Speaker's name : Ulf Teichgräber

☑ I have the following potential conflicts of interest to declare:

Potential conflicts of interest <u>related</u> to the presentation:

o   Research grant: iVascular, Endoscout

Potential conflicts of interest <u>not related </u>to the presentation:

o   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

o   Master research agreements with Siemens Healthineers, GE Healthcare

Study design

Investigator initiated, prospective, multicenter, randomized controlled trial

Study objective

To assess efficacy and safety of Luminor-35 paclitaxel-coated balloon angioplasty in SFA/PA lesions up to 24 months

Sponsor

University of Jena, Germany

Investigational Product

luminor
Paclitaxel coated balloon
(3,0 µg/mm²)

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
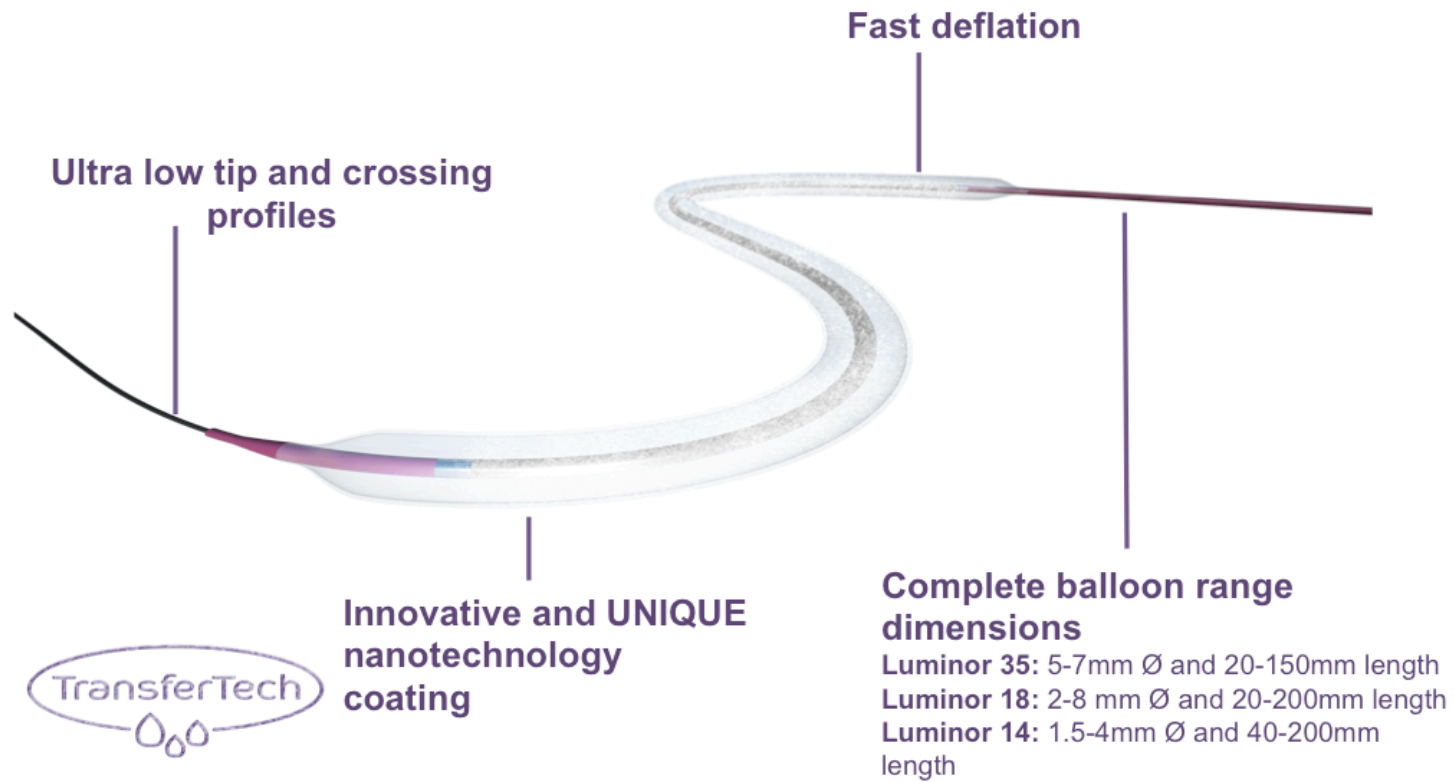
1. Jena   Universitätsklinikum   R. Aschenbach

