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

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# Background

- First generation Absorb bioresorbable vascular scaffolds (BVS) have been associated with higher rates of TLF and device thrombosis than contemporary metallic DES, in part due to suboptimal technique in early studies
- In addition, prior ABSORB trials excluded commonly treated patient subgroups (e.g. troponin+ NSTEACS)
- We therefore performed the ABSORB IV trial in an expanded patient population, in which avoidance of small vessels was mandated and aggressive pre-dilatation and routine high-pressure post-dilatation were encouraged

# Trial Design

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**

# Major Inclusion Criteria

- ≥18 years old
- SIHD, NSTEACS, STEMI >72 hours; troponin pos or neg
- 1, 2 or 3 *de novo* target lesions in up to 2 native coronary arteries (max 2 lesions per artery) ± 1 non-target lesion
- Diameter stenosis ≥50% and <100% with TIMI flow ≥1
  - If DS <70%, abnormal noninvasive or invasive functional test, unstable angina or NSTEMI within 2 weeks, or STEMI >72 hours but ≤2 weeks.
- RVD ≥2.50 mm and ≤3.75 mm (visually estimated)
  - QCA or IVUS/OCT strongly recommended if visually estimated RVD ≤2.75 mm and 2.5 mm device intended
- Lesion length ≤24 mm (visually estimated)

# Major Exclusion Criteria

- LVEF <30%
- GFR <30 ml/min/1.73mm$^2$ or dialysis
- Any contraindication to DAPT for ≥ 12 months
- Target lesion: left main, ostial, bifurcation with SB ≥2 mm or stenosis >50% or requiring dilatation, in or distal to bypass graft, or within 5 mm of prior stent
- Proximal vessel or target lesion: mod/severe calcification, extreme angulation (≥90°) or excessive tortuosity (≥two 45° angles)
- Target vessel PCI within prior 12 months, or any future planned PCI (except staged procedures for study lesions)
- Receiving or will require chronic oral anticoagulation
- Unsuccessful pre-dilatation

# Powered Endpoints

**Primary endpoint #1:** TLF at 30 days (non-inferiority)

- Cardiac death, or
- Myocardial infarction attributed to the target vessel (TV-MI), or
  - Peri-procedural MI: CK-MB >5x ULN w/i 48 hours
- Ischemia-driven target lesion revascularization (ID-TLR)

**Primary endpoint #2:** TLF between 3 years and 7/10 years (pooled with ABSORB III) (sequential non-inferiority and superiority)

**Secondary endpoint #1:** TLF at 1 year (non-inferiority)

**Secondary endpoint #2:** Angina at 1 year (sequential non-inferiority and superiority)

# Statistical Design

## 30-day TLF primary endpoint

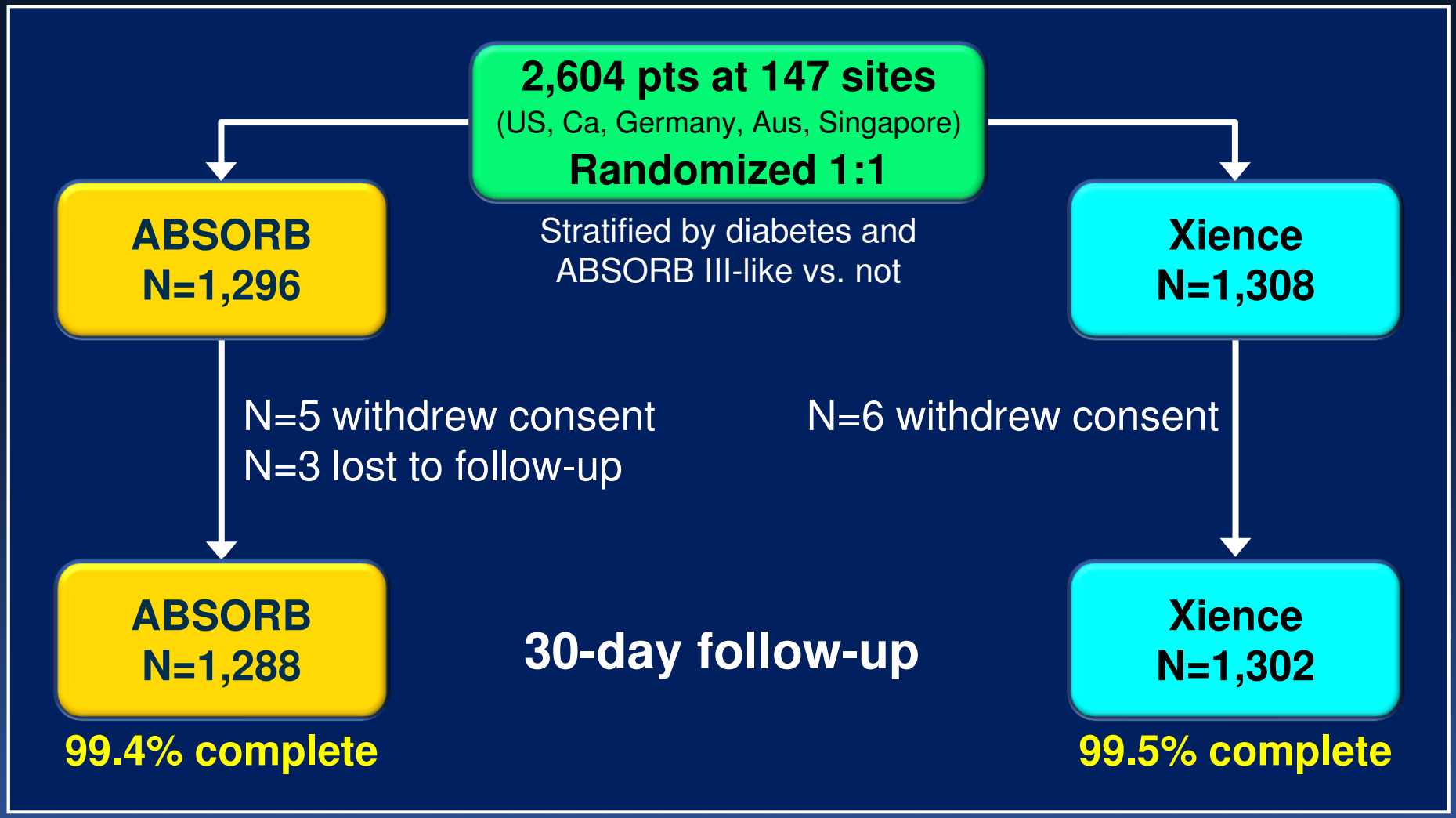
**Non-inferiority analysis (ITT population) with the following assumptions:**

