I. What are the key questions to be answered in these guidelines:
   1. What are the goals of antiretroviral therapy
   2. Pretreatment evaluation
   3. What is new in these guidelines
   4. When should antiretroviral therapy be started
   5. Which regimens are preferred for initial therapy
   6. What to avoid
   7. Immune reconstitution inflammatory syndrome (IRIS)
   8. Monitoring tools
   9. When should resistance testing be offered
   10. When to switch and what to switch to
   11. Address special populations

II. Goals of therapy:
- Reduce HIV related morbidity and mortality
- Improve quality of life
- Restore and preserve immune function
- Maximally and durably suppress viral load
- Reduce the risk of transmission:
  o non professional exposures:
    ▪ sexual partner(s),
    ▪ infants,
  o professional exposures,

In deciding on therapy, the following have to be considered:
- Clinical stage
- Immunological stage (viral load is at best used as an adjunct to decision but cannot be considered alone as an indication for therapy in the current guidelines)
- Patient readiness and his/her understanding of treatment, the need of adherence and follow-up, and what to expect as far as efficacy and toxicities
- Patient support and counseling
- Preventive measures
- Antiretroviral therapy is part of a comprehensive care process which includes counseling, prevention, management and prevention of opportunistic infections

III. Pretreatment evaluation:
Along with thorough history and physical examination, there is a need to evaluate:
- Social and economic issues
- Mental illness
- Substance abuse including smoking, alcohol, psychotropic drugs and illegal drugs
- Co-morbidities particularly diabetes and dyslipidemias

The following laboratory tests should be performed for each new patient during initial visit:
- HIV antibody testing with confirmation (see laboratory diagnosis algorithm)
- CD4+ cell count
- Plasma HIV viral load
- CBCD, creatinine, transaminases level, urinalysis
- VDRL, PPD tuberculin skin test (unless there is a history of tuberculosis or positive PPD), HAV IgG, HBsAg, HBc IgG, HCV IgG
- PAP smear in women
- Fasting blood glucose and lipid profile if history of such or if risk of cardiovascular disease and prior to initiation of antiretroviral therapy
- Optional: *Toxoplasma* IgG
- Optional: Resistance genotype if patient ARV experienced and viral load > 1000 copies/ml

**CD4+ cell counting interpretation:**
- Strongest predictor of disease progress
- Significant change: 30% change in absolute number or 3% change in CD4 percentage
- Adequate response to ARVs: increase in CD4 cell count of 100-150 cell/mm³ per year
- CD4 cell counting should be determined every 3 to 6 months

**Viral load monitoring:**
- Evaluation of response to therapy
- Determination of virologic failure
- Significant change: 0.5 log or three fold change
- Goal of therapy: undetectable level: <400 copies/ml in the regular assay and <50 copies/ml in the ultrasensitive assay (Roche Amplicor HIV-1, version 1.5)
- Undetectable level should be achieved by 16-24 weeks of therapy
- Viral load monitoring should be determined before treatment, at 2-8 weeks after treatment or treatment changes (there should be a 1.0 log drop). If response, testing should be repeated every 3-4 months or as clinically indicated.

**Resistance testing:**
- Currently unavailable in Lebanon. Such testing usually is done in foreign laboratories with what it entails in terms of excessive costing. It is expected that genotypic resistance testing will be offered in Lebanon starting summer 2007 at reasonable costs.
- Genotypic resistance testing should be performed in case of virologic failure while the patient is taking his/her antiretroviral drugs (or less than 4 weeks after discontinuing them).
- So far, there is no data as far as transmitted resistance to recommend genotypic resistance testing prior to initiation of therapy or in acute infection. In case such studies are done or such transmitted resistance is documented, genotypic resistance testing in naïve patients should be done only if transmitted resistance to drugs from more than one class is documented in more than 5% of naïve patients.
- Genotypic resistance testing should not be done in persons with viral load <1000 copies/ml.

**IV. When to start ART:**
1. General guidelines:
- All patients with history of an AIDS defining illness or severe symptoms of HIV infection regardless of CD4 cell count
- Asymptomatic patients with CD4 cell counts <350/mm³
- In patients with CD4 cell counts between 350 and 500/mm³, antiretroviral therapy may be advised. Consideration will be given on a case per case according to minor clinical findings (such as oral candidiasis, oral hairy leukoplakia, diarrhea, weight loss (< 10% of body weight), low grade fever, night sweats), progression of CD4 counts and to viral load if higher than 100,000 RNA copies/ml.
- If the viral load is higher than 100,000/ml, and if treatment is deferred, these patients should be monitored by CD4 cell counting and eventually viral load monitoring every three months.
- Regardless of CD4 count, antiretroviral therapy is strongly recommended for individuals with:
  - Pregnancy (see Prevention of Mother to Child Transmission guidelines)
  - History of an AIDS defining illness
  - HIV associated nephropathy
  - Viral Hepatitis B or C co-infection
- Antiretroviral therapy should be offered for individuals who are at risk of transmitting HIV to sexual partners such as in discordant couples.

2. Revised clinical classification of HIV infected adults and adolescents (WHO 2006):

<table>
<thead>
<tr>
<th>Classification of HIV associated disease</th>
<th>WHO clinical stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>1</td>
</tr>
<tr>
<td>Mild</td>
<td>2</td>
</tr>
<tr>
<td>Advanced</td>
<td>3</td>
</tr>
<tr>
<td>Severe</td>
<td>4</td>
</tr>
</tbody>
</table>

3. Immunological assessment:

CD4 criteria for the initiation of ART in adults and adolescents

<table>
<thead>
<tr>
<th>CD4 cell count /mm³</th>
<th>Treatment recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 350</td>
<td>Treat irrespective of clinical stage</td>
</tr>
<tr>
<td>350 – 500</td>
<td>Treatment may be advised (see note above) and initiate treatment before CD4 count drops below 200 /mm³</td>
</tr>
<tr>
<td>&gt; 500</td>
<td>Do not initiate treatment (unless special considerations are met)</td>
</tr>
</tbody>
</table>

Patients in clinical stage 4 should be treated regardless of CD4 count. In all patients, a CD4 level of 350 /mm³ or less is considered to be a level below which treatment should be considered. For example, patients with pulmonary tuberculosis or severe bacterial infections should be considered for ART when their CD4 cell count falls below 350/mm³. It is also recommended to treat a pregnant woman regardless of CD4 count. For patients with clinical stages 1 or 2, a CD4 cell count below 350/mm³ is a clear indication to initiate ART. In individuals where therapeutic decision is to be made solely on CD4 counts, it is recommended to repeat the count before initiation of therapy, since fluctuation may occur.

