



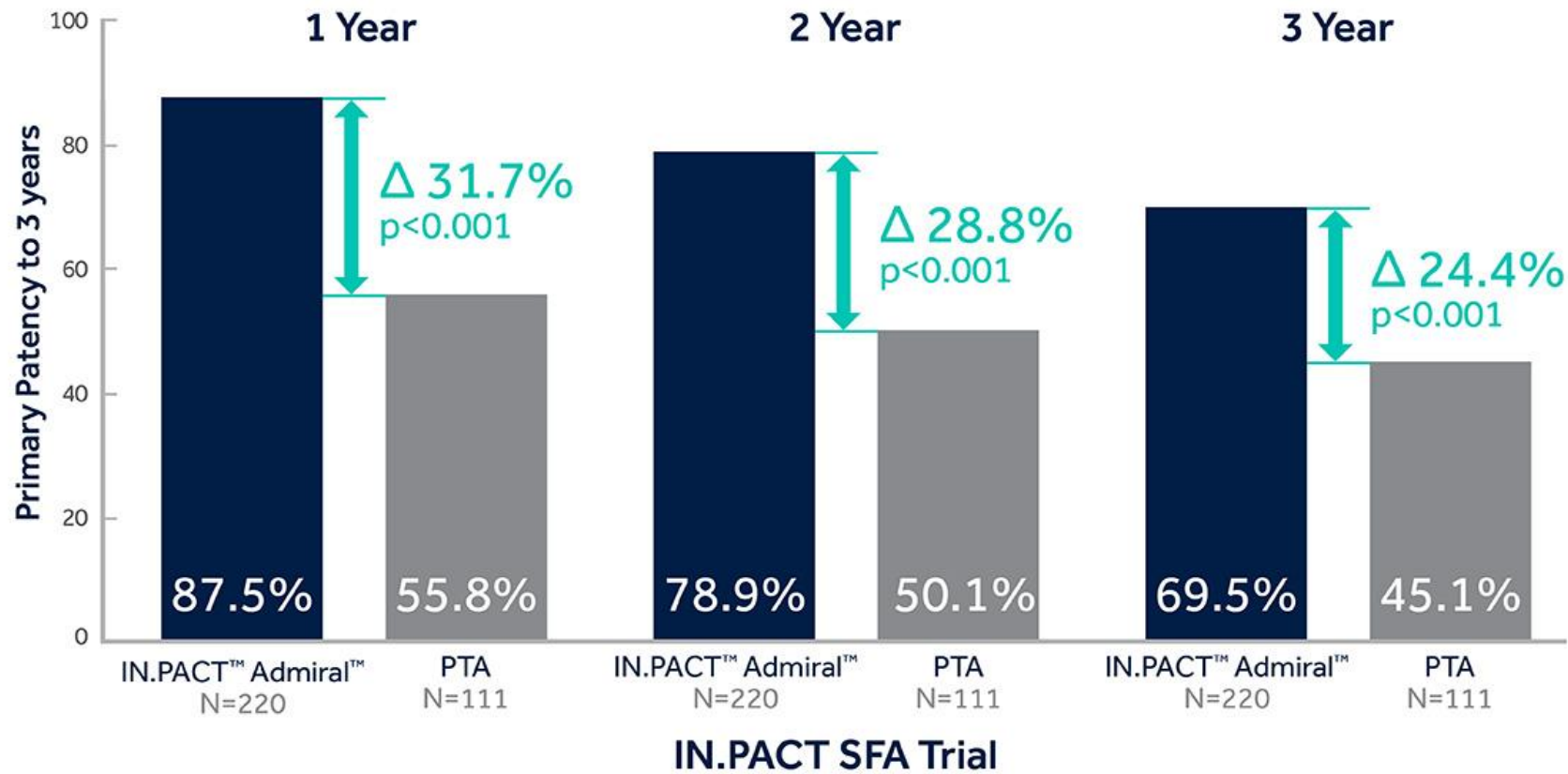
VASCUPEDIA

Overview DCB treatment in BTK arteries

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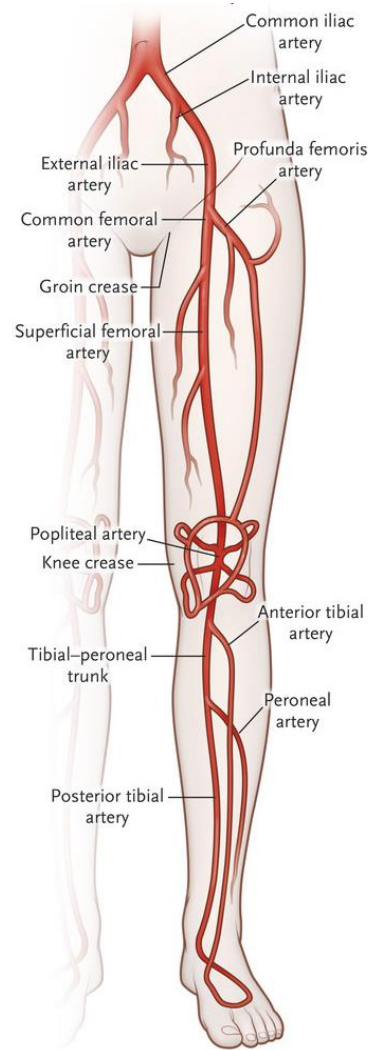
DCB proven to work in SFA



