

STANDARDS AND GUIDELINES

An Expert Consensus of Integrated Chinese and Western Medicine Treatment on Lung Cancer

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ABSTRACT Lung cancer is a malignant tumor of the lung originating from the bronchial mucosa, glands or alveolar epithelium. With the population aging and environmental pollution getting increasingly severe, lung cancer has become the malignant tumor with the highest incidence and mortality rate in China, seriously endangering people's life and health. However, there is no standardized guideline for the integrated Chinese and Western medicine treatment of lung cancer in China. In order to standardize and improve integrated Chinese and Western medicine diagnosis and treatment of lung cancer in China, the First Affiliated Hospital of Guangzhou University of Chinese Medicine, together with oncologists from the Sun Yat-sen University Cancer Center, compiled this consensus under the coordination of the Medical Policy Department of the National Administration of Traditional Chinese Medicine, taking into account the main results of the pilot project of Chinese and Western Medicine Clinical Collaboration for Major Difficult Diseases (lung cancer).

KEYWORDS Lung cancer; Integrated traditional Chinese and Western medicine; Diagnosis and treatment; Expert consensus

According to the data released by the National Cancer Center in 2019, the incidence of lung cancer in China was 57.26/100,000 in 2015, of which 73.9/100,000 were men and 26.7/100,000 were women, ranking the 2nd in malignant tumors.^[2] The mortality of lung cancer reaches 45.87/100,000, and lung cancer has become the malignant tumor with the highest incidence and mortality rate in China, endangering people's life and health. Following the three conventional treatments of surgery, chemotherapy and radiotherapy, Chinese medicine treatment of lung cancer has carried out numerous high-level evidence-based medical studies in recent years, and gradually formed the theory and methods of integrated Chinese and Western medicine treatment of lung cancer, which has improved the efficacy of comprehensive treatment of lung cancer. Therefore, it's urgently needed and of clinical value that we provide medical practitioners in oncology specialty with the treatment specification or expert consensus on integrated Chinese and Western medicine treatment of lung cancer, so as to maximize the efficacy and level of integrated Chinese and Western medicine treatment of lung

cancer in China.

The pilot project of Chinese and Western Medicine Clinical Collaboration for Major Difficult Diseases (lung cancer) was approved by the National Administration of Traditional Chinese Medicine in February 2018 in conjunction with National Health Commission the People Republic of China and the Health Bureau of the Central Military Commission Logistics Security Department, with The First Affiliated Hospital of Guangzhou University of Chinese Medicine as the lead unit and the Sun Yat-sen University Cancer Center as the collaborating unit. Since the approval of the project, the two units have actively responded to the call of the relevant departments at the higher level, and with the foundation of years of cooperation, they have joined forces, supported each other, and explored the model of collaborative treatment of Chinese and Western medicine with lung cancer as a pilot project. Through the implementation of the project, the two units have developed and optimized a unique integrated Chinese and Western medicine treatment plan for lung cancer, formed a good mechanism

for cooperation between Chinese and Western medicine, and further promoted the development of integrated Chinese and Western medicine for lung cancer discipline in China.

In August 2020, under the coordination of the Medical Policy Department of the National Administration of Traditional Chinese Medicine. The First Affiliated Hospital of Guangzhou University of Chinese Medicine, together with oncologists from the Sun Yat-sen University Cancer Center, combined the main results of the pilot project of Chinese and Western Medicine Clinical Collaboration for Major Difficult Diseases (lung cancer) to compile this *A Pilot Project of Chinese and Western Medicine Clinical Collaboration for Major Difficult Diseases-Integrated Chinese and Western Medicine Treatment for Lung Cancer*. The Consensus was finalized and validated by oncologists from many hospitals in China, and was drafted three times. As a practical professional consensus with both theoretical and practical contents, it describes the etiology, clinical manifestations, and diagnostic principles of lung cancer from the perspective of integrating Chinese and Western medicine, and focuses on the ideas, principles, and specific treatment routines of integrating Chinese and Western medicine in the treatment of lung cancer. It is hoped that through the study of this consensus, medical oncologists can further master the treatment of lung cancer by integrating Chinese and Western medicine. Therefore, it may lay a solid foundation for further clinical and scientific research in oncology.

1 Research Scope

Relying on the pilot project of Chinese and Western Medicine Clinical Collaboration for Major Difficult Diseases (lung cancer), the Consensus is developed for patients with lung malignancies. It introduces in detail the pathogenesis and etiology of lung malignant tumors, the key points of diagnosis and the whole management of integrated Chinese and Western medicine treatment in postoperative rehabilitation, chemotherapy, radiotherapy, targeted therapy and Chinese medicine treatment of lung cancer. The consensus highlights the characteristics of integrated Chinese and Western medicine in the treatment of lung malignant tumors, insists on the

equal importance of Chinese and Western medicine, and promotes the mutual complementation of Chinese medicine and Western medicine. It is suitable for medical personnel in oncology, respiratory medicine, Chinese medicine and related departments of integrated Chinese and Western medicine, especially for clinicians' reference.

2 Definition of Lung Cancer

Lung cancer, or primary bronchopulmonary cancer, is a malignant tumor of the lung that originates from the bronchial mucosa, glands or alveolar epithelium. Lung cancer can be broadly divided into two categories: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), of which non-small cell lung cancer accounts for 80%-85%, and the rest is small cell lung cancer. The incidence and mortality rate of lung cancer in China have been on the rise.^[1]

Lung cancer belongs to lung accumulation and lung amassment in TCM, which are now collectively known as "lung cancer disease" in Chinese medicine.

3 Pathogenesis and Etiology of Lung Cancer

Common etiologies associated with lung cancer include smoking, occupational and environmental pollution, but also ionizing radiation, genetics, and viruses. Smoking is the primary risk factor for lung cancer. Specific occupational exposures such as asbestos can increase the incidence of lung cancer. Carcinogens in outdoor air pollutants, including benzopyrene, are associated with the development of lung cancer. The presence of familial aggregation among lung cancer patients suggests that genetic factors may play an important role in the population and/or individuals susceptible to environmental carcinogens.

The development of lung cancer is also a multifactorial and multistep process. The main genes known to be associated with clinical management of non-small cell lung cancer are KRAS, EGFR, ALK, ROS1, RET, NTRK, etc.. The oncogenes associated with non-small cell lung cancer mainly include P53, PTEN, TSC1, ARID1A, etc.. In small cell lung cancer, the mutation rate of both P53 and RB genes

are more than 90%. The functions of these mutated genes requires further study so as to provide information for future precise diagnosis, treatment and monitoring of the disease.

TCM believes that the etiologies of lung cancer are excess resulted from deficiency and intermingled deficiency and excess. Lung cancer starts with the deficiency of positive qi, which leads to the imbalance of yin and yang. The six climatic exopathogens then enter the body taking advantage of the qi deficiency and stagnate in the lung, resulting in the disharmony of the lung qi, disturbance of diffusion and downbearing, disorder of qi movement, obstruction of blood flow, disorder of fluids distribution, which then lead to coagulation of phlegm, stagnation of qi-blood blocking the meridians. "Deficiency", "phlegm", "stagnation" and "toxicity" are the four major pathogenic factors of lung cancer and are relevant to the entire pathogenesis of lung cancer. In the case of deficiency manifestation, qi deficiency, yin deficiency and deficiency of both qi and blood are the most common, while in the case of excess root, phlegm coagulation, qi stagnation, blood stasis and poisonous constipation are the most common.

