REPRIEVE

Randomized Trial to Prevent Vascular Events in HIV

Site Newsletter 6/8/2015

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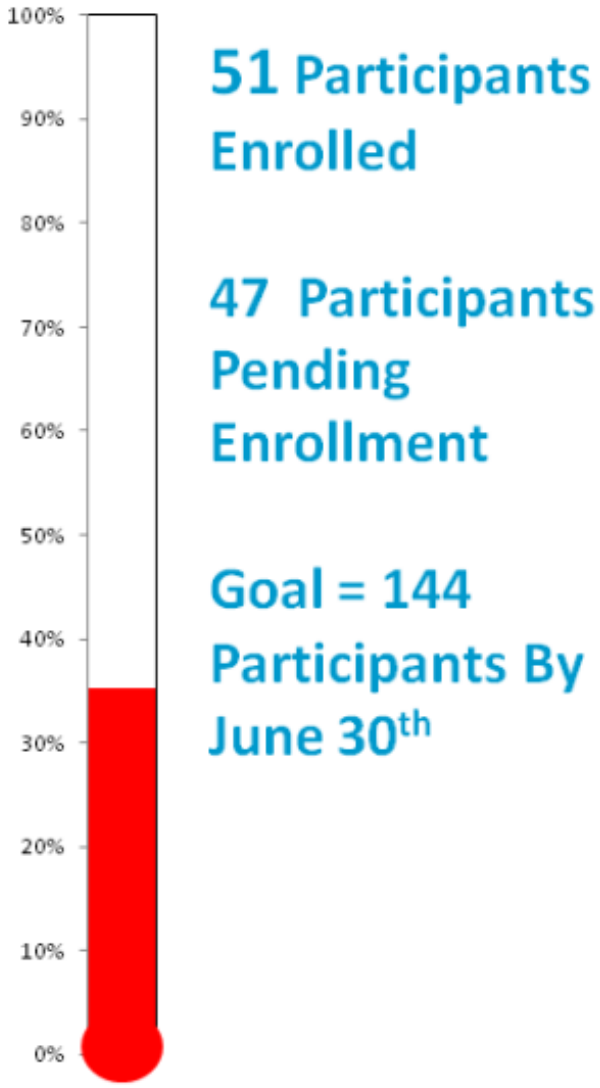
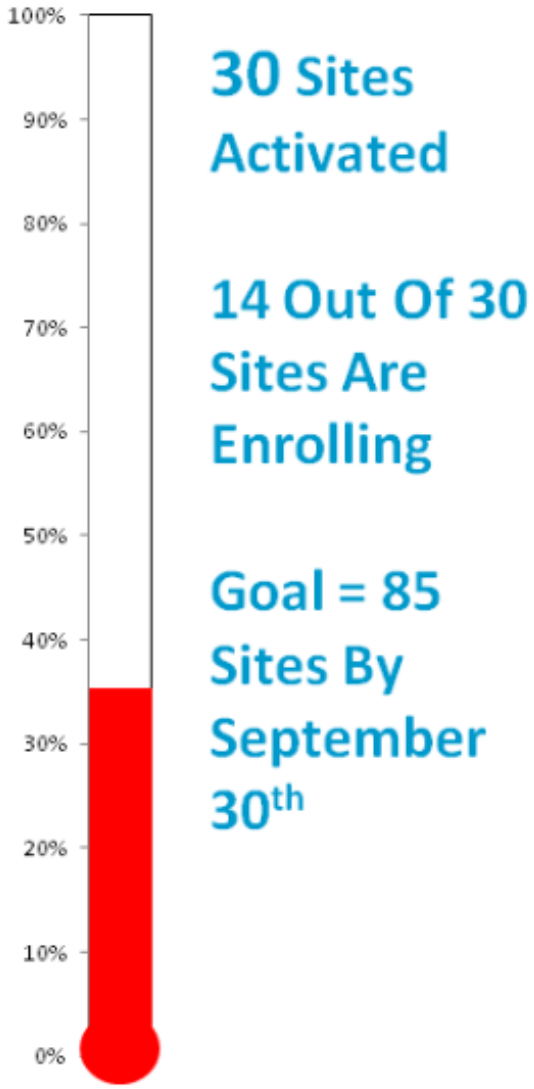
Trial Status





REPRIEVE (A5332) Updates

Welcome Newly Activated Sites!

