IV Congresso
Novas Fronteiras em Cardiologia

# Stents ou BVS

## Bioabsorbable Vascular Scaffolding

7 a 9 de Fevereiro 2014
Hotel Vila Galé Ericeira

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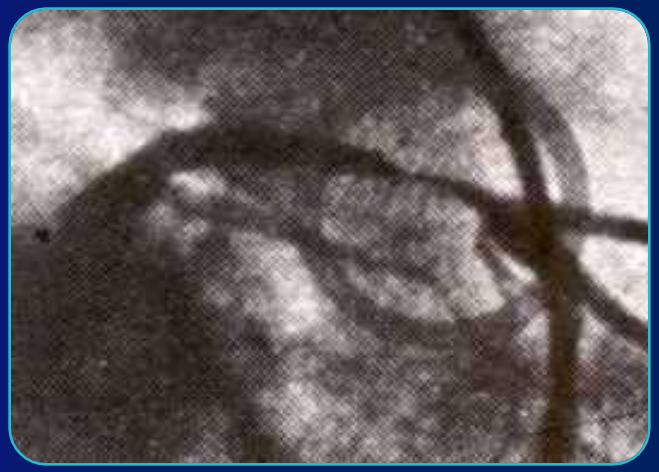
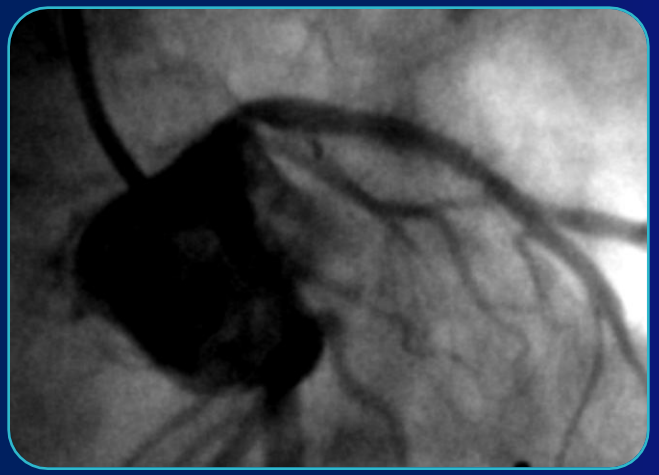
# First PTCA and 23-Year Follow Up

**1977**



**2000**



In patients who did not suffer sub-acute closure due to dissections, or restenosis due to negative remodeling in the first few months, long term results following balloon angioplasty were very encouraging and durable, with loss in MLD not seen until 17 years post procedure[1]

1. Hatrick, R., et al. *EuroIntervention*. 2009;5:121-126.

# Evolution of PCI Therapy Improving Patient Outcomes

**1977**

**Balloon Angioplasty (PTCA)**

**1986**

**Bare Metal Stents (BMS)**

**2001**

**Coronary Drug Eluting Stents (DES)**

**2006**

**Bioresorbable Vascular Scaffold (BVS)**

Advancements in PCI

# What is Required of a Fully Biorebsorbable Scaffold to Fulfill the Desire for a 'Vascular Restoration Therapy'?

*Revasculascularization*

0 to 3 months

**Performance should mimic that of a standard DES**

- Good deliverability
- Minimum of acute recoil
- Hight acute radial strength
- Controlled delivery of drug to abluminal tissue

*Restoration*

3 to ~ 6-9 months +

**Transition from scaffolding to discontinous structure**

- Gradually lose radial strenght
- Struts must be incorporated into the vessel wall (strut coverage)
- Become structurally discontinuous
- Allow the vassel to respond naturally to physilogical stimuli

*Resorption*

~9 months +

**Implant is discontinous and inert**

- Resorb in a benign fashion

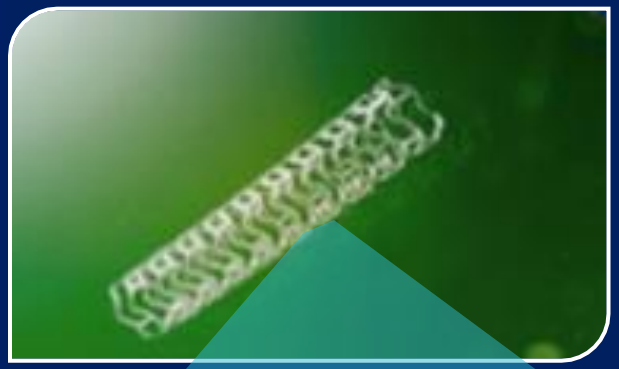
# BVS Advantage

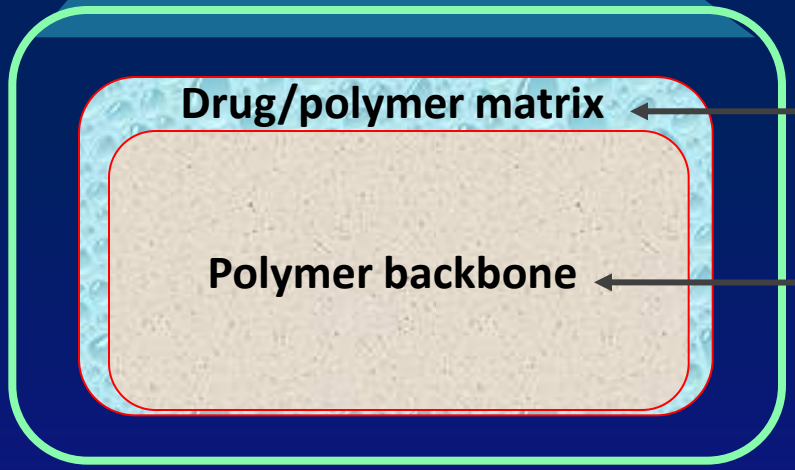
| | Balão | BMS | DES | BVS |
|---|---|---|---|---|
| Oclusão aguda | – | + | + | + |
| Trombose aguda *stent*/BVS | NA | – | +/– | + |
| Trombose subaguda *stent*/BVS | NA | – | – | + |
| Trombose tardia *stent*/BVS | NA | – | – | + |
| Recolha elástica | – | + | + | + |
| Remodelação constritiva | – | + | + | + |
| Hiperplasia da neoíntima | – | – | + | + |
| Remodelação expansiva | – | – | – | + |
| Aumento tardio do lúmen | + | – | – | + |
| Vasomotricidade tardia do vaso | – | – | – | + |
| Preservação dos colaterais | – | – | – | + |
| Preservação para pontagem | + | – | – | + |
| Reavaliação não invasiva | + | – | – | + |

# Bioabsorbable Vascular Scaffolds

| Companhia | Dispositivo | Descrição/Estudo | Fármaco | Estado |
|---|---|---|---|---|
| Abbott | ABSORB | PLLA totalmente absorvido em dois anos<br>ABSORB program | Everolimus | Marca CE |
| A.R.T. | A.R.T. Bioresorbable stent | PLA (2009) | Não | FIM em curso |
| Biotronik | DREAMS | Magnésio em liga 93%<br>BIOSOLVE-I (2007-2013) | Paclitaxel | FIM concluído |
| Elixir | DESolve | PLLA<br>DESSOLVE-I (2013) | Novolimus | Marca CE |
| Huaan | Xinsorb | PLLA (2012) | Sirolimus | FIM concluído |
| Kyoto Medical | Igaki-Tamai | PLLA absorvido em dois anos (2000) | Não | FIM concluído |
| REVA Medical | REVA-ReZolve | Policarbonato de tirosina absorvido em 18 meses, libertação por deslizamento e fecho<br>RESORB, (2007, não publicado) | Não | FIM concluído |
| Bioabsorbable Therapeutics | Ideal Biostent | Polisalicilato absorvido em 12 meses<br>WISPHER (2009, não publicado) | Sirolimus | FIM concluído |