2. Arnsberg   Klinikum Arnsberg   M. Lichtenber

3. Bad Krozingen   Herzzentrum   T. Zeller

4. Berlin   Ihre Radiologen   K. Brechtel

5. Hamburg   Angiologikum   S. Sixt

6. Kusel   Westpfalz Klinikum   P. von Flotow

7. Karlsbad   SRH Klinikum   E. Blessing

8. Leipzig   Universitätsklinikum   D. Scheinert

9. München   LMU München   M. Treitl

10. Sonneberg   Medios Kliniken   M. Thieme

11. Heidelberg   Universitätsklinik   B. Vogel

ClinicalTrial.gov Identifier: NCT02540018
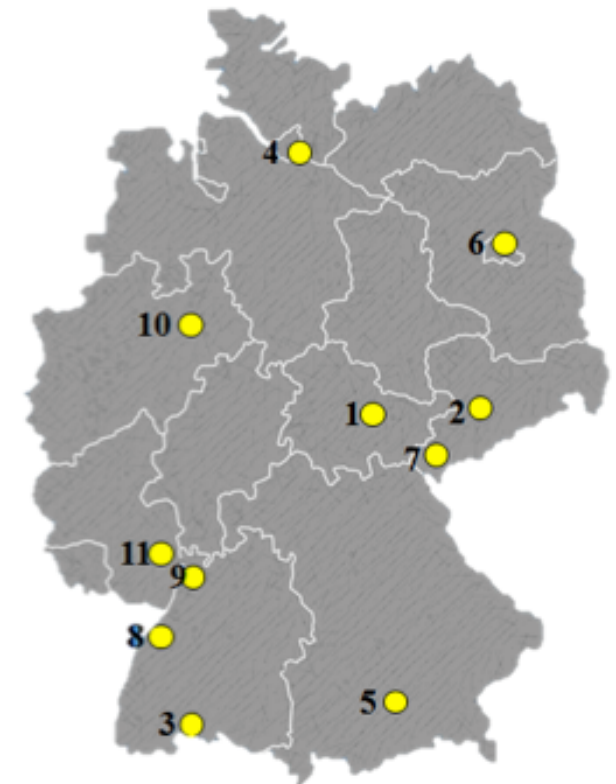
Primary Endpoint

- LLL at 6 months

Secondary Endpoints

- Binary restenosis
- Primary patency
- Freedom from TLR
- Freedom from TVR
- Rutherford category
- WIQ-score
- ABI
- EQ-5D score

- All-cause mortality
- Target limb amputation

Inclusion

- Rutherford category 2-4
- De-novo stenotic/restenotic or occluded (≥ 70%) SFA/prox. PA lesions
- Lesion length ≤ 150 mm
- 1 lesion/patient
- Successful pre-dilation

Exclusion

- Previous TV surgery
- Major amputation TL
- Severly calcified lesions (PTA resistant)
- In-stent restenosis
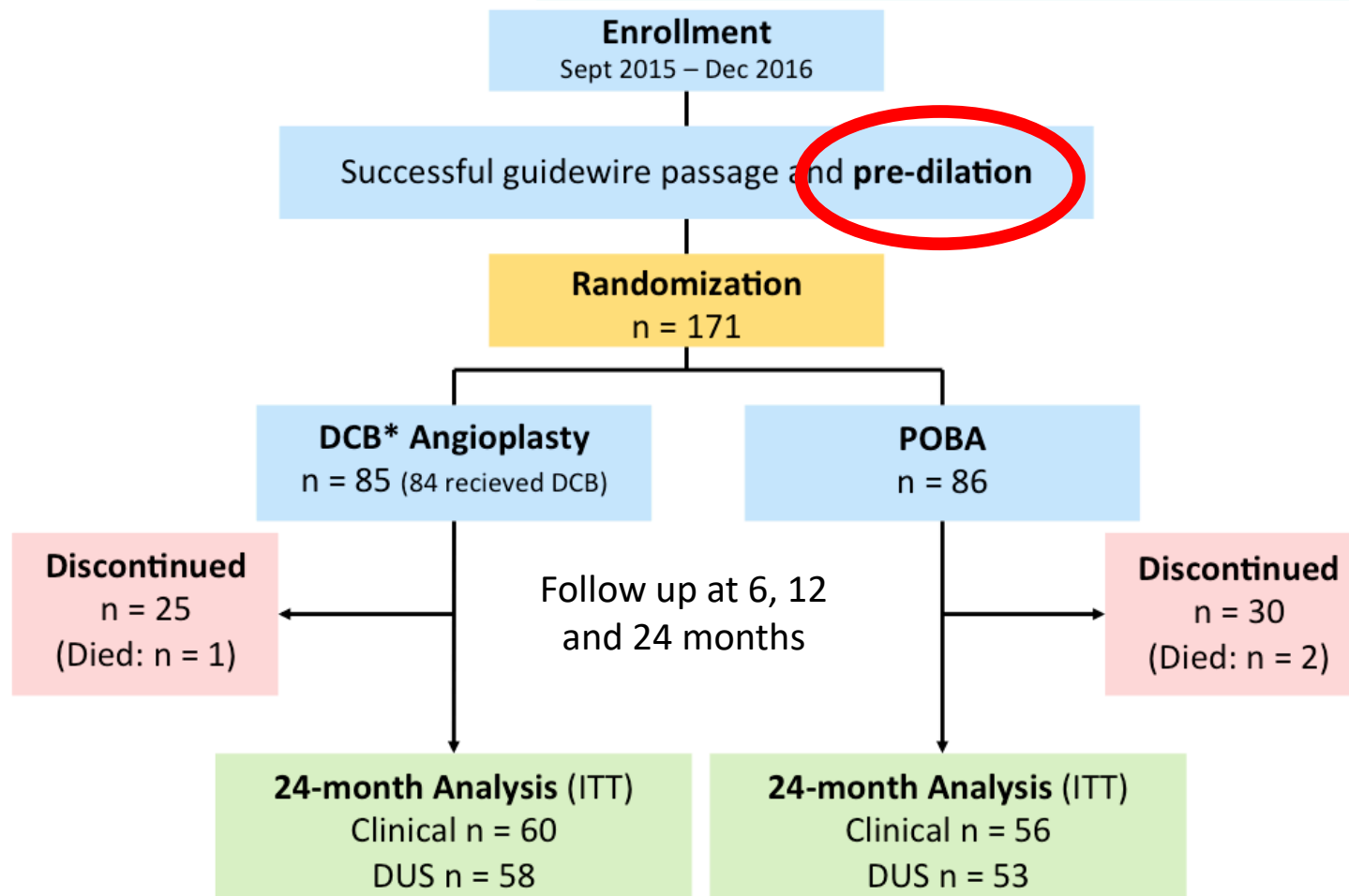
Luminor-35: paclitaxel 3 µg/mm², organic ester excipient (iVascular, Barcelona)

