Six versus Twelve Months Dual Antiplatelet Therapy After Drug-Eluting Stent Implantation in ST-Elevation Myocardial Infarction Primary Results from the DAPT-STEMI Trial

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On behalf of the DAPT-STEMI Investigators and Steering Committee

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Consulting Fees/Honoraria, travel fees or institutional grants	• Medtronic, Abbott, Meril, OrbusNeich, Boston Scientific, Astra Zeneca, Pfizer

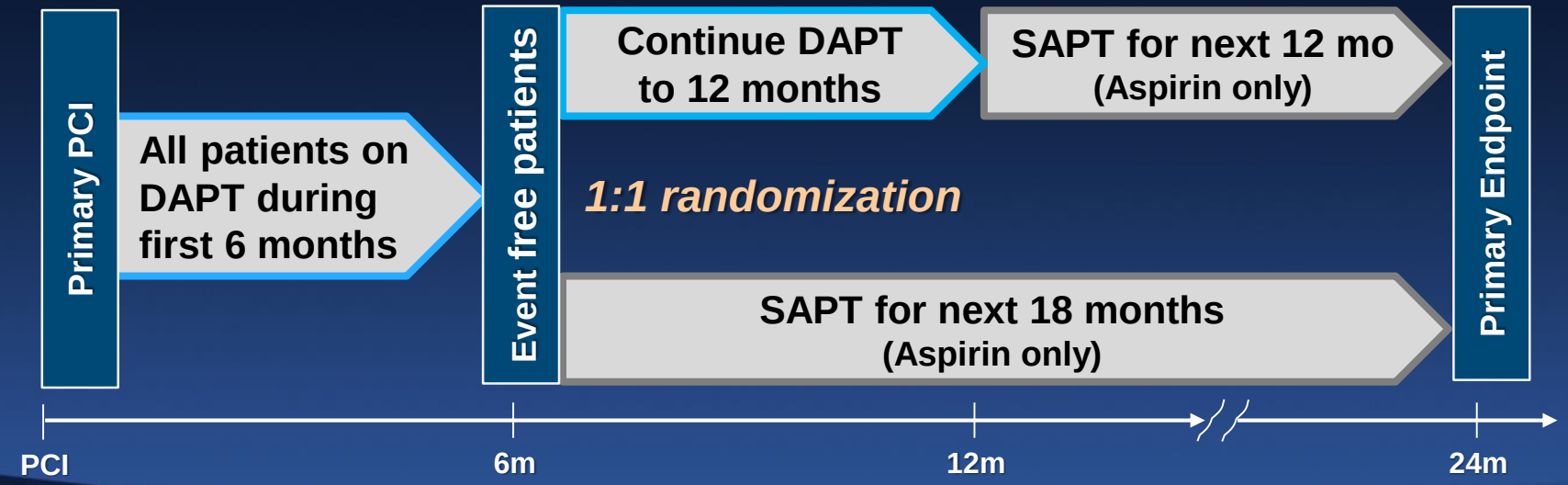
Introduction

- International guidelines recommend 12-months of DAPT after primary PCI with DES in setting of STEMI
- While longer DAPT reduces the risk of ST and thromboembolic events in general, it is also associated with a higher risk of bleeding, which sometimes can be fatal
- Second-generation DES have consistently shown superior safety outcomes than their predecessors even in STEMI patients, questioning the need for a long duration of DAPT
- Whether a shorter DAPT duration is feasible also in STEMI patients has not been studied previously

DAPT – STEMI Trial Design

Prospective, International, Randomized, Non-inferiority Trial
STEMI Patients undergoing primary PCI with a second-generation Zotarolimus-eluting stent (Resolute Integrity)

Enrollment took place in 17 centers in The Netherlands, Poland, Switzerland and Norway



Trial Population

Inclusion Criteria

- STEMI patients requiring primary PCI
- Age 18-85 years
- Eligible for DES implantation

Key Exclusion Criteria – Enrollment

- Planned elective surgery necessitating DAPT interruption ≤ 6 months after PPCI
- History of stent thrombosis
- DES in left main coronary artery
- Active bleeding, known bleeding diathesis or coagulopathy
- Oral anticoagulant therapy

