TCTAP 2022
MAnagement of high bleeding risk patients post bioresorbable polymer coated STEnt implantation with an abbReviated versus prolonged DAPT regimen
MASTER DAPT

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On behalf of the MASTER DAPT Investigators

Presented at ESC2021 by Dr Marco Valgimigli

Disclosure

- I, (Fazila Malik) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Background and objectives

- Studies with 1 month dual antiplatelet therapy (DAPT) after DES implantation suggested that this regimen may mitigate bleeding without compromising safety
- These studies were either nonrandomized, did not select high bleeding risk (HBR) pts or included pts at low ischemic risk
- To determine whether an abbreviated compared with a standard DAPT regimen preserves net and major clinical events, and, if so mitigates the bleeding risk in a broadly inclusive HBR population who underwent percutaneous coronary intervention (PCI)

Study Organization

Grant Supplier: Terumo Corp

PIs: M. Valgimigli P. C. Smits

Sponsor: ECRI

CROs: CERC Cardialysis CVQuest

Sites: 140

Countries: 30 countries

CEC: S. Leonardi (Chair) C. Hanet
R. Lopes E.P. McFadden P. Radke
R. O. Roine

DMC: M. Bertrand S. Pocock P. Urban

Stats: D. Heg P Juni J. Tjissen

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F. Mahfoud R. Kornowski
M. Lesiak P.J. Ong
Y. Ozaki A.E. Rodriguez
M. Roffi C. Schultz
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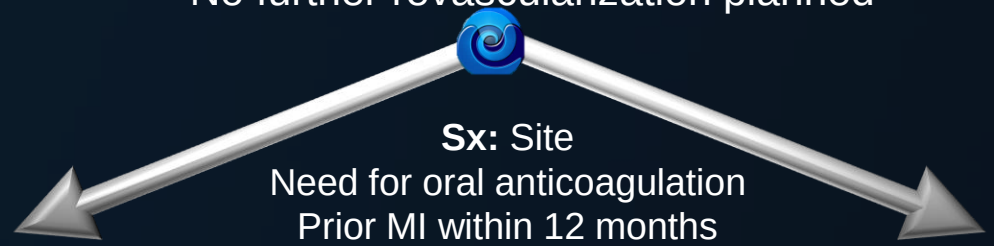
MASTER DAPT Trial

Screened Population: **HBR pts, treated exclusively with Ultimaster stent, with no restriction based on clinical presentation or PCI complexity**

Randomization and Regimens

30 (+14) Days after PCI

Free from cardiac and cerebral ischemic events
and active bleeding
No further revascularization planned



Sx: Site
Need for oral anticoagulation
Prior MI within 12 months

Abbreviated DAPT

Immediate DAPT discontinuation

followed by SAPT for 11 months
or 5 months if OAC is indicated

Standard DAPT

DAPT for ≥ 2 or 5 months in pts with or without OAC indication, respectively

followed by SAPT up to 11 months

HBR: high bleeding risk; DAPT: dual antiplatelet therapy; SAPT: single antiplatelet therapy; MI myocardial infarction: OAC: oral anticoagulation

High Bleeding Risk Definition

Patients are at high bleeding risk if at least one of the following criteria applies:

1. Clinical indication to oral anticoagulants (OAC) for at least 12 months
2. Recent (<12 months) non-access site bleeding episode(s), which required medical attention
3. Previous bleeding episode(s) which required hospitalization if the underlying cause has not been definitively treated (i.e. surgical removal of the bleeding source)
4. Age ≥75 years
5. Systemic conditions associated with an increased bleeding risk
6. Documented anemia (Hb<11 g/dL) or transfusion within 4 weeks before randomization
7. Need for chronic treatment with steroids or non-steroidal anti-inflammatory drugs
8. Diagnosed malignancy (other than skin) considered at high bleeding risk
9. Stroke at any time or transient ischemic attack (TIA) in the previous 6 months
10. PRECISE DAPT score ≥25

Exclusion Criteria

- Treatment with stents other than the Ultimaster® stent at index PCI or within 6 months before
- Treatment for in-stent restenosis or stent thrombosis at index PCI or within 6 months before
- Treatment with Bioresorbable scaffolds at any time

