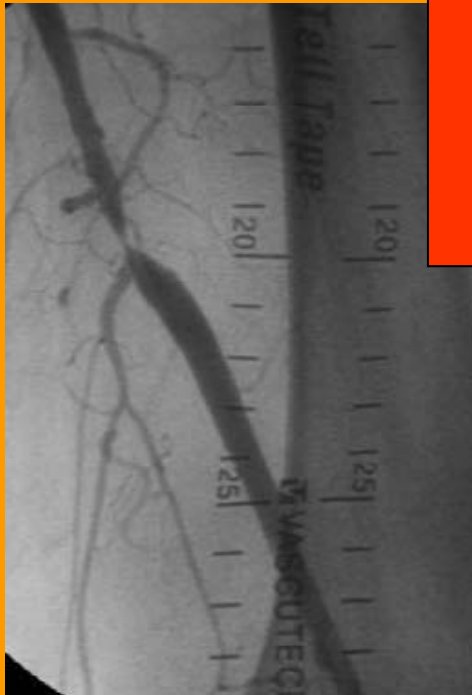


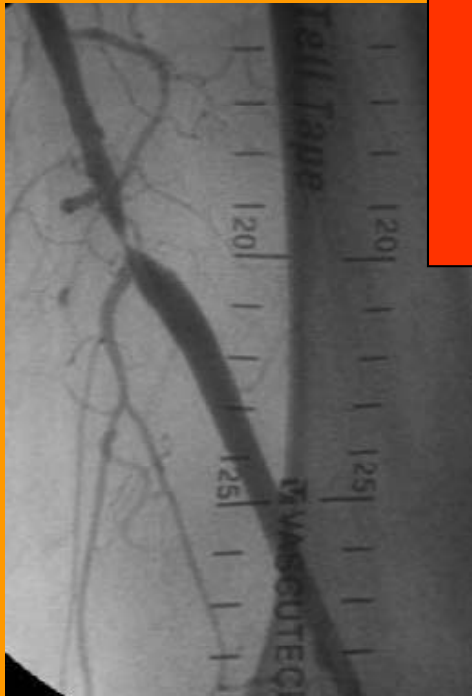
Will Drug-coated Balloons and Drug-coated Stents Shift the Paradigm for Superficial Femoral Artery Disease



Mark W. Burket, MD
University of Toledo Medical Center



Yes!!



Mark W. Burket, MD
University of Toledo Medical Center

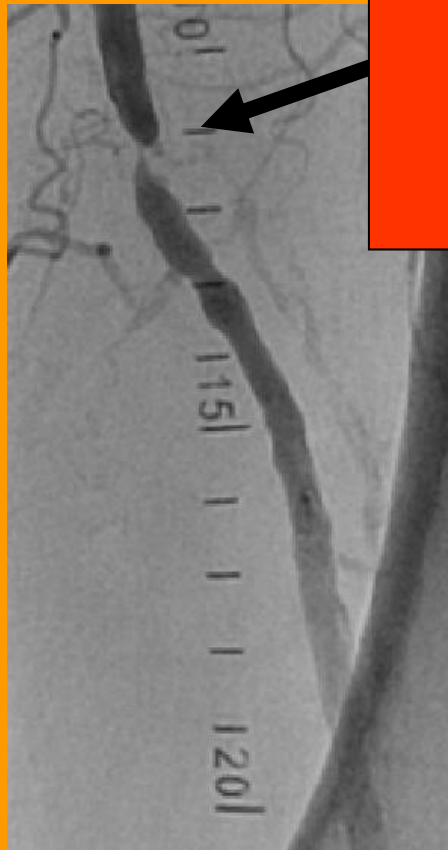




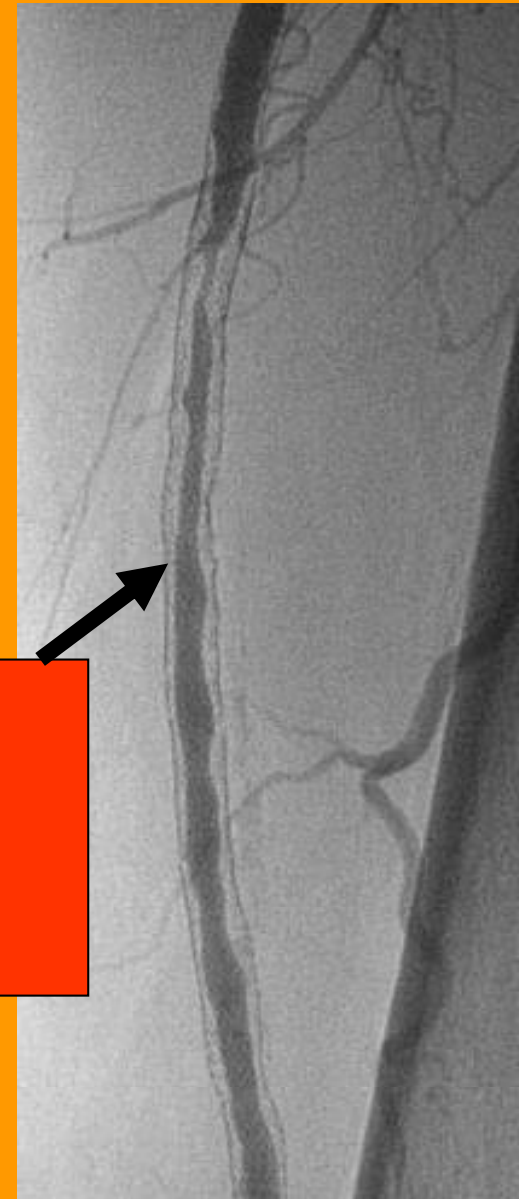
The New Game

- In which country do you practice?
- What is your budget?
- Can the patient comply with prolonged thienopyridine use?
- What is this person's risk of restenosis?
- What treatment combination(s) make sense?

Not all SFA disease is the same



Discrete lesion
Predictably good result
Inexpensive procedure
Reasonably durable



Diffuse in-stent restenosis
Expensive procedure
Questionable durability

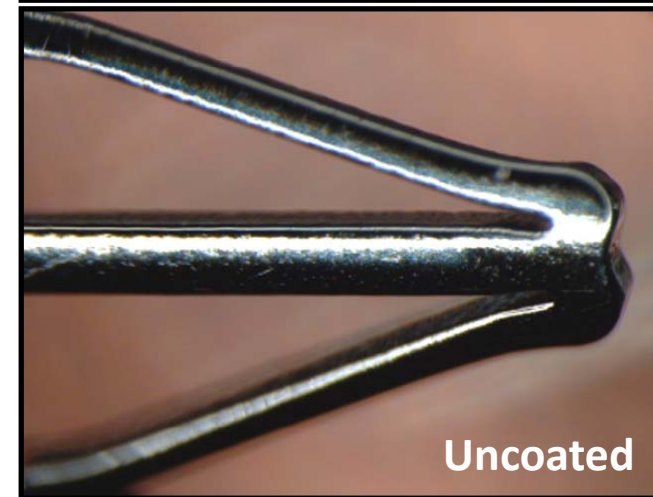
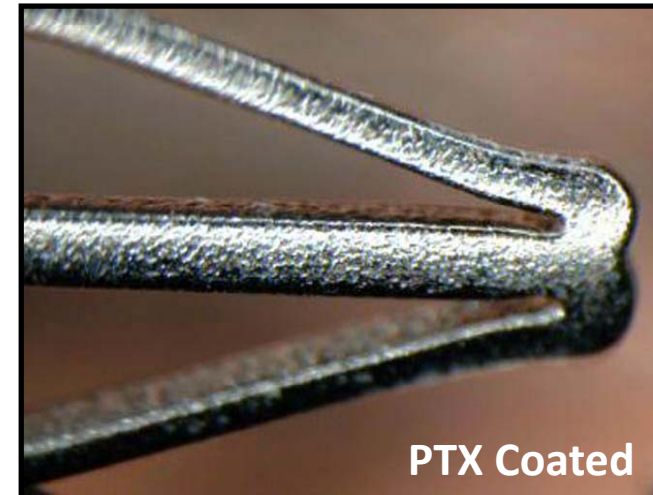
The Big Question in Percutaneous SFA Treatment

How can I keep it open?

