Everolimus-eluting Bioresorbable Vascular Scaffolds in Patients with Coronary Artery Disease: ABSORB III Trial 2-Year Results

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ABSORB III/IV

Program Objectives

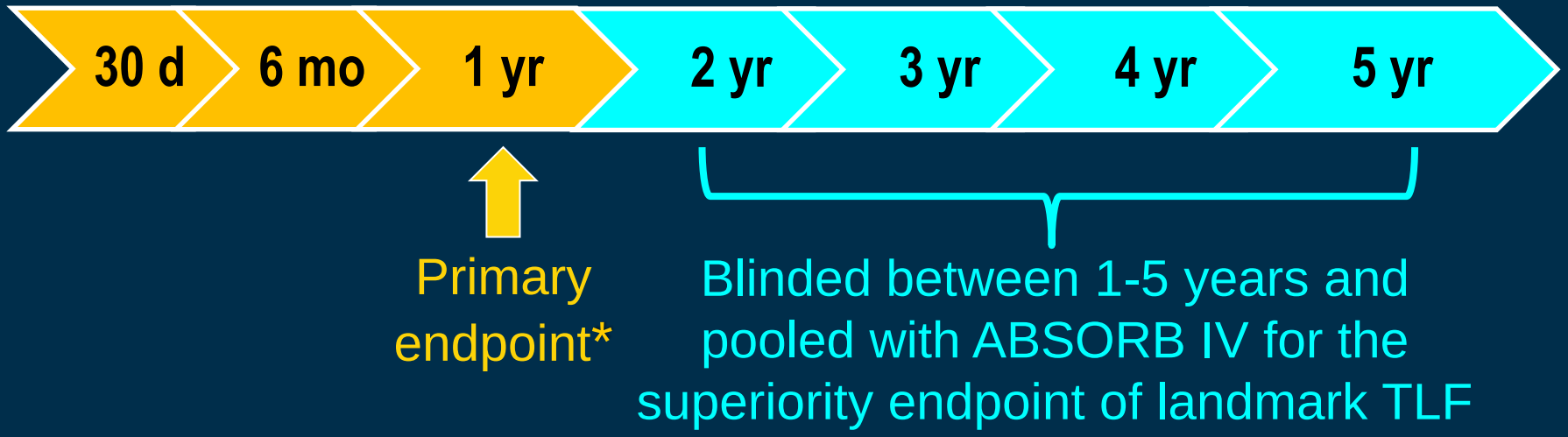
Two integrated randomized trials designed to:

- Short-term: Demonstrate similar (non-inferior) results with ABSORB BVS compared to Xience CoCr-EES
- Long-term: Demonstrate superior results with ABSORB BVS compared to Xience CoCr-EES

Initial ABSORB III Study Design

Prospective, multicenter, single-blind, trial
~2,000 patients randomized
2:1 Absorb BVS vs. Xience CoCr-EES

Clinical follow-up:

