Best DCB outcomes in SFA TASC A&B lesions: EFFPAC-RCT 12-months follow-up

Ulf Teichgräber, MD, MBA
on behalf of the investigators

Teichgräber U, Aschenbach R, Scheinert D, Zeller T, Brechtel K, Blessing E, Treitl M, Lichtenberg M, von Flotow P, Vogel B, Werk M, Riambau V, Wienke A, Lehmann T, Sixt S, Thieme M

NCT02540018 | Teichgräber et al. Trials (2016) DOI 10.1186/s13063-016-1657-x

Disclosure of conflict of interest

- Speaker name: Ulf Teichgräber, MD, MBA

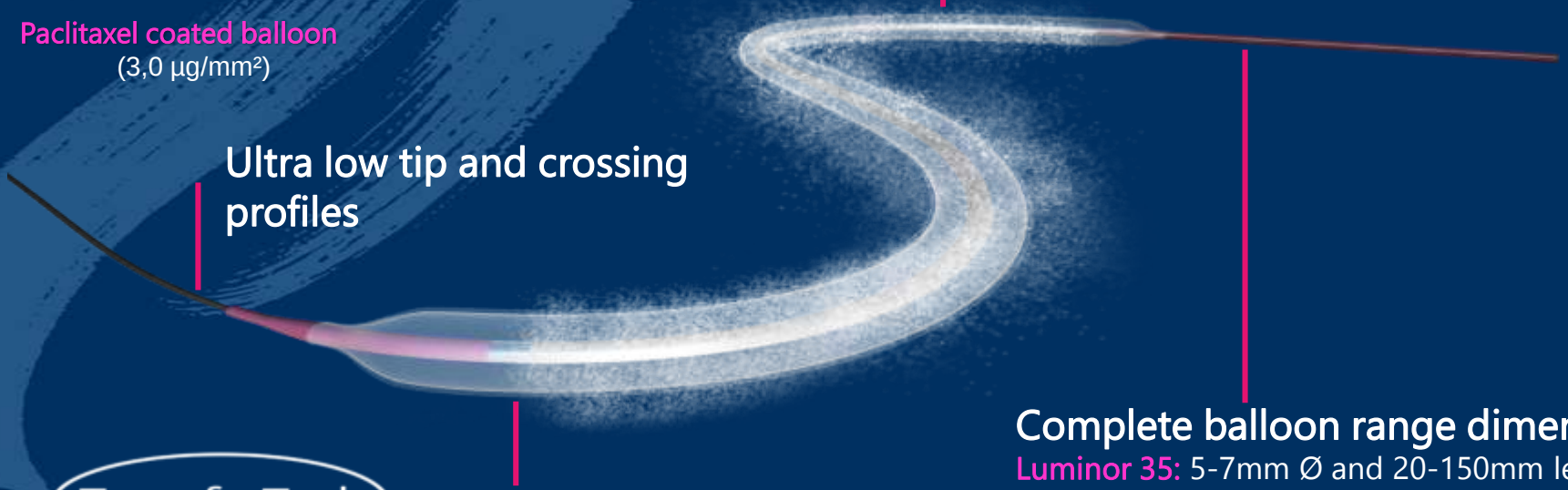
- Potential conflicts of interest related to the presentation:
  - Research grant: iVascular, Endoscout

- 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)

iVascular
therapies for living



Fast deflation

Ultra low tip and crossing profiles

Innovative and UNIQUE nanotechnology coating

TransferTech

Complete balloon range dimensions

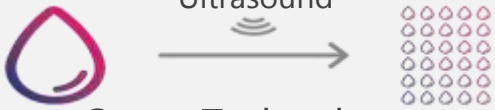
Luminor 35: 5-7mm Ø and 20-150mm length
Luminor 18: 2-8 mm Ø and 20-200mm length
Luminor 14: 1.5-4mm Ø and 40-200mm length