Baseline Patient Characteristics

	DCB n = 85	POBA n = 86	P value
Age, years	68.0 $\pm$ 7.5	68.1 $\pm$ 8.8	p = 0.979
Male, %	60.0	69.8	p = 0.239
Diabetes, %	36.5	40.4	p = 0.681
Hypertension, %	87.1	84.9	p = 0.850
Hyperlipidemia, %	70.7	68.6	p = 0.144
Current smoker, %	40.5	43.0	p = 0.856
Critical limb ischemia, %	3.6	1.2	p = 0.613
ABI	0.73 $\pm$ 0.23	0.74 $\pm$ 0.23	p = 0.929

Lesion and Procedure Characteristics

	DCB (n = 85)	POBA (n = 86)	P value
Lesion length, mm	59.1 ± 43.4	55.8 ± 39.1	p = 0.732
CTO, %	20.2	25.6	p = 0.492
Calcification, %			p = 0.232
Severe	3.6	11.6	
Moderate	42.2	44.2	
Mid / dist. popliteal artery, %	18.8	14.0	p = 0.248
Pre-dilation, %	98.8	98.8	p = 0.993
Dissection, %	37.6	40.7	p = 0.801
Bailout stenting, %	15.3	18.8	p = 0.709
Residual DS, %			
post-angioplasty	15.5 ± 16.7	14.9 ± 16.2	p = 0.807
post-treatment	7.5 ± 9.3	8.3 ± 10.1	p = 0.699

Primary Endpoint – 6-Month LLL

Study	DCB 6-month LLL	Control 6-month LLL	Difference DCB vs POBA (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 2018 Luminor (iVascular)	**0.14** [CI: -0.38; 0.67]	**1.06** [CI:0.54; 1.59]	**-0.92** [CI:-1.364; -0.49] p < 0.001
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

p = 0.188*

p = 0.740*

p = 0.021*

Patients, %

DCB POBA — Baseline
DCB POBA — 6
DCB POBA — 12
DCB POBA — 24 months
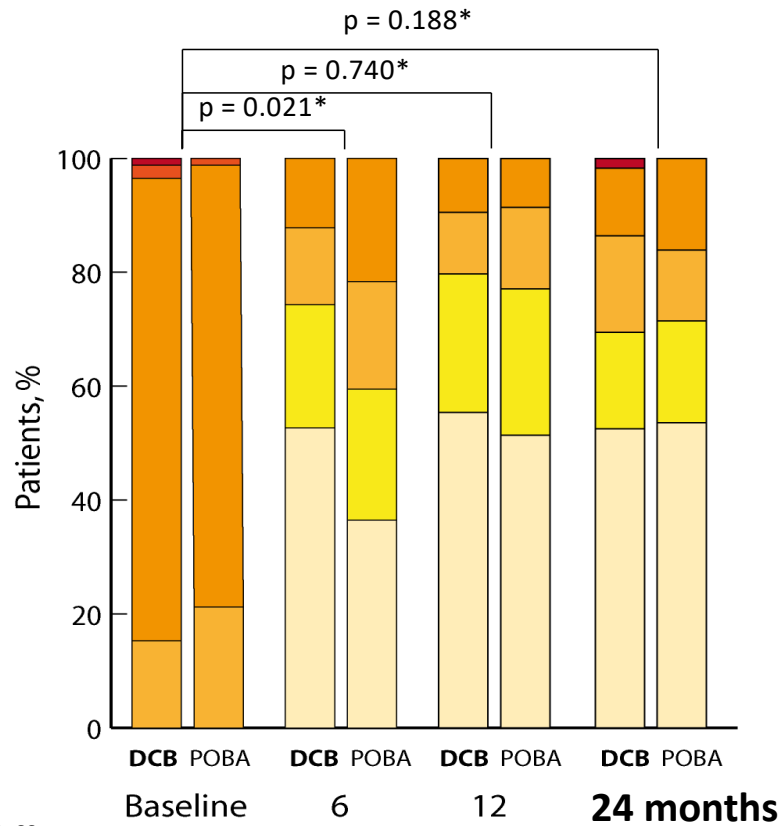
P-value for difference in change from baseline to 24 months between DCB and POBA

Rutherford-Becker category (RBC)

0 1 2 3 4 5

Improvement by ≥ 1 Rutherford category
DCB **88.1%** vs. POBA **85.5%** ($p = 0.441$)

