Update on the Ranger clinical trial programme

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on behalf of the RANGER SFA investigators

Disclosure

Speaker's name: Dierk Scheinert

I have the following potential conflicts of interest to report:

Advisory Board /Consultant:

Abbott, Biotronik, Boston Scientific, Cook Medical, Cordis, CR Bard, Gardia Medical/Allium, Medtronic, TriReme Medical, Trivascular, Upstream Peripheral Technologies

Ranger™ Drug Coated Balloon

Next generation DCB

Design:

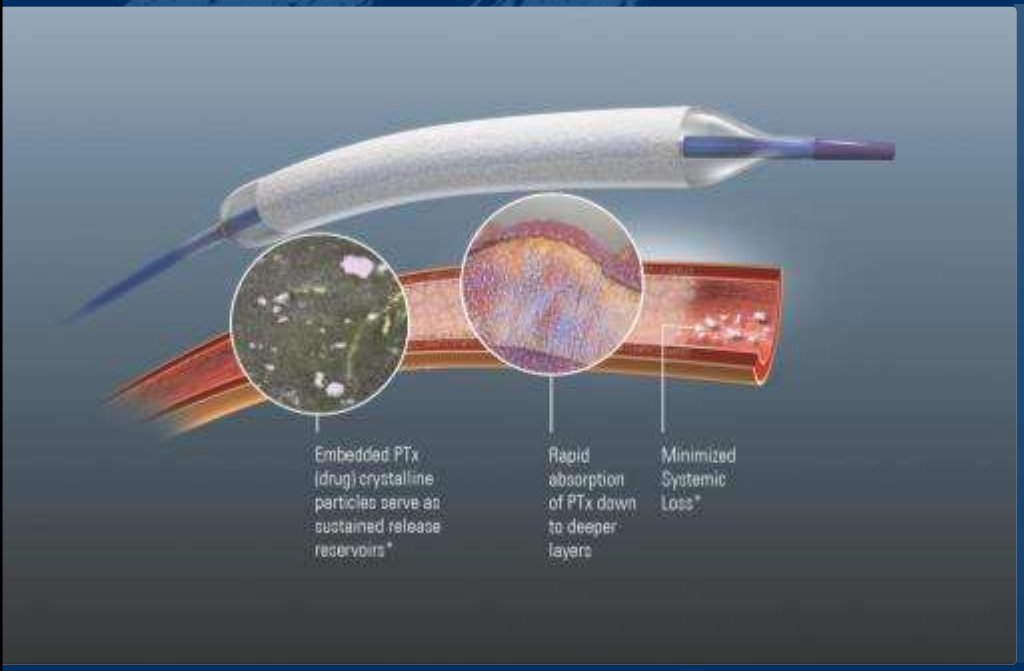
- Sterling balloon platform
- TransPax™ coating technology
  - Paclitaxel
- Ranger™ DCB Loading Tool
  - Designed to protect the drug coating
- Size matrix:
  - SFA: 4-8 mm; 30-100 mm
  - BTK: 2-4 mm; up to 150 mm

Ranger Drug Coated Balloon is an investigational device, not available for sale in the United States.

Ranger™ Drug Coated Balloon

TransPax™ Technology

Paclitaxel, Excipient: Citrate ester (acetyl tributyl citrate – ATBC)



Designed to:

- Balance hydrophilic and hydrophobic properties
- Allow adhesion to the balloon during tracking and deployment
- Allow transfer to the vessel wall during balloon inflation
- Minimize particulate loss

Ranger Drug Coated Balloon is an investigational device, not available for sale in the United States.

Ranger-SFA FIM Study

Clinical Study Overview: Ranger	Study follow-up complete through 6M
Name	Ranger-SFA
Primary Investigator	Dierk Scheinert, MD
Study Sponsor	Hemoteq AG (Würseln, Germany)
Study Device	Ranger™ Paclitaxel-Coated PTA Balloon Catheter Sizes available for the RANGER SFA study: 4-7 mm diameter; 40-100 mm length
Objective	To prove the superior performance of the Ranger™ paclitaxel-coated PTA balloon catheter for angioplasty for femoropopliteal artery lesions when compared to non-coated balloons at six months post-procedure when comparing Late Lumen Loss (LLL).
Study Design	Prospective, randomized, multicenter, controlled trial (2:1 Ranger DCB vs. uncoated balloon)
Subjects	105 patients with femoropopliteal artery lesions
Investigational Centers	10 sites (Germany, France, and Austria)
Endpoints	Primary endpoint : • In-segment late lumen loss of the treated segment, as observed by angiography at six months post-procedure Secondary Endpoints: • Restenosis and patency rates • Rutherford classification / clinical success • Ankle-brachial index / hemodynamic success • Quality of life (WIQ, EQ5D, SF12)

