Lower extremity interventions: Is there a "best" strategy?

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

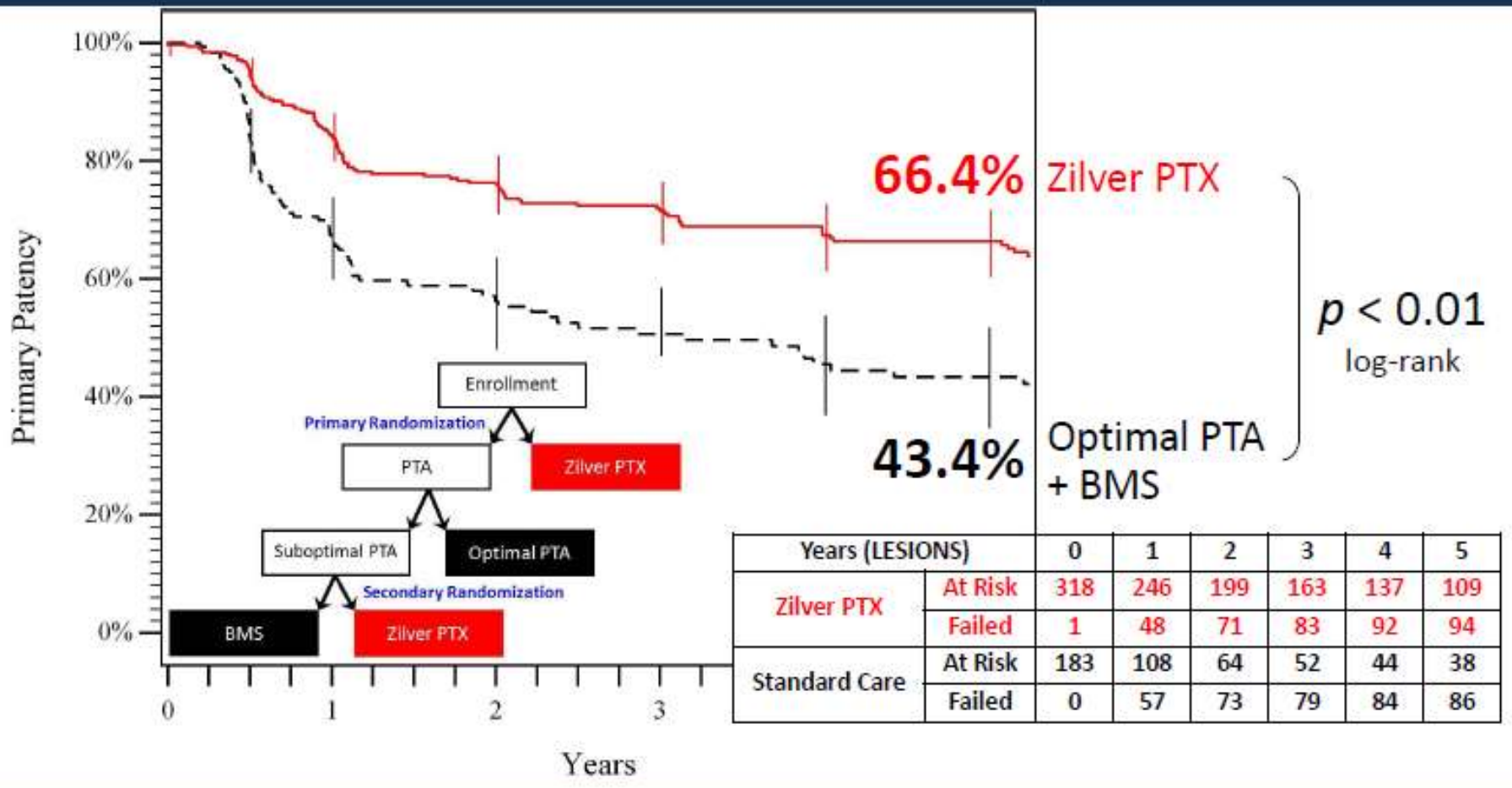
Affiliation/Financial Relationship	Company
• Grant/Research Support	• Abbott, Covidien/Medtronic
• Consulting (non-compensated)	• Covidien/Medtronic, Boston Scientific, Abbott
• Major Stock Shareholder/Equity	• Arsenal, Primacea, TissueGen, CV Ingenuity, Spirox, Scion Cardiovascular, Syntervention, Essential Medical
• Royalty Income	• None
• Ownership/Founder	• Innovation Vascular Partners, Consulting
• Intellectual Property Rights	• None
• Other Financial Benefit	• None

ZilverPTX

		PTA	Zilver PTX	*P*-value
Lesions		251	247	
Normal-to-normal lesion length (mm)		63 ± 41	66 ± 39	0.35
Stenosed lesion length (mm)[1,2]		53 ± 40	54 ± 41	0.76
Diameter stenosis (%)[1]		78 ± 17	80 ± 17	0.44
Total occlusions		25%	30%	0.20
De novo lesions		94%	95%	0.69
Lesion calcification[1]	None	5%	2%	< 0.01*
	Little	38%	26%	
	Moderate	22%	35%	
	Severe	35%	37%	

[1] Angiographic core lab assessment
[2] Region with > 20% diameter stenosis
*Statistically significant

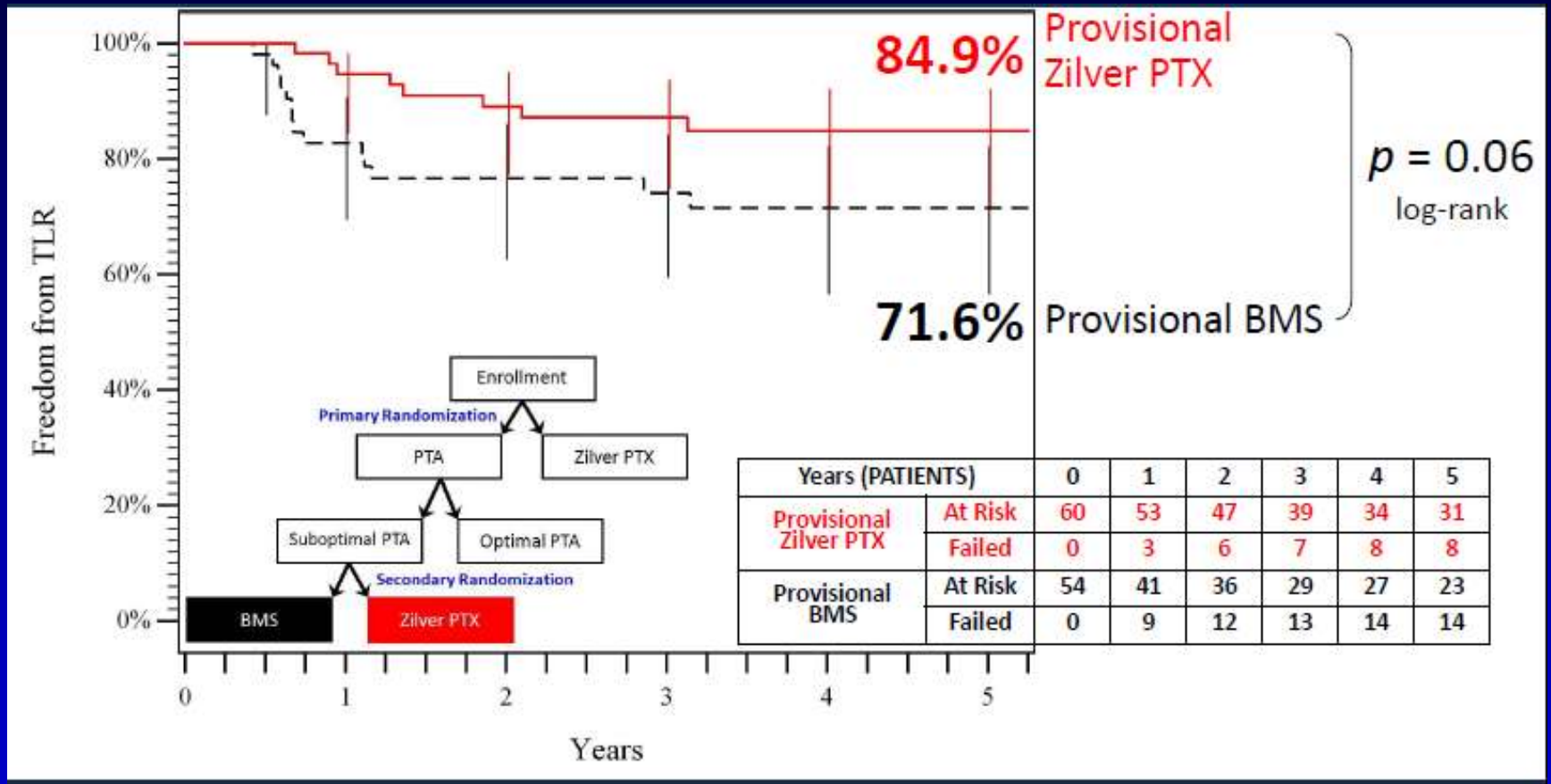
5-Year Primary Patency (PSVR < 2.0)
Zilver PTX vs. Standard Care



