Pipeline Report » 2019

HIV Vaccines, Passive Immunization, and Antibody Gene Transfer

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HIV Vaccines, Passive Immunization, and Antibody Gene Transfer Pipeline 2019

By Richard Jefferys

Taking center stage in this year's HIV vaccine pipeline update is the prime-boost approach being developed by Janssen Vaccines & Prevention B.V., part of the Janssen Pharmaceutical Companies of Johnson & Johnson. A large phase III efficacy trial—MOSAICO—is due to start recruiting imminently, with a plan to enroll 3,800 cisgender men and transgender individuals who have sex with cisgender men and/or transgender individuals. Locations will include the United States, Argentina, Brazil, Italy, Mexico, Peru, Poland, and Spain.

The vaccine candidate comprises adenovirus serotype 26 (Ad26) vectors encoding four different mosaic HIV antigens (codenamed Ad26.Mos4.HIV), which are designed to induce immune responses against diverse HIV variants, followed by a bivalent booster containing two versions of the HIV gp140 envelope protein (one from a clade C virus and the other a mosaic of multiple clades).

The new phase III trial complements an ongoing phase IIb trial, known as Imbokodo or HPX2008/HVTN 705, which is studying efficacy among 2,600 women in five southern African countries. In May of this year, the company announced that this trial is now fully enrolled. The only difference between the vaccine regimens being administered in the two trials is that the booster in Imbokodo contains only the clade C HIV gp140 envelope protein and not the mosaic version.

MOSAICO is taking a novel approach to addressing the availability of pre-exposure prophylaxis (PrEP), which is a key challenge facing researchers attempting to design ethical HIV vaccine efficacy trials (or any efficacy trial of new biomedical prevention interventions). Potential participants who are using PrEP will not be eligible to join the trial, but any enrollees who decide to start PrEP after receiving their first vaccination will be provided means of access according to a study site plan and allowed to continue in the study. Individuals deemed not eligible at screening due to PrEP use will be permitted to return for re-screening if they subsequently stop.

There are now three large ongoing HIV vaccine efficacy trials: MOSAICO, Imbokodo, and HVTN 702 (Uhambo), which began in South Africa in 2016 and is testing a prime-boost combination of an ALVAC vector and clade C Env protein (a regimen based on the only HIV vaccine trial to show evidence of efficacy to date, RV144).[1]

A variety of vaccine candidates remain in something of a holding pattern in middle-phase clinical trials; information is being gleaned about optimal methods for inducing different HIV-specific immune responses, but the ideal protective response remains unknown. If results from the ongoing efficacy trials shed light on the types of immune response that can achieve a significant level of protection, this could guide decisions about which of the many contenders deserves to advance further along the pipeline.

The phase I stage of HIV vaccine testing is becoming dominated by protein constructs that aim to jostle B cells along a pathway toward the generation of broadly neutralizing antibodies (bNAbs). These candidates typically include variants of the HIV envelope protein that have been painstakingly designed to mimic the natural 'native' structure. None of these candidates are expected to instantly generate bNAbs—the idea is to induce B-cell responses that could be coaxed toward that goal by additional immunization strategies. As their name suggests, bNAbs can inhibit a broad array of HIV variants from multiple clades, and inducing them with vaccines is viewed as a critical objective by researchers.

An alternative but less practical means of providing bNAbs is to deliver them directly via intravenous infusion or subcutaneous injection, an approach called passive immunization. Multiple bNAbs are now being tested in this context, both alone and in combination. Two very large efficacy trials—HVTN 704/HPTN 085 and HVTN 703/HPTN 081—are evaluating whether infusions of VRC01, one of the first bNAbs to be discovered, can protect against HIV infection.[1]

In an effort to create a more user-friendly version of passive immunization, researchers are also studying antibody gene transfer. The concept borrows from the field of gene therapy and uses adeno-associated virus (AAV) vectors to deliver bNAbs into the body. After a single injection, an AAV vector modified to encode a bNAb can take up residence in muscle tissue and—in theory—act as a factory that delivers an ongoing supply of the antibody into the circulation. Promising results have been seen in macaque studies.

Unfortunately, the antibody gene transfer pipeline for prevention is currently stalled because the results of the first trial were disappointing (see table entry below for a link to the open-access journal article describing the results). The major problem that has emerged is that the body makes antibodies against the AAV-encoded bNAbs, preventing the achievement of detectable bNAb levels. In the phase I trial sponsored by the International AIDS Vaccine Initiative (IAVI), all participants developed antibodies against the bNAb being delivered, PG9.

