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Dr. Reddy is the Ruimy Family President’s Distinguished Professor of Medicine and Professor of Medicine in Surgery in the Division of Gastroenterology/Hepatology at the University of Pennsylvania in Philadelphia, Pennsylvania. He is the Director of Hepatology, Medical Director of Liver Transplantation, and the Director of the Viral Hepatitis Center. A Fellow of the American College of Physicians, American College of Gastroenterology, and the Royal College of Physicians (UK), and Dr. Reddy is also a Fellow of the American Association for the Study of Liver Diseases. He has held several Visiting Professorships at Medical Schools throughout the World. He has trained several fellows and mentored numerous research assistants throughout his career.

Dr. Reddy has authored or co-authored over 400 peer-reviewed papers on a spectrum of hepatobiliary topics that include liver transplantation, chronic C viral hepatitis, HIV and the liver, and hepatocellular carcinoma. In addition, he has edited and contributed to several text books, and has participated in numerous scientific presentations at National and International meetings. He serves on the editorial boards of prestigious journals such as Liver Transplantation, Hepatology, Liver International, and is an ad-hoc reviewer for several journals.

Dr. Reddy also has participated in a number of clinical trials that have advanced the understanding of the therapy of chronic viral hepatitis. He has been the recipient of both federal and non-federal funding for clinical research. His current research interests include areas of liver transplantation, viral hepatitis, and hepatocellular carcinoma.

Abstract: Reactivation of hepatitis B in clinical trials with immune suppressive drugs

Reactivation of Hepatitis B (HBVr) is associated with significant morbidity and mortality. It is well recognized that this is a preventable consequence of hepatitis B infection. (HBVr) is known to occur spontaneously although lately the attention has been on cases of HBVr seen in the context of immunosuppressive therapy and in those who received oral directly acting anti-viral (DAA) hepatitis C (HCV) therapy. HBVr reactivation occurs more often in those with positive hepatitis B surface antigen (HBsAg) but can be seen in those with resolved HBV infection (negative HBsAg, but positive anti-HBc with or without positive anti-HBs). Although specific cellular immunologic mechanisms have not been fully delineated, the initial event is believed to be a disruption in the ability of the host immune system to control hepatitis B virus (HBV) replication.

There have been heterogeneous definitions of HBVr that are based on viral, biochemical, and
clinical characteristics. Although the definition of HBVr has varied, it is desirable to prevent the end clinical manifestation of hepatic decompensation or acute liver failure. Several aspects of HBVr prevention remain unclear, including the optimal population to screen for risk for HBVr, in whom to use prophylaxis with anti-HBV agents, the best specific agent to use, the duration of prophylaxis, and the type and duration of monitoring if prophylaxis is not used in those at risk.

The risk of HBVr varies with the type of immunosuppression and the serologic status. While there is relatively sparse data in most situations, there is concrete data in certain situations where the risk of HBVr in quite high even in those with isolated anti-HBc, such as those exposed to the B-cell depleting agents (e.g., Rituximab, ofatumumab), and anthracycline derivatives (e.g., doxorubicin, epirubicin). Based on experiences published in the literature, those at risk for HBVr can be categorized into high risk (> 10% risk), moderate risk (1-10%), and low risk (< 1%) groups and the recommendations for prophylaxis vary according to the risk and the serologic status.

More recent data have emerged suggesting that those with HCV who are co-infected with hepatitis B virus (HBV) may be at risk for HBVr during or following HCV treatment. This most often included those who were HBsAg positive but infrequently was seen in those who were hepatitis B surface antigen (HBsAg) and hepatitis B surface antibody (anti-HBs) negative, but hepatitis B core antibody (anti-HBc) positive. In early October 2016, the U.S. Food and Drug Administration (FDA) released a black box warning about the risk of HBVr following treatment with DAAs for chronic HCV infection. This reactivation has been noted to occur in the background of current or previous HBV infection. According to the FDA, 24 cases of hepatitis B reactivation were identified in HBV/HCV co-infected patients over 20 months from 2013-2016. Of these, two patients died and one required a liver transplant. To that end, the AASLD/IDSA Guidance document recommends that all patients initiating HCV DAA therapy be assessed for HBV coinfection with HBsAg, anti-HBs, and anti-HBc. For those who are HBsAg positive but not on HBV suppressive therapy, monitoring of HBV DNA levels during and immediately after DAA therapy for HCV is recommended and antiviral treatment for HBV be initiated if treatment criteria for HBV are met. No specific recommendations for the monitoring of patients testing positive either for anti-HBc alone (isolated anti-HBc) or for anti-HBs and anti-HBc (immune recovery) have been made because of the lack of robust data in such situations. In summary, HBVr can be a serious and life threatening clinical manifestation and is well recognized to occur, but with variable risk, after exposure to a spectrum of drugs. Most often high quality data are lacking to make strong recommendations regarding prophylaxis versus only follow up. Large data base analyses and prospective studies are needed to specifically examine the risk in certain situations such as those receiving DAA HCV therapy. This particularly applies to HBV endemic areas where HCV is quite prevalent and while there are efforts towards global eradication of HCV.