ABSORB II
3 years
Implication for Clinical Practice ?

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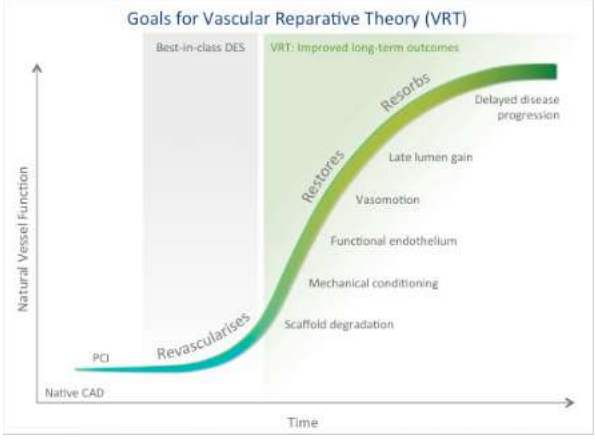
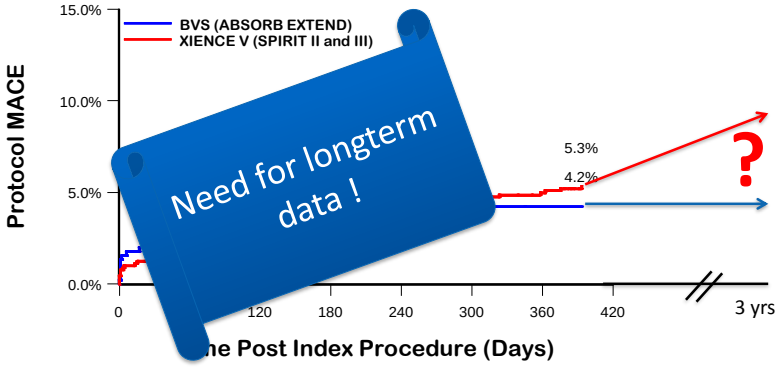
Bioresorbable Vascular Scaffold
A new paradigm

providing temporary vessel support and then allow the physiology to recover and evolve naturally.

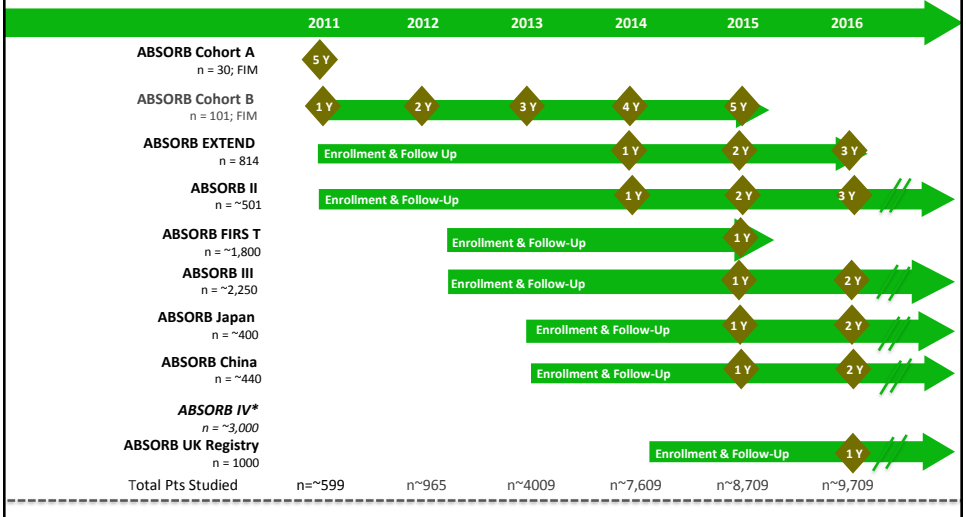


Time Course: Will events eventually stop ?



BVS (ABSORB EXTEND) At Risk:	**450**	**439**	**436**	**429**
XIENCE V (SPIRIT II and III) At Risk:	**892**	**877**	**857**	**814**

ABSORB: Clinical Trial Program



Each trial n reflects total patients. Data effective September 2013
*ABSORB IV trial is in the planning stage and subject to change.

