Drug eluting therapies:
Just do it !

Y. Gouëffic, MD, PhD

Department of vascular surgery, University hospital of Nantes, France

l'institut du thorax

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Disclosure

Speaker name: Yann Gouëffic

☒ have the following potential conflicts of interest to report:

☒ Receipt of grants/research support
Details: Abbott; Bard; Medtronic; Terumo; WL Gore

☒ Receipt of honoraria and travel support
Details: Abbott; Bard; Boston Sc; Cook; WL Gore; Medtronic; Perouse; Spectranetics

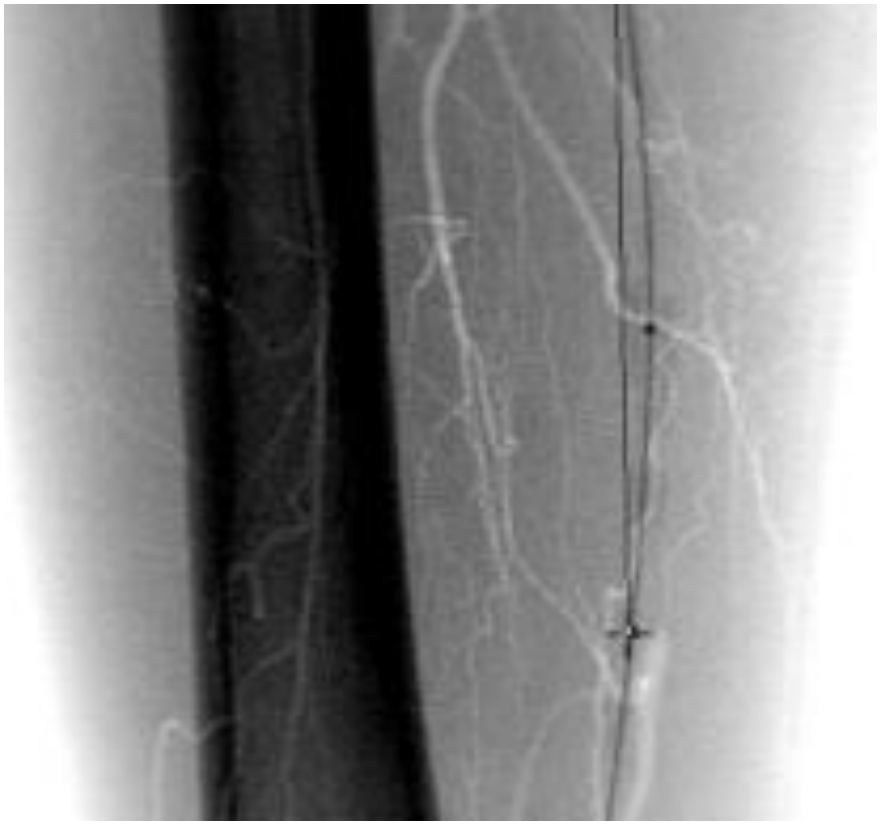
☐ Employment in industry
Details: /

☐ Shareholder in a healthcare company
Details: /

☐ Owner of a healthcare company
Details: /

☐ do not have any potential conflicts of interest to report

What is the best strategy for femoropopliteal lesions?



