The Zilver PTX® Randomized Trial of Paclitaxel-Eluting Stents for Femoropopliteal Disease: **24-Month Update**

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On behalf of the Investigators

Overview

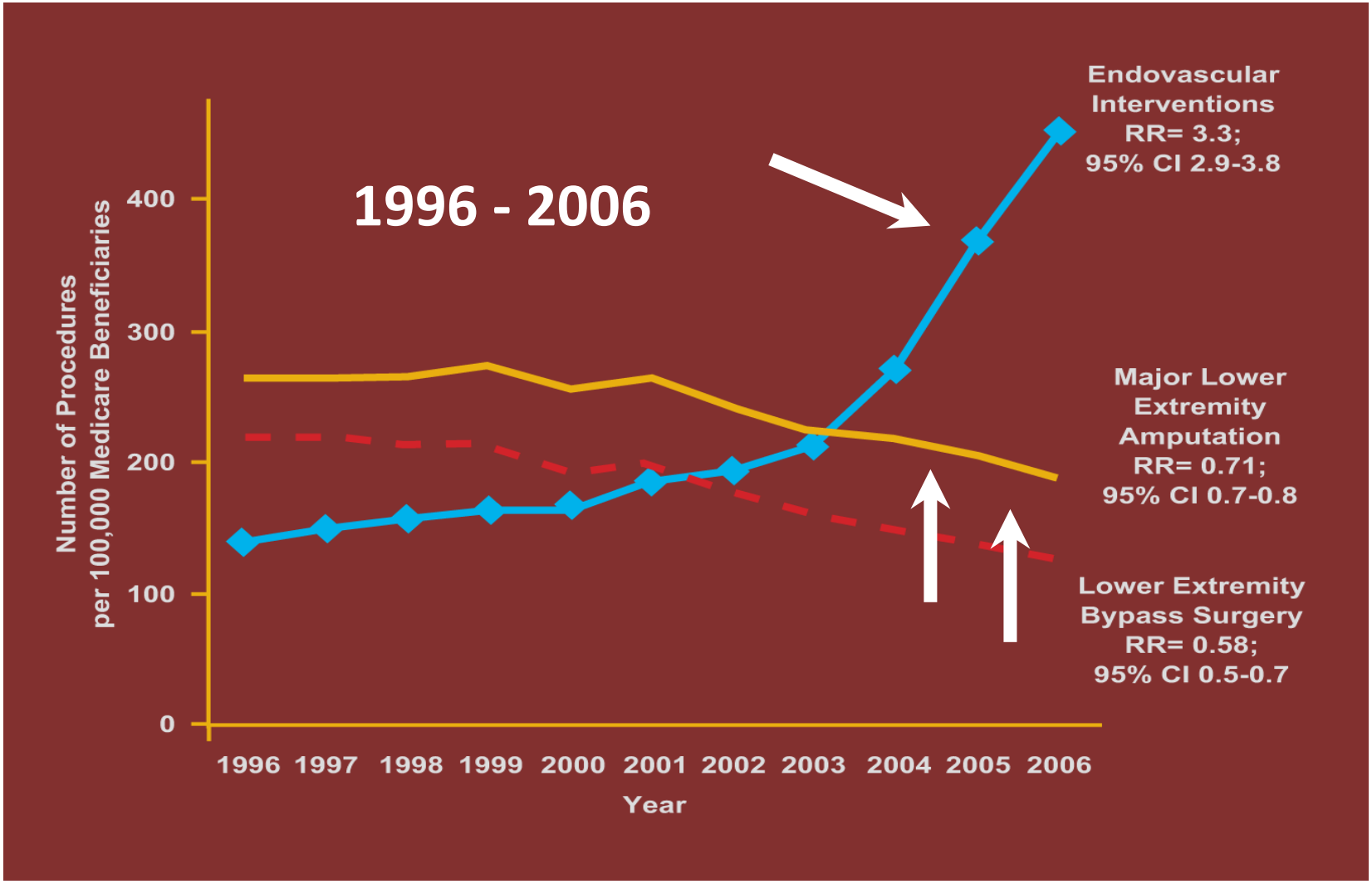
- Background
  - Drug-eluting stents for SFA treatment
  - Zilver PTX® drug-eluting stent
  - Trial design
  - Patient demographics/lesions

- Zilver PTX Randomized Trial – 24-month update
  - Safety
  - Effectiveness – Primary Patency
    - **81.2% Zilver PTX® vs. 62.7% BMS**

