State of play – contemporary use of DCB and Ranger Investigator Sponsored Research

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- 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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Disclosure

Speaker name:

Michael Lichtenberg

I have the following potential conflicts of interest to report:

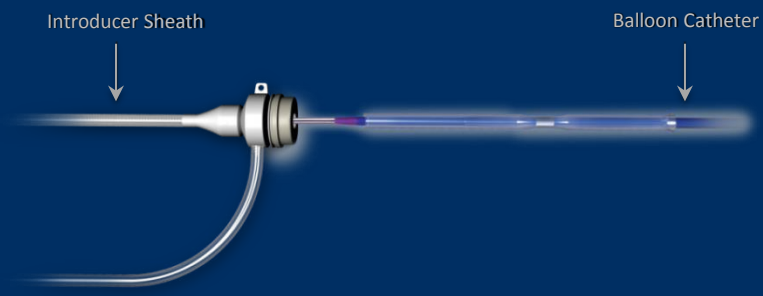
- [x] Consulting (Boston, CR Bard, Biotronik, Straub Medical, Optimed)
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [x] I do not have any potential conflict of interest

Ranger™ Drug Coated Balloon

- Sterling balloon platform
- TransPax™ coating technology
  (Paclitaxel, Excipient: Citrate estecitrate – ATBC)

- 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



BSC Peripheral DCB Clinical Program

Ranger DCB SFA

Prospective, multicenter, RCT
n = 105

DCB China
FPI: ~4Q 2015

Prospective, multicenter, single-arm, open label
n= 123

DCB SFA Global Pivotal
FPI: ~3Q 2016

Study Design TBD
n = ~300-600

Ongoing Ranger-SFA Clinical Study

Clinical Study Overview: Ranger	
Name	Ranger-SFA
Primary Investigator	Dierk Scheinert, MD
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	Planned 105 patients with femoropopliteal artery lesions
Investigational Centers	11 sites (Germany, France, and Austria)
Primary Endpoint	**The primary endpoint is in-segment late lumen loss of the treated segment, as observed by angiography at six months post-procedure**

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

Ranger-SFA Study
Patient Characteristics

	Control	Ranger DCB
N	30	63
Age (years)	67±9	68±8
Male	67%	73%
General Medical History		
Diabetes mellitus	33%	40%
Hyperlipidemia	60%	71%
Hypertension	73%	83%
Smoking		
Current	50%	40%
Previous	20%	46%
Cardiac History		
Congestive heart failure	3%	6%
Coronary artery disease	43%	35%
Myocardial infarction	17%	14%
Renal History		
Renal insufficiency	3%	13%
Peripheral Vascular History		
Claudication	93%	98%
Other peripheral endovascular interventions	33%	38%
Peripheral vascular surgery	0%	11%

Albrecht, T. CIRSE 2015.

