21st CardioVascular Summit
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Leave light thing behind

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Key Findings of FP Revascularization Based on Current Guideline
-Stenting for FP lesions-

ESC 2011: Primary stent implantation **should be considered** in femoropopliteal TASC B lesions. *(IIA, level B)*

AHA 2013: Primary stent placement **is not recommended** in the femoral, popliteal, or tibial arteries. *(Level of Evidence: C)*

SVS 2015: For intermediate-length lesions in the SFA, we recommend the **adjunctive use** of self-expanding nitinol stents (with or without paclitaxel) to improve the midterm patency of angioplasty. *(Grade 1, level B)*

Some practice guidelines advise against primary stenting in patients with intermittent claudication, whereas others recommend primary stenting in short- or intermediate-length lesions or in the event of acute PTA failure.

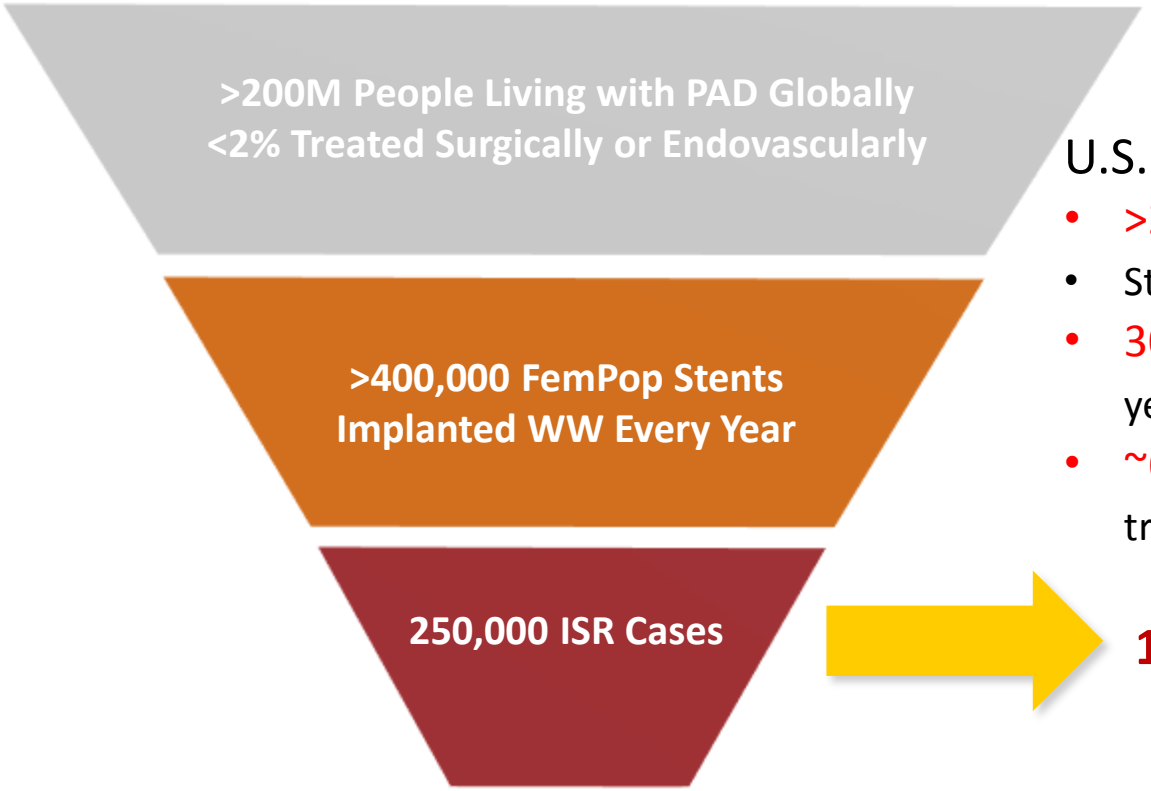
Incidence of In-Stent Restenosis (ISR)

Summary of 1-Year Restenosis Rate After BMS Implantation

Studies	Stent	Mean lesion length (mm)	1 Year restenosis rate (%)
FAST	Luminexx (BARD)	45	32
RESILIENT	Life stent (BARD)	62	20
Zilver PTX	Zilver flex (Cook)	63	27
STROLL	S.M.A.R.T (Cordis)	77	12
SIROCCO II	S.M.A.R.T (Cordis)	82	8
SIROCCO I	S.M.A.R.T (Cordis)	85	23
DURABILITY II	Protégé EverfLex (Covidien)	89	23
DURABILITY I	Protégé EverfLex (Covidien)	96	28
ASTRON	Astron (Biotronik)	99	25
ABSOLUTE	Absolute (Abbott)	101	27

Endovascular therapy (EVT) by using bare-metal nitinol stent is safe and effective for the treatment of the SFA and proximal popliteal arterial lesions at 1 year.

