Current Status of Clinical Trials versus Optimal Outcomes

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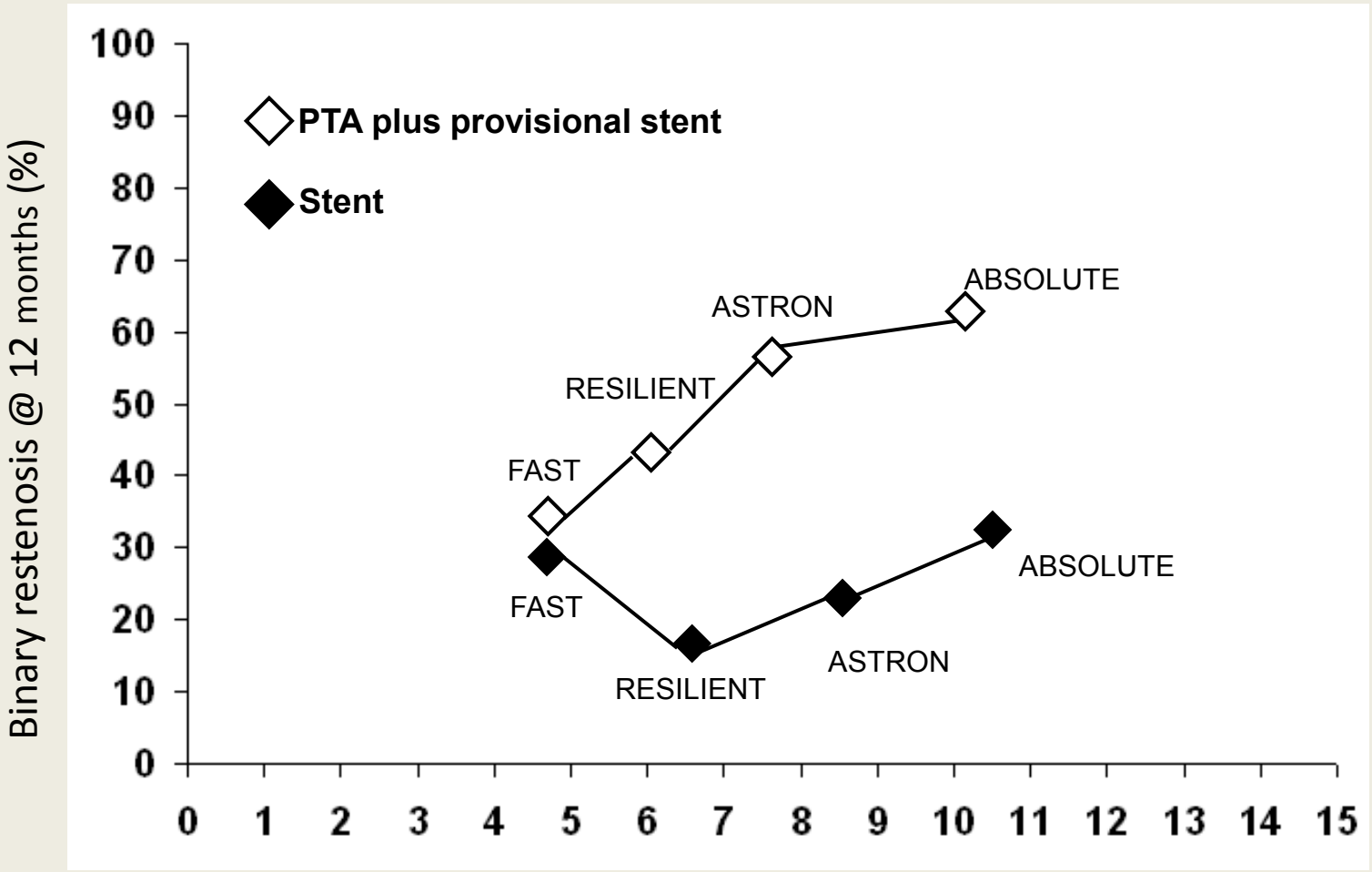
Bare-metal Stents

PTA and Stent



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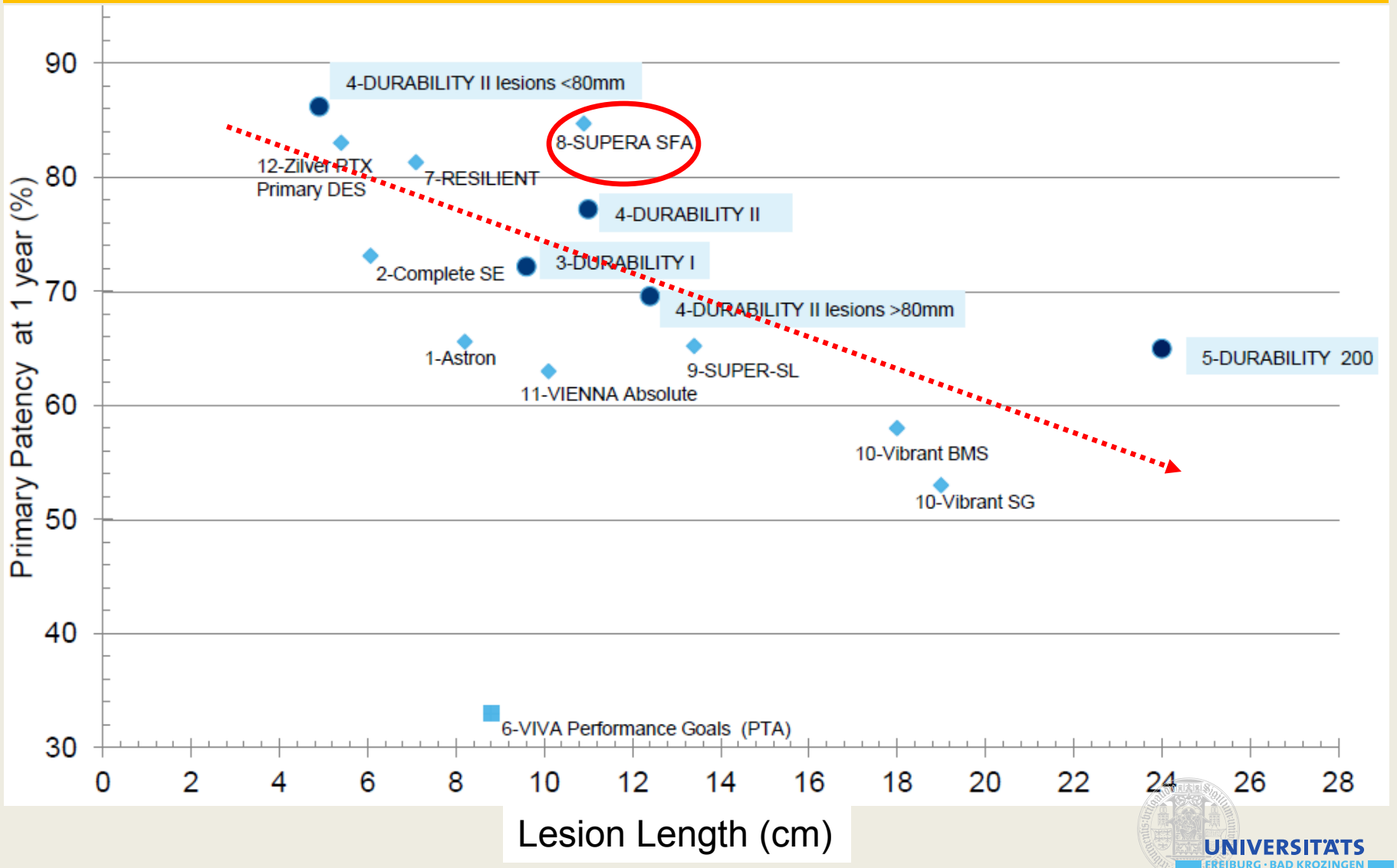
SFA Stent Trials

Primary Patency at 1year vs. Lesion Length



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SUPERA Trial: Retrospective, single-centre, single-arm

	Baseline	1 year	2 years
Patients (n)	107		
Lesion length (mm)	90.2 (10-240)		
Stents/Lesion	1.6		
Primary patency		84.7%	76.1%
TLR		15%	23%
Limb salvage		97.7%	96.2%
Stent-FX		0%	
ABI	0.68±0.14		0.87±0.10
Rutherford-Becker	3.3±0.7		2.0±1.0

Scheinert et al. JEVT 2011

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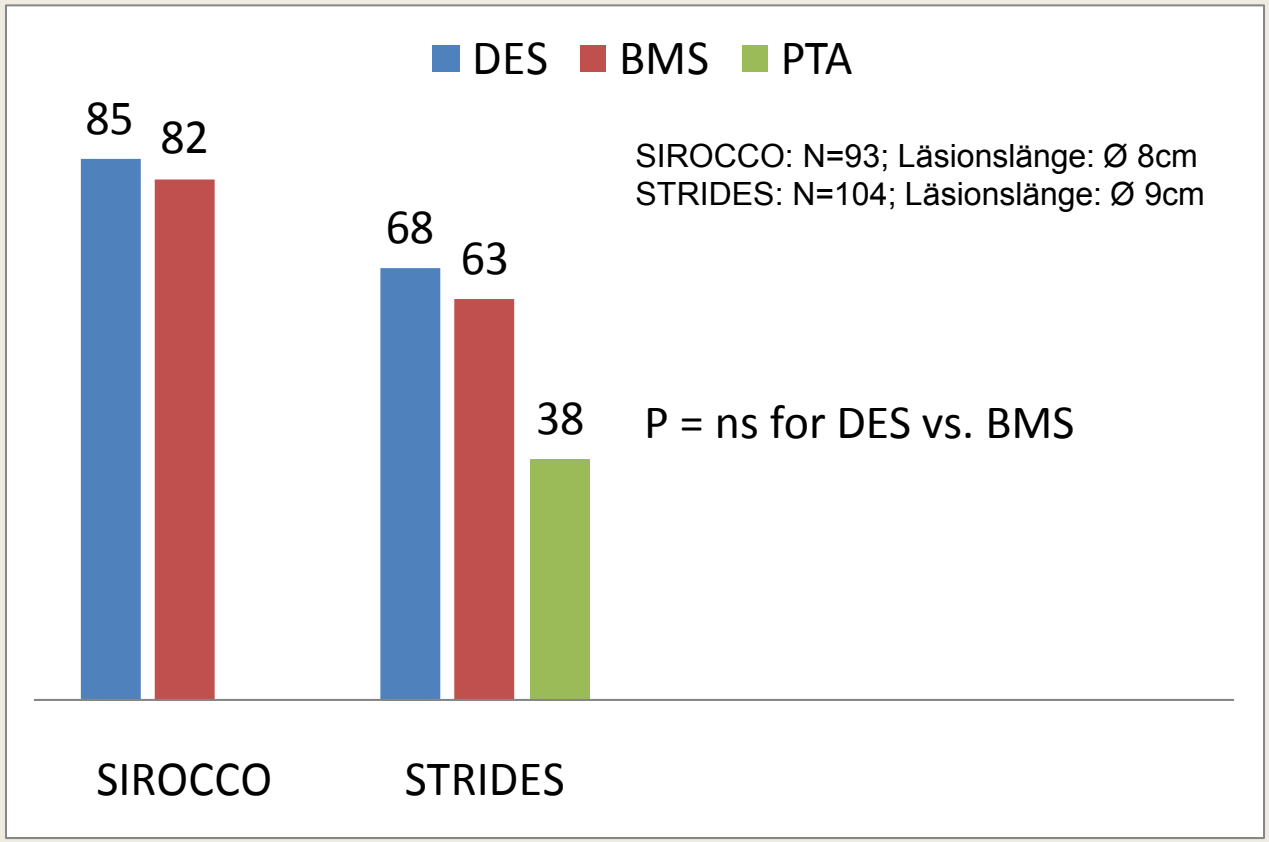
Drug-eluting Stents

