Onyx ONE

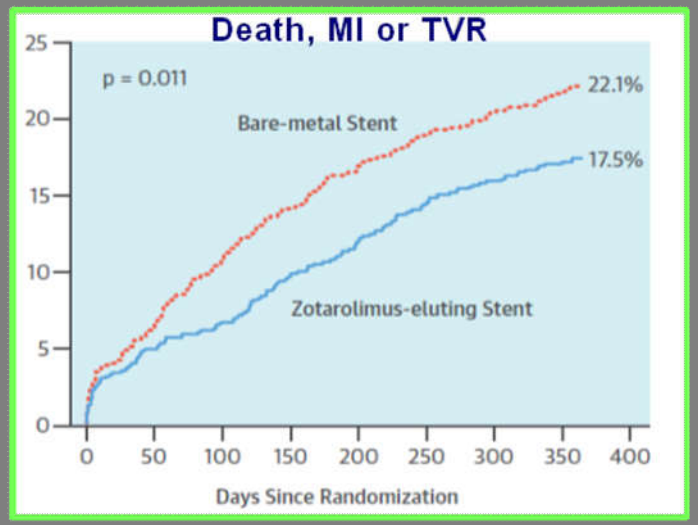
A Randomized Trial of a Durable-Polymer Drug-Eluting Stent vs. A Polymer-Free Drug-Coated Stent in Patients at High Risk of Bleeding on 1-Month DAPT

Gilles Montalescot

DOI @ action-coeur.org

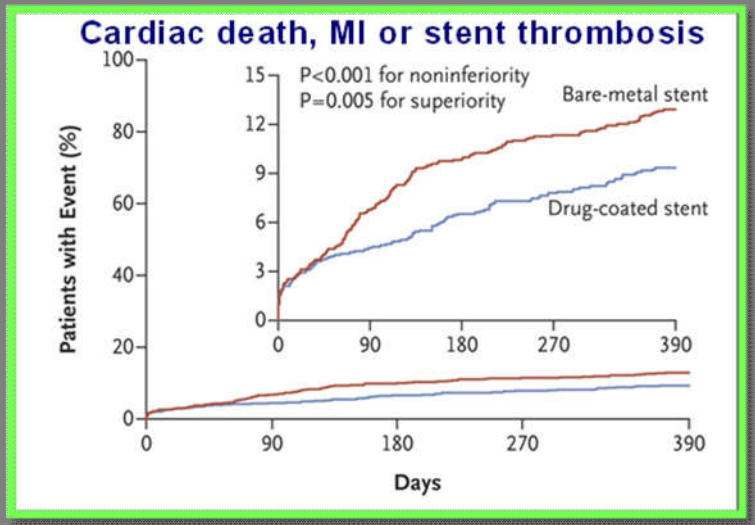
Stent comparisons with 1 month DAPT in HBR patients

ZEUS study (n=1606)



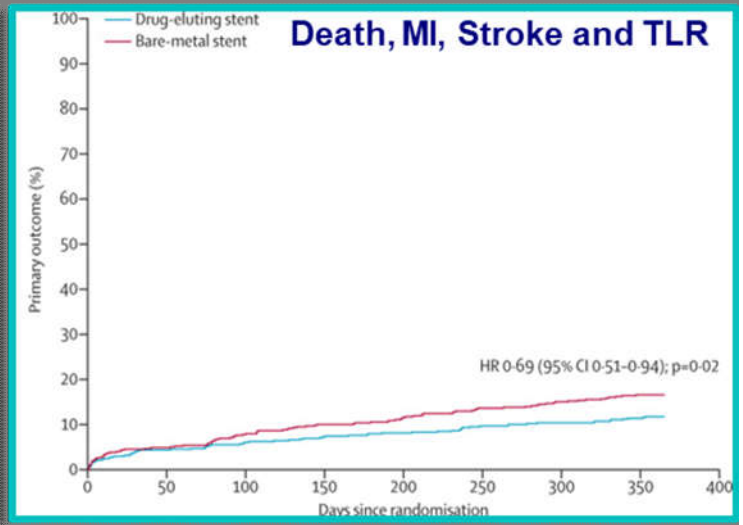
Valgimigli et al. JACC 2015;65:805-815

LEADERS-FREE study (n=2466)



Urban P et al. N Engl J Med 2015;373:2038-2047

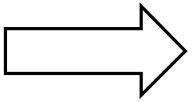
SENIOR study (n=1200)



