March 26th, 2018

**Trial Status**

- **6210** participants are enrolled
- **60** participants enrolled last week!
- **402** participants are in screening
- **119** sites are open for enrollment
- **27** sites enrolled at least 1 participant in the past week
- **38** sites screened at least 1 participant in the past week

Since the last newsletter, **123** participants have been enrolled. **Thank you for the excellent effort that all teams are putting forth to enroll participants in REPRIEVE.**

---

**Thank You to All Sites Enrolling Participants Week of March 19th, 2018!**

- University of Pittsburgh CRS
- The Miriam Hosp (TMH) CRS
- Penn Therapeutics CRS
- Weill Cornell Uptown CRS
- Wits Helen Joseph Hospital CRS (Wits HJH CRS)
- Barranco CRS
- San Miguel CRS
- Chennai Antiviral Research and Treatment (CART) CRS
- Joint Clinical Research Centre (JCRC)/Kampala CRS
- Gaborone CRS
- Les Centres GHESKIO Clinical Research Site (GHESKIO-INLR) CRS
Parirenyatwa CRS
Trinity Health and Wellness Center
Houston AIDS Research Team CRS
GHESKIO Institute of Infectious Diseases and Reproductive Health
Alabama CRS
University of Cape Town Lung Institute
Thai Red Cross AIDS Research Center
Wake Forest University
Mt Sinai West CRS
Chronic Viral Illness Service of McGill University
School of Medicine, Federal University of Minas Gerais CRS
HGNI HIV Family Care Clinic HHFCC
Capital Medical Associates
Tropical Medicine Foundation
Augusta University
Palmetto Health Clinical Trial Department

Full Speed to 1500
Full Speed to 1500 Challenge Updates!

Since the Full Speed to 1500 Challenge began on December 4th, 2017, 1083 participants have been enrolled, we are getting closer to the goal of enrolling 1500 participants! If 70 participants are enrolled each week between now and the first week of May we will meet the challenge. Stay tuned for updates.

Don't forget prizes include:

- $500 gift card for 1st place
- $250 gift card for 2nd place
- All other sites that enroll 15 participants by May 1st will win a $100 gift card

Check out the standings below!
Non-Adjudicated Events

Don't forget that detailed information is being collected on events of interest. These events do not go through a formal adjudication process which is why they are referred to as "Non-Adjudicated Events".

Non-Adjudicated Events include:

<table>
<thead>
<tr>
<th>Site #</th>
<th>Site name</th>
</tr>
</thead>
<tbody>
<tr>
<td>11701</td>
<td>Chennai Antiviral Research and Treatment (CART) CRS</td>
</tr>
<tr>
<td>31441</td>
<td>Byramjee Jeejeebhoy Government Medical College (BJMC) CRS</td>
</tr>
<tr>
<td>12401</td>
<td>Joint Clinical Research Centre (JCRC)/Kampala CRS</td>
</tr>
<tr>
<td>31946</td>
<td>Tropical Medicine Foundation</td>
</tr>
<tr>
<td>11301</td>
<td>Barranco CRS</td>
</tr>
<tr>
<td>31802</td>
<td>Thai Red Cross AIDS Research Center</td>
</tr>
<tr>
<td>31924</td>
<td>Instituto de Infectologia Emilio Ribas CRS</td>
</tr>
<tr>
<td>30222</td>
<td>Les Centres GHESKIO Clinical Research Site (GHESKIO-NLRL) CRS</td>
</tr>
<tr>
<td>31954</td>
<td>Centro de Referencia e Treinamento</td>
</tr>
<tr>
<td>12701</td>
<td>Gaborone CRS</td>
</tr>
<tr>
<td>31730</td>
<td>GHESKO Institute of Infectious Diseases and Reproductive Health</td>
</tr>
<tr>
<td>11302</td>
<td>San Miguel CRS</td>
</tr>
<tr>
<td>31927</td>
<td>HGNI HIV Family Care Clinic HHFCC</td>
</tr>
<tr>
<td>31879</td>
<td>Mount Sinai Downtown CRS</td>
</tr>
<tr>
<td>31984</td>
<td>UT Southwestern</td>
</tr>
<tr>
<td>31925</td>
<td>Hospital Escola Sao Francisco de Assis</td>
</tr>
<tr>
<td>31917</td>
<td>Centro de Pesquisas Clinicas ICHCFMUSP CRS</td>
</tr>
<tr>
<td>31915</td>
<td>School of Medicine, Federal University of Minas Gerais CRS</td>
</tr>
<tr>
<td>31784</td>
<td>Chiang Mai University HIV Treatment CRS</td>
</tr>
<tr>
<td>11101</td>
<td>Wits Helen Joseph Hospital CRS (Wits HJH CRS)</td>
</tr>
<tr>
<td>31980</td>
<td>Palmetto Health Clinical Trial Department</td>
</tr>
<tr>
<td>6101</td>
<td>University of Colorado Hospital CRS</td>
</tr>
<tr>
<td>6201</td>
<td>Penn Therapeutics CRS</td>
</tr>
<tr>
<td>2501</td>
<td>Case CRS</td>
</tr>
<tr>
<td>8950</td>
<td>Family Clinical Research Unit</td>
</tr>
<tr>
<td>12301</td>
<td>SOWETO</td>
</tr>
<tr>
<td>31788</td>
<td>Alabama CRS</td>
</tr>
<tr>
<td>30329</td>
<td>Columbia Physicians and Surgeons CRS</td>
</tr>
<tr>
<td>1601</td>
<td>Duke University Medical Center</td>
</tr>
<tr>
<td>31918</td>
<td>Hospital Federal dos Servidores do Estado</td>
</tr>
<tr>
<td>11201</td>
<td>Durban International CRS</td>
</tr>
<tr>
<td>1001</td>
<td>University of Pittsburgh CRS</td>
</tr>
<tr>
<td>31786</td>
<td>New Jersey Medical School-Clinical Research Ctr. CRS</td>
</tr>
<tr>
<td>31889</td>
<td>Toronto General Hospital</td>
</tr>
<tr>
<td>31871</td>
<td>Bluegrass Care ClinicUniversity of Kentucky Research FDN CRS</td>
</tr>
</tbody>
</table>
Non-cardiovascular Disease Events not Associated with Death

