

CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE
CONTROVERSIES & UPDATES IN VASCULAR SURGERY

JANUARY 19-21 2017

MARRIOTT RIVE GAUCHE & CONFERENCE CENTER

PARIS, FRANCE



Drug coated balloon vs
drug eluting stent in
complex SFA lesions
Yes, **DCB** are definitely
superior

Frank Vermassen



Disclosure

Speaker name: Frank Vermassen

I have the following potential conflicts of interest to report:

- Consulting: Medtronic, Abbott Vascular, Terumo, Boston Scientific, Spectranetics,
- Employment in industry
- Shareholder in a healthcare company
- Owner of a healthcare company
- Other(s)



Primary vs selective stenting in the SFA

Survival free of vascular events

1st local vascular event

Log-rank test : $p=0.0178$

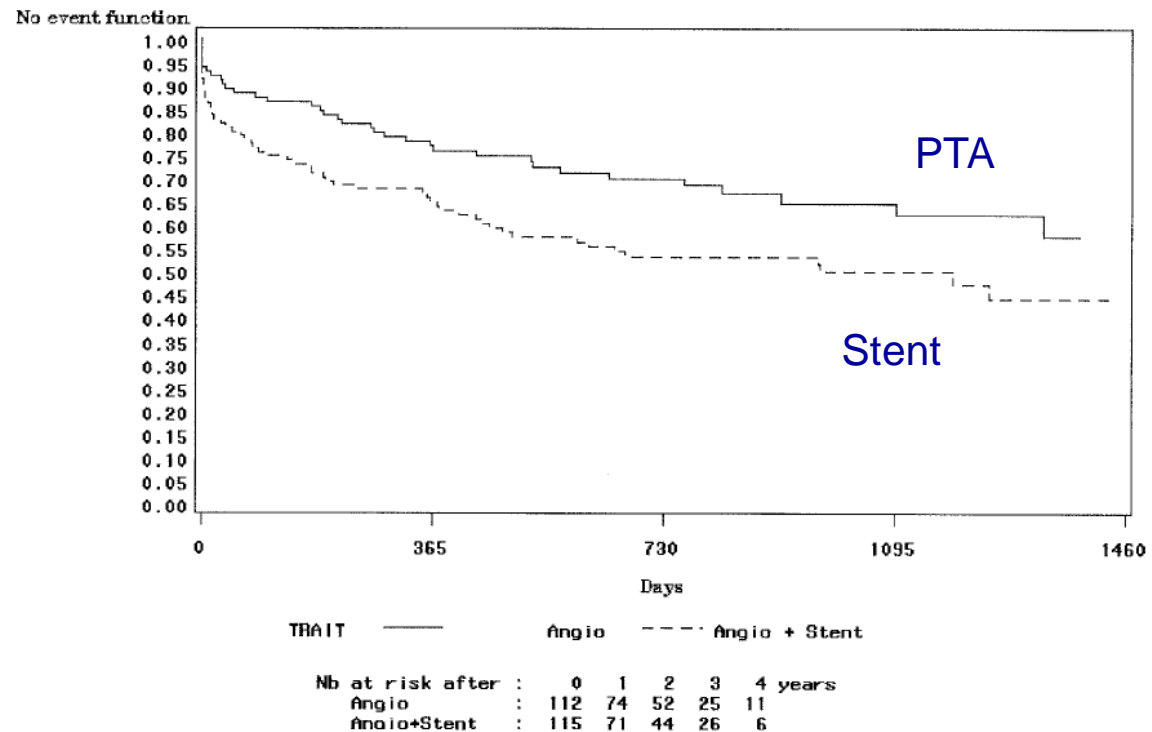
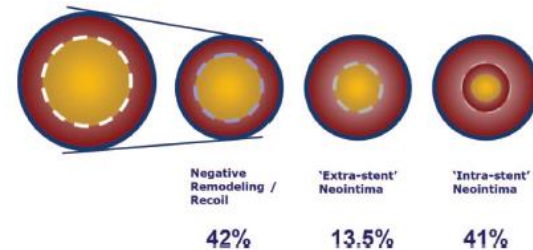
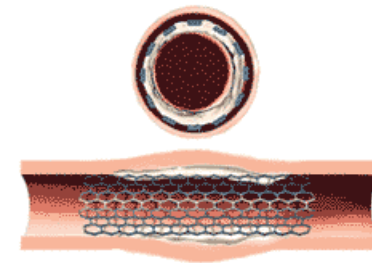


Fig 2. Comparison of balloon angioplasty and stenting in superficial femoral artery. Cumulative survival free of vascular critical events on the ipsilateral leg.



Reasons for restenosis

- Early recoil, dissection
- Negative vessel remodelling
- Neo-intimal hyperplasia





Stents cause restenosis

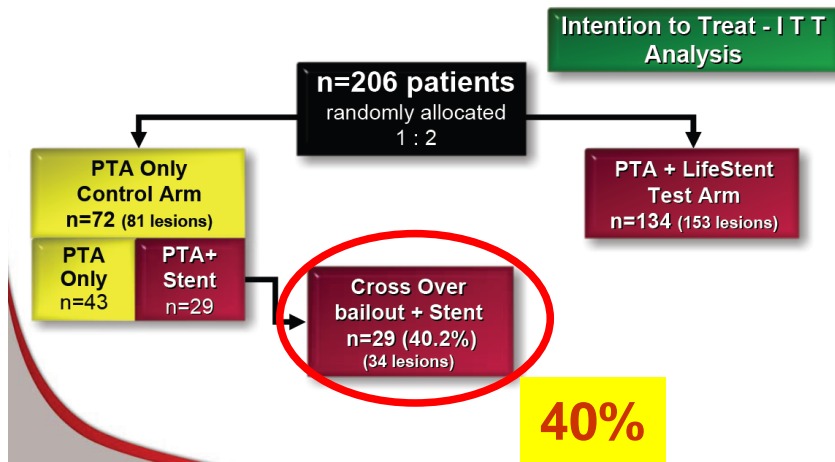
- Stents exert a
- persistent pressure on the vessel wall,
- causing a continuous trauma,
- promoting injury-repair phenomenon,
- causing restenosis





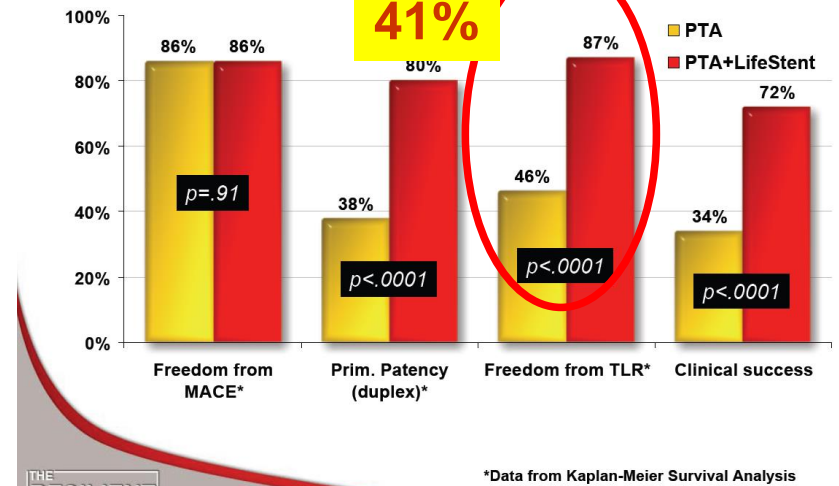
Resilient trial

Actual Enrollment Pattern



THE RESILIENT TRIAL

12-Month Results



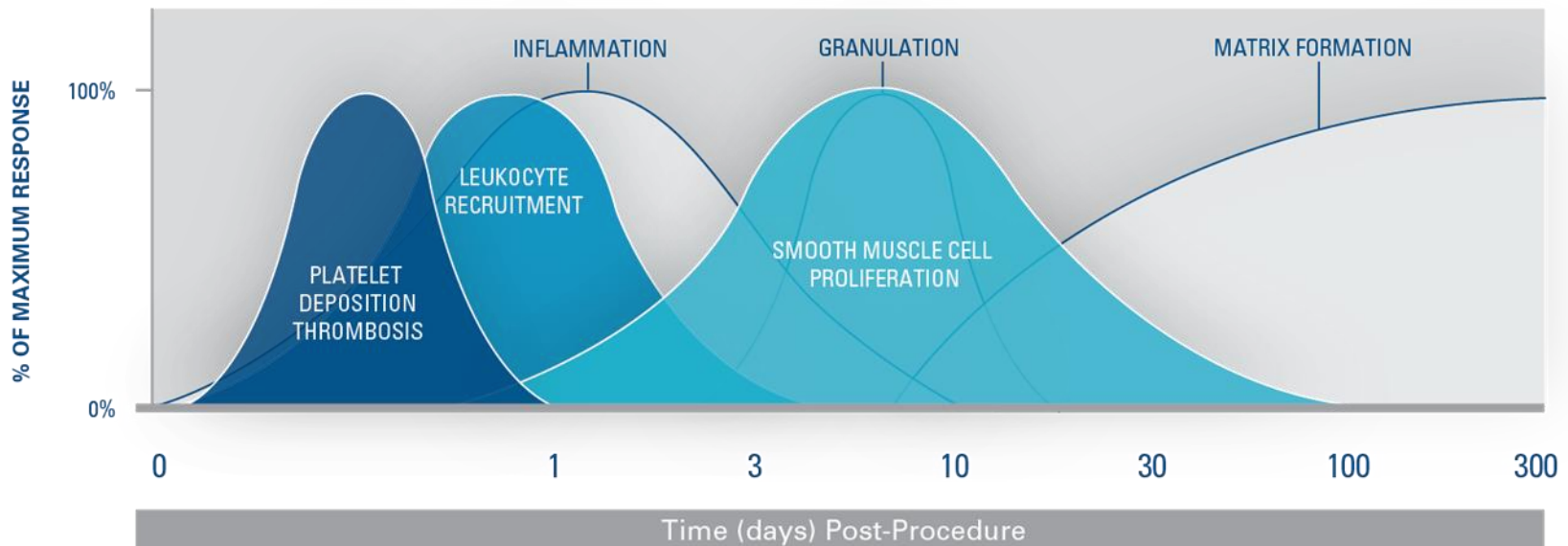
THE RESILIENT TRIAL

Difference entirely due to cross-overs during intervention
No difference in later restenosis rate



