Outcomes of Absorb Bioresorbable Scaffolds with Improved Technique in an Expanded Patient Population: The Blinded ABSORB IV Randomized Trial

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ABSORB IV

Background

- Prior studies have demonstrated more adverse events with coronary bioresorbable vascular scaffolds (BVS) compared with metallic DES, although in the ABSORB II trial angina was reduced with BVS
- However, these early studies were unblinded, lesions smaller than intended for the scaffold were frequently enrolled, technique was suboptimal, and patients with recent MI in whom BVS may be well-suited were excluded

Trial Design (Blinded FU)

NCT01751906

~2,600 pts with SIHD or ACS
1 - 3 target lesions w/RVD
2.5-3.75 mm and LL ≤24 mm

Randomize 1:1
Stratified by diabetes and ABSORB III-like vs. not

Absorb BVS
N=1,300

Xience EES
N=1,300

BVS technique:
Pre-dil: 1:1; NC balloon recommended
Sizing: IV TNG; QCA/IVUS/OCT strongly recommended if visually estimated RVD ≤2.75 mm and 2.5 mm device intended; <2.5 mm ineligible!
Post-dil: 1:1, NC balloon, ≥16 atm strongly recommended

DAPT for ≥12 months
Clinical/angina follow-up: 1, 3, 6, 9, 12 months, yearly through 7-10 years
SAQ-7 and EQ-5D: 1, 6, 12 months and 3 and 5 years
Cost-effectiveness: 1, 2, and 3 years

Primary endpoints: TLF at 30 days; TLF between 3 and 7-10 yrs (pooled with AIII)
Secondary endpoints: TLF at 1 year; angina at 1 year

No routine angiographic follow-up

Novel Study Procedures

Patients:

- Allowed troponin + pts, lsns with thrombus, 1-3 lsns (1-2 vessels)

Technique:

- Extensive training not to enroll small vessels (visual RVD <2.5 mm)
- IV imaging/QCA strongly recommended if visual RVD ≤2.75 mm
- ACL measured RVD within 72 hours and sites were placed on hold/re-trained if lesions with QCA RVD <2.25 mm were enrolled
- Aggressive pre-dilatation and routine NC-balloon high pressure post-dilatation were strongly recommended (but not mandated)

Blinding:

- Of pts/family/all post-PCI caregivers and clinical assessors
- Specific training/conscious sedation/headphones/bills masked
- Blinding/perception questionnaire administered at discharge & 1-year

Angina assessment:

- 6-page CRF questionnaire of specific angina symptoms
- Angina type and severity adjudicated by blinded CEC

Power Analysis

Endpoints hierarchically tested

Endpoint	Test	Assumptions*	Power with 2600 pts
1° endpoint 30-day TLF	Non-inferiority	Rate 4.9% in both groups NI margin 2.9% risk difference 1-sided alpha 0.025	92%
2° endpoint 1-year TLF	Non-inferiority	Rate 9.7% in both groups NI margin 4.8% risk difference 1-sided alpha 0.025	98%
2° endpoint 1-year angina	Non-inferiority	Rate 22.6% in both groups NI margin 7% risk difference 1-sided alpha 0.025	99%
2° endpoint 1-year angina	Superiority	Rate 22.6% EES, 17.7% BVS 2-sided alpha 0.05	86%

*Assumed attrition: 99% 30-day follow-up; 95% 1-year follow-up

Study Leadership

- Principal Investigator and Study Chair
  - Gregg W. Stone, MD, Columbia University Medical Center, NY, NY
- Co-Principal Investigators
  - Stephen G. Ellis, MD, Cleveland Clinic, Cleveland, OH
  - Dean J. Kereiakes, MD, The Christ Hospital, Cincinnati, OH
- Clinical Events Committee
  - Cardiovascular Research Foundation, New York, NY
    Steven Marx, MD, chair
- Angiographic Core Laboratory
  - Cardiovascular Research Foundation, New York, NY
    Ziad Ali, MD, director; Philippe Genereux, MD, former director
- Data Safety Monitoring Board
  - Axio Research, Seattle, WA; Robert N. Piana, MD, chair
- Sponsor
  - Abbott Vascular, Santa Clara, CA