Ranger-SFA Study
Lesion Characteristics and Procedural Success

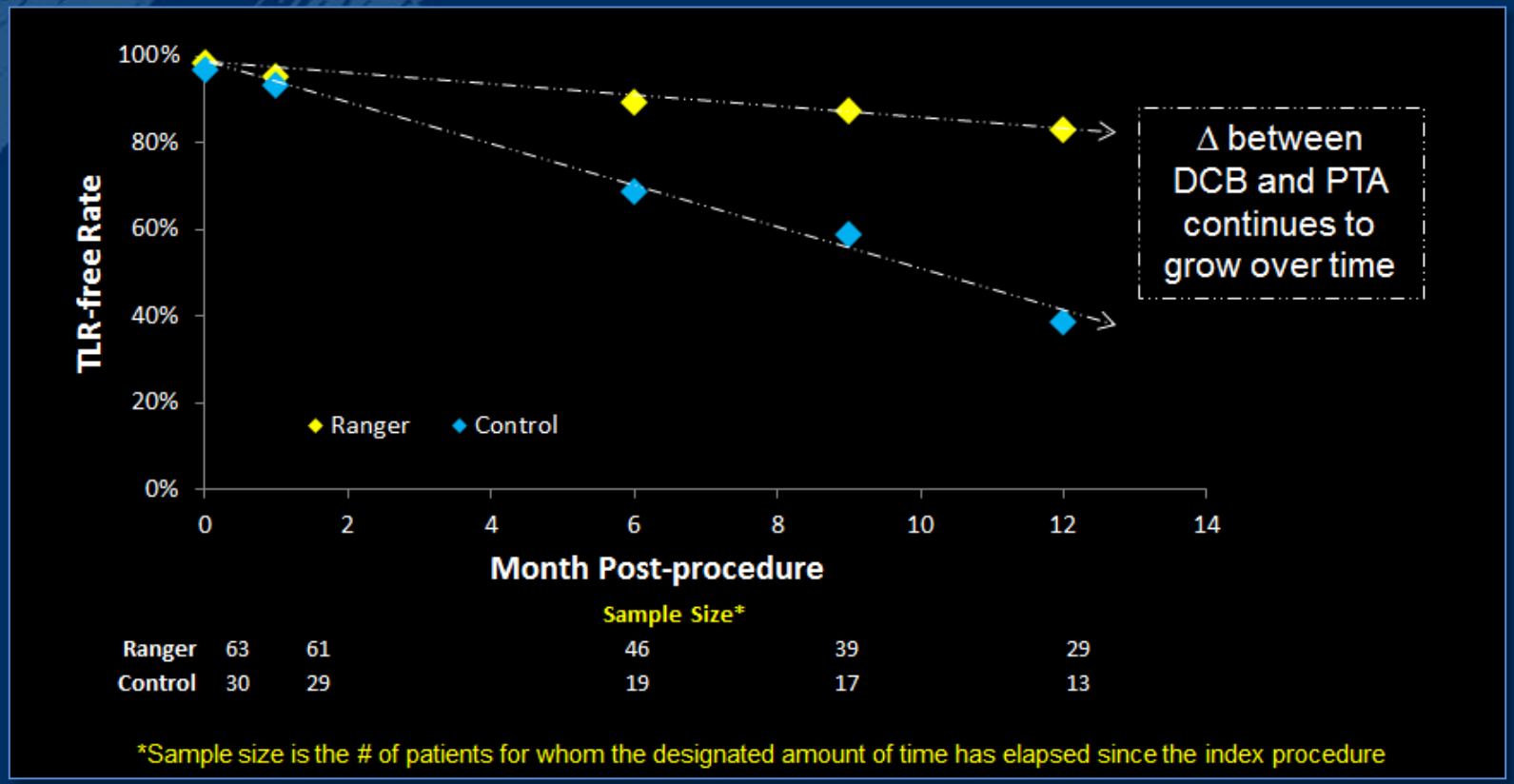
	Control (N=30)	Ranger DCB (N=63)
Lesion length (mm)	83 ± 66	73 ± 43
Lesion location		
Proximal SFA	7%	19%
Middle SFA	47%	41%
Distal SFA	43%	35%
Proximal popliteal	3%	5%
Reference vessel diameter (mm)	5.1 ± 1.1	5.2 ± 0.7
Percent diameter stenosis	89% ± 11%	91% ± 9%
TASCII		
A	77%	59%
B	23%	38%
C	0%	2%
D	0%	2%
Procedure	**Control**	**Ranger DCB**
Technical success	100% (30/30)	93.7% (59/63)
Procedural success	96.7% (29/30)	93.7% (59/63)
Residual angiographic stenosis	12% ± 12%	15% ± 17%

Albrecht, T. CIRSE 2015.

