CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE
CONTROVERSIES & UPDATES IN VASCULAR SURGERY
JANUARY 19-21 2017
MARRIOTT RIVE GAUCHE & CONFERENCE CENTER
PARIS, FRANCE

Drug coated stents versus bare metal stents: are DCS superior? **Proof are lacking**

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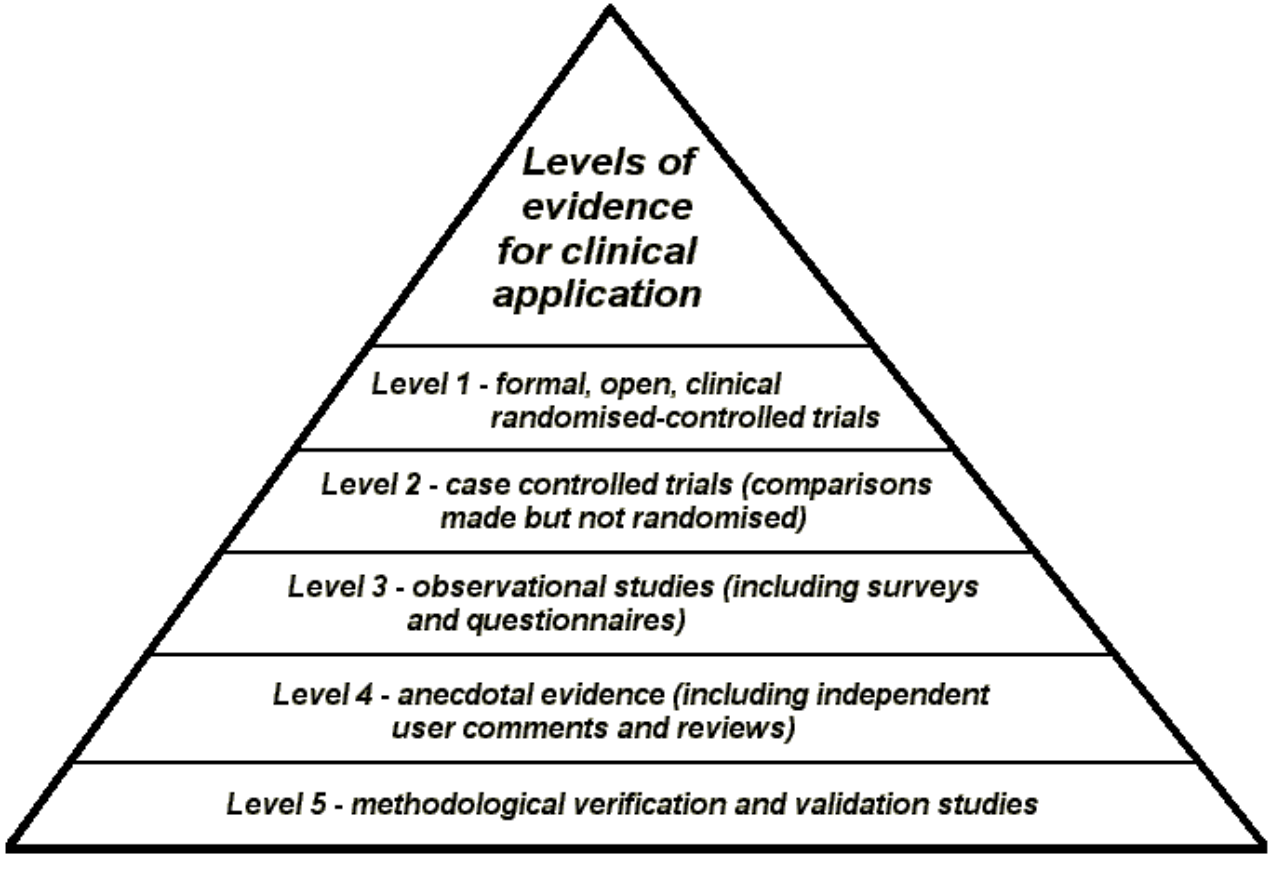
www.cacvs.org

Disclosures

Research grants /Consulting/Honoraria for

- Abbott
- Bard
- Boston Sc
- Cook
- Medinol
- Medtronic
- Perouse
- Spectranetics
- Terumo
- WL Gore

5 levels of evidence



Drug eluting stent trials for TASC A/B femoropopliteal lesions

Sirocco

(Duda, J Endovasc Ther 2006)