EUDAMED CIV-13-07-011514; ClinicalTrials.gov NCT02013193

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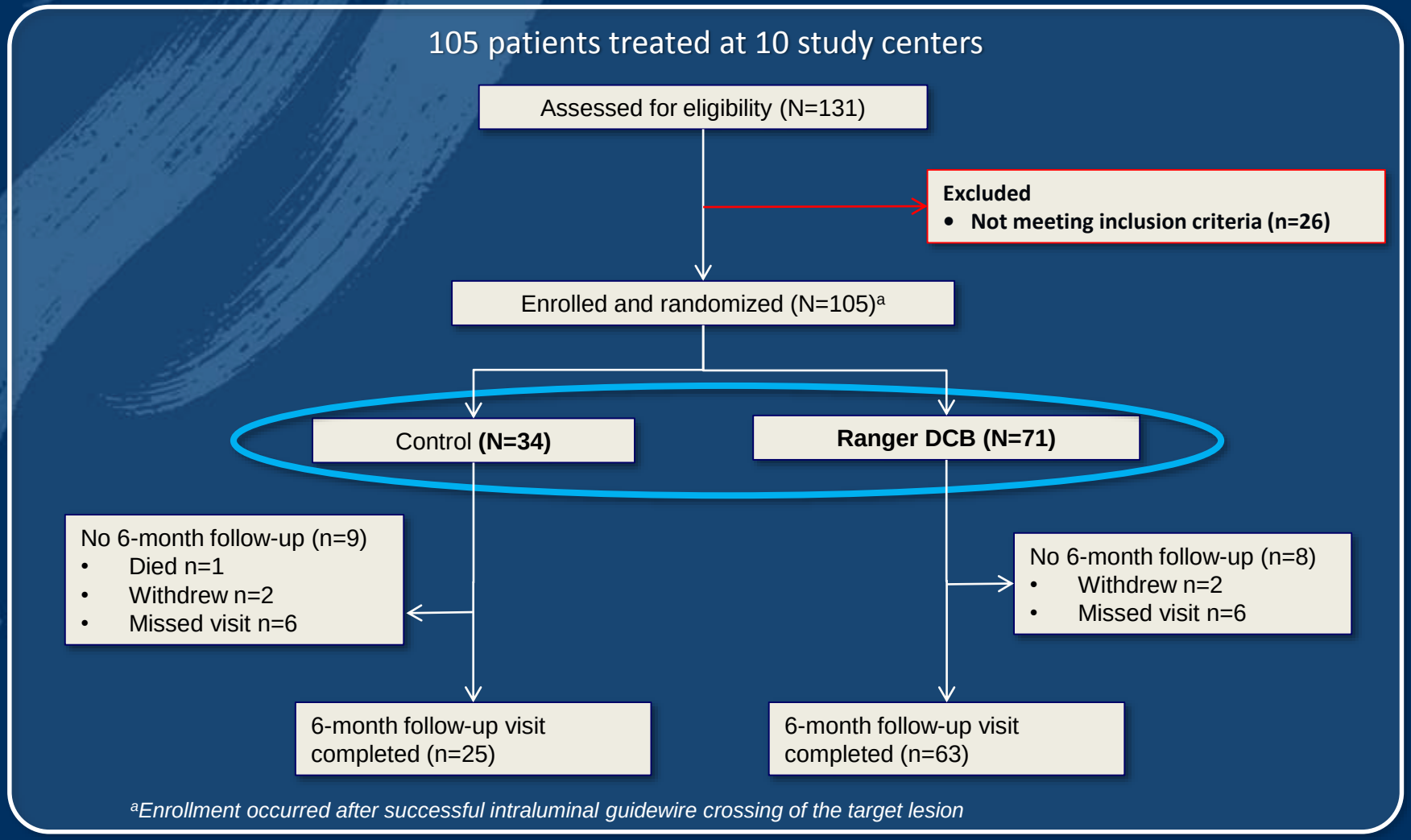
Ranger-SFA FIM Study

