RANGER II SFA: Randomized Trial of Ranger DCB vs. PTA in the SFA

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On behalf of the RANGER II SFA Investigators

Disclosure

Speaker name:

Brodmann Marianne, MD

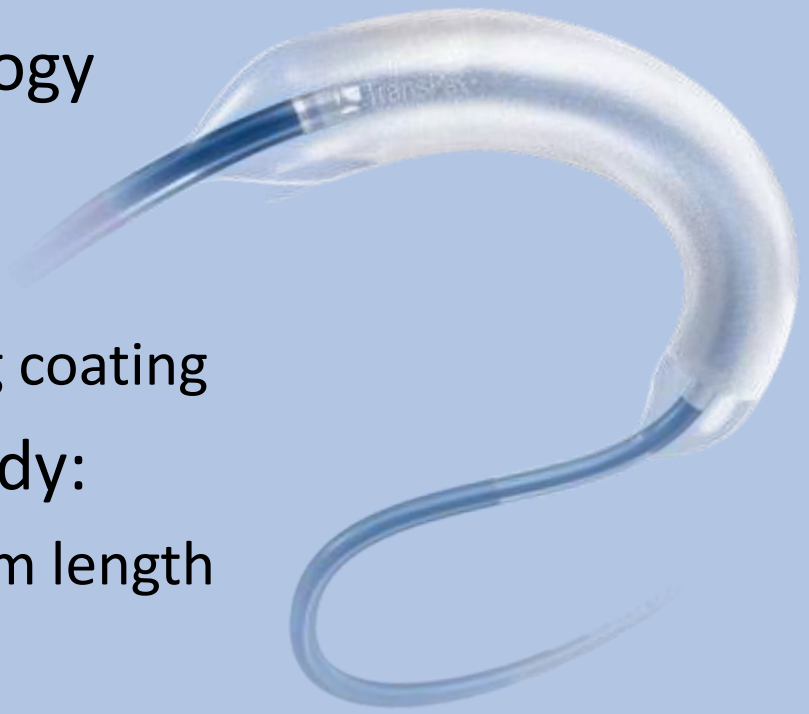
I have the following potential conflicts of interest to report:

- [x] 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

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 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