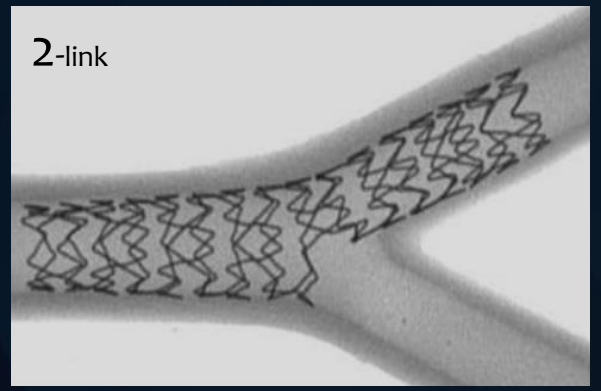
Ultimaster Stent

Stent Platform

Open Cell 2-link Design

CoCr L-605 Alloy

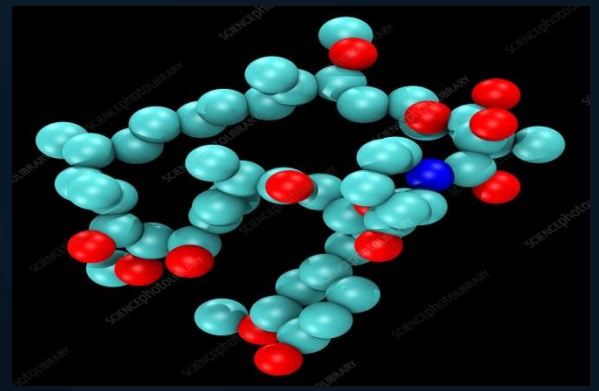
Strut thickness:
80 µm



Drug

Sirolimus

3.9 µg/mm stent length

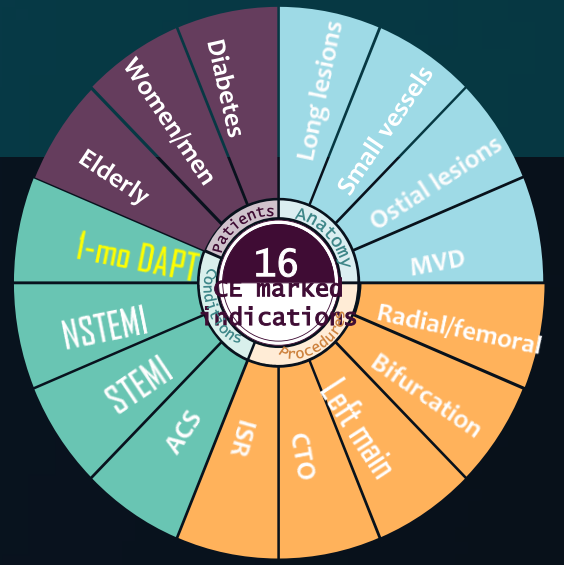


Polymer Coating

Abluminal, PDLLA-PCL **gradient coating**

Simultaneous polymer resorption and drug release in 3-4 months

CE Marks



Study Endpoints

The study has 3 primary endpoints to be tested in an hierarchical order:

Net adverse clinical events (NACE): the composite of all-cause death, MI, stroke, and major bleeding defined as BARC type 3 or 5

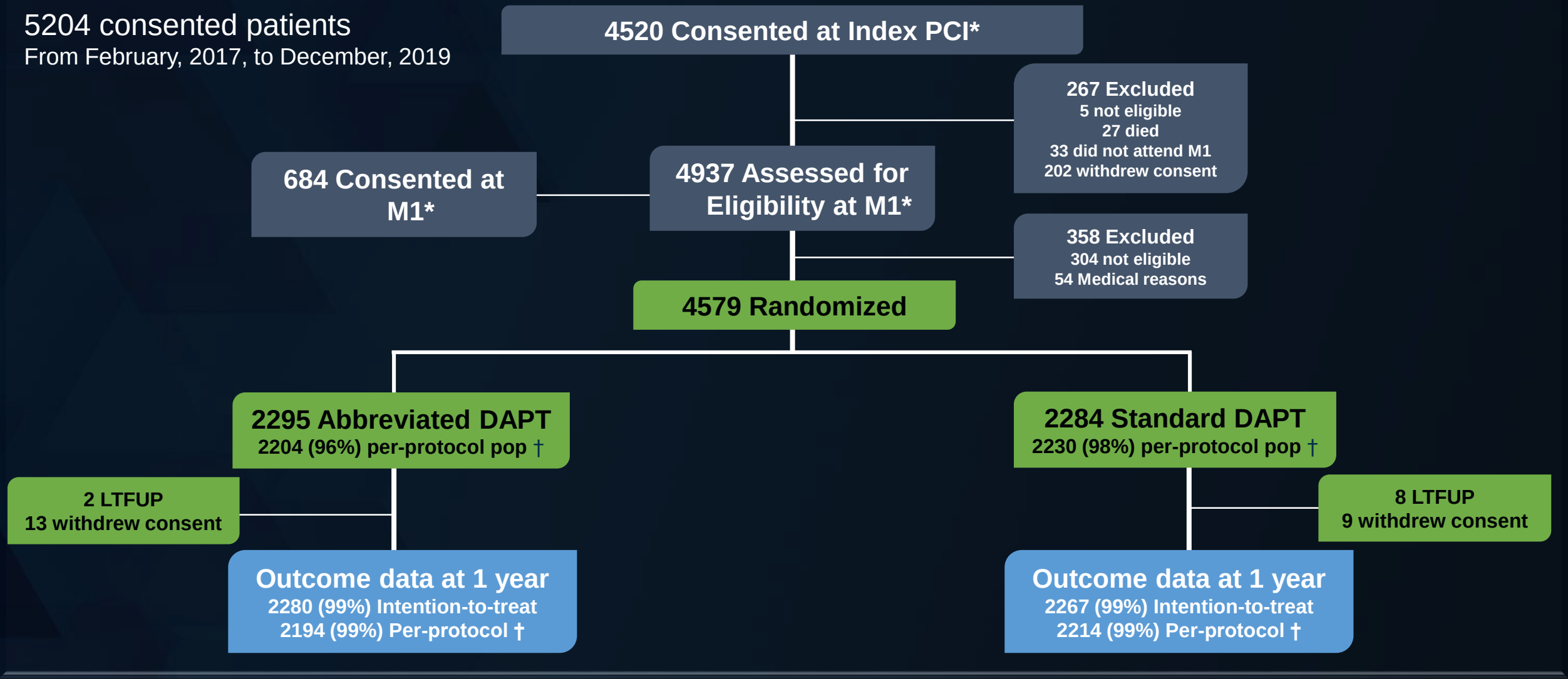
Major adverse cardiac and cerebral events (MACCE): the composite of all-cause death, MI, and stroke

