Second Generation Drug-Eluting Stents Implantation Followed by Six Versus Twelve-Month - Dual Antiplatelet Therapy - The SECURITY Randomized Clinical Trial

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Disclosures: Antonio Colombo is a Minor shareholder of Direct Flow Inc.

All faculty disclosures are available on the CRF Events App and online at www.crf.org/tct

Methods

- The SECURITY trial [NCT00944333] was a prospective, randomized, non-inferiority, investigator-driven, multicenter, international study.

- 3 Countries, 38 centers (Italy: 31; Spain: 6; the Netherlands: 1)

- Second-generation DES used in the study were the Endeavor Resolute (Medtronic, MA), Xience (Abbott Park, Illinois), Promus (Boston Scientific, MN), Nobori™ (Terumo Corporation, Tokyo, Japan) and the Biomatrix™ (Biosensors Europe S.A.).

Inclusion Criteria

- Diagnosis of angina pectoris / unstable angina pectoris / documented silent ischemia, all treated with a second generation drug eluting stent
- Presence of one or more de novo stenosis equal or greater than 70% in a native coronary artery, treated with a drug eluting stent
- Patient is > 18 years of age (or minimum age as required by local regulations).
- The patient has consented to participate by signing the “Patient Informed Consent Form”.
- Any type of lesion or number of lesions can be included in this trial unless specifically detailed in the exclusion criteria.
- No other DES implanted before the target procedure
- No BMS implanted in the 3 months before the target procedure

Exclusion Criteria

- Patients treated for lesions in venous or arterial grafts / in-stent restenosis / Unprotected Left Main lesions / ST elevation myocardial infarction in the 48 hours prior to the procedure / Non ST elevation myocardial infarction in the previous six months
- Patients with LVEF≤30%
- Patients with hypersensitivity or allergies to study drug or devices.
- Patients with chronic renal insufficiency (creatinine >2mg or mg or 180 μmol/l)
- Current medical condition with a life expectancy of less than 24 months.
- The subject is participating in another device or drug study.

Study Objectives

- **Primary Endpoint**
  - Composite of cardiac death, MI, stroke, definite or probable stent thrombosis or bleeding academic consortium criteria (BARC) type 3 or 5 bleeding at **12 months**.
- **Secondary Endpoints**
  - Composite of cardiac death, spontaneous MI, stroke, definite or probable stent thrombosis or BARC type 2, 3 or 5 bleeding at **12 and 24 months.**
  - MI, Urgent Target Vessel Revascularization (coronary artery by-pass surgery or percutaneous coronary intervention because of acute cardiac ischemia), All-bleeding events and All-cause mortality at **30 days, 6, 12** and **24 months**.

