

6. Hyperlipidemia – premature cases of coronary artery disease have been described in patients on ARVs.

7. Osteoporosis, osteonecrosis and osteopaemia has been described.

8. Skin rash – may be severe or fatal. Steven Johnson syndrome or toxic epidermal necrosis have been described with NNRTI especially nevirapine and this should be permanently stopped if this occurs.

Interruption of ARV;

In the event of a failing regimen it is better to stop 2 or more drugs and change than to do it singly.

Viral resistance tests are not available locally but should be part of long term policy considerations.

Monitoring of ARV;

Should be;

- Clinical
- Biological
- Monitoring for side effects and adherence

Clinical

Should be to watch for development of OIs and side effects. Weight should be monitored.

Biological

- ◆ Routine laboratory tests – FBC, U/E, LFTs, urine dipstix, blood sugars.
- ◆ Immunological – CD4/ CD8 every 3 months
- ◆ Virological if available – 6 weeks and 3 months after commencing ARVs and 3 months after that.

Protocols should be developed for monitoring adherence. A form of DOT may need to be implemented



HAQOCI

HIV/AIDS Quality of Care Initiative



Clinical Epidemiology Resource & Training Centre - University of Zimbabwe Medical School

Anti Retroviral Therapy Practical Issues and Policy Considerations



Since the mid 1990s and increasing number of antiretroviral (ARV) drugs have become available for combating the HIV virus.

These have made a significant impact on the HIV pandemic especially in the developed world. Due to various initiatives and pricing adjustments they are becoming increasingly more available locally. Patients are becoming more aware of the ARVs and are beginning to demand their use.

The use of ARVs is a complex matter which needs prior careful consideration before commencing the medication.

ARVs are not a “cure” for AIDS, the HIV virus may persist in “sanctuary sites” and may still be isolated in patients who have undetectable HIV RNA plasma levels.

Who administers ARVs?

For the programme to make a meaningful impact on a national scale practitioners have to be trained to administer the drugs and must be aware of the complexities involved.

Who gets ARVs?

The HIV test is a prerequisite for getting ARVs- only patients who have been for-

mally tested and confirmed to be HIV positive should be given ARVs. The exception to this is for post exposure prophylaxis (PEP) in HIV negative workers exposed occupationally to HIV during their work. (In this case, ARVs are started prior to getting the HIV result for the health worker)

In addition to a positive HIV test patients who are symptomatic from HIV (wasting, unexplained fever for more than 2 weeks) or AIDS accordingly to either WHO or CDC criteria are entitled to be commenced on ARVs.

To maximize benefits in the presence of limited budgets symptomatic patients with a CD4 count less than 200/mm² or a viral load greater than 30 000 copies/ml of plasma should be treated.

Controversy exists concerning treatment of asymptomatic HIV positive people and these should be closely monitored with CD4 counts and viral loads if available. To maximize adherence symptomatic patients only should be offered ARVs, asymptomatic ones should be followed up carefully.

In the situation in Zimbabwe some patients are already getting ARVs without viral load tests and sometimes without CD4 counts.

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Formal clinical research and protocols are required to address this issue.

Aim of ARV therapy

The aim of therapy is full suppression of viral replication to below detectable levels by the most sensitive assays available.

Even with this aim achieved, there are still reservoirs of HIV in patients on ARVs. Viable virus has been retrieved from patients who have been well suppressed on triple therapy for up to two years. Massive rebound viraemia has been known to occur on stopping ARVs.

Other aims of therapy include;

- Restoration and/or preservation of immunological function.
- Improvement of quality of life.
- Reduction of HIV related morbidity and mortality

ARV Treatment: Steps to Follow

1. HIV pretest counselling
2. Obtain informed consent
3. HIV testing
4. HIV post test counselling
5. Medical consultation
 - Medical history
 - Physical examination
 - STD screening
 - TB screening (to include CXR)
 - Routine haematological and biochemical tests
 - Other tests to diagnose OI if indicated
 - Pregnancy test (if indicated)
 - CD4 count, viral load if available

Classes of ARVs.

1. Reverse transcriptase inhibitors
 - Nucleoside (NsRTI) e.g. AZT
 - Nucleotide (NtRTI) e.g.

- Tenofovir
 - Non-nucleoside (NNRTI) e.g. Nevirapine
2. Protease inhibitors
 3. Fusion inhibitors
 4. Integrase inhibitors

The last two groups of drugs are still in their early stages of use and are not commonly available.

	Column A	Column B
Strongly recommended	Efavirenz Indinavir Nelfinavir Ritonavir + Indinavir Ritonavir + Lopinavir Ritonavir + Saquinavir (SBC or HBC)	Didanosine + Lamivudine Stavudine + Didanosine Stavudine + Lamivudine Zidovudine + Didanosine Zidovudine + Lamivudine
	Column A	Column B
Recommendations alternative	Abacavir Amprenavir Delavirdine Nelfinavir + Saquinavir - SBC Nevirapine Ritonavir Saquinavir SBC	Zidovudine + Zalcitabine
	Column A	Column B
Not recommended	Saquinavir MGC	All monotherapies, whether column A or B Stavudine + Zidovudine Zalcitabine + Didanosine Zalcitabine + Lamivudine Zalcitabine + Stavudine

The recommended first line for Zimbabwe in adults; who are not pregnant is;

- Zidovudine 300mg bd
- Lamivudine 150mg bd plus
- Nevirapine 200mg od for 14 days then 200mg bd

Second line treatment in Zimbabwe in adults.

	Weight <60kg	Weight >60kg
Didanosine	250mg od	400mg od
Stavudine	30mg bd	40mg bd
Indinavir	800mg tds	800 mg tds

The first line treatment is also recommended for children and pregnant women in the appropriate doses.



For pregnant women

Avoid starting treatment in the first trimester to reduce teratogenicity.

Protease inhibitors do not cross the placenta.

Efavirenz has been described to cause teratogenicity in animal studies and is better avoided in pregnancy. The same has been found of hydroxy-gurea.

Adherence: Other issues with ARVs

Only patients who will comply with treatment for life should be given ARVs. Adherence with treatment should be at least 95% to reduce resistance.

Continuing patient counselling must be conducted on subsequent visits.

Terminal HIV patients with advanced malignancies are better treated with appropriate palliation rather than ARVs.

Avoiding over the counter preparations (OTCs) which may interact with ARVs. ARVs interact with TB drugs especially Rifampicin. Continued supervision of patients in the community should be strongly considered

Side Effects of ARVs

These can be serious and patients should be warned of these from the beginning. Patients should be monitored appropriately to detect early side effects.

1. Lactic acidosis
 - NsRTI
 - NtRTI
2. Mitochondrial disease with hepatic steatosis.
3. Hepatotoxicity is more common in females on NNRTI especially nevirapine and especially if there is coinfection with hepatitis B or C.
4. Hyperglycaemia – seen with PI
5. Fat maladministration sometimes called lipodystrophy syndrome.