

Contemporary Treatment Options for In-stent Restenosis: What Is the Best?



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Potential conflicts of interest

Speaker's name: **Massimiliano Fusaro**

I have the following potential conflicts of interest to report:

- Research contracts
- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

X I do not have any potential conflict of interest

Self-expanding stents
13 companies
29 medical products

Problem dimensions

US ~325.000 per year

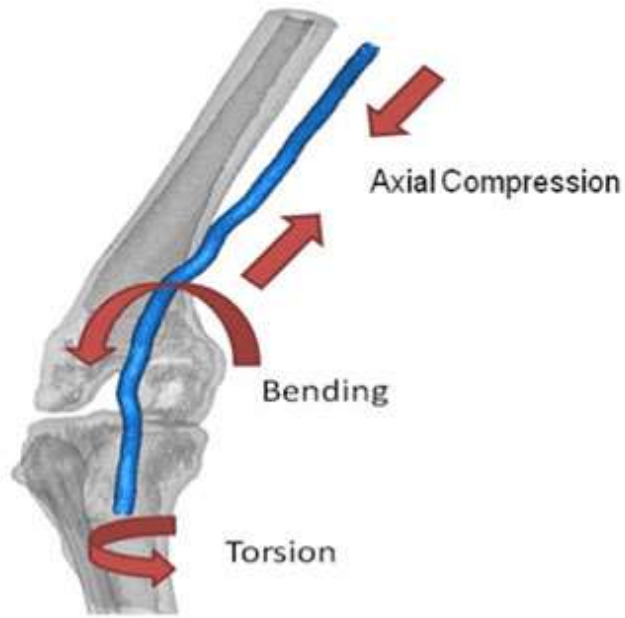
ROW ~245.000 per year

TOT ~570.000 per year

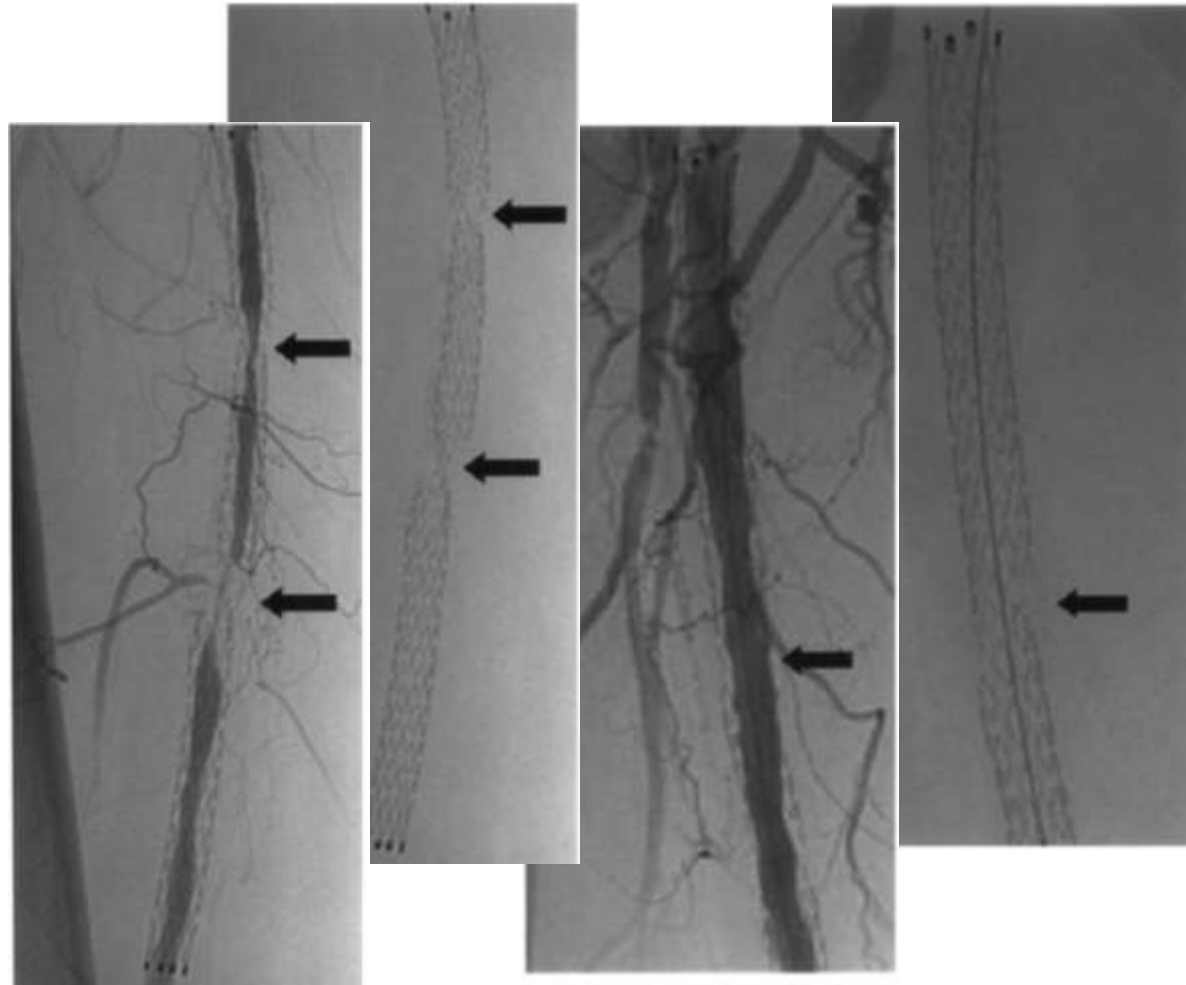
	FAST	Vienna Study	Resilient
Mean lesion length	45.2mm	101mm	61.8mm
ISR rate @ 12mo	32%	36%	20%
Fracture rate	12%	2%	2.9%

Source: Industry

Bio-mechanical Problems in the Superficial Femoral Artery (SFA)



Biomechanical forces challenging femoropopliteal artery territory



Scheinert D, J Am Coll Cardiol 2005;45:312-5

Classification In Stent Restenosis (ISR)