Researchers are pursuing multiple strategies that aim to circumvent this induction of immunity against AAV-delivered bNAbs, but at the present time no additional prevention studies of antibody gene transfer are taking place. The lone ongoing trial is evaluating a slightly different AAV variant encoding the bNAb VRC07 in people with HIV on antiretroviral therapy. The results should contribute to efforts to assess the viability of the approach for both treatment and prevention.

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1. On June 21, 2019, HVTN announced that all their large, ongoing biomedical prevention trials are now fully enrolled. The total numbers are as follows:

- HVTN 702/Uhambo: 5,407 participants.
- HVTN 705/Imbokodo: 2,637 participants.
- HVTN 703 & 704/Antibody Mediated Prevention (AMP) studies: 4,625 participants.

Table: HIV Vaccines, Passive Immunization, and Antibody Gene Transfer Pipeline 2019

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor	Status
HIV VACCINES				
Ad26.Mos4.HIV, clade C and mosaic gp140 HIV/ alum	Ad26 vectors encoding four mosaic Env, Gag, and Pol antigens (Ad26.Mos1.Gag-Pol, Ad26.Mos2.Gag-Pol, Ad26.Mos1.Env, Ad26.Mos2S.Env) Clade C and mosaic gp140 protein in alum adjuvant	NCT03964415 (HPX3002/ HVTN 706)	Janssen Vaccines & Prevention B.V.	Phase III
■ Stieh DJ, Callewaert K, Sarnecki M, et al. Primary analysis of TRAVERSE: A phase 1/2a study to assess safety/tolerability and immunogenicity of 2 Different prime/boost HIV vaccine regimens (Abstract OA02.06LB). Paper presented at: R4P; 2018 October 21-25; Madrid, Spain.				
ALVAC-HIV (vCP2438), bivalent clade C gp120/ MF59	Canarypox vector encoding HIV-1 clade C gp120, clade B gp41, Gag, and protease + protein boost comprising two clade C Env proteins (TV1.Cgp120 and 1086.Cgp120)	NCT02968849 (HVTN 702)	NIAID/HVTN/Bill & Melinda Gates Foundation/South African Medical Research Council/Sanofi Pasteur/ GlaxoSmithKline	Phase IIb/ III
■ NIAID (Press Release). First new HIV vaccine efficacy study in seven years has begun. 2016 November 27. ■ Bekker LG, Moodie Z, Grunenberg N, et al. Subtype C ALVAC-HIV and bivalent subtype C gp120/MF59 HIV-1 vaccine in low-risk, HIV-uninfected, South African adults: a phase 1/2 trial. Lancet HIV. 2018 Jun 8. doi: 10.1016/S2352-3018(18)30071-7. [Epub ahead of print]				
Ad26.Mos4.HIV, clade C gp140/alum	Ad26 vectors encoding four mosaic Env, Gag, and Pol antigens (Ad26.Mos1.Gag-Pol, Ad26.Mos2.Gag-Pol, Ad26.Mos1.Env, Ad26.Mos2S.Env) Clade C gp140 protein	NCT03060629 (HPX2008/ HVTN 705)	Janssen Vaccines & Prevention B.V.	Phase IIb
■ NIH (Press Release). NIH and partners launch HIV vaccine efficacy study. 2017 November 30.				
HIV DNA-rTV	DNA prime and replication-competent Tiantan vaccinia virus vector boost encoding Gag, Pol, and Env proteins from HIV-1 CN54	ChiCTR1900021422	Beijing Youan Hospital, Capital Medical University/Center for STD/AIDS Prevention, and Control of China CDC/Beijing Bioproducts Research Institute Company, Ltd.	Phase IIa
■ Shao Y, Li T, Wolf H, et al. The safety and immunogenicity of HIV-1 vaccines based on DNA and replication competent vaccinia vector in phase I clinical trial (Abstract P14-15 LB). Retrovirology. 2009;6(Suppl 3):P404. doi: 10.1186/1742-4690-6-S3-P404.				