POBA

Bare metal stent

Drug eluting stent

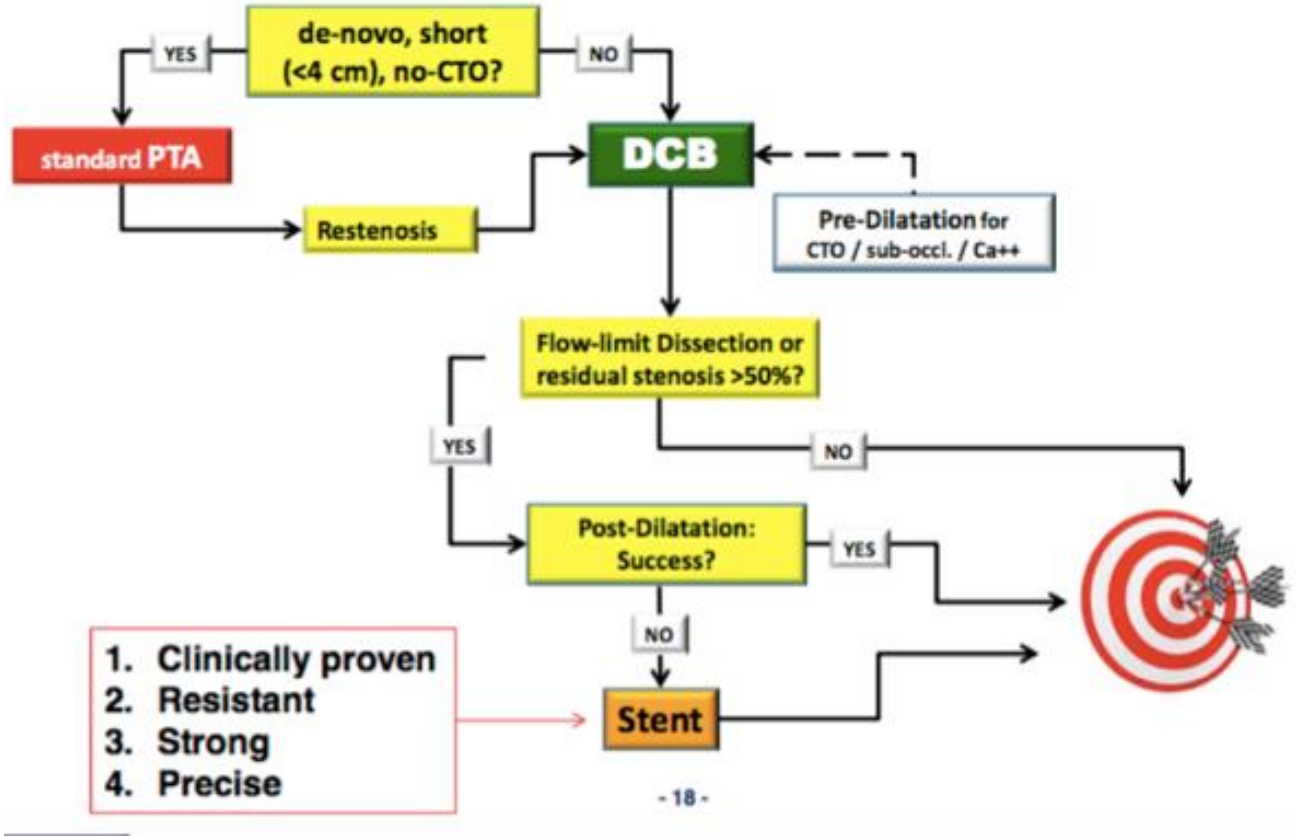
Drug eluting balloon

Covered stent

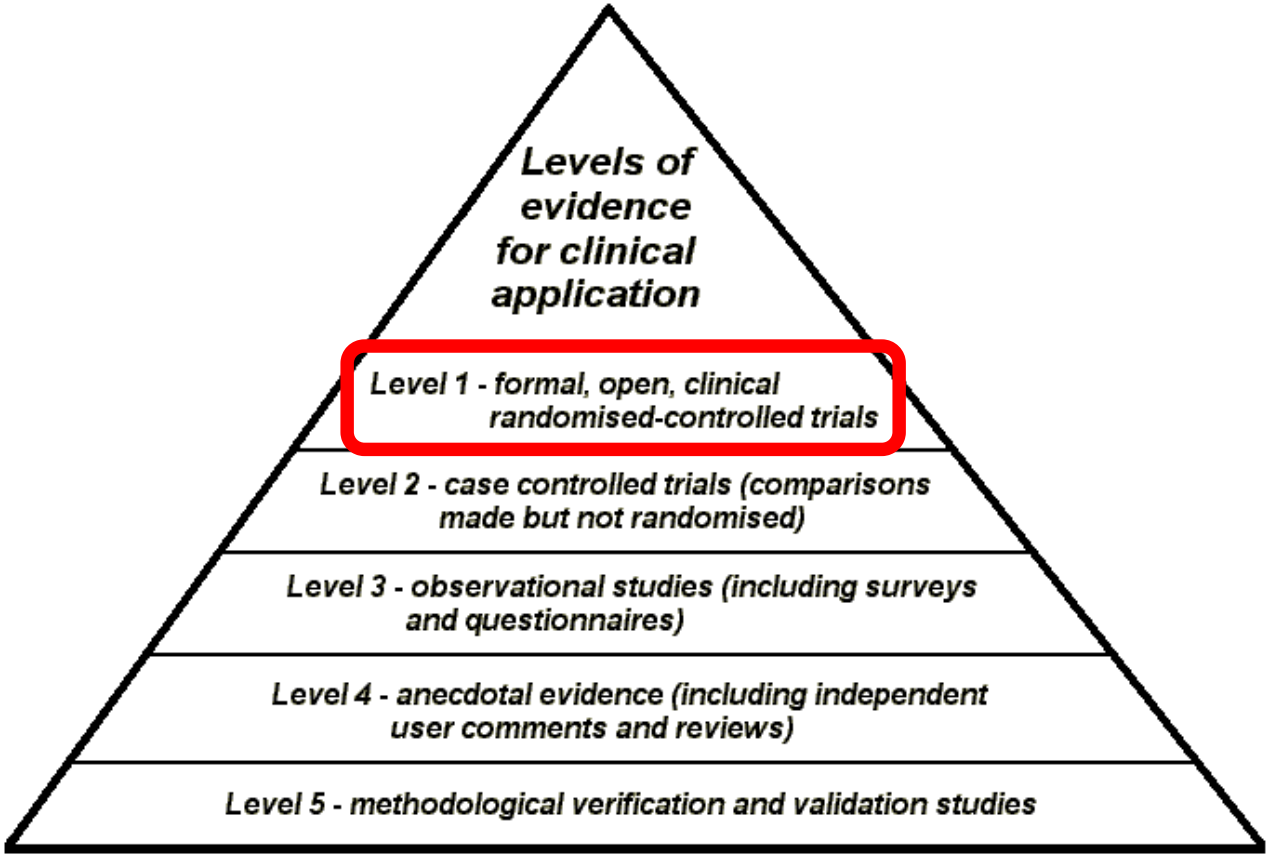
Bioresorbable stent

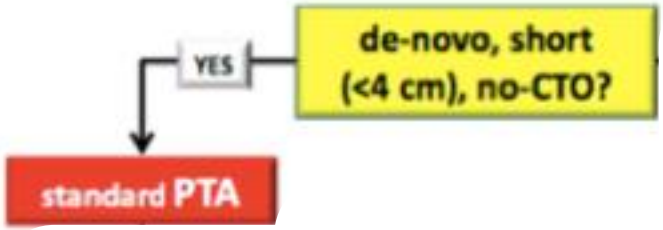
…

Algorythm


de-novo, short (<4 cm), no-CTO?
YES
NO
standard PTA
DCB
Restenosis
Pre-Dilatation for CTO / sub-occl. / Ca++
Flow-limit Dissection or residual stenosis >50%?
YES
NO
Post-Dilatation: Success?
YES
NO
Stent
1. Clinically proven
2. Resistant
3. Strong
4. Precise
- 18 -

5 levels of evidence





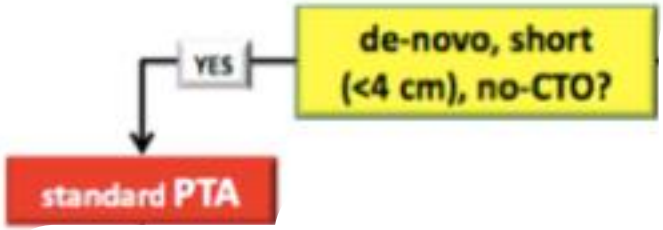
Systematic versus selective stent placement after superficial femoral artery balloon angioplasty: A multicenter prospective randomized study

Jean-Pierre Becquemin, MD,[a] Jean-Pierre Favre, MD,[b] Jean Marzelle, MD,[c] Chantal Nemoz, PhD,[d] Caroline Corsin,[d] and Alain Leizorovicz, MD,[d] *Créteil, St Etienne, Antony, and Lyon, France*

Nitinol Stent Implantation Versus Percutaneous Transluminal Angioplasty in Superficial Femoral Artery Lesions up to 10 cm in Length : The Femoral Artery Stenting Trial (FAST)

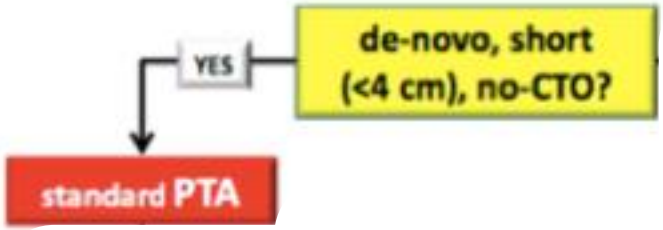
Hans Krankenberg, Michael Schlüter, Hermann J. Steinkamp, Karlheinz Bürgelin, Dierk Scheinert, Karl-Ludwig Schulte, Erich Minar, Patrick Peeters, Marc Bosiers, Gunnar Tepe, Bernhard Reimers, Felix Mahler, Thilo Tübler and Thomas Zeller

Becquemin, J Vasc Surg, 2003
Krankenberg, Circulation, 2007



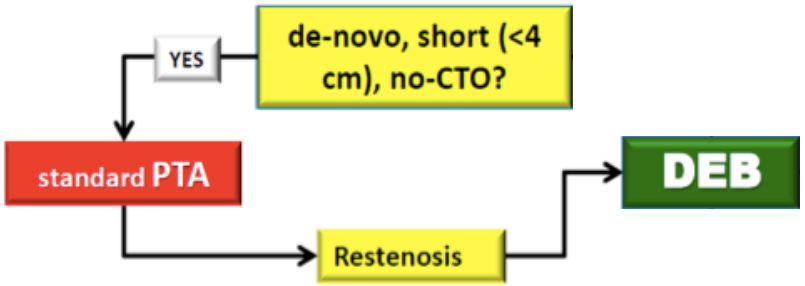
	Zilver PTX	MAJESTIC
Length	≤14-cm	≥30 mm and ≤110 mm
Mean treated length (cm)	61.8mm	70.8±28.1

