**Table 1 Indications for HIV testing – BHIVA guidelines [6] adapted to include rheumatological conditions**

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|  | **AIDS-defining conditions** | **Other conditions where HIV testing should be offered** |
| **Respiratory** | Tuberculosis | Bacterial pneumonia |
|  | Pneumocystis | Aspergillosis |
| **Neurology** | Cerebral toxoplasmosis | Aseptic meningitis/encephalitis |
|  | Primary cerebral lymphoma | Space occupying lesion of unknown cause |
|  | Cryptococcal meningitis | Cerebral abscess |
|  | Progressive multifocal leucoencephalopathy | Guillain–Barré syndrome |
|  |  | Transverse myelitis |
|  |  | Peripheral neuropathy |
| **Dermatology** | Kaposi’s sarcoma | Severe or recalcitrant seborrhoeic dermatitis |
|  |  | Severe or recalcitrant psoriasis |
|  |  | Multidermatomal or recurrent herpes zoster |
| **Gastroenterology** | Persistent cryptosporidiosis | Oral candidiasis |
|  |  | Oral hairy leukoplakia |
|  |  | Chronic diarrhoea of unknown cause |
|  |  | Weight loss of unknown cause |
|  |  | Salmonella, shigella or campylobacter |
|  |  | Hepatitis B infection |
|  |  | Hepatitis C infection |
| **Oncology** | Non-Hodgkin’s lymphoma | Anal cancer or anal intraepithelial dysplasia |
|  |  | Lung cancer |
|  |  | Seminoma |
|  |  | Head and neck cancer |
|  |  | Hodgkin’s lymphoma |
|  |  | Castleman’s disease |
| **Gynaecology** | Cervical cancer | Vaginal intraepithelial neoplasia |
|  |  | Cervical intraepithelial neoplasia Grade 2 or above |
| **Haematology** |  | Any unexplained blood dyscrasia including:  • thrombocytopenia  • neutropenia  • lymphopenia |
| **Ophthalmology** | Cytomegalovirus retinitis | Infective retinal diseases including herpesviruses and toxoplasma |
|  |  | Any unexplained retinopathy |
| **ENT** |  | Lymphadenopathy of unknown cause |
|  |  | Chronic parotitis |
|  |  | Lymphoepithelial parotid cysts |
| **Other** |  | Other Mononucleosis-like syndrome (primary HIV infection) |
|  |  | Pyrexia of unknown origin |
|  |  | Any lymphadenopathy of unknown cause |
|  |  | Other Mononucleosis-like syndrome (primary HIV infection) |
|  |  | Any sexually transmitted infection |
| **Rheumatological** |  | Sexually-acquired reactive arthritis or reactive arthritis with unknown mode of acquisition  Suggested rheumatological presentations to add to BHIVA guidance |
|  |  | Keratoconjunctivitis sicca symptoms in the absence of anti-Ro or anti-La antibodies (DILS) |
|  |  | Atypical lupus |
|  |  | Vasculitis |
|  |  | Unexplained autoantibodies |

Note: HIV antibody testing (and Hepatitis B and C) is also recommended for rheumatological patients prior to commencement of biologic therapies

**Table 3 A review of the use of disease-modifying anti-rheumatic drugs and biologics among patients with known HIV infection for control of inflammatory diseases, transplant patients and skin psoriasis**

