LUTONIX® BTK Trial

A Prospective, Multicenter, Single Blind, Randomized, Controlled Trial Comparing the Lutonix Drug Coated Balloon vs. Standard Balloon Angioplasty for Treatment of Below-the-Knee (BTK) Arteries

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Disclosures

Consultant to:

- Abbott Vascular
- Bard Peripheral Vascular/Lutonix
- Boston Scientific
- Cardiovascular Systems, Inc.
- Cook Medical
- Covidien/Medtronic
- Spectranetics
- Terumo Medical

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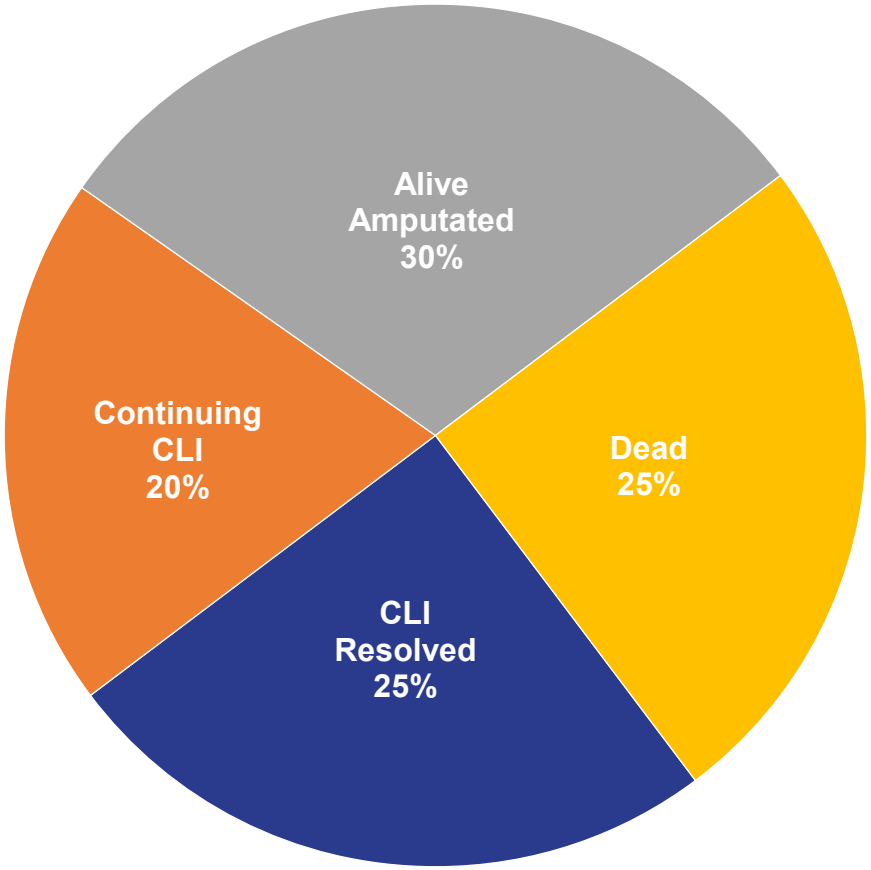
CLI Impact

1 year after primary treatment for CLI



Norgren et al, TASC II. (2008). JOURNAL OF VASCULAR SURGERY Volume 45, Number 1, Supplement S

- Approximately 120,000 amputations are performed annually
- The estimated lifetime direct healthcare cost for an amputee patient is $794,027
- When aggregated for the total number of lower extremity amputation patients annually, the expected lifetime cost is estimated at roughly $95.2 billion USD

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LUTONIX® Global Below-the-Knee Study

Enrollment by Geography

US	275
EU	122
Japan	40
Canada	5

442 Randomized Subjects

(DCB - 287, PTA - 155)

Multicenter participation:

51 sites

8 countries

Enrollment: Jun 2013 – Dec 2017

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Study Synopsis

Objective
To demonstrate the superior efficacy and non-inferior safety of the Lutonix DCB by direct comparison to standard PTA for treatment of stenosis or occlusion of below-the-knee arteries

Study Design
Prospective, Multicenter, Single Blind, Randomized, Safety and Efficacy

Test Device
LUTONIX® 0.014” OTW Drug Coated PTA Dilatation Catheter

Randomization
Subjects will be randomized 2:1 to Lutonix DCB or standard PTA catheter.

