Status of the BEST-CLI—A RCT of CLI treatments; Laudable but difficult; It will provide useful information
Alik Farber, M.D.
Professor and Chief
Division of Vascular and Endovascular Surgery
Boston Medical Center
Boston University School of Medicine

BEST-CLI Trial Leadership

Clinical Coordinating Center: Brigham and Women’s Hospital
Alik Farber
Matthew Menard
Kenneth Rosenfield
Michael Strong

Date Coordinating Center: New England Research Institutes (NERI)
Sandra Siami
Susan Assmann

Cost Effectiveness Core: Brigham and Women’s Hospital
Jerry Avorn
Niteesh Choudhry

Sponsor: National Heart Lung and Blood Institute
Diane Reid
George Sopko

A Growing Problem

An Expensive Problem

National health care costs of peripheral arterial disease in the Medicare population

- Medicare expenditure on CLI > $4 billion
  (CHF = $3.9B, Cerebrovascular disease = $3.7B)
  - 90% inpatient care
  - $1,700 per patient (>2X avg beneficiary)
  - 3% of total Medicare budget (THR = 0.9%, THR 2.7%)

Exponential Rise Health Care Spending (as % GDP)

Disclosures

- BEST-CLI Trial co-Chair
Its all about value!

What Is “Value” in Health Care?

Value = dollars spent per health-related outcome

Which FIRST Revascularization Option in CLI Has the BEST Value?

VS

Bypass Surgery (LEB)
Endovascular Therapy (Endo)

Current State of Affairs in CLI

Endovascular-first Approach has been adopted by many...

• “There is paucity of high quality comparative effectiveness data to support choice of revascularization” (Jones. Am Heart J, 2014)

• Some CLI patients do worse with endovascular compared to surgical revascularization (Sachs JVS 2011)

• Results of bypass after endovascular therapy are inferior (Bradbury JVS 2010, Nolan JVS 2011)

• ...Endovascular-first approach in all patients with CLI is a strategy that is not supported by good science

What is the best way to answer “Which FIRST Revascularization Option in CLI Has the BEST Value” question?

• Registry/observational study?
• Randomized controlled trial?

Advantages and Disadvantages of Different Trial Designs

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<tr>
<th>Clinical Trial Design</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Registries and Observational Studies</td>
<td>-ideal for descriptive data -Less restrictive for patient entry -“Real world” patient population ➔ Generalizable</td>
<td>-Data variability -Selection bias -Confounding factors cannot often be well adjusted for despite advanced statistics ➔ Not suited for comparative outcomes research</td>
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<tr>
<td>Randomized Clinical Trial</td>
<td>- Confounders eliminated</td>
<td>- Time intensive</td>
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<td>- Treatment selection bias minimized</td>
<td>- Expensive</td>
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<td>- Spurious causality reduced</td>
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<td>- Highly selected populations due to selection criteria and investigator selection bias</td>
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<td>- Less generalizable</td>
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James, S. et al. (2015) Registry-based randomized clinical trials—a new clinical trial paradigm
Nat. Rev. Cardiol. doi:10.1038/nrcardio.2015.33

Comparison of open and endovascular treatment of patients with critical limb ischemia in the Vascular Quality Initiative
Jeffrey J. Stinson, MD; Harleen S. Nizard, MD; Mohammed H. Eldan, MD; Jeffrey A. Stable, MD; William F. Robertson, MD; Robert T. Hechtman, MD; Naim Al-Hamad, MD; and Ali F. Fayad, MD
For the Vascular Quality Initiative, Rene and Winters, Elsevier

BEST-CLI Trial

- Prospective, randomized, pragmatic, multicenter, international, multispecialty open-label superiority trial
- 2100 patients at 160 clinical sites
- Funded by National Institutes of Health

Goal: to assess clinical outcomes, quality of life, cost and value in patients with CLI who are candidates for both vascular surgery and endovascular therapy

BEST-CLI is unique?

- Well powered and designed
  - Real world pragmatic trial
  - Two cohort design
    - SGSV (optimal conduit) – 1620 patients
    - All conduits are allowed – 480 patients
  - Stratification by clinical presentation and anatomy
  - Novel endpoints
    - MALE-free Survival is optimal endpoint
    - Death, amputations AND major re-interventions
    - Hemodynamic success, clinical success
  - Comprehensive quality & economic analysis planned
- All specialties involved
  - Planned by a multidisciplinary group of CLI experts

BEST-CLI is positioned

- Define which treatment approach has best value
- Define an evidence-based standard of care
- Inform the next set of scientific and clinically relevant questions
Enrollment Update

As of 11/15/2017

- 129 sites open for enrollment
- 1118 subjects randomized

Next Milestone:
1,368 subjects by December 31, 2017

What do we know now?

- Enrolled subjects are representative of a typical CLI cohort
- Trial compliance is excellent
- ~75% of enrolling sites are multidisciplinary
- 8 Sites in Europe, Israel and New Zealand are being on-boarded
- Efforts on the way to obtain funding for a prospective companion CLI registry at trial sites that will include patients not eligible for RCT

RCT’s are hard...

Treasure trove of relevant data...

Conclusions

- BEST-CLI is a laudable effort
- RCT’s are VERY DIFFICULT to conduct
- CLI Registries alone will never be able to answer which therapy provides best value in CLI...
- There are some questions that only a well designed and powered RCT can answer
- BEST-CLI
  - will not answer all questions about CLI
  - will provide powerful, Level I data that will help to shape a much-needed evidence based approach to CLI