Next Generation DES and DEB

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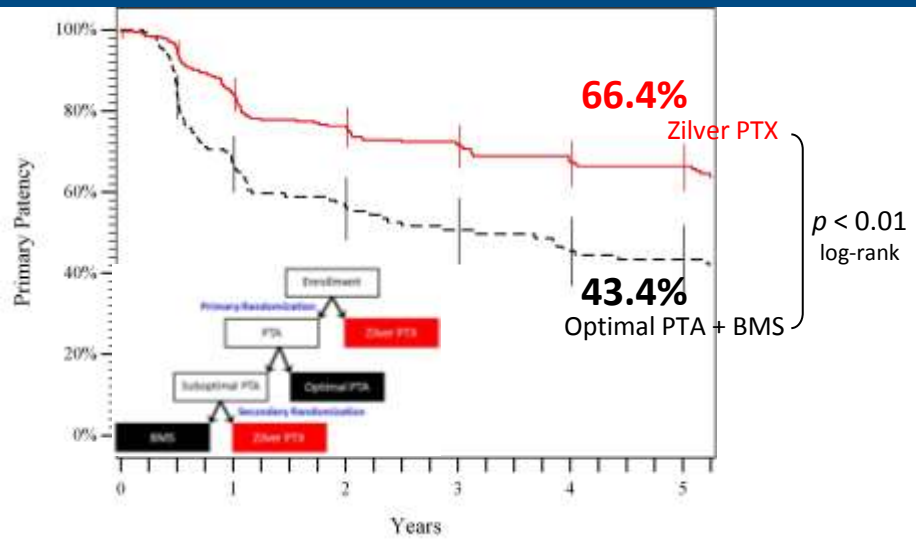
Disclosure Information

Abbott Vascular C, P, SB
Ablative Solutions EI
Boston Scientific AB, C, EI, P, SB
Cook Medical, Inc. C, P
Cordis Endovascular C, EI
Covidien, Inc. C, P
Medtronic Vascular C, P
Omeros Corp, EI
QT Vascular, EI
Sapheon, Inc. EI
St. Jude Medical C
Transverse Medical AB, EI, SO
Vatrix Medical EI
W.L. Gore C, P

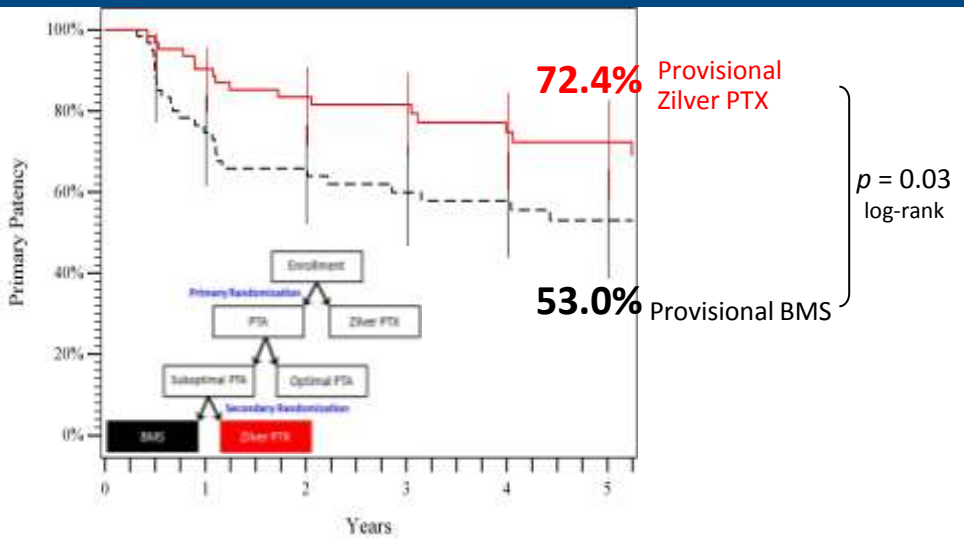
AB: Advisory Board
C: Consulting Relationship
EI: Equity Interest
GS: Grant Support
P: Proctor or Training Course Sponsorships
SB: Speakers Bureau
SE: Spouse Employee
SO: Stock Options or Positions

PTX Zilver 5-Year Primary Patency

Primary Randomization



Provisional Stenting PTX vs. BMS

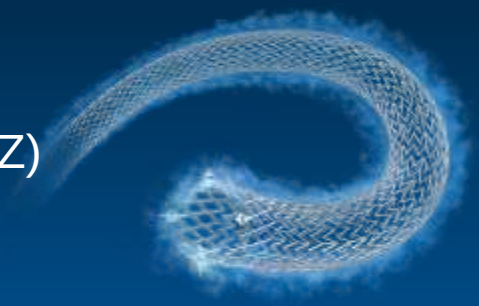


Paclitaxel 3 µg/mm2 with no polymer or binder

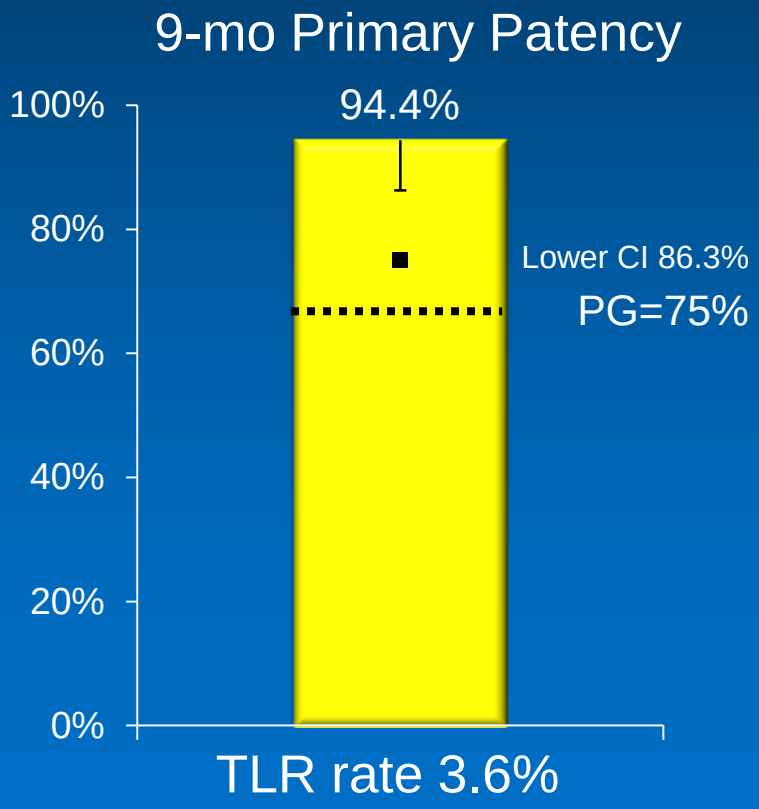
Dake MD et al *Circ Cardiovasc Interv* 2011; 4: 495-504
Dake MD VIVA 2014

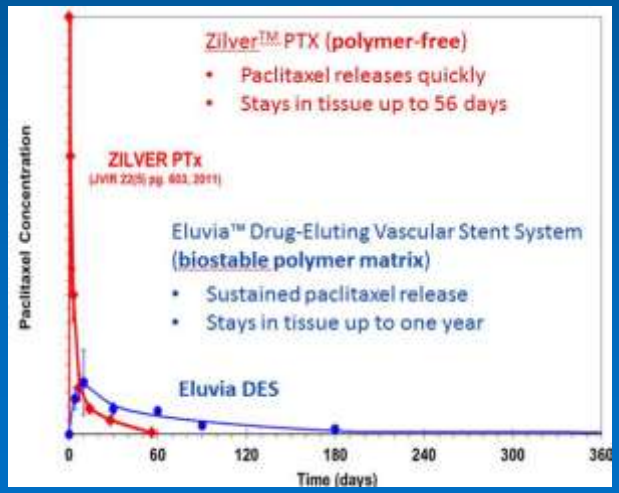
Eluvia™ SES

- Fluorocopolymer coated paclitaxel-eluting stent
- Innova self-expanding stent platform
- MAJESTIC CE Mark trial (57 pts at 14 sites in Europe, Aus/NZ)



