INTERESTING CLINICAL CASES: HIV diagnostic and treatment dilemmas

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Goals of the programme (2013 SA ARV guidelines – public sector)

- Save lives and improve the quality of life of people living with HIV
- Achieve best health outcomes in the most cost-efficient manner
- Implement nurse-initiated treatment
- Decentralise service delivery to PHC facilities
- Integrate services for HIV, TB, MCH, SRH and wellness
- Diagnose HIV earlier
- Prevent HIV disease progression
- Avert AIDS-related deaths
- Retain patients on lifelong therapy
- Prevent new infections among children, adolescents, and adults
- Mitigate the impact of HIV and AIDS

SA – first line ARV regimens (adults)

- 2004 2010 2013

D4T/3TC/EFV or NVP

TDF/3TC/EFV or NVP

TDF/FTC/EFV (FDC)

Contra-indication to TDF and AZT

- use d4T or ABC

Baseline HIV VL

No baseline HIV VL

SA – first line ARV regimens (children)

	2004	2010	2013
<3 years (or >10 kg)	D4T/3TC/LPV-r	ABC/3TC/LPV-r	ABC/3TC/LPV-r
>3 years (and >10kg)	D4T/3TC/EFV	ABC/3TC/EFV	ABC/3TC/EFV

NVP prophylaxis - for 6 weeks for children born to HIV infected mothers

Baseline HIV VL *** Baseline HIV VL *** Baseline HIV VL

VL & CD4 MONITORING IN PUBLIC SECTOR

	Baseline	6mo	12mo	18mo	
<u>Adults</u>					
2013	----	VL	VL	----	annually
	CD4 count	----	CD4 count	----	----
<u>Children 5 – 15 years</u>					
2013	VL	VL	VL	----	annually
	CD4 count	----	CD4 count	----	annually
<u>Children <5 years</u>					
2013	VL	VL	VL	VL	every 6 months
	CD4 count	----	CD4 count	----	annually

2013 South African Antiretroviral Treatment Guidelines.

Ms HM – 20 month old child

- HAART since 7 weeks of age – ABC/3TC/LPVr
- HIV ELISA @ 18 months = NEGATIVE
- HIV PCR @ 19 months = NEGATIVE
- HIV VL @ 20 months = LDL (lower than
- Baseline test results @ 6 weeks
  - HIV ELISA - POSITIVE
  - PCR = POSITIVE
  - HIV VL = 311 705 copies/ml

<u>ISSUES</u>

➢Significance of baseline tests

➢Negative HIV ELISA ≥18 months

➢Negative PCR

➢? Functional cure

NEGATIVE HIV ELISA IN CHILDREN 18 MONTHS OR OLDER

- Seroreversion in children infected with HIV-1 who are treated in the first months (esp. in ≤3 months) of life is not a rare event

Hainaut M, et al. CID 2005:41; 1820.

Persaud D, et al. AIDS Research And Human Retroviruses 2007: 23; 381–390.

SEROREVERSION IN A CORHOT OF 12 CHILDREN

NEGATIVE HIV ELISA >18 MONTHS

Subject	Age at start of HAART (months)	Baseline HIV VL (log_{10} c/ml)	Time to LDL VL (months)	Duration of suppression (years)	Age tested for HIV ELISA in study (years)
C102	1.6	>5.8	3	3.4	2.8
C103	1.8	5.7	2.9	5.6	5.1
C104	2.4	>5.8	2.5	4.5	4.3
C107	3.8	>5.8	2.3	0.7	0.71
C108	2.5	5.5	5.8	2.2	2
C109	1.4	5.6	1.9	4.7	4.7
C110	1.7	>5.8	1.9	5.1	4.8
C112	2	4.8	2.1	2.2	2.5

POSITIVE HIV ELISA >18 MONTHS

C101	1.8	>5.8	5.4	4.9	4.5
C105	3.4	>5.8	3.2	2.4	2.6
C106	4.8	4.2	1.2	4.6	5
C111	0.6	4.9	3.3	1.4	1.3

Adapted from Persaud D, et al. AIDS Research And Human Retroviruses 2007: 23; 381–390.

Ms HM – 20 month old baby

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<u>ISSUES</u>

➢Significance of baseline tests ✓

➢Negative ELISA a⁺ or after 18 months ✓

➢Negative PCR

➢? Functional cure

DETECTION LIMITS OF HIV MOLECULAR ASSAYS USED IN NHLS LABORATORIES

Qualitative HIV PCR on DBS card (Roche CAP/CTM v2): 300 copies/mL

Qualitative HIV PCR on whole blood (Roche CAP/CTM v2): 20 copies/mL

Abbott HIV viral load assay (m2000): 40 copies/mL

Roche HIV viral load assay (CAP/CTM v2): 20 copies/mL

Roche and Abbot HIV PCR & viral loads packages inserts.

Performance of HIV-1 DNA or HIV-1 RNA Tests for Early Diagnosis of Perinatal HIV-1 Infection during Anti-Retroviral Prophylaxis

- Screening for HIV by PCR was done at:
  - **birth** and at ages **1 month**, **3 months**, and **6 months**
  - Prophylaxis for 4 – 6 weeks: AZT or AZT + 3TC or 2 NRTIs + PI

<u>At 1 month</u>

- 30 infected infants with at least one positive PCR test at birth
  - 90% had a positive PCR result in both PCR tests at 1 month

- 17 infected infants with negative PCR results at birth
  - 76% had positive results in both PCR tests at 1 month

<u>At 3 Months</u> (prophylaxis had been stopped and HAART not initiated)

- the sensitivity of both assays was 100%.

Burgard M, et al. J Pediatr 2012; 160: 60-6.

MISSISSIPI BABY

Ms HM – 20 month old baby

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ISSUES

- Significance of baseline tests
- Negative ELISA at or after 18 months
- Negative PCR
- ? Functional cure

?? FUNCTIONAL CURE IN A 30 MONTH OLD CHILD

- Born to an HIV infected mother who had no prenatal care, and not on ARVs
  - HIV diagnosis established @ delivery (ELISA & WB)
  - 24 hrs after delivery: HIV VL = 2423 copies/ml,
  - 14 days later: CD4+ count = 644 cells/mm^3

Persaud D, et al. N Engl J Med 2013; 369:1828-1835.

?? FUNCTIONAL CURE IN A 30 MONTH OLD CHILD

Test	Result	ART
HIV-1 DNA, at 30 hr	Positive	AZT
HIV-1 RNA, at 31 hr	19,812 copies/ml	AZT/3TC/NVP
HIV-1 RNA, at 6 days	2617 copies/ml	AZT/3TC/NVP
HIV-1 RNA, at 11 days	516 copies/ml	AZT/3TC/LPVr
HIV-1 RNA, at 19 days	265 copies/ml	AZT/3TC/LPVr
HIV-1 RNA, at 29 days	<48 copies/ml	AZT/3TC/LPVr
CD4+ T-cell percentage, at 8 days	69%	AZT/3TC/LPVr
HIV-1 DNA, at 24 mo	Negative	
HLA typing, at 26 mo	A3, A68, B7, B39, and Cw7	None
Mutation status in CCR5 delta32, at 26 mo	Nonmutated	None

Persaud D, et al. N Engl J Med 2013; 369:1828-1835.

?? FUNCTIONAL CURE IN A 30 MONTH OLD CHILD

- Proviral DNA detected on PBMCs resting CD4+ cells & monocyte-derived adherent cells from samples taken at 24 and 26 months (@ very low levels)
- Residual viremia in plasma = 1 copy/ml @ 24 months, and <2 copies/ml @ 26 months
- No recovery of infectious virus

Persaud D, et al. N Engl J Med 2013; 369:1828-1835.