LINC 2019 – U. Teichgräber et al. – Best DCB outcomes in SFA TASC A&B lesions – EFFPAC-RCT 12-months follow-up –Discussion Forum, 22.01.2019

luminor

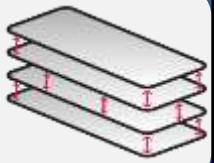
iVascular

UNIQUE nanotechnology coating



Spray Technology
Dosage of uniform diameter nanodrops by ultrasonic deposition

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



TransferTech

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

Excipient
- Organic ester
- Biocompatible
- Lipophilic

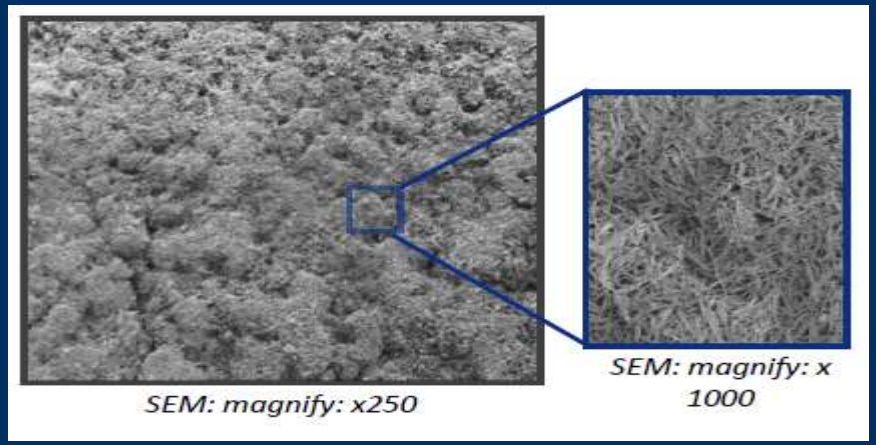
Paclitaxel
- Lipophilic
- Inhibition of stenosis
- Specific cellular receptors

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

Coating Technology

- Ultrathin **multilayer** coating:
  - Increases **adhesion** to balloon
    - **Lower loss** related to manipulation
  - Improves **durability**:
    - **Lower loss** during navigation
  - Improves mechanical properties
  - **Fast absorption:** 30-60s

Dosage of uniform diameter nanodrops by direct ultrasonic deposition



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-randomized 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 Safety and Monitoring Board (DSMB):

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

Dr. Vicenc Riambau, Hospital Clinic de Barcelona, Spain

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

Monitoring (VascuScience GmbH): Dr. Christin Ott, Svenja Peters, Leipzig, Germany

Project Management: Nicole Brillinger, Tabitha Heller, University Hospital Jena, Germany

SAE Management: Monique Philipp, University Hospital Jena, Germany

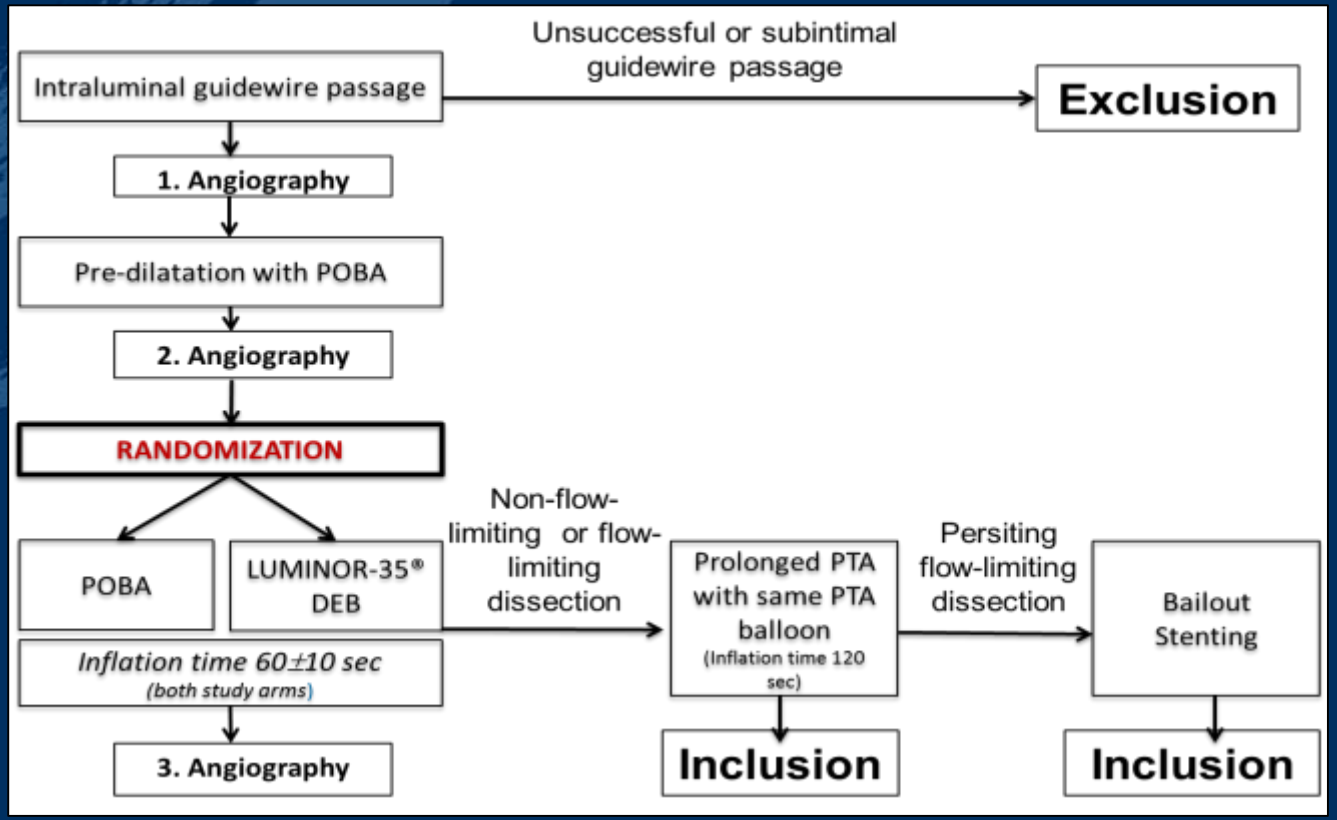
Data Mangement: Cornelia Eichhorn, University Hospital Jena, Germany

