Drug-Eluting Stents
vs.
Drug-Coated Balloons

When to Choose?

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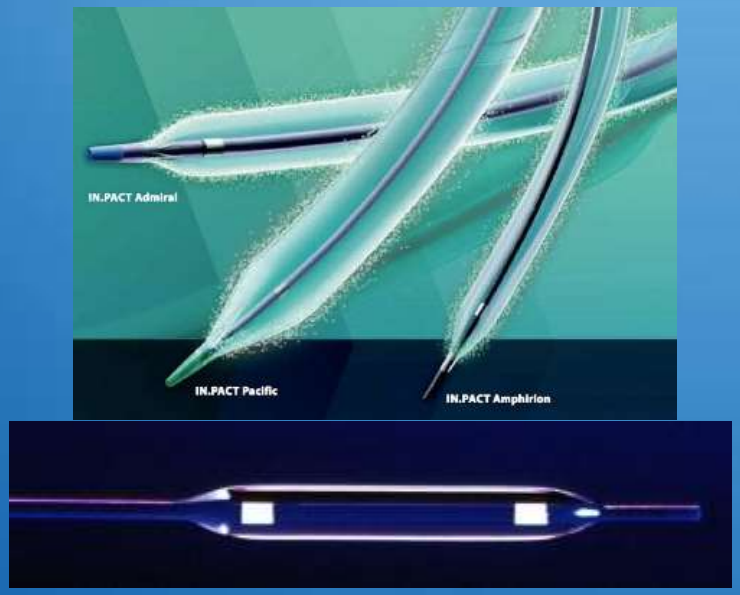
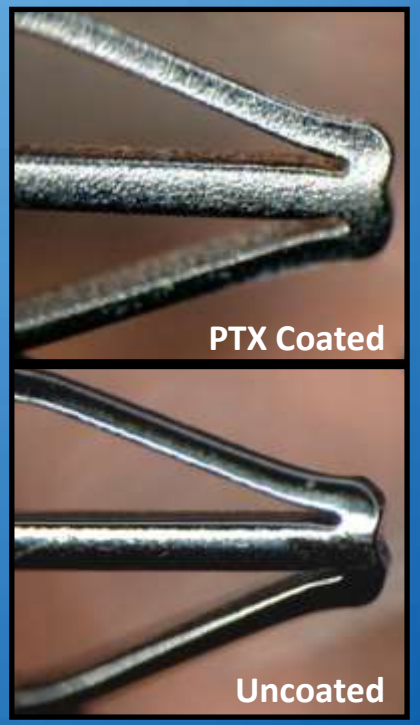
THE UNIVERSITY OF TOLEDO
HEART AND VASCULAR CENTER

Is This a Race Too Close to Call?

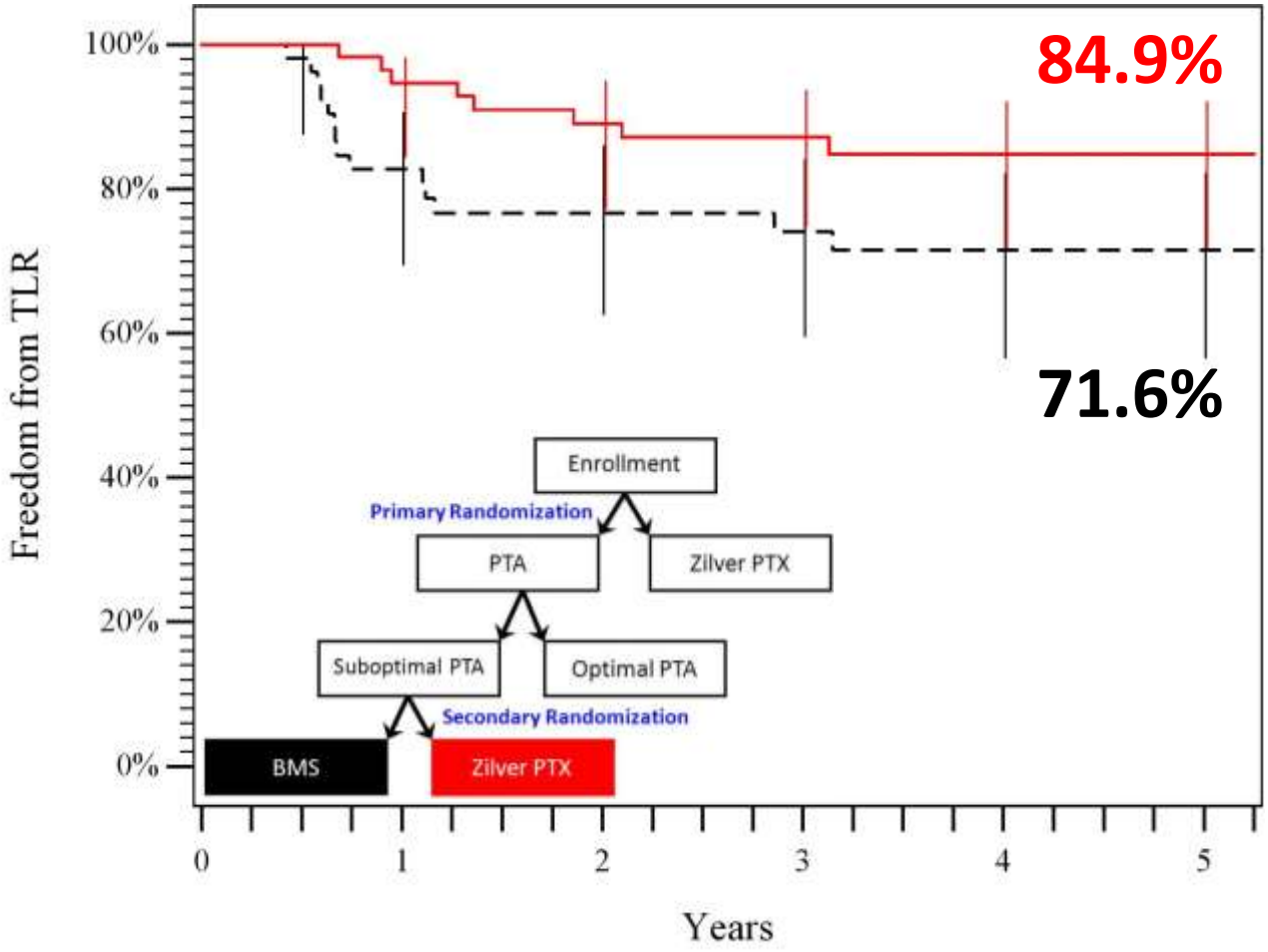
Clinical Trials Have Proven:

- Zilver PTX stents are superior to bare Zilver stents, and superior to plain angioplasty (PTA)
- Drug-coated balloons (DCB) are superior to PTA





5-year Freedom from TLR
Provisional Zilver PTX vs. BMS



Provisional Zilver PTX

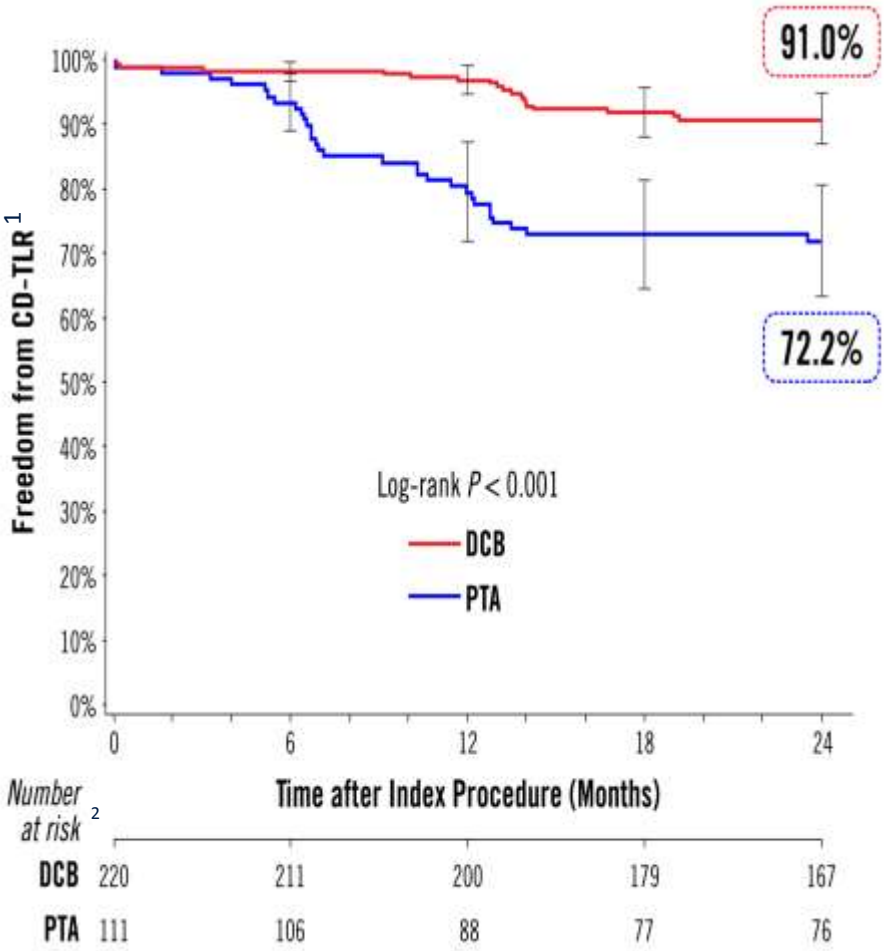
Provisional BMS

$p = 0.06$
log-rank

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

IN.PACT SFA TRIAL EFFICACY OUTCOMES THROUGH 2 YEARS

SUSTAINED PERFORMANCE BENEFIT OF IN.PACT™ ADMIRAL™ DCB OVER PTA THROUGH TWO YEARS



1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 24 months (adjudicated by a Clinical Events Committee blinded to the assigned treatment).
2. Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval.

Can We Compare DES with DCB?

