LEVANT 2 Clinical Trial

Ken Rosenfield, MD
Massachusetts General Hospital; Boston, MA
Levant 2 Co-Primary Investigator

A Prospective, Multicenter, Single Blind, Randomized, Controlled Trial Comparing DCB vs. Standard Balloon Angioplasty for Treatment of Femoropopliteal Arteries

BARD

Kenneth Rosenfield, MD Disclosure

- **Consultant**
  - Abbott Vascular
- **Equity**
  - Primacea
- **Research or Fellowship Support**
  - Abbott Vascular
  - Atrium
  - Lutonix-Bard
  - IDEV
- Board Member
  - VIVA Physicians
    - www.vivapvd.com

BARD

LEVANT 2 Trial Summary

Primary endpoints	Safety and primary patency of target lesion at 1 year
Number of patients/sites	476 Randomized (2:1) / 55 global sites
Follow-up	**Clinical:** 6, 12, 24 Months **Duplex Ultrasound (DUS):** 0–30 days, 6,12, 24 months **Telephone:** 1, 36, 48, 60 Months
National principal investigators	**Ken Rosenfield:** Mass General, Boston **Dierk Scheinert:** Park Hospital, Leipzig, Germany
Status	First Patient Enrolled July 2011 Last Patient Enrolled July 2012 12 month follow-up visits now complete and monitored

LEVANT 2 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)

