REPRIEVE

Randomized Trial to Prevent Vascular Events in HIV

Site Newsletter 01/25/2016

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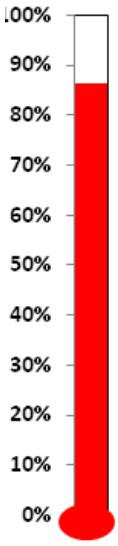
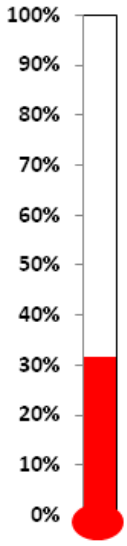
Trial Status: 01/18/2016-01/25/2016

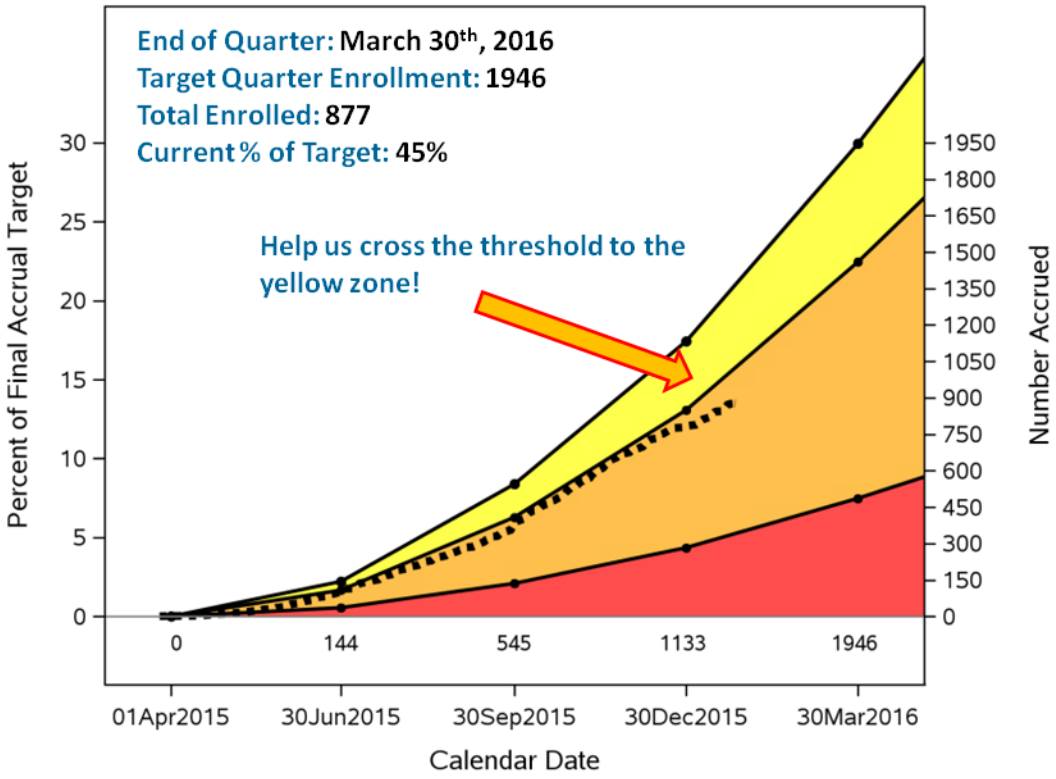
REPRIEVE is ***extremely*** close to having over 1,000 participants enrolled! And we will exceed 1,000 participants in only 2 weeks if each activated site enrolls at least 1 participant each week. Help us meet the goal of having over 1,000 participants enrolled well in advance of the 1st anniversary of the first participant enrolled (March, 2016).



86% of Activated Sites are Enrolling!



32% of Activated Sites Enrolled at Least 1 Participant Last Week!



Dotted line shows actual accrual progress.
Colored bands denote predefined NIH target enrollment zones: yellow (100% to 75%), orange (75% to 25%), red (<25%).

