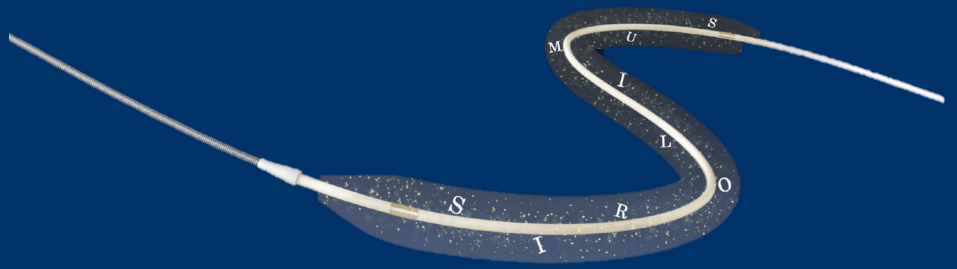


Discussion: SIRONA Trial Design

Head-to-Head Comparison of **SIRO**limus versus Paclitaxel Drug-Eluting Balloo**N** **A**ngioplasty in the Femoropopliteal Artery

Ulf Teichgräber, MD, MB

Disclosure

Speaker name:

Ulf Teichgräber, MD, MBA

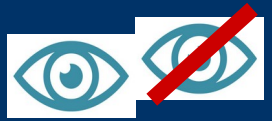
I have the following potential conflicts of interest to report:

I am the leading principal investigator of the randomised-controlled SIRONA trial, a head-to-head comparison trial of sirolimus versus paclitaxel drug-eluting balloon angioplasty in the femoropopliteal artery

Sirona at a glance

Safety and Efficacy of the Magic Touch PTA

Randomized (1 : 1)



Patient blinded, Investigator unblinded

478 patients

29 site in 2 countries

24 months recruitment

Study Sites

Nr	Ort	Hauptprüfer
01	Jena	Aschenbach
02	Bad Krozingen	Zeller
03	Immenstadt	Ito
04	Leipzig	Scheinert
05	Münster SFH	Stavroulakis
06	Sonneberg	Thieme
07	Berlin Charite	De Bucourt
08	Halle	Wohlgemuth
09	Flensburg	Müller-Hülsbeck
10	Heidelberg	Erbel
11	Mainz	Balzer
12	Münster UKM	Malyar
13	Dresden	Hoffmann
14	Augsburg	Kröncke
15	Rendsburg	Wissgott
16	Krefeld	Freyhardt
17	Essen	Rammos
18	Bruchsal	Andrassy
19	Torgau	Maiwald
20	Graz	Brodmann
21	Klagenfurt	Hausegger
22	Wien AKH	Wolf
23	Wien Hanusch	Werner
24	Langen	Donas
25	Berlin St. Gertrauden	Langhoff
26	Rosenheim	Tepe
27	Radebeul	Waßmer
28	Riesa	Waßmer
29	München	Heilmeier

Trial Design and Endpoints

Endpoints		Baseline	1 month	6 month	12 month	24 month	36 month	48 month	60 month
Efficacy	**Primary**	Patency Rate*		Patency Rate	Patency Rate	Patency Rate			
	Secondary	Composite of: - freedom from device and procedure-related **death** through 12 months - **freedom from target limb major amputation** and - clinically-driven **TVR**	WIQ	• TLR rate • Rutherford improvement • Walking capacity • EQ-5D-3L					
				Binary restenosis (via DUS)					
Safety	**Primary**	Composite of: - freedom from device and procedure-related **death** through 60 months - **freedom from target limb major amputation** and - clinically-driven **TVR**	• Composite of: - freedom from all-cause death - freedom from target limb amputation - freedom from TVR						

Study Endpoints

Primary Endpoint

Efficacy: patency rate after one year defined as absence of clinically driven TLR (due to symptoms and drop of ABI of ≥ 20% or > 0.15 when compared to post-procedure) or restenosis with PVR > 2.4 evaluated by duplex ultrasound

Primary Safety: Composite of freedom from device and procedure-related death through 12 months post procedure as well as freedom from both target limb major amputation and clinically-driven target vessel revascularization

Secondary Endpoint

1. **TLR rate** at 6, 12, 24, 36, 48 and 60 months

2. **Sustained clinical improvement:** an improvement shift in the Rutherford classification of one class in amputation and TVR free surviving patients at 12 months

3. **Walking capacity assessment:**

a) Walking distance test measured by treadmill
b) "Corridor" pain-free walking distance test
c) Walking Impairment Questionnaire at 6, 12, 24, 36, 48 and 60 months.

4. **Duplex-defined binary restenosis** (PSVR >2.4) of the target lesion post-procedure and at 6, 12 and 24 months or at any time of re-intervention

5. **Quality of life assessment** by EQ5D at 6, 12, 24, 36, 48 and 60 months

6. **Secondary Safety:** Composite of freedom from device and procedure-related, all cause death through 60 months post procedure as well as freedom from both target limb major amputation and clinically-driven target vessel revascularization.

