Zilver PTX Five Year –Clinical Data

What Does This Mean to Clinical Practice?

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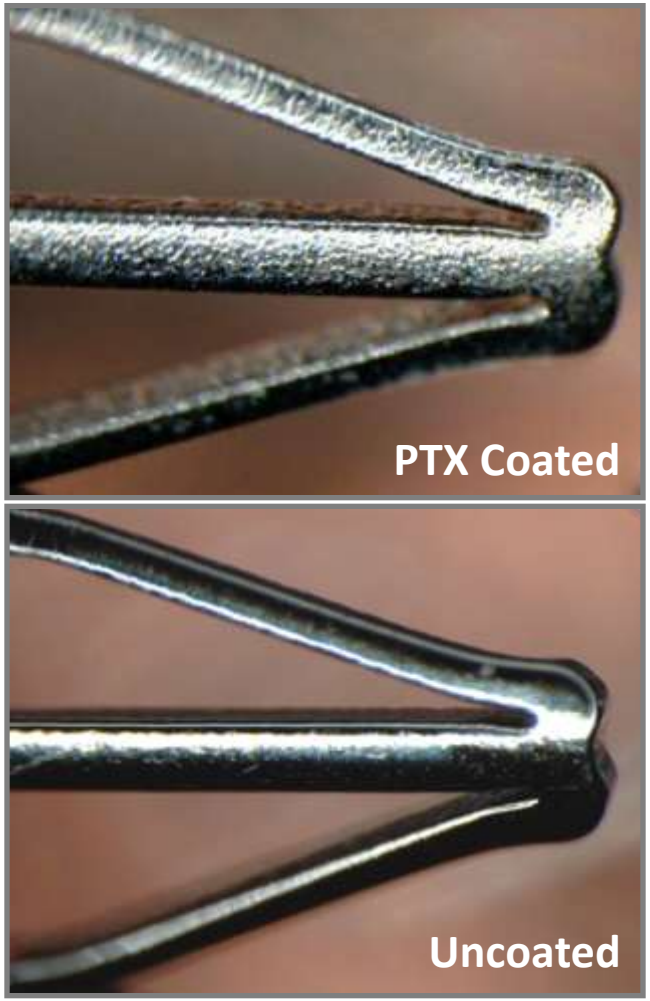
Zilver PTX drug-eluting peripheral stent

- Available in over 50 countries
- Approved in EU, Japan, and US

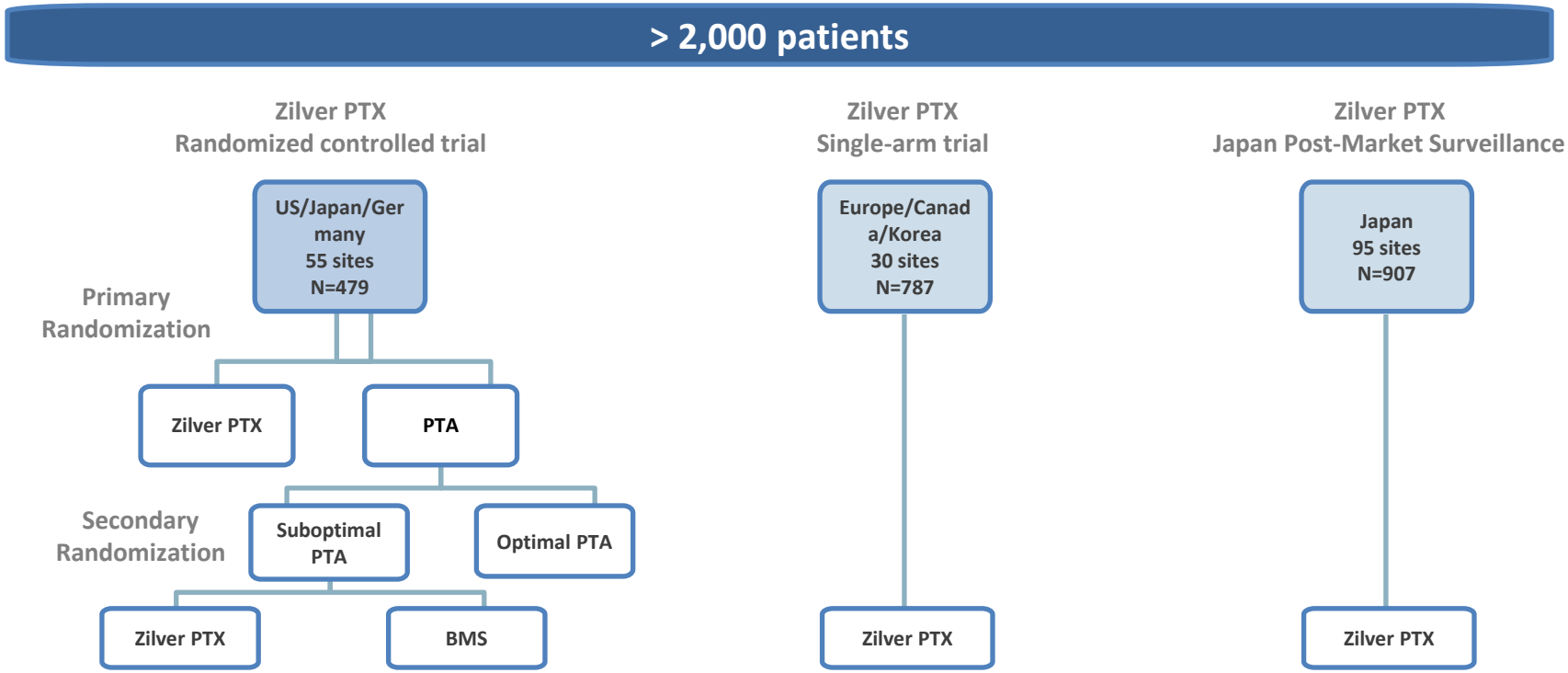
  - **Mechanical scaffold:** Zilver Flex® Stent Platform
  - **Drug therapy:** Paclitaxel only
    - No polymer or binder
    - 3 µg/mm^2 dose density



The proven drug effect of Zilver PTX[1]

Zilver PTX randomized controlled trial (RCT) and single-arm study (SAS):
largest endovascular SFA study ever conducted.

- Nearly 2,200 patients in the three trials
- RCT with completed 5-year follow up



1. Refer to Instructions for Use (IFU) for full prescribing information, including indications, contraindications, warnings, precautions, and clinical data.