Patients at 24 months, %

1.7% 0% 10.2% 14.5% 22.0% 18.2% 22.0% 27.3% 44.1% 40.0%

Rutherford category improved by

-2 0 1 2 3

DCB   POBA
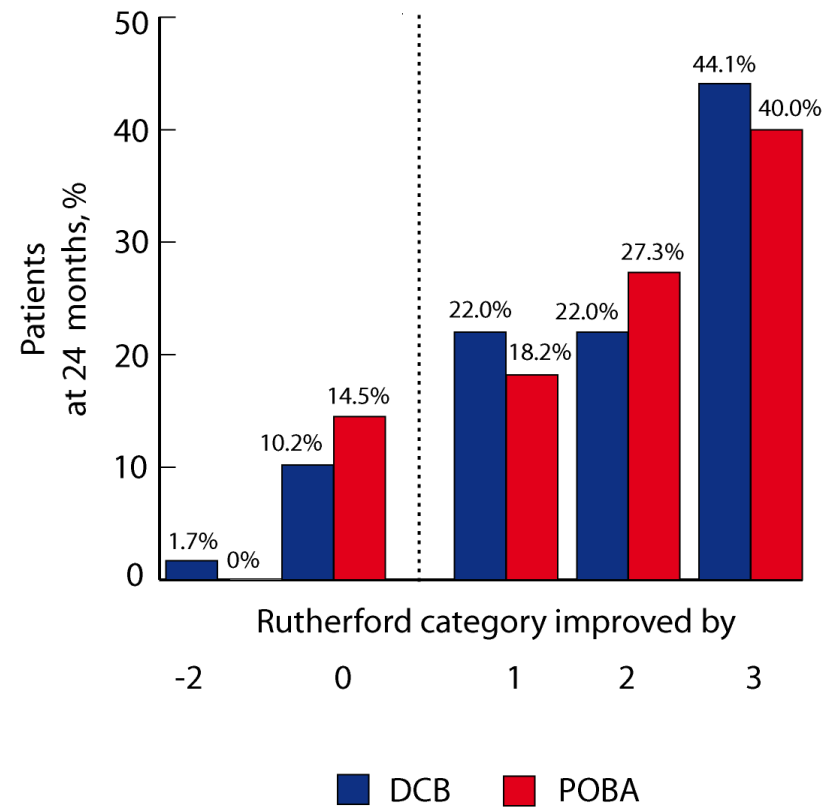
WIQ score

Change **DCB** vs. **POBA**: p = 0.8825
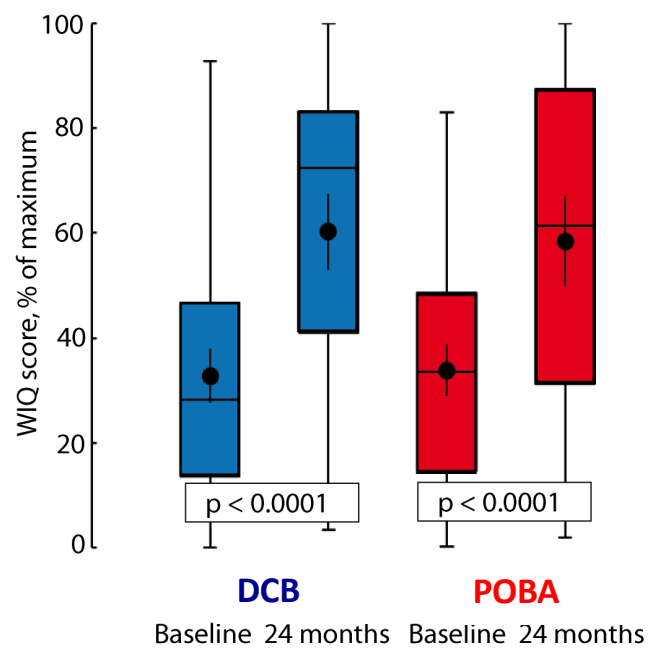
	Baseline	24 months	Baseline	24 months
Mean	32.8%	60.2%	33.8%	58.4%
± SD	23.5%	27.7%	22.9%	31.8%

EQ-5D index

Change **DCB** vs. **POBA**: p = 0.1953
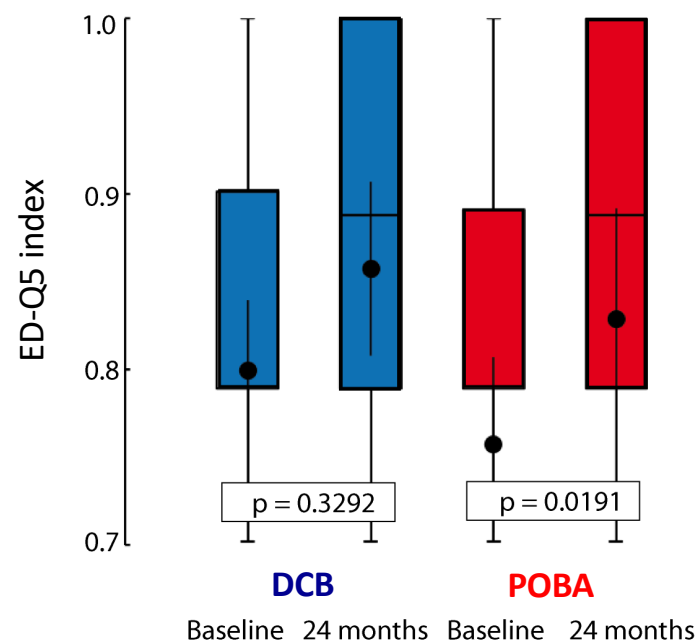
	Baseline	24 months	Baseline	24 months
Mean	0.80	0.86	0.76	0.83
± SD	0.18	0.19	0.23	0.23

Primary Patency – 24 Months

DCB: **90.2%**

POBA: **62.7%**

Log-rank p = 0.0004

	12 months	24 months
DCB	**94.7%** (86.4 to 98.0)	**90.2%** (80.4 to 95.2)
POBA	**71.3%** (59.4 to 80.3)	**62.7%** (50.0 to 73.0)

