Many Many Stents: What Should I Select?

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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

- Grant/Research Support
- Scientific Advisory Board
- Executive Physician Council

Company

- Abbott Vascular, Medtronic
- Medtronic, Abbott Vascular
- Boston Scientific Corp

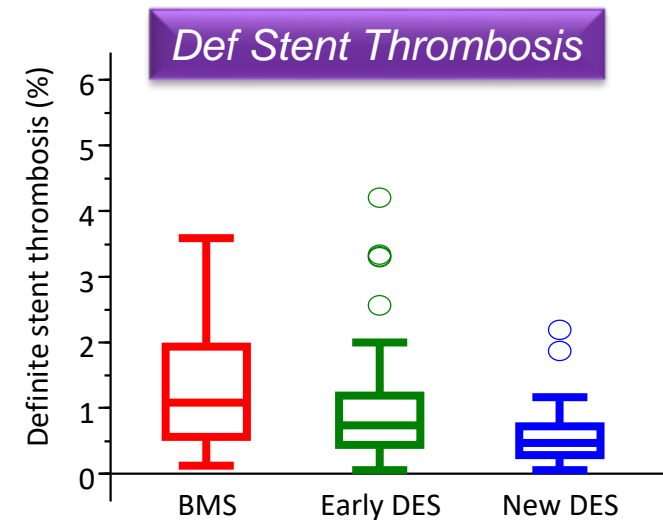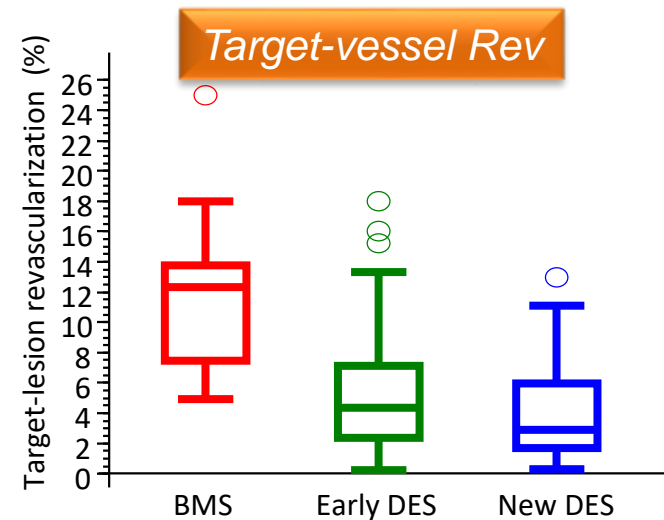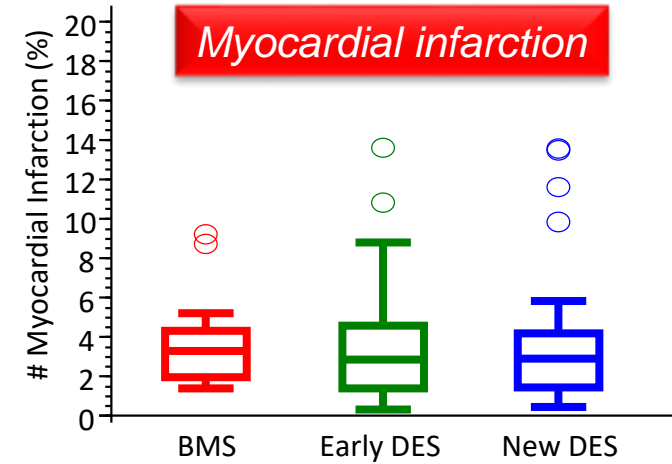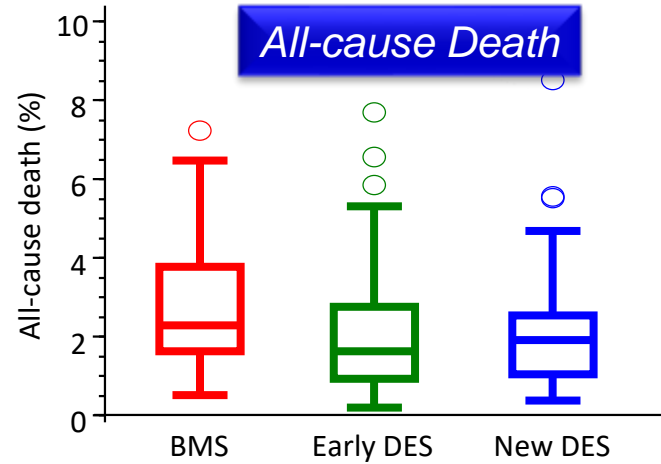# PROGRESS WITH METALLIC DRUG-ELUTING STENTS
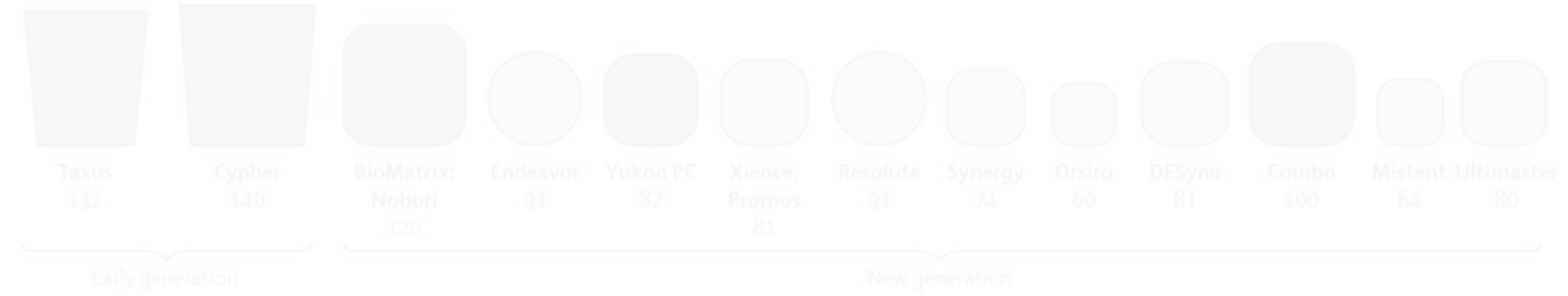
SAFETY AND EFFICACY OF BMS, EARLY-DES AND NEW-DES

Byrne et al. *Eur Heart J* 2015;36:2608-20

Systematic Review of 158 RCTs

Median rate per 100 person-yrs

Clinical outcomes at 9-12 months

RECOMMENDATIONS FOR DES USE

New-generation DES are recommended in all lesion and patient subsets!

Myocardial revascularization

Neumann et al. *Eur Heart J 2018;40:204-212*

DES are recommended over BMS for any PCI irrespective of:
- clinical presentation
- lesion type
- planned non-cardiac surgery
- anticipated duration of DAPT
- concomitant anticoagulant therapy.[100,578,579,640]

I **A**

Chronic coronary syndrome

Knuuti et al. *Eur Heart J 2019*

The use of DES is recommended in elderly patients.[508,509]

I **A**

NSTE-ACS

Roffi et al. *Eur Heart J 2016;37:267-315*

Stenting with new-generation DES is recommended over BMS for primary PCI.[148-151,178,179]

I **A**

STEMI

Ibanez et al. *Eur Heart J 2017;39:119-177*

In patients undergoing PCI, new-generation DESs are recommended.

I **A**

Current Iterations of DES Technology
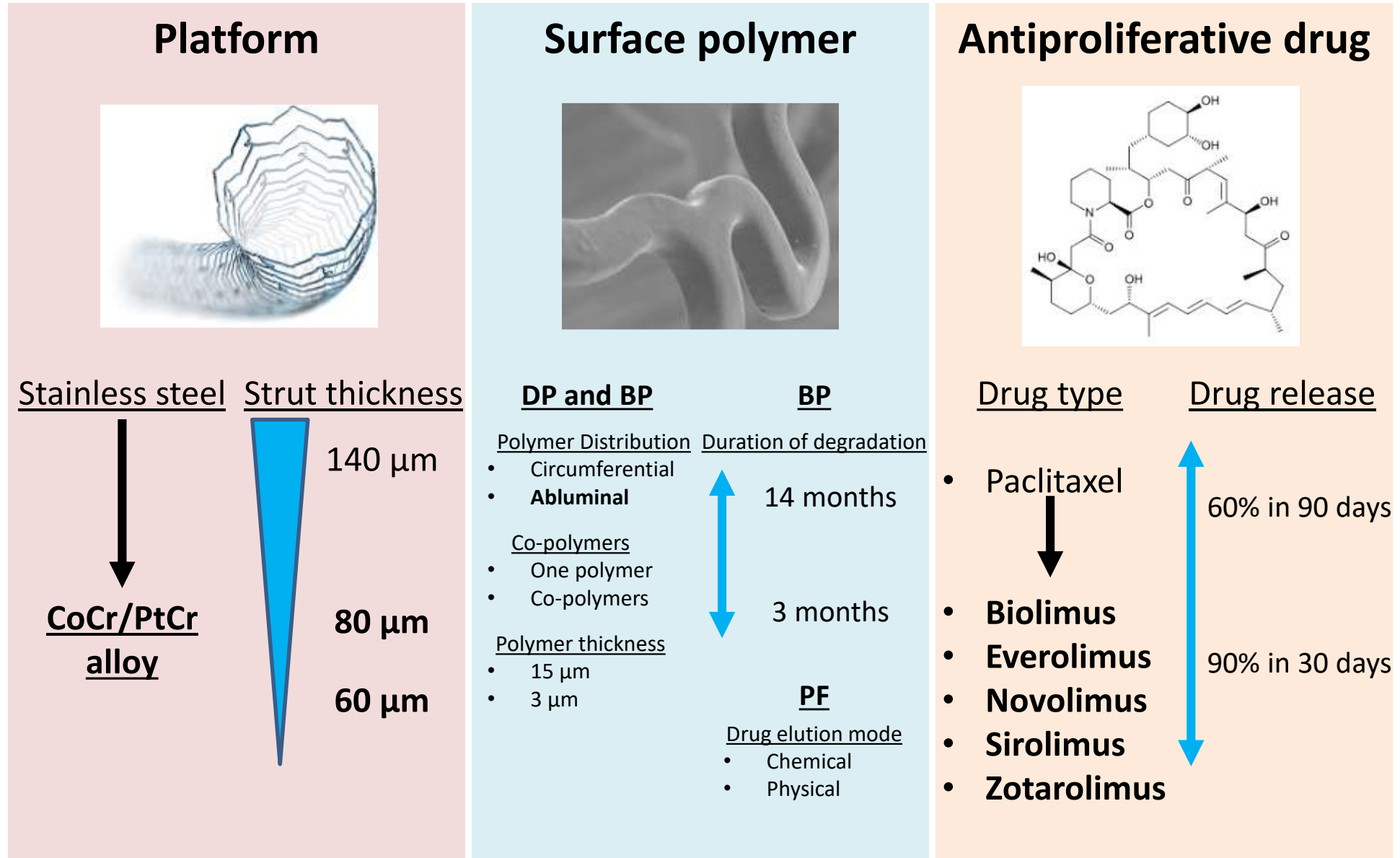
Thinner Struts

