UNIVERSITÄTS KLINIKUM jena

Department of Radiology

EffPac - Trial:

Effectiveness of LUMINOR® DCB versus POBA in the SFA: primary endpoint and 6 months results

Ulf Teichgräber
on behalf of the Investigators

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Disclosure of conflict of interest

Speaker name: Ulf Teichgräber, MD, MBA

Potential conflicts of interest related to the presentation:

- **Research grant: iVascular, Endoscout**

Potential conflicts of interest not related to the presentation:

- **Consulting Fees, Honoraria, Research Grants, Advisory Boards: ab medica, Abbott Vascular, B.Braun Melsungen, Boston Scientific, Celonova, C.R. Bard, COOK, Endoscout, GE Healthcare, iVascular, Kimal, Maquet, Medtronic, Philips Healthcare, Siemens Healthineers, Spectranetics, W.L.Gore**
- **Master research agreements with Siemens Healthineers, GE Healthcare**

luminor

Paclitaxel coated balloon
(3,0 µg/mm²)

Fast deflation

Ultra low tip and crossing profiles

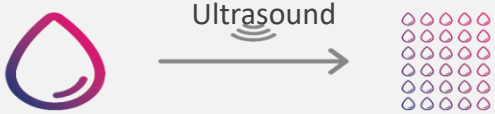
Innovative and UNIQUE nanotechnology coating

Complete balloon range dimensions

Luminor 35: 5-7mm Ø and 20-150mm length
Luminor 18: 2-8 mm Ø and 20-200mm length
Luminor 14: 1.5-4mm Ø and 40-200mm length

luminor

UNIQUE nanotechnology coating

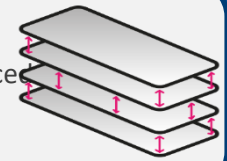


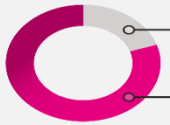
Spray Technology
Dosage of uniform diameter nanodrops by ultrasonic deposition

TransferTech

Proprietary nanotechnology dosage system for an **uniform, flexible** and **ultrathin coating**

Multi-layer technology
- Coating durability during the proce
- No cracking





Excipient
- Organic ester
- Biocompatible
- Lipophilic

Paclitaxel
- Lipophilic
- Inhibition of stenosis
- Specific cellular receptors

Dry-off
- Microcrystalline structure
- Optimal drug transfer to the vessel wall within 30-60s seconds

Study Title

Multicenter Randomized Controlled Trial to assess the

Effectiveness of Paclitaxel-coated Luminor® Balloon Catheter

vs.

Uncoated Balloon Catheter

in the Superficial Femoral and Popliteal Arteries to Prevent Vessel Restenosis or Reocclusion

EffPac-Trial

Design:

Investigator-initiated, prospective, multi-centre, intention-to-treat trial and 2 arms randomised study

Objective:

Safety and efficacy of the Luminor® paclitaxel drug-eluting balloon in inhibiting restenosis and in ensuring long-term patency

Sponsor: **University of Jena, Germany**

Representative of the sponsor: **Prof. Dr. Ulf Teichgräber, Jena University Hospital**

EFFPac-Trial

CoreLab

Dr. Ulrich Beschorner, coreLab Bad Krozingen GmbH, Germany

Data Management and Safety Board (DMSB)

Dr. Michael Werk, Martin Luther Krankenhaus, Berlin, Germany

Dr. Vicenc Riambau, Hospital Clinic de Barcelona, Spain

Prof. Dr. Wienke, University Halle-Wittenberg, Germany

Monitoring and SAE Reporting (VascuScience GmbH)

Dr. Christin Ott and Lars Mahler, Leipzig, Germany

Project Management

Tabitha Heller, Cornelia Eichorn, Nicole Brillinger, Dr. Andrea Rößler, University Jena, Germany

