The Valentines Trial

Professor Dr. Sigmund Silber, Munich, Germany
on behalf of the Valentines-I trial investigators

Background

- **The treatment of in-stent restenosis (ISR) following BMS or DES implantation is challenging.**
- **With the use of vascular brachytherapy or DES for ISR, the re-restenosis rates still range from 10-20% at 12 months.**
- **As an alternative, drug-eluting balloons (DEB) have emerged as a treatment option of ISR in BMS with < 10% recurrence rate.**
- **The efficacy and safety of DEB for the treatment of ISR following DES is unknown.**

The Valentines Trial

Study Objective:

To assess the efficacy of the paclitaxel-eluting balloon Dior®-II for ISR following BMS and DES implantation at 6-9 months.

Clinical Outcomes (MACE):

- **any death**
- **any myocardial infarction**
- **target vessel revascularization**
- **stent thrombosis (both early and late occurrences) of the target lesion**

The Valentines Trial

Methods:

- **Multi-center, international registry study**
- **Goal: of up to 300 patients to be recruited in over 100 centers**
- **Snapshot enrollment during 9 days (starting Valentine's day, i.e. 14th - 23rd of Feb. 2010)**
- **PCI for treatment of ISR in native vessels with the DIOR®-II DEB (shellac)**
- **Bailout stenting was allowed**
- **Follow-up for 6-9 months**
- **Online-CRF, data management and statistical analysis was performed by MEDSTAR** (Ron Waksman)

The Valentines Trial

Inclusion Criteria:

- ✓ **Patients over the age of 18 year**
- ✓ **Stable or unstable angina, and/or clinical evidence of ischemia**
- ✓ **Planned PCI for ISR**
- ✓ **Target lesion in a native vessel**
- ✓ **Target lesion stenosis is ≥ 50%**
- ✓ **Up to two lesions per patient**

The Valentines Trial

Exclusion Criteria:

- **Acute MI within last 48 hours**
- **Co-morbid illness likely to limit life expectancy to less than 12 months**
- **Lesion requiring an a priori additional stenting**
- **Previous therapeutic brachytherapy to target vessel**
- **Unable to take dual antiplatelet therapy for at least 6 months**