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor	Status
ALVAC-HIV vCP1521, AIDSVAX B/E	Canarypox vector encoding HIV-1 CRF01_AE Env, clade B Gag, the protease-encoding portion of the Pol protein, and a synthetic polypeptide encompassing several known CD8+ T-cell epitopes from the Nef and Pol proteins AIDSVAX B/E recombinant protein vaccine containing gp120 from HIV-1 clades B and CRF01_AE	NCT01931358 NCT01435135	U.S. Army Medical Research and Materiel Command	Phase II
■ Akapirat S, Karnasuta C, Vasan S, et al. Characterization of HIV-1 gp120 antibody specificities induced in anogenital secretions of RV144 vaccine recipients after late boost immunizations. PLoS One. 2018 Apr 27;13(4):e0196397. doi: 10.1371/journal.pone.0196397. ■ Rerks-Ngarm S, Pitisuttithum P, Excler JL, et al. Randomized, double-blind evaluation of late boost strategies for HIV-Uninfected vaccine recipients in the RV144 HIV vaccine efficacy trial. J Infect Dis. 2017 Apr 15;215(8):1255-63. doi: 10.1093/infdis/jix099. ■ Easterhoff D, Moody MA, Fera D, et al. Boosting of HIV envelope CD4 binding site antibodies with long variable heavy third complementarity determining region in the randomized double blind RV305 HIV-1 vaccine trial. PLoS Pathog. 2017 Feb 24;13(2):e1006182. doi: 10.1371/journal.ppat.1006182.				
HIVIS DNA MVA-CDMR CN54rgp140	HIVIS DNA encoding Env, Gag, reverse transcriptase, and Rev proteins, administered by Zetajet with or without Derma Vax electroporation MVA-CMDR encoding Env, Gag, and Pol proteins Trimeric recombinant subtype C HIV-1 gp140 Env glycoprotein	NCT01697007	Muhimbili University of Health and Allied Sciences	Phase II
■ Viegas EO, Kroidl A, Munseri PJ, et al. Optimizing the immunogenicity of HIV prime-boost DNA-MVA-rgp140/GLA vaccines in a phase II randomized factorial trial design. PLoS One. 2018 Nov 29;13(11):e0206838. doi: 10.1371/journal.pone.0206838.				
Ad26.Mos.HIV MVA-Mosaic gp140 protein	Ad26 vectors encoding mosaic Env, Gag, and Pol MVA vectors encoding mosaic Env, Gag, and Pol + gp140 protein boost	NCT02315703	Janssen Vaccines & Prevention B.V./NIAID/ MHRP/ IAVI/Beth Israel Deaconess Medical Center	Phase I/IIa
■ Barouch DH, Tomaka FL, Wegmann F, et al. Evaluation of a mosaic HIV-1 vaccine in a multicentre, randomised, double-blind, placebo-controlled, phase 1/2a clinical trial (APPROACH) and in rhesus monkeys (NHP 13-19). 2018 Jul 6. Lancet. doi: 10.1016/S0140-6736(18)31364-3. [Epub ahead of print]				
ALVAC-HIV (vCP2438) Bivalent clade C gp120/ MF59 Bivalent clade C gp120/ alum Bivalent clade C gp120	Canarypox vector encoding HIV-1 clade C gp120, clade B gp41, Gag, and protease + protein boost comprising two clade C Env proteins (TV1.Cgp120 and 1086.Cgp120) with MF59 or alum adjuvant, or without adjuvant	NCT03284710 (HVTN 107)	NIAID/ HIV Vaccine Trials Network/Sanofi Pasteur/ GlaxoSmithKline	Phase I/IIa

