

# **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 Treated With 1-Month DAPT**

**Stephan Windecker**

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**on behalf of the Onyx ONE Investigators**

# Disclosure Statement of Financial Interest

**I, Stephan Windecker, declare the following:**

- Research grants to the institution from Abbott, Amgen, Bayer, BMS, Boston Scientific, Biotronik, CLS Behring, Edwards Lifesciences, Medtronic, Polares and Sinomed


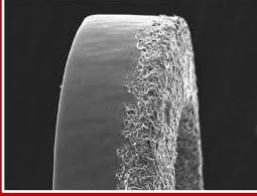
# Background

- Up to 40% of patients undergoing PCI have high bleeding risk (HBR) characteristics
- Guidelines recommend 3-6 months of DAPT for HBR patients undergoing PCI with consideration for DAPT duration as short as 1 month in selected patients
- LEADERS FREE established superiority of polymer-free biolimus-A9 coated stents (BioFreedom) over otherwise identical BMS in terms of both safety and effectiveness in HBR patients treated with 1-month DAPT
- Current generation polymer-based DES have not been compared to polymer-free drug-coated stents (DCS) in HBR patients treated with 1-month DAPT

# Objective

To compare the **safety** and **efficacy** of a **durable polymer-based zotarolimus-eluting stent (Resolute Onyx)** with a **polymer-free biolimus A9-drug coated stent (BioFreedom)** among **HBR** patients undergoing PCI with planned **1-month DAPT**

# Study Devices

	 <b>Resolute Onyx™ DES</b>	 <b>BioFreedom™ DCS</b>
<b>Metallic stent material</b>	CoCr with platinum iridium core	316L Stainless steel
<b>Antiproliferative drug</b>	Zotarolimus	Biolimus A9™
<b>Stent surface characteristic</b>	BioLinx™, biocompatible durable polymer	Polymer-free, selectively micro-structured abluminal surface
<b>Strut thickness (µm)</b>	81 – 91 µm	112 µm
<b>Available stent diameters</b>	2.0 – 5.0 mm	2.25 – 4.0 mm

# Onyx ONE Global Study Design

Prospective, Multicenter, Single-blind Randomized Trial



Clinical Follow-up



- 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  $\geq 75$  years



Thrombocytopenia ( $<100,000/\text{mm}^3$ )



OAC planned after PCI



Cancer diagnosed or treated within 3 yrs



Renal failure (CrCl  $<40$  ml/min)



Stroke within 1 year or any prior ICH



Planned surgery  $<1$  year



Severe chronic liver disease



Anemia (Hgb  $<11$  g/dl)



Long-term NSAID or steroid use

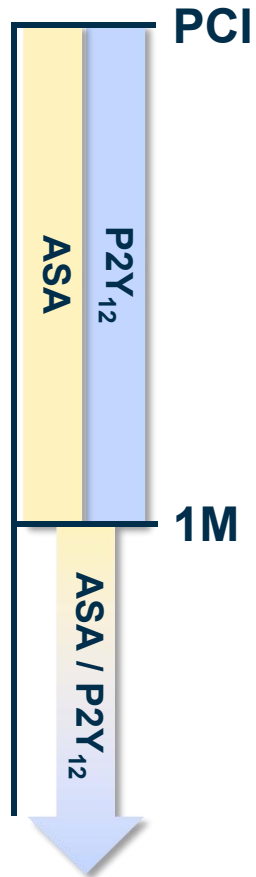


Hospitalization for bleeding within 1 year



Expected DAPT non-compliance

# Antithrombotic Therapy



- **After PCI, 1-month DAPT was prescribed, including:**
  - Daily dose of aspirin (75-100 mg) AND
  - P2Y<sub>12</sub> inhibitor (clopidogrel preferred, others allowed)
    - Patients receiving OAC could receive single or dual antiplatelet therapy during this 1<sup>st</sup> month after PCI
- **After 1-month DAPT, single antiplatelet therapy was prescribed (at physician discretion):**
  - Either aspirin OR
  - P2Y<sub>12</sub> inhibitor



# 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% <sup>1</sup> for both arms	11% for both arms
Non-inferiority margin	4.1%	4.4%
One-sided type I error ( $\alpha$ )		0.05
Power		>90%
Lost to follow-up		10%

**Total sample size: 2000 patients**

# Trial Organization

## Principal Investigators

S. Windecker (Lead PI)  
A. Latib, E. Kedhi (Co-PIs)

## Executive Committee

G. Stone (Program Chair)  
A. Abizaid, D. Kandzari, E. Kedhi, A. Kirtane, A. Latib, R. Mehran, M. Price, D. Simon, S. Windecker, S. Worthley, A. Zaman

## DSMB

JP. Carrozza (Chair)  
Cardiovascular Research Foundation, New York NY, USA

## CEC

S. Marx (Chair)  
Cardiovascular Research Foundation, New York NY, USA

## Angiographic Core Lab

Cardiovascular Research Foundation, New York NY, USA

## Statistics

Medtronic (Analysis) and  
Baim Institute for Clinical Research, Boston MA, USA (Independent Validation)

## Data Management & Monitoring

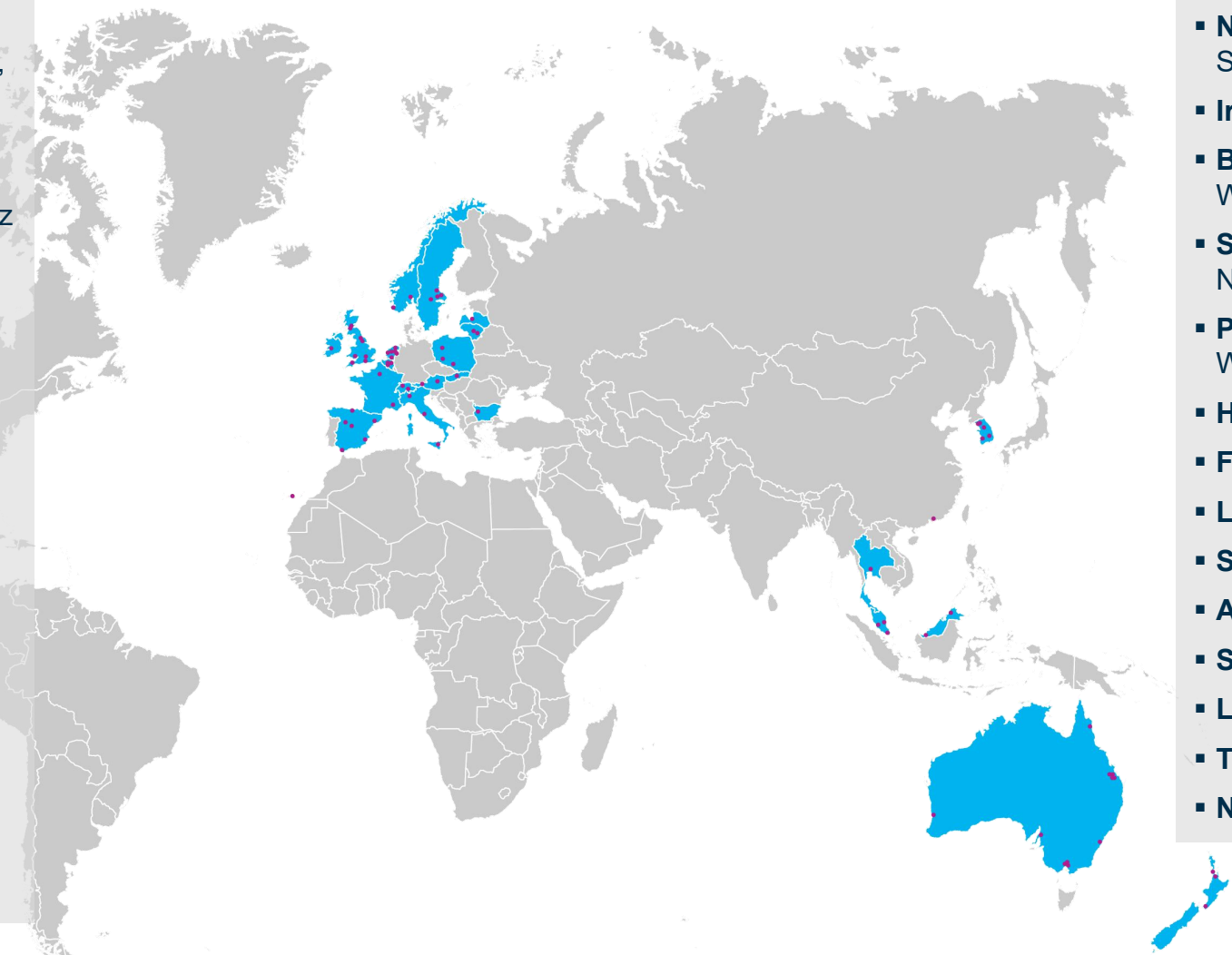
Medtronic, Santa Rosa CA, USA

## Sponsor

Medtronic, Santa Rosa CA, USA


# 84 Participating Centers

- **Republic of Korea:** HS Kim, SH Hur, YS Jang, IH Chae, MH Jeong, JH Yoon, HC Gwon, KY Chang, SJ Park
- **Spain:** E Pinar, R Moreno, F Bosa Ojeda, B Vaquerizo, J de la Torre Hernández, Á Cequier, V Mainar, I Cruz
- **Slovakia:** M Hudec
- **Malaysia:** AKA Ghapar, TK Ong, HB Liew, AA Nuruddin
- **Australia:** C Tie, A Conradie, A Walton, C Hammett, P Garrahy, C Raffel, G Starmer, A Sinhal, S Shetty, R Bhindi, R Whitbourn
- **Italy:** F Fabbicchi, A Latib/M Montorfano, G Sardella, C Tamburino
- **Netherlands:** E Kedhi, A Van 't Hof, R Troquay, MJ Suttorp, S Somi, P van der Harst
- **Bulgaria:** I Petrov
- **United Kingdom:** D Muir, K Oldroyd, A Ludman, R Anderson, N Uren, A Zaman, S Kalra, B. Anantharam