Cascade of events leading to wound healing also leads to restenosis

BIOLOGY OF RESTENOSIS



Drug-elution to inhibit SMC proliferation and intimal hyperplasia

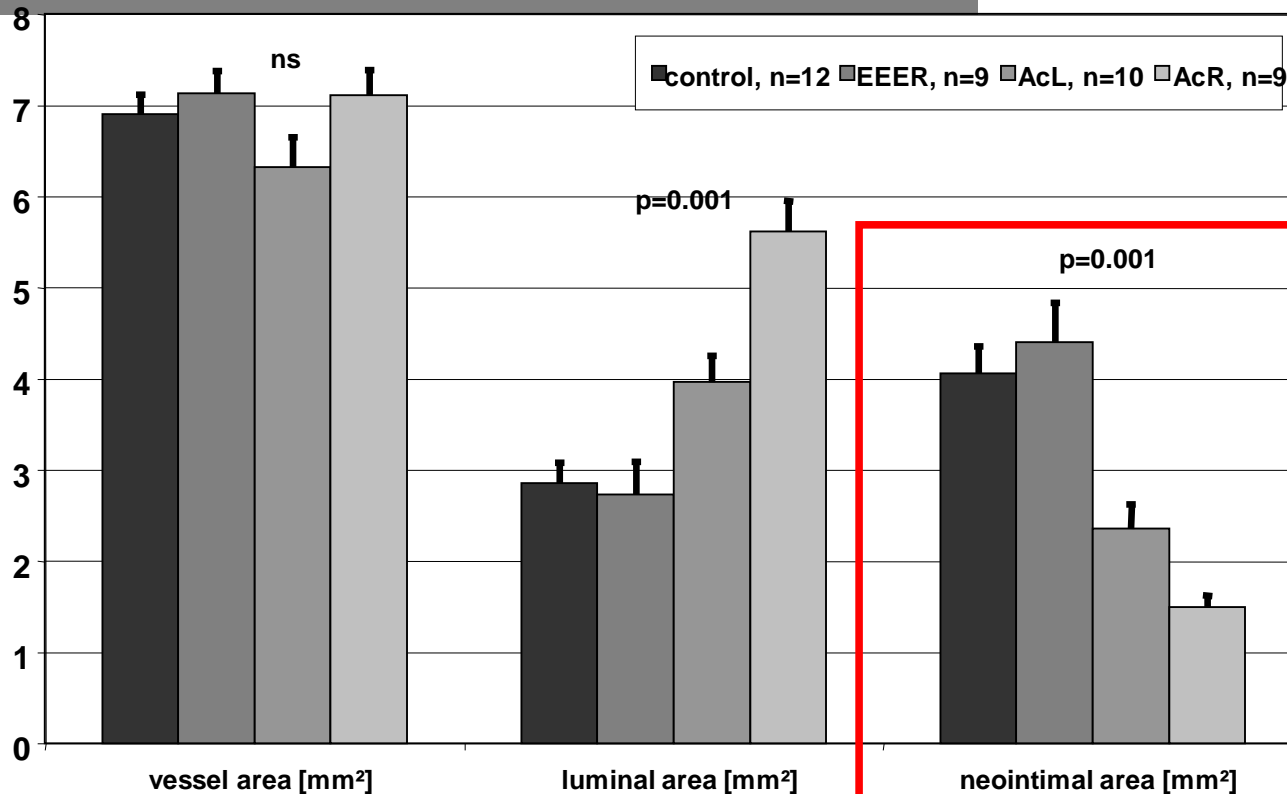


DEB: Proof of concept

DEB- porcine restenosis study

- coronary stent implantation LAD + CX with study balloon:
- uncoated control, EEER, AcL, AcR; 28 days follow-up, n=40

- - POBA control
- - Paclitaxel 2.5 $\mu\text{g}/\text{mm}^2$ WITHOUT additive
- - Paclitaxel 1.3 $\mu\text{g}/\text{mm}^2$ + Ultravist additive
- - Paclitaxel 2.5 $\mu\text{g}/\text{mm}^2$ + Ultravist additive

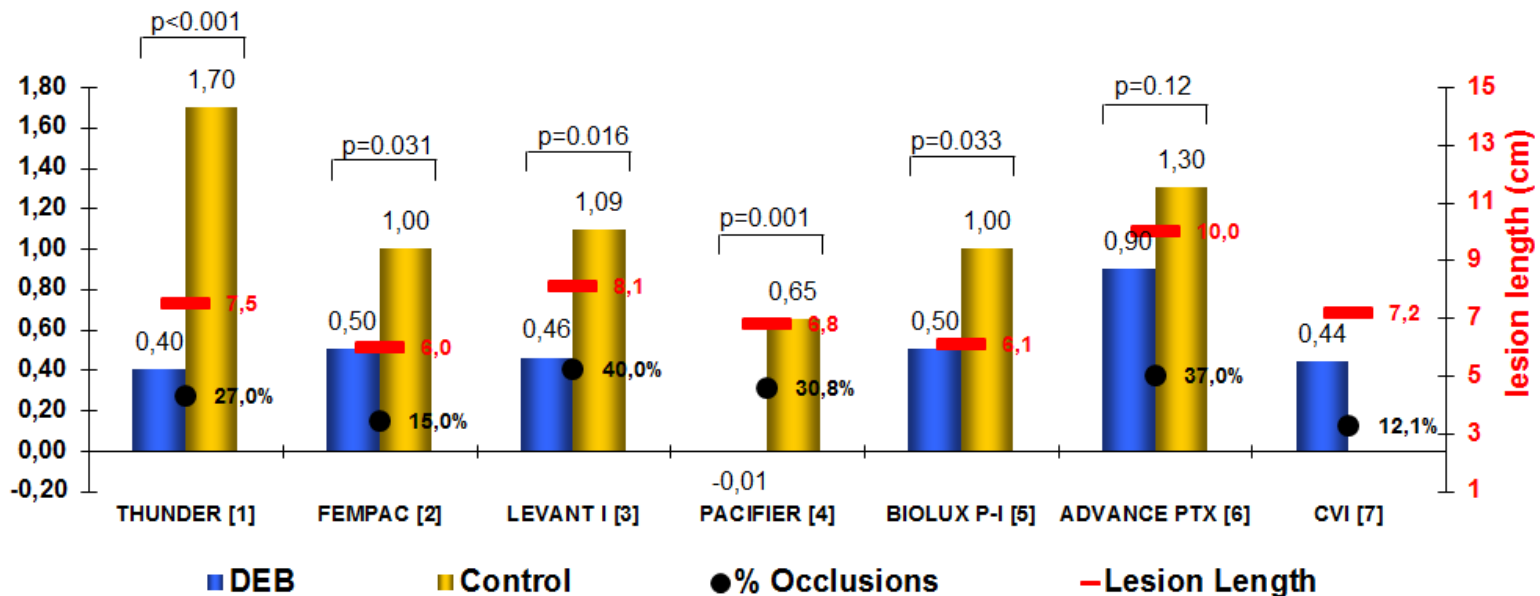




Short term results

6 DEB Technologies / 7 Trials (6-month LLL Primary Endpoint)

6-month LLL (Primary Endpoint)





Paclitaxel-Coated Versus Uncoated Balloon Angioplasty Reduces Target Lesion Revascularization in Patients With Femoropopliteal Arterial Disease

A Meta-Analysis of Randomized Trials

Salvatore Cassese, MD*; Robert A. Byrne, MB, BCh, PhD*; Ilka Ott, MD; Gjin Ndrepepa, MD; Mateja Nerad, MD; Adnan Kastrati, MD; Massimiliano Fusaro, MD

A Target lesion revascularization

Study or Subgroup	PCB		UCB		Weight	Odds Ratio M-H, Random, 95% CI	Year	Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total				
THUNDER	7	48	28	54	32.1%	0.16 [0.06, 0.42]	2008	
FemPac	6	45	21	42	27.3%	0.15 [0.05, 0.44]	2008	

A Binary restenosis

Study or Subgroup	PCB		UCB		Weight	Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total			
THUNDER	7	41	21	48	38.8%	0.26 [0.10, 0.71]	
FemPac	10	31	22	34	36.1%	0.26 [0.09, 0.73]	

B Late lumen loss

Study or Subgroup	PCB			UCB			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
THUNDER	0.4	1.2	41	1.7	1.8	48	19.6%	-1.30 [-1.93, -0.67]	
FemPac	0.5	1.1	31	1	1.1	34	25.2%	-0.50 [-1.04, 0.04]	
LEVANT I	0.4	1.1	39	1.09	1	35	29.7%	-0.69 [-1.17, -0.21]	
PACIFIER	-0.05	1.1	40	0.61	1.3	39	25.5%	-0.66 [-1.19, -0.13]	
Total (95% CI)			151			156	100.0%	-0.75 [-1.06, -0.45]	

Heterogeneity: Tau² = 0.02; Chi² = 3.95, df = 3 (P = 0.27); I² = 24%
 Test for overall effect: Z = 4.78 (P < 0.00001)

-2 -1 0 1 2
 PCB Better UCB Better



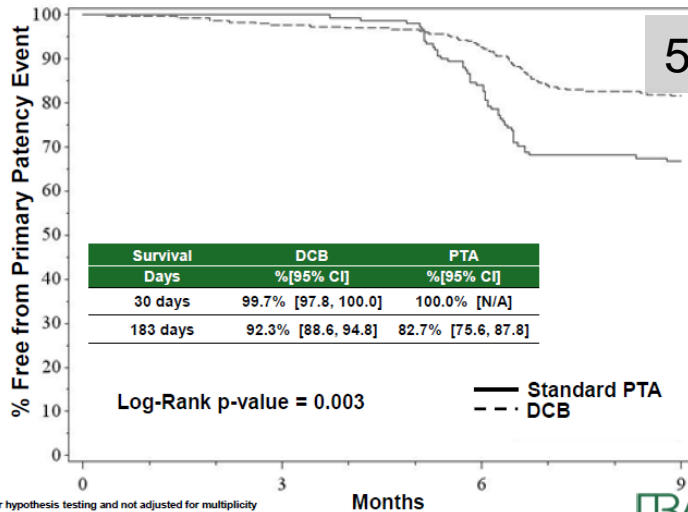
LEVANT II – 1 yr

1 yr¹⁴

Primary Patency - KM¹

62.5%

52.6%



¹Not pre-specified for hypothesis testing and not adjusted for multiplicity

CAUTION: Investigational Device- Limited by Federal (USA) Law to Investigational Use



- Lutonix DEB vs POBA
- 476 patients randomized 2:1
- Rutherford cat: 2-4
- Single de novo lesions > 70%
- < 15 cm length
- SFA or prox. PA
- Mean lesion length: 6.3 cm