Global PAD/ISR Scope of Problem



U.S. ISR Incidence

- >200,000 Stents / Year implanted
- Stent volume growing 6-7% annually
- 30-40% 1st time ISR Incidence within 2 years of implant
- ~65% of ISR will recur post-PTA treatment within 2 years

115,000 US ISR Cases

FP-ISR remains a common problem with an incidence up to 37% for lesion length of <150mm and 60% for longer lesions.

Dippel EJ et al. JACC Cardiovasc Interv. 2015;8:92-101.

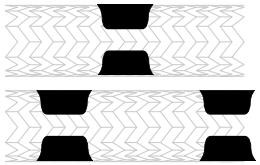
Classification and Clinical Impact of Restenosis After Femoropopliteal Stenting

Study subjects: 116 patients (133 limbs)
Lesion length: 91.4 ± 67.1 mm
RVD: 5.4 ± 0.7 mm

Visual estimate on angiography

Class I: 29%
Class II: 38%
Class III: 33%

Class I
Focal ISR group
(≤ 50 mm in length)



Class II
Diffuse ISR group
(> 50 mm in length)

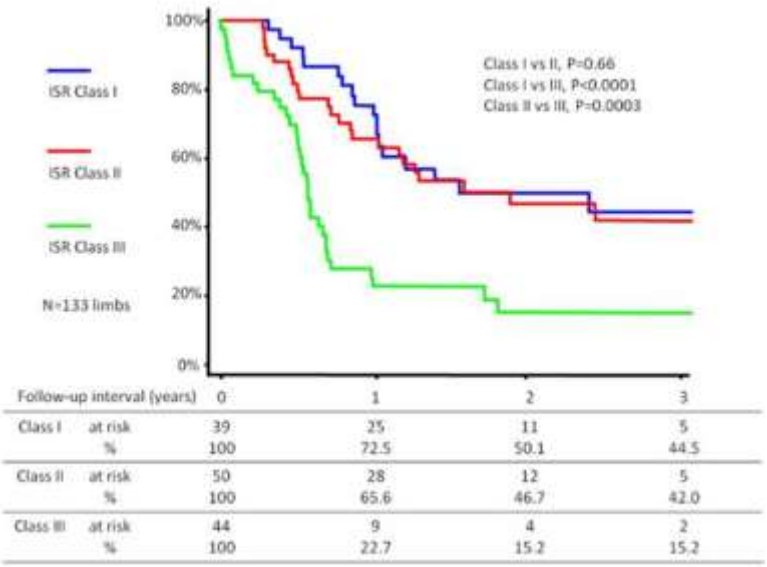
Class III
Totally occluded ISR group

Predictors of Recurrent ISR

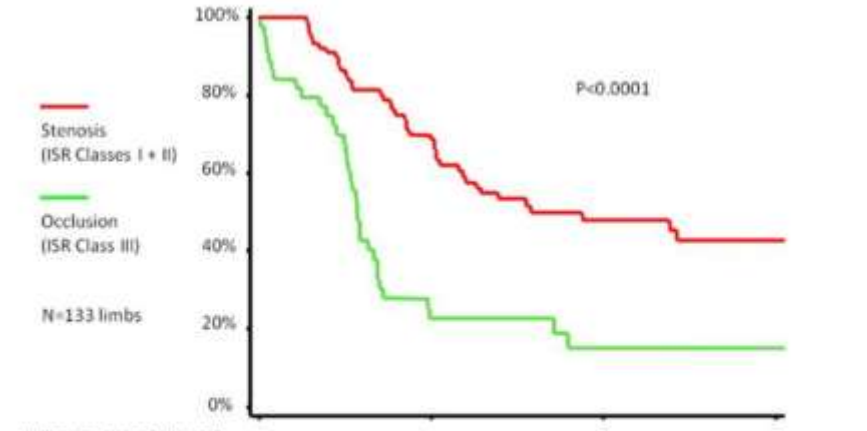
Variables	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	p Value	HR (95% CI)	p Value
ISR class III	**2.90 (1.83–4.56)**	**< 0.01**	**2.44 (1.33–4.48)**	**< 0.01**
Lesion length	1.004 (1.002–1.007)	< 0.01	1.001 (0.998–1.005)	0.50
Reference vessel diameter	**0.62 (0.44–0.87)**	**< 0.01**	**0.63 (0.44–0.89)**	**< 0.01**
Early restenosis	1.92 (1.13–3.23)	0.02	1.60 (0.94–2.73)	0.09

Tosaka A, Soga Y, Iida O, et al. J Am Coll Cardiol. 2012;59:16–23.