Trial population

- ***Exclusion criteria – Randomization at 6 Months:***
  - **Occurrence of *death, myocardial infarction, stroke, stent thrombosis and target vessel* or *any revascularization (beyond 45 days) during the first* 6 months after PPCI**
  - **Bleeding requiring discontinuation of DAPT during the first 6 months after PPCI**
  - **Oral anticoagulant therapy**

Endpoints

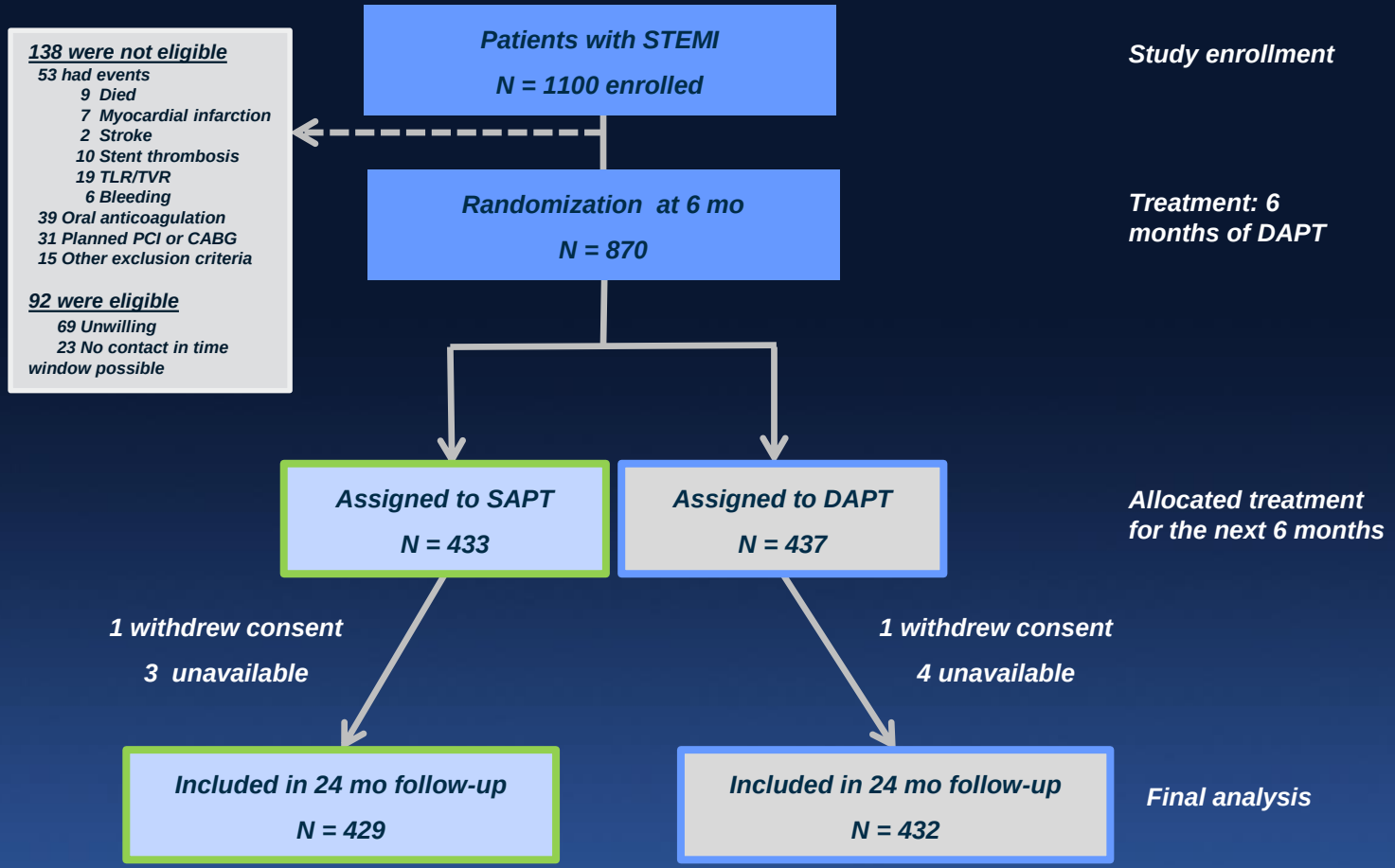
- **The primary endpoint : *all-cause mortality, myocardial infarction, any revascularization, stroke, TIMI major bleeding* at 18-month follow-up after randomization**

