



DOLUTEGRAVIR RESISTANCE

CASE STUDIES FROM R K KHAN HOSPITAL

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DOLUTEGRAVIR ROLLOUT

- SINCE 2020, SWITCHED VIREMIC OR SUPPRESSED
- WELL TOLERATED
- HIGH GENETIC BARRIER TO RESISTANCE
- MINIMAL SIDE EFFECTS
- MINIMAL DRUG DRUG INTERACTIONS

- WHY ARE SOME PATIENTS VIRAEMIC ON DTG REGIMEN?
- WHAT DO WE DO?

TLD1 VS TLD 2

- TLD1 = PATIENTS WHO HAVE NEVER VIROLOGICALLY FAILED (IRRESPECTIVE THEIR STARTING AND SUBSEQUENT REGIMEN) AND WAS SWITCHED TO TLD
- TLD2 = PATIENTS WHO STARTED ON FIRST LINE THERAPY (IRRESPECTIVE OF STARTING AND SUBSEQUENT REGIMEN), WHO, AFTER 2 CONSECUTIVE VL>1000 AND WAS SWITCHED TO SECOND LINE THERAPY WHICH WAS AZT/3TC/LPV/R. WHO WERE THEN VIROLOGICALLY SUPPRESSED AND CHANGED TO TLD AS PER GUIDELINES. (PATIENTS PREVIOUSLY EXPOSED TO A PI)
- WHY IS THAT IMPORTANT?

APPROACHES TO VF ON DTG BASED REGIMEN

NATIONAL GUIDELINES FOR THE MANAGEMENT OF TLD 1 FAILURE FROM 46 COUNTRIES WITH THE HIGHEST PREVALANCE OF HIV.

- 1. EMPIRIC SWITCH TO PI BASED SECOND LINE REGIMEN 61%
- 2. GRT TO GUIDE REGIMEN SELECTION 30%
- 3. CONTINUE TLD WITHOUT GRT 7%
- 4. EMPIRIC SWITCH TO PI BASED REGIMEN WITH
CONCURRENT GRT 2%

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Two or more VLs ≥ 1000 c/mL

On TLD for **at least 2 years**
and 2 elevated VLs were taken two or more years after starting TLD regimen

On TLD for **less than 2 years**,
irrespective of VL

Adherence > 80%
Proven by an objective measurement¹

Adherence < 80%¹

**Repeat VL at next scheduled
routine VL** (i.e., in 6 months' time)

TLD 2
Clients who have failed a
previous ART regimen

TLD 1
Clients who have never failed a previous
ART regimen

As a rule,
resistance testing is **not
indicated**
for clients on
TLD1²

Special circumstances⁴
e.g., incorrect classification as TLD1
(including perinatally infected
adolescents), or drug interactions

