CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE

CONTROVERSIES & UPDATES IN VASCULAR SURGERY

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The latest evidences from the DES trials in peripheral arterial disease

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Disclosure

Speaker name: Michael D. Dake

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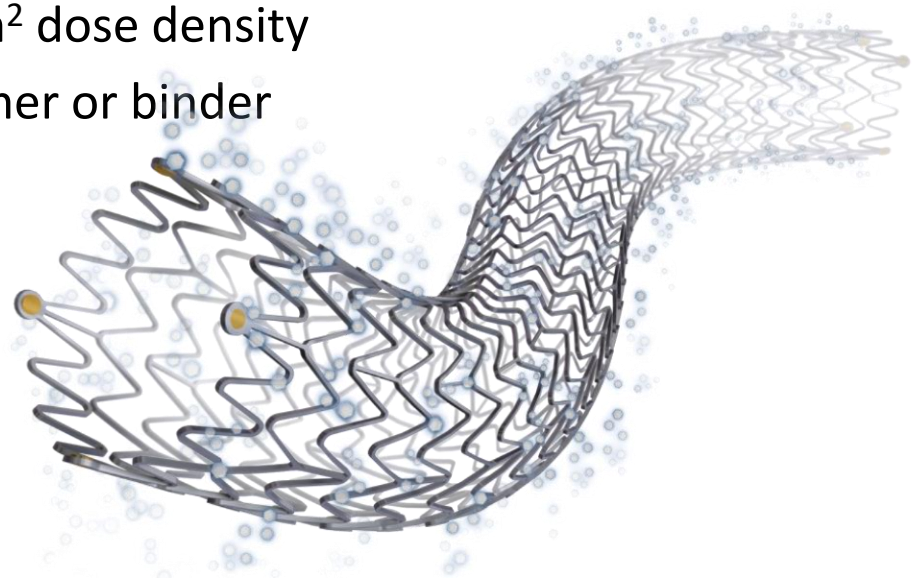
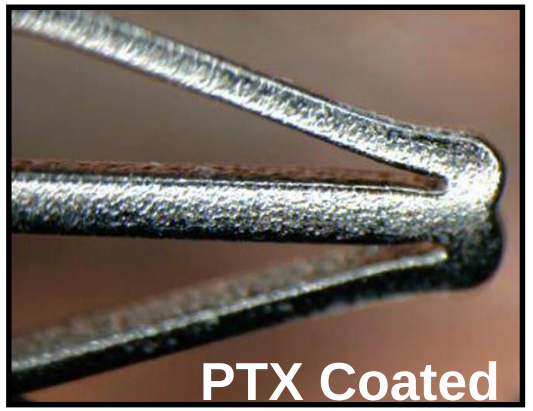
- [x] I have the following potential conflicts of interest to report:
- [x] Consulting
- [ ] Employment in industry
- [ ] Shareholder in a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)
- [ ] I do not have any potential conflict of interest

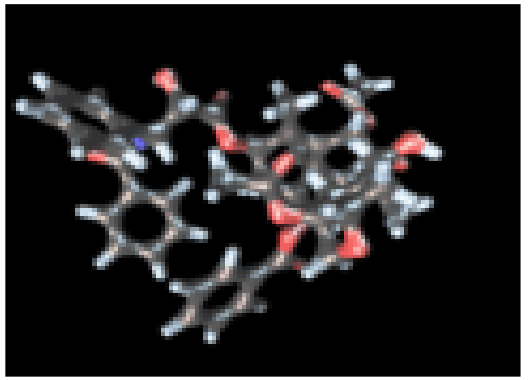
Zilver PTX Drug-Eluting Peripheral Stent

- **Mechanical scaffold:**
  Zilver Flex® Stent Platform

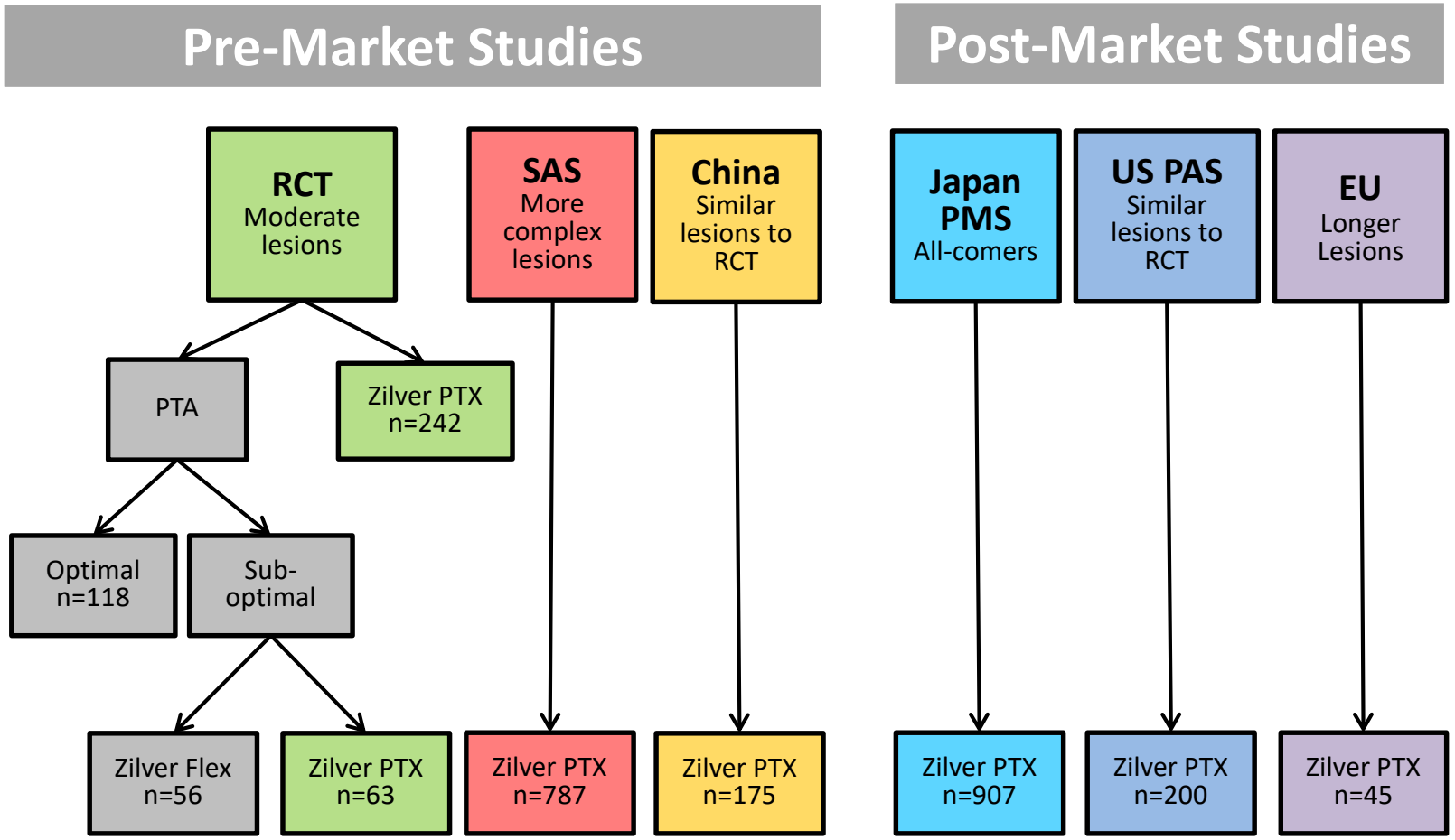
- **Drug therapy:** Paclitaxel only
  - 3 µg/mm² dose density
  - No polymer or binder







