



2nd Long-Acting Treatment and Prevention Conference

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Long-acting agents - where do these products fit in the African context?

Professor Catherine Orrell, Desmond Tutu HIV Centre, UCT.





What is available NOW?

CAB and CAB / RPV: q8w IM injections – registrations increasing: South Africa, Botswana...

HPTN 083 and 084: success in PrEP in diverse populations

ATLAS, ATLAS2M and FLAIR studies – showed success in viral suppression (1.4% failure); non-inferior to oral ART.

- 3ml injection, into (each) gluteal muscle every 8 weeks.
- Vast majority of data in Rx has been after switch with VS on oral medication.



Orkin, Lancet HIV 2021; Swindells, AIDS 2022; Jaeger, Lancet HIV; 2021; Overton, CROI 2022.

2nd LA ARVs Conference



What is coming up?

- **Lencapavir** (Gilead): capsid inhibitor in phase III, sc q24w injections. SUCCESS in Purpose 1 and Purpose 2.
- **Islatravir** (MSD): reverse transcriptase and translocation inhibitor in phase III. Once daily, once weekly and once per month tablet. ISLEND studies.
- **MK-8507**: (MSD): novel HIV-1 non-nucleoside reverse transcriptase inhibitor in phase II; once a week oral regimen.
- **bNabs**: Phase I and II studies exploring various bNabs are ongoing – combinations and with CAB. Possible sc dosing every 2-6 months.



Possible options for PrEP...



6-monthly subcutaneous injections i.e Lenacapavir



Vaginal rings
e.g. Dapivirine



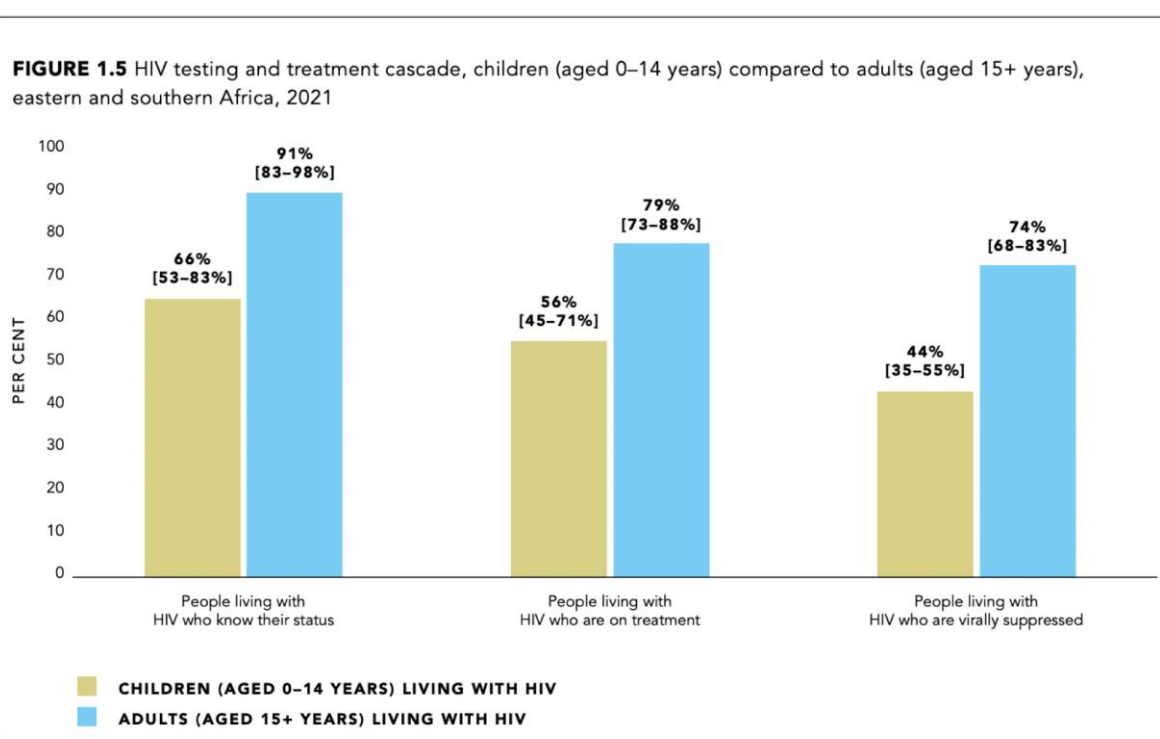
2-monthly intramuscular injections i.e. CAB

