



UNIVERSITY OF TM
KWAZULU-NATAL
INYUVESI
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HIV DRUG RESISTANCE CLINICAL MANAGEMENT

Richard Lessells



EDGEWOOD CAMPUS



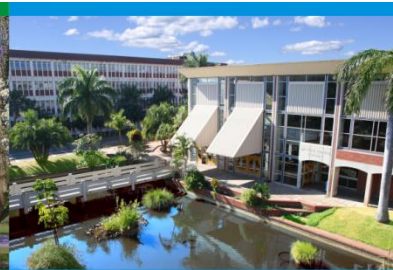
HOWARD COLLEGE CAMPUS



NELSON R MANDELA SCHOOL OF MEDICINE



PIETERMARITZBURG CAMPUS



WESTVILLE CAMPUS

UKZN INSPIRING GREATNESS

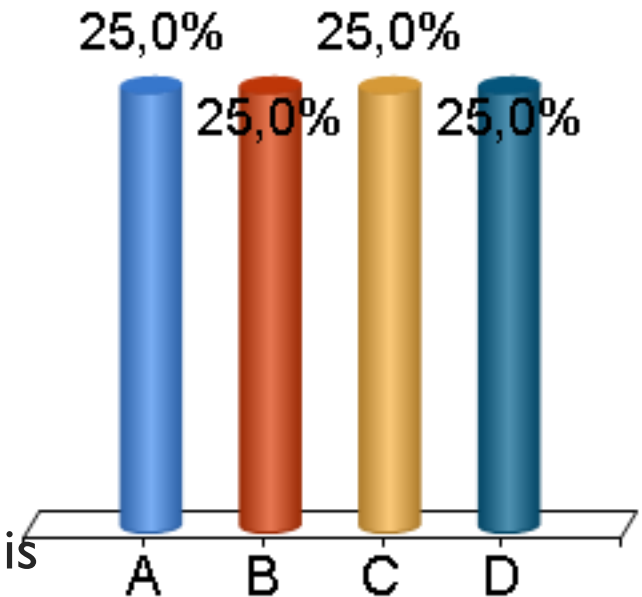
Question

Have you ordered an HIV drug resistance test?

A. Yes

B. No

C. I don't know what an HIV drug resistance test is



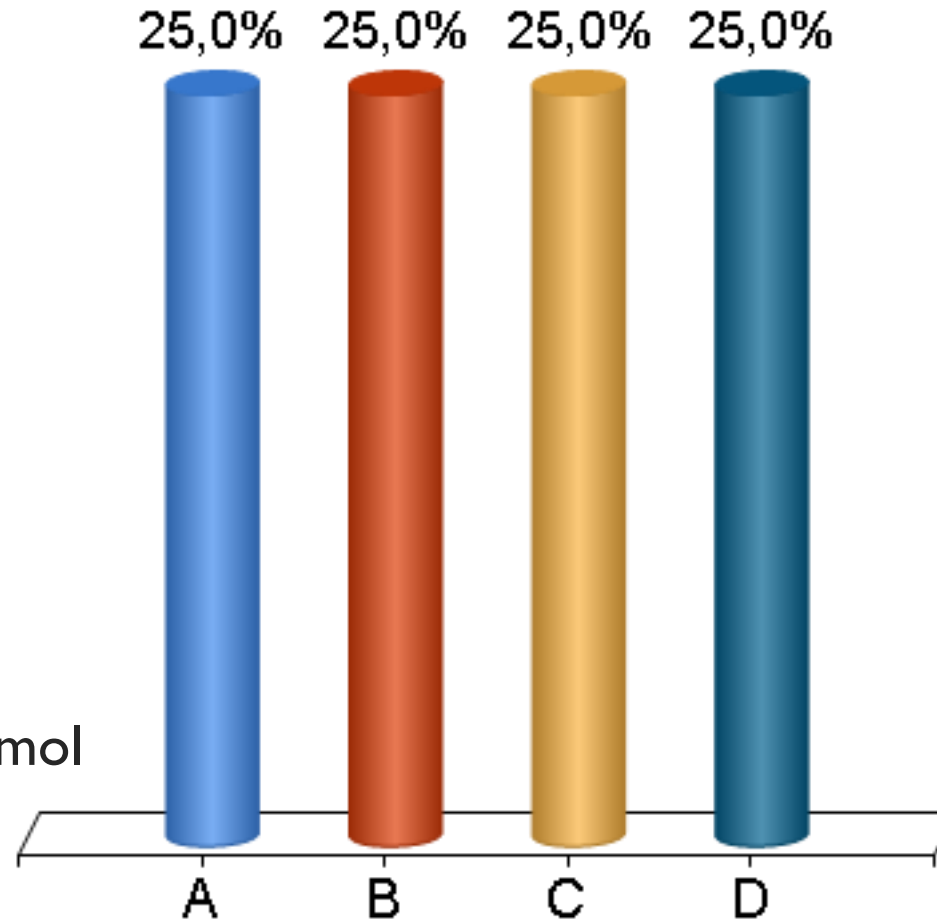
Question

Have you ordered and prescribed third-line antiretroviral therapy?

A. Yes

B. No

C. I haven't even prescribed paracetamol



Clinical case



44-year old HIV-positive male

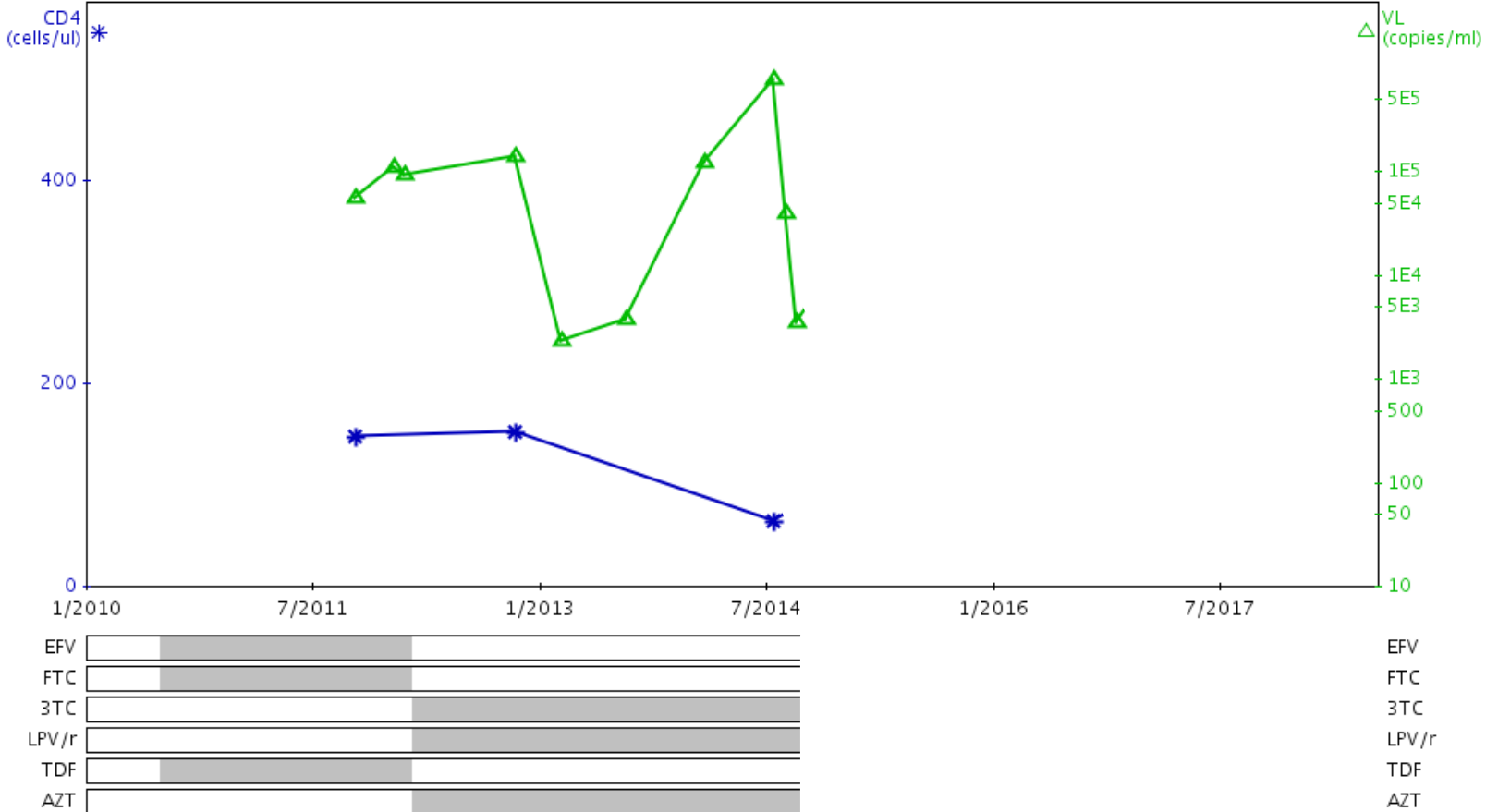
HIV diagnosis 2010

Pre-treatment CD4+ count not known

Initiated first-line ART (TDF/FTC/EFV) in private sector
2010 – transferred into public sector Oct 2011

