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Observation on the Effect of Interventional Therapy Combined with Lenvatinib and Sintilimab in the Treatment of Advanced Liver Cancer

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Abstract: *Objective*: To observe the control effect of interventional therapy combined with lenvatinib and sintilimab in patients with intermediate and advanced liver cancer. *Methods*: 82 patients with intermediate and advanced liver cancer who visited from January 2022 to January 2025 were selected as samples and randomly divided into two groups. Group A received interventional therapy combined with lenvatinib and sintilimab, while Group B received interventional therapy combined with lenvatinib. Disease remission rate, adverse reactions, liver function indicators, and tumor marker indicators were compared between the two groups. *Results*: The disease control rate (DCR) in Group A was higher than that in Group B ($P < 0.05$). There was no difference in adverse reaction rates between Group A and Group B ($P > 0.05$). Total bilirubin (TBil), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels in Group A were lower than those in Group B ($P < 0.05$). Carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), and alpha-L-fucosidase (AFU) levels in Group A were also lower than those in Group B ($P < 0.05$). *Conclusion*: Intermediate and advanced liver cancer patients receiving interventional therapy combined with lenvatinib and sintilimab showed reduced tumor marker levels, lessened liver function damage, and a high disease control rate and treatment safety.

Keywords: Intermediate and advanced liver cancer; Sintilimab; Lenvatinib; Interventional therapy

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1. Introduction

Advanced liver cancer is characterized by a high metastasis rate, strong invasiveness, and severe liver function impairment, which can shorten the survival time and reduce the quality of life of patients. Therefore, early treatment is essential. In the early stage of liver cancer, symptoms are not typical. However, in the advanced stage, symptoms such as jaundice, ascites, abdominal pain, and weight loss become apparent. A few patients may develop

abdominal masses, and most patients have a poor prognosis. Clinically, transcatheter arterial chemoembolization (TACE) is commonly used to manage patients with advanced liver cancer. This technique delivers antitumor drugs to the target area, reducing the toxicity and side effects of chemotherapy. However, drug resistance remains a challenge, necessitating the exploration of combined treatment regimens. Lenvatinib, a targeted drug, is used in the management of advanced liver cancer. It blocks the activity of vascular endothelial growth factor receptors, inhibiting tumor angiogenesis and prolonging patient survival. Sintilimab, a PD-1 inhibitor, mediates T-cell immune responses, blocking the proliferation of tumor cells and slowing tumor growth. Studies have shown that the combination of lenvatinib and PD-1 inhibitors has a synergistic effect in the treatment of advanced liver cancer [1]. Based on this, this article explores the efficacy of interventional therapy combined with lenvatinib and sintilimab using a sample of 82 patients with advanced liver cancer who were treated between January 2022 and January 2025.

2. Materials and methods

2.1. Materials

From January 2022 to January 2025, 82 patients with advanced liver cancer who visited our hospital were selected as samples and randomly divided into groups by drawing. There was no difference in liver cancer data between Group A and Group B, with $P > 0.05$. See **Table 1**.

Table 1. Analysis of advanced liver cancer data

Group *n*		Gender (%)		Age (years)		BCLC staging (%)	
		Male	Female	Range	Mean	Stage B	Stage C
Group A	41	22 (53.66)	19 (46.34)	46–70	59.42 ± 2.49	25 (60.98)	16 (39.02)
Group B	41	23 (56.10)	18 (43.90)	46–71	59.39 ± 2.52	26 (63.41)	15 (36.59)
χ^2/t	-	0.0492		0.0542		0.0519	
P	-	0.8244		0.9569		0.8198	

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Meet the criteria for liver cancer in the "Guidelines for the Diagnosis and Treatment of Primary Liver Cancer (2024 Edition)" [2]; (2) Signed informed consent; (3) Predicted survival > 12 months; (4) Not taken anti-tumor drugs before enrollment.

Exclusion criteria: (1) Organ dysfunction; (2) Autoimmune diseases; (3) Myelosuppression; (4) Solid organ transplantation.

2.3. Treatment methods

Group A: (1) Interventional therapy: During TACE, select oxaliplatin (50–120mg) + tegafur (20–30mg) + doxorubicin (40–60mg) for treatment, once every 4–6 weeks, adjusting the dosing regimen based on the physiological status of the liver cancer patient. (2) Targeted therapy: Oral administration of lenvatinib, a single dose of 8mg, once a day. (3) Immunotherapy: Intravenous injection of sintilimab, a single dose of 240mg, once every 2 weeks. Treatment for 3 months.

Group B: The interventional therapy + targeted therapy medication regimen and cycle are the same as Group A.

2.4. Observation indicators

Disease control rate: Complete response (CR) is recorded when the tumor lesion disappears; partial response (PR) is recorded when the tumor lesion volume reduction is >30% and the number reduction is >50%; stable disease (SD) is recorded when the tumor lesion volume and number remain unchanged or the increase does not meet the above criteria; disease progression (PD) is recorded when the tumor lesion increases.

Adverse reactions: Record platelet decline, hypothyroidism, decreased white blood cell count, and hypoproteinemia.

Liver function: Fully automated biochemical analyzer to detect TBil, AST, and ALT indicators.

Tumor markers: Enzyme-linked immunosorbent assay to detect CEA, AFP, and AFU indicators.

2.5. Statistical analysis

Data were processed using SPSS 23.0, with a chi-square test used for counting data (recorded as %) and a *t*-test used for measurement data (recorded as mean ± standard deviation [SD]). Statistical difference exists when $P < 0.05$.

3. Results

3.1. Disease control rate

The DCR of Group A was higher than that of Group B, $P < 0.05$. As shown in **Table 2**.

Table 2. Disease control rate in advanced liver cancer [*n* (%)]

Group	CR	PR	SD	PD	DCR
Group A ($n = 41$)	1 (2.44)	19 (46.34)	18 (43.90)	3 (7.32)	38 (92.68)
Group B ($n = 41$)	1 (2.44)	15 (36.59)	14 (34.15)	11 (26.83)	30 (73.17)
χ^2	-	-	-	-	5.5126
P	-	-	-	-	0.0189

3.2. Adverse reaction rate

There was no difference in the adverse reaction rate between Group A and Group B, with $P > 0.05$. See **Table 3**.

Table 3. Adverse reaction rate in advanced liver cancer [*n* (%)]

Group	Thrombocytopenia	Hypothyroidism	Leukopenia	Hypoproteinemia	Incidence rate
Group A ($n = 41$)	4 (9.76)	3 (7.32)	6 (14.63)	5 (12.20)	18 (43.90)
Group B ($n = 41$)	5 (12.20)	5 (12.20)	6 (14.63)	4 (9.76)	21 (51.22)
χ^2	-	-	-	-	0.4401
P	-	-	-	-	0.5071

3.3. Liver function indicators

After treatment, the TBil, AST, and ALT indicators in Group A were all lower than those in Group B, with $P < 0.05$. See **Table 4**.

Table 4. Analysis of liver function indicators in advanced liver cancer (mean ± SD)

Group	TBil (μmol/L)		AST (U/L)		ALT (U/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A (n = 41)	31.18 ± 1.62	14.69 ± 1.02	50.47 ± 2.88	26.31 ± 1.88	75.28 ± 4.11	41.89 ± 2.06
Group B (n = 41)	31.21 ± 1.59	20.48 ± 1.44	50.42 ± 2.91	34.33 ± 2.06	75.31 ± 4.16	55.73 ± 3.44
t	0.0846	21.0093	0.0782	18.4133	0.0328	22.1016
P	0.9328	0.0000	0.9379	0.0000	0.9739	0.0000

3.4. Tumor markers

After treatment, the CEA, AFP, and AFU indicators in Group A were all lower than those in Group B, with $P < 0.05$. See **Table 5**.

Table 5. Analysis of tumor marker indicators in advanced liver cancer (mean ± SD)

Group	CEA (ng/ml)		AFP (ng/ml)		AFU (U/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A (n = 41)	35.82 ± 2.41	16.11 ± 1.25	329.25 ± 11.26	104.24 ± 6.16	72.62 ± 3.88	34.82 ± 1.58
Group B (n = 41)	35.79 ± 2.39	24.33 ± 1.73	329.31 ± 11.29	155.73 ± 8.43	72.59 ± 3.91	50.33 ± 2.61
t	0.0566	24.6604	0.0241	31.5777	0.0349	32.5510
P	0.9550	0.0000	0.9808	0.0000	0.9723	0.0000

4. Discussion

The pathogenesis of advanced liver cancer is complex, related to fatty liver, high blood glucose, and viral infections. Additionally, continuous damage to the liver caused by hepatitis and alcoholic liver disease can also increase the risk of liver cancer. In patients with advanced liver cancer, the increase in tumor diameter can elevate the tension of the liver capsule, exacerbating pain symptoms in the liver area. If it involves the digestive tract, it can induce nausea, vomiting, low appetite, abdominal distension, and other symptoms. For those with excessively large tumor volumes, a lump may be palpable upon touching the abdomen, and complications such as jaundice and portal hypertension may occur, leading to conditions like low body weight, anemia, fever, fatigue, ascites, jaundice, and even secondary blood coagulation disorders [3]. As liver cancer progresses and the liver continues to be damaged, it can reduce the patient's survival time.

Currently, interventional procedures are commonly used in the clinical treatment of advanced liver cancer, with TACE being frequently employed. By directly delivering chemotherapy drugs to the target hepatic artery, it can enhance the drug concentration in the tumor area, achieving local therapeutic effects. Compared to conventional chemotherapy, TACE technology can reduce damage to healthy tissues, restore the patency of the liver's blood supply arteries, and alleviate liver cancer-related symptoms [4].

Lenvatinib is a targeted drug that can inhibit tumor-related receptor kinases, slowing down tumor growth. It can also block tumor cell pathways, accelerate tumor cell apoptosis, and reduce the number of local new blood vessels, thus lowering the tumor metastasis rate. Sintilimab can enhance the activity of immune cells, promoting their ability to kill tumor cells. It can also strengthen the ability of T cells to infiltrate tumor tissue, deactivate NK

cells, and delay tumor tissue growth [5].

Furthermore, sintilimab can enhance the management of liver cancer through multiple pathways: upon entering the body, sintilimab binds to PD-1 molecules on the surface of T cells, enhancing their ability to recognize and kill liver cancer cells, thereby strengthening the immune response. Its pharmacologically active components express immune molecules, blocking the activity of adjacent immune cells and creating an immunosuppressive microenvironment for immune monitoring of tumor cells. When combined with antitumor drugs such as lenvatinib, it can enhance the efficacy of killing tumor cells and improve disease control rates through multiple synergistic mechanisms. This drug has high safety, with only a few patients experiencing minor complications such as pneumonia, abnormal liver function, and skin rash, which can be alleviated with symptomatic treatment.

In this paper, the combination of TACE with lenvatinib and sintilimab can activate the immune response and improve prognosis.

Based on the data analysis in this article, the DCR of Group A is higher than that of Group B, with $P < 0.05$. The reason for this is analyzed as follows: Lenvatinib, a tyrosine kinase inhibitor, can block tumor angiogenesis and cell proliferation through multiple targets. Combined with sintilimab, it can act on PD-1 receptor antibodies, inhibit tumor cell escape mechanisms, and enhance tumor control effects [6]. Another set of data shows that there is no difference in the adverse reaction rate between Group A and Group B, with $P > 0.05$. This suggests that the combination therapy does not increase adverse reactions and has high treatment safety. Another set of data indicates that the TBil, AST, and ALT levels in Group A are lower than those in Group B, with $P < 0.05$. The analysis of the reasons is that tumor cells in patients with advanced liver cancer invade healthy tissues, leading to increased permeability of liver cell membranes, increased cell necrosis, and elevated levels of ALT and AST in the blood. Additionally, impaired liver metabolism and disordered glucose and lipid metabolism can further elevate ALT and AST levels. Widespread damage to liver cells in patients with advanced liver cancer can induce hepatocellular jaundice, resulting in increased TBil levels [7]. The combined treatment approach in this article includes TACE, which can inhibit tumor-supplying arteries, protect residual kidney function, and restore blood supply to non-tumor areas, favoring hepatocyte regeneration. Combined with lenvatinib, it can deactivate vascular endothelial growth factor receptors, blocking nutrient supply to tumor cells and inhibiting their proliferation, thereby delaying tumor growth. Additionally, combined with sintilimab, the PD-1/PD-L1 signaling pathway is blocked, and T cells are activated, enhancing the immune system's ability to recognize and kill tumor tissue. Monoclonal antibody therapy can reverse immunosuppression and accelerate the immune system's clearance of tumor tissue, thereby protecting liver function [8]. The combined intervention of interventional therapy, lenvatinib, and sintilimab can reduce liver damage caused by tumor tissue, leading to improved TBil, AST, and ALT levels. The final set of data shows that CEA, AFP, and AFU levels in Group A are lower than those in Group B, with $P < 0.05$. The analysis of the reasons is that patients with advanced liver cancer secrete CEA, and impaired liver function leads to abnormal CEA metabolism, resulting in elevated CEA levels. AFP is a glycoprotein substance, and liver cancer cells have dedifferentiation characteristics that enable them to secrete large amounts of AFP, allowing for the assessment of tumor type and differentiation degree by monitoring AFP levels. AFU participates in the body's metabolism of oligosaccharides, glycolipids, and glycoproteins, and as liver damage increases, AFU metabolism levels decrease, leading to elevated AFU levels in patients [9]. Based on interventional therapy, this article combines lenvatinib and sintilimab to treat advanced liver cancer, inhibiting tumor cell proliferation through multiple pathways. This activation of the immune system and reduction of tumor marker levels, combined with multi-modality treatment, can reduce tumor malignancy, achieve multi-pathway tumor control, and improve tumor marker levels [10]. Patients with advanced liver cancer should seek medical attention if they experience severe fever, abdominal pain, or gastrointestinal reactions during treatment, and regularly

undergo liver function testing. Treatment plans for liver cancer should be adjusted based on the results of these tests.

5. Conclusion

In summary, patients with advanced liver cancer who receive interventional therapy combined with lenvatinib and sintilimab experience decreased tumor marker levels, improved liver function, and enhanced disease control rates, indicating the value of this treatment approach for widespread application.

Disclosure statement

The authors declare no conflict of interest.

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