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CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

Understanding Innovations in HIV Treatment

INTEREST Virtual Symposium, 30 November 2020

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CAPRISA hosts a DST-NRF Centre of Excellence in HIV Prevention

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UNAIDS

CAPRISA is the UNAIDS Collaborating Centre for HIV Research and Policy

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Overview

1. **Innovations in :**
   - **Therapeutics including new drug classes**
   - **Diagnostics**

2. **Suitability and scalability of innovations to vulnerable populations**

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Innovations in HIV Therapeutics 2020

- Currently available antiretroviral drug classes inhibit one of four steps in the HIV replication cycle:
  - Viral entry
  - Reverse transcription
  - Viral DNA integration
  - Proteolysis of viral polyproteins

- Therapeutic Innovations include alternate drug targets within the HIV replication cycle:
  - NRTTI's
  - Monoclonal antibodies
  - Rev inhibitors
  - Capsid inhibitors
  - Maturation inhibitors

Long Acting Injectables

- Many new agents are long-acting drug products:
  - require less frequent administration therefore improved adherence
  - suitable for pre-existing multiclass ART resistance,
  - provides sustained viral suppression and additional treatment options for PLWH

- Noteworthy data for dual LA ART use:
  - New data from Flair, Atlas and Atlas-2M
    - LA CAB + LA RPV non-inferior to a 3-drug oral ART in maintaining virologic suppression

  - Islatravir (MK-8591) demonstrated HIV-1 suppression for ≥ 7 days with a single 0.5 mg dose
    - Currently being evaluated in a Phase 2 clinical trial (NCT03272347) for treatment of HIV-1 infection in combination with doravirine.

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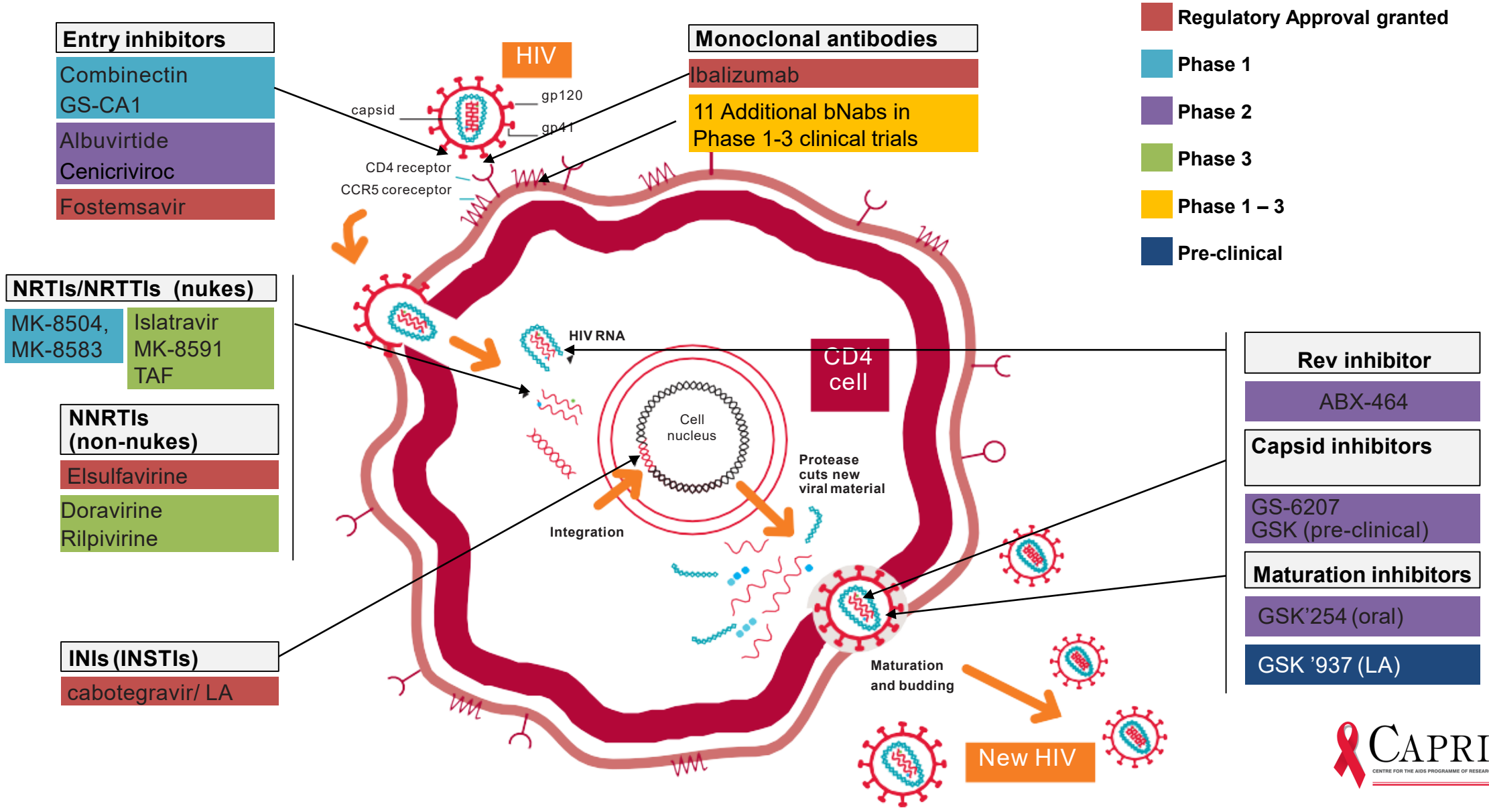
The Current HIV Therapeutics Pipeline



