When, How, and with Which Devices Are Endovascular Treatments the Best Way to Treat BTK Disease Causing CLTI ?

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Company	Affiliation/Financial Relationship
• Abbott	• Consulting Fees / Honoraria
• Boston Scientific	• Consulting Fees
• Medtronic	• Consulting Fees / Honoraria
• Penumbra	• Honoraria
• BD / Bard	• Consulting Fees

Endovascular Treatment of BTK Disease: *When, How, & with Which Devices?*

BEST-CLI RANDOMIZED CONTROLLED TRIAL


The NEW ENGLAND JOURNAL of MEDICINE

Surgery or Endovascular Therapy for Chronic Limb-Threatening Ischemia

Farber A, et al. NEJM 2022

- RCT of bypass vs best endovascular therapy
- Cohort 1 (Adequate GSV): 1420 patients randomized
- Cohort 2 (Alternative conduit): 393 patients randomized

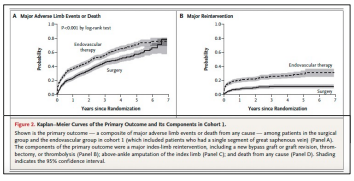

Figure 2. Kaplan-Meier Curves of the Primary Outcome and Its Components in Cohort 1.
Shown is the primary outcome — a composite of major adverse limb events or death from any cause — among patients in the surgical group and the endovascular group in cohort 1 (which included patients who had a single segment of great saphenous vein) (Panel A). The components of the primary outcome were a major index-limb reintervention, including a new bypass graft or graft revision, thrombectomy, or thrombolysis (Panel B); above-ankle amputation of the index limb (Panel C); and death from any cause (Panel D). Shading indicates the 95% confidence interval.

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BASIL-2 RANDOMIZED CONTROLLED TRIAL

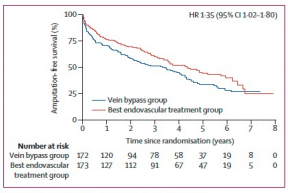


Figure 2: Amputation-free survival Kaplan-Meier curve

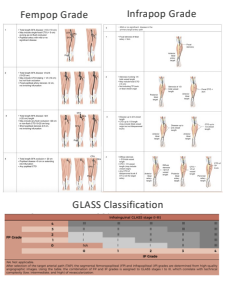

A vein bypass first versus a best endovascular treatment first revascularisation strategy for patients with chronic limb-threatening ischaemia who required an infra-popliteal, with or without an additional more proximal infra-inguinal revascularisation procedure to restore limb perfusion (BASIL-2): an open-label, randomised, multicentre, phase 3 trial

Endovascular 1st strategy associated with better amputation-free survival, driven largely by fewer deaths in endovascular group

Endovascular Treatment of BTK Disease: *When, How, & with Which Devices?*

When?

- Identifiable Targe Artery Path
- Adequate Level of Perfusion
- Durable Arterial Patency
- Absence of Complications



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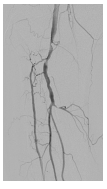
How?

Two Main Challenges to Solve

Biologic

- Inflammation
- Intimal Hyperplasia
- Biologic restenosis



Mechanical

- Flow-limiting Dissections
- Residual Plaque Burden
- Elastic Recoil

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With Which Devices?

Current Treatment Landscape

Balloon Angioplasty

- Elastic recoil
- Residual plaque
- Restenosis
- PP 0-50% (TASC II)

Atherectomy

- Device variability
- Lack of data
- Embolization risk

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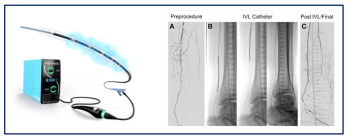
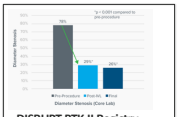
With Which Devices?

Current Treatment Landscape

Intravascular Lithotripsy





DISRUPT BTK II Registry

- 250 pts, 38 sites
- 85% moderate/severe Ca
- 91mm lesion length
- 98% procedure success
- <5% stent rate

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With Which Devices?

Emerging Treatment Landscape

Emerging Therapy for BTK Space

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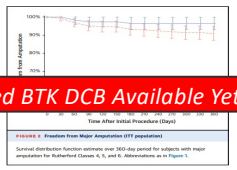
With Which Devices?

Current Treatment Landscape



No FDA-Approved BTK DCB Available Yet in the U.S.

IN.PACT DEEP: failed to meet primary endpoint; trend toward amputation noted

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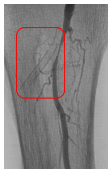
Drug-Eluting Coronary Stents

- DES shows benefit over BMS/PTA in multiple RCTs
- DES shows best patency results in BTK space and can address acute recoil / residual mechanical burden

- 12mo Primary patency:

	DES	BMS/PTA
ACHILLES (vs PTA)	75%	57%
IDEAS (vs DCB PTA)	72%	42%
DESTINY (vs BMS)	85%	54%
YUKON-BTX (vs (BMS)	81%	56%



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Endovascular Treatment of BTK Disease: *When, How, & with Which Devices?*

Bioresorbable Vascular Scaffolds

	Inhibit NIH	Minimize recoil & repair dissections	Leave nothing behind
Ideal treatment	✓	✓	✓

DRUG
Inhibit restenosis and provide drug-modulated healing for sustained patency

SCAFFOLD
Provide transient support in the vessel to address recoil and dissections

TEMPORARY
Resorbable scaffold

DRS = ***D***rug-eluting ***R***esorbable ***S***caffold

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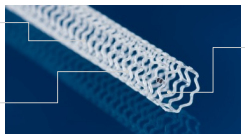
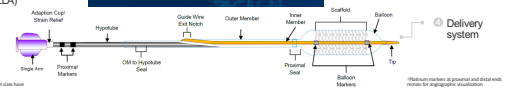
Esprit™ BTK Drug-eluting Resorbable Scaffold (DRS)