*The initiation of ART is recommended for all HIV infected pregnant women regardless of stage or clinical manifestations, and for all HIV infected individuals with CD4 counts below 350/mm³ and pulmonary tuberculosis or severe bacterial infections.
4. Virological assessment:
Plasma viral load measurement is not necessary for making a decision whether to initiate ART. It is however useful in order to make decisions to monitor response to therapy and to make decisions whether to switch therapy. It has been recognized that at similar levels of CD4 cell counts, women tend to have lower viral loads; however, decisions to treat on clinical or immunological grounds are the same in both men and women.
### WHO Staging

#### CLINICAL STAGE 1
- Asymptomatic
- Persistent generalized lymphadenopathy

#### CLINICAL STAGE 2
- Unexplained moderate weight loss (<10% of presumed or measured body weight)
- Recurrent upper respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulcerations
- Papular pruritic eruptions
- Seborrheic dermatitis
- Onychomycosis

#### CLINICAL STAGE 3
- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhea for more than one month
- Unexplained persistent fever (intermittent or constant for more than one month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis
- Severe bacterial infections (pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia, severe pelvic inflammatory disease)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anemia (< 8 g/dl), neutropenia (< 500/mm3), thrombocytopenia (< 50,000/mm3)

#### CLINICAL STAGE 4
- HIV wasting syndrome
- *Pneumocystis jiroveci* pneumonia
- Recurrent bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal for more than a month)
- Esophageal candidiasis
- Extrapulmonary tuberculosis
- Recurrent septicemia (including non typhoidal *Salmonella*)
- Cytomegalovirus infection (retinitis, other organs)
- Central nervous system toxoplasmosis
- Atypical disseminated leishmaniasis
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (coccidiomycosis, histoplasmosis)
- Kaposi sarcoma
- Lymphoma (cerebral or B cell non-Hodgkin)
- Invasive cervical carcinoma
- HIV encephalopathy
V. What to start: recommended first-line ARV regimens

1. Considerations for treatment

The following issues should be considered when selecting ARV regimens:

a. Availability of drugs and doses.

b. Drug formulation and number of pills. Consider using fixed drug combinations.

c. Friendly dosing schedules to foster adherence.

d. Toxicity profile and need for toxicity monitoring.

e. Preservation of future treatment options (preserving drug families)

f. Co-morbidities (especially tuberculosis and viral hepatitis)

g. Pregnancy and child bearing potential

h. Price and cost-effectiveness

i. Eventually, special issues related to HIV-2 infections that are naturally resistant to NNRTIs. HIV-2 is rare but has been regularly reported in Lebanon.

2. Drug formulary currently available in Lebanon:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Generic Name</th>
<th>Brands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleoside Reverse Transcriptase Inhibitors and Nucleotide Reverse Transcriptase Inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZDV</td>
<td>Zidovudine</td>
<td>Zidovir, Retrovir</td>
</tr>
<tr>
<td>3TC</td>
<td>Lamivudine</td>
<td>Lamivir, Epivir</td>
</tr>
<tr>
<td>ddl</td>
<td>Didanosine</td>
<td>Dinex, Videx</td>
</tr>
<tr>
<td>TDF</td>
<td>Tenofovir</td>
<td>Tenvor, Viread</td>
</tr>
<tr>
<td>ABC</td>
<td>Abacavir</td>
<td>Abamune, Ziagen</td>
</tr>
<tr>
<td>Non Nucleoside Reverse Transcriptase Inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td>Nevirapine</td>
<td>Nevimune, Viramune</td>
</tr>
<tr>
<td>EFV</td>
<td>Efavirenz</td>
<td>Efavir, Stocrin, Sustiva</td>
</tr>
<tr>
<td>Protease Inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LPV/r</td>
<td>Lopinavir/ritonavir</td>
<td>Lopimune, Kaletra, Aluvia</td>
</tr>
<tr>
<td>RTV</td>
<td>Ritonavir</td>
<td>Ritonum, Norvir</td>
</tr>
<tr>
<td>Integrase Inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAL</td>
<td>Raltegravir</td>
<td>Isentress</td>
</tr>
<tr>
<td>Combinations</td>
<td>Zidovudine/Lamivudine</td>
<td>Duovir, Combivir</td>
</tr>
<tr>
<td>TDF/FTC</td>
<td>Tenofovir/Emtricitabine</td>
<td>Tenvor EM, Truvada</td>
</tr>
<tr>
<td>TDF/FTC/EFV</td>
<td>Tenofovir/Emtricitabine/Efavirenz</td>
<td>Viraday, Atripla</td>
</tr>
</tbody>
</table>

3. Background information necessary in building needs:

a. No continuous knowledge of basic resistance and transmitted resistance.

b. Apparently high level of co-infection with HBV in persons with sexually transmitted HIV and HCV in persons with IDU transmitted HIV.

c. The prevalence of tuberculosis appears relatively high as OI although it does not reach levels reported in other countries in the region.

4. Basic recommendations:
a. The first line regimen would include two NRTIs and one NNRTI.
b. NVP or EFV may be used. EFV is the preferred agent because of ease of single dose administration and because of lower prevalence of rash. However, NVP remains the drug of choice in pregnancy and EFV is preferred in case of tuberculosis or co-infection with hepatitis viruses.
c. 3TC or FTC may be used interchangeably.

5. First-line regimen:
   a. Preferred regimen:
      \[ \text{TDF 300 mg od + 3TC 150 mg bid + EFV 600 mg od.} \]
      \[ \text{TDF 300 mg / FTC 200 mg / EFV 600 mg Single pill combination OD} \]
      i. Advantages:
         1. Limited number of pills (according to availability in Lebanon):
            one pill TDF, 2 pills 3TC and one pill EFV or in the second option a single drug.
      ii. Disadvantages:
         1. Lack of continuous supply of TDF or of the triple combination.
         2. Neuropsychiatric toxicity and teratogenicity of EFV.