Varenne O et al. Lancet 2017

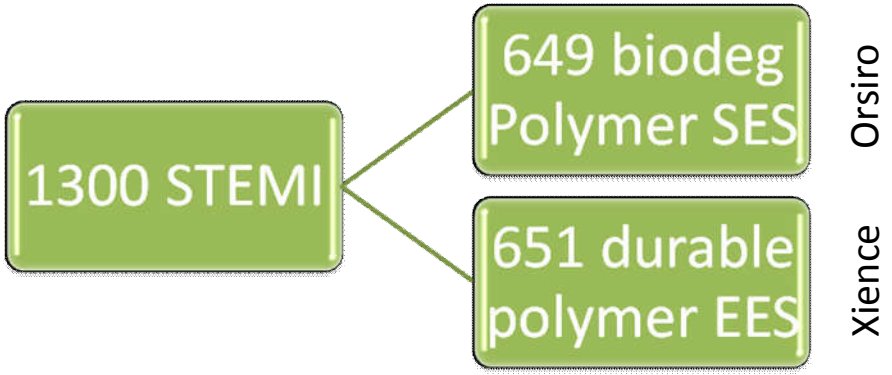
Current guidelines

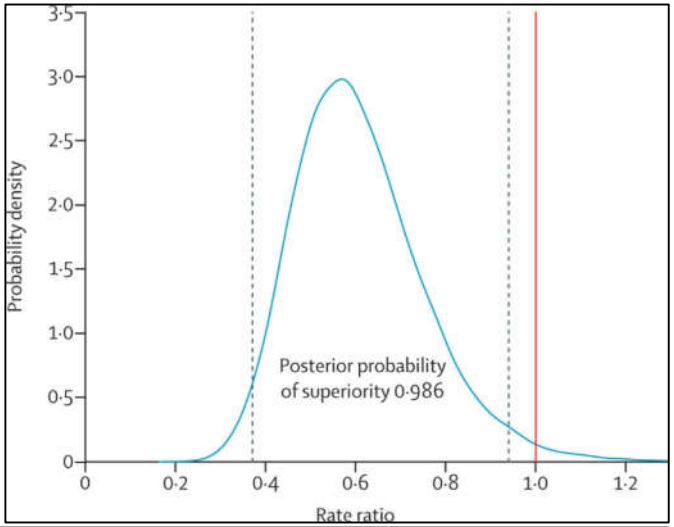
Recommendations	Class[a]	Level[b]
DES are recommended over BMS for any PCI irrespective of: • clinical presentation • lesion type • planned non-cardiac surgery • anticipated duration of DAPT • concomitant anticoagulant therapy.[100,578,579,640]	I	A

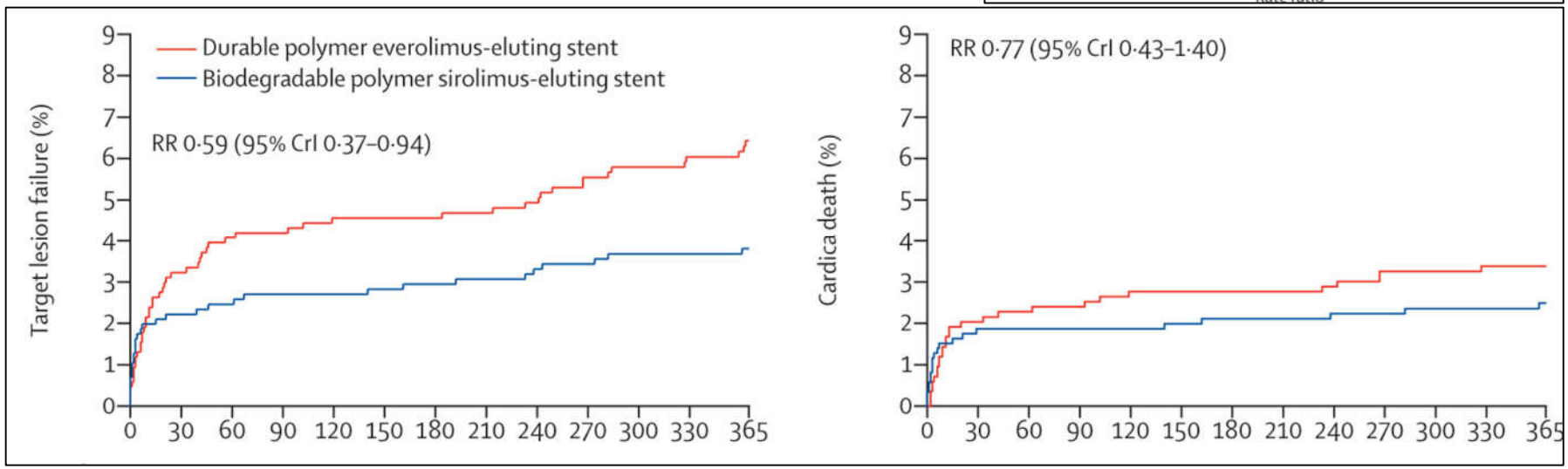


Shall we challenge this?

