BEST-CLI – The Shortest Month with the BEST Updates!

From the Desktop of Alik Farber, M.D

The BEST-CLI trial is in full swing as we close in on the 1,000 patients-enrolled milestone. Questions, however, still persist about how to manage iliac and common femoral disease in patients with critical limb ischemia (CLI) who are considered for enrollment. I would like to reiterate that patients with CLI who have significant infrainguinal disease and have coexistent iliac or common/deep femoral arterial occlusive disease are fully allowed into the trial. There are nuances that relate to the management of patients who have rest pain alone and those who have tissue loss. It is important to remind everyone of our central premise that for the purpose of the BEST-CLI trial, the common femoral artery (CFA) and profunda femoris artery (PFA), like the aorta and iliac arteries, are considered inflow arteries. In the setting of a patient enrolled into the trial, endovascular treatment of the aorta or iliac arteries and surgical or endovascular treatment of the CFA or PFA does not obligate a delay for the randomized index procedure.

Let's consider the following illustrative examples:

A patient with CLI, significant infrainguinal occlusive disease and tissue loss has associated significant aortoiliac occlusive disease.

This patient can be randomized into BEST-CLI. The aortoiliac disease can be treated with endovascular therapy at any point between diagnostic imaging (angiography, or in appropriate cases, CTA or MRA) and index revascularization.

A nice feature of the trial is that endovascular treatment of the aortoiliac disease can be staged.

- One can randomize and treat the inflow disease and infrainguinal disease at the same time.
- One can randomize, treat the inflow disease separately, and then come back and treat the infrainguinal disease (as long as it is within 30 days of randomization)
- One can treat the inflow disease separately and then come back, randomize, and treat the infrainguinal disease

If one chooses to treat the aortoiliac disease with surgical bypass (aortobifemoral, iliofemoral, axillofemoral or femorofemoral bypass), then one must wait 6 weeks before treatment of the infrainguinal disease.

A patient with CLI, significant infrainguinal occlusive disease and rest pain alone has associated significant aortoiliac occlusive disease.

If aortic or iliac stenosis > 70% (or occlusion) is present then the patient cannot be enrolled into the trial. The aortoiliac stenosis/occlusion has to be treated first to ensure that the inflow disease is not the cause of the rest pain. If after endovascular treatment of the inflow disease, 1) symptoms of rest pain persist and 2) non-invasive hemodynamic parameters still support the diagnosis of CLI, then the patient can be randomized into BEST-CLI without any further waiting period.

If aortic or iliac stenosis of < 70% is present then the patient can be randomized into BEST-CLI. The aortoiliac disease can be treated, or not, with endovascular therapy at the discretion of the investigator at any point between diagnostic angiography and index revascularization (as in the above example for tissue loss).

If one chooses to treat the aortoiliac disease with surgical bypass (aortobifemoral, iliofemoral, axillofemoral or femorofemoral bypass), then one must wait 6 weeks before treatment of the infrainguinal disease.

A patient with CLI, significant infrainguinal occlusive disease and tissue loss has associated significant common femoral or deep femoral occlusive disease.

This patient can be randomized into BEST-CLI. The common femoral or deep femoral disease can be treated either with **surgical endarterectomy** or **endovascular therapy**. Then, occlusive disease distal to the common femoral artery can be treated according to randomization (endovascular therapy or bypass).

The same 3 options exist to staging of treatment of the CFA/PFA disease as for aortoiliac disease. i.e. *a) before randomization*, b*) at the same time as the index infrainguinal revascularization, or c) after randomization but preceding the index infrainguinal revascularization (as along as within 30 days of randomization).* For logistical reasons we do not recommend option a. unless the plan is to treat the CFA/PFA lesion using endovascular therapy. This is so, because, if the patient is randomized to surgery and CFA/PFA endarterectomy is chosen then most investigators would choose to do both endarterectomy and bypass in one setting. We want to avoid the possibility of having a patient undergo a common femoral endarterectomy first and then if randomized to bypass need to have another surgical procedure.

If the patient is randomized to endovascular therapy, and CFA/PFA endarterectomy is chosen, then investigators will have a choice between doing both procedures at the same sitting or doing the CFA/PFA endarterectomy first and distal endovascular therapy in a second sitting (within 30 days).