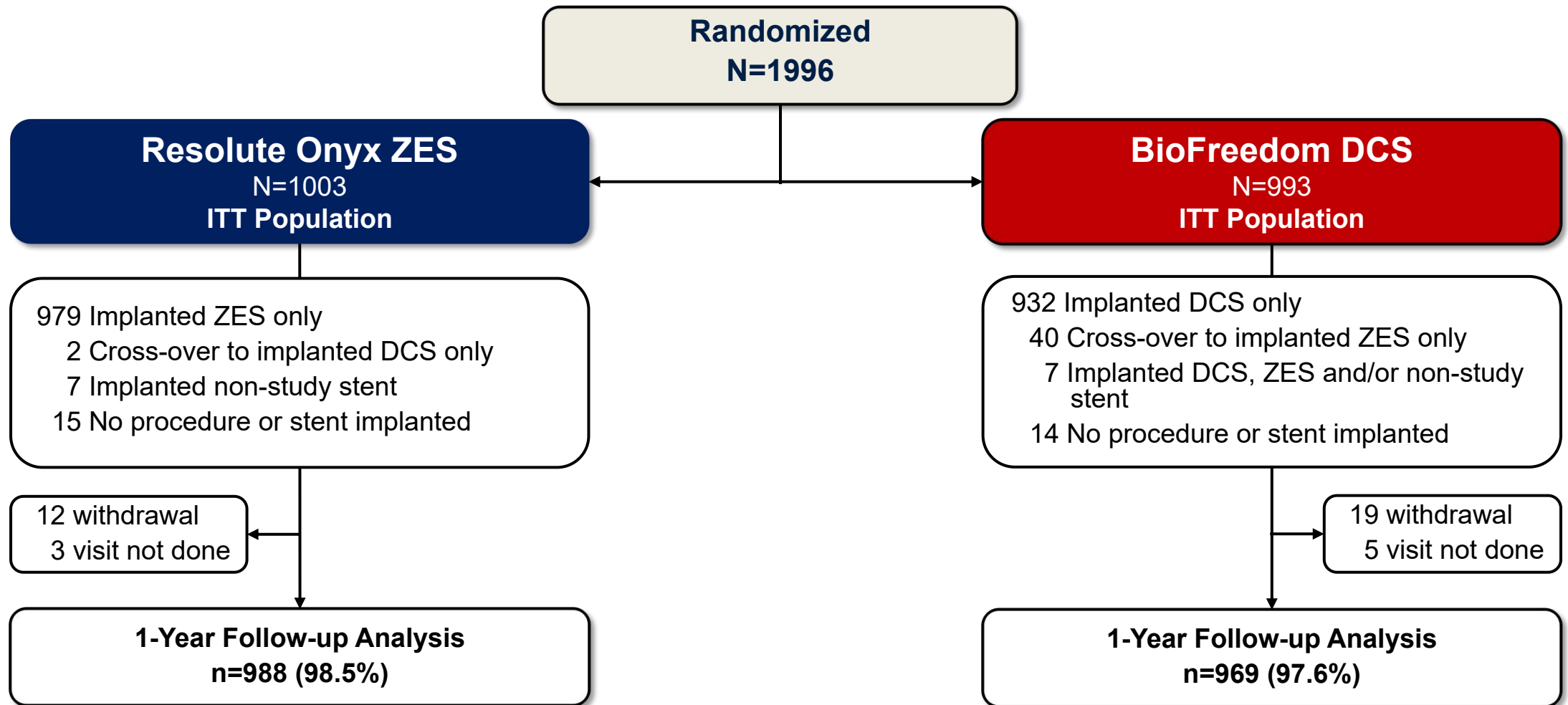


- **New Zealand:** S Pasupati, S Harding, M Webster
- **Ireland:** D Mylotte
- **Belgium:** A Aminian, P Lancellotti, W Desmet
- **Sweden:** E Diderholm, R Kastberg, N Witt, O Fröbert, L Henareh
- **Poland:** A Włodarczak, M Lesiak, W Wojakowski
- **Hong Kong:** FCC Tam, MKY Lee
- **France:** B Chevalier, M Silvestri
- **Latvia:** A Ērglis, A Kalniņš
- **Switzerland:** T Moccetti, S Windecker
- **Austria:** G Toth, G Friedrich
- **Singapore:** PJJ Ong, KH Chan
- **Lithuania:** A Baranauskas, R Unikas
- **Thailand:** D Tresukosol
- **Norway:** A Opdahl, AI Larsen

# Top Enrolling Sites

Site Principal Investigator	Hospital	Location		Patients Randomized
Martin Hudec	Stredoslovensky Ustav Srdcovych a Cievnych Chorob	Banska Bystrica, Slovakia		209
Kahar Abdul Ghapar	Hospital Serdang	Kajang Selangor, Malaysia		153
Ivo Petrov	Acibadem City Clinic	Sofia, Bulgaria		109
Darren Mylotte	University Hospital Galway	Galway, Ireland		63
Eduardo Pinar	Hospital Clínico Universitario Virgen de la Arrixaca	El Palmar, Spain		57
Raul Moreno	Hospital Universitario La Paz	Madrid, Spain		54
Franco Fabbicchi	Centro Cardiologico Monzino	Milan, Italy		53
Sanjeevan Pasupati	Waikato Hospital	Hamilton, New Zealand		52
Hyo Soo Kim	Seoul National University Hospital	Seoul, Korea		50
Adel Aminian	C.H.U. de Charleroi	Charleroi, Belgium		43
Elvin Kedhi	Isala Ziekenhuis	Zwolle, Netherlands		42
Charles Tie	St Andrew's Hospital	Adelaide, Australia		42
Adrian Włodarczak	Mieziowe Centrum Zdrowia	Lubin, Poland		42

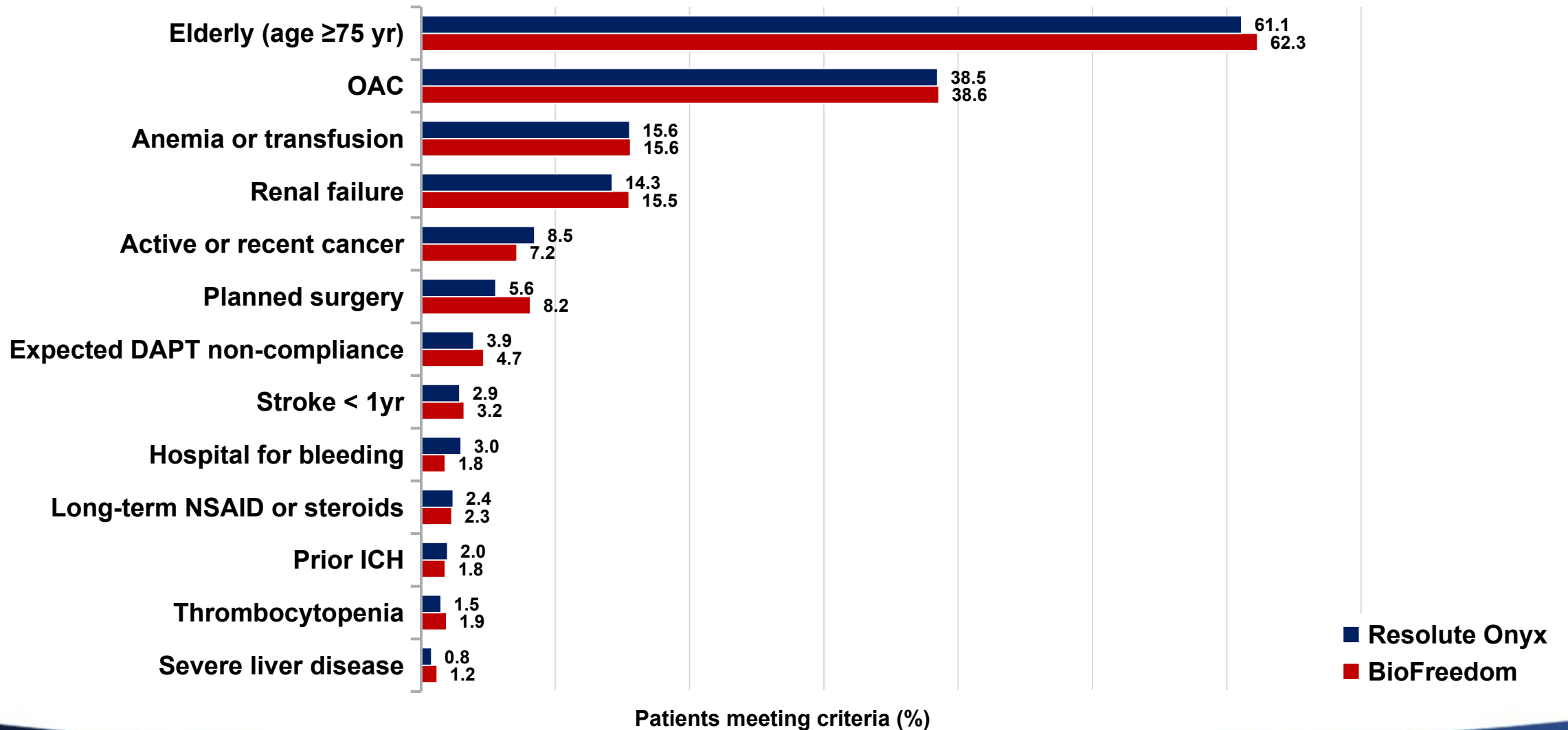
# Patient Flowchart



# 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

# HBR Inclusion Criteria (Mean 1.6 Criteria / Pt)



# Lesion Characteristics

% or mean ± SD	Resolute Onyx (N=1003)	BioFreedom (N=993)	P-value
Radial access	75.0	75.1	0.96
Staged procedure (performed)	2.6	4.7	0.01
<i>Lesion location</i>			
LAD	55.2	59.0	0.09
LCX	25.9	26.1	0.92
RCA	34.5	31.6	0.18
Left main	1.3	1.9	0.29
Bypass graft	2.4	2.0	0.65
Bifurcation	15.2	16.8	0.26
Moderate/severe calcification	46.4	48.5	0.30
B2/C lesion class	79.7	79.9	0.96
Number of treated lesions per patient	1.3 ± 0.6	1.3 ± 0.6	0.85
Number of stents per patient	1.7 ± 1.0	1.7 ± 1.0	0.73
Total stent length per patient (mm)	37.9 ± 25.2	37.3 ± 25.0	0.61