Strides

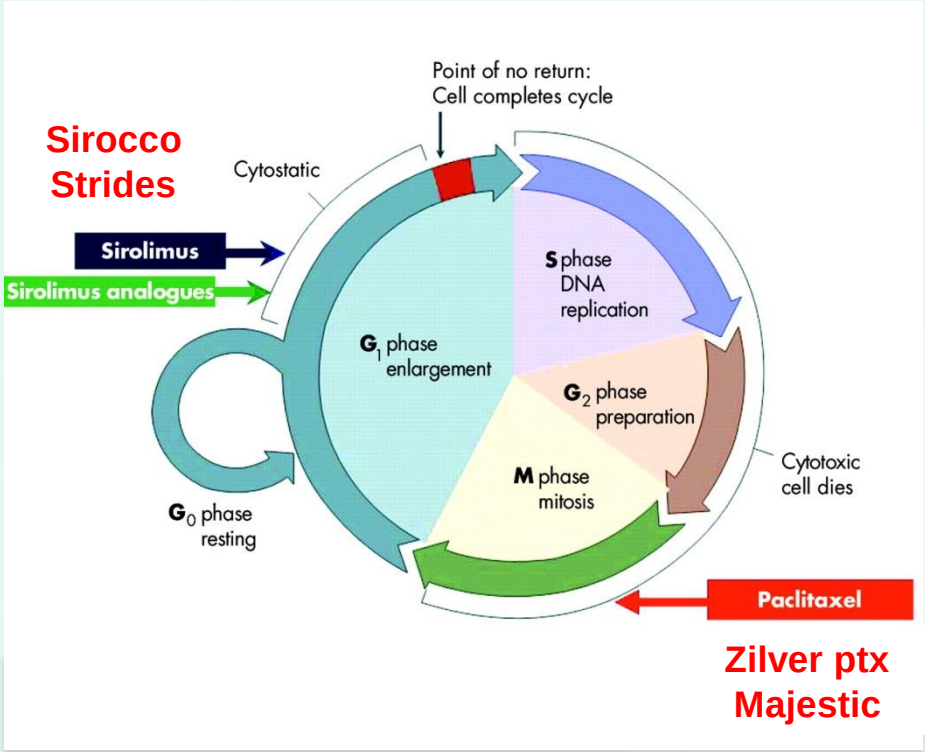
(Lammer, J Vasc Surg, 2011)

Zilver ptx

(Dake, Circ Cardiovasc Interv 2011)

Majestic

(Müller-Hülsbeck, J Endovasc, Ther, 2016)



Cytostatic drug eluting stents failed to prevent ISR

Sirocco

(Duda, J Endovasc Ther 2006)

Duplex Ultrasound In-Stent Restenosis Rates

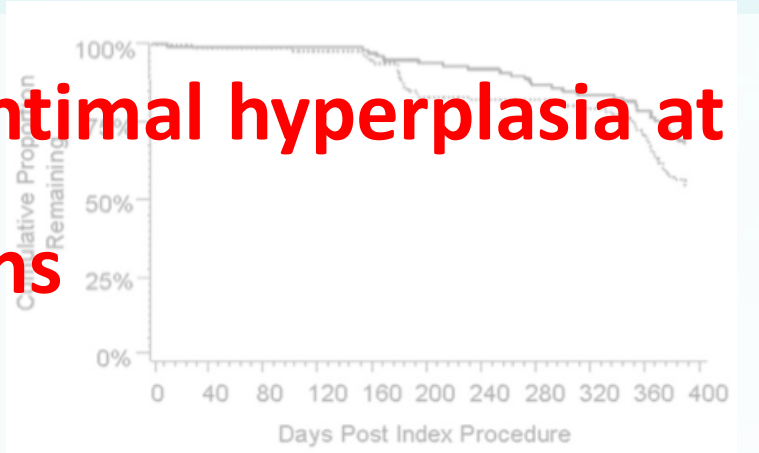
	Sirolimus Stent	Bare Stent
6 Months	4.8%; 0.6% to 16.2% (n=42)	4.5%; 0.6% to 15.5% (n=44)
9 Months	7.1%; 1.5% to 19.5% (n=42)	11.1%; 3.1% to 2[illegible]% (n=36)
18 Months	18.4%; 7.7% to 34.3% (n=38)	12.8%; 4.3% to 2[illegible]% (n=[illegible])
24 Months	22.9%; 10.4% to 40.1% (n=35)	21.1%; 9.6% to 37.3% (n=38)

Data presented as the rate and 95% Clopper-Pearson confidence intervals.

ISR: *NS*

Strides

(Lammer, J Vasc Surg, 2011)



Iry patency: 68±4,6%
TLR: 28%

No sustained inhibition of intimal hyperplasia at 12 months

Clinical Investigation

JOURNAL OF ENDOVASCULAR THERAPY

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

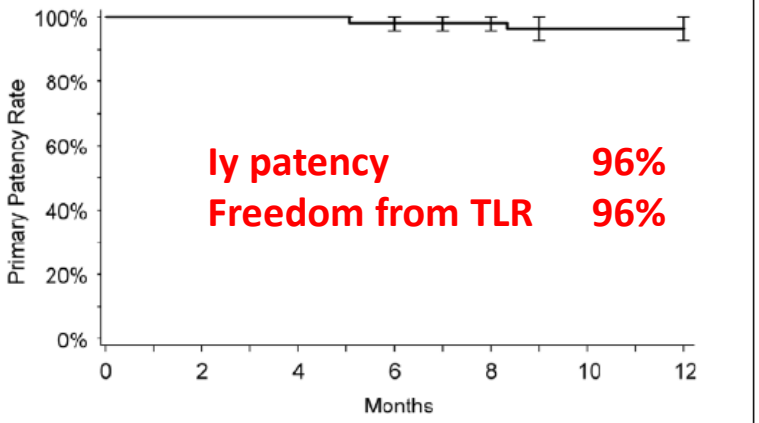
DOI: 10.1177/1526602816650206
www.jevt.org
SAGE

