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Efficacy of tislelizumab combined with gemcitabine and resulting changes in CT imaging for advanced non-small cell lung cancer

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► ***Original article***

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ABSTRACT

Background: The purposes of this study were to evaluated the efficacy and changes in computed tomography (CT) imaging associated with tislelizumab combined with gemcitabine for advanced non-small cell lung cancer (NSCLC). ***Material and Methods:*** This study examined 122 patients with advanced NSCLC who were treated at our hospital between January 2021 and October 2023. Subjects were categorized into the control group (gemcitabine monotherapy) and study group (tislelizumab + gemcitabine), with 61 patients in each group. Clinical efficacy, CT imaging changes (maximum lesion diameter, CT value, short diameter of metastatic lymph nodes), serum tumor markers (CA125, CEA, NSE), quality of life (FACT-L), drug safety, and survival outcomes were compared between groups. ***Results:*** The study group showed higher rates of objective remission (42.62%) and clinical control (86.89%) compared to the control group (18.03% and 62.30%, respectively, x^2=8.728, 9.731, P<0.05). CT parameters (maximum diameter, CT value, and short diameter of metastatic lymph nodes) were remarkably shorter in the study group (P<0.05). Serum CA125, CEA, and NSE levels were decreased in the study group, and their FACT-L score was higher (P<0.05). No remarkable discrepancy was found in complication rates. At the one-year follow-up, the survival rate was 70.49% in the study group and 44.26% in the control group (x^2=13.571, P<0.05). ***Conclusion:*** Tislelizumab combined with gemcitabine improves short-term efficacy, reduces serum tumor markers, enhances life quality, increases survival rates in advanced NSCLC patients, and has a good safety profile.

INTRODUCTION

Lung cancer (LC) occurs in the bronchial lungs and is a common malignancy. Patients often present with clinical symptoms like cough, sputum production, and fever [1]. If left untreated, as the disease progresses, it may lead to the proliferation and spread of tumor cells to other organs and tissues around the bronchial lungs, endangering the patient's life [2]. According to relevant reports, there are as many as 787,000 new cases of LC in China each year, and the five-year survival rate is 19.7%. Its high incidence rate and mortality are related to smoking, environmental pollution, occupational exposure, and other factors [3].

LC can be divided into two types based on its histopathological characteristics: small-cell carcinoma and non-small-cell LC (NSCLC) [4]. NSCLC accounted for approximately 85% [5], and for affected patients, early detection and corresponding treatment can significantly improve the prognosis. However, early diagnosis of NSCLC is difficult, and many patients have already reached advanced stages by the time they seek medical attention, so they cannot receive surgical treatment. Although radiotherapy and chemotherapy are options, they are limited in their efficacy and are associated with significant negative effects [6, 7]. Therefore, there is an urgent need for clinical methods with lower toxicity and better efficacy.

With research on the pathogenesis and biological behavior of NSCLC, as well as developments in biotechnology and immunology [8], immunotherapy has emerging as a novel treatment choice for advanced NSCLC [9]. Programmed cell death-1 (PD-1) inhibitors are important immunotherapeutic medicines that restore anti-tumor activity of T-cells by preventing binding of PD-1 and programmed cell death ligand-1 (PD-L1), thereby achieving immune killing of tumors [10]. Tislelizumab is a PD-1 inhibitor that mainly inhibits tumor cells from evading recognition and clearance by the immune system by blocking the binding of PD-1 to its ligand, PD-L1 (11). It also preserves the number and functions of effector T-cells, promotes T lymphocyte activation, plays a role in cellular immunity, and enhances the inhibitory effect the immune system on tumor occurrence and development. Furthermore, it increases the affinity

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and binding sites for PD-1, which can be blocked on a larger scale and for a longer period of time, thus improving therapeutic efficacy [12, 13]. Therefore, tislelizumab has been used in the treatment of tumors such as Hodgkin's lymphoma [14].

Computed tomography (CT) imaging is an essential detection to monitoring tumor progression and evaluating treatment efficacy [15, 16]. Multiple studies have confirmed that CT can clearly display changes in lung structure and abnormal lesions through X-ray cross-sectional imaging techniques to evaluate therapeutic efficacy [17]. At present, there is a lack of unified standards for clinical management of advanced NSCLC patients, and due to relatively short time that tislelizumab has been on the market in China, there is a relative lack of reports on its efficacy when combined with gemcitabine for advanced NSCLC. In view of this, this study focuses on advanced NSCLC patients enrolled in our hospital explores the efficacy and CT imaging changes of combined therapy of tislelizumab and gemcitabine for NSCLC.

A novelty of this study is that it focuses on the combination of tislelizumab and gemcitabine, which has been on the market for a short period of time. This is important in view of the current situation of inconsistency in the clinical standard of treatment for advanced NSCLC, which is different from the common combination model. The study also fills the gap in the evidence for non-platinum immune combination therapy and provides a certain basis for the expansion of clinical application of PD-1 inhibitors by analyzing their therapeutic efficacy and changes in CT imaging.

