Lessons from RANGER II SFA

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Disclosure

Speaker name:

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I have the following potential conflicts of interest to report:

- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

- ☐ I do not have any potential conflict of interest

- IMPORTANT INFORMATION: These materials are intended to describe common clinical considerations and procedural steps for the on-label use of referenced technologies as well as current standards of care for certain conditions. Of course, patients and their medical circumstances vary, so the clinical considerations and procedural steps described may not be appropriate for every patient or case. As always, decisions surrounding patient care depend on the physician's professional judgment in light of all available information for the case at hand.
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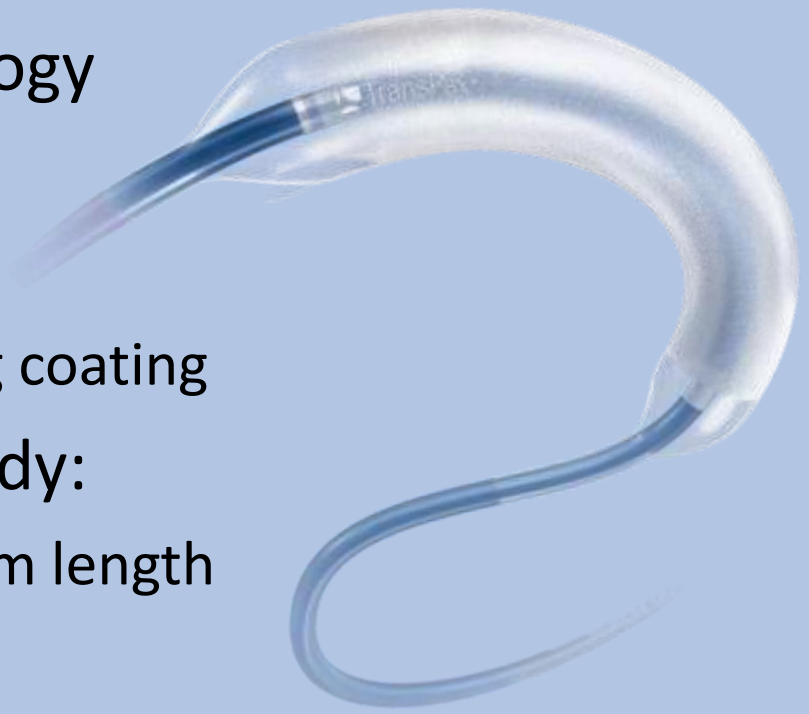
Ranger™ Drug-Coated Balloon

- 0.018” Sterling balloon platform
- TransPax™ coating technology
  - Paclitaxel 2 µg/mm^2
- Loading Tool
  - Designed to protect the drug coating
- Size matrix available for study:
  - 4-8 mm diameter; 30-100 mm length



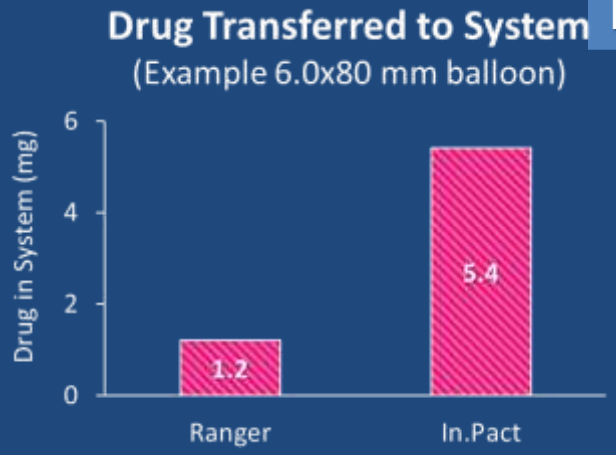
Ranger DCB is an investigational device and not available for sale in the US.

