Lutonix DCB in BTK – Update on the BTK real world registry and RCT

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Disclosures

Speaker: **Prof. Dr. med. Dierk Scheinert**

I have the following potential conflicts of interest to report:

Advisory Board /Consultant: Abbott, Biotronik, Boston Scientific, Cook Medical, Cordis, CR Bard, Gardia Medical, Medtronic/Covidien, TriReme Medical, Trivascular, Upstream Peripheral Technologies

Drug-Coated Balloon BTK

Trials which failed to show a benefit / superiority for DCBs BTK

– In.Pact DEEP multicenter, randomized, controlled trial
  - In.Pact Amphirion PTX-eluting balloon vs.
  - Uncoated Amphirion Deep

Zeller et al. *JACC* 2014

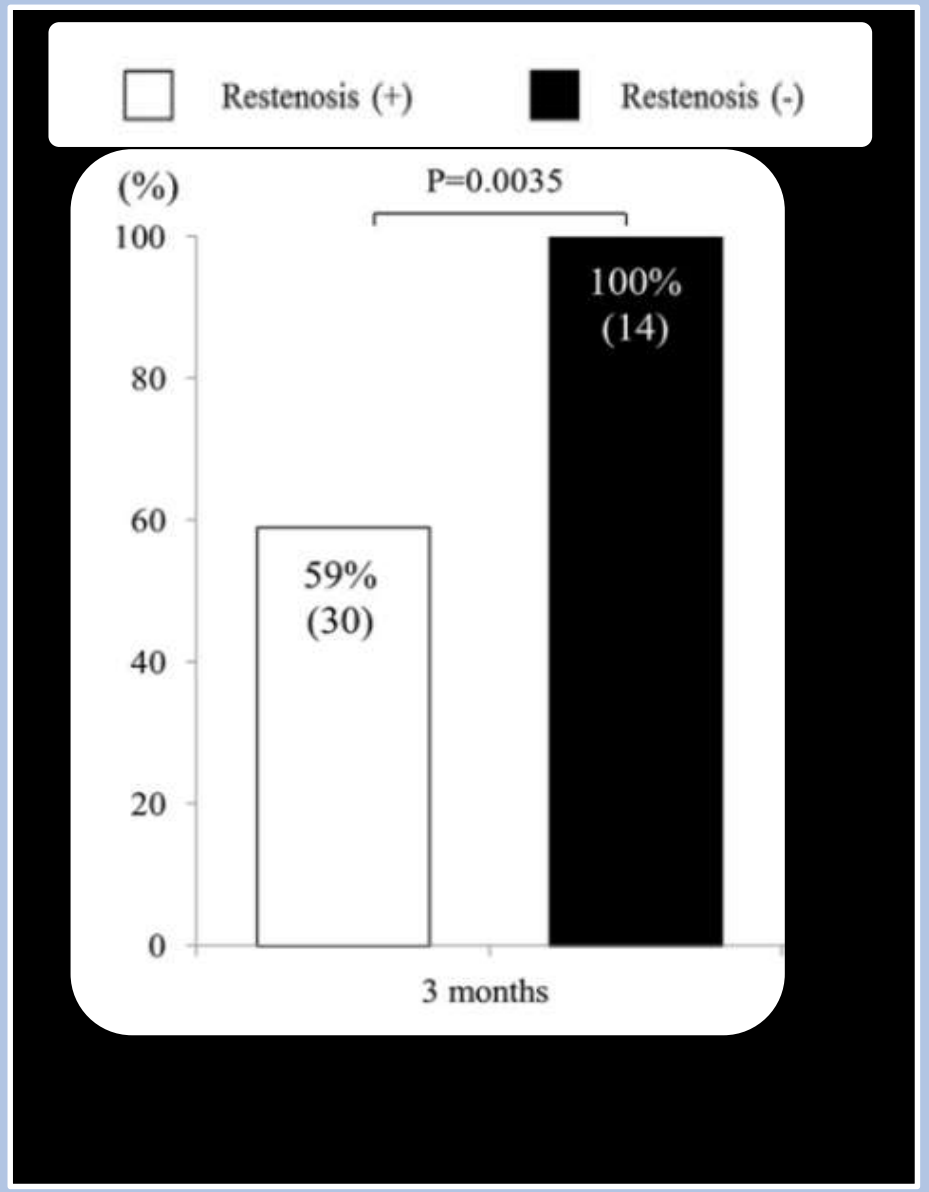
✘ Biolux-P-II multicenter, randomized, controlled trial
  - ✓ Passeo-18 LUX PTX-eluting balloon vs.
  - ✓ Uncoated Passeo-18

Zeller et al. *JACC* Intervent 2015

POBA for CLI Treatment

- 68 CLI patients due to BTK lesions
- Lesion length: 140 ± 90 mm
- **Restenosis at 3 months: 73%**

- Restenosis delays healing



Iida O.. et al. EJVES 2012; 44:425-31.

