

21st CardioVascular Summit

TCTAP 2016

April 26-29, 2016

Coex, Seoul, Korea

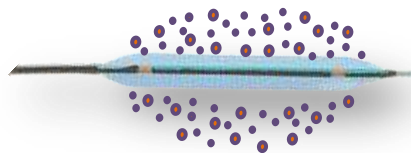
Updated Data for DEB 2016: De Novo Lesions and ISR Lesions

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Role of DEBs in PCI

DEBs area a new and effective PCI treatment option

Advantages of DEB over direct stent approach

- **Reduction in DAPT**
- **No foreign object left behind (vascular restoration possible)**

Current and potential indications include

- **ISR**
- **small vessels**
- **patients on oral anticoagulation or at high risk for initiation of oral anticoagulation**
- **True Bifurcations with long (>5mm) SB lesions or complex SB ISR difficult to treat with DES**

DEB Clinical Trials : DES for ISR

Study	Devices	Number of patients	Primary outcome/follow-up	TLR, %/follow-up	Bail-out rate,	Reference
PACCOCATH-ISR I	Paccocath vs. UCB	54	LLL 0.03 mm vs. 0.74 mm/6 mos	0 vs. 23/12 mos		8
PACCOCATH-ISR I/II	Paccocath vs. UCB	108	LLL 0.14 mm vs. 0.81 mm/6 mos MACE 15% vs. 32%/5 yrs	3 vs. 20/24 mos 5 vs. 21/5		9, 10
PEPCAD II	SeQuent Please vs. TAXUS	131	LLL 0.17 mm vs. 0.38 mm/6 mos		3	11
PEPCAD-DES	SeQuent Please vs. UCB	110	LLL 0.43 mm vs. 1.03 mm/6 mos		1	12
Habara et al	SeQuent Please vs. UCB	50	LLL 0.18 mm vs. 0.74 mm/6 mos		—	13
ISAR-DESIRE 3	SeQuent Please vs. TAXUS Liberté vs. POBA	472	Diameter 37.5 vs. 37.5 mm/6 mos 37.5 vs. 37.5 mm/6 mos	13.5 vs. 43.5/6-8 mos	—	14
SeQuent Please worldwide registry	SeQuent Please	1,200		3.8 for BMS ISR, 9.6 for DES ISR/9 mos	—	15
Spanish multicentre registry	DIOR I/II			12 (9 for BMS ISR, 15 for DES ISR)/12 mos	4	16
Valentines I	DIOR II			7.4/8 mos	5	17
PEPPER		21	LLL 0.07 mm (BMS ISR -0.005 mm, DES ISR 0.19 mm)/6 mos	3.9/6 mos 9.2/12 mos	—	18
DELUX registry		1,064	MACE 8.7%/6 mos	3.9/6 mos	—	19
Cremers et al		23	LLL 0.07 mm/6 mos	4/6 mos	—	20

BMS: bare metal stent; balloon

Efficacy in treating ISR similar to DES and superior to conventional balloon

2014 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Restenosis			
Repeat PCI is recommended, if technically feasible.	I	C	
DES are recommended for the treatment of in-stent re-stenosis (within BMS or DES).	I	A	501,502,508 511,524
Drug-coated balloons are recommended for the treatment of in-stent restenosis (within BMS or DES).	I	A	507– 511,524
IVUS and/or OCT should be considered to detect stent-related mechanical problems.	IIa	C	

Clinical Data on DEB for De Novo lesions in different subsets :

Table 4. Complex coronary lesions.

Study	Devices	Number of patients	Primary outcome/follow-up	TLR, %/follow-up	Bail-out stent rate, %	Reference
Diffuse lesion						
Pilot long lesion study	DCB+BMS	12	LLL 0.48 mm/6 mos	16/6 mos	—	34
Diabetes mellitus						
PEPCAD IV	SeQuent Please+BMS vs. TAXUS	84	LLL 0.51 mm vs. 0.53 mm/6 mos	7.7 vs. 8.3/9 mos		35
DEAR	DIOR II+BMS (vs. DES vs. BMS)		MACE 13.2% (vs. 18.6% vs. 32.3%) /12 mos	6.6/12 mos		36
Chronic total occlusion						
PEPCAD CTO	BMS + SeQuent Please (vs. TAXUS)	49	LLL 0.64 mm/6 mos			37

Table 2. Coronary small vessel disease.

Study	Devices	Number	Primary outcome/follow-up	TLR, %/follow-up	Bail-out stent rate, %	Reference
PEPCAD I	SeQuent Please vs. TAXUS	100	LLL 0.73 in vs. 0.73 in/6 mos	4.9 in DCB-only, 27.1 in DCB+BMS/12 mos	28	23
PICCOLETTTO	SeQuent Please vs. TAXUS	100	LLL 0.51 mm vs. 0.53 mm/6 mos	32.1 vs. 10.3/9 mos	36	24
Spanish DIOR regis.	DIOR II+BMS (vs. DES vs. BMS)	103	LLL 0.34 mm/6 mos	3/12 mos	7	25
BELLO	IN.PACT Falcon vs. TAXUS	182	LLL 0.08 mm vs. 0.29 mm/6 mos	4.4 vs. 7.6/6 mos	20	26

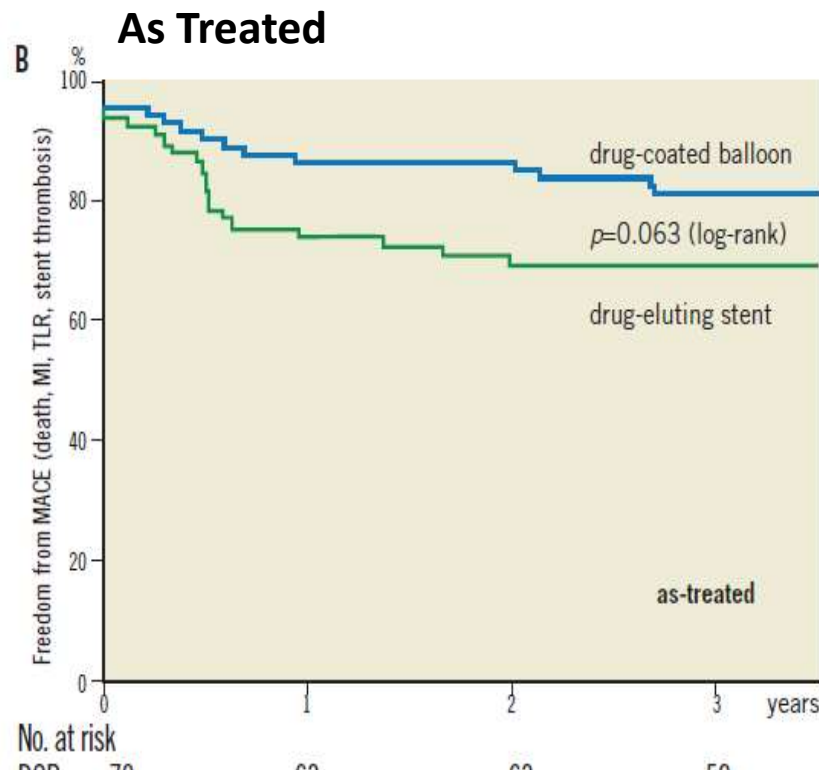
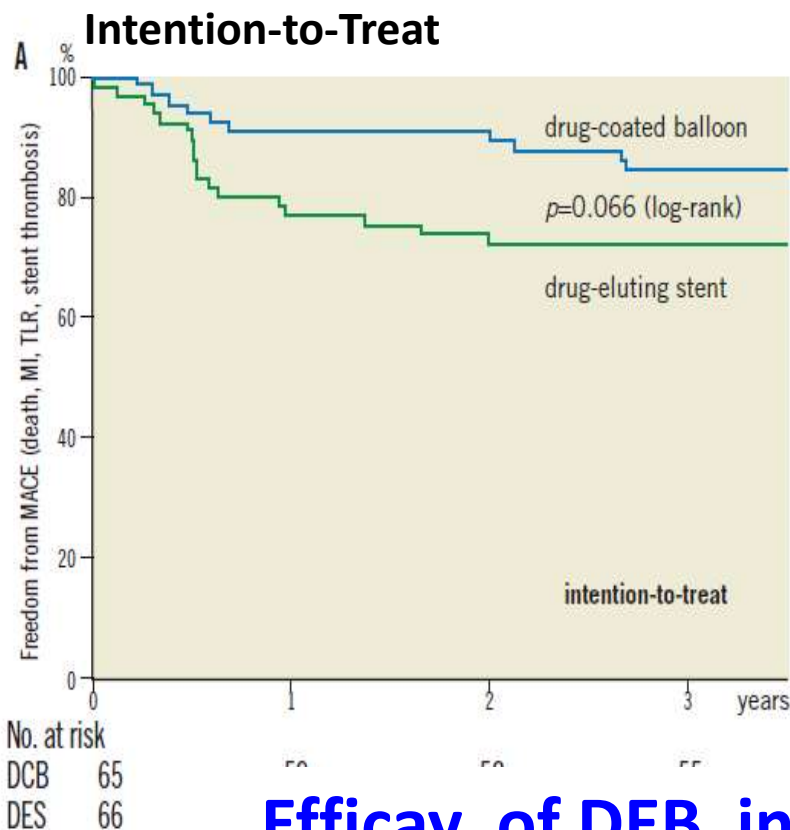
BMS: bare metal stent; DCB: drug-coated balloon; LLL: late luminal loss; TLR: target lesion revascularisation