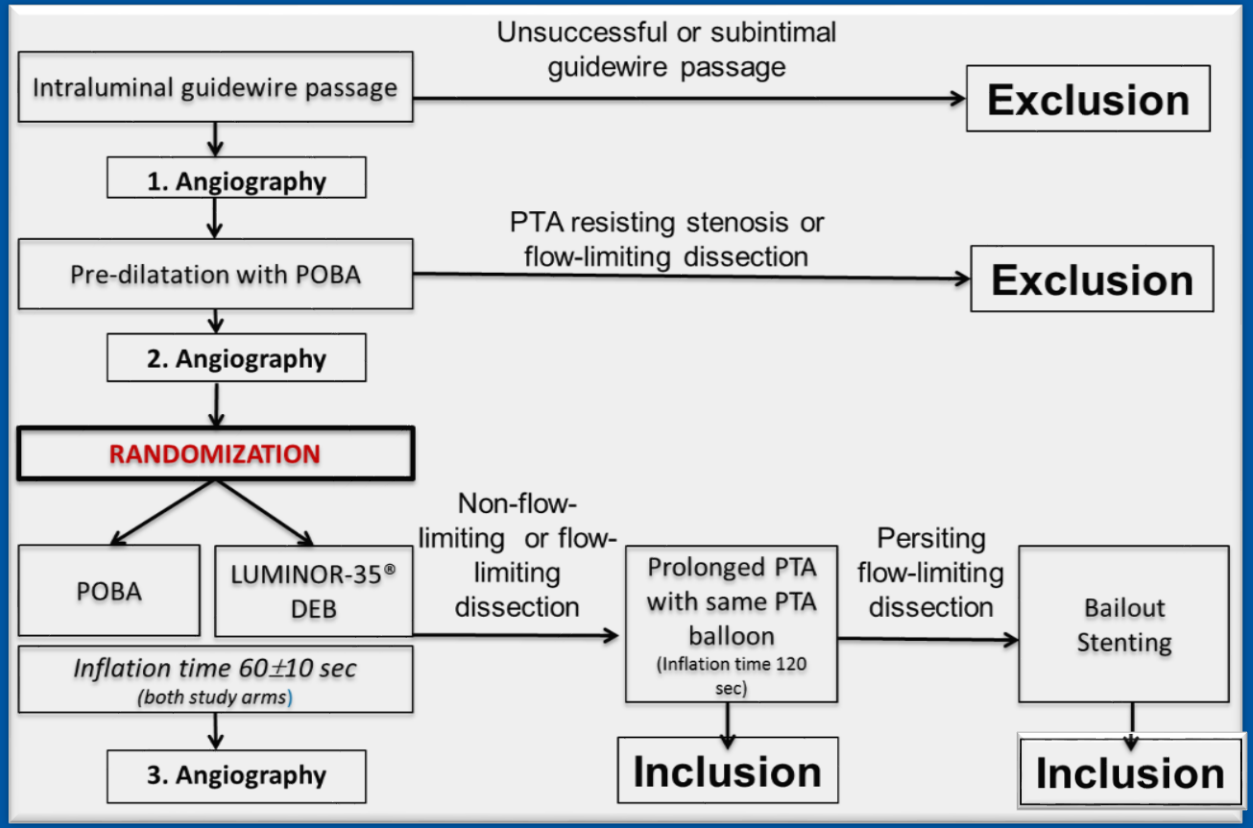
Producer of the Investigational Product

Life Vascular Devices Biotech, S.L., Barcelona, Spain

11 Participating Sites

01 Jena	PD Dr. R. Aschenbach, *University Hospital Jena*
02 Leipzig	Prof. Dr. Dierk Scheinert, *University Hospital Leipzig*
03 Bad Krozingen	Prof. Dr. Thomas Zeller, *Heart Center*
04 Hamburg	Dr. S. Sixt, *Angiologikum*
05 München	PD Dr. M. Treitl, *University Hospital*
06 Berlin	Prof. Dr. K. Brechtel, *„Ihre Radiologen"*
07 Sonneberg	Dr. M. Thieme, *Medinos Clinic*
08 Karlsbad	Prof. Dr. E. Blessing, *SRH-Clinic*
09 Heidelberg	Dr. B. Vogel, University Heidelberg
10 Arnsberg	Dr. M. Lichtenberg, *Clinic Arnsberg*
11 Krusel	Dr. P. von Flotow, *Westpfalz Clinic*