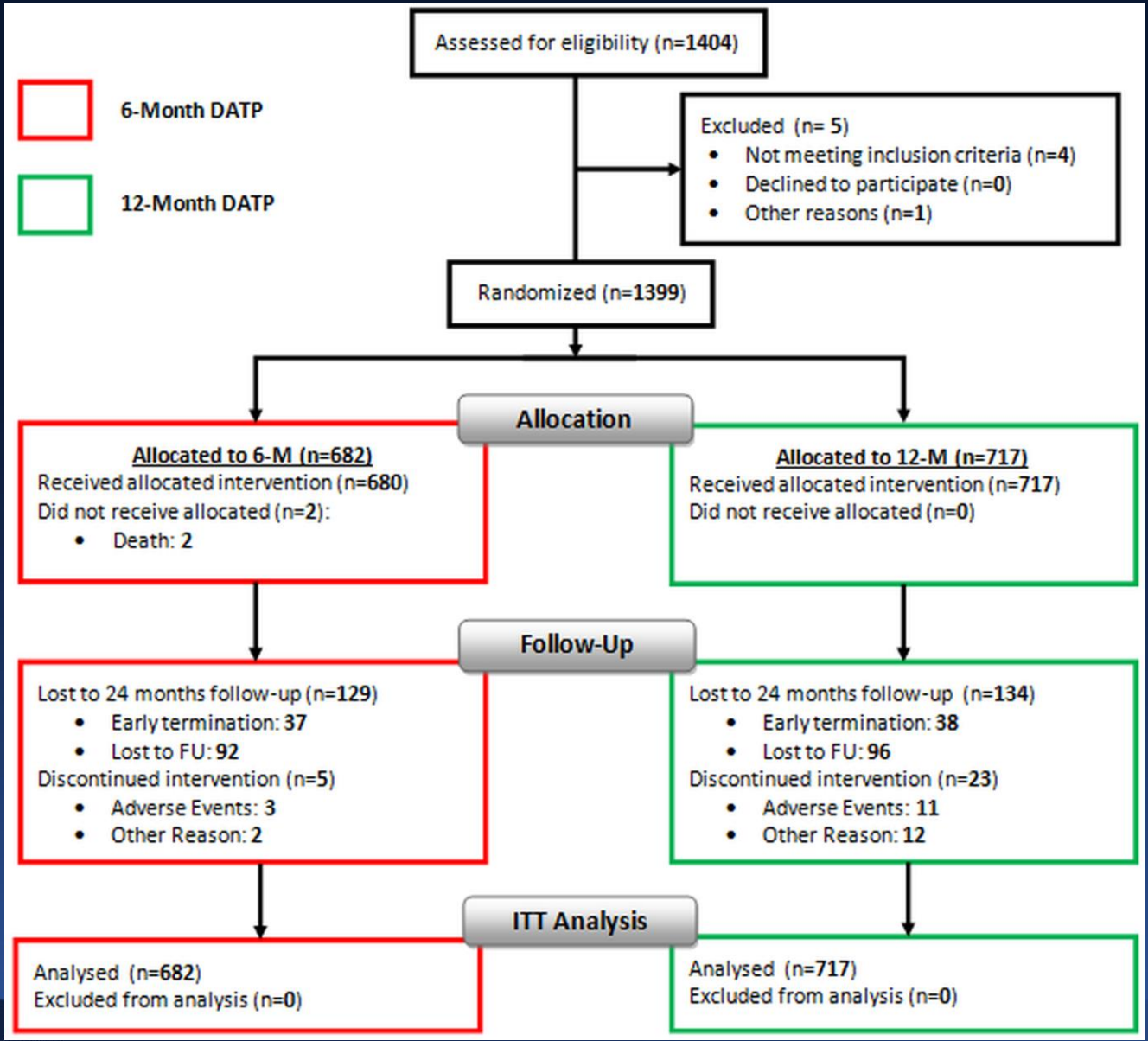
Statistical Methods

- Powered to test the non-inferiority of the primary composite endpoint between 6 and 12 months DAPT following 2nd-generation DES Implantation.
- To validate the incidence of the primary endpoint, a **Safety Interim Analysis** was conducted by an independent statistician when the first 1000 randomized patients completed 12 months follow-up. Results of the interim analysis were evaluated by the data monitoring committee. The incidence of the primary endpoint at 12 month after randomization was of 4.5%. Considering this low incidence and keeping the **absolute non-inferiority margin of 2.0%** , a **power of 0.80** and a **significance level of 0.05 (one-tail)** it was estimated that **1,370 patients were needed in each group** instead of the first sample size of 1.800 estimated on a prevalence basis of 6%.

Study Population – Top 10 Enrolling Centers

	Center	PI	Patients
1	Policlinico Umberto I - Roma	G. Sardella	199 (14.2%)
2	Ospedale San Raffaele - Milano	A. Colombo	193 (13.7%)
3	ASL Trapani - P.O. Sant'Antonio Abate-Erice	A. Frasheri	92 (6.6%)
4	S. Giovanni Bosco Hospital - Torino	R. Garbo	54 (3.9%)
5	Hospital Clínic, Barcelona	M. Masotti	55 (3.9%)
6	Hospital del Mar, Barcelona	N. Salvatella	55 (3.9%)
7	Hospital Puerta de Hierro Madrid	J. F. Oteo Dominguez	50 (3.6%)
8	Hesperia Hospital- Modena	A. Benassi	50 (3.6%)
9	Azienda Ospedaliera di Padova	G. Tarantini	48 (3.4%)
10	IRCCS Humanitas- Rozzano	P. Presbitero	46 (3.3%)

Study Population



Baseline Clinical Characteristics

Characteristics	6-Month DAPT (N = 682)	12-Month DAPT (N = 717)
Age (years), mean ± SD	64.9 ± 10.2	65.5 ± 10.1
Female sex, n (%)	[illegible]	166 (23.2)
Diabetes Mellitus, n (%)	206 (30.4%)	223 (31.4%)
Hypertension, n (%)	[illegible]	510 (71.1)
Dyslipidemia, n (%)	446 (65.4)	436 (60.8)
Smoker Status, n (%)		
Never Smoked	274 (40.5)	261 (37)
Previous Smoker	239 (35.3)	238 (33.7)
Active Smoker	139 (20.5)	172 (24.4)
Previous MI, n (%)		
NSTEMI > 48 h	65 (9.5)	71 (9.9)
STEMI > 48 h	80 (11.7)	73 (10.2)
Previous PCI, n (%)	132 (19.4)	116 (16.2)
Previous CABG, n (%)	38 (5.6)	39 (5.4)
LVEF (%), mean ± SD	56.3 ± 8.7	56.6 ± 8.2
Clinical Presentation, n (%)		
Stable Angina	[illegible]	368 (61.6)
Unstable Angina	213 (38.4)	229 (38.4)
Baseline Medications		
Aspirin, n (%)	616 (90.3)	621 (86.6)
Clopidogrel, n (%)	301 (44.1)	305 (42.5)
Statin, n (%)	489 (71.7)	494 (68.9)
Heparin, n (%)	377 (55.3)	401 (55.9)

