

Zilver PTX Experiences for Femoropopliteal Artery Disease in Japan

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■ I have the following potential conflicts of interest to report:

Research contracts

Consulting- Fukudadensi, Kaneka, Medicon, Japan Life Line

Employment in industry

Stockholder of a healthcare company

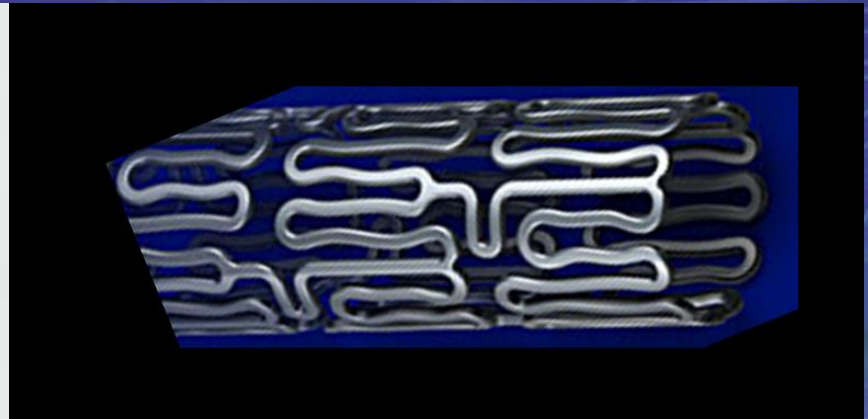
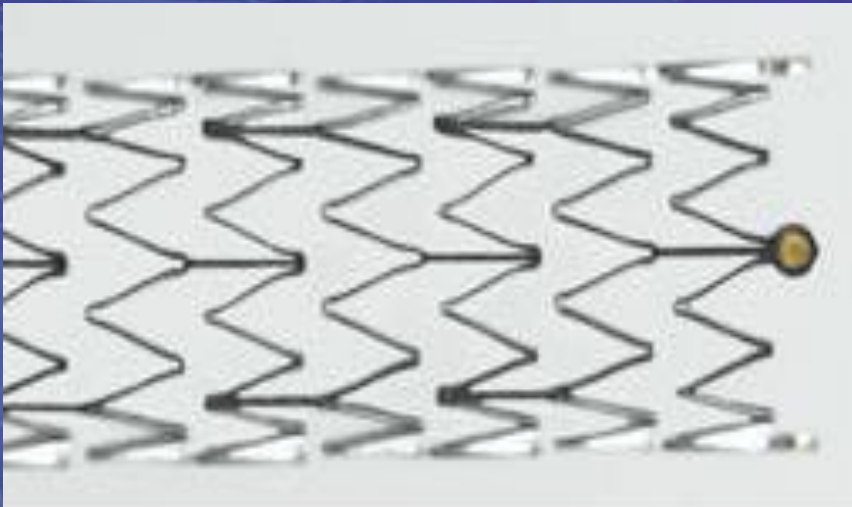
Owner of a healthcare company

Other(s)

I do not have any potential conflict of interest

High expectations of New SFA DES

- Success in Coronary DES
- Restenosis of SFA BMS
- High rate of restenosis and stent fracture in long and multi stent use



Zilver PTX[®] Japan Post-Market Surveillance Study of Paclitaxel-Eluting Stents for Femoropopliteal Artery Disease: 12-Month Results in Real-World Patients

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Japan

On behalf of the Investigators



2014

Zilver PTX Clinical Program

	Randomized Clinical Trial (RCT)	Single-Arm Study (SAS)¹	Japan Post-Market Surveillance Study (PMS)¹
Patients	479	787	907
Regions	US, Japan, Germany	EU, Korea, Canada	Japan
Key Study Criteria	No significant untreated inflow tract stenosis		ALL patients treated with Zilver PTX enrolled (up to enrollment limit), NO exclusion criteria
	At least one patent runoff vessel		
	Maximum 2 Zilver PTX stents per lesion	Maximum 4 Zilver PTX stents per patient	
	Lesion length ≤ 14 cm	No exclusions	
	One lesion per limb		
	No prior stent in SFA	In-stent restenosis	
Excluded if serum creatinine > 2.0, renal failure, or dialysis	No exclusions		
Antiplatelets	Clopidogrel or ticlopidine recommended for 60 days, aspirin indefinitely		
Follow-up	5 years	2 years	5 years
Patency	Core laboratory analysis	Site analysis	
Stent Integrity	X-ray core laboratory analysis		

Increasingly complex patients and lesions 



¹ These studies included patients with lesions > 140 mm in length and previously stented lesions that are outside of the approved indication for use in the US.

Patient Demographics and Comorbidities

	RCT	SAS	Japan PMS
Patients	236	787	907
Age (years)	68 ± 10 *	67 ± 10 *	74 ± 9
Male	66%	73%	70%
Diabetes	50% *	36% *	59%
High cholesterol	76% *	58%	61%
Hypertension	89%	80% *	85%
Pulmonary disease	19% *	9%	8%
Renal disease	10% *	11% *	44% ¹

* $p < 0.01$ compared to Japan PMS

¹ Of patients with renal disease in the Japan PMS, 82% were in renal failure, defined as eGFR < 60 and/or dialysis

Japan PMS patients are older and have a higher prevalence of diabetes and renal disease

Baseline Lesion Characteristics

	RCT	SAS	Japan PMS	
Lesions	247	900	1081	
Lesion length (cm)	6.6 ± 3.9 *	10.0 ± 8.2 *	14.7 ± 9.7	
Diameter stenosis (%)	80 ± 17 *	85 ± 16 *	92 ± 11	
Total occlusions	33% *	38%	42%	
In-stent restenosis (ISR)	0% *	15%*	19%	
Patent runoff vessels	0	0%	0%	7%
	1	22%	19%	32%
	2	35%	35%	32%
	3	42%	45%	29%
Rutherford 4-6 (CLI)¹	9% *	11% *	20%	

* $p < 0.05$ compared to Japan PMS

¹ p -value based on all reported Rutherford values (classes 1 through 6)

Japan PMS lesions are more complex (e.g., longer, more ISR, fewer patent runoff vessels, greater incidence of CLI)

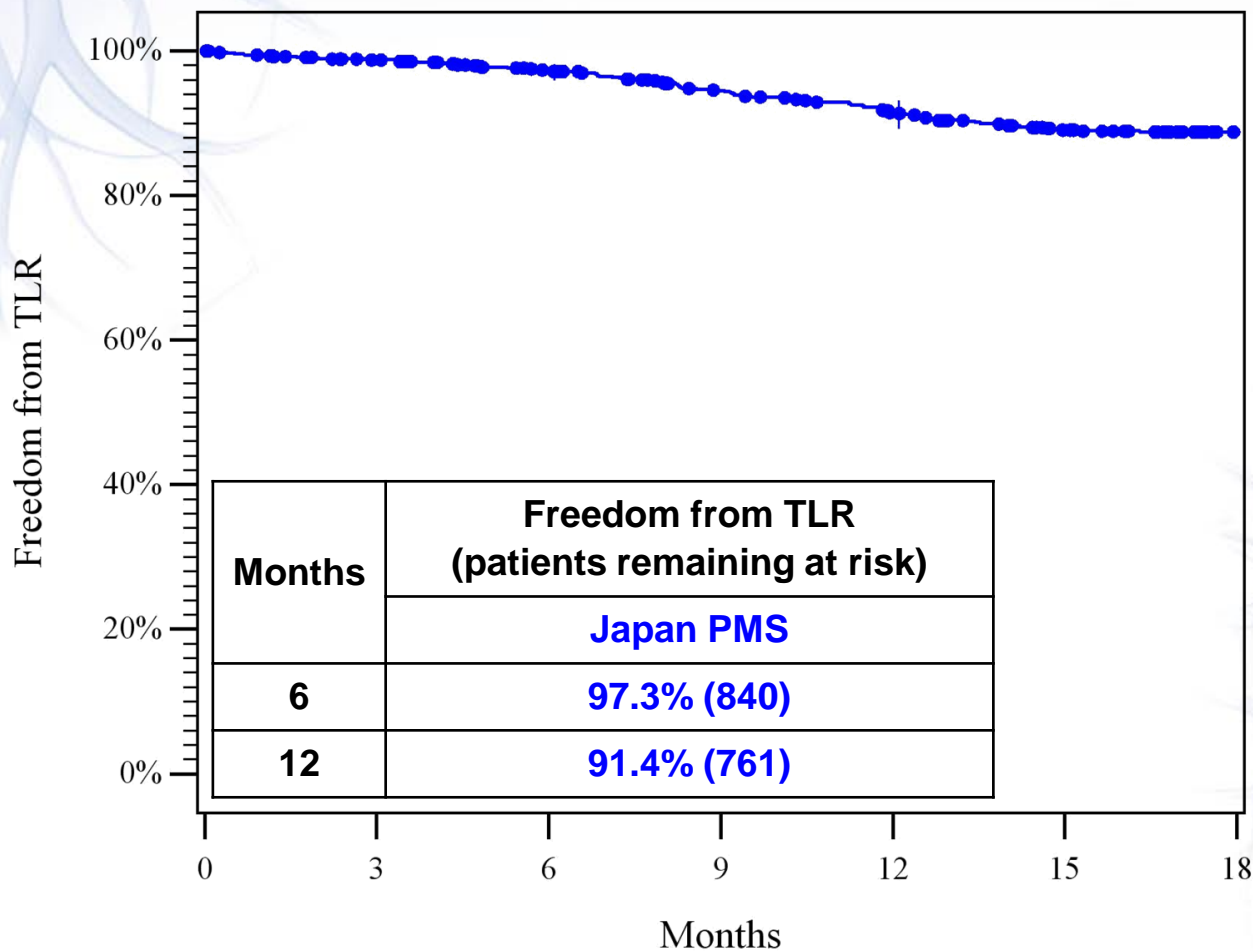
Stent Integrity Through 12 Months

- 1066 stents were evaluated by sites in Japan PMS
 - 17 total fractures (1.6%)