- 30-day TLF rate of 4.9% in both groups
- Non-inferiority margin of 2.9%
- 1-sided alpha of 0.025
- 99% 30-day follow-up
- 2600 subjects → 92% power

# 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
    Philippe Genereux, MD, director
- Data Safety Monitoring Board
  - Axio Research, Seattle, WA; Robert N. Piana, MD, chair
- Sponsor
  - Abbott Vascular, Santa Clara, CA

# Study Flow and Follow-up



ABSORB IV

# 140 Enrolling Centers

## US, Canada, Germany, Australia, Singapore


Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

# 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% |
| Biomarker positive ACS | 22.9% | 23.2% |
| BMI (kg/m$^2$) | 30.3 ± 5.9 | 30.2 ± 6.1 |

# 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

# 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 |
| Unassigned device implanted | 0.8% | 0.4% | 0.19 |
| Unplanned overlapping devices | 7.8% | 6.3% | 0.15 |
| 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

# 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 |
| Study device diameter (mm) | 3.05 ± 0.38 | 3.05 ± 0.39 | 0.91 |
| Device dia./QCA-RVD ratio | 1.06 ± 0.10 | 1.06 ± 0.09 | 0.74 |
| Total study device length (mm) | 20.5 ± 8.3 | 20.1 ± 7.9 | 0.25 |
| Device length/QCA-LL ratio | 1.43 ± 0.52 | 1.42 ± 0.51 | 0.54 |
| 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 |
| Pressure (atm.) | 16.0 ± 3.4 | 16.4 ± 3.4 | 0.046 |
| Bailout scaffold/stent required | 7.0% | 5.7% | 0.15 |