Patient Enrollment & Follow-up



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Ranger-SFA FIM Study

Lesion Characteristics – Angiographic Core Lab

Similar lesion characteristics between Ranger and control groups

	Control (N=34)	Ranger DCB (N=71)	P
Lesion length (mm)	60 ± 48	68 ± 46	0.7314
Total occlusion	34%	34%	1.0000
Calcification			
None	16%	10%	0.2359
Mild	28%	27%	
Moderate	34%	24%	
Severe	22%	36%	
Location			
Proximal SFA	6%	17%	0.2885
Middle SFA	38%	44%	
Distal SFA	53%	36%	
Proximal popliteal	3%	3%	
TASC II			
A	69%	66%	0.6196
B	22%	27%	
C	6%	7%	
D	0.0%	0.0%	
% Diameter stenosis	82 ± 18	85 ± 15	0.5740
Reference vessel diameter	4.5 ± 0.83	5 ± 0.89	0.0389

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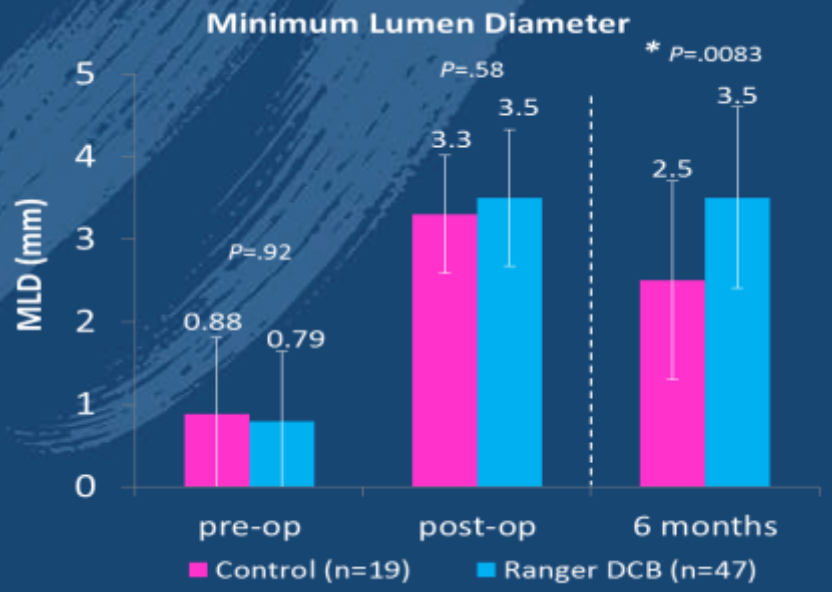
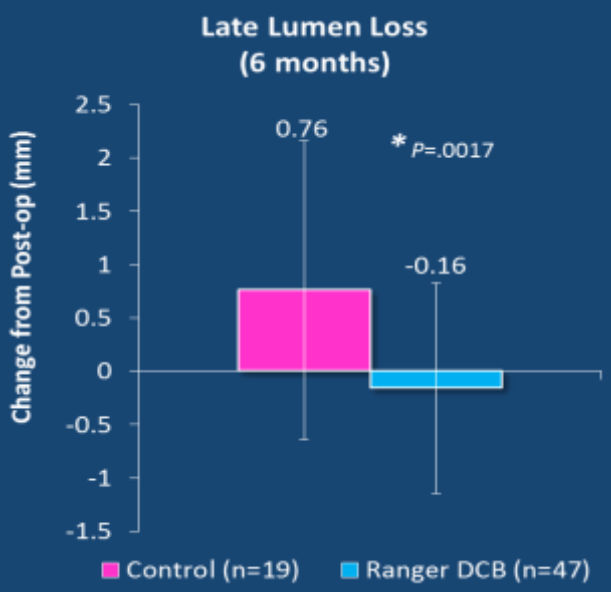
Ranger-SFA FIM Study

Efficacy and Safety – 6 months





- LLL was significantly less for Ranger DCB than for control (*P*=.0017)
  - Primary endpoint was met
- Cumulative TLR rate through 6 months: 12% control vs 5.6% Ranger (P=.47)
- Similar AE and SAE rates between groups
  - No target limb amputations
  - 1 death within 6 months (control group)
- No USADE reported

