1-Year and Landmark 6-12 Month Clinical Outcomes from the INFINITY-SWEDEHEART Randomized Clinical Trial:

Bioadaptor Implant Compared to a Contemporary Drug-Eluting Stent Among Patients in Complex Lesion Subsets

David Erlinge, M.D., Ph.D. on behalf of Stefan James, M.D., Ph.D. and the INFINITY-SWEDEHEART investigators

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Disclosure of Relevant Financial Relationships

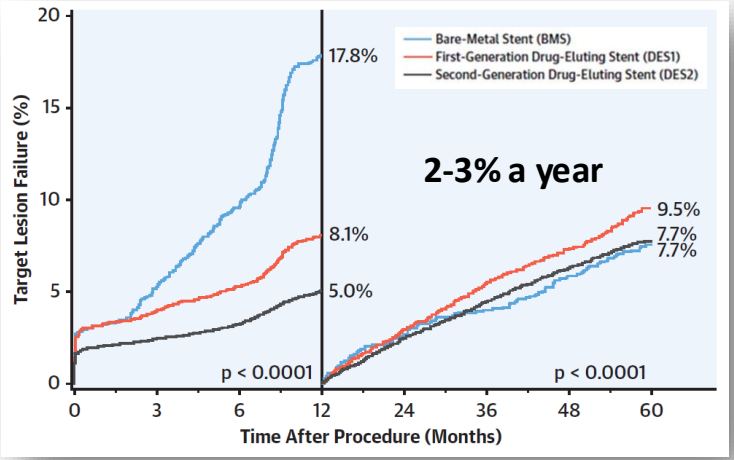
Within the prior 24 months, I, *David Erlinge*, have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

Nature of Financial Relationship	**Ineligible Company**
Consultant Fees/Honoraria	Amgen, AstraZeneca, Chiesi, Sanofi, NovoNordisk, InfraredX/Nipro and Kaminari Medical

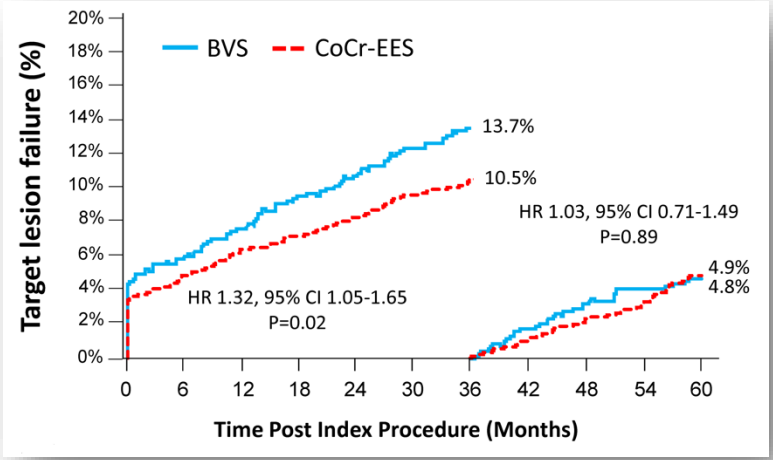
All Relevant Financial Relationships have been mitigated.
Faculty disclosure information can be found on the app

Background

- Stent related adverse events continue to accrue after the first year at a non-plateauing rate of 2-3% a year, with no difference between 2nd generation DES, 1st generation DES and BMS[1].



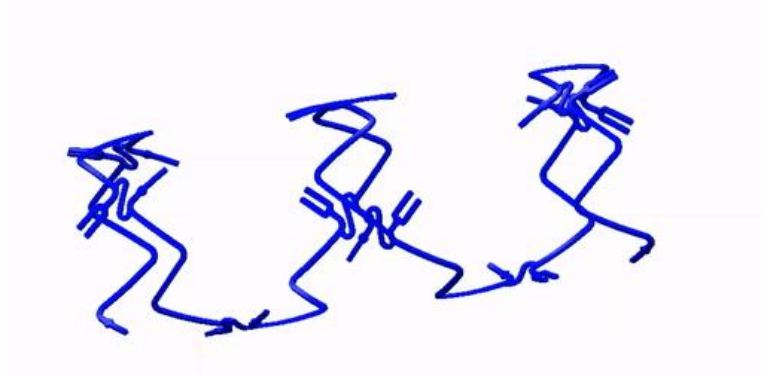
- "Leave nothing behind" concept of Bioresorbable Scaffolds failed at improving short or long-term outcomes compared to DES, driven by poor acute performance and loss of long-term vessel dynamic support following scaffold resorption[2].



1. Madhavan MV et al. J Am Coll Cardiol 2020;75:590-604
2. Stone GW et al. Five-Year Clinical Outcomes After Coronary Bioresorbable Scaffolds and Drug-Eluting Stents: The ABSORB IV Randomized Trial. J Am Coll Cardiol 2023

Study Device: Bioadaptor Implant

Bioadaptor is a novel coronary implant (DynamX®, Elixir Medical, California) that is designed to adapt to vessel physiology to restore vessel function and address device related adverse events[1,2].



