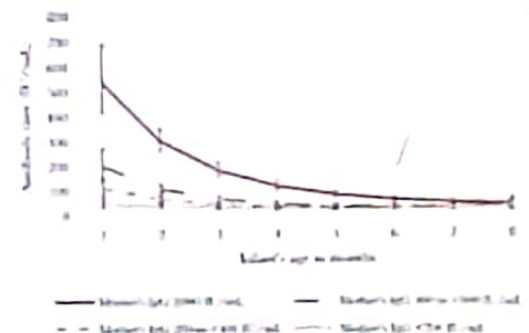

Care of HIV infected infants and children

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HIV diagnosis in infants

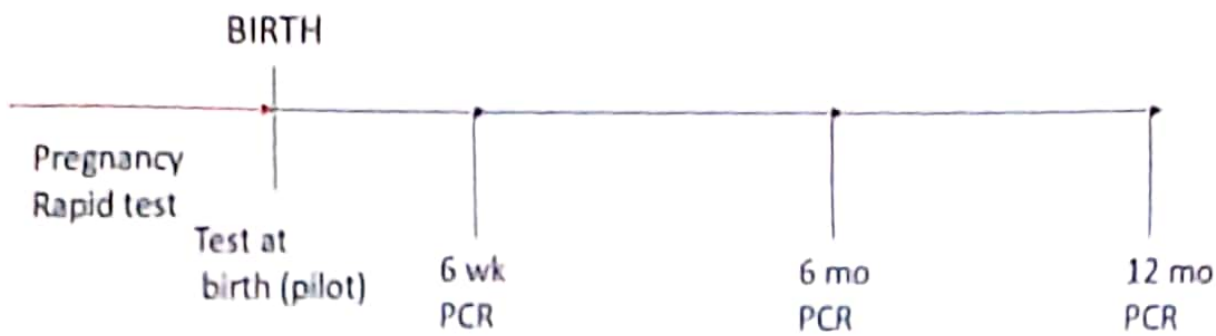
- Maternally acquired **HIV specific IgG antibodies** persist in infants upto 15-18 months
- HIV diagnosis in young infants **is based on identifying the virus** rather than antibodies
- HIV-1 DNA PCR (or RNA PCR) is used to confirm diagnosis



Testing time points (Exposed infants)

- Establish **HIV exposure** before or at birth
 - (Rapid HIV test in mother)
- All HIV exposed infants get PCR test at
 - 6 weeks, 6 months , 12 months
- Rapid HIV test HIV exposed infants 18 months
- Testing at birth:
 - Chance to identify infants infected in-utero