?? FUNCTIONAL CURE IN A 30 MONTH OLD CHILD

- Controlled HIV-1 viremia for 12 months while not receiving ART
  - absence of rebound viremia,
  - undetectable replication-competent virus,
  - almost-complete disappearance of cell associated HIV-1 DNA, &
  - absence of HIV-1–specific immune responses while the child was not receiving ART

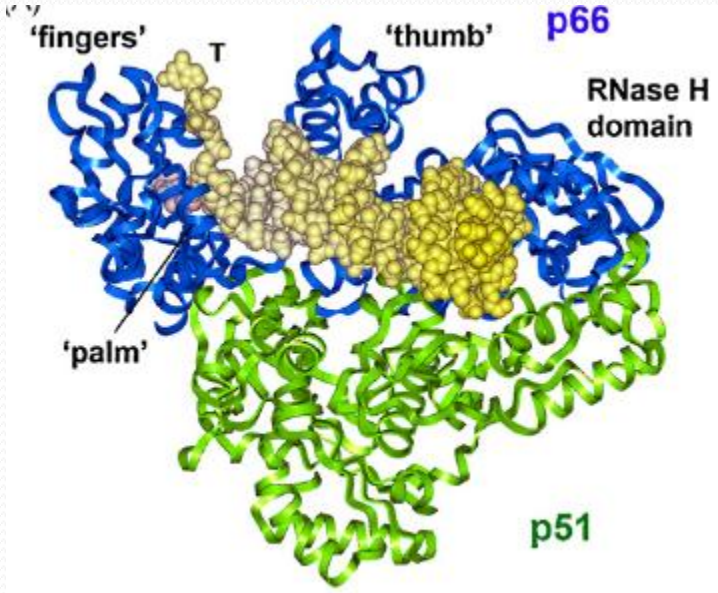
- Suggest that replication-competent HIV-1 reservoirs may not have been established or were markedly abated, if not extinguished

Persaud D, et al. N Engl J Med 2013; 369:1828-1835.

ONLY ONE MISSISSIPI BABY SO FAR!

MECHANISMS OF NRTI RESISTANCE

- Impaired nucleotide analogue incorporation - e.g. M184V
- Excision of nucleoside analogue RT inhibitors
  - e.g. thymidine analogue mutations (TAMs)



Menendez-Arias L. Antiviral Research 2010; 85: 210–231.

Mutations associated with impaired nucleotide analogue incorporation

Mutations	Nucleoside analogue
K65R	Tenofovir
	Didanosine
	Abacavir
	Lamivudine
	Emtricitabine
	Zalcitabine
K70E	Tenofovir
L74V	Abacavir
	Didanosine
V75I	Acyclovir
V75T	Stavudine
Q151M	Zidovudine
	Stavudine
	Didanosine
	Zalcitabine
	Abacavir
M184V	Lamivudine
	Emtricitabine
	Abacavir

Menendez-Arias L. Antiviral Research 2010; 85: 210–231.

THYMIDINE ANALOGUE MUTATION (TAM) PATHWAYS

- TAM-1 pathway - M41L, L210W and T215Y
  - confer higher levels of AZT resistance and are responsible for more extensive cross-resistance to other NRTIs

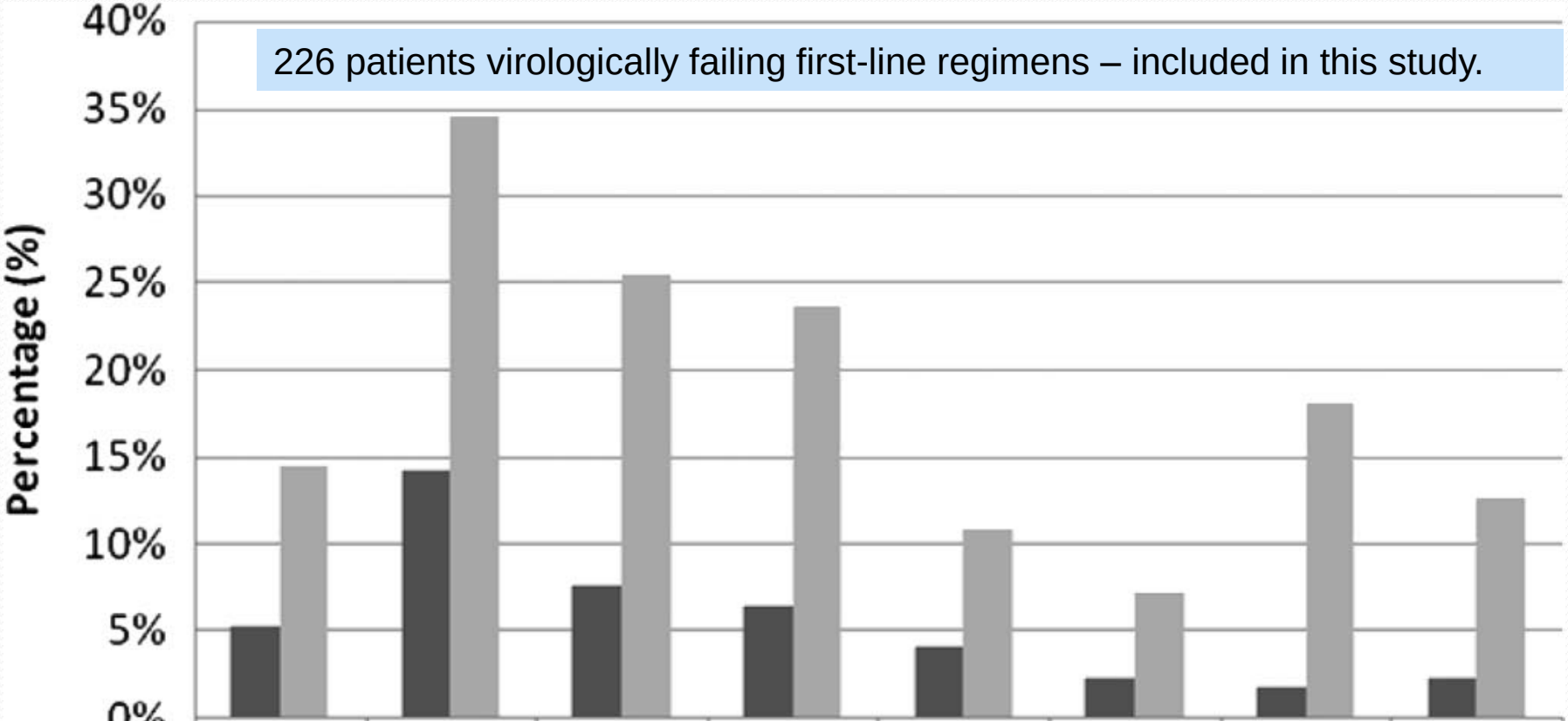
- TAM-2 pathway - D67N, K70R and K219E/Q, and sometimes T215F
  - resistance is usually limited to zidovudine and stavudine

Menendez-Arias L. Antiviral Research 2010; 85: 210–231.

Marconi VC, et al . CID 2008; 46:1589–97.

Patterns of HIV-1 Drug Resistance on Failing First-Line ART in South Africa

226 patients virologically failing first-line regimens – included in this study.



	M41L	D67N	K70R	T215Y	T215F	K219E	K219Q	L210W
d4t	5%	14%	8%	7%	4%	2%	2%	2%
AZT	15%	35%	25%	24%	11%	7%	18%	13%

Wallis CL et al. J Acquir Immune Defic Syndr 2010; 53(4): 480 -84.