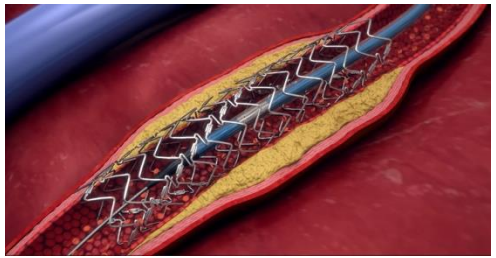
- *Three helical sinusoid strands (CoCr 71µm) are temporary connected by bioresorbable polymer coating eluting antiproliferative agent*
- *Following polymer resorption after 6 months, the helical strands unlock and separate*

1. Saito S et al. 12-Months Outcomes BIODAPTOR-RCT. The Lancet eClinicalMedicine. 2023;65:102304.
2. Verheye S et al. 12-Months Clinical and Imaging outcomes MECHANICSTIC Study, EuroIntervention 2020, 16(12);E974

Study Device: Bioadaptor Mechanism of Action

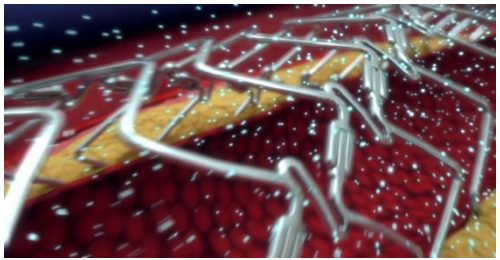
Bioadaptor (DynamX®, Elixir Medical, CA) is a novel technology designed to *restore hemodynamic modulation of the vessel.*

0 – 6 months → **after 6 months**



1. Locked:
Establish Flow Lumen

Restore flow and achieve high acute gain and low residual %DS[1,2]



2. Unlocked:
Maintain Flow Lumen

Restore adaptive remodeling and maintain low %DS[1,2]

3. Dynamic Support:
Restore Hemodynamic Modulation

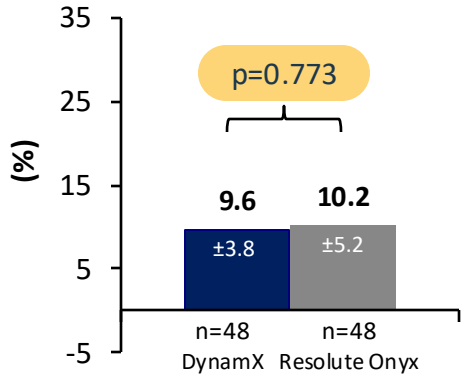
Restore pulsatility, compliance, adaptive coronary flow[1-3]

1. Saito S et al. 12-Months Outcomes BIODAPTOR-RCT. The Lancet eClinicalMedicine. 2023;65:102304.
2. Verheye S et al. Twelve-month clinical and imaging outcomes of the uncaging coronary DynamX bioadaptor system, *EuroIntervention 2020*, *16*(12);E974
3. Kwak BR et al. Biomechanical factors in atherosclerosis: mechanisms and clinical implications. European heart journal. 2014 Nov 14;35(43):3013-20.

Study Device: Bioadaptor Mechanism of Action

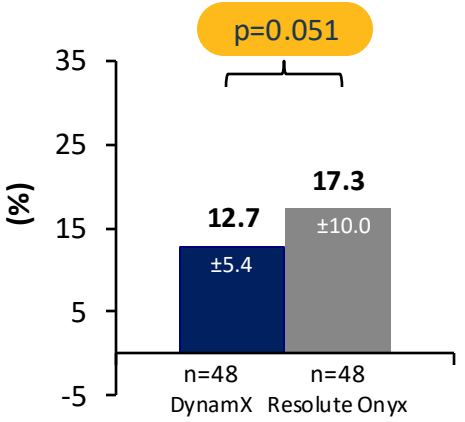
Results from the BIOADAPTOR-RCT[1] imaging cohort

