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HIV DRUG RESISTANCE

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Introduction

The introduction of antiretroviral drug therapy (ART) has reduced morbidity and mortality associated with human immunodeficiency virus (HIV) infection and resulted in long-term survival of HIV patients (1). Unfortunately, the effectiveness of ART has been reduced by the emergence of HIV drug resistance (HIVDR) (1). HIVDR refers to the ability of HIV to replicate in the presence of drugs that usually suppress its replication. Exposure to ART selects for resistant HIV strains, whereas Drug-naive patients may be infected with strains of the virus that is resistant to drug therapy (2).

The former is referred to as acquired HIVDR and the latter is primary HIVDR. The presence of ART resistance is an important cause of treatment failure in HIV patients and the resistance has often been documented to cut across multiple classes of ART (1), significantly complicating HIV therapy. A significant population-level HIVDR could potentially restrict future therapeutic options and increase treatment costs by requiring new and more expensive antiretroviral (ARV) regimens. HIVDR could also hinder progress towards the global goal of ending the epidemic by 2030.

In Uganda, since the early 2000s, the Ministry of Health (MoH) has progressively rolled-out the public sector ART programme that provides free ART through accredited health facilities. The number of people on ART has increased from 20,000 in 2003 to 1,312,974 by the end of September 2021 (3). In 2014, MoH adopted the WHO/UNAIDS 2020 targets and by the end of September 2021, it was estimated that there were 1,414,183 people living with HIV in Uganda – Coag Report. Of these, 1,382,265 (98%) knew their HIV status; of those who knew their HIV status, 1,312,917 (95%) were on treatment and of those on treatment, 1,202,244 (92%) had viral suppression (3).

Editor's Note

Hello and welcome to this quarter's ATIC newsletter! We at IDI hope that you are well, and using your knowledge and skills to manage your patients better.

Over the last quarter, the ATIC Call Centre received lots of questions on HIV drug resistance (HIVDR) both in adults and in children. So, we decided to focus this quarter's newsletter on that so that we can equip you with the knowledge and skills you need to manage your clients who may be facing drug resistance.

You will read about the HIV life cycle and how variants arise; causes of, and how HIVDR happens; adherence and its implications on HIVDR; third-line regimens. You will also read about laboratory eligibility criteria for testing drug resistance in both ART and in PLHIV in Uganda. As always, we answer all your other questions in the ASK ATIC column.

We welcome all your health-related questions to our Call Centre. You can reach us through our toll-free number: 0800200055 or WhatsApp: +256787311883 or on email: training@idi.co.ug. Stay safe, healthy, and informed!

Carolyne Amuge,
Research & Communications Officer

In 2016, MoH supported by Uganda Virus Research Institute (UVRI) and US Centers for Disease Control and Prevention (CDC) conducted an HIVDR survey among adults initiating or reinitiating ART, yielding an overall weighted HIVDR prevalence of 18.2%
(4) with the highest noted for Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) at 14.1% (4).

A study done in Uganda by Joint Clinical Research Centre (JCRC) showed 10% prevalence of primary HIV drug resistance (HIVDR) among all children, and 15.2% among children under three years (7). The high level of resistance was attributed to previous PMTCT exposure that occurred in 35.7% of prevention of mother-to-child transmission (PMTCT)-exposed children (7).

According to the MoH HIV DR database, as of March 2022, HIV DR cascade is facing a number of challenges from client identification, completion of intensive adherence counselling (IAC), repeat viral load (VL), case discussion and provision of appropriate regimes to clients. Below is a summary of the current national HIV DR cascade (Jan - Mar 2022):