Primary patency, %

Time since randomization, months

Patients at risk

DCB	85	76	68	52	43
POBA	86	71	49	35	31
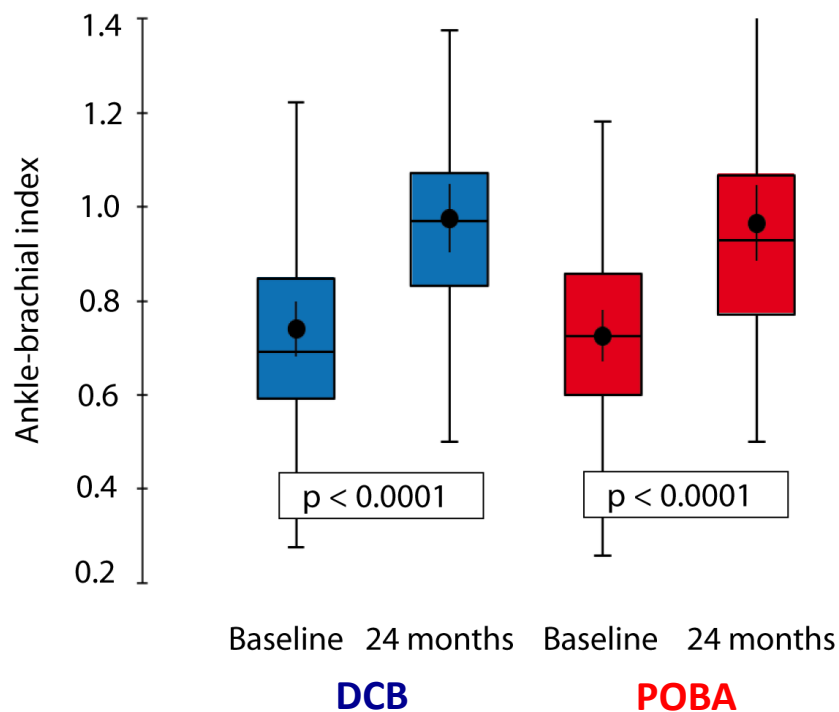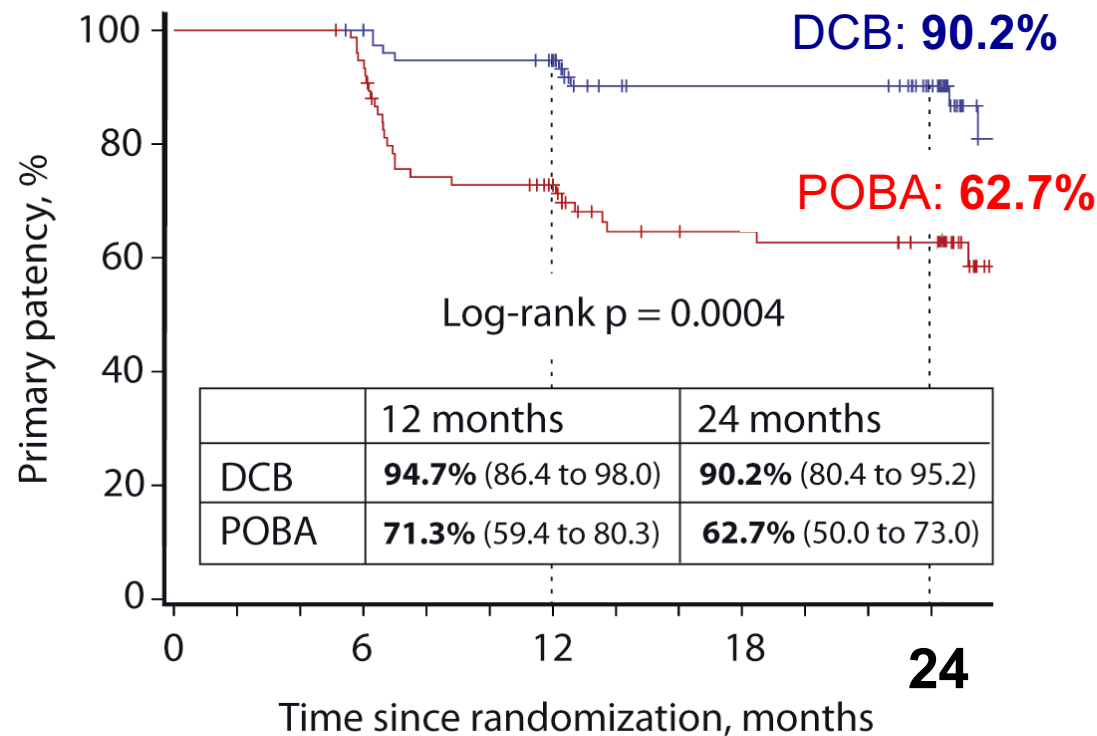
Primary patency:
Freedom from restenosis (determined by duplex ultrasound PSVR < 2.5) and freedom from TLR

DCB: **97.2%**

POBA: **78.0%**

Log-rank p = 0.0010

	12 months	24 months
DCB	**98.7%** (91.1 to 99.8)	**97.2%** (89.1 to 99.3)
POBA	**81.6%** (71.0 to 88.7)	**78.0%** (66.5 to 86.0)