Not all lesions are the same

ABOVE THE KNEE

- Mixed morphology (multiple plaque types & thrombus)
- Medium to large vessels (4-9mm)



BELOW THE KNEE

- Lesions more commonly calcified
- Tortuous, challenging anatomy
- Small vessels (1.5 – 3.5mm)

BTK revascularization challenges

- Long, complex, often calcified nature of lesions
- Often associated with multilevel disease, thus success inflow- and outflow-dependent
- High restenosis rate
- Limb salvage poorly correlated to primary patency
- Literature landscape dominated by small series and case studies, with limited level I evidence

Leipzig Registry (IN.PACT BTK) – DCB

- 104 patients – single arm study DCB (compare to historical PTA data)
- Primary Endpoint:
Angiographic Binary Restenosis @3-month

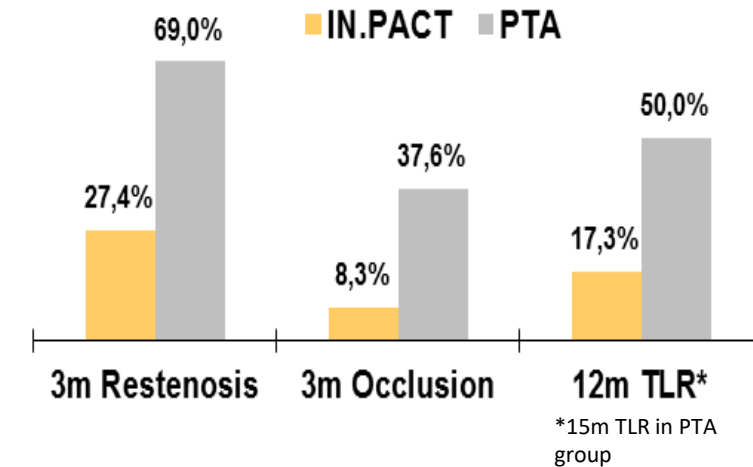
Inclusion criteria:

- ✓ CLI or severe claudication
- ✓ Stenosis >70% or occlusion of the BTK arteries
- ✓ LL ≥80mm

Leipzig Registry – DCB - Results

BTK RCTs/registries	IN.PACT BTKregistry – LeipzigSchmidt et al. 2011[46]
DCB system	IN.PACT™
	DCB
Number of patients	104
Lesion lengths (mm)	176 ± 88
De novo lesion type (%)	65
Total occlusions (%)	62
Calcified lesions (%)	
Severe calcification (%)	
Diabetic patients (%)	71
PAD CLI patients (%)	82

FU ≥ 12 months	
LLL	
TLR (%)	17
PP (%)	
Restenosis rate (%)	
Improvement in clinicaloutcome/RU (%)	Yes
Distal embolization (%)	
Improvement in ABI	
Major amputationrate (%)	

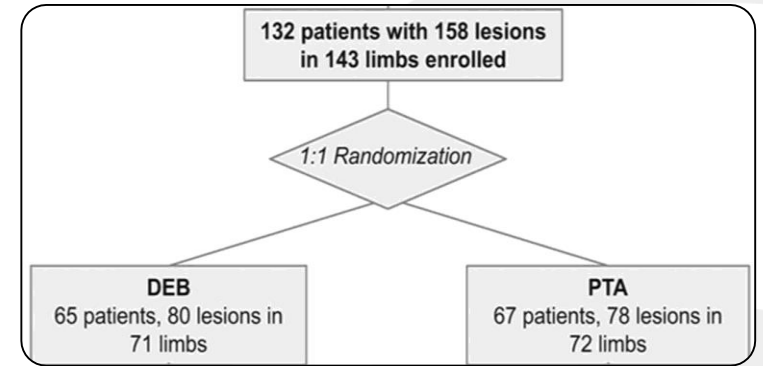


DEBATE-BTK – DCB vs PTA

- 132 patients – RCT : IN.PACT Amphirion vs PTA
- Primary Endpoint:
Angiographic binary restenosis @12M

Inclusion criteria:

- ✓ CLI & diabetic patients
- ✓ Stenosis >50% or occlusion of the BTK arteries
- ✓ LL not specified



DEBATE-BTK study – DCB vs PTA - Results

BTK RCTs/registries	DEBATE-BTK Liistro et al. 2013 [43]		
DCB system	IN.PACT™ Amphirion		
	DCB	PTA	P-value
Number of patients	65	67	
Lesion lengths (mm)	129 ±83	131 ±79	
De novo lesion type (%)	100	100	
Total occlusions (%)	77	82	
Calcified lesions (%)			
Severe calcification (%)			
Diabetic patients (%)	100	100	
PAD CLI patients (%)	100	100	

FU ≥ 12 months			
LLL			
TLR (%)	18	43	0.002
PP (%)			
Restenosis rate (%)	27	74	<0.001
Improvement in clinical outcome/RU (%)			0.06
Distal embolization (%)			
Improvement in ABI	Yes		<0.001
Major amputation rate (%)	0	1.5	n.s.