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, Dr. S. Brucks, *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, Dr. C. Erbel, University Heidelberg
10 Arnsberg	Dr. M. Lichtenberg, *Clinic Arnsberg*
11 Kusel	Dr. P. von Flotow, *Westpfalz Clinic*

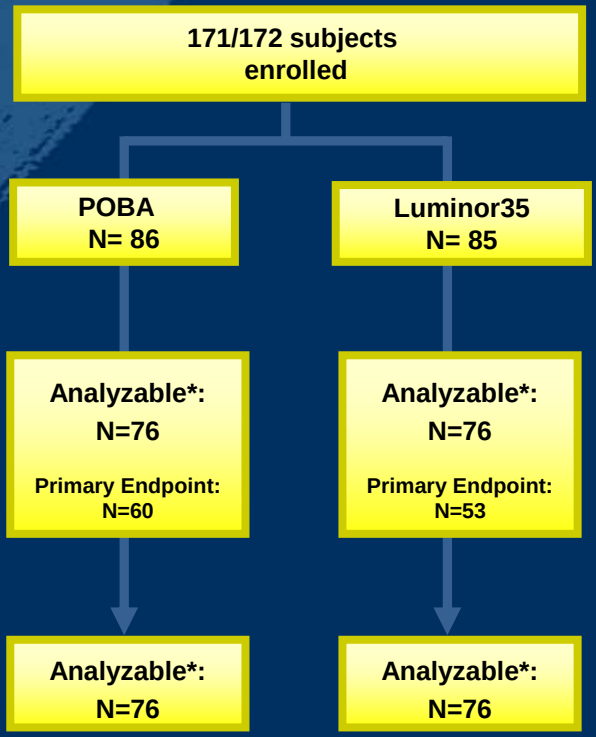
Flowchart


Intraluminal guidewire passage
Unsuccessful or subintimal guidewire passage
Exclusion
1. Angiography
Pre-dilatation with POBA
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)	-	-
Efficacy	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		

Patient Flow



Recruitment completed on 31.12.2016

Randomization (1:1)

6 month follow-up

Data Lock: 31.08.2017

12 month follow-up

Data Lock: 31.01.2018

* Patients with data of at least one endpoint

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)

Rutherford at Baseline

		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)

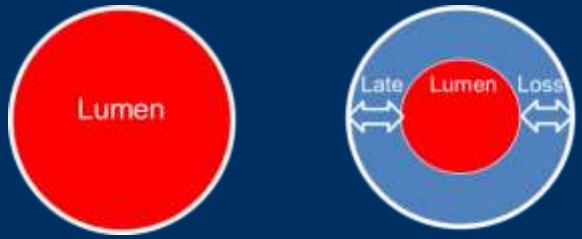
Baseline Angiographic Data

	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)	

Procedural Characteristics

	LUMINOR®	POBA	p value
Vessel preparation: Pre-dilatation performed	100% (84/84)	98.8% (85/86)	1.000
Dissection	37.6% (32/85)	40.7% (35/86)	0.755
Stent rate	15.3% (13/85)	18.8% (16/85)	0.684