# 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 |

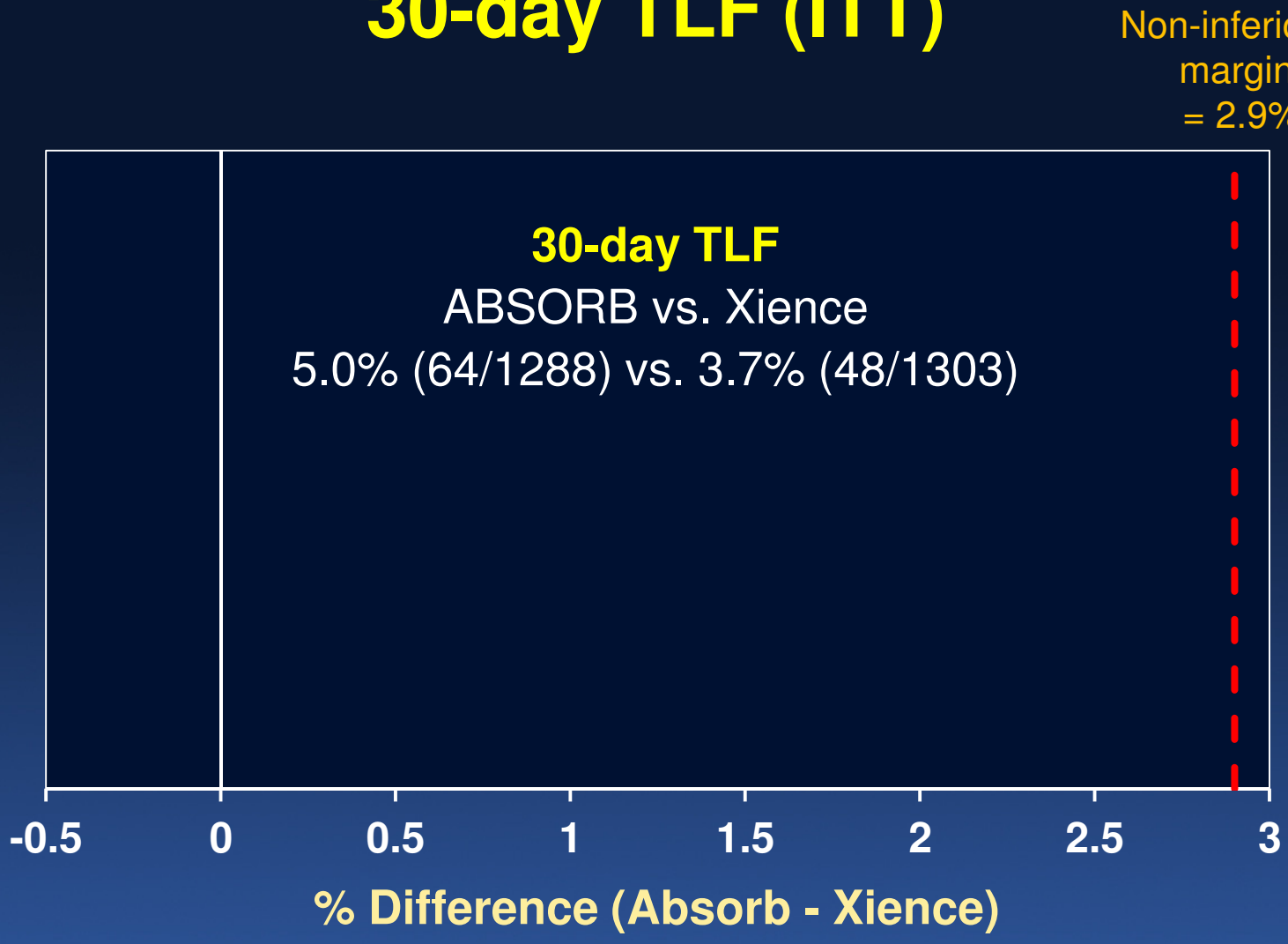
N= number of patients
L= number of lesions

# Acute Success

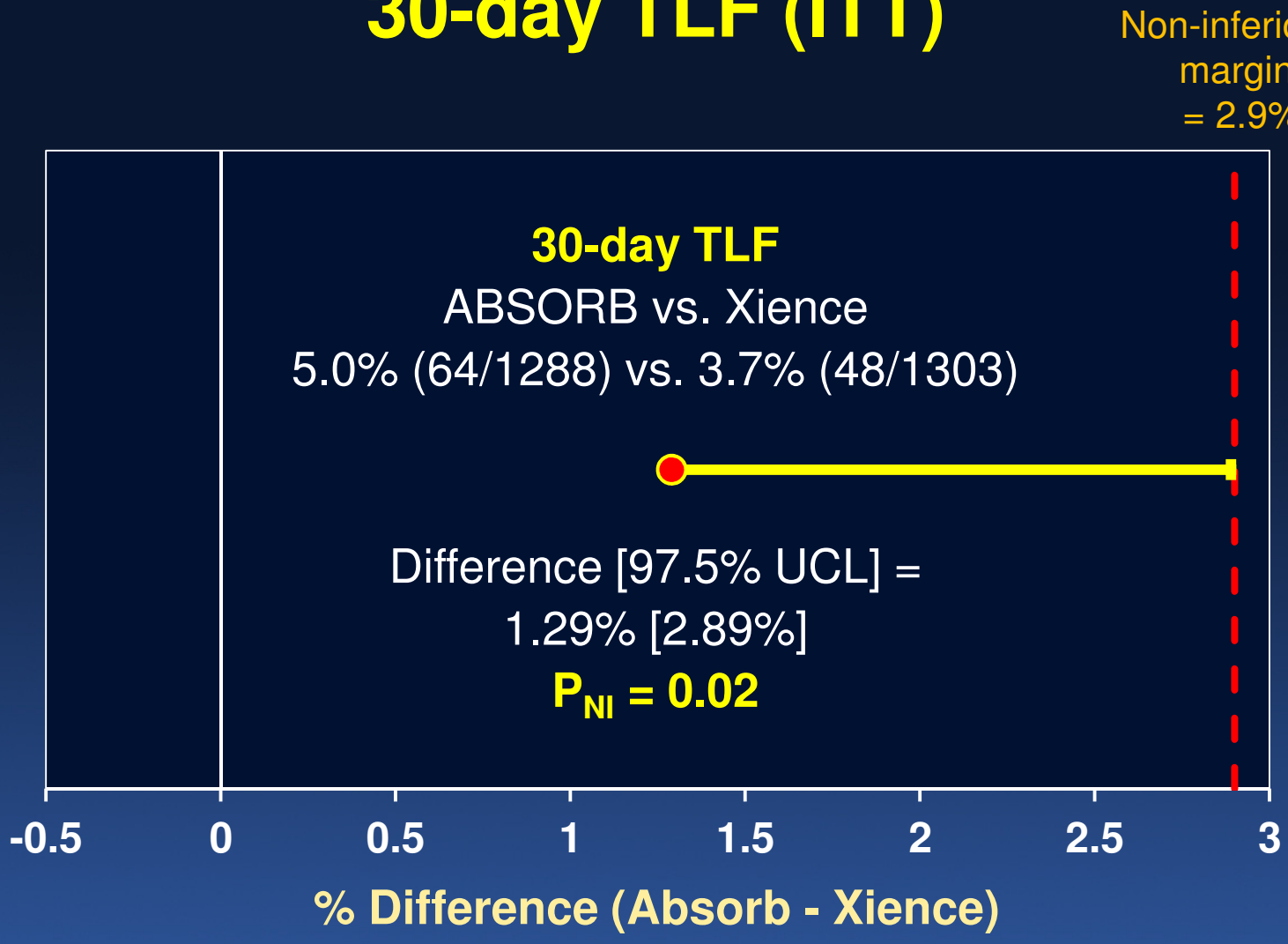
| | Absorb (N=1296) (L=1446) | Xience (N=1308) (L=1457) | p-value |
|---|---|---|---|
| Device Success | 94.6% | 99.0% | <0.0001 |
| Procedural Success | 93.8% | 95.9% | 0.02 |