Lutonix® 014 Drug Coated Balloon IDE BTK Trial

Study Synopsis

OBJECTIVE	To demonstrate the superior efficacy and non-inferior safety of the Lutonix DCB by direct comparison to standard PTA catheter for treatment of stenosis or occlusion of below-the-knee arteries.
STUDY DESIGN	Prospective, Multicenter, Single Blind, Randomized, Safety and Efficacy
STUDY DEVICE	Lutonix® 0.014" OTW Drug Coated PTA Dilatation Catheter (Lutonix DCB Catheter)
RANDOMIZATION	2:1 Lutonix DCB to standard PTA
PRIMARY ENDPOINTS	Safety at 30 days Limb salvage & primary patency at **6 months**
NUMBER OF SUBJECTS/SITES	Up to 840 randomized subjects at 75 global sites
FOLLOW-UP	**Clinical:** 1, 6, 12, 24, and 36 Months **Duplex Ultrasound (DUS):** 1, 6,12, 24, & 36 months **Telephone:** 48 and 60 Months

Primary Endpoints

SAFETY

Freedom from Major Adverse Limb Events (MALE) & All-Cause Perioperative Death (POD) at **30 DAYS**

★ Amputation (above ankle)

★ Major re-intervention

- New bypass graft
- Jump/Interposition graft revision
- Thrombectomy/Thrombolysis

EFFICACY

Composite of Limb Salvage and Primary Patency at **6 Months**

Defined as freedom from the composite of above ankle amputation, target vessel occlusion, and clinically-driven target lesion re-intervention. ★