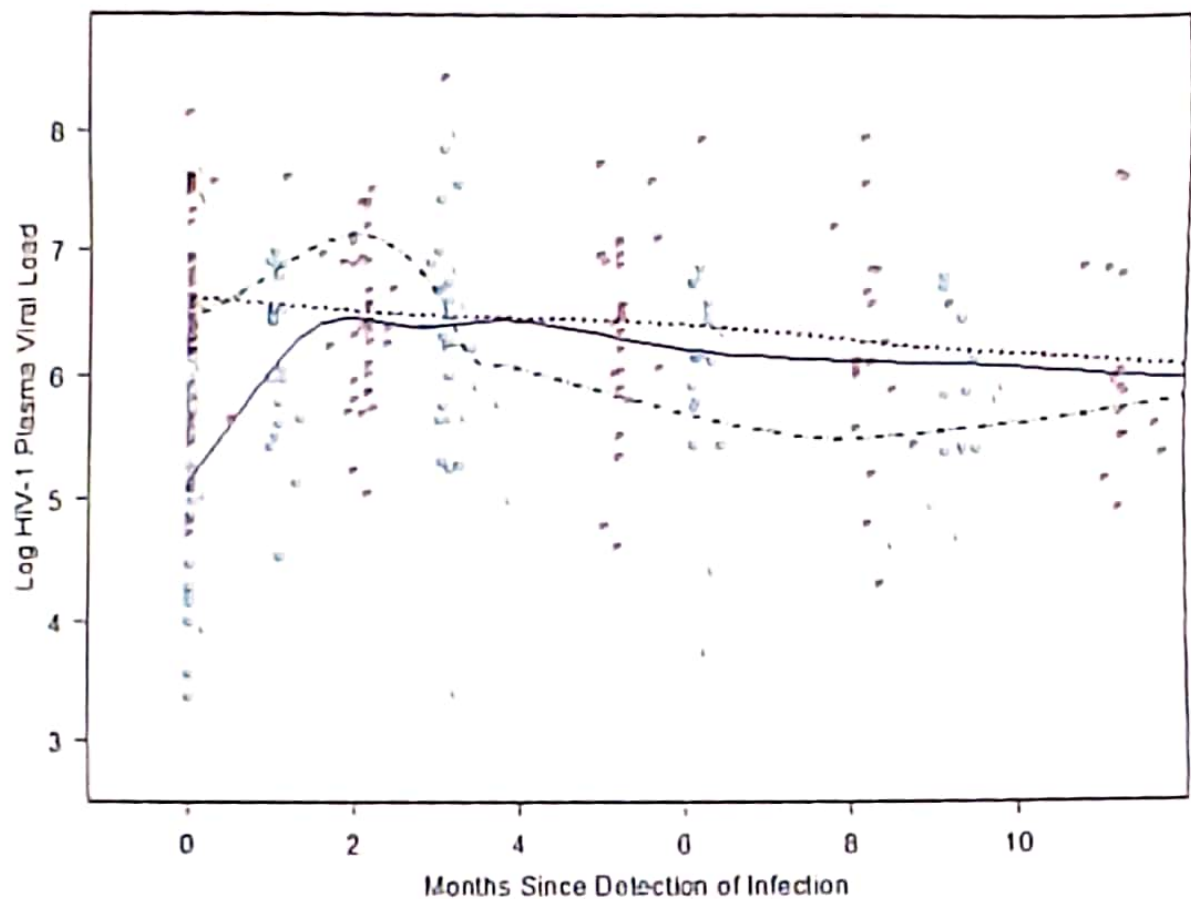
Testing time points (Exposed infants)



Progression of (untreated) HIV disease

- HIV disease progression is **more rapid** in children than adults
 - Highest rate of progression seen in infants infected in utero and during birth
 - Late (breastmilk transmission) slower progression