BIOSTEMI







Iglesias J et al. Lancet 2019

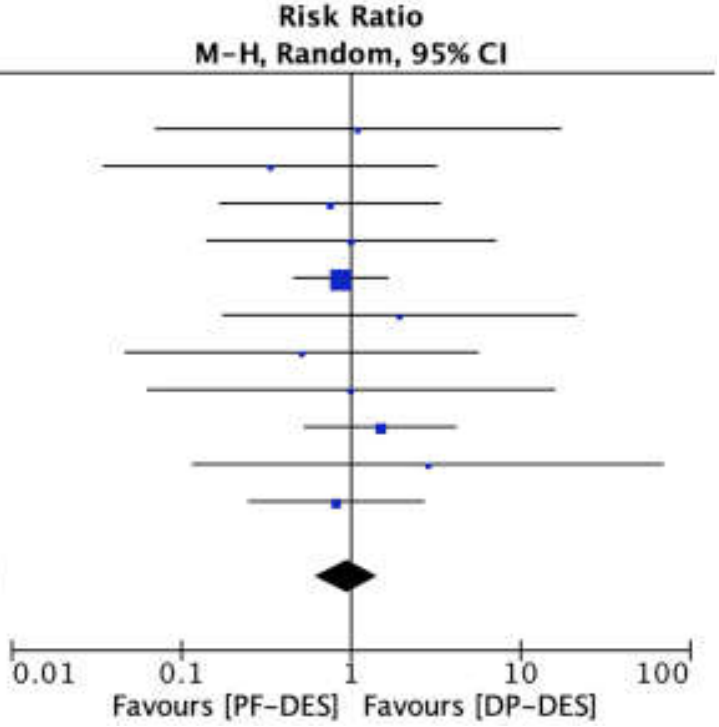
Polymer-free drug-eluting stents (PF-DES) vs. Durable polymer drug-eluting stents (DP-DES)

Definite or probable stent thrombosis

Study or Subgroup	PF-DES Events	PF-DES Total	DP-DES Events	DP-DES Total	Weight	Risk Ratio M-H, Random, 95% CI
BioFreedom FIM 2016	0	122	0	60		Not estimable
Dang 2012	1	50	1	55	2.3%	1.10 [0.07, 17.12]
ISAR-TEST 2013	1	225	3	225	3.4%	0.33 [0.03, 3.18]
ISAR-TEST-2 2010	3	333	4	335	7.8%	0.75 [0.17, 3.35]
ISAR-TEST-3 2009	2	201	2	202	4.5%	1.00 [0.14, 7.07]
ISAR-TEST-5 2016	26	2002	15	1000	43.3%	0.87 [0.46, 1.63]
LIPSIA Yukon 2014	2	118	1	114	3.0%	1.93 [0.18, 21.02]
Nano 2014	1	132	2	136	3.0%	0.52 [0.05, 5.61]
NEXT 2012	1	148	1	148	2.3%	1.00 [0.06, 15.84]
ReCre8 2018	9	747	6	744	16.3%	1.49 [0.53, 4.18]
Shiratori 2014	1	84	0	80	1.7%	2.86 [0.12, 69.17]
Zhang 2013	5	327	6	321	12.4%	0.82 [0.25, 2.65]
Total (95% CI)		**4489**		**3420**	**100.0%**	**0.94 [0.62, 1.43]**
Total events	52		41			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.88$, df = 10 (P = 0.98); $I^2 = 0\%$

Test for overall effect: Z = 0.29 (P = 0.77)



JJ Wu et al. Ann Med Surg. 2019 Feb; 38: 13–21

Onyx ONE Study Design

Prospective, Multicenter, Single-blind Randomized

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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**

HBR Inclusion Criteria (One or More)

- Elderly age ≥75 years
- OAC planned after PCI
- Renal failure (CrCl <40 ml/min)
- Planned surgery <1 year
- Anemia (Hgb <11 g/dl)
- Hospitalization for bleeding within 1 year
- Thrombocytopenia (<100,000/mm^3)
- Cancer diagnosed or treated w/i 3 years
- Stroke within 1 year or any prior ICH
- Severe chronic liver disease
- Long-term NSAID or steroid use
- Expected DAPT non-compliance

Sample Size Estimation (Powered for Non-inferiority)