Patient Eligibility

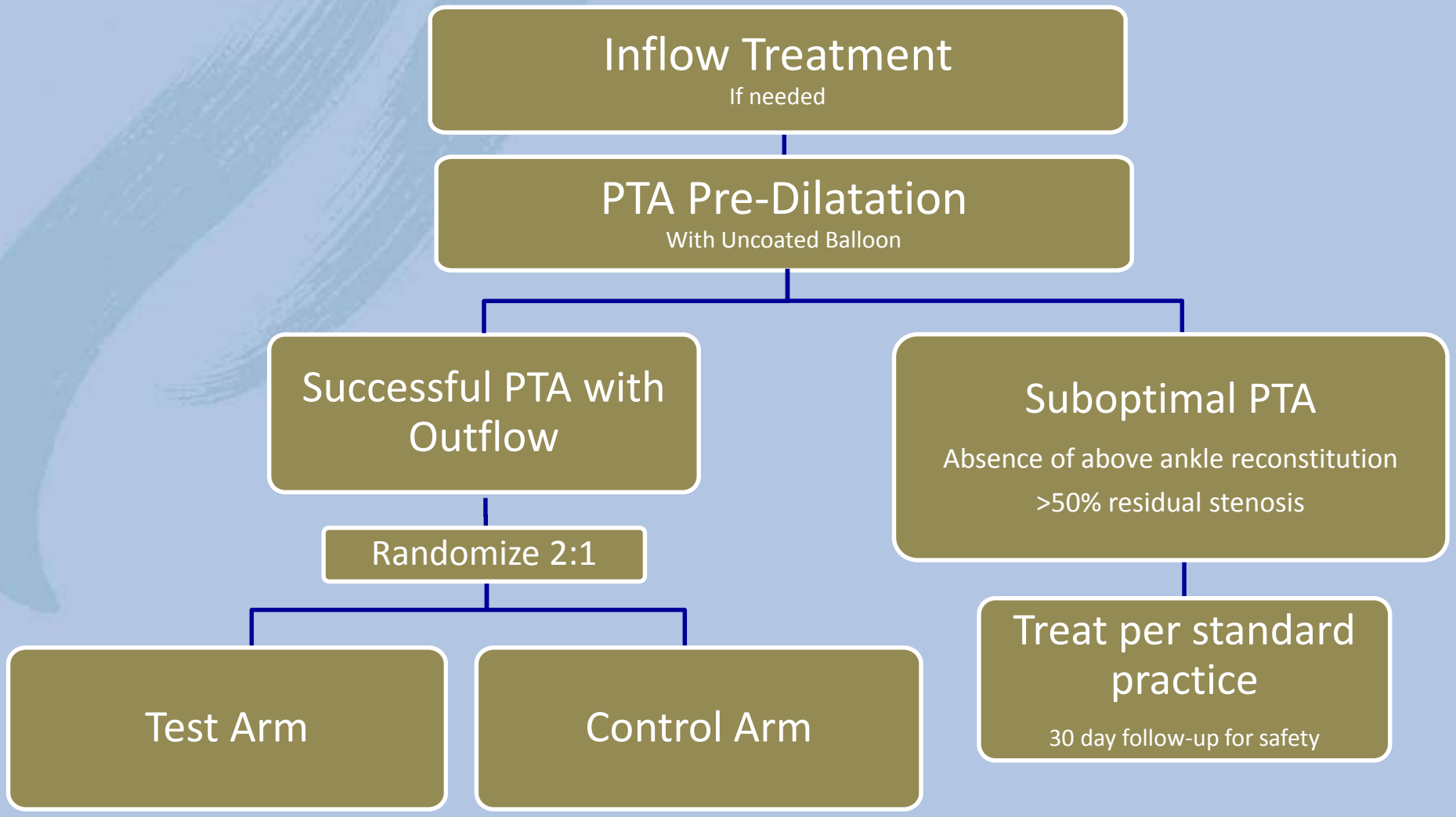
Inclusion Criteria

- Male or non-pregnant female ≥18 years of age
- Rutherford 3-5
- Life expectancy ≥ 1 year
- Significant stenosis (≥70%)
- A patent inflow artery
- Target vessel(s) diameter between 2 and 4 mm
- Target vessel(s) reconstitute(s) at or above the ankle

Exclusion Criteria

- Pregnant or planning on becoming pregnant
- History of stroke within 3 months
- History of MI, thrombolysis or angina within 30 days of enrollment
- GFR ≤ 30 ml/min per 1.73m^2
- Acute limb ischemia
- In-stent restenosis of target lesion

Study Flowchart



Current Status of Lutonix 014 BTK IDE Study

- 382 Randomized Subjects
- 12 subjects with a Major Amputation (3.2%)
- The Data Monitoring Committee (DMC) has met 11 times and unanimously recommended continuation of the study with no modifications.

Preliminary Demographic Information

	All Randomized Subjects* (N=375)
Age (Years), Mean ± SD (n)	72.9 ± 9.77 (375)
Median (Min, Max)	74.0 (45.0, 96.0)
Gender, % (n/N)	
Female	32.0% (120/375)
Male	68.0% (255/375)
Race, % (n/N)	
American Indian	0.3% (1/375)
Asian	9.6% (36/375)
Black or African American	10.9% (41/375)
Other	1.1% (4/375)
White	78.1% (293/375)
Height (cm), Mean ± SD (n)	170.0 ± 10.3 (367)
Median (Min, Max)	170.0 (140.0, 193.0)
Weight (kg), Mean ± SD (n)	81.3 ± 20.53 (367)
Median (Min, Max)	80.0 (38.0, 202.0)
BMI (kg/m^2), Mean ± SD (n)	28.0 ± 6.07 (367)
Median (Min, Max)	27.4 (14.1, 69.9)
BMI >= 30, % (n/N)	33.2% (122/367)

*Site reported data, enrollment ongoing may change as more subjects enroll.

Preliminary Selected Medical History

	All Randomized Subjects* (N=375)
Current or Previous Smoker, % (n/N)	57.7% (210/364)
Diabetes, % (n/N)	68.4% (249/364)
Dyslipidemia, % (n/N)	75.0% (273/364)
Hypertension, % (n/N)	92.0% (335/364)
CAD, % (n/N)	49.2% (179/364)
Heart Failure, % (n/N)	10.4% (38/364)
MI, % (n/N)	20.3% (74/364)
COPD, % (n/N)	12.6% (46/364)
Osteomyelitis, % (n/N)	6.0% (22/364)
Renal Failure, % (n/N)	20.9% (76/364)

*Site reported data, enrollment ongoing may change as more subjects enroll.

Preliminary Baseline Angio Data

	All Randomized Subjects* (N=375)
Number of Treated Lesions, % (n/N)	
1	74.7% (254/340)
2	20.6% (70/340)
3	4.1% (14/340)
4	0.6% (2/340)
Total Target Lesion (mm), Mean ± SD (n)	136.4 ± 97.63 (336)
Median (Min, Max)	111.0 (6.0, 442.0)
Maximum Stenosis (%DS), Mean ± SD (n)	88.3 ± 13.84 (340)
Median (Min, Max)	94.0 (32.0, 100.0)
CTO, % (n/N)	45.0% (153/340)
Average RVD (mm, Site), Mean ± SD (n)	2.52 ± 0.56 (338)
Median (Min, Max)	2.41 (1.27, 5.32)
Any Calcification, % (n/N)	59.1% (201/340)
Severe Calcification	25.8% (51/198)
Location(s) Treated, n (%)**	
Popliteal, % (n/N)	10.9% (37/340)
Tibioperoneal Trunk, % (n/N)	30.0% (102/340)
Anterior Tibial, % (n/N)	45.0% (153/340)
Posterior Tibial, % (n/N)	27.1% (92/340)
Peroneal, % (n/N)	27.1% (92/340)

*Site reported data, enrollment ongoing may change as more subjects enroll.
**More than one vessel may be treated

Preliminary Rutherford Classification

	All Randomized Subjects* (N=375)
Baseline Rutherford Classification, % (n/N)	
3	7.9% (29/368)
4	37.8% (139/368)
5	54.3% (200/368)
92.1% have CLI**	

*Site reported data, enrollment ongoing may change as more subjects enroll.
**Based on Rutherford Classification 4 & 5

Summary

- Primary Endpoints
  - Safety at 30 days
  - Limb salvage & primary patency at 6 months
- Current Study Population
  - 92.1% CLI
  - 54.3% RCC 5
  - 68.4% diabetic
  - 32.0% females
- Low major amputation rate - 3.2%
- The Data Monitoring Committee (DMC) has met 11 times and deemed the study safe to continue with no modifications to protocol.