ABSORB IV

Between August 15, 2014 and March 31, 2017

2604 Pts Enrolled at 147 Sites

US, Canada, Germany, Australia, Singapore

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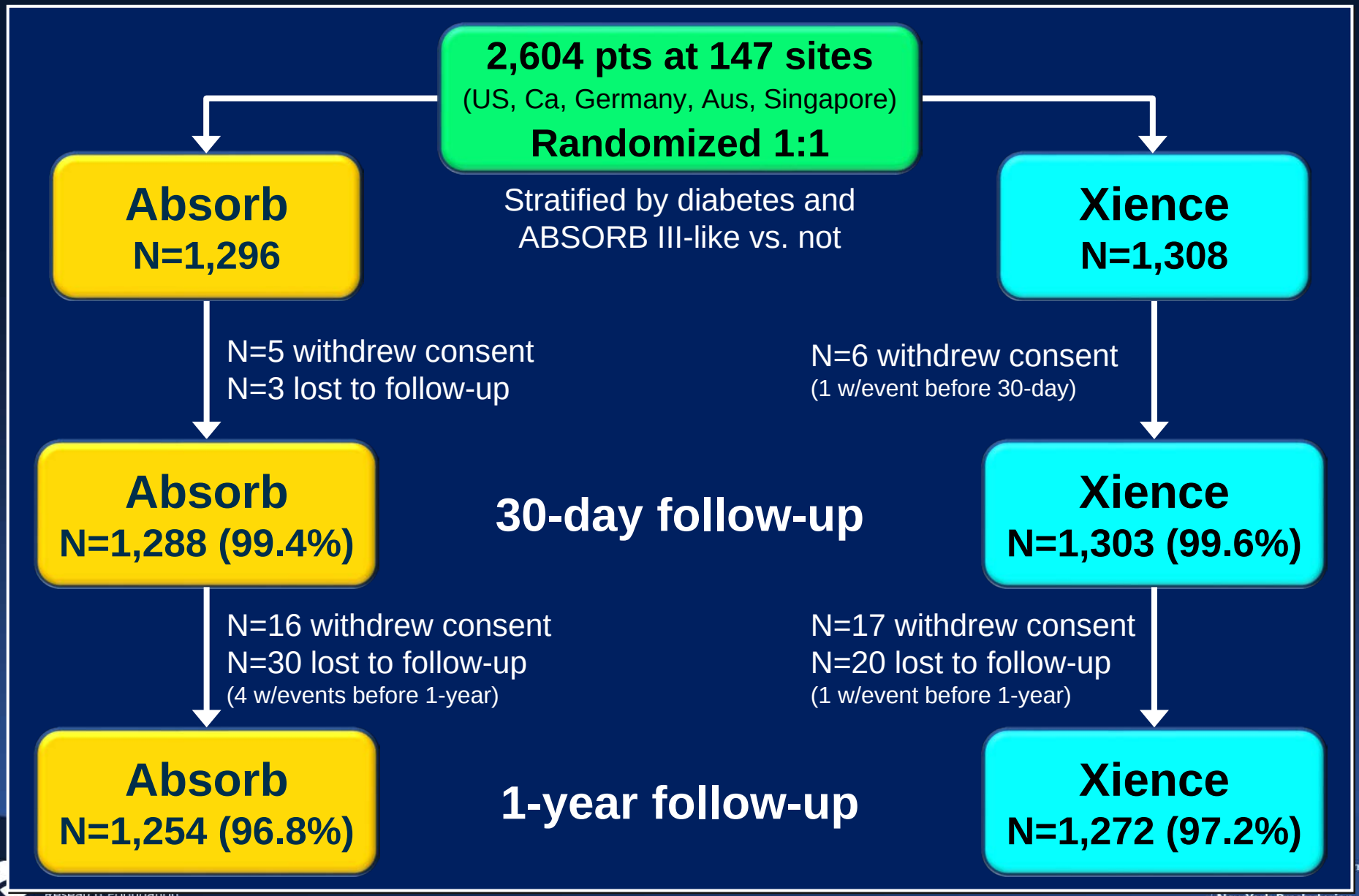
Study Flow and Follow-up



Top Enrollers (2,604 patients)

1. Dr. Gori (89)
Johannes Gutenberg-Universitaet Langenbeckstr, Mainz, Germany

2. Dr. Metzger (75)
Holston Valley Wellmont Medical Center, Kingsport, TN

3. Drs. Cambier & Stein (74)
Morton Plant Hospital, Clearwater, FL

4. Dr. Erickson (65)
Royal Perth Hospital, WA, Australia

5. Dr. Torzewski (63)
Kliniken Oberallgäu GmbH, Immenstadt, Germany

6. Dr. Williams (62)
Presbyterian Hospital, Charlotte, NC

7. Dr. Gruberg (62)
Stony Brook University Medical Center, Stony Brook, NY

8. Dr. Broderick (56)
The Christ Hospital, Cincinnati, OH

9. Dr. Kabour (55)
Mercy St. Vincent Medical Center, Toledo, OH

10. Dr. Piegari (53)
St. Joseph Medical Center, Wyomissing, PA

11. Drs. Fortuna & Cavendish (52)
Scripps Memorial Hospital La Jolla, La Jolla, CA

12. Dr. Bertolet (51)
North Mississippi Medical Center, Tupelo, MS

13. Dr. Choi (51)
Baylor Jack and Jane Hamilton Heart and Vascular Hospital, Dallas, TX

14. Drs. Waksman & Satler (47)
MedSTAR Washington Hospital Center, Hyattsville, MD

15. Dr. Whitbourn (46)
St. Vincent's Hospital Melbourne, VIC, Australia

16. Dr. Gaither (42)
Winchester Medical Center, Winchester, VA

17. Dr. Zidar (41)
Rex Hospital, Inc., Raleigh, NC

18. Dr. Wöhrle (40)
Universitätsklinik um Ulm ALBERT- EINSTEIN, Ulm, Germany

19. Dr. Wang (36)
MedSTAR Union Memorial Hospital, Hyattsville, MD

20. Dr. Litt (36)
Baptist Medical Center, Jacksonville, FL

21. Dr. Caputo (36)
St. Joseph's Hospital Health Center, Liverpool, NY

Baseline Characteristics

Characteristic	Absorb (N=1296)	Xience (N=1308)
Age (mean)	63.1 ± 10.1	62.2 ± 10.3
Male	71.5%	72.4%
Race (Caucasian)	87.6%	88.7%
Current tobacco use	22.1%	23.3%
Hypertension	78.5%	78.6%
Dyslipidemia	80.0%	79.2%
Diabetes	31.6%	31.9%
Insulin-treated	11.6%	11.1%
Prior MI	18.0%	19.4%
Prior coronary intervention	30.1%	33.3%
Recent MI (biomarker +)	24.0%	23.8%
BMI (kg/m^2)	30.3 ± 5.9	30.2 ± 6.1

There were no significant differences between groups

Baseline Characteristics (QCA)

Per lesion	Absorb (N=1296) (L=1446)	Xience (N=1308) (L=1457)
# of target lesions treated	1.1 ± 0.3	1.1 ± 0.3
One	88.4%	88.8%
Two	10.6%	10.7%
Three	0.6%	0.4%
Target lesion		
LAD	43.6%	43.7%
RCA	25.9%	25.9%
LCX	30.5%	30.4%
Lesion length, mm	14.9 ± 6.2	15.1 ± 6.9
>24 mm	9.9%	9.9%
RVD, mm	2.90 ± 0.39	2.89 ± 0.38
<2.25 mm	2.5%	2.9%
MLD, mm	0.82 ± 0.35	0.81 ± 0.34
%DS	71.8 ± 11.2	71.8 ± 10.9

N= number of patients; L= number of lesions

There were no significant differences between groups

Procedural Characteristics

Per patient	Absorb (N=1296) (L=1446)	Xience (N=1308) (L=1457)	p-value
Bivalirudin use	26.5%	27.7%	0.52
GP IIb/IIIa inhibitor use	13.4%	12.6%	0.54
Cangrelor use	0.3%	0.5%	0.75
Only assigned device implanted	92.6%	99.2%	<0.0001
Unplanned overlapping devices	5.9%	4.6%	0.14
Intravascular imaging use	15.6%	12.8%	0.04
Procedure duration (min)	46.2 ± 25.2	38.1 ± 21.1	<0.0001