Studies and registries including small cohorts of patients with conflicting data

What is new in more recent studies ?

Paclitaxel-coated balloon catheter versus paclitaxel-coated stent for the treatment of coronary in-stent restenosis: the three-year results of the PEPCAD II ISR study

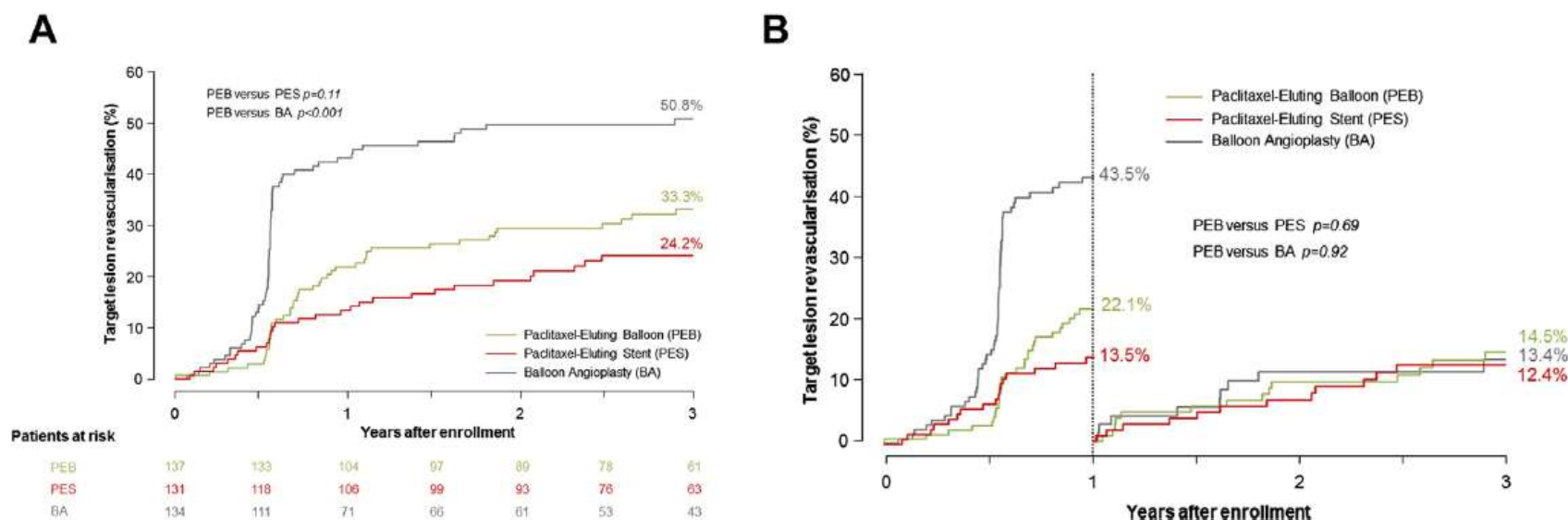
MACE at 3 years



Efficacy of DEB in treating ISR is durable !

Long Term Efficacy and Safety of Paclitaxel-Eluting Balloon for the treatment of Drug_Eluting Stent Restenosis. 3-year Results of a Randomized Controlled Trail (ISAR-DESIRE 3 Trial)

FIGURE 1 Cumulative Survival Analysis Curves and Landmark Analysis for TLR



Cumulative survival analysis curves at 3 years (A) and landmark analysis from 1 to 3 years (B) for target lesion revascularization (TLR) by treatment group. BA = balloon angioplasty; PEB = paclitaxel-eluting balloon; PES = paclitaxel-eluting stent(s).

ISAR-DESIRE 4 Trial

Intercoronary Stenting and Angiographic Results : Optimizing Treatments of Drug Eluting Stent
In-Stent Resstenosis

Design

PRIMARY ENDPOINT:

Percent diameter stenosis at follow-up angiography

TEST HYPOTHESES:

neointimal modification with scoring balloon pre-dilation before DCB would be superior to standard balloon pre-dilation before DCB

%DS= 26.25% vs. 35%

2-sided α -level = 0.05

power = 80%

101 patients per group

252 patients with DES-restenosis enrolled between June 2012 and December 2014 in 4 centers in Germany

Scoring balloon plus paclitaxel-coated balloon (N=125)

Standard balloon plus paclitaxel-coated balloon (N=127)

