BEST-CLI – Leaf it to BEST!

With fall in full swing, BEST sites are giving thanks for a bountiful harvest of enrollments this season! It's time to gobble up the cornucopia of benefits from the protocol amendment and reach our accrual goal!

From the Desktop of Kenneth Rosenfield, MD

Greetings from New England! The leaves have fallen and the days are shorter; Thanksgiving is upon us. While it may be chilly here, **BEST-CLI is heating up** more than ever. Nearly 350 of your patients have been randomized between "open" and "endo", but we still need everyone to strap on your boots, put on your ski hats, and **ramp up your efforts to enroll every CLI patient at your institution!**

To make this easier, the trial leadership has made **major changes in the protocol**. Significant adjustments to eligibility criteria have eliminated virtually every possible barrier to enrollment, while still retaining the integrity of the trial. You should now be able to randomize **most** patients you see with CLI. Among the most impactful adjustments are:

- Inclusion of patients with CFA disease
- Ability to do hybrid procedures (e.g. common femoral endarterectomy), in association with the assigned distal treatment, both endo or open
- Shortened "time to eligibility" following prior percutaneous revascularization, from six months to three months
- Shortened "time to eligibility" following surgical inflow procedures to six weeks
- Elimination of thrombophilia, immunosuppressive therapy, and stainless steel or nitinol allergies as exclusions
- Increased site payments to an additional $500 per enrolled patient, plus $750 for resubmission of protocol amendment to the IRB and payment for source documents
- Payment to patients of $25 for each follow up visit

Many sites have already received IRB approval for the protocol amendment and have implemented these changes. The feedback from sites has been that the changes have truly opened the floodgates for enrollment. However, even with these changes, **we must still commit** as investigators, to enroll every eligible patient with CLI into the trial. As the saying goes…**Just do it!**

With enrollment progressing, we are entering the **follow-up and retention phase** for many of your patients. This takes hard work, both on the part of investigators and coordinators. But, please keep in mind that this is the *essence* of BEST-CLI! It is critical that you track patients' progress and capture all events – first major reintervention, repeat revascularizations, repeat hospitalizations, MI, stroke and other adverse events. Remember, the endpoints of the trial, both primary and secondary, must be captured in order for the trial to maintain its integrity and fidelity. The most challenging events to track are those involving admission and/or treatment at another hospital. We suggest that you as physicians and coordinators establish "great personal connections" with your BEST-CLI patients and their families; ask them to call for any events or changes in their medical care, or admission to another hospital.

Thank you in advance for your diligence in connecting with patients, being constantly aware of their status, and tracking them down before they are "lost".

Rigorous follow-up is essential and every patient counts!

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

Montefiore Medical Center

Site Spotlight

From back to front, left to right: Dr. Evan Lipsitz, Dr. David Slovut, Dr. Karan Garg, Juan Garcia. Front row, left to right: Yvette Ash, Rebecca Meli, Dr. Saadat , and Suzy Moran. Missing from the team picture is Dr. Kenneth Goldstein, Dr. Issam Koleilat, Dr. Michael Vitti, Dr. Eric Trestman, Dr. Jeffry Kirk and Dr. Francis Porreca.

The BEST-CLI team at Montefiore Medical Center is honored to be participating in this clinical trial. The study team is led by Dr. Evan Lipsitz (Chief of Vascular and Endovascular Surgery) and Dr. David Slovut (Associate Professor of Clinical CT Surgery), in a collaborative effort. The team is further comprised of physicians from vascular surgery, CT surgery and interventional cardiology, as well as a PA and three study coordinators, who meet regularly to discuss potential patients and ways to constantly improve screening and enrollment. Our success stems from each team member being actively engaged in recruiting efforts to identify patients who would qualify for the trial and ultimately benefit from participation. We have been very aggressive in these efforts, and they have translated into successful patient randomization across both of our campuses (Moses and Einstein).

Our team enjoys working collaboratively to identify those patients who are at high risk of CLI and to determine their participation in the trial. We at Montefiore believe that by participating in the BEST Trial, we are offering our patients the most innovative clinical care and research involvement with respect to critical limb ischemia and its treatment.

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 be paid!

FAQ CORNER

Q: If the initial index procedure is not a technical success, is it necessary to continue to follow the patient?

A: A very important question. Yes, even if the index procedure is a technical failure, the subject is still a participant in the trial, and study personnel need to continue to follow the patient following the failed index procedure. All subsequent revascularization procedures should be captured and recorded.

346 Subjects Randomized as of 11/20/2015!

Site #1288, Kaiser Hawaii randomized our 300th Subject!

