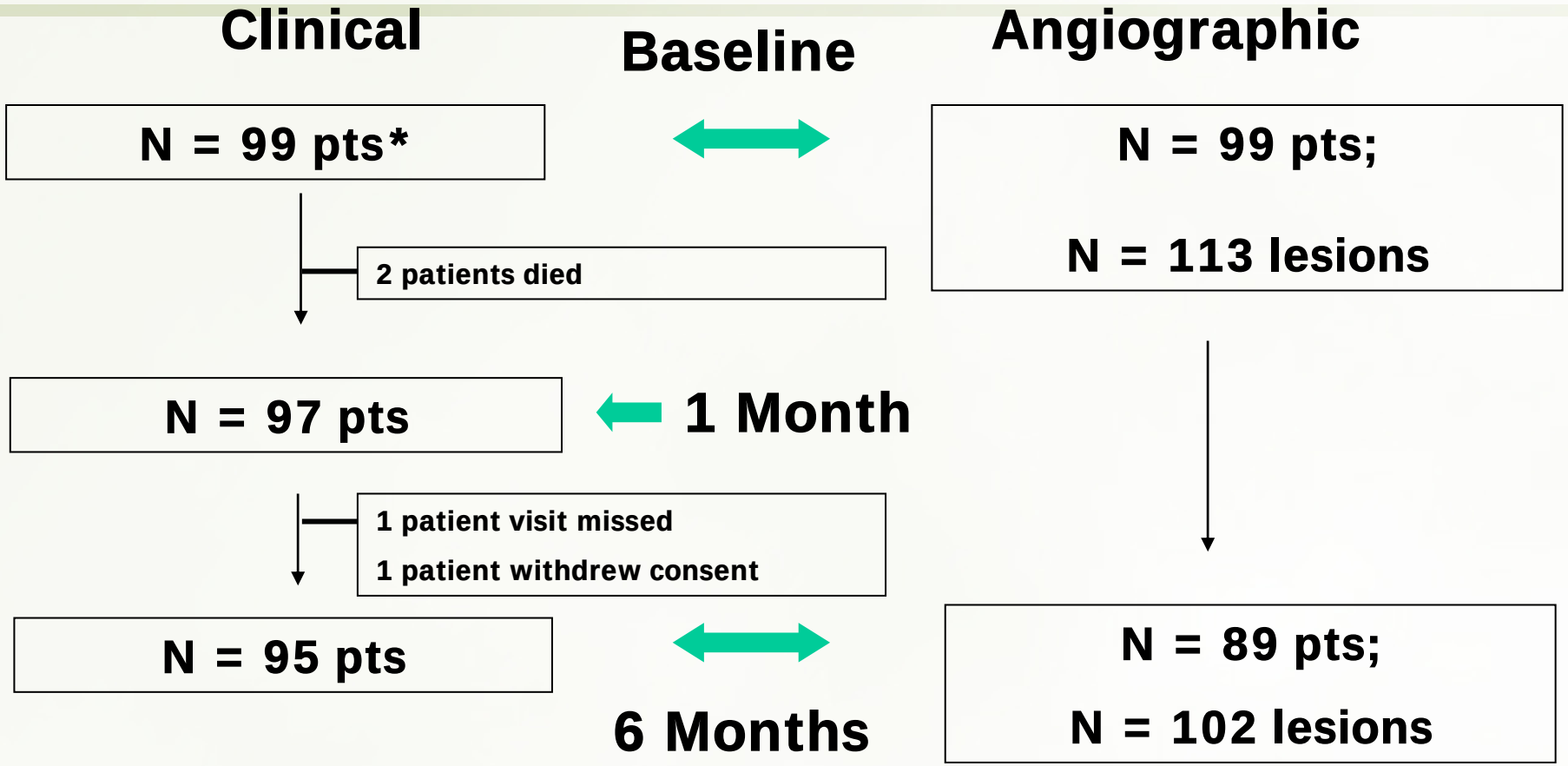


Healing 2B

6 Months follow-up results

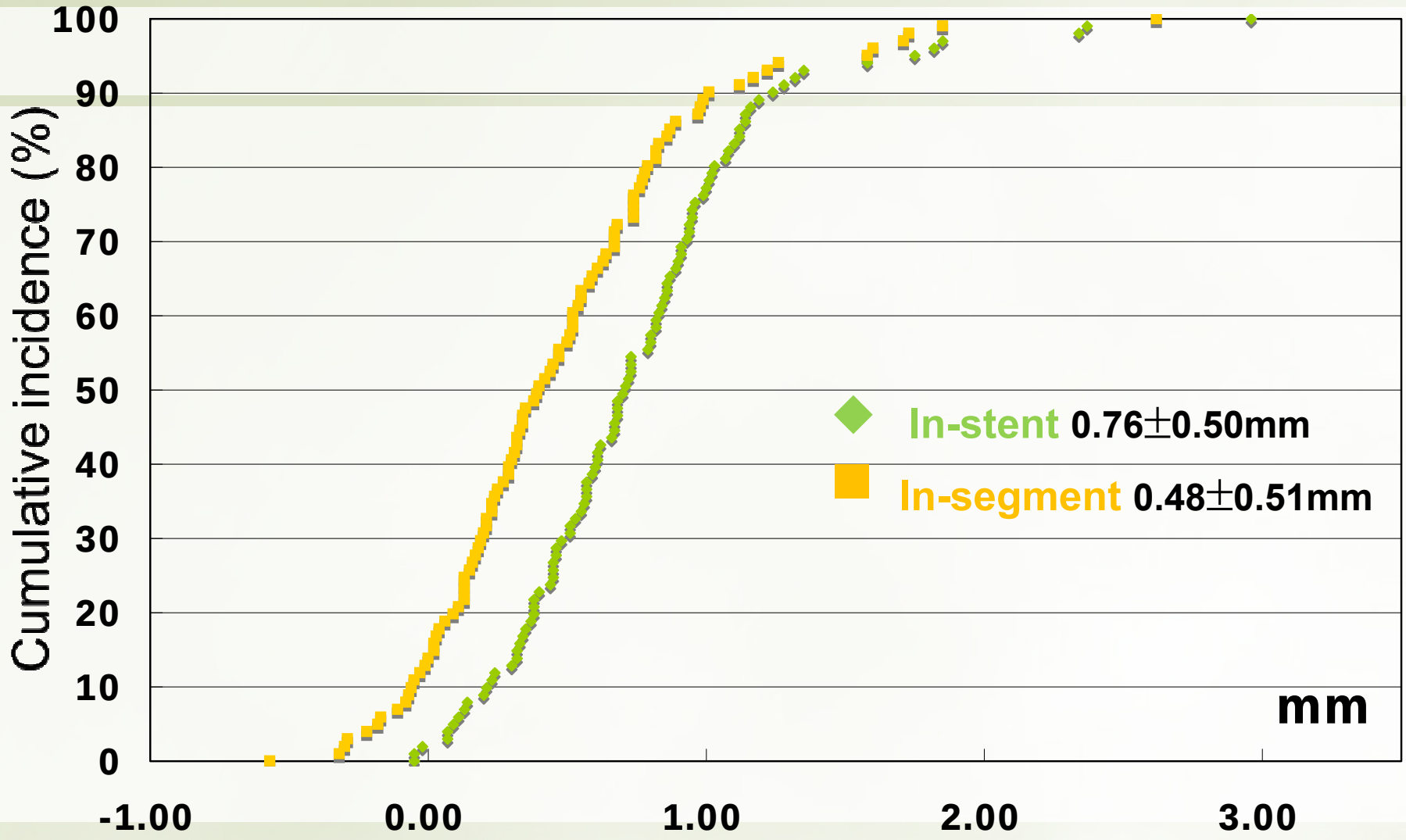
Patients Flow Chart of Per protocol (PP) population

1. Pre-treated with 80mg atorvastatin for 2 weeks
2. Device success* in at least one lesion treated with a Genous stent (device success defined as postprocedurel %DS is <30% by QCA).



* After 100 patients were enrolled, 1 patient (pt. 1139) was excluded from PP analysis: DS post procedure = 32%

Cumulative curve of in-stent Late Loss in matched QCA (n=102)