Dake, Circ Cardiovasc Interv. 2011
Müller-Hülsbeck, J Endovasc, Ther, 2016



	IN-PACT SFA	LEVANT 2	ILLUMINATE RCT
Length (Inclusion criteria)	4-18 cm length or occulsion with lengths of ≤10 cm	≤15 cm	3-20 cm
Mean treted length (cm)	8.94±4.89	6.28±4.10	7.2± 5.2

Tepe, Circulation, 2014; Rosenfield, NEJM, 2015;
Schroeder, Circulation, 2017



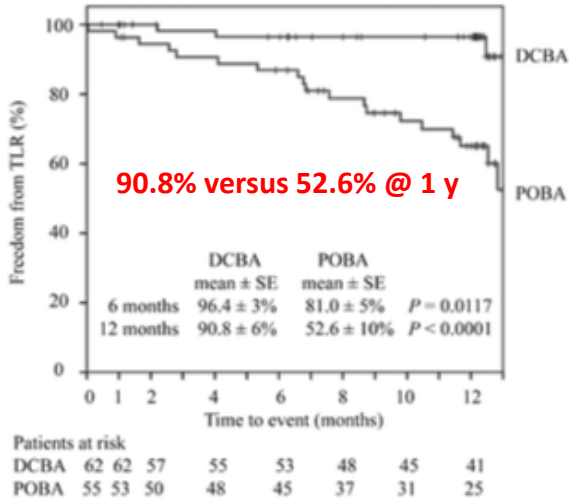
Interventional Cardiology

Drug-Coated Balloon Versus Standard Balloon for Superficial Femoral Artery In-Stent Restenosis

The Randomized Femoral Artery In-Stent Restenosis (FAIR) Trial

Hans Krankenberg, MD*; Thilo Tübler, MD*; Maja Ingwersen, DVM; Michael Schlüter, PhD; Dierk Scheinert, MD; Erwin Blessing, MD; Sebastian Sixt, MD; Arne Kieback, MD; Ulrich Beschorner, MD; Thomas Zeller, MD

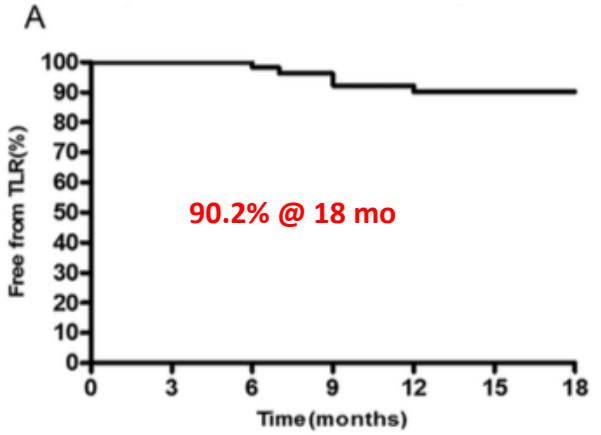
Mean lesion length: 82.2±68.4 mm
Complete occlusion: 28.6%



Femoropopliteal In-stent Restenosis Repair: Midterm Outcomes After Paclitaxel Eluting Balloon Use (PLAISIR Trial)

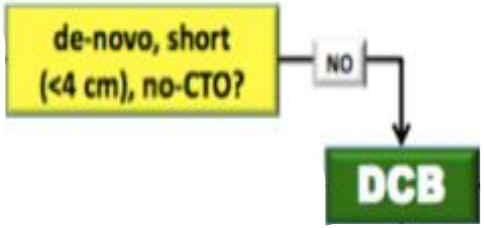
N. Bague [a], P. Julia [b], A. Sauguet [c], J.M. Pernès [d], P. Chatelard [e], J.F. Garbé [f], S. Penillon [g], J.M. Cardon [h], P. Commeau [i], O. Planché [j], B. Guyomarch [a], Y. Gouëffic [a,k,l,*]

Prospective registry (In Pact Admiral,Medtronic)
53 patients



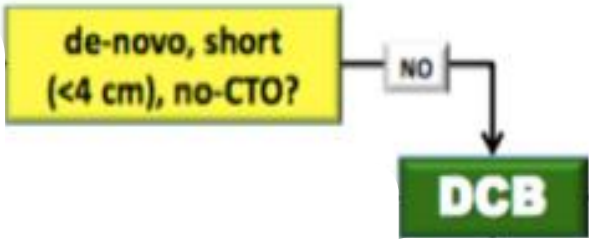
Months	0	3	6	12	18
Patients at risk (n)	55	54	53	44	40
Rate (%+/-SD)	100	100	98.1+/-1.9	90.2+/-4.2	90.2+/-4.2

Krankenberg, Circulation, 2015
Bague, Eur J Vasc Endovasc Surg, 2016



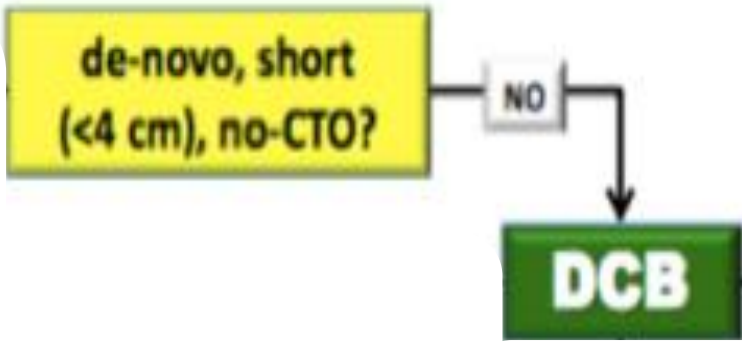
	IN-PACT SFA (DEB arm)	LEVANT 2 (DEB arm)	ILLUMINATE RCT (DEB arm)	RANGER SFA (DEB arm)
Patients (n)	220/111	316/160	222/72	71/34
Mean age	67.5±9.5	67.8±10.0	67±9	68±8
Intermittent claudication (%)	91	92.1	98	/
Mean length (cm)	8.94±4.89	6.28±4.10	7.2± 5.2	6.8±4.6
Severe calcifications (%)	8.1	10.4	13	36
Occlusions	25.8	21	19	34

Tepe, Circulation, 2014; Rosenfield, NEJM, 2015 ; Schroeder, Circulation, 2017; Bausback, J Endovasc Ther ,2017