SFA Treatment Overview

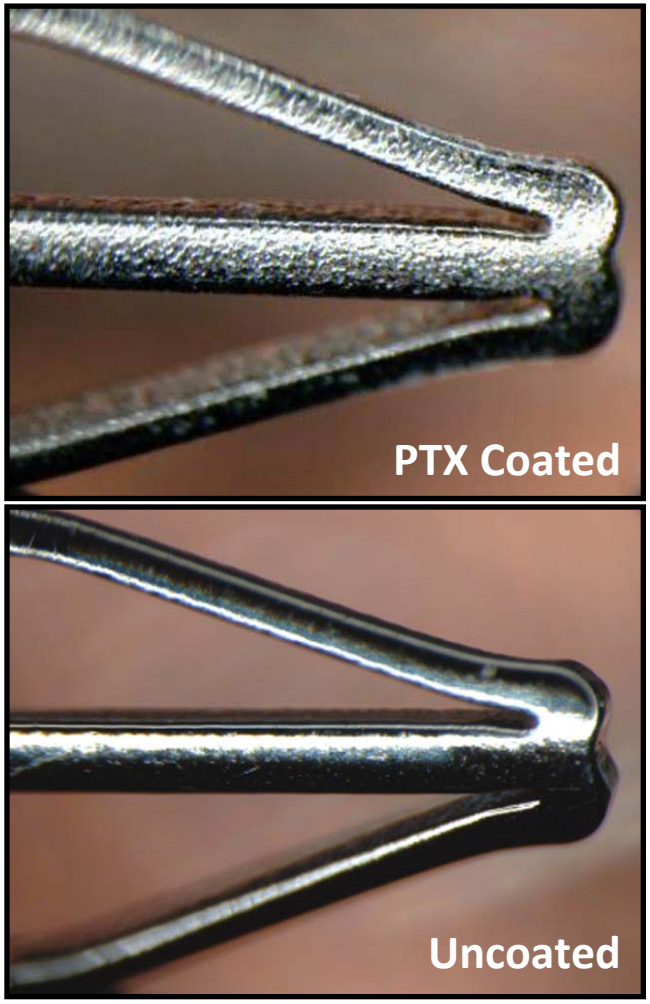
- **Medical therapy** – small population
- **Exercise** – effective when supervised; not reimbursed
- **Surgery** – invasive
- **PTA** – limited effectiveness (12-mo. patency rates ≈35%)
- **BMS** – more effective than PTA (12-mo. patency rates ≈70%)
- **Atherectomy** – no randomized data
- **Cryoplasty** – no randomized data
- **Previous DES (polymer-based, limus drug coatings)** – no sustained difference from BMS
- **Paclitaxel-coated balloons** – promising in short, simple lesions

What is Driving Increased Device Use?

