UC San Diego

UC San Diego Previously Published Works

Title

Participant experiences in HIV cure-directed trial with an extended analytical treatment interruption in Philadelphia, United States.

Permalink

https://escholarship.org/uc/item/2f58j0vq

Journal

HIV Research & Clinical Practice, 24(1)

Authors

Bilger, Andrea

Plenn, Eion

Barg, Frances

et al.

Publication Date

2023-10-06

Peer reviewed

eScholarship.org Powered by the California Digital Library
University of California

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

HIV Res Clin Pract. Author manuscript; available in PMC 2024 October 14.

Published in final edited form as:

HIV Res Clin Pract. 2023 October 06; 24(1): 2267825.

Participant Experiences in HIV Cure-Directed Trial with an Extended Analytical Treatment Interruption in Philadelphia, United States

Andrea Bilger[*,1], **Eion Plenn**[*,1], **Frances K. Barg**[1], **Katharine A. Rendle**[1], **William B. Carter**[2], **Andrea Lamour-Harrington**[2], **Nora Jones**[2], **Beth Peterson**[3], **John A. Sauceda**[4], **Pablo Tebas**[5], **Karam Mounzer**[6], **David Metzger**[7], **Luis J. Montaner**[3], **Karine Dubé**[8,9]

[1]Department of Family Medicine and Community Health, University of Pennsylvania, Pennsylvania, PA, USA

[2]BEAT-HIV Delaney Collaboratory Community Advisory Board, Philadelphia, PA, USA

[3]Wistar Institute, Philadelphia, PA, USA

[4]Division of Prevention Sciences, Department of Medicine, Center for AIDS Prevention Studies (CAPS), University of California, San Francisco, CA, USA

[5]Hospital of the University of Philadelphia, University of Pennsylvania, Pennsylvania, PA, USA

[6]Philadelphia FIGHT Community Health Centers, Philadelphia, PA, USA

[7]Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Pennsylvania, PA, USA

[8]University of California San Diego School of Medicine, Division of Infectious Diseases and Global Public Health, Chapel Hill, NC, USA

[9]Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Abstract

Background: A feature of HIV cure trials is the need to interrupt treatment to test the efficacy of experimental interventions – a process known as analytical treatment interruptions (ATIs).

Objectives: We report the experiences of participants after they completed an extended ATI.

Corresponding Author Karine Dubé, DrPH, MPhil, UCSD School of Medicine, Division of Infectious Diseases and Global Public Health, 9500 Gilman Drive, MC, 0507, La Jolla, CA, 92093-0507, kdube@health.ucsd.edu.

*Eion Plenn and Andrea Bilger are joint first authors.

Authorship Contribution Statement

Conceptualization: F.K.B., K.A.R., D.M., and K.D. Data Curation: A.B., E.P. Project Administration: A.B., E.P. Formal Analysis and Investigation: K.D., F.K.B., K.A.R., N.J. Funding Acquisition: F.K.B., K.A.R., L.J.M. Supervision: F.K.B., K.A.R., L.J.M. Writing – original draft preparation: A.B., E.P., L.J.M. and K.D. All authors reviewed and edited manuscript drafts including the final draft of the manuscript.

Authors' Disclosure

KD provides advisory services to Gilead Sciences, Inc. All other authors declare that they have no competing interests.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Methods: From April – November 2022, we conducted post-ATI in-depth interviews with BEAT2 clinical trial (NCT03588715) participants who stopped ART while receiving an immunotherapy regimen. We used conventional content analysis to code the data.

Results: We conducted interviews with 11 Black/African American and 3 White/Caucasian participants (11 males, 2 females and 1 transgender woman). The mean ATI was 38 weeks. Participants noted several significant experiences surrounding the interventions' side effects, ATI, and returning to medication. Some participants had positive experiences in the ATI. Other participants were nervous during the ATI. Rising viral loads led some to feel a sense of failure. Although trial experiences were heterogeneous, participants unanimously had positive interactions with the clinical trial staff which facilitated their retention in the trial. Participants shared their experiences with the trial, including changes in expectations, experiences with experimental interventions and procedures, compensation as a measure of respect, effort, transportation, and effects of COVID-19 during the trial. Based on these results, we provide considerations for the conduct of future HIV cure-directed clinical trials involving ATIs.

Conclusions: Managing expectations, focusing on participants' contributions, and providing support to reduce feelings of having failed the research team and/or the HIV community following viral rebound should be part of HIV cure trial design. Discussing the mental health impact of rebound during consent, distinct from risk, is needed. Continued efforts to understand how people with HIV experience ATIs will improve future designs of HIV cure clinical trials.

Keywords

HIV cure research; socio-behavioral research; people with HIV; analytical treatment interruptions; participant experiences; qualitative research

Introduction

Research towards an HIV cure represents a scientific priority for the United States (U.S.) National Institutes of Health (NIH), industry, private foundations, and the community of people with HIV [1]. HIV cure-directed research pursues two scientific aims – either complete elimination of HIV from the body or durable antiretroviral (ART)-free virologic suppression. Several HIV cure-directed strategies are currently being investigated, including immune-based approaches such as broadly neutralizing antibodies, cell and gene therapies, latency-reversal or permanent silencing agents, or combinatorial approaches [2]. These novel HIV cure-directed research interventions remain in the early stage and have limited prospects of direct clinical benefits for trial participants [3,4].

A distinctive feature of HIV cure-directed trials is the need to interrupt treatment to test the efficacy of experimental interventions aimed at keeping HIV suppressed in the absence of therapy – a process known as analytical treatment interruptions (ATIs). In recent years, the field of HIV cure-directed research has witnessed growing consensus that extended periods of treatment interruptions lasting a few weeks to a few months may be necessary to test investigational HIV cure-directed approaches aimed at modulating the immune system to reduce HIV burden [5]. ATI strategies in cure-directed research may also include allowance for periods of viremia before restarting ART to allow for viral control if it is

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

to be observed. ATIs present physical and psychosocial risks for participants (e.g., the possibility of developing resistance to ART or anxiety related to being off ART causing disease progression), in addition to the risk of transmitting HIV to sex partners [5]. For safety reasons, careful monitoring of people with HIV is required during and after ATIs, which requires frequent trial visits and biological sampling. Involving community members in co-creating socio-behavioral research efforts on the impact of ATIs on trial participants helps honor the long history of community engagement in HIV-related research [6-10].

The last decade has observed accumulating knowledge about the ethics of HIV cure trials and ATIs [5,11-20]. Ethical issues specific to ATIs include ensuring acceptable risks/benefits to participants [15], and protecting sex partners from acquiring HIV [21-24]. Studies involving ATIs must also meet basic ethical criteria, such as strong scientific rationale and robust informed consent [14]. Most efforts to understand patient/participant perspectives undergoing ATIs have focused on short-term ATIs lasting a few days to few weeks. Little is known about how people with HIV experience extended ATIs that may require periods of viremia in individuals who have previously been undetectable on ART.

The BEAT-HIV Delaney Collaboratory (https://beat-hiv.org/) was created in 2016 to help advance the search towards an HIV cure. In 2019, the Collaboratory initiated a clinical trial titled "*A Pilot Phase I Randomized Study to Evaluate Innate Immune Activation Predictors of Sustained Viral Control in Adults with HIV Undergoing an Analytical Treatment Interruption after Administration of Pegylated Interferon (PEG-IFN) Alpha 2b in Combination with Two Intravenous Broadly HIV-1 Neutralizing Antibodies 3BNC117 and 10-1074*" (NCT03588715) (hereafter referred to as BEAT2 trial). In this trial, all participants stopped ART while receiving 24 weeks of immunotherapy (seven infusions of two broadly neutralizing antibodies and weekly pegylated interferon alpha 2b) before an open-ended follow-up without any further intervention (Table 1). Participants were off ART (and immunotherapy) until they met criteria to resume ART. The BEAT2 trial overlapped with the COVID-19 pandemic.