Classification and Clinical Impact of Restenosis After Femoropopliteal Stenting



Follow-up interval (years)		0	1	2	3
Class I	at risk	39	25	11	5
	%	100	72.5	50.1	44.5
Class II	at risk	50	28	12	5
	%	100	65.6	46.7	42.0
Class III	at risk	44	9	4	2
	%	100	22.7	15.2	15.2



Follow-up interval (years)		0	1	2	3
Stenosis	at risk	89	53	23	10
	%	100	68.6	48.0	42.9
Occlusion	at risk	44	9	4	2
	%	100	22.7	15.2	15.2

Class III

Totally occluded ISR group

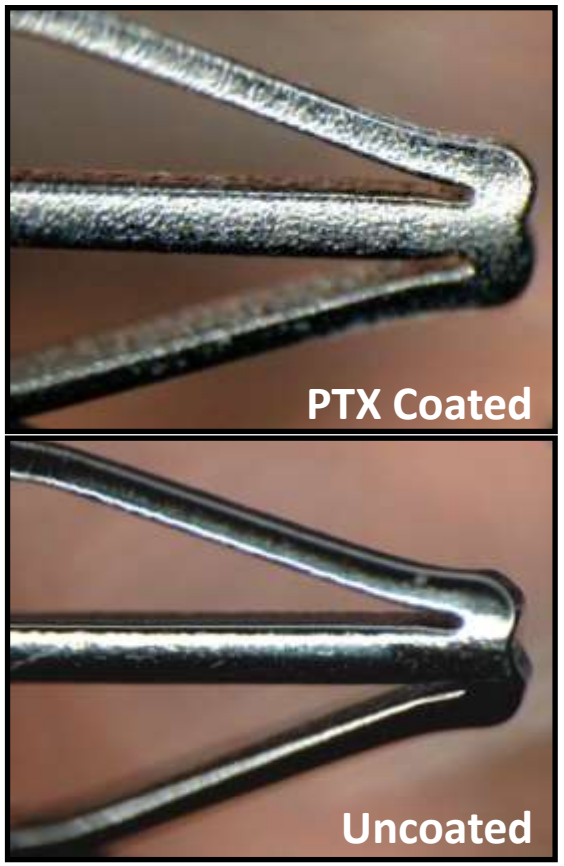
Conclusion:

Although balloon angioplasty for the stenotic ISR group is feasible, the freedom from recurrent ISR and occlusion after balloon angioplasty are remarkable low for **totally occluded ISR**.

Tosaka A, Soga Y, Iida O, et al. J Am Coll Cardiol. 2012;59:16–23.

Zilver PTX® Drug-Eluting Stent

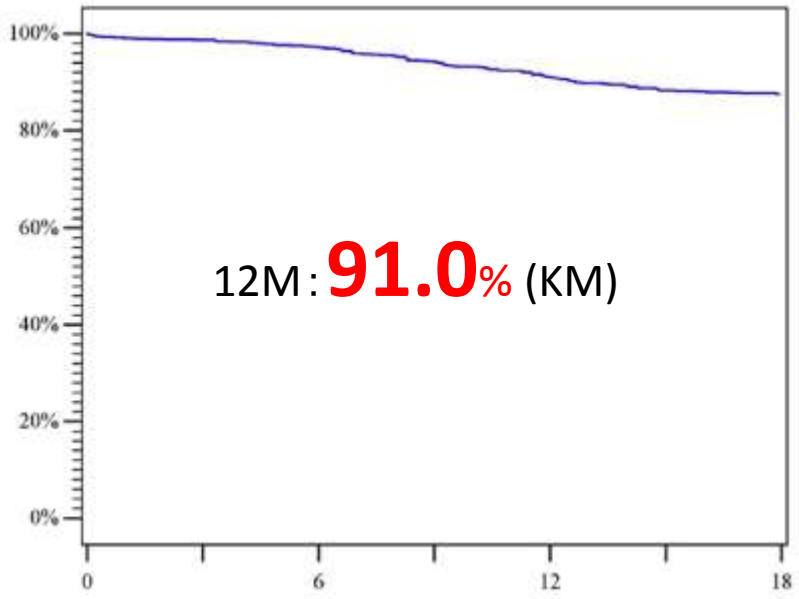
- Designed for the SFA
- Approved in EU/Japan
- Approval pending in US
- Dual therapy
  - **Mechanical scaffold:**
    Zilver Flex® Stent Platform
  - **Drug therapy: Paclitaxel only**
    - **No polymer or binder**
    - 3 µg/mm^2 dose density
- Sponsor: **Cook Medical**



Zilver PTX PMS in Japan, 12-Month Results

	n=907
Age	73.5±8.5
DM	58.8%
Dialysis	30%
CLI	21.5%
CTO	41.6%
ISR	18.6%
Lesion Length(cm)	14.7±9.7
Lesion Length>15cm	42.0%