- AIDS-defining events (including AIDS-defining cancers)
- Non-AIDS-defining cancers (except squamous/basal cell of the skin)
- End-stage kidney disease (requiring initiation of dialysis or renal transplantation, see 6.2.4 below)
- End-stage liver disease (cirrhosis or hepatic decompensation requiring hospitalization)
- Incident diabetes mellitus requiring the use of hypoglycemic agents

Other Events Requiring Reporting

- Incident hypertension
- Incident active hepatitis B (HBV) infection
- Incident active hepatitis C (HCV) infection
- Incident venous thromboembolism (VTE)
- Incident pulmonary thromboembolism (PTE)

Identifying these events and reporting them as per section 6.2 of the REPRIEVE (A5332) MOPS is very important!

Q. Is Herpes Simplex virus (HSV) exclusionary per section 4.2.14 of the protocol? What is considered active or resolved HSV?
A. In most situations, HSV infection does not automatically exclude a person from participation, eg, an HSV oral or genital outbreak would not be exclusionary. However, a person with a serious HSV infection (eg, HSV encephalitis or esophagitis requiring IV treatment or hospitalization) would be excluded per 4.2.13 of the protocol.

Q. A potential participant’s blood pressure was slightly elevated at screening although previous measurements were always normal. The elevated BP will make the 10-year ASCVD risk score too high for eligibility--what should I do?
A. Blood pressure is somewhat variable and can be intermittently elevated depending on a number of things (caffeine, activity prior to the visit, etc.). It would be appropriate to recheck the blood
pressure. Have participants return, assure they are relaxed, sitting in a quiet area without their legs crossed, and check the blood pressure again. You may use any blood pressure reading within the 90 day window specified in the protocol and you can use the lowest blood pressure obtained when it is rechecked.

---

Measuring Site Performance

Curious about how your site's performance is measured by the Site Performance and Selection Committee (SSPC)? Read on for details!

- Site performance is evaluated on a continual basis.
  - Important issues brought to the attention of site PI.
- Twice a year (in January and July) the SSPC formally reviews cumulative performance and letters are sent to PIs.
- The Site Selection and Performance Committee (SSPC) evaluates each site's:
  - Enrollment
  - Retention / On and Off Treatment Rates
  - Specimen management
  - Data management
  - EAE reporting

---

Important Targets to be Aware of

- Enrollment
  - Target is approximately 2-4 participants enrolled per month per site
- Retention / Study Treatment
  - Target is ≤ 5% annual loss to follow up
  - Target is ≤ 5% off study treatment and still on study.
- Data management
  - Target is complete data entry within 3 weeks of visit
  - Target is to address data queries within 3 weeks of receipt
- Laboratory management
  - Target is to ship 100% of specimens within 90 days of data entry
  - Target is to ship specimens according to the rules in the Lab Processing Chart (on the PSWP)
- EAE Reporting
  - Target is 100% of EAEs reported within 3 reporting days of site awareness

For more details, please review the Site Performance Plan (SPP) on the REPRIEVE PSWP

https://mailchi.mp/27c8e7caec42/c46vbcmmx9-1343921
LDMS Training Resources

The Laboratory Data Management System (LDMS) website (https://www.ldms.org) offers links to numerous training resources that can help familiarize laboratory staff with the LDMS.

