Bioresorbable vascular scafolds: Current limitations and future perspectives

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CE-marked bioresorbable scaffolds

Main device characteristics

Stent Name (Manufacturer)	Stent Platform	Strut Thickness	Coating Material	Coating Thickness	Drug	Reported Release Profile	Drug Dose
BVS 1.1 (Abbott)	PLLA	157 μm	PLLA	2–4 μm	Everolimus	75% of loaded everolimus within 30 days	100 μg/cm²
DESolve (Elixir)	PLLA	150 μm	Bioresorbable polymer	<3 μm	Novolimus	More than 85% of the drug is released over 4 wk	5 μg/mm
ART Pure (ART)	PDLLA	170 μm	…	…	No drug	NA	NA
Magmaris (Biotronik)	93% Mg and 7% rare earth elements	150 μm	PLLA	1 μm	Sirolimus	Over 3 to 6 mo	1.4 μg/mm²

BVS indicates bioresorbable vascular scaffold; NA, data not available; PDLLA, poly(L-lactide-co-D,L-lactide); and PLLA, poly-L-lactide.

Absorb BRS is the only device with clinical outcome data from RCTs

Sotomi et al. | Circ Res 2017

Increased rate of scaffold thrombosis!

- GHOST-EU all comers registry

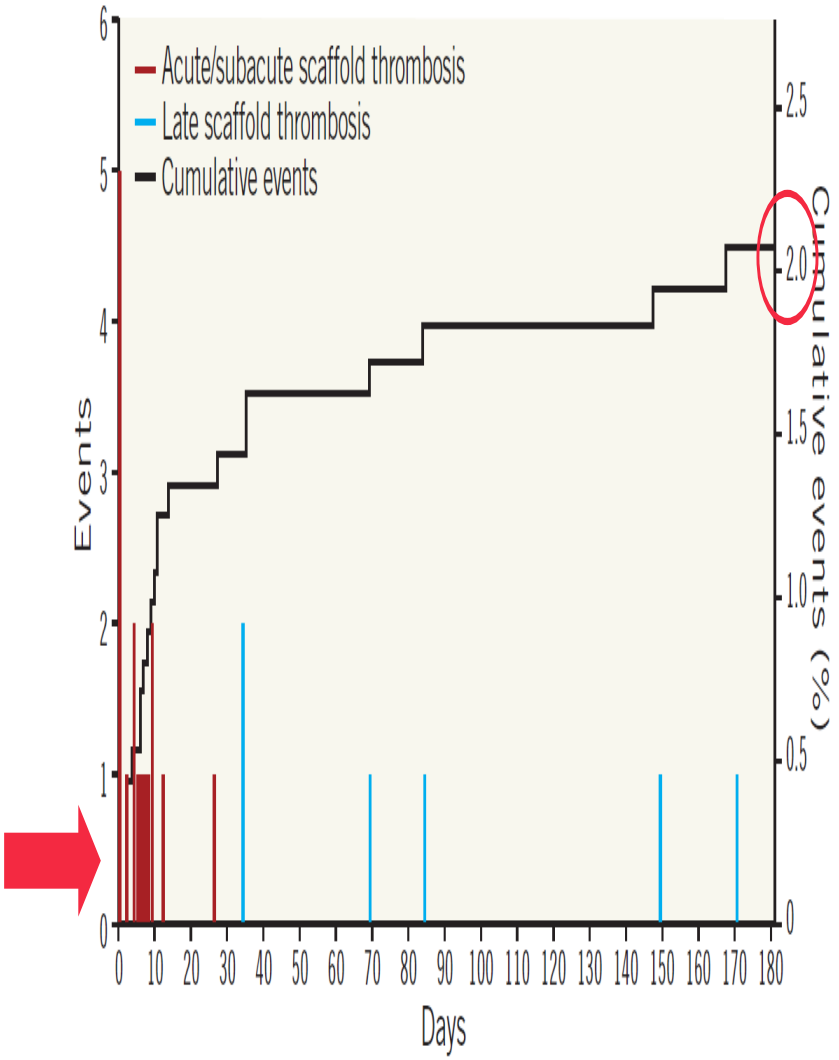


Figure 2. *Distribution and cumulative incidence of scaffold thrombosis up to six months.*

Source: Capodanno D. et al., GHOST-EU registry, *EuroIntervention* 2014

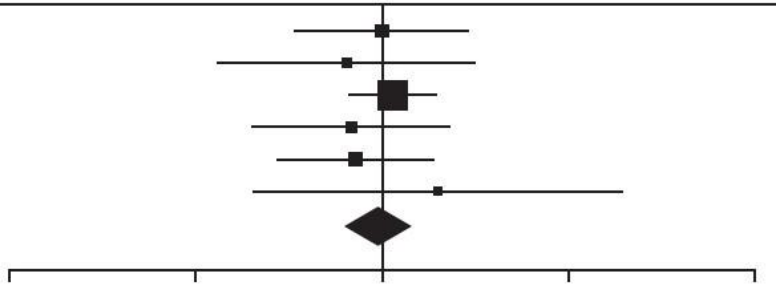
Meta-analysis of 6 RCTswith Absorb BRS

Primary endpoint results (at or before 12 months)