- **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

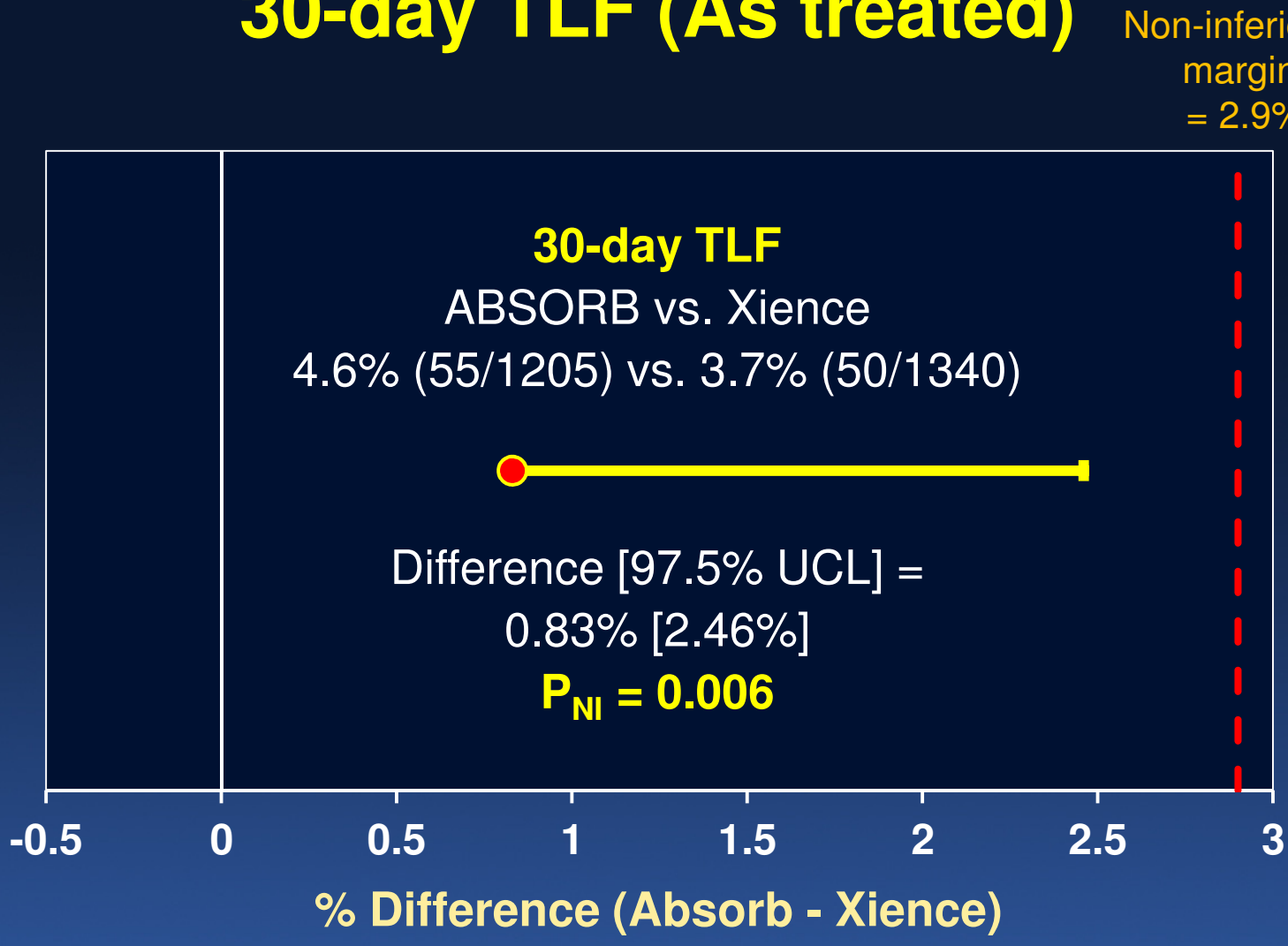
# Primary Endpoint
## 30-day TLF (ITT)