Freedom from clinically driven-TLR

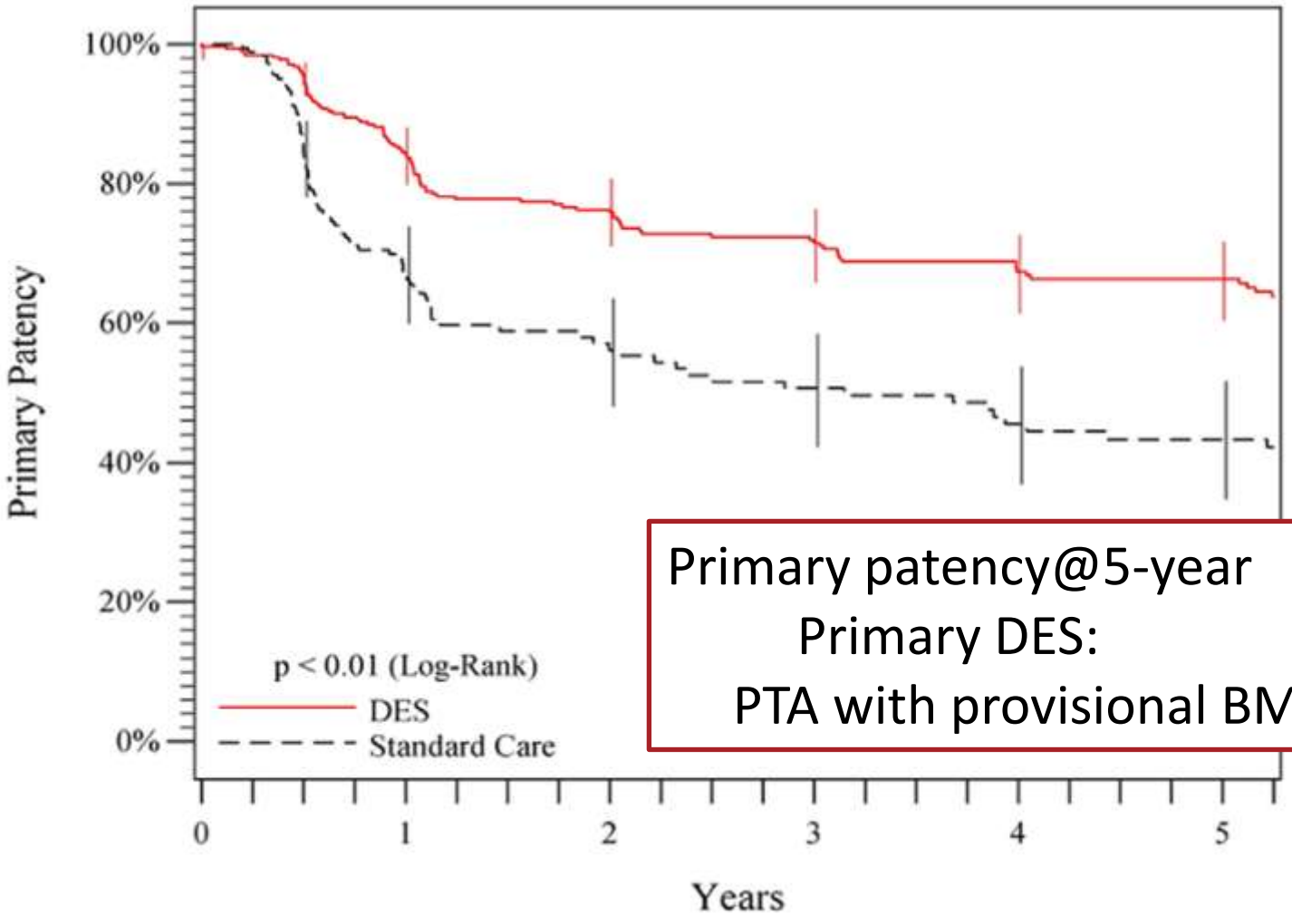


Stent Fracture rate(12M): **1.5%**

Stent Thrombosis rate(12M): **3.8%**

Yokoi H, et al. JACC Cardiovasc. Interv. 2016;9:271–277.

Sustained Safety and Effectiveness of PES for FP Lesions; 5-Year Follow-Up



Primary patency@5-year

Primary DES: **66.4%**

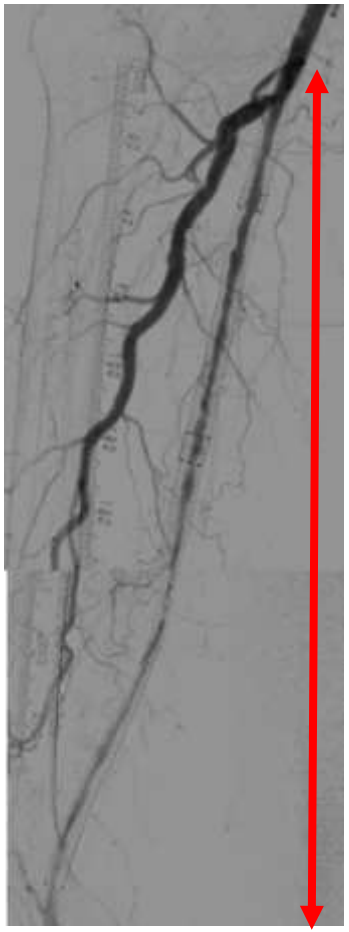
PTA with provisional BMS: **43.4%**

Dake MD, et al. Circulation. 2016;133:1472-1483.