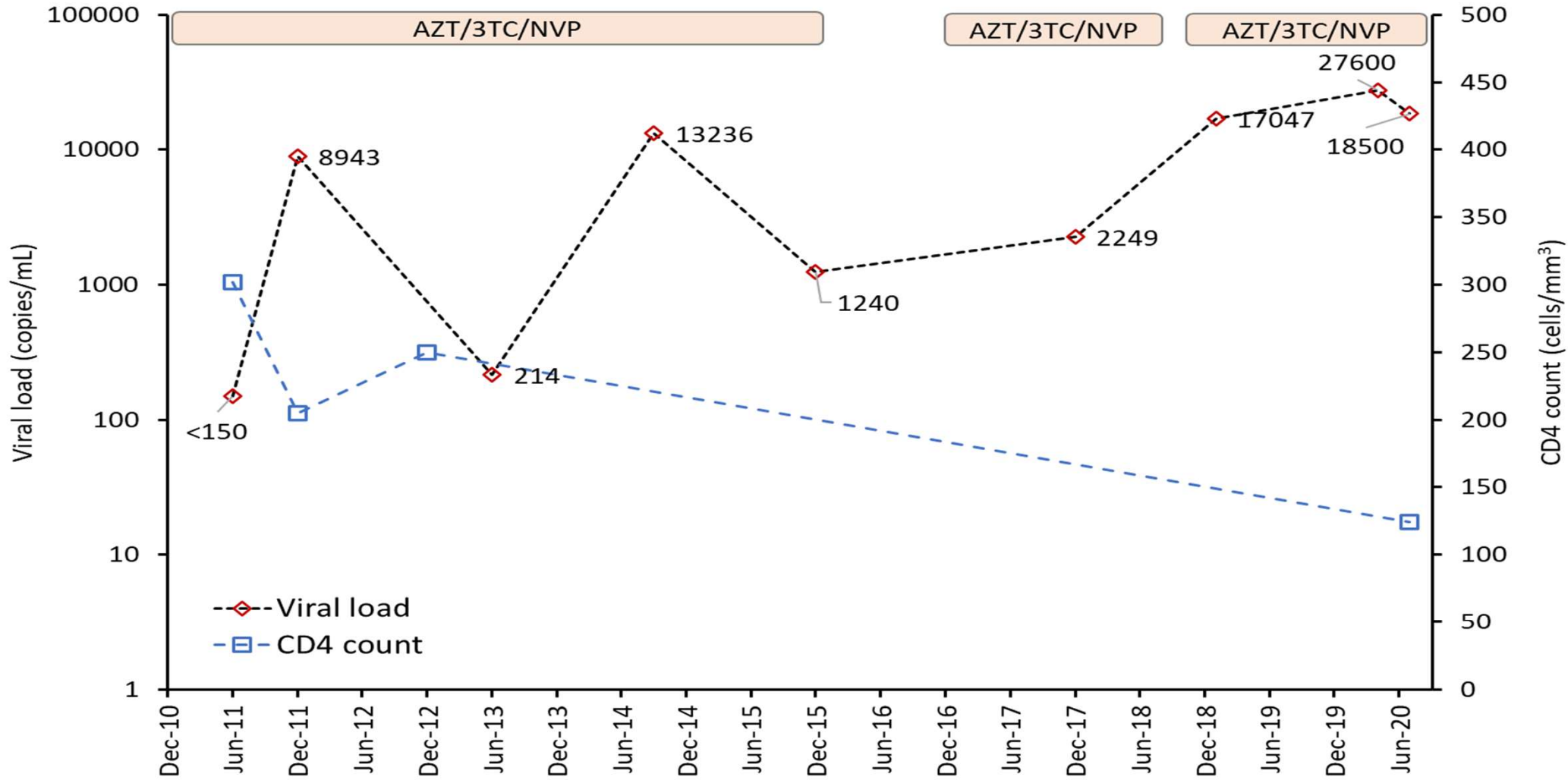
Discuss with an HIV expert⁵
to authorise and interpret a resistance test*

Individualised regimen