Freedom from TLR, %

Time since randomization, months
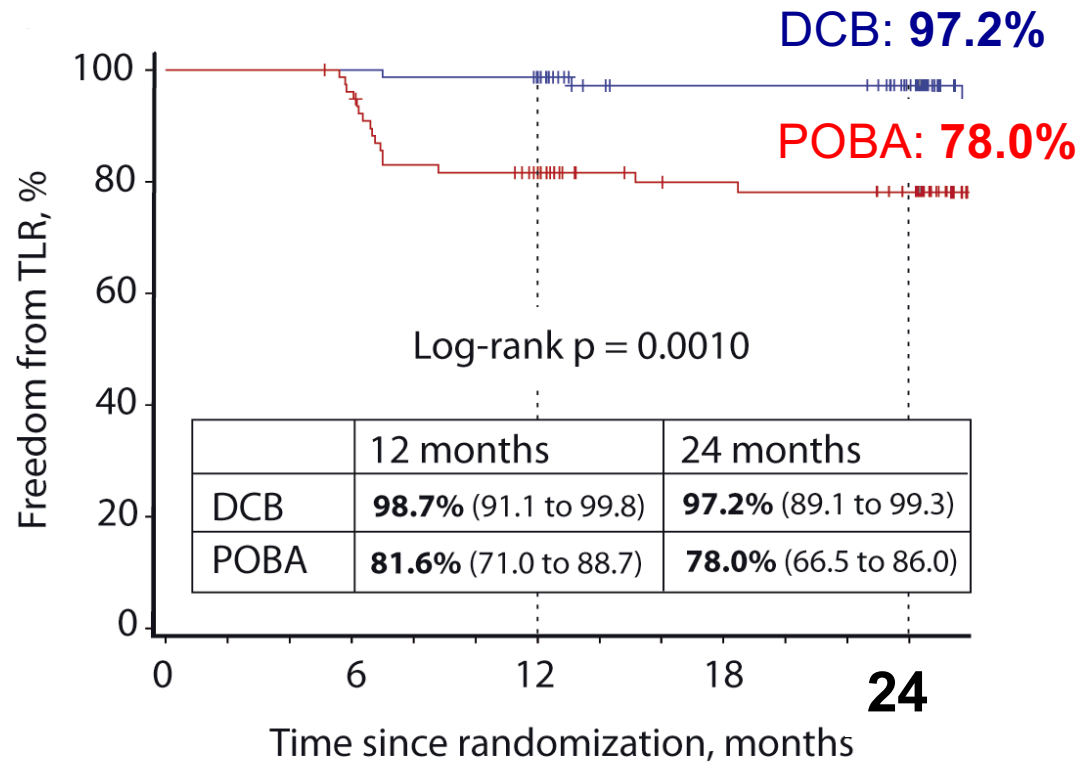
| 85 | 77 | 74 | 59 | 50 |
| 86 | 74 | 58 | 44 | 39 |

Consitent treatment effect across subgroups
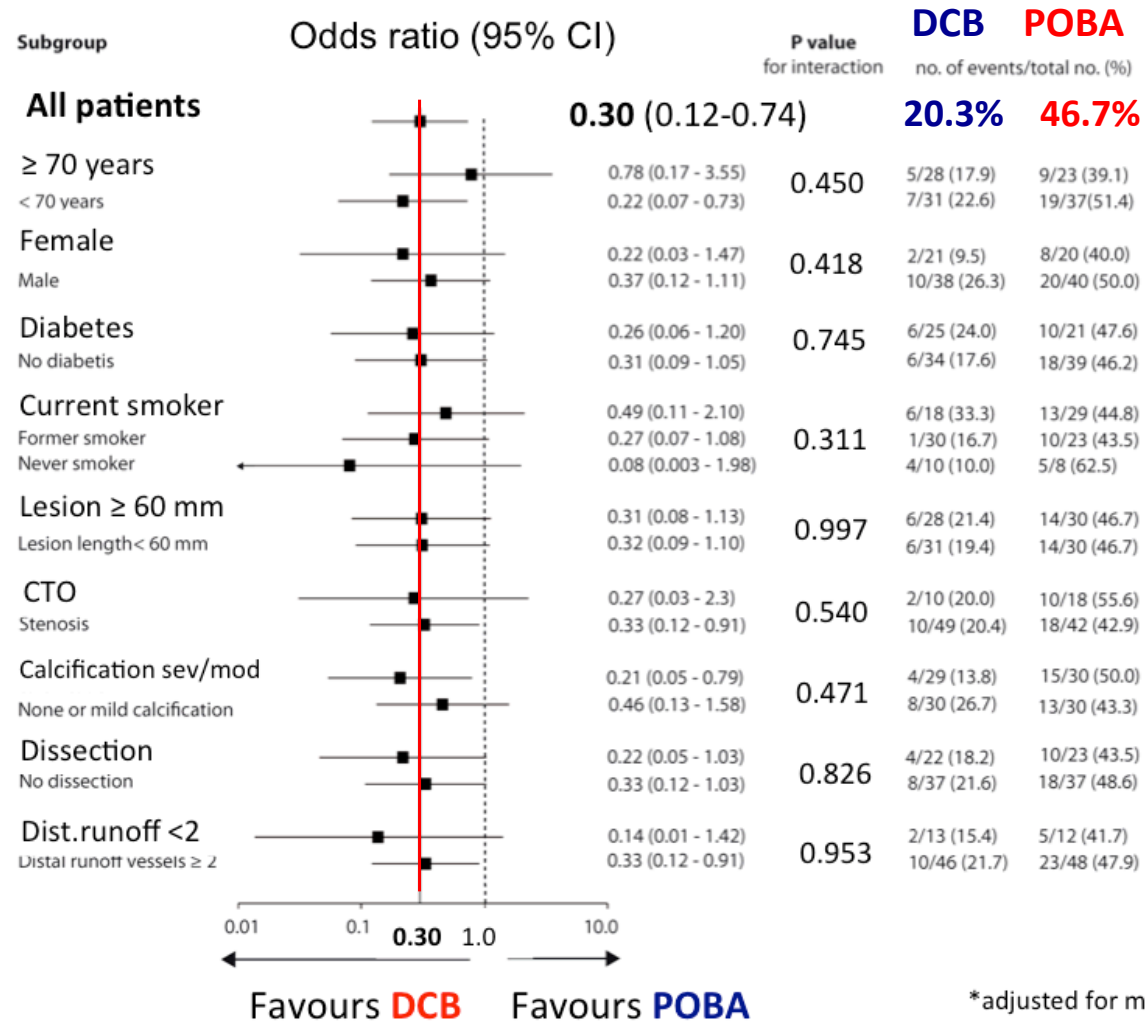
Binary restenosis:
PSVR ≥ 2.5, CorLab adjudicated
* adjusted for multiple centers