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor	Status
ALVAC-HIV (vCP2438) Bivalent clade C gp120/ MF59 Bivalent clade C gp120/ ASO1B	Canarypox vector encoding HIV-1 clade C gp120, clade B gp41, Gag, and protease + protein boost comprising two clade C Env proteins (TV1.Cgp120 and 1086.Cgp120) with either MF59 or AS01B adjuvant	NCT03122223 (HVTN 120)	NIAID/GlaxoSmithKline/ Sanofi Pasteur	Phase I/IIa
LIPO-5, MVA HIV-B, GTU-MultiHIV	Five lipopeptides comprising CTL epitopes from Gag, Pol, and Nef proteins MVA vector encoding Env, Gag, Pol, and Nef proteins from HIV clade B DNA vector encoding fusion protein comprising elements from six different HIV proteins Given in four different prime-boost combinations	NCT02038842	INSERM-ANRS	Phase I/II
■ Lelièvre J-D, Lacabaratz C, Wiedemann A, et al. Immunogenicity and safety of 4 prime-boost combinations of HIV vaccine candidates (MVA HIV-B; LIPO-5; GTU-MultiHIV B) in healthy volunteers: ANRS/INSERM VRI01 phase I/II randomized trial. Paper presented at: 9th IAS Conference on HIV Science (IAS 2017); 2017 July 23-26; Paris, France.				
MYM-V101	Virosome-based vaccine designed to induce mucosal IgA antibody responses to HIV-1 Env	NCT01084343	Mymetics	Phase I/II
■ Leroux-Roels G, Maes C, Clement F, et al. Randomized phase I: Safety, immunogenicity and mucosal antiviral activity in young healthy women vaccinated with HIV-1 Gp41 P1 peptide on virosomes. PLoS One. 2013;8(2):e55438. doi: 10.1371/journal.pone.0055438.				
GEO-D03 DNA + MVA/ HIV62B	Prime: DNA vaccine with GM-CSF adjuvant Boost: MVA vector Both vaccines encode Gag, Pol, and Env proteins from HIV-1 clade B and produce VLPs	NCT01571960 (HVTN 094)	GeoVax/NIAID	Phase I
■ Buchbinder SP, Grunenberg NA, Sanchez BJ, et al. Immunogenicity of a novel clade B HIV-1 vaccine combination: Results of phase 1 randomized placebo controlled trial of an HIV-1 GM-CSF-expressing DNA prime with a modified vaccinia Ankara vaccine boost in healthy HIV-1 uninfected adults. PLoS One. 2017 Jul 20;12(7):e0179597. doi: 10.1371/journal.pone.0179597.				
MAG-pDNA, rVSVIN HIV-1 Gag	Multiantigen DNA vaccine encoding the Env, Gag, Pol, Nef, Tat, and Vif proteins of HIV-1 and GENEVAX, IL-12 pDNA adjuvant, attenuated replication-competent rVSV vector encoding HIV-1 Gag	NCT01578889 (HVTN 087)	Profectus Biosciences/ HVTN	Phase I
■ Elizaga ML, Li SS, Kochar NK, et al. Safety and tolerability of HIV-1 multiantigen pDNA vaccine given with IL-12 plasmid DNA via electroporation, boosted with a recombinant vesicular stomatitis virus HIV Gag vaccine in healthy volunteers in a randomized, controlled clinical trial. PLoS One. 2018 Sep 20;13(9):e0202753. doi: 10.1371/journal.pone.0202753. eCollection 2018. ■ Li SS, Kochar NK, Elizaga M, et al. DNA priming increases frequency of T-cell responses to a vesicular stomatitis virus HIV vaccine with specific enhancement of CD8+ T-cell responses by interleukin-12 plasmid DNA. Clin Vaccine Immunol. 2017 Nov 6;24(11):e00263-17. doi: 10.1128/CVI.00263-17.				

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor	Status
pSG2.HIVconsv DNA + ChAdV63.HIVconsv, or MVA.HIVconsv	Prime: DNA vaccine pSG2 Boost: chimpanzee adenovirus vector ChAdV63 or MVA vector All contain the HIVconsv immunogen, designed to induce cross-clade T-cell responses by focusing on conserved parts of HIV-1	NCT01151319	University of Oxford	Phase I
■ Moyo N, Borthwick NJ, Wee EG, et al. Long-term follow up of human T-cell responses to conserved HIV-1 regions elicited by DNA/simian adenovirus/MVA vaccine regimens. PLoS One. 2017 Jul 18;12(7):e0181382. doi: 10.1371/journal.pone.0181382. eCollection 2017. ■ Hayton EJ, Rose A, Ibrahimsa U, et al. Safety and tolerability of conserved region vaccines vectored by plasmid DNA, simian adenovirus and modified vaccinia virus ankara administered to human immunodeficiency virus type 1-uninfected adults in a randomized, single-blind phase I trial. PLoS One. 2014 Jul 9;9(7):e101591. doi: 10.1371/journal.pone.0101591.				
SeV-G(NP), Ad35-GRIN	Sendai virus vector encoding HIV-1 Gag protein delivered intramuscularly or intranasally, Ad35 vector encoding HIV-1 clade A Gag, reverse transcriptase, integrase, and Nef	NCT01705990	IAVI/DNAVEC	Phase I
■ Nyombayire J, Anzala O, Gazzard B, et al. First-in-human evaluation of the safety and immunogenicity of an intranasally administered replication-competent Sendai virus-vectored HIV type 1 Gag vaccine: induction of potent T-cell or antibody responses in prime-boost regimens. J Infect Dis. 2017 Jan 1;215(1):95-104. doi: 10.1093/infdis/jiw500.				
GTU-MultiHIV	DNA vector encoding fusion protein comprising elements from six different HIV proteins, administered by intramuscular, intradermal, or transcutaneous routes	NCT02075983	Imperial College London/ European Commission-CUT'HIVAC Consortium	Phase I
■ Haidari G, Cope A, Miller A, et al. Combined skin and muscle vaccination differentially impact the quality of effector T cell functions: the CUTHIVAC-001 randomized trial. Sci Rep. 2017 Oct 12;7(1):13011. doi: 10.1038/s41598-017-13331-1.				
DNA Nat-B Env DNA CON-S Env DNA mosaic Env MVA-CMDR	Prime: DNA vector encoding Nat-B, CON-S, or mosaic Env proteins Boost: MVA vector encoding Env (E), Gag (A), and Pol (E) proteins	NCT02296541 (HVTN 106)	NIAID/CHAVI/IPPOX/ MHRP/HVTN	Phase I
■ Frahm N, Fiore-Gartland A, Harman Malhi H, et al. Increased breadth of T-cell responses after mosaic HIV vaccination in humans (HVTN 106) (Abstract OA07.01). Paper presented at: R4P; 2018 October 21-25; Madrid, Spain.				
MVA mosaic	MVA vectors encoding HIV-1 mosaic proteins	NCT02218125	Crucell/MHRP/NIAID/ Beth Israel Deaconess Medical Center	Phase I
■ Baden LR, Walsh SR, Seaman MS, et al. First-in-human randomized controlled trial of mosaic HIV-1 immunogens delivered via a modified vaccinia Ankara vector. J Infect Dis. 2018 Apr 13. doi: 10.1093/infdis/jiy212. [Epub ahead of print]				
DNA-HIV-PT123 AIDSVAXB/E	DNA vectors encoding HIV-1 clade C Gag, gp140, and Pol-Nef AIDSVAX B/E recombinant protein vaccine containing gp120 from HIV-1 clades B and CRF01_AE	NCT03391375	EuroVacc/IAVI/Uganda Medical Research Council/UVRI Uganda Research Unit on AIDS/ Centre Hospitalier Universitaire Vaudois	Phase I