Ranger Drug Kinetics Profile

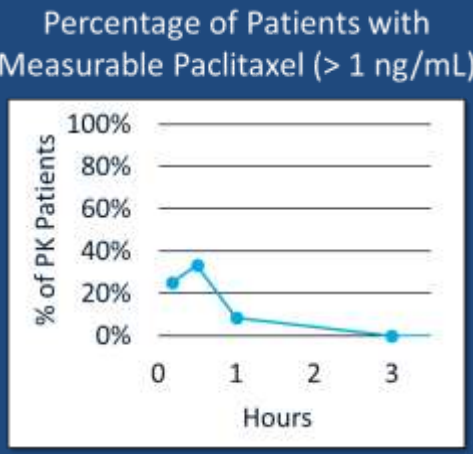
In Box

Balloon Length	Ranger (6mm) PTX µg	In.Pact (6mm) PTX µg	Ratio
40	1467	3170	0.46
60	2200	4489	0.49
80	3108	5809	0.54
120	4809	8448	0.57

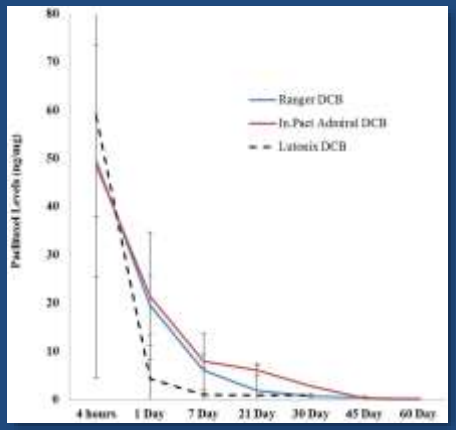
In Procedure



In Circulation



In Lesion



DCB drug kinetics “fingerprints” are unique

Data on File Boston Scientific. In.Pact DFU. Gongora CA, et al. JACC Cardiovasc Interv. 2015;8(8):1115-1123. Preclinical results may not necessarily be indicative of clinical outcomes.

RANGER II SFA Global Study Overview

Primary Investigators	Global: Prof. Thomas Zeller, MD United States: Ravish Sachar, MD, FACC	
Study Design	RCT (Ranger™ DCB vs Standard PTA) • 3:1 randomized • Single-blind • Superiority design for effectiveness	Pharmacokinetic Sub-study (Ranger) • Single-arm
Patients	N=376 Ranger DCB N=278 vs PTA N=98	N=12
Investigational Centers	67 study centers: United States, Japan, New Zealand, Europe, Canada	

- **Full cohort 12-month analysis presented here**
- Interim analysis: first 306 subjects to complete 12-month follow-up were included in a prespecified interim analysis presented at VIVA 2019 (Sachar)