The BEAT-HIV Community Advisory Board (CAB) together with larger Community Engagement Group (CEG) [25] helped co-create a nested socio-behavioral sub-study to assess how participants perceived and experienced the trial. The BEAT-HIV CEG decided to conduct qualitative interviews with participants at two timepoints in the BEAT2 trial: 1) shortly following enrollment, and 2) after participants had resumed their ART following the extended ATI. Results from enrollment interviews were previously published [6] reporting participants' motivations for joining the trial. The most prominent motivation reported was the altruistic desire to help find a cure for HIV and to benefit the HIV community [6]. Building on these results, we describe in this report the perspectives and experiences of BEAT2 participants following completion of the trial inclusive of an extended ATI.

Methods

Participants and Setting

We followed principles of community-based participatory research (CBPR) [26,27] to design the BEAT2 participant experiences study. BEAT-HIV CEG members collaborated

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

with investigators to design and implement the study, analyze the data, and discuss implications of the findings. We chose qualitative interviews to elicit participants' experiences with the clinical trial, the extended ATI, and returning to HIV medication after the trial, from their perspective. Secondarily, interviews shed light on the effects of COVID-19 and participant perspectives on COVID-19 vaccination during the clinical trial [28,29].

All interview participants were people who participated in the BEAT2 trial [6]. Participants provided informed consent prior to the interview. To be eligible, participants had to be 18 years or older, speak English, meet the inclusion and exclusion criteria for the clinical trial such as history of viral suppression and confirmation at entry and absence of major medical issues. All trial participants were people chronically living with HIV on stable ART regimens (sustained adherence) with long-standing relationship with their provider (> 7 years) and were engaged in their medical care with 4 to 6 visits per year. Prior to undergoing an ATI in the parent trial, participants were counseled on safer sex, and had an in-depth discussions regarding the value of pre-exposure prophylaxis (PrEP) offered for their sex partners without HIV.

Data Collection

From April – November 2022, we conducted post-ATI interviews with BEAT2 clinical trial participants. Trained interviewers from the University of Pennsylvania Mixed Methods Research Lab (MMRL) conducted all interviews by telephone with audio recording with the participants' permission. All interviewees were asked questions from the Institutional Review Board (IRB)-approved interview guide (Table 2). Interviews lasted approximately 30 minutes (range 15–53 minutes) and elicited participant experiences during the trial and the extended ATI, expectations about the trial, positive and negative aspects, experiences with ART restart, time and effort put into the clinical trial, hopes, and worries, concerns about COVID-19, and suggestions to improve the conduct of future clinical trial. Participants received $USD 50 following their interview.

Data Analysis

We transcribed all interviews verbatim, removed all potential identifiers, and entered the transcripts into NVivo Plus (version 1.6, Burlington, Massachusetts) for coding and analysis. We used conventional content analysis [30] to code the qualitative data. We developed the codebook iteratively to closely match key themes identified in the interviews. Two coders from the University of Pennsylvania MMRL established strong inter-rater reliability with three (23%) interviews. The remaining interviews were reviewed and coded independently. After coding all data, two research analysts examined each code for patterns and identified key themes.

Ethical Considerations

The University of Pennsylvania IRB reviewed and approved the participant experience study.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Results

In total, 14 persons with HIV participated in the BEAT2 clinical trial and all of them also completed the post-ATI interview. Most were aged above 50 years old. Participants included 11 Black/African American and 3 White/Caucasian participants. There were 11 males, 2 females and 1 transgender woman (Table 3). The mean ATI was 38 weeks in duration.

Overall Experiences in the Clinical Trial

Motivations for Continuing Participation in the Clinical Trial and undergoing an ATI—The most common reasons people chose to continue participation in the clinical trial was their connection to the HIV community and a desire to prevent HIV transmission to others now or in the future. Participants also felt that being in the clinical trial gave meaning to their lives. To some, participation also had a deeper meaning of being a part of history. Some of these participants also had previous experiences in HIV research prior to enrolling in the clinical trial, which may have served as a motivating factor to continue in the trial, together with helping address HIV-related stigma.

> So, I've worked in HIV research since 2014. I've been living with HIV since 2007 and I feel like this is one of those things that my heart pulls towards helping to find a cure, helping to end stigma, finding ways of prevention. So, my [continued] participation in the study was me adding to the overall scheme of what I'm doing with my life.

> I feel the same way I thought about day one. I believe you hope that my contribution to this study will help give doctors or scientists more data to finding a cure. Finding a way to help people suppress their virus and again, helping people to prevent the spread of HIV.

Additionally, most participants had a desire to see the trial results after completion. Participants mainly expressed an interest in trial conclusions. Some participants asked to be contacted if there was any important information that could impact their health. Other participants wanted to know about the intervention efficacy and if the trial would lead to “something bigger,” such as a breakthrough in HIV cure research. One participant wanted to know what they specifically contributed to the research, while another had hoped they would help others with their participation.

Trust between participants and the clinical research staff was a key motivator and reason why many participants continued in the clinical trial and completed an ATI. A few participants explained that their trust with their clinical research staff made them less concerned about the side effects during the trial.

> Just kind of leery because I had never been off of the meds. So, I was a little leery, but me, personally, I really have a lot of faith in my doctors and… when I talk with them and they assure me that, "If anything was to take place, that we’ll go back to what it is that you need to do that, we're not forcing you to make this decision, that this is definitely a decision on your own. If you don't want to do it, you don't have to.” So, that's how I go along with my doctors, so if they feel like that, I'm going to

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

> be okay, I have enough trust in them that I believe that I'm going to be okay, and I was.

Change in Expectations—Many participants mentioned their expectations of the clinical trial changed since their baseline interview [6]. Some participants expressed the trial was more time consuming than they initially intended. Another participant mentioned their expectations shifted from remuneration to improving things for people with HIV in the future. Other participants expected to have a longer period of being undetectable for HIV during the ATI. When this was not the case, participants expressed disappointment in themselves for letting the HIV community down, a feeling they did not expect when entering the trial.

> I was hoping to make it through the three-month period after being taken off of everything, but I only made it about six weeks because my viral load started going up again. So, I'm back on my HIV medication now… I kind of feel like I let our community down. I mean, I'm not depressed about it, but I don't know. I was hoping I make it through the whole three-month area and then I could stay off my medications, but I don't know. I'm not saying I feel like a failure, but I just feel like I'd let the whole HIV community down.

Conversely, another participant mentioned their expectations changed in a positive way. This participant started into the trial thinking they would have a negative experience and was able to relax as the trial went on.

Perceived and Experienced Side Effects—Many participants said they did not experience any substantial physical side effects from the trial intervention or the ATI period. While the majority of participants reported an increase in viral load after the ATI, most said they had felt no physical effects associated with their increase in viral load. These participants said they expected to feel differently due to not being on their HIV medications and were relieved they did not experience any negative health outcomes. Overall, participants expressed relief at the lack of long-term physical side effects.

Perceived Experiences with Analytical Treatment Interruption

Perceived Positive Experiences from the ATI—Many participants mentioned feeling positive emotions towards ATIs, while other participants described negative experiences during this phase of the trial. Positive experiences included not taking HIV medication daily, having an undetectable viral load without taking HIV medication, appreciation for the lack of side effects and involvement in HIV research, and hope for the future of HIV therapeutics. As a result, participants felt more empowered, self-reliant, hopeful, and optimistic about living with HIV and the HIV pandemic.