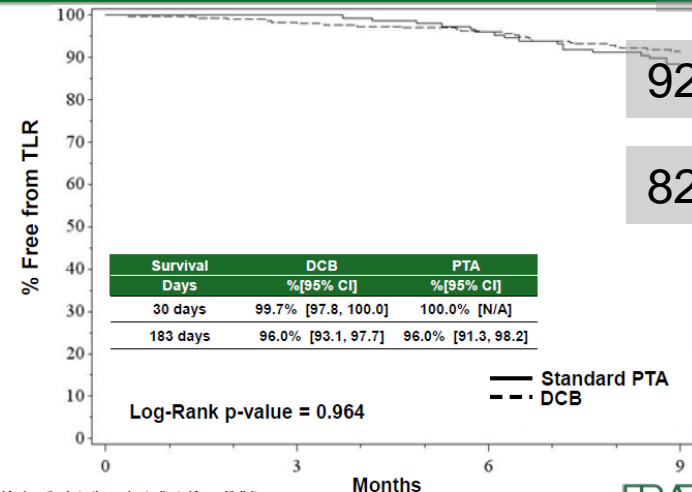
C-15

Freedom from TLR - KM¹

1 yr

92.3%

82.7%



¹Not pre-specified for hypothesis testing and not adjusted for multiplicity

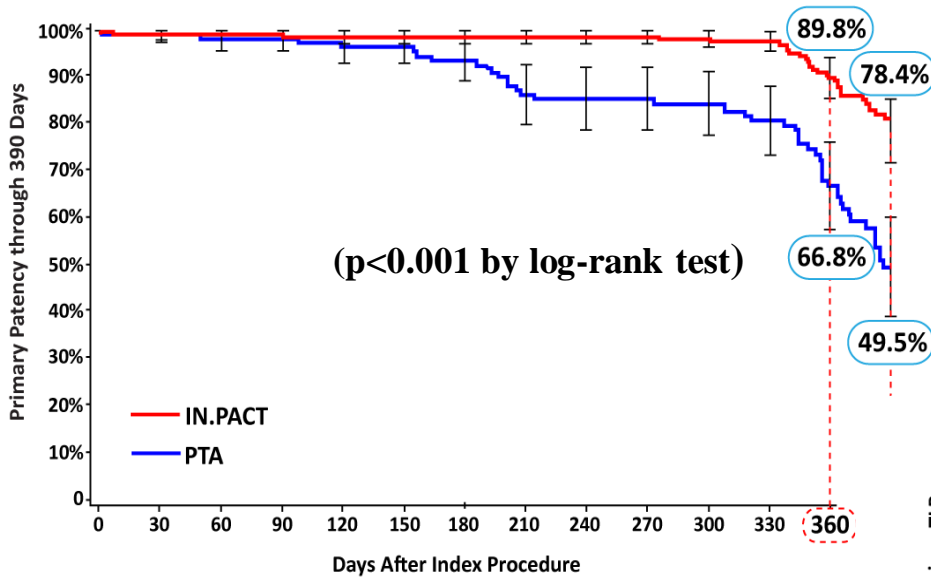
CAUTION: Investigational Device- Limited by Federal (USA) Law to Investigational Use





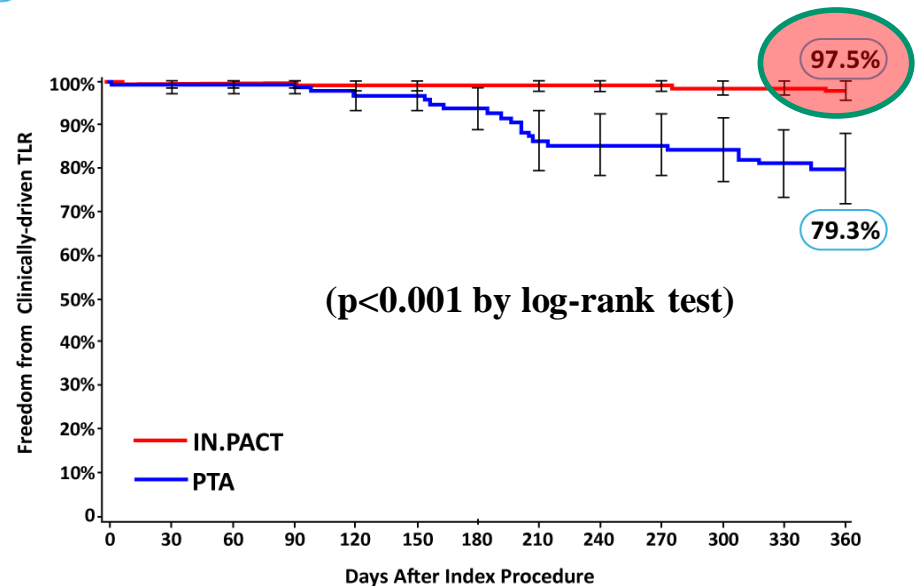
IN.PACT SFA – 1 yr

- IN.PACT admiral vs POBA
- 331 patients randomized 2:1
- Rutherford cat: 2-4
- Single de novo lesions > 70%
- 4-18 cm length (occlusions < 10 cm)
- SFA or prox. PA
- Mean lesion length: 8.9 cm



Freedom from binary restenosis

Freedom from CD-TLR

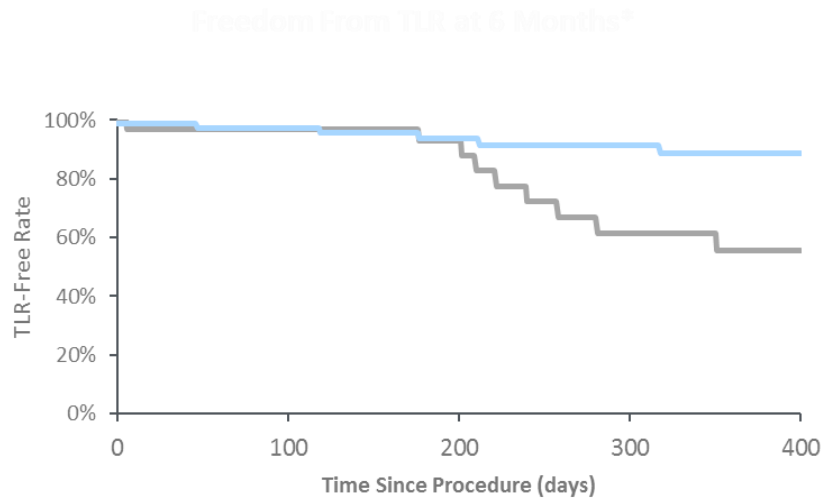




Preliminary results with other DCB

Ranger (Boston Scientific)

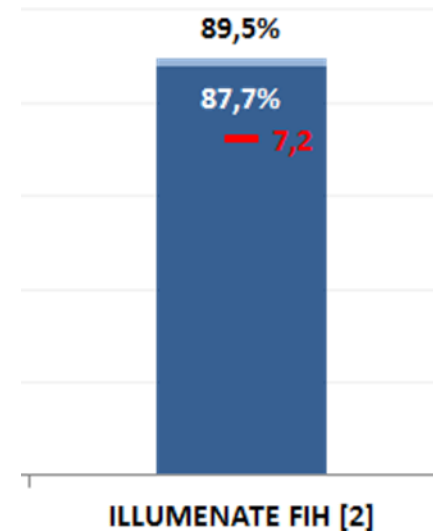
RCT: DCB vs POBA 2:1
105 Patients



Freedom from TLR

Illuminate (Spectranetics)

First in men study
50 DCB – 1 yr

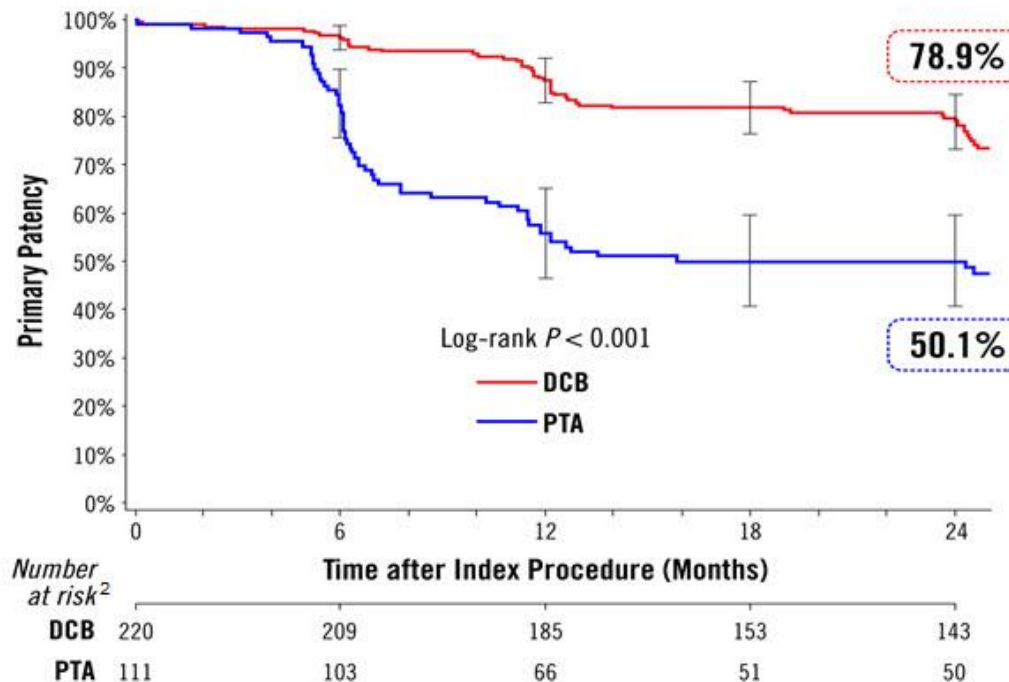


Primary patency



In.Pact SFA – 2 year results

Primary Patency¹ Results through 2 Years



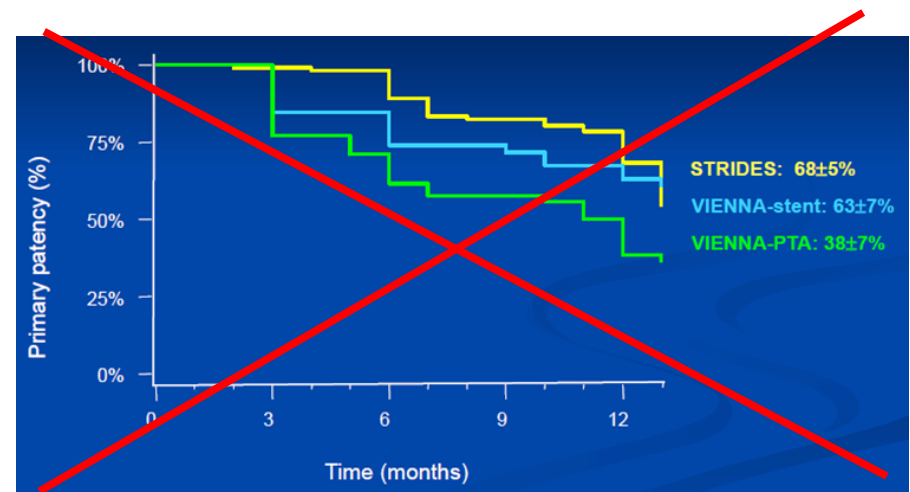
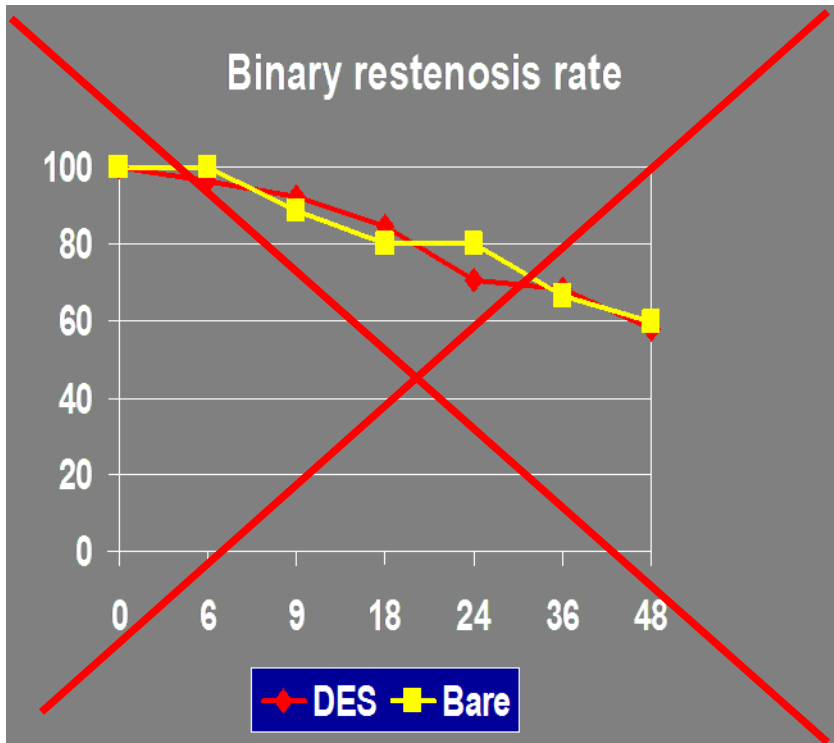
CD-TLR: 9.1% vs 28.3%



