Randomized Comparison of Genous Stent Versus Chromium-Cobalt stent for Treatment of ST-Elevation Myocardial Infarction. 6-month Clinical, Angiographic and IVUS Follow-up. GENIUS-STEMI trial.

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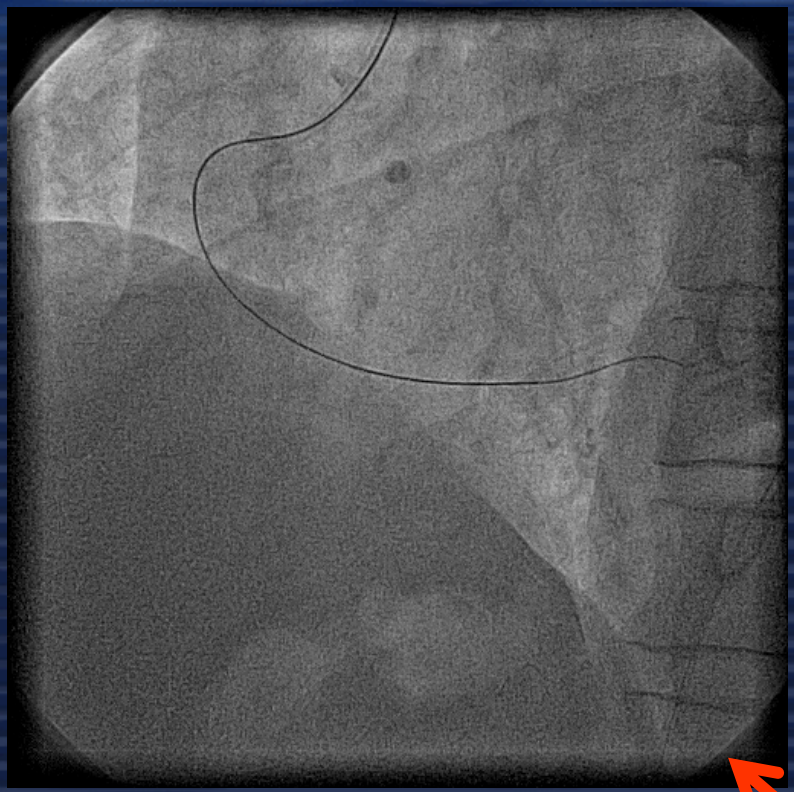
(Orlando, 28th March,2008)

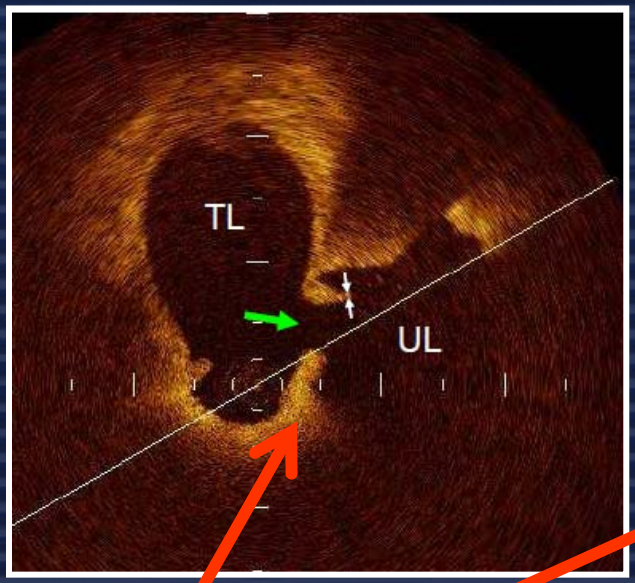
GENIUS-STEMI

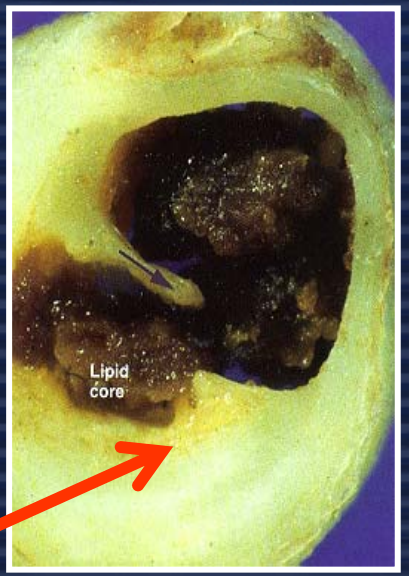
Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

Acute coronary syndromes

(STEMI or UAP/NSTEMI)







Plaque rupture/errosion + thrombosis

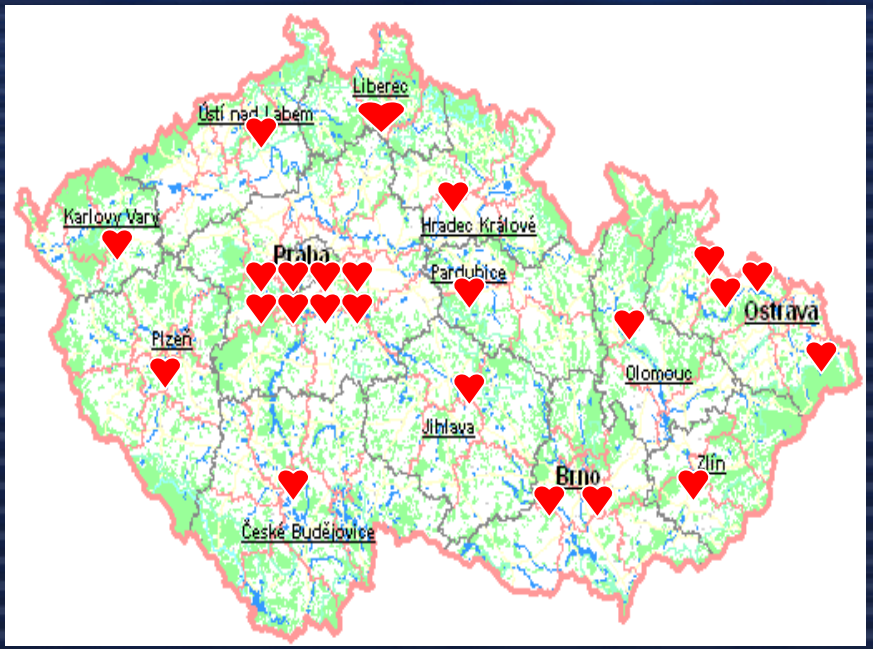
GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ *P-PCI is prefered treatment of STEMI* **IA**