- **The major secondary endpoints**
  - **all-cause mortality, MI, stroke, ST, or TIMI major bleeding at 15 and 18-month follow-up after randomization**
  - **Individual components of the primary endpoint**

Power Calculation

- **The sample size:**
  - *α = 0.05 for a two-sided test* (0.025 for a one-sided test)
  - *Power of 85%*
  - Non-inferiority margin: *HR and upper 95% CI of 1.66*
  - The assumed *primary endpoint rate in both arms* was *15 %*

- The *sample size* needed was *1000 patients*
- To compensate for the patients who met a randomization exclusion criteria in the first 6 months *1100 patients were enrolled*


Patients with STEMI
N = 1100 enrolled
Study enrollment
138 were not eligible
53 had events
9 Died
7 Myocardial infarction
2 Stroke
10 Stent thrombosis
19 TLR/TVR
6 Bleeding
39 Oral anticoagulation
31 Planned PCI or CABG
15 Other exclusion criteria
92 were eligible
69 Unwilling
23 No contact in time window possible
Randomization at 6 mo
N = 870
Treatment: 6 months of DAPT
Assigned to SAPT
N = 433
Assigned to DAPT
N = 437
Allocated treatment for the next 6 months
1 withdrew consent
3 unavailable
1 withdrew consent
4 unavailable
Included in 24 mo follow-up
N = 429
Included in 24 mo follow-up
N = 432
Final analysis

Baseline Results

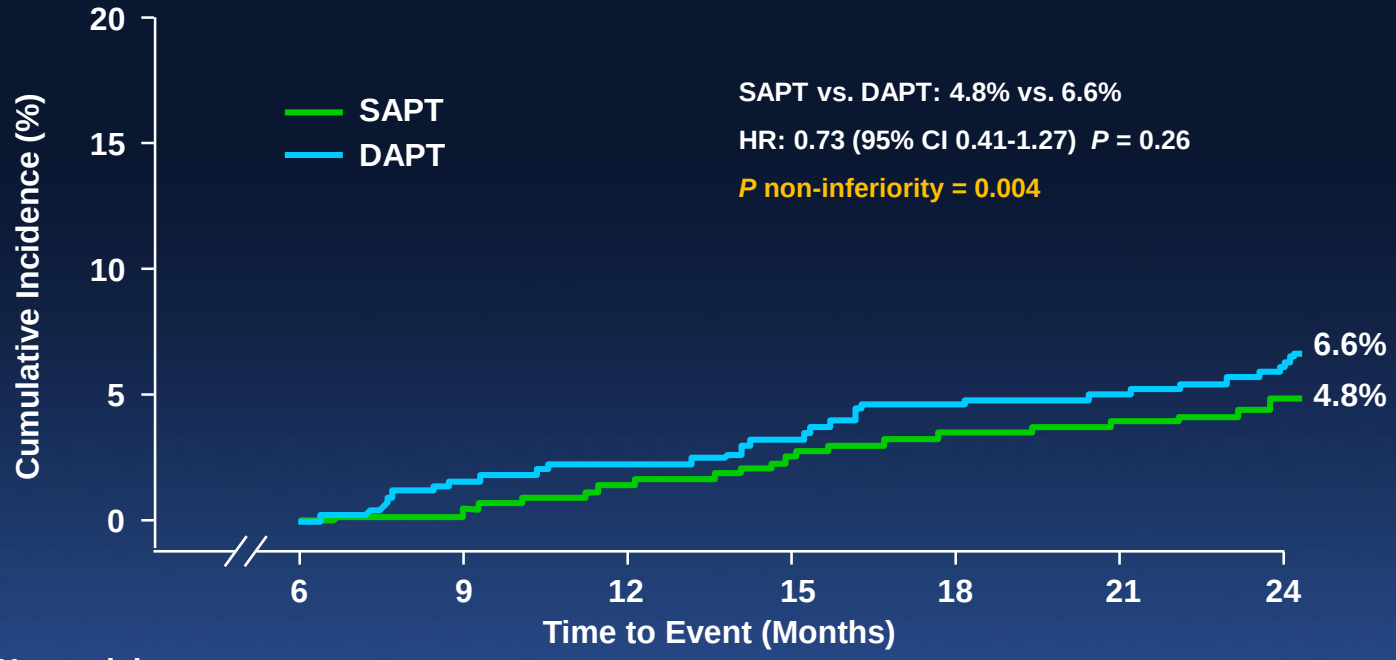
% or mean ± SD	SAPT N=433	DAPT N=437	P-Value
Patient characteristic			
Age – years	59.8 ± 10.7	60.2 ± 10.3	0.57
Male gender	337/433 (78%)	332/437 (76%)	0.52
Medical history			
Prior CABG	8/433 (2%)	2/437 (0.5%)	0.06
Prior PCI	29/433 (7%)	18/437 (4%)	0.09
Prior myocardial infarction	26/433 (6%)	20/436 (5%)	0.35
Stroke or TIA	14/433 (3%)	8/436 (2%)	0.19
Risk factors			
Diabetes mellitus	54/433 (13%)	61/437 (14%)	0.52
Hypertension	193/433 (45%)	195/436 (45%)	0.96
Dyslipidaemia	120/433 (28%)	125/436 (29%)	0.75
Current cigarette smoker	218/431 (51%)	205/437 (47%)	0.31
Family history of CAD	143/431 (33%)	144/436 (33%)	0.96