Clinical Follow-up
1, 6, 12, 24, 36 Months

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Primary Endpoints

SAFETY

Freedom from Major Adverse Limb Events (MALE) & All-Cause Perioperative Death (POD) at 30 Days

★ ***Amputation (above ankle)***
★ ***Major re-intervention***
- New bypass graft
- Jump/interposition graft revision
- Thrombectomy/thrombolysis

EFFICACY

Composite of Limb Salvage and Primary Patency at 6 Months

★ ***Defined as freedom from a composite of above ankle amputation, target vessel occlusion, and clinically-driven target lesion revascularization***

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Patient Eligibility

Inclusion Criteria

✓ Male or non-pregnant female ≥18 years of age

✓ Rutherford 3-5

✓ Life expectancy ≥ 1 year

✓ Significant stenosis (≥70%)

✓ A patent inflow artery

✓ Target vessel(s) diameter between 2 and 4 mm

✓ Target vessel(s) reconstitute(s) at or above the ankle

Exclusion Criteria

✓ History of stroke within 3 months

✓ History of MI, thrombolysis or angina within 30 days of enrollment

✓ GFR ≤ 30 ml/min per 1.73m^2

✓ Acute limb ischemia

✓ In-stent restenosis of target lesion

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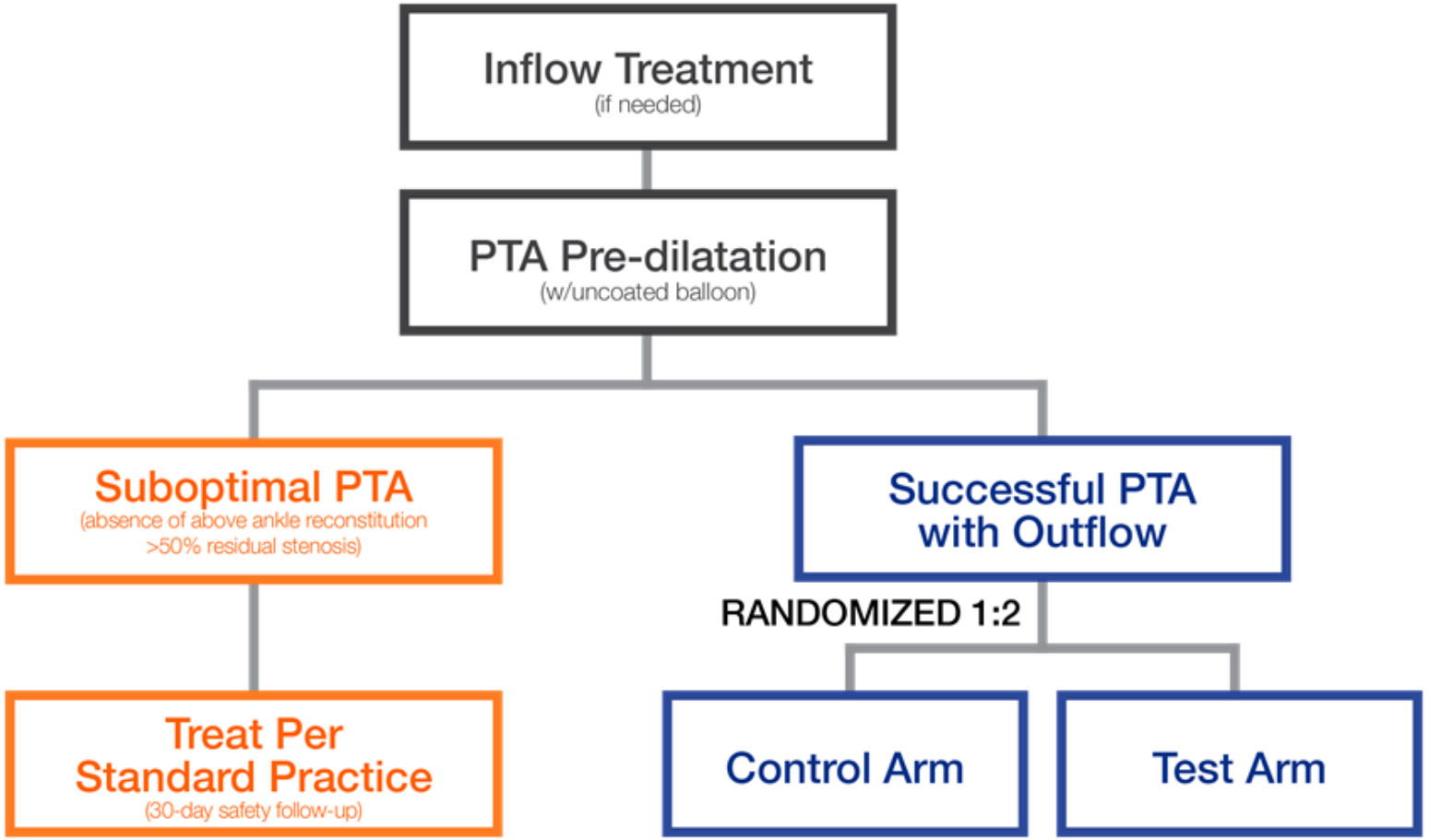
Study Flowchart



