One-month dual antiplatelet therapy followed by aspirin monotherapy after drug-eluting stent implantation: Randomized One-Month DAPT trial

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Background

- **Dual-antiplatelet therapy (DAPT)**
  - A 6–12 months of DAPT is currently recommended after drug-eluting stent (DES) implantation.

    Valgimigli M, et al. Eur Heart J 2018;39:213-60
    Levine GN, et al. J Am Coll Cardiol 2016;68:1082-115
  - It is necessary to determine the appropriate minimal duration of DAPT followed by aspirin monotherapy to minimize unnecessarily long DAPT.

- **Hypothesis**
  - One-month DAPT followed by aspirin monotherapy is noninferior to the currently recommended 6–12-month DAPT for the composite endpoint of cardiovascular events or major bleeding at 1-year follow-up.

Study Design

- A randomized, open-label, noninferiority, multi-center trial
- At 23 centers in Korea
- Enrollment period: December 2015 and September 2019
- Key inclusion criteria
  - Patient age ≥19 years
  - Patients with ischemic heart disease considered for coronary revascularisation by non-emergent percutaneous coronary intervention
  - Significant de novo coronary lesion
- Key exclusion criteria
  - Acute myocardial infarction
  - Complex lesion morphologies, such as aorto-ostial, unprotected left main lesion, chronic total occlusion, graft, thrombosis, or a heavily calcified or extremely tortuous lesion
  - Cardiogenic shock or previous cardiopulmonary resuscitation

Study Design

Patients with who presented to the cardiac catheterization laboratory for elective percutaneous coronary intervention
N = 3020

1-month DAPT
followed by aspirin monotherapy
after polymer-free drug-coated stent implantation (Biofreedom stent), n=1507

6–12-months DAPT
followed by aspirin monotherapy
after contemporary DES implantation (Biomatrix or Ultimaster stent), n=1513

Clinical follow-up at 12 months

The composite outcome of cardiac death, nonfatal myocardial infarction, target-vessel revascularisation, cerebrovascular accident, or major bleeding (STEEPLE criteria)

Trial Registration: Clinicaltrial.gov Identifier: NCT02513810

Statistical Analysis

- **Sample size calculation**
  - An estimated event rate for patients in the 6–12-month DAPT group was 6.2%.

Urban P, et al. Catheter Cardiovasc Interv 2015;86:1151-60
Serruys PW, et al. JACC Cardiovasc Interv 2013;6:777-89
Kim BK, et al. J Am Coll Cardiol 2012;60:1340-8

  - A 3.0% noninferiority margin, giving the study a power of 90% with a one-sided alpha error rate of 2.5% and allowing for at least 10% loss to follow-up.
    → A sample size of 3,020 patients (1,510 patients in each group) was required.

  - Noninferiority would be declared if the upper limit of the one-sided 97.5% CI for the difference in primary endpoint incidences between groups was <3.0%.

Study Flow

3020 Patients underwent randomization

1507 Assigned to receive 1-month DAPT	1513 Assigned to receive 6–12-month DAPT
1232 Received allocated antiplatelet therapy 275 Did not receive allocated therapy 253 Received DAPT > 1 month 22 Did not continue aspirin monotherapy after DAPT	1452 Received allocated antiplatelet therapy 61 Did not receive allocated therapy 52 Received DAPT < 6 months 9 Did not continue aspirin monotherapy after DAPT
13 Died 19 Lost to follow-up 5 Withdrew consent	20 Died 24 Lost to follow-up 3 Withdrew consent
1507 Included in intention-to-treat analysis	**1513 Included in intention-to-treat analysis**