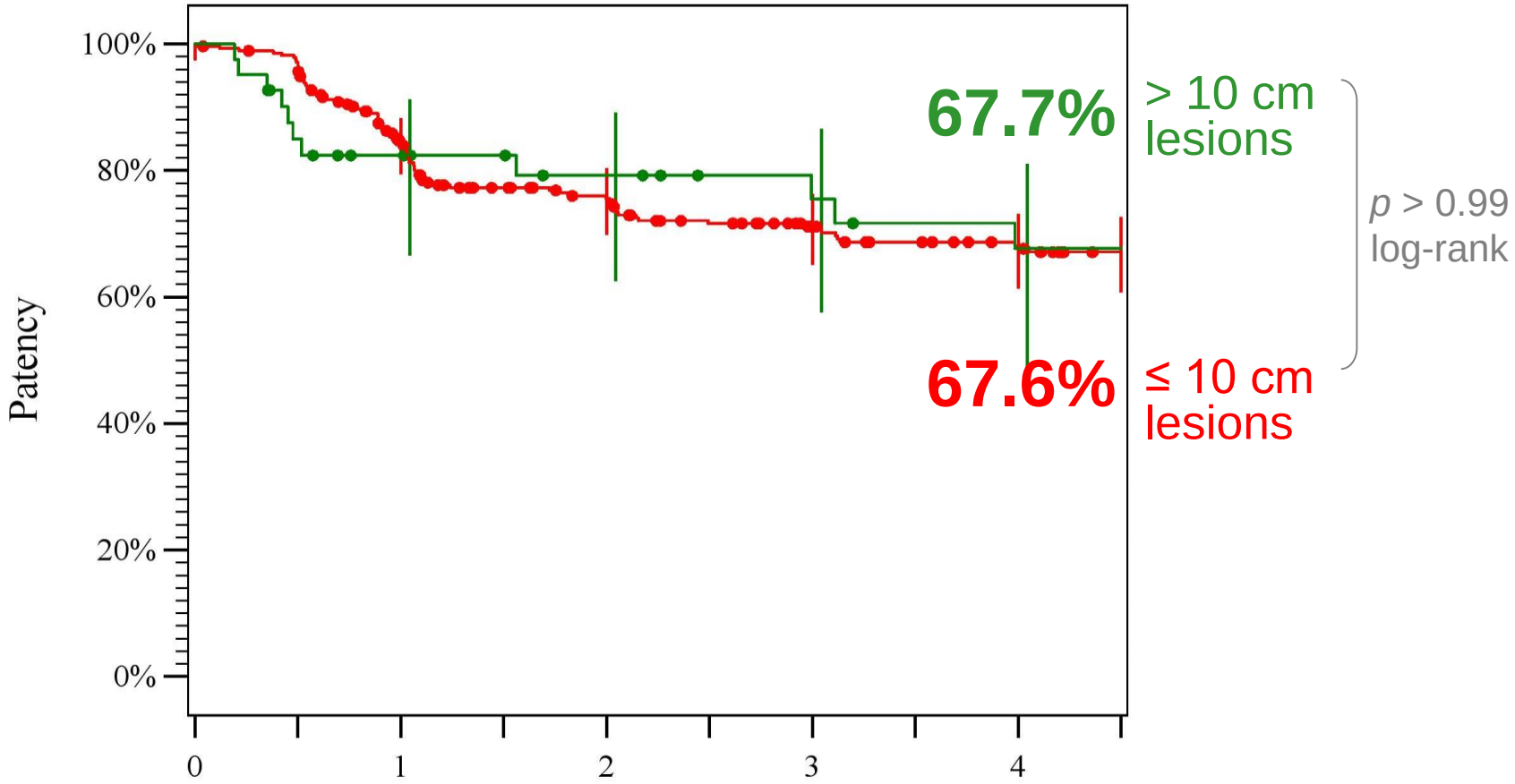
Global Clinical Program



More than 2400 patients included in the current Zilver PTX clinical program

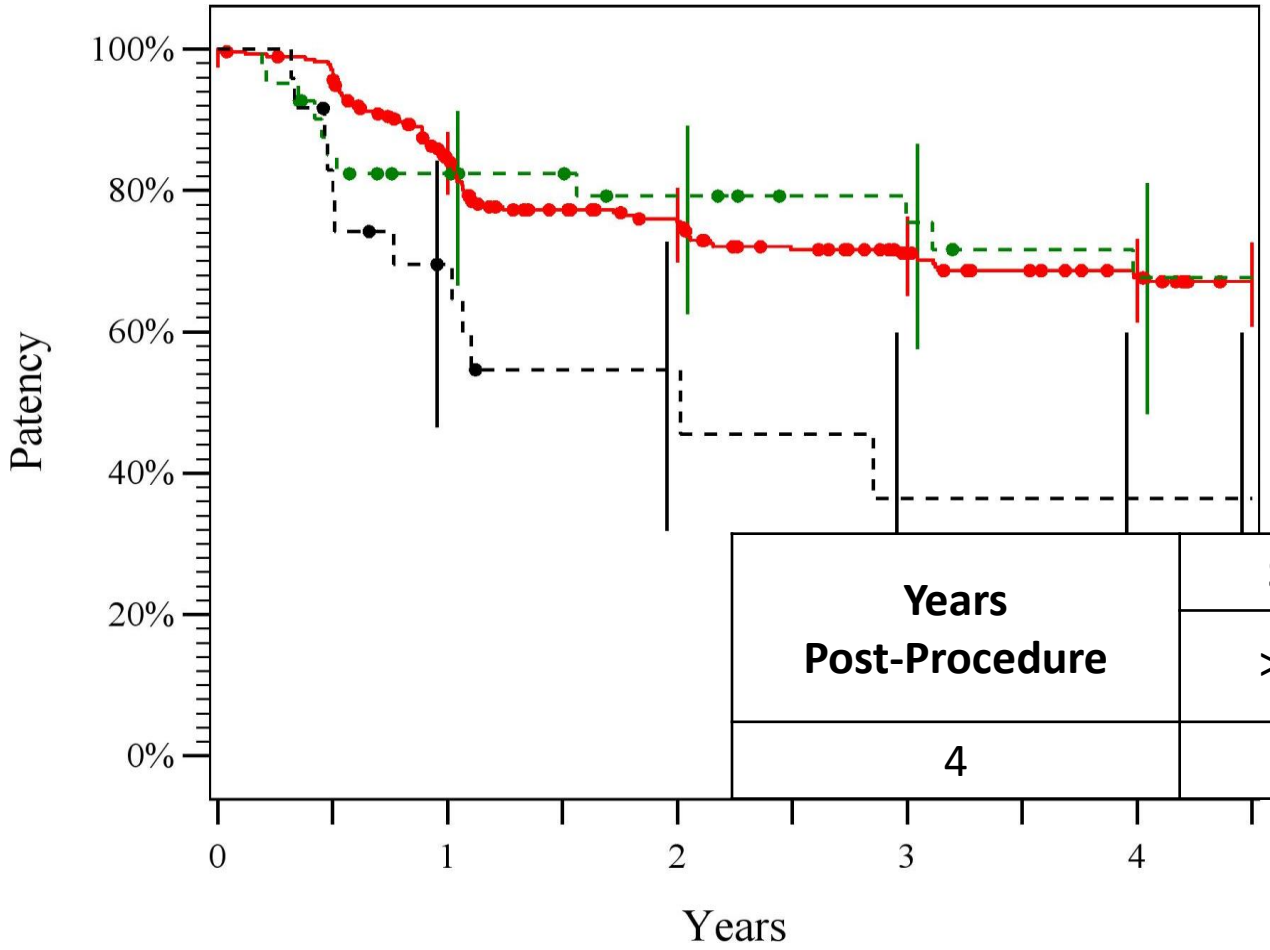
But, what about the effect when treating longer, more complicated, real world lesions?

4-Year Primary Patency in > 10 cm Lesions



Zilver PTX results are similar in lesions ≤ 10 cm and lesions > 10 cm

4-Year Primary Patency in > 10 cm Lesions



Years Post-Procedure	Standard Care	Zilver PTX	
	> 10 cm lesions	≤ 10 cm lesions	> 10 cm lesions
4	36.4%	67.6%	67.7%

Zilver PTX results are superior to standard care in lesions > 10 cm

Global Clinical Program

	Zilver PTX RCT	Zilver PTX SAS	Zilver PTX Japan PMS
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	**ISR included**	
	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	**DUS core laboratory analysis**	**DUS site analysis**	
Stent Integrity	X-ray core laboratory analysis		