ABSORB 1-Year Meta-analysis

Conclusions from 4 trials and 3,389 randomized patents

For treatment of simple and moderately complex lesions in pts with stable CAD and stabilized ACS, the ABSORB BVS, compared to the Xience CoCr-EES, resulted in:

1. Similar rates of the patient-oriented and device-oriented composite endpoints, consistent with comparable overall outcomes at 1 year
2. Non-significantly different rates of major safety outcomes, including death, MI, and device thrombosis
   - No significant difference in peri-procedural MI, but a small increase in TV-MI
3. Comparable measures of efficacy, including ID-TLR, ID-TVR and all revascularization

Modified from PW Serruys presentation

TCT 2016, Washington convention center
Main arena I, Sunday Oct. 30, 12:30-12:40 pm
Plenary Session VI First Report Investigations 1

ABSORB II: Three-year Clinical Outcomes from a Prospective, Randomized Trial of an Everolimus-Eluting Bioresorbable Vascular Scaffold vs. an Everolimus-Eluting Metallic Stent in Patients with Coronary Artery Disease

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Yoshinobu Onuma MD. PhD.[3]
on behalf of ABSORB II investigators
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2. Institut Jacques Cartier, Massy, France
3. Cardialysis, Rotterdam, the Netherlands / Erasmus university

Imperial College London · Abbott · Erasmus MC · CARDIALYSIS Clinical Trial Management - Core Laboratories · tct2016

Background

- Absorb BRS was CE-mark approved in December 2010 based on the data of the first in man trial (ABSORB Cohort B trial).
- "At the time of the study design in July 2011, clinical evidence has been attained without use of a comparator (Xience)." *
- The absorb II study has been powered to demonstrate two mechanistic co primary end points
  - Superiority of the bioresorbable scaffold Absorb on the metallic stent Xience in vasomotion post intracoronary nitrate
  - Non inferiority in late loss post intracoronary nitrate

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*Serruys et al. Lancet October 30, 2016—16:30 (GMT)

Design and Methods

- ABSORB II trial, prospective, randomized, single blind
- 501 patients randomized 2:1 to either Absorb or Xience
- Trial protocol allowed up to 2 de novo coronary lesions
- Device sizing based on online QCA Dmax
- Pre-dilatation with undersized balloon by 0.5 mm
- Post-dilatation: 61% in Absorb vs. 59% in Xience
- Clinical follow-up at 30 and 180 days and 1, 2, and 3 years
- Repeat invasive imaging (QCA and QIVUS) at 3 years
- QCA pre and post nitrate to assess vasomotion
- Seattle angina questionnaires pre-implantation, at 30 and 180 days and 1, 2, and 3 years
- Exercise testing with ECG: ST-T depression of ≥0.1 mV or chest pain, indicative of ischemia

Study Sponsor- Abbott Vascular Abbott

Co-primary endpoints

- **Vasomotion** assessed at 3-year follow-up by change in mean lumen diameter assessed by QCA pre and post intracoronary nitrate and assumed to be 0.07 mm for Absorb and 0.0 mm for Xience Prime.
  - **Superiority test** using a 2-sided t-test.
- **Angiographic late luminal loss** at 3-year follow-up (minimum lumen diameter [MLD] at 3 years post-nitrate minus MLD post-procedure post-nitrate)
  - **Non-inferiority test** using a one-sided asymptotic test, against a non-inferiority margin of 0·14 mm.

- **Multiple matched angiographic views for assessment of vasomotion and late loss.**

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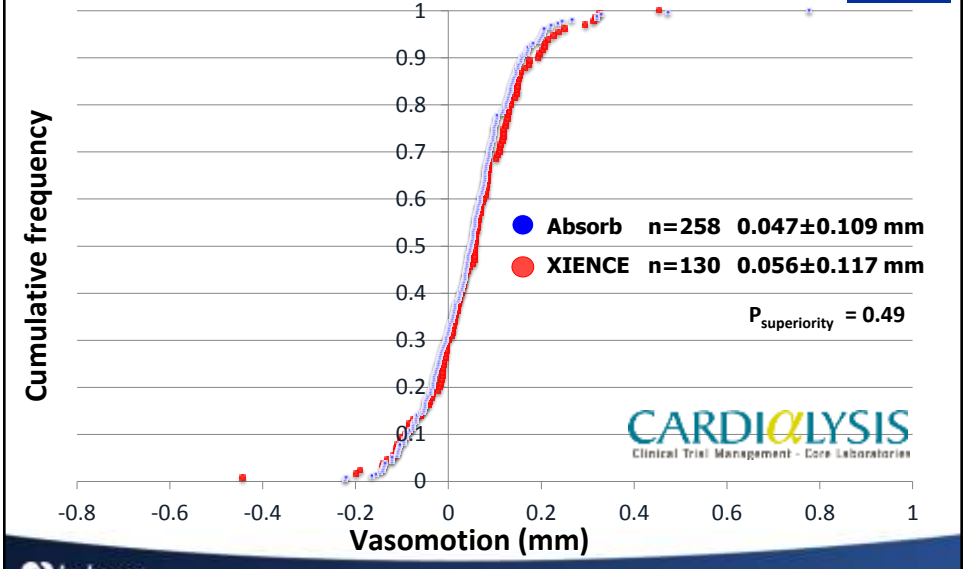
Co-primary endpoint: in-device vasomotion in ABSORB II