6. Alternative first line regimens:
   a. \text{ABC 300 mg bid + 3TC 150 mg bid + EFV 600 mg od.}
      i. Advantages:
         1. Avoidance of a thymidine analogue and associated mitochondrial toxicity and possibility of preexistent TAMs.
      ii. Disadvantages:
         1. Allergic reactions to abacavir. These allergic reactions may be fatal. The presence of the HLA B-5701 allele has been found to be associated with these allergic reactions to abacavir and its determination is recommended for the assessment of such predisposition. This determination is not readily available in Lebanon, thus rendering the use of this drug relatively hazardous.
         2. Limited availability of the drug in the country.
   b. \text{ZDV 300 mg bid + 3TC 150 mg bid + EFV 600 mg od.}
      i. Advantages:
         1. Availability of combinations of ZDV/3TC, thus the advantage of low number of pills (3 per day: one ZDV/3TC in the morning, one ZDV/3TC in the evening and one EFV at bedtime.
         2. Preservation of PI for second line, and avoidance of lipid abnormalities related to PIs.
         3. Long standing experience and proven long term efficacy.
      ii. Disadvantages:
         1. Use of a thymidine analogue with its associated mitochondrial toxicity and lipodystrophy.
         2. Myelosuppression due to ZDV.
3. ZDV has been present in use for a long time hence the possibility of transmitted TAMs reducing the efficacy of this regimen.
4. Neuropsychiatric toxicity of EFV.
5. Need to determine child bearing potential because of the possible teratogenicity of EFV.

c. ddI 400 mg od + 3TC 150 mg bid + EFV 600 mg od.
   i. Advantages:
      1. Availability.
      2. Low cost.
      3. Desirable in case of unavailability of TDF or of bone marrow insufficiency or toxicity.
   ii. Disadvantages:
      1. Marked neuropathy and GI intolerance.
      2. Neuropsychiatric toxicity and teratogenicity of EFV.

d. Same protocols with substitution of NVP 200 mg bid in lieu of EFV.
   i. Advantages:
      1. Avoidance of neuropsychiatric toxicity of EFV.
      2. Possibility of use in women with child bearing potential or pregnant.
   ii. Disadvantages:
      1. Hepatotoxicity of NVP.
      2. Problem in combination with anti-tuberculous medications.
      3. Severe rash and Stevens Johnson associated with NVP.
      4. NVP should be avoided in naïve women with CD4 counts above 250/mm3 and in naive men with CD4 cell count above 400/mm3 because of increased risk of hepatotoxicity.

e. The only co-formulations of NRTIs available in Lebanon are ZDV/3TC, TDF/FTC, TDF/FTC/EFV.

f. Schematic representation of the recommended initial regimen:

```
+ 3TC + EFV or NVP
```

TDF or ABC or ZDV or ddI

or FTC

7. The following should be avoided:
   a. Monotherapy
   b. Dual NRTI therapy
   c. As part of any regimen:
      i. d4T: Unacceptable mitochondrial toxicity and fatal lactic acidosis
      ii. d4T + ZDV: antagonism, similar resistance profile
      iii. d4T + ddI: combined toxicity (neuropathy, pancreatitis, lactic acidosis)
iv. 3TC + FTC: similar resistance profile, minimal additive antiviral activity
v. EFV in the first trimester of pregnancy and in women with child bearing potential not on effective contraception
vi. NVP in treatment naïve women with CD4 cell counts > 250 cells/mm³ or in treatment naïve men with CD4 cell counts > 400/mm³ (life threatening hepatotoxicity)
d. TDF + ddl + NNRTI: high rate of failure. However, this combination of TDF + ddl may be used along with a PI as salvage therapy.
e. Triple NRTIs regimens: Although they have the advantage of preserving both PIs and NNRTIs for future treatment options, these regimens have inferior virological suppression efficacy as compared to other classical regimens. Combinations that have been used with some relative efficacy are: (ZDV + 3TC + ABC) and (ZDV + 3TC + TDF). Other combinations such as (3TC + ABC + TDF) or (3TC + ddl + TDF) have been associated with unacceptable high virological failure rates and should be avoided.

8. The following combinations or regimens are not recommended because of insufficient evidence or because of non-superiority over current regimens. However, such combinations may be decided upon according to resistance criteria and genotyping. The final decision will be made through case by case evaluation and discussion.
   a. NRTI sparing regimen: Combination of NNRTI and PI (or ritonavir boosted PI)
   b. Triple class regimens (NRTI + NNRTI + PI)
   c. Quadruple class regimens (NRTI + NNRTI + PI + EI)
   d. Quadruple NRTI regimens
   e. Regimens containing 5 or more active agents
   f. Triple NRTI and NNRTI

9. PIs should be reserved for second line options. However, regimens including two NRTIs backbone with one PI may be an option as initial regimen in the following situations:
   a. Viral types with intrinsic resistance to NNRTIs such HIV-2
   b. In women with CD4 counts over 250/mm³.
   c. Severe toxicity due to NNRTI.
Recommended PIs are:
   o Preferred PIs (all are ritonavir boosted): Only one available in Lebanon:
     ▪ Lopinavir/ritonavir twice daily

However, since the prevalence of NNRTI resistant strains is rapidly increasing worldwide, it is worthwhile considering to initiate therapy with a PI based regimen if the patient seems to have acquired HIV from a country with heavy NNRTI experience or from an individual heavily experienced with NNRTIs. Until the prevalence of transmitted resistance is determined in Lebanon, the initial recommended regimen in naïve individuals remains NNRTI based.

10. Response to therapy:
A favorable response to therapy is defined by:
   o clinical criteria [absence or resolution of illnesses of immunosuppression (opportunistic infections, malignancies); weight gain],
o immunological criteria [rise in CD4 cell count];
o virological criteria [drop in HIV viral load to undetectable levels]. Virological success of treatment is defined as an undetectable plasma viral load after 6 months of treatment.