Boston Scientific

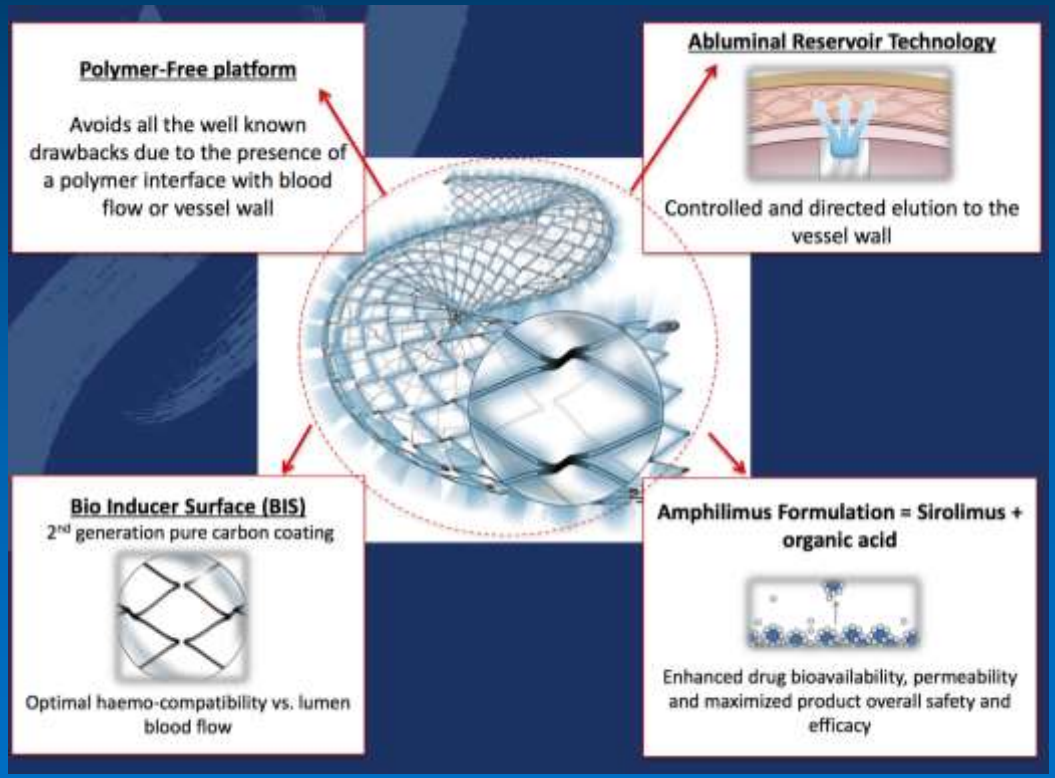


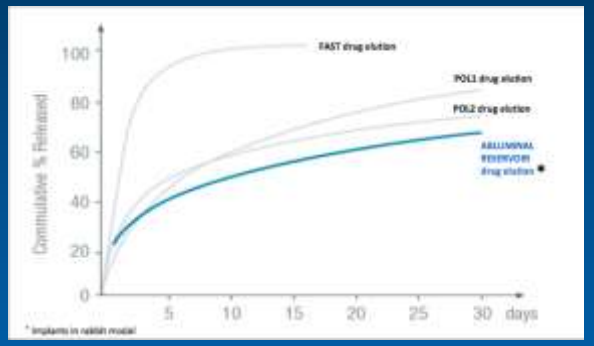


Müller-Hülsbeck S Charing Cross 2015

NiTiDES SES

- Polymer-free abluminal reservoir technology
- Amphilimus™ formulation (Sirolimus + organic acid) for prolonged elution
- Carbon coated for rapid endothelialization



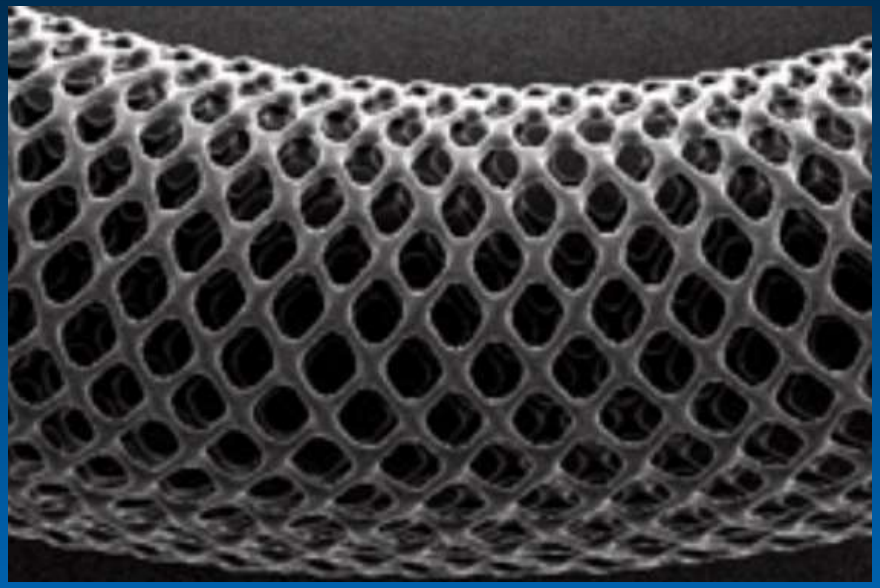



Endothelialization at 7 days

ILLUMINA Trial (100 pts with SFA-popliteal stenoses)
Enrollment completed March 3, 2017

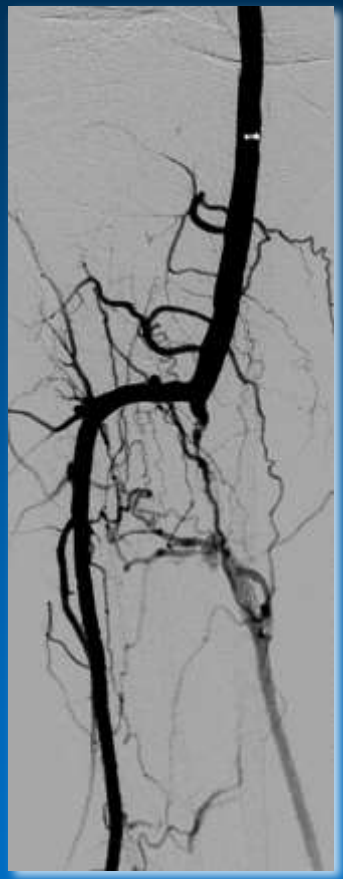
Scheinert D LINC 2014

Stanza™ Self-Expanding Bioresorbable Scaffold System



- Flexible, self-expanding design with stiffness similar to nitinol
- Composite structure of strong PLGA fibers + elastomer
- Resorbs in approximately one year
- A drug-eluting version is in clinical trial (SPIRIT)

Meta-analysis of BTK DES Trials



A Target lesion revascularization

Study or Subgroup	DES Events	DES Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
ACHILLES	8	80	14	85	27.6%	0.56 [0.22, 1.43]
BELOW	1	10	6	28	5.6%	0.41 [0.04, 3.88]
DESTINY	7	74	22	66	27.4%	0.21 [0.08, 0.53]
Falkowski et al.	3	25	14	25	13.0%	0.11 [0.03, 0.45]
YUKON-BTK	7	82	15	79	26.3%	0.40 [0.15, 1.04]
Total (95% CI)		**271**		**283**	**100.0%**	**0.31 [0.18, 0.54]**
Total events	26		71			

Heterogeneity: Tau² = 0.06; Chi² = 4.69, df = 4 (P = 0.32); I² = 15%
Test for overall effect: Z = 4.19 (P < 0.0001)

Odds Ratio M-H, Random, 95% CI
0.1 0.2 0.5 1 2 5 10
Favors DES Favors control

B Restenosis

Study or Subgroup	DES Events	DES Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
ACHILLES	15	67	31	74	27.1%	0.40 [0.19, 0.84]
BELOW	2	10	19	28	8.2%	0.12 [0.02, 0.68]
DESTINY	17	75	36	73	28.2%	0.30 [0.15, 0.61]
Falkowski et al.	4	25	19	25	11.6%	0.06 [0.01, 0.25]
YUKON-BTK	12	62	28	63	24.8%	0.30 [0.13, 0.67]
Total (95% CI)		**239**		**263**	**100.0%**	**0.25 [0.15, 0.43]**
Total events	50		133			

Heterogeneity: Tau² = 0.14; Chi² = 6.48, df = 4 (P = 0.17); I² = 38%
Test for overall effect: Z = 5.02 (P < 0.00001)

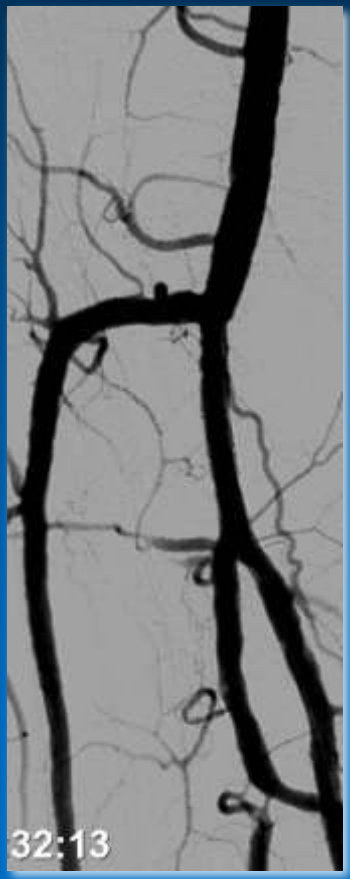
Odds Ratio M-H, Random, 95% CI
0.1 0.2 0.5 1 2 5 10
Favors DES Favors control

C Amputation

Study or Subgroup	DES Events	DES Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
ACHILLES	11	80	17	85	61.7%	0.64 [0.28, 1.46]
BELOW	2	10	8	28	13.8%	0.63 [0.11, 3.61]
DESTINY	1	74	2	66	7.2%	0.44 [0.04, 4.95]
YUKON-BTK	2	82	9	79	17.3%	0.19 [0.04, 0.93]
Total (95% CI)		**246**		**258**	**100.0%**	**0.50 [0.26, 0.97]**
Total events	16		36			

Heterogeneity: Tau² = 0.00; Chi² = 1.82, df = 3 (P = 0.61); I² = 0%
Test for overall effect: Z = 2.06 (P = 0.04)