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%

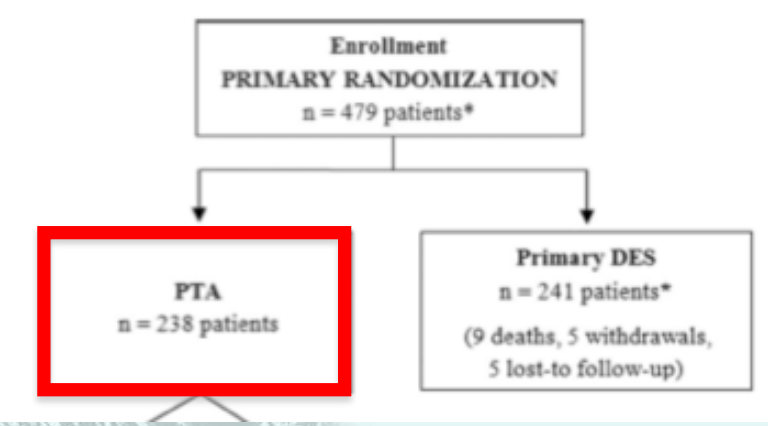


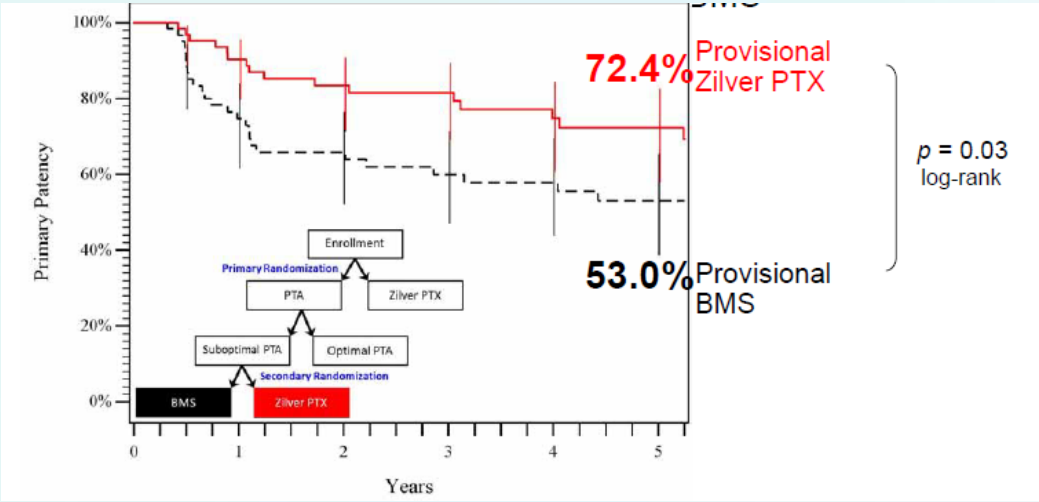
Number of patients:	Time from index procedure (months)				
	0	1	6	9	12
At Risk	57	56.5	56	54.5	37
Censored	0	1	0	1	32
Events	0	0	1	1	0
Patency Rate	100%	100%	98.2%	96.4%	96.4%