as recommended by HIV expert⁵

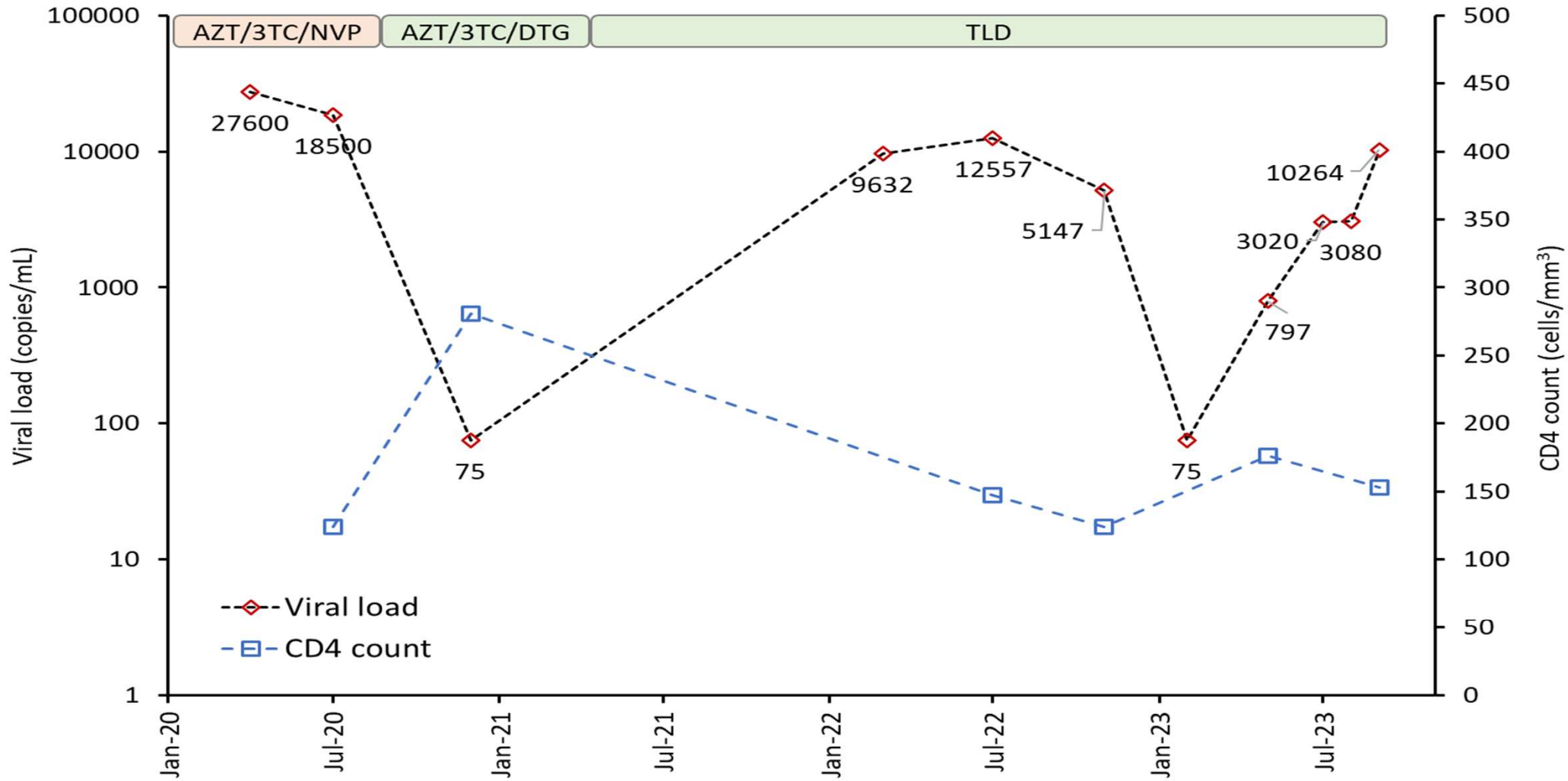
Repeat VL 3 months after starting the new regimen
to confirm viral re-suppression