Increasingly complex patients and lesions

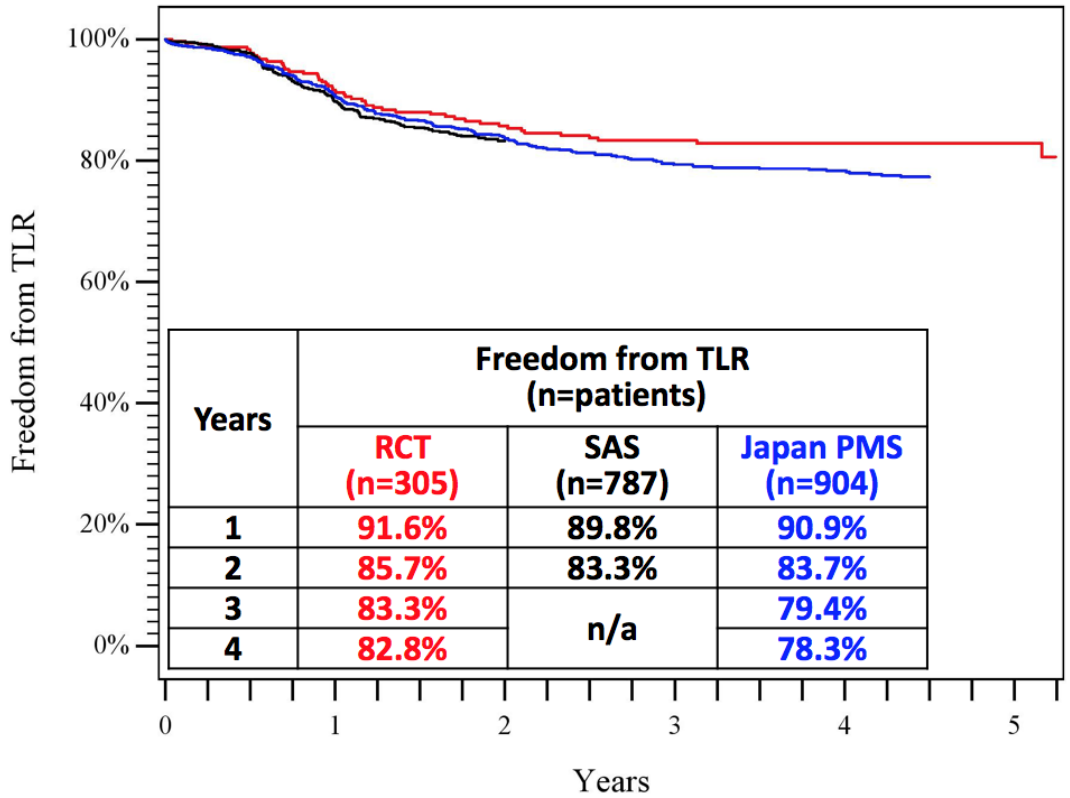
Patient Demographics and Comorbidities

	RCT	SAS	Japan PMS
Patients	236	787	907
Age (years)	68 ± 10	67 ± 10	74 ± 9
Diabetes	50%	36%	59%
High cholesterol	76%	58%	61%
Hypertension	89%	80%	85%
Renal disease[1]	10%	11%	44%
Lesion length (cm)	6.6 ± 3.9	10.0 ± 8.2	14.7 ± 9.7
Total occlusions	33%	38%	42%
In-stent restenosis (ISR)	0%	15%	19%
Rutherford 4-6 (CLI)	9%	11%	20%

[1] Of patients with renal disease in the Japan PMS, 82% were in renal failure (eGFR < 60 and/or dialysis)

Increasingly complex patients and lesions

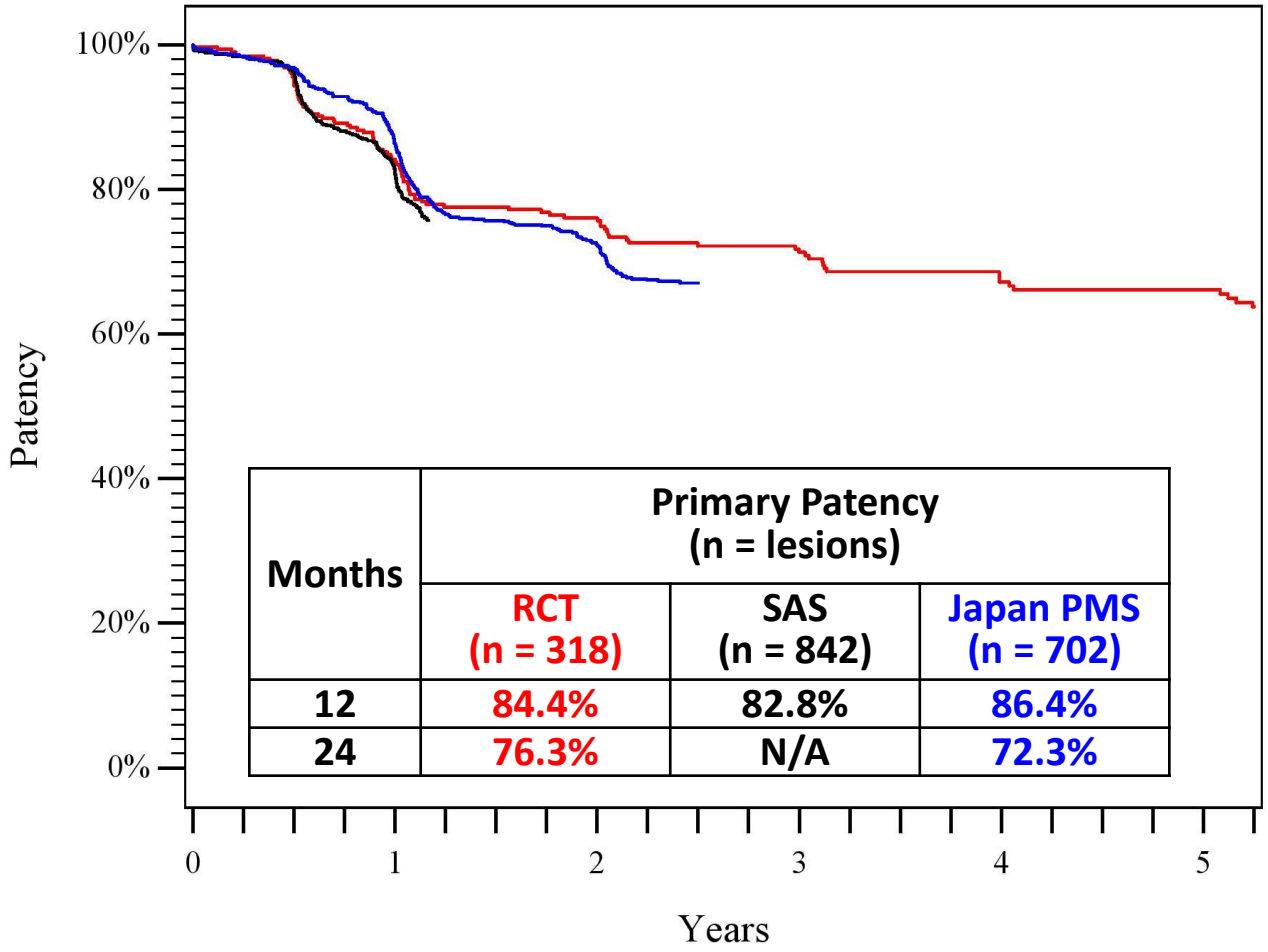
Freedom from TLR



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%	83.7%
3	83.3%	n/a	79.4%
4	82.8%		78.3%

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

Primary Patency by DUS



Months	Primary Patency (n = lesions)		
	RCT (n = 318)	SAS (n = 842)	Japan PMS (n = 702)
12	84.4%	82.8%	86.4%
24	76.3%	N/A	72.3%

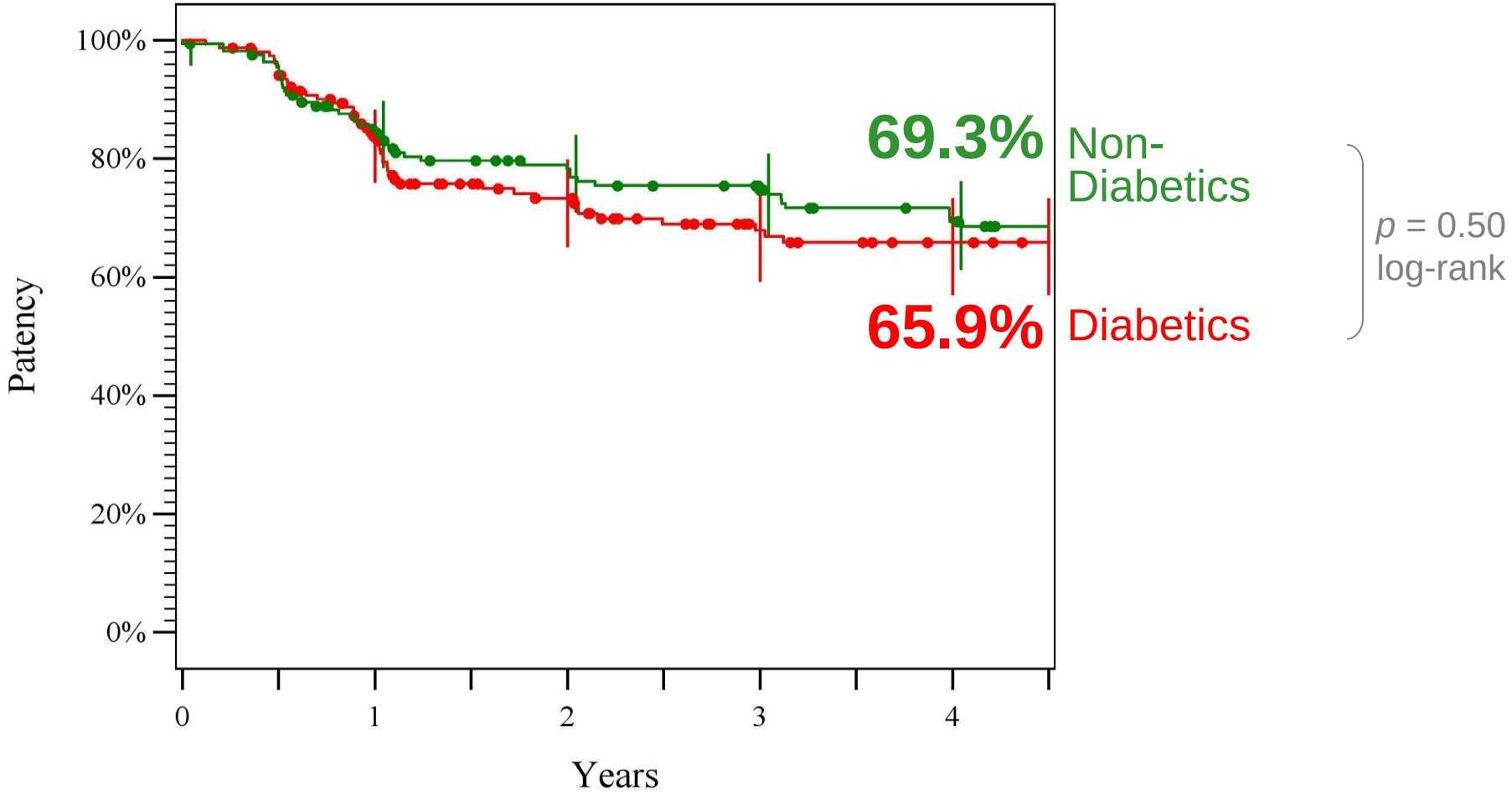
Primary patency rate is consistent across studies