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Demographics and Risk Factors

	DCB N=287	PTA N=155	P-Value
Age, Mean ± SD (n)	72.9 ± 9.65 (287)	72.9 ± 9.62 (155)	0.9586
Gender, % (n/N) Male Female	 70.4% (202/287) 29.6% (85/287)	 67.1% (104/155) 32.9% (51/155)	0.5173
Race, % (n/N) American Indian or Alaska Native Asian Black or African American White Other	 0.3% (1/287) 8.7% (25/287) 11.5% (33/287) 78.7% (226/287) 0.7% (2/287)	 0 9.7% (15/155) 7.7% (12/155) 81.9% (127/155) 0.6% (1/155)	0.7468

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Demographics and Risk Factors

	DCB N=287	PTA N=155	P-Value
History of Risk Factors, % (n/N) Diabetes Dyslipidemia Hypertension Cigarette Smoking Current Former	99.3% (285/287) 71.1% (204/287) 78.4% (225/287) 92.0% (264/287) 59.2% (170/287) 15.0% (43/287) 44.3% (127/287)	100.0% (155/155) 68.4% (106/155) 74.8% (116/155) 95.5% (148/155) 57.4% (89/155) 12.3% (19/155) 42.5% (70/155)	0.5436
Subject has Undergone Any Previous Cardio Vascular Interventions	72.8% (209/287)	74.8% (116/155)	0.735
Subject has Undergone Previous Peripheral Vascular Interventions	53.7% (154/287)	54.2% (84/155)	0.921

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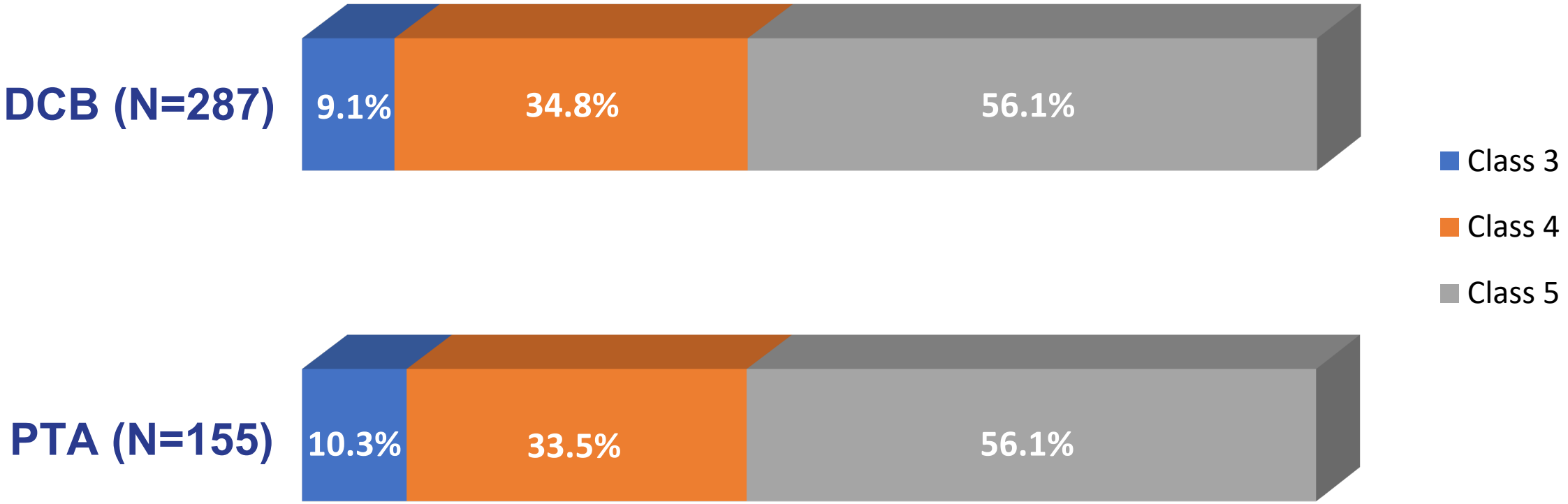
Baseline Rutherford Category