Treatment of STEMI in CR
(!!93% CAG!!)

dPCI	83%
dPCI+CABG	3%
CAG+conservative	6%
TL	1%
Nothing	7%



(Registry of ACS of CR; 2006)

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ *Concerns about DES thrombosis in patients with STEMI*

European Heart Journal (2009) **30**, 321–329
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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

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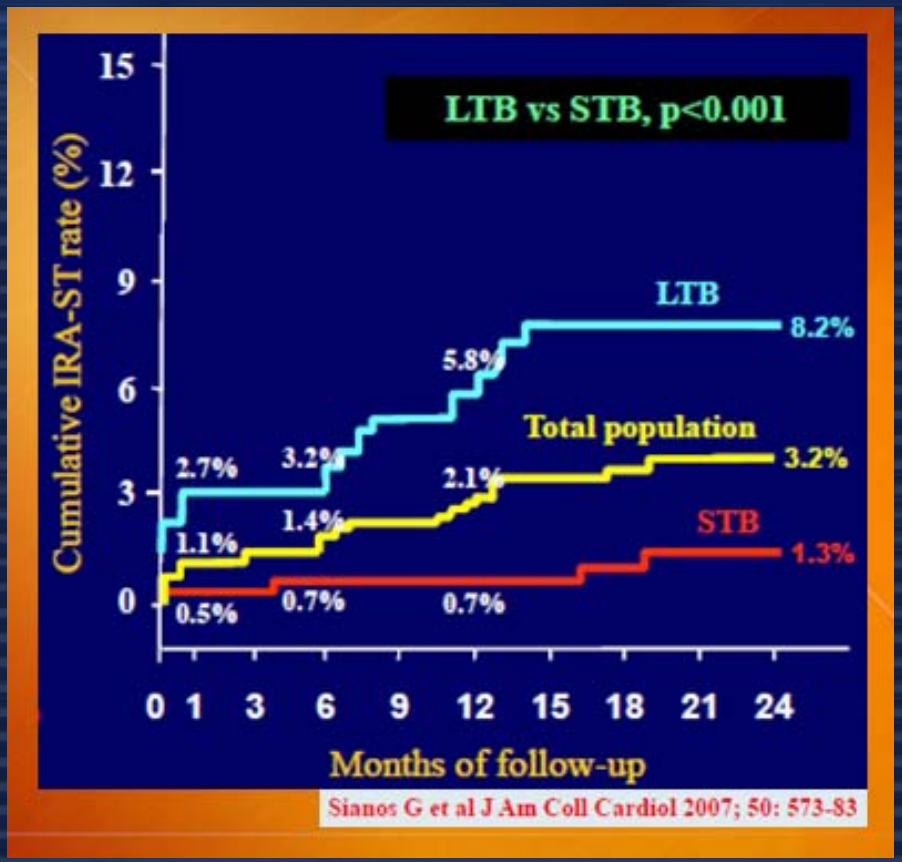
Aims To assess mortality after drug-eluting stent (DES) or bare-metal stent (BMS) for ST-segment elevation myocardial infarction (STEMI).

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.



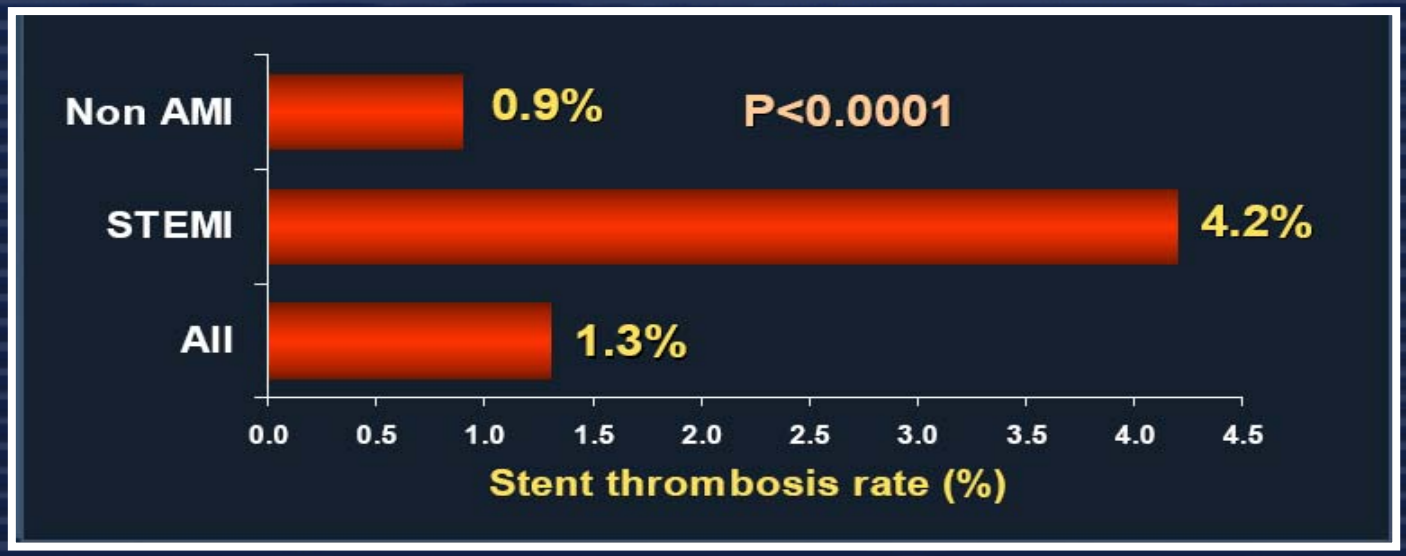
(de la Torre Hernandez JM, et al. JACC 2008;51:986-90)

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

Concerns about DES thrombosis in patients with STEMI

The Spanish ESTROFA Registry
N=23 500 pts; 63% PES, 37% SES



(de la Torre Hernandez JM, et al. JACC 2008;51:986-90)