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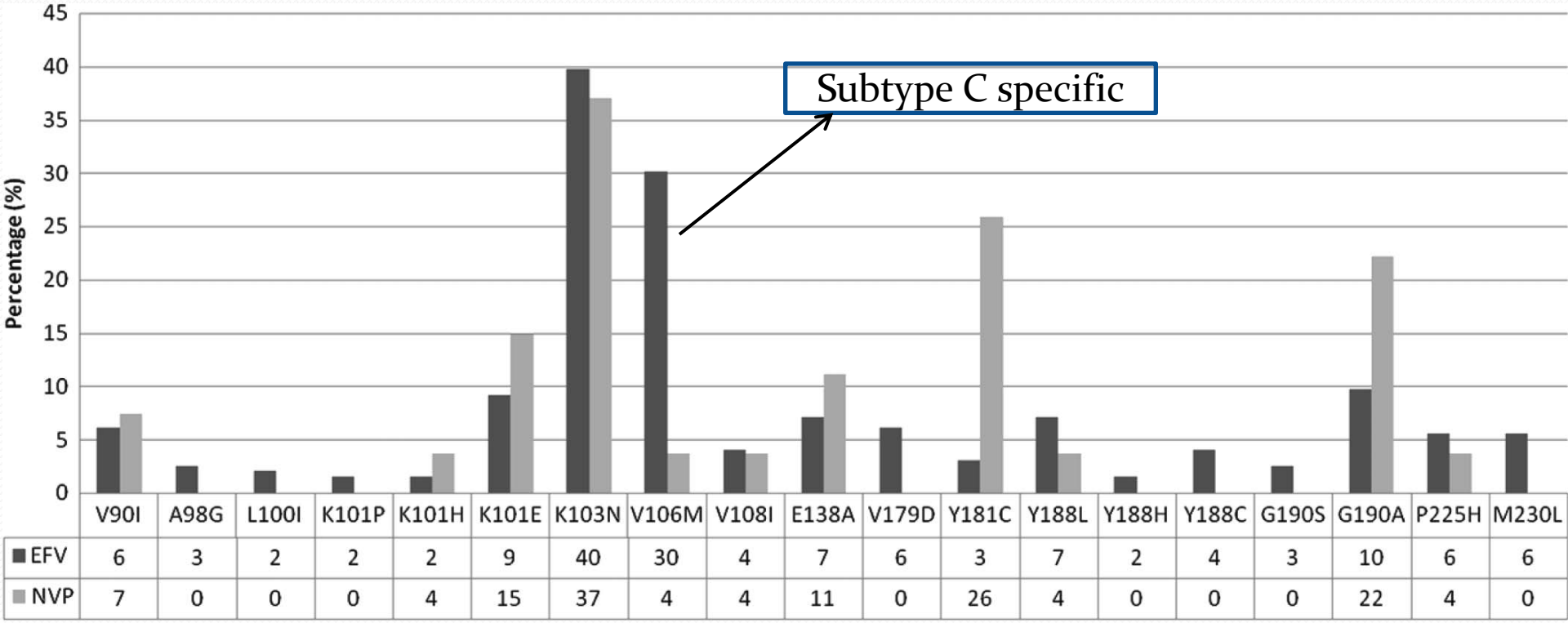


	V90I	A98G	L100I	K101P	K101H	K101E	K103N	V106M	V108I	E138A	V179D	Y181C	Y188L	Y188H	Y188C	G190S	G190A	P225H	M230L
EFV	6	3	2	2	2	9	40	30	4	7	6	3	7	2	4	3	10	6	6
NVP	7	0	0	0	4	15	37	4	4	11	0	26	4	0	0	0	22	4	0

Wallis CL et al. J Acquir Immune Defic Syndr 2010; 53(4): 480 - 84.

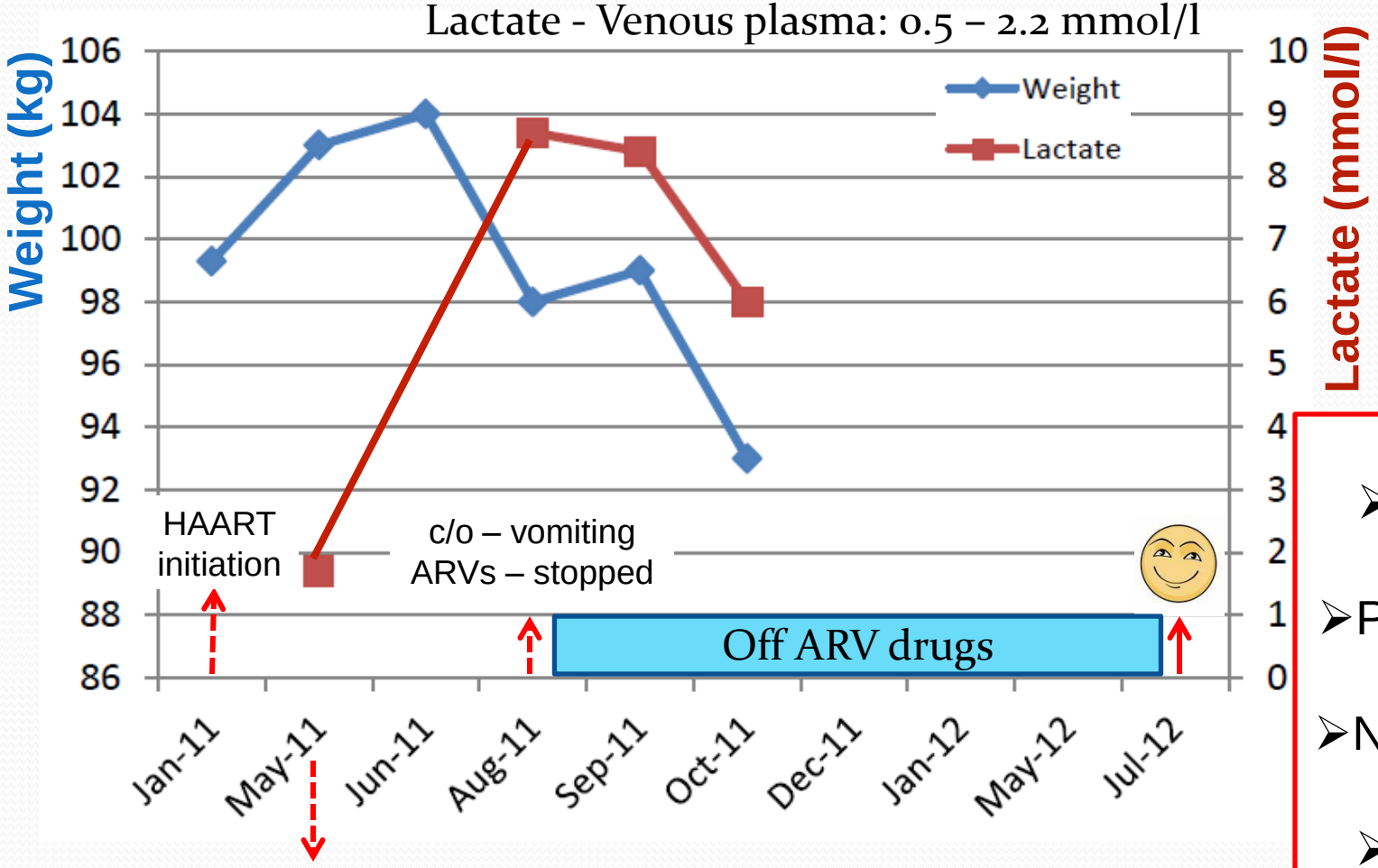
Ms LC - 52 year old lady

- HIV infected, completed TB Rx in Dec 2010

- Diabetes and hypertension on treatment
  - Metformin, then later changed to insulin injection
  - Hydrochlorothiazide / adalat / atenolol / perindopril

- Nov 2010
  - Hb = 9.0 g/dl (12.1 – 16.3), ALT = 21 U/l (10 - 40),
    Cr = 93 µmol/l (49 – 90), eGFR >60; CD4 = 337 cells/mm^3
- Jan 2011
  - HAART initiation at Tshwane ARV clinic = D4T/3TC/EFV
  - BP – 133/78

Ms LC - 52 year old lady



Cr = 64 µmol/l (49 – 90),
eGFR >60
HIV VL = LDL, CD4 = 247

ISSUES

- Side effect
- Poor follow up
- NNRTI half life
- DM & HPT
- Weak health care system

Ms LC - 52 year old lady

- July 2012
  - HIV VL = 9416, CD4 count = 222 cells/mm^3
  - Glucose =15.2 (post-prandial), Triglycerides = 2.3,
    Cholesterol – 3.6
  - Hb = ↓10.3 g/dl, ALT = 18 U/l, Cr = 67 µmol/l (eGFR >60)

TDF/3TC/EFV

- Dec 2012
  - HIV VL = LDL
  - Hb = ↓ 10.7 g/dl, Cr = 76 µmol/l (eGFR >60)

- Oct 2013
  - HIV VL = LDL, CD4 count = 519 cells/mm^3
  - Hb = 11.3 g/dl, Cr = 87 µmol/l (eGFR = 59), ALT =17, Lactate =1.7

ISSUES

- Side effect
- Poor follow up
- NNRTI half life
- DM & HPT
- Weak health care system