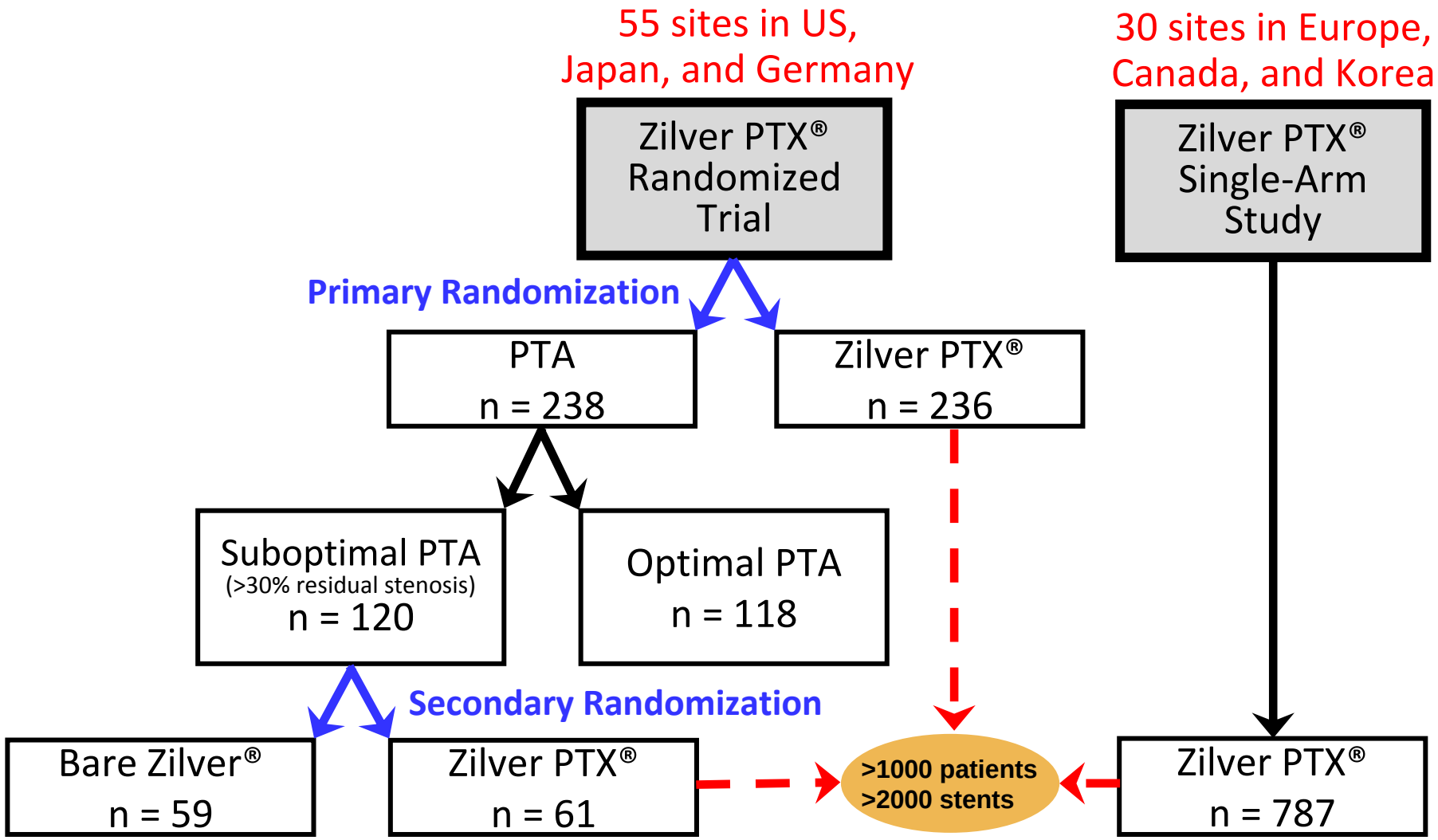


Zilver PTX® Drug-Eluting Stent

- Designed for the SFA
- CE Marked
  - Investigational in the US and Japan
- Dual therapy stent
  - **Mechanical support:** Zilver Flex® Stent Platform
  - **Drug coating:** Paclitaxel only
    - No polymer or binder
    - 3 µg/mm^2 dose density
- Sponsor: Cook Medical



Complementary Zilver PTX® Clinical Studies



Complementary Studies

Zilver PTX®	Single-Arm Study	Randomized Study
Protocol	Prospective, detailed case report forms, extensive monitoring	
Antiplatelets	Clopidogrel for 60 days, aspirin indefinitely	
Outcomes	Patency by ultrasound, stent integrity by X-ray, clinical benefit	
Patients	Symptomatic PAD with Rutherford score ≥ 2	
Control Group(s)	None	PTA ± provisional BMS
Lesions	*De novo* or restenotic, > 50% diameter stenosis,	
	Real-world: •Unlimited per limb •Included in-stent restenosis •Length not limited •Unlimited Zilver PTX® stents per lesion*	**Controlled/Moderate:** •One lesion per limb •No prior stent in study vessel •Length ≤ 14 cm •Maximum of 2 Zilver PTX® stents per lesion
Imaging Analysis	Site-based	Core laboratories (duplex ultrasound, angiography, X-ray)
Primary Analysis	12 months	
Ongoing Follow-up	2 years	5 years

* Maximum four per patient

Zilver PTX® Randomized Trial

- **Prospective, multinational trial**
  - Protocol approved by FDA, PMDA and German regulatory authorities
- **CEC and DSMB** oversight, and imaging **Core Lab** analyses
- **Key inclusion/exclusion criteria**
  - Rutherford classification ≥ 2
  - Reference vessel diameter 4-9 mm
  - Lesion length ≤ 14 cm
  - *De novo* or restenotic lesions (no in-stent restenosis)
  - > 50% diameter stenosis
  - One lesion per limb (bilateral treatment allowed)

Zilver PTX® Randomized Trial

- **12-month event-free survival –** Primary safety endpoint
  - Per patient freedom from death, amputation, target lesion revascularization, or worsening Rutherford score (by 2 classes or to class 5 or 6)
- **12-month primary patency –** Primary effectiveness endpoint
  - Per lesion patency by duplex ultrasonography, patent = PSVR < 2.0 (or angiography if available, patent = diameter stenosis < 50%)
  - One lesion per limb, bilateral treatment allowed
- **5 year** ongoing follow-up
  - 2, 3, 4, and 5 year patency evaluations for all stent patients and a randomly selected subset of patients with acutely successful PTA
  - 3 and 5 year stent radiographs

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%	49%	0.13
High cholesterol	70%	76%	0.12
Hypertension	82%	89%	0.02*
Past/current smoker	84%	86%	0.70