*FDA Approved IDE G130007

Initial Look at the Global Lutonix DCB BTK Registry Study 6 Month Outcomes

A Prospective, Multicenter, Single-Arm Real-World Registry Investigating the Clinical Use and Safety of the Lutonix Drug Coated Balloon PTA Catheter for Treatment of Below-the-Knee (BTK) Arteries

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Study Design

Study Design	Prospective, Multicenter, Single Arm Registry
Objective	To demonstrate safety and assess the clinical use and outcomes of the Lutonix DCB for treatment of stenosis or occlusion of native below-the-knee arteries in a heterogeneous patient population in real world clinical practice
Number of patients/sites	Up to 500 subjects to be enrolled at up to 35 international sites
Inclusion Criteria	Rutherford Class: 3-5, ≥ 70% stenosis lesion, target vessel(s) reconstitute(s) at or above the ankle with inline flow to at least one patent
Exclusion Criteria	Neurotrophic ulcer or heel pressure ulcer or ulcer potentially involving calcaneus (index limb)
Primary Endpoints	Safety: Freedom from BTK MALE+POD at 30-days Efficacy: Freedom from TLR at 6 months
Follow-up	1, 6, 12 and 24 Months

Study Centers

PI Name	
Prof. Willfort-Ehringer	
Dr. Loewe	
Prof. Brodmann	
Prof. Hausegger	
Dr. Lerut	
Dr. Lansink	
Dr. Husmann	
Dr. Banyai	
Dr. Zech	
Dr. Giménez-Gaibar	
Dr. Albuquerque e Castro	
Prof. Sapoval	
Dr. Lichtenberg	
Dr. Thieme	
Prof. Scheinert	

Study Centers

PI Name	
Prof. Eckstein	
Dr. Sunderdiek	
Prof. Tepe	
Dr. Perez Delgado	
Prof. Zeller	
Prof. Karnabatidis	
Prof. Brountzos	
Dr. Rossato	
Dr. Cioppa	
Dr. Tolva	
Dr. Fanelli	
Dr. Van den Heuvel	
Dr. Butterfield	
Dr. Al-Shammari	

Demographics / Baseline Characteristics

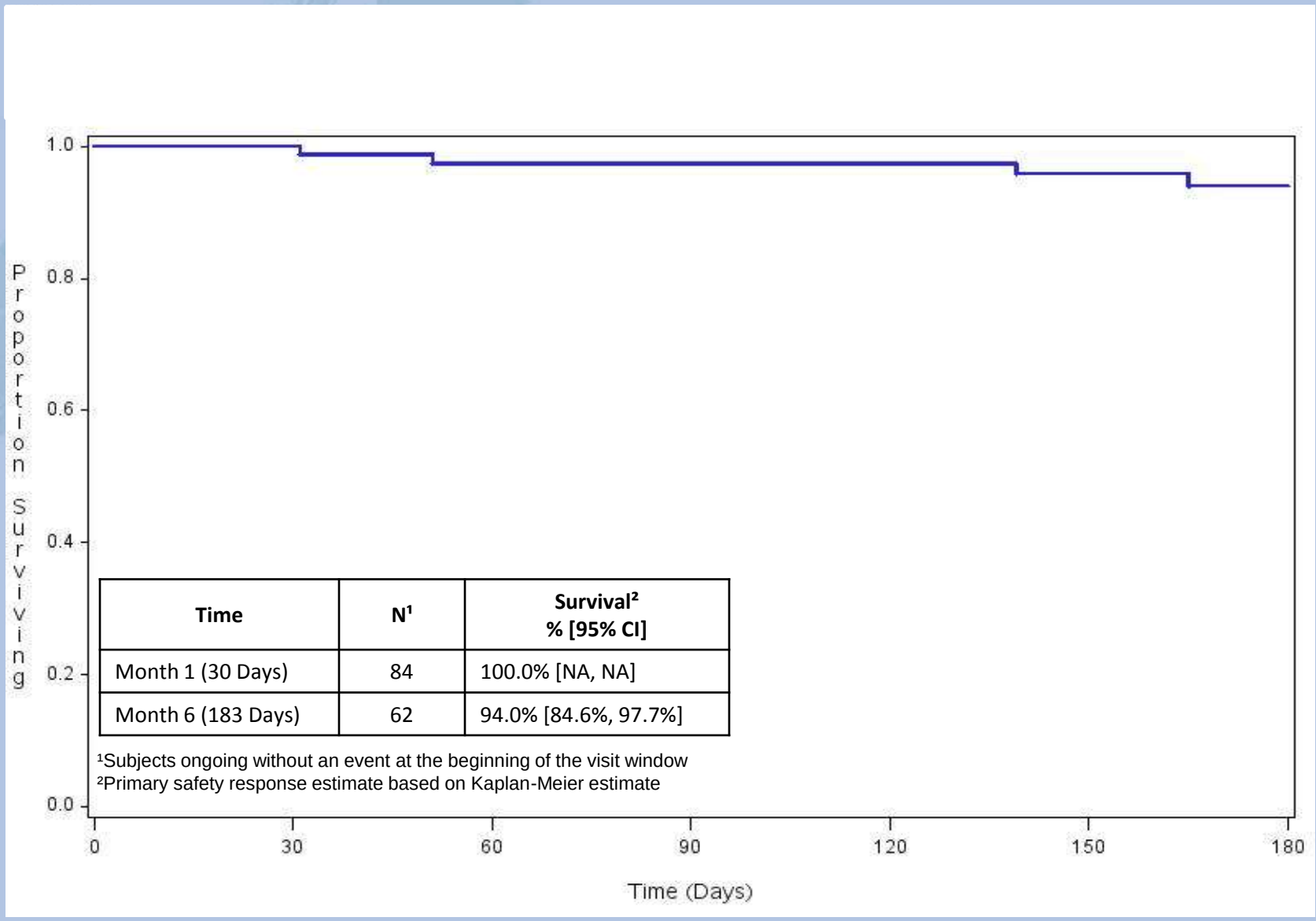
Description	BTK Study Registry (N=85)
Age (Years), Mean ± SD (n)	73.9 ± 10.2 (85)
Gender, % (n/N)	
Female	29.4% (25/85)
Male	70.6% (60/85)
BMI ≥30 kg/m², % (n/N)	25.0% (21/84)
Hypertension, % (n/N)	87.1% (74/85)
Dyslipidemia, % (n/N)	60.0% (51/85)
Current/Previous Smoker, % (n/N)	47.1% (40/85)
Diabetes	57.6% (49/85)
Rutherford Category	
3	19.0% (16/84)
4	16.7% (14/84)
5	64.3% (54/84)

