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

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On behalf of the Investigators

Overview

- Background
  - Drug elution in the periphery
  - Zilver PTX® drug-eluting stent
  - Trial design
  - Patient demographics and lesion characteristics

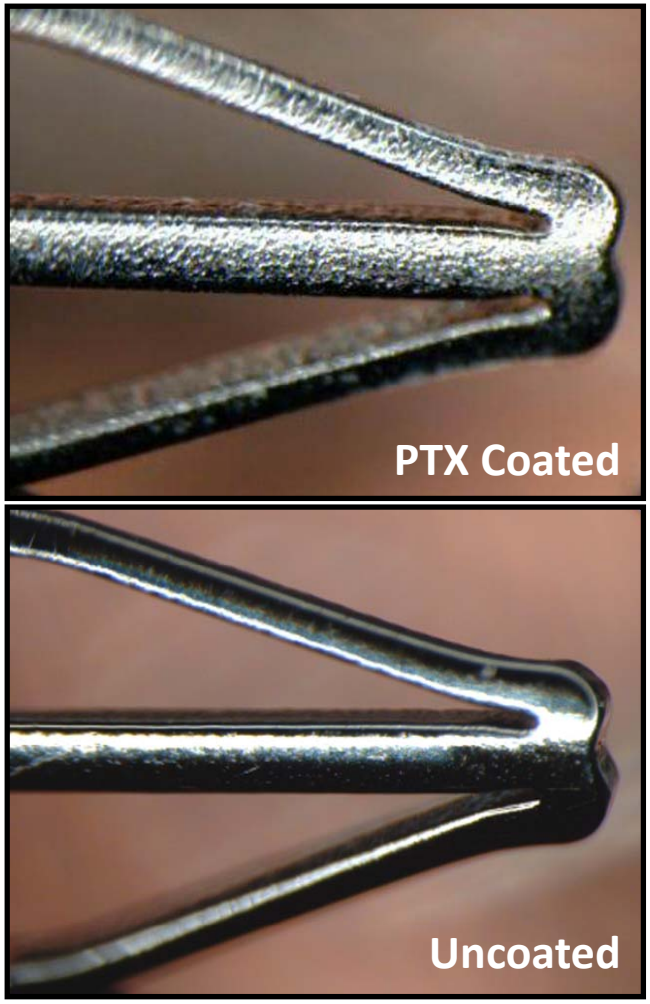
- Zilver PTX® Randomized Trial – 24-month update
  - Safety: significantly better safety than PTA ($p < 0.01$)
  - Effectiveness: proven drug effect vs. BMS
    - Patency: **83.4% Zilver PTX® vs. 64.1% BMS**

Drug Elution in the Periphery

- Multiple drug-eluting stent and drug-eluting balloon trials underway
- Six companies with peripheral drug-eluting technology
- Cook Medical offers both drug-eluting stents and drug-eluting balloons for the periphery

Zilver PTX® Drug-Eluting Stent

- Designed for the SFA
- Approved in EU/Japan
- Approval pending in US
- Dual therapy
  - **Mechanical scaffold:** Zilver Flex® Stent Platform
  - **Drug therapy:** Paclitaxel only
    - No polymer or binder
    - 3 µg/mm^2 dose density
- Sponsor: Cook Medical



