



# **First line ARV Drugs: Mechanism of action, dosage and storage**

**Part B: Module B1  
Session 3**



# Objectives

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1. Describe how the different classes of ARVs work
2. Identify the drugs to include in the first-line ARV regimen
3. Discuss the use of these regimens in reference to Nigerian guidelines
4. Discuss dosages and administration of ARVs
5. Discuss storage and availability in country

# Desired Characteristics of a First Line Regimen

- The simplest three-drug combination as the first line therapy. Simple =
  - As few pills a day as few times as possible
  - Lower likelihood of side effects
  - Of sufficient potency to have desired effect
  - Scalable / Affordable
  - Practical in the Nigerian Setting
    - for example – not requiring refrigeration
  
- There is no perfect first line regimen.



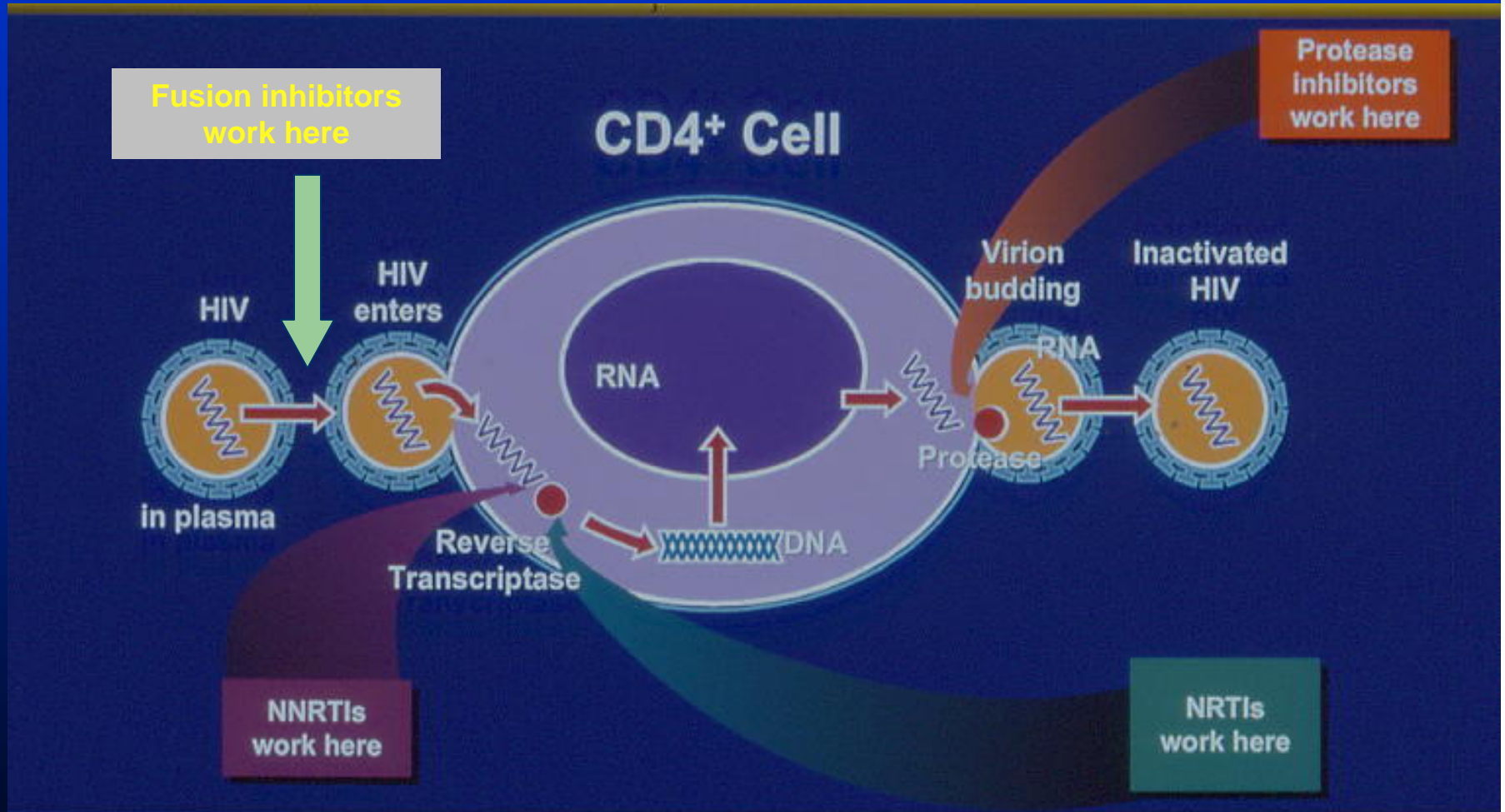
# What Therapy to Begin With

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- At least three antiretrovirals are needed in combination to achieve the following desirable outcomes of antiretroviral therapy:
  - Dramatically reduce viral replication
  - Reduce the risk of resistance and treatment failure
- Choices\* include
  - Seven nucleoside reverse transcriptase inhibitors (NRTIs)
  - One nucleotide reverse transcriptase inhibitor (NtRTI)
  - Three non-nucleoside reverse transcriptase inhibitors (NNRTIs) and
  - Eight protease inhibitors (PIs)
  - One fusion inhibitor

\* Most, but not all, of these are available in Nigeria

# HIV Lifecycle and Antiretroviral Therapy





# Antiretroviral therapies: Mode of action

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- Antiretroviral drugs (ARVs) act on HIV by interfering with its reproductive cycle.
- The main stages of the cycle where these drugs act to inhibit replication of the virus are:
  - NRTIs and NNRTIs prevent formation of proviral DNA
    - *Mechanism: inhibit reverse transcriptase enzyme*
    - *NRTIs and NNRTIs work by two different mechanisms*
  - PIs inhibit maturation of virion