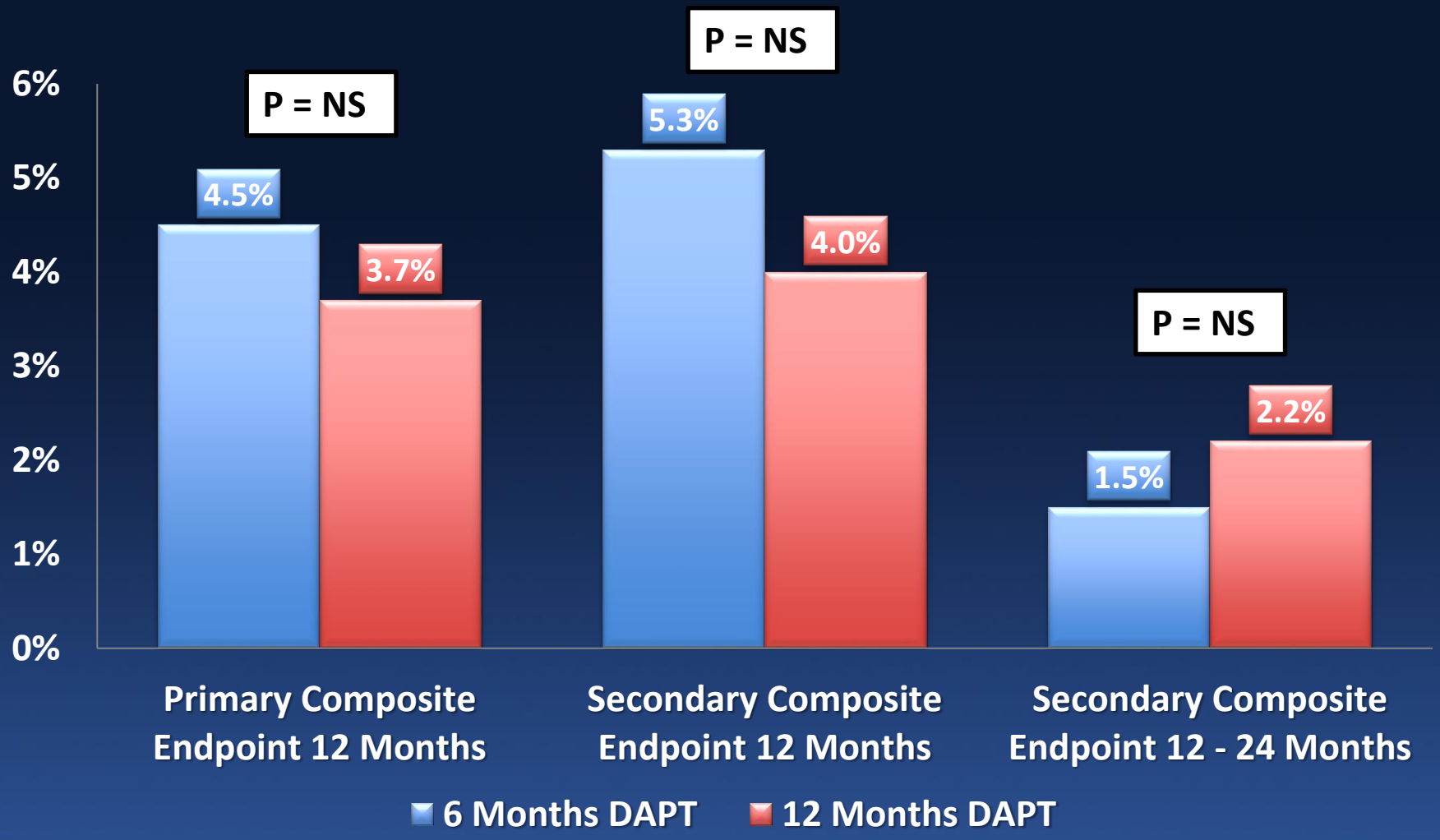
Baseline Lesion Characteristics

Characteristic	6-Month DAPT (N = 682)	12-Month DAPT (N = 717)
Number of Lesions, n (%)		
1-Vessel disease	383 (56.2)	424 (59.1)
2-Vessel disease	221 (32.4)	210 (29.3)
3-Vessel disease	77 (11.3)	82 (11.4)
4-Vessel disease	1 (0.1)	1 (0.1)
Main Branch Lesion Distribution, n (%)		
Left Anterior Descending Artery	402 (43)	423 (44)
Left Circumflex Artery	133 (14.3)	137 (14.2)
Diagonal Artery	38 (4)	32 (3.3)
OM and RI Arteries	106 (11.2)	118 (12.3)
Right Coronary Artery	206 (22)	207 (21.6)
Bifurcation, n (%)	97 (10.4)	105 (10.9)
Baseline TIMI flow < 3	140 (15.3)	145 (15.5)
AHA / ACC Classification		
Class B	603 (64.5)	617 (64.3)
Class C	197 (21.1)	201 (21)
Baseline visual estimate, mean ± SD		
Lesion length (mm)	17.6 ± 9.8	18.1 ± 10.8
Reference vessel diameter (mm)	2.9 ± 0.4	2.9 ± 0.4
Minimal lumen diameter (mm)	0.6 ± 0.5	0.6 ± 0.6
Diameter stenosis, n (%)	84 ± 10.1	84.4 ± 9.7

Use of Medication During The Trial

Characteristic	6-Month DAPT (N = 682)	12-Month DAPT (N = 717)
DAPT Therapy at 6 Months		
Clopidogrel only	2 (0.3)	6 (0.9)
ASA only	3 (0.5)	5 (0.7)
ASA + clopidogrel	618 (97.3)	655 (97.6)
ASA + prasugrel	8 (1.3)	2 (0.3)
ASA + ticagrelor	4 (0.6)	3 (0.4)
DAPT Therapy at 12 Months		
Clopidogrel only	11 (1.8)	8 (1.2)
ASA only	392 (63.6)	13 (2.0)
ASA + clopidogrel	208 (33.8)	622 (96.1)
ASA + prasugrel	0	1 (0.2)
ASA + ticagrelor	0	1 (0.2)
Drug Therapy at 24 Months		
Aspirin, n (%)	525 (96.5)	563 (97.9)

Primary and Secondary Composite Endpoints

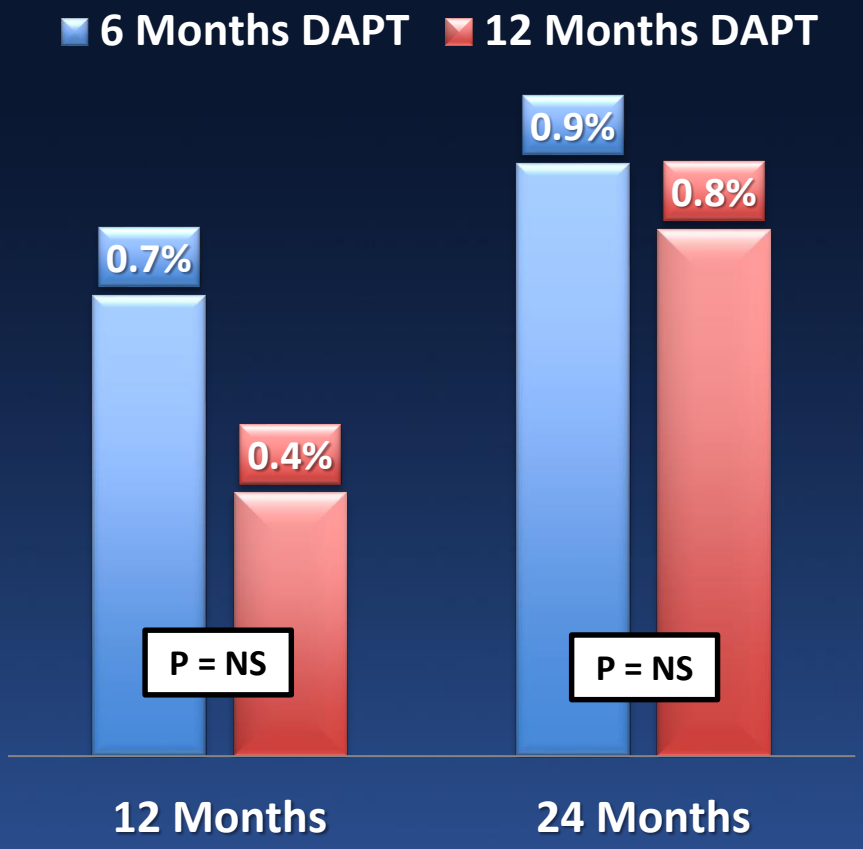


Outcome rates at 24 months according to treatment groups – Cox proportional hazards