Daily oral tablets
e.g. TDF/FTC;
TAF/FTC





Finding the niche in LMIC



People less likely to be virally suppressed:

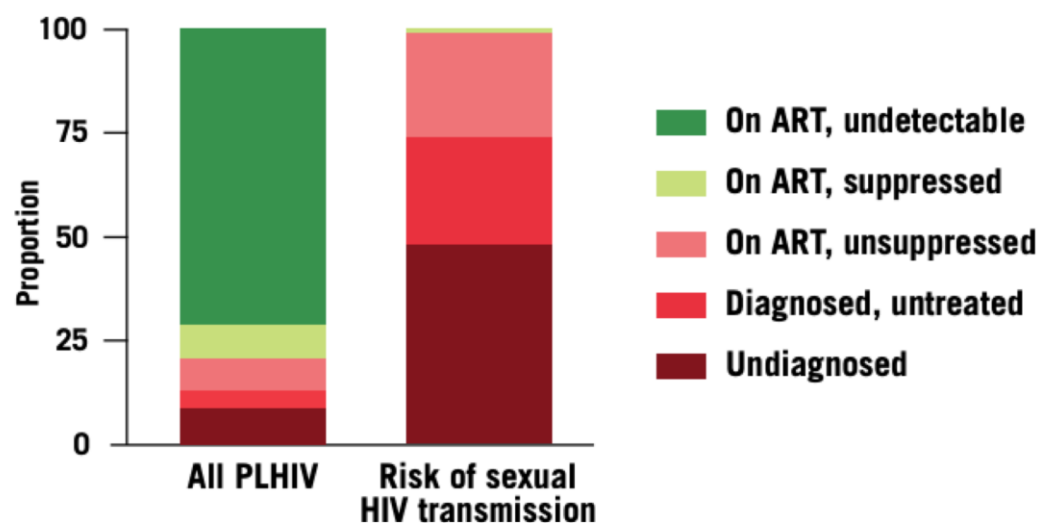
- Younger people (adolescents and children)
- Pregnant women
- Poorer people - often substantial disparity in ART access across districts within the same country.

(UNAIDS Update 2022; Orrell JAIDS 2015; Haberer JIAS 2019)



Critical to achieve viral suppression.

- Individual health
- Reduction in transmission



Viral load categorisation: all PLWH, and those at risk of sexual transmission. Viraemic people drive the epidemic.

The role of HIV viral suppression in improving individual health and reducing transmission: policy brief. Geneva: World Health Organization; 2023. Licence: CC BY-NC-SA 3.0 IGO.



Options for treatment...



Daily oral tablets.

2-monthly intramuscular injections i.e. CAB/RPV



FASTPrEP



FASTPrEP Hub and Spokes Model



Differentiated Service Delivery Model (DSD)

