# *EVOLUTION IN HIV/AIDS TREATMENT AND FUTURE DEVELOPMENT*

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**Abstract:** *HIV being life threatening infectious and cancerous, it is very difficult to understand, cure and stop infection completely. After the release of zidovudine and first anti-retroviral therapy (ART) in 1987, treatment of HIV has improved so much but still isn't curable it can only be controlled.*
*Over past 5 years, advancement in human immunodeficiency virus type 1 (HIV-1) clinical research and data on the effectiveness of potent combination therapy have substantially influenced the general perspective of the long-term management of HIV-1 disease.*
*Moving on to evolution, anti-retroviral therapy its development, nitric oxide based anti-retroviral therapy and stem cell therapy have been proved a boost in the treatment and management of HIV/AIDS. On a continued research and development in the complete cure and management of HIV/AIDS drugs like Azvudin in phase III trial, drug in the way of development to target different stages of HIV life cycle like Isltravir and fostemsavir are under progress. In case of long acting anti-retroviral, cabotegravir LA and rilpivirine LA are under progress which can be a leading step to the development in the treatment of HI/AIDS.*

**Key words:** HIV/AIDS, Anti-Retroviral Therapy, Stem Cell Therapy, Drug Development, AIDS transmission

## I. INTRODUCTION

### HIV

To understand what HIV is, let's break it down: -
**H – (Human) –** This particular virus can only infect citizenry.

**I – (Immunodeficiency) –** HIV weakens our immune system by destroying important cells that fight disease and infection. A "deficient" system can't protect us.

**V – (Virus) –** an epidemic can only reproduce itself by taking over a cell in the body of its host.

HIV can hide for long periods of your time in the cells of your body and that it attacks a key part of our immune system (T-cells or CD4 cells). Our body has got to have these cells to fight infections and disease, but HIV invades them, uses them to form more copies of itself, then destroys them.
Over time, HIV can destroy numerous of our CD4 cells that our body can't fight infections and diseases anymore. When that happens, HIV infection can cause AIDS.

### AIDS

To understand what AIDS is, let's break it down: -
**A – (Acquired) –** AIDS isn't something you inherit from your parents. We acquire AIDS after birth.

**I – (Immuno) –** Our body's system includes all the organs and cells that work to fight off infection or disease.

**D – (Deficiency) –** You get AIDS when your system is "deficient," or isn't working the way it should.

**S – (Syndrome) –** A syndrome may be a collection of symptoms and signs of disease.

AIDS may be a syndrome, instead of a single disease, because it's a complex illness with a wide range of complications and symptoms. Acquired Immunodeficiency Syndrome is the ultimate stage of HIV infection. People at this stage of HIV disease have badly damaged immune systems, which put them in danger for opportunistic infections (OIs).

### ❖ Infection and transmission of HIV

AIDS is caused by HIV, a really fragile RNA type of retro virus, which like all other microorganism lives inside the living cells of the human body. Outside body it doesn't survive for quite half an hour. There are two sorts of HIV virus, i.e. HIV-1 and HIV-2. HIV-1 is present everywhere the world and in India more than 80% people are affected by it. HIV-2is mainly found in Africa and also present in India. Some people are infected with both the virus. People only infected with HIV-2 live longer than those infected with HIV-1 and chances of transmission of HIV-2 from mother to child are very rare. Once in body, HIV attacks CD4 sort of white blood cells (WBCs) in blood and gradually kills them. These CD4 sorts of white blood cells help us to fight against various infections. Once they're destroyed our body's resistance to fight infections goes down and person suffers from lots of infections. This end stage of HIV infection is named AIDS. It takes a few years for AIDS to develop and till that time infected person usually remain healthy.

### ❖ Detection and diagnosis of HIV

The infected person looks perfectly healthy and feels well for years. The infection can only have detected by doing a biopsy. the foremost commonly used HIV testes detect HIV antibodies – the substances the body creates in response to becoming infected with HIV. most of the people infected with HIV develop specific antibodies (i.e. seroconvert) within three to 12 weeks of initial infection. Diagnosis of primary HIV before seroconversion is completed by measuring HIV-RNA or p24 antigen. Positive results obtained by antibody or PCR testing are confirmed either by a special antibody or by PCR. There are tests that search for HIV's genetic material or proteins directly; these may be used to find out if someone has been infected with HIV.
Window period: - window period is that the time between first infection and when the test can reliably detect that infection. In antibody-based testing, the window period depends on the time taken for seroconversion. Antibody test may give false negative (no antibodies were detected despite the presence of HIV) results during the window period, an interval of three weeks to 6 months between the time of HIV infection and the production of measurable antibodies to HIV seroconversion. Most of the people develop detectable antibodies approximately 30 days after infection, although some seroconversion later. The overwhelming majority of people (97%) have detectable antibodies by three months after HIV infection; six-month window is extremely being with modern antibody testing.