IMPACT OF STRUT THICKNESS ON ARTERIAL HEALING AND THROMBOGENICITY

Koppara et al. *Circ Cardiovasc Interv* 2015;8:e002427

Endothelialization

Endothelialization above struts
rabbit, 28 days

Synergy 74μm — BioMatrix 120μm — Absorb 150μm
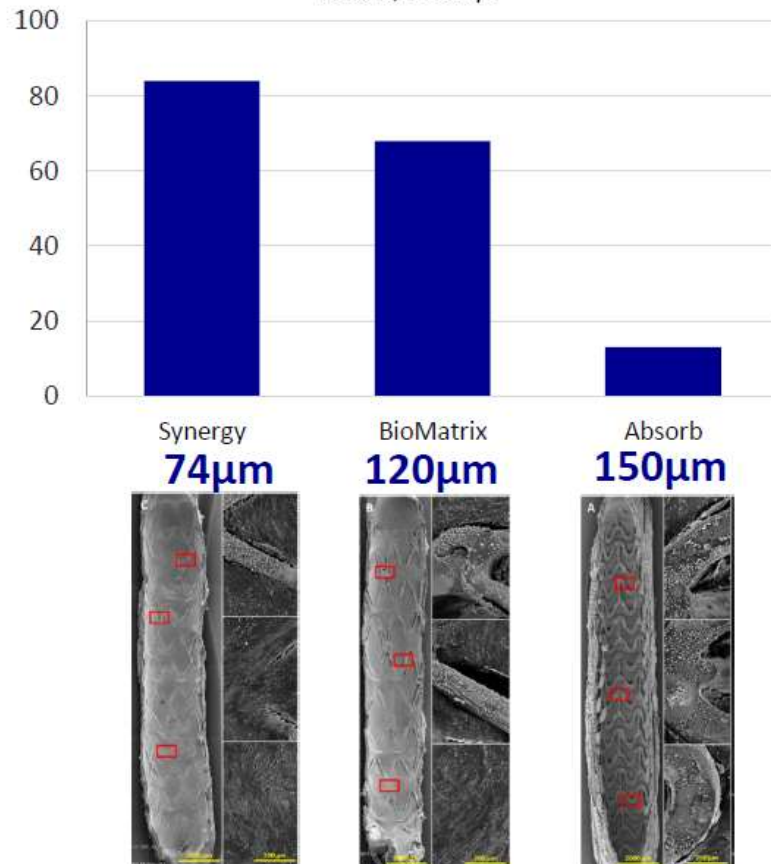
Platelet Deposition

Immuno-fluoroscent staining (CD61/CD42b)
in porcine ex-vivo arterio-venous shunt model

Strut thickness

PtCr PLGA 74 μm — PtCr bare 74 μm — 316L PLA 120 μm — PLLA PDLA 150 μm

Synergy — Omega — Biomatrix — Absorb
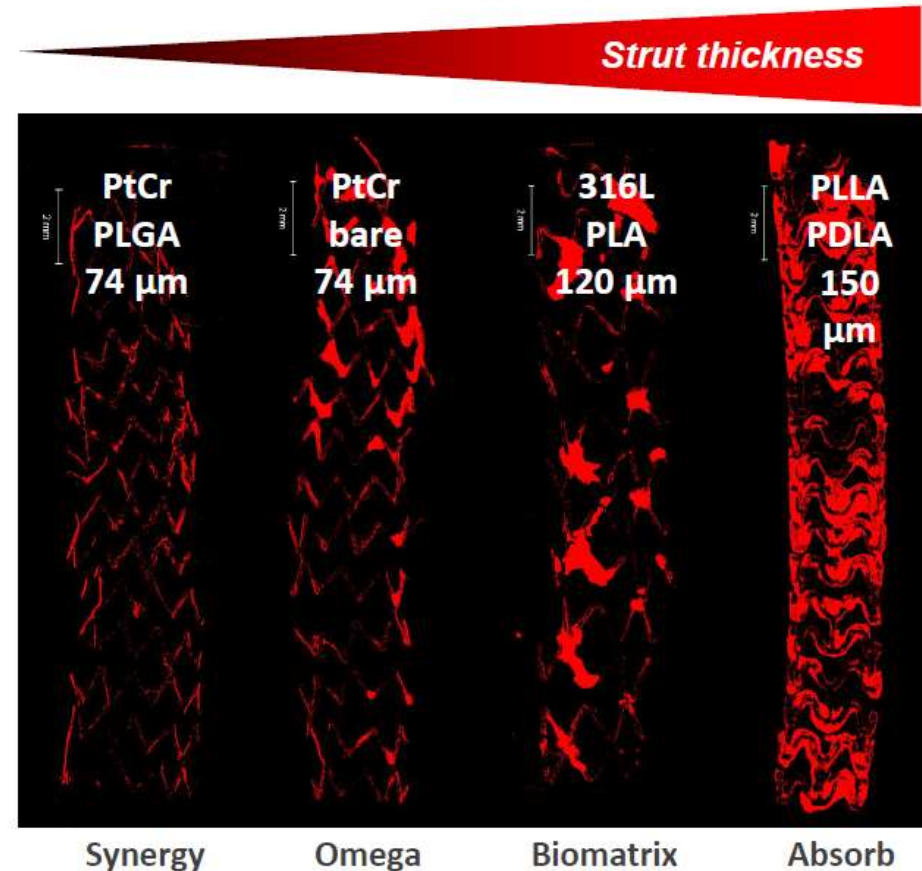
ULTRATHIN VS. THICK STENT STRUTS

Bangalore et al. *Circulation* 2018;138:2216-2226

- Meta-analysis of 11658 pts in 10 RCTs comparing ultrathin vs. thicker 2G DES
- Primary endpoint: TLF at 1 year
- Orsiro 46%, MiStent 6%, BioMime 1%, Xience 24%, Resolute 11%, Nobori 11%
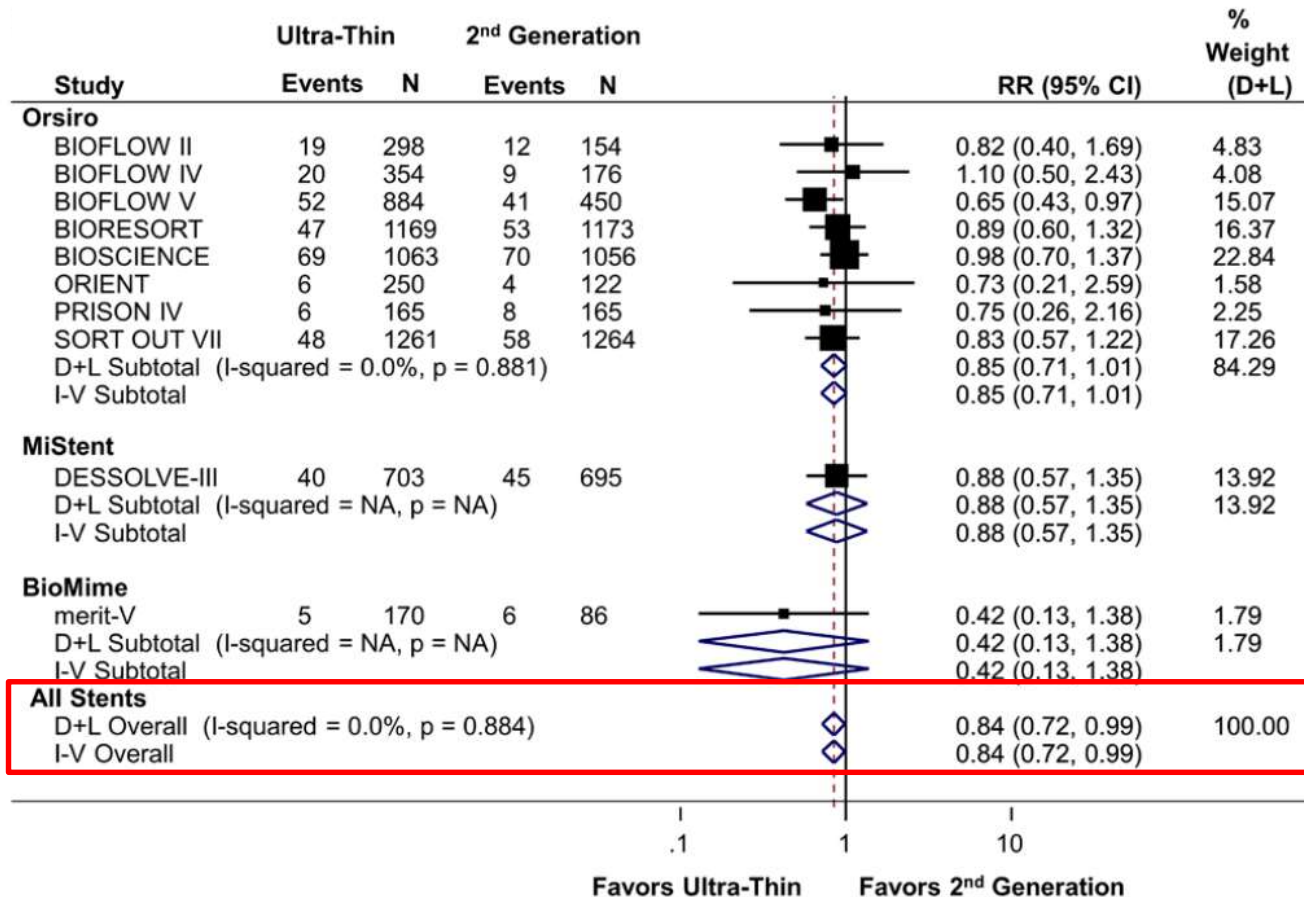
1 year TLF
16% risk reduction
Driven by TV-MI