Years (LESIONS)		0	1	2	3	4	5
Zilver PTX	At Risk	318	246	199	163	137	109
	Failed	1	48	71	83	92	94
Standard Care	At Risk	183	108	64	52	44	38
	Failed	0	57	73	79	84	86

At 5 years, Zilver PTX demonstrates a 41% reduction in restenosis compared to standard care

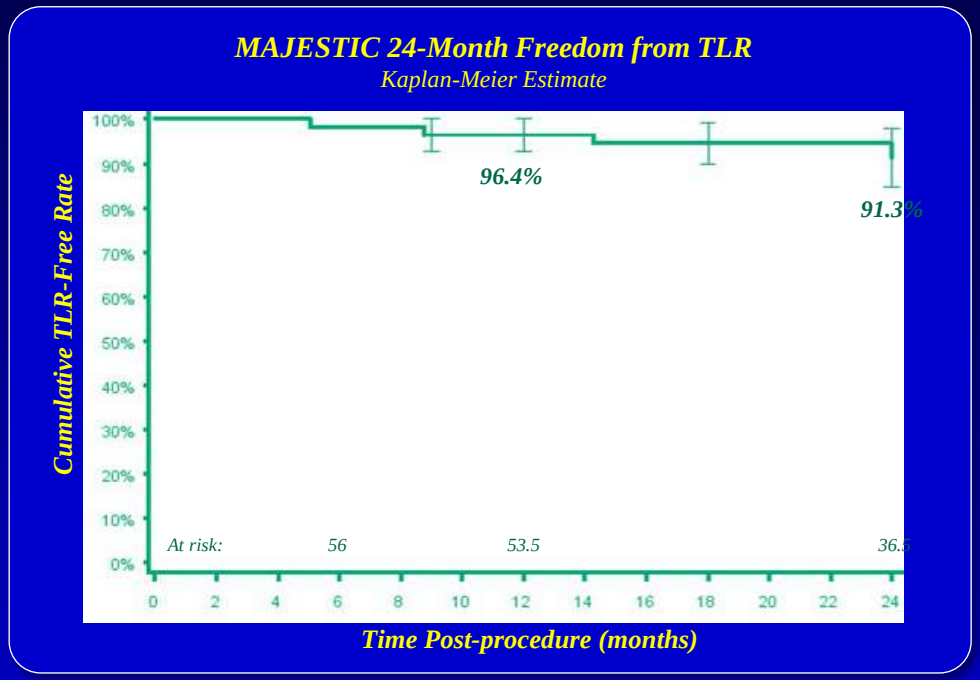
5-Year Freedom from TLR
Zilver PTX vs. Standard Care



Years (PATIENTS)		0	1	2	3	4	5
Provisional Zilver PTX	At Risk	60	53	47	39	34	31
	Failed	0	3	6	7	8	8
Provisional BMS	At Risk	54	41	36	29	27	23
	Failed	0	9	12	13	14	14

At 5 years, Zilver PTX demonstrates a 47% reduction in reintervention compared to BMS

MAJESTIC
24 month outcomes



24-Month Safety Profile

- 92.5% (49/53) TLR free rate
  - Only 2 additional TLRs were reported between one and two years
- No target limb major amputations
- 1 death at >365 days post-procedure, unrelated

Stent Integrity

- No stent fractures

	12 Months	24 Months
Primary Patency[a]	**96.4%**	**78.2%**
Assisted Primary Patency[b]	**98.2%**	**84.7%**

Note: Kaplan-Meier Estimates.
[a]Duplex ultrasound peak systolic velocity ratio ≤2.5 and absence of TLR or bypass.
[b]No TLR and those with TLR not for complete occlusion or bypass who were free of restenosis at 24 months.

Müller-Hülsbeck, S. CIRSE 2016.

TLR, target lesion revascularization.

MAJESTIC 3 year

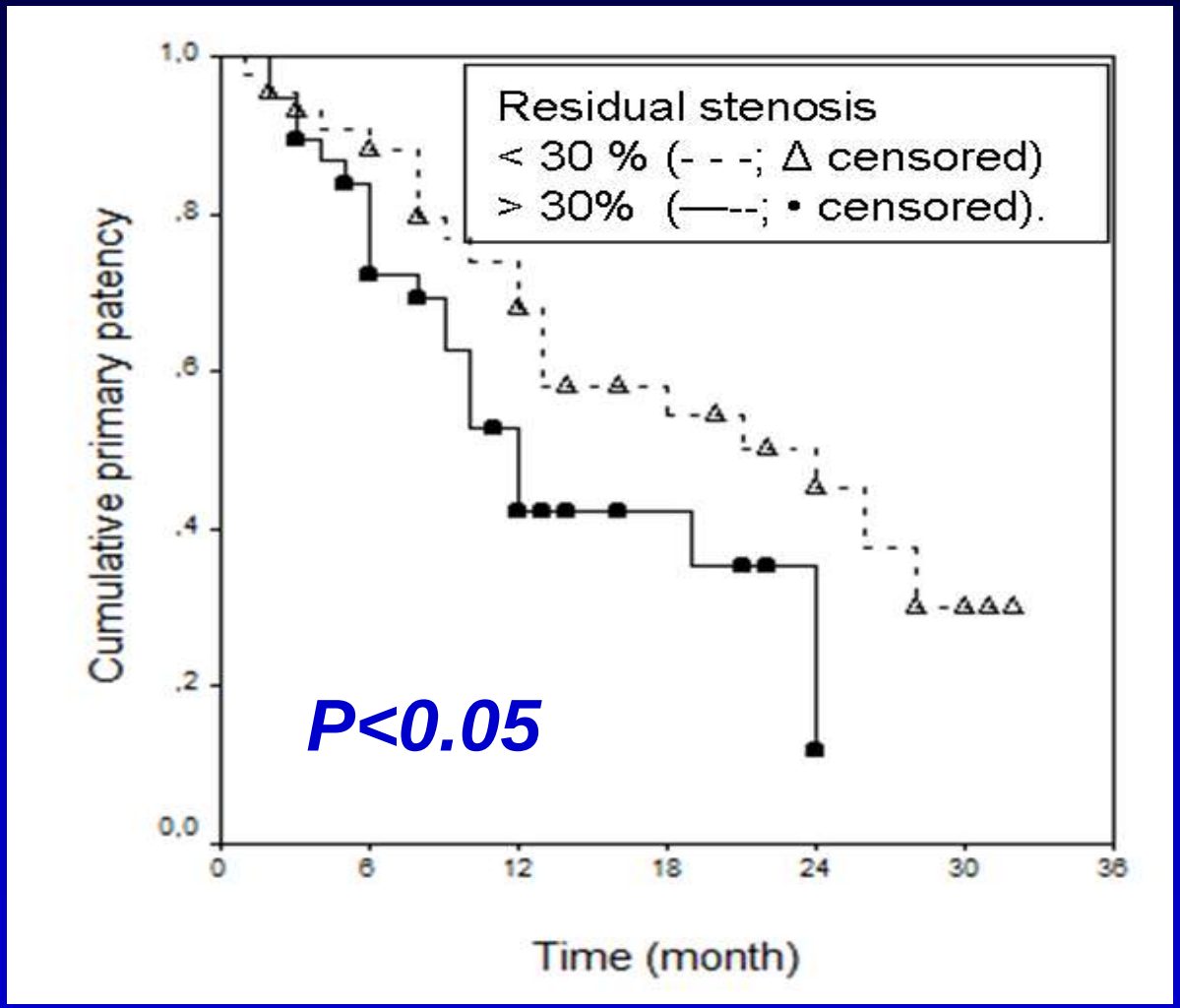
- TLR 85.3% at 36 months
- No stent fracture
- Primary patency not reported at 36 months