4 x episodes pulmonary TB (last 2010)

Clinical chart



↑
PTB

↑
Virological failure

↑
Genotype

Genotypic resistance test report

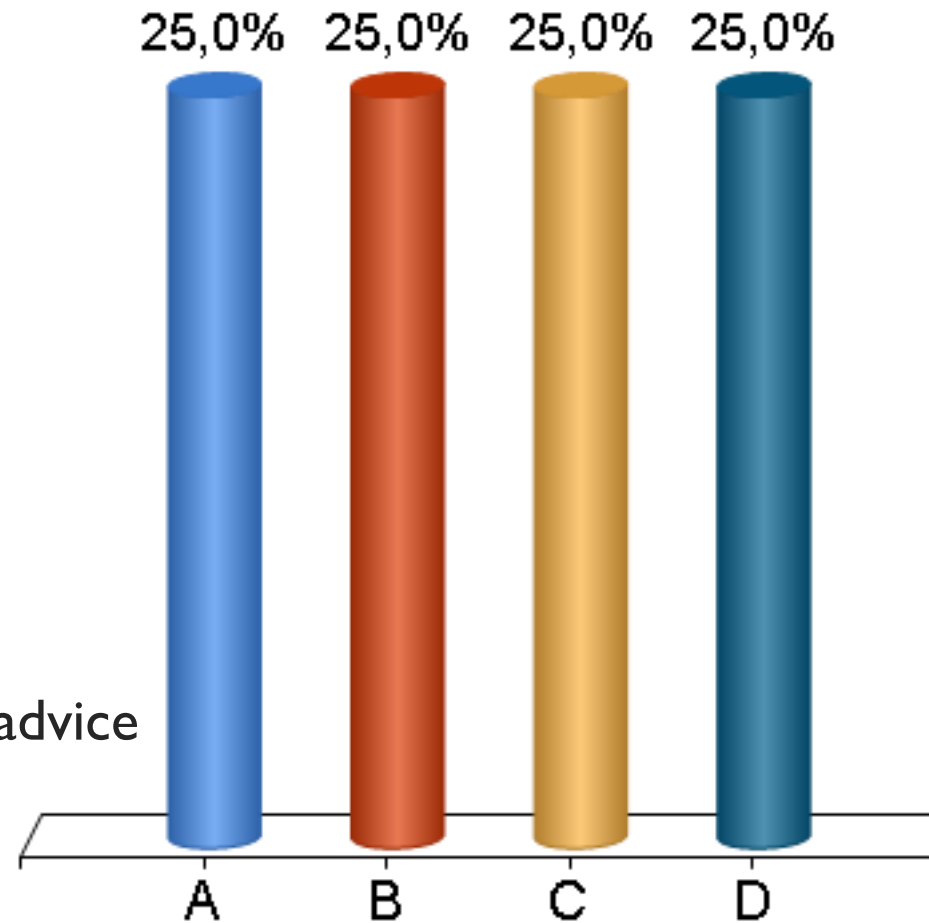
Antiretroviral experience: TDF, FTC, EFV, AZT, 3TC, LPVr
Subtype: HIV-1 Subtype C
Resistance interpretations: HIVdb 8.6

Drug	Mutations	Description	Score
Zidovudine	M184V,T215S	Potential low-level resistance	10
Lamivudine	M184V	High-level resistance	60
Abacavir	M184V,T215S	Low-level resistance	20
Emtricitabine	M184V	High-level resistance	60
Tenofovir	M184V,T215S	Susceptible	-5
Nevirapine	-	Susceptible	0
Efavirenz	-	Susceptible	0
Etravirine	-	Susceptible	0
Lopinavir/r	-	Susceptible	0
Atazanavir/r	-	Susceptible	0
Darunavir/r	-	Susceptible	0

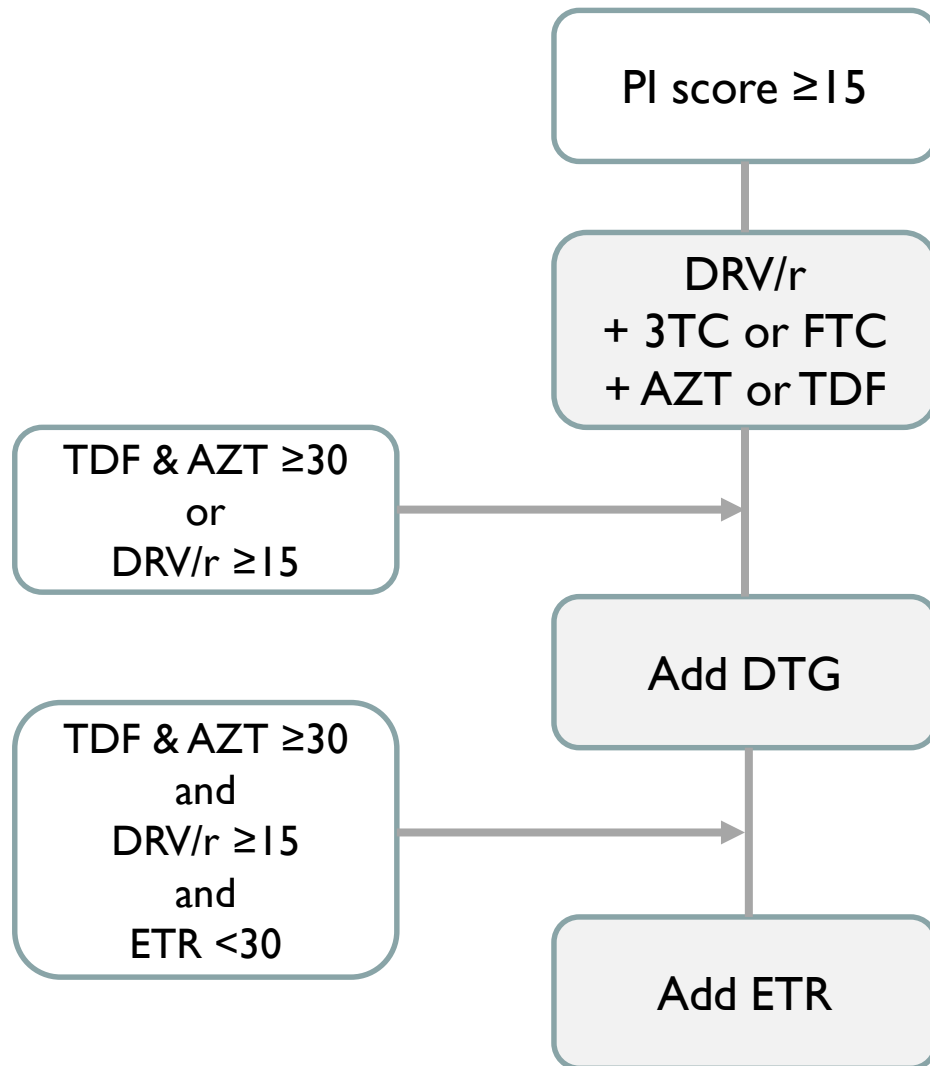
Question

Would you submit a request for third-line antiretroviral therapy now?

- A. Yes
- B. No
- C. I would phone ID/virology for advice



Third-line ART decision tree



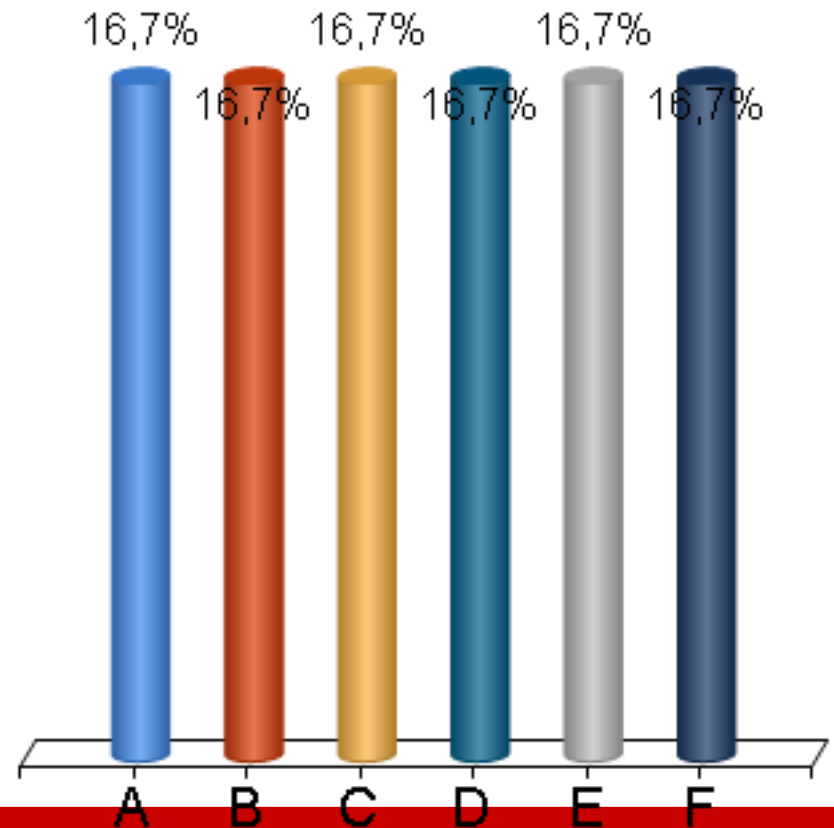
Penalty scores & predicted resistance

- <10 Susceptible
- 10-14 Potential low-level resistance
- 15-29 Low-level resistance
- 30-59 Intermediate resistance
- ≥60 High-level resistance

Question

You strengthen adherence counselling and support. He reports no specific side-effects. What will you do with his ART regimen?

