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REPRIEVE

Randomized Trial to Prevent Vascular Events in HIV

June 2022 Table of Contents

Hot Off the Press!

Proteomic Signature of Subclinical Coronary Artery Disease in People With HIV: Analysis of the REPRIEVE Mechanistic Substudy

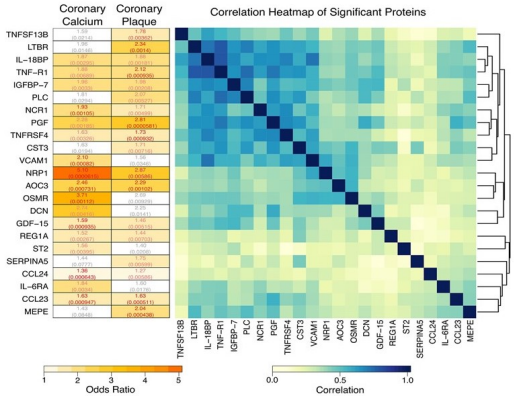
Márton Kolossváry, Chris deFilippi, Michael T. Lu, Markella V. Zanni, Evelynne S. Fulda, Borek Foldyna, Heather Ribaudo, Thomas Mayrhofer, Ann C. Collier, Gerald S. Bloomfield, Carl Fichtenbaum, Edgar T. Overton, Judith A. Aberg, Judith Currier, Kathleen V. Fitch, Pamela S. Douglas, Steven K. Grinspoon ✉

Author Notes

The Journal of Infectious Diseases, jiac196, https://doi.org/10.1093/infdis/jiac196

The REPRIEVE team recently published a report on Proteomic Signature of Subclinical Coronary Artery Disease in People With HIV. This publication was recently featured on the National Institute of Allergy and Infectious Diseases's twitter page!

Don't forget to check our publications page on the REPRIEVE website for



links to all publications and plain language summaries to share with participants.

Reporting Non-Adjudicated Events

Three things to know about non-adjudicated events in REPRIEVE:

1. They are considered as secondary and/or safety events.
2. They should be assessed for at every visit.
3. They do not go through an adjudication process.

There are two groups of non-adjudicated events to remember:

1. Non-cardiovascular Disease Events not Associated with Death, that include:

- 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 section 6.2.4 below)
- End-stage liver disease (cirrhosis or hepatic decompensation requiring hospitalization)
- Incident diabetes mellitus requiring the use of hypoglycemic agents

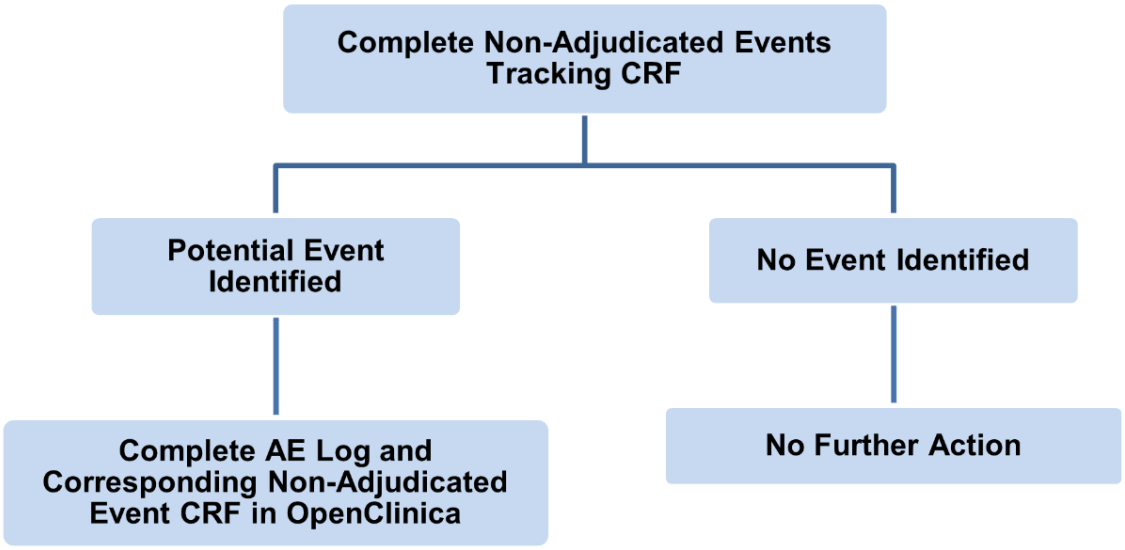
2. Other Events Requiring Reporting, that include:

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

The event-specific CRFs for non-adjudicated events require the signature of the local PI or designee confirming that they have reviewed the documentation and agree with the diagnosis and the level of evidence.

For more information, refer to the A5332 MOPS, section 6.2.

Below is a workflow on how to report non-adjudicated events.



A Reminder About Expedited Adverse Events (EAEs)

All Serious Adverse Events (SAEs) are reported to DAIDS as Expedited Adverse Events (EAEs) ***except*** the following:

1. Any REPRIEVE MACE, Cerebrovascular Event, Heart Failure Event, or AIDS-Defining Event (see Appendix I of MOPS).

- NOTE: If a REPRIEVE MACE, Cerebrovascular Event, Heart Failure Event, or AIDS-defining Event is felt to be related to pitavastatin or placebo for pitavastatin, *it is* to be reported to DAIDS as an EAE.