Angiographic follow-up at 6-8 months in 80.4% (N=203)*

Clinical follow-up at 12 months

*no significant differences across groups

Angiosculpt scoring balloon



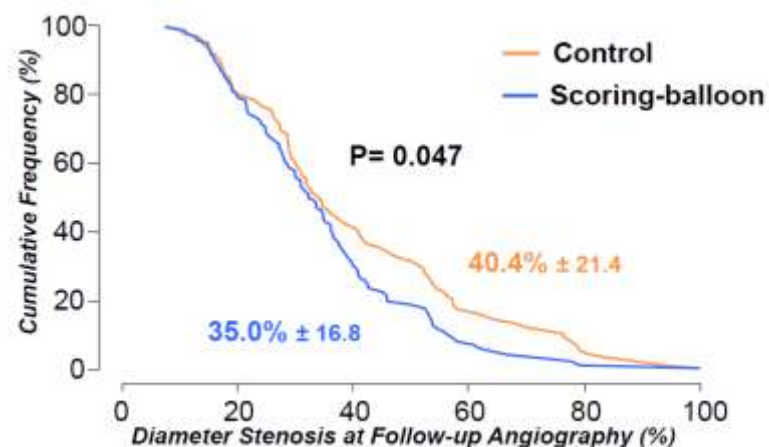
Pantera Lux paclitaxel-coated balloon



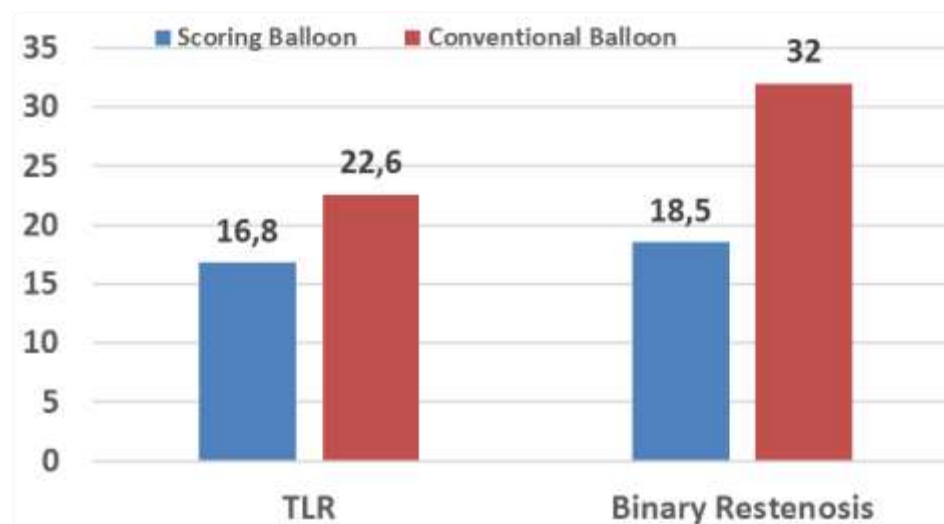
**Predilatation with scoring balloon before DEB inflation
can improve the clinical outcome**

ISAR-DESIRE 4 Trial

Primary Endpoint :Diameter Stenosis at Follow-up Angiography



Secondary endpoints : TLR and Restenosis



Original Studies

A Novel Drug-Coated Scoring Balloon for the Treatment of Coronary In-Stent Restenosis: Results From the Multi-Center Randomized Controlled PATENT-C First in Human Trial

61patients:

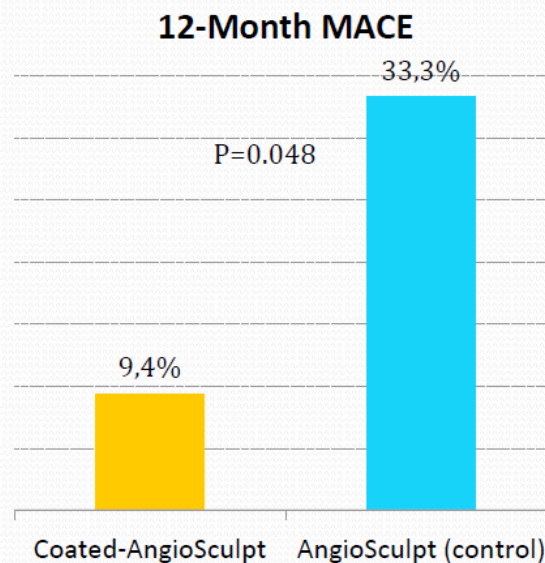
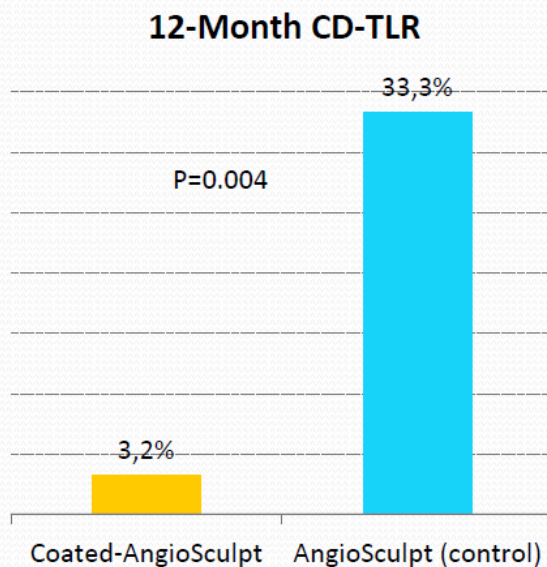
28 uncoated and 33 coated

Clinical follow-up at 30 days, 6 months, 1 and 2 years

6 –month repeat angiogram

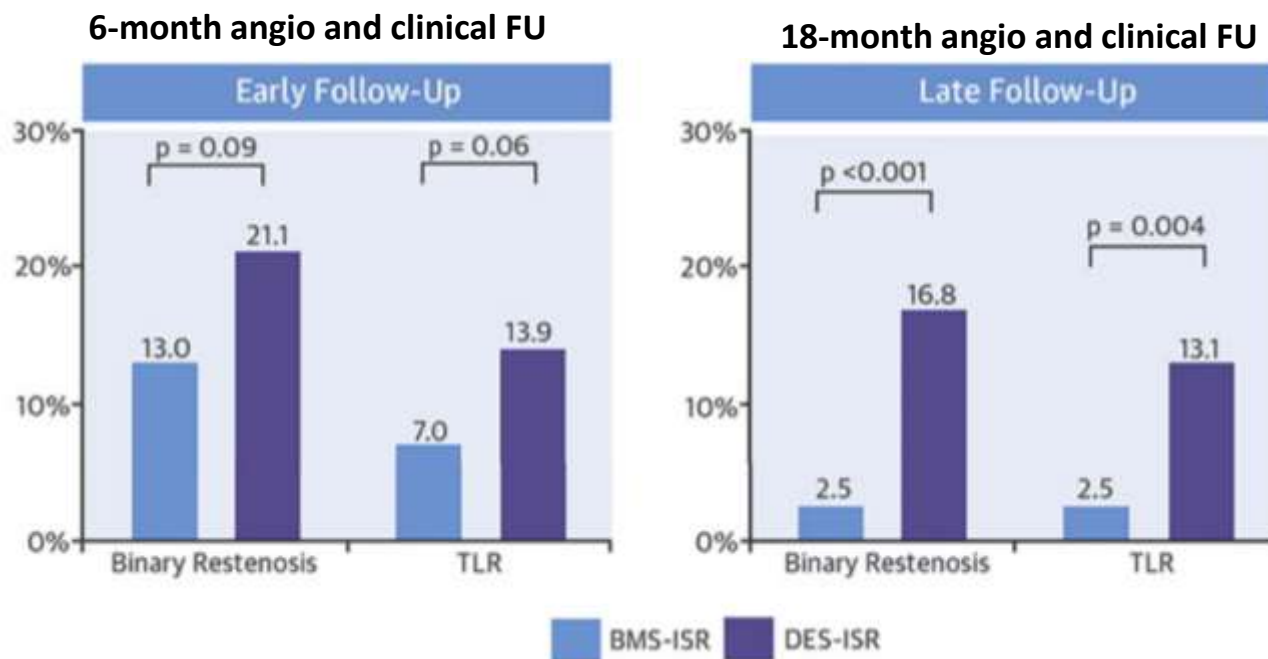
1-Year Results

➤ Significant reduction in clinically-driven TLR and MACE rates at 1-year with DCAS



