

# Analysis of the Effect of Bevacizumab as an Anti-VEGFR Pathway Drug in the Clinical Treatment of Lung Cancer

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**Abstract:** *Objective:* To analyze the effect of treatment with bevacizumab, an anti-vascular-endothelial-growth-factor (anti-VEGFR) pathway drug, in patients with lung cancer. *Methods:* 60 patients with lung cancer that were admitted from October 2021 to February 2023 were used as research subjects, the patients were divided into two groups using the random number table. Group A was treated with bevacizumab + protein bound paclitaxel combined with carboplatin + cisplatin, and Group B was treated with protein-bound paclitaxel combined with carboplatin + cisplatin. The efficacy of both treatments and the tumor marker levels, the immune function, and the toxicity and side effects between the two groups were compared. *Results:* The efficacy of the lung cancer therapy in group A was higher than that in group B,  $P < 0.05$ ; serum tumor markers such as carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), carbohydrate antigen 125 (CA125) of the patients of group A were significantly higher than those in group B,  $P < 0.05$ ;  $CD4^+$ ,  $CD8^+$ ,  $CD4^+/CD8^+$  and other immune indicators of the patients in group A were better than those in group B,  $P < 0.05$ ; the toxicity and side effects of the treatment received in group A was no different than group B,  $P > 0.05$ . *Conclusion:* Bevacizumab, an anti-VEGFR pathway drug, is effective and feasible in treating lung cancer. Besides, it inhibits the progression of cancer, regulates the body's immune function, thus prolonging the survival of patients.

**Keywords:** Anti-VEGFR drugs; Bevacizumab; Lung cancer; Efficacy

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## 1. Introduction

Lung cancer is one of the most common malignant tumors and a leading cause of patient mortality. The most common pathological type is non-small cell lung cancer (NSCLC). Following the onset of lung cancer, tumor cell proliferation is typically slow, and metastasis occurs later in the disease course. Patients often remain asymptomatic during the early stages of the illness, which can lead to a delay in the optimal timing of surgery once the diagnosis is established <sup>[1]</sup>. Chemotherapy is commonly used in treating patients with advanced lung cancer. The drugs used are protein-bound paclitaxel combined with carboplatin, cisplatin, etc., which can prolong the survival of patients. However, the chances of a 5-year survival of lung cancer patients are still relatively low <sup>[2]</sup>. In recent years, targeted drugs have been gradually used in the treatment of lung cancer, such

as bevacizumab, which can act on vascular endothelial growth factor (VEGF), block the growth of tumor blood vessels, and induce tumor cell death. It is applicable to the treatment of advanced malignant tumors<sup>[3]</sup>. In this paper, 60 patients with lung cancer who were treated from October 2022 to February 2023 were used as a sample to explore the treatment effect of bevacizumab.

## 2. Materials and methods

### 2.1. Information

60 lung cancer patients from October 2021 to February 2023 were included in this study, and the patients were divided into 2 groups by the random number table method. Group A consisted of 19 males and 11 females, aged 40–72 years, average  $52.88 \pm 1.89$  years; group B, 21 males, 9 females, aged 41–73 years, average  $53.01 \pm 1.91$  years old. There was no difference in the data of patients with lung cancer in group A and group B,  $P > 0.05$ .

### 2.2. Inclusion and exclusion criteria

Inclusion criteria: (i) expected survival of more than 3 months, (ii) imaging and pathology results suggest lung cancer, (iii) signed an informed consent, (iv) requires chemotherapy.

Exclusion criteria: (i) patients with mental and intellectual abnormalities, (ii) patients with secondary malignant tumors, (iii) patients allergic to chemotherapy drugs or bevacizumab, (iv) patients with cardiac dysfunction.

### 2.3. Treatment methods

The chemotherapy regimen of group A is the same as that of group B. As for the patients in group A (manufactured by Hengrui Pharmaceutical Company; approval number: S20100024) 7.5 mg/kg bevacizumab was administered intravenously once a day, and one course of treatment lasted for 4 weeks. A total of 4 courses of treatment were carried out for each patient.