MATERIALS AND METHODS

Study design

This retrospective controlled clinical study was undertaken in the clinical diagnosis and treatment center of our hospital from January 2022 to October 2024. A total of 130 patients were initially recruited, and the final total was 122 cases. Based on treatment methods, participants were categorized to two groups of 61 each: the study group receiving trastuzumab and gemcitabine and control group receiving gemcitabine monotherapy. All patients were followed up.

Participants

The study involved 122 patients with advanced NSCLC and a total of 175 lesions. Through multidisciplinary consultations in oncology, respiratory medicine, thoracic surgery, and radiotherapy, comprehensive diagnosis and preoperative evaluation were conducted through chest CT, X-ray, tissue, and cytology examinations to ensure diagnostic accuracy. The inclusion criteria: ① meets the criteria for the diagnosis of advanced NSCLC [18] with a diagnosis by chest CT and X-ray detection, as well as age ≥18 years; ② complete clinical and imaging data; ③ no recent treatment with related drugs; ④ predicted survival time >3 months; ⑤ normal mental health, good cognition, and good compliance; ⑥ having at least one measurable lesion; and ⑦ patients with a histological or cytological diagnosis who could not undergo surgery or radiotherapy. The exclusion criteria were ① diagnosis with small-cell LC; ② complications with other serious chronic diseases and unstable condition; ③ immune-system diseases or mental illness; ④ patients with an impaired hematopoietic system, heart, liver, or kidney function; ⑤ allergy to the study drugs; ⑥ cognitive or speech disorders; and ⑦ pregnant or lactating women. The drop-out criteria were ① not meeting the inclusion criteria or having incomplete data; ② poor compliance; ③ loss to follow-up or refusal to continue to participate in the study; and ④ having other diseases occur during the study and changes in the treatment plan.

Ethical considerations

This study strictly follows the principles of the Declarations of Helsinki, and all research procedures complied with international ethical standards. Approval was obtained from the unit and region where the hospital is located. A signed a consent form was obtained for all patients, and in emergency situations, the consent form may have been signed by the patient's representative or guardian. All data involved in the research process have been anonymized to guarantee the participants' privacy and confidentiality.

Treatment options

During the treatment, patients in both groups received routine hydration therapy, corrective measures for electrolyte disorders, and anti-allergy treatment. Adverse reactions were closely monitored, and reasonable work and rest time was arranged. The patients were also instructed to maintain sufficient sleep. Patients were advised to eat a light diet, eliminate irritating food, avoid smoking and alcohol, etc. All patients were treated with 3 consecutive treatment courses, and a single course lasted 21 days.

The control group was treated with gemcitabine at the dose of 1000 mg/m^2 for the first and eighth days of chemotherapy. Study group was treated with tislelizumab in combination with gemcitabine, and gemcitabine chemotherapy regimen was the same as that of the control group. 200 ml of tislelizumab and 200 ml of 0.9% sodium chloride injection were mixed and administered with a slow intravenous drip once every 3 weeks. The following were used in the treatment process: infusion sets (GuoMeinZhuQi 20213140222, Weihai Weigao Pharmaceutical Packaging Co., Ltd., China), gemcitabine (Drug Registration No. H20190023, Gemzar Corporation, USA), tislelizumab (National Drug Certificate No.

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S20200009, Baizi Shenzhou (Suzhou) Biotechnology Co., Ltd., China), sodium chloride injection (National Drug License No. H20053804, Cinnabar Pharmaceuticals Co., Ltd., China), physiological saline (State Drug License H20054770, Sichuan Kelun Pharmaceutical Co., Ltd., China), various blood test kits (National Instruments No. 20212400001, Shenzhen Myriad BioMedical Electronics Co., Ltd., China), and Neusoft Medical NeuViz Series Diagnostic Imaging Software (National Instruments No. 20212210032, Neusoft Medical Systems Co., Ltd., China).

Observation indicators

Clinical efficacy was evaluated in terms of patient outcomes based on the criteria for evaluating the efficacy on solid tumors (RECIST1.1) [19]. Outcomes were classified as disease progression (PD), stable disease (SD), partial remission (PR), and complete remission (CR). Calculate objective remission rate (CR+PR) and clinical control rate (CR+PR+SD) were calculated.

CT imaging was performed using a General Electric (GE) Revolution Multilayer Spiral CT scanner (National Instruments No. 20153062261, Avionics General Electric Medical Systems Ltd., China). The patient fasted for 6 h prior to the examination, and after being placed in a supine position, the midline of the body was aligned with that of the scanning bed. After respiratory training, patients held their breath at the end of deep inhalation, and the scanning procedure was initiated with a full-range scan from the thoracic inlet to the middle of the kidneys.

The contrast agent was iohexol (300 mg/ml, National Drug Code H20000591, GE Pharmaceuticals (Shanghai) Co., Ltd., China), which was injection at 4.5 ml/s into the anterior elbow vein via a double-barreled high-pressure syringe (National Instruments No. 20202060116, Shanghai Hongkang Medical Equipment Co., Ltd., China). The total dose was adjusted to 80–100 ml according to the patient's body mass. A two-phase scanning protocol was used. The arterial phase scan was conducted 30 s after injection to capture the enhancement of tumor vasculature, and the venous phase scan was conducted 60 s to observe the enhancement of tumor parenchyma and lymph nodes. Scanning parameters: helical scanning mode, frame rotation time 0.28 s/rev, pitch 0.55, electron tube current 280–350 mA with an automatic milliamperage technique, tube voltage 140 kV, layer thickness 0.625 mm, reconstruction interval 1.250 mm, and a scanning field of view (FOV) of 350 mm × 350 mm.