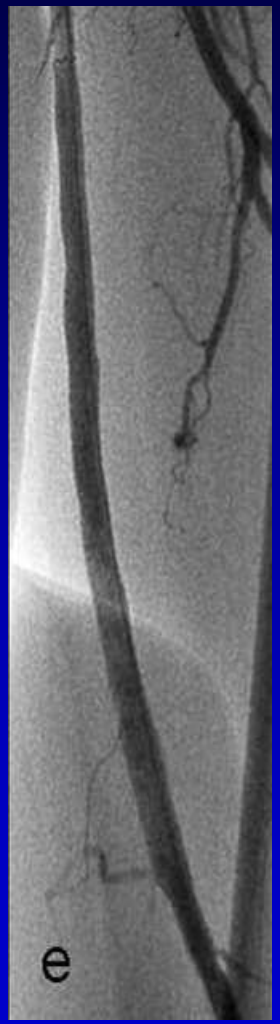
Muller-Hulsbeck et al CVIR Dec 2017

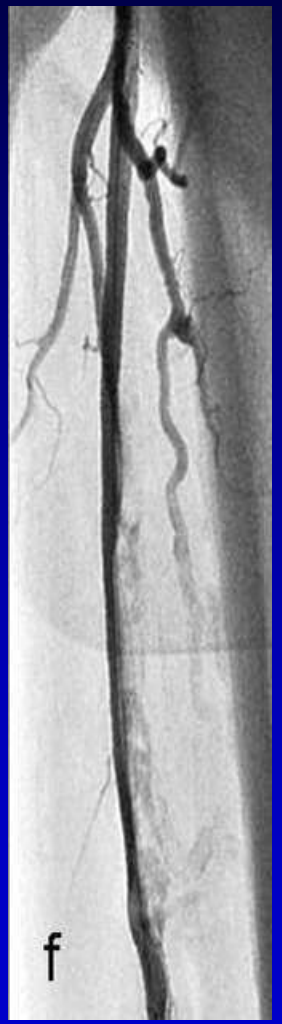
NiTiDES

- NiTiDES (Alvimedica) Illumina study
- Completed enrollment 100 patients 2017
- Results pending