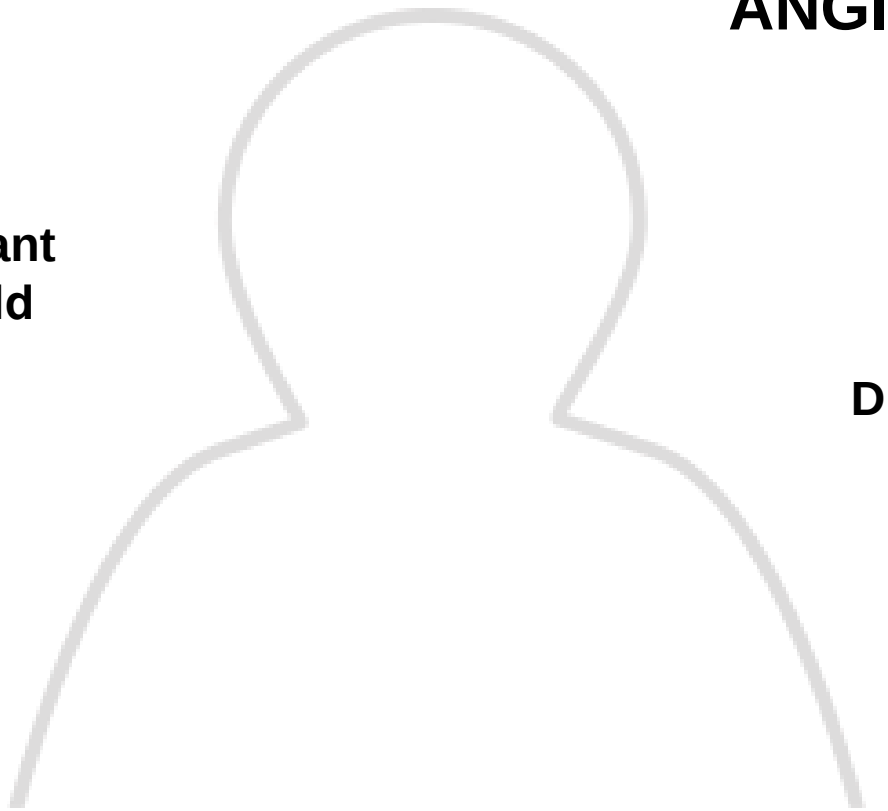
Major Inclusion Criteria

CLINICAL CRITERIA

Male or non-pregnant female ≥18 years old

Rutherford 2–4

Patient is willing to
- Consent
- Comply with follow up schedule



ANGIOGRAPHIC CRITERIA

Length ≤15 cm

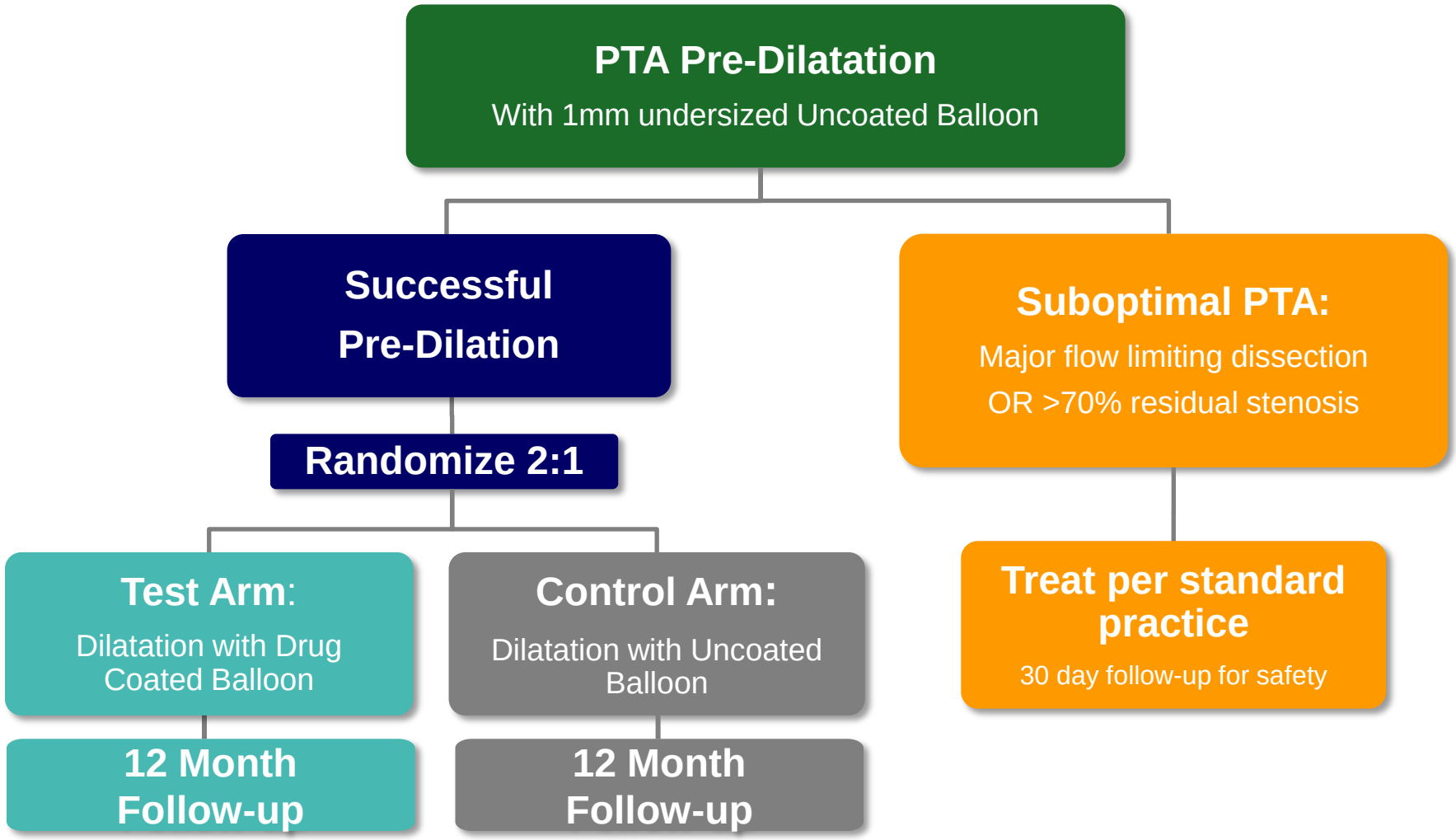
Diameter 4-6 mm

≥70% stenosis

No in-stent restenosis

BARD

Study Designed to Reduce Bias Against Control Group



BARD

Bail-out Stenting Not Considered a TLR or Failure in LEVANT 2

- Unlike some pivotal stent studies for PMA
- Purpose: to assess and compare long-term performance of the treatment modalities alone
- More rigorous way to assess a device