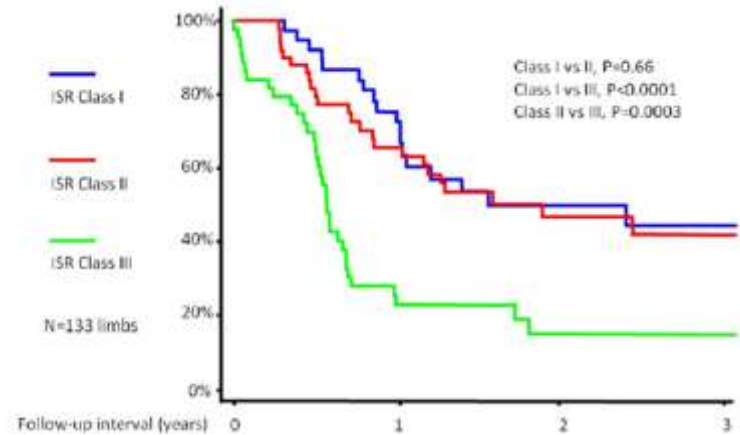
CLINICAL RESEARCH

Interventional Cardiology

Classification and Clinical Impact of Restenosis After Femoropopliteal Stenting

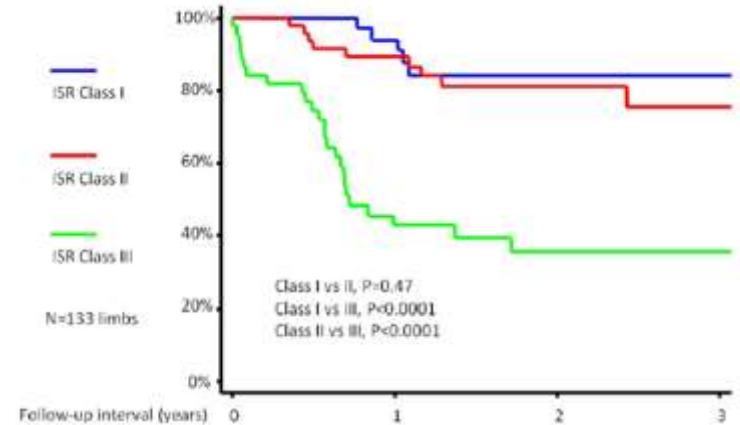
Atsushi Tosaka, MD,* Yoshimitsu Soga, MD,* Osamu Iida, MD,† Takayuki Ishihara, MD,† Keisuke Hirano, MD,‡ Kenji Suzuki, MD,§ Hiroyoshi Yokoi, MD,* Shinsuke Nanto, MD,|| Masakiyo Nobuyoshi, MD*

Kitakyushu, Amagasaki, Yokohama, Sendai, and Suita, Japan



Freedom From Recurrent ISR by ISR Class

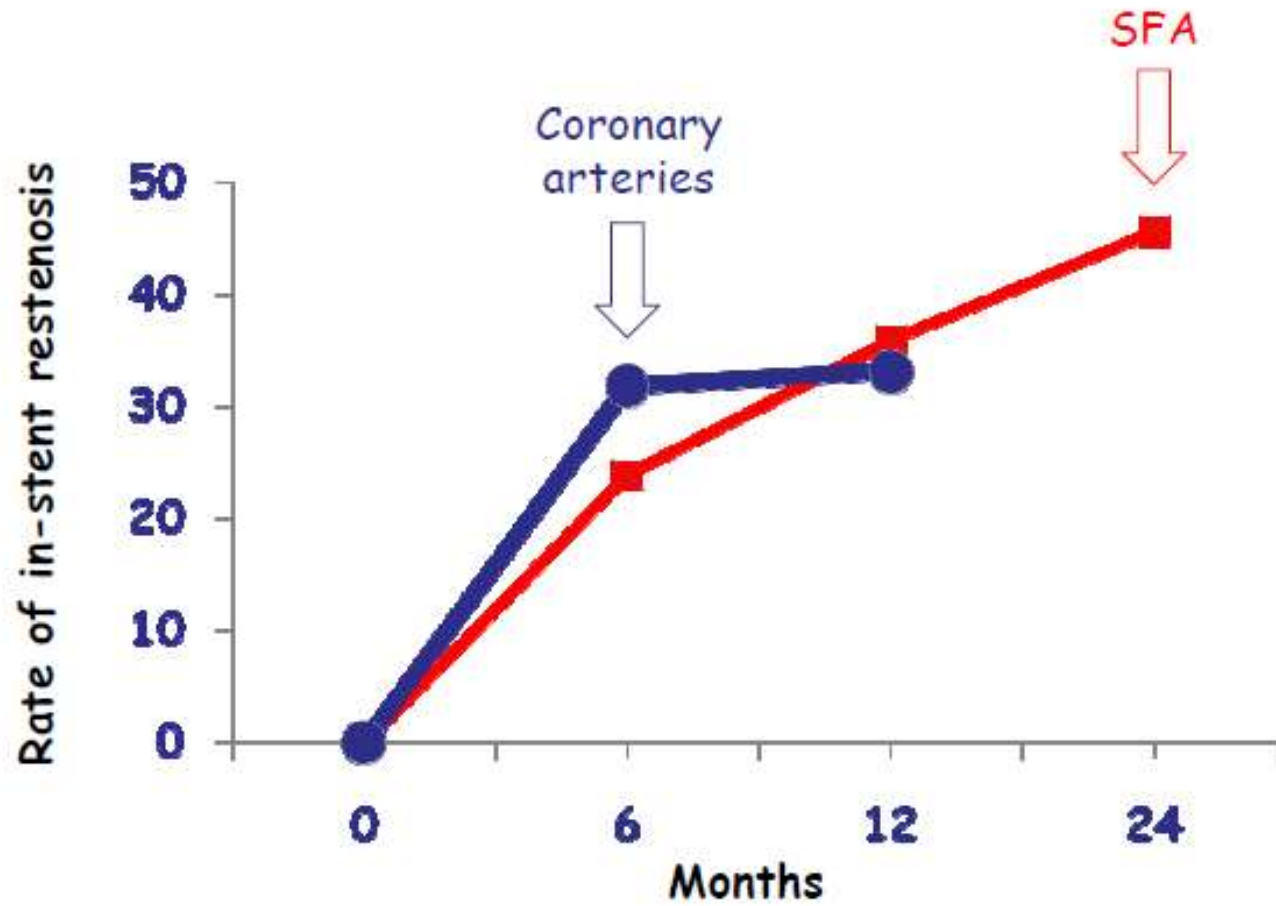
Classified by visual estimate on angiography