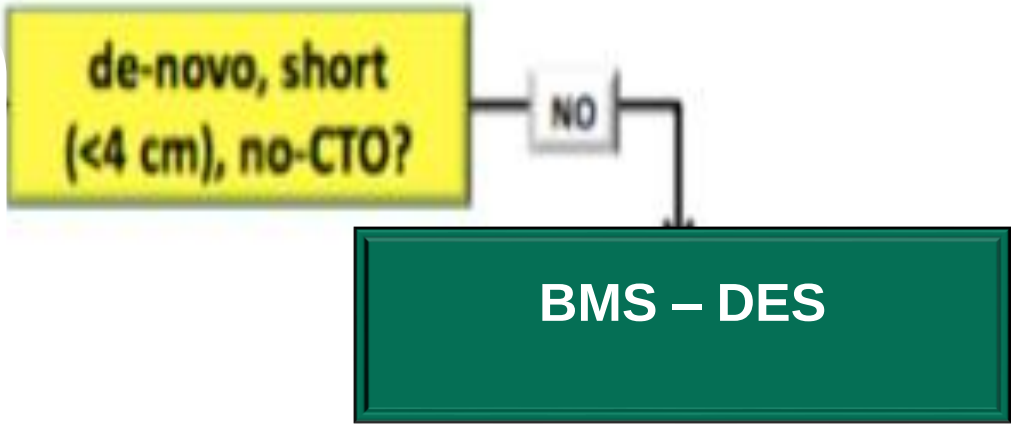
	IN-PACT SFA	LEVANT 2	ILLUMINATE RCT	RANGER SFA
Provisionnal stenting (%)	7.3	2.5	15	21
Iy patency rates at 12 months (%) (proportional rate)	82.2 vs. 52.4 p <0.001	65.2 vs. 52.6 p <0.02	83.9 vs. 60.6 p <0.001	86 vs 56 P<0.001
Iy patency rates at 24 months (%)	78.9 vs. 50.1 p < 0.001	58.6 vs. 53.0 p=0.05	89 vs 65 p <0.001	NA

Tepe, Circulation, 2014; Rosenfield, NEJM, 2015 ; Schroeder, Circulation, 2017; Bausback, J Endovasc Ther ,2017



In/Ex critieria ?

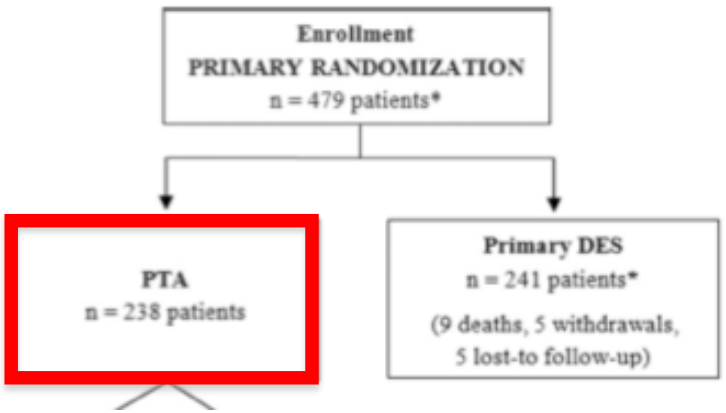
- Long lesions
- Failure of vessel prep
- Severe calicification

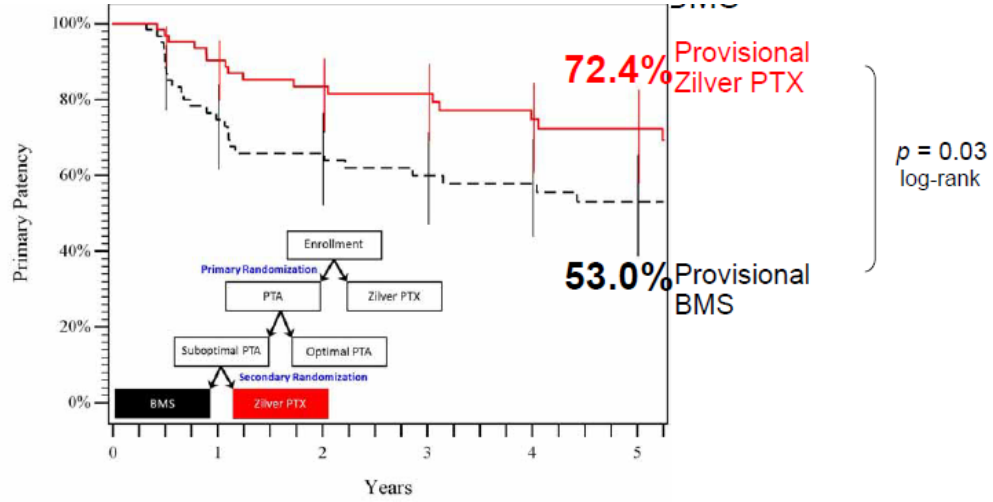

de-novo, short
(<4 cm), no-CTO?
NO
BMS – DES

?

Zilver PTX RCT

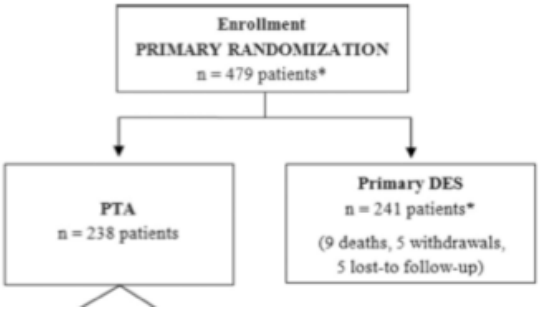
Zilver PTX vs POBA for TASC A/B femoropopliteal lesions
At 5 years, sustained clinical, morphological and hemodynamic outcomes





Dake, Circ Cardiovasc Interv. 2011
Dake, Circulation, 2016

Samples size calculation of Zilver-PTX RCT



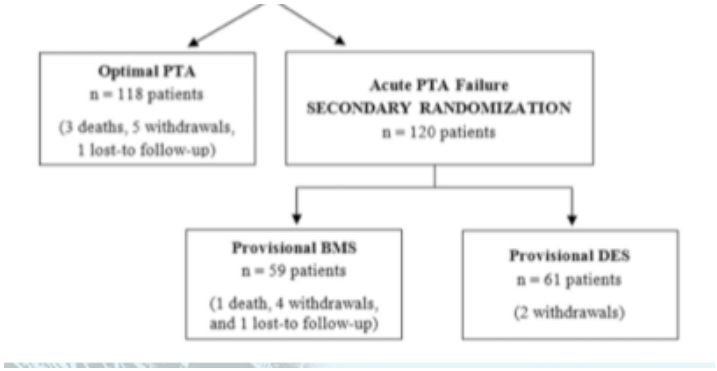
First arm of randomization

Primary end point

12-month rates of event-free survival and patency in the primary DES and PTA groups

describing femoropopliteal PTA outcomes.[21–26] The calculation assumed the 12-month primary patency rates were 65% and 80% in the PTA and DES groups, respectively. Power analysis was performed

479 patients to include



Second arm of randomization

- Sub groups
- Secondary endpoints

Dake, Circ Cardiovasc Interv. 2011

Clinical Investigation

JOURNAL OF ENDOVASCULAR THERAPY

Journal of Endovascular Therapy
2016, Vol. 23(5) 701–707

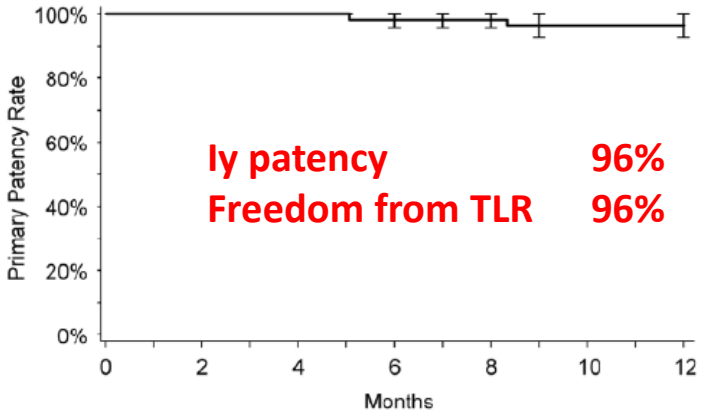
DOI: 10.1177/1526602816650206
www.jevt.org
SAGE