Indicator	1- 4 Yrs	5-9 Yrs	10-14 Yrs	15-19 Yrs	20-24 Yrs	25+
Non-suppressed ART clients who had a repeat VL testing that remained non-suppressed	97	75	176	134	39	260
Clients failing on 1st line therapy referred for HIV DR Test	26	16	56	29	1	0
Clients failing on 2nd line therapy referred for HIV DR Test	0	7	34	44	30	173
Clients failing on 3rd line therapy referred for HIV DR Test	1	1	2	4	1	10
% Receiving a DR Test	27.8%	32.0%	52.3%	57.5%	82.1%	70.4%
Non-suppressed ART clients who had a repeat VL testing that remained non-suppressed with DR test results ***SWITCHED*** to a higher Regimen	11	22	40	20	7	84
Non-suppressed ART clients who had a repeat VL testing that remained non-suppressed with DR test results ***SUBSTITUTED*** to a higher Regimen	8	14	37	23	6	42
Non-suppressed ART clients who had a repeat VL testing that remained non-suppressed with DR test results ***MAINTAINED*** on their regimen following review	14	21	62	67	18	103
Non-suppressed ART clients who had a repeat VL testing that remained non-suppressed ***PENDING CASE REVIEW*** with DR test results	27	50	109	115	53	224
% Switched and/or Substituted to Higher Regimen	31.7%	33.6%	31.0%	19.1%	15.5%	27.8%
Proportion of clients with HIVDR test results pending case review	45.0%	46.7%	44.0%	51.1%	63.1%	49.4%

There is visible age-disproportionate performance across the HIV DR cascade with children as the most affected group. One critical driver of poor out comes in children is suboptimal ART regimens (8). This is secondary to lack of palatable paediatric formulations, higher cost of protease inhibitors (PIs), and scarcity of paediatric-trained clinicians which contributes to prolonged use of failing regimens in children (9).

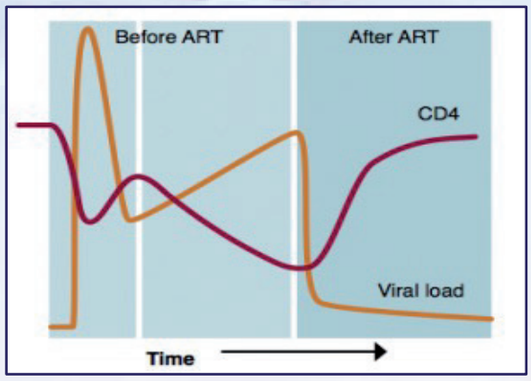
Many children living with HIV in Uganda have been faced with multiple biopsychosocial challenges leading to adherence issues that stem from medicine-related, care-giver, and health facility challenges. These challenges lead to viral non- suppression, thus limited growth and disease progression (10).

HIVDR testing is proving to be a powerful tool that can help clinicians tailor their treatment regimen to the specific HIV strain(s) that infect their patients. In addition, numerous new agents and classes of ART are currently under development in an effort to keep pace with emerging HIVDR. Successful treatment of HIV requires a detailed knowledge of the various mechanisms by which resistance can arise as well as an understanding of strategies for overcoming resistance once it occurs.

HIV Basic Information

HIV is a virus that attacks the body's immune system and if not treated, leads to acquired immunodeficiency syndrome (AIDS) (11). With and without ART, the natural history of HIV is shown in (fig 1) below depicting viral load and CD4. In its spread, HIV is transmitted sexually, vertically through mother to child transmission during pregnancy, delivery, breastfeeding, and through contact with infected blood or sharps (11).

Fig 1: HIV Natural History



HIV LIFE CYCLE

The HIV life cycle is typically divided into seven distinct stages, from the attachment of the virus to the host cells, to the budding of new free-circulating HIV virions (11). Figure 2 below shows the steps in HIV's replication, mistakes due to the lack of proofreading are made. This results in multiple variants from the original species (11). It's very important to understand these stages because this is where the ARVs target.

Figure 2 below shows the HIV life cycle is typically divided into seven distinct stages:

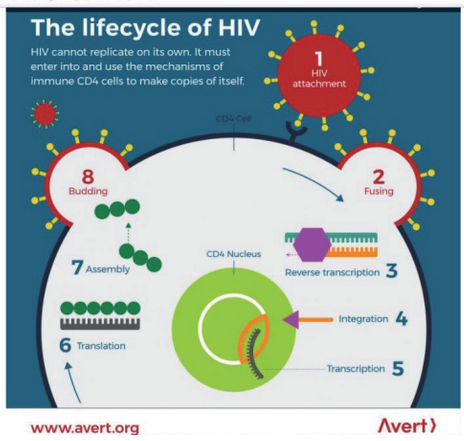


Figure showing the HIV lifecycle. See details at https://www.avert.org/infographics/lifecycle-hiv