Subgroup	Odds ratio (95% CI)	P value for interaction	DCB no. of events/total no. (%)	POBA no. of events/total no. (%)
All patients	**0.30 (0.12-0.74)**		**20.3%**	**46.7%**
≥ 70 years	0.78 (0.17 - 3.55)	0.450	5/28 (17.9)	9/23 (39.1)
< 70 years	0.22 (0.07 - 0.73)		7/31 (22.6)	19/37(51.4)
Female	0.22 (0.03 - 1.47)	0.418	2/21 (9.5)	8/20 (40.0)
Male	0.37 (0.12 - 1.11)		10/38 (26.3)	20/40 (50.0)
Diabetes	0.26 (0.06 - 1.20)	0.745	6/25 (24.0)	10/21 (47.6)
No diabetis	0.31 (0.09 - 1.05)		6/34 (17.6)	18/39 (46.2)
Current smoker	0.49 (0.11 - 2.10)		6/18 (33.3)	13/29 (44.8)
Former smoker	0.27 (0.07 - 1.08)	0.311	1/30 (16.7)	10/23 (43.5)
Never smoker	0.08 (0.003 - 1.98)		4/10 (10.0)	5/8 (62.5)
Lesion ≥ 60 mm	0.31 (0.08 - 1.13)	0.997	6/28 (21.4)	14/30 (46.7)
Lesion length< 60 mm	0.32 (0.09 - 1.10)		6/31 (19.4)	14/30 (46.7)
CTO	0.27 (0.03 - 2.3)	0.540	2/10 (20.0)	10/18 (55.6)
Stenosis	0.33 (0.12 - 0.91)		10/49 (20.4)	18/42 (42.9)
Calcification sev/mod	0.21 (0.05 - 0.79)	0.471	4/29 (13.8)	15/30 (50.0)
None or mild calcification	0.46 (0.13 - 1.58)		8/30 (26.7)	13/30 (43.3)
Dissection	0.22 (0.05 - 1.03)	0.826	4/22 (18.2)	10/23 (43.5)
No dissection	0.33 (0.12 - 1.03)		8/37 (21.6)	18/37 (48.6)
Dist.runoff <2	0.14 (0.01 - 1.42)	0.953	2/13 (15.4)	5/12 (41.7)
Distal runoff vessels ≥ 2	0.33 (0.12 - 0.91)		10/46 (21.7)	23/48 (47.9)

0.01 0.1 **0.30** 1.0 10.0

⟵ Favours **DCB**   Favours **POBA** ⟶

*adjusted for multiple centers

Safety – 24 Months

	DCB	POBA	P value
All-cause mortality, %	1.6* (1/61)	3.4** (2/58)	p = 0.877

Amputation, %
    Major
    Minor
	
	0.0
	0.0
		
		0.0
		1.8 (1/56)
			
			p = 0.972

Binary restenosis, %	20.3 (12/59)	46.7 (28/60)	p = 0.004
TLR, %	4.9 (3/61)	27.1 (16/59)	p = 0.010

Periprocedural complication, %
    Dissection
    False aneurysm
    Thromb. embolization
	
	37.6 (32/85)
	0.0
	1.2 (1/85)
		