Impaired primary patency due to residual stenosis

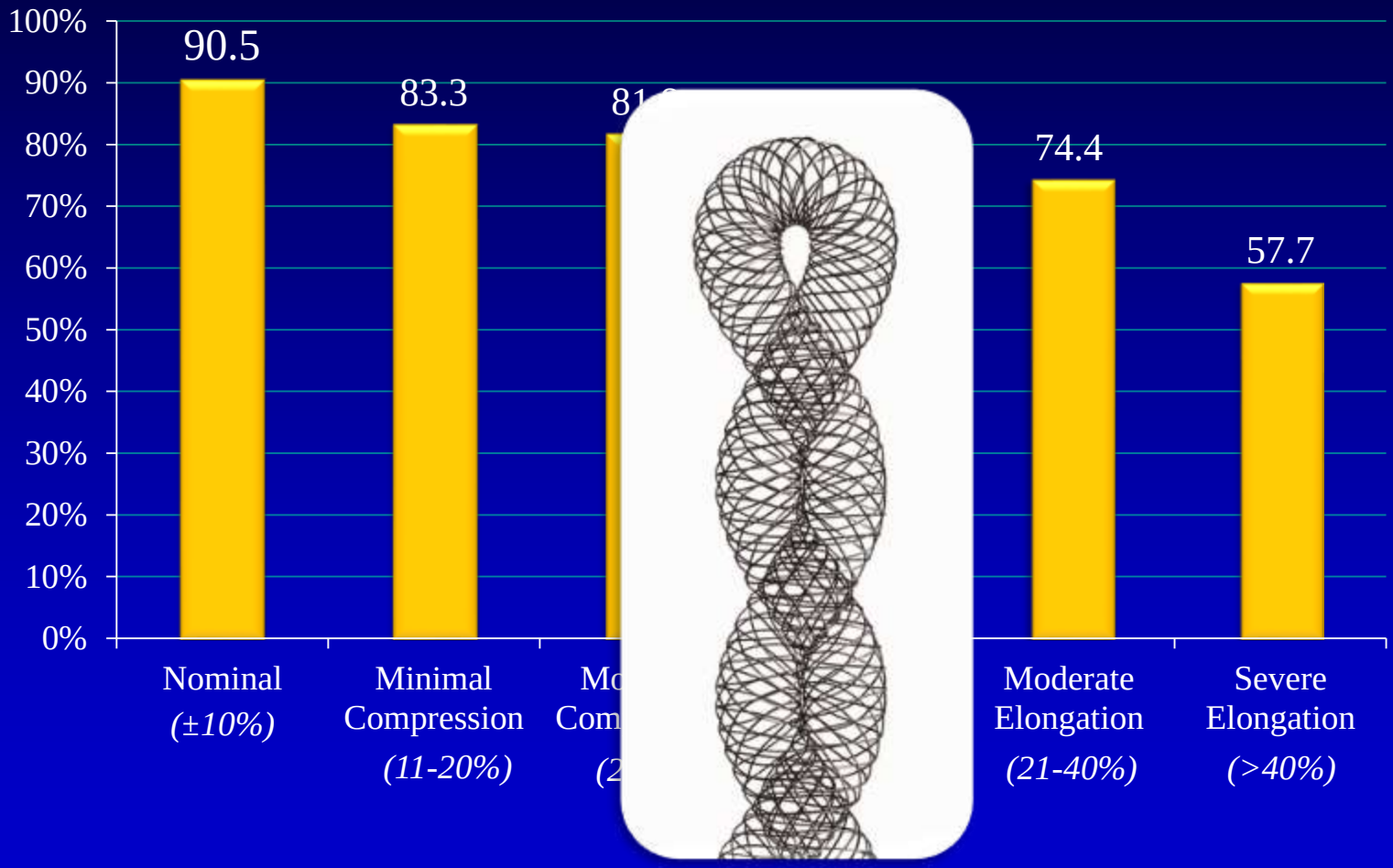




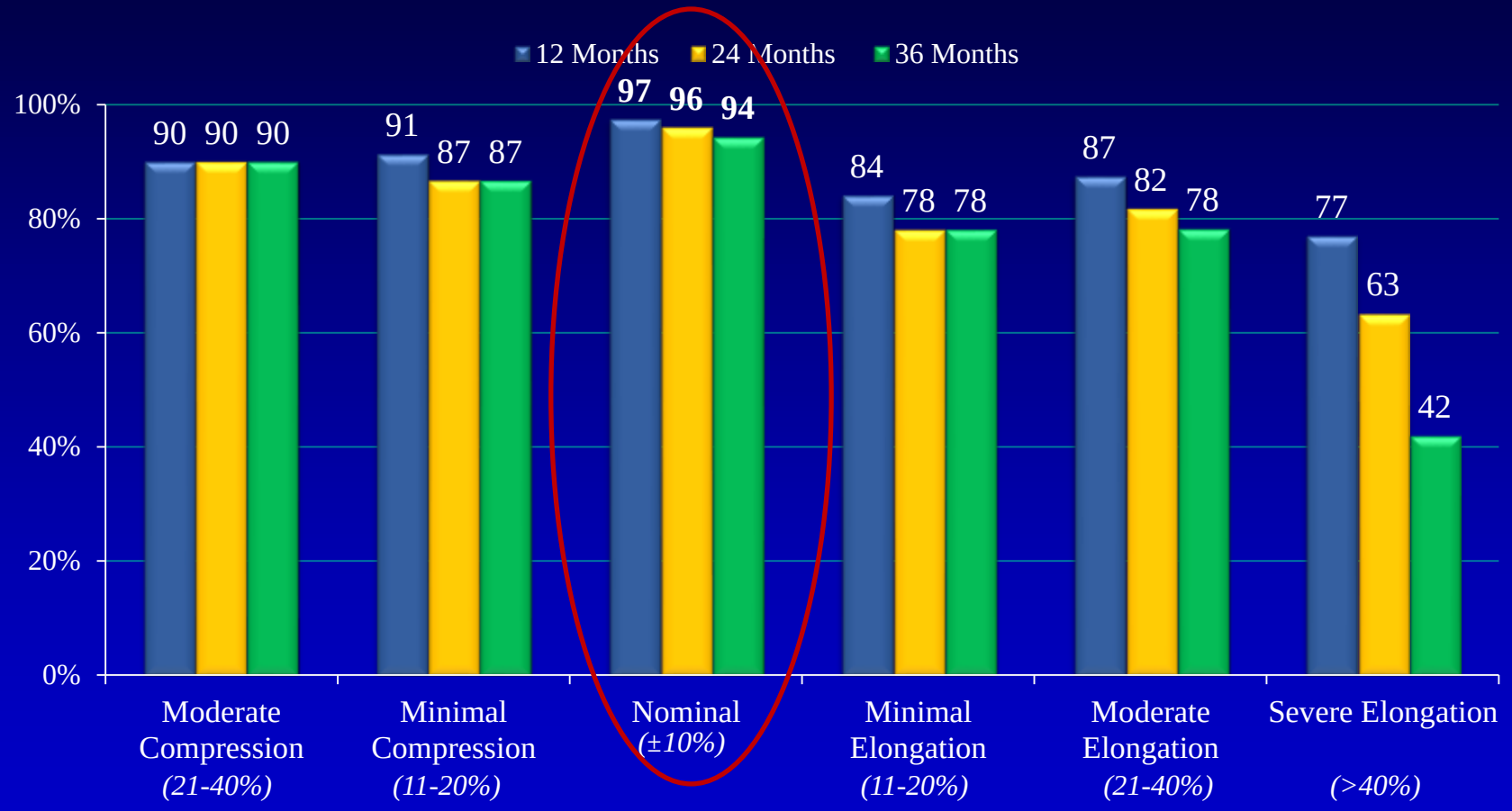


Y Bausback et al, J Endovasc Ther 2011

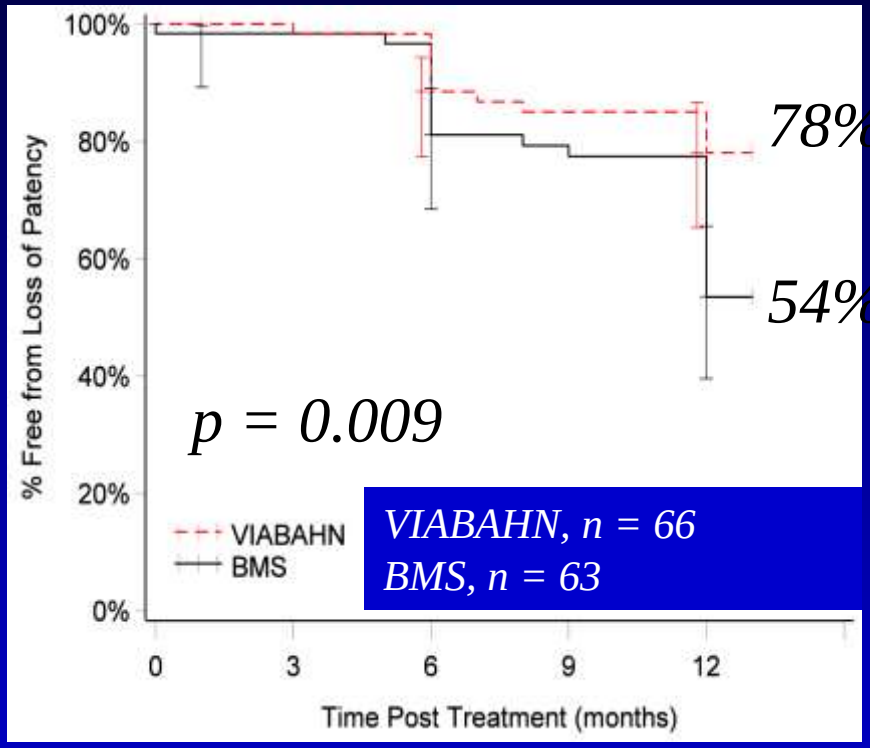
SUBERB
Deployment on 12-Month Patency

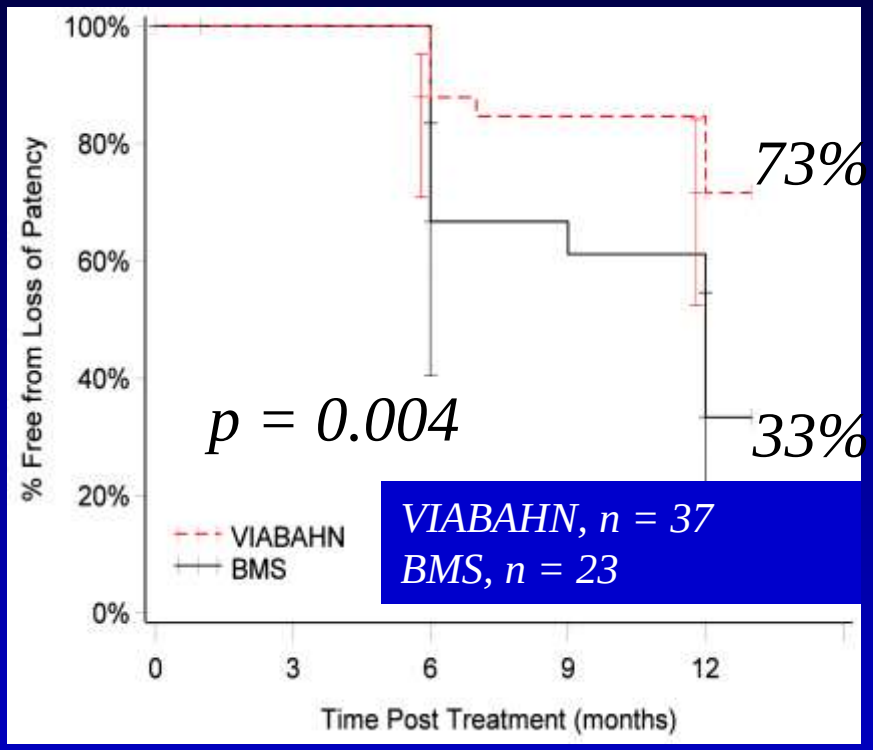


Deployment Technique Impact on Freedom From TLR



VIASTAR Trial: 1-Year Primary Patency Stratified to Lesion Length





Patency improvements with VIABAHN amplified in lesions ≥20 cm.

Lammer, et al. JACC. 2013.