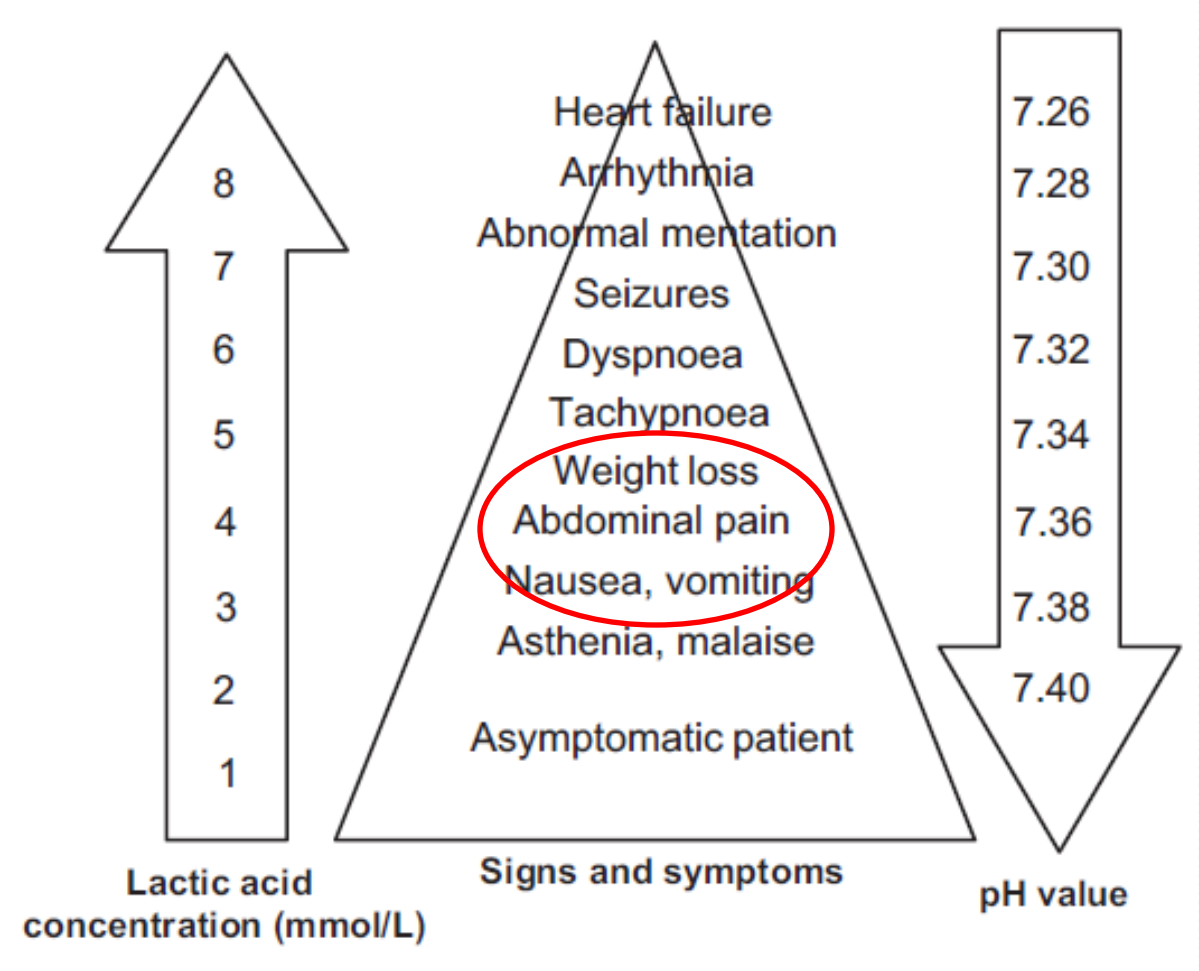
Hyperlactataemia / lactic acidosis during ART

- Hyperlactataemia is defined as a mild-to-moderate increase in serum lactate concentration (2 – 5mmol/l),
  - with normal pH value and bicarbonate level
    (pH≥7.35 and bicarbonate concentration ≥20mmol/l)

- Lactic acidosis is defined as persistently and remarkably elevated serum lactate level (generally >5 mmol/l),
  - associated with metabolic acidosis
    (pH <7.35 and bicarbonate concentration <20 mmol/l)

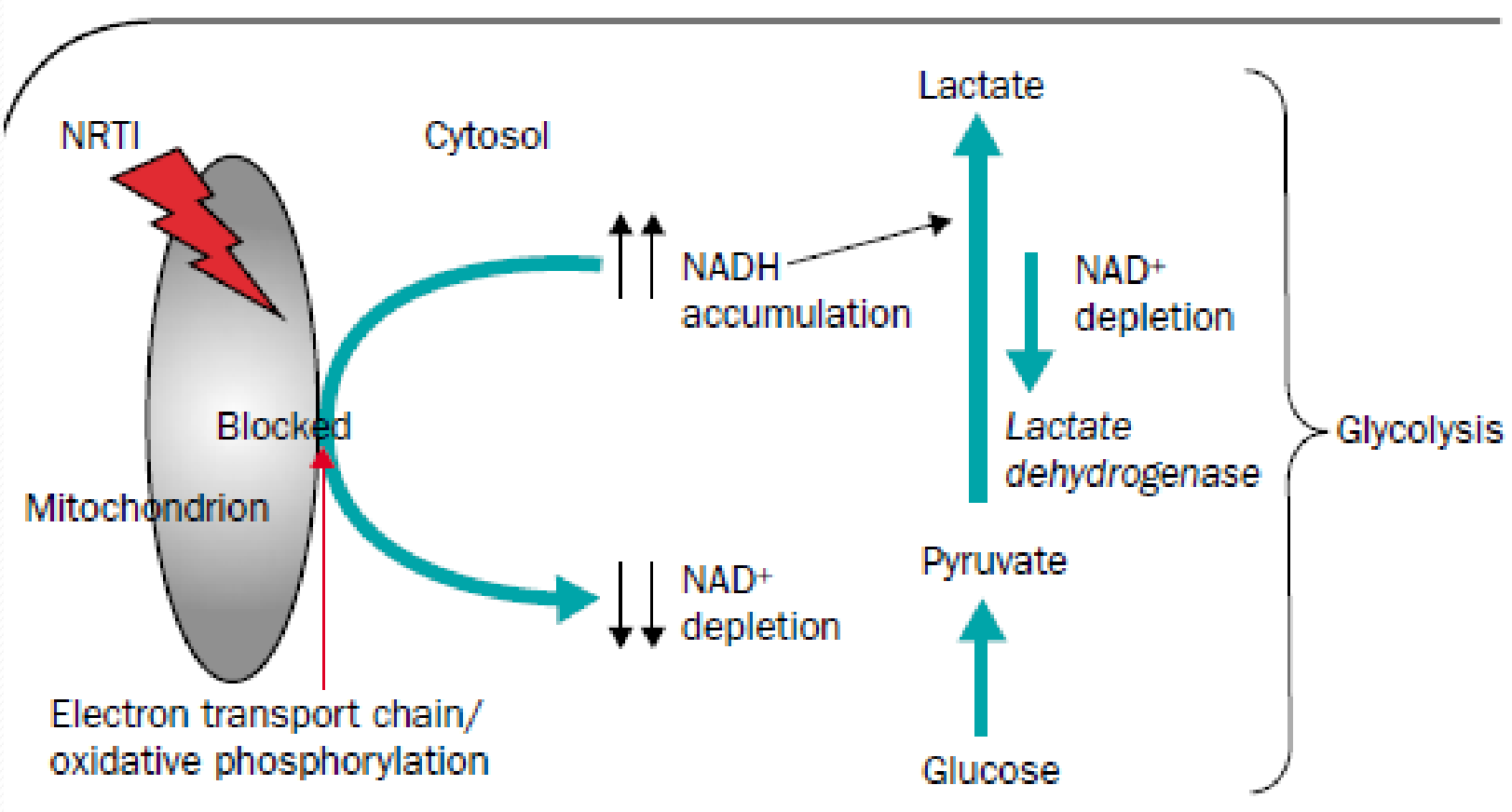
Calza L, et al. Clinical Nutrition 2005: 24; 5–15.