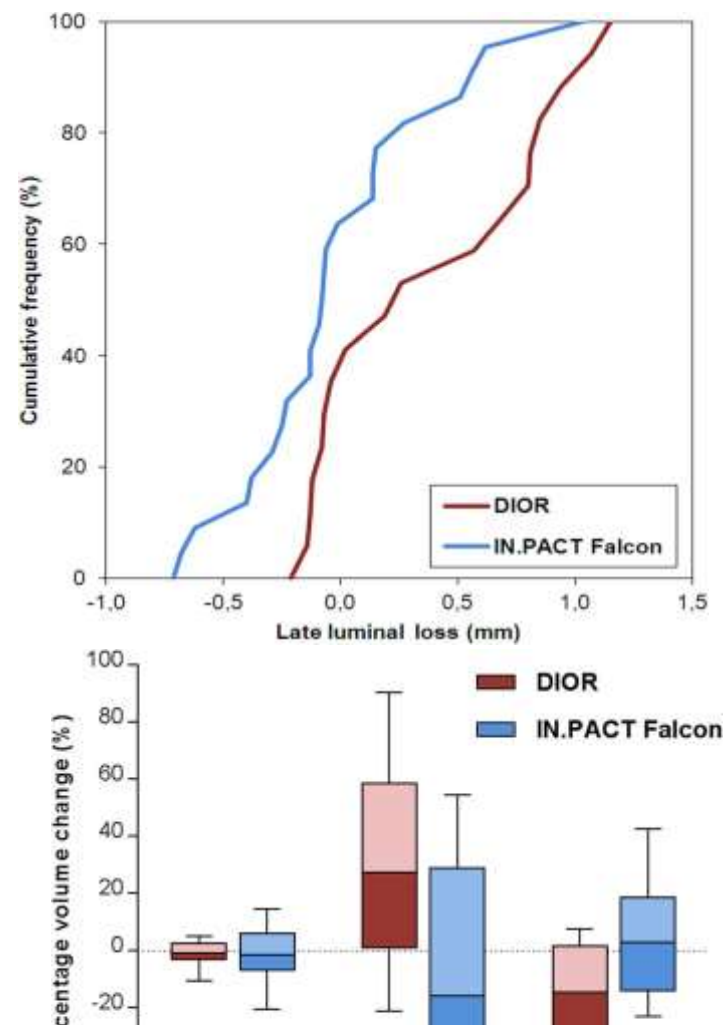
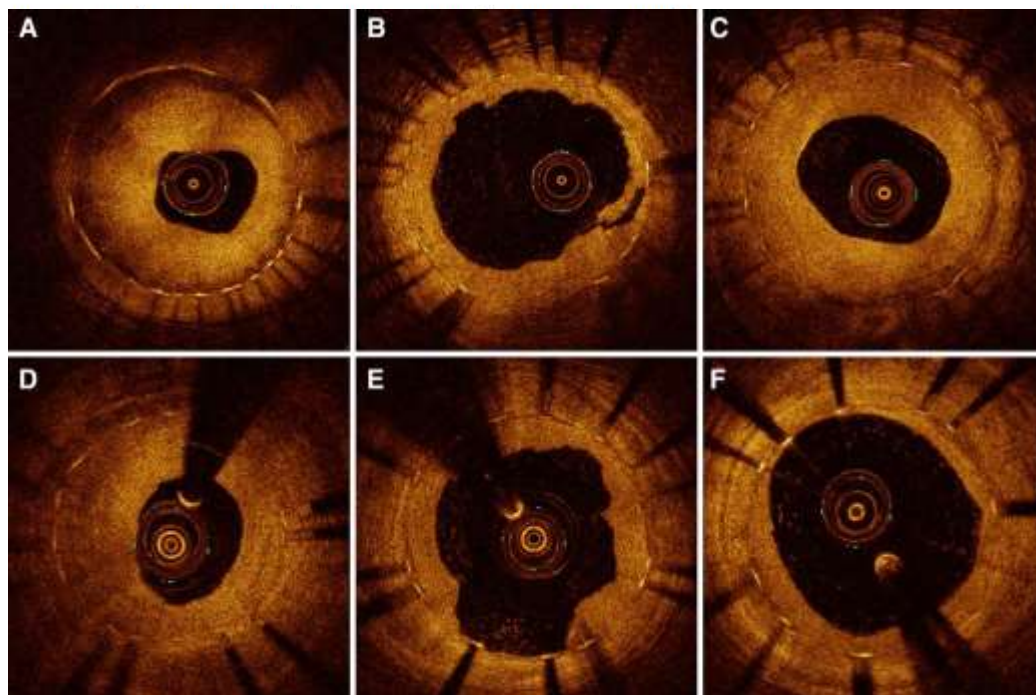
Late Restenosis After Paclitaxel-Coated Balloon Angioplasty Occurs in Patients With Drug-Eluting Stent Restenosis

Izawa, MD; Shunsuke Kubo, MD; Yusuke Hyodo, MD; Suguru Otsuru, MD; Daiji Hasegawa, MD; Takeshi Tada, MD; Hiroyuki Tanaka, MD; Yasushi Fuku, MD; Tsuyoshi Goto, MD; Kazuaki Mitsudo, MD



Early and Late Restenosis After Paclitaxel-Coated Balloon Angioplasty

Comparative assessment of the antirestenotic efficacy of two paclitaxel drug-eluting balloons with different coatings in the treatment of in-stent restenosis



Conclusions The IN.PACT Falcon DEB showed higher antirestenotic efficacy than the DIOR in the treatment of ISR, demonstrating that DEB with an excipient-based coating is not equally effective.

RESEARCH ARTICLE

Open Access

Drug eluting balloons for *de novo* coronary lesions – a systematic review and meta-analysis

Georg M Fröhlich¹, Alexandra J Lansky², Dennis T Ko³, Olga Archangelidi⁴, Rodney De Palma¹, Adam Timmis⁵ and Pascal Meier^{1,2*}

Table 2 Baseline characteristics of included trials

Study	Paclitaxel eluting balloon	Controls stent type(s)	Setting	Clopidogrel (mts)	Follow-up (mts)	Primary endpoint	MACE	TLR	Bare metal stenting
DEB-AMI	DIOR 2 nd generation	TAXUS DES, Genius Magic Euroscore BMS	STEMI	12	6	LLL	death, MI, TVR	restenosis >50% ischemia	100%
Stella et al	DIOR 1 st generation	TAXUS DES, Liberté BMS	stable/unstable CAD, bifurcation	3 after BMS, 12 after DES	12 (angio 6)	LLL	death, MI, TVR	restenosis >50% ischemia	100%

Conclusion:

- DEB are not superior to current standard therapies (BMS or drug eluting stent (DES)) in treating *de novo* coronary lesions.
- DEB efficacy seems to lie in between DES and BMS with a trend towards superiority over BMS alone.
- DEB may be considered in patients with contraindications for DES.