Müller-Hülsbeck, J Endovasc ther, 2016

Zilver PTX RCT

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

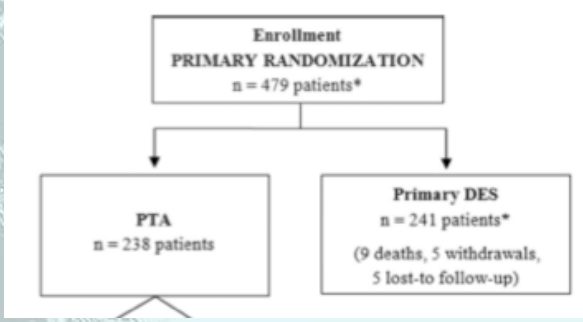




Dake, Circ Cardiovasc Interv. 2011

Dake, Circulation, 2016

Samples size calculation of Zilver-PTX RCT



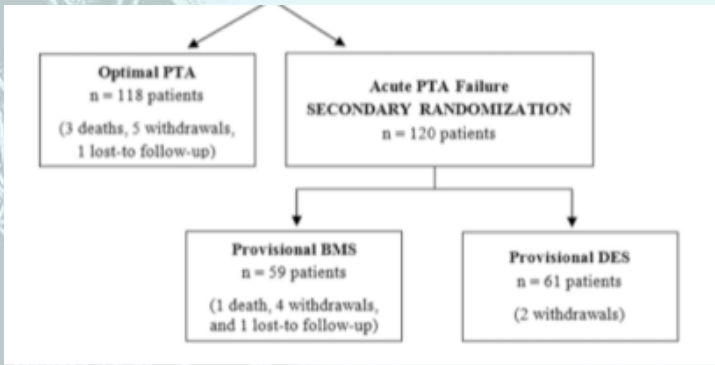
First arm of randomization

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

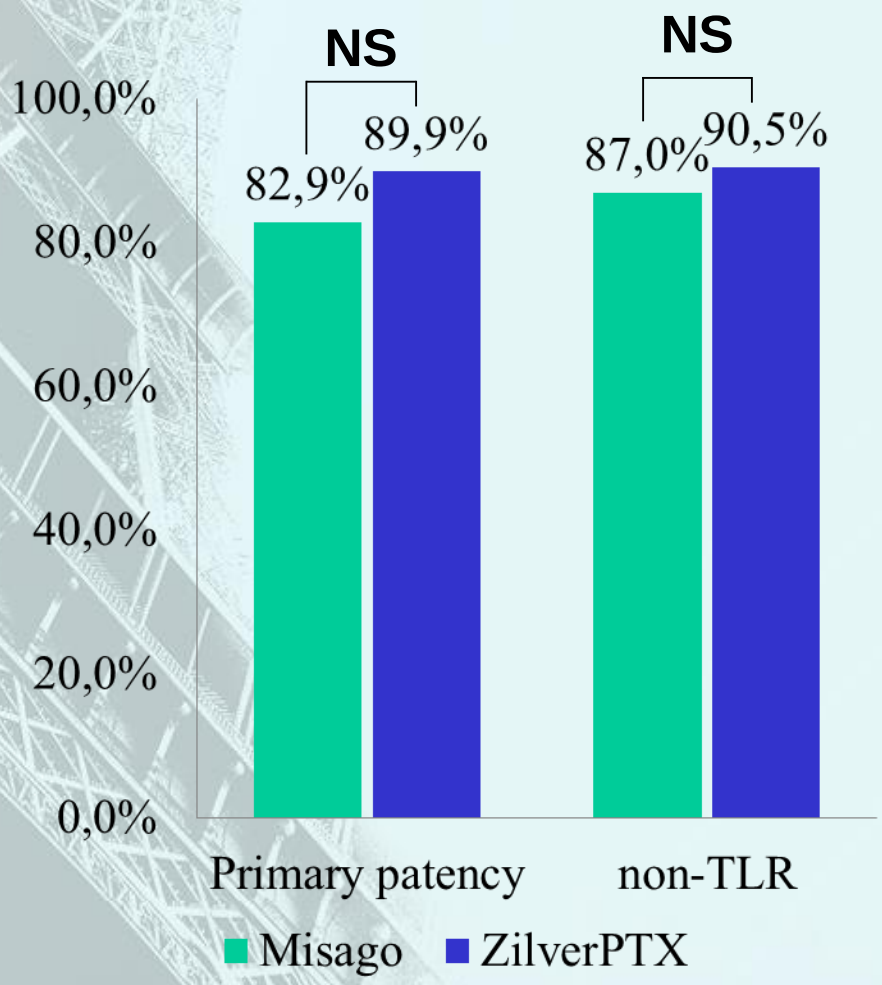
Dake, Circ Cardiovasc Interv. 2011

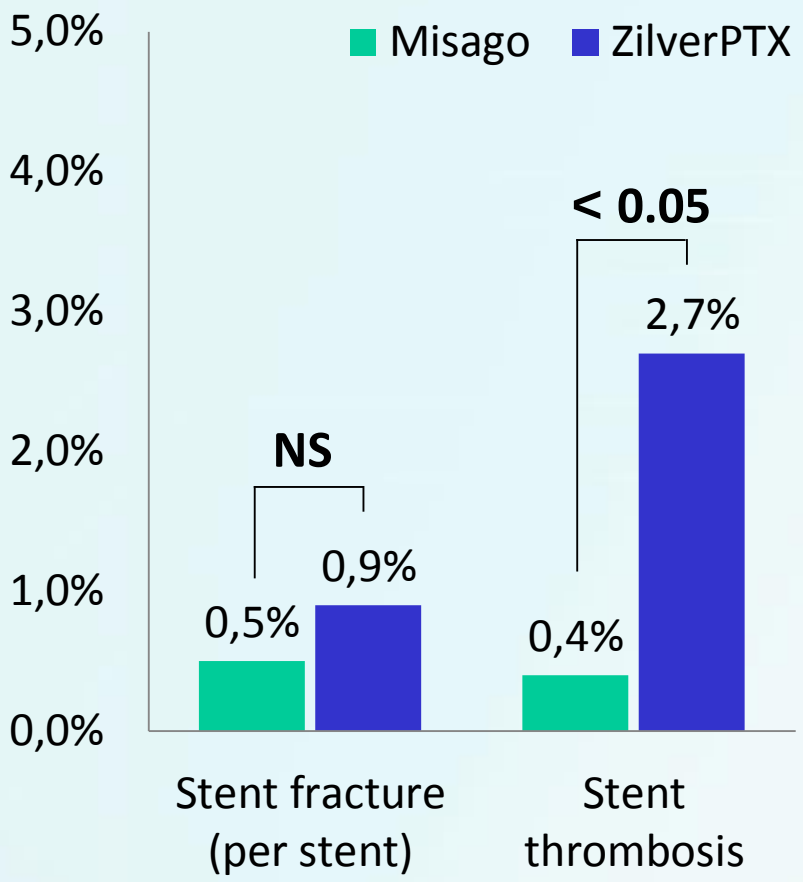
Sub groups and secondary endpoints analysis