No difference in
cardiac death and ID-TLR

BP vs DP vs no P

BP- vs. DP-DES: Meta-analysis

Mridha et al. *Eur Heart J Qual Care Clin Outcomes* 2019 pii:qcz031

TLR @ 3-5 years
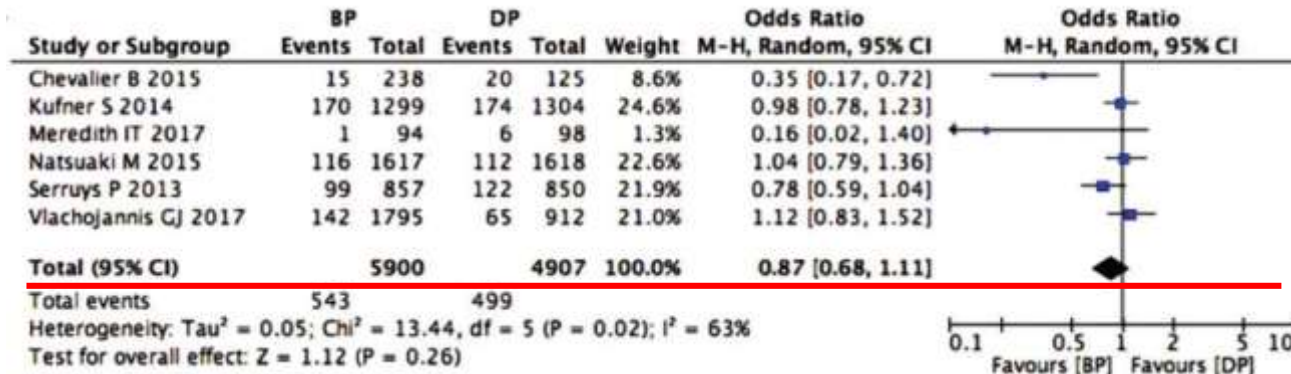
El-Hayek et al. *JACC Cardiovasc Interv* 2017;10:462-473

TVR @ 1 year
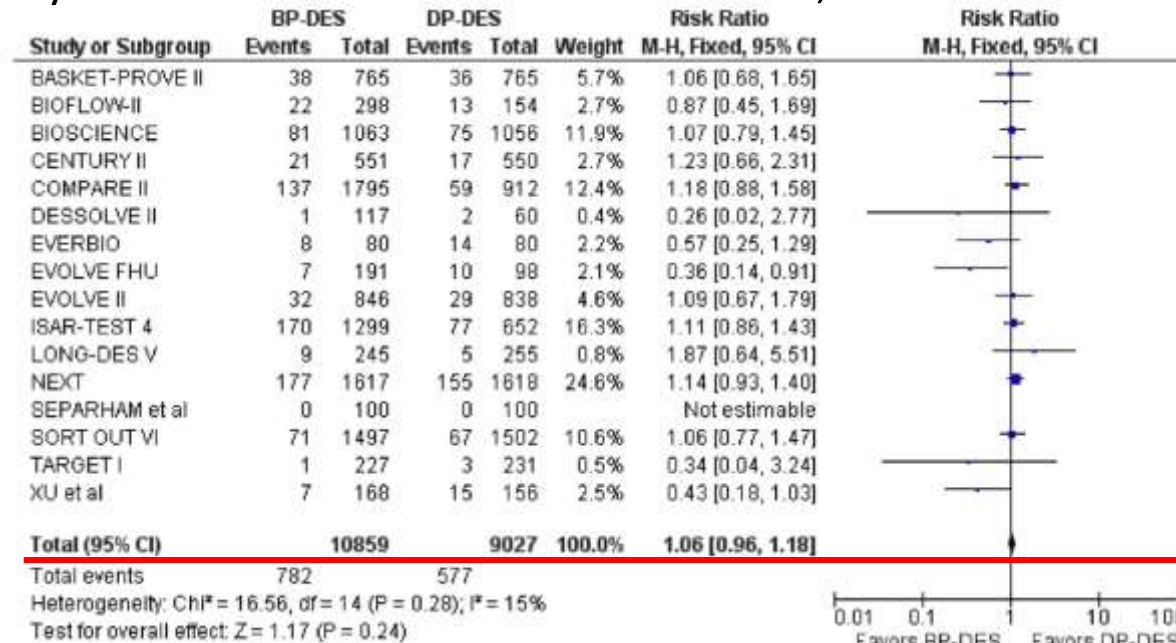
BP VS. DP DES: FROM SCAAR REGISTRY

Buccheri et al. *Eur Heart J* 2019;40:2607-2615

- Patients with CAD enrolled into SCAAR registry from 2011 to 2016
- Age 67 yo, Male 73%, DM 22%, ACS 78%
- BP: Orsiro 5%, Synergy 10%, Ultimaster 2%
- DP: Xience 17% , Resolute 34%, Promus 32%

No significant difference between BP- and DP-DES

■ DP-DES (n=47454) ■ BP-DES (n=10032)   ■ DP-DES (n=79106) ■ BP-DES (n=16504)

P=0.918

6.8   7.8

P=0.404

5.4   5.4

P=0.151

0.7   0.5

P=0.670

1.4   1.2

Death @2Y   MI @2Y   Def ST @2Y   ISR @2Y
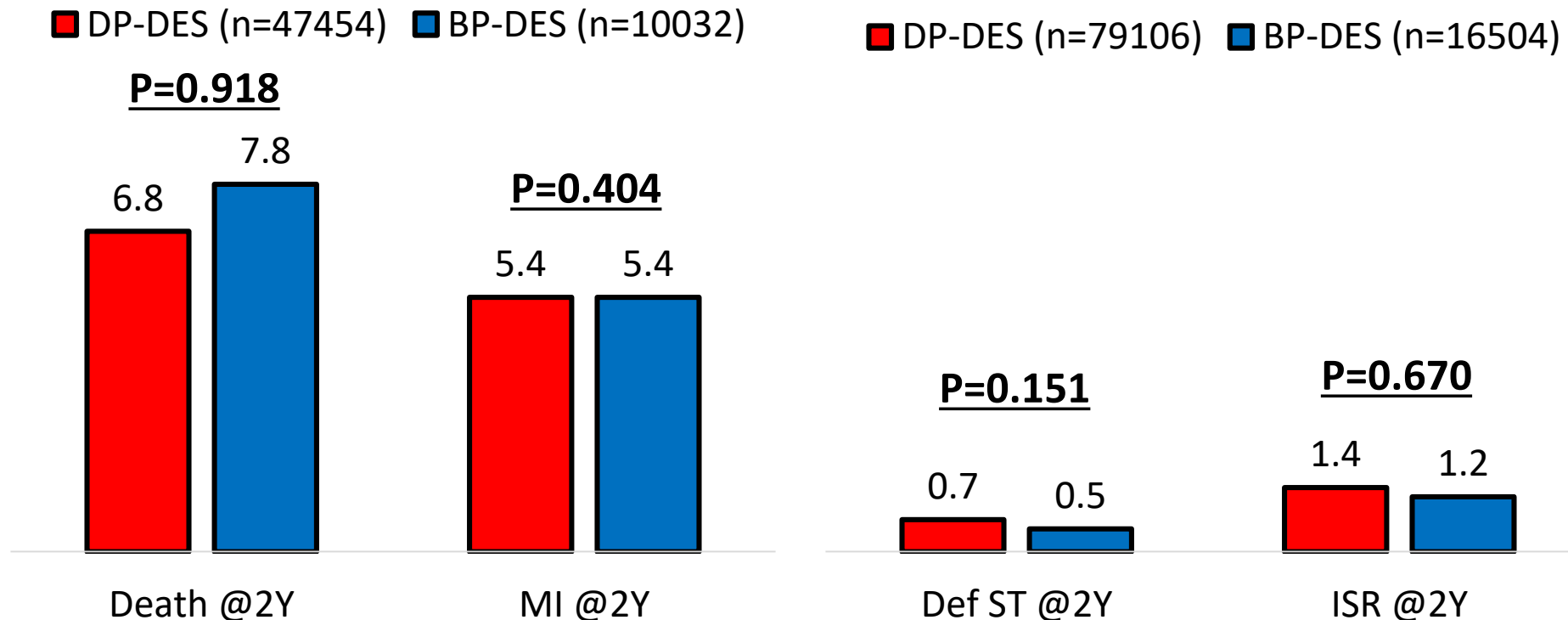
NEOATHEROSCLEROSIS IN BP VS. DP DES

Guagliumi et al. *Eur Heart J* 2018;39:2448-2456

- 90 patients with MVD randomized to BP-EES vs DP-ZES
- Primary endpoint: % of patients with neoatherosclerosis at 18 months
- Age 64 yo, Male 80%, DM 174%, ACS 70%