Exclusion of Bail-out Stenting as TLR Makes a Difference

Bail-out Stent considered a failure	RESILIENT[1]		Zilver® PTX[2]	
	%	%	%	%
	LifeStent®	PTA	Zilver® PTX	PTA
12-Month Primary Patency (KM)	81.5	36.7	83.1	32.8
Stent vs. PTA only (Bail-out stents excluded)	**LifeStent® ITT**	**PTA (as treated)**	**Zilver® PTX ITT**	**PTA (optimal)**
12-Month Primary Patency (KM)	81.5	61.5	83.1	65.3

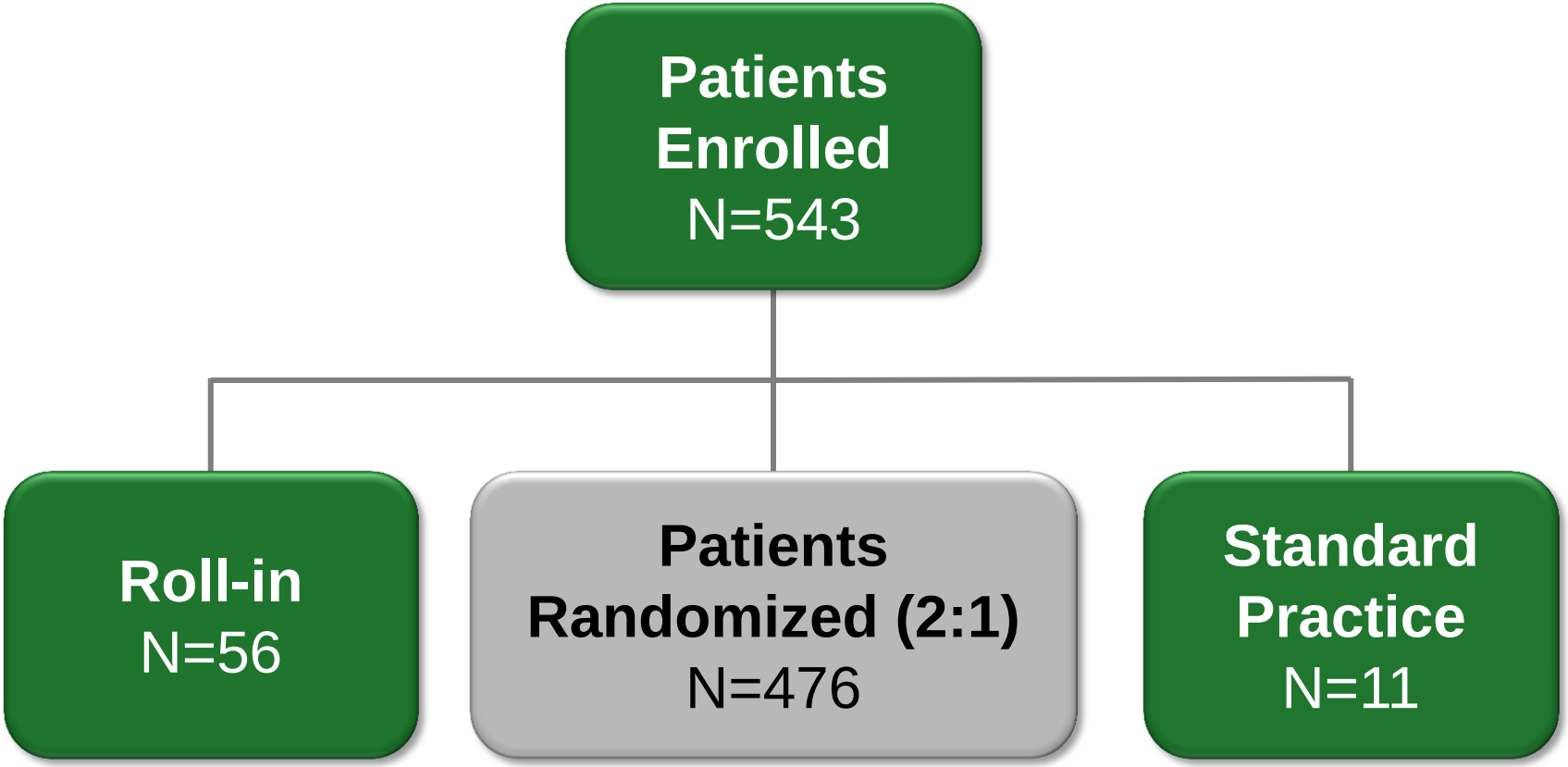
[1] Circ Cardiovasc Interv 2010;3:267-276 & J Endovasc Ther 2012;19:1-9.