N= number of patients
L= number of lesions

ABSORB IV

Procedural Technique

Per Lesion	Absorb (N=1296) (L=1446)	Xience (N=1308) (L=1457)	p-value
Pre-dilatation performed	99.8%	99.2%	0.02
NC/cutting/scoring balloon	43.9%	40.4%	0.06
Balloon/QCA-RVD ratio	1.00 ± 0.12	0.99 ± 0.12	0.22
Pressure (atm.)	12.6 ± 3.5	12.6 ± 3.5	0.99
Max device diameter (mm)	3.22 ± 0.44	3.16 ± 0.44	<0.0001
Device dia./QCA-RVD ratio	1.12 ± 0.12	1.10 ± 0.11	<0.0001
Total study device length (mm)	20.5 ± 8.3	20.1 ± 7.9	0.25
Post-dilatation performed	82.6%	54.1%	<0.0001
NC balloon	98.1%	96.1%	0.007
Balloon diameter (mm)	3.25 ± 0.45	3.26 ± 0.46	0.74
Balloon/QCA-RVD ratio	1.13 ± 0.12	1.12 ± 0.11	0.12
Max pressure (atm.)	16.3 ± 3.1	15.9 ± 3.1	0.002

N= number of patients
L= number of lesions

Post-Procedural QCA

Per lesion	Absorb (N=1296) (L=1446)	Xience (N=1308) (L=1457)	p-value
RVD (mm)	2.96 ± 0.40	2.95 ± 0.39	0.61
In-Device			
MLD (mm)	2.66 ± 0.39	2.74 ± 0.41	<0.0001
Acute gain (mm)	1.85 ± 0.46	1.92 ± 0.46	<0.0001
%DS	9.9 ± 8.3	7.2 ± 7.9	<0.0001
In-Segment			
MLD (mm)	2.41 ± 0.40	2.41 ± 0.41	0.71
Acute gain (mm)	1.59 ± 0.47	1.60 ± 0.46	0.72
%DS	18.6 ± 8.5	18.2 ± 8.4	0.24

N= number of patients
L= number of lesions

ABSORB IV

Acute Success

	Absorb (N=1296) (L=1446)	Xience (N=1308) (L=1457)	p-value
Device Success	94.6%	99.0%	<0.0001
Procedural Success	93.8%	95.9%	0.02

- **Device Success (lesion basis)**
  - Successful delivery and deployment of study scaffold/stent at intended target lesion
  - Successful withdrawal of delivery system and final in-scaffold/stent DS <30% (QCA)
- **Procedure Success (patient basis)**
  - Successful delivery and deployment of at least one study scaffold/stent at intended target lesion
  - Successful withdrawal of delivery system and final in-scaffold/stent DS <30% (QCA)
  - No in-hospital (maximum 7 days) TLF

Antiplatelet Agent Usage

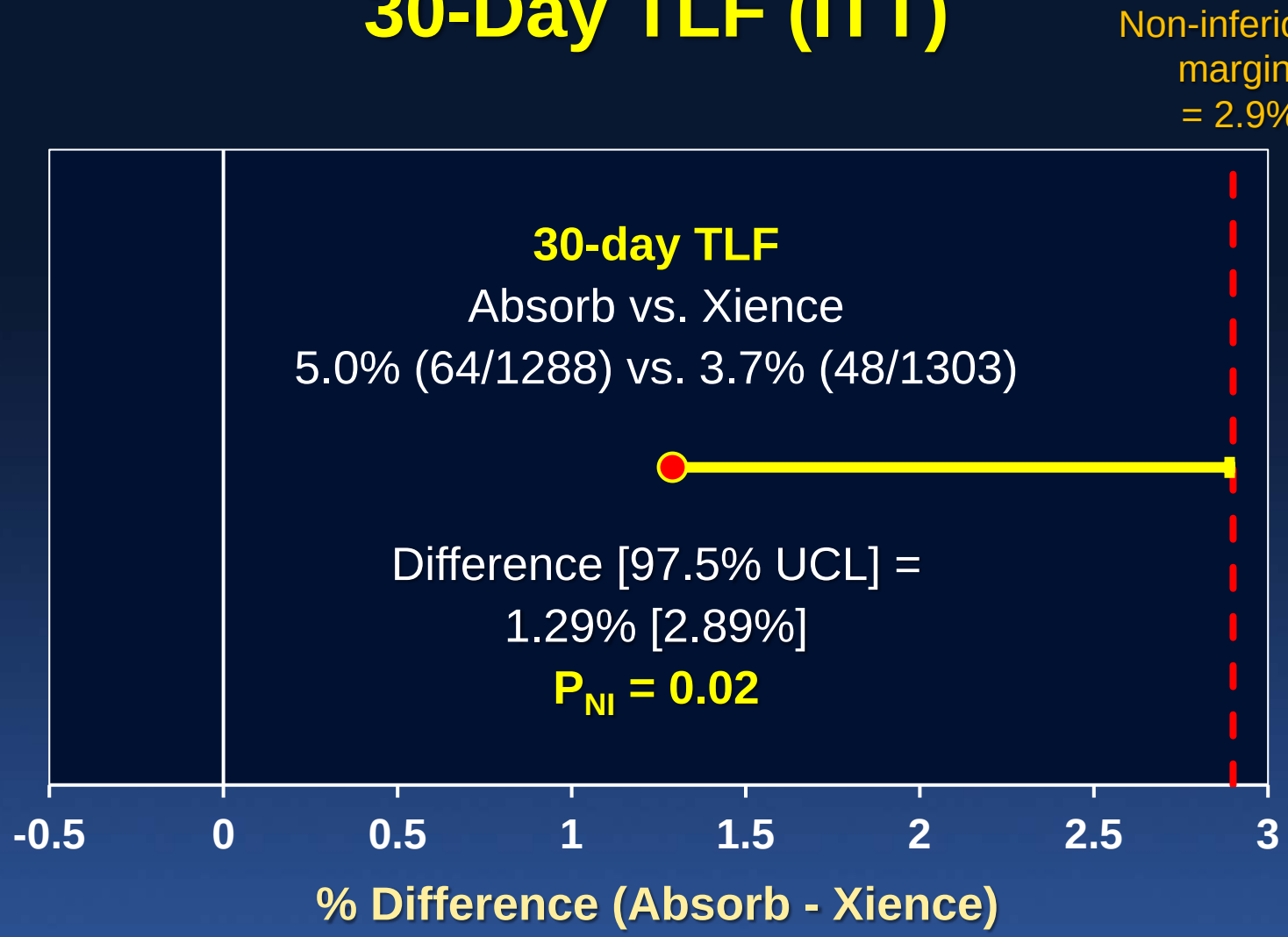
	Absorb (N=1296)	Xience (N=1308)	p-value
At index procedure			
Aspirin	99.3%	99.8%	0.08
P2Y12 inhibitor	99.3%	99.5%	0.43
Clopidogrel	55.4%	54.9%	0.79
Prasugrel	18.0%	18.7%	0.62
Ticagrelor	29.2%	29.8%	0.75
At 30 days			
Aspirin usage	99.5%	99.1%	0.26
P2Y12 inhibitor	99.4%	99.5%	0.78
Clopidogrel	62.1%	60.9%	0.55
Prasugrel	16.5%	17.2%	0.63
Ticagrelor	23.0%	23.2%	0.88
At 1 year			
Aspirin usage	93.9%	94.6%	0.41
P2Y12 inhibitor	90.9%	92.2%	0.25
Clopidogrel	61.1%	61.0%	0.98
Prasugrel	13.5%	13.7%	0.87
Ticagrelor	16.6%	17.5%	0.52