The pathogenic point of Lung cancer is located in the lung and is closely related to the dysfunction of the lung, spleen, and kidney.^[3] Qi deficiency of lung and spleen is the root cause of lung cancer. In the early stage of the disease, stagnated lung qi with phlegm stasis are the most common causes, so treatment is based on ventilating lung qi, regulating qi-flowing, dissipating phlegm and eliminating stasis. In the middle stage of the disease, spleen qi is damaged, transportation and transformation function is disturbed, and phlegm-dampness are accumulated in interior. The syndrome differentiation is qi deficiency of lung and spleen or spleen deficiency with phlegm-damp, so treatment is based on benefiting qi and invigorating spleen, banking up earth to generate metal. As the disease develops, qi and yin are depleted and deficiency involves the kidney, resulting in deficiency of both qi and yin, and deficiency of kidney yang, so the treatment is based on benefiting qi, nourishing yin, warming yang and tonifying kidney. In terms of the excessive pathogens,

the intermingling of "phlegm", "stasis", and "toxin" is the main pathological factor of lung cancer. As a result of the disharmony of the lung, spleen and kidney, the fluid is not well distributed and warmed, which leads to the accumulation of dampness and phlegm, and the constipation of phlegm and toxin. Therefore, in the treatment of TCM, while strengthening vital qi, it is also necessary to eliminate pathogenic factor, and to flexibly apply the treatment methods of dissipating phlegm and dampness, activating blood and resolving stasis, and removing toxic substance and dispersing constipation.

4 Diagnosis and Staging

4.1 Diagnosis

The diagnostic idea of lung cancer is based on the clinical symptoms and signs of patients, imaging examination that helps determine the clinical diagnosis and TNM staging, and the pathology (including histology or cytology) and molecular diagnosis that are further clarified. Early diagnosis of lung cancer is of great clinical significance, and only when the lesion is diagnosed and treated at an early stage can we obtain better curative effect.

4.1.1 Symptoms

The symptoms of lung cancer in early stage are not obvious. The common symptoms of lung cancer patients include cough, bloody phlegm, chest pain, shortness of breath and fever, among which the most common symptom is cough and the most diagnostic symptom is bloody phlegm. When the tumor invades the surrounding tissues in the thoracic cavity, hoarseness, superior vena cava obstruction syndrome and Horner's syndrome involving the recurrent laryngeal nerve may appear. When the tumor metastasizes distantly to bone, brain, liver, adrenal gland, subcutaneous and other organs, it may cause clinical manifestations of metastasis in corresponding organs. In addition, some patients may develop paraneoplastic syndromes, including abnormal antidiuretic hormone secretion syndrome, hypercalcemia, Cushing's syndrome, carcinoid syndrome and hypertrophic pulmonary osteoarthropathy, etc..

4.1.2 Signs

The signs lung cancer in early stage are not

obvious. When the tumor grows to the bronchus or metastatic lymph node compresses the main airway causing partial airway obstruction, there may be dyspnea, shortness of breath and wheezing, and croup may be found during auscultation. Supraclavicular lymph node is a common site of lung cancer metastasis. Typically, they are located in the anterior oblique muscle area, fixed and firm, fusible, and mostly painless. There may be tenderness points when the ribs and spine are invaded, and pain may involve the affected area in the chest when the tumor compresses the intercostal nerve. Some patients have varying degrees of pleural fluid, decreased breath sounds in the affected lung, and turbid percussion sounds. In the presence of superior vena cava syndrome, the patient may have stasis edema of the head, face and upper body, swelling of the neck and dilated jugular veins.

Dilated venous collateral circulation is seen in the anterior thoracic wall. Supraglottic sulcus tumors tend to compress the sympathetic nerve in the neck, causing ptosis, pupillary constriction, and inversion of the eyeball on the affected side, and little or no sweating on the ipsilateral forehead and chest wall.

4.1.3 Major examinations

(1) Imaging examination

Chest X-ray examination: It is one of the most basic imaging examination methods for lung cancer. However, because of the low resolution of chest X-ray and its blind area, it is not routinely recommended for the screening and examination of lung cancer.

CT examination: Chest CT can effectively detect early peripheral lung cancer and clarify the location and extent of lesion involvement, which is important for lung cancer diagnosis, staging, efficacy evaluation and post-treatment follow-up, and is also the most important and commonly used imaging examination. Patients without contrast allergy usually receive enhanced CT examination to distinguish tumor lesions from adjacent blood vessels and soft tissues. Abdominal CT can be used to examine the liver, adrenal glands, abdominal lymph nodes, etc. for the presence of metastasis. In addition, low-dose chest CT is recommended for lung cancer screening.

MRI: It is suitable for examining whether there are metastases in brain, spinal cord and bone and assessing the treatment efficacy.

Ultrasonography: It can be used to check whether there are metastases in solid important organs of the abdomen, abdominal cavity and retroperitoneal lymph nodes. In addition, ultrasound is often used to localize hydrothorax and pericardial effusion during puncture and aspiration.

Radionuclide bone scan: It is a common test for bone metastasis of lung cancer.

PET-CT examination: It is one of the important methods for lung cancer diagnosis, staging and re-staging, efficacy and prognosis assessment, and also the best method for pre-surgical evaluation of lung cancer.

(2) Pathological examination methods

They include phlegm cytology, CT-guided percutaneous lung aspiration biopsy, thoracentesis, pleural biopsy, resection or excisional biopsy of metastatic lesions, endoscopy, etc.. Endoscopic examination is mainly to obtain cells or tissues for pathological examination, and can also be used to determine the stage of tumor. It mainly includes bronchoscopy, transbronchial needle aspiration biopsy, ultrasonic bronchoscopy, ultrasonic bronchoscopy-guided TBNA, transbronchial lung biopsy, thoracoscopy and mediastinoscopy.

(3) Tumor marker detection

Lung cancer-related serum tumor markers may be useful for disease identification, early diagnosis and prevention, and monitoring during treatment. Common clinical tumor markers of lung cancer include carcinoembryonic antigen (CEA), cytokeratin fragment 19 antigen (CYFRA21-1), squamous epithelial cell carcinoma-associated antigen (SCC), gastrin-releasing peptide precursor (ProGRP) and neuron-specific enolase (NSE).

4.2 Histologic classification, molecular pathologic diagnosis, and staging of lung cancer

4.2.1 Histological classification

Lung cancer can be categorized into non-

small cell lung cancer and small cell lung cancer. Non-small cell lung cancer histologically includes squamous carcinoma, adenocarcinoma, adenosquamous carcinoma, and large cell carcinoma, etc.. Specific histological typing should be based on the 2015 WHO histological classification of lung cancer. Immunohistochemical indexes for adenocarcinoma identification are Napsin-A and TTF-1; indexes for squamous carcinoma identification are P40, CK5/6, P63; indexes for small cell identification are CD56, Syno, NSE, CgA, Ki-67, TTF-1. Specific histological classification can be found in the 2015 WHO histological classification of lung cancer (Appendix A).

4.2.2 Staging

The staging of lung cancer is based on the UICC/AJCC 8th edition TNM staging criteria, including stages I (I A, I B), II (II A, II B), III (III A, III B, III C), and IV (IV A, IV B). The specific staging can be found in the UICC/AJCC 8th edition of TNM staging of lung cancer (Appendix B).

4.2.3 Molecular pathology diagnosis

(1) Single gene detection: EGFR gene mutation, ALK and ROS1 fusion gene detection should be performed on tumor tissues. MET amplification, MET exon 14 jump mutation, HER-2 mutation, RET fusion gene, NTRK fusion, BRAF mutation, etc. are feasible if available.

(2) Second-generation sequencing technology (NGS): A high-throughput sequencing method to discover targetable driver genes at once, which is more suitable for patients with a small amount of advanced lung cancer tissue specimens.^[4]

(3) Liquid biopsy ctDNA detection: including plasma, pleural fluid, cerebrospinal fluid, suitable for those with unavailable tumor tissue specimens.

(4) PD-L1 expression detection: PD-L1 expression is detected by immunohistochemistry on tissue specimens.

