e-BioMatrix PMS Registry – A post market surveillance registry for the BioMatrix™ DES

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On behalf of the e-BioMatrix PMS Registry Investigators:
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e-BioMatrix Registry

Prospective, Multi-Center, Observational Study
to assess outcomes of
Real World, All Comers Patients

More than 5000 patients in 81 International centers

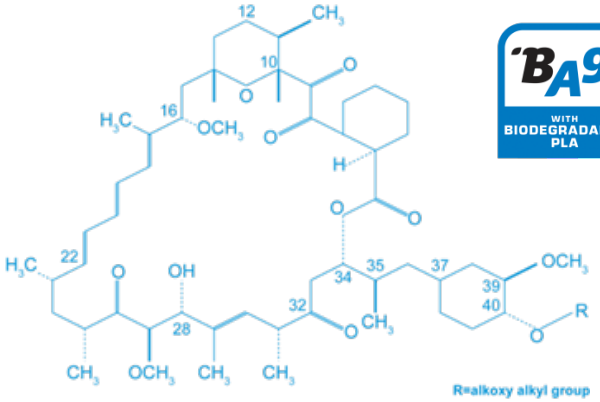
Follow-Up

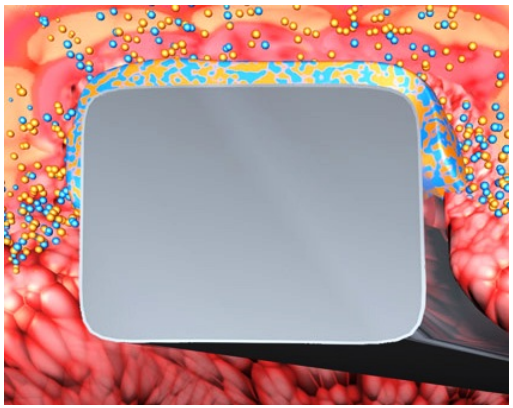
1° Endpoint:	MACE* in overall population at 12 months
Key 2° Endpoints:	MACE* at 30 days, 6 months and 2, 3 and 5 years Stent Thrombosis (ARC) & Total Revascularization Rate at 30 days, 6 months, 1, 2, 3 and 5 years

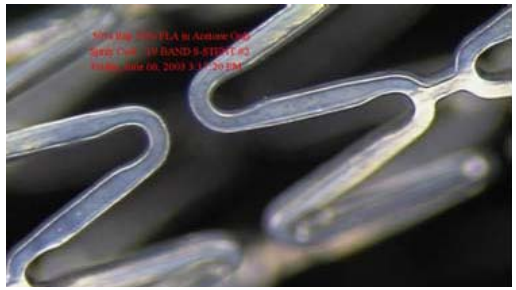
MACE = Composite of Cardiac Death, MI and clinically driven TVR

DAPT Duration (as per IFU):	Min. 6 months, recommended up to 12 months ASA indefinitely

BioMatrix™ Stent







- Biolimus is a semi-synthetic sirolimus analogue with 10x higher lipophilicity and similar potency as sirolimus.
- Biolimus is immersed at a concentration of 15.6 μg/mm into a biodegradable polymer, polylactic acid, and applied solely to the abluminal stent surface by a fully automated process.
- Polylactic acid is co-released with biolimus and completely dissolves into carbon dioxide and water after 6-9 months.
- The stainless steel stent platform has a strut thickness of 120 μm with a quadrature link design.

Registry Design

e-BioMatrix PMS REGISTRY

e-BioMatrix PMR REGISTRY

Identical Protocol

1,000 + patients

100% Source data verification of informed consent, baseline data & index hospital stay
+ 100% MACE*

4,000 + patients

verification of 100% informed consent

+100% MACE (Source data verification)

Independent CEC
Angiography core lab evaluation of all reported stent thromboses

*100% SDV of patient file until last reported MACE

Registry Enrollment

	e-BioMatrix PMS	e-BioMatrix PMR
Number of centers	9	72
Status	12-month FU available (N=1102)	Enrolling (N=4272)
First Enrollment	March 2008	April 2008
Final Enrollment	September 2009	Expected in October 2011
12-month follow-up	Completed (in 97.6%)	ongoing

Clinical Trial Organization

- **Steering Committee**
  - Philip Urban (PI), David Hildick-Smith, Marco Roffi, Mariano Valdes, Keith Oldroyd, Franz-Xaver Kleber, Jacques Berland, David Iosseliani, Al Haddad
- **CEC**
  - Adnan Kastrati (Chair), Alaide Chieffo, Lisette Okkels Jensen, Jan Z Peruga, Tudor-Constantin Poerner, Peter W. Radke, Jochen Wöhrle
- **Data Monitoring**

  PREMIER RESEARCH (CH), Biosensors Europe
- **EDC system**

  MERGE Healthcare (former KIKA Medical)
- **Statistical analysis**

  Biosensors Europe

e-BioMatrix Registry

e-Biomatrix PMS

✓ Inclusion Criteria:

1. Age ≥18 years
2. Patients treated with one or more BioMatrix™ DES
3. Presence of one or more coronary artery stenoses in a native coronary artery or a saphenous bypass graft from 2.25 to 4.0 mm in diameter that can be covered with one or multiple stents
4. No limitation for the number of treated lesions, number of treated vessels, or lesion length

× Exclusion Criteria:

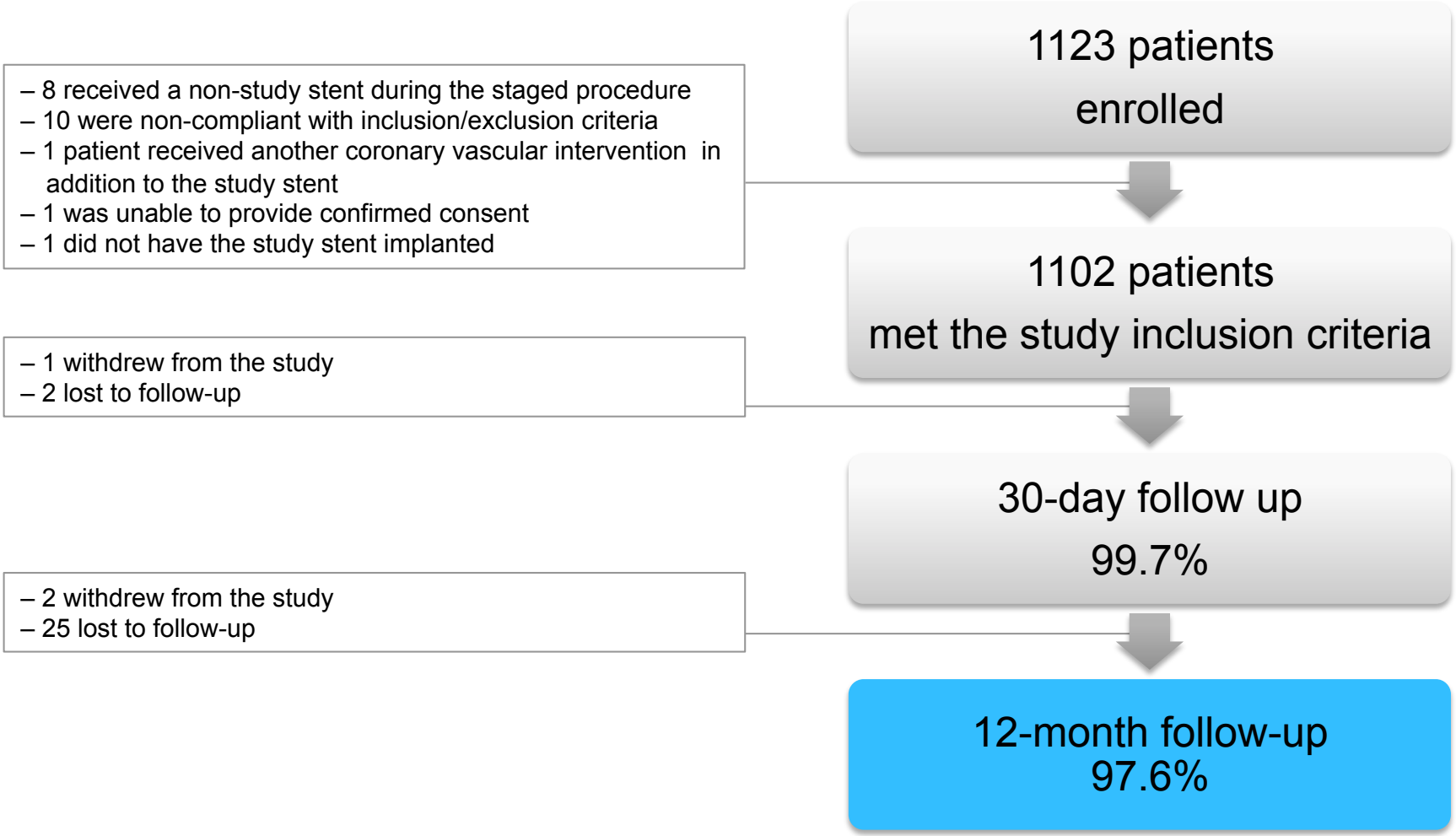
1. Inability to provide informed consent
2. Patients needing additional stent(s) not of the BioMatrix type
3. Patients with lesions not ultimately treated with a BioMatrix stent

Site Enrollments

1102 patients enrolled from March 2008 to September 2009

Country	Center	PI	# Patients
CH	Stadtspital Triemli - Zurich	F. Eberli	256
CH	Hôpitaux Universitaires de Geneve	M. Roffi	176
ES	Hospital Universitario Virgin de la Arrixaca - Murcia	M.Valdes	164
CH	Hôpital de la Tour – Geneva	P.Urban	101
CH	Cardiocentro Ticino – Lugano	G. Pedrazzini	100
CH	Hôpital Fribourgeois	JJ. Goy	100
UK	Brighton and Sussex University Hospitals NHS Trust	D. Hildick-Smith	88
CH	Inselspital Bern	S. Windecker	65
UK	Manchester Royal Infirmary	M. El-Omar	52