Procedural Results

% or mean ± SD	SAPT N=433	DAPT N=437	P-Value
P2Y12 inhibitors at start			
Clopidogrel	180/433 (42%)	182/437 (42%)	0.98
Prasugrel	128/433 (29%)	132/437 (30%)	0.84
Ticagrelor	125/433 (29%)	123/437 (28%)	0.81
Infarct related artery			
LAD	169/433 (39%)	188/437 (43%)	0.24
RCA	175/433 (41%)	179/437 (41%)	0.95
RCX	89/433 (21%)	70/437 (16%)	0.80
Lesion type culprit			
B2	158/428 (37%)	158/433 (36%)	0.94
C	108/428 (25%)	101/433 (24%)	0.53
Procedure data			
No. of treated lesions	1.09 ± 0.3	1.10 ± 0.3	0.60
No. of stents total	1.42 ± 0.8	1.48 ± 0.8	0.29
Total stent length total – mm	28.5 ± 16	29.8 ± 16	0.22

Primary Endpoint:

Death, MI, Revascularization, Stroke and Major Bleeding



No. at risk							
SAPT	433	428	424	419	413	411	408
DAPT	437	430	426	421	412	409	403

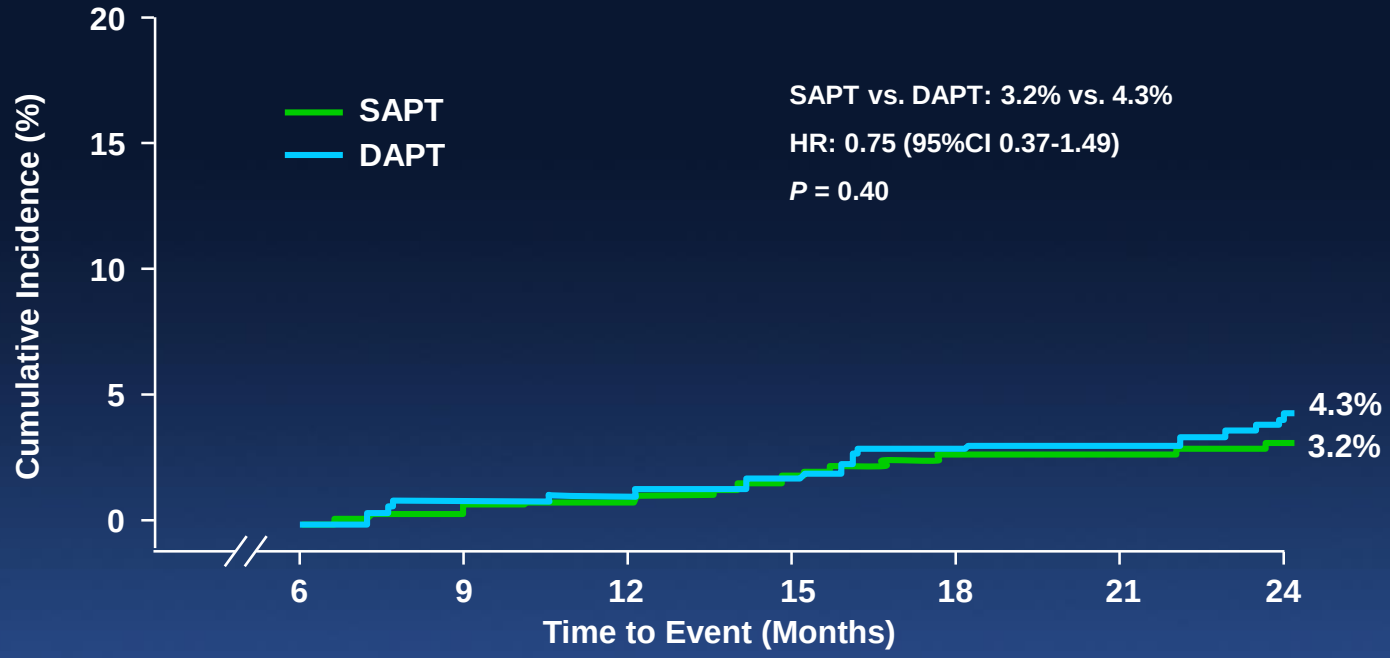
Primary Endpoint:

Death, MI, Revascularization, Stroke and Major Bleeding

Non-inferiority could be declared

Secondary Endpoint:

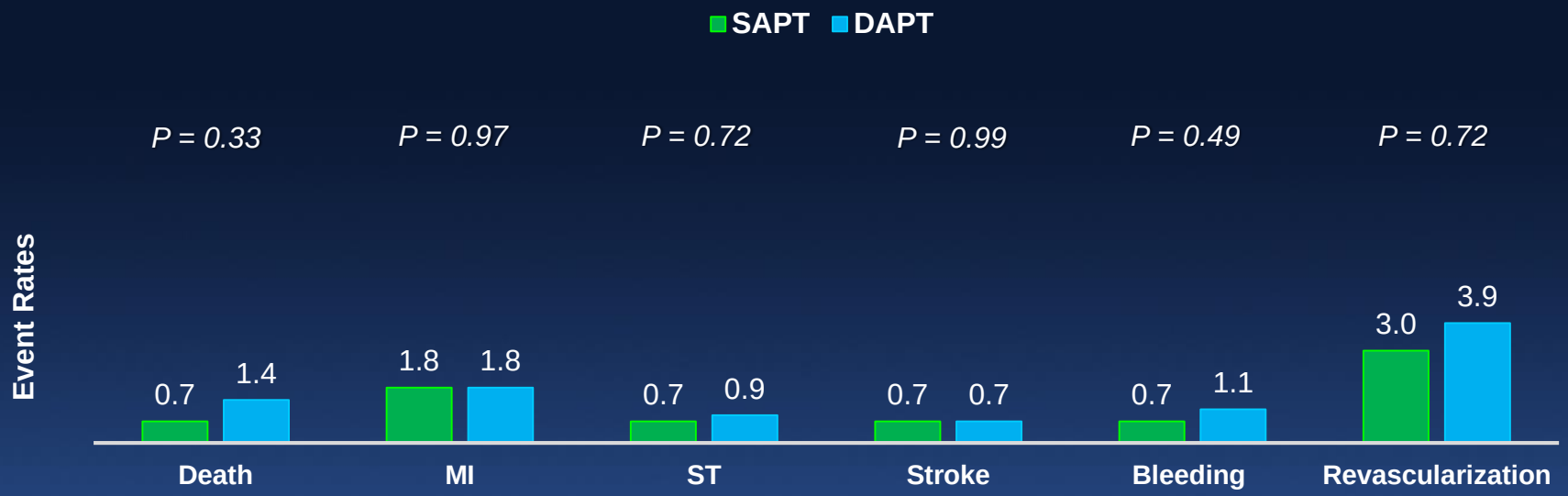
Death, MI, Stroke, ST, or TIMI Major Bleeding