Study follow-up complete through 6M

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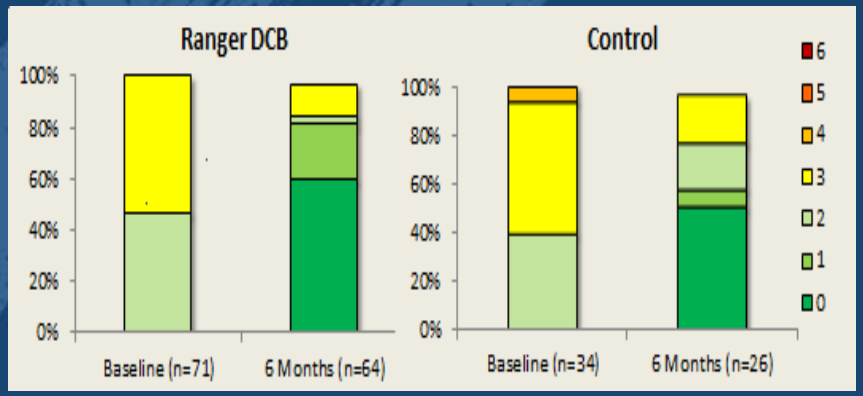
Ranger-SFA FIM Study

Clinical Outcomes

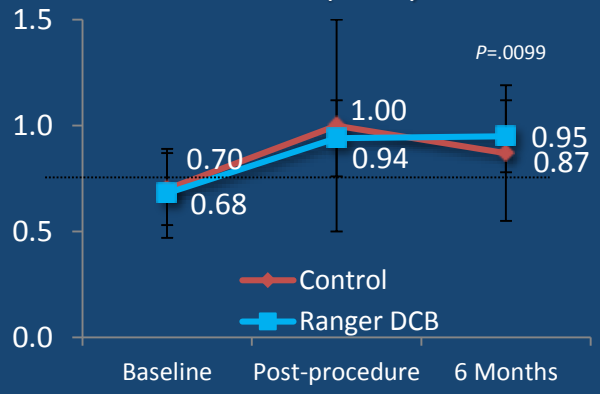
Rutherford Classification



- 81% of subjects in Ranger DCB group presented with no or mild symptoms (category 0-1) at 6-month follow-up
- Distributions for both Control and Ranger DCB groups show a shift to lower Rutherford Categories (improvemed)
  - Not significantly different between groups

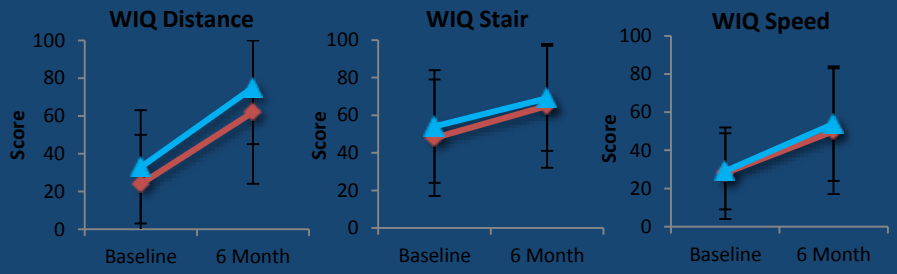
ABI/Hemodynamic Success

Significant improvement in both groups at 6 months (P<.05)



Walking Function and QoL

No significant differences between groups for WIQ, EQ5D, or SF12



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Boston Scientific Global Pivotal Study
RANGER II SFA

Clinical Study Overview: RANGER II SFA	
Title	A 3:1 Randomized Trial Comparing the Boston Scientific RANGER Paclitaxel Coated Balloon vs Standard Balloon Angioplasty for the Treatment of Superficial Femoral Arteries (SFA) and Proximal Popliteal Arteries (PPA)
Primary Investigators	Global: Prof. Thomas Zeller, MD - Germany National: Ravish Sachar, MD, FACC – United States
Objective	To evaluate the safety and effectiveness of the RANGER™ Paclitaxel Coated Balloon for treating lesions located in the SFA and PPA
Study Design	The trial consists of the following: • Prospective, multicenter, single-blind, superiority, RCT 3:1 (RANGER DCB : Standard PTA) • A concurrent, non-blinded, single-arm, pharmacokinetic(PK) sub-study
Subjects	396 patients • At least 376 patients into the randomized arm • 12 to 20 subjects in the non-randomized PK Sub-study
Investigational Centers	Up to 70 study centers in Canada, Europe (Austria, Belgium, Germany, Poland), Japan, New Zealand, and U.S.
Primary Efficacy Endpoint	Primary Patency of lesion • Determined by DUS and absence of clinically driven TLR
Primary Safety Endpoint	Occurrence of MAEs • All-cause death at 1 Month • TLR at 12 Months • Target limb major amputation at 12 Months