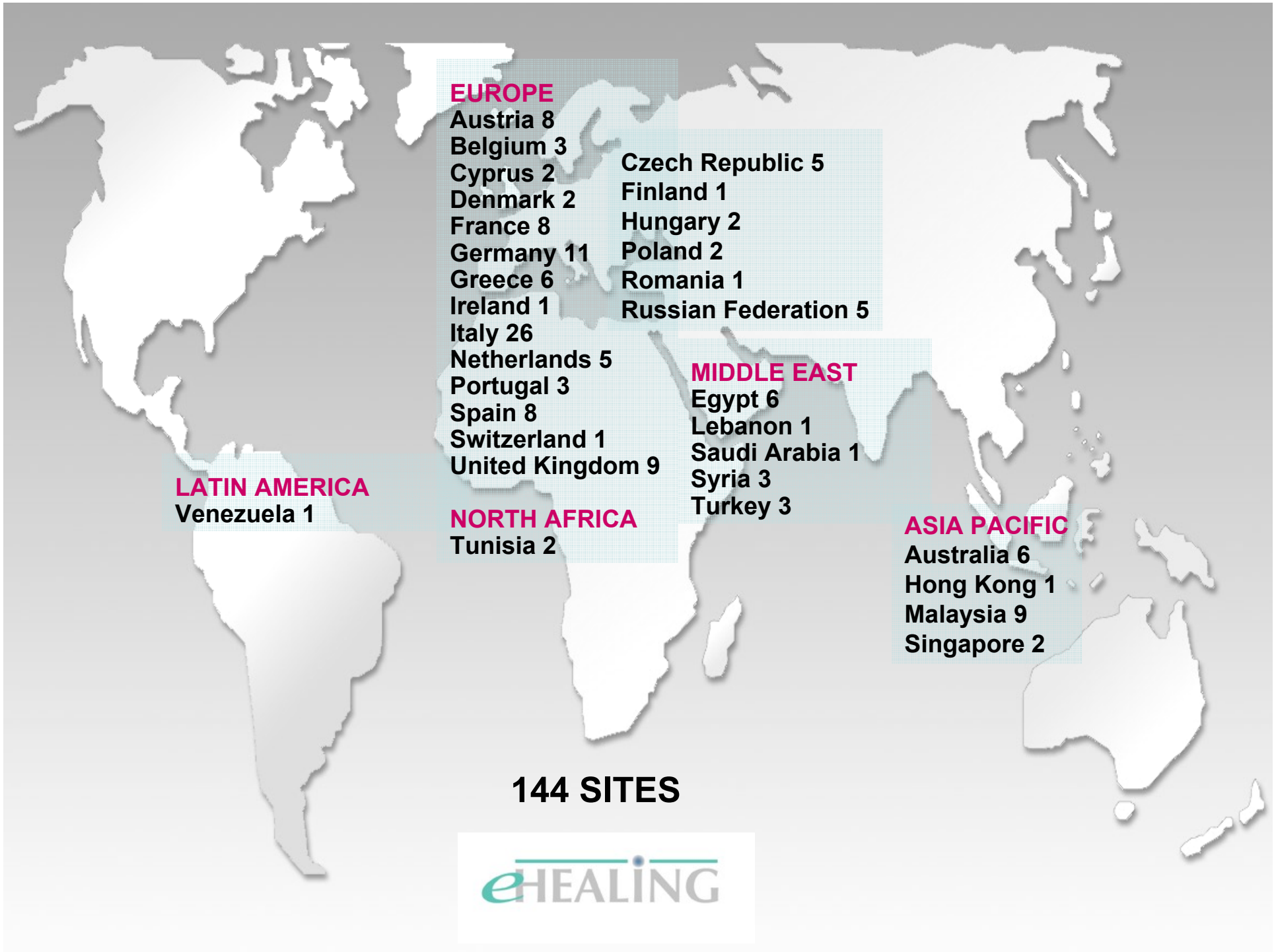


HEALING 2B 6M interim results, AHA 2008

Non-Hierarchical Events
(pt. may be counted under more than one event type)

	Up to Discharge	Up to 30 days	Up to 180 days	Up to 210 days
N= 99	%	%	%	%
Cardiac Death	**1.0**	**2.0**	**2.0**	**2.0**
MI	**4.0**	**5.1**	**5.1**	**5.1**
Q-wave	1.0	2.0	2.0	2.0
Non Q-wave	3.0	3.0	3.0	3.0
Cardiac Death + MI	**4.0**	**5.1**	**5.1**	**5.1**
Non TV rePCI	0.0	0.0	0.0	1.0
ID TLR CABG	0.0	0.0	0.0	1.0
ID TLR PCI	1.0	2.0	6.1	8.1
ID TLR (PCI + CABG)	**1.0**	**2.0**	**6.1**	**9.1**
all TLR PCI (ID + non ID)	1.0	2.0	6.1	11.1
All PCI	**1.0**	**2.0**	**6.1**	**12.1**
MACE*	**4.0**	**5.1**	**9.1**	**12.1**

*MACE: Cardiac death + MI + ID TLR (PCI or CABG)


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
Patient Demographics as of Sep 17, 2008

Age	62.8 years
Males	78.7%
Diabetics	25.0%
Hypertension	68.4%
Hypercholesterolemia	74.5%
Current Smokers	24.9%
Family History	28.1%
Previous MI	36.7%
Previous PCI	19.2%
Previous CABG	6.2%
Previous Stroke	6.0%

e-HEALING
Lesion Characteristics as of Sep 17, 2008

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

Lesion Classification	
Type A	**15.3%**
Type B1	**35.4%**
Type B2	**29.7%**
Type C	**19.6%**

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

Clinical Events all patients with 12 month follow-up

Interim results as of Sep 17, 2008**, n=3196**

	30 days	6 months	12 months
Cardiac Death	**0.6 %**	**1.3 %**	**1.9 %**
MI	**1.2 %**	**1.5 %**	**1.6 %**
Q-wave	0.2 %	0.2 %	0.2%
Non Q-wave	1.0 %	1.3 %	1.4%
TLR (Clinically Driven)	**0.2 %**	**2.9 %**	**5.0 %**
PCI	0.2 %	2.6 %	4.6%
CABG	0.0 %	0.3 %	0.4%
MACE	**1.9 %**	**5.8 %**	**8.5 %**
Acute stent thrombosis		**0.2 %**	
Sub-acute stent thrombosis		**0.4 %**	
Late stent thrombosis		**0.3 %**	

Patients treated before Feb 22, 2007

All events reported before Aug 12, 2008; all events adjudicated by CEC

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

e-HEALING

Clinical Events diabetic patients with 12 month follow-up

Interim results as of Sep 17, 2008, **n=851**

	30 days	6 months	12 months
Cardiac Death	**0.8 %**	**2.5 %**	**3.6 %**
MI	**0.6 %**	**1.3 %**	**1.3 %**
Q-wave	0.1 %	0.1 %	0.1 %
Non Q-wave	0.5 %	1.2 %	1.2 %
TLR (Clinically Driven)	**0.2 %**	**3.2 %**	**4.9 %**
PCI	0.2 %	2.8 %	4.5 %
CABG	0.0 %	0.4 %	0.5 %
MACE	**1.6 %**	**6.9 %**	**9.9 %**