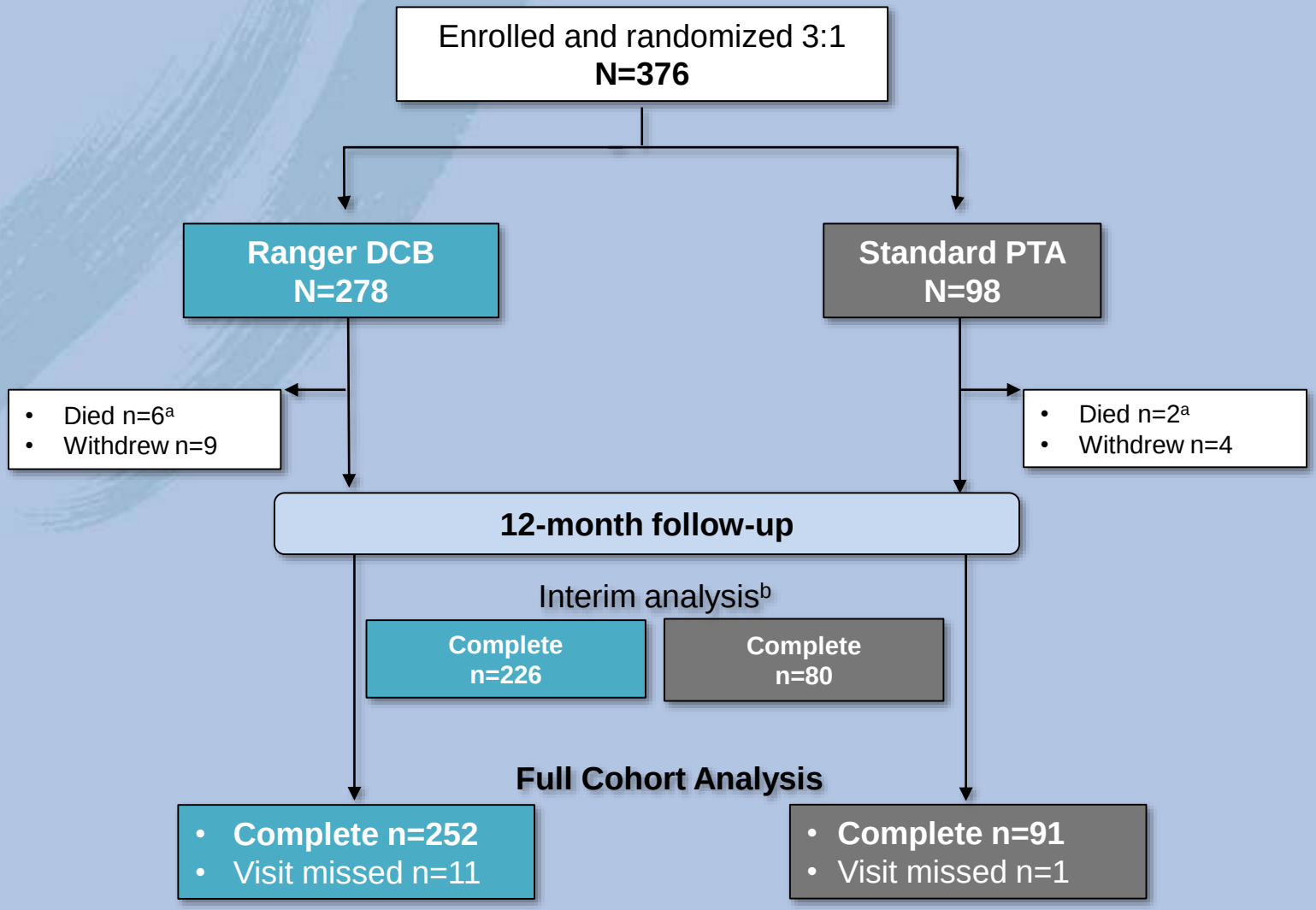
Inclusion

- 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



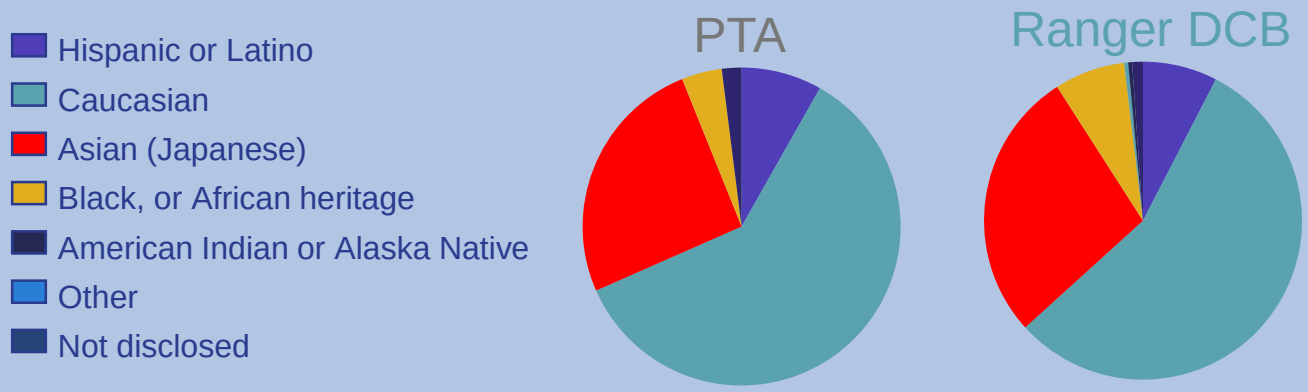
[a]Death less than 395 days post-procedure with no 12-month visit performed.

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

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



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

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.

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.