### ❖ Following tests are used to detect HIV infection:

- Enzyme linked immunosorbent assay (ELISA).
- Western blot (WB) test.
- CD4 count.
- Viral load.

## II. TREATMENT OF AIDS

The HIV virus that causes AIDS may be a retro virus, an RNA virus that uses the cell's machinery to transcribe itself into DNA and integrate itself into the genetic material of the cell before creating more RNA, viral particles to send and infect other cells.

### ❖ Antiretroviral therapy (ART)

Medications used to treat HIV have very low rate and less effective, medical professionals developed antiretroviral treatment in 1996. A diagnosis with a very dismal prognosis was transformed into a treatable health condition with the use of three antiretroviral medications. There are two ways that antiretroviral therapy impacts the body. In the beginning, it boosts the body's immune cell count. Additionally, it reduces the quantity of viral cells. These drugs aid in maintaining health and avoiding other infections. HIV does not spread to other people when a patient is receiving effective antiretroviral therapy.

**Goals of ART: -** The goals of treatment with antiretroviral drugs are to inhibit viral replication while minimizing toxicities and side effects related to the available drugs. The inhibition of virus replication permits restoration of the system. Viral eradication from the host genome isn't achievable, thus a cure for HIV isn't yet possible. By using highly active antiretroviral therapy (HAART), it's possible to promote growth in children and prolong the survival of all HIV infected patients, reduce their morbidity and improve their quality of life. In summary the goals of ART are:

- The suppression of HIV replication, as reflected in plasma HIV concentration, to as low as possible and for as long as possible
- The preservation or enhancement of the immune function (CD4 restoration), thereby preventing or delaying the clinical progression of HIV disease
- Quality of life improvement
- Reduction in HIV related morbidity and mortality

## ❖ Available agents for Anti-Retroviral Therapy (ART): -

At present antiretroviral drugs come in six classes, each of which attacks a special site or stage of the HIV life cycle thereby interfering with its reproduction:

- **Entry inhibitors also called HIV fusion inhibitors (e.g., enfuvirtide or T-20)** prevent the HIV virus particle from infecting the helper T cell.
- **CCR5 antagonists (e.g., Maraviroc)** block the CCR5 coreceptor molecules that HIV uses to infect new target T cells. Some sorts of HIV use a different coreceptor and thus some patients may not benefit from maraviroc.
- **Nucleoside polymerase inhibitors (NsRTIs)** incorporate themselves into the DNA of the virus, thereby stopping the building process. The resulting DNA is incomplete and can't create new virus.
- **Nucleotide polymerase inhibitors (NtRTIs)** e.g. Tenofovir
- **Non-nucleoside polymerase inhibitors (NNRTIs)** stop HIV production by binding directly onto the reverse transcriptase enzyme thus preventing the conversion of RNA to DNA.
- **Integrase inhibitors (e.g., Raltegravir)** interfere with the power of the HIV DNA to insert itself into the host DNA and thereby copy itself.
- **Protease inhibitors (PIs)** work on the last stage of the virus reproduction cycle. They prevent HIV from being successfully assembled and released from the infected helper T cell. Boosted Protease inhibitors are combinations of low-dose Ritonavir (RTV) with a PI for pharmacoenhancement.

There are currently over 30 approved antiretroviral agents for the treatment of HIV-1 infection by Food and Drug Administration (FDA), a US Drug regulatory authority. Given in table. 1 and table. 2.