4.3 TCM identification and staging

Clinically, the integration of Chinese and Western medicine treatment for lung cancer is

adopted in the whole process of postoperative rehabilitation, chemotherapy, radiotherapy, targeted therapy and other treatments to realize the whole management of Chinese and Western medicine treatment. Clinically, lung cancer is a mixture of deficiency and reality, and can be seen in several types, often divided into the following five basic types: stagnated lung qi with phlegm stasis, spleen deficiency with phlegm-damp, yin deficiency with phlegm-heat, deficiency of both qi and yin, and kidney-yang deficiency.

5 Integrated Chinese and Western Medicine Treatment of Lung Cancer

5.1 Treatment principles

For early stage non-small cell lung cancer patients, radical surgical resection should be performed, and local radiotherapy or radiofrequency ablation should be given to patients who cannot tolerate surgery because of cardiopulmonary insufficiency. For locally advanced patients, concurrent radiotherapy and chemotherapy are the standard treatment, and some patients can be considered for surgery if the imaging reassessment suggests that the lesion can be completely resected after induction therapy. Advanced patients should receive a comprehensive treatment based on systemic therapy, and individualized treatment strategies should be formulated according to the patient's pathological type, molecular pathological characteristics and performance status in order to prolong survival time, control disease progression and improve quality of life. The treatment of most small cell lung cancers is based on the principle of systemic chemotherapy-based comprehensive therapy.^[5,6]

For lung cancer patients who receive surgery, radiotherapy, chemotherapy, and targeted therapy and are eligible for treatment, an integrated treatment of Chinese and Western medicine is adopted. It can help recovery, resist recurrence and metastasis, reduce toxicity and increase efficiency, relieve symptoms and enhance survival quality in different stages. While considering disease differentiation, the treatment is also based on syndrome differentiation. Basing on the idea that the deficient vital qi is the root cause, the

intermingling of "phlegm", "stasis" and "toxin" is the basic pathogenesis, the treatment flexibly applies the basic treatment principle of "strengthening vital qi" and "eliminating pathogen". The emphasis of strengthening vital qi is on invigorating lung and spleen, benefiting qi and nourishing yin and warming spleen and kidney, while of eliminating pathogen on dissipating phlegm and dispersing constipation and removing blood stasis and toxic substance. With the rising and falling of vital qi and pathogen, the strategies of "strengthening vital qi" and "eliminating pathogen" are adjusted accordingly.^[7] Specific treatment strategies are as follows.

5.1.1 Surgery combined with TCM treatment

During the perioperative period, the treatment is mainly to invigorating lung and spleen and strengthening vital qi to help postoperative recovery; for patients with early-stage lung cancer who do not need adjuvant therapy or have completed adjuvant therapy after surgery, the treatment should lay equal emphasis on eliminating pathogen and strengthening vital qi; during the stable postoperative period, the treatment is invigorating the spleen and dissipating phlegm, softening and resolving hard mass and improving the immune function of the body to reduce the risk of recurrence. For patients in stable postoperative stage, the recommended TCM treatment period is 1 to 2 years.

5.1.2 Chemotherapy combined with TCM treatment

It refers to the TCM treatment adopted during chemotherapy stage. In this stage, patients often manifest as disharmony between stomach and spleen, deficiency of both qi and blood, spleen-kidney deficiency and other patterns. The treatment should focus on harmonizing stomach for descending adverse qi, replenishing qi and nourishing blood flexibly apply the methods of harmonizing the stomach and lowering the rebellion, benefiting the qi and nourishing the blood, and warming the spleen and kidney, so as to alleviate toxic and side reactions and improve the tolerance of treatment.^[8] The TCM treatment cycle is synchronized with chemotherapy.

5.1.3 Radiotherapy combined with TCM treatment

Radiotherapy is a "heat-toxicity" pathogen,

which can easily cause qi and yin injury, or stagnation of lung qi, and the intermingling of phlegm and fire, and therefore injure liver and kidney yin in the long run. The main treatment of TCM is to benefit qi and nourish yin, clear heat and remove toxicity, and nourish liver and kidney, so as to sensitize radiotherapy and reduce adverse reactions. The TCM treatment cycle is synchronized with radiotherapy.

5.1.4 Targeted therapy combined with TCM treatment

It refers to the combined TCM treatment used during targeted therapy. Patients are prone to complications such as target drug-associated rash, diarrhea, oral mucositis, etc., and manifest as stagnated heat of lung channel, damp obstruction due to spleen deficiency, deficiency of both qi and yin, etc.. Treatment should be flexibly applied basing on syndrome differentiation, adopting the methods of clearing the lung and dissipating phlegm, regulating qi-flowing and relieving qi stagnation, invigorating the spleen and resolving dampness, and benefiting qi and nourishing yin according to the evidence, so as to reduce the related toxic and side reactions and improve patients' quality of life.^[9] The TCM treatment cycle is synchronized with targeted drug therapy.

5.1.5 TCM maintenance therapy

For cancer patients in stable condition after chemoradiotherapy, TCM can be used as a maintenance treatment. Basing on the principle that strengthening vital qi while eliminating pathogen, the treatment method should focus on invigorating the spleen and dissipating phlegm, and removing toxic substance and dispersing constipation, in order to slow down the disease progression and improve the patient's quality of life,^[10] with 3 months as a treatment cycle.

5.1.6 TCM can be used as the main treatment for elderly lung cancer patients

Elderly patients with lung cancer mostly have deficiency of vital qi and insufficiency of kidney essence, which make it difficult for them to tolerate purgation method, so the treatment is mainly to strengthen vital qi. TCM takes the dominant position in treating elderly lung cancer patient, focusing

on strengthening vital qi and tonifying spleen and kidney, with 3 months as a treatment cycle.^[11]

5.1.7 Precancerous lesions of lung cancer

Lung cancer precancerous lesions include carcinoma in situ, atypical hyperplasia, and ground glass nodules. The treatment focuses on eliminating pathogen, and the treatment is based on ventilating lung qi, regulating qi-flowing, removing toxic substance and dispersing constipation, which can block precancerous lesions to a certain extent. But regular review and follow-up are still needed, and surgery is performed if necessary.

5.1.8 Chinese medicine relieves symptoms and alleviates toxic and side reactions

TCM is good at relieving symptoms and alleviating toxic and side reactions, and boasts rich experience in treating cough, shortness of breath, fatigue, constipation, nausea and vomiting, and pain of lung cancer patients. It also has good efficacy in alleviating adverse effects related to lung cancer treatment, such as bone marrow suppression, radiation pneumonia, and oral mucositis, which can be treated clinically according to disease differentiation and syndrome differentiation.^[12]

In conclusion, TCM treatment can be applied throughout the whole treatment process of lung cancer, and there are different treatment strategies in different stages that should be applied clinically in accordance to the syndrome differentiation.

5.2 Treatment of lung cancer

5.2.1 Western medicine treatment

(1) Treatment of non-small cell lung cancer (NSCLC)

For patients with early-stage NSCLC, surgical treatment is preferred, and whether to perform postoperative adjuvant chemotherapy or postoperative targeted therapy is assessed according to the postoperative pathological stage. For patients with resectable locally advanced NSCLC, integrated multidisciplinary treatment (including surgery, medical oncology, radiotherapy, etc.) is the best choice; for unresectable locally advanced NSCLC, radical simultaneous radiotherapy is recommended. Patients with advanced NSCLC

are treated individually according to molecular pathological features, distant metastases, PS status and combined concomitant diseases. Clinicians need to make a comprehensive assessment of the short-term efficacy (PFS, objective remission rate), long-term efficacy (OS, full management of follow-up treatment), safety, survival quality, medical insurance coverage, donated medicine and economic cost when selecting treatment regimens, so that patients can obtain a more desirable effect of tumor treatment. For detailed information, please refer to *Integrated Chinese and Western Medicine Treatment for Lung Cancer (non-small cell type): An Expert Consensus*.