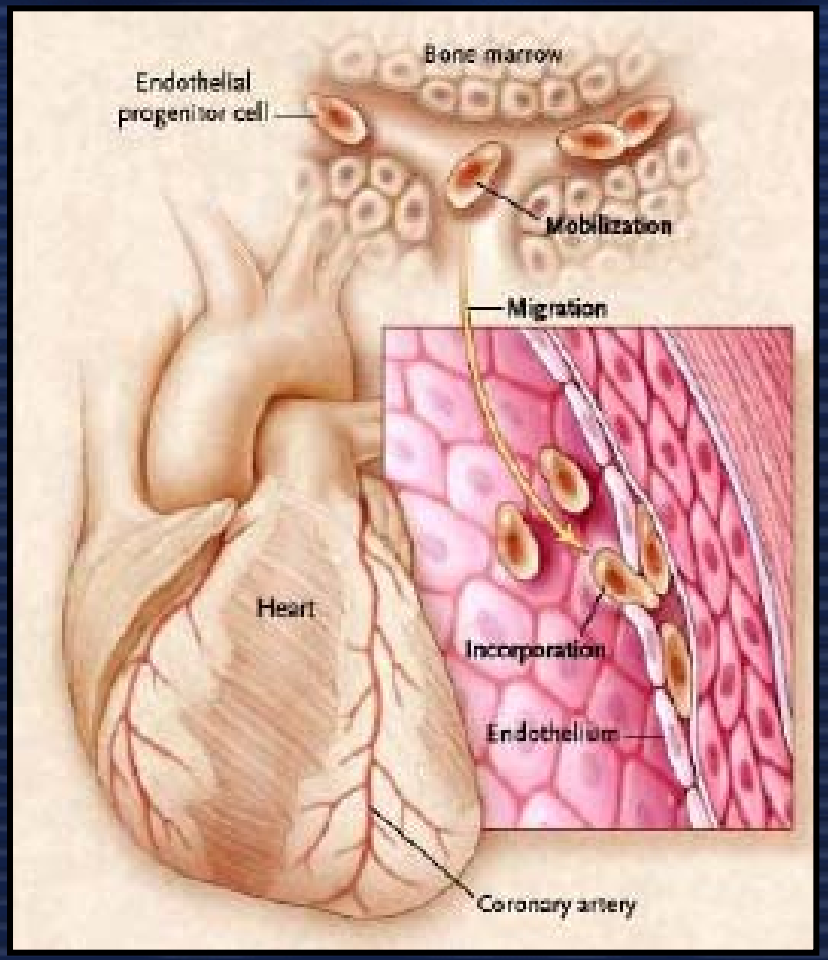
Endothelial progenitor cells (EPCs)

Cells in the general circulation that are genetically predisposed repopulate areas of vascular injury and endothelial disruption.
Their presence was first described by *Asahara et al* in 1996

EPCs physiology is rapidly emerging, critical importance in vascular disease, wound healing and vascular health

EPCs are bone marrow derived and circulate in the adult

They have the ability to differentiate into mature functional endothelial cells

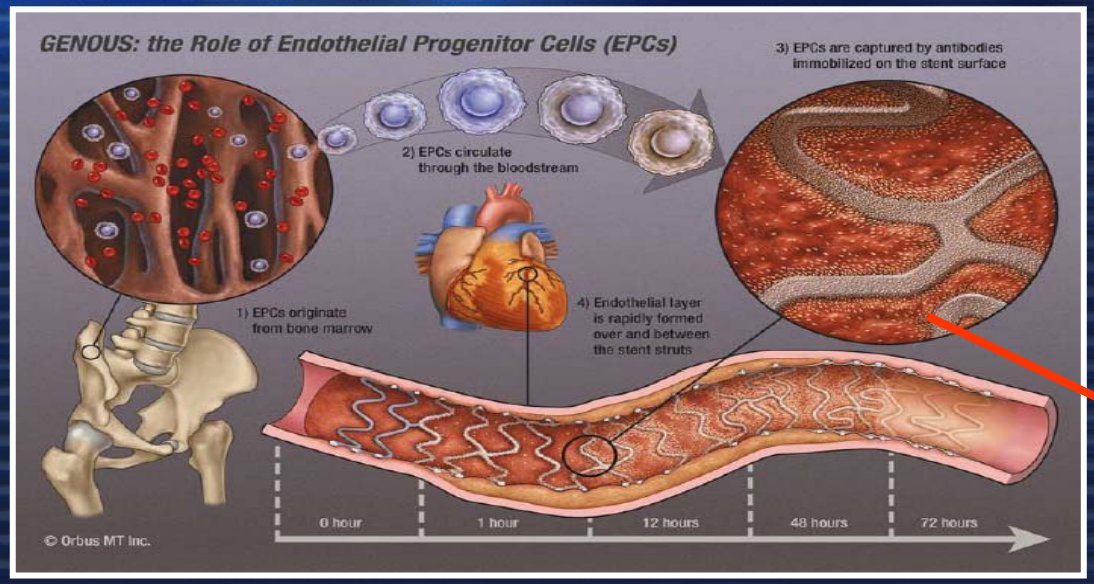


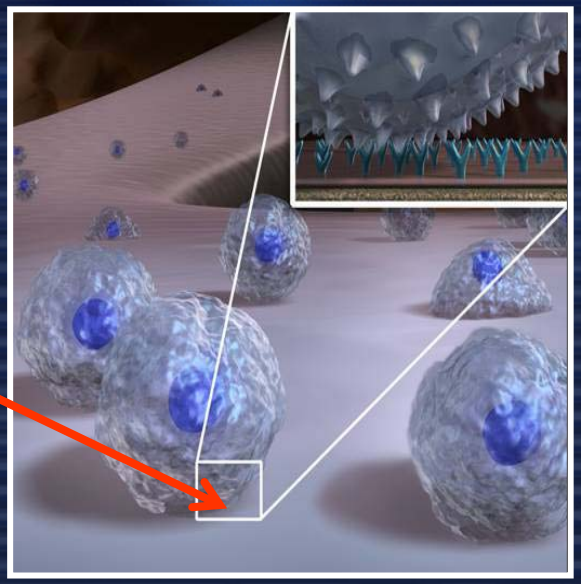
(Rosenweig A et al. NEJM 2003;348:581-2)