Freedom From Recurrent Occlusion by ISR Class

Tosaka a et al. JACC 2012

ISR in coronary and peripheral arteries



Smooth Muscle Cells-actin in atherosclerotic plaque is associated with restenosis: analysis of ex-vivo atherectomy sample from SFA

Study Protocol

65 patients with PAD stage >IIb (Fontaine)

Atherectomy (*SilverHawk, EV3*), extraction of plaque material
duplex ultrasonography after 12 months

Fixation of the plaque material in formalin, embedded in paraffin and staining with hematoxylin-eosin (HE), Sudan Red and Elastica by Gieson. Immunohistochemical work-up with: anti-CD3, anti-CD15, anti-CD68, anti-CD31, anti-CD61 and anti-SMC

Methods

Microscopic sections were analysed blindly on a semi quantitative scale in order to assess: lipid content and foam cells, smooth muscle cells, inflammation cells, platelets and apoptosis

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2

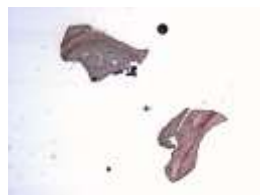
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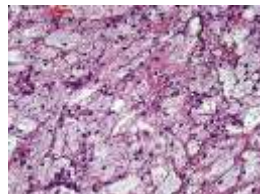
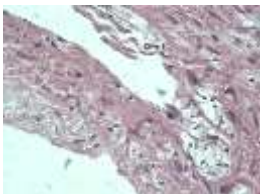
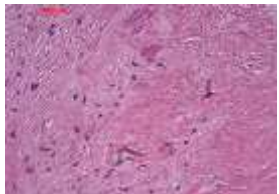
Smooth Muscle Cells



Lipids



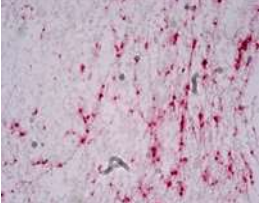
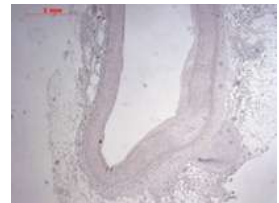
Foam cells



inflammation



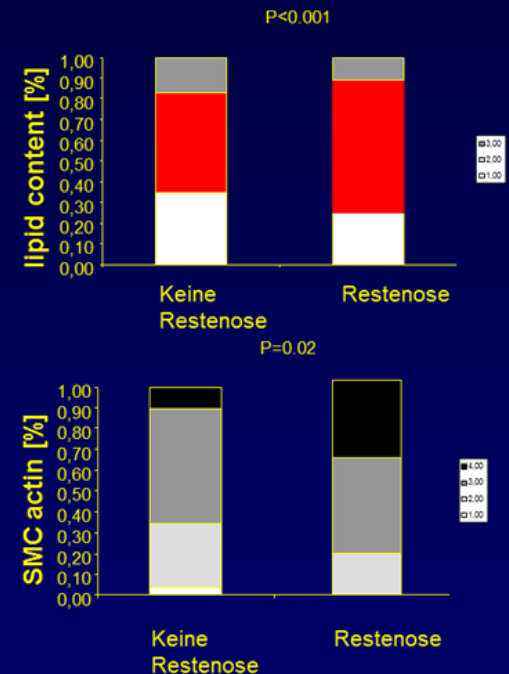
Platelets



In patient with restenosis the plaque analysis demonstrated high level of smooth muscle cells and lipid contents in ex vivo sample from atherectomy

Multivariate analysis between lesion length, occlusion, SMC actin content, percentage of CD68 + cells or lipid content of the plaques and restenosis:

	Beta	P
Lesions lenght	0.107	0.475
Occlusion	0.055	0.724
SMC actin (Smooth cells)	0.300	0.041
Inflammatory cells	-0.103	0.514
Lipid content	-0.396	0.010
ANOVA	0.009	



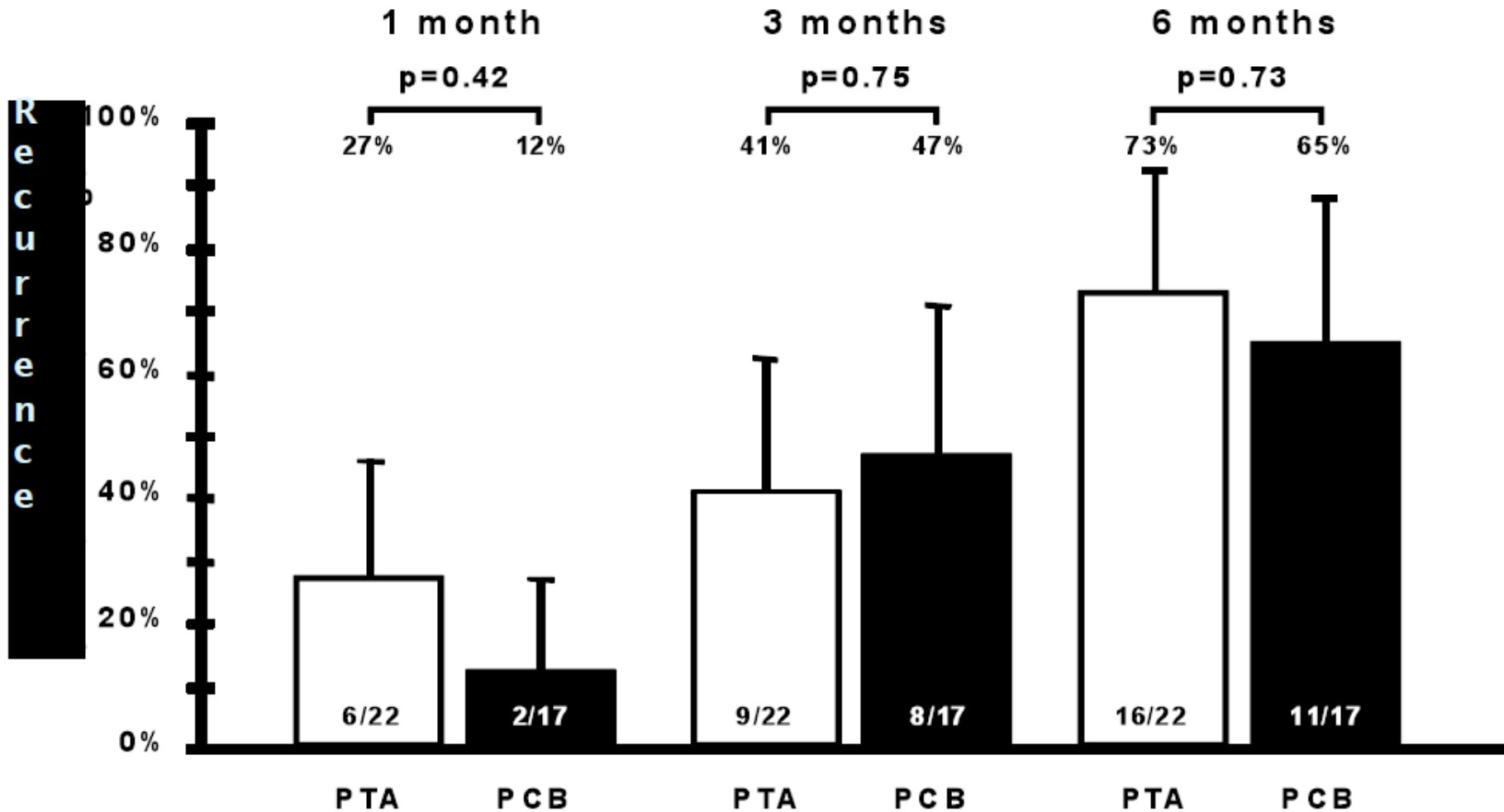
Endovascular Treatment of SFA In-stent Restenosis – a “New” Disease