- **Table 1: -** Drugs Used in the Treatment of HIV Infection/ Available nucleoside reverse transcriptase inhibitors

| | **Generic name** | **Brand/Trade name (s)** |
|---|---|---|
| Nucleoside Reverse Transcriptase Inhibitors (NRTIs) | | |
| Single Drug Medicines | Abacavir (ABC) | Ziagen |
| | Didanosine (ddI) | Videx |

| | | |
|---|---|---|
| (SDMs) | Emtricitabine (FTC) | Emtriva |
| | Lamivudine (3TC) | Epivir, Lamivir, Lamivox, avolam, Virolam |
| | Stavudine (d4T) | Zerit, Stavir, Stag, Atavex, Avostav, Virostav |
| | Tenofovir disopropyl fumarate (TDF) | Viread |
| | Zalcitabine (ddC) | Hivid |
| | Zidovudine (AZT) (ZDV) | Retrovir, Zidovir, Zido-H, Zidovex |
| Fixed Dose Combinations (FDCs) | Abacavir + Lamivudine (ABC/3TC) | Epzicom |
| | Abacavir + Zidovudine + Lamivudine (ABC/AZT/3TC) | Trizivir |
| | Stavudine + Lamivudine (d4T/3TC) | Zidolam, Stavex L, Virolis, |
| | Tenofovir + Emtricitabine (TDF/FTC) | Truvada |
| | Zidovudine + Lamivudine (AZT/3TC) | Combivir, Duovir |
| Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) | | |
| Single Drug Medicines | Delavirdine (DLV) | Rescriptor |
| | Efavirenz (EFV) | Sustiva, Stocrin, Efavir, Estiva, Viranz |
| | Nevirapine (NVP) | Viramune, Nevipan, Nevimune, Nevirex |
| | Etravirine (ETV) | TMC 125 (ETV) |
| Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) | | |
| Single Drug Medicines | Amprenavir (APV) | Agenerase |
| | Atazanavir sulfate (ATV) | Reyataz |
| | Darunavir (DRV) | Prezista |
| | Fosamprenavir calcium (FOS-APV) | Lexiva |
| | Indinavir (IDV) | Crixivan |
| | Nelfinavir mesylate (NFV) | Viracept |
| | Ritonavir (RTV) | Norvir |
| | Saquinavir mesylate (SQV) | Invirase |
| | Tipranavir (TPV) | Aptivus |
| FDC | Lopinavir/Ritonavir (LPV/r) | Kaletra, Aluvia |
| Fusion Inhibitors | | |

| | | |
|---|---|---|
| SDM | Enfuvirtide (T-20) | Fuzeon |
| Integrase inhibitors | | |
| SDM | Raltegravir | Isentress |
| CCR5 antagonist | | |
| | Maraviroc | Celsentri |
| Multi-class Combination Products | | |
| Fixed Dose Combinations (FDCs | Stavudine + Lamivudine + Nevirapine (d4T/3TC/NVP) | Triomune, Virolans, Nevilast, Stavex LN |
| | Zidovudine + Lamivudine + Nevirapine (AZT/3TC/NVP) | Combipack, Duovir-N |
| | Tenofovir DF + Emtricitabine + Efavirenz (TDF/FTC/EFV) | Atripla |

- **Table 2:** - Drugs Used in the Treatment of HIV Infection/ Available Antiretroviral Agents

| Antiretroviral Drug | Primary toxicities | Minor toxicities | Monitoring/Management |
|---|---|---|---|
| Zidovudine (ZDV) | Haematological (Anaemia, neutropenia, thrombocytopenia), myopathy, GI intolerance | Blue to black discoloration of nails, nausea and headache | For severe anaemia: -<br><br>Reduce dose or change to d4T or transfuse<br><br>For myopathy: -<br><br>Discontinue if CPK high |
| Lamivudine (3TC) | Painful peripheral neuropathy, pancreatitis | Skin rash, headache | Do serum amylase. Discontinue if elevated. Restart when resolved or change to ABC |
| Stavudine (d4T) | Painful peripheral neuropathy, lipoatrophy, lactic acidosis, hepatitis, pancreatitis | Insomnia, anxiety, panic attacks | Severe peripheral neuropathy, abnormal serum amylase and transaminases, discontinue therapy |
| Didanosine (ddI) | Pancreatitis, painful peripheral neuropathy | Abdominal cramps, diarrhoea | Discontinue if neuropathy severe, raised serum amylase and transaminases |
| Tenofovir (TDF) | Renal dysfunction | | Monitor renal function at baseline, and every 6 months. Avoid use in pregnant women except if other alternatives are not available. |
| Abacavir (ABC) | Hypersensitivity reaction, | Lactic acidosis | Discontinue therapy and don't restart when resolved |