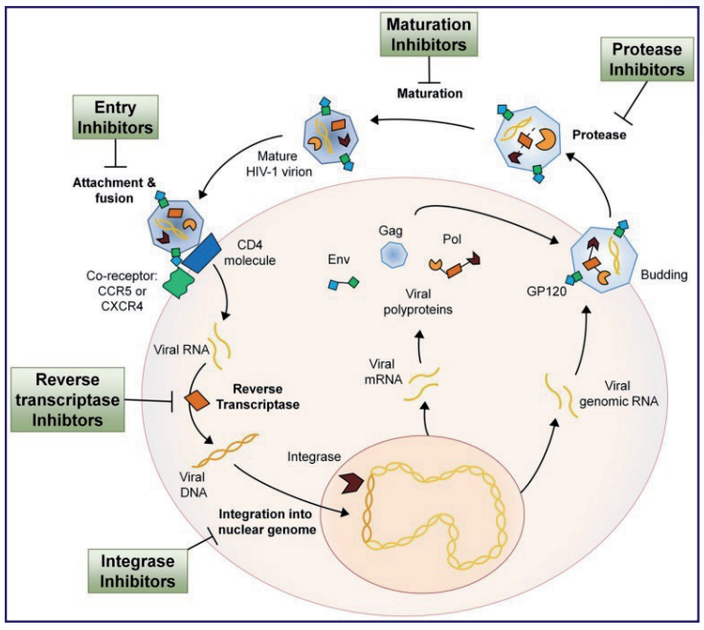
- STEP I (Viral attachment): To infect the cell, HIV must attach itself by way of a lock-and-key system onto CD4 cells using gp120 and gp41 (11).
- STEP II (Binding and fusion): Once attached to the cell, HIV injects proteins of its own into the cytoplasm of the CD4 cell. This causes fusion of the cell membrane to the outer envelope of the HIV virion via co-receptors CCR5 and CXCR4. The virus then un-coats (11).
- STEP III (Reverse transcription): The single-stranded RNA of HIV must be converted to the double stranded DNA. It accomplishes this by use of enzyme reverse transcriptase. Once converted to DNA, the genetic machine has the coding needed to enable viral replication (11).
- STEP IV (Integration): For HIV to hijack the host cell's genetic machinery, it must integrate the newly formed DNA into the nucleus of the cell, thus integration into host DNA (11).
- STEP V (Transcription and translation): Upon integration, more transcription occurs leading to formation of mRNA and translation into viral polyproteins (Env, Gag, Pol) (11).
- STEP VI (Assembly): HIV must manufacture protein building blocks that it uses to assemble new viruses. It does so with the protease enzyme which chops protein into smaller bits and then assembles the bits into new, fully formed virions (11).
- STEP VII (Maturation and budding): Once the virions are assembled, they go through the final stage in which the mature virions bud off from the infected host cell. Once released into free circulation, these virions go on to infect other host cells and begin the cycle yet again (11).

ANTIRETROVIRAL THERAPY (ART)

These are drugs that have been developed to hinder HIV viral replication with the major goal of achieving viral suppression that progressively would result in immune reconstitution, reduced morbidity and mortality, good quality of life and lastly, reduced HIV transmission (11). Currently, there are six classes of approved ARVs available that act at the different stages of the HIV life cycle. These are:

- CCR5 inhibitors like Maraviroc.
- Fusion inhibitors like Enfurvirtide.
- Nucleoside reverse transcriptase inhibitors (NRTIs) like Abacavir, Tenofovir, Zidovudine, Lamivudine, Emtricitabine.
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs) like Efavirenz, Nevirapine and Etravirine.
- Integrase inhibitors like Dolutegravir, Raltegravir, Elvitegravir.
- Protease inhibitors like Lopinavir, Atazanavir, Darunavir (all boosted by ritonavir).