A Target lesion revascularisation

	BVS Events	BVS Total	EES Events	EES Total	Weight (%)	Fixed-effects odds ratio (95% CI)
ABSORB China	7	238	7	237	13·2	1·00 (0·34–2·88)
ABSORB II	4	335	3	166	5·9	0·64 (0·13–3·12)
ABSORB III	42	1313	19	677	51·6	1·14 (0·67–1·95)
ABSORB Japan	7	265	5	133	10·1	0·68 (0·20–2·31)
EVERBIO II	8	78	11	80	16·3	0·72 (0·28–1·87)
TROFI II	2	95	1	96	2·9	1·98 (0·20–19·29)
Overall	**70**	**2324**	**46**	**1389**	**100**	**0·97 (0·66–1·43)**

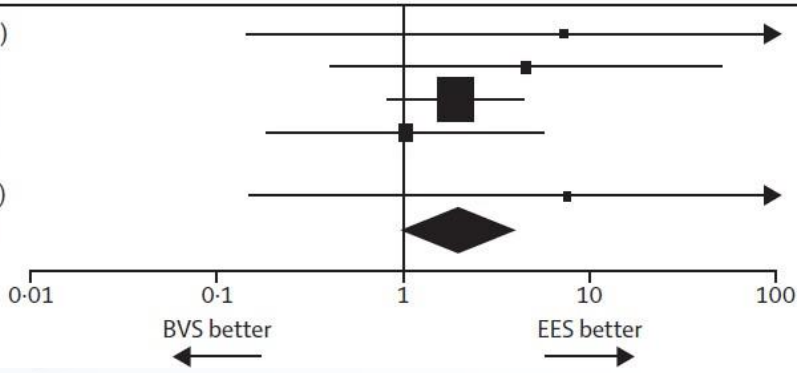
Heterogeneity: χ^2=1·69, df=5; p=0·89; I^2=0%
Test for overall effect: Z=0·16; p=0·87
Random-effects odds ratio 0·97 (95% CI 0·66–1·43)