- Retrospective review* of 228 patients treated with DCB or DES
- REAL PTX

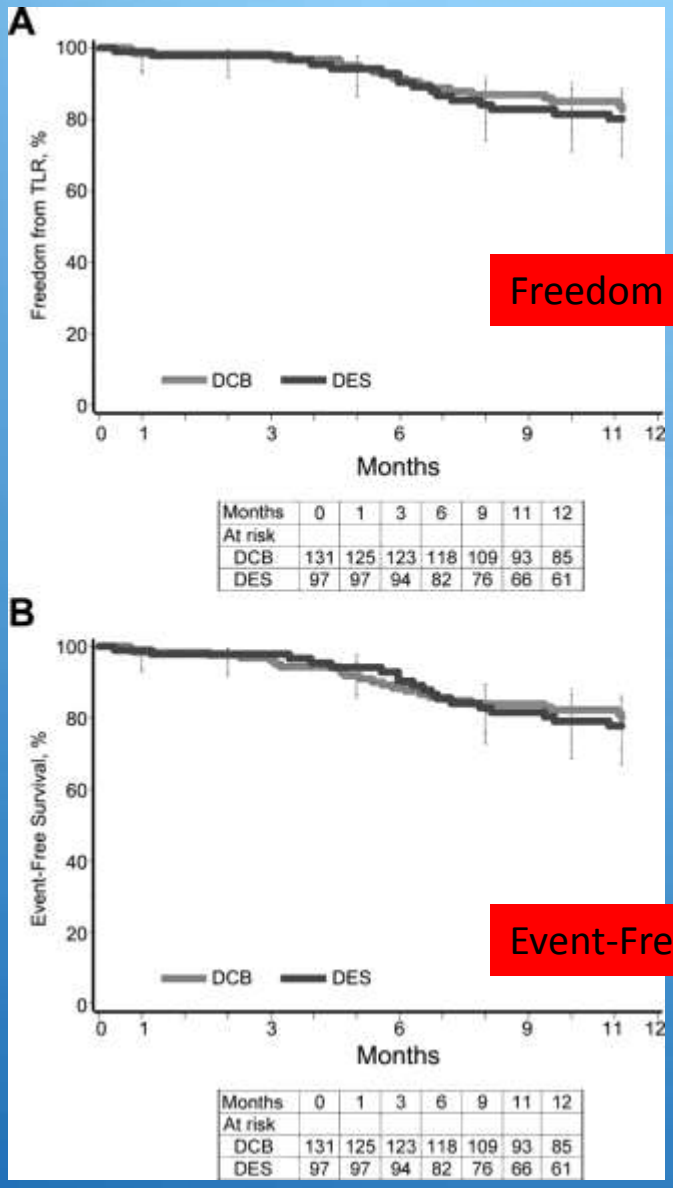
*Zeller. J Endovasc Ther. 2014;21:359-368

Retrospective Comparison

- 228 patients treated with DES or DCB
- Similar lesion length (195 mm vs 194 mm)
- Included restenosis
- Total occlusions 63% DES, 53% DCB
- Severe calcification 9% DES vs 20% DCB
- 18% provisional stenting in DCB patients
- Restenosis 30% DES, 24% DCB (p=0.319)

*Zeller. J Endovasc Ther. 2014;21:359-368
IN.PACT vs Zilver PTX

Retrospective Comparison



Months	0	1	3	6	9	11	12
At risk							
DCB	131	125	123	118	109	93	85
DES	97	97	94	82	76	66	61

Freedom from TLR

Months	0	1	3	6	9	11	12
At risk							
DCB	131	125	123	118	109	93	85
DES	97	97	94	82	76	66	61

Event-Free Survival

Event-free survival: freedom from procedure- or device-related death, CD TLR, bypass, amputation, surgical repair.

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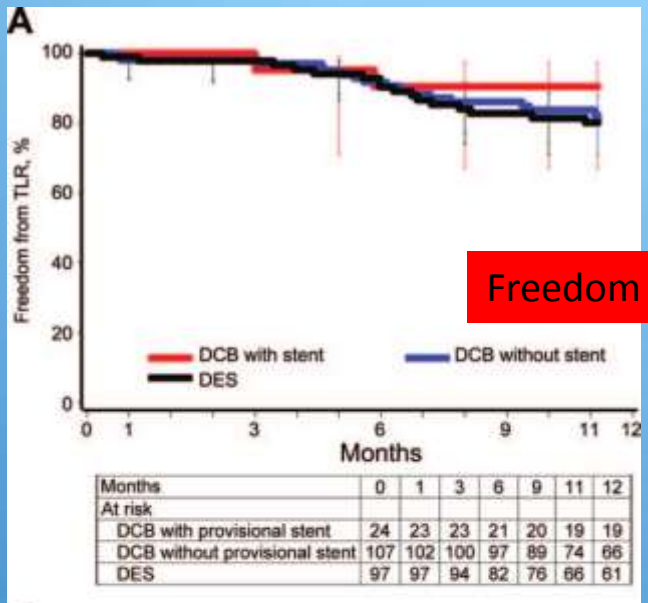
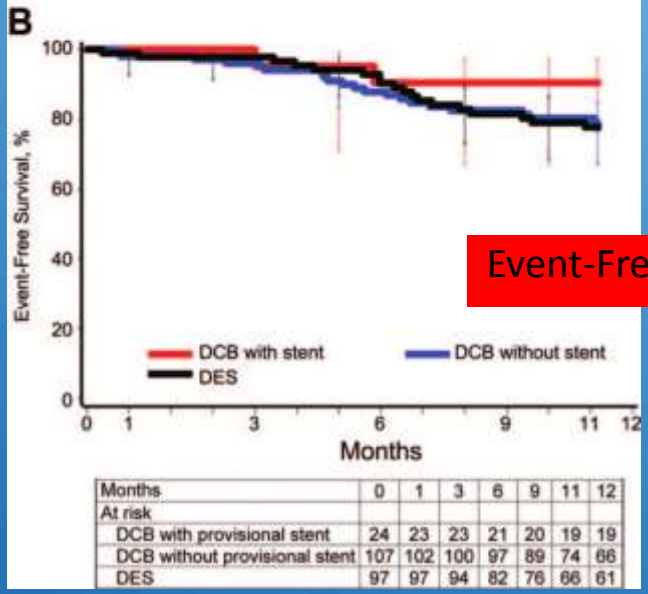
Retrospective Comparison



