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A Landscape Analysis of HIV Cure-Related Clinical Research in 2019—Community Summary

by Richard Jefferys, Treatment Action Group, New York and Liz Barr, AIDS Clinical Trials Group, Baltimore, MD; University of Maryland, Baltimore County

INTRODUCTION

Since 2014, TAG has published an online listing of HIV cure-related clinical trials and observational studies derived from information contained in trial registries (primarily clinicaltrials.gov). In 2018, the Bill & Melinda Gates Foundation contracted TAG to survey the researchers conducting the studies in our listing to obtain more detailed information about the status of their work and assess how the overall HIV cure research field is progressing. Results from this analysis are available in an article in the *Journal of Virus Eradication* and on TAG's website.

In 2019, TAG undertook a second survey to assess how the landscape of HIV cure-related clinical research has evolved, also under contract with the Bill & Melinda Gates Foundation. Results are now available in the *Journal of Virus Eradication* and are briefly summarized here.

CURRENT HIV CURE-RELATED RESEARCH

A total of 97 interventional trials and 36 observational studies were ongoing at the time of this analysis in August 2019 (for the current listing, see: https://www.treatmentactiongroup.org/cure/trials/). A diverse range of possible therapeutic interventions are being evaluated in 24 different categories. Most of the research is at the earliest stage (phase I or II) and the aim is to generate leads that might eventually result in the development of broadly effective curative interventions.

The majority of studies are located in the United States, but there are 23 countries in which at least one cure-related study is taking place.

ENROLLMENT AND PARTICIPANT DEMOGRAPHICS

Researchers responsible for 65 of these studies responded to our survey. Respondents reported that, on average, studies are about half-way enrolled (53% of the planned enrollment target has been achieved).

The demographics of trial participants were obtained in two ways: from information provided by survey respondents, and from presentations or publications of study results that have occurred over the past year. A summary of the results is below.

Proportions of study participants based on gender and race/ethnicity (total number of participants in parentheses)

	Surveys	Presented/ published studies
Women	18.5% (1241)	14% (1165)
Men	81.5% (1241)	86% (1165)
Transgender	1.4% (1233)	0.09% (1165)

White	53.4% (219)	42.7% (768)
Black	32.4% (219)	33.8% (768)
Hispanic	11.9% (219)	4% (768)
Asian	5.5% (219)	12.4% (768)
Native American	N/A	0.78% (768)
Indigenous Canadians	N/A	1.4% (768)

TRIAL COMPLETION

Most studies anticipate completion by the end of 2020, with results likely to become available over the course of 2021. The hope is that the knowledge

gained will help refine and guide future research, bringing the field closer to developing effective curative approaches.

FUNDING

According to the survey results, government agencies or networks (primarily the National Institutes of Health) were responsible for the majority of funding (57%). Other sources included industry (18%), nonprofit organizations (11%), universities/hospitals (7%), and "other" (7%), which includes self-funding, the European Commission, and a combination of other funders.

INVASIVE PROCEDURES

Cure-related research often employs complex and potentially invasive procedures, largely due to the difficulty of measuring the low levels of HIV that persist in people on antiretroviral therapy (ART). The most commonly used invasive procedure, reported by 30/65 (46%) of survey respondents, was the extraction of white blood cells using a lengthy process called leukapheresis. Gut-associated lymphoid tissue (GALT) biopsies are also prevalent (cited by 18 out of 65). In many cases these procedures were optional for participants, not mandatory.

Analytical treatment interruptions (ATIs) were part of the study protocol for 15 out of 65 survey respondents (23%). Overall, out of the 133 studies open at the time of this analysis, 30 include ATIs.

COMMUNITY INPUT

Approximately two-thirds of survey respondents reported some degree of consultation with community members during the development of their study. The main mechanism was through regional, local, or research network community advisory boards (CABs). Disappointingly however, 31% felt that community input was not required.

REPEAT RESPONDERS

Of the 65 respondents, 37 had also completed our previous survey in 2018. When asked if enrollment into their study had progressed as originally anticipated, 23% responded affirmatively, and 10% noted it had been faster than expected. However, a concerning proportion (67%) reported that enrollment has progressed slower than planned.

CONCLUSIONS

There remains an encouragingly broad array of interventions under evaluation in HIV cure-related research, but the current pipeline should be considered exploratory. A broadly effective, safe, and affordable curative approach is not on the immediate horizon.

There are several issues of concern to highlight. The underrepresentation of women in the research is extremely problematic because there is evidence of biological sex differences that affect the immune response to HIV and how the virus persists in the body. Furthermore, HIV is highly prevalent in young women on the African continent, where the burden of the epidemic is greatest. The narrow geographic diversity of current HIV cure-related research also threatens to limit the generalizability of findings to the most affected populations.

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Participant diversity continues to be suboptimal, with relatively little representation of people of Hispanic descent, Native Americans/Indigenous Peoples and transgender individuals.

The slower than anticipated enrollment for many studies also has implications for the speed at which HIV cure research can progress. This slow enrollment rate may relate to the complex ethical challenges associated with conducting trials of experimental interventions in an era of highly effective HIV treatment.

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Study procedures could also represent an obstacle—a significant proportion of studies include ATIs, which can carry a risk to both the individual involved in the study and, potentially, to their sexual partners (depending on how high the HIV viral load is allowed to rebound). There have now been two reports of HIV transmission during ATIs; it is critical that researchers and community collaborate to generate best practices for mitigating this risk, including the provision of pre-exposure prophylaxis for HIV-negative partners when appropriate (an initial set of recommendations has been published on the topic).

More broadly, increasing the amount of accessible information on HIV cure research will be essential for educating people about the parameters of study participation and the overall state of the field.

For more details on this landscape analysis of HIV cure-related clinical research, including tables and figures, see the article in the *Journal of Virus Eradication*.