Acute stent thrombosis	**0.0 %**
Sub-acute stent thrombosis	**0.2 %**
Late stent thrombosis	**0.8 %**

Patients treated on or before Feb 22, 2007

All events reported before Aug 12, 2008; all events adjudicated by CEC

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

e-HEALING

Clinical Events diabetic patients with 12 month follow-up

Interim results as of Sep 17, 2008, **n=851**

	30 days	6 months	12 months
Cardiac Death	**0.8 %**	**2.5 %**	3.6 % **(+1.7%)**
MI	**0.6 %**	**1.3 %**	1.3 % **(-0.3%)**
Q-wave	0.1 %	0.1 %	0.1 %
Non Q-wave	0.5 %	1.2 %	1.2 %
TLR (Clinically Driven)	**0.2 %**	**3.2 %**	4.9 % **(-0.1%)**
PCI	0.2 %	2.8 %	4.5 %
CABG	0.0 %	0.4 %	0.5 %
MACE	**1.6 %**	**6.9 %**	9.9 % **(+1.4%)**
Acute stent thrombosis		0.0 % **(-0.2%)**	
Sub-acute stent thrombosis		0.2 % **(-0.2%)**	
Late stent thrombosis		0.8 % **(+0.5%)**	

Patients treated on or before Feb 22, 2007

All events reported before Aug 12, 2008; all events adjudicated by CEC

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

e-HEALING compared to the DES groups of recent randomized studies

	Genous (e-HEALING)	Cypher (LEADERS)	BioMatrix (LEADERS)	Taxus (SYNTAX)
Inclusion criteria	**all comers**	**all comers**	**all comers**	**3-VD / Left main**
Number of patients	**3196**	**850**	**857**	**903**
Duration of follow-up	**12 months**	**9 months**	**9 months**	**12 months**
Cardiac death	**1.9 %**	**2.5 %**	**1.6 %**	**4.3 %** (any)
MI	**1.6 %**	**4.6 %**	**5.7 %**	**4.8 %**
TLR Clinically Driven	**5.0 %**	**4.9 %**	**4.3 %**	**13.7 %**
MACE	**8.5 %** [1]	**10.5 %** [2]	**9.2 %** [2]	**17.2 %** [3]
Stent thrombosis	**0.9 %**	**2.2 %** [4]	**2.7 %** [4]	**3.4 %** [4]
Dual antiplatelet therapy	**4 weeks**	**12 months**	**12 months**	**12 months**

Patients treated on or before Feb 22, 2007

All events reported before Aug 12, 2008; all events adjudicated by CEC

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

[2] MACE = Cardiac Death, MI TVR [3]MACE = any death, MI, TVR, [4]ARC definite + probable

Single-center TRIAS HR study

Academic Medical Center
Amsterdam
The Netherlands

To compare the feasibility and efficacy of the Genous EPC capturing stent with the Taxus paclitaxel-eluting stent in the treatment of coronary artery stenosis in patients / lesions with high risk of restenosis.