# Procedural Characteristics

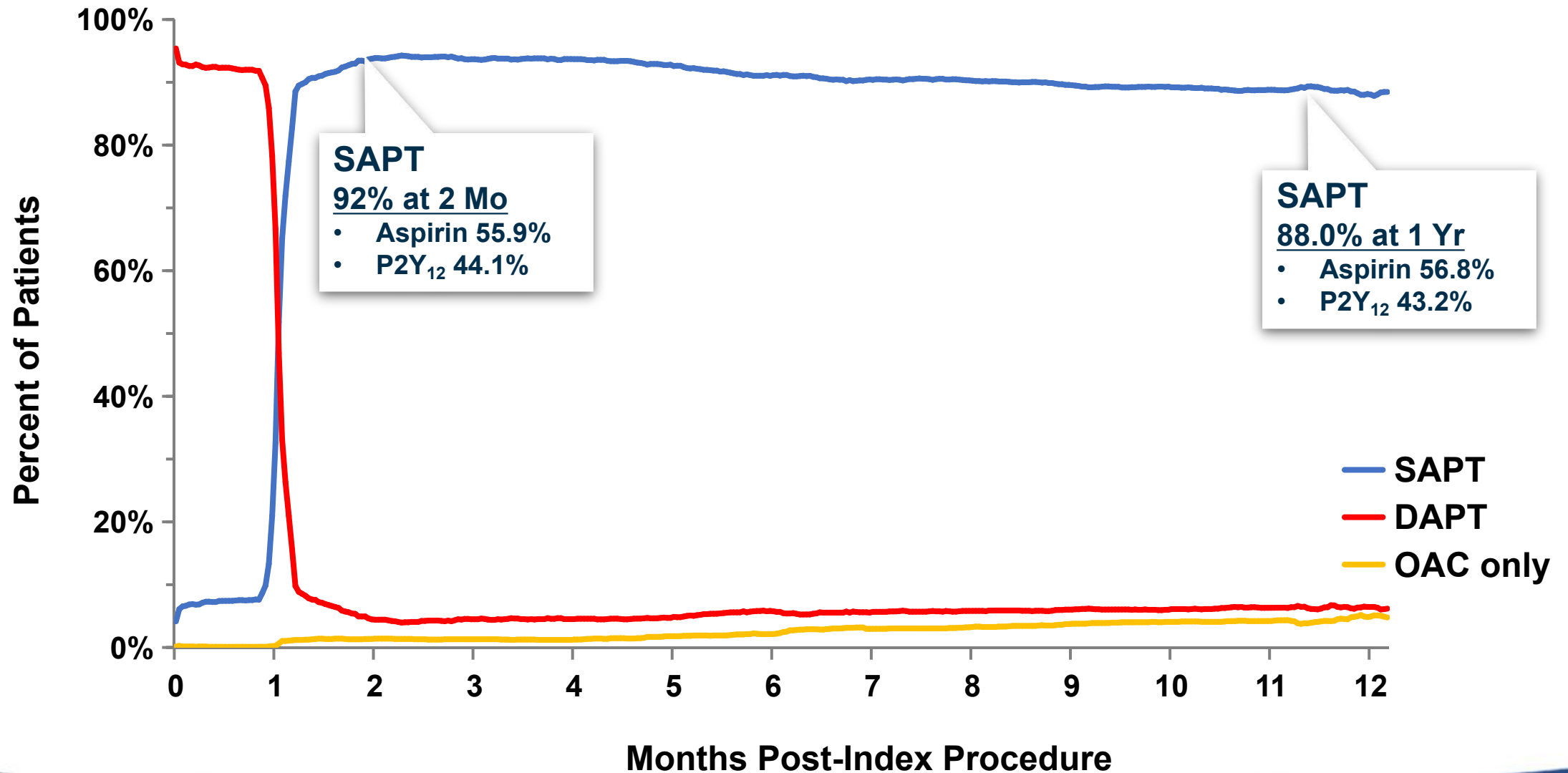
% or mean ± SD	Resolute Onyx (N=1003)	BioFreedom (N=993)	P-value
Cross-over to other study stent	0.2 (2)	4.0 (40)	<0.001
<i>Pre-procedural QCA</i>			
Lesion length (mm)	21.2 ± 12.5	20.8 ± 12.7	0.48
RVD (mm)	2.84 ± 0.46	2.83 ± 0.44	0.74
MLD (mm)	0.89 ± 0.41	0.90 ± 0.41	0.42
% Diameter stenosis	68.6 ± 13.4	68.2 ± 13.2	0.44
<i>Post-procedural QCA</i>			
% 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 <sup>1</sup>	93.8	94.2	0.67
Device success <sup>2</sup>	92.8	89.7	0.007
Procedure success <sup>3</sup>	83.3	86.2	0.09

<sup>1</sup> The attainment of <30% residual stenosis by QCA (or <20% by visual assessment) and TIMI flow 3 after the procedure, using any percutaneous method.

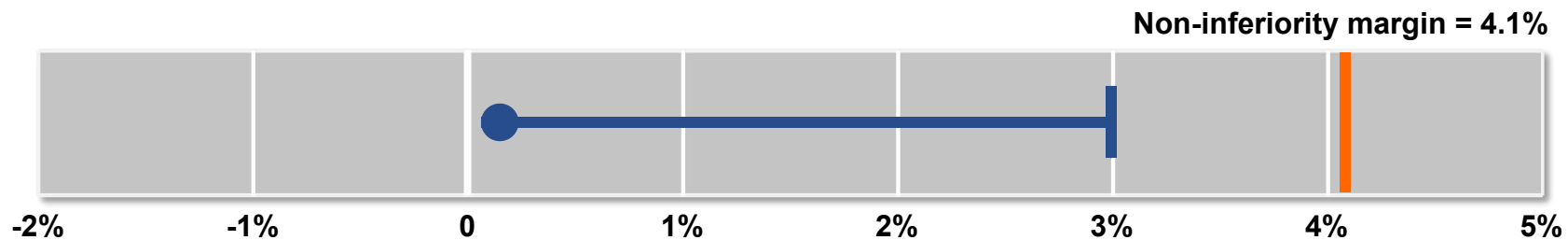
<sup>2</sup> The attainment of <30% residual stenosis by QCA (or <20% by visual assessment) and TIMI flow 3 after the procedure, using the assigned device only.

<sup>3</sup> The attainment of <30% residual stenosis by QCA (or <20% by visual assessment) and TIMI flow 3 after the procedure, using any percutaneous method without the occurrence of MACE during the hospital stay.