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What's in the horizon?

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pipeline HIV -lite 2020

New drugs in development

htb supplement: 2020 Vol 21:(1)

Recent regulatory approvals/ submissions for antiretroviral agents

Table 1: Recent regulatory approvals and submissions

Compound/formulation	Class	Approved / submitted	Company
ibalizumab	bNAb.	Approved US: April 2018. Approved EU: Sep 2018.	Theratechnologies
fostemsavir	gp120 attachment inhibitor.	Submitted US: Dec 2019. Submitted EU: Jan 2020.	ViiV Healthcare
cabotegravir LA and rilpivirine LA injections	INSTI + NNRTI injections.	Submitted US: Apr 2019 Submitted EU: July 2019	ViiV Healthcare Janssen
cabotegravir oral	INSTI - oral formulation used for lead-in dosing.	Submitted US: Apr 2019 Submitted EU: July 2019	ViiV Healthcare Janssen
elsulfavirine, prodrug of VM-1500A	NNRTI - similar activity to efavirenz. Long-acting monthly IM/SC injections. 96-week phase 2 results at AIDS 2018.	Apparently licensed in Russia. No published phase 3 data or submission to FDA or EMA.	Viriom

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Implications of Novel Therapeutics for Vulnerable populations in disease endemic settings

Pros

- Simplified ART
- Long-acting compounds enables less frequent dosing compared to daily oral ART
- Rescue treatment for people with multiclass HIV resistance
  - Several new drug classes can potentially overcome pre-existing resistance
  - bNAbs - offers a mechanism to overcome pre-existing resistance

Cons

- Costs and Resources
- Cold chain requirement of some new agents
- Insufficient data from vulnerable groups such as women, including in pregnancy, and in adolescents to inform scale up
- Injectables in high burden resource poor settings→ long queues, health facility congestion, needle safety

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Early Infant Diagnosis: SOC vs POC

Evaluation of a routine point-of-care intervention for early infant diagnosis of HIV: an observational study in eight African countries

Flavia Bianchi, Jennifer Cohn*, Emma Sacks, Rebecca Bailey, Jean-Francois Lemaire, Rhoderick Machekano, on behalf of the EGPAF POC EID Study Team†*

SOC

Caregiver presents with infant for HIV testing → Sample collected by a health worker → Sample packaged + sent to referral laboratory → Sample tested at laboratory → Results recorded and sent back to facility → Requesting facility receives and logs results → Caregiver returns to facility to receive results → **ART initiation after 55 days**