Early DCB-BTK evidence showed high promise to **reduce restenosis and reintervention rates** vs standard PTA

However, there is **no consistence** between trials and registries on hard clinical endpoints

No major **differences in hard clinical outcomes** across all studies between any DCB and control arm.

PTA

DCB

Leipzig Registry

Leipzig Registry

DEBATE-BTK

DEBATE-BTK

BIOLUX P-II study – DCB vs PTA

- 72 patients – RCT: Passeo-18 LUX vs Passeo-18
- Primary Endpoint:
6-month Target Lesion Patency at 6-months

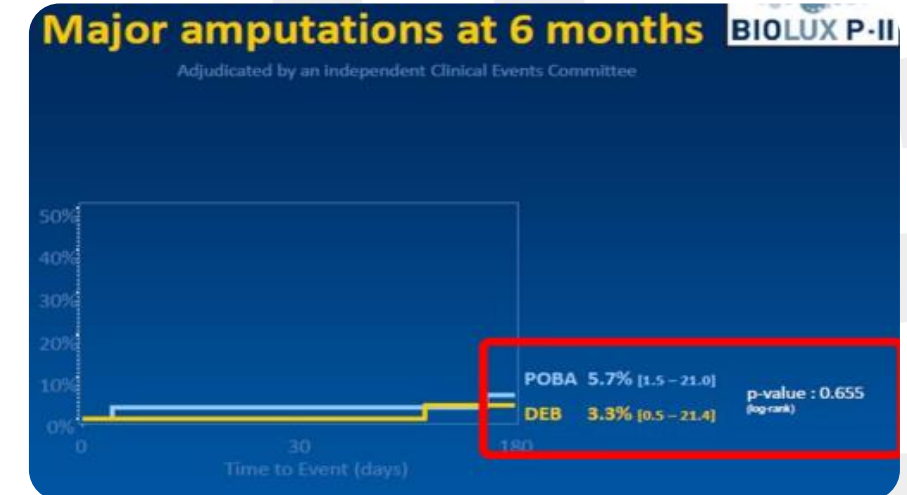
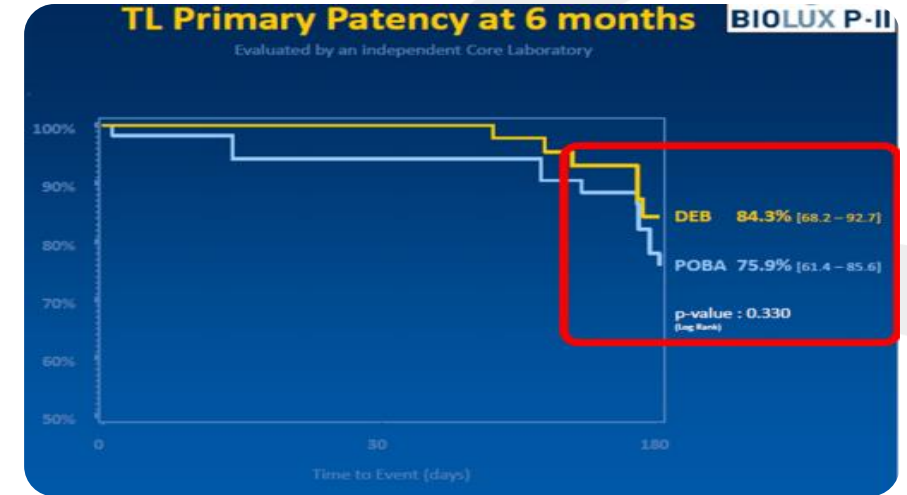
Inclusion criteria:

- ✓ RCC not specified
- ✓ Stenosis >70% or occlusion of the BTK arteries
- ✓ LL \geq 30mm

BIOLUX P-II study – DCB vs PTA - Results

BTK RCTs/registries	BIOLUX-PII Brodmann 2015 [45]		
DCB system	Passeo-18 Lux		
	DCB	PTA	P-value
Number of patients	36	36	
Lesion lengths (mm)	113 ±88	115 ±87	
De novo lesion type (%)			
Total occlusions (%)			
Calcified lesions (%)			
Severe calcification (%)			
Diabetic patients (%)	61	72	
PAD CLI patients (%)			

FU 6 months			
LLL (mm)			
TLR (%)			
PP (%)	84.3	75.9	n.s.
Restenosis rate (%)			
Improvement in clinical outcome/RU	59	47	n.s.
Improvement in ABI			
Major amputation rate (%)	3.3	5.7	n.s.



