New Biomarkers for Early Detection of Hepatocellular Carcinoma

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Although considerable progress has been made in treatments of hepatocellular carcinoma (HCC), no effective systemic cytotoxic chemotherapy has been established (Lopez et al., 2006). Surgical resection or percutaneous intervention (radiofrequency ablation and ethanol injection) therapy is effective only at an early stage of HCC. Approximately 70% of these patients develop recurrent tumors within five years. Transarterial chemoembolization is reserved for patient intermediate stage HCC without portal invasion or extrahepatic metastasis. Molecular target therapy, especially that targeting the angiogenesis pathway, is now developing as a novel anti-HCC therapy. However, to date, none of these novel has exhibited superior efficacy to sorafenib. Although, sorafenib is the only currently available therapeutic option for patients with advanced-stage HCC, they are required to have a performance status of 0–2 and an A Child–Pugh classification (Llovet and Bruix, 2008). Overall, with the currently available diagnostic techniques and therapies, the prognosis of HCC depends on the stage of the disease at the time of diagnosis and remaining liver function. Thus, lesions detected at screening must be aggressively investigated because treatment of early HCC has a high cure rate.

Patients at risk for HCC should undergo surveillance with ultrasonography, CT scan, or MRI at 6-monthly intervals. Serum-α-fetoprotein (AFP) and protein induced vitamin K absence (PIVKA)-II are the most common markers available to detect HCC. Des gamma carboxyprothrombin (DCP), α-fetoprotein (AFP) containing regimen, and are approved for treating patients with HCV genotype 1 infections. These drugs demonstrate significant improvements in sustained virological response (SVR) rates (Jacobson et al., 2011). Recently, asunaprevir and daclatasvir represent the first all oral, interferon free direct-acting anti viral agents (DAA) containing regimen and are approved for treating patients with HCV genotype 1 infections. These drugs demonstrate significant improvements in SVR rates without interferon related side-effects. Likewise, nucleoside analogues are recognized as more effective agents for chronic hepatitis B patients compared with that of interferon therapy: Lamivudine, adefovir (in 2002), entecavir (in 2005), telbivudine (in 2006), and tenofovir disoproxil fumarate (in 2008) have been licensed. These nucleoside analogues suppress HBV replication through inhibition of reverse transcriptase and DNA polymerase, and inhibit reverse transcription of pregenomic RNA to HBV DNA. Previous studies have shown that successful anti-viral therapy can improve biochemical liver function parameters as well as histological findings (Shiratori et al., 2000). Patients with mild liver fibrosis are likely to show histologically evident decreases in fibrosis and inflammation after a SVR in response to IFN treatment against HCV infection (Shiratori et al., 2000). Furthermore, treated patients show marked reductions in decompensated liver disease and HCC occurrence (Yoshida et al., 1999; Morgan et al., 2010). Patients with advanced fibrosis, however, retain relatively low but still considerable risks of HCC occurrence despite having attained SVR (Morgan et al., 2010).

Risk of HCC development increases in proportion to the degree of liver fibrosis in patients persistently infected with hepatitis virus. Antiviral therapy has been shown to decrease the risk of hepatic decompensation (Morgan et al., 2010) and HCC occurrence (Yoshida et al., 1999) among sustained virologic responders. In chronic HCV infected patients,
prevention of unfavorable disease outcome seems most effective when therapy is given before development of cirrhosis (Morgan et al., 2010). On the other hand, oral nucleoside analogues are beneficial for patients with even decompensated HBV-related cirrhosis and HCC (Deng et al., 2013). Improvement of anti-viral therapy will decrease the incidence of HCC. However, surveillances to detect HCC at an early stage are still indispensable to those who achieved SVR. Serum autoantibodies to TAA can be used as a new predictive biomarker for early assessment of HCC.

**Disclosure**

The author declares no conflicts of interest.

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