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor	Status
PENNVAX-GP HIV-1 DNA vaccine IL-12 DNA adjuvant	DNA vector encoding Gag, Pol, and Env proteins + DNA vector encoding IL-12 adjuvant, delivered via intradermal or intramuscular electroporation	NCT02431767 (HVTN 098)	NIAID	Phase I
■ Edupuganti S, De Rosa S, Huang Y, et al. Immune responses to PENNVAX-GP® HIV DNA vaccine plus IL-12 are equivalent or superior when delivered by intradermal vs. intramuscular electroporation (Abstract OA11.06LB). Paper presented at: R4P; 2018 October 21-25; Madrid, Spain.				
IHV01 (FLSC-001)	Full-length single-chain gp120-CD4 complex vaccine	NCT02756208	University of Maryland/ Bill & Melinda Gates Foundation/Profectus BioSciences, Inc.	Phase I
■ Fouts TR. Development of the full length single chain gp120-CD4 (FLSC), a novel vaccine for HIV prevention. Paper presented at: 10th Euro Global Summit and Expo on Vaccines & Vaccination; 2016 June 16-18; Rome, Italy.				
HIV DNA-C CN54ENV + recombinant HIV CN54gp140	DNA vector encoding HIV-1 clade C Env delivered intramuscularly and intradermally Clade C Env protein boost	NCT02589795	Imperial College London	Phase I
■ Cheeseman HM, Day S, McFarlane LR, et al. Combined skin and muscle DNA priming provides enhanced humoral responses to a human immunodeficiency virus type 1 clade C envelope vaccine. Hum Gene Ther. 2018 Sep;29(9):1011-28. doi: 10.1089/hum.2018.075.				
HIV-1 Nef/Tat/Vif, Env pDNA + HIV-1 rVSV envC	DNA vector encoding HIV-1 Nef/ Tat/Vif and Env Attenuated replication-competent rVSV vector encoding HIV-1 clade C Env	NCT02654080 (HVTN 112)	NIAID	Phase I
■ Wilson G, Rodriguez B, Elizaga M, et al. Safety and immunogenicity of a pDNA clade B Env prime, rVSV clade C Env boost HIV-1 vaccination regimen in a phase 1 clinical trial (Abstract OA02.02). Paper presented at: R4P; 2018 October 21-25; Madrid, Spain.				
Ad4-mgag, Ad4-EnvC150	Live, replication-competent recombinant Ad4 vectors encoding HIV-1 clade C Env and HIV-1 mosaic Gag proteins Formulated either as enteric-coated capsules for oral administration or as an aqueous formulation for tonsillar administration	NCT01989533	NIAID/PaxVax, Inc.	Phase I
Ad4-mgag, Ad4-EnvC150 + AIDSVAX B/E	Orally administered replication-competent Ad4 HIV vaccine in combination with AIDSVAX B/E recombinant protein vaccine containing gp120 from HIV-1 clades B and CRF01_AE	NCT02771730 (HVTN 110)	PaxVax, Inc./NIAID	Phase I
Ad4-EnvCN54, MVA-CN54, CN54gp140/MPLA	Orally administered replication-competent Ad4 vector and MVA vector encoding clade C Env protein, clade C Env protein in MPLA adjuvant	NCT03408262	Imperial College London	Phase I
■ Alexander J, Mendy J, Vang L, et al. Pre-clinical development of a recombinant, replication-competent adenovirus serotype 4 vector vaccine expressing HIV-1 envelope 1086 clade C. PLoS One. 2013 Dec 3;8(12):e82380. doi: 10.1371/journal.pone.0082380.				

