Drug-Eluting Stents in the SFA

(Zilver PTX or Eluvia)

Why Not Now?

What is Needed for the Future?

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THE UNIVERSITY OF TOLEDO
HEART AND VASCULAR CENTER

Controversies in Cardiovascular Medicine

Are Drug-Eluting Stents Now the Default Strategy for Superficial Femoral Artery Intervention?

Drug-Eluting Stents Are the Default Strategy for Superficial Femoral Artery Intervention Now

Mark W. Burket, MD

Drug-eluting stents (DES) are the default strategy for superficial femoral artery (SFA) intervention in 2015 because they have been evaluated in a large number of patients over a long follow-up period with outcomes superior to other treatment options. No other therapy can make that claim.

Response by Garcia on p 329

The SFA and the contiguous popliteal artery constitute the femoropopliteal (FP) segment, which is among the human body's most hostile vascular environments. It is extremely

options is broad, ranging from exercise therapy as the least intrusive option, to bypass surgery as the most intrusive.[4] In between these extremes lies a seemingly endless variety of endovascular options.

Less Is Less

Perhaps the most universally available and cheapest treatment strategy for symptomatic lower extremity vascular disease is exercise therapy. Supervised exercise programs are more effective than unsupervised and have received a class I recommendation from the American College of Cardiology and the American Heart Association.[5,6] The requirement

whose ambulatory goals include thousands of meters per day for occupational or recreational pursuits.

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Drug-Eluting Stents Are the Default Strategy for Superficial Femoral Artery Intervention Now

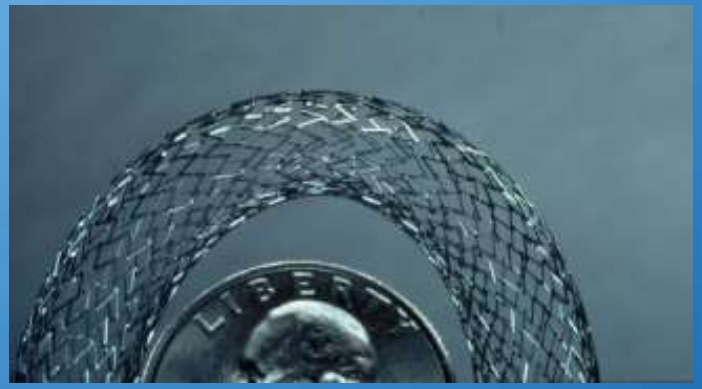
Circulation. 2016;133:320-329.

Drug-Eluting Stents

- Randomized controlled trial data with 5 year follow-up
- High patient enrollment numbers
- Randomized comparison to:
  - Balloon angioplasty
  - Bare nitinol stents
  - Provisional stenting

No Longer in the Race

- Simple balloon angioplasty
- Bare metal nitinol stents



Appealing…But Unproven
Atherectomy

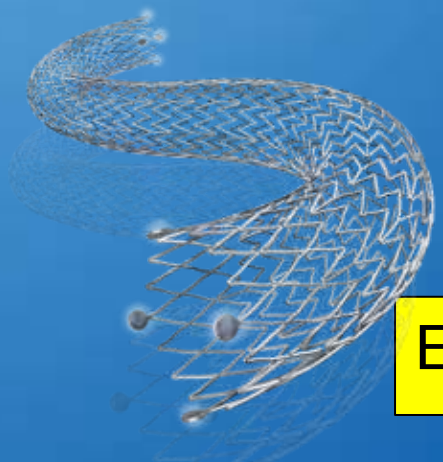
- “Nothing left behind”
- Randomized trial data lacking
- Initial equipment cost 3X DES