(2) Small cell lung cancer (SCLC) treatment

① Treatment of T1~2N0 limited stage SCLC

Radical surgical treatment + adjuvant chemotherapy (EP regimen or EC regimen, 4-6 cycles) is feasible for patients who are suitable for surgery (evidence type 2A). Adjuvant chemotherapy ± mediastinal lymph node radiation therapy is recommended if postoperative N1 (evidence type 2A); adjuvant chemotherapy + mediastinal lymph node radiation therapy is recommended for postoperative N2 (evidence type 2A). Postoperative prophylactic brain irradiation is feasible^[13] (evidence type 1). If surgery is inappropriate or unacceptable for the patient, chemotherapy after stereotactic radiation therapy (evidence type 2A), and chemotherapy combined with synchronous or sequential radiotherapy (evidence type 1) are recommended. For patients achieved CR (complete remission), prophylactic brain radiotherapy is recommended (evidence type 1).

② Treatment of limited stage SCLC beyond T1 to 2N0

Preference is given to concurrent chemoradiotherapy (evidence type 1); if patients cannot tolerate concurrent chemoradiotherapy, sequential chemoradiotherapy is also a viable option (evidence type 1). For patients achieved CR, prophylactic brain radiotherapy is recommended (evidence type 1).

③ Treatment of extensive stage SCLC

First-line treatment: EP regimen chemotherapy combined with Atezolizumab (evidence type

1A) or Durvalumab (evidence type 1A) or EP regimen chemotherapy alone (evidence type 1) is recommended;^[14,15] for patients achieved CR, prophylactic brain radiotherapy is recommended (evidence type 2A), and for patients with brain metastases, local or whole-brain radiotherapy (evidence type 2A).

Second-line treatment: for those with relapse or progression after first-line chemotherapy within less than or equal to 6 months, topotecan (evidence type 1), irinotecan (evidence type 2A), gemcitabine (evidence type 2A), paclitaxel monotherapy (evidence type 2A) or nivolumab monotherapy (evidence type 2A) or in combination with Ipilimumab immunotherapy (evidence type 2A) are recommended. The initial treatment regimen is recommended for those with disease relapse or progression after 6 months. However, for patients who have relapsed after 6 months of previous maintenance treatment with atezolizumab or durvalumab, a combination regimen of PD-L1 inhibitor and chemotherapy is not recommended. Regimens of carboplatin combined with etoposide or cisplatin combined with etoposide are recommended.

Third-line and beyond: it is recommended to use anlotinib (evidence type 2A), nabolutumab (evidence type 2A), pembrolizumab (evidence type 2A) or participate in clinical trials.

5.2.2 TCM Treatment

(1) Treatment based on syndrome and pattern differentiation

Clinically, lung cancer is a intermingling of deficiency and excess, manifesting as several patterns, often divided into the following five basic patterns.

① Stagnated lung qi with phlegm stasis

Main symptoms: Cough with poor circulation, blood in the phlegm, pain in the chest or chest tightness and shortness of breath, purple lips, dry mouth, constipation, dark red tongue with petechiae or petechial dots, white or yellow fur, and smooth string pulse.

Treatment method: ventilating lung qi and Qi,

resolving blood stasis and removing phlegm.

Formula: Modified *Qianjin Weijing* Decoction (*Arcane Essentials from the Imperial Library*): *Weijing* (*Phragmites Stem*) 15 g, *Taoren* (*Semen Persicae*) 10 g, *Miyiren* (*Semen Coix*) 30 g, *Dongguaren* (*Semen Benincasae*) 15 g, *Shengnanxing* (*Rhizoma Arisaematis*) 15 g 10 g, *Yiyiren* (*Semen Coix*) 30 g, *Dongguaren* (*Semen Benincasae*) 15 g, *Shengnanxing* (*Rhizoma Arisaematis*) 15 g (decocted earlier), *Shengbanxia* (*Rhizoma Pinelliae*) 15 g (decocted earlier), *Pinelliae* 15 g (decocted earlier), *Jiegeng* (*Radix Platycodonis*) 12 g, *Yuxingcao* (*Herba Houttuyniae*) 30 g, *Quangualou* (*Fructus Trichosanthis*) 15 g, *Tianqi* (*Radix et Rhizoma Rhizoma*) 15 g (decocted earlier), and *C. p. Tianqi* (*Radix et Rhizoma Notoginseng*) 6g, *Zhebeimu* (*Bulbus Fritillariae Thunbergii*) 10 g.

Variant Formula: Add *Ezhu* (*Rhizoma Curcumae*) 15 g, *Yanhusuo* (*Rhizoma Corydalis*) 15 g for patients with pain and distension in chest and hypochondrium; Add *Baimaogen* (*Rhizoma Imperatae*) 30 g, *Xianhecao* (*Herba Agrimoniae*) 30 g, *Hanliancao* (*Herba Ecliptae*) 20 g for patients with hemoptysis; add *Mudanpi* (*Cortex Moutan*) 15 g, *Lianqiao* (*Fructus Forsythiae*) 15 g, *Huangqin* (*Radix Scutellariae*) 10 g for patients with fever, blood in the phlegm and a dark tongue.

② Spleen deficiency with phlegm-damp

Main symptoms: cough with phlegm, oppression in chest and shortness of breath, fatigue and laziness to speak, anorexia and emaciation, abdominal distension and loose stool, teeth-printed tongue, white and greasy tongue fur, soggy, slow and slippery pulse.

Treatment method: Invigorating the spleen and eliminating dampness, regulating qi-flowing for eliminating phlegm.

Formula: Modified *Chenxia Liujunzi* Decoction (*Yixue Zhengzhuan*). *Dangshen* (*Radix Codonopsis*) 30 g, *Fuling* (*Poria*) 20 g, *Baizhu* (*Rhizoma Atractylodis Macrocephalae*) 15 g, *Chenpi* (*Pericarpium Citri Reticulatae*) 6 g, *Shengbanxia* (*Rhizoma Pinelliae*) 15 g (decocted earlier), *Shengnanxing* (*Rhizoma*

Arisaematis) 15 g (decocted earlier), *Yiyiren* (*Semen Coix*) 30 g, *Gualoupi* (*Pericarpium Trichosanthis*) 15 g, *Jiegeng* (*Radix Platycodonis*) 12 g, *Zhebeimu* (*Bulbus Fritillariae Thunbergii*) 10 g, *Gancao* (*Radix et Rhizoma Glycyrrhizae*) 10 g.

Variant Formula: Add *Baijiezi* (*Semen Sinapis*) 15 g, *Zhishi* (*Fructus Aurantii Immaturus*) 15 g for patients with phlegm congestion and excessiveness; add *Renshen* (*Radix et Rhizoma Ginseng*) 10 g, *Huangqi* (*Radix Astragali*) 30 g for patients with fatigue and analeptic.

③ Yin deficiency with phlegm-heat

Main symptoms: cough with little phlegm, dry cough without phlegm, or phlegm with blood, hemoptysis, chest tightness and shortness of breath, tidal fever and night sweating, dizziness and tinnitus, dysphoria and thirst, red urine and constipated stool, red and crimson tongue, peeled tongue fur or mirror-like tongue, thin, rapid and weak pulse.

Treatment method: Nourishing kidney and clearing lung, dissipating phlegm and dispersing constipation.

Formula: Modified *Baihe Gujin* Decoction (*Shenzhai Yishu*): *Shengdi* (*Radix Rehmanniae*) 20 g, *Baihe* (*Bulbus Lilii*) 15 g, *Xuanshen* (*Radix Scrophulariae*) 15 g, *Danggui* (*Radix Angelicae Sinensis*) 10 g, *Zhebeimu* (*Bulbus Fritillariae Thunbergii*) 10 g, *Shougong* (*Gekko japonicus Dumeril et al. Angelicae Sinensis*) 10 g, *Zhebeimu* (*Bulbus Fritillariae Thunbergii*) 10 g, *Shougong* (*Gekko japonicus Dumeril et Bibron*) 6 g, *Xiakucuo* (*Spica Prunellae*) 15 g, *Gualoupi* (*Pericarpium Trichosanthis*) 15 g, *Zhuling* (*Polyporus*) 20 g, *Biejia* (*Carapax Trionycis*) 30 g (decocted earlier), *Gancao* (*Radix et Rhizoma Glycyrrhizae*) 10 g.