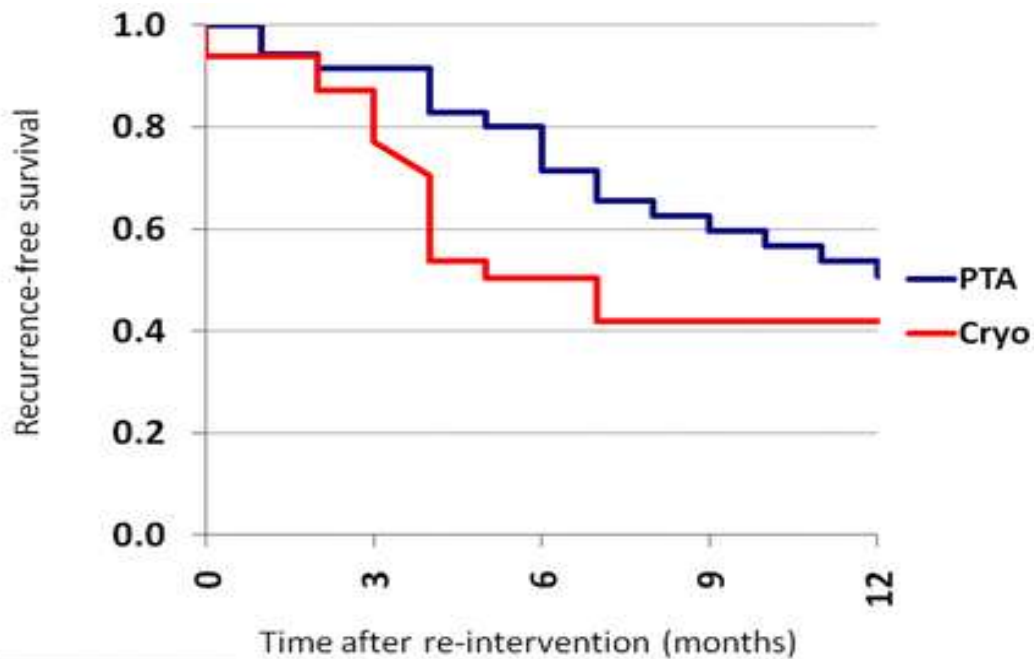
How to approach SFA-ISR?

- **POBA**
- **Cutting balloon**
- **Cryoplasty**
- **Debulking (Laser, Atherectomy)**
- **Stent-in-stent**
- **Covered Stent**
- **Brachytherapy**
- **DEB**
- **DES**

PTA versus Cutting Balloon



Cryoplasty versus PTA



Number at risk					
CBA	39	36	32	26	23
Cryoplasty	37	33	22	20	20

Figure 1

Kaplan–Meier re-stenosis free survival estimate

Laser versus PTA

[J Endovasc Ther](#). 2014 Feb;21(1):52-60. doi: 10.1583/13-4538R.1.

Photoablation using the turbo-booster and excimer laser for in-stent restenosis treatment: twelve-month results from the PATENT study.

[Schmidt A¹](#), [Zeller T](#), [Sievert H](#), [Krankenbergh H](#), [Torsello G](#), [Stark MA](#), [Scheinert D](#).



CONCLUSION: The PATENT study has established excimer laser atherectomy as safe for the treatment of femoropopliteal ISR, achieving high procedure success. Recurrence of restenosis indicates that removing hyperproliferative tissue alone does not solve the problem of ISR. New concepts, such as the combination of ELA with drug-eluting balloons, may prove beneficial.