P-Value 0.9181

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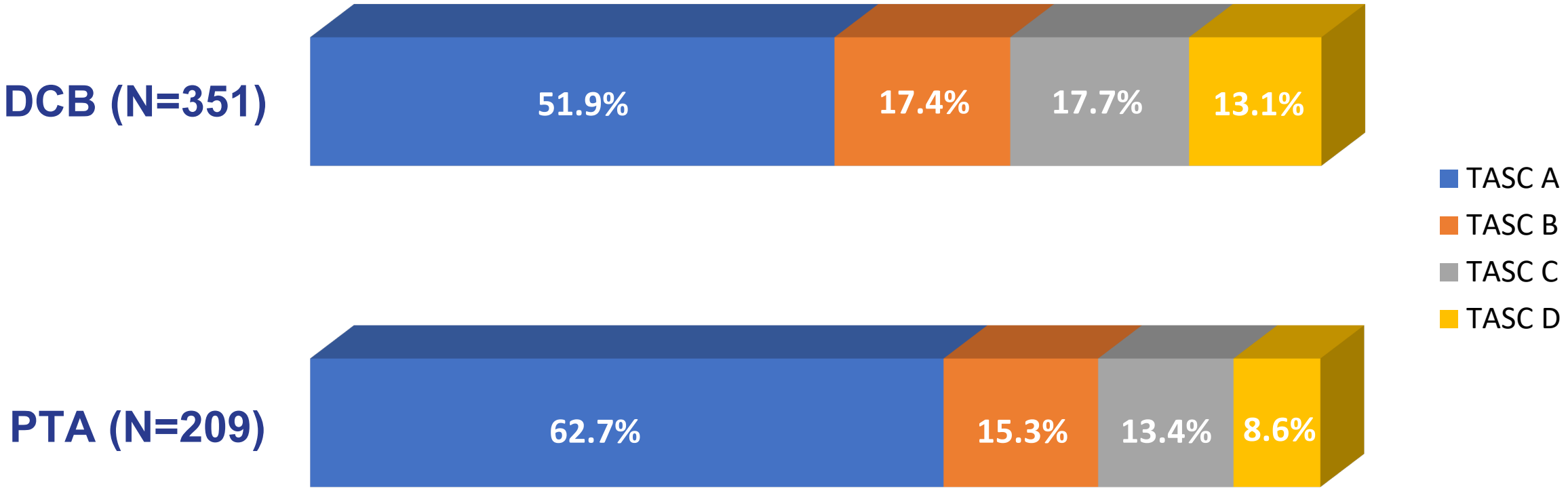
Lesion Characteristics



P Value 0.073

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Preliminary Baseline Angio Data

	Treated Lesions DCB	Treated Lesions PTA
Number of Lesions by Vessel, % (n/N) 1 2 3 6	 85.4% (275/322) 12.1% (39/322) 2.2% (7/322) 0.3% (1/322)	 79.2% (145/183) 18.6% (34/183) 2.2% (4/183) 0.0% (0/183)
Mean Target Lesion Length, mm (n/N)	111.8 ± 92.6 mm (349/352)	94.7 ± 85.4 mm (206/213)
Mean Initial % Stenosis, % (n/N)	86.7 ± 14.5% (352/352)	84.8 ± 14.5% (212/213)

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Preliminary Baseline Angio Data (Cont.)

	Treated Lesions DCB	Treated Lesions PTA
Mean RVD, mm (n/N)	2.5 ± 0.61 mm (350/352)	2.6 ± 0.62 mm (213/213)
Run-off Present through Foot, % (n/N)	94.5% (310/328)	95.0% (192/202)
Any Calcification, % (n/N)	59.9% (211/352)	54.2% (115/212)
Severe Calcification, % (n/N)	15.1% (53/352)	13.2% (28/212)
CTO, % (n/N)	36.1% (137/380)	33.3% (75/225)

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Preliminary Baseline Angio Data (Cont.)