- A. Continue AZT/3TC/LPV/r
- B. Switch to TDF/FTC/LPV/r
- C. Switch to AZT/3TC/ATV/r
- D. Switch to TDF/3TC/DTG (TLD)
- E. Switch to AZT/3TC/DTG



National HIV guidelines



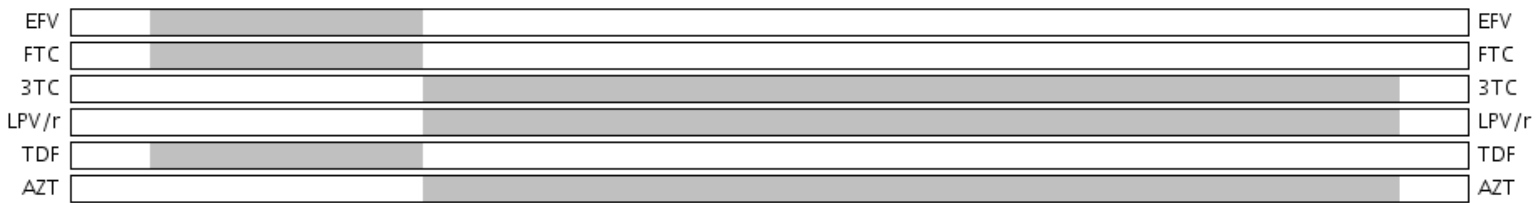
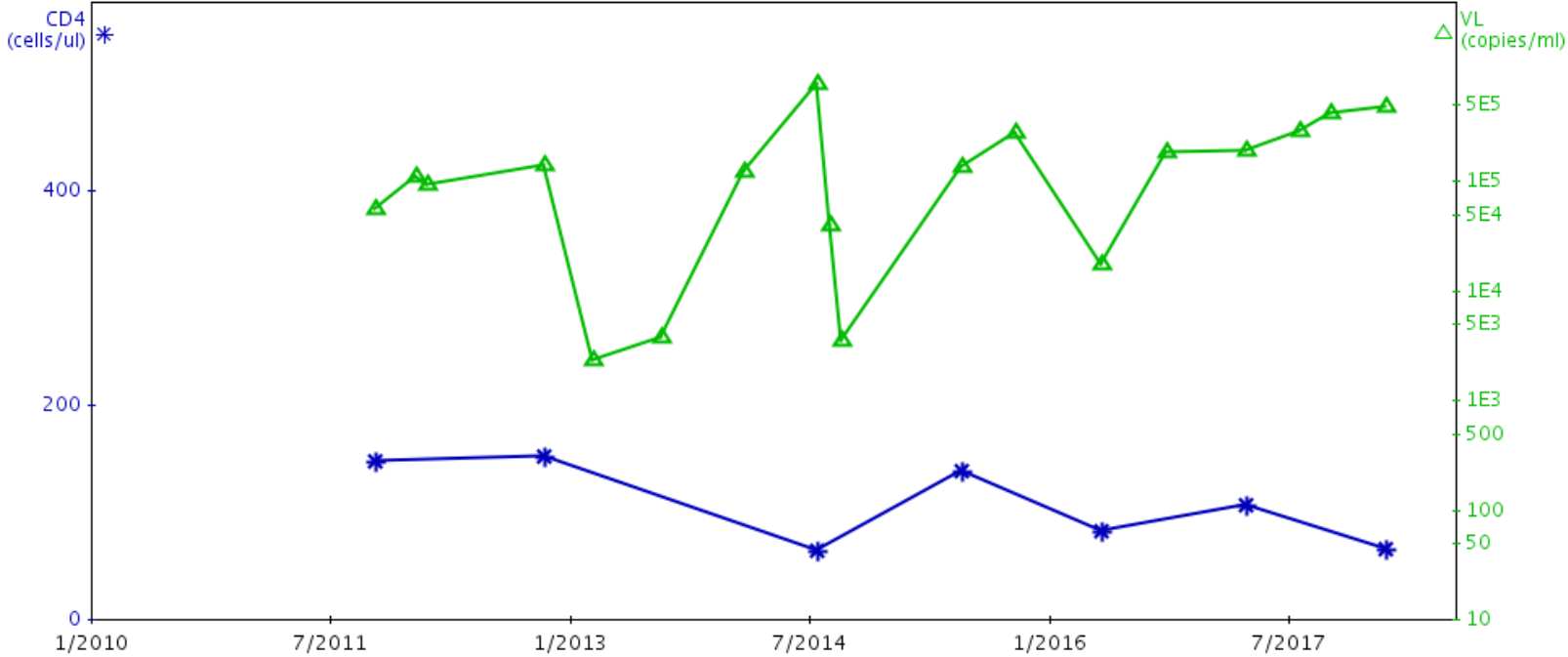
	First-Line Regimens				Second-Line Regimens	
	NNRTI-based Regimen		InSTI-based Regimen for > 2 years		PI-based Regimen for > 2 years	
Regimen	TDF + 3TC/FTC + EFV/NVP		TDF + 3TC/FTC + DTG		AZT/TDF + 3TC/FTC + LPV/r or ATV/r	
Resistance Testing	Resistance test <u>not</u> required		Resistance testing may be required under expert consultation ⁵		Resistance test required	
Resistance Test results	Not applicable		Not applicable		No PI resistance	PI resistance
HBV Co-infection Status ¹	HBV-negative	HBV-positive	HBV-negative	HBV-positive	HBV-positive or -negative	
New Regimen	AZT + 3TC/FTC + DTG ²	TDF ¹ + AZT + 3TC/FTC + DTG ²	AZT + 3TC/FTC + LPV/r	TDF + 3TC/FTC + LPV/r ⁴	Continue current regimen and address adherence. If intolerance to LPV/r is affecting adherence, discuss possible substitutions with an expert	Refer to Third-Line Committee. Regimen will be determined by results of resistance test
	If DTG not suitable ² , AZT + 3TC/FTC + LPV/r	If DTG not suitable ² , TDF + 3TC + LPV/r ⁴				

Genotypic resistance test report

Antiretroviral experience: TDF, FTC, EFV, AZT, 3TC, LPVr
Subtype: HIV-1 Subtype C
Resistance interpretations: HIVdb 8.6

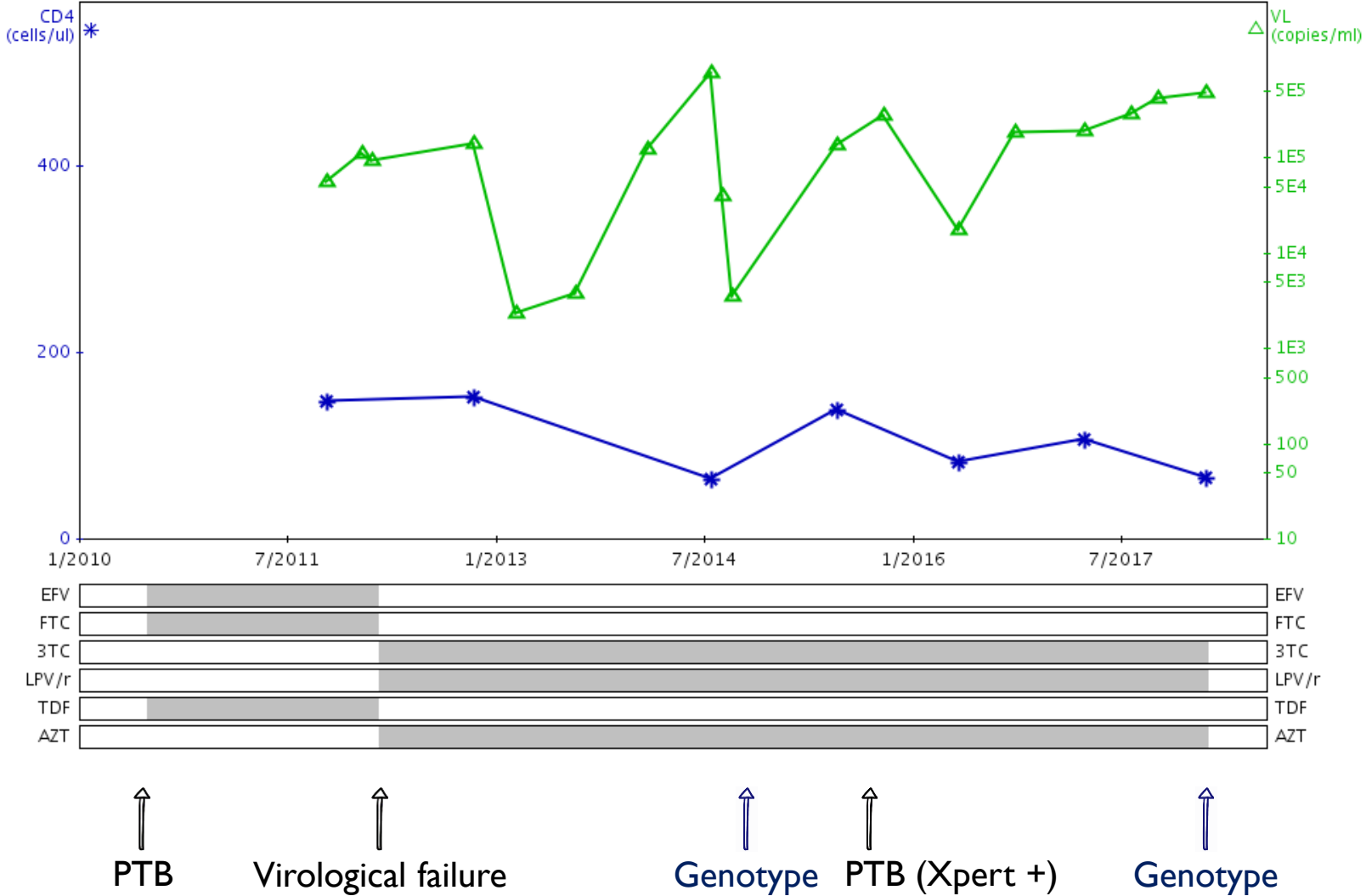
Drug	Mutations	Description	Score
Zidovudine	M184V,T215S	Potential low-level resistance	10
Lamivudine	M184V	High-level resistance	60
Abacavir	M184V,T215S	Low-level resistance	20
Emtricitabine	M184V	High-level resistance	60
Tenofovir	M184V,T215S	Susceptible	-5
Nevirapine	-	Susceptible	0
Efavirenz	-	Susceptible	0
Etravirine	-	Susceptible	0
Lopinavir/r	-	Susceptible	0
Atazanavir/r	-	Susceptible	0
Darunavir/r	-	Susceptible	0