To reiterate, unlike with the aorta or iliac arteries, surgical treatment of the CFA or PFA does not obligate a 6 week delay**.**

Article continued on Page 5.

Funded by: NIH National Heart, Lung, and Blood Institute

Site Spotlight

Yale University

Pictured above, from left to right: Bennett Cua MD, David Halpin MD, Rob Attaran MD, Sophia Altin MD, Carlos Mena-Hurtado MD, Jackie Gamberdella MS, Sunny Jhamnani MD

At Yale University, our process to enrollment into BEST-CLI is to aim to maximize the opportunity to deliver care to patients with CLI in the tri-state area. We have developed a large multidisciplinary practice within the Heart and Vascular Center with Interventional Cardiology, Interventional Radiology, Vascular Surgery, Podiatry and other surgical and medical specialties. Patients are referred to both the inpatient and outpatient service, they are evaluated in a comprehensive manner and as part of that BEST CLI trial, is offered to patients and if qualified the process of enrollment begins since the Initial encounter. Our research coordinators and fellows work diligently to ensure that everyone involved is educated on the protocol and the importance of a study like BEST-CLI. Ultimately, we are making efforts to advance our knowledge and understanding of therapies for CLI and we see this trial as a great opportunity to accomplish this, we have gotten significant momentum by getting buy in from all our referring doctors.

BEST- CLI was "slow" to get up and running. One of our biggest challenges was to develop the multidisciplinary team that the study required to be successful. This took a great deal of effort and the various "teams" needed to become comfortable working together and not be concerned that one group was *stealing* patients from the other. We continue to work on fostering this relationship and building on this trust.

Patients are seen in our Vascular Clinic by interventional cardiology, interventional radiology, and vascular surgery. If a potential patient is identified as a possible subject for BEST-CLI, the research coordinator is contacted to further screen and ultimately consent the subject for study participation.

January Top Enrollers

2 subjects each!

1017 / Henry Ford

1018 / Inova Fairfax

1113 / Oregon Health and Science University

1154 / Yale University

1279 / NC Heart and Vascular Research

Q4 2016 Site Payments Complete!

All site payments for worked performed in Q4, 2016 have been distributed to qualified sites.

The next data freeze for site payments is currently scheduled for **March 31, 2017.**

Have a question regarding site payments?
Please send them to BEST@neriscience.com.

Angiogram of the Month!

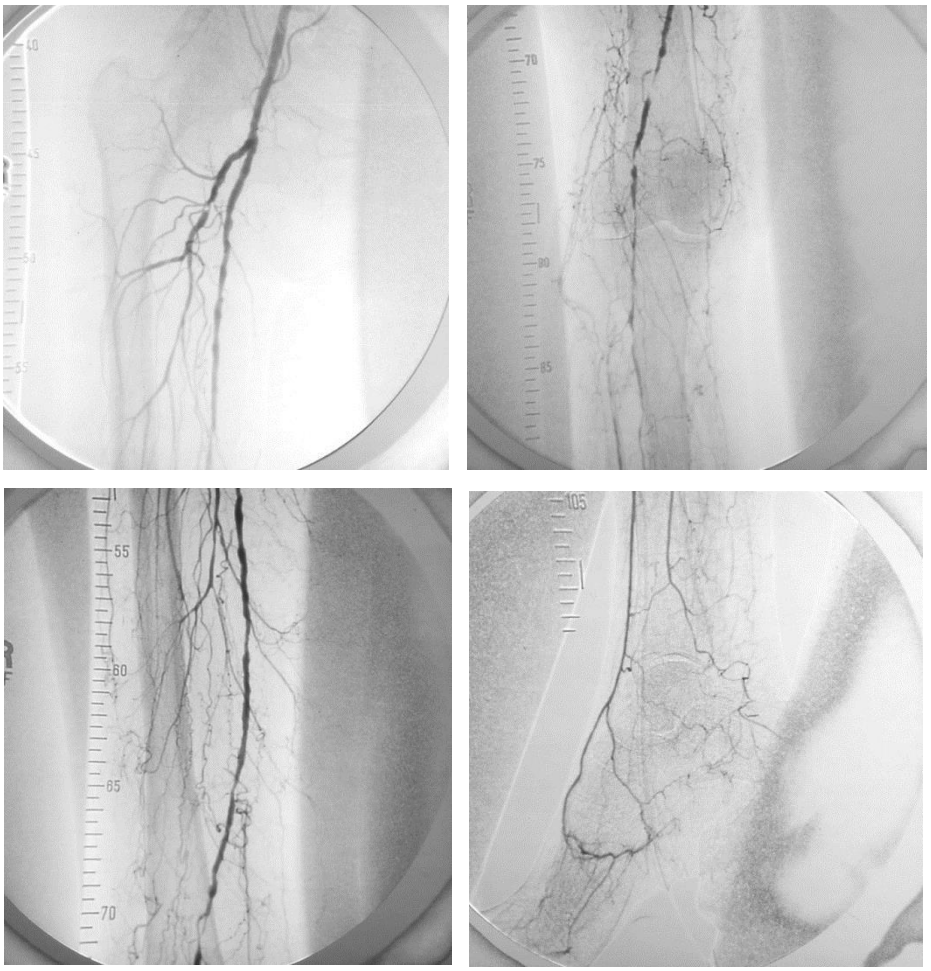
A 75yo female presented with a 3 week history of right toe gangrene
Her past medical history was significant for hypertension and diabetes

