

In response to the issues raised in peer review, the following content has been added.

The incidence rate of HCC is increasing year by year, which is, of course, related to the improvement of diagnostic mode and the shortening of cancer monitoring interval. In the past, viral hepatitis was the main epidemiological cause of hepatocellular carcinoma, but with the implementation of hepatitis B vaccination and hepatitis C treatment plan worldwide, the annual incidence rate of hepatocellular carcinoma with viral hepatitis as the main cause decreased. And increasing evidence suggests that non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) contribute to the development of HCC and are becoming increasingly common causes of HCC worldwide. With the implementation of viral hepatitis treatment plans, the epidemiological etiology of HCC is likely to shift from viral hepatitis to non-alcoholic steatohepatitis.

In systematic treatment regimens, advanced HCC patients can generally be treated with tyrosine kinase inhibitors (TKIs). With the increasing understanding and characterization of the immune characteristics of the tumor microenvironment, immune checkpoint inhibitors (ICI) methods further expand the systemic treatment of HCC. The current emerging systemic comprehensive treatment method combines the above two methods, and there is evidence that the combination therapy of ICI+TKI has achieved certain results. However, existing research evidence suggests that the treatment options currently used in clinical practice are still relatively ineffective. In fact, although the efficacy has significantly improved after the introduction of ICI, the objective response rate to treatment is still largely insufficient. Most patients do not have good returns, and the 5-year OS of metastatic HCC is still unsatisfactory. Currently, efforts should mainly focus on expanding treatment targets and searching for reliable biomarkers as much as possible, which will help adjust treatment choices and avoid the risks and costs associated with drug ineffectiveness and side effects.