

# The Switch

ACTION Project

Abuja

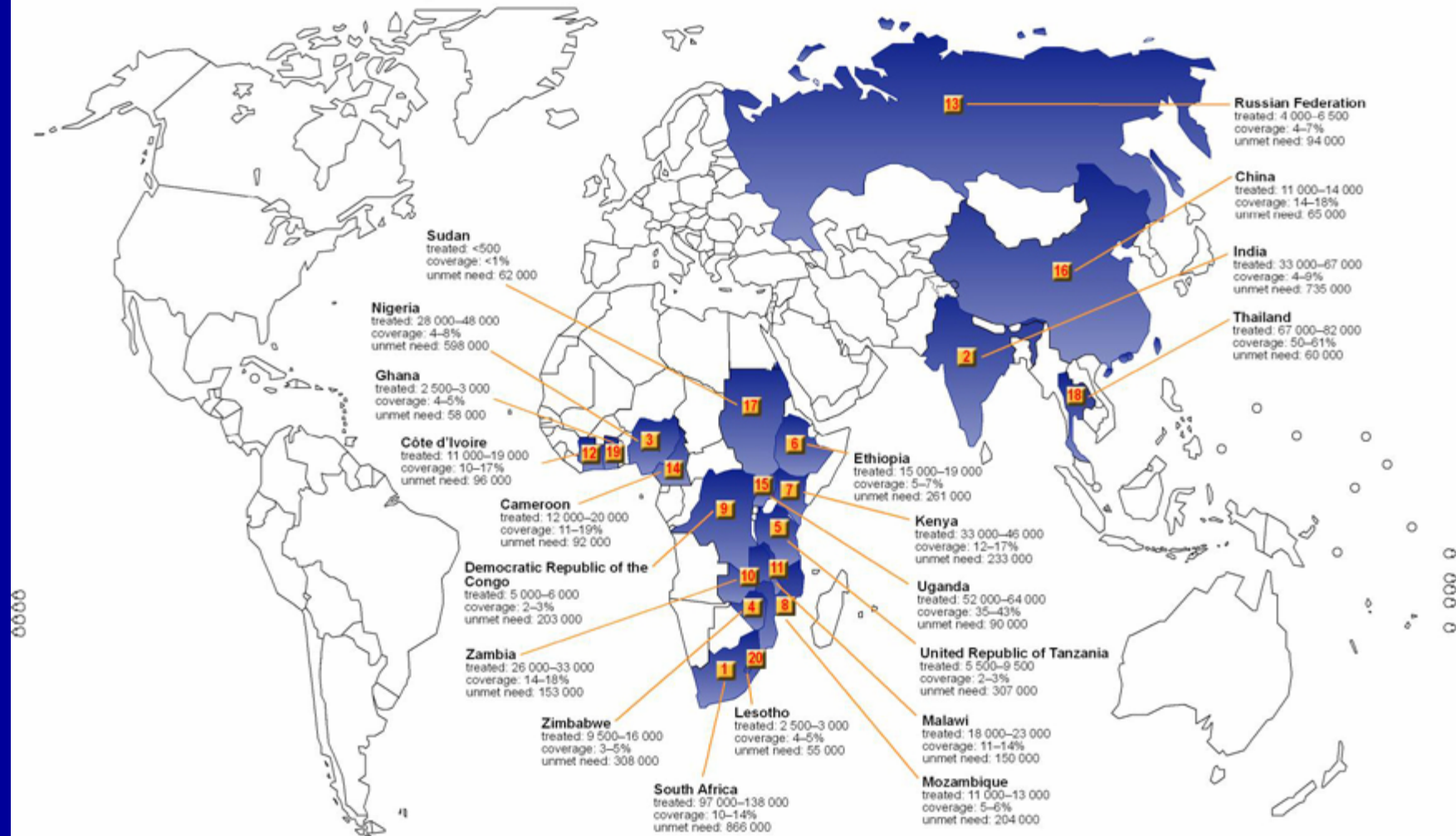
October 2005



# Stavudine

- Made by Bristol-Myers-Squibb
- Since 1998, not favored in the USA
- Mitochondrial toxicities, neuropathies
- Use replaced by zidovudine in FDC
  - Combivir, Trizivir
- PEPFAR programs start worldwide in 2004
- #1 first-line regimen Stavudine/Lamivudine/Nvp (WHO 2003)

## Estimated number of people receiving ARV therapy and percentage coverage in 20 countries with the highest unmet need, June 2005<sup>a</sup>



<sup>a</sup>Unmet need is expressed as the total number of people aged 0-49 in need of antiretroviral treatment in 2005 minus the estimated number of people on treatment in June 2005.