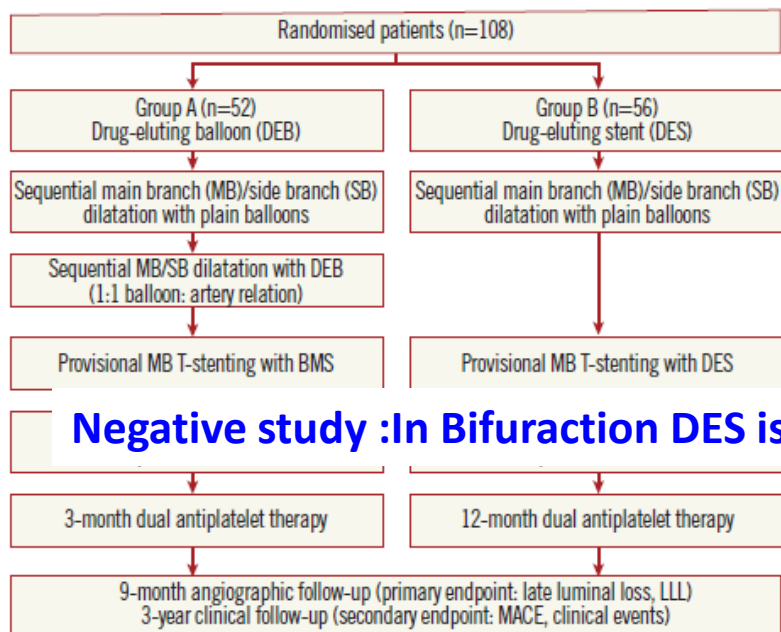
A prospective randomised study of the paclitaxel-coated balloon catheter in bifurcated coronary lesions (BABILON trial): 24-month clinical and angiographic results

José Ramón López Mínguez^{1*}, MD, PhD; Juan Manuel Nogales Asensio¹, MD, PhD; Luis Javier Doncel Vecino¹, MD; Jorge Sandoval², MD; Sebastián Romany³, MD; Pedro Martínez Romero⁴, MD; José Antonio Fernández Díaz⁵, MD; Javier Fernández Portales³, MD, PhD; Reyes González Fernández¹, MD, PhD; Ginés Martínez Cáceres¹, MD; Antonio Merchán Herrera¹, MD, PhD; Fernando Alfonso Manterola², MD, PhD; on behalf of the BABILON Investigators

24-month follow-up clinical events.

	All patients n=108	pDEB group n=52	DES group n=56	p-value
Death	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Non-fatal MI	4 (3.7%)	2 (3.8%)	2 (3.6%)	1
Stroke	1 (0.9%)	1 (1.9%)	0 (0.0%)	0.477
CABG	2 (1.9%)	1 (1.9%)	1 (1.8%)	1
New PCI	17 (15.7%)	11 (21.2%)	6 (10.7%)	0.125
TVR	11 (10.2%)	9 (17.3%)	2 (3.6%)	0.018
TLR	10 (9.3%)	8 (15.4%)	2 (3.6%)	0.045
Other vessel PCI	9 (8.3%)	5 (9.6%)	4 (7.1%)	0.734

Restenosis (global)	12 (11.1%)	9 (17.3%)	3 (5.4%)	0.048
MB restenosis	8 (7.4%)	7 (13.5%)	1 (1.8%)	0.027
SB restenosis	5 (4.6%)	3 (5.8%)	2 (3.6%)	0.670
MB stent occlusion	2 (1.9%)	1 (1.9%)	1 (1.8%)	0.958



Negative study :In Bifurcation DES is superior to DEB followed + BMS !!

Drug eluting balloons as stand alone procedure for coronary bifurcational lesions: results of the randomized multicenter PEPCAD-BIF trial

Franz X. Kleber¹ · Harald Rittger² · Josef Ludwig² · Antonia Schulz¹ ·
Detlef G. Mathey³ · Michael Boxberger⁴ · Ralf Degenhardt⁵ · Bruno Scheller⁶ ·
Ruth H. Strasser⁷

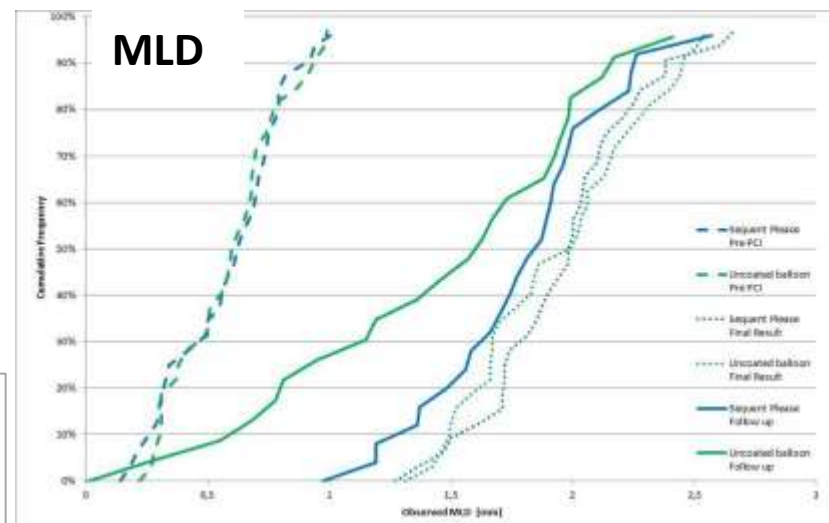
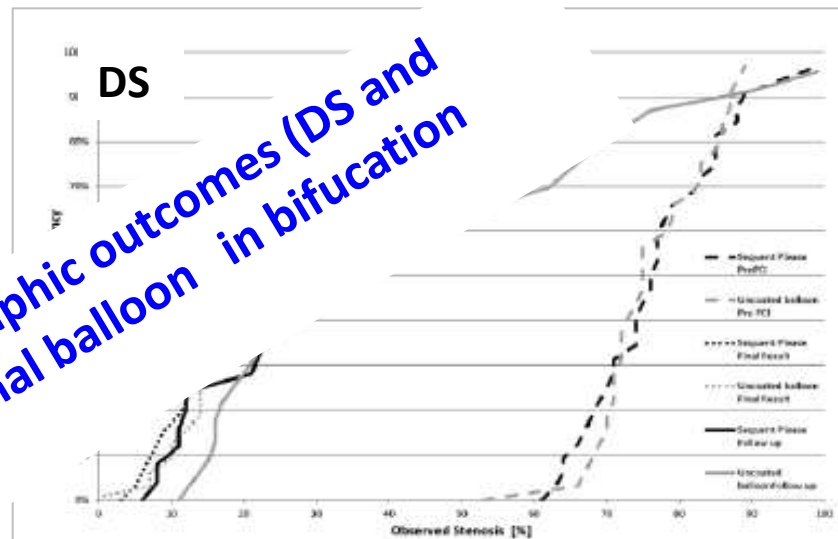
	DCB, N = 25	POBA, N = 23
Reference diameter (mm)	2.40 ± 0.37	2.37 ± 0.37
MLD (mm)	1.78 ± 0.37	1.78 ± 0.37
Stenosis grade in lesion (%)	25.7 ± 12.8	25.7 ± 12.8
MLD in segment (mm)	1.76 ± 0.36	1.76 ± 0.36
Stenosis grade in segment (%)	26.6 ± 12.8	26.6 ± 12.8
LLL in lesion (mm)	1.76 ± 0.36	1.76 ± 0.36
LLL in segment (mm)	1.76 ± 0.36	1.76 ± 0.36
LLL Index in lesion	1.76 ± 0.36	1.76 ± 0.36
LLL Index in segment	1.76 ± 0.36	1.76 ± 0.36
Binary restenosis grade (≥50 %) (n)	9 ^a (25.7 %)	9 ^a (25.7 %)

^a Two of them had been stented

Conclusion

In bifurcation lesions that show only class A or B dissection and recoil not beyond 30 % the use of DCBs is a sound strategy.