Major or clinically relevant non-major bleeding (MCB): the composite of BARC type 2, 3 and 5 bleeding

The first two primary endpoints were to be tested on a non-inferiority basis in the per protocol population. If non-inferiority was met for both, the third primary endpoint was to be tested on superiority basis in the Intention to treat population. The main analyses evaluate the occurrence of the primary endpoints between randomization and 335 after index PCI

Patient Disposition

5204 consented patients
From February, 2017, to December, 2019



*: From February 28, 2017 through December 5, 2019 † : Per-protocol population: met eligibility criteria and implemented study Tx within 14 days after Rx

Baseline Characteristics and Clinical Presentation

Mean±SD 2.1±1.1 HBR criteria	Abbreviated DAPT *(N=2295)*	Standard DAPT *(N=2284)*
Age — yr	76.1±8.7	76.0±8.8
Male sex — no. (%)	1590 (69.3)	1581 (69.2)
Diabetes mellitus — no. (%)	754 (32.9)	784 (34.3)
Prior MI— no. (%)	434 (18.9)	430 (18.8)
Prior PCI— no. (%)	594 (25.9)	594 (26.0)
Prior CVA— no. (%)	268 (11.7)	302 (13.2)
Chronic kidney disease— no. (%)	418 (18.2)	458 (20.1)
Atrial fibrillation — no. (%)	770 (33.6)	720 (31.5)
Oral anticoagulant — no. (%)	849 (37.0)	820 (35.9)
CCS– no. (%)	1167 (50.8)	1201 (52.6)
Non–ST-elevation ACS– no. (%)	855 (37.2)	818 (35.8)

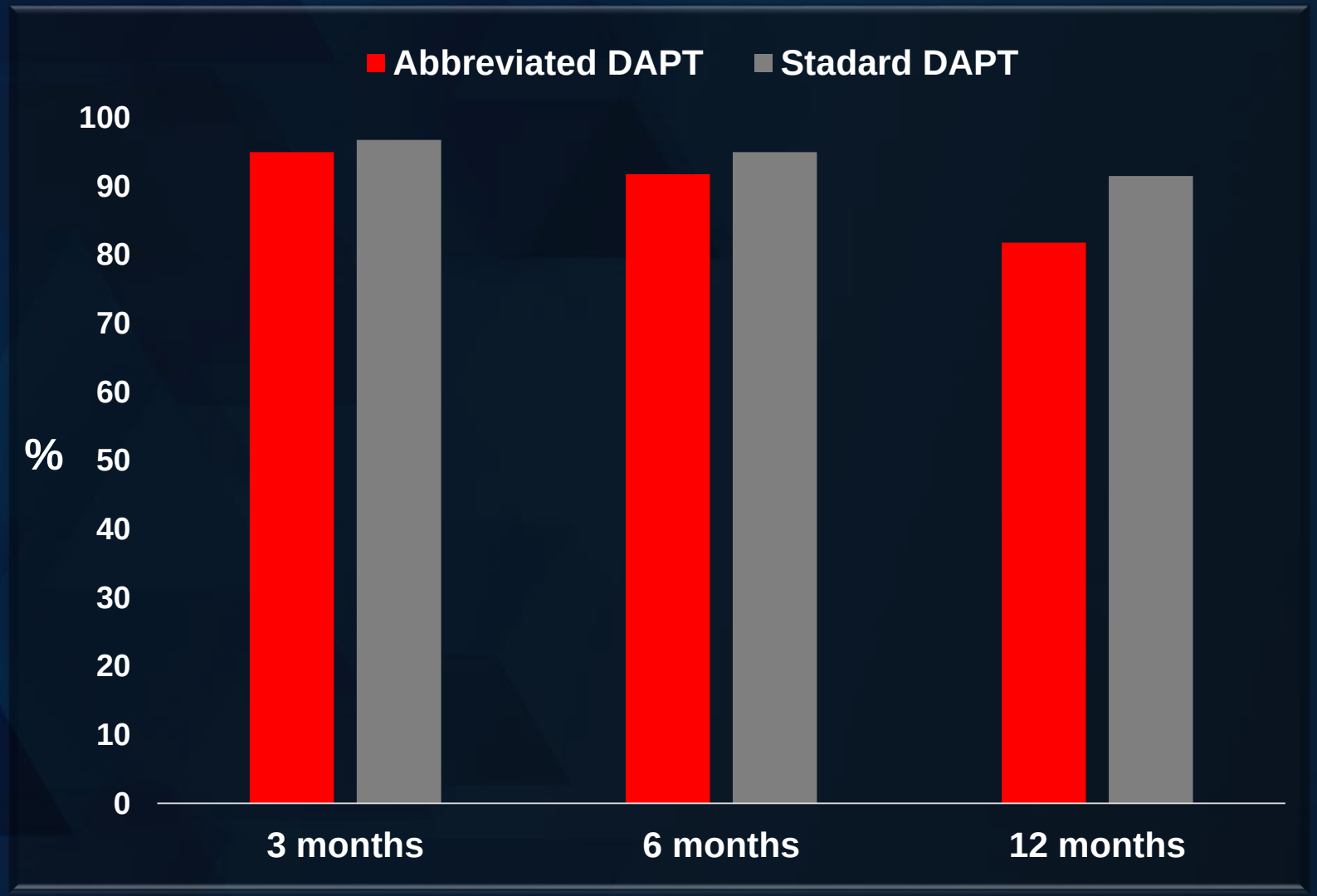
Procedural Characteristics

Biodegradable polymer sirolimus-eluting stents were used in 99.8% of the treated lesions in both study groups