Clinical chart



↑ PTB ↑ Virological failure ↑ Genotype ↑ PTB (Xpert +)

Clinical chart



Genotypic resistance test report

Antiretroviral experience: TDF, FTC, EFV, AZT, 3TC, LPVr
Subtype: HIV-1 Subtype C
Resistance interpretations: HIVdb 8.6

Drug	Mutations	Description	Score
Zidovudine	M41L, M184V, T215S	Intermediate resistance	55
Lamivudine	M41L, M184V, T215S	High-level resistance	65
Abacavir	M41L, M184V, T215S	Intermediate resistance	45
Emtricitabine	M41L, M184V, T215S	High-level resistance	65
Tenofovir	M41L, M184V, T215S	Low-level resistance	15
Nevirapine	A98G	Intermediate resistance	30
Efavirenz	A98G	Low-level resistance	15
Etravirine	A98G	Potential low-level resistance	10
Lopinavir/r	L10F, M46I, I54V, V82A	High-level resistance	80
Atazanavir/r	M46I, I54V, V82A	High-level resistance	60
Darunavir/r	L10F	Susceptible	5

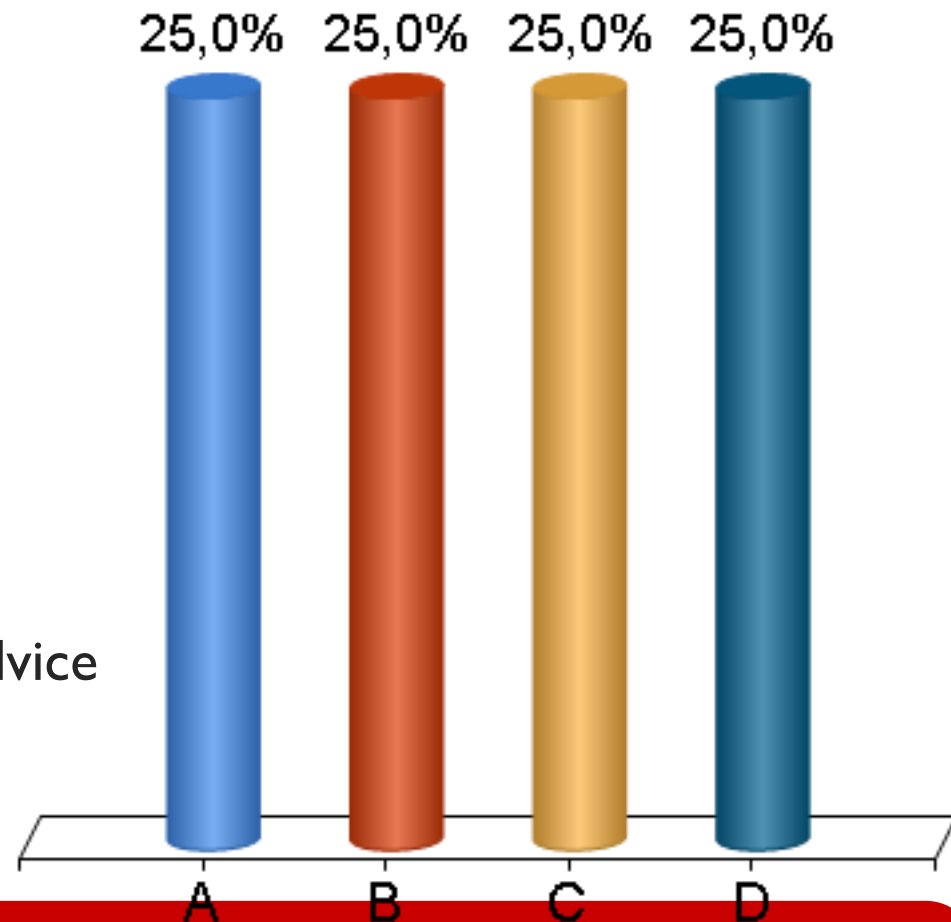
Question

Would you submit a request for third-line antiretroviral therapy now?