Drug-eluting Stents: Primary patency at 1-year



Duda SH et al. J Endovasc Ther 2006
Lammer J et al. J Vasc Surg 2011

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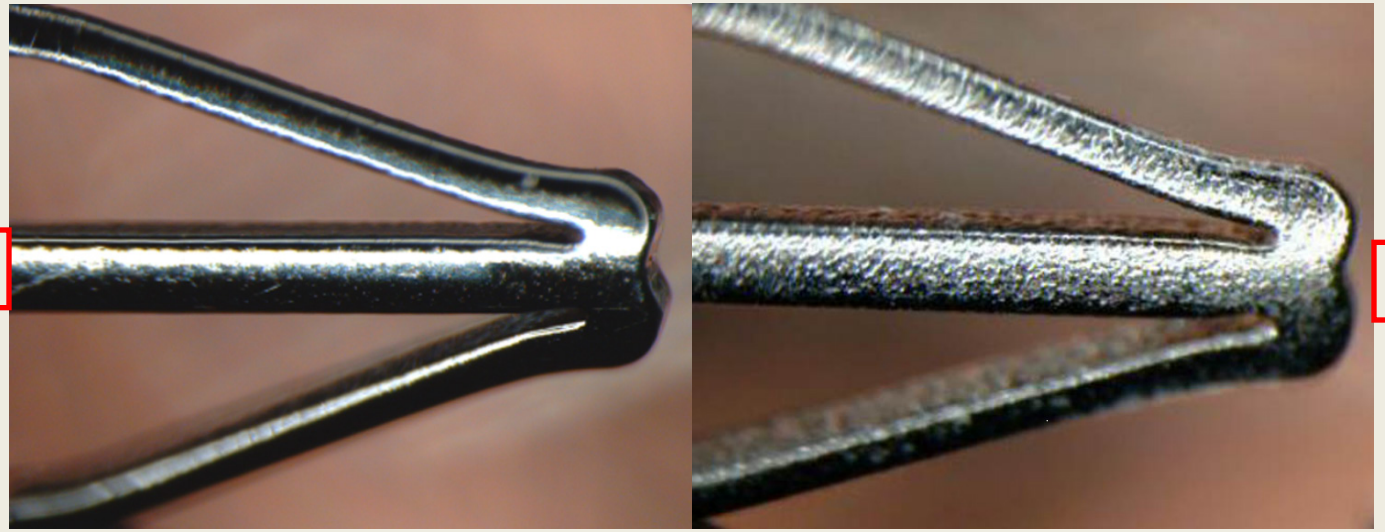
Zilver® PTX® -Stent

Nitinolstent mit Paclitaxel-Beschichtung (3 µg/mm²)



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Zilver® PTX® prospective, multi-centre, single-arm

	Baseline	1 year	P
Lesions (patients)	900 (787)		
Mean lesion length	99.5±82.1mm		
Stents/Lesion	1.9		
Primary patency		86.2%	
TLR		9.5%	
Event-free survival		89%	
Stent-FX		1.5%	
ABI	0.6±0.3	0.9±0.2	0.001
Rutherford-Becker	3	0	0.001

Dake et al. JEVT 2011

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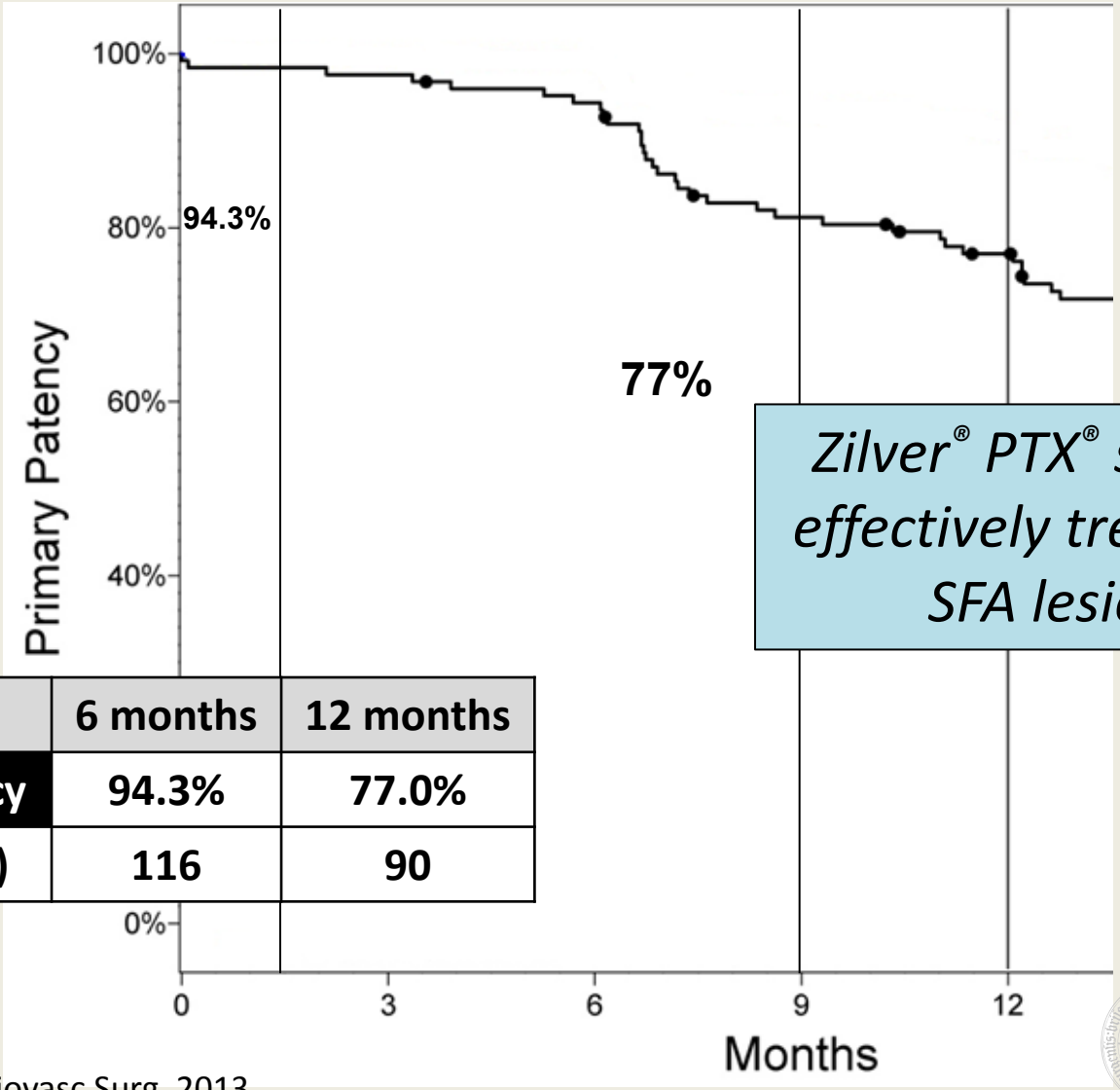
Zilver® PTX® Effectiveness in *de novo* lesions >15 cm

(N=135 lesions; mean length 226± 44)