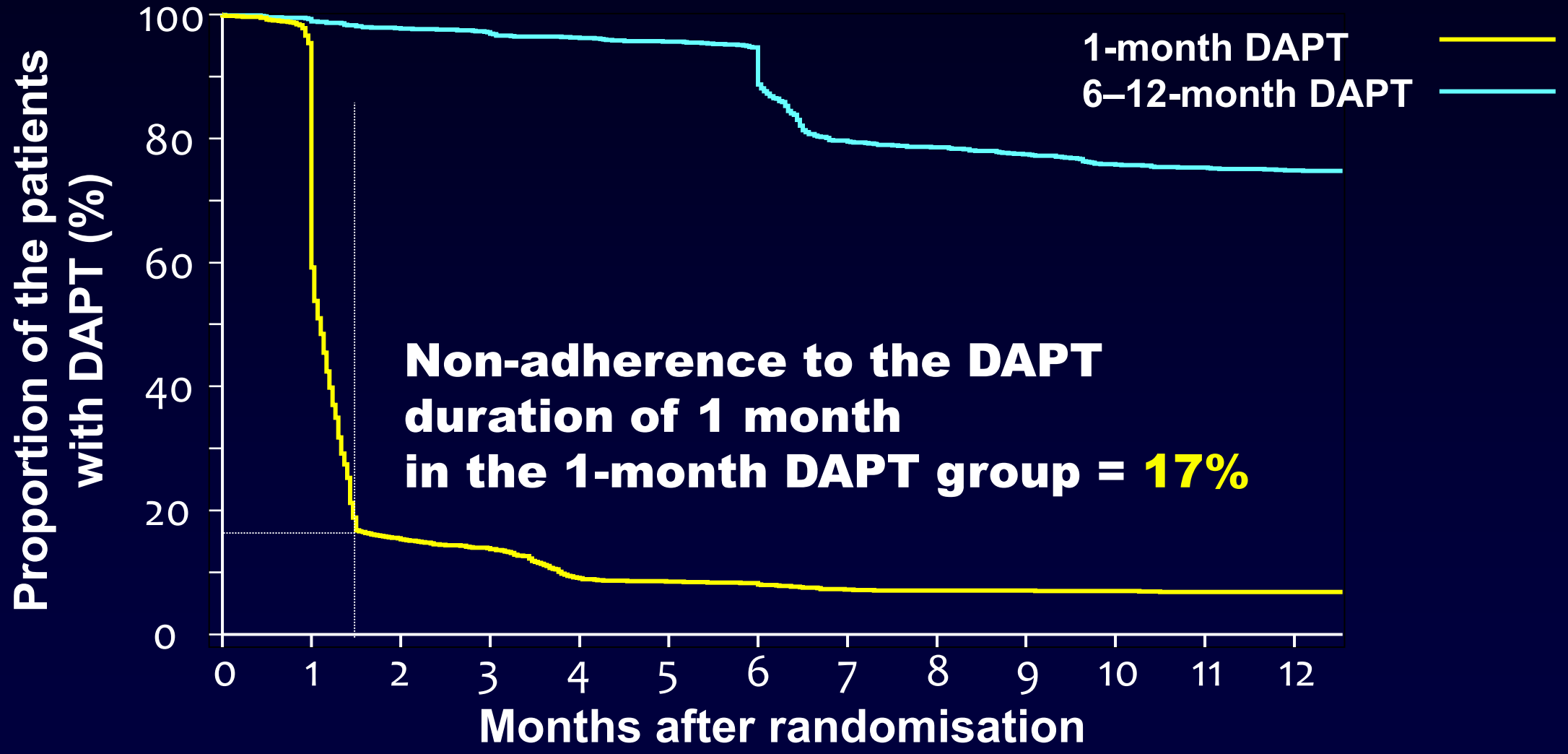
Baseline clinical characteristics

	1-month DAPT (n=1507)	6–12-month DAPT (n=1513)
Age, y	67 ± 10	67 ± 10
Men	1039 (69%)	1048 (69%)
Hypertension	1007 (67%)	1002 (66%)
Diabetes mellitus	564 (37%)	571 (38%)
Chronic kidney disease	202 (13%)	206 (14%)
Dyslipidaemia	1220 (81%)	1234 (82%)
Prior percutaneous coronary intervention	247 (16%)	274 (18%)
Prior stroke	92 (6%)	109 (7%)
Prior myocardial infarction	54 (4%)	54 (4%)
Prior coronary bypass graft	20 (1%)	24 (2%)
Clinical presentation		
Stable angina	933 (62%)	895 (59%)
Acute coronary syndrome	574 (38%)	618 (41%)
Left ventricular ejection fraction, %	63 ± 9	63 ± 9