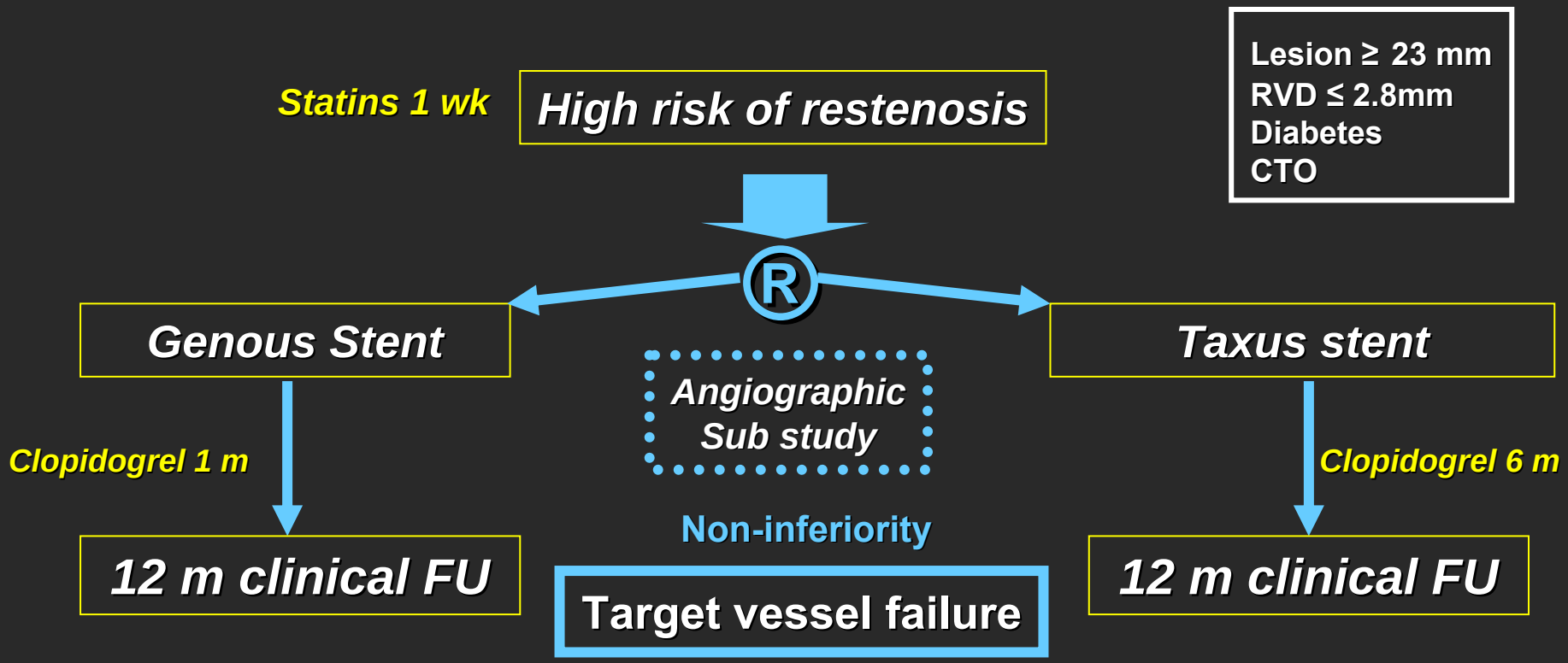
Single-center TRIAS HR study *Design*

- **Inclusion period: February 2006 - April 2007**
- **On statin therapy for at least 1 week prior to PCI**

High risk of restenosis is defined as:

- ♥ **Lesion ≥ 23 mm in length**
- ♥ **Lesions in vessels ≤ 2.8 mm in diameter**
- ♥ **Any lesion in diabetic patients**
- ♥ **Chronic total occlusion**

Single-center TRIAS HR study — Design



Single-center TRIAS HR study — *Results*

Clinical characteristics

	Genous N = 98	Taxus N = 95	P-value
Age	62 ±10	63 ±11	NS
Diabetes	14 (14%)	26 (27%)	0.025
Requiring oral medication	11 (11%)	18 (19%)	
Requiring Insulin	3 (3%)	8 (8%)	
Hypertension	45 (46%)	53 (56%)	NS
Hypercholesterolemia	62 (63%)	50 (53%)	NS
Family history of CAD	52 (52%)	61 (64%)	NS
Current smoker	32 (33%)	30 (32%)	NS
Angina pectoris			
Stable	80 (82%)	81 (85%)	NS
Unstable	18 (18%)	14 (15%)	NS
Statin therapy	98 (100%)	93 (98%)	NS

Single-center TRIAS HR study — *Results*

Lesion characteristics

	Genous N = 121	Taxus N = 125	P-value
Type of lesion			
A	0 (0%)	2 (2%)	
B1	10 (8%)	15 (12%)	
B2	54 (45%)	52 (42%)	Ns
C	57 (47%)	52 (42%)	Ns
Total chronic occlusion	39 (32%)	30 (24%)	Ns
Lesions ≥ 23 mm	101 (83%)	100 (80%)	Ns
Vessels ≤ 2.8 mm	9 (7%)	25 (20%)	0.004
Treated vessel			Ns
RCA	41 (34%)	49 (39%)	
LM	1 (1%)	1 (1%)	
LAD	48 (40%)	46 (37%)	
CX	31 (26%)	29 (23%)	