# ABSORB BVS





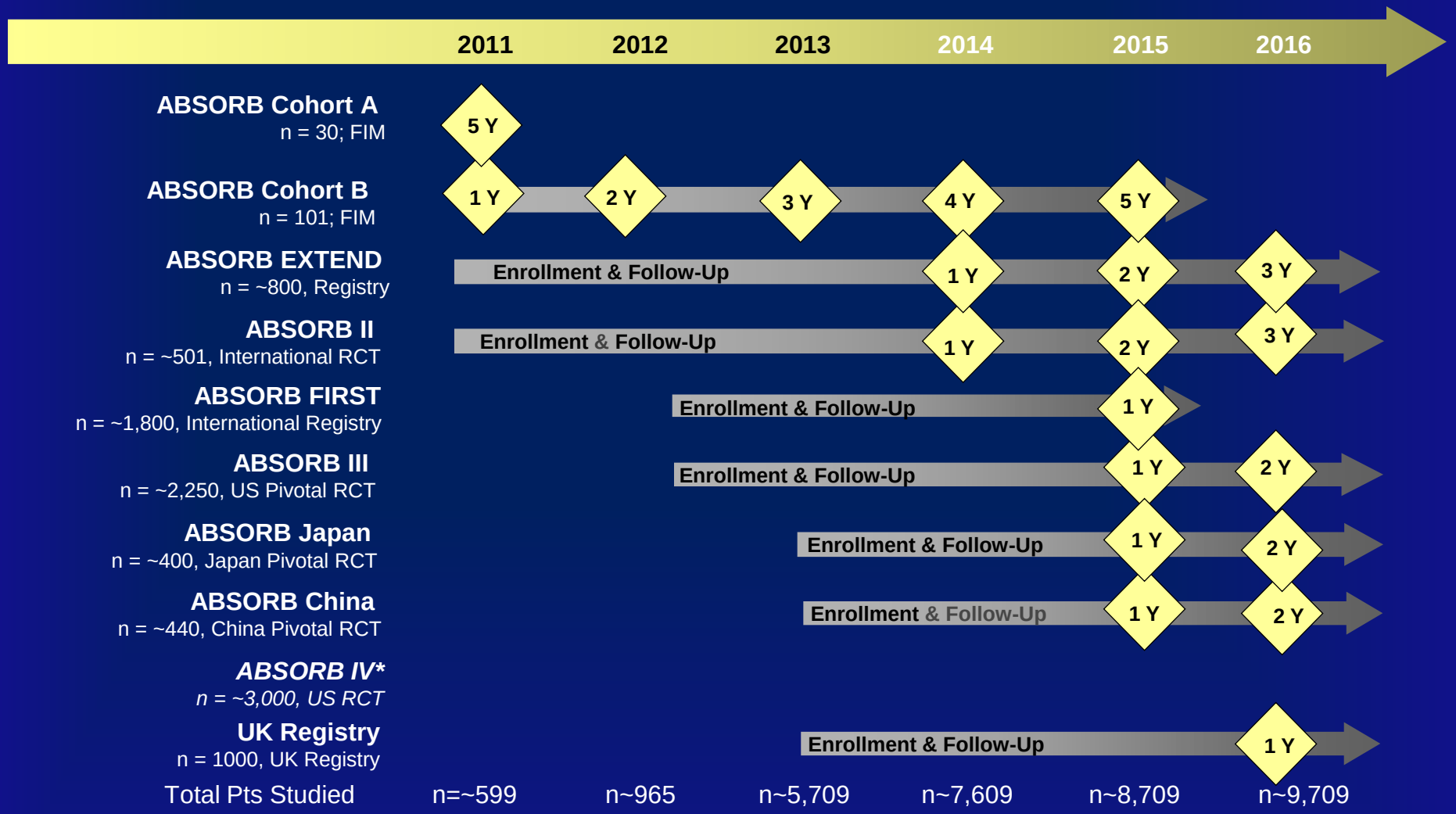

**Everolimus/PDLLA Matrix Coating**

- Thin layer
- Amorphous (non-crystalline)
- 1:1 ratio of Everolimus/PDLLA matrix
- Conformal coating, 2-4 μm thick
- Controlled drug release

**PLLA Scaffold**

- Semi-crystalline
- Provides device structure
- Processed for required radial strength

# Absorb
## Comprehensive AV-Sponsored Clinical Trial Program




Each trial n reflects total patients. Data effective September 2013

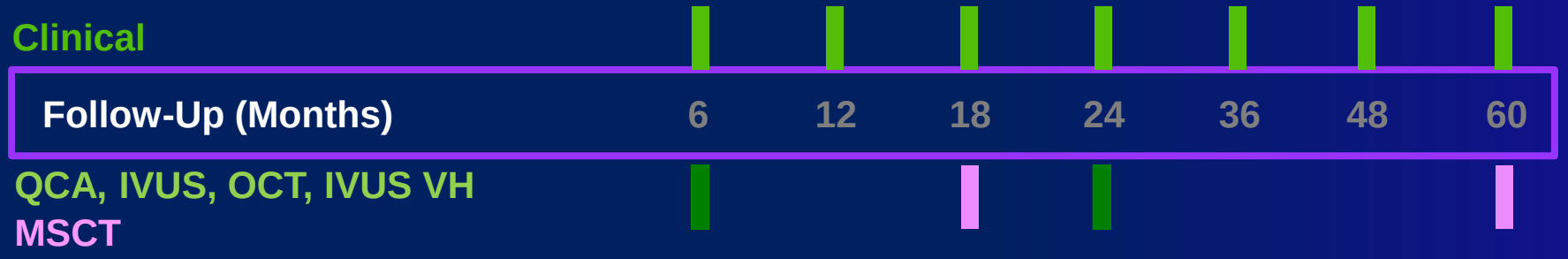
*ABSORB IV trial is in the planning stage and subject to change.

# Investing in a Comprehensive ABSORB Clinical Program – Investigator Sponsored Trials

| Study Title | Design | Number of Patients | Primary Endpoint | Patient FU (Years) |
|---|---|---|---|---|
| **Randomized Controlled Trials (2,764 Pts)** | | | | |
| AIDA | All – comers RCT vs Xience | 2194 | 2-Yr TVF | 5 |
| TROFI II | STEMI RCT vs XIENCE | 190 | 6-Mo neo-intimal healing score | 3 |
| PROSPECT II ABSORB | RCT vs OMT in unstable asymptomatic pts | 300 | 2-Yr IVUS MLA | 3 |
| PROACTIVE | RCT vs XIENCE | 20 | Peri-Proc Platelet Reactivity | 1 |
| VANISH | RCT vs XIENCE | 60 | Evolution of myocardial blood flow values over time | 3 |
| **Registries (10,030 Pts)** | | | | |
| BVS EXPAND | All – comers Registry (excl STEMI) | 300 | 1 – Yr MACE | 5 |
| ASSURE | All – comers Registry | 180 | Safety and Efficacy | 3 |
| ABSORB CTO | Feasibility in CTO | 20 | Safety and Performance | 2 |
| PABLOS | Feasibililty in Bifurcations | 30 | Device, Procedural, Main and Side Branch Success | 2 |
| IT-DISSAPEARS | MVD and Long Lesion Registry | 1000 | Safety and Efficacy | 5 |
| GABI-R | All – comers Registry | 5000 | Safety and Efficacy | 5 |
| REPARA | All – comers Registry | 1500 | 1- Yr MACE | 1 |
| POLAR ACS | ACS Registry | 100 | Safety, clinical device, procedure success and in-hospital MACE | 1 |
| France ABSORB | Feasibility in de novo lesions | 2000 | 1 – Yr MACE | 1 |