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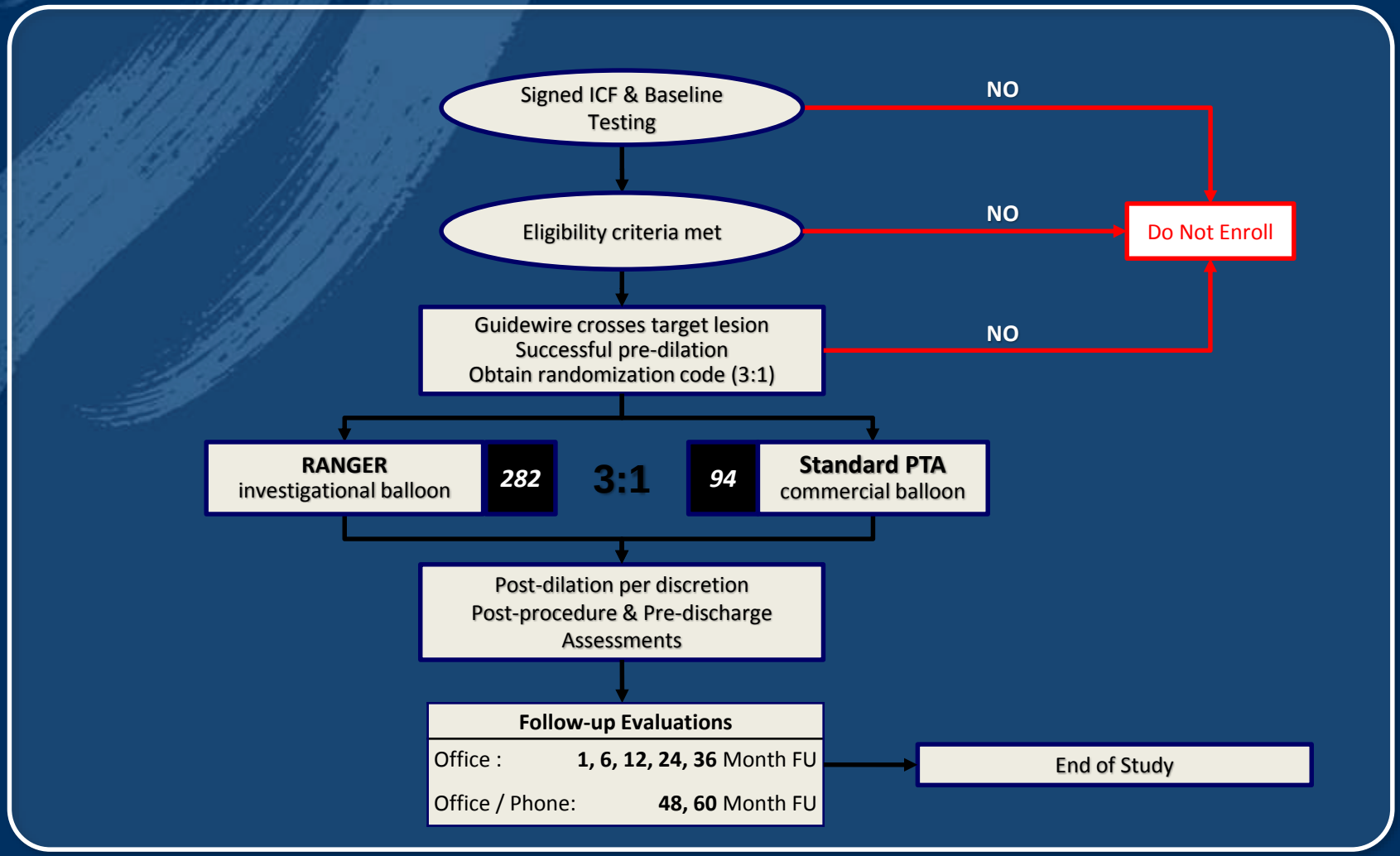
RANGER II SFA
Study Flow



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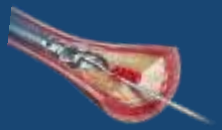
Boston Scientific Drug Elution
Clinical Program