Key Eligibility Criteria

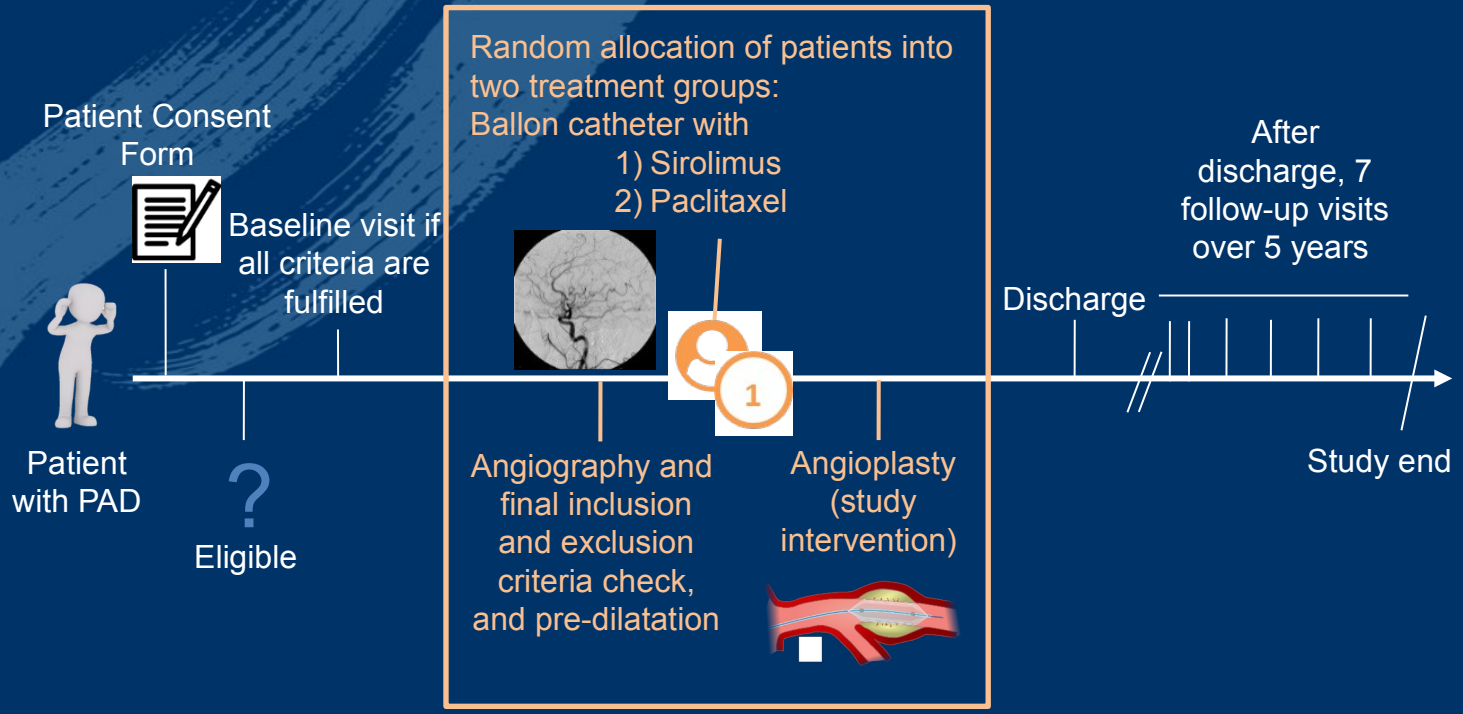
Inclusion

- Rutherford category 2-4
- De-novo stenotic / restenotic lesion with ≥ 70% stenosis
- Lesion length ≥ 2 cm and ≤ 20 cm
- Reference vessel diameter (RVD) ≥ 4 mm and ≤ 6.5 mm

Exclusion

- Severe calcified lesions (PTA resistant)
- Major amputation
- Previous surgery
- SFA or PPA disease in the opposite leg that requires treatment at the index procedure

Study Workflow



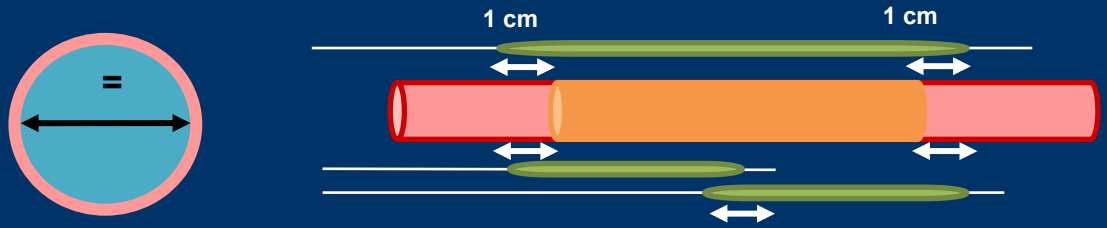
Index procedure

Balloon length:

- Balloon sizing must match the reference vessel diameter distal to the target lesion and fully cover and extend slightly beyond the lesion length (about 1 cm of margin for both edges)
- Balloon inflation pressure should be at or beyond the nominal pressure, but the rated burst pressure (RBP) should never be exceeded

Inflation and pre-dilatation:

- Inflation time: min. 60 sec or longest time after SoC
- Dilatation time of **180 seconds** (3 minutes) is strongly recommended



≥ 60 sec.

Follow-Up

On-site

- Physical examination with duplex of thigh concerned
- Queries about medication, health condition, walking test
- Walking capacity assessment

Phone FU

- Queries about medication, health condition, walking test

Hypothesis

DCB has been questioned after Katsanos et al. (2018) and Klumb et al. (2019) described an association between paclitaxel dose and mortality risk.

The authorities, such as BfArM, unanimously recommend further evaluation given the widespread use of paclitaxel in peripheral interventions in clinical practice.

SIRONA trial is currently the first trial worldwide that is ready to be initiated to collect additional evidence on patient level regarding this topic.

The safety alert initiated by the above-mentioned systematic reviews leads to the search of an alternative to PTX DCB.