Zilver PTX® Randomized Trial

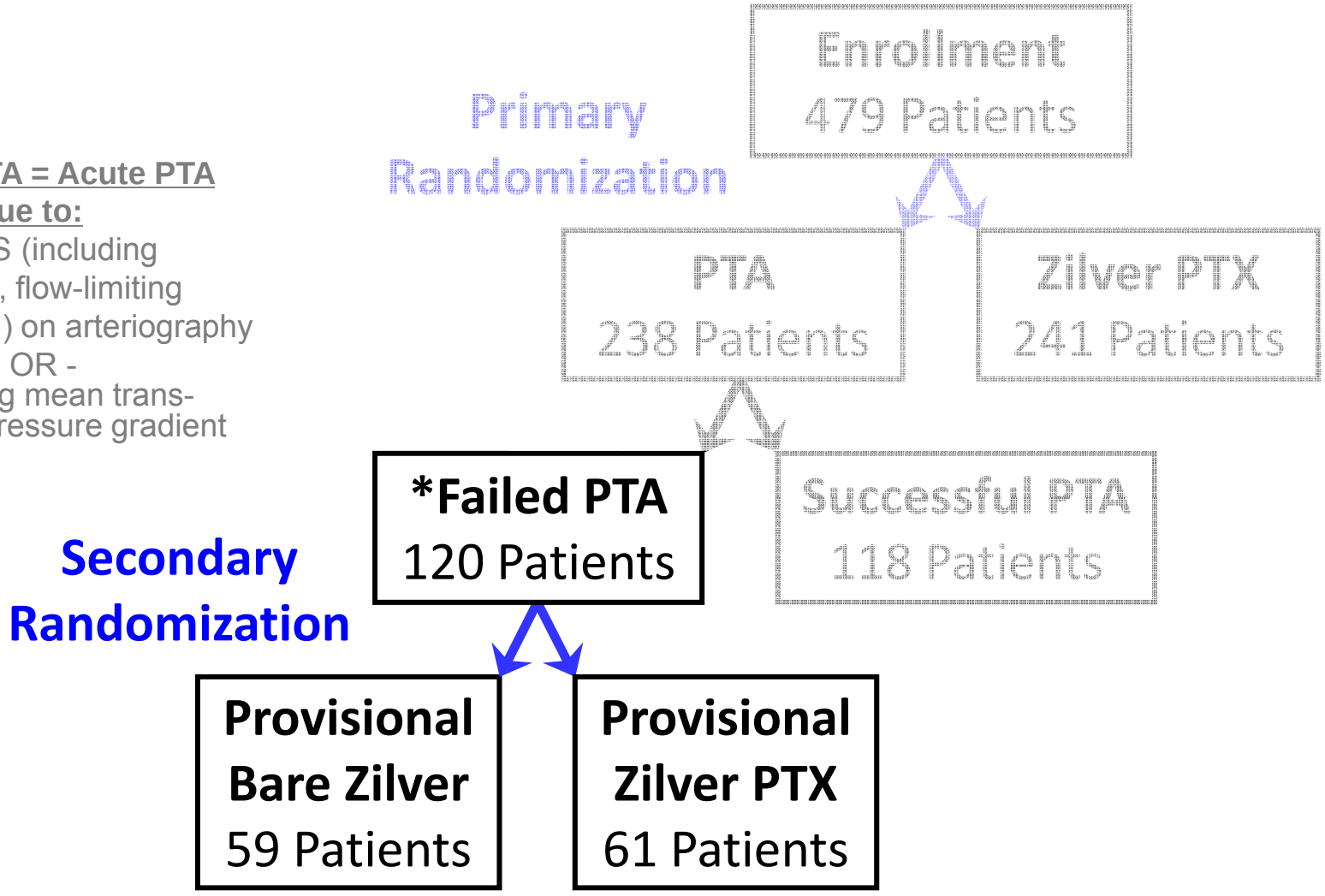
- **Prospective, multinational trial**
  - Protocol approved by FDA, PMDA, and German regulatory authorities
- **CEC and DSMB** oversight, and imaging **Core Lab** analyses
- **Key inclusion/exclusion criteria**
  - Rutherford classification ≥ 2
  - Reference vessel diameter 4-9 mm
  - Lesion length ≤ 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

Clinical Trial Design

* **Failed PTA = Acute PTA Failure Due to:**
- ≥ 30 %DS (including persistent, flow-limiting dissection) on arteriography
- OR -
- ≥ 5 mmHg mean trans-stenotic pressure gradient