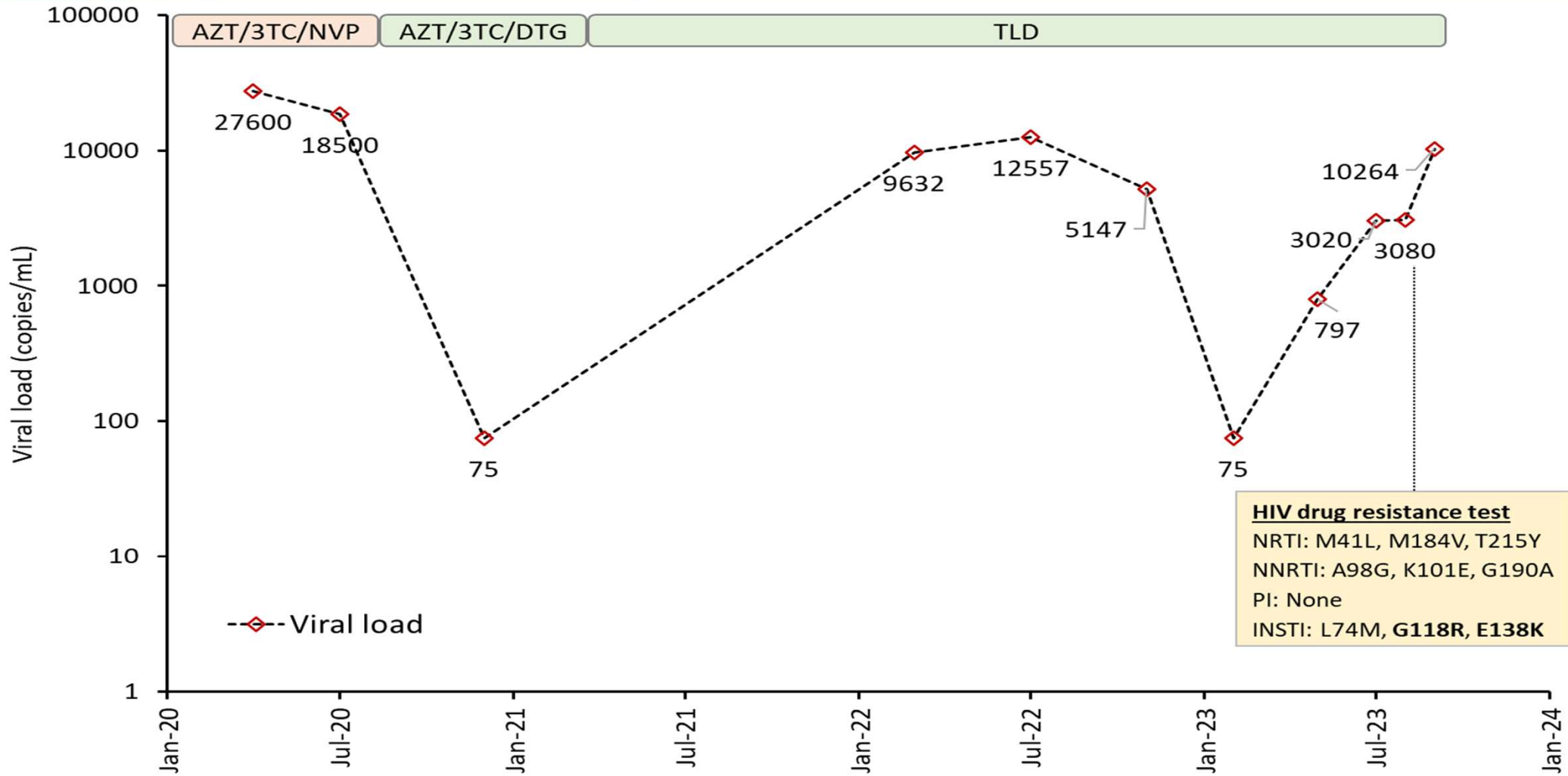
ZD initial NNRTI-based ART



ZD switch from NNRTI- to DTG-based ART

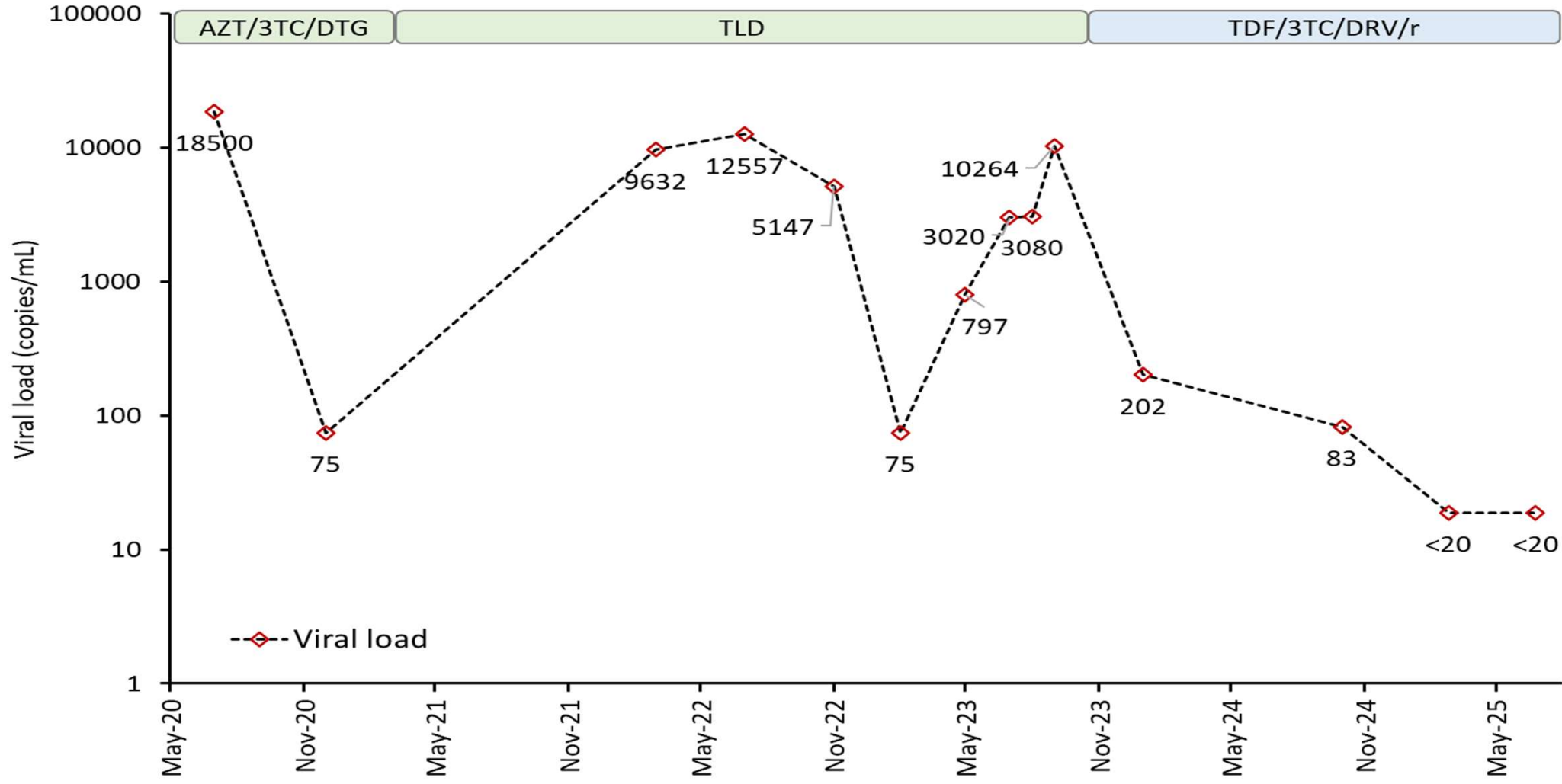


ZD TLD virological failure & HIVDR testing

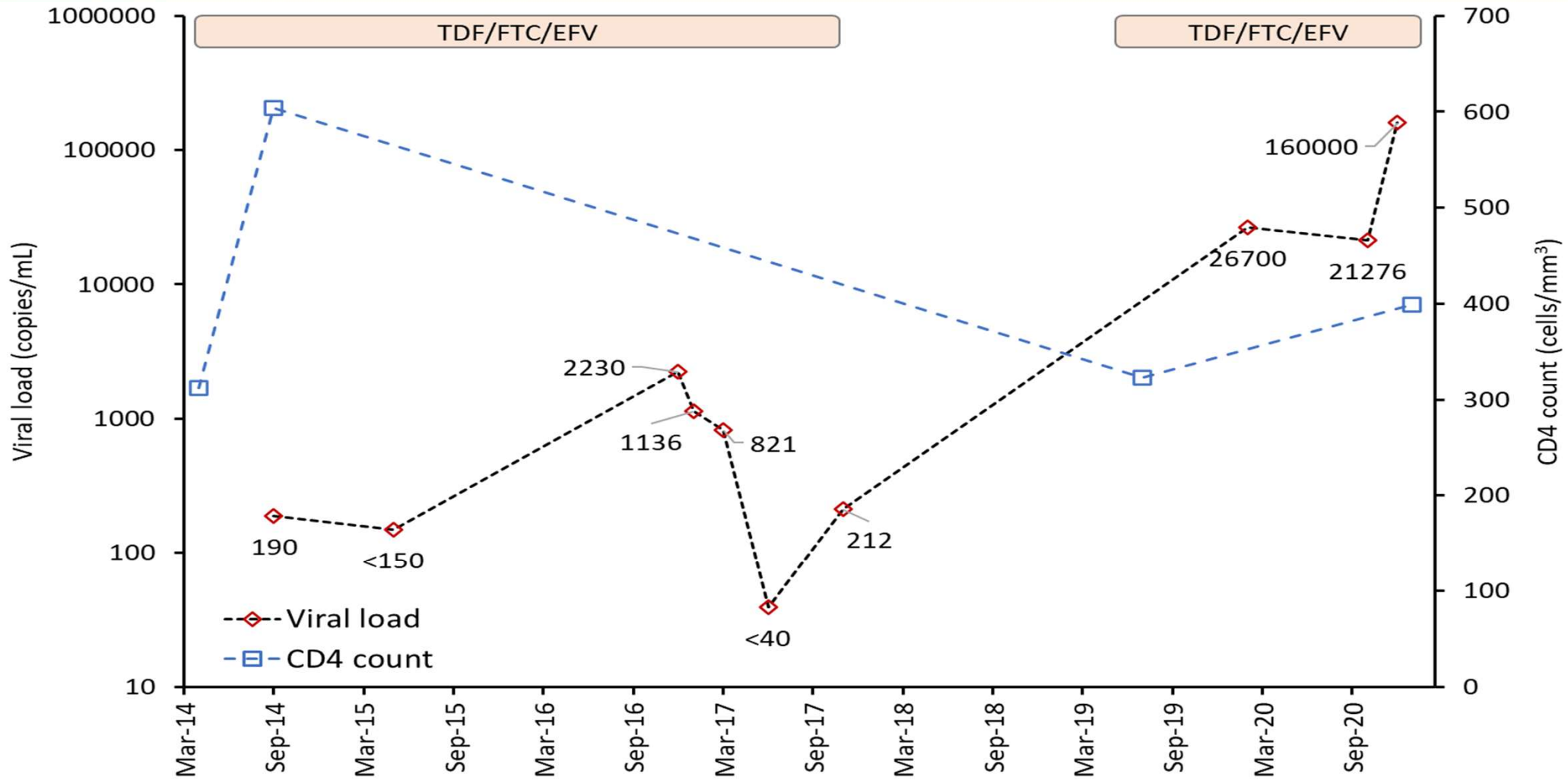


| | | | | |
|-------|------------|--|----------|-----|
| GRT | 14/08/2023 | | ABC | ILR |
| NRTI | M184V | | AZT | HLR |
| | M41L | | D4T | ILR |
| | T215Y | | DDI | ILR |
| NNRTI | A98G | | FTC | HLR |
| | G190A | | 3TC | HLR |
| | K101E | | TDF | LLR |
| PI | NONE | | EFV | HLR |
| INI | E138K | | ETR | ILR |
| | G118R | | NVP | HLR |
| | L74M | | RPV | HLR |
| | | | DTG | HLR |
| | | | EVG | HLR |
| | | | RAL | HLR |
| | | | ALL PI's | S |
| | | | | |