Drug eluting balloons and drug eluting stents
are the best answer to this question in 2011.

Zilver[®] PTX[®] Drug-Eluting Stent

- Designed for the SFA
- Drug coating: paclitaxel only
 - No polymer or binder
 - 3 $\mu\text{g}/\text{mm}^2$ dose density



Randomized Clinical Trial Design

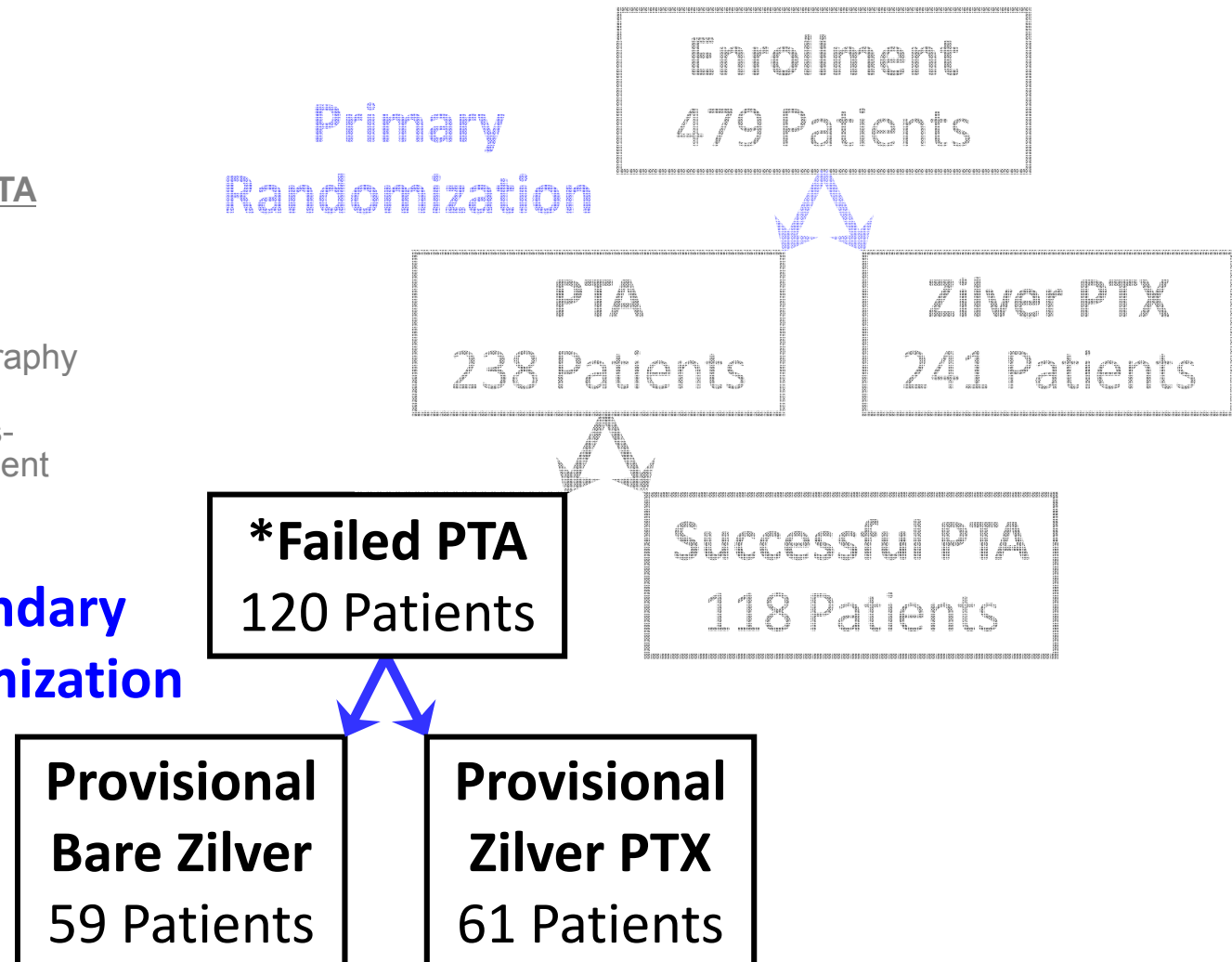
*** Failed PTA = Acute PTA**

Failure Due to:

- ≥ 30 %DS (including persistent, flow-limiting dissection) on arteriography
- OR -
- ≥ 5 mmHg mean trans-stenotic pressure gradient