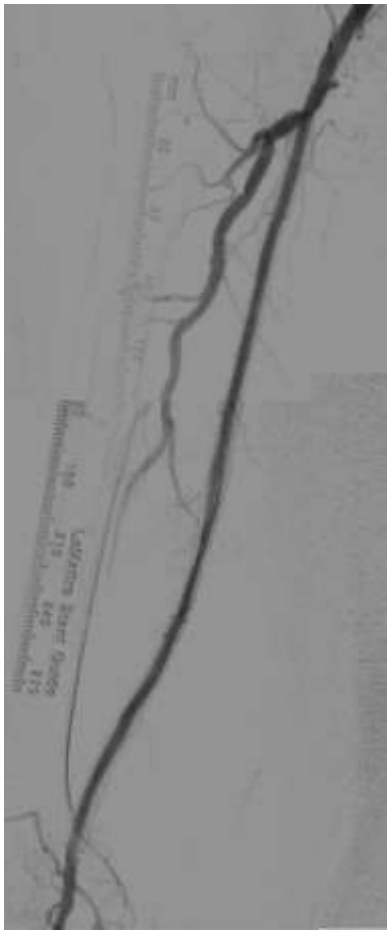
Case: 80-YO, Male

Zilver PTX DES for ISR Class II (Pre, Post, 1 Year Angiogram)

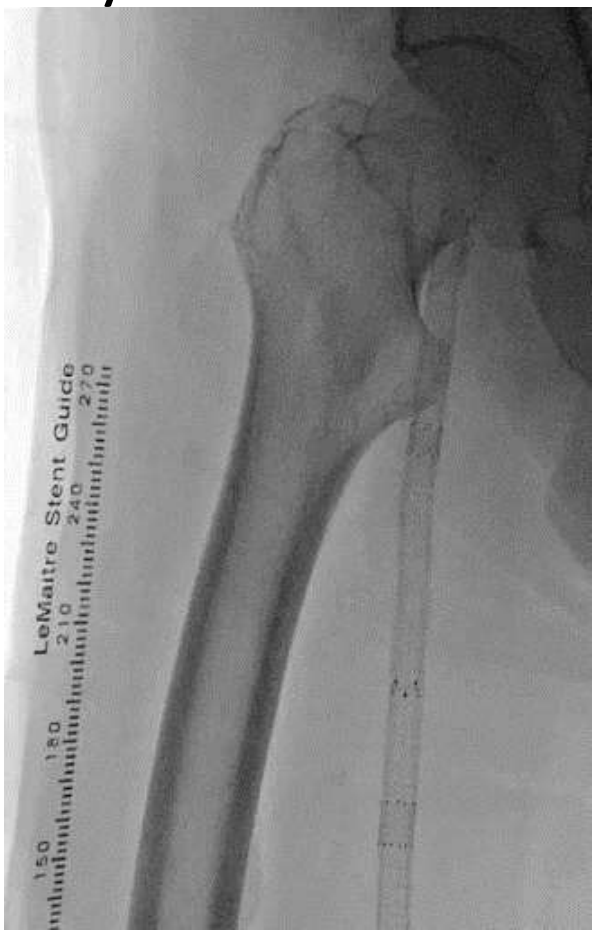
Pre



Post



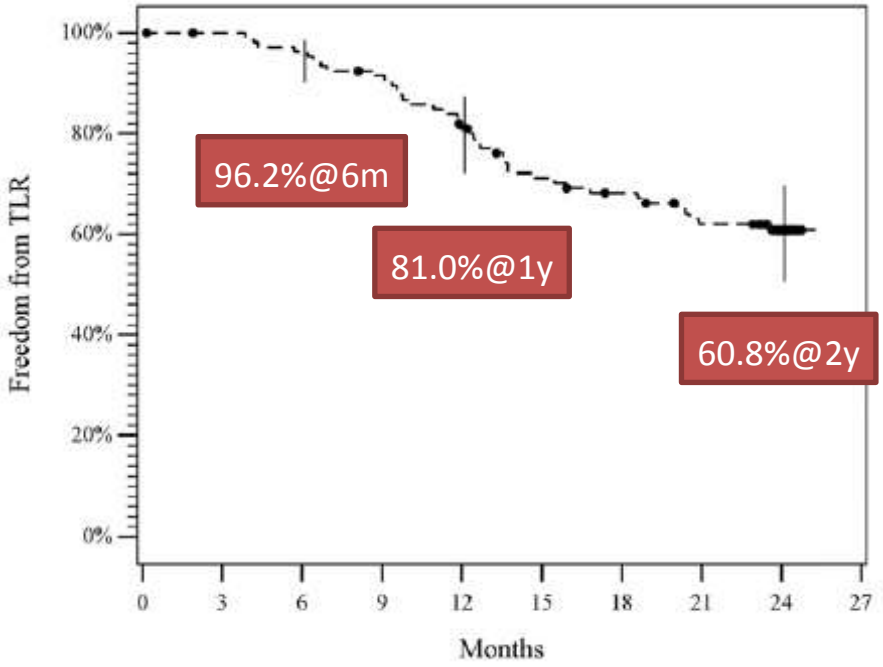
3 years after EVT



Lt-SFA: 90% (ISR) →0% (Zilver PTX 7×120 mm 3 stents)

Treatment of Femoropopliteal ISR with Paclitaxel-Eluting Stents

Study subjects:108 patients
(119 ISR lesions, class III: 31%)
Lesion length: 133.0 ± 91.7 mm



Conclusion:
The Zilver PTX stent achieves favorable outcomes at 2 years in treating femoropopliteal lesions with in-stent restenosis.