Cumulative frequency distribution curves of vasomotion at 3 years

Change in mean lumen diameter



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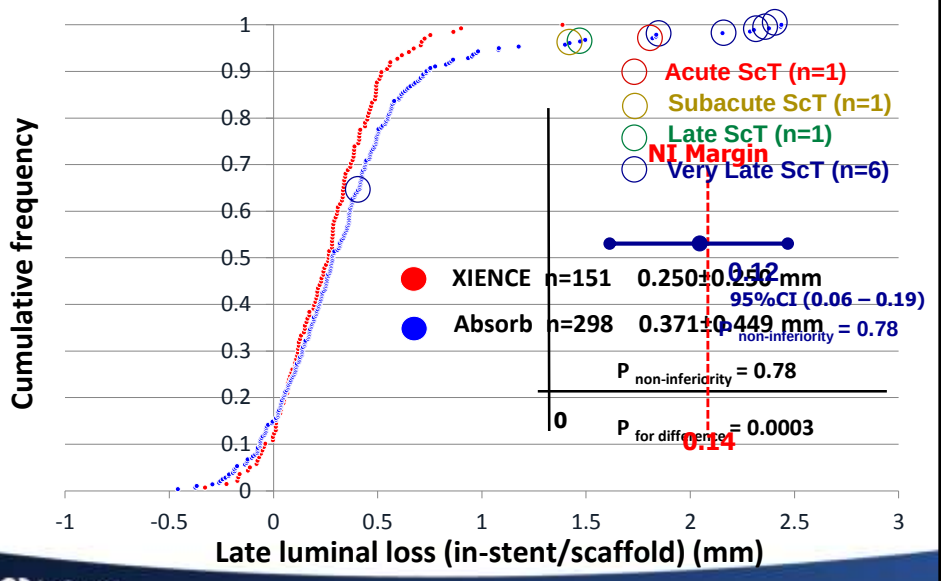
Co-primary endpoint: angiographic late luminal loss

Cumulative frequency distribution curves of late luminal loss at 3 years



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Scaffold or stent thrombosis

2 : 1 randomization

	Absorb 335 patients	Xience 166 patients	p value
Definite	**2·5% (8)**	**0·0% (0)**	**0·06**
Acute (0–1 day)	**0·3% (1)**	**0·0% (0)**	**1·0**
Sub-acute (2–30 days)	**0·3% (1)**	**0·0% (0)**	**1·0**
Late (31–365 days)	**0·0% (0)**	**0·0% (0)**	**1·0**
Very late (>365 days)	**1·8% (6)**	**0·0% (0)**	**0·19**
Definite or probable	**2·8% (9/320)**	**0·0% (0/159)**	**0·03**
Acute (0–1 day)	0·3% (1)	0·0% (0)	1·0
Sub-acute (2–30 days)	0·3% (1)	0·0% (0)	1·0
Late (31–365 days)	**0·3% (1)**	**0·0% (0)**	**1·0**
Very late (>365 days)	1·8% (6)	0·0% (0)	0·19

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Secondary angiographic endpoints

	Absorb 298 lesions		Xience 151 lesions	p value
In-scaffold/stent assessment				
Minimum lumen diameter				
Pre-procedure diameter (mm)	**1·06**	=	**1·06**	0·81
Acute gain (mm)	**1·16**	<	**1·45**	<0·0001
Post-procedure diameter (mm)	**2·22**	<	**2·50**	<0·0001
Late loss (mm)	**0·37**	>	**0·25**	0·0003
Follow-up diameter (mm)	**1·86**	<	**2·25**	<0·0001
Net gain (mm)	**0·80**	<	**1·20**	<0·0001
Percent Diameter stenosis				
Pre-procedure (%)	**59%**	=	**59%**	0·83
Post-procedure (%)	**15·6%**	>	**10·1%**	<0·0001
Follow-up (%)	**25·8%**	>	**15·7%**	<0·0001
In-device binary restenosis (%)	**7·0%**	>	**0·7%**	0·003
In-segment binary restenosis (%)	**8·4%**	>	**3·3%**	0·042