MAJESTIC (DES)	Prospective, multicenter, single-arm, open label n= 57 (2yr follow-up complete)
IMPERIAL (DES)	Prospective, multicenter, RCT 2:1 (Eluvia : Zilver PTX) n = 485 (Enrolling)
EMINENT (DES/BMS)	Prospective, multicenter, RCT 2:1 (Eluvia : BMS) n = 750 (Enrolling)
REGAL (DES)	Prospective, multicenter, single-arm, open label n = 500 (Enrolling)
Ranger FIM (DCB)	Prospective, multicenter, randomized n = 105
Ranger II (DCB)	Prospective, multicenter, RCT 3:1 (Ranger : PTA) n = 376
Ranger China (DCB)	Prospective, multicenter, single-arm n = 123

Investigator Sponsored Research

Drug Elution (DES and DCB)



SPORTS	**Prospective, multicenter, RCT 1:1:1 (DES:DCB:BMS)** **N = 222**
Hemodialysis AVF Rescue	**Prospective, multicenter, RCT 1:1** **N = 200**
SFA RCT (COMPARE)	**Prospective, RCT 1:1 (Ranger : InPact)** **N = 150**
SFA Registry	**Prospective, multicenter, registry** **N = 180**
BTK Angiographic	**Feasibility, observational, angio F/U** **N = 30**
BTK Clinical	**Prospective, RCT 1:1 (Ranger : PTA)** **N = 70**
JET-PCB (IDE)	**Prospective, multicenter, RCT 2:1 (JS+Ranger : PTA+Ranger)** **N = 250**

These investigator-sponsored studies are supported by grant funding from Boston Scientific. Boston Scientific is not responsible for the collection, analysis or reporting of these studies which remain the sole responsibility of the investigators. Information for the use in countries with applicable product registrations.

Ranger SFA Registry

Ranger All-Comer Registry Treatment of femoro-popliteal atherosclerotic lesions using the Drug eluting Balloon Ranger: An All Comers Registry	
PI	Michael Lichtenberg
Design	Multicentre, all comer registry
Centres	Germany (Dr. von Bilderling (Munich), Dr. Ranft, Dr. Niemöller (Bottrop), Dr. Grell (Trier) and Switzerland (Dr. Saucy, Lausanne)
Population	Planned 180 patients
Key Inclusion Criteria	PAOD SFA – PIII, Rutherford II - V
Primary Safety Endpoint	Major Adverse Events (MAE): composite of device or procedure related mortality and major target limb amputation at 6 months
Primary Efficacy Endpoint	Primary patency at 12 and 24 months, defined as freedom from ≥ 50% restenosis as indicated by duplex ultrasound peak systolic velocity ratio (PSVR) ≥2.4 in the target lesion with no re-intervention

Lesion Characteristics

Average lesion length 135 mm (50 –400 mm)

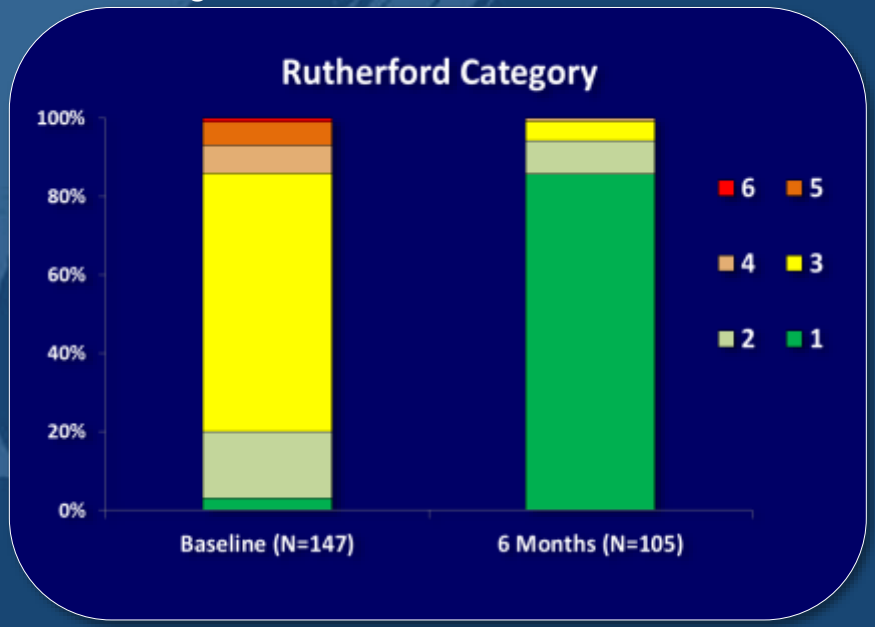
TASC II – A (20%), B (21%), C (21%), D (38%)