DCB Considerations

Potential advantages:

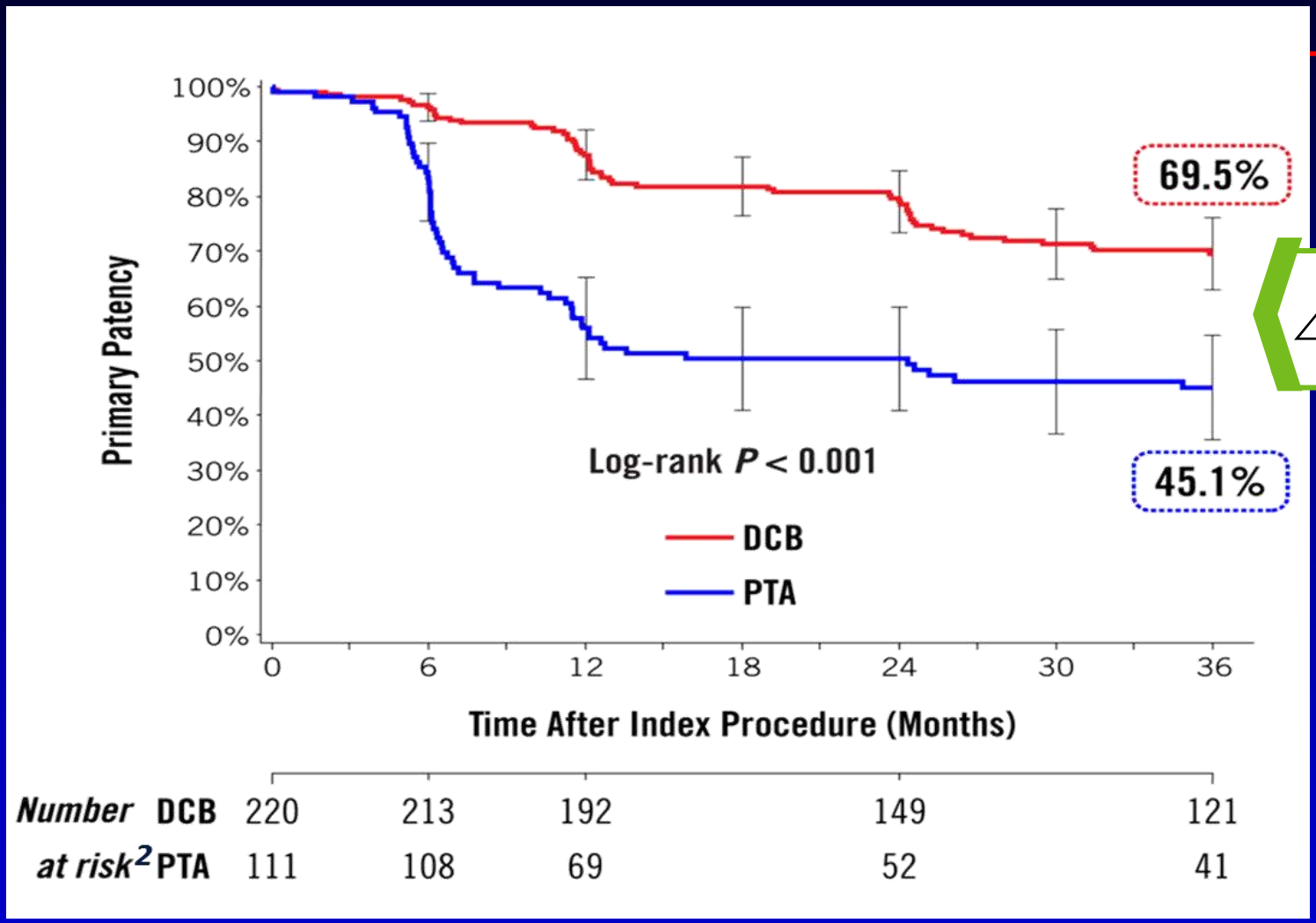
- May be used in lesions where drug-eluting stents cannot be delivered or do not perform well:
  - Torturous or small vessels
  - Bifurcated lesions/avoid obstructing side branches
- Leave no implant
- Reduced duration of antiplatelet therapy

Potential limitations:

- Dosing control (drug transfer and retention)
- Severe calcification
- Need for bail-out stenting
- Cost considerations

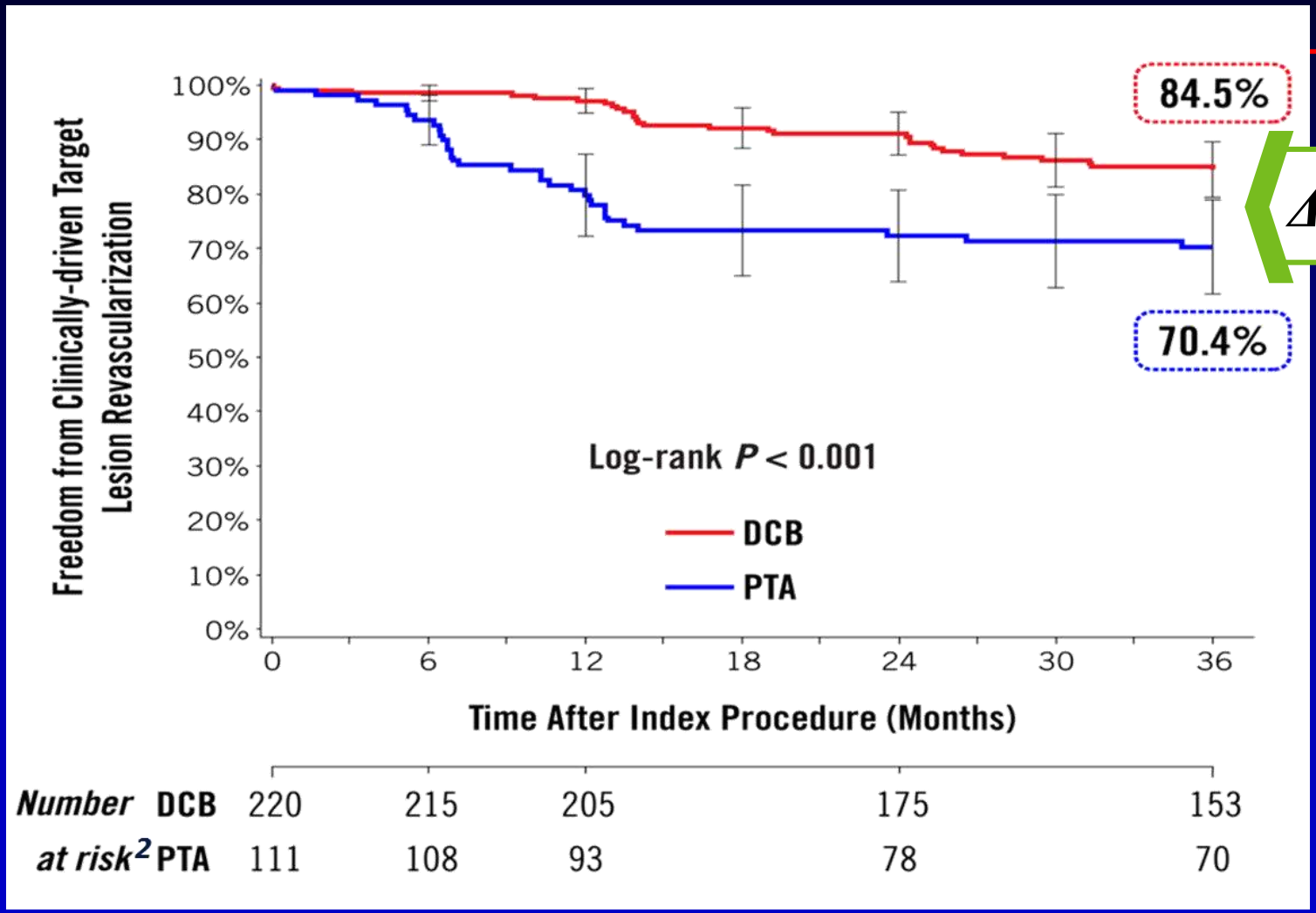
Loh JP, et al. EuroIntervention. 2013;9:979-88.
Krokidis M, et al. Cardiovasc Intervent Radiol. 2013;36:281-91.

IN.PACT SFA Trial:
Primary Patency[1] through 3 Years



1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 36 months (adjudicated by a Clinical Events Committee blinded to the assigned treatment).
2. Number at risk represents the number of evaluable subjects at the beginning of each 30-day window.