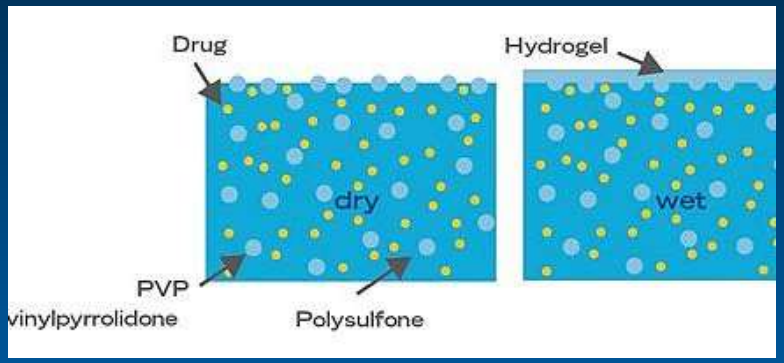
Odds Ratio M-H, Random, 95% CI
0.1 0.2 0.5 1 2 5 10
Favors DES Favors control

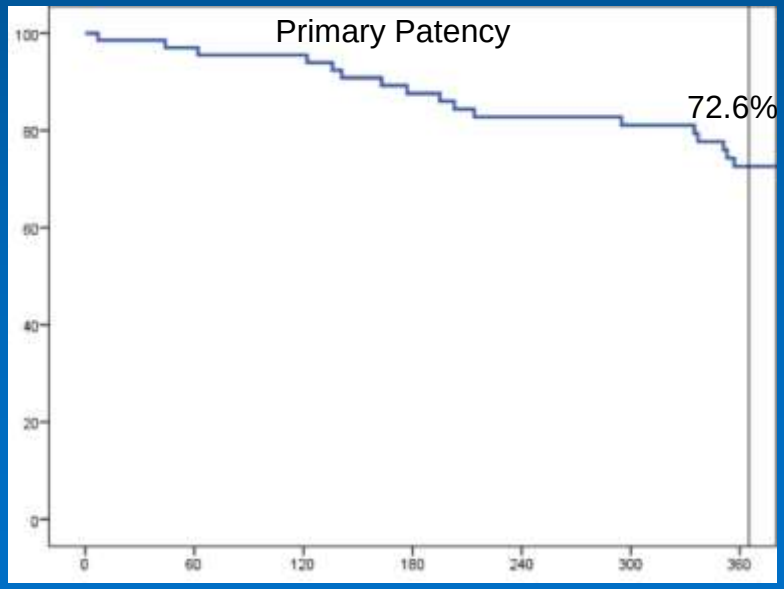


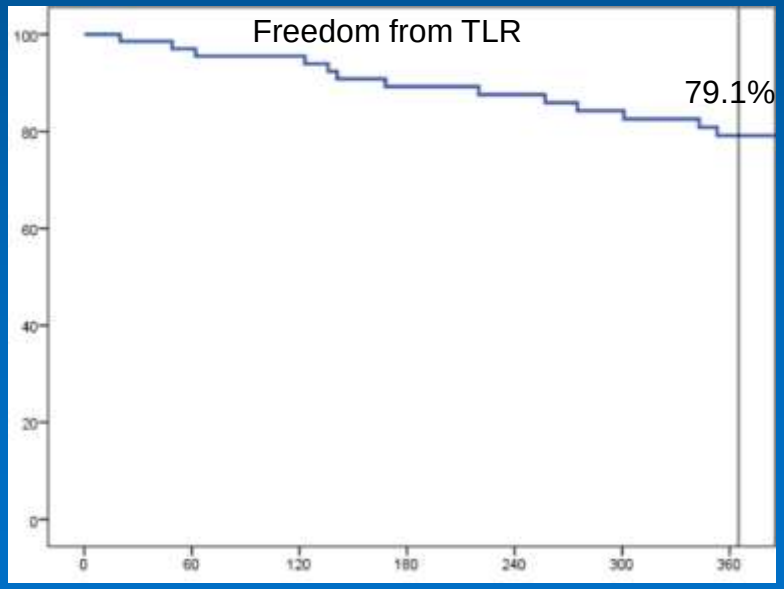
Fusaro M et al *JACC Cardiovasc Interv* 2013; 6(12): 1284-1293

Stentsys BTK-70 Trial

- 70 pts with Rutherford IV-V CLI
- Paclitaxel eluting SES
- Mean lesion length 19.7 mm



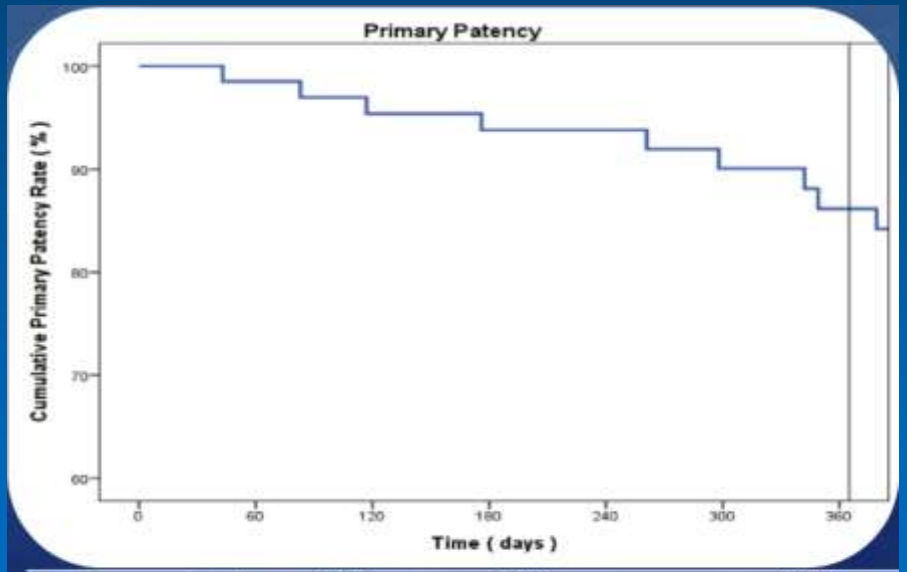




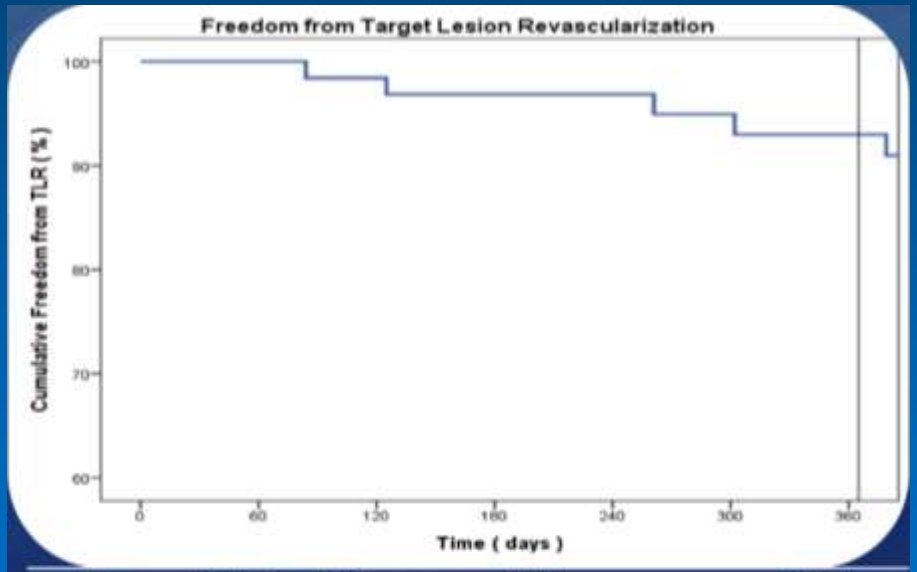
Bosiers M LINC 2015

PREVENT BTK Trial

- Promus Premier™ platform
- Prospective single arm study in 70 patients at 5 sites
- 12-mo primary patency 86.2%, TLR 7%



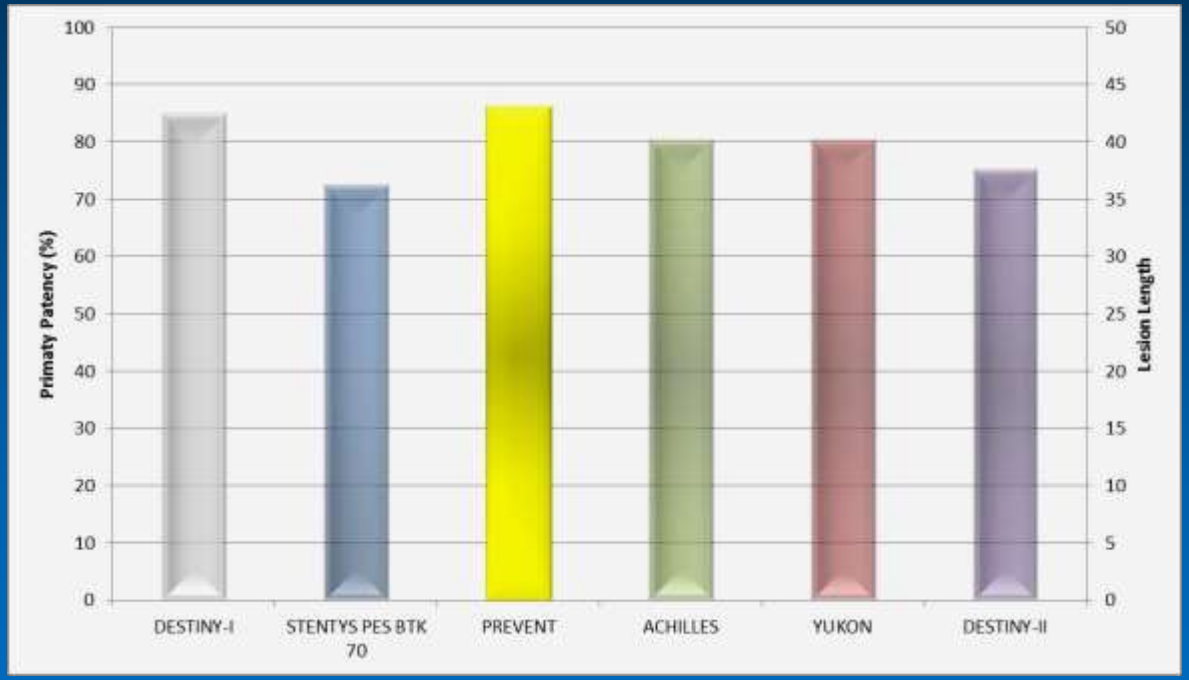
time	baseline	1MFU	6MFU	12MFU
at risk	70	67	58	44
%	100	100	93.8	86.2