Twelve-Month Results From the MAJESTIC Trial of the Eluvia Paclitaxel-Eluting Stent for Treatment of Obstructive Femoropopliteal Disease

Stefan Müller-Hülsbeck, MD[1], Koen Keirse, MD[2], Thomas Zeller, MD[3], Herman Schroë, MD[4], and Juan Diaz-Cartelle, MD[5]

Prospective, multicentre, single-arm, open label (n= 57)

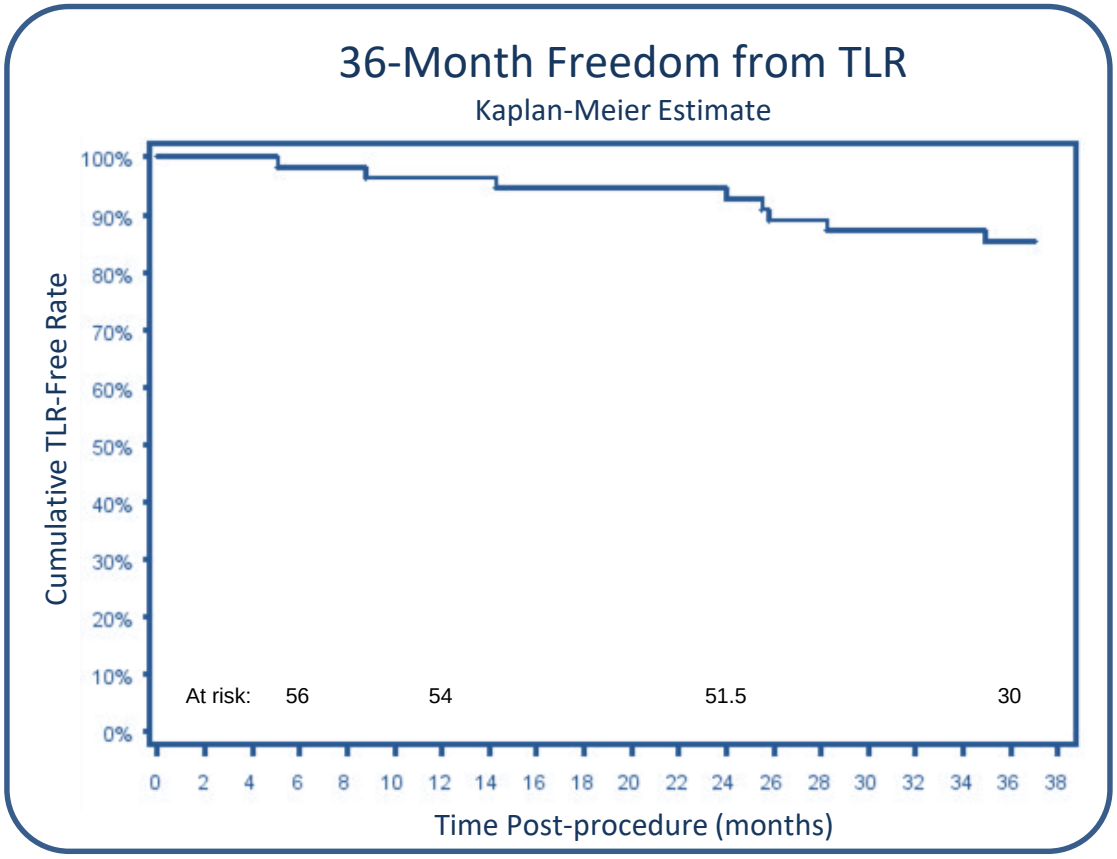
Mean age	69±9 years
Diabetes	35%
Restenotic lesions	-
Mean lesion length	70.8±28.1 mm
Occlusions	46%
TASC A/B	90%



Number of patients:	Time from index procedure (months)				
	0	1	6	9	12
At Risk	57	56.5	56	54.5	37
Censored	0	1	0	1	32
Events	0	0	1	1	0
Patency Rate	100%	100%	98.2%	96.4%	96.4%

Müller-Hülsbeck, J Endovasc ther, 2016

Majestic at 36 months



85.3% freedom from TLR rate (K-M estimate)

No target limb major amputations

2 deaths at >365 days post-procedure, unrelated to study device or procedure

No stent fractures

	12 Months	24 Months
TLR	**96.4%**	**92.8%**
Primary Patency[b]	**96.4%**	**83.5%**
Assisted Primary Patency	**98.2%**	**88.9%**

Müller-Hülsbeck S. CIRSE 2017. Müller-Hülsbeck S. et al, Cardiovasc Interv Radiol 2017, doi: 10.1007/s00270-017-1771-5.