We can not draw any conclusions from the second arm of randomization

MeReC Briefing (2005);30:1-7.
Best Pract Res Clin Obstet Gynaecol. 2005;19(1):15-26.
Wiebe S. The principles of evidence-based medicine.Cephalalgia. 2000;20 Suppl 2:10-3.
Drug and Therapeutics Bulletin 2006; 44(3):21.

Indirect Comparison between BMS (Misago) and DES (Zilver PTX) *(Results @ 12months)*





Ohki A. et al. Journal of Vascular Surgery 2016

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 du thorax, service de chirurgie vasculaire, Nantes, France
[b] Laboratoire de physiopathologie de la résorption osseuse, UMR-957, Nantes, France
[c] CHU Nantes, l'institut du thorax, centre d'investigation clinique, Nantes, France

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. TESSAREK [3], K. DELOOSE [1], S. STRICKLER [4]
FOR THE ZILVER PTX SINGLE-ARM STUDY INVESTIGATORS

Clinical Investigation

JOURNAL OF ENDOVASCULAR THERAPY

Journal of Endovascular Therapy
2016, Vol. 23(6) 889–895

DOI: 10.1177/1526602816666261
www.jevt.org
SAGE

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

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

Demographic and morphologic data for long FP lesions

	STELLA-ptx	Zilver-ptx	Zephyr
Limbs (n)	48	135	192
Mean Rutherford stage	4.1	-	-
IC/CLI (%)	52/48	-	69/31
TASC C/D (%)	58/42	-	-
Mean length of treated segment (mm)	252	226	205
Mean number of stent/limb	2.9	3.4	-

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

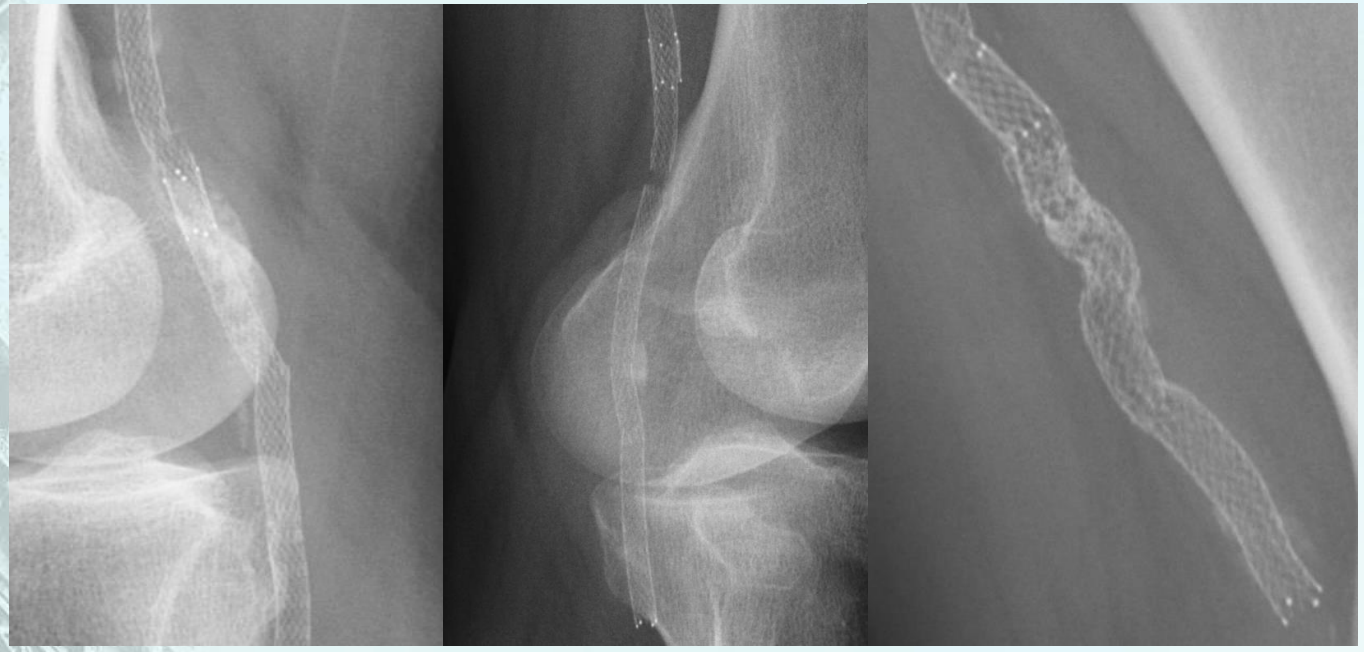
Clinical and morphological outcomes for long FP lesions @ 1 year