Key Eligibility Criteria

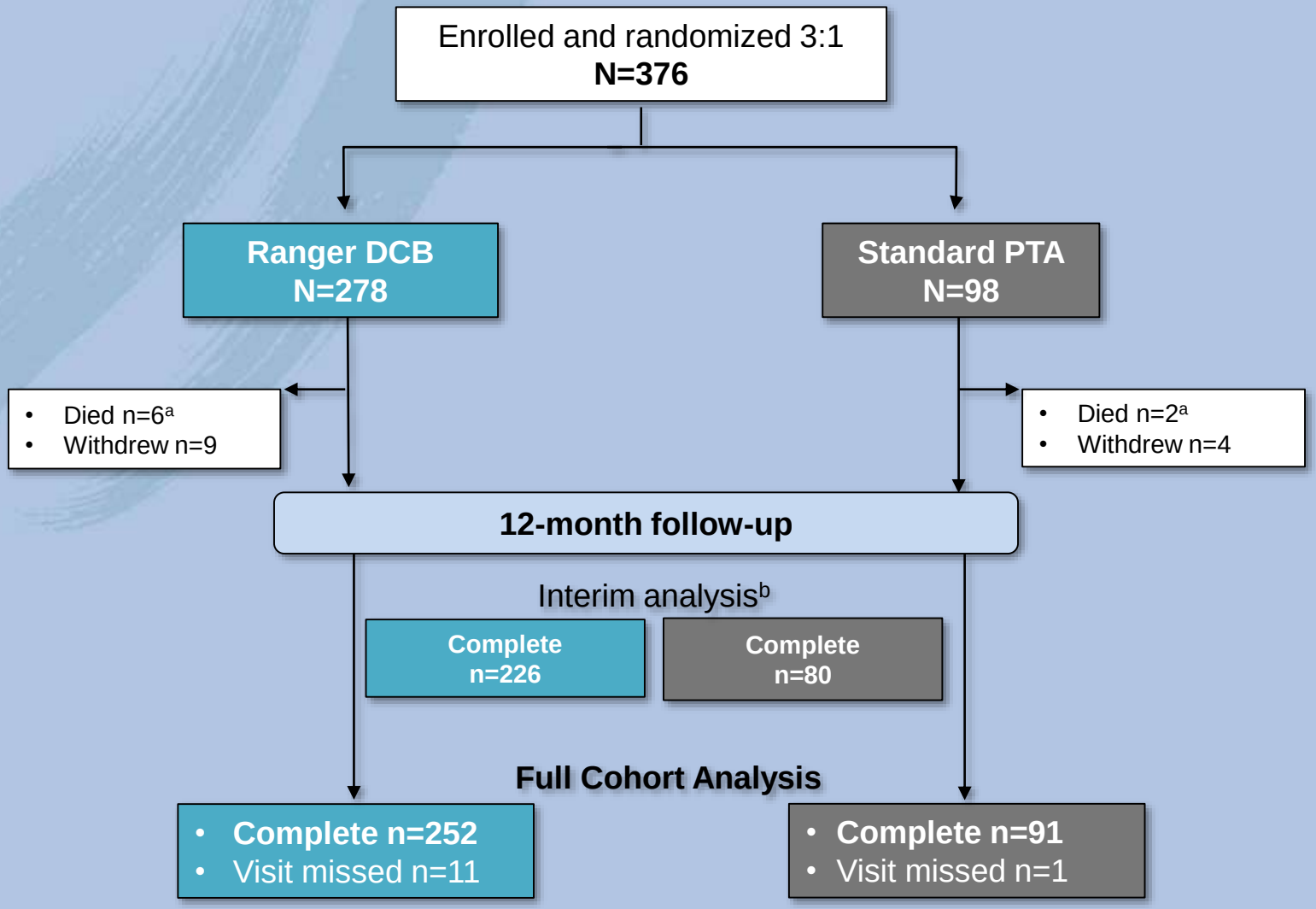
Inclusion

- Rutherford classification 2, 3, or 4
- Lesions in the native SFA and/or PPA
- Angiographic evidence for:
  - 70%-99% stenosis with total lesion length up to 180 mm; or
  - Occlusion with total lesion length ≤100 mm
- Reference vessel diameter 4-8 mm

Exclusion

- Failure to successfully pre-dilate the target vessel
- Use of adjunctive primary treatment modalities (e.g., debulking devices)
- Previous treatment with stent (i.e., in-stent restenosis) or surgery
- Treatment with atherectomy or a DCB in the past 12 months
- Dialysis

RANGER II SFA RCT Patient Flow



[a]Death less than 395 days post-procedure with no 12-month visit performed.

[b]The first 306 evaluable subjects were included in the prespecified interim analysis presented at VIVA 2019.