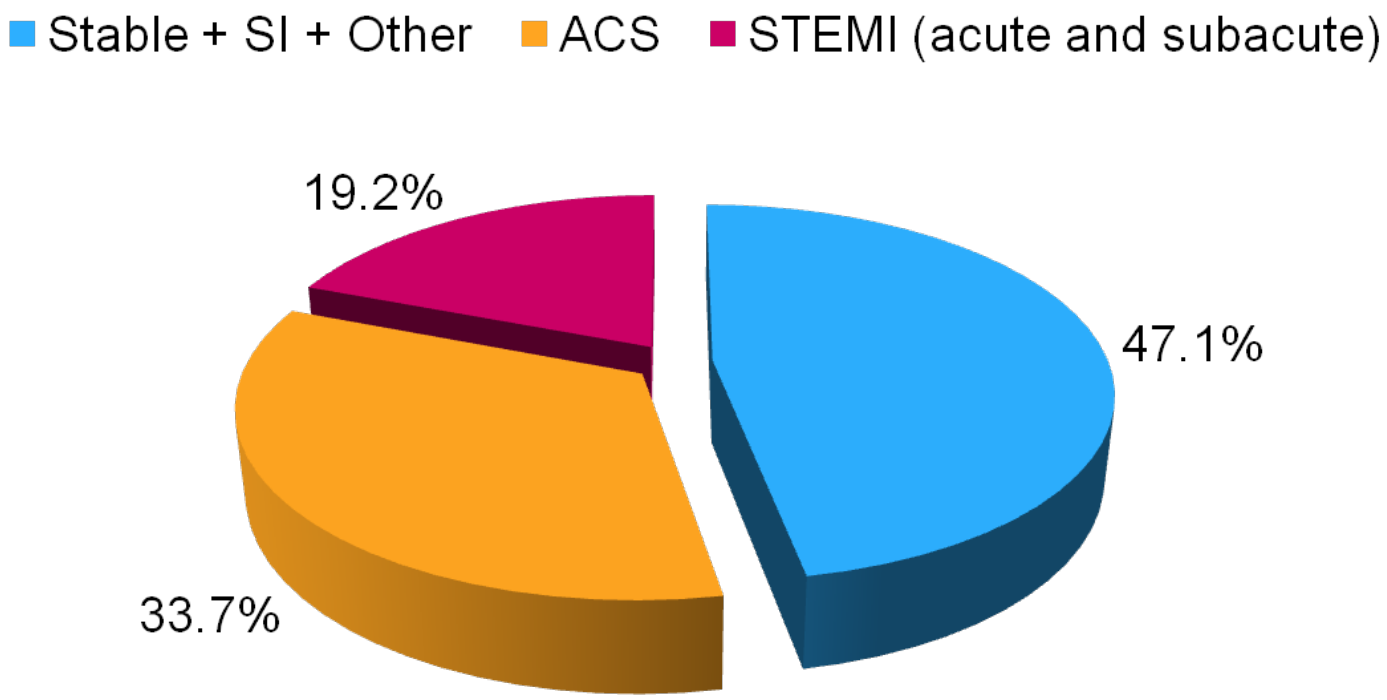
Patient Flow



Indication for PCI

N = 1102 patients

Anginal Status

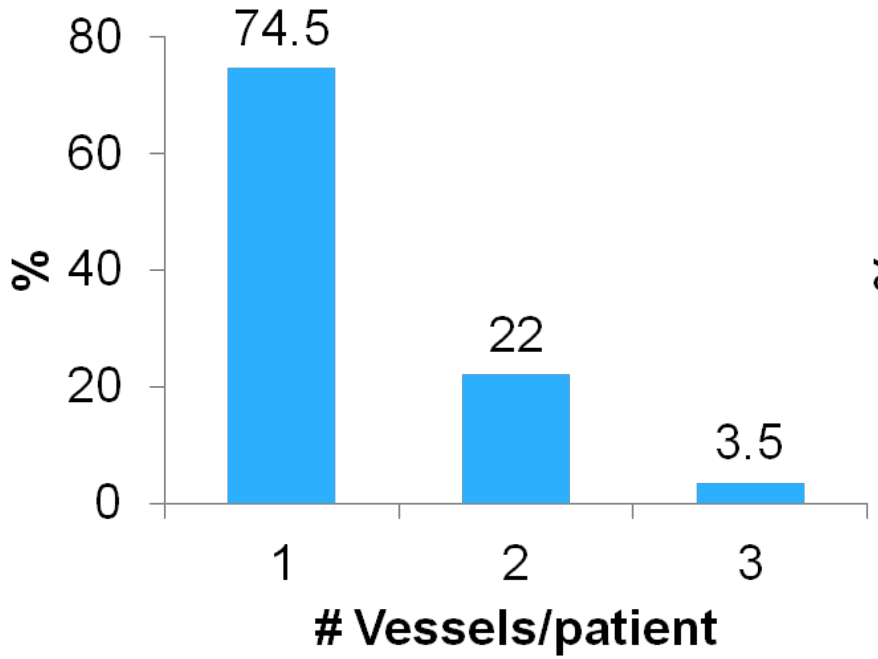


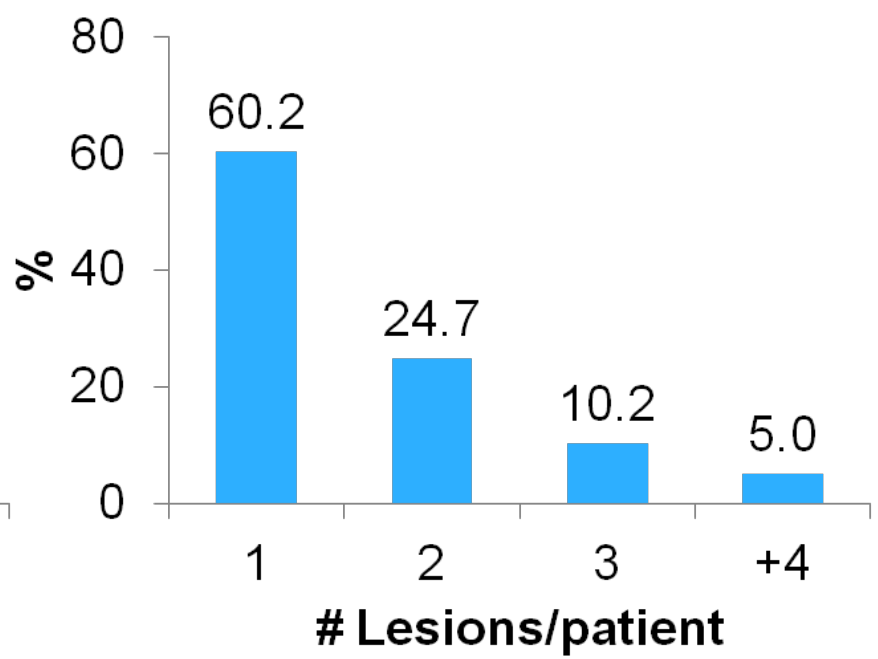
Demographics

	Percent (%)
Age (mean)	64.1 ± 10.9
Male gender	77.4
Obese (BMI >= 30)	24.8
LVEF < 40%	8.7
Prior PCI	24.5
Prior CABG	9.3
Prior MI	21.4
Peripheral vascular disease	7.2
Cerebrovascular disease	5.3
Hypertension	66.5
Hypercholesterolemia	67.5
Current smoker	28.1
Diabetes Mellitus	24.0
Charlson Comorbidity Index score (mean ±SD)	1.2 ± 1.5

Number of Vessels/Lesions Treated

Including 123 patients (11.2%) with a staged procedure*





*defined as a 2nd PCI planned at the time of the first index procedure, and taking place within 90 days

Index PCI

Including 123 patients (11.2%) with a staged procedure*

Nominal BES diameter** (mm)	3.0 ± 0.4
Total BES length**/patient (mm)	34.0 ± 22.4
Total BES length**/lesion (mm)	21.6 ± 10.4
Number of treated lesions/patient	1.6 ± 0.9
Number of stents/lesion	1.2 ± 0.5

Multiple BES/lesion	17.7%
≥ 3 stents/lesion	2.8%
Multiple BES/patient	51.0%
≥ 3 stents/patient	23.8%
Number of BES/patient	1.9 ± 1.2

*defined as a 2nd PCI planned at the time of the first index procedure, and taking place within 90 days

**BioMatrix™ stent is available in the following lengths and diameters
Diameter (mm): 2.25 / 2.5 / 2.75 / 3.0 / 3.25 / 3.5 / 4.0
Length (mm).: 8 / 11 / 14 / 18 / 23-24 / 28