Blinding/Perception Questionnaire Results at Discharge and 1 Year

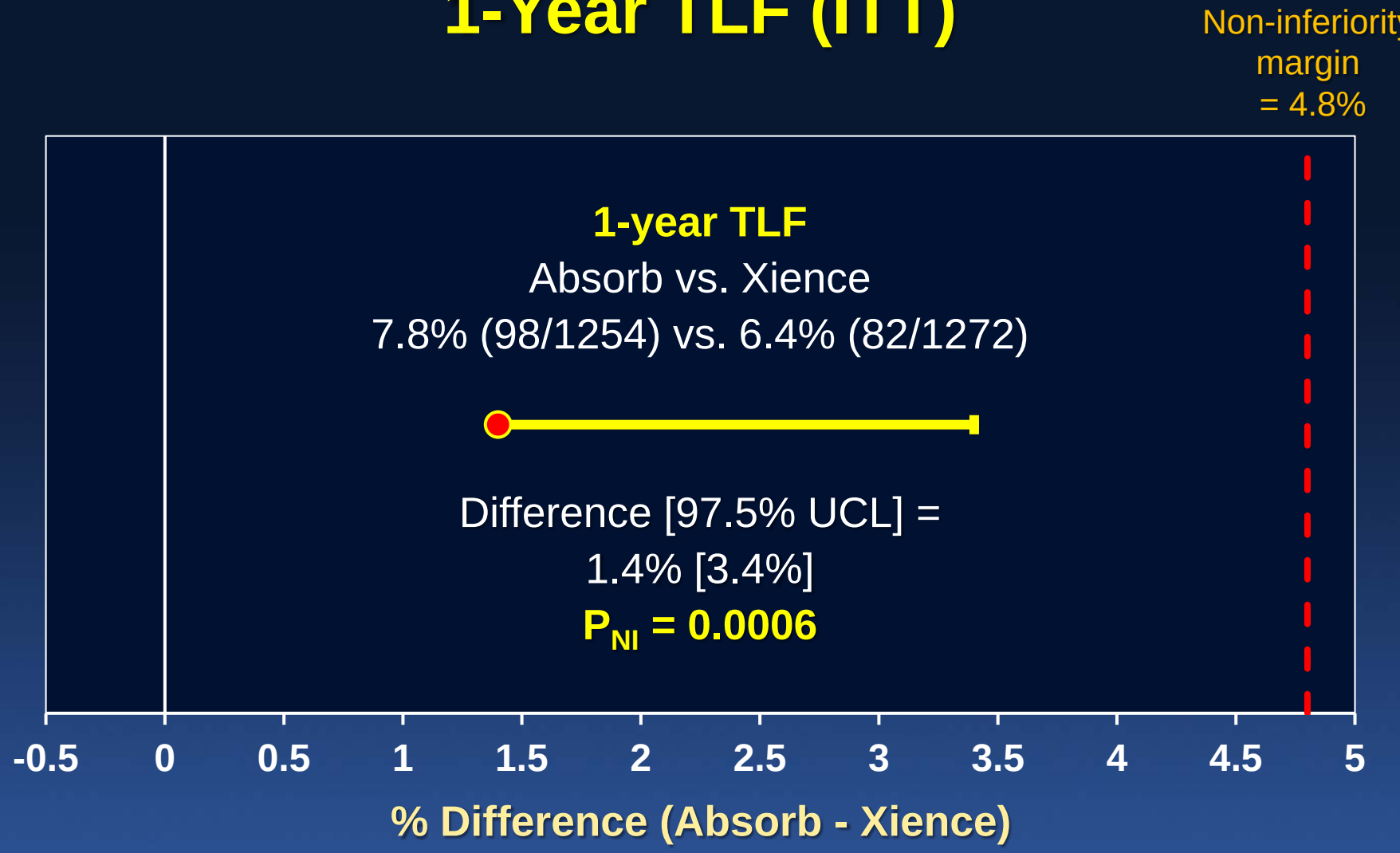
Question	At discharge			At 1 year		
	Absorb scaffold (N=1296)	Xience stent (N=1308)	P-value	Absorb scaffold (N=1296)	Xience stent (N=1308)	P-value
Do you think you know which device you received?						
- Yes	11.0%	9.4%	0.20	18.4%	16.4%	0.23
- No	89.0%	90.6%	0.20	81.6%	83.6%	0.23
If yes, which device do you think you received?						
- Standard metal stent	11.0%	5.4%	0.12	11.7%	17.5%	0.13
- Temporary dissolving stent	89.0%	94.6%	0.12	88.3%	82.5%	0.13
If yes, are you certain?						
- Yes	25.4%	35.1%	0.10	51.7%	37.3%	0.008
- No	74.6%	64.9%	0.10	48.3%	62.7%	0.008