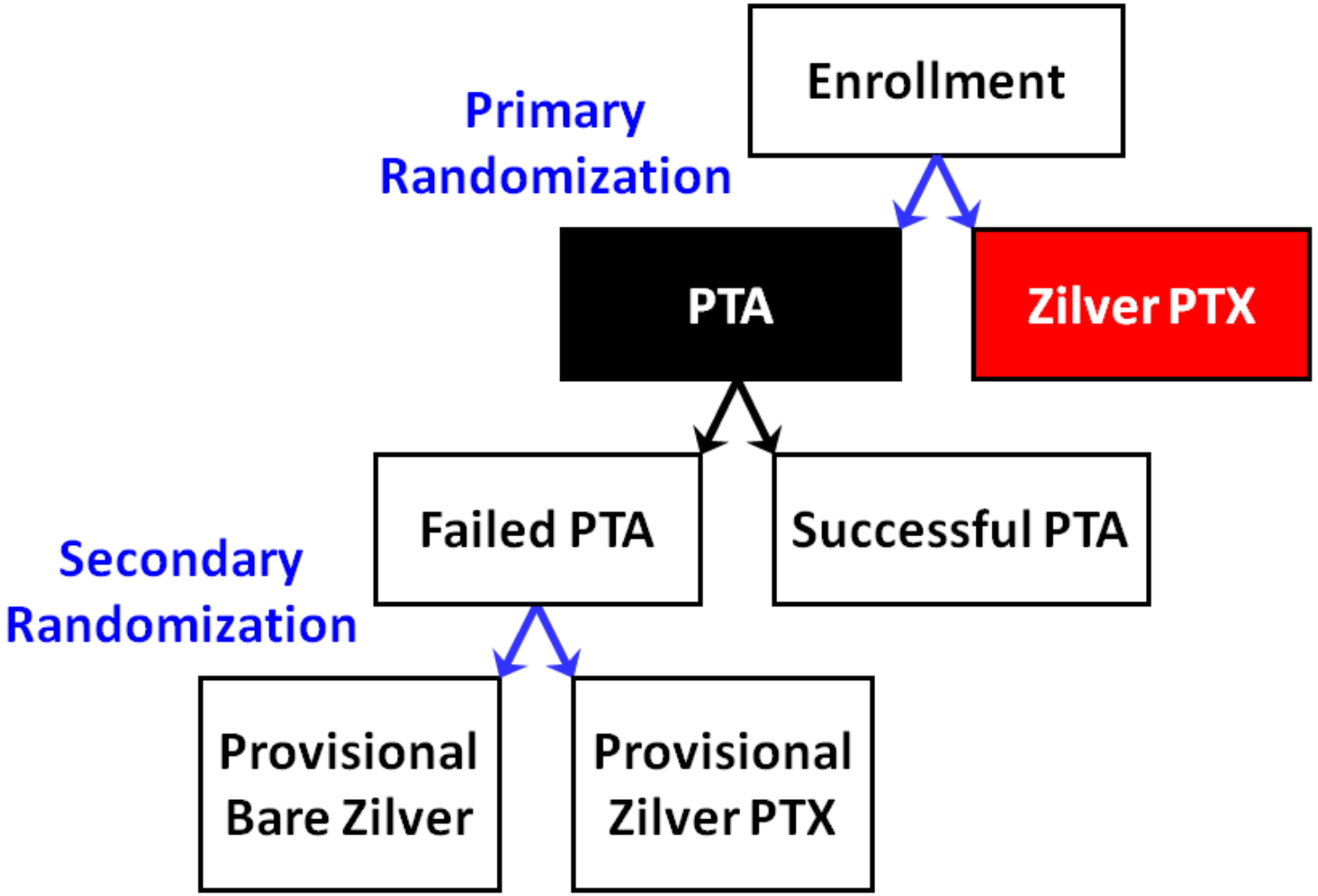
* Statistically significant

Baseline Lesion Characteristics

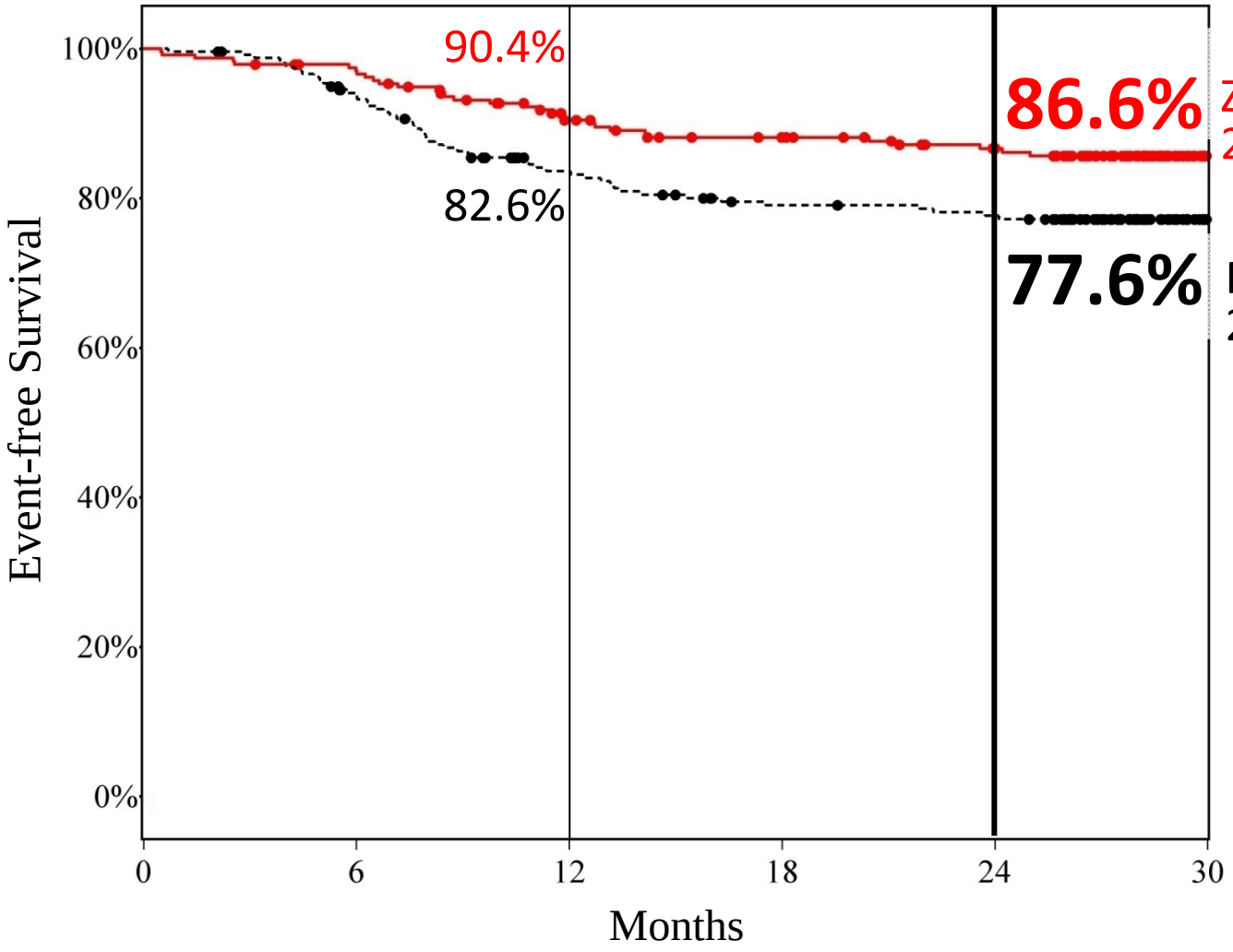
		PTA	Zilver PTX®	*P*-value
Lesions		251	247	
Normal-to-normal lesion length (mm)		63 ± 41	66 ± 39	0.35
Stenosed lesion length (mm)[1,2]		53 ± 40	54 ± 41	0.76
Diameter stenosis (%)[1]		78 ± 17	80 ± 17	0.44
Total occlusions		25%	30%	0.20
***De novo* lesions**		94%	95%	0.69
Lesion calcification[1]	**None**	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