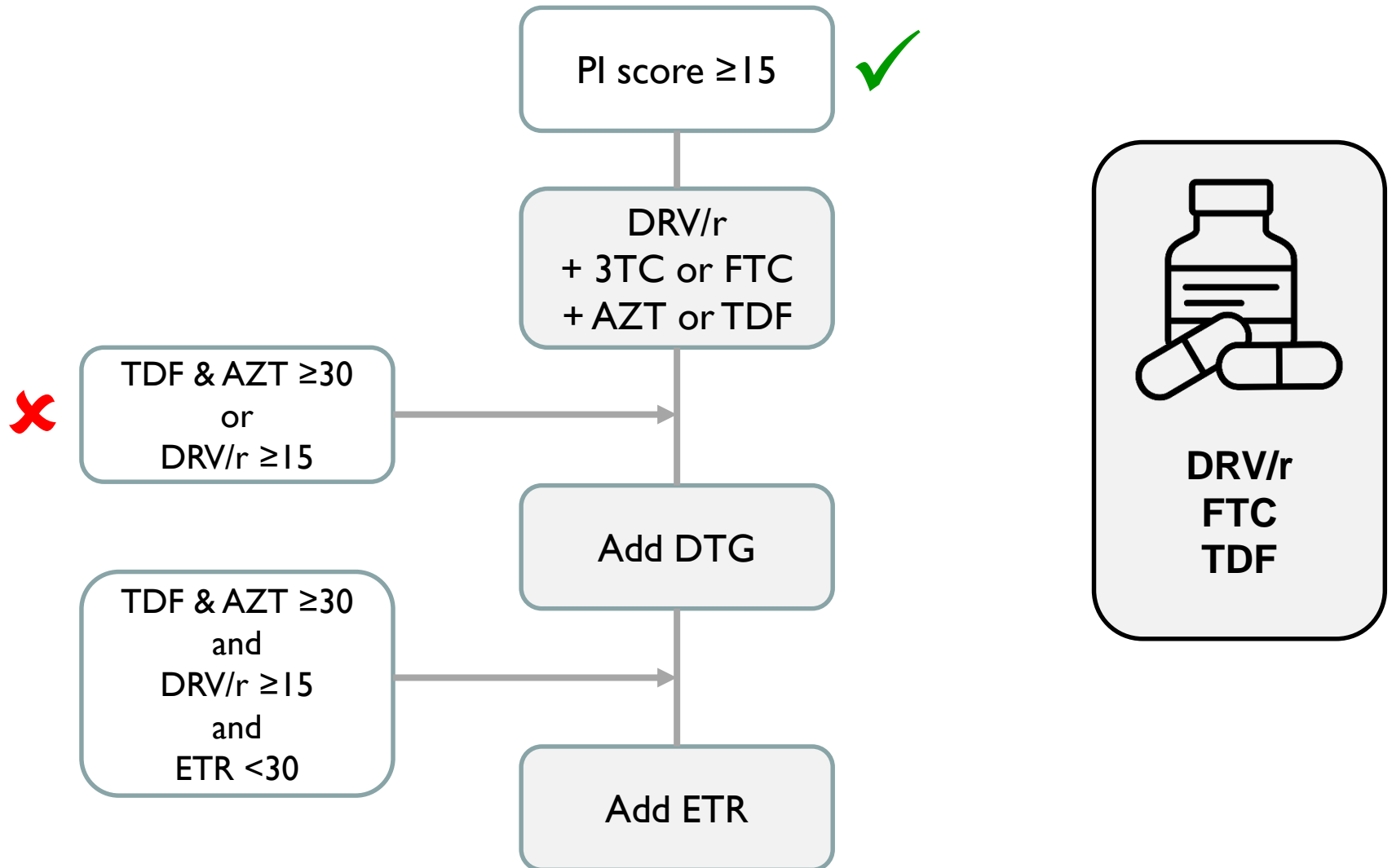
A. Yes

B. No

C. I would phone ID/virology for advice



Third-line ART decision tree



Requesting third-line ART

APPLICATION - THIRD LINE ANTIRETROVIRAL THERAPY					
PLEASE ENSURE ALL FIELDS ARE COMPLETED BEFORE SUBMITTING					
Patient First Name					
Patient Surname					
Date of Birth day/month/year	Patient number				
Identity number	Age		Gender		
Weight	BMI (kg/m ²)	Height (child)			
FACILITY DETAILS					
Facility Name					
Province					
Doctor In Charge Of Patient/ Authorised Prescriber					
Doctor's Contact Number					
Doctor and Pharmacist Email Addresses					
Signature of Authorised Prescriber		Date day/month/year			
PAST MEDICATION HISTORY					
Timelines day/month/year	Past Regimens Only	Reason for discontinuation	Concurrent TB therapy?		
Date started					
Date stopped					
Date started					
Date stopped					
Date started					
Date stopped					
Date started					
Date stopped					
<i>Reason for discontinuation codes: SE = Side effect, F= Failure, FC = Formulary change, NC = Non adherent</i>					
CURRENT REGIMEN ONLY					
Date started day/month/year	Regimen				
CHILDREN: PMTCT HISTORY					

Was the mother on therapy during pregnancy or breastfeeding?				
What treatment did the mother take and for how long?				
Was child breastfed?				
Did child receive any ARV at birth/ after birth/ during breastfeeding? State ARV and duration				
ADHERENCE IN LAST 3 – 6 MONTHS				
Regular clinic attendance				
On-time pharmacy refill				
Correct pill counts				
Treatment partner observes taking of medication				
Alcohol / drug abuse				
Severe GIT or other side effects experienced				
If adherence problem, what interventions were undertaken to address the issue?				
CD 4 COUNT			VIRAL LOAD	
DATE day/month/year	RESULT	Children CD4 %	DATE day/month/year	RESULT
Date:			Date:	
Date:			Date:	
Date:			Date:	
Most recent available tests		Date	Results of Viral Resistance Test - submit together with application to: TLART@HEALTH.GOV.ZA	
Hb (g/dL)				
ALT (U/L)				
Creatinine (µmol/L)				
Creatinine Clearance (mL/min/1.73 m ²)				
White cell count (x 10 ⁹ /L)				
Hepatitis B status (HbsAg pos/neg)				

Case progress



Admitted to hospital while waiting for third-line ART
with cough, fever and chest pain

Sputum Xpert Ultra MTB detected, rifampicin
resistance not detected

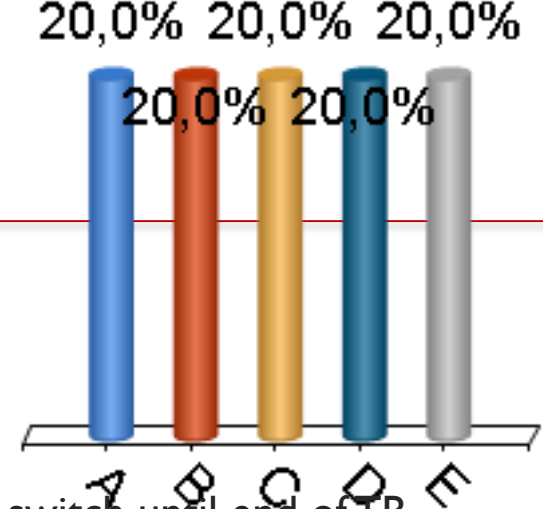
Commenced on RHZE

Discharged to follow-up at HIV clinic

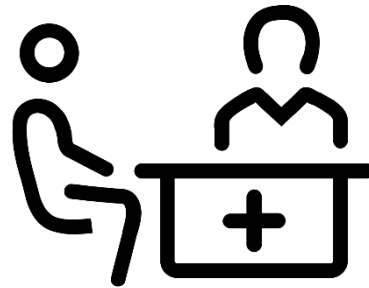
Question

How will you manage the TB treatment and ART now?

- A. Continue HRZE and continue AZT/3TC/LPV/r^{800/200} (delay ART switch until end of TB treatment)
- B. Continue HRZE and switch to TDF/FTC/DRV/r
- C. Change TB treatment to HZE + levofloxacin then switch to TDF/FTC/DRV/r after 2 weeks
- D. Change TB treatment to HZE + rifabutin then switch to TDF/FTC/DRV/r after 2 weeks