Post Procedure QCA: Low %Diameter Stenosis



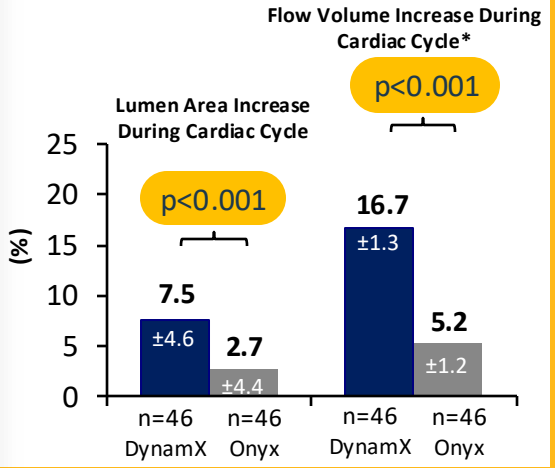
Establish Flow Lumen

1-Year QCA: Lower % Diameter Stenosis



Maintain Flow Lumen

1-Year IVUS: Restored Pulsatility and Adaptive Coronary Flow Volume



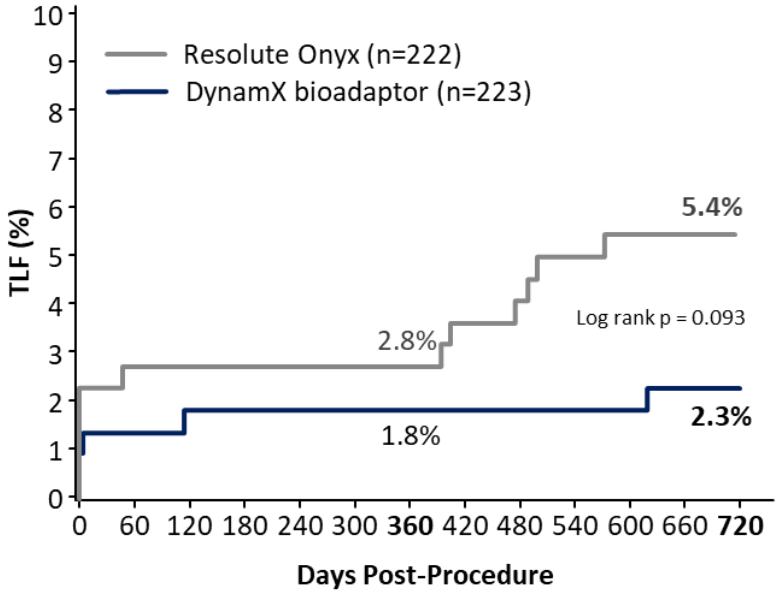
Restore Hemodynamic Modulation

* Estimated by Hagen-Poiseuille flow equation

1. Saito S et al. 12-Months Outcomes BIODAPTOR-RCT. The Lancet eClinicalMedicine. 2023;65:102304.

BIOADAPTOR-RCT Demonstrated Events Plateau After 6 Months

- 12- and 24-month results from BIOADAPTOR RCT (n=445) demonstrated safety and efficacy of DynamX bioadaptor and established benchmarks in restoring vessel function
  - TLF primary endpoint at 12 months was met (p<0.001 for non-inferiority)[1]
  - Reduction and plateauing in TLF, TVF through 2 years[2]
  - Statistically significantly lower %DS and LLL versus DES, and uniquely demonstrated pulsatility in intravascular imaging endpoints[1]
  - Novel finding of plaque stabilization and regression[1]



1. Saito S et al. 12-Months Outcomes BIODAPTOR-RCT. The Lancet eClinicalMedicine. 2023;65:102304.
2. Saito S. BIOADAPTOR-RCT 24-month Clinical Outcomes. EuroPCR 2024

INFINITY-SWEDEHEART RCT
Objectives and Powered Endpoints:

Objectives

- To evaluate the safety and efficacy of the bioadaptor implant compared to the DES in a large multi-center RCT
- To evaluate potential superior clinical benefit after 6 months on reducing non-plateauing event rates compared with a contemporary DES in a representative patient population, including:
    - High risk patients with Acute Coronary Syndrome (ACS) and complex lesion subsets

Powered Endpoints

Primary endpoint (non-inferiority):
Target lesions failure (TLF) at 1 year

Powered Secondary endpoints (superiority):
Landmark analysis of:

1. TLF from 6 months to End of Follow-up
2. TVF from 6 months to End of Follow-up
3. TLF in ACS from 6 months to End of Follow-up

Study Management and Site Enrollment

INFINITY-SWEDEHEART

UCR

- Study/Site Management, Data Mgmt., Statistics, CEC, DSMB

PI	Hospital Name	# Enrolled
Jonas Andersson, MD, PhD	Umeå University Hospital	316
Stefan James, MD, PhD	Uppsala University Hospital	275
David Erlinge, MD, PhD	Skåne University Hospital, Lund	221
Ole Fröbert, MD, PhD	Örebro University Hospital	215
Mattias Törnerud, MD	Danderyd Hospital, Stockholm	198
Mehmet Hamid, MD	Mälarsjukhuset, Eskilstuna	170
Thomas Kellerth, MD	Central Hospital, Karlstad	146
Per Grimfjärd, MD, PhD	Västerås hospital,	133
Daniel Ohm, MD	Capio St Göran Hospital, Stockholm	107
Carl-David Dolata, MD	Helsingborg Hospital	84

CERC European Cardiovascular Research Center

- Imaging Core Lab

PI	Hospital Name	# Enrolled
Sammy Zwackman, MD	Linköping University Hospital	81
Juliane Jurga, MD, PhD	Karolinska University Hospital, Huddinge	76
Martin Adielsson, MD	Halland Hospital, Halmstad	69
Patrik Alström, MD	Södersjukhuset, Stockholm	67
Elli Masoe, MD	Sundsvall Hospital	57
Juliane Jurga, MD, PhD	Karolinska University Hospital, Solna	49
Anders Ulvenstam, MD, PhD	Östersund Hospital	48
Jonas Millgård, MD, PhD	Sunderby Hospital, Luleå	43
Maria Tafesse, MD	Blekinge Hospital, Karlskrona	29
Mats Birgander, MD, PhD	Skåne University Hospital, Malmö	15