	Primary Safety Endpoint	Secondary Efficacy Endpoint
Definition	Cardiac death, MI or ST	TLF (cardiac death, TV-MI or CD-TLR)
Expected event rate	9.4%[1] for both arms	11% for both arms
Non-inferiority margin	4.1%	4.4%
One-sided type I error (α)	0.05	
Power	>90%	
Lost to follow-up	10%	

Total sample size: 2000 patients

[1] *Urban P, et al. N EnglJ Med. 2015;373:2038-4*

Baseline Characteristics

% or mean ± SD	Resolute Onyx (N=1003)	BioFreedom (N=993)
Age (yrs)	74.0 ± 9.5	74.1 ± 9.8
Female	32.5	34.2
Diabetes	38.7	38.5
Hypertension	79.4	81.3
Hyperlipidemia	64.1	62.3
Previous MI	26.3	25.1
Previous revascularization	31.3	29.8
Atrial fibrillation	32.7	31.8
Silent ischemia	9.1	11.0
Chronic coronary syndrome	38.1	38.6
Acute coronary syndrome	52.8	50.4
STEMI	6.2	5.1
Non-STEMI	27.1	27.0
Unstable angina	19.5	18.3

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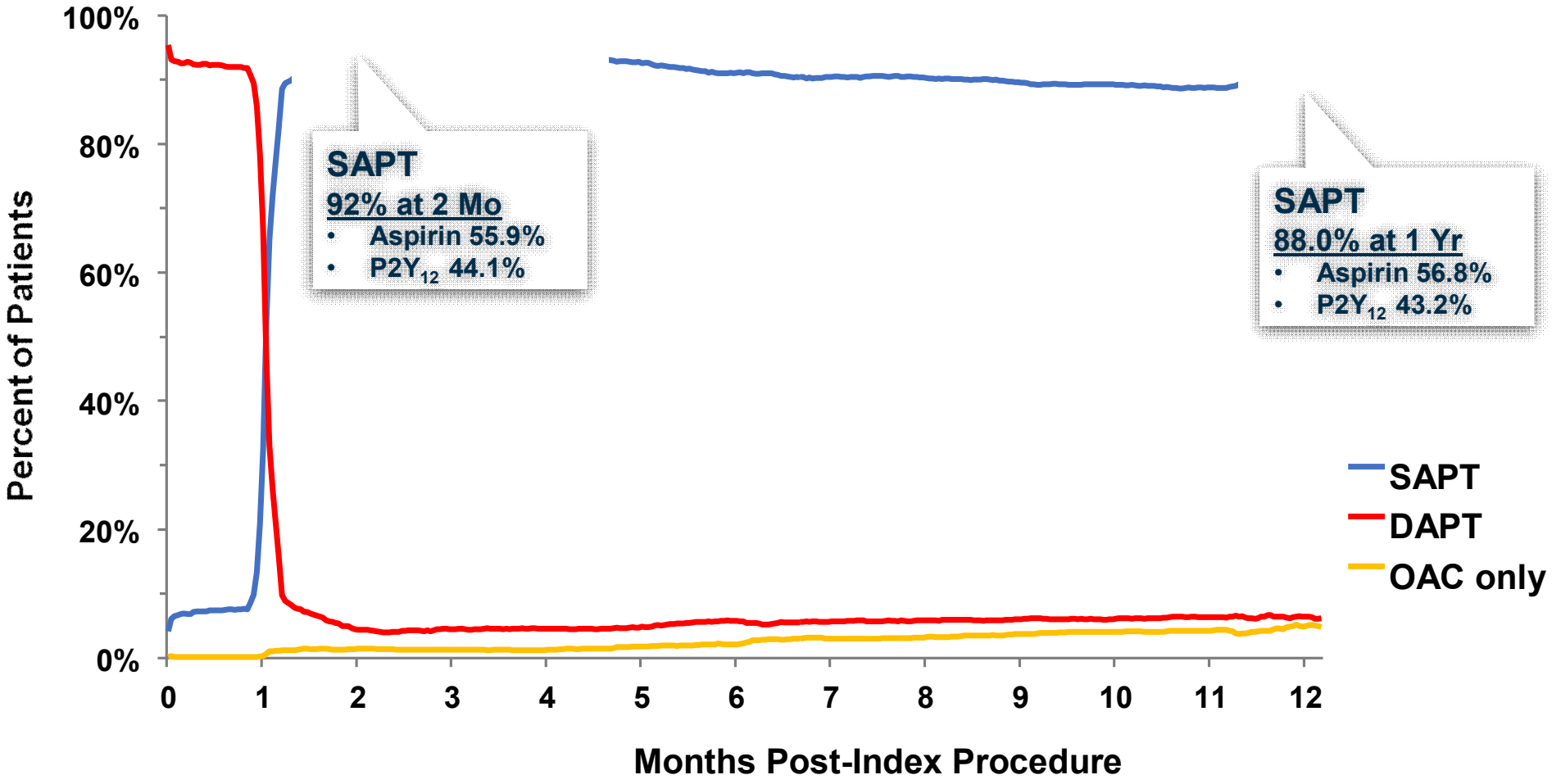
Procedural Characteristics

% or mean ± SD	Resolute Onyx (N=1003)	BioFreedom (N=993)	*P*-value
Cross-over to other study stent	0.2 (2)	4.0 (40)	<0.001
Pre-procedural QCA			
Lesion length (mm)	21.2 ± 12.5	20.8 ± 12.7	0.48
RVD (mm)	2.84 ± 0.46	2.83 ± 0.44	0.74
MLD (mm)	0.89 ± 0.41	0.90 ± 0.41	0.42
% Diameter stenosis	68.6 ± 13.4	68.2 ± 13.2	0.44
Post-procedural QCA			
% Diameter stenosis (in-stent)	9.9 ± 8.7	11.2 ± 9.4	<0.001
% Diameter stenosis (in-segment)	20.2 ± 9.8	21.2 ± 10.3	0.02
Acute gain (mm, in-stent)	1.72 ± 0.49	1.67 ± 0.48	0.004
Acute gain (mm, in-segment)	1.43 ± 0.50	1.39 ± 0.50	0.045
Lesion success[1]	93.8	94.2	0.67
Device success[2]	92.8	89.7	0.007
Procedure success[3]	83.3	86.2	0.09

Antithrombotic Therapy Transition After PCI



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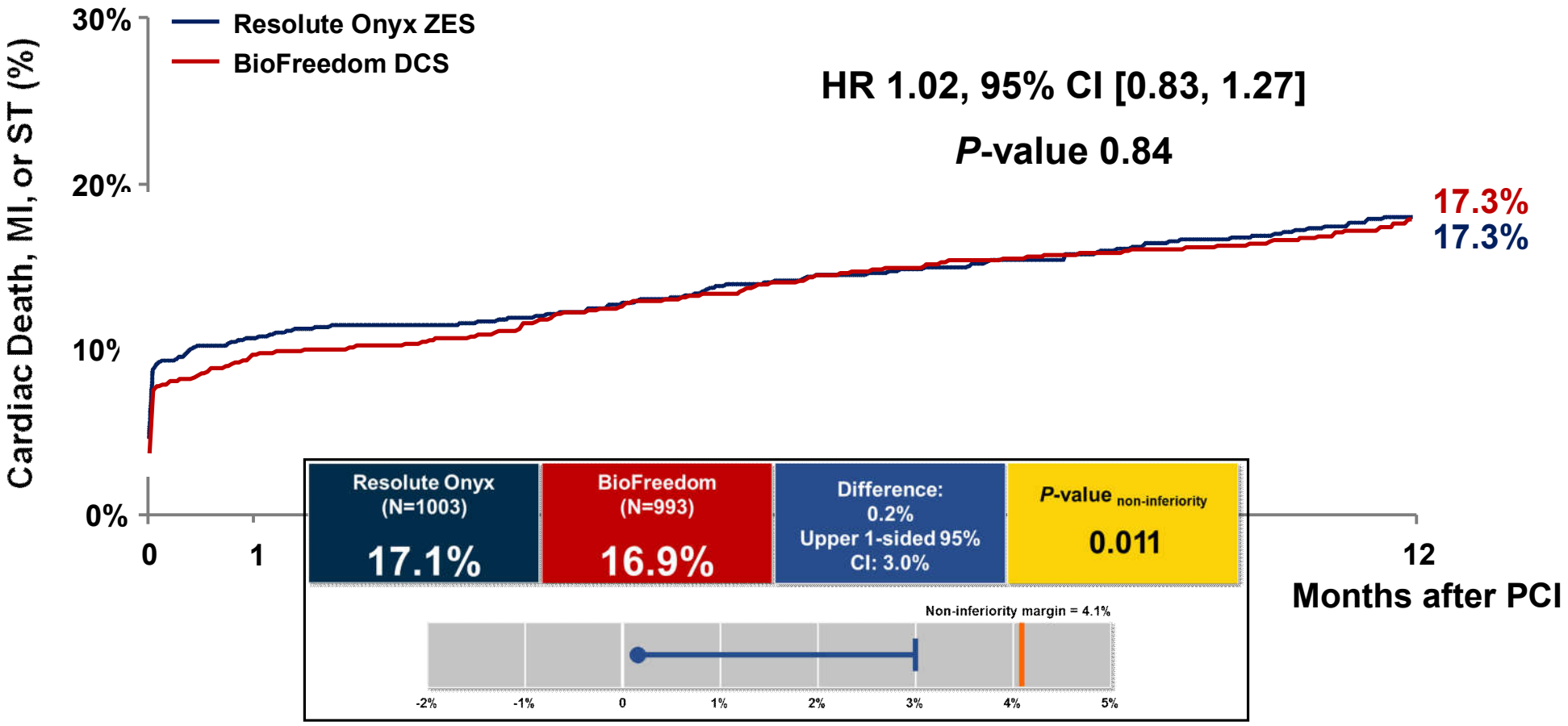
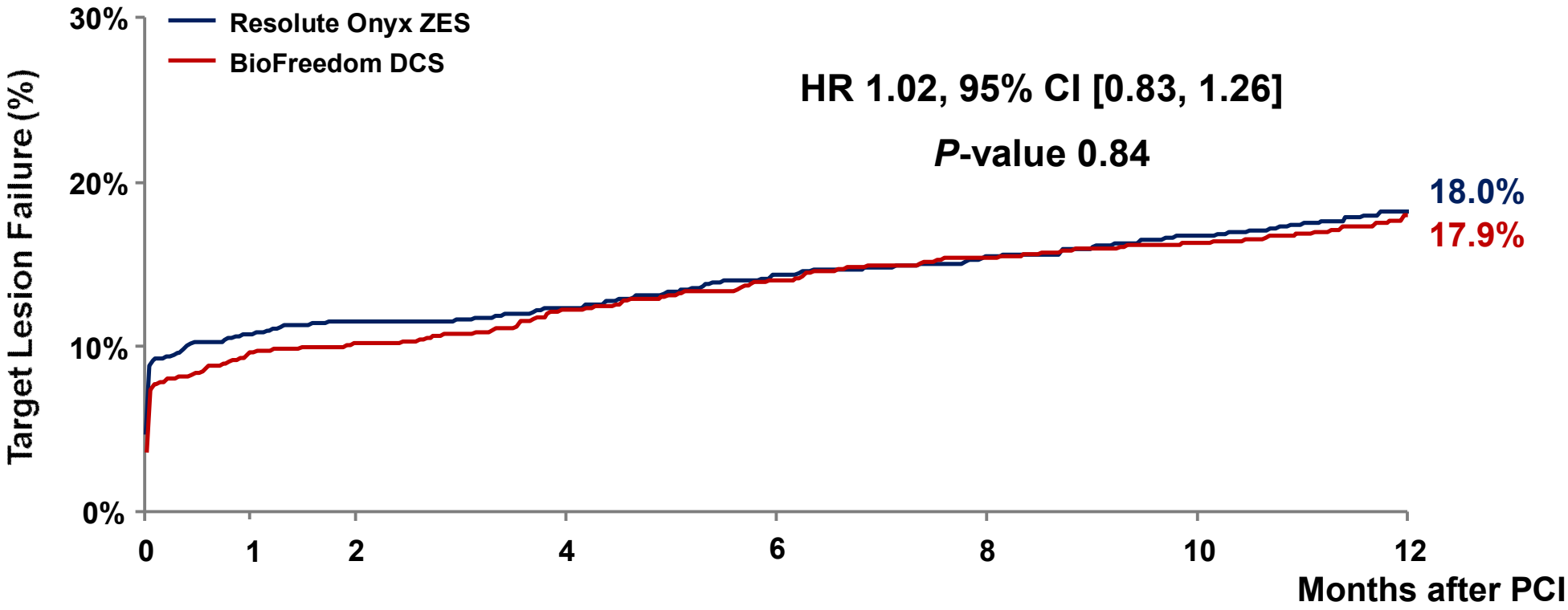
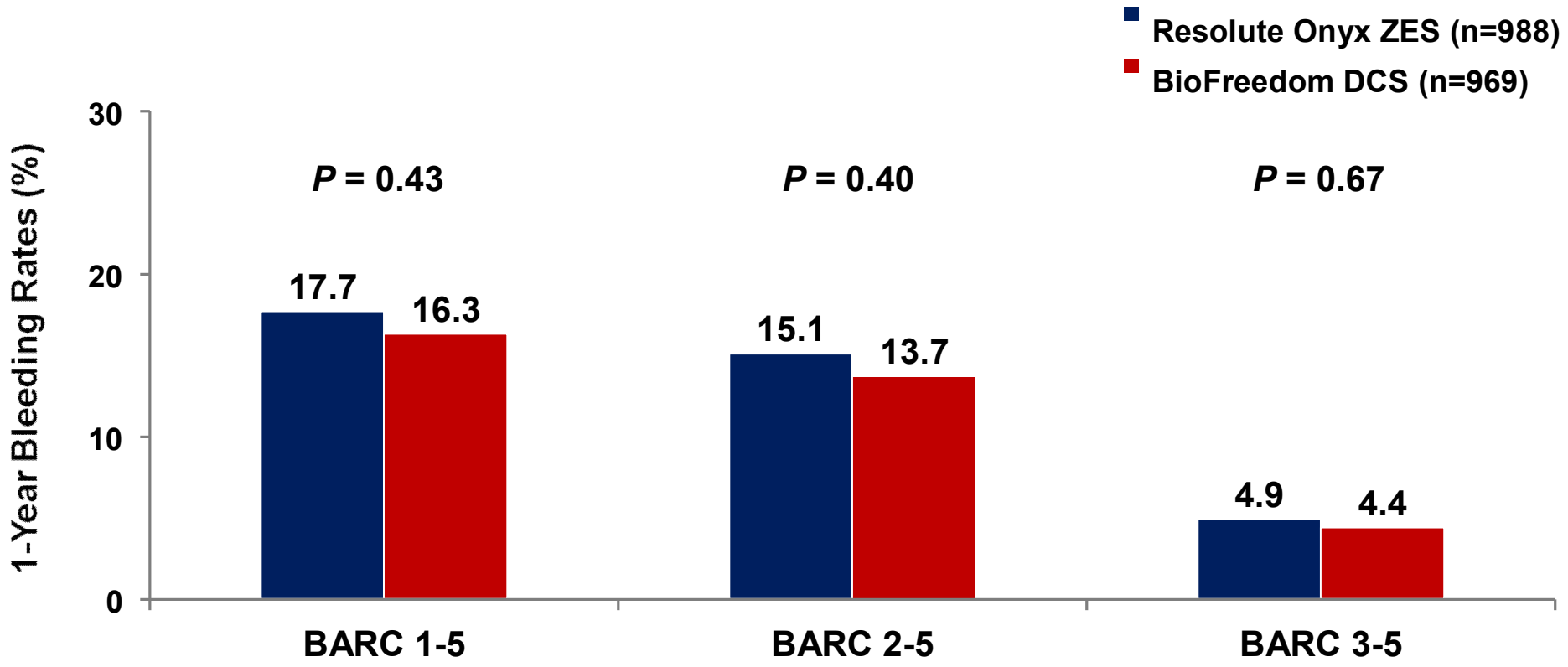
Primary Safety Endpoint: Cardiac Death, MI, or ST