	Abbreviated DAPT *(N=2295)*	Standard DAPT *(N=2284)*
Arterial access site		
Femoral	360 (15.7)	293 (12.8)
Radial	1930 (84.1)	1984 (86.9)
Multivessel Intervention — no. (%)	579 (25.2)	635 (27.8)
Treated vessel(s)— no. (%)		
Left main	126 (5.5)	134 (5.9)
Left arterial descending artery	1240 (54.0)	1271 (55.6)
Left circumflex artery	652 (28.4)	689 (30.2)
Right coronary artery	854 (37.2)	806 (35.3)
Bypass graft	38 (1.7)	38 (1.7)
≥ one complex lesion B2 or C — no. (%)	1562 (68.1)	1579 (69.1)
Number of stents per patient	1.74±1.13	1.76±1.11
Total stent length per patient	39.3±29.2	39.7±28.4
Overlapping stenting — no. (%)	488 (21.3)	450 (19.7)
Bifurcation/trifurcation stenting — no. (%)	83 (3.6)	101 (4.4)

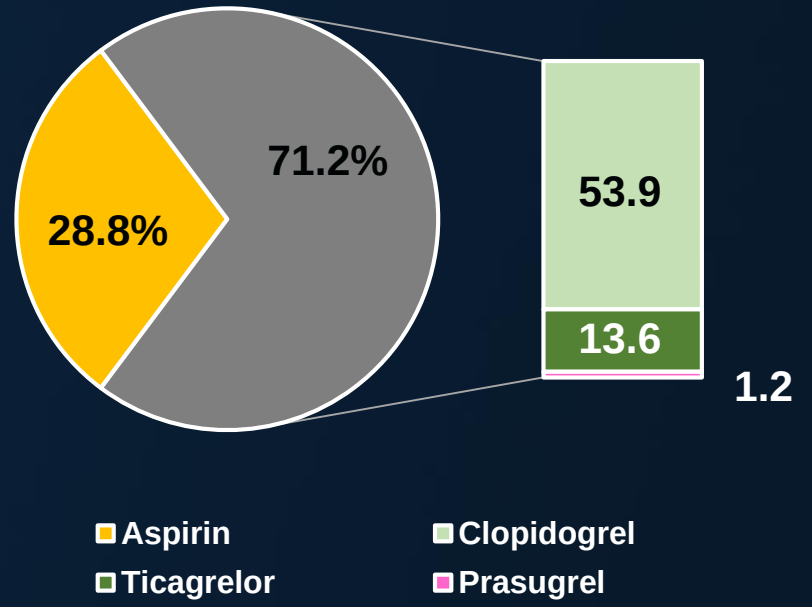
NARC 0 Adherence Rates* and Regimens

*: *Perfect* adherence rate, defined as 100% intake of protocol mandated regimen, counted on a daily basis



The median DAPT duration from the index coronary intervention was 34 days (IQR, 31-39) in the abbreviated- and 193 days (IQR, 102-366) in the standard-treatment groups.