Key Inclusion and Exclusion Criteria

INFINITY-SWEDEHEART

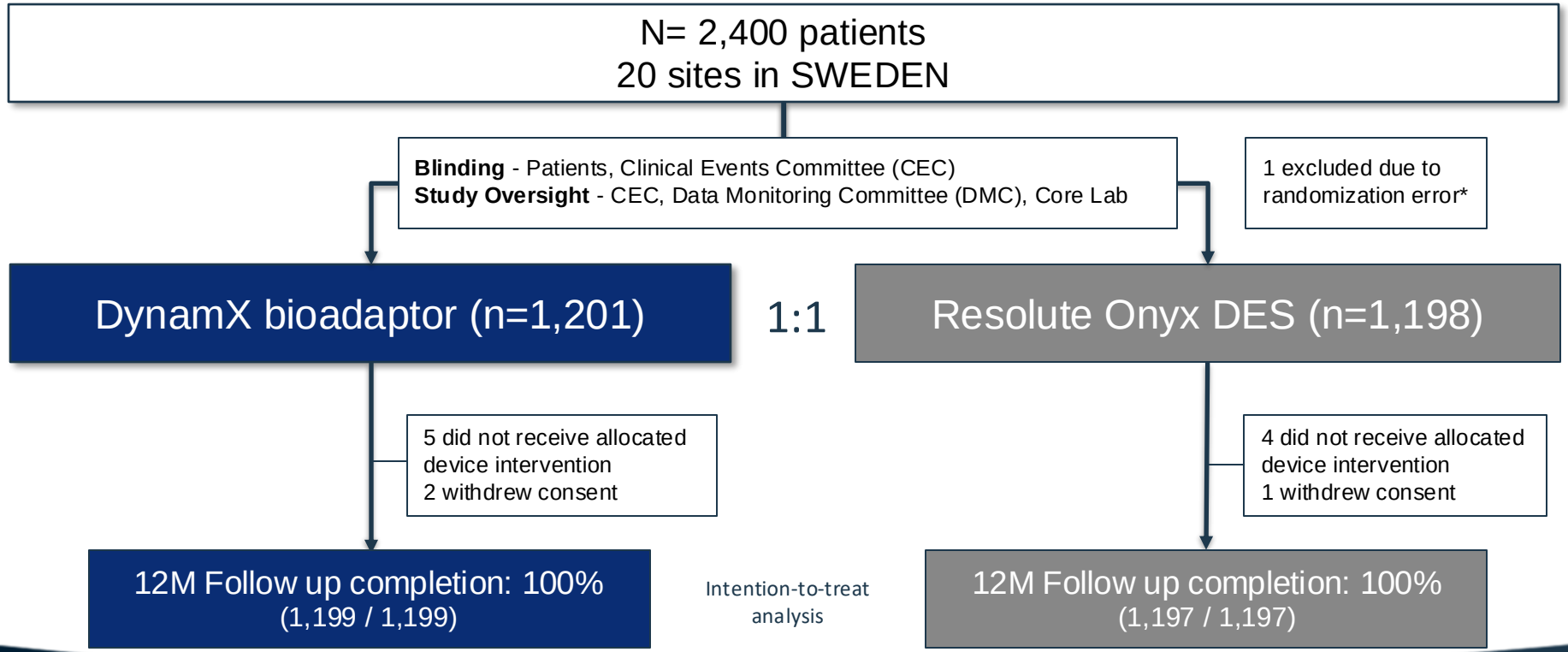
KEY INCLUSION

- Patient age ≥ 18 and ≤ 85 years
- **Patients with CCS or ACS indicated for PCI with stent implantation**
- Successful pre-dilation of at least 1 Target Lesion
- **Maximum of 3 Lesions may be treated**
  - Up to 3 Target Lesions, or
  - Up to 2 Target Lesions and 1 Non-Target Lesion, which must be without complications prior to randomization
- Target Lesion vessel diameter and lesion length suitable for implantation with either study device

KEY EXCLUSION

- Life expectancy < 2 years
- Prior PCI in the target vessel within 12M
- AMI with Killip class III/IV
- Chronic heart failure with LVEF < 30%
- On renal dialysis or with known eGFR < 30 ml/min
- **Lesions in the Left Main artery**
- **Venous or arterial bypass grafts**
- **In-stent restenosis**
- **Chronic total occlusion**
- **Lesions < 3 mm from ostium**

12-M Follow up completion: 100%



*randomization error of a patient who did not sign consent

Patient Baseline Characteristics

Baseline Characteristics	DynamX (N=1,201)	Onyx (N=1,198)
Age, years	68.2 ± 9.7	68.1 ± 9.6
Female	290 (24.1%)	285 (23.8%)
Hypertension	722 (60.5%)	710 (59.9%)
Hyperlipidemia	544 (45.6%)	492 (41.5%)
Diabetes Mellitus	231 (19.3%)	198 (16.6%)
Prior MI	**144 (12.1%)**	**141 (11.9%)**
Prior PCI	**176 (14.7%)**	**165 (13.9%)**
Prior CABG	**12 (1.0%)**	**8 (0.7%)**
Current Smoking	164 (14.2%)	187 (16.1%)

Clinical Presentation	DynamX (N=1,201)	Onyx (N=1,198)
Acute Coronary Syndrome (ACS)	**925 (77.0%)**	**913 (76.2%)**
STEMI	282 (23.5%)	317 (26.5%)
NSTEMI	458 (38.1%)	437 (36.5%)
Unstable Angina	185 (15.4%)	159 (13.3%)
Chronic Coronary Syndrome (CCS)	**276 (23.0%)**	**285 (23.8%)**

Baseline Lesion Characteristics

Baseline Characteristics	DynamX (N=1,201) (L=1,419)	Onyx (N=1,198) (L=1,431)
Target Lesion Location		
LAD	726 (51.2%)	728 (50.9%)
RCA	365 (25.7%)	384 (26.8%)
LCx	327 (23.0%)	318 (22.2%)
Lesion Classification		
A	160 (11.4%)	170 (11.9%)
B1	639 (45.4%)	666 (46.7%)
B2/C	609 (43.3%)	590 (41.4%)
Bifurcation	165 (11.8%)	161 (11.3%)
Calcified lesion*	239 (16.9%)	204 (14.3%)
Tortuous lesion*	109 (7.7%)	105 (7.3%)

Baseline Characteristics	DynamX (L=1,419)	Onyx (L=1,431)
Number of target lesions per subject, n (%)		
1	1009 (84.1%)	987 (82.6%)
≥2	191 (15.9%)	208 (17.4%)
RVD, mm	3.2 ± 0.5	3.2 ± 0.5
Lesion Length, mm	**24.4 ± 9.1**	**24.7 ± 9.4**
%DS, pre-procedure	**87.0 ± 12.1**	**87.3 ± 11.7**
%DS, post-procedure	**1.0 ± 5.4**	**0.6 ± 3.5**
Successful pre-dilation	1413 (99.7%)	1429 (99.9%)
Post-dilation	819 (58.5%)	754 (52.9%)

