BEST-CLI – Happy Holidays from BEST!

Let's deck the halls with more enrollments in BEST! We wish CLI teams peace, joy, and all the BEST this wonderful holiday season has to offer!

Common Femoral Conundrums and Considerations…
From the Desktop of Kenneth Rosenfield, MD

Some investigators have been confused regarding enrollment of patients with Common Femoral Artery (CFA) disease: Can my patients with CFA stenosis be enrolled? If so, how can I treat the CFA? Is there a mandated sequence for treatment and randomization? This memo will provide answers to these excellent questions!

Patients with CFA disease are now eligible for BEST-CLI! The original protocol did exclude patients with >50% CFA disease, but the latest protocol amendment has changed all that. **CFA disease is no longer an exclusion**. Moreover, the protocol does not proscribe the treatment modality for the CFA: the investigator can treat the CFA using open surgical or endovascular techniques.

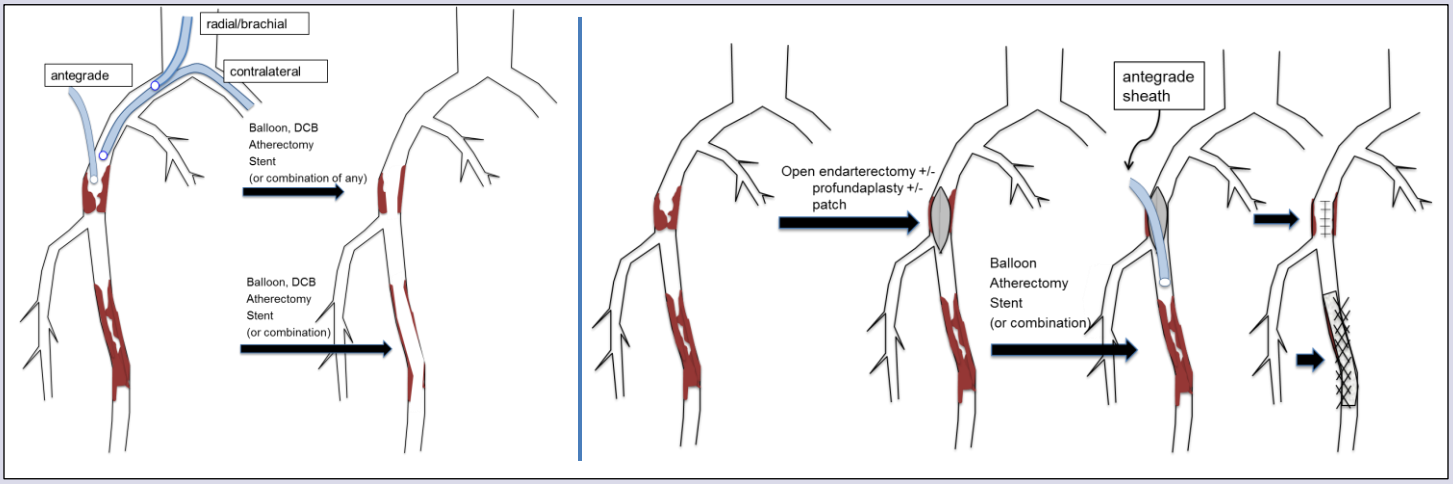
"Inflow" and "outflow"
In BEST-CLI, the common femoral artery will now be considered as an "inflow vessel", in the same way as the ipsilateral iliac arteries and aorta. As such, the CFA is not subject to randomization. Rather, the trial focuses on randomization of the infra-inguinal vessels by which we mean the vessels distal to the common femoral artery.

Defining what constitutes the "CFA"?
For purposes of this trial, when discussing matters involving the CFA, we intend to include the CFA itself, proximal profunda (PFA), and the origin/very proximal portion of the SFA, (if the plaque is contiguous with high grade CFA plaque). Everything below this is considered as "outflow" and is subject to randomization in BEST-CLI.

Treatment of CFA (with contiguous segments: PFA and very proximal SFA): options and sequence
If a BEST-CLI patient has CFA disease that requires treatment, then the options are not limited in any way. As seen on the accompanying schematic diagrams, the patient whose infrainguinal disease randomizes to "endo" can, in the same sitting as the trial-related infrainguinal *endovascular* procedure, first undergo *open* CFA endarterectomy (+/- profundaplasty) and patch angioplasty. Trial-related distal endo revascularization can be performed via the open CFA arteriotomy, either with or without a sheath, prior to, during or after the CFA endarterectomy/patch.