Variant Formula: Add *Yuxingcao* (*Herba Houttuyniae*) 30 g, *Zhimu* (*Rhizoma Anemarrhenae*) 15 g, *Sangbaipi* (*Cortex Mori*) 10 g for patients with yellow phlegm like pus with fishy smell; add *Danpi* (*Cortex Moutan*) 15 g, *Huangbai* (*Cortex Phellodendri Chinensis*) 15 g for patients with dysphoria with feverish sensation in chest; Add *Tianhuafen* (*Radix Trichosanthis*) 20 g, *Tiandong*

(*Radix Asparagi*) 15 g for patients with thirst and desire to drink; Add *Huomaren* (*Fructus Cannabis*) 15 g, *Houpo* (*Cortex Magnoliae Officinalis*) 10 g for patients with dry stool.

④ Deficiency of both qi and yin

Main symptoms: dry cough with little phlegm, low cough sound, or little phlegm with blood, withered-yellow complexion, mental fatigue and lack of strength, dry mouth and shortness of breath, anorexia and emaciation, light red or fat tongue, white dry tongue fur or no fur, thin pulse like silk.

Treatment method: Benefiting qi and nourishing yin, strengthening vital qi and removing stagnation.

Formula: Modified *Dabu Yuanjian* Decoction (*The Orthodox Materia Medica*) *Renshen* (*Radix et Rhizoma Ginseng*) 15 g, *Shanyao* (*Rhizoma Dioscoreae*) 30 g, *Shudihuang* (*Radix Rehmanniae Praeparata*) 15 g, *Danggui* (*Radix Angelicae Sinensis*) 10 g, *Shanyurou* (*Fructus Corni*) 10 g, *Xianhecao* (*Herba Agrimoniae*) 30 g, *Xiyangshen* (*Radix Panacis Quinquifolii*) 10 g, *Maidong* (*Radix Ophiopogonis*) 15 g, *Maidong* (*Fructus Schisandrae Chinensis*) 10 g, *Zhuling* (*Polyporus*) 20 g, *Shanhailuo* (*Radix Codonopsis Lanceolatae*) 30 g.

Variant Formula: For sticky phlegm with difficulty in coughing, add *Sangye* (*Folium Mori*) 10 g, *Jiangcan* (*Bombyx Batryticatus*) 10 g, *Haigeqiao* (*Concha Meretricis seu Cyclinae*) 30 g; for swollen face and limbs, add *Tinglizhi* (*Semen Lepidii*) 15 g, *Fuling* (*Poria*) 25 g, *Zexie* (*Rhizoma Alismatis*) 15 g; *Quanxie* (*Scorpio*) 5 g, *Wugong* (*Scolopendra*) 3 g, *Shichangpu* (*Rhizoma Acori*) 15 g, *Tatarinowii* 15 g.

⑤ Kidney-yang deficiency

Main symptoms: shortness of breath, shortness of breath on exertion, possible withered complexion, facial and eyelid edema, cold sweating, soreness and weakness of the waist and knees, cough with little phlegm, fear of cold and timidity, pale, tender and enlarged tongue, deep and thin pulse.

Treatment: Warming yang and tonifying kidney, controlling respiring qi and calming panting.

Formula: Modified *Renshen Gejie* Powder (*Yilei Yuanrong*): *Gejie* (*Geckoi*) 1 pair, *Renshen* (*Radix et Rhizoma Ginseng*) 15 g, *Beixingren* (*Semen Armeniaca Amarum*) 10 g, *Beimu* (*Bulbus Fritillaria*) 10 g, *Sangbaipi* (*Cortex Mori*) 15 g, *Fuling* (*Poria*) 15 g, *Duzhong* (*Cortex Eucommiae*) 15 g, *Rougui* (*Cortex Cinnamomi*) 6 g, *Chenxiang* (*Lignum Aquilariae Resinatum*) 10 g, *Shufupian* (*Radix Aconiti Lateralis Praeparata*) 10 g (decocted earlier).

Variant Formula: Add *Tinglizi* (*Semen Lepidii*) 15 g, *Dazao* (*Fructus Jujubae*) 15 g for patients who breathe more and inhale less, coughing and wheezing; add *Suzi* (*Fructus Perillae*) 15 g, *Qianhu* (*Radix Peucedani*) 15 g, *Juhong* (*Exocarpium Citri Rubrum*) 10 g for patients with congested phlegm and shortness of breath on exertion; add *Ganjiang* (*Rhizoma Zingiberis*) 10 g, *Danggui* (*Radix Angelicae Sinensis*) 10 g, *Lujiangshuang* (*Cornu Cervi Degelatinatum*) 15 g for patients with physical cold and cold limbs.

Syndrome differentiation is the core of TCM treatment. In the process of diagnosis and treatment, we can also refer to the academic thought and experience of lung cancer treatment by famous Chinese medical oncologists, national medical masters and national famous TCM practitioners, such as Zhu Liangchun, Liu Jiaxiang, Zhou Daihan, Piao Bingkui, Pan Minqiu, Yu Rencun, Li Peiwen, Liu Weisheng and Liu Yaxian. The duration of TCM treatment should be flexibly adjusted according to the patient's physical status, clinical stage, treatment modality and prognostic indicators; overall, it is recommended that the duration of TCM treatment should be more than 1 year, and blood analysis, urinalysis, liver and kidney function should be checked regularly during the course of treatment.

(2) Prescribe basing on syndrome differentiation

Clinically, cough, hemoptysis, chest pain, fatigue, hydrothorax and other symptoms are common in lung cancer patients, and may coexist with multiple symptoms. It is suggest that modify the formulas according to syndrome differentiation.

① Cough

Cough is located in the lung and is related to

the spleen and liver, and in the long run may affect the kidney. In the syndrome differentiation of cough, the first step is to distinguish between exogenous disease and internal damage, and whether the symptoms are deficient or excessive. Most patients with lung cancer have coughs due to internal damages, such as deficiency of lung qi, spleen deficiency generating phlegm, liver fire invading lung or kidney failing to govern inspiration, which lead to lung qi failing in dispersing and adverse rising of lung qi. In terms of treatment, the basic principle should be ventilating lung qi for dissipating phlegm, and to prescribe according to the intermingled deficiency and excess and syndrome differentiation of zang-fu viscera.^[16-18]

The syndromes of cough with itchy throat, thin white phlegm, clear runny nose, aversion to cold and fever are mostly due to external assault by wind-cold. The treatment is to relieve superficies syndrome with pungent and warm natured drugs, ventilate lung for relieving cough, including *Mahuang* (*Herba Ephedrae*), *Jingjie* (*Herba Schizonepetae*), *Zisugeng* (*Caulis Perillae*), *Xingren* (*Semen Armeniaca Amarum*), *Jiegeng* (*Radix Platycodonis*), etc. are recommended.

The syndromes of dry cough, sore throat, little phlegm and difficult to cough, or blood in the phlegm, red and dry tongue, thin yellow fur, floating and rapid pulse, are mostly due to wind-dry injuring lung. The treatment is to clear lung-heat and moisten dryness. *Sangye* (*Folium Mori*), *Beixingren* (*Semen Armeniaca Amarum*), *Chuanbei* (*Bulbus Fritillariae Cirrhosae*), *Shashen* (*Radix Adenophorae seu Glehniae*), *Pipaye* (*Folium Eriobotryae*), etc. are recommended.