*moderate to severe

Target Lesion Failure at 12 Months

INFINITY-SWEDEHEART

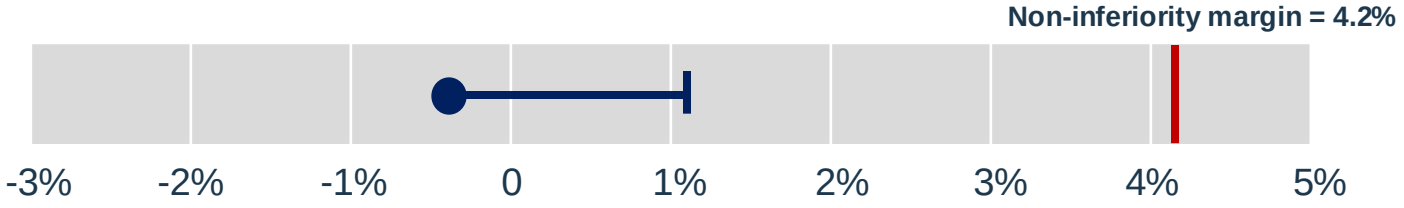
Primary Non-Inferiority Endpoint Met

DynamX
(N=1,189)
2.35%

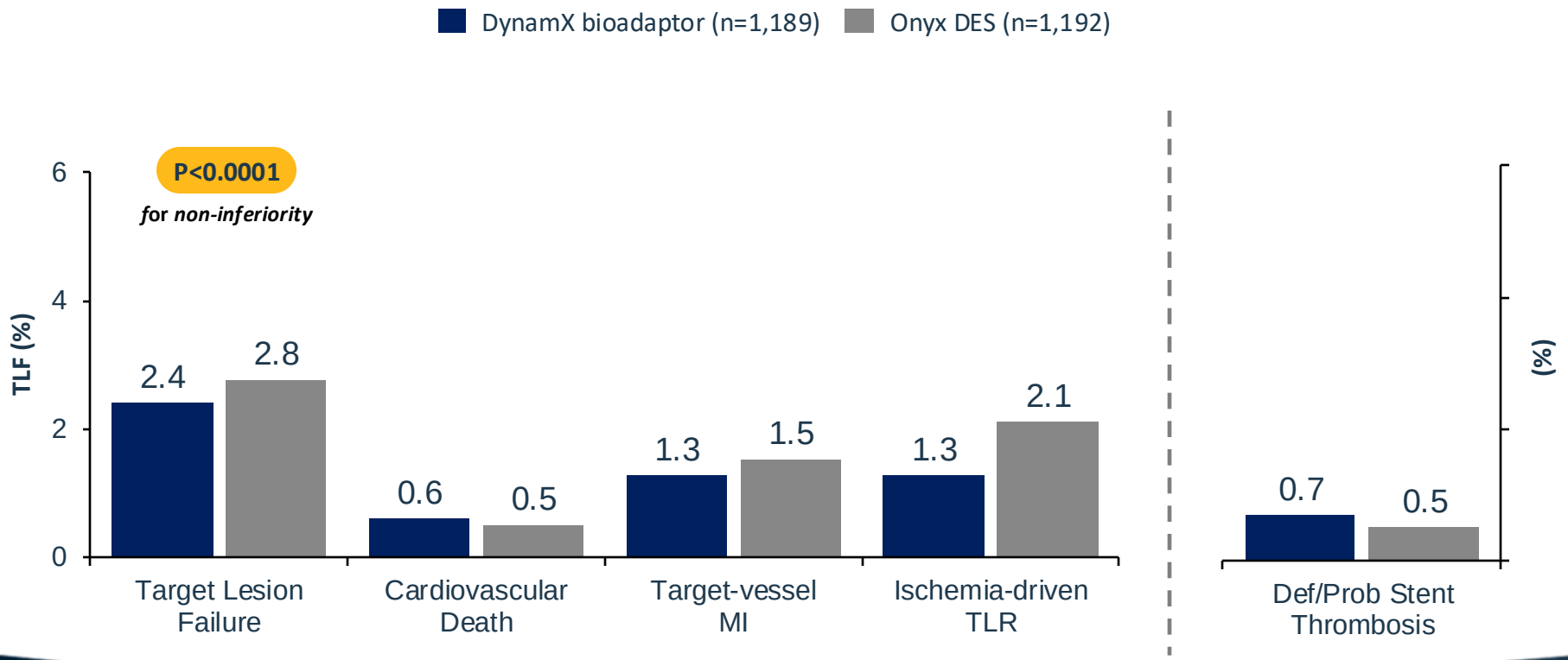
p-value <0.0001

Difference: - 0.41%
[-1.94%, 1.11%]