Figure 3: Antiretroviral drugs - sites of action Copyright (12).



These ARTs have dramatically reduced morbidity and mortality associated with HIV infection achieving the major goals. Unfortunately, the effectiveness of ART has been markedly reduced by the emergence of HIVDR. In 1987, the first ARV drug was developed (Zidovudine) (11), and later, other drugs. In the early treatment of HIV Zidovudine was successful, however, HIV resistance emergence towards it complicated the situation. Research that followed showed that the use of combination drug therapies could significantly improve HIV patients' chances for long-term survival by delaying the occurrence of drug resistance.

HIV DRUG RESISTANCE

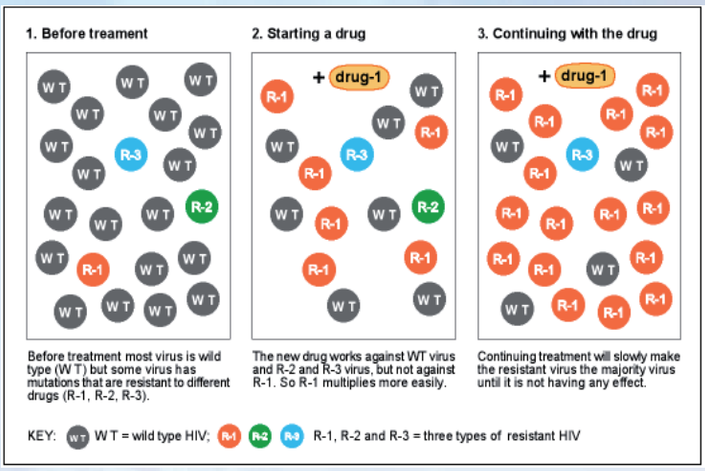
The WHO defines two forms of HIVDR (3):

1. **Acquired HIVDR (ADR):** This develops when HIV mutations emerge due to viral replication in individuals receiving ARV drugs.
2. **Primary/Transmitted HIVDR (TDR):** This is detected in ARV drug-naive people with no history of ARV drug exposure. TDR occurs when previously uninfected individuals are infected with a virus that has drug resistance mutations. Below are some important terms used in drug resistance.

Causes and How HIVDR Happens

HIVDR is caused by changes in the genetic structure of HIV that affects the ability of drugs to block replication of the virus. Initially, resistant mutations are caused by the rapidly multiplying error-prone virus even before initiating ART (13) but after ART initiation, the selective drug pressure will cause more mutations and even more complicated resistant patterns (9). Figure four below, obtained from HIV i-base (14) demonstrates how mutations happen before treatment, at start of treatment with good adherence in presence of mutations, and at holding of the medication.

Fig 4: Mutations before treatment



It is clear from the figure above that we already have a resistant virus even before treatment. Because HIV RNA is prone to mistakes as it multiplies, there are usually many variants as an outcome. The variants are usually less fit as compared to the wild type (15) and that is why the figure before treatment is predominated by the wild type of virus. With the initiation of ART, the wild type that is sensitive to ART is wiped out leaving the resistant type, which with continued treatment, multiplies and becomes dominant. Now, the ART has selected for the mutant type of virus hence it's wrong to say that ART causes resistance. With stoppage of ART the wild type, being more fit, will multiply and suppress the previously selected resistant type while on treatment.

The commonest risk factor associated with drug resistance is poor adherence to ART (16,17). Others could be drug interactions, malabsorption, and primary resistance.

Adherence is the extent to which a patient follows an agreed upon prescribed treatment regimen, that is, right drug, right dose, right route and frequency. The common red flags to non-adherence are missing appointments, wrong (high or under) doses of medicine, sharing drugs, taking drugs at the wrong time, drug holiday (16,18).