[2] Circ Cardiovasc Interv 2011;4:495-504.

BARD

6-month Data for Randomized Cohort

Patients Enrolled



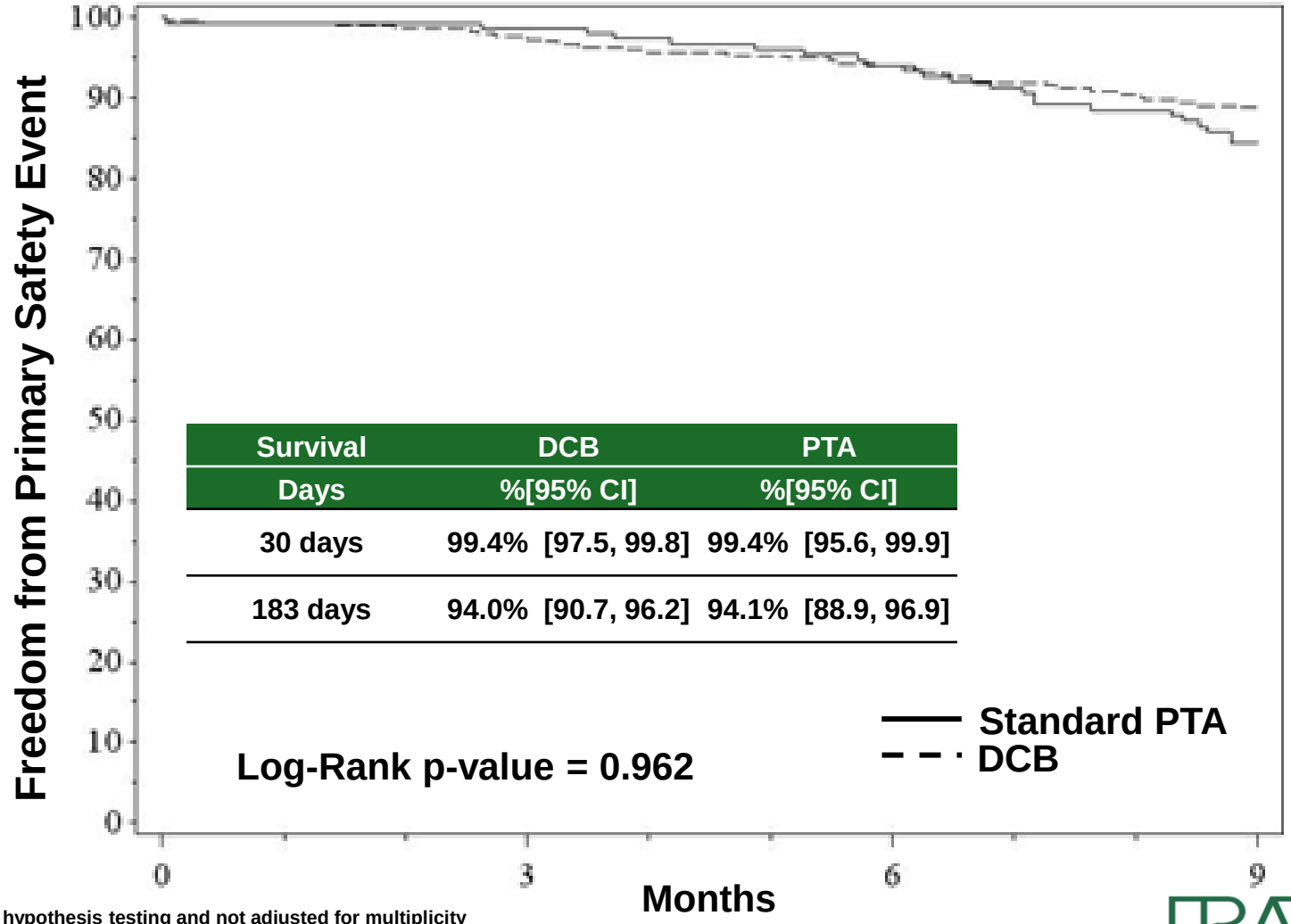
Baseline Demographics (ITT)