Efficacy: Late Lumen Loss - LLL



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

	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	-0.92
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: Negative Remodeling*

	LUMINOR®	POBA	Relative Risk**, 95% CI (LUMINOR® vs. POBA)	Number needed to treat (NNT)	p value
Negative Remodeling(%)	30.2 (16/53)	15.0 (9/60)	1.91 [0.87; 4.16]	7	0.069

* **Negative Remodeling :** LLL < 0mm after 6 months

** Interpretation: Relative chance for negative remodeling is increased by 91% in the LUMINOR® group (Cochran-Mantel-Haenszel estimate, adjusted for center)

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
TLR 12M (%)	1.3 (1/76)	18.7 (14/75)	0.077 [CI: 0.011; 0.526]*	6	<0.001

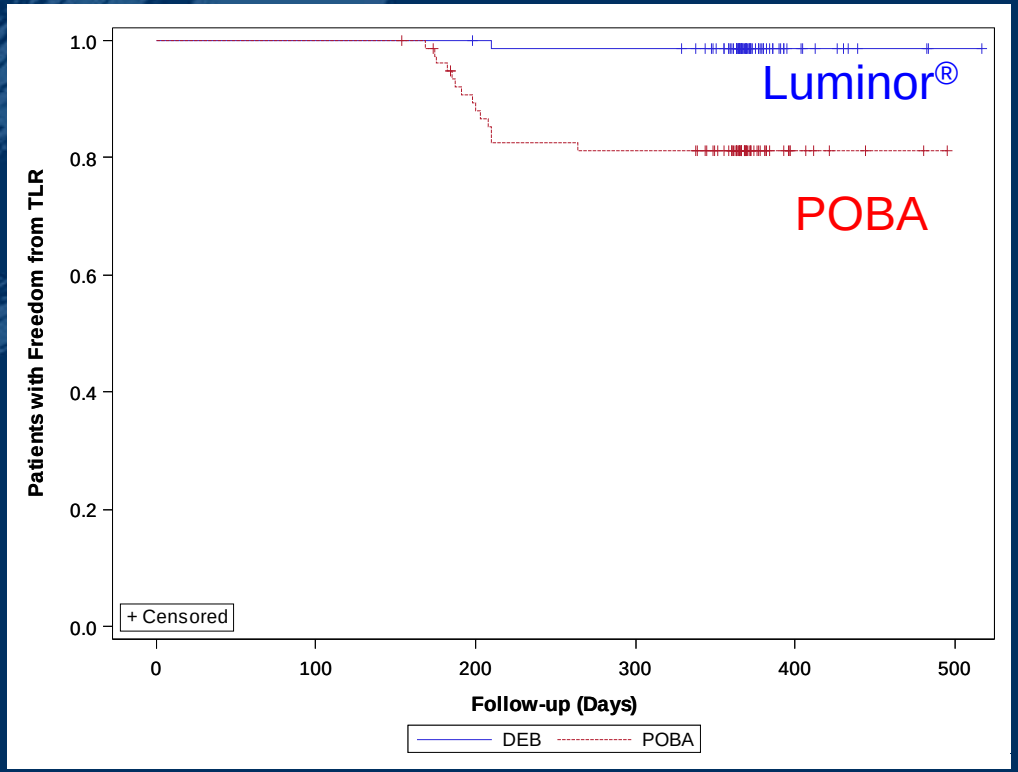
*Relative Risk Reduction (RRR) = 91.8%, Cochran-Mantel-Haenszel estimate, adjusted for center

Efficacy: Target Lesion Revascularization (TLR)

Study	DCB 12 mo TLR (%)	Control 12 mo TLR (%)
EFFPAC 2017 Luminor (iVascular)	**1.3 (1/76)**	**18.7 (14/75)**
IN.PACT Tepe et al. 2014 IN.PACT Admiral DCB	2.4 (5/207)	20.6 (22/107)
ILLUMINATE Schroeder et al. 2017 Stellarex DCB	5.2 (n=220)*	14.7 (n=72)*
AcoArt I Trial Jia et al. 2016 Orchid (Acotec)	7.2 (7/97)	39.6 (38/96)
RANGER Bausback et al. 2017 Ranger DCB	8.5 (6/71)	26.5 (9/34)
THUNDER Tepe et al. 2008 Paccocath coating	10.4 (5/48)	48.2 (26/54)
BIOLUX P-I Trial Scheinert et al. 2015 Passeo-18 Lux (Biotronik)	15.4 (4/26)*	41.7 (10/24)*
CONSEQUENT 2017 SeQuent Please (B. Braun)	17.8 (13/73)	37.7 (26/69)
LEVANT II Rosenfield et al. 2015 Lutonix DCB	38.0 (35/92)	37.5 (24/64)