Measuring Adherence

There is no gold standard for measuring adherence but there are many validated tools or strategies including clinic attendance, pharmacy records, pill counts, review of treatment charts, patient/care-giver self-report, electronic measurement devices like bottle caps/MEMS and therapeutic drug levels.

$$\% \text{ Adherence} = \frac{\text{(Number of pills taken)}}{\text{(Total number of pills expected to have been taken)} \times 100\%}$$

Table 1: Determining adherence levels from self-report and pill count and recommended action

Missed doses per months		Percent adherence	Adherence ranking	Recommended Action
Oncedaily dosing	Twice daily dosing			
<2 doses	≤ 2 doses	≥95%	Good	• Review adherence plan • Support to continue adhering well.
2-4 doses	4-8 doses	85–94%	Average	• Address the causes of average/poor adherence • Review adherence plan
≥5 doses	≥9 doses	<85%	Poor	
Note: Adherence >105% could imply potential drug sharing or other inconsistencies in dosing and should be investigated.				

Good adherence aims at viral suppression and avoiding resistance which are good indicators of excellent response to ARVs.

Common Class Resistance Mutations

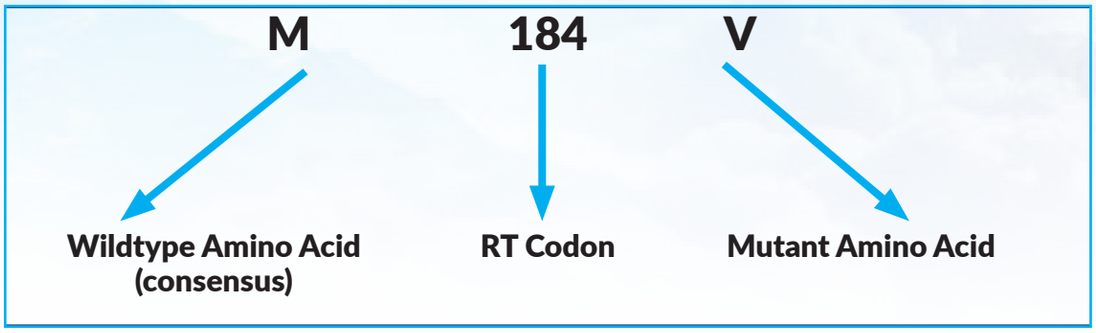
As noted earlier, there are different stages during HIV viral multiplication and different classes of ARVs have been developed to inhibit viral multiplication at these different stages. The virus will develop resistance to particular ARVs by developing changes in their genetic makeup (mutations). This can happen either as a result of prolonged periods of time on treatment or, more commonly, as a result of suboptimal treatment adherence.

Characteristics of mutations:

- Some mutations have clinical significance while others don't. Those with clinical significance cause resistance to ART targeted by that mutation.
- Some mutations affect only one drug while others cause cross-resistance across the whole class. For example, K103N affects Nevirapine and Efavirenz.
- Some mutations are pathognomonic of drugs, for example, K65R- resistance to Tenofovir.
- Wild type virus is more fit than mutated virus.
- Mutations can emerge within days of insufficient drug pressure.
- Mutations persist indefinitely and can re-emerge if the same drug is stopped and re-started resulting in archived mutations.
- Major mutations have a big impact on drug resistance. M184V results in high-level resistance to 3TC/FTC and low-level resistance to ABC but it (M184V) gives a half crippling effect on the virus increasing its susceptibility to TDF, AZT, and others.
- Minor mutations only have a small impact on drug resistance.

Figure 5 below shows the nomenclature of mutations. This means, in this particular virus at position 184, the original amino acid methionine has been replaced by amino valine forming a new mutant virus.

Figure 5 showing the nomenclature of mutations



Usually, the NRTIs work at the active site of the reverse transcriptase (RT) enzyme by actively competing with the naturally occurring substrates for the active site (11). The drug is picked-up and added to the polypeptide chain being formed hence blocking the addition of more proteins (11). The resistance to this pathway follows two mechanisms:

Discrimination pathway: The RT enzyme is able to avoid binding of the NRTI while retaining the ability to recognize the natural nucleotides. Examples of mutations using this are K65R, L74V, Q151M and M184V (11).

Primer unblocking: The enhanced phosphorolytic removal of the chain-terminating NRTI from the 3'-terminus of the primer after it has been incorporated into the viral DNA (11). This pathway is used by Thymidine Analogue Mutations (TAMs).