Group B was given protein-bound paclitaxel combined with carboplatin (manufactured by Jiangsu Hansoh Pharmaceutical Group Co., Ltd.; approval number: H20093996) combined with cisplatin (manufactured by Dezhou Deyao Pharmaceutical Co., Ltd.; approval number: H20093996). Protein-bound paclitaxel combined with  $500 \text{ mg/m}^2$  carboplatin and  $75 \text{ mg/m}^2$  cisplatin were administered once a day, both by intravenous infusion. one course of treatment lasted for 4 weeks. A total of 4 courses of treatment were carried out for each patient. During chemotherapy, it is important to pay attention to the management of allergies and nausea, and the patient should also be well hydrated.

### 2.4. Observation indicators

Efficacy was assessed as follows: Complete remission (CR) indicated the absence of lung cancer lesions for four consecutive weeks, partial response (PR) meant a reduction of over 30% in the sum of the largest tumor diameters for four consecutive weeks, stable disease (SD) was recorded for  $\leq 30\%$  reduction or  $< 20\%$  increase in the sum of the largest tumor diameters for four consecutive weeks, progressive disease (PD) was noted for a  $\geq 20\%$  increase in the sum of the largest tumor diameters for four consecutive weeks. The disease control rate (DCR) was calculated as CR rate + PR rate + SD rate. Tumor markers, including carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), and carbohydrate antigen 125 (CA125), were monitored before and after medication, as well as changes in  $\text{CD4}^+$ ,  $\text{CD8}^+$ , and  $\text{CD4}^+/\text{CD8}^+$  ratios. Toxic and side effects such as abnormal liver function, bone marrow suppression, and chemotherapy-induced thrombocytopenia were recorded for both groups.

## 2.5. Statistical analysis

The data from lung cancer patients were analyzed using SPSS 21.0 software. Count data for lung cancer patients were expressed as percentages and analyzed using the  $\chi^2$  test, while mean  $\pm$  standard deviation was used for measurement data of lung cancer patients and analyzed with a  $t$ -test. Statistical significance was set at  $P < 0.05$ .

## 3. Results

### 3.1. Efficacy

The efficacy of the treatment received by group A was higher than that in group B,  $P < 0.05$ . As in **Table 1**.

**Table 1.** Efficacy of treatment received by group A and group B ( $n$  [%])

Group	CR	PR	SD	PD	DCR
Group A ( $n = 30$ )	0 (0.00)	9 (30.00)	18 (60.00)	3 (10.00)	27 (90.00)
Group B ( $n = 30$ )	0 (0.00)	3 (10.00)	13 (43.33)	14 (46.67)	16 (53.33)
$\chi^2$	-	-	-	-	9.9316
$P$	-	-	-	-	0.0016

### 3.2. Tumor markers

Before treatment, there was no difference in the tumor markers between group A and group B,  $P > 0.05$ . After treatment, the tumor markers such as CEA, NSE, and CA125 in group A were better than those in group B ( $P < 0.05$ ), as shown in **Table 2**.

**Table 2.** Comparison of tumor markers (mean  $\pm$  standard deviation)

Group	CEA ( $\mu\text{g/L}$ )		NSE ( $\mu\text{g/L}$ )		CA125 (mg/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A ( $n = 30$ )	124.14 $\pm$ 2.36	25.41 $\pm$ 1.51	17.87 $\pm$ 2.43	5.59 $\pm$ 1.84	275.36 $\pm$ 3.28	27.11 $\pm$ 2.36
Group B ( $n = 30$ )	124.19 $\pm$ 2.39	49.31 $\pm$ 1.69	17.91 $\pm$ 2.39	9.71 $\pm$ 1.96	275.41 $\pm$ 3.31	45.73 $\pm$ 2.87
$t$	0.0815	57.7614	0.0643	8.3941	0.0588	27.4472
$P$	0.9353	0.0000	0.9490	0.0000	0.9533	0.0000

### 3.3. Immune function

Before treatment, there was no difference in the immune function indexes between group A and group B,  $P > 0.05$ . After treatment, immune indexes such as CD4<sup>+</sup>, CD8<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup> in group A were better than those in group B,  $P < 0.05$ , as shown in **Table 3**.