	RCT	SAS	Japan PMS
Fracture Rate	0.9%	1.5%	1.6%
Number of Stents Evaluated	470	1889	1066

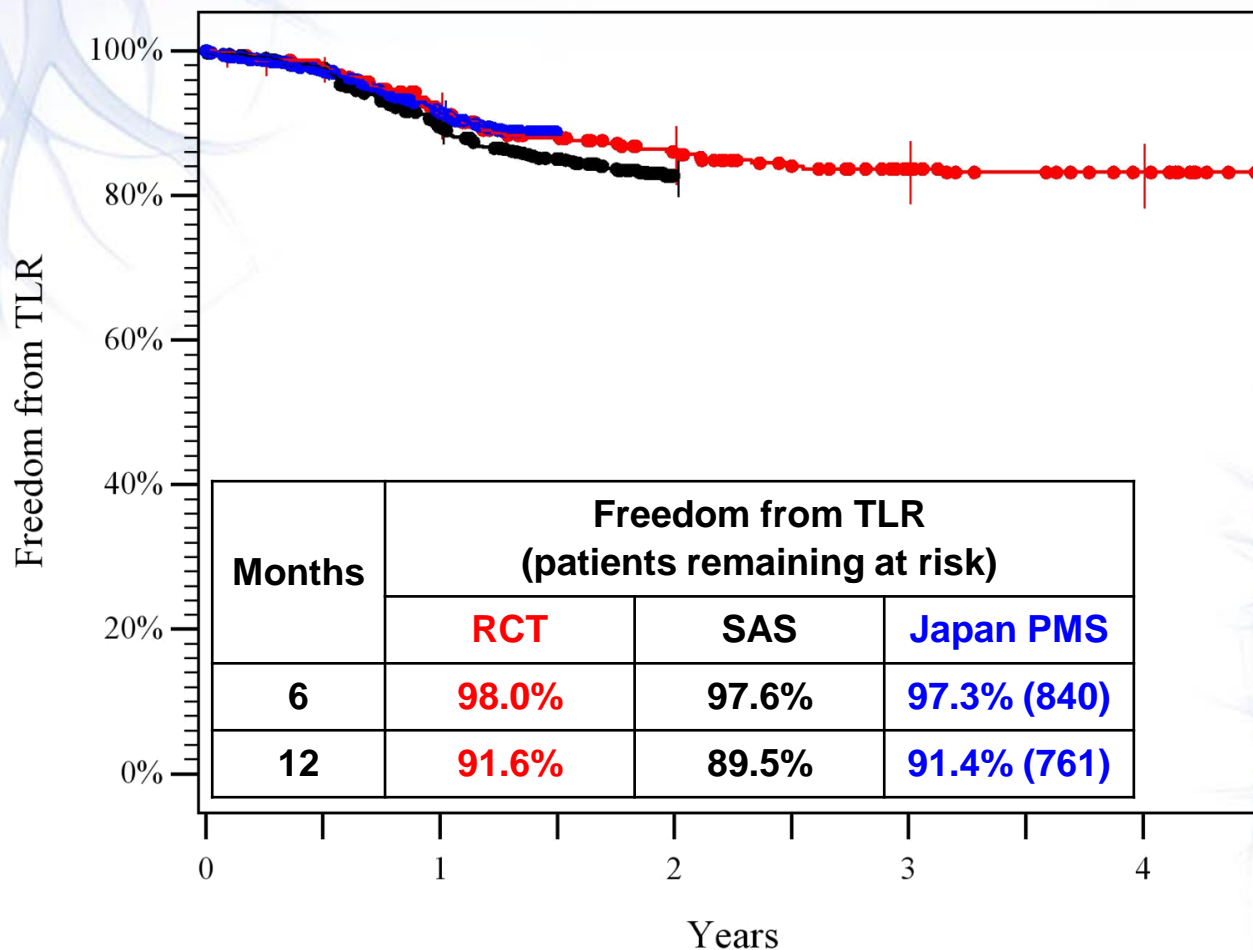
Low fracture rate; not significantly greater than in pre-market studies despite more complex lesions (e.g., longer, more ISR, fewer patent runoff vessels)

Freedom from TLR



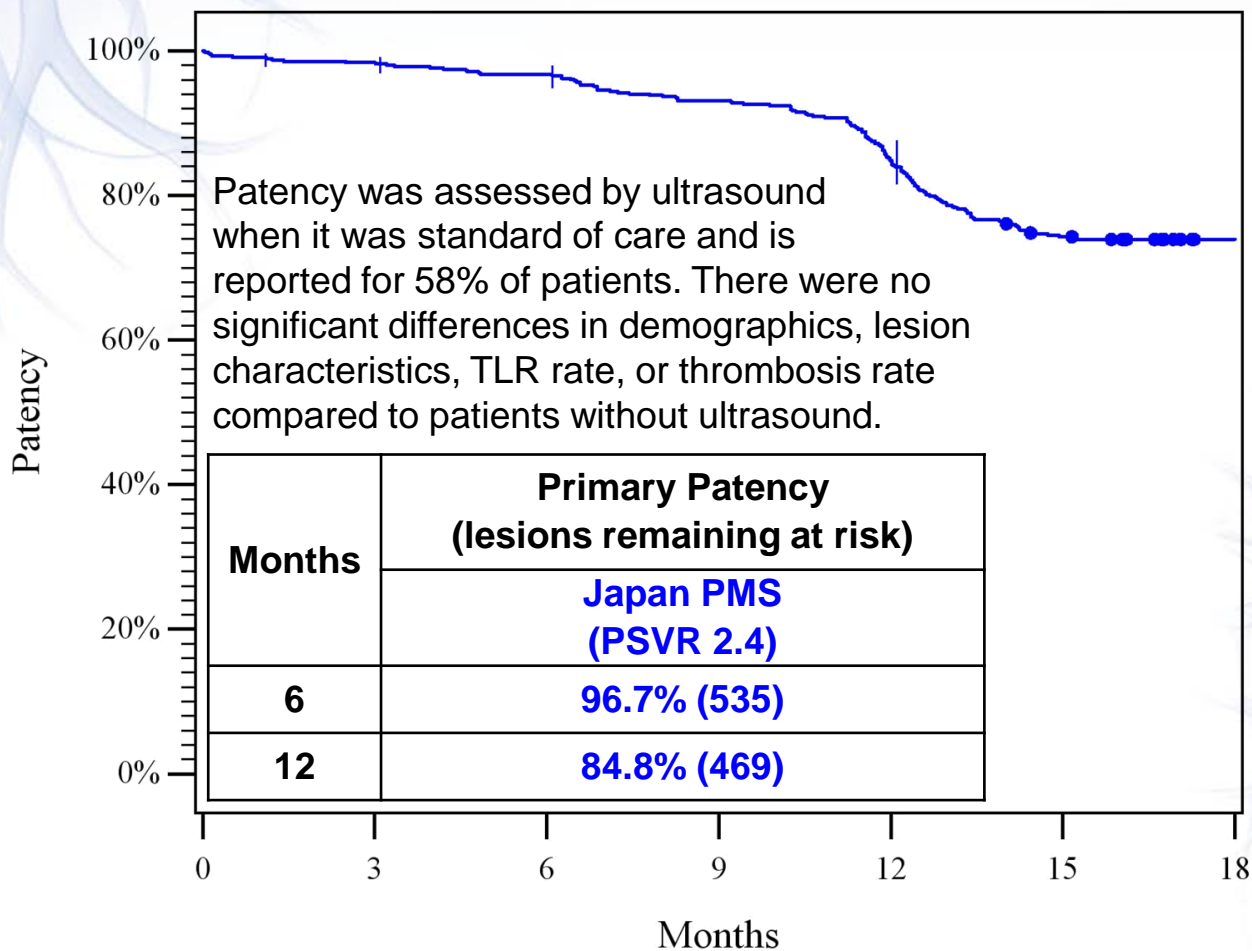
Freedom from TLR is 91.4% through 12 months in the Japan PMS