    - *Mechanism: interrupt the protein processing and virus assembly*
  - Fusion inhibitors prevent attachment of HIV to CD4 cells

## Antiretroviral therapies: Mode of action, continued

- Nucleoside reverse transcriptase inhibitors (NsRTIs) and nucleotide reverse transcriptase inhibitors (NtRTI), or NRTI as a whole group
  - Lead to premature termination of the production of the HIV DNA chain
  - Are competitive inhibitors of reverse transcriptase
  - Are active against both HIV 1 and 2
  - NRTIs not recommended as monotherapy (one drug regimen)---this leads to the rapid development of resistance



# Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

- NNRTIs work to change the conformation of reverse transcriptase, inhibiting it from functioning properly
  - Non-competitive inhibitors (NRTIs are competitive)
- NNRTIs do not work in HIV-2 and HIV-1 group O infection
- Delavirdine and Nevirapine are antagonistic in action on the HIV reverse transcriptase activity---do not use together
- Interaction with some drugs occurs due to induction and/or inhibition of cytochrome P450 enzymes in liver

## Nigerian Guidelines Recommended First Line Regimen for Adults/Adolescents

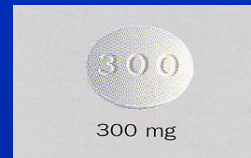
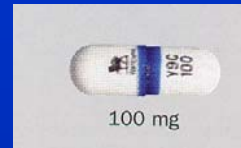
- d4T (stavudine) + 3TC (lamivudine) + NVP (nevirapine)
- ZDV (zidovudine) + 3TC (lamivudine) + NVP (nevirapine)

## Alternative First Line Regimens for Special Categories of Adults/Adolescents

- Pregnant women or women who are likely to become pregnant whose CD4 count is < 250
  - ZDV (zidovudine) + 3TC (lamivudine) + NVP (nevirapine)
- Patients with HIV and Tuberculosis
  - ZDV (zidovudine) OR d4T (stavudine) + 3TC (lamivudine) + NVP (nevirapine)
    - (during non-Rifampicin containing continuation phase)
  - ZDV (zidovudine) OR d4T (stavudine) + 3TC (lamivudine) + EFV (efavirenz)
    - (during Rifampicin containing intensive or continuation phase)

# Zidovudine/Retrovir (AZT)

- 100mg capsules
- 300 mg tablet
- 10mg/ml yellow liquid, strawberry flavoured
- Intravenous formulation



