Zilver PTX Post-Market Surveillance Study of Paclitaxel-Eluting Stents for Treating Femoropopliteal Artery Disease in Japan: 3-Year Results

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On behalf of the Investigators

Disclosure

Speaker name:

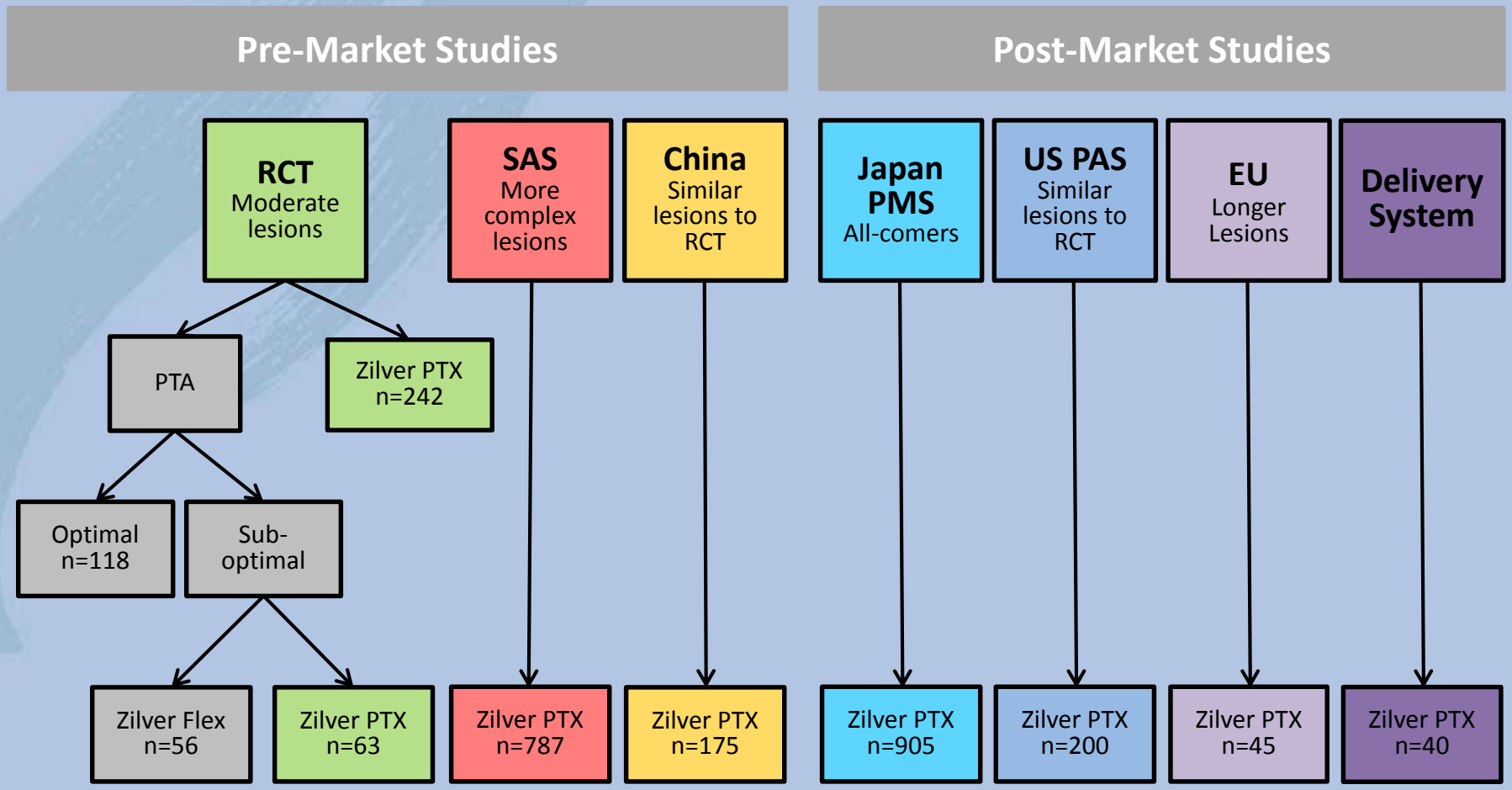
.....Hiroyoshi Yokoi., M.D.....