Months	0	1	3	6	9	11	12
At risk							
DCB with provisional stent	24	23	23	21	20	19	19
DCB without provisional stent	107	102	100	97	89	74	66
DES	97	97	94	82	76	66	61

Freedom from TLR



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REAL PTX

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

REAL PTX - Randomized Evaluation of the Zilver **PTX** Stent vs. Paclitaxel-Eluting Balloons for Treatment of Symptomatic Peripheral Artery Disease of the Femoropopliteal Artery

This study has been completed.

No Study Results Posted

- 150 patients
- Germany, Belgium
- Primary outcomes: 12 month primary patency, freedom from TLR

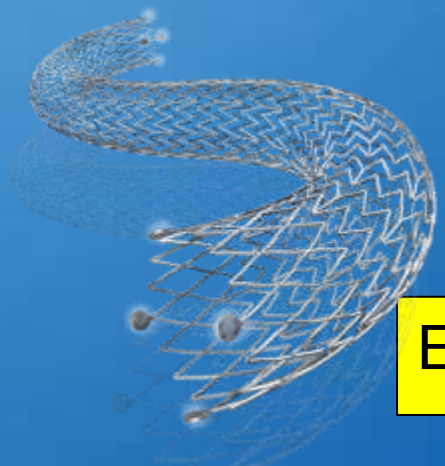
Making the Best Comparison

- Prospective, randomized study
- Assuming class effect: any DES vs any DCB
- No class effect: best DES vs best DCB

