Antiretroviral agents

Other separate articles related to human immunodeficiency virus (HIV) include Human Immunodeficiency Virus (HIV), Congenital HIV and Childhood AIDS, Complications of HIV Infection, Management of HIV In Pregnancy, Acquired Immune Deficiency Syndrome (AIDS), and HIV and Skin Disorders.

The human immunodeficiency virus (HIV) is a retrovirus that causes immunodeficiency by infecting and destroying cells of the immune system, particularly the CD4 cells. Acquired immune deficiency syndrome (AIDS) occurs when the number of CD4 cells fall to below 200 cells/microlitre; opportunistic infections and malignancies (AIDS-defining illnesses) can develop.

The prognosis of HIV and AIDS has greatly improved due to more effective and better tolerated antiretroviral therapy (ART). If on ART for 6 months and viral load is undetectable, HIV can't be transmitted.

Antiretroviral therapy aims to achieve an undetectable viral load, to preserve immune function, to reduce the mortality and morbidity associated with chronic HIV infection, and to reduce onward transmission of HIV, whilst minimising drug toxicity. Treatment with a combination of ART aims to improve the physical and psychological well-being of infected people.

Antiretroviral agents[1]

Drugs that are licensed for the treatment of HIV/AIDS are as follows:

- Nucleoside reverse transcriptase inhibitors (NRTI or 'nucleoside analogue'): abacavir, emtricitabine, lamivudine, tenofovir alafenamide fumarate, tenofovir disoproxil fumarate, and zidovudine.
- Non-nucleoside reverse transcriptase inhibitors (NNRTI): doravirine, efavirenz, etravirine, nevirapine, and rilpivirine.

- Protease inhibitors: atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, and saquinavir.
- CCR5 antagonists: maraviroc.
- Integrase inhibitors: bictegravir, cabotegravir, dolutegravir, elvitegravir, and raltegravir.
- Fusion inhibitors: enfuvirtide.
- Attachment inhibitors: fostemsavir.
- Pharmacokinetic enhancers: cobicistat, and low-dose ritonavir (boost the concentrations of other antiretrovirals metabolised by CYP3A4).

Initiation of treatment[2]

All patients with suspected or diagnosed HIV should be reviewed promptly by a HIV specialist. All patients diagnosed as being HIV positive should be offered immediate treatment, irrespective of CD4 cell counts. Low adherence to treatment can be associated with drug resistance, progression to AIDS, and death.

Treatment of HIV infection in treatment-naive patients is initiated with a combination of two nucleoside reverse transcriptase inhibitors (NRTIs) plus one of the following as a third drug:

- An integrase inhibitor.
- A non-nucleoside reverse transcriptase inhibitor (NNRTI).
- A boosted protease inhibitor.

The combination of two nucleoside reverse transcriptase inhibitors (NRTIs) usually includes emtricitabine and either tenofovir disoproxil or tenofovir alafenamide. An alternative is abacavir and lamivudine. The third drug of choice is either atazanavir or darunavir both boosted with ritonavir, or dolutegravir, or elvitegravir boosted with cobicistat, or raltegravir, or rilpivirine. Efavirenz may be used as an alternative third drug.

Patients who require treatment for both HIV and chronic hepatitis B should be treated with antivirals active against both diseases as part of fully suppressive combination ART. Regimens of choice are tenofovir disoproxil and emtricitabine, or tenofovir alafenamide and emtricitabine. Deterioration of the condition (including clinical, virological, and CD4 cell count changes) may require a change in therapy.[2]

HIV infection in pregnancy[3]

Management of HIV infection should focus on ensuring that the ART regimen maximally suppresses viral replication as early as possible (if possible before conception) in order to minimise vertical transmission of HIV.

Information on the teratogenic potential of most antiretroviral drugs is limited, however, all pregnant women living with HIV who conceive whilst on effective ART should continue this treatment throughout their pregnancy. All other women should start ART during their pregnancy.