**Table 3.** Comparison of immune function (mean  $\pm$  standard deviation)

Group	CD4 <sup>+</sup> (%)		CD8 <sup>+</sup> (%)		CD4 <sup>+</sup> /CD8 <sup>+</sup> (%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A ( $n = 30$ )	27.01 $\pm$ 1.87	29.43 $\pm$ 2.01	23.21 $\pm$ 1.42	19.43 $\pm$ 1.32	1.25 $\pm$ 0.21	1.39 $\pm$ 0.17
Group B ( $n = 30$ )	27.05 $\pm$ 1.91	23.43 $\pm$ 1.63	23.24 $\pm$ 1.39	22.08 $\pm$ 1.36	1.23 $\pm$ 0.19	1.08 $\pm$ 0.09
$t$	0.0820	12.6991	0.0827	7.6584	0.3868	8.8272
$P$	0.9350	0.0000	0.9344	0.0000	0.7003	0.0000

### 3.4. Toxicity and side effects

The toxicity of both types of treatment were no different ( $P > 0.05$ ), as shown in **Table 4**.

**Table 4.** Comparison of the toxicity and side effects of both groups ( $n$  [%])

Group	Abnormal liver function	Myelosuppression	Thrombocytopenia	Incidence rate
Group A ( $n = 30$ )	1 (3.33)	1 (3.33)	3 (10.00)	6 (20.00)
Group B ( $n = 30$ )	2 (6.67)	1 (3.33)	2 (6.67)	5 (16.67)
$\chi^2$	-	-	-	0.1113
$P$	-	-	-	0.7386

## 4. Discussion

Lung cancer is a relatively common malignant tumor, and it comes with several symptoms. (i) Coughing: Coughing is the primary symptom of lung cancer. This is because the function of bronchial mucus secretion will be impaired due to tumor cell infiltration. Paroxysmal dry cough is common among lung cancer patients, which cannot be treated with conventional cough medicine. In addition, smoking further aggravates coughing. (ii) Hemoptysis: Tumor tissue possesses an abundant blood supply, and severe coughing can lead to the rupture of blood vessels within it, potentially triggering hemoptysis. This is especially significant in cases where larger blood vessels rupture, resulting in more substantial episodes of hemoptysis. (iii) Chest pain: Most patients with lung cancer experience chest tightness or chest pain, and in severe cases, throbbing pain. (iv) Chest tightness: Central lung cancer patients often experience chest tightness, and if secondary lung failure develops, it can be accompanied by dyspnea. This is often associated with factors such as airway obstruction, atelectasis, pleural effusion, and lymph node metastasis, making treatment challenging. (v) Hoarseness is an uncommon symptom in lung cancer patients and is typically associated with lymph node metastasis and blockage of the recurrent laryngeal nerve. In severe cases, it can lead to airway obstruction and impaired respiratory function<sup>[5,6]</sup>.

There are several causes of lung cancer. (i) Smoking: The incidence of lung cancer is associated with the duration of smoking. (ii) Occupational exposure: working in special environment for a long time, such as exposure to ammonia, formaldehyde, coal tar and other substances. (iii) Air pollution: vehicle exhaust emissions and industrial waste gas increase the risk of lung cancer. (iv) Ionizing radiation: Long-term high-dose exposure to ionizing radiation can induce lung cancer. (v) Diet: Individuals with a low daily intake of fruits and vegetables often have low levels of  $\beta$ -carotene in their bodies. (vi) History of pulmonary diseases: Those with history of bronchiectasis and pulmonary tuberculosis are more likely to develop lung cancer. Since there are no specific signs in the early stages of lung cancer, when it advances to the middle and late stages, it becomes necessary to combine chemotherapy regimens to stabilize the disease, delay the progression of cancer foci, and enhance the 5-year survival rate of patients<sup>[7,8]</sup>.

At present, protein-bound paclitaxel combined with carboplatin is mostly used in the treatment of lung cancer patients. Taxol protein-bound combined with carboplatin is a targeted cytotoxic drug that acts on multiple targets, disrupting various enzyme activation processes within the human body. It inhibits dihydrofolate reductase and other catalytic reactions, subsequently counteracting the body's synthesis of purine and thymidine nucleotides. This inhibition suppresses tumor cell RNA and DNA replication, leading to a slowdown in tumor proliferation.<sup>[9,10]</sup> Cisplatin is administered intravenously and directly acts on tumor cells, allowing water molecules to replace chloride ions in tumor cells, causing water molecules to enter the nucleus of tumor cells. The water molecules are then replaced by guanine, which results in the inhibition of DNA transcription of

tumor cells, leading to apoptosis, thus delaying tumor progression<sup>[11,12]</sup>. As per relevant literature, the 5-year survival rate for patients treated with protein-bound paclitaxel in combination with carboplatin + cisplatin chemotherapy for lung cancer remains relatively low. This outcome is associated with tumor cell metastasis, which is closely linked to both neovascularization and the infiltration of tumor cells<sup>[13]</sup>. When the tumor cells in lung cancer patients exceed 2 mm in diameter, independent vasculature is needed to supply energy to the tumor cells. However, new tumor blood vessels in the body need the help of vascular endothelial growth factor (VEGF) and other cytokines. Therefore, VEGF and vascular endothelial growth factor (VEGFR) targeted therapy can be carried out during the treatment of lung cancer patients. Bevacizumab is a novel targeted therapy drug that contains human genes (93.00%) and mouse genes (7.00%). The two gene fragments competitively inhibit each other and have the ability to bind to endogenous VEGFR, resulting in the inactivation of VEGF. This process effectively disrupts the proliferation of endothelial cells and blocks the formation of new blood vessels in the tumor's surrounding area. Furthermore, it can also inhibit the functioning of the tumor cell implantation system. By disrupting the supply of nutrients and oxygen to the tumor tissue, it effectively hinders tumor growth, thus demonstrating anti-tumor properties. Additionally, bevacizumab can increase blood vessel permeability, leading to a higher concentration of locally administered chemotherapeutic drugs and thereby enhancing treatment efficacy<sup>[14]</sup>. Protein-bound paclitaxel combined carboplatin + platinum chemotherapy, combined with bevacizumab therapy can optimize the prognosis of lung cancer patients.

Combined with the data analysis in this paper, the lung cancer treatment in group A was higher than that in group B ( $P < 0.05$ ); serum tumor markers such as CEA, NSE, and CA125 in group A were lower than those in group B ( $P < 0.05$ ); group A's CD4<sup>+</sup>, CD8<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup> and other immune indicators were better than those in group B ( $P < 0.05$ ); the incidence of toxic and side effects in patients with lung cancer in group A was not different from that in group B, ( $P > 0.05$ ). It is suggested that conventional chemotherapy + bevacizumab treatment can enhance the immune function of patients and delay the progression of cancer. Besides, the addition bevacizumab does not increase the toxicity of the treatment. Bevacizumab belongs to the main monoclonal antibody, which can prevent edema, induce tumor cell apoptosis by blocking VEGF activity, and has the effect of anti-angiogenesis in the adjacent area of the tumor, which is beneficial to the prognosis of lung cancer patients.

## 5. Conclusion

In summary, bevacizumab, an anti-VEGFR pathway drug, can regulate the immune function of the body and delay the progression of lung cancer for lung cancer patients. Besides the addition of bevacizumab does not increase the toxicity and side effects, which helps prolong the survival of lung cancer patients and has promotion value.

## Disclosure statement

The author declares no conflict of interest.

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