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Show Me The Road
Randomized Trials of Antiproliferative Therapies:

LEVANT II, In.PACT SFA, Zilver PTX, and DEFINITIVE AR

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Disclosure Statement of Financial Interest

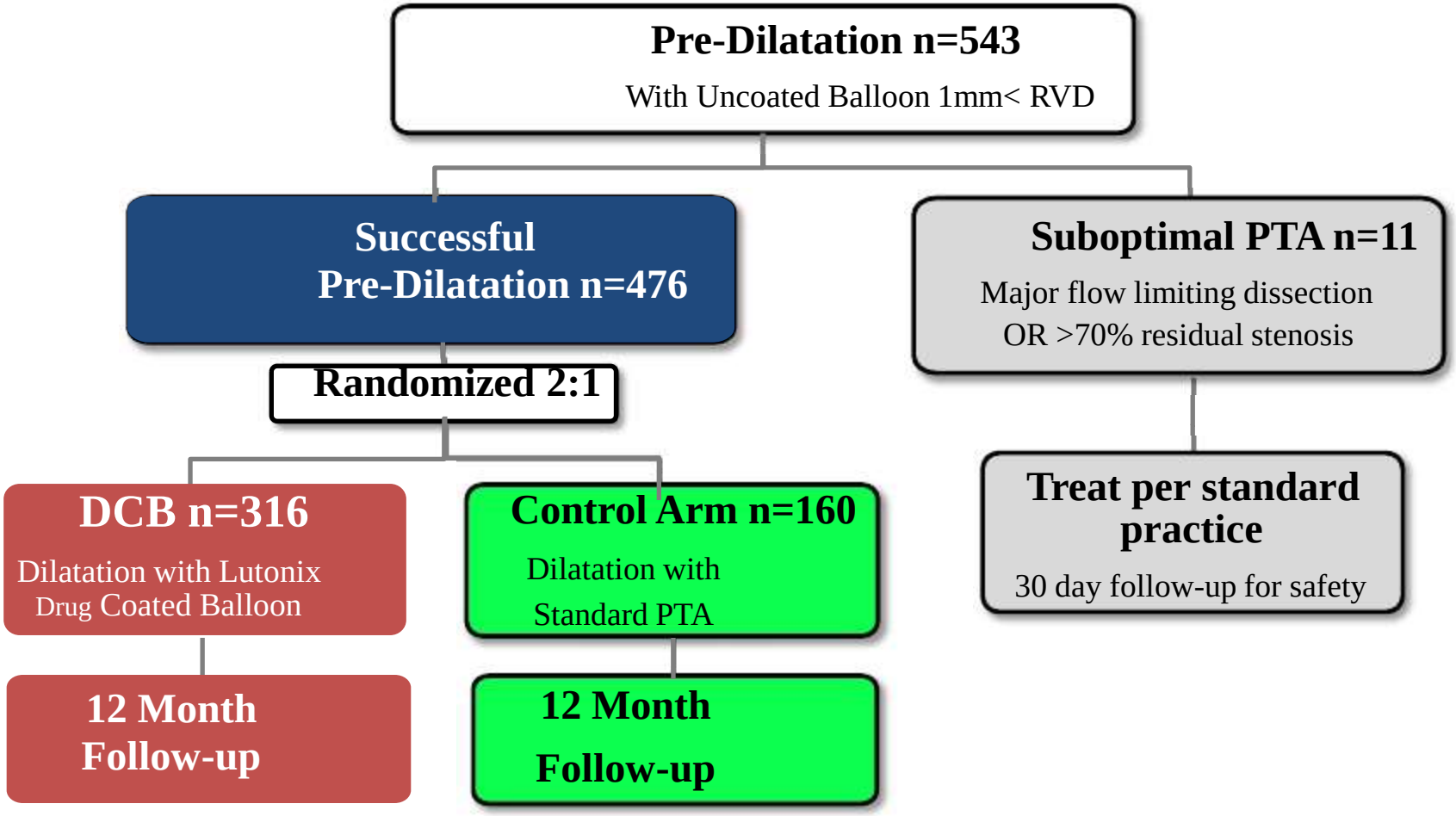
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• Medtronic, Boston Scientific, Gore
• Consulting Fees/Honoraria	• Medtronic, Boston Scientific
• Ownership/Founder	• Contego Medical
• Other Financial Benefit	• CardioMEMs

Randomized Trials for Femoro-Popliteal Disease

- Levant 2
- In.Pact SFA
- Zilver PTX
- Definitive AR

Levant 2 Trial



Patients and follow up physician were blinded

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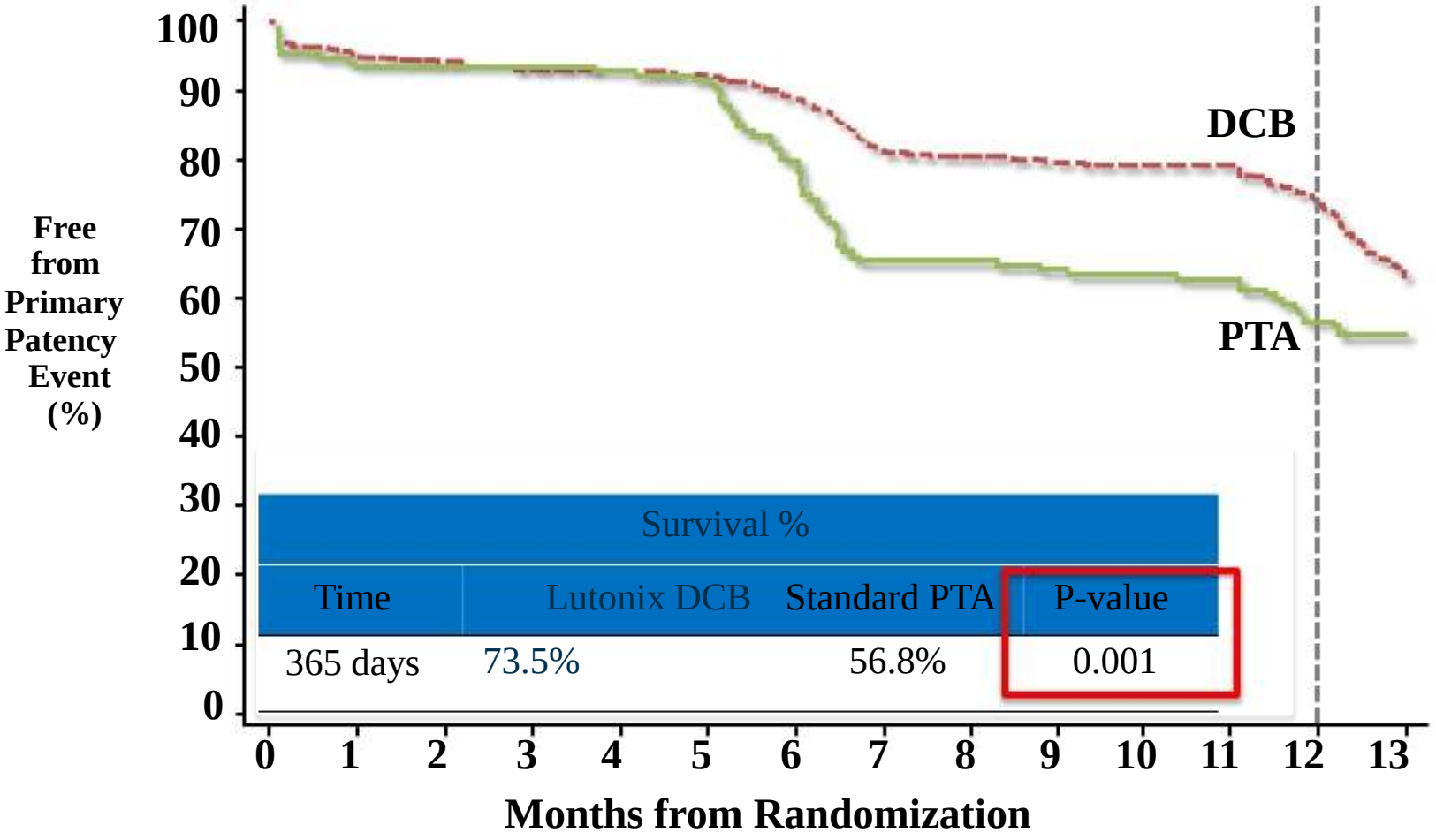
Levant 2 Trial - Primary Endpoints

Safety	Efficacy
Composite of freedom from all-cause peri-operative death & freedom at **1 YEAR** in the index limb from: • Amputation (above or below the ankle) • Re-intervention • Index-limb-related death	Primary patency of the target lesion at **1 YEAR**: • Absence of restenosis (defined by DUS PSVR < 2.5 & freedom from target lesion revascularization (TLR)

Angiographic Characteristics (ITT)