Other participants expressed positive feelings after remaining undetectable during the ATI. One participant even mentioned their viral load was lower during the ATI than it had been before joining the trial.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

> Then [the clinical staff] were like, yes, we're finding fewer than four copies, and I'm like, holy crap, I am more undetectable than I was [before the trial], so yeah, there were some good times with that.

Some participants found comfort in their contributions to science, despite the shift from undetectable to detectable status. Others found comfort in not experiencing any side effects or getting sick during their ATI, despite their viral load increasing.

While emotions towards the ATI varied, many participants agreed that support from the clinical trial team eased their nerves and fears during the ATI.

Perceived Negative Experiences from the ATI—All participants who expressed negative feelings attributed these feelings to an increase in their viral load following viral rebound. The most common negative feelings included frustration, annoyance, anger, and despair. The second most common negative feelings were feelings of discomfort, nervousness, and "being scared." Many participants felt angered or frustrated that their status changed from undetectable to detectable. Some participants expressed feelings of disappointment because of their trial outcome and hoped the experimental intervention would last longer.

> I was hoping that there was a rare chance that these antibodies would really – like they were long-lasting but that they were really long lasting and that I would still be undetectable with just the antibodies, that's what I was hoping for. Like I knew it wouldn't last forever. So, I am grateful that from October to February without any antibodies maybe a little bit longer I was undetectable. That was exciting to me. Yeah so, I was just hoping it would be a little bit longer.

Overall, these feelings made many participants anxious about their health and made them fear they would get "kicked out" of the clinical trial.

> I did get a little frustrated, because I did not want to be kicked off the program. I knew… the least effect of the study was basically to see if there's a way of clearing the sanctuary spots… and I thought that was at least beneficial.

Of the participants who were frustrated or annoyed during the ATI, these feelings mainly revolved around an increase or "spike" in their viral load after being undetectable for many years. The increase in viral load during the ATI also made some participants feel uncomfortable and unsure.

> Because they've been, because I've been undetected [undetectable] for so long. Even before the study, I've been undetected for such a long time and just to see those numbers go up like that, I was kind of like and I was kind of worried like, okay, are they going to keep going up and not going to come back down, but they were certainly up, they are starting to decrease again, so and I just know that and a week or two, I think that I'll be undetectable again, so.

A couple of participants said they were initially nervous about the ATI but continuously monitoring their viral load eased some of their anxieties, such as fearing they could transmit the virus to their partners.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Experiences with ART Resumption—When asked what it felt like returning to HIV medication after the ATI, participants also expressed varying positive and negative emotions. Participants who expressed positive emotions mentioned returning to HIV treatment made them feel relieved and gave them a “peace of mind” since they could return to their previous undetectable status. Another participant mentioned feeling relieved because they could return to their HIV medications and resume work.

Participants also expressed a newfound appreciation for their HIV medications, saying they no longer take them for granted.

> So, I felt safe, and it was nice to take a break from them, but I was glad to go back on them when the numbers went bad. So, unfortunately, it didn't take long for the numbers to get back up to good again. So, I got a greater appreciation for my regular ART.

Negative emotions while limited were expressed through feelings of disappointment by going back to taking HIV pills, as participants had hoped the ATI would last longer.

> So, I’m back on a regimen that I didn't have to be on. So, it was depressing to me. I'm like, I need this to survive. I finished my interferon… and I think it was January or February. So not taking nothing to take even though I only take one pill to take in something like I said, I was depressed for a little over a week and I had to, I had to speak to the people that I use for sounding boards and for therapy. So, but it was depressing to me. Do I like taking [the pills]? No.

Some participants did not express any emotions towards returning to medication, saying that it was just an aspect of their life as a person with HIV, or that it just returned them back to the suppressed viral load that they started at.

Relationships with the Clinical Research Team—The most common positive experience was their relationship with clinical trial staff, which included nurses, physicians, administrators, and environmental services. Participants reported that these interpersonal connections made difficult experiences such as side effects of the interventions or anxieties of being off ART, more manageable. Participants valued when the clinical trial staff was caring, accommodating, effective communicators, and trustworthy. Participants appreciated the research team taking the time to get to know them during this trial, as this made the participants feel valued “like a human” or “feel like somebody.”

> So, I felt like I was in safe hands and that always makes a person feel valued. That makes them feel like, I'm not just a guinea pig or I'm not just a number and grand number of participants. I wasn't just a participant, I was a person.

One participant expressed feeling upset prior to an appointment and valued the research team’s empathetic and caring response to their emotional state.

Moreover, a few participants appreciated the staff’s ability to be effective communicators during the clinical trial process. Examples of effective communications included researchers explaining complicated research procedures, potential side effects, and what was going on in the participant’s bodies during the ATI.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Perceptions of Trial Procedures and Logistics—Some of the themes to come out of trial experience discussions were participants' perceptions of trial procedures and logistics. Some participants mentioned apheresis was the most time-consuming part of the trial; however, they did not feel like this negatively affected their trial experience. A couple of participants reported that a high number of blood draws and adhesive bandages used after injections made participation unpleasant; otherwise, there were no significant concerns mentioned with the trial procedures or interventions.

Several participants expressed appreciation for the clinical monitoring provided during the trial that gave them insight into their health status. This included biopsies, eye exams, and routine blood work.

When asked about experiences travelling to the trial site, participants reported minimal barriers to transportation and had no difficulty scheduling appointments. A few participants who did not always take public transportation said they had difficulty parking on site while another participant talked about the distance to the trial site. Participants also valued accommodations made for them by the staff. Accommodations included setting up transportation and coordinating appointments around participants' hectic schedules.

Perceptions of Compensation and Effort

Perceptions of Compensation—In general, most participants were either satisfied with their compensation during the trial or did not feel like compensation was important to their participation. However, one participant felt that compensation made a difference in their decision to participate, and a minority of participants felt like compensation was not enough or could have been more. Many participants were grateful for the compensation, as they could cover costs of transportation, time off from work, and even a "lunch out." Still, many participants expressed compensation was not important to them to be part of the trial. These participants said they would have participated regardless due to their own intrinsic motivating factors.

Perceived Effort—Half of the participants said the effort required to put into the trial was minimal or the trial only required "a little bit" of effort. The other half of the participants said they put in a lot of time and effort. Some participants expressed feeling overwhelmed during the clinical trial. These feelings were often due to the participants' employment or living situation, as well as difficulties with transportation.

Overall, regardless of the amount of effort put in, participants unanimously agreed that the time and effort put into the trial was worth it for the trial outcome. Like compensation, they would do the trial regardless of the amount of effort required because of their intrinsic motivations to participate and helping find a cure for HIV.

Perceived Effects of COVID-19—For most participants, the COVID-19 pandemic did not negatively affect their participation in the trial. This was due to protocols being in place at the research site, such as routine COVID-19 testing and masking requirements, as well as precautions exercised by individual participants, such as physical distancing. Participants highlighted these precautions and said they made them feel safer during the trial and did not

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

interfere with it. A participant who took public transportation during COVID-19 expressed having negative experiences getting to trial visits.

Participant Suggestions to Improve Future HIV Cure-Directed Clinical Trials— Overall, most participants were satisfied with the clinical trial experience and did not have any substantial suggestions for improving the clinical trial experience. A few participants offered various suggestions, such as the emphasis of the positive experience with the clinical trial staff and suggested future trial operations emulate similar staff practices. One participant emphasized participant education and informing future participants on the details of the trial procedures, such as the number of blood draws. Another participant mentioned providing a follow-up survey to participants for evaluating their mental health.

Table 4 provides additional quotes related to the above themes.