No significant difference between BP- and DP-DES

Patients with frames of neoatherosclerosis

BP-EES 11,6%
DP-ZES 15,9%
p=0.56
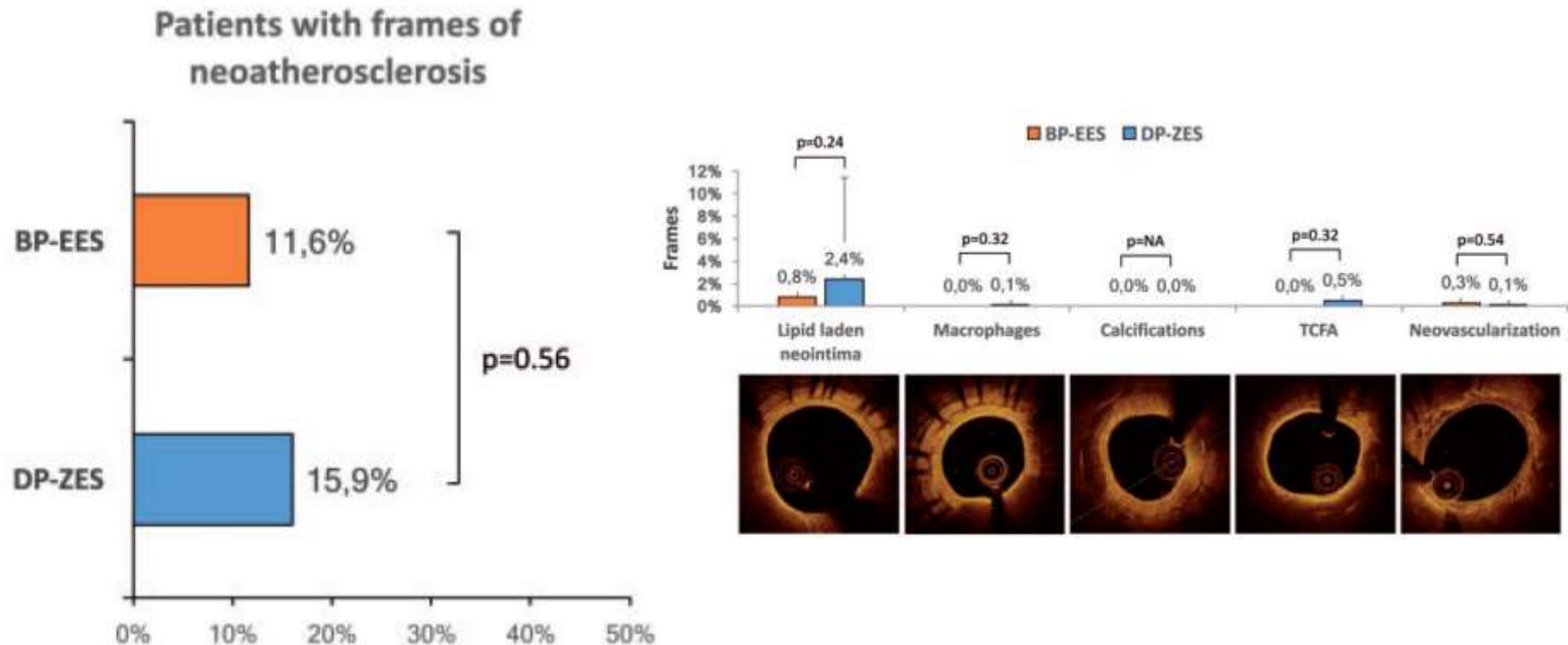
BioFreedom Drug Coated Stent (DCS)

120 um thick stainless steel stent
Selectively micro-structured surface holds
drug in abluminal surface structures
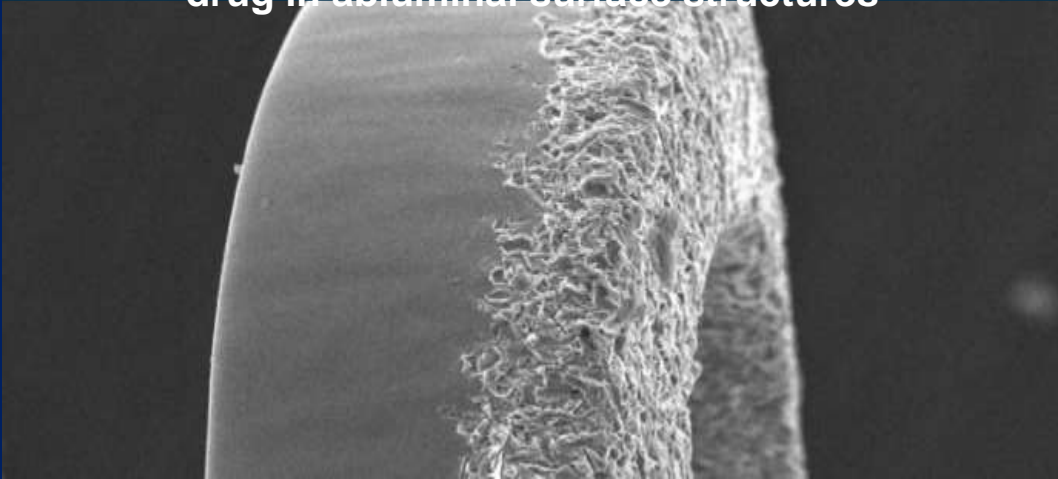
12 mo in-stent LL ~0.17 mm (n=31)

Biolimus A9 is 10x more lipophilic than sirolimus[1]

±2.8% (valid for all drugs test)

Potential Advantages:

- Rapid drug transfer to vessel wall (98% within one month[2])
- Avoid possible polymer-related adverse effects
- Safe to shorten DAPT?
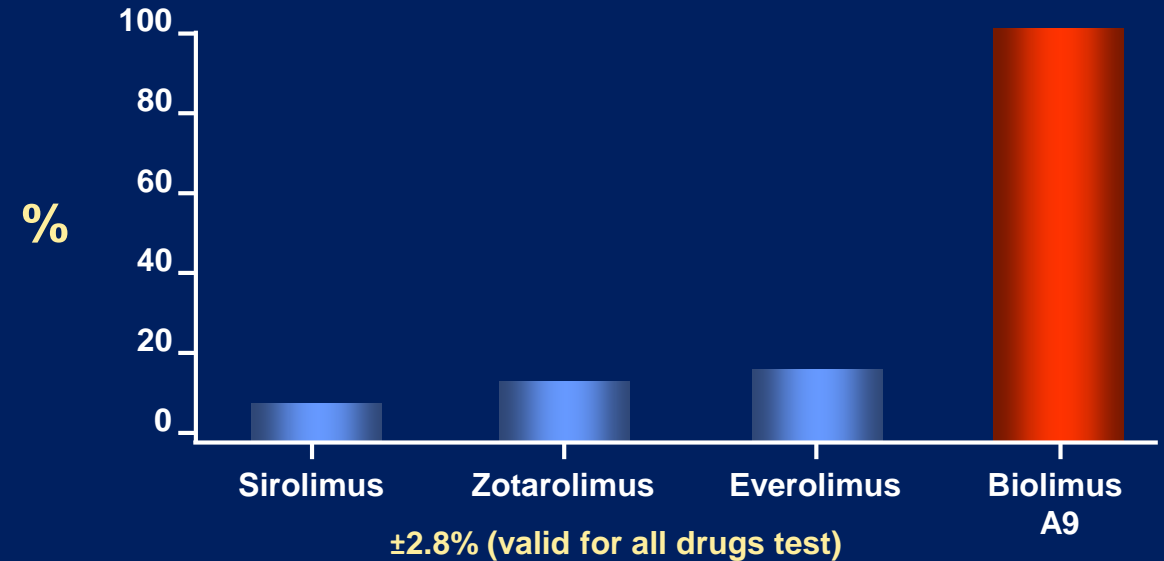
1. Data on file at Biosensors Intl
2. Tada et al. *Circ Cardiovasc Interv* 2010;3;174-183

Leaders Free: Primary Efficacy Endpoint (Clinically-Driven TLR)

Urban P et al. *NEJM* 2015;373:2038-47
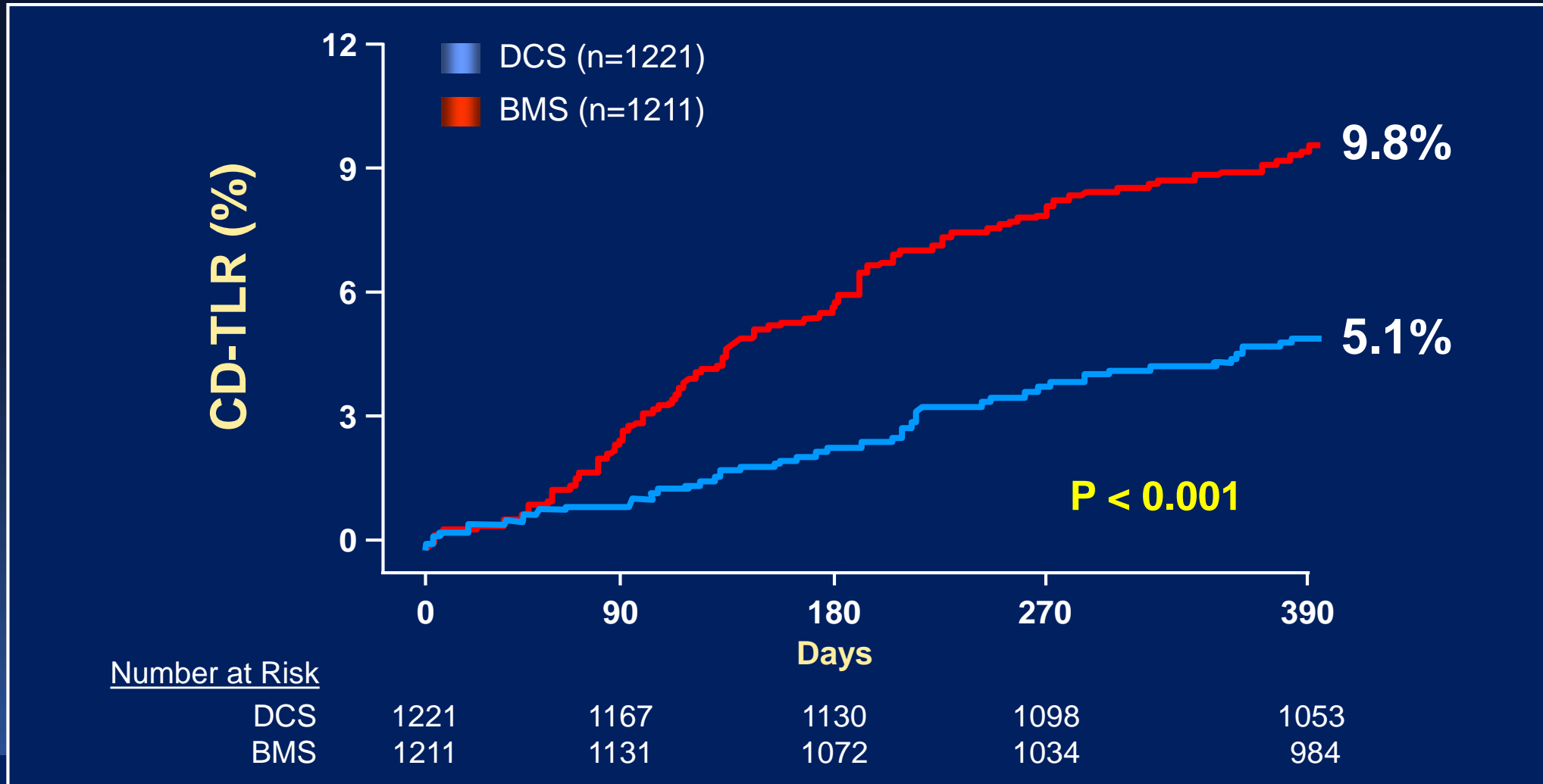
SORT OUT IX