	STELLA-ptx	Zilver-ptx	Zephyr (Sub/intra)
Iry sustained clinical improvement (%)	63.3	84.7	-
Freedom from TLR (%)	64	85.4	-
Primary patency (%)	52.5	77.6-	-
ISR (%)	25	-	35-45

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

Stent fractures

	STELLA-ptx	Zilver-ptx	Zephyr (Sub/intra)
Stent fracture in a limb basis (%)	12.5	2.1	-



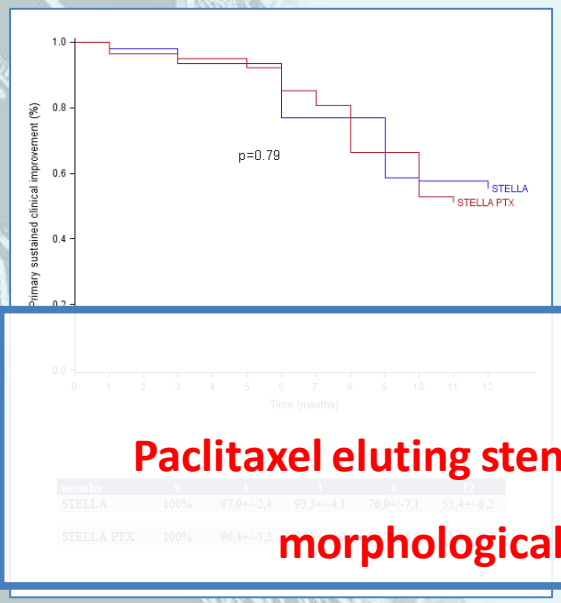
Davaine, Eur J Vasc Endovasc Surg, 2015

Original report

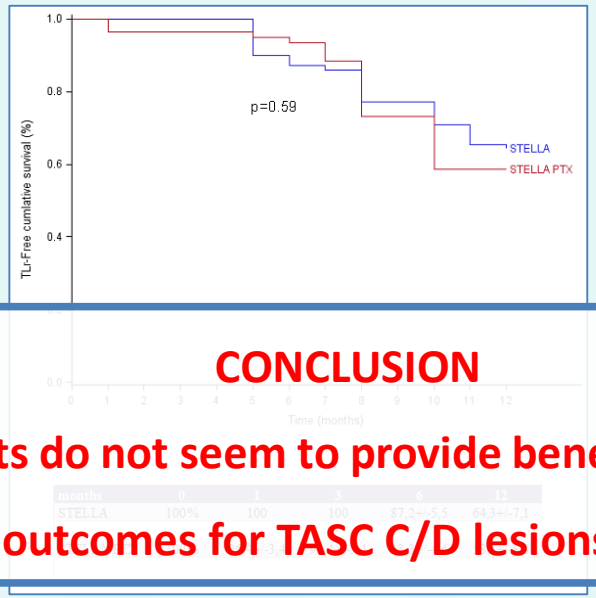
Bare metal versus paclitaxel eluting stents for long femoropopliteal lesions: prospective cohorts comparison using a propensity-score matched analysis.

Pierre-Alexandre Vent[1], Adrien Kaladji[2], Jean-Michel Davaine[1], Béatrice Guyomarch[3-4-5-6], Philippe Chaillou[1], Alain Costargent[1], Thibaut Quillard[7], Yann Gouëffic[1, 6, 7]

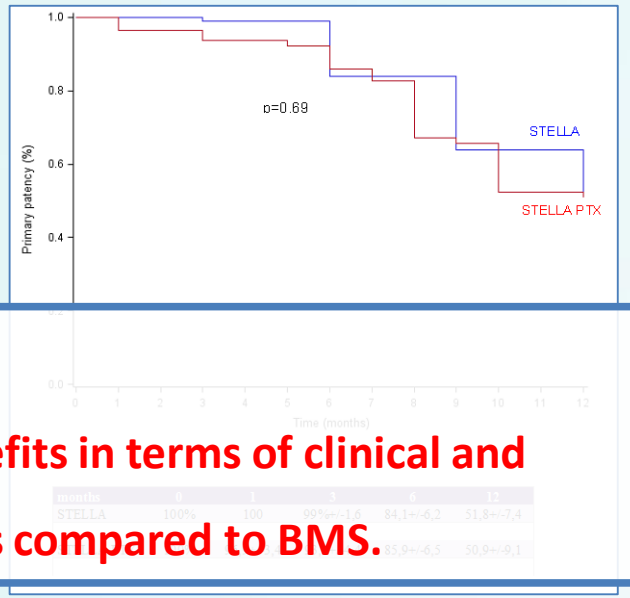
Sustained primary clinical improvement with adjusted data



TLR-free cumulative survival with adjusted data



Patency cumulative survival with adjusted data



CONCLUSION

Paclitaxel eluting stents do not seem to provide benefits in terms of clinical and morphological outcomes for TASC C/D lesions compared to BMS.