Safety
Event-free Survival



24-Month Safety
Event-free Survival



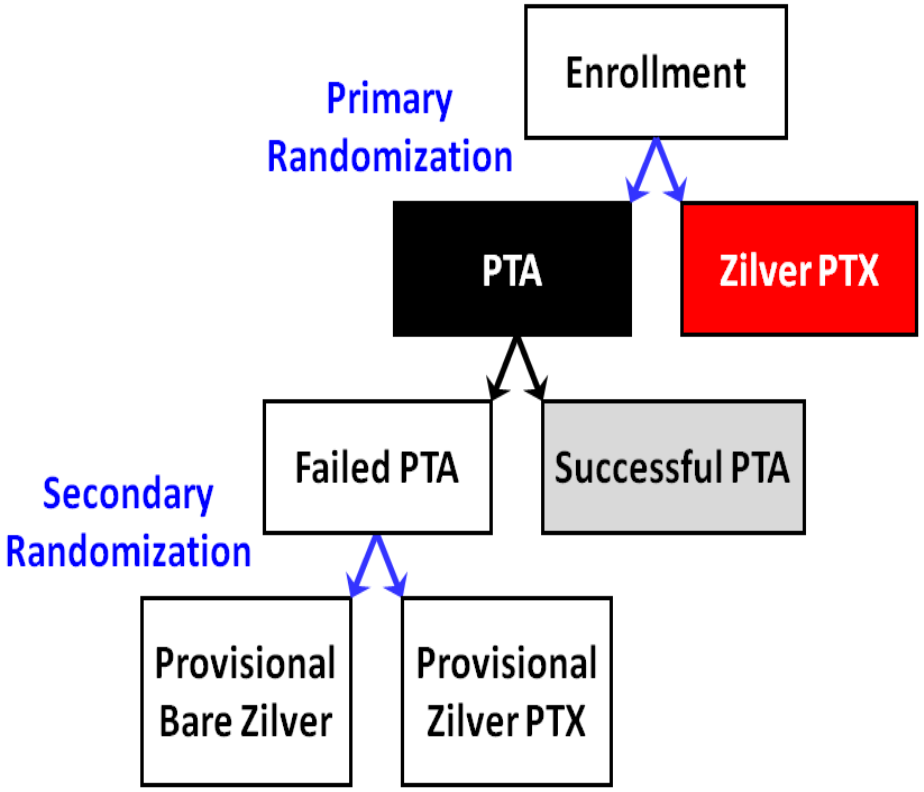
Event-free Survival: Freedom from CEC-adjudicated death, amputation, and target lesion revascularization, or worsening Rutherford score (by 2 classes or to class 5 or 6)