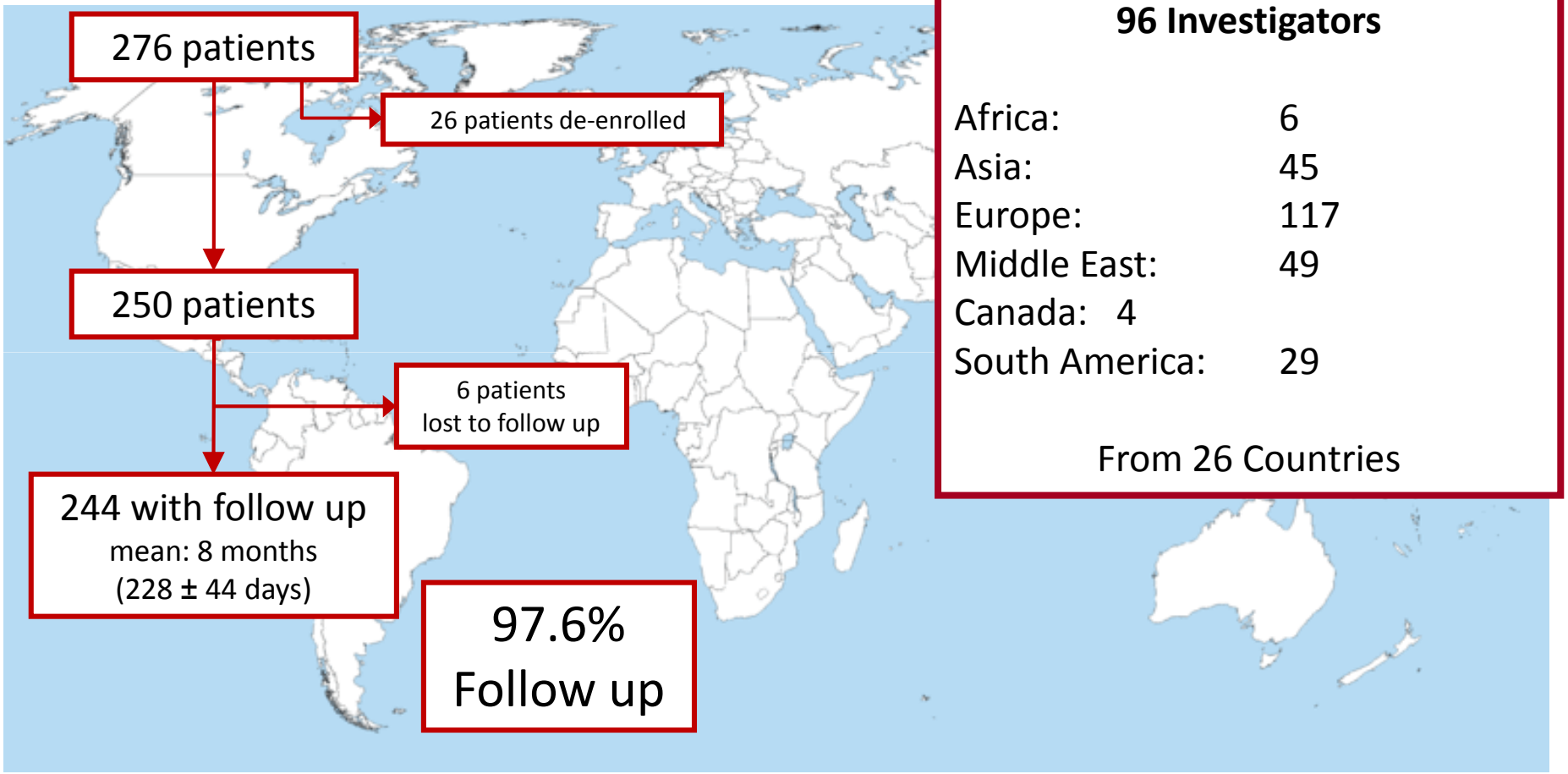
The Valentines Trial

Enrollment:

- **276 patients were initially enrolled**
- **26 patients were then de-enrolled due to:**
  - **11 not having met the incl./excl. criteria**
  - **13 not filling out the CRF forms**
  - **2 having violated the required treatment regimen**

The Valentines Trial

Enrollment:



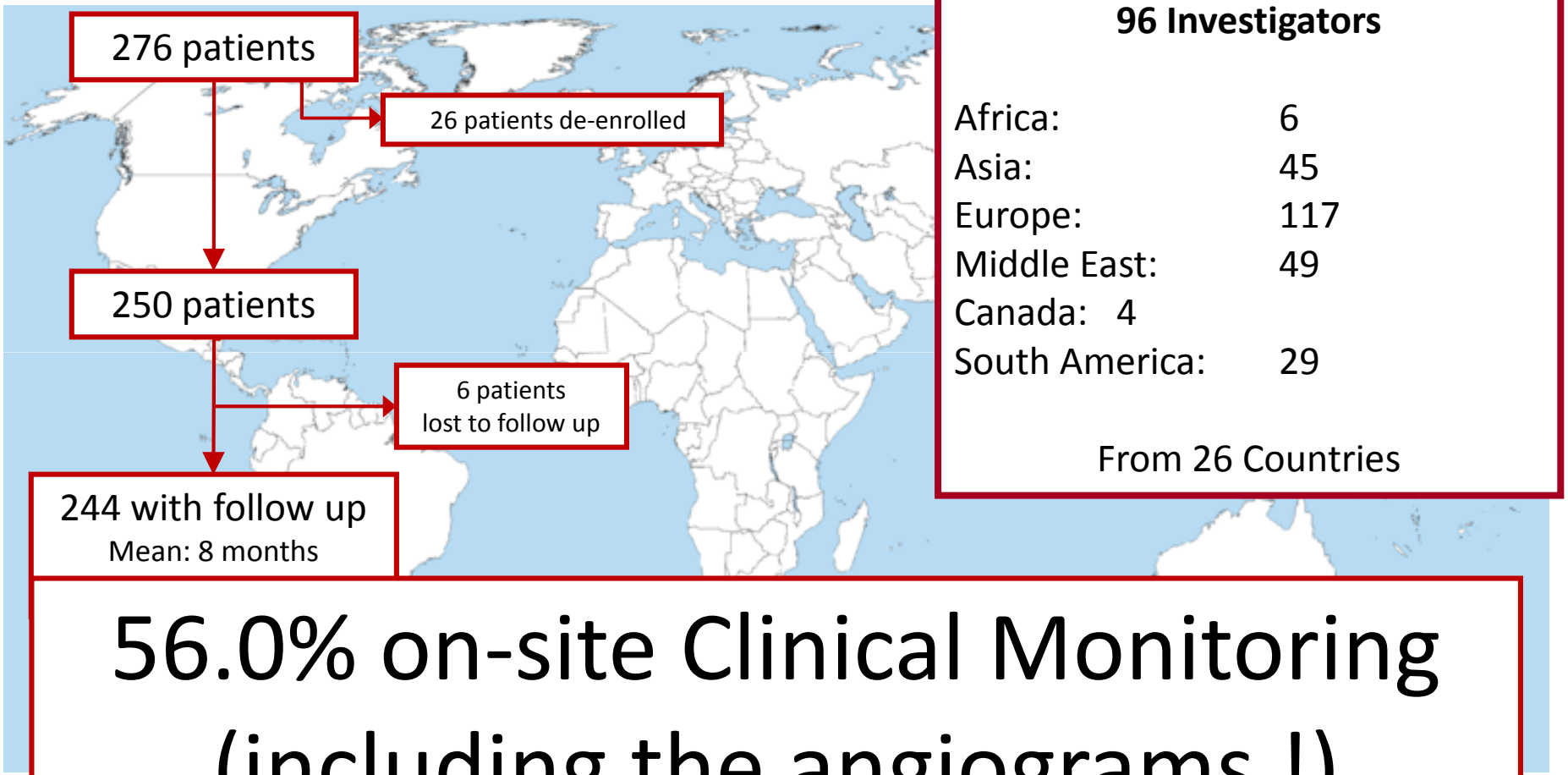
96 Investigators

Africa:	6
Asia:	45
Europe:	117
Middle East:	49
Canada:	4
South America:	29

From 26 Countries

The Valentines Trial

Enrollment:



96 Investigators

Africa:	6
Asia:	45
Europe:	117
Middle East:	49
Canada:	4
South America:	29

From 26 Countries

56.0% on-site Clinical Monitoring (including the angiograms !)

The Valentines Trial

Baseline Demographics

	n = 250 patients
Male	77.2%
Age (years)	61.7 ± 10.1 yrs
Previous MI	46.4%
Previous CABG	9.6%
Diabetes Mellitus	31.6%
Insulin Dependent Diabetes Mellitus	6.4%
Smoking (any)	23.2%
Smoking (active)	8.0%
Hyperlipidemia	60.4%
Hypertension	80.4%
Renal Insufficiency	7.2%
Dialysis	0.4%
Peripheral Vascular Disease	2.0%

The Valentines Trial

Baseline Demographics

	n = 250 patients
Male	77.2%
Age (years)	61.7 ± 10.1 yrs
Previous MI	46.4%
Previous CABG	9.6%
Diabetes Mellitus	31.6%
Insulin Dependent Diabetes Mellitus	6.4%
Smoking (any)	23.2%
Smoking (active)	8.0%
Hyperlipidemia	60.4%
Hypertension	80.4%
Renal Insufficiency	7.2%
Dialysis	0.4%
Peripheral Vascular Disease	2.0%

The Valentines Trial

Baseline ISR Lesion Characteristics

	n = 265 lesions n= 250 patients
Number of lesions per patient	1.1± 0.3
Pre Diameter Stenosis (visual estimate)	81 ± 14 %
RCA	25.3%
LAD	50.2%
LCx	24.5%
Lesion Location	
Ostial	3.8%
Proximal	41.7%
Mid	40.2%
Bifurcation	2.3%
Pattern of Restenosis	
Focal	21.1%
10 to 20 mm	21.9%
Diffuse	40.6%
Proliferative	3.9%
Occlusive or Multi-focal	12.5%

The Valentines Trial

Baseline ISR Lesion Characteristics

	n = 265 lesions n= 250 patients
Number of lesion per patient	1.1± 0.3
Pre Diameter Stenosis (visual estimate)	81 ± 14 %
RCA	25.3%
LAD	50.2%
LCx	24.5%
Lesion Location	
Ostial	3.8%
Proximal	41.7%
Mid	40.2%
Bifurcation	2.3%
Pattern of Restenosis	
Focal	21.1%
10 to 20 mm	21.9%
Diffuse	40.6%
Proliferative	3.9%
Occlusive or Multi-focal	12.5%