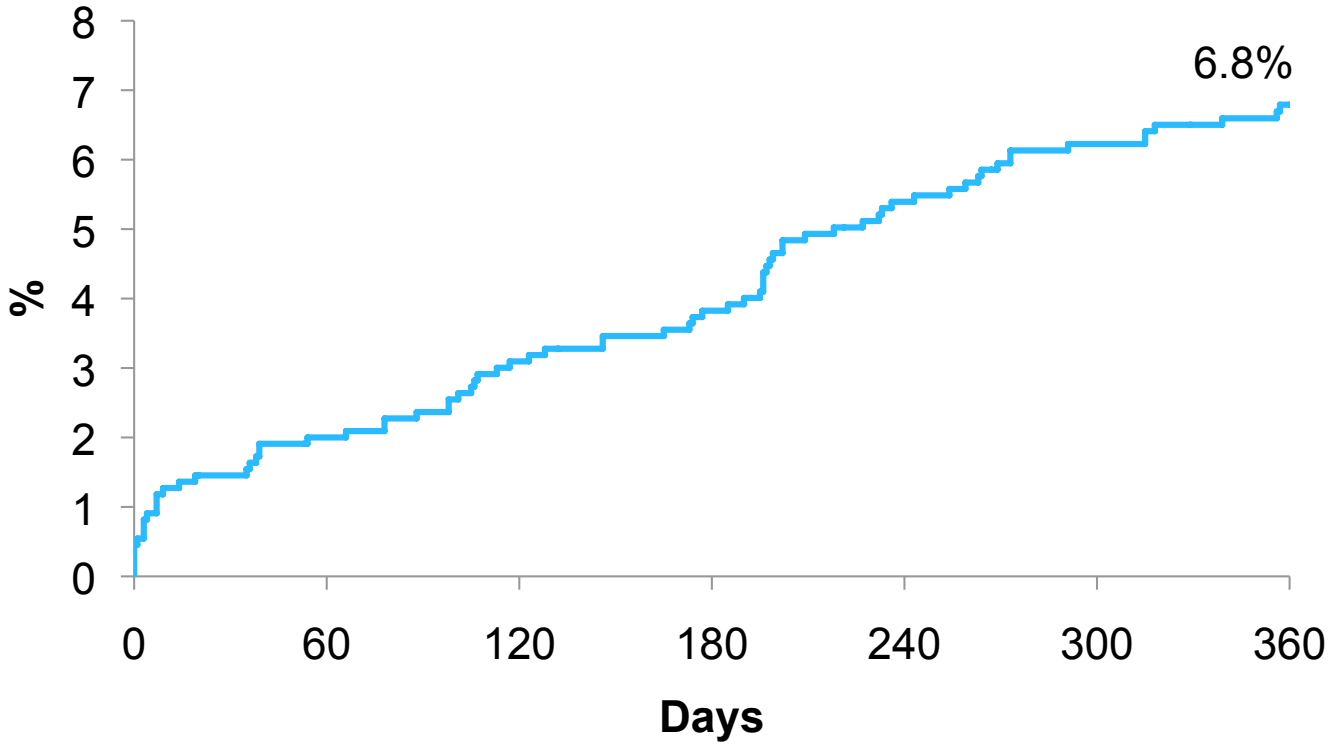
12-month Outcomes

	30 days %	6 months %	12 months %
MACE[1]	1.5	3.8	6.7
Cardiac Death	0.4	1.4	1.7
MI	1.2	1.8	2.5
Q-wave MI	0.4	0.5	0.5
Non Q-wave MI	0.8	1.4	2.0
ci-TVR[2]	0.5	1.9	4.3
ci-TLR[3]	0.5	1.5	3.3
All Death	0.5	1.6	2.5
Death or MI	1.5	3.1	4.4

[1] MACE = composite of cardiac death, MI and ci-TVR =primary endpoint
[2] ci-TVR: clinically indicatedt target vessel revascularization
[3] ci-TLR: clinically indicated target lesion revascularization