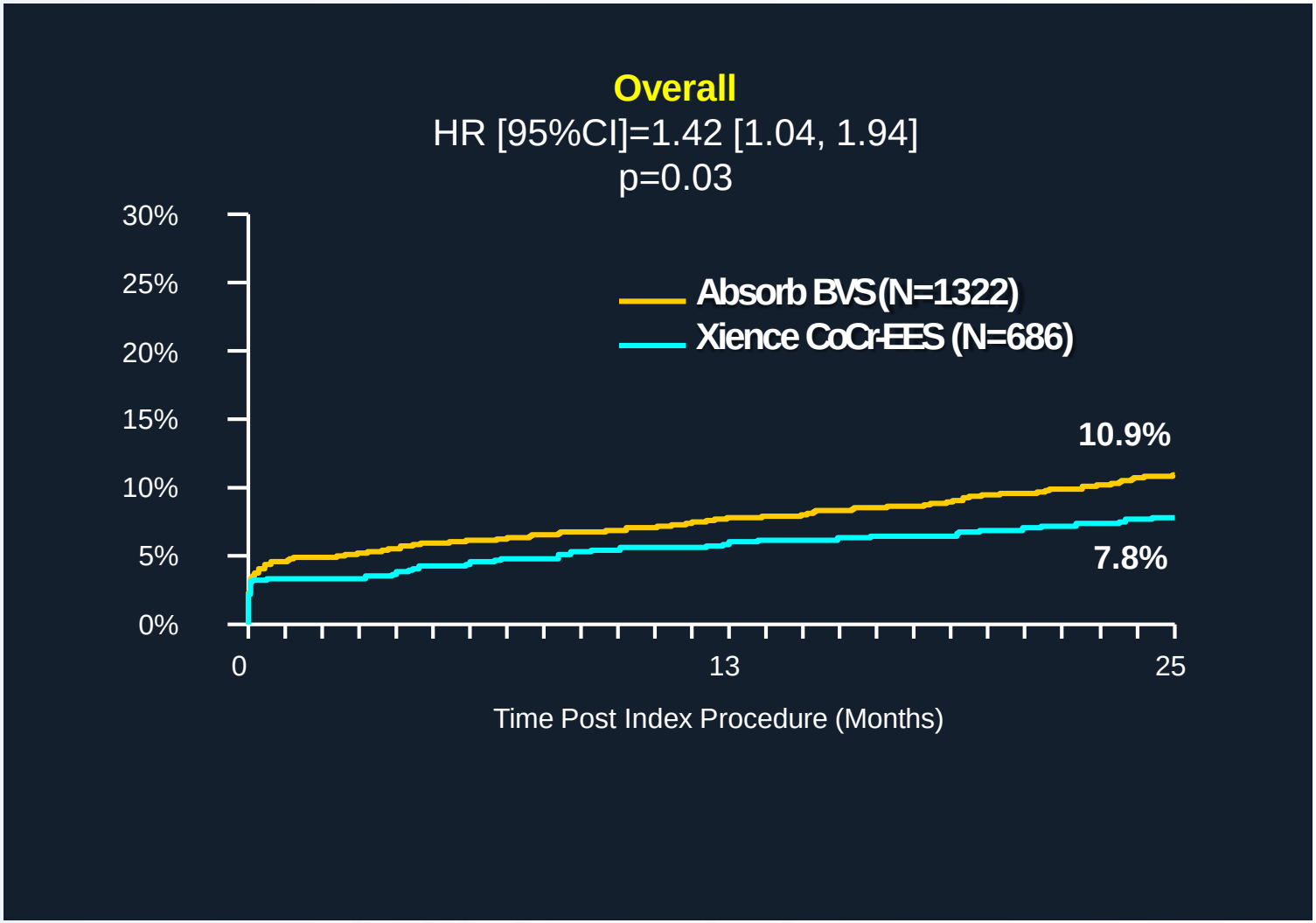
B Definite or probable stent thrombosis

	BVS Events	BVS Total	EES Events	EES Total	Weight (%)	Fixed-effects odds ratio (95% CI)
ABSORB China	1	238	0	232	3·1	7·21 (0·14–363·23)
ABSORB II	3	335	0	166	8·2	4·49 (0·04–49·92)
ABSORB III	20	1301	5	675	69·1	1·89 (0·82–4·34)
ABSORB Japan	4	262	2	133	16·5	1·02 (0·18–5·58)
EVERBIO II	0	78	0	80		Not estimable
TROFI II	1	95	0	96	3·1	7·47 (0·15–376·35)
Overall	**29**	**2309**	**7**	**1382**	**100**	**1·99 (1·00–3·98)**

Heterogeneity: χ^2=1·90, df=4; p=0·75; I^2=0%
Test for overall effect: Z=1·96; p=0·05
Random-effects odds ratio 1·99 (95% CI 1·00–3·98)