- multiple delivery platforms
- multiple PrEP modalities



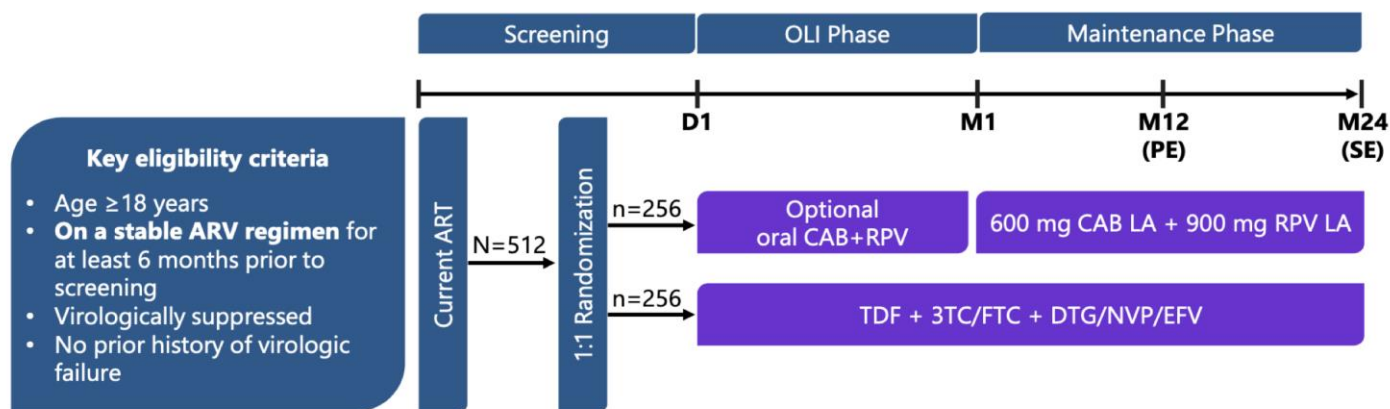
Implementation science-
evaluating uptake, coverage
and effectiveness of a youth-
focused, decentralized PrEP
program.



CARES

CARES: Study Design (Kenya, South Africa, Uganda)

Objective: Efficacy and safety in adults on stable cART in SSA



Primary outcome

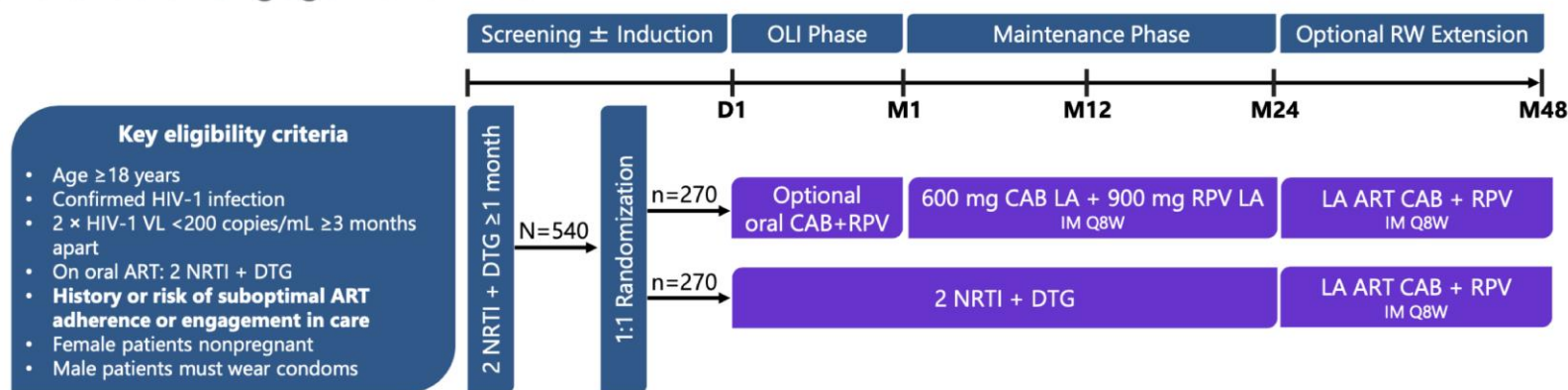
- Noninferiority of CAB + RPV LA every 2 months vs daily cART over 12 months in a resource-limited setting



IMPALA

IMPALA: Study Design (Kenya, South Africa, Uganda)

Objective: Efficacy and retention in care for adults with a history or risk of suboptimal adherence or engagement in SSA