After scanning, the raw data were transferred to an AW 4.7 post-processing workstation for multiplanar reconstruction (MPR) and maximum density projection (MIP). Image interpretations were independently performed by two associate radiologists who had experience in diagnostic chest CT for more than 10 years. A blind method was used to assess the three-dimensional spatial position of the target lesion, the maximum diameters (taking the average of the vertical bi-directional diameter), the CT value of the plain scan (region-of-interest area of ≥100 mm^2, avoiding necrotic and vascular areas), as well as the metastatic lymph nodes with a short diameter of ≥1 cm. In cases of measurement error >5% or qualitative disagreement, the chief physician organized a case discussion and made the final decision. CT image analysis included the target lesion location, the maximum diameter of the lesion, the CT value of the plain scan, and the size of metastatic lymph nodes.

Serum tumor markers were measured using 3.5 ml of venous blood collected after fasting and before and after treatment. Immediately after blood collection, the samples were centrifuged according to set speed and time parameters to obtain the supernatant. Levels of cancer antigen 125 (CA125), carcinoembryonic antigen (CEA), and neuron-specific enolase (NSE) were measured using an automatic chemiluminescence immunoassay analyzer (National Instrument No. 20173400326, Mike's Medical Electronics Co., Ltd., China). Quality-control samples were included in each batch to ensure accuracy and reliability of the test results, and all procedures were performed in strict accordance with the standard operating procedures of the instrument and the instructions of the relevant reagents.

The FACT-L Cancer Treatment Scale [19] was applied to evaluate the patients' life quality [20]. The scale consists of 36 items in five dimensions: daily life (7 items), social/family life (7 items), emotions (6 items), mobility (7 items), and other factors (9 items). The items are rated on a 5-point scale from 0 to 4, and the patients were instructed to complete the scale independently. Standardized instructions were given to patients with reading difficulties to ensure consistency and objectivity of the assessment process. The final scoring results showed a positive correlation between the scores and the patients' life quality, and the impact of the treatment on the patients' quality of life was analyzed accordingly.

For safety evaluation, the research team closely monitored the patients after they received the treatment. Information on the patient's physical condition was collected daily through face-to-face consultations and symptom questionnaires, and drug-related adverse reactions were observed and recorded in detail. Adverse effects included nausea and vomiting, loss of appetite, bone-marrow suppression, and leucopenia. Prognosis and survival were also examined through follow up once a month for 1 year to observe the 1-year survival rate of patients.

Statistical analysis

Data were analyzed using SPSS 25.0, and the

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number table method was used for grouping. The variables with similar conditions or similar main influencing factors were paired, and then the two variables from each pair were allocated to each of the two groups. Before the experiment, a standard deviation test or Q test was used to verify the consistency of the initial index scores of the two groups, and outliers in the data were eliminated. Enumeration data were displayed as n (%), the $\chi 2$ test was used. Measurements were calculated by t-test and expressed as mean ± standard deviation (±s). P<0.05 was considered statistical significance.

RESULTS

Basic data and clinical efficacy

No marked difference among groups in terms of age, sex, type of pathology or general data (P>0.05, table 1). This helped to fairly evaluate the impact of the two treatment modalities on advanced NSCLC. After treatment, the objective response rate (42.62%) and clinical control rate (86.89%) of the study group were above the control group (18.03%, 62.30%) (χ^2=8.728, 9.731; P<0.05, table 2), indicating that the combination therapy of trastuzumab and gemcitabine has improved clinical efficacy for patients.

Table 1. Comparisons of basic clinical data of the two groups of patients [(¯x±s), n (%)].

Index	Control group(*n*=61)	Study group (*n*=61)	*t*/χ^2-value	*P* value
Age (years)	54.62±7.93	53.82±6.28	0.620	0.536
Sex				
male	48 (78.69)	44 (72.13)	0.707	0.400
female	13 (21.31)	17 (56.67)		
Pathological type				
Squamous cell carcinoma	29 (47.54)	23 (37.70)	1.207	0.272
Adenocarcinoma	32 (52.46)	38 (62.30)		
Location of the lesion				
left lung	27 (44.26)	21 (34.43)	1.236	0.266
right lung	34 (55.74)	40 (65.57)		
Number of lesions (number)				
1	38 (62.30)	36 (59.02)	0.463	0.793
2	20 (35.79)	23 (37.70)		
3	3 (4.92)	2 (3.28)		
Smoking status				
Yes	52 (85.25)	46 (75.41)	1.867	0.172
No	9 (14.75)	15 (24.59)		
Drinking history				
Yes	55 (90.16)	57 (93.44)	0.436	0.509
No	6 (9.84)	4 (6.56)		
Marital status				
married	48 (78.69)	52 (85.25)	0.887	0.346
other	13 (21.31)	9 (14.75)		
Payment Method				
medical insurance	37 (60.66)	45 (73.77)	2.380	0.123
self-funded	24 (39.34)	16 (26.23)		

Table 2. Comparisons of short-term outcomes of both groups of patients [n(%)].

