Clinical Outcomes Of Sirolimus-Eluting BioResorbable Peripheral Scaffold System In Arteries Below- the-Knee:

CREDENCE BtK-1 Study

INTRODUCTION

- Critical limb ischemia (CLI) is a limb and life-threatening condition with a yearly incidence of around 220 new cases per million populations[1]
  - Infrapopliteal arterial occlusive disease is a leading source of CLI[1]
- Infrapopliteal percutaneous endovascular methods such as angioplasty and stenting, are currently supported by clinical evidence as the first line treatment of BtK arterial occlusive disease[1]
- However, several unresolved issues for permanent DES implants remain, mainly due to the unnecessary long-term arterial irritation, leading to in-stent restenosis[2]
- The concept of bioresorbable scaffolds coated with anti-proliferative drugs is an attractive concept to solve problems associated with metallic DES[3]
- It helps to achieve excellent acute and long-term results with completely disappearing scaffold[4]

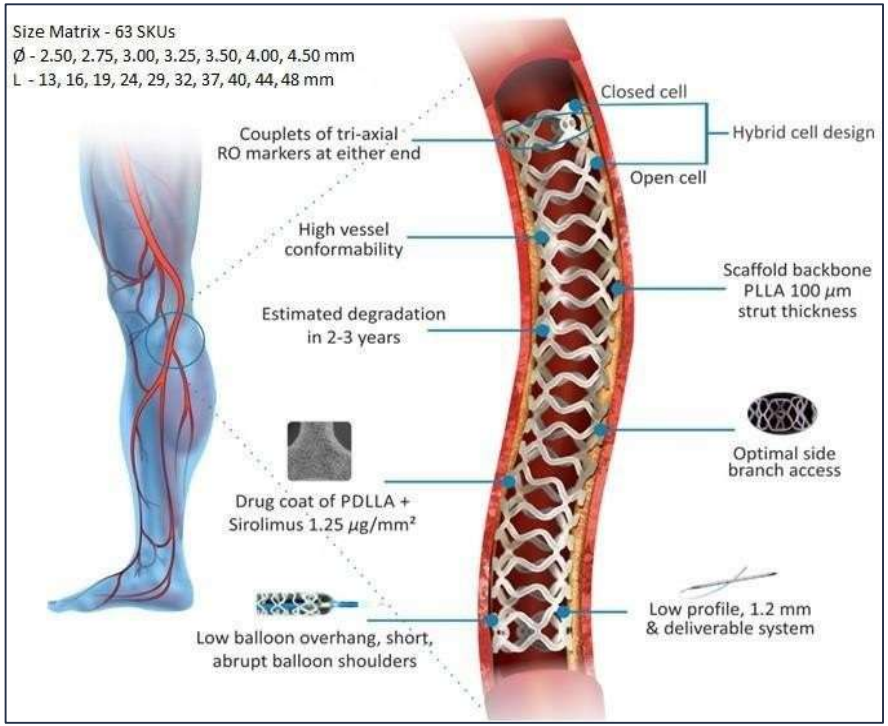
1. Farber A, et al. *J Vasc Surg.* 2019; 69(2): 470-481.
2. Ali Z.A., et al. *EuroIntervention.* 2021; 17(2): e105-e123.
3. Drelich J.W., et al. *Curr Opin Biomed Eng.* 2022; 100411.
4. Jinnouchi H, et al. *Nat Rev Cardiol.* 2019: 16(5): 286-304.

RATIONALE

- Despite the widespread adoption of bare-metal stents for the treatment of critical limb ischemia, it presents with several critical challenges:
  - Stent thrombosis
  - Permanent metal implant
  - Persistent inflammation
  - Neoatherosclerosis within the stented segment
  - Inability to restore normal vessel architecture due to the presence of permanent metallic stent remain unresolved
- Bioresorbable vascular scaffold has potential to address above challenges
- This study was carried out to evaluate the safety and performance of CREDENCE BtK sirolimus-eluting bioresorbable peripheral scaffold system in patients with critical limb ischemia following percutaneous transluminal angioplasty of below-the-knee arteries