ABSORB IV

Primary Endpoint
30-Day TLF (ITT)

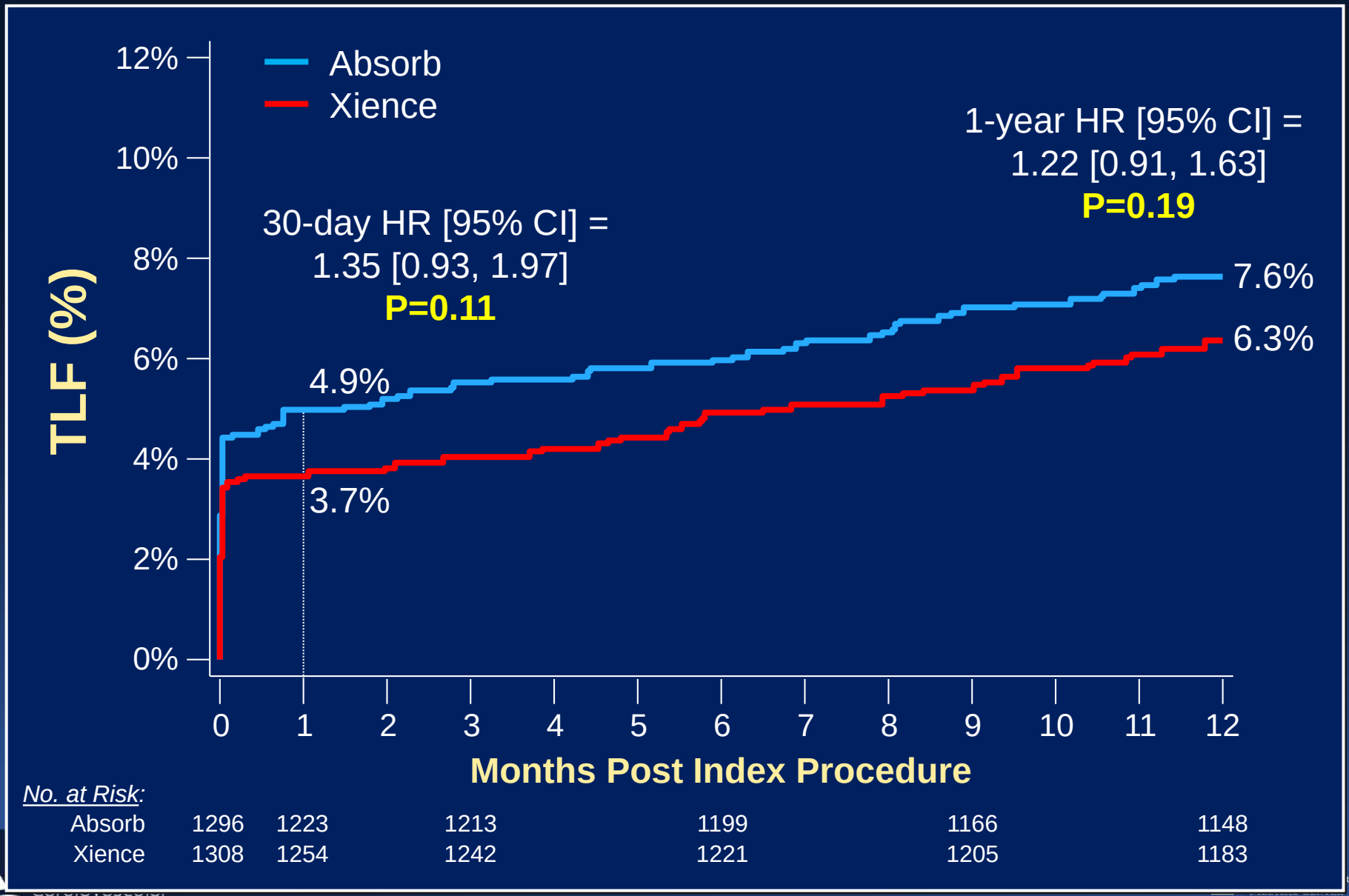


Secondary Endpoint
1-Year TLF (ITT)



ABSORB IV

Target Lesion Failure



ABSORB IV

30-Day Endpoints

	Absorb (N=1296)	Xience (N=1308)	p-value
TLF	4.9% (64)	3.7% (48)	0.11
- Cardiac death	0.1% (1)	0% (0)	0.32
- TV-MI	4.4% (57)	3.6% (47)	0.29
- ID-TLR	1.0% (13)	0.2% (3)	0.02
TVF (CD, MI, ID-TVR)	5.1% (66)	3.7% (48)	0.08
PoCE (death, MI, revasc)	5.2% (67)	4.1% (53)	0.17
- All-cause death	0.1% (1)	0.1% (1)	0.99
- MI	4.5% (58)	3.6% (47)	0.25
- Peri-procedural MI	3.8% (49)	3.4% (44)	0.56
- Spontaneous	0.8% (10)	0.2% (3)	0.05
- All revascularization	1.5% (19)	0.6% (8)	0.03
- ID-TVR	1.2% (16)	0.2% (3)	0.003

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Data are KM estimates (n events)

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ABSORB IV

1-Year Endpoints

	Absorb (N=1296)	Xience (N=1308)	p-value
TLF	7.6% (98)	6.3% (82)	0.19
- Cardiac death	0.8% (10)	0.6% (8)	0.62
- TV-MI	5.8% (75)	4.5% (58)	0.12
- ID-TLR	2.9% (37)	1.9% (24)	0.08
TVF (CD, MI, ID-TVR)	8.7% (111)	7.6% (99)	0.33
PoCE (death, MI, revasc)	9.7% (124)	8.6% (112)	0.35
- All-cause death	1.3% (16)	1.1% (14)	0.69
- MI	6.2% (80)	5.0% (65)	0.18
- Peri-procedural MI	3.8% (49)	3.4% (44)	0.56
- Spontaneous	2.6% (33)	1.7%(22)	0.12
- All revascularization	4.9% (63)	3.9% (50)	0.19
- ID-TVR	4.0% (51)	2.9% (37)	0.11