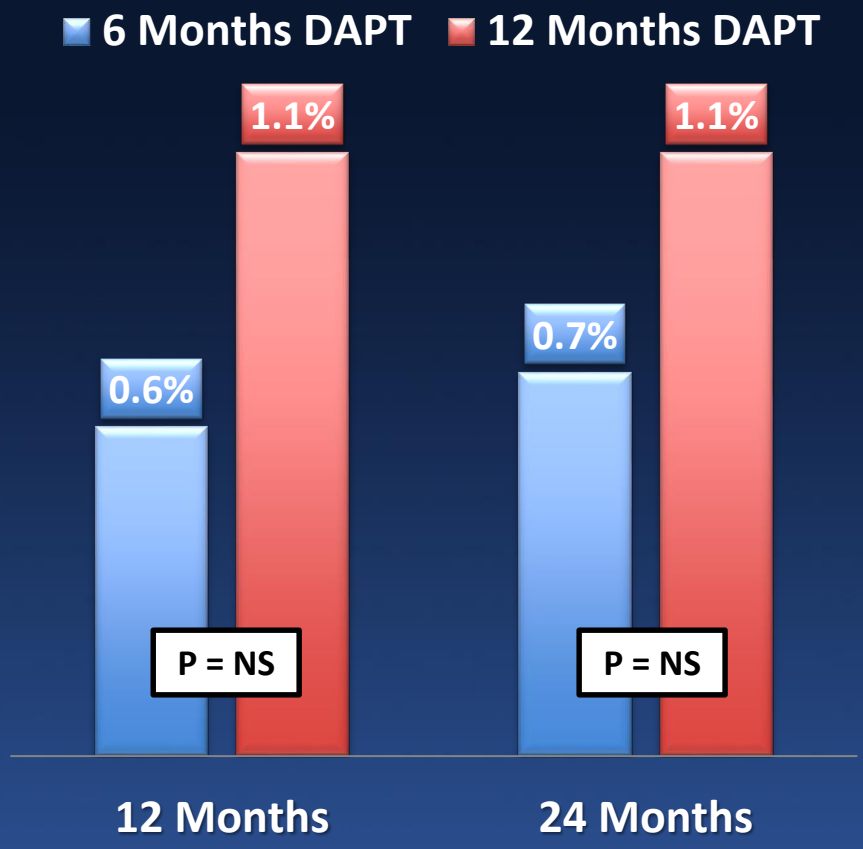
	6-Month DAPT (N = 682)	12-Month DAPT (N = 717)	Hazard ratio 95% CI	P-value
Cardiac death	6 (0.9%)	6 (0.8%)	1.05 (0.34 to 3.26)	0.925
Myocardial Infarction	21 (3.1%)	19 (2.6%)	1.16 (0.62 to 2.16)	0.636
Stroke	6 (0.9%)	3 (0.4%)	2.10 (0.52 to 8.40)	0.636
Definite/probable ST	3 (0.4%)	3 (0.4%)	1.05 (0.21 to 5.20)	0.951
BARC 3 or 5	5 (0.7%)	8 (1.1%)	0.69 (0.25 to 1.96)	0.496