1. Bioresorbable scaffold backbone comprised of 100% poly(L-lactide) (PLLA) and strut thickness of 99 µm*
2. Coating comprised of the active pharmaceutical ingredient everolimus and bioresorbable poly (D,L-lactide) (PDLLA)



3. Four platinum markers of the same mass, two each embedded at the proximal and distal ends of the scaffold for radiopacity†
4. Delivery system



* ±1.0 mm size; 3.5-3.75 mm sizes have 120 µm strut thickness.
†Platinum markers at proximal and distal ends remain for angiographic visualization

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LIFE-BTK Randomized Multicenter Trial

Prospective, randomized, multicenter, US and OUS single-blind trial

261 patients randomized
2:1 Esprit BTK vs. PTA

Evaluate the safety and efficacy of the Esprit BTK DRS System, compared to PTA, for the treatment of infrapopliteal artery disease in patients with CLTI.
ClinicalTrials.gov: NCT04227899

FDA approval on April 26, 2024

Clinical Follow-Up:

TCT 2023 — VIVA 2024

14 D** | 30 D | 42 D** | 90 D** | 6 M | 1 Y | 2 Y | 3 Y | 4 Y | 5 Y

** Follow up focused on index wound assessment

Funded by Abbott.

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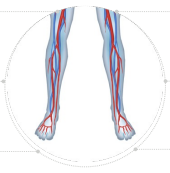
Key Inclusion Criteria

Study Population LIFE-BTK

- Proximal 2/3 of native infrapopliteal arteries
- Maximum 2 *de novo*/restenotic (from prior PTA) infrapopliteal lesions, each with ≥ 70% stenosis
- Successful treatment of all inflow artery(ies)* through standard of care prior to target lesion treatment
- The total scaffold length per patient ≤ 170 mm (in 1 lesion, or divided among the 2 target lesions)
- RVD ≥ 2.5 mm and ≤ 4.0 mm
- CLTI subjects with RB 4 or 5



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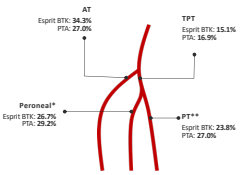
	Esprit BTK	PTA
Lesion length (mm)	43.78 ± 31.84 (172)	44.75 ± 29.07 (89)
RVD pre-intervention (mm)	2.94 ± 0.77 (147)	2.82 ± 0.74 (80)
Site-Reported Calcification		
None/Mild	69.3% (124/179)	69.6% (64/92)
Moderate	27.4% (49/179)	28.3% (26/92)
Severe	3.4% (6/179)	2.2% (2/92)
TASC II classification		
A	48.3% (83/172)	52.8% (47/89)
B	35.5% (61/172)	25.8% (23/89)
C	16.3% (28/172)	21.3% (19/89)
D	0.0% (0/172)	0.0% (0/89)
% DS pre-intervention	72.6 ± 18.9 (172)	73.7 ± 21.0 (89)



Number of Target Lesions Per Subject
Esprit BTK = 1.0 (1,2)
PTA = 1.0 (1,2)

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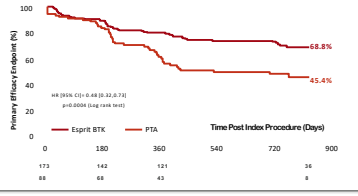
Composite of Limb Salvage & Primary Patency at 2 Years

ITT population	Esprit BTK	PTA	Difference [95% CI]‡
	61.5% (75/122)	32.8% (21/64)	28.66% (13.59%, 41.76%)



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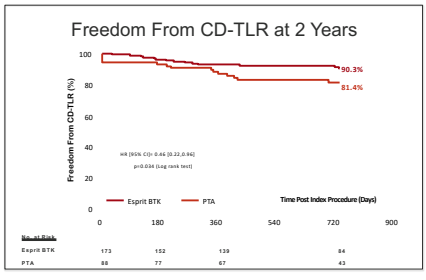
Freedom From CD-TLR at 2 Years



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Scaffolds, Stents, and Drug-Coated Devices for BTK Disease

Enrolling / Completed Trials with BTK DRS Devices

Company	Device	Scaffold Material	Drug	Status
Abbott	ESPRIT BTK	PLLA	Everolimus	Randomized LIFE-BTK IDE Trial completed, Presenting @ TCT2023 (n=261) PI: Varco, DeRubertis, Parikh
Reva	Motiv	Tyrocore (Tyrosine-derived polycarbonate)	Sirolimus	CE Mark obtained. Single-arm FIH study (N=60). MOTIV-I Randomized IDE trial, approx 150 pts enrolled (N=292) PI: Armstrong, Schmidt
R3 Vascular	Magnitude	High molecular weight PLLA	Sirolimus	Single-arm FIH RESOLVI in follow-up (N=30). Randomized IDE Trial planned (N=300) PI: Brodman, Secemsky, Varcoe
Biotronik	Magmaris	Magnesium	Sirolimus	Retrospective 24mo single center study completed (N=28)
Meril	MeRes	PLLA	Sirolimus	Non-randomized CREDENCE BTK single-arm study enrolling (N=30)

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Conclusions

- Tibial disease in CLTI patients remains a challenging area to treat.
- To effectively treat BTK disease in tibial arteries, one must confront both the mechanical and biologic challenges that are present below the knee, ideally without limiting future therapeutic options.
- Drug-eluting Resorbable Scaffolds (DRS) have proven effective in the LIFE-BTK trial and may represent a major advance in BTK therapy.

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