Congratulations to Sites Enrolling Participants

Week of 01/18/16

UCSD Antiviral Research Center CRS

Thai Red Cross AIDS Research Center

University of Colorado Hospital CRS

Cincinnati CRS

Columbia Physicians and Surgeons CRS
Weill Cornell Uptown CRS
The Ponce de Leon Ctr. CRS
Chiang Mai University HIV Treatment CRS
Case CRS
University of Washington AIDS CRS
Massachusetts General Hospital CRS
Ohio State University CRS
Harbor UCLA CRS
University of Rochester Adult HIV Therapeutic Network CRS
Johns Hopkins University CRS
Whitman-Walker Health CRS
University of Southern California CRS
University of Illinois at Chicago
UT Southwestern
Denver Public Health
Florida Department of Health
University of Nebraska Medical Center
Orlando Immunology Center CRS
Louisiana Community AIDS Research Program

Our site is awaiting final approval for LOA #1 that increased the 10-year ASCVD risk score exclusion from ≥7% to >10%. In the meantime, there are a few participants I have screened whose blood pressure was slightly elevated at their screen visit, due to this their 10-year ASCVD score would be slightly above 10%. However, all blood pressures have been in the normal range at previous clinic visits. How should I proceed?

Blood pressure is somewhat variable and can be intermittently elevated depending on a number things (caffeine, activity prior to the visit etc.), therefore it would be appropriate to recheck the blood pressure. Have the participants return, assure that they are relaxed, sitting in a quiet area without their legs crossed and recheck the blood pressure. Once the LOA is approved by your local IRB, re-consent the participant; screening assessments completed within protocol specified windows do not need to be repeated.

Now that our IRB has approved the new 10-year ASCVD risk score cutoff, I

am contacting patients that screen failed due to the previous ASCVD cutoff. If a patient returns, which number do I use: the Screening Number or the PID?

Screening Failures are associated with Screening Numbers and not PIDs. A participant could potentially have multiple Screening Numbers, but never more than one PID.

A Screening Number is still valid and is associated with a participant until one of two things happens:

1. A Screening Outcome Form is completed indicating the participant will not enroll or,
2. 90 days have elapsed since the screening number was assigned and the participant has not been enrolled. If this happens, the screening number expires.

You could use the same Screening Number for a participant who did not meet the original enrollment checklist criteria but does meet the new enrollment checklist criteria if the two conditions above are met.

You should complete the Screening Checklist for the participant if either of the conditions are met.

If the participant fails enrollment under a new Screening Number, complete the Screening Outcome form that is now associated with the new Screening Number indicating why they screen failed.

Tips from the Data Management Center

Be mindful of the Informed Consent date you provide in the enrollment checklist. We use the Informed Consent date in OpenClinica to compare to your visit dates.

We do not anticipate any Screening Visit to occur before the Informed Consent date.

Reminder

Don't forget to submit the VERSION 2.0 LOA # 1 (Letter of Amendment) to the DAIDS Protocol Registration Office (PRO)! If you have any questions about the process, please contact the Protocol Registration Office via e-mail at protocol@tech-res.com, or by phone at 301-897-1707. You can implement the LOA immediately upon receiving final IRB/EC and any other applicable regulatory entity approvals for this LOA (without waiting for successful LOA registration).

Protocol Amendment Status Update

The full protocol amendment (which will be VERSION 3.0) will complete the sponsor's regulatory review shortly, we anticipate distributing the final amendment to you in early February. Specific changes will be reviewed on the February 18 Monthly Team Site Call.

Helpful Tips From the Network Coordinating Center

What is an Email Group?

- An email group (the "prot logon") has been created for REPRIEVE. This email group is the primary means of communication from the study team to site staff. Information that will be communicated to sites via this email logon includes download instructions for protocol clarifications and amendments, revised MOPS and LPCs, DSMB summaries, important reminders and other study-related documents, and conference call logistics.
- Each site is responsible for identifying staff members who need to receive this information and contacting actg.user.support@fstrf.org to add those staff members to the "A5332 prot logon." You do not have to wait for successful protocol registration to do this. At a minimum, we recommend that you add your Principal Investigator, CRS leader, investigator of record, CRS coordinator, pharmacist, data manager, and laboratory staff to the email group. Alternatively, add your CRS Leader, CRS Coordinator, and at least one study nurse, and designate one person to forward emails to the relevant site staff.

Helpful Resources

- Site approval: your site's DAIDS OCSO Program Officer or OCSOREPRIEVETeam@mail.nih.gov
- DAIDS Protocol Registration: Protocol@tech-res.com
- DAIDS Regulatory Support Center: http://rcc.tech-res.com/default.aspx

- Site protocol activation: ACTGSiteCoordination@s-3.com
- Contract & payment inquiries: ACTG.Finance@fstrf.org
- Lab questions: reprieve.labcom@fstrf.org
- Study drug and pharmacy: PABREPRIEVEPEP@mail.nih.gov
- Data management/eCRFs and OpenClinica: reprieve.dmc@fstrf.org
- Email team with all other questions: actg.corea5332@fstrf.org and we will see that you get the help you need.

