BEST-CLI Trial
Study Concept and Current Status

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Conflicts of Interest

- **Consultant**
  - Abbott Vascular
  - Capture Vascular
  - Cardinal Health
  - Contego
  - CRUZAR Systems
  - Endospan
  - Eximo
  - InspireMD
  - MD Insider
  - Micell
  - Shockwave
  - Silk Road
  - Surmodics
  - Valcare
  - Volcano/Philips

- **Equity**
  - CardioMEMs
  - Contego
  - Embolitech
  - Icon
  - Janacare
  - MD Insider
  - Micell
  - PQ Bypass
  - Primacea
  - Shockwave
  - Vortex

- **Research or Fellowship Support**
  - Abbott Vascular
  - Atrium
  - NIH
  - Lutonix-Bard

- **Board Member**
  - VIVA Physicians
    - www.vivapvd.com
Trends in PAD Therapy

Redefining the Treatment of Peripheral Artery Disease
Role of Percutaneous Revascularization

Jeffrey M. Isner, MD, and Kenneth Rosenfield, MD

The times, they are a changin'.
Bob Dylan

The application of a catheter-based approach to the treatment of arterial occlusion of the lower extremities was proposed by Dotter and Judkins\(^1\) nearly 30 years ago; 13 years later, Gruentzig\(^2\) provided a widespread basis to convert total occlusions into subtotal or less lengthy occlusions that may be recanalized with less technical difficulty and greater therapeutic efficacy. Plain old balloon angioplasty (“POBA”) is

Isner and Rosenfield
Circulation 1993

Jeffrey Michael Isner, M.D. 1947-2001
75 year old woman with right toe gangrene
Revascularization Options in CLI

Bypass Surgery

Endovascular Therapy

Which is best initial approach?
% of Patients with CLI and Intrainguinal PAD treated using Surgical Bypass (vs. Endovascular Therapy)

All VQI Centers Mean = 31%

Procedure Selection Variation
Limitations of Current Data

- Retrospective
- Poorly controlled
- Endo technique limited to balloon only
- Suboptimal endpoints
  - Amputation free survival
  - Target lesion revascularization
  - Target vessel revascularization
  - Patency
- Sponsor bias
- Operator bias
- Inclusion of claudicants
- Short or incomplete follow up
Little Agreement re: Ideal “outcome” in CLI

- Acute result
- Long term Patency
- Pain reduction
- Wound healing
- Quality of life
- Functional status
- Return to work
- Mortality
Comparative effectiveness of endovascular and surgical revascularization for patients with peripheral artery disease and critical limb ischemia: Systematic review of revascularization in critical limb ischemia

W. Schuyler Jones, MD, a,b Rowena J. Dolor, MD, a,c Vic Hasselblad, PhD, a Sreekanth Vemulapalli, MD, a,b Sumeeet Subherwal, MD, a Kristine Schmit, MD, a,c Brooke Heidenfelder, PhD, a,c and Manesh R. Patel, MD,a,b

“The currently available literature suggests that there is no difference in clinical outcomes for patients with CLI treated with endovascular or surgical revascularization. There is a paucity of high-quality data available to guide clinical decision-making…”

Conclusions The currently available literature suggests that there is no difference in clinical outcomes for patients with CLI treated with endovascular or surgical revascularization. There is a paucity of high-quality data available to guide clinical decision making, especially as it pertains to patient subgroups or anatomical considerations. [Am Heart J 2014;167:489-498.e7.]
Sponsored by the National Heart Lung and Blood Institute
Prospective, randomized, pragmatic, multicenter, open label superiority trial

2,100 patients at 140 clinical sites in United States and Canada

Each patient will have at least 2 year follow-up
To compare treatment efficacy, functional outcomes and cost in patients with CLI undergoing best open surgical or best endovascular revascularization.
Patients with **CLI and infrainguinal PAD** who are candidates for **both** infrainguinal bypass **and** endovascular therapy, in the eyes of the individual investigator.
Definition of “Best Treatment” is left to the investigator