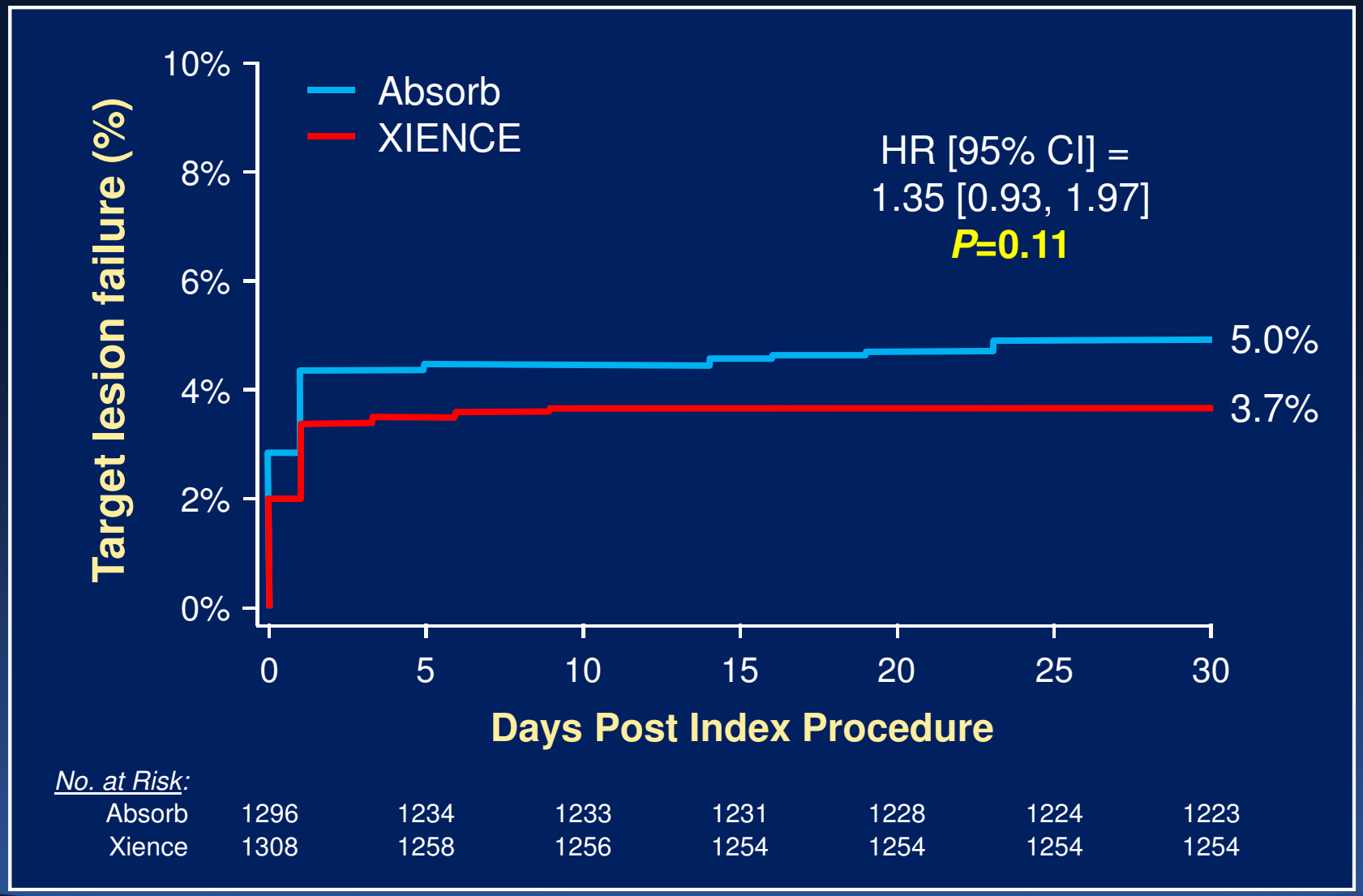
# Primary Endpoint
## 30-day TLF (ITT)