Vent, Ann Vasc Surg, In press

Take home message

Proofs are lacking to show the superiority of DES/BMS:

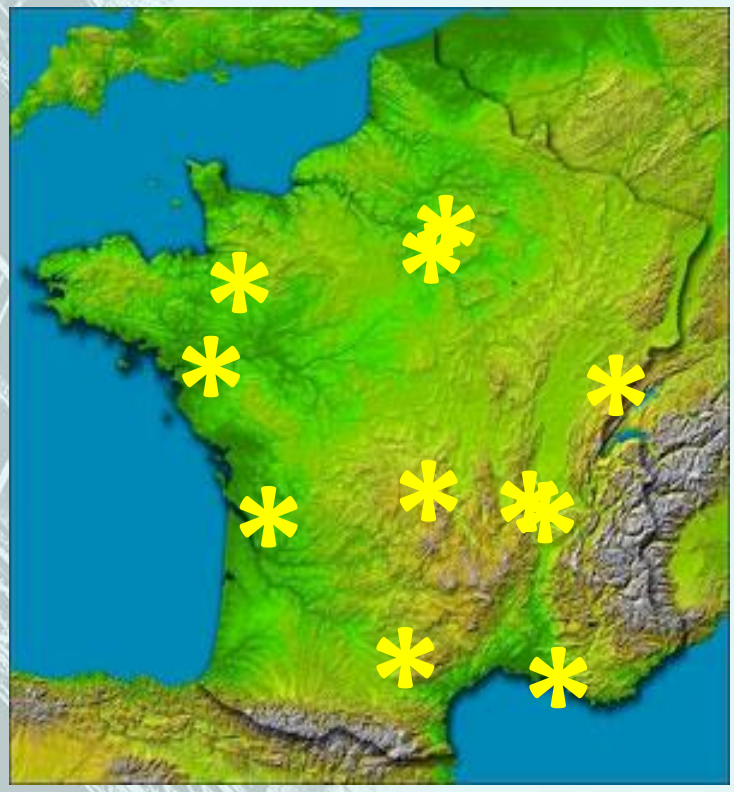
- *No head to head comparison*
- *Cohorts with similar results*
- *Contreversies about long femoropopliteal lesions*

Further studies are required

BATTLE trial

(*ClinicalTrials.gov number, NCT02004951)*

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



10 centers: Clinique d'Antony (Jean-Marc PERNES); CHU de Besançon (Simon RINCKENBACH); CHU de Bordeaux (Eric DUCASSE) ; CHU de Clermont Ferrand (Eugenio ROSSET) ; AP-HP, Hôpital Henri Mondor (Pascal DESGRANGES) ; CH de Lyon (Patrick FEUGIER) ; CH de Bourgouin (Patrick LERMUSIAUX); Clinique Ollioules (Philippe COMMEAU) ; 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).

BATTLE Trial

Perioperative interim analysis

- Enrollment completed: **186 patients**

- Perioperative interim analysis with **186 patients** will be communicated at the JET in **February 2017**

- Primary endpoint completion date: **September 2017**
- BATTLE trial completion date: **September 2018**

IMPERIAL trial

Clinical Study Overview: IMPERIAL

Ongoing

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

The ELUVIA Stent system is an investigational device, not available for sale in the European Economic Area (EEA).

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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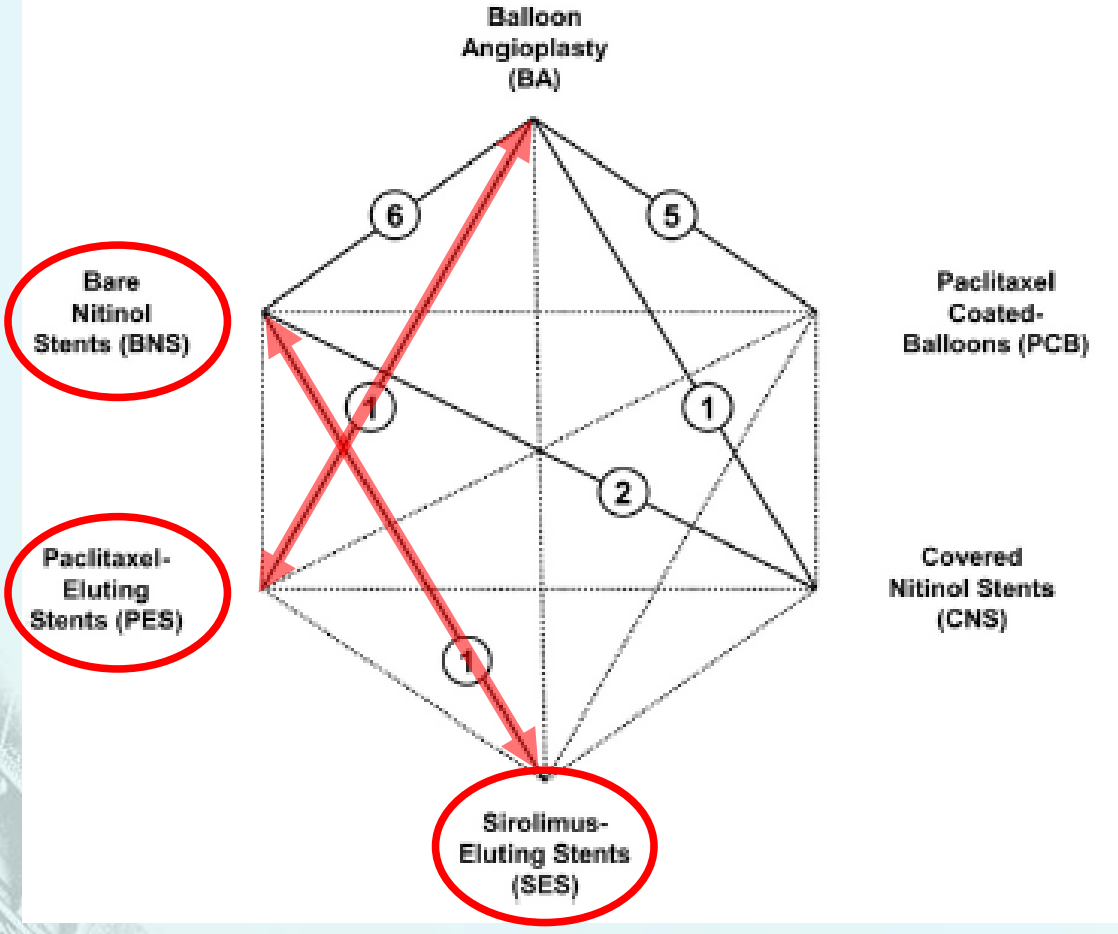
Few head to head comparison between devices for FP lesions treatment