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="8">Key Sudy Criteria</td><td colspan="2">No significant untreated inflow tract stenosis</td><td rowspan="8">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 ≤ 14cm</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>In-stent restenosis 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>Core laboratory analysis</td><td colspan="2">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

Patient Demographics and Comorbidities

	Zilver PTX RCT	Zilver PTX SAS	Zilver PTX 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%

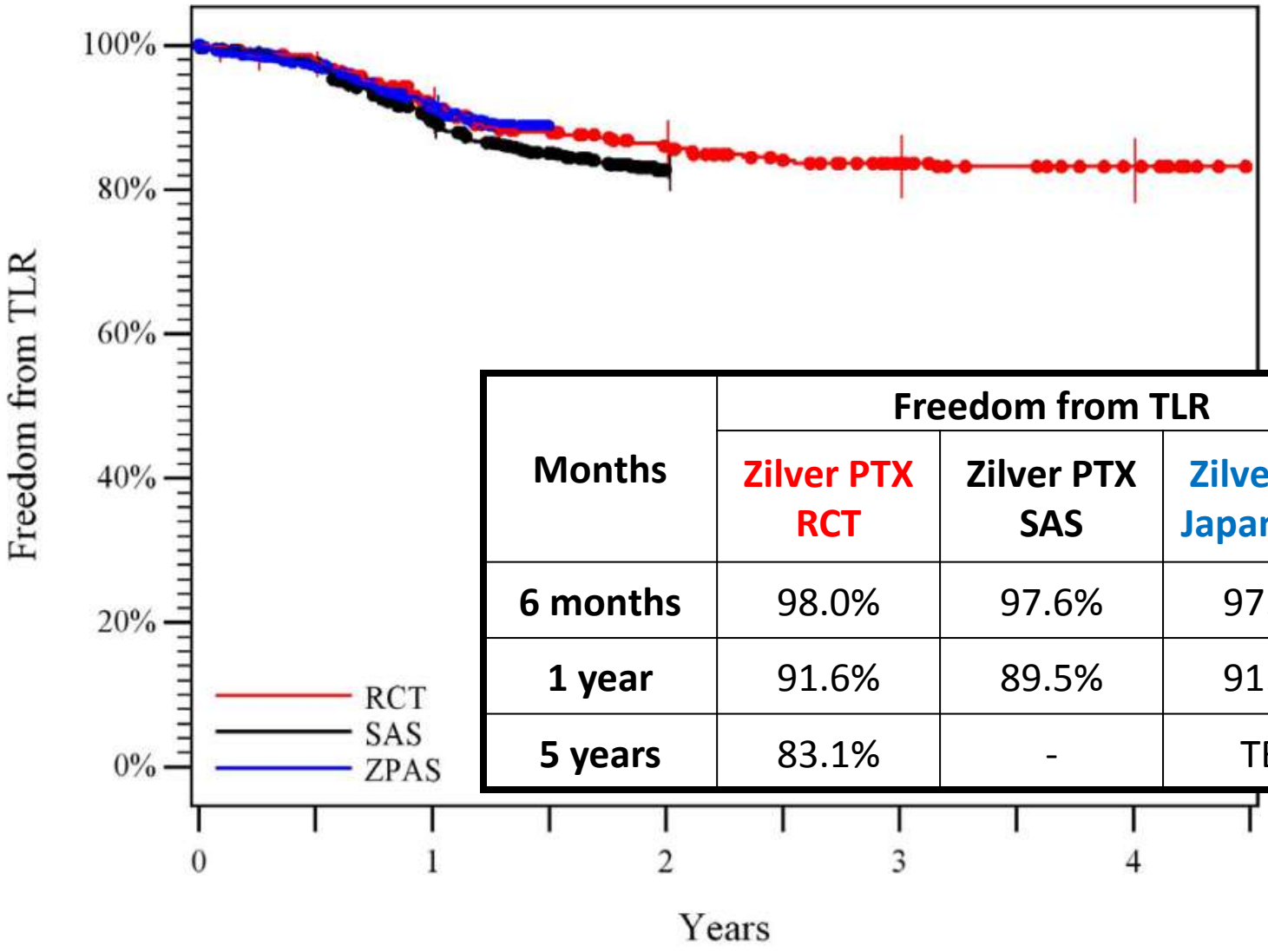
Baseline Lesion Characteristics

		Zilver PTX RCT	Zilver PTX SAS	Zilver PTX Japan PMS
Lesions		251	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		30%	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%