Zeller T, et al. J Am Coll Cardiol Intv. 2013;6:274–81.

Zephyr

Study design: Prospective, multicenter registry

Subjects: 690 PAD Pt with 831 femoro-popliteal lesion treated with **Zilver PTX**

Primary endpoint: Primary patency, Incidence of stent thrombosis

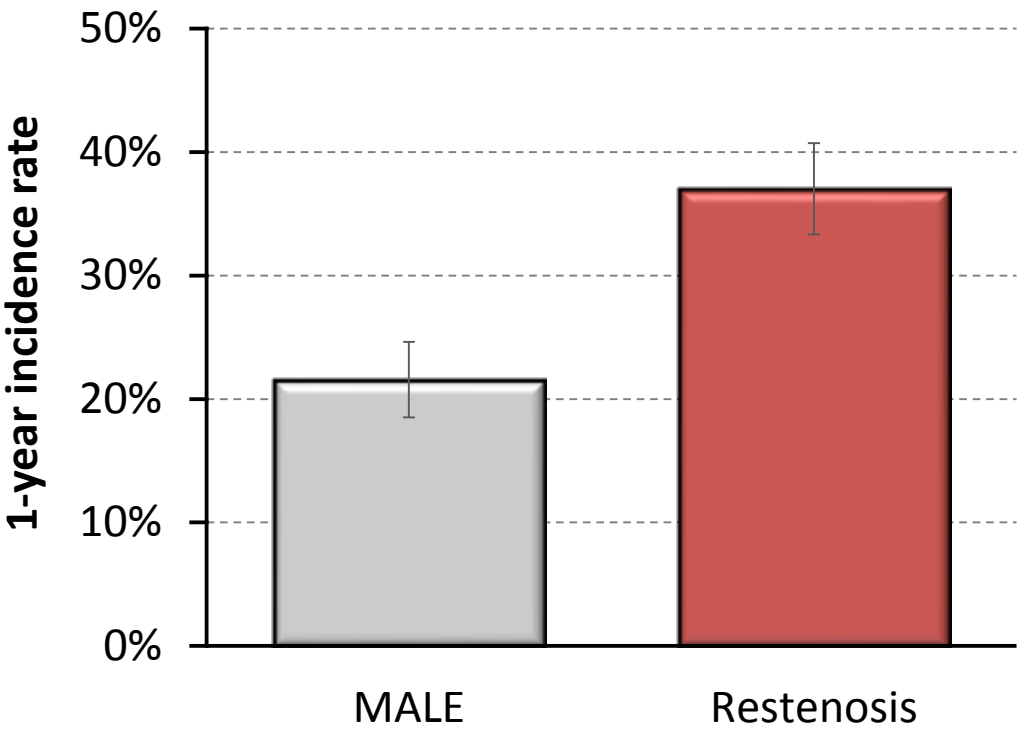
Procedure: Initial: **IVUS** was routinely used for assessing vessel diameter.

12 months: restenosis was evaluated by follow-up **angiography**.

Iida O, et al. JACC Cardiovasc Interv. 2015;8:1105-12.

One-year Incidence of Restenosis and MALE

	n=690
Age	73.6±8.8
DM	69%
Hemodialysis	30%
CLI	32%
CTO	45%
Restenosis	24%
ISR	15%
Lesion length(cm)	17±10
Calcification	65%



One-year incidence of restenosis was estimated to be 37%, while 1-year MALE was observed in 22%, indicating that MALE accounted for 58% in lesions with restenosis.

Iida O, et al. JACC Cardiovasc Interv. 2015;8:1105-12.

