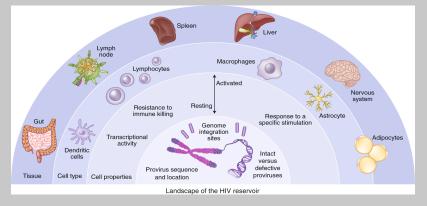
HIV cure update

STEPS 8: A Community Initiative to Design the Pathway to a Long-Term Remission of HIV Infection

23 October 2022

Simon Collins, i-Base.info







Few comments...

- IAS cure roadmap: resource. Recent progress/issues
- Diversity, inclusion and access/scalability.
- Personal impact of joining an ATI study.



IAS 2021 roadmap

- 3rd IAS 5-year review: Nature Medicine: covers 170 new studies. [1]
- Summary for medical journalists (English, French, Portuguese, Spanish).
- Non technical Q&A: everyday language. [2] Reading age 11-12. Easy for translations.

1. IAS, Nature Medicine (1 Dec 2021), 2. i-Base.info

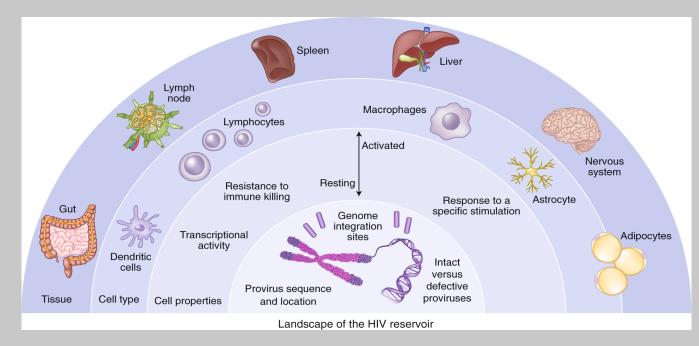




Research priorities for an HIV cure: Internationa

AIDS Society Global Scientific Strategy 202

Diverse reservoir



Smaller reservoir - but not small.

10¹⁰ viral DNA after years of ART – even if 99% might be defective.

Refs: IAS Roadmap to an HIV Cure, Nature Med, 2021. Estes et al. Nat Med, 2017. Bruner et al. Nature, 2019).

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Community.1

- Broaden awareness: to 40 million people living with HIV and engagement beyond advocates and CABs.
- Inclusive research: balance for race / sex / gender / age / country and in entry criteria.
- Include social research in clinical studies.

Refs: Barr L, Jefferys R: A landscape analysis of HIV cure-related clinical research in 2019. J Virus Erad, 2018 and 2019.

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Community.2

- Ethics disconnect between participants and researchers: "I might be cured".
- Global research involve and fund research site in different countries and all regions.
- Use community-preferred language.
- Extend follow-up on reported cases.

Ref: AVAC: Community preferred language for an HIV cure.

TAG: Baseline demographics in 122 studies 2018–2022

Total # of participants	4475	*Includes two transgender participants reported
Total from studies reporting sex and gender	4375	
Female	885 (20.2%)	
Male	3437 (78.5%)	additively to data
Transgender or non-binary	19 (0.4%)*	presented on sex assigned at birth
Missing/not reported	36 (0.8%)	

https://www.treatmentactiongroup.org/cure/resource-on-the-demographics-of-participation-in-hiv-cure-related-clinical-research/

TAG: Baseline demographics in 122 studies 2018–2022

Total from studies reporting race/ethnicity	2607
Asian	208 (8%)
Black	587 (22.5%)
Hispanic	244 (9.4%)**
White	1373 (52.7%)
Native American/Native Hawaiian, American Indian/Alaskan Native	8 (0.3%)
Pacific Islander	2 (0.08%)
Indigenous Australian	1 (0.04%)
More than one race/ethnicity	25 (1%)
Other/unknown/not reported	306 (11.7%)

**Includes 147 participants of Hispanic ethnicity reported additively to data on race (with their race not specified)

Include women and all ages

- Including women in cure research is essential and achievable. ...on principle AND supported by biological differences in viral load and reservoir dynamics (including hormone exposure and immune differences.
- Expand age criteria to include children and much older adults.

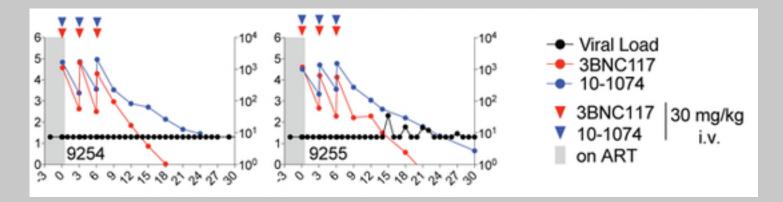
Ref: Eileen Scully, "Ready for a Cure: Where are the Women and Children?, July 2022.

What is meant by a cure?