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Photoablative Atherectomy Followed by a Paclitaxel-Coated Balloon to Inhibit Restenosis in Instent Femoro-popliteal Obstructions (PHOTOPAC)

Example: "Heart attack"
Search for studies:
[Advanced Search](#)

EXCITE ISR Clinical Trial

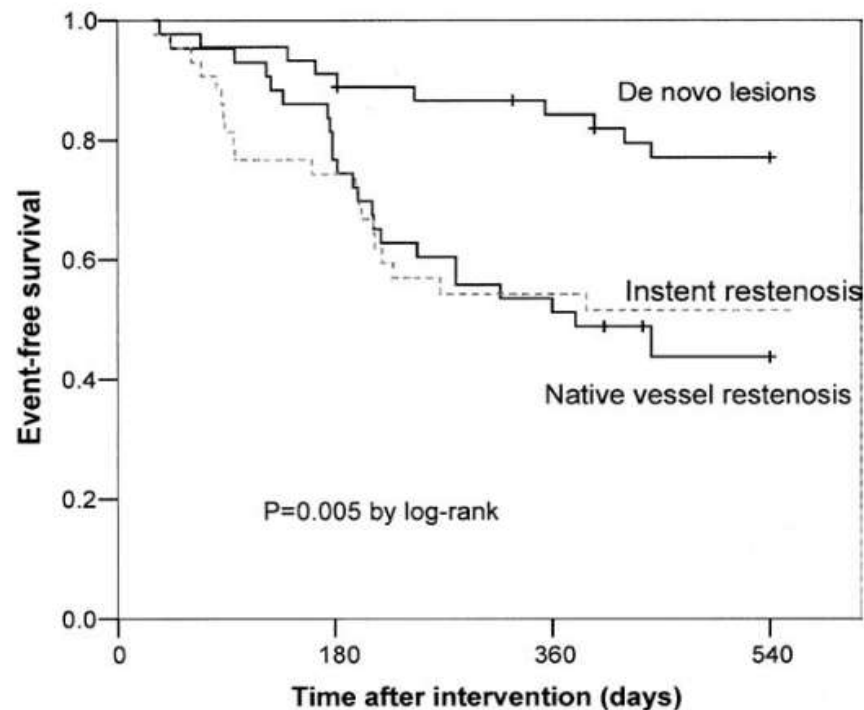
EXCimer Laser Randomized Controlled Study for Treatment of Femoropopliteal In-Stent Restenosis – THE EXCITE ISR TRIAL

Study Purpose

To evaluate the safety and efficacy of the Spectranetics Excimer Laser Atherectomy (ELA) with adjunctive percutaneous transluminal angioplasty (PTA), compared to PTA alone, in the treatment of subjects with chronic peripheral arterial disease (PAD), Rutherford Class 1-4 associated with femoropopliteal artery in-stent restenosis (ISR) in bare nitinol stents, in vessels ≥ 5.0 mm

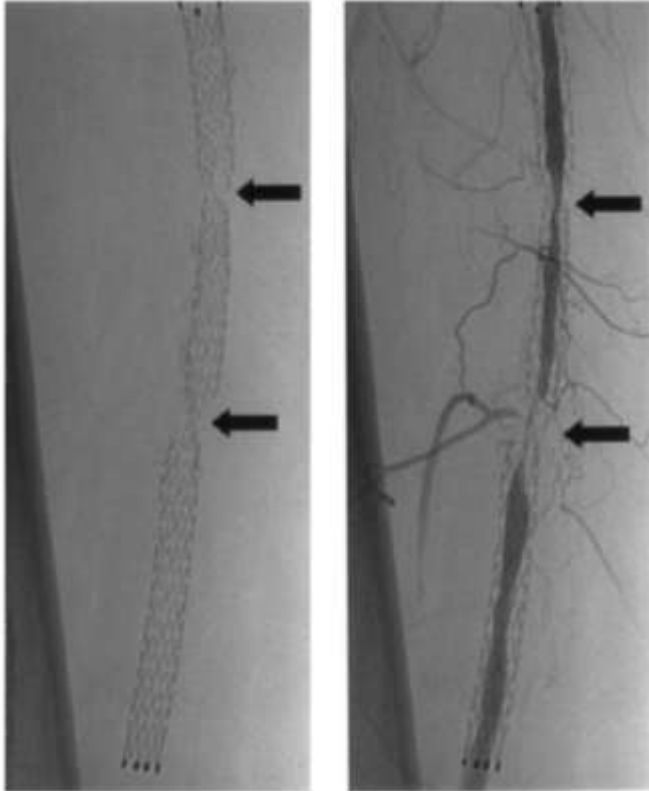
Atherectomy and ISR

Long-Term Results After Directional Atherectomy of Femoro-Popliteal Lesions



CONCLUSIONS Long-term technical and clinical results after directional atherectomy of femoro-popliteal lesions are in favor of de novo lesions compared with restenotic lesions.

ISR by stent fractures therapeutic options

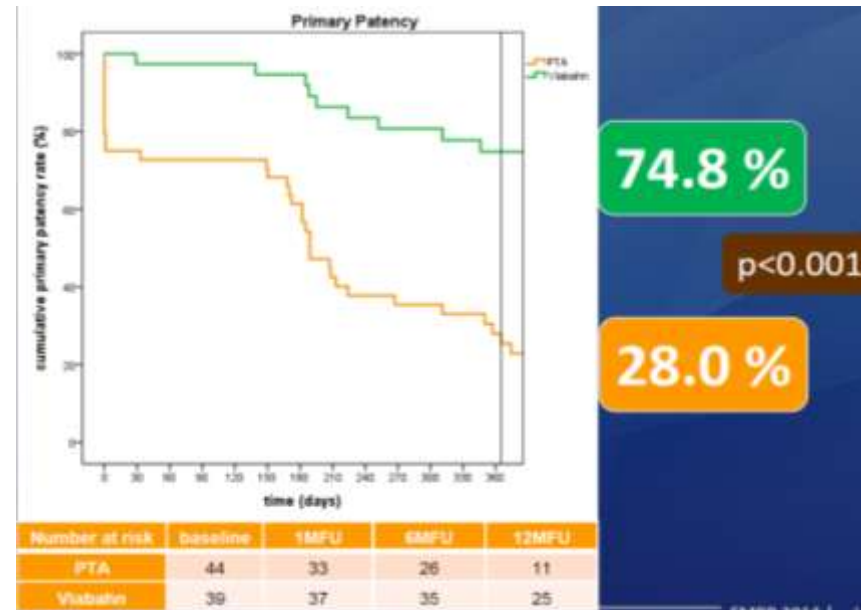
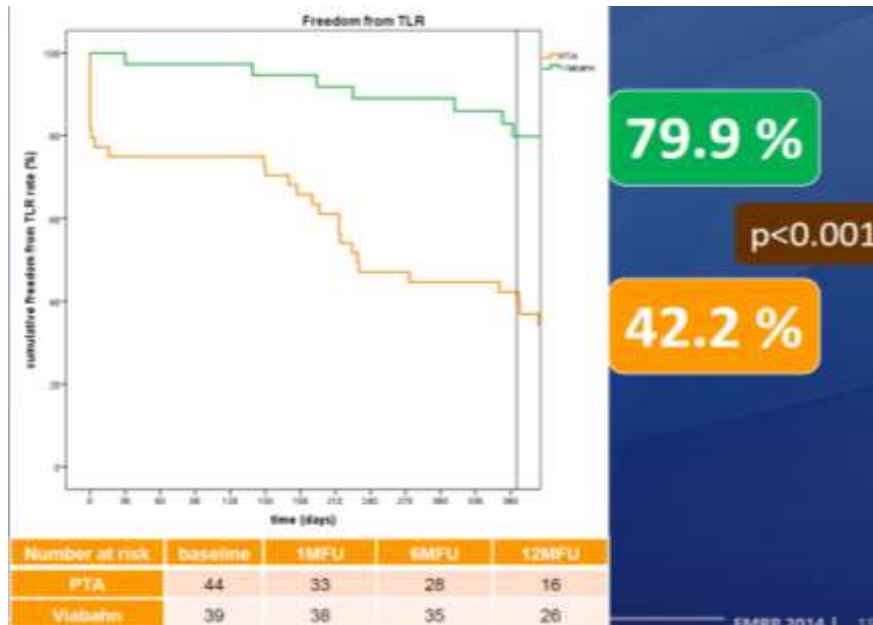