Group	n	CR	PR	SD	PD	Objective response rate	clinical control rate
Study group	61	4 (6.56)	22 (36.07)	27 (44.26)	8 (13.11)	26 (42.62)	53 (86.89)
Control group	61	0 (0.00)	11 (18.03)	27 (44.26)	23 (37.70)	11 (18.03)	38 (62.30)
χ^2**-value**						8.728	9.731
***P* value**						0.003	0.002

Note: CR represents complete remission, PR represents partial remission, SD represents stable disease, PD represents disease progression.

CT imaging parameters and serum tumor markers

Before treatment, no marked difference in the maximum diameter of lesions, CT value, and short diameter of metastatic lymph nodes among both groups (P>0.05), which was helpful for fair comparison of the two treatment methods. After treatment, the maximum diameter of lesions, CT value, and short diameter of metastatic lymph nodes were reduced in both groups, but lower in the study group (P<0.05, table 3, figure 1). This indicates that combination therapy can effectively inhibit the growth of tumors in patients.

Table 3. Comparisons of CT imaging indexes of both groups of patients([(¯x±s).

Group	*n*	Maximum diameter of lesion (mm)		CT value (HU)		Short diameter of metastatic lymph nodes (mm)	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Study group	88	42.57± 8.08	24.59± 7.45*	49.59±7.04	32.27± 8.66*	15.86± 4.52	9.76± 3.35*
Control group	87	42.68± 7.43	35.88± 9.85*	50.05± 8.37	42.64± 9.12*	15.97±3.45	12.08± 4.21*
***t*-value**		-0.092	-8.552	-0.398	-7.713	-0.185	-4.027
***P* value**		0.927	<0.001	0.691	<0.001	0.854	<0.001

Note: Compared with that before treatment, *P<0.05, the same as below. CT represents computed tomography.

No marked difference in pre-treatment serum levels of CA125, CEA, and NSE between groups (P>0.05), which was helpful to compare the effects of the two treatment methods on serum tumor markers. After treatment, the serum indicator levels in both groups were decreased, but lower in the study group (P<0.05, table 4). This suggests that combination therapy can effectively control the patients' serum levels of tumor markers.

Quality of life, safety assessment, and prognosis

No marked difference in pre-treatment FACT-L scores among groups (P>0.05). After treatment, all dimensions and total scores of the FACT-L scale increased in both groups, but higher in the study group (P<0.05, table 5). This indicates that the combination therapy effectively improved patients' quality of life.

No marked difference was observed in the overall complication incidence in both groups (P<0.05), and the adverse reaction incidence was reduced in both groups, indicating that the treatment methods were safe (table 6). After 1 year of follow-up, the survival

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incidence in study group was 70.49%, which was above incidence of 44.26% in control group (χ^2=13.571, P<0.05). The survival curve of the K–M method is shown in figure 2, which indicates that tislelizumab combined with gemcitabine for advanced NSCLC can effectively improve short-term survival.

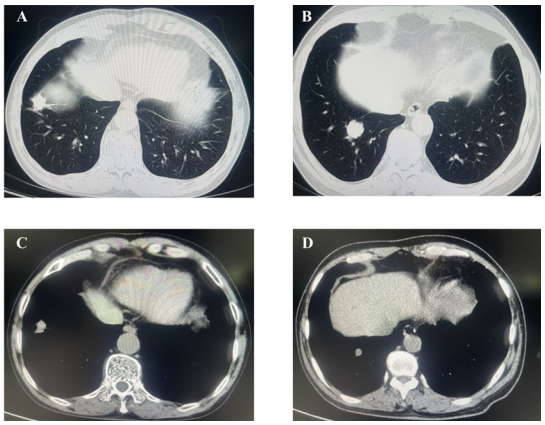

Figure 1. CT images of the two groups before and after treatment. **(A)** control group before treatment; **(B)** control group after treatment; **(C)** study group before treatment; **(D)** study group after treatment.

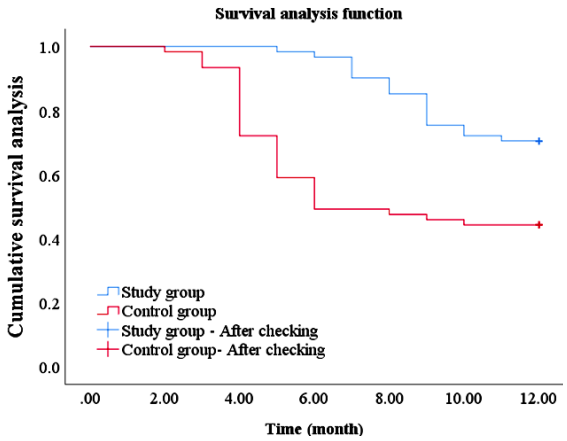

Figure 2. Survival curve analysis of the two groups of patients.

Table 4. Comparisons of CA125, CEA and NSE of both groups of patients (¯x±s).