| | | | |
|---|---|---|---|
| Nevirapine (NVP) | Skin rash, Stevens-Johnson syndrome, hepatoxicity | | Low-dose over first 2 weeks minimizes rash occurrence. If mild or moderate continue cautiously or substitute with EFV. If severe discontinue NVP and permanently if hepatitis confirmed |
| Efavirenz (EFV) | Nightmares, rash, hepatitis | Dizziness, | Rash in 10% but rarely severe <1%; CNS symptoms often resolve 2-4 weeks. Discontinue if hepatitis is confirmed. |
| Lopinavir/Ritonavir | Diarrhoea, skin rash | Headache, weakness | Diarrhoea rarely severe |
| Nelfinavir (NFV) | Diarrhoea, lipid, glucose & liver abnormalities, | | Diarrhoea occurs 10-30% at start of therapy but often resolves on its own |
| Indinavir (IDV) | Nephrolithiasis, hepatitis, lipid, glucose abnormalities | Headache, rash, retinoid-like effects, alopecia, | Ensure adequate rehydration (1.5 L/day). Monitor liver enzymes |
| Emtricitabine (FTC) | Lactic acidosis with hepatic steatosis | Hyperpigmentation Skin coloration | Do serum lactate if suspicious symptoms exist |

## *III. PROGRESS IN TRATMENT OF HIV*

### ❖ The evolution in anti-retroviral therapy

Anti-retroviral therapy (ART) was being used by over 7 million people at the time (21% of all HIV-positive individuals), while the annual mortality toll from AIDS was roughly 1.8 million. The majority of low-income and middle-income countries (LMICs) were in the process of switching from Stavudine/lamivudine/nevirapine to zidovudine/lamivudine/nevirapine, and the median cost of a first-line regimen was 160 USD per patient per year. In order to increase the harmonization of adult (including pregnant and lactating women) and pediatrics ARV regimens, CADO-1 established the principles of drug escalation and defined the target product profiles, which included safety, efficacy, tolerability, durability, stability, convenience, accounting for special populations, and achieving lower treatment costs.

### ❖ Changes to new anti-retroviral options

There was discussion on low-dose EFV (EFV 400 mg) as an alternate first-line option in the event that DTG is unavailable or patients face tolerability issues. Several fixed-dose DTG dual therapy regimens have recently been developed, notably DTG combined with rilpivirine and DTG with DRV/r. These weren't given a priority at that time, as existing clinical test data with these regimens were limited, particularly with reference to populations of concern in resource-limited settings. Medium-term opportunities include the role of regimens including the new Tenofovir prodrug (TAF) and new DRV formulations, with critical research that specialize in the efficacy/safety, switch regimens, dose-reduction and/or the utilization of Nano formulations, particularly for DRV. Long-term goals include long-acting formulations of latest compounds, maturation and capsid inhibitors and biologicals.

Furthermore, harmonization of adult and paediatric and key populations has been a goal for HIV treatment, ideally as FDCs. DTG offers great potential as a first-line regiment options, particularly as a generic fixed dose combination – requires less quantity of active pharmaceutical ingredient, once daily dosing, favourable side-effect profile compared to EFV.

### ❖ Target product profile for an ideal antiretroviral

HIV treatment agenda for resource-limited settings, that specialize in first-line and second-line treatments and understanding new technologies that may help to give long-term durability and affordability to ARV regimens. This shift focused was reflected with a new set of recommendations established in the second conference on drug optimization (CADO-2) held in 2013. therein year, the amount of people on ART increased to almost 10 million (28% of all PLHIV), but the amount of AIDS deaths had only slightly decreased to 1.6 million per annum. Transition from zidovudine/lamivudine/nevirapine to Tenofovir/lamivudine/efavirenz (EFV) because the preferred first-line regimen already had started in LMICs. The CADO-2 main objective was to determine an HIV-treatment research agenda for resource-limited settings over the next 5–10 years, identifying a priority list of affordable first-line and second-line ART regimens, increasing the main target on development of once daily generic FDCs, ideally together tablet a day, the intersection of HIV with concurrent illnesses/comorbidities, particularly TB and hepatitis B, also as incentivizing novel treatment regimens and strategies at a time when there was declining investment in HIV treatment research. Two investigational drugs of high interest at that point were the dolutegravir (DTG) and a new Tenofovir prodrug-Tenofovir alafenamide (TAF). There was also a perception that optimizing the security, convenience and availability of ART would help prevent more HIV infections.