Ranger-SFA Study
Interim Safety Data – MAEs

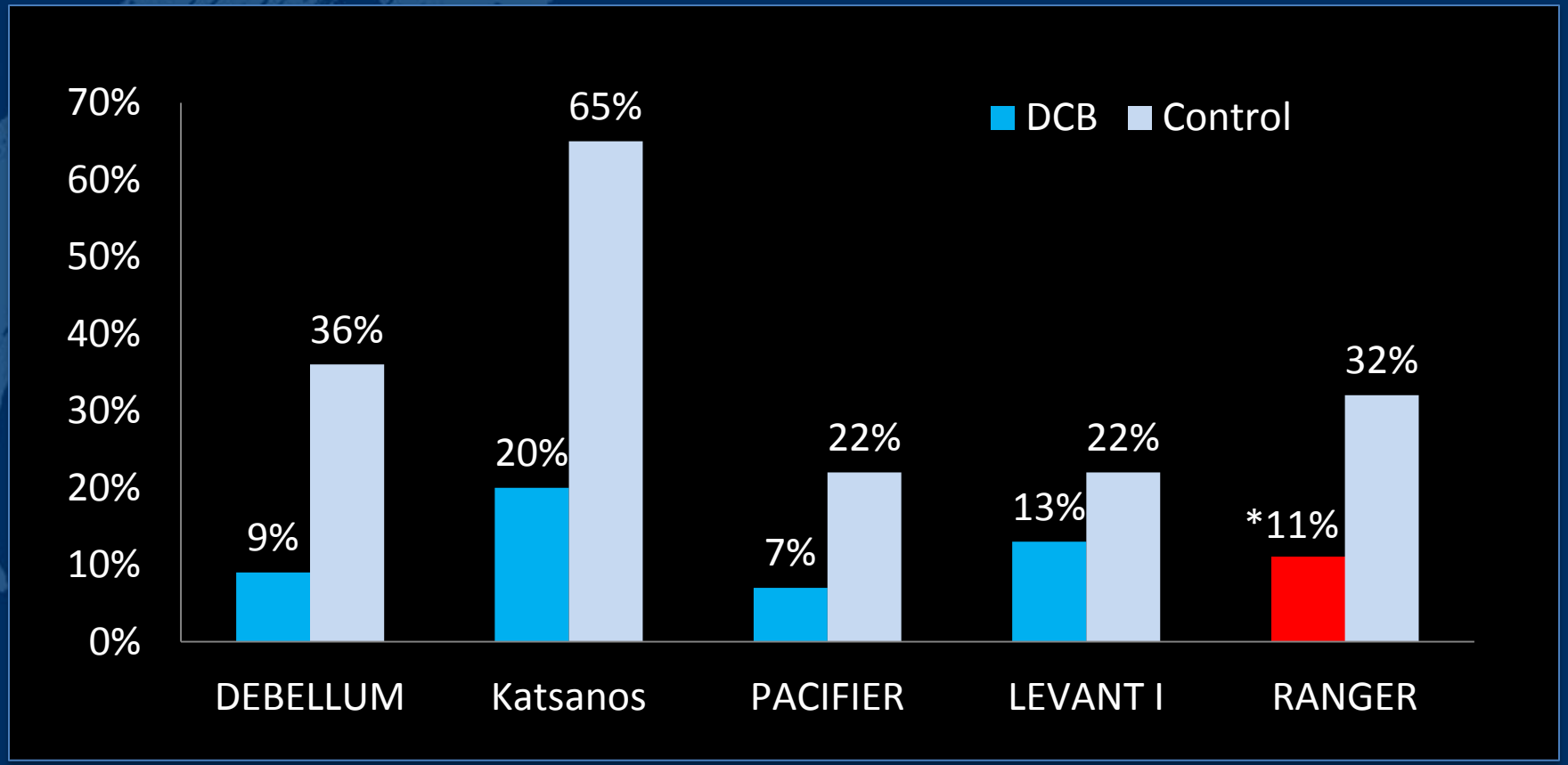
As of August 2015, interim snapshot of SAE and MAEs

- No SADE, no deaths or major amputations reported
- 8 TLR in the Control group and 5 TLR in the Ranger DCB group



Albrecht, T. CIRSE 2015.