She never smoked.

On physical examination, a small gangrenous ulcer over the right distal great toe was noted. She had a normal right femoral and no distal pulses. Her right ankle pressure was 40 mm Hg. Right tibial Doppler waveforms were monophasic. Vein mapping of the right great saphenous vein revealed it to be 3-4 mm throughout. A cardiac stress test was negative for ischemia. Below is her right leg angiogram.

Questions:
1. Is this patient a candidate for the BEST-CLI Trial?
2. Trial aside, what is the best way to revascularize this patient?

Answers on page 5.



Get the BEST Updates on Social Media!

Tweet us @BEST_CLI

Join our Linkedin group!

Visit our website for updates!

BEST Quarterly Site Progress Reports On Their Way!

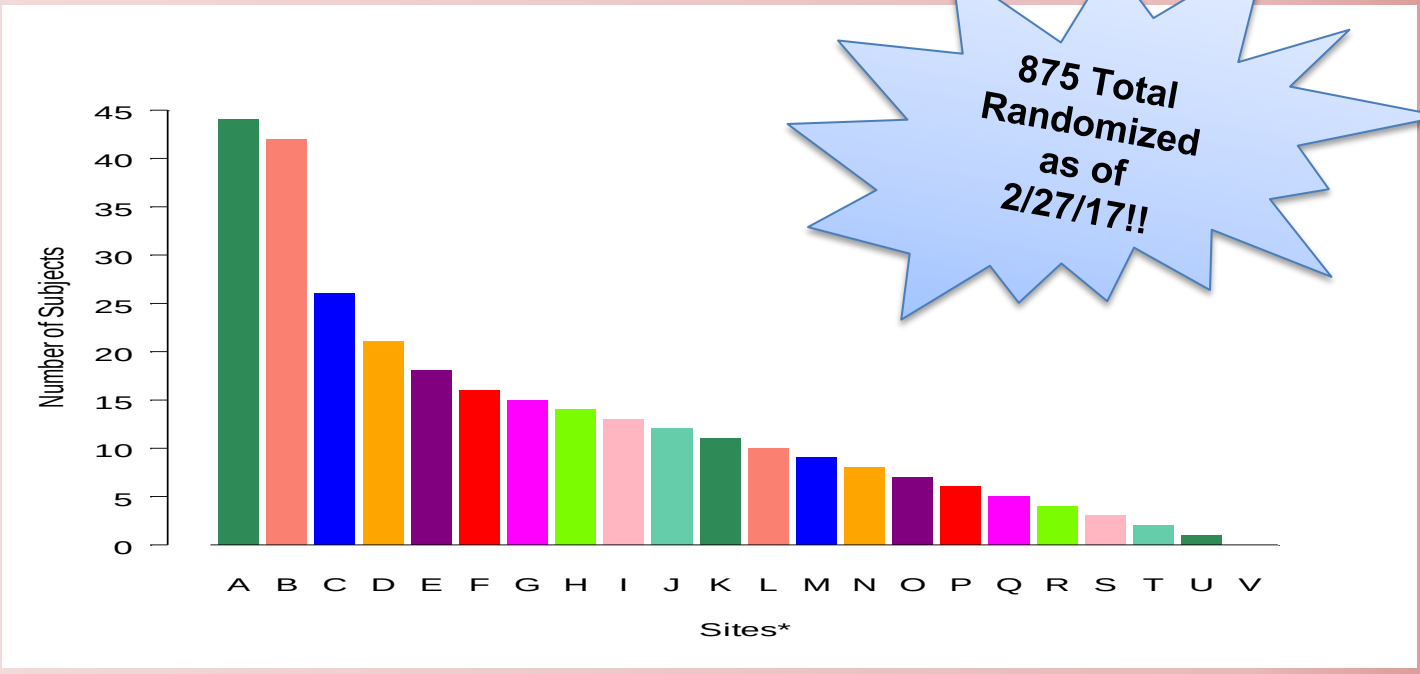
Curious about how your site is doing?