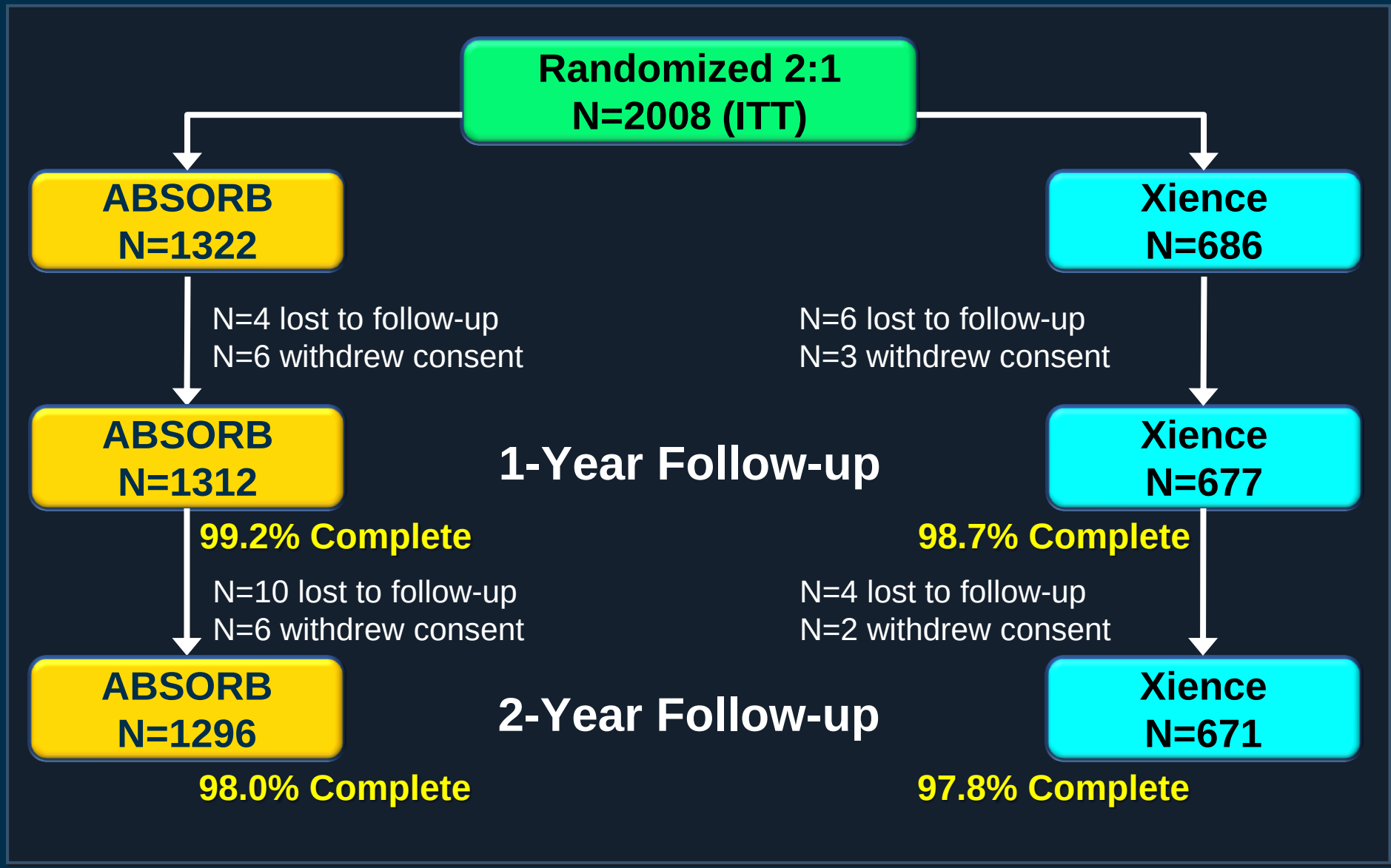


* Non-inferiority of TLF

Protocol Revision

- Superiority of Absorb BVS is not likely to emerge before the bioresorption process is complete (approximately 3 years), consistent with emerging reports of very late events between 1-3 years with BVS in small studies
- In consultation with the study PIs and the FDA, the landmark TLF endpoint of ABSORB III/IV was revised from between 1 and 5 years in the initial protocol to between 3 and 7 (or up to 10) years
- This change allows unblinding of clinical endpoints between 1 and 3 years in the ABSORB III and ABSORB IV trials

Study Flow and Follow-up



Baseline Characteristics

	Absorb (N=1322) (L=1385)	**Xience** (N=686) (L=713)	**p-value**
Patient Characteristics			
Age (mean)	63.5 ±10.6	63.6±10.3	0.75
Male	70.7%	70.1%	0.80
Diabetes	31.5%	32.7%	0.60
Unstable angina	26.9 %	24.5%	0.25
Lesion Characteristics			
Lesion length, mm	12.6 ± 5.4	13.1 ± 5.8	0.048
RVD, mm	2.67 ± 0.45	2.65 ± 0.46	0.36

As previously published, there were no major inter-group differences between baseline patient and lesion characteristics