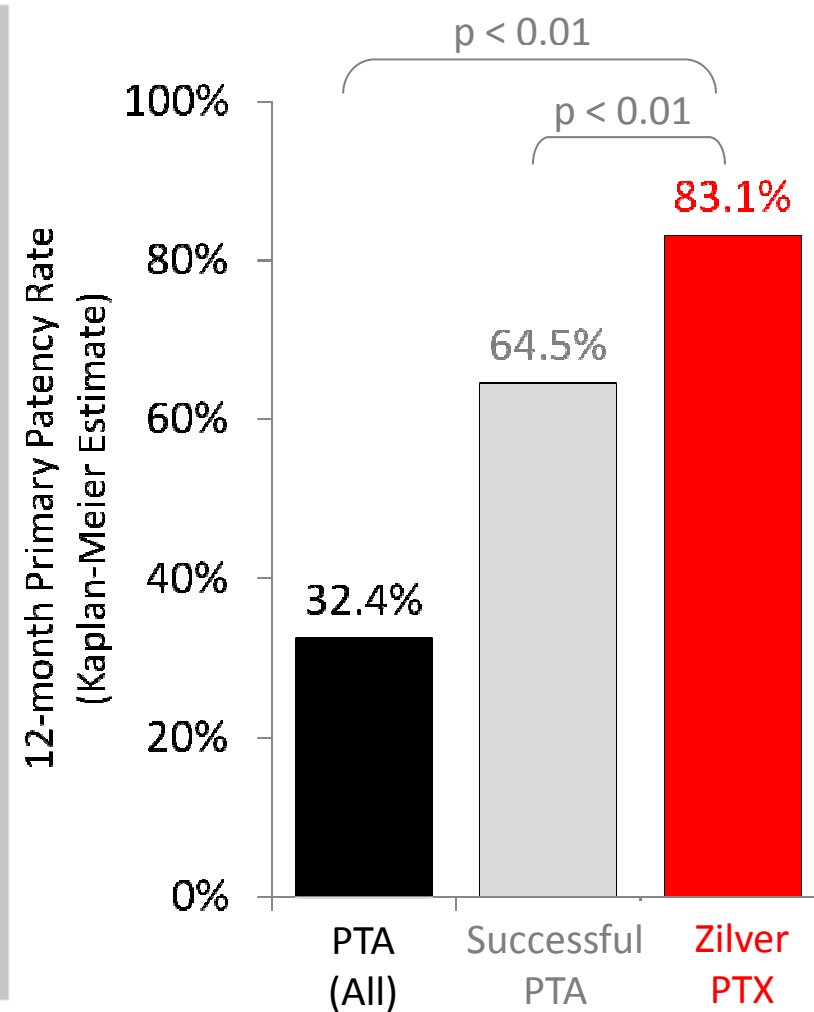
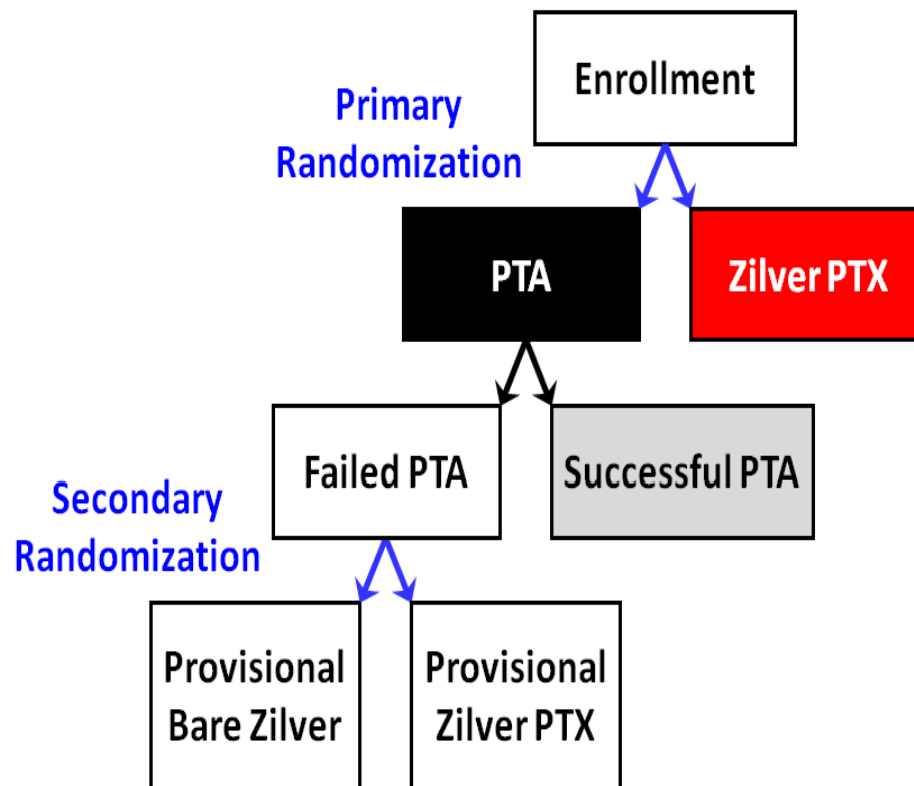
**Secondary
Randomization**

**Primary
Randomization**



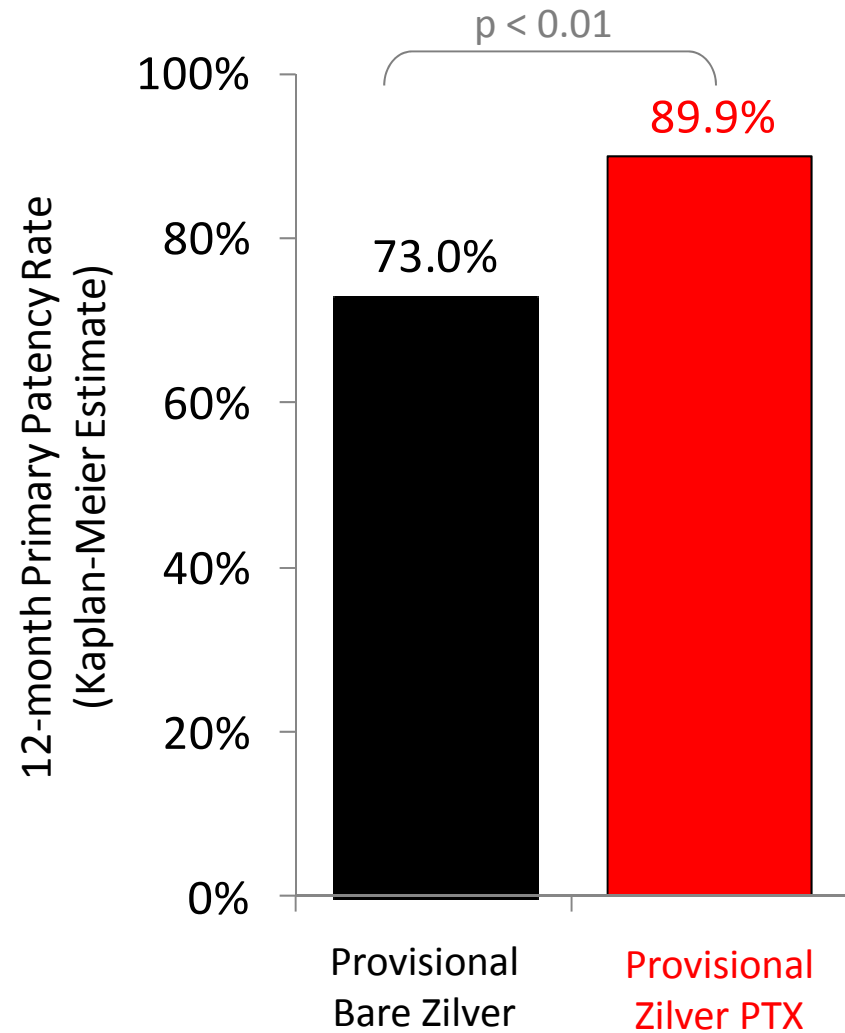
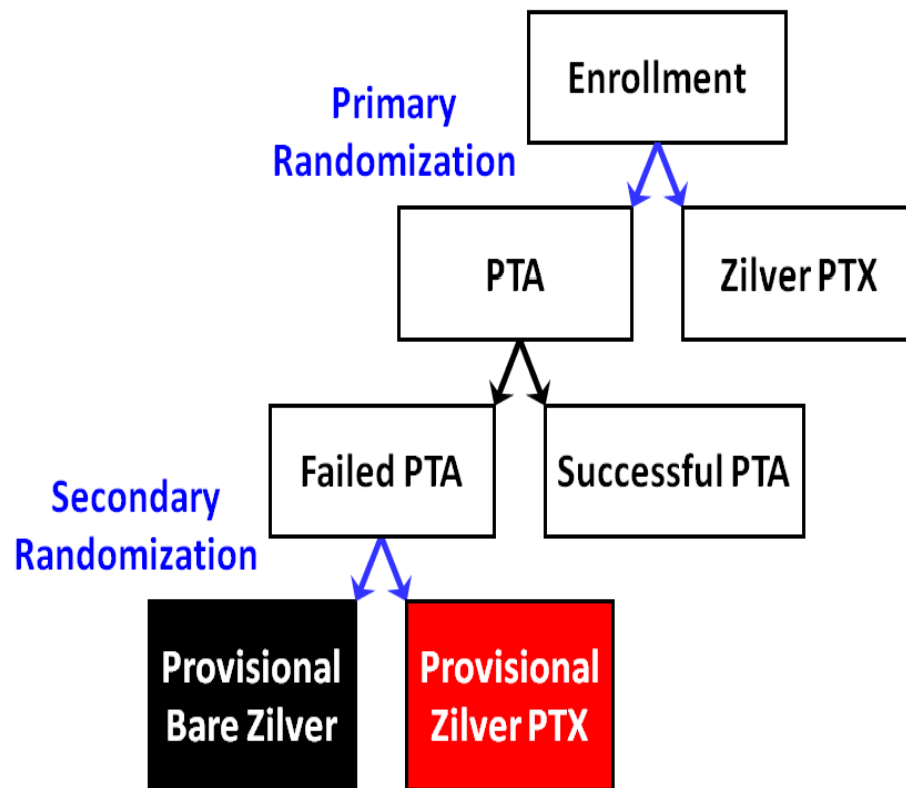
12-Month Effectiveness