HIV-1 RNA levels remain high in untreated infants



Common presentation of HIV in children

Growth Failure

- Wasting
- Stunting
- Milestones

Recurrent infections

- Mild to severe
- Respiratory, Skin
- Neurologic

Organ dysfunction

- Cardiomyopathy
- Nephropathy
- Hepatitis,
- Encephalopathy

Malignancy

- B-cell lymphoma
- Kaposi's sarcoma

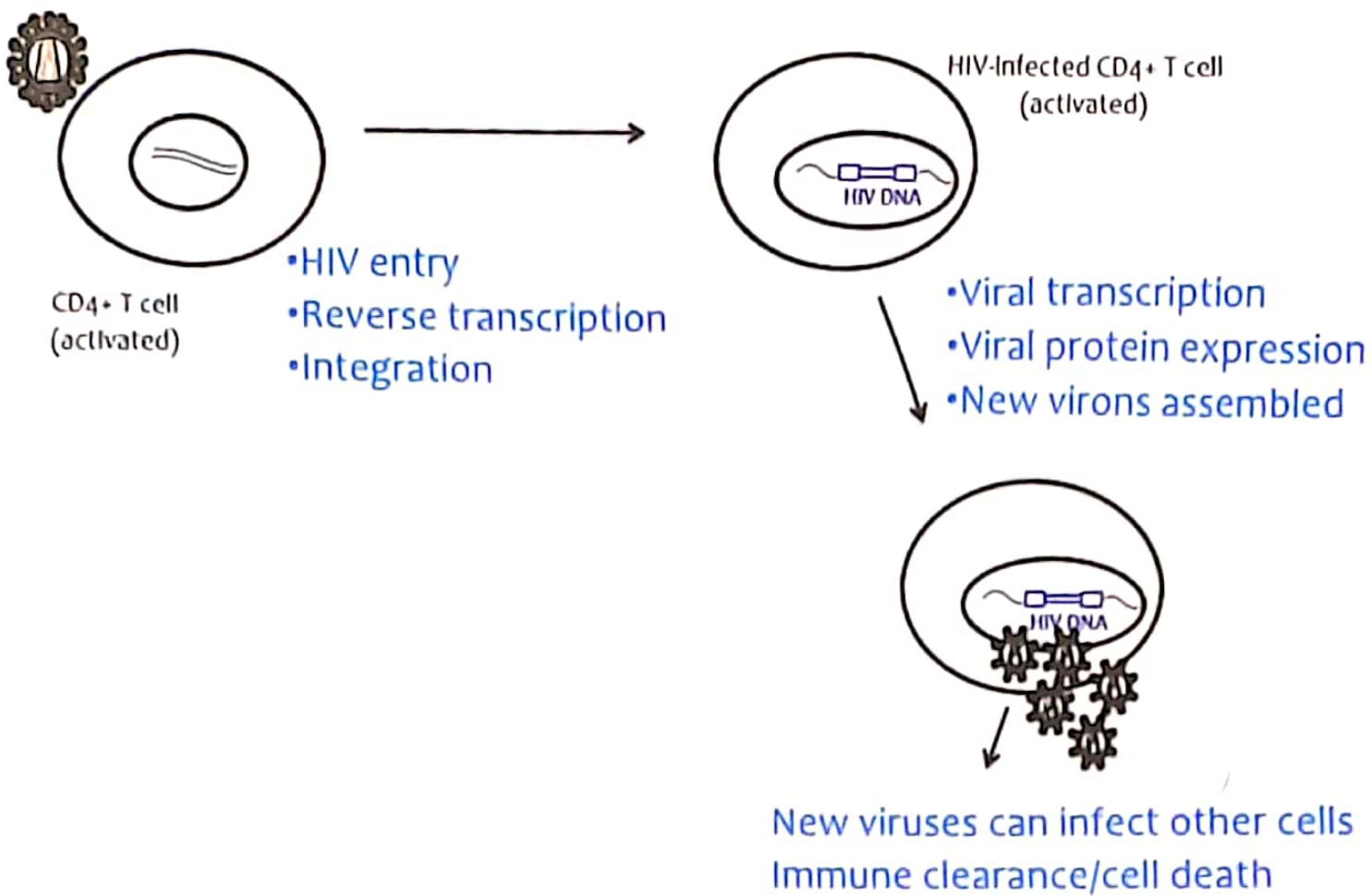
Care package for CWHIV

- Prompt initiation of combination antiretroviral therapy
- Growth monitoring and Nutrition counselling
- Opportunistic infection prevention
 - Cotrimoxazole prophylaxis
 - Isoniazid preventive therapy
 - Regular deworming
- Careful assessment and early treatment of infections
- Psychosocial support and counselling
- Complete Immunization