Appealing…And Proven

Drug-Eluting Stents

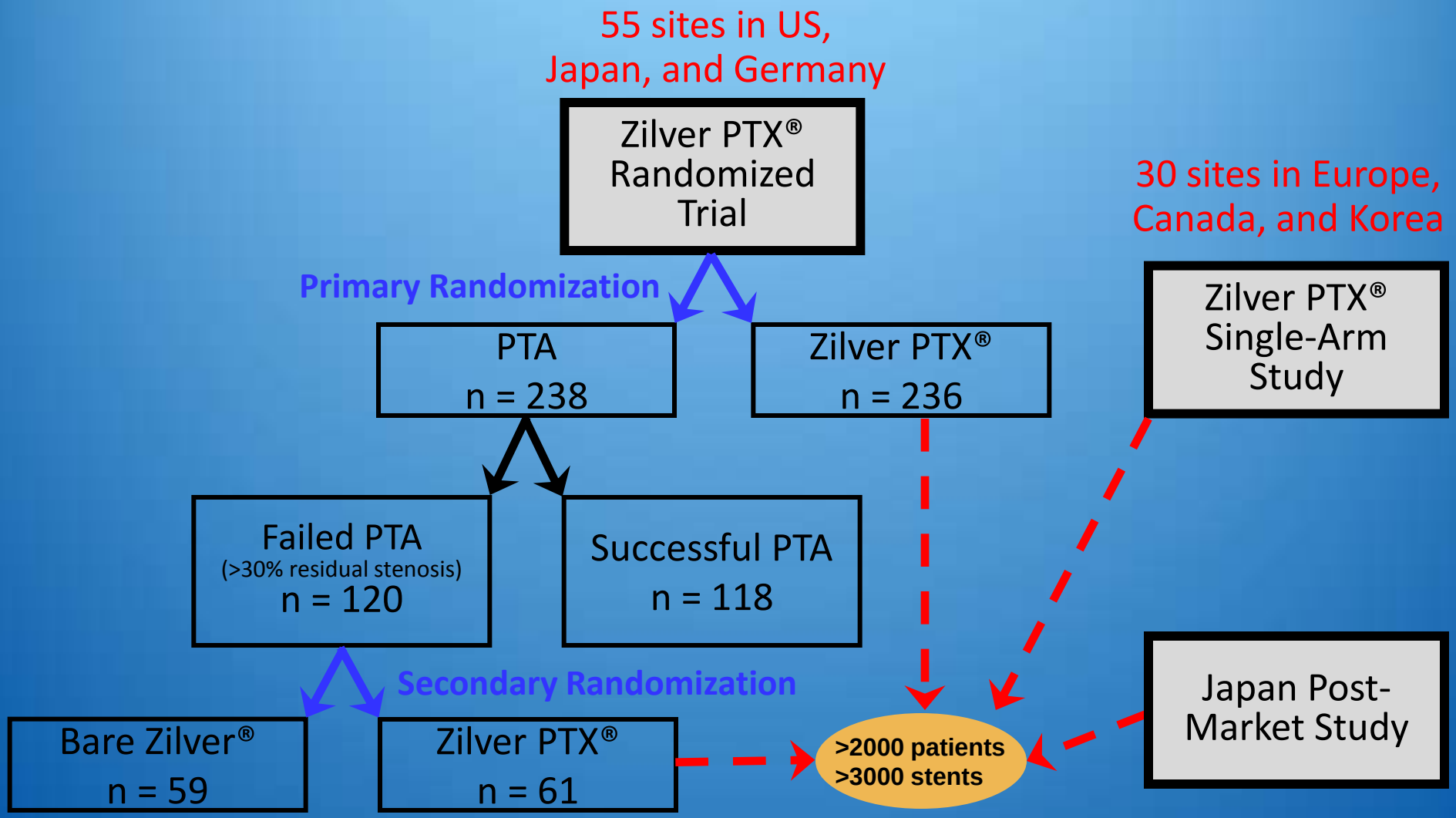
- Zilver PTX
  - Cook Medical
  - US and CE approval (> 50 countries)
- Eluvia
  - Boston Scientific
  - CE approval 2016