Time	6 months	12 months
Primary patency	94.3%	77.0%
Lesions (at risk)	116	90

Zilver® PTX® stenting effectively treats long SFA lesions

Bosiers M et al. J Cardiovasc Surg. 2013

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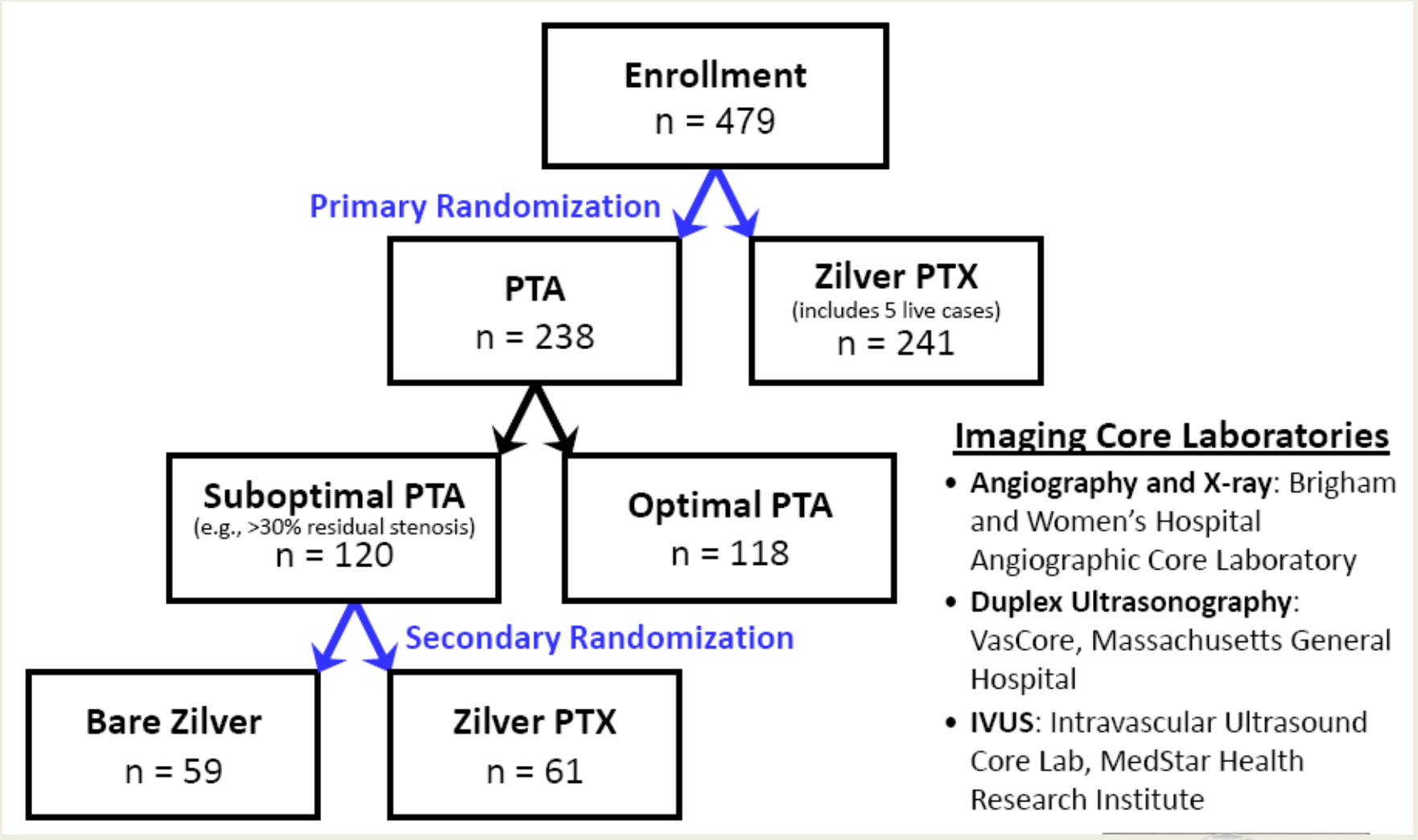
Study design Zilver-PTX vs. PTA



M. D. Dake et al., Circ Cardiovasc Interv 2011

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Sustained Safety and Effectiveness of Paclitaxel-Eluting Stents for Femoropopliteal Lesions

2-Year Follow-Up From the Zilver PTX Randomized and Single-Arm Clinical Studies

Michael D. Dake, MD,* Gary M. Ansel, MD,† Michael R. Jaff, DO,‡ Takao Ohki, MD,§ Richard R. Saxon, MD,‖ H. Bob Smouse, MD,¶ Scott A. Snyder, PHD,# Erin E. O'Leary, PHD,# Gunnar Tepe, MD,** Dierk Scheinert, MD,†† Thomas Zeller, MD,‡‡ on Behalf of the Zilver PTX Investigators

Stanford and Oceanside, California; Columbus, Ohio; Boston, Massachusetts; Tokyo, Japan; Peoria, Illinois; West Lafayette, Indiana; Rosenheim, Leipzig, and Bad Krozingen, Germany

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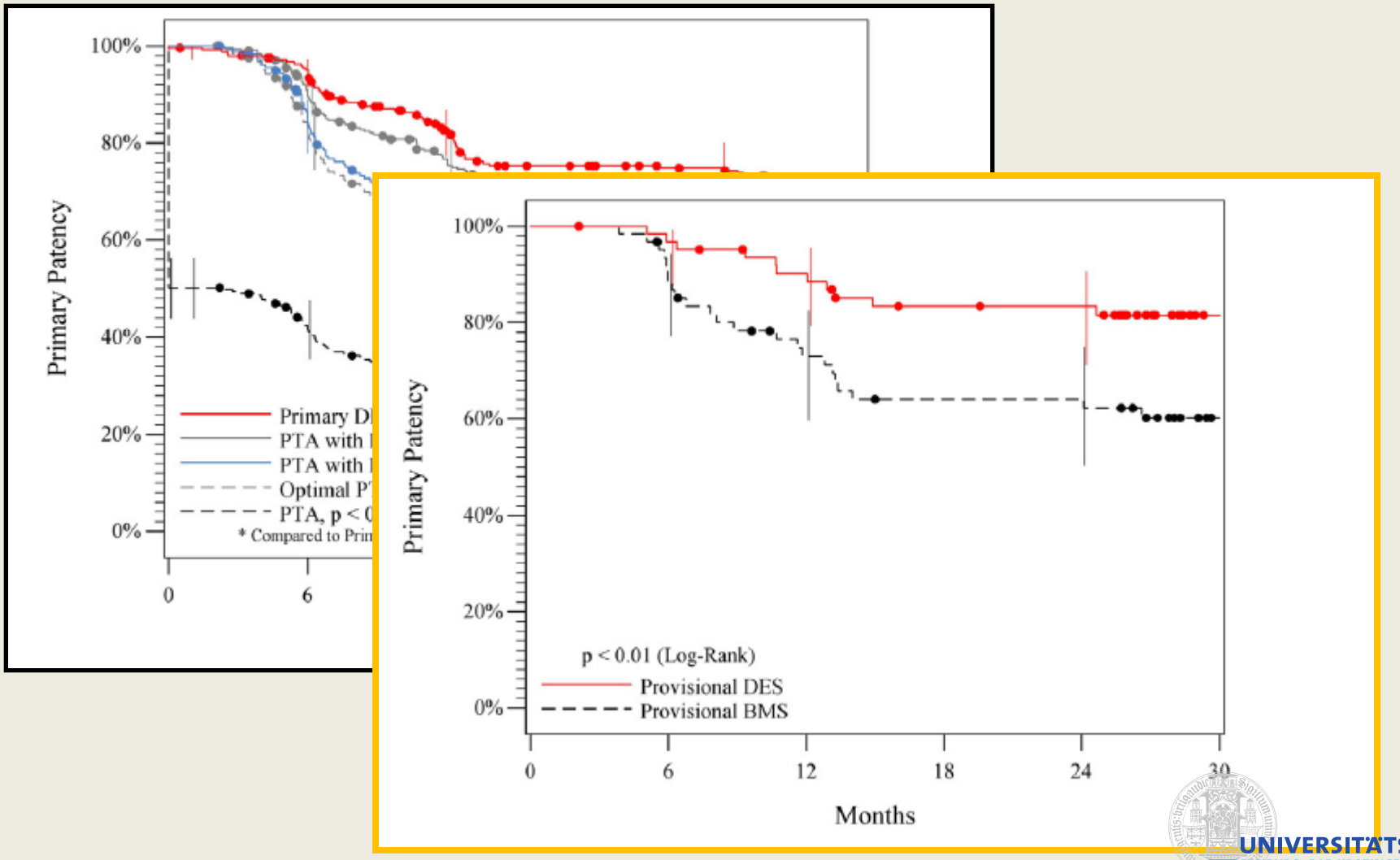
Zilver® PTX®: 2-Year follow-up



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Endoprothesen

Studien: AFS Läsionen/Endoprothese

	Boufi et al. J Vasc Surg. 2010	**Farraj et al.** J Int. Cardiol. 2009	**Saxon et al.** J Vas Inter Rad. 2008
Design	Retrospektiv, monozentrisch Endoprot. vs. PTA	Prospektiv, monozentrisch single arm	Randomisiert, multizentrisch Endoprot. vs. PTA
Patientenzahl	53	30	197
Läsionslänge Ø	20 cm	15 cm	<13 cm
Technischer Erfolg	94.5%	94%	95% vs. 66% (P=0.0001)
1-J Pri. Patency	61.8% vs. 78.9% (P=0.49)	80%	65% vs. 40% (P=0.0003)
1-J Sec. Patency	88.2% vs. 78.9% (P=0.22)	86%	
Beinerhalt	94.1% vs. 100%	100%	100%

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Vibrant: Randomized, multi-center study

	Viabahn (N=72)	Bare-Nitinol (N=76)	P
Läsionslänge Ø	19±8 cm	18±7 cm	0.87
Okklusionen	59.7%	56.6%	0.74
Technischer Erfolg	97%	97%	1
1-Jahr Pr. Patency	53%	58%	0.58
3-Jahres Pr. Patency	24.2%	25.9%	0.39
3-Jares Sec. Patency	89.3%	79.5%	0.30
Beinerhalt	100%	100%	1

1-Jahres Restenose der Viabahn in 87% durch „edge“-Stenosen verursacht

Geraghty PJ et al. J Vasc Surg 2013

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VIASTAR-Trial (randomized, multi-center)

Characteristic	VIA (N = 72)	BMS (N = 69)	p Value
Age – yr *	68.85 ± 8.59	69.44 ± 8.96	0.69

Variable	VIA (N = 72)	BMS (N = 69)	p Value
Length of target lesion — mm*	189.8±63	173.2± 66	0.13
Length of stented segment — mm*	236.8±77	203.1±77	0.01
Target vessel diameter — mm*	6.08±0.6	6.25±0.7	0.88
Occlusion — no. (%)	56 (79)	46 (70)	0.21

Renal failure – no. (%)	12 (17)	5 (7)	0.14

Lammer J et al.; 2013 (review)