Recruitment

Are You Giving Provider Talks in Your Area About REPRIEVE?

We have had many requests for a sample provider presentation that can be used to promote REPRIEVE. The REPRIEVE Clinical Coordinating Center has used the attached presentation for many provider talks. Please feel free to use this as a template.

We are currently updating these slides and will distribute a revised set as soon as they are completed. In the meantime, please use the sample slides attached.

Need a Brief Summary About REPRIEVE?

When you are working with your local advocacy groups, providers, case managers, social workers etc. to promote REPRIEVE, providing copies of the articles listed below may be really helpful to provide background information about REPRIEVE.

- New Med Could Prevent Heart Disease in People Living with HIV. *HIV Equal*, January, 2016. (this article has really a catchy tagline! **"Call it PrEP to protect against heart disease in people living with HIV"**)
- NIH Launches REPRIEVE, First Large-Scale Cardiac HIV Prevention Study, *Edge Media Network, December, 2015.*
- NIH to Fund First Large-Scale Trial for Heart Disease Prevention Among People With HIV, *LGBT Weekly, November, 2015.*
- REPRIEVE Clinical Trial on Preventing HIV-Related Heart Disease Still Seeking Participants, *HIV Plus Magazine, November, 2015.*
- HIV-Related Cardiovascular Disease, Statins, and the REPRIEVE Trial, *Topics in Antiviral Medicine, October/November 2015.*
- Getting to the Heart of the Matter, *Poz, October, 2015.*

Please Join Us For Our Monthly Team-Site Calls

These calls are held on the third Tuesday of every month at 1 PM ET. The phone number, access code, and agenda are sent by email before the call to the protocol logon (email group).

These calls are meant to be an open forum where site staff can share best practices, discuss their experiences recruiting, screening, and implementing the study, raise any issues they are facing, and share successes.

If you have questions or concerns that you'd like to raise but you cannot attend the call, please send them to the core team.

A summary of the team-site calls will be distributed to the protocol logon, and recent summaries are posted on the protocol-specific web page here: » A5332 » Protocol Training » Site Calls for reference.

Notes From The CT Expert

Michael Lu, MD
Co-Chair, REPRIEVE Mechanistic Substudy A5333s

Thank you to the sites participating in A5333S!
Because of you, we are exceeding our enrollment milestones!