	DCB	Standard PTA	P-value
Two lesions treated	1.9%(6/316)	3.1%(5/160)	0.400
Total Lesion Length(mm)	62.9±41.5(315)	63.6±40.3(160)	0.866
Treated Length(mm)	107.7±47.0 (316)	107.3±49.3 (160)	0.933
Calcification	59.2%(187/316)	57.5%(92/160)	0.726
Total Occlusion	20.6%(65/316)	21.9%(35/160)	0.741
%DS post-treatment	23.4±12.3(316)	23.8±12.3(158)	0.703
Bail-outStenting	2.5%(8/316)	6.9%(11/160)	0.022
Dissection	63.7%(200/314)	72.3%(115/159)	0.060
Procedural Success (corelab)	88.9%(281/316)	86.8%(138/159)	0.497
DeviceSuccess(no of balloons)	99.5%(430/432)	100%(180/180)	0.367

Levant II Trial: 12 Month Kaplan Meier Freedom from Primary Patency Event



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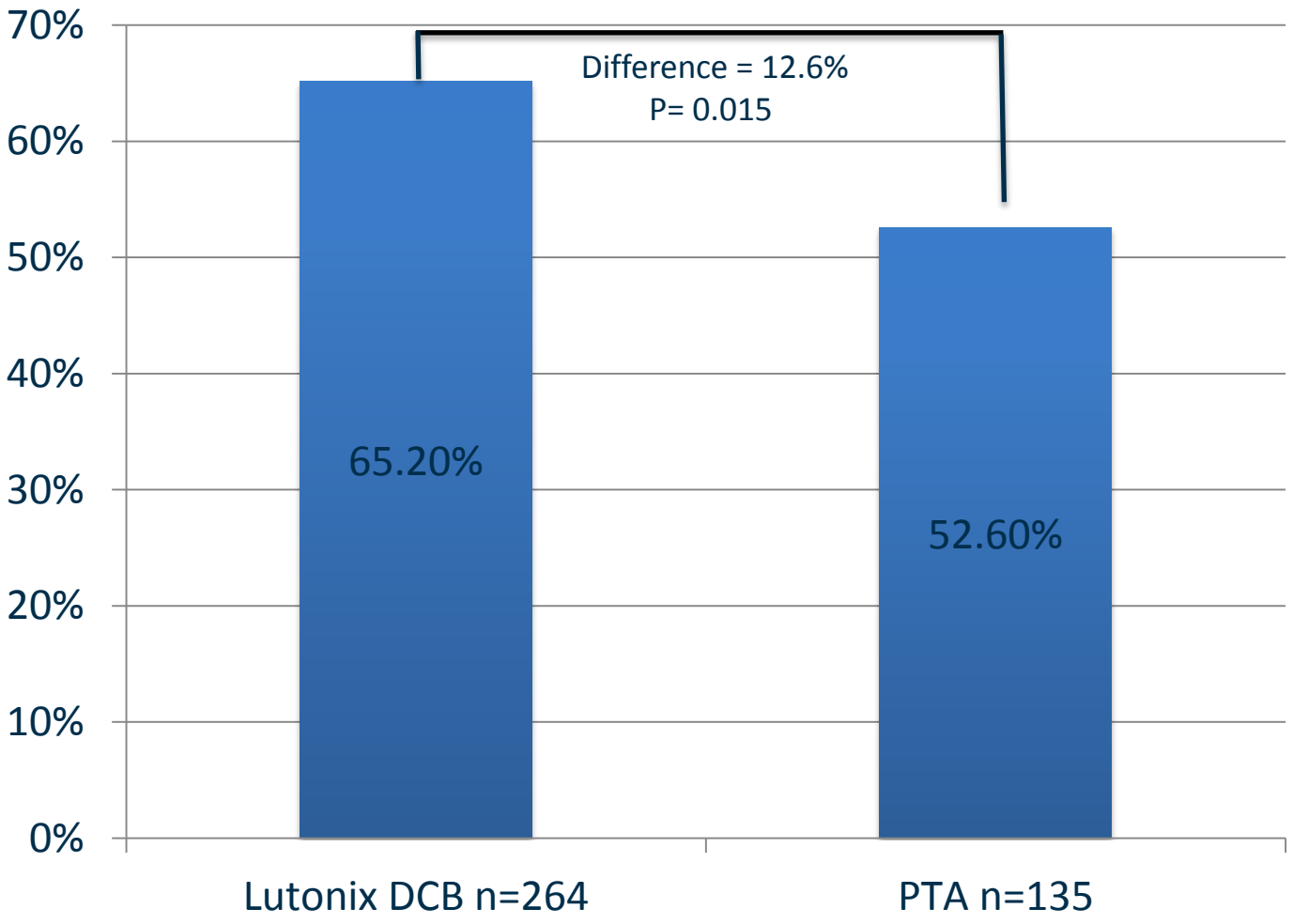
LEVANT II Trial

1-Year Primary Patency - PSVR<2.5



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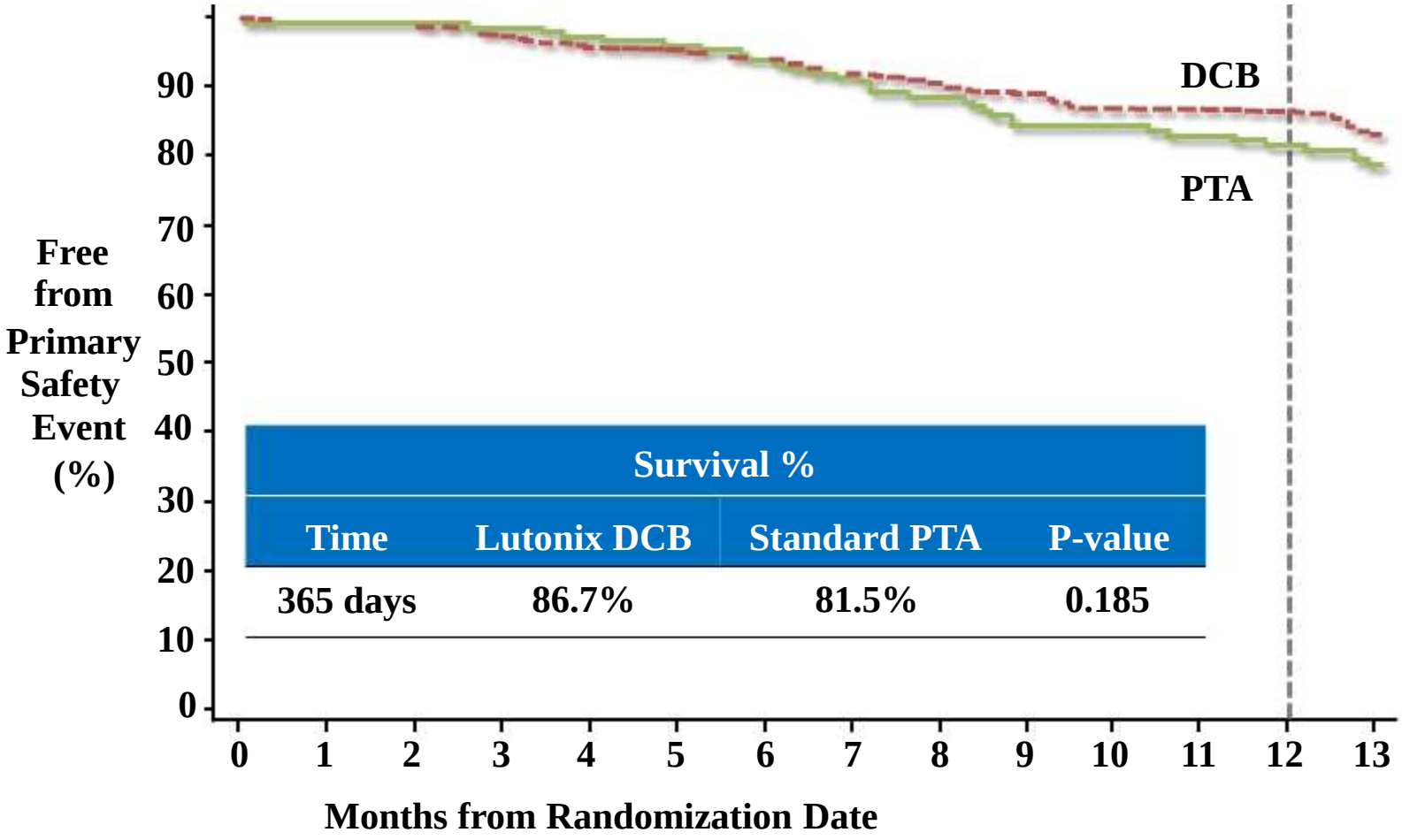
Levant II Trial:

12 Month Freedom from Primary Safety Event



Survival %			
Time	Lutonix DCB	Standard PTA	P-value
365 days	86.7%	81.5%	0.185

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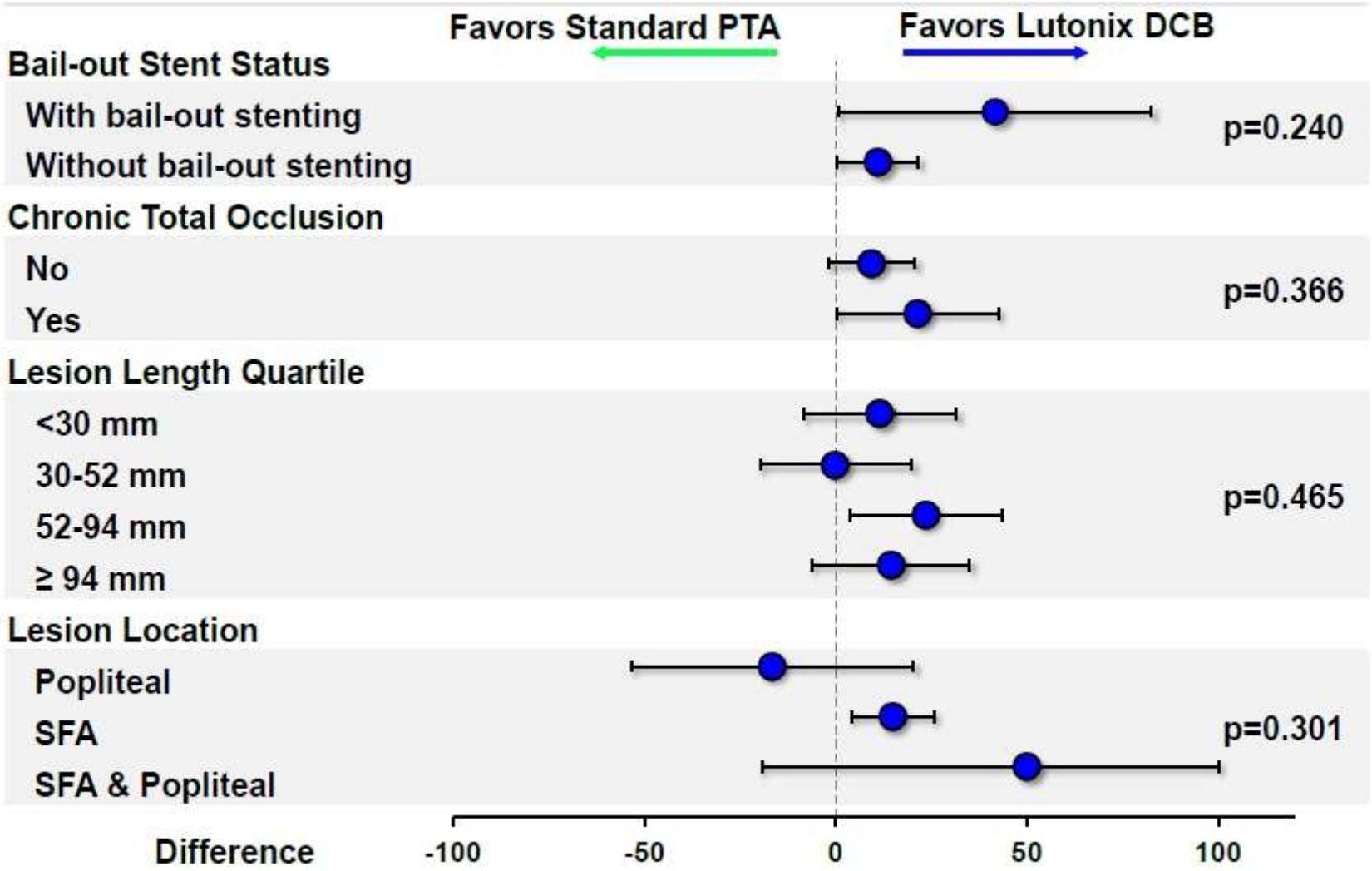
Levant II Trial

1-Year Subgroup Analyses



Levant II Trial
Subset Analysis: Gender

Gender	Endpoint	Lutonix DCB Adjusted%	Control PTA Adjusted %	Adjusted Difference %	Unadjusted Difference %
US Female	Freedom from Primary Safety Event	74.6%	77.4%	-2.6%	-5.6%
	Primary Patency	50.8%	63.9%	-13.1%	-19.7%
US Male	Freedom from Primary Safety Event	87.6%	86.3%	1.3%	1.3%
	Primary Patency	81.2%	49.8%	31.4%	21.9%

Levant II Trial

Subset Analysis: Geography

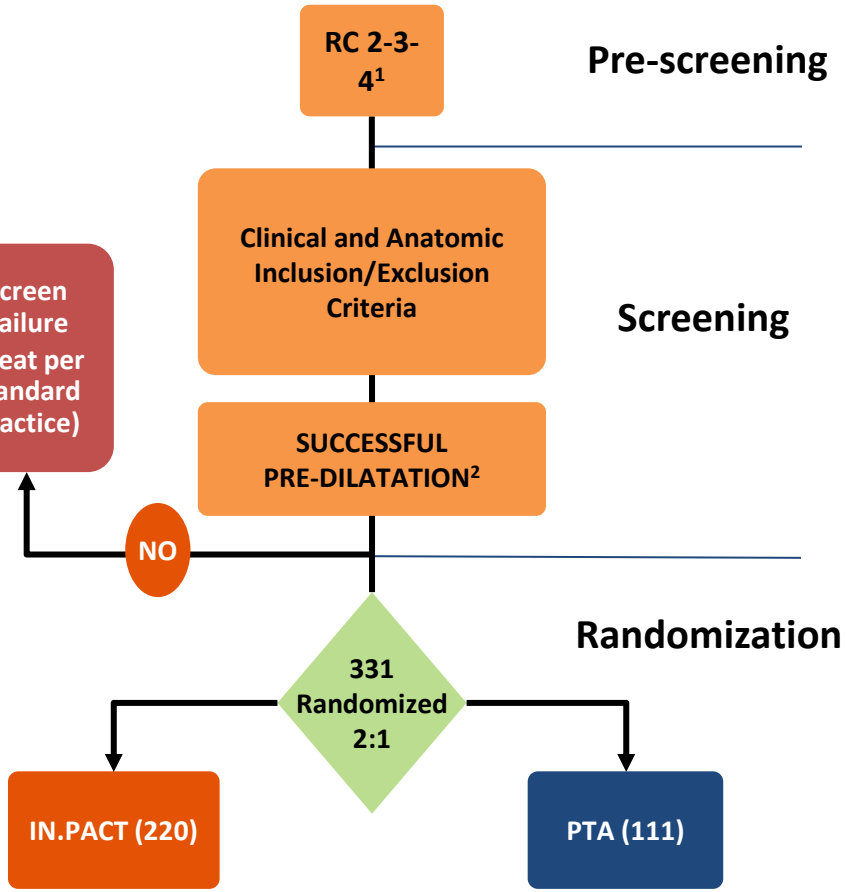
	Geography	Lutonix DCB	Control PTA	Difference %	P-value
Freedom from Primary Safety Event	OUS	88.7%	71.7%	17%	0.02
	US	81.1%	83.3%	-2.2%	
Primary Patency	OUS	69.1%	46.0%	23.1%	0.12
	US	62.9%	56.5%	6.4%	

Levant II Trial

24 Month Primary Patency, Freedom from TLR, and Composite Safety

	Lutonix	PTA	
Patency @730 days	58.6%	53%	P=0.05
Composite Safety	78.7%	70.9%	P=0.08

IN.PACT SFA TRIAL DESIGN



IN.PACT SFA
Aggregate dataset from Phase I and II

Primary Endpoints:

- **Efficacy**: 12-month Primary Patency
- Freedom from clinically-driven TLR and duplex ultrasound derived restenosis (PSVR ≤2.4)
- **Safety**: Freedom from 30-day device/procedure death, 12-month amputation, 12-month clinically-driven TVR

Key Inclusion Criteria:

- Rutherford 2-3-4
- SFA and proximal popliteal
- Lesion length 4-18 cm
- Total occlusion ≤10 cm

1.With symptoms of claudication and/or rest pain and angiographic evidence of SFA/PPA stenosis
2.Pre-dilatation mandatory for all subjects in IN.PACT SFA II phase only.