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

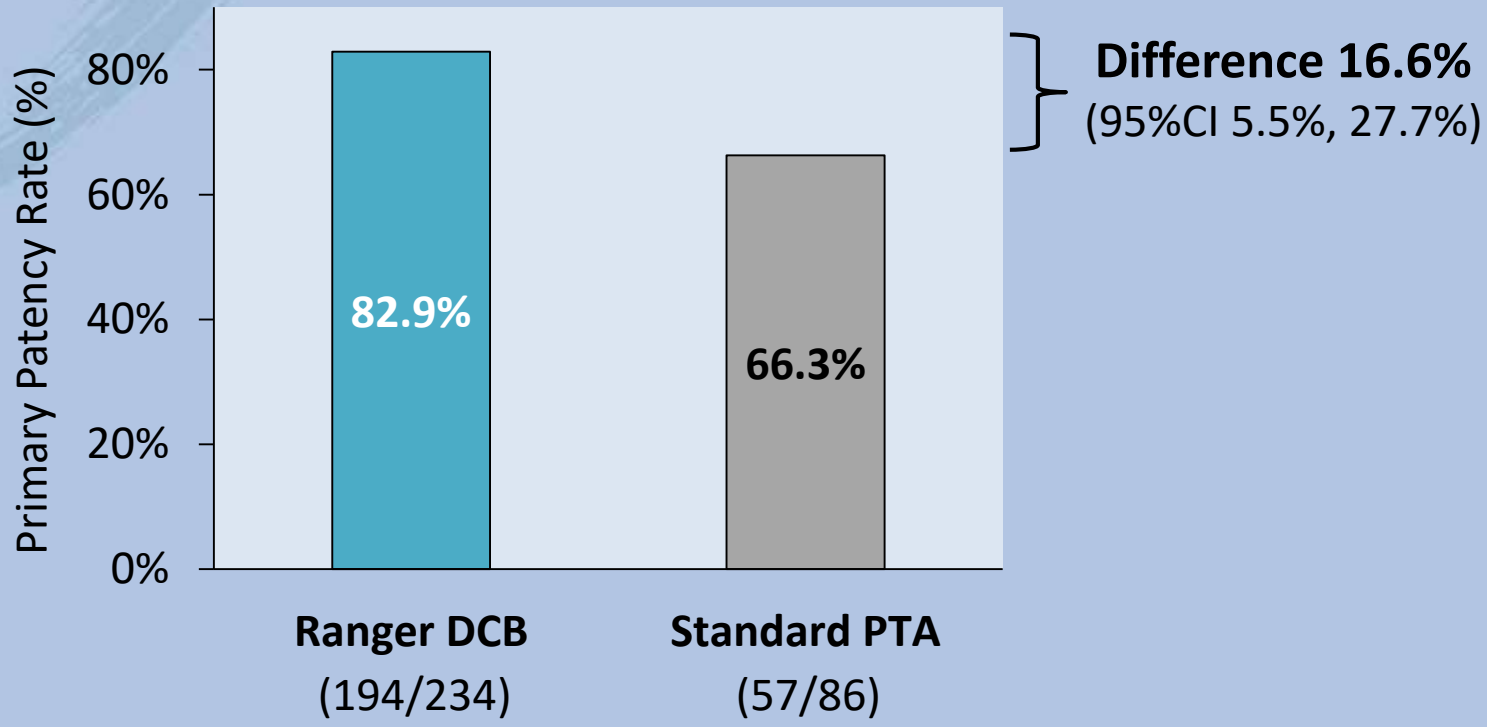
Clinical Events Committee (CEC) adjudicated deaths occurring within 365 days post-procedure.

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

Effectiveness | Primary Patency

Full Cohort

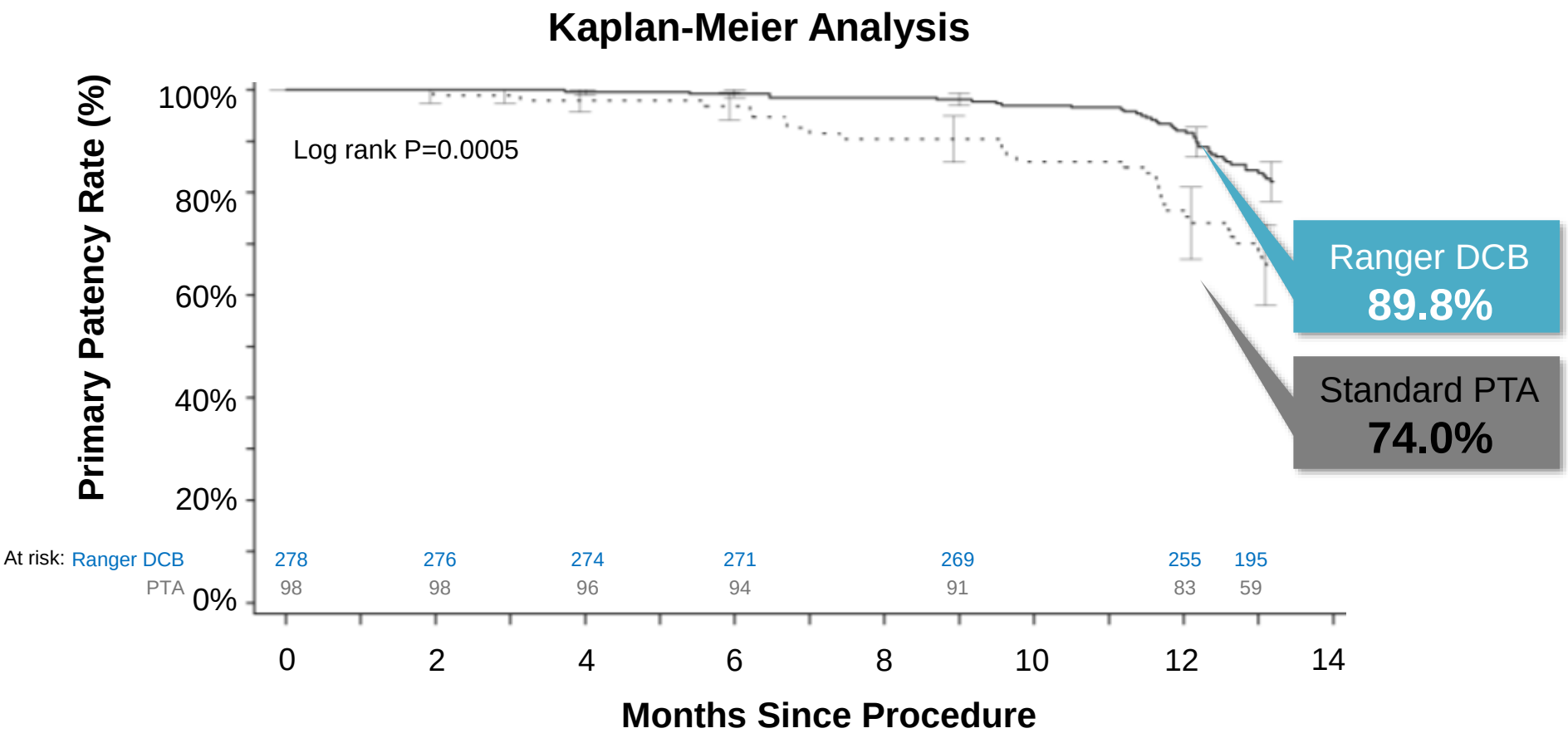
- Superior primary patency at 12 months for Ranger DCB vs PTA (P=0.0017)