Lesion Characteristics

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)	2.7 ± 0.57 (85)
(min, max)	(2.0, 4.0)
Calcification, % (n/N)	63.8% (51/80)
Severe Calcification, % (n/N)	10.5% (8/76)

[1]Subjects may be in more than one category.

Freedom from Primary Safety Events



Time	N[1]	Survival[2] % [95% CI]
Month 1 (30 Days)	84	100.0% [NA, NA]
Month 6 (183 Days)	62	94.0% [84.6%, 97.7%]

[1]Subjects ongoing without an event at the beginning of the visit window
[2]Primary safety response estimate based on Kaplan-Meier estimate

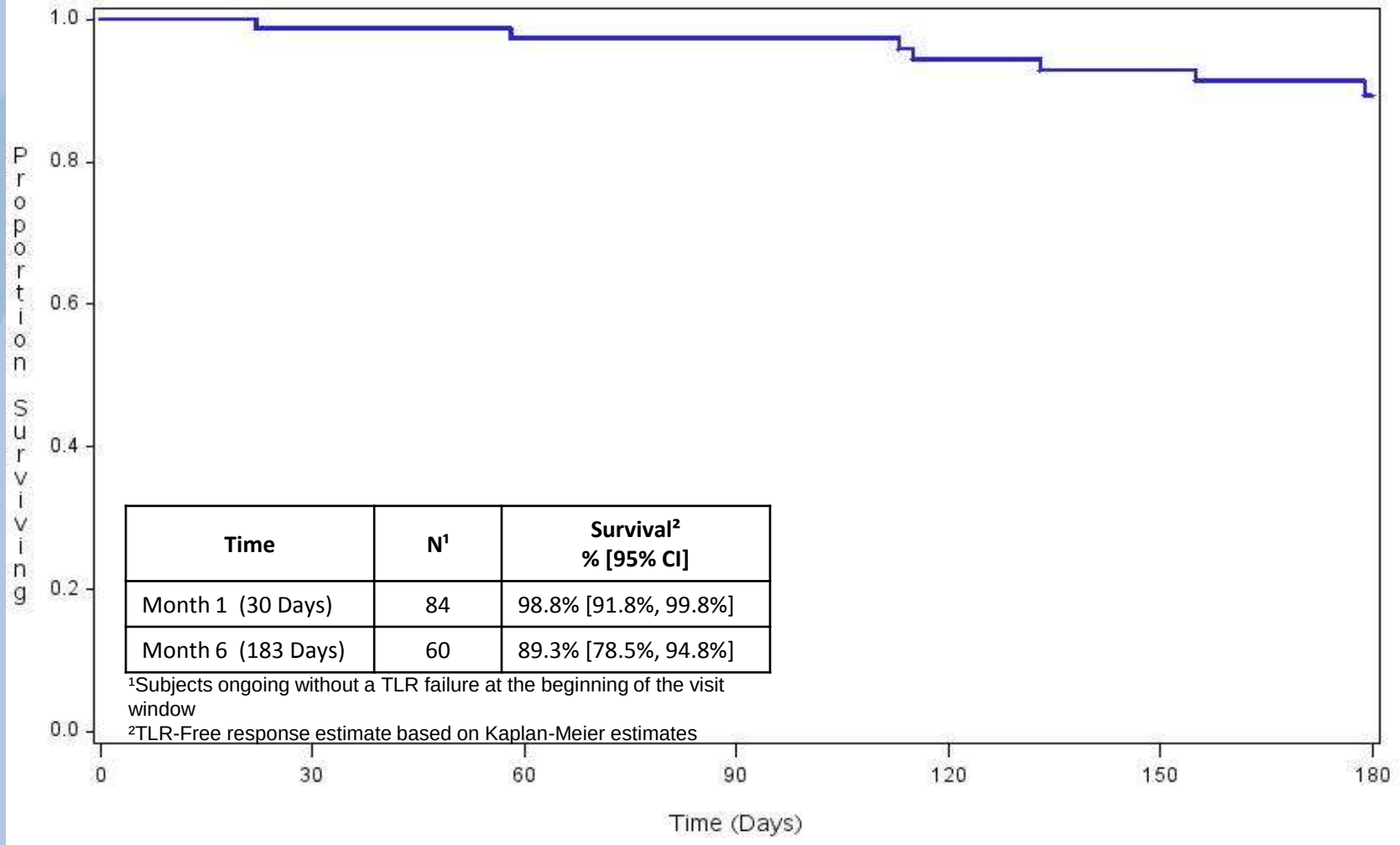
Freedom at 30-Days from the composite of all-cause death, above-ankle amputation or major re-intervention, i.e., new bypass graft, jump/interposition graft revision, or thrombectomy/thrombolysis of the index limb involving a below-the-knee artery.