Drug eluting stents

Sirocco –trial (Cordis)
Sirolimus-eluting Smart
RCT

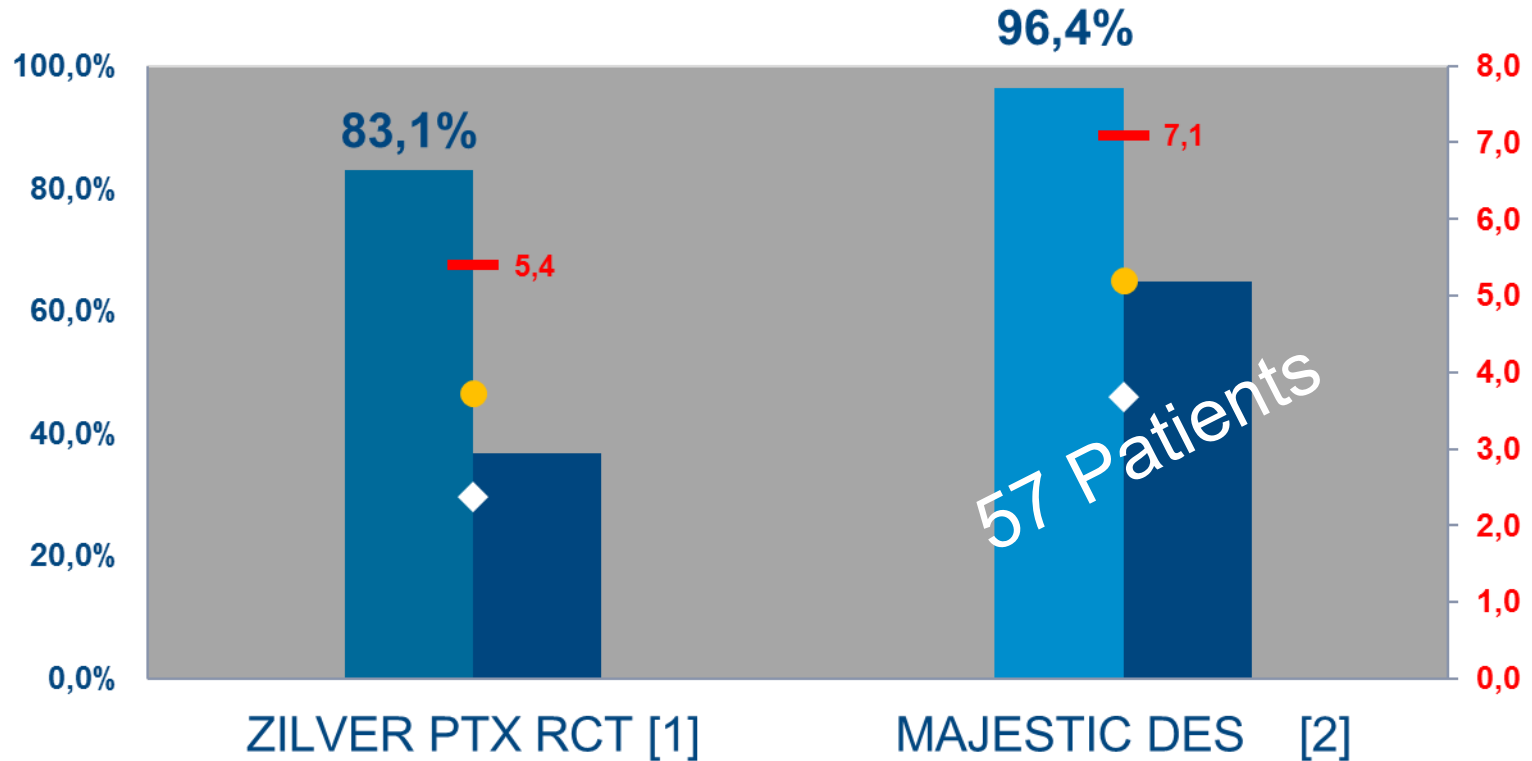
Strides (Abbott)
Everolimus-eluting Dynalink
Historical controls





Drug-eluting stents

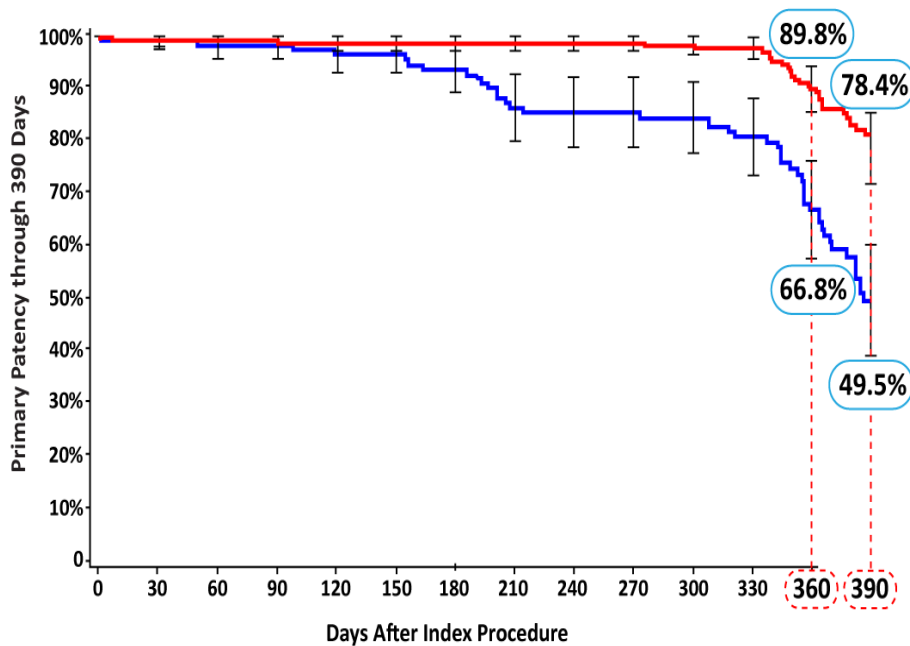
■ 12M Patency (KM 360 days) ■ Ca++ (%) ● RC≥3 (%) CTO (%) — L length (cm)





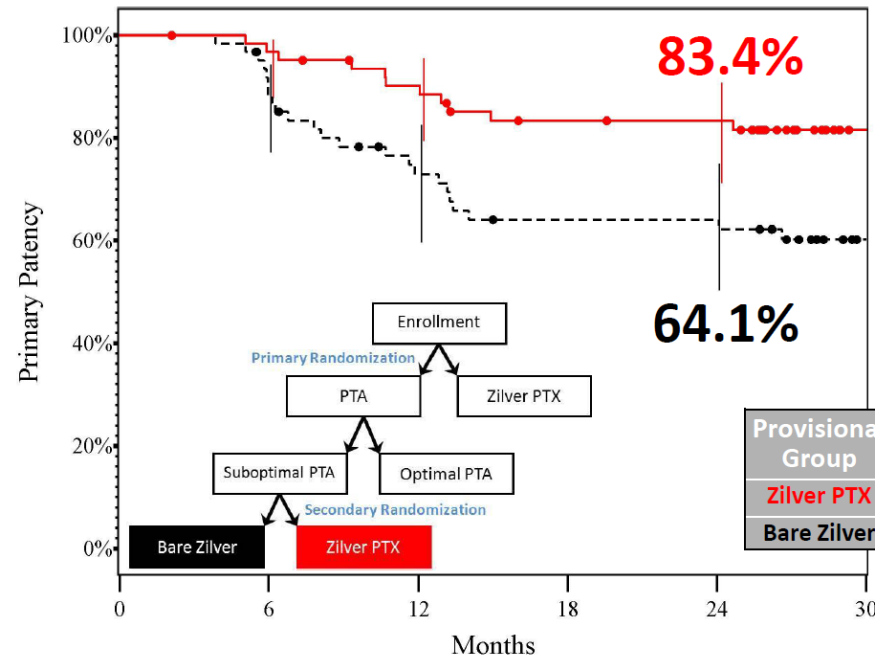
IN.PACT SFA vs Zilver PTX study: Primary patency