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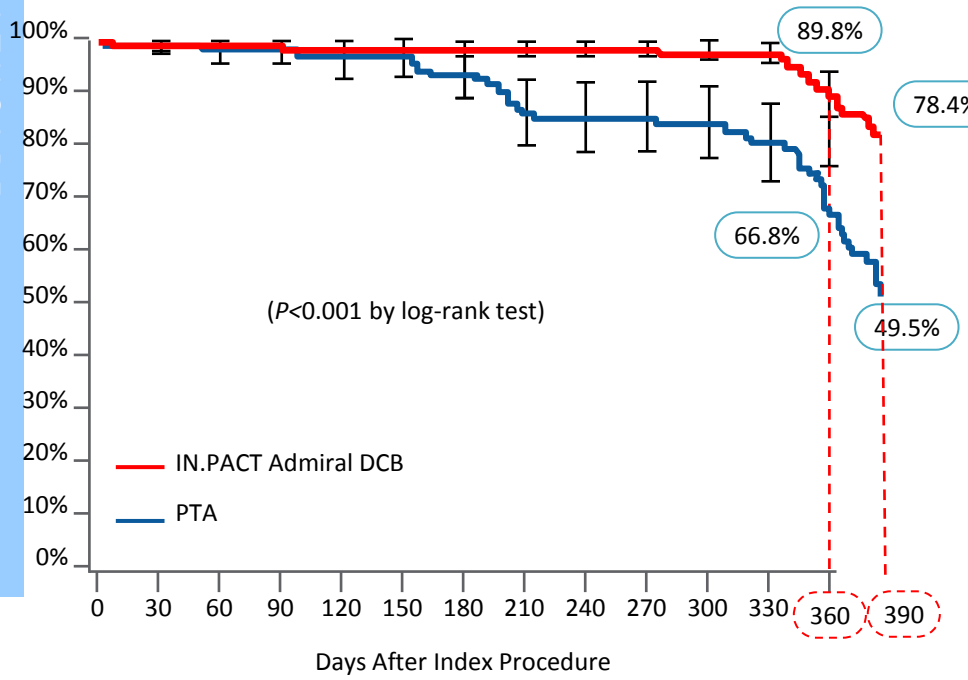
IN.PACT SFA Baseline Characteristics

Clinical + Angiographic Baseline

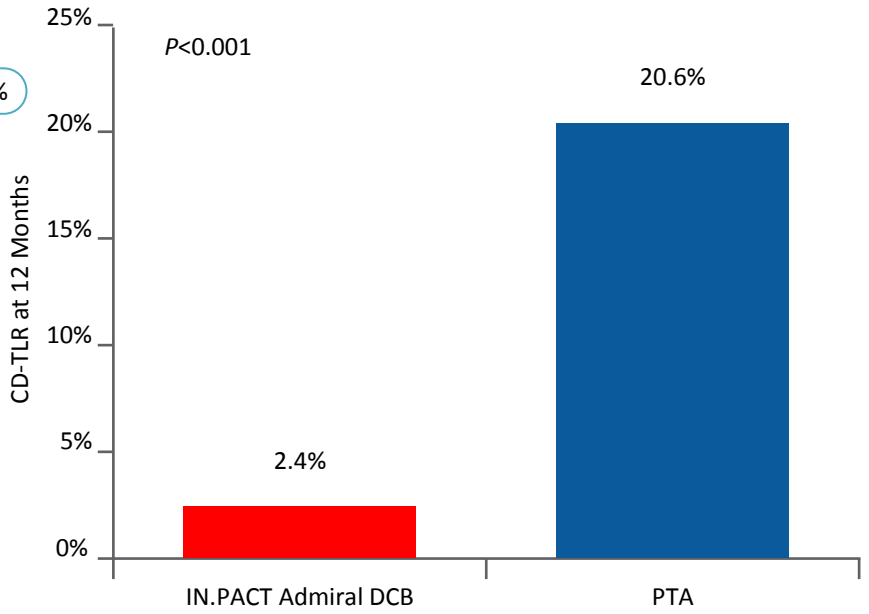
	IN.PACT DCB (N=220) (N=221 lesions)	PTA (N=111) (N=113 lesions)	P-value
Age	67.5 y ± 9.5	68.0 y ± 9.2	0.612
Male Gender	65.0% (143/220)	67.6% (75/111)	0.713
Diabetes	40.5% (89/220)	48.6% (54/111)	0.161
Current Smoker	38.6% (85/220)	36.0% (40/111)	0.719
Hypertension	91.4% (201/220)	88.3% (98/111)	0.431
Hyperlipidemia	84.5% (186/220)	82.0% (91/111)	0.637
Lesion Length	8.9 cm ± 4.9	8.8 cm ± 5.1	0.815
Total Occlusions	25.8% (57/221)	19.5% (22/113)	0.222
RVD	4.6 mm ± 0.8	4.7 mm ± 0.8	0.728
Diameter Stenosis	81.1% ± 15.5	81.3% ± 13.7	0.946

IN.PACT SFA 12-Month Efficacy Outcomes

Primary Patency Kaplan Meier (All ITT)[1]



Clinically-Driven Target Lesion Revascularization (CD-TLR)[2]



1. Primary patency is defined as freedom from clinically-driven TLR and freedom from restenosis as determined by DUS PSVR ≤2.4
2. Clinically-driven TLR defined as any re-intervention due to symptoms or drop of ABI/TBI of >20% or >0.15 compared to post-procedure ABI/TBI

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InPact: 12 Month Effectiveness

	IN.PACT DCB	PTA	p
Primary Patency (PSVR ≤ 2.4)	82.2% (157/191)	52.4% (54/103)	<0.001
Clinically-driven TLR	2.4% (5/207)	20.6% (22/107)	<0.001
All TLR	2.9% (6/207)	20.6% (22/107)	<0.001
Sustained Clinical Improvement	85.2% (167/196)	68.9% (73/106)	<0.001
ABI / TBI	0.951 ±0.221	0.886 ±0.169	0.002

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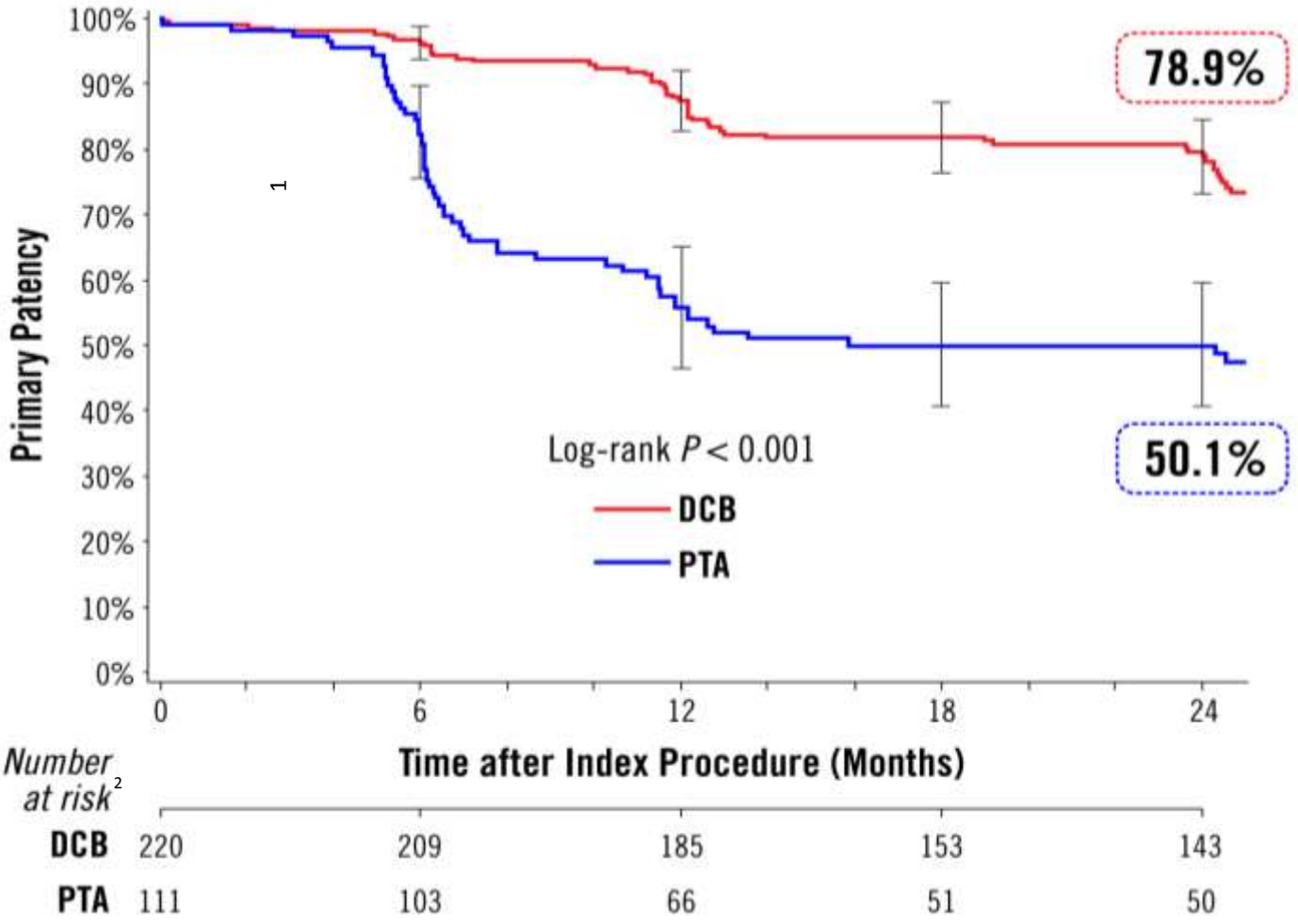
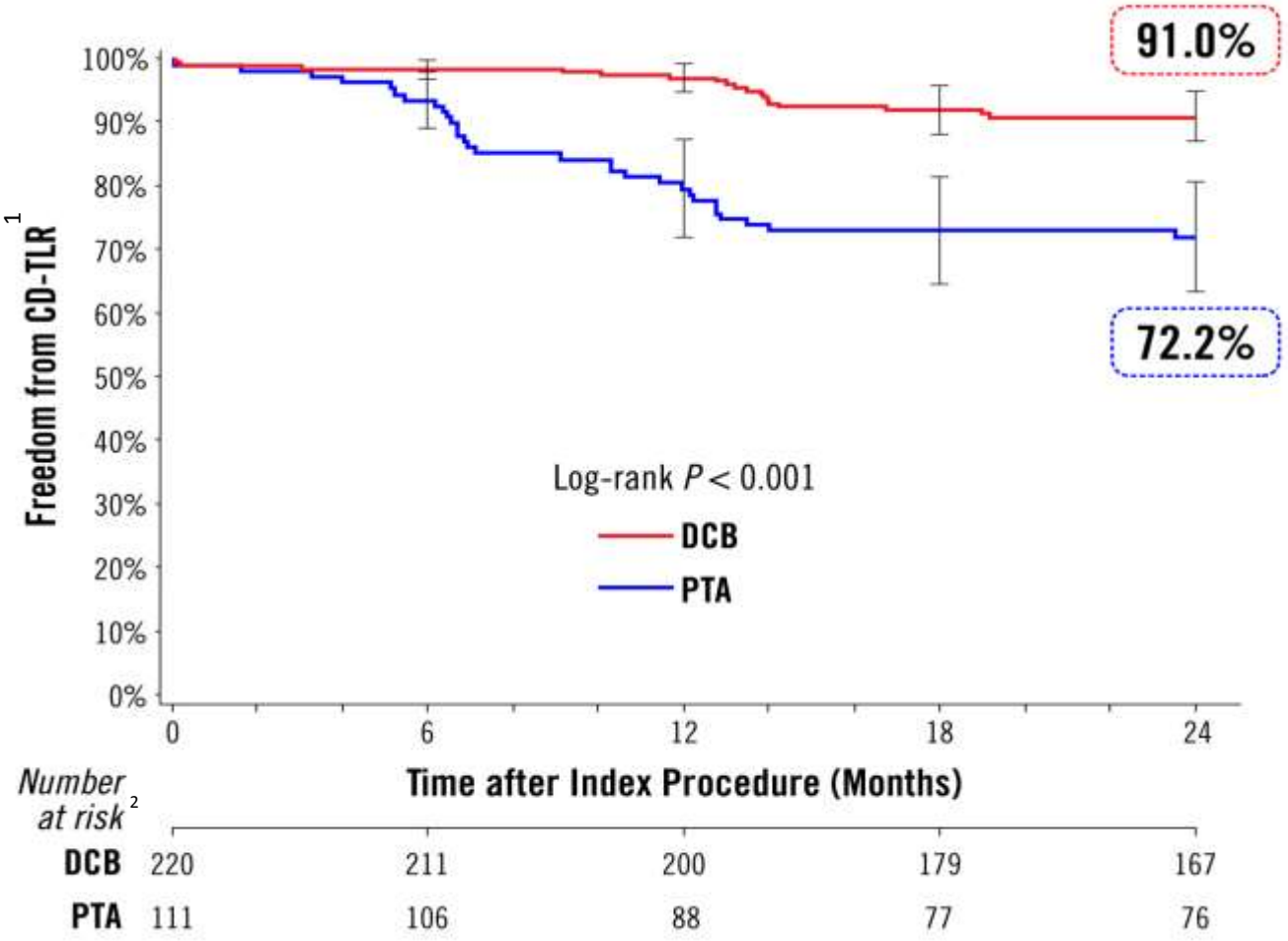
IN.PACT SFA TRIAL EFFICACY OUTCOMES THROUGH 2 YEARS