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

EPC Capture Coating Technology (GENOUS™ stent)



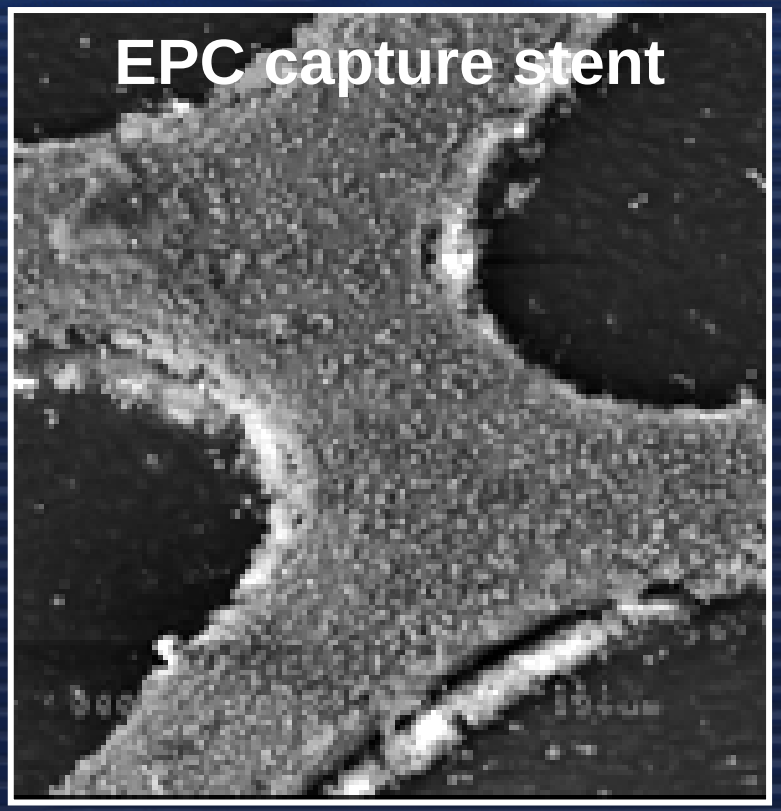


- Orbus has succesfully applied EPC capture technology to 316L stainless steel and NiTi stent
- Antibodies (murine monoclonal antihuman CD34) immobilizied on the stent surface are directed towards cell surface antigens on EPC
- By recruiting the body´s own EPCs to the site of vascular injury/stent, an acceleration of the normal endothelisation process would occur