Design
Randomized, multicenter, single-blind, all-comers, two-arm, non-inferiority trial comparing BioFreedom to Orsiro

Objective
To compare the safety and efficacy of the polymer free biolimus A9-coated BioFreedom stent and the thin strut biodegradable polymer sirolimus-eluting Orsiro stent in an all-comer population

Primary Endpoint
Target lesion failure: a composite of cardiac death, myocardial infarction (not related to other than index lesion) or target lesion revascularization within 1 year

3,151 Patients across 4 centers in Denmark

1:1 randomization

BioFreedom
n = 1,572

Orsiro
n = 1,572

30-day clinical follow-up

12-month clinical follow-up

5-year clinical follow-up
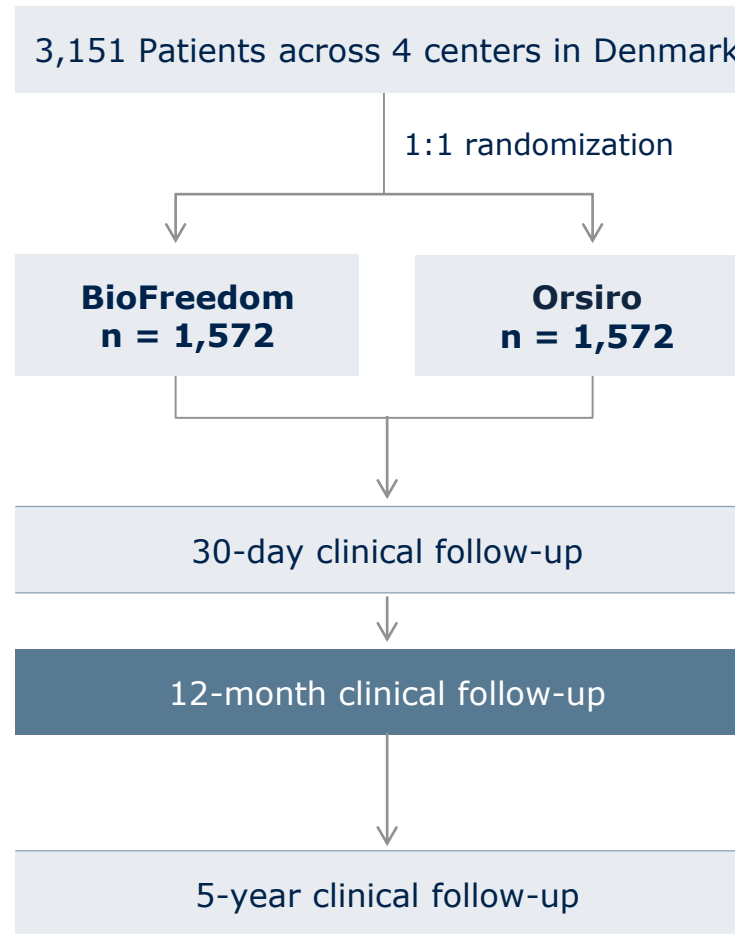
STEMI 24%
B2/C 61%
Bifurcation 20%
CTO 5%

NCT02623140

Okkels Jensen et al. on behalf SORT OUT IX Investigators, TCT 2018 – Oral presentation

SORT OUT IX
Primary Endpoint: TLF at 1 Year
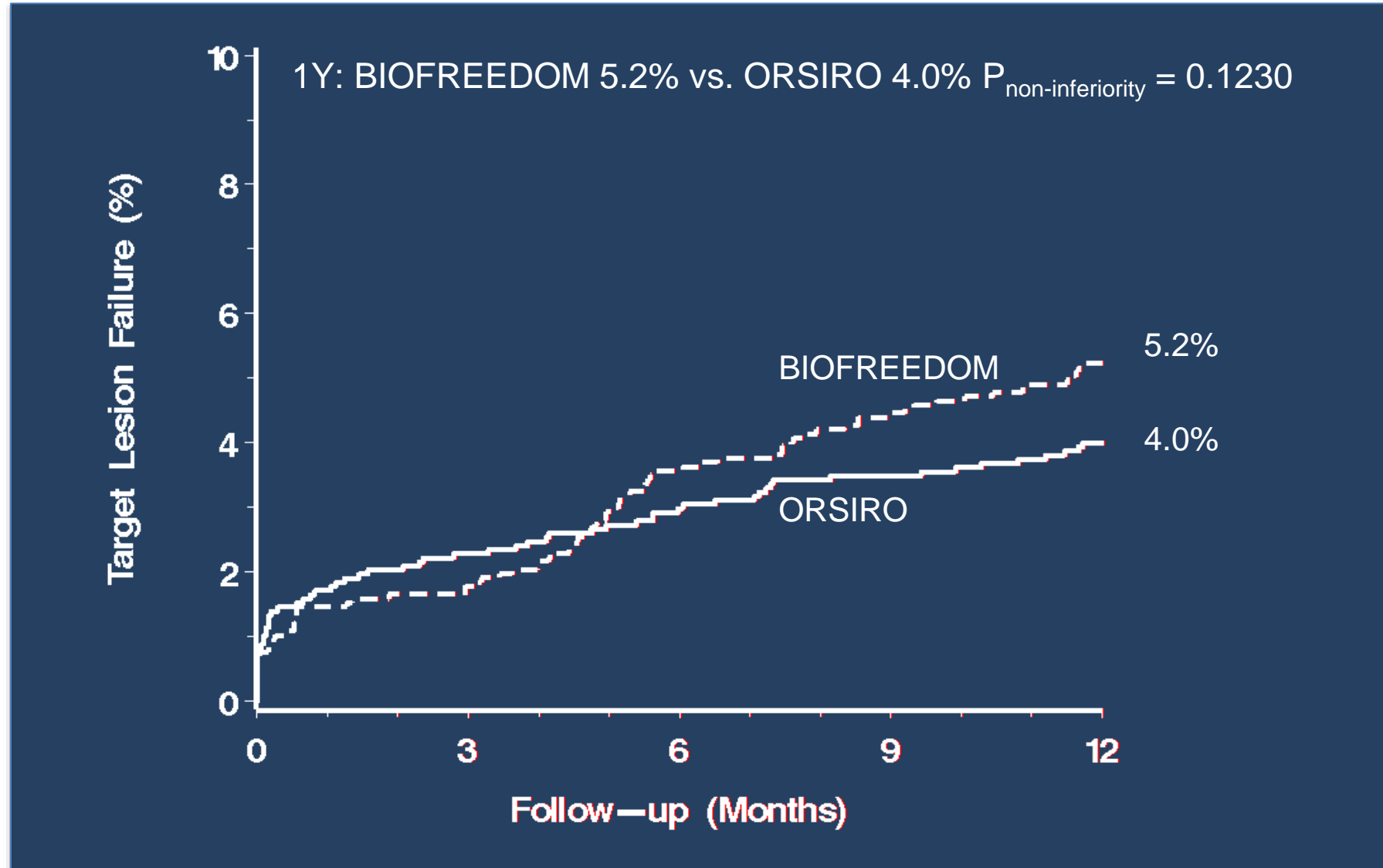
SORT OUT IX
Target Lesion Revascularization at 1 Year