Drug-Coated Balloons
(Randomized Trials)
TLR Rates at 6 months*

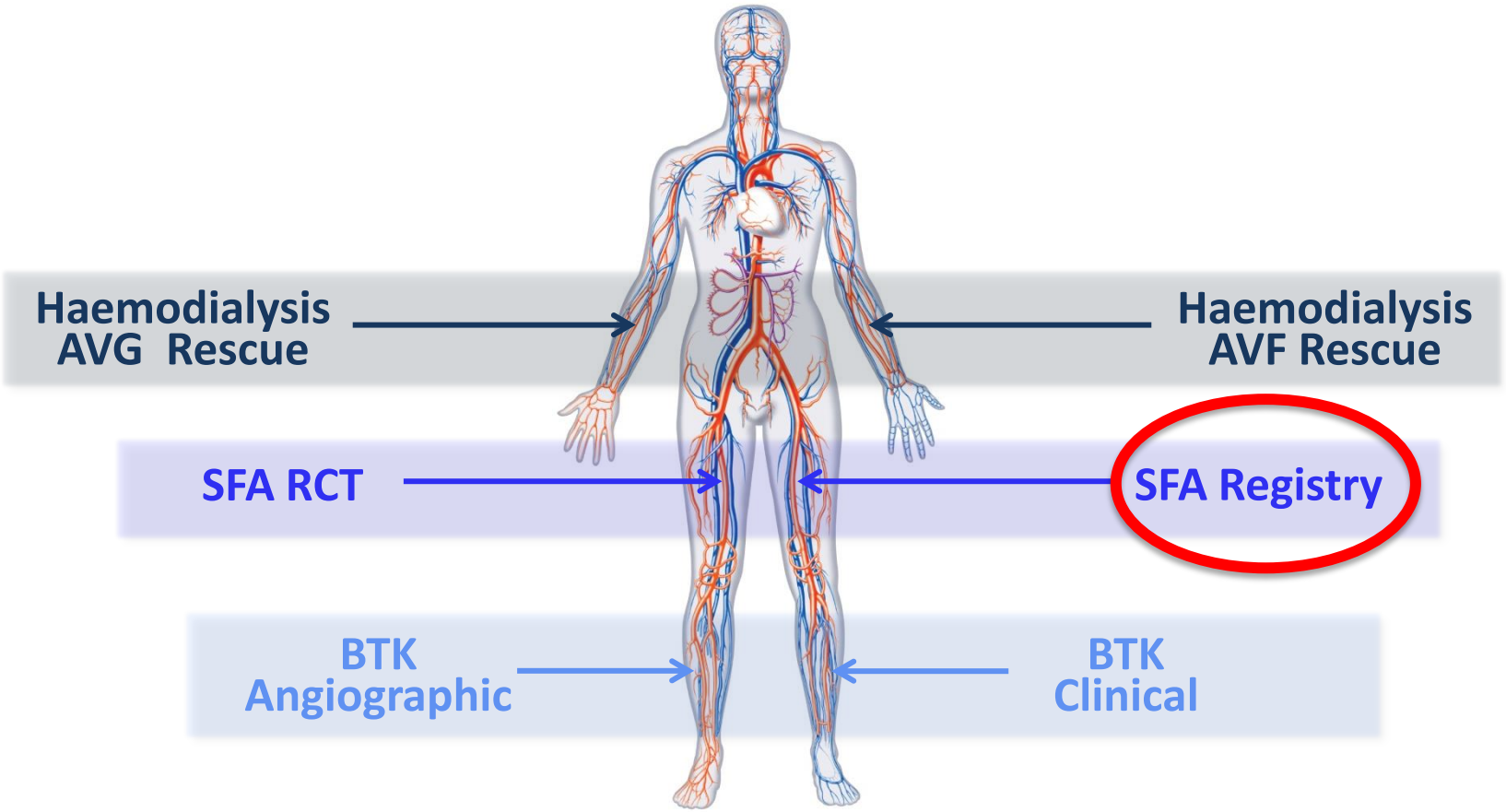


*Ranger Interim Trial analysis, monitoring ongoing

*Clinical trials were not designed to be comparable. Biondi-Zoccai G, et al. Int J Cardiol. 2013;168(1):570-1.
Data on file at Boston Scientific.