- **Stent-in-Stent (DES? Nitinol?)**
- **Covered Stent**
- **Surgery in case of re-occlusion**

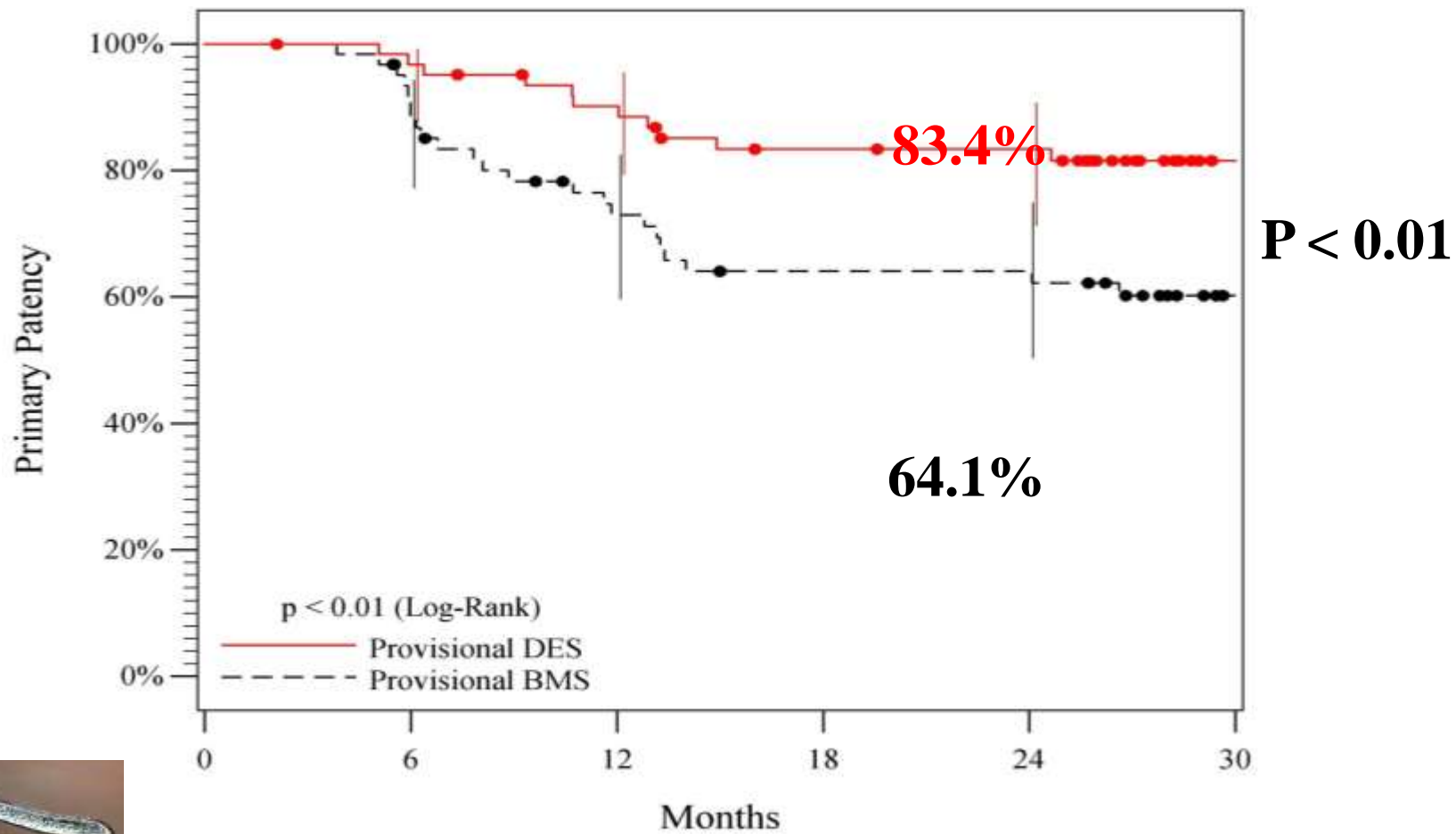
Scheinert D, JACC 2005;45:312–5

The RELINE Trial

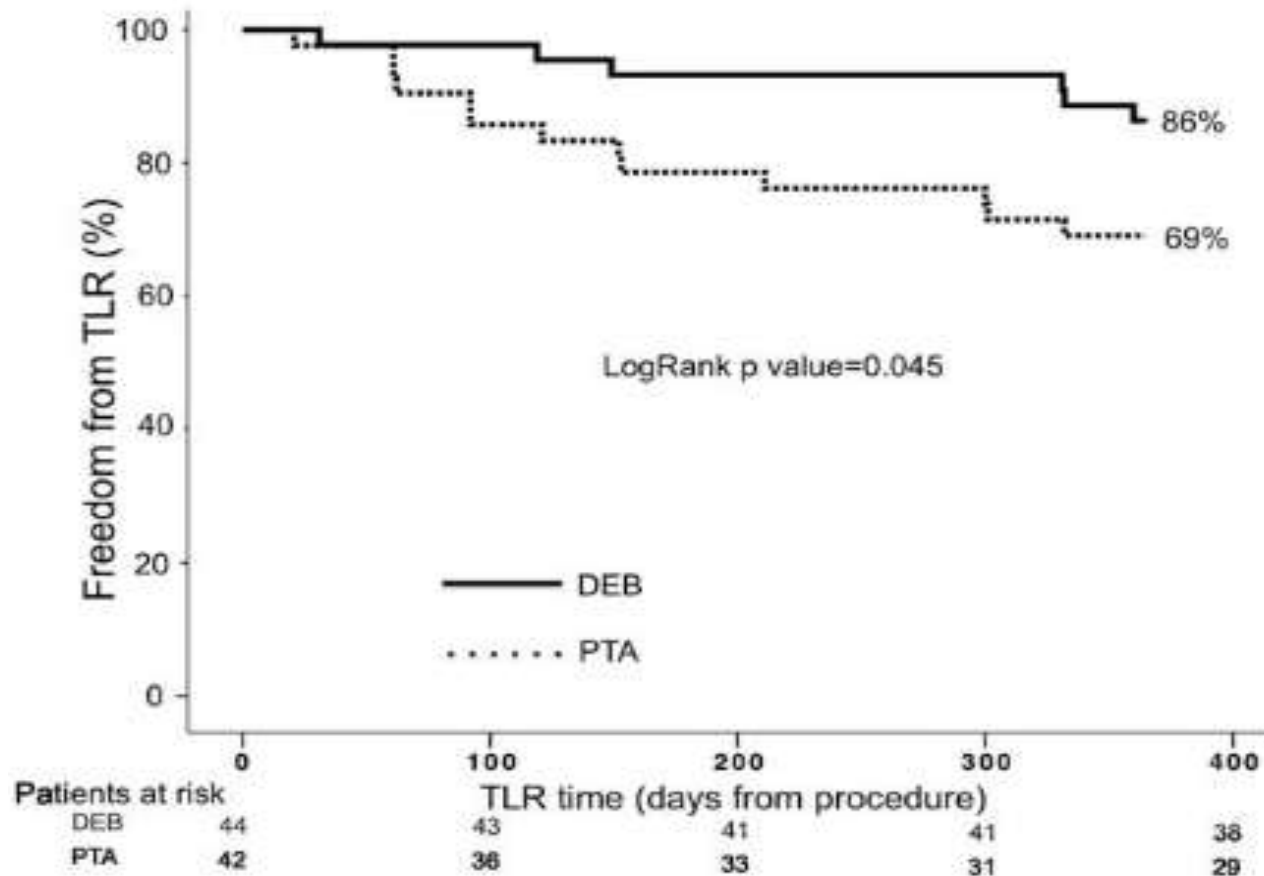
Physician initiated, randomized, controlled, multi-center trial comparing the new generation Viabahn endoprosthesis (Gore & Associates) and POBA in the treatment of femoral in-stent restenosis