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

- ***Scanning electron micrographs (SEMs): 1 hour***



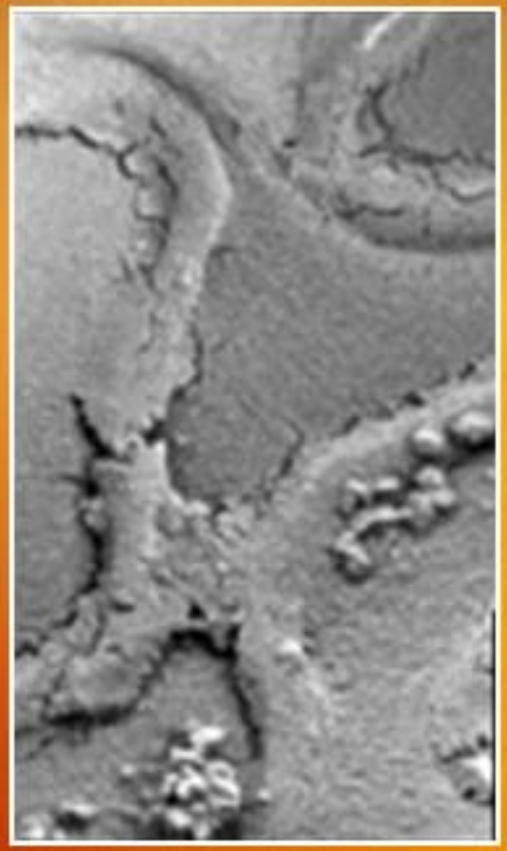
almost complete cellular coverage

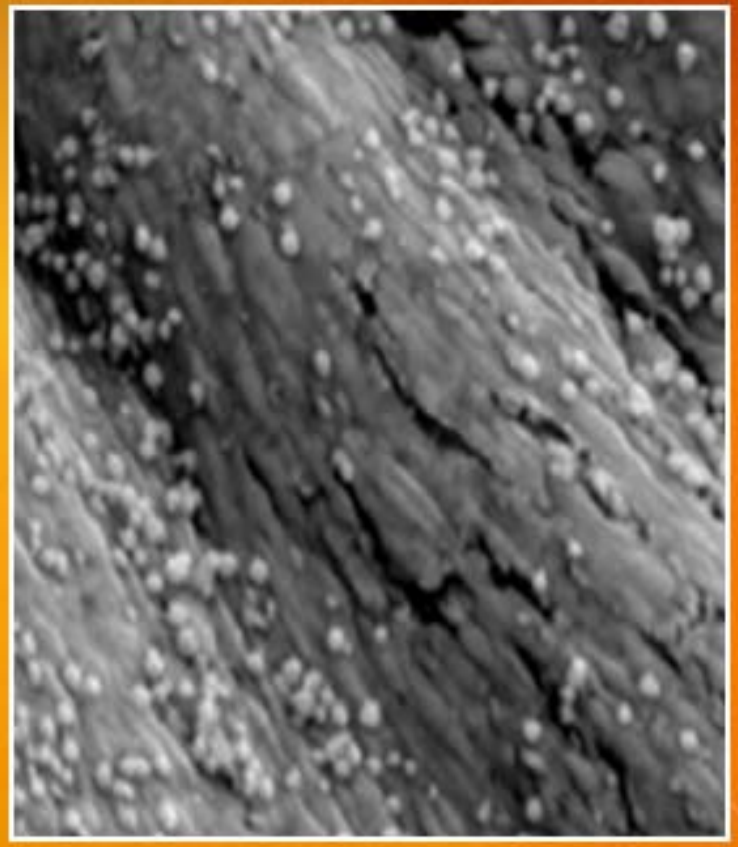
sparse cellular coverage

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

Scanning electron micrographs (SEMs): 48 hours





GENIUS-STEMI

Krajská zdravotní, a.s.
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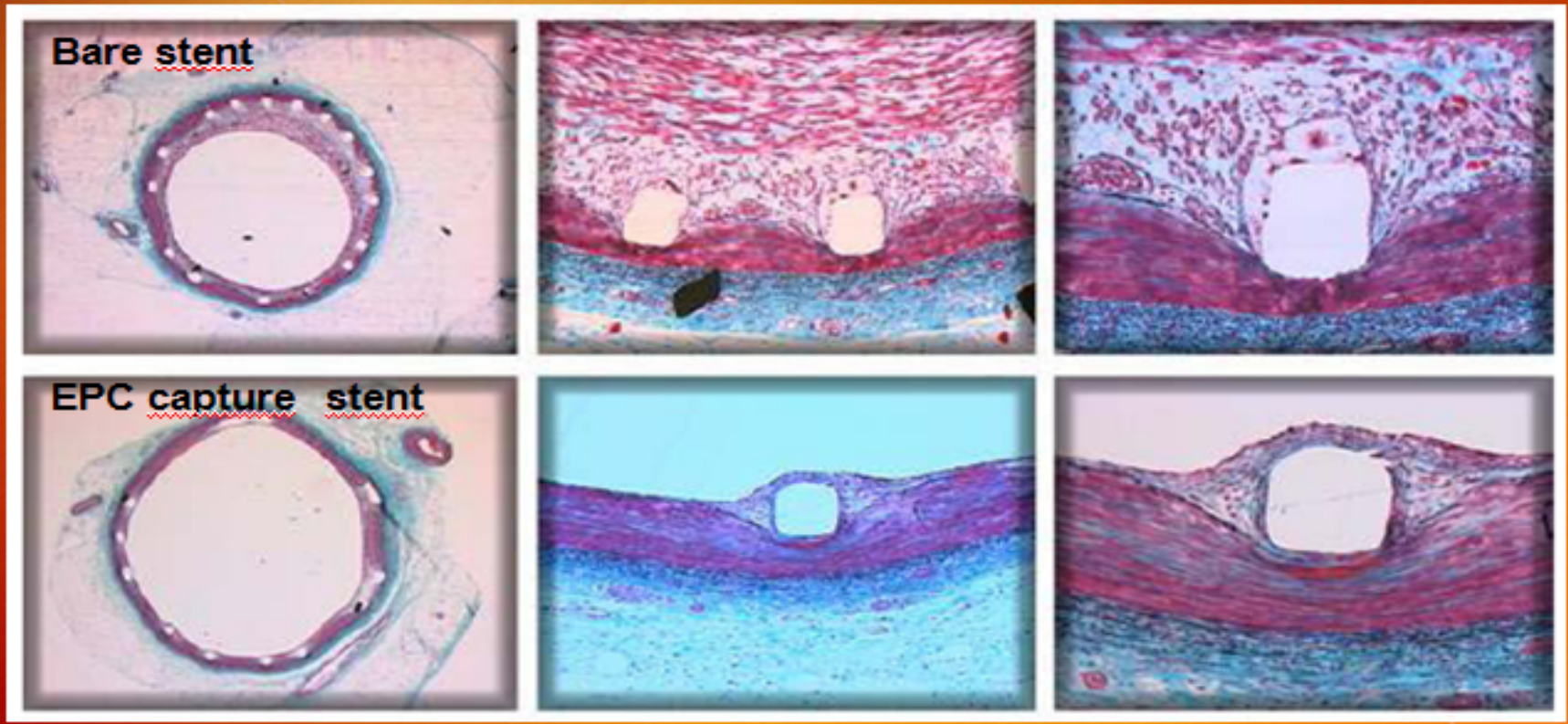
Histopathologic analysis: 28 days



Mature neointima with minimal inflammation

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ Purpose

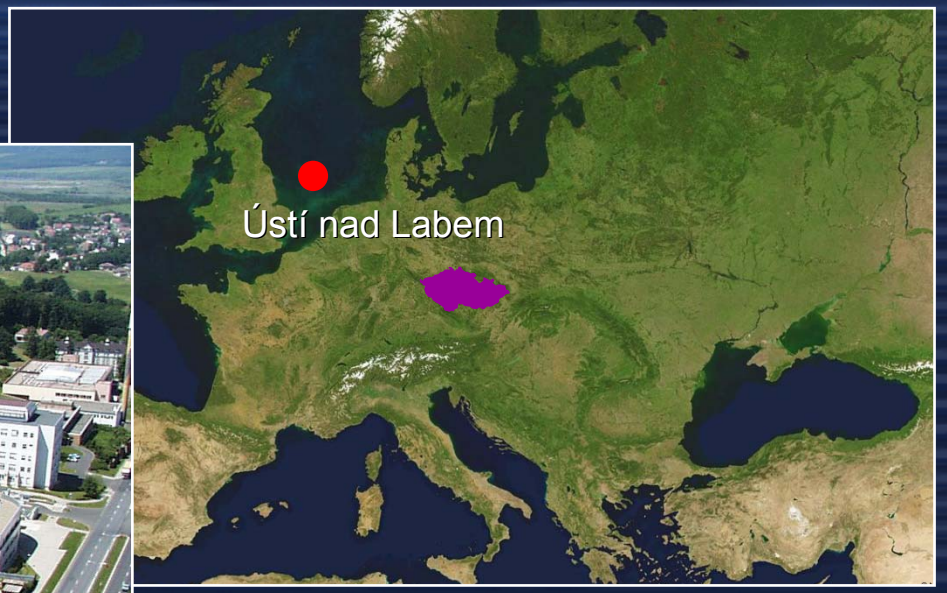
The objective of this trial was to assess the feasibility and safety of the use of EPC capture stent for treatment of STEMI and comparison of 30-day and 6-month outcome with chromium-cobalt stents.

The use of EPC stent may result in more rapid healing process and improve clinical outcome.