		40.7 (35/86)
		1.2 (1/86)
		0.0
			
			p = 0.801
			p = 1.000
			p = 1.000

* One DCB patient died for unknown reason at 9 months
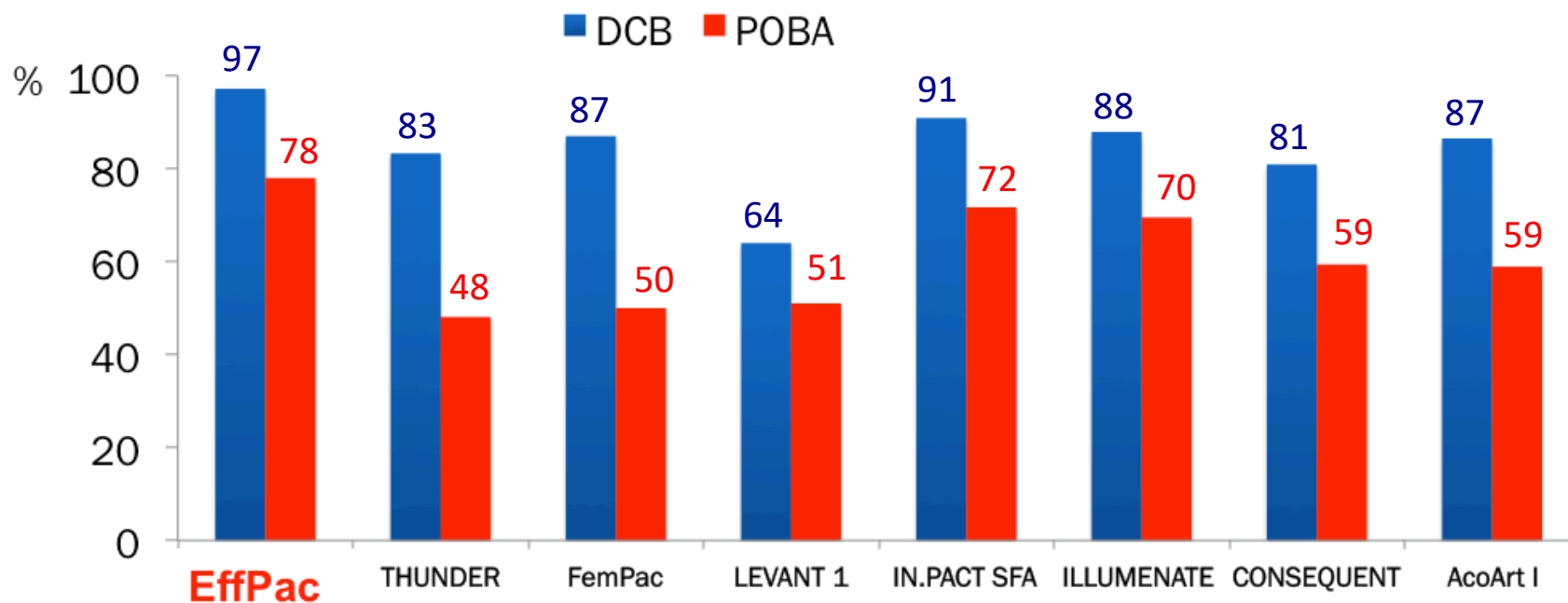 (patient was multimorbid: severe COPD, coronary artery disease, alcoholism)

** One POBA patient died of sepsis at 4 months
 Another POBA-patient committed suicide at 7 months

Primary Patency – 24 Months

%

Legend: ■ DCB ■ POBA

- EffPac: DCB 90, POBA 63
- THUNDER: (no bars)
- FemPac: (no bars)
- LEVANT 1: DCB 57, POBA 40
- IN.PACT SFA: DCB 79, POBA 50
- ILLUMENATE: DCB 76, POBA 61
- CONSEQUENT: DCB 72, POBA 48
- AcoArt I: DCB 65, POBA 31

	EffPac	THUNDER	FemPac	LEVANT 1	IN.PACT SFA	ILLUMENATE	CONSEQUENT	AcoArt I
Les. length cm	6/6 DCB/POBA	8/7	4/5	8/8	9/9	7/7	14/12	15/15
CTO %	17/20	27/26	13/19	41/42	26/20	19/19	23/29	57/52
Sev. calc. %	3/10				8/6	13/10		
Bailout stent %	13/16	4/22	9/14	3/16	7/12	15/11	14/19	19/21
Reference	Teichgräber 2019	Tepe 2015	Werk 2008	Scheinert 2014	Laird 2015	Brodmann 2018	Albrecht 2018	Xu 2018

	EffPac	THUNDER	FemPac	LEVANT 1	IN.PACT SFA	ILLUMENATE	CONSEQUENT	AcoArt I
Les. length cm	6/6 DCB/POBA	8/7	4/5	8/8	9/9	7/7	14/12	15/15
CTO %	17/20	27/26	13/19	41/42	26/20	19/19	23/29	57/52
Sev. calc. %	3/10				8/6	13/10		
Bailout stent %	13/16	4/22	9/14	3/16	7/12	15/11	14/19	19/21
Reference	Teichgräber 2019	Tepe 2015	Werk 2008	Scheinert 2014	Laird 2015	Brodmann 2018	Albrecht 2018	Xu 2018

All-Cause Mortality – 24 Months

Study or Subgroup	DCB Events	Total	POBA Events	Total	Weight	Risk Ratio M–H, Random, 95% CI
EffPac	1	61	2	58	3.1%	0.48 [0.04, 5.10]
LEVANT I	4	42	5	41	11.2%	0.78 [0.23, 2.71]
ILLUMENATE EU	13	199	3	59	11.6%	1.28 [0.38, 4.36]
AcoArt I	8	96	6	95	16.6%	1.32 [0.48, 3.66]
LEVANT II	21	278	7	140	25.0%	1.51 [0.66, 3.47]
THUNDER	7	48	5	54	14.8%	1.57 [0.53, 4.64]
CONSEQUENT	2	70	1	65	3.1%	1.86 [0.17, 20.00]
FemPac	7	45	3	42	10.4%	2.18 [0.60, 7.88]
INPACT SFA	16	198	1	106	4.3%	8.57 [1.15, 63.70]
Total (95% CI)		1037		660	100.0%	1.47 [0.97, 2.23]
Total events	79		33			

Heterogeneity: Tau² = 0.00; Chi² = 5.53, df = 8 (P = 0.70); I² = 0%

Overall effect: Z = 1.89, p = 0.07

Favours **DCB**   Favours **POBA**

At 2 years, DCB angioplasty (Luminor-35®) of medium length SFA/PA lesions resulted in

- a significant clinical and hemodynamic improvement from baseline

- a significantly lower incidence of binary restenosis compared to POBA

- significantly less need for TLR

DCB angioplasty (Luminor-35®) was safe through 2 years (RR<1)