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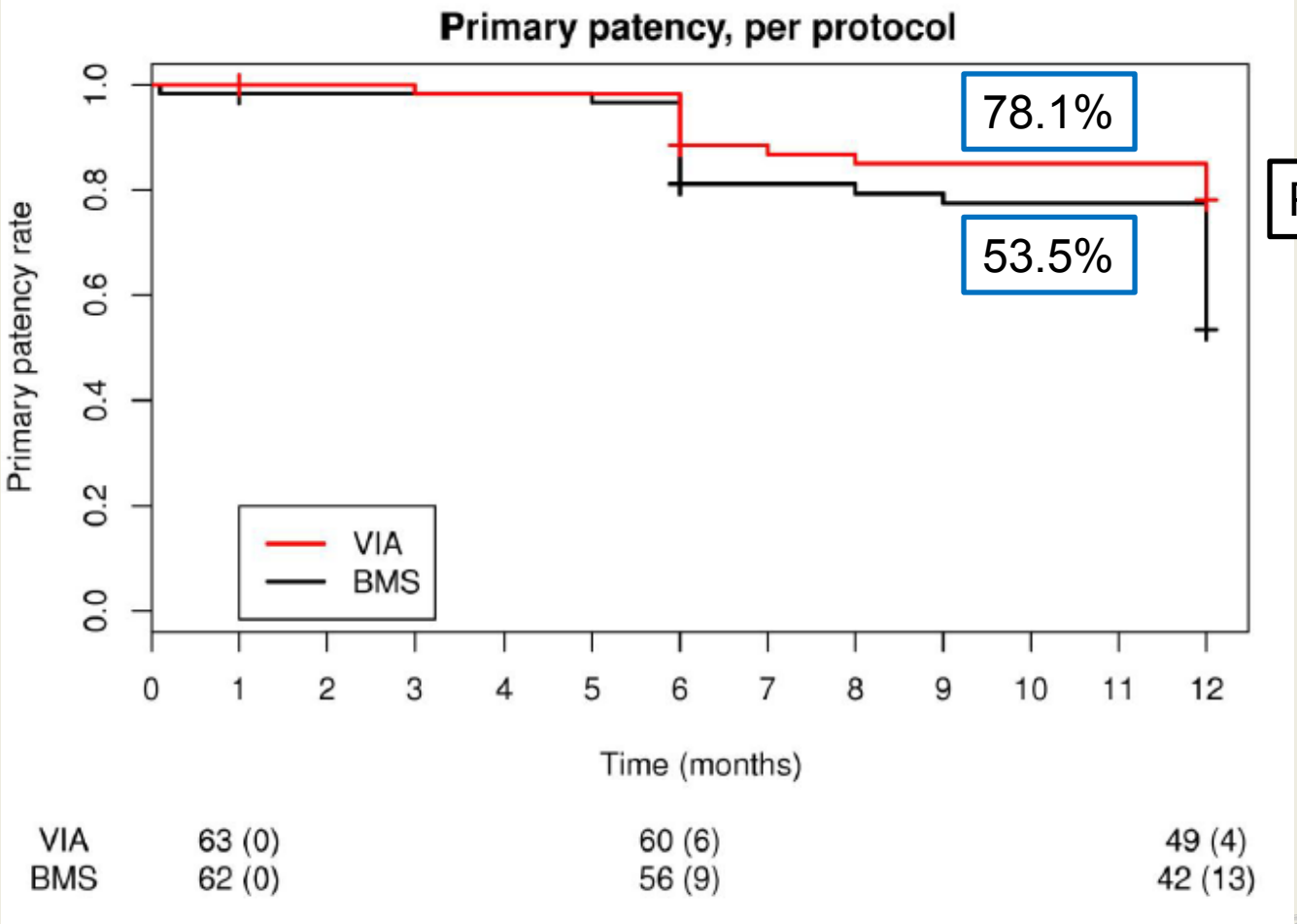
VIASTAR-Trial



Lammer J et al.; 2013 (review)

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VIPER-Trial (single-arm, multi-center)

119 limbs (113 patients; 69 men; mean age, 67 y), including 88 with Rutherford category 3-5 disease and (TASC II) C or D lesions of the FPA

	Viabahn (N=113)	Oversiz.<20%	Ovesiz.>20%	P
Läsionslänge Ø	19±4 cm			
Okklusionen	56%			
1-J- Pr. Patency	73%	88%	70%	0.047
1-J-Sec. Patency	92%			

Primary patency was not significantly affected by lesion length (≤20 cm vs>20 cm).

Saxon RR, et al. J Vasc Inter Radiol 2013

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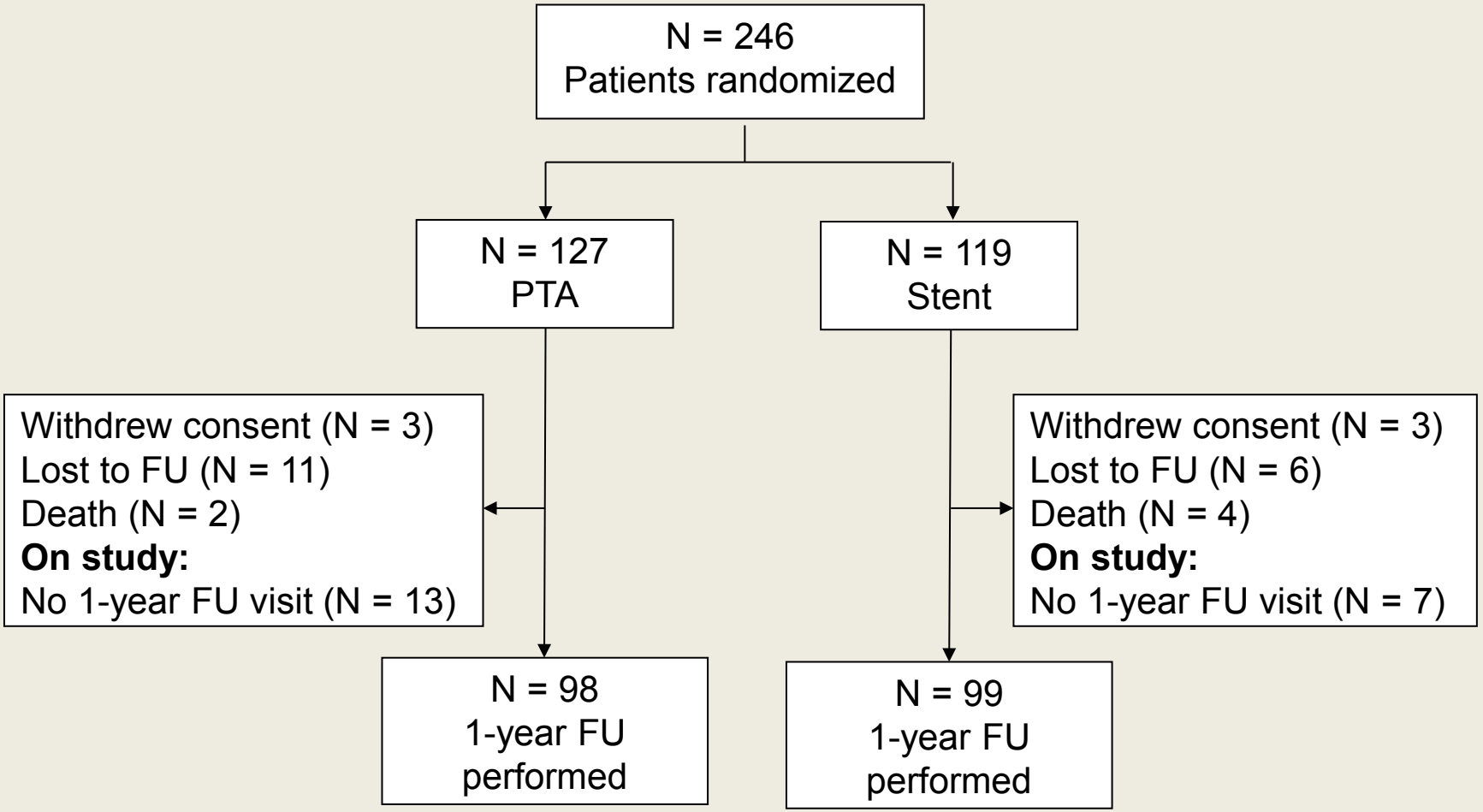
Arteria poplitea

Stent Placement versus Balloon Angioplasty for the Treatment of Obstructive Lesions of the Popliteal Artery: A Prospective, Multi-centre, Randomized Trial

ETAP-Trial

Final Data

ETAP: Study Design



Rastan et al. *Circulation* 2013

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ETAP: Baseline Characteristics

	All Patients (N=246)	Stent (N=119)	PTA (N=127)
Age (years, range)	72 (41-89)	72 (42-89)	73 (41-89)
Male sex (%)	64.2	63.9	64.6
Body-mass-Index	26±4	27±4	26±4
Diabetes mellitus (%)	37	36.1	37.8
Dyslipidemia (%)	78.9	75.6	81.9
Hypertension (%)	85.4	82.4	88.2
Occlusion (%)	32.9	32.8	33.1
Length of the lesion (mm)	42.3±30	41.3±31	43.2±28

Rastan et al. *Circulation* 2013

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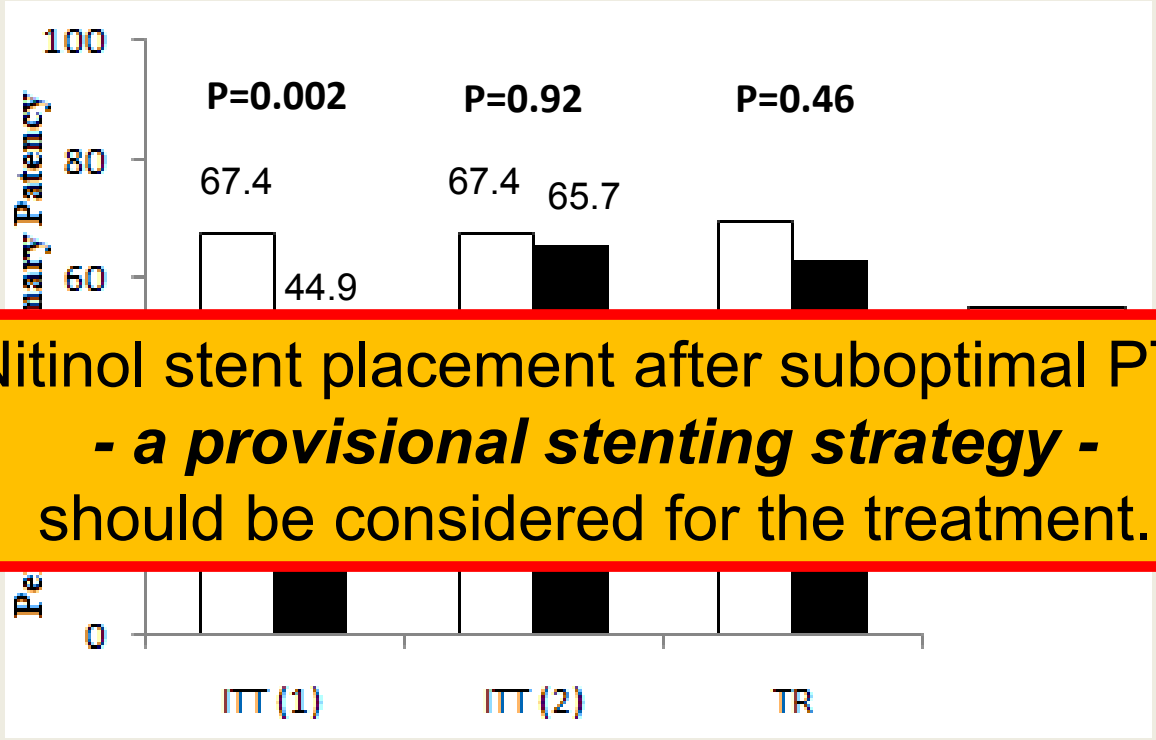
ETAP: Primary Patency at 1-year



Nitinol stent placement after suboptimal PTA
- a provisional stenting strategy -
should be considered for the treatment.