Powered Secondary Effectiveness Endpoint: TLF



BARC Bleeding Rates at 1 Year



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Summary

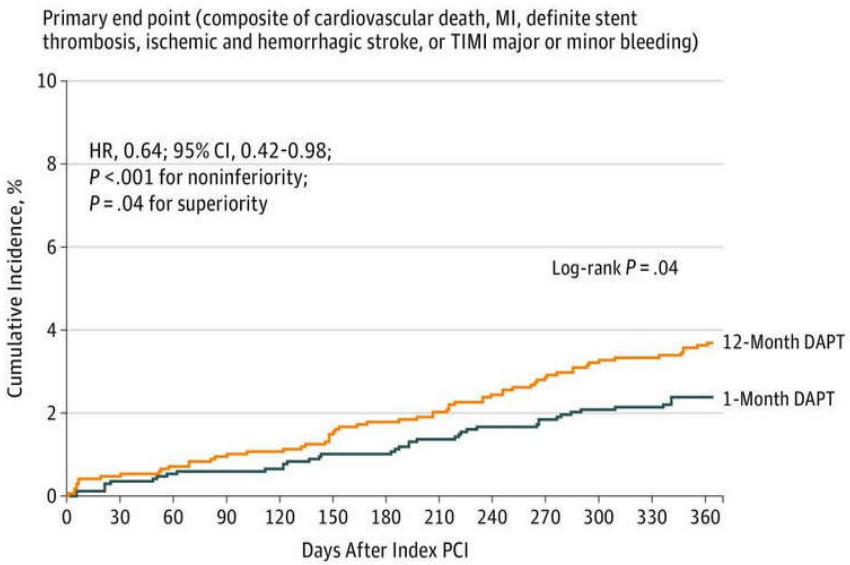
- **ONYX ONE is a contemporary trial:**
  - **First trial comparing DES versus DCS**
  - **Investigating 1-month DAPT**
  - **Very complex HBR patient and lesion population**
- **Among HBR patients treated with 1-month DAPT after PCI, Resolute Onyx was as safe and effective as BioFreedom**
- **Resolute Onyx had improved angiographic outcomes and greater device success post-PCI**