1. Yang X, et.al *US Cardiology Review*. 2017;11:25-30.

CREDENCE BtK
Sirolimus-Eluting Bioresorbable Peripheral Scaffold System



CREDENCE™ BtK: Sirolimus eluting BRS

STUDY DESIGN

CREDENCE BtK : Study Design

First-in-man prospective, multi-center clinical study
Total number of patients: 30
CTRI No. - CTRI/2016/11/007473

Baseline assessment, informed consent process and eligibility assessment

1-month clinical follow-up → **6-month clinical and angiographic follow-up** → **12-month clinical follow-up** → **Annual follow-up up to 5-year**

Safety Endpoints
Major amputation or any cause of death

Performance Endpoints
Primary patency, target lesion revascularization, Technical success, clinical success and improvement of ankle-brachial index

Imaging Endpoints
Late lumen loss and primary patency by quantitative vessel analysis
Independent core laboratory
(Stanford University,
Stanford, CA, USA)

ELIGIBILITY CRITERIA

Key Inclusion Criteria

- Stenotic (>50%) or occlusive atherosclerotic disease of below the knee arteries
- Length of lesion ≤56 mm, Reference vessel diameter 2.25-4.50 mm
- A maximum of two lesions in one of the below the knee arteries treated in the study, or in two vessels of two different legs
- Symptomatic Critical Limb Ischemia (Rutherford IV and V)
- Life expectancy of >6 months
- No child-bearing potential or negative pregnancy test within 7 days of the index procedure
- Patient willing and able to return at the appropriate follow-up times for the duration of the study

ELIGIBILITY CRITERIA

Key Exclusion Criteria

- Patient refusing treatment
- Reference segment diameter not suitable for available scaffold design
- Length of lesion requiring more than one scaffold implantation
- Previously implanted stent(s) or PTA at the same lesion site
- Lesion lying within or adjacent to an aneurysm
- Inflow-limiting arterial lesions left untreated
- Patient has a known allergy to heparin, aspirin, or other anticoagulant/antiplatelet therapies or a bleeding diatheses, or is unable, or unwilling, to tolerate such therapies
- Patient taking phenprocoumon (Marcumar)
- Patient history of prior life-threatening contrast medium reaction
- Patient currently enrolled in another investigational device or drug trial
- Patient currently breastfeeding, pregnant, or intending to become pregnant
- Patient mentally ill or retarded

INVESTIGATING SITES

INVESTIGATING SITES

STUDY RESULTS

Baseline Demographic Characteristics

Baseline and demographic characteristics	n = 30 Patients
Age, Years, Mean±SD	67.4 ± 10.0
Gender, n (%)	
Male	26 (86.7)
Female	4 (13.3)
Body Mass Index, kg/m^2 , Mean±SD	22.5 ± 4.0
Heart rate, bpm, Mean±SD	85.7 ± 11.8
Disease Vessel, n (%)	
Single Vessel	12 (40.0)
Double Vessel	10 (33.3)
Triple Vessel	8 (26.7)

Values are presented as number, n (%) or mean±SD

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Summary of Medical History

Medical History, n (%)	n = 30 Patients
Diabetes mellitus	25 (83.3)
Dyslipidemia	3 (10)
Hypertension	19 (63.3)
Ischemic heart disease	10 (33.3)
Renal insufficiency	1 (3.3)
Anemia	2 (6.7)
Coronary artery disease	3 (10)
Coronary artery bypass graft	3 (10)
Diabetic retinopathy	1 (3.3)
Right tibial angioplasty	1 (3.3)
Greater toe abscess	1 (3.3)
Right leg cellulitis	1 (3.3)
Diabetic foot	2 (6.6)
Ankle-brachial index, pre-procedure, mean ±SD	**0.76 ± 0.36**

