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Clinical Efficacy of Tirilizumab in Combination with Conventional Chemotherapeutic Agents in Patients with Advanced Non-small Cell Lung Cancer

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Abstract: *Objective:* To explore the analysis of the application effect of tirilizumab combined with conventional chemotherapeutic drugs (paclitaxel + carboplatin) in the clinical treatment of advanced non-small cell lung cancer patients. *Methods:* Seventy-five patients with advanced non-small cell lung cancer who received chemotherapy treatment in a hospital from July 2023 to June 2024 were selected as objects, and grouped according to the choice of chemotherapy drugs, 37 patients who received regular chemotherapy drugs (paclitaxel + carboplatin) were included in the control group, and the other 38 patients who received tirilizumab + paclitaxel and carboplatin chemotherapy were included in the observation group, and the clinical efficacy of the two groups was compared. *Results:* Before treatment, the difference in serum tumour marker levels between the two groups was not significant ($P > 0.05$); after treatment, the levels of glycan antigen 125 (CA125), carcinoembryonic antigen (CEA), neuron-specific enolase NSE, and squamous carcinoembryonic antigen (SCC) in the patients of the two groups were significantly reduced, and the level in the observation group was lower than that in the control group ($P < 0.05$); before treatment, the level of immune function in the patients of the two groups, there was no statistically significant difference between the immune function levels of patients in the two groups ($P > 0.05$); after treatment, the levels of $CD3^+$, $CD4^+$ and $CD4^+$ /$CD8^+$ were significantly higher and $CD8^+$ were lower in the two groups, and the indicators of the observation group were better than those of the control group ($P < 0.05$); the incidence rate of toxic side effects such as nausea, vomiting, bone marrow suppression, liver and kidney function abnormalities, and so on, during the period of treatment of the observation group was significantly lower than that of the control group (5.26%) and the difference had a significant difference of 24.32%, the difference was statistically significant ($P < 0.05$); before treatment, there was no statistically significant difference in the quality of life SF-36 scores between the two groups ($P > 0.05$); after three courses of treatment, the quality of life SF-36 scores of the two groups were significantly higher, and the observation group was higher than the control group ($P < 0.05$). *Conclusion:* Tirilizumab combined with conventional chemotherapy drugs (paclitaxel + carboplatin) has remarkable efficacy in the treatment of advanced non-small cell lung cancer, which can effectively reduce the level of tumour markers and the risk of toxic and side effects, improve the immune function and enhance the quality of life of patients, and has positive clinical promotion value.

Keywords: Advanced non-small cell lung cancer; Tirilizumab; Chemotherapy; Tumour markers; Immune function; Quality of life SF-36

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1. Introduction

Advanced non-small cell lung cancer (NSCLC) is one of the most common malignancies worldwide, and since most patients are diagnosed at an advanced stage, surgical resection is often not possible, and only systemic chemotherapeutic treatment is available. For a long time, traditional chemotherapeutic agents such as paclitaxel and carboplatin have always occupied an important position in the treatment of NSCLC [1]. Paclitaxel induces apoptosis in tumour cells by inhibiting microtubule protein polymerization and interfering with the process of cell division; carboplatin, on the other hand, inhibits DNA replication by binding to the DNA of the tumour cells, thereby preventing cell proliferation [2]. Although chemotherapy has prolonged the survival time of patients to a certain extent, its efficacy is limited, especially for patients with advanced NSCLC, and drug resistance and toxicity remain major challenges. In recent years, with the rapid development of tumour immunology, the emergence of immune checkpoint inhibitors (e.g., anti-PD-1/PD-L1 monoclonal antibodies) has brought new therapeutic options for patients with advanced NSCLC [3]. Tirelizumab is an anti-PD-1 monoclonal antibody, which is used in the treatment of tumour diseases to inhibit tumour growth by blocking the PD-1 pathway and restoring T-cell activity [4]. Relevant medical research shows that in the clinical treatment of tumour patients, the combined use of immunotherapy and chemotherapy has a certain synergistic effect. On the one hand, chemotherapeutic agents can directly kill tumour cells and release tumour antigens, thus enhancing the recognition ability of the immune system [5]. On the other hand, immune checkpoint inhibitors can further activate anti-tumour immune responses and enhance the therapeutic effect of chemotherapy [6]. Therefore, exploring the efficacy and safety of the combination of tirilizumab with conventional chemotherapeutic agents in the treatment of patients with advanced NSCLC is of great clinical significance. In this study, we took patients with advanced NSCLC as research subjects and analyzed the application effect of tirilizumab combined with chemotherapy (paclitaxel + carboplatin) in the clinic, aiming to provide a more optimal treatment plan for this type of patient.