The immune reconstitution inflammatory syndrome (IRIS) is defined as a combination of symptoms and signs due to the improved ability to mount an inflammatory response because of immune restoration. It may present as the development of a previously subclinical or unrecognized OI, a paradoxical recrudescence of manifestations of preexistent OI, or as an autoimmune disease. It usually occurs within 2 to 12 weeks after initiation of ART, but later occurrences have been reported. Therefore the development of an OI soon after initiation of ART is not an indication of treatment failure and is not an indication to stop or switch therapy. If possible with no overwhelming or combined toxicity, the OI should managed along with the continued administration of ART. If impossible because of combined toxicity, such as is the case in tuberculosis, ART may be discontinued momentarily (according to adequate schedule of discontinuation, taking in consideration the half lives of the drugs used in combination) and resumed as soon as the clinical condition permits. The management of IRIS consists of the management of the OI, continuation of ART and eventually the use of prednisone at 0.5 mg/kg for 5 to 10 days in cases of moderate to severe reaction.

11. Antiretroviral drug toxicities:

<table>
<thead>
<tr>
<th>Common ARV toxicities</th>
<th>Clinical manifestations</th>
<th>Most commonly involved ARV drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematological</td>
<td>Anemia, neutropenia, thrombopenia</td>
<td>ZDV</td>
</tr>
<tr>
<td>Mitochondrial</td>
<td>Lactic acidosis, hepatic toxicity, pancreatitis, peripheral neuropathy, lipoatrophy and lipodystrophy, myopathy</td>
<td>NRTIs especially thymidine analogues (d4T ++, ZDV, ddC, ddI)</td>
</tr>
<tr>
<td>Renal toxicity</td>
<td>Nephrolithiasis</td>
<td>IDV</td>
</tr>
<tr>
<td></td>
<td>Renal tubular dysfunction</td>
<td>TDF</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>Hyperlipidemia, fat accumulation, insulin resistance, diabetes, osteopenia</td>
<td>PIs</td>
</tr>
<tr>
<td>Allergic reactions</td>
<td>Skin rashes, hypersensitivity reactions, Stevens-Johnson</td>
<td>NNRTIs ABC Some PIs</td>
</tr>
<tr>
<td>Central nervous system toxicity</td>
<td>Insomnia, hypersomnia, nightmares, severe neurologic disturbances</td>
<td>EFV</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Abnormal liver function tests</td>
<td>Thymidine analogues NVP PIs</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Hyperbilirubinemia</td>
<td>ATV</td>
</tr>
</tbody>
</table>
Mild toxicity does not require switching drugs although it might affect adherence to therapy. Moderate to severe toxicities might necessitate switching therapy. However, some drugs have cross toxicity and should be avoided while substituting (for example severe allergy to NNRTIs).

In managing toxicity, one must consider the following principles:

- Severity of the adverse reaction.
- Ensure that the adverse reaction is due to the ARVs and not to concurrent medications used for example for the treatment or the prevention of OIs.
- Ensure that the reaction is not due to an OI or an on-going illness or co-morbidity.
- Maintain adherence despite toxicity in mild to moderate reaction.
- If discontinuation of ART is deemed necessary because of severe to potentially lethal side-effect, all ARVs should stopped according to appropriate schedule and reinitiated once patient is stabilized with appropriate substitutions.

**Common toxicities of first line regimens and suggested substitutions**

<table>
<thead>
<tr>
<th>ARV drug</th>
<th>Common associated toxicity</th>
<th>Suggested substitution</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZDV</td>
<td>Severe anemia, neutropenia</td>
<td>TDF or ABC or d4T</td>
</tr>
<tr>
<td>ZDV</td>
<td>Severe GI intolerance</td>
<td></td>
</tr>
<tr>
<td>d4T</td>
<td>Lactic acidosis</td>
<td>TDF or ABC</td>
</tr>
<tr>
<td>d4T</td>
<td>Lactic acidosis, Lipoatrophy, metabolic syndrome</td>
<td>TDF or ABC</td>
</tr>
<tr>
<td>ABC</td>
<td>Hypersensitivity</td>
<td>ZDV or TDF or ABC</td>
</tr>
<tr>
<td>TDF</td>
<td>Renal tubular dysfunction</td>
<td>ZDV or ABC or d4T</td>
</tr>
<tr>
<td>ddI</td>
<td>Severe GI intolerance, Neuropathy, pancreatitis</td>
<td>3TC or FTC</td>
</tr>
<tr>
<td>EFV</td>
<td>Persistent and severe CNS toxicity</td>
<td>NVP or any PI or TDF or ABC</td>
</tr>
<tr>
<td>EFV</td>
<td>Potential teratogenicity (first trimester of pregnancy)</td>
<td>NVP or any PI or ABC</td>
</tr>
<tr>
<td>NVP</td>
<td>Hepatitis</td>
<td>EFV or any PI</td>
</tr>
<tr>
<td>NVP</td>
<td>Hypersensitivity reaction including Stevens-Johnson</td>
<td>Any PI or ABC or TDF</td>
</tr>
</tbody>
</table>

In mild hypersensitivity reaction such as simple rash due to NVP, EFV may be used with careful monitoring.

12. Antiretroviral treatment failure and when to switch therapy

Considering the limited available financial resources for laboratory monitoring particularly viral load measurement and the limited choice in antiretroviral drugs, the decision to switch upon failure of therapy is difficult. It is recognized that maintaining a patient on a failing regimen leads to more recruitment of resistance mutations and the accumulation of NAMs. In addition, only second line regimen may be available. Therefore, caution should be used and strict definitions of treatment failures should be implemented prior to switching therapy. Decisions to switch are only based on assumptions and on history of prior experience with ARVs, since genotyping is not yet available to define resistance mutations. Once this is available, choices may be rendered easier albeit at a cost.
However, the IAS recommends more stringent definitions of failure of therapy and these should be taken in consideration to define a sub-group of patients to be followed and reevaluated with close scrutiny:

IAS recommendations

<table>
<thead>
<tr>
<th>Clinical failure</th>
<th>New or recurrent HIV related event after at least 3 months on ART, excluding IRIS</th>
</tr>
</thead>
</table>
| Immunological failure | • Failure to increase CD4 cell count by 25-50 cells/mm³ above baseline over the first year on ART; OR  
                          • Decrease below pre-treatment CD4 level |
| Virological failure | • Repeatedly detectable HIV RNA level >200 copies/ml after 24 weeks on ART |

The mean rise in CD4 cell count with initial ARV regimens in ART naive patients is expected to be approximately 150 cells/mm³ over the first year on treatment. Most patients with adequate virologic response at 24 weeks had a 1 log drop in HIV RNA at 1-4 weeks on ART.