# Primary Endpoint
## 30-day TLF (As treated)



# Target Lesion Failure



# 30-Day Endpoints (i)

| | Absorb (N=1296) | Xience (N=1308) | p-value |
|---|---|---|---|
| TLF (CD, TV-MI, ID-TLR) | 5.0% (64) | 3.7% (48) | 0.11 |
| TVF (CD, MI, ID-TVR) | 5.1% (66) | 3.7% (48) | 0.07 |
| PoCE (death, MI, revasc) | 5.2% (67) | 4.1% (53) | 0.17 |
| - Death | 0.1% (1) | 0.1% (1) | 0.99 |
| - MI | 4.5% (58) | 3.6% (47) | 0.25 |
| - TV-MI | 4.4% (57) | 3.6% (47) | 0.29 |
| - Non-TV-MI | 0.1% (1) | 0.1% (1) | 0.99 |
| - Peri-procedural MI | 3.8% (49) | 3.4% (44) | 0.55 |
| - Non-peri-procedural MI | 0.8% (10) | 0.2% (3) | 0.049 |
| - Q-wave MI | 0.5% (6) | 0.2% (2) | 0.15 |
| - Non-Q-wave MI | 4.1% (53) | 3.5% (46) | 0.44 |

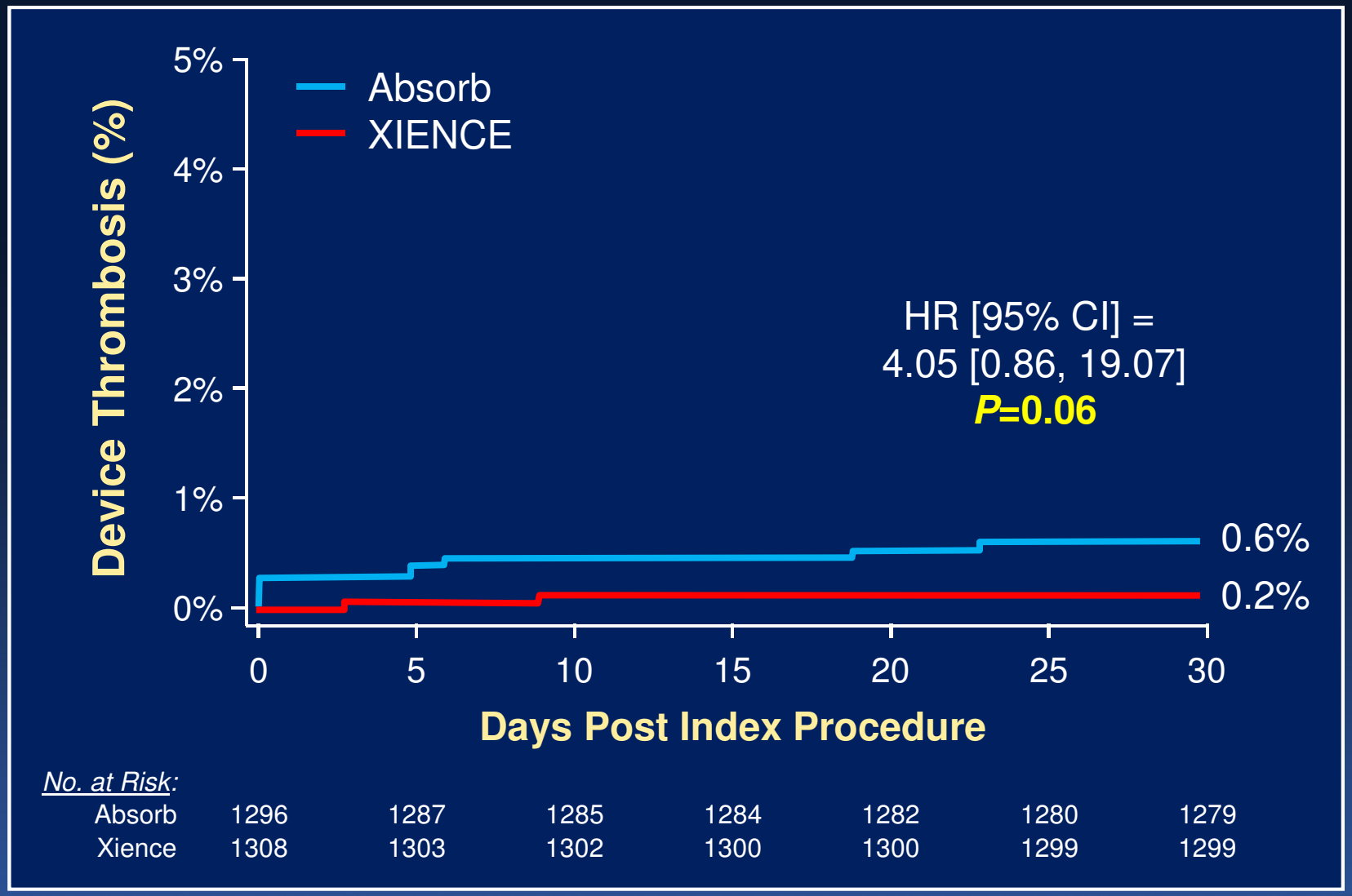
Data are KM estimates (n events)