Comparing Different DES: The IMPERIAL Trial

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

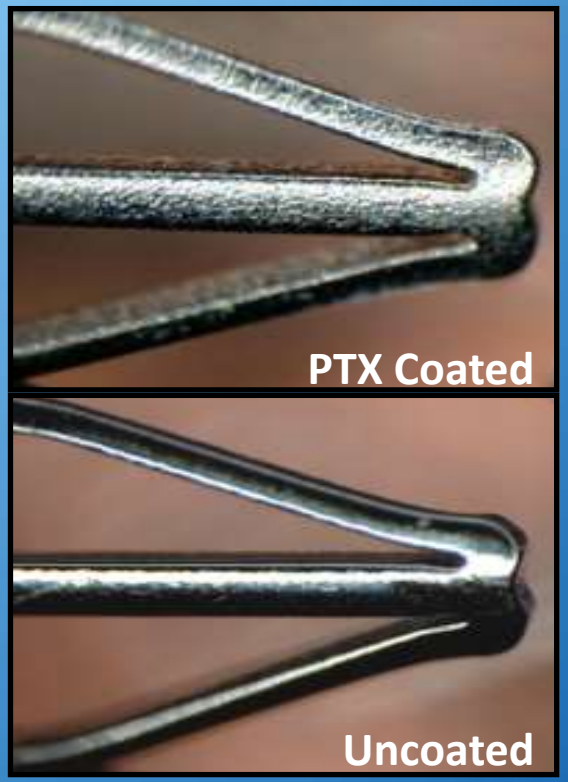
Zilver PTX



Eluvia

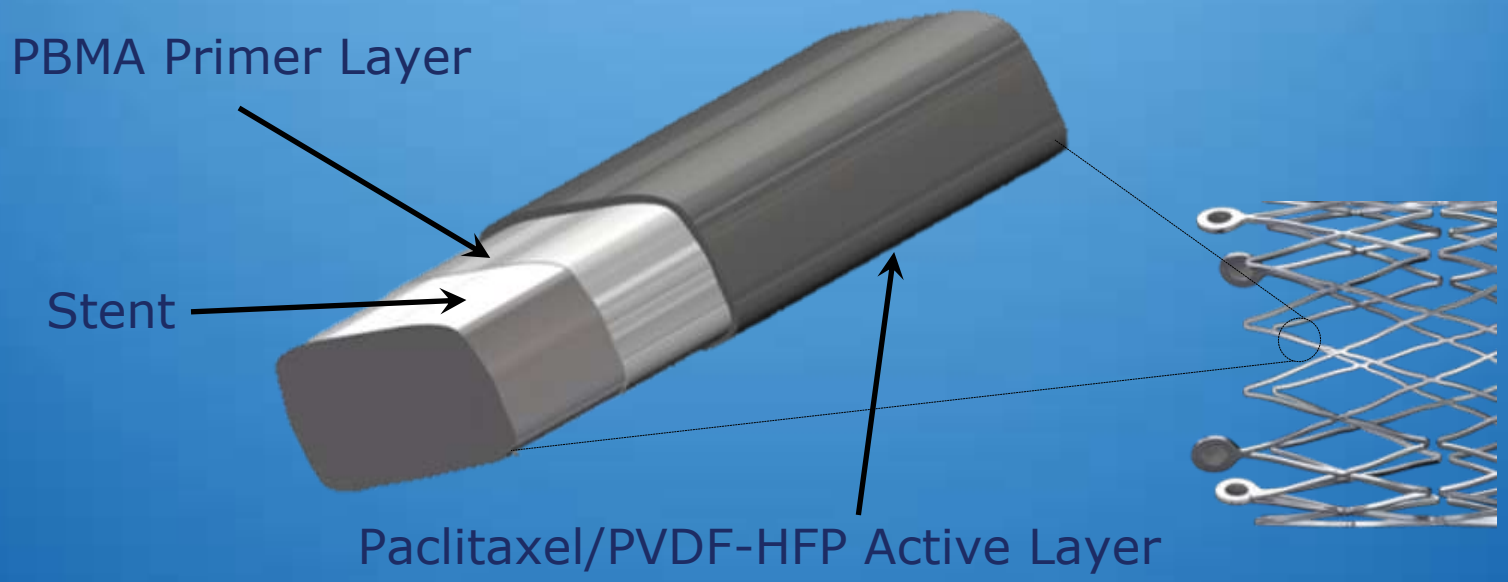
Zilver PTX

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



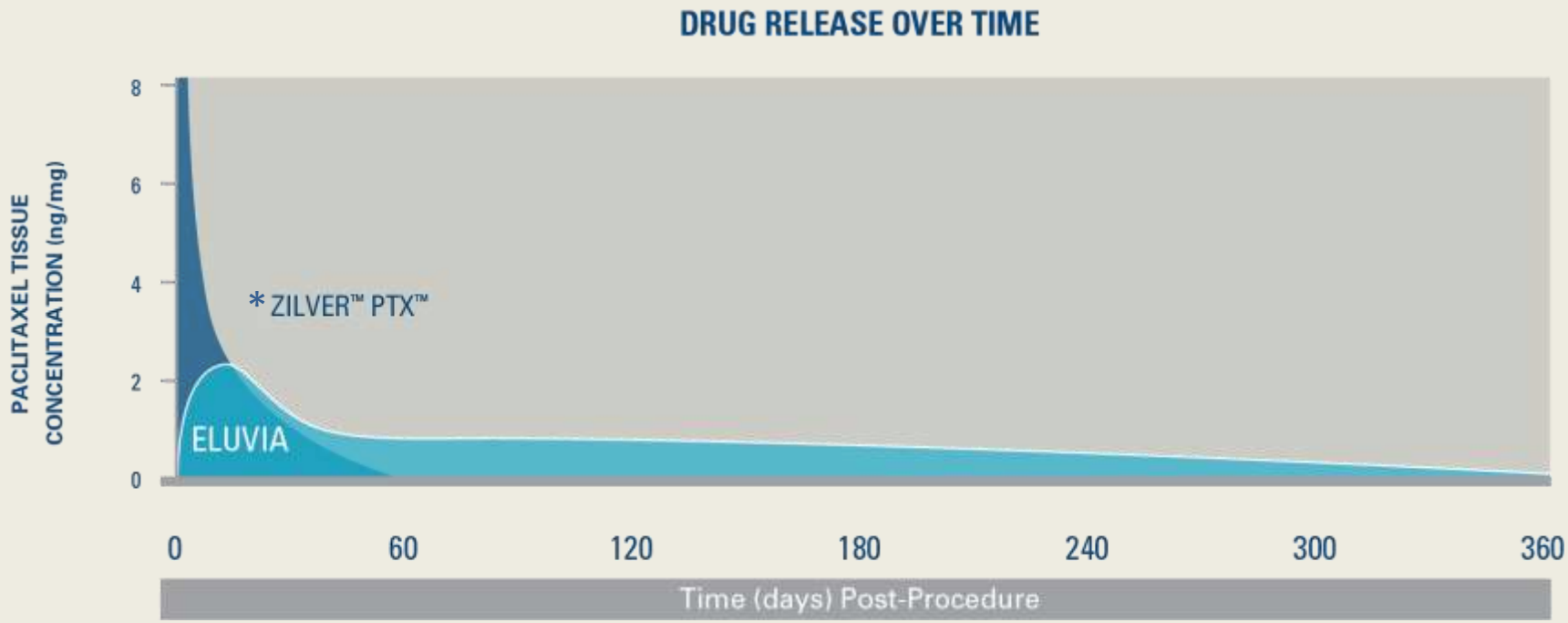
Eluvia

- 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.
Eluvia is an investigational device. Limited under U.S. law for investigational use only.