Group	*n*	CA125 (U/ml)		CEA(μg/L)		NSE(ng/mL)	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Study group	61	104.59±5.44	42.35±3.36*	65.08±0.28	20.07±1.58*	38.15±2.12	10.60±1.35*
Control group	61	104.93±5.08	78.82±4.37*	65.12±0.50	36.88±2.42*	38.60±2.42	25.48±2.16*
t-value		-0.357	-51.688	-0.528	-45.398	-1.156	-45.615
P value		0.722	<0.001	0.599	<0.001	0.250	<0.001

Note: CA125 represents Cancer antigen 125; CEA represents carcinoembryonic antigen; NSE represents neuron-specific enolase.

Table 5. Comparison of FACT-L scale of both groups of patients ((¯x±s, score).

Group	*n*	Everyday life		Social/family life		mood	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Study group	61	14.84±2.82	21.48±2.59*	13.70±1.88	20.97±2.32*	12.25±1.77	19.11±1.43*
Control group	61	14.28±2.10	17.20±2.32*	13.16±1.71	17.10±2.27*	12.00±2.01	15.95±2.09*
t-value		1.239	9.641	1.659	9.315	0.718	9.755
P value		0.218	<0.001	0.100	<0.001	0.474	<0.001
Group	*n*	Capacity for mobility		Other Factors		Total score	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Study group	61	16.57±2.06	22.70±2.21*	21.89±2.17	29.08±2.16*	79.25±4.81	113.34±4.63
Control group	61	16.70±1.51	19.87±2.07*	22.07±2.18	25.89±1.63*	78.21±3.97	96.00±4.86
t-value		-0.401	7.318	-0.458	9.212	1.293	20.187
P value		0.689	<0.001	0.648	<0.001	0.198	<0.001

Table 6. Comparisons of complication rates of both groups of patients (n %)

Group	n	Nausea and vomiting	Bone Marrow suppression	Loss of appetite	Decreased white-cell count	Overall Incidence
Study group	61	1 (1.64)	1 (1.64)	3 (4.92)	1 (1.64)	6 (9.84)
Control group	61	2 (3.28)	1 (1.64)	4 (6.56)	0 (0.00)	7 (11.48)
χ^2-value						0.086
P value						0.769

DISCUSSION

NSCLC is a type of malignant tumor that is significantly invasive and grows rapidly, and its occurrence is related to multiple factors. Most patients are diagnosed in advanced stages and cannot undergo surgery, which greatly reduces the effectiveness of treatment and shortens the patient's survival time [21]. For advanced NSCLC, treatment options are relatively limited, and chemotherapy is often considered the standard therapy.

However, even with standard treatment, the survival of patients is still limited, and the prognosis is poor [22]. Therefore, the urgent need exists to exploring new drugs to improve their survival rate. In recent years, immunotherapy has received much clinical attention [23], the PD-1 inhibitor tislelizumab enhanced the body's anti-tumor responses by blocking the bindings of PD-1 to its ligands [24]. Thus, the present study investigated effectiveness of trastuzumab combined with gemcitabine for advanced NSCLC.

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CT images can clearly display information such as the size, shape, location, and density of tumors, which intuitively reflect the changes in tumors. Medical staff can predict the prognosis of patients by observing changes in CT images and develop more reasonable follow-up treatment plans based that are more effective [25, 26]. For example, the maximum diameter of a lesion directly reflects the tumor volume [27], and changes in its CT value are often related to the internal structure, composition, or metabolic status of the tumor [28]. Therefore, a decrease in CT value may indicate changes in certain components or structures within the tumor, such as decreased blood vessels, increased necrosis, or decreased cell density.

Additionally, a decrease in the short diameter of metastatic lymph nodes may indicate that the disease is being controlled or has improved, and the immune system is effectively fighting against pathogens or cancer cells [29]. This study suggests that after treatment, the clinical efficacy of study group was higher, and he maximum diameter of the lesion, CT value, and short diameter of metastatic lymph nodes were lower. This indicates that the integration of tislelizumab and gemcitabine for advanced NSCLC can improve the clinical efficacy and effectively inhibit tumor growth.

Xiang *et al.* studied tilizumab combined with gemcitabine plus cisplatin chemotherapy for localized advance or metastatic bladder cancer. They reported significant efficacy and significant improvement in disease control after combination therapy [30],which is similar to the findings of this study. It is speculated that as an immune checkpoint inhibitor, tislelizumab can blocks the binding of PD-1 and PD-L1, release its inhibitory effect on T cells, enhance the anti-tumor immune responses, and exert anti-tumor effects, enabling more effective recognition and killing of tumor cells [31]. Under normal circumstances, T cells are able to kill infected cells (32). However, in the tumor microenvironment, tumor cells evade immune system attacks by expressing immunosuppressive molecules such as PD -L1.