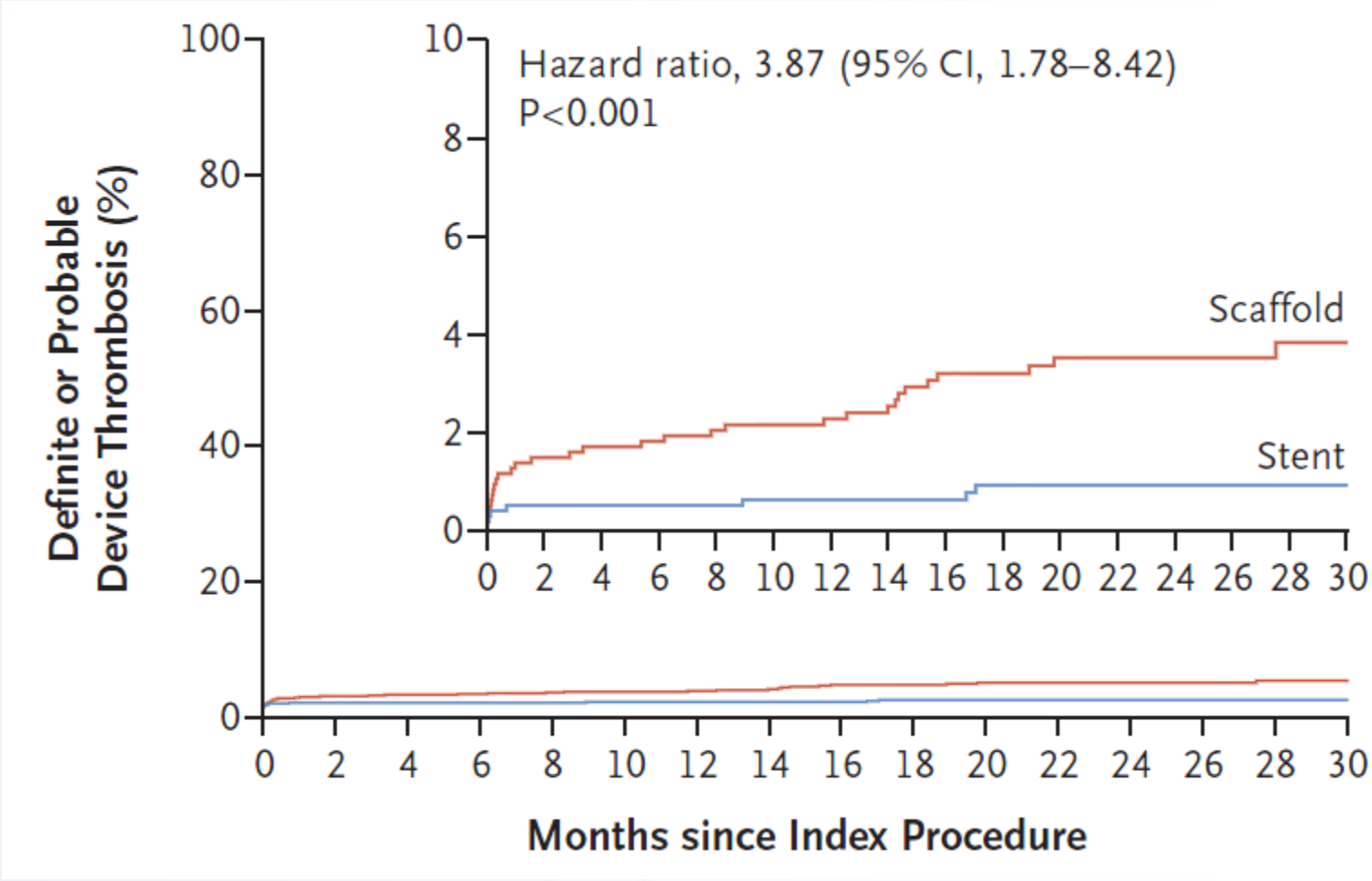


TLF by 2 years



AIDA Trial

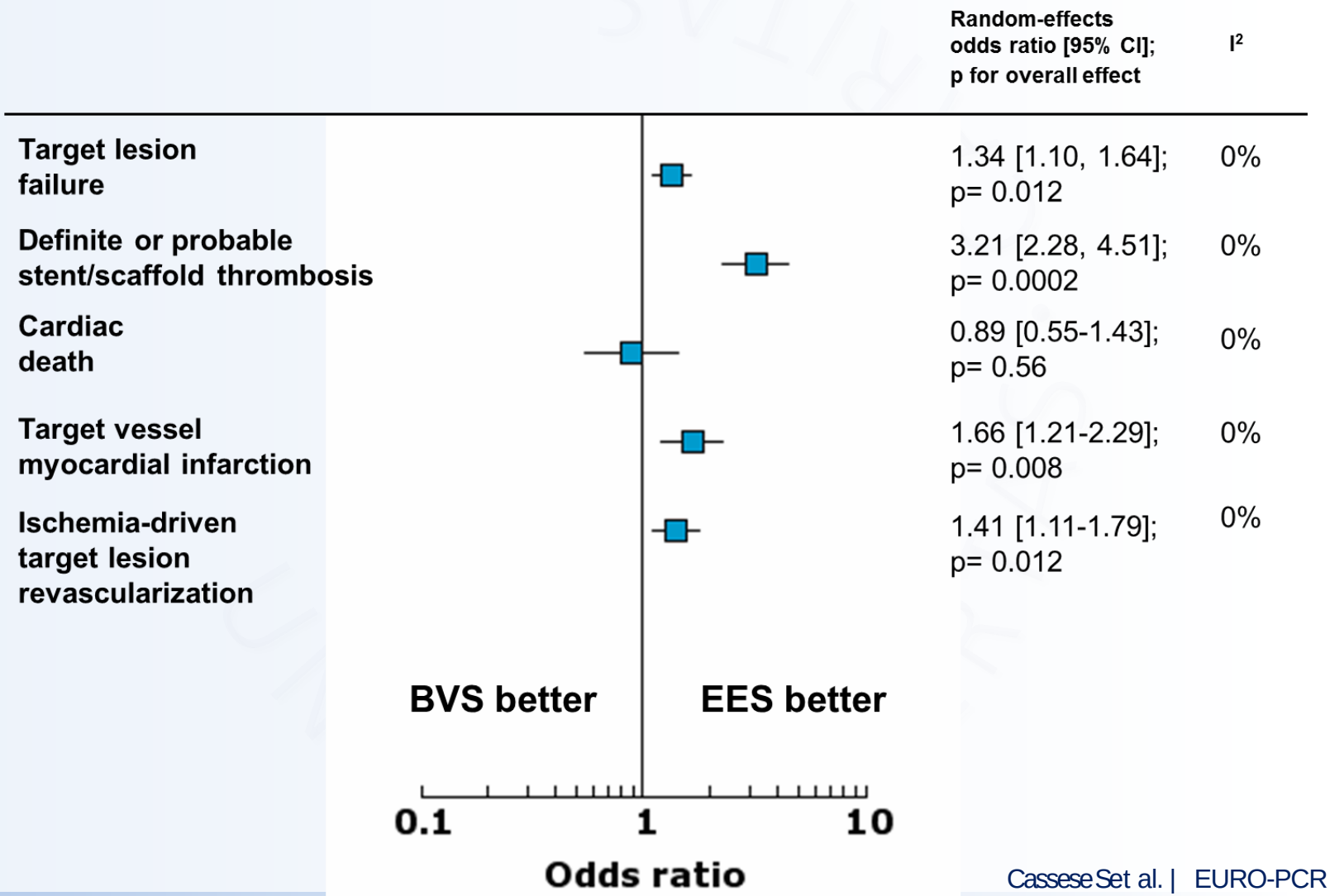
Definite or probable stent/scaffold thrombosis