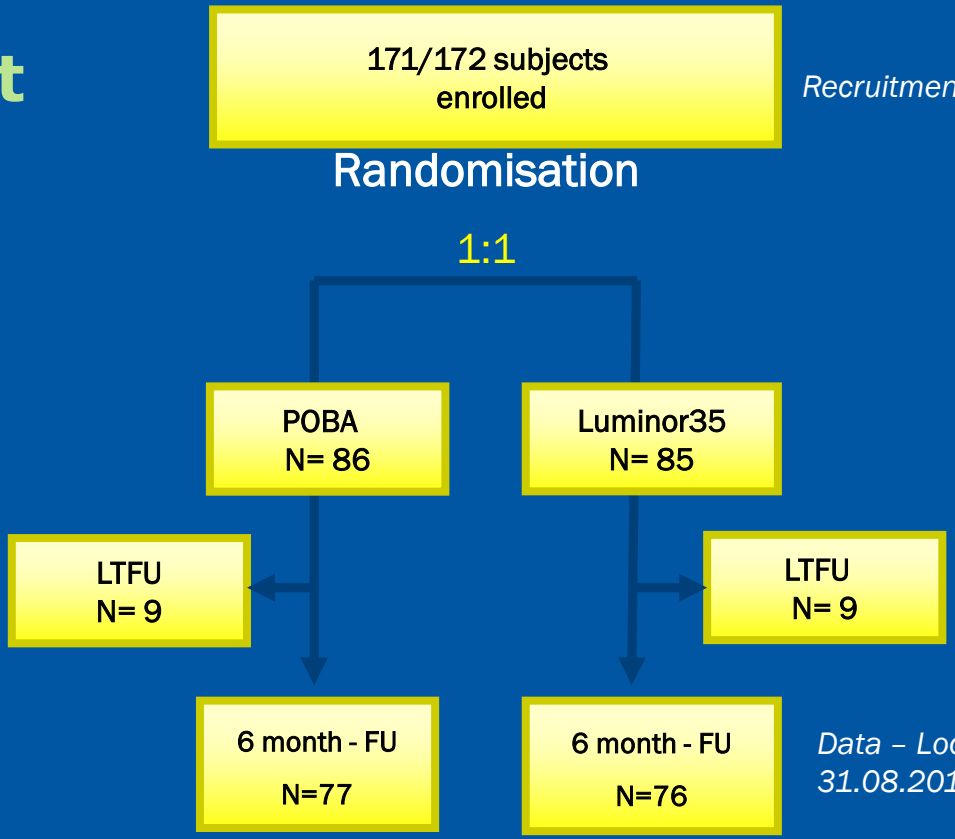
Flowchart


Intraluminal guidewire passage
Unsuccessful or subintimal guidewire passage
Exclusion
1. Angiography
Pre-dilatation with POBA
PTA resisting stenosis or flow-limiting dissection
Exclusion
2. Angiography
RANDOMIZATION
POBA
LUMINOR-35® DEB
Inflation time 60±10 sec
(both study arms)
3. Angiography
Non-flow-limiting or flow-limiting dissection
Prolonged PTA with same PTA balloon
(Inflation time 120 sec)
Inclusion
Persiting flow-limiting dissection
Bailout Stenting
Inclusion

Trial Design and Endpoints

Endpoints		Baseline	6 month	12 month	24 month
Efficacy	Primary	Vessel diameter (mm)	• Late Lumen Loss (LLL)*	-	-
	Secondary		• Freedom from Target Lesion Revascularization (TLR/TVR) • Patency • Change of ABI, Rutherford stage, QoL (WIQ) , EQ-5D		
Safety	Primary		• Major and minor amputation rate at index limb • Mortality, independently of cause		

Flowchart



Recruitment completed on 31. Dec. 2016

Data – Lock – Point for 6 month-FUP on 31.08.2017

Baseline Patient Characteristics

	LUMINOR®	POBA
Age - yr	68.0 ± 7.5 (85)	68.1 ± 8.8 (86)
Male - % (no.)	60.0% (51/85)	69.8% (60/86)
Diabetes mellitus - % (no.)	36.5% (31/85)	40.7% (35/86)
Hypertension - % (no.)	87.1% (74/85)	84.9% (73/86)
Hyperlipidemia - % (no.)	70.6% (60/85)	68.6% (59/86)

Baseline Patient Characteristics

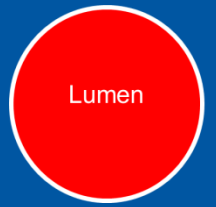
		LUMINOR®	POBA
Rutherford Clinical Category			
Mild claudication	1	0% (0/85)	0% (0/85)
Moderate claudication	2	15.3% (13/85)	21.2% (18/85)
Severe claudication	3	81.2% (69/85)	77.6% (66/85)
Ischemic rest pain	4	2.4% (2/85)	1.2% (1/85)
Minor tissue loss	5	1.2% (1/85)	0% (0/85)
Major tissue loss	6	0% (0/85)	0% (0/85)
ABI (treated leg)		0.73 ± 0.23 (69)	0.74 ± 0.23 (69)