IN.PACT SFA



Mean Lesion length: 8,9 cm

Zilver PTX study

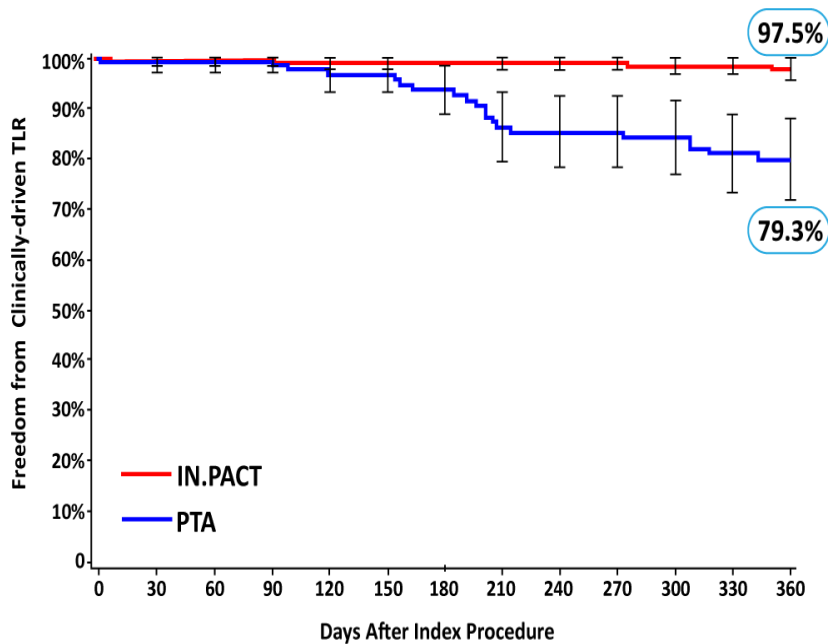


Mean Lesion length: 6,6 cm



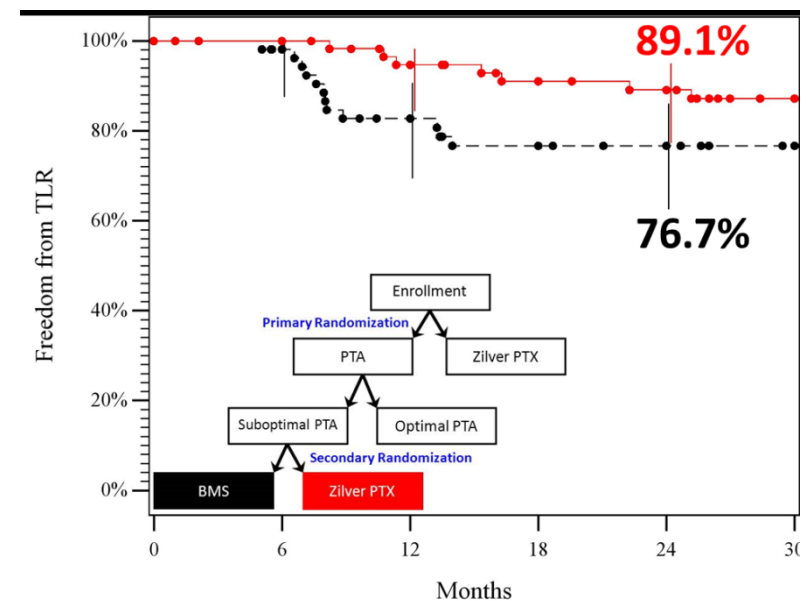
IN.PACT SFA vs Zilver PTX study: Freedom from CD-TLR

IN.PACT SFA



Mean Lesion length: 8,9 cm

Zilver PTX study



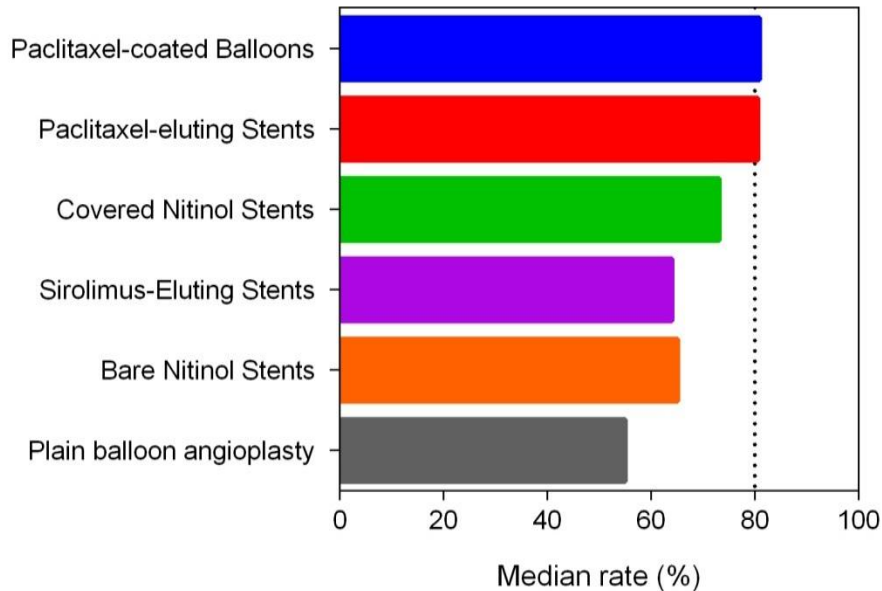
Mean Lesion length: 6,6 cm



1-year SFA results (%)

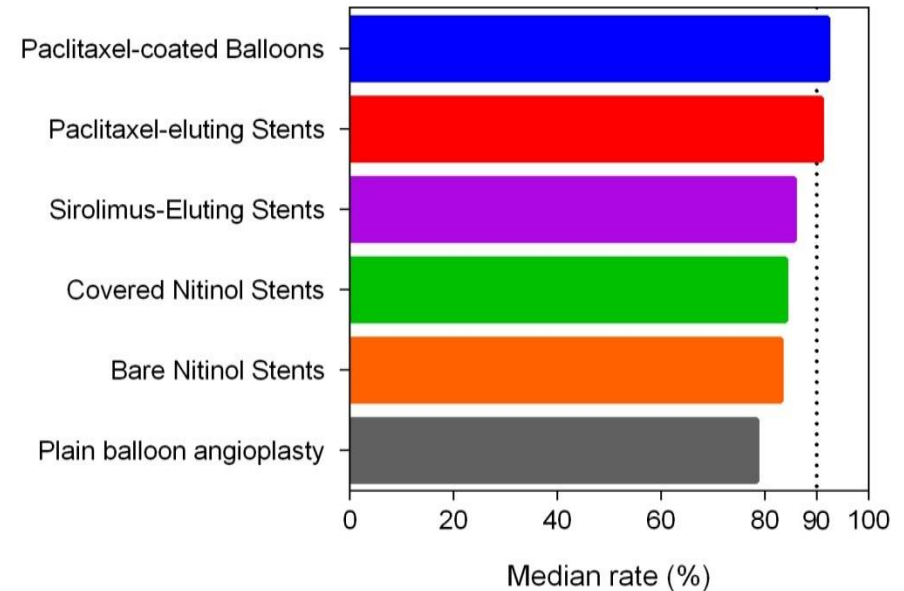
Freedom from Restenosis at 1 Year

Freedom from Restenosis @ 1 year



Freedom from TLR at 1 Year

Freedom from TLR @ 1 year



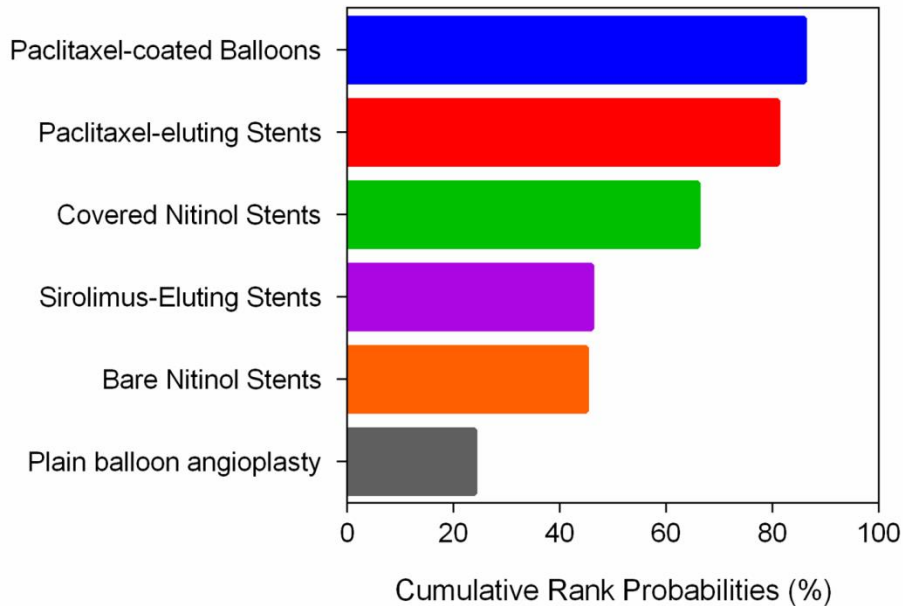
Baseline risk adjusted random effects mixed treatment comparison