time	baseline	1MFU	6MFU	12MFU
at risk	70	67	59	46
%	100	98	96.8	93.0

Bosiers M LINC 2016

1-Year Primary Patency of BTK DES

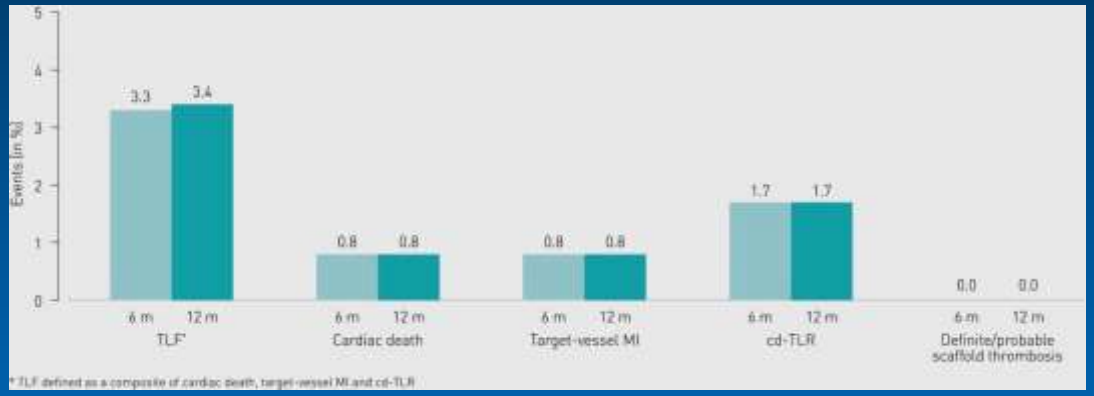


	Primary Patency	Lesion Length
DESTINY-I	85.2	15.9
STENTYS	72.6	19.7
PREVENT	86.2	22.8
ACHILLES	80.6	26.9
YUKON	80.6	31.0
DESTINY-II	75.4	47.4

Bosiers M LINC 2016

Magmaris BIOSOLVE II Trial 12 Month Results

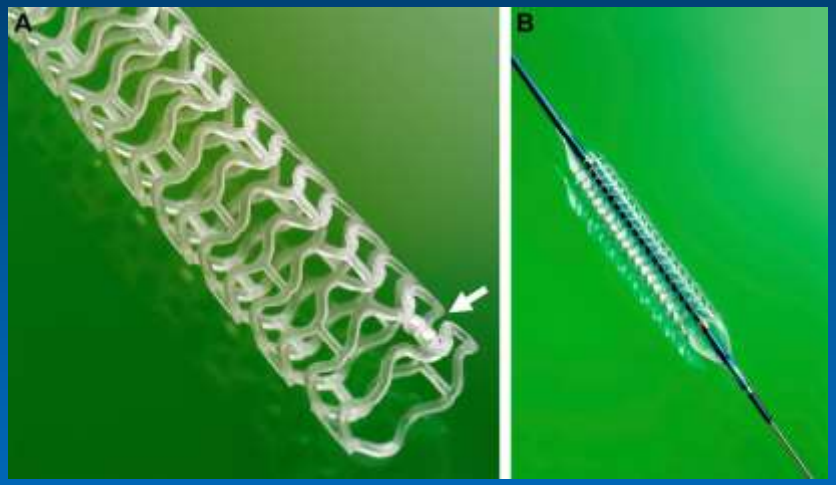
123 patients with up to 2 de novo lesions
in 2 separate coronary arteries

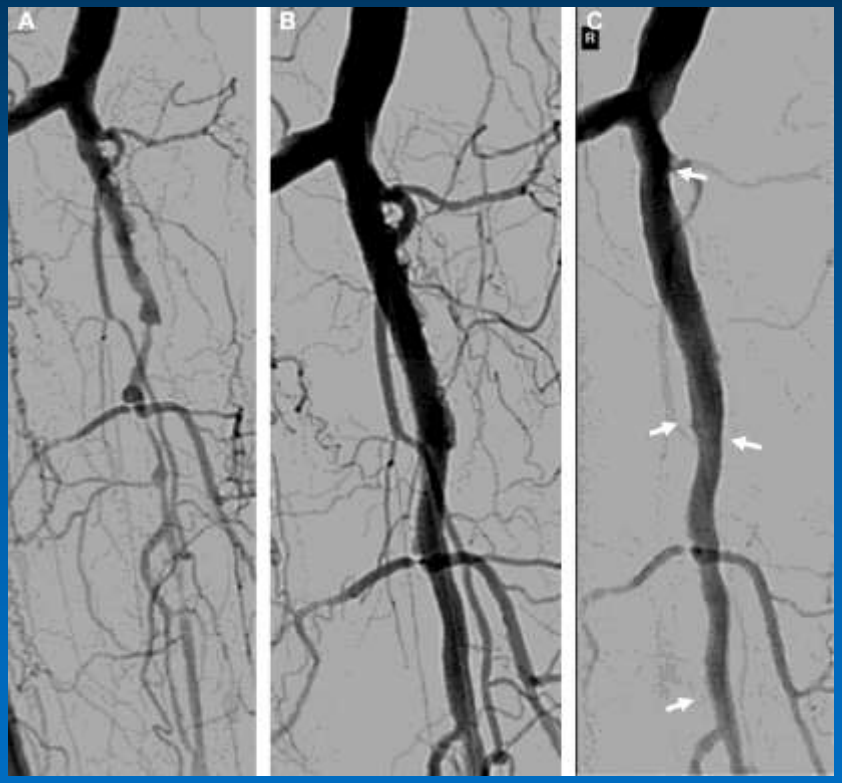


- Late lumen loss 0.27 mm
- TLF rate 3.4%
- No scaffold thrombosis at 12 months
- Vasomotion present in 80% of patients at 6 and 12 months

ABSORB BTK DES

ABSORB BVS BTK Trial



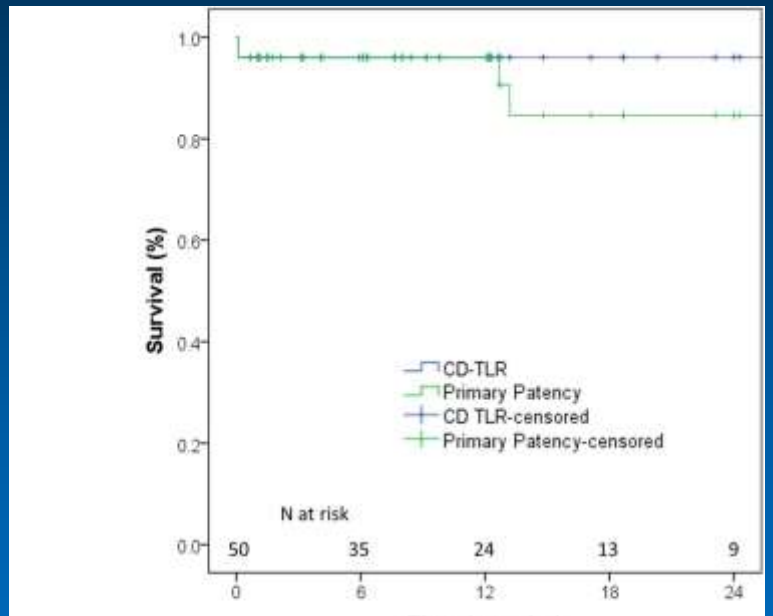


43 lesions with mean lesion length 19.2 ± 11.6 mm

Varcoe RL et al *JACC Interv* 2016; 9(16): 1721-1728

ABSORB BTK DES

ABSORB BVS BTK Trial



CD-TLR (%)	100	96.0	96.0	96.0	96.0
SE (%)	0	2.8	2.8	2.8	2.8
Primary Patency (%)	100	96.0	96.0	84.6	84.6
SE (%)	0	2.8	2.8	8.0	8.0

Primary patency 96% at 12 mo and 84.6% at 24 mo
TLR 4% at 12 and 24 mo.