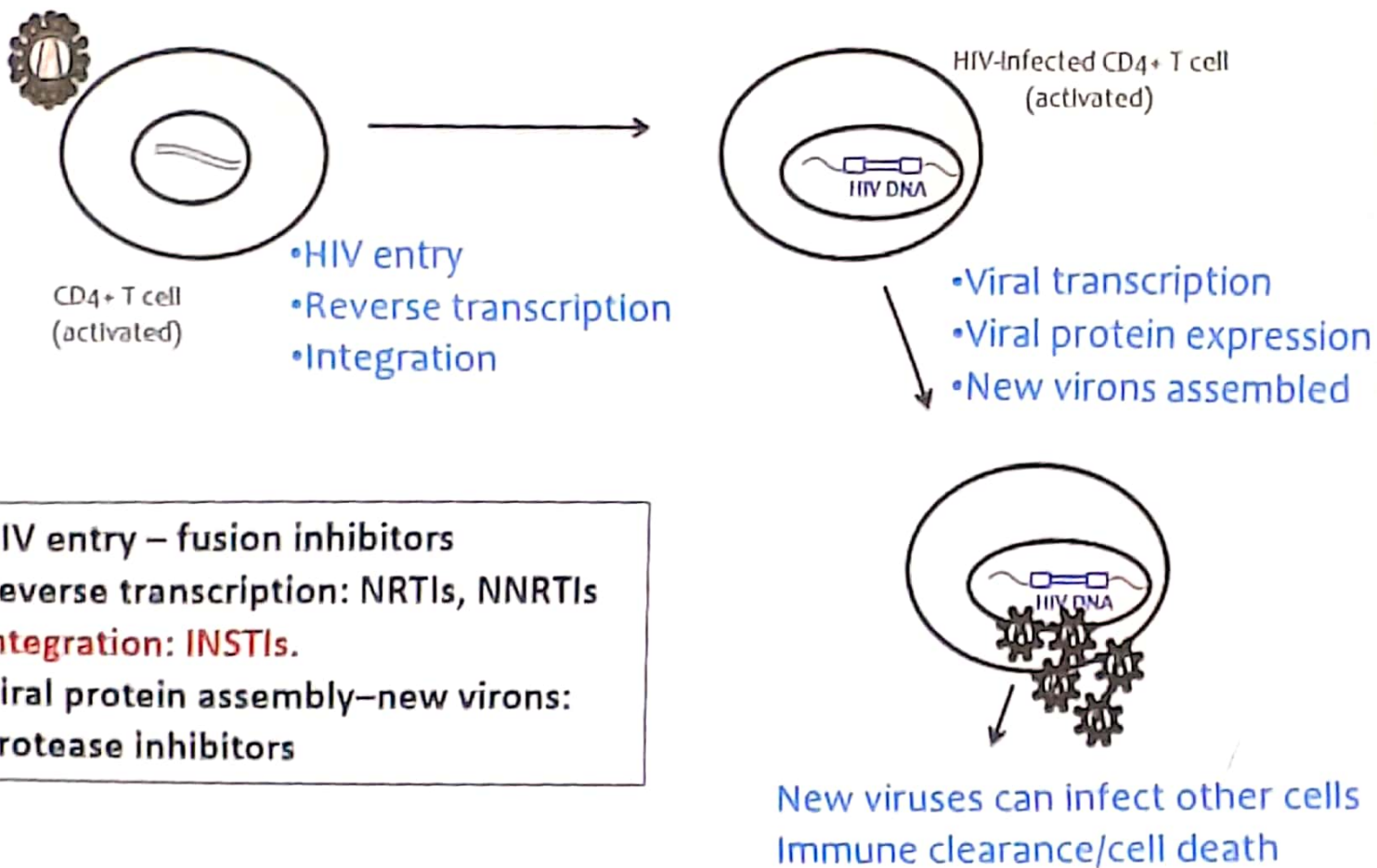
Care package for Adolescents LWHIV

- Adherence and Psychosocial support including disclosure and mental health screening
- Reproductive health services:
 - Pregnancy screening
 - Family planning services
 - Sexually transmitted disease screening and treatment
- Clinical evaluation and early treatment of infections
- Prophylaxis against TB and Cotrimoxazole(PCP)
- Prevention of HIV transmission –partner tracing