# 30-Day Endpoints (ii)

| | Absorb (N=1296) | Xience (N=1308) | p-value |
|---|---|---|---|
| All revascularization | 1.5% (19) | 0.6% (8) | 0.03 |
| ID-revascularization | 1.4% (18) | 0.6% (8) | 0.046 |
| - ID-TVR | 1.2% (16) | 0.2% (3) | 0.003 |
| - ID-TLR | 1.0% (13) | 0.2% (3) | 0.01 |
| - ID-TVR, non-TLR | 0.4% (5) | 0.1% (1) | 0.10 |
| - ID-non-TVR | 0.4% (5) | 0.5% (6) | 0.78 |

Data are KM estimates (n events)

# Device Thrombosis




*No. at Risk:*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Absorb | 1296 | 1287 | 1285 | 1284 | 1282 | 1280 | 1279 |
| Xience | 1308 | 1303 | 1302 | 1300 | 1300 | 1299 | 1299 |

# AIII-like vs. Not AIII-like Patients

1918/2604 pts (73.7%) enrolled in ABSORB IV were "ABSORB III-like";
686 were not (20.8% troponin+ ACS, 0.5% 3 lesions treated, 2.1% thrombus)

| | AIII-like | | | Not AIII-like | | | |
|---|---|---|---|---|---|---|---|
| **30-day outcomes** | Absorb (N=958) | Xience (N=960) | HR [95%CI] | Absorb (N=338) | Xience (N=348) | HR [95%CI] | P-value interaction |
| TLF | 5.0% | 3.0% | 1.67 [1.05, 2.65] | 4.7% | 5.5% | 0.87 [0.45, 1.68] | 0.11 |
| - Cardiac death | 0.1% | 0% | - | 0% | 0% | - | 1.00 |
| - TV-MI | 4.5% | 2.9% | 1.55 [0.96, 2.49] | 4.1% | 5.5% | 0.76 [0.38, 1.51] | 0.09 |
| - ID-TLR | 0.7% | 0.1% | 7.05 [0.87, 57.32] | 1.8% | 0.6% | 3.09 [0.62, 15.33] | 0.54 |
| Stent thrombosis | 0.4% | 0% | - | 1.2% | 0.6% | 2.06 [0.38, 11.24] | 0.99 |