# Introduction
# ABSORB Cohort A

**30 subjects**
(Non-randomized) 4 sites in Europe & New Zealand




| | |
|---|---|
| **Study Objective** | **First In Man, Single Arm – safety/performance** |
| **Endpoints** | **Typical PCI clinical and imaging endpoints** |
| **Treatment** | **Single, *de novo* native coronary lesion in a vessel with a reference vessel diameter of 3.0 mm** |
| **Device Sizes** | **3.0 x 12 mm scaffolds (3.0 x 18 mm scaffolds available after enrolment start and used in 2 pts)** |

# ABSORB Cohort A
# Excellent Long-Term Data Out to 5 Years

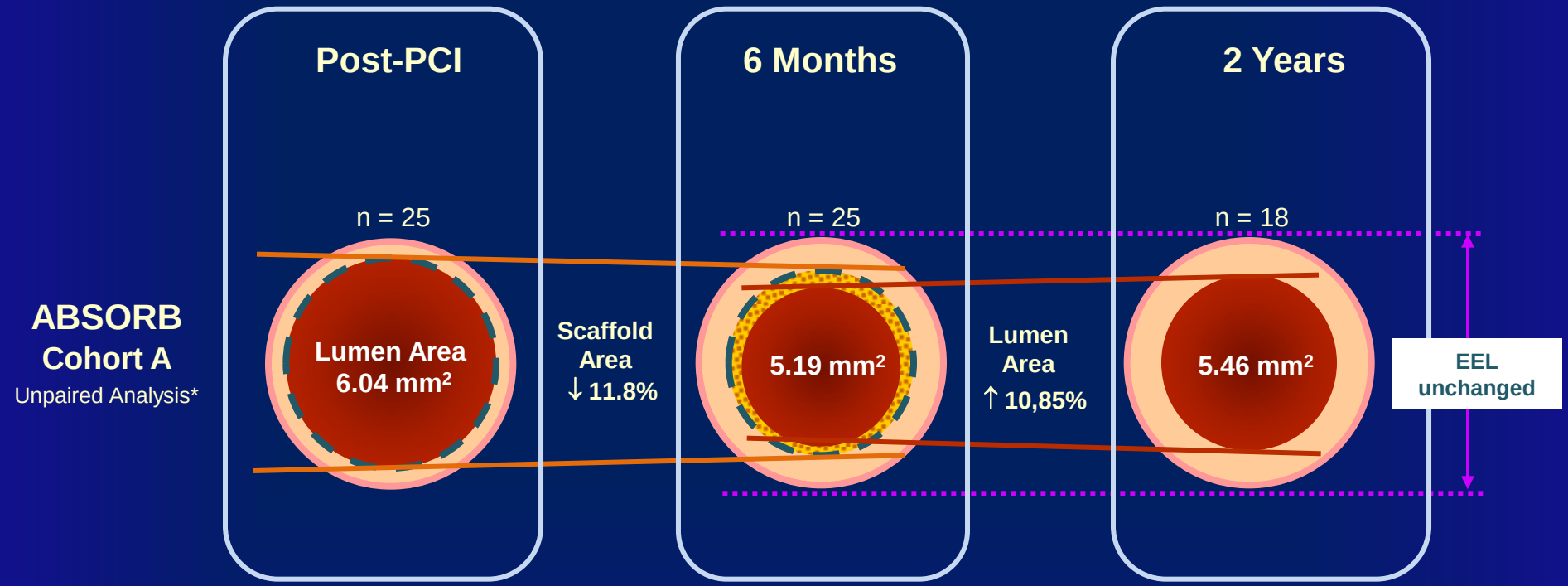
- **ABSORB Cohort A Clinical Results at Each Phase: Intent to Treat**

| | RESTORATION | | RESORPTION | |
|---|---|---|---|---|
| Hierarchical | 6 Months<br>30 Patients | 1 year<br>29 Patients** | 2 Year<br>29 Patients** | 5 Year<br>29 Patients** |
| Ischemia Driven MACE*** | 1 (3.3%)* | 1 (3.4%)* | 1 (3.4%)* | 1 (3.4%)* |
| Cardiac Death | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| MI | 1 (3.3%)* | 1 (3.4%)* | 1 (3.4%)* | 1 (3.4%)* |
| Q-Wave MI | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Non Q-Wave MI | 1 (3.3%)* | 1 (3.4%)* | 1 (3.4%)* | 1 (3.4%)* |
| Ischemia Driven TLR | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| by PCI | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.%) |
| by CABG | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.%) |

**No scaffold thrombosis by ARC or Protocol**

*Same patient – this patient also underwent a TLR, not qualified as ID-TLR (DS = 42%). **One patient withdrew consent and missed the 9, 12, 18 month and 2, 3, and 4 year visits; two patients died from a non-cardiac causes, one at 706 days and one at 888 days post procedure. ***MACE – Composite endpoint comprised of cardiac death, myocardial infarction (MI) and ischemia-driven target lesion revascularization (TLR) by PCI or CABG.

# ABSORB Cohort A
# Temporal Lumen Dimensional Changes, Per Treatment

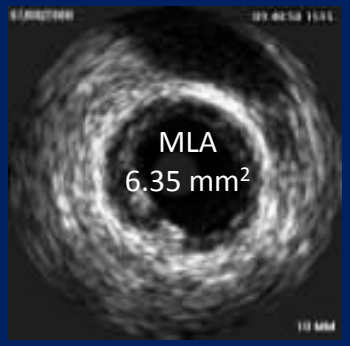
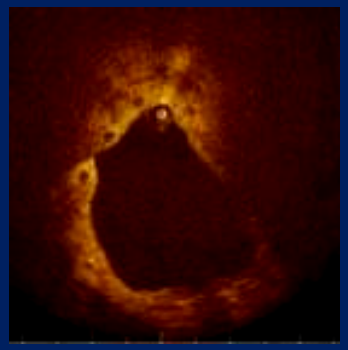
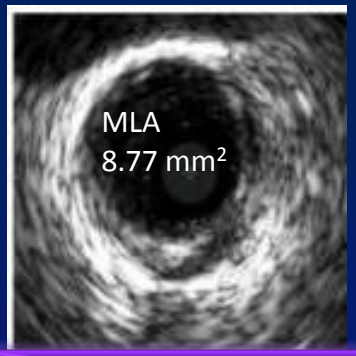
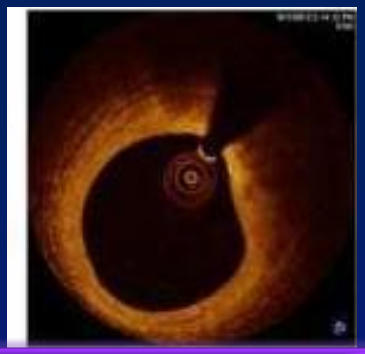



- Late lumen loss at 6 months mainly due to reduction in scaffold area
- Very late lumen gain noted from 6 months to 2 years

*Adapted from Serruys, PW, ABSORB Cohort A 2-year IVUS and OCT results; ACC 2009.