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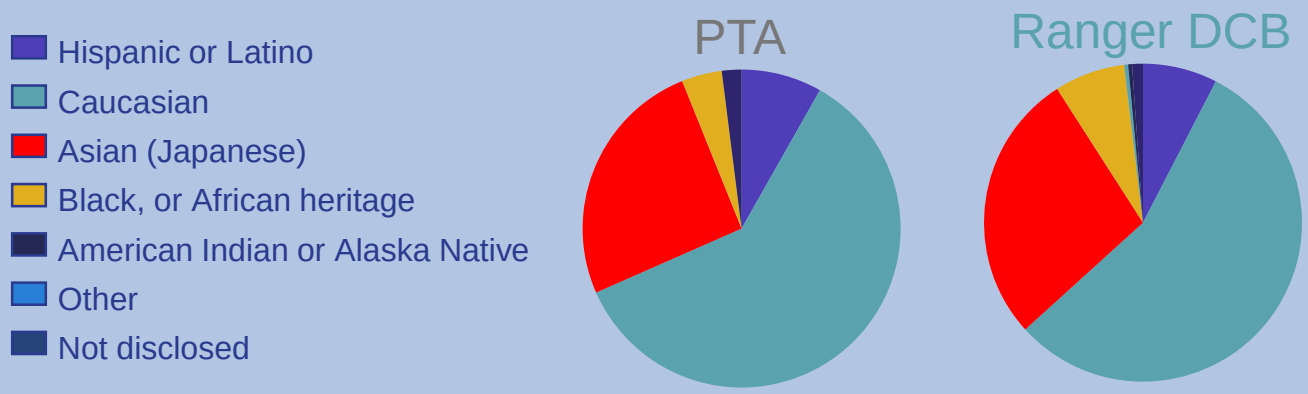
Baseline characteristics similar between groups

Demographics and Clinical History

	Ranger DCB (N=278)	Standard PTA (N=98)	P
Age (Year)	70.6±9.5	69.1±10.3	0.189
Female	37.8%	31.6%	0.277
Smoking History			
Current	31.3%	45.9%	0.009
Previous	54.0%	38.8%	0.010
Diabetes Mellitus	42.4%	43.9%	0.806
Hyperlipidemia	75.9%	79.6%	0.456
Hypertension	90.3%	81.6%	0.023
Chronic Obstructive Pulmonary Disease	18.9%	21.4%	0.589
Coronary Artery Disease	47.5%	44.9%	0.662
History of Cerebrovascular Accident	13.0%	11.2%	0.641
History of Renal Insufficiency	10.8%	5.2%	0.100



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Baseline characteristics similar between groups

Lesion Characteristics (core lab)

	Ranger DCB (N=278)	Standard PTA (N=98)	P
Lesion Location			
pSFA	17.3%	18.4%	0.805
mSFA	52.5%	44.9%	0.195
dSFA	24.8%	32.7%	0.133
pPopliteal	4.3%	4.1%	>0.99
mPopliteal	1.1%	0.0%	0.571
Lesion Length (mm)	82.5±48.9	79.9±49.3	0.655
PACSS Calcification			
Grade 0	35.3%	22.4%	0.019
Grade 1	12.6%	14.3%	0.668
Grade 2	2.5%	1.0%	0.686
Grade 3	36.3%	52.0%	0.006
Grade 4	11.5%	10.2%	0.724
TASC II			
A	59.4%	61.2%	0.745
B	30.2%	30.6%	0.942
C	9.0%	6.1%	0.374
D	1.4%	2.0%	0.653
% Diameter Stenosis	73.7±16.9	78.2±18.4	0.029
100% (Occlusion)	18.3%	29.6%	0.019

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Procedure Characteristics

	Ranger DCB (N=278)	Standard PTA (N=98)	P-value
Pre-dilatation	100%	100%	Undef
Post-dilatation	13.3%	21.4%	0.056
Bailout stent (bare metal)	5.0%	9.2%	0.141
Technical success[a]	99.6%	NA	NA
Procedural success[b] (core lab)	96.8%	99.0%	0.464
Clinical success[c]	96.0%	98.0%	0.527

[a]Technical Success: Successful delivery, balloon inflation and deflation and retrieval of the intact trial device without burst below the rated burst pressure. Only collected for Ranger DCB.

[b]Procedural Success: Residual stenosis of ≤50% (non-stented) or ≤30% (stented) by core laboratory evaluation.

[c]Clinical Success: Procedural success without CEC-adjudicated complications (e.g., death, major target limb amputation, clinically-driven TLR) or thrombosis of the target lesion prior to discharge.