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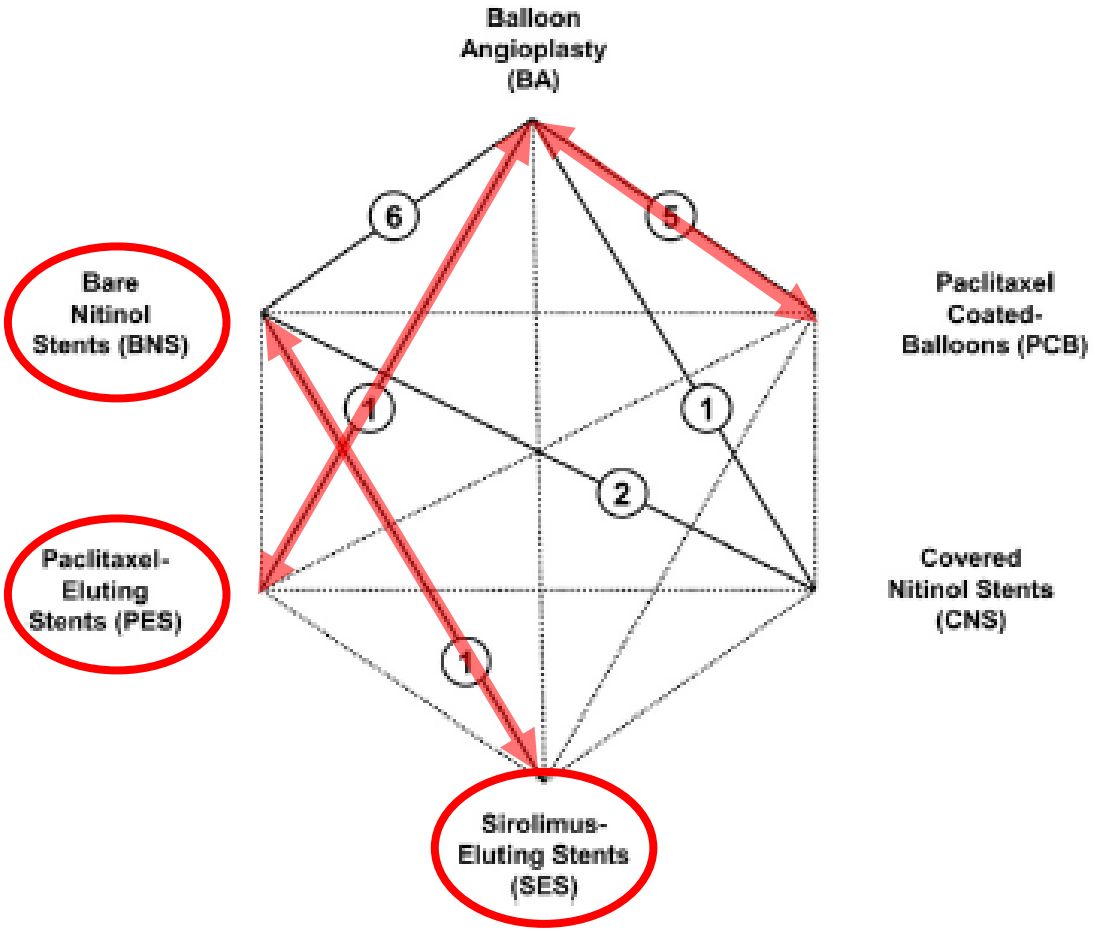
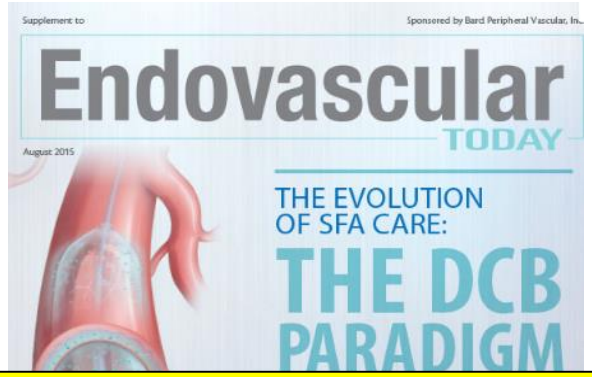
Few head to head comparison between devices for FP lesions treatment

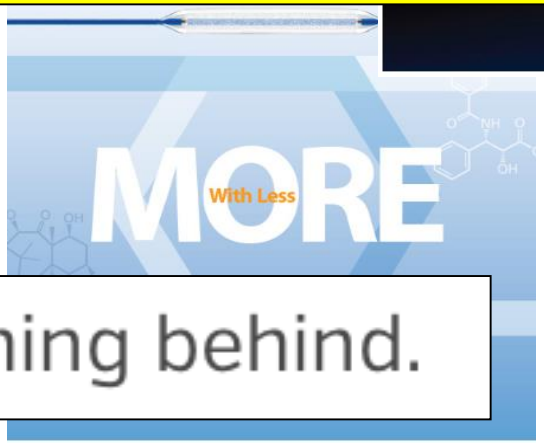


Katsanos, J Vasc Surg, 2014

POBA
the weakest competitor



No high level evidence support an algorythm to treat femoropopliteal lesions > 4-cm



leaving nothing behind.

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CLASH OF THE TITANS
LEGENDARY PICTURES
real 3D
WARNER BROS. PICTURES

BATTLE trial

(ClinicalTrials.gov number, NCT02004951)

French multicentric randomized clinical trial comparing MISAGO vs. ZILVER PTX for the treatment of intermediate femoropopliteal lesions

12-months outcomes with 186 patients will be released in 2018

10 centers: Clinique d'Antony (Jean-Marc PERNES); CHU de Besançon (Simon RINCKENBACH); CHU de Bordeaux (Eric DUCASSE) ; CHU de Clermont Ferrand (Eugenio [illegible]ndor (Pascal DESGRANGES) ; CH de Lyon (Patrick FEUGIER) ; [illegible] (Patrick LE[illegible]RMUSIAUX); Clinique Ollioules (Philippe COMM[illegible]EAU) ; CHU de Rennes (Alain CARDON) ; Clinique Pasteur (Antoine SAUGUET); CHU de Nantes (Yann GOUËFFIC)

Principal investigator: Pr Gouëffic
Sponsor: **Nantes University Hospital**
Granted from the French ministry of health (PHRC 2010 DGOS 20-03)

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IMPERIAL trial

Clinical Study Overview: IMPERIAL	Enrollment completed
Title	A randomIzed trial coMParing the ELUVIA dRug-elutIng stent versus Zilver PTX stent for treatment of superficiAL femoral and/or proximal popliteal arteries
Primary Investigators	Global: William A. Gray, MD European: Prof. Dr. med Stefan Müller-Hülsbeck
Objective	To evaluate the safety and effectiveness of the ELUVIA Drug-Eluting Vascular Stent System (ELUVIA Stent) for treating Superficial Femoral Artery (SFA) and/or Proximal Popliteal Artery (PPA) lesions up to 140 mm in length.
Study Design	The trial consists of the following: •A prospective, multicenter, 2:1 randomized (ELUVIA vs Zilver PTX), controlled, single-blind, non-inferiority trial (RCT) •A concurrent, non-blinded, non-randomized, single-arm, pharmacokinetic (PK) substudy A subject may be enrolled in the RCT or the substudy; but not in both

EMINENT Clinical Study

Clinical Study Overview: EMINENT	Ongoing
Title	A Randomized Trial Comparing the ELUVIA™ Drug-Eluting Stent versus Bare Metal Self-Expanding Nitinol Stents in the Treatment of Superficial Femoral and/or Proximal Popliteal Arteries
Coordinating Principal Investigators	Prof. Yann Goueffic, Nantes, France Prof. Giovanni Torsello, Münster, Germany
Objective	To confirm superior effectiveness of the ELUVIA Drug-Eluting Vascular Stent System (ELUVIA Stent) for treating Superficial Femoral Artery (SFA) and/or Proximal Popliteal Artery (PPA) lesions up to 140 mm in length when compared against bare metal stents, and collect additional data including health economics data.
Study Design	Prospective, multi-centre, single-blind, superiority trial (RCT) Randomized 2:1 (Eluvia : Self Expanding BMS)
Subjects	750 subjects to receive treatment •Test Device – Eluvia Drug Eluting Vascular Stent System • N=500 subjects •Control device N=250 • Self Expanding Bare Nitinol Stents with US approval and CE marking

Caution: Eluvia is an investigational device limited under US law for investigational use only. Not available for sale in the U.S.