Zilver PTX Stenting

in the Diabetic Patient Population

(Results from SAS, RCT, Japan PMS)

4-Year Primary Patency (PSVR < 2.0) Zilver PTX in Diabetics

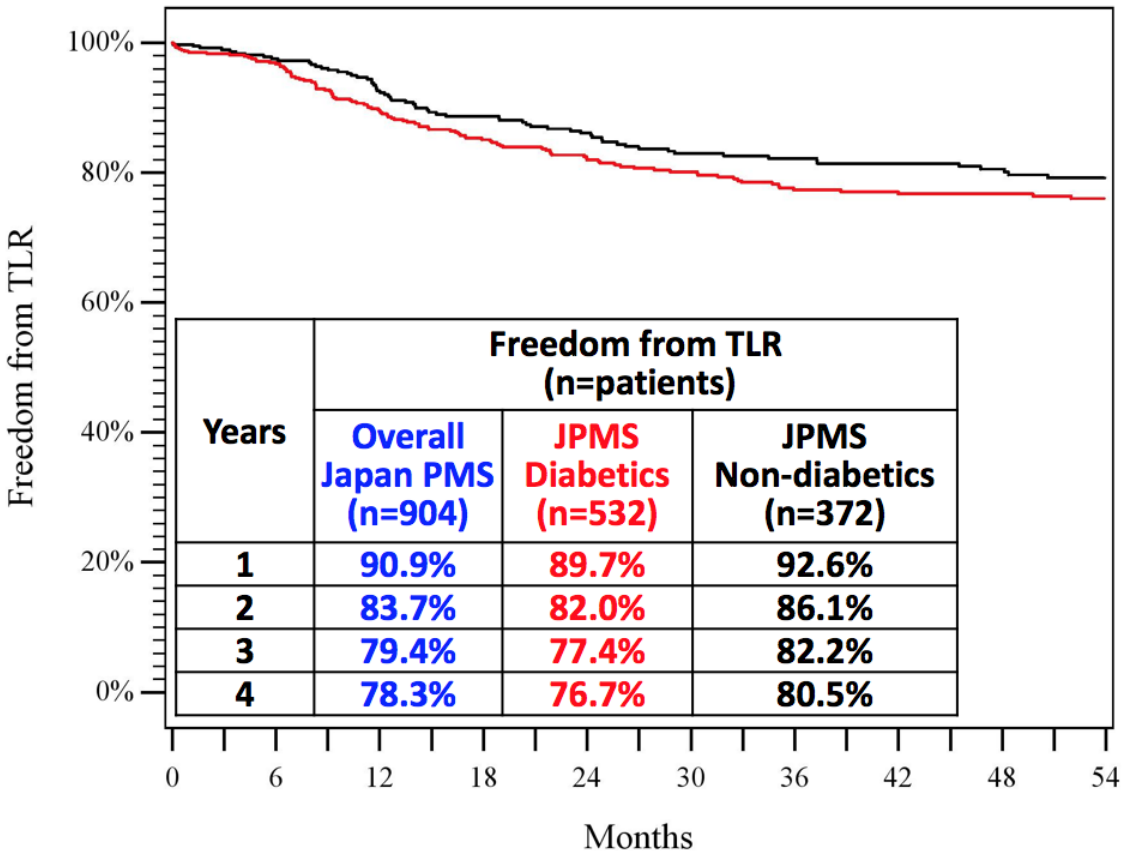


Zilver PTX results are similar in diabetic and non-diabetic patients

Patient Demographics and Comorbidities

	Overall Zilver PTX Japan PMS	JPMS Diabetics	JPMS Non-diabetics	*p*-value
Patients	905	532	373	-
Age (years)	74 ± 9	72 ± 8	75 ± 9	< 0.01
Male	70%	71%	69%	NS
Diabetes	59%	100%	0%	-
High cholesterol	61%	69%	50%	< 0.01
Hypertension	85%	88%	82%	< 0.01
Pulmonary disease	8%	7%	10%	NS
Renal disease	44%	49%	36%	< 0.01
Renal failure (eGFR < 60 and/or "on dialysis")	35%	42%	27%	< 0.01

Freedom from TLR



Years	Freedom from TLR (n=patients)		
	Overall Japan PMS (n=904)	JPMS Diabetics (n=532)	JPMS Non-diabetics (n=372)
1	90.9%	89.7%	92.6%
2	83.7%	82.0%	86.1%
3	79.4%	77.4%	82.2%
4	78.3%	76.7%	80.5%

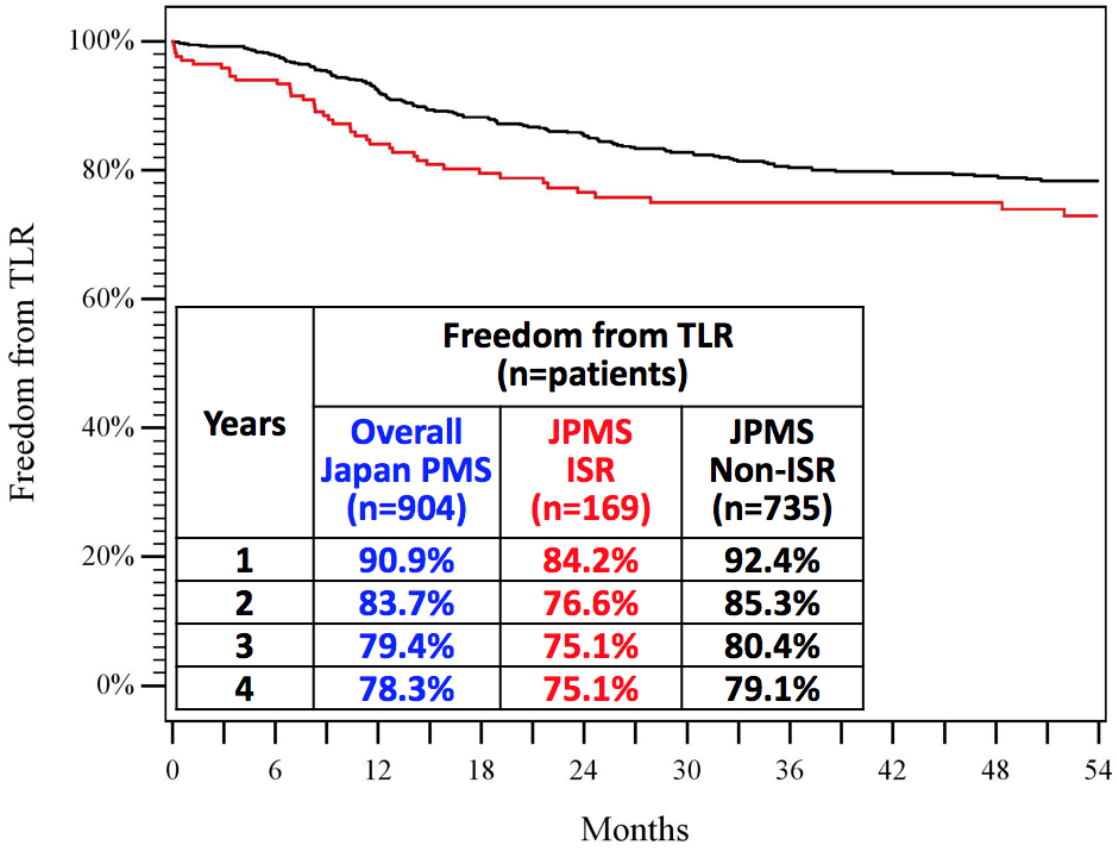
Similar outcomes for diabetic and non-diabetic patients