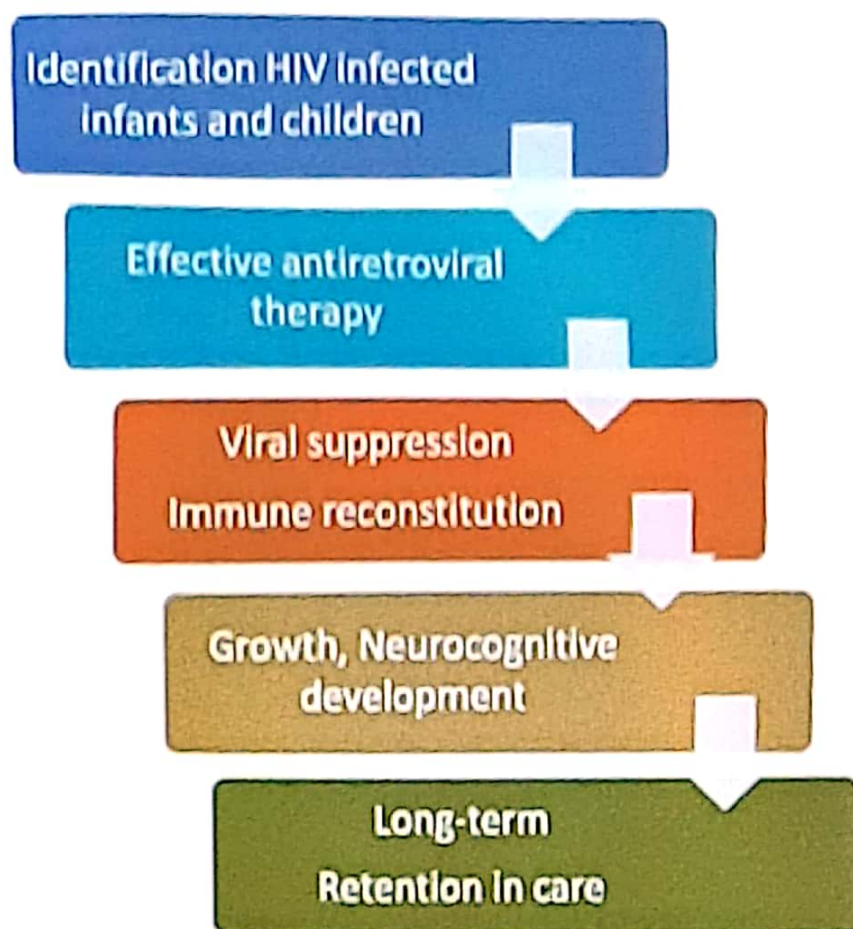
Targets for Antiretroviral drugs



Targets for Antiretroviral drugs



Target of Paediatric HIV treatment



Prevent
HIV drug resistance
Loss to follow-up
Mortality

Recommendations: When to start ART

- ART should be initiated as soon as possible after HIV diagnosis preferably within 2 weeks.
 - Same day initiation for infants preferable
 - Baseline lab tests should not delay ART initiation
- Special considerations
 - Cryptococcal meningitis – defer 4-6 weeks
 - Tuberculosis – may defer upto 2 weeks
 - Anticipated major problems with adherence – soon as adherence addressed

Readiness assessment – 1a

Psychosocial/Knowledge Criteria (patients/caregivers)

1. Understands nature of HIV infection and benefits of ART
2. Screened negative for alcohol/other drug use/depression other psychiatric illness, or is stable on treatment
3. Willing to disclose/has disclosed HIV status, ideally to a family member or close friend
4. Received demonstration of how to take/administer ART and other prescribed medication

Readiness assessment – 2b

Support Systems for patients/caregivers)

5. Received information on side effects of ART ,understands what steps to take
6. Caregiver is committed to long-term support of the patient, daily administration of ART
7. Barriers to adherence been identified - plan in place to address them : e.g. frequent travel for work, unexpected travel, distance from clinic
8. Provided accurate locator information and contact details
9. Patient/caregiver feels ready to start ART today

Preferred 1st line ART (NASCOP 2019)

Age/Weight	Preferred Regimen
Birth – 4 weeks	AZT + 3TC + RAL ¹
< 20 kg (above 4 weeks old)	ABC ² + 3TC + LPV/r ³
20 kg – 35 kg	ABC ² + 3TC + DTG ^{4,5}
> 35 kg	TDF ² + 3TC + DTG ^{5,6}

1. If RAL is not available use NVP instead (switch to ABC/3TC+LPV/r at 1 month)
2. TAF will be the preferred NRTI once appropriate formulations are available
3. DTG will replace LPV/r as preferred ART for children < 20 kg once appropriate formulations are available
4. Effective contraception should be offered to adolescent girls of childbearing potential.
5. DTG can be prescribed for adult women and adolescent girls of childbearing age or potential who wish to become pregnant or who are not otherwise using or accessing consistent and effective contraception if they have been fully informed of the potential increase in the risk of neural tube defects
6. For adolescent girls who choose not to use DTG, then LPV/r 400mg (if <35 kg) or ATV/r 300/100mg (if ≥35 kg) can be used and are safe in pregnancy