*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 6M (%)	94.7 (72/76)	75.0 (57/76)	1.26 [CI: 1.100; 1.443]	6	<0.001
Patency 12M (%)	90.3 (65/72)	65.3 (47/72)	1.38* [CI: 1.146; 1.664]	4	<0.001

* Interpretation: Relative chance for patency is increased by 38% in the LUMINOR® group

Primary patency: Freedom from restenosis (determined by duplex ultrasound PSVR <2.5) and freedom from TLR at 12 months

Efficacy: Patency

* Patency based on freedom from target lesion revascularization and restenosis, restenosis by angiography (>50%DS) at 12M

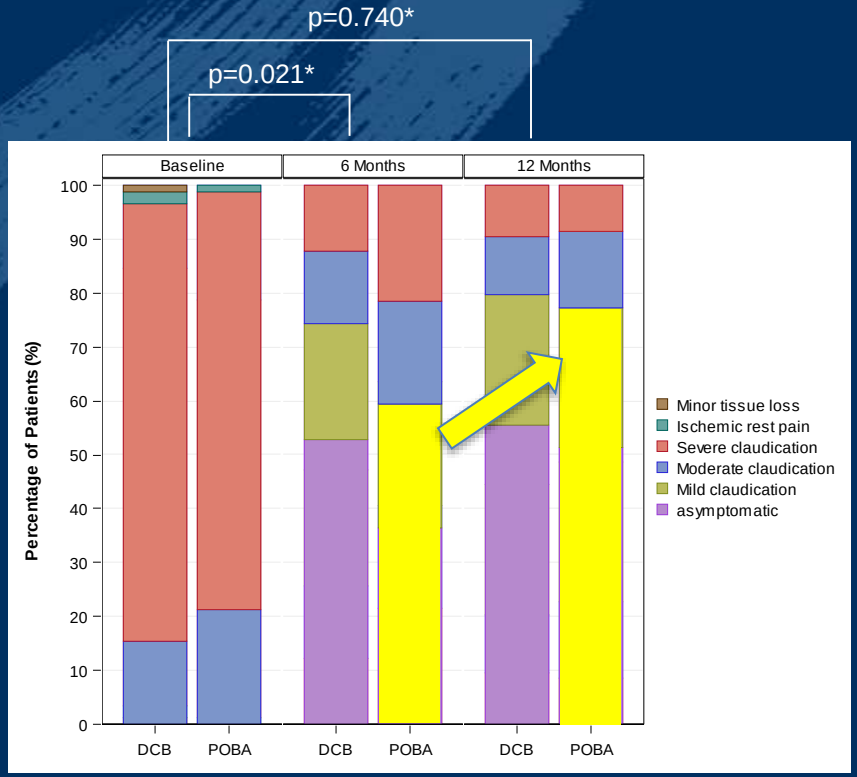
** Kaplan-Meier estimates

Study	DCB 12 mo Patency (%)	Control 12 mo Patency (%)	NNT
EFFPAC 2018 Luminor (iVascular)	**90.3(65/72)**	**65.3 (47/72)**	**4**
IN.PACT Tepe et al. 2015 IN.PACT Admiral DCB	82.2 (157/191)	52.4 (54/103)	4
ILLUMINATE Schroeder et al. 2017 Stellarex DCB	83.9 (188/224)	60.6 (40/66)	5
AcoArt I Trial Jia et al. 2016 Orchid (Acotec)	76.1 (67/88)	33.7 (30/89)	3
LEVANT I Scheinert et al. 2014 Lutonix DCB	66.7 (30/45)**	54.8 (23/42)**	9
RANGER-SFA 2017 Ranger DCB	86.0**	56.0**	4

Efficacy: Improvement of Rutherford

	after 6 months*		after 12 months**	
Improvement of Rutherford-Becker	Paclitaxel-Coated Balloon (n=74)	Standard Angioplasty Balloon (n=72)	Paclitaxel-Coated Balloon (n=74)	Standard Angioplasty Balloon (n=68)
Deterioration of 1 stage	1 (1.4)	0 (0.0)	1 (1.4)	1 (1.5)
No improvement	10 (13.5)	18 (25.0)	6 (8.1)	7 (10.3)
Improvement of 1 stage	9 (12.2)	15 (20.8)	13 (17.6)	12 (17.6)
Improvement of 2 stages	21 (28.4)	19 (26.4)	17 (23.0)	21 (30.9)
Improvement of 3 stages	33 (44.6)	20 (27.8)	37 (50.0)	27 (39.7)