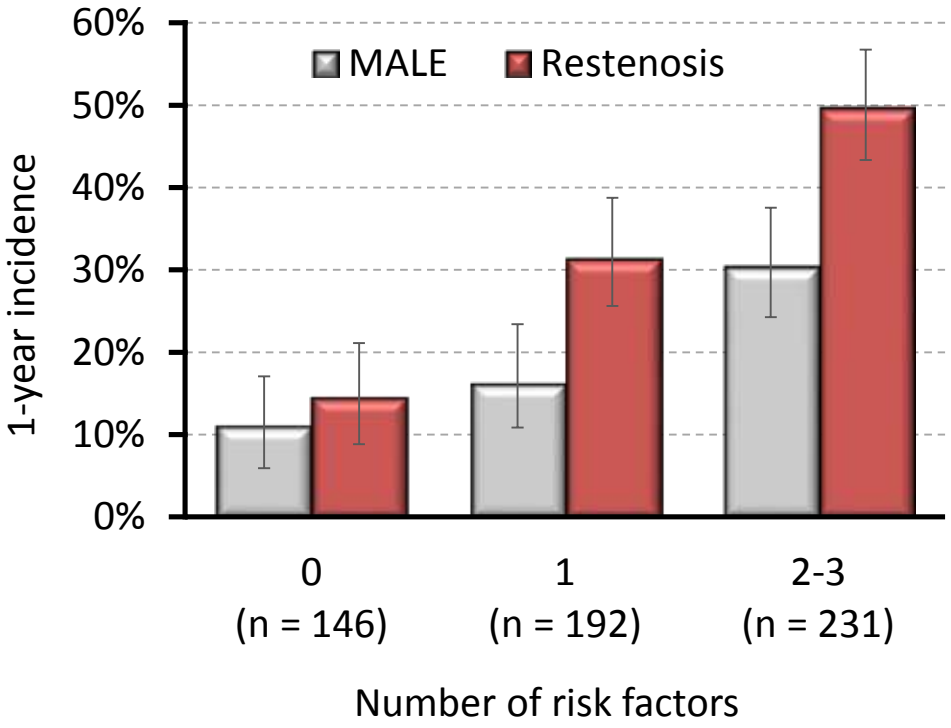
No. of Risk Factors & Restenosis/MALE Incidence

Risk factors for restenosis

1) lesion length ≥ 16 cm

2) EEM area ≤ 27 mm^2

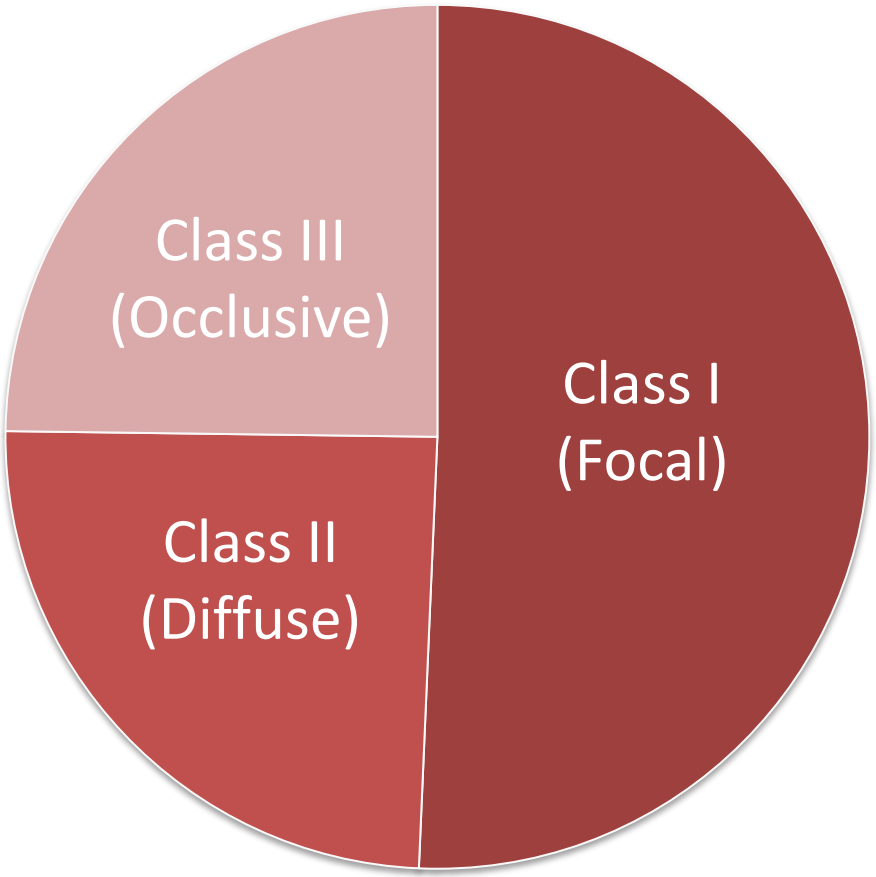
3) MSA ≤ 12 mm^2



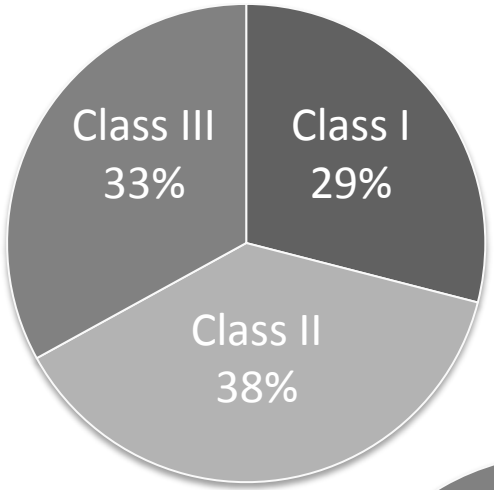
1-year restenosis rate was as low as 15% in cases with none of these risk factors, whereas it reached 51% in those with ≥ 2 risk factors

Iida O, et al. JACC Cardiovasc Interv. 2015;8:1105-12.