At the top of 2017, a 3rd global conference on ARV optimization (CADO-3) was convened with an objective to better define the critical research necessary to optimize second-line and third-line treatment regiments and also promote adequate sequencing and recycling of key antiretroviral agents in the context of public health. the worldwide number of people on ART reached 21 million (57% of all PLHIV), the amount of AIDS deaths declined to less than 1 million per year and transition from EFV to DTG containing regimens has started in many countries. The median price of first-line regimens per patient has reduced to 85 USD/year. At CADO-3, there was a stress on ensuring that optimal products elected as preferred options for HIV treatment should be well tolerated, safe and effective across specific populations – namely pregnancy and breastfeeding women, TB/HIV coinfection also as other comorbidities. Specific emphasis was also placed on the emergence of HIV drug resistance, particularly within the context of service delivery models that reduced contact with health services.

### ❖ Nitric oxide based Anti-retroviral therapy

Nitric oxide (NO) is a gasotransmitter of great significance to developing the innate immune response to many bacterial and viral infections, while also modulating vascular physiology. The generation of NO from the upregulation of endogenous gas synthases serves as an efficacious method for inhibiting viral replication in host defence and warrants investigation for the development of antiviral therapeutics. With increased incidence of worldwide pandemics concerning several respiratory-based viral infections, it's necessary to develop broad therapeutic platforms for inhibiting viral replication and enabling more efficient host clearance, also as to fabricate new materials for deterring viral transmission from medical devices. Recent developments in creating stabilized NO donor compounds and their incorporation into macromolecular scaffolds and polymeric substrates has created a replacement paradigm for developing NO-based therapeutics for long-term NO release in applications for bactericidal and blood-contacting surfaces. Despite this abundance of research, there has been little consideration of NO-releasing scaffolds and substrates for reducing passive transmission of viral infections or for treating several respiratory viral infections. The aim of this review is to spotlight the recent advances in developing gaseous NO, NO prodrugs, and NO donor compounds for antiviral therapies; discuss the restrictions of NO as an antiviral agent; and outline future prospects for guiding materials design of a next generation of NO-releasing antiviral platforms.

### ❖ Stem cell therapy

Stem cells are highly specialized cell types that can be found in adult (body tissues of adults), embryonic (embryos), mesenchymal (connective tissue or stroma), and induced pluripotent sources. They have a remarkable capacity for self-renewal and the capacity to differentiate into one or even more distinct cell types, which is crucial for the regulation and healing of damaged tissues.

It's interesting to note that this technique significantly improved procedure results not long after beginning antiretroviral therapy.15 Many currently incurable diseases can be treated by stem cell transplantation. They could also be used to improve the management of immunologic disorders like HIV infection and develop a fresh anti-infection therapeutic strategic plan.

The clinical importance of HIV infection was once thought to be influenced by stem cell transplantation, however viral modulation was not achieved in the field. This area of HIV cell management has also been greatly expedited by advancements in stem cell transplants that use synthetic or natural resistant cell resources, novel genetic manipulation techniques, or the development of cytotoxic anti-HIV effector cells.

60 HIV can be treated using a variety of strategies, including increasing immune responses to the viral infection or shielding cells from infectious disease. 30 The different approaches are as follows: Human umbilical cord mesenchymal stem cell transplantation, autologous stem cell transplantations, hematopoietic stem cell transplantation, genetic modification of hematopoietic stem cells (HSCT), HSCT and HAART therapeutic approach, mesenchymal stem/stromal cell (MSC) applications, CCR5 Delta32/Delta32 stem-cell transplantation, CRISPR and stem cell applications, and applications involving induced pluripotent stem.

### ❖ Mobile application for detecting HIV

This application is developed with Java serving as its primary programming language, Android Studio was used to create the iOS and Android-compatible AR Predictor. The Nginx Server hosts the app system, while the Retrofit Library manages network calls made using the LA ravel PHP framework. For ARVPredictor, DigitalOcean provides a dependable and high-performance cloud computing platform. This mobile application is described as a "ARVPredictor" on the Google Play Store, and the source code is accessible via a GitHub repository with an MIT permissive license.

A total of 100 known HIV sequences were examined to see if there was any consistency between the ARVPredictor and Stanford HIV Database in identifying the HIV subtype and NNRT and NRTI mutations.