The recommended regimen is a NRTI backbone of either tenofovir disoproxil or abacavir with either emtricitabine or lamivudine; the third drug should be efavirenz or atazanavir boosted with ritonavir. All treatment options require careful assessment by a specialist.

Breast-feeding by HIV-positive mothers may cause HIV infection in the infant and should be avoided.

Pre-exposure prophylaxis[4]

Emtricitabine with tenofovir disoproxil may be appropriate for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in combination with safer sex practices in adults at high risk.

Tenofovir disoproxil alone is an alternative for HIV-negative heterosexual individuals when emtricitabine is contra-indicated.

PrEP is widely available throughout the UK from genitourinary medicine (GUM) clinics, as part of a risk management programme which will include regular testing.

Post-exposure prophylaxis[5]

Prompt prophylaxis with antiretroviral drugs [unlicensed indication] may be appropriate following exposure to HIV-contaminated material. Immediate expert advice should be sought.

Prompt prophylaxis with antiretroviral drugs [unlicensed indication] may also be appropriate following potential sexual exposure to HIV where there is a significant risk of viral transmission.
The recommended treatment for post-exposure prophylaxis is emtricitabine with tenofovir disoproxil plus raltegravir for 28 days.

Post-exposure prophylaxis should be initiated as soon as possible after exposure, preferably within 24 hours. Post-exposure prophylaxis should not be initiated beyond 72 hours after exposure.

Adverse effects of antiretroviral therapy[6]

Antiretroviral therapy (ART) can have multiple adverse effects. Always consider whether specialist advice or hospital admission is required. Do not stop any ART or adjust the dose without specialist advice. Some minor adverse effects may herald a major adverse effect, and so have a low threshold for seeking specialist advice. Serious adverse effects may present in unusual ways such as osteoporosis, Fanconi syndrome, or lactic acidosis.

Adverse effects include: (always check the British National Formulary [BNF] for detailed information)

- Hypersensitivity: typically causes a rash but can cause non-specific symptoms such as fever, vomiting, or myalgia. Hypersensitivity can be life threatening.
- Neurological and psychiatric: nightmares, sleep disturbance, mood or behaviour changes may occur. Psychosis and suicidal ideation. Peripheral neuropathy.
- Hyperlipidaemia (common): increases in cholesterol or triglycerides can be extreme. Lipids need to be regularly monitored and managed. Drug interactions with statins and fibrates occur frequently and can be serious (seek specialist advice before prescribing). .

- Lipodystrophy (changes in the distribution of body fat) and lipoatrophy (loss of subcutaneous fat).
    - May be associated with diabetes, and hyperlipidaemia.
    - Deep dermal injection of non-absorbable gel polymer for HIV-related lipoatrophy is available but infection, granuloma formation and migration are common side effects. NICE recommends that the procedure should only be used with special arrangements for clinical governance, consent and audit or research.[7]
    - See also the leaflet on Lipodystrophy Syndrome.
- Type 2 diabetes mellitus: most likely occurs through insulin resistance and can be associated with ART.
- Bone density loss: higher risk of osteopenia, osteoporosis, and fractures.
- Renal problems: decline in renal function may indicate Fanconi's syndrome (dysfunction of the proximal tubule). Seek specialist advice. Ureteric colic, renal and ureteric stones may also occur.
- Lactic acidosis and hepatic toxicity: may present with non-specific symptoms such as nausea, anorexia, or abdominal pain. It is potentially life threatening.
- Bone marrow suppression.
- Pancreatitis (most often associated with older ART).

Further reading

- Cote J, Godin G, Ramirez-Garcia P, et al; Virtual intervention to support self-management of antiretroviral therapy among people living with HIV. J Med Internet Res. 2015 Jan 6;17(1):e6. doi: 10.2196/jmir.3264.
- Cabotegravir with rilpivirine for treating HIV-1; NICE Technology appraisal guidance, January 2022

Authored by:	Peer Reviewed by: Dr Toni Hazell	
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