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



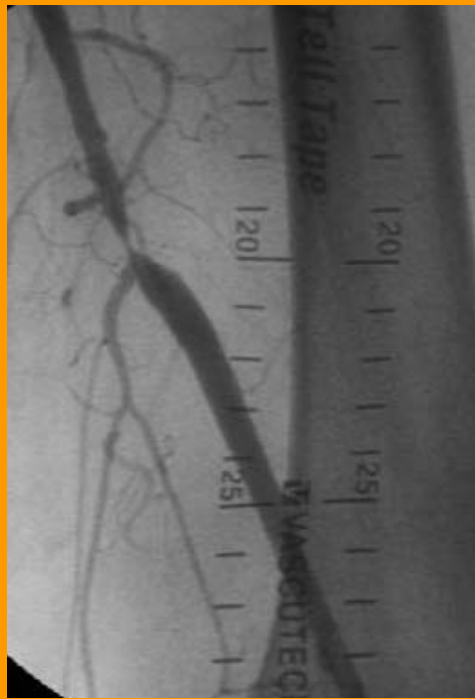
12-Month Paclitaxel Effect

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



Zilver PTX Registry

Real World SFA Disease



Zilver PTX Single-Arm Registry

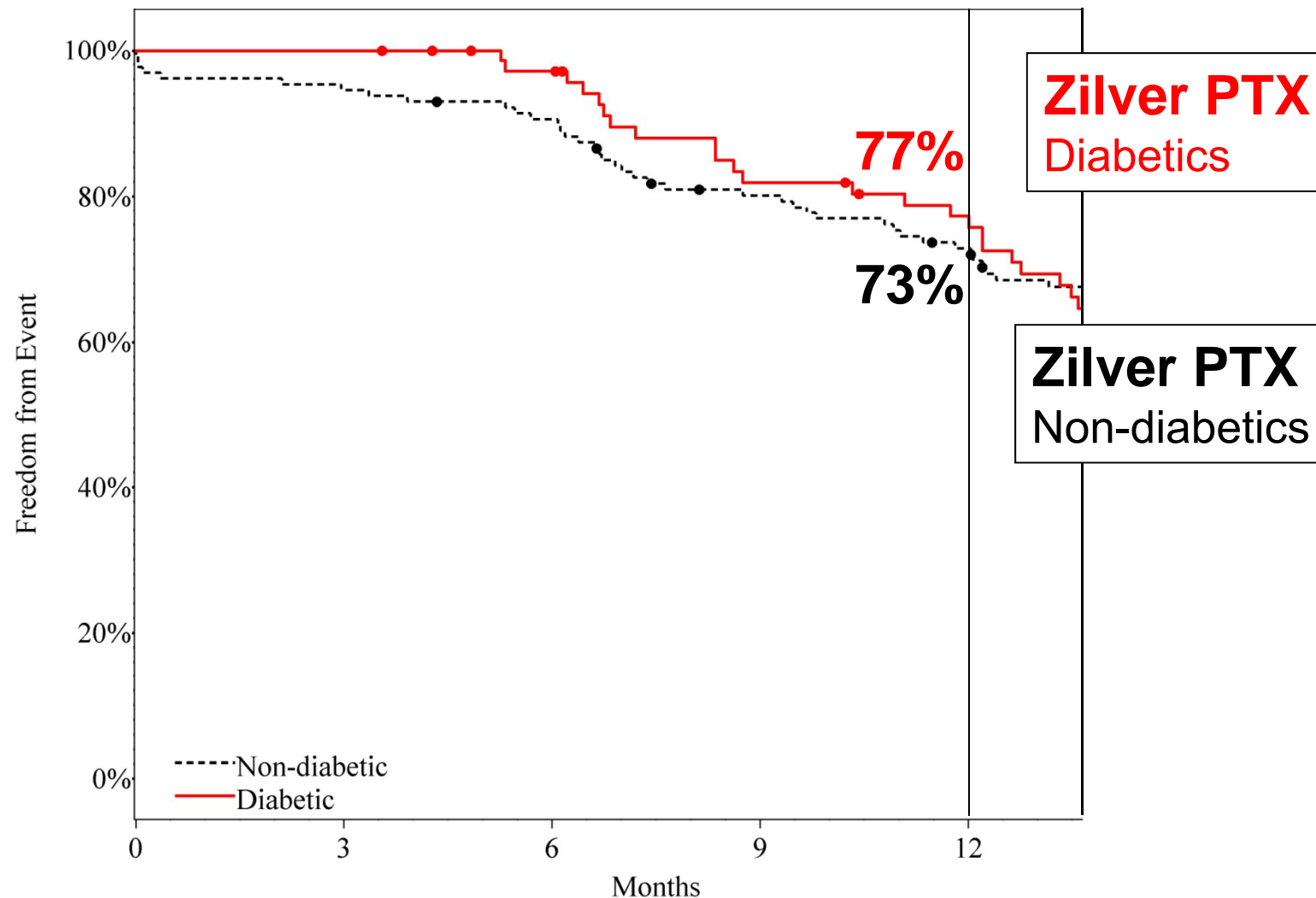
- No lesion length limit
- Up to 4 stents per patient
- Included restenosis, including in-stent restenosis
- Prospective, nonrandomized, multinational

Baseline Lesion Characteristics

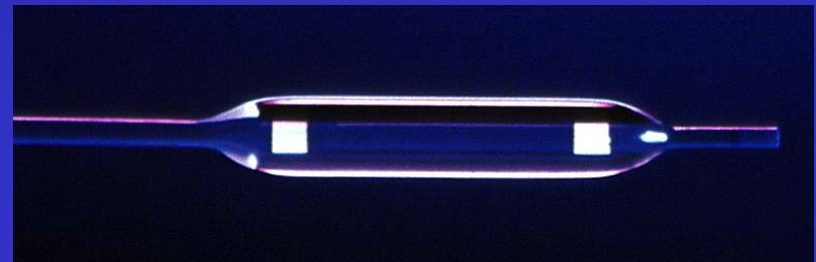
Lesions		900
Lesion length (mm)		100 ± 82
Diameter stenosis		85 ± 16%
TASC 2000 class	A	26%
	B	29%
	C	25%
	D	14%
Lesions > 7 cm		48%
Lesions > 15 cm		22%
Total occlusions		38%
Restenosis (all)		24%
In-stent restenosis (ISR)		14%

Zilver PTX in long lesions (> 15 cm)

Primary Patency (PSVR < 2.5)



Is the stent really necessary?