	DCB	Standard PTA	P-value	Pooled
Age, Mean ± SD (n)	67.8 ± 10.0 (316)	69.0 ± 9.0 (160)	0.207	68.2 ± 9.7 (476)
Male gender, % (n/N)	61.1% (193/316)	66.9% (107/160)	0.216	63.0% (300/476)
Obesity	34.8% (110/316)	30.6% (49/160)	0.360	33.4% (159/476)
Current Smoker	35.1% (111/316)	33.8% (54/160)	0.548	34.7% (165/476)
Dyslipidemia	89.6% (283/316)	85.6% (137/160)	0.208	88.2% (420/476)
Diabetes	43.4% (137/316)	41.9% (67/160)	0.758	42.9% (204/476)
Hypertension	89.2% (282/316)	87.5% (140/160)	0.572	88.7% (422/476)
CAD	49.7% (157/316)	48.1% (77/160)	0.748	49.2% (234/476)
Rutherford Grade			0.521	
2	29.4% (93/316)	34.4% (55/160)		31.1% (148/476)
3	62.7% (198/316)	57.5% (92/160)		60.9% (290/476)
4	7.9% (25/316)	8.1% (13/160)		8.0% (38/476)
ABI	0.7 ± 0.2 (306)	0.7 ± 0.2 (156)	0.364	0.7 ± 0.2 (462)

Lesion/Procedural Characteristics (ITT)

	DCB	Standard PTA	P-value	Pooled
Two lesions treated	1.9% (6/316)	3.1% (5/160)	0.400	2.3% (11/476)
Total Lesion Length (mm)	62.9 ± 41.5 (315)	63.6 ± 40.3 (160)	0.866	63.2 ± 41.1 (475)
Treated Length (mm)	107.7 ± 47.0 (316)	107.3 ± 49.3 (160)	0.933	107.6 ± 47.7 (476)
Calcification	59.2% (187/316)	57.5% (92/160)	0.726	58.6% (279/476)
Severe	17.6% (33/187)	13.0% (12/92)	0.326	16.1% (45/279)
Total Occlusion	20.6% (65/316)	21.9% (35/160)	0.741	21.0% (100/476)
%DS post-treatment	23.4 ± 12.3 (316)	23.8 ± 12.3 (158)	0.703	23.5 ± 12.3 (474)
Bail-out Stenting	2.5% (8/316)	6.9% (11/160)	0.022	4.0% (19/476)
Dissection	63.7% (200/314)	72.3% (115/159)	0.060	66.6% (315/473)
Final Procedural Dissection Grade			0.075	
Grade A	59.5% (119/200)	53.9% (62/115)		57.5% (181/315)
Grade B	36.5% (73/200)	35.7% (41/115)		36.2% (114/315)
Grade C	4.0% (8/200)	10.4% (12/115)		6.3% (20/315)
Procedural success (core lab)	88.9% (281/316)	86.8% (138/159)	0.497	88.2% (419/475)
Geographic Miss (core lab)	7.9% (24/316)	21.9% (35/160)	<0.001	12.6% (60/476)