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.

IN.PACT SFA TRIAL EFFICACY OUTCOMES THROUGH 2 YEARS

Freedom from CD-TLR



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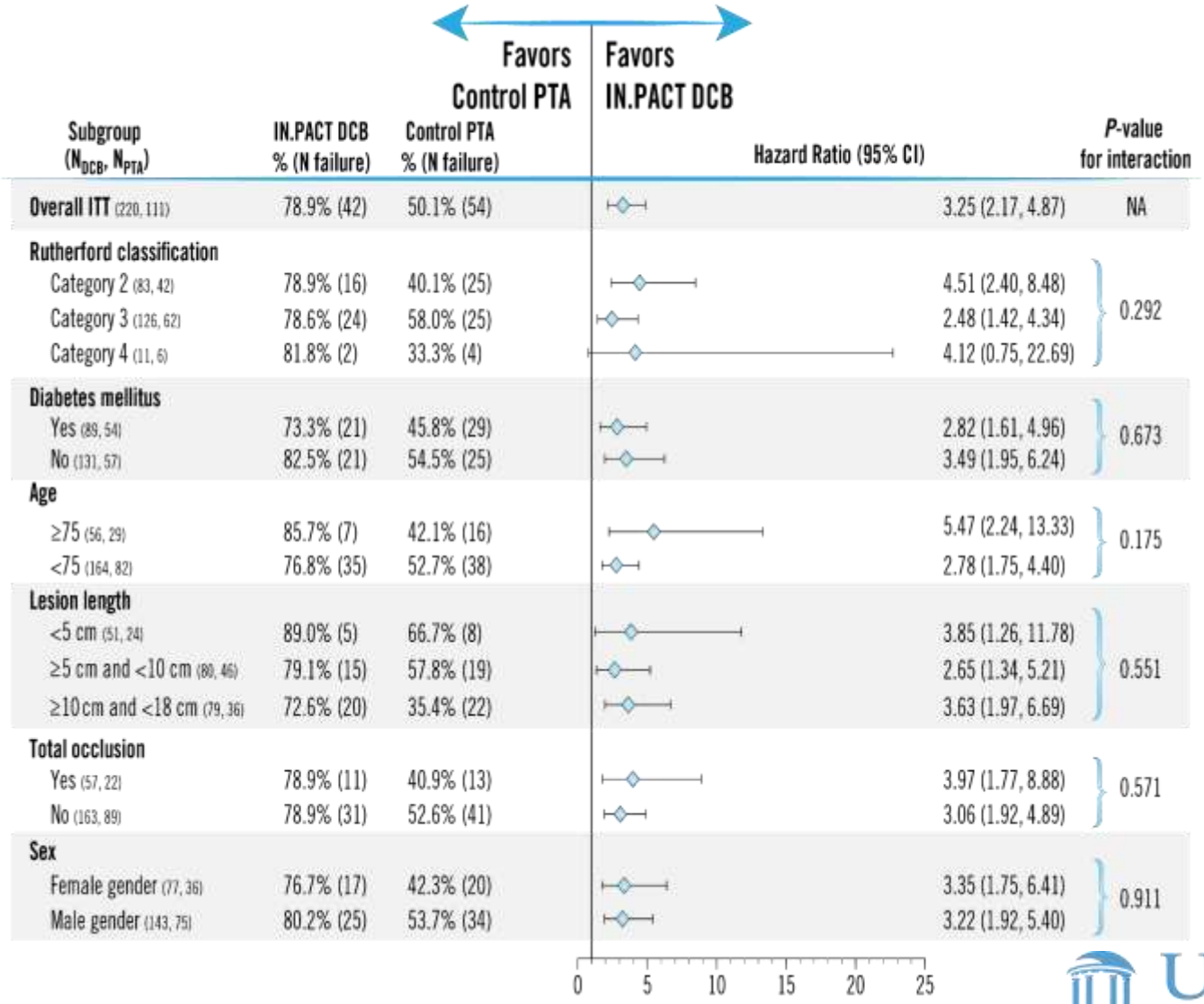
IN.PACT SFA TRIAL SUBGROUP PRIMARY PATENCY THROUGH 2 YEARS



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IN.PACT SFA TRIAL SUBGROUP PRIMARY PATENCY THROUGH 2 YEARS

Gender

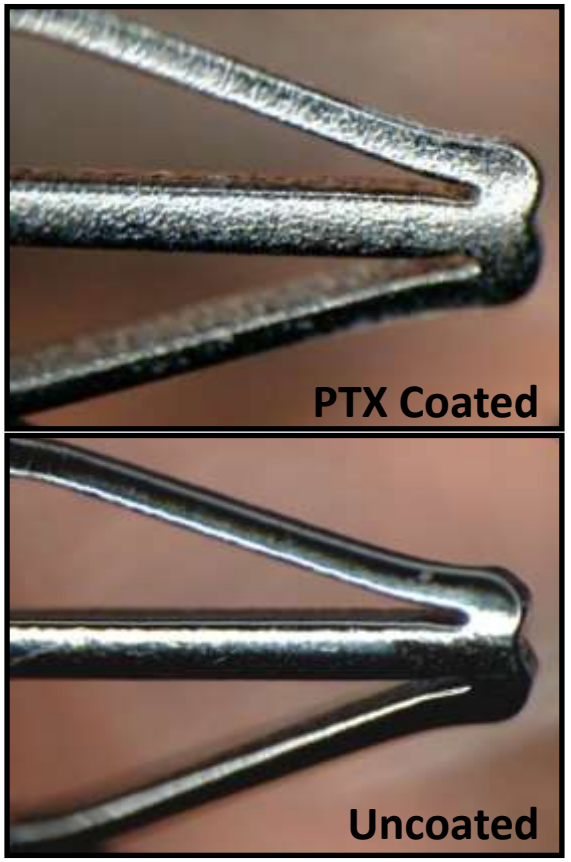
Subgroup	Variable (N_{DCB}, N_{PTA})	IN.PACT™ Admiral™ DCB % (N failure)	PTA % (N failure)	*P*-value[1]
Gender	**Female** (77, 36)	**76.7%** (17)	**42.3%** (20)	<0.001
	Male (143, 75)	**80.2%** (25)	**53.7%** (34)	<0.001

Primary patency defined as 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).