In patients failing therapy, the following should be assessed:

- Adherence to therapy and identification of reasons for non-adherence: One of the main reasons for non-adherence in Lebanon appears to be shortage of drugs and difficult access to medications.
- Intolerance to treatment and toxicity: In this case, symptomatic treatment may be used. If a specific side effect is identified, the responsible drug may be switched to another drug of the same class with different tolerance profile. Eventually, drug class may be changed (from NNRTI to PI, for example).
- Pharmacokinetic issues such as relationship of drug intake to food intake, and drug-drug interactions within the regimen or with other agents used for OIs especially anti-mycobacterial agents or for co-morbidities such as psychotropic agents, anti-acid drugs, anti-convulsive therapy etc...

Decision to switch therapy depends on all three criteria (clinical, immunological and eventually virological). Once virological failure is documented, the regimen should be changed as soon as possible.

a. In case of a clinical event while on ART, decision depends on the following:
   i. Consider the possibility of immune reconstitution syndrome. This usually occurs during the first 3 months on treatment. If there is no virologic failure, treatment switch is not warranted.
   ii. If there is a stage 2 event, it is important to assess adherence. The event should be managed. A decision should be made to reevaluate the patient within the next 3 months and repeat CD4 cell counting.
   iii. In case of a stage 3 or 4 event, and it is not compatible with IRIS, the event should be managed. If ART has been on for more than 6 months, check CD4 cell count and consider switching therapy. If possible, resistance testing should be done and therapy change is done according to results.
b. Tuberculosis may occur at any CD4 level and does not indicate treatment failure. This is also true for recurrent bacterial infections or esophageal candidiasis responding well to specific therapy.

c. CD4 cell counting should be performed before any treatment change. Eventually, this should be repeated twice (according to resources).

d. An undetectable viral load indicates that ART should not be switched regardless of the CD4 cell count or the clinical stage.

e. The following table gives the WHO recommendations for switching therapy:

<table>
<thead>
<tr>
<th>Treatment failure criteria</th>
<th>CD4 failure (Viral load not available)</th>
<th>CD4 failure and viral load failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO Stage 1</td>
<td>Do not switch regimen. Follow patient for clinical signs and symptoms. Repeat CD4 in 3 months.</td>
<td>Consider switching to second line regimen.</td>
</tr>
<tr>
<td>WHO Stage 2</td>
<td>Do not switch regimen. Follow patient for further clinical progression. Repeat CD4 in 3 months.</td>
<td>Consider switching to second line regimen.</td>
</tr>
<tr>
<td>WHO Stage 3</td>
<td>Consider switching to second line regimen.</td>
<td>Recommend switching to second line regimen.</td>
</tr>
<tr>
<td>WHO Stage 4</td>
<td>Recommend switching to second line regimen.</td>
<td>Recommend switching to second line regimen.</td>
</tr>
</tbody>
</table>

CD4 failure is defined as a fall to or below pretreatment baseline, a 50% drop from the on-treatment peak level or persistent levels below 100/mm3 after 6 months of treatment.

Every time clinical, virological or immunological failure is being evaluated, it is essential to evaluate patient’s adherence to therapy, pharmacokinetic factors and toxicity features.

13. What to switch to: Second line regimens:

The following are recommendations for switching therapy after failure of a first line regimen:

<table>
<thead>
<tr>
<th>Regimen class</th>
<th>Initial regimen</th>
<th>Recommend second line</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTI</td>
<td>2 NRTIs + NNRTI</td>
<td>• 2 different NRTIs (based on resistance testing + PI with ritonavir boosting)</td>
</tr>
</tbody>
</table>
| PI            | 2 NRTIs + PI (with ritonavir boosting) | • 2 different NRTIs (based on resistance testing) + NNRTI  
                      • 2 different NRTIs (based on resistance testing) + alternative PI with ritonavir boosting, (based on resistance testing)  
                      • 2 different NRTIs (based on resistance testing) + NNRTI + alternative PI with ritonavir boosting (based on resistance testing) |
In second line regimens, DDI is frequently used. Second line regimens offering more activity include TDF/ABC or DDI/ABC. The combination of DDI and TDF should be used with caution because of suboptimal CD4 response and should be used only along with a boosted PI. Some experts recommend maintaining 3TC even in the setting of resistance because it may maintain residual antiviral activity and reduction of viral fitness.

In some cases of multiple resistance mutations to NRTIs in heavily experienced patients, it is recommended to combine all three families of drugs with DDI or 3TC along with a boosted PI and an NNRTI. Some even recommend NNRTI + boosted PI combinations, but this should only be used as an ultimate recourse and with resistance studies available demonstrating multiple NRTI resistance mutations. In some situations, the addition of an integrase inhibitor (raltegravir) should be considered. Examples:

<table>
<thead>
<tr>
<th>First line regimen</th>
<th>Second line regimen</th>
<th>PI component</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZDV + 3TC + EFV or NVP</td>
<td>DDI + ABC or TDF + ABC or TDF + 3TC (+/- ZDV)</td>
<td>PI/r</td>
</tr>
<tr>
<td>TDF + 3TC + EFV or NVP</td>
<td>DDI + ABC or DDI + 3TC (+/- ZDV)</td>
<td></td>
</tr>
<tr>
<td>ABC + 3TC + EFV or NVP</td>
<td>DDI + 3TC (+/- ZDV) or TDF + 3TC (+/- ZDV)</td>
<td></td>
</tr>
</tbody>
</table>

**Special Salvage Regimens and Medications:**
In some situations with evidence of multidrug resistant viruses, there is a need to secure a limited amount of medications for use in these cases. Although these drugs and regimens are included in first line regimens in the International AIDS Society Guidelines, however, it is deemed advisable to restrict their usage for special multidrug resistant cases, particularly concerning their cost. Raltegravir (an integrase inhibitor) is the only such drug currently registered in Lebanon. Other agents are obtained on special requests and should be registered in Lebanon such as the protease inhibitors, atazanavir and darunavir and the non nucleoside reverse transcriptase inhibitor, etravirine.