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Safety

- Primary safety endpoint met (non-inferiority P<0.0001)
- 12-month MAE-free rate

  94.1% (241/256) Ranger DCB vs 83.5% (76/91) PTA; P=0.002
- Significantly lower MAE and TLR rates for Ranger DCB vs PTA

	Ranger DCB (N=256)	Standard PTA (N=91)	Difference [95% CI]	P-value
12-Month MAE	**5.9% (15/256)**	**16.5% (15/91)**	**-10.6% [-18.8%, -2.5%]**	**0.002**
All Causes of Death at 1 Month	0.4% (1/256)	0.0% (0/91)	0.4% [-0.4%, 1.2%]	>0.99
Target Limb Major Amputation	0.0% (0/256)	0.0% (0/91)	0.0% [NA, NA]	Undef
Clinically-Driven TLR	**5.5% (14/256)**	**16.5% (15/91)**	**-11.0% [-19.1%, -2.9%]**	**0.001**

MAEs were adjudicated by a Clinical Events Committee.

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Mortality Summary

- No significant difference in survival through 1 year for Ranger DCB vs PTA (log-rank P=0.8794)[a]
  - Mortality rate **1.9% (5/260) Ranger DCB** vs **2.1% (2/92) PTA** at day 365[a]

Group	Site-Reported Cause of Death	CEC Adjudication	Days from Index Procedure
Ranger DCB	Coronary artery disease	Cardiac	3
	Respiratory failure	Non-cardiovascular	112
	Myocardial infarction	Cardiac	116
	Accidental (burns)	Non-cardiovascular	325
	Cardiac arrest	Cardiac	337
Standard PTA	Unknown	Cardiac	129
	Pneumonia	Non-cardiovascular	160

Clinical Events Committee (CEC) adjudicated deaths occurring within 365 days post-procedure.

[a]Cumulative events through 365 days log rank p=0.8794.

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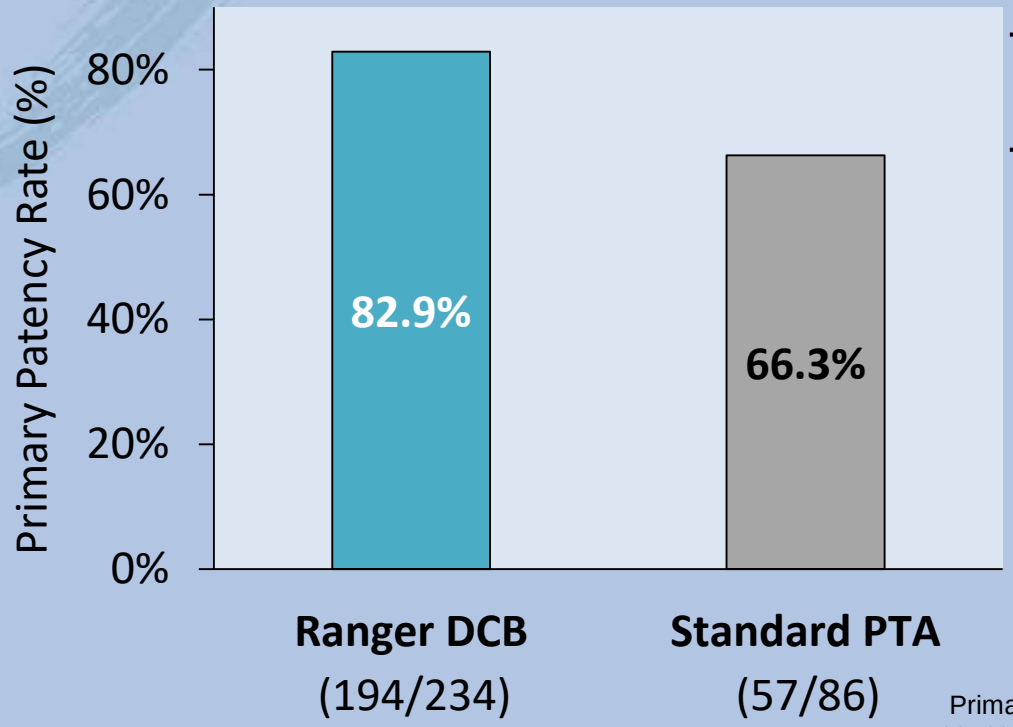
Effectiveness | Primary Patency

Full Cohort

- Superior primary patency at 12 months for Ranger DCB vs PTA (P=0.0017)



Primary patency defined as duplex ultrasound PSVR ≤2.4, in the absence of clinically-driven target lesion revascularization or bypass of the target lesion, as assessed by the DUS core lab.