* Zilver PTX is indicated for lesions up to 140mm per leg and 280mm per patient

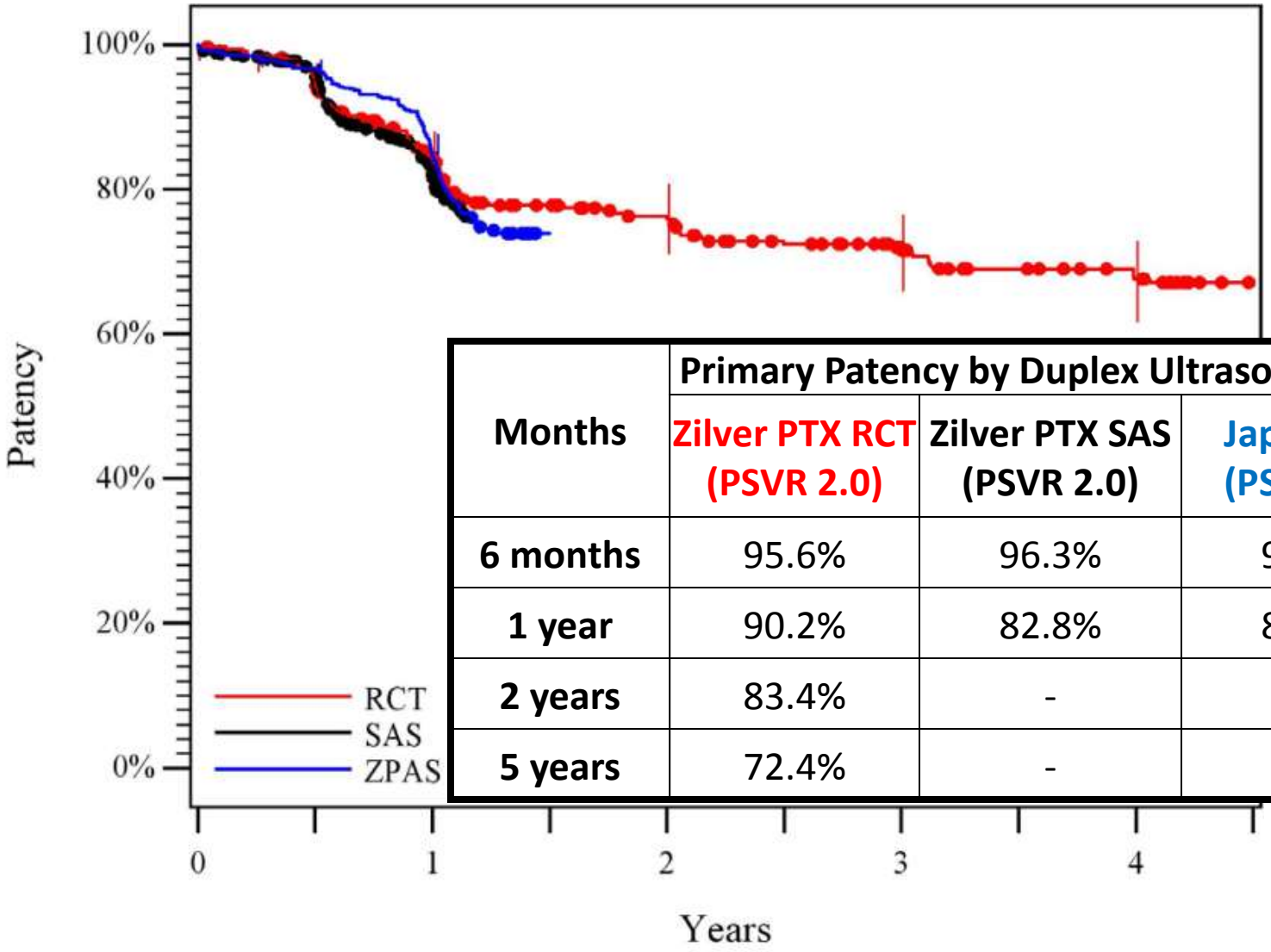
** Zilver PTX is not indicated for the treatment of in-stent restensosis

Results:
Freedom from TLR



Months	Freedom from TLR		
	Zilver PTX RCT	Zilver PTX SAS	Zilver PTX Japan PMS
6 months	98.0%	97.6%	97.3%
1 year	91.6%	89.5%	91.4%
5 years	83.1%	-	TBD

Primary Patency by Duplex Ultrasonography

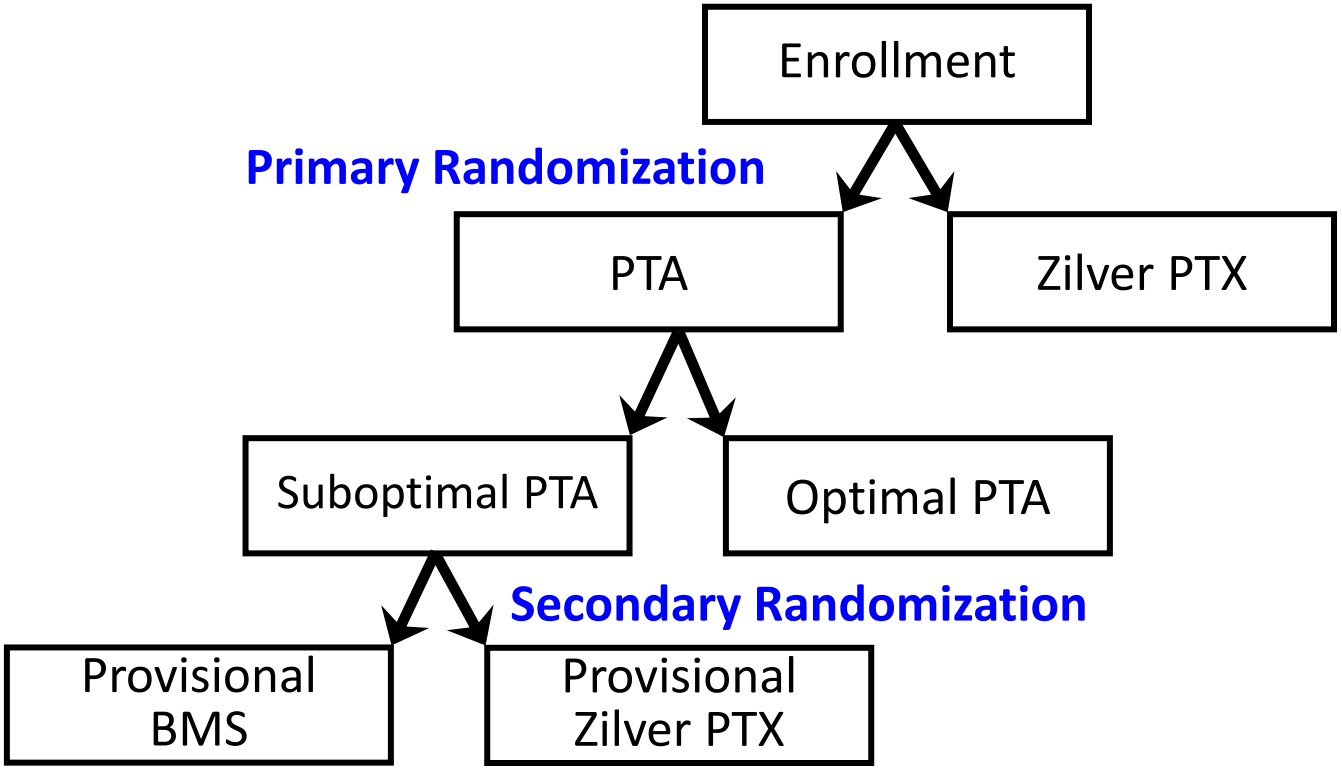


Months	Primary Patency by Duplex Ultrasonography		
	Zilver PTX RCT (PSVR 2.0)	Zilver PTX SAS (PSVR 2.0)	Japan PMS (PSVR 2.4)
6 months	95.6%	96.3%	96.7%
1 year	90.2%	82.8%	84.8%
2 years	83.4%	-	TBD
5 years	72.4%	-	TBD

Section 2:

The Zilver® PTX® randomized controlled trial of paclitaxel-eluting stents for femoropopliteal disease: **5-year results**

