

Therapy switch

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44 year old woman

- Married
- Spouse: HIV serostatus unknown to her (declined to go for HIV test)
- Children: 4 in school, youngest 8 years
- Sells second hand clothes
- No prior use of ARVs

September 2003: 1st visit to the IDC

- Papular pruritic eruption for 7 months
- Diarrhoea + abdominal pain for 1 month
- Oesophageal candidiasis
- **Treatment:** Fluconazole, metronidazole, cetirizine, cotrimoxazole

Lab results

- CD4 count: 1/ μ L
- WBC: 2,300/ mm^3 lymphocytes: 800/ mm^3
- Hb 7.8 g/dl
- Stool exam – no pathogens

A week later

- Diarrhoea had stopped, still with prurigo and abdominal pain

Management:

- Counseled and started on ARVs (D4T, 3TC, NVP)
- Ferrous sulphate and folic acid

During the following 4 months

- Prurigo progressively decreased
- Recurrent episodes of oral candidiasis

6 months after starting HAART

- Only complaint was pruritis at night
- She had gained 9 kg since the start of ARVs
- She reported good adherence to the ARVs and cotrimoxazole

Expected lab result?

Lab results

CD4 count: $1/\text{mm}^3$

WBC: $1.5 \times 10^3/\mu\text{l}$

lymphocytes: $0.5 \times 10^3/\mu\text{l}$

Hb: 7.9 g/dl

8 months after starting HAART

- Presented with history of fever and odynophagia for 2 weeks
- Lost 3 kg, was afebrile, moderate pallor and extensive oral thrush, only prurigo scars

Expected lab result?

Lab results

- CD4 count: $1/\text{mm}^3$
- WBC: $2.3 \times 10^3/\mu\text{l}$
- lymphocytes: $0.5 \times 10^3/\mu\text{l}$
- Hb: 7.9 g/dl

12 months on HAART

- Weight loss 11kg
- Unexplained prolonged fevers
- Recurrent oral candidiasis
- Prurigo

What next?

Goals of Antiretroviral Therapy

- **Maximal and durable suppression of viral load**
- **Restoration or preservation of immunologic function**
- **Improvement in quality of life**
- **Reduction of HIV-related morbidity and mortality**

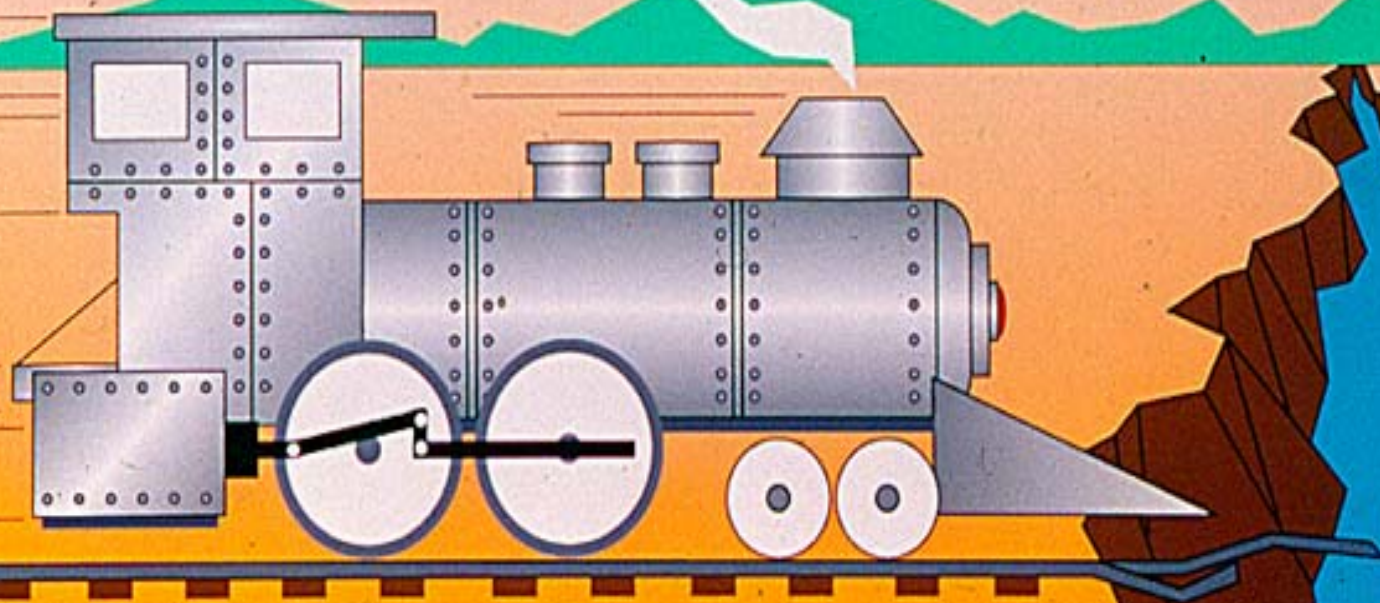
Tools to Achieve Goals of Therapy

- **Maximize adherence to the antiretroviral regimen**
- **Rational sequencing of drugs**
- **Preservation of future treatment options**
- **Use of drug-resistance testing in selected clinical settings**

Development of AIDS: Like an Impending Train Wreck

Viral load = Speed of the train

CD4 count = Distance from site of crash



Who should be treated ?

Biological & clinical criteria

- CD4 lymphocyte count $< 200/\text{mm}^3$
- Clinical evidence of severe immune deficiency (WHO stage 3 or 4)

Other criteria

- Commitment for long term ARV treatment
- Medical and biological follow-up possible

When to change therapy

- Treatment failures
- Drug toxicity
- Drug interactions

Patient Evaluation

- History and physical examination.
- Relevant basic lab investigations e.g. change in CD4 where available.
- Assessment of adherence and remaining treatment options considered.

Changing for treatment failure

- **Clinical**: disease progression with development of an OI or malignancy on drugs for at least six months. (differentiate from IRIS which can be seen within the first eight weeks if sub-clinical infection present)
- **Immunological**: a fall in CD4 counts more than 30% on two or more occasions from the peak value or a return to, or below, the pre-therapy baseline. (TLC decline)

- **Virological**: continued detectable viraemia is indicative of incomplete viral suppression. Not an option in many developing countries

Causes of treatment failure

- Poor adherence
- Infected with a viral resistant strain
- Poor ARV regimen
- Impaired drug absorption
- Drug interactions

Changing for toxicity and interactions

- If there is a good therapeutic response;
 - development of **definable toxicity** results in switch of one drug e.g. AZT anaemia to D4T
 - Development of **unclear source** of intolerable toxicity that decrease adherence, complete regimen switch.

Recommended regimens

1ST Line regimen	Pregnancy and TB considerations
D4T/3TC + NVP or EFV OR ZDV/3TC+ NVP or EFV	Give NVP in pregnant women or women for whom effective contraceptive cant be assured. Give EFZ for patients requiring simultaneous ART and TB therapy including rifampicin.

Recommended regimens

1st line regimen	Second line regimen for treatment failure
D4T/3TC + NVP or EFV OR ZDV/3TC+ NVP or EFV	ZDV/DDI + LPV/r D4T/DDI + LPV/r

Switching ARV's for toxicity

Zidovudine ↔ **stavudine** ↔ **abacavir**

Lamivudine ↔ **didanosine** ↔ **abacavir**

Nevirapine ↔ **efavirenz**

Nelfinavir ↔ **indinavir**

Standard 1 st line	Side Effects	Alternative 1 st line
d4T + 3TC + Nevirapine	Rash	AZT + 3TC + Efavirenz 600 mg
	Neuropathy	AZT + 3TC + NVP
	Severe hepatitis	3TC + d4T + Indinavir/RTV
	On initial phase TB at the start	AZT/3TC + EFV (800 mg)
	Develops TB > 2 months after start HAART	D4T/3TC + EFV (800 mg)
Pregnancy		
AZT/3TC/NVP	Aneamia	3TC/d4T/NVP
AZT/3TC/NVP	Rash	AZT/3TC/Nelfinavir

Decision to change a treatment regimen must take into account:

- The **adherence** of the patient in the past and the adherence with the second line often more complicated seconding treatment regimen.
- The cost of the new treatment options
- The possibilities to access new ARVs in the near future

Decision to change a treatment regimen must take into account:

- **The degree of immunodeficiency, the CD4 nadir**
- **The tolerance and side effects of the actual regimen and potential new treatment options**
- **The remaining treatment options (including the possibility of the patient to access a new regimen)**

THANK YOU