Boston Scientific DCB Investigator Sponsored Research

Patient centric program to study DCB use in various anatomies



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**
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**
Key Inclusion Criteria	**PAOD SFA – PIII, Rutherford II - V**

Ranger SFA Registry
Patient Demographics

	Ranger DCB
N	134
Mean Age (years)	70
Male	63 %
ABI	0.70 (0.1-1.4)
General Medical History	
Diabetes mellitus	34 %
Hyperlipidemia	95 %
Hypertension	93 %
Smoking	
Current	34 %
Previous	43 %
Renal History	
Renal insufficiency	20 %
Rutherford stage	
II	18 %
III	70 %
IV	7 %
V	5%

Ranger SFA Registry
Lesion Characteristics

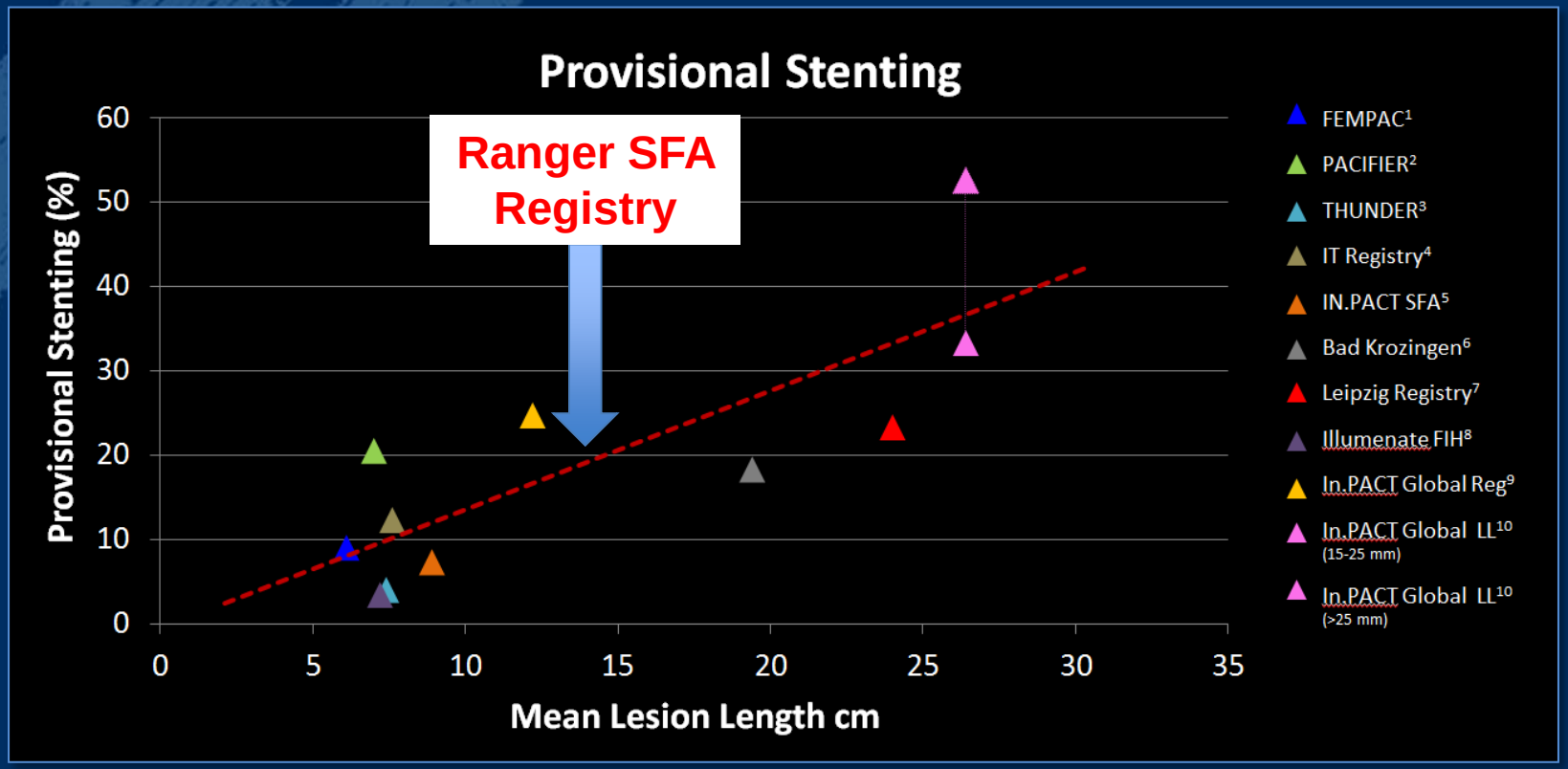
	Ranger DCB
Lesion (n)	188
SFA	126
APOP	62
Lesion length (mm)	142 mm (6 – 223 mm)
Lesion location	
Reference vessel diameter (mm)	5.3 mm ± 1.2
Percent diameter stenosis	89 % ± 11%
TASCII	
A	19 %
B	22 %
C	21 %
D	38 %

Ranger SFA Registry
Procedure Characteristics

Procedure	
TLD Number	
1	69 %
2	20 %
3	6 %
4	2.5 %
5	0.5 %
Predilatation before DCB	81.2 %
Bail out stent rate	**26%**
Procedure Outcomes	
Technical success for DCB only (no flow limiting dissection)	74 %
Procedural success DCB plus adjunctive therapy (stent)	100 %
Residual angiographic stenosis	10.7 %

Stents used in DCB studies

- Longer mean lesion length in DCB studies is correlated with higher provisional stenting rate



Provisional Stenting in Randomized Controlled Trials may not be representative of actual stenting in studies due to study design

Results from different trials are not directly comparable. Information provided for educational purposes.

[1]Werk M et al. Circulation 2008; [2]Werk et al. Circ Cardiovasc Interv 2012; [3]Tepe G et al. N Engl J Med 2008; [4]icari A Et al. J Am Coll Cardiol Intv 2012; [5]Tepe et al. Circulation 2015; [6]Zeller T et al. J Endovasc Therapy 2014; [7]Schmidt A. LINC 2013; [8]Schroeder H et al. Catheter Cardiovasc Interv 2015; [9]Laird J. Endovacsular Today Feb 2015. [10]Ansel G. TCT 2015.

Interim Analysis

Too early

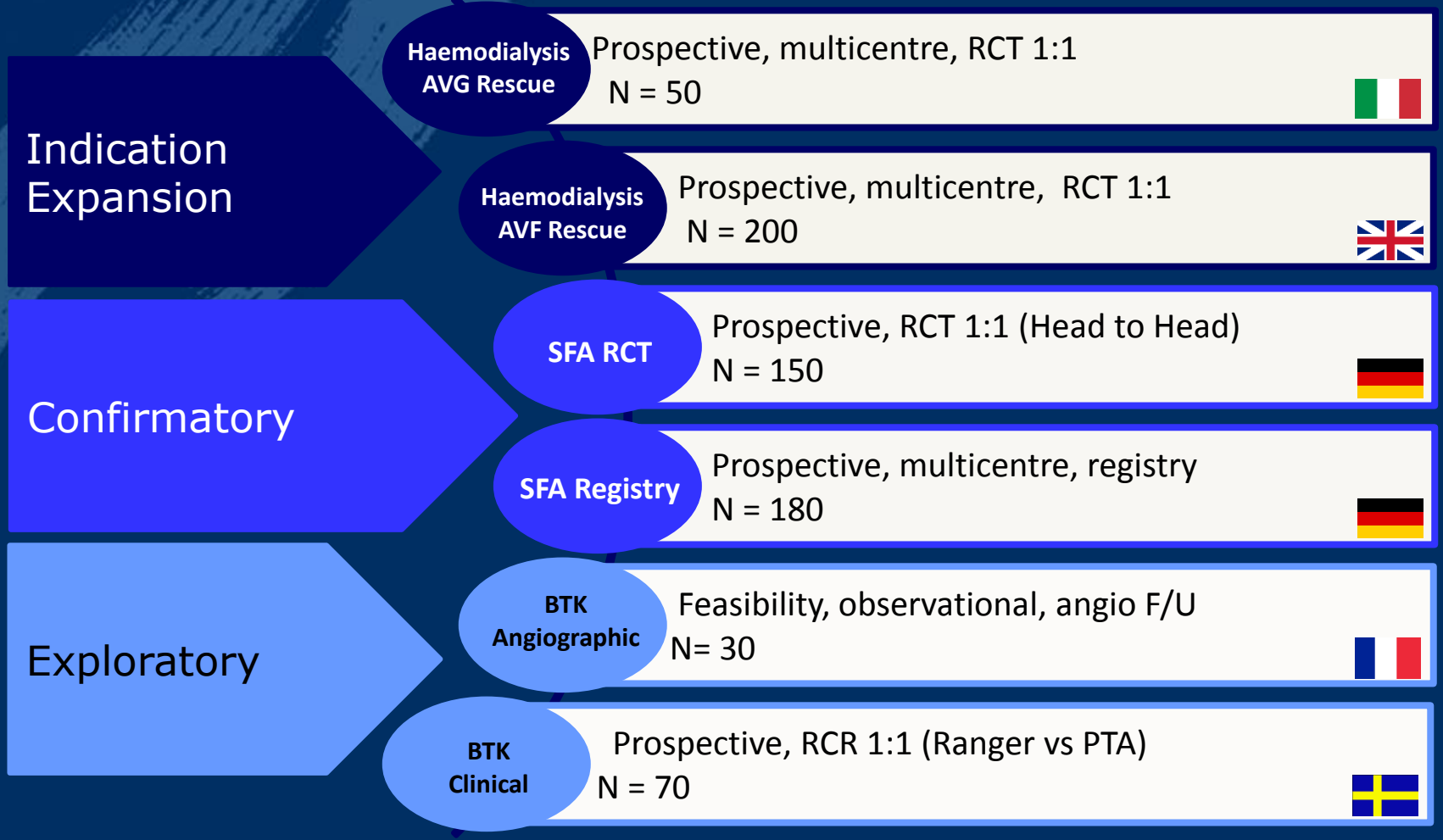
20. January 2016: 20 patients with 6 month FU

So far no TLR

Future of DCB

Areas of investigation for using DCB

Boston Scientific DCB Investigator Sponsored Research



Boston Scientific DCB Investigator Sponsored Research

COMPARE I Pilot Treatment of Subjects with Symptomatic Femoropopliteal Artery Disease with the Ranger™ DCB vs. the IN.PACT™ DCB	
PI	**Dierk Scheinert**
Design	**Multicentre, RCT 1:1**