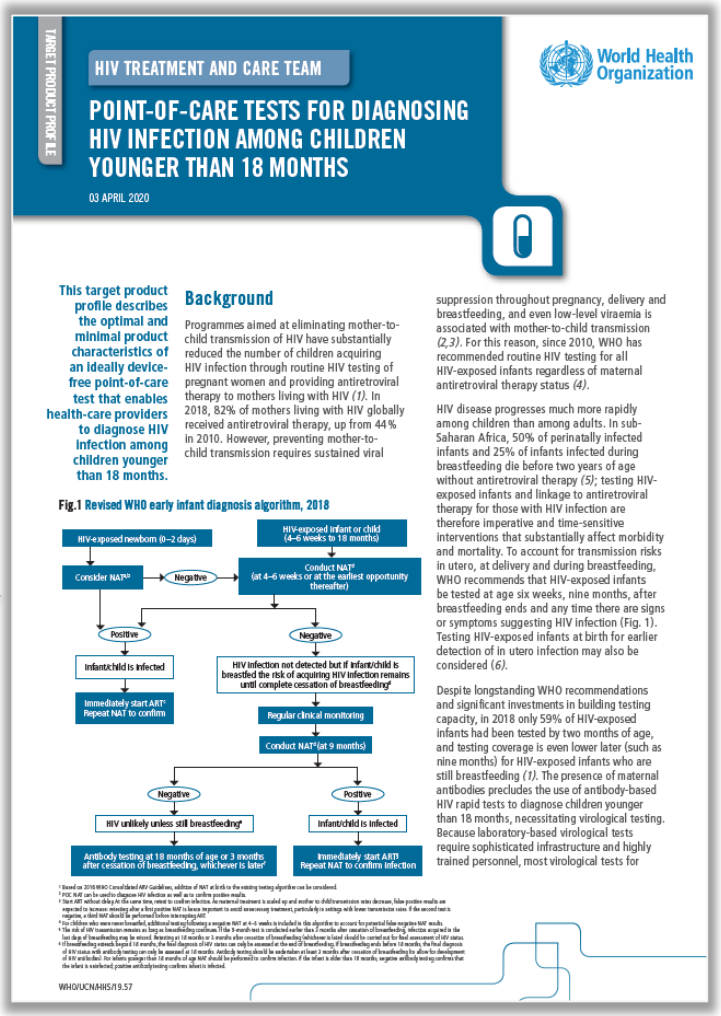
POC

Caregiver presents with infant for HIV testing → Sample tested using POC EID assays within 52-90 mins and results are recorded → Caregiver receive results and ART is initiated → **ART initiation after 0 days**

Innovations in diagnostics: Point of care testing for Early Infant Diagnosis

- In 2019 only 60% of HIV exposed infants received an HIV test within 2 months of birth
- Mortality of untreated, in utero-HIV-infected infants peak at 2-3 months ~ 35% die by 12 months and 52% by 24 months
- Early infant diagnosis of HIV combined with early ART reduces infant mortality
- HIV diagnostic tests providing same day results are now approved by regulatory authorities & are available
- Several systemic reviews on POC testing for EID provide compelling evidence that POC/same day testing:
  - Significantly reduced the time to result return to caregivers – same day result provided in 97%
  - ART treatment initiation occurred within 2 days in 75% of patients diagnosed early in 6/7 studies

WHO released target product profile for POC nucleic acid EID



TARGET PRODUCT PROFILE

HIV TREATMENT AND CARE TEAM

World Health Organization

POINT-OF-CARE TESTS FOR DIAGNOSING HIV INFECTION AMONG CHILDREN YOUNGER THAN 18 MONTHS

03 APRIL 2020

This target product profile describes the optimal and minimal product characteristics of an ideally device-free point-of-care test that enables health-care providers to diagnose HIV infection among children younger than 18 months.

Background

Programmes aimed at eliminating mother-to-child transmission of HIV have substantially reduced the number of children acquiring HIV infection through routine HIV testing of pregnant women and providing antiretroviral therapy to mothers living with HIV *(1)*. In 2018, 82% of mothers living with HIV globally received antiretroviral therapy, up from 44% in 2010. However, preventing mother-to-child transmission requires sustained viral suppression throughout pregnancy, delivery and breastfeeding, and even low-level viraemia is associated with mother-to-child transmission *(2,3)*. For this reason, since 2010, WHO has recommended routine HIV testing for all HIV-exposed infants regardless of maternal antiretroviral therapy status *(4)*.