I have the following potential conflicts of interest to report:

- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☒ Other(s) Cook, Termo, BSJ,

☐ I do not have any potential conflict of interest

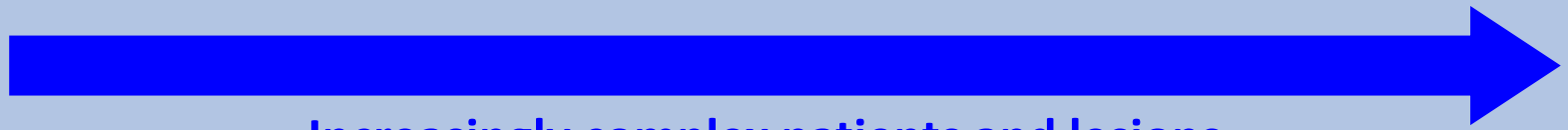
Global Clinical Program



More than 2400 patients to be included in current Zilver PTX clinical program

Japan PMS Compared to RCT and SAS

<table>
<tr><th></th><th>Zilver PTX RCT</th><th>Zilver PTX SAS</th><th>Zilver PTX Japan PMS</th></tr>
<tr><td rowspan="7">Key Study Criteria</td><td colspan="2">No significant untreated inflow tract stenosis</td><td rowspan="7">ALL patients treated with Zilver PTX enrolled (up to enrollment limit), NO exclusion criteria</td></tr>
<tr><td colspan="2">At least one patent runoff vessel</td></tr>
<tr><td>Maximum 2 Zilver PTX stents per lesion</td><td>Maximum 4 Zilver PTX stents per patient</td></tr>
<tr><td>Lesion length ≤ 14 cm</td><td rowspan="2">No exclusions</td></tr>
<tr><td>One lesion per limb</td></tr>
<tr><td>No prior stent in SFA</td><td>ISR included</td></tr>
<tr><td>Excluded if serum creatinine > 2.0, renal failure, or dialysis</td><td>No exclusions</td></tr>
<tr><td>Antiplatelets</td><td colspan="3">Clopidogrel or ticlopidine recommended for 60 days, aspirin indefinitely</td></tr>
<tr><td>Follow-up</td><td>5 years</td><td>2 years</td><td>5 years</td></tr>
<tr><td>Patency</td><td>DUS core laboratory analysis</td><td colspan="2">DUS site analysis</td></tr>
<tr><td>Stent Integrity</td><td colspan="3">X-ray core laboratory analysis</td></tr>
</table>



Increasingly complex patients and lesions

3-year Follow-up for Japan PMS

- 905 patients with 1080 lesions treated with 1877 Zilver PTX stents
- 3-year results currently available for 84% of eligible patients (526/623)
  - 18% (160/905) lost to follow-up or withdrawn through 3 years
  - 13% (114/905) mortality through 3 years
    - None adjudicated as device- or procedure-related

Patient Demographics and Comorbidities

	Zilver PTX RCT	Zilver PTX SAS	Zilver PTX Japan PMS
Patients	236	787	905
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%
Renal failure (eGFR <60 and/or "on Dialysis")	0% *	Not assessed	35%

* $p<0.05$ compared to Japan PMS

Japan PMS patients were older, more diabetic, and had more renal failure

Baseline Lesion Characteristics

		Zilver PTX RCT		Zilver PTX SAS		Zilver PTX Japan PMS
Lesions		247		900		1080
Lesion length (cm)		6.6 ± 3.9 *		10.0 ± 8.2 *		14.6 ± 9.6
Diameter stenosis (%)		80 ± 17 *		85 ± 16 *		92 ± 11
Total occlusions		33% *		38%		42%
In-stent restenosis		0% *		15%*		19%
Patent runoff vessels	**0**	0%		0%		7%
	1	22%	*	19%	*	32%
	2	35%		35%		33%
	≥3	42%		46%		29%

* $p<0.05$ compared to Japan PMS

Japan PMS lesions were more complex (e.g., longer, more ISR, fewer patent runoff vessels)

