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Non-systemic non-surgical therapy for HCC with PVTT

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Lecture : The presence of portal vein tumor thrombosis (PVTT) is regarded as a hallmark of advanced hepatocellular carcinoma (HCC). The prognosis of HCC with PVTT is dismal, with a median survival of 2.7–4.0 months if left untreated. PVTT is regarded as being indicative of an advanced stage of HCC with little hope for a cure. Until very recently, the BCLC system, based on randomized clinical trials (RCT), only recommended sorafenib for HCC with PVTT. However, the heterogeneous nature of HCC-PVTT calls for individualized management strategies. This short summary briefly provides clinical data on treatment outcomes with transarterial chemoembolization (TACE), transarterial radioembolization (TARE), external beam radiotherapy (EBRT), and hepatic arterial infusion chemotherapy (HAIC) in patients with HCC with PVTT.

Radiotherapy can be used for treating PVTT. In most clinical situations, EBRT has been used as an adjuvant therapy to improve survival outcomes. In a large nationwide study from South Korea, median overall survival of patients with PVTT was 10.2 months in combination with intra-arterial therapies. Recently, a randomized trial from South Korea showed a significantly prolonged overall survival (OS) and time to progression (TTP) with TACE plus EBRT versus sorafenib alone. In other series, the addition of radiotherapy to TACE often resulted in promising OS in comparison with TACE alone. Despite the promising results for the use of radiotherapy to treat PVTT, few have been obtained with a high level of evidence. Currently, EBRT alone, or in combination with other therapies is recommended for the treatment of HCC and PVTT in only eastern guidelines, but not in western guidelines.

TACE is frequently used for treatment of HCC with PVTT, especially segmental or sub-segmental PVTT. The median OS was reported to be 10-19 months in several prospective and retrospective studies of PVTT treated with TACE. In a meta-analysis of 13 studies with 1933 TACE-treated patients, median OS was 8 months, with only 1% and 18% having liver failure and post-treatment complications, respectively. Among the trails of combined TKIs, only the TACTICS trial showed a benefit with TACE plus sorafenib compared with TACE alone. A retrospective-controlled study from China also showed improved OS in patients with HCC with first-order or lower-branch PVTT when compared with patients who underwent TACE alone. Whereas most of the western guidelines do not recommend TACE as a standard treatment for HCC with PVTT, the aforementioned data indicate that TACE can be used as a readily acceptable option for selected patients with HCC with PVTT.

Two open-label, randomized controlled phase 3 trials, the SARAH and SIRveNIB studies, showed that overall survival did not significantly differ between TARE and sorafenib for patients with locally advanced HCC. Subgroup analysis also showed similar results for patients with MVI. Nevertheless, the positive safety profile and general tolerability of TARE make it the preferable treatment choice in selected patients. By contrast, several retrospective studies identified that TARE was associated with a more prolonged survival than was sorafenib for patients with HCC and PVTT.

Hepatic arterial infusion chemotherapy (HAIC) has the potential to deliver higher local concentrations of drugs to the tumor with reduced systemic distribution to non-tumorous parts of the patient. Studies of HAIC have been reported from Asian countries, mostly Japan, showing median OS ranging between 6 and 17 months, with response rates ranging from 12% to 52% for patients with advanced HCC. Randomized studies from South Korea (HAIC vs. sorafenib) and China (combination of HAIC and sorafenib vs. sorafenib alone) have shown significantly increased OS, whereas an RCT from Japan failed to show benefits with HAIC plus sorafenib compared with sorafenib alone for patients with advanced HCC with PVTT. Despite the promising results on its treatment effects, HAIC is not widely implemented and mostly performed for advanced HCC with PVTT in selected institutions.

Tremendous progress has been made with promising results for the treatment of HCC with PVTT. However, the efficacy among such patients requires validation and more elaboration before their active application to the clinical practice. Advanced HCC represents complicated diseases, accompanying with cirrhosis, decreased

hepatic function, and other comorbidities. Due to the complexity, it is highly likely that personalized, multidisciplinary management may be necessary to achieve optimal outcomes among this particular patent group.

Keywords: Liver cancer, Portal vein invasion, Conventional therapy