IN.PACT DEEP study – DCB vs PTA

- 358 patients – RCT (2:1) – IN.PACT Amphirion (239) vs PTA (119)
- Primary Endpoint:
Late Lumen Loss @ 12M
Clinically driven TLR @ 12M

Inclusion criteria:

- ✓ CLI patients (RCC 4,5,6)
- ✓ Stenosis >70% or occlusion of the BTK arteries
- ✓ LL ≤100mm

IN.PACT DEEP study – DCB vs PTA - Results

BTK RCTs/registries	IN.PACT DEEP Zeller et al. 2014 [44]		
DCB system	IN.PACT™ Amphirion		
	DCB	PTA	P-value
Number of patients	239	119	
Lesion lengths (mm)	101 ±91	129 ±95	0.002
De novo lesion type (%)	93	96	
Total occlusions (%)	39	46	
Calcified lesions (%)	75	78	
Severe calcification (%)	14	11	
Diabetic patients (%)	76	69	
PAD CLI patients (%)	100	99	

FU 6 months			
Major amputation rate (%)	8.8	3.6	0.080
FU ≥ 12 months			
LLL	0.6 ±0.8	0.6 ±0.8	n.s.
TLR (%)	9.2	13.1	n.s.
PP (%)			
Restenosis rate (%)	41	36	n.s.
Improvement in clinical outcome/RU (%)			
Distal embolization (%)	2.8	0.6	n.s.
Improvement in ABI			
Major amputation rate (%)	8.8	3.6	0.08

Failure to meet Primary Efficacy Endpoint

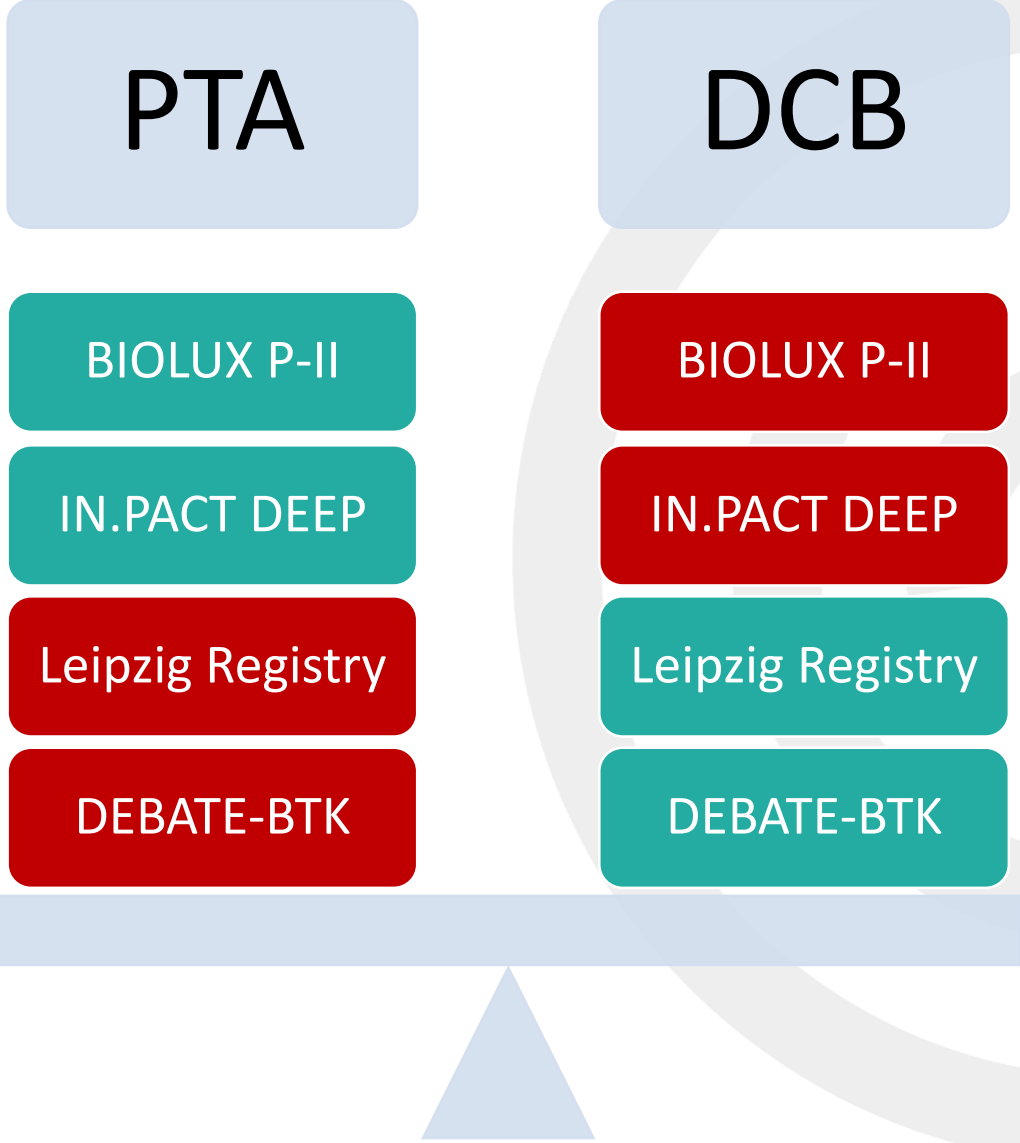
Trend towards higher Major Amputation Rate in DCB arm

No difference in primary patency rates
between DCB & PTA at 6MFU
in the BIOLUX P-II study

Also, **no difference in amputation rates**

IN.PACT DEEP showed **no superior treatment effect of DCB over PTA**

Trend towards a **higher amputation rate in the DCB arm.**



What was the problem with BIOLUX P-II?