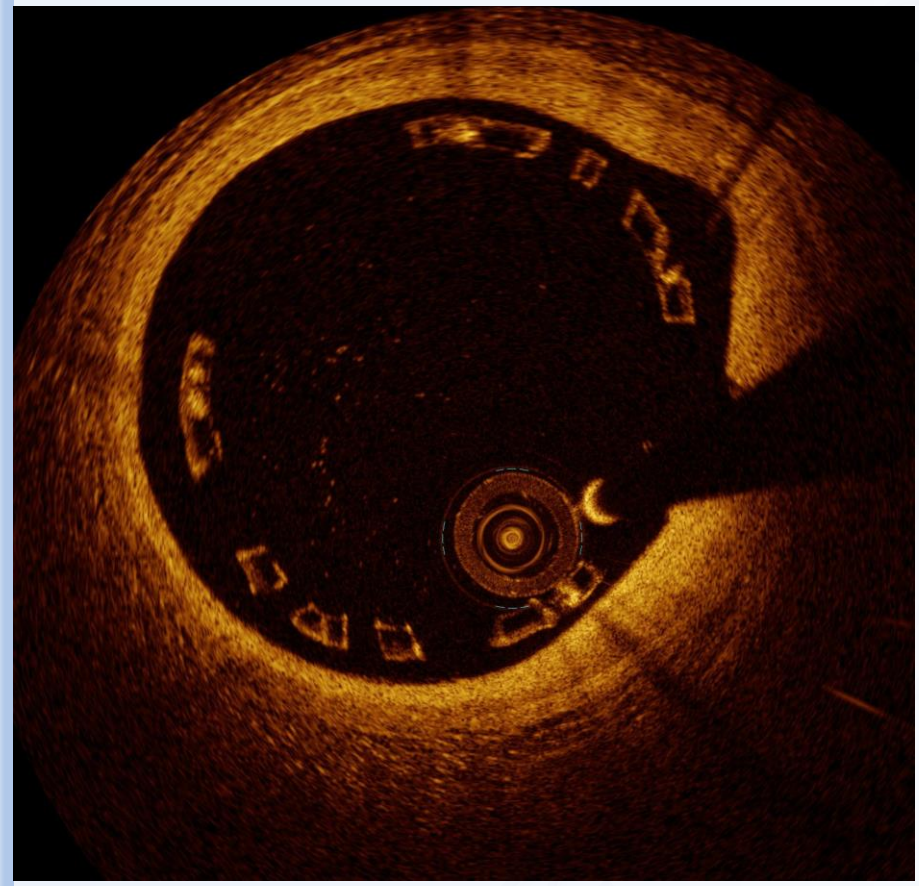
Wykrzykowska et al. | New Engl J Med *online 29th March 2017*

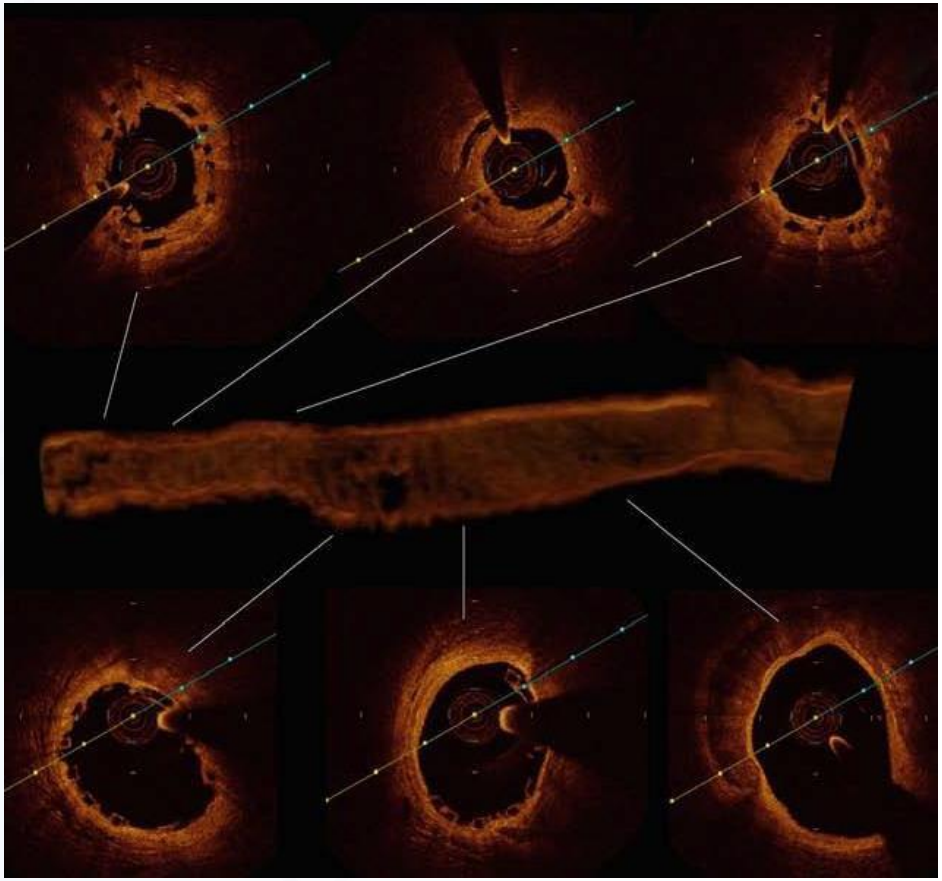
Absorb BRS: Metaanalysis (6/2017)

Data available from 7x RCTs with 2yr+ FU



Factors responsible for scaffold failure: Undersizing and underexpansion !!!





Scaffold **underexpansion**, **undersizing** and **geographical miss** → early ScT.