Freedom from TLR



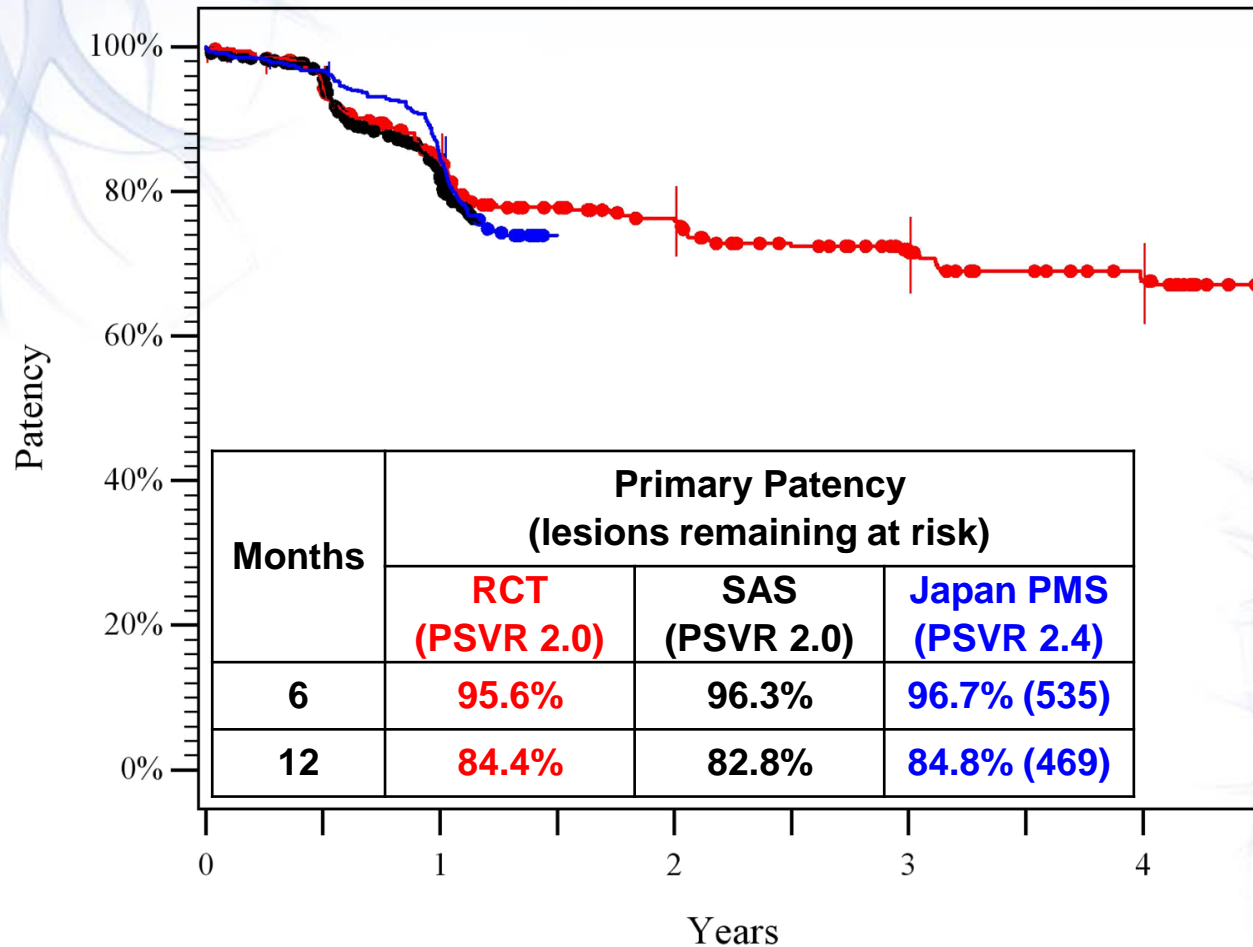
Freedom from TLR in the Japan PMS is similar to both pre-market studies

Primary Patency by Duplex Ultrasound



Primary patency rate is 84.8% through 12 months in the Japan PMS

Primary Patency by Duplex Ultrasound



Primary patency rate in the Japan PMS is similar to both pre-market studies

Results in RCT-Like and More Complex Lesions

- Classification as an RCT-like lesion required all of
 - ≤ 14 cm length
 - At least 1 patent runoff vessel
 - No in-stent restenosis
- Classification as a more complex lesion required at least one of
 - > 14 cm length
 - 0 patent runoff vessels
 - In-stent restenosis
- There were no significant differences in patient demographics and comorbidities for the RCT-like versus more complex lesion groups

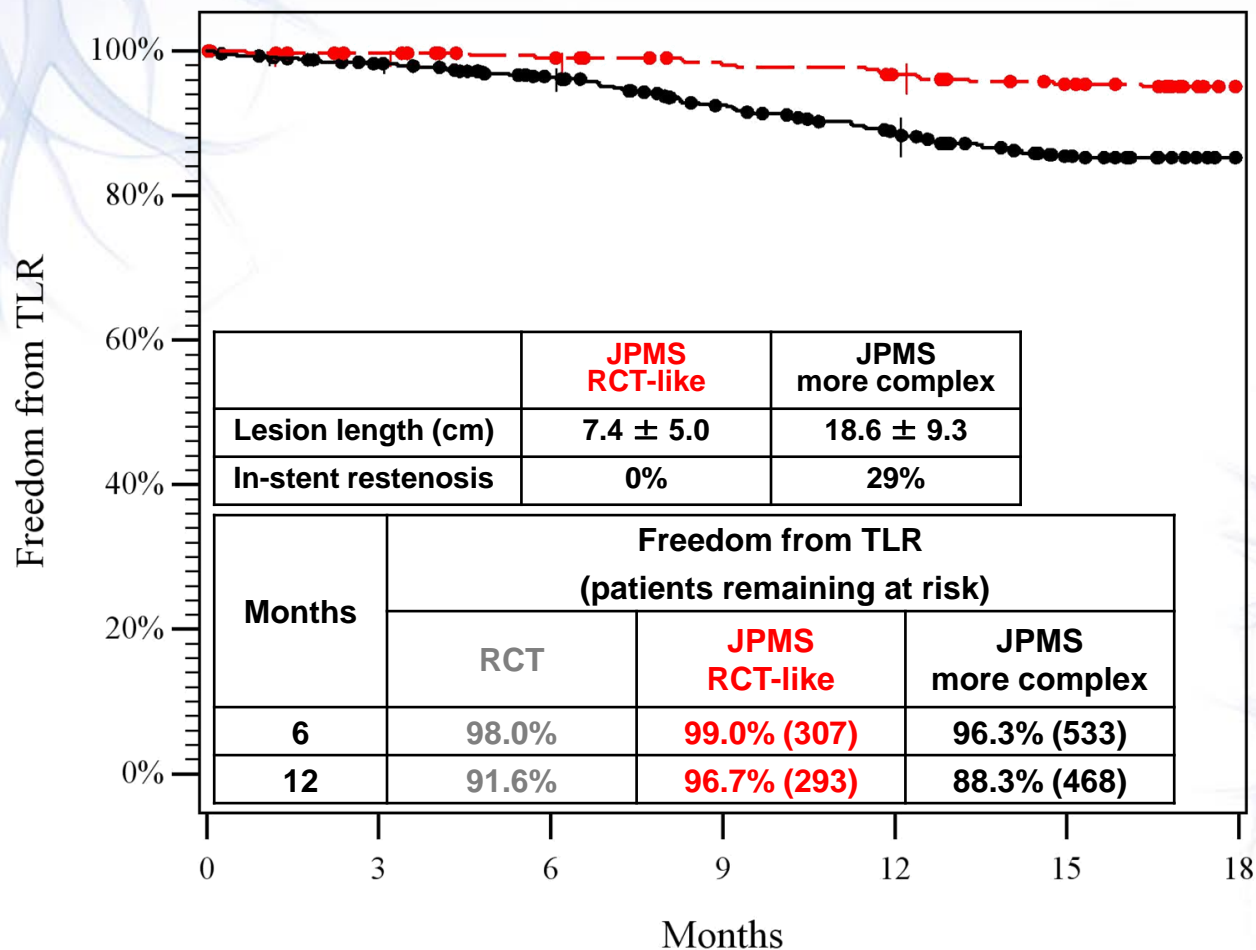
RCT-Like and More Complex Lesions

		Zilver PTX RCT	JPMS RCT-like	JPMS more complex	<i>p-value*</i>
Lesions		247	378	703	
Lesion length (cm)		6.6 ± 3.9	7.4 ± 5.0	18.6 ± 9.3	< 0.001
Diameter stenosis (%)		80 ± 17	89 ± 12	93 ± 9	< 0.001
Total occlusions		33%	28%	49%	< 0.001
In-stent restenosis		0%	0%	29%	< 0.001
Patent runoff vessels	0	0%	0%	10%	< 0.001
	1	22%	29%	33%	
	2	35%	36%	30%	
	3	42%	34%	27%	