BEST Fall Highlights

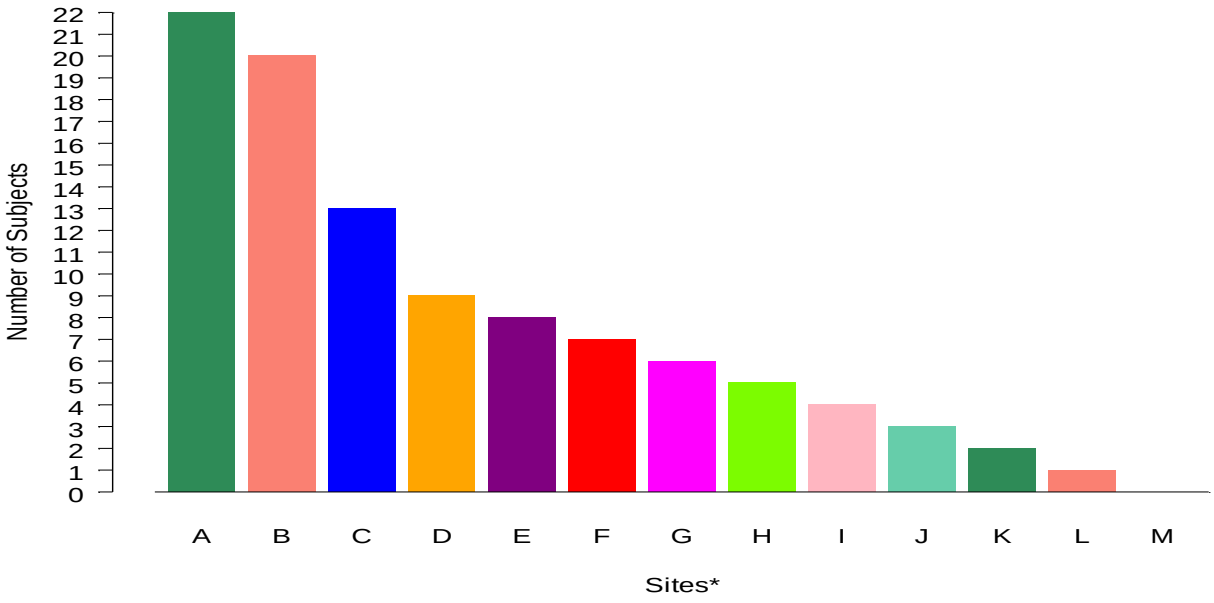
Number of Sites Activated under Protocol Amendment: 63

Top Enroller:

1346/Gundersen Health System

Sites Enrolling 1st Subject: 7

Enrollment Leaderboard*



Sites*

A: 1160 - Keck MC of USC
B: 1258 - Boston MC
C: 1238 - Univ. of Massachusetts Medical School
D: 1288 - Kaiser Foundation Hosp.
E: 1009 - Dartmouth Hitchcock MC; 1030 - Montefiore MC; 1272 - St. Boniface General Hosp.; 1282 - Carondelet Heart & Vascular Institute
F: 1005 - Brigham and Women's Hosp.; 1274 – Univ. of Oklahoma Health Sciences Ctr.
G: 1013 - Harbor-UCLA MC; 1101 - Albany MC; 1105 - Medical College of Wisconsin; 1310 - Harborview MC; 1314 - VA Boston Healthcare System; 1332 - Denver VA MC
H: 1041 - San Francisco Veterans Affairs MC; 1055 - Mount Sinai MC; 1095 - Johns Hopkins Hosp.; 1108 - Michigan Heart Hosp.; 1217 – Univ. of California Davis MC; 1260 - Greenville Memorial Hosp.; 1261 - Indiana Univ. Medical School; 1308 - The Ohio State Univ.; 1309 - Mercy Hosp. MC; 1316 - Holy Name MC
I: 1029 - Michael E. DeBakey VA MC ; 1066 - Arizona Heart Hosp.; 1169 - Case Western Reserve; 1234 – Univ. of Toledo MC; 1275 - MUSC; 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; 1311 - Dallas VA MC; 1340 – Wake Forest Baptist Hosp.
J: 1003 – Alleghany General Hosp.; 1010 - Emory Univ.; 1046 - Steward St. Elizabeth's MC; 1104 - VA Palo Alto; 1113 - Oregon Health and Science Univ.; 1125 – Univ. of California San Francisco MC; 1182 - Providence Heart and Vascular Institute; 1256 - Beth Israel Deaconess MC; 1264 - Minneapolis Heart Hosp; 1269 - Ohio Health Research Institute; 1271 - Southern Illinois Univ. SOM; 1273 – Univ. of Florida (Gainesville); 1306 – McGill; 1318 – Univ. of North Carolina Hosp.; 1323 – Univ. of Nebraska MC; 1326 - The Miriam Hosp.-Brown Medical School; 1346 – Gunderson Health System; 1347 – Maine MC
K: 1023 – MGH.; 1026 - Medstar Washington Hosp. Center; 1054 - Univ. of Colorado Hosp.; 1061 - Baptist Hosp. of Miami; 1072 - Univ. of Wisconsin – Madison; 1076 - Northwestern Memorial Hosp.; 1135 - Univ. of Pittsburgh MC; 1137 - The Univ. of Vermont MC, LLC; 1259 - Rhode Island Hosp.; 1270 - Scott and White – Temple; 1290 - Loma Linda Univ. MC; 1293 - Univ. Health System: LSU Health Sciences; 1331 - Pinnacle Health System