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.

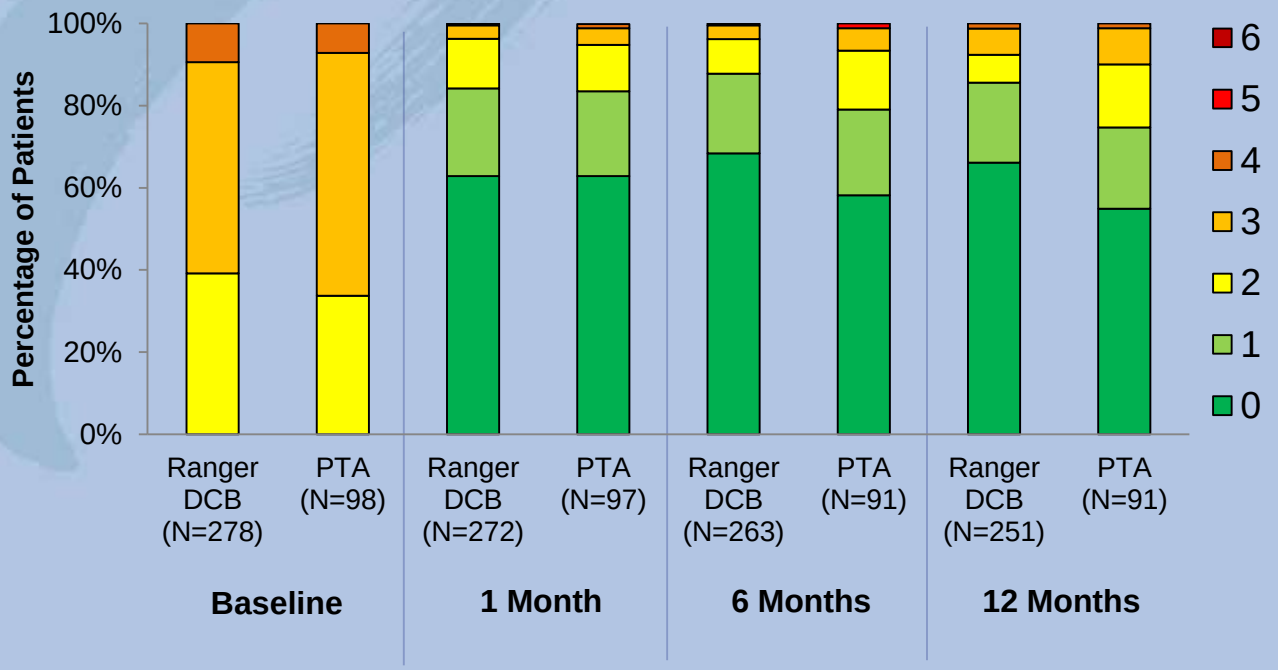
Effectiveness | Primary Patency



Error bars are SE.

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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RANGER II SFA | Pharmacokinetics Substudy

- All patients treated with Ranger DCB (N=12)
- Treated lesion length 154.2±92.8 mm
- Plasma paclitaxel less than the limit of quantification (<1 ng/mL):
  - 11 of 12 patients by 1 hour following DCB deployment and removal
  - all patients by 3 hours
- 1 death, non-cardiovascular, 79 days post-procedure

Protocol required blood draws: baseline, 10 minutes, 30 minutes, 1, 3, 6, 24 or 48 hours, 7 days and 30 days after last Ranger DCB treatment and removal.

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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