No. at risk							
SAPT	433	427	426	422	416	415	414
DAPT	437	433	431	427	419	419	414

Secondary Endpoints

18 Months Post Randomization



Results: 18 Months Post Randomization

N (%)	SAPT N=433	DAPT N=437	HR SAPT vs. DAPT (95% CI interval)	P-Value
Death	3 (0.7%)	6 (1.4%)	0.51 (0.13-2.02)	0.33
Cardiac	2 (0.5%)	4 (0.9%)	0.51 (0.09-2.76)	0.43
Stroke	3 (0.7%)	3 (0.7%)	1.02 (0.21-5.03)	0.99
Myocardial infarction	8 (1.8%)	8 (1.8%)	1.02 (0.38-2.71)	0.97
Stent thrombosis	3 (0.7%)	4 (0.9%)	0.76 (0.17-3.39)	0.72
Target lesion failure	5 (1.2%)	8 (1.8%)	0.63 (0.21-4.06)	0.42
Revascularization	13 (3.0%)	17 (3.9%)	0.87 (0.42-1.83)	0.72
Urgent	8 (1.8%)	13 (3.0%)	0.83 (0.34-1.99)	0.67
TLR	4 (0,9%)	10 (0,9%)	1.02 (0.25-2.18)	0.98
Bleeding	3 (0.7%)	5 (1.1%)	0.61 (0.15-2.53)	0.49
TIMI major	1 (0.2%)	2 (0.5%)	0.51 (0.05 -5.57)	0.58
BARC type 3	2 (0.5%)	4 (0.9%)	0.50 (0.09-2.75)	0.43

Limitations

- The *lower than estimated event rates in both arms* might reflect the trial design: only event-free patients at 6 months, were randomized, however to anticipate for this eventuality we chose an non-inferiority margin based on HR

- *Fewer patients than predicted were randomized at 6m FU* reflecting higher than expected rate of informed consent withdrawal as well as the treatment of non-culprit coronary lesions outside the pre-specified time window

- Although *a non-inferiority margin of 1.66 might appear large*, it should be noted that it represents the *upper limit of the 95%CI of the HR* and that it takes into account the impact of random fluctuation in a trial like DAPT-STEMI

Conclusions

Six-month DAPT is non-inferior **in regards to a combined endpoint of safety, efficacy and bleeding as compared** ***to 12-month DAPT after primary PCI*** **with second-generation zotarolimus-eluting stent**

This trial, for the first time showed that**, in modern DES era, event free** ***STEMI patients do not benefit from a prolonged DAPT beyond 6 months as currently recommended,*** **and sets the stage for further dedicated research in this important topic**

Onyx ONE Clinical Study

Leading Investigator: Prof. Stephan Windecker
Co-PIs: Elvin Kedhi & Azeem Latib

Prospective, Multicenter, Single Blinded Randomized Study for High Bleeding Risk patients undergoing PCI[1]

Resolute ONYX™ DES
with 1 Month DAPT
(N=1000)

2000 Patients
85 Global sites
1:1 Randomization

BioFreedom™ DCS
with 1 Month DAPT
(N=1000)

Primary Endpoint: Cardiac Death, Myocardial Infarction and Stent Thrombosis (def/prob) at 1 yr

Powered Secondary Endpoint: Target Lesion Failure (TLF) at 1 year

Antiplatelet Therapy: all patients to discontinue DAPT at 1 month, thereafter SAPT only

[1]CAD patients (ACS + stable angina) undergoing PCI who are at increased risk of bleeding or in whom DAPT >1 month is undesirable, see inclusion criteria for HBR definition.

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