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.
Eluvia is an investigational device. Limited under U.S. law for investigational use only.

PI-308709-AD Feb 2016

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)

PI-308709-AD Feb 2016

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	S) at 12 months post- y.
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

Enrollment Complete February 15, 2017!!

PI-308709-AD Feb 2016

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

Comparing Different DCB: The TRANSCEND Trial

- Randomized controlled trial with 3 year follow-up
- 446 patients
- 1:1 IN.PACT vs SurVeil
- Enrollment start target July 2017

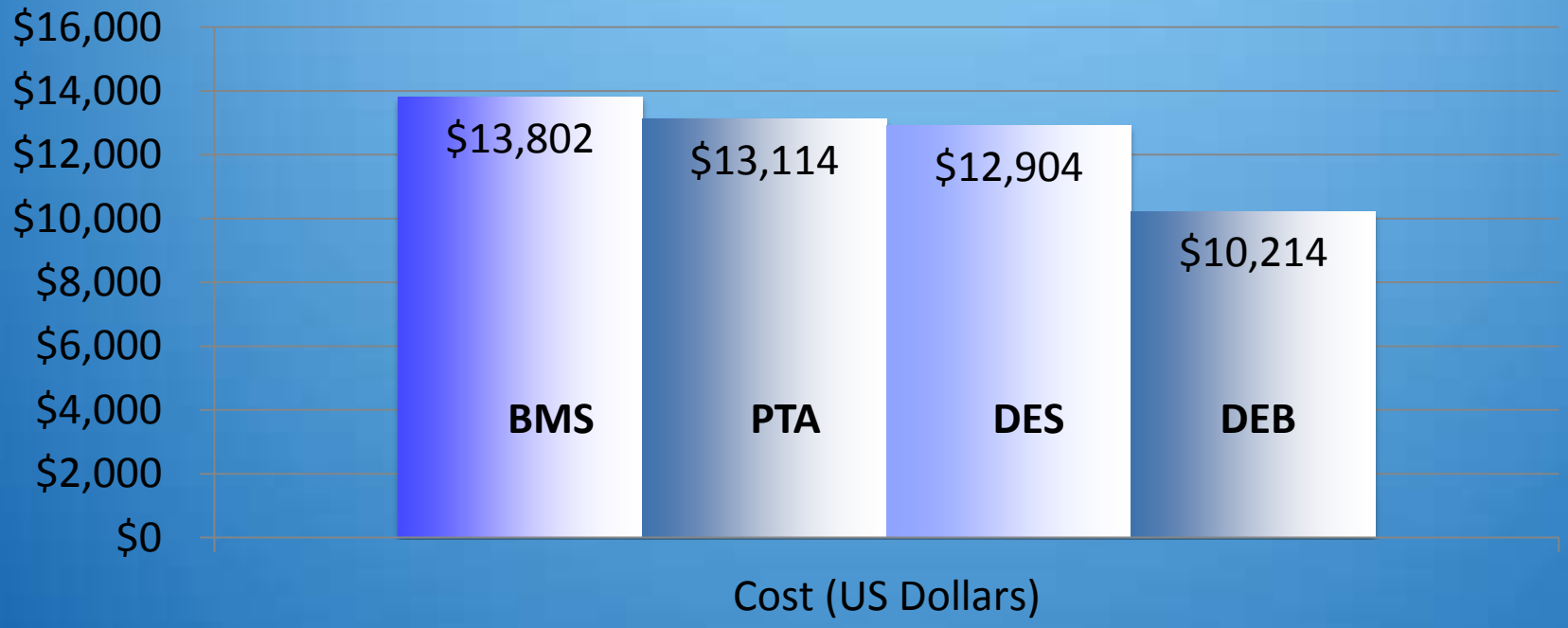
Comparing Cost

Device	Length	Cost
Angioplasty Balloon		$90
Bare Metal Stent		$650
Drug Coated Balloon	<150 mm	$1330
	150 mm	$1470
Drug Eluting Stent	80-100 mm	$1795
	120 mm	$1995

Note: numbers will vary from region to region.
Lowest cost option chosen for angioplasty balloon and bare metal stent.

2-Year Total Cost

Budget Impact Model



Similar outcome in German healthcare system

Pietzsch J. Catheter Cardiovasc Interv. 2014 Oct 1;84(4):546-554.

What's This Cost…You?