Baseline Clinical Assessment

Pre-procedure Clinical Assessment		Zilver PTX RCT		Zilver PTX SAS		Zilver PTX Japan PMS
Rutherford	1	0%		0.5%		8%
	2	53%		32%		27%
	3	38%	*	56%	*	44%
	4	6%		5%		10%
	5	3%		6%		10%
	6	0%		0.2%		1%
ABI		0.67 ± 0.20	*	0.64 ± 0.28		0.63 ± 0.18

* $p<0.01$ compared to Japan PMS

Japan PMS had significantly more CLI patients

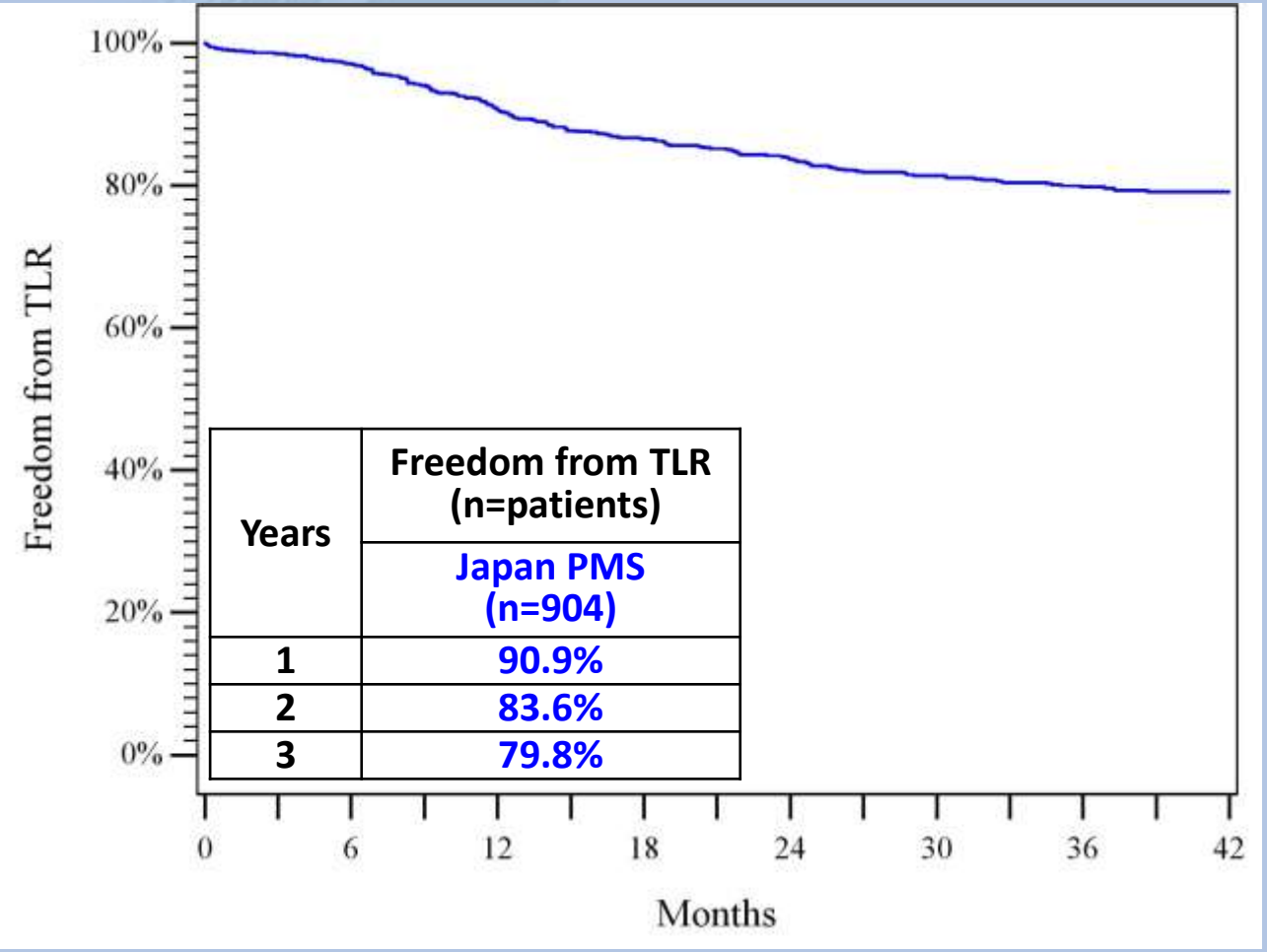
Stent Integrity

- 1142 stents were evaluated by X-ray at 1 year
  - 17 fractures identified
  - 1.5% (17/1142) stent fracture rate through 1 year
