

SUPPLEMENTARY MATERIAL

1. Hepatitis B Virus (HBV)

Hepatitis B virus (HBV) is a DNA virus that belongs to the Hepadnaviridae family. HBV replicates in hepatocytes and also integrates within the host DNA (1). About 350 million people worldwide including 2.2 million in United States have chronic HBV infection that may eventually cause liver failure, cirrhosis or hepatocellular carcinoma (2, 3). A recent, prospective multi-center study in Spain, Registro Hepatitis Enfermedad Inflamatoria Intestinal (REPENTINA), showed that the prevalence of HBV infection in IBD patients is similar to that of the general population (4). Patients with ongoing HBV infection who are Hepatitis B surface antigen (HBsAg) positive can be active {circulating Hepatitis B e antigen (HBeAg) or anti-HBe and have a viral load ≥ 2000 IU/ml, abnormal alanine aminotransferase [ALT], and signs of hepatic disease}, or inactive (serum anti-HBe positive, persistently normal ALT levels and HBV DNA < 2000 IU/ml) carriers (1). Patients with resolved HBV infection are HBsAg negative and have antibody to Hepatitis B core antigen (anti-HBc), usually defined as ‘anti-HBc carriers’ (5). The risk of HBV reactivation in HBsAg-negative/anti-HBc-positive patients with rheumatological disorders or IBD receiving anti-TNF therapy appears to be low (5). Risk factors for HBV reactivation in the IBD population are high serum HBV DNA levels, exposure to more than one immunosuppressant, prolonged immunosuppression and absence of antiviral prophylaxis (5). Reactivation ranges from asymptomatic self-limiting hepatitis to a more severe and potentially fatal hepatitis and chronic hepatitis (1, 6, 7). The American Association for the Study of Liver Disease (AASLD) and the European Association for the Study of the Liver (EASL) recommend early treatment with nucleoside/ nucleotide analogues (lamivudine,

entecavir or tenofovir) for HBsAg-positive patients requiring immunosuppressive therapies (1, 8). Patients with chronic active hepatitis on immunosuppression should receive lifelong antiviral treatment with the later generation nucleoside/nucleotide analogues, while the inactive HBV carriers should receive prophylaxis with lamivudine (1, 8). Entecavir or tenofovir are preferred in patients expected to be on immunosuppression for more than 1 year, to minimize the emergence of drug resistance (9). For HBsAg –positive patients with IBD receiving immunosuppression, prophylaxis should begin 1-3 weeks prior to start of immunosuppression, and continue at least 6 months after withdrawal (5, 9). This is essential as cases of hepatitis B flare-ups have been reported 2-3 months after withdrawal of immunosuppression (6). Systemic prophylaxis is not recommended for Anti HBc positive patients, although periodic monitoring of liver function tests and HBV DNA is recommended (1, 8-10). All patients diagnosed with IBD should undergo HBV screening at the time of diagnosis, and be vaccinated against HBV, if they are not immune (1, 8).

2. Hepatitis C virus (HCV)

HCV virus is a major cause of parenterally acquired viral hepatitis, and affects over 170 million people worldwide (11). The acute infection is generally benign, although 60-70% of cases progress to chronic disease; sequelae of chronic disease involving cirrhosis or hepatocellular carcinoma (5, 12). The risk of reactivation of HCV during immunomodulator/ immunosuppressive therapy is extremely low; hence, universal screening of IBD patients is currently not recommended and even ECCO consensus guidelines could not reach a consensus (9). EASL and AASLD have not considered the IBD population on immunosuppressants as an at-risk group for whom universal screening is mandated (12, 13). However, both CDC and

USPSTF have recently recommended one time screening for persons born during 1945-1965 for hepatitis C without any risk factor or known liver disease (14, 15). Case series of HCV-infected patients with arthropathy and psoriasis treated with methotrexate or TNF- α inhibitors have not shown any detrimental results, with the exception of a few patients having elevated ALT or AST level (16-18). To summarize, immunosuppression in HCV patients seems to be low risk, but serial monitoring of liver functions tests (3 monthly if patient is on anti-TNF- α inhibitors) is recommended (5).

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