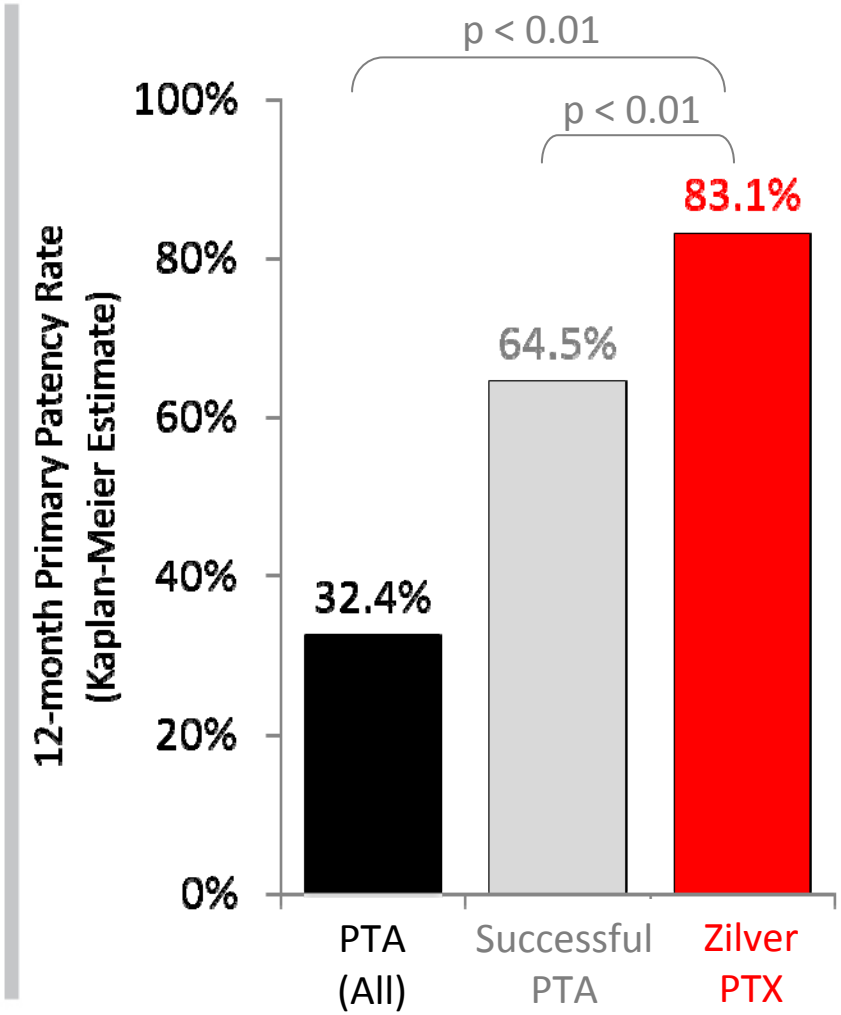
Low Stent Fracture Rate

- 546 stents implanted
  - 453 Zilver PTX (average of 1.5 stents per patient)
  - 93 Zilver BMS
- X-ray core laboratory analysis of 457 stents at 12 months
- Four stent fractures
  - No associated adverse events

0.9% stent fracture rate through 12 months (next evaluations at 3 and 5 years)

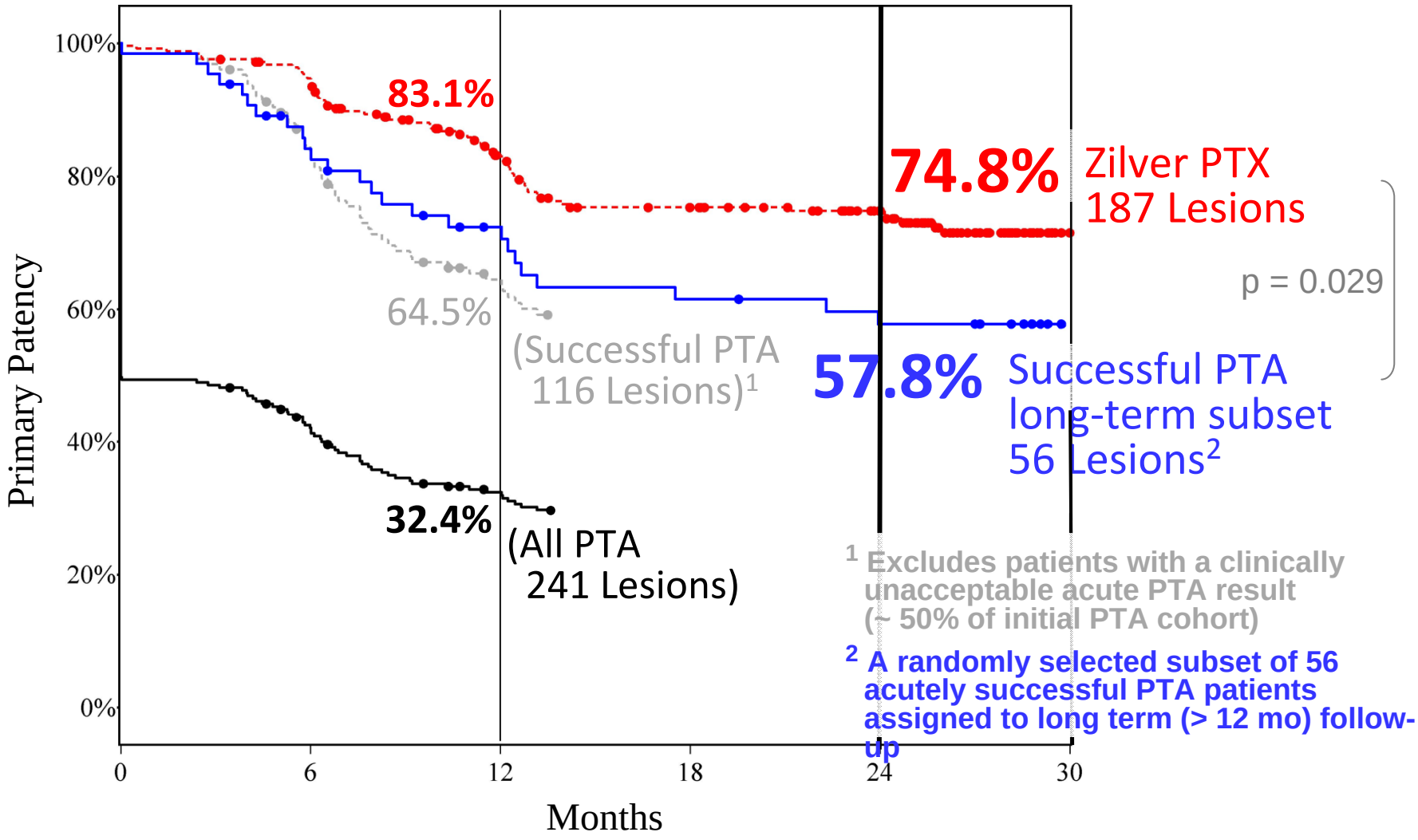
12-Month Effectiveness
Primary Patency (PSVR < 2.0): **Zilver PTX vs. PTA**