Katsanos, J Vasc Surg, 2014

Original report

Bare metal versus paclitaxel eluting stents for long femoropopliteal lesions: prospective cohorts comparison using a propensity-score matched analysis.

Pierre-Alexandre Vent[1], Adrien Kaladji[2], Jean-Michel Davaine[1], Béatrice Guyomarch[3-4-5-6], Philippe Chaillou[1], Alain Costargent[1], Thibaut Quillard[7], Yann Gouëffic[1, 6, 7]

- Single centre study
- 2 consecutive and prospective cohorts
- TASC C/D FP de novo lesions
- Similar inclusion and exclusion criteria
- BMS vs PES (LifeStent®, Zilver® PTX)
- Propensity score (IPTW) stratification was used to minimise bias.

Vent, Ann Vasc Surg, In press

BMS and Zilver ptx literature

(TASC <15cm)

	Vienna	Durability I	Fast	Resilient	Astron	Misago 2	Zilver-ptx trial	Zilver ptx registry
Stent	Absolute (Abbott)	Everflex (Covidien)	Luminexx (Bard)	Lifestent (Bard)	Astron (Biotronik)	Misago (Terumo)	Zilver ptx (Cook)	Zilver ptx (Cook)
Lesion length	101mm	96.4mm	45.2mm	70.5mm	82mm	63.9mm	61,8mm	99mm
TVR/ TLR	28%	20.9%	15%	12.7%	/	10.1%	9.5%	9.5%
ISR	37%	27.8%	32%	19%	34.4%	12.4%	16.9%	13.8%
PSVR	/	<2.5	<2.4	<2.5	<2.4	<2.4	<2.0	<2.5

Schillinger, NEJM, 2006 ; Bosiers, J Endovasc Ther, 2009 ; Krankenberg, Circulation, 2007 ; Laird, Circ Cardiovasc Interv, 2010 ; Dick, Catheter Cardiovasc Interv, 2009 ; Schulte, J Endovasc Ther, 2012 ; Dake, Circ Cardiovasc Interv, 2011 ; Dake, J Endovasc Ther 2011.

Indirect comparison between BMS and DES

(IN/EX Criteria)

	OSPREY*	Zilver PTX trial**
Age	≧ 18	≧ 18
Rutherford classifications	2 - 4	≧ 2
Resting ABI	< 0.9	< 0.9
Lesion	*de novo*	*de novo* or restenotic lesions
Lesion length	40 - 150 mm	≦ 140mm
RVD	4 - 7 mm	4 - 9 mm
Severe Calcification	Exclude	No criteria
Thrombus	Exclude	Exclude

*Ohki A. et al. Journal of Vascular Surgery 2016
**Dake, Circ Cardiovasc Interv. 2011

Indirect Comparison between BMS and DES

- Lesion Characteristics -

	OSPREY*	Zilver PTX**	P
Lesions (n)	261	247	
Lesion length (mm)	83.8 ± 41.3	66.4±38.9	<0.001
RVD (mm)	5.1 ± 1.0	5.1 ± 0.9	NS
Segment MLD (mm)	1.1 ± 0.9	1.0±0.9	NS
Calcification **None/Mild**	33.3% (87/261)	27.6%(66/239)	NS
Moderate	35.2% (92/261)	35.6%(85/239)	NS
Severe	31.4% (82/261)	36.8%(88/239)	NS

*Ohki A. et al. Journal of Vascular Surgery 2016
**Dake, Circ Cardiovasc Interv. 2011