Discussion

Our nested qualitative interview study provides a window into the perspectives and experiences of BEAT2's trial participants having completed an extended ATI period. Participants noted several significant experiences surrounding the interventions' side effects, ATI, and returning to medication. Some participants found positive experiences in the ATI and noted it made them feel self-confident, empowered, and brought a newfound appreciation for their HIV medications. Other participants were frustrated, anxious, and nervous during the ATI, especially after experiencing viral rebound. Although trial experiences were highly heterogeneous, participants unanimously had positive interactions with the clinical trial staff which facilitated their retention in the trial and brought them a sense of comfort, together with the close clinical monitoring. At the time of interview, participants had completed the ATI and had just returned to their HIV medications and their perceptions reflected this. Participants also shared their experiences with the trial, including changes in expectations, experimental interventions, procedures, compensation, effort, transportation, and effects of COVID-19. Most participants noted that they had an overall positive experience in the clinical trial.

Our socio-behavioral study advances the multi-disciplinary literature [31,32] on HIV cure-directed research by documenting experiences of predominantly Black/African American participants in an extended ATI trial in Philadelphia, United States. Indeed, in the global landscape of HIV cure-directed research [33-36], the BEAT2 trial is significant in terms of participant demographics. To our knowledge, the parent trial is one of the first to report predominant enrollment of Black/African American participants in an extended ATI in the United States [6]. As Seifer and colleagues proposed over a decade ago, clinical trial participation has become an issue of social justice [27].

Altruistic motivations for continued participation and trial completion remained consistent throughout the BEAT2 trial and mirrored those found during the baseline interviews [6]. The sense of accomplishment from participating in the BEAT2 trial observed during baseline interviews [6] was validated during the post-ATI interviews. Prior research similarly documented scientific altruism among ATI trial participants [12,17,37,38]. BEAT2

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

participants understood the trial in terms of production of incremental scientific knowledge [39]. A small proportion of participants expressed hope for a good personal outcome, a phenomenon known as therapeutic optimism, which may not be ethically problematic [40]. Nevertheless, a small proportion of participants in our study expressed a desire to have HIV taken out of their bodies and their lives, possibly representing a form of therapeutic or even curative misestimation – i.e., overestimating benefits and under-estimating risks – particularly for cure strategies aimed at durable ART-free suppression [40]. While some levels of therapeutic misestimation in HIV cure-directed trials is expected in a minority of trial participants, as shown elsewhere [16,17,37,38], this finding underscores the importance of robust informed consent and providing regular information to participants during early-phase HIV cure-directed clinical trials aimed at sustained ART-free control [37,41].

The fact that BEAT2 participants were interested in seeing the trial results and knowing how they individually contributed to HIV cure-directed research speaks to the critical importance of disseminating data in lay terms to them and other community members in a timely manner following completion of clinical trials. This aligns with the philosophy that trial participants are critical partners in research as noted in baseline interview [6]. Some BEAT2 participants experienced shorter post-intervention control than expected and were disappointed in themselves and worried about letting the HIV community down. This finding critically emphasizes that research teams have an important role in managing expectations about the potential outcomes of clinical trials and designing counseling strategies in support of study participants at the start of viremia during an ATI. Specifically, study staff need to emphasize participants' contributions and provide support to reduce feelings of having failed the research and the HIV community following viral rebound. Further, while the usual ethical emphasis is on communicating risks and benefits (or lack thereof) to trial participants, much less guidance has been offered around communicating uncertainty or dealing with periods of potential emotional distress such as viral rebound period. Apart from trial risks, emphasizing at consent and during trial visits that outcomes may involve the probability of rebound. As a result, a lack of viral control is not a failure as it informs scientific effort. Stressing the real possibility and unpredictable nature of viral rebound in the context of ATIs could help advance the science of communicating scientific uncertainty [42,43].

Moreover, BEAT2 participants recounted mixed experiences with resuming ART following their ATI. For most, ART restart provided peace of mind and a newfound appreciation for HIV medications, while other participants expressed disappointment with resuming ART and worried about the long-term side effects of treatment. These findings echo those of two prior studies which showed greater awareness of feeling in control of HIV while resuming ART post-ATI [17,37]. Our study revealed that some participants may need closer counseling and support during the period of ART resumption. Medical providers should also be sensitized to communicate to participants the anticipated period that may be needed before re-suppression is established. At the time of writing this manuscript, all BEAT2 participants had re-suppressed viral loads to undetectable levels. Our findings emphasize adopting a journey approach to HIV cure-directed trial participation and providing adequate support to participants throughout the entire process.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

While most participants did not experience an impact of the trial on their mental and emotional health, our findings that some participants experienced episodes of anxiety from being off ART warrant attention as current clinical trial protocols (including the current parent trial) do not mandate any customized support to identify participants where this may be occurring. There is increasing evidence, beyond anecdotal reports, that persons with HIV experience anxiety during ATIs [17,37]. A similar nested socio-behavioral study in Belgium found participants under-estimated the emotional impact for their ATI, which was accompanied with a sense of losing control [37]. In that study, many participants found the ATI alienating, burdensome and stressful, corroborating findings from our study. This cumulative evidence of mental health impact underscores the importance of capturing the diverse psychosocial trajectories of participants in real-time before, during and after clinical trials. In our study, worries appeared more prominent following viral load rebound and during the period of viral load re-suppression. Based on these findings and explicit suggestions from BEAT2 trial participants, we recommend frequent mental health checks during ATI trials, having health psychologists as part of the trial team to help mitigate psychological effects, and adopting holistic person-centered clinical trial designs. We also recommend research teams to include some of the concerns of extended ATIs noted in this study (e.g., anxiety of being off ART) in future informed consent forms to adequately portray ATI-related risks to prospective trial participants. There should also be adequate support for partner protections during ATI trials to reduce feelings of anxiety [21,22].

The close relationship with the clinical team and the feeling of trust facilitated trial retention and were reported as highlights for all trial participants. In baseline interviews, BEAT2 participants praised the clinical research team for their professionalism and communication [6]. Two similar studies [12,37] showed the critical importance of interpersonal aspects of clinical research participants, which in turn blurred the boundaries between research and clinical care [12]. Participants in our study appreciated routine clinical monitoring procedures, which conferred feelings of oversight and medical awareness. These ancillary or indirect benefits – also called inclusion benefits [44,45] – counter-balanced ATI-related worries and contributed to participation satisfaction. Another socio-behavioral study conducted in North Carolina showed that almost all (16/17) participants valued these indirect health care benefits [46].

Our study called some attention to the importance of logistical and practical factors, such as transportation, time commitments, and burdens of participation. These themes are consistent with prior socio-behavioral research focused on HIV cure-directed studies [17,38,46]. While compensation was not the main reason BEAT2 participants joined the trial, it was still perceived as a sign of appreciation and respect. Ethical guidelines have focused on avoiding the possibility of coercion and undue inducement in deciding trial payments [47]. Our study revealed that adequate payments can go a long way in making participants feel valued for their contributions. Finally, the BEAT2 trial persisted despite the COVID-19 pandemic. Risk mitigation measures, adaptations during the trial [48], and encouraged vaccination offset the risks of COVID-19 and allowed HIV cure-directed research efforts to continue.

Table 5 summarizes considerations for future HIV cure clinical research emerging from our findings. These points for consideration were developed in close collaboration with the

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

BEAT-HIV CAB in the hopes that they would generate critical dialogue about extended ATIs among key stakeholders.