The Valentines Trial

DIOR®-II drug-eluting PTCA balloons (Eurocor GmbH) used in the Valentine's Trial:

- **2.0, 2.5, 2.75, 3.0 and 3.5 mm in diameter**
- **15, 20, 25 and 30 mm in length**

The Valentines Trial

DEB Procedure Details

	N=265 lesions
Balloons per lesion	1.1 ± 0.3
Balloon Diameter (mm)	3.0 ± 0.4
Balloon Covered Length (mm)	24 ± 9.1
Number of inflations	1.6 ± 0.9
Maximum Inflation Pressure (atm)	12.7 ± 3.7
Total Balloon Inflation time (seconds)	66.7 ± 38.8
Device related complications	0.8%

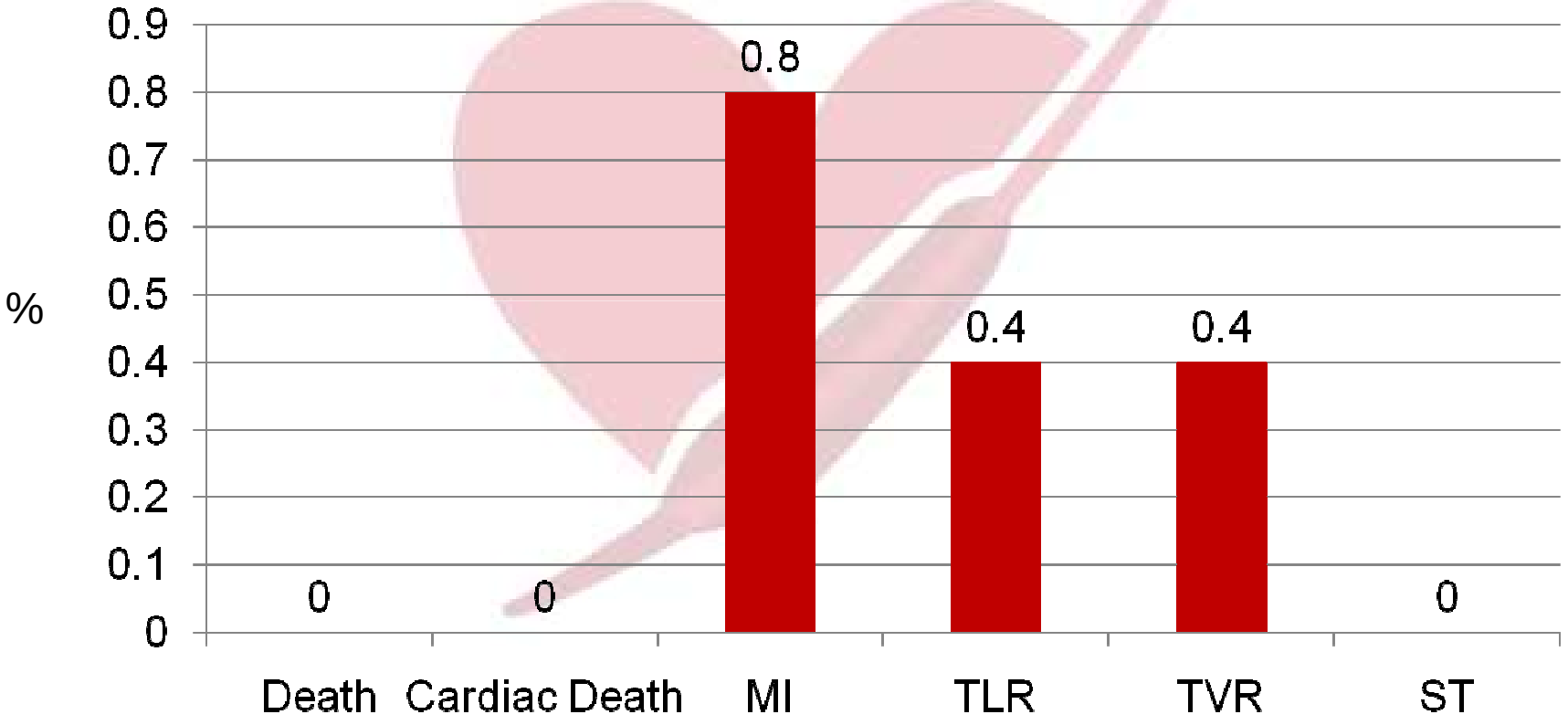
The Valentines Trial

Post DEB Treatment

	N=265 lesions
Stent Implantation	4.9%
Plain Old Balloon	3.4%
IVUS	7.7%
Angiographic Success	96.6%
Intra-procedural Thrombus	0%
Dissection	3.1%
Abrupt Closure	0.4%
No Reflow	1.2%
TIMI Flow	
III	98.1%
II	1.9%
I	0%
0	0%