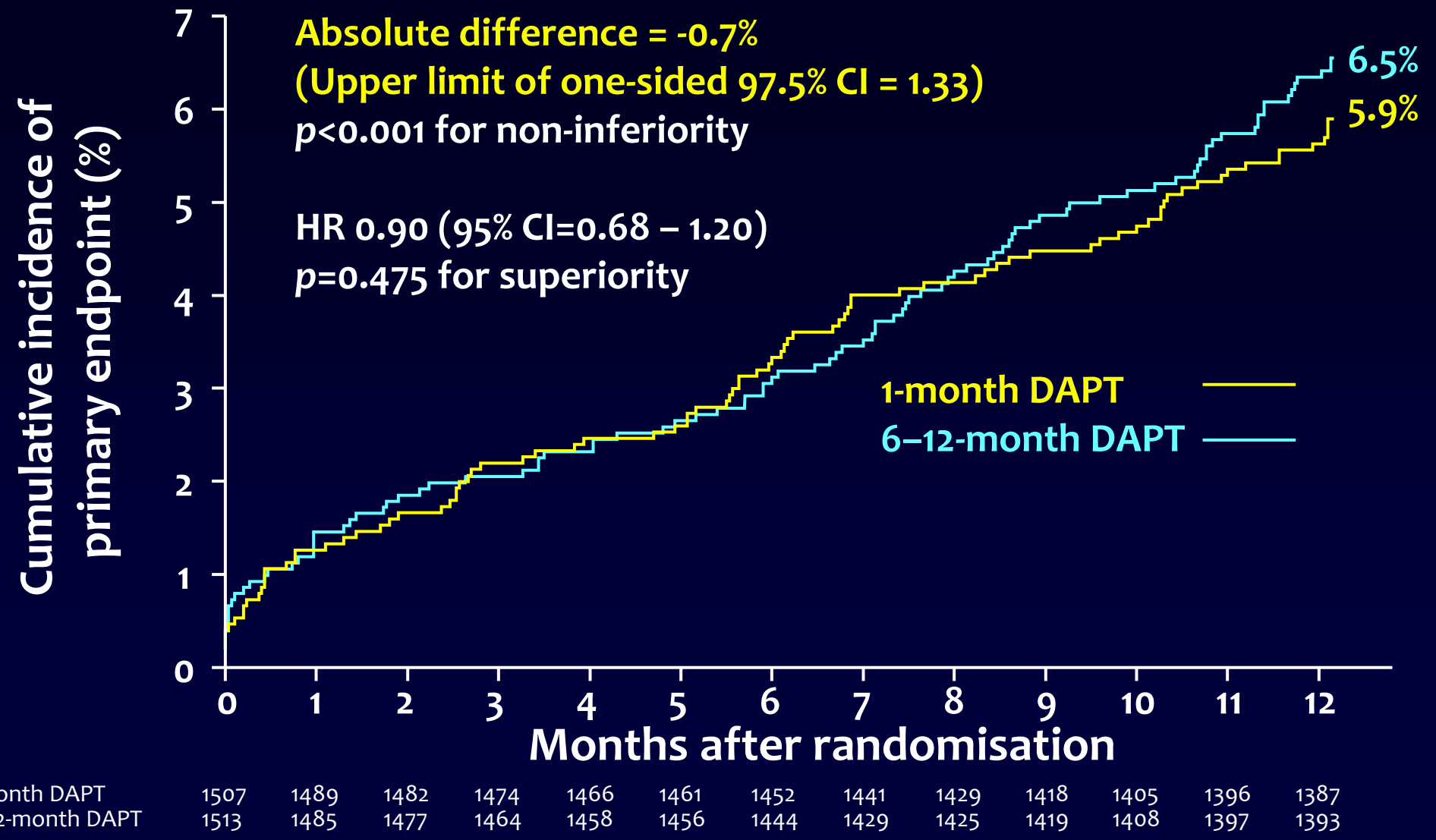
Angiographic and procedural Characteristic