Zilver PTX



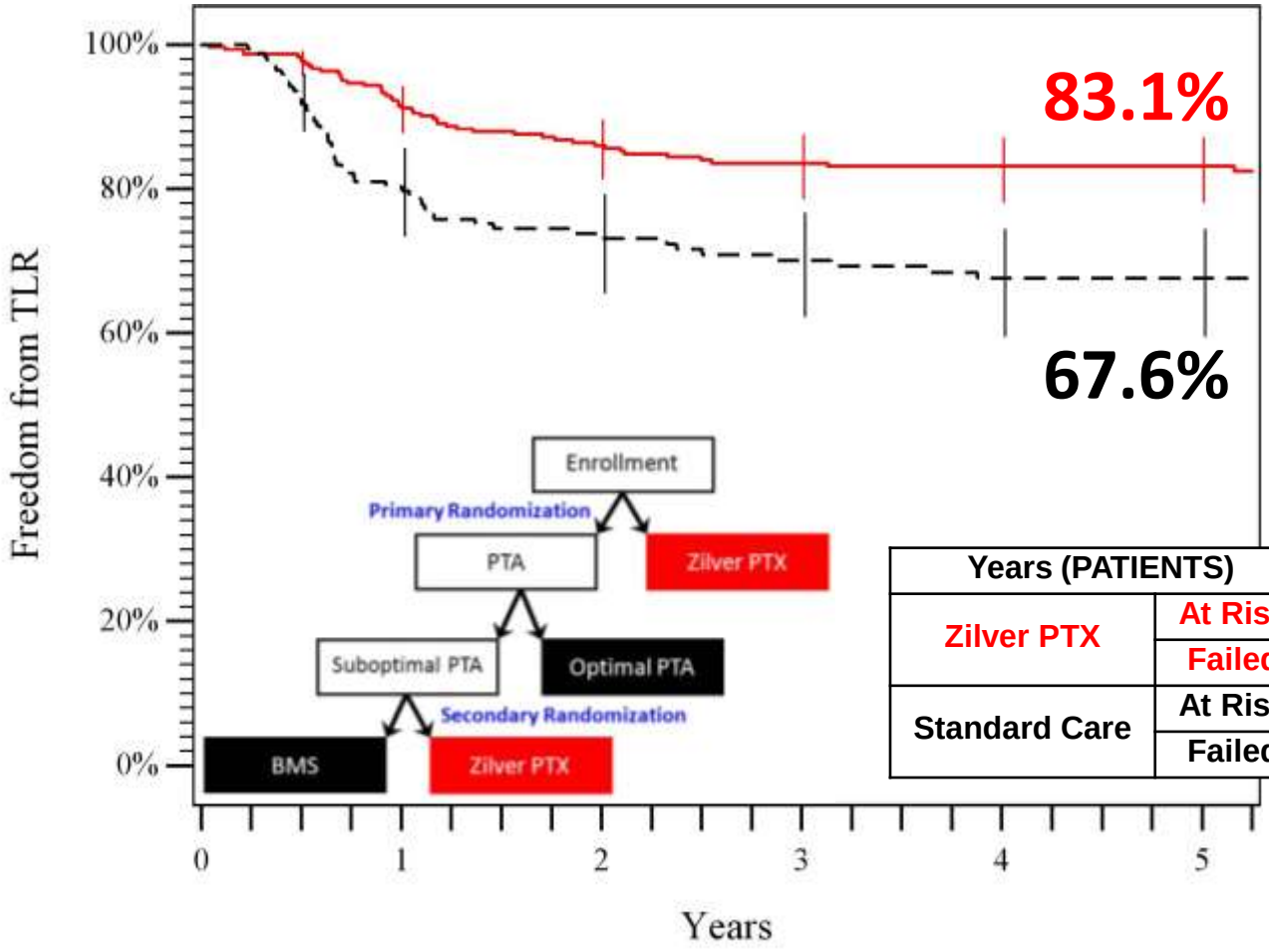
Eluvia

Multiple Zilver PTX® Clinical Studies



5-year Freedom from TLR

Zilver PTX vs. Standard Care



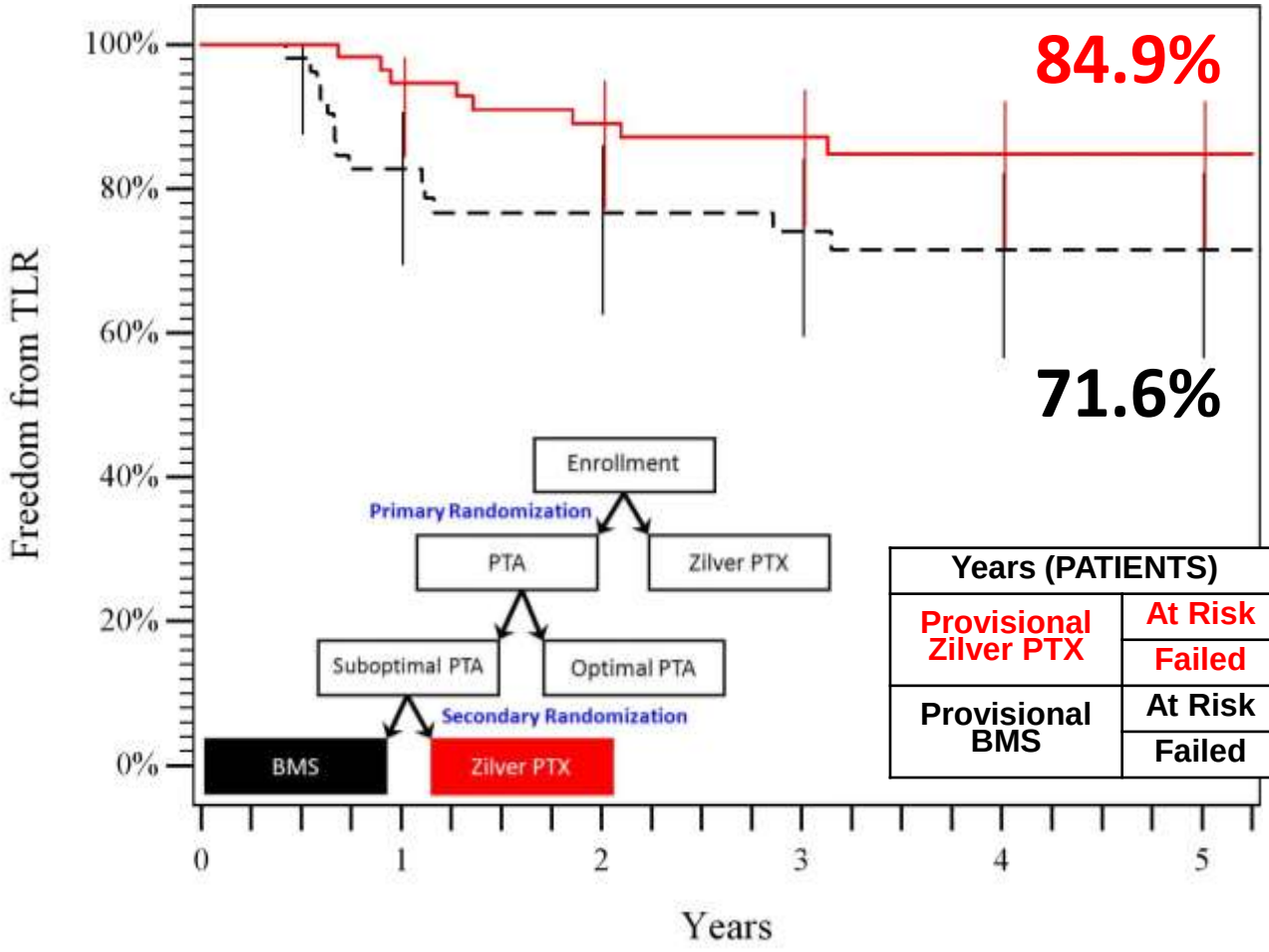
$p < 0.01$
log-rank

Years (PATIENTS)		0	1	2	3	4	5
Zilver PTX	At Risk	305	260	220	187	164	133
	Failed	0	25	40	46	47	47
Standard Care	At Risk	172	125	106	88	78	69
	Failed	0	33	44	48	51	51