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

- Single center, Prospective, Randomized (envelope)
- No sponsor



- Medical ethics committee of our institution approved the study protocol

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ Method

Between August and December 2007, 100 consecutive patients with STEMI were randomly assigned (sealed envelope) to receive either EPC capture stent (N=50) (Genous™ stent) or chromium-cobalt stent (either Driver™ or Coroflex Blue™) (N=50).

Dual antiplatelet treatment was administered for 30 days in both groups.

A 6-month clinical, angiographic and IVUS follow-ups were assessed in both groups.

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ Endpoints

MACEs' (CV death, MI, clinically driven TLR)

at 6 month follow-up

GENIUS-STEMI

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- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ Definitions

Deaths - cardiac or noncardiac
- undetermined causes reported as cardiac

Myocardial infarction

Q wave MI: new, pathological Q waves in≥2 contiguous leads with post-PCI increase
CK double the upper limit of normal and CK-MB>10% of CK level

Non-Q-wave MI: elevation of CK level to double the upper limit of normal, CK-MB>10% of CK level and no Q-waves

TLR – reinterventions inside the stent or within 5mm proximal or distal to the stent

Stent thrombosis (according to the Academic Research Consorcium)

- early (0-30 days) - late (31-360days) - very late (>361 days)

- definite: ACS+angiographic or autopsy evidence of thrombus or occlusion
- probable: unexplained deaths within 30 days of the procedure or acute MI involving the target-vessel teritory without angiography
- possible: all unexplained deaths>30 days after the procedure

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➢ Statistical analysis (NCSS&PASS)

Continuous variables are expressed as the mean ±SD

Categorical variables as percentages

Continuous variables were compared by means of the Student´s *t- t.*

Categorical variables were compared by the means of the X^2 t.

A two-tailed value of $p<0.05$ was considered to be statistically significant

GENIUS-STEMI

Krajská zdravotní, a.s.
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➢ Study flow chart

2007: 400 P-PCI

100 patients included

(Randomization)

50 Genous™ | **50 CrCo**

ASA 100mg/day+clopidogrel 75mg/day 30 days; GPIIb/IIIa inhibitors and thromboaspiration at the discretion of the physician

6-month clinical, angio and IVUS FU

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ Baseline demographic, clinical and angiographic charcteristics

	Genous N=50	Cr-Co N=50	P value
Age (years)	57±10	57±11	NS
Male (%)	79	76	NS
Hypertension (%)	50	57	NS
Diabetes mellirus (%)	29	20	NS
Hyperlipoproteinemia (%)	35	45	NS
Smoking (%)	68	75	NS
Time			
- onset to PCI (minutes)	230	203	NS
Myocardial infarction (%)			
- anterior	47	45	NS
- lateral	6	6	NS
- diaphragmatic	47	51	NS
Killip classification (%)			
I	94	97	NS
II	5	2	NS
III	0	0	NS
IV	1	1	NS
Intervened vessel (%)			
LAD	47	46	NS
LCX	12	9	NS
RCA	38	45	NS
SVG	1	0	NS
TIMI flow			
0-1 (%)	70	61	NS
2-3 (%)	30	39	NS
Stenosis (%)	94.6±10.4	95.3±8.7	NS
MLD (mm)	0.24±0.45	0.19±0.39	NS
Reference diameter (mm)	3.22±0.30	3.40±0.38	NS

