



Updates in the Pipeline: What would you like
seen added in the guidelines

**Southern African HIV Clinicians Society Guidelines for ART in Adults:
2023 update Masterclass**

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Summerstrand, Gqeberha

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HOT TOPICS

- HIV treatment long actings
- HIV prevention long actings



So then why all this excitement about long-actings? Especially injections?

Imagine

- Giving a patient 28 tablets for 6 months?
 - Injections every 2, 3 or 6 months
 - Or one injection!!!
-
- Adherence has been a huge issue in ART, PrEP, in adolescents in treatment, in certain key-populations (drug users, 'chaotic lives') – already shown success in LMICs



What are we talking practically? Few Long Acting Injectables (LAI) treatment agents currently

- Only 3 formulations registered by the FDA
- *Cabotegravir with rilpivirine* for treatment
- *Lenacapavir* subcutaneous 6-monthly for treatment - in highly experienced patients
- Multiple other agents (*islatravir, mAbs*) under investigation in phase 2, some of above in phase 3; off-label use happening (combinations, in 'no-hope' situations, in increasing variety of environments)



Agent 1: Cabotegravir (ViiV Healthcare)

- Next generation integrase inhibitor, high(ish) resistance barrier
- (Oral lead in - ?need), nanotechnology intramuscular injectable
- T $\frac{1}{2}$ 21-50 days, studies found it detectable out to year!
- Monthly and 2-monthly dosing: CROI 2024 - ?longer
- This 'tail' a double-edged sword – great for dosing, but lots of time to:
 - to get breakthrough HIV if on PrEP
 - and resistance if on other antiretrovirals for treatment
- Safety excellent (oral and injectable, injection site reactions) (erythema, nodules, intravenous administration can be scary))



Cabotegravir IMI administration is complex

- Separate injection, in a different buttock region, relatively large volume
- Special training required to administer
- Special needle needed for people with obesity
- Other sites (thigh) being tested – similar pk, but patients largely preferred buttocks (CROI, 2023)
- Self-administration devices being tested (2023)



Politics of costs and access to CAB LA

- ViiV initially announced it would make the world's CAB LA
- No immediate access price, no immediate access plan, restrictions on access to drug for operational/investigator studies (us!)
- Immediate reaction was immediate and angry
- Led to licencing to Medicine's Patent Pool (MPP) and granting of 3 licences (Cipla, Viatrix, Aurobindo) – protracted process ?2027, ?will happen
- Cabotegravir is complex
 - technology transfer
 - expensive manufacturing equipment
 - Important QA processes



Politics of costs and access to CAB LA

- Initial cost of ViiV offering of CAB LA high - >\$40 (R720)/dose, now UK£29 (R667)/dose
- Modelling work emerged re CAB LA vs oral PrEP – huge benefits (could avert 3x more infections, save 3x more life-years)
- But needed to be \$9-15 (R270) (CHAI estimates for manufacturing)



Agent 2: Rilpivirine (J&J/Jansen)

- Next generation non-nucleoside reverse transcriptase inhibitor
- Oral agent available for > decade as FDC, injectable now used with CAB LA (oral $\frac{1}{2}$ life 45-50 hours, IMI 13-28 weeks)
- Dosed 2 monthly – unlikely higher
- Given IMI, needs cold chain, painful (very viscous), needs HCW training
- Side effects – local reactions, but actually pretty well tolerated
- Higher barrier to resistance vs older NNRTIs, but still vulnerable
- In HIC, prior resistance/lack of resistance testing a contraindication
- Access issues- No Patent



Agent 3: Lenacapavir (Gilead Sciences)

- Translocation inhibitor
- Oral (daily, weekly) or subcutaneous (3, 6 monthly)
- Well tolerated (subcutaneous nodules?), resistance barrier high(ish)
- Approved for heavily pretreated ARV patients in small study, on optimised backbone – registered FDA/EMA 2022



South African Timeline

- 2022 December: The South African Health Products Regulatory Authority (SAHPRA) approved the CAB-LA for PrEP
- 2024 July: US Government through Pefar announces donation of 231 000 doses
- Future: Roll out strategy
 - : Guidelines
 - : Training of healthcare workers
 - : Public awareness
 - : Patient acceptability



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The End

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