Ellis SG et al. *N Engl J Med* 2015;373:1905-15

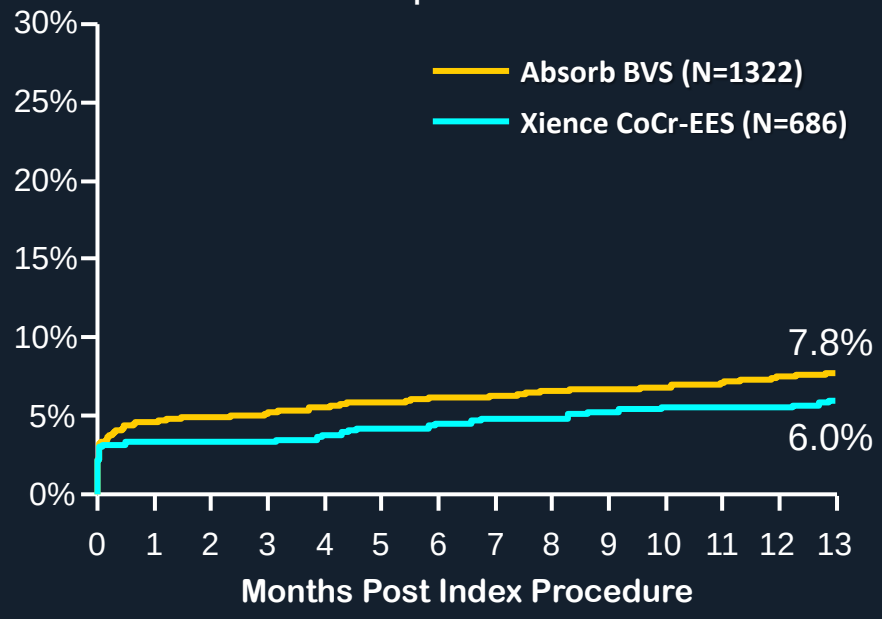
Antiplatelet Agent Usage

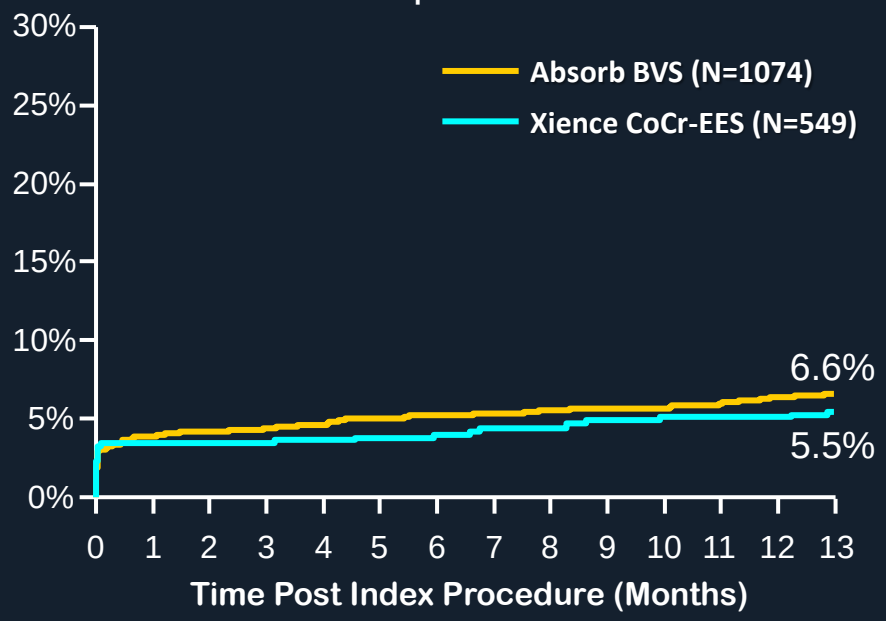
	Absorb (N=1322)	Xience (N=686)	p-value
At 1 year			
Aspirin	95.2%	95.6%	0.69
P2Y12 inhibitor	92.4%	92.3%	0.95
Clopidogrel	67.1%	71.1%	0.06
Prasugrel	17.0%	13.1%	0.02
Ticagrelor	8.5%	8.2%	0.77
DAPT	90.2%	90.7%	0.72
At 2 years			
Aspirin	92.4%	92.6%	0.87
P2Y12 inhibitor	68.2%	67.1%	0.59
Clopidogrel	50.4%	54.1%	0.12
Prasugrel	11.6%	7.7%	0.01
Ticagrelor	6.3%	5.2%	0.35
DAPT	66.0%	65.6%	0.84

ABSORB III Very Small Vessel Analysis at 1 Year

- The primary endpoint of 1-year TLF non-inferiority was met
- ABSORB III eligibility criteria included vessels with RVD 2.5 mm – 3.75 mm (visual estimation)
- ~19% of patients had a target lesion with RVD <2.25 mm by QCA (correlates with visual estimate ~2.5 mm)
- Post-hoc subgroup analysis revealed an increased 1-year risk associated with treating very small vessels (QCA RVD <2.25 mm)
- In collaboration with the FDA, Absorb IFU was updated with specific guidance to avoid BVS implantation in vessels with RVD <2.5 mm