Schematic Diagrams

Option 1 *Option 2*



Common Femoral Conundrums and Considerations…continued
From the Desktop of Kenneth Rosenfield, MD

Alternatively, the operator/patient might prefer to avoid a groin incision and instead perform a procedure that is completely endovascular, using the contralateral femoral approach, the radial/brachial approach, or even ipsilateral antegrade CFA access above the stenosis (assuming there is enough space for sheath placement).

Similarly, a patient with CFA disease who randomizes to "open" can undergo treatment of the CFA disease by either open or endo means at the time of the trial-related infrainguinal *open* procedure.

An additional available option in both scenarios is to completely separate the CFA and infrainguinal procedure in time: i.e. perform either operative or endo repair of the CFA in one sitting, followed by a second stage with index treatment of the randomized infrainguinal segment. If these procedures are staged, they should be performed within 30 days of each other.

Patients with rest pain: For patients with rest pain and a >70% stenosis of the CFA and/or PFA, one must first treat the CFA and/or PFA disease (by either open or endo means). If the rest pain persists and the patient continues to meet the definition of CLI on repeat hemodynamic testing, the patient is eligible for randomization. Please note, this is the only scenario in which an "inflow" **open** procedure (unlike femoro-femoral, ilio-femoral, axillo-femoral and aorto-femoral bypasses) does not obligate waiting six weeks prior to randomization.

In summary, the sequence and approach are completely up to the investigator (after discussion with the patient). The only requirement is that the CFA "inflow" is repaired adequately to supply the randomized infrainguinal segment.

Which endovascular therapies are allowed for CFA?
If endovascular treatment is selected for the CFA, all options are allowed: balloon angioplasty, cutting/scoring balloon, atherectomy, and stenting. Yes, even a stent is allowable in the common femoral artery, if the investigator feels that's the best or most proper therapy.

What about "isolated" CFA disease in the setting of tibial disease?
Another variation to consider is the patient who has the combination of CFA disease and tibial disease. Surgical bypass in such patients may not even involve the isolated CFA, so the investigator may repair the CFA disease percutaneously or surgically, then randomize the tibial segment.

When there is concomitant CFA disease, does this affect treatment options for the randomized infrainguinal segment?
Whether randomized to "open" or "endo", the randomized infrainguinal segment should be treated with the endovascular device(s) or bypass that is considered "best practice".

What if CFA plaque extends into the SFA?
Generally, the origin of the SFA is considered part of the infra-inguinal segment and should be treated as part of the randomized index treatment. However, an endarterectomy and patch angioplasty of disease that extends into the very proximal SFA as an extension of a concomitant CFA endarterectomy is acceptable, even for the patient who has randomized in BEST-CLI to the "endo" cohort. An isolated endarterectomy of the proximal SFA is not allowed.

The bottom line: There are currently no limitations with respect to CFA disease in BEST-CLI. The only decisions to be made are: a) the investigator's preferred sequence and modality of revascularization for the CFA and its contiguous segments (PFA and proximal SFA) for that individual patient; and b) the choice of specific percutaneous device(s) or - if randomized to "open" - surgical bypass conduit(s) for the infrainguinal segment that has been randomized.

The CCC investigators are always available to discuss patient candidacy for BEST-CLI, as well as therapeutic strategy.
Call anytime:
Alik Farber (310-968-6083)
Matthew Menard (617-512-1372)
Ken Rosenfield (617-480-8080)

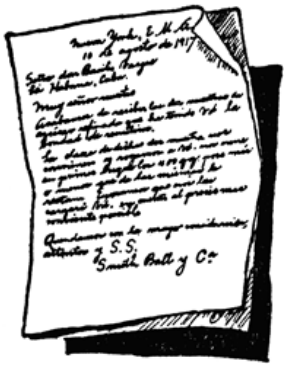
You may also call the BEST-CLI Hotline:
1-844-237-8120

St. Boniface Hospital

The BEST CLI team at St. Boniface Hospital is committed to providing optimal care to all of our patients and welcomes the opportunity to collaborate in this important clinical trial. Our team is led by Dr. Randy Guzman (Regional Lead, Section of Vascular Surgery) and consists of an Interventional Radiologist, Dr. Siuchan Sookhoo, and a Research Nurse, Wendy Weighell. Our key element for successful recruitment is ongoing communication. We have set up a central communication process that is available to all CLI team members to identify and follow critical limb ischemia patients and their potential inclusion in the trial. We have weekly meetings to review all potential trial patients and plan steps for efficient identification, communication and optimal care in these patients.

Informational Letter Coming Soon!

Our project officers at NHLBI will be sending informational letters to site leadership in the near future to recognize each site's performance and provide each site with some general information and updates on overall progress in the trial.