- For hospitals and office based labs (OBL), reimbursement is as important as cost
- Varies from country to country
- Varies at different times
- In the USA
  - OBL are penalized for using DES or DCB
  - Hospitals are penalized for using DES
  - Hospitals are incentivized to use 1 DCB

Economics May Favor a Third Option

- Reimbursed DCB
- Inexpensive bare metal stent

DEBAS TREATMENT APPROACH

Pulsar-18 / 35 SE stent

PASSEO-18 LUX DCB

Predilate lesion

↓

Implant SE Stent in diseased segment

↓

Deliver DCB to entire stented segment

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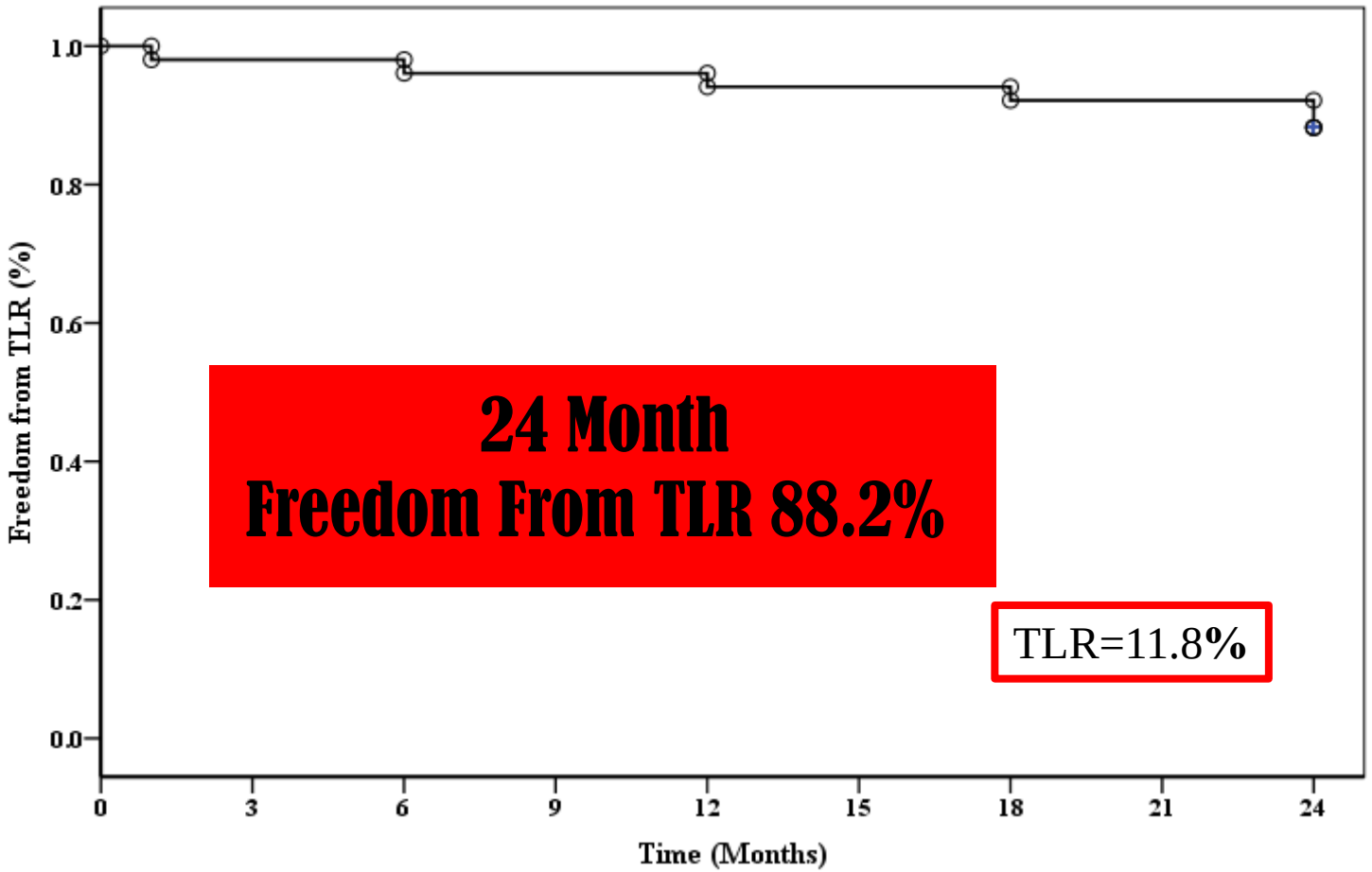
School of Surgery, University of Western Australia Perth

Patient and Lesion Characteristics

Rutherford Classification - n (%)	
Class III = Severe claudication	21 (41.18%)
Class IV = Ischemic Rest Pain	16 (31.37%)
Class V = Minor Tissue Loss	14 (27.45%)
ABI	0.39 ± .01*