## Zidovudine/Retrovir (AZT)

- Was first available antiretroviral medication
- Initially used for cancer but taken off market for that indication (due to toxicity concerns at higher doses than are being used now for ART)
- Adolescent and adult dose
  - 300 mg PO BD

# Zidovudine/Retrovir (AZT)

- Also comes in combination forms

- *Combivir*

AZT + 3TC

- *Trizivir*

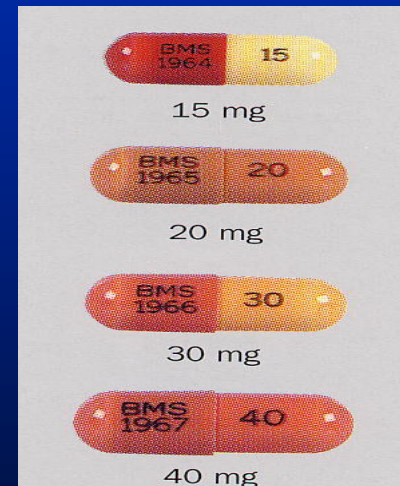
AZT + 3TC + ABC

## Zidovudine/Retrovir (AZT)

- Tablets and capsules can be stored at room temperature
- Protect capsules from moisture
- May be taken with or without food

# Stavudine/Zerit (d4T)

- Capsules: 15 mg, 20 mg, 30 mg, 40mg
- Solution: 1 mg/ml

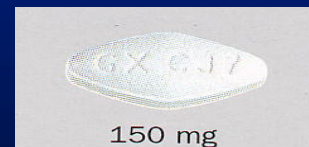


## Stavudine/Zerit (d4T)

- Can be given with or without food
- Capsules can be opened and sprinkled on mashed potatoes, porridge or other soft foods
- Dose
  - > 60 kg            40 mg bid
  - < 60 kg            30 mg bid

# Lamivudine/Epivir (3TC)

- Tablets: 150 mg, 300mg
- 10 mg/ml clear solution
- Epivir HBV: 5 mg/ml solution , 100 mg tab



# Lamivudine/Epivir (3TC)

- Adolescents/Adults
  - < 50 kg: 2 mg/kg twice daily
  - ≥ 50 kg: 150 mg twice daily or 300 mg once daily
- Also comes in Combivir and Trizivir

## Lamivudine/Epivir (3TC)

- Can be given with or without food
- Store oral solution at room temperature
- Dosage should be decreased in patients with renal impairment

# Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

- NVP, Nevirapine (Viramune)
- EFV, Efavirenz (Sustiva)
- DLV, Delaviridine (Rescriptor)\*

\*Not used in Nigeria

# Nevirapine/Viramune (NVP)

- Oval White tablet 200 mg
- Oral solution 10 mg/ml

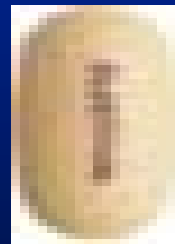


# Nevirapine/Viramune (NVP)

- Adolescent/Adult
  - Oral: 200 mg every 12 hours
- INITIATE THERAPY WITH ONCE DAILY DOSING FOR 14 days for ALL patients. If no rash or other problems, then increase to full dose.
- Because of the long half-life of nevirapine, when you discontinue it, continue other antiretroviral medications for three to seven days so as to reduce the likelihood of resistance (NNRTI tail)

# Efavirenz/Sustiva (EFV)

- Capsules: 50 mg, 100 mg, 200 mg
- Tablets: 600 mg
- No oral suspension



## Efavirenz/Sustiva (EFV)

- Adolescents and Adults
  - 600 mg once daily
  - Increase to 800 mg once daily if used with rifampicin
- Because of the long half-life of efavirenz, when you discontinue it, continue other antiretroviral medications for three to seven days so as to reduce the likelihood of resistance (NNRTI tail)

## Efavirenz/Sustiva (EFV)

- Can be administered with or without food, but avoid high fat meals
- Capsules can be opened and added to liquids or foods; grape jelly masks the peppery taste well
- Tolerability of CNS side effects can be improved by bedtime dosing



# Antiretroviral Therapy Combinations

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Do not use the following drugs in combination

AZT + d4T

ddl + ddC

d4T + ddC

3TC+ ddC

ddl + d4T

ddl + Indinavir