Effectiveness of Combination Therapy of Stereotactic Body Radiation Therapy with Lenvatinib in Advanced Hepatocellular Carcinoma

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ABSTRACT

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and has a high mortality rate, especially in advanced stages. Treatment of advanced HCC remains a significant challenge due to limited effective therapeutic options. This study examines the effectiveness of combining Stereotactic Body Radiation Therapy (SBRT) and Lenvatinib in advanced HCC patients. SBRT is a high-precision radiation technique that allows high-dose irradiation of tumor targets with minimal damage to surrounding healthy tissues. At the same time, Lenvatinib is a multikinase inhibitor that inhibits several critical molecular pathways in angiogenesis and tumor cell proliferation. The results showed that the combination of SBRT and Lenvatinib significantly improved overall survival (OS) by reducing the risk of death by 63%, progression-free survival (PFS) reduced the risk of tumor progression by 67%, intrahepatic tumor progression-free survival (IHPFS) showed a decrease of 71%, objective remission rate (ORR) was also higher in the combination group (56.8%), and disease control rate (DCR) of 91.9% which was higher than the use of Lenvatinib alone. However, this combination therapy also carries a higher risk of side effects, including hypertension and diarrhea, which require close monitoring and dose adjustment. This study suggests combining SBRT and Lenvatinib may be a more practical approach to treating advanced HCC. However, the treatment strategy needs to be tailored to the patient's condition to minimize the risk of toxicity.

Keywords: *Hepatocellular carcinoma (HCC), lenvatinib, Stereotactic Body Radiation Therapy (SBRT), terapi kombinasi*

ABSTRAK

Hepatocellular carcinoma (HCC) adalah jenis kanker hati primer yang paling umum dan memiliki tingkat kematian yang tinggi, terutama pada stadium lanjut. Pengobatan HCC stadium lanjut masih menjadi tantangan yang signifikan karena terbatasnya pilihan terapi yang efektif. Studi ini menguji efektivitas kombinasi Terapi Radiasi Tubuh Stereotaktik (Stereotactic Body Radiation Therapy/SBRT) dan Lenvatinib pada pasien HCC stadium lanjut. SBRT adalah teknik radiasi presisi tinggi yang memungkinkan penyinaran dosis tinggi pada target tumor dengan kerusakan minimal pada jaringan sehat di sekitarnya. Sementara itu, Lenvatinib adalah penghambat multikinase yang menghambat beberapa jalur molekuler penting dalam angiogenesis dan proliferasi sel tumor. Hasil studi menunjukkan bahwa kombinasi SBRT dan Lenvatinib secara signifikan meningkatkan overall survival (OS) dengan menurunkan risiko kematian sebesar 63%, progression-free survival (PFS) menurunkan

risiko perkembangan tumor sebesar 67%, intrahepatic tumor progression-free survival (IHPFS) menunjukkan penurunan sebesar 71%, objective remission rate (ORR) juga lebih tinggi pada kelompok kombinasi (56,8%), dan disease control rate (DCR) sebesar 91,9% yang lebih tinggi dibandingkan penggunaan Lenvatinib saja. Namun, terapi kombinasi ini juga memiliki risiko efek samping yang lebih tinggi, termasuk hipertensi dan diare, yang memerlukan pemantauan ketat dan penyesuaian dosis. Studi ini menunjukkan bahwa kombinasi SBRT dan Lenvatinib mungkin merupakan pendekatan yang lebih praktis untuk mengobati HCC stadium lanjut. Namun, strategi pengobatan perlu disesuaikan dengan kondisi pasien untuk meminimalkan risiko toksisitas.

Kata kunci: *Hepatocellular carcinoma (HCC), lenvatinib, Stereotactic Body Radiation Therapy (SBRT), combination therapy*

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer and is the leading cause of cancer mortality in the world. HCC accounts for approximately 75% of all liver cancer cases in the world. The epidemiology of HCC shows an uneven geographical distribution, and the highest incidence rates are recorded in East Asia and Sub-Saharan African regions, which can mainly be explained by ting. In Asia, Mongolia has the highest incidence rate with 93.7 per 100,000 people, followed by China, which, in absolute relation to its enormous population, also has the highest cases of hepatocyte cell cancer with a high incidence rate. In the Western world, such as in the United States and Europe, cases of hepatocyte cell cancer have also been steadily increasing in recent decades, with incidence rates attributable to HB. In these places, the dominating risk factors are non-alcoholic fatty liver disease (NAFLD) associated with obesity and syndrome.[1]