Use of Alternative ARVs in First-Line Regimens

Age/Weight	Scenario and ARV Affected	Recommended Alternative ARV to Use
Birth – 4 weeks	RAL: Not available or unable to tolerate	Use NVP
	AZT: Infant Hb < 9.5 g/dL	Defer ART until 4 weeks of age, then start ABC+3TC+LPV/r
< 20 kg (above 4 weeks old)	ABC: Develops ABC hypersensitivity reaction	Use AZT (if Hb ≥ 9.5 g/dL); if Hb < 9.5 g/dL consult Regional or National HIV Clinical TWG
	LPV/r: Unable to tolerate	Use RAL
	LPV/r: Currently on anti-TB medications	Use LPV/r + RTV If not able to tolerate super-boosted LPV/r + RTV then use RAL double-dose (if ≥ 2 years old) or ABC+3TC+AZT (if < 2 years old)
20 kg – 35 kg	ABC: Develops ABC hypersensitivity reaction	Use AZT (if Hb ≥ 9.5 g/dL); if Hb < 9.5 g/dL consult Regional or National HIV Clinical TWG
	DTG: Unable to tolerate	Use LPV/r If unable to tolerate LPV/r then use RAL
	DTG: Currently on rifampicin-containing TB treatment	Use RAL at double standard weight-based dose until 2 weeks after completing TB treatment, then switch to DTG
> 35 kg	TDF: Impaired renal function (CrCl < 60 ml/min) or unable to tolerate	Use ABC
	DTG: Unable to tolerate	Use LPV/r If unable to tolerate LPV/r then use RAL
	DTG: Currently on rifampicin-containing TB treatment	Increase DTG to 50 mg BD until 2 weeks after completing TB treatment, then revert back to DTG 50 mg once daily

Dolutegravir (DTG)