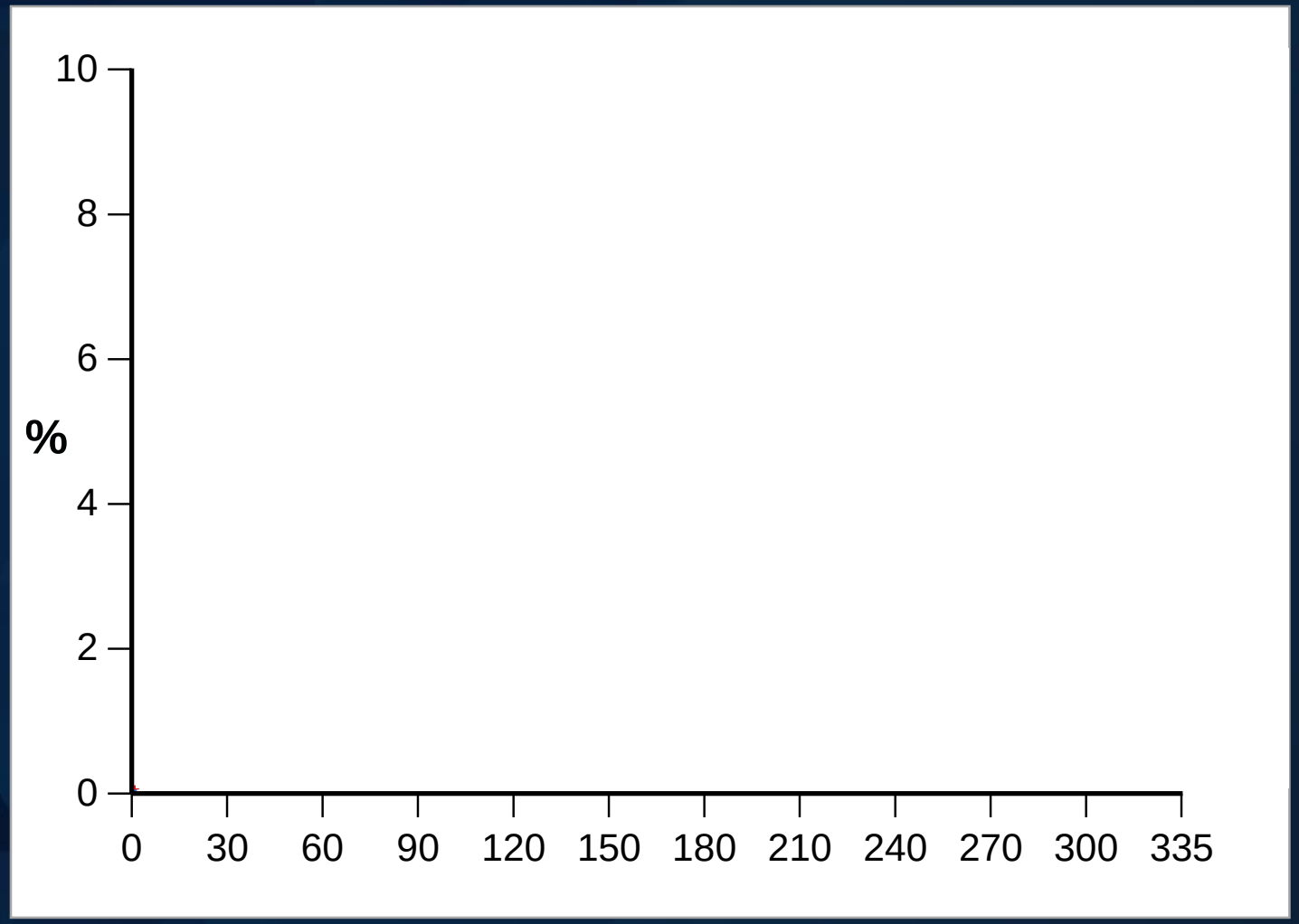
Type of SAPT in the abbreviated DAPT



*:NARC definition and Framework, Eur Heart J. 2019 Jul 1; 40(25): 2070–2085.

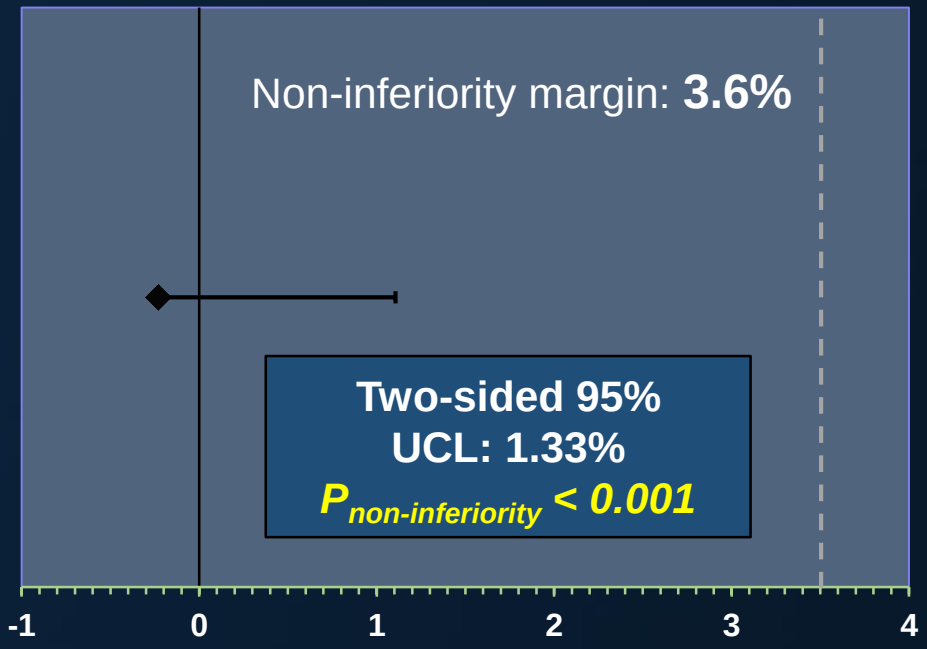
Net adverse clinical events (NACE)