Limitations

We must acknowledge study limitations. Our sample size was small and predominantly male, consistent with the parent BEAT2 clinical trial. We leave open the possibility that we did not achieve thematic saturation [49]. Our results may have been thinner on some topics (e.g., effects of COVID-19). Due to the qualitative nature of this study, the results were emergent, and we did not quantify the number of participants who responded in certain ways. The hallmark of qualitative research is particularity, not generalizability. Interviews did not delve into partner protections used during the ATI, and we did not capture psychosocial experiences prospectively during the ATI. We suspect some recall bias with the retrospective study design. We did not capture the reactions of researchers upon hearing about the present findings, as this would constitute a separate sub-study. It would be important, however, to question researchers on their perspectives as well. This was a single-institution study and findings cannot be generalized to other clinical trial sites outside of Philadelphia, United States. Nevertheless, the findings reported here have internal validity with respect to the participants who took part in the BEAT2 extended ATI trial.

Conclusions

Our nested socio-behavioral study highlights the feasibility and importance of multi-disciplinary HIV cure research to examine and appreciate participant values and lived experiences, and improve trial designs inclusive of steps to address mental wellness. We identified key points for intervention and participant support during HIV cure-directed studies involving extended ATIs. Managing expectations, focusing on participants' contributions, and providing psychosocial support to reduce feelings of having failed the research team and/or the HIV community following viral rebound should be critical components of future trial design. Continued efforts to understand how persons with HIV experience ATIs will improve future clinical trial designs and lead us closer to a human-centered cure.

Acknowledgements

The authors are indebted to all the BEAT2 trial participants. We are also grateful to the BEAT-HIV Collaboratory, the BEAT-HIV Community Engagement Group (CEG), Philadelphia FIGHT Community Health Centers, and the University of Pennsylvania. We would like to thank Rease Maddox, Roy Hayes, Marcus Hill, Christopher Roebuck and William (Bill) Freshwater from the BEAT-HIV CAB, and Waheedah Shabazz-El who chaired the CAB when the socio-behavioral study was first conceptualized. We would also like to thank Kenneth M. Lynn from the Hospital of the University of Pennsylvania and Linden Lalley-Chareczko from Philadelphia FIGHT Community Health Centers. We are grateful to Jim Riley from the BEAT-HIV CEG, and Amy Onorato who serves as BEAT-HIV Community Engagement Coordinator. We would like to thank Rebecca Neergaard and Caroline O'Brien from the University of Pennsylvania Mixed Methods Research Laboratory.

Funding Statement

This work was funded by a pilot grant from the Penn Mental Health AIDS Research Center (PMHARC), an NIH-funded program (P30 MH 097488). It was also supported by UM1AI126620 and UM1AI164570 (BEAT-HIV Collaboratory) which is co-supported by the National Institute of Allergies and Infectious Diseases (NIAID), the National Institute of Mental Health (NIMH), the National Institute of Neurological Disorders and Stroke (NINDS), the National Institute on Drug Abuse (NIDA), and the Robert I. Jacobs Fund of The Philadelphia Foundation. LJM

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

is also supported by the Herbert Kean, M.D., Family Professorship. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. J.A.S. and K.D. received support from R01-MH126768.

References

1. Deeks SG, Archin N, Cannon P, Collins S, Jones RB, de Jong M, et al. Research Priorities for an HIV Cure: International AIDS Society Global Scientific Strategy 2021. Nat Med. 2021. doi:10.1038/s41591-021-01590-5
2. TAG. Research Toward a Cure Trials. 2023. Available: http://www.treatmentactiongroup.org/cure/trials
3. Dresser R. First-in-Human HIV-Remission Studies: Reducing and Justifying Risk. J Med Ethics. 2017;43: 78–81. doi:10.1136/medethics-2015-103115 [PubMed: 27143494]
4. Dubé K, Henderson GE, Margolis DM. Framing Expectations in Early HIV Cure Research. Trends Microbiol. 2014;22: 547–9. doi:10.1016/j.tim.2014.08.003 [PubMed: 25280965]
5. Julg B, Dee L, Ananworanich J, Barouch D, Bar K, Caskey M, et al. Recommendations for Analytical Treatment Interruptions in HIV Research Trials. Report of a Consensus Meeting. Lancet HIV. 2019;6: e259–68. [PubMed: 30885693]
6. Neergaard R, Jones NL, Roebuck C, Rendle KA, Barbati Z, Peterson B, et al. "I know that I was a part of making a difference": Participant Motivations for Joining a Cure-Directed HIV Trial with an Analytical Treatment Interruption. AIDS Res Hum Retroviruses. 2022;39: 414–21. doi:10.1089/aid.2022.0040 [PubMed: 35979886]
7. The Denver Principles. In: ACT Up Historical Archive [Internet]. 1983 [cited 4 Oct 2021]. Available: https://actupny.org/documents/Denver.html
8. AIDS United. Meaningful Involvement of People with HIV/AIDS (MIPA). 2021 [cited 5 Oct 2021]. Available: https://www.aidsunited.org/resources/meaningful-involvement-of-people-with-hivaids-mipa
9. Lau J, Smith M, Allan B, Dubé K, Young A, Power J. Time for Revolution? Enhancing Meaningful Involvement of People Living with HIV in HIV Cure-Focused Science. J Virus Erad. 2020;6: 100018. [PubMed: 33251026]
10. Karris MY, Dubé K, Moore AA. What Lessons It Might Teach Us? Community Engagement in HIV Research. Curr Opin HIV AIDS. 2019;Dec 30. doi:10.1097/COH.0000000000000605
11. Henderson GE, Waltz M, Meagher K, Cadigan RJ, Jupimai T, Phanuphak N, et al. Going Off Antiretroviral Treatment in a Closely Monitored HIV "Cure" Trial: Longitudinal Assessments of Acutely Diagnosed Trial Participants and Decliners. Journal of the International. 2019;22: e25260. doi:10.1002/jia2.25260
12. Henderson GE, Peay HL, Kroon E, Cadigan RJ, Meagher K, Jupimai T, et al. Ethics of Treatment Interruption Trials in HIV Cure Research: Addressing the Conundrum of Risk/Benefit Assessment. J Med Ethics. 2018;44: 270–6. doi:10.1136/medethics-2017-104433 [PubMed: 29127137]
13. Dubé K, Evans D, Dee L, Sylla L, Taylor J, Weiner BJ, et al. "We Need to Deploy Them Very Thoughtfully and Carefully": Perceptions of Analytical Treatment Interruptions in HIV Cure. AIDS Res Hum Retroviruses. 2018;34: 67–79. doi:10.1089/aid.2017.0067 [PubMed: 28562069]
14. Garner SA, Rennie S, Ananworanich J, Dubé K, Margolis DM, Sugarman J, et al. Interrupting Antiretroviral Treatment in HIV Cure Research: Scientific and Ethical Considerations. J Virus Erad. 2017;3: 82–4. [PubMed: 28435691]
15. Eyal N, Holtzman LG, Deeks SG. Ethical Issues in HIV Remission Trials. Curr Opin HIV AIDS. 2018;13: 422–7. doi:10.1097/COH.0000000000000489 [PubMed: 30015634]
16. Diepstra KL, Barr L, Palm D, Hogg E, Mollan KR, Henley L, et al. Participant Perspectives and Experiences Entering an Intensively Monitored Antiretroviral Pause: Results from the AIDS Clinical Trials Group A5345 Biomarker Study. AIDS Res Hum Retroviruses. 2021;37: 489–501. doi:10.1089/aid.2020.0222 [PubMed: 33472545]
17. Dubé K, Eskaf S, Barr L, Palm D, Hogg E, Simoni JM, et al. Participant Perspectives and Experiences Following an Intensively Monitored Antiretroviral Pause in the United States: Results from the AIDS Clinical Trials Group A5345 Biomarker Study. AIDS Res Hum Retroviruses. 2022;38: 510–7. [PubMed: 35323030]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