Clinical case



46-year old HIV-positive female

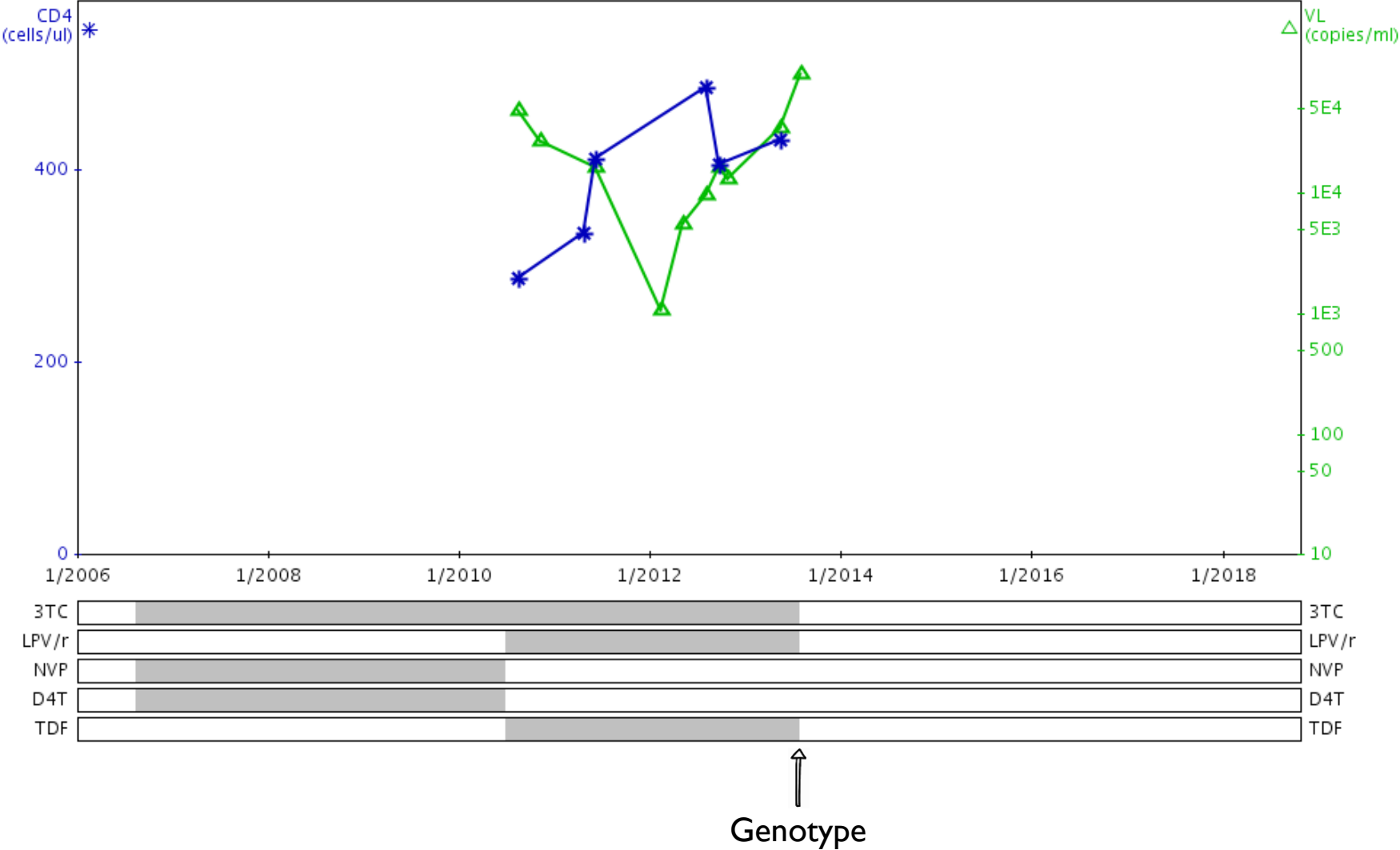
HIV diagnosis 2006

Pre-treatment CD4+ count 160 cells/ μ L

First-line ART – d4T/3TC/NVP 2006 – 2010

Second-line ART – TDF/3TC/LPVr 2010 - 2013

Clinical chart

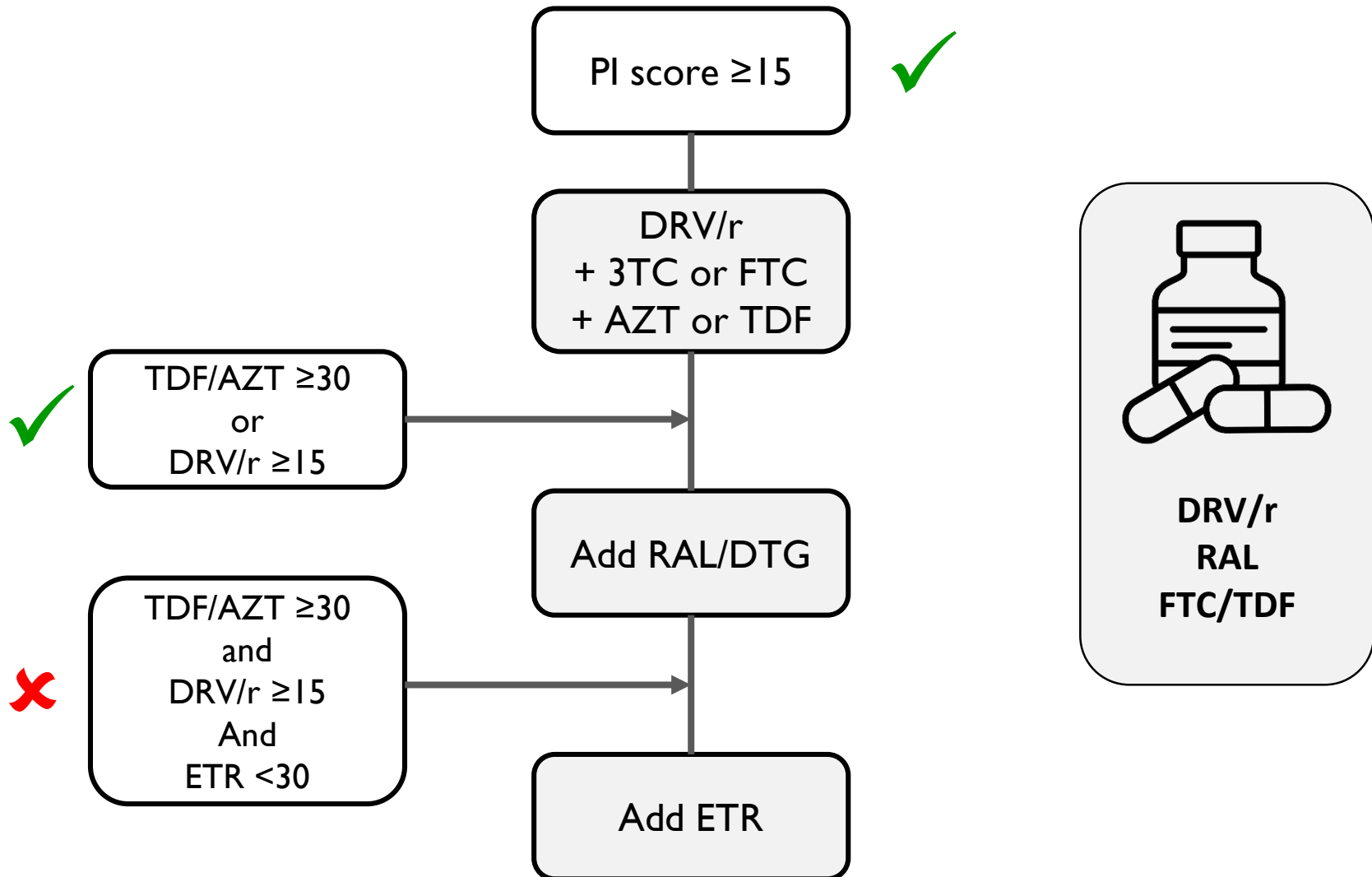


Genotypic resistance test report

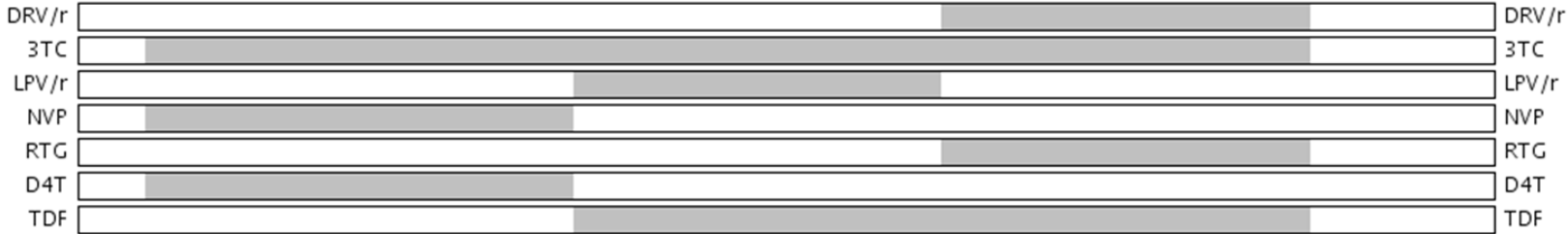
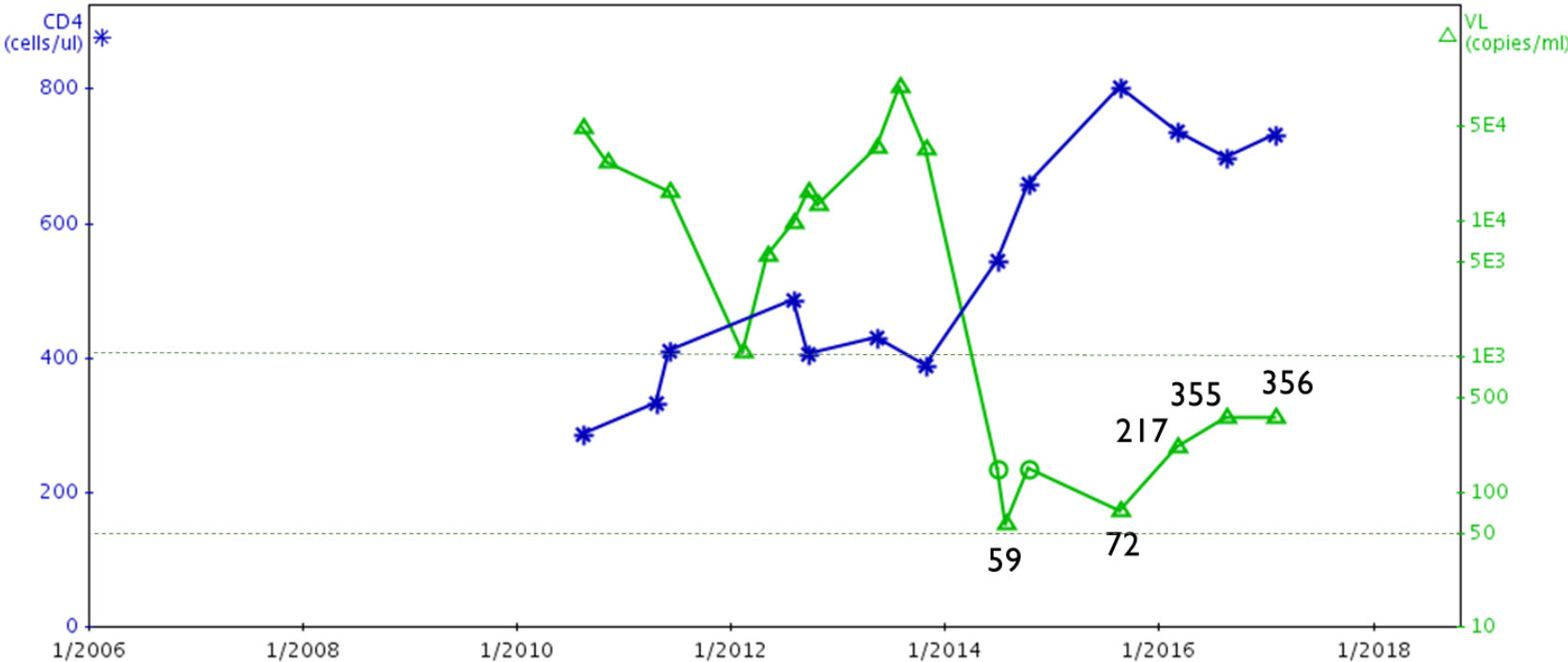
Antiretroviral experience: d4T, 3TC, TDF, NVP, LPVr
Subtype: HIV-1 Subtype C
Resistance interpretations: HIVdb 8.6.1