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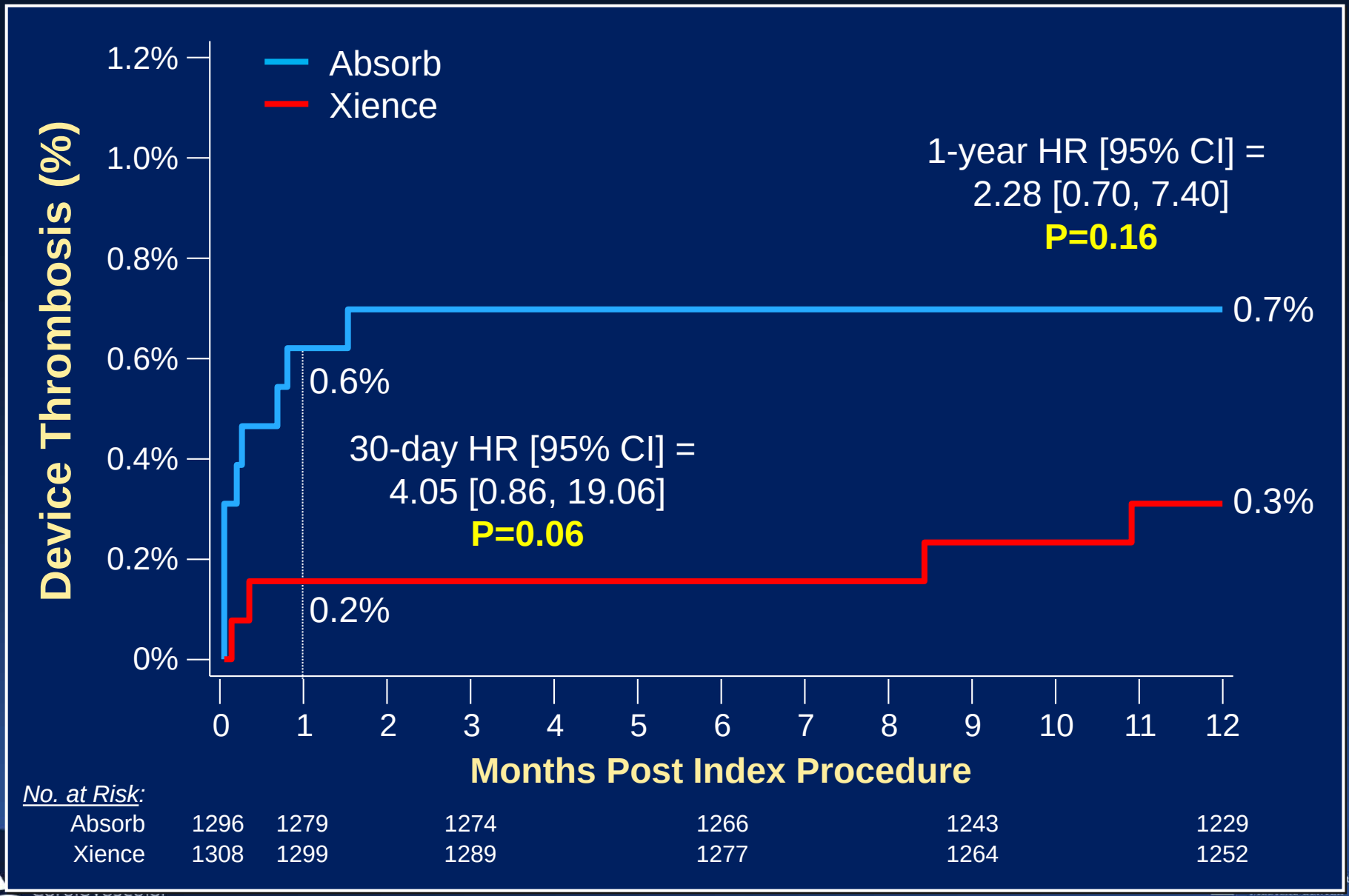
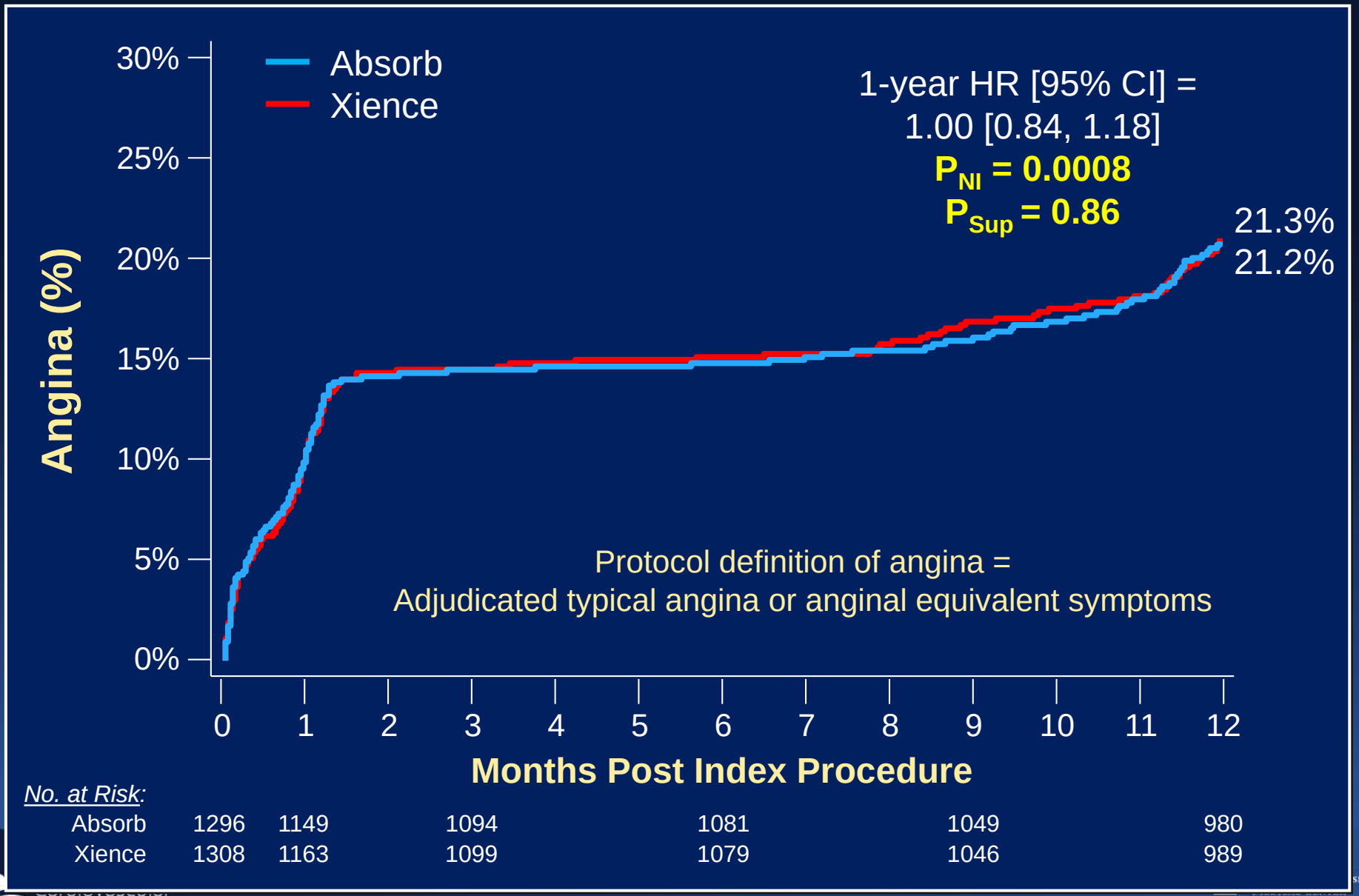
Device Thrombosis



