Universe
Scientific Publishing

# Clinical analysis of tenofovir combined with sorafenib in patients with hepatitis B-related intermediate to advanced primary liver cancer

**Min Zhao, Fangcheng Zhao***

**The Second Hospital of Dalian Medical University. Dalian 116023, China.**

***Abstract:*** **Aim:** To investigate the clinical efficacy of tenofovir combined with sorafenib in the treatment of patients with hepatitis B-related intermediate to advanced primary liver cancer. **Methods:** Sixty patients with hepatitis B-related intermediate to advanced primary liver cancer admitted to our hospital between January 2021 and December 2021 were selected and divided into 30 cases each in the study group and the control group according to the random number table method, in which the control group was treated with sorafenib and the study group was treated with tenofovir on top of the control group. Finally, the liver function indexes and clinical efficacy of the two groups of patients were observed and compared. **Results:** The total effective rate of treatment in the study group was 83.33%, while the total effective rate of treatment in the control group was 46.67%, There was a significant difference ($P < 0.05$) between the two groups comparing, Liver function indexes such as TBIL, ALB, PT and AFP before treatment in the study group were not significantly different from those in the control group ($P > 0.05$)，there were significant differences in liver function indexes such as TBIL, ALB, PT and AFP after treatment compared with the control group ($P < 0.05$). **Conclusion:** The short-term clinical efficacy and safety of tenofovir in combination with sorafenib in the treatment of patients with hepatitis B-related intermediate to advanced primary liver cancer is remarkable and worthy of clinical application.

***Keywords:*** Tenofovir; Sorafenib; Hepatitis B; Primary Liver Cancer

## Introduction

Liver cancer is a kind of malignant tumor that seriously endangers human health. One of the important causes of primary liver cancer in China is hepatitis B virus infection (HBV), which is already in the middle or late stages when detected early and has lost the possibility of liver transplantation or surgical treatment, and radiotherapy and chemotherapy often fail to achieve the desired results.[1] How to improve the survival rate of patients with intermediate and advanced liver cancer is an urgent clinical research topic at present, therefore, looking for an effective treatment can greatly improve patient' quality of life. In this paper, we conducted a preliminary investigation of the therapeutic effects of tenofovir in combination with sorafenib in hepatitis B-related intermediate to advanced hepatocellular carcinoma, the report was as follows:

# 1. Materials and Methods

# 1.1 General Information

Sixty patients with hepatitis B-related intermediate and advanced primary liver cancer admitted to our hospital during January 2021-January 2022 were selected and divided into 30 cases in the study group and 30 cases in the control group, including 17 males and 13 females in the study group, aged 55-85 years, with a mean age of (70±15) years. There were 16 male and 14 female cases in the control group, aged 54-87 years, with a mean age of (70.5±16.5) years. The basic information of the patients in both groups was comparable ($P > 0.05$). All patients and their families were informed of the study and signed it. Permission for this study was obtained from the hospital ethics committee.

## 1.2 Methods

All patients were given liver protection and supportive symptomatic treatment with tenofovir fumarate (GlaxoSmithKline Tianjin Co., Ltd., State Drug Administration H20153090) 300 MG was given orally, 1 time/D； In the observation group, on the basis of tenofovir fumarate treatment, sorafenib mesylate (Bayer Pharma AG, approval number/registration certificate number H20160201, execution standard import drug registration standard JX20060053) 0.4G was given orally, 2 times/d, and observed for 12 months.

## 1.3 Observation indicators

Patients with an improvement of at least 20 points in Karnofsky score after treatment according to the Karnofsky Quality of Survival Scale were assessed as having a significant effect； After treatment, the patient's Karnofsky score improved by 10 to 20 points and was rated as effective； Patients with an improvement of <10 points or no change in Karnofsky score after treatment were rated as stable；Patients with reduced Karnofsky scores after treatment were assessed as ineffective. [2]

## 1.4 Statistical Methods

The study was analyzed by SPSS24.0 statistical package, and the measurement data were expressed by ($\bar{x}\pm s$), and the t-test was used for comparison between two groups, the count data were expressed by relative numbers, and the X2 test was used for comparison between two groups, and SPEARMAN correlation analysis was used for correlation analysis between non-variables, and $P < 0.05$ meant that the difference was statistically significant.

# 2. Results

## 2.1 Comparison of clinical efficacy between the two groups

The total effective rate of treatment in the study group was 83.33% compared with 46.67 in the control group, with a significant difference between the two groups ($P < 0.05$), as shown in Table 1.

**Table 1 Comparison of clinical efficacy between two groups of patients [n(%)]**

| Groups | Number of cases | Significant effect | Effective | Stable | Ineffective | Total efficiency rate |
|---|---|---|---|---|---|---|
| Study Group | 30 | 9 | 16 | 4 | 1 | 25（83.33） |
| Control group | 30 | 4 | 10 | 9 | 7 | 14（46.67） |
| $X^2$ | | | | | | 8.865 |
| $P$ | | | | | | 0.003 |

## 2.2 Comparison of liver function indexes between two groups of patients

Liver function indexes such as TBIL, ALB, PT and AFP in the study group before treatment were not significantly different from those in the control group ($P > 0.05$)，Significant differences in liver function indexes such as TBIL, ALB, PT and AFP compared with the control group after treatment ($P < 0.05$)，as shown in Table 2.

**Table 2 Comparison of liver function indexes between the two groups ($\bar{x}\pm s$)**

| Groups | Number of cases | TBIL（μMOL/L） | | ALB（μMOL/L） | | PT（μMOL/L） | | AFP（μMOL/L） | |
|---|---|---|---|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Study Group | 30 | 35.4±18.1 | 20.6±10.1 | 27.6±3.6 | 37.7±2.7 | 13.8±2.1 | 13.2±1.1 | 760.3±210.4 | 430.5±80.5 |
| Control group | 30 | 35.7±17.9 | 32.7±12.3 | 28.3±3.1 | 31.6±2.4 | 14.4±2.6 | 14.8±1.9 | 770.5±220.3 | 530.7±101.8 |
| *T* | | 0.065 | 4.164 | 0.807 | 9.249 | 0.983 | 3.992 | 0.183 | 4.229 |
| *P* | | 0.949 | 0.000 | 0.423 | 0.000 | 0.330 | 0.000 | 0.855 | 0.000 |

# 3. Discussion

The liver plays an important role in maintaining the balance of the coagulation system, mainly by synthesizing coagulation factors, physiological anticoagulation factors, and fibrinolytic factors in the liver. Patients with intermediate to advanced hepatocellular carcinoma will have more complete liver damage when their liver function is decompensated. The more severely the liver function is damaged, the synthesis of coagulation factors will be reduced and the coagulation ability will be decreased. Therefore, there is a certain correlation between liver function and coagulation function, and coagulation function is a good indicator. Prothrombin time (PT) is a method to detect the function of the human exogenous coagulation system by over-screening, which can be used to diagnose congenital coagulation and acquired bleeding disorders of the exogenous coagulation system, as well as to diagnose severe hepatitis and early cirrhosis.[3] The activated partial thromboplastin time (APTT) is a relatively sensitive assay that reflects the coagulation activity of the endogenous coagulation system, and it is an important test that reflects the combined viability of the endogenous coagulation pathways, especially the first phase of coagulation factors. TT is an indicator of anticoagulant substances in the body. Duration of TT indicates hyperfibrinolysis, and TT shortening is not clinically relevant in cases of hypofibrinogenesis, DIC and heparin-like substances. Plasma fibrinogen, a common blood clotting factor, is a protein found in plasma.

Alpha fetoprotein is a highly specific marker of HCC sensitivity that is made by juvenile cells similar to hepatocytes and can be detected at an early stage of hepatocyte development. Serum A-fetoprotein is elevated earlier than imaging, that is, earlier than ultrasound or CT, so it is best for early diagnosis. The detection rate of alpha fetoprotein in liver cancer is around 80%. If the content of alpha fetoprotein is high, it indicates that the prognosis is poor. Therefore, the detection of alpha fetoprotein is an important indicator of the efficacy of liver cancer [4]. Hepatitis B-associated liver cancer is a relatively common malignant tumor with a high incidence, usually in the middle and late stages, which cannot be treated surgically; radiotherapy and chemotherapy often fail to achieve the desired therapeutic effect. Hepatitis B virus binds to human chromosomes, which is the causative agent of liver cancer, making liver cells susceptible to mutation under a series of stimuli. Under the influence of different stimulating factors and growth factors, liver cells are altered, some proto-oncogenes are activated and oncogenes are mutated; therefore, to a certain extent, controlling the level of HBVDNA can be of great help in improving the quality of life of patients. [5]

Tenofovir fumarate is a new antiviral drug that can effectively and rapidly inhibit HBVDNA replication. It can reduce inflammation in the patients' liver and provide effective treatment for liver damage. Sorafenib is a novel multitargeted new anticancer drug that can inhibit tumor cell proliferation by blocking RAF/MEK/ERK-mediated cell signaling pathways and can indirectly inhibit tumor cell growth by inhibiting VEGFR, PDGF and other receptors for the treatment of liver cancer, so as to achieve the purpose of treating liver cancer.[6] The results of this study showed that the combination of tenofovir with sorafenib for the treatment of hepatitis B-related intermediate and advanced HCC significantly improved liver function and reduced AFP levels. This is due to the better synergistic effect of the two drugs, which can better improve the liver function of patients.

In conclusion, tenofovir combined with sorafenib in combination with hepatitis B-related intermediate and advanced hepatocellular carcinoma is a feasible method to effectively improve liver function and reduce the level of AFP; it has obvious effects in the short term and deserves further clinical testing.

# References

[1] Liu J, Hu SJ, Guo JY, et al, A comparative analysis of the clinical characteristics of hepatitis B virus associated cirrhotic liver cancer and non cirrhotic liver cancer [J] From Journal of Clinical Gastroenterology, 2022, 34 (02): 115-119.

[2] An XQ, Li Y, et al. A clinical observation on tenofovir combined with sorafenib in the treatment of patients with hepatitis B related advanced primary liver cancer [J] From Journal of practical Hepatology, 2021,24 (04): 600-602.

[3] Zhang XR, Li W, Correlation of serum AFP, VEGF and AFU levels with microvascular invasion in patients with hepatitis B-associated hepatocellular carcinoma [J]. From Laboratory Medicine and Clinics,2021,18(22):3294-3297.

[4] Wang HX, Yu ZJ, Liu JP, and Zhao WX, The correlation between TCM evidence and T lymphocytes and biochemical indicators in patients with HBV-related primary liver cancer[J]. From the Journal of Hainan Medical College, 2021, 27(22): 1692- 1697+1703.

[5] Tang M, Chen Q, Guo S, The detection of liver cancer patients with low serum viral load HBV-DNA hepatitis B related hepatocytes [J] From contemporary medicine, 2021,27 (23): 91-93.

[6] Hou J, Ye FS, Qiu SJ, and Song YM, The correlation analysis between hepatitis B virus DNA load and immune function in patients with hepatitis B primary liver cancer[J]. From Chinese and Foreign Medical,2021,40(17):15-17.