Treatment of end-stage HCC is a significant challenge due to the lack of adequate and numerous treatment options. The heterogenicity of HCC and its rapidly mutating nature make therapy outcomes in late-stage systems. Some personalized therapies, such as targeted molecular therapy and immunotherapy, have shown promising results but are low in consistency and severe in toxicity. On the other hand, there are delays in diagnosis and lost opportunities. With an abysmal five-year prognosis in HCC at advanced stages, multidisciplinary planning is designed using supportive, local, and systemic therapies to be effective in improving clinical outcomes.[2]

This paper reviews the effectiveness of combining Stereotactic Body Radiation Therapy (SBRT) with Lenvatinib therapy in advanced HCC and presents evidence from clinical studies that support or question this combination. The writer searched and collected journal articles through PubMed and Google Scholar using the keywords “Hepatoma”, “Hepatocellular Carcinoma (HCC)”, “Stereotactic Body Radiation Therapy (SBRT)”, “Lenvatinib”, and “Combination Therapy”. Furthermore, the information used in this paper was summarized and carefully selected.

OVERVIEW OF HEPATOCELLULAR CARCINOMA (HCC)

Definition and Pathophysiology of HCC

Hepatocellular carcinoma is the third leading cause of cancer-related deaths worldwide. With recent advances in the treatment of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, the burden of hepatocellular carcinoma due to these viruses is decreasing. However, the prevalence of non-alcoholic fatty liver disease (NAFLD) is rapidly increasing. Nearly one-third of the world's population has NAFLD, with about 20% of them having non-alcoholic steatohepatitis, which can progress to cirrhosis and hepatocellular carcinoma. NAFLD is currently the fastest-growing cause of hepatocellular carcinoma in the United States and some European countries. It is expected to continue to rise as the global obesity epidemic increases.[3]

There are multiple factors involved in the pathophysiology of HCC. First, autophagy and apoptotic pathways are dysregulated. One type of planned cell death that helps get rid of damaged or superfluous cells is called apoptosis. Many cancer cells have increased production of anti-apoptotic proteins like Bcl-xL and decreased expression of pro-apoptotic proteins like BAX. This indicates that apoptotic pathways can be disturbed in HCC. The growth of cancer cells is encouraged by this imbalance. Additionally, autophagy is the mechanism by which damaged cellular materials are recycled by breaking down cellular components. Autophagy has two roles in HCC. Preventing the buildup of damaged proteins and organelles acts as a protective mechanism in the early

stages of cancer. Preserving cellular homeostasis can help cancer cells survive in the later stages.[3]

Second, oxidative damage and Endoplasmic Reticulum (ER) stress are involved. An buildup of incorrectly folded proteins in the ER lumen, which can be brought on by a pathogen infection, genetic changes, or an increase in metabolic load, is known as ER stress. genetic mutations, or increased metabolic load. ER stress activates the unfolded protein response (UPR), which can trigger apoptosis or promote autophagy depending on the level of stress experienced. Furthermore, oxidative stress is caused by excessive production of reactive oxygen species (ROS), which can damage DNA and other cell components, contributing to the initiation and progression of HCC.[3]

Mutations in genes like the TERT promoter, p53 tumor suppressor gene, or Wnt/β-catenin, AKT/mTOR, and MAPK signaling pathways can lead to HCC. Epigenetic modifications like DNA methylation, histone modification, and RNA silencing also regulate gene expression. In addition, microRNA (miRNA) and Long Non-Coding RNA (lncRNA) can act as oncogenes or tumor suppressor genes. They can regulate critical molecular pathways associated with HCC initiation and progression. For example, some miRNAs regulate the PI3K/AKT/mTOR and Wnt/β-catenin pathways involved in liver carcinogenesis.[3]

Other factors contribute to the pathogenesis of HCC. Exosomes can transport proteins, DNA, and RNA from liver cancer cells to normal cells, triggering local or systemic reactions that participate in the initiation and progression of HCC. Furthermore, Calcium (Ca2+) plays a role in initiating HCC by affecting ion homeostasis within cells, potentially promoting metastatic cell formation and reducing cell death.[3]

Advanced Stages of HCC

In contrast to other cancers, the prognosis and treatment options for patients with hepatocellular carcinoma (HCC) depend not only on the stage of the tumor but also on the degree of liver dysfunction. Staging systems are needed to help predict survival outcomes and can help to decide on optimal medical treatment. The most commonly used staging system in clinical studies is the Barcelona Clinic Liver Cancer System (BCLC) **(Figure 1),** which classifies patients into four stages depending on tumor burden, liver function (Child-Pugh score), and overall health. Pathological diagnosis is based on tumor-node-metastasis (TNM) classification and staging according to UICC (Union for International Cancer Control) criteria.[4]

In the case of advanced-stage HCC (BCLC C), it is often referred to as unresectable HCC as the tumor is not eligible for resection therapy given the severity of the disease. The prognosis for patients with advanced HCC is generally worse compared to earlier stages, as cancer has spread to the significant hepatic blood vessels (portal invasion) or other parts of the body outside the liver (extrahepatic spread). The median survival time of advanced-stage HCC patients is <2 years. However, the specific prognosis may vary depending on various factors, including the response to systemic therapy and the patient's overall health.[4]

STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN THE TREATMENT OF HCC

Basic Principles of SBRT

Stereotactic body radiation therapy, or SBRT, is a new method of radiation therapy in cancer that allows the delivery of high doses with high

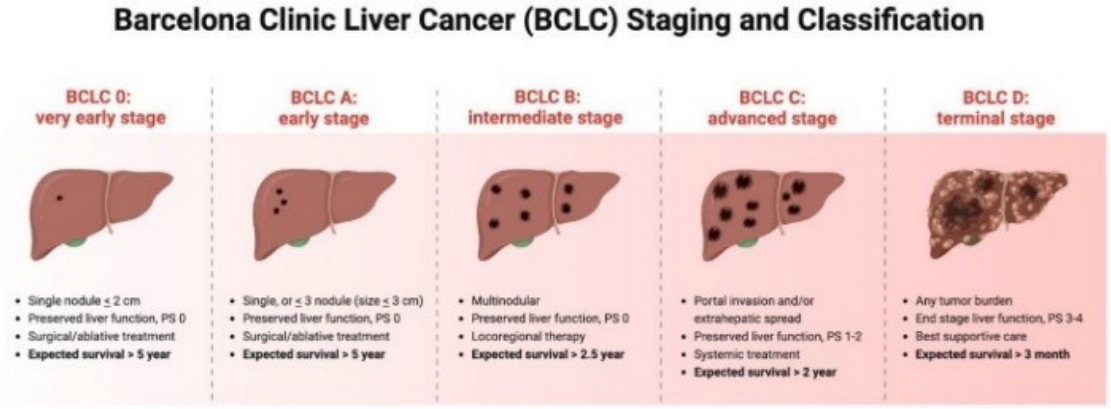

Figure 1. BCLC Staging and Classifcation.[4]

accuracy to a small and specific target area in the body. This therapy can be performed with a single dose or multiple doses with a very high level of precision. The total radiation dose can be divided into smaller, fractionated doses delivered over several days to help spare normal tissue.[5] SBRT requires high precision, accuracy, and consistency throughout therapy. To ensure the patient remains in the desired place, reducing movement and using stereotactic localization techniques is necessary. The patient immobilization system must be exact, and the radiation equipment must be able to deliver radiation with a mechanical tolerance of ±2 mm. To minimize damage to healthy tissue around the target, high-dose delivery should be precisely directed at the target, and rapid dose reduction from the target can be performed using multiple coplanar and non-coplanar static fields or arc therapy. Quality assurance and safety are essential parts of this entire process.[6]

Stereotactic body radiation therapy, or SBRT shows remarkable results in local tumor control with reduced rates of long-term complications. The main difference between SBRT and conventional radiation treatment is the delivery of large doses in one or multiple sessions, resulting in a highly effective biological dose. Other distinctive features of SBRT are small irradiation volume, inhomogeneous dose distribution, and relatively short therapy time.[6] SBRT can be used in various tumor types, including prostate, liver, spinal cord, kidney, oligo metastasis, and pancreas.[7]

Effectiveness of SBRT in Advanced HCC

International guidelines have recommended SBRT as a treatment option for hepatocellular carcinoma or HCC. Most guidelines recommend SBRT as an alternative therapy for early-stage HCC and recommend SBRT as a treatment for symptomatic relief in advanced or metastatic HCC. In Asia, SBRT is often chosen as a step before hepatic transplantation. In the United States, SBRT is usually offered to patients with good liver function (Child-Pugh A/CP A). In addition, SBRT is also often combined with other local therapies in mainland China and America.[5] Miften et al. recommend an average SBRT dose limit for primary liver disease of 13 Gy or 3 fractions to 18 Gy or 6 fractions.[8]

The following are among the indications for SBRT in HCC patients, per Hu et al. :[5]

1. A biopsy or a characteristic enhancement pattern on dynamic CT, dynamic MRI, or perflubutane-enhanced ultrasonography was used to diagnose primary HCC;
2. Refuses the procedure or is unable to undertake surgery or ablation as judged by a multidisciplinary specialist;
3. tumours with one or more nodules that are within the radiation area's reach, including those with portal vein thrombosis (PVTT);
4. The Eastern Cooperative Oncology Group (ECOG) reports a performance status of 0–2.
5. Normal liver volume > 700 ml;
6. Leukocyte count ≥ 3,000/mm3, platelet count ≥ 30,000/mm3, hemoglobin ≥ 8.0 g/dL, total bilirubin ≤ 2.0 mg/dL, and other indicators of good organ function;
7. No prior abdominal radiation would have compromised the infusion of a sufficient SBRT dosage.

The results of studies conducted in 18 countries with a total subject of 1536 HCC patients treated with SBRT showed that the local control rate in HCC patients treated with SBRT for two years was 93%. In addition, the overall survival rate in HCC patients treated with SBRT for one year showed that it was 69%, while the overall survival rate in HCC patients treated with SBRT for two years was 54%.[5]

Several prospective studies have reported that the local control rate in HCC patients with tumours larger than 5 cm treated with SBRT for one year was 56%-92%, and the overall survival rate in HCC patients with tumours larger than 5 cm treated with SBRT for one year was 32%-62%. The NCCN (National Comprehensive Cancer Network) recommends SBRT for tumours that are 2 cm or more prominent, but there is no clear tumour size limit. These findings imply that SBRT can improve acceptable survival for large tumours and provide local control.[5]

Limitations and Challenges of SBRT

Stereotactic body radiation therapy (SRBT) in the treatment of HCC patients with CP A disease has well-tolerated side effects, such as mild acute fatigue, lack of appetite, nausea due to lesions located near the abdomen, and radiation-induced liver disease (RILD). Long-term effects may include gastrointestinal bleeding in patients with tumors located near the intestine.[9]

An association of liver cancer experts in the Asia-Pacific region recommends SBRT for early detection only. In addition, SBRT, which generally uses higher radiation doses, can cause liver and gastrointestinal complications. The dose increase is influenced by tumor size, liver function, and the location of the tumor with other organs.[10]

LENVATINIB AS SYSTEMIC THERAPY FOR HCC

Lenvatinib Mechanism of Action

Lenvatinib is a multikinase tyrosine kinase inhibitor (TKI) that has antitumor effects by inhibiting several molecular pathways critical in angiogenesis and tumor cell proliferation. The main pathways targeted by lenvatinib include vascular endothelial growth factor receptors (VEGFR) 1, 2, and 3, fibroblast growth factor receptors (FGFR) 1 to 4, platelet growth factor receptor (PDGFR) alpha, KIT, and REarranged during Transfection (RET). Lenvatinib interferes with intracellular signals essential for tumor growth and spread by inhibiting these receptors. Inhibition of VEGFR and FGFR, for example, suppresses tumor angiogenesis by reducing the formation of new blood vessels necessary for tumor growth. In addition, lenvatinib also inhibits other signaling pathways, such as PDGFR and RET, which are involved in cell proliferation and tumor metastasis. Clinically, lenvatinib is an active agent in controlling tumor growth and prolonging progression-free survival in several cancers, including thyroid and hepatocellular cancers.[11]

Lenvatinib Mechanism of Action

The effectiveness of lenvatinib varies depending on the condition of each patient. Liver function is one of the influencing factors. The drug is stated to be relatively capable of prolonging the patient's Overall Survival (OS) or lifetime. Based on Wang et al. (2022), the combined mean Progression-Free Survival (PFS), Objective Response Rate (ORR), and Disease Control Rate (DCR) for lenvatinib were 6.68 months, 35% and 75%, respectively. Lenvatinib is considered quite effective in slowing disease progression, helping to prolong the period before the tumor grows back, and is able to show a good ORR. On the other hand, lenvatinib may trigger various side effects, such as hypertension or weight loss in patients. However, the prognosis of lenvatinib-induced hypertension is relatively good.[11]

Side Effects And Limitations Of Lenvatinib

Depending on the course of treatment, patients with HCC may have specific long-term adverse effects after finishing it. About a year after receiving a liver transplant, a tiny percentage of patients develop a chronic liver rejection reaction, in which the body begins to reject the new liver. Anti-rejection medications can be used to manage this, although some individuals need a second liver transplant. Side effects from radiotherapy can include diarrhea and bowel disturbances, abdominal pain, and long-lasting skin abnormalities in the treated area. These side effects can develop gradually over time. Even if new side effects appear months or years after receiving radiation therapy, it is imperative to report them to the physician or nurse. Notifying the physician or nurse of any new or persistent symptoms is crucial because HCC and its treatment can negatively influence one's physical and mental well-being. A customized survival care plan will also be developed by the physician or nurse. These adverse effects will be managed or prevented with assistance from the physician or nurse. Throughout the course of treatment, blood pressure will be tracked, and if necessary, antihypertensive medication will be administered.[12]

Combination of SBRT with Lenvatinib in Advanced HCC

The most common cause of cancer-related deaths is hepatocellular carcinoma (HCC), and its incidence is expected to rise. According to the biology of HCC and hepatic anatomy, HCC frequently invades nearby blood arteries. The most common type of macrovascular invasion is portal vein tumour thrombosis (PVTT), which has an autopsy incidence of 44-62%. When HCC with PVTT is treated with supportive care alone, the overall survival (OS) might be as low as 2.7–4 months, making it an advanced stage with a dismal prognosis.[13]

Based on research on the combination of SBRT and Levantinb is facing several challenges in the treatment of hepatocellular carcinoma (HCC) with portal vein tumor thrombosis (PVTT), the following results were obtained **(Table 1) :**

1. Improved overall survival (OS). Patients who received the combination of SBRT and Lenvatinib had better overall survival (OS) than those who received Lenvatinib alone. The median OS in the combination group was 19.3 months, while that in the Lenvatinib alone group was 11.2 months. This suggests that combination therapy can reduce the

risk of death by 63% (HR 0.37, $p < 0.001$).[13]

2. The combination of SBRT with Lenvatinib can lower the risk of tumour progression by 67% (HR 0.33, $p < 0.001$), as evidenced by improved progression-free survival (PFS), which was also longer in the combination group (10.3 months) than in the Lenvatinib alone group (5.3 months).[13]
3. Improved Intrahepatic Tumor Progression Survival (IHPFS). Patients receiving this combination therapy also showed a significant improvement in IHPFS survival, with a median IHPFS of 10.7 months compared to 5.3 months in the monotherapy group. This showed a 71% reduction in the risk of intrahepatic tumor progression (HR 0.29, $p < 0.001$).[13]
4. Improved Objective Remission Rate (ORR). The ORR, which includes complete and partial responses, was also higher in the combination group (56.8%) compared to the Lenvatinib alone group (20.8%). This suggests that the combination therapy is more effective in controlling tumor growth.[13]
5. Better Disease Control Rate (DCR). DCR, which includes complete response, partial response, and stable disease, was also higher in the combination group (91.9%) compared to the Lenvatinib alone group (64.9%).[13]

Table 1. Comparison of Effectiveness of Combination Therapy And Monotherapy. [13]

	Combination Therapy	Monotherapy
Overall Survival (OS)	19.3 months	11.2 months
Progression-Free Survival (PFS)	10.3 months	5.3 months
Intrahepatic Tumor Progression Survival (IHPFS)	10.7 months	5.3 months
Objective Remission Rate (ORR)	56.8%	20.8%
Disease Control Rate (DCR)	91.9%	64.9%

Indications and Contraindications for Combination Therapy of SBRT with Lenvatinib

The combination of SBRT + Lenvatinib is focused on managing advanced-stage HCC cases (BCLC C). Several things, namely characterize advanced-stage HCC:

1. Massive tumor spread to invade significant blood vessels (e.g., portal vein thrombosis) or to other organs outside the liver (extrahepatic metastasis).[4]
2. Liver function by child-pugh assessment **(Figure 2).** In this combination therapy, the patient's child-pugh assessment is critical. This therapy can be given to patients with liver function with Child-Pugh A and Child-Pugh B assessments.[4]

Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points) Class A = 5 to 6 points (least severe liver disease) Class B = 7 to 9 points (moderately severe liver disease) Class C = 10 to 15 points (most severe liver disease)			

Figure 2. Child Pugh Score in Liver Disease.[14]

Patients with a child-pugh score of C should not receive this combination therapy as the side effects of this combination therapy may worsen the patient's disease prognosis. Child-Pugh C is a classification that indicates the most severe degree of liver cirrhosis, with severely impaired liver function. Patients with Child-Pugh C often have serious complications such as severe ascites, hepatic encephalopathy, and elevated bilirubin, reflecting the inability of the liver to perform its function. The use of lenvatinib can have hepatotoxic side effects, including elevated liver enzymes (AST, ALT), hyperbilirubinemia, and even liver failure. In patients with poor liver function such as Child-Pugh C, the risk of hepatotoxicity increases significantly, as the severely damaged liver cannot metabolize the drug properly.[15]

In addition to the side effects of lenvatinib, SBRT radiation can also severely compromise patients with a child-pugh C score and can exacerbate remaining liver function impairment and increase the risk of acute liver failure.[15]

TREATMENT OF BCLC A AND B

In BCLC stages 0 and A, curative therapies such as surgical resection, liver transplant, and ablation may be considered, while for patients with BCLC B, palliative treatment with Transarterial chemoembolization (TACE) is recommended. The therapeutic approach for BCLC A varies according to the number of tumors and the severity of liver function impairment. If there is no clinically significant portal hypertension (CSPH), resection may be considered, while ablation is prioritized for small tumors or low-risk sites. In patients with CSPH, laparoscopic resection or LT is considered, but the decision depends on the tumor location and degree of CSPH.[16]

Chemotherapy with sorafenib can be given as palliative therapy for BCLC C. In contrast, supportive treatment can still be given to terminal-stage patients (BCLC D) with a life expectancy of more than three months. TACE is a way to treat liver cancer (HCC) by killing tumor cells by administering chemotherapy drugs directly through the arterial blood vessels that feed the tumor (arterial feeder). Because it is administered directly, the concentration of drugs in the cancer will be higher, and the side effects will be minimal compared to conventional chemotherapy administered through a vein. TACE attacks cancer in 2 ways, namely cytostatics or chemotherapy drugs locally/regionally and embolization, which will close the blood flow path that supplies the tumor to prolong the contact between cytostatics and cancer and will further increase the concentration of chemotherapy drugs in the tumor TACE is performed by interventional radiology doctors with the help of angiography tools. A needle is punctured through the femoral artery in the groin, and a catheter is inserted into the arterial blood vessel that feeds the tumour. Once the arterial feeder is identified, chemotherapy drugs are injected at the prescribed dose. The procedure takes 1-2 hours and can be repeated at 6 to 12 weeks.[17]

POTENTIAL BENEFITS AND CHALLENGES OF COMBINATION

Based on previous studies, there are significant and positive results from the combination of SBRT with Lenvatinib in improving tumor control and patient survival. The prognosis of patients receiving this combination therapy was significantly better than those receiving only Lenvatinib monotherapy. However, based on research conducted by Ji et al., it is known that there are several challenges in the combination of SBRT and Levantinb is facing several challenges in the treatment of hepatocellular carcinoma (HCC) with portal vein tumor thrombosis (PVTT), including:

1. Side Effects and Tolerability: Although side effects arising from combination therapy are generally manageable, there is an increased risk of side effects, such as hypertension and diarrhea, which require close monitoring and dose adjustment. Approximately 91% of patients in the combination therapy group experienced side effects requiring a dose reduction or temporary treatment discontinuation.[13]
2. Complexity of Management of Patients with PVTT: The management of patients with HCC who also have PVTT is complex as the condition is already in an advanced stage and has a poor prognosis. Combination therapy has the potential to increase the toxicity burden and requires a cautious approach, especially in patients with compromised liver function.[13]
3. Response Variability According to the PVTT classification, Treatment results are influenced by PVTT categorization, and the degree of thrombosis can affect how well a patient responds to this combination of medications. Based on the Japanese Hepatocellular Carcinoma Research Group's proposed classification system, which takes into account anatomical structure and the degree of tumour thrombosis, researchers divided PVTT into five categories: PVTT is absent in VP0, distal but not involved in second-order PV branches; invasive in second-order branches; present in first-order branches; and extending into contralateral portal vein branches in VP4. Patients with milder PVTT (Vp1-2) have better results than those with more severe PVTT (Vp3-4).[13]

CONCLUSION

The combination of SBRT and Lenvatinib in hepatocellular carcinoma (HCC) patients with portal vein tumor thrombosis (PVTT) proved more effective than Lenvatinib alone. This combination therapy significantly improved overall survival (OS), progression-free survival (PFS), intrahepatic tumor progression-free survival (IHPFS), objective remission rate (ORR), and disease control rate (DCR). The results show that this combination can better prolong life and control tumor progression than Lenvatinib monotherapy. However, the treatment strategy needs to be customized cautiously so as not to cause a poor prognosis.

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