Resistance to Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

NNRTIs usually work in an allosteric way. They do not work at the active site but attach on the side of the RT enzyme called the hydrophobic pocket (11). With this, they change the shape of the active site where the natural substrates can no longer fit or attach. In resistance to these NNRTIs, the virus makes changes in the hydrophobic pocket where the NNRTIs can no longer attach (11).

Resistance to Protease Inhibitors (PIs)

PIs bind specifically to the active site of the enzyme thereby preventing the HIV-1 protease from cleaving onto the two Gag and Gag Pol precursor proteins, which results in the formation of immature non-infectious virus particles (11).

The development of PI resistance is believed to be a stepwise process (11). These first resistance mutations to develop are also referred to as primary mutations (11). They are located near the substrate binding of the enzyme resulting in conformational changes. By changing the structure of the substrate-binding cleft, these primary mutations interfere with the binding of the PI to the viral protease, resulting in resistance to PIs (11).

The altered structure of the substrate-binding cleft has a knock-on effect and the viral protease is less able to cleave its natural substrate, resulting in a reduced replicative capacity of the virus (11). Thus, the development of PI resistance comes with a fitness cost for the virus. During continuous PI therapy, additional mutations emerge in the protease, which are commonly referred to as secondary or accessory mutations. Secondary mutations may also be compensatory, restoring protease enzyme activity and/or enhance the resistance of primary mutations.

Resistance to Integrase

This inhibits the integrase enzyme from performing strand transfer by binding to the active site of integrase (11). Changes are at the active site of the integrase enzyme where the drugs can no longer attach.

Monitoring of response to ART can be done through viral load monitoring (19). Viral load (VL) monitoring is done starting at six months after initiation of ART, at 12 months on ART and thereafter, annually for adults who are virally suppressed (19). For children, adolescents, pregnant and lactating mothers, however, the viral load testing is conducted every six months (19).

When a viral load is >1000 copies/ml, IAC is done for at least three months to assist the client to overcome their specific barriers to adherence, then viral load testing is repeated.

HIVDR is suspected when two consecutive viral loads are >1000 copies/ml despite IAC (19). Detection of drug resistant virus can be done for patients that are suspected to be failing on treatment so as to determine the next best regimen.

The rationale for the threshold of 1000 copies/ml was based on two main sources of evidence: First, viral blips or intermittent low-level viremia (50–1000 copies/ml) can occur during effective treatment but have not been associated with an increased risk of treatment failure unless low-level viremia is sustained (20). Second, clinical and epidemiological studies show that the risk of HIV transmission and disease progression is very low when the viral load is lower than 1000 copies/ml (20).

Laboratory Eligibility Criteria for Testing ART Drug Resistance

HIVDR is not performed for all patients with a detectable viral load in Uganda. For patients to be eligible for HIVDR testing, they should have been adherent to their ART for at least one month before the sample is taken off, and have: **(1)**. A confirmed detectable VL from two independent consecutive samples collected after an undetectable measurement, or **(2)**. A steady or increasing VL after the initiation of medications (HIV RNA levels >1000 copies/ mL), or **(3)**. A detectable VL six months after treatment initiation (20).

Laboratory Eligibility Criteria for Testing Drug Resistance in PLHIV in Uganda

All children below 15 years failing on first-line (20). This allows for all children below 15 years in three categories:

1. Children on NNRTIs based regimens with a non-suppressed viral load.
2. Infants born to mothers failing treatment (first-, second-, or third-line).
3. Children on LPV/r or DTG-based regimens with a non-suppressed repeat VL following two consecutive good IAC sessions.

Adults should be considered when they are on second-line regimen, and they have non-suppressed repeat viral load results following three consecutive IAC sessions. From the HIV 2020 guidelines, these categories were also added to the above:

- Patients failing on a PI-based regimen irrespective of the line of care.
- Patients with prior exposure to a PI and failing on a DTG-based regimen.
- All patients failing on their third-line ART.