Drug	Mutations	Description	Score
Zidovudine	D67N, T69D, K70R, M184V, K219Q	Intermediate resistance	55
Abacavir	D67N, T69D, K70R, M184V, K219Q	High-level resistance	60
Tenofovir	D67N, T69D, K70R, M184V, K219Q	Low-level resistance	15
Lamivudine	D67N, T69D, K70R, M184V, K219Q	High-level resistance	70
Emtricitabine	D67N, T69D, K70R, M184V, K219Q	High-level resistance	70
Nevirapine	Y181C	High-level resistance	60
Efavirenz	Y181C	Intermediate resistance	30
Etravirine	Y181C	Intermediate resistance	30
Rilpivirine	Y181C	Intermediate resistance	45
Lopinavir/r	L10F, M46I, I54V, A71V, L76V, V82A	High-level resistance	120
Atazanavir/r	L10F, M46I, I54V, A71V, L76V, V82A	High-level resistance	60
Darunavir/r	L10F, M46I, I54V, A71V, L76V, V82A	Low-level resistance	25

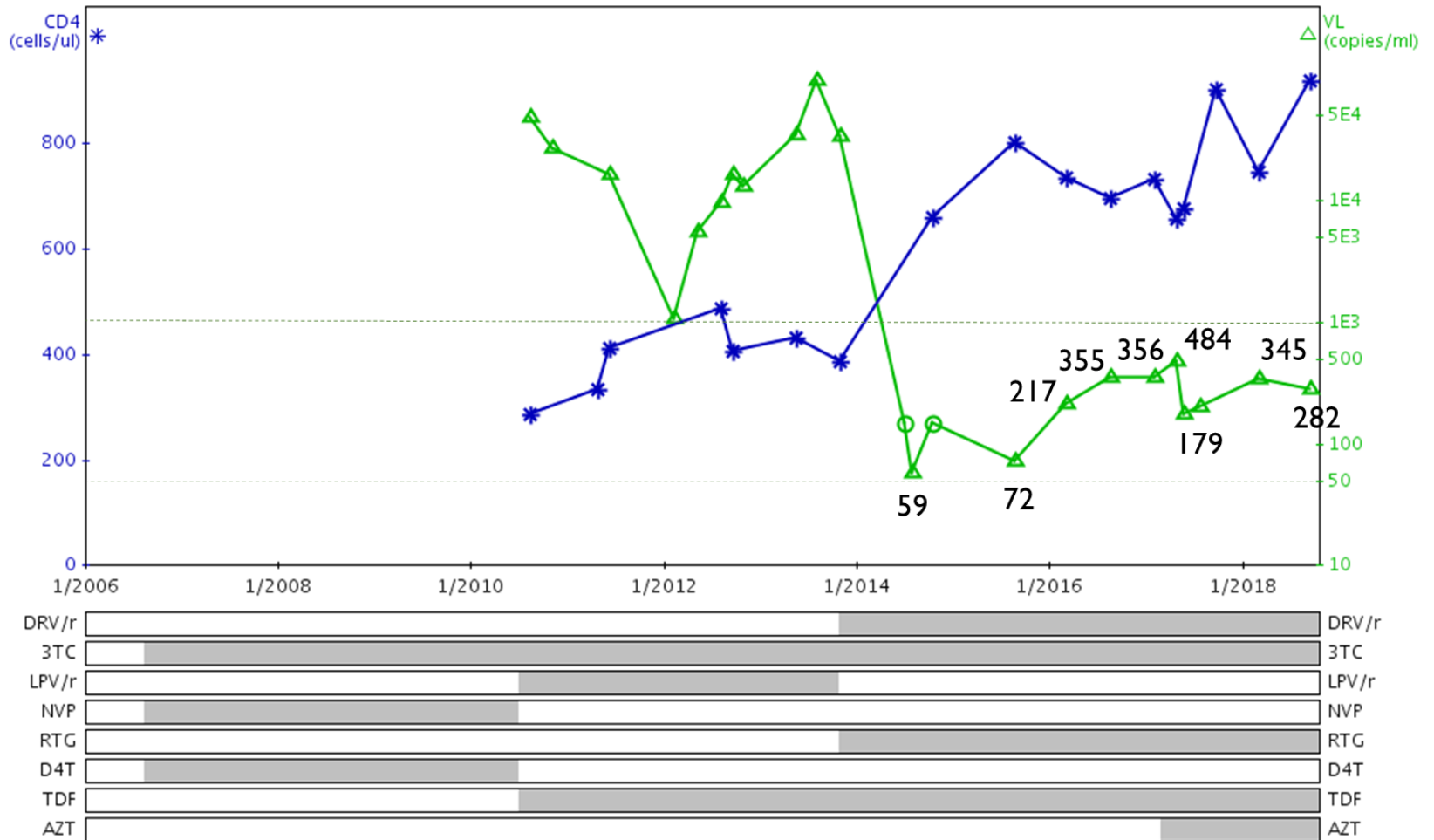
Third-line ART decision tree



Clinical chart

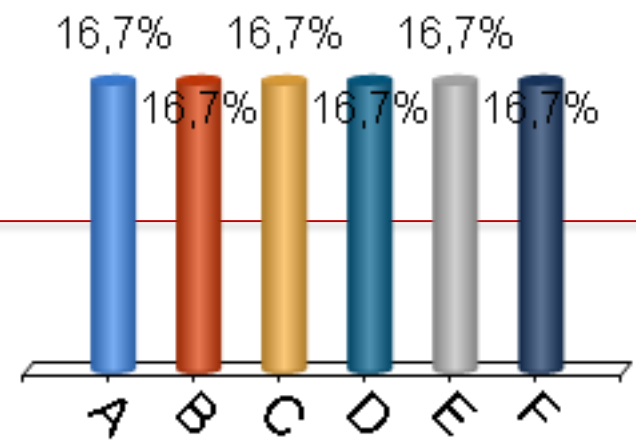


Clinical chart



Question

What is the most important action now?



- A. Thorough clinical assessment for the cause of elevated VL
- B. Thorough clinical assessment for the cause of elevated VL
- C. Thorough clinical assessment for the cause of elevated VL
- D. Thorough clinical assessment for the cause of elevated VL
- E. Panic

Clinical assessment

Adherence

Subjective and objective assessment – excellent adherence

Takes ARVs 0900 & 2100

Uses cell phone alarm as reminder

Niece often also reminds her to take ARVs

Only person on ARVs at home, but disclosed to all household members

Note MCV 111 (cf. 88 prior to AZT introduction)

Tolerability/toxicity

No problem swallowing pills (ARV total pill burden - 9 pills)

No reported side-effects

Significant weight gain (~10 kg ↑ on third-line ART – 75kg to 85kg)

Lipodystrophy (dating back to stavudine use)

Clinical assessment

Comorbidities

Hypertension 2014

Genital warts (Rx podophyllin) 2014

Right salpingo-oophorectomy (haemorrhagic corpus luteum cyst) 2016

Avascular necrosis & osteoarthritis left talus (ankle) 2017

Persistent microscopic haematuria (awaiting urology review) since 2014

Polypharmacy

Hypertension – hydrochlorothiazide, enalapril, amlodipine

Analgesia – Tramadol, amitriptyline, carbamazepine

Total pill burden (ARVs & others) – at least 19 pills per day

Useful resources

University of Liverpool HIV Drug Interactions

The screenshot shows the desktop version of the website. At the top, there is a navigation bar with the University of Liverpool logo and name, a 'Donate Now' button, and a dropdown menu for 'Apps'. Below this is a secondary navigation bar with links for 'About Us', 'Interaction Checkers', 'Prescribing Resources', 'Videos', 'Site News', 'Contact Us', and 'Support Us'. The main content area features a header with the text 'Having trouble viewing the interactions? Click here for the Interaction Checker Lite.' Below this is a search interface with three columns: 'HIV Drugs', 'Co-medications', and 'Drug Interactions'. Each column has a search bar and a filter menu with options for 'A-Z', 'Class', and 'Trade'. The 'HIV Drugs' and 'Co-medications' columns show a list of selected drugs with checkboxes and information icons. The 'Drug Interactions' column is currently empty, displaying the message 'Drug Interactions will be displayed here'.

Website

The screenshot shows the mobile app interface. At the top, there is a navigation bar with 'Welcome' and 'Update' buttons. Below this is the University of Liverpool logo and the title 'Liverpool HIV iChart'. The main content area features a large blue button labeled 'Search For Drug Interactions'. Below this are three smaller blue buttons labeled 'Sponsors', 'Privacy', and 'Disclaimer'. The background is a light gray color.