# Restoration and Resorption
# Late Lumen Enlargement

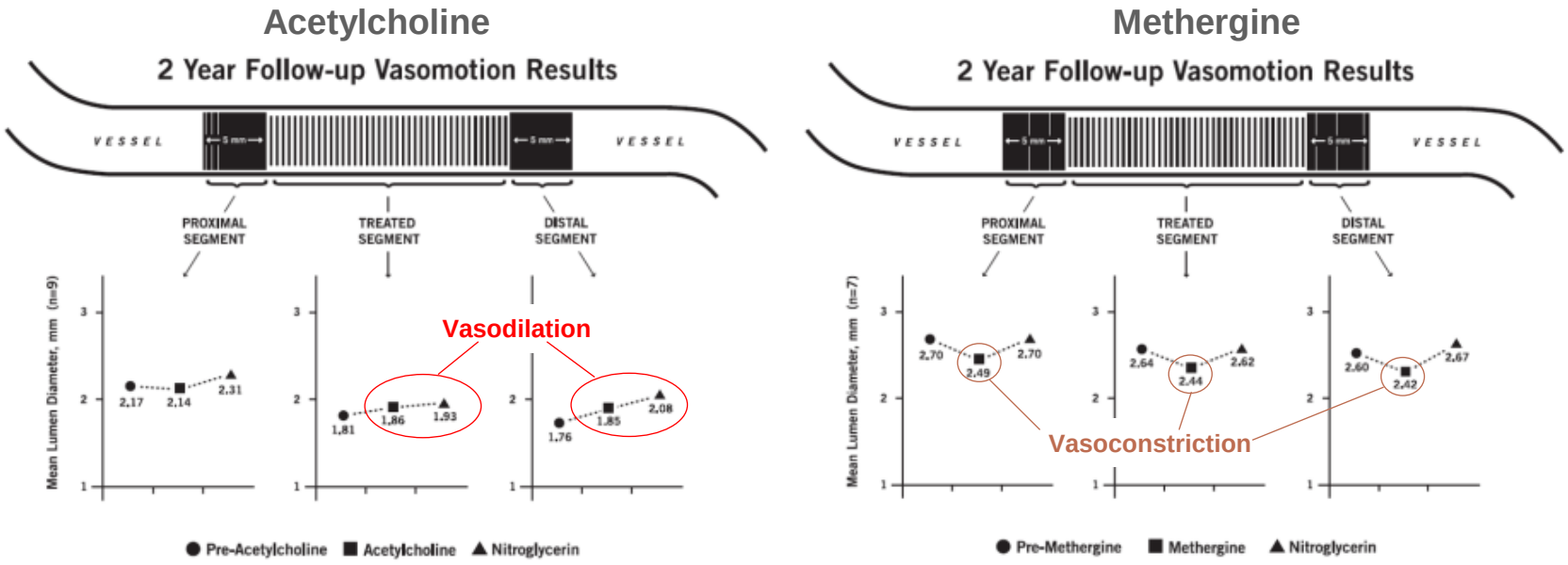
**ABSORB A 5 Yr**

| | IVUS | OCT |
|---|---|---|
| 6 month follow up |   |  |
| **Δ 1.42mm** | | |
| 5 year follow up |   |  |

**Late lumen enlargement/gain and 'characteristic 'final golden tube' on OCT illustrating functional reparation of the vessel**

# ABSORB Cohort A
# Vasomotor Function Testing at 2 Years

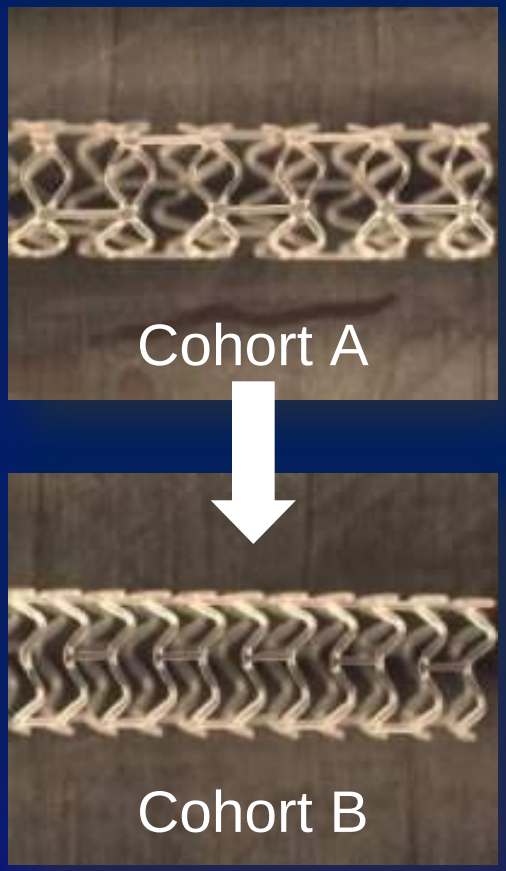
## ABSORB Cohort A at 2 years




**The reappearance of vasomotion in the proximal, distal, as well as treated segments in response to methergine or acetylcholine suggests that vessel vasoreactivity has been restored and that a physiological response to vasoactive stimulus might occur anew.**

Serruys, PW, et al. *Lancet* 2009; **373**: 897-910.

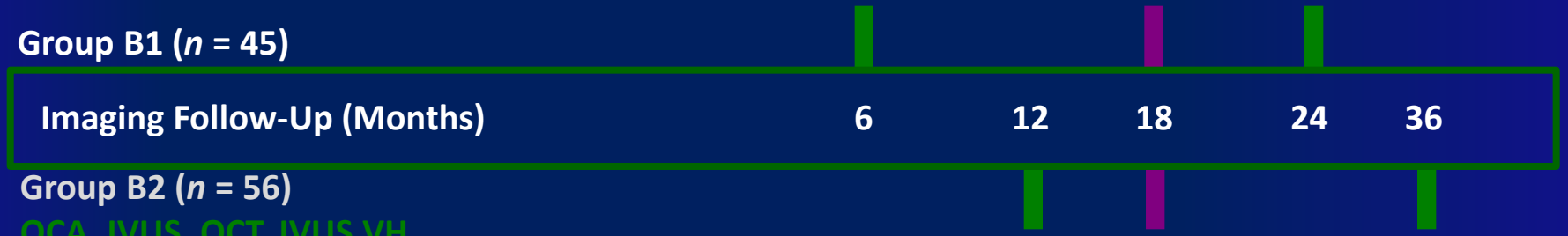
# BVS Device Optimization Objectives




- **More uniform strut distribution**
- **More even support of arterial wall**
- **Lower late scaffold area loss**
  - Maintain radial strength for at least 3 months
- **Storage at room temperature**
- **Improved device retention**
- **Unchanged:**
  - Material, coating and backbone
  - Strut thickness
  - Drug release profile

# Introduction
# ABSORB Cohort B

**101 subjects**
(Non-randomized) 12 sites in Europe, Australia, New Zealand




| | |
|---|---|
| Study Objective | First In Man, Single Arm – safety/performance |
| Endpoints | Typical PCI clinical and imaging endpoints |
| Treatment | Up to 2 *de novo* lesions in different epicardial vessels<br>Reference vessel diameter of 3.0 mm, lesions ≤ 14 mm in length |
| Device Sizes | 3.0 x 18 mm devices |