24-Month Effectiveness

Primary Patency (PSVR < 2.0): **Zilver PTX vs. PTA**

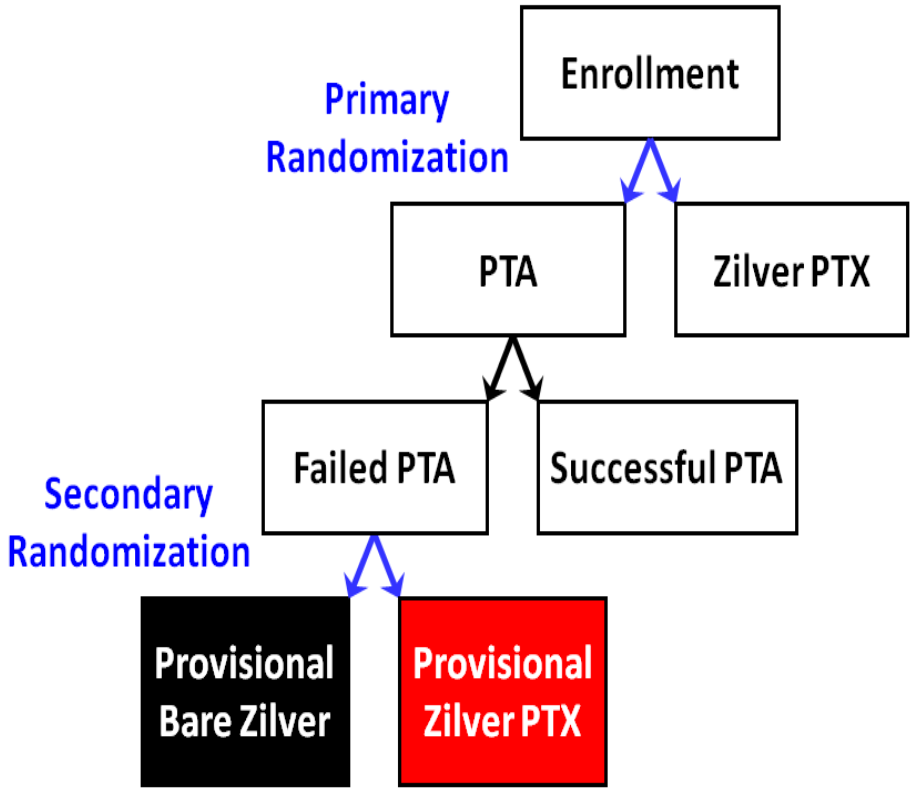


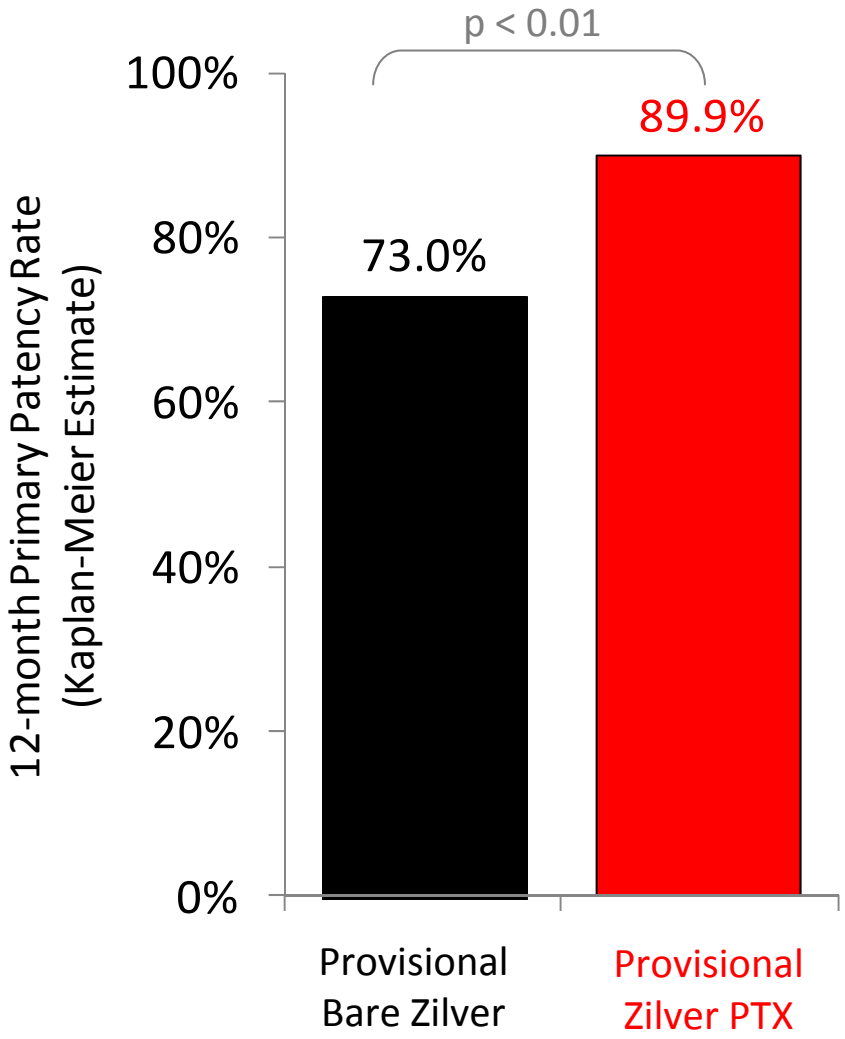
[1] Excludes patients with a clinically unacceptable acute PTA result (~ 50% of initial PTA cohort)

