2021 WHO Product Development for Vaccines Advisory Committee (PDVAC)
Virtual Consultation: HIV mAbs Preferred Product Characteristics
15 April 2021
CHAIR: David Kaslow

Concept Note and Agenda

Background

The HIV epidemic continues to cause extensive morbidity and mortality globally. Despite progress in reaching 61% of people living with HIV with antiretroviral therapy (ART),[1] gaps in HIV prevention and treatment contributed to 1.7 million new infections and 690,000 HIV-related deaths in 2019.[2]

With the exception of voluntary medical male circumcision, the existing arsenal of prevention tools, including oral pre-exposure prophylaxis (PrEP), condoms, and medication-assisted treatment for people who inject drugs (PWIDs), require frequent usage contributing to implementation challenges. New and forthcoming products that offer longer duration of protection are poised to have a significant impact on HIV prevention efforts. The dapivirine (DVP) vaginal ring for women recently received a positive opinion from the EMA as a monthly prevention option and was found to reduce the risk of HIV infection by 31% overall in cisgender women aged 18 to 45 years.[3,4] Additionally, in the HPTN083 and HPTN084 trials, long-acting pre-exposure prophylaxis with cabotegravir (CAB-LA), administered as a bi-monthly injection, demonstrated high effectiveness in preventing HIV infection among cisgender men who have sex with men (MSM), transgender women (TGW) who have sex with men, and cisgender women in sub Saharan Africa.[5,6]

Alongside these promising developments, the continued need to identify interventions that can provide durable, or even life-long, protection against HIV infection has been identified by WHO and UNAIDS as a top public health priority.[7] Several HIV vaccine and monoclonal antibody (mAbs) candidates are currently advancing through clinical development. Given their ability to directly target specific epitopes, antibodies represent a promising preventative modality against HIV. Two parallel antibody-mediated protection (AMP) efficacy proof-of-concept trials were recently completed, testing intravenous delivery of the single broadly neutralizing antibody, VRC01, among men who have sex with men (MSM) and transgender persons in the Americas, and among women in Eastern and Southern Africa (NCT02716675 and NCT02568215).[8,9] The studies demonstrated proof-of-concept that the VRC01 broadly neutralizing antibody (bnAb) was effective at preventing the acquisition of HIV strains that were sensitive to the bnAb (at 75.4% efficacy), but suggested the need to assess combinations of antibodies that provide broader, more potent protection than VRC01 alone, as the overall efficacy was only 8.8% (95% CI: -45.1 to 42.6, P=0.70) in cisgender women and 26.6% (95% CI: -11.7 to 51.8, P=0.15) MSM and transgender persons.[10,11,12] A number of putatively more potent combinations and engineered antibodies are also undergoing early clinical evaluation.[13]

WHO and IAVI entered into a project collaboration agreement in November 2019 to co-develop preferred product characteristics (PPC) for HIV antibody products. A WHO Working Group on HIV Vaccines and Monoclonal Antibodies was established in 2020 and contributed to the development of this PPC. In November 2020, a virtual stakeholder consultation was held to review the draft PPC with a broad range of stakeholders. This was done prior to the results of the AMP trial of VRC01. Following the stakeholder consultation, the WHO Working Group on HIV Vaccines and mAbs met to discuss the implications of the AMP trials on the PPC.

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The goal of this virtual session is to facilitate PDVAC review of the draft HIV mAbs PPC document. The circulated draft has incorporated feedback from the stakeholder meeting but has not yet undergone public consultation. The intended outcome is to finalize the draft PPC for public comment.

A second goal is to highlight critical aspects that require further consideration to facilitate future research, policy and implementation discussions for development and use of HIV mAbs. Such aspects would be reported separately in a scientific journal.

Objectives of the meeting

1. Present the rationale and context for developing WHO PPC guidance for HIV monoclonal antibodies including in the context of other prevention products on the market or on the horizon.
2. Evaluate the draft PPC document tables and discuss the following characteristics and issues:
    - priority target populations
    - delivery strategies
    - efficacy
    - schedule and duration of protection
    - route of administration and amount of mAb required
3. Gather input on key issues/research priorities to include in an article in a peer reviewed journal.

Outcomes of the meeting

1. Recommendations for finalization of the HIV mAb PPC document as a draft for public consultation.
2. Identification of critical product attributes/characteristics that require further consideration or evidence to facilitate future research prioritization, policy and implementation discussions.