Cuculi, Puricel et al. – Circ Interv. 2015

Bioresorbable Coronary Scaffold Thrombosis

Multicenter Comprehensive Analysis of Clinical Presentation, Mechanisms, and Predictors

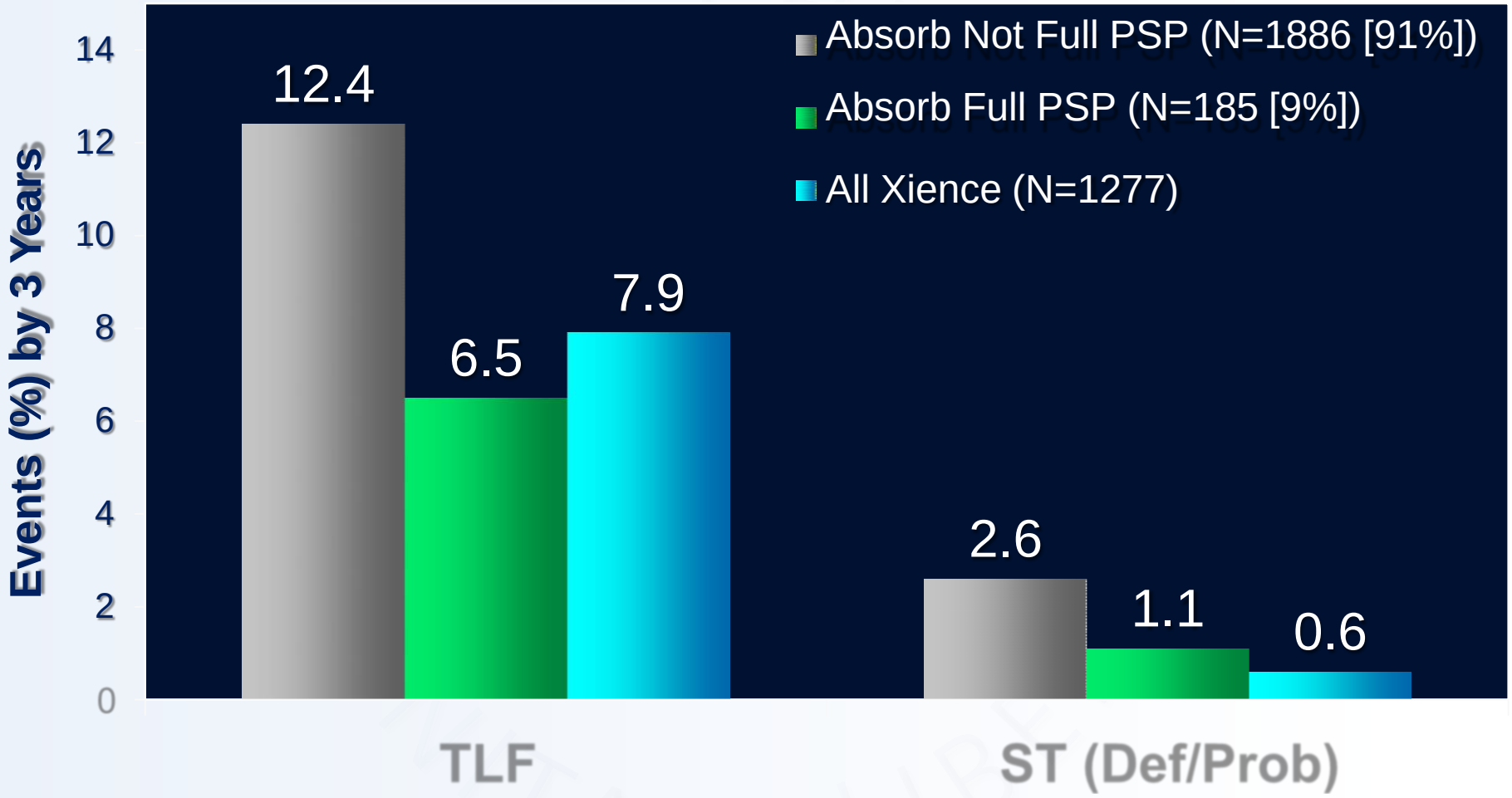
4C Frankfurt Fribourg Luzern Mainz Cities Registry

- 1305 patients, 1870 BVS, all-comers
- Incidence of probable and definite ScT
  - 1.8 %at 1 month
  - 3.0 %at 12 months
- Independent predictors of ScT
  - Ostial lesions, impaired LV-Function
- ScTrates rapidly increased for post-procedural lumen diameters < 2.4 mm (2.5-3.0 mm scaffold) and < 2.8 mm (3.0 mm scaffold)
- **Improved strategy (PSP) dropped ScTrates to 1 %!**

Puricel, Cuculi et al. – JACC2016

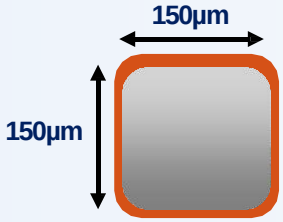
Impact of Full PSP* on 0-3 Year Outcomes

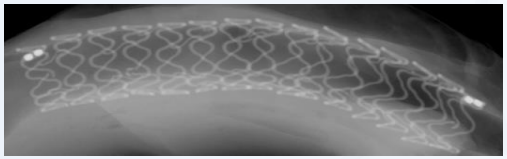
Pooled ABSORB Trials, As-Treated Population**