Per protocol population



Non-inferiority Analysis

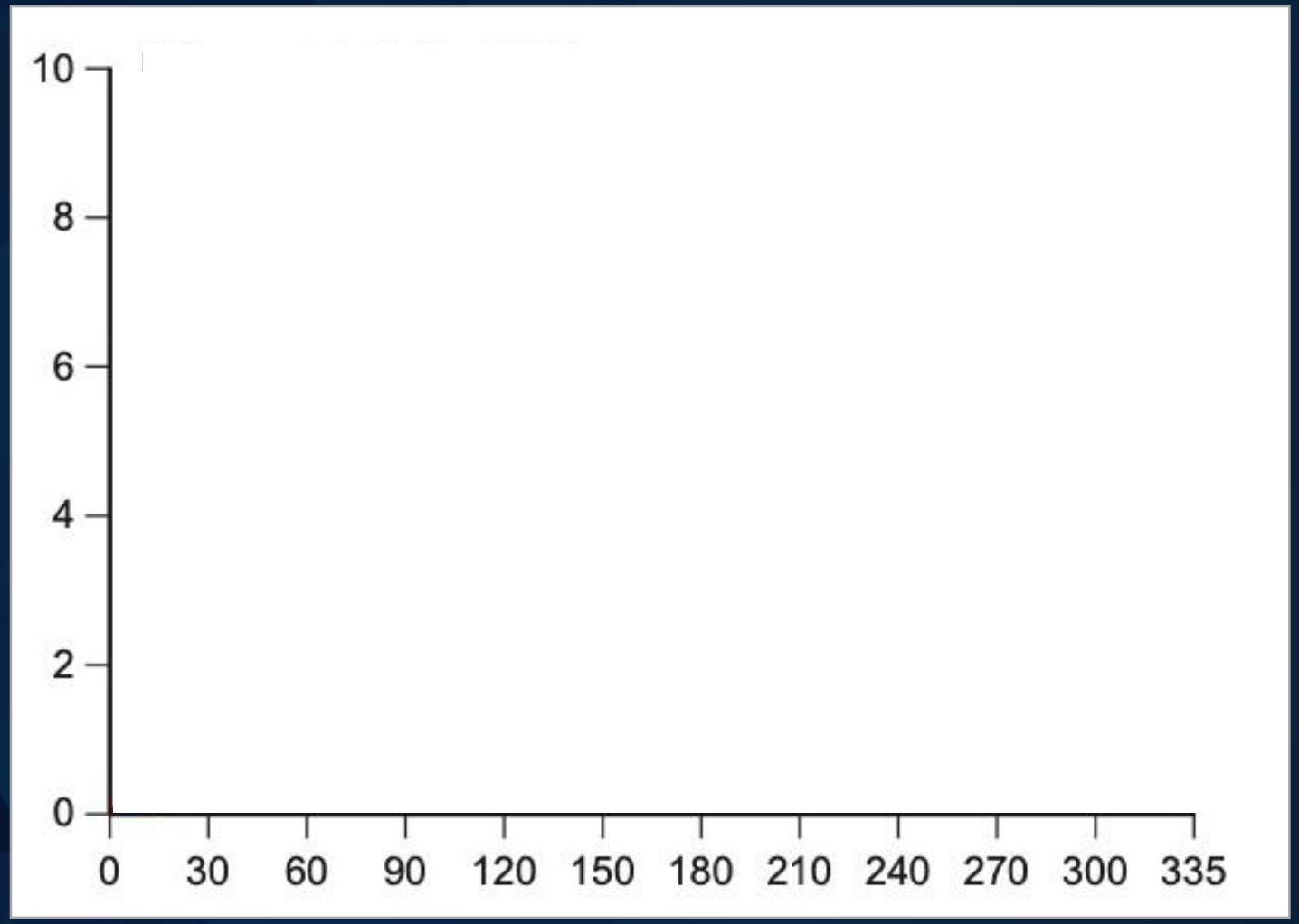
Difference in cumulative incidence, -0.23



NACE: *All-cause death, MI, stroke, and major bleeding events defined as BARC 3 or 5*

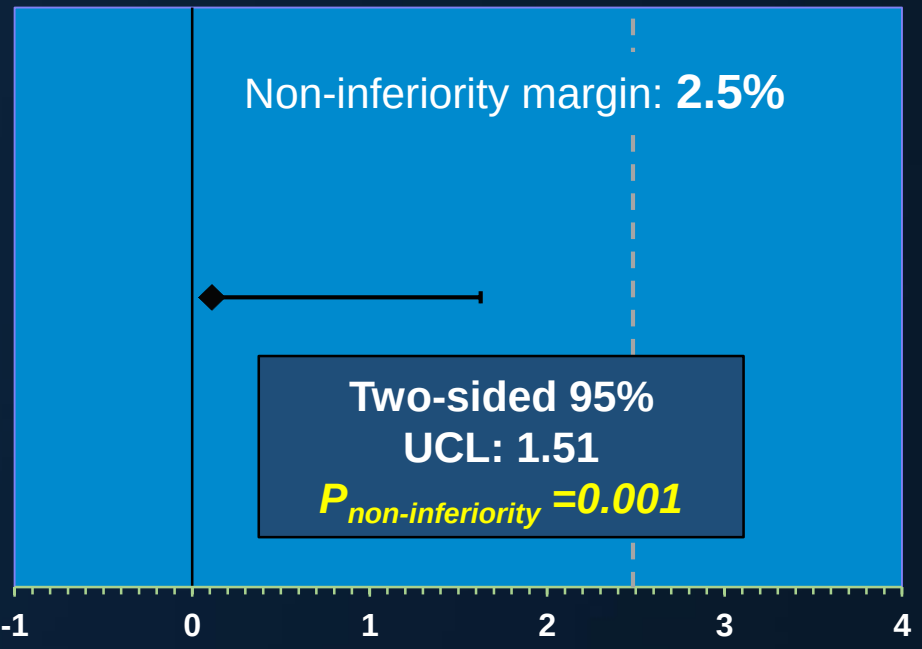
Major adverse cardiac and cerebral events (MACCE)