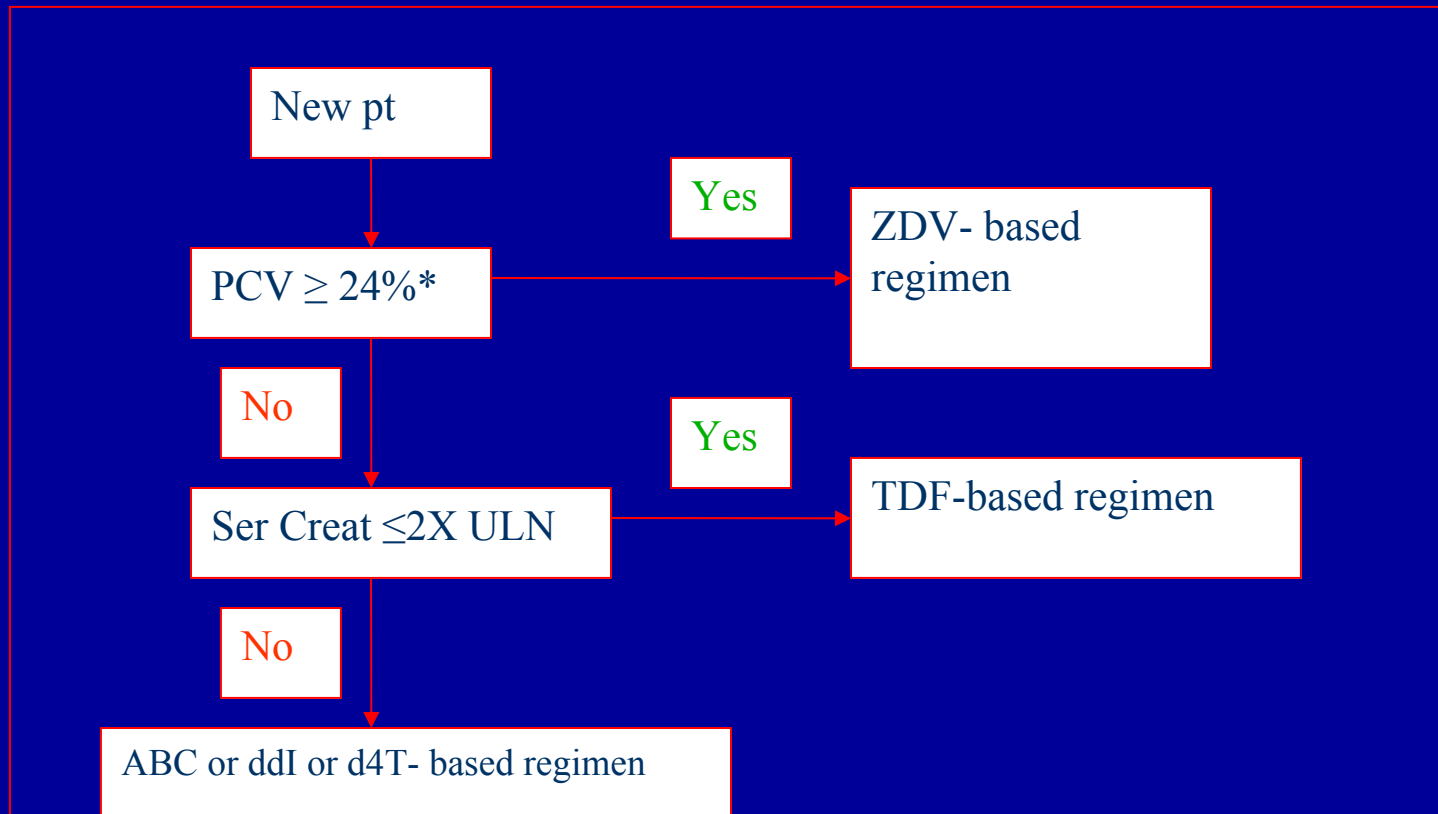
# PEPFAR in Nigeria

- UMD/ACTION
  - Harvard/APIN
  - GHAIN
  - Columbia
- 
- All have run out of stavudine for new patients
    - Stock available for maintenance of current patients
  - BMS is unlikely to make more stavudine