Additional Safety Profile

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]

[1]Subjects ongoing without a failure at the beginning of the visit window
[2]Survivor rate based on Kaplan-Meier Estimate

Freedom from TLR

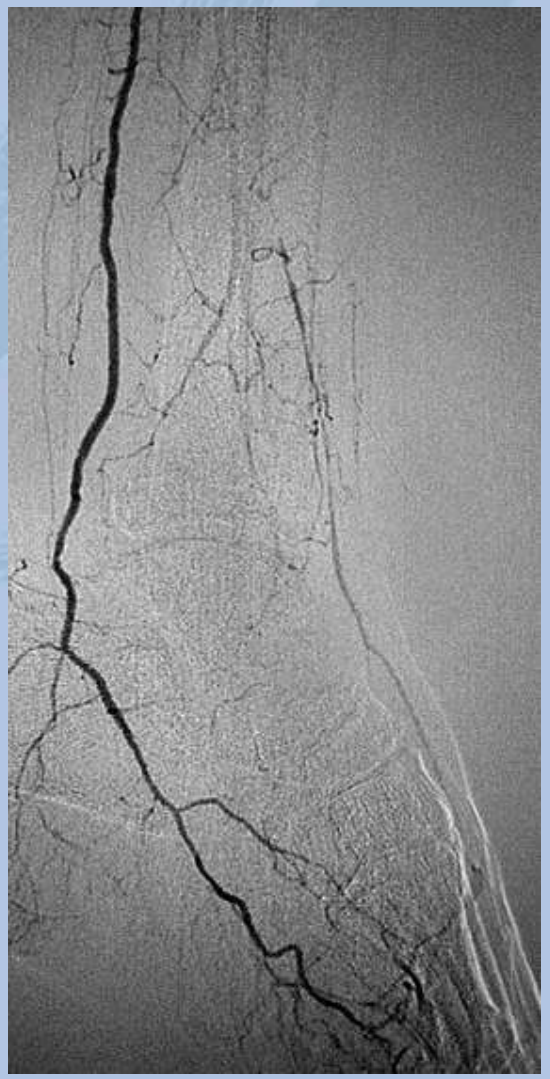


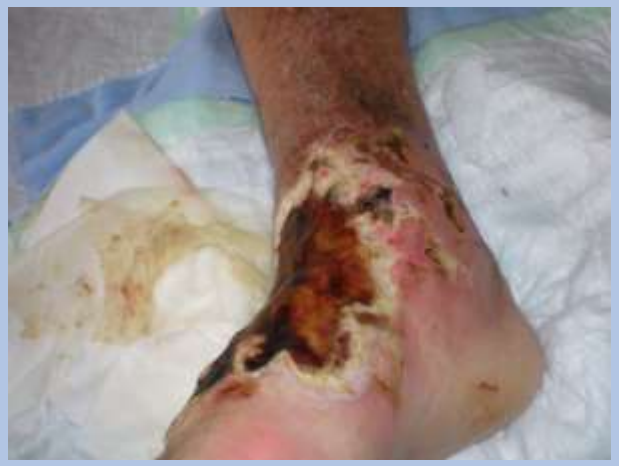
Time	N[1]	Survival[2] % [95% CI]
Month 1 (30 Days)	84	98.8% [91.8%, 99.8%]
Month 6 (183 Days)	60	89.3% [78.5%, 94.8%]