In addition, tislelizumab can also inhibit angiogenesis, thereby suppressing the growth and spread of the tumor [33]. Gemcitabine interferes with the normal synthesis process of DNA by incorporating into DNA strands, leading to DNA damage and death of tumor cells [34]. In addition, it can also block tumor cells in the G1/S or S phase of the cell cycle, thereby preventing them from entering the next division cycle and inhibiting tumor growth [35]. It also has a certain anti-angiogenic effect of inhibiting the formation of tumor neovascularization, cutting off the nutritional supply of tumor cells, and inhibiting their growth [36]. Therefore, while chemotherapy can widely kill tumor cells, tislelizumab selectively inhibits residual tumor cells, thereby reducing their immune evasion ability. Both works together to effectively inhibit tumor growth and enhance treatment efficacy.

Serum tumor markers are key indicators for monitoring tumor progression and treatment efficacy and have high value for evaluating the development status and treatment effectiveness of tumors [37]. CEA is a complex soluble glycoprotein with human embryonic antigen properties that is applied in the diagnosis, treatment efficacy evaluation, and postoperative monitoring of malignant tumors [38]. CA125 is a mucin-like glycoprotein [39], NSE are critical enzymes in the glycolytic pathway that is mainly distributed in nerve cells and neuroendocrine cells. When tumor cells grow or proliferate, there is often an abnormal increase in CEA, CA125, and NSE levels [40].

The integration of tislelizumab and gemcitabine treatment resulted in lower serum CA125, CEA, and NSE levels compared to gemcitabine treatment alone. This mainly occurred because tislelizumab can inhibit the immune escape mechanism and restart the immune response, effectively suppressing the growth of tumor cells and reducing tumor marker levels [41]. Secondly, gemcitabine, a cytotoxic drug, has significant therapeutic effects on advanced NSCLC [42]. However, when used in combination with tislelizumab, it can produce synergistic effects, enhance anti-tumor effects, and reduce tumor-marker levels.

Liang *et al*. studied sintilimab combined with chemotherapy for advanced NSCLC. They reported that the combination therapy significantly reduced serum levels of tumor markers and improved cellular immune function in patients [43], which is consistent with the results of the present study. In addition, in this study, the FACT-L scale score was higher in the study group after treatment, and no marked difference was observed in adverse reactions among both groups. It can be seen that the combination does not increase the adverse reactions of patients, has high safety, and can enhance patients' quality of life.

This study also found that after 1 year of follow-up, the survival rate of the study group was higher, suggesting that the combination therapy of tislelizumab and gemcitabine can improve the short-term survival rate. This may have occurred because tislelizumab enhances the formation of immune memory by promoting the reactivity of T cells [44]. This a quick response to tumor recurrence and provides immune protection for patients [45]. In addition, long-term use of gemcitabine can easily lead to drug resistance, but tislelizumab can reduce the development of resistance by restoring the anti-tumor activity of the immune system [46]. This allows gemcitabine to continue to exert its therapeutic effects and improve survival rates.

Limitations

There were limitations to this study that snot be

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ignored. The limited sample size could have affected the long-term effectiveness and applicability of the results. In addition, the mortality and recurrence rates of advanced NSCLC are relatively high, and it is challenging to comprehensively evaluate the long-term efficacy in advanced NSCLC patients due to the follow-up time of only 1 year. The evaluation of CT-imaging changes may have a certain degree of subjectivity, and different radiologists or even the same doctor may interpret the same image differently at different time points. There was also a lack of cost-benefit analysis for joint use.

The next step is to increase the sample size and conduct multicenter randomized trials to improve the reliability and generalizability of the research results. In addition, the follow-up period should be extended, and a long-term patient follow-up database should be established to comprehensively track the long-term efficacy, safety, and potential adverse reactions of combination therapy. At the same time, the subjectivity of CT image interpretation should be avoided, and a more solid theoretical basis should be provided for clinical application.

CONCLUSION

This study has examined the use of tislelizumab combined with gemcitabine for patients with advanced NSCLC. The results indicate that the combination can improve the short-term efficacy. Furthermore, it can control serum levels of tumor markers, improve patients' life quality, and increase survival rates, while it also has good safety characteristics.

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***Consent to participate*:** We secured a signed informed consent form from every participant.