Secondary Endpoints

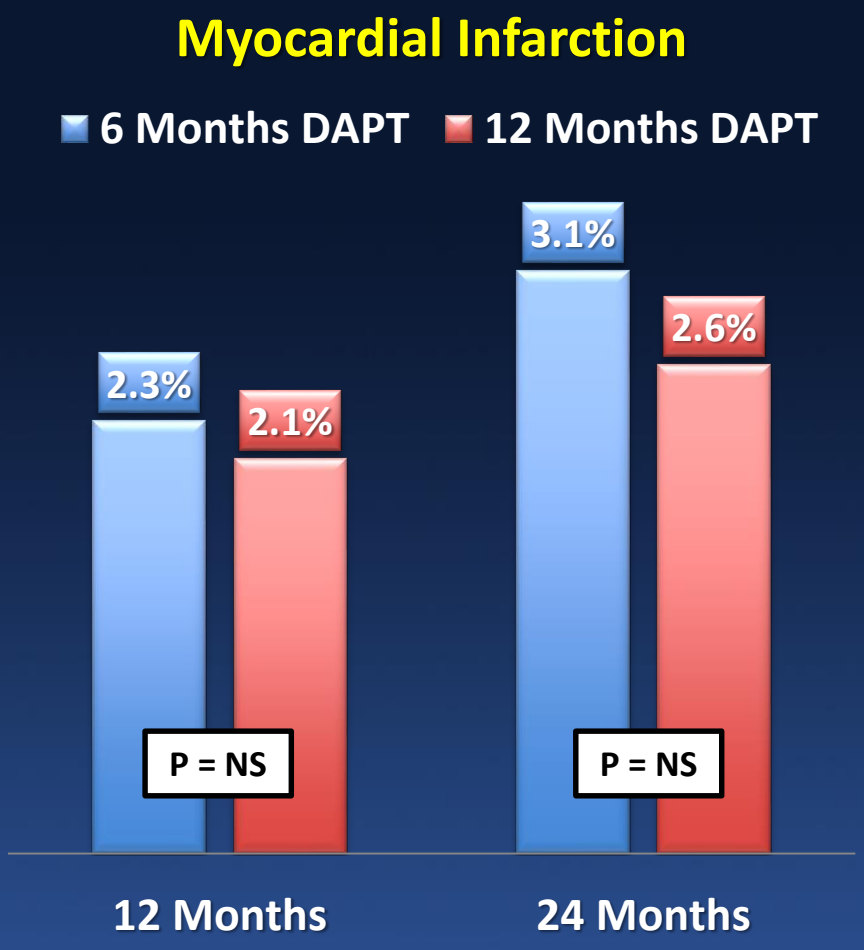
Cardiac Mortality

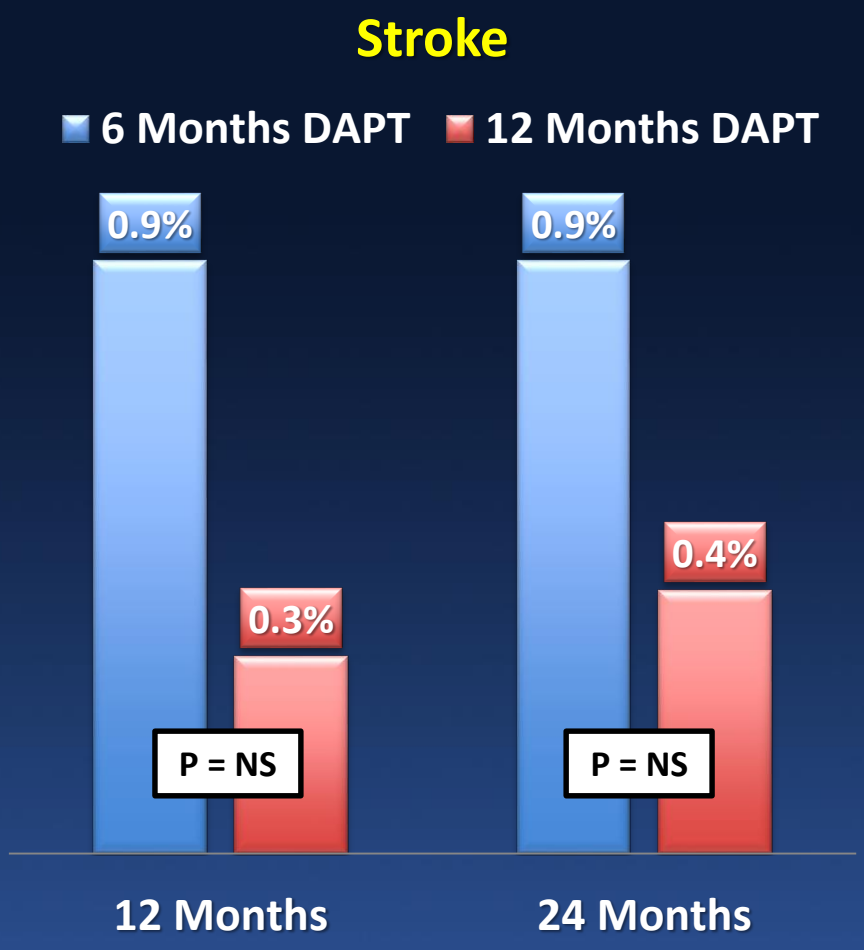


BARC 3 or 5 Bleeding

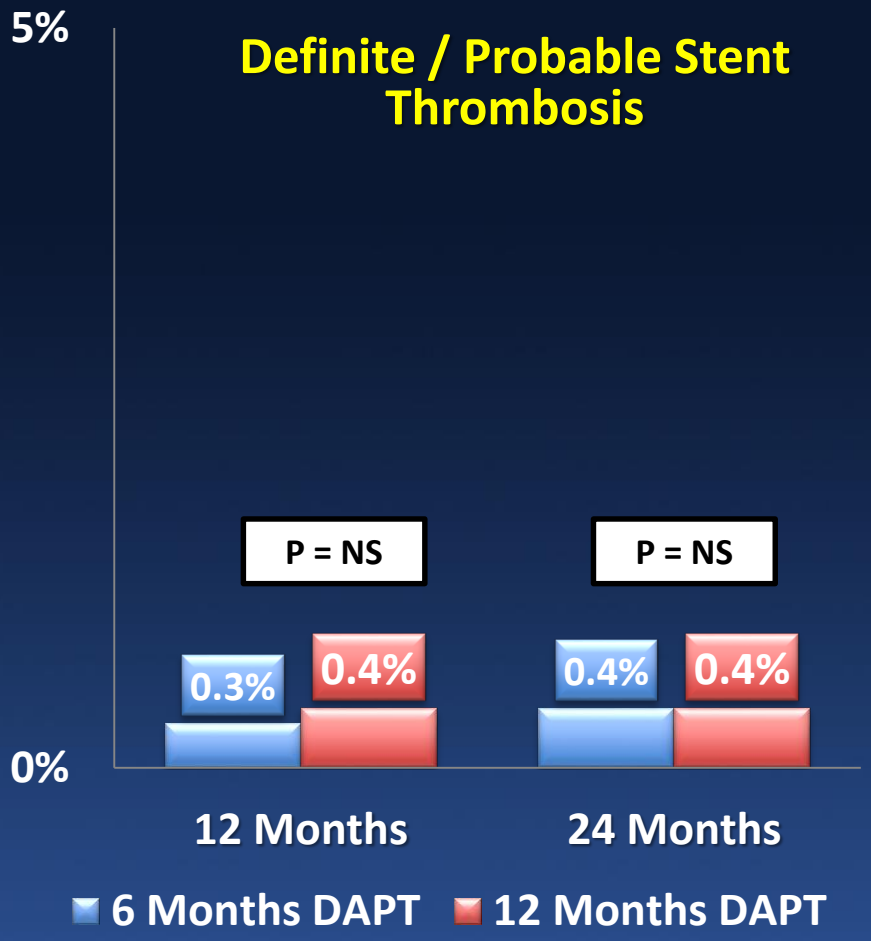


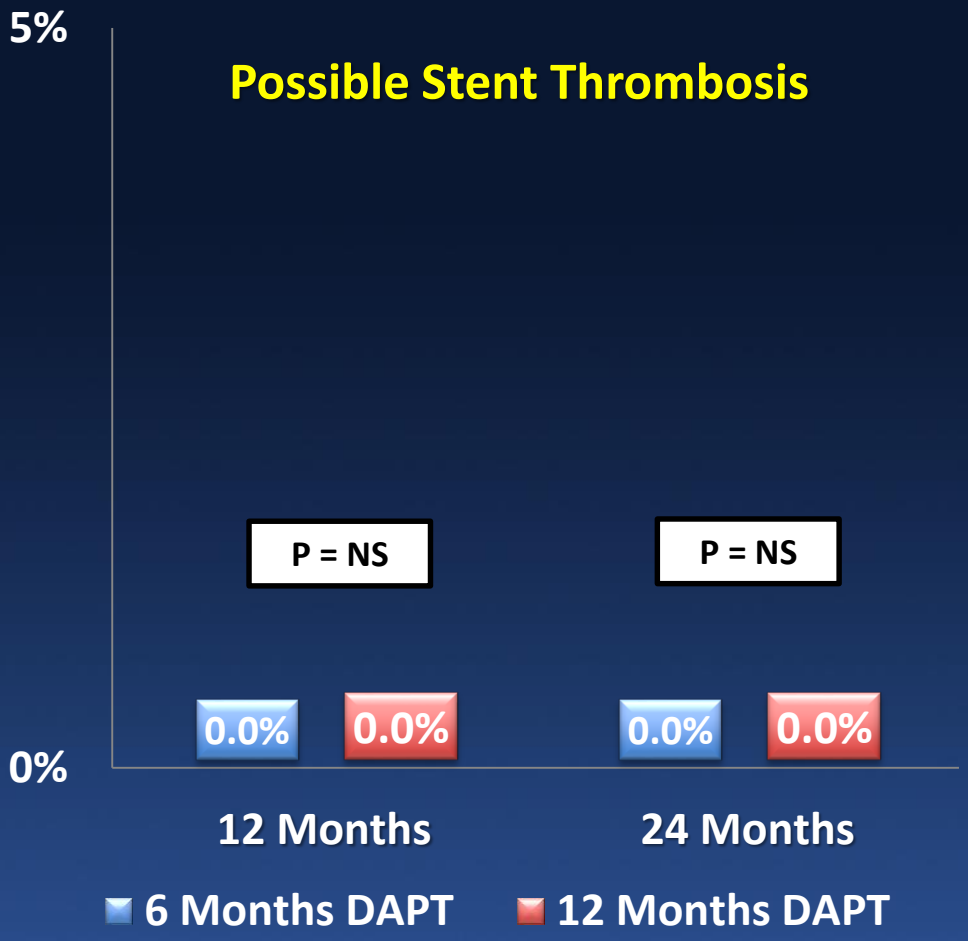