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

5-year Freedom from TLR

Provisional Zilver PTX vs. BMS



Provisional Zilver PTX

Provisional BMS

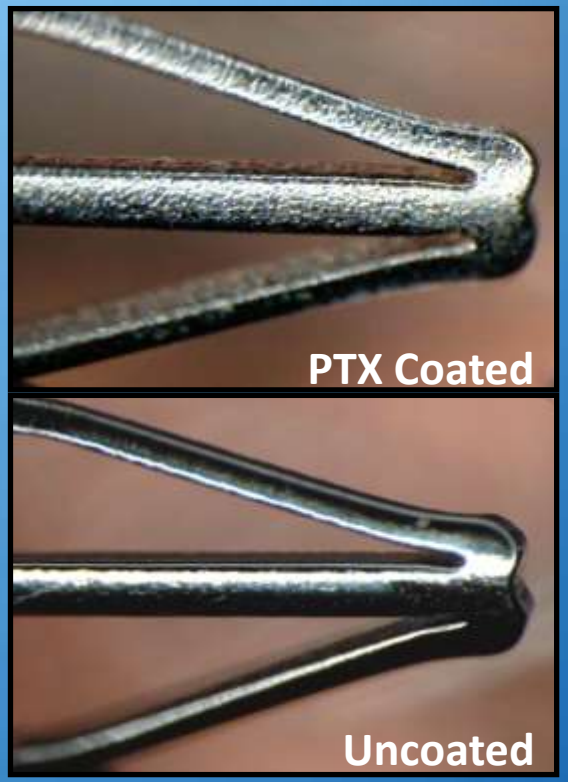
$p = 0.06$
log-rank

Years (PATIENTS)		0	1	2	3	4	5
Provisional Zilver PTX	At Risk	60	53	47	39	34	31
	Failed	0	3	6	7	8	8
Provisional BMS	At Risk	54	41	36	29	27	23
	Failed	0	9	12	13	14	14

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

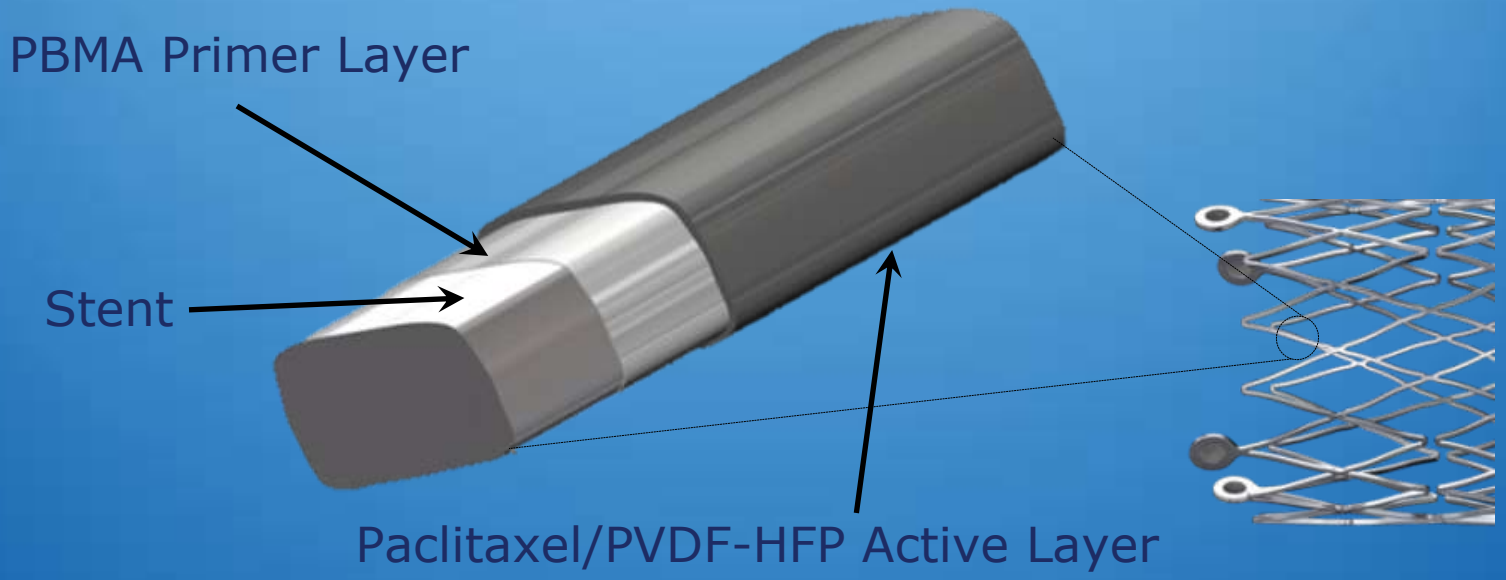
Zilver PTX

- Paclitaxel bound directly to stent without polymer
- Rationale: short-term exposure leads to long-term anti-restenotic effect