DEB improves surrogate angiographic outcomes (DS and MLD) as compared to conventional balloon in bifurcation lesions

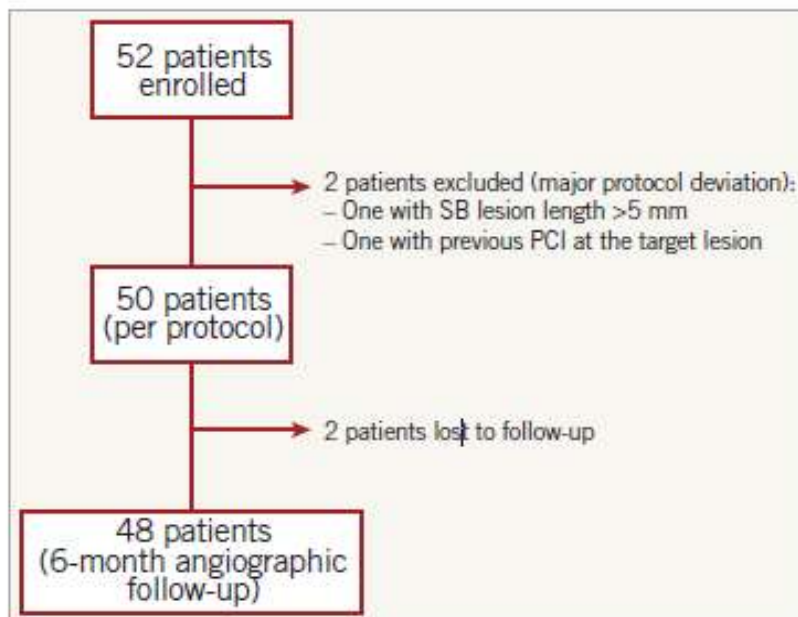


DANUBIO - a new drug-eluting balloon for the treatment of side branches in bifurcation lesions: six-month angiographic follow-up results of the DEBSIDE trial

Jacques Berland^{1*}, MD; Thierry Lefèvre², MD, FESC, FSCAI; Philippe Brenot³, MD; Jean Fajadet⁴, MD; Pascal Motreff⁵, MD, PhD; Patrice Guerin⁶, MD, PhD; Patrick Dupouy⁷, MD; Christian Schandrin⁸, MD; DEBSIDE trial investigators

Table 3. Side branch late lumen loss at six months in DEBSIDE and previous trials.

Trial	Study device	Technique	Months	SB LLL (mm)
DEBSIDE (2014)	DANUBIO	Predilatation: conventional balloon in MB+SB MB: DES SB: DEB	6	-0.04±0.34
PEPCAD V (2011) ⁸	SeQuent Please	MB+SB: DEB MB: BMS	9	0.21±0.47
DEBIUT (2011) ⁷	DIOR I	Predilatation: DEB in MB+SB MB: BMS	6	0.19±0.66
Herrador et al (2013) ¹⁰	SeQuent Please	Predilatation: conventional balloon in MB or SB SB: DEB MB: DES	12	0.09±0.40
BABILON (2014) ⁹	SeQuent Please	Predilatation: conventional balloon in MB+SB MB+SB: DEB MB: BMS	9	-0.04±0.64



Treatment of Small Vessel Disease With the Paclitaxel Drug-Eluting Balloon: 6-Month Angiographic and 1-Year Clinical Outcomes of the Spanish Multicenter Registry

Multicenter Registry

- 104 patients with native coronary lesions in small
- PEB
- Regular ball
- Angiographic

Promising results in small vessel disease , but
 DEB should not be followed by BMS
 ... 45–60 sec
 ... implantation due to coronary dissection)

Predictors of Adverse Event s at 12- Months

MACE	HR	IC 95%	P-Value
DEB + Bailout BMS	18.74	2.58–135.84	0.004
STEMI	9.99	1.40–71.18	0.022
Complete Revascularization	0.10	0.01–0.87	0.038
TLR			
DEB + Bailout BMS	30.99	2.79–344.07	0.005
Restenosis			
Pts with stent implanted out of the TL	9.439	1.19–74.72	0.03
Bifurcated lesion	6.707	0.84–53.16	0.07

Native vessels with diffuse disease

The Role of Drug-Eluting Balloons Alone or in Combination With Drug-Eluting Stents in the Treatment of De Novo Diffuse Coronary Disease

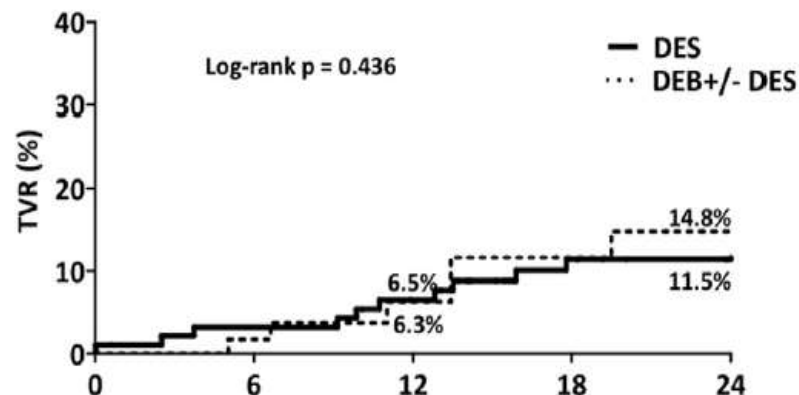
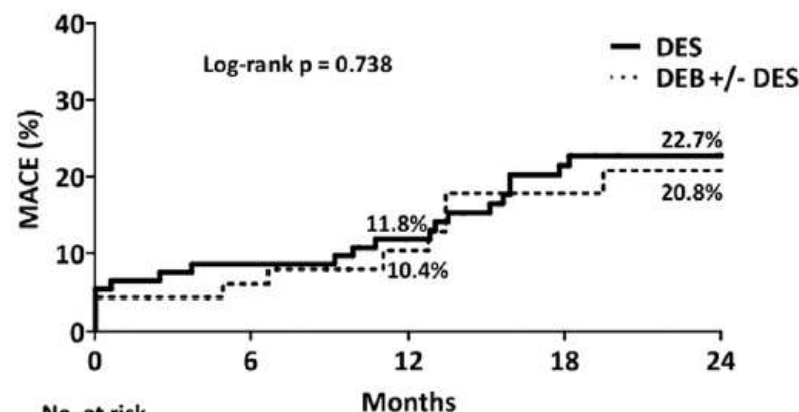
Charis Costopoulos, MD,*†, Azeem Latib, MD,*†, Toru Naganuma, MD,*†, Alessandro Sticchi, MD,* Filippo Figini, MD,* Sandeep Basavarajiah, MD,*†, Mauro Carlino, MD,* Alaide Chieffo, MD,* Matteo Montorfano, MD,* Charbel Naim, Masanori Kawaguchi, MD,*†, Francesco Giannini, MD,* Antonio Colombo, MD,*†

Table 2. Lesion and Procedural Characteristics

Characteristic	DEB ± DES Strategy (n = 93)	DES-Alone Strategy (n = 93)	p Value
Vessel treated			0.48
Left anterior descending artery	37 (39.8)	43 (46.2)	
Circumflex artery	16 (17.2)	18 (19.4)	
Right coronary artery	40 (43.0)	32 (34.4)	
Location of lesion in treated vessel			0.10
Proximal	4 (4.3)	10 (10.8)	
Mid/distal	89 (95.7)	83 (89.2)	
Balloon pre-dilation	80 (86.0)	84 (90.3)	0.36
Procedural adjuncts			
IVUS	37 (39.8)	30 (32.3)	0.28
Rotablation	3 (3.2)	4 (4.3)	0.70
Device characteristics			
DEB diameter, mm	2.52 ± 0.29	NA	
DES diameter, mm	2.95 ± 0.42	2.79 ± 0.25	<0.01
Total stent length,* mm	29.0 ± 9.1	50.2 ± 18.2	<0.01

Values are n (%) or mean ± SD. *DEB ± DES (n = 41), DES alone (n = 93).