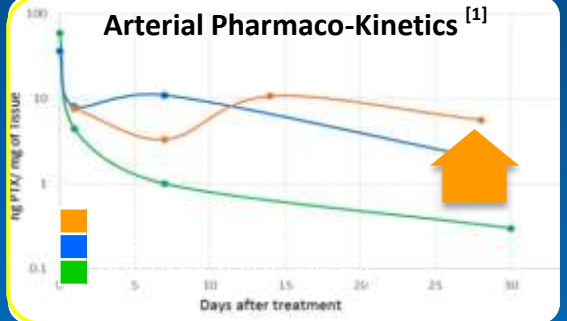
Varcoe RL et al *JACC Interv* 2016; 9(16): 1721-1728

Stellarex DCB

Spectranetics Proprietary open-folded coating technology

- Low dose (2 µg/mm^2) paclitaxel
- Hybrid-crystalline formulation

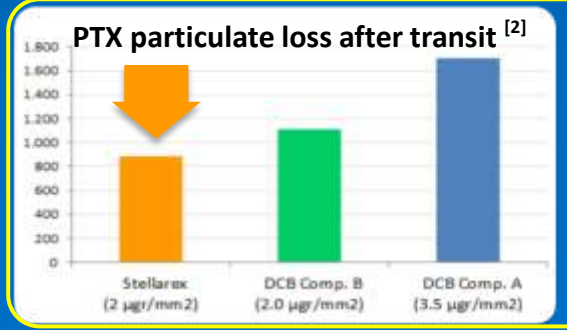
Arterial Pharmaco-Kinetics [1]



- Effective drug tissue transfer and residency (≥ 28 days)

1. Superimposed PK curves from different datasets: R.Melder, EuroPCR 2012; Yazdani et.al. Catheterization and Cardivascular Interventions 83:132-140 (2014); data on file at Spectranetics

PTX particulate loss after transit [2]

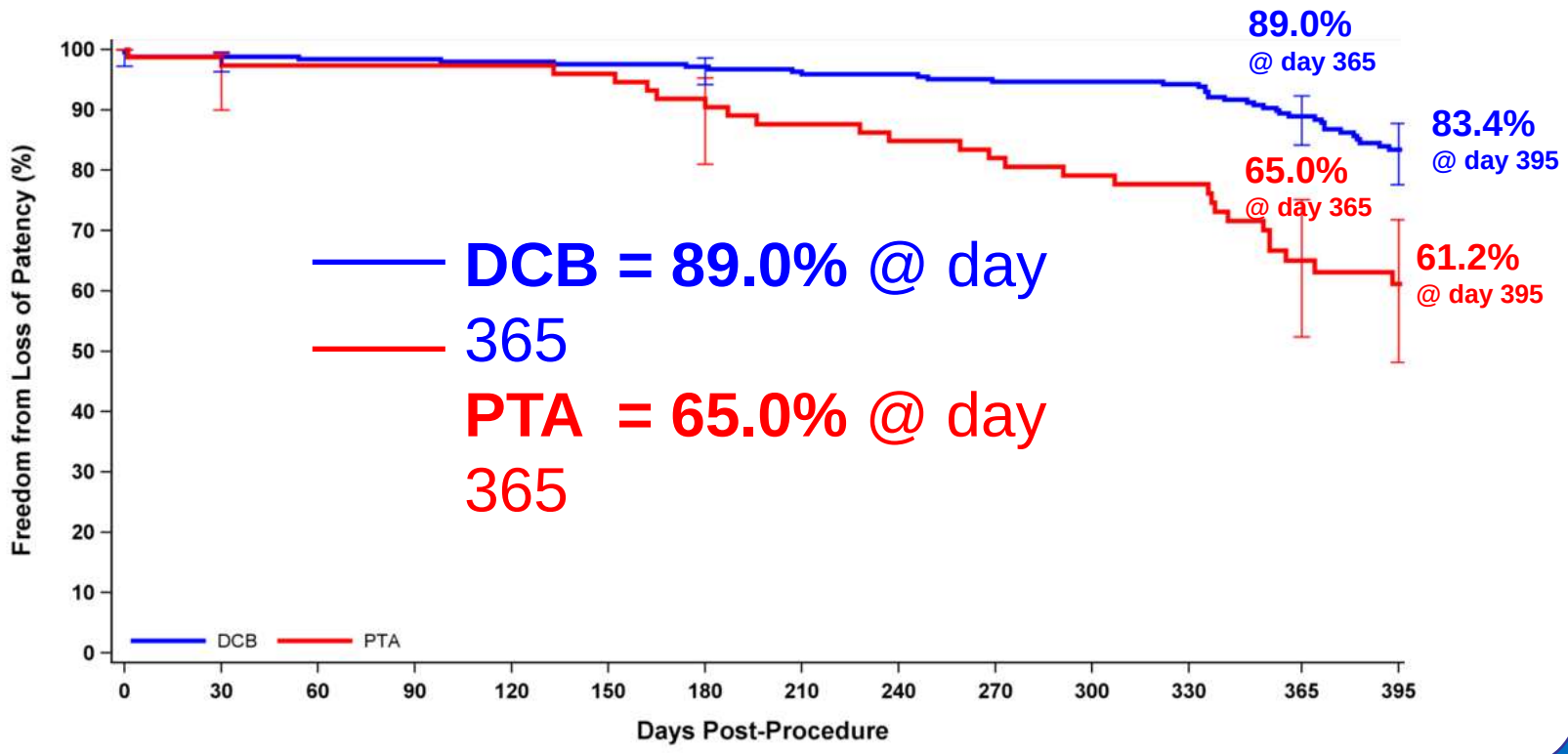


- Limited drug loss

2. Number of particulates ≥10µm/mm of DCB length lost during transit. Data on file at Spectranetics

ILLUMENATE EU RCT

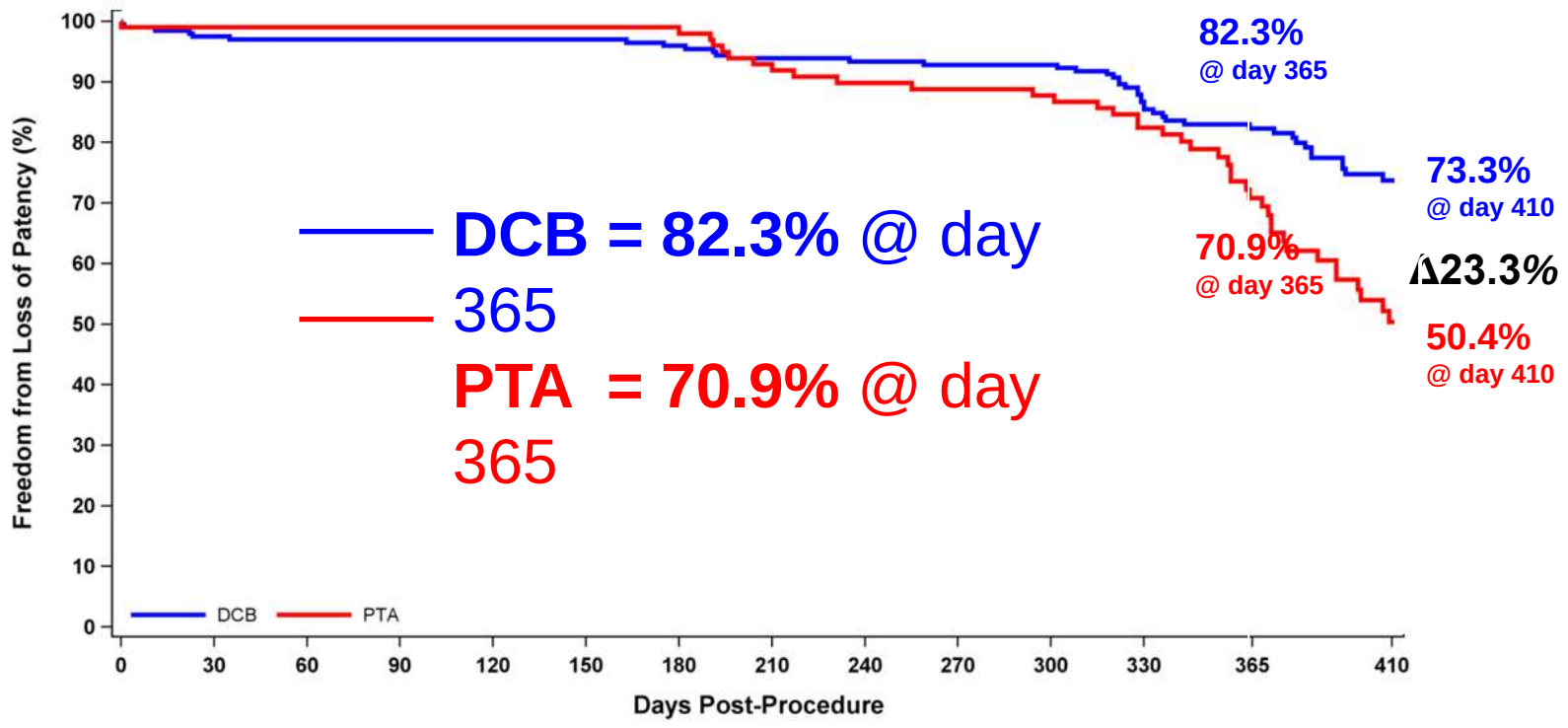
Primary patency 89% at 12 months



Primary patency defined as freedom from restenosis (determined by duplex ultrasound with PSVR ≤2.5) and freedom from clinically-driven TLR at 12 months. Assessed per lesion. KM estimates reported at day 395 to capture all patients and events within the full (and legitimate) 335-395 follow-up window. Rates from the middle of the protocol visit window (365 days) reported for consistency and comparative purposes with other trials.