Study is sponsored by Klinikum Arnsberg

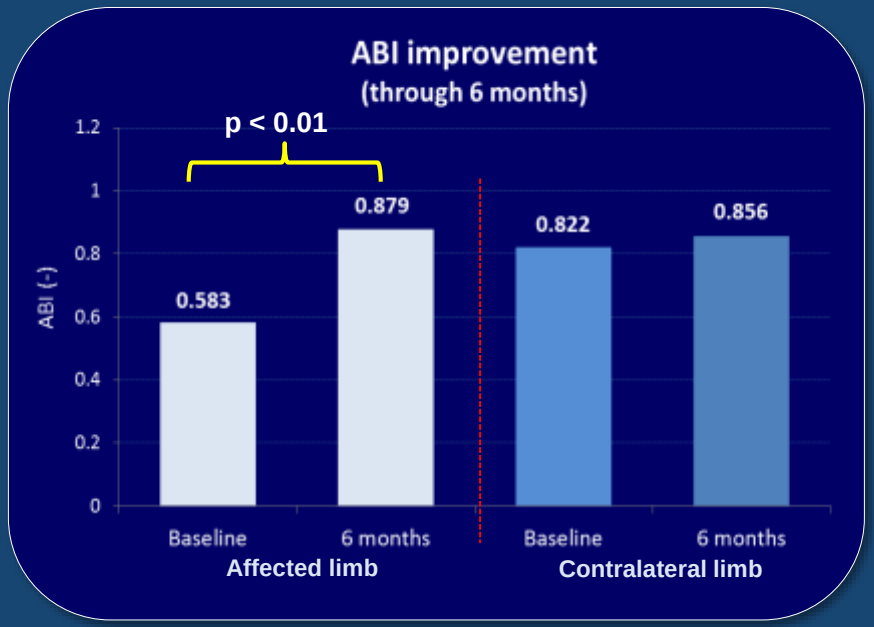
Lichtenberg, M. DGA 2016.

Ranger SFA Registry - Interim
Patient Outcomes

- 91% of patients improved by at least 1 Rutherford category at 6M
- 80% of patients improved ≥2 Rutherford categories at 6M



- Statistically significant ABI improvement from baseline to 6M in the affected limb



Study is sponsored by Klinikum Arnsberg
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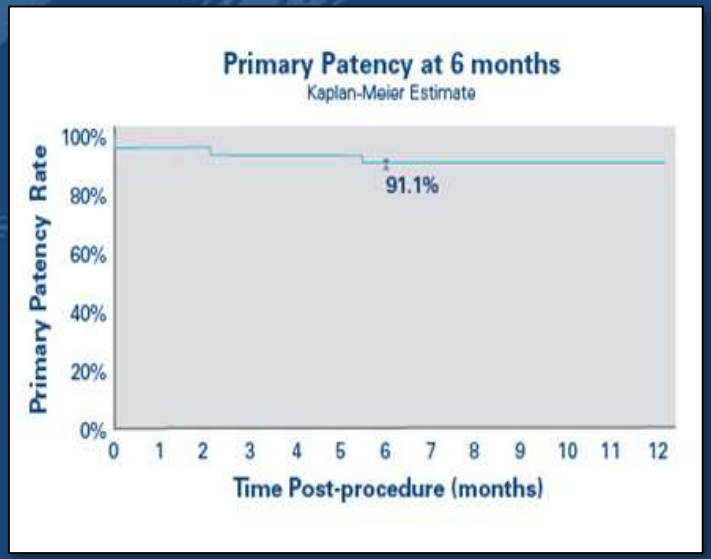
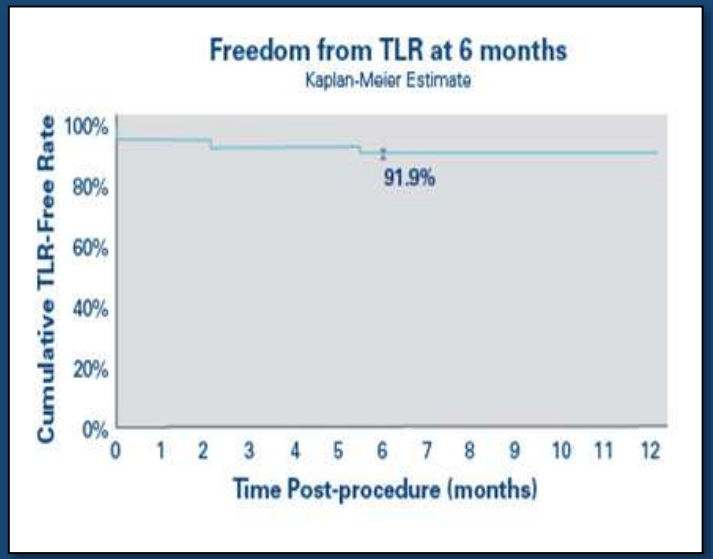
Ranger SFA Registry - Interim
Efficacy and Safety at 6M