	DCB	PTA
Vessel Locations, % (n/N)		
Popliteal	10.2% (33 / 322)	9.3% (17 / 183)
Tibioperoneal Trunk	28.0% (90 / 322)	31.1% (57 / 183)
Anterior Tibial	41.0% (132 / 322)	35.5% (65 / 183)
Posterial Tibial	24.2% (78 / 322)	27.3% (50 / 183)
Peroneal	23.6% (76 / 322)	24.6% (45 / 183)

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Primary Endpoints (30-Day Safety*)

	DCB N=287 % (n/N)	PTA N=155 % (n/N)	Difference in Response % (95% CI)	P-Value
Free from Primary Safety Event at 30 Days	99.3% (283/285)	99.4% (154/155)	-0.1% (-3.9%, 3.8%)	<.0001

*Freedom at 30 days from TVR, major index limb amputation, and device and all cause death.

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Primary Endpoints (6 Month Efficacy*)

	DCB N=287	PTA N=155	Difference in Response (95% CI)	P-Value
Free from Primary Efficacy Failure at 6 Months	73.7% (196/266)	63.5% (87/137)	10.2% (-0.2%, 18.7%)	0.0273

*Freedom at 6 months from major index limb amputation, target lesion occlusion and CD-TLR.

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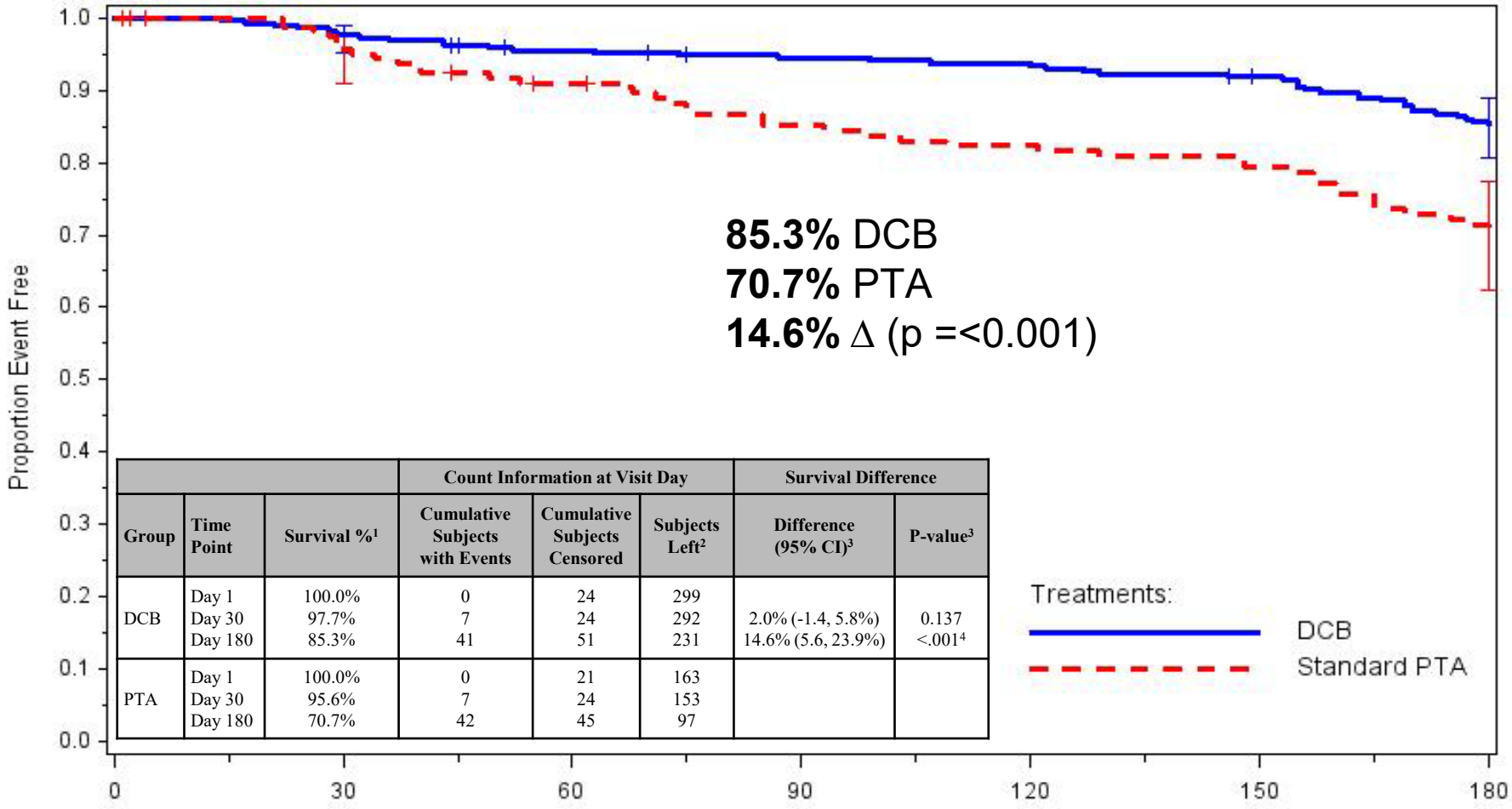
Primary Endpoints (KM 6 Month Efficacy)



