HIV Cure
Target Product Profile

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What will a cure need to do?

Ideal product profile

- A truly transformative intervention will need to address the needs of those unable to access, adhere, afford, tolerate and respond to ART
  - Effective for decades
  - Safe, affordable, scalable
  - Works in all populations, including those who are viremic
  - Prevents re-infection
- Aspirational but possible: Single-dose administration

Although the characteristics of an ideal cure are easily defined, those that might at a minimum be acceptable requires careful consideration and discussion from all stakeholders

HIV Cure: Target Product Profile

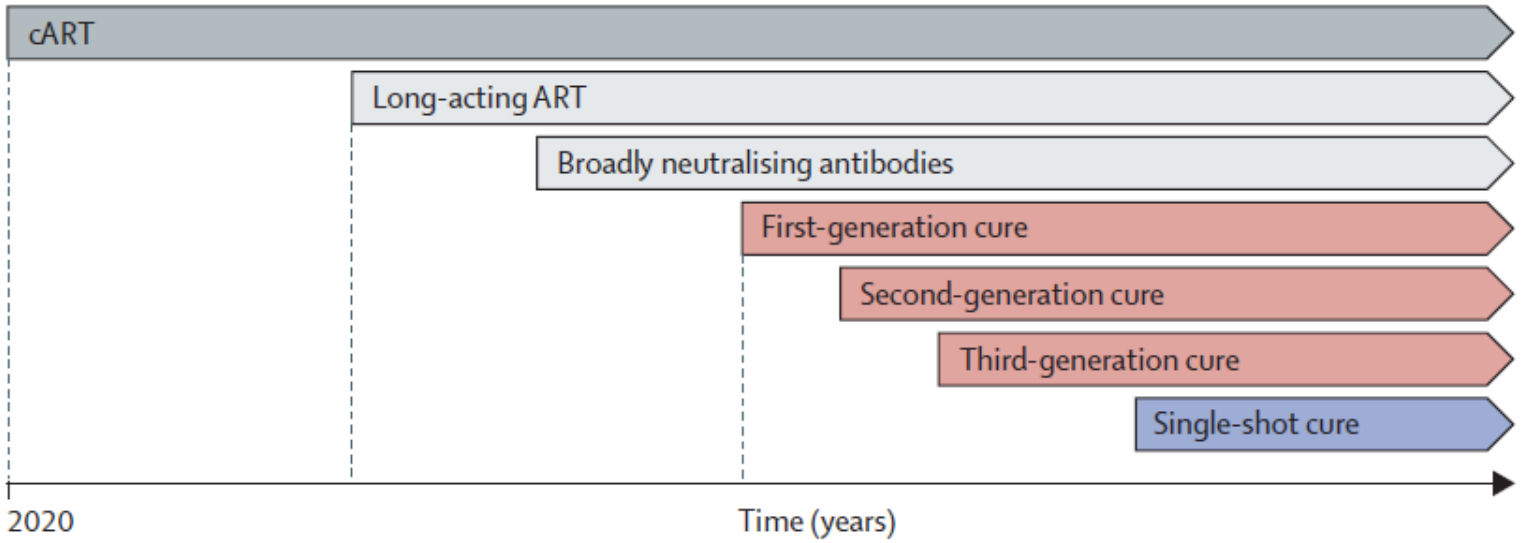
HCAAP

HIV Cure Africa Acceleration Partnership

- Leaders from industry, academia, advocacy groups, and funders were assembled in February 2019 to discuss cure and its global implementation
- Consensus reached that “target product profiles” for various cure strategies (e.g., immunotherapy, gene therapy)
- TPP should be applicable to all regions
- Process
  - Key stakeholders contacted
  - Delphi exercise completed
  - Consensus obtained, published
  - Living document maintained by HCAAP

Treatment evolution and a cure/remission

The first generation of cures are expected to complex and difficult-to-scale, as were the initial antiretroviral regimens



THE LANCET HIV

Multi-stakeholder consensus on a target product profile for an HIV cure

Sharon R Lewin*, Timothy Attoye, Cathy Bansbach, Brian Doehle, Karine Dubé, Mark Dybul, Devi SenGupta, Adam Jiang, Rowena Johnston, Rosanne Lamplough, Joseph M McCune, Gary J Nabel, Thumbi Ndung'u, John Pottage, David Ripin, James F Rooney, Izukanji Sikazwe, Moses Nsubuga, Mitchell Warren, Steven G Deeks*, on behalf of the Sunnylands 2019 Working Group

What is a target product profile?