Per protocol population



Non-inferiority Analysis

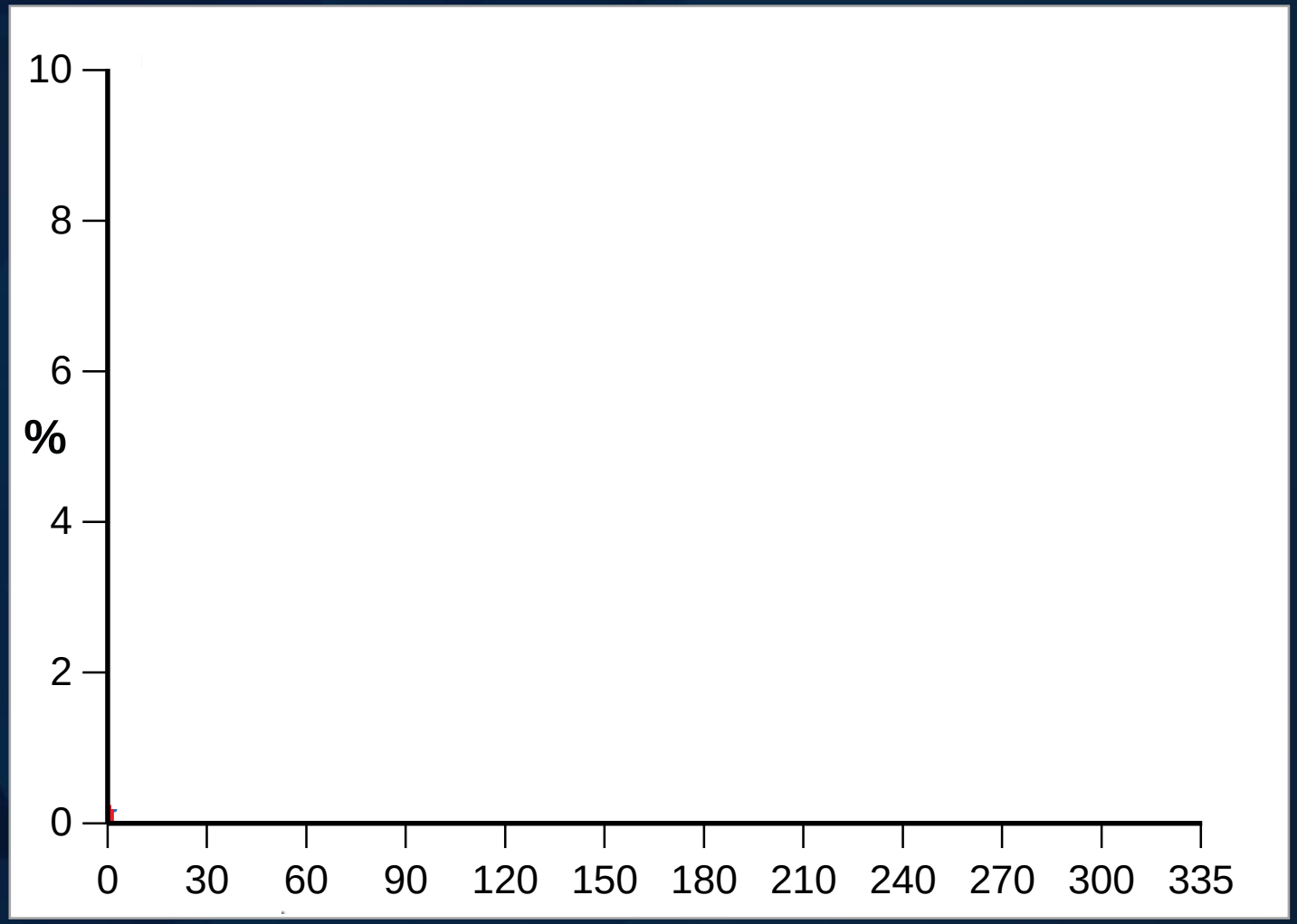
Difference in cumulative incidence, 0.11