# Antithrombotic Therapy Transition After PCI

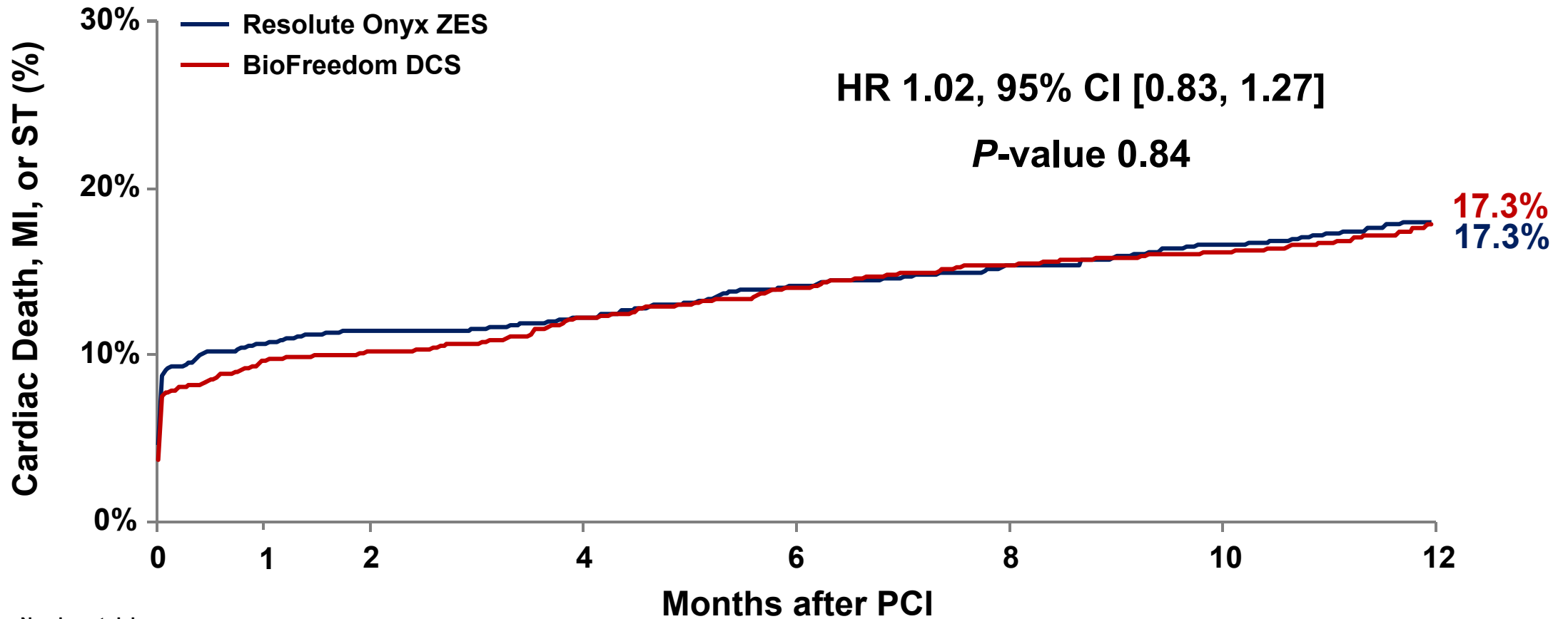


# Primary Safety Endpoint: Cardiac Death, MI, ST



**Non-Inferiority Endpoint Met**

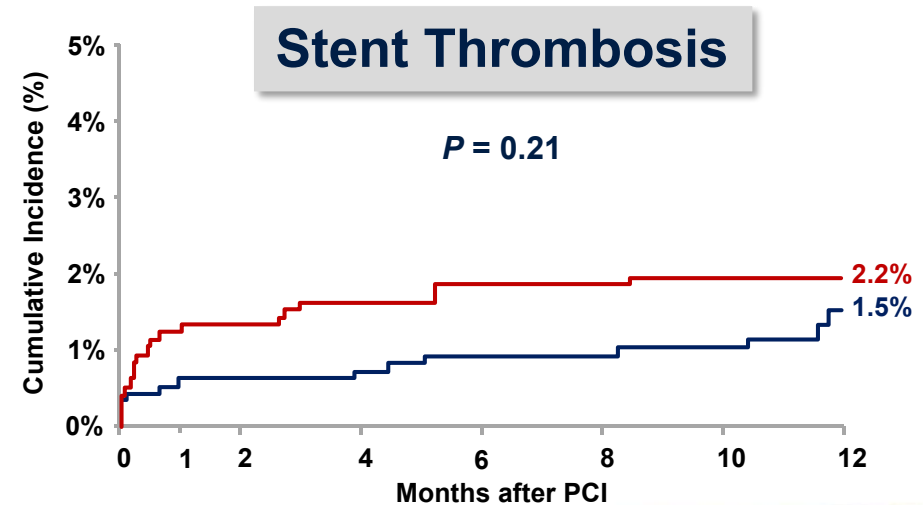
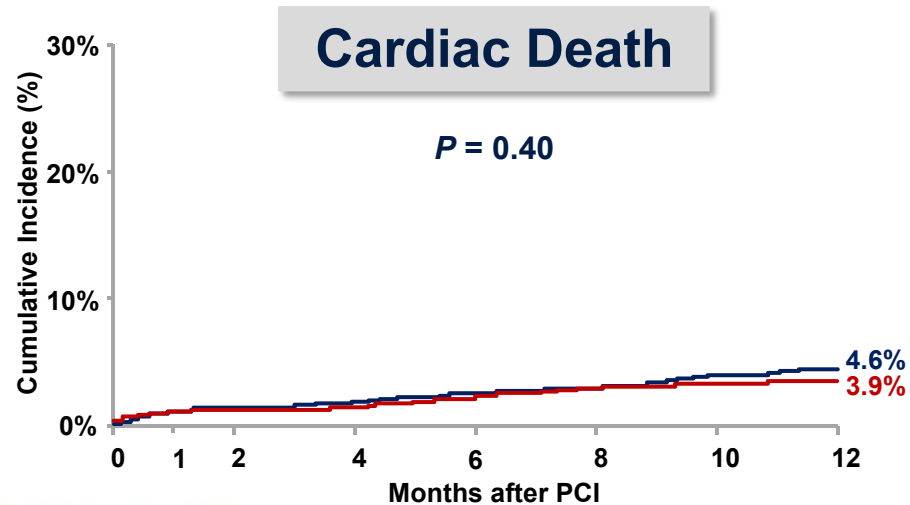
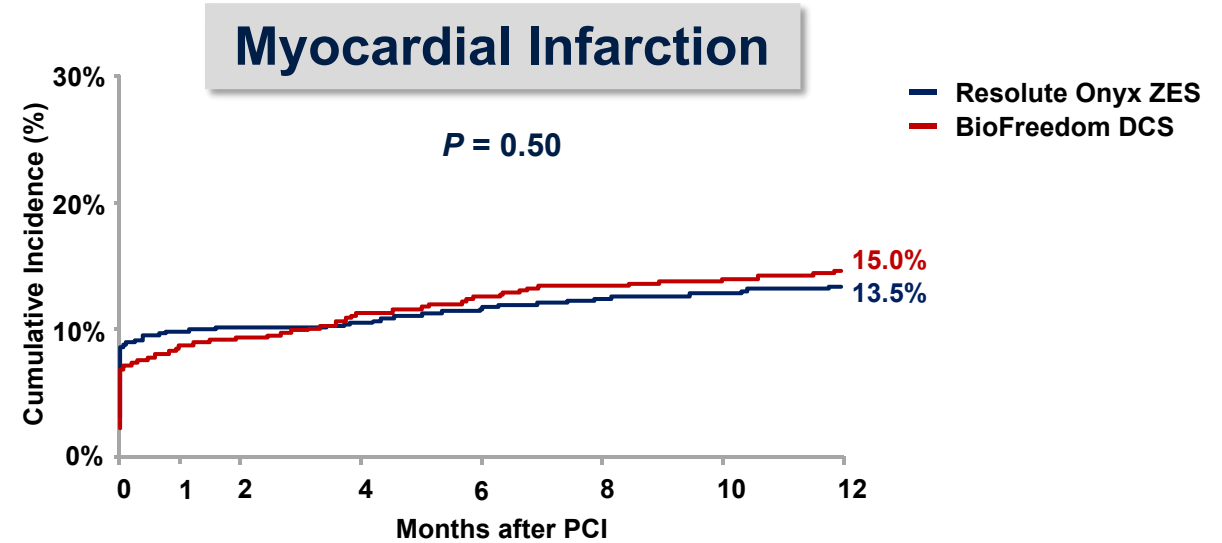
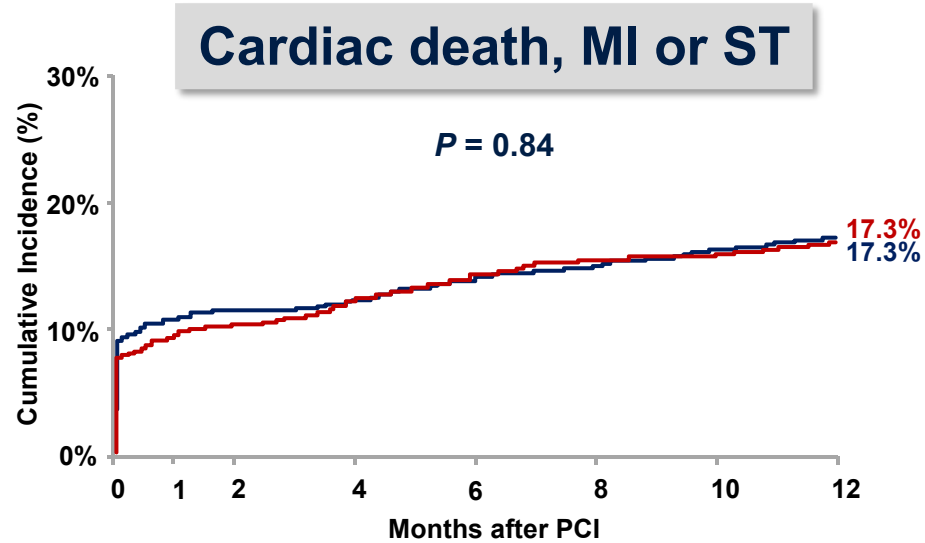
# Primary Safety Endpoint: Cardiac Death, MI, or ST