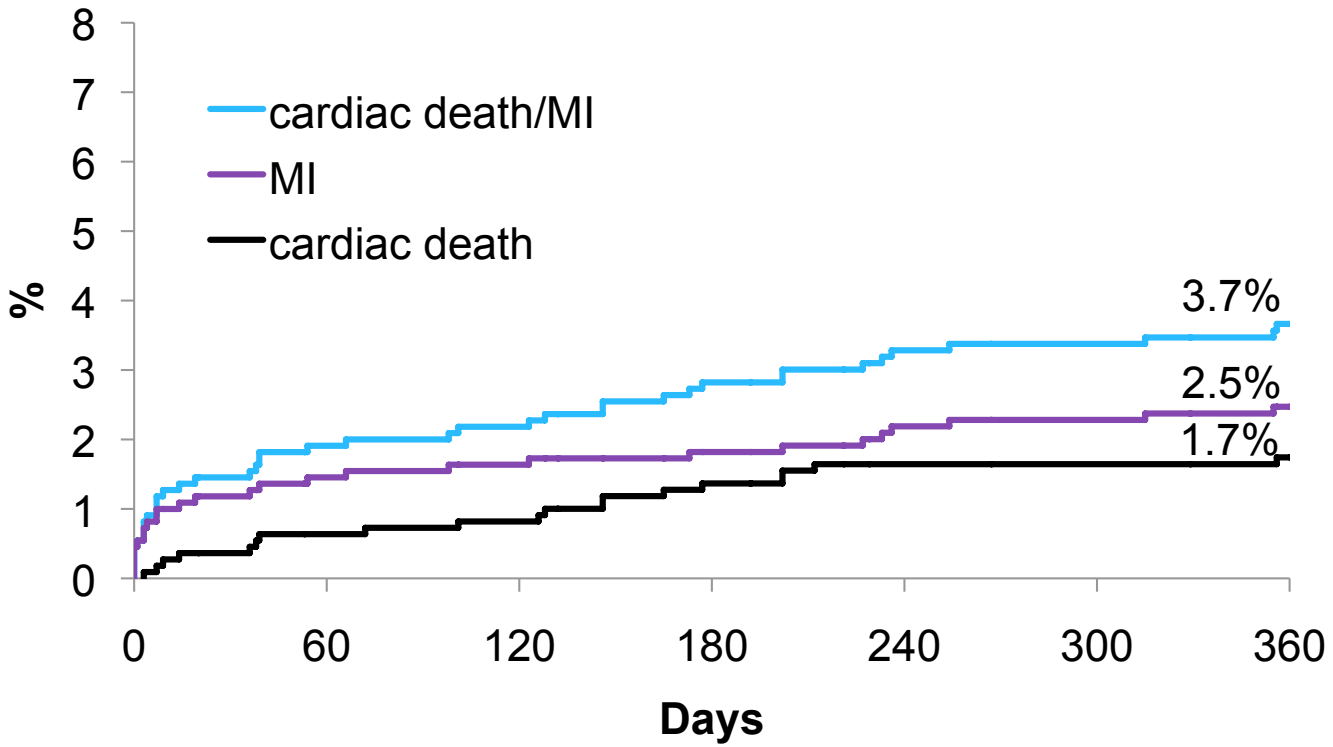
MACE

Cardiac Death, MI, ci-TVR = primary endpoint

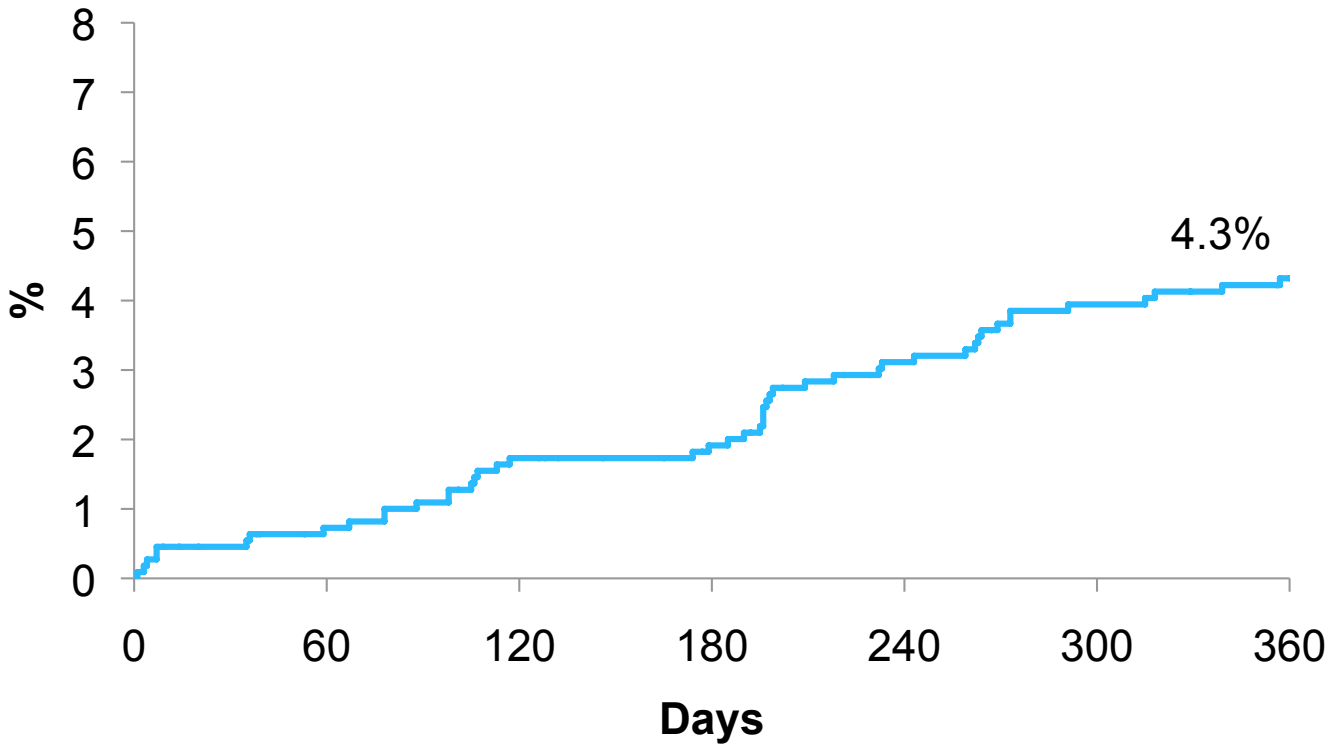


Number at risk	1102	1073	1060	1049	1018	1008	917

Safety Outcomes



Clinically indicated TVR



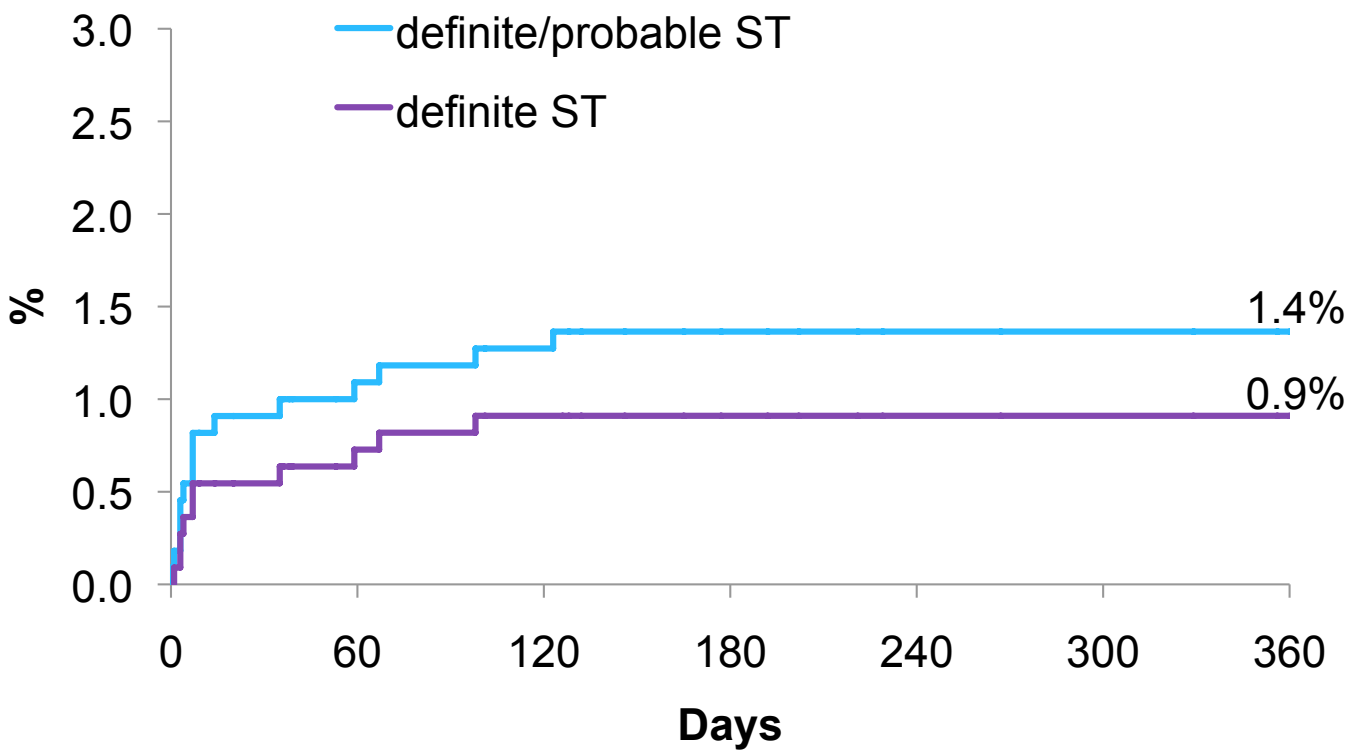
Number at risk	1102	1082	1069	1058	1029	1019	949

ARC-defined[1] Stent Thrombosis & Major Bleeding[2]

	Acute %	Sub-Acute %	Late %	Total %
Definite/Probable ST	0.2	0.7	0.5	1.4
Definite ST	0.1	0.5	0.4	0.9
Probable ST	0.1	0.3	0.1	0.4
Possible ST	0	0	0.7	0.7
Total ST	0.2	0.7	1.2	2.1
Major Bleeding (STEEPLE)	1.0	0.1	1.0	2.1