Ohio State University
Rush University
Puerto Rico AIDS CT
Chelsea Cornell

We have reached the milestone of 30 sites activated by July 30th, 2015!

June Enrollment Goal:

For all activated sites to enroll 5 participants!

REPRIEVE has more than doubled in enrollment since the last newsletter! 123 participants have screened, 51 participants are enrolled and 47 are awaiting enrollment.

Mechanistic Substudy (A5333s) Updates

Welcome Newly Activated Sites!

Ohio State University
Weill Cornell Uptown
Clinic 1917 at UAB

- 10 participants enrolled
- 13 sites activated
- 4 out of 13 activated sites have enrolled

Cincinnati CRS and UCLA Care Center are the top enrolling sites for A5333s!

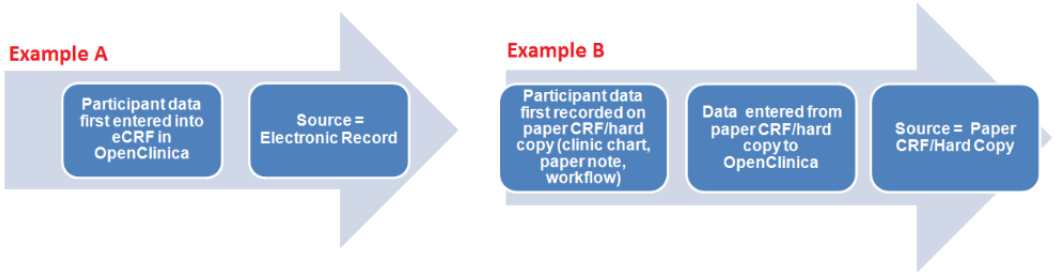
REPRIEVE Source Documentation and Monitoring

In the boxes below are details regarding source documentation and monitoring for REPRIEVE. Several questions were brought up regarding this topic on the last monthly site call. We hope the information below clarifies this topic, we plan to follow up in more detail during the next site call on June 16th, 1:00PM EST. The REPRIEVE (A5332) MOPS is also in the process of being revised and will include the details below.

REPRIEVE Source Documentation

For the REPRIEVE study a new EDC (electronic data capture) system, OpenClinica is being used. The system allows for different options to be utilized for entering and managing data. The system will also allow monitors to have direct access to the study visit data once it is entered into OpenClinica by the site staff. Our plan is to try to conduct some of the monitoring visits as "remote visits" where the monitors will review the PID data via computer from their offices and flag data that requires clarification or correction. While the monitors will be able to review the data electronically there is still a GCP requirement for adequate source data. Since many clinical investigations are now using new technology and computerized systems the FDA published a guidance document in May 2007, Guidance for Industry: Computerized Systems Used in Clinical Investigations. We would like to provide some guidance to sites regarding the requirements for source documentation, what monitors will be looking for and how this study will be monitored.

Source data and source documentation must still meet the same requirements of data quality (e.g. attributable, legible, contemporaneous, original and accurate) as would be expected when using paper records. For the REPRIEVE study, participant data may be entered directly into OpenClinica via the site's computers (Example A). In this case, the electronic record is the source document if the original observations are entered directly into the computerized system. If the site staff first record participant information in a clinic chart, institution medical record or any other hardcopy method (paper notes etc.) and then enters the data into OpenClinica, the clinic chart, medical record or hardcopy is the source document (Example B).



Monitoring REPRIEVE

The investigator must retain records as required under 21 CFR 312.62, 511.1(b). This requirement applies to the retention of original source document or a copy of the source documents.

As referenced in sections 5.18.1.b, 5.15.1 & 6.10 of the ICH Guidelines for Good Clinical Practice E6, the trial sponsor and investigator are required to ensure that monitors are provided direct access to source data consisting of original documents, data and records (source documentation). In the case where source data is collected electronically through direct entry, monitors will access and review source data directly from the electronic database utilized. Providing the monitor direct access to the electronic capture method ensures that contemporaneous and accurate data are reviewed. Monitoring from a printed version of an open electronic database is not recommended as there is very often no way to guarantee that data in the electronic version has not been revised between the time of printing and the time when monitoring of that data is finalized. This could result in a risk to participant safety and data integrity, as well as multiple printouts of the same data being required.