* JPMS RCT-like lesions compared to JPMS more complex lesions

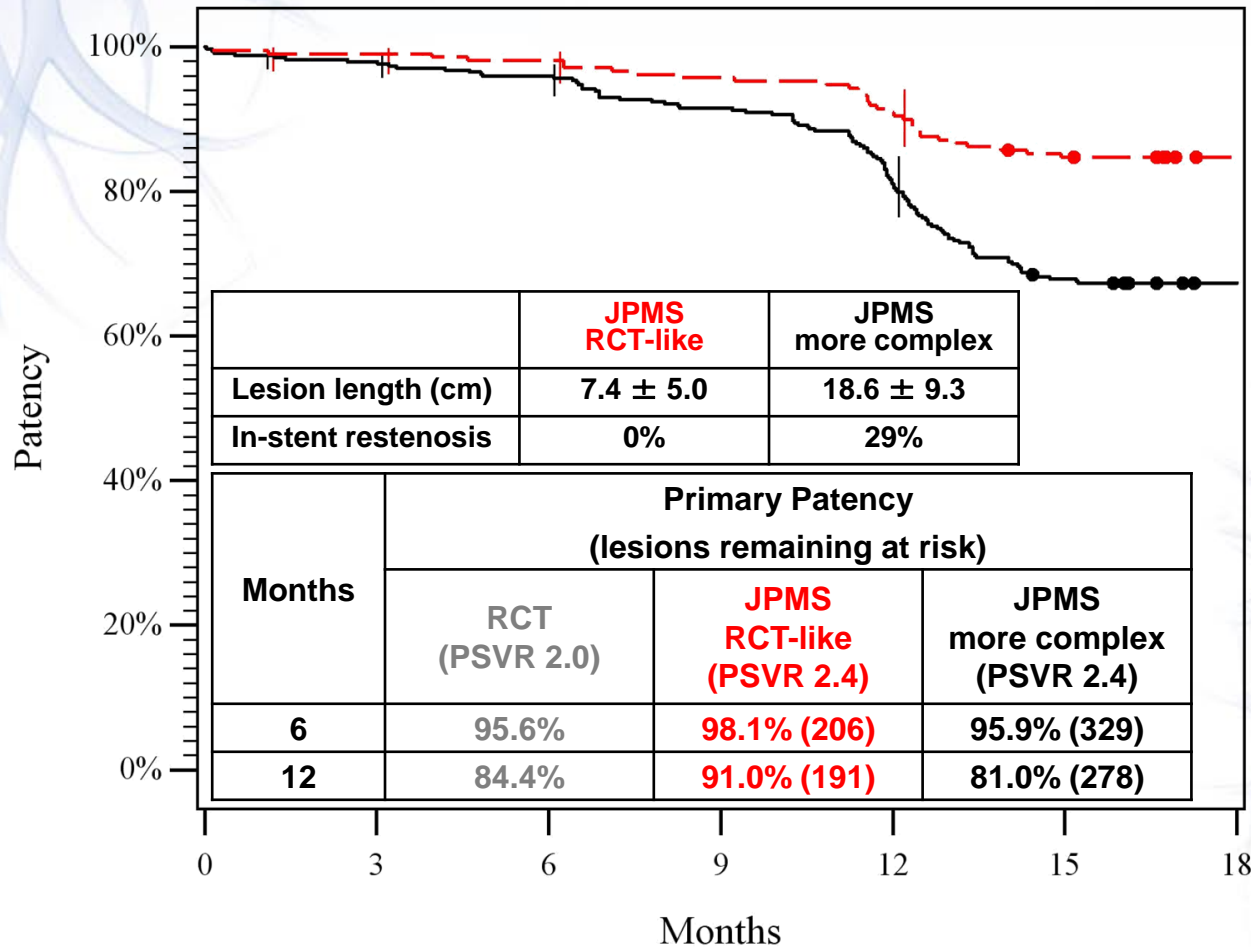
The more complex lesions are longer, have higher incidence of total occlusions and in-stent restenosis, and have fewer patent runoff vessels

Freedom from TLR



Freedom from TLR is excellent in more complex lesions, and as expected, lower than in RCT-like lesions

Primary Patency by Duplex Ultrasound



Primary patency rate is excellent in RCT-like lesions, and as expected, lower in more complex lesions

Conclusions

- Large amount of clinical data for Zilver PTX, ranging from carefully controlled Level I evidence to large, global, real-world experience
- As expected, patient population and lesion characteristics become more challenging in real-world, all-comer studies
- Japan PMS results through 1 year confirm the benefit of the Zilver PTX technology for treating femoropopliteal artery disease
 - Favorable results in both RCT-like and more complex lesions
 - Consistency across studies provides added assurance of the performance of the Zilver PTX drug-eluting stent

The Zilver PTX[®] Randomized Trial of Paclitaxel-Eluting Stents for Femoropopliteal Artery Disease: 5-Year Results

Michael D. Dake, MD

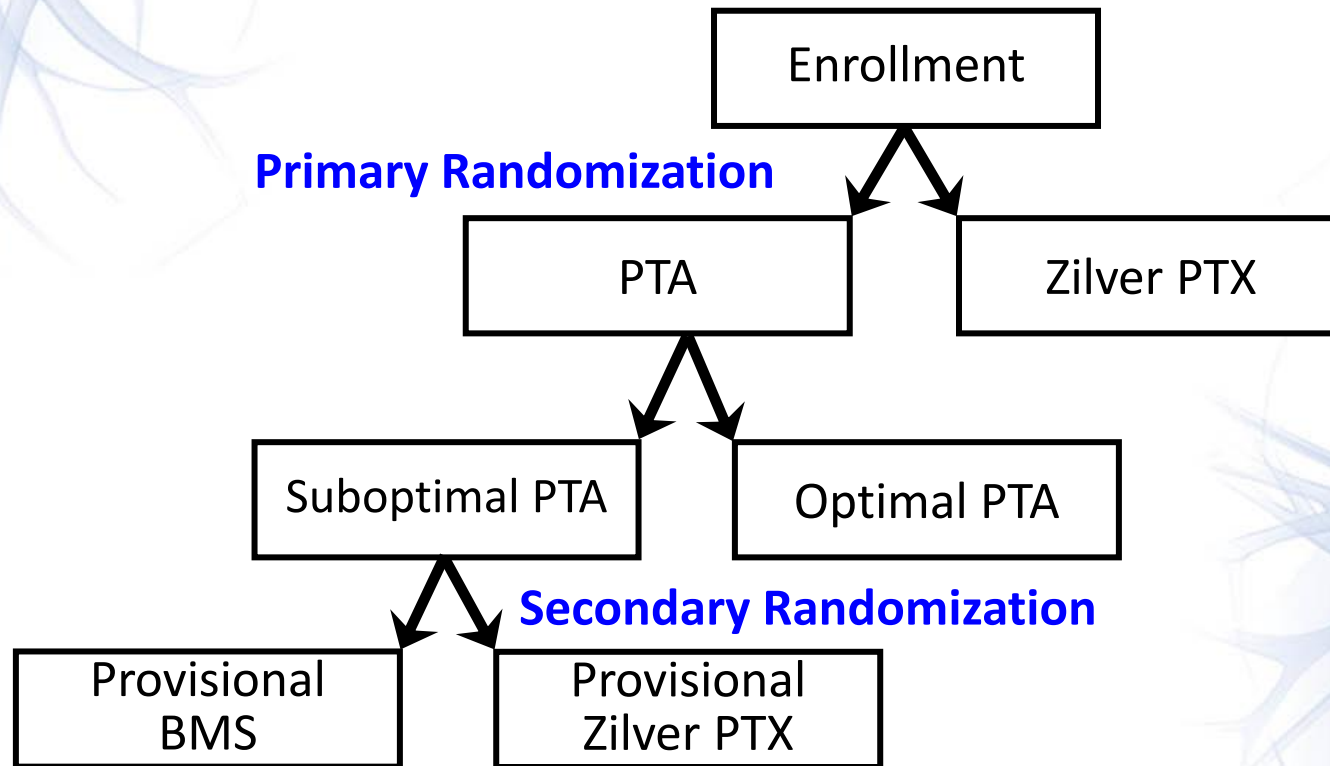
*Department of Cardiothoracic Surgery
Stanford University School of Medicine
Stanford, California*