Values are presented as number, n (%) or mean±SD

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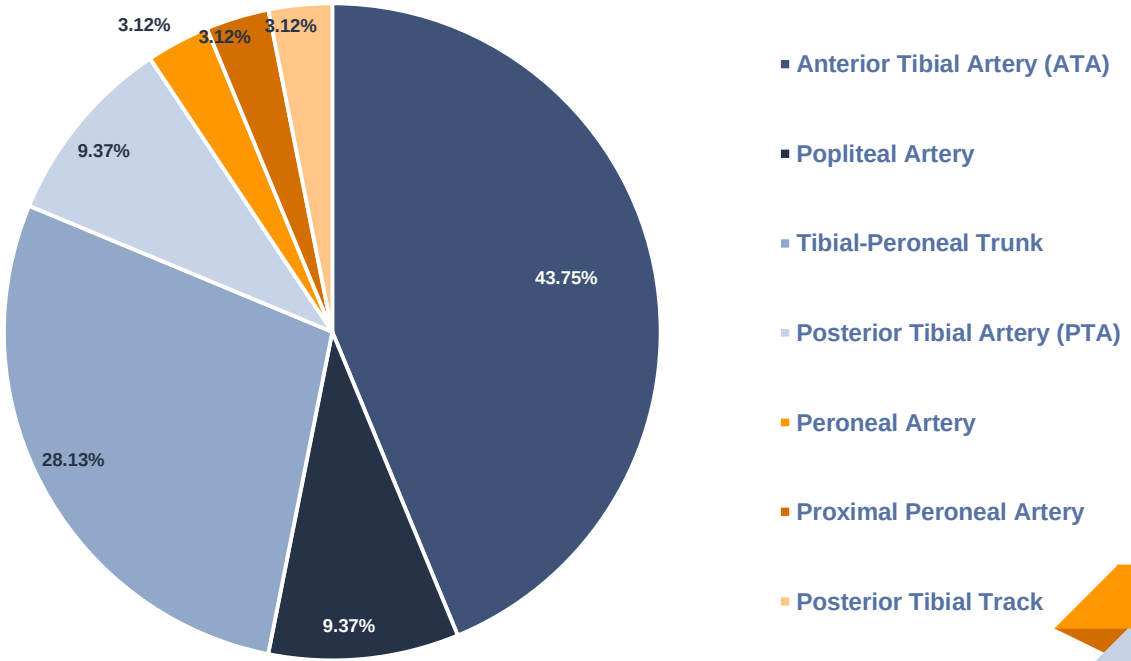
Procedure And Lesion Characteristics

Variables	N = 32 lesions / 30 Patients
Total number of lesions treated with study device	32
Lesion treated per patient	1.1
Technical success, n (%)	**30 (100)**

Lesion Location



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CREDENCE BtK Scaffolds Used in the Study

Scaffold Length

Length/ Diameter (mm)	19	24	29	32	37	40
2.75	2 (6.2)	3 (9.3)	1 (3.1)	1 (3.1)	0	1 (3.1)
3.00	0	1 (3.1)	0	1 (3.1)	5 (15.6)	4 (12.5)
3.50	1 (3.1)	2 (6.2)	2 (6.2)	1 (3.1)	0	3 (9.3)
4.00	1 (3.1)	0	1 (3.1)	0	1 (3.1)	1 (3.1)

Values are presented as number, n (%)

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Procedural Details

Access Site Location, n (%)	N=30 Patients
Left Femoral Artery	18 (60.0)
Right Femoral Artery	12 (40.0)
Average Scaffold Length, mm, mean±SD	31.7 ± 7.7
Pre-dilatation, n (%)	30 (93.8)
Post-dilatation, n (%)	19 (59.4)