Choice of sample

While plasma is the preferred sample for HIVDR genotyping, plasma analysis requires sophisticated laboratory equipment, personnel, space, and stringent storage conditions for maintenance of sample integrity and transport. The field has gained substantial experience with the dried blood spot (DBS) technique as an alternative. Laboratories that have built capacities to collect plasma samples do collect them for HIVDR testing while those who aren't able to collect plasma samples collect DBS samples. All laboratory staff must be properly trained and deemed competent to collect, store and transport samples according to standard operating procedures.

Sample collection

Proper sample collection is a very vital part of laboratory investigations. Whole venous blood is collected in plasma-separating tubes (PST) to obtain plasma while DBS samples can be collected using either finger prick or venous blood. Blood collected using PST is first left to separate and thereafter kept in the freezer at -20°C (21).

Storage

Plasma samples are stored at -20°C if the samples won't be tested immediately while the DBS samples can be stored at room temperature until they are tested (21).

Transportation

In situations where sample collection happens away from the laboratory, plasma is transported at room temperature to the laboratory on the same day. Clinic staff should ensure that DBS samples are dried completely away from direct sunlight, rodents and dust. These are then packaged in Ziploc bags with a desiccant and humidity indicator at room temperature and transported to the laboratory at room temperature. These samples are then triple-packaged and transported to the central public reference laboratories for HIVDR testing at appropriate temperature using the hub sample transport network.

Interpretation of results

Drug-resistant mutations may be related to the transmission of a drug-resistant virus at the time of initial infection or may arise due to continued virus replication in the presence of a drug due to poor drug adherence (11). In treatment-experienced patients with virologic failure, it is preferable to obtain resistance testing while the patient is taking ART or is within weeks of discontinuing treatment. However, this might not be possible in patients who are non-adherent to their regimen. In the absence of drug pressure, the wild-type HIV strain may become dominant. Although some mutations may persist off ART, the results can be misleading if drug resistance testing is performed when patients are not receiving ART.

Similarly, resistance testing is less reliable at detecting resistance to classes of drugs no longer being taken (11). These limitations emphasize the importance of taking a complete medication history.

To achieve viral suppression, ART programmes require

Way Forward For Children

targeted efforts to provide specific health facility requirements, psychological and economic needs of patients. and ART-treated children and their caregivers. Integration of HIV treatment with programs for orphans and vulnerable children may improve viral suppression rates (22).

Other facilitators of adherence that were reported included: the child's knowledge and understanding of HIV, assistance or increased psychosocial support from a vigilant caregiver or other family member, having a routine or strategy to maintain good adherence like keeping medicine in the same spot, setting alarms to remind about time for taking medicine, and motivators for children including gifts but some used fear of the effects of missed doses (23).

A study on drug resistance mutations among South African children living with HIV (24) recommended the following:

- Use of PI-based ART regimens as the first-line for all young children.
- Overcome logistic barriers to always avail palatable paediatric regimens.
- Always super-boost PIs or provide alternative regimens for children with HIV/TB co-infection.
- When appropriate, use Dolutegravir (DTG)-based regimen like for children >20Kg or when dispersible DTG is available.
- More studies to estimate the extent of primary HIVDR in paediatric patients in order to inform current treatment guidelines.

Recommendations for use of either AZT or TDF-based second line regimens have be made because the M184V mutation causes hyper-susceptibility of HIV to AZT and TDF, not ABC (25).

THIRD-LINE REGIMENS

When a patient has treatment failure on second- line regimens, and a drug susceptibility test is done, a switch meeting is usually convened to discuss the possible third-line regimen. This depends on the level of resistance detected to the different drugs, but also the drug interactions, pill burden, side effects, and psychosocial issues. The common third-line available drugs in Uganda are Dolutegravir (DTG), Raltegravir (RAL), Darunavir (DRV), Ritonavir, Etravirine, Tenofovir Alafenamide (TAF) (19).