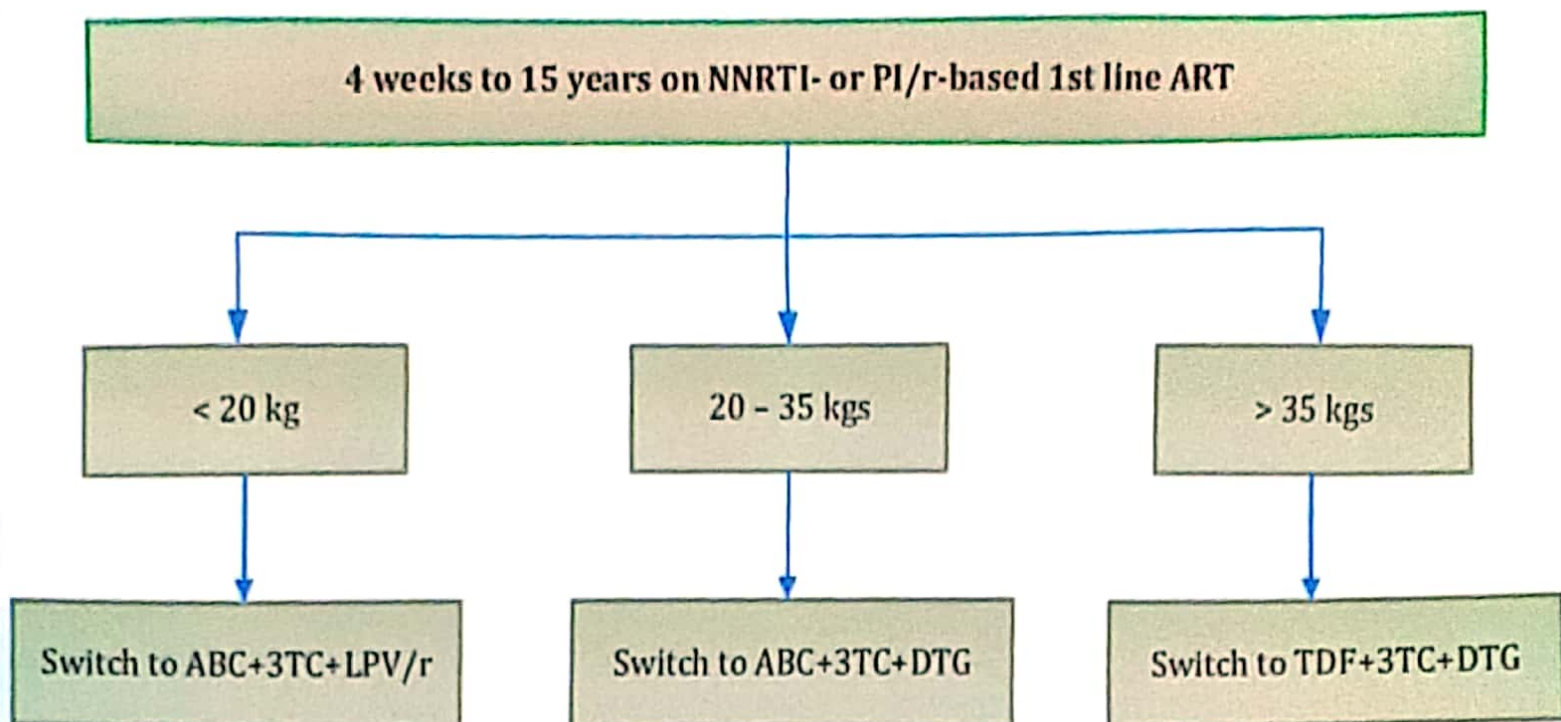


- DTG is a second generation INSTI that retains activity in presence of resistance mutations to other INSTIs
 - DTG is approved for children ≥ 6 years with a weight ≥ 15 kg (FDA & EMA)
 - DTG widely available for children ≥ 20 kg (dose 50 mg once daily)- WHO approval reflects availability
 - Dosing formulation for children < 15 kg expected in 2020
- DTG 50 mg twice daily dosing for concurrent Rifampicin based TB treatment (weight ≥ 35 kg)

Rationale for 2019 WHO updates

- Compared with EFV-based regimens DTG has:
 - Higher viral suppression & more rapid viral suppression
 - Lower risk of discontinuing treatment (tolerability)
 - Lower risk of developing HIV drug resistance (high genetic barrier)
 - Lower potential for drug–drug interactions
- However DTG results in:
 - increased risk for sleep disorders and headache

Transition to Preferred 1st line Regimens for Children and Adolescents



Treatment failure : Clinical failure

- New or recurrent HIV associated condition indicating severe immune deficiency (WHO 3/4 condition)
 - Sufficient time on ART : at least 6 months
 - Exclude IRIS
 - Always confirm with a viral load test

Treatment failure in : Virologic failure

- Persistent high viral load ≥ 1000 copies/ml
- Results of TWO viral loads measured at least 3 months apart with intensified adherence support between
- Patient must have been on ART at least 6 months

Preferred 2nd Line ART Regimens for Children and Adolescents (NASCOP 2019)

Failing 1 st -line regimen	Preferred 2 nd -line regimen	Alternative 2 nd -line regimen
ABC (or TDF)+3TC+LPV/r	AZT+3TC +DTG ^b	AZT+3TC+RAL
AZT+3TC+EFV (or NVP)	ABC ^a +3TC+DTG ^b	ABC ^a +3TC+LPV/r (or ATV/r)
ABC+3TC+EFV (or NVP)	AZT+3TC+DTG ^b	AZT+3TC+LPV/r (or ATV/r)
AZT+3TC+DTG	ABC ^a +3TC+LPV/r (or ATV/r)	ABC ^a +3TC+DRV/r
ABC+3TC+DTG	AZT+3TC+LPV/r (or ATV/r)	AZT+3TC+DRV/r
a. TDF is preferred to ABC if appropriate formulations are available. Adult formulation of TDF (300mg once daily) can be used for children 35 kg and above b. Adult formulation of DTG (50mg once daily) can be used for children 20 kg and above. For children 15 – 20 kg DTG can be used once appropriate formulations are available		

Case 3

A 5 year old boy on AZT/3TC/NVP and weighing 21kgs with a VL of 2345 copies/ml done 12 months ago is brought to your facility today.

A decision to change his current ARV regimen is made due to the NVP phase-out.

What regimen will you choose for him?