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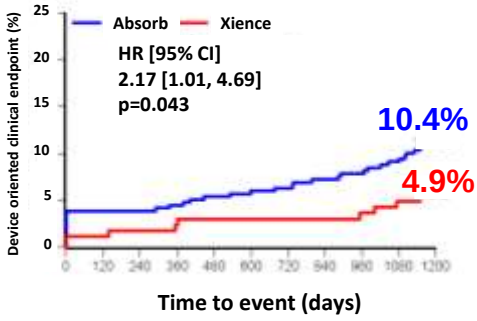
Secondary Intravascular ultrasound endpoints

	Absorb 247 lesions		Xience 136 lesions	p value
Mean lumen area				
Pre-procedure (mm^2)	**4·81**	=	**5·02**	0·1568
Post-procedure (mm^2)	**6·05**	<	**6·81**	<0·0001
Follow-up (mm^2)	**6·12**	<	**6·66**	0·003
Major secondary endpoint				
Mean Change in mean lumen area from postprocedure to 3 years (mm^2)	**+ 0·07**	>	**- 0·15**	0·02
Minimal lumen area				
Pre-procedure (mm^2)	**2·01**	=	**2·11**	0·2714
Acute gain (mm^2)	**2·89**	<	**3·64**	<0·0001
Post-procedure (mm^2)	**4·88**	<	**5·72**	<0·0001
Late loss (mm^2)	**0.56**	>	**0.33**	0.0401
Follow-up (mm^2)	**4·32**	<	**5·38**	<0·0001

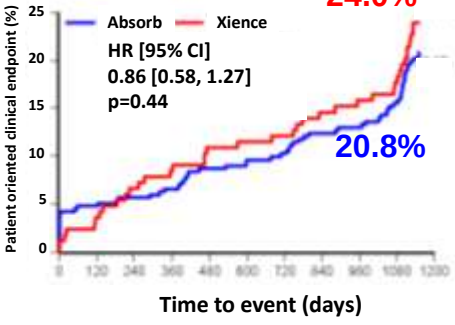
Secondary clinical endpoints (Arc definition ; WHO MI definition)

Kaplan Meier curves for Device- and Patient- oriented composite endpoints (DOCE and POCE)

DOCE Cardiac death, TV-MI, CI-TLR



POCE All-cause death, Any-MI, Any revascularization



Three-year protocol mandated imaging triggered subsequent revascularizations, clinically indicated or not.

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Secondary Clinical endpoints

