Update on the LIFE-BTK RCT Investigating a Drug Eluting Bioresorbable Scaffold Below-the-Knee

Sahil A. Parikh, MD, FACC, FSCAI on behalf of the LIFE-BTK investigators.

6 | June | 2023
Disclosure

Speaker name:

I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☐ I do not have any potential conflict of interest
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.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td><em>Institutional Research Support</em></td>
<td>• Abbott Vascular, Veryan Medical, Acotec, Concept Medical, Shockwave Medical, TriReme Medical, Surmodics, Boston Scientific, MedAlliance</td>
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<td><em>Advisory Board</em></td>
<td>• Abbott, Medtronic, Boston Scientific, Cordis, Philips</td>
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<td>• Terumo, Abiomed, Penumbra, Canon</td>
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<td><em>Equity</em></td>
<td>• Encompass Vascular, Adv NanoTherapies, eFemoral</td>
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BACKGROUND RATIONALE

CLTI is an underdiagnosed disease with high mortality rates

- Amputation rates as high as 40% within 6 months\(^2\)
- Nearly **HALF** of the major amputations occur with no prior diagnostic evaluation\(^2\)
- 25% of CLTI patients die within 1 year\(^3\) and 60% die over 5 years\(^1\)
- Diagnostic angiography lowers the odds of having a CLTI amputation by **90%**\(^4\)

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BACKGROUND RATIONALE AND OBJECTIVE

Current treatment options for BTK have inherent limitations

CURRENT TREATMENT OPTIONS FOR TIBIAL CIRCULATION*

**ANGIOPLASTY**
- Elastic recoil
- Restenosis
- Dissection
- Primary patency 20%–50% (TASC II)

**BMS**
- Restenosis
- No on-label BMS (U.S.)
- Permanent implant
- Short lengths
- Surgical reintervention

**DES**
- No on-label DES (U.S.)
- Permanent implant
- Short lengths
- Surgical reintervention

**DCBs**
- Elastic recoil
- Residual plaque
- Dissection
- Failed RCTs
- No approved DCB (U.S.)

**ATHERECTOMY**
- Device variability
- Embolization
- Lack of data

TO EFFECTIVELY TREAT BTK DISEASE:

<table>
<thead>
<tr>
<th>Drug (inhibit NIH)**</th>
<th>Scaffold (resist recoil)</th>
<th>Leave nothing behind</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angioplasty</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Atherectomy</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>DCB</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>BMS</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>DES</td>
<td>✓</td>
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UNMET NEED

*Adapted from Varcoe, R., LINC 2020. **NIH = Neointimal Hyperplasia.
INVESTIGATIONAL DEVICE

- Esprit™ BTK (Drug-eluting Resorbable Scaffold) - Temporary scaffold that will fully resorb over time

COMPONENTS

1. Bioresorbable scaffold backbone comprised of 100% poly(L-lactide) (PLLA)

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
Objective: To evaluate the safety and efficacy of the Esprit™ BTK System*, compared to PTA, in the planned treatment of diseased infrapopliteal lesions in patients with critical limb ischemia with up to two de novo lesions in separate vessels.

Prospective, randomized, multicenter, US and OUS single-blind trial
261 patients randomized
2:1 Esprit™ BTK vs. PTA

Safety Endpoint @ 6 months:
MALE+POD

Efficacy Endpoint @ 12 months:
Primary Patency + Limb Salvage

5-YEAR FOLLOW-UP

TRIAL LEADERSHIP
Ramon Varcoe MBBS, MS, FRACS, PhD; Sahil Parikh MD, FACC, FSCAI; Brian DeRubertis MD, FACS

ClinicalTrials.gov: NCT04227899
LIFE-BTK Sites and Enrollment

- Total enrolled sites: 50
- Total randomized patients: 261
# Study Design and Endpoint Assessments

## Primary Endpoints

<table>
<thead>
<tr>
<th>PRIMARY EFFICACY ENDPOINT</th>
<th>PRIMARY SAFETY ENDPOINT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ENDPOINT</strong></td>
<td><strong>MALE + POD</strong></td>
</tr>
<tr>
<td>Limb Salvage + Primary Patency</td>
<td>Freedom from MALE + POD (Major Adverse Limb Event + Peri-Operative Death)</td>
</tr>
</tbody>
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### Definition