IVUS = intravascular ultrasound; NA = not applicable; other abbreviations as in Table 1.



Hybrid strategy with a bioresorbable scaffold and a drug-coated balloon for diffuse coronary artery disease: the “no more metallic cages” multicentre pilot experience

Hybrid Strategy : patients with diffuse *de novo* or in-stent restenosis treated with

- BRS implantation (larger proximal segment)
- DCB inflation (smaller distal segment or bifurcation side branch)

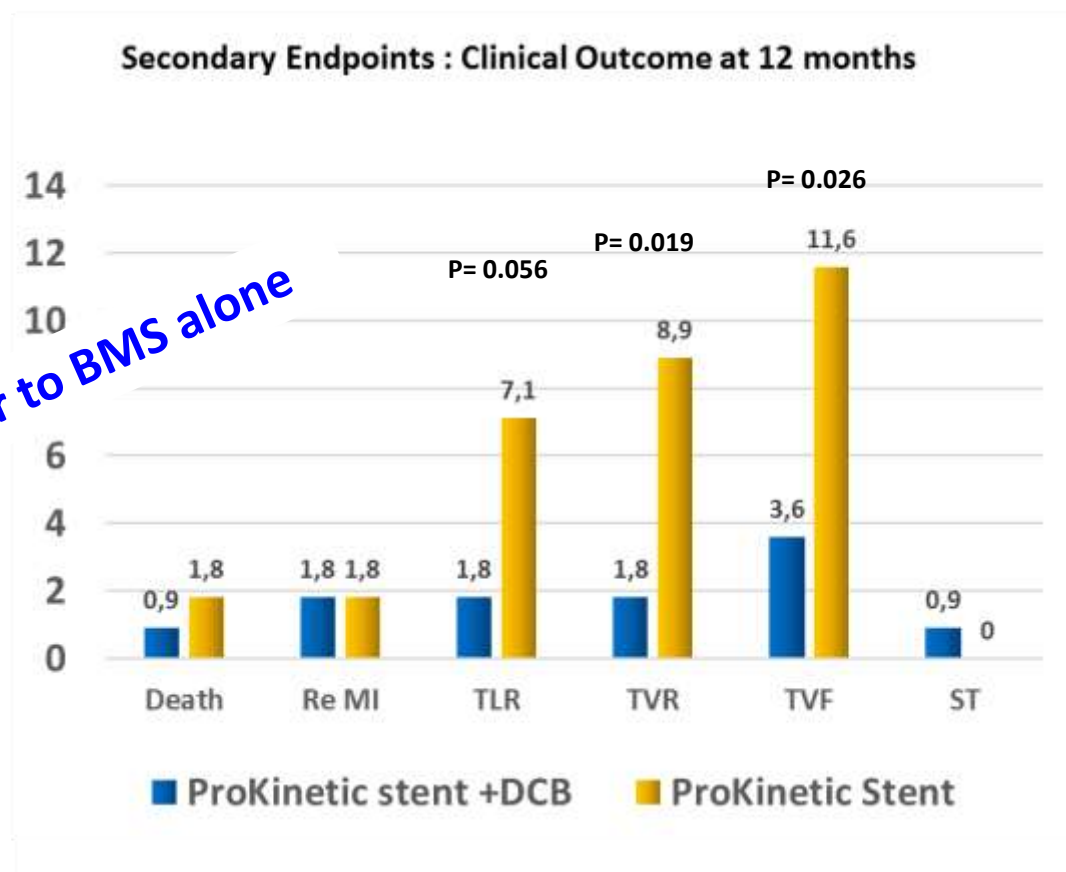
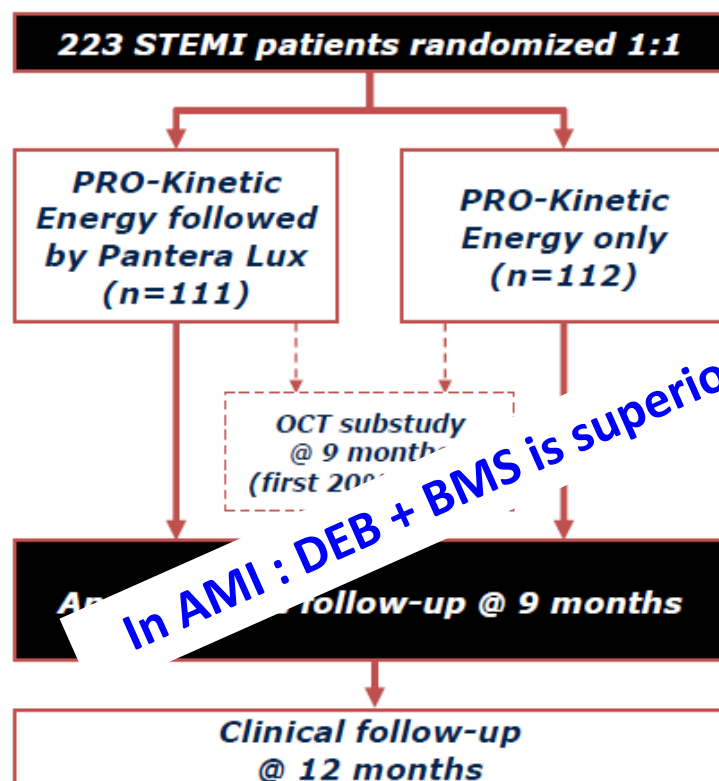
Lesion and procedural characteristics

	Patients, n=42
Target vessel	
Left anterior descending	29 (69.0)
Left circumflex	8 (19.0)
Right coronary artery	5 (12.0)
Radiol approach	17 (40.5)
Hybrid (BRS plus DCB) indication	
<i>De novo</i> diffuse or tandem coronary disease	37 (88.1)
CTO	2 (5.4)
Bifurcation (side branch >2.0 ≤2.75 mm)	9 (24.3)
Diffuse BMS ISR	5 (11.9)
Rotational atherectomy	1 (2.4)
Scoring balloons	5 (11.9)
Intracoronary imaging	
OCT	5 (11.9)
IVUS	18 (42.9)
BMS: bare metal stent; BRS: bioresorbable scaffold; CTO: chronic total occlusion; DCB: drug-coated balloon; ISR: in-stent restenosis; IVUS: intravascular ultrasound; OCT: optical coherence tomography; PCI: percutaneous coronary intervention	

Clinical outcomes following BRS plus DCB hybrid strategy (median FU = 12 months)