2. Information and methodology

2.1. General information

Seventy-five patients with advanced non-small cell lung cancer who were treated with chemotherapy in a hospital from July 2023 to June 2024 were selected and grouped according to the treatment method, and 37 patients who were treated with conventional chemotherapeutic drugs (paclitaxel + carboplatin) were included in the control group. Among them, 21 cases were male and 16 cases were female, the age range was 45–78 years old, with an average of (62.42 ± 8.56) years old; clinical stage: 14 cases of stage III and 23 cases of stage IV. Another 38 patients who received tirilizumab + paclitaxel and carboplatin chemotherapy were included in the observation group. Among them, there were 20 males and 18 females, with an age range of 43–79 years old, mean (61.91 ± 8.63) years old; clinical stage: 13 cases of stage III and 25 cases of stage IV. The difference in general information between the two groups of patients was not statistically significant ($P > 0.05$) and was

comparable.

Inclusion criteria: (1) non-small cell lung cancer (NSCLC) stage III or IV diagnosed by pathology or cytology [7]; (2) age between 43 and 79 years old, no gender restriction; (3) no contraindication to immunotherapy and no previous treatment with immune checkpoint inhibitors; (4) patients with quality of life SF-36 scores of > 50, able to tolerate chemotherapy and immunotherapy; (5) voluntary participation in the study and signed an informed consent form.

Exclusion criteria: (1) the presence of other malignant tumours or recently received other anti-tumour therapy (such as radiotherapy, targeted therapy, etc.); (2) previous history of severe cardiac, hepatic, renal function abnormalities or active autoimmune diseases; (3) the presence of uncontrolled infections (e.g., active tuberculosis, hepatitis B, hepatitis C, or HIV infection) disease; (4) patients who participated in a clinical trial of other drugs in the 6 months prior to the start of the study.

2.2. Methodology

During the treatment period, patients in both groups received hydration, correction of electrolyte disorders and anti-allergic conventional supportive therapy, meanwhile, healthcare personnel closely monitored the patients, focusing on the occurrence of toxic side effects, and took corresponding measures in time to ensure the safety of the patients and the smooth progress of the treatment. The control group adopts a conventional chemotherapy regimen (paclitaxel + carboplatin), every 21 days as a course of treatment, which lasts until the disease progresses or the patient is unable to tolerate the toxicity. The specific chemotherapy procedure was as follows: on days 1, 8 and 15 of each course, patients received paclitaxel intravenous drip (135 mg/m^2), (Beijing Shuanglu Pharmaceutical Co., Ltd., specification 5 mL/30 mg, State Pharmaceutical Licence No.: H20066640), which was diluted with 250 mL of saline and slowly infused. Meanwhile, on day 1 of each treatment course, patients received carboplatin intravenous drip (about 50 g based on AUC5 dose), the drug was produced by Qilu Pharmaceutical Co. Ltd. (National Pharmaceutical Standard H20020180). Throughout the treatment process, standardized toxicity management was strictly implemented and adverse reactions were closely monitored to ensure the safety and efficacy of chemotherapy.