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

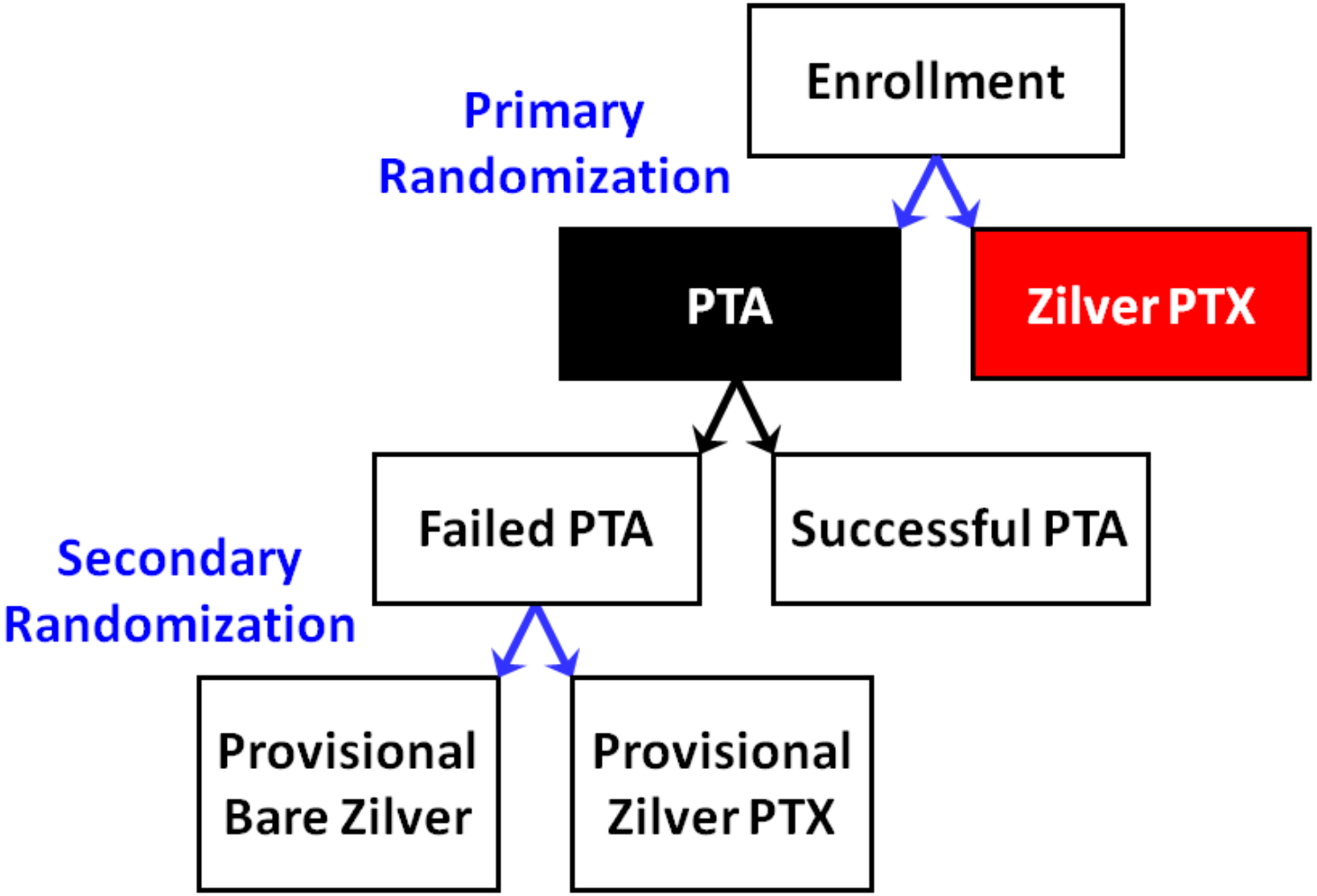
		PTA	Zilver PTX®	*P*-value
Lesions		251	247	
Normal-to-normal lesion length (mm)		63 ± 41	66 ± 39	0.35
Stenosed lesion length (mm)[1,2]		53 ± 40	54 ± 41	0.76
Diameter stenosis (%)[1]		78 ± 17	80 ± 17	0.44
Total occlusions		25%	30%	0.20
***De novo* lesions**		94%	95%	0.69
Lesion calcification[1]	**None**	5%	2%	< 0.01*
	Little	38%	26%	
	Moderate	22%	35%	
	Severe	35%	37%	