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



Paclitaxel-Eluting Balloon vs. Standard Angioplasty to Reduce Recurrent Restenosis in Diabetic Patients With In-Stent Restenosis of the Superficial Femoral and Proximal Popliteal Arteries: The DEBATE-ISR Study



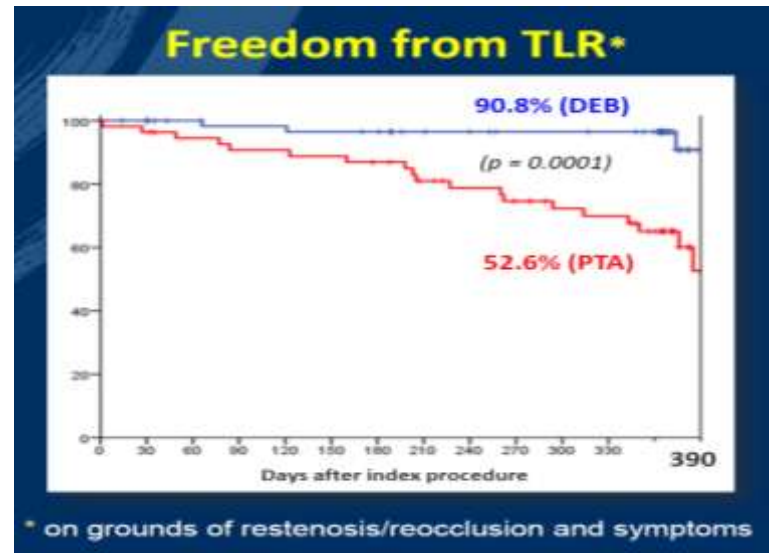
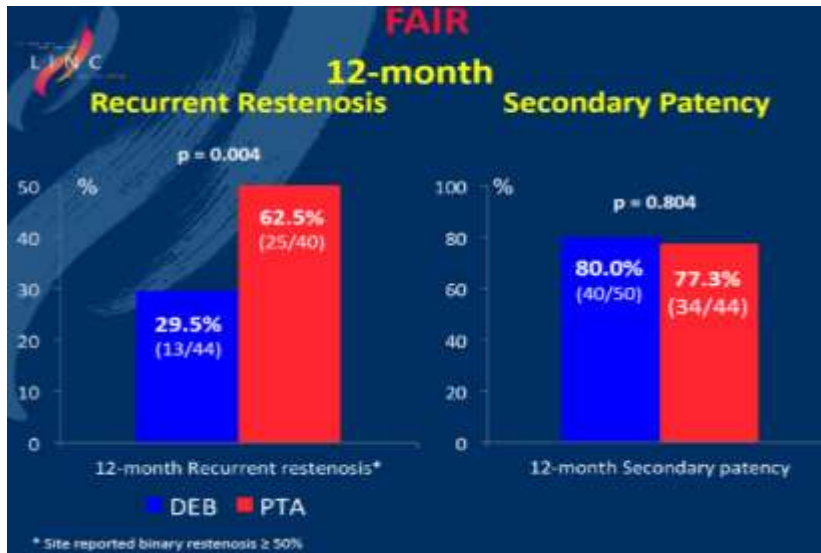
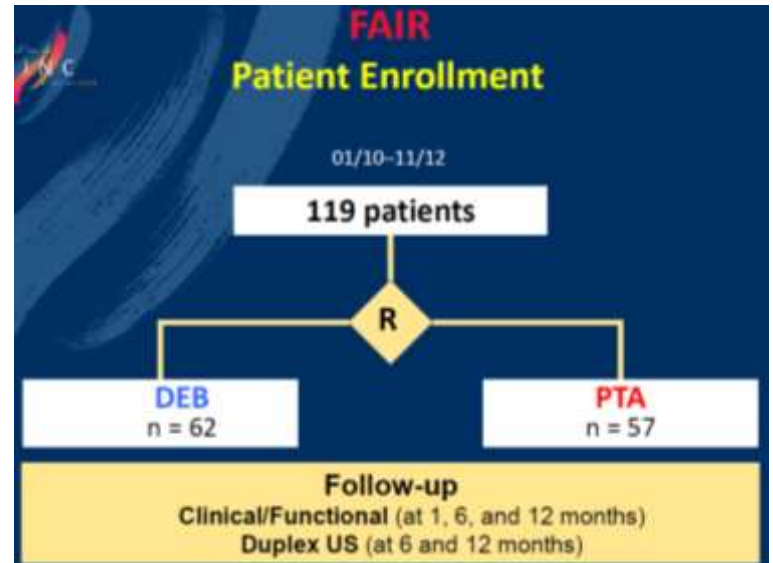
FAIR