What ONYX-ONE does not validate

- **What stent characteristic is best:**
  - **Zotarolimus vs. Biolimus A9**
  - **Polymer vs. no polymer**
  - **Strut size and shape**

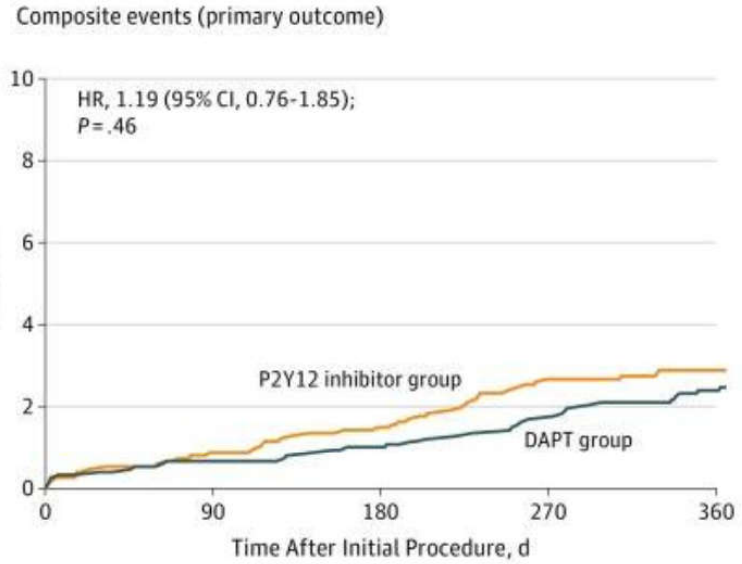
- **What DAPT is best**
- **What SAPT is best @ 1 month**
- **What DAPT duration is optimal in HBR patients**

STOP-DAPT-2



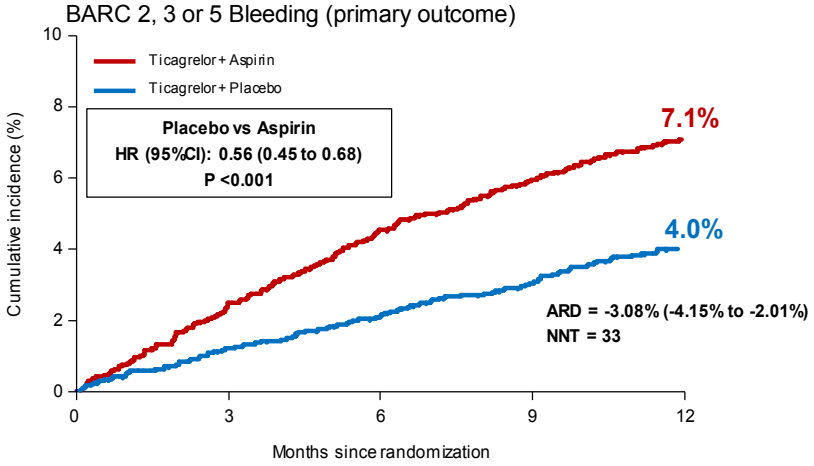
H. Watanabe, JAMA. 2019 Jun 25;321(24):2414-2427

SMART-CHOICE



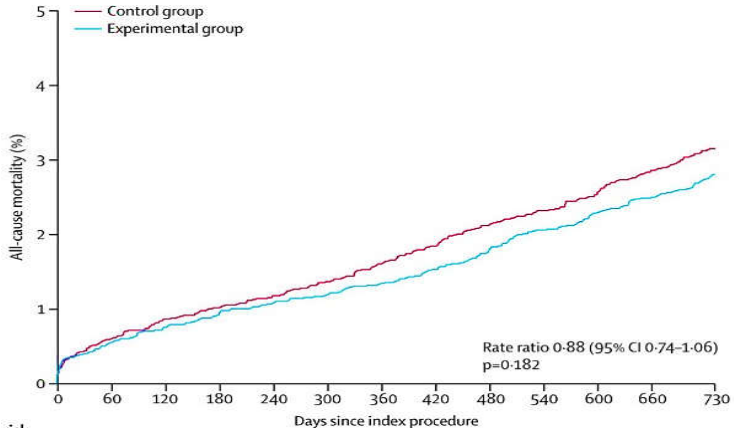
JY Hahn – JAMA. 2019 Jun 25;321(24):2428-2437

TWILIGHT



Mehran R et al. N Engl J Med. 2019 Nov 21;381(21):2032-2042

GLOBAL-LEADERS



Vranckx P et a. Lancet 2018

One-Month Landmark Analyses (Time of DAPT Discontinuation)