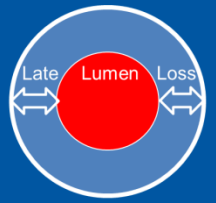
Baseline Angiographic Data

	LUMINOR®	POBA	p value
Lesion Length (cm)	5.9 ± 4.3 (84)	5.6 ± 3.9 (86)	0.731
Total Occlusion	20.2% (17/84)	25.6% (22/86)	0.468
Calcification			0.094
none/mild	54.2% (45/83)	44.2% (38/86)	
moderate	42.2% (35/83)	44.2% (38/86)	
severe	3.6% (3/83)	11.6% (10/86)	
Diameter Stenosis (%)	88.0 ± 9.8 (85)	90.1 ± 8.8 (86)	0.191
Reference Vessel Diameter (mm)	5.4 ± 0.6 (85)	5.4 ± 0.7 (86)	0.732
# of Patent Run-off Vessel			0.311
0	0% (0/85)	1.2% (1/86)	
1	22.4% (19/85)	22.1% (19/86)	
2	41.2% (35/85)	31.4% (27/86)	
3	36.5% (31/85)	45.3% (39/86)	

Efficacy:
Late Lumen Loss - LLL

*** LLL =** difference between the diameters (in mm) at 6 months follow-up minus post-procedure





	LUMINOR®	POBA	Difference, 95% CI (LUMINOR® vs. POBA)	p value
LLL 6M (mm)*	0.14 [CI: -0.38; 0.67]	1.06 [CI: 0.54; 1.59]	-0.92 [CI: -1.36; -0.49]	<0.001

* Estimated LLL (Mean, 95% CI) from linear mixed model adjusted for center

Efficacy: Late Lumen Loss - LLL

Study	Drug-coated balloon 6 mo LLL (mm)	Control 6 mo LLL (mm)	LLL Difference (mm)
THUNDER Tepe et al. 2008 Paccocath coating	0.4±1.2	1.7±1.8	-1.3
AcoArt I Trial Jia et al. 2016 Orchid (Acotec)	0.05±0.73	1.15±0.89	-1.1
EFFPAC 2017 Luminor (iVascular)	**0.14 [CI: -0.38; 0.67]**	**1.06 [CI:0.54; 1.59]**	**-0.92**
RANGER Bausback et al. 2017 Ranger DCB	-0.16±0.99	0.76±1.4	-0.60
LEVANT I Scheinert et al. 2014 Lutonix (Bard)	0.46±1.13	1.09±1.07	-0.63
BIOLUX P-I Trial Scheinert et al. 2015 Passeo-18 Lux (Biotronik)	0.51±0.72	1.04±1.0	-0.53
FEMPAC Werk et al. 2008 Paccocath DCB	0.5±1.1	1.0±1.1	-0.5
CONSEQUENT 2017 SeQuent Please (B. Braun)	0.35 [CI: 0.19; 0.79]	0.72 [CI: 0.68; 1.22]	-0.37

Efficacy: Improvement of Rutherford after 6M

Improvement of Rutherford Stages	LUMINOR®	POBA
Deterioration of 1 stage	1.4% (1/74)	0% (0/82)
No improvement	13.5% (10/74)	25.0% (18/82)
Improvement of 1 stage	12.2% (9/74)	20.8% (15/82)
Improvement of 2 stages	28.4% (21/74)	26.4% (19/82)
Improvement of 3 stages	44.6% (33/74)	27.8% (20/82)

Significant higher improvement of LUMINOR® compared to POBA (p=0.021)

Efficacy: Target Lesion Revascularization (TLR)

	LUMINOR®	POBA	Relative Risk, 95% CI (LUMINOR® vs. POBA)	Number needed to treat (NNT)	p value
TLR 6M (%)	1.3 (1/76)	17.1 (13/76)	0.082 [CI: 0.012; 0.560]*	7	<0.001