Rates of Primary Patency at 1-Year
Based on the “intention-to-treat” analysis (Typ 1 and Type 2), and the “treatment-received” analysis.

Rastan et al. *Circulation* 2013

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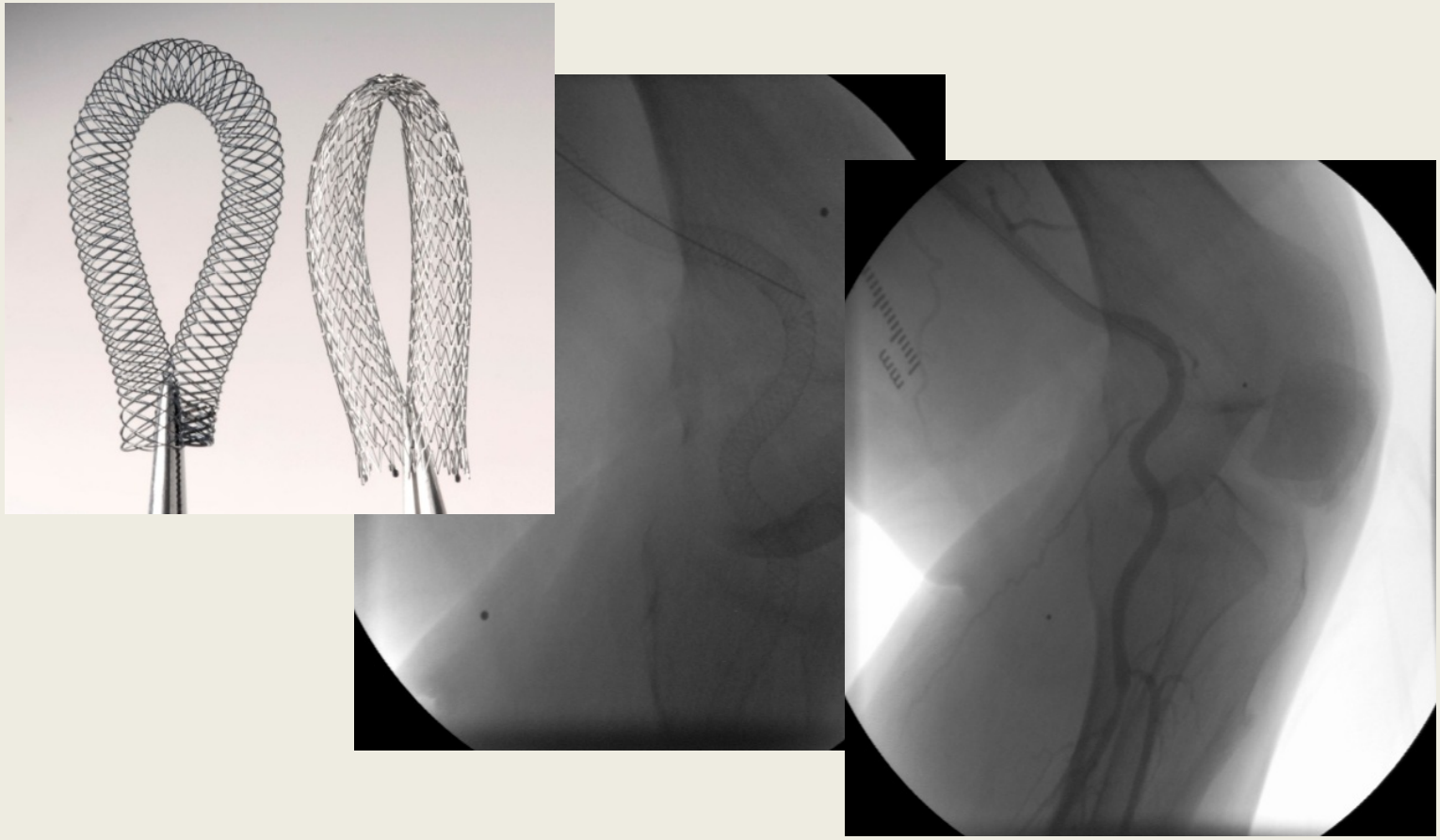
Interwoven Stent (SUPERA)



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Popliteal artery Trials: Interwoven Stent (Supera)

Single-center Registries

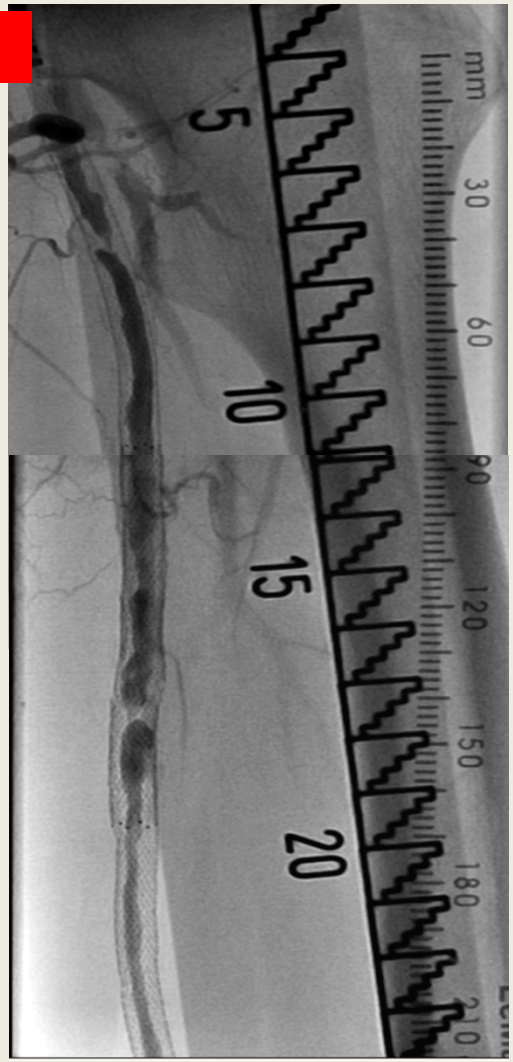
	Scheinert et al.[1]	Goltz et al.[2]	Scheinert et al.[3]
Patients (n)	107	40	101
Rutherford-Becker	1-5	3-5	1-5
Lesion length (mm)	90.2 (10-240)	79±40	58.4 (10-200)
Occlusion (%)	30.8	87.5	47.5
Stents/Lesion (ø)	1.6	1.3	1.3
1-year Primary patency	84.7%	68.4%	87.7%
TLR (%)	15	17.5	6.9
Limb salvage (%)	97.7	95	99
Stent-FX (%)	0	0	0
ABI	P<0.05	P<0.05	P<0.05
Rutherford-Becker	P<0.05	UKN	P<0.05

1 Scheinert et al. JEVT 2011
2 Glotz et al. JEVT 2012
3 Scheinert et al. JACC cardiovasc interv 2013

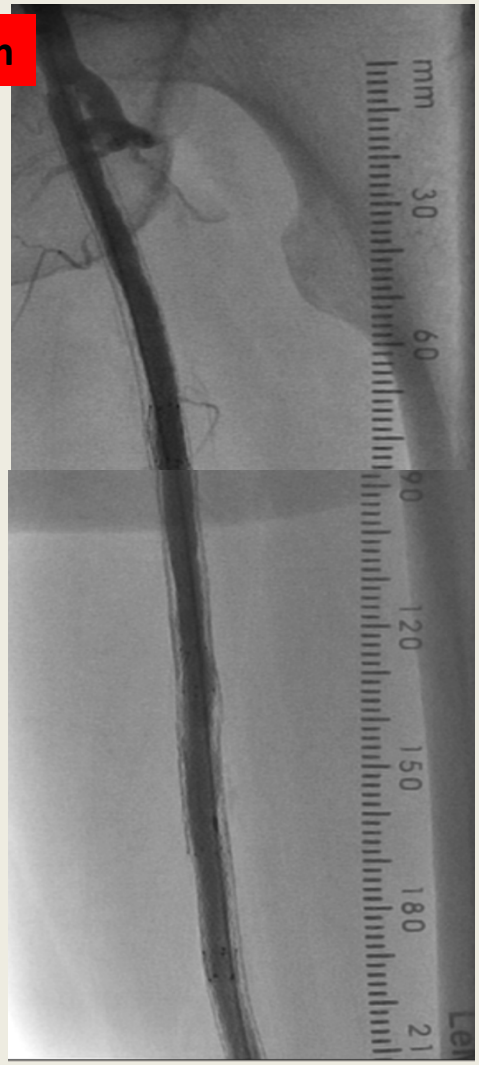
In-Stent Stenose

AFS In-stent Stenose

Vor Intervention



Nach Intervention



In-Stent Stenose (ISR): Inzidenz und Therapie

1-Jahres Risiko einer ISR der AFS: 19% - 37%
→mit der Stentlänge steigt das Risiko!