			Count Information at Visit Day			Survival Difference	
Group	Time Point	Survival %[1]	Cumulative Subjects with Events	Cumulative Subjects Censored	Subjects Left[2]	Difference (95% CI)[3]	P-value[3]
DCB	Day 1 Day 30 Day 180	100.0% 97.7% 85.3%	0 7 41	24 24 51	299 292 231	 2.0% (-1.4, 5.8%) 14.6% (5.6, 23.9%)	 0.137 <.001[4]
PTA	Day 1 Day 30 Day 180	100.0% 95.6% 70.7%	0 7 42	21 24 45	163 153 97		

[1] Kaplan-Meier estimate of proportion of subjects without a composite failure event at the visit day
[2] Subjects ongoing without an event at the visit day
[3] 95% CI for difference and p-value for one-sided test that DCB response is less than or equal to Standard PTA response obtained from Kaplan-Meier estimates and standard error estimates from Greenwood's method

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Primary Endpoints by Gender

	DCB	PTA	P-Value
Primary Safety			
Gender, % (n/N)			
Male	99.0% (198/200)	100.0% (104/104)	<0.0001
Female	100.0% (85/85)	98.0% (50/51)	0.0001
Pooled	99.3% (283/285)	99.4% (154/155)	<0.0001
Primary Efficacy			
Gender, % (n/N)			
Male	73.3% (140/191)	62.1% (59/95)	0.077
Female	74.7% (56/75)	66.7% (28/42)	0.404
Pooled	73.7% (196/266)	63.5% (87/137)	0.027

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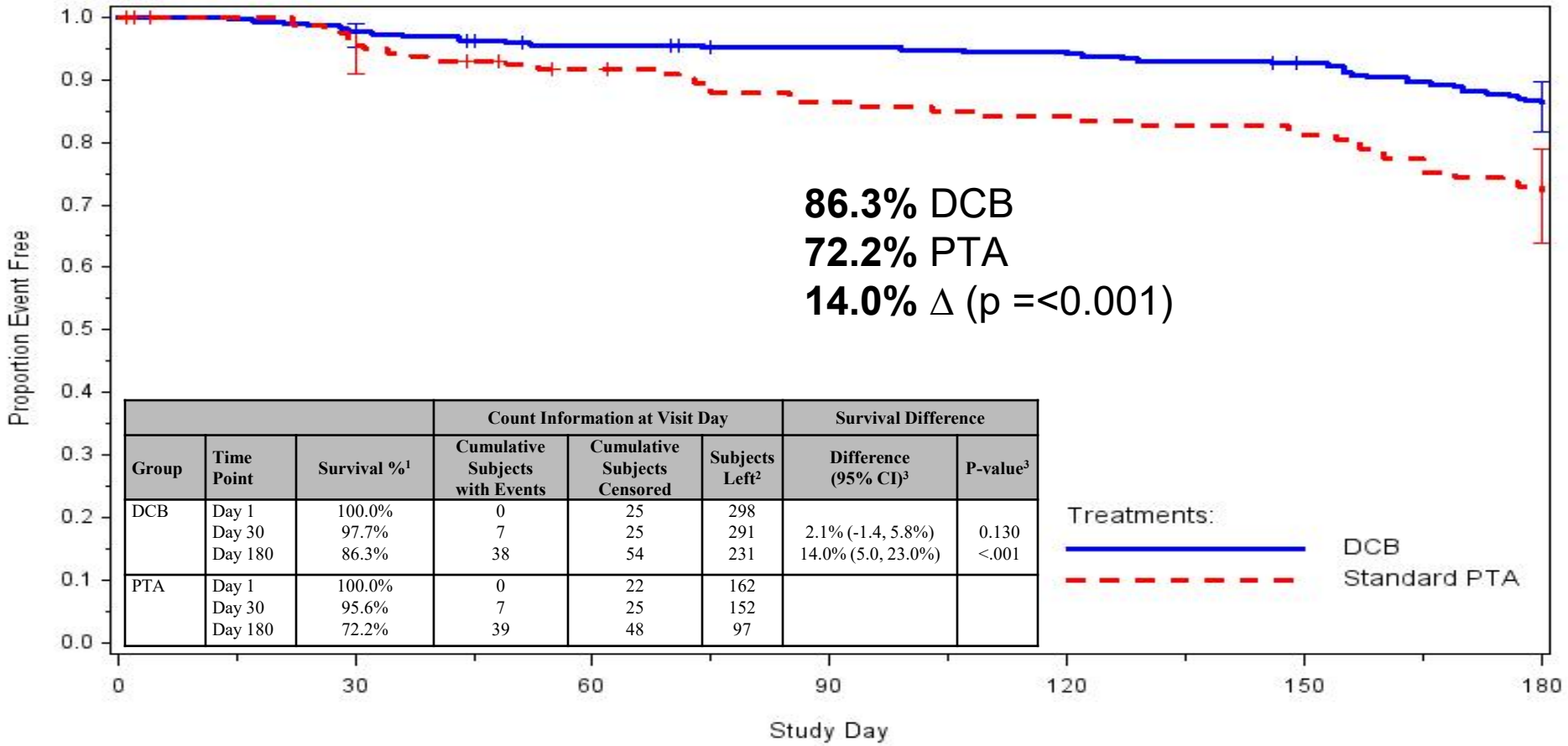
Secondary Endpoint