ILLUMENATE US Pivotal

Primary patency 82.3% at 12 months

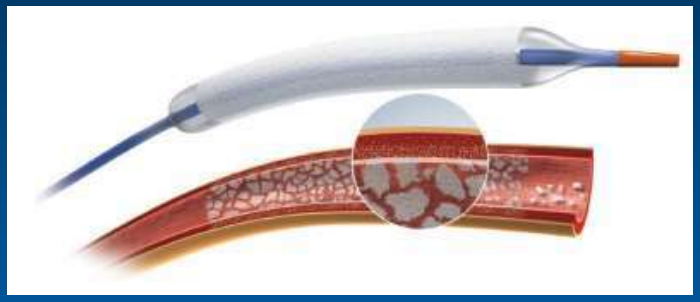


Primary patency defined as freedom from restenosis determined by duplex ultrasound PSVR ≤2.5 and freedom from clinically-driven TLR at 12 months. Assessed per lesion. KM estimates reported at day 410 to capture all patients and events within the full 320-410 follow-up window. Rates from the middle of the protocol visit window (365 days) reported for consistency and comparative purposes with other trials.

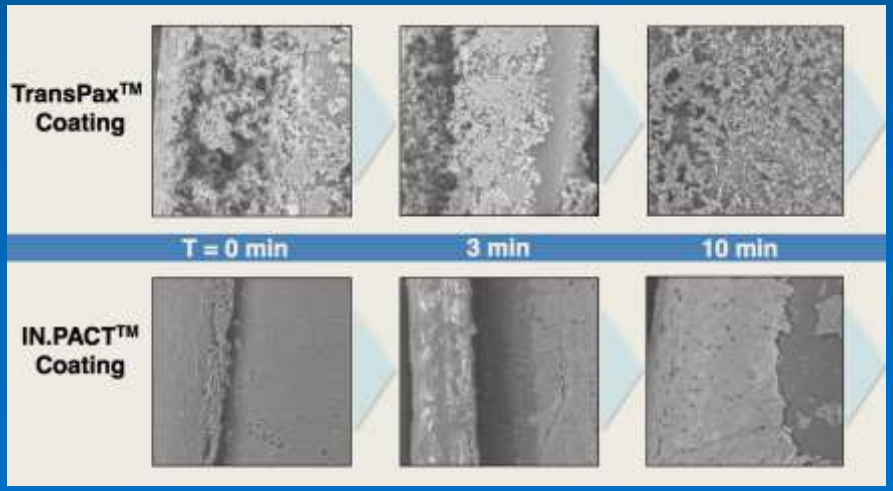
S.Lyden TCT 2016

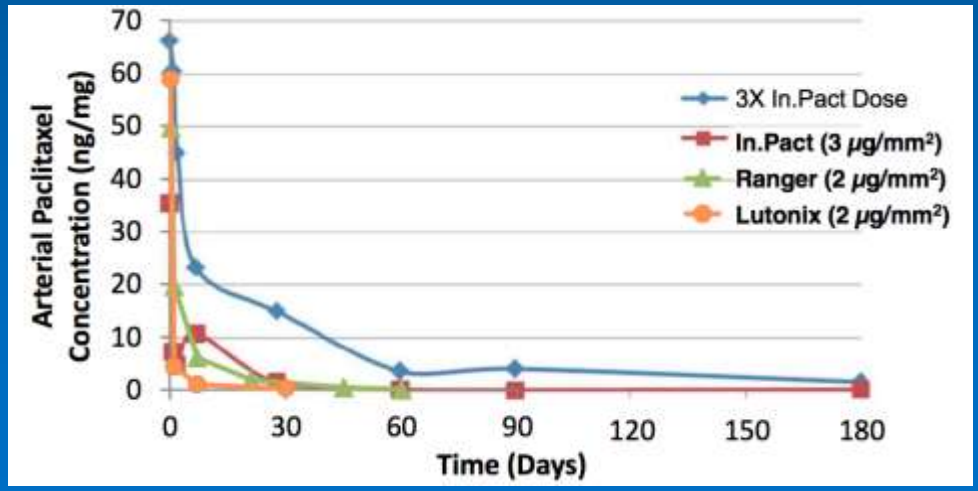
Ranger™ DCB

TransPaxTM Technology



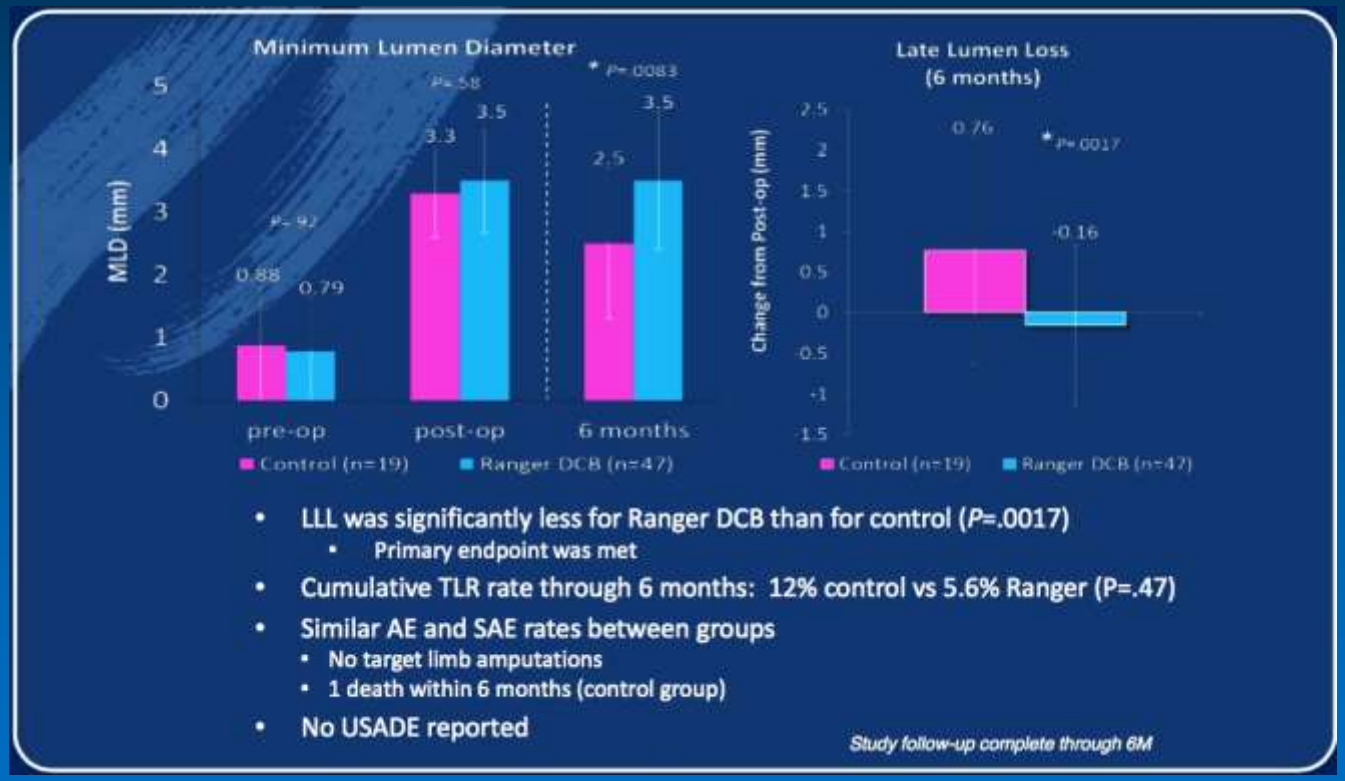
- Paclitaxel 2 µg/mm^2
- Citrate ester (acetyl tributyl citrate – ATBC)
- Balanced hydophyllic/hydrophobic excipient enhances drug retention and transfer





RANGER-SFA Trial

Prospective 2:1 randomized trial in 105 patients



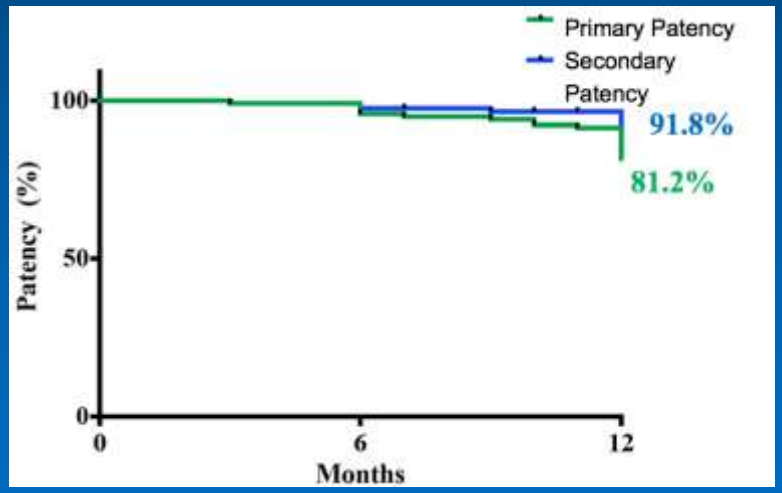
SFA: 4-8mm; 30-100mm
BTK: 2-4 mm; up to 150 mm