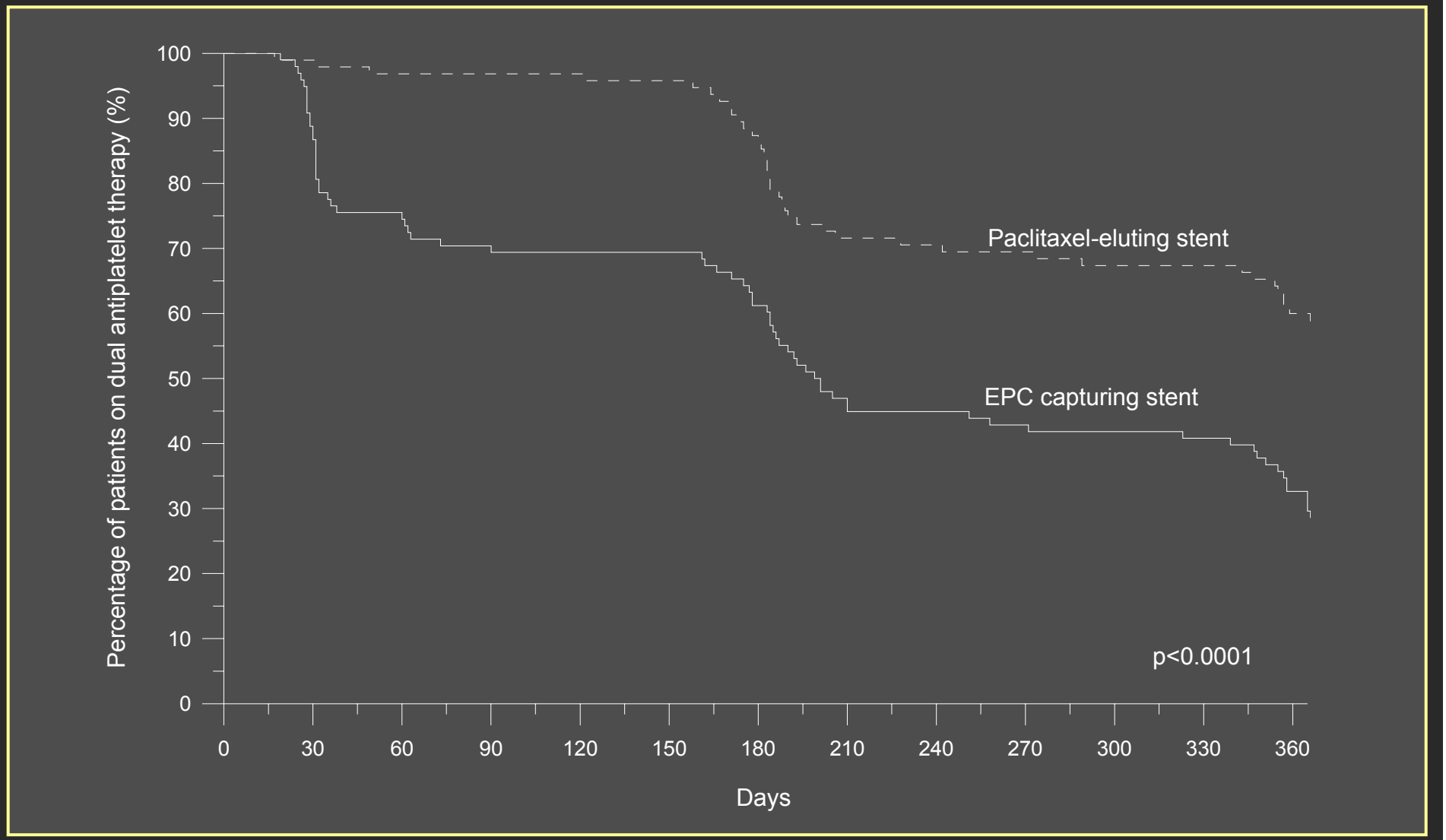
Single-center TRIAS HR study *Results*

Procedural characteristics

	Genous N = 121	Taxus N = 125	P-value
Pre-procedure TIMI 3 flow	74 (61%)	83 (66%)	Ns
Pre-dilatation	108 (89%)	111 (89%)	Ns
Stents per lesion	1.2 ± 0.54	1.2 ± 0.48	Ns
Lesion length, mm	26.8 ± 12	25.4 ± 10	Ns
Ref vessel diameter, mm	3.3 ± 0.4	3.2 ± 0.5	Ns
Total stent length, mm	31.7 ± 14.3	30.7 ± 12	Ns
Max Atm stent placement	13 ± 2.6	14 ± 2.5	Ns
Post dilatation	88 (73%)	88 (70%)	Ns
Max Atm post dilatation	18.6 ± 3.6	18 ± 3.5	Ns
Procedural success	119 (98%)	124 (99%)	Ns

Single-center TRIAS HR study

DAPT during 1-year follow-up



Single-center TRIAS HR study — *Results*

12-month clinical outcome

Stent thrombosis:

Genous

No Stent thrombosis (CEC adjudication)

Taxus

@ 24 hours	MI, TLR
@ 10 days	no MI, TLR
@ 155 days	MI, TLR
@ 200 days	MI, TLR

♥ All ST were angiographically documented

♥ All on dual antiplatelet therapy at time of ST

Single-center TRIAS HR study — *Results*

12-month clinical outcome

	Genous N=98	Taxus N=95	P-value
Cardiac death	0	0	
Non cardiac death	1 (1.0%)	2 (2.1%)	Ns
MI	3 (3.1%)	5 (5.3%)	Ns
TLR			
PCI	12 (12.2%)	8 (8.4%)	Ns
CABG	1 (1.0%)	1 (1.1%)	Ns
TVR/ no TLR	2 (2.0%)	0 (0%)	Ns
Non TVR	8 (8.2%)	14 (14.7%)	Ns
Target vessel failure*	**17 (17.3%)**	**10 (10.5%)**	**0.172**

*Target vessel failure: Cardiac death, MI, TVR

All events CEC adjudication

TRIAS HR Pilot study

Conclusions

♥ In this small, single center, randomized trial on ‘high risk’ patient, both Genous and Taxus treated patients showed good clinical outcome at 1 year

♥ There was a slightly higher incidence of target lesion repeat revascularization in patients treated with Genous

♥ There was a higher incidence of stent thrombosis in patients treated with Taxus