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor	Status
Tetravalent Ad26.Mos4. HIV + clade C gp140 ± mosaic gp140	Ad26 vectors encoding two mosaic HIV-1 Envs and mosaic Gag and Pol + clade C HIV Env protein boost ± mosaic HIV Env protein boost	NCT02935686	Janssen Vaccines & Prevention B.V.	Phase I
MVA/HIV62B + AIDSVAX B/E	MVA vector encoding Gag, Pol, and Env proteins from HIV-1 clade B to produce VLPs + AIDS-VAX B/E recombinant protein vaccine containing gp120 from HIV-1 clades B and CRF01_AE	NCT02852005 (HVTN 114)	NIAID	Phase I
▪ Goepfert P, Casapia M, Elizaga M, et al. HVTN114: A phase 1 trial to evaluate late boosts with AIDSVAX B/E of participants previously vaccinated with MVA/HIV62B in DNA/MVA or MVA regimens (Abstract P05.14LB). Paper presented at: R4P; 2018 October 21-25; Madrid, Spain.				
DNA-HIV-PT123 Bivalent clade C gp120/ MF59 Bivalent clade C gp120/ ASO1B	DNA vaccine encoding HIV-1 clade C Gag, gp140, and Pol-Nef + protein boost comprising two clade C Env proteins (TV1. Cgp120 and 1086.Cgp120) with either MF59 or AS01B adjuvant	NCT02915016 (HVTN 108)	NIAID	Phase I
DNA-HIV-PT123 + clade C gp120/MF59	DNA vaccine encoding HIV-1 clade C Gag, gp140, and Pol-Nef + protein boost comprising two clade C Env proteins (TV1. Cgp120 and 1086.Cgp120) in MF59 adjuvant	NCT02997969 (HVTN 111)	NIAID/HVTN/IPPOX Foundation/Novartis Vaccines	Phase I
▪ Moodie Z, Innes C, Hosseinipour M, et al. DNA-prime induces higher magnitude humoral responses than ALVAC-prime in HIV vaccine regimens with the same protein boost (Abstract OA02.04LB). Paper presented at: R4P; 2018 October 21-25; Madrid, Spain.				
EnvSeq-1 Envs adjuvanted with GLA-SE DNA Mosaic-Tre env	Four individual EnvSeq-1 Env proteins (CH505TF, CH505w53,CH505w78, CH505w100), DNA vaccine encoding mosaic Env antigen	NCT03220724 (HVTN 115)	NIAID	Phase I
gp145 C.6980/alum	Oligomeric gp145 Clade C Env protein vaccine + alum adjuvant	NCT03382418 (HVTN 122)	NIAID	Phase I
p24CE1/2 DNA vaccine p55^gag DNA vaccine/IL-12 DNA adjuvant	DNA vaccines encoding Gag p24 conserved elements and/or Gag p55 + DNA vector encoding IL-12 adjuvant, delivered via intramus-cular electroporation	NCT03181789 (HVTN 119)	NIAID	Phase I
Env/gag DNA vaccine gp120 protein vaccine/ GLA-SE adjuvant	Polyvalent DNA vaccine encoding Envs from HIV-1 clades A, B, C, and A/E and clade C Gag + polyvalent gp120 protein vaccine + GLA-SE adjuvant	NCT03409276 (HVTN 124)	NIAID	Phase I