Eluvia

- Primer Layer (PBMA): Promotes Adhesion of Active Layer
- Active Layer (PTx, PVDF-HFP)– Controls Release of Paclitaxel
  - 0.167µg PTx/mm^2 stent surface area
- Over 10 million coronary implants



Boston Scientific Data on File.
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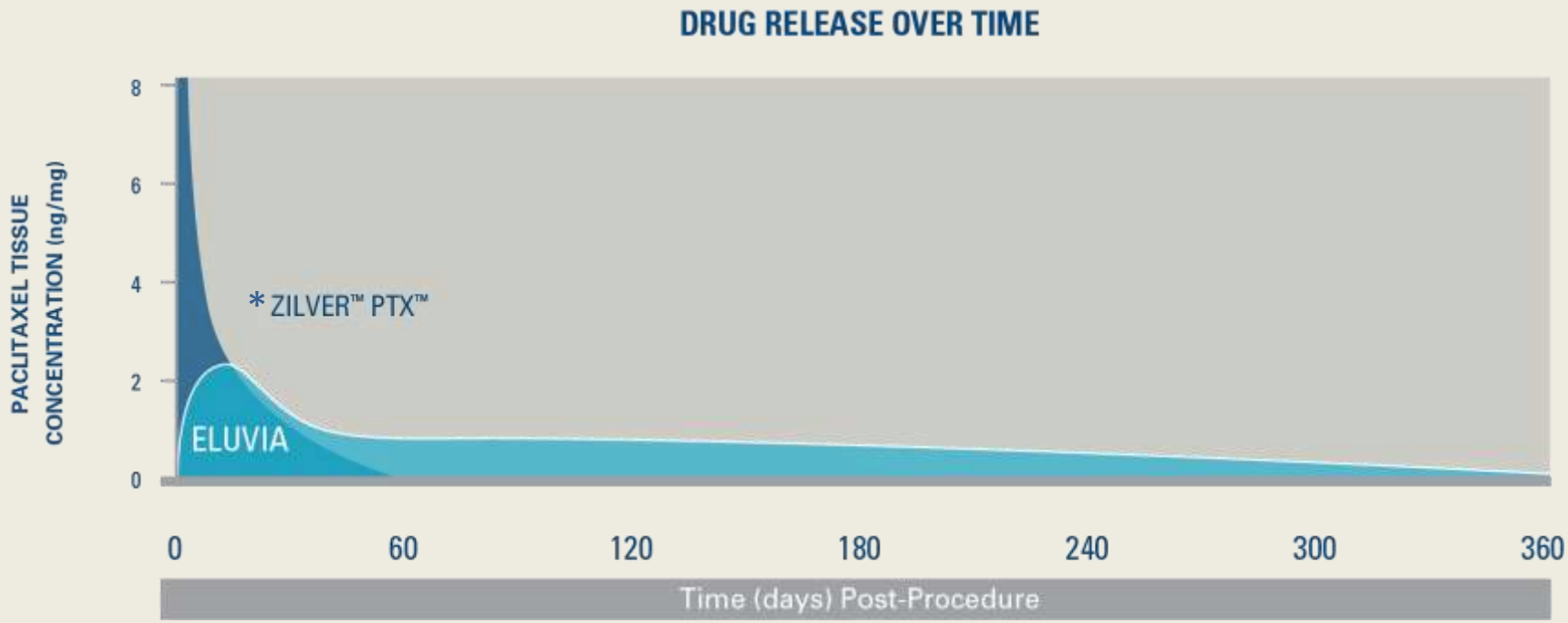
Sustained Drug Release