	Minimum	Optimum
Target population	Adults ages >16 and <65 years regardless of sex and gender who are healthy, on stable ART, and virologically suppressed (HIV-1 RNA <200 copies per mL) with a CD4 count >500 cells per μL	All people living with HIV
Clinical efficacy	Viral load below the transmission threshold (conservatively defined as <200 copies HIV RNA per mL), effective in ≥20% of individuals, average relapse rate <10% per year and remission duration >2 years	Viral load below the detection threshold (<50 copies HIV RNA per mL), effective in ≥90% of subjects, average relapse rate <2% per year and remission duration >3 years or complete eradication of virus, including the rebound-competent reservoir, as detected by a diagnostic biomarker
Safety and tolerability	No serious adverse events, frequency of grade 3 reversible adverse events dependent on clinical efficacy (<5% with near 20% efficacy rate or <20% with >80% efficacy rate), frequency of significant irreversible adverse events (eg, neuropathy, liver cirrhosis, and carcinogenicity) <1%	No grade 3 or 4 adverse events
Frequency of discontinuation during therapy	<20%	<5%
Frequency of significant irreversible adverse events	<1%	<1%
Protection from re-infection	None	Full
Special populations	Safe and effective in individuals likely to experience common drug–drug interactions (eg, individuals having opioid substitution therapy, using recreational drugs, or consuming alcohol)	Safe and effective in all populations, including pregnant women, children, infants, and newborns
Contraindications	Low CD4 counts, scarce ART options, renal insufficiency (eg, chronic kidney disease), hepatic insufficiency (eg, liver cirrhosis), co-infections (eg, hepatitis B, hepatitis C, herpes simplex virus, and tuberculosis), cancer	None
Dosing and administration	Oral preferred but parenteral (including infusions) acceptable	Single administration, oral preferred, but subcutaneous administration (volume ≤1 mL) acceptable
Maximum regimen duration	12 months	3 months
Adjunct treatments	Stable ART as lead-in therapy for at least 3 months	None
Need for screening	HIV RNA level, CD4 count	None
Need for monitoring	Must be safe and accessible, particularly if relapse risk is high, qualitative viral load monitoring: every 1–4 weeks during treatment, after ART interruption, for 8–12 weeks; every 4 weeks for 6 months after completion of regimen; every 3 months after 6 months of completion of regimen and stable viral suppression	None
Need for booster	At most, once a year	None
Storage and handling	Cold chain (2–8°C) requirement acceptable, other specialised storage permissible, small molecules: stable for 12 months at 30°C plus or minus 2°C and 75% relative humidity plus or minus 5%	Stable at ambient temperatures (no cold chain requirement), small molecules: same as minimum
Product registration path	Approval by stringent regulatory authority (eg, Food and Drug Administration, European Medicines Agency) leading to WHO prequalification[29]	Approval by stringent regulatory authority (eg, Food and Drug Administration, European Medicines Agency) leading to WHO prequalification[29]
Target delivery setting	Any, including tertiary or quaternary medical systems with corresponding complex infrastructure (eg, highly trained and specialised medical staff, isolation units for immunosuppressed patients from conditioning, and inpatient care and laboratories)	Settings capable of delivering ART in the current setting (ie, primary or secondary settings not necessarily requiring a physician for day-to-day care)
Cost of goods sold	Any	Target will be informed by cost-effective and cost-saving analyses
Expected financing source	Global Fund, US President's Emergency Plan for AIDS Relief in the short term, domestic government and local health insurance in the longer term	National governments

ART=antiretroviral therapy.

- An agreed set of minimally-acceptable and optimistic characteristics of a new product
- Helps to align all stakeholders by broadly defining the product the community wants to deliver to the field
- Will evolve based on scientific developments and changing patient needs

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Key areas of debate and consensus building

- Consensus that first generation cures might be cumbersome, non-scalable, expensive and less effective than ART
  - Need to start somewhere
  - Process will be iterative
  - First generation cures not meant to replace ART in those with access who are doing well
- Will PWH/clinicians/regulators accept any detectable viremia?
  - At what viral load threshold will transmission become a concern?
- Should a cure be comparable to ART in terms of safety?
  - No permanent, potentially disabling adverse events
- How important is a biomarker for a cure?
  - Higher tolerance of a less effective strategy if there is a way to prove the therapy was curative and unnecessary ART interruptions avoided
- Prevention of re-infection important public health implications

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towards an HIV cure
people focused science driven

THE ANNENBERG RETREAT AT SUNNYLANDS

BILL & MELINDA GATES foundation