Zilver PTX Study Design



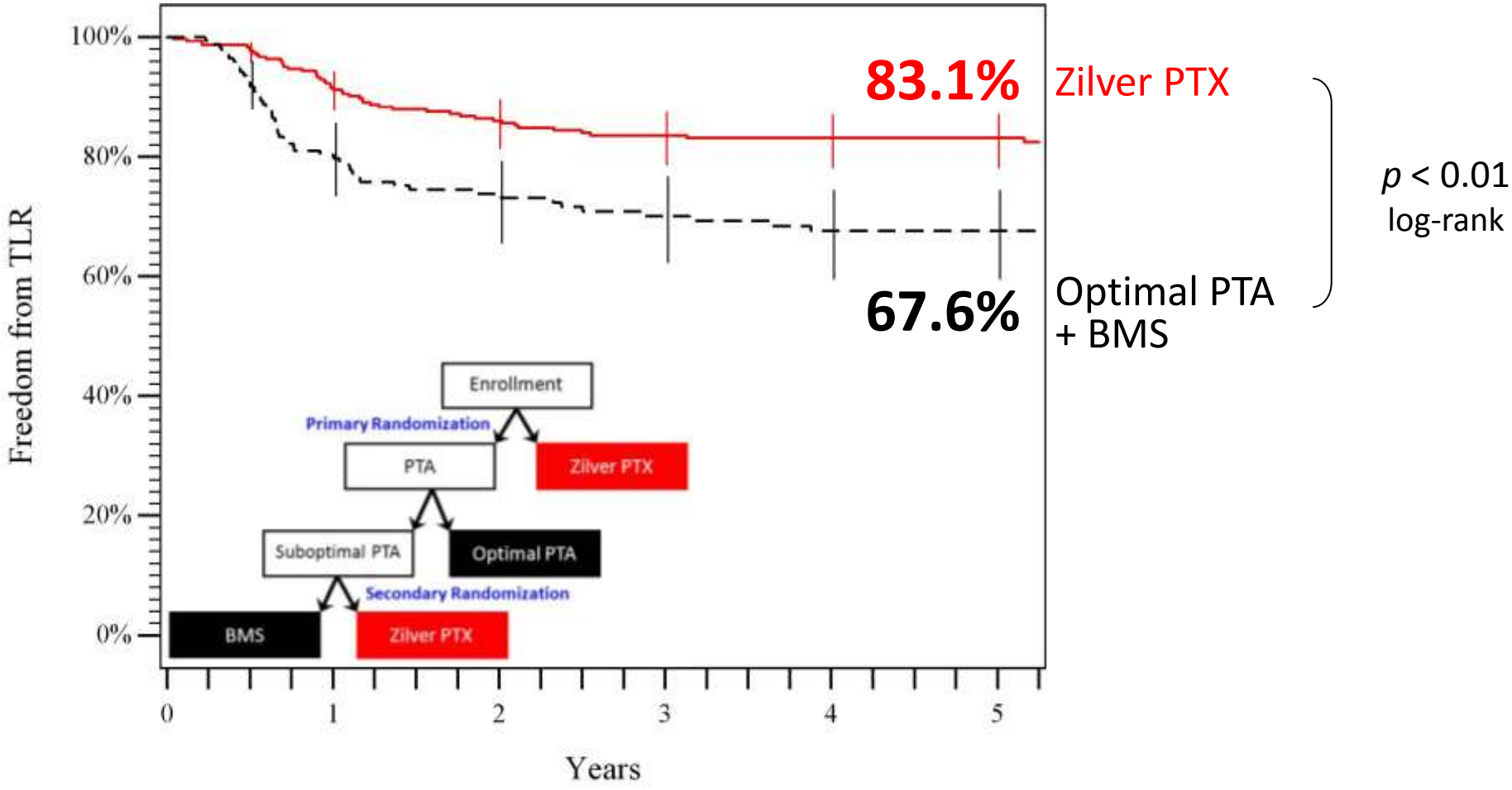
5-year Stent Integrity

Study Period	Number of New Events	Fracture Rate[1]
Enrollment	0	0.0%
1-year	4	0.9%
3-year	3	1.9%
5-year	0	1.9%

[1] Kaplan-Meier estimates

Zilver PTX has excellent durability in challenging SFA environment

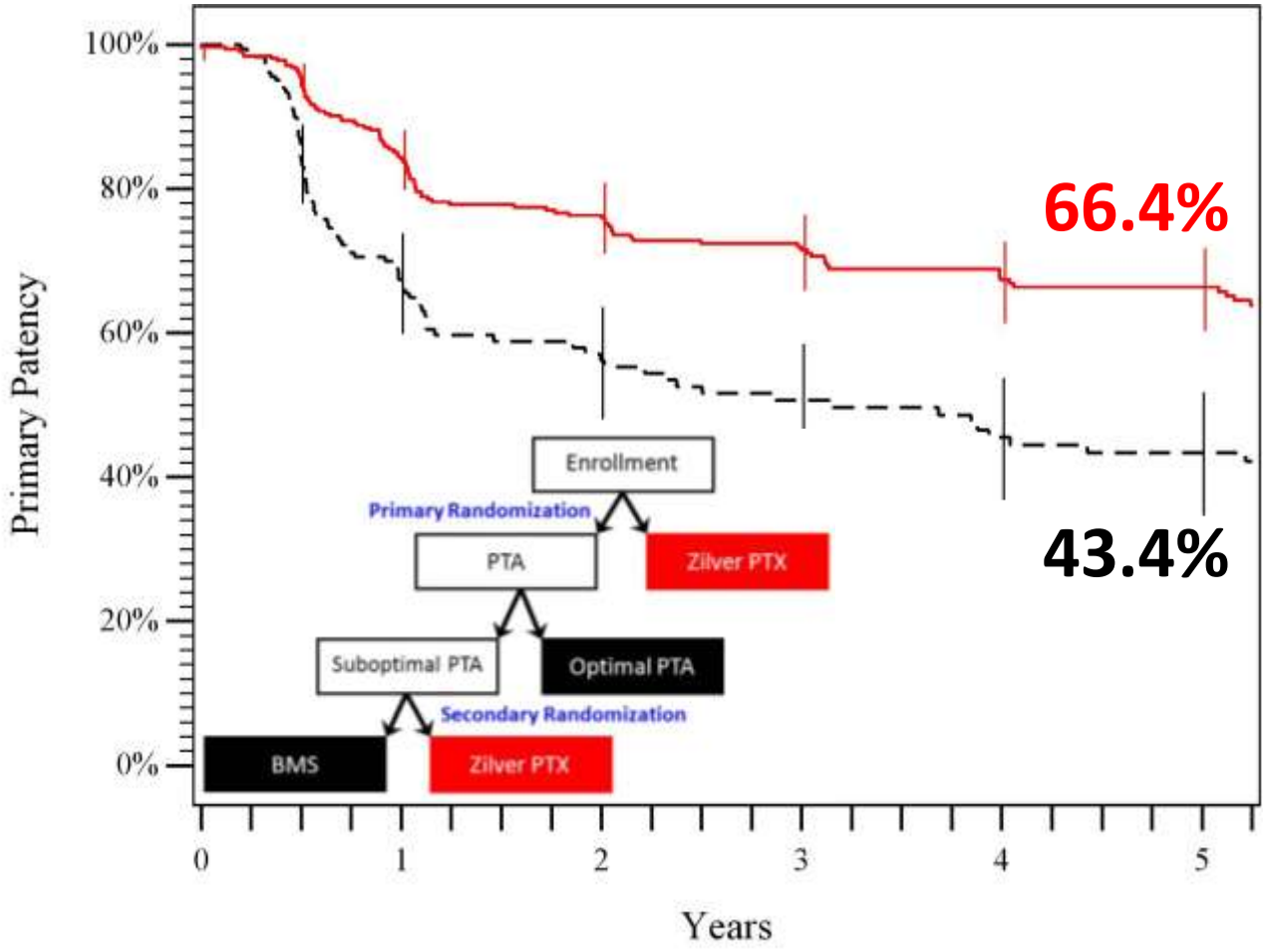
5-year Freedom from TLR
Zilver PTX vs. Standard Care