On behalf of the Investigators



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Zilver PTX Study Design

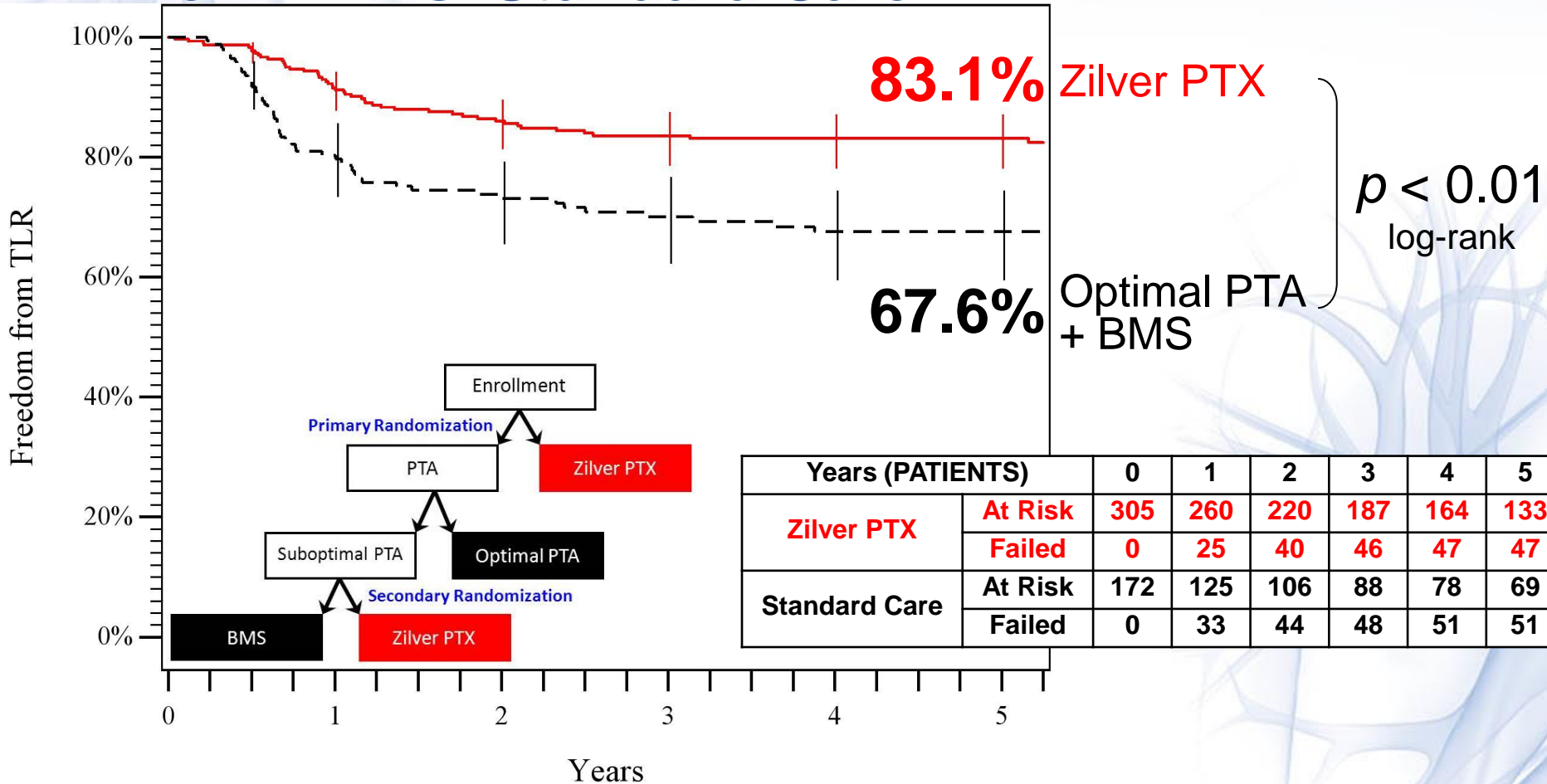


Outline

- Study design and baseline characteristics
- Safety results through 5 years
 - Stent integrity
- **Effectiveness results through 5 years**
 - **Zilver PTX vs. standard care**
 - **Provisional Zilver PTX vs. Provisional BMS**
- Conclusions

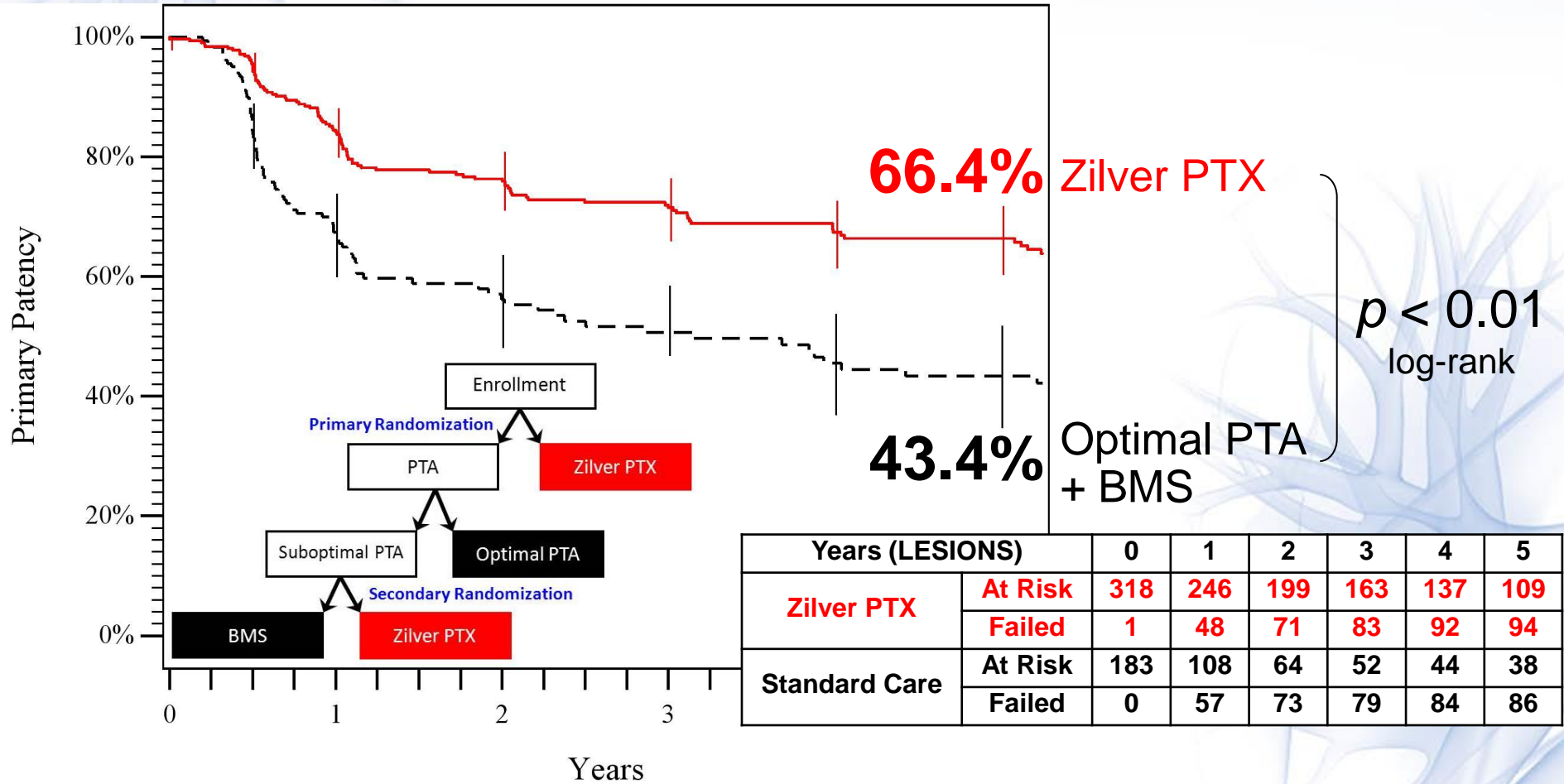
5-year Freedom from TLR

Zilver PTX vs. Standard Care



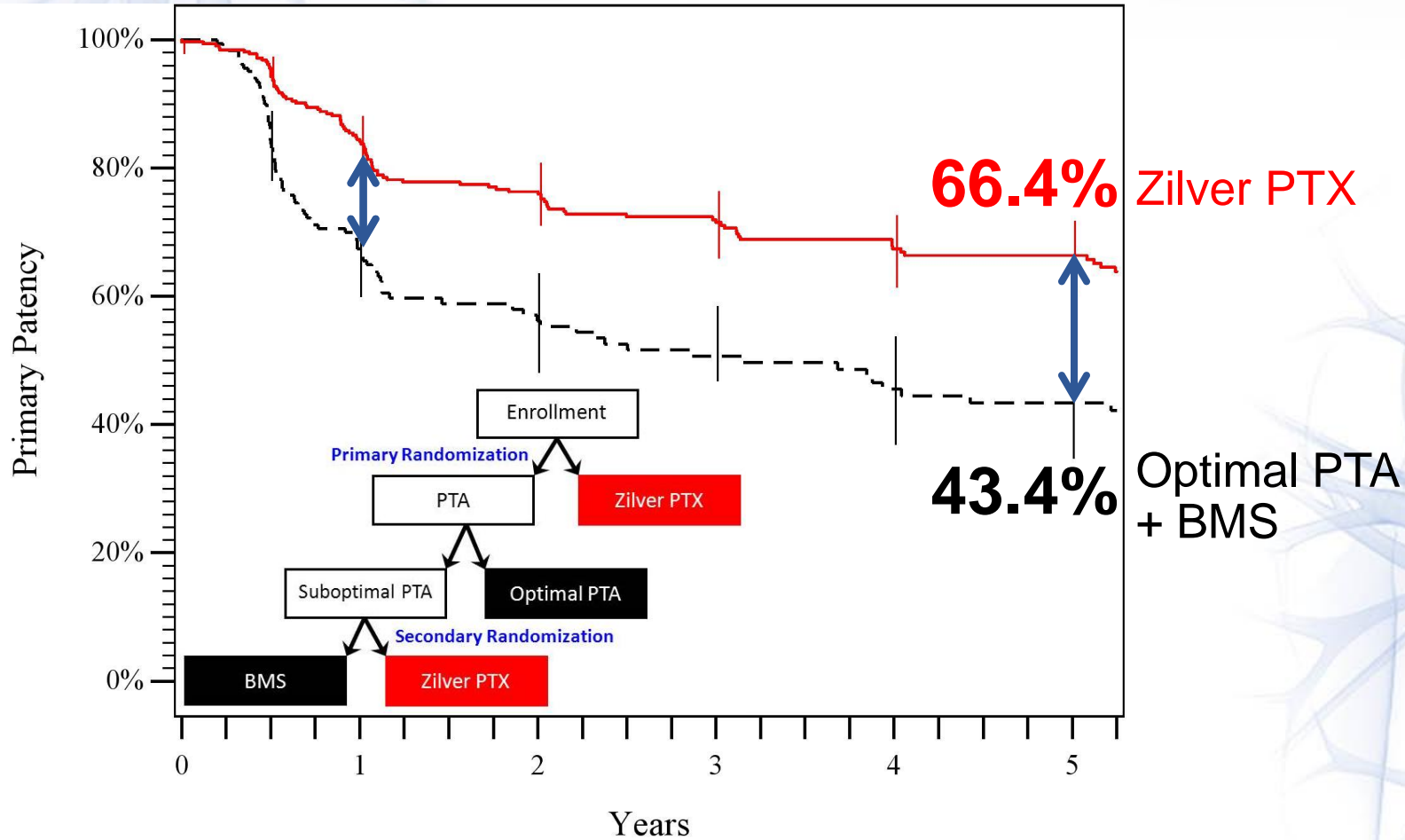
At 5 years, Zilver PTX demonstrates a 48% reduction in reintervention compared to standard care

5-year Primary Patency (PSVR < 2.0)



At 5 years, Zilver PTX demonstrates a 41% reduction in restenosis compared to standard care