Primary outcome

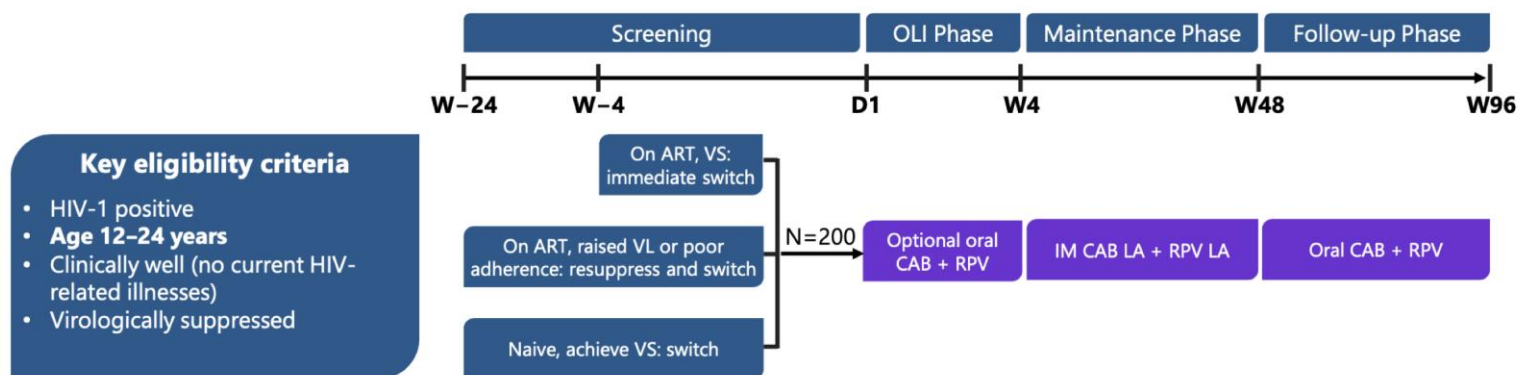
- Noninferiority of CAB + RPV LA every 2 months vs daily cART over 12 months in people with a history or risk of suboptimal adherence



AFINAty

AFINAty: Study Design (South Africa)

Objective: Effectiveness, acceptability, and feasibility of community AYA implementation in SSA



Key eligibility criteria

- HIV-1 positive
- **Age 12-24 years**
- Clinically well (no current HIV-related illnesses)
- Virologically suppressed

Primary outcomes

- Acceptability and tolerability of IM delivery
- Feasibility of IM delivery in a community setting
- Adherence



Benefits

NO TABLETS

- For those who are busy
- For those who are on the move
- Privacy
- Acceptance

“...I feel so good because I do not have to worry about taking my medication at a certain time or waiting for people to leave the room so I can take it.”
(24 YO, Male)

“...I would say that using injectables makes you feel as if you don't have the HIV virus, as if you're just leaving your life and feeling free”
(14 yr, Male)

“...You know how sometimes you want to go out and party, but you have to bring your medication with you because you have to drink it in the morning? The injection simplifies my life, and when I am away from home in the evening, I do not have to rush home to take medication”.
(22 yr, Female)



Challenges – health system

- Medicalisation – current focus is on DSD i.e. give more Rx → move people out of clinics.
- Injections – large volume, painful. Currently need a health care worker to administer. Cold chain.
- Visits become critical: need to attend, reminders, tracing.

DSD building block	Optimized DSD model (future LAIs)
WHEN: frequency of treatment refills and clinical appointment	6-12 monthly injections (SC self injections/implants) 6-12 monthly clinical visits
WHERE: Where are the service provided	Use of non-traditional health care models (pharmacies, minute clinics, community-based organizations, mobile vans, home visits)
WHO: Who can provide the services	ART prescription in HIV clinic/primary care /community /mobile/home services (with referral system) SC self -injection / implant
WHAT: What are the services	Same as current DSD + SC self injection/implant (strong community support)



Challenges - formulation

- Too frequent dosing; RPV needs cold chain.
- Concomitant TB treatment: cannot be given with RFN-based TB treatment.
- Does not treat Hepatitis B (4-9% prevalence in SA: Ive, PlosOne 2013)
- Children – data is coming...
- Pregnancy – some PK data from HPTN084, Purpose 1.



Challenges - costing

- As yet unknown.
- Cost-effectiveness data not yet available. Modelling suggests will need to be targeted to those with reduced adherence (Phillips, The Lancet 2021)



Way forward...

MORE...

- Data beyond clinical trials...
- Implementation in our settings...
- Data on populations who might most benefit.

BUT:

- CAB and CAB/RPV are the beginning, not the final formulation/s
- Learning will occur rapidly as registrations progress.

Thank you!