[1] Angiographic core lab assessment

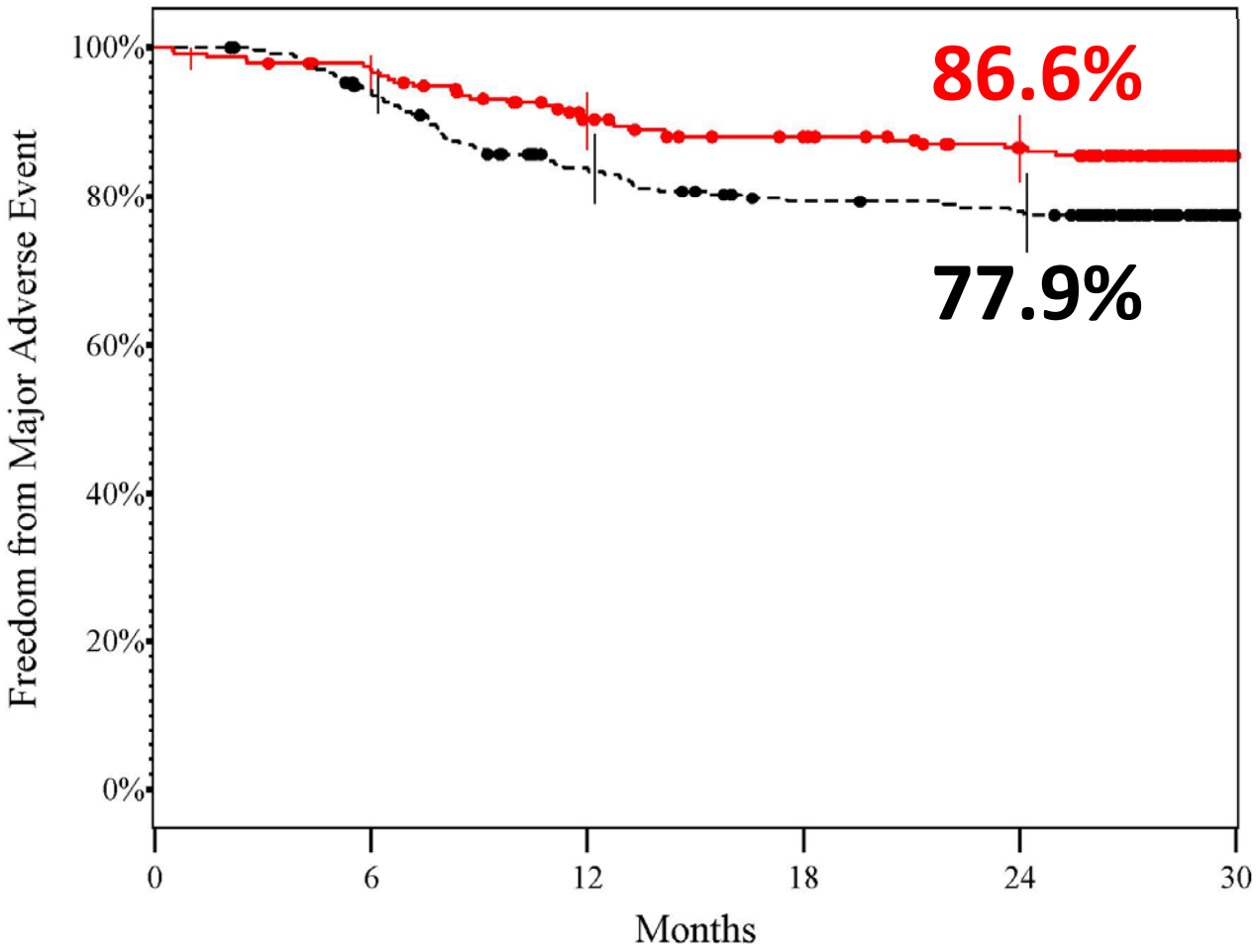
[2] Region with > 20% diameter stenosis

*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)