$p < 0.01$
log-rank

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

5-year Primary Patency (PSVR < 2.0)
Zilver PTX vs. Standard Care



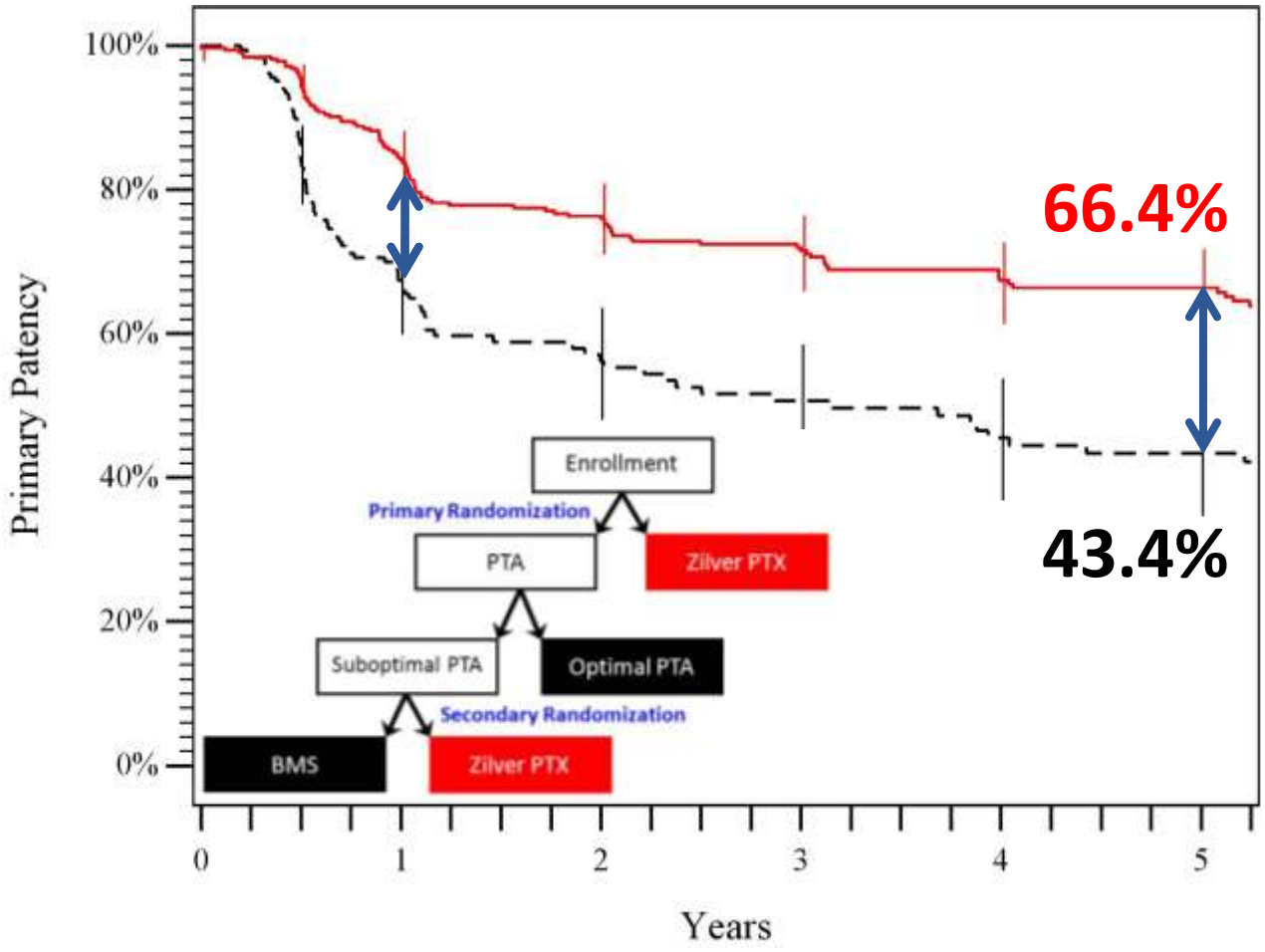
66.4% Zilver PTX

43.4% Optimal PTA + BMS

$p < 0.01$ log-rank

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