- Between 1 and 3 years, 494 stents evaluated by X-ray
  - 4 additional stent fractures identified between 1 and 3 years
  - 0.8% (4/494) stent fracture rate between 1 and 3 years
- Fracture rate remains low and similar to RCT (1.9%) through 3 years
- Next X-ray at 5 years

Stent Thrombosis/Occlusion

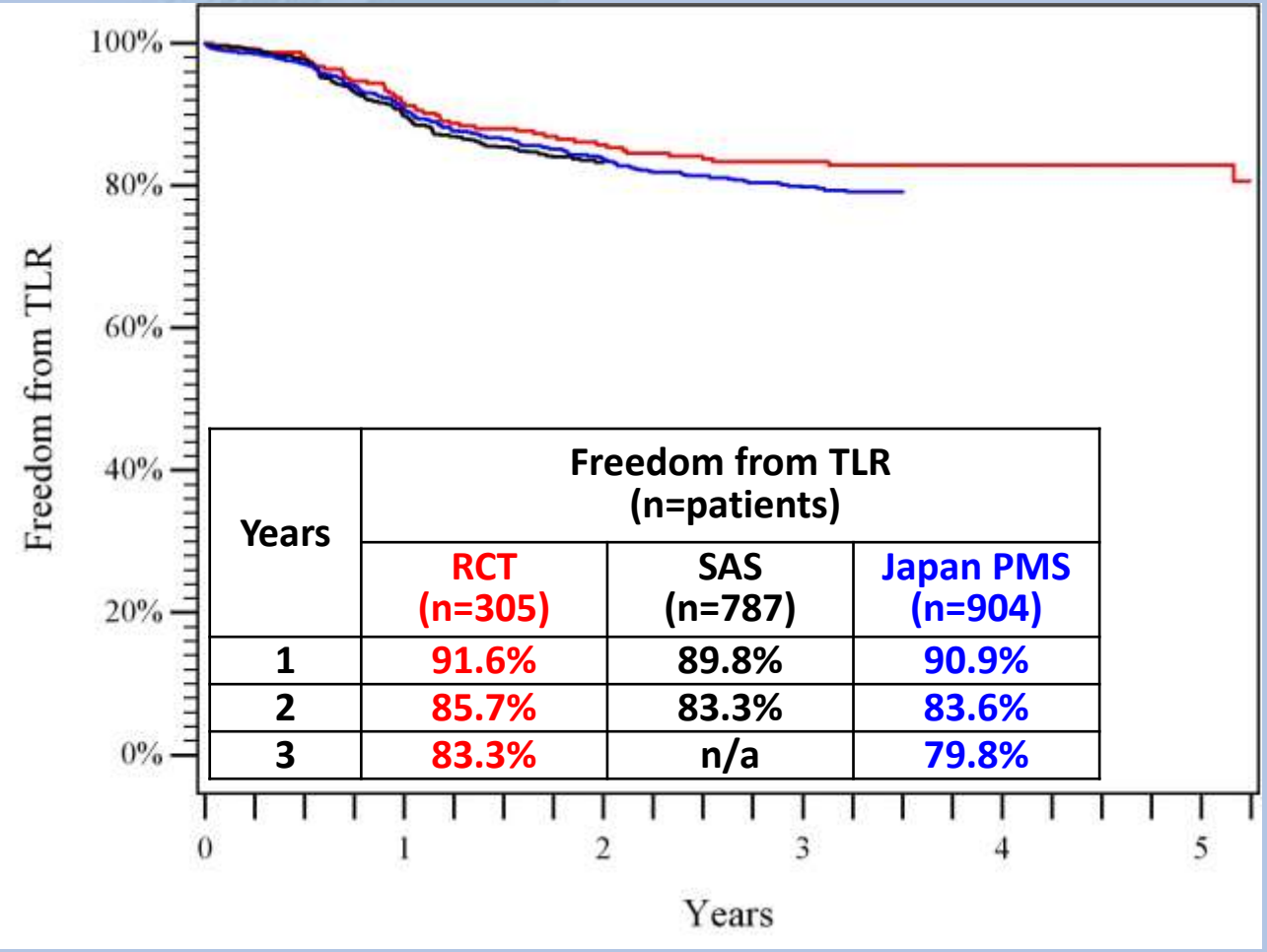
- No occlusions of site-suspected thrombotic origin reported between 2 and 3 years
  - No evidence of change in thrombosis profile compared to previous Zilver PTX studies, bare Zilver, or other bare metal stents