Hyperlactataemia / lactic acidosis during ART



Calza L, et al. Clinical Nutrition 2005: 24; 5–15.

Hyperlactataemia / lactic acidosis during ART



Ogedegbe AO, et al. *Lancet Infect Dis 2003; 3: 329–37.*

Hyperlactataemia / lactic acidosis during ART

- The mean time to developing lactic acidosis is 10–12 weeks after initiation of combination ART

- d4T > ddI = ZDV > TDF=ABC=3TC=FTC

Blazes DL. Lancet Infect Dis 2006; 6: 249–52.

DHHS guidelines 2009.

ISSUES

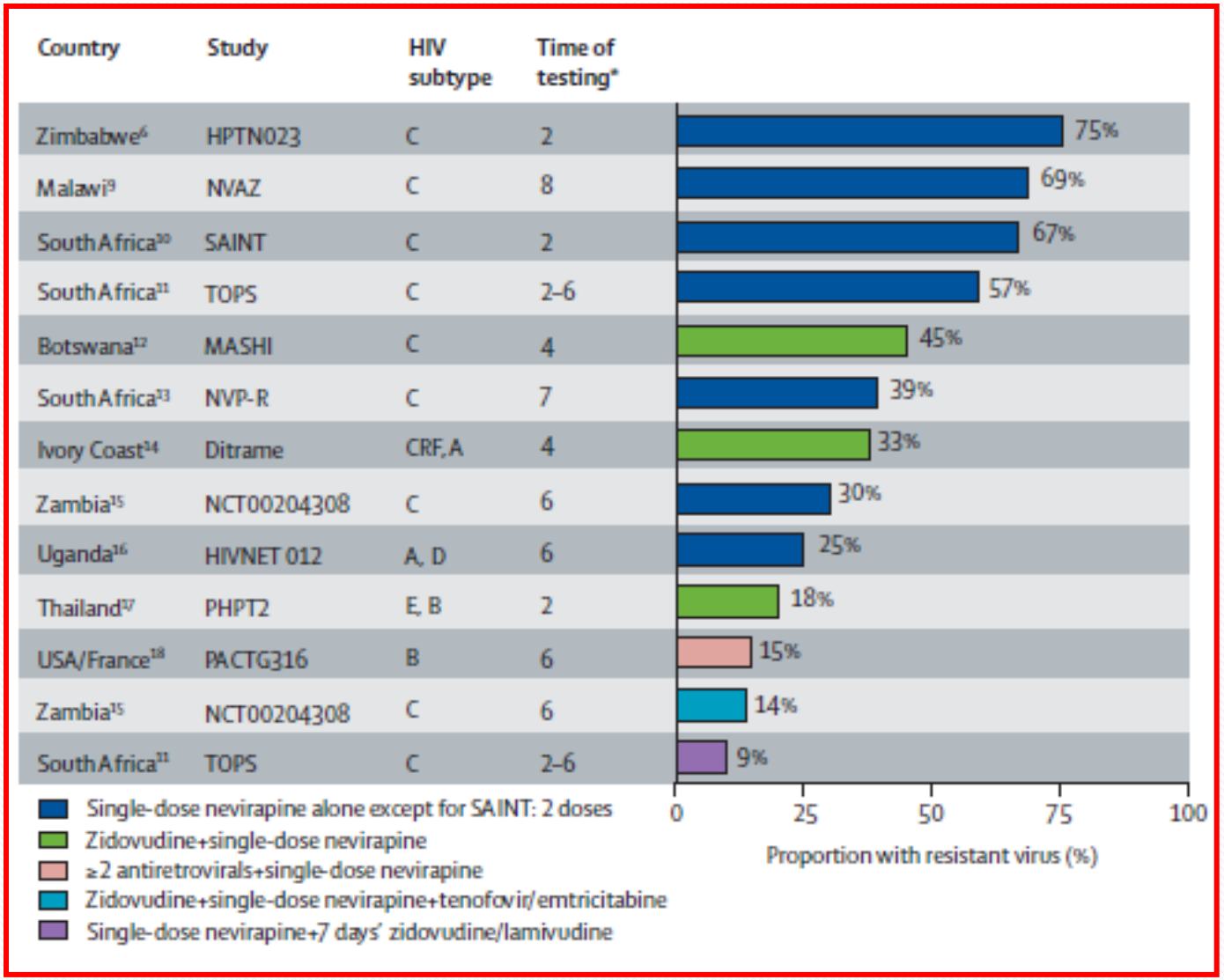
- Side effects 
- Poor follow up
- NNRTI half life - prolonged
- DM & HPT
- Weak health care system

Stopping rules for ARV therapy

- **Simultaneous stop**
  - for half-life balanced regimens: i.e. three short or long half-life drugs can be stopped simultaneously
- **Staggered stop**
  - for unbalanced regimens: i.e. the long half-life drug or drugs are discontinued before the short half-life drugs of the regimen
- **Replacement stop**
  - where the drug with the long half-life is replaced by a drug with a short half-life and a high genetic barrier for a short period of time; for example replacement of EFV with LPV/r; the correct length of LPV/r intake is unknown, but 4 weeks is probably advisable with this strategy
- **Protected stop**
  - when the drugs are stopped simultaneously despite their different half-lives and LPV/r is administered for 4 weeks; clinical data are being collected to investigate whether this strategy could be recommended

British HIV Association guidelines 2008.

RISK OF RESISTANCE AFTER STOPPING NVP



Lockman S & McIntyre JA. Lancet 2007: 370; 1668 – 70.

Response to Antiretroviral Therapy after a Single, Peripartum Dose of Nevirapine

- Women who received a single dose of nevirapine to prevent perinatal transmission of HIV-1 had higher rates of virologic failure with subsequent nevirapine-based antiretroviral therapy than did women without previous exposure to nevirapine.

- However, this applied only when nevirapine-based antiretroviral therapy was initiated within 6 months after receipt of a single, peripartum dose of nevirapine.

Lockman S, et al. N Engl J Med 2007;356:135-47.

Viral kinetics after HAART interruption

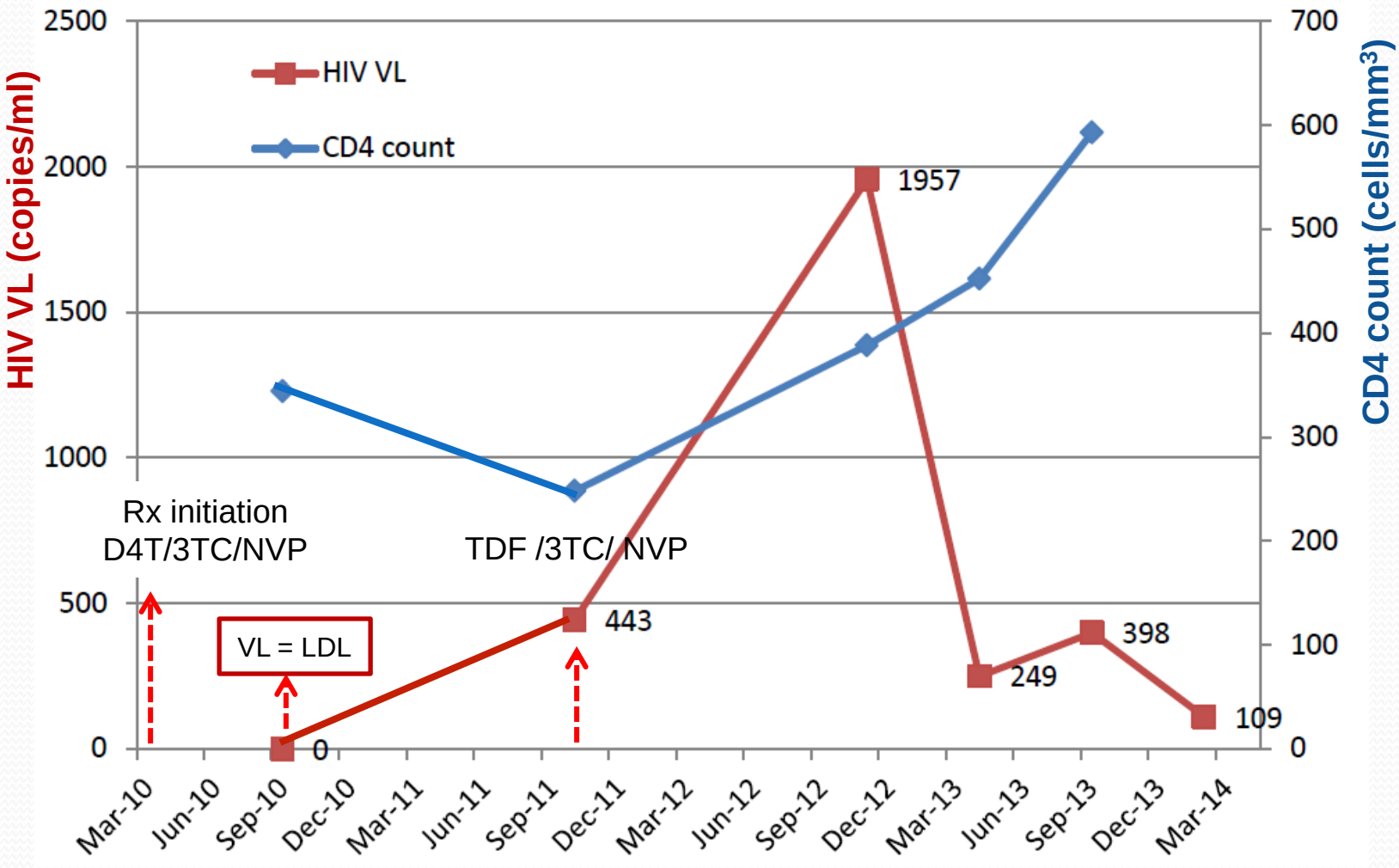
HIV VL was detectable (>50 copies/ml) on:

- day 7 - in 5 patients
- day 14 – in 8 patients, &
- day 28 - in 18 patients (90%)

- In 2 patients HIV VL remained undetectable for 4 weeks

Sanchez R, et al. Journal of Infection 2007:54; 159 -166.

Ms PP – 35 year old



Ms PP – 35 year old

ISSUES

- Low level viraemia
- Poor follow up
- Single drug substitution
- ?Partner status

Ms PP – 35 year old

- Good adherence
- No clinical problems
- Partner - HIV positive on HAART (Mamelodi day hospital)
- ARV drug resistance testing – (VL was 1200 during resistance testing – April 2014)

Ms PP's ARV RESISTANCE RESULTS

- **Sequence includes PR: codons: 16 - 99**
- **Sequence includes RT: codons: 1 - 445**
  - *There are no insertions or deletions*

- *Subtype and % similarity to closest reference isolate:*
  - 1. *PR: C (94.0%)*
  - 2. *RT: C (94.1%)*

Mr PP's ARV RESISTANCE RESULTS

- **NRTI Resistance Mutations:**
  - M184V
- **NNRTI Resistance Mutations:**
  - A98G, K103N, V108I
- **Other Mutations:**
  - V35T, E36A, T39E, S48T, V60I, K122E, D123G, I135T, K173A, Q174K, D177E, T200A, Q207N, R211K, F214L, V245Q, A272P, T286A, E291D, V292I, I293V, D324E, Q334N, G335D, R356K, G359T, T377L, K390R, A400I, E404D, V435A

Mr PP's ARV RESISTANCE RESULTS

Nucleoside RTI	
3TC	High-level resistance
ABC	Low-level resistance
AZT	Susceptible
D4T	Susceptible
DDI	Potential low level resistance
FTC	High-level resistance
TDF	Susceptible

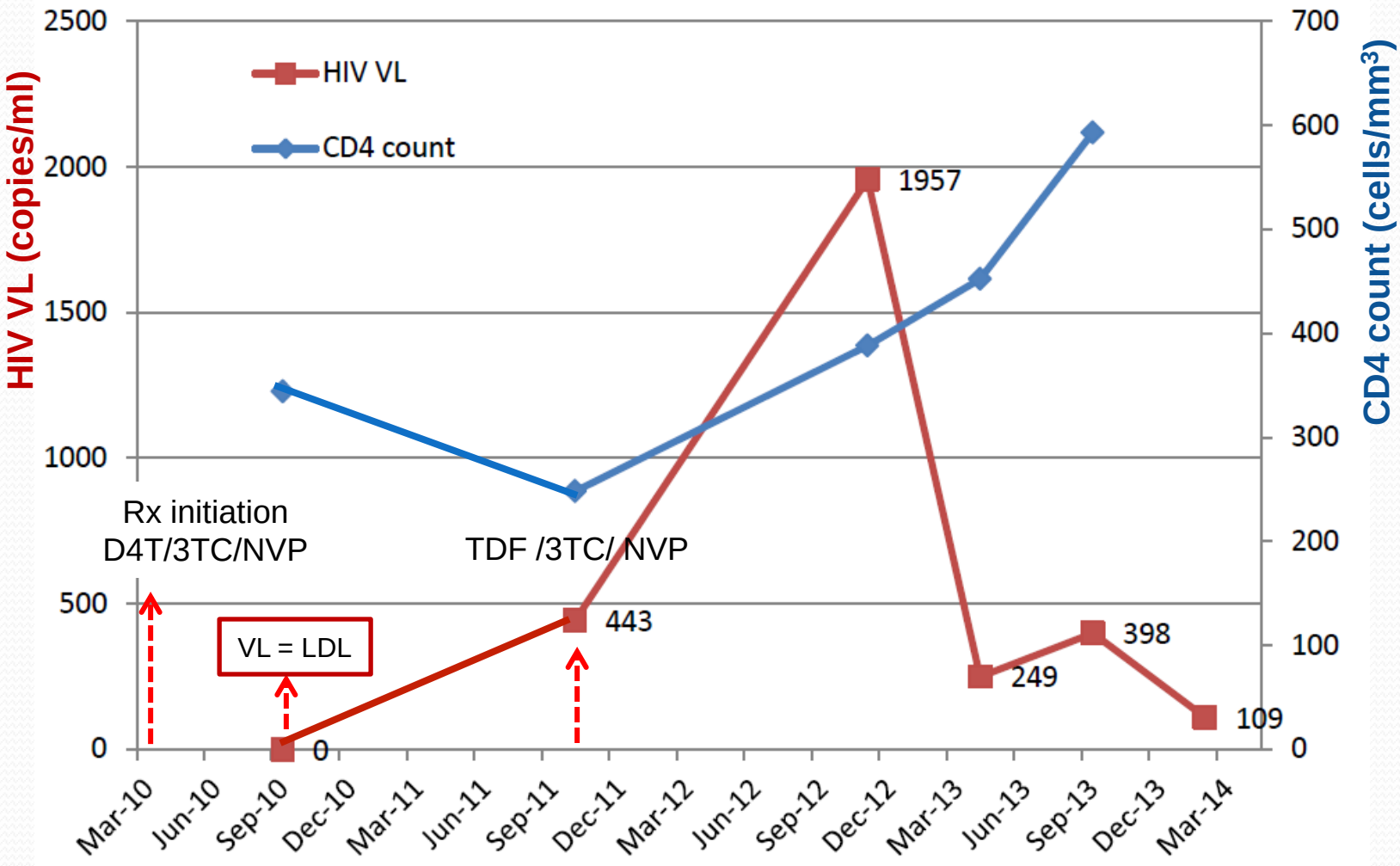
Non-Nucleoside RTI	
EFV	High-level resistance
ETR	Potential low-level resistance
NVP	High-level resistance
RPV	Low-level resistance

Mr PP's ARV RESISTANCE RESULTS

- **PI Major Resistance Mutations:** None
- **PI Minor Resistance Mutations:** T74S
- **Other Mutations:** L19T, E35D, M36I, R41K, K45R, H69K, L89M, I93LV

- **Protease Inhibitors**
  - **atazanavir/r (ATV/r)** Susceptible
  - **darunavir/r (DRV/r)** Susceptible
  - **fosamprenavir/r (FPV/r)** Susceptible
  - **indinavir/r (IDV/r)** Susceptible
  - **lopinavir/r (LPV/r)** Susceptible
  - **nelfinavir (NFV)** low-level resistance
  - **saquinavir/r (SQV/r)** Susceptible
  - **tipranavir/r (TPV/r)** Susceptible

Ms PP – 35 year old



TDF/3TC/LPVr – April 2014

ASSESSMENT OF TREATMENT FAILURE

- Clinical assessment
- Immunological assessment, e.g. CD4 count
- Virological assessment, e.g. HIV VL

The value of clinical and immunological monitoring of ARVs

- Consequent immunologic failure and clinical events after initiation of HAART generally occur 6 months to 2 years after virologic failure.