New England Journal, February 14, 2008

Gunnar Tepe, MD

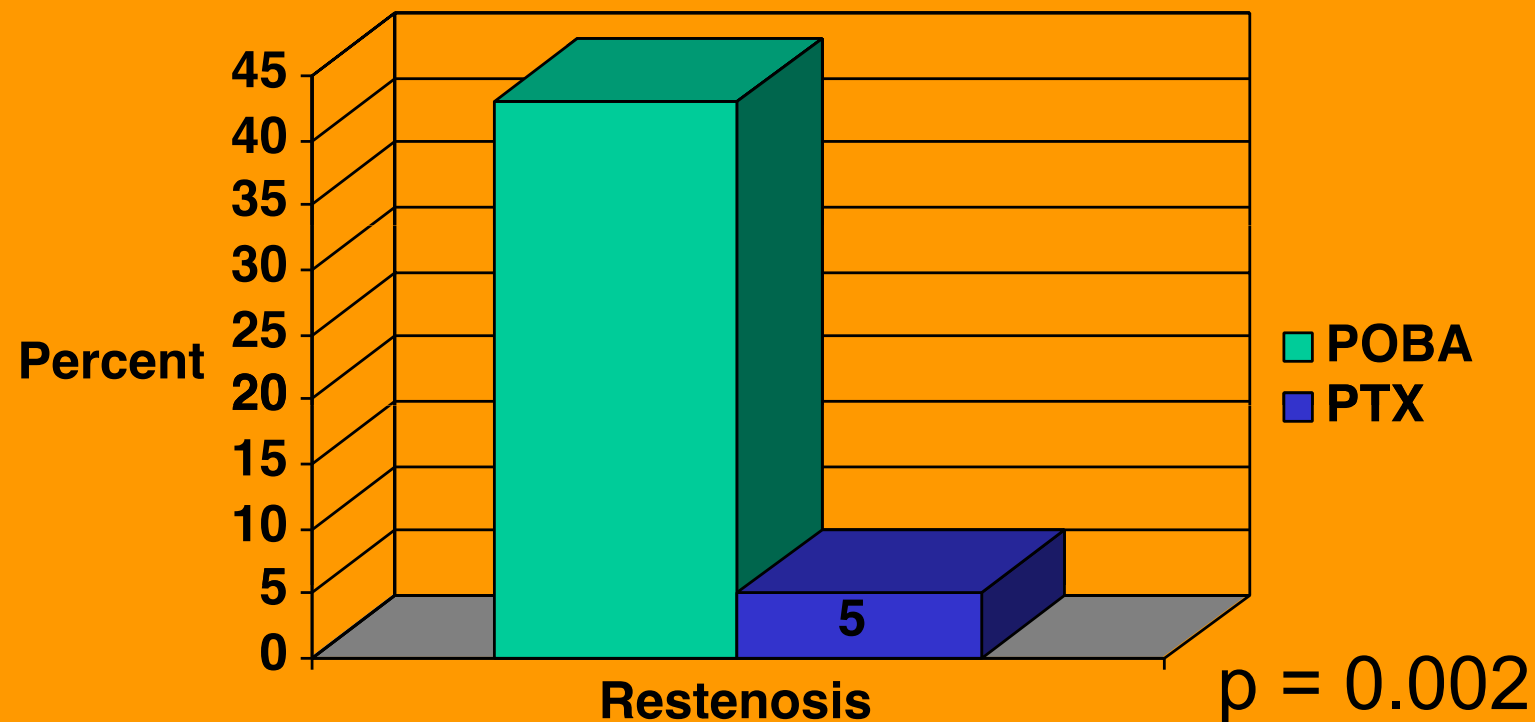
- Hypothesis: short-term exposure to paclitaxel can inhibit cell growth
- 2004: PTX coated balloon reduces ISR in porcine model
- 2006: 52 patients with coronary ISR randomized to POBA vs PTX coated balloon

Scheller Circulation 2004;110:810

Scheller N Engl J Med 2006;355:2113

6 Month Binary Restenosis

(second restenosis in coronary ISR)