TLF by 1 Year (13 Months)





No. at Risk:

Absorb	1322	1225	1193	1074	1006	982
Xience	686	647	634	549	522	512

Note: The 1-year window allowed follow-up through 13 months

Clinical Endpoints by 1 Year (13 Months)

	Overall		QCA RVD ≥ 2.25mm	
	Absorb (N=1322)	XIENCE (N=686)	Absorb (N=1074)	XIENCE (N=549)
TLF	7.8% (102)	6.1% (41)	6.7% (71)	5.5% (30)
Cardiac Death	0.6% (8)	0.1% (1)	0.6% (6)	0.2% (1)
TV-MI	6.0% (79)	4.6% (31)	5.2% (55)	4.6% (25)
ID-TLR	3.0% (40)	2.5% (17)	2.2% (24)	1.5% (8)
ST (Def/Prob)	1.5% (20)	0.7% (5)	0.9% (9)	0.6% (3)

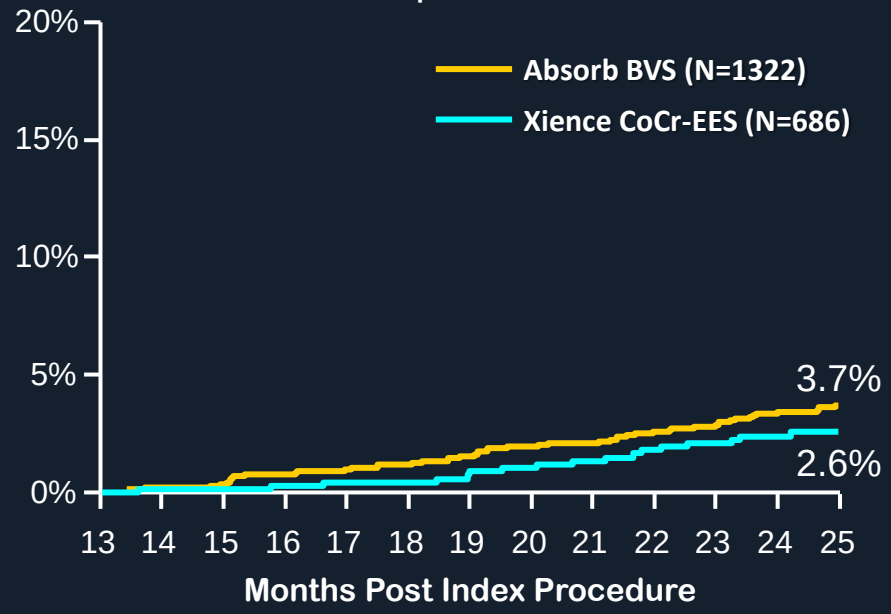
P-value >0.05 for all comparisons

Note: The 1-year window allowed follow-up through 13 months

TLF Between 1 and 2 Years (13 – 25 Months)