Secondary Endpoints



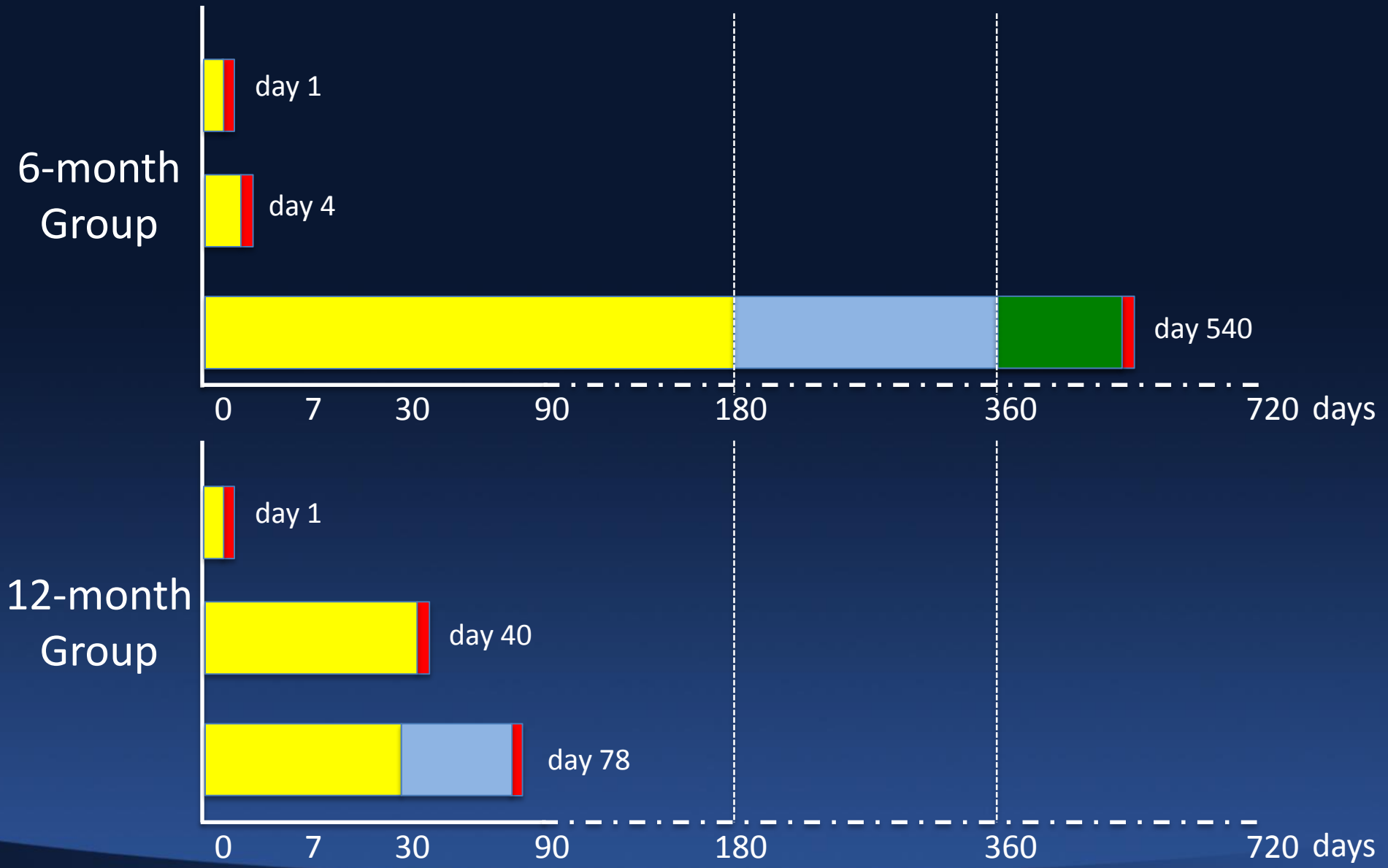


Stent Thrombosis





Stent Thrombosis – Events Timeline



DAPT | ASA Only | No APT | ST

Stent thrombosis – ARC classification