Dick et al. Radiology 2008

40 Patienten mit AFS In-Stent-Stenosen bis 200mm (ø80mm).
PTA vs. **Cutting-balloon**:

Restenoserate nach 6 Monaten: **65%** vs. **73%** (P=0.73)

Tosaka et al. JACC 2012

133 AFS In-Stent Stenosen (ø91mm) mit **PTA** behandelt.

(Class I: ≤50mm; Class II: >50mm; Class III: Occlusion)
Restenoserate nach **24 Monaten**: **49.9%** vs. **53.3%** vs. **84.8%** (P=0.73)

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Drug-Eluting Balloon for Treatment of Superficial Femoral Artery In-Stent Restenosis

Eugenio Stabile, MD, PHD, Vittorio Virga, MD, Luigi Salemme, MD, Angelo Cioppa, MD, Vittorio Ambrosini, MD, Giovanni Sorropago, MD, Tullio Tesorio, MD, Linda Cota, MD, Grigore Popusoi, MD, Armando Pucciarelli, MD, Giancarlo Biamino, MD, Paolo Rubino, MD

Mercogliano, Italy

1-year Primary patency: 92.1%
Secondary patency: 100%
Ankle-brachial index improvement: P<0.05
Rutherford-class improvement from baseline P<0.05

Table 1 Pat

Male	
Age (yrs)	
Diabetes (%)	
Hypertension (%)	
Hypercholesterole	
Smoking history	
eGFR <30 (ml/min)	
Rutherford class	2.9 ± 0.7
BTK patent vessels	
≥2	31 (79.5)
1	8 (20.5)

	5–262.5)
	± 78.9
	5–5)
	0–120)
	-6)
	-2)
	20–250)
Fractured stents	4 (10.3)
Ballout stenting (%)	4 (10.3)
Procedural success	39 (100)

N = 39. Values are n (%) or mean ± SD.
BTK = below-the-knee; eGFR = estimated glomerular filtration rate.

J Am Coll Cardiol 2012

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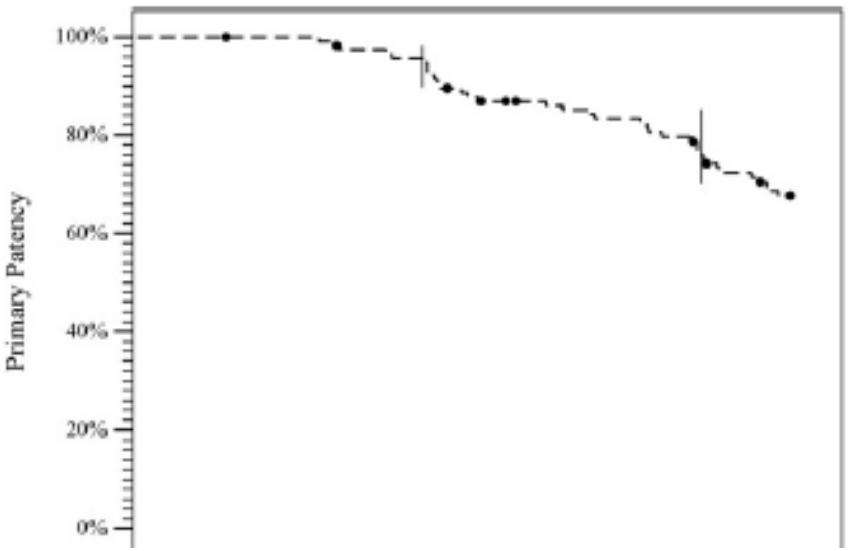
Treatment of Femoropopliteal In-Stent Restenosis With Paclitaxel-Eluting Stents

Thomas Zeller, MD,* Michael D. Dake, MD,† Gunnar Tepe, MD,‡ Klaus Brechtel, MD,‡
Elias Noory, MD,* Ulrich Beschorner, MD,* Patricia L. Kultgen, PHD,§
Aljoscha Rastan, MD*

Bad Krozingen and Rosenheim, Germany; Stanford, California; and West Lafayette, Indiana

Table 2. Baseline Lesion Characteristics

Characteristic
Length, mm
>70
>150
Proximal reference vessel diameter, mm
Distal reference vessel diameter, mm
Minimum lumen diameter, mm
Diameter stenosis, %
TASC I class
A
B
C
D
Not assessed
Total occlusion



Kaplan Meier Estimates of Primary Patency by Lesion

Months Post-procedure	Patency ± Standard Error	Cumulative Failed	Cumulative Censored	Remaining at Risk
6	95.7% ± 1.9%	5	2	110
12	78.8% ± 3.8%	24	7	86

J Am Coll Cardiol Intv 2013

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Drug-coated balloon angioplasty after directional atherectomy improves outcome in restenotic femoropopliteal arteries

Sebastian Sixt, MD,[a,b] Oscar Gerardo Carpio Cancino, MD,[a] András Treszl, MD,[c] Ulrich Beschorner, MD,[a] Roland Macharzina, MD,[a] Aljoscha Rastan, MD,[a] Hans Krankenberg, MD,[b] Franz-Josef Neumann, MD,[a] and Thomas Zeller, MD,[a] *Bad Krozingen and Hamburg, Germany*

Table I. Patient baseline characteristics

Variables[a]	*Entire cohort (n = 89)*	*PTA (n = 60)*	*DCB (n = 29)*	*Standardized difference*[b]	P
Male	52 (58)	37 (62)	15 (52)	−0.202	.492
Age, years	69 ± 11	68 ± 10	70 ± 13	0.178	.409
Diabetes mellitus type 2	40 (45)	26 (43)	14 (48)	0.099	.820
Arterial hypertension	79 (89)	55 (92)	24 (83)	−0.269	.284
Hypercholesterolemia	76 (85)	55 (92)	21 (72)	−0.518	.024
Smoker	52 (58)	38 (63)	14 (48)	−0.307	.251

Results: Lesion location was in the stent (DCB [n = 27] vs PTA [n = 36]) and in native restenotic vessels (DCB [n = 2] vs PTA [n = 25]). The 1-year Kaplan-Meier freedom from restenosis estimates (95% confidence intervals) in the DCB and PTA groups were 84.7% (70.9%-98.5%) and 43.8% (30.5%-57.1%), respectively. In a multivariable Cox model for restenosis, DCB treatment had a hazard ratio (95% confidence interval) of 0.28 (0.12-0.66; $P = .0036$) compared with the PTA group. In the multivariable model for procedural success, the effect of treatment did not differ between PTA and DCB ($P = .134$).

J Vasc Surg 2013

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Zusammenfassung I
femoro-popliteale Arterien

- Die Stentimplantation (BMS) ist der PTA im Vergleich der Offenheitsraten überlegen (AFS).

- Bei der Behandlung der AP ist der Stent der PTA nicht überlegen und sollte daher nur als bail-out zum Einsatz kommen (ETAP-Studie).

- Zunehmende Evidenz bei Wirksamkeit/Überlegenheit der DES gegenüber dem BMS und der PTA.

Zusammenfassung II
femoro-popliteale Arterien

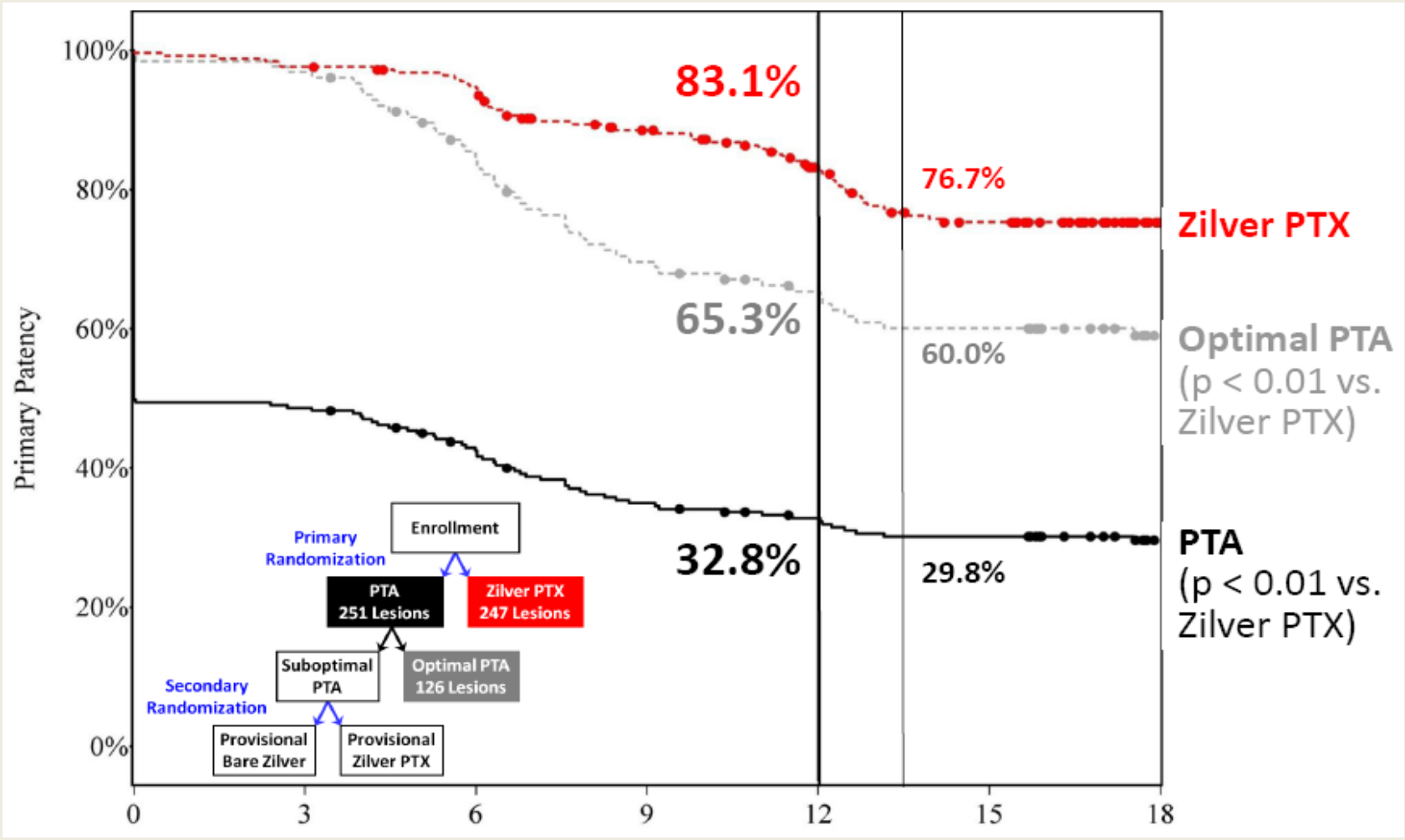
- Eine Verbesserung der Offenheitsraten der AFS durch Einsatz von Endoprothesen ist weiterhin fraglich.