Primary superiority effectiveness endpoint met. One-sided lower 97.5% confidence bound on the difference (5.53%) greater than zero; p=0.0017.

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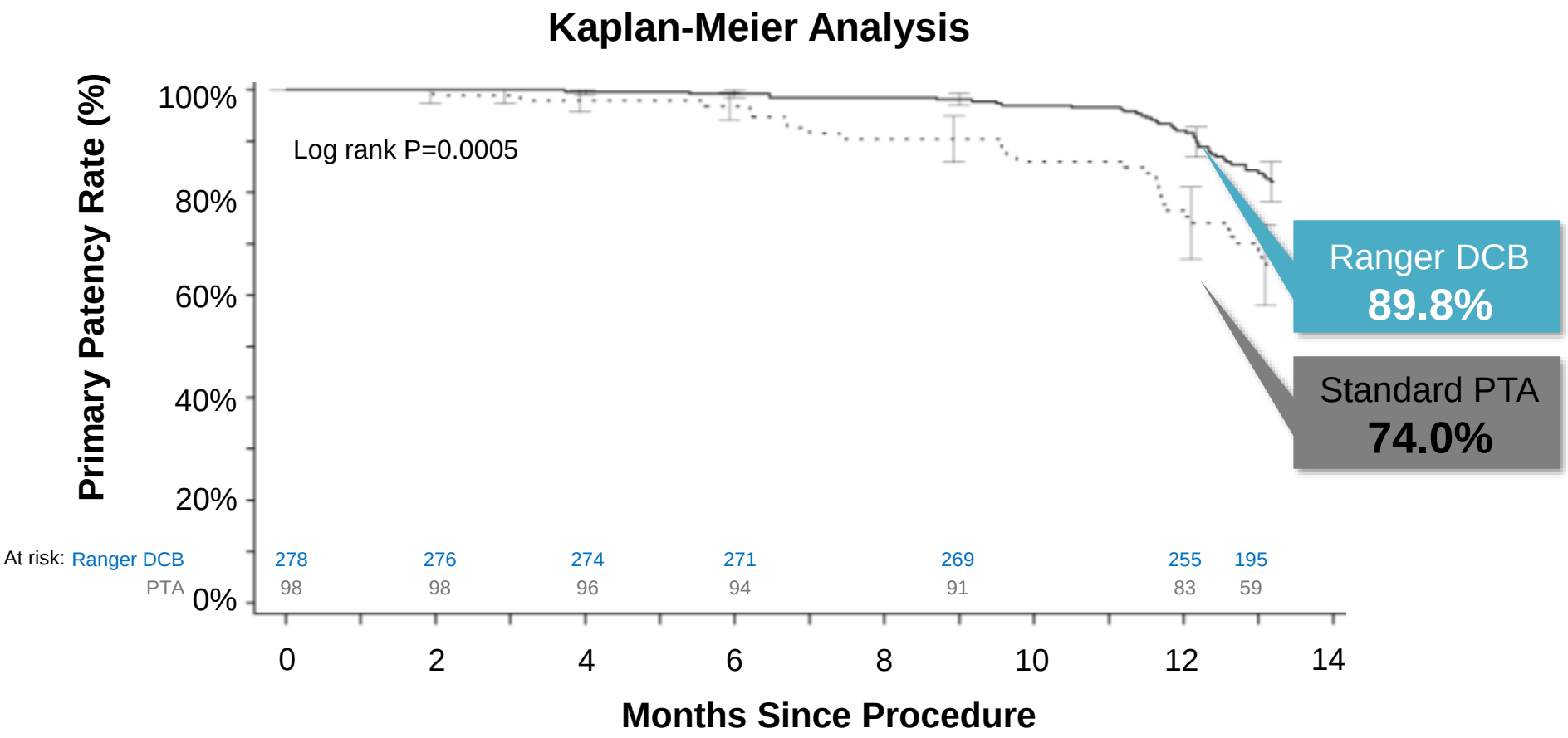
Effectiveness | Primary Patency