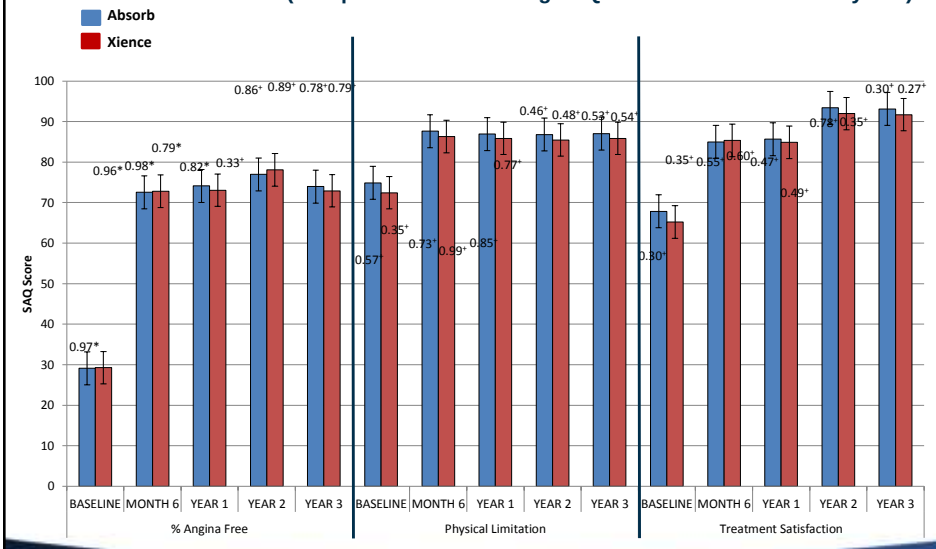
2 : 1 randomization

Non-hierarchical	Absorb 325 patients	Xience 161 patients	Relative Risk	p value
Device-oriented composite endpoint [DOCE]	10.5%	5.0%	2·11 [1·00, 4·44]	0·04
Cardiac death	0.9%	1.9%	0·50 [0·10, 2·43]	0·40
Target vessel MI	7.1% (23)	1.2% (2)	5.70 [1.36, 23.87]	0.0061
Periprocedural MI (WHO)	3.9%(13)	1.2% (2)	3.22 [0.74, 14.11]	0.16
Spontaneous MI (WHO extended)	3.1% (10)	0% (0)	NC [NC]	0.06
Clinically indicated TLR	6.2%(20)	1.9% (3)	3.30 [1.00, 10.95]	0.036

- **Out of 20 CI-TLR, 8 had a definite scaffold thrombosis with STEMI.These 8 definite scaffold thromboses are also tabulated in the category spontaneous MI in the hierarchical presentation.**
- **Out of 10 spontaneous MI, 9 were due to scaffold thrombosis (8 definite and 1 probable) and 1 definite thrombosis case died. This case is also tabulated in the category cardiac death in the hierarchical presentation.**

Seattle Angina Questionnaire

angina stability, frequency, physical limitation, disease perception, and treatment satisfaction (Compliance in answering SAQ: 93% for both arms at 3 years)



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Conclusions 1/2

- **The data presented in our report are the first randomized data published after a period of observation of 3 years.**
- **The trial did not meet its mechanistic co-primary endpoints of superior vasomotor reactivity because Xience showed unexpected vasomotion which had been hypothesised to be zero.**
- **The trial did not meet its co-primary endpoints of non-inferior late luminal loss with respect to Xience that was found to have lower late luminal loss than Absorb.**
- **Serial intravascular ultrasound follow-up showed a significant difference between the stable mean lumen area of Absorb as opposed to a significant loss in mean lumen area for Xience.**

Conclusions 2/2

- **A higher rate of device oriented composite endpoint due to target vessel myocardial infarction largely driven by peri-procedural myocardial infarction was observed in the Absorb arm.**
- **The incidence of very late scaffold thrombosis warrants further careful monitoring of the patient having a clinical follow-up of longer than 2 years.**
- **The patient oriented composite endpoint, exercise testing and anginal status (compliance: 93%) were not statistically different between both devices at 3 years with treatment satisfaction of >90% in both arms.**

THELANCET-D-16-06222R3
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Embargo: October 30, 2016—16:30 (GMT)

Articles

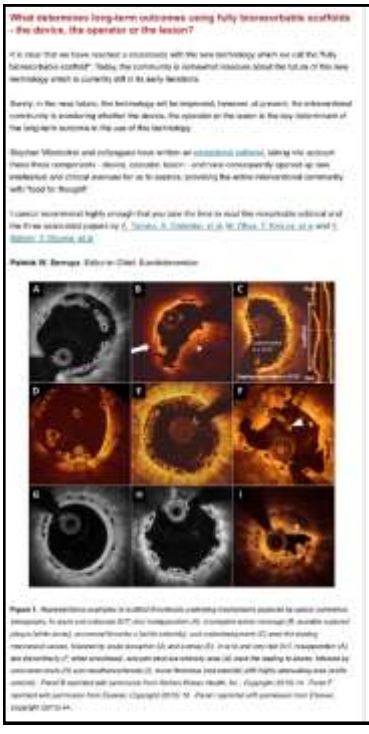
Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial

Patrick W Serruys, Bernard Chevalier, Yohei Sotomi, Angel Cequier, Didier Carrié, Jan J Piek, Ad J Van Boven, Marcello Dominici, Dariusz Dudek, Dougal McClean, Steffen Helqvist, Michael Haude, Sebastian Reith, Manuel de Sousa Almeida, Gianluca Campo, Andrés Iñiguez, Manel Sabaté, Stephan Windecker, Yoshinobu Onuma

"Future studies should investigate the clinical impact of accurate intravascular imaging in sizing the device and in optimizing the scaffold implantation. The benefit and need for prolonged dual antiplatelet therapy after bioresorbable scaffold implantation could also become a topic for future clinical research."

ABSORB II
Conclusions

- Disappointing late results
  - No difference in vasomotion (i.e. normalisation)
  - No difference in efficiency
- Late stent thrombosis



Ongoing discussion

Data awaited:

AIDA

Absorb III 2 years unblinded

ACC 2017