HIV disease progresses much more rapidly among children than among adults. In sub-Saharan Africa, 50% of perinatally infected infants and 25% of infants infected during breastfeeding die before two years of age without antiretroviral therapy *(5)*; testing HIV-exposed infants and linkage to antiretroviral therapy for those with HIV infection are therefore imperative and time-sensitive interventions that substantially affect morbidity and mortality. To account for transmission risks in utero, at delivery and during breastfeeding, WHO recommends that HIV-exposed infants be tested at age six weeks, nine months, after breastfeeding ends and any time there are signs or symptoms suggesting HIV infection (Fig. 1). Testing HIV-exposed infants at birth for earlier detection of in utero infection may also be considered *(6)*.

Despite longstanding WHO recommendations and significant investments in building testing capacity, in 2018 only 59% of HIV-exposed infants had been tested by two months of age, and testing coverage is even lower later (such as nine months) for HIV-exposed infants who are still breastfeeding *(1)*. The presence of maternal antibodies precludes the use of antibody-based HIV rapid tests to diagnose children younger than 18 months, necessitating virological testing. Because laboratory-based virological tests require sophisticated infrastructure and highly trained personnel, most virological tests for

Fig.1 Revised WHO early infant diagnosis algorithm, 2018

WHO/UCN/HHS/19.57

POC Viral Load Testing for ART monitoring

Point-of-Care HIV Viral Load Testing: an Essential Tool for a Sustainable Global HIV/AIDS Response

Paul K. Drain,[a,b,c] Jienchi Dorward,[d,e] Andrew Bender,[f] Lorraine Lillis,[g] Francesco Marinucci,[h] Jilian Sacks,[i] Anna Bershteyn,[j] David S. Boyle,[g] Jonathan D. Posner,[b,f] Nigel Garrett[d,k]

- POC HIV VL testing improves HIV management by reducing TAT for VL test results
- Same day results provided 99% of the time

Point-of-care HIV viral load testing combined with task shifting to improve treatment outcomes (STREAM): findings from an open-label, non-inferiority, randomised controlled trial

Paul K Drain, Jienchi Dorward, Lauren R Violette, Justice Quame-Amaglo, Katherine K Thomas, Natasha Samsunder, Hope Ngobese, Koleka Mlisana, Pravikrishnen Moodley, Deborah Donnell, Ruanne V Barnabas, Kogieleum Naidoo, Salim S Abdool Karim, Connie Celum, Nigel Garrett

- Point-of-care viral load testing combined with task shifting significantly improved viral suppression and retention in HIV care
- Improved rates of switching to SLART, and monitoring of viraemia on FLART
- Enhanced referral of stable patients to community ART centres

POC VL testing simplifies HIV treatment & improves outcomes for HIV-positive adults receiving ART in resource-limited settings

Implications of Novel Diagnostics for Vulnerable populations disease endemic settings

Pros

- Simply diagnostic and treatment algorithms
- Enhanced diagnosis and linkage to care
- Earlier ART initiation and earlier treatment switch in failing patients
- Minimize retention losses, and costs from multiple health facility visits
- Increased likelihood of clinical action from test result
- Decentralisation of testing

Cons

- Need for trained personnel to perform and interpret tests
- Congestion and queues due to limited test through-put, and longer health visits
- Re-purposing lab infrastructure for POC
  - may cannibalize vulnerable programmes e.g. TB diagnostics
  - Costs and Resources

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Summary and Conclusions

- Innovations in HIV Management include new diagnostics and new drugs incl. new drug classes
  - These innovations holds the promise of a bright and exciting new era in HIV treatment
- Impact of new interventions on therapeutic outcomes in treatment naïve and experienced patients is still poorly understood
- To optimise use of new diagnostics and drugs →need to identify:
  - Who would most likely to benefit
  - Where to locate service
  - What triage system, would be most appropriate
  - How to deliver & integrate innovations within busy health services
- Empiric data guiding implementation: cost effectiveness, access, suitable patient and provider criteria, and advocacy, is required
- Innovations carry enormous potential to simplify and enhance chronic HIV care

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Thank you!

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