Scheller N Engl J Med 2006;355:2113

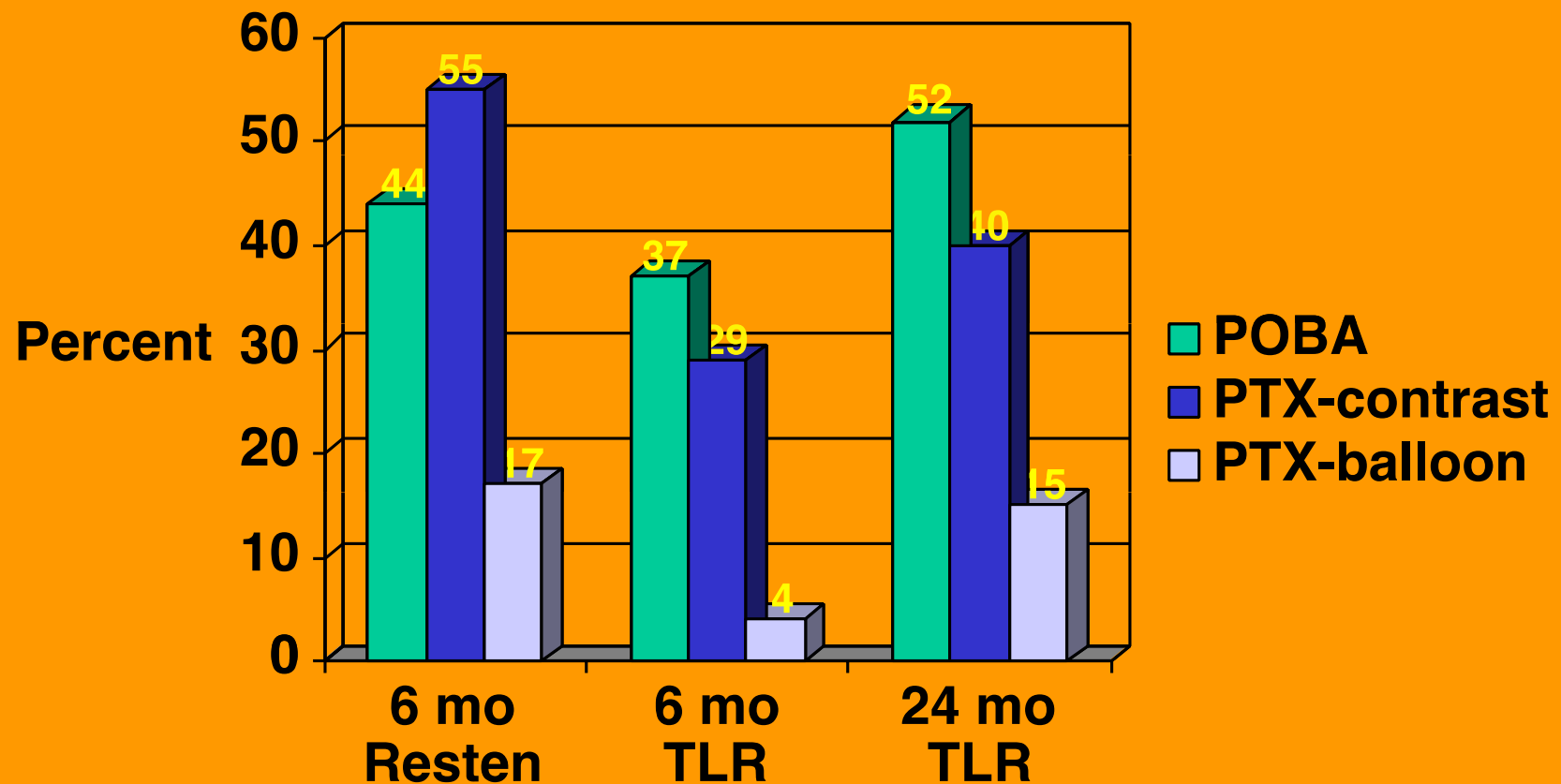
New England Journal, February 14, 2008

Gunnar Tepe, MD

- 154 patients with femoropopliteal disease
- 3 arm study
 - POBA without PTX
 - PTX in contrast medium
 - PTX coated balloons
- Balloons coated with 3 μg per sq mm

Tepe N Engl J Med 2008;358:689

Outcomes After PTX Treatment



Tepe N Engl J Med 2008;358:689



Pre Post
 PTA 6 Mo



Pre Post
 PTA 6 Mo

Tepe N Engl J Med 2008;358:689-99

A More Complex Chess Game

- Drug eluting balloons and drug eluting stents: most well-established benefit
- The lesson of history: FDA approval of coronary DES



The Impact of Country

- EU: approval of Zilver PTX and drug eluting balloons
- US: likely first approval of Zilver PTX
- With identical approval, application will vary
 - Reimbursement structures
 - Cultural and legal climates



The Impact of Cost

- Price points will determine usage
- Available stent (and balloon) length will determine usage
- Patients with most to gain will have greatest financial burden



A More Complex Chess Game

- Simple lesions: POBA
- Thienopyridine contraindications
 - POBA or bare nitinol stent
- Moderate disease
 - POBA with provisional PTX stent
 - PTX balloon with provisional bare nitinol stent
 - (or non PTX options only)
- Diffuse disease, restenosis
 - PTX stent(s)
 - PTX balloon with provisional stent
 - Mix of PTX treatment and POBA





The Attack on Restenosis

- Radiation therapy
- Photoactivation
- Cryotherapy
- Atherectomy
- Nitinol stents
- Stent grafts
- Drug eluting stents
- Drug eluting balloons

Paclitaxel Coated Balloons

- Commercially available in Europe
- Clinical trial site selection in US
 - LEVANT 2 (Lutonix)
 - RIVER (Medrad Interventional)

Effective Attacks

- Radiation therapy
- Nitinol stents
- Stent grafts
- Drug eluting stents
- Drug eluting balloons

Available* Attacks

- Nitinol stents
- Stent grafts
- Drug eluting stents
- Drug eluting balloons

* Outside US

Schillinger



- Mean treated length 13 cm
- 32% randomized to PTA received stents
- 12 month MWD and ABI significantly better with stents
- Benefit also in FAST and RESILIENT



Zilver PTX Randomized Trial

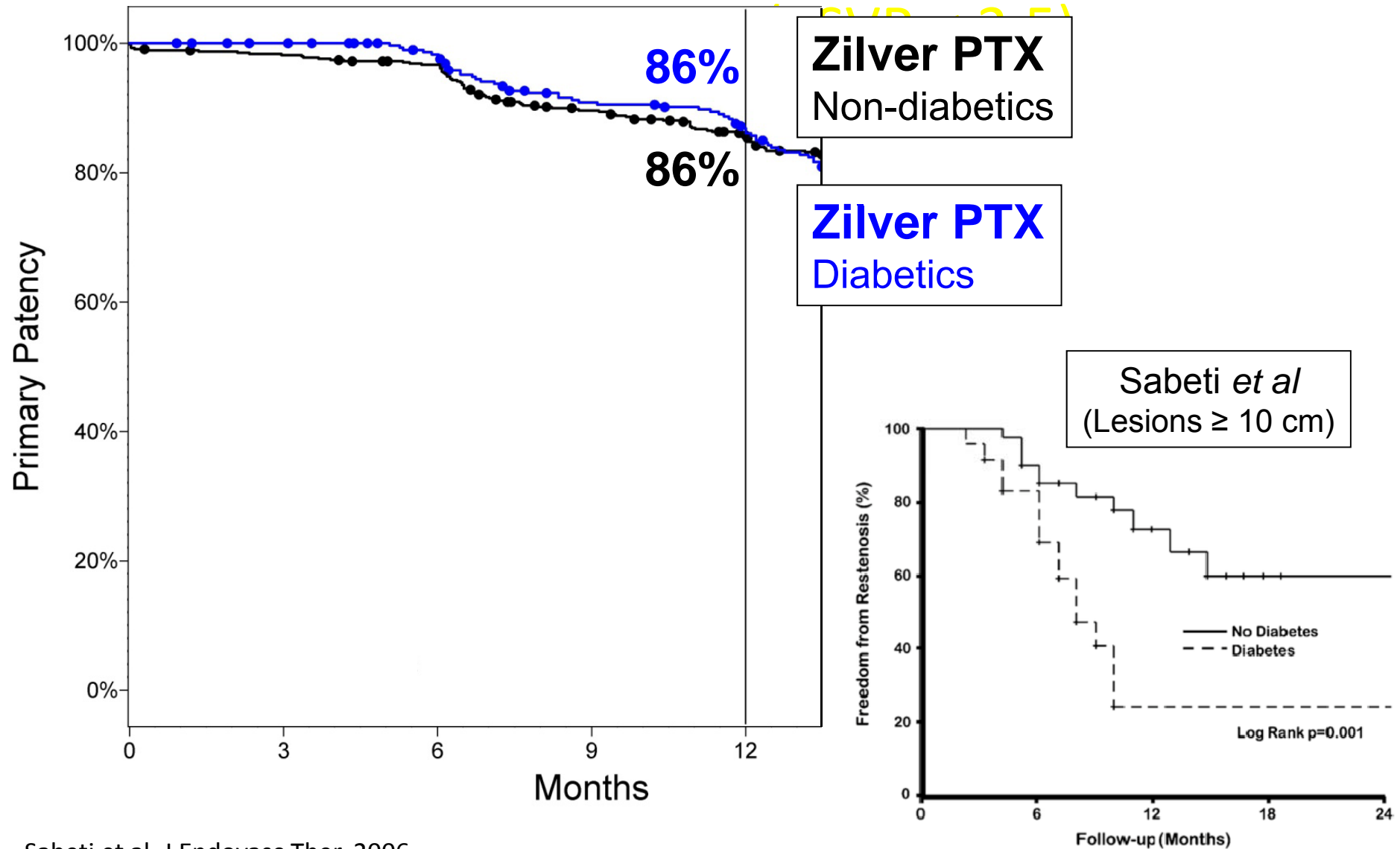
- Rutherford classification ≥ 2
- Reference vessel diameter 4-9 mm
- Lesion length ≤ 14 cm
- *De novo* or restenotic lesions (no in-stent restenosis)

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)***

Zilver PTX stenting is effective in diabetics



Sabeti et al, J Endovasc Ther, 2006

Zilver PTX Patency Compared to BMS

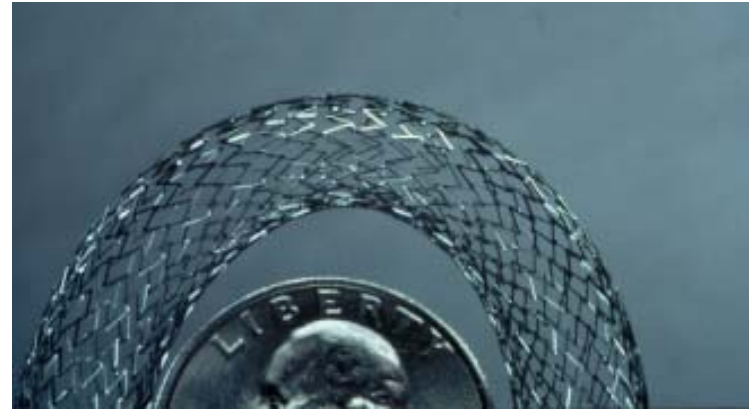
Matched Zilver PTX Cohort: matched inclusion/exclusion criteria and PSVR threshold for each published study



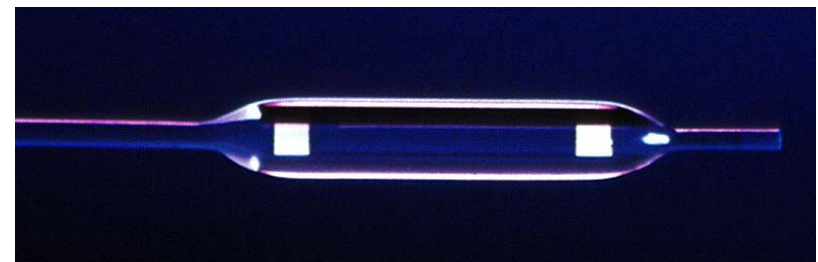
Zilver PTX stenting increases 12-month patency rates relative to BMS published literature

Nitinol Stents

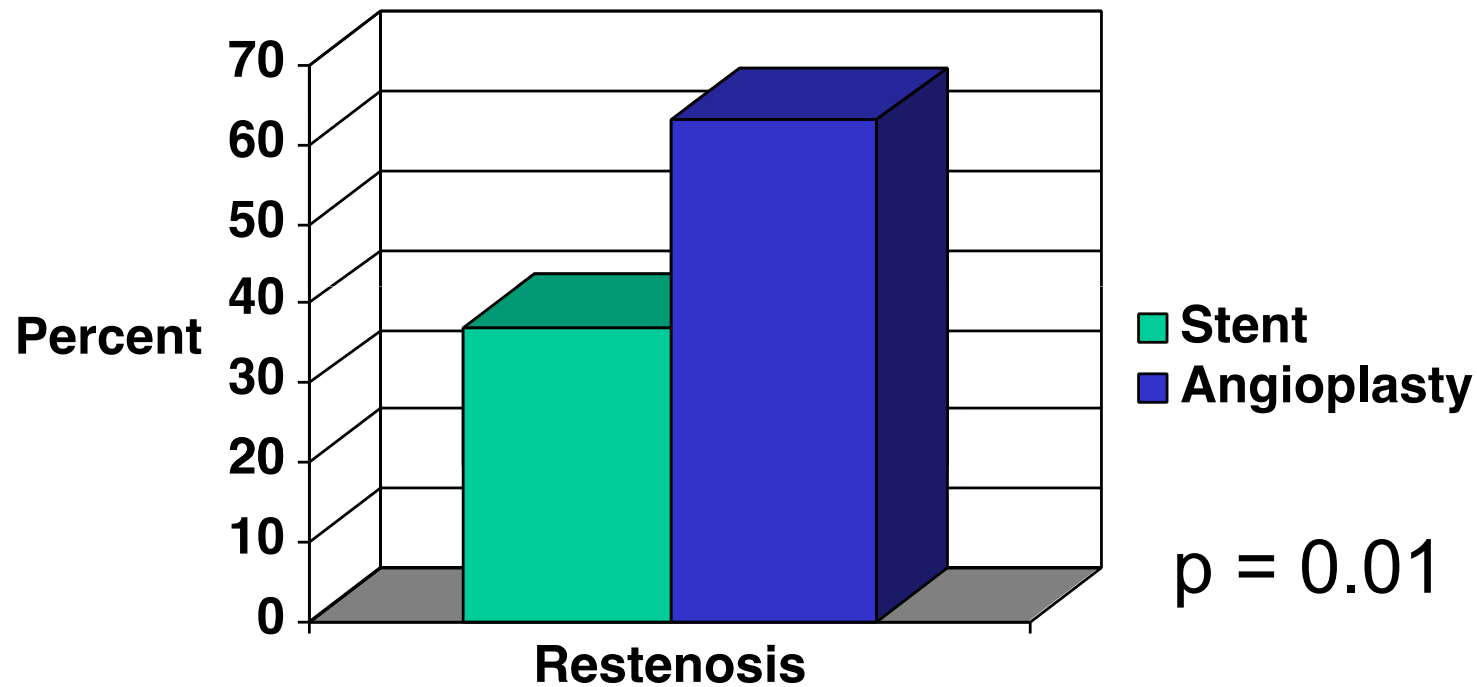
to reduce restenosis



- Prospective series with nitinol encouraging
- Schillinger randomized 104 patients
 - 51 primary stent (Dynalink or Absolute)
 - 53 angioplasty



12 Month Restenosis by Duplex



Benefit also in FAST and RESILIENT

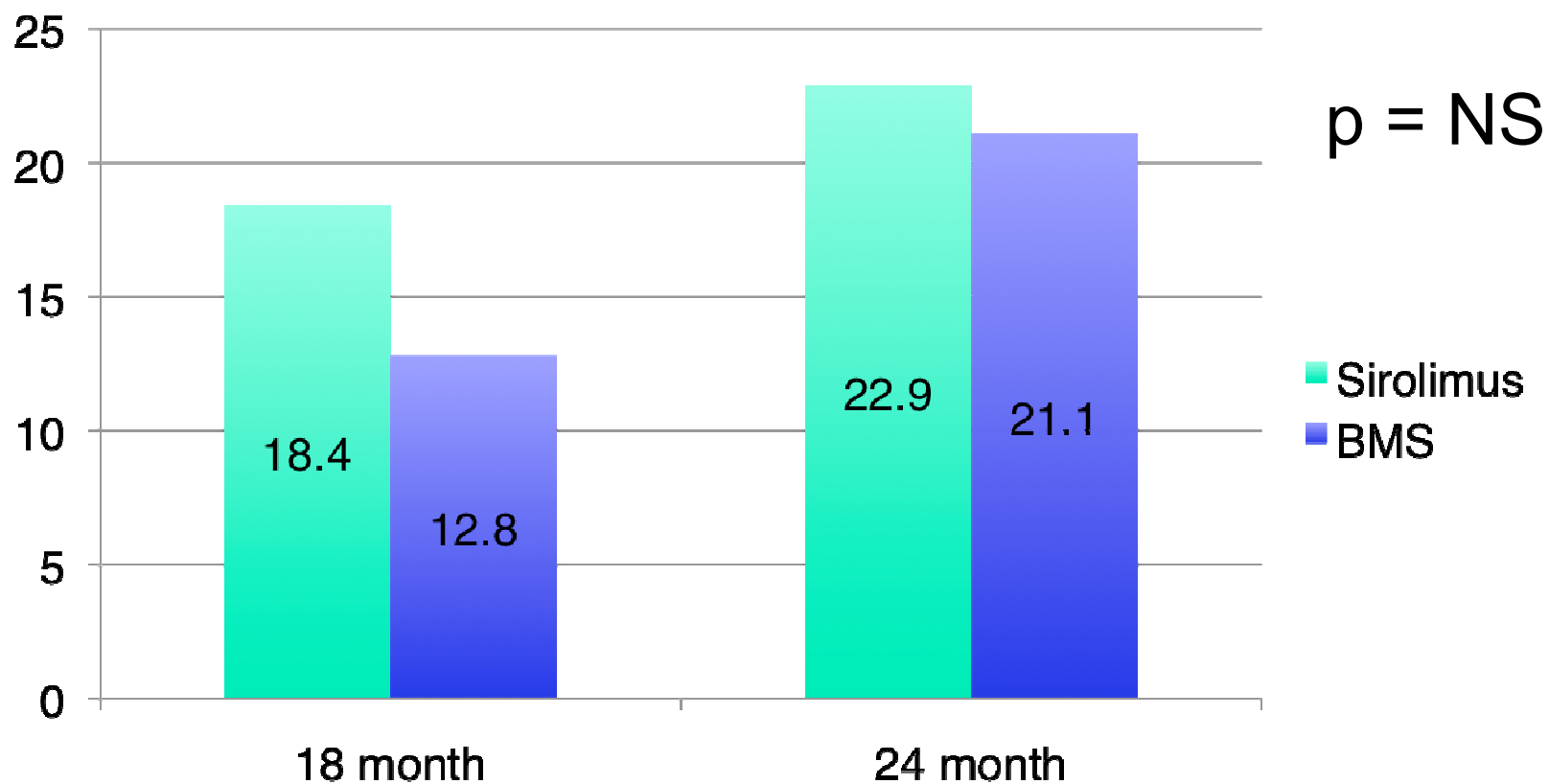
Drug Eluting Stent Disappointments

- SIROCCO
 - SMART + polymer + sirolimus
- STRIDES
 - Dynalink-E + polymer + everolimus

SIROCCO

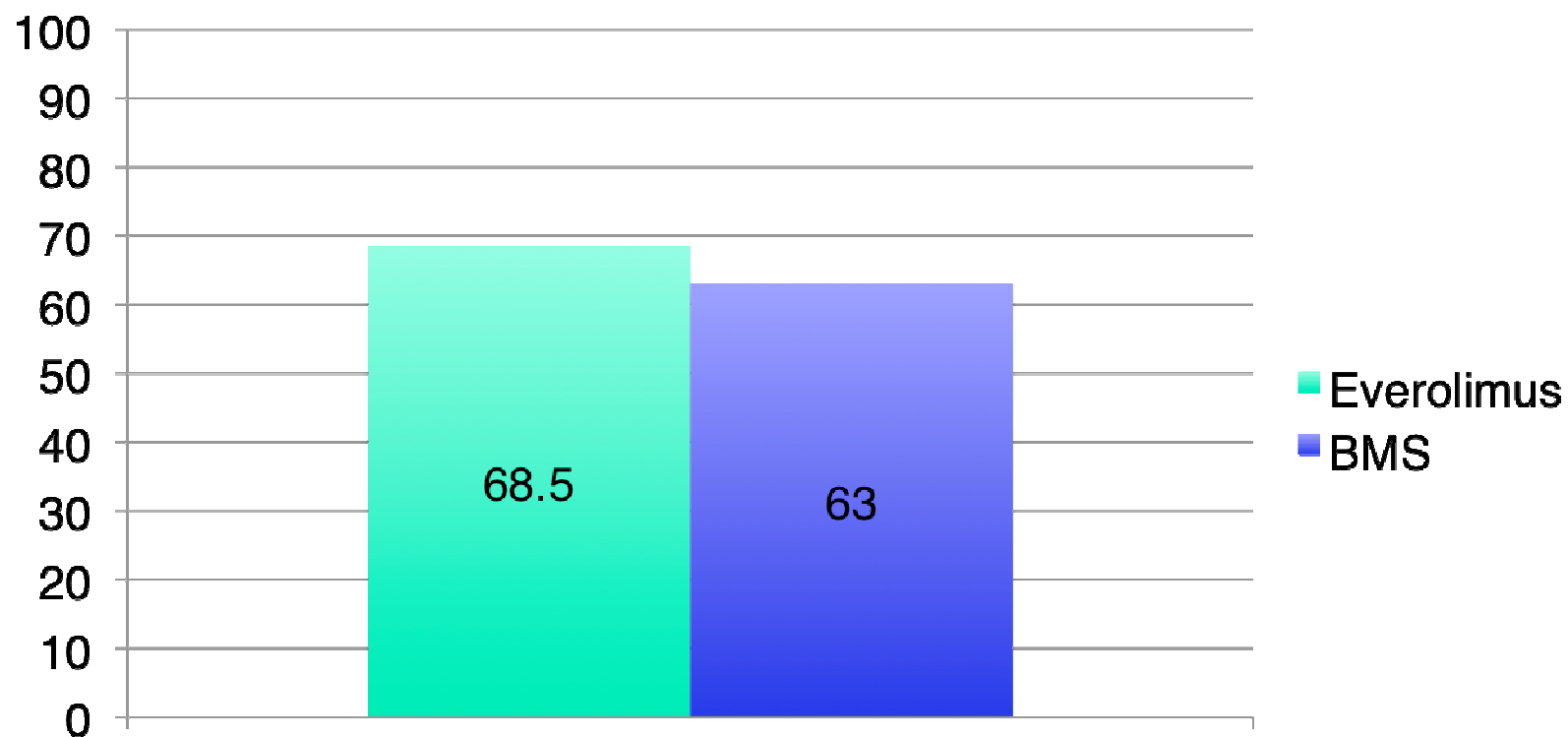
In-stent Restenosis

(by duplex ultrasound)



STRIDES

12 Month Patency (duplex ultrasound)



SIROCCO and STRIDES

what went wrong?

- “imus” drugs?
- Wrong elution rate?
- Wrong dose?
- Wrong stent?
- Polymer?

Polymer Breakdown