Freedom from TLR



Years	Freedom from TLR (n=patients)
	Japan PMS (n=904)
1	90.9%
2	83.6%
3	79.8%

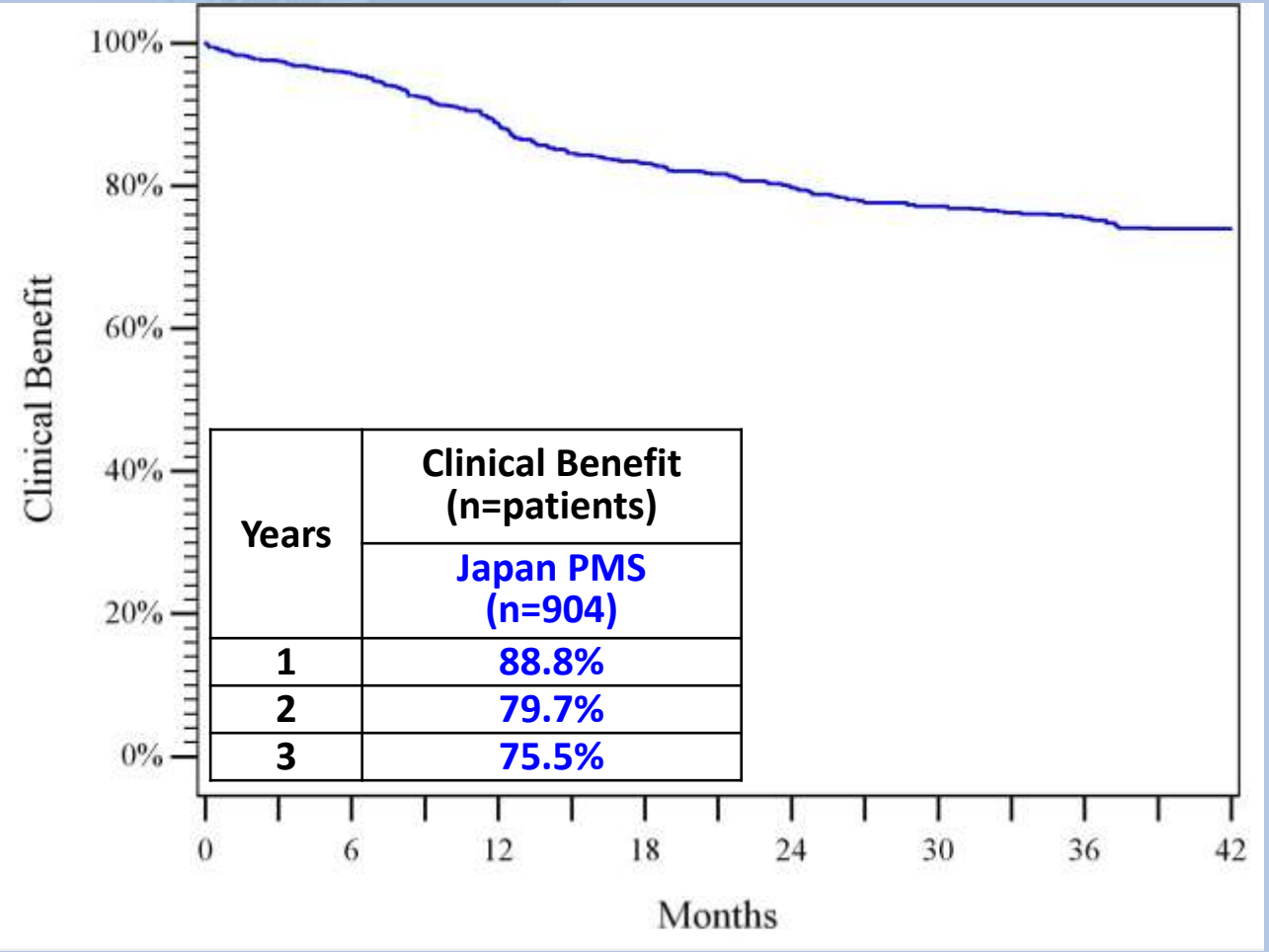
Freedom from TLR



Years	Freedom from TLR (n=patients)		
	RCT (n=305)	SAS (n=787)	Japan PMS (n=904)
1	91.6%	89.8%	90.9%
2	85.7%	83.3%	83.6%
3	83.3%	n/a	79.8%

Japan PMS TLR rate consistent with pre-market studies despite more complex lesions