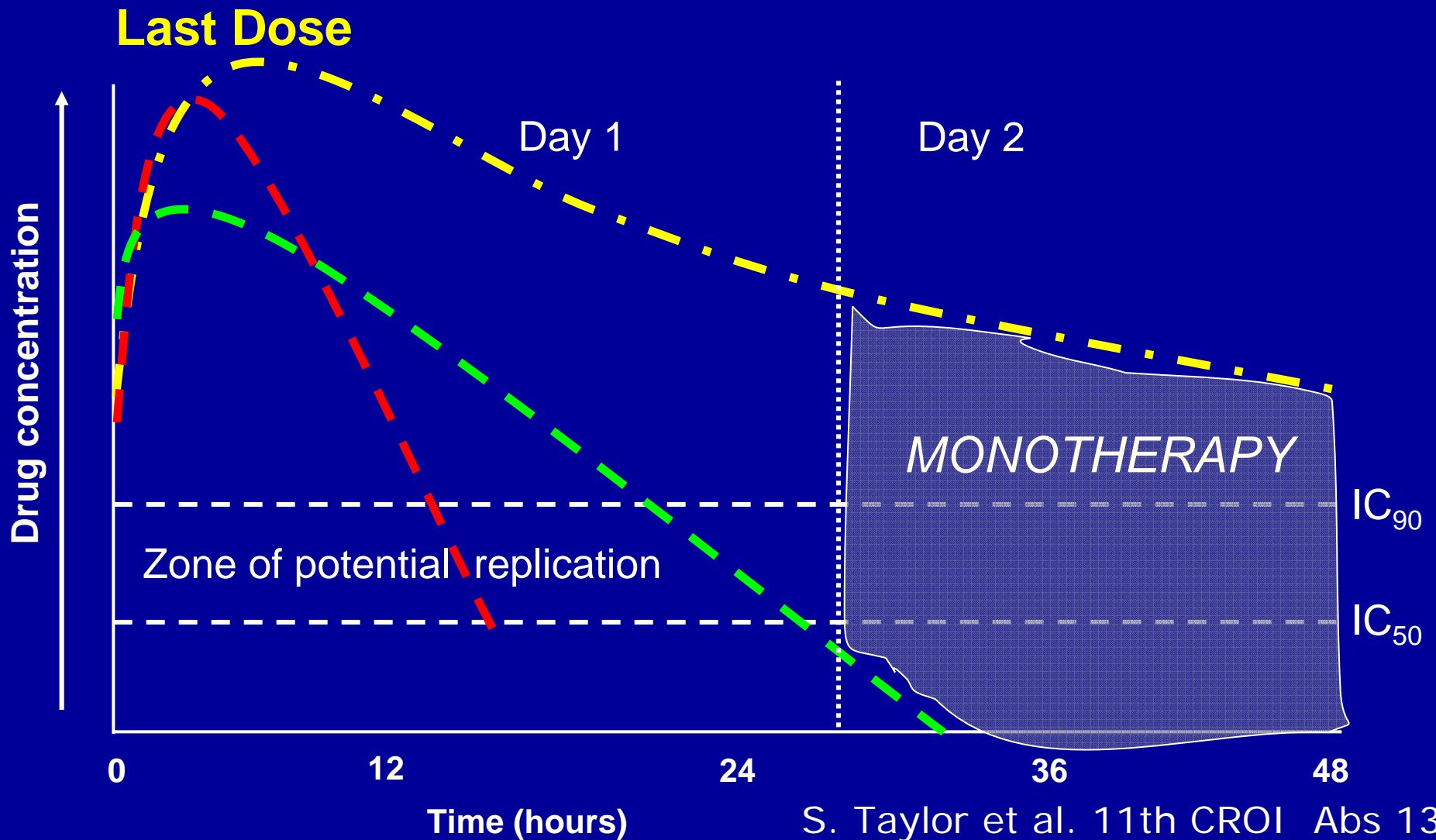
# Recommended Nigerian regimens

First line	Second line
AZT or d4T or TDF or ABC	TDF or AZT or ddl or d4T or ABC
3TC or FTC +	3TC or FTC +
NVP or EFV	IDV/r or SQV/r or LPV/r

# The Switch



# Stopping a Triple ARV combination when ARVs have different half lives



# Special Cases

- For patient on NVP
  - ALT at baseline, 2 weeks and at 1 month
- For patient on ZDV
  - Hemoglobin at baseline, week 4-6, then every 3 months, or more frequently if clinically indicated
- For patient on PIs
  - Blood sugar, Lipid panel, every ???
- For patient on Tenofovir
  - Renal function at baseline, every ???

# Prior experience

- Antivir Ther. 2005;10(5):615-24



**Haematological changes in adults receiving a zidovudine-containing HAART regimen in combination with cotrimoxazole in Cote d'Ivoire.**

Moh R, Danel C, Sorho S, Sauvageot D, Anzian A, Minga A, Gomis OB, Konga C, Inwoley A, Gabillard D, Bissagnene E, Salamon R, Anglaret X.

Programme PAC-CI, Abidjan, Cote d'Ivoire.