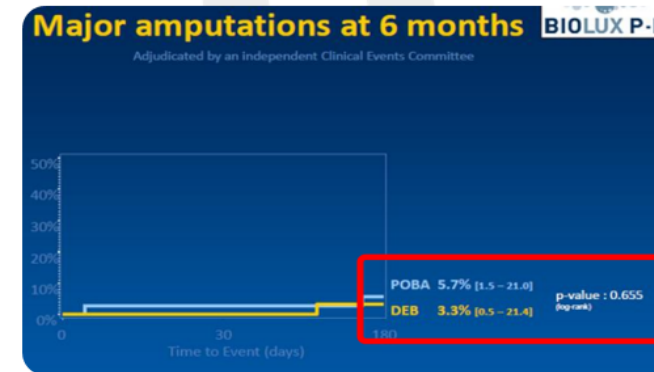
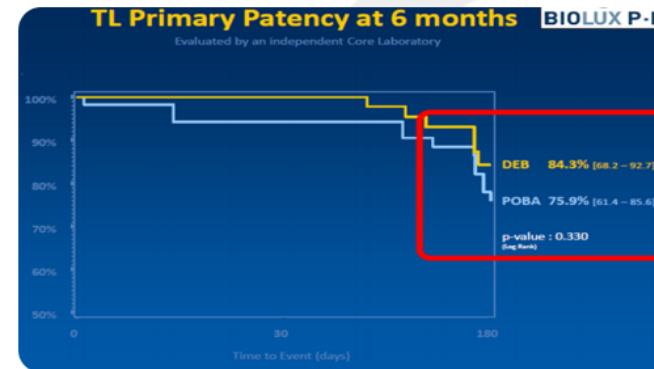
BIOLUX P-II study – DCB vs PTA - Results

BIOLUX P-II study – Passeo-18 LUX vs Passeo-18

BTK RCTs/registries	BIOLUX-P II Brodmann 2015 [45]		
DCB system	Passeo-18 Lux		
	DCB	PTA	P-value
Number of patients	36	36	
Lesion lengths (mm)	113 ±88	115 ±87	
Diabetes			
Cholesterol			
Severe stenosis			
Dialysis			
PAD CLI patients (%)			

FU 6 months			
LLL (mm)			
TLR (%)			
PP (%)	84.3	75.9	n.s.
Restenosis rate (%)			
Improvement in clinical			

**Underpowered study!
Too small sample size!**

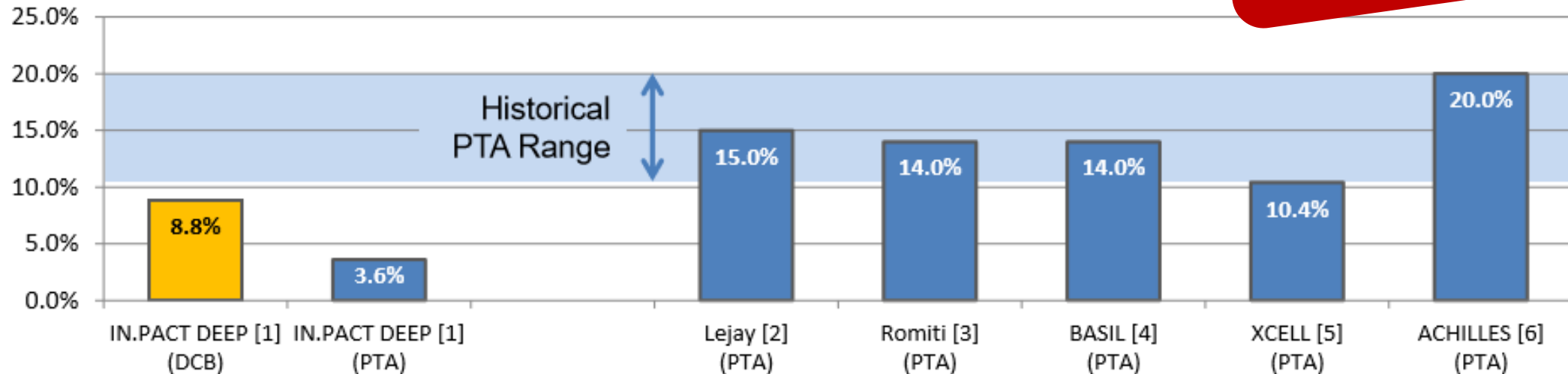


What was the problem with IN.PACT DEEP?