14. Special issues for women of childbearing potential or pregnant women:

a. Women of child bearing potential: The first line regimen in a woman of child bearing potential should consist of a NVP based regimen unless effective and consistent use of a contraceptive method is documented. EFV should be avoided in women of child bearing potential unless adequate contraception is used, because of potential teratogenicity. Because of potential interaction between some antiretroviral drugs such as EFV or PIs and oral contraceptives, women should use effective barrier contraception instead of oral contraceptives.

b. Pregnant women are managed the same way as non-pregnant adults. The optimal time to initiate ART in a pregnant woman is in women with stage 3 or 4 disease or in those with clinical stage 1 or 2 if the CD4 count is below 200/mm³. It is also recommended in women with stage 3 and a CD4 cell count less than 350/mm³. The benefits of starting therapy according to these criteria even in the first trimester of pregnancy clearly outweigh the risks and
therapy should be initiated if indicated. Antiretroviral therapy for prevention of mother to child transmission should be initiated at best at the second trimester and at least before the third trimester regardless of clinical or immunological status (see PMTCT). Once started, ART should be continued post-partum.

c. What to choose: The greatest experience is with the ZDV/3TC backbone. Alternative choices could include ABC or DDI. Because of limited experience, TDF should only be considered if other regimens are contraindicated or not effective. NVP is the NNRTI of choice; however, because of toxicity, it should be avoided in women with a CD4 cell count above 250/mm3. Therefore, in such a situation the following options are offered:

i. Treat with NVP and maintain close monitoring of liver tests for the first 12 weeks of therapy. If ALT or AST exceeds 5 times ULN without another explanation, or if symptoms suggestive of hepatic toxicity, including rash, NVP should be permanently discontinued.

ii. Start EFV and ensure adequate and effective use of barrier contraception.

iii. Start a PI based regimen (preferred regimen in pregnant women)

d. If the decision is made to start a PI, the only formulation available in Lebanon with adequate experience and efficacy is LPV/r.

e. Women should be counseled regarding the avoidance of breastfeeding.

f. If treatment has been initiated in a pregnant women for the usual indications, treatment should continue post partum. For women who initiated ART for the sole purpose of PMTCT, they are encouraged to continue therapy post partum. However, if they choose to discontinue therapy, and if therapy includes nevirapine, simultaneous cessation of all drugs may lead to functional NVP monotherapy because of the longer half life of this drug, hence leading to the development of resistance mutations. One recommendation is to switch temporarily to a PI based regimen for about one month before complete discontinuation of therapy.

15. Patients with tuberculosis:

Antiretroviral therapy should be started in all HIV infected individuals with extrapulmonary tuberculosis (stage 4) and all those with pulmonary tuberculosis with a CD4 cell count below 350/mm3.

a. Special considerations in TB:

- Drug interactions with rifampicin with both NNRTI and PIs
- Immune reconstitution inflammatory syndrome
- Pill burden
- Overlapping toxicities especially hepatotoxicity
- Adherence issues

b. When to start ART in a patient with TB-HIV co-infection:

- In patients already on ART at the time anti-TB treatment is initiated, the ART regimen has to be reassessed and modified to manage the drug drug interaction with rifampicin, eventually shifting to an EFV based regimen if not already used.
- In persons with CD4 cell count below 50/mm3, ART should be initiated as early as possible within 2 weeks after initiating anti-TB therapy.
In patients with CD4 cell count above 50/mm3 presenting with severe clinical disease, ART should be started within 2 to 4 weeks of starting TB treatment.

In patients with CD4 cell count above 50 cells/mm3 with no severe clinical disease, ART may be delayed beyond 2 to 4 weeks of starting TB therapy but should be initiated within 8 to 12 weeks.

c. What to start:
The standard regimen of 2 NRTIs + NNRTI is the recommended regimen. EFV is the preferred option because of easier to manage interactions with rifampicin. When rifampicin is used, the dose of EFV should be increased to 800 mg per day in patients weighing more than 60 kgs. In patients weighing less than 60 kgs, the standard 600 mg per day dosage is used. NVP is the alternative in pregnant women or women of child bearing age but it carries the risk of hepatotoxicity.

In women of child bearing potential or pregnant, EFV based regimen has to be avoided in the first trimester, but may be used in the second or third trimester of pregnancy, or with adequate contraception in women of child bearing potential. Another option is to use a triple NRTI combination of ZDV + 3TC + ABC, changing it to an EFV based regimen after delivery. A pregnant woman with TB started on an EFV based regimen during pregnancy may be shifted to a NVP based regimen as soon as the TB treatment is completed.

In HIV-2 infection, a PI based regimen is the preferred option.

The development of TB during the first 6 months of therapy is not considered as treatment failure and may be part of IRIS. If an episode of TB develops more than six months after the initiation of ART and data on the CD4 cell count and viral load are available, the decision about whether the TB diagnosis represents ART failure is based on the CD4 cell count and, if available, the viral load. If a CD4 cell count is not available the decision on whether the TB diagnosis constitutes ART failure depends on whether the TB is pulmonary or extrapulmonary. Extrapulmonary TB should be considered as indicating ART failure, although simple lymph node TB or uncomplicated pleural disease may be less significant than disseminated TB.
ART recommendations for patients who develop TB within 6 months of starting a first line or second line ART regimen

<table>
<thead>
<tr>
<th>First or second line ART</th>
<th>ART regimen at the time TB occurs</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>First line ART</td>
<td>2 NRTIs + EFV</td>
<td>Continue with 2 NRTIs + EFV</td>
</tr>
<tr>
<td></td>
<td>2 NRTIs + NVP</td>
<td>• Substitute to EFV or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Substitute to triple NRTIs or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Continue with 2 NRTIs + NVP in pregnant women or women of child bearing potential with careful hepatic monitoring</td>
</tr>
<tr>
<td>Second line ART</td>
<td>2 NRTIs + PI</td>
<td>Substitute to or continue (if already started) LPV/r and adjust dose of RTV</td>
</tr>
</tbody>
</table>

16. HBV and HCV co-infection:
The rates of HBV co-infection is relatively high in HIV-infected patients who acquired HIV through sexual contact, with rates of 7% of HBsAg positivity and up to 25% HBc antibody alone status (Ramia and Mokhbat, 2007). HCV seems more prevalent in the IDU subgroup of patients, with up to 25% HCV seropositivity (but very limited numbers). HIV impacts negatively the course of liver disease due to either HCV or HBV.