Wait no further as site progress reports are coming this week!

Have a progress report question? Feel free to reach out to your site assigned CRA or BEST@neriscience.com

Funded by: NIH National Heart, Lung, and Blood Institute

Enrollment Leaderboard



Sites*

A: 1258 - Boston MC

B: 1160 - Keck MC of USC

C: 1238 - Univ. of Massachusetts Medical School

D: 1260 - Greenville Memorial Hosp.

E: 1154 - Yale.; 1274 – Univ. of Oklahoma Health Sciences Ctr

F: 1005 - Brigham & Women's Hosp; 1009 - Dartmouth MC; 1284 – Chu de Quebec.; 1309 - Iowa Heart

G: 1273 - Univ. of Florida (Gainesville); 1282 - Carondelet Heart & Vascular Institute.

H: 1261 - Indiana Univ. Medical School; 1272 - St. Boniface General Hosp.

I: 1101 - Albany MC; 1288 - Kaiser Foundation Hosp.(Hawaii).

J: 1104 - VA Palo Alto; 1105 - Medical College of Wisconsin.

K: 1013 - Harbor-UCLA MC; 1017 – Henry Ford Hosp; 1113 - Oregon Health and Science Univ.

L: 1041 - San Francisco VAMC; 1217 – Univ. California Davis MC; 1256 - BIDMC; 1332 - Denver VAMC.

M: 1030 - Montefiore MC; 1055 - Mount Sinai MC; 1066 - Arizona Heart Hosp.; 1095 - Johns Hopkins Hosp; 1135 - Univ. of Pittsburgh MC; 1276 - Memorial Hermann Hosp. TMC; 1281 - VA Western NY Healthcare System; 1310 - Harborview MC; 1318 – Univ. of North Carolina Hosp; 1342 – Regina Qu'Appelle; 1346 – Gundersen Health

N: 1061 - Baptist Hosp. of Miami;.; 1305 - Univ. of Virginia; 1308 - The Ohio State Univ; 1311 - Dallas VA MC; 1323 – Univ. of Nebraska MC; 1340 – Wake Forest Baptist Hosp.

O: 1010 - Emory Univ; 1108 - Michigan Heart Hosp; 1169 - Case Western Reserve; 1234 – Univ. of Toledo MC; 1259 - Rhode Island Hosp; 1275 - MUSC; 1293 - Univ. Health System: LSU Health Sciences; 1306 – McGill.

P: 1023 – Massachusetts General Hosp; 1026 - Medstar Washington Hosp. Center; 1029 - Michael E. DeBakey VA MC; 1075 - Swedish MC; 1277 - The Univ. of Utah; 1285 – Duke Univ; 1314 - VA Boston Healthcare System.

Q: 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; 1188 - Toronto General Hosp; 1264 - Minneapolis Heart Hosp; 1271 - Southern Illinois Univ. SOM; 1290 - Loma Linda Univ. MC; 1316 - Holy Name MC; 1337 – Loma Linda VA MC; 1344 – Michigan Vascular Center; 1349 – Queens Elizabeth II Health Science Center.

R: Alleghany General Hosp; 1076 - Northwestern Memorial Hosp; 1134 - Univ. of Michigan Health System; 1137 - The Univ. of Vermont MC, LLC; 1140 – Greater Los Angeles VA; 1156 – Minneapolis VAMC; 1182 - Providence Heart and Vascular Institute; 1300 - Tampa General Hosp.; 1304 - CAMC Clinical Trials Center; 1325 - Deborah Heart and Lung Center; 1326 - The Miriam Hosp.-Brown Medical School; 1331 - Pinnacle Health System; 1334 – Stanford; 1345 – Los Angeles MC, Kaiser Permanente; 1347 – Maine MC; 1350 - Benaroya Res. Inst. At Virginia Mason.; 1351 – KP NCAL

Enrollment Leaderboard Continued

S: 1007 – Cleveland Clinic Foundation; 1008 – Columbia Univ. MC; 1024 – Mayo Clinic (Rochester); 1034 – Ochsner MC/Clinic Foundation; 1263 - Kaiser Permanente (San Diego); 1269 - Ohio Health Research Institute; 1270 - Scott and White – Temple; 1279 - North Carolina Heart and Vascular Research; 1307 – Univ. of Rochester; 1341 – Meriter Wisconsin Heart; 1367 - Englewood Hospital and Medical Center.

T: 1018 - Inova Fairfax Medical Campus; 1019 - Jewish General Hosp.; 1229 - Penn State Milton S. Hershey MC; 1257 - Univ. of Arkansas for Medical Services; 1283 – Univ. of Oklahoma College of Medicine; 1287 - Providence Sacred Heart MC; 1294 - North Central Heart Institute; 1301 – UCSD-Sulpizio Cardiovascular Center; 1336 - Staten Island Univ. Hosp.; 1348 – New Mexico Heart Institute; 1352 - San Diego VAMC; 1355 - Vancouver General Hospital; 1359 – The Ottawa Hospital.

U: 1059 - The Univ. of Alabama;1116 - Rush Univ. MC; 1121 – Temple Univ; 1126 - Univ. of Chicago Medicine; 1131 – Univ. of Maryland; 1151 - William Beaumont Hosp; 1226 – St. Paul's Hospital (U. Saskatchewan); 1278 – Univ. of California Irvine; 1292 – Munroe Regional MC; 1299 - Univ. of Tennessee MC; 1302 - UCLA-Gonda Vascular Surgery; 1315 - George Washington Univ. Hosp; 1320 - Portland VA MC; 1339 – Cadence Health (Chicago); 1356 - South Shore Hosp.

V: 1085 – Cedars Sinai; 1327 - Wellmont Holston Valley MC; 1357 – St. Francis Hospital; 1358 - Vascular Health Partners, CCP; 1360 - Midwest Cardiovascular Research Foundation; 1361 - Midwest Aortic Vascular Institute (MAVI); 1362 - Mount Sinai Medical Center (Miami, FL); 1363 - University of Missouri, Columbia; 1368 - Sentara Vascular Specialists; 1369 – Milwaukee VAMC; 1370 – Rutgers New Jersey Medical Center; 1371 – MetroHealth Cleveland; 1373 - Baton Rouge General Medical Center; 1375 - West Haven VA (WHVA); 1376 - University of Western Ontario; 1377 - Decatur Memorial Hospital.

*Data frozen on 02/22/2017
** Site names abbreviated to accommodate space

Answers to Angiogram of the Month!

1. This patient is absolutely a candidate for the BEST-CLI Trial. Her disease pattern can be treated using either endovascular therapy or surgical bypass.

2: It all depends on whom you ask! We have shown this case to more than 500 investigators at 90 participating sites. When queried, ~60% of investigators choose endovascular therapy while ~ 40% choose bypass as the best way to treat her.

Cover article continued from Page 1

A patient with CLI, significant infrainguinal occlusive disease and <u>rest pain alone</u> has associated significant common femoral or deep femoral occlusive disease.

If common femoral/deep femoral stenosis > 70% (or occlusion) is present then the patient cannot be enrolled into the trial. The common femoral/deep femoral stenosis/occlusion has to be treated with endarterectomy or endovascular therapy as this in many cases will successfully treat ischemic rest pain. If after such intervention rest pain persists and non-invasive hemodynamic parameters still support the diagnosis of CLI then the patient can be randomized into BEST-CLI without any further waiting period.

If common femoral/deep femoral stenosis < 70% is present then the patient can be randomized into BEST-CLI. The common femoral or deep femoral disease can be treated either with endarterectomy or endovascular therapy, at the discretion of the investigator, at any point between diagnostic angiography and index revascularization. Then, occlusive disease distal to the common femoral artery can be treated according to randomization (endovascular therapy or bypass) as above.