Recurrent Angina



Type and Severity of Angina During 1-Year Follow-up Adjudicated

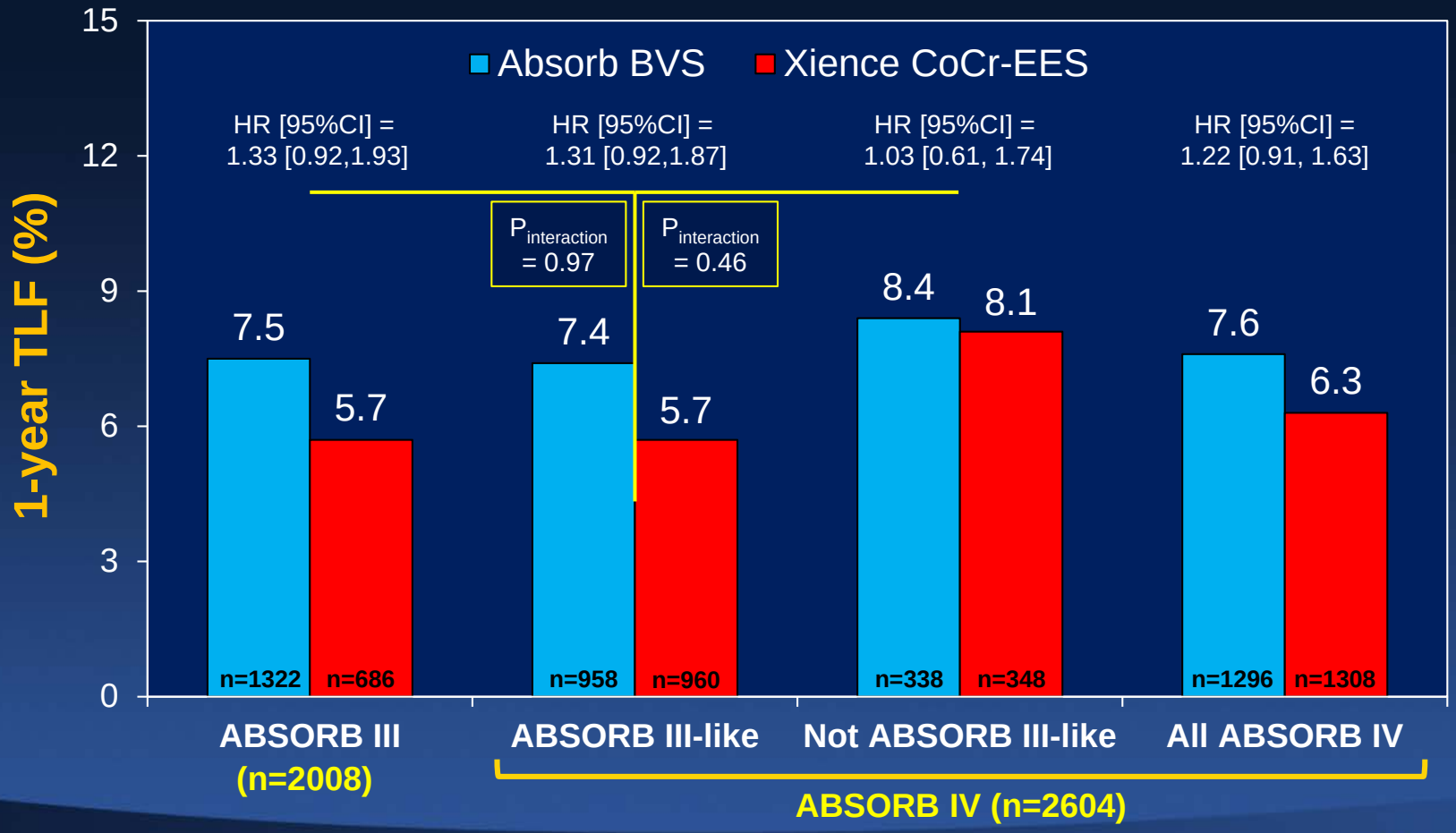
	Absorb (N=1296)	Xience (N=1308)	p-value
Symptom adjudication type*			
- Angina	13.0%	13.3%	0.88
- Anginal equivalent	8.2%	8.3%	0.92
- Non-anginal chest pain and/or non-cardiac shortness of breath	25.4%	25.1%	0.85
Protocol angina**	20.3%	20.5%	0.89
Anginal severity worst class, pts with protocol angina			
- I	16.6%	18.9%	0.98
- II	41.1%	33.2%	
- III	26.5%	35.5%	
- IV	15.8%	12.4%	

*Categories are non-exclusive; patients may have more than one type of symptom during follow-up. **Defined as adjudicated angina or anginal equivalent symptoms.