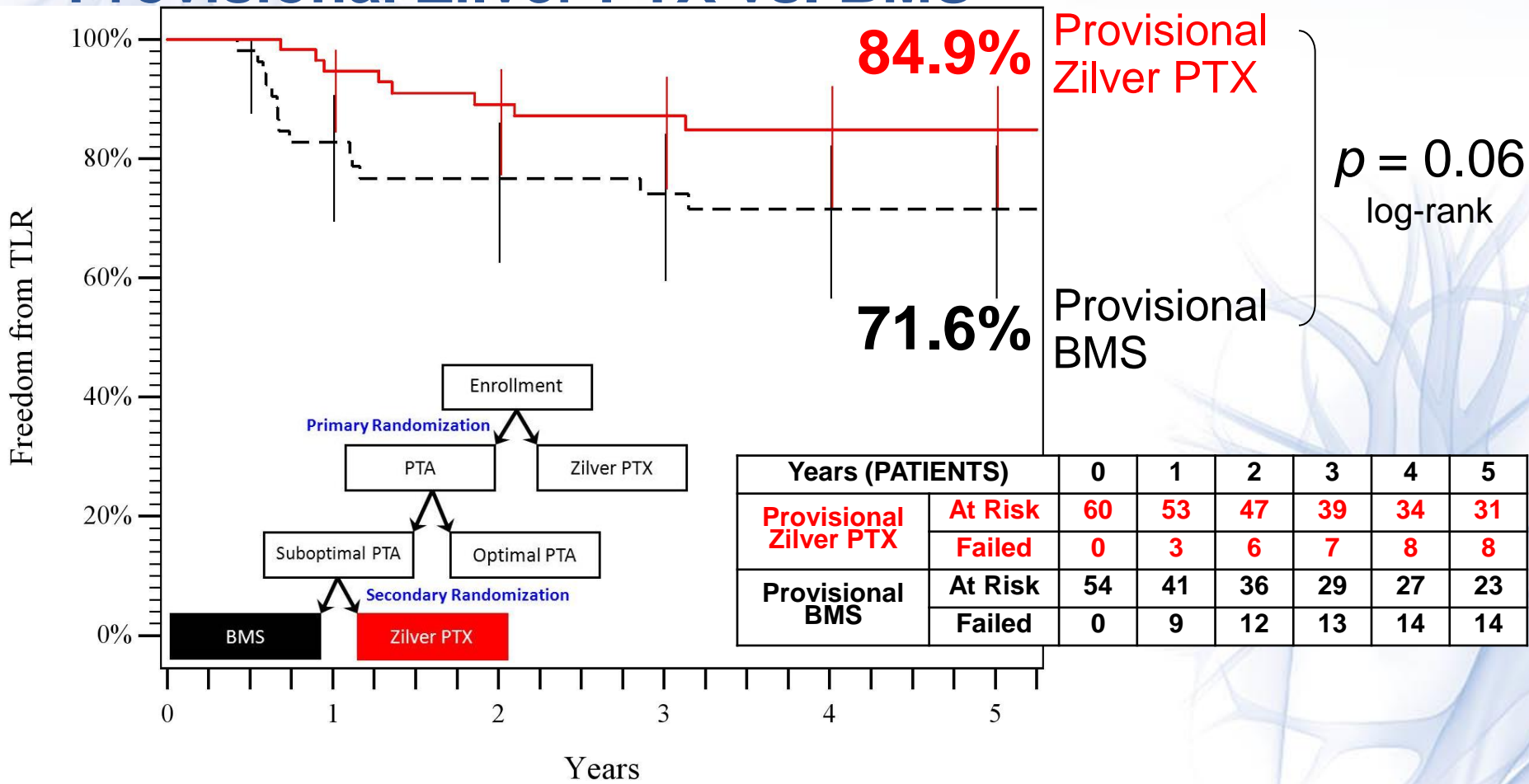
5-year Primary Patency (PSVR < 2.0)



From 1-5 years, the relative separation increases by 35%

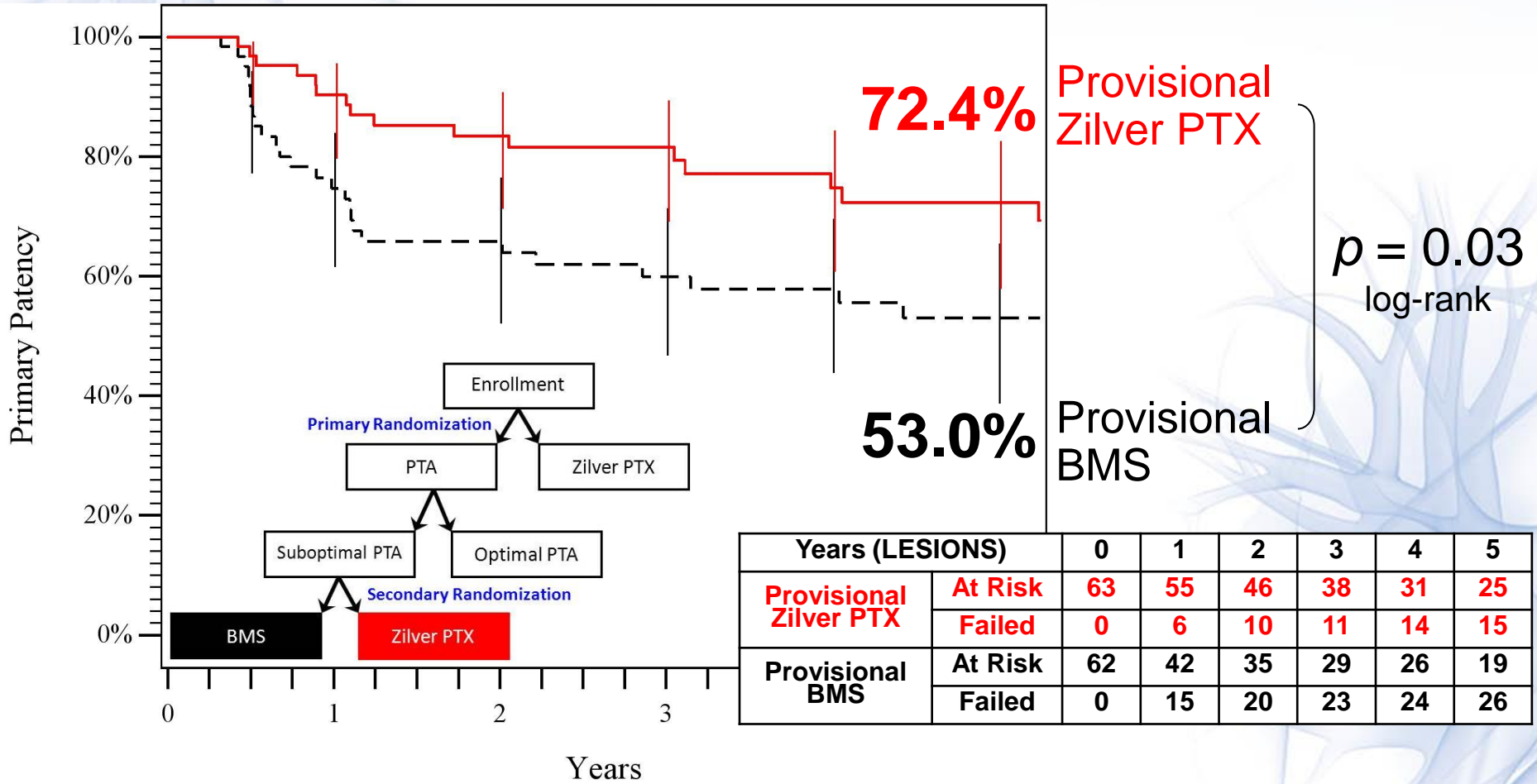
5-year Freedom from TLR

Provisional Zilver PTX vs. BMS



At 5 years, Zilver PTX demonstrates a 47% reduction in reintervention compared to BMS

5-year Primary Patency (PSVR < 2.0)



At 5 years, Zilver PTX demonstrates a 41% reduction in restenosis compared to BMS

Conclusions for 5-year Zilver PTX RCT

- As the first randomized controlled SFA device trial with 5-year follow-up, these results with the Zilver PTX stent provide important insights regarding long-term outcomes for endovascular treatment
- 5-year data for Zilver PTX versus standard care
 - Greater than 40% reduction in reintervention and restenosis
 - Superior clinical benefit
 - These benefits increase with time – results with Zilver PTX continue to diverge from standard care over 5 years with no late catch-up
- 5-year results confirm long-term superiority of Zilver PTX versus bare metal stents