Centres	**Germany and Austria**
Population	**150 patients**
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**

Boston Scientific DCB Investigator Sponsored Research

Exploration Studies

Ranger BTK A safety and efficacy study to evaluate Ranger drug-eluting balloon for below the knee angioplasty in patients with critical limb ischemia		**CRURAL DEB** Randomized trial comparing drug coated balloon vs plain balloon angioplasty in critical limb ischemia and treatment of long lesions in crural arteries	
PI	Marc Sapoval	PI	Torbjorn Fransson
Design	Prospective, single centre, non-controlled, open-label	Design	Prospective, single centre, randomized
Centres	France	Centres	Sweden
Population	30 patients	Population	70 patients
Primary Efficacy Endpoint	Primary patency (no stenosis >50%) and Late Lumen Loss (LLL) of the Target Lesion measured by Quantitative Vascular Angiography (QVA) at 6 months adjudicated by independent core lab	Primary Efficacy Endpoint	12 month primary patency
Primary Safety Endpoint	Composite of all death and major amputation at 6 and 12 months	Secondary Endpoints	TLR, Event Free Survival, MRA analysis

Conclusion

- DCB provide increased efficacy in short to medium term over plain PTA
- Early data on Ranger DCB is reassuring
- Ongoing Ranger SFA trials will provide further evidence in real world **Ranger SFA study** and head to head in **COMPARE I**
- Growing body of data on the effect of lesion characteristics on DCB outcome – calcium, occlusion, length / bail-out stenting

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