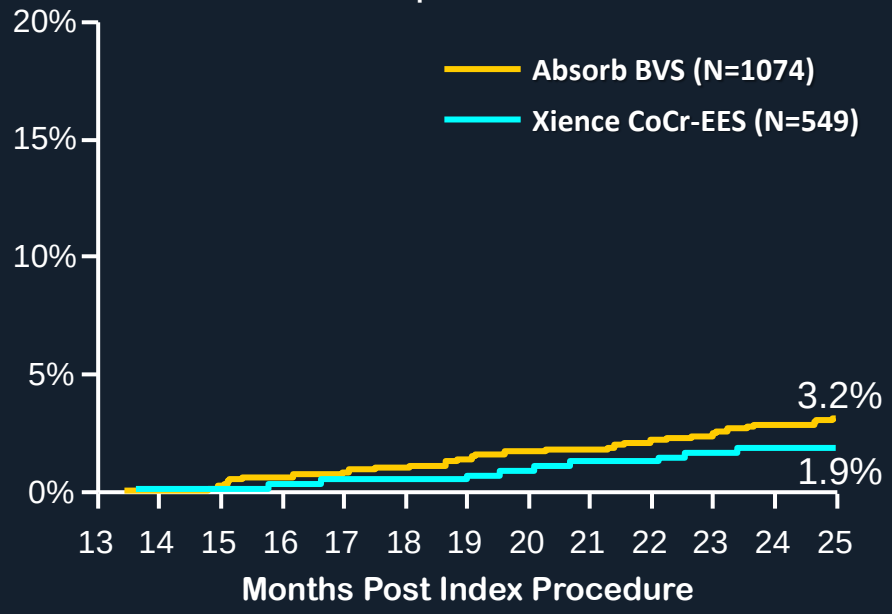
Overall

HR [95%CI]=1.45 [0.83, 2.52]
p=0.19



QCA RVD ≥ 2.25 mm

HR [95%CI]=1.71 [0.84, 3.47]
p=0.13



No. at Risk:

Absorb	1284	1255	1225	1046	1023	1002
Xience	673	658	641	540	532	521

Note: The 1-year window allowed follow-up through 13 months, and the 2-year window allowed follow-up through 25 months

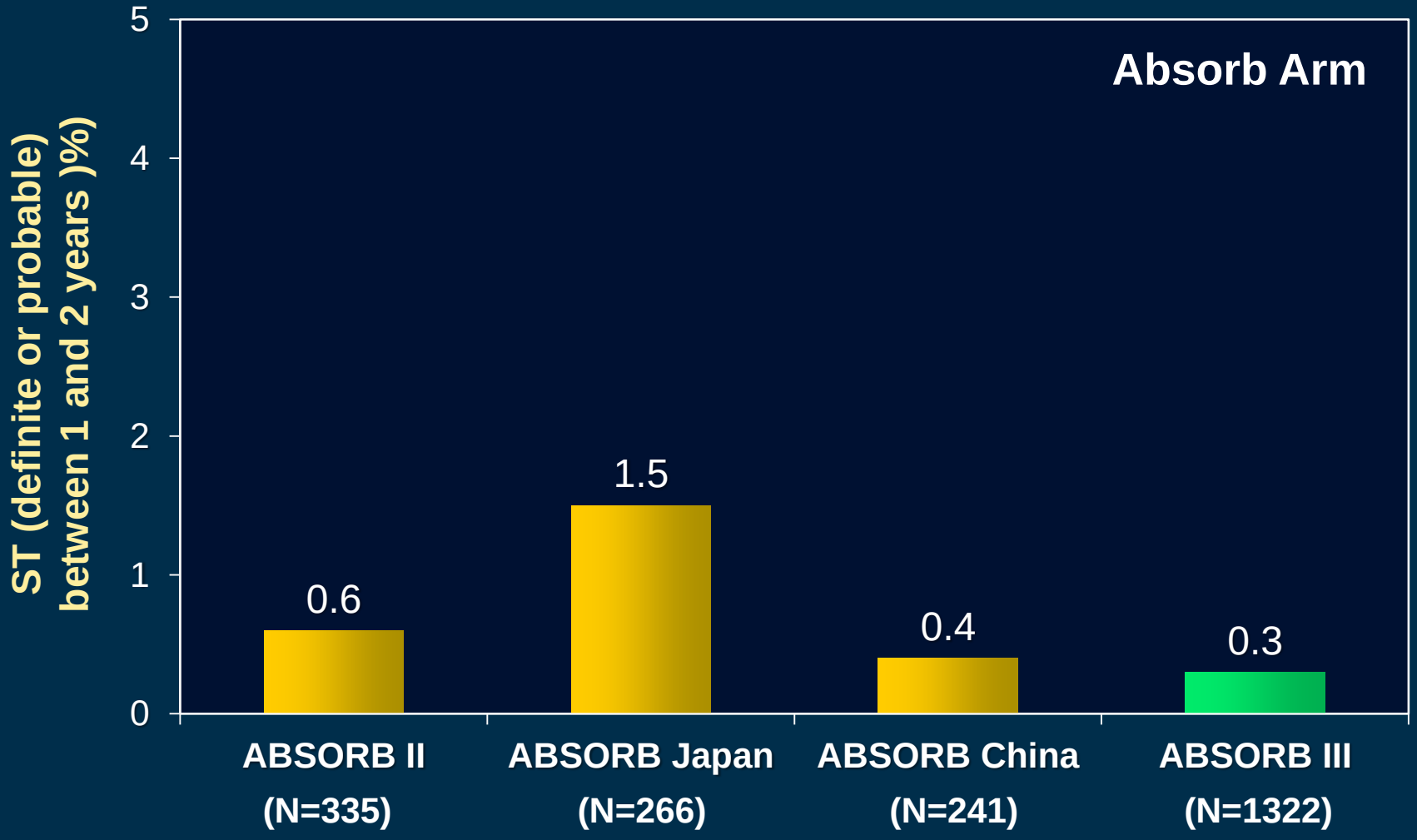
Clinical Endpoints from 1 to 2 Years (13 to 25 Months)