DREAMS-2G (MAGMARIS)
Sirolimus Eluting Mg Scaffold

Sirolimus + PLLA (BIOlute)





90-Day Faxitron, porcine explant

- 6-crown 2-link design,
- 150µm strut thickness
- 150µm strut width
- Optimized scaffold design for
  - Higher bending flexibility
  - Higher acute radial force
  - Slower absorption rate: 95% at 12 months
- Sirolimus drug elution & PLLA (ORSIRO BIOlute coating)
- Tantalum radiopaque markers
- Gained CE mark in June 2016

BIOSOLVE-II Clinical data out to 24-month

	6-month		12-month		24-month	
	N=120	%	N=118	%	N=120	%
TLF†	**4**	**3.3**	**4**	**3.4**	**7**	**5.9**
Death	2	1.7	2	1.7	4	3.3
Cardiac Death†	0	0.0	0	0.0	0	0.0
Non-cardiac death	1[1]	0.8	1[1]	0.8	2[1,2]	1.7
Unknown death†	1[3]	0.8	1[3]	0.8	2[3,4]	1.7
Target Vessel MI†	1	0.8	1	0.8	1	0.8
Clinically driven TLR†	2	1.7	2	1.7	4	3.3
CABG†	0	0.0	0	0	0	0.0
Scaffold Thrombosis definite or probable	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**

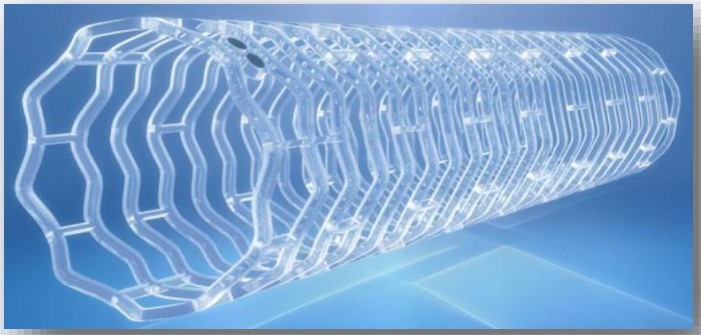
† Composite of TLF: cardiac and unknown death, target vessel myocardial infarction, clinically driven target lesion revascularization and CABG

- TLF (5.9%) and TLR (3.3%) rates in BIOSOLVE-II remain low and comparable to other absorbable scaffolds and permanent drug-eluting stents out to 24-month when the DREAMS-2G is already fully absorbed
- TLF in BIOSOLVE-III confirm the low TLF and TLR rates of the BIOSOLVE-II trial despite more complex lesions being treated in BIOSOLVE-III
- There was no definite or probable scaffold thrombosis up to 24-month FUP with DAPT termination at 12-month latest
- In-segment and in-scaffold late lumen loss remained stable between 6- and 12-month FUP in 42 patients with serial angiographic assessment in BIOSOLVE-II

DESolve® Bioresorbable Coronary Scaffold

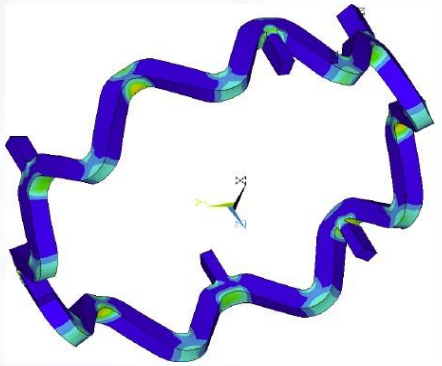
Engineered to fulfill the promise of BRS

- **PLLA-based polymer**
- **Early degradation at 6 months and near complete resorption (mass loss) in 1 year[1]**
- **Self-correction mechanism that minimizes malapposition and chronic recoil**
- **Novolimus, metabolite of Sirolimus dosed at 5µg/mm for sustained neointimal inhibition**



Designed for advanced vessel support

- Open cell body for flexibility and side- branch access
- Strut thickness: 150µm (and 120µm)
- Fracture Resistant up to 5mm
- Low acute and chronic recoil[2]
- Early lumen and scaffold enlargement at 6-mo.[2]
- Sustained efficacy out to 4 years[3]



[1]~70% resorption in developmental preclinical data; on file at Elixir Medical
[2]Abizaid et al. JACC Cardiovasc Interv. 2016;9(6):565-74; [3]Abizaid, DESolve NX 4 YR, TCT 2016

DESolve® Post-Market Clinical Follow-up (PMCF) study

Variable	DESolve Nx[1]	DESolve PMCF
N (pat/lesions)	126/126	102/109
Sites	13	10
Diabetes	21%	26%
LAD	38%	47%
Scaffold implant	122/126	100/102
Lesion length, mm	11.23	17.27
Reference diameter, mm	3.00	3.03
Type C lesion	3%	51%
Long-term FU at 24 months		
- Cardiac death	2.5%	0%
- Target vessel MI	0.8%	1%
- Clinically indicated TLR	4.1%	3%
- Scaffold thrombosis	0.8%	1%