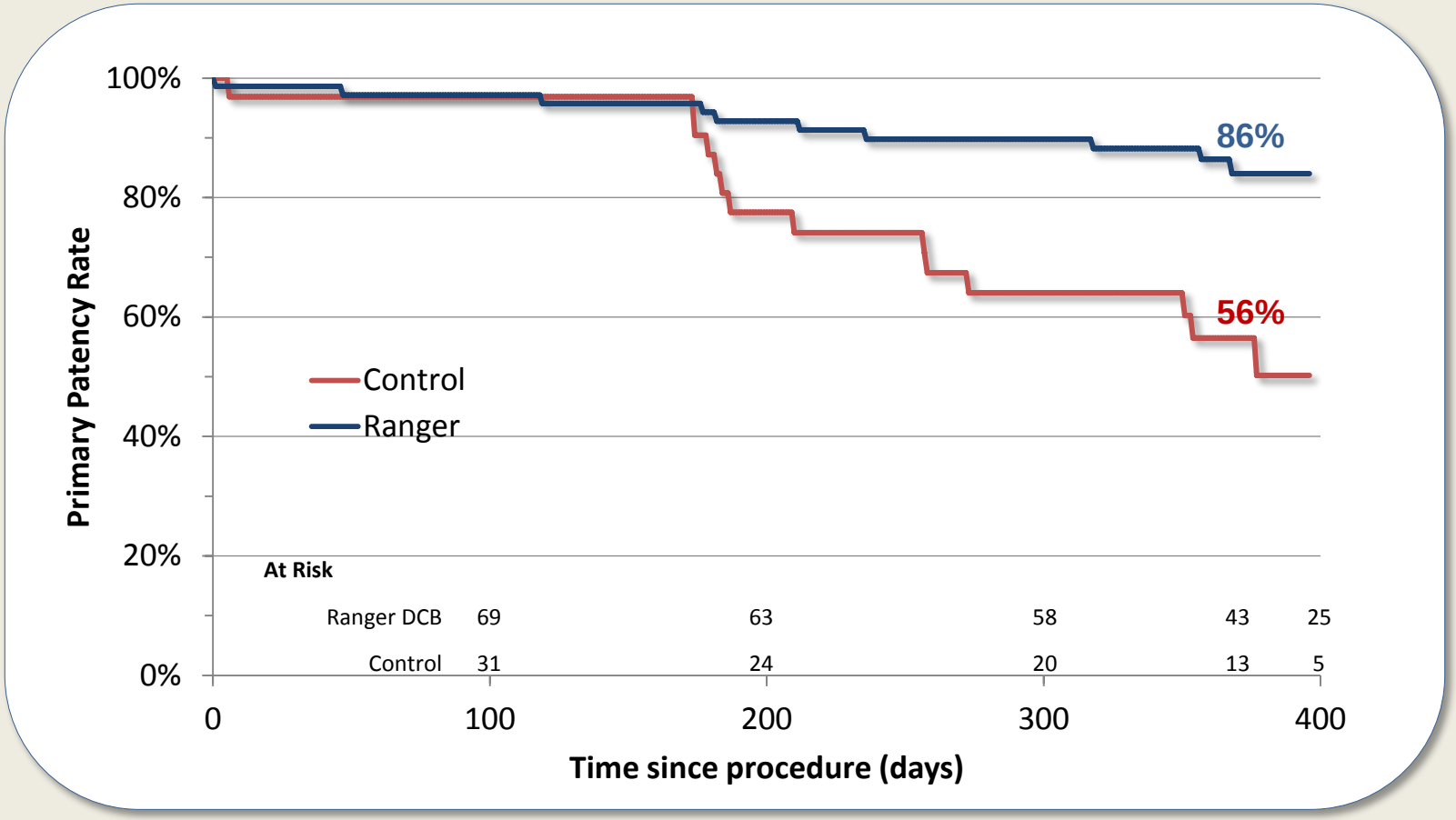
IN.PACT SFA Trial:
Freedom from CD-TLR[1] through 3 Years



1. Clinically-driven TLR adjudicated by an independent Clinical Events Committee, blinded to the assigned treatment based on any re-intervention at the target lesion due to symptoms or drop of ABI of ≥20% or >0.15 when compared to post-procedure baseline ABI.
2. Number at risk represents the number of evaluable subjects at the beginning of each 30-day window.

Ranger-SFA Study
Primary Patency – 12 Months

- Kaplan Meier estimate of primary patency rate at 12 months:
  - **86% Ranger DCB vs 56% Control**
- Significantly greater time to failure (survival time) for Ranger DCB than control (log-rank *P*<.001)



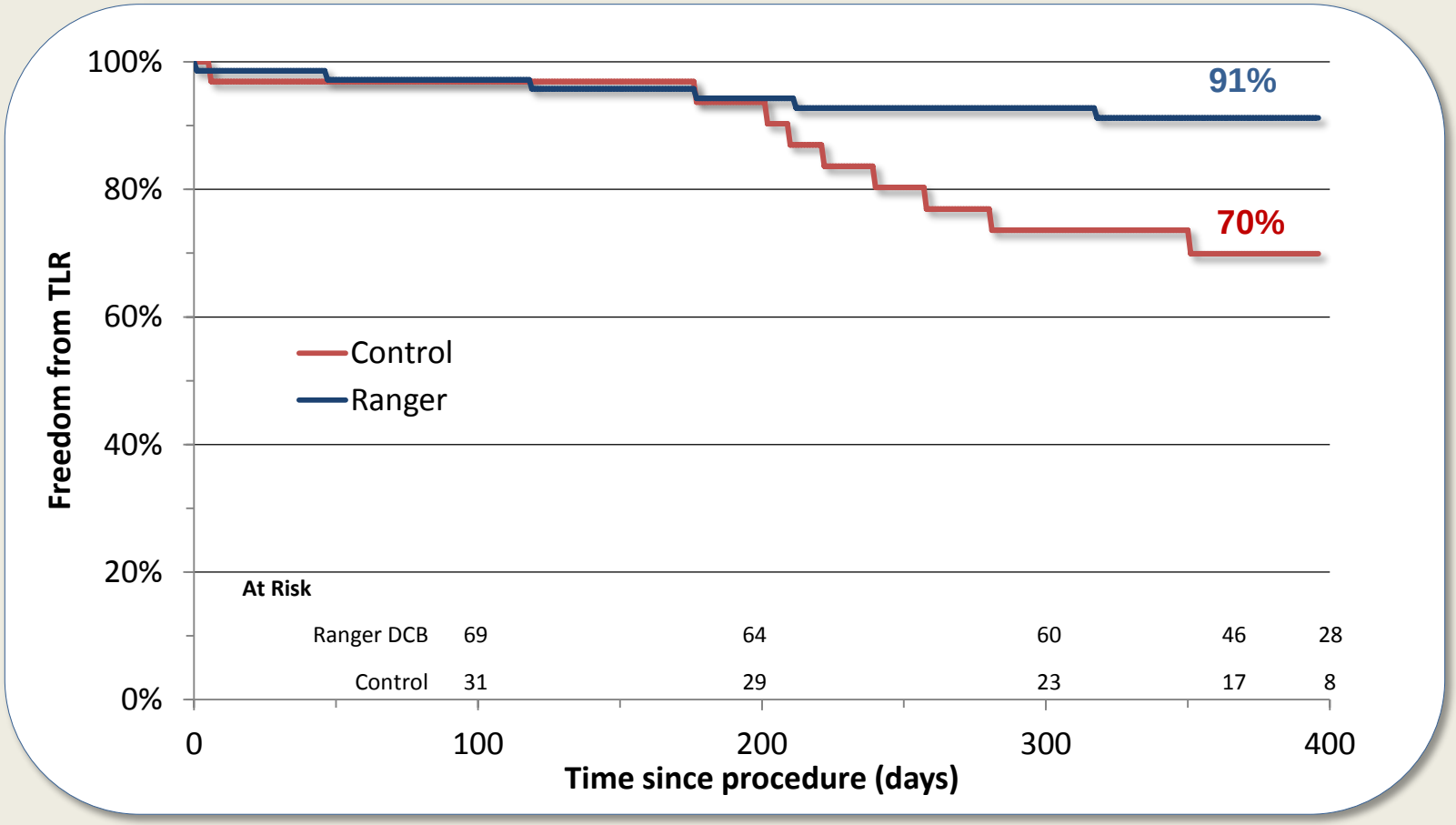
Scheinert, D. Charing Cross 2017.
Ranger DCB is an investigational device and not available for sale in the US.