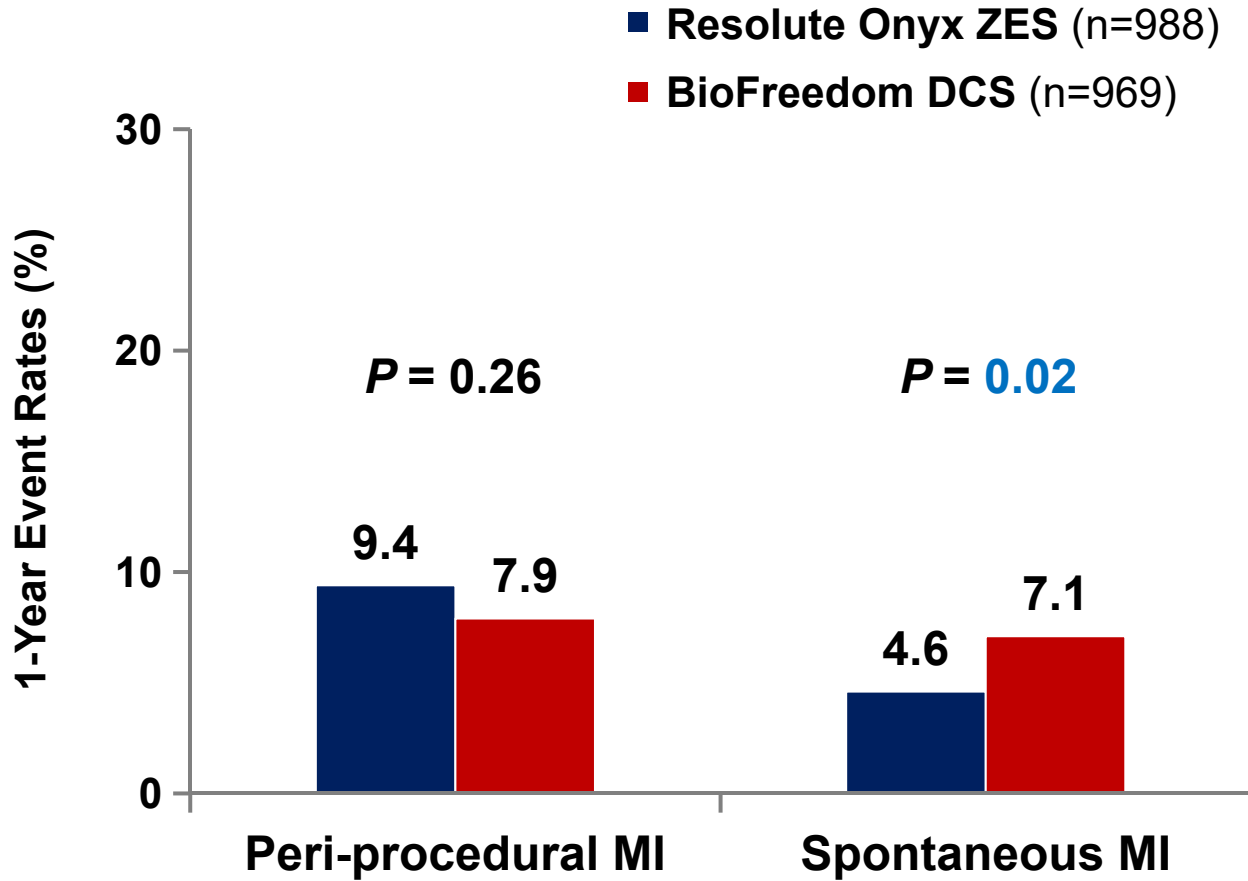
Number at risk

ZES	1003	955	844	790
DCS	993	949	833	782

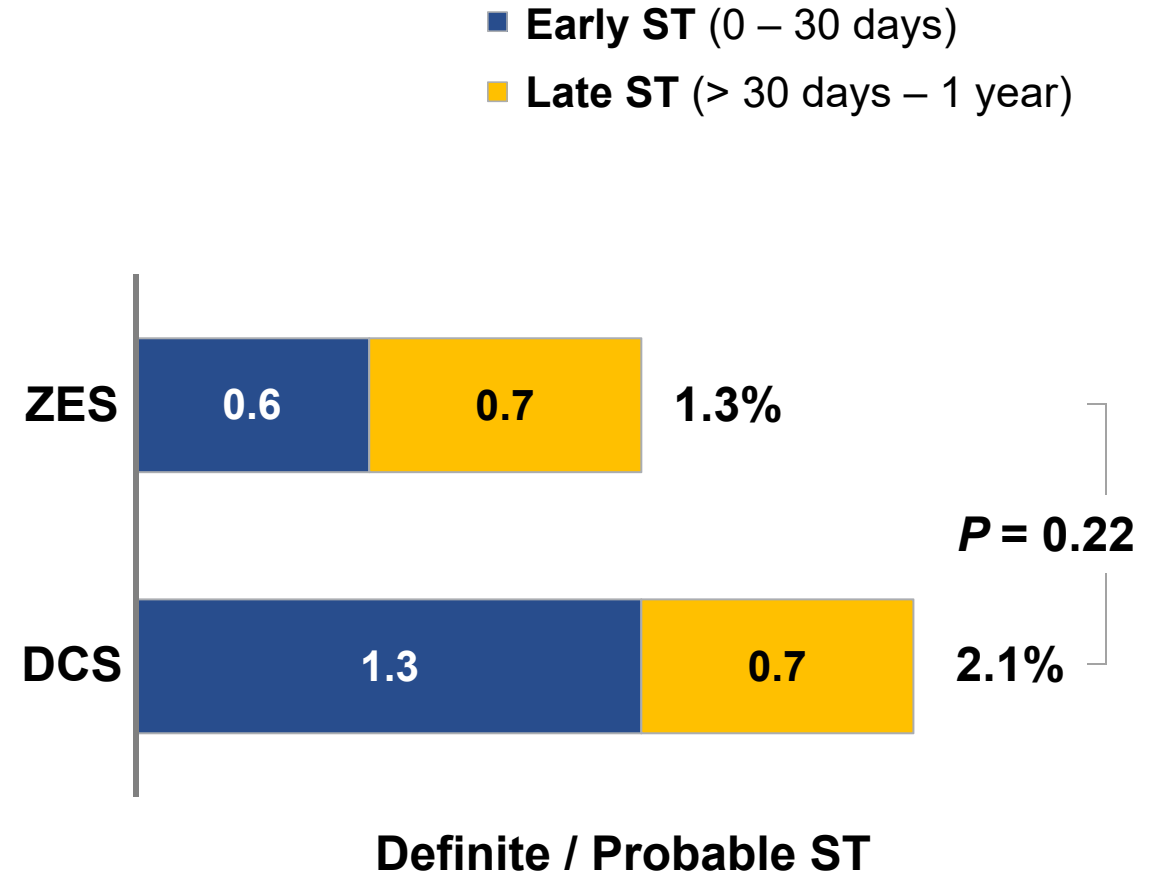
# Primary Safety Endpoint and Components



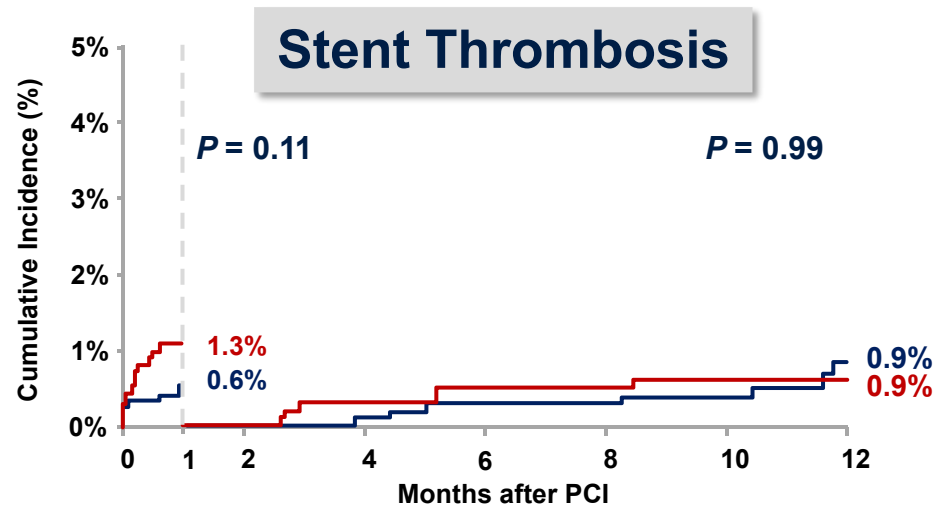
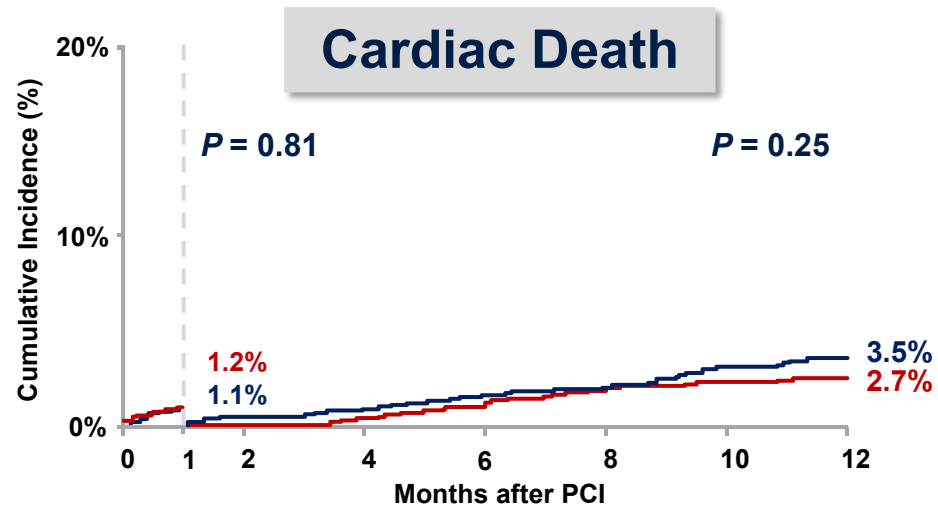
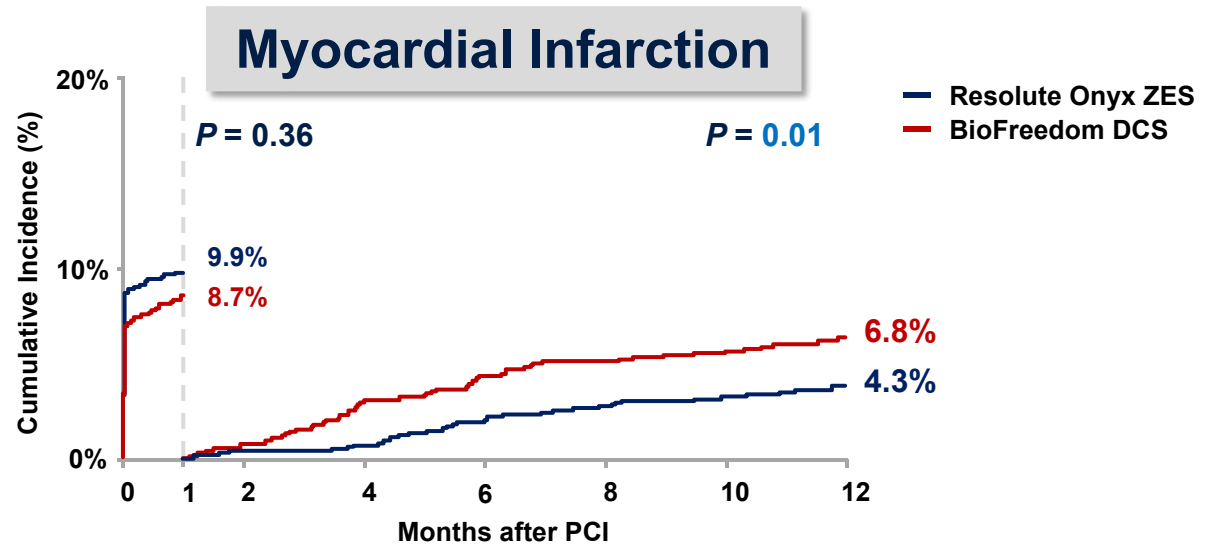
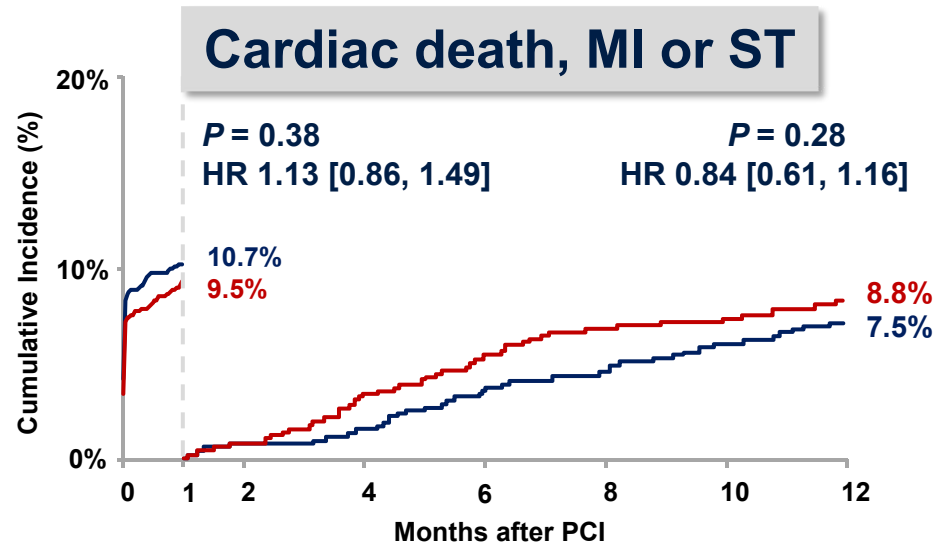
# Myocardial Infarction