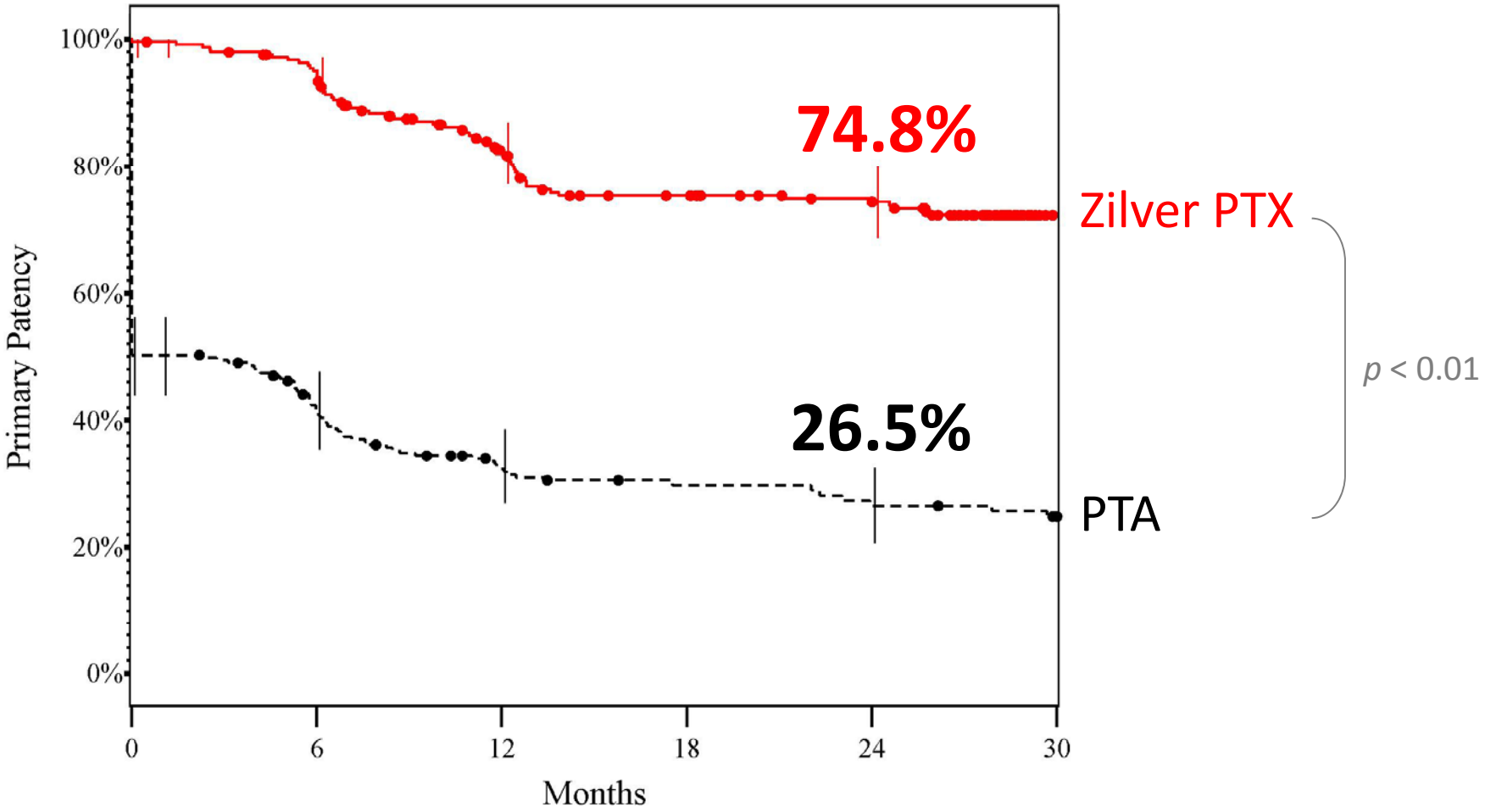
High Stent Integrity

- 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
- High stent integrity - four stent fractures
  - No associated adverse events