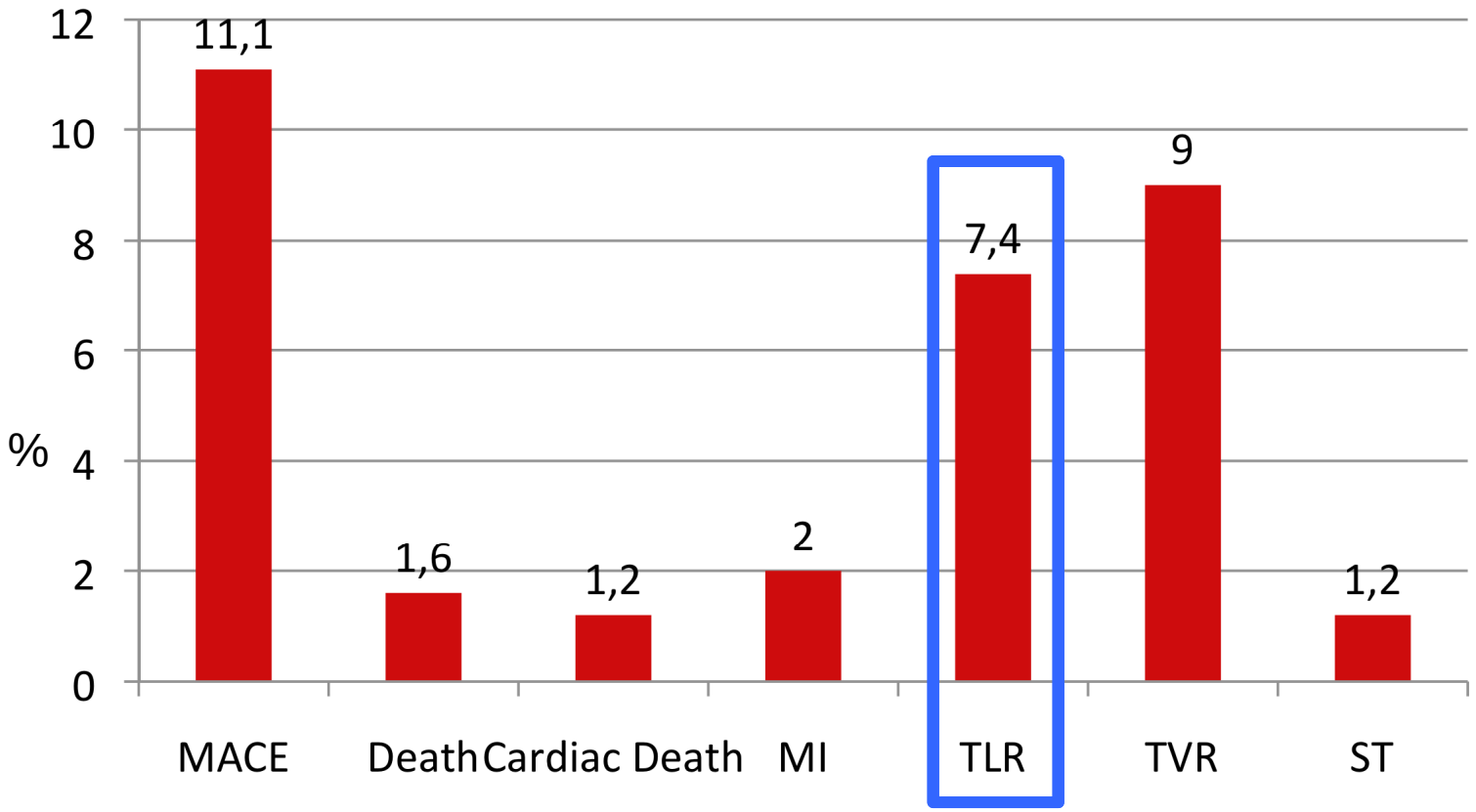
The Valentines Trial

Results: In Hospital



The Valentines Trial

Results: Follow-up (8 Months)