[2] A randomly selected subset of 56 acutely successful PTA patients assigned to long term (> 12 mo) follow-up

12-Month Paclitaxel Effect

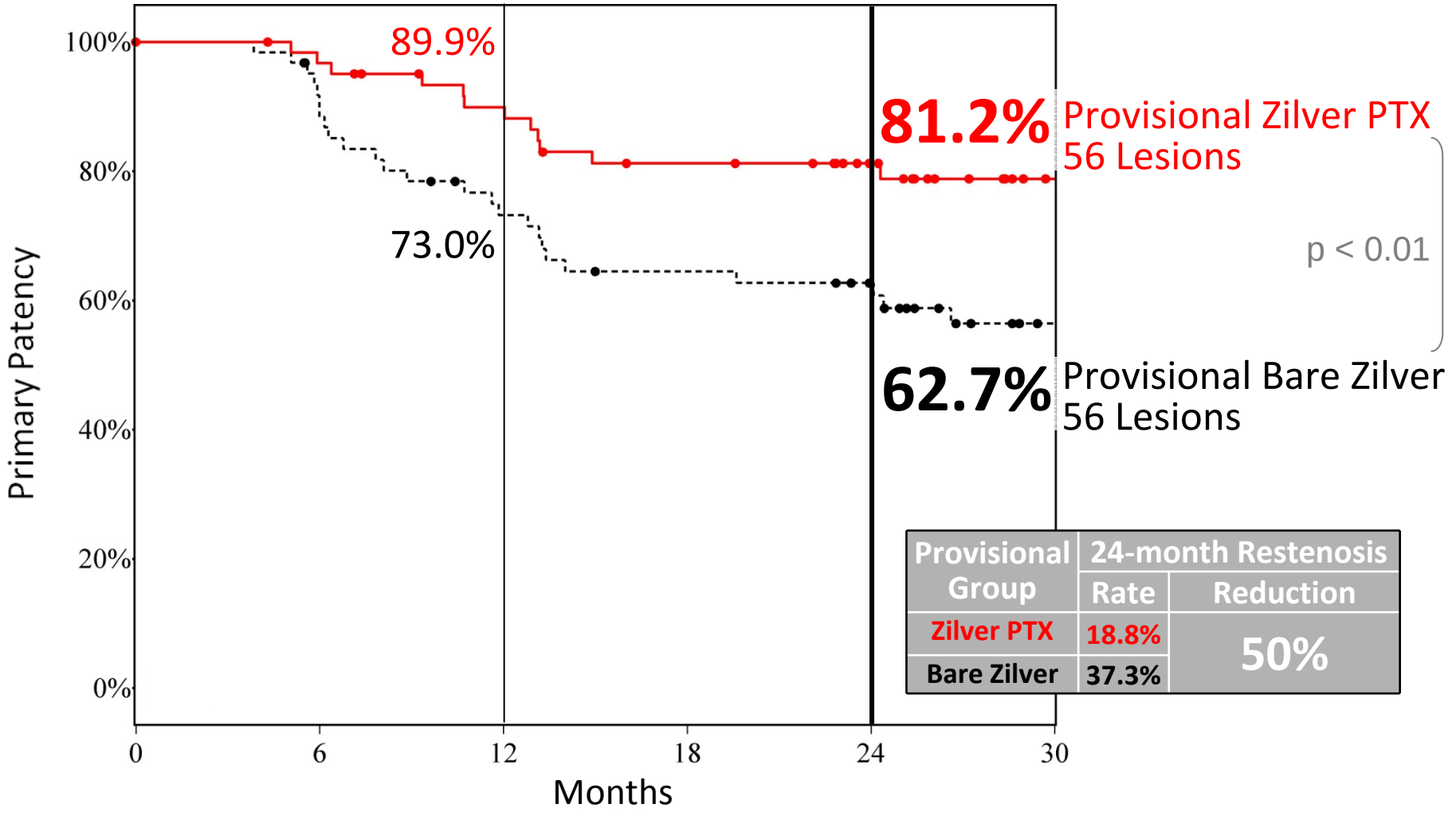
Patency (PSVR < 2.0): **Provisional Zilver PTX vs. BMS**





24-Month Paclitaxel Effect

Patency (PSVR < 2.0): **Provisional Zilver PTX vs. BMS**



Provisional Group	24-month Restenosis Rate	24-month Restenosis Reduction
Zilver PTX	18.8%	50%
Bare Zilver	37.3%	

Conclusions

- **24-month results** support sustained safety and effectiveness
  - Primary Zilver PTX significantly better patient safety than PTA ($p < 0.01$)
  - Primary Zilver PTX patency of 74.8%
  - Provisional Zilver PTX patency (81.2%) significantly higher than provisional BMS patency (62.7%, $p < 0.01$)
  - PTX coating reduces 24-month restenosis rates by 50%