Long-term: Probability best

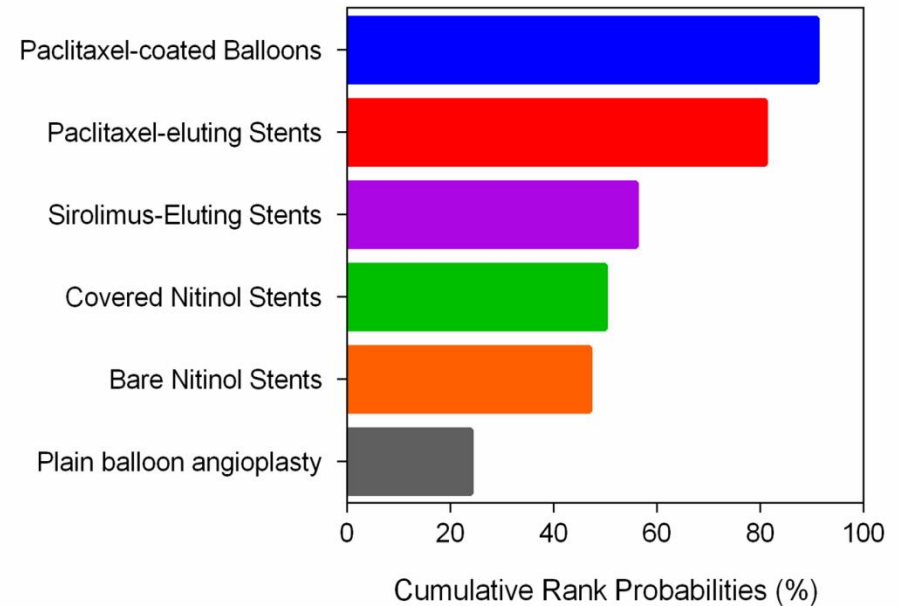
Freedom from Restenosis

Vascular Restenosis



Freedom from TLR

Freedom from Target Lesion Revascularization

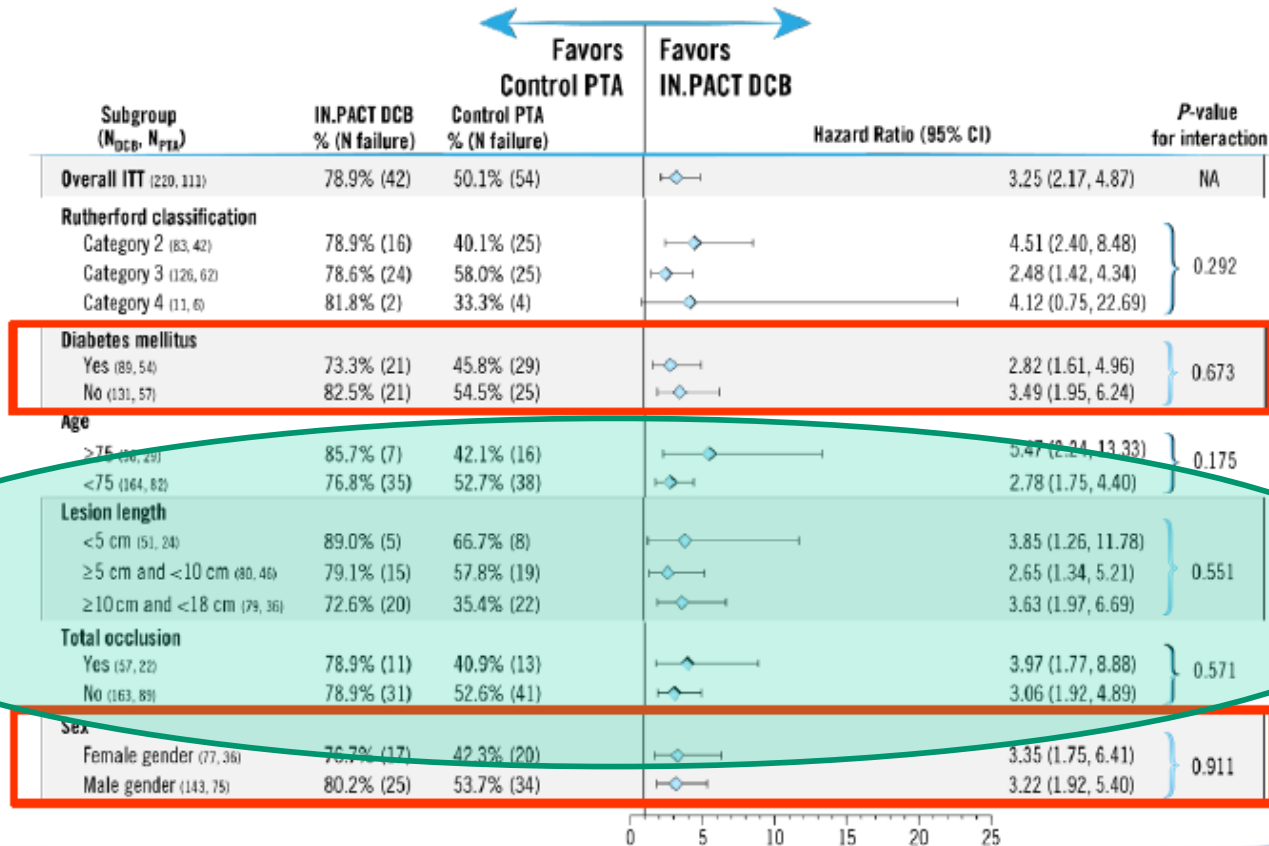


Baseline risk adjusted random effects mixed treatment comparison



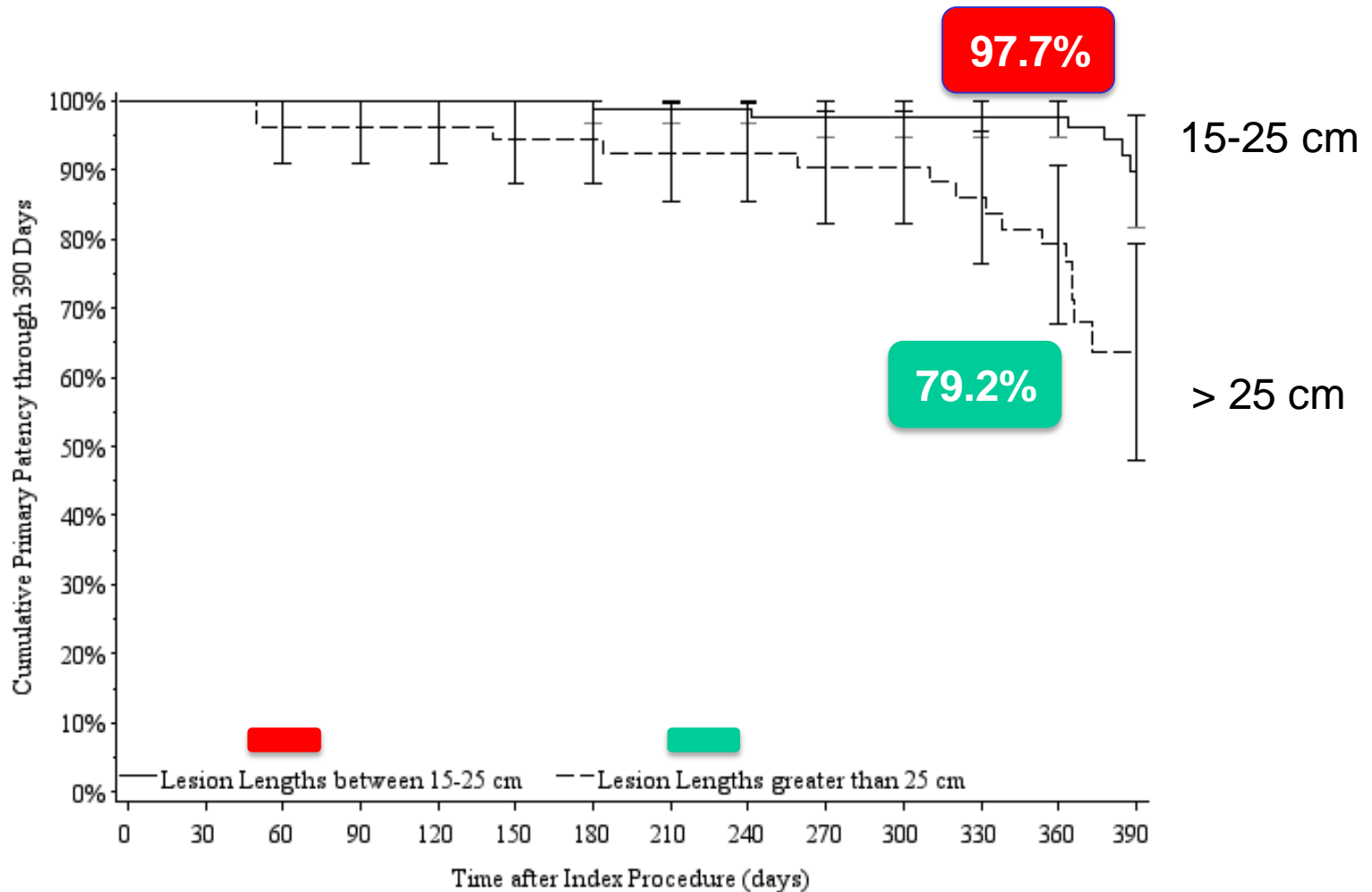
In.Pact SFA subgroups

IN.PACT SFA Trial Subgroups Primary Patency Outcomes Through 2 Years





IN.PACT Global Long Lesions

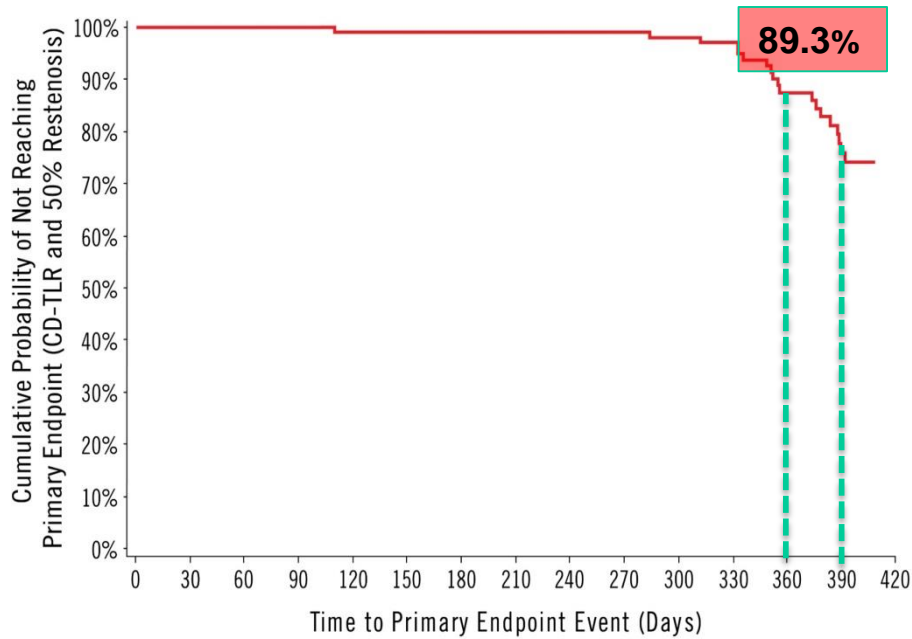




IN.PACT Global LL vs Zilver PTX study: Primary patency

IN.PACT Global

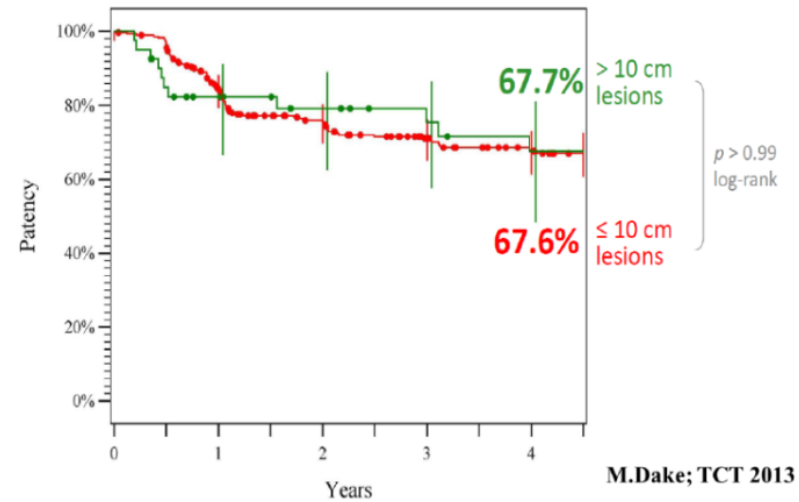
Primary Patency



Lesion length > 15 cm

Zilver study

4-Year Primary Patency in > 10 cm Lesions



Lesion length > 10 cm

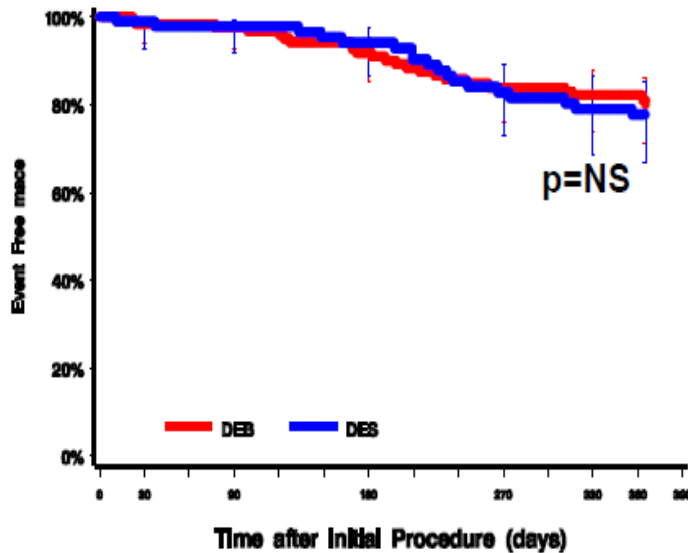


DEB vs. DES in long SFA lesions

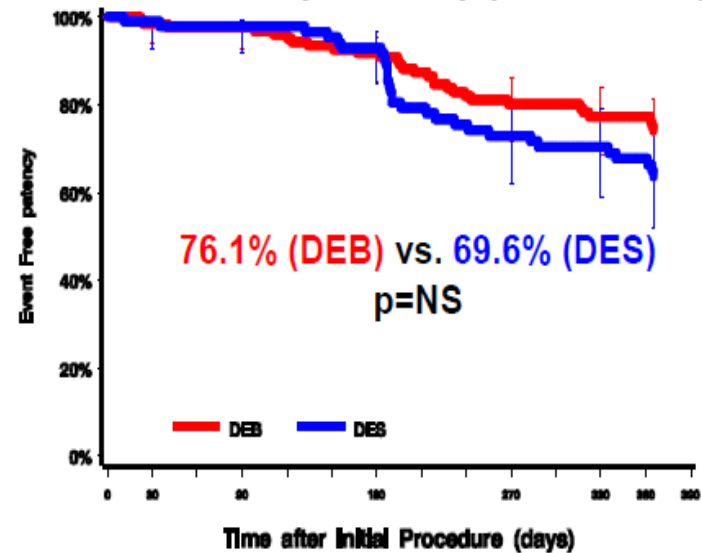
228-Patients retrospective, propensity score analysis