12-month Major Amputation Rate

- Literature Review PTA : 10-20%
- IN.PACT DEEP DCB: 8.8%
- IN.PACT DEEP PTA: 3.6%

Historical good PTA results compared to literature!



1. Zeller T. et al., JACC 64:1568-76 (2014)
2. Lejay A. et al. Acta Chir Belg 110:684-93 (2010)
3. Romiti M. et al., J Vasc Surg 47:975-81 (2008)

4. Adam D. et al., Lancet 366:1925-34 (2005)
5. Rocha-Singh K. et al., Catheter Cardiovasc Interv 80:1042-51 (2012)
6. Scheinert D. et al., JACC 60:2290-5 (2012)

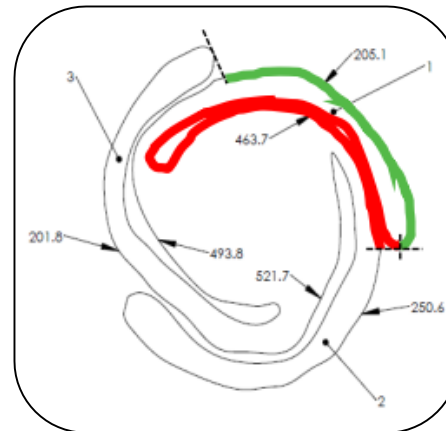
What was the problem with IN.PACT DEEP?

	DCB	PTA	P
12-month LLL (mm)	0.61 ± 0.78	0.62 ± 0.78	0.950



Lack of drug effect by older technology?

	“Old” IN.PACT Amphirion	“New” (Next Gen) IN.PACT Pacific/Admiral
Coating Method	Manually-coated on folded balloon	Automatically-coated on inflated balloon
Balloon Material	High surface energy	Low surface energy



Green denotes example of coating on folded balloon

Red denotes incremental surface area coated on inflated balloon

Animal studies confirmed balloon material can impact drug delivery:

- New design delivered more drug to vessel → Folds protect the drug
- New design had less residual drug on balloon → Better drug release

What was the problem with IN.PACT DEEP?

Multiple factors may have contributed:

- Potentially underpowered study design (2:1 randomization)
- Poor compliance to angiographic follow-up
- PTA group outcomes not consistent with historical results
- Procedural differences
- Lack of pre-specified assessment of wound-related artery by core labs
- Insufficient drug delivery to the lesion?
- No dedicated wound care schedule

Need for new studies! Upcoming / Ongoing

Lutonix BTK Registry

Luminor BTK Registry

BIOLUX P-III

Illuminate BTK

IN.PACT BTK

Global Lutonix DCB BTK registry – DCB

- +/- 500 patients single arm study - Lutonix DCB
- Primary Endpoint:
Freedom from clinically driven TLR @ 6M
Limb Salvage Rate @ 6M

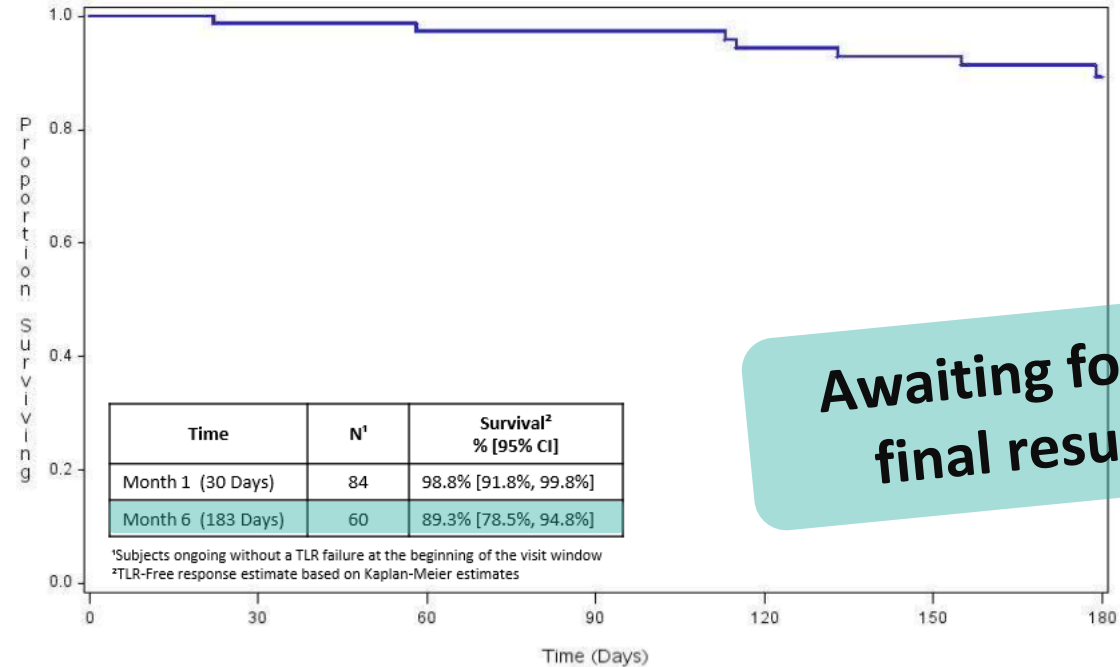
Inclusion criteria:

- ✓ RCC 3,4,5
- ✓ Stenosis >70% or occlusion of the BTK arteries
- ✓ LL not specified

Global Lutonix DCB BTK registry – DCB – preliminary Results

- MLL : 102 ± 79.5mm
- F-TLR @6M : 89.30%

Description	BTK Study Registry (N=85)
Lesion Location ¹	
Popliteal	9.4% (8/85)
Tibioperoneal Trunk	27.1% (23/85)
Anterior Tibial	34.1% (29/85)
Posterior Tibial	24.7% (21/85)
Peroneal	25.9% (22/85)
Total Target Length (mm), Mean ± SD (n)	102 ± 79.5 (85)
Average RVD (mm), Mean ± SD (n) (min, max)	2.7 ± 0.57 (85) (2.0, 4.0)
Calcification, % (n/N)	63.8% (51/80)
Severe Calcification, % (n/N)	10.5% (8/76)



Freedom From	N ¹	Survival ² % [95% CI]
All Cause Death Survival	63	89.2% [79.5%, 94.4%]
Major Amputation	63	95.2% [85.8%, 98.5%]
Re-intervention for Thrombosis/Thrombolysis	62	96.1% [84.9%, 99.0%]
Re-intervention For Distal Embolization	63	100.0% [NA, NA]
TVR	59	89.8% [79.8%, 95.0%]
Unexpected Device or Drug Related Event	63	100.0% [NA, NA]

Luminor Registry : BTK Cohort

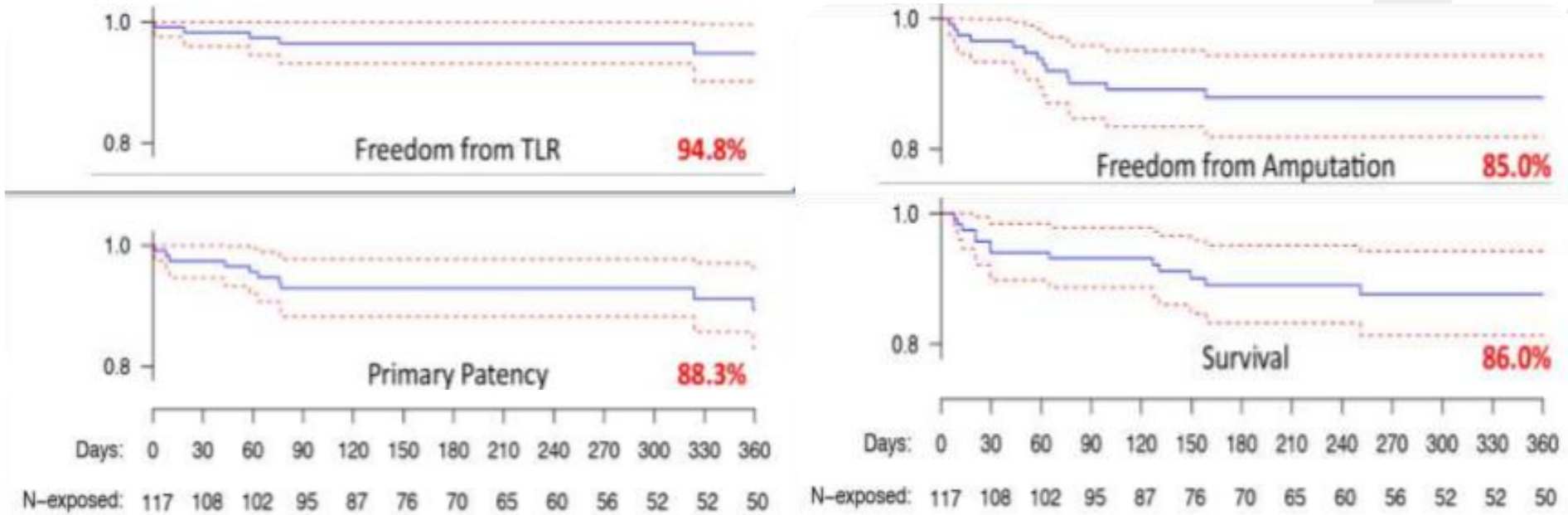
- Preliminary 98 patients – 116 lesions
- All comers study in infra-inguinal arteries - BTK cohort
- Primary Endpoint:
Primary Patency Rate @ 12M

Inclusion criteria:

- ✓ RCC 2,3,4,5
- ✓ Stenosis >50% or occlusion (of the tibial arteries)
- ✓ LL 20 to 200mm

Luminor Registry : BTK Subgroup – Preliminary Results

- MLL : 77.90mm



Awaiting for the final results!