Onyx DES
(N=1,192)
2.77%



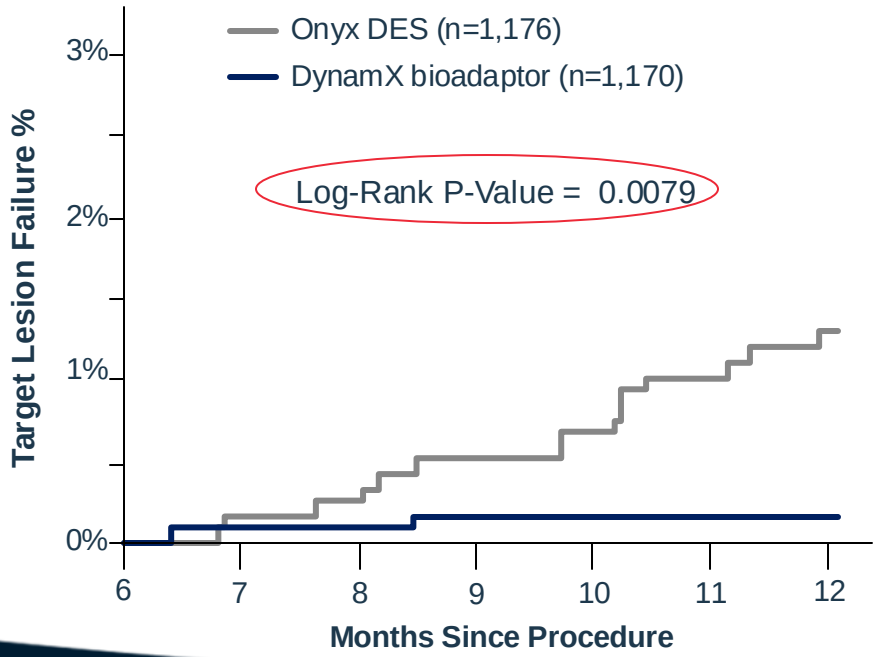
TLF and Components, Stent Thrombosis at 12 Mos



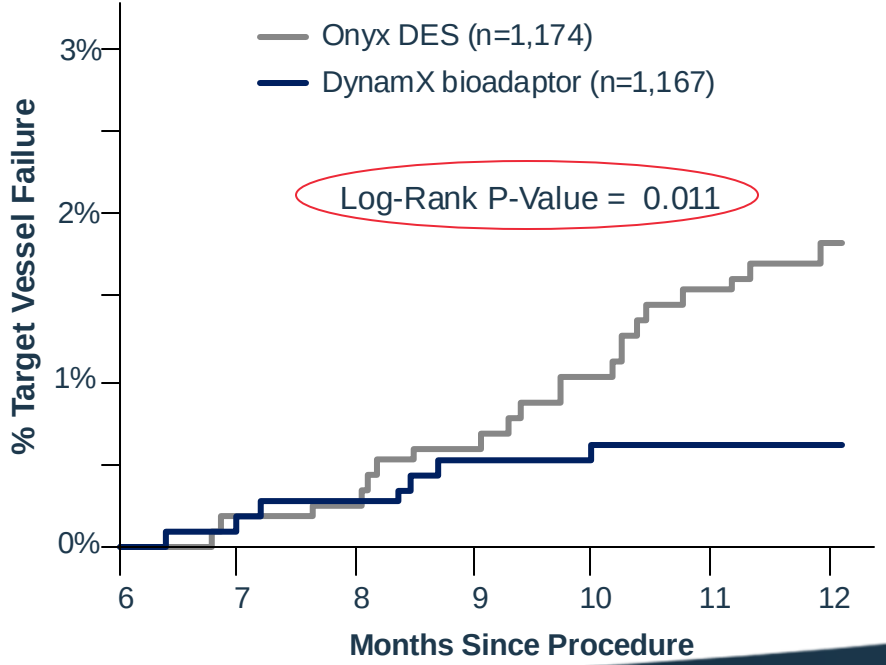
Powered Secondary Endpoints, 6-12 Mos

Significant Reduction and Plateau in TLF and TVF After 6 Mos

#1: TLF, Landmarked at 6 Months

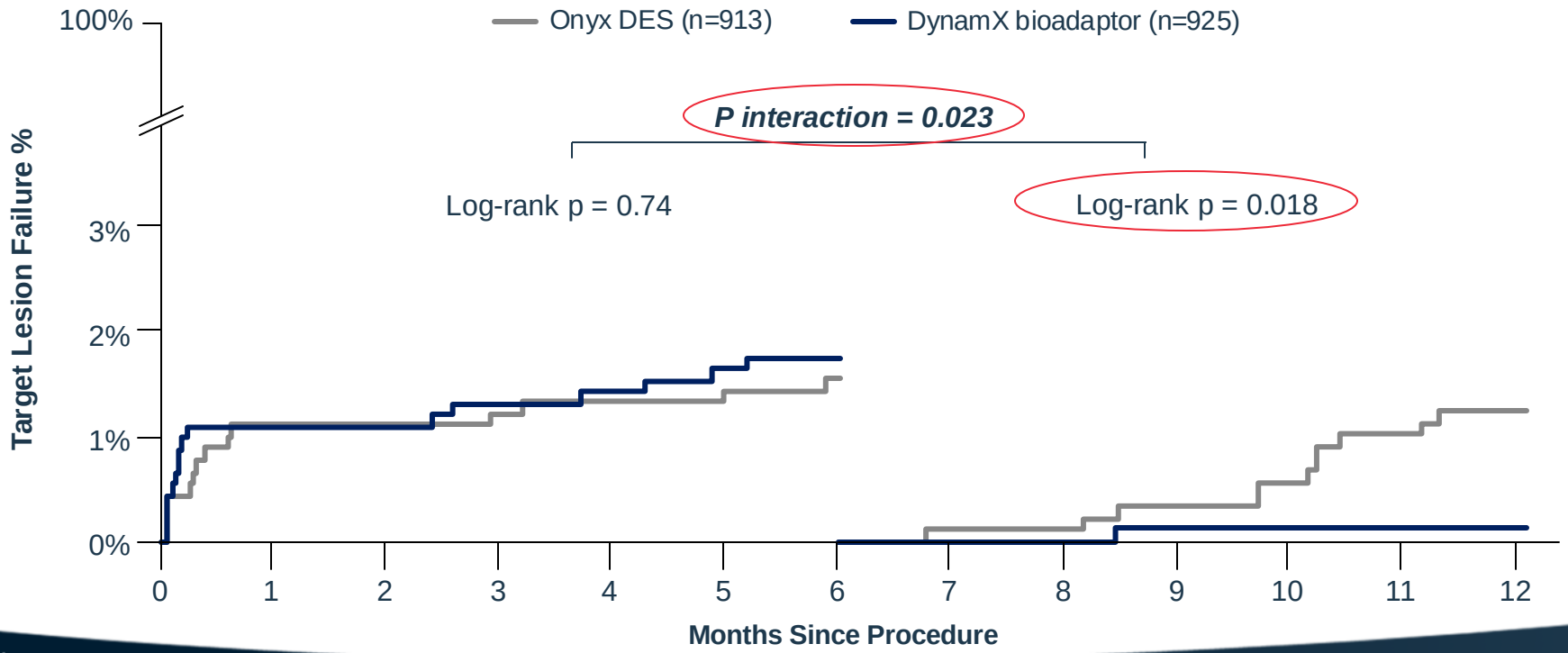


#2: TVF, Landmarked at 6 Months



Powered Secondary Endpoint: TLF in ACS, 6-12 Mos

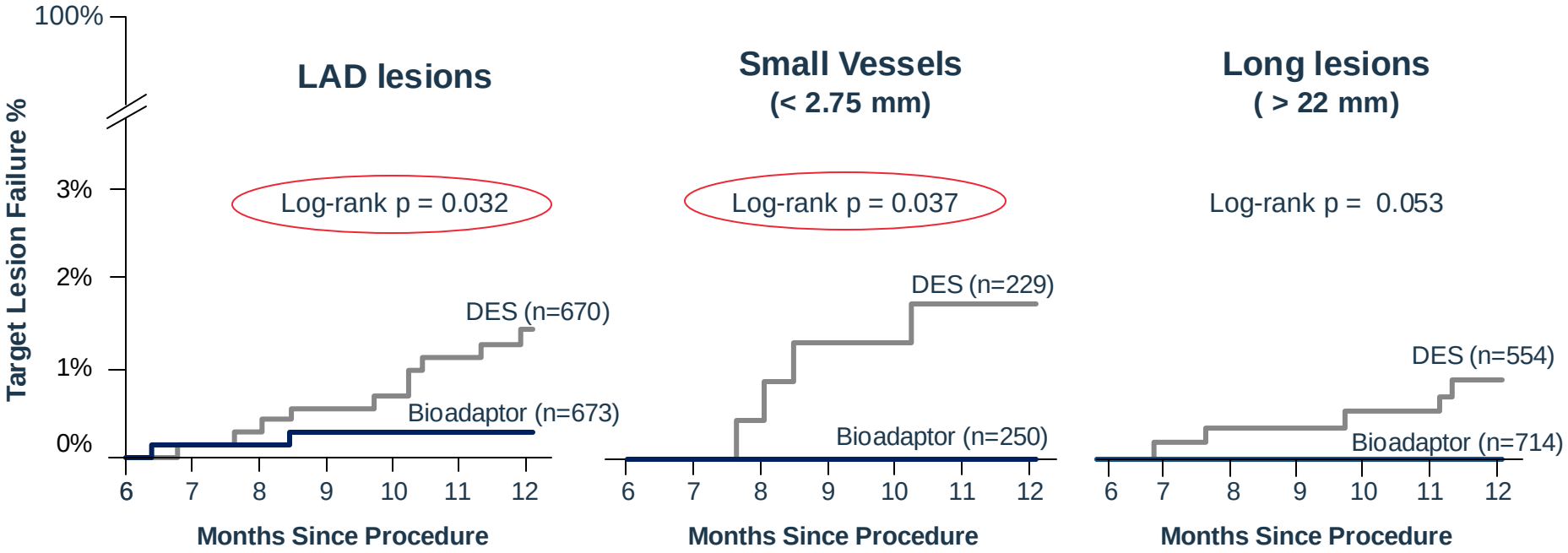
Significant Reduction and Plateau in TLF After 6 Months



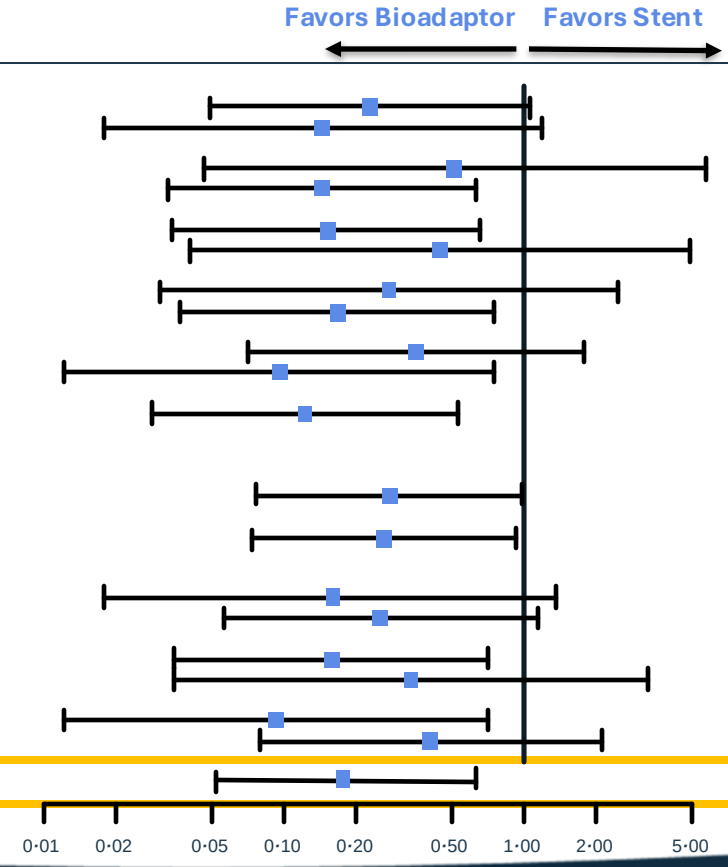
*0-6M analysis was not prespecified in the study protocol