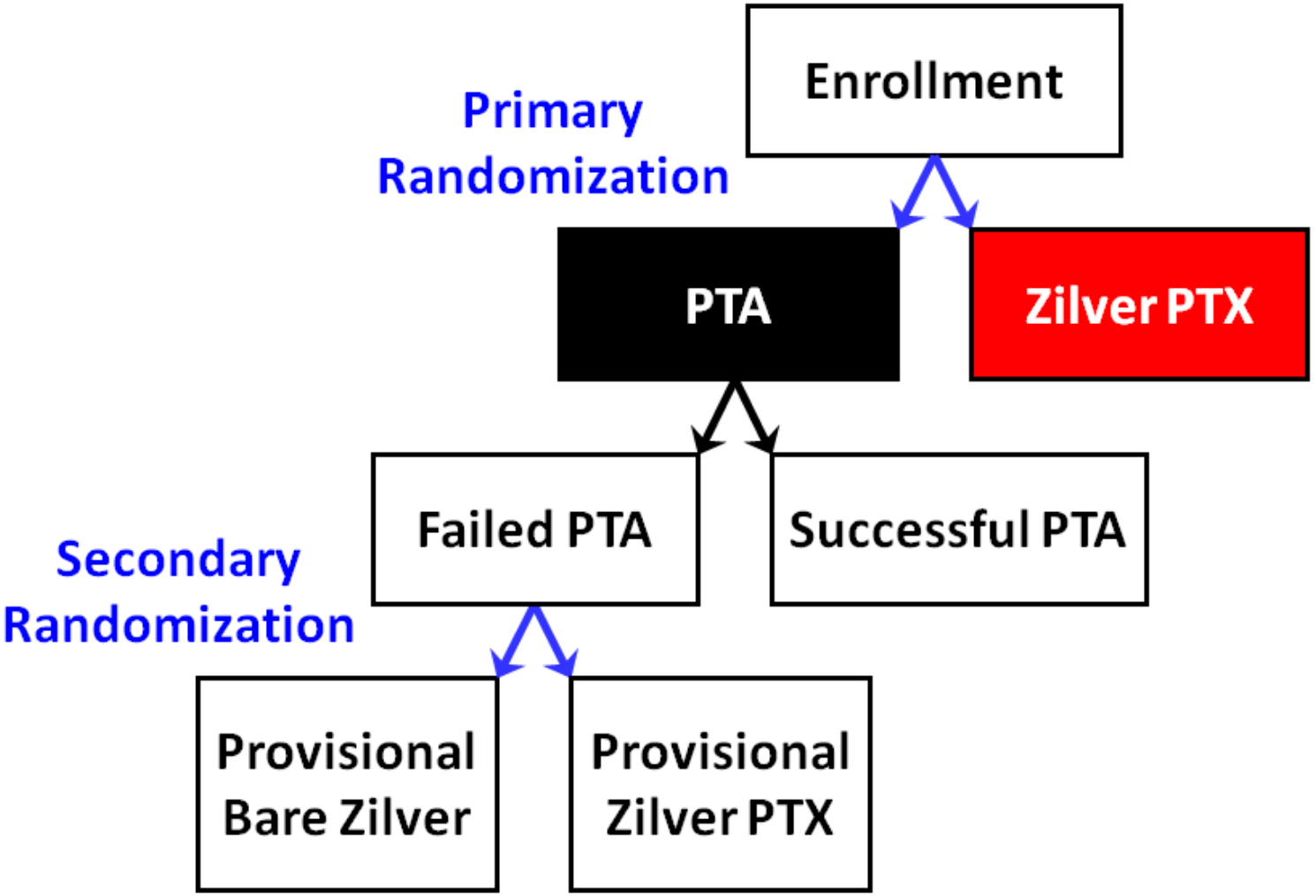
The Zilver® PTX® randomized controlled trial of paclitaxel-eluting stents for femoropopliteal disease: **5-year results**