Values are presented as number, n (%) or mean±SD

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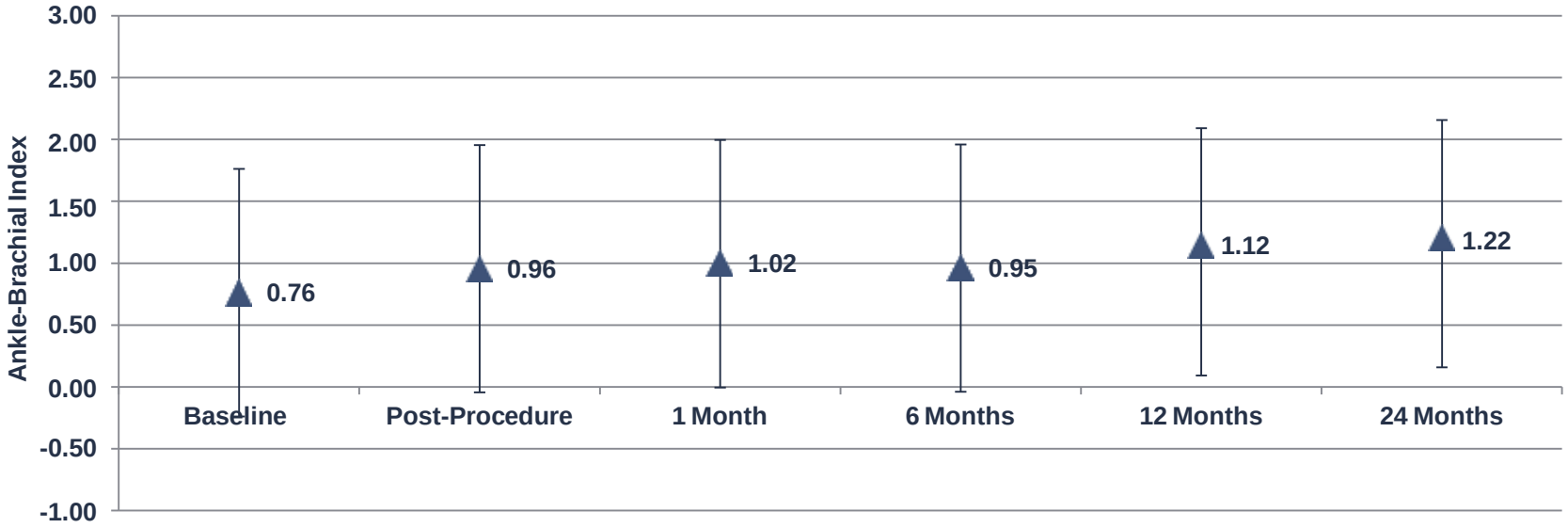
Ankle-brachial Index
Up to 24-month follow-up



Improvement of Ankle-Brachial Index from baseline up to 24-month follow-up

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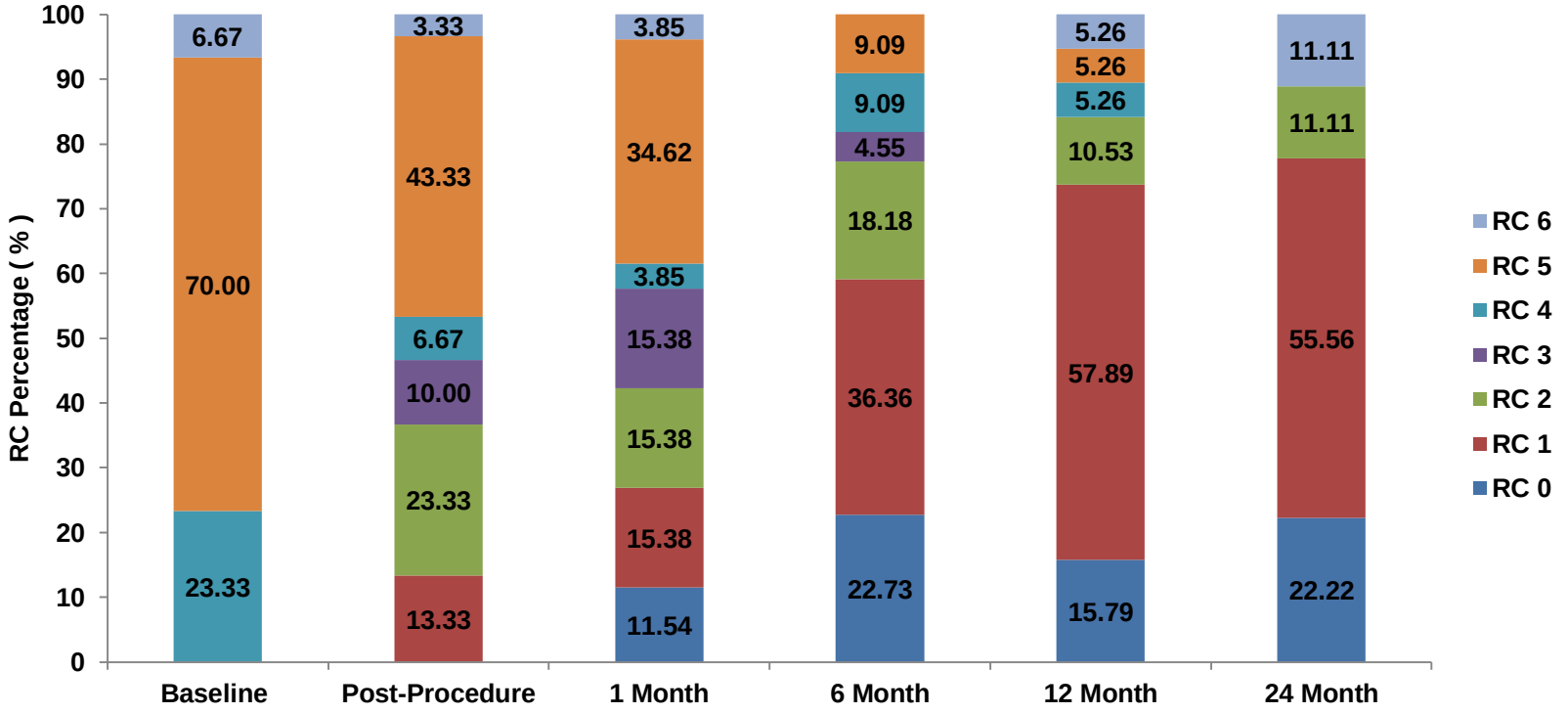
Rutherford-Becker Class up to 24-month Follow-up