- Drug release from the Eluvia system is sustained over time
  - >90% of drug is released at 1 year
  - Drug release coincides with the restenotic cascade

Based on pre-clinical PK analysis. Data on file at Boston Scientific.
*Dake MD, et al. J Vasc Interv Radiol. 2011;22(5):603-610.
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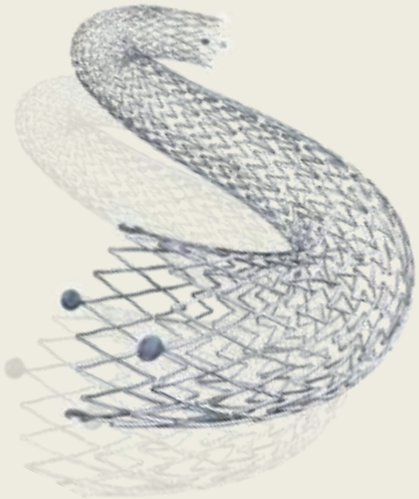
Eluvia™ Clinical Studies



MAJESTIC

Prospective, multicentre, single-arm, open label

n= 57 (1yr follow-up complete)

IMPERIAL

Prospective, multicenter, RCT 2:1

(Eluvia:Zilver PTX)

n = 485 (Enrolling)

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Eluvia™

MAJESTIC Clinical Study

Study Design	Prospective, multicentre, single-arm, open label
Subjects	57 patients with femoropopliteal artery lesions
Investigational Centers	14 sites (Europe, Australia, New Zealand)
Follow-up	Baseline, Procedure 1 month, 9 months, 1 year, 2 years, 3years
Primary Endpoint	Primary patency of target lesion at 9 months by duplex ultrasound

Core Lab
Clinical Events Committee

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Clinicaltrials.gov Identifier: NCT01820637

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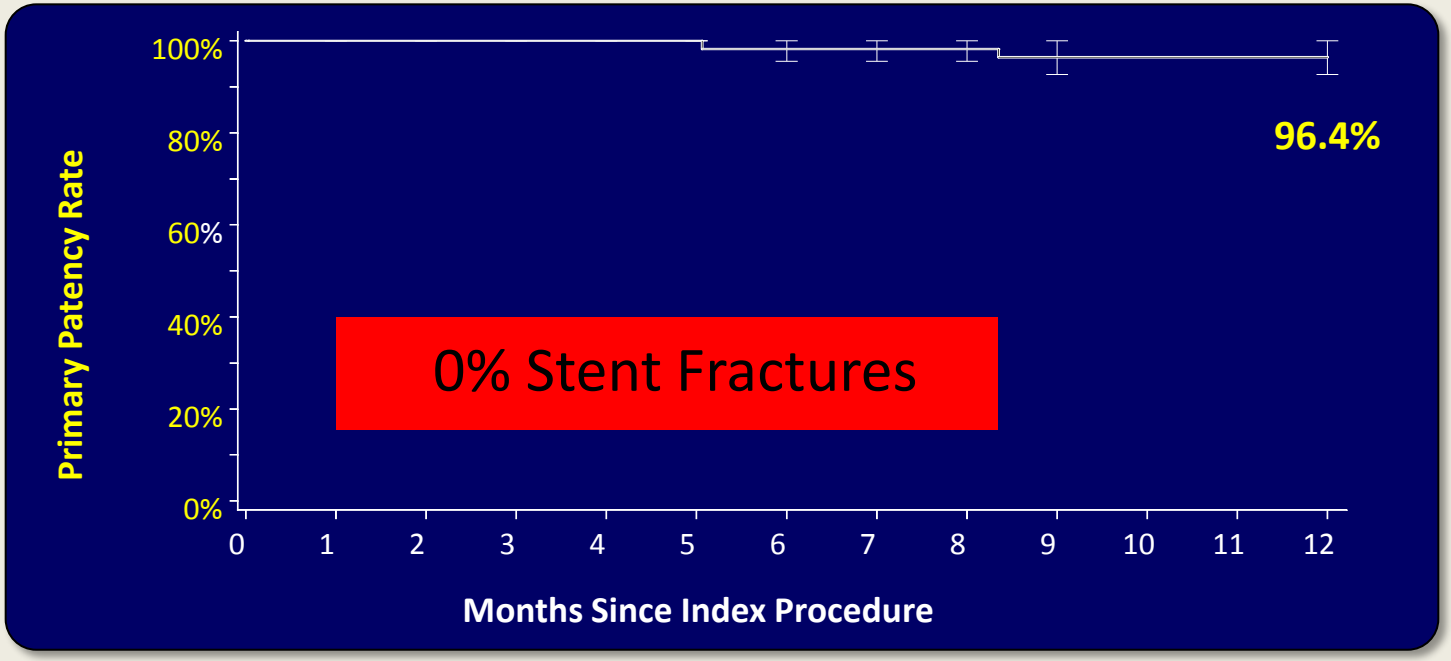
Primary Patency*: 12 Months