a. HBV: Three ARV agents have anti-HBV activity (3TC, FTC and TDF). In co-infected patients who qualify for ARV treatment, it is recommended to use 3TC or FTC and to combine with TDF because of the risk of HBV resistance to 3TC if used alone. EFV is the preferred NNRTI since NVP may be associated with increased risk of hepatotoxicity. HBV may flare during ARV therapy as part of IRIS and anti HBV drugs must be maintained. It is also noted that discontinuation of anti-HBV drugs or all ART may be associated with severe HBV reactivation and should be avoided.

b. HCV: The treatment of HCV consisting of pegylated interferon and ribavirin may have interactions with ARVs and therefore appropriate monitoring is indicated. For example:
   i. Ribavirin and DDI: increased risk of pancreatitis and lactic acidosis (to be avoided)
   ii. Ribavirin and ZDV: increased risk of anemia.
   iii. Interferon and EFV: worsened depression.
If CD4 is high, it is preferable to treat HCV first. If ART is indicated, it is preferable to delay anti-HCV therapy because better responses are obtained after immune reconstitution.

The recommend ARV regimen is similar to non-co-infected individuals, with EFV being the NNRTI of choice. Eventually, if EFV is contraindicated (allergy or pregnancy), a triple NRTI regimen may be used (ZDV + 3TC + ABC).

17. Injecting drug users:
The recommended ARV regimens in these cases are similar to the general population, but special attention should be placed on potential co-morbidities such as HCV and HBV, TB and on the issues of adherence. Management of drug use is part of the management of these patients. Special attention should be placed on the psychiatric risks of EFV and on potential drug drug interactions between ARVs and illicit substances of abuse. The blood levels of methadone may decrease after initiation of BNNRTIs or LPV and therefore, the dose of methadone should be increased 7 days after initiating an NNRTI or LPV. Methadone increases the blood levels of ZDV increasing its side effects. Methadone decreases the blood levels of the buffered tablet of DDI. Buprenorphine seems to have less significant drug interactions with ARVs.

18. Dosages of Antiretroviral drugs for adults and adolescents:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS</strong></td>
<td></td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
<td>300 mg twice daily or 600 mg once per day</td>
</tr>
<tr>
<td>Zidovudine (ZDV)</td>
<td>300 mg twice daily</td>
</tr>
<tr>
<td>Emtricitabine (FTC)</td>
<td>200 mg once daily</td>
</tr>
<tr>
<td>Didanosine (DDI)</td>
<td>60 kg: 400 mg once daily</td>
</tr>
<tr>
<td></td>
<td>&lt; 60 kg: 250 mg once daily</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>150 mg twice daily or 300 mg once per day</td>
</tr>
<tr>
<td><strong>NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS</strong></td>
<td></td>
</tr>
<tr>
<td>Tenofovir (TDF)</td>
<td>300 mg once per day</td>
</tr>
<tr>
<td><strong>NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS</strong></td>
<td></td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
<td>600 mg once per day at bedtime</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>200 mg once daily for 14 days, followed by 200 mg twice daily</td>
</tr>
<tr>
<td><strong>PROTEASE INHIBITORS</strong></td>
<td></td>
</tr>
<tr>
<td>Atazanavir + ritonavir (ATV/r)</td>
<td>300 mg + 100 mg once per day</td>
</tr>
<tr>
<td>Darunavir + ritonavir (DRV/r)</td>
<td>600 mg + 100 mg twice per day</td>
</tr>
<tr>
<td>Lopinavir + ritonavir (LPV/r)</td>
<td>3 capsules twice per day</td>
</tr>
<tr>
<td>(Capsules 133.3 mg/33.3 mg)</td>
<td>4 capsules twice daily if combined with an NNRTI</td>
</tr>
<tr>
<td>Need refrigeration</td>
<td></td>
</tr>
<tr>
<td>Lopinavir + ritonavir (LPV/r)</td>
<td>Treatment naive : 2 tabs twice daily</td>
</tr>
<tr>
<td>(Heat stable 200 mg/50 mg)</td>
<td>Treatment experienced : 3 tabs twice daily</td>
</tr>
<tr>
<td><strong>INTEGRASE INHIBITORS</strong></td>
<td></td>
</tr>
<tr>
<td>Raltegravir</td>
<td>400 mg twice per day</td>
</tr>
</tbody>
</table>

All antiretroviral may be stored at room temperature (< 30°C) except for ritonavir and lopinavir/ritonavir capsules which need refrigeration at 2-8°C.
19. Management of ARV toxicities (symptom oriented)