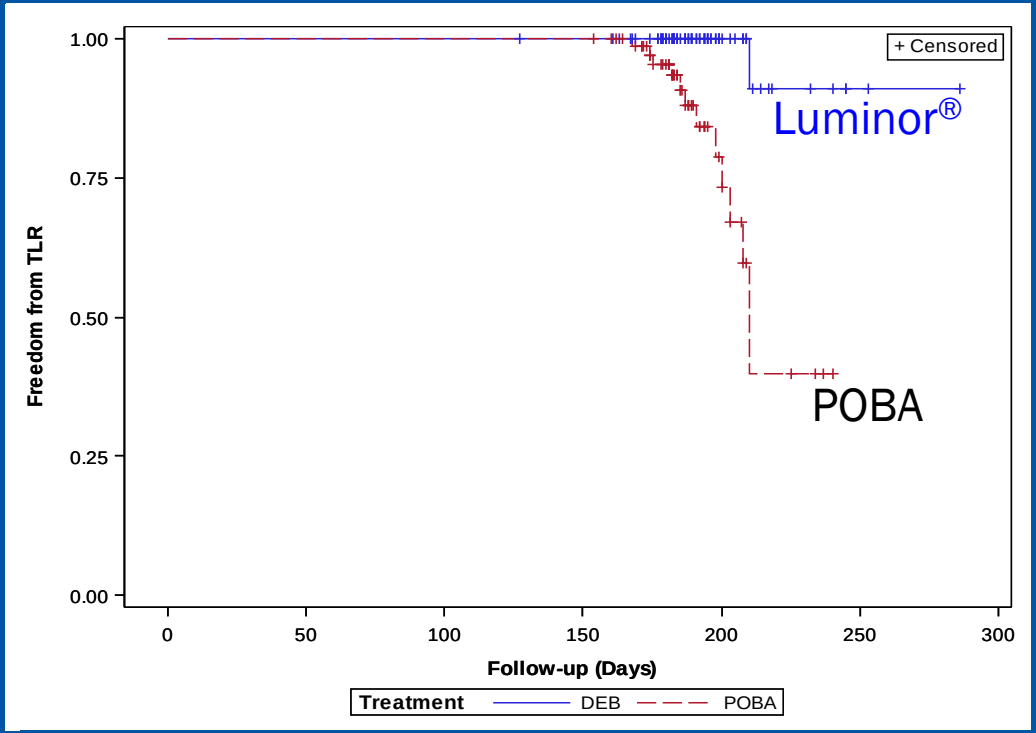
*Relative Risk Reduction (RRR) = 91.8%, Cochran-Mantel-Haenszel estimate, adjusted for center

Efficacy: Target Lesion Revascularization (TLR)

Study	DCB 6 mo TLR (%)	Control 6 mo TLR (%)
EFFPAC 2017 Luminor (iVascular)	**1.3 (1/76)**	**17.1 (13/76)**
THUNDER Tepe et al. 2008 Paccocath coating	4.2 (2/48)	37.0 (20/54)
AcoArt I Trial Jia et al. 2016 Orchid (Acotec)	6.1 (6/99)	38.8 (38/98)
FEMPAC Werk et al. 2008 Paccocath DCB	6.7 (3/45)	33.3 (14/42)
CONSEQUENT 2017 SeQuent Please (B. Braun)	8.9 (7/78)	30.7 (23/75)
RANGER Bausback et al. 2017 Ranger DCB	5.6 (4/71)	12.0 (4/34)
BIOLUX P-I Trial Scheinert et al. 2015 Passeo-18 Lux (Biotronik)	3.8 (1/26)*	4.2 (1/24)*

*Kaplan-Meier estimates, clinically driven TLR

Efficacy: Target Lesion Revascularization (TLR)



Efficacy: Patency

	LUMINOR®	POBA	Relative Risk*, 95% CI (LUMINOR® vs. POBA)	Number needed to treat (NNT)	p value
Patency (%)	94.7 (72/76)	75.0 (57/76)	1.26 [CI: 1.100; 1.443]	6	<0.001

* Interpretation: Relative chance for patency is increased by 26% in the LUMINOR® group

Primary patency: Freedom from restenosis (determined by duplex ultrasound PSVR <2.5) and freedom from TLR at 6 months

Efficacy: Patency

Study	DCB 6 mo Patency (%)	Control 6 mo Patency (%)
LEVANT I Scheinert et al. 2014 Lutonix DCB	71.8 (28/39)**	41.4 (17/41)**
RANGER-SFA 2017 Ranger DCB	87.0 (62/71)	60.0 (20/34)
EFFPAC 2017 Luminor (iVascular)	**94.7 (72/76)**	**75.0 (57/76)**
FEMPAC Werk et al. 2008 Paccocath DCB	93.5 (29/31)	94.1 (32/34)

* Interpretation: Increase of relative chance for patency DCB vs. POBA

** Patency based on freedom from target lesion revascularization and restenosis, restenosis by angiography (>50%DS) at 6M

Safety: Adverse Events

	LUMINOR®	POBA	p value
Minor Amputation (%)	0 (0/85)	1.2 (1/86)	1.000
Major Amputation (%)	0 (0/85)	0 (0/86)	1.000
Death (not related, %)	0 (0/85)	2.3 (2/86)	0.497

Conclusions

The LUMINOR® Paclitaxel-coated balloon catheter demonstrates to be clinical highly effective and safe in inhibiting restenosis compared to POBA

The innovative coating technique matters and is shown not only in the patency, LLL and TLR data, but also in an improvement of the Rutherford stage

The results of the study allow direct comparison to other already-completed RCTs applying Paclitaxel-coated DEB from different manufacturers in the same target vessel

EffPac-Trial results of 12-months follow-up will be presented on Apirl 2018