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

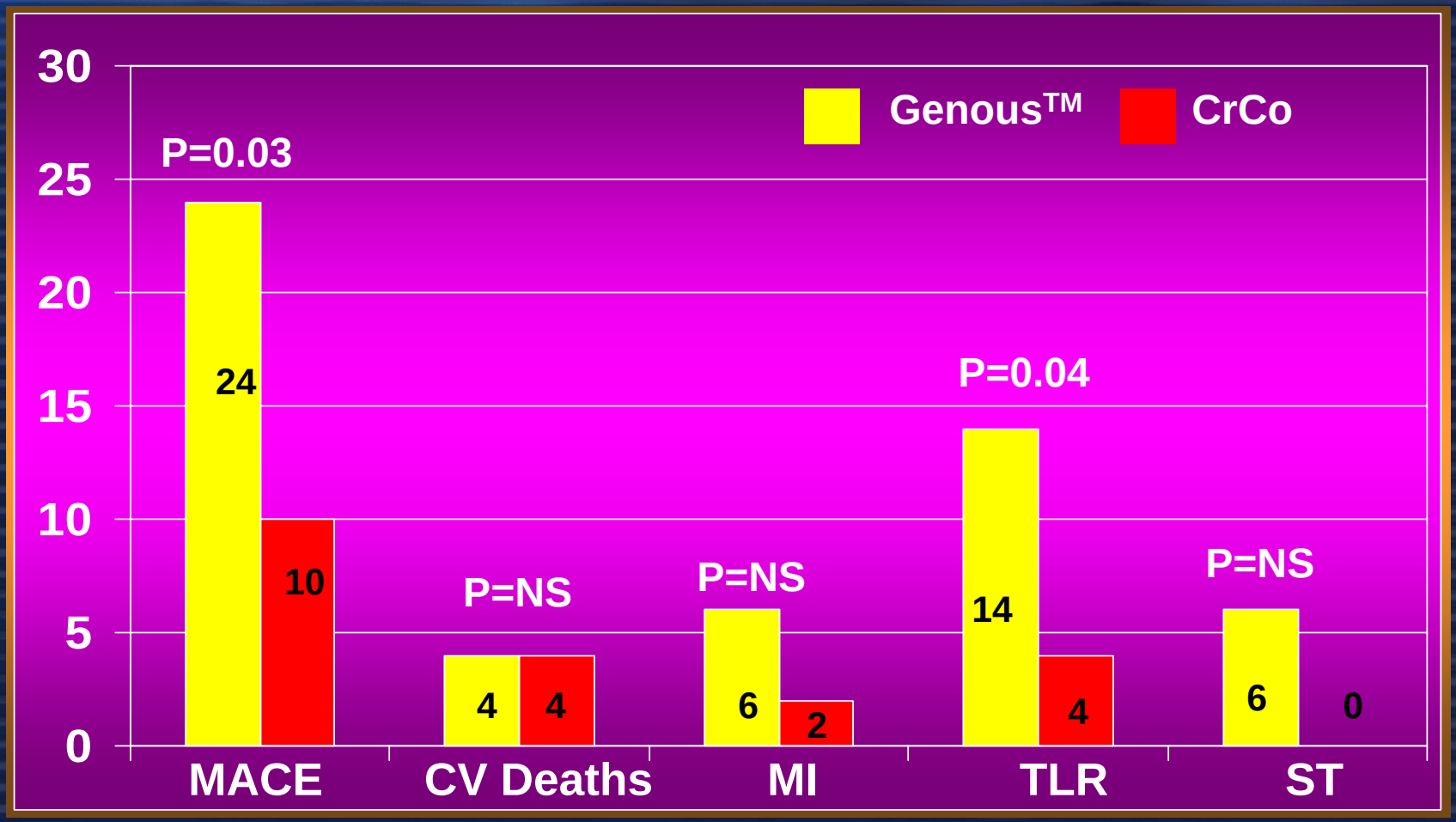
➢ Procedural characteristics

	Genous	Cr-Co	P value
	N=50	N=50	
Stenosis (%)	5.2±4.5	3.9±3.7	NS
MLD (mm)	3.56±0.42	3.62±0.39	NS
TIMI flow			
0-1 (%)	0	0	NS
2	6	3	NS
3	94	97	NS
Number of stents	1.20	1.26	NS
Length of the stents (mm)	20.42	22.30	NS
GP IIb/IIIa inhibitors (%)	32	22	NS
Thromboaspiration (%)	17	25	NS

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ 6-month clinical outcome

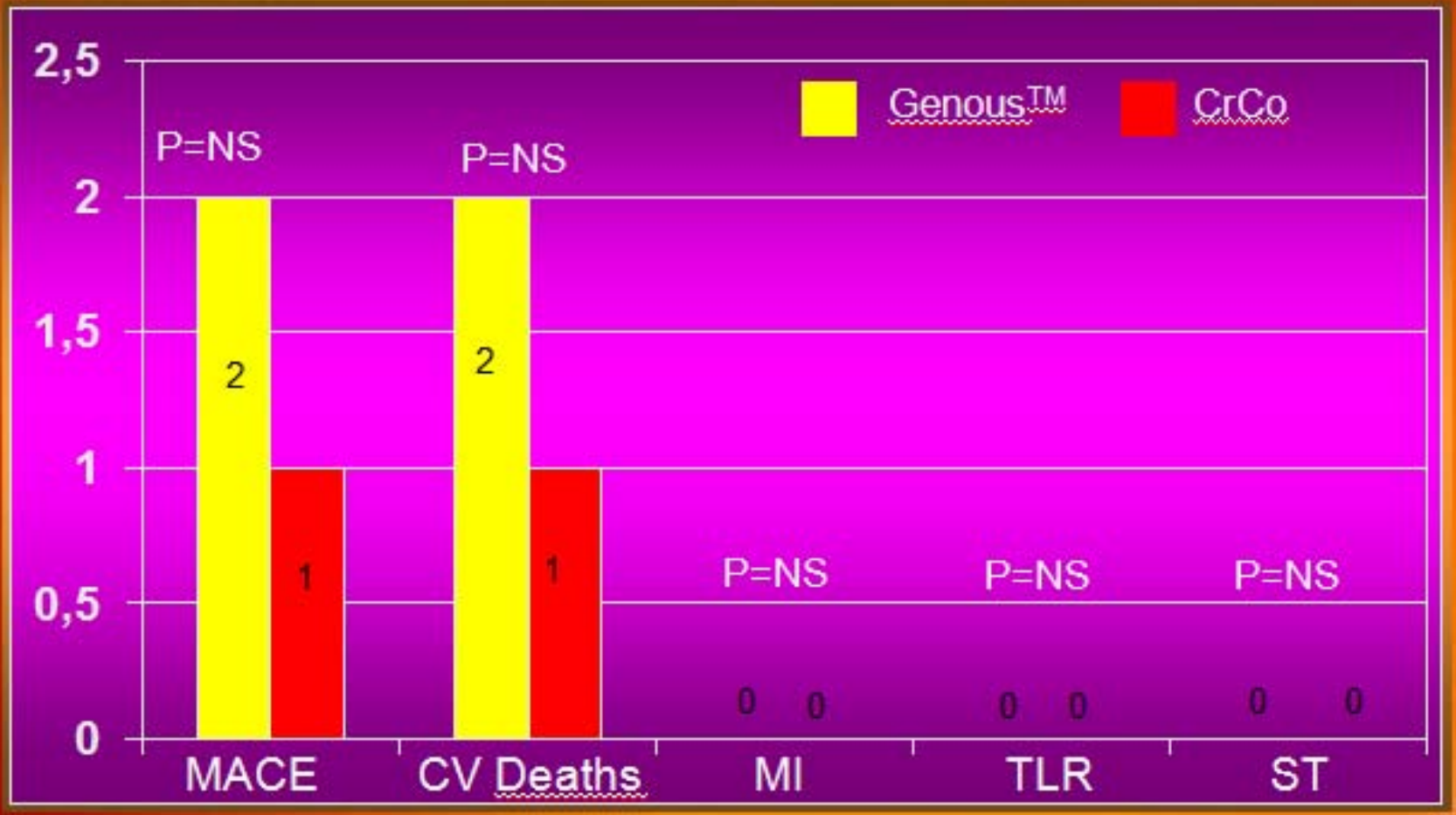


(Non hierachical)

GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ 30 day outcome



(Non hierachical)

GENIUS-STEMI

Krajská zdravotní, a.s.
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➢6 month angio and IVUS data

	Genous N=44	Cr-Co N=47	P value
ANGIO DATA			
Late lumen loss (mm)	0.89±0.59	0.79±0.47	NS
Restenosis (>50%)	20	13	NS
IVUS			
mean in-stent NIH (mm^3)	49.7±48	40.0±22.8	NS