TLF in High-Risk Lesions, 6-12 Mos

Significant Reduction and Sustained Treatment Effect



Consistency of 6-12M Outcomes Across Subgroups



	Bioadaptor (n=*1,201*)	DES (*n=1,198*)	HR (95% CI)	$P_{interaction}$
Age < 65 Years				0·73
Yes	2/416 (0·7%)	9/429 (2·2%)	0·23 (0·05-1·05)	
No	1/748 (0·1%)	7/746 (1·5%)	0·14 (0·02-1·17)	
Sex				0·38
Female	1/279 (0·4%)	2/280 (0·7%)	0·51 (0·05-5·64)	
Male	2/885 (0·3%)	14/895 (2·0%)	0·14 (0·03-0·63)	
Diabetes				0·45
No	2/942 (0·3%)	14/975 (1·5%)	0·15 (0·03-0·65)	
Yes	1/219 (0·5%)	2/195 (3·2%)	0·44 (0·04-4·88)	
Clinical Presentation				0·71
CCS	1/264 (0·4%)	4/281 (1·5%)	0·27 (0·03-2·44)	
ACS	2/900 (0·3%)	12/894 (1·8%)	0·17 (0·04-0·74)	
NSTEMI				0·33
No	2/717 (0·4%)	6/747 (0·8%)	0·35 (0·07-1·74)	
Yes	1/447 (0·2%)	10/428 (3·5%)	0·09 (0·01-0·74)	
STEMI				NA
No	2/892 (0·2%)	16/863 (2·4%)	0·12 (0·03-0·53)	
Yes	1/272 (0·6%)	0/312 (0·0%)		
LAD lesion				NA
No	0/493 (0·0%)	5/504 (1·0%)		
Yes	3/670 (0·6%)	11/669 (2·2%)	0·27 (0·08-0·98)	
Small Vessel				NA
No	3/915 (0·4%)	12/994 (1·7%)	0·26 (0·07-0·92)	
Yes	0/248 (0·0%)	4/229 (1·8%)		
Lesion Length				0·73
> 22mm	1/709 (0·3%)	5/554 (0·9%)	0·16 (0·02-1·35)	
≤ 22mm	2/439 (0·5%)	11/610 (2·5%)	0·25 (0·06-1·13)	
Bifurcation				0·58
No	2/998 (0·3%)	13/1013 (1·3%)	0·16 (0·04-0·69)	
Yes	1/152 (0·7%)	3/153 (5·3%)	0·34 (0·04-3·25)	
Complex Lesion (B2/C)				0·27
No	1/646 (0·2%)	11/652 (2·3%)	0·09 (0·01-0·71)	
Yes	2/517 (0·6%)	5/524 (1·0%)	0·41 (0·08-2·09)	
Overall	3/1201 (0·3%)	16/1198 (1·7%)	**0·19 (0·06-0·65)**	**0·0079**

Stratified Analysis of TLF from 6 to 12 month Across Subgroups

*NA: Not available/evaluable due to limited number of events

Conclusions

- The INFINITY-SWEDEHEART is a large-scale, multicenter RCT comparing bioadaptor implant versus DES in a representative, clinically complex ischemic patient population.
  - **Low and non-inferior TLF rates at 12 months** (2.4% versus 2.8%, p<0.0001)
  - **Significant reduction in TLF (p=0.008) and TVF (p=0.011) and flattening of event curves after 6 months in favor of bioadaptor,** in prespecified landmark analyses
  - **Substantial clinical benefit for the high-risk subgroups including ACS (p=0.018)** after 6 months in prespecified landmark analysis and **consistent effect across prespecified subgroups** including LAD, small vessels, long lesions.
- Evidence from the large-scale INFINITY-SWEDEHEART RCT confirms the results from the BIOADAPTOR-RCT trial and suggests bioadaptor may represent the long-awaited solution to flatten the event curve following PCI, marking a significant advancement in coronary interventions

INFINITY-SWEDEHEART Primary Outcomes Simultaneous Publication in the Lancet

Articles

Bioadaptor implant versus contemporary drug-eluting stent in percutaneous coronary interventions in Sweden (INFINITY-SWEDEHEART): a single-blind, non-inferiority, registry-based, randomised controlled trial

David Erlinge, Jonas Andersson, Ole Fröbert, Mattias Törnerud, Mehmet Hamid, Thomas Kellerth, Per Grimfjärd, Oscar Winnberg, Juliane Jurga, Henrik Wagner, Sammy Zwackman, Martin Adielsson, Patrik Alström, Elli Masoe, Anders Ulvenstam, Jonas Millgård, Felix Böhm, Claes Held, Henrik Renlund, Jonas Oldgren, Pieter C Smits, Candace Elek, Andrea Abizaid, Stefan James