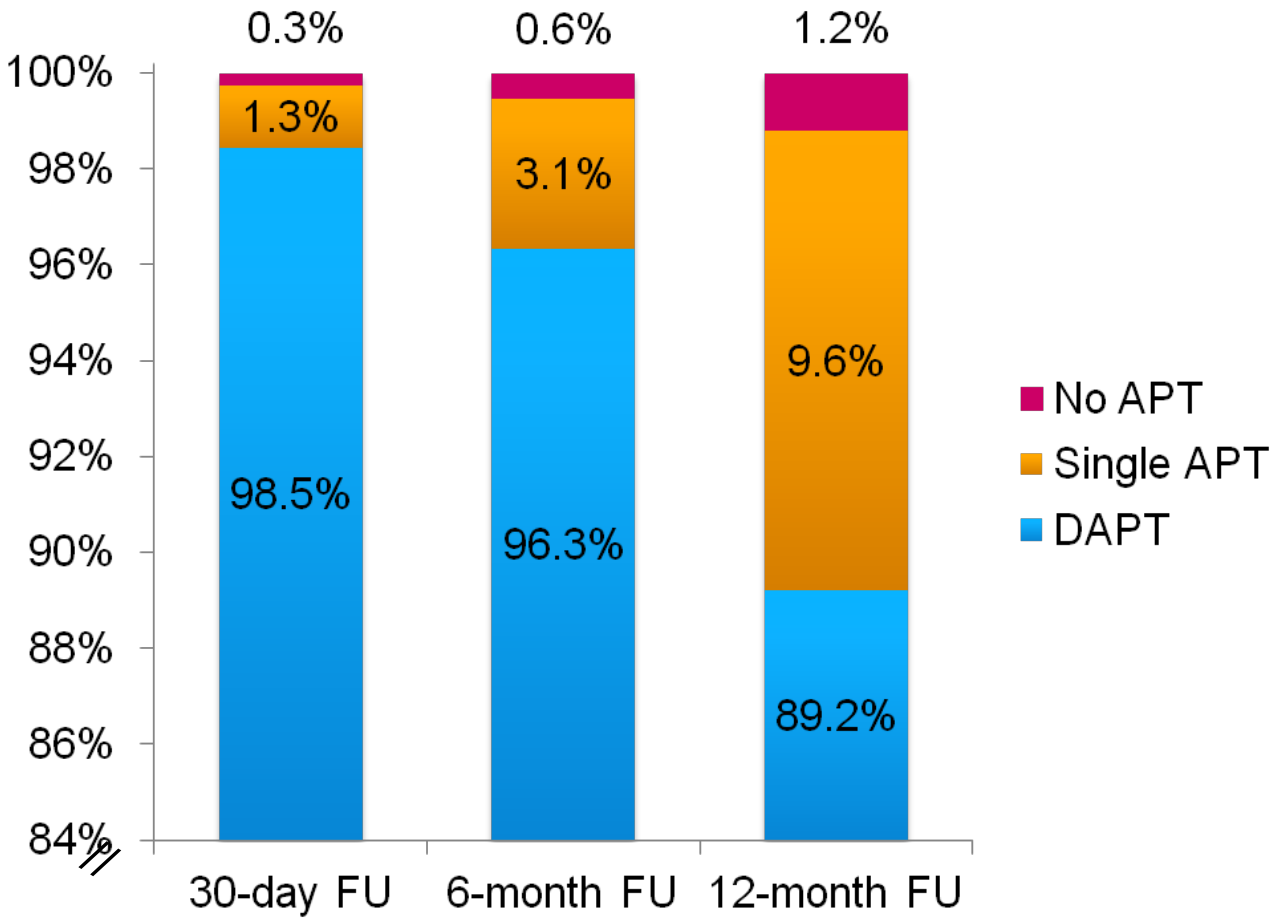
1) Cutlip D et al, Circulation 2007; 115: 2344-51
2) Montalescot G et al, NEJM 2006; 355: 1006-17