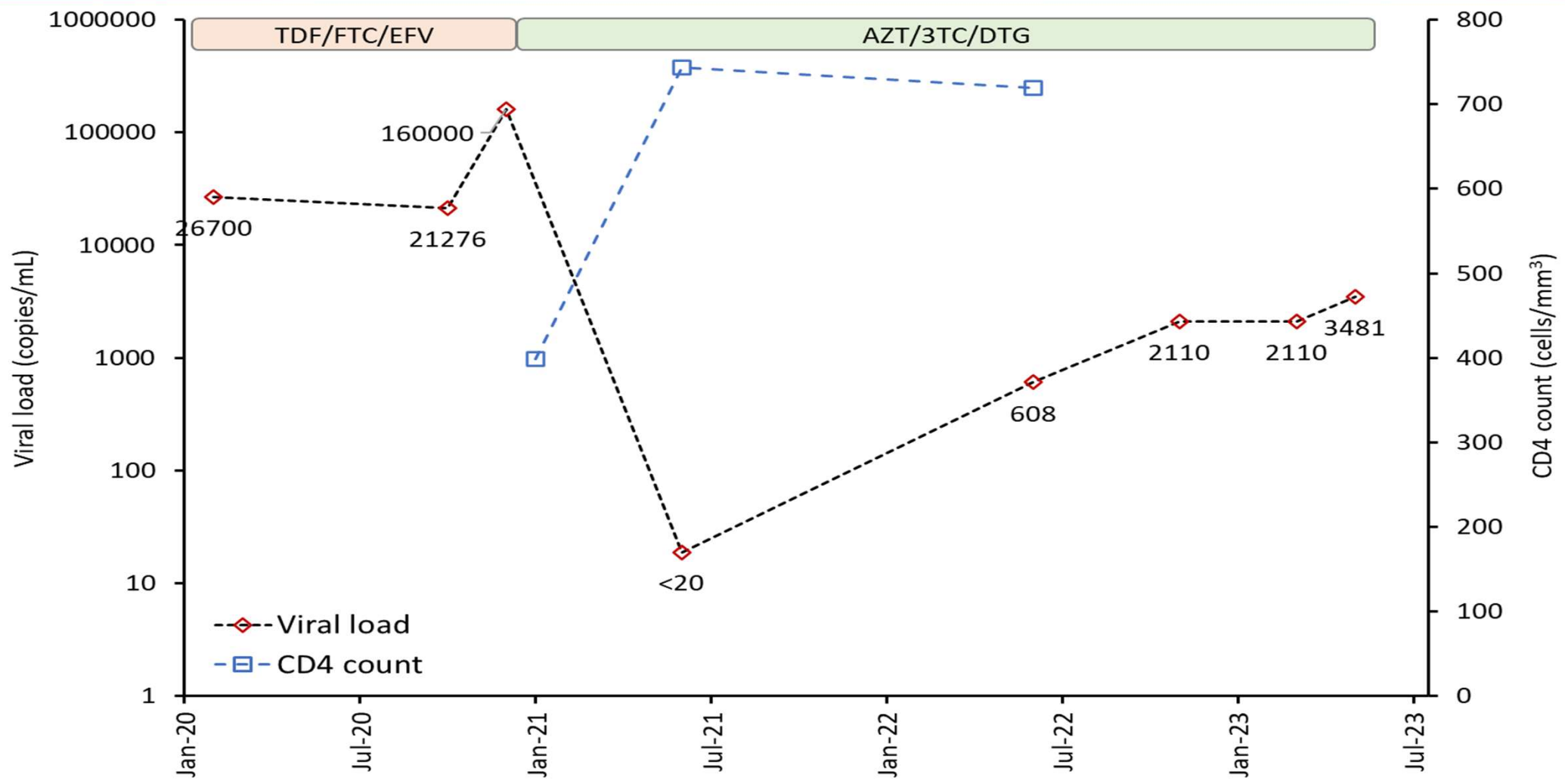
ZD switch from DTG- to DRV/r-based ART



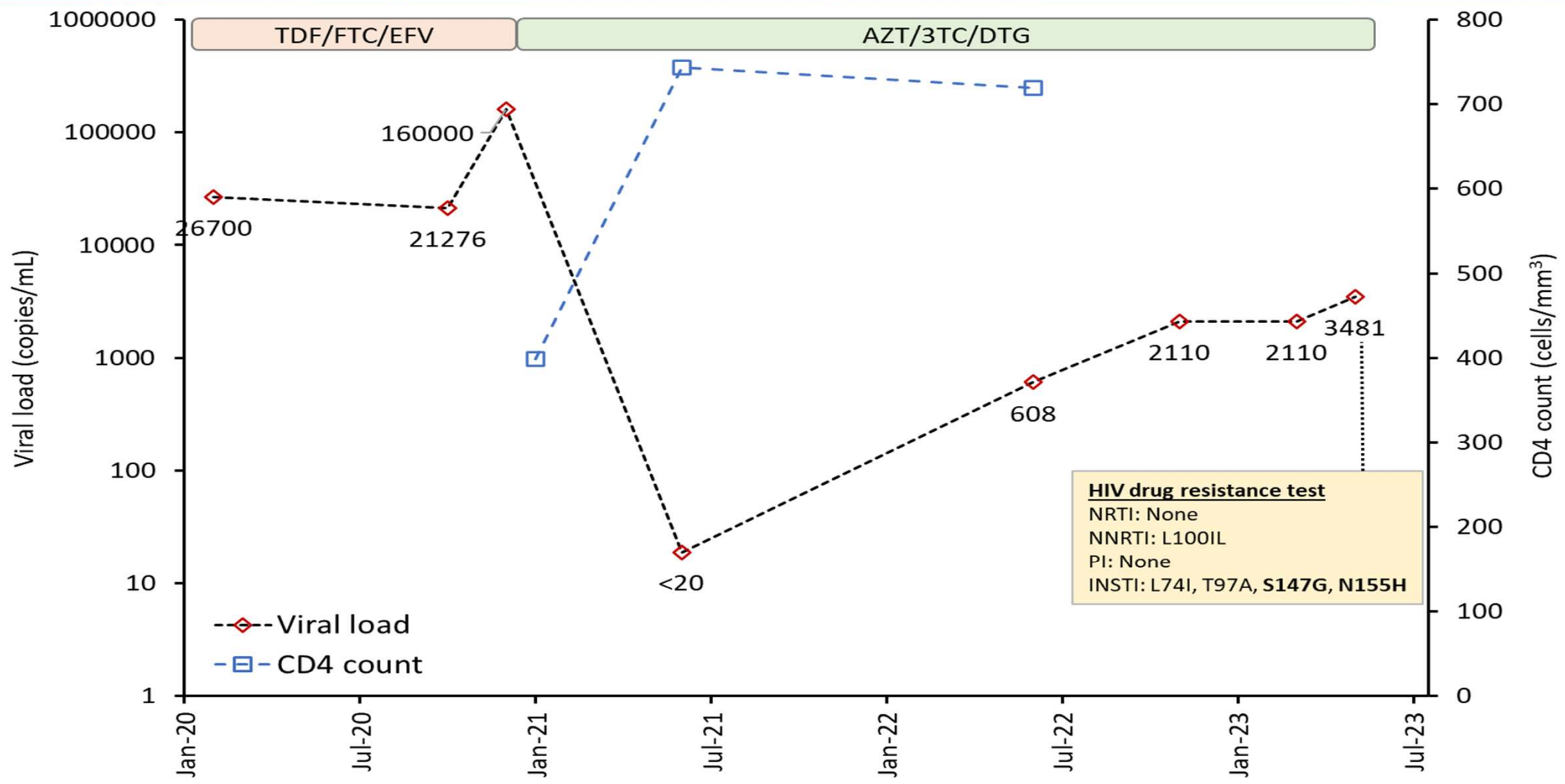
HM initial NNRTI-based ART



HM switch from NNRTI- to DTG-based ART

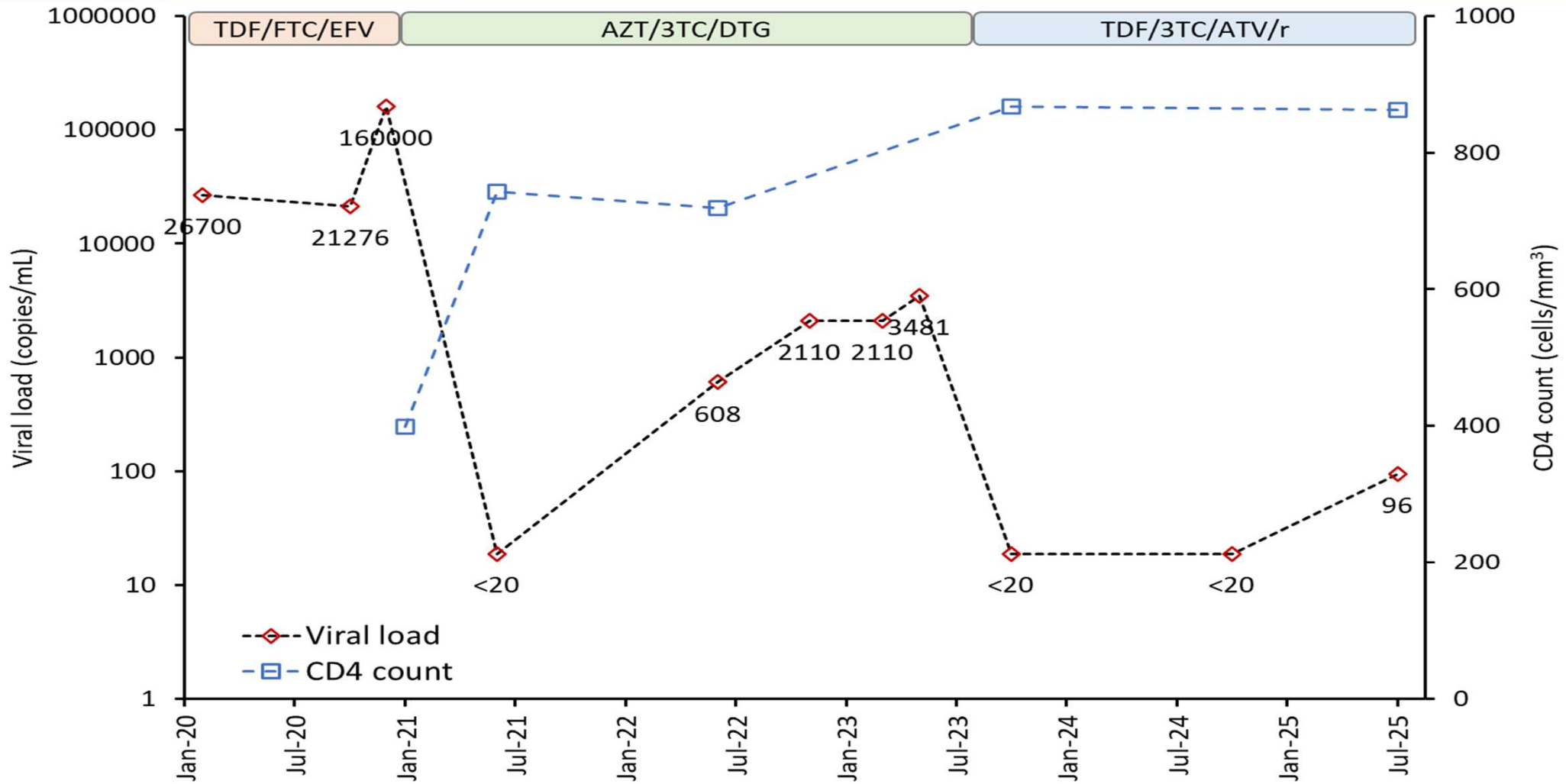


HM AZT/3TC/DTG virological failure & HIVDR testing



| | | | | |
|-------|------------|--|----------|-----|
| GRT | 11/05/2023 | | ABC | S |
| NRTI | NONE | | AZT | S |
| NNRTI | L100I/L | | D4T | S |
| PI | NONE | | DDI | S |
| INI | NI55H | | FTC | S |
| | S147G | | 3TC | S |
| | T97A | | TDF | S |
| | L471 | | EFV | HLR |
| | S119R | | ETR | ILR |
| | | | NVP | HLR |
| | | | RPV | HLR |
| | | | DTG | ILR |
| | | | EVG | HLR |
| | | | RAL | HLR |
| | | | ALL PI's | S |

HM switch from DTG- to ATV/r-based ART



RISK FACTORS FOR DTG RESISTANCE

- Exposure to DTG
- Treatment experienced
- Viraemia on former regimen at switch
- Underlying NRTI resistance
- DTG dual or mono therapy
- Previous experience with Raltegravir
- Childhood compared to adulthood.
- Other emerging risk factors

The background is a teal-to-blue gradient. In the corners, there are decorative white lines resembling a circuit board or neural network, with small circles at the end of the lines.

VIGILANCE

IMPLICATIONS FOR SA

THOUGHTS AND QUESTIONS