When compared to the Stanford HIV Database, the ARVPredictor found similar HIV subtypes in 98 out of 100 sequences (=0.98, indicating almost perfect agreement).

Similar to the Stanford HIV Database, ARVPredictor identified 89 out of 100 important NNRTI and NRTI mutations (=0.89, suggesting almost perfect agreement). ARVPredictor categorized eight mutations that the Stanford HIV Database had deemed significant as other mutations.

## IV. LOOKING TO THE FUTURE

Given the high efficacy, safety, tolerability and convenience of current ARV therapy, it is often challenging to identify where and to what extent further improvements can be made. New agents under investigation are challenging the present treatment paradigm of three active antiretroviral medications taken orally every day to maintain viral suppression. Several two-drug therapy options are under study and should simplify treatment and reduce cost. Long-acting medications dosed hebdomadally or month, or longer, could also be easier for some patients, improve medication adherence and increase cost-effectiveness. some longer acting ARVs in development will provide additional oral therapy options, but the bulk of novel regimens will likely be delivered via alternative drug delivery systems. This includes the potential delivery of some new agents like cabotegravir and rilpivirine as long-acting injectable formulations or as a subdermal implant. These methods of drug, while new for HIV treatment, are common in other therapeutic areas like hormonal contraception and psychiatry and may represent an additional way to improve medication adherence and effective treatment.

### ❖ Major new ARVs in phase III studies

The state drug administration (NMPA) has given azvudine (FNC), a novel nuclear nucleoside reverse transcriptase inhibitor, approval for clinical study. FNC makes itself a better candidate to be co-formulated in other anti-HIV

medicines, improving patient compliance. FNC has successfully finished its phase I–II clinical investigations. This clinical trial involves multiple centres and is randomised, double-blind, double-placebo, and active-control. While subjects in the active control arm receive 3TC+TDF+EFV+FNC placebo, those in the experimental arm receive FNC+TDF+EFV+3TC placebo. While FNC and 3TC are conducted using a double-blinded design, the background medications in both arms are done so under an open-label protocol.

### ❖ HIV Drug Development to target HIV lifecycle

In the meantime, NIAID keeps funding studies to create novel antiviral medications with distinct modes of action. Such medications would probably be successful against HIV strains that are resistant to other medication classes.
For instance, the creation of the experimental drug islatravir (also known as EFdA or MK-8591), which is a member of the class of medications known as nucleoside reverse transcriptase translocation inhibitors, or NRTTIs, was aided by fundamental research funded by the NIAID. The maturation inhibitors, which target the same stage of the HIV lifecycle as protease inhibitors but work via a different mechanism, were also developed in part thanks to NIAID research.
Additionally, scientists are aiming to focus on other phases of the HIV lifecycle. For instance, by binding to the gp120 protein on the surface of the virus, the investigational inhibitor fostemsavir prevents HIV from infecting immune cells. Another illustration is the creation of inhibitors that prevent the viral capsid, the protein shell that encases HIV's genetic material, from being assembled.

### ❖ Long acting HIV drugs

Researchers funded by NIAID are working to create a new class of HIV medications, including longer-acting pills and alternate dosage forms like injections, patches, and implants. Due to the difficulty of creating such products, NIAID formed a group of professionals who can promote interactions between the various sorts of researchers required to turn an idea for a long-acting HIV treatment into a practical solution. The effectiveness of two novel long-acting HIV medications, cabotegravir LA and rilpivirine LA, in patients who have had trouble adhering to traditional antiretroviral therapy will also be studied by NIAID. Another research will examine whether cabotegravir LA monthly injections and monthly infusions of VRC01LS, a broadly neutralising antibody developed by the NIAID, can maintain HIV suppression in individuals whose infection was previously under the control of antiretroviral therapy.

## V. CONCLUSION

In summary, the worldwide ARV optimization framework was initially focused on improving global access to key ARV drugs available at that time by reducing cost and simplifying manufacturing processes, aiming the rapid reduction in mortality from HIV, preservation of life and prevention of progression to AIDS and therefore the risk of HIV transmission at the population level.
With the evolving science of HIV, New steps were taken to make sure a transition to new drugs and formulations with better efficacy, lower toxicity, limited contraindications and better durability against drug resistance, to scale back the need to switch to more complex and expensive regimens and also to reduce the risk of HIV transmission at population level.

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