The syndromes of short breath, low voice, white phlegm, spontaneous sweating, aversion to cold, tiredness and weakness, pale tongue, white fur, weak pulse, are mostly due to the deficiency of lung and spleen. The treatment is to invigorate spleen and nourish lung, replenish earth to generate gold, *Dangshen* (*Radix Codonopsis*), *Baizhu* (*Rhizoma Atractylodis Macrocephalae*), *Chenpi* (*Pericarpium Citri Reticulatae*), *Faxia* (*Rhizoma Pinelliae Praeparatum*), etc.^[12] are recommended.

The syndromes of dry cough, short cough, dry mouth and throat, hoarseness, tidal fever in the afternoon, night sweats, emaciation, red tongue, little fur, thin and rapid pulse, are mostly due to loss of lung yin. The treatment is to nourish yin and clear heat, moisten lung for arrest cough. *Maidong* (*Radix Ophiopogonis*), *Tiandong* (*Radix Asparagi*), *Tianhuafen* (*Radix Trichosanthis*), *Kuandonghua* (*Flos Farfarae*), *Ziwan* (*Radix et Rhizoma Asteris*), etc. are recommended.

If the phlegm is white and thin with a pale tongue and white smooth fur, it is cold phlegm. The treatment is to warmly resolve cold-phlegm. *Xixin* (*Radix et Rhizoma Asari*), *Ganjiang* (*Rhizoma Zingiberis*), *Gejie* (*Geckoi*), *Banxia* (*Rhizoma Pinelliae*), etc. are recommended. If the cough is deep and harsh, the phlegm is white and sticky and there are stuffiness and oppression in chest, it is phlegm-damp amassing in lung. The treatment is to dry dampness and dissipate phlegm, regulate qi and arrest coughing. *Banxia* (*Rhizoma Pinelliae*), *Fuling* (*Poria*), *Chenpi* (*Pericarpium Citri Reticulatae*), *Baijiezi* (*Semen Sinapis*), *Cangzhu* (*Rhizoma Atractylodis*), *Huajuhong* (*Exocarpium Citri Grandis*), etc. are recommended.

The syndromes of cough with chest pain, thick phlegm or yellow phlegm, dry mouth and desire to drink, red tongue, yellow greasy fur, and slippery pulse are mostly phlegm and heat in the lung. The treatment is to clear heat, resolve phlegm, and astring lung for relieving cough. *Huangqin* (*Radix Scutellariae*), *Zhimu* (*Rhizoma Anemarrhenae*), *Gualoupi* (*Pericarpium Trichosanthis*), *Pugongying* (*Herba Taraxaci*), *Yuxingcao* (*Herba Houttuyniae*), etc. are recommended.

After radiotherapy, patients often have dry cough, dry and burning throat, yellow and thick phlegm that is difficult to cough, occasional fever, red tongue, little fur, slippery and rapid or thin and rapid pulse. The symptoms are mostly due to injury of both qi and yin or pathogenic heat congesting lung. The treatment is to benefit qi and nourish yin or nourish yin and clear heat, can use *Shashen* (*Radix Adenophorae seu Glehniae*), *Maidong* (*Radix Ophiopogonis*), *Lianqiao* (*Fructus Forsythiae*),

Zhimu (*Rhizoma Anemarrhenae*), *Jiegeng* (*Radix Platycodonis*), *Shengdi* (*Radix Rehmanniae*), etc. are recommended.

② Hemoptysis

Hemoptysis belongs to the category of "blood pattern", and is located in the collateral. In the syndrome differentiation of hemoptysis, it is necessary to distinguish between deficiency and actuality. Excessive symptoms are mostly caused by fire-heat and blood stasis, fire-heat burning, bleeding due to blood heat, or blood overflowing outside the veins and stasis of blood blocking the collateral; deficient symptoms are generally caused by deficiency of qi and blood not returning to the meridians. In terms of treatment, we should focus on treating fire, qi and blood, and prescribe according to the syndrome differentiation of intermingled deficiency and excess.

The syndromes of blood in the phlegm or hemoptysis, dry mouth and itchy throat or sore throat, aversion to wind and fever and headache are mostly due to dry-heat invading lung. The treatment is to clear heat and moisten lung, calm the collateral and stop bleeding. *Sangye* (*Folium Mori*), *Shashen* (*Radix Adenophorae seu Glehniae*), *Oujie* (*Nodus Nelumbinis Rhizomatis*), *Cebaiye* (*Cacumen Platycladi*), etc. are recommended.

If there is blood in the phlegm or hemoptysis, coughing with pain involving the chest and hypochondrium, irritability, red eyes and bitter taste in mouth, red tongue, thin yellow fur, and stringy and rapid pulse, it's due to liver fire invading lung. The treatment is to clear liver-fire and purge lung, cool blood for hemostasis. *Xianhecao* (*Herba Agrimoniae*), *Huangqin* (*Radix Scutellariae*), *Shigao* (*Gypsum Fibrosum*), *Zhimu* (*Rhizoma Anemarrhenae*), *Qiancaogen* (*Radix et Rhizoma Rubiae*), etc. are recommended.

The syndromes of blood in the phlegm or hemoptysis in purple and dark color, fixed stabbing pain in the chest and hypochondrium, cyanotic tongue with ecchymosis, astringent pulse, are mostly due to blood stasis blocking collateral. The treatment is to remove blood stasis, cool the

blood and stop bleeding. *Tianqi* (*Radix et Rhizoma Notoginseng*), *Danshen* (*Radix et Rhizoma Salviae Miltiorrhizae*), *Shengdi* (*Radix Rehmanniae*), *Biejia* (*Carapax Trionycis*), etc.^[19] are recommended.

The syndromes of massive hemoptysis in light color, tiredness and weakness, poor appetite, pale tongue with white fur and thin pulse are mostly due to failure of keeping fluid due to qi deficiency and spleen failing to manage blood. The treatment is to benefit qi and control blood. *Renshen* (*Radix et Rhizoma Ginseng*), *Huangqi* (*Radix Astragali*), *Fuling* (*Poria*), *Ejiao* (*Colla Corii Asini*), *Qiancao* (*Rhizoma Rubiae*), *Paojiangtan* (*Rhizoma Zingiberis Praeparatum*), etc. are recommended.

③ Hydrothorax

Hydrothorax belongs to the category of "phlegm and fluid retention" and "suspending fluid", and is located in the Sanjiao (BL 22). Phlegm and fluid retention is mostly due to deficiency and root vacuity and tip repletion. The first thing to identify is the primary and secondary aspects of the two. Suspending fluid are mainly caused by breakdown of qi transformation in Sanjiao (BL 22), and dysfunction of lung, spleen and kidney, which are retained in the hypochondrium. In treatment, the priority is to warm yang and transform qi, and meanwhile, to prescribe according to the syndrome differentiation of intermingled deficiency and excess.

The symptoms of pain in the chest and hypochondrium, difficulty in breathing, coughing and asthma, unable to lie down, or only able to lie down on the side where fluid suspends, fullness between the ribs on the sick side, pale tongue with white fur, deep and stringy or striny and slippery pulse are mostly due to fluid retained in chest and hypochondrium. The treatment is to eliminating pathogens from lung for expelling fluid retention. *Tinglizi* (*Semen Lepidii*), *Sangbaipi* (*Cortex Mori*), *Zhuling* (*Polyporus*), *Cheqianzi* (*Semen Plantaginis*), *Fangji* (*Radix Stephaniae Tetrandrae*), etc. are recommended.

The symptoms of frequent coughing, dry mouth and throat, tidal fever in the afternoon, feverishness in palms and soles, red tongue with little fur, thin and

rapid pulse are mostly because of endogenous heat due to yin deficiency. The treatment is to nourish yin and clear heat. *Shashen* (*Radix Adenophorae seu Glehniae*), *Maidong* (*Radix Ophiopogonis*), *Sangbaipi* (*Cortex Mori*), *Tianhuafen* (*Radix Trichosanthis*), *Taizishen* (*Radix Pseudostellariae*), *Shihu* (*Caulis Dendrobii*), *Yuzhu* (*Rhizoma Polygonati Odorati*), etc. are recommended.