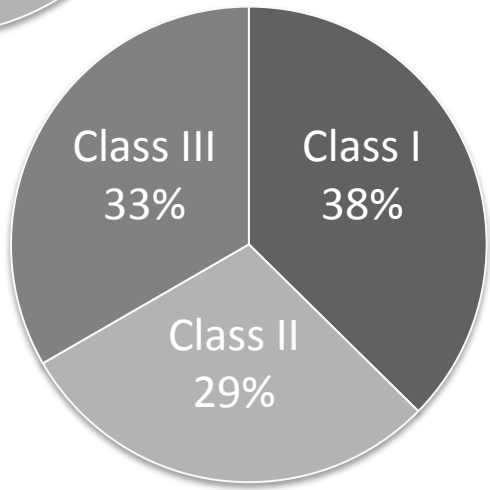
Distribution of DES-ISR at 12 months



DES-ISR, Iida O
JACC interv 2016



BMS-ISR
Tosaka A
JACC 2012



BMS-ISR
Armstrong EJ
CCI 2013

Iida O, et al. JACC Cardiovasc Interv. 2016 in press.
Tosaka A, Soga Y, Iida O, et al. J Am Coll Cardiol. 2012;59:16–23.
Armstrong EJ, et al. Catheter Cardiovasc Interv. 2013;82:1168-74.

One-year stenotic status and baseline characteristics at DES implantation

Variables	Class I (focal) (n = 106)	Class II (Diffuse) (n = 52)	Class III (occlusive) (n = 52)	P value for trend
Age (years)	73 ± 9	73 ± 8	72 ± 10	0.771
Male sex	76 (72%)	33 (63%)	32 (62%)	0.171
Diabetes mellitus	81 (76%)	36 (69%)	32 (62%)	0.051
Regular dialysis	34 (32%)	19 (37%)	11 (21%)	0.238
Smoking	24 (23%)	13 (25%)	14 (27%)	0.546
Critical limb ischemia	26 (25%)	13 (25%)	14 (27%)	0.755
Prior history of EVT	31 (29%)	10 (19%)	20 (38%)	0.391
Calcification	67 (63%)	37 (71%)	28 (54%)	0.188
Chronic total occlusion	**44 (42%)**	**28 (54%)**	**35 (67%)**	**0.009**
Lesion length (cm)	17 ± 9	20 ± 10	19 ± 10	0.113
IVUS-evaluated EEM area (mm^2)	**27 ± 10**	**25 ± 8**	**22 ± 5**	**0.017**
IVUS-evaluated MSA (mm^2)	14 ± 4	13 ± 4	13 ± 3	0.219

Iida O, et al. JACC Cardiovasc Interv. 2016 in press.

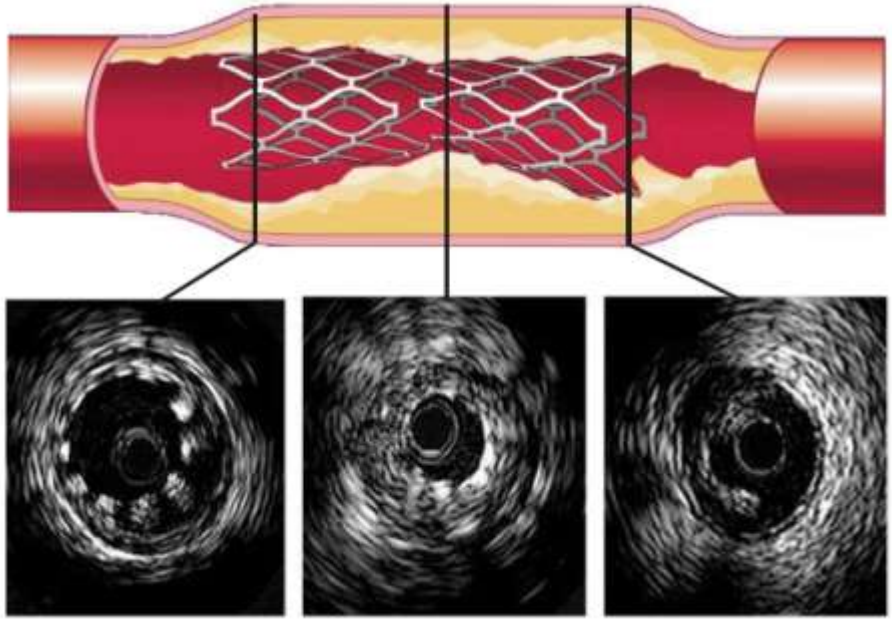
Current findings in SFA treatment
-Learn from ZEPHYR study-

<u>Predictors after DES implantation</u>

- Lesion length
- Distal EEM area
- MSA

<u>Factors associated with morphology of DES-ISR</u>

- Distal EEM area
- CTO



More focusing on primary results

MSA: minimum stent area EEM: external elastic membrane