Tweet us @BEST_CLI

Follow us on Facebook!
www.facebook.com/BESTCLI

Next Round of Site Payments!

The data freeze for the next round of site payments is scheduled for **December 31st**. Be sure your enter your data and respond to queries in eCOS to ensure proper payment!

Albany Medical Center

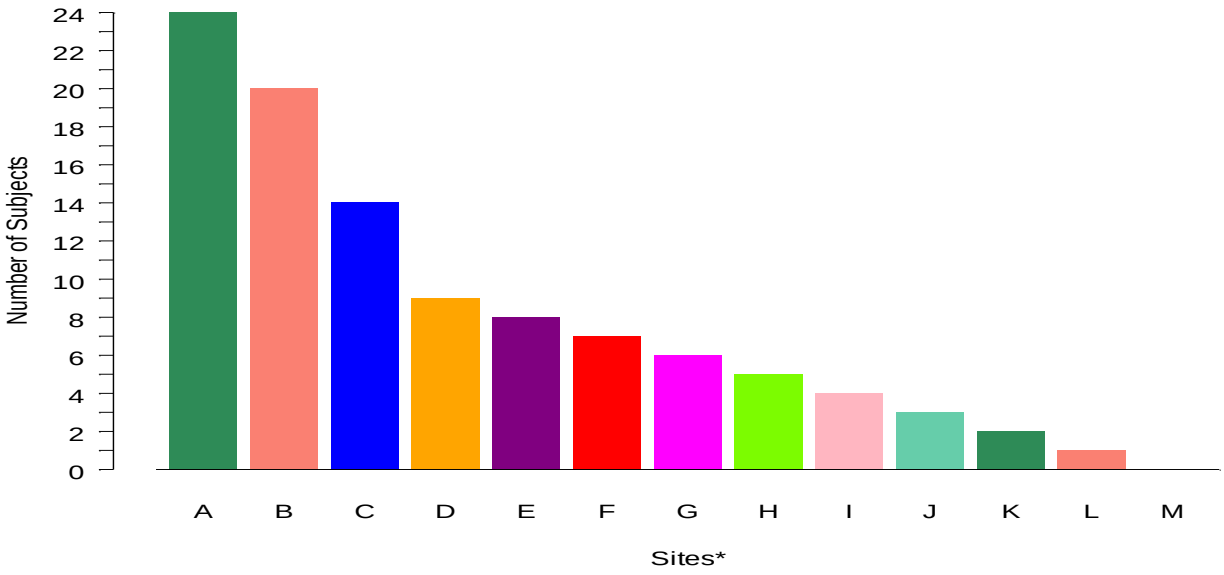
Site Spotlights

Left to Right: Dr. Barbara Melendez, Dr. Courtney Warner, Dr. R. Clement Darling, Jaime Kepner LPN, Nancy Giebelhaus RN, Ryan Kaim RN, Megan Ferguson RN, and Tara Patire LPN.

The BEST-CLI Team at Albany Medical Center is led by Dr. R. Clement Darling along with nine other Vascular Surgeons. Our team includes many of our office LPN's, NP's, Fellows, Surgical Residents and our three Research Nurses. As we are the busiest Level 1 Trauma Center in New York State that services 14 counties, our patient population is vast. The team meets weekly to discuss clinic patients and the inpatient population to identify potential BEST-CLI candidates. Communication within the Research Team is critical from the time of screening to enrollment. Our system ensures that several team members have thoroughly screened potential subjects before randomization to ensure subject compliance and retention.

Our team feels that the BEST-CLI Trial will provide crucial information on future treatment of patients suffering with CLI and will change standard of care. We believe this trial is of utmost importance and are thrilled to be a part of such a revolutionary trial!

Enrollment Leaderboard*



Sites*

A: 1160 - Keck MC of USC

B: 1258 - Boston MC

C: 1238 - Univ. of Massachusetts Medical School

D: 1009 - Dartmouth Hitchcock MC; 1030 - Montefiore MC; 1282 - Carondelet Heart & Vascular Institute; 1288 - Kaiser Foundation Hosp.

E: 1101 - Albany MC; 1272 - St. Boniface General Hosp.