18. Arnold M, Evans D, Vergel N. Recruitment and Ethical Considerations in HIV Cure Trials Requiring Treatment Interruption. J Virus Erad. 2015;1: 43–48. [PubMed: 27482394]
19. Lo B, Grady C. Ethical Considerations in HIV Cure Research: Points to Consider. Curr Opin HIV AIDS. 2013;8: 243–9. doi:10.1097/COH.0b013e32835ea1c5 [PubMed: 23422260]
20. Dubé K, Kanazawa J, Taylor J, Dee L, Jones N, Roebuck C, et al. Ethics of HIV Cure Research: An Unfinished Agenda. BMC Med Ethics. 2021;22: 1–14. doi:10.1186/s12910-021-00651-1 [PubMed: 33388052]
21. Peluso MJ, Dee L, Campbell D, Taylor J, Hoh R, Rutishauser RL, et al. A Collaborative, Multidisciplinary Approach to HIV Transmission Risk Mitigation during Analytic Treatment Interruption. J Virus Erad. 2020;6: 34–7. [PubMed: 32175090]
22. Dubé K, Kanazawa JT, Dee L, Taylor J, Campbell DM, Brown BJ, et al. Ethical and Practical Considerations for Mitigating Risks to Sexual Partners during Analytical Treatment Interruptions in HIV Cure-Related Research. HIV Res Clin Pract. 2021;Mar 24: 1–17. doi:doi: 10.1080/25787489.2021.1902116
23. Dawson L. Human Immunodeficiency Virus Transmission Risk in Analytical Treatment Interruption Studies: Relational Factors and Moral Responsibility. J Infect Dis. 2019;220: S12–15. doi:10.1093/infdis/jiz090 [PubMed: 31264689]
24. Eyal N. How to Address the Risk of HIV Transmission in Remission Studies With Treatment Interruption: The Low-Hanging Fruit Approach. J Infect Dis. 2019;220: S7–11. doi:10.1093/infdis/jiz163 [PubMed: 31264692]
25. Dubé K, Peterson B, Jones NL, Onorato A, Carter WB, Dannaway C, et al. Community Engagement Group Model in Basic and Biomedical Research: Lessons Learned from the BEAT-HIV Delaney Collaboratory Towards an HIV-1 Cure. Res Involv Engagem. 2023;9: 1–17. doi:10.1186/s40900-023-00449-y [PubMed: 36739420]
26. Wallterstein N, Duran B, Oetzel J, Minkler M. Community-Based Participatory Research for Health: Advancing Social and Health Equity. Jossey-Bas. San Francisco, CA; 2017.
27. Seifer SD, Michaels M, Collins S. Applying Community-Based Participatory Research Principles and Approaches in Clinical Trials: Forging a New model for Cancer Clinical Research. Prog Community Health Partnersh. 2010;4: 37–46. [PubMed: 20364077]
28. Cresswell J. Research Design. Qualitative, Quantitative, and Mixed Methods Approaches. 4th ed. Sage Publications; 2013.
29. Cresswell J. Turning the Story. Qualitative Inquiry and Research Design. 1998. pp. 219–29.
30. Hsieh HF, Shannon SE. Three Approaches to Qualitative Content Analysis. Qual Health Res. 2005;15: 1277–88. doi:10.1177/1049732305276687 [PubMed: 16204405]
31. Grossman CI, Ross AL, Auerbach JD, Ananworanich J, Dubé K, Tucker JD, et al. Towards Multidisciplinary HIV-Cure Research: Integrating Social Science with Biomedical Research. Trends Microbiol. 2016;24: 5–11. doi:10.1016/j.tim.2015.10.011 [PubMed: 26642901]
32. Dubé K, Auerbach JD, Stirratt MJ, Gaist P. Applying the Behavioural and Social Sciences Research (BSSR) Functional Framework to HIV Cure Research. J Int AIDS Soc. 2019;22: e25404. [PubMed: 31665568]
33. Barr L, Jefferys R. A Landscape Analysis of HIV Cure-Related Clinical Trials and Observational Studies in 2018. J Virus Erad. 2019;5: 212–9. [PubMed: 31754444]
34. Barr L, Jefferys R. A Landscape Analysis of HIV Cure-Related Clinical Research in 2019. J Virus Erad. 2020;6: 100010. doi:10.1016/j.jve.2020.100010 [PubMed: 33294212]
35. Johnston R, Heitzeg M. Sex, Age, Race and Intervention Type in Clinical Studies of HIV Cure: A Systematic Review. AIDS Res Hum Retroviruses. 2015;31: 85–97. [PubMed: 25313793]
36. Roberts C, Creamer E, Bonne C, Young A, Magnus M. Short Communication: Population Representative in HIV Cure Research: A Review of Diversity within HIV Cure Studies based in the United States. AIDS Res Hum Retroviruses. 2022;38: 631–44. [PubMed: 35018803]
37. De Scheerder M, Van Bilsen WPH, Dullaers M, Martinez-picado J, Davidovich U, Vandekerckhove L. Motivations, Barriers and Experiences of Participants in an HIV Reservoir Trial. J Virus Erad. 2021;7: 100029. doi:10.1016/j.jve.2021.100029 [PubMed: 33598311]
38. Dubé K, Hosey L, Starr K, Evans D, Hoffman E, Campbell D, et al. Participant Perspectives in an HIV Cure-Related Trial Conducted Exclusively in Women in the United States: Results

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

from AIDS Clinical Trials Group (ACTG) 5366. AIDS Res Hum Retroviruses. 2020;36: 268–82. doi:doi: 10.1089/AID.2019.0284 [PubMed: 32160755]

39. Dubé K, Taylor J, Sylla L, Evans D, Dee L, Burton A, et al. 'Well, It's the Risk of the Unknown … Right ?': A Qualitative Study of Perceived Risks and Benefits of HIV Cure Research in the United States. PLoS One. 2017;12: e0170112. [PubMed: 28122027]
40. Horng S, Grady C. Misunderstanding in Clinical Research: Distinguishing Therapeutic Misconception, Therapeutic Misestimation, and Therapeutic Optimism. IRB. 2003;25: 11–6.
41. Henderson GE. The Ethics of HIV 'Cure' Research: What Can We Learn from Consent Forms? AIDS Res Hum Retroviruses. 2015;31: 56–63. [PubMed: 25406579]
42. Simpkin AL, Armstrong KA. Communicating Uncertainty: A Narrative Review and Framework for Future Research. J Gen Intern Med. 2019;34: 2586–2591. doi:10.1007/s11606-019-04860-8 [PubMed: 31197729]
43. Hare C. Risk and Radical Uncertainty in HIV Research. J Med Ethics. 2017;43: 87–9. doi:10.1136/medethics-2015-103117 [PubMed: 27670811]
44. Lantos J. The "Inclusion Benefit" in Clinical Trials. Journal of pediatrics. 1999; 130–131.
45. Rennie S, Day S, Mathews A, Gilbertson A, Luseno W, Tucker J, et al. The Role of Inclusion Benefits in Ethics Committee Assessment of Research Studies. Ethics Human Res. 2019;41: 13–22. [PubMed: 31108576]
46. Gilbertson A, Kelly EP, Rennie S, Henderson G, Kuruc J, Tucker JD. Indirect Benefits in HIV Cure Clinical Research: A Qualitative Analysis. AIDS Res Hum Retroviruses. 2019;35: 100–7. doi:10.1089/aid.2017.0224 [PubMed: 30009625]
47. Gelinas L, Largent EA, Cohen IG, Kornetsky S, Bierer BE, Lynch HF. A Framework for Ethical Payment to Research Participants. N Engl J Med. 2018;378: 766–71. [PubMed: 29466147]
48. Peluso MJ, Dee L, Shao S, Taylor J, Campbell D, Collins S, et al. Operationalizing HIV Cure-Related Trials with Analytic Treatment Interruptions during the SARS-Cov-2 Pandemic: A Collaborative Approach. Clinical Infectious Diseases. 2021;72: 1843–9. [PubMed: 32841311]
49. Guest G. How Many Interviews Are Enough?: An Experiment with Data Saturation and Variability. Field methods. 2006;18: 59–82. doi:10.1177/1525822X05279903