- 12-month primary patency was **96.1%** (49/51)
- Kaplan-Meier estimate: 96.4%



	0	1	2	3	4	6	9	12
Entered	57	57	56	56	56	56	55	53
Events	0	0	0	0	0	1	1	0
Event Rate	0%	0%	0%	0%	0%	1.8%	3.6%	3.6%

*Primary patency defined as duplex ultrasound peak systolic velocity ratio ≤2.5 and absence of TLR or bypass

Müller-Hülsbeck, S. VIVA 2015.

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Global Pivotal Study
IMPERIAL Trial

IMPERIAL CLINICAL TRIAL

First Patient Enrolled Dec 2015

Title	A randomIzed trial coMParing the ELUVIA dRug-elutIng stent versus Zilver PTX stent for treatment of superficiAL femoral and/or proximal popliteal arteries
Primary Investigators	Global: William A. Gray, MD European: Prof. Dr. med Stefan Müller-Hülsbeck
Target Vessel	Superficial Femoral Artery and/or Proximal Popliteal Artery lesions up to 140 mm in length.
Study Design	Prospective, multicenter, 2:1 randomized (Eluvia vs Zilver PTX), controlled, single-blind, non-inferiority trial (RCT)

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The Eluvia Stent system is an investigational device, not available for sale in the European Economic Area (EEA).

IMPERIAL Trial

IMPERIAL
CLINICAL TRIAL

Clinical Study Overview: IMPERIAL	
Subjects	• 465 subjects treated with Eluvia (N=310) or Zilver PTX (N=155)
Investigational Centers	Up to 75 study centers worldwide: • US, Canada, New Zealand, Belgium, Germany, Austria, and Japan
Primary Efficacy Endpoint	**Primary vessel patency** as assessed by duplex ultrasound (DUS) at 12 months post-procedure and adjudicated by an independent core laboratory.
Primary Safety Endpoint	**Major Adverse Event (MAE) rate** defined as • All cause death through 1 month • Target limb major amputation through 12 months • Target lesion revascularization (TLR) through 12 months

The Real Race in 2016

DES vs DCB

*

- DCB results consistently superior to plain angioplasty
- Strong appeal of “nothing left behind”
- Retrospective review** of 228 patients treated with DCB or DES
  - No significant difference in restenosis (12 months)
  - No significant difference in TLR
- Still lacking: long-term data for DCB

*Daytona 500, 21 February 2016, won by 0.011 sec

**Zeller. J Endovasc Ther. 2014;21:359-368

What We Need

*

- 5 year results with DCB
- Randomized results: DCB vs DES (Real PTX, etc)
- Comparative DES results (IMPERIAL)
- Appropriate reimbursement for DES

*Daytona 500, 21 February 2016, won by 0.011 sec

What Winning Looks Like in the Future

- Resolution of the in-stent restenosis problem
  - Avoidance:
    - very low TLR rates
    - bioabsorbable stents
    - proven non-stent strategies
  - Durable, economical, user-friendly treatment of ISR
- Reimbursement that rewards best clinical outcomes

Summary

- In 2016, DES are the best option for many patients
- We know a lot…
- but we need to know a whole lot more!