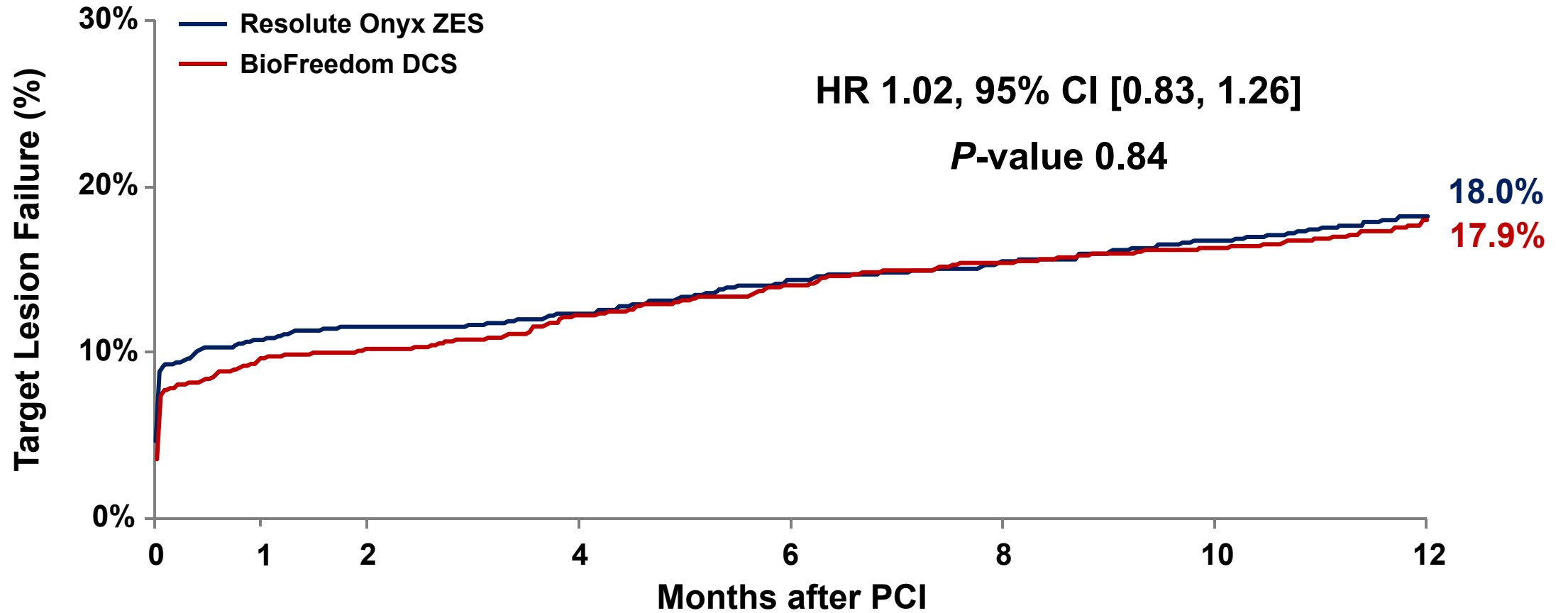
# Stent Thrombosis



# One-Month Landmark Analyses (Time of DAPT Discontinuation)



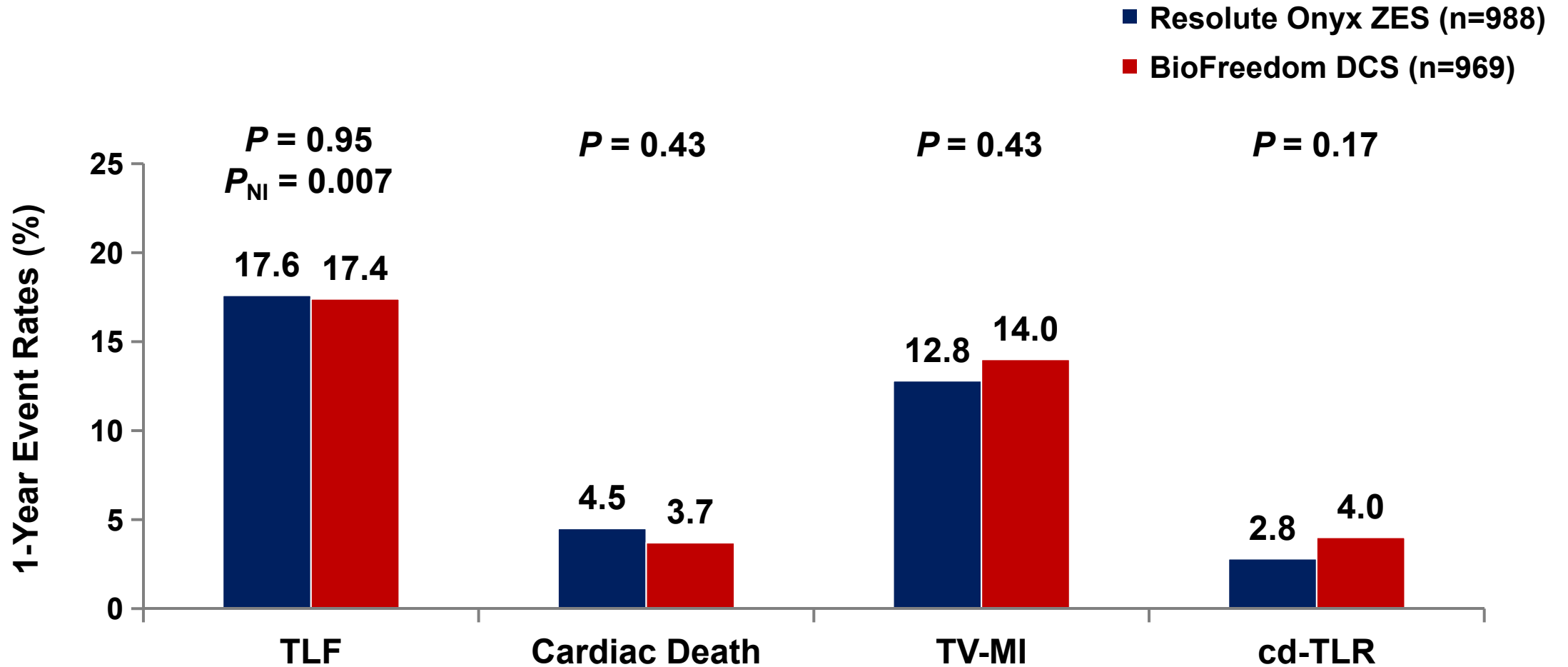
# Powered Secondary Effectiveness Endpoint: TLF