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1:

BEAT2 Trial Scheme

	Time Period	Study Steps
Step 1	0 weeks	ART* + Baseline evaluation (innate response measures, leukapheresis /rectal biopsy, ophthalmic evaluation) ***Qualitative Interview*** [6]
Step 2	4 weeks	ART + Pegintron injections
Step 3	26 weeks	ATI + Pegintron injections + Broadly Neutralizing Antibodies Intravenous (IV) infusions
Step 4	12 weeks	ATI + Follow Up
Step 5	12 weeks	Return to ART, optional continued ATI **Qualitative Interview**

*ART = Antiretroviral Therapy; ATI = Analytical Treatment Interruption

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2:

BEAT2 Participant Experience Study Post-ATI Interview Guide

1. What has been your experience in the clinical trial up to now?
2. Let's think about what you expected about been off HIV treatment when you first joined the clinical study. What were some of your original expectations of being in the clinical trial?
3. What, if any, have been some positive experiences that stood out to you during the clinical trial so far?
4. What, if any, have been some negative experiences that have stood out to you during the clinical trial so far?
5. You have just decided to return to taking your HIV treatments after taking some time off of them for the trial, correct? What was that like for you?
6. How much time and effort do you feel you are putting into this clinical trial?
7. What do you hope to get out of being in this clinical trial?
8. What excites/excited you about being in this clinical trial?
9. What worries/worried you about being in this clinical trial?
10. At a time when we are all concerned about COVID-19, how has COVID-19 affected your trial experience?
11. Do you have any recommendations for how we could improve the experience for people who participate in future clinical trial?
12. Is there anything you would like from the research team at the end of the trial?
13. What would you like the study investigators to know about your experience in this clinical trial?

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3:

Participant Demographics (Age, Race, Sex)

Age		**Race**		**Sex**	
30-40	2	Black	11	Male	11
41-45	2	White	3	Female	2
46-50	1	Asian	0	Trans (MtF)	1
51-55	4	Other	0	Total	14
56-60	5	Total	14		
Total	14				

* MtF = Male to Female

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 4:

Additional Quotes – Participant Experiences in HIV Cure-Directed Trials with an Extended Analytical Treatment Interruption (Philadelphia, United States, 2022)

Themes	Quotations
Overall Experiences in the Clinical Trial	
Motivations for Continuing Participation in the Clinical Trial	
Adding meaning to their lives	*The main reason why I want [to be in] this study [is] because it could actually take HIV out of somebody's life, anyone's life, out of the world, like, for good.*
Contributing to scientific community	*The study itself because this is cure research and I know that this is not going to cure me, but again if this is a step closer. I'm a part of history at this point so that's exciting. Even if this particular study isn't, the procedure is gonna [sic] be taken to do a cure. It was a contribution to the overall. So, I'm a part of history and it's exciting.*
Interest in trial conclusions	*I was hoping that it would, you know, my blood work and be off meds, which would be a good thing, but maybe it would go on to some good results for somebody.*
Change in Expectations	
Expectations changed in a positive way	*Because first of, I didn't think that I was going to qualify for it. Second of, I didn't think I would last in it, because I just like everyone else, just knew every, I just thought of all the negative things, but once I decided to just to play it out, listen to see how it is and got in tune in all my personal questions were answered and I got to relax and like I said, I have a little bit more privilege than others… I'm going to say I had the pleasure and honor to participate, because everybody doesn't qualify for it. So… I don't have anything negative to say about this particular program.*
Perceived and Experienced Side Effects	
Chills following infusion	*I only had one set of… side effects. That was on my very first infusion, but that was something that I told I may or may not experience and that could go through the whole entire study… I just experienced cold chills and the people at the study site gave me a bunch of warm blankets. I was fine. It lasted maybe like 20 – 25 minutes.*
Relieved did not experience negative health outcomes	*I didn't get sick. So, I know that it was possible to not be on medication and not really get sick from it or didn't have any of the side effects that could've taken place. So, that was positive for me because, of course, you get a lot of leery when they tell you they're taking you off the meds or they're using this stuff to input into your body and what is it, what can happen, because they give you all the side effects that can happen; and to see that nothing happened, for me, that was a positive thing for me.*
Perceived Impact of Clinical Trial on Mental and Emotional Health	
Positive effects on mental and emotional health	*Again, I think it's about peace of mind number one. So, considering that during the study, I was monitored every week and that gave me peace of mind and then seeing my viral load stay undetectable for so long always make me feel like superman.*
	This clinical study has helped give me self-confidence, encouragement. Before I got involved in this, I hadn't worked in 14 years due to being ill, but they, I'm going to say, it helped give me back my life.
Perceived Experiences with Analytical Treatment Interruption	
Perceived Positive Experiences from the ATI	
Not having to take daily medications	*It felt good, like it was, it's hard to explain how good it feels not to take one pill… I didn't have to take the HIV medicine. Every day I went without taking it, just makes it feel so good. I was just focused and keep going… Okay, I made it this long, good.*
	I mean, it was nice to… not hav[e] to take a pill every day… I've stayed undetectable the whole time that I was on the study drug, and I mean, I don't know, it was nice not to have to be on my medicine.
Remaining undetectable during the ATI	*To a degree, I believe it was helping. I must say, I stayed undetectable for a long time, even off of my meds. So, I believe something was working and I don't know what took place or transpired that caused it to jump, but I was off my meds for, I guess, about a year maybe and that was a year that was the longest I had been without my meds, since I started taking the medication. So, I guess it was doing its job.*
Comfort in not having side effects during ATI	*Nothing happened. I was well, I didn't get sick… Well, I didn't have any side effects. Let me say that I didn't have any, nothing went wrong after coming off of my meds, I got to say, up until, at the end, towards the end of the whole trial for me that my viral spiked, but other than that, I was good. Even when the viral load spiked, I didn't get sick, my CD4 count didn't drop. Those were still good numbers. Just my viral load has spiked. So, other than that, everything else was good.*
Perceived Negative Experiences from the ATI	