# ABSORB III vs. ABSORB IV

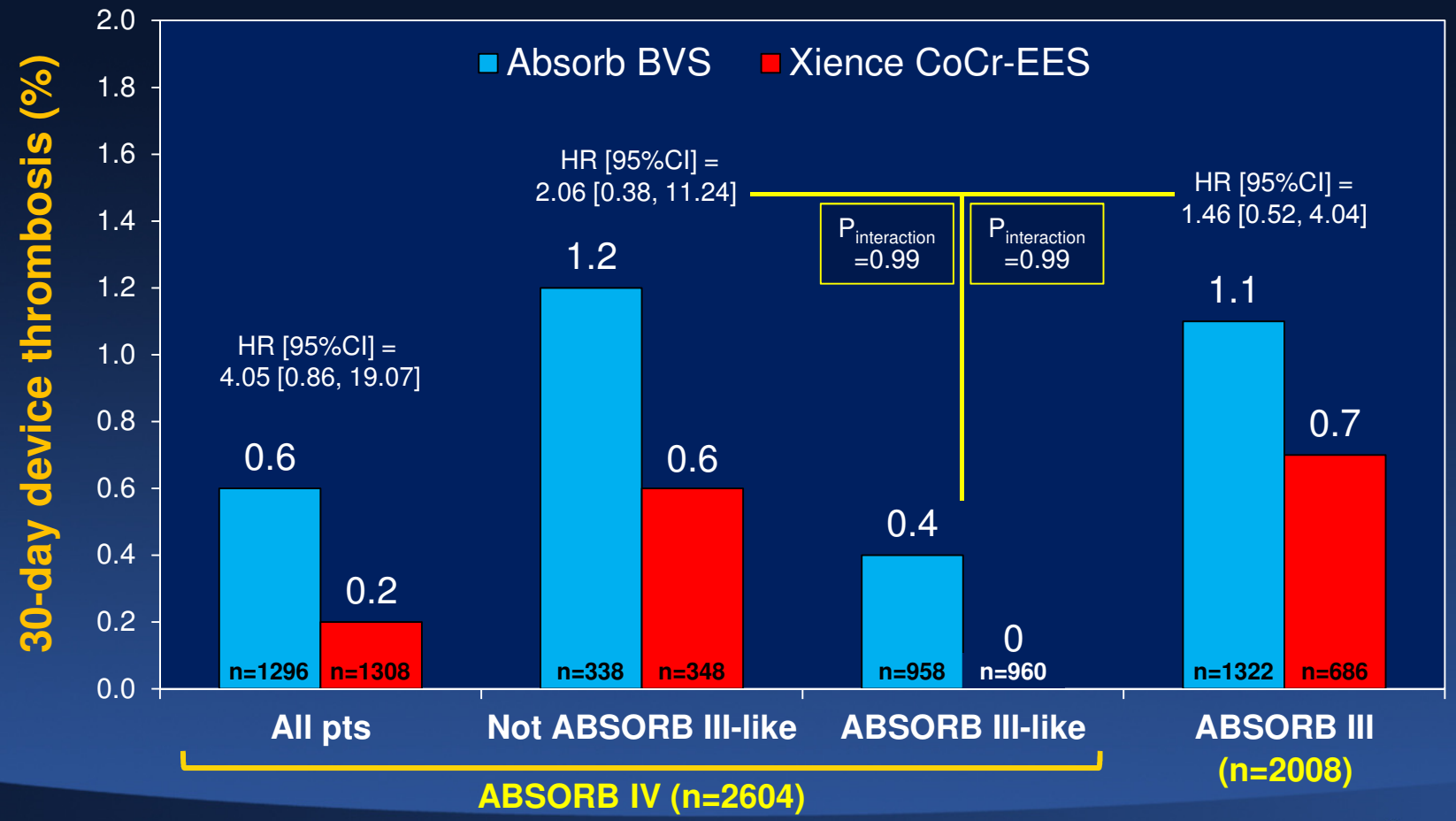
| | ABSORB III | | | ABSORB IV | | |
|---|---|---|---|---|---|---|
| | All pts (N=2008) (L=2098) | Absorb (N=1322) (L=1385) | Xience (N=686) (L=713) | All pts (N=2604) (L=2903) | Absorb (N=1296) (L=1446) | Xience (N=1308) (L=1457) |
| ABSORB III-like | 100% | 100% | 100% | 73.7% | 73.9% | 73.4% |
| Not ABSORB III-like | 0% | 0% | 0% | 26.3% | 26.1% | 26.6% |
| - troponin+ ACS | 0% | 0% | 0% | 20.8% | 20.4% | 21.1% |
| - 3 target lesions | 0% | 0% | 0% | 0.5% | 0.6% | 0.4% |
| - thrombotic lesion | 0% | 0% | 0% | 2.1% | 1.9% | 2.3% |
| [1]QCA RVD mean, mm | 2.66 | 2.67 | 2.65 | 2.89 | 2.90 | 2.89 |
| [1]QCA RVD <2.25 mm | 18.3% | 17.8% | 19.4% | 2.7% | 2.5% | 2.9% |
| [1]Pre-dil mean b/a ratio | 1.09 | 1.09 | 1.08 | 1.00 | 1.00 | 0.99 |
| [1]Pre-dil mean, atm. | 12.1 | 12.1 | 12.1 | 12.6 | 12.6 | 12.6 |
| [1]Post-dil performed | 59.8% | 64.8% | 49.9% | 68.3% | 82.6% | 54.1% |
| [1]Post-dil mean, atm. | 15.6 | 15.6 | 15.8 | 16.2 | 16.0 | 16.4 |

N= number of patients
[1] L= number of lesions

# Device Thrombosis

## ABSORB IV vs. ABSORB III

1918/2604 pts (73.7%) enrolled in ABSORB IV were “ABSORB III-like”;
686 were not (20.8% troponin+ ACS, 0.5% 3 lesions treated, 2.1% thrombus)

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# 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 in BVS patients
- Trial was underpowered for low frequency events, especially at 30 days
- Longer-term follow-up is required to understand the true safety and efficacy profile of BVS during and beyond its complete bioresorption

# Summary and Conclusions (1)

- Absorb BVS was non-inferior to Xience CoCr-EES for TLF at 30 days (primary endpoint met)
  - The relative rates of TLF and device thrombosis between BVS and CoCr-EES were similar in the non-ABSORB III-like pts (mostly troponin positive) and the more stable ABSORB III-like pts
- Compared to ABSORB III, reducing the number of very small vessels treated in ABSORB IV substantially reduced the device thrombosis rate with BVS, but also with CoCr-EES

# Summary and Conclusions (2)

- Rates of non-peri-procedural MI and ID-TLR at 30 days were greater with BVS than with CoCr-EES, and a trend toward greater stent thrombosis with BVS was present
- These data, which are largely consistent with those from earlier ABSORB trials, emphasize the need for advancements in device technology and standardized technique to further improve the early safety profile of BVS