The Valentines Trial

BMS vs. DES

The Valentines Trial

BMS vs. DES: Baseline Demographics

	BMS N=157 patients	DES N=83 patients	p
Male	75.8%	78.3%	0.66
Age (years)	61.3 ± 10.1	62.7 ± 10.3	0.29
Previous MI	53.5%	32.5%	0.002
Previous CABG	7.0%	14.5%	0.06
Diabetes Mellitus	28.0%	39.8%	0.06
Insulin Dependent Diabetes Mellitus	6.4%	6.0%	0.92
Smoking (any)	26.8%	14.5%	0.03
Smoking (active)	9.6%	4.8%	0.2
Hyperlipidemia	59.9%	60.2%	0.96
Hypertension	79.6%	79.5%	0.99
Renal Insufficiency	7.6%	6.0%	0.64

The Valentines Trial

BMS vs. DES:
Baseline ISR Lesion Characteristics

	BMS N=168 lesions N=157 patients	DES N=86 lesions N=83 patients	p
Number of lesion per patient	1.1± 0.3	1.0± 0.2	0.244
Pre Diameter Stenosis (visual estimate)	80 ± 13%	82 ± 16%	0.307
RCA	22.0%	27.9%	0.299
LAD	53.0%	46.5%	0.329
LCx	25.0%	25.6%	0.920
Lesion Location			
Ostial	4.8%	2.3%	0.502
Proximal	42.5%	38.4%	0.526
Bifurcation	3.0%	1.2%	0.667
Pattern of Restenosis			
Focal	16.4%	27.5%	0.041
10 to 20 mm	23.0%	21.3%	0.754
Diffuse	44.2%	35.0%	0.168
Proliferative	4.2%	2.5%	0.722
Occlusive or Multi-focal	12.7%	18.8%	0.841