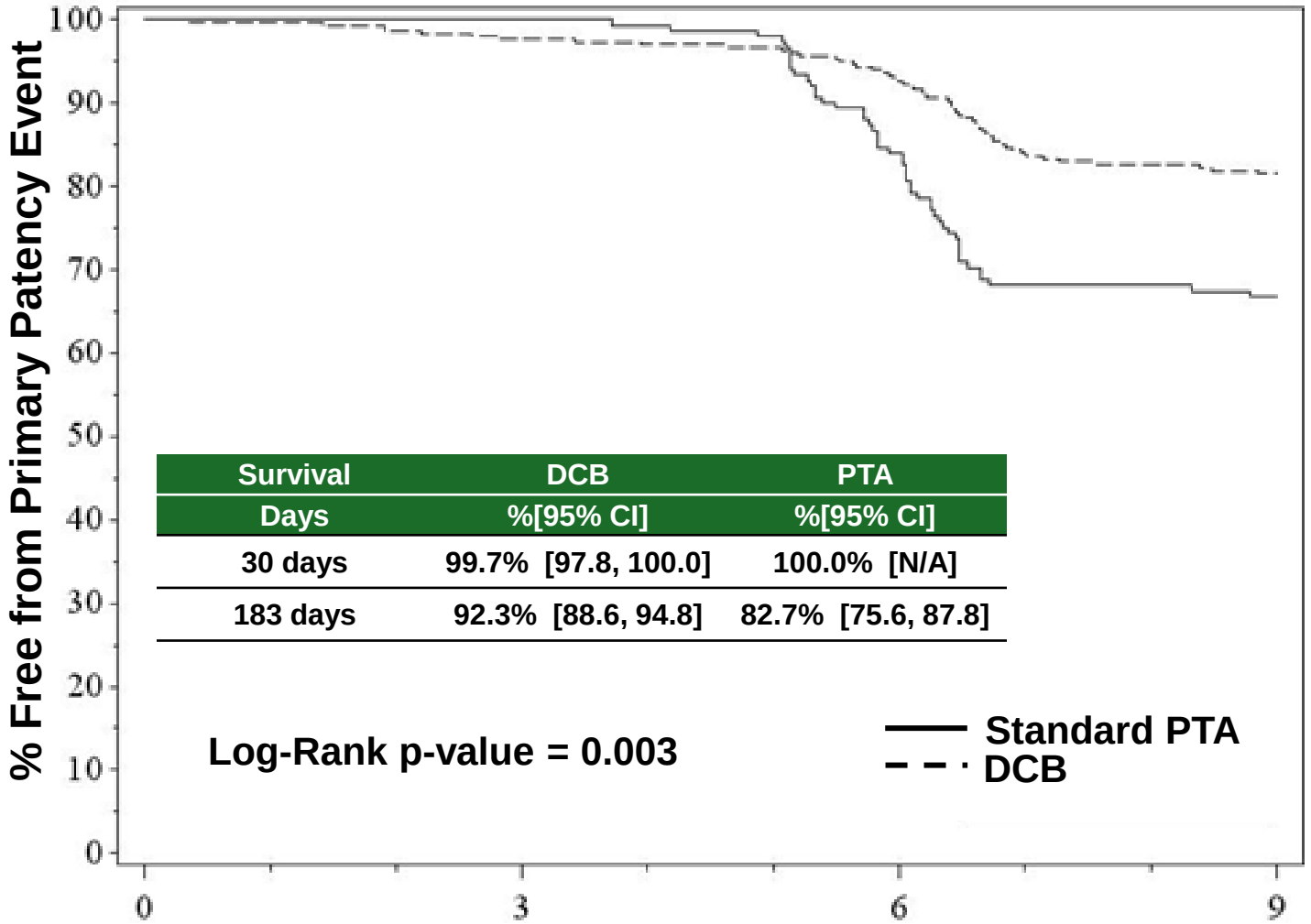
Composite Safety Endpoint - KM[1]



Survival	DCB	PTA
Days	%[95% CI]	%[95% CI]
30 days	99.4% [97.5, 99.8]	99.4% [95.6, 99.9]
183 days	94.0% [90.7, 96.2]	94.1% [88.9, 96.9]