Limitations

1 More more complex lesion in Japan

2 Poor delivery system

3 Stent variation $\leq 10\text{cm}$

4 Appropriate DAPT

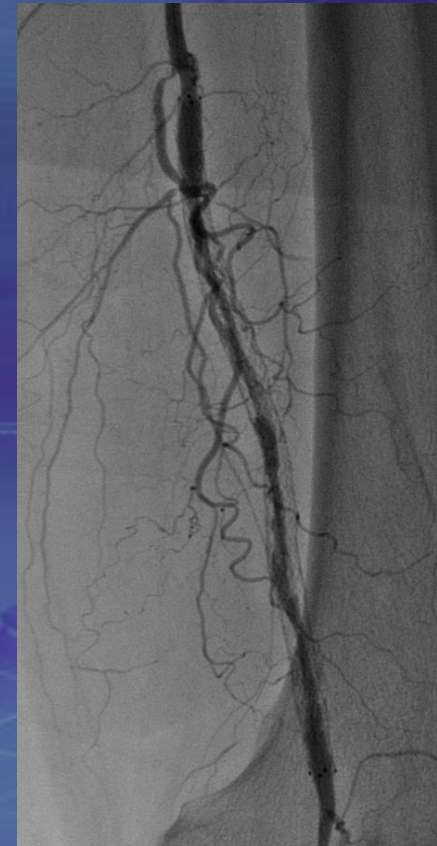
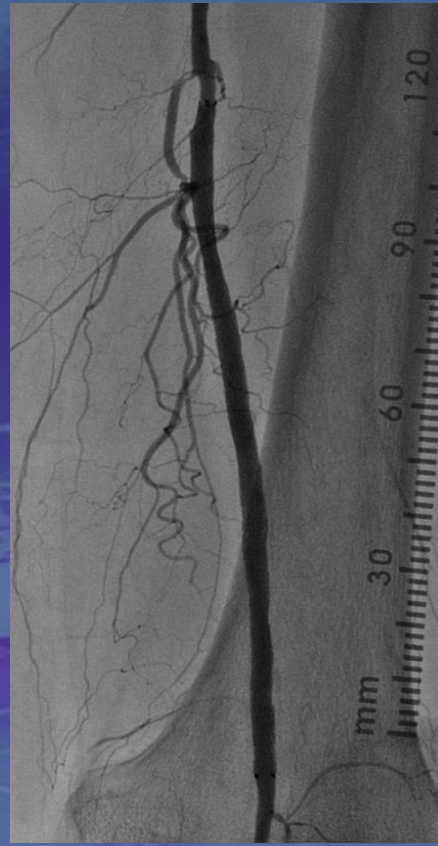
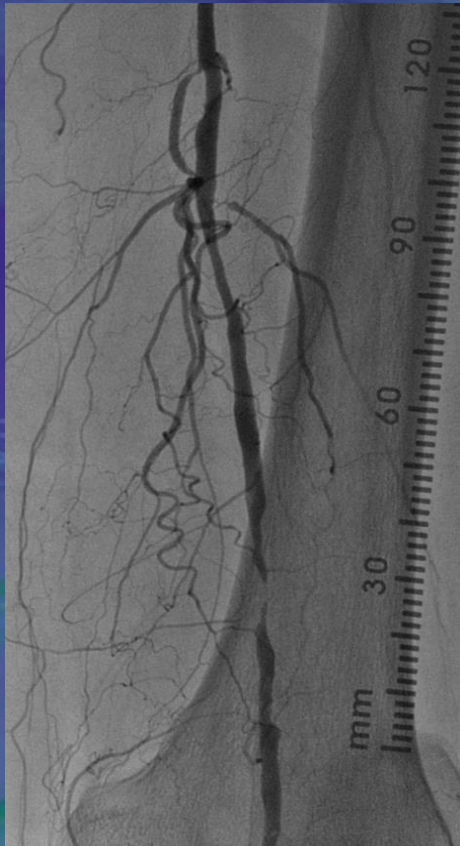
Original recommendation 2 months

Case 3: 70's Female R-3

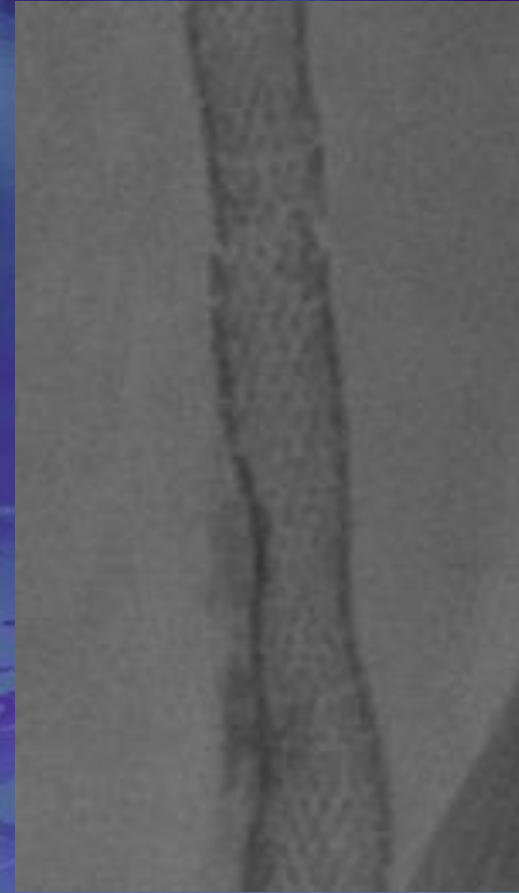
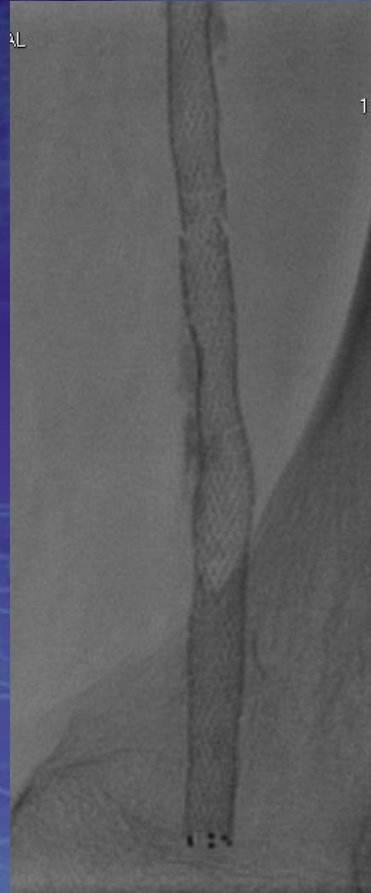
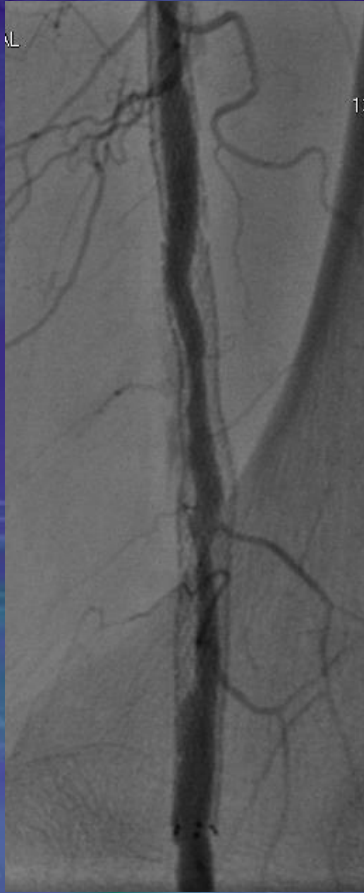
Pre

Post

12 months



Case-4: 60`s Female R-3,HD



Case 5: 60's Male R-3

Zilver PTX

6x120mm+6x60mm

On 24th day Reocclusion



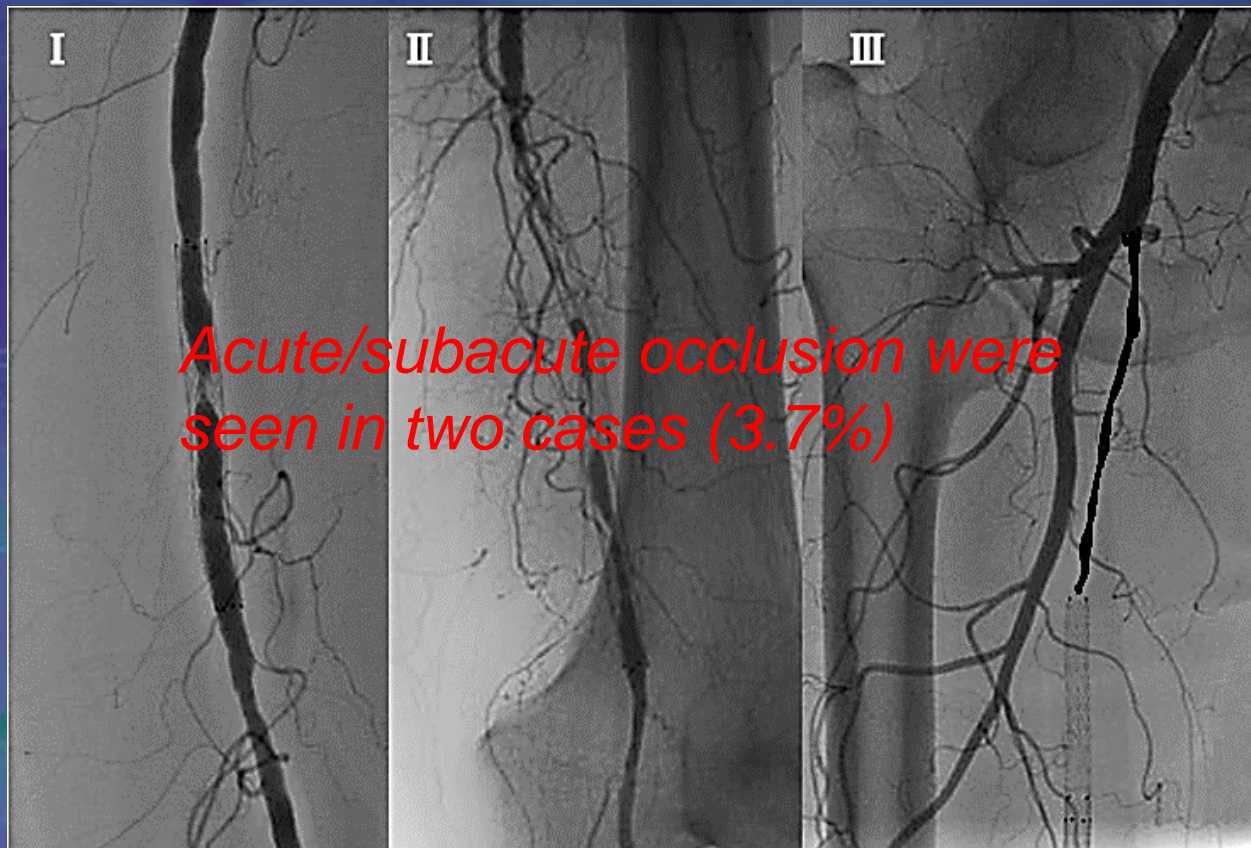
Angiographic Restenotic Pattern of Zilver PTX