Drug Eluting Balloon vs. PTA for Superficial Femoral Artery In-Stent Restenosis 12-month Results

Hans Krankenberg

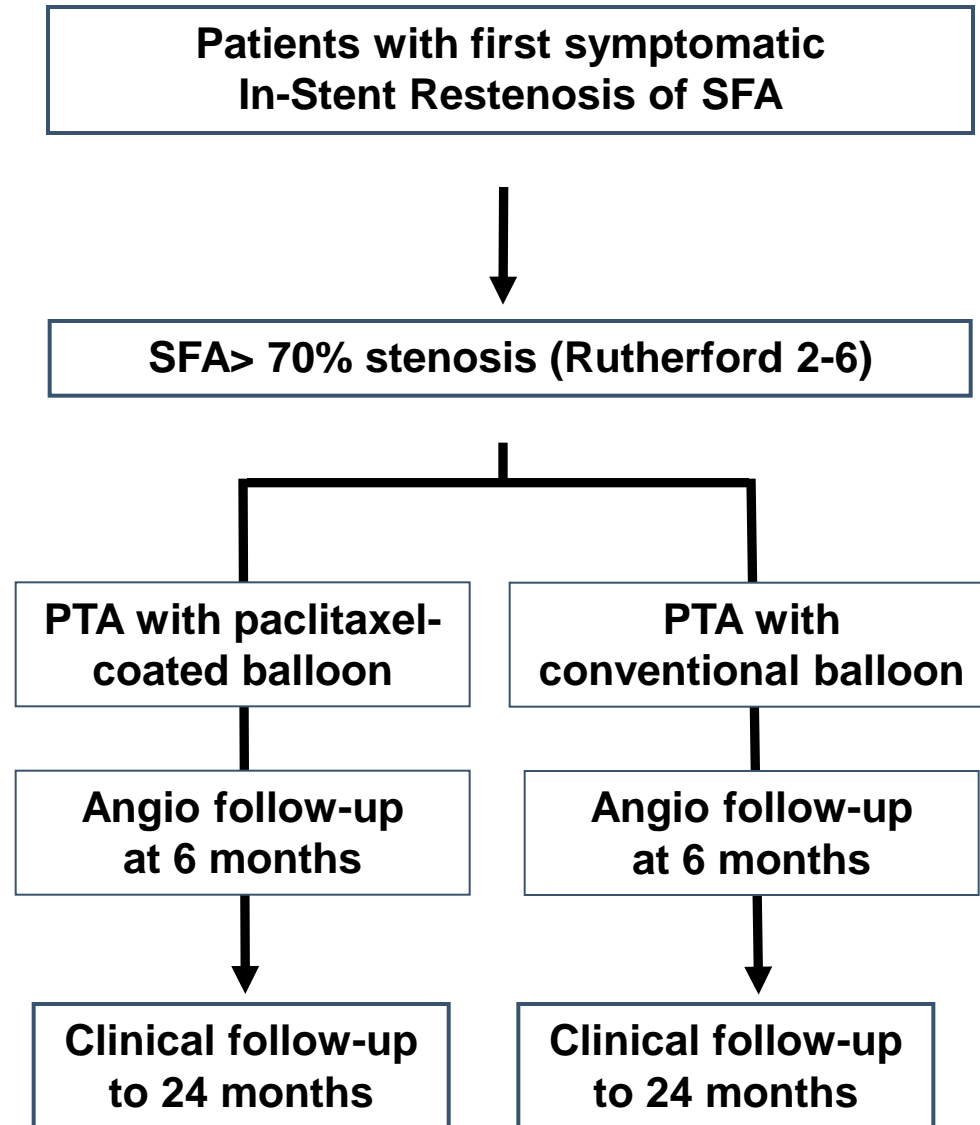
(Heart and Vascular Center Bad Bevensen, Germany)
on behalf of the FAIR Trial Investigators

ClinicalTrials.gov NCT01305070



Design

- **DESIGN:** Prospective, randomized control trial
- **HYPOTHESIS:** PTA with paclitaxel-coated balloon is superior to PTA with conventional balloon
- **PRIMARY ENDPOINT**
Angiographic percent diameter stenosis at 6 months



Contemporary Treatment Options for In-stent Restenosis: What Is the Best?

- Failure: POBA, Debulking, Cutting and Cryoplasty
- Promising: Drug Coated Ballons
- In stent restenosis + stent fracture: DES, Covered



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Thank You

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