- Bei der Behandlung der In-Stent Stenose zeigen sowohl der DES als auch DEB vielversprechende Ergebnisse. Weitere Verbesserung durch eine Kombination mit Atherektomie?

Thank you!

Questions?

Primary Patency Zilver-PTX vs. PTA



M. D. Dake et al., Circ Cardiovasc Interv 2011

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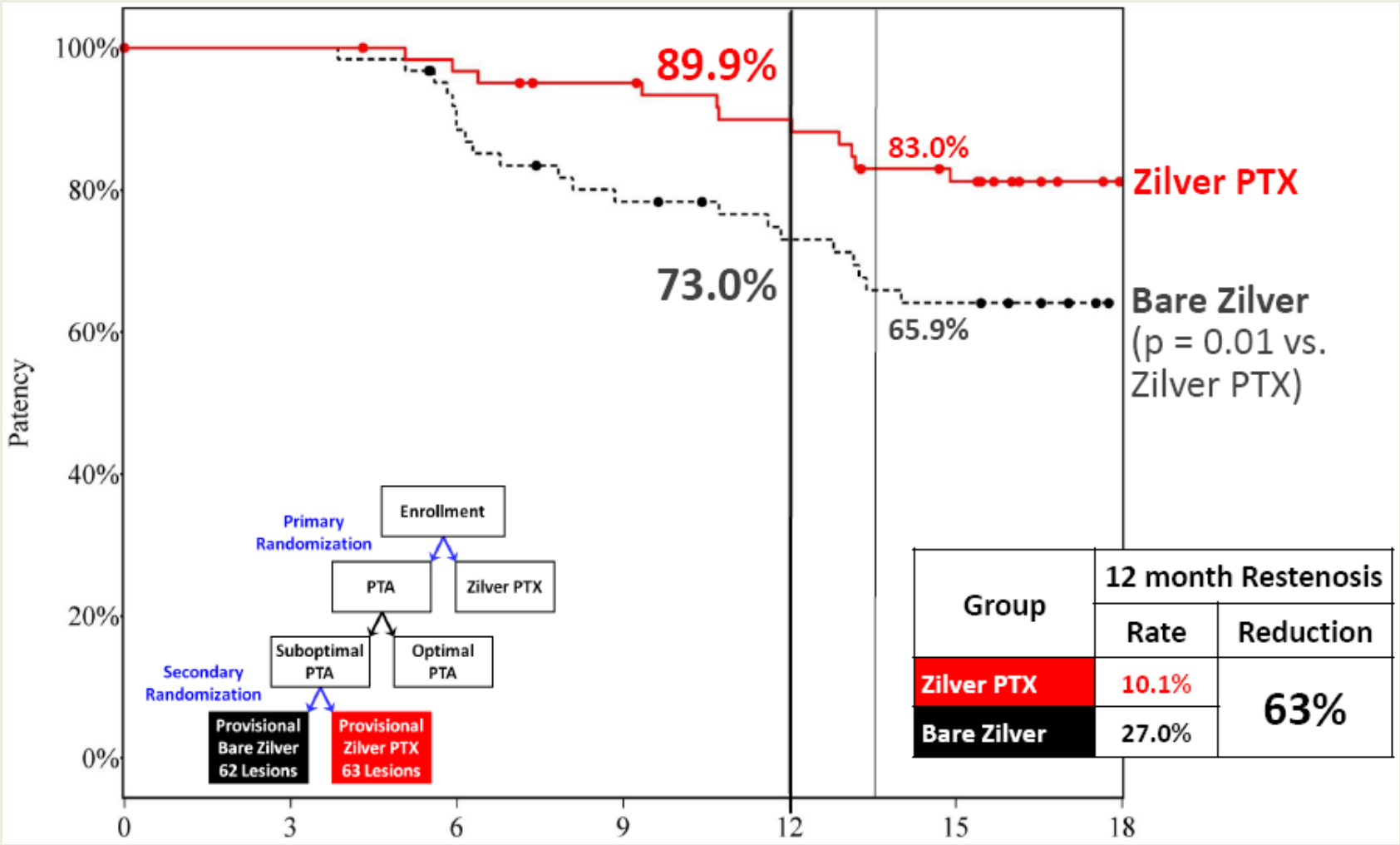
Primary Patency Zilver PTX vs. BMS



Group	12 month Restenosis	
	Rate	Reduction
Zilver PTX	10.1%	63%
Bare Zilver	27.0%	

M. D. Dake et al., Circ Cardiovasc Interv 2011

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Atherektomie

DEFINITIVE LE Trial: Final Data

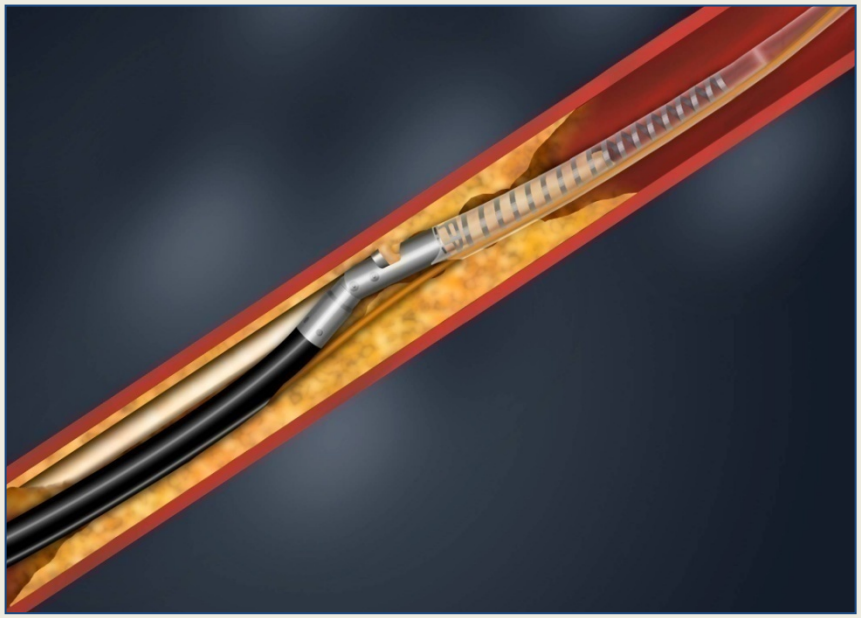
Study Design

- Primary Objective:

To evaluate effectiveness of stand-alone SilverHawk™ /TurboHawk™ Systems for treatment of peripheral arterial disease in the femoro-popliteal and tibio-peroneal arteries.

- Details & Oversight:

- Prospective, non-randomized study
- CEC and Steering Committee oversight
- Angiographic and duplex-ultrasound core laboratory analyses



SilverHawk™ /TurboHawk™ Peripheral Plaque Excision Systems used in study

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Baseline Lesion Characteristics

Core Lab Reported

Characteristic	Claudication (RCC 1-3)	CLI (RCC 4-6)	All Subjects (RCC 1-6)
Number of Patients	598	201	799
Number of Lesions	743	279	1022
Mean Length (cm)	7.5	7.2	7.4
Baseline Stenosis (%)	73	76	74
Occlusions (%)	17	30	21
Anatomic location based on proximal edge of lesion treatment, % (n)			
SFA	72% (536)	48% (135)	66% (671)
Popliteal	15% (114)	17% (48)	16% (162)
Infrapopliteal	13% (93)	34% (96)	18% (189)

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Pre-Dilation and Adjunctive Therapy

Analysis by Lesion

Therapy	
Pre-Directional Atherectomy PTA	**9%**
Post-Directional Atherectomy PTA (no stent)	**33%**
Mean pressure	6.6 atm
Bail-Out Stent	**3%**