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Themes	Quotations
Overall Experiences in the Clinical Trial	
Motivations for Continuing Participation in the Clinical Trial	
Uncertainty related to increase in viral load	*It's been good for the most part, I think towards the end, a few weeks back, my numbers, my viral load jumped up high… unusual for me. So, it had me a little scared, because I had never seen my numbers in that area, in that range since I've been diagnosed. So, it kind of threw me a little bit. So, I was a little worried and made a decision to go back on my medication.*
Monitoring of viral load eased anxiety	*[The analytical treatment interruption] made me nervous at first, but I trust the process. We were monitoring my levels the entire time. So that did give me comfort, but it was still the idea of knowing that I would be off with my treatments long enough to get a little bit of a spike. So, I am a sexually active person so that made me – don't put a pause on some things for a while, but other than that like I said, I really am interested in the study and the findings. So, I'm willing to do what I have to do to make sure we can get what we need.*
Experiences with ART Resumption	
Relief with returning to HIV medications	*As I mentioned earlier it gave me peace of mind, because like I said, I am undetectable… So, if I can't do what I need to do to be healthy, then I have to put that on pause. So that part made me a little bit concerned. It didn't take long before the PI [Principal Investigator] and the Study Coordinator were saying hey your levels are really high so let's get back on treatment and once that happened, I was happy.*
Appreciation for HIV medications	*Right. Because, I took them for so many years, you kind of just take it for granted and then when you see those numbers change, and then you go back on it, and then you see the numbers go good again, you're like, okay, this is, we took it for granted, because… everything was well until it wasn't and then we saw it kick in, so.*
Relationships with the Clinical Research Team	
Positive relationships with clinical research team	*After dealing with the staff, I have to honestly admit, when going to my treatment and whatnot, they were so sweet, I mean, extra sweet. They were nurturing and they cared about their job. It wasn't just a job for them and they would remember you by name.*
Empathetic and caring response from clinical research team	*I want to say this much, all of the staff and everyone… really made the bar very high for bedside manner, caring about how you [are] feeling. One day I went in the office, they could tell I was upset mentally, but physically I was doing okay, you know what I mean, and they made me take a moment to sit like, no, something [is] wrong. I was really having a major, major mental episode, and if it wasn't for [the clinical research staff] and his staff, I would have been in probably driving and having a mental episode.*
Effective communication during the ATI trial	*No, I didn't think too much about it. It was like, okay I met my appointments and they're going over like my medical, not medical history but like what's going on over my body. Everything was discussed right then and there and there was no alarm to me at that point.*
Perceptions of Trial Procedures and Logistics	
Appreciation for clinical monitoring during the trial	*I guess some of the positive things that came out of it was, because I was staying up with them, there was a lot of medical stuff that was taken care of, you know, blood pressure was taken on a regular I got the you know, the biopsy was done and you know, I went and got my eyes checked again, you know, difficult things like that I guess that was some of the positives that came off of it.*
Transportation or parking issues	*So, there were two different locations I would have to go to depending on what I was doing. Most of my study visits was a little bit more of a community finding. Parking was a lot of the times a hassle or public transportation. It took more to get there. The one that was closer, obviously that was easier because I could walk there.*
Perceptions of Compensation and Effort	
Perceptions of Compensation	
Compensation makes a difference	*I really wasn't doing it for money but HIV -- it doesn't matter. I wasn't doing it for money. That was making a difference.*
Perceived Effort	
Minimal effort for the ATI trial	*There wasn't much time required. Like the times that were scheduled, like to travel or whatever… that is nothing, like putting the necessary time, but nothing extra, does that makes sense. And overtime, I didn't waste any time, like I even count the transportation as part of the study.*
ATI trial took time and effort	*Well, it was a really big effort for me and my husband, because both of us live in [city name], which is almost to [state name], trying to get back and forth to doctor's appointment, get to be much considering the fact, I do work two full time jobs… You know, all that kind of stuff took a toll on my job, and the distance it took to get here, and, you know, it was a bit much, but I would do it again.*
Perceived Effects of COVID-19	
COVID-19 did not affect trial participation	*They checked everybody and you had to, I know, at least [hospital name], you had to, they asked you questions before you came and they gave you a green pass that you had to answer the questions over your phone and they*

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Themes	Quotations
Overall Experiences in the Clinical Trial	
Motivations for Continuing Participation in the Clinical Trial	
	gave you a green pass, you showed that and they still checked your temperature, you didn't sit near anybody and for the most part, the most people that I've ever had to sit in a waiting room was two others and we were nowhere near each other… So, like I said, I don't have a bad experience.
Impact of COVID-19 on trial logistics	*The only bad part was COVID-19. That's what made it a little bit taxing. But it wasn't this process of maintenance, but it was the COVID-19 precautions, the max, and because of COVID-19, the buses weren't running as much. They were running on like a Sunday schedule, that was a little bit longer. That was the only kind of drawback, but that was beyond anybody's control.*
Suggestions to Improve Future HIV Cure-Directed Clinical Trials	
Mental health assessments	*I think you all could ask people when, even if they drop out, or if they complete the study and how did that experience like you doing now, affects you and if you are experiencing some type of depression for it, you can like recommend them, sure they do, but I'm saying, but that could be written in there that they do that and use people like myself to, you can ask them, because everything is not about a compensation, I want to say that because I know we talked, talked about that, but the reward would come from.*

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 5:

Considerations for Future HIV Cure-Directed Clinical Research Generated in Collaboration with BEAT-HIV Community Advisory Board

1. Community-based participatory practice (CBPR) approaches can enhance socio-behavioral research practices embedded as part of HIV cure research efforts.
2. HIV cure clinical trial participants are motivated by altruistic desires to help advance HIV cure science and the HIV community. It is important to manage participants' expectations, focus on participants' contributions, communicate uncertainty, and provide support to reduce feelings of having failed the research team and/or the HIV community following viral rebound.
3. At the start of the clinical trial, it is important to provide information to participants that the trial is addressing an unknown question (e.g., whether the experimental intervention will have an impact on ability to keep HIV suppressed in the absence of ART) and will most likely not cure them. Providing regular and accurate information to participants during the trial is important to reduce the risk of therapeutic (or curative) misestimation or misconception. There should be adequate support for partner protections during the ATI (e.g., referral to of provision of pre-exposure prophylaxis (PrEP) for partners without HIV).
4. It is important to emphasize time commitments, blood draws and procedures needed during HIV cure clinical trials.
5. Participants' experiences during ATI trials are heterogeneous. HIV cure clinical research teams should be attuned to participants' tolerance for physical and psychosocial side effects. Capturing side effects from the participants' perspectives can yield useful insight about how they experience clinical trials, and how to mitigate potential psychosocial risks during ATIs. Capturing participants' lived experiences can complement biomedical assessments.
6. The mental, emotional, and social impact of HIV cure-directed clinical trials on trial participants should not be underestimated. We recommend embedding frequent mental health checks as part of extended ATI trials involving viremia and ART restart periods, having health psychologists available as part of the trial team, and utilizing holistic person-centered clinical trial designs. Mental and emotional impacts can stem from the experimental interventions, ATIs (e.g., anxiety of being off ART) and even monitoring or additional procedures. Participants can be provided additional resources during the trial related to HIV or the ATI. We also recommend research teams to include some of the concerns of extended ATIs noted in this manuscript (e.g., anxiety of extended ATIs) as part of their informed consent forms.
7. HIV cure trial participants must weigh the trade-offs of possible positive and negative effects of the ATI – e.g., not taking HIV medications versus the worry of viral rebound and passing HIV to sex partner(s). Apprehensive feelings may be more prominent in people who have experienced undetectable HIV for many years. Close clinical monitoring and ongoing support from the clinical trial team are essential during the ATI and the period of viral load re-suppression to alleviate those feelings of worries.
8. ART resumption following the extended ATI can be accompanied with both positive and negative feelings. These can include peace of mind from being on ART and can be mixed with disappointment about viral relapse. Some participants may need closer counseling and support with ART adherence following the ATI. Sensitization of medical providers of the time needed for viral re-suppression may be necessary.
9. HIV cure trial participants value the relationships with and communications from the clinical trial team which can make a meaningful difference in their participation. Clinical trial teams should try to understand each participant's unique circumstances during the trial. Trust is an important factor affecting retention in clinical trials.
10. HIV cure trial participants may appreciate indirect or inclusion benefits, such as close medical monitoring.
11. Clinical research teams should endeavor to reduce trial burdens and participation barriers as much as possible (e.g., offering ride share over public transportation). Adequate compensation makes participants feel appreciated and valued.
12. It is important to disseminate data in lay terms to trial participants and community members following clinical trials.
13. To help ensure meaningful involvement of critically under-represented groups in HIV cure research, we recommend adopting intentional social, racial and gender justice approaches to clinical trial designs and partnerships with community-based organizations well-versed in those issues.