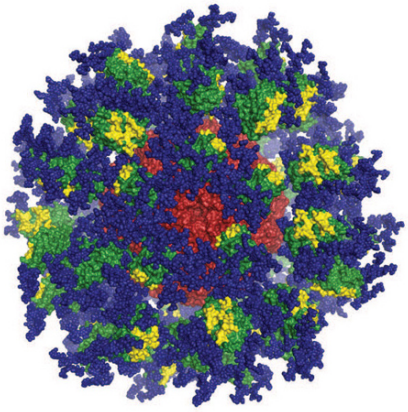

Caption: eOD-GT8 60mer, a self-assembling nanoparticle of engineered HIV Env proteins linked to a spherical protein structure. Courtesy Joseph Jardine, Sergey Menis, William Schief, Scripps Research and IAVI

Fact sheet

Understanding the results from IAVI G001 presented at HIV R4P // Virtual 2021

Study profile

- IAVI G001 is a Phase I study that began in 2018 to test an innovative engineered HIV vaccine candidate.
- The trial was designed to assess the safety of the vaccine candidate and to test the hypothesis that an immunogen could activate naïve B cells of the immune system that produce precursors to a certain type of broadly neutralizing antibody (bnAb). This type of bnAb, known as a VRC01-class antibody, targets an area on the HIV surface protein Env known as the CD4 binding site. The strategy of targeting naïve B cells with specific properties is called “germline targeting,” as these B cells display antibodies encoded by unmutated, or “germline,” genes.
- IAVI G001 enrolled 48 healthy, HIV-negative adults. Participants received two doses of the vaccine candidate or placebo, spaced two months apart.
- 24 participants were enrolled in a low-dose group, and 24 were enrolled in a high-dose group.
- IAVI G001 was conducted at two sites: George Washington University in Washington, D.C., and the Fred Hutchinson Cancer Research Center in Seattle, Washington.

Outcome of analysis (n=48)

- No safety concerns arose among participants.
- 97% of participants who were vaccinated developed detectable VRC01-class immunoglobulin G (IgG) B cells.
- The frequency of these responses — meaning how frequently these VRC01-class B cells were detected among all IgG B cells — was high enough to be considered promising for boosting as a next step.

- The results establish proof of principle for germline targeting in humans, and support extending this strategy to other targets on HIV and to other pathogens.

Caring for study participants

- Participants are monitored for safety and immune responses for 12 months after the last vaccination.
- Participants will be notified of the trial results once the trial is completed and the study is unblinded, which should occur later this year.

Profile of the experimental vaccine candidate evaluated in IAVI G001

- The candidate was developed in the laboratory of William Schief, Ph.D., executive director of vaccine design for IAVI's Neutralizing Antibody Center (NAC) at Scripps Research and professor, Department of Immunology and Microbiology, at Scripps Research.
- The candidate, eOD-GT8 60mer (pronounced *ee-oh-dee gee-tee-ayt sixtee-mer*) is the first in a sequence of engineered HIV vaccine candidates that Schief and his colleagues are developing.
- eOD-GT8 60mer is a self-assembling nanoparticle of engineered HIV Envelope (Env) proteins linked to a spherical protein structure. The engineered proteins are designed to engage with cells of the immune system that produce a certain type of antibody that can eventually evolve into a bnAb, or one capable of neutralizing a wide range of HIV variants. The approach underlying the immunogen engineering is considered a reverse vaccinology 2.0 approach, because previously discovered bnAbs were used to guide the design of the vaccine immunogen. The approach is also a structure-based vaccine approach, because molecular structure information on the HIV gp120 protein and its interactions with bnAbs were used to guide the design of the vaccine immunogen.
- A vaccine candidate based on eOD-GT8 60mer would be administered as part of the first stage of a multi-step vaccine regimen aimed at eliciting many different types of bnAbs.
- The immunogen was combined with an adjuvant developed by GSK. Adjuvants are substances added to some vaccines to boost the immune response.

Next steps

- IAVI, Scripps Research, the Bill & Melinda Gates Foundation, Moderna, and other partners are planning to launch further trials of the candidate. Additionally, the Schief lab is working with collaborators in pre-clinical studies to develop and test sequential vaccines to guide the B cells even further along the path to produce mature bnAbs.
- Moderna will apply its mRNA vaccine platform, recently validated in their COVID-19 vaccine Phase III trial, to delivery of the eOD-GT8 60mer immunogen. A Phase I trial is expected to begin in the third quarter of 2021.
- Researchers think the approach used in this trial for HIV could also be applied to vaccines for other challenging pathogens such as influenza, dengue, Zika, and hepatitis C viruses and the malaria parasite.

Partners and funders of IAVI G001

- IAVI and Scripps Research developed the vaccine candidate with funding from the Bill & Melinda Gates Foundation, an HIV Vaccine Research and Development (HIVRAD) grant (P01 AI094419 titled "Optimizing HIV immunogen-BCR interactions for vaccine development") from the National

Institute of Allergy and Infectious Diseases (NIAID), the Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery (CHAVI-ID) at the NIAID and Scripps Research, and the Scripps Consortium for HIV/AIDS Vaccine Development (CHAVD). Other collaborating organizations include Duke Human Vaccine Institute, Karolinska Institutet, and La Jolla Institute. See the press release for other funding and partner information.

Media Contacts

IAVI Media Contact
Karie Youngdahl
kyoungdahl@iavi.org
+1 484 343 1731

Scripps Research Media Contact
Kelly Quigley
kquigley@scripps.edu
+ 1 858 997 9462