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor	Status
eOD-GT8 60mer/AS01B/ DPBS sucrose	Engineered priming immunogen designed to activate B cell precursors as a step toward induction of bNAbs + AS01B adjuvant	NCT03547245	IAVI	Phase I
■ Jardine JG, Ota T, Sok D, et al. Priming a broadly neutralizing antibody response to HIV-1 using a germline-targeting immunogen. Science. 2015 Jul 10;349(6244):156-61. doi: 10.1126/science.aac5894.				
BG505 SOSIP.664 gp140/ ASO1B	Native-like HIV-1 Env trimer + AS01B adjuvant	NCT03699241	IAVI	Phase I
■ Dey AK, Cupo A, Ozorowski G, et al. cGMP production and analysis of BG505 SOSIP.664, an extensively glycosylated, trimeric HIV-1 envelope glycoprotein vaccine candidate. Biotechnol Bioeng. 2018 Apr;115(4):885-99. doi: 10.1002/bit.26498. ■ IAVI (Press Release). IAVI announces first-in-human clinical trial of native-like HIV envelope vaccine candidate. 2019 March 27.				
Ad4-Env145NFL, Ad4-Env150KN + VRC-HIVRGP096-00-VP (Trimer 4571) /alum	Replication-competent Ad4 HIV vaccines encoding Env proteins + native-like HIV-1 Env trimer with alum adjuvant	NCT03878121	NIAID	Phase I
VRC-HIVRGP096-00-VP (Trimer 4571) /alum	Native-like HIV-1 Env trimer with alum adjuvant	NCT03783130	NIAID	Phase I
■ Caringal RT, Fleischman M, Chaudhuri R, et al. Development of a stable formulation for stabilized HIV-1 Env trimer vaccine candidate (HIV-1 trimer 4571) (Abstract W1030-12-094). Paper presented at: AAPS PharmSci 360; 2018 November 4-7; Washington DC.				
ConM SOSIP.v7 gp140/ MPLA liposomes	Native-like HIV-1 envelope vaccine adjuvanted with monophosphoryl lipid A (MPLA) liposomes	NCT03961438	Academisch Medisch Centrum - Universiteit van Amsterdam (AMC-UvA)	Phase I
ConM SOSIP, EDC ConM SOSIP, ConS UFO, EDC ConS UFO, mosaic SOSIPs/ MPLA	Prime-boost combinations of model immunogens based on HIV-1 envelope proteins with MPLA adjuvant	NCT03816137	Imperial College London	Phase I
■ Sliepen K, Han BW, Bontjer I, et al. Structure and immunogenicity of a stabilized HIV-1 envelope trimer based on a group-M consensus sequence. Nat Commun. 2019 May 29;10(1):2355. doi: 10.1038/s41467-019-10262-5. ■ Markus S. EAVI2020 announces start of new HIV vaccine trial. Imperial College London. 2019 April 2.				
Stable CH505TF gp120, transient CH505TF gp120/ GLA-SE	CH505TF gp120 produced from stably transfected cells or CH505TF gp120 produced from transiently transfected cells, with GLA-SE adjuvant	NCT03856996 (HVTN 123)	NIAID	Phase I
■ Saunders KO, Verkoczy LK, Jiang C, et al. Vaccine Induction of Heterologous Tier 2 HIV-1 Neutralizing Antibodies in Animal Models. Cell Rep. 2017 Dec 26;21(13):3681-3690. doi: 10.1016/j.celrep.2017.12.028.				
HIV-1 gp41 MPER-656 liposome vaccine/alum	Priming immunogen designed to activate B cell precursors as a step toward induction of bNAbs + alum adjuvant	NCT03934541 (HVTN 133)	NIAID	Phase I

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor	Status
PASSIVE IMMUNIZATION				
VRC01	Monoclonal bNAb administered intravenously	NCT02716675 (HVTN 704/HPTN 085) NCT02568215 (HVTN 703/HPTN 081)	NIAID/HVTN/HPTN	Phase IIb
■ NIAID (Press Release). NIH launches large clinical trials of antibody-based HIV prevention. 2016 April 7.				
PGT121 + VRC07-523LS ± PGDM1400	Monoclonal bNAbs administered intravenously	NCT03721510	IAVI	Phase I/IIa
10-1074	Monoclonal bNAb administered intravenously	NCT02511990	Rockefeller University	Phase I
■ Caskey M, Schoofs T, Gruell H, et al. Antibody 10-1074 suppresses viremia in HIV-1-infected individuals. Nat Med. 2017 Feb;23(2):185-91. doi: 10.1038/nm.4268.				
3BNC117 + 10-1074	Monoclonal bNAbs administered intravenously	NCT02824536	Rockefeller University	Phase I
■ Cohen YZ, Butler A, Levin R, et al. A phase 1 trial of the combination of 3BNC117 and 10-1074 in HIV-uninfected adults (Abstract 1062). Paper presented at: 2018 Conference on Retroviruses and Opportunistic Infections; 2018 March 4-7; Boston, MA.				
P2G12	Monoclonal neutralizing antibody administered intravenously	NCT02923999	St George's, University of London	Phase I
PGT121	Monoclonal bNAb administered intravenously	NCT02960581	IAVI	Phase I
VRC01	Monoclonal bNAb administered subcutaneously or intravenously	NCT01993706 NCT02165267 NCT02256631 NCT02797171	NIAID	Phase I (adults and HIV-exposed infants)
■ Mayer KH, Seaton KE, Huang Y, et al. Safety, pharmacokinetics, and immunological activities of multiple intravenous or subcutaneous doses of an anti-HIV monoclonal antibody, VRC01, administered to HIV-uninfected adults: Results of a phase 1 randomized trial. PLoS Med. 2017 Nov 14;14(11):e1002435. doi: 10.1371/journal.pmed.1002435. ■ Ledgerwood JE, Coates EE, Yamshchikov G, et al. Safety, pharmacokinetics and neutralization of the broadly neutralizing HIV-1 human monoclonal antibody VRC01 in healthy adults. Clin Exp Immunol. 2015 Dec;182(3):289-301. doi: 10.1111/cei.12692.				
VRC01LS	LA monoclonal bNAb administered subcutaneously or intravenously	NCT02256631 NCT02599896 NCT02797171	NIAID	Phase I
VRC07-523LS	LA monoclonal bNAb administered intravenously	NCT03015181 NCT03387150 NCT03735849	NIAID	Phase I
3BNC117-LS	A monoclonal bNAb administered intravenously	NCT03254277	Rockefeller University	Phase I
10-1074-LS + 3BNC117-LS	LA monoclonal bNAbs administered subcutaneously or intravenously	NCT03554408	Rockefeller University	Phase I
VRC07-523LS + 10E8VLS	LA monoclonal bNAbs administered subcutaneously	NCT03565315 (suspended)	NIAID	Phase I