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EMINENT enrollment by country

Country	Enrollment	Sites Activated to Enroll
AT	21	3
BE	25	7
CH	8	4
DE	62	20
ES	13	1
FR	42	13
IE	1	1
IT	12	3
NL	6	3
UK	10	8
Total	200	63

Enrollment as of 23Jan2018

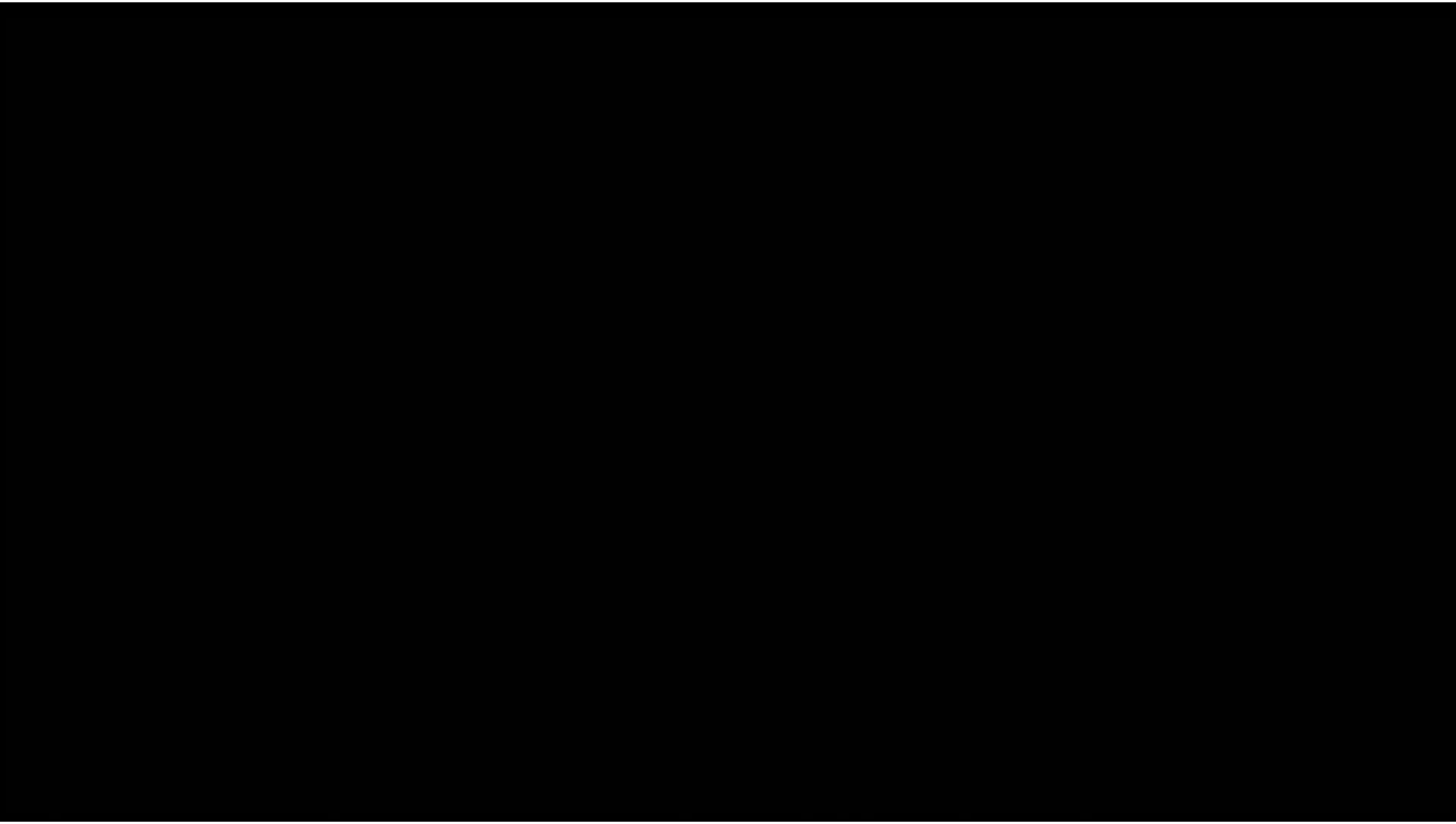
Activated centers to enroll in France

City	Center	Investigator	Enrollment
Nantes	CHU NANTES	Goueffic	11
Lille	CHU Lille	Sobocinski	5
Clermont-Ferrand	CHU CLERMONT-FERRAND	Rosset	5
Toulouse	CL SARRUS TEINTURIERS	Sauguet	4
Paris	Hôpital Européen Georges-Pompidou	Del Guidice	4
Saint Nazaire	CHU de Saint-Nazaire	Guillemot	3
Lyon	HEH (CHU - HCL)	Feugier	2
Strasbourg	CHU STRASBOURG	Thaveau	2
Nancy	CHU Nancy	Settembre	2
Valenciennes	CHU Valenciennes	Bianchini	2
Dijon	CHU DIJON	Steinmetz	1
Champigny	Hôpital Privé Paul d'Egine	Becquemin	1
Créteil	CHU MONDOR (CHU - APHP)	Desgranges	0
Marseille	SCAPP TIMONE (CHU - APHM)	Bartoli	0