Zilver PTX Stenting
in the ISR Patient Population
(Results from Japan PMS)

Baseline Lesion Characteristics

		Overall 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 ± 9	92 ± 11	NS
Total occlusions		41%	36%	43%	NS
In-stent restenosis		19%	100%	0%	-
Patent runoff vessels	**0**	7%	6%	7%	NS
	1	32%	31%	32%	
	2	33%	37%	32%	
	3	29%	27%	29%	

Freedom from TLR



Years	Freedom from TLR (n=patients)		
	Overall Japan PMS (n=904)	JPMS ISR (n=169)	JPMS Non-ISR (n=735)
1	90.9%	84.2%	92.4%
2	83.7%	76.6%	85.3%
3	79.4%	75.1%	80.4%
4	78.3%	75.1%	79.1%

Nearly similar outcomes for ISR and non-ISR patients

Zilver PTX Stenting

Comparison of Total Occlusions and Stenoses (Results from Japan PMS)

Comparison of Total Occlusions and Stenoses

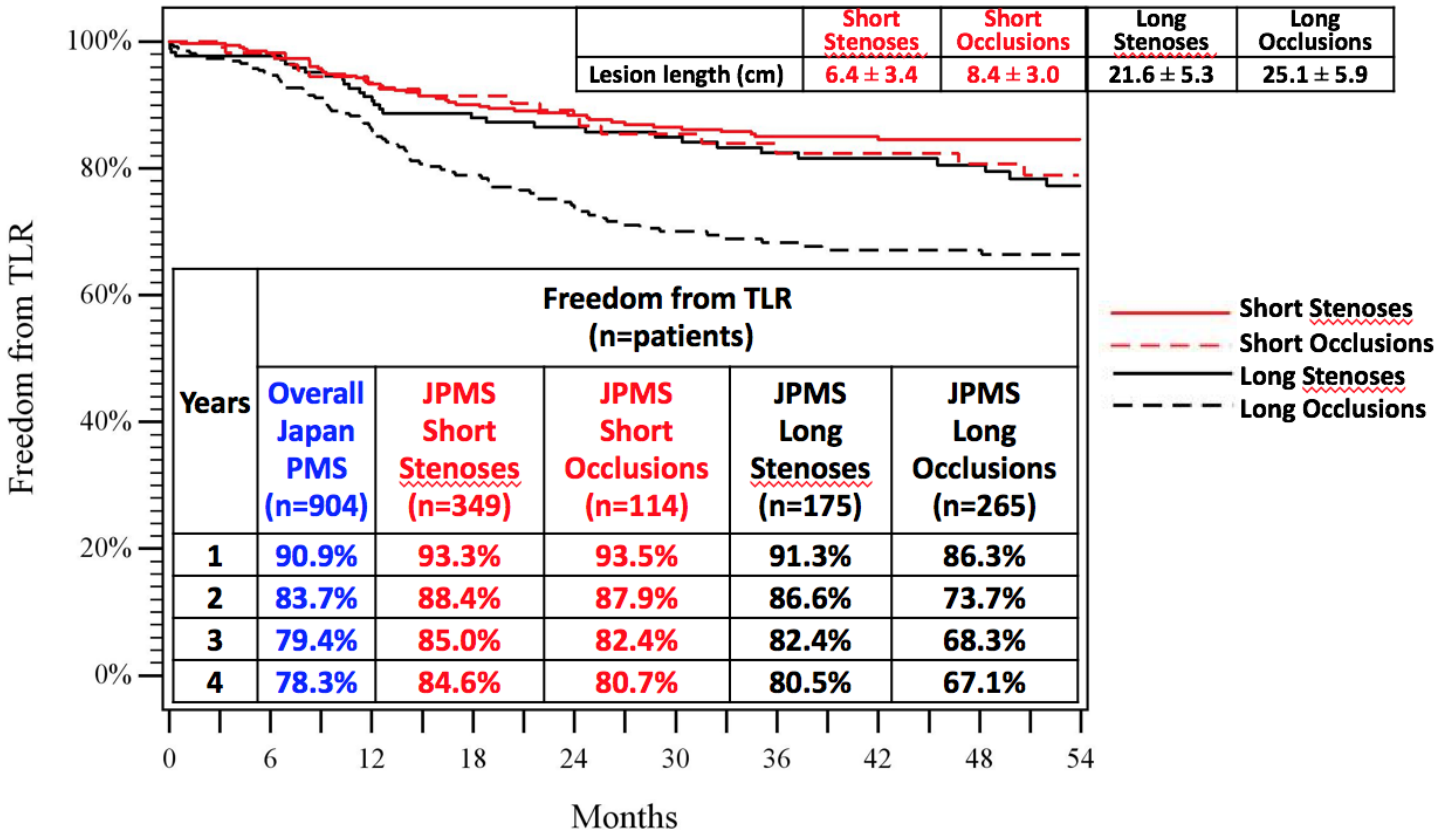
	Overall Zilver PTX Japan PMS	JPMS Occlusions	JPMS Stenoses	*p*-value
Lesions	1080	448	632	-
Lesion length (cm)	14.6 ± 9.6	19.7 ± 9.3	11.0 ± 8.1	< 0.01

- Interaction between occlusion/stenosis and lesion length

	Length < 14 cm	Length ≥ 14 cm
Stenoses	75% (440/583)	39% (192/496)
Occlusions	25% (143/583)	61% (304/496)

- Analysis looked at each of these 4 groups

Freedom from TLR



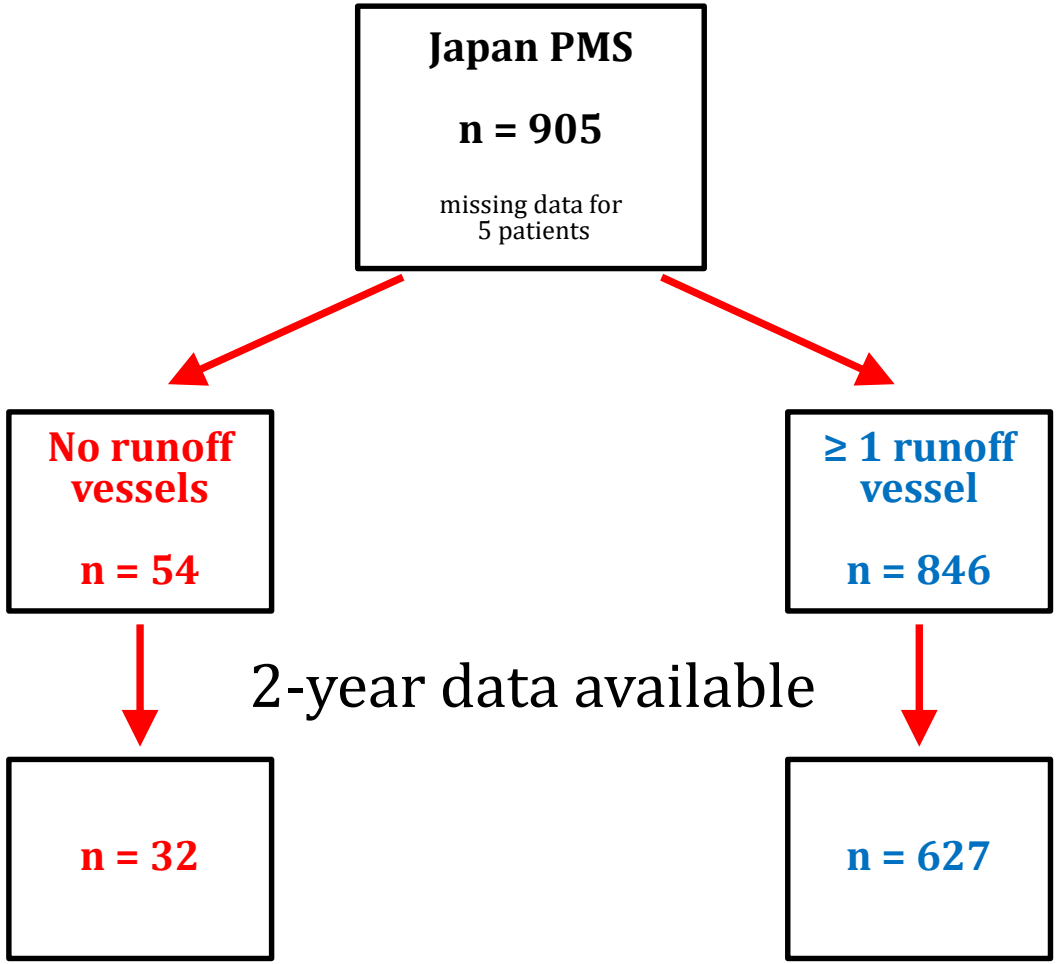
	Short Stenoses	Short Occlusions	Long Stenoses	Long Occlusions
Lesion length (cm)	6.4 ± 3.4	8.4 ± 3.0	21.6 ± 5.3	25.1 ± 5.9