- Primary Patency of **91.1%** at 6M by Kaplan Meier Estimate



- Freedom from TLR of **91.9%** at 6M by Kaplan Meier Estimate



Study is sponsored by Klinikum Arnsberg
VonBilderling, P. CIRSE 2016.

COMPARE I Pilot

Investigator Sponsored Research

Enrollment complete August 2016

Clinical Study Overview: COMPARE I Pilot Study	
Title	Prospective, Randomized, Multi-center Study for the Treatment of Subjects with Symptomatic Femoropopliteal Artery Disease with the Ranger™ Paclitaxel Coated PTA Balloon Catheter (study arm) vs. the IN.PACT™ Drug Eluting Balloon (control arm)
	Dierk Scheinert, MD – Germany University of Leipzig – Leipzig, Germany
Objective	To compare two different Paclitaxel coated balloons in the treatment of high grade stenotic or occluded lesions in the SFA and/of PPA
Study Design	Prospective, multicenter, RCT 1:1 (Ranger DCB : InPact DCB)
Subjects	150 patients
Investigational Centers	15 centers in Germany
Primary Efficacy Endpoint	Patency rate after 1yr defined as absence of clinically driven TLR (due to symptoms and drop of ABI of ≥ 20% or > 0.15 when compared to post-procedure baseline) or restenosis with PVR > 2.4 evaluated by DUS
Primary Safety Endpoint	Composite of freedom from device and procedure-related death through 12m post procedure as well as freedom from both target limb major amputation and clinically-driven TVR

COMPARE I Extension
Investigator Sponsored Research

Clinical Study Overview: COMPARE I ~~Pilot Study~~ Extension	
Title	Prospective, Randomized, Multi-center Study for the Treatment of Subjects with Symptomatic Femoropopliteal Artery Disease with the Ranger™ Paclitaxel Coated PTA Balloon Catheter (study arm) vs. the IN.PACT™ Drug Eluting Balloon (control arm)
Primary Investigator / Sponsor	Dierk Scheinert, MD – Germany University of Leipzig – Leipzig, Germany
Objective	To compare two different Paclitaxel coated balloons in the treatment of high grade stenotic or occluded lesions in the SFA and/of PPA
Study Design	Prospective, multicenter, RCT 1:1 (Ranger DCB : InPact DCB)
Subjects	~~150 patients~~ **414 patients**
Investigational Centers	15 centers in Germany
Primary Efficacy Endpoint	Patency rate after 1yr defined as absence of clinically driven TLR (due to symptoms and drop of ABI of ≥ 20% or > 0.15 when compared to post-procedure baseline) or restenosis with PVR > 2.4 evaluated by DUS
Primary Safety Endpoint	Composite of freedom from device and procedure-related death through 12m post procedure as well as freedom from both target limb major amputation and clinically-driven TVR

Conclusions

Real world studies and RCT testing the Ranger DCB have shown low rates of freedom from TLR at and improvement in patient outcomes at 6M

Boston Scientific has a broad portfolio of clinical studies with the goal of advancing the evidence for various PAD treatment technologies

- Large Head-to-head randomized trials
- Complex lesions being studied
- Adjunctive therapies being studied
- Inclusion of more endpoints including cost effectiveness

The future is exciting in the landscape for endovascular treatment for PAD, specifically in regards to Drug Elution technologies

Update on the Ranger clinical trial programme

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on behalf of the RANGER SFA investigators