Primary patency defined as the percentage of lesions without a hemodynamically significant stenosis on duplex ultrasound (PSVR > 2.4) and without TLR or bypass of the target lesion.

PI-342608-AD 2017

Ranger-SFA Study
Freedom from TLR – 12 Months

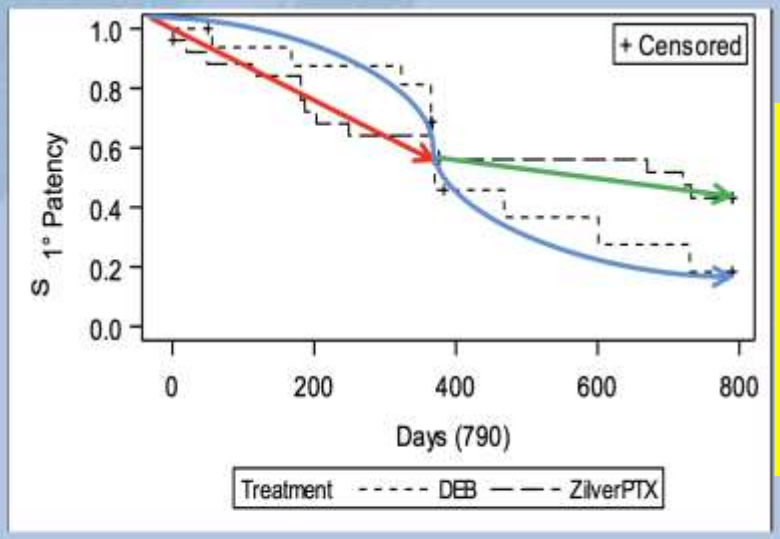
- Kaplan Meier estimate of freedom from TLR at 12 months:
  - **91% Ranger DCB vs 70% Control**
- Significantly greater TLR-free time for Ranger DCB than control (log-rank *P*=.010)



Scheinert, D. Charing Cross 2017.
Ranger DCB is an investigational device and not available for sale in the US.

REAL PTX RCT of DES vs. DCB

Primary Patency @ 24 Month
Long Lesion Group
Zilver PTX vs DCB only



Treatment	PP
DCB	18.3%
Zilver PTX*	43.1%

Mean lesion length 152.6 ±88.2mm

**> 40% had >30% residual stenosis*

Imperial

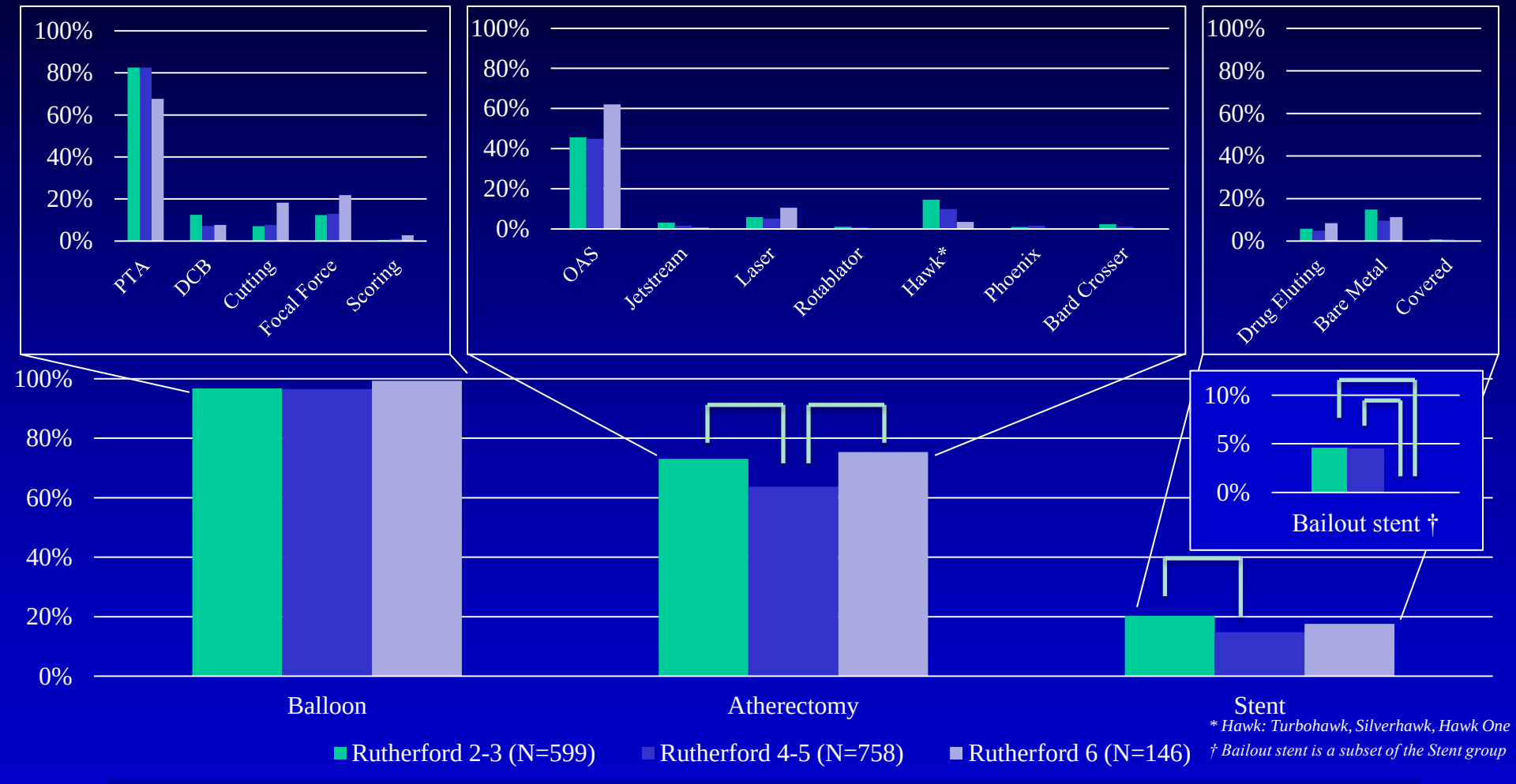
- Randomized trial BSC
- Eluvia compared with ZilverPTX
- Results to be presented TCT 2018

DEFINITIVE LE

Subgroup	Claudicants (n=743)		CLI (n=279)	
	Patency (PSVR ≤ 2.4)	Lesion Length (cm)	Patency (PSVR ≤ 2.4)	Lesion Length (cm)
All (n=1022)	**78%**	**7.5**	**71%**	**7.2**
Lesion type				
Stenoses (n=806)	81%	6.7	73%	5.8
Occlusions (n=211)	64%	11.1	66%	10.3
Lesion Location				
SFA (n=671)	75%	8.1	68%	8.6
Popliteal (n=162)	77%	6.0	68%	5.4
Infrapopliteal (n=189)	90%	5.5	78%	6.0

LIBERTY Device Usage by Lesion

Balloon and/or atherectomy were preferred devices with orbital atherectomy (OAS) the most frequently used atherectomy device. RC6 subjects saw significantly higher use of focal force/cutting balloons, OAS, and laser atherectomy. Bailout stenting was significantly less frequent in RC6 compared to either RC2-3 or RC4-5.