Efficacy: Improvement of Rutherford

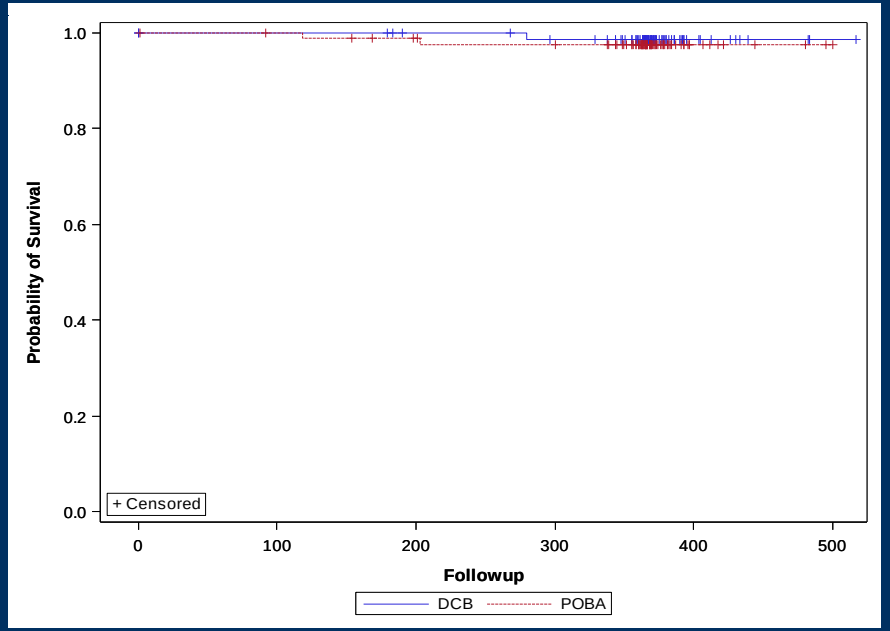


* Cochran-Mantel-Haenszel method was applied to compare the change of RBC at 6 and 12 months to baseline between DCB- and POBA-group

Safety: Mortality after 12 months

	LUMINOR®	POBA	p value
Death (%)	1.2 (1*/85)	2.3 (2*/86)	1.000

* Not related to device or procedure



Safety: Amputation after 12 months

	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

Classification of SAEs*

*to the causality to study procedure and investigational device/control product

SAE		Procedure		Total
		related	not related	
Investigational device (DCB)	related	2**	0	2
	not related	0	53	53
	Summe	2	53	55
Control product (POBA)	related	0	0	0
	not related	10	63	73
	Summe	10	63	73
	Summation	12	116	128

**thrombosis and persisting claudication

Classification of mortality

Mortality		Procedure		Total
		related	not related	
Investigational device (DEB)	related	0	0	0
	not related	0	1*	1
	Total	0	1	1
Control product (POBA)	related	0	0	0
	not related	0	2**	2
	Total	0	2	2
	Summation	0	3	3

* Exact cause of death: unknown; patient was multimorbid and suffered of severe lung disease (COPD) and emphysema, a coronary heart disease and abused of alcohol.
**Aortic and mitral valve infection with septic shock and suicide.

Safety: conclusions

When EffPac trial was initiated in 2015, POBA was the golden standard as comparative device to drug-eluting balloon catheters and LLL was imperative as primary endpoint to demonstrate technical efficacy.

A head-to-head study between two Paclitaxel-coated balloon catheters is necessary today and would bring more evidence about efficacy and safety of DCBs.

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

Best DCB outcomes in SFA TASC A&B lesions: EFFPAC-RCT 12-months follow-up

Ulf Teichgräber, MD, MBA
on behalf of the investigators

Teichgräber U, Aschenbach R, Scheinert D, Zeller T, Brechtel K, Blessing E, Treitl M, Lichtenberg M, von Flotow P, Vogel B, Werk M, Riambau V, Wienke A, Lehmann T, Sixt S, Thieme M

NCT02540018 | Teichgräber et al. Trials (2016) DOI 10.1186/s13063-016-1657-x