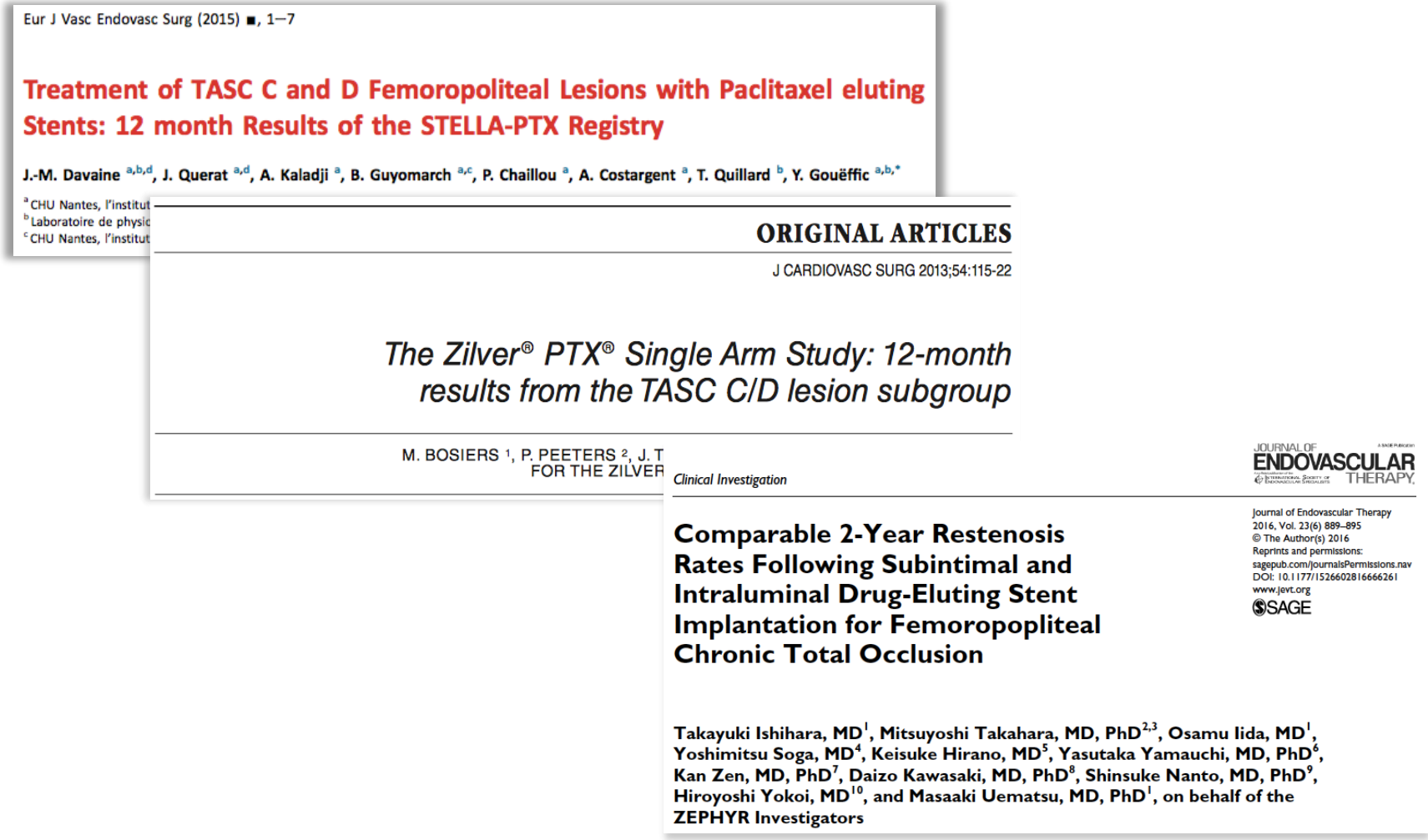
Enrollment as of 23Jan2018

Take home message

- **Lesions de novo < 4-cm: POBA**
- **Restenosis: DCB**
- **Lesions de novo > 4-cm: BMS, DES, DCB BUT POBA**



Drug eluting stent trials for TASC C/D femoropopliteal lesions



Eur J Vasc Endovasc Surg (2015) ■, 1—7

Treatment of TASC C and D Femoropoliteal Lesions with Paclitaxel eluting Stents: 12 month Results of the STELLA-PTX Registry

J.-M. Davaine [a,b,d], J. Querat [a,d], A. Kaladji [a], B. Guyomarch [a,c], P. Chaillou [a], A. Costargent [a], T. Quillard [b], Y. Gouëffic [a,b,*]

[a] CHU Nantes, l'institut
[b] Laboratoire de physic
[c] CHU Nantes, l'institut

ORIGINAL ARTICLES

J CARDIOVASC SURG 2013;54:115-22

The Zilver® PTX® Single Arm Study: 12-month results from the TASC C/D lesion subgroup

M. BOSIERS [1], P. PEETERS [2], J. T
FOR THE ZILVER

Clinical Investigation

JOURNAL OF ENDOVASCULAR THERAPY

Comparable 2-Year Restenosis Rates Following Subintimal and Intraluminal Drug-Eluting Stent Implantation for Femoropopliteal Chronic Total Occlusion

Journal of Endovascular Therapy
2016, Vol. 23(6) 889–895
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sagepub.com/journalsPermissions.nav
DOI: 10.1177/1526602816666261
www.jevt.org
SAGE

Takayuki Ishihara, MD[1], Mitsuyoshi Takahara, MD, PhD[2,3], Osamu Iida, MD[1], Yoshimitsu Soga, MD[4], Keisuke Hirano, MD[5], Yasutaka Yamauchi, MD, PhD[6], Kan Zen, MD, PhD[7], Daizo Kawasaki, MD, PhD[8], Shinsuke Nanto, MD, PhD[9], Hiroyoshi Yokoi, MD[10], and Masaaki Uematsu, MD, PhD[1], on behalf of the ZEPHYR Investigators

Davaine, Eur J Vasc Endovasc Surg, 2015
Bosiers, J Cardiovasc Surg, 2013
Ishihara, J Endovasc Ther, 2016

2-Year Results of Paclitaxel-Coated Balloons for Long Femoropopliteal Artery Disease

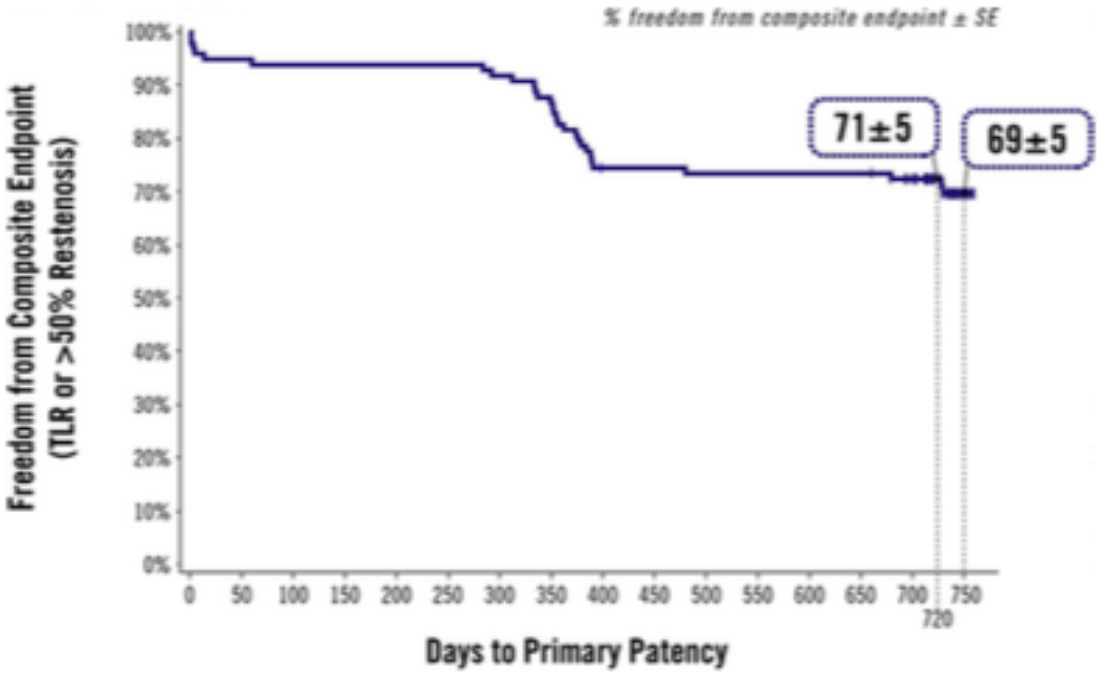
Evidence From the SFA-Long Study

Antonio Micari, MD, PhD,[a] Roberto Nerla, MD,[a] Giuseppe Vadalà, MD,[b] Fausto Castriota, MD,[a] Chiara Grattoni, MD,[a] Armando Liso, MD,[c] Paolo Russo, MD,[d] Paolo Pantaleo, MD,[e] Giuseppe Roscitano, MD,[f] Alberto Cremonesi, MD[a]

Prospective,multicenter,single-arm study

Age 68±9 years;
Limbs: 105
IC/CLI: 89.5/10.5
Diabetes: 57.2%
De novo lesions: 91.4%
Lesion length (mm)251.71±78.9mm
Total occlusions: 49.5%

Bailout stenting rate was 10.9%.



Micari, J Am Coll Cardiol Intv 2017