Reporting and Ordering for Third-line ART Medicines:

Supplies for third-line ARV medicines have been streamed as follows;

- Public and private not-for-profit (PNFP) health facilities with patients on third-line outside Kampala and Wakiso will receive their third-line ARV medicines through the regional referral hospitals in their region which get their supply from National Medical Stores (NMS).
- Centres of Excellence (CoE) like Joint Clinical Research Centre (JCRC), Baylor Mulago, The AIDS Support Organisation (TASO) and Mildmay Uganda, receive their third-line ART supplies from the attached regional referral hospital as follows: Kiruddu National Referral Hospital: JCRC, TASO Entebbe and Mildmay Uganda. China-Uganda Friendship Hospital Naguru, Baylor, IDI and TASO Mulago.
- PNFP health facilities in Kampala and Wakiso with patients on third-line will receive third-line ARVs through the nearby CoEs.
- Public health facilities with patients on third-line in Kampala and Wakiso will receive their third-line ARVs through China-Uganda Friendship Hospital Naguru.

ASK ATIC

Dear ATIC, what is the current guidance on DTG dosing in relation to weight among children?

Answer: According to the 2020 Ministry of Health (MoH) guidelines, DTG can be used for children ≥3kg. MoH has procured DTG 10mg for use in children below 20kg.

Dear doctor, I have a client on ART, who has been on fluconazole for two years. Serum CrAg today was positive but the client has no symptoms and signs of meningitis.

Answer: The MoH guidelines recommend discontinuation of fluconazole for those with VL<1000copies/mm3 and CD4 of at least 200 after 12 and 18 months of treatment.

Dear Doctor, I have a 26 kg adolescent on LPV/r with a non-suppressed viral load. He suggests changing his dosing to one in the morning and two in the evening to increase his adherence to the medication. Is this something I can do?

Answer: No, you may not make such dose adjustments because this will be inappropriate dosing for the age. The therapeutic range will not be reached and the virus will continue to multiply in presence of a low drug in the blood which creates a conducive environment for mutations that may pose a risk of drug resistance.

Dear ATIC, I am a midwife in a HC III. How do I prevent neonatal hepatitis B infections in babies born to hepatitis B-positive mothers?

Answer: All hepatitis B positive mothers with a viral load greater than 200,000 IU/ml or positive hepatitis B antigen should be initiated on prophylactic treatment with TDF at earliest contact.

WHO also recommends an immunoglobulin and hepatitis B vaccine be given to the baby within 72 hours of delivery. Subsequent hepatitis B vaccines are given at six weeks and six months.

Hello ATIC, can I vaccinate a person on cART and non-suppressed viral load for COVID-19?

Answer: Yes, people living with HIV at any CD4 cell count appear to be at increased risk for severe outcomes and death due to COVID-19 compared with people without HIV. The currently available vaccine products are not live vaccines - they include genetic material from SARS-CoV-2 which cannot replicate. Therefore, these vaccines are not expected to be less safe in people who are immunocompromised.

Hello Doctor, I have a middle-aged woman with a one-month history of progressive hair loss (see attached image). How best can I manage the client?

The case in question is for Alopecia areata, a rare disorder of hair growth that results in loss of hair. Kindly refer the client to a skin specialist for better management.

Dear Doctor, I have a 9-year-old on ABC/3TC/LPV/r weighing 15kg with three consecutive non-suppressed viral loads. What is their best choice of second-line regimen?

Answer: MoH recommends a DTG based regimen as a second-line for all persons failing on the first line. Do a Drug susceptibility test and switch the patient to AZT/3TC/DTG.

Dear Doctor, I have someone under our care who is on anticonvulsants (Carbamazepine) and TDF/3TC/EFV. How can we best optimize this client considering the interactions between DTG and anticonvulsants?

Answer: Many anticonvulsants (Sodium Valproate is an exception) decrease the plasma concentrations of DTG. Double the dose of DTG to achieve the therapeutic dose.

Dear ATIC, can I switch a client failing on TDF/3TC/EFV to ABC/3TC/DTG?

Answer: No, mutations to TDF have a crippling effect on the future use of ABC. In cases of blind switching, a regimen containing AZT is recommended.

Dear Doctor, can ABC/3TC 120/60mg dispersible tablet (or other dispersible backbones) and DTG be dispersed and administered simultaneously in the same solution?

Answer: Yes, DTG 10mg DTs can be dispersed and administered in the same solution of clean water as ABC/3TC 120/60mg dispersible tablets.

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