Rate Ratio 2.77 95% CI 1.66-4.62; p<0.0001

BIOFREEDOM — 3.5%

ORSIRO — 1.3%
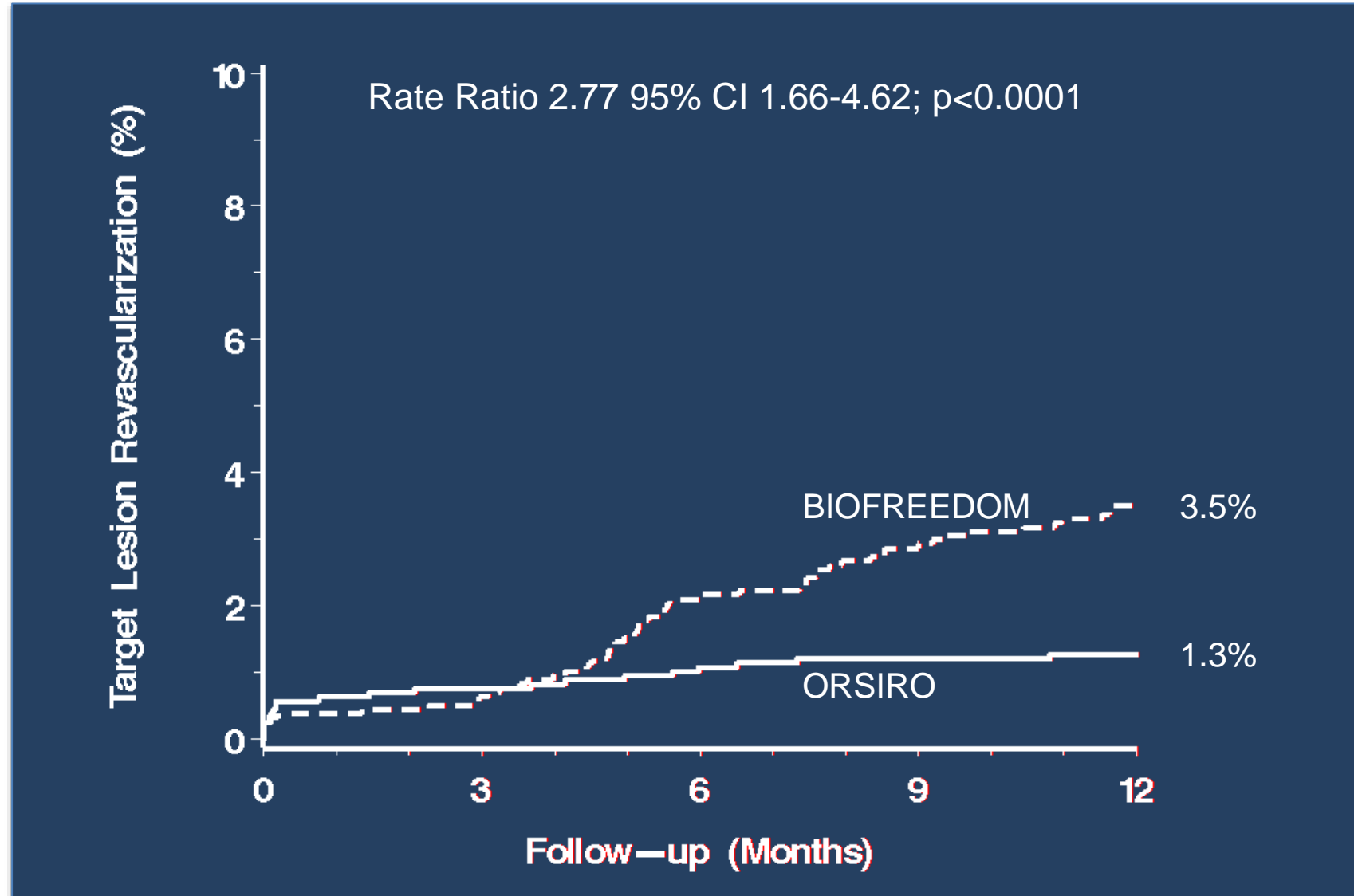
SORT OUT IX
TLF at 1 Year: Subgroup Analysis

Pre-specified Subgroups	Risk Ratio	Events (%)		P Value for Interaction
		Biolimus-eluting Stent	Sirolimus-eluting Stent	
Acute Coronary Syndrome No	1.74 (1.08 – 2.79)	48 (6.4)	27 (3.7)	
Acute Coronary Syndrome Yes	0.97 (0.61 – 1.56)	34 (4.1)	36 (4.2)	0.09
Age <=65	1.60 (0.86 – 2.97)	25 (3.8)	17 (2.4)	
Age >65	1.17 (0.79 – 1.73)	57 (6.3)	46 (5.3)	0.40
Diabetes Melitus No	1.34 (0.90 – 1.99)	57 (4.5)	43 (3.4)	
Diabetes Melitus Yes	1.23 (0.68 – 2.23)	25 (8.2)	20 (6.6)	0.83
LAD No	1.52 (0.93 – 2.48)	41 (5.2)	27 (3.4)	
LAD Yes	1.15 (0.73 – 1.80)	41 (5.2)	36 (4.5)	0.40
Lesion Type C	1.21 (0.76 – 1.92)	41 (6.9)	33 (5.6)	
Lesion Type Not C	1.40 (0.87 – 2.24)	41 (4.2)	30 (3.0)	0.68
Male No	1.14 (0.57 – 2.30)	17 (4.8)	15 (4.2)	
Male Yes	1.36 (0.93 – 1.98)	65 (5.3)	48 (3.9)	0.67
Multivessel Disease No	1.24 (0.85 – 1.79)	63 (4.8)	51 (3.9)	
Multivessel Disease Yes	1.62 (0.78 – 3.36)	19 (7.3)	12 (4.5)	0.52
One Stent Per Patient No	1.16 (0.75 – 1.78)	45 (4.5)	39 (3.9)	
One Stent Per Patient Yes	1.50 (0.88 – 2.56)	34 (6.0)	23 (4.0)	0.45
Previous MI No	1.33 (0.91 – 1.93)	65 (5.0)	49 (3.8)	
Previous MI Yes	1.62 (0.70 – 3.77)	14 (6.3)	9 (3.8)	0.36
Previous PCI No	1.22 (0.81 – 1.84)	52 (4.3)	43 (3.5)	
Previous PCI Yes	1.75 (0.92 – 3.30)	27 (8.4)	15 (4.8)	0.98
STEMI No	1.39 (0.96 – 2.02)	68 (5.6)	48 (4.1)	
STEMI Yes	1.01 (0.50 – 2.10)	14 (3.8)	15 (3.8)	0.44
Overall	1.31 (0.94 – 1.82)	82 (5.2)	63 (4.0)	

Biolimus-eluting Stent better   Sirolimus-eluting Stent better

SUB-GROUPS OF CAD PATIENTS
CAN WE EXPECT DIFFERENCES?

STEMI	In-stent restenosis
DM	**HBR (short DAPT)**
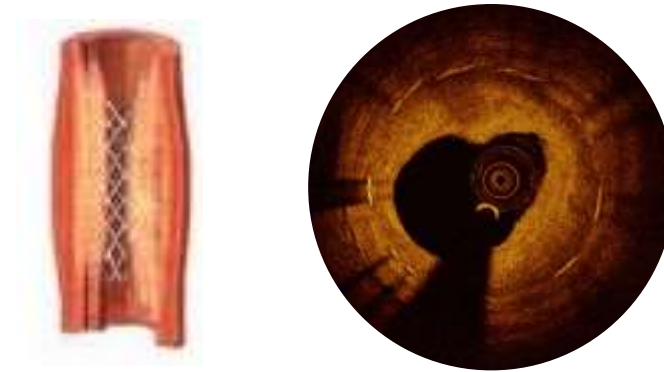
BIOSTEMI

DESIGN
Prospective, multicenter, randomized, controlled, superiority trial.

OBJECTIVE
To investigate the superiority of ultrathin-strut Orsiro BP-SES to Xience DP-EES in STEMI patients undergoing primary PCI.

COORDINATING CLINICAL INVESTIGATORS
Prof. Dr. Thomas Pilgrim, Bern, Switzerland
Dr. Juan F. Iglesias, Lausanne, Switzerland
PD Dr. Olivier Muller Lausanne, Switzerland

PRIMARY ENDPOINT
Target Lesion Failure (TLF) at 12 months, defined as a composite of cardiac death, target vessel re-infarction, or clinically-indicated TLR.

BIOSCIENCE STEMI subgroup (n=407)	BIOSTEMI trial (n=1,250)
Orsiro 1:1 Xience	Orsiro 1:1 Xience
Clinical follow-up at 30 days	Clinical follow-up at 30 days
Clinical follow-up at 12 months	Clinical follow-up at 12 months
Superiority analysis for target lesion failure at 12 months employing Bayesian approach	
Clinical follow-up at 2 years	Clinical follow-up at 2 years
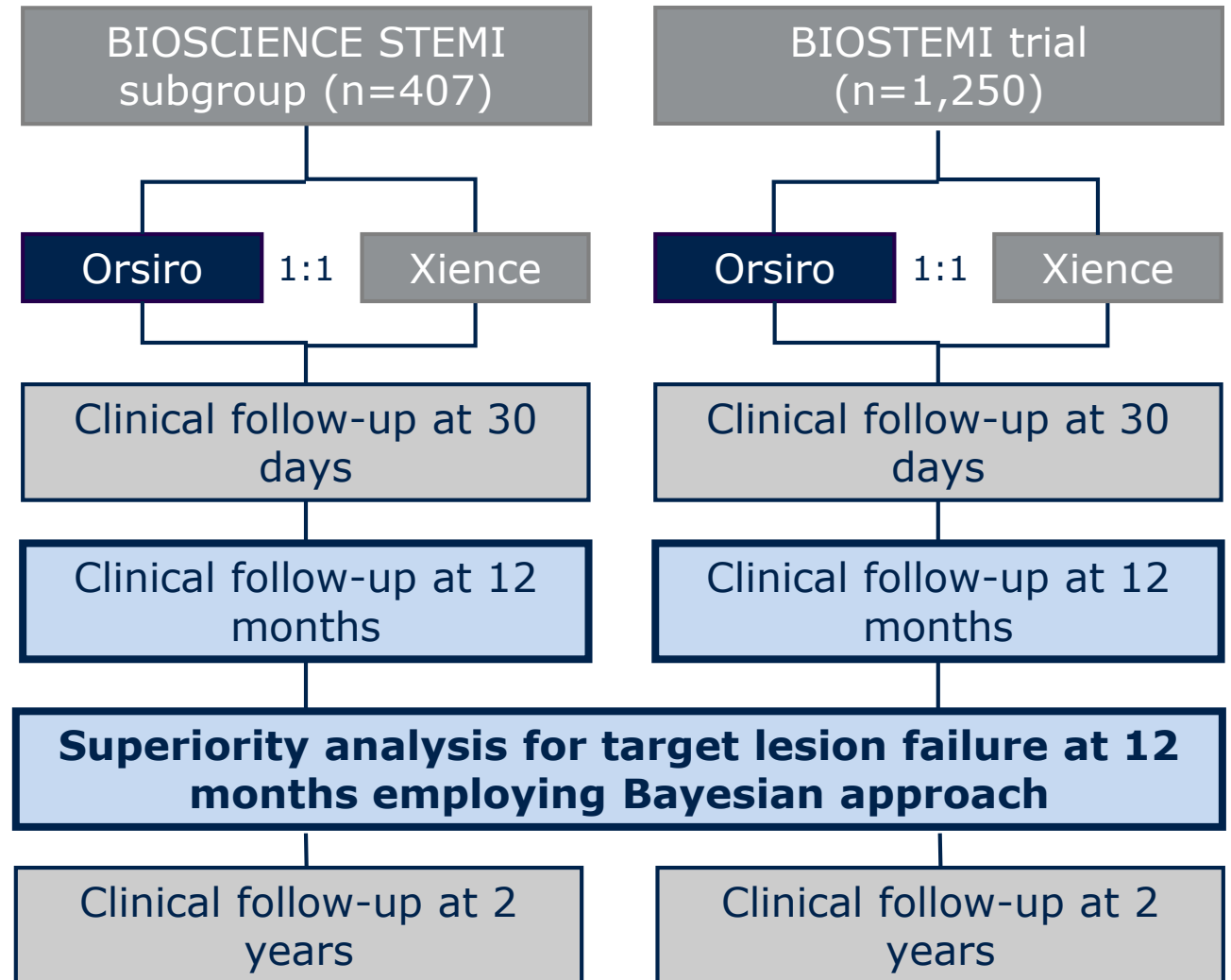
BIOSTEMI