- Different things:
- Not being a risk to partners?
- Freedom from stigma and disclosure?
- Testing HIV negative? Etc
- Not needing meds? long-acting ART achieves some of these things - but this also will need viral load home testing/sampling.

Long-acting ART and bNAbs

Dual bNAb studies included viral load staying <50 copies/mL for >1 year during an ATI off-ART.



Mendoza et al. Nature 2018.

Personal impact of studies

- Cure studies often involve intensive routines: many hospital visits (time, travel, cost), infusions (time, practical issues), placebo (questioning benefit.
- ATIs disrupt being stable and undetectable, risk of reinfection, risk to partners, disorientating experiences, difficulty returning to oral ART.
- COVID, MPX risk from travel and crowds.

Thanks

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Back-up slides

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Impossible dream...

Activist focus on a cure. 38m adults & children. 6m not yet diagnosed. 28m on ART, 1.5m new cases. 0.7m people died. Limited ART and monitoring.



Source: UNAIDS, 2021 data. https://www.unaids.org/en/resources/fact-sheet

Global need...



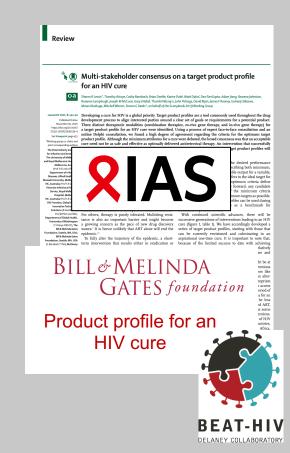
- >85% in global south.
- ~50% are women.

65% from key populations: *sex workers; people who are trans; gay and bisexual men; people using drugs etc.* Issues of poverty, housing, healthcare. Link to aid: \$30b a year. *"I don't want to worry about who is the next US President"* – Moses Supercharger.

Source: UNAIDS, 2021 data. https://www.unaids.org/en/resources/fact-sheet

Profiles for a cure...

Safe = low risk. Affordable in all settings. Effective for all populations. Permanent – no reinfection. Easy to deliver and use.



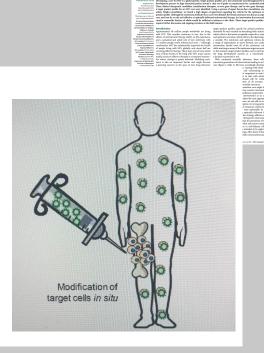
Refs: Lewin S et al. Multi-stakeholder consensus. Lancet HIV, Jan 2021, McCune M, Jonathan Lax lecture 2022.

Profiles for a cure... Minimal dosing... long duration: maybe every three years? No risk to partners + easy monitoring for rebound. Timeline: 10 years – in stages LA-ART > bNAbs > 1st/2nd/3rd cures > single shot.

Refs: Lewin S et al. Multi-stakeholder consensus. Lancet HIV, Jan 2021, McCupe M. Jopethan Lax Josture 2022, https://boot.biv.org/iopethan.lax.award.loctures

McCune M, Jonathan Lax lecture 2022. https://beat-hiv.org/jonathan-lax-award-lectures/

EATG/STEP HIC Cre Workshop, Glasgow, 2022



eview

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

Community highlights

- Real people who have been cured. Each one brings hope.
- Advances in understanding the reservoir in context of ART.
- That researchers are working collaboratively and internationally.

Current cures and/or remission

- Four stem cell cures in patients from Berlin (Timothy Ray Brown) in 2008, London (Adam Castillejo) in 2019, Düsseldorf in 2019, and the US in 2022.
- Loreen Willenberg, Esperanza patient.
- Visconti cohort (control without ART).
- IAS 2022: City of Hope, Barcelona pt.

Photos: Timothy Ray Brown, Adam Castillejo, Loreen Willenberg.



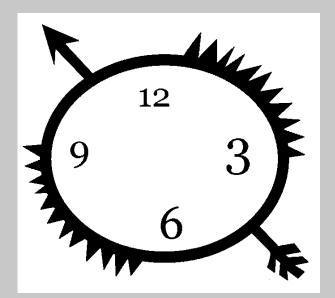




Timeline...

An HIV cure, like a vaccine, is always 10 years away...

But, even being cautious, the 10 years now feels closer than it has ever been ...





- Broader community inclusion and participation in research and consent.
- Expand sites to fund countries globally.
- Care over language and reporting.
- Including cure as part of treatment literacy.
- Optimism and hope for treatment, a vaccine and a cure.

Thanks

Investigators and funders for cure-related research.

Participants in cure-related studies.

And for comments on slides: Lynda Dee, Richard Jefferys, Cissy Kityo, Udom Likhitwonnawut, Michael Louella, Moses Supercharger, Jeff Taylor and community members of the IAS writing group.

Disclosure

No personal financial conflict of interest

Future cure...?

- Increasing focus on cure research.
- International networks.

Either

(i) Eradication (cure) or(ii) Remission (whereviral load staysundetectable withoutneed for ART).

