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Personalized Therapy of Chronic Hepatitis C and B Dually Infected Patients With Pegylated Interferon Plus Ribavirin

A Randomized Study

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Abstract: We aimed to investigate whether response-guided therapy (RGT) with peginterferon-alpha plus ribavirin by using hepatitis C virus (HCV) genotype, pretreatment HCV RNA levels, and rapid virological response (RVR, undetectable HCV RNA at treatment week 4) could be applied for active HCV/hepatitis B virus (HBV) dually infected patients, without compromised the treatment efficacy.

A total of 203 patients, seropositive of HCV antibody, HCV RNA and HBV surface antigen (HBsAg), and seronegative for HBV e antigen for >6 months, were randomized to receive peginterferon-alpha/ribavirin by either genotype-guided therapy (GGT, n = 102: HCV genotype 1 [HCV-1], 48 weeks; HCV-2/3, 24 weeks) or RGT (n = 101: HCV-1, 48 or 24 weeks if patients with baseline VL <400,000 IU/mL and RVR; HCV-2/3, 24 or 16 weeks if patients with RVR). The primary endpoint was HCV-sustained virological response (SVR).

The HCV SVR rate was comparable between the GGT (77.5%, 79/102) and RGT groups (70.3%, 71/101, $P = 0.267$), either among HCV-1/HBV (69.4% [43/62] vs 63.5% [40/63], $P = 0.571$) or among HCV-2/3/HBV (90.0% [36/40] vs 81.6% [31/38], $P = 0.342$) dually infected patients based on intention-to-treat analysis. In HCV-1/HBV dually infected patients, RVR (odds ratio [OR]: 6.05; 95% confidence intervals [CI]: 2.148–17.025, $P = 0.001$) and lower pretreatment blood glucose levels (OR: 0.97; CI: 0.944–0.989, $P = 0.003$) were independent predictors of HCV SVR. Although RVR (OR: 10.68; CI: 1.948–58.514, $P = 0.006$) was the only significant factor associated with HCV SVR in HCV-2/3/HBV dually infected patients. HBsAg loss at 1 year posttreatment was observed in 17 of 185 (9.2%) patients. The rates of discontinuation and adverse events were similar between the 2 groups.

RGT with peginterferon-alpha/RBV may be considered for HBeAg-negative HBV/HCV dually infected patients.

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Abbreviations: AE = adverse event, Anti-HCV = HCV antibodies, DAA = directly acting antiviral agent, EOTVR = end-of-treatment virological response, EVR = early virological response, GGT = genotype-guided therapy, HBeAg = hepatitis B e antigen, HBsAg = HBV surface antigen, HBV = hepatitis B virus, HCV = hepatitis C virus, HCV-1 = HCV genotype 1, ITT = intent-to-treat, LVL = low baseline viral load, Peg-IFN = PEGylated interferon-alpha, PP = per-protocol, RBV = ribavirin, RGT = response-guided therapy, RVR = rapid virological response, SAE = serious adverse events, SVR = sustained virological response, ULN = upper limit of normal, VL = viral load.

INTRODUCTION

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are the leading causes of liver cirrhosis and hepatocellular carcinoma.[1,2] In HBV and HCV high endemic areas, such as the Asia-Pacific region, dual infection with HBV and HCV is not uncommon. Approximately 10% of patients are dually infected with both viruses in Taiwan.[3] Dually infected patients have been at a much higher risk for the aggravation and progression of liver disease than those with monoinfection.[4,5]

Current guidelines for the management of HBV/HCV dual infections suggest that which virus is dominant for patients with concurrent HBV/HCV dual infections should be determined and to accordingly treat patients as monoinfections.[6] PEGylated interferon (Peg-IFN) and ribavirin (RBV) combination therapy is the currently standard of care for HBV/HCV dually infected

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