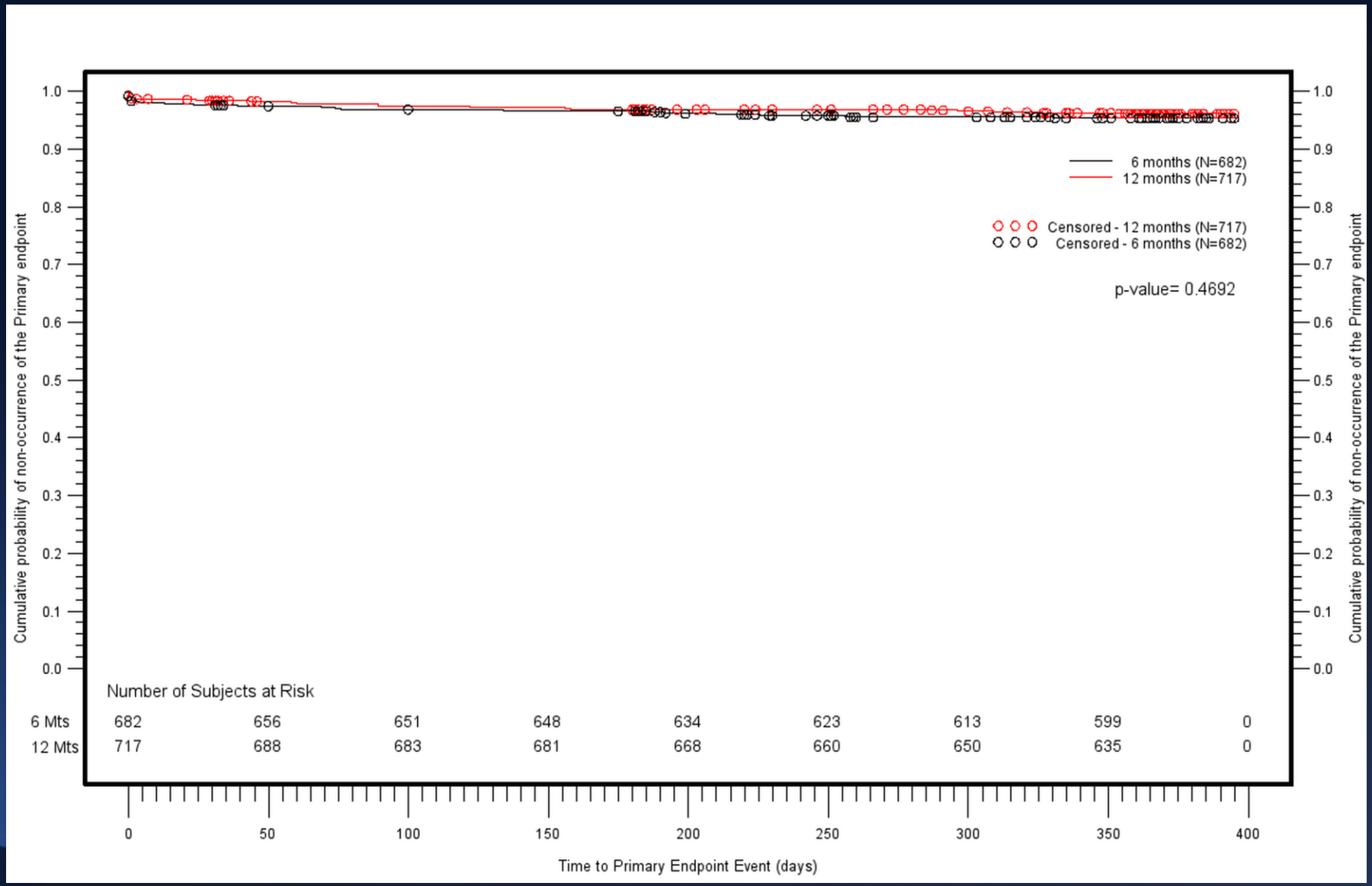
	6-Month DAPT (N = 682)	12-Month DAPT (N = 717)
Acute	1	1
Sub-acute	1	-
Late	-	2
Very late	1	-

All patients were under DAPT at the time of ST (but the very late case)