Years	Freedom from TLR (n=patients)				
	Overall Japan PMS (n=904)	JPMS Short Stenoses (n=349)	JPMS Short Occlusions (n=114)	JPMS Long Stenoses (n=175)	JPMS Long Occlusions (n=265)
1	90.9%	93.3%	93.5%	91.3%	86.3%
2	83.7%	88.4%	87.9%	86.6%	73.7%
3	79.4%	85.0%	82.4%	82.4%	68.3%
4	78.3%	84.6%	80.7%	80.5%	67.1%

Similar outcomes for patients with stenosed lesions and total occlusions < 14 cm; somewhat lower freedom from TLR for total occlusions ≥ 14 cm

Zilver PTX Stenting
in the No Run-off Patient Population
(Results from Japan PMS)

Subgroup of No Patent Runoff Vessels in Patients from the Japan PMS



Patient Demographics and Comorbidities

	No-Runoff	Runoff
Patients (n)	**54**	**846**
Age (years)	74 ± 9	73 ± 9
Male	69%	70%
Diabetes	70%	58%
High cholesterol	61%	61%
Hypertension	89%	85%
Pulmonary disease	7%	8%
Critical limb ischemia	**44.8%**	**19.7%**

No statistically significant differences except higher proportion of CLI

Baseline Lesion Characteristics

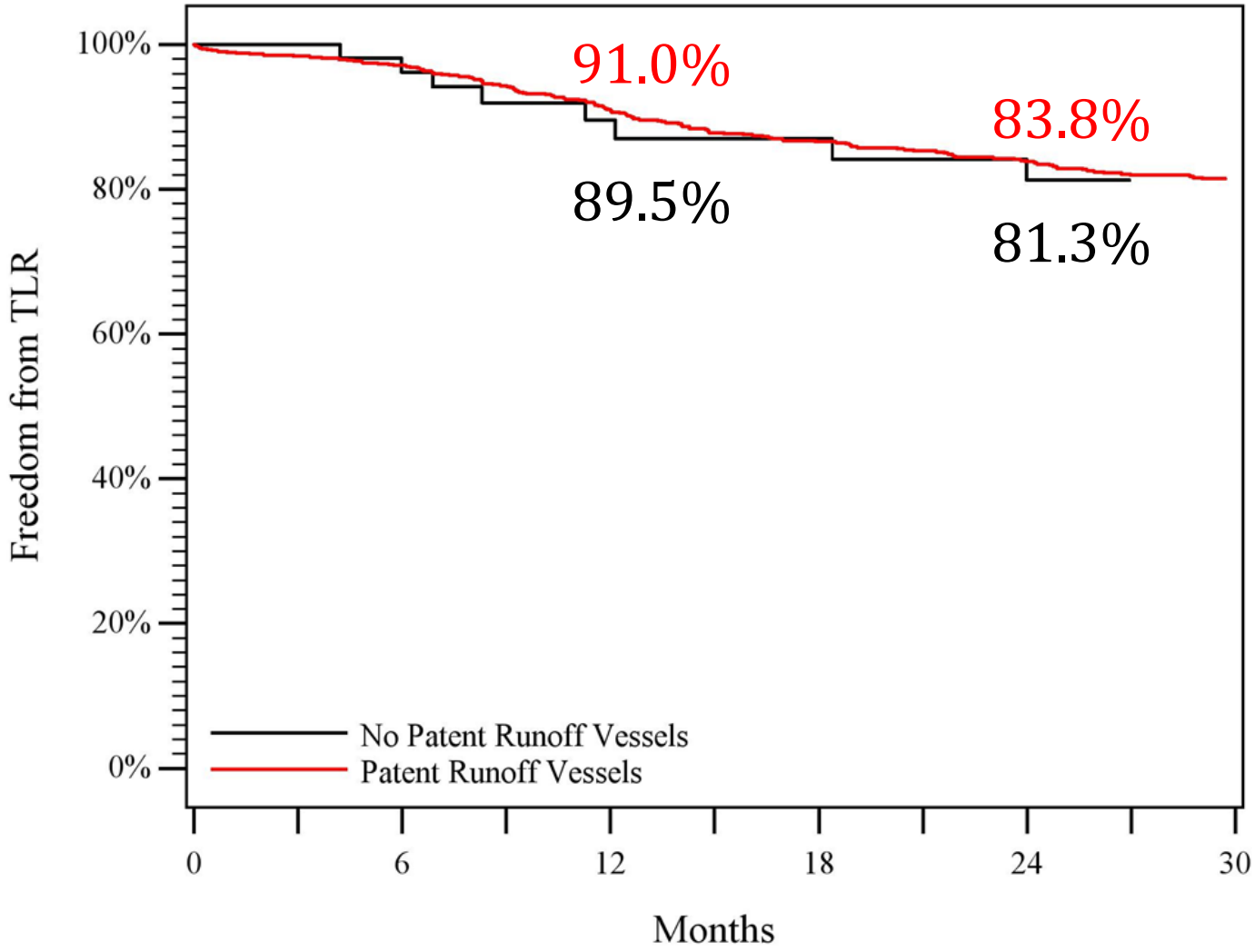
		No-Runoff	Runoff
Lesions (n)		**71**	**1003**
Lesion length (mm)		**138** ± 96	**147** ± 96
Diameter stenosis (%)		93 ± 9	92 ± 11
Total occlusions		44%	41%
In-stent restenosis		17%	19%
Patent runoff vessels	**0**	100%	N/A
	1		34%
	2	N/A	35%
	≥3		31%