ARC-defined* Stent Thrombosis

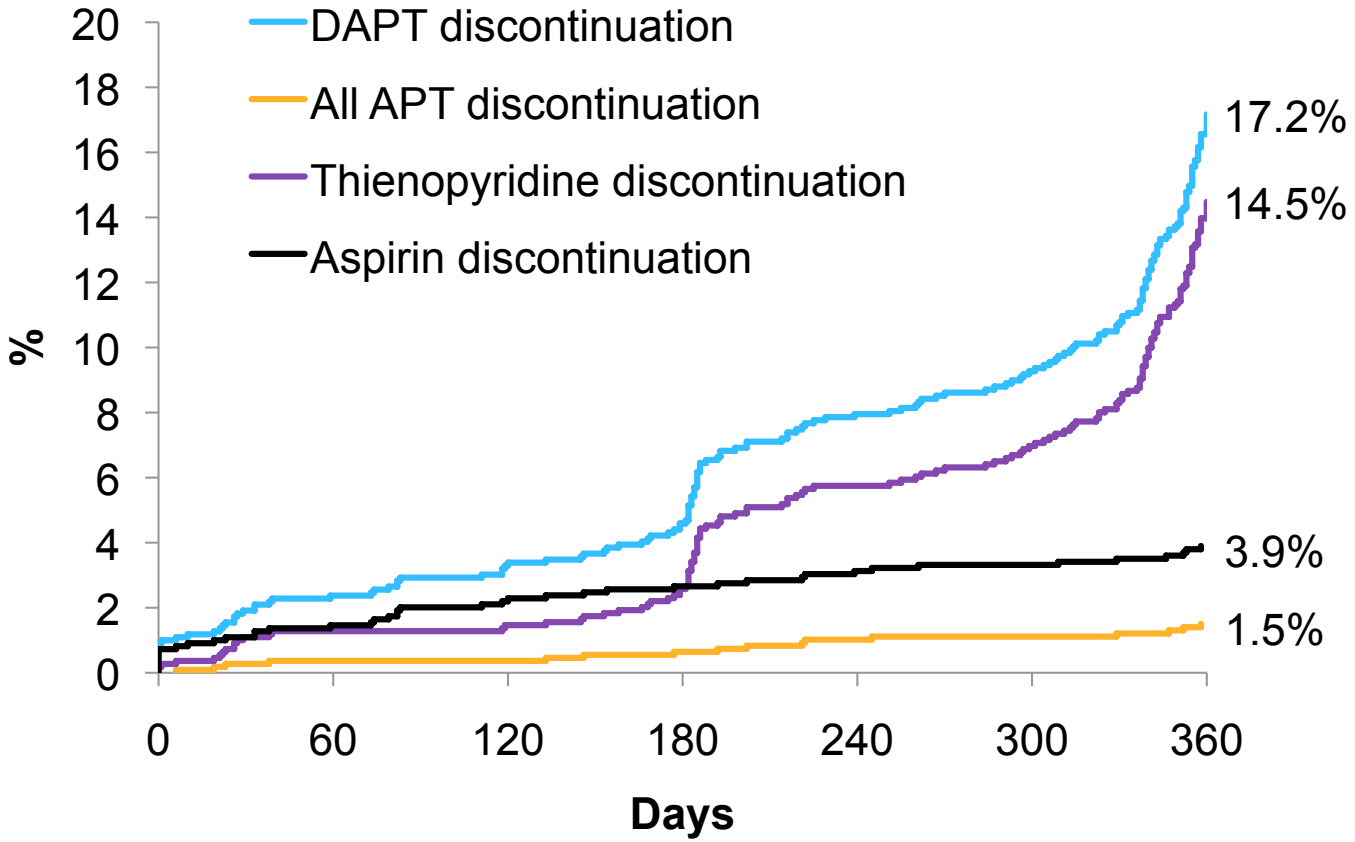


*Cutlip D et al, Circulation 2007; 115: 2344-51

Compliance with Antiplatelet Regimen

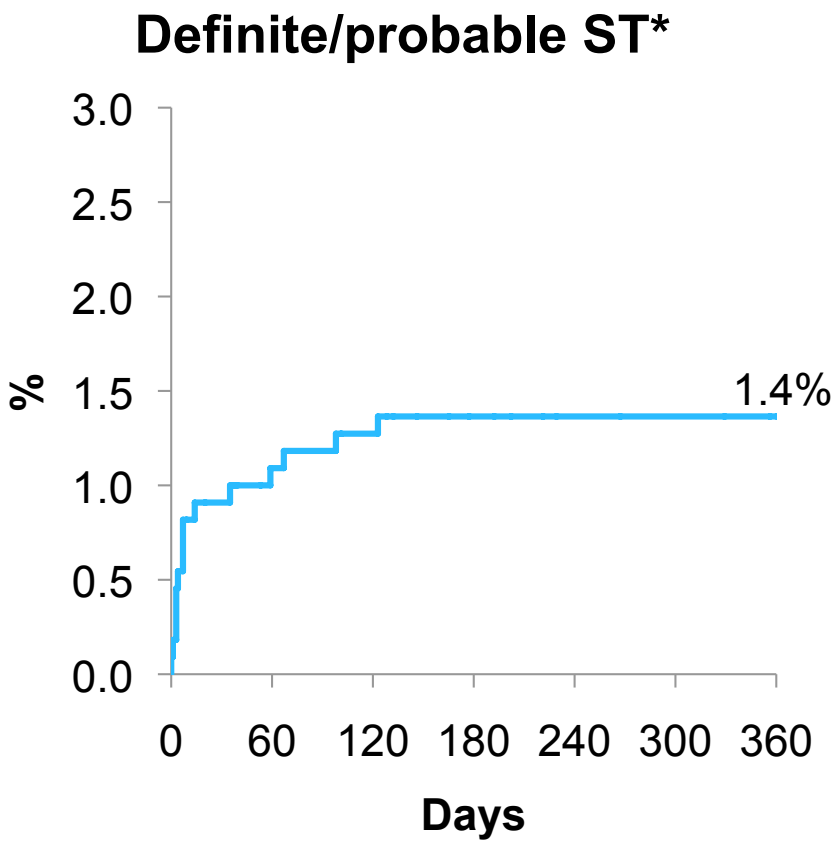


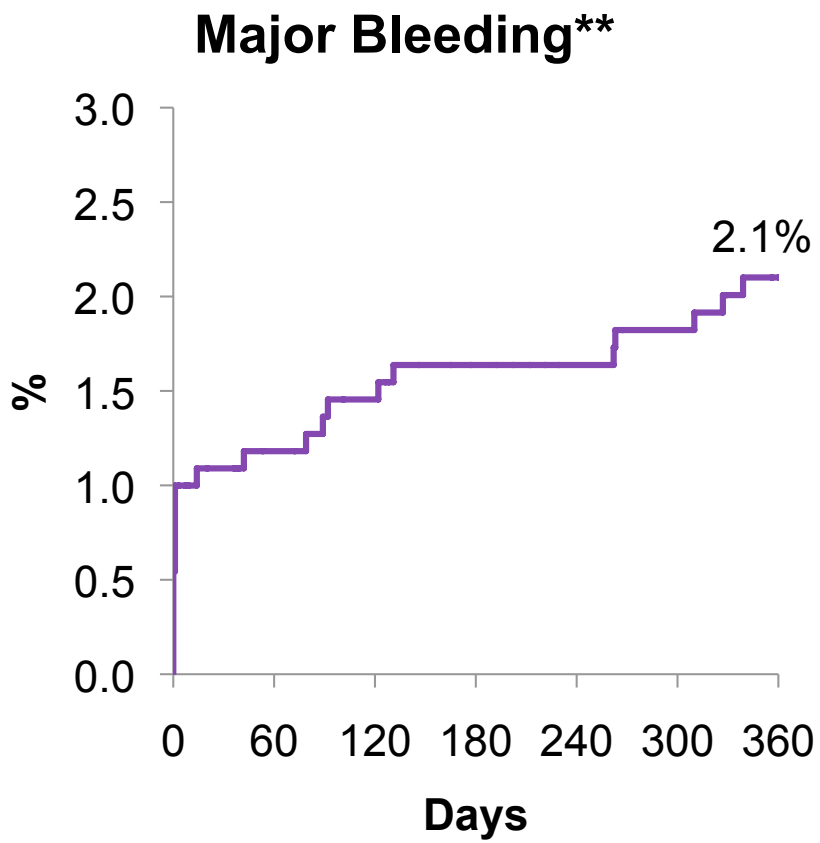
DAPT Discontinuation



DAPT discontinuation: Time when either Aspirin or Thienopyridine was discontinued
All APT discontinuation: Time when both Aspirin and Thienopyridine were discontinued

ARC Definite/Probable ST & Major Bleeding

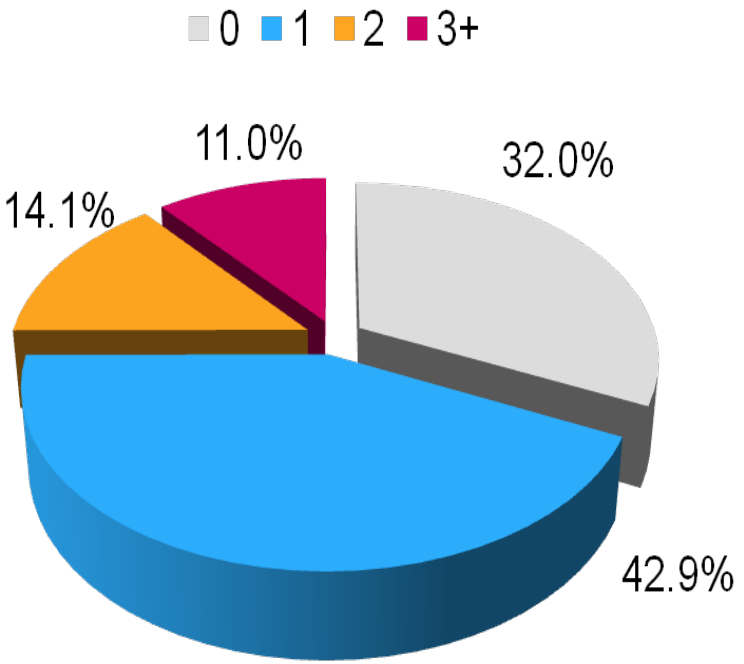




* Cutlip D et al, Circulation 2007; 115: 2344-51
** STEEPLE - Montalescot G et al, NEJM 2006; 355: 1006-17