- **PRIMARY EFFICACY ENDPOINT**
  - Freedom from above ankle amputation in index limb, 100% total occlusion of target vessel, binary restenosis of target lesion, and CD-TLR at 12 months

- **PRIMARY SAFETY ENDPOINT**
  - MALE = Above ankle amputation in index limb, major re-intervention at 6 months
  - POD = Perioperative (30-day) mortality

### Test

- **PRIMARY EFFICACY ENDPOINT**
  - Superiority of Esprit™ BTK against PTA with a 1-sided α of 0.025

- **PRIMARY SAFETY ENDPOINT**
  - Non-inferiority of Esprit™ BTK against PTA with a 1-sided α of 0.025

### Statistical Assumptions

- **PRIMARY EFFICACY ENDPOINT**
  - Assumed rates:
    - PTA: 55%
    - Esprit™ BTK: 75%
  - Assumed treatment effect:
    - 20% favoring Esprit™ BTK

- **PRIMARY SAFETY ENDPOINT**
  - Assumed rates:
    - PTA: 95%
    - Esprit™ BTK: 95%
# Study Design and Endpoint Assessments

## Powered Secondary Endpoints

<table>
<thead>
<tr>
<th>Secondary Endpoint</th>
<th>Test</th>
<th>Statistical Assumptions</th>
</tr>
</thead>
</table>
| 1. Binary restenosis of the target lesion | Superiority of Esprit™ BTK against PTA with a 1-sided α of 0.025 | Assumed rates:  
- PTA: 35%  
- Esprit™ BTK: 15% |
| 2. Freedom from above ankle amputation in index limb, 100% total occlusion of target vessel and clinically-driven target lesion revascularization (CD-TLR) | Superiority of Esprit™ BTK against PTA with a 1-sided α of 0.025 | Assumed rates:  
- PTA: 65%  
- Esprit™ BTK: 83% |
INCLUSION/EXCLUSION CRITERIA

Study Population LIFE-BTK

CLTI Subjects with RB 4 or 5

Proximal $\frac{2}{3}$ of native infrapopliteal arteries

RVD $\geq 2.5$ mm and $\leq 4.0$ mm

Maximum 2 de novo/restenotic (from prior PTA) infrapopliteal lesions, each with $\geq 70\%$ stenosis

The total scaffold length per patient $\leq 170$ mm (in one lesion, or divided among the 2 target lesions)
LIFE-BTK Pharmacokinetics (PK) Sub-study

SUB-STUDY TO DETERMINE THE PK OF EVEROLIMUS DELIVERED BY ESPRIT™ BTK SCAFFOLD

Objective: To determine pharmacokinetics of everolimus delivered by the Esprit™ BTK scaffold in a separate, non-randomized cohort of subjects receiving the Esprit BTK for the planned treatment of narrowed infrapopliteal lesions

Prospective, single-arm, open-label, non-blinded, non-randomized sub-study

Approximately 7 patients

- 4 subjects treated with Esprit BTK in below the knee artery(ies) in whom drug-coated balloons (DCB) were not used
- 3 subjects treated with Esprit BTK in below the knee artery(ies) in whom DCB were used for treatment of inflow disease
- Clinical pharmacokinetic analysis on all registered subjects

5-YEAR FOLLOW-UP

ClinicalTrials.gov: NCT04227899
Unique Characteristics of LIFE-BTK

PATIENT DIVERSITY AND INCLUSION

- Service for follow-up visit in patient’s home
- Direct patient reimbursement for travel expenses
- Rideshare service for travel to and from clinical site
- Travel agent for hotel and airfare booking
- Translations services available 24/7
- LIFE-BTK.com website

IMPLANTATION ALGORITHM

- Vessel preparation
- Careful vessel sizing to ensure implantation of appropriate size scaffold
- Post-dilatation to ensure vessel wall apposition

CORE LAB ADJUDICATED DATA

- Angio, IVUS, OCT core lab
- Duplex Ultrasound core lab
- Wound core lab

WOUND ASSESSMENT BY CORE LAB

- Wound etiology
- Quantitative wound measurements from baseline to 1-year
- Determination of healed vs. not healed
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