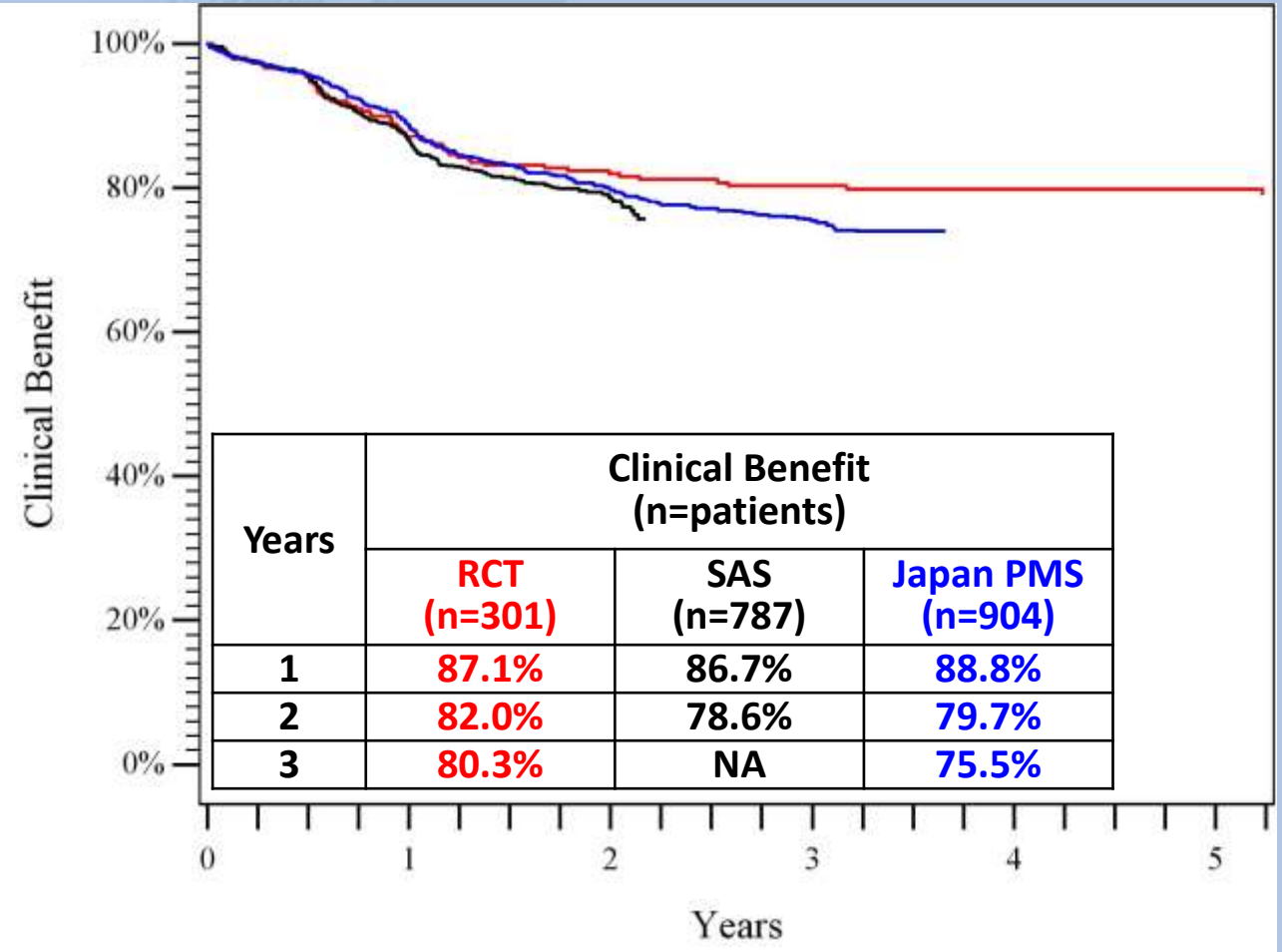
Clinical Benefit



Years	Clinical Benefit (n=patients)
	Japan PMS (n=904)
1	88.8%
2	79.7%
3	75.5%

Clinical benefit is defined as freedom from persistent or worsening claudication, rest pain, ulcer, or tissue loss

Clinical Benefit



Years	Clinical Benefit (n=patients)		
	RCT (n=301)	SAS (n=787)	Japan PMS (n=904)
1	87.1%	86.7%	88.8%
2	82.0%	78.6%	79.7%
3	80.3%	NA	75.5%

Clinical benefit in the Japan PMS is similar to both pre-market studies

Comparison of ISR Patients and Non-ISR Patients from Japan PMS

Patient Demographics and Comorbidities

	Zilver PTX Japan PMS	JPMS ISR	JPMS Non-ISR	*p*-value*
Patients	905	175	730	-
Age (years)	74 ± 9	74 ± 8	73 ± 9	NS
Male	70%	66%	71%	NS
Diabetes	59%	62%	58%	NS
High cholesterol	61%	70%	59%	< 0.01
Hypertension	85%	88%	85%	NS
Pulmonary disease	8%	9%	8%	NS
Renal disease	44%	41%	44%	NS
Renal failure (eGFR <60 and/or "on Dialysis")	35%	31%	36%	NS

* *p*-value comparing ISR and non-ISR subgroups

More hypercholesterolemia in ISR patients

Baseline Lesion Characteristics

		Zilver PTX Japan PMS	JPMS ISR	JPMS Non-ISR	*p*-value*
Lesions		1080	202	878	-
Lesion length (cm)		14.6 ± 9.6	17.8 ± 10.4	14.0 ± 9.3	< 0.01
Diameter stenosis (%)		92 ± 11	92 ± 10	92 ± 11	NS
Total occlusions		42%	36%	43%	NS
In-stent restenosis		19%	100%	0%	-
Patent runoff vessels	**0**	7%	6%	7%	NS
	1	32%	31%	32%	
	2	33%	36%	32%	
	3	29%	27%	29%	