	1-month DAPT (n=1507)	6–12-month DAPT (n=1513)
Extent of coronary artery disease		
2-vessel disease	491 (33%)	470 (31%)
3-vessel disease	376 (25%)	408 (27%)
Multivessel intervention	200 (13%)	189 (13%)
Treated lesions per patients	1.2 ± 0.5	1.2 ± 0.4
Total number of stents per patient	1.3 ± 0.6	1.3 ± 0.6
Total stent length per patient, mm	31 ± 18	31 ± 18
Number of treated lesions	1804	1800
Treated lesion		
Left anterior descending	1009 (56%)	992 (55%)
Left circumflex	348 (19%)	326 (18%)
Right	447 (25%)	482 (27%)
Type of drug-eluting stents		
BioFreedom	1797 (>99%)	0
Biomatrix	0	1205 (67%)
Ultimaster	0	585 (33%)
Other drug-eluting stents	4 (<1%)	10 (<1%)
Balloon angioplasty alone	3 (<1%)	0
Average stent diameter, mm	3.1 ± 0.4	3.1 ± 0.4

Proportion of patients receiving DAPT during the study period

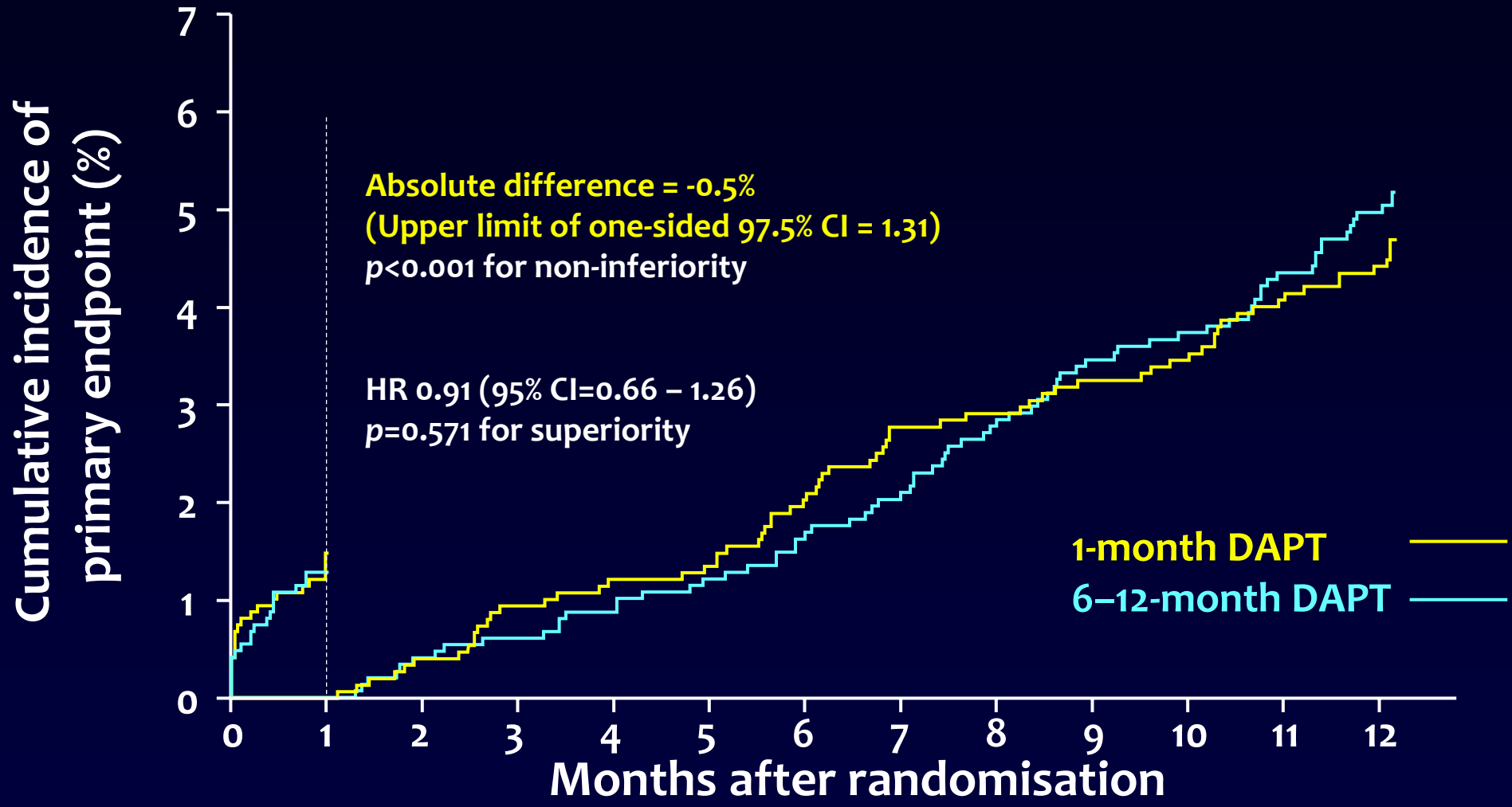


Primary Endpoint



1-month DAPT	1507	1489	1482	1474	1466	1461	1452	1441	1429	1418	1405	1396	1387
6–12-month DAPT	1513	1485	1477	1464	1458	1456	1444	1429	1425	1419	1408	1397	1393

Primary Endpoint; 1 month Landmark Analyses



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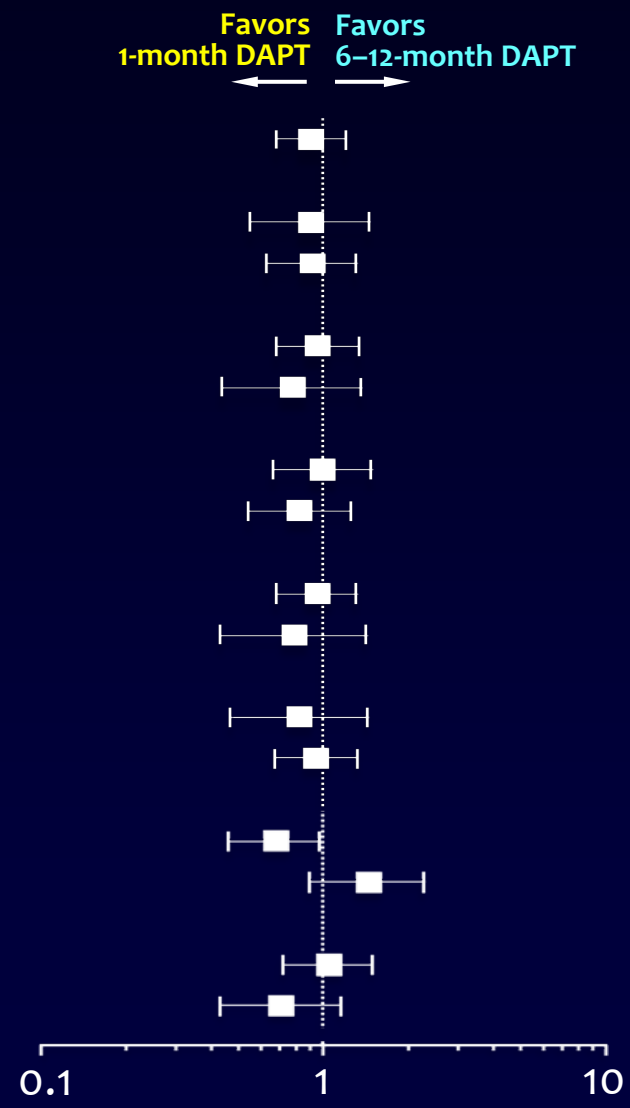
Clinical Outcomes at 1 year