GENIUS-STEMI

Krajská zdravotní, a.s.
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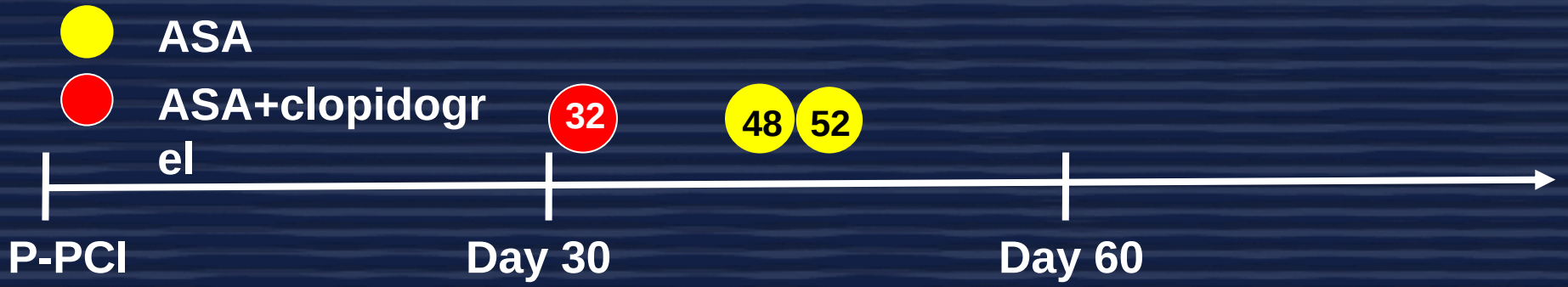
➢ Stent thrombosis in Genous™ group

Patient	Age	TIMI Pre	TIMI Post	LBT	iGP II	Vessel	EF	Stent	Days	Treatment	Stat.
J.J. Alive	61	2	3	Y	Y	RCA	60	1; 2.75/23	48	dPOBA	
P.U. Alive	26	0	3	Y	Y	LAD	45	1; 3/23	32	dPCI+G	
							2	2; 3.5/23+18	52	dPOBA	

ARC definition: 3x definite; 3x late



GENIUS-STEMI

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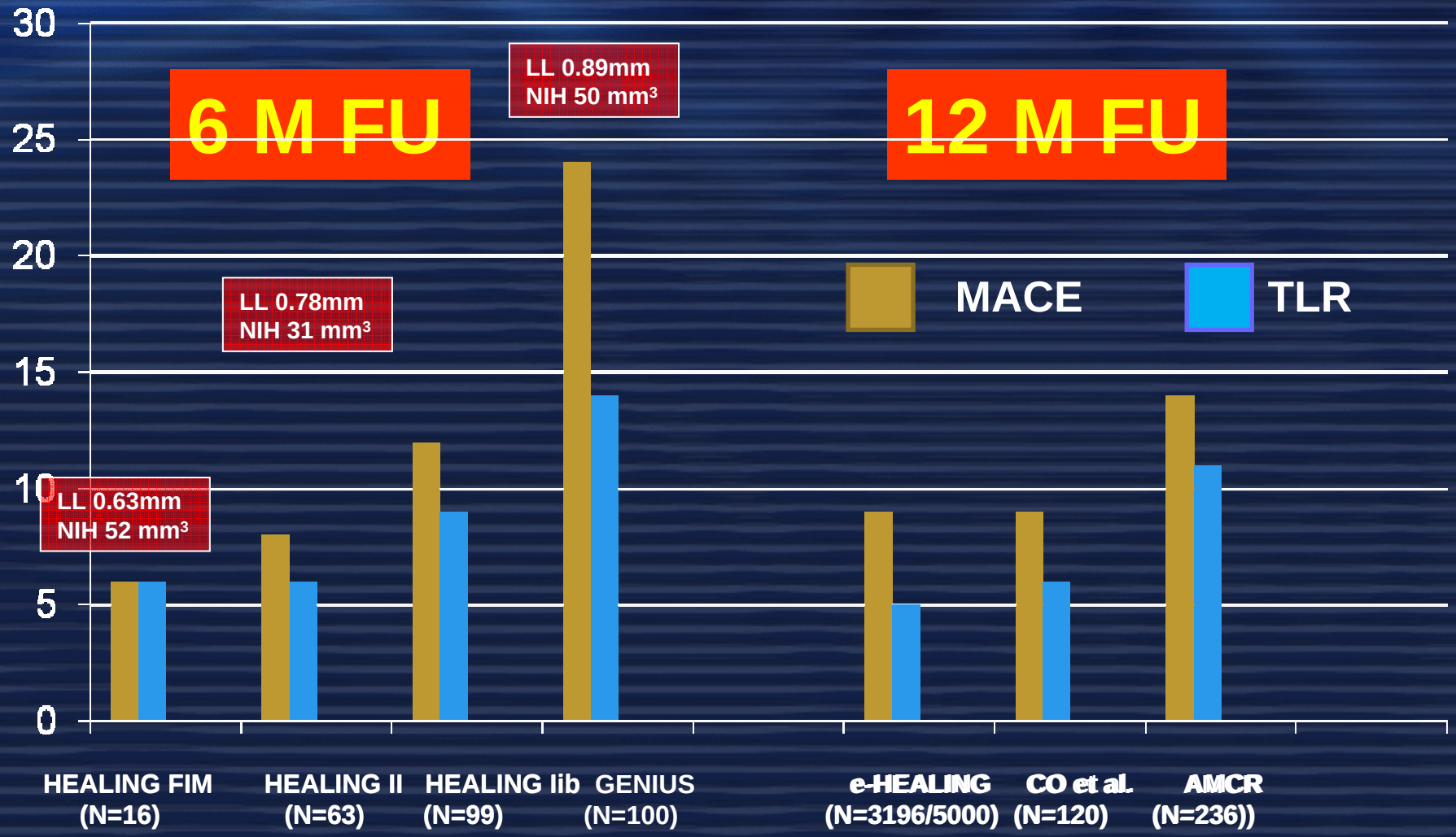
➢ Studies with EPCs capture stent



GENIUS-STEMI

Krajská zdravotní, a.s.
- Masarykova nemocnice v Ústí nad Labem, o.z.

➢ Conclusions:

The use of EPC capture stents in the setting of STEMI is feasible and save.

Caveats:

Small single-center trial

However, the rate of MACE at 6-month FU was significantly higher in Genous™ group when compare to CrCo stents.

No core lab

Warrisome is the rate of late stent thrombosis in EPCs capture stent group

Larger randomized trials are mandatory.