- A.ABC/3TC/DTG
- B.ABC/3TC/LPV/r
- C.TDF/3TC/LPV/r
- D.AZT/3TC/LPV/r

TB co-infection in CALWHIV

Ago	Scenario	Recommendation
<20kgs ^a	ABC/3TC/LPV/r	Super Boost LPV/r ^c
20kgs-35kgs	ABC/3TC/DTG	RAL at x2 standard weight-based BD dosing until 2 weeks after completion of Anti TBs
>35kg	TDF/3TC/DTG	DTG ^b x2 standard dose BD dosing
a. For children who cannot tolerate LPV/r + RTV (usually because of GI side-effects), the alternative regimen is RAL (double-dose) if ≥ 2 years old, if < 2 years old use triple-NRTI regimen of ABC + 3TC + AZT for the duration of TB treatment, then return to weight based ARV regimen upon completion of TB. b. For children >35kgs HIV-TB co-infected to use DTG x2 standard dose BD dosing. Those who cannot tolerate DTG, the alternative is RAL at X2 standard weight-based BD dosing		

TB co-infection in CALWHIV

Age	Scenario	Recommendation
<20kgs ^a	ABC/3TC/LPV/r	Super Boost LPV/r ^c
20kgs-35kgs	ABC/3TC/DTG	RAL at x2 standard weight-based BD dosing until 2 weeks after completion of Anti TBs
>35kg	TDF/3TC/DTG	DTG ^b x2 standard dose BD dosing
a. For children who cannot tolerate LPV/r + RTV (usually because of GI side-effects), the alternative regimen is RAL (double-dose) if ≥ 2 years old, if < 2 years old use triple-NRTI regimen of ABC + 3TC + AZT for the duration of TB treatment, then return to weight based ARV regimen upon completion of TB. b. For children >35kgs HIV-TB co-infected to use DTG x2 standard dose BD dosing. Those who cannot tolerate DTG, the alternative is RAL at X2 standard weight-based BD dosing		

Case 4

A 14 year old female, weighing 30 kg on ABC/3TC/DTG is diagnosed with TB and started on 1st line Anti TB. Before initiation of Anti TBs, it is recommended that the regimen be adjusted.

What changes will be made to the regimen before initiating Anti TB?

- A. Double the dose of DTG
- B. Switch DTG to Super Boosted LPV/r
- C. Switch to RAL at x2 standard weight-based BD dosing
- D. Switch DTG to EFV

Monitoring response to ART

- The **most reliable** indicator of response to ART is viral suppression
- Viral suppression in infants and young children **may take longer** than in adults CD4
- HIV-1 RNA testing schedule: baseline, 6 and 12 months then annual
- CD4 count and percentage are important makers of immune reconstitution:
 - baseline, 6 monthly until reconstituted and as indicated

Laboratory monitoring

Test	Schedule
CD4 count	Baseline and if Treatment failure
HIV viral load	Baseline, 6, 12 months, annually if VL < 1000 copies/ml
Serum CRAG	Baseline (adolescents CD4 < 100 copies/ml)
Hb	Baseline, symptom-directed On AZT baseline, 2,4,12 week
Urinalysis, creatinine	Baseline and annually if on TDF
Lipids, Glucose	Baseline and annually
ALT	Specific clinical indication

Common significant adverse drug reactions

Drug	Adverse reaction
Abacavir	Hypersensitivity
AZT	Anemia, neutropenia Lactic acidosis, lipoatrophy
TDF	Renal dysfunction
NVP, EFV, ETV	Skin rash/hypersensitivity
Efavirenz	CNS side effects, gynaecomastia
NVP	Hepatotoxicity
PIs	GI intolerance, dyslipidemia,
ATZ	Hyperbilirubinemia
DRV	Skin rash/hypersensitivity
INSTIs	Rash/hypersensitivity
DTG	Insomnia, glucose intolerance

ARV adverse events principles of management

- Rule out other medication as causes.
- Consider other disease processes including IRIS.
- Mild reaction (grades 1):
 - continue ARV and monitor.
- Moderate (grade 2):
 - continue ARV and offer symptomatic treatment
- Severe reaction (Grade 3):
 - Single drug substitution
- Life-threatening (Grade 4)
 - Stop all medications including ARV and manage condition.
 - When recovered introduced modified regimen

Modifiable factors - treatment failure in children

- Suboptimal ART regimens
- Inappropriate drug formulations
- Family and caregiver dynamics
- Societal and cultural barriers