(KM 6 Month Primary Patency – Total Occlusion / CD-TLR)



			Count Information at Visit Day			Survival Difference	
Group	Time Point	Survival %[1]	Cumulative Subjects with Events	Cumulative Subjects Censored	Subjects Left[2]	Difference (95% CI)[3]	P-value[3]
DCB	Day 1	100.0%	0	25	298		
	Day 30	97.7%	7	25	291	2.1% (-1.4, 5.8%)	0.130
	Day 180	86.3%	38	54	231	14.0% (5.0, 23.0%)	<.001
PTA	Day 1	100.0%	0	22	162		
	Day 30	95.6%	7	25	152		
	Day 180	72.2%	39	48	97		

[1] Kaplan-Meier estimate of proportion of subjects without a composite failure event at the visit day
[2] Subjects ongoing without an event at the visit day
[3] 95% CI for difference and p-value for one-sided test that DCB response is less than or equal to Standard PTA response obtained from Kaplan-Meier estimates and standard error estimates from Greenwood's method

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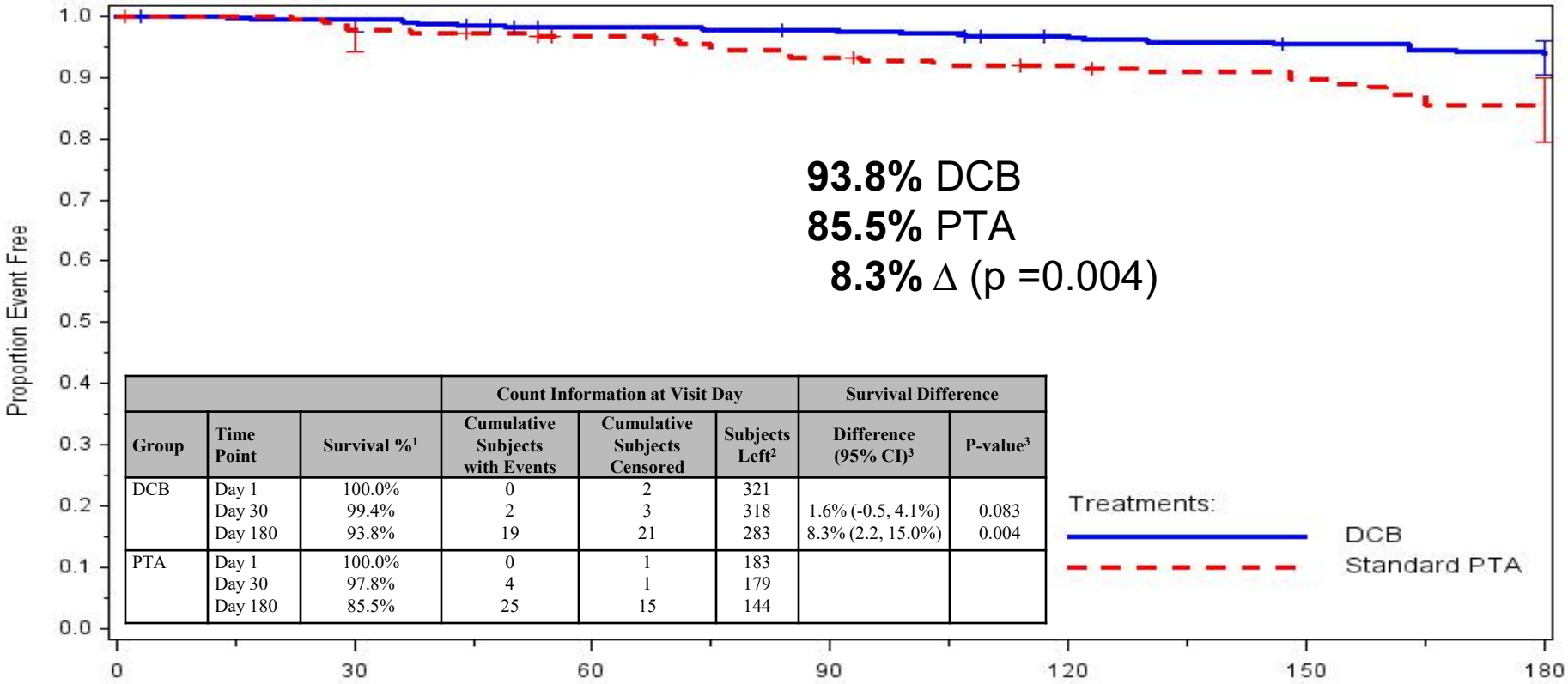
Secondary Endpoint (KM 6 Month CD-TLR Free)



			Count Information at Visit Day			Survival Difference	
Group	Time Point	Survival %[1]	Cumulative Subjects with Events	Cumulative Subjects Censored	Subjects Left[2]	Difference (95% CI)[3]	P-value[3]
DCB	Day 1	100.0%	0	2	321		
	Day 30	99.4%	2	3	318	1.6% (-0.5, 4.1%)	0.083
	Day 180	93.8%	19	21	283	8.3% (2.2, 15.0%)	0.004
PTA	Day 1	100.0%	0	1	183		
	Day 30	97.8%	4	1	179		
	Day 180	85.5%	25	15	144		

[1] Kaplan-Meier estimate of proportion of subjects without a composite failure event at the visit day
[2] Subjects ongoing without an event at the visit day