Lesions ~19 cm

12-month freedom from death and TLR



12-month freedom from loss of Primary Patency (PSVR < 2.4)



IN.PACT[®] Global CTO Imaging Cohort

Lesions (N)	128
Lesion type	
- de novo	92.2% (118/128)
- restenosis	7.8% (10/128)
- ISR	0%
Lesion Length (mean ±SD)	22.90± 9.75 cm
Occluded Lesion Length	11.97± 8.11
Calcification	71.2%% (89/125)
RVD (mm ±SD)	5.056 ± 0.657
Diameter Stenosis (% ±SD)	100%
Dissections: None	32.8% (42/128)
A-C	43.8% (56/128)
D-F	23.4% (30/128)

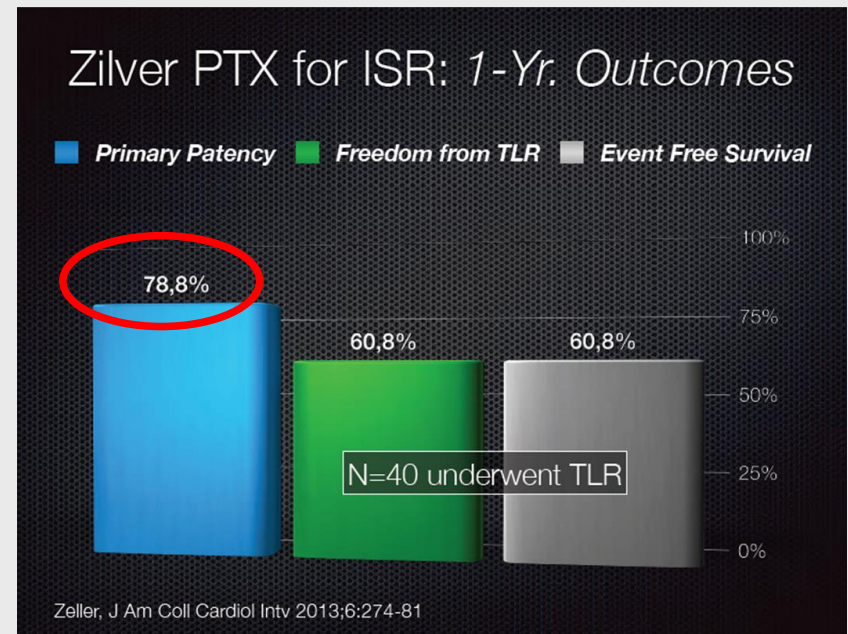
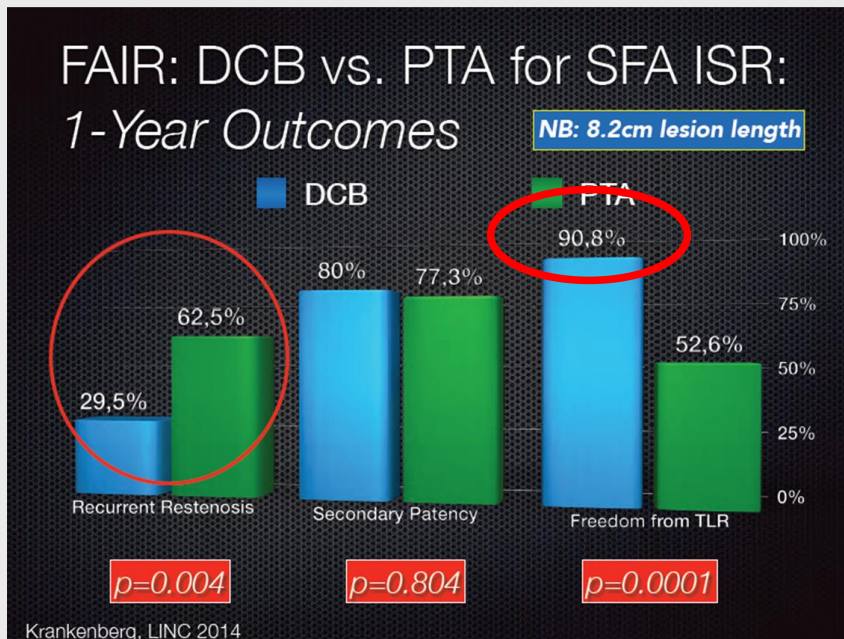
Procedure Success	100% (125/125)
Clinical Success	99.2% (124/125)
Pre-dilatation	94.4% (119/126)
Post-dilatation	50% (62/126)
Provisional Stent	46.8% (59/126)

**Primary patency rate at 12 Mo
= 84.4% (95 cases)**



DEB vs DES for In stent restenosis

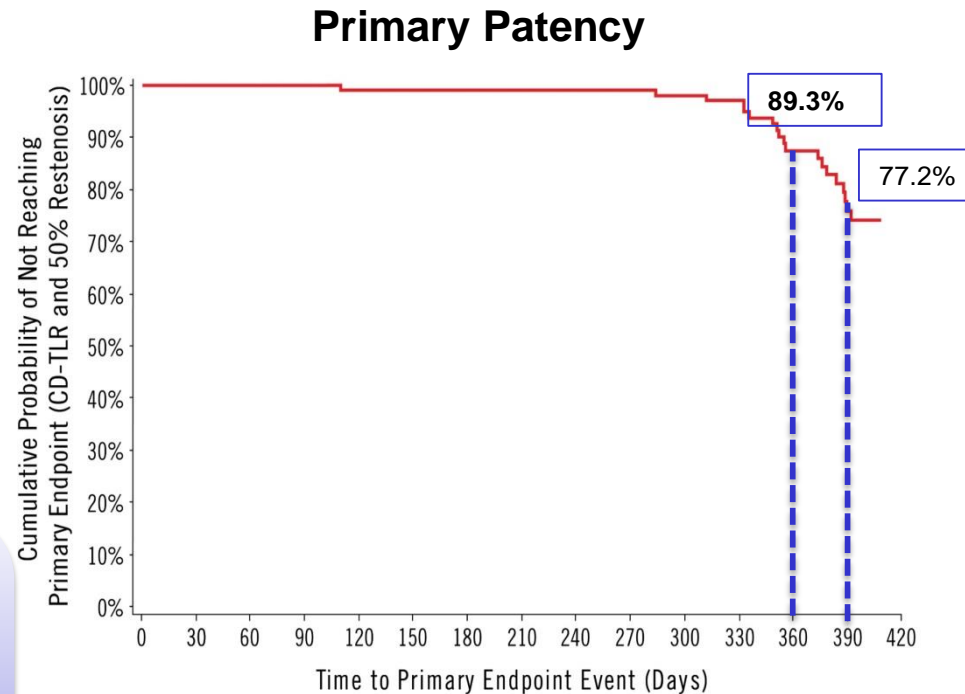
- Freedom from TLR superior with DCB over DES



TASC C & D - SFA- Long Study at 1 Yr

- Independent, prospective, multicentre single arm study
- 105 pts
- **Lesion length 251.71 ±78.89 mm.**
 - De novo 94.6%
 - CTO 49.5%
 - Provisional stenting 10.5%

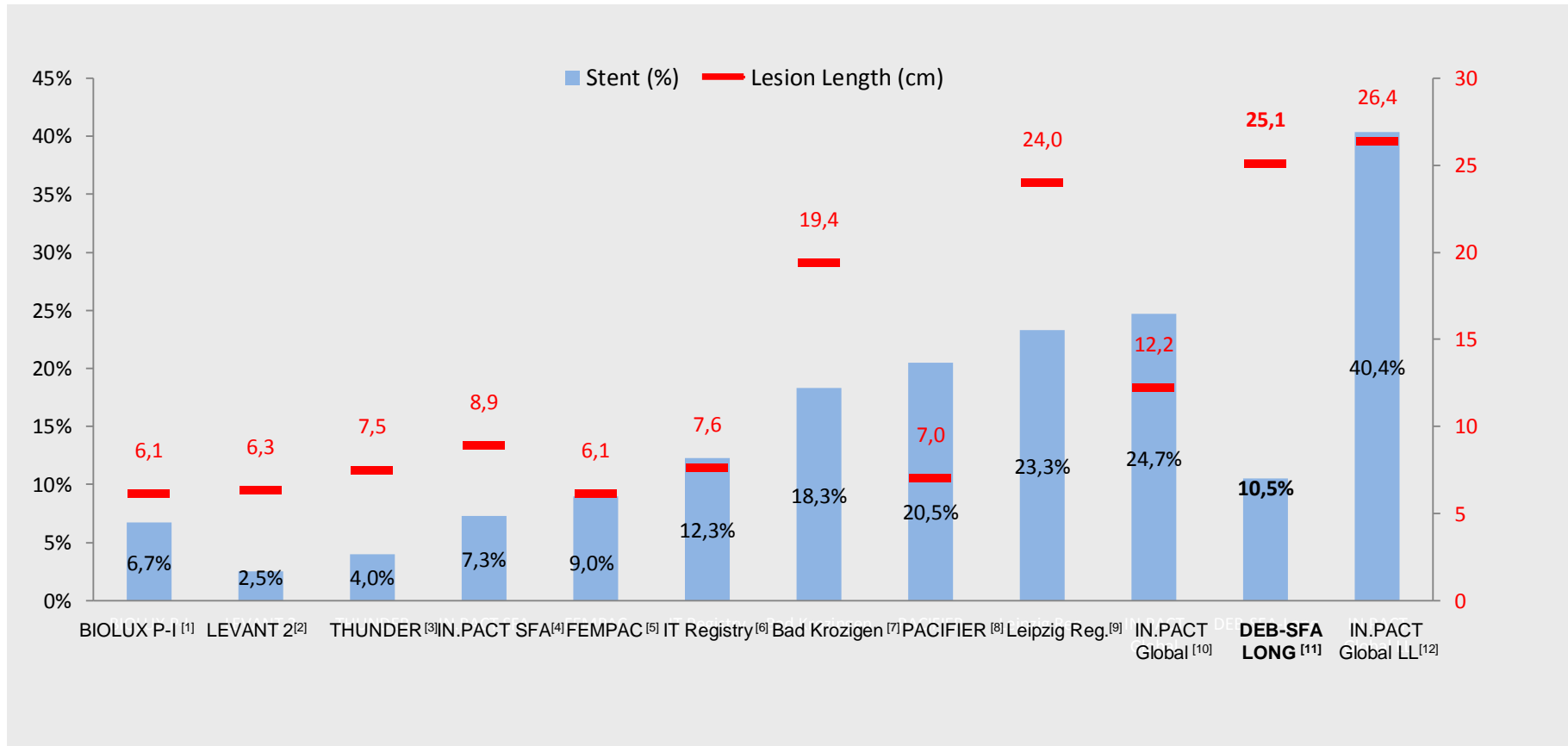
- **Primary patency at 360 days 89.3%**
- **Freedom from CD-TLR 96%**
- MAE composite at 12mo 6.9%
- Thrombosis: 1% (1 event)