<table>
<thead>
<tr>
<th>ADVERSE EFFECT</th>
<th>RESPONSIBLE ARV</th>
<th>RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute pancreatitis</td>
<td>D4T, DDI</td>
<td>Discontinue ART. Supportive care. Laboratory monitoring. Resume ART with an NRTI with low pancreatic toxicity such as ZDV, ABC, 3TC, ABC.</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>DDI, LPV/r</td>
<td>Usually self-limited. Symptomatic treatment. No change of therapy needed.</td>
</tr>
<tr>
<td>Drug eruptions (mild to severe, including Stevens-Johnson syndrome or toxic epidermal necrolysis)</td>
<td>NVP, EV</td>
<td>In very mild cases, antihistamines and strict observation; regression may occur spontaneously. If mild/moderate rash, non-progressing and without mucosal involvement or systemic signs, consider a single NNRTI substitution (i.e. from NVP to EFV). In moderate and severe cases, discontinue ART and give supportive treatment. After resolution, resume ART with three NRTIs or two NRTIs + PIs</td>
</tr>
<tr>
<td>Dyslipidaemia, insulin resistance and hyperglycaemia</td>
<td>PIs</td>
<td>Consider replacing the suspected PI by drugs with less risk of metabolic toxicity. Adequate diet, physical exercise and antilipaemic drugs should be considered.</td>
</tr>
<tr>
<td>Condition</td>
<td>ARVs</td>
<td>Management</td>
</tr>
<tr>
<td>-----------</td>
<td>------</td>
<td>------------</td>
</tr>
<tr>
<td>GI intolerance, with taste changes, nausea, vomiting, abdominal pain and diarrhea.</td>
<td>All ARVs (less frequent with d4T, 3TC, FTC and ABC)</td>
<td>Usually self-limited, without need to discontinue ART. Symptomatic treatment.</td>
</tr>
<tr>
<td>Hematological toxicities (particularly anemia and leukopenia)</td>
<td>ZDV</td>
<td>If severe (Hg &lt;6.5 g% and/or ANC &lt;500 cells/mm3), replace by an ARV with minimal or no bone marrow toxicity (e.g. d4T, ABC or TDF) and consider blood transfusion.</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>All ARVs (particularly with NVP and ritonavir boosted PIs)</td>
<td>If ALT is at more than five times the basal level, discontinue ART and monitor. After resolution, replace the drug most likely associated with the condition.</td>
</tr>
<tr>
<td>Hyperbilirubinaemia (indirect)</td>
<td>ATV</td>
<td>Generally asymptomatic but can cause scleral icterus (without ALT elevations). Replace ATV with other PI.</td>
</tr>
<tr>
<td>Hypersensitivity reaction with respiratory symptoms, fever and without mucosal involvement.</td>
<td>ABC</td>
<td>Discontinue ABC and do not restart. Symptomatic treatment. Re-exposure may lead to a severe and potentially life threatening reaction.</td>
</tr>
<tr>
<td>Lactic acidosis</td>
<td>All NRTIs (particularly d4T and ddI)</td>
<td>Discontinue ART and give supportive treatment. After clinical resolution, resume ART, replacing the offending NRTI. ABC, TDF and 3TC are less likely to cause this type of toxicity.</td>
</tr>
<tr>
<td>Lipoatrophy and lipodystrophy</td>
<td>All NRTIs (particularly d4T)</td>
<td>Early replacement of the suspected ARV drug (e.g. d4T for TDF or ABC). Consider esthetic treatment and physical exercises.</td>
</tr>
<tr>
<td>Neuropsychiatric changes (sleep disturbances; depression; behavioural, concentration and personality changes)</td>
<td>EFV</td>
<td>Usually self-limited, without the need to discontinue ART. Symptomatic treatment if required. Effects may be enhanced by alcohol and...</td>
</tr>
</tbody>
</table>
Renal toxicity (nephrolithiasis) | IDV | IDV may be continued with hydration, laboratory monitoring and symptomatic treatment (50% recurrence rate). Consider replacing IDV with another PI.

Renal toxicity (renal tubular dysfunction) | TDF | Discontinue TDF and give supportive treatment. After clinical resolution, resume ART, replacing TDF.

Peripheral neuropathy | D4T, DDI | Consider replacement by an NRTI with minimal or no neurotoxicity (AZT, TDF or ABC). Symptomatic treatment with gabapentin should be considered.

20. Recommendations for drug resistance testing:
   a. Resistance testing is recommended:
      - With virologic failure
      - With suboptimal suppression of viral load
      - Testing prior to therapy is currently under investigation depending of transmitted resistance. If this is higher than 5%, pre-treatment resistance assay may be warranted.
   b. Resistance testing is not recommended:
      - After discontinuation of drugs (drug resistance testing should be done during treatment or at a maximum of 1 month within discontinuation of treatment)
      - When plasma viral load is less than 1000 copies/ml.

CONCLUSION:
This review considered the current knowledge about therapeutic approach to HIV infection. It is clear that the science behind such therapy is complex and rapidly evolving. HIV care requires open communication and partnership and a continuous discussion between the health care partners to provide the best care.
It is to be made clear that in the current state of knowledge and of treatment approach, the provision of HIV care and antiretroviral therapy is a life long program, based on commitment and adherence. These elements are based on the effective dialogue between caregiver and patient as well as the optimal and timely delivery of drugs by pharmaceutical suppliers and the governmental drug distribution system. The medical and pharmaceutical aspects cannot succeed without the legal support securing the rights of persons living with HIV to decent care, work and education, free from stigma and discrimination.
In the vision to provide efficiency and efficacy as well as simplicity to improve adherence and reduction of toxicity, the program provided a list of drugs that are considered best options in the current situation.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Generic Name</th>
<th>Brands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleoside Reverse Transcriptase Inhibitors and Nucleotide Reverse Transcriptase Inhibitors</td>
<td>ZDV Zidovudine</td>
<td>Zidovir, Retrovir</td>
</tr>
<tr>
<td></td>
<td>3TC Lamivudine</td>
<td>Lamivir, Epivir</td>
</tr>
<tr>
<td></td>
<td>ddl Didanosine</td>
<td>Dinex, Videx</td>
</tr>
<tr>
<td></td>
<td>TDF Tenofovir</td>
<td>Tenvor, Viread</td>
</tr>
<tr>
<td></td>
<td>ABC Abacavir</td>
<td>Abamune, Ziagen</td>
</tr>
<tr>
<td>Non Nucleoside Reverse Transcriptase Inhibitors</td>
<td>NVP Nevirapine</td>
<td>Nevimune, Viramune</td>
</tr>
<tr>
<td></td>
<td>EFV Efavirenz</td>
<td>Efavir, Stocrin, Sustiva</td>
</tr>
<tr>
<td>Protease Inhibitors</td>
<td>LPV/r Lopinavir/ritonavir</td>
<td>Lopimune, Kaletra, Aluvia</td>
</tr>
<tr>
<td></td>
<td>RTV Ritonavir</td>
<td>Ritomune, Norvir</td>
</tr>
<tr>
<td>Integrase Inhibitors</td>
<td>RAL Raltegravir</td>
<td>Isentress</td>
</tr>
<tr>
<td>Combinations</td>
<td>ZDV/3TC Zidovudine/Lamivudine</td>
<td>Duovir, Combivir</td>
</tr>
<tr>
<td></td>
<td>TDF/FTC Tenofovir/Emtricitabine</td>
<td>Tenvor EM Truvada</td>
</tr>
<tr>
<td></td>
<td>TDF/FTC/EFV Tenofovir/Emtricitabine/Efavirenz</td>
<td>Viraday, Atripla</td>
</tr>
</tbody>
</table>

Additional agents of interest for salvage regimens
- Darunavir (Prezista)
- Atazanavir (Reyataz)
- Etravirine (Intelence)