Significant improvement according to change in Rutherford-Becker class from baseline to 24-month FU



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Angiographic Assessment of Target Lesion

Parameters	Pre-procedure	Post-procedure	6-Month	p-value
In-Segment				
Percentage Stenosis (%)	62.18 ± 20.67	21.28 ± 10.07	23.92 ± 12.17	0.0004
MLD (mm)	1.37 ± 0.77	2.65 ± 0.44	2.11 ± 0.59	0.0503
RVD (mm)	3.21 ± 0.70	3.41 ± 0.66	3.07 ± 0.96	0.3347
Late Lumen Loss (mm)	-	-	0.47 ± 0.39	-
In-Scaffold		**Post-procedure**	**6-Month**	**p-value**
Percentage Stenosis (%)	-	21.37 ± 13.46	25.07 ± 15.70	-
MLD (mm)	-	2.74 ± 0.45	2.22 ± 0.69	-
RVD (mm)	-	3.46 ± 0.61	3.12 ± 0.96	-
Late Lumen Loss (mm)	-	-	0.41 ± 0.35	-

Values are in mean ± SD, MLD: Minimal Lumen Diameter, RVD: Reference Vessel Diameter
Data are mean (SD) unless otherwise stated.
Note: p-values are between pre-procedure and 6-month follow-up, and are given for exploratory analysis only

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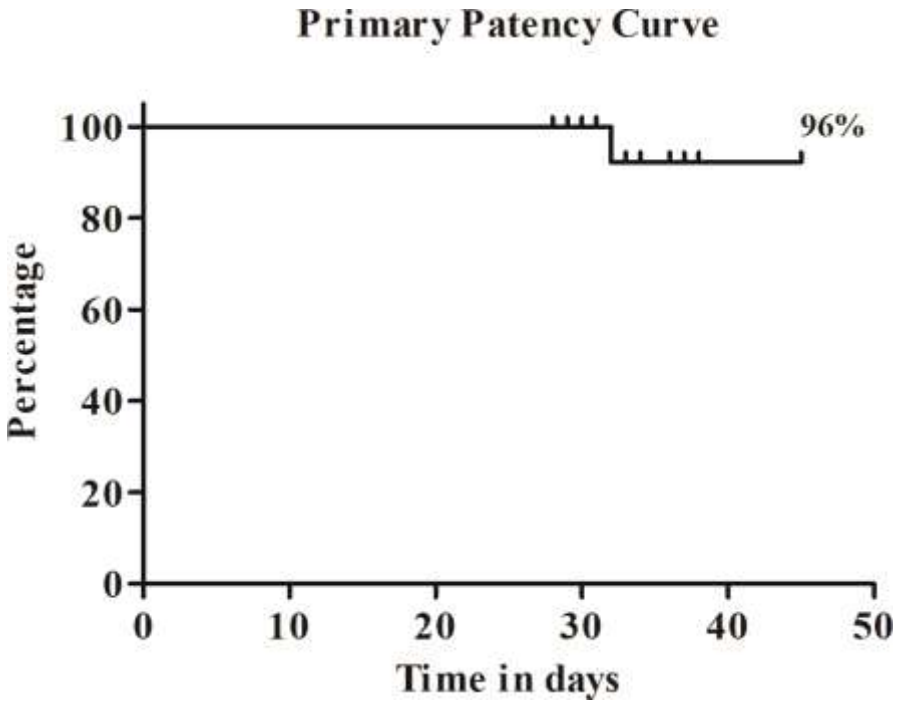
Core Lab: Stanford University, Stanford, CA, USA