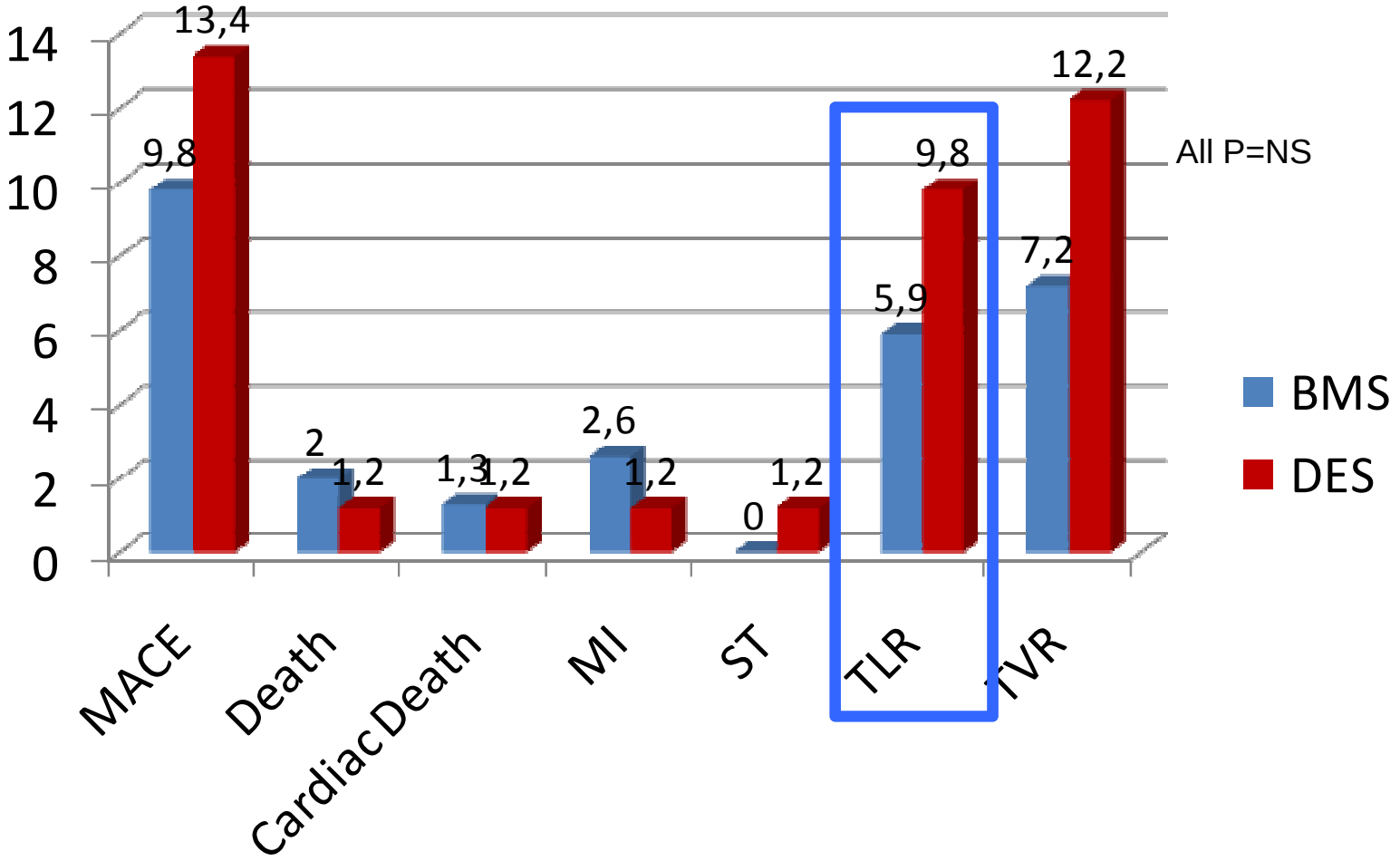
The Valentines Trial

BMS vs. DES: DEB Procedure Details

	BMS N=168 lesions	DES N= 86 lesions	p
Balloons per lesion	1.0 ± 0.3	1.1 ± 0.3	0.106
Balloon Diameter (mm)	2.9 ± 0.4	3.0 ± 0.4	0.408
Balloon Covered Length (mm)	23.6 ± 7.6	25.1± 11.8	0.317
Number of inflations	1.5 ± 0.9	1.6 ± 0.9	0.570
Maximum Inflation Pressure (atm)	12.7 ± 3.6	12.5 ± 3.8	0.724
Total Balloon Inflation time (seconds)	63.2 ± 34.3	73.0 ± 46.9	0.089
Device related complications	1.2%	0	0.550