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REFERENCES

1. Harðardottir H, Jonsson S, Gunnarsson O*, et al.* (2022) Advances in lung cancer diagnosis and treatment - a review. *Laeknabladid,* ***108*** *(1):17-29*.
2. Deshpand R, Chandra M, Rauthan A (2022) Evolving trends in lung cancer: Epidemiology, diagnosis, and management. *Indian J cancer,* ***59****(Supplement): S90-s105*.
3. Daylan AEC, Miao E, Tang K*, et al.* (2023) Lung cancer in never smokers: Delving into epidemiology, genomic and immune landscape, prognosis, treatment, and screening. *Lung,* ***201****(6): 521-9*.
4. Abu Rous F, Singhi EK, Sridhar A*, et al.* (2023) Lung cancer treatment advances in 2022. *Cancer Invest,* ***41****(1): 12-24*.
5. Alduais Y, Zhang H, Fan F*, et al.* (2023) Non-small cell lung cancer (NSCLC): A review of risk factors, diagnosis, and treatment. *Medicine,* ***102****(8): e32899*.
6. Mithoowani H and Febbraro M (2022) Non-small-cell lung cancer in 2022: A review for general practitioners in oncology. *Curr Oncol,* ***29****(3): 1828-39*.
7. Awad MM, Govindan R, Balogh KN*, et al.* (2022) Personalized neoantigen vaccine NEO-PV-01 with chemotherapy and anti-PD-1 as first-line treatment for non-squamous non-small cell lung cancer. *Cancer Cell,* ***40****(9): 1010-26.e11*.
8. Gayen S, Parui A, Arshad A*, et al.* (2025) Decrypting the crosstalk mechanisms between cGAS-STING and TBK1 signaling pathways in cancer immunotherapy: A comprehensive review. *Journal of Cancer Biomoleculars and Therapeutics,* ***2****(1): 89-104*.
9. Patil NS, Nabet BY, Müller S*, et al.* (2022) Intratumoral plasma cells predict outcomes to PD-L1 blockade in non-small cell lung cancer. *Cancer Cell,* ***40****(3): 289-300.e4*.
10. Kim Y, Kim G, Kim S*, et al.* (2024) Fecal microbiota transplantation improves anti-PD-1 inhibitor efficacy in unresectable or metastatic solid cancers refractory to anti-PD-1 inhibitor. *Cell Host Microbe,* ***32****(8): 1380-93.e9*.
11. Yang Y, Pan J, Wang H*, et al.* (2023) Tislelizumab plus chemotherapy as first-line treatment for recurrent or metastatic nasopharyngeal cancer: A multicenter phase 3 trial (RATIONALE-309). *Cancer Cell,* ***41****(6): 1061-72.e4*.
12. Zhou C, Huang D, Fan Y*, et al.* (2023) Tislelizumab versus docetaxel in patients with previously treated advanced NSCLC (RATIONALE-303): A phase 3, open-label, randomized controlled trial. *J Thorac Oncol,* ***18****(1): 93-105*.
13. Xu J, Kato K, Raymond E*, et al.* (2023) Tislelizumab plus chemotherapy versus placebo plus chemotherapy as first-line treatment for advanced or metastatic oesophageal squamous cell carcinoma (RATIONALE-306): a global, randomised, placebo-controlled, phase 3 study. *Lancet Oncol,* ***24****(5): 483-95*.
14. Song Y, Gao Q, Zhang H*, et al.* (2022) Tislelizumab for relapsed/refractory classical Hodgkin lymphoma: 3-year follow-up and correlative biomarker analysis. *Clin Cancer Res,* ***28****(6): 1147-56*.
15. Perumal V, Narayanan V, Rajasekar SJS (2021) Prediction of COVID criticality score with laboratory, clinical and CT images using hybrid regression models. *Comput Methods Programs Biomed,* ***209****: 106336*.
16. Gong X and Huang C (2024) Clinical value of CT imaging features to predict infiltration degree and pathological subtype of ground glass lung adenocarcinoma. *Int J Radiat Res,* ***22****(4): 909*.
17. Avila RS, Krishnan K, Obuchowski N*, et al.* (2023) Calibration phantom-based prediction of CT lung nodule volume measurement performance. *Quant Imaging Med Surg,* ***13****(9):6193-204*.
18. Postmus PE, Kerr KM, Oudkerk M*, et al.* (2017) Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol,* ***28****(suppl-4): iv1-iv21*.
19. Frentzas S, Austria Mislang AR, Lemech C*, et al.* (2024) Phase 1a dose escalation study of ivonescimab (AK112/SMT112), an anti-PD -1/VEGF-A bispecific antibody, in patients with advanced solid tumors. *J Immunother Cancer,* ***12****(4): e008037.*
20. Hircock C, Wang AJ, Goonaratne E*, et al.* (2024) Comparing the EORTC QLQ-LC13, EORTC QLQ-LC29, and the FACT-L for assessment of quality of life in patients with lung cancer - an