Sheinert D CIRSE 2016

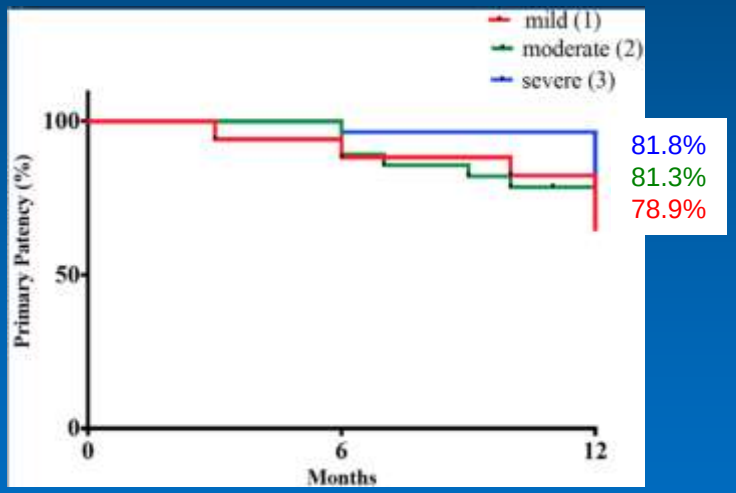
AngioSculpt DCB

PANTHER Registry (N=121 patients, 124 lesions)

- 37.1% Angiosculpt alone (N-46)
- 32.3% Angiosculpt plus DCB (N=40)
- 30.6% Angiosculpt plus stent (N=38)



Overall results



PP by extent of calcification

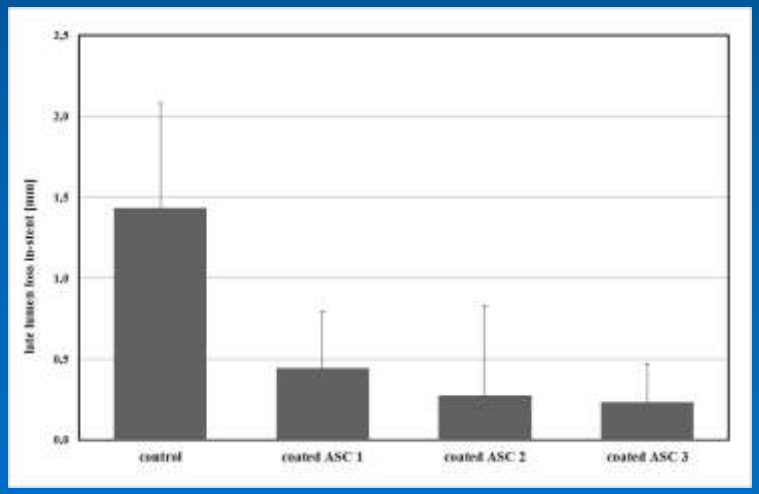
BIOTRONIK
excellence for life

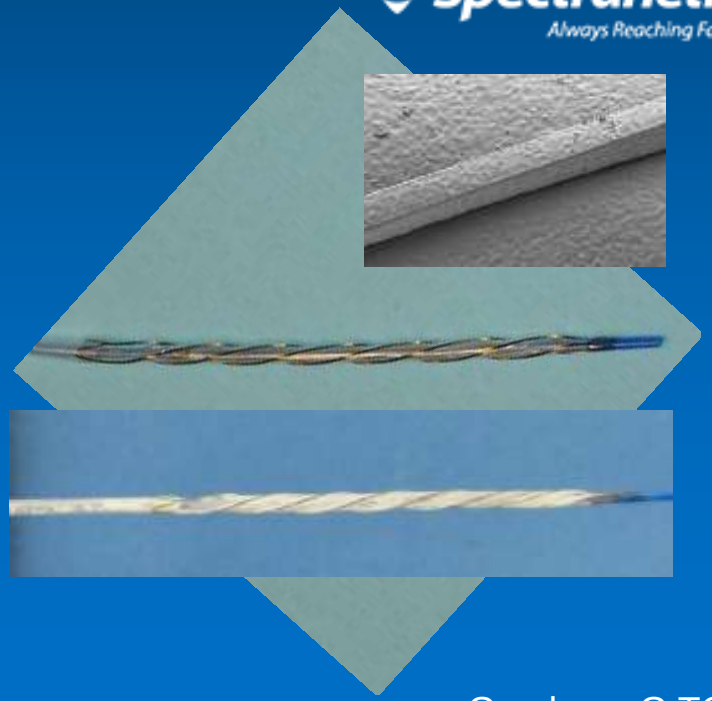
Pantera LUX™ DCB

Blessing E LINC 2014

AngioScore DCB

- 60 patient single-arm registry (4 sites)
- 3 µgr/mm2 paclitaxel with Ultravist excipient (switch to PEG?)
- Coronary ISR (endovascular application now being considered)





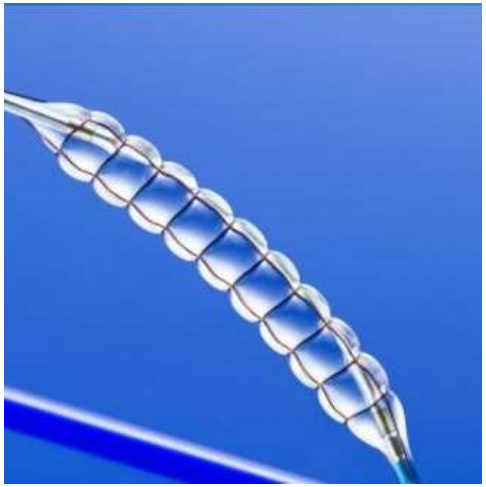
30-day LLL porcine overstretched BMS model (N=30)

Gershony G TCT 2012

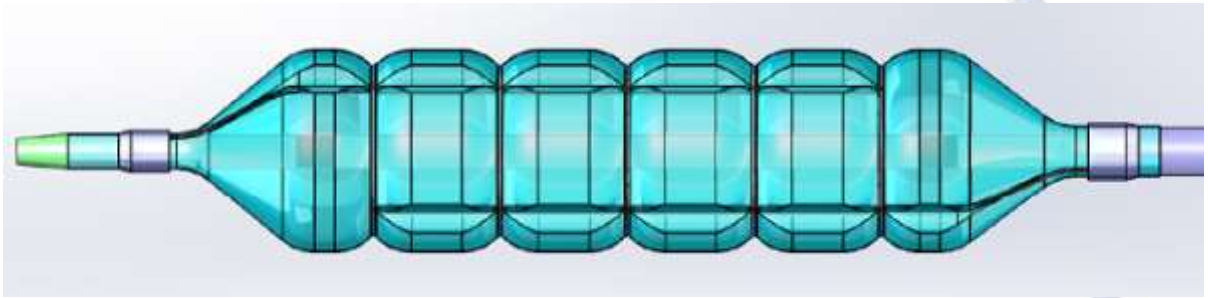
Chocolate Touch DCB

TriReme Medical

- Nominal dose density of paclitaxel on Chocolate Touch is 3µg/mm^2, similar to other drug coated balloons.
- Excipient is a GRAS substance used in the pharmaceutical and in the food industry for 65yrs.