Mobile app

Useful resources

NATIONAL HIV & TB HEALTH CARE WORKER HOTLINE



0800 212 506
021 406 6782



E-MAIL
pha-mic@uct.ac.za



SMS/PLEASE CALL ME/WHATSAPP
071 840 1572



WEBSITE
www.mic.uct.ac.za



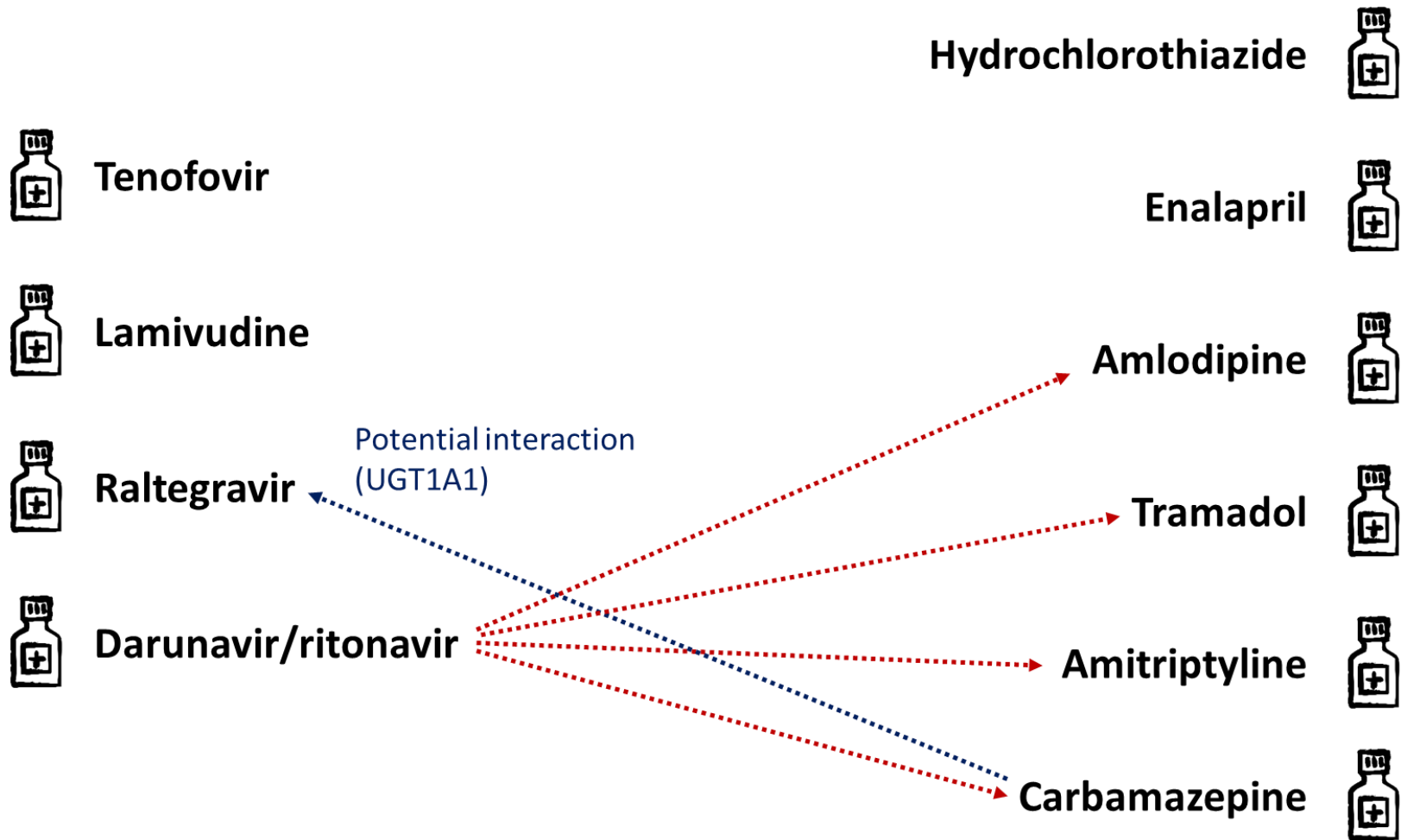
FACEBOOK
**HIV & TB Health Care Worker
Hotline, South Africa**



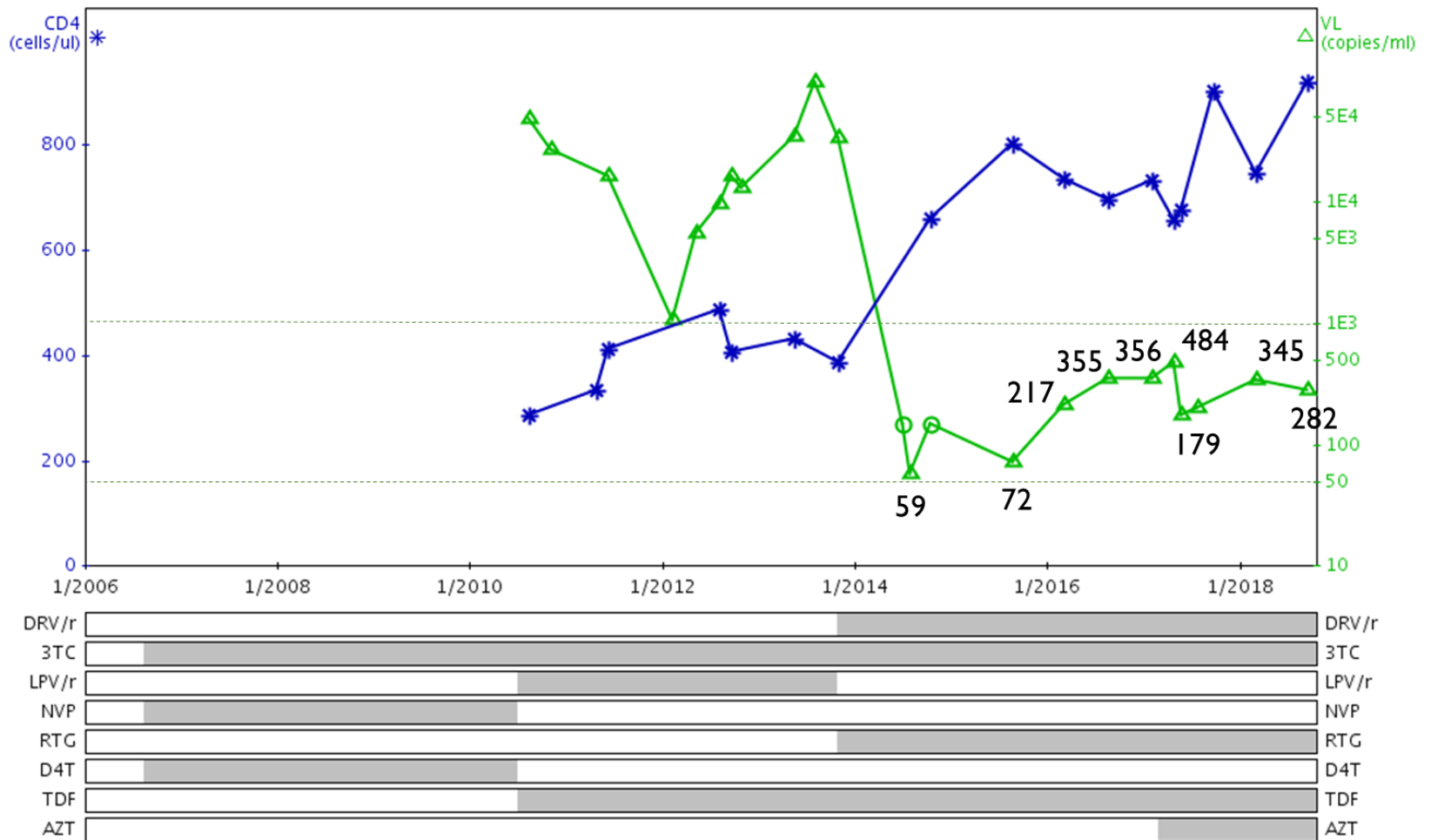
FREE APP ON GOOGLE PLAY
SA HIV/TB Hotline

Contact us - we will gladly assist you! This service is free

Potential drug-drug interactions



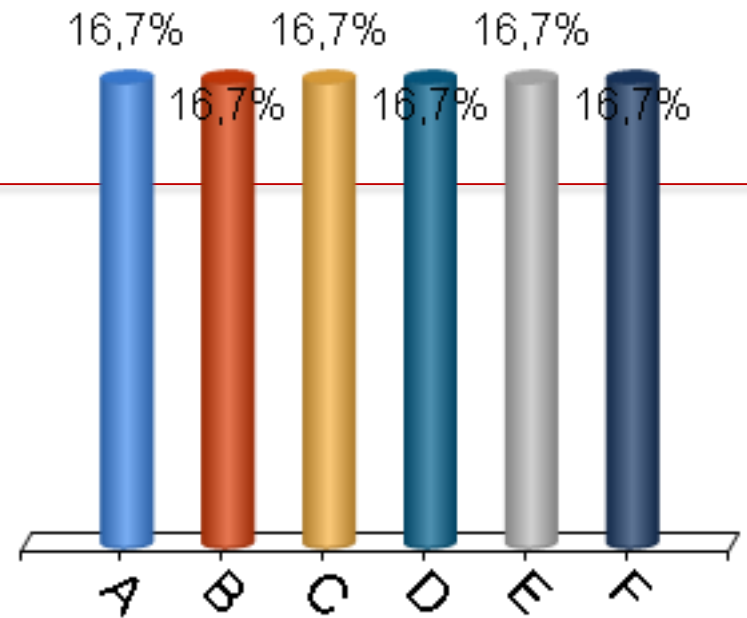
Clinical chart



Question

What will you do now?

- A. Refer to adult ID clinic
- B. Send blood for genotypic resistance testing
- C. Submit request to third-line committee for switch RAL → DTG
- D. Send blood for drug level testing (especially RAL)
- E. Add etravirine



Acknowledgments

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