The observation group was treated with tirilizumab in combination with the control group's chemotherapy regimen in courses of 21 days each, continuing until disease progression or patient intolerance of toxicity. The specific treatment procedure was as follows: on day 1 of each course, patients received paclitaxel (135 mg/m^2) and carboplatin (AUC5 dose, approximately 50 g) intravenously, in combination with tirilizumab injection (Guangzhou Baizi Divine Bio-Pharmaceutical Co., Ltd., State Drug Licence S20190045). Tirilizumab was added into 100 mL 0.9% sodium chloride injection at a dose of 200 mg/dose and mixed evenly for intravenous drip. Throughout the treatment process, healthcare professionals strictly monitored the patients' drug reactions, paid close attention to possible adverse reactions, and took appropriate measures to deal with them to ensure the safety and effectiveness of the combined treatment protocol.

2.3. Observation indicators

2.3.1. Serum tumour markers

Before treatment and after completing 3 courses of treatment, serum samples were collected from patients, and serum tumour marker levels were detected using a fully automated chemiluminescent immunoassay analyzer (Maglumi2000PLUS). The test indicators include squamous carcinoma antigen (SCC), carcinoembryonic

antigen (CEA), neuron-specific enolase (NSE) and glycan antigen 125 (CA125). The dynamic changes of these indicators are used to assess the effectiveness of treatment and disease progression.

2.3.2. Immune function testing

Before treatment and after completing 3 courses of treatment, flow cytometry (model: FACSCalibur, BD, USA) was used to test the immune function of patients. The detection indexes include the expression levels of T-lymphocytes CD3+, helper T-cells CD4+ and cytotoxic T-cells CD8+, and the CD4+/CD8+ ratio is calculated to assess the functional status of the immune system.

2.3.3. Quality of life scores

The patient's physical and mental health were comprehensively measured using The Short Form-36 Health Survey (SF-36), which consists of 8 dimensions, namely Physical Functioning (PF), Role Physiology (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Emotional Functioning (RE) and Mental Health (MH). Scores for each dimension range from 0– 100, with higher scores indicating better quality of life.

2.3.4. Toxic side effects

Observe and record the occurrence of toxic side effects such as nausea, vomiting, bone marrow suppression, liver, and kidney function abnormalities, etc., during the treatment of the two groups, and the incidence rate = the number of cases/the total number of cases × 100%.

2.4. Statistical methods

The software SPSS 23.0 was applied to statistically analyze the data of this study. General data such as gender distribution, clinical stage and count data such as toxic side effects were expressed as [n (%)], and the χ^2 test was used; the measurement data such as mean age, serum tumour marker expression, immune function level, SF-36 quality of life score were expressed as mean ± standard deviation (SD), and the comparison between groups was made using the t-test, and the difference between groups was expressed by $P < 0.05$ to indicate statistical significance.

3. Results

3.1. Comparison of serum tumour marker levels between the two groups of patients before and after treatment

Before treatment, there was no statistically significant difference in the levels of serum CA125, CEA, NSE, and SCC between the two groups of patients ($P > 0.05$). After treatment, the levels of various indexes in the two groups decreased significantly, and the observation group was lower than the control group, and the difference was statistically significant ($P < 0.05$). See **Table 1**.

Table 1. Comparison of serum tumour marker levels before and after treatment in the two groups (mean ± SD)

Groups	CA125 (U/mL)		CEA (ng/mL)		NSE (ng/mL)		SCC (ng/mL)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Control group (n = 37)	103.75 ± 5.21	62.37 ± 2.32*	65.72 ± 0.23	30.34 ± 2.30*	38.59 ± 2.34	21.75 ± 1.59*	48.86 ± 5.02	25.46 ± 3.42*
Observation group (n = 38)	103.97 ± 5.23	37.78 ± 2.36*	65.81 ± 0.25	19.85 ± 2.26*	39.02 ± 2.25	17.12 ± 1.43*	49.23 ± 4.78	21.17 ± 3.35*
t	0.1825	45.4923	1.6213	19.9222	0.8113	13.2670	0.3270	5.4878
p	0.8557	< 0.01	0.1093	< 0.01	0.4198	< 0.01	0.7446	< 0.01

Note: *P < 0.05 compared to pre-treatment.

3.2. Comparison of immune function levels between the two groups before and after treatment

Before treatment, the difference between the immune function levels of the two groups of patients was not statistically significant (P > 0.05). After treatment, the $CD3^+$, $CD4^+$ and $CD4^+$ /$CD8^+$ of the two groups were significantly higher, and $CD8^+$ was significantly lower, and the indicators of the observation group were better than those of the control group, and the difference was statistically significant (P < 0.05). See **Table 2**.

Table 2. Comparison of immune function levels between the two groups of patients before and after treatment (mean ± SD)

Groups	CD3+ (%)		CD4+ (%)		CD8+ (%)		CD4+ /CD8+ (%)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Control group (n = 37)	42.12 ± 6.75	52.57 ± 8.69*	28.58 ± 4.39	34.19 ± 4.06*	29.48 ± 2.34	23.25 ± 3.35*	0.98 ± 0.22	1.54 ± 0.24*
Observation group (n = 38)	41.83 ± 6.85	60.52 ± 8.39*	28.03 ± 4.46	40.21 ± 4.25*	29.02 ± 2.25	20.14 ± 2.36*	0.97 ± 0.19	2.11 ± 0.32*
t	0.1846	4.0310	0.5381	6.2696	0.8679	4.6579	0.2109	8.7088
p	0.8540	< 0.01	0.5922	< 0.01	0.3883	< 0.01	0.8336	< 0.01

Note: *P < 0.05 compared to pre-treatment.

3.3. Comparison of toxic side effects between the two groups of patients

The incidence of toxic side effects in patients in the observation group was significantly lower than that in the control group, and the difference was statistically significant (P < 0.05). See **Table 3**.

Table 3. Comparison of the occurrence of toxic side effects in the two groups (n, %)

Groups	Nauseating	Vomiting	Myelosuppression	Abnormalities in liver and kidney function	Rate of occurrence
Control group (n = 37)	3 (8.11)	2 (5.40)	3 (8.11)	1 (2.70)	9 (24.32)
Observation group (n = 38)	1 (2.63)	0	1 (2.63)	0	2 (5.26)
χ^2					5.4422
p					0.0197

3.4. Comparison of quality of life between the two groups

Before treatment, there was no statistically significant difference in the quality of life SF-36 scores between the two groups ($P > 0.05$). After 3 courses of treatment, the quality of life SF-36 scores of the two groups increased significantly, and the observation group was higher than the control group, with a statistically significant difference ($P < 0.05$). See **Table 4**.

Table 4. Comparison of quality of life SF-36 scores between the two groups before and after treatment (mean ± SD, points)

Groups	Pre-treatment	3 courses of treatment	*t*	*p*
Control group (*n* = 37)	50.56 ± 5.83	65.24 ± 4.72	11.9042	< 0.01
Observation group (*n* = 38)	50.21 ± 6.02	82.31 ± 5.03	25.2240	< 0.01
t	0.2557	15.1465		
p	0.7989	< 0.01		

4. Discussion

Advanced non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for approximately 85% of all lung cancer cases [8]. NSCLC has insidious symptoms in the early stages of the disease and patients lack specific manifestations in the early stages of the disease, which are often diagnosed only when the disease has progressed to advanced stages. Early-stage NSCLC patients can be treated with radical surgery, but most advanced NSCLC patients are unable to receive surgical treatment due to extensive lesions or physical conditions that do not allow them to undergo surgical treatment, making treatment options limited [9]. Currently, the conventional treatment option for advanced NSCLC is the TP regimen (paclitaxel combined with carboplatin). Although this regimen has some efficacy in controlling disease progression, its overall therapeutic efficacy is still limited, and chemotherapy-related toxicities (e.g., nausea, vomiting, myelosuppression, and abnormalities in hepatic and renal functions) have also affected patients' tolerability and quality of life to a certain extent. Patients' overall survival (OS) and progression-free survival (PFS) have remained short, with an overall poorer prognosis [10]. There is an urgent clinical need to develop new drugs and therapeutic strategies for the unsatisfactory treatment of advanced NSCLC. The emergence of immune checkpoint inhibitors such as tirilizumab provides new therapeutic hope for NSCLC patients. By blocking the PD-1/PD-L1 signaling pathway, tirilizumab restores T-cell activity and enhances anti-tumour immune responses in patients, thus playing a key role in the treatment of advanced NSCLC [11]. Combining tirilizumab with standard chemotherapeutic regimens may improve the survival outcome of patients while increasing efficacy and become an important breakthrough direction in the treatment of advanced NSCLC.

The results of this study showed that serum tumour marker levels, immune function levels, the incidence of toxic side effects, quality of life and other qualitative changes in the observation group of patients who received tirilizumab combined with a conventional chemotherapy regimen were significantly better than those in the control group who received conventional TP regimen. Analysis of the reasons suggests that this efficacy advantage stems from the synergistic effect of tirilizumab and chemotherapeutic agents, which optimizes the therapeutic effect of advanced non-small cell lung cancer (NSCLC) in many ways [12]. Tirilizumab enhances the immune clearance of tumour cells by blocking the PD-1/PD-L1 signaling pathway and restoring T-cell

function. Paclitaxel and carboplatin, on the other hand, further reduced the tumour load by disrupting tumour cell division, which synergistically significantly reduced tumour marker levels, reflecting a higher tumour control rate. Tirilizumab activates the patient's immune system by lifting T-cell immunosuppression, restoring its recognition and killing function against tumour cells.

Combined chemotherapy with paclitaxel and carboplatin further reduces tumour load by interfering with tumour cell division and proliferation. Paclitaxel acts as a microtubule protein inhibitor and prevents tumour cell mitosis, while carboplatin induces apoptosis by binding to DNA to form crosslinks and inhibiting DNA replication and transcription. Both act synergistically to significantly reduce tumour marker levels and improve tumour control.

Tirelizumab, as a PD-1 monoclonal antibody, activates the anti-tumour immune response of patients by blocking the PD-1/PD-L1 pathway and restoring the ability of T-cells to recognize and kill tumour cells. Compared with the mechanism of single killing of tumour cells by traditional chemotherapy, tirilizumab combined with chemotherapy not only enhances the anti-tumour effect, but also improves the immune status, providing patients with stronger anti-tumour ability. Tirilizumab may reduce the damage of chemotherapeutic drugs to normal cells by improving the immune environment, especially in the recovery speed of myelosuppression and the maintenance of liver and kidney functions, which helps patients to better tolerate the treatment and ensures the continuity of treatment. Tirilizumab combination chemotherapy not only improves the clinical outcome of patients, but also helps patients to achieve a better state of life both physically and psychologically by reducing the burden of symptoms and improving immune function. The traditional chemotherapeutic drugs paclitaxel and carboplatin achieve efficacy mainly by directly killing tumour cells. However, a single chemotherapeutic agent has limited effect on improving the microenvironment and immunosuppressive status of tumours, whereas tirilizumab plays a role in targeting the immunosuppressive characteristics of the tumour microenvironment, which is complementary to chemotherapy in terms of mechanism. This synergistic mechanism not only improves anti-tumour efficacy but also slows down the emergence of drug-resistance, which results in a more lasting benefit to the patients.

5. Conclusion

Tirilizumab combined with conventional chemotherapeutic agents has significant clinical advantages in the treatment of advanced NSCLC, which provides an important breakthrough in the comprehensive treatment of NSCLC by improving efficacy, survival outcomes and quality of life of patients through the synergistic effect of multiple mechanisms.

Disclosure statement

The authors declare no conflict of interest.

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