F: 1005 - Brigham and Women's Hosp.; 1105 - Medical College of Wisconsin; 1261 - Indiana Univ. Medical School;1274 – Univ. of Oklahoma Health Sciences Ctr.; 1318 – UNC, Chapel Hill

G: 1013 - Harbor-UCLA MC; 1104 - VA Palo Alto; 1108 - Michigan Heart Hosp.; 1217 – Univ. of California Davis MC; 1310 - Harborview MC; 1314 - VA Boston; 1332 - Denver VAMC

H: 1041 - San Francisco VAMC; 1055 - Mount Sinai MC; 1095 - Johns Hopkins Hosp.; 1113 - Oregon Health & Science Univ.; 1169 - Case Western Reserve; 1260 - Greenville Memorial Hosp.; 1308 - Ohio State Univ.; 1309 - Mercy Hosp. MC; 1311 - Dallas VAMC; 1316 - Holy Name MC

I: 1010 - Emory Univ.; 1029 - Michael E. DeBakey VA MC ; 1066 - Arizona Heart Hosp.; 1234 – Univ. of Toledo MC; 1256 - Beth Israel Deaconess MC; 1259 - Rhode Island Hosp.; 1273 – Univ. of Florida (Gainesville); 1275 - Medical Univ. of South Carolina; 1276 - Memorial Hermann Hosp. TMC; 1277 - The Univ. of Utah; 1281 - VA Western NY Healthcare System; 1284 – Chu de Quebec; 1304 - CAMC Clinical Trials Center; 1340 – Wake Forest Baptist Hosp.

J: 1003 – Alleghany General Hosp.; 1046 - Steward St. Elizabeth's MC; 1054 - Univ. of Colorado Hosp.; 1072 - Univ. of Wisconsin – Madison; 1125 – Univ. of California San Francisco MC; 1173 – SUNY Upstate; 1182 - Providence Heart and Vascular Institute; 1264 - Minneapolis Heart Hosp; 1269 - Ohio Health Research Institute; 1271 - Southern Illinois Univ. SOM; 1290 - Loma Linda Univ. MC; 1306 – McGill; 1323 – Univ. of Nebraska MC; 1326 - The Miriam Hosp.-Brown Medical School; 1346 – Gunderson Health System; 1347 – Maine MC

K: 1023 – Massachusetts General Hosp.; 1026 - Medstar Washington Hosp. Center; 1061 - Baptist Hosp. of Miami; 1076 - Northwestern Memorial Hosp.; 1135 - Univ. of Pittsburgh MC; 1137 - The Univ. of Vermont MC, LLC; 1270 - Scott and White – Temple; 1285 – Duke Univ.; 1293 - Univ. Health System: LSU Health Sciences; 1305 - Univ. of Virginia; 1331 - Pinnacle Health System;1342 – Regina Qu'Appelle

Enrollment Leaderboard Continued*

L: 1007 – Cleveland Clinic Foundation; 1024 – Mayo Clinic (Rochester); 1034 – Ochsner MC/Clinic Foundation; 1075 - Swedish MC; 1116 - Rush Univ. MC; 1151 - William Beaumont Hosp.; 1188 - Toronto General Hosp.; 1257 - Univ. of Arkansas for Medical Services; 1263 - Kaiser Permanente (San Diego); 1279 - North Carolina Heart and Vascular Research; 1287 - Providence Sacred Heart MC; 1294 - North Central Heart Institute; 1299 - Univ. of Tennessee MC; 1325 - Deborah Heart and Lung Center; 1334 – Stanford; 1336 - Staten Island Univ. Hosp.; 1344 – Michigan Vascular Center

M: ***

*Data frozen on 12/16/2015.
**Site names abbreviated to accommodate space.
***Full list of sites can be found on NERI Connect

DSMB Memo on NERI Connect!

The BEST-CLI DSMB completed its third meeting on Tuesday, November 24, 2015. A DSMB memo, which was a result from the first meeting, has been posted to NERI Connect.

Click Here

Please follow your institutional guidelines when it comes to notifying your IRB.

Data Management FAQ Corner

Q: What if I can't provide an answer to a question in eCOS?

A: If you cannot and will not be able to answer a question the field should be left blank, and the reason should be provided in the query response.

Please do not enter, dummy values such as 000 or 999 as these will likely result in additional queries.

If you cannot answer a question, but expect to receive the data at a later time, the query can be left open or a query response can be added noting that the data will be entered at a later time.

These queries will remain at the answered status until the data is provided, or may be re-opened, if no further updates are made within 30 days.

BEST Holiday Highlights

# of Sites Activated under Protocol Amendment: 98

Top Enroller: UNC, Chapel Hill

# of Subjects Randomized: 395

NEW Re-Consent Form in eCOS

The re-consent form is available to sites that have received protocol 4.1 IRB approval and who have re-consented their subjects with the amended ICF.

To add this form, go to the addable visit column and select the magnifying glass icon 🔍, then select ⊕ Add to open the form. The subject ID and the reconsent questions should be completed for all patients. A date should be provided if 'Yes' is selected for the reconsent question.

This update has been made due to the modified clinical trial agreements that allows for additional payments for visits completed after patients are re-consented.