No statistically significant differences between the two groups

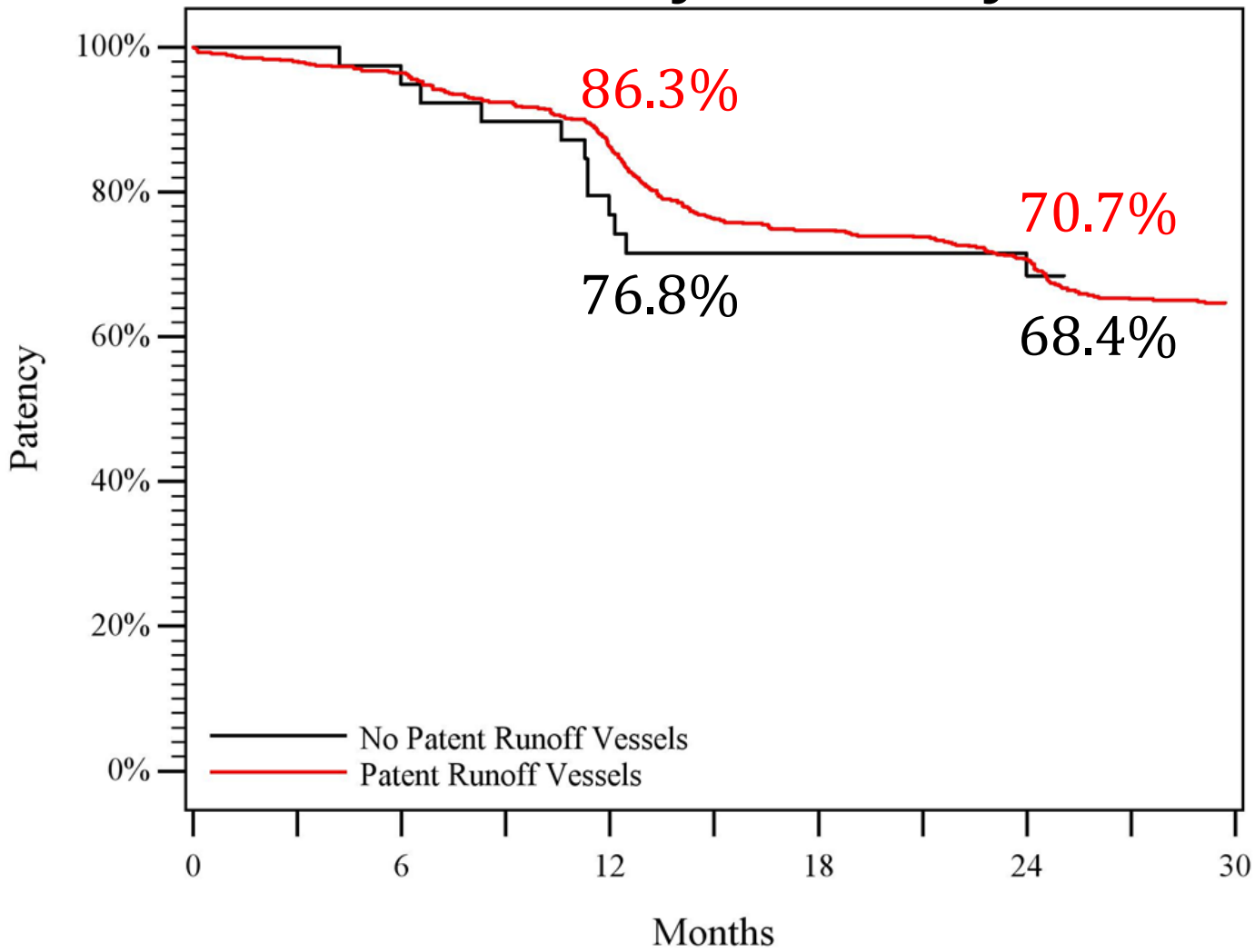
Safety

- No device or procedure related deaths
- Stent integrity through 1 year
  - 0.0% fracture rate in no runoff group
  - 2.5% fracture rate in runoff group
- Low rate of thrombosis through 2 years
- Three patients in the no runoff group and seven patients in the runoff group had an amputation through 2 years
  - All three amputations in the no runoff group occurred within 2 months of the initial procedure likely reflecting a more advanced stage of PAD

Freedom from TLR

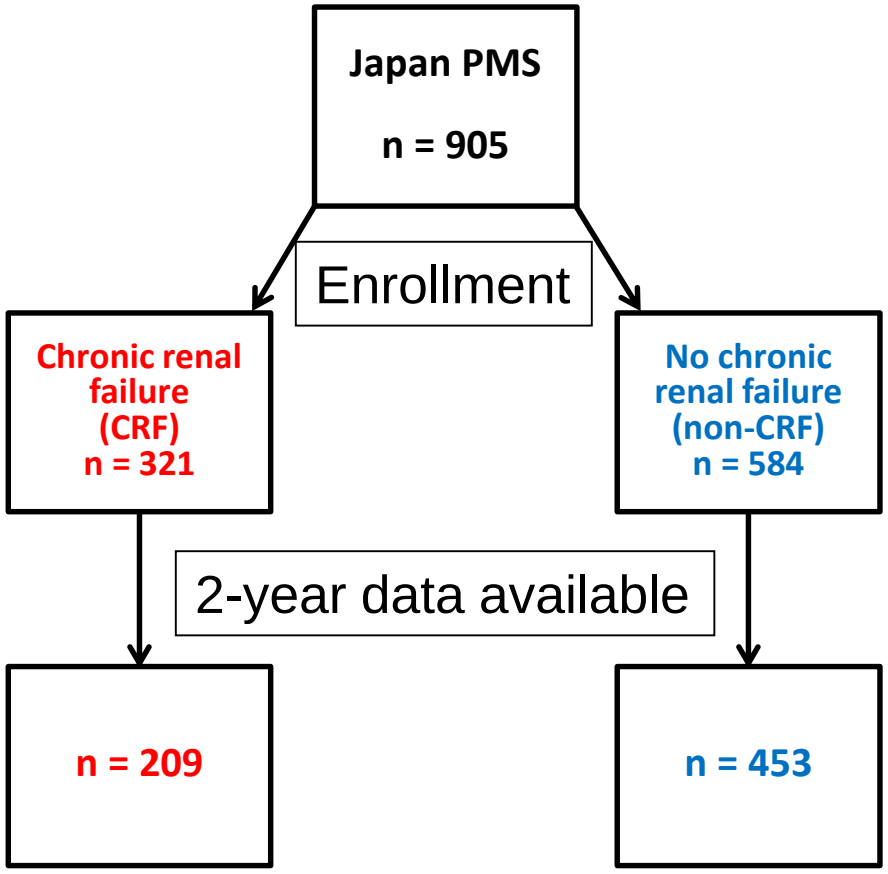


Primary Patency



Zilver PTX Stenting
in the Renal Failure Patient Population
(Results from Japan PMS)

Chronic Renal Failure Patients from the Japan PMS



CRF was defined as eGFR < 60 mL/min/1.73m^2 and/or dialysis

Patient Demographics and Comorbidities

	CRF	Non-CRF
Patients	321	584
Age (years)*	72 ± 9	74 ± 8
Male	68%	72%
Diabetes*	69%	53%
High cholesterol	57%	63%
Hypertension	86%	85%
Pulmonary disease*	19%	6%
* $p<0.05$		

Higher incidence of diabetes and pulmonary disease in the CRF group

Baseline Lesion Characteristics

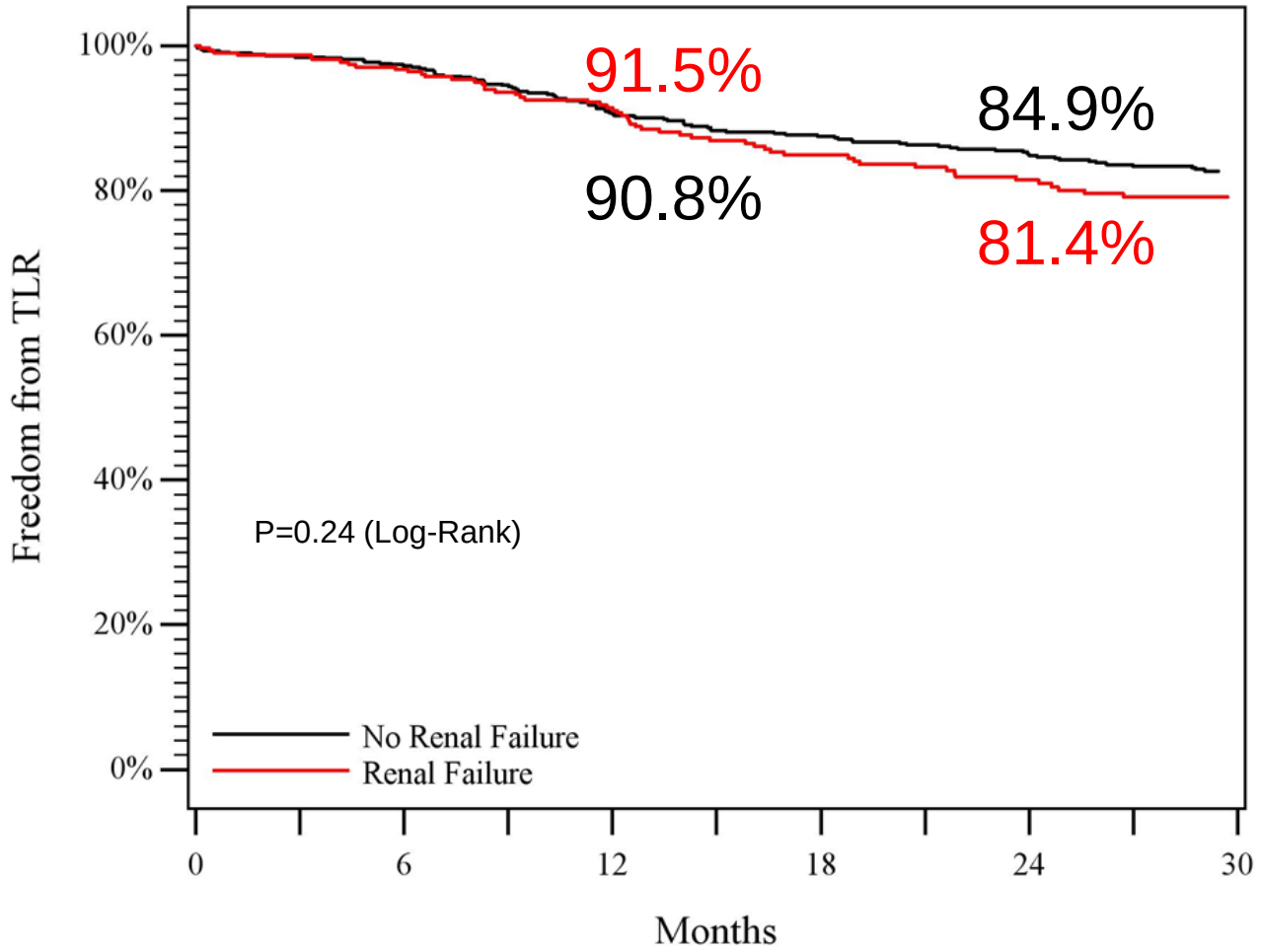
		CRF	Non-CRF
Lesions		381	699
Lesion length (mm)		146 ± 93	147 ± 98
Diameter stenosis (%)		91 ± 10	92 ± 11
Total occlusions*		34%	45%
In-stent restenosis		17%	20%
Severe calcification*		32%	9%
CLI; Rutherford (≥4) *		33%	15%
Patent runoff vessels	0	7%	7%
	1	35%	30%
	>2	58%	63%
* $p<0.05$			