	Patients, n=42
Procedural success, n (%)	42 (100)
Periprocedural MI (CK MB >5 times the upper limit of normal), n (%)	2 (4.7)
Median follow-up period, months	12 (IQR 6-18)
Angiographic follow-up, n (%)	22 (52.4)
Events from hospital discharge to the longest available follow-up	
All-cause death, n (%)	0
TLR per patient, n (%)	5 (11.9)
ID-TLR per patient, n (%)	2 (4.7)
BRS segment TLR, n (%)	4 (9.5)
BRS segment ID-TLR, n (%)	2 (4.7)
DCB segment TLR, n (%)	1 (2.3)
Definite/probable BRS/DCB segment thrombosis, n (%)	0
BRS: bioresorbable scaffold; CK MB: creatine kinase MB; DCB: drug-coated balloon; ID: ischaemia-driven; MI: myocardial infarction; TLR: target lesion revascularisation	

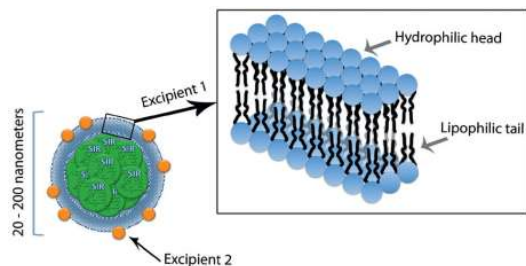
PEBSI: A Randomized Trial of Paclitaxel-Eluting Balloon After Bare Metal Stent Implantation vs Bare Metal Stent in ST Elevation Myocardial Infarction



What is Next ?

Drug-coated AngioSculpt

- AngioSculpt Platform
- Paclitaxel ($3 \mu\text{g}/\text{mm}^3$) + proprietary excipient
- Diameters 2.0, 2.5, 3.0, 3.5 mm
- Lengths 10 – 15 – 20 mm
- 6F GC compatible



Magic Touch

The Chocolate Touch™ Balloon



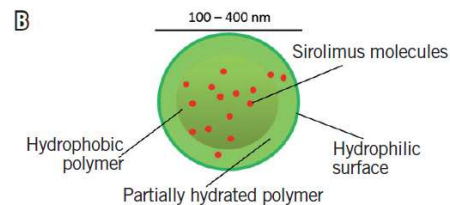
Advantages of Chocolate Platform



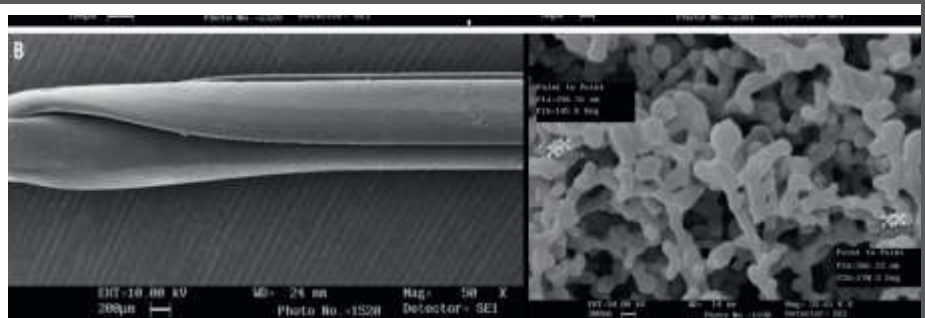
- The CS is designed to cover the coated balloon during insertion, delivery through tortuosity, and balloon unfolding
- The inflated Chocolate has a larger surface area vs. POBA
- The inflated balloon opens the vessel by angioplasty, while passively transferring the vessel wall to paclitaxel
- Upon deflation, the CS and balloon are removed from the vessel; no part of the device remains



Virtue™ nanoparticle



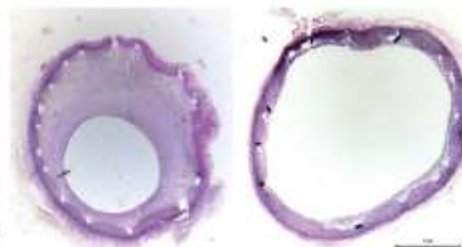
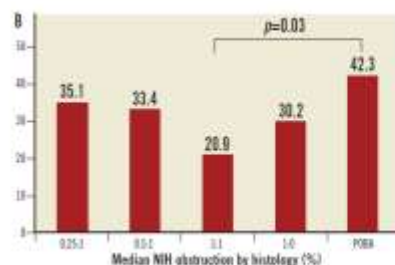
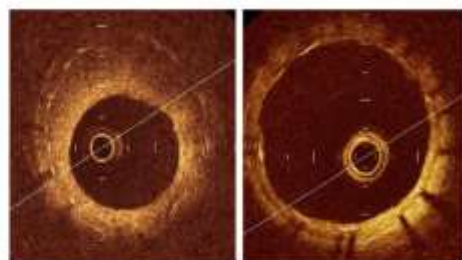
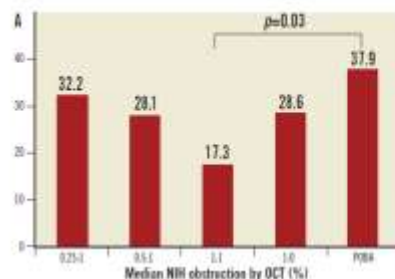
Innovative Balloon Coating Technology for “II Generation DEB “



Magic Touch™



Hydrophilic head

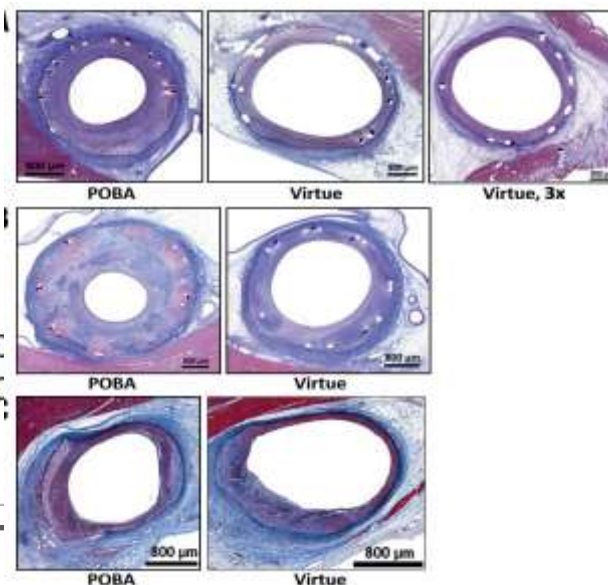


PA Lemos et al ; EuroIntervention 2013;9:148-156



Virtue™ nanoparticle

B



ecules

Hydrophilic

ilic

J F Granada et al; EuroIntervention 2015;11-online publish-ahead-of-print October 2015

Take Home Messages:

- ❑ Established efficacy and safety in treating coronary ISR (both BMS and DES ISR). So far DEBs are recommended in recent ESC Guidelines for the treatment of both BMS and DES ISR (Class I - Evidence A)
- ❑ Promising data (but still conflicting) for additional indications (*side branches in bifurcation lesions, de-novo lesions , small vessels, diffuse disease*) . Larger randomised trials (vs newer generation DES) using clinical rather than surrogate angiographic outcomes are warranted .
- ❑ New limus-eluting balloons with innovative coating approaches (Nanotechnology) are on arrival for clinical use and might add a further improvement in clinical outcome
- ❑ Not all DEBs are equal : different manufacturing and drug release kinetics. Need for head to head comparison for a more appropriate use

Thank You for Your Kind Attention !!

EuroIntervention 2013;9:148-156