	Overall		QCA RVD ≥ 2.25mm	
	Absorb (N=1322)	XIENCE (N=686)	Absorb (N=1074)	XIENCE (N=549)
TLF	3.7% (47)	2.5% (17)	3.2% (33)	1.9% (10)
Cardiac Death	0.5% (6)	0.4% (3)	0.4% (4)	0.2% (1)
TV-MI	1.3% (17)	0.7% (5)	1.3% (14)	0.4% (2)
ID-TLR	2.6% (33)	1.8% (12)	2.2% (23)	1.5% (8)
ST (Def/Prob)	0.3% (4)	0.0% (0)	0.4% (4)	0.0% (0)

P-value >0.05 for all comparisons

Note: The 1-year window allowed follow-up through 13 months, and the 2-year window allowed follow-up through 25 months

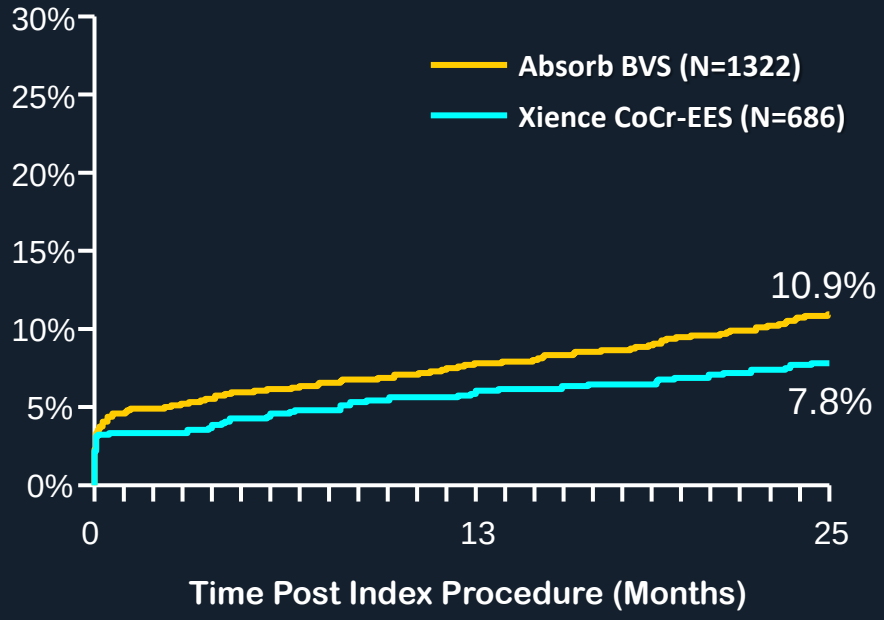
Scaffold Thrombosis Rates Between 1 and 2 Years in Perspective



TLF by 2 Years (25 Months)