[1]Not pre-specified for hypothesis testing and not adjusted for multiplicity

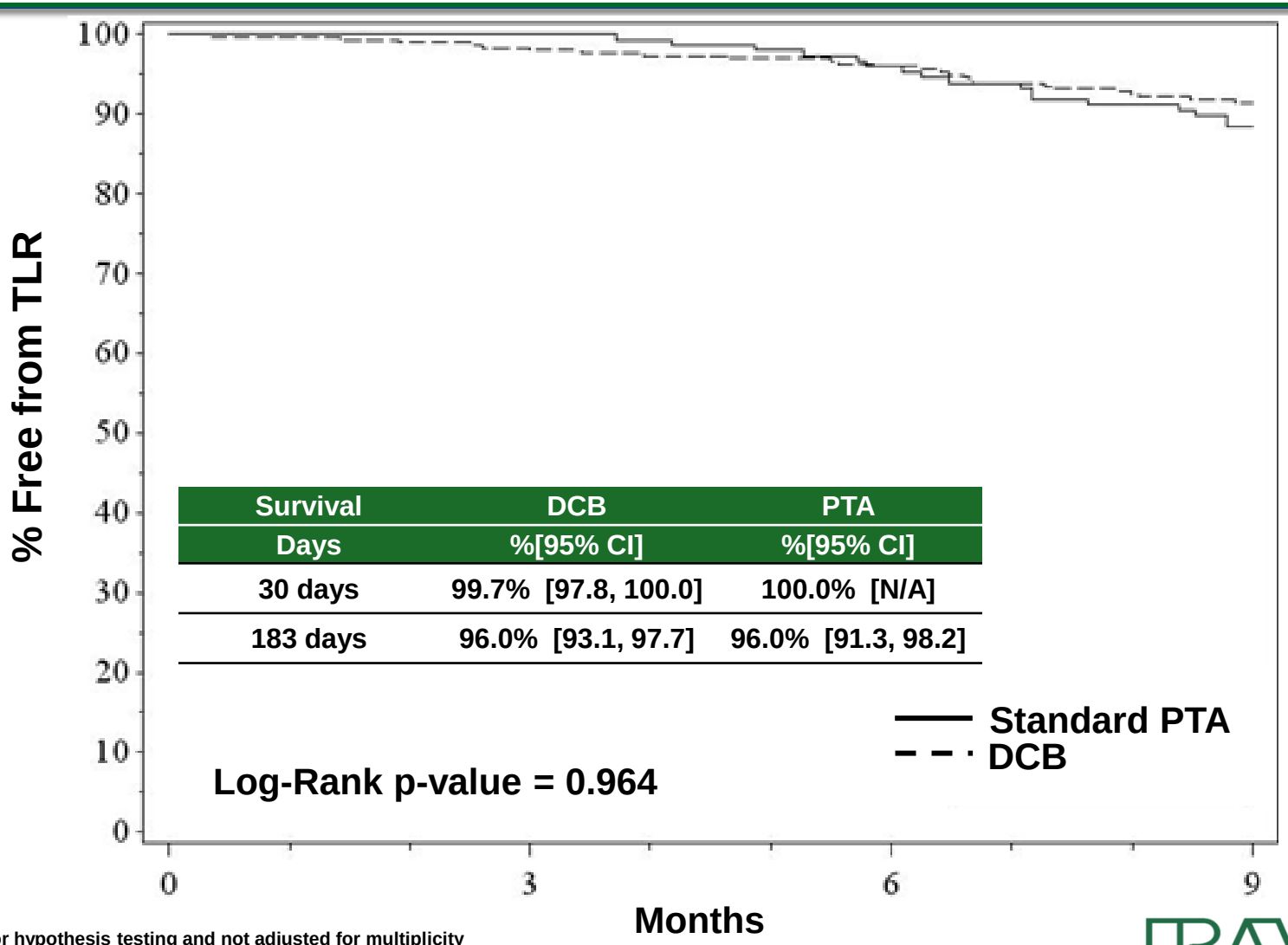
Primary Patency - KM[1]



Survival	DCB	PTA
Days	%[95% CI]	%[95% CI]
30 days	99.7% [97.8, 100.0]	100.0% [N/A]
183 days	92.3% [88.6, 94.8]	82.7% [75.6, 87.8]

[1]Not pre-specified for hypothesis testing and not adjusted for multiplicity

Freedom from TLR - KM[1]



Survival Days	DCB %[95% CI]	PTA %[95% CI]
30 days	99.7% [97.8, 100.0]	100.0% [N/A]
183 days	96.0% [93.1, 97.7]	96.0% [91.3, 98.2]

