In patients with very low CD4 counts (well below the normal range of 800–1200/μL), ART may cause exacerbation of hepatitis due to recovery of cellular immunity, in a phenomenon known as Immune Reconstitution Inflammatory Syndrome (IRIS). In the majority of cases, IRIS is observed within 16 weeks of starting ART. It can be difficult to distinguish between IRIS and drug-induced liver injury.

An issue with ART is the potential for drug-induced liver injury associated with the use of anti-HIV agents, particularly protease inhibitors (PI) and non-nucleoside reverse transcriptase inhibitors (NNRTI). The risk of liver injury generally decreases during ongoing ART;[362] it is however more likely in patients with advanced liver fibrosis, and particularly cirrhosis. Cessation of ART or a change in the agents used should be considered if liver injury is detected or hepatic function deteriorates.

Prolonged administration of tenofovir and/or adefovir can lead to renal damage.[363] In the case of tenofovir, this may be irreversible.[364] For this reason, changes in the drug regimen should be considered before the estimated glomerular filtration rate (eGFR) falls below 60% or phosphorus reabsorption falls below 70%.

6.4.3 Problems with treatment and responses

Before commencing ART including anti-HBV agents, it is important to check for a history of treatment with anti-HBV agents such as lamivudine, adefovir, entecavir or any of the anti-HIV drugs listed in Table 16. If any of these agents have been administered in the past, an infectious diseases specialist should be consulted regarding the choice of ART agents.

Functional hepatic reserve should also be evaluated prior to commencing ART including anti-HBV agents, given that IRIS can potentially exacerbate hepatitis in patients with a low hepatic reserve. Protease inhibitors and NNRTIs known to cause hepatic dysfunction should be avoided with these patients.

Entecavir is not recommended for patients coinfected with HIV and HBV not being administered anti-HIV agents, as it can lead to the emergence of drug-resistant HIV.

All the abovementioned factors should be considered in selecting the ART regimen. The ART regimen should consist of a backbone of either tenofovir (TDF) with emtricitabine (FTC), or tenofovir (TDF) with lamivudine (3TC), together with a key drug (integrase inhibitor, NNRTI or PI).

Where IRIS occurs during ART including anti-HBV agents, it is usually only transient in nature. Although it is generally held that cessation of ART should be considered when transaminase levels reach more than five to ten times the baseline level, it is preferable to address the problem without interrupting ART.

If it proves necessary to cease administration of an anti-HIV drug with anti-HBV activity (such as lamivudine, emtricitabine, tenofovir or Truvada (emtricitabine+tenofovir)) due to adverse reactions associated with ART, there is a danger of recurrence or aggravation of hepatitis. Where possible, two anti-HBV agents should be administered instead. Consideration should be given to entecavir+adefovir combination therapy.

It is rare for treatment to be indicated for HBV alone, and "treatment of HIV infection not indicated or not wanted". If this situation does arise, Peg-IFNα-2a therapy should be considered.

Specific directions regarding coinfections with HBV and HIV are set out in the HIV Guidelines.[365,366]

Recommendations

- *In patients with very low CD4 counts (well below the normal range of 800–1200/μL), ART may exacerbate hepatitis due to recovery of cellular immunity.*
- *When administering ART, we should take into consideration the potential for anti-HIV agents to cause drug-induced liver injury.*
- *Before commencing ART involving anti-HBV agents, it is important to check for a history of treatment with anti-HBV agents.*
- *Before commencing ART involving anti-HBV agents, it is important to evaluate functional hepatic reserve.*
- *The ART regimen should consist of a backbone of either tenofovir (TDF) with emtricitabine (FTC), or tenofovir (TDF) with lamivudine (3TC), together with a key drug (integrase inhibitor, non-nucleoside reverse transcriptase inhibitor or protease inhibitor).*
- *If it is necessary to cease administration of an anti-HIV drug with anti-HBV activity due to adverse reactions associated with ART, there is a danger of recurrence or aggravation of hepatitis. Where possible, two anti-HBV agents should be administered instead. Consideration should be given to entecavir+adefovir combination therapy.*

CONFLICTS OF INTEREST

THE MEMBERS OF Drafting Committee for Hepatitis Management Guidelines have received consultant

fees from GlaxoSmithKline, royalty from SRL, lecture fees from Ajinomoto Pharmaceuticals, MSD, Daiichi-Sankyo, Dainippon-Sumitomo Pharma, Mitsubishi Tanabe Pharma, Chugai Pharmaceutical, Bristol-Myers-Squibb, and research support from Eisai, MSD, Kan Research Institute, GlaxoSmithKline, Chugai Pharmaceutical, Bristol-Myers-Squibb, Daiichi-Sankyo, Mitsubishi Tanabe Pharma, Dainippon-Sumitomo Pharma, Toray, Minophagen Pharmaceutical.

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