ULTRATHIN BP-DES VS. THIN DP-DES IN STEMI

Iglesias et al. *Lancet* 2019

- 1300 STEMI patients randomized to BP-SES vs. DP-EES
- Primary enpdoint: TLF at 1 year
- Age 62 yo, male 80%, DM 10%, mean stent length 32mm

TLF

BP-SES: **4**% vs. DP-EES: **6**%
Rate ratio: 0.59 (0.37-0.94)

Clinically-driven TLR

BP-SES: **1**% vs. DP-EES: **3**%
Rate ratio: 0.55 (0.26-1.13)
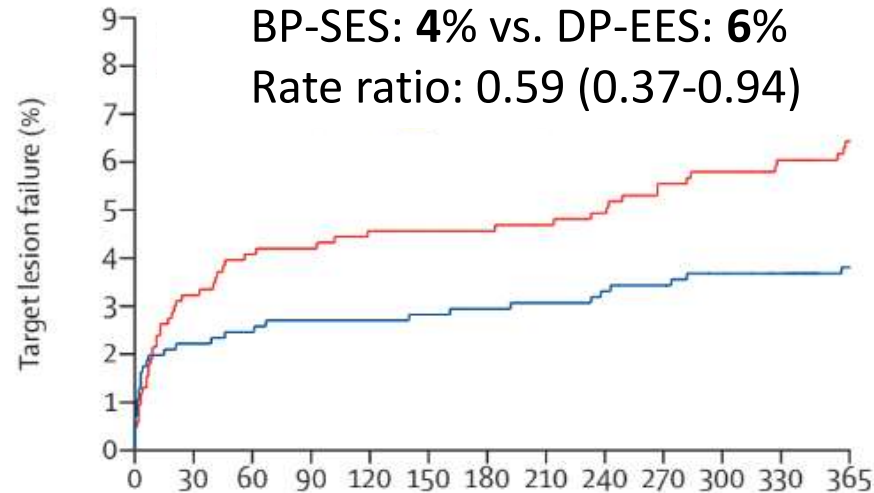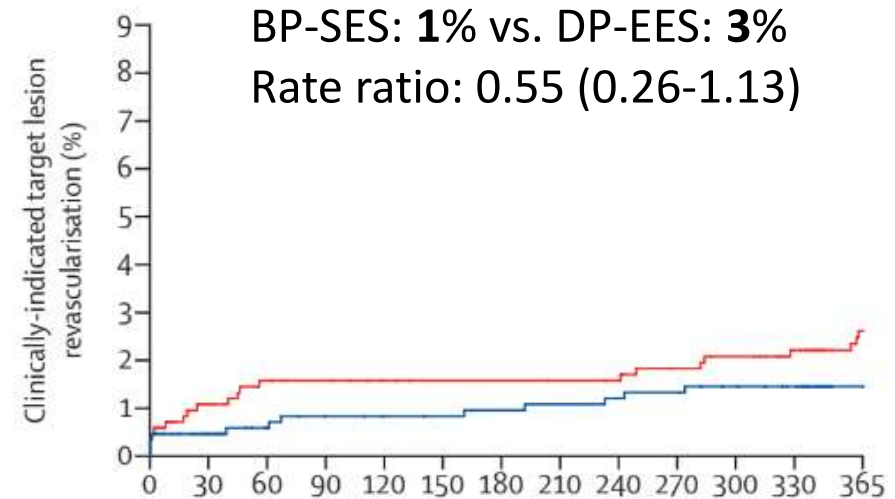
*DES with **biodegradable polymer** and **ultrathin struts** may be the best practice in STEMI patients.*

PCI STRATEGY FOR IN-STENT RESTENOSIS

Siontis et al. *Lancet* 2015;386:655-664

- Meta-analysis of 5923 ISR patients from 27 trials

Estimated differences of %DS

	EES	DCB	SES	PES
EES	99·6 (0·98)	−9·0% (−15·8 to −2·2)	−9·4% (−17·4 to −1·4)	−10·2% (−18·4 to −2·0)
DCB	..	73·7 (0·00)	−0·2% (−6·2 to 5·6)	−1·2% (−6·4 to 4·2)
SES	..	..	72·8 (0·01)	−0·8% (−6·4 to 4·6)
PES	..	..	..	67·7 (0·01)

- EES was associated with the best angiograpic and clinical outcomes
- DCB provided favourable results without a new stent layer

Odds ratios for TLR

	EES	DCB	PES	SES
EES	99·1 (0·97)	0·36 (0·14–0·94)	0·34 (0·12–1·00)	0·34 (0·12–0·97)
DCB	..	73·7 (0·01)	0·93 (0·51–1·71)	0·93 (0·55–1·58)
PES	..	..	70·7 (0·02)	1·00 (0·59–1·68)
SES	..	..	..	70·0 (0·01)

SYNERGY in Short DAPT Trials:

>5,000 pts studied

SENIOR

- Elderly Pts (>75 yrs)
- 1m DAPT Stable pts
- 6m DAPT ACS pts

1,200 pts

EVOLVE Short DAPT

- HBR pts
- 3m DAPT

2,009 pts

POEM

- Real-world HBR pts
-1m DAPT

1,023 pts

SYNIVUS-DAPT

- HBR pts
- 1m DAPT

100 pts

IDEAL LM

- Pts w/ LM Disease
- 4m DAPT SYNERGY
-12m DAPT XIENCE

818 pts

EVOLVE Short DAPT: Mauri, TCT 2015; SENIOR: Varenne, O. et al. *Lancet* 2017; POEM: Clinicaltrials.gov NCT03112707; IDEAL LM: Van Geuns, EuroPCR 2017

EVOLVE Short DAPT Study Design

Prospective, multicenter, single-arm study powered to define safety of 3-month DAPT in high bleeding risk (HBR) patients treated with SYNERGY

Analysis period

PCI

DAPT (Aspirin optional if on chronic anticoagulation)

Clinical follow-up

Aspirin Only (patients eligible† for discontinuation of P2Y12 inhibitor)

Final follow-up

0   3   15

Time in months after SYNERGY stent implantation
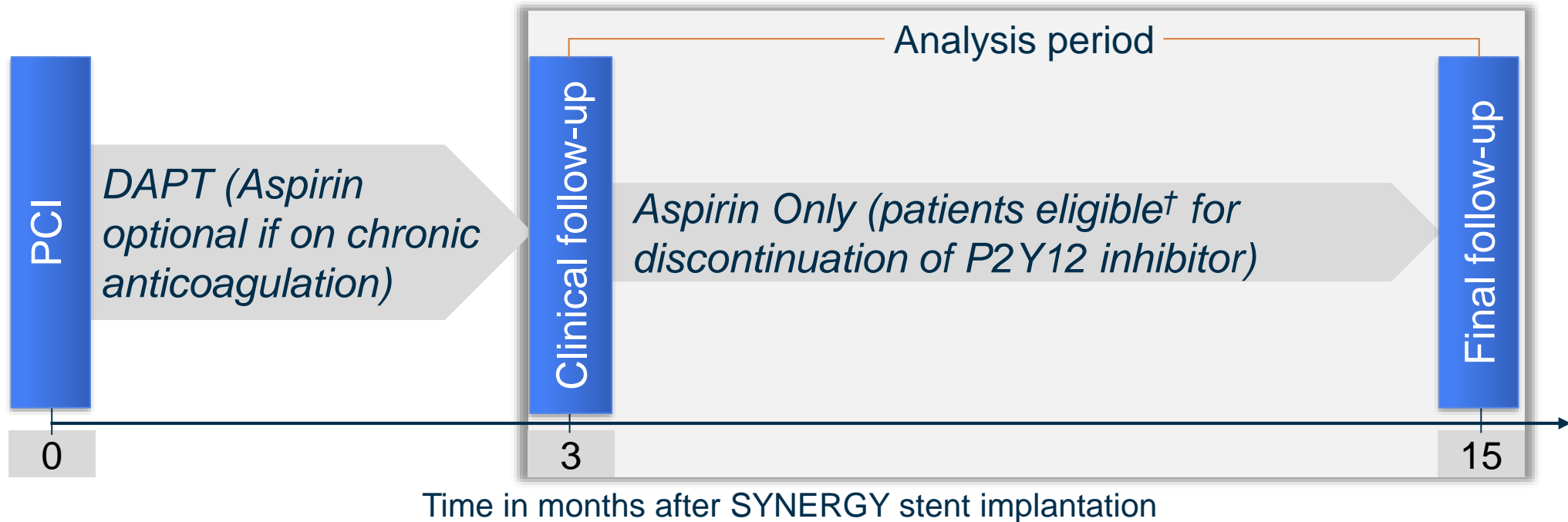
Co-Primary endpoints: Death/MI and ARC definite/probable ST between 3-15 months
Secondary endpoint: BARC 2/3/5 bleeding between 3-15 months (patients not on chronic anticoagulation)

†Subjects free from stroke, MI, revascularization and ST between 0-3 months eligible to discontinue; Mauri et al. *AHJ* 2018

EVOLVE Short DAPT

EVOLVE Short DAPT Patient Disposition

2009 patients implanted with at least 1 SYNERGY stent at 110 global sites

Withdrawn*: n=44
Death: n=37
Missed visit: n=16

Clinical follow-up at 3 months: N=1912 (95.2%)