Higher rates of severe calcification and CLI in the CRF group

Safety

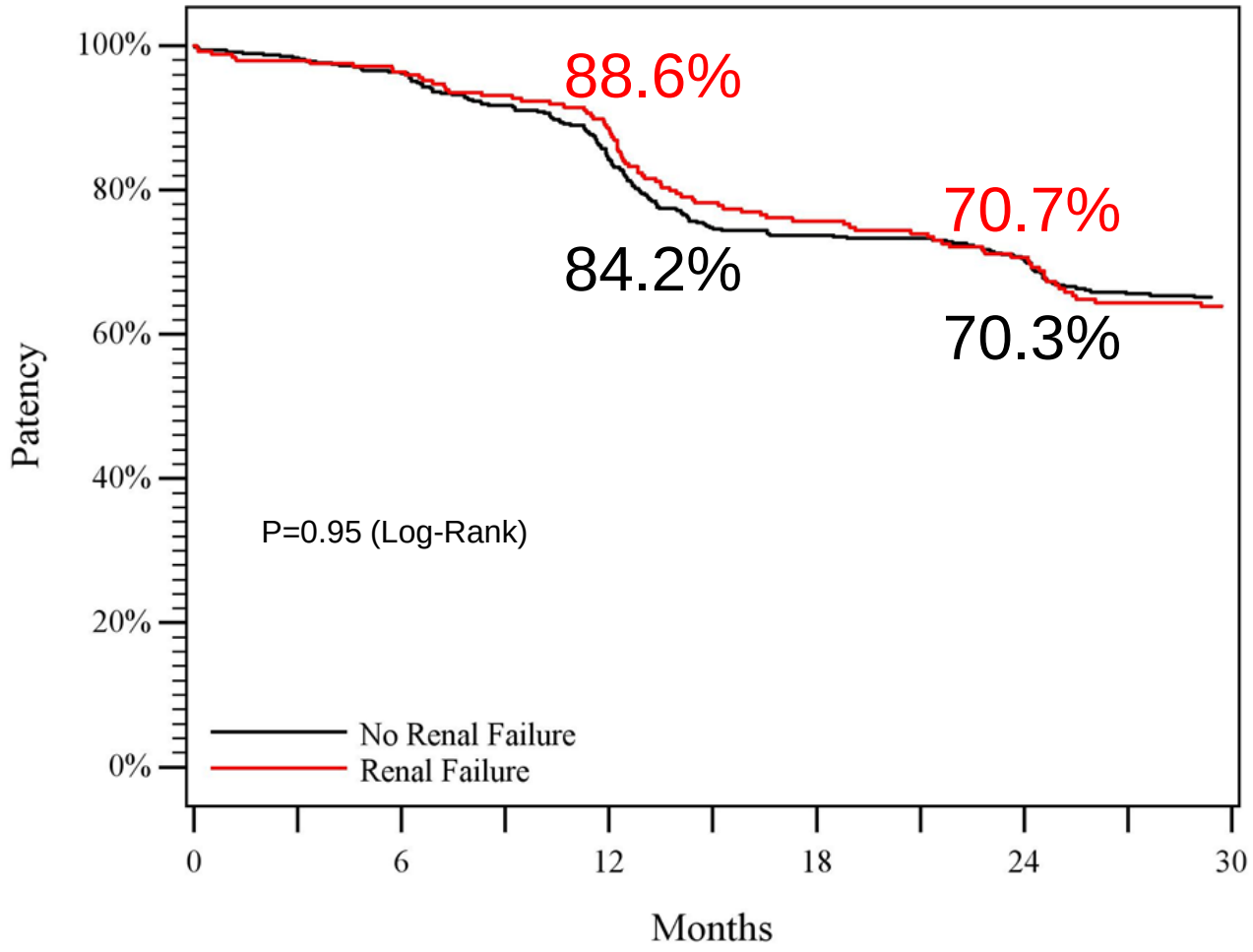
- No device or procedure related deaths
- 1249 stents implanted
  - -0.5% fracture rate in CRF group through 1 year
  - -3.7% fracture rate in non-CRF group through 1 year
- Through 2 years, low rate of thrombosis
- Through 2 years, 8 patients in the CRF group (2.5%) and 2 patients in the non-CRF group (0.3%) had an amputation
  - -Four of these occurred within 2 months from the initial procedure likely reflecting a more advanced stage of PAD

Freedom from TLR



Freedom from TLR rates are similar through 2 years

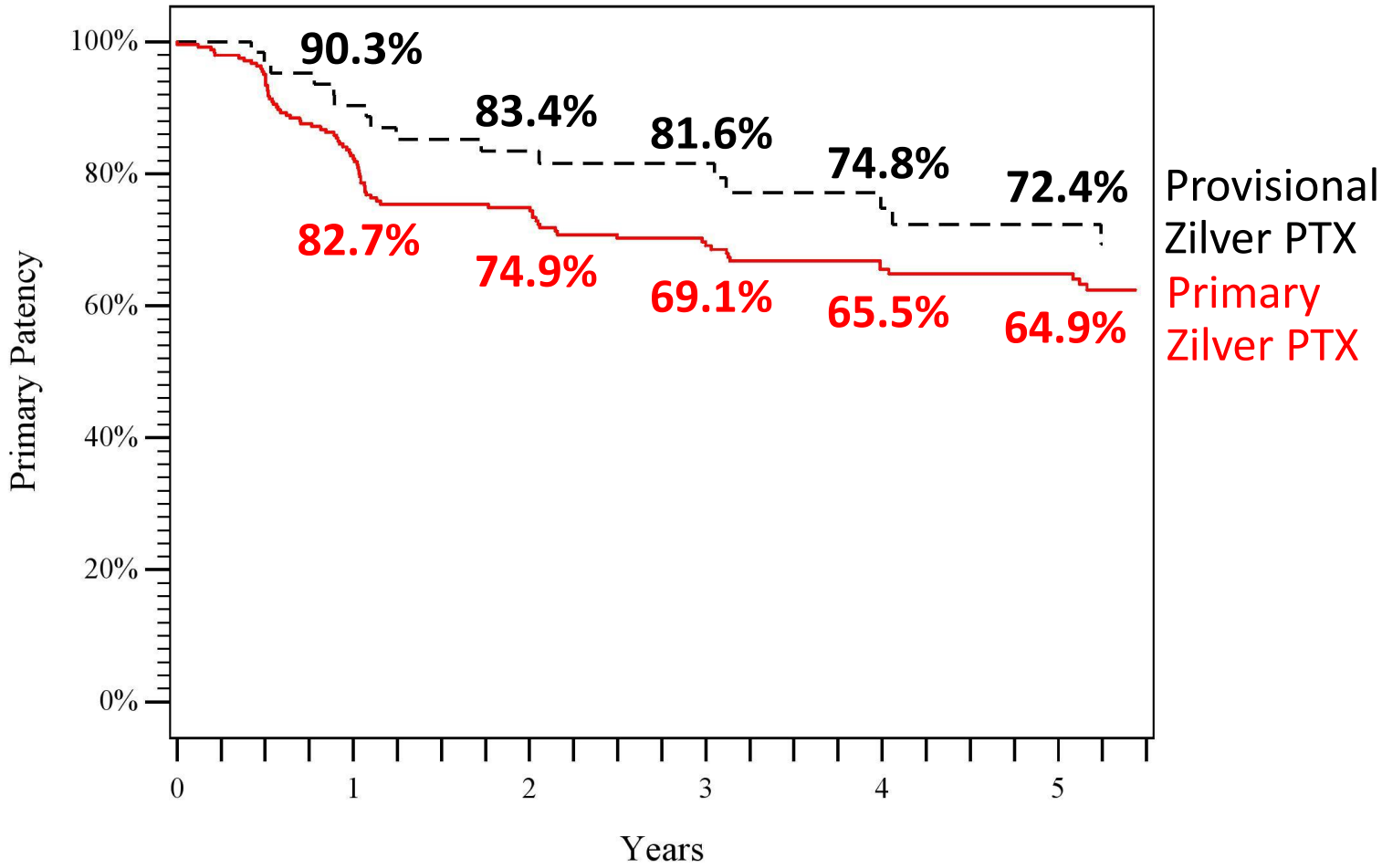
Primary Patency



Primary patency rates are similar through 2 years

5-year Primary Patency (PSVR < 2.0)

Primary Zilver PTX vs. Provisional Zilver PTX



4 & 5 year Overall 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
- 4-year Japan PMS and 5-year RCT results are positive and confirm the long-term benefit of Zilver PTX
  - Freedom from TLR remains consistent across studies and provides added support for the established performance of the Zilver PTX stent