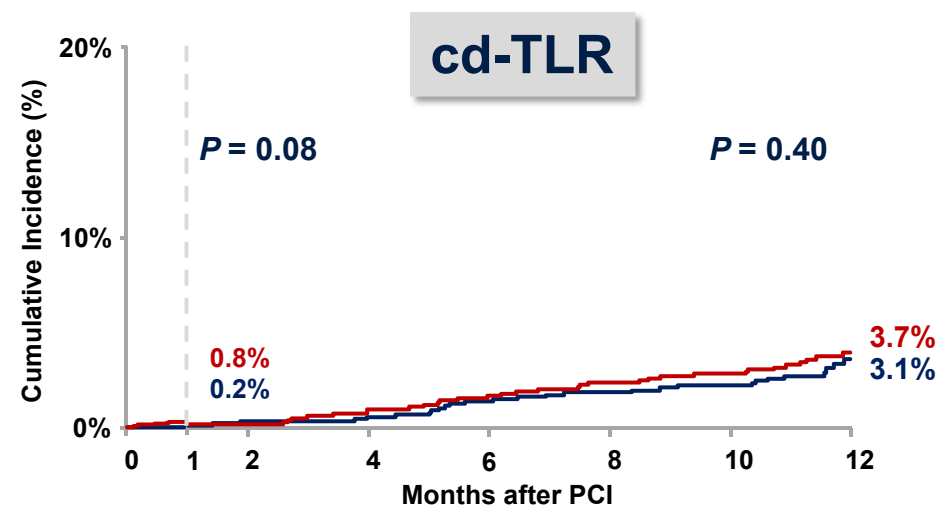
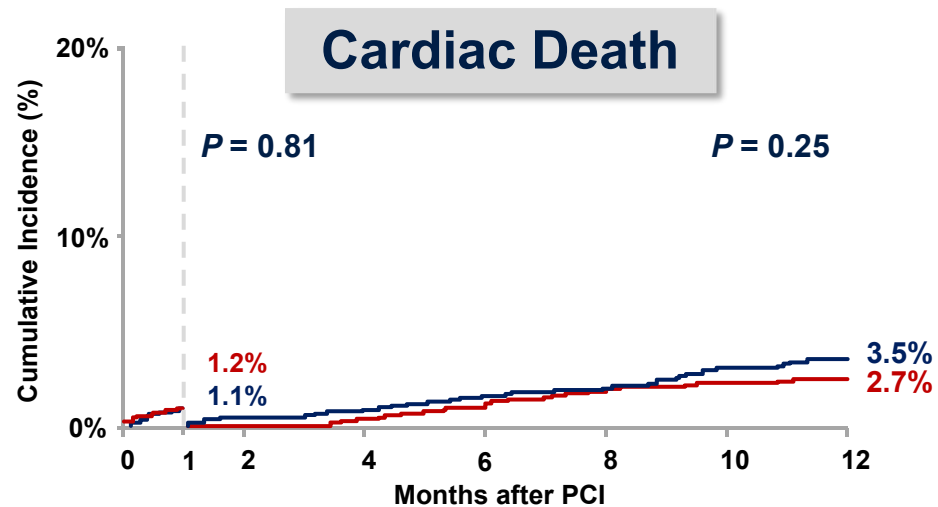
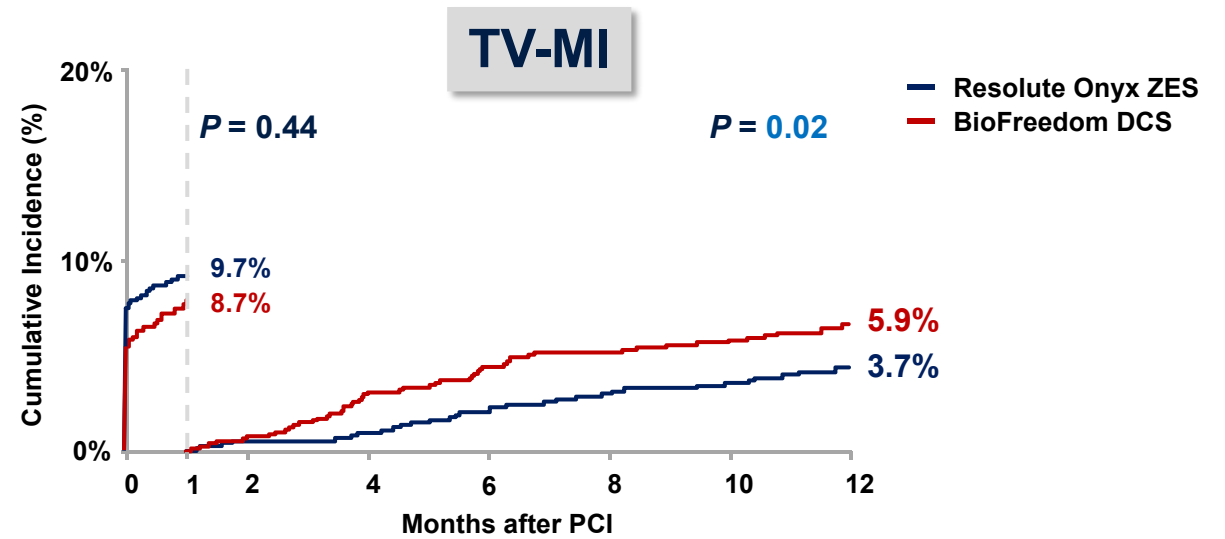
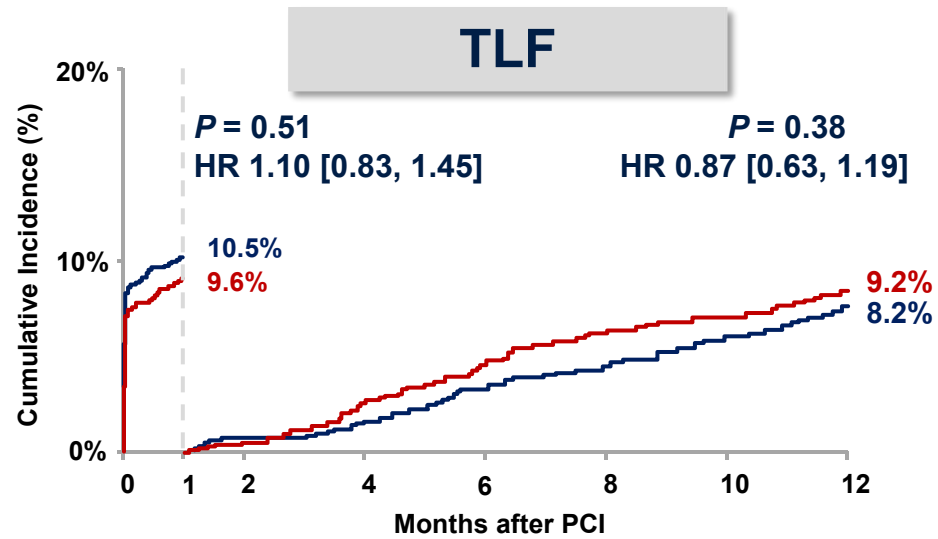
Number at risk				
	0	1	6	12
ZES	1003	956	845	787
DCS	993	949	835	779



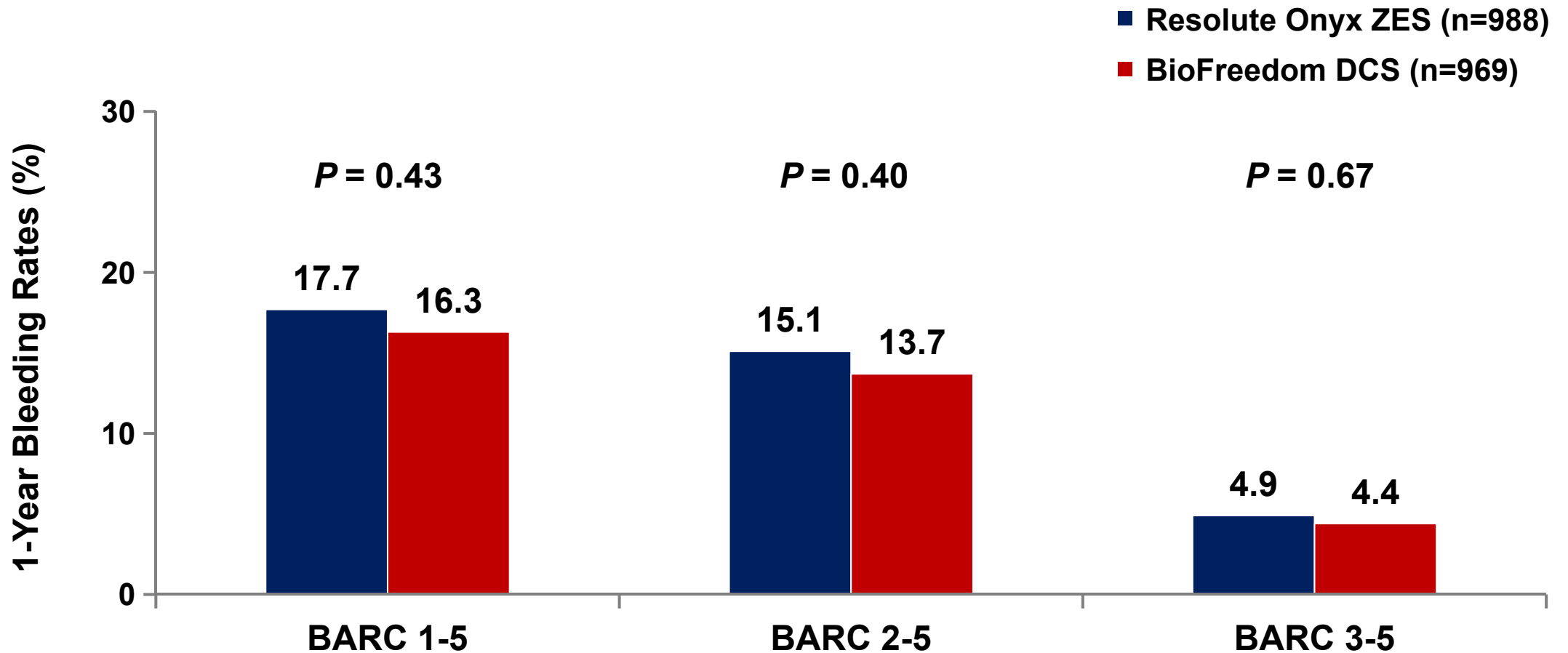
# Powered Secondary Effectiveness Endpoint: TLF at 1 Year