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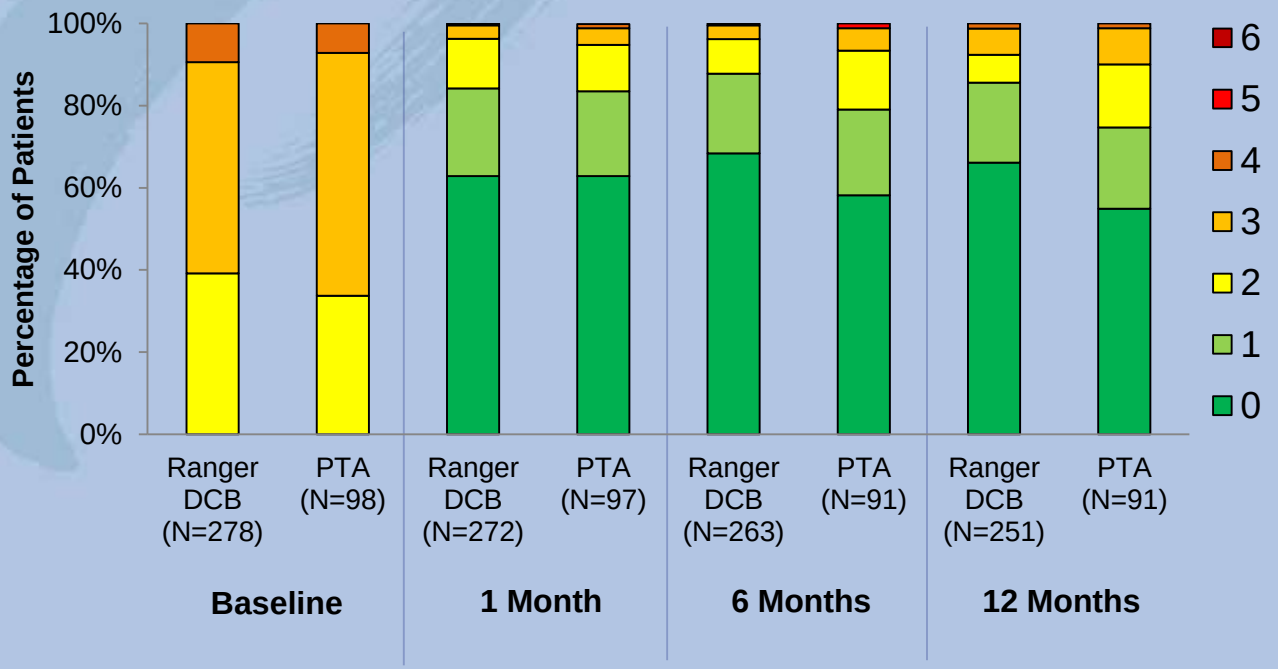
Clinical Outcomes at 12 Months

Primary sustained clinical improvement[a]	Ranger DCB	Standard PTA	Difference	95%CI	P-value
	87.6% (220/251)	**75.8%** (69/91)	11.8%	2.1%, 21.5%	0.0076



- No or minimal symptoms (Rutherford Category 0-1) at 12 months
  - 85.7% Ranger DCB
  - 74.7% PTA

[a]Improvement in Rutherford classification of one or more categories as compared to baseline without TLR.

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Summary

- Primary superiority effectiveness and non-inferiority safety endpoints were met
- Superior primary patency for Ranger DCB vs Standard PTA (Δ 16.6%) at 12 months (P=0.0017)
- Significantly lower CD-TLR for Ranger DCB vs PTA (5.5% vs 16.5%; P=0.001)
- No difference in 1-year mortality between groups
- Clinical outcome improvement rates achieved with fewer reinterventions

Conclusion

The low-dose Ranger DCB demonstrated effectiveness superior to standard PTA through 1 year, with fewer reinterventions and an equivalent safety profile

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