[3] 95% CI for difference and p-value for one-sided test that DCB response is less than or equal to Standard PTA response obtained from Kaplan-Meier estimates and standard error estimates from Greenwood's method

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Wound Assessment

	DCB		PTA	
	Baseline	**6 Months**	**Baseline**	**6 Months**
Any Wound Present, % n/N*	59.2% 161/272	43.4% 99/228	58.0% 87/150	45.4% 54/119

*Site reported, Non-standardized, Non-adjudicated

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Conclusion

- Primary safety endpoint met - no difference between DCB and PTA (p=<0.0001*) at 30 days
- By Kaplan Meier estimate at 6 months: no difference in primary safety (DCB - 97.8% / PTA - 95.3%, p=0.096)
- Primary efficacy endpoint at 6 months: DCB - 73.7% / PTA - 63.5% (Δ10.2%, p=0.0273)
- By Kaplan Meier estimate at 6 month: primary efficacy DCB - 85.3% / PTA - 70.7% (Δ14.6%, p=<0.001*)

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* Statistically significant

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Conclusion (Cont.)

- Sustained hemodynamic improvement through 6 Months
- No gender differences - Primary Safety and Primary Efficacy
- By Kaplan Meier estimate at 6 month: Primary Patency DCB - 86.3% / PTA - 72.2% (Δ14.0%, p=<0.001*)
- By Kaplan Meier estimate at 6 month: TLR Free DCB - 93.8% / PTA - 85.5% (Δ8.3 %, p=<0.004*)
- Reduction in the presence of any wound at 6 months compared to enrollment; no difference between DCB and PTA

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* Statistically significant

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