BIOLUX P-III : DCB

- 882 patients total cohort -> 150 pts BTK cohort
All comers study in infra-inguinal arteries with BTK cohort
- Primary Endpoint:
Freedom from clinically driven TLR @ 12M

Inclusion criteria:

- ✓ RCC not specified
- ✓ Stenosis not specified
- ✓ LL not specified

BIOLUX P-III : DCB - Results

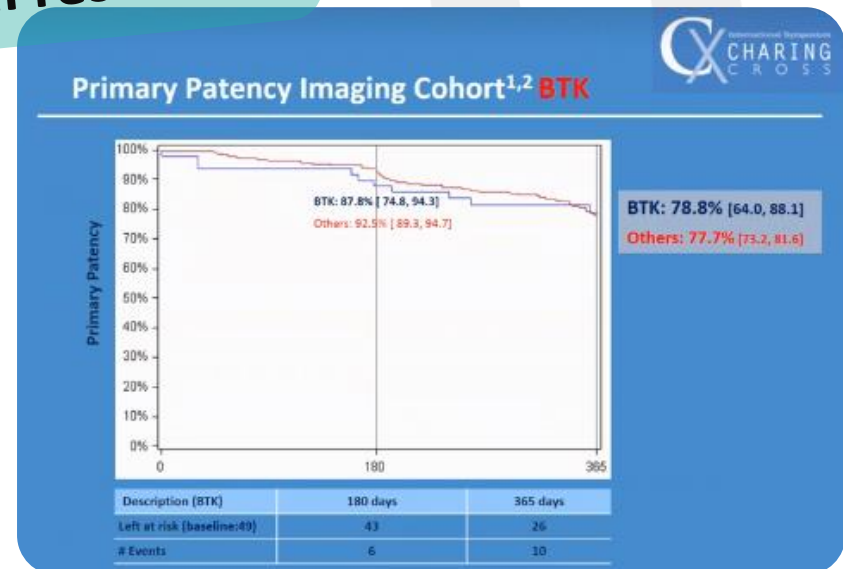
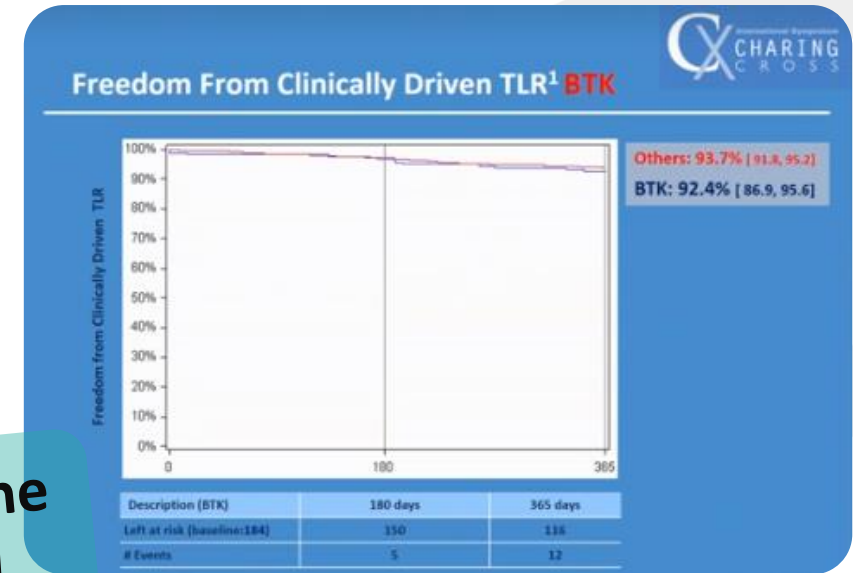
MLL : 79 mm
 62.70% diabetics / 76.70% CLI patients

f-TLR @ 12M : 92.40%

PP @ 12M : 78.80%

f-major AMP @ 12M : 92.20%

Awaiting for the final results!



ILLUMENATE BTK Post Market Study (BTK PMS)

- +/- 75 patients – single arm – Stellarex DCB
All comers study in infra-inguinal arteries with BTK cohort
- Primary Endpoint:
Composite Patency (flow/no flow) + Limb Salvage @6M

Inclusion criteria:

- ✓ RCC 3,4,5
- ✓ Stenosis not specified
- ✓ LL not specified

**Enrolling patients
Waiting for the first results!**

IN.PACT BTK – DCB vs PTA

- 60 patients – RCT– IN.PACT Admiral DCB vs PTA
- Primary Endpoint:
LLL @ 9M

Inclusion criteria:

- ✓ RCC 4,5
- ✓ Stenosis not specified
- ✓ LL not specified

**Enrolling patients
Waiting for the first results!**

Conclusion

- DCB concept for SFA can not be transferred into the challenging BTK region
- Initial promising results with DCB in the BTK area (DEBATE-BTK & IN.PACT BTK) could not be duplicated into the IN.PACT DEEP & BIOLUX P-II studies
- Existing new enthusiasm waits for the results of ongoing studies: Lutonix BTK Registry, Luminor BTK Registry, Biolux P-III, Illumenate BTK-PMS, IN.PACT BTK,...
- Still remains the question in BTK / CLI treatment:
What are the right endpoints , correct strategy, the most efficient follow-up and the absolute need for multi-disciplinary approach.