Drug therapy: Paclitaxel only

- No polymer or binder
- 3 µg/mm^2 dose density



Zilver PTX RCT: Study Design

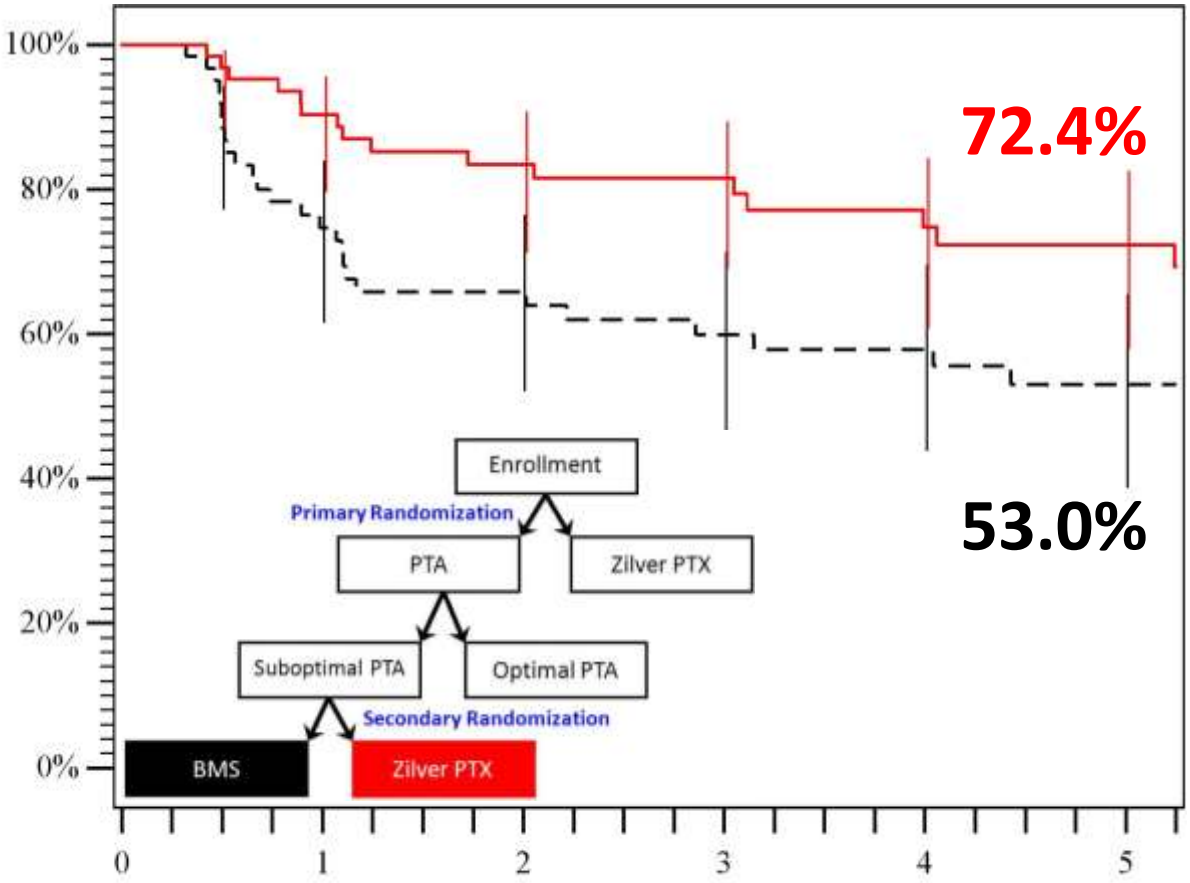


Baseline Lesion Characteristics

		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

5-year Primary Patency (PSVR < 2.0)
Provisional Zilver PTX vs. BMS



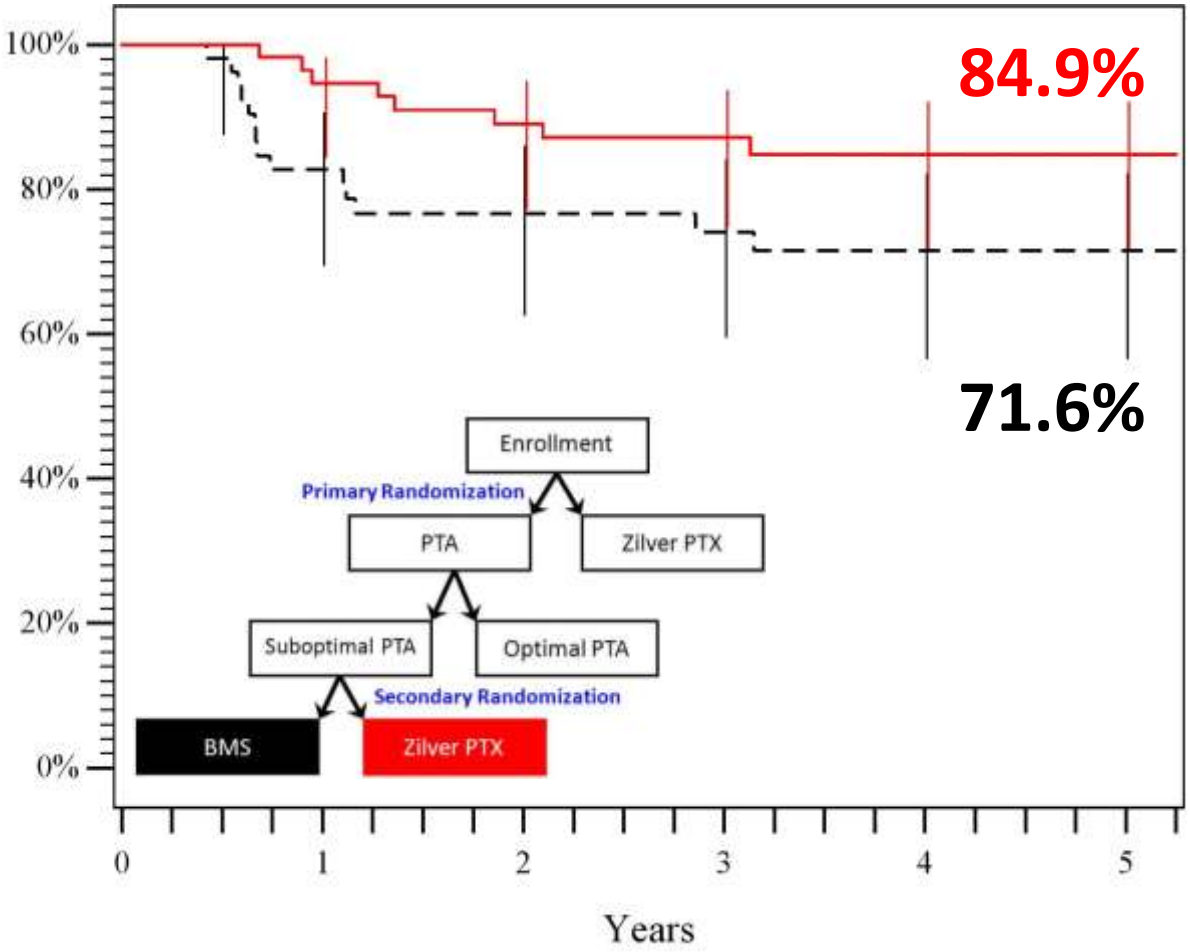
Provisional Zilver PTX

Provisional BMS

$p = 0.03$
log-rank

At 5 years, Zilver PTX shows a sustained drug effect.
There is a 41% reduction in restenosis compared to BMS.

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 shows a sustained drug effect.
There is a 47% reduction in reintervention compared to BMS

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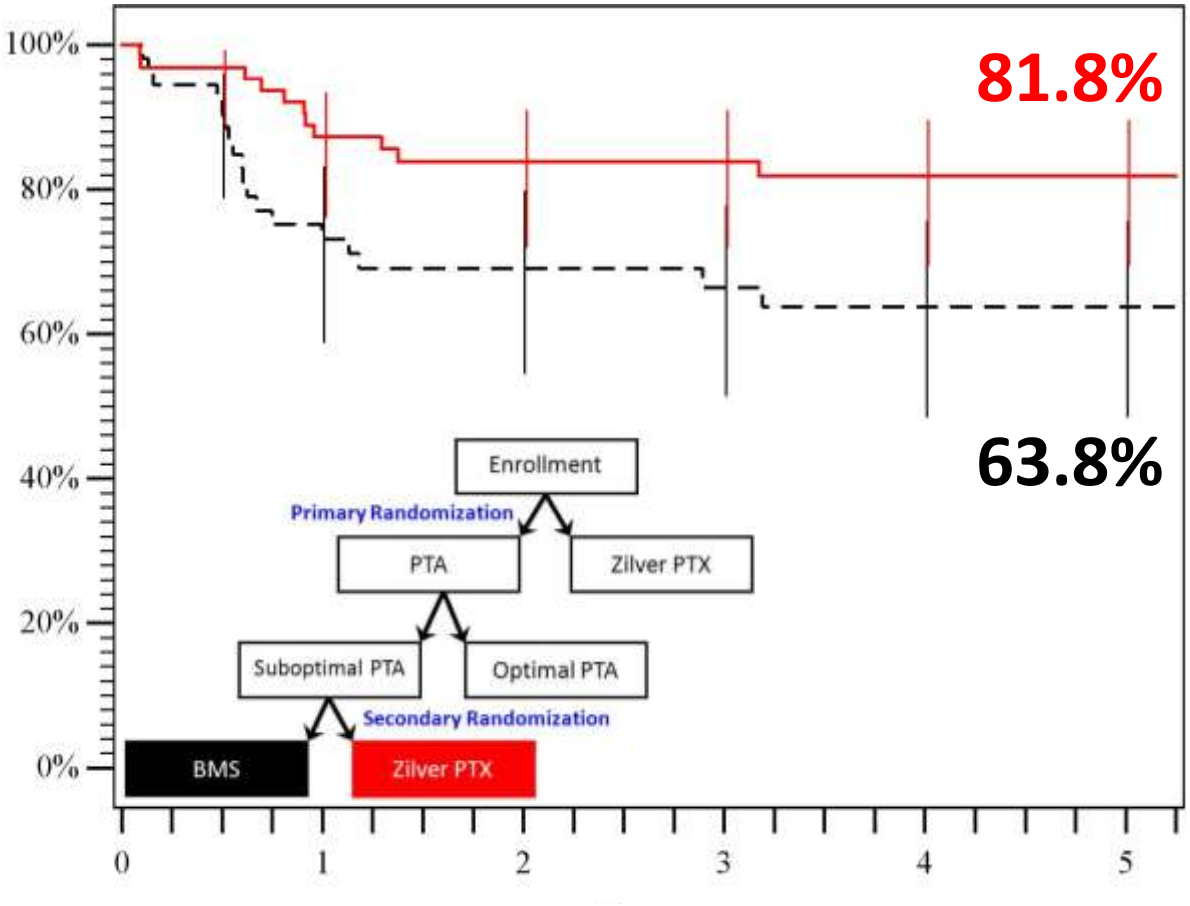
5-year Clinical Benefit Index
Provisional Zilver PTX vs. BMS



At 5 years, Zilver PTX has a superior rate of freedom from persistent or worsening claudication, rest pain, ulcer, or tissue loss

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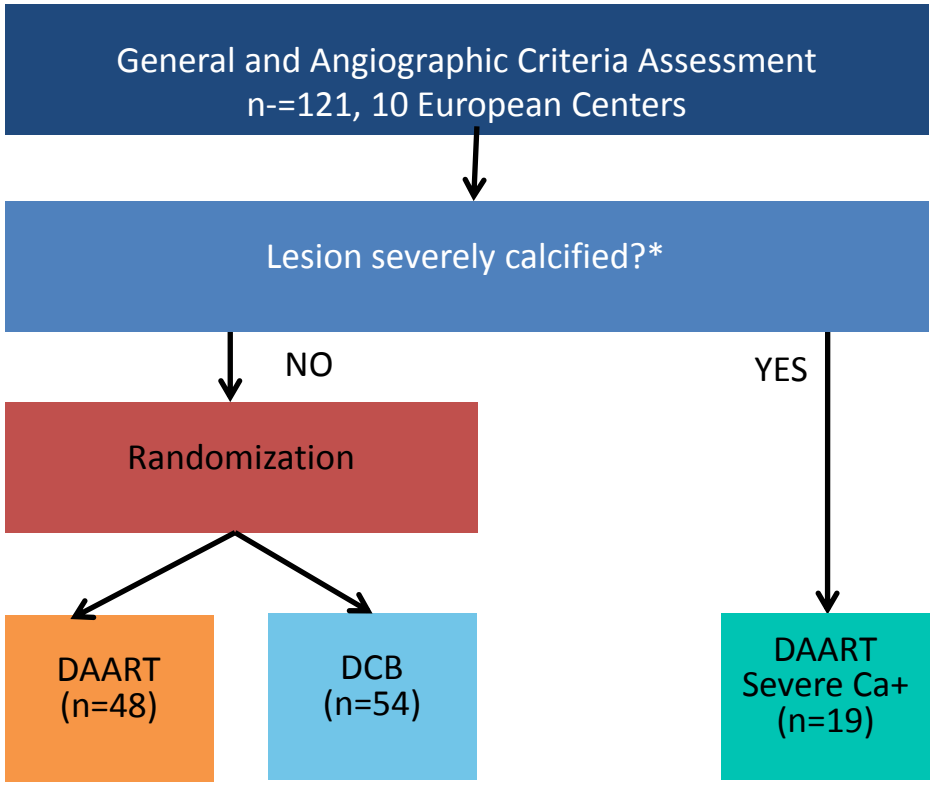
DEFINITIVE AR