Deeks S, et al. J Infect Dis 2004; 189:312–21.

The value of clinical and immunological monitoring of ARVs

Reasons for treatment failure	%
Clinical failure	46
Decrease in CD4 cell count to less than or equal to baseline value	2
50% Decrease in CD4 cell count from peak value	37
Persistent CD4 cell count <100 cells/μL	15
>1 Major mutation with drug resistance to NRTIs	90
>1 Major mutation with drug resistance to NNRTIs	65
⩾2 major NNRTI and/or NRTI mutations	88 *
No NRTI or NNRTI mutations	5

Kumarasamy N, et al. CID 2009; 49:306–9.

MANAGEMENT OF VIROLOGICAL FAILURE (2013 SA ARV guidelines – public sector)

- If plasma HIV RNA >1000 copies/ml
  - check for adherence, compliance, tolerability and drug- drug interaction and assess psychological issues
- Repeat VL test 2 months later
- If plasma VL confirmed >1000 copies
  - change regime to second line therapy

The South African Antiretroviral Treatment Guidelines 2013

Detection Virologic Failure (other guidelines)

- **SA HIV Clinicians Society guidelines (private sector)**
  - HIV viral load of >1000 copies/ml in 2 measurements taken 1 - 3 months apart
- **2013 WHO guidelines**
  - HIV viral load of >1000 copies/ml based on two consecutive viral load measurements after 3 months
- **2014 DHHS guidelines (USA)**
  - the inability to achieve or maintain suppression of viral replication to an HIV RNA level <200 copies/ml
- **2013 British HIV Association guidelines**
  - a single VL >400 copies/ml should be investigated further, as it is indicative of virological failure

Drug resistance at low viraemia in HIV-1-infected patients with antiretroviral combination therapy

Soo Aleman[a], Karin Söderbärg[b], Ubaldo Visco-Comandini[c], Gisela Sitbon[b] and Anders Sönnerborg[a,d]

- Conclusion: Low viraemia after virological treatment failure can select for virus with several new drug resistance mutations, despite a concomitant increase in CD4 T cell counts.

- This serial accumulation of mutations is likely to exhaust future drug options.

AIDS 2002, 16:1039 – 1044.

ISSUES

- Low level viraemia 
- Poor follow up
- Single drug substitution 
- ?Partner status

Mr PS – husband to Ms PP

- Baseline CD4 count = 11 cells/mm^3
- June 2013 - HAART initiation (TDF/3TC/EFV)
- March 2014 – HIV VL = 9387
  - CD4 count = 8 cells/mm^3
- 27 May 2014 
  - diarrhoea since he started ARVs – wakes him up at 3 – 4 a.m. daily
  - only loose stools in the morning, but fine later in the day
  - adherence assessment – good
  - ARV resistance testing - pending

Mr PS – husband to Ms PP

ISSUES

- Side effect
- Poor follow up
- Weak health care system
- Partners treated at different sites

TENOFOVIR ADVERSE EFFECTS

	FTC + TDF + EFV[b]	AZT/3TC + EFV
	N=257	N=254
Gastrointestinal Disorder		
Diarrhea	9%	5%
Nausea	9%	7%
Vomiting	2%	5%
General Disorders and Administration Site Condition		
Fatigue	9%	8%
Infections and Infestations		
Sinusitis	8%	4%
Upper respiratory tract infections	8%	5%
Nasopharyngitis	5%	3%
Nervous System Disorders		
Headache	6%	5%
Dizziness	8%	7%

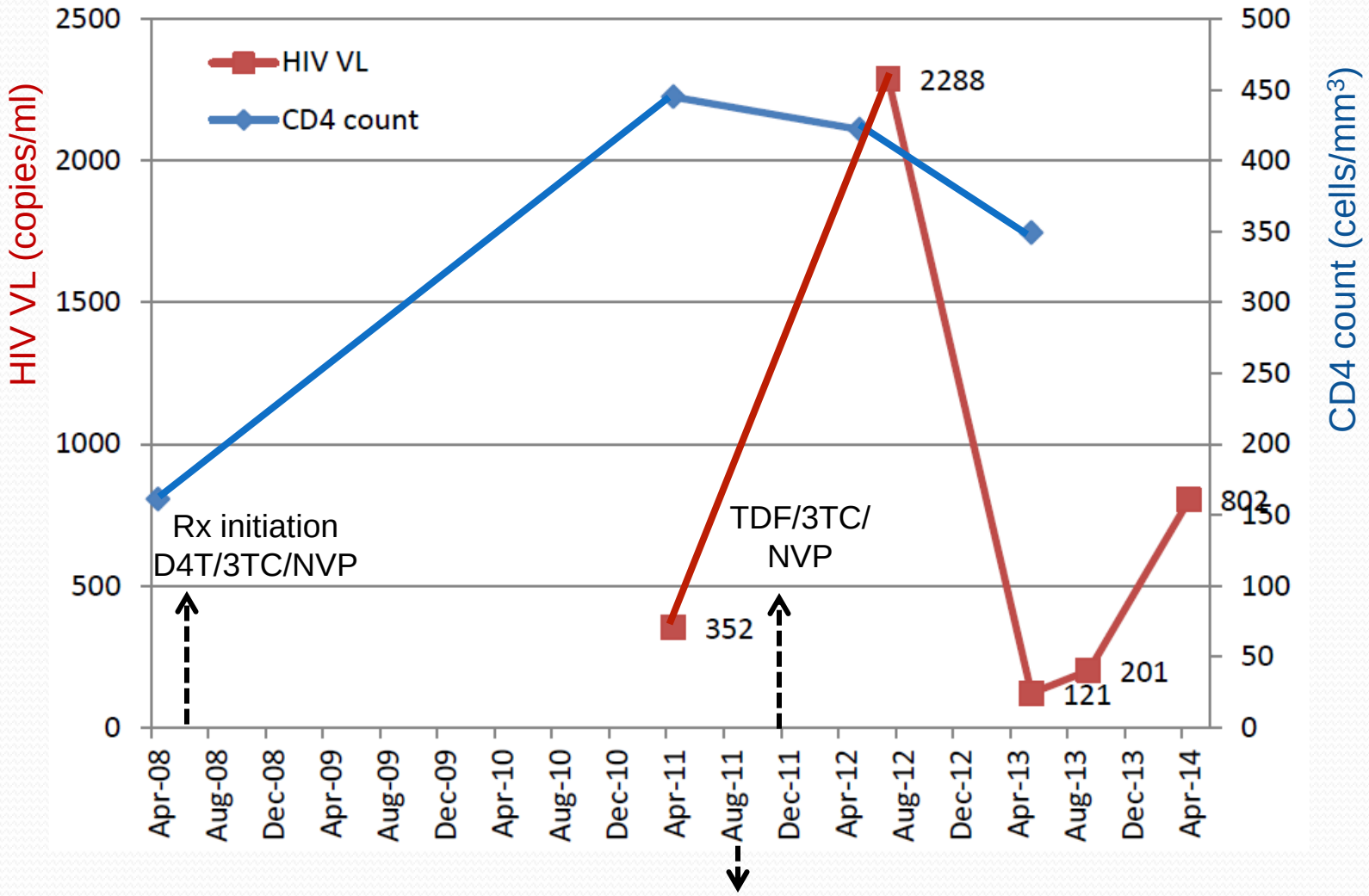
Truvada package insert. Revised December 2013

Pharmacokinetics and Tolerability of Tenofovir

- The most frequently reported AE was diarrhea, which occurred in 3 subjects (21%), 2 cases of which were considered by the investigator as possibly related to the study medication.