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/ Sponsor	Status
PGDM1400 + PGT121	Monoclonal bNAbs administered intravenously	NCT03205917	IAVI	Phase I
N6LS	LA monoclonal bNAb administered subcutaneously or intravenously	NCT03538626	NIAID	Phase I
■ Huang J, Kang BH, Ishida E, et al. Identification of a CD4-binding-site antibody to HIV that evolved near-pan neutralization breadth. Immunity. 2016 Nov 15;45(5):1108-21. doi: 10.1016/j.immuni.2016.10.027.				
PGT121, PGDM1400, 10-1074, VRC07-523LS	Monoclonal bNAbs administered intravenously	NCT03928821	NIAID	Phase I
10E8.4/iMab	Bispecific monoclonal antibody administered subcutaneously or intravenously	NCT03875209		Phase I
■ Padte NN, Yu J, Huang Y, Ho DD. Engineering multi-specific antibodies against HIV-1. Retrovirology. 2018 Aug 29;15(1):60. doi: 10.1186/s12977-018-0439-9. ■ Huang Y, Yu J, Lanzi A, et al. Engineered bispecific antibodies with exquisite HIV-1-neutralizing activity. Cell. 2016 Jun 16;165(7):1621-31. doi: 10.1016/j.cell.2016.05.024.				
ANTIBODY GENE TRANSFER				
rAAV1-PG9DP	Recombinant AAV vector encoding the PG9 broadly neutralizing antibody	NCT01937455	IAVI/NIAID/CHOP	Phase I
■ Priddy FH, Lewis DJM, Gelderblom HC, et al. Adeno-associated virus vectored immunoprophylaxis to prevent HIV in healthy adults: a phase 1 randomised controlled trial. Lancet HIV. 2019 Apr;6(4):e230-9. doi: 10.1016/S2352-3018(19)30003-7.				

Shaded entries represent additions since the 2018 Pipeline Report.

TABLE ABBREVIATIONS

AAV: adeno-associated virus

Ad4: adenovirus serotype 4

Ad26: adenovirus serotype 26

Ad35: adenovirus serotype 35

bNAb: broadly neutralizing antibody

CAVD: Collaboration for AIDS Vaccine Discovery

CHAVI: Center for HIV/AIDS Vaccine Immunology

CHOP: Children's Hospital of Philadelphia

CMDR: Chiang Mai double recombinant

CTL: cytotoxic T lymphocyte

DPBS: Dulbecco's phosphate-buffered saline

GLA-AF: glucopyranosyl lipid adjuvant (aqueous formulation)

GLA-SE: glucopyranosyl lipid adjuvant formulated in a stable emulsion

GM-CSF: granulocyte-macrophage colony–stimulating factor

Hsp70: heat shock protein 70

HVTN: HIV Vaccine Trials Network

IAVI: International AIDS Vaccine Initiative

IHV: Institute for Human Virology

IL: interleukin

INSERM-ANRS: French National Institute for Health and Medical Research-French National Agency for Research on AIDS and Viral Hepatitis

LA: long-acting

MHRP: U.S. Military HIV Research Program

MPER: membrane-proximal external region

MPLA: monophosphoryl lipid A

MVA: modified vaccinia Ankara strain

NIAID: U.S. National Institute of Allergy and Infectious Diseases

rVSV: recombinant vesicular stomatitis virus

UVRI: Uganda Virus Research Institute

VLP: virus-like particle

VRC: The Dale and Betty Bumpers Vaccine Research Center

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EIN 13-3624785