SARS-CoV-2 Vaccination in the Context of Ongoing HIV Cure-Related Research Studies

To the Editors:

The SARS-CoV-2 pandemic has affected research efforts worldwide. Previously, we described our strategy to mitigate COVID-19 transmission risk during an ongoing HIV cure-related clinical trial.[1] SARS-CoV-2 vaccines recently have been authorized for emergency use and will become available to people with HIV imminently.[2–4] As a result, researchers must determine how to adjust study protocols to incorporate the likelihood that participants may be vaccinated.

In many cases, SARS-CoV-2 vaccination is unlikely to interact with study interventions or outcomes, either because of the nature (eg, not involving mechanisms that would be expected to be altered by immune activation or inflammation) or timing (eg, a single therapy administered regularly for a duration of months or years) of the investigational interventions or measurements. In such cases, it is possible that the effects caused by a highly immunogenic vaccine are likely to be transient and unlikely to interfere with study interventions or outcomes over the long term. Furthermore, some studies can be postponed. However, ongoing HIV cure-related studies involving immunotherapy or analytic treatment interruption (ATI) face substantial challenges. First, study interventions, particularly immunotherapy or ATI, might affect the safety and/or efficacy of the SARS-CoV-2 vaccine. Second, the immunologic effects of vaccination might confound the study's scientific findings. Third, previous counseling and informed consent is not likely to have included detailed discussion around SARS-CoV-2 vaccination.

To address these challenges (Table 1), our biomedical study team, social scientists, and community advisory board met to determine the optimal approach to SARS-CoV-2 vaccination within an ongoing study in which immunotherapies are followed by an ATI (NCT04357821), then broadened our considerations to our larger immunotherapy program.

Our team believed that it was unacceptable to discourage or even delay SARS-CoV-2 vaccination during the study period. We recognized that participants could be offered vaccination from diverse sources contingent on local guidelines, making it unlikely that all participants would be offered vaccination simultaneously or at a predictable time.

Our goals were as follows: (1) to avoid delays in accessing SARS-CoV-2 vaccination, once it is available, (2) to minimize the effects of study interventions on vaccine safety and efficacy, and (3) to minimize the effects of SARS-CoV-2 vaccination on study results. Before the COVID-19 pandemic, the study protocol outlined that a participant should not receive any vaccination within 7 days of enrollment or be exposed to any experimental vaccination within 90 days of enrollment. Participants were

TABLE 1. Key Considerations Related to SARS-CoV-2 Vaccination

Participant considerations
When is SARS-CoV-2 vaccination expected to be available to each study participant?
Where will each participant receive their SARS-CoV-2 vaccination?
Which SARS-CoV-2 vaccine will be made available to each study participant?
How should a participant be counseled regarding the risks and benefits of SARS-CoV-2 vaccination during the study?
Effect of the study on vaccine safety and/or efficacy
Can enrollment into the study be delayed?
Which study interventions might affect the safety and/or efficacy of the SARS-CoV-2 vaccine?
How can the study schedule be adjusted to accommodate SARS-CoV-2 vaccination?
How should the study approach a situation in which a participant has already begun a phase of the study that could affect vaccine response?
Effect of the vaccine on the study
Are there study results that could be affected by SARS-CoV-2 vaccination?
Will delaying study product administration lead to logistical challenges regarding product availability or viability?
How should SARS-CoV-2 vaccination be accounted for in the analysis phase?
Other considerations
Can the study navigate participants to COVID-19 vaccination?
Should study participants be required to be vaccinated for SARS-CoV-2?
Should participants be asked to provide documentation of SARS-CoV-2 immunization before enrolling or continuing in the study?
Should additional considerations be made based on the details of the SARS-CoV-2 vaccine, ie, made available to the participant (eg, manufacturer, single dose versus two-dose series, and adenovirus vector versus lipid nanoparticle)?
How should a situation in which a participant declines to report SARS-CoV-2 vaccination plans or status be addressed?
What approach should be taken if the second vaccine in a 2-vaccine series is delayed?
What approach should be taken if a participant chooses not to be vaccinated and later changes his or her mind?