Abizaid et al. EuroIntervention

Considerations

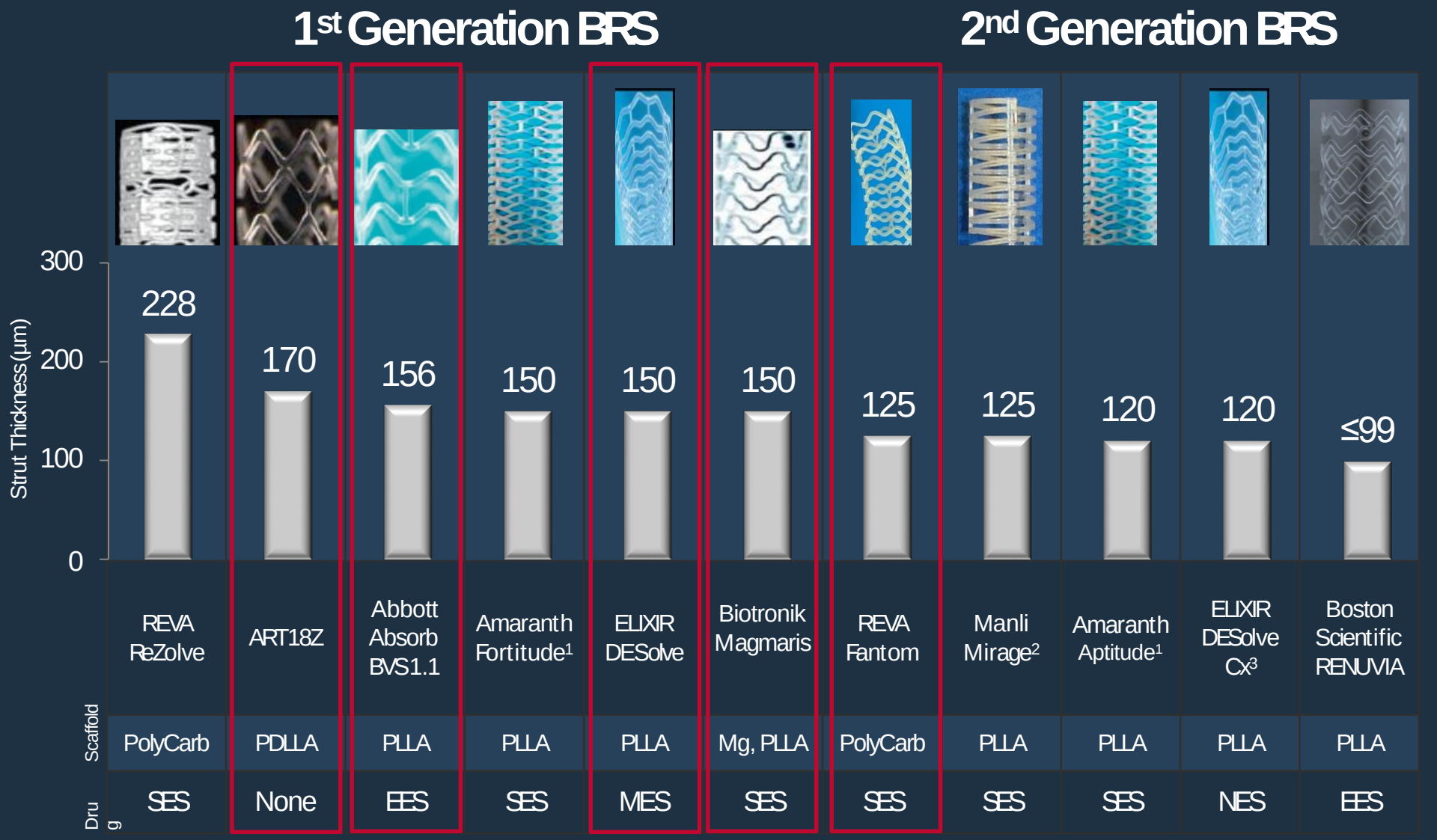
Potential implications for BRS

The DESolve Scaffold offers potentially important key differences as compared to other BRS:

- Early degradation at 6 months and near complete resorption in one year
- Fracture resistance with the ability to over-expand across an extended range of diameters
- New user-friendly designs
  - DESolve Cx: Thinner 120µm struts
  - DESolve NXT: 120µm contoured struts for improved embeddedness
  - TRANSFORM balloon technology for preferentially enhanced force transmission

Collectively these features allow DESolve to demonstrate confirmatory safety and effectiveness at 2 yrs

Bioresorbable Scaffolds in Perspective



Tenekecioglu, et al. *BMC Cardiovasc Disord* .2016:2-11. [1]Colombo. Presented at JIM 2016. [2]Santoso. Presented at TCT2014. [3]Abizaid. Presented at JIM 2016.

Outlook

Important points to consider to further improve BVS performance:

- Patient selection and lesion characteristics
  (not in ostial lesions, calcified lesions, small vessels <2.5mm)
- Lesion preparation and implant technique (PSP)
- Duration of DAPT
- Duration of bioresorption (faster may be better)
- Novel scaffold designs (thinner scaffolds, less turbulent flow)