5-year Primary Patency (PSVR < 2.0)
Zilver PTX vs. Standard Care

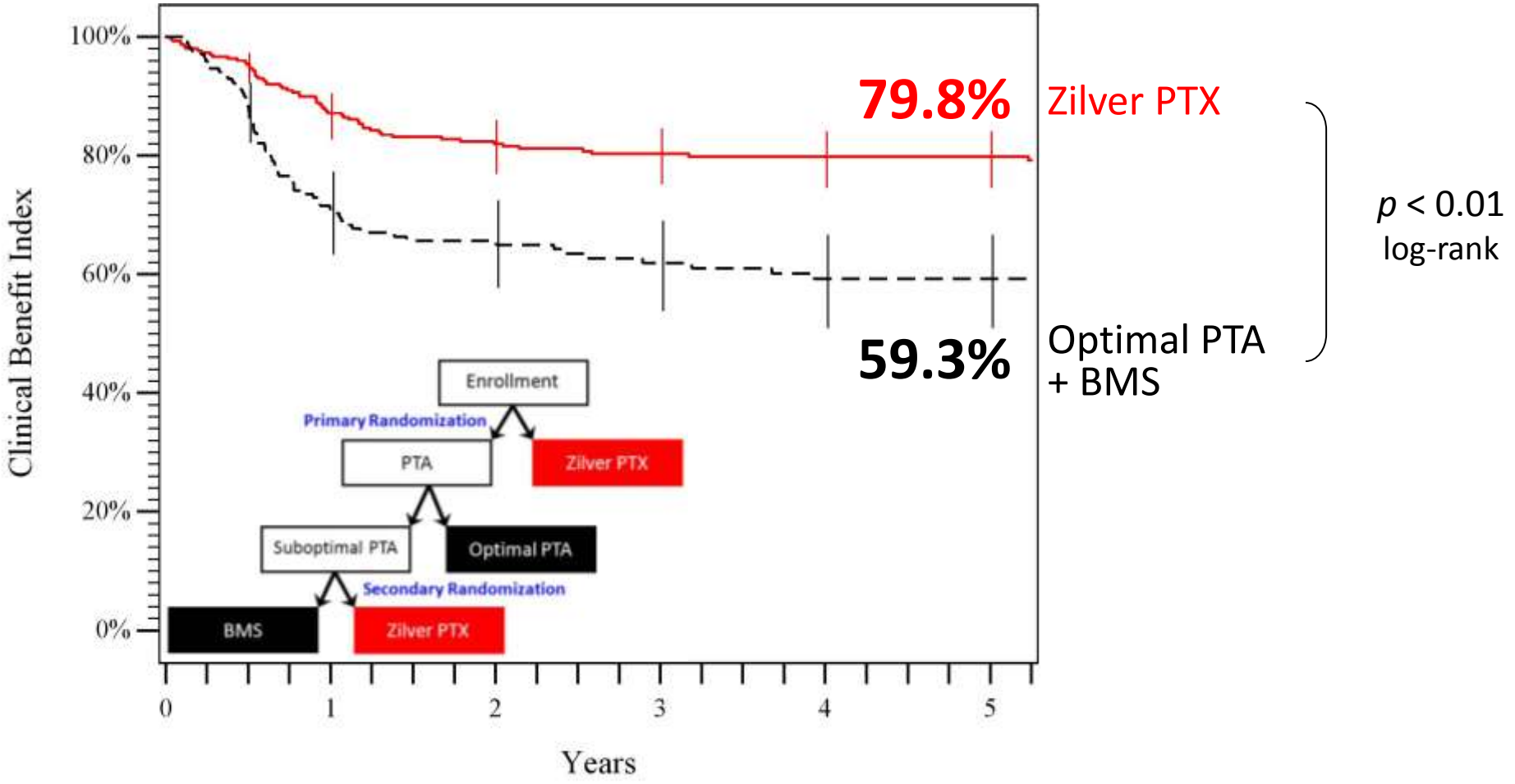


66.4% Zilver PTX

43.4% Optimal PTA + BMS

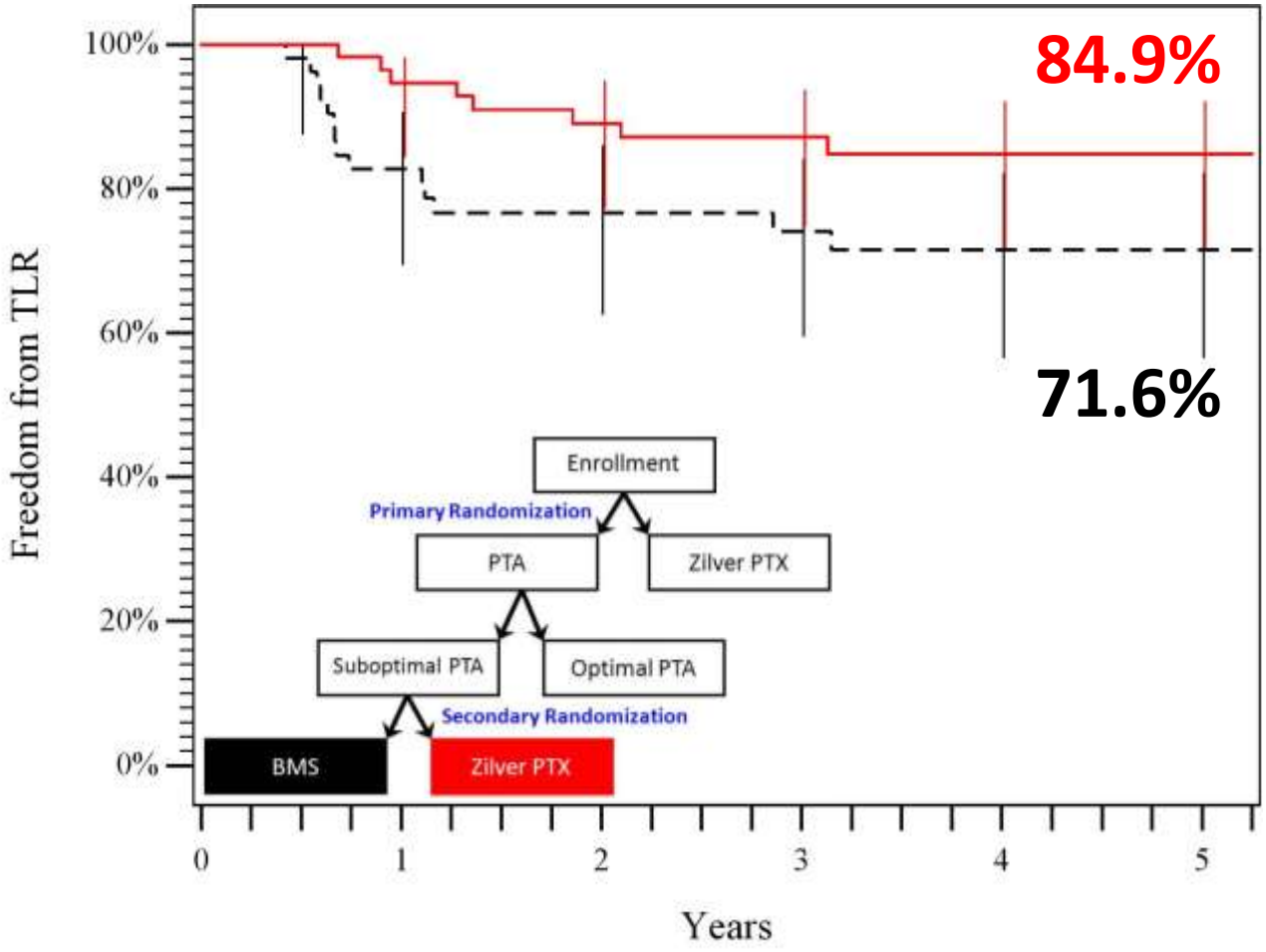
From 1-5 years, the relative separation increases by 35%