The symptoms of shortness of breath on exertion, oppression in chest, little appetite, physical cold and cold limbs, mental fatigue and lack of strength, pale and enlarged tongue, white smooth fur, deep and thin pulse are mostly due to the deficiency of spleen and kidney yang. The treatment is to warm spleen and tonify kidney. *Fuzhi* (*Radix Aconiti Lateralis Praeparata*), *Guizhi* (*Ramulus Cinnamomi*), *Ganjiang* (*Rhizoma Zingiberis*), *Huangqi* (*Radix Astragali*), *Baizhu* (*Rhizoma Atractylodis Macrocephalae*), *Buguzhi* (*Fructus Psoraleae*), *Gejie* (*Geckoi*), etc. are recommended.

④ Chest pain

Chest pain belongs to the category of "pain" and is located in the collateral. When there is stoppage, there is pain. Lung cancer disease chest pain is root vacuity and tip repletion, when it attacks, the treatment is based on tip repletion and when it relieves, the treatment is based on root vacuity. In treatment, "before the onset we should focus on strengthening vital qi, while after the onset, we should eliminating pathogen".^[20]

The symptoms of pain involving the chest and hypochondrium, intensifies with mood swings, red eyes and bitter taste in the mouth, red tongue, thin yellow fur, and stringy and rapid pulse are mostly due to liver fire invading the lung. *Pugongying* (*Herba Taraxaci*), *Huangqin* (*Radix Scutellariae*), *Shigao* (*Gypsum Fibrosum*), *Zhimu* (*Rhizoma Anemarrhenae*), etc. are recommended.

The symptoms of fixed stabbing pain in the chest and hypochondrium on exertion, cyanotic tongue with ecchymosis, stringy pulse, mostly due to blood stasis blocking the collateral. The treatment is to remove obstruction in collaterals and promote blood circulation for relieving pain. *Tongluo* (*Radix*

et Rhizoma Notoginseng), *Dilong* (*Pheretima*), *Biejia* (*Carapax Trionycis*), *Shougong* (*Gekko japonicus* *Dumeril et Bibron*), *Dilong* (*Pheretima*), *Jiangcan* (*Bombyx Batryticatus*), etc. are recommended.

The symptoms of stuffy pain in the chest with variable location that aggravates by rainy days, white, greasy and sticky phlegm are mostly due to phlegm-damp amassing in lung. The treatment is to dry dampness and dissipate phlegm, regulate qi and relieve pain. *Banxia* (*Rhizoma Pinelliae*), *Fuling* (*Poria*), *Chenpi* (*Pericarpium Citri Reticulatae*), *Zhihe* (*Fructus Aurantii*), etc. are recommended.

The symptoms of dull pain in chest, shortness of breath, more inhalation and less exhalation, low voice, sweating and cold extremities, pale tongue with thin white fur, deep and weak pulse are mostly due to deficiency of both lung and kidney. The treatment is to benefit lung and tonify kidney, *Fuzhi* (*Radix Aconiti Lateralis Praeparata*), *Gejie* (*Geckoi*), etc. are recommended.

(3) Prescribe basing on disease differentiation

On the basis of treatment according to disease differentiation, two to three herbs with disease-specific anti-cancer properties can be added, such as *Baihuasheshecao* (*hedyotis*), *Zhebeimu* (*Bulbus Fritillariae Thunbergii*), *Bihu* (*Gekko japonicus* *Dumeril et Bibron*), *Banzhilian* (*Herba Scutellariae Barbatae*), *Banbianlian* (*Herba Lobeliae Chinensis*), *Shancigu* (*Pseudobulbus Cremastrae seu Pleiones*), *Maozhuacao* (*Radix Ranunculi Ternati*), *Lufengfang* (*Nidus Vespae*), *Yuxingcao* (*Herba Houttuyniae*), *Longkuicao* (*Herba Solani Nigri*), *Shemei* (*Herba Duchesneae Indicae*), etc.^[20] are recommended.

(4) Prescribe basing on syndrome differentiation

① Oral Chinese patent medicine

According to the condition, we can choose to use Chinese patent medicines such as *Heshan* Tablet,^[21] *Kanglaite* Soft Capsule,^[22] *Xiaoaping* Capsule,^[23] *Ankangxin* Capsule,^[24] *Shenyi* Capsule^[25] (evidence type D), *Yadanzhiyou* Soft Capsule, Compound *Hongdoushan* Capsule,^[26] *Yifeiqinghua* Granules,^[27] *Jinfukang* Oral Liquid^[28] (evidence type B), *Zhengyuan* Capsule,^[29] *Huisheng* Oral Liquid.^[30]

② Intravenous drip of TCM injections

According to the condition, we can choose to apply *Kanglaite* Injection^[31] (evidence type B), *Aaidi* Injection^[32] (evidence type C), *Xiaoaping* Injection (evidence type D), *Yadanzhiyou* Injection^[33] (evidence type B), *Kang'ai* Injection^[34] (evidence type B), *Huachansu* Injection^[35] (evidence type B), *Shenqi Fuzheng* Injection^[36] (evidence type C), *Lanxiangxiru* Injection^[37] (evidence type B), etc..

(5) TCM special therapy

① External application of Chinese herbs for cancer pain

Chanwu Babu Paste, composed of *Chansu* (*Venenum Bufonis*), *Chuanwu* (*Radix Aconiti*), *Liangmianzhen* (*Radix Zanthoxyli*), *Chonglou* (*Rhizoma Paridis*), *Guanbaifu* (*Radix Aconiti Coreani*), *Sanleng* (*Rhizoma Sparganii*), *Ezhu* (*Rhizoma Curcumae*), *Xixin* (*Radix et Rhizoma Asari*), *Dingxiang* (*Flos Caryophylli*), *Rougui* (*Cortex Cinnamomi*), *Ruxiang* (*Olibanum*), *Bingpian* (*Borneolum Syntheticum*), etc., is used for pain caused by lung cancer, with the effect of promoting blood circulation for removing blood stasis, eliminating detumescence and relieving pain. Usage and dosage: for external use, apply the medicine directly to the painful area, or apply it to Tiantu (RN 22), Danzhong (RN 17), etc.. Apply 1 patch at a time and change it once in 1 to 2 days.

Ailitong, composed of *Baiyao* Paste, *Chansu* (*Venenum Bufonis*), *Zhimaqianzi* (*Semen Strychni Praeparata*), *Maoshexiang* (*Moschus*), *Liaodiaozhu* (*Arundina graminifolia*), *Dameipian* (*Borneolum Syntheticum*), *Jinniupi* (*Herba Ardisiae japonicae*), *Bingpian* (*Borneolum Syntheticum*), etc., is used for pain caused by lung cancer, with the effect of promoting blood circulation for removing blood stasis, eliminating detumescence and relieving pain. Usage and dosage: for external use, wash the skin of the affected area before applying externally, Apply 1 patch softened by heat, to local or painful parts, massage gently with hands on it for 3 to 5 minutes to make it adhere closely. 2 times a day, 10 days as a course of treatment.

② Intrathoracic administration of drugs for cancerous hydrothorax

Intrathoracic administration of drugs has a good

therapeutic effect on lung cancer hydrothorax. After the extraction and drainage of hydrothorax in lung cancer patients, relevant drugs such as *Yadanzhiyou* Injection and *Lanxiangxiru* Injection (evidence type D) are administered intrathoracically, which can inhibit the formation of hydrothorax to varying degrees.