# ABSORB Cohort B Groups 1&2 Clinical Results – Intent to Treat

| | 30 Days | 6 Months | 1 Year | 2 Years | 3 Years |
|---|---|---|---|---|---|
| **Non-Hierarchical** | **n = 101** | **n = 101** | **n = 101** | **n = 100*** | **n = 100*** |
| **Cardiac Death %** | **0** | **0** | **0** | **0** | **0** |
| **Myocardial Infarction % (n)** | **2.0 (2)** | **3.0 (3)** | **3.0 (3)** | **3.0 (3)** | **3.0 (3)** |
| **Q-wave MI** | 0 | 0 | 0 | 0 | 0 |
| **Non Q-wave MI** | 2.0 (2) | 3.0 (3) | 3.0 (3) | 3.0 (3) | 3.0 (3) |
| **Ischemia driven TLR % (n)** | **0** | **2.0 (2)** | **4.0 (4)** | **6.0 (6)** | **7.0 (7)** |
| **CABG** | 0 | 0 | 0 | 0 | 0 |
| **PCI** | 0 | 2.0 (2) | 4.0 (4) | 6.0 (6) | 7.0 (7) |
| **Hierarchical MACE % (n)** | **2.0 (2)** | **5.0 (5)** | **6.9 (7)** | **9.0 (9)** | **10.0 (10)** |
| **Hierarchical TVF % (n)** | **2.0 (2)** | **5.0 (5)** | **6.9 (7)** | **11.0 (11)** | **13.0 (13)** |

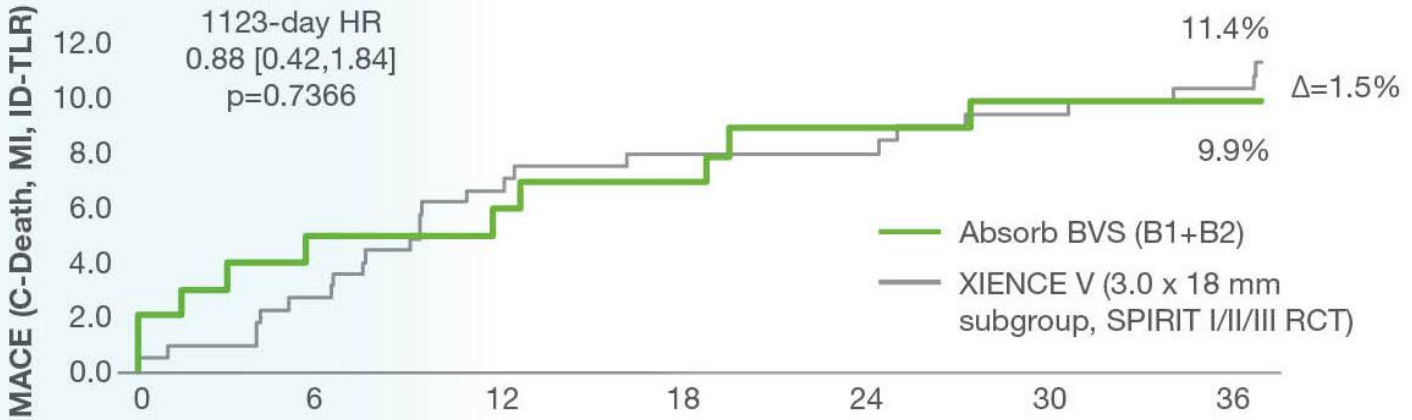
**No scaffold thrombosis by ARC or Protocol out to 3 Years only 3 additional TLR events between 1 and 3 years**

Serruys, PW, ABSORB Cohort B 3-year results; ACC 2013 / *One patient missed the 2 year FUP

MACE: Cardiac death, MI, ischemia-driven TLR
TVF: Cardiac death, MI, ischemia-driven TLR, ischemia-driven TVR

# ABSORB Cohort B Clinical Results – MACE

## Numerically Lower Long-Term Event Rates versus a Best-in-Class DES



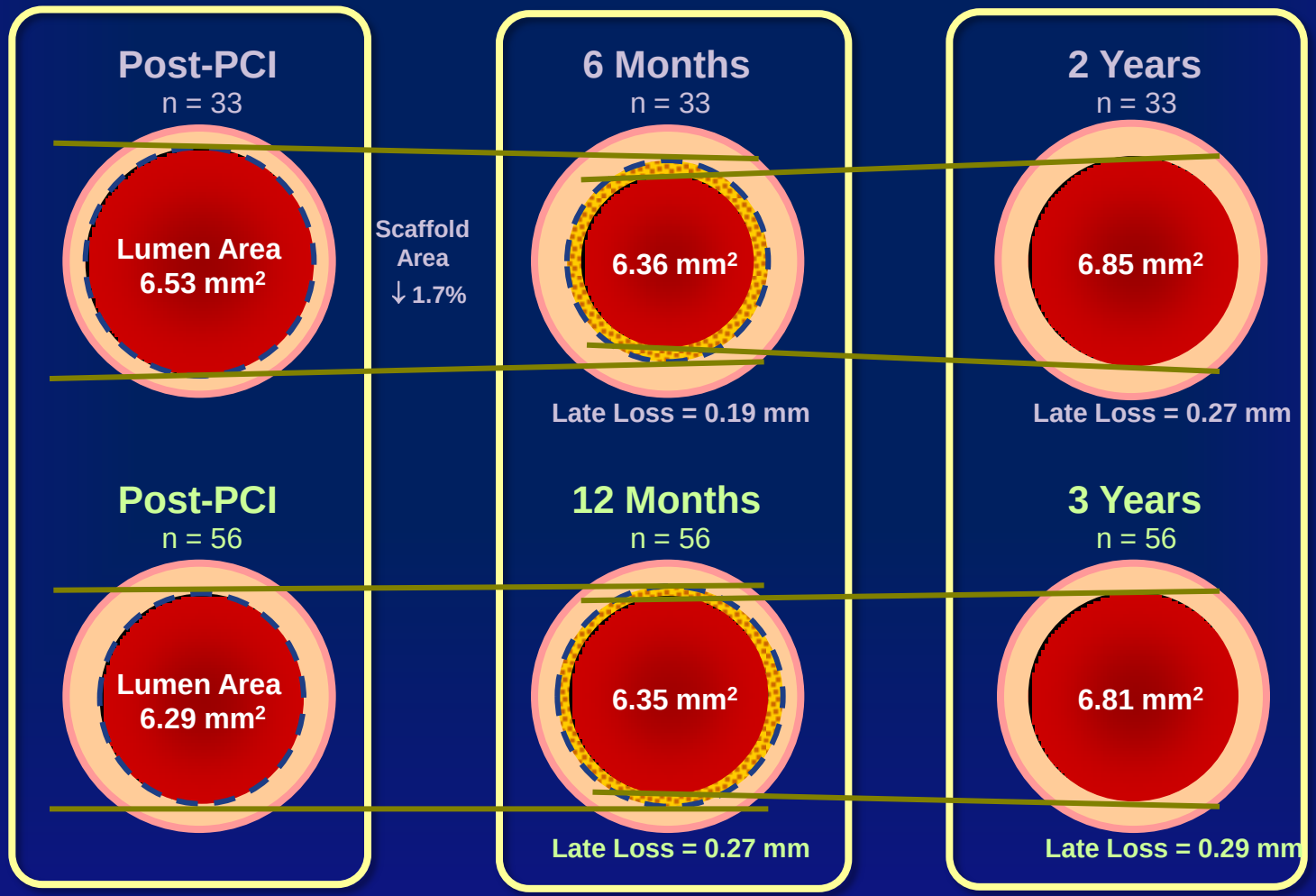

**Number at Risk**

| Time After Index Procedure (Days) | 0 | 37 | 194 | 284 | 393 | 573 | 758 | 1123 |
|---|---|---|---|---|---|---|---|---|
| Absorb BVS (B1+B2) | 101 | 99 | 96 | 96 | 94 | 92 | 91 | 89 |
| XIENCE V (3.0 x 18 mm subgroup, SPIRIT I/II/III) | 227 | 224 | 219 | 211 | 204 | 202 | 191 | 182 |

*Note: The datasets are from different trials, and displayed for descriptive purposes only.*

Serruys PW, ABSORB Cohort B 3Year Data, Rotterdam EuroPCR Focus on BVS 2013

# ABSORB Cohort B
# Temporal Lumen Dimensional Changes

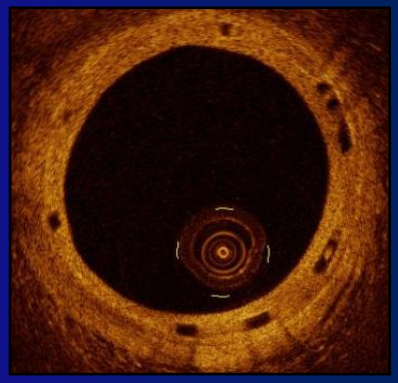



*Serruys, PW., ABSORB Cohort B 2-year results; TCT 2011
**Serruys, PW., ABSORB Cohort B 3-year results; ACC 2013

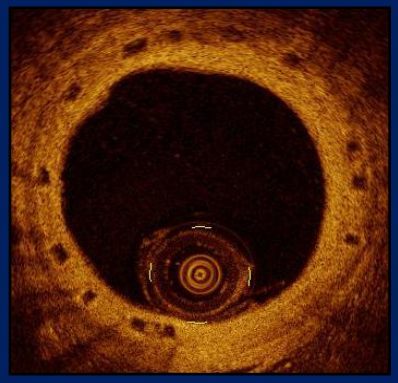
1. Patient-level serial analysis
2. Calculated from overall mean values

# Resorption: Vascular Response

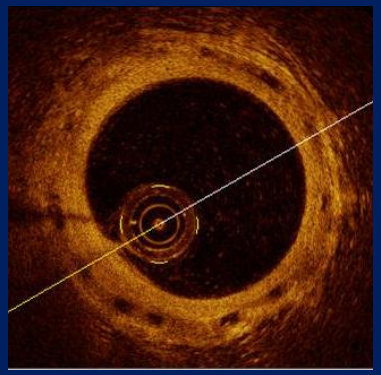
**Cohort B, Preclinical OCT Images**



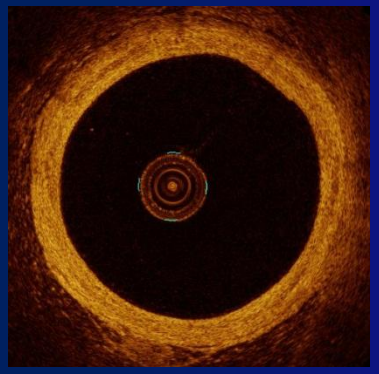
**6 months**



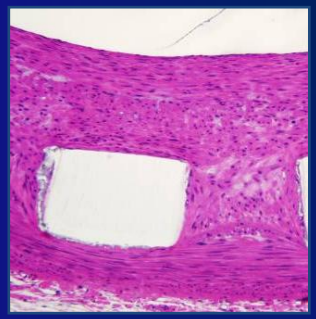
**24 months**

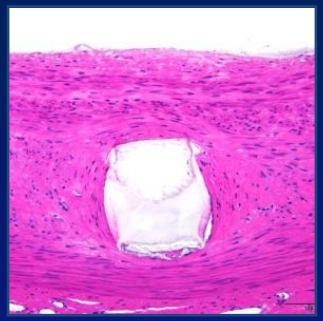


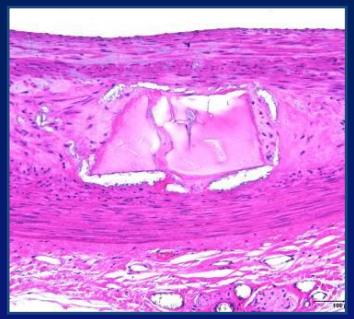
**36 months**

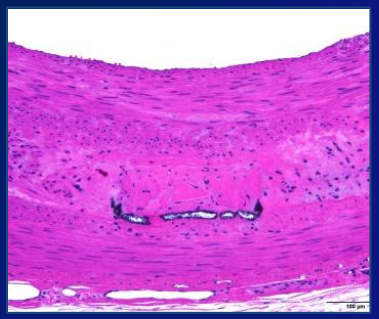


**42 months**



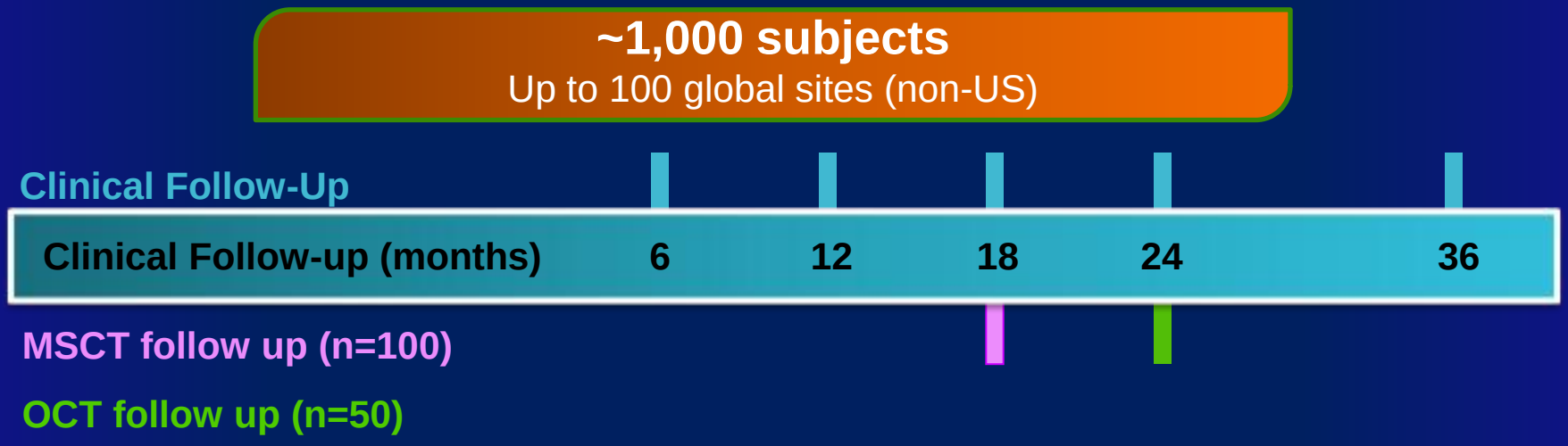






Representative photomicrographs of porcine coronary arteries, 20x, Hematoxylin and Eosin

# ABSORB EXTEND
# Non-Randomized, Single-Arm, Continued Access Trial




| | |
|---|---|
| Study Objective | Continued Access trial. FPI: Jan 11, 2011 |
| Endpoints | Typical PCI clinical endpoints |
| Treatment | Up to 2 *de novo* lesions in different epicardial vessels<br>Planned overlapping allowed in lesions >22 and ≤ 28 mm |
| Device Sizes | Scaffold diameters: 2.5, 3.0, 3.5 mm<br>Scaffold lengths: 12*, 18, 28 mm |

# ABSORB EXTEND
# Clinical Results – Intent to Treat; Interim Snapshot

| Non-Hierarchical | 6 Months* n = 450 | 12 Months* n = 450 |
|---|---|---|
| **Cardiac Death % (n)** | **0.2 (1)**** | **0.2 (1)**** |
| **Myocardial Infarction % (n)** | **2.7 (12)** | **2.9 (13)** |
| Q-wave MI | 0.7 (3) | 0.9 (4) |
| Non Q-wave MI | 2.0 (9) | 2.0 (9) |
| **Ischemia Driven TLR % (n)** | **0.4 (2)** | **1.8 (8)** |
| PCI | 0.4 (2) | 1.6 (7) |
| CABG | 0.0 (0) | 0.2 (1) |
| **Hierarchical MACE % (n)** | **2.9 (13)** | **4.2 (19)** |
| **Scaffold Thrombosis (ARC Def/Prob) % (n)** | **0.7 (3)** | **0.9 (4)** |

*Reflects an interim snapshot with only cleaned data as of the cut-off date of 03 December 2012.
**No Absorb BVS was implanted in the target lesion

MACE: cardiac death, MI, ischemia-driven TLR

Chevalier, ABSORB EXTEND 12-month outcomes in the first 450 patient enrolled, Rotterdam EuroPCR Focus on BVS 2013

# ABSORB EXTEND
# Diabetic Subgroup 12-Month Clinical Outcomes

| Non-Hierarchical | Diabetic n = 119 | Non-Diabetic n = 331 | P-value |
|---|---|---|---|
| **Cardiac Death %** | **0.0** | **0.3*** | **1.00** |
| **Myocardial Infarction %** | **3.4** | **2.7** | **0.75** |
| Q-wave MI | 0.0 | 1.2 | 0.58 |
| Non Q-wave MI | 3.4 | 1.5 | 0.25 |
| **Ischemia Driven TLR %** | **1.7** | **1.8** | **1.00** |
| PCI | 1.7 | 1.8 | 1.00 |
| CABG | 0.0 | 0.6 | 1.00 |
| **Hierarchical MACE %** | **4.2** | **4.2** | **0.63** |
| **Hierarchical TLF%** | **4.2** | **4.2** | **1.00** |

P-values are not from formal hypotheses testing and are displayed for exploratory purpose only
*Day 108, no Absorb BVS was implanted in the target lesion

MACE: cardiac death, MI, ischemia-driven TLR

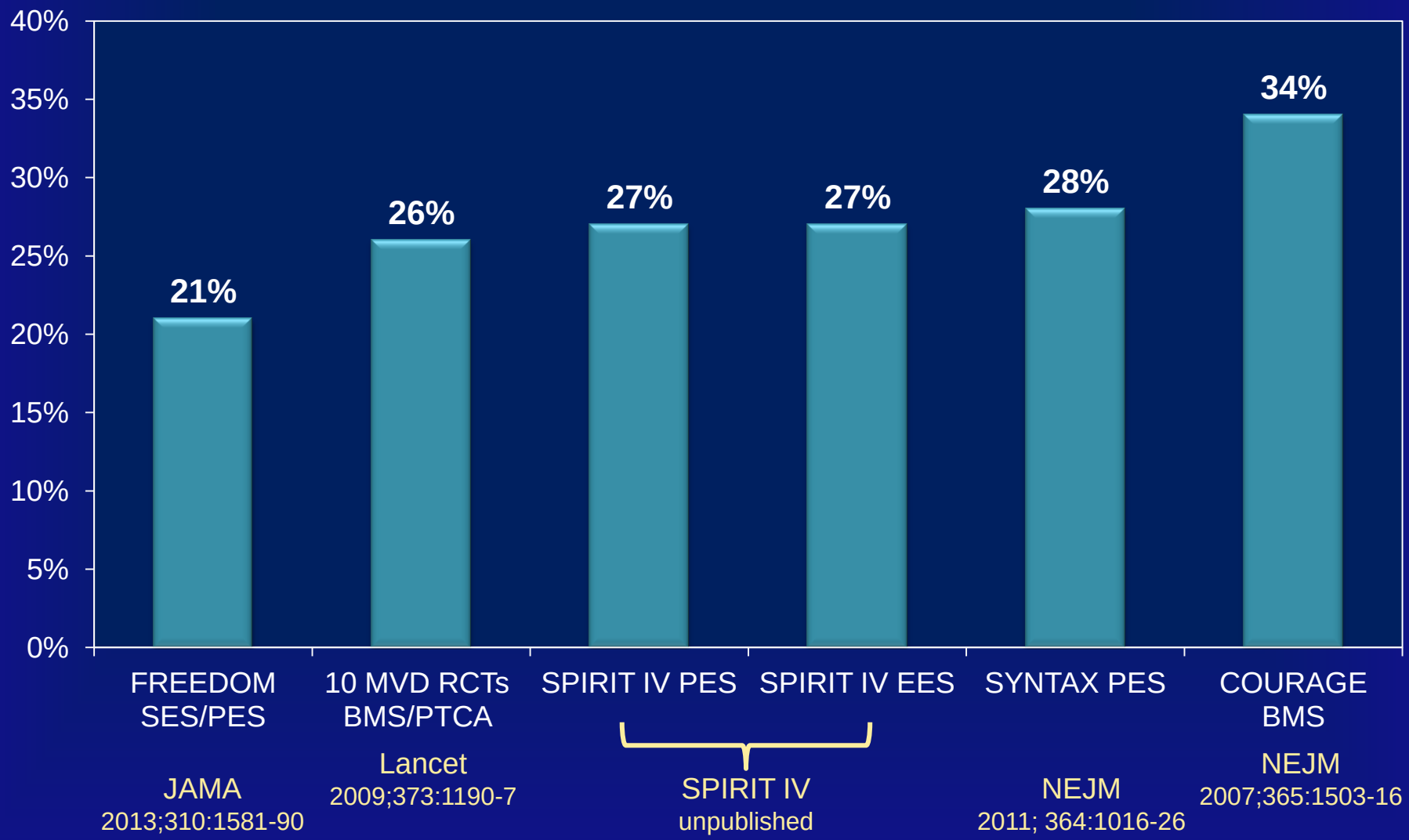
Van Geuns, RJ. ABSORB EXTEND Diabetic Subset; Rotterdam EuroPCR Focus on BVS 2013

# Absorb BVS (B+EXTEND) vs. XIENCE V (SPIRIT I, II, III)
## Diabetic Subgroup – Unadjusted 1Y Clinical Outcomes

| Non-Hierarchical | Absorb BVS (N=170) | XIENCE V (N=252) | Unadjusted P-value |
|---|---|---|---|
| Cardiac Death % | 0.0 | 1.2 | 0.55 |
| Myocardial Infarction % | 2.9 | 4.4 | 0.59 |
| Q-wave MI | 0.0 | 0.8 | 0.54 |
| Non Q-wave MI | 2.9 | 3.6 | 1.00 |
| Ischemia driven TLR % | 1.5 | 4.4 | 0.15 |
| CABG | 0.0 | 0.4 | 1.00 |
| PCI | 1.5 | 4.0 | 0.23 |
| **Hierarchical MACE %** | **3.7** | **8.4** | **0.09** |
| **Hierarchical TVF %** | **3.7** | **10.8** | **0.02** |
| **Scaffold Thrombosis (def/prob) %** | **0.7** | **1.6** | **0.66** |

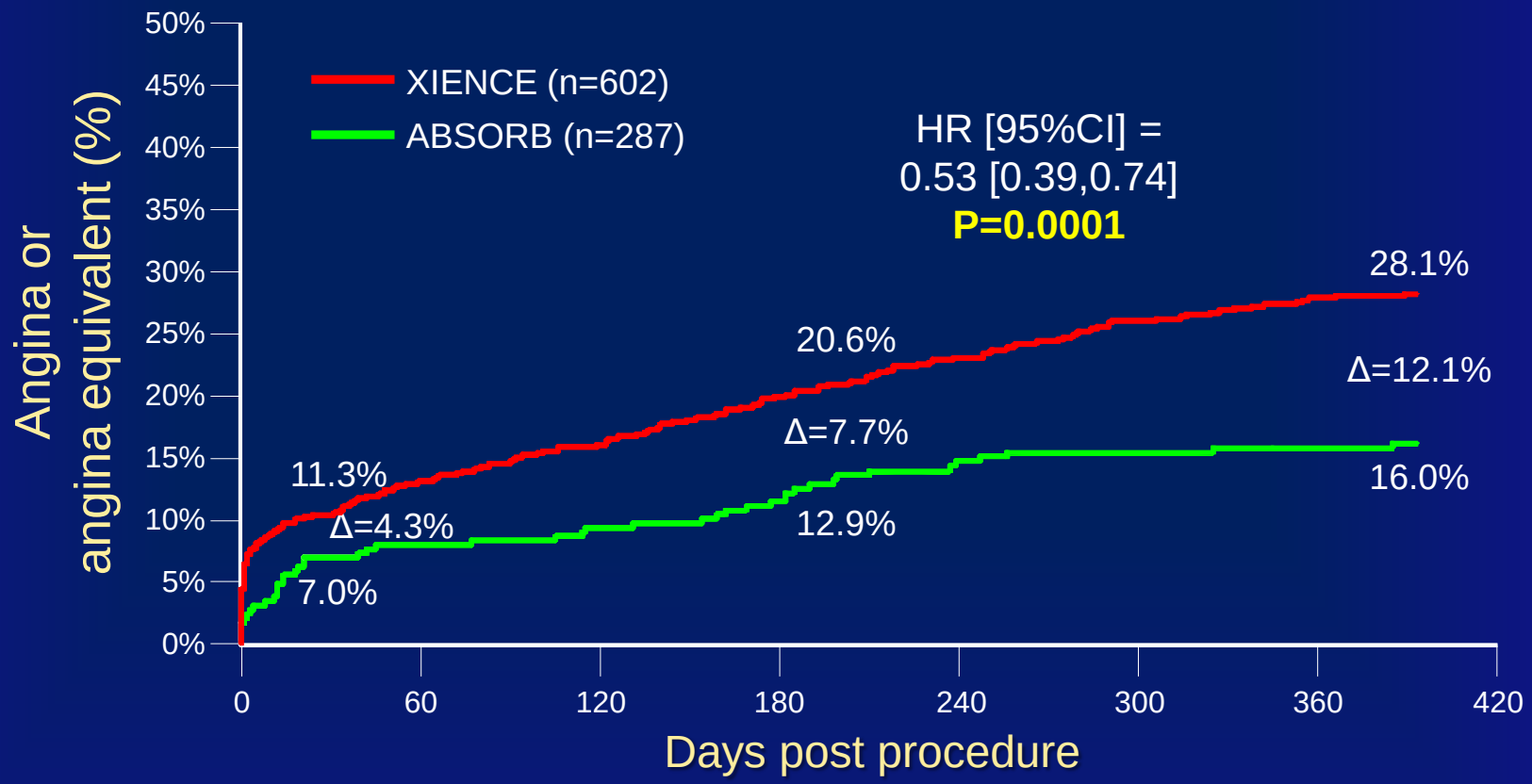
P-values are descriptive and are displayed for exploratory purpose only. Study funded by Abbott Vascular.
C. Naber, Patients I Select to Treat with BVS, EuroPCR 2013

# Angina at 1 Year After PCI



# Angina Status: EXTEND* vs. SPIRIT IV**

## Propensity matched cohorts




| Days post procedure | 0 | 37 | 194 | 393 |
|---|---|---|---|---|
| Absorb pts at risk: | 287 | 267 | 250 | 240 |
| Xience pts at risk: | 602 | 535 | 478 | 429 |

*Excludes non-Japanese Asian pts because of low event reporting rates; **Excludes complex pts and lesions (3 vessel PCI; PCI of 2 lesions per vessel; RCA aorto-ostial lesions; bifurcation lesions)

# Indicações para implantação de BVS

## Indicações apropriadas, consensuais

1. Idade Jovem (< 50 anos)
2. Diabéticos
3. Lesões em segmentos potencialmente pontáveis, preferencialmente a artéria descendente anterior
4. Vasos que apresentem lesões longas (> 30 mm) e/ou doença difusa com elevado potencial de revascularização secundária

## Indicações possíveis, menos consensuais

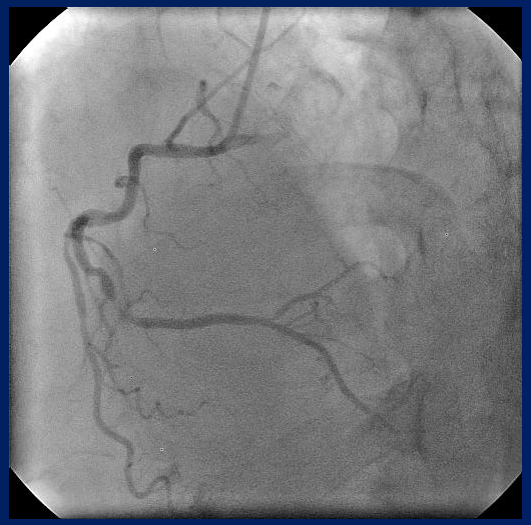
1. Lesões envolvendo pequenos ramos colaterais (< 1.5 mm)
2. Síndrome coronário agudo sem supra desnivelamento ST, estabilizado, apresentando placas intermédias e/ou instáveis
3. Síndrome coronário agudo com supra desnivelamento ST, estabilizado, apresentando placas intermédias e/ou instáveis

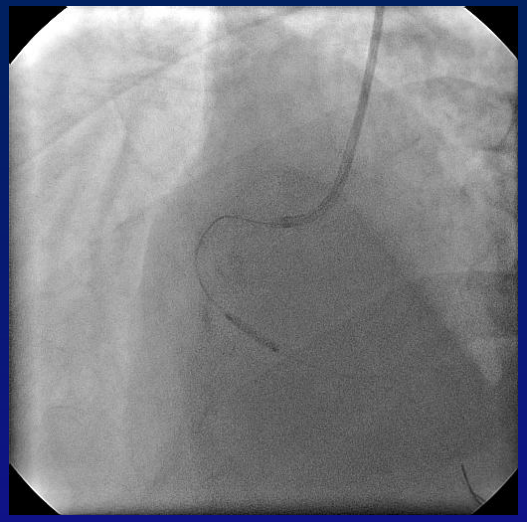
## Indicações desaconselhadas

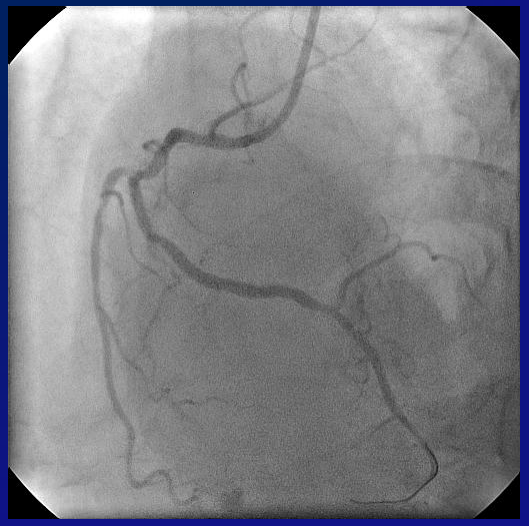
1. Lesões do tronco comum
2. Anatomia com tortuosidade moderada/grave
3. Lesões com calcificação grave

# Caso clinico

55 anos, sexo masculino
DMNID, HTA, Dislipidémia
ECG de esforço positivo para isquémia
Coronariografia: lesão única na CD







# Conclusões

- Os Stents bioabsorviveis constituem uma terapêutica válida no tratamento actual da Doença Coronária.

- Apresentam uma eficácia e segurança sobreponivel à dos stents com fármaco.

- Na sua utilização devem ser previligiadas as indicações mais consensuais.