Hu C, et al. Clinical Therapeutics 2013: 35; 1884 - 89.

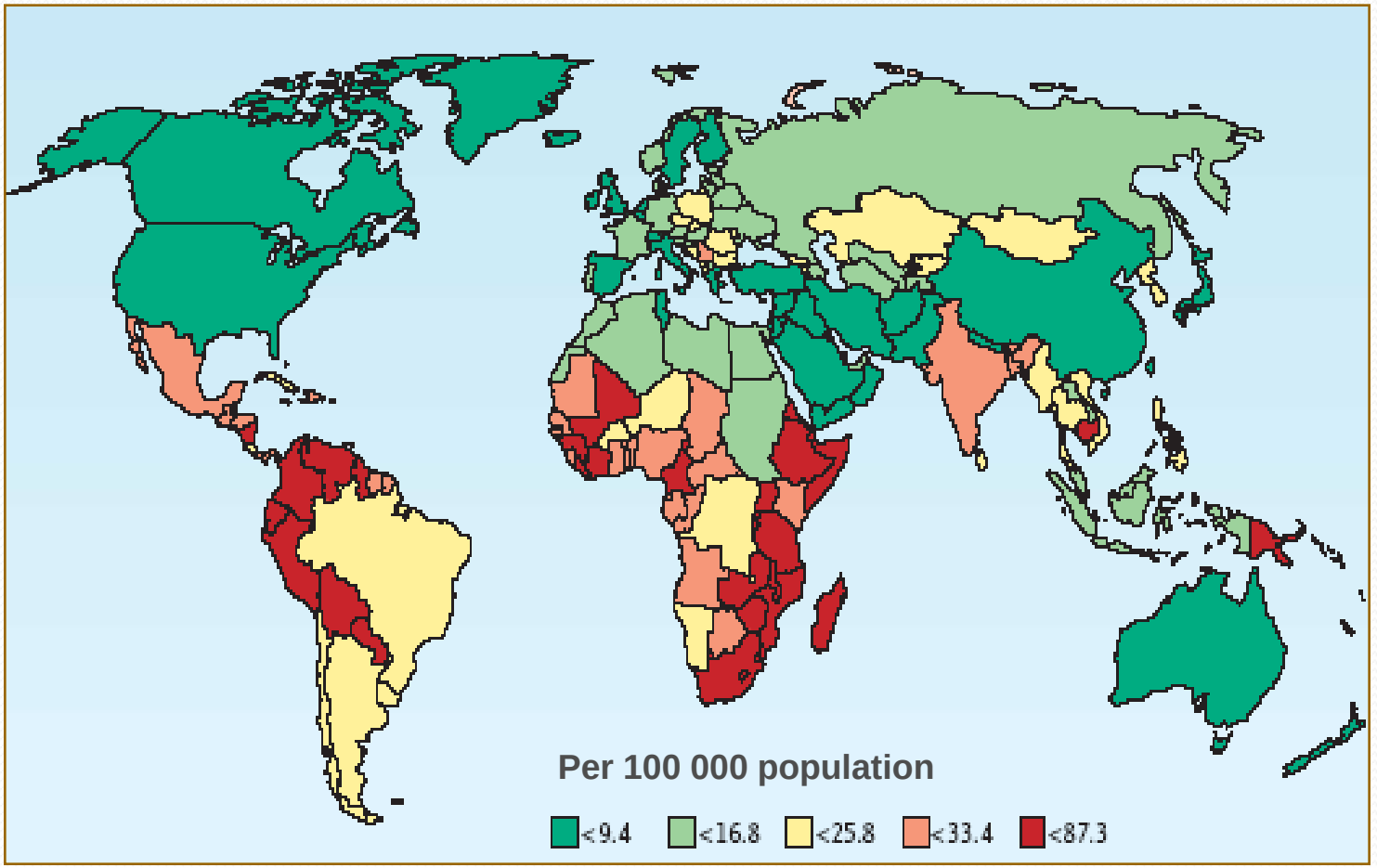
Ms PW



Pap smear - Keratinising HSIL – LLETZ done the same year

HUMAN PAPILLOMA VIRUS (HPV) = causes CERVICAL CANCER

- ~ 510 000 new cases of invasive cervical cancer / year
  - ~80% occurs in the developing world



2013 SA HIV MANAGEMENT GUIDELINES

Patients with CD4 above 350, Not yet eligible for ART

- CD4 testing 6-monthly, HIV reduction counselling, INH prophylaxis for TB
- Provide counselling on nutrition and contraceptive & do annual pap smear

2013 WHO HIV MANAGEMENT GUIDELINES

- Cervical cancer screening leads to early detection of precancerous and cancerous cervical lesions that will prevent serious morbidity and mortality.
- Thus, all women with HIV should be screened for cervical cancer regardless of age

2010 SA guidelines for cervical cancer screening

- The national policy on cervical screening allows for 3 smears in a woman's lifetime taken at 10 year intervals from 30 years of age.

Botha H, et al. South Afr J Gynaecol Oncol 2010;2:23-26

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CLINICAL ARTICLE

Outcome of loop electrosurgical excision for HIV-positive women in a low-resource outpatient setting

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Kietpeerakool C, et al. International Journal of Gynecology and Obstetrics 2009:105;10–13.

Abnormal cervical cytology following LEEP/LLETZ in 6 HIV-infected women

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	25	35	40	35	41	30
Time interval, mo	8	8	9	4	12	4
Integrated HAART	Yes	Yes	Yes	Yes	Yes	Yes
CD4 count at 1st LEEP	53	450	370	323	449	201
First histologic result	CIN 2,3	CIN 2,3	CIN 1	CIN 2,3	CIN 1,2,3	CIN 2,3
Margin involvement	Endo	Ecto	Ecto/endo	Ecto	Ecto	Endo
Lesion grades at involved margins	CIN 2,3	CIN 2,3	Negative	CIN 2,3	CIN 1	CIN 1
Cytologic type	ASC-H	LSIL	ASC-US	ASC-H	ASC-US	LSIL
Second histologic result	Chronic cervicitis	not done	CIN 1	Chronic cervicitis	not done	CIN 1

Kietpeerakool C, et al. International Journal of Gynecology and Obstetrics 2009:105;10–13.

OUTCOMES OF LLETZ OR LEEP IN HIV-INFECTED WOMEN

- HIV-infected women have a higher risk of resection margin involvement after cervical conization, which may reflect a more extensive lesion

- Margin involvement after conization has been found to be an independent predictor for persistent or recurrent disease

- Severe immunosuppression (CD4 cell count <200 cells/μL) may be a predictor of margin involvement

Kietpeerakool C, et al. International Journal of Gynecology and Obstetrics 2009:105;10–13.

BMC Cancer

BioMed Central

Research article

Open Access

Predictors of persistent cytologic abnormalities after treatment of cervical intraepithelial neoplasia in Soweto, South Africa: a cohort study in a HIV high prevalence population

Yasmin Adam*[1,2], Cyril J van Gelderen[1,2], Guy de Bruyn[3], James A McIntyre[3], Diane A Turton[2,4] and Neil A Martinson[3,5]

- The median time between LLETZ and first follow-up Pap smear was short - at 122 days.
- Persistent cytological abnormalities occurred in 49% of our patients after LLETZ.

BMC Cancer 2008, ***8:211***

2013 WHO guidelines for screening and treatment of precancerous cervical lesions in HIV+ women

If screening with cytology & followed by colposcopy (with or without biopsy)

- Normal cytology – rescreen within 3 years
- ASCUS or greater & colposcopy negative - rescreen within 3 years
- ASCUS or greater & colposcopy positive (no biopsy) – cryotherapy or LLETZ
  - post-treatment follow up at 1 year
- ASCUS or greater & colposcopy positive (biopsy)
  - CIN 2+ - cryotherapy or LLETZ – post-treatment follow up @1 year
  - CIN 1 or less – rescreen within 3 years

SUMMARY

- Infant diagnosis in the era of PMTCT and early HAART
- LDL – main goal of HAART
- ARV resistance testing – not part of SA guidelines yet (limited access through research labs)
- Side effects of ARVs
- Think beyond guidelines sometimes