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updated systematic review. *Curr. Opin. Support. Palliat Care,* ***18****(4): 260-8*.
21. Miao D, Zhao J, Han Y*, et al.* (2024) Management of locally advanced non-small cell lung cancer: State of the art and future directions. *Cancer Commun (Lond),* ***44****(1): 23-46*.
22. Mitsudomi T, Ito H, Okada M*, et al.* (2024) Neoadjuvant nivolumab plus chemotherapy in resectable non-small-cell lung cancer in Japanese patients from CheckMate 816. *Cancer Sci,* ***115****(2): 540-54*.
23. (2024) Advances in combination therapy for gastric cancer: Integrating targeted agents and immunotherapy. *Adv Clin Pharm Ther,* ***1****(1): 1-15*.
24. Liu SY and Wu YL (2020) Tislelizumab: an investigational anti-PD-1 antibody for the treatment of advanced non-small cell lung cancer (NSCLC). *Expert Opin Investig Drugs,* ***29****(12): 1355-64*.
25. Curti M, Fontana F, Piacentino F*, et al.* (2022) Dual-layer spectral CT fusion imaging for lung biopsies: more accurate targets, diagnostic samplings, and biomarker information? *Eur Radiol Exp,* ***6****(1):34*.
26. Le L, Narula N, Zhou F*, et al.* (2024) Diseases involving the lung peribronchovascular region: A CT imaging pathologic classification. *Chest,* ***166****(4): 802-20*.
27. Gao F, Li H, Du C*, et al.* (2023) Causes of endoscopic misdiagnosis of gastrointestinal cyst as solid lesion. *BMC Gastroenterol,* ***23****(1): 10*.
28. Wei W, Zhong W, Kang W*, et al.* (2023) Reference range of CT value in NC-CBBCT based on female breast structure. *Current Medical Imaging,* ***19****(13): 1523-32*.
29. Xu R, Xu W, Liu D*, et al.* (2025) Application value of low-dose computed tomography combined with serum tumor markers in diagnosis of early non-small cell lung cancer. *Int J Radiat Res,* ***23*** *(1): 77*.
30. Ren X, Tian Y, Wang Z*, et al.* (2022) Tislelizumab in combination with gemcitabine plus cisplatin chemotherapy as first-line adjuvant treatment for locally advanced or metastatic bladder cancer: a retrospective study. *BMC Urol,* ***22****(1): 128*.
31. Wang Z, Bi H, Wang YD*, et al.* (2024) Tislelizumab, a novel PD-1 monoclonal antibody in urothelial cancer: A real-world study. *Actas Urol Esp,* ***48****(4): 295-303*.
32. Zhao Y, Shao Q, Peng G (2020) Exhaustion and senescence: two crucial dysfunctional states of T cells in the tumor microenvironment. *Cell Mol Immunol,* ***17****(1): 27-35*.
33. Wang X, Pan H, Cui J*, et al.* (2024) SAFFRON-103: a phase Ib study of sitravatinib plus tislelizumab in anti-PD-(L)1 refractory/resistant advanced melanoma. *Immunother,* ***16****(4): 243-56*.
34. McElree IM, Steinberg RL, Mott SL*, et al.* (2023) Comparison of sequential intravesical gemcitabine and docetaxel vs *Bacillus Calmette-Guérin* for the treatment of patients with high-risk non-muscle-invasive bladder cancer. *JAMA Netw Open,* ***6****(2): e230849*.
35. Koh EK, Lee HR, Son WC*, et al.* (2023) Combinatorial immunotherapy with gemcitabine and ex vivo-expanded NK cells induces anti-tumor effects in pancreatic cancer. *Sci Rep,* ***13****(1): 7656*.
36. Rohila D, Park IH, Pham TV*, et al.* (2023) Syk inhibition reprograms tumor-associated macrophages and overcomes gemcitabine-induced immunosuppression in pancreatic ductal adenocarcinoma. *Cancer Res,* ***83****(16): 2675-89*.
37. Yousef A, Yousef M, Zeineddine MA*, et al.* (2024) Serum tumor markers and outcomes in patients with appendiceal adenocarcinoma. *JAMA Netw Open,* ***7****(2): e240260*.
38. Baskiran DY, Sarigoz T, Baskiran A*, et al.* (2023) The significance of serum tumor markers CEA, Ca 19-9, Ca 125, Ca 15-3, and AFP in patients scheduled for orthotopic liver transplantation: Do elevated levels really mean malignancy? *J Gastrointest Cancer,* ***54*** *(2): 442-6*.
39. Li G, Zhang H, Zhang L*, et al.* (2022) Serum markers CA125, CA153, and CEA along with inflammatory cytokines in the early detection of lung cancer in high-risk populations. *BioMed Res Int,* ***2022****: 1394042*.
40. Sun A (2023) Clinical role of serum tumor markers SCC, NSE, CA 125, CA 19-9, and CYFRA 21-1 in patients with lung cancer. *Lab Med,* ***54****(6): 638-45*.
41. Al-Sawaf O, Ligtvoet R, Robrecht S*, et al.* (2024) Tislelizumab plus zanubrutinib for Richter transformation: the phase 2 RT1 trial. *Nat Med,* ***30****(1): 240-8*.
42. Zhou C, Wu L, Fan Y*, et al.* (2021) Sintilimab plus platinum and gemcitabine as first-line treatment for advanced or metastatic squamous NSCLC: Results from a randomized, double-blind, phase 3 trial (ORIENT-12). *J Thorac Oncol,* ***16****(9): 1501-11*.
43. Liang X and Wei Z (2021) Effect of sintilimab combined with chemotherapy on tumor markers and immune function of advanced non-small cell lung cancer. *Pak J Med Sci,* ***37****(4): 1063-8*.
44. Zhang Y, Geng H, Zeng L*, et al.* (2024) Tislelizumab augment the efficacy of CD19/22 dual-targeted chimeric antigen receptor T cell in advanced stage relapsed or refractory B-cell non-Hodgkin lymphoma. *Hematol Oncol,* ***42****(1): e3227*.
45. Gao XN, Su YF, Li MY*, et al.* (2023) Single-center phase 2 study of PD-1 inhibitor combined with DNA hypomethylation agent + CAG regimen in patients with relapsed/refractory acute myeloid leukemia. *Canc Immunol Immunother,* ***72****(8): 2769-82*.
46. Yan X, Duan H, Ni Y*, et al.* (2022) Tislelizumab combined with chemotherapy as neoadjuvant therapy for surgically resectable esophageal cancer: A prospective, single-arm, phase II study (TD-NICE). *Int J surg,* ***103****: 106680*.

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