The Training menu includes:

- upcoming workshops and webinars and a link to register for training and,
- more information about the content and format of training events.

The Resources menu includes:

- LDMS user manuals
- general and project-specific documentation
- training materials (workbooks and quizzes)
- LDMS video tutorials such as:
  - Completing PBMC Processing Information
  - Locating Specimens Not Stored,
  - Shipping for REPRIEVE
  - Specimen Management for REPRIEVE
  - Storage Management for REPRIEVE,
  - Specimens Not in Storage Report
  - These tutorials are also on the Frontier Science YouTube channel: https://www.youtube.com/user/FSTRFFilms

Next REPRIEVE DSMB Meeting is June 4th, 2018
The timeline below lists important tasks and deadlines for the upcoming Data and Safety Monitoring Board (DSMB) review of the REPRIEVE trial.

Please mark these dates on your calendar and note that **Monday, Apr 9** is the data entry deadline.

<table>
<thead>
<tr>
<th>Task</th>
<th>Deadline*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sites Latest date for the occurrence of an</td>
<td>Mar 31 (Sat)</td>
</tr>
<tr>
<td>evaluation for which complete data will be</td>
<td></td>
</tr>
<tr>
<td>included in this DSMB review</td>
<td></td>
</tr>
<tr>
<td>Sites All data for visit through Mar 31 entered</td>
<td>Apr 9 (Mon)</td>
</tr>
<tr>
<td>Sites All adjudication packets for potential MACE</td>
<td>Apr 13 (Fri)</td>
</tr>
<tr>
<td>events with a work-up complete by Mar 31</td>
<td></td>
</tr>
<tr>
<td>submitted to DCC (MGH)**</td>
<td></td>
</tr>
<tr>
<td>Sites All outstanding queries resolved</td>
<td>Apr 23 (Mon)</td>
</tr>
<tr>
<td>Sites Respond to last minute outstanding queries</td>
<td>May 11 (Fri)**</td>
</tr>
<tr>
<td>All DSMB Meeting</td>
<td>June 4 (Mon)</td>
</tr>
</tbody>
</table>

*Deadlines are Close of Business on the given date unless otherwise noted

** Please ensure that you have responded to all queries and clarifications from the DCC regarding source documents submitted for potential adjudicated events. This will ensure that the DCC is able to submit complete packets to TIMI for adjudication prior to the DSMB.

***Please note this date has been updated from the email that was distributed

---

Did You Miss the Monthly Site Call?

If so, please find the March call slides attached.

Topics discussed:

- Version 4.0 full protocol amendment (status update!)
- Protocol registration and submission requirements; change of key personnel
- Non-adjudicated events
- Measuring Site Performance
- Specimen Shipping
- CROI Meeting Summary

If you have suggestions for a monthly site call in the future, we would love to hear from you! Please email Katie Fitch at kfitch@partners.org.
REPRIEVE (A5332): Are you up to date?
For A5332 please use

**Current Protocol Documents:**
- Protocol Version 3.0 dated 01/28/2016
- Clarification Memo #1 dated 04/04/2016
- Clarification Memo #2 dated 04/12/2016 (corrects an error in CM #1)
- Clarification Memo #3 dated 12/27/2016
- Letter of Amendment, Version 3.0 #1 dated 08/17/16
- Letter of Amendment, Version 3.0 #2, dated 04/14/17
- Letter of Amendment, Version 3.0 #3, dated 01/19/2018

**MOPS Version 3.0:** dated 09/20/2017
- A5332 LPC for ACTG Sites: Version 3.0 dated 02/02/2018
- A5332 LPC for Non-ACTG Sites: Version 3.0 dated 09/21/2017

These documents are on the [A5332 PSWP](#).

Mechanistic Substudy of REPRIEVE (A5333s): Are you up to date?
For A5333s please use

**Protocol:** Version 3.0 dated 01/28/2016
**MOPS:** Version 3.0 dated 06/05/2017
**A5333s LPC:** Version 3.0, dated 09/21/2017

These documents are on the [A5333s PSWP](#).

For future reference, all newsletters are available on the [REPRIEVE Website](#).
We welcome ideas and suggestions for future newsletters. Please submit any comments or suggestions to the REPRIEVE News team at reprieve.news@fstrf.org

---

REPRIEVE Trial Clinical Coordinating Center
Massachusetts General Hospital
55 Fruit Street, 5LON 207
Boston, MA USA 02144

Our mailing address is: