中文題目：系統性治療在主要門靜脈栓塞之晚期肝癌的療效

英文題目：Lenvatinib with or without Immune Checkpoint Inhibitors for Advanced Hepatocellular Carcinoma with Major Portal Venous Invasion

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**Background:** Hepatocellular carcinoma (HCC) with major portal vein invasion, including Vp3 and Vp4, indicates poor survival outcome and systemic therapy is the key treatment option for such condition. However, high-risk patients such as main portal vein thrombosis (Vp4) were mostly excluded from previous clinical trials, including REFLECT and Keynote 240. Whether these patients could be beneficial from sorafenib or lenvatinib-based treatment and their responses to the thrombosed portal vein were unclear.

**Method:** One hundred and five consecutive HCC patients with vp3/ vp4 portal vein thrombosis received sorafenib or lenvatinib with or without immunotherapy in the first-line setting in Taipei Veteran General Hospital from Jan. 2018 to Sep. 2021 were retrospectively recruited. The tumor and portal vein specific response rates were assessed by an independent radiologist according to RECIST 1.1 criteria.

**Results:** Of them, 61 patients received sorafenib monotherapy, 20 received lenvatinib monotherapy, and 24 received lenvatinib plus pembrolizumab. Significantly better overall objective response rate (ORR: 29.5% vs. 8.2%, p=0.004), disease control rate (DCR: 77.3% vs. 29.5%, p<0.001), median PFS (5.8 vs. 2.2 months, p<0.001) and median OS (12.2 vs. 6.3 months, p=0.043) were observed in patients received

lenvatinib-based treatment as compared with sorafenib treatment. The portal vein specific ORR (70% vs. 16.1%, p<0.001) and DCR (95% vs. 61.3%, p=0.007) were also significantly higher in the lenvatinib-based treatment subgroup. The findings were consistent in the 51 patients with main portal vein (Vp4) thrombosis. In multivariate analysis, extrahepatic metastasis (HR=1.799, p=0.020) and lenvatinib-based treatment (HR=0.491, p<0.009) were significant factors associated with OS. However, a higher risk of hepatic encephalopathy (15.9% vs.3.3%, p=0.033) was noted in lenvatinib-based treatment as compared with sorafenib treatment.

**Conclusion:** Lenvatinib-based treatment could provide better ORR, PFS, and OS for HCC patients with Vp3/Vp4 portal vein invasion. However, the risk of hepatic encephalopathy by lenvatinib treatment should be aware.