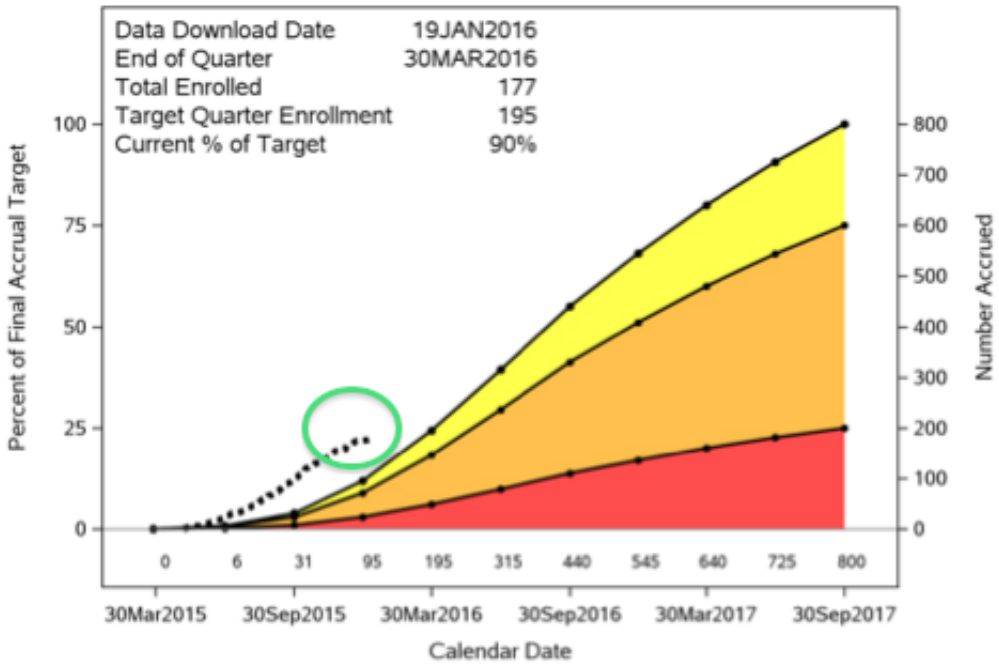


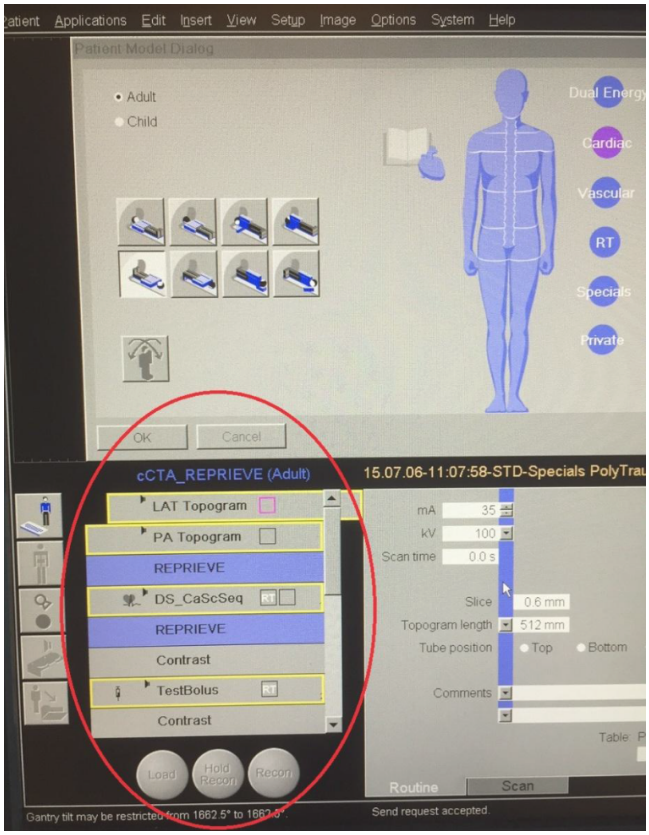
Image quality has been outstanding, with >80% of coronary CTs of excellent or good quality. Image transfer has also exceeded expectations, with the majority of CTs sent within a week of image acquisition.

Radiation Dose:

Overall radiation dose has been below our target of 3 to 8 mSv, with only a handful of high dose CTs above 12 mSv. Most high dose CTs have been due to pulsing windows set too wide despite a low heart rate. For heart rates <65 bpm, a brief period of diastole should be sufficient for good visualization of the coronary arteries. Also, please use an automatic (e.g. CarekV for Siemens) or manual BMI-based (e.g. 100 kV for BMI≤30) kV setting.

Establish a "REPRIEVE Coronary CTA protocol" at your scanner:

Sites with consistently low radiation dose and high quality images have setup a REPRIEVE specific protocol at the scanner. Example from the Massachusetts General Hospital site:



When acquiring and submitting images, ensure that the following series are included:

1. Noncontrast calcium score CT
    a. Small field of view (FOV) limited to the heart
    b. Full FOV including entire portion of imaged body
2. Contrast CT angiogram
    a. Small FOV limited to the heart
    b. Full FOV including entire portion of imaged body
3. Radiation dose report/protocol page

Training Opportunities

ECG Training Dates

- **Session 1 = 27 Jan 2016, 1pm EST**
- **Session 2 = 24 Feb 2016, 1pm EST**
- **Session 3 = 30 Mar 2016, 1pm EST**

This training will include information on the ECG machine, supplies, performance, and

transmission of data. **At least one person from your site must attend one training to meet protocol activation requirements.** If you have participated already but would like a refresher, please feel free to attend.

You do not have to have an ECG machine onsite to participate in this training. We encourage you to have all staff that will work with the Quintiles ECG machine attend the training (eg, PI, study coordinator, CRA, backup personnel).

Calendar invites with call details have been sent out. Please email Katie Fitch, kfitch@partners.org, if you did not receive the invites.

Site Start Up Calls

Site start up calls will be scheduled soon. Dates will be included in future newsletters and sent via email. Stay tuned...

REPRIEVE (A5332): Are you up to date?

For A5332 please use

Protocol: Version 2.0 dated 12/19/2014

Letter of Amendment #1: 09/18/2015

Clarification Memo #1: 02/02/2015

Clarification Memo #2: 08/28/2015

Clarification Memo #3: 09/10/2015

MOPS: 11/09/15

A5332 LPC for ACTG Sites: dated 09/17/2015

A5332 LPC for Non-ACTG Sites:dated 09/17/2015

These documents are on the A5332 PSWP

REPRIEVE Mechanistic Substudy (A5333s): Are you up to date?

For A5333s please use

Protocol: Version 2.0 dated 12/19/14

MOPS: dated 11/10/2015

A5333s LPC : dated 9/21/15

These documents are on the A5333s PSWP

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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