5-year Clinical Benefit Index
Zilver PTX vs. Standard Care



At 5 years, Zilver PTX has a superior rate of freedom from persistent or worsening claudication, rest pain, ulcer, or tissue loss

5-year Freedom from TLR
Provisional Zilver PTX vs. BMS



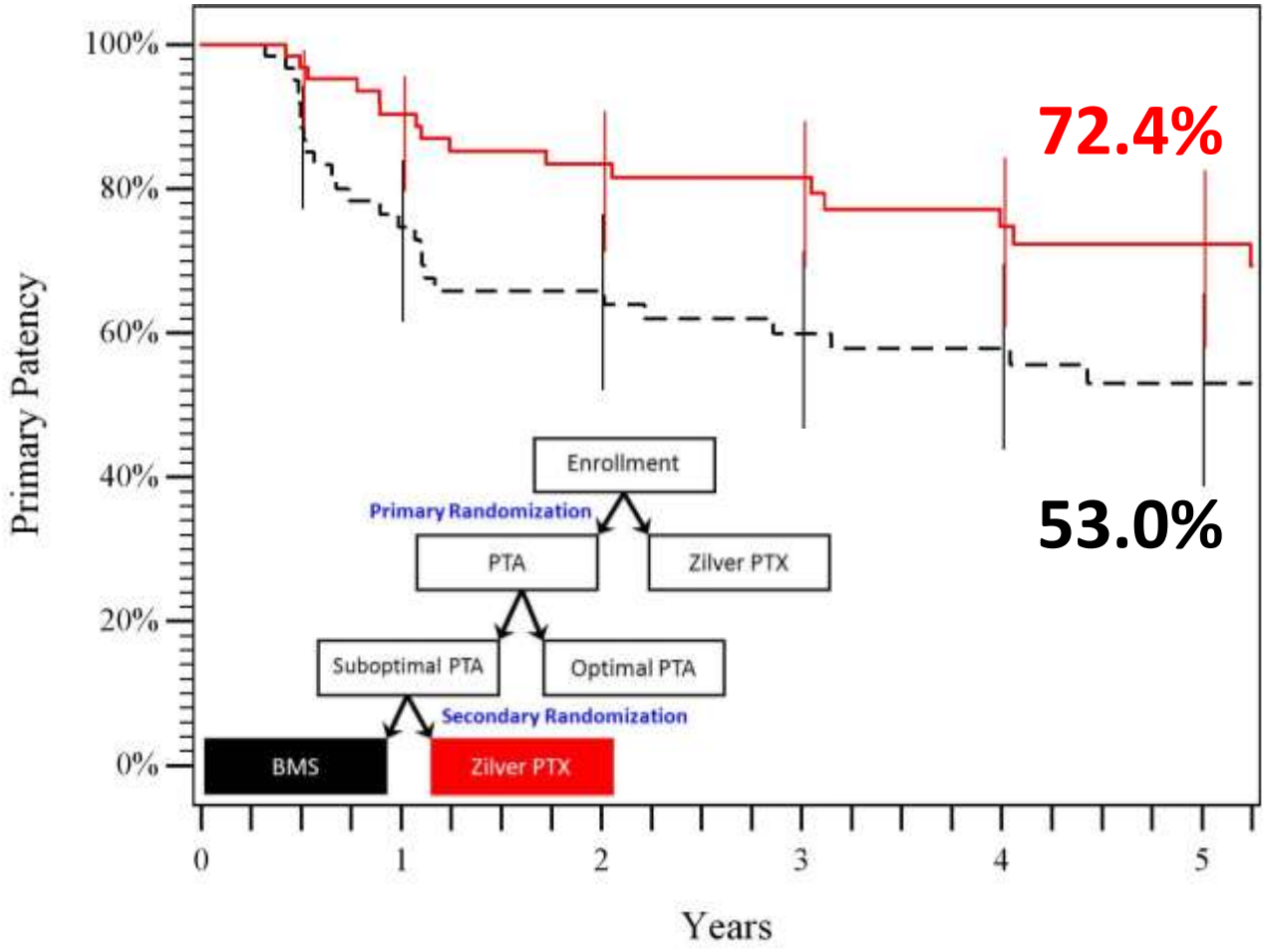
Provisional Zilver PTX

Provisional BMS

$p = 0.06$
log-rank

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

5-year Primary Patency (PSVR < 2.0)
Provisional Zilver PTX vs. BMS



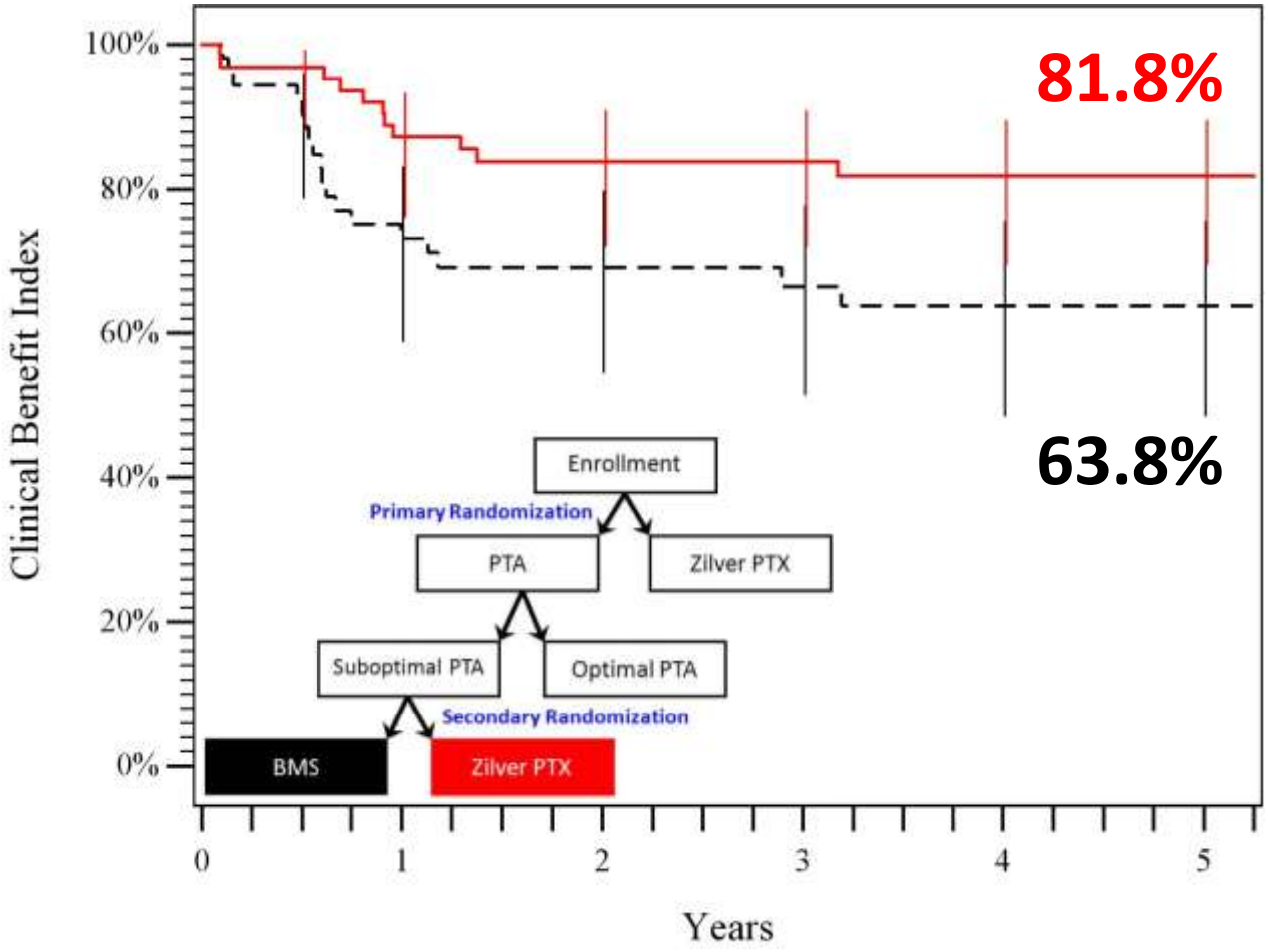
Provisional Zilver PTX

Provisional BMS

$p = 0.03$ log-rank

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

5-year Clinical Benefit Index
Provisional Zilver PTX vs. BMS



Provisional Zilver PTX

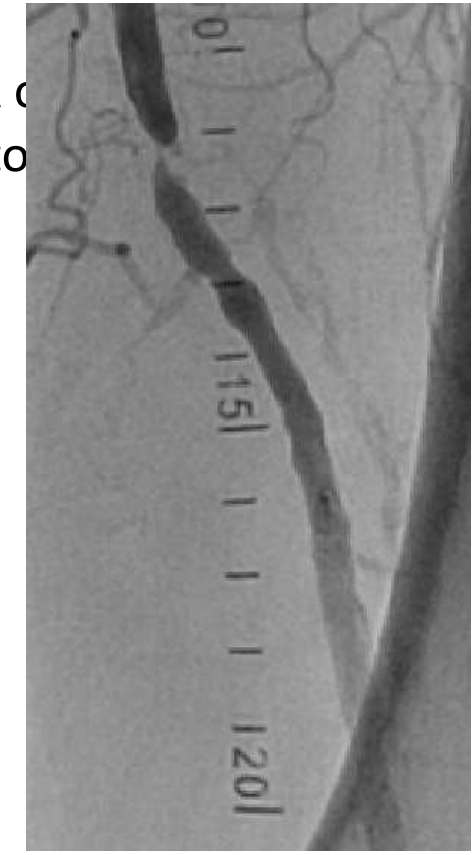
Provisional BMS

$p = 0.02$
log-rank

At 5 years, Zilver PTX has a superior rate of freedom from persistent or worsening claudication, rest pain, ulcer, or tissue loss

What Do The 5-year Zilver PTX Results Mean?

- No other SFA treatment has data as robust as Zilver PTX
- Less need for TLR
  - Lower long-term cost than PTA c
  - *Much* lower cost than atherecto
- Well supported role for
  - Moderate to severe disease
  - ISR
- Complementary role
  - Very simple lesions
  - Densely calcified lesions



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

Drug elution now in the periphery