**OBJECTIVE:** Neutropenia is the most frequent side effect of cotrimoxazole in sub-Saharan Africa. We estimated the incidence of haematological disorders during the first 6 months of a zidovudine-containing highly active antiretroviral therapy (HAART) regimen in sub-Saharan African adults receiving cotrimoxazole. **METHODS:** Prospective cohort study in Abidjan, with blood cell count measurement at baseline (HAART initiation), month 1, month 3 and month 6. **RESULTS:** A total of 498 adults [baseline: 80% currently on cotrimoxazole prophylaxis; median CD4 count 237/mm<sup>3</sup> [interquartile range (IQR) 181;316]; median neutrophil count 1647/mm<sup>3</sup> (IQR 1221;2256); median haemoglobin 113 g/l (IQR 102;122)] started zidovudine (AZT)/lamivudine/efavirenz. During follow-up, 118 patients had a grade 3-4 neutropenia [(56.3/100 person-years (PY)], 23 had a grade 3-4 anaemia (9.6/100 PY) and no cases of grade 3-4 thrombocytopenia. Of the 118 patients with grade 3-4 neutropenia, 86 (73%) had to stop cotrimoxazole because neutropenia persisted, and one (<1%) had to stop AZT because of persistent neutropenia after cotrimoxazole was stopped (neutropenia-related HAART modification: 0.4/100 PY). Of the 23 patients with grade 3-4 anaemia, 11 had to stop AZT (anaemia-related HAART modification: 4.4/100 PY). In patients who stopped cotrimoxazole but not AZT, the median gain in neutrophils at 1 month was +540/mm<sup>3</sup> (IQR +150;+896). **CONCLUSIONS:** At baseline, most patients had a normal neutrophil count and 80% of them were already receiving cotrimoxazole. An unexpectedly high rate of grade 3-4 neutropenia occurred shortly after introduction of AZT. Almost all of the persistent severe neutropenia disappeared after cotrimoxazole was stopped. This suggests an accentuated drug interaction between the two drugs in these sub-Saharan African individuals. Grade 3-4 anaemia was much less frequent, but remained the first cause of AZT discontinuation

# Another study

- Niger J Med. 2005 Jan-Mar;14(1):33-8.



**Some haematological parameters in human immunodeficiency virus (HIV) infected Africans: the Nigerian perspective.**

Erhabor O, Ejele OA, Nwauche CA, Buseri FI.

Department of Haematology and Blood Transfusion, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.

**BACKGROUND:** Haematologic abnormalities are among the most common manifestations of advanced human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS). A specific diagnosis of cause, severity and mechanism of cytopenia should be sought because of specific treatments or intervention may be indicated for its correction. This study was to determine some haematological parameters in HIV/AIDS infected Nigerians.

**METHOD:** One hundred HIV/AIDS infected previously antiretroviral naive adult Nigerians, aged 18-58 year (males 47 and females 53) consisting of 88 symptomatic and 12 asymptomatic patients recruited into the antiretroviral pilot project in the Haematology department of the University of Port Harcourt Teaching Hospital between June 2002 to July 2003 were studied. Haematological parameters of hemoglobin, white cell count, platelet count, erythrocyte sedimentation rate and differential leucocyte count were determined. Data was analyzed using a multipurpose statistical package version 9 SPSS.

**RESULT:** The mean haemoglobin was 10.25 +/- 1.97 g/dl (range 6.31-14.2 g/dl), severe anaemia occurred in 80% of subjects while 20% were non-anaemic.

# Tenofovir nephrotoxicity

- AIDS Patient Care STDS. 2005 Jul;19(7):421-4



**Low frequency of renal function impairment during one-year of therapy with tenofovir-containing regimens in the real-world: a case-control study.**

**Padilla S, Gutierrez F, Masia M, Canovas V, Orozco C.**

Infectious Diseases Unit, Internal Medicine Department, Hospital General Universitario de Elche, Alicante, Spain.

Concern exists about the risk of nephrotoxicity using tenofovir (TDF) in HIV-infected patients. We performed a retrospective case-control study including 122 consecutive TDF-naive patients who started treatment with TDF-containing regimens and 194 patients receiving antiretroviral therapy with other antiretroviral drugs. During a 12-month observation period 5 (4.1%) patients in the TDF group versus 1 (0.5%) in the control group developed grade 1 or higher serum creatinine elevations ( $p = 0.018$ ). Only 2 (1.6%) patients discontinued TDF treatment as a result of serum creatinine level elevations. In 4 of the 5 patients developing creatinine elevations TDF was combined with lopinavir-ritonavir. The use of TDF in clinical practice during a 12-month period is associated with low risk of mild renal failure. Further studies to assess long-term renal safety of this drug are needed.

# Fixed dose combinations

- Combivir (ZDV + 3TC) one pill twice a day



- Truvada (TDF + FTC) one pill once a day