Charlson Comorbidity Index Score

Prior myocardial infarct	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Congestive heart failure	1
Chronic pulmonary disease (COPD)	1
Ulcer disease	1
Diabetes Mellitus	1
Mild liver disease	1
Dementia	1
Connective tissue disease	1
Moderate to Severe Renal Disease	2
Diabetes with retinopathy, neuropathy or nephropathy	2
Hemiplegia	2
Any Tumor	2
Lymphoma or Leukemia	2
Moderate to Severe Liver Disease	3
Metastatic Solid Tumor	6
AIDS	6



Charlson ME et al, Journal of Chronic diseases 1987; 40: 373-383

Main components of the Charlson Comorbidity Index Score

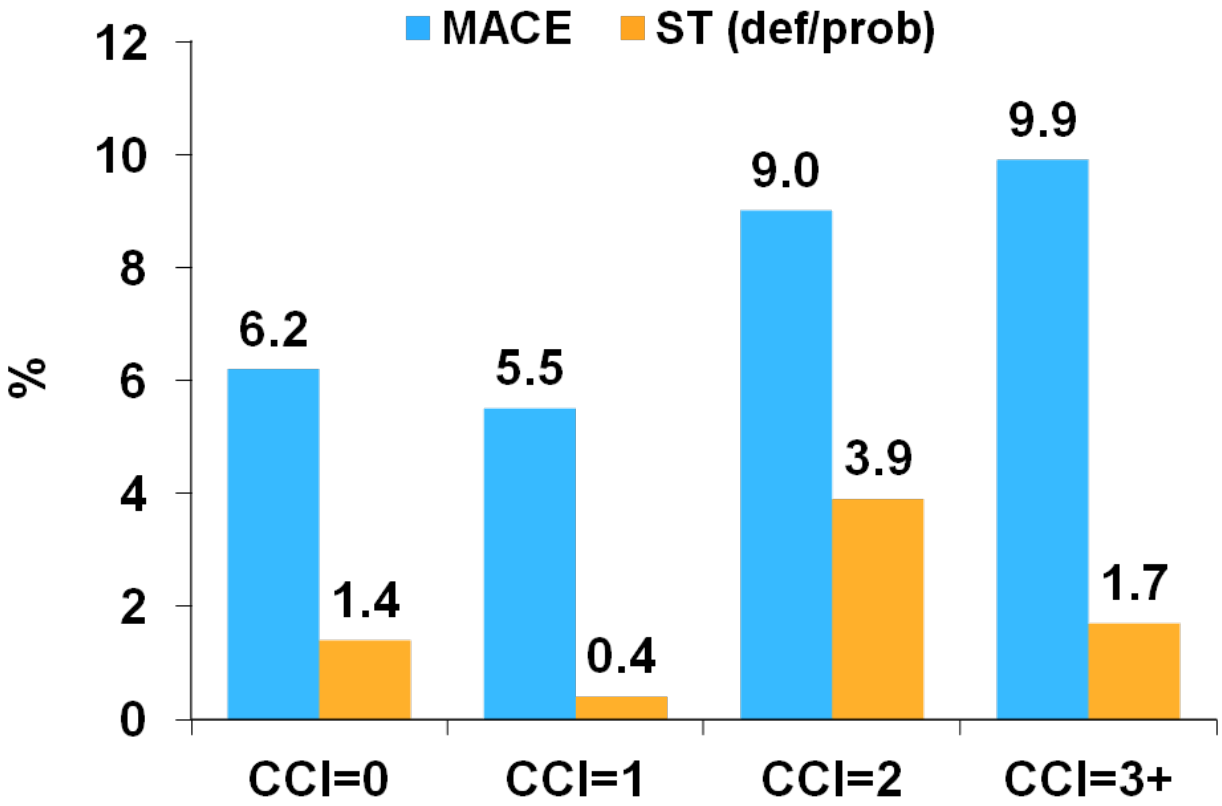
CCI SCORE	0 32%	1 43%	2 14%	3+ 11%	All N=1102
Prior myocardial infarction	0	66.3	62.6	63.6	44.4
Diabetes Mellitus	0	21.2	53.9	58.3	23.1
DM with retino-, neuro- or nephropathy	0	0	0.7	24.0	2.7
Hemiplegia	0	0	0	3.4	0.4
Peripheral vascular disease	0	2.5	14.5	26.7	6.0
Cerebrovascular disease	0	2.8	13.6	19.8	5.3
Ulcer disease	0	2.5	9.3	6.6	3.1
Moderate to Severe Renal Disease	0	0	2.0	41.7	4.8
Chronic pulmonary disease (COPD)	0	2.3	12.4	17.4	4.7
Congestive heart failure	0	1.9	7.2	16.7	3.7
Any Tumor	0	0	9.2	20.2	3.5
AIDS	0	0	0	0.8	0.1

Charlson ME et al, Journal of Chronic diseases 1987; 40: 373-383

Charlson Comorbidity Index Score

CCI Score	0 32%	1 43%	2 14%	3+ 11%	All N=1102
Age	63	64	65	68	64±10
Gender (M)	77.6	77.6	77.4	76	77.4
BMI ≥30	20.5	21.2	33.1	40.7	24.8
LVEF <40%	2.8	7.8	12.1	25.3	8.7
Prior PCI	15.3	25.4	32.3	38	24.5
Prior CABG	8.8	7.8	9	16.5	9.3
Hypertension	62.3	60.5	82.6	81.8	66.5
Hypercholesterolemia	65.2	69.6	65.2	69.4	67.5
Current smoker	28.3	32.8	23.9	14.9	28.1

MACE and ST vs. CCI



* MACE : composite endpoint of cardiac death/MI/ci-TVR
** Stent thrombosis defined by ARC (Cutlip et al,. *Circulation, 2007)*

Conclusions

- The e-BioMatrix PMS confirms the excellent 12 months safety profile for the BioMatrix™ stent in an all-comers population, with:
  - low MACE rate of 6.7%
  - low def/prob ST rate of 1.4% (all during the first 6 months)
  - compliance with DAPT of 96.3% at 6 months and 89.2% at 12 months, associated with a major bleeding rate of 2.1%
- The 7.1% DAPT discontinuation rate between 6 and 12 months did not translate into any stent thrombosis events, while 0.5% major bleeding events occurred during the same period. These data raise the question whether six months DAPT may be sufficient, and perhaps safer, for a majority of patients treated with BES in routine clinical practice.
- Co-morbidity, as assessed by the Charlson Comorbidity Index, is an important predictor of MACE during follow-up