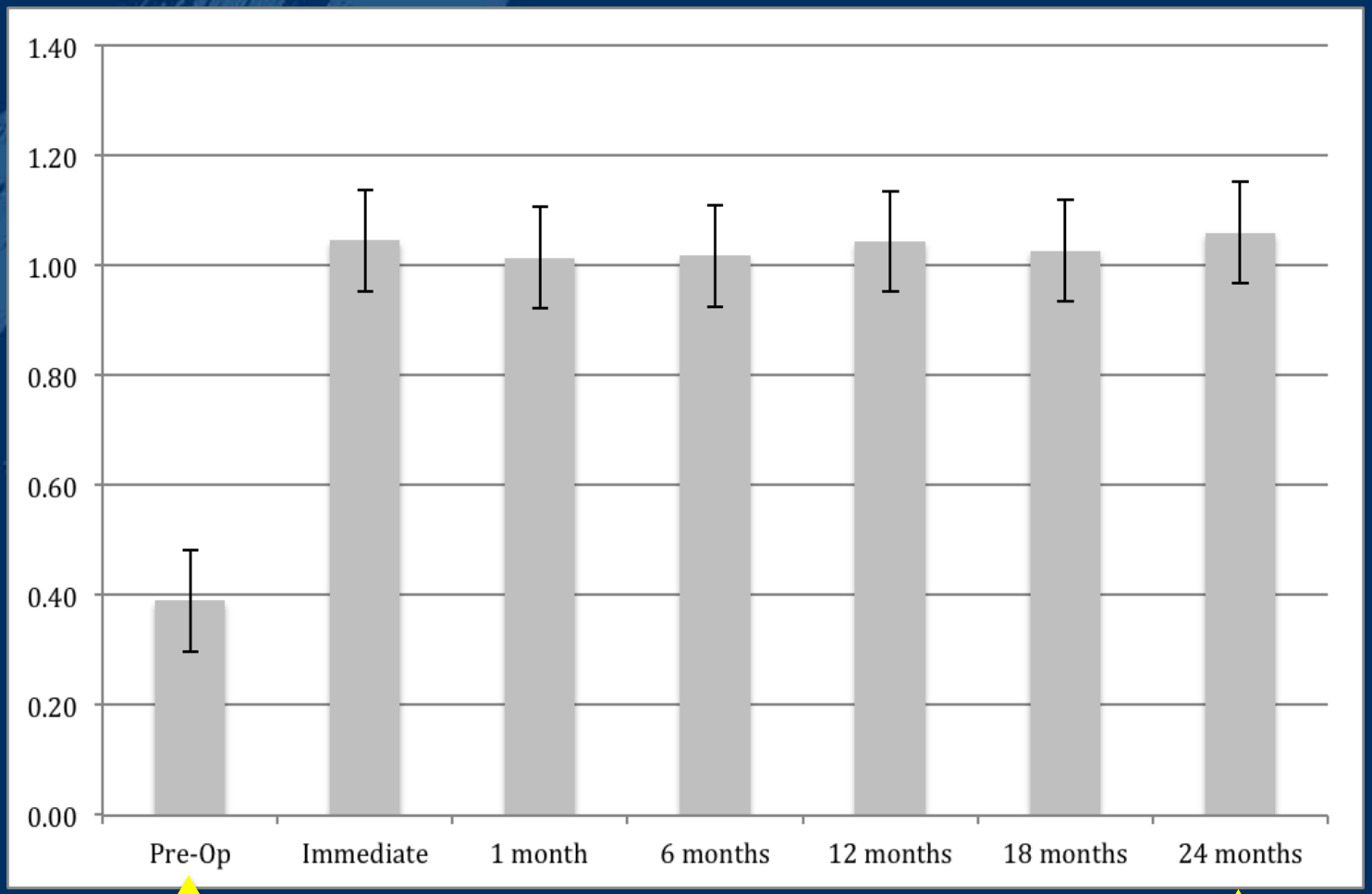
Lesion Length (mm)	**187.55 ± 74.55***	**167.09 – 208.01**
Total Occlusions	41 (80.4%)	.45 - .82
Calcification - n (%)		
None or mild	17 (33. 33%)	.19 – .47
Moderate	**22 (43.14%)**	**.29 – .59**
Severe	**12 (23.53%)**	**.13 – .39**
TASC Classification		
TASC A	0 (0%)	.00 - .09
TASC B	2 (3.92%)	.01 - .15
TASC C	**23 (45.10%)**	**.31 - .60**
TASC D	**26 (50.98%)**	**.36 - .66**

KAPLAN MEIER CURVE OF FREEDOM FROM TLR



	1 Month	6 Months	12 Months	18 Months	24 Months
Patients at risk (n)	50	49	48	46	45
Freedom From TLR	**98**	**96.1**	**94.1**	**92**	**88.2**
Standard Error (%)	1.9	2.7	3.3	3.6	4.5

IMPROVEMENT OF ANKLE-BRACHIAL INDEX (ABI)



Mean ABI = 0.39
95%CI 0.36 – 0.42

Mean ABI = 1.06
95%CI 1.03 -1.09

ISAR-STATH

- Randomized
  - DCB + bare metal stent (BMS)
  - Plain balloon angioplasty + BMS
  - Directional atherectomy (with bailout BMS)
- DCB + BMS superior in:
  - Angiographic percent stenosis at 6 months
  - Binary restenosis
  - Freedom from TLR at 24 months

Ott. Circulation April 2017

Conclusions

- Some lesions always require stents
  - Persistent recoil
  - Flow-limiting dissection
- For the rest: the race is nearly even
- Economics favor DCB
- Looking for volunteers to complete a DES/DCB randomized trial!