MACCE: *All-cause death, MI, stroke*

Major or clinically relevant nonmajor bleeding

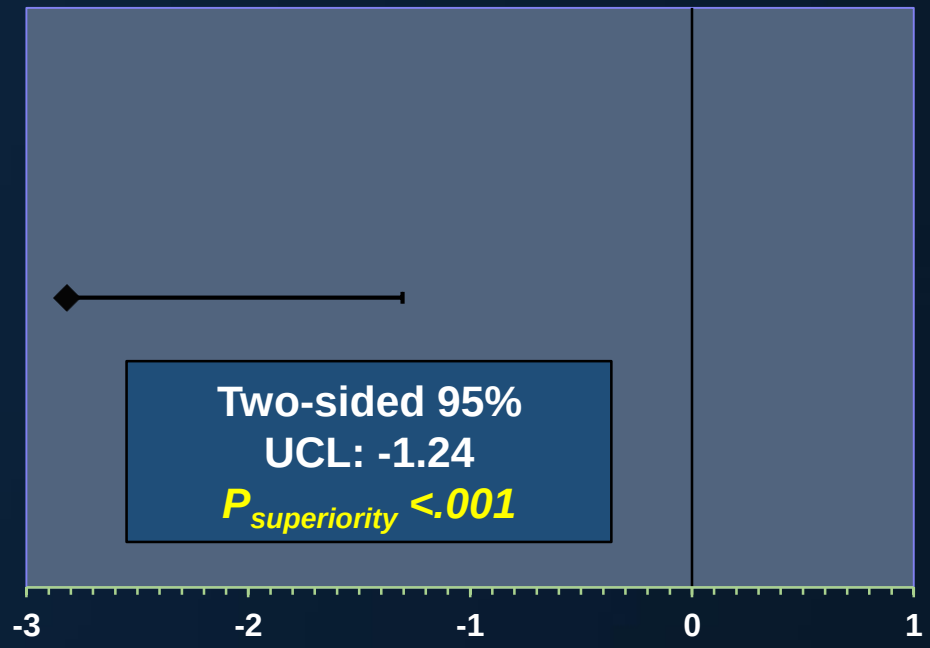
Intention to treat population



MCB: *BARC 2, 3 or 5*

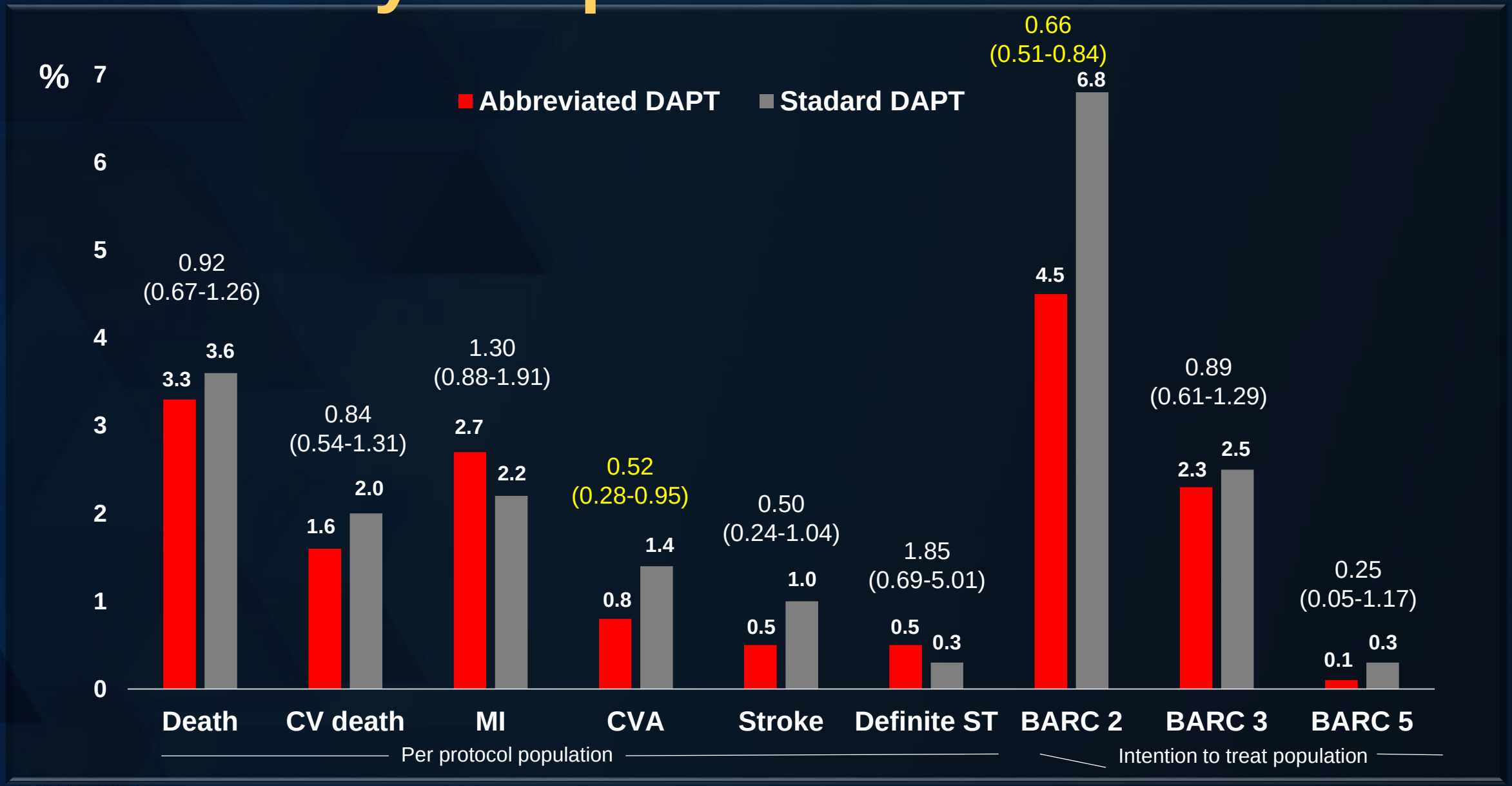
Superiority Analysis

Difference in cumulative incidence, -2.82



NNTB: 35

Secondary Endpoints



Study Limitations

- Open label study
- DAPT duration was heterogenous in the standard DAPT group, which reflects current clinical practice
- DAPT duration in both arms was longer than what is currently recommended for OAC patients
- This study was not designed to assess the role of type of SAPT after DAPT discontinuation
- Non-inferiority margins were relatively wide and the observed event rates were lower than expected for NACE and MACE
- Our results may not apply to patients not treated with biodegradable-polymer sirolimus eluting stents

Conclusions

In patients at HBR who had undergone implantation of a biodegradable-polymer ULTIMASTER sirolimus-eluting stent, the discontinuation of DAPT at a median of 34 days compared with continuation of treatment for a median of 193 days after PCI was:

- noninferior for the incidence of net adverse clinical events
- noninferior for the incidence of major adverse cardiac or cerebral events
- associated with a lower incidence of major or clinically relevant nonmajor bleeding

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dual Antiplatelet Therapy after PCI in Patients at High Bleeding Risk

M. Valgimigli, E. Frigoli, D. Heg, J. Tijssen, P. Jüni, P. Vranckx, Y. Ozaki, M.-C. Morice, B. Chevalier, Y. Onuma, S. Windecker, P.A.L. Tonino, M. Roffi, M. Lesiak, F. Mahfoud, J. Bartunek, D. Hildick-Smith, A. Colombo, G. Stanković, A. Iñiguez, C. Schultz, R. Kornowski, P.J.L. Ong, M. Alasnag, A.E. Rodriguez, A. Moschovitis, P. Laanmets, M. Donahue, S. Leonardi, and P.C. Smits, for the MASTER DAPT Investigators*