DCB and Provisional Stenting

Provisional Stent Rates in DCB Trials Trend with Lesion Length

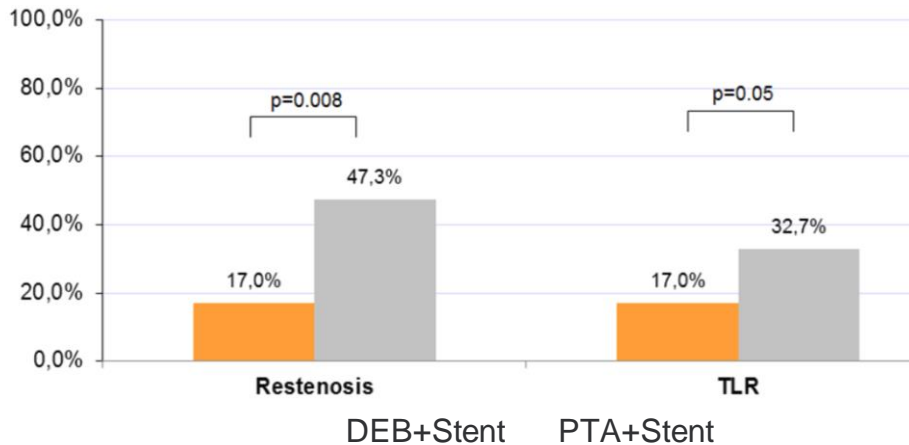


[1] J Endovasc Ther. 2015 Feb;22(1):14-21; [2] N Engl J Med. 2015 Jul 9;373(2):145-53; [3] N Engl J Med. 2008 Feb 14;358(7):689-99; [4] Circulation. 2015 Feb 3;131(5):495-502; [5] Circulation. 2008 Sep 23;118(13):1358-65; [6] JACC Cardiovasc Interv. 2012 Mar;5(3):331-8; [7] Zeller T CX 2013 oral presentation; [8]. Circ Cardiovasc Interv. 2012 Dec;5(6):831-40; [9] Schmidt A LINC 2013 oral presentation; [10] Ansel G TCT 2014 oral presentation; [11] Micari A EuroPCR 2015 oral presentation; [12] Scheinert D EuroPCR 2015 oral presentation



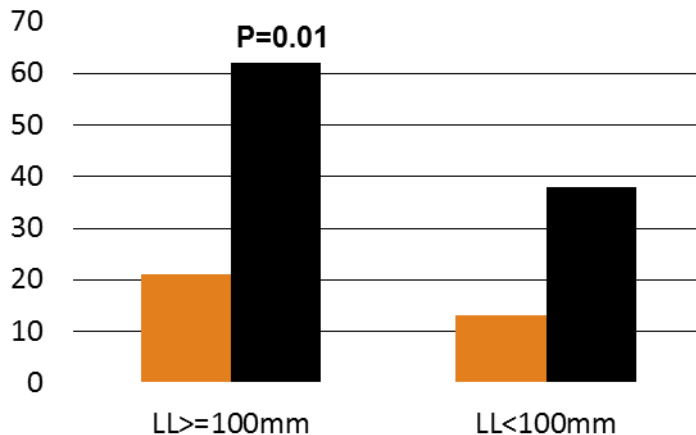
DEB and STENTS: DEBATE SFA

12-month Restenosis and TLR (per lesion)

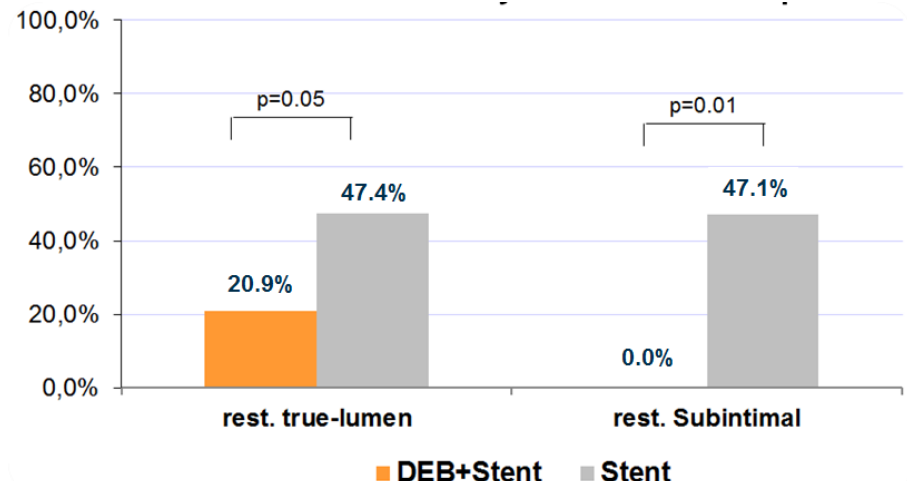


- DEB + stent vs PTA + stent
- Single centre RCT (Liistro F.)
- 110 patients randomized 1:1
- Rutherford cat: 3-6
- SFA or prox. PA
- Concomitant PTA BTK > 50%
- Mean lesion length: 9.5 cm

Restenosis per lesion length



Restenosis per Revasc Technique





Per protocol 12 mths outcome – Stent vs no stent

Primary Efficacy, Primary Patency ^[1]	IN.PACT DCB	PTA	Difference [95% CI] ^[2]	p ^[2]
Non-stented ITT	82.9%	52.2%	29.0% [16.2%, 41.8%]	<0.001
All ITT	82.2%	52.4%	26.2% [15.1%, 37.3%]	<0.001
Primary Safety Composite ^[3]	IN.PACT DCB	PTA	Difference [97.5% CI] ^[4] Difference [95% CI]	p
Non-stented ITT	95.8%	77.7%	12.2% [1.2%, ∞] ^[4, 5] 18.2% [9.3%, 27.0%] ^[4]	NA <0.001 ^[6]
All ITT	95.7%	76.6%	19.0% [11.5%, ∞] ^[4] 19.0% [10.5%, 27.5%]	NA <0.001 ^[6]

1.

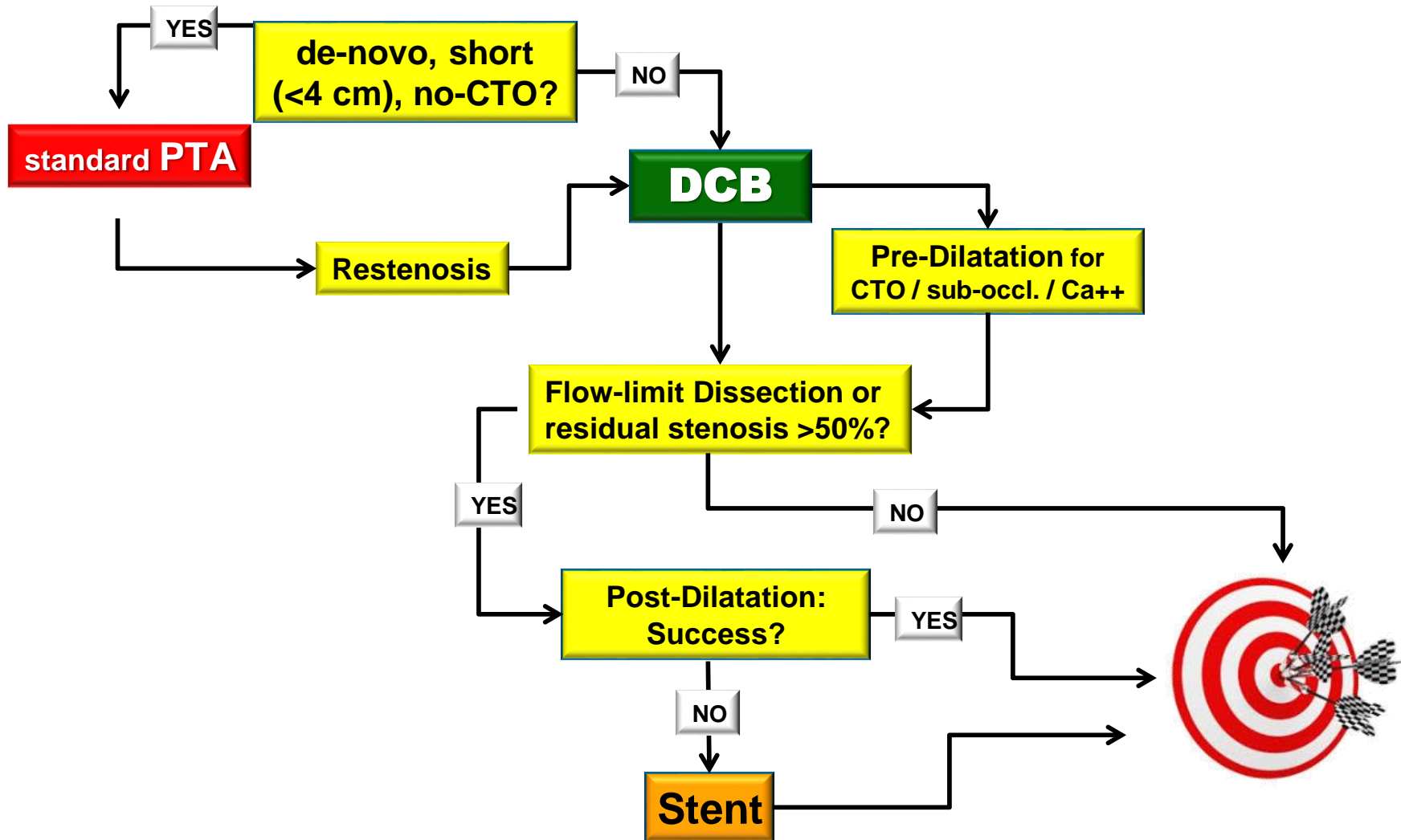
2. Primary patency comparative statistics imputed missing data and non-stented ITT were adjusted for Propensity Score

3. Primary safety composite is defined as freedom from device and procedure-related 30-day death and freedom from target limb major amputation and clinically-driven TVR through 12 months

4. Non-inferiority margin –10% 5. Non-stented ITT cohort difference adjusted for Propensity Score 6. p-value associated with sequential superiority test



Algorithm for treatment of SFA-lesions





Conclusions

- DCB results are at least equivalent to DES results, even in complex lesions
- DCB does not leave a metallic implant, causing continuous harm to the vessel wall, and hampering later treatment
- If needed DCB can be combined with a bare metal stent without influencing the results
- DCB with provisional stenting is more cost-effective than routine DES implantation



DCB always wins