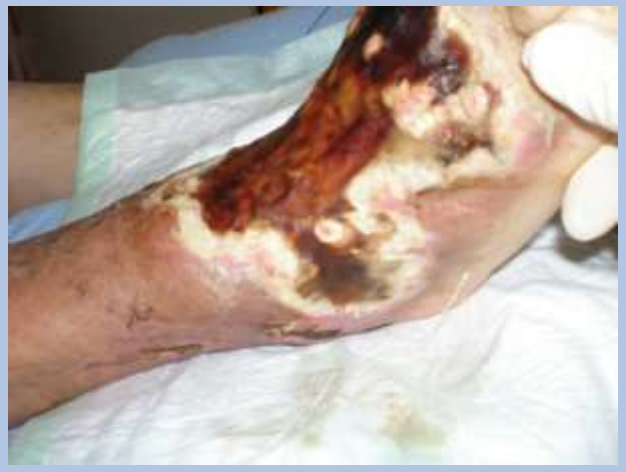
[1]Subjects ongoing without a TLR failure at the beginning of the visit window

[2]TLR-Free response estimate based on Kaplan-Meier estimates

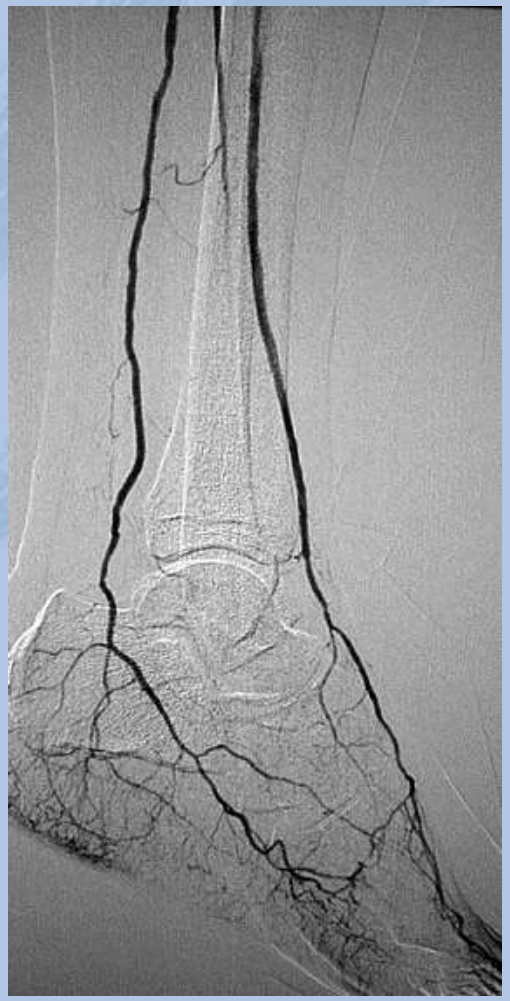
Male, 70 J, Diabetes, Endstage Renal Insufficency