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06:00 Seattle; 08:00 Lima; 9:00 Washington DC; 13:00 London; 15:00 Geneva; 15:00 Johannesburg; 18:30 New Delhi, 21:00 Beijing; 22:00 Seoul

Time (Geneva CEST)	Topic	Duration	Detail	Moderators, speakers
15.00 – 15.05	Introduction	5’	• Welcome remarks, roll call, agenda and objectives	Martin Friede (WHO) Birgitte Giersing (WHO) David Kaslow (PATH)
15.05 – 15.20	The context for development of PPCs for HIV monoclonal antibodies	15’	• Public health need (epidemiology and different target populations) • Current WHO recommendations/schedule for PrEP and PMTCT and issues with current products (access, adherence, side-effects, resistance) • UNAIDS and WHO updated Guidance on Ethical considerations in HIV prevention trials, overview & implications	Michelle Rodolph (WHO)
15.20 – 16.00	Update on development of HIV prevention products	15’ 10’ 5’ 10’	• Long acting ARVs (e.g CAB-LA and others in the pipeline) • The dapivirine (DVP) vaginal ring • Results of the AMP trials of VRC01 (HIV mAb) • Other mAbs in the pipeline • Brief overview of vaccines in the pipeline • Questions	Sinead Delany-Moretlwe (Wits) Barney Graham (NIH) Jerome Kim (IVI)
16.00 – 16.20	The rationale for development of PPCs for HIV monoclonal antibodies	10’ 10’	• Value proposition: Potential contribution of mAbs to HIV prevention options • Discussion	Susan Buchbinder (SFDH)

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Time (Geneva CEST)	Topic	Duration	Detail	Moderators, speakers
16.20 – 17.00	Facilitated discussion on selected PPCs for HIV mAbs Note: *if time runs over part of this discussion can move to the closed session*	40’	• HIV mAbs PPC overview and discussion • Focus on: o Target populations o Efficacy o Dose regimen o Route of Administration	Erin Sparrow (WHO)
16 April 15.00-16.30 Chair: David Kaslow	**Discussion (closed session) – PDVAC only** What are PDVAC’s recommendations with respect to the draft text for the product attributes listed above and which issues should be highlighted that require further consideration to facilitate future research, policy and implementation discussions for development and use of HIV mAbs.			

[1] UNAIDS, HIV treatment, https://www.unaids.org/en/topic/treatment (Accessed April 13, 2020)
[2] WHO, HIV/AIDS Factsheet, https://www.who.int/news-room/fact-sheets/detail/hiv-aids
[3] EMA, Vaginal ring to reduce the risk of HIV infection for women in non-EU countries with high disease burden, July 24, 2020. https://www.ema.europa.eu/en/news/vaginal-ring-reduce-risk-hiv-infection-women-non-eu-countries-high-disease-burden (Accessed August 17, 2020).
[4] Nel A et al, Safety, adherence, and HIV-1 seroconversion among women using the dapivirine vaginal ring (DREAM): an open-label, extension study, Lancet HIV, Feb 2021, https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(20)30300-3/fulltext
[5] HPTN, Long-acting injectable cabotegravir is highly effective for the prevention of HIV infection in cisgender men and transgender women who have sex with men, May 18, 2020. https://www.hptn.org/news-and-events/press-releases/long-acting-injectable-cabotegravir-highly-effective-prevention-hiv (Accessed Sept 10, 2020)
[6] HPTN, HPTN 084 Study Demonstrates Superiority of Injectable Cabotegravir to Oral FTC/TDF for the Prevention of HIV in Cisgender Women in Sub-Saharan Africa, November 9, 2020 https://www.hptn.org/news-and-events/announcements/hptn-084-study-demonstrates-superiority-of-injectable-cabotegravir-to. (Accessed February 2, 2021).
[7] UNAIDS, UNAIDS urges a scaling up of HIV vaccine research to stop new infections, May 17, 2018, https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2018/may/hiv-vaccine-awareness-day.

[8] ClinicalTrials.gov, https://clinicaltrials.gov/ct2/show/NCT02716675 (Accessed April 13, 2020)
[9] ClinicalTrials.gov, https://clinicaltrials.gov/ct2/show/NCT02568215 (Accessed April 13, 2020)
[10] HPTN, Most advanced clinical trials testing broadly neutralizing antibody against HIV demonstrate efficacy against sensitive strains, Jan 26, 2021. https://www.hptn.org/news-and-events/press-releases/most-advanced-clinical-trials-testing-broadly-neutralizing-antibody. (Accessed February 2, 2021).
[11] AMP study results presentation: https://ampstudy.org/assets/docs/AMP-Trials-Efficacy-Results-Community-Slides_01OCT2020.pdf
[12] Corey L, Gilbert P, Jurshka M, *et al*, Two Randomized Trials of Neutralizing Antibodies to Prevent HIV-1 Acquisition, NEJM, 18 Marh 2021. https://www.nejm.org/doi/full/10.1056/NEJMoa2031738
[1313] AVAC, Broadly Neutralizing Antibody Combinations, https://www.avac.org/sites/default/files/infographics/bNAbCombos_july2019.pdf (Accessed April 13, 2020)