# One-Month Landmark Analyses (Time of DAPT Discontinuation)



# BARC Bleeding Rates at 1 Year



# Limitations

- **Single-blinded trial**
  - More frequent crossover in pts allocated to BioFreedom
  - Patients and outcome assessors were blinded to allocation
- **Trial not powered for low frequency 2° endpoints (TLR, ST)**
  - Powered for non-inferiority of 1° safety and 2° effectiveness EP
- **Periprocedural MI prior to DAPT interruption at 30 days significantly contributed to 1° EP and powered 2° EP**
  - Results were consistent in 30-day landmark analyses
- **Lack of control arm of 3- or 6-month DAPT**














# 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**

# Conclusion

**These data demonstrate that  
Resolute Onyx is safe and effective  
in complex high bleeding risk  
patients who receive 1-month DAPT**

# Participating Centers (1)














Principal Investigator	Hospital	Location		Patients Randomized
Martin Hudec	Stredoslovenský ústav srdcových a cievnych chorôb	Banská Bystrica, Slovakia		209
Abd Kahar Abd Ghapar	Hospital Serdang	Kajang, Malaysia		153
Ivo Petrov	Acibadem City Clinic	Sofia, Bulgaria		109
Darren Mylotte	University Hospital Galway	Galway, Ireland		63
Eduardo Pinar	Hospital Clínico Universitario Virgen de la Arrixaca	El Palmar, Spain		57
Raul Moreno	Hospital Universitario La Paz	Madrid, Spain		54
Franco Fabbicchi	Centro Cardiologico Monzino	Milan, Italy		53
Sanjeevan Pasupati	Waikato Hospital	Hamilton, New Zealand		52
Hyo-Soo Kim	Seoul National University Hospital	Seoul, South Korea		50
Adel Aminian	C.H.U. de Charleroi	Charleroi, Belgium		43
Elvin Kedhi	Isala Ziekenhuis	Zwolle, Netherlands		42
Charles Tie	Adelaide Cardiology	Adelaide, Australia		42
Adrian Włodarczak	Mieziowe Centrum Zdrowia	Lubin, Poland		42

# Participating Centers (2)














Principal Investigator	Hospital	Location		Patients Randomized
Seung-Ho Hur	Keimyung University Dongsan Medical Center	Daegu, South Korea		41
Andre Conradie	Bundaberg Cardiology - Friendly Society Private Hospital	Bundaberg, Australia		35
Frankie Chor Cheong Tam	Queen Mary Hospital	Hong Kong		33
Azeem Latib	Ospedale San Raffaele	Milan, Italy		31
Yangsoo Jang	Severance Hospital	Seoul, South Korea		30
In-Ho Chae	Seoul National University Bundang Hospital	Seongnam-si, South Korea		29
Antony Walton	The Alfred Hospital	Melbourne, Australia		26
Francisco Bosa Ojeda	Hospital Universitario de Canarias	La Laguna, Spain		26
Beatriz Vaquerizo	Hospital del Mar	Barcelona, Spain		25
Douglas Muir	The James Cook University Hospital - South Tees Hospitals NH	Middlesbrough, United Kingdom		25
Bernard Chevalier	Hôpital Privé Jacques Cartier	Massy, France		24
Tiong Kiam Ong	Sarawak Heart Centre	Kota Samarahan, Malaysia		24
Arnoud Van 't Hof	Maastricht Universitair Medisch Centrum (MUMC)	Maastricht, Netherlands		24
















# Participating Centers (3)

Principal Investigator	Hospital	Location		Patients Randomized
José María de la Torre Hernández	Hospital Universitario Marques de Valdecilla	Santander-Cantabria, Spain		23
Christopher Hammett	Royal Brisbane and Women's Hospital	Herston, Australia		22
Houng Bang Liew	Hospital Queen Elizabeth II	Kota Kinabalu, Malaysia		22
Gennaro Sardella	Umberto I - Policlinico di Roma	Rome, Italy		21
Myung Ho Jeong	Chonnam National University Hospital	Gwangju, South Korea		21
Ángel Cequier	Hospital Universitari Bellvitge	Barcelona, Spain		21
Junghan Yoon	Wonju Severance Christian Hospital	Wonju, South Korea		20
Hyeon-Cheol Gwon	Samsung Medical Center	Seoul, South Korea		20
Paul Garrahy	Princess Alexandra Hospital	Woolloongabba, Australia		19
Corrado Tamburino	Presidio Ospedaliero Gaspare Rodolico	Catania, Italy		18
Andrējs Ērglis	Paula Stradiņa Klīniskā universitātes slimnīca	Riga, Latvia		17
Roel Troquay	VieCuri Medisch Centrum voor Noord-Limburg - Locatie Venlo	Venlo, Netherlands		17
Erik Diderholm	Västmanlands Sjukhus	Västerås, Sweden		17

# Participating Centers (4)

Principal Investigator	Hospital	Location		Patients Randomized
Tiziano Moccetti	Cardiocentro Ticino	Lugano, Switzerland		17
Keith Oldroyd	Golden Jubilee National Hospital - NHS Trust	Glasgow, United Kingdom		17
Paul Jau Leung Ong	Tan Tock Seng Hospital	Singapore		16
Gabor Toth	LKH - Universitätsklinikum Graz	Graz, Austria		15
Kiyuk Chang	Seoul St. Mary's Hospital	Seoul, South Korea		15
Andrew Ludman	Royal Devon and Exeter NHS Foundation Trust	Exeter, United Kingdom		15
Seung-Jung Park	Asan Medical Center	Seoul, South Korea		14
Richard Anderson	Cardiff and Vale University Health Board - (UHW)	Cardiff, United Kingdom		14
Christopher Raffel	The Prince Charles Hospital	Chermside, Australia		13
Gregory Starmer	Cairns Hospital	Cairns, Australia		13
Maarten Jan Suttorp	St. Antonius Ziekenhuis	Nieuwegein, Netherlands		13
Robert Kastberg	Gävle sjukhus	Gävle, Sweden		12
Neal Uren	Royal Infirmary of Edinburgh	Edinburgh, United Kingdom		12



# Participating Centers (5)

Principal Investigator	Hospital	Location		Patients Randomized
Scott Harding	Wellington Hospital	Newtown, New Zealand		11
Vincente Mainar	Hospital General Universitario de Alicante	Alicante, Spain		11
Ignacio Cruz	Hospital Clinico Universitario de Salamanca	Salamanca, Spain		11
Nils Witt	Södersjukhuset	Stockholm, Sweden		11
Ajay Sinhal	Flinders Medical Centre	Bedford Park, Australia		10
Samer Somi	HagaZiekenhuis - Locatie Leyweg	Den Haag, Netherlands		10
Ole Fröbert	Universitetssjukhuset Örebro	Örebro, Sweden		10
Patrizio Lancellotti	CHU de Liège - Hôpital du Sart Tilman	Liège, Belgium		9
Walter Desmet	UZ Leuven - Campus Gasthuisberg	Leuven, Belgium		9
Michael Kang Yin Lee	Queen Elizabeth Hospital	Hong Kong		9
Artis Kalniņš	Riga East University Hospital	Riga, Latvia		9
Azfar Zaman	The Newcastle upon Tyne Hospitals	Newcastle upon Tyne, United Kingdom		9
Arvydas Baranauskas	Vilnius University Hospital Santariskiu Klinikos	Vilnius, Lithuania		8

# Participating Centers (6)

Principal Investigator	Hospital	Location		Patients Randomized
Guy Friedrich	A.ö. Landeskrankenhaus - Universitätskliniken Innsbruck	Innsbruck, Austria		7
Mark Webster	Auckland City Hospital	Auckland, New Zealand		7
Loghman Henareh	Karolinska Universitetssjukhuset	Stockholm, Sweden		7
Stephan Windecker	Inselspital - Universitätsspital Bern	Bern, Switzerland		7
Sharad Shetty	Fiona Stanley Hospital	Perth, Australia		6
Ramūnas Unikas	Hospital of Lithuanian University of Health Sciences Kauno Klinikos	Kaunas, Lithuania		6
Pim van der Harst	Universitair Medisch Centrum Groningen	Groningen, Netherlands		6
Koo Hui Chan	National University Heart Center Singapore	Singapore		6
Maciej Lesiak	Szpital Kliniczny Przemienienia Panskiego	Poznań, Poland		5
Sundeep Kalra	Royal Free Hospital	London, United Kingdom		5
Ravinay Bhindi	Royal North Shore Hospital	St. Leonards, Australia		4
Wojciech Wojakowski	Górnośląskie Centrum Medyczne im prof Leszka Gieca Śląskiego Uniwersytetu Medycznego w Katowicach	Katowice, Poland		4
Damras Tresukosol	Siriraj Hospital	Bangkok, Thailand		4

# Participating Centers (7)

Principal Investigator	Hospital	Location		Patients Randomized
Marc Silvestri	Clinique Axiom	Aix en Provence, France		3
Brijesh Anantharam	Queen Alexandra Hospital	Portsmouth, United Kingdom		3
Robert Whitbourn	Saint Vincent's Hospital Melbourne	Fitzroy, Australia		1
Amin Ariff Nuruddin	Institut Jantung Negara	Kuala Lumpur, Malaysia		1
Anders Opdahl	Oslo - Ullevål Universitetssykehus	Oslo, Norway		1
Alf Inge Larsen	Stavanger Universitetssjukehus - Helse Stavanger HF	Stavanger, Norway		1