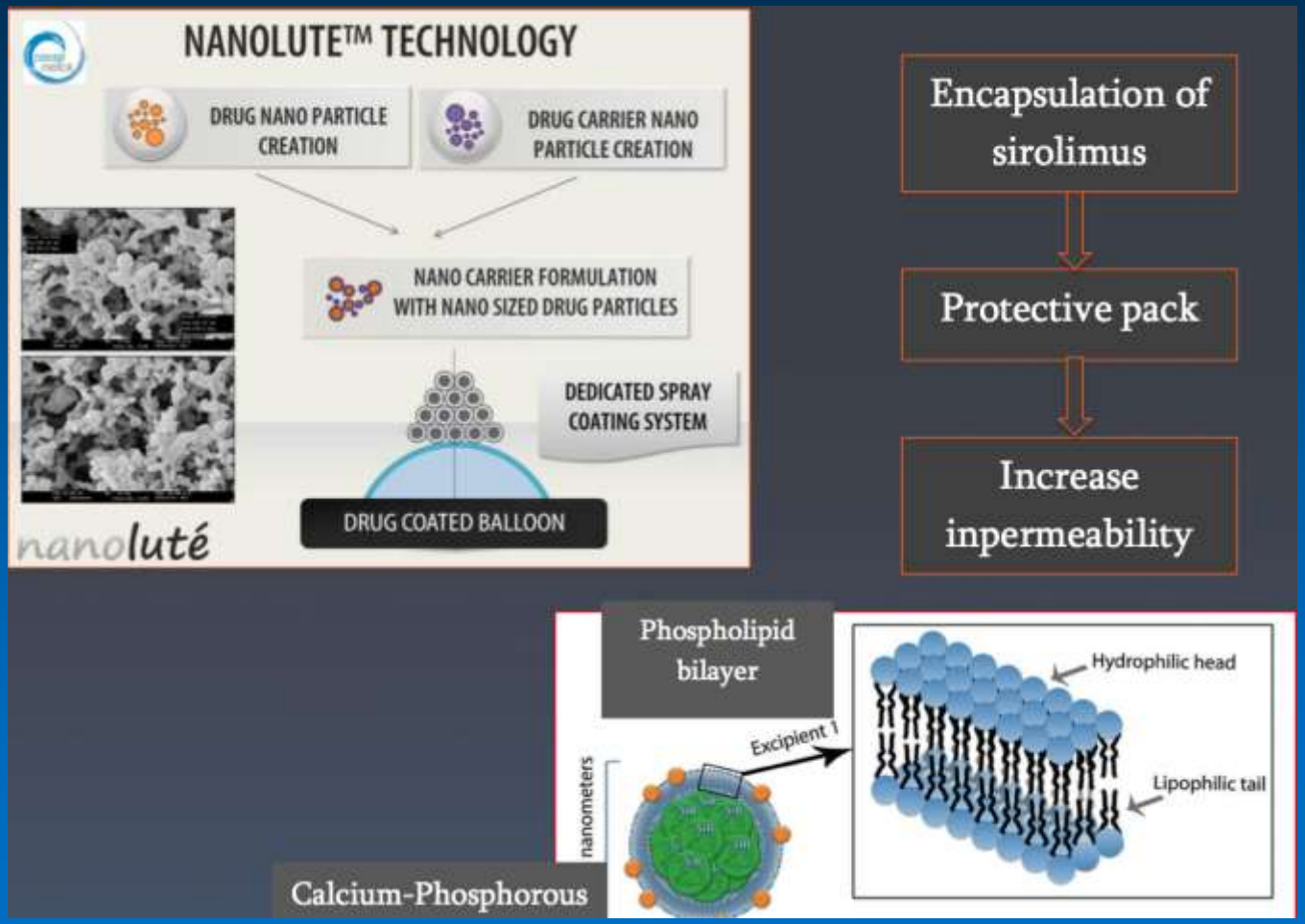
Coating Application



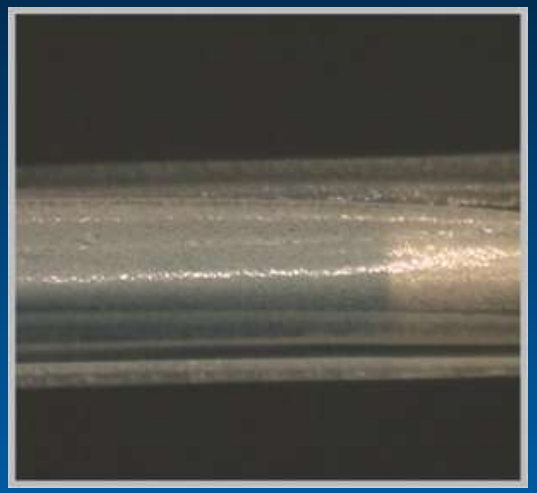
GRAS: Generally Recognized as Safe
Investigational device. Not approved for human use.

CHOCOLATE TOUCH
Drug-Coated PTA Balloon Catheter

Magic Touch Nanolute Technology



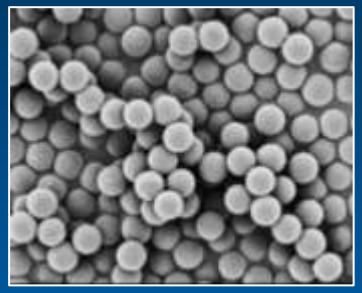
Xtreme Touch Neo Endovascular DCB



Catheter Configuration	Over-The-Wire (OTW)
Available Balloon Lengths	Up to 150 mm
Available Balloon Diameters	Up to 12.00 mm
Effective Catheter Length	130 cm (1300 mm) and 150 cm (1500 mm)
Radiopaque Marker Bands	2
Guide wire compatibility (max)	0.014" / 0.018" / 0.035"
Coating Formulation	Active Pharmaceutical Ingredient: Sirolimus Drug Excipients: Phospholipid
Drug Dose	3µg/mm^2

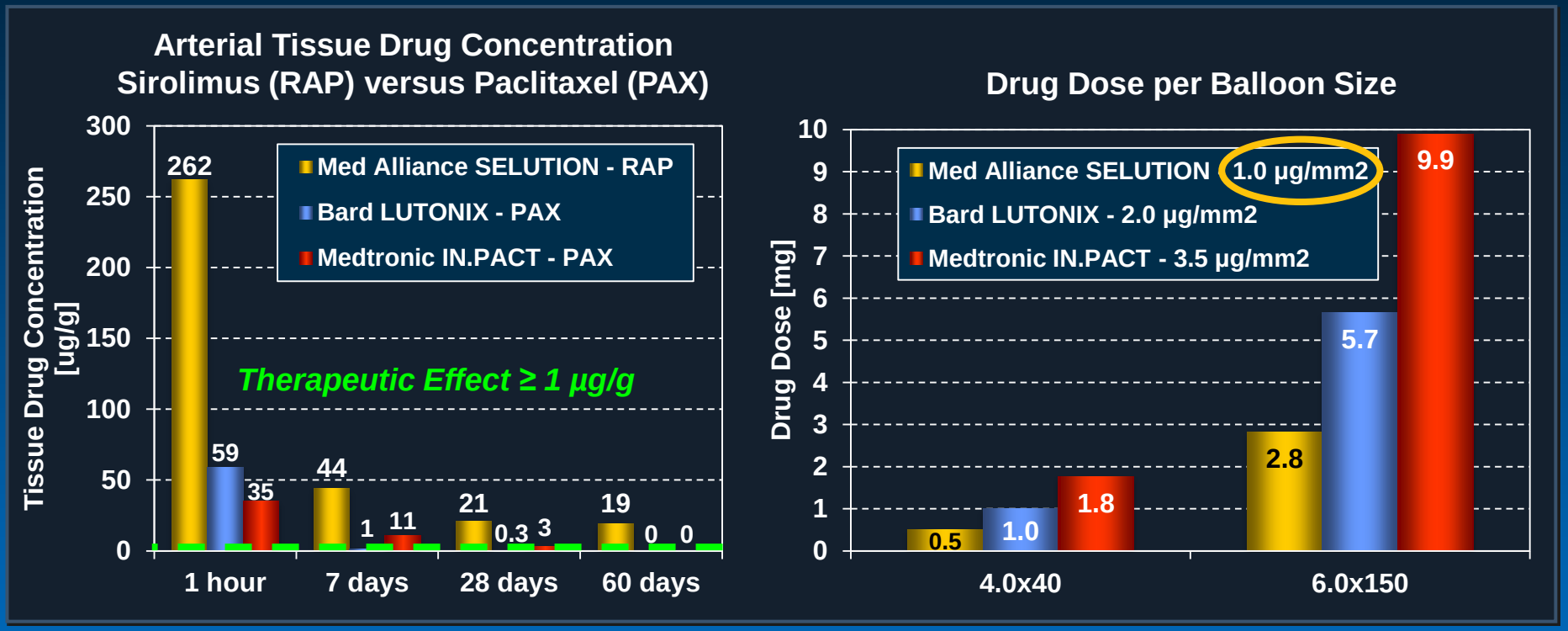
SELUTION™ Sirolimus DCB

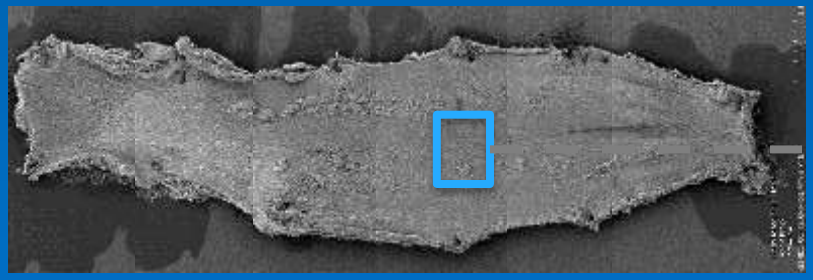
- Use of micro-reservoirs made out of biodegradable polymer intermixed with Sirolimus
  - **Controlled** and **sustained** drug release
  - **Long-term distribution** of Sirolimus into tissue to maintain therapeutic levels



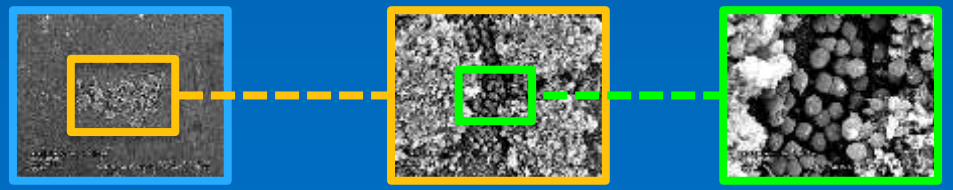
- Novel Cell Adherent Technology – CAT™
  - **Minimizes wash-off** during insertion, tracking and lesion crossing
  - **Optimizes drug transfer** to tissue during short-term balloon dilatation

SELUTION™ Sirolimus DCB





En Face Scanning Electron Microscope at 24 hours



Med Alliance – PK Study (2014-004)
Medtronic – Presentation R.J. Melder (LINC 2012)
Bard – *Catheterization and Cardiovascular Interventions* 83:132–140 (2014)

SELUTION™ FIH Fem-Pop Trial

Objective	To show non-inferiority of **SELUTION™ DCB** in terms of safety and efficacy for treatment of Superficial Femoral (SFA) or Popliteal (PA) Artery lesions
Design	▫ Prospective, Multi-Center, Single Blinded, Single Arm Controlled ▫ N=50
Primary Endpoint	▫ **Angiographic Late Lumen Loss (LLL) by QVA** ▪ **6 months**
Secondary Endpoints	▫ Major Adverse Events (Death, TLR, Thrombosis, Amputation) ▪ 6 months ▫ Primary Patency – Freedom from CD-TLR and Restenosis by DUS ▪ 6, 12 and 24 months ▫ Angiographic Binary Restenosis (ABR) by QVA ▪ 6 months ▫ Composite of Freedom from Amputation and Freedom from CD-TVR ▪ 12 and 24 months ▫ Change of ABI, WIQ and QoL ▪ 6, 12 and 24 months