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| --- | --- | --- | --- | --- |
| **Drug** | **Comment** | **Efficacy /safety** | **Interactions with cART** | **Personal experience** |
| Hydroxychloroquine | Hydroxycholoroquine (HCQ) inhibits HIV infectivity through immunomodulatory effects, inhibits viral replication and increases circulating CD4+ T cells [76-78]. Chloroquine and Hydroxychloroquine under investigation for use in suppressing immune activation that remains despite effective viral suppression with cART [79]. | Generally safe and well-tolerated. Appears to have been widely used in HIV patients, particularly for dermatological disease. | None identified | Used safely in several patients without safety issues and with good benefit |
| Sulfasalazine | Possible immunomodulatory effect on HIV viral infectivity [80] | From three published reports including 17 patients with HIV and seronegative spondyloarthropathy, there is evidence of a good response in the majority of patients (14/17= 82%) (often in < 1 month) and no bone marrow, renal or liver toxicity [81]. | None identified but hypothetical interaction with zidovudine (extra monitoring required) | Used safely in several patients without safety issues and with good benefit |
| Methotrexate | Used in combination chemotherapy for lymphoma patients | Most reports in the pre-cART era reported poor outcomes, and even death [8,62]. Since however, there have been increasing numbers of case reports of its safe, effective use among patients with psoriasis, psoriatic arthritis, RA and dermatomyositis over the course of months and even years [54,82]. It may be that methotrexate does not adversely affect the natural course of HIV disease but the literature reflects publication bias. The use of methotrexate is now recommended for the treatment of refractory severe psoriasis by the National Psoriasis Foundation in their 2009 guidance (grade III evidence) [83]. | No identified interactions with any cART but very low quality evidence as co-administration has not been studied at rheumatological doses. In high dose chemotherapy, MTX elimination half-life was not influenced use of non-nucleoside reverse transcriptase inhibitors or integrase inhibitors (p = 0.15). Similarly, different NRTI backbones did not affect MTX elimination kinetics despite the potential overlapping competition for active renal tubular transporters between MTX and tenofovir [84]. | Used in 5 patients with suppressed viral activity and CD4+ > 200 without side effects |
| Leflunomide | Leflunomide has been shown to have virostatic properties against several viruses, including HIV-1, so that it may be a safe drug to use in the context of HIV [85]. |  | No data on interactions | Not used personally. Anecdotal report of safe use in two patients |
| Azathioprine |  | There were few data on azathioprine but a recent review of its use in 7 patients suggested that it had been used safely, without opportunistic infections, over a median of 12 months although two died but the authors stated ‘neither death was associated with azathioprine therapy’ [86]. Of note, the only rheumatic syndrome treated with azathioprine in this series was myositis in one patient. | For most cART, no interactions expected. Azathioprine is partly inactivated via the enzyme xanthine oxidase, which also metabolises didanosine and zidovudine so competition could possibly increase the risk of toxicity and monitoring of haematological parameters is recommended. | Used in 2 patients with suppressed viral activity and CD4+ > 200 without side effects |
| Ciclosporin-A |  | Ciclosporin-A has been used in HIV patients, particularly in the context of organ transplantation, those with nephritis and dermatological patients – very few data from rheumatological use | There are complex drug interactions between Ciclosporin-A and protease inhibitors and non-nucleoside reverse transcriptase inhibitors | Not used personally |
| Mycophenolate mofetil | There have been in vitro and in vivo studies showing that MMF has some promising anti-viral activity against HIV-1. | There are few data on the use of Mycophenolate (MMF), except in renal and SLE patients [55,87-88]. | Interactions only studied for: Abacavir, Indinavir, Ritonavir, Nevirapine, Didanosine, 3TC. Results suggest increased clearance of nevirapine. Co-administration of inducers or inhibitors of glucuronidation, such as some PIs and NNRTIs, could alter mycophenolate levels. Concentration monitoring of mycophenolate is recommended. Close monitoring of renal function recommended if co-administered with Tenofovir. | Used twice safely in patients with viral suppression and CD4+ count>200 |
| Gold | Auranofin under investigation for possible beneficial effects on HIV viral activity [89] | No published data on use of Myocrisin in HIV | No data on interaction | Not used personally |
| Anti-TNFɑ | TNFɑ is involved in viral replication and pathogenesis of HIV. TNFɑ production elevated even in patients taking cART with complete viral suppression. Trials in HIV infected patients showed TNFɑ suppression achieved with inhibitors [90]. | There have been increasing numbers of case reports and series of use of anti TNFɑ therapies in HIV, including: Infliximab, Etanercept and Adalimumab. They have been successfully used in psoriasis, psoriatic arthropathy, AS, RA, Crohn’s, colitis, Spondyloarthropathy and Reiter’s syndrome [91-95]. | Review reported published use in 27 patients [95] Largest series was 8 patients [93], all with CD4+ cell count > 200 cells /mm3 and viral load < 60,000 copies/ml. No patients experienced HIV progression or opportunistic infections over 48 months follow-up. In one case report, the patient experienced frequent secondary infections which required discontinuation after 4 months (CD4<50) [92]. There are few long term data published presently but one patient, co-infected with HIV and Hepatitis C was successfully treated with infliximab over 11 years of follow-up without serious infection [94]. | Infectious complications seen in 4/27 (15%) of patients. Particular caution over screening for TB in patients with HIV considered for anti-TNFɑ therapy. Used safely in three patients. |
| Rituximab |  | Widely used as part of lymphoma treatment. Two studies of rituximab monotherapy in HIV-associated multicentric Castleman disease showed no increased risk of infection but a potential for reactivation of Kaposi sarcoma [97-98]. HIV viral load and absolute CD4 counts were not affected during therapy [98]. Successful and safe use to induce pemphigus remission [96]. | No recognised drug interactions. Theoretical risk of haematological toxicity with zidovudine | Caution: HIV associated with increased risk of PML. Used safely in 1 patient who had received previously for lymphoma. |