[1]Not pre-specified for hypothesis testing and not adjusted for multiplicity

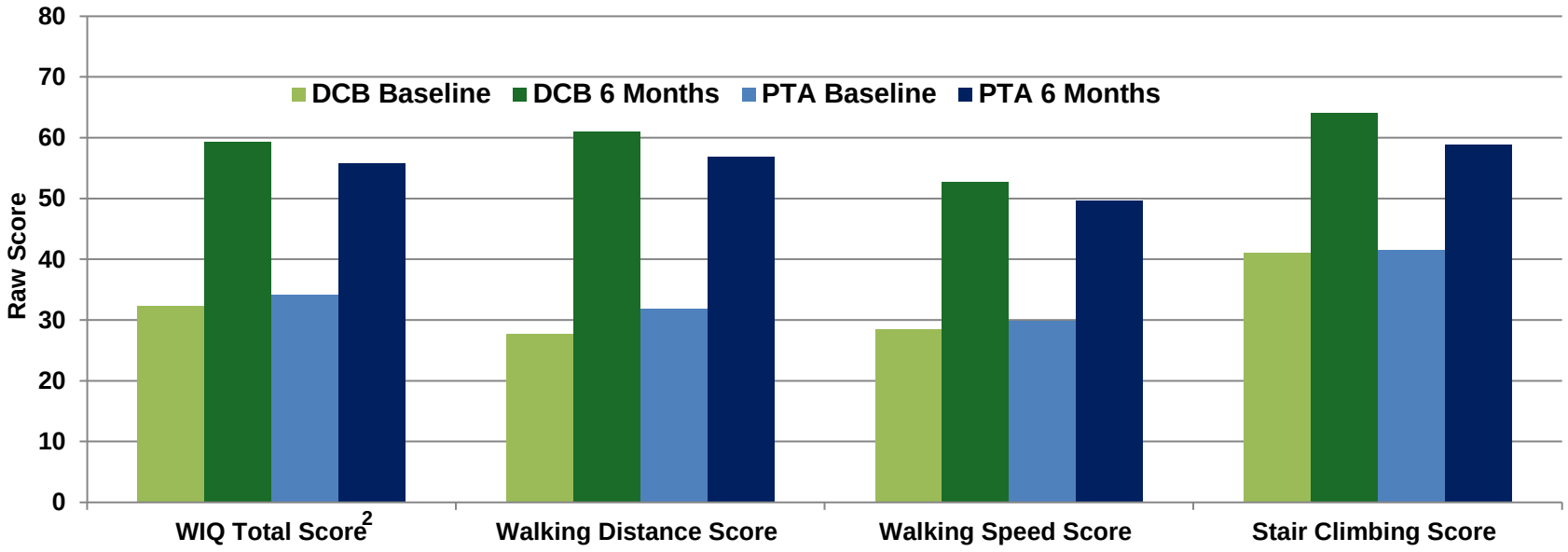
BARD

Other Secondary Endpoints at 6 Months[1]

Measure	DCB % (n/N)	PTA % (n/N)	Difference[2]	P-value[2]
Binary Restenosis	17.4% (47/270)	33.8% (47/139)	-16.4%	<0.001
Composite Safety Endpoint Failure	8.0% (24/299)	8.6% (13/151)	-0.6%	0.016 (non-inferiority)
TVR	6.7% (20/298)	7.9% (12/151)	-1.2%	0.633
Death	0.7% (2/301)	1.3% (2/152)	-0.7%	0.497
Amputation	0.3% (1/299)	0.0% (0/151)	0.3%	0.366
Embolization (any during index procedure)	0.6% (2/316)	1.9% (3/160)	-1.2%	0.226
Re-intervention for Thrombosis or Embolism (target vessel)	0.3% (1/298)	0.7% (1/151)	-0.4%	0.623

[1]Proportions through close of 6-month follow-up window (212 days)
[2]Not pre-specified for hypothesis testing and not adjusted for multiplicity

Walking Impairment Questionnaire



Change From Baseline[1]	DCB-PTA Difference % (95% CI)
WIQ Total Score[2]	6.0% (0.1, 12.0)
Walking Distance Score	7.6% (0.1, 15.2)
Walking Speed Score	4.3% (-1.9, 10.5)
Stair Climbing Score	6.7% (-0.2, 13.5)

[1]Not pre-specified for hypothesis testing and confidence intervals not adjusted for multiplicity

[2]Combined score is calculated as the mean of the distance, speed, and stair scores.

BARD

Summary

- Rigorous trial designed to reduce bias
  - Controlled pre-dilatation prior to randomization to limit the number of bail-out stents
  - Did not count bail-out stenting as TLR
  - Blinded clinician to DUS
- Six month data is promising regarding safety and efficacy