Primary Patency Rate

as determined by Duplex ultrasound/Color flow Doppler ultrasound



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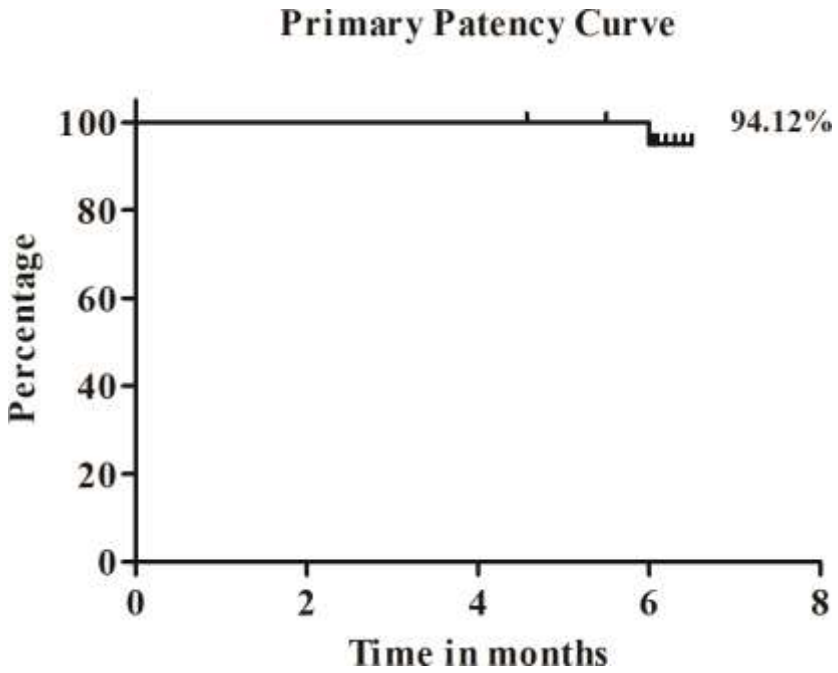
Primary Patency

based on angiography at average 6.6 months



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Clinical Outcomes

Up to 3-Year follow-up

Event description	Post-procedure (n=30)	1-Month (n=30)	6-Month (n=29[a])	1-Year (n=27[b])	2-Year (n=23[c])	3-Year (n=21[d])
Death[@]	0	1	3	4	5	8
TLR	0	0	0	0	0	0
Major Amputation[#]	0	1	4	4	4	4

[@]All deaths were not related to study device. Out of nine deaths, one death occurred due to accidental fall (caused head injury) at 1-month follow-up; one patient died due to cardiac arrest at 6-month follow-up; one death was due to road traffic accident at 6-month follow-up; one due to sudden bradycardia at 12-month follow-up; one death due to pineal region tumor at 24-month follow-up; one natural death, one death with unknown cause and one death due to cardiac failure at 36-month follow-up; [#]New lesions in great toe and heel were responsible for amputation in one patient, infected left foot with necrosis caused amputation in another patient, third patient amputation was due to non-healing wound on right foot and in fourth patient, there was debridement and below the knee amputation of left lower limb

a- one patient was LTF at 6-month follow-up, b- two patient withdrew consent at 1-Year follow-up, c- four patients withdrawn from the study at 2-Year follow-up, d- two patients were LTF at 3-Year follow-up

TLR: Target Lesion Revascularization, LTF: Lost to Follow-up

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Conclusions

- Our study results have demonstrated favourable safety and performance of the CREDENCE BtK sirolimus-eluting bioresorbable scaffold with zero TLR up to 36 months follow-up
- Primary patency at 1 month is 96% (evaluated by color-flow doppler ultrasound) and 94.12% at average 6.6 months (evaluated by angiography)
- Encouraging patency at 6 months and freedom from target lesion revascularization at 36 months follow-up suggest that the device has significant potential as therapy in this group of patients
- Further larger trials in larger populations are warranted

THANKS!