- Multiple drug-eluting stent and drug-eluting balloon trials underway
- Multiple companies with peripheral drug-eluting technology
- Cook Medical is the only company to offer drug-eluting stents for the SFA.*

* This device may not be approved or available for sale in all regions.

Patient Demographics and Comorbidities

	PTA	Zilver PTX	*p*-value
Patients	238	236	
Age (years)	68 ± 11	68 ± 10	0.88
Male	64%	66%	0.70
Height (in)	66 ± 4	67 ± 4	0.55
Weight (lbs)	179 ± 44	180 ± 40	0.62
Diabetes	42%	50%	0.11
High cholesterol	70%	76%	0.12
Hypertension	82%	89%	0.02*
Past/current smoker	84%	86%	0.70

* Statistically significant

Baseline Lesion Characteristics

		PTA	Zilver PTX	*p*-value
Lesions		251	247	
Normal-to-normal lesion length (mm)		63 ± 41	66 ± 39	0.36
Stenosed lesion length (mm)[1,2]		53 ± 40	55 ± 41	0.71
Diameter stenosis (%)[1]		78 ± 17	80 ± 17	0.38
Total occlusions		27%	33%	0.20
***De novo* lesions**		94%	95%	0.68
Lesion calcification[1]	**None**	5%	2%	< 0.01*
	Little	38%	26%	
	Moderate	22%	35%	
	Severe	35%	37%	

[1] Angiographic core lab assessment
[2] Region with > 20% diameter stenosis
* Statistically significant

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

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High stent integrity

Years	Fracture Rates		
	Zilver PTX RCT (457 stents)	Zilver PTX SAS (1889 stents)	Japan PMS (1066 stents)
1	0.9%	1.5%	1.6%
3	1.9%	-	TBD
5	1.9%	-	TBD