* *p*-value comparing ISR and non-ISR subgroups

ISR patients had longer lesions

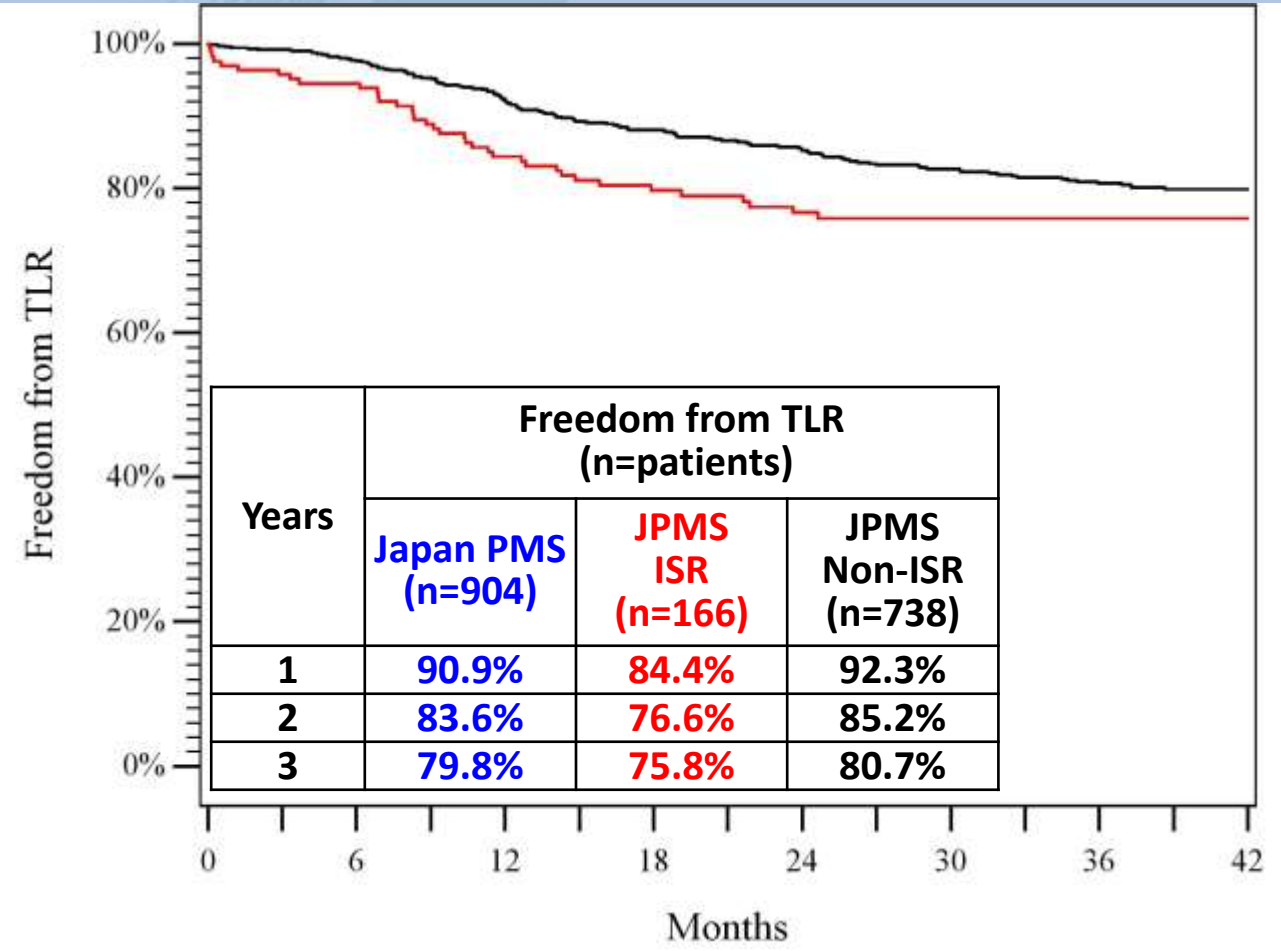
Baseline Clinical Assessment

Pre-procedure Clinical Assessment		Zilver PTX Japan PMS	JPMS ISR	JPMS Non-ISR	*p*-value*
Rutherford	1	8%	9%	8%	NS
	2	27%	22%	28%	
	3	44%	47%	43%	
	4	10%	14%	10%	
	5	10%	9%	10%	
	6	1%	0%	2%	
ABI		0.63 ± 0.18	0.59 ± 0.16	0.64 ± 0.18	< 0.01

* *p*-value comparing ISR and non-ISR subgroups

ISR patients had lower ABI

Freedom from TLR



Years	Freedom from TLR (n=patients)		
	Japan PMS (n=904)	JPMS ISR (n=166)	JPMS Non-ISR (n=738)
1	90.9%	84.4%	92.3%
2	83.6%	76.6%	85.2%
3	79.8%	75.8%	80.7%

Nearly similar outcomes for lesions with and without ISR

Conclusions

- Large amount of clinical data 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
- 3-year Japan PMS results are positive and continue to support the long-term benefit of the Zilver PTX technology
  - Reaffirm Zilver PTX safety
  - Consistent results across studies provide added support for the established performance of the Zilver PTX stent
- Zilver PTX performs well in ISR lesions

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