2. An SAE occurring before exposure to pitavastatin or placebo for pitavastatin.
3. Immune reconstitution inflammatory syndrome (IRIS), even if the event otherwise meets the reporting criteria. IRIS is an intense immune reaction that may result from a response to HIV treatment and is an anticipated event for antiretroviral therapies.

- NOTE: Any adjudicated event that is rejected as a REPRIEVE MACE, cerebrovascular event, or heart failure event must be assessed as to whether it meets classification as an EAE. If it meets the threshold, the site is expected to report the event in DAERS within 3 reporting days of the Downgraded Events Memo. Sites will not be penalized for late reporting of events that were initially reported for adjudication.

EAEs should be reported in the DAERS Reporting System within 3 reporting days of the event or on the DAIDS EAE Report form. EAEs ***are not to be reported*** to the REPRIEVE Data Coordinating Center (DCC).

See Section 7.0 of the REPRIEVE MOPS for more information.

FAQs

Q: We have a participant who was recently prescribed ezetimibe (Zetia) by their provider. We wanted to confirm that this medication is not prohibited or precautionary? This specific medication nor its drug class is mentioned in the list of precautionary or prohibited meds but we wanted to be sure since it is a cholesterol-lowering medication.

A: Ezetimibe is permitted for REPRIEVE participants and is not considered prohibited or precautionary.

Protocol A5332, Version 6.0, dated16May2022 is Available!

In case you missed the email, the amended protocol for REPRIEVE (A5332), Version 6.0, 16May2022, titled “Randomized Trial to Prevent Vascular Events in HIV – REPRIEVE (A5332)”, is now ready for download from the A5332 PSWP.

All sites that have received protocol registration approval for the previous protocol version (Version 5.0) must submit the Version 6.0 protocol amendment to their local institutional review boards or ethics committees (IRBs/ECs) as soon as a possible.

Upon receiving final IRB/EC and any other applicable regulatory entity approval(s) for this amendment, sites should implement the amendment immediately. Sites are required to submit an amendment registration packet to the DAIDS PRO at the RSC. For additional information on the protocol registration process and specific documents required for initial and amendment registrations, refer to the current version of the DAIDS Protocol Registration Manual and section 4.0 of the protocol document.

Reminder:

Sites are required to enter dates for the following information electronically via your site's study affiliations page on the ACTG member website:

- IRB/EC Submission for Protocol Version 6.0
- MTA/STA Executed (if applicable)

Please enter these dates as soon as possible after completion of the respective task. Also, at this time you may wish to revise your anticipated total and monthly accrual figures.

Please contact the team (actg.corea5332@fstrf.org) if you have any questions.

Training for Version 6.0 will take place during the July 19th site call, an invite for this call has been sent, if you haven't received it please email Nada Saleh at nada.saleh@dlhcorp.com.

NOTE: Because the ICF template has been revised as part of this amendment sites have asked if participants need to be reconsented. We have asked for sites to please consult with their local IRB/EC to make this determination.

Please be sure to **complete the Specimen Tracking Form in a timely manner and ensure the collection time entered on the Specimen Tracking CRF and in LDMS are identical**. This is important for monitoring the specimen collection status of the trial as well as to prevent lab data queries.

Do you have a questions about lab processing question, shipping specimens, or responding to LDSMS queries?

We will also be hosting our annual Shipment/Query refresher call in September 2022! Stay tuned for more details about this call.
Lab Tips

Tokens of Appreciation Are Back In Stock!

Tote bags

Birthday cards

Thank you cards

We have REPRIEVE-branded tote bags, 'Happy Birthday' cards, and 'Thank You' cards. These tokens are a great way to show appreciation for our dedicated REPRIEVE participants.

Click Here to Order Swag for Your Site!

Next Team/Site Call!
July 19th

Please send any REPRIEVE related question you might have prior to the call to kfitch@mgh.harvard.edu!

1:00 PM US (EDT)
1:00 PM HAITI (EDT)
1:00 PM PERU (PET)
2:00 PM PUERTO RICO (ADT)
3:00 PM BRAZIL (BRT)
8:00 PM BOTSWANA (CAT)***
8:00 PM SOUTH AFRICA (SAST)***
8:00 PM ZIMBABWE (CAT)***
9:00 PM UGANDA (EAT)***
11:30 PM INDIA (IST)***
1:00 AM 04/20/2021 THAILAND (ICT)***
****We do not expect site staff to join these calls during their off-work hours*. Instead we will update you on other scheduled calls, e.g., your calls with the ACTG NCC.

Remember that questions are always welcome at actg.corea5332@fstrf.org and if there are slides used for a call, they are available on the PSWP in the Protocol Training >> Site Calls folder.

REPRIEVE (A5332): Are You Up to Date?

For A5332 please use:
***New version!* Protocol Version 6.0** *dated 05/16/2022*
***New version!* MOPS Version 6.0** *dated 06/10/2022*
***Revised version!* LPC for ACTG Sites Version 6.0** *dated 06/03/2022*
***Revised version!* LPC for Non-ACTG Sites Version 6.0** *dated 06/10/2022*
These documents are on the A5332 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

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