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.; 1173 – SUNY Upstate; 1188 - Toronto General Hosp.; 1257 - Univ. of Arkansas for Medical Services; 1263 - Kaiser Permanente (San Diego); 1279 - North Carolina Heart and Vascular Research; 1285 – Duke Univ.; 1287 - Providence Sacred Heart MC; 1294 - North Central Heart Institute; 1299 - Univ. of Tennessee MC; 1305 - Univ. of Virginia; 1325 - Deborah Heart and Lung Center; 1334 – Stanford; 1336 - Staten Island Univ. Hosp.; 1342 – Regina Qu'Appelle

M: ***

*Data frozen on 11/19/2015.
**Site names abbreviated to accommodate space.
***Full list of sites can be found on NERI Connect

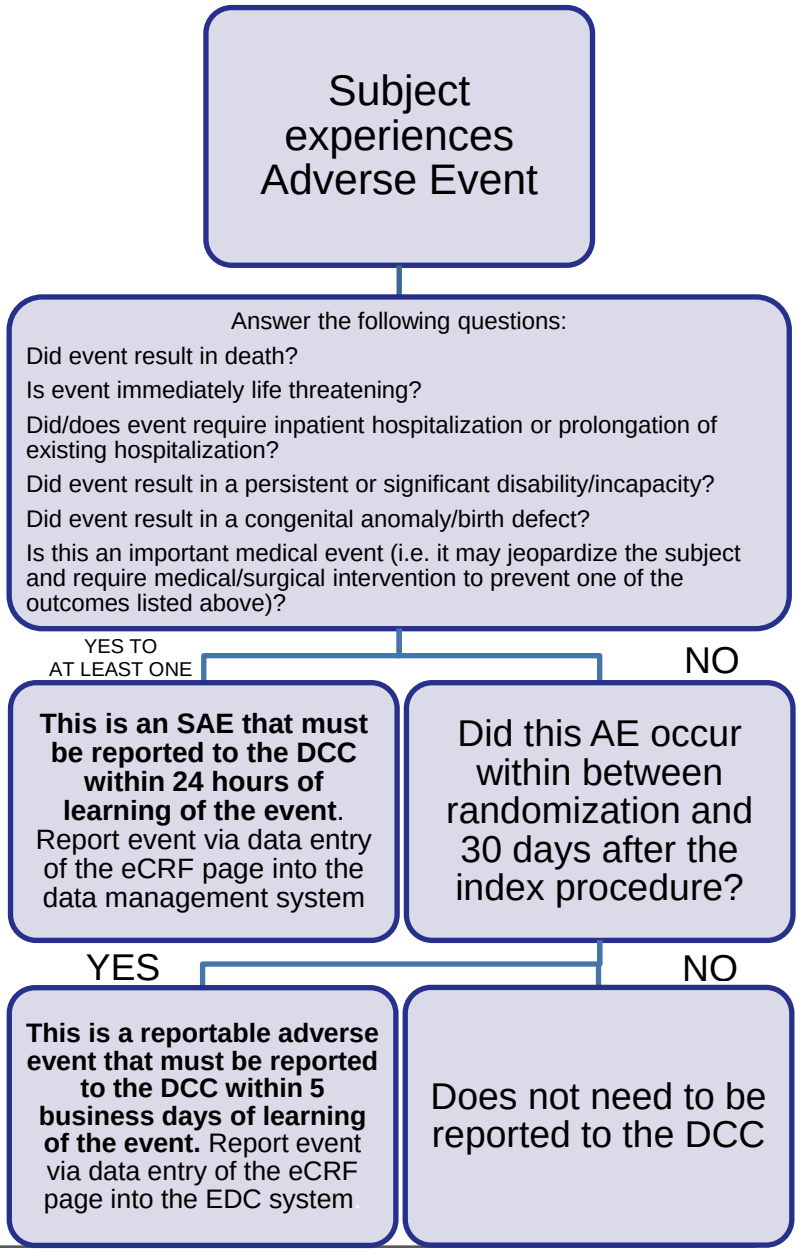
A Lesson in Entering AE Terms

Data Management has noticed a need to issue queries on the AE term field and would like to provide a reminder to sites of how these should be entered in eCOS.

An adverse event (AE) is defined as "any untoward/unfavorable medical experience occurring in a subject during participation in a clinical trial." While a procedure, action, or outcomes is considered an AE, they should not be listed as the AE term. Only signs, symptoms, or disease should be listed as the AE term.

For example, if a patient was hospitalized because they underwent an amputation to treat their osteomyelitis, it is the osteomyelitis that should be entered as the event term because it is the root cause of the hospitalization (an action) and the amputation (the outcome). If during this hospitalization, the patient contracted sepsis, a new AE, 'sepsis' should be entered as a separate AE term because it is an unique diagnosis.

For more details regarding AEs, please see the Manual of Operations, Chapter 6, flow chart (right) or contact BEST@neriscience.com. The FDA also issued a Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Report to IRBs – Improving Human Subject Protection in January 2009.



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