In accordance with the definition of original data, the monitor will apply vigilance to ensure that the electronic database is being used as the first point of entry for all applicable data points. Wherever data is initially collected in another format, this becomes the original data and therefore monitoring of those documents will be required. It is a recommendation for sites to retain a source document SOP defining data collected directly via electronic medium vs. data collected in any other manner as defined in ICH E6 1.52 (Source Documents). Clinical Research Site staff are advised to be thoughtful of the logistics, practicalities and infrastructure required for entering data directly in an electronic database prior to compiling such a document. This document would provide guidance to site staff, monitors, IRB/EC, auditors or other entities appropriately authorized to view source data directly.

Helpful Definitions

Original Data: For the purpose of this guidance, original data are those values that represent the

first recording of study data. FDA is allowing original documents and the original data recorded on those documents to be replaced by copies provide the copies are identical and have been verified as such.

Source Documents: Original documents and records including, but not limited to, hospital records, clinical and office charts, laboratory notes, memoranda, subject's diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in a clinical trial.

Direct Entry: Direct entry is recording data where an electronic record is the original means of capturing the data. Examples are the keying by an individual or original observations into a system, or automatic recording by the system of the output of a balance that measures subject's body weight.

Reference

Guidance for Industry: Computerized Systems Used in Clinical Investigations, U.S. food and Drug Administration, May 2007

http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm070266.pdf

Reminders

Reminder to newly DAIDS Approved Sites: After successfully registering to the DAIDS PRO, you will need to ensure that you have addressed all necessary protocol requirements prior to activation. These requirements are included in the Site Protocol Activation Checklist. To access, please have your site Leader or Coordinator login to the ACTG Member website, click affiliations and then click on the link under the column titled, "Site Protocol Activation Checklist" for the study. Once you've confirmed that all requirements have been met, submit the completed checklist to proceed with protocol activation. **You should not begin screening subjects for enrollment until you have received the notice stating your site has been activated for this study**.

Reminder to Sites participating in REPRIEVE Substudy A5333s: A separate activation notification is required. Once your site has completed all requirements please verify, by submitting the site protocol activation checklist located on the ACTG Member website. **You should not begin screening subjects for enrollment until you have received the notice stating your site has been activated for this study**.

Contact Stephanie Holland (sholland@s-3.com) with any questions regarding the checklist or for assistance with completing protocol requirements.

TRAINING OPPORTUNITIES

Training Opportunities

All training call dates and call details are listed on the REPRIEVE website calendar.

85 sites have participated in a site start up call, 80 have participated in data management training!

52 sites have already participated in ECG training.

Need a A5332 or A5333s Site Training Call Refresher?

- Slides from the A5332 training calls are available in the Training Folder of the A5332 PSWP, there is also an audio recording available.
- Slides from the A5333s training calls are available in the Training Folder of the A5333s PSWP.

ECG Training

- ECG training has begun and is required for site activation for those sites that have not already activated. This requirement was added to the Site Activation Checklist on May, 27th, 2015.
- For all sites if you have not done so already, please plan to attend one of the sessions noted below, *there are only 3 more sessions available for sites in the US and Canada.*
- Your site does not need to be DAIDS approved or protocol registered, nor do you need to have your Site Qualification Form (SQF) signed or the Quintiles ECG machine onsite to participate in this training.
- We encourage you to have all staff that will work with the Quintiles ECG machine to attend the training, e.g., PI, study coordinator.
- Training Sessions:
  - **Tuesday, June 9th (1:00 - 1:30 PM EST)**
  - **Tuesday, June 9th (11:00 - 11:30 PM EST) -- For Thai sites only**
  - **Thursday, June 11th (11:00 - 11:30 AM EST)**
  - **Wednesday, June 17th (3:00 - 3:30 PM EST)**
- See the REPRIEVE calendar for details to access the webinars. Please note, the url and dial in number for these calls were recently modified, therefore please check the calendar in case you did not receive the updates.

ACTG Network Meeting (attendance is voluntary), June 22-26, Washington DC

https://meetings.actgnetwork.org/meeting/2015ACTG

If you are at a non-ACTG site and in the DC area please join us!