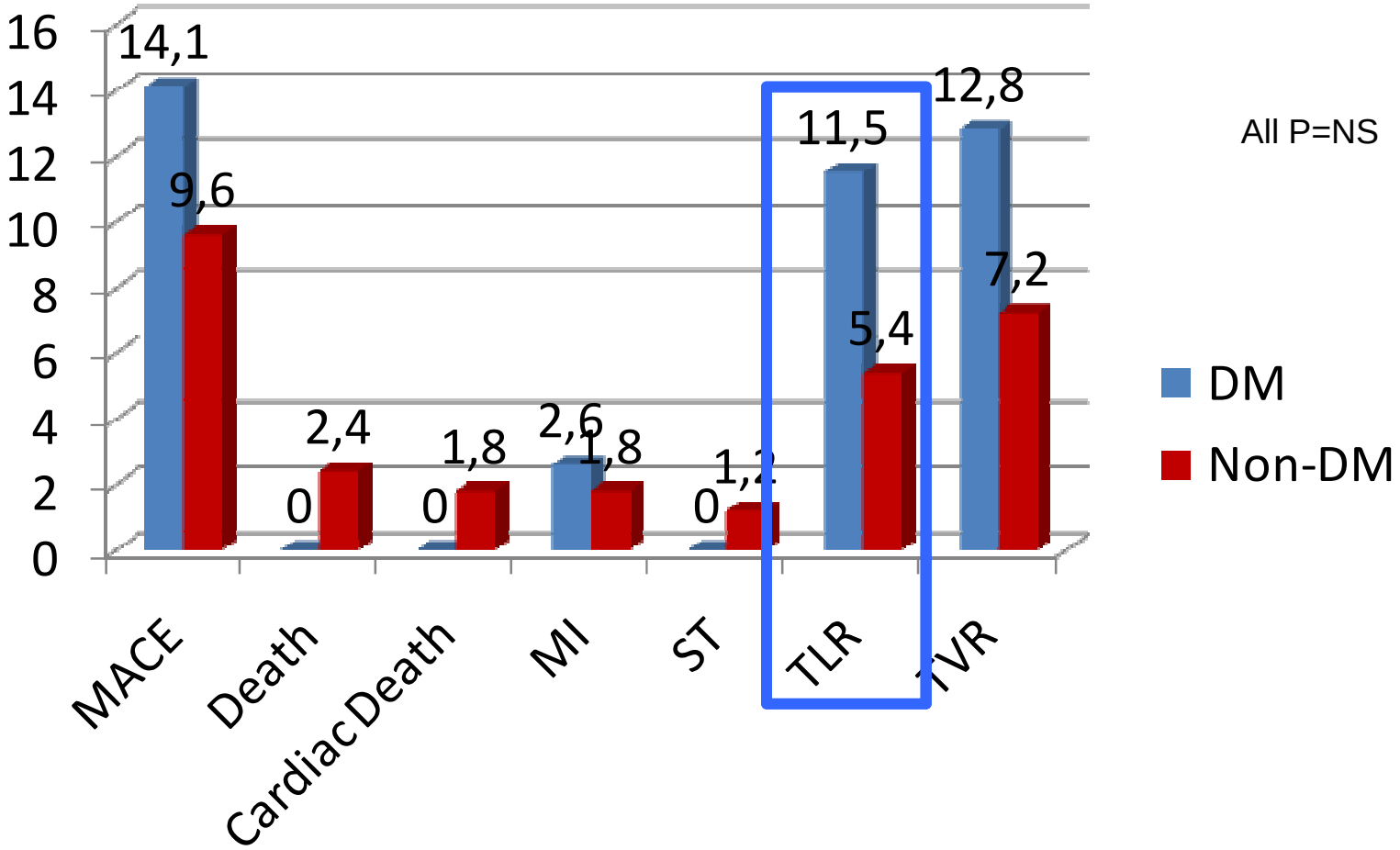
The Valentines Trial

Results: BMS vs. DES: Follow-up (8 Months)



The Valentines Trial

Results: Diabetes vs. no Diabetes: Follow-up (8 Months)



The Valentines Trial

Summary:

- **The VALENTINE'S snaphot registry is the largest study with a DEB in patients with in-stent restenosis (ISR), also including ISR after drug-eluting stents.**
- **External monitoring of 56% is exceptionally high for registries.**
- **The follow-up rate of 98% was also very high for registries.**
- **In these patients with appr. one third diabetes and over 50% long and diffuse ISR, the overall clinical restenosis rate of the target lesion (TLR) after 8 months was 7.4%.**

The Valentines Trial

Conclusions

In this international, multi-center registry study, the DIOR®-II drug-eluting Balloon seems to be effective, demonstrating a single-digit TLR rate at 8 months post treatment for in-stent restenosis of both bare metal and drug-eluting stents.

Thank You!!

Principle Investigators

G. Sangiorgi | S. Silber | P. Stella

International Steering Committee

A. Rodriguez | J. Yu | M. Gyöngyösi | A. Serra

K. Samer | K. Chin | K. Upranda

Local Investigators

Yu	Menown	Serruys	Narain	Yarkov
Sgueglia	Canbay	Roguin	Puri	Ganiukov
Petrovski	Çavusoglu	Trehan	Chong	Mironkov
Becirovic	Birdane	Hong Co Tek	Saxsena	Demin
Bertrand	Döven	Jebavy	Utech	Loenko
Stella	Özdemir	Jagtap	Battikh	Osherov
Silber	Kanadasi	Tiwari	Boughzela	Dashibalova
Denchev	Demir	Arneia	Marouen	Beliakov
Mrózek	Dagdeviren	Chin	Yucel	P. Kumar
Pfeiffer	Merkely	S. Kumar	Sitar	Hiremath
Wilke	Nagybaczoni	Srinivas Rao	Iakovou	Bhandari
Tonev	Dering	Mahesh	Coufal	V. Pramod
Jorgova	Fernandez	Rao	Garcia	Burgos
Rodriguez	Isaac	P. Chandra	Estrada	Benchimol
Serra	Tinageros	Skvaril	Notheis	Vargas
Vaquerizo	Corral	Prohaska	Grosse	Pastrana
Vester	Bula	Finsterer	Moncada	Deshpande
Auer	Lievano	Kapoor	Tovar	Krishna
Malik	Draganov	S. Chandra	Lacativa	Caicedo
			Carvalho	Hobikoglu