All commercially available endovascular therapies allowed as long as accepted as standard of care

All surgical bypass techniques and conduits allowed
BEST-CLI Trial Design: Two Cohorts

- **Cohort #1** Patients with adequate single segment great saphenous vein (SSGSV) N=1620
  
  Open surgery vs. Endovascular treatment

- **Cohort #2** Patients without adequate SSGSV (if randomized to OPEN conduit may include arm vein, short saphenous vein, composite vein, cryopreserved vein, and prosthetic conduit) N=480

  Open surgery vs. Endovascular treatment
Major Adverse Limb Event (MALE) – free survival

**MALE defined as:**

Above ankle amputation

**Major re-intervention**

- new bypass graft
- jump/interposition graft revision
- thrombectomy/thrombolysis
Key Secondary Endpoints

Reintervention and Amputation (RAS)-free Survival

Defined as survival without:

Above ankle amputation

**Major** re-intervention

**Minor** re-intervention

- patch angioplasty
- balloon angioplasty
- atherectomy
- stent/stentgraft
Selected Clinical Secondary Endpoints

Freedom from hemodynamic failure

- Major amputation or any re-intervention to maintain patency in the index limb
- Failure to increase ABI by at least .15 post-procedure
- Decrease of ABI by .15 or greater during follow-up
- Duplex diagnosed treated artery/graft occlusion or critical graft stenosis (PSV > 300 cm/sec and velocity ratio > 3.0)
- Angio diagnosed treated artery/graft occlusion or stenosis >50% with recurrent clinical symptoms

Freedom from clinical failure

- Death, MALE, non-healing or recurrence of index limb wound, worsening of Rutherford category, recurrence of ischemic rest pain that resolved after rx

Freedom from critical limb ischemia
Functional, QOL and CE Endpoints

- Numerical Rating Scale (NRS) for pain
- VascuQoL
- EuroQoL EQ-5D
- SF-12

- Treatment-associated costs
- Incremental CE measured in dollars per quality adjusted life years (QALY)
How is BEST Different?

Collaboration
Interventional Cardiology
- Kenneth Rosenfield, Massachusetts General Hospital
- Christopher White, Ochsner Medical Center

Interventional Radiology
- Michael Dake, Stanford
- John Kaufman, Oregon Health Sciences University

Vascular Medicine
- Mark Creager, Brigham and Women’s Hospital
- Michael Jaff, Massachusetts General Hospital

Vascular Surgery
- Michael Conte, UCSF
- Alik Farber, Boston Medical Center
- Matthew Menard, Brigham and Women’s Hospital
- Richard Powell, Dartmouth-Hitchcock Medical Center
**CLI Team**

**Consists** of Specialists at a given site who treat patients with CLI **within the confines of the BEST-CLI Trial**

- **Specialty PIs and Co-investigators**
  - Interventional Cardiologists
  - Interventional Radiologists
  - Vascular Medicine Specialists
  - Vascular Surgeons

- **Research Nurses and Coordinators**

**Mission is** to maximize interdisciplinary collaboration within each site to ensure best practices, optimal outcomes, and successful conduct of BEST-CLI
Map of BEST-CLI Sites
Enrollment Update

- 1st patient randomized 28/Aug/2014

As of 1/19/2016

- 125 sites open for enrollment
- 416 subjects randomized

Next Milestone: 685 subjects by March 31, 2016
What questions will BEST-CLI answer?

- How does infrainguinal bypass with optimal conduit (SSGSV) fare against endovascular therapy?
- How does bypass with non-optimal conduit fare against endovascular therapy?

Will assess

- Comparative effect of clinical presentation and anatomy
- Comparative QOL and cost effectiveness
- Outcomes of revascularization as it relates to presence of tibial disease, clinical presentation, gender, race, age, diabetes, heel ulcer, renal dysfunction

Define an evidence-based standard of care

revascularization to clinical outcomes
Email contact:
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Krosenfield1@partners.org

Website: www.BestCLI.com

NIH: ClinicalTrials.gov NCT0206030
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