1-Year Target Lesion Failure

ABSORB IV vs. ABSORB III

1918/2604 pts (73.7%) enrolled in ABSORB IV were “ABSORB III-like”; 686 (26.3%) were not (23.9% troponin+ ACS, 0.5% 3 target lesions treated, 2.1% thrombus)

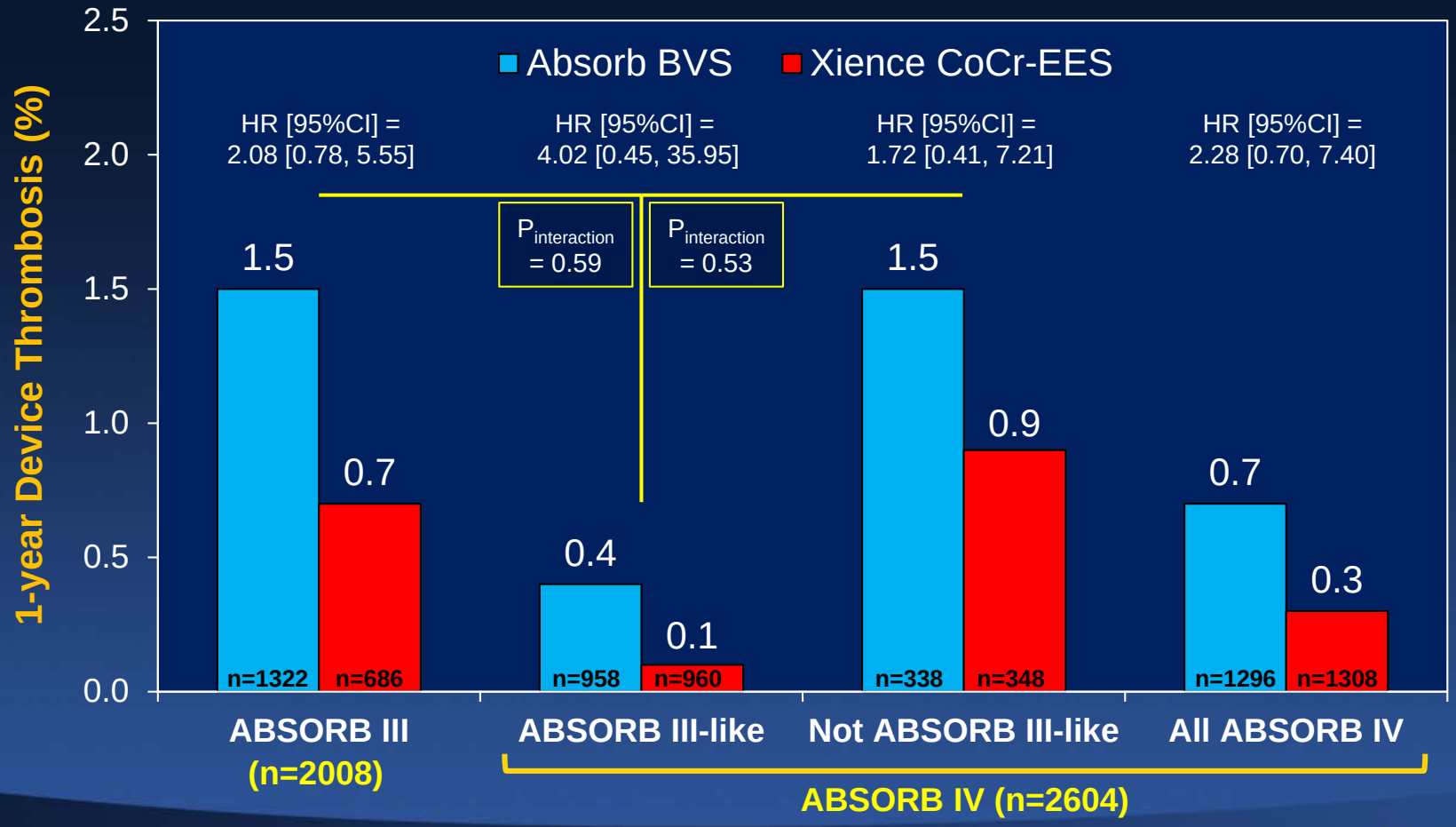


Data are Kaplan-Meier rates

1-Year Device Thrombosis

ABSORB IV vs. ABSORB III

1918/2604 pts (73.7%) enrolled in ABSORB IV were “ABSORB III-like”; 686 (26.3%) were not (23.9% troponin+ ACS, 0.5% 3 target lesions treated, 2.1% thrombus)



Data are Kaplan-Meier rates

Limitations

- Although troponin-positive patients were enrolled, ABSORB IV excluded STEMI and complex lesions (e.g. large bifurcations, diffuse disease, CTO, LM); results may not be generalizable to such patients
- While the trial methodology was successful at eliminating most very small vessels, “optimal” PSP rates were still low, and use of IV imaging was uncommon
- Longer-term follow-up is required to understand the true safety and efficacy profile of BVS during (0-3 years) and beyond (3-10 years) its complete bioresorption
  - The beneficial effects of high-pressure post-dilatation on ensuring scaffold-wall apposition may principally impact very late results (>1 year)

Summary and Conclusions 1

In this large-scale, blinded randomized trial:

- Absorb BVS was non-inferior to Xience CoCr-EES for TLF at 30 days and 1 year
- Compared with ABSORB III, nearly eliminating treatment of very small vessels in ABSORB IV substantially reduced the scaffold thrombosis rate with BVS, but also with CoCr-EES
- Angina recurred in a relatively high but nearly identical rate in both arms, with a bimodal pattern suggesting contributions from incomplete revascularization, restenosis, and possibly non-CAD-related mechanisms

Summary and Conclusions 2

- Despite better pt and lesion selection (larger vessels, troponin+ ACS) and improved technique, 30-day and 1-year rates of MI, ID-TLR and device thrombosis still tended to be greater with BVS than with CoCr-EES
- These data, which are largely consistent with those from earlier ABSORB trials, emphasize the need for further advancements in device technology and improvements in technique (e.g. routine IV imaging) to further improve the early safety profile of BVS if the benefits of late scaffold bioresorption are to be realized