STUDY DESIGN



*Defined as: dense circumferential calcification extending > 5 cm

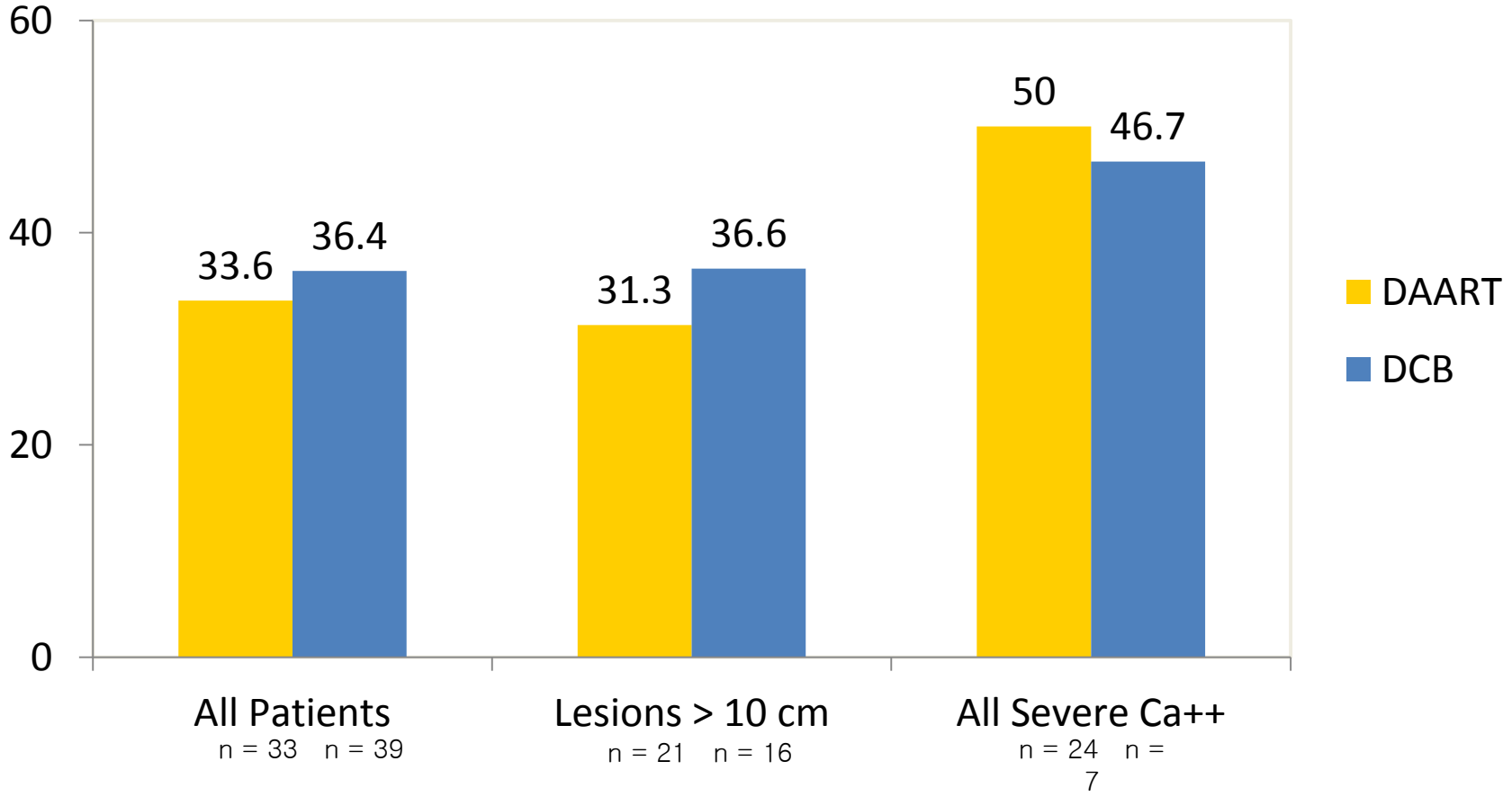
DCB: PaccoCath – Not commercially available

Baseline Lesion Characteristics
Per Core Lab Assessment

	DAART Severe Ca++ Arm (N=19)	DAART (N= 48)	DCB (N = 54)
Lesion Length (cm)	11.9	10.6	9.7
Diameter Stenosis	88%	82%	85%
Reference vessel diameter (mm)	5.1	4.9	4.9
Minimum lumen diameter (mm)	0.7	1.0	0.8

DEFINITIVE AR

STENOSIS AT 12 MONTHS
Core lab angiographic evaluation

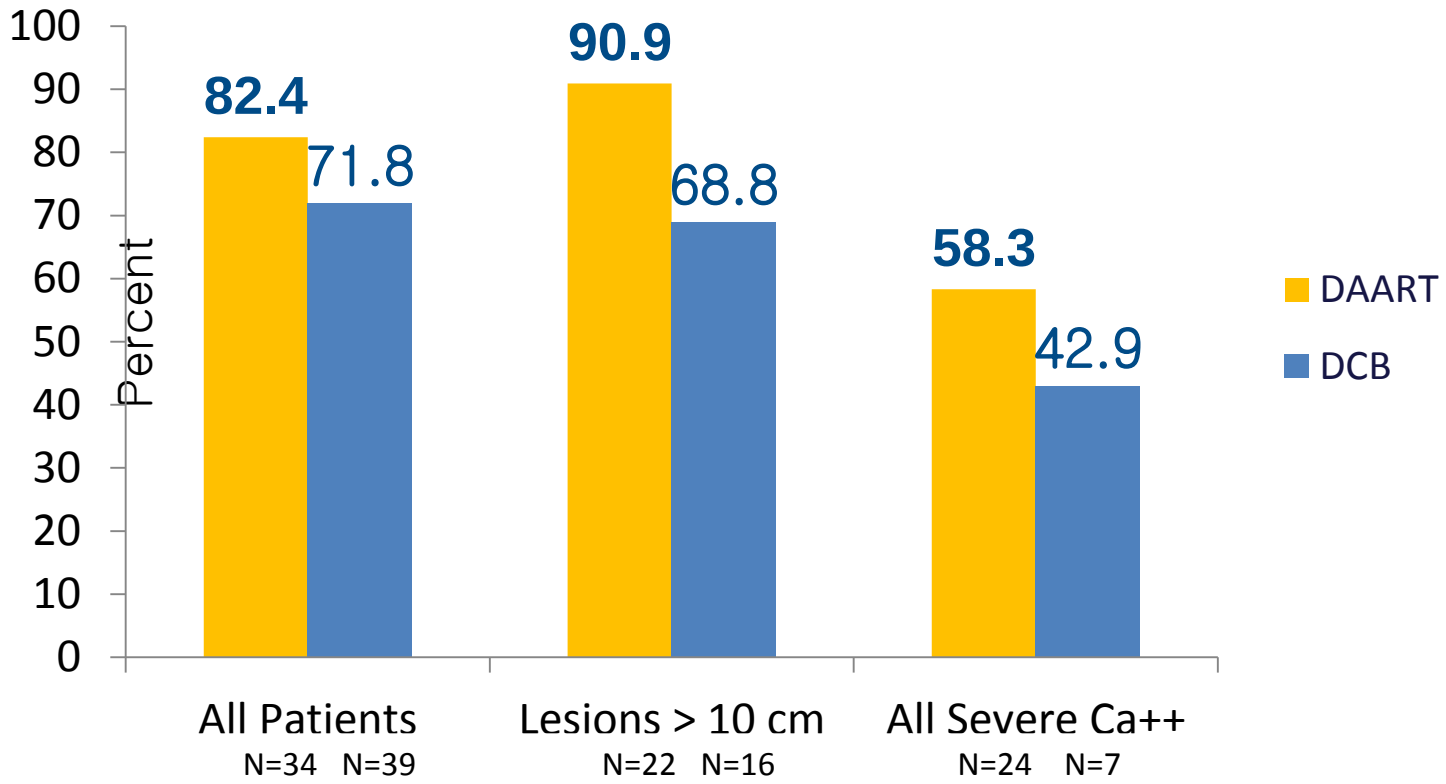


Per Core Lab Assessment. "All Severe Ca++ " group includes all patients with severe calcium (including randomized and non-randomized)

DEFINITIVE AR

ANGIOGRAPHIC PATENCY

Angiographic data shows similar pattern



Per Core Lab Assessment. "All Severe Ca++" group includes all patients with severe calcium (including randomized and non-randomized). Results for all patients who returned for angiographic follow-up.

Hypotheses Generated

- Is there a benefit of atherectomy prior to DCB in patients with
  - Lesions > 10 cm
  - Severe Ca++

Summary

- Large randomized trials show that use of anti-proliferative therapy is safe and beneficial for fem-pop disease
- There does not appear to be a class effect, but hard to compare trials
- Long term data show a benefit for DES, but lesion length studied is short
- Await longer term data from DEB Trials and results from the Imperial Trial for the BSC Eluvia DES randomized against Zilver PTX

Thank You!