	1-month DAPT (n=1507)	6–12-month DAPT (n=1513)	Absolute difference (confidence interval)	p value*	Hazard ratio (95% confidence interval)	p value†
Primary endpoint						
Composite of cardiac death, nonfatal myocardial infarction, target-vessel revascularisation, stroke, or major bleeding	88 (5.9%)	98 (6.5%)	-0.7% (1.3)	<0.001	0.90 (0.68 to 1.20)	0.475
Secondary endpoints						
All-cause death	13 (0.9%)	20 (1.3%)	-0.5% (-1.2 to 0.3)	–	0.65 (0.32 to 1.31)	0.225
Cardiac death	6 (0.4%)	10 (0.7%)	-0.3% (-0.8 to 0.3)	–	0.60 (0.22 to 1.66)	0.321
Nonfatal myocardial infarction	17 (1.1%)	22 (1.5%)	-0.3% (-1.1 to 0.5)	–	0.78 (0.41 to 1.46)	0.426
Target-vessel revascularisation	41 (2.8%)	39 (2.6%)	0.1% (-1.0 to 1.3)	–	1.05 (0.68 to 1.63)	0.814
Stent thrombosis	11 (0.7%)	12 (0.8%)	-0.1% (-0.7 to 0.6)	–	0.90 (0.41 to 2.09)	0.842
Definite	7	6				
Probable	4	6				
Stroke	13 (0.9%)	16 (1.1%)	-0.2% (-0.9 to 0.5)	–	0.81 (0.39 to 1.69)	0.581
Ischemic	9	5				
Haemorrhagic	4	11				
Major bleeding	26 (1.7%)	38 (2.5%)	-0.8% (-1.8 to 0.2)	–	0.69 (0.42 to 1.13)	0.136

Subgroup Analyses for Primary Endpoint

Subgroup	No. /Total (%) 1-month DAPT	6–12-month DAPT	HR (95% CI)	p value for interaction
All patients	88/1507 (5.9)	98/1513 (6.5)	0.90 (0.68 - 1.20)	
Age, years				0.941
<65	31/616 (5.1)	35/615 (5.8)	0.89 (0.55 - 1.44)	
≥65	57/891 (6.4)	63/898 (7.1)	0.91 (0.63 - 1.30)	
Sex				0.532
Men	66/1039 (6.4)	70/1048 (6.8)	0.95 (0.68 - 1.33)	
Women	22/468 (4.8)	28/465 (6.1)	0.77 (0.44 - 1.35)	
Diabetes mellitus				0.519
Yes	48/564 (8.6)	49/571 (8.7)	0.99 (0.66 - 1.47)	
No	40/943 (4.3)	49/942 (5.3)	0.82 (0.54 - 1.24)	
Hypertension				0.594
Yes	69/1007 (6.9)	73/1002 (7.3)	0.94 (0.68 - 1.30)	
No	19/500 (3.9)	25/511 (5.0)	0.78 (0.43 - 1.41)	
Chronic kidney disease				0.688
Yes	23/202 (11.6)	28/206 (13.9)	0.82 (0.47 - 1.42)	
No	65/1305 (5.0)	70/1307 (5.4)	0.93 (0.67 - 1.31)	
Clinical presentation				0.013
Stable angina	47/933 (5.1)	67/895 (7.6)	0.67 (0.46 - 0.97)	
Acute coronary syndrome	41/574 (7.2)	31/618 (5.1)	1.43 (0.89 - 2.27)	
Multivessel disease				0.212
Yes	60/867 (7.0)	59/878 (6.8)	1.04 (0.72 - 1.48)	
No	28/640 (4.4)	39/635 (6.2)	0.70 (0.43 - 1.15)	



Conclusion

- To our knowledge, this study is the first randomised trial comparing 1-year clinical outcomes of **1-month DAPT followed by aspirin monotherapy** after polymer-free DCS implantation versus currently recommended DAPT after next-generation DES implantation in a diverse group of patients (both HBR and non-HBR).

- DAPT for 1 month followed by aspirin monotherapy was not inferior to 6–12 months of DAPT in terms of 1-year outcomes among patients receiving a DES.


Dreams will
come true