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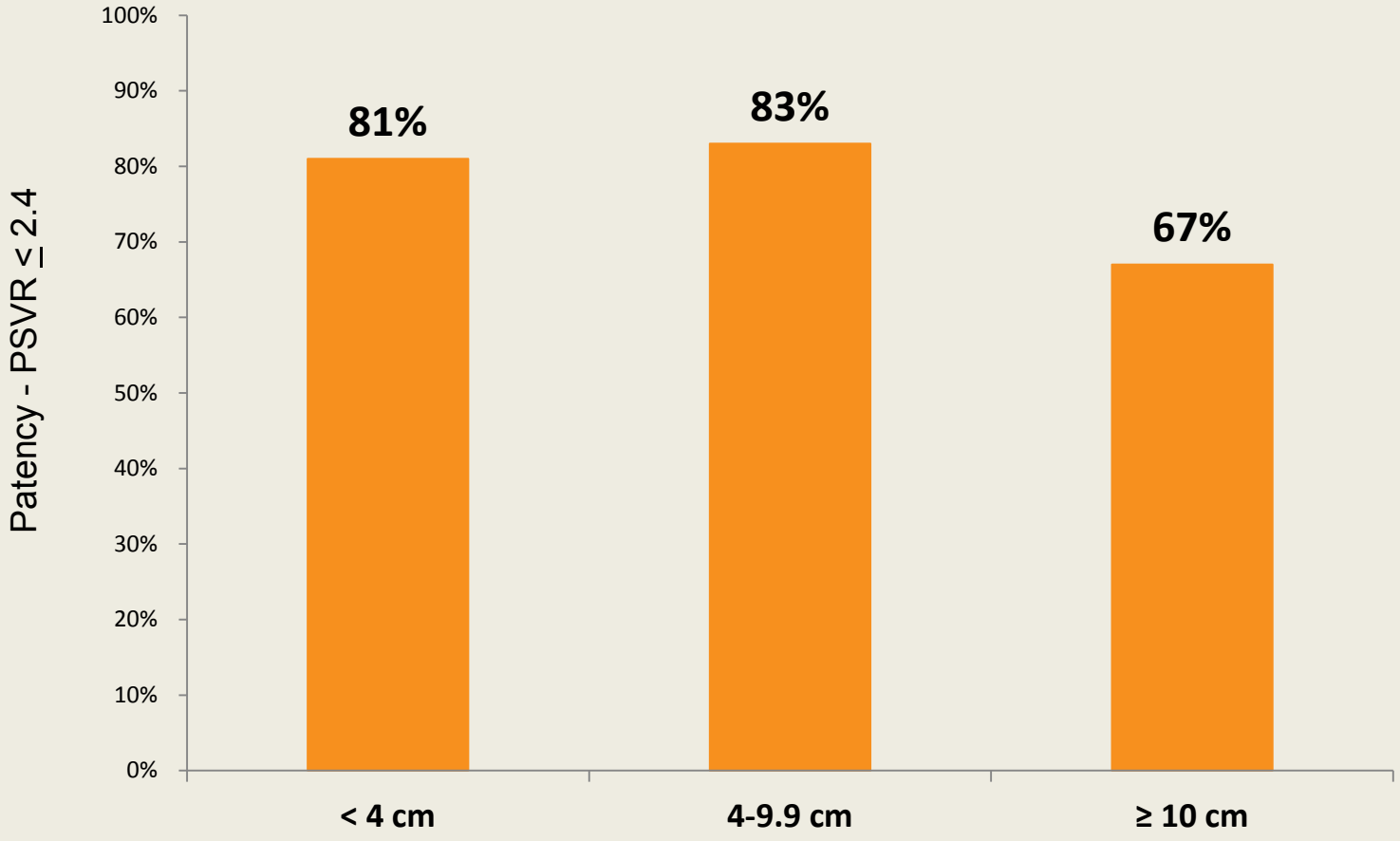
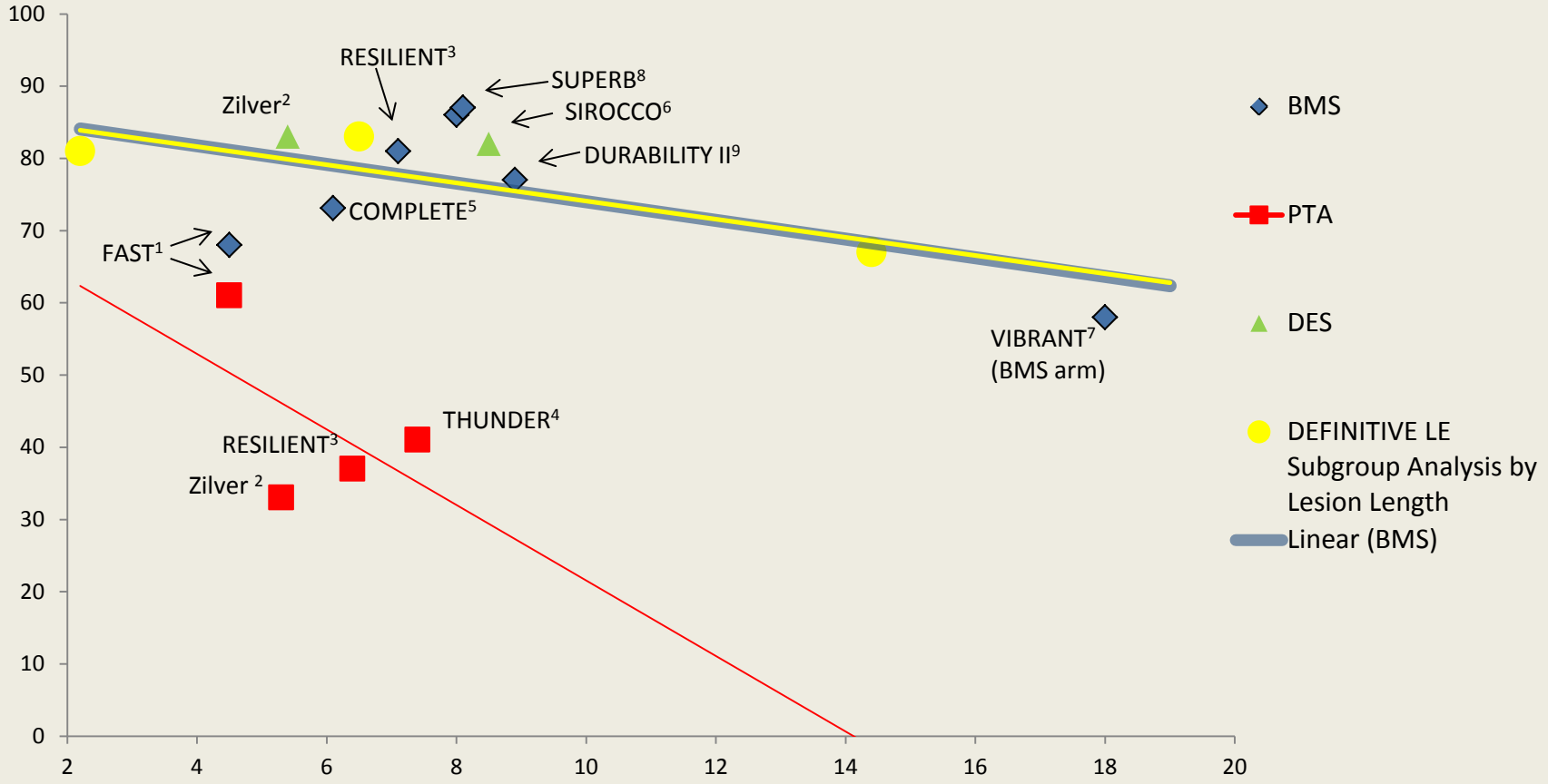
Primary Patency at 12 Month by Lesion Length



Mean length :	**2.2 cm**	**6.5 cm**	**14.4 cm**
Number of lesions:	**220**	**307**	**214**

SFA 12-Month Primary Patency

PTA, BMS, DES and DEF LE Sub-analyses by Lesion Length



1. Krankenberg et al. Circulation. 2007;
2. Dake et al. Circ Cardiovasc Interv. 2011
3. Laird et al. Circ Cardiovasc Interv. 2010
4. Tepe et al. NEJM 2008;358:689-99
5. Laird, ISET 2012
6. Duda et al. J Endovasc Ther 2006
7. Ansel, VIVA 2010
8. Rosenfield VIVA 2012
9. Matsumura ISET 2012

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Functional outcomes improved at 30 days and were maintained out to 1 year*

Outcome	Baseline	30-day	1-year
Mean Rutherford	3.1 ± 1.1	1.5 ± 1.7	1.3 ± 1.4
Mean ABI	0.65 ± 0.16	0.90 ± 0.18	0.83 ± 0.21
WIQ (Claudicants)			
Pain	54.9 ± 26.0	77.3 ± 23.6	79.1 ± 24.1
Distance	19.9 ± 24.2	46.5 ± 39.1	49.5 ± 38.0
Speed	20.3 ± 20.7	36.9 ± 29.4	39.4 ± 28.8
Stair Climbing	32.0 ± 31.0	49.9 ± 38.9	53.9 ± 37.6
EQ-5D Quest			
EQ-5D Index	0.71 ± 0.19	0.80 ± 0.19	0.81 ± 0.19
VAS Score	65.0 ± 19.2	71.0 ± 20.1	71.8 ± 18.8

*All outcomes significantly improved from baseline ($p < 0.001$)

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SFA Stent Trials

	TRIAL	TRIAL DESIGN	PSVR	PATIENTS Stent Arm		PRIMARY PATENCY %	REFERENCES
				Enrolled	At 1 year	Stent Arm - 1 year -	
1	Astron	Prospective, Randomized, Single center	PSVR<2.4	34	32	65,6	Dick P. et al, Catheter Cardiovasc Interv. 2009;74:1090-5.
2	Complete SE	Prospective, Single arm, Multicenter, Core lab controlled	PSVR≤2.0	196	175	73,1	Laird J. et al, The Complete SE SFA Trial. LINC 2012, Leipzig.
3	DURABILITY I	Prospective, Single arm, Multicenter, Core Lab controlled	PSVR≤2.4	151	134	72,2	Bosiers M. et al, J Endovasc Ther. 2009;16:261-269.
4	DURABILITY II	Prospective, Single arm, Multicenter, Core lab controlled	PSVR≤2.0	287	226	<80mm: 86,2 Mean: 77,2 >80mm: 69,6	Matsumura J. et al, DURABILITY II. ISET 2012, Miami.
5	DURABILITY 200	Prospective, Single arm, Multicenter	PSVR≤2.4	100	55	65,0	Bosiers M. et al, J Vasc. Surg. 2011;54:1042-1050.
6	VIVA Performance Goals	Meta Analysis	Statistical analysis of 3 RCT PMA and 5 published RCT trials	Meta Analysis	307	33,0	Rocha-Singh K. et al, Catheter Cardiovasc Interv. 2007;69:910-919.
7	RESILIENT	Prospective, Randomized, Multicenter, Core lab controlled	PSVR≤2.5	134	112	81,3	Laird J. et al, Circ Cardiovasc Interv. 2010;3:267-76.
8	SUPERA SFA	Retrospective, Single arm, Single center registry	PSVR≤2.4	107	88	84,7	Scheinert D. et al, J Endovasc Ther. 2011;18:745–752
9	SUPER-SL	Prospective, Randomized, Multicenter	PSVR≤2.5	96	N.A.	65,2	Duda S. et al, The SUPER-SL study. LINC 2009, Leipzig.
10	VIBRANT	Prospective, Randomized, Multicenter, Core lab controlled	PSVR≤2.5	72 76	N.A. N.A.	53,0 58,0	Ansel G. et al, Gore ViBRANT Trial. VIVA 2009, Las Vegas.
11	VIENNA Absolute	Prospective, Randomized, Single center	PSVR≤2.5	51	49	63,0	Schillinger M. et al, N Engl J Med. 2006;354:1879-1888.
12	Zilver PTX	Prospective, Randomized, Multicenter, Core lab controlled	PSVR≤2.0	Primary DES 241	222	83,0	Dake M. et al, Circ Cardiovasc Interv. 2011;4:495-504.