** Hawk: Turbohawk, Silverhawk, Hawk One*

† Bailout stent is a subset of the Stent group

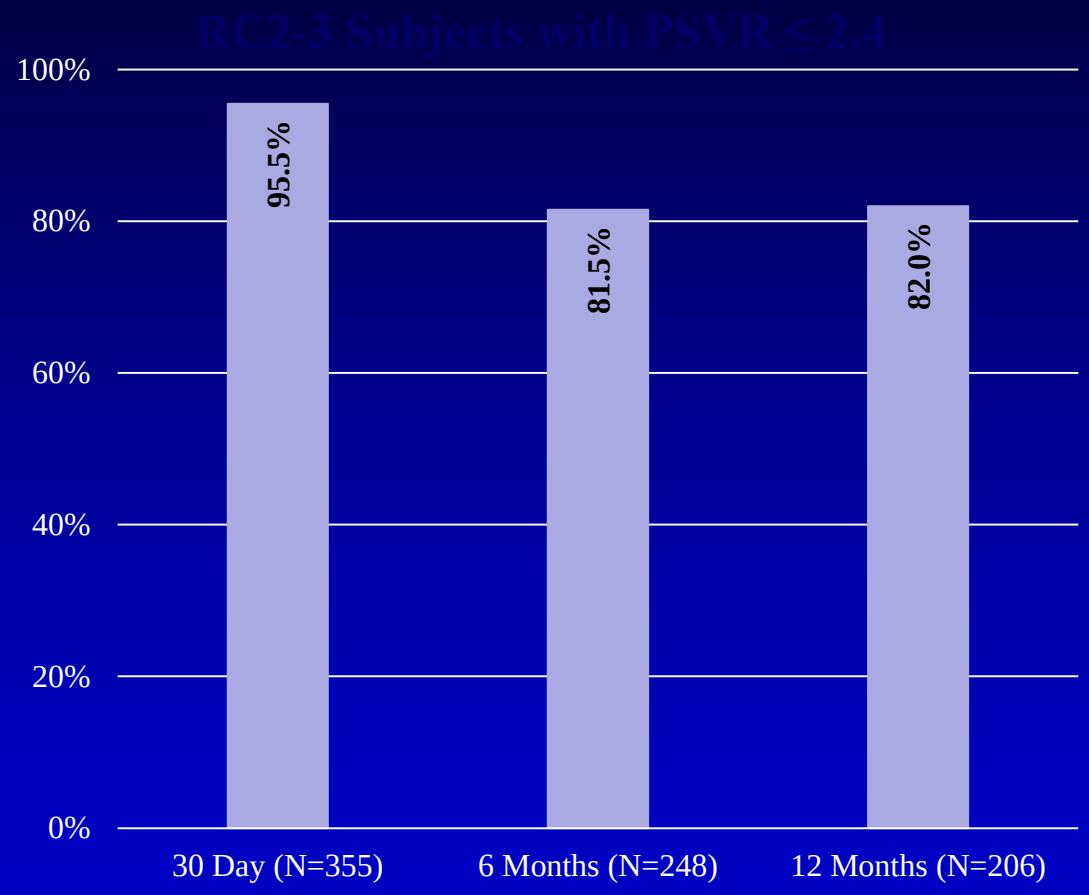
LIBERTY 360: Prospective, observational, multi-center study to evaluate procedural and long-term clinical and economic outcomes of endovascular device interventions in patients with symptomatic lower extremity PAD (N=1,204 Subjects)

Core Lab reported lesions (Lesions with reported values may be less than total number of lesions treated in each arm).
23-May-2017 Data

Comparison between Rutherford categories significant ($p<0.05$)

LIBERTY Duplex Ultrasound (DUS)

High long-term patency rate in RC2-3 subjects.

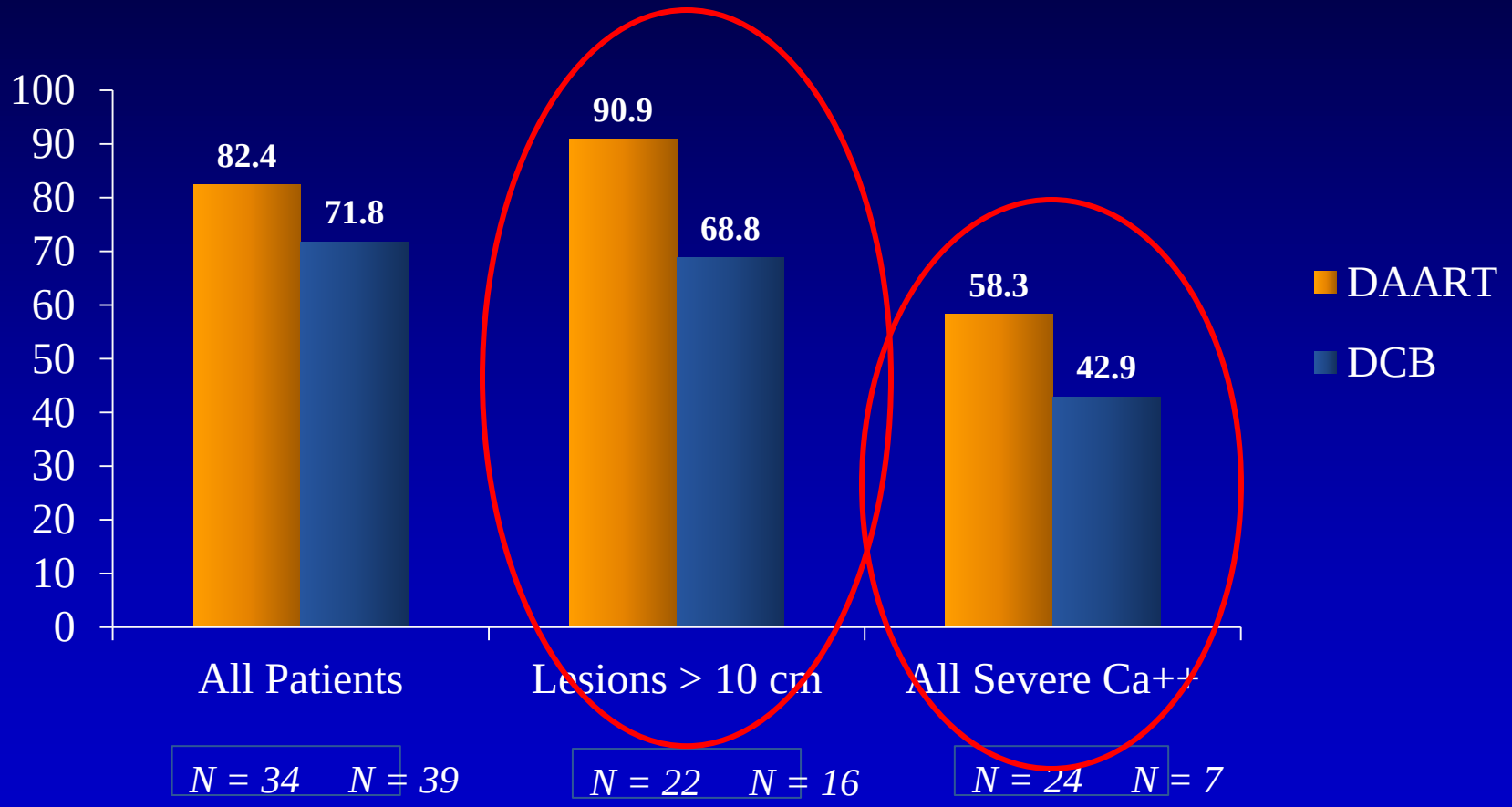


LIBERTY 360: Prospective, observational, multi-center study to evaluate procedural and long-term clinical and economic outcomes of endovascular device interventions in patients with symptomatic lower extremity PAD (N=1,204 Subjects)

VasCore Core Lab Assessed (Patients with reported values may be less than total number of patients enrolled in each arm).
DUS required only for RC2-3 Subjects
At baseline, previous Peripheral Vascular Intervention on target limb in 30% of RC 2-3 subjects
23-May-2017 Data

Key Study Outcome at 12 Months

Angiographic Patency shows similar pattern



Results for all patients who returned for angiographic follow-up

What's the benchmark?

- Unfortunately, current stent data have been limited mostly to around 5 to 8 cm
- DES gain is persistent to 5 years
- "real world" SFA lengths VIBRANT 53/58% primary patency at 12 months and recent VIPER 70% in a similar lesion cohort
- Newer stent technologies (interwoven nitinol) may afford improved patency without fracture
- Non-stent technologies, atherectomy or DCB data for above the knee application (IN-Pact) has exceptional outcomes on a 9cm LL, RANGER is compelling at 12 months, Lutonix may have missed the mark
  - Registry data compelling though must understand adjunctive rx
- Combined therapy appear compelling though not fully tested
- Unfortunately without head to head trials "what's best" remains at your discretion