- **REPRIEVE Team-Site Meeting**

- Wednesday, June 24th 8:00-9:00 AM EDT

- **Question and Answer Session with the REPRIEVE Team**
  - Wednesday, June 24th 12:30-1:30 PM EDT, Room 5
- **DMC Demo Room at ACTG Network Meeting**
  - Monday, June 22nd
    - 9:00 AM EDT: OpenClinica Overview
    - 3:00 PM EDT: Survival Guide to Reporting Events for REPRIEVE
- **LDMS demo room will be open from 9:00 AM – 5:00 PM**
  - Tuesday, June, 23rd – Thursday, June, 25th
  - LDMS trainers available to answer questions regarding the LDMS. I encourage anyone who has questions about LDMS and/or how to use it for REPRIEVE to stop by.

REPRIEVE (A5332)
Are you up to date?

For A5332 please use

Protocol: Version 2.0 dated 12/19/14
MOPS: dated 04/20/15 **(a revised version will be released soon!)**
A5332 LPC for ACTG Sites only: dated 05/06/2015
A5332 LPC for Non-ACTG Sites only: dated 05/06/2015

These documents are on the A5332 PSWP

Mechanistic Substudy (A5333s)
Are you up to date?

For A5333s please use
MOPS: dated 03/16/2015
A5333s LPC: dated 05/07/2015

Questions on CT Activation? Contact the MGH CT Core Lab MGHReprieve@partners.org

These documents are on the A5333s PSWP

REPRIEVE In the News

Check out recent articles about REPRIEVE!

- Novel mechanism and potential treatment strategies for CVD in HIV patients, *Infectious Disease News*
- Drug that lowers cholesterol could be next advancement in HIV treatment, *St. Louis Post-Dispatch*
- CVD prevention, treatment challenging as patients with HIV and HCV live longer, *Cardiology Today*

We would like to introduce. . .

Lab Technologists Francoise Giguel and Joan Dragavon!

Francoise Giguel. REPRIEVE is my first project as a Laboratory Technologist and I am very fortunate to be Joan's mentee. I helped developing the Laboratory Processing Charts for both A5332 and A5333s.

I joined Ann Gershon's WITS lab at Columbia University in the mid nineties, then Marty Hirsch's ACTG lab at Massachusetts General Hospital in 1997 and finally Dan Kuritzkes' lab in 2002. I served as the Harvard Virology Specialty Lab manager since 2010. A public servant at heart, I started working in clinical labs when only AZT was available. I am extremely grateful for the opportunity that was given to me all along the amazing transformation that renders HIV a manageable disease. I am honored to be part of REPRIEVE and I hope that the results of this important study will be ultimately be beneficial to the public at large.

Joan Dragavon. My interest in viruses developed during high school when my neighbor, a virologist at a poultry disease research facility, hired me as a "gofer" to "wash lab dishes" the summer of my junior year. I learned to draw blood from mostly uncooperative chickens, aseptic technique to make cell culture media and observed the preparing and maintaining of chick embryo fibroblast cell cultures and plaque formation assays for Rous Sarcoma virus and its helper Rous-associated adenovirus. (I was hooked!) I helped finance college as a student helper in veterinary virology.

After graduation I was fortunate to land a position in a growing clinical and research virology laboratory. The research was first SIDS, next Herpes, and then HIV. In the mid-90s, I moved into Retrovirology in an ACTG/PACTG laboratory working for Dr. Coombs. I currently work on projects for the ACTG and for the HVTN, always learning new virology things.

We will assist sites and labs to maintain a smooth flow of our participants' specimens, preserving their integrity through training, team work and availability for questions to all ACTG and non-ACTG labs participating in REPRIEVE. Our goal is to ensure the quality of the specimens that the REPRIEVE participants so graciously provide. To that end, the details of processing, documentation, storage and shipping are so very important. We encourage the labs to contact the REPRIEVE lab team with questions at any time: reprieve.labcom@fstrf.org; we are here to help.

For future reference, all newsletters are available on the REPRIEVE Website

We welcome suggestions and ideas for upcoming newsletters. Please submit any comments or suggestions to the REPRIEVE News Team at reprieve.news@fstrf.org.

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