N=19

Focal

Diffuse

Reocclusion



18%

26%

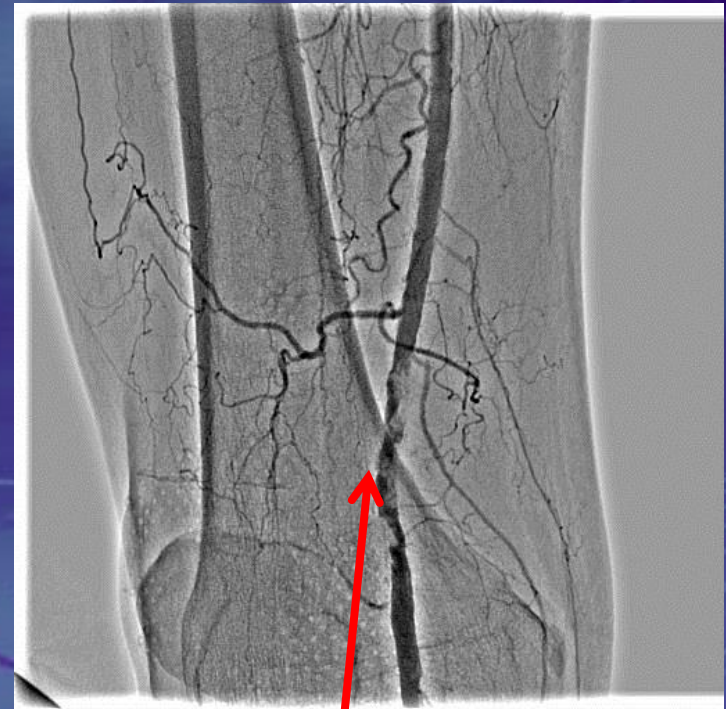
58%

JCR 2014

Delivery system



No calcification and tortuosity in the iliac artery
Moderate sharp angle between bilateral iliac arteries
Easy to use cross-over technique

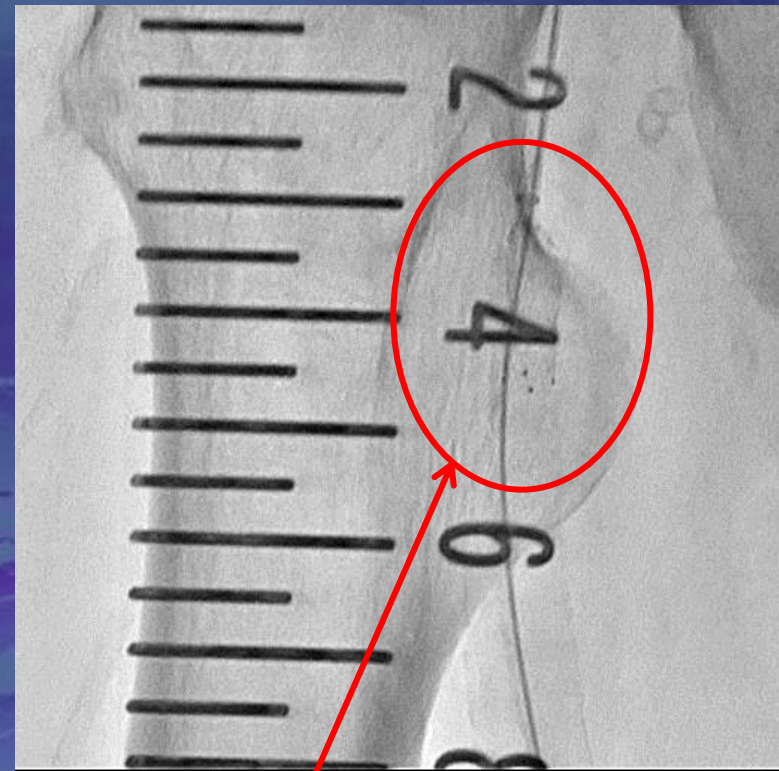


Calcified short lesion

Delivery system

6.0x120mm Zilver PTX

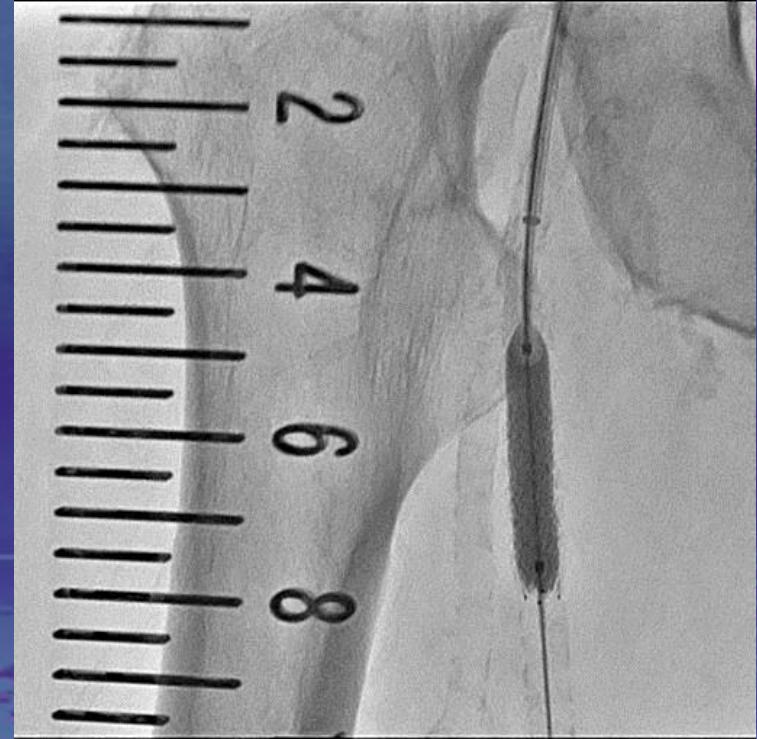
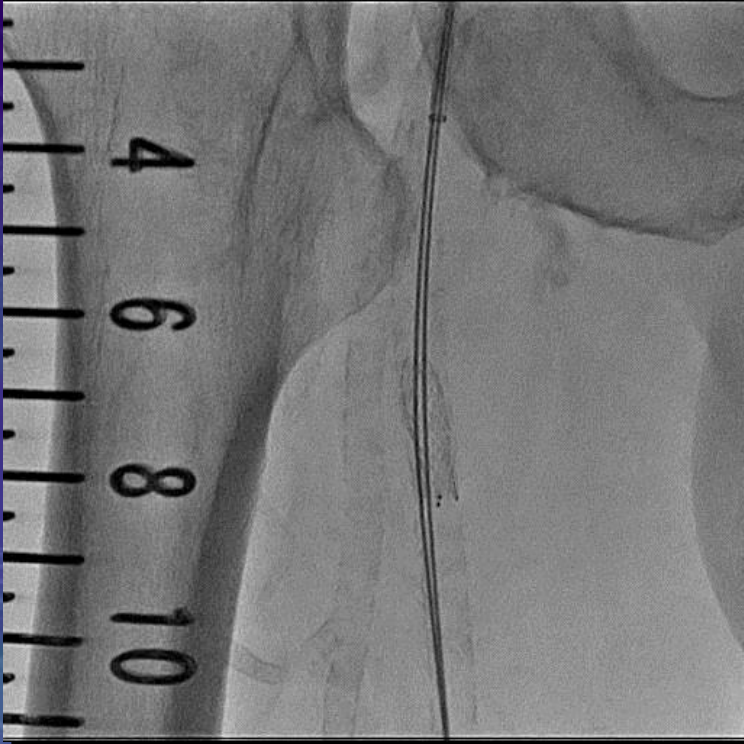
- ① Switched from 0.014 GW to 0.035Amplatz Super Stiff wire
- ② No resistant during the advancement of stent
- ③ Could not pull back outer sheath after the partial stent delivery (30mm)
- ③ Tried to retrieve the whole segment of stent
- ④ Outer sheath was ruptured
- ⑤ Fragmentated stent remained in the SFA



Fragmentation of stent

JCR 2014

Delivery system



Express LD 7.0/27mm was implanted into the broken stent

*Temporary withdrawn from the market
Shorten from 120mm to 100mm*

My personal conclusion

- 1 PTA coating reduced restenosis compared to the balloon angioplasty and conventional BMS in RCT and PMS
- 2 Safety concern regarding the stent delivery system and stent thrombosis
- 3 Not cost effectiveness (Maximum stent length $\leq 100\text{mm}$)
- 4 Appropriate duration of DAPT is not determined