Eligible to discontinue P2Y12 inhibitor at 3 months†: N=1487 (77.7%)
Analysis population: Death/MI and ST, n=1487; BARC 2,3,5 bleeding, n=1032 (excluded 455 patients on anticoagulation)

Not eligible to discontinue P2Y12 inhibitor at 3 months: N=425 (22.3%)
Not event-free (52); DAPT non-compliant (34); DAPT interruption ≥14 days (31); other (24); investigator decision (183); subject decision (152)‡

Withdrawn*: n=36
Death: n=66

Withdrawn*: n=40
Death: n=19

15-month follow-up: N=1385 (93.1%)

15-month follow-up: N=366 (86.1%)

*withdrawn due to adverse event, lost to follow-up, investigator discretion, or other reasons;
†patients free from stroke, MI, revascularization and ST between 0-3 months eligible to discontinue;
‡patients may have had multiple reasons for not being eligible

EVOLVE Short DAPT

Clinical Outcomes between 3-15 Months

Analysis Population (N=1457)
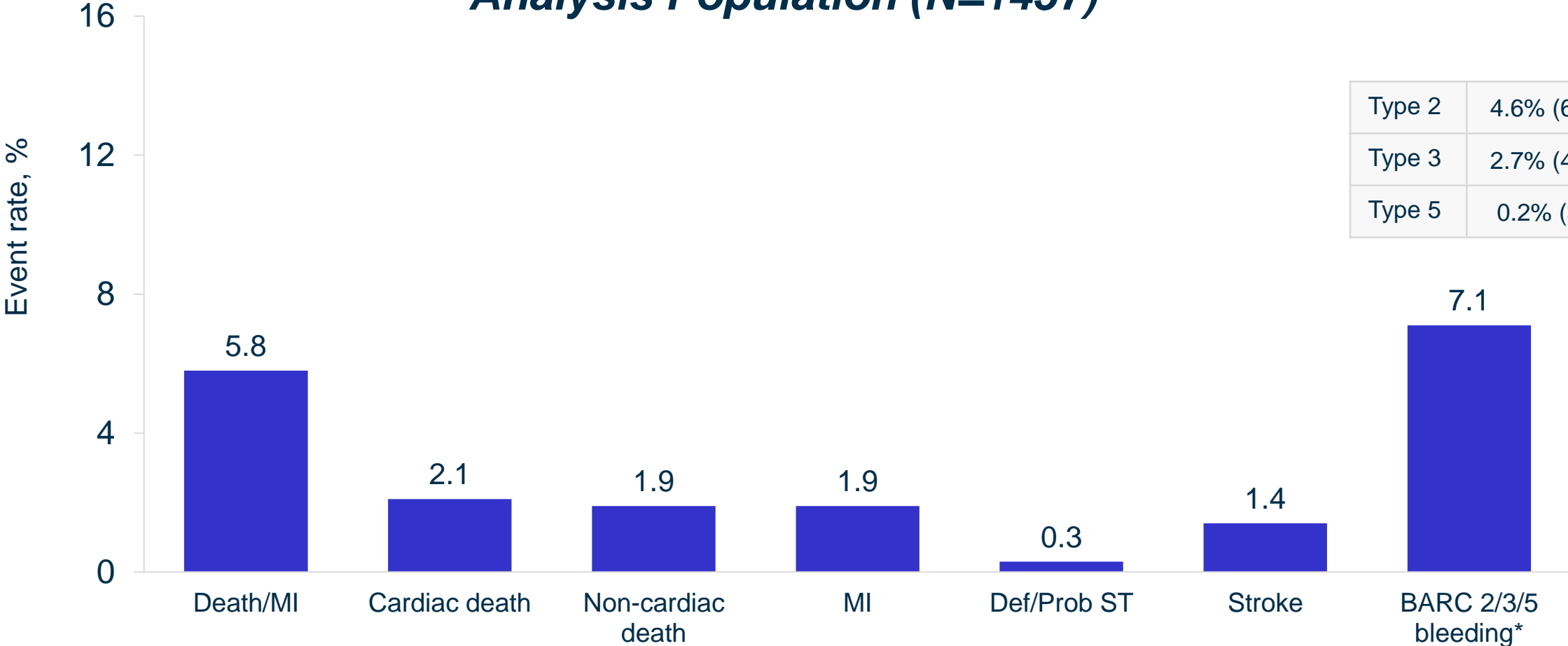
Type 2	4.6% (67)
Type 3	2.7% (40)
Type 5	0.2% (3)

Event rate, %

- Death/MI: 5.8
- Cardiac death: 2.1
- Non-cardiac death: 1.9
- MI: 1.9
- Def/Prob ST: 0.3
- Stroke: 1.4
- BARC 2/3/5 bleeding*: 7.1

Binary rates; denominator includes patients with sufficient f/u or having a CEC event; *Non-hierarchical

tct2019

EVOLVE Short DAPT
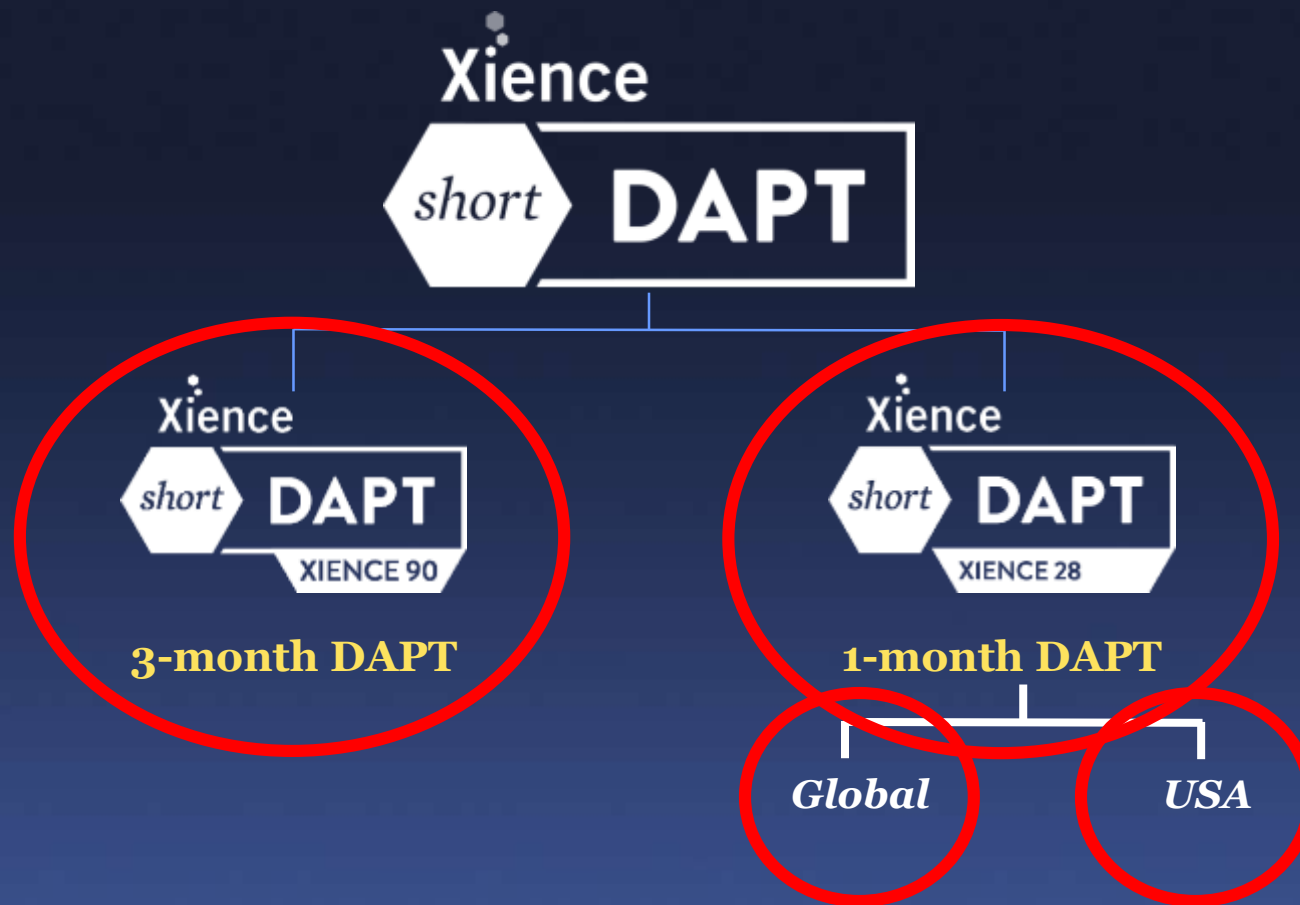
ONYX ONE MONTH DAPT PROGRAM

STUDYING 1-MONTH DAPT

IN HIGH BLEEDING RISK PATIENTS

Onyx ONE Global Study
Stephan Windecker

Prospective, Multicenter, Single-blind Randomized Trial

**High Bleeding Risk patients undergoing PCI
(no lesion, vessel limitations)**

Resolute Onyx ZES
with 1 Month DAPT
(N=1000)

**1:1 randomization
84 global sites
Enrollment Nov 2017 – Sep 2018**

BioFreedom DCS
with 1 Month DAPT
(N=1000)

Clinical Follow-up

| 1mo | 2mo | 6mo | 1yr | 2yr |

Primary safety endpoint: Cardiac death, MI or stent thrombosis (def/prob) at 1 year

2°   Efficacy endpoint (powered):   Target Lesion Failure (TLF; cardiac death, TV-MI or CD-TLR)
        at 1 year

Other secondary endpoints: Lesion, device and procedure success rates, BARC bleeding,
        individual components of primary endpoints

Primary Safety Endpoint: Cardiac Death, MI, or ST

HR 1.02, 95% CI [0.83, 1.27]

P-value 0.84

- Resolute Onyx ZES
- BioFreedom DCS

17.3%
17.3%

Number at risk

ZES	1003	955	844	790
DCS	993	949	833	782

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Onyx ONE

STENT CHOICE: DECISION TREE