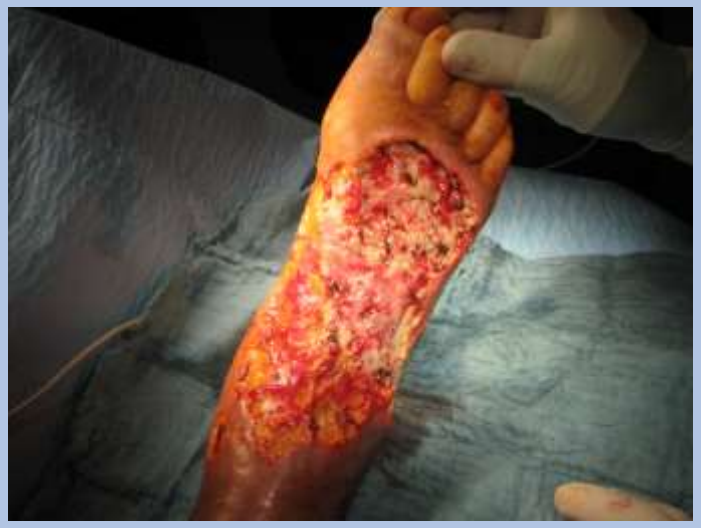


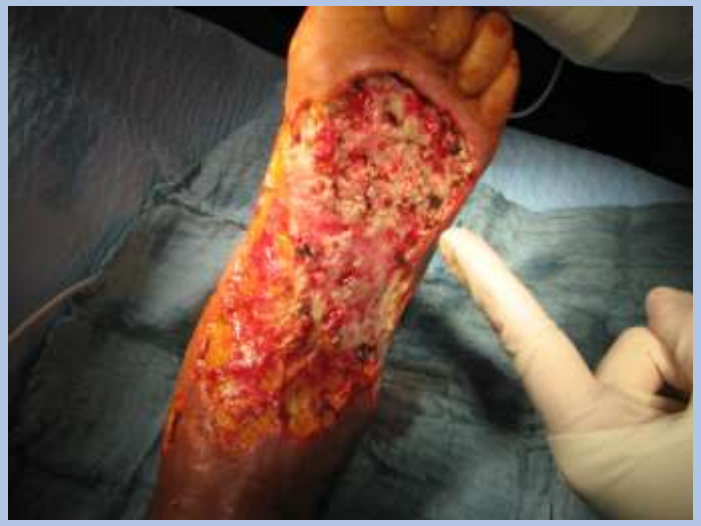




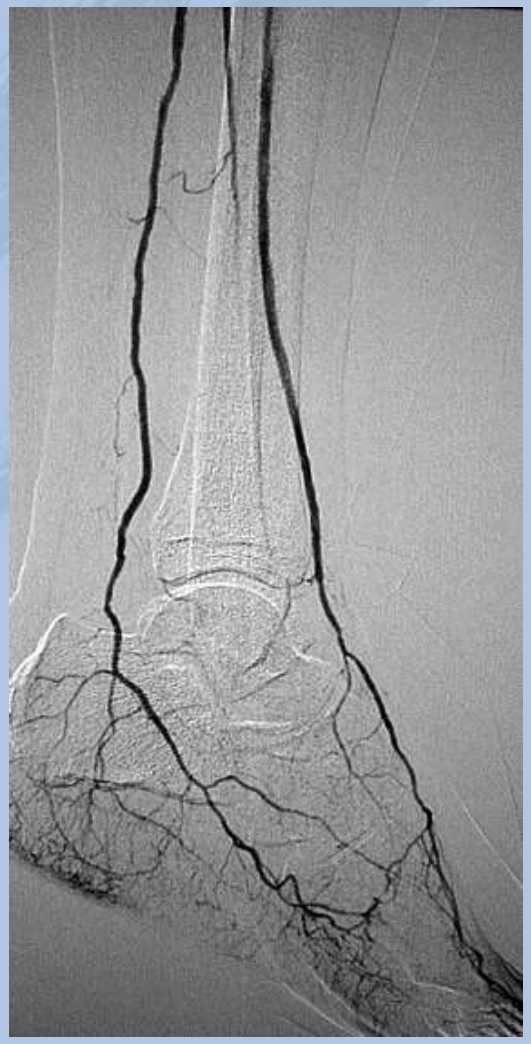
Recanalisation with DCB Lutonix 2.5mm

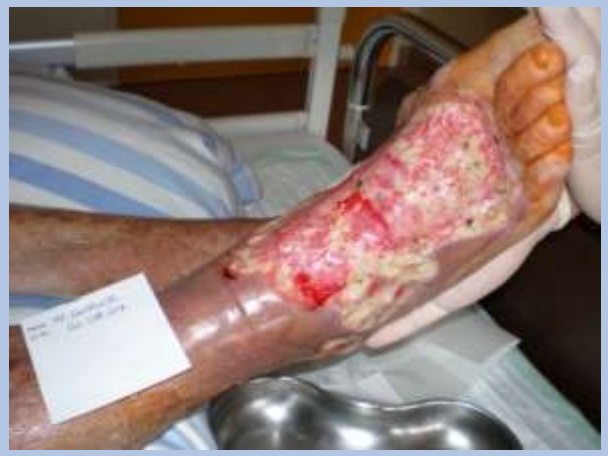


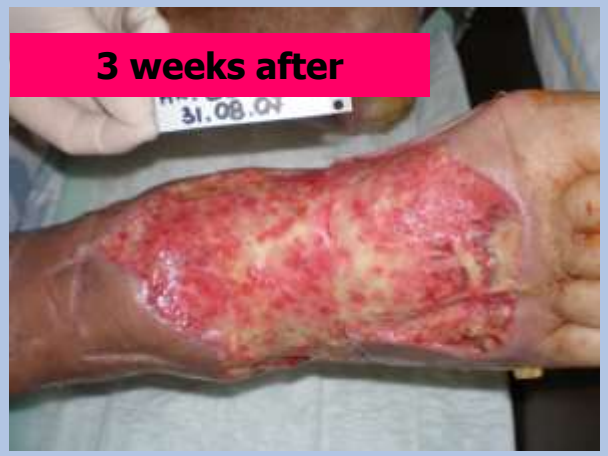




Follow-up







Klinikum Arnsberg

Conclusions

- Only BTK Registry Multi Center On-going Study
- Promising Treatment Effect in Below-the–Knee Arteries
- Safety Consistent with the Strong Safety Profile of the Lutonix DCB in PAD
- Freedom from TLR 89.3%
- Less than 5% Amputation Rate
- ZERO Re-interventions for Distal Embolizations

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