♥ A larger multicenter randomized study is needed

Conclusions

♥ **HEALING FIM, HEALING II, HEALING IIb show promising results**

- Healing II: 6 mFU: LL 0.78mm vs.18 mFU: 0.95mm = ↓24.4%
- Healing IIb: in-stent LL 0.76mm

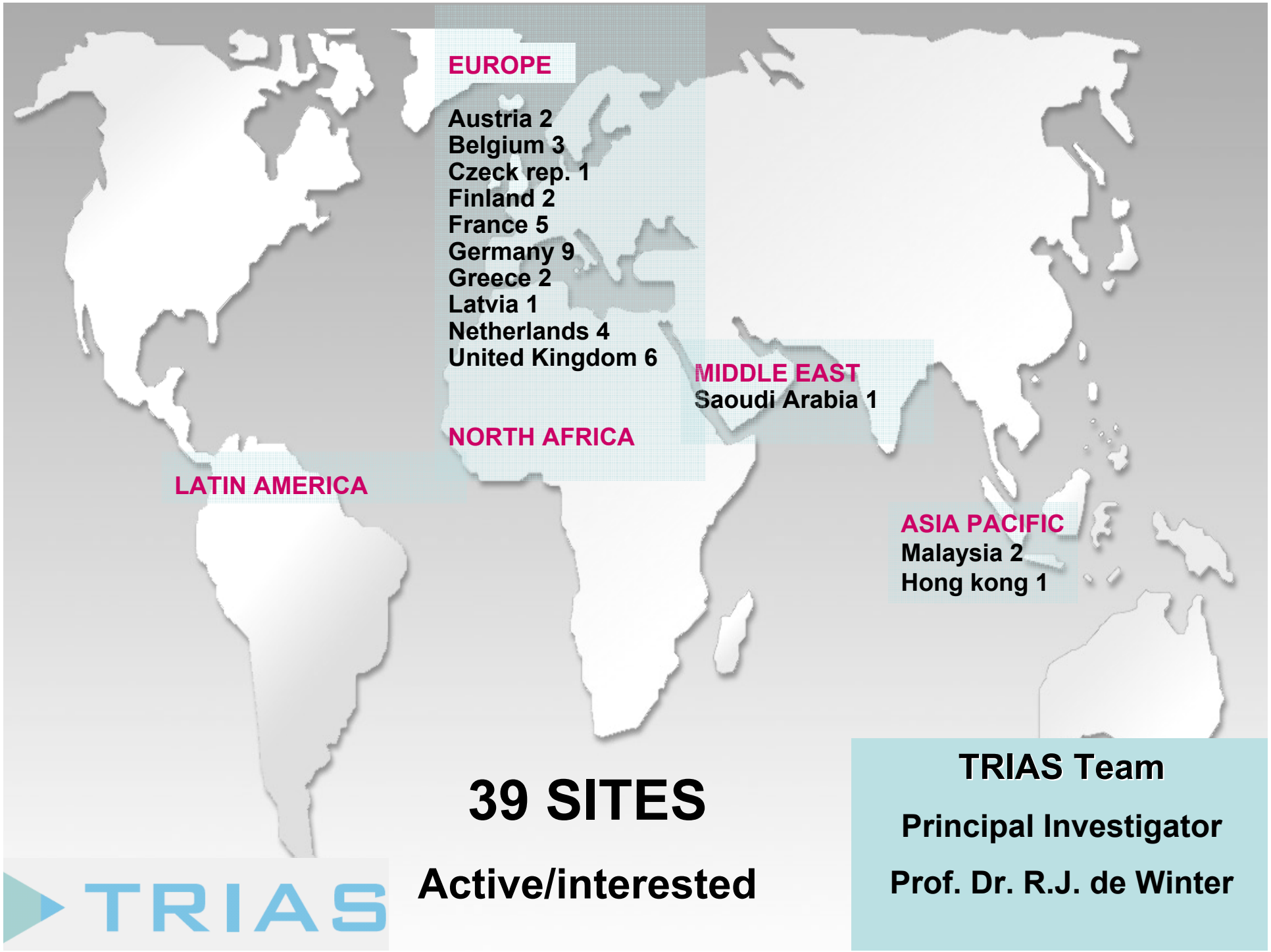
♥ **e-HEALING registry shows good clinical 1-year outcome**

√ MACE at 1 year: 8.5%

♥ **AMC TRIAS Pilot study shows good 1-year outcome**

√ TVF 17.3% vs 10.5%

√ stent thrombosis 0% vs 4.3%


EUROPE
Austria 2
Belgium 3
Czeck rep. 1
Finland 2
France 5
Germany 9
Greece 2
Latvia 1
Netherlands 4
United Kingdom 6
MIDDLE EAST
Saoudi Arabia 1
NORTH AFRICA
LATIN AMERICA
ASIA PACIFIC
Malaysia 2
Hong kong 1
39 SITES
Active/interested
TRIAS
TRIAS Team
Principal Investigator
Prof. Dr. R.J. de Winter

TRIAS study design

Study questions:

- **Genous better than BMS ?**
- **Genous safer than DES ?**

TRIAS

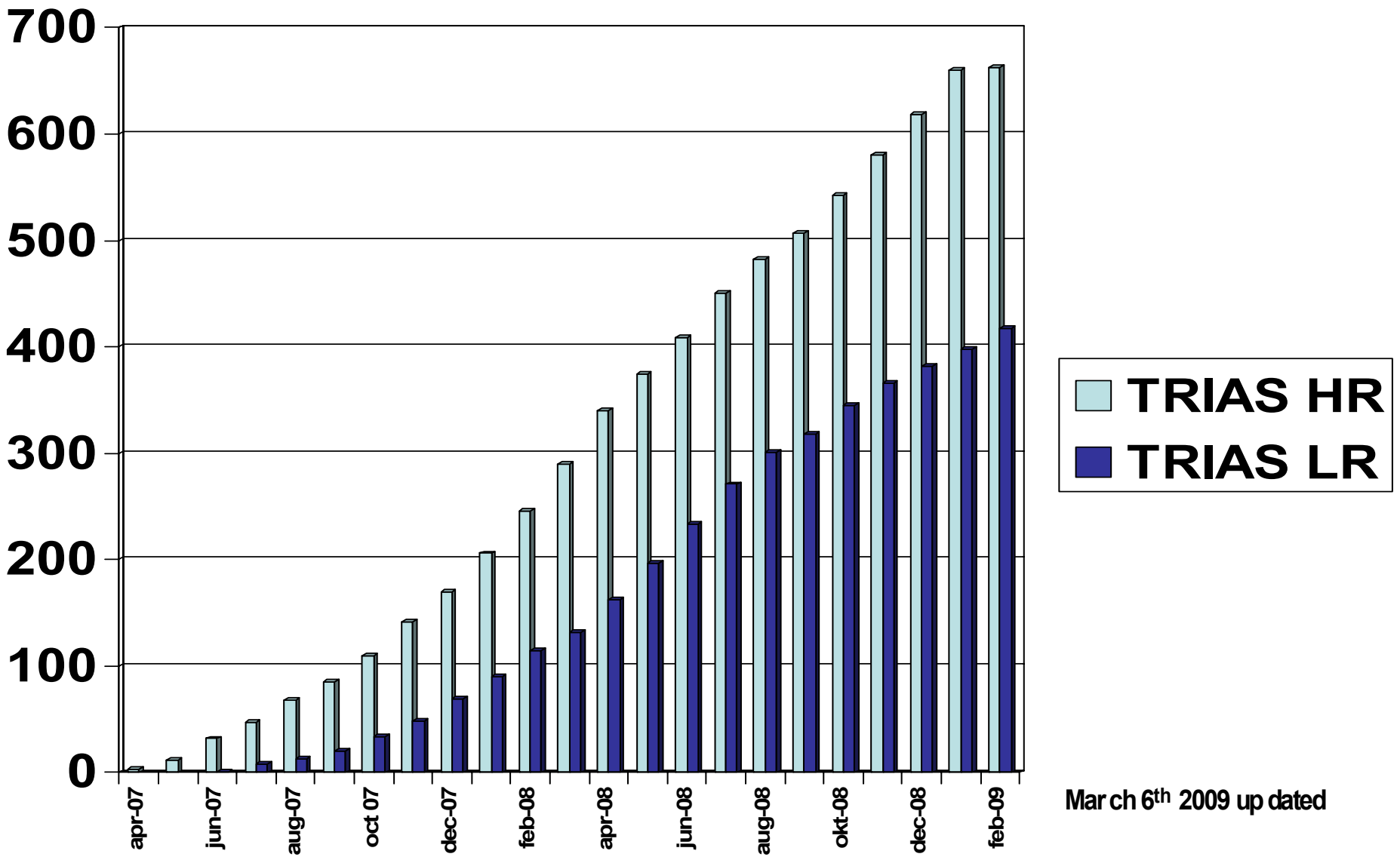
TRIAS study design

High risk of restenosis	*Low risk of restenosis*
TRIAS HR	**TRIAS LR**
RCT **Genous versus DES**	**RCT** **Genous versus BMS**
N = 1300	**N = 1260**

Clinical endpoint: TLF at 1 year FU

TRIAS

Current enrollment



Mar ch 6th 2009 up dated

TRIAS HR

Feb'09: Prospectively planned DSMB safety analysis (N=650)

- MACE:
  - No difference in cardiac death and MI. But slightly higher TLR in Genous group partially due to a better than expected TLR in DES population:
    - therefore *highly unlikely* to expect equivalence in TLR at 12 months follow-up
  - ➢ Recommendation: discontinuation patient enrollment in the TRIAS HR trial.

TRIAS

TRIAS LR

N=350

- DSMB: No concerns
- Advise: continue enrollment and follow-up

Genous Technology

GENOUS clinical trial program

• **HEALING FIM**	Published
• **HEALING II**	Published
• **HEALING IIb**	**12m outcome**
• **e-HEALING**	**EuroPCR 2009**
• **TRIAS Single Center**	**Submitted**
• **TRIAS HR**	***Continuation of FU***
• ***TRIAS LR***	***Actively enrolling***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THANK YOU