Supported by funding from the National Institute for Allergy and Infectious Disease at the National Institutes of Health to MJP (T32 AI60530-12), the amfAR Institute for HIV Cure Research (amfAR 109301), the Delaney AIDS Research Enterprise (DARE) (UM1AI126611), and the National Institute of Mental Health to K.D. (R21MH118120). M.J.P. receives support from the UCSF Resource Allocation Program.

S.G.D. reports grants and/or personal fees from Gilead Sciences, Merck & Co, and Viiv, consulting fees from AbbVie, and serves on the Scientific Advisory Board of Enochian BioSciences. The remaining authors have no funding or conflicts of interest to disclose.

The authors are pleased to make available the materials referred to in this article on request. Please contact michael.peluso@ucsf.edu to request the most recent version of these materials.

encouraged to receive routine vaccinations before enrollment, but clinically required vaccinations are allowed during the study period as long as they are spaced 1 week from study interventions or measurements. Most participants are able to carefully plan for routine vaccinations based on the anticipated study schedule. However, the need for participants to urgently receive a highly immunogenic vaccine, in most cases requiring 2 doses with unpredictable availability, to protect against a newly identified pathogen associated with substantial morbidity and mortality was not anticipated when the study was initially implemented.

The study consists of 5 phases of interventions, including immunotherapy and ATI, and takes place over up to 2 years. To address the issues related to SARS-CoV-2 vaccination, our team reviewed the protocol and identified key time points where interventions would be expected to affect vaccine efficacy. This included periods of immunotherapy and the ATI, during which vaccine responses could be suboptimal due to iatrogenic immune suppression. We then identified the study's key biological endpoints, using these determinations to identify optimal time points for SARS-CoV-2 vaccination, and developing plans to pause the study at these points if it was likely vaccination would be offered to the participant imminently. We also identified periods when vaccination would be particularly problematic, and developed contingencies if vaccination is offered during these periods. Throughout, we made an effort to openly and clearly communicate these changes and their rationale to study participants.

To implement this plan, we submitted an IRB amendment describing an informed consent addendum to counsel participants about their options and a script to standardize discussion of COVID-19 vaccination with participants. All materials were developed in English, corresponding to participants' primary language.

Finally, we recognized that even with the best laid plans, vaccine availability will be unpredictable and participants' plans could change rapidly. Realizing that we cannot plan for all contingencies, we anticipate protocol deviations and violations will occur, which our IRB agreed was to be expected.

Through this process, we hope to be able to continue the study while maximizing participants' safety and minimizing the impact on trial results.

ACKNOWLEDGMENTS

The authors would like to acknowledge the contributions of the amfAR and DARE Community Advisory Boards. The authors thank Dr. Rowena Johnston from amfAR for her support.

Michael J. Peluso[a]
Lynda Dee[b,c,d,e]
Jeff Taylor[c,e,f,g]
Danielle M. Campbell[d,e,h]
Adam Ehm[d,i]
Moisés Agosto-Rosario[d,j]
Shirley Shao[a]
Meghann C. Williams[a]
Rebecca Hoh[a]
Rachel L. Rutishauser[k]
Steven G. Deeks[a,l]
John A. Sauceda[m]
Karine Dubé[m,n]

[a]Division of HIV Infectious Diseases, and Global Medicine University of California San Francisco (UCSF) San Francisco, CA
[b]AIDS Action Baltimore Baltimore, MD
[c]amfAR Institute for HIV Cure Research Community Advisory Board
[d]Delaney AIDS Research Enterprise (DARE) Community Advisory Board
[e]Martin Delaney Collaboratory Community Advisory Board
[f]HIV + Aging Research Project (HARP-PS), Palm Springs, CA
[g]University of California San Diego (UCSD) AntiViral Research Center (AVRC) Community Advisory Board San Diego, CA
[h]Charles R. Drew University of Medicine and Science Los Angeles, CA
[i]Living Positive Victoria, Victoria, Australia
[j]National Minority AIDS Council Washington, D.C.
[k]Division of Experimental Medicine University of California San Francisco, CA
[l]amfAR Institute for HIV Cure Research San Francisco, CA and New York City, NY
[m]Center for AIDS Prevention Studies (CAPS) UCSF, San Francisco, CA
[n]UNC Gillings School of Global Public Health, Chapel Hill, NC

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