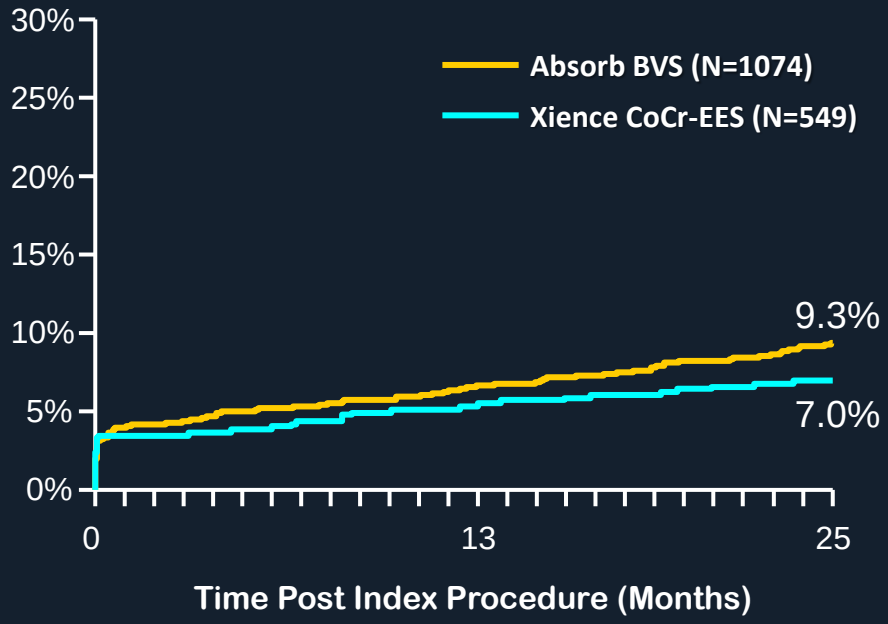
Overall

HR [95%CI]=1.42 [1.04, 1.94]
p=0.03



QCA RVD ≥ 2.25 mm

HR [95%CI]=1.35 [0.93, 1.96]
p=0.12



No. at Risk:

Absorb	1322	1193	1141	1074	982	943
Xience	686	634	608	549	512	496

Note: The 2-year window allowed follow-up through 25 months

Clinical Endpoints by 2 Years (25 Months)

	Overall		QCA RVD ≥ 2.25mm	
	Absorb (N=1322)	XIENCE (N=686)	Absorb (N=1074)	XIENCE (N=549)
TLF	11.0% (143)*	7.9% (53)*	9.4% (99)	7.0% (38)
Cardiac Death	1.1% (14)	0.6% (4)	0.9% (10)	0.4% (2)
TV-MI	7.3% (95)**	4.9% (33)**	6.5% (68)	4.8% (26)
ID-TLR	5.3% (69)	4.3% (29)	4.1% (43)	3.0% (16)
ST (Def/Prob)	1.9% (24)	0.8% (5)	1.3% (13)	0.6% (3)

* P-value=0.03. ** P-value=0.04. P-value >0.05 for all other comparisons
Note: The 2-year window allowed follow-up through 25 months

Limitations

- ABSORB III enrolled patients with stable ischemic heart disease and stabilized ACS, and excluded specific complex lesions (e.g. CTO, LM, large bif); results may therefore not be generalizable to higher-risk patients and more complex disease
- Underpowered for low frequency events
- BVS is a first generation device and was used for the first time by most operators within this trial
- Results should be viewed in context that Xience was the control device which has been associated with low rates of ST and TLF
- The optimal implantation technique was still evolving during the initiation and enrollment of ABSORB III

Blinded, Pooled, Interim ABSORB IV Outcomes: Comparison to ABSORB III

ABSORB III: 2008 pts randomized 2:1 BVS:EES (1322:686)
ABSORB IV: 3000 pts being randomized 1:1 BVS:EES

	ABSORB III Pooled (N=2008)[1]	**ABSORB IV Pooled** (N=2546)[2,3]
QCA RVD < 2.25 mm	19%	4%
Post-dilatation (BVS)	66%	83%
	Pooled Stent/Scaffold Thrombosis	
30 days	0.9%	0.4%
1 year	1.1%	0.5%

1. Assuming the observed event rates for each arm in ABSORB III, but adjusted for the 1:1 randomization ratio in ABSORB IV. The actual observed pooled ST rates in ABSORB III were 1.0% at 30 days and 1.3% at 1 year.
2. Based on February 15, 2017 data cut (N=2397 with 30-day FU and N=1415 with 1-year FU).
3. ABSORB IV includes ~25% non A-III like subjects (troponin+ ACS, 3 lesions treated, and planned staged procedures).

Summary and Conclusions

- In the large-scale randomized ABSORB III trial, the safety and efficacy profile of Absorb BVS between 1 and 2 years in patients with stable CAD and stabilized ACS was acceptable
  - In particular, the scaffold thrombosis rate between 1 and 2 years was only 0.3% (NNH=317) for Absorb
- The cumulative 2-year TLF rates were higher with Absorb than Xience (11.0% vs 7.9%, p=0.03), but in patients with appropriately sized vessels the difference was smaller (9.4% vs 7.0%, p=0.11)
- Longer-term data from the ABSORB III/IV program will determine whether better patient selection and technique improves short-term outcomes, and whether Absorb improves late outcomes compared to Xience