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

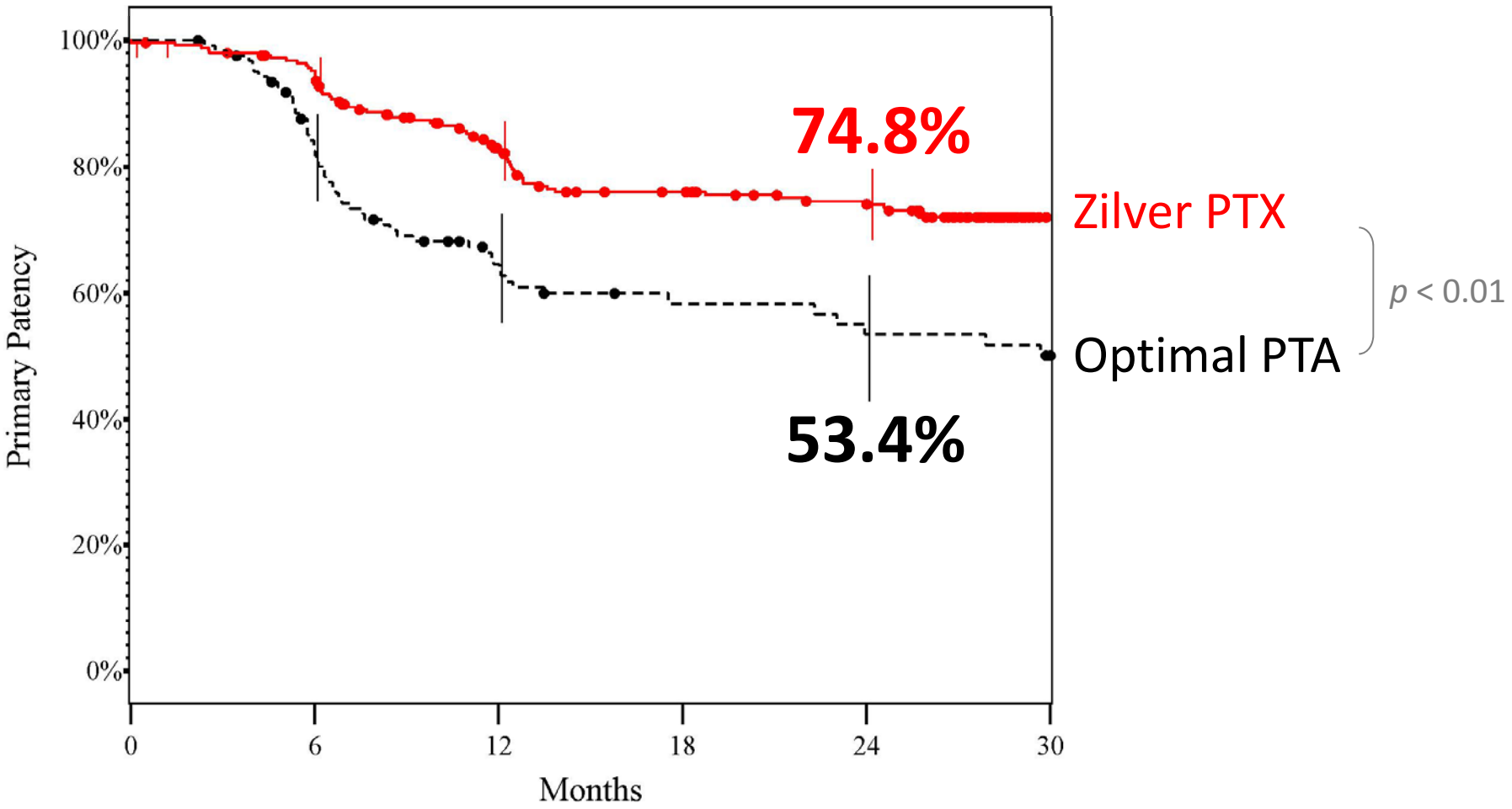
24-Month Effectiveness

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

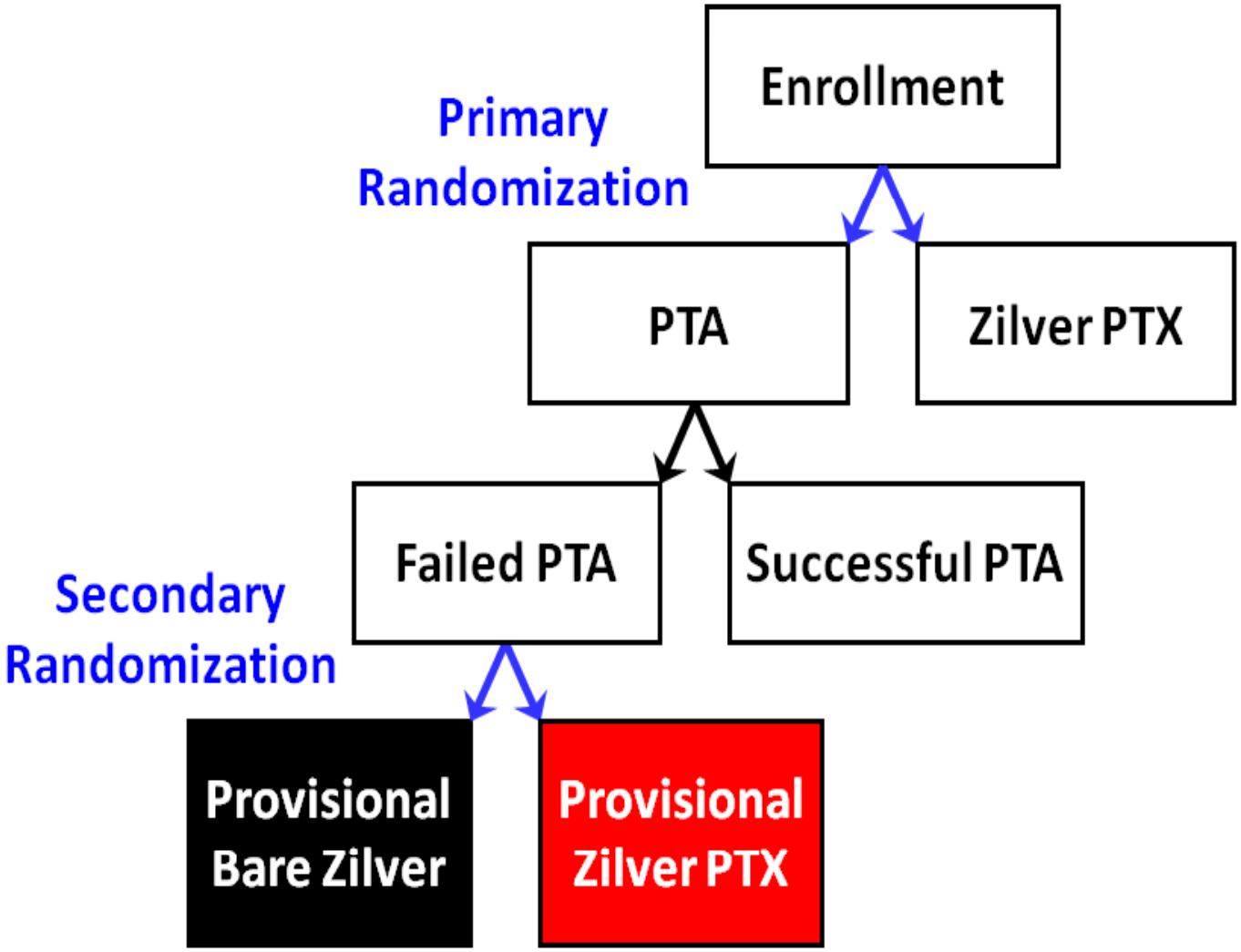


24-Month Secondary Effectiveness

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

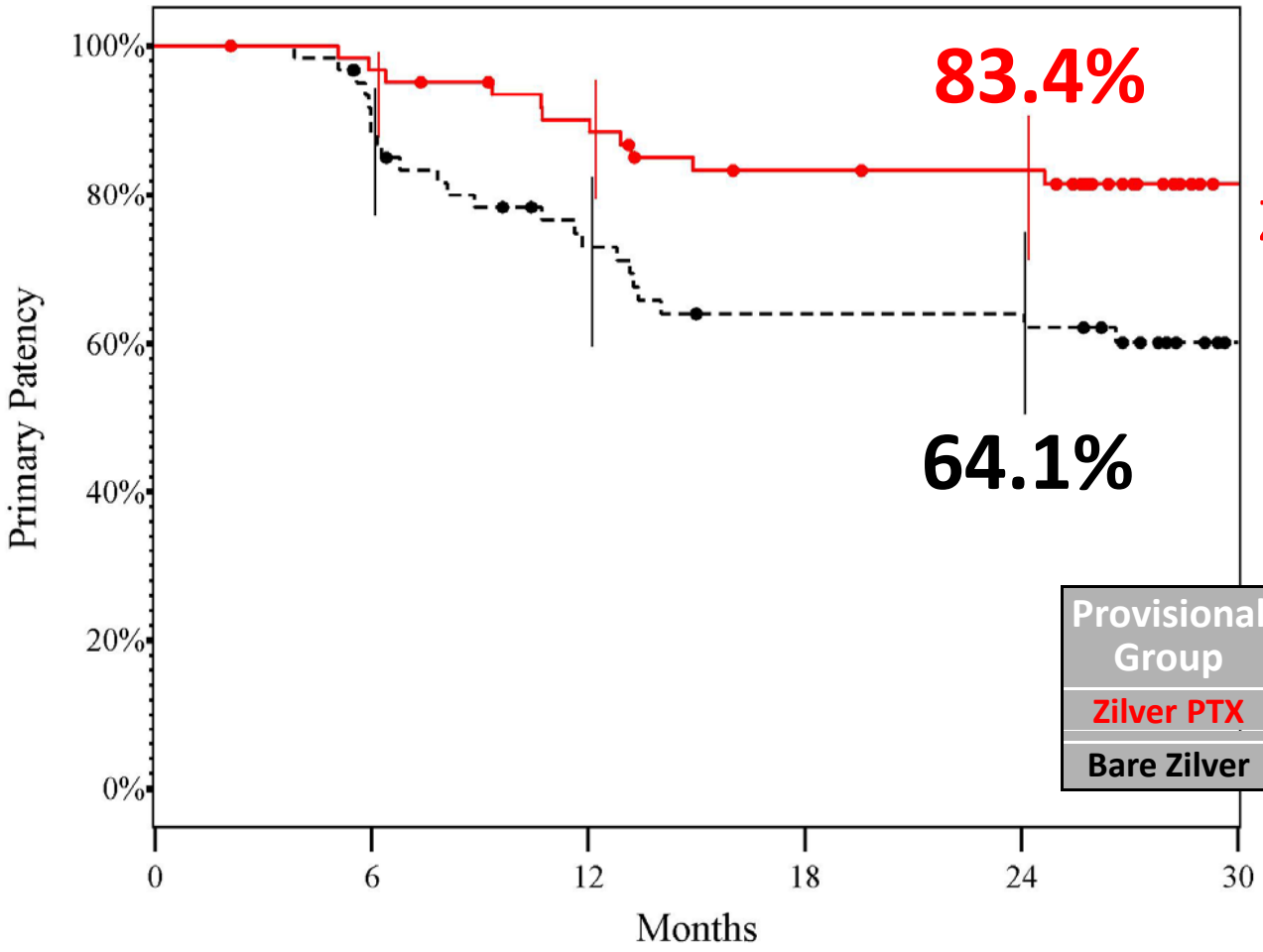


Provisional Zilver PTX vs Bare Metal Stent



Proven Drug Effect at 24-Months

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



Provisional Group	24-month Restenosis Rate	24-month Restenosis Reduction
Zilver PTX	16.6%	54%
Bare Zilver	35.9%	

Conclusions

- **24-month results** support sustained safety and effectiveness
  - Safety
    - Primary Zilver PTX significantly better patient safety than PTA ($p < 0.01$)
  - Effectiveness
    - Primary Zilver PTX patency of 74.8%
  - Proven Drug Effect
    - Provisional Zilver PTX patency (83.4%) significantly higher than provisional BMS patency (64.1%, $p < 0.01$)
    - PTX coating reduces 24-month restenosis rates by 54%