Urgent Target Vessel Revascularization

All-Bleedings

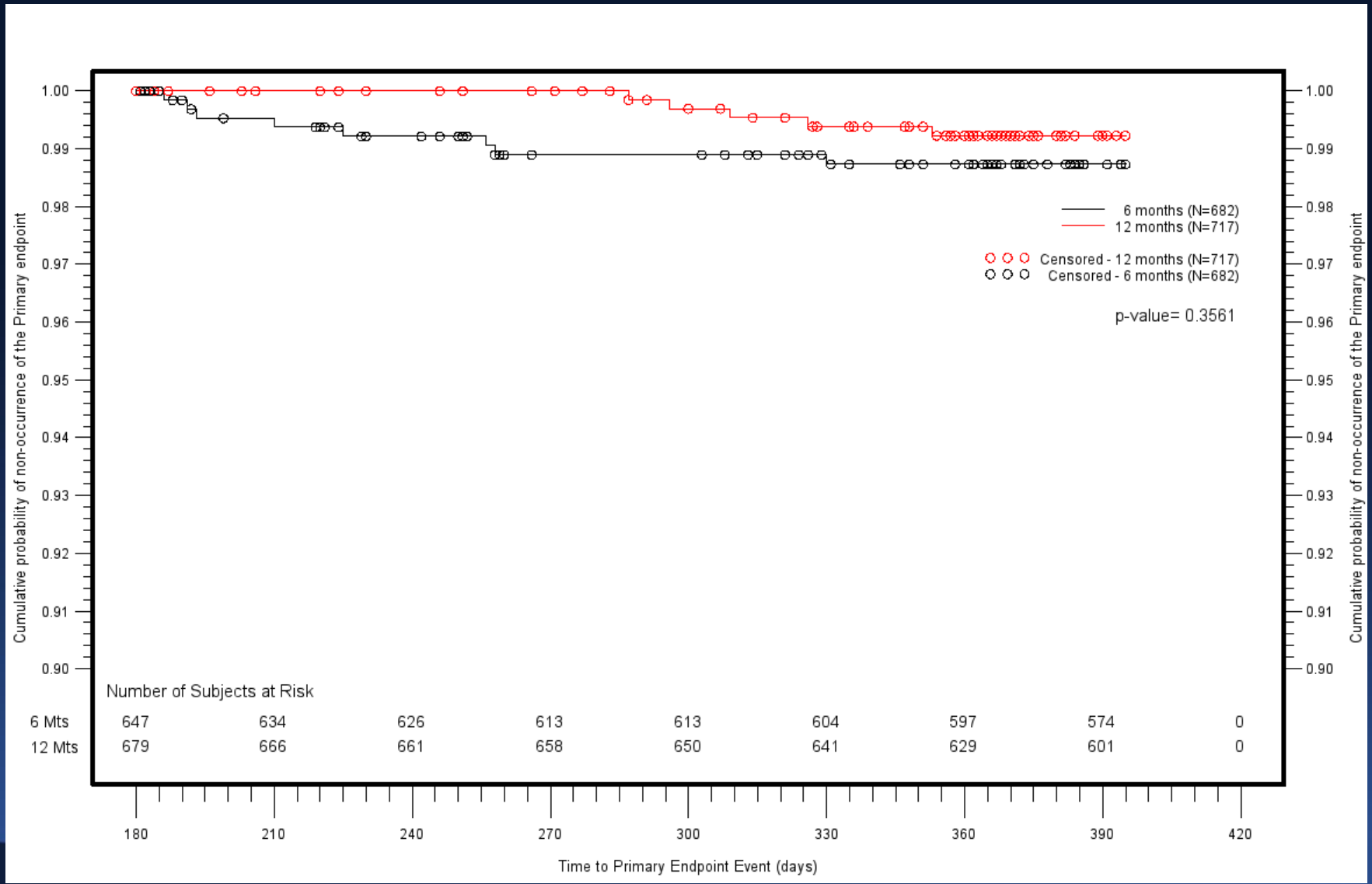
KM – Primary Endpoint 12 Months



Predictors of the PE at Multivariable Analysis

Variables in the Model	HR	95% CI	p value
Age ≥ 75 years	2.211	1.234 – 3.962	0.007
Stent Type			0.019
Endeavor Resolute Vs. Biomatrix / Xience / Promus	2.336	1.051 – 5.190	
Mean Number of Stents (for each unit increase)	1.410	1.128 – 1.741	0.002
Mean Stents Length (for each 5 units increase)	1.383	1.135 – 1.685	0.001
Mean Stent Size (for each 2.5 units increase)	1.326	1.106 – 1.590	0.002
Diabetes Mellitus			0.069
NIDDM Vs. None	0.895	0.464 – 1.729	
IDDM Vs. None	2.349	1.080 – 5.106	
DAPT 6- vs. 12-month	1.272	0.754 – 2.145	0.367
Female sex	1.596	0.897 – 2.838	0.111

Landmark analysis



Events after 6 months

	6-Month DAPT (N = 682)		12-Month DAPT (N = 717)	
	M12	M24	M12	M24
Cardiac death	-	1 (0.2%)	1 (0.2%)	3 (0.5%)
Myocardial Infarction	2 (0.3%)	5 (0.9%)	2 (0.3%)	4 (0.7%)
Stroke	3 (0.5%)	-	-	1 (0.2%)
Definite/probable ST	-	1 (0.2%)	-	-
BARC 3 or 5	1 (0.2%)	1 (0.2%)	2 (0.3%)	-

Conclusions

- Six months DAPT appeared to be non-inferior to a 12 months regimen in patients undergoing PCI with 2nd-generation DES regarding the primary composite end point of cardiac death, MI, stroke, definite or probable ST or BARC type 3 or 5 bleeding at 12 months of clinical follow-up.

- Multivariable analysis found as significant independent predictors of the primary endpoint age ≥ 75 years, stent type used, mean number of stents implanted, mean stent length and mean stent size. Of note, DAPT 6 versus 12 months resulted not significant following multivariable adjustment.

- The 6 months DAPT appeared to be non-inferior to 12 months regarding the incidence of the secondary composite endpoints defined by the study protocol.

Accepted Manuscript

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PII: S0735-1097(14)06155-5

DOI: 10.1016/j.jacc.2014.09.008

Reference: JAC 20588

To appear in: *Journal of the American College of Cardiology*