③ Acupuncture and moxibustion

Body acupuncture, scalp acupuncture, electro-acupuncture, ear acupuncture, wrist and ankle acupuncture, eye acupuncture, moxibustion and catgut embedment in acupoint can be applied according to the patient's condition. For patients with lung cancer combined with cough, Lieque (LU 7), Feishu (BL 13), Tiantu (RN 22), Fengfu (DU 16), Fengmen (BL 12), Bailao (EX-HN 15), etc. are recommended; for patients with post-lung cancer resection pain, Hegu (LI 4), Yanglingquan (GB 34), Waiqiu (GB 36), Sanyangluo (SJ 8) and ashi point are recommended; for patients with bone metastases from lung cancer, Dazhui (DU 14), Huatuojiagi (EX-B2), Mingmen (DU 4), Shenshu (BL 23), Weizhong (BL 40) and ashi point are recommended; for patients with other concomitant symptoms, such as abdominal distension and constipation, the points can also be taken by following the meridians.

④ Ear acupuncture to prevent chemotherapy-induced gastrointestinal reactions

Main acupoints: Stomach, sympathetic, Shenmen (HT 7), subcortex. Treatment: harmonizing stomach for descending adverse qi and suppressing vomiting. Points combination: lung, trachea and large intestine, etc..

⑤ Main selection of acupressure points.

Feishu (BL 13), Gaohuang (BL 43), Geshu (BL 17), Danshu (BL19). It is effective in regulating lung qi, tonifying lung deficiency and promoting blood circulation to remove blood stasis. (evidence type C2)

5.2.3 TCM treatment of common side reactions of lung cancer

(1) Toxic and side reactions due to chemotherapy

① Digestive tract reactions

Gastrointestinal reactions are common toxic and side reactions of chemotherapy for lung cancer patients, and are often associated with

anorexia, nausea, aversion to grease, vomiting and belching. In TCM, it is believed to be related to the malfunction of spleen and stomach's transportation and transformation, and the pathogenesis is damp retention due to spleen deficiency and disharmony between ascending and descending. Chemotherapy drugs are cold in nature and can damage spleen and yang, resulting in failure of stomach qi to descend.

Treatment: Harmonizing the stomach and subduing rebellion, strengthening the spleen and dispelling dampness.

Formula: Modified *Jianpi Hewei* Decoction: *Dangshen* (*Radix Codonopsis*), *Baizhu* (*Rhizoma Atractylodis Macrocephalae*), *Fuling* (*Poria*), *Zhigancao* (*Radix et Rhizoma Glycyrrhizae Praeparata cum Melle*), *Chenpi* (*Pericarpium Citri Reticulatae*), *Fabanxia* (*Rhizoma Pinelliae Praeparatum*), *Muxiang* (*Radix Aucklandiae*), *Sharen* (*Fructus Amomi*), *Houpo* (*Cortex Magnoliae Officinalis*), *Jineijin* (*Endothelium Corneum Gigeriae Galli*), *Shanzha* (*Fructus Crataegi*), etc..

Variant formula: ① For those with anorexia, difficulty in digestion, distention and stuffiness of stomach, preferring warmth and pressure, etc., it's due to deficiency-cold in spleen and stomach, add *Ganjiang* (*Rhizoma Zingiberis*), *Dingxiang* (*Flos Caryophylli*), *Gaoliangjiang* (*Rhizoma Alpiniae Officinarum*), *Maiya* (*Fructus Hordei Germinatus*), *Laifuzi* (*Semen Raphani*), *Doukouren* (*Semen Fructus Amomi Rotundus*), *Shenqu* (*Massa Medicata Fermentata*); ② For recurrent retching, dry mouth and throat and stomach upset, it's due to stomach-yin deficiency, add *Maidong* (*Radix Ophiopogonis*), *Tiandong* (*Radix Asparagi*), *Shihu* (*Caulis Dendrobii*), *Huafen* (*Radix Trichosanthis*), *Zhimu* (*Rhizoma Anemarrhenae*), *Jingmi* (*Oryza Sativa* L.); ③ For vomiting with putrid sour, frequent belching, dry stools with foul odor, it's due to liver qi offending stomach, add *Huangqin* (*Radix Scutellariae*), *Huanglian* (*Rhizoma Coptidis*), *Wuzhuyu* (*Fructus Evodiae*), *Chaihu* (*Radix Bupleuri*), *Zhishi* (*Fructus Aurantii Immaturus*), *Xuanfuhua* (*Flos Inulae*), *Zheshi* (*Haematitum*), *Xiangfu* (*Rhizoma Cyperi*), *Chuanlianzi* (*Fructus Toosendan*), *Yujin* (*Radix Curcumae*); ④ For vomiting clear water, oppression

and stuffiness in the chest, dizziness and palpitations, it's due to phlegm-damp, add *Zhuru* (*Caulis Bambusae in Taenia*), *Jupi* (*Pericarpium Citri Reticulatae*).

⑤ For vomiting with undigested food, accompanied by sweating and cold extremities, soreness and weakness of waist and knees, pale and enlarged tongue and deep and thin pulse, add *Fuzhi* (*Radix Aconiti Lateralis Praeparata*), *Rougui* (*Cortex Cinnamomi*), *Gaolishen* (*Rhizoma Alpiniae Officinarum*). As the stomach qi of tumor patients has been injured, fishy and foul-smelling products or those that can irritate stomach should be avoided in the prescription, such as *Dilong* (*Pheretima*), *Shuizhi* (*Hirudo*), *Ruxiang* (*Olibanum*), *Moyao* (*Myrrha*), etc. Those with light and aromatic smell that can awaken spleen are preferred.

Other treatments:

Acupuncture: For deficiency-cold of spleen and stomach, acupuncture points Tanzhong (RN 17), Zhongwan (RN 12) and Guanyuan (RN 4) are recommended, 20 minutes each time; for deficiency of stomach yin, acupuncture points Neiguan (PC 6), Zusanli (ST 36), Zhongwan (RN 12), Hegu (LI 4) and Gongsun (SP 4) are recommended, conventional acupuncture with even reinforcing-reducing method; for liver qi offending stomach, acupuncture points Neiguan (PC 6), Zusanli (ST 36), Zhongwan (RN 12), Yanglingquan (GB 34), Taichong (LV 3) are recommended, conventional acupuncture with even reinforcing-reducing method. (evidence type D)

Local application of medicinals on acupuncture points: for deficiency of spleen and stomach, double Feishu (BL 13), Pishu (BL 20), Weishu (BL 21), Zusanli (ST 36) are recommended; for deficiency of stomach yin, double Feishu (BL 13), Weishu (BL 21), Zusanli (ST 36), Neiguan (PC 6) are recommended; for liver qi offending the stomach, double Feishu (BL 13), Pishu (BL 20), Yanglingquan (GB 34), Taichong (LV 3) are recommended. The treatment is performed once a day, removed after four hours. (evidence type C)

Ear acupuncture: For deficiency of spleen and stomach, subcortical, stomach, spleen and kidney

points are recommended; for stomach yin deficiency, sympathetic, stomach, cardia, esophagus, and Shenmen (HT 7) points are recommended; for liver qi offending the stomach, sympathetic, Shenmen (HT 7), stomach, liver and spleen points are recommended. The treatment is performed once two days, self-pressure for 3 to 5 minutes, 3 to 4 times a day.

② Myelosuppression

Bone marrow suppression is one of the most common side effects of chemotherapy. According to its clinical manifestations, such as dizziness, weakness, soreness and weakness of waist and knees, susceptible to exogenous infection and fever, and bleeding, this disease belongs to "consumptive disease" and "blood deficiency" in Chinese medicine, and its main etiology is deficiency of spleen and kidney, and loss of nourishment of the marrow. Chemotherapeutic drugs are toxic and can injure spleen and stomach, resulting in disharmony between spleen and stomach and a lack of source of transformation and transportation of qi and blood; and can injure kidney, resulting in a deficiency of kidney essence and kidney yang, the essence not nourishing the marrow and malnutrition of marrow, thus leading to deficiency of both yin and blood.

Treatment: invigorating spleen and tonifying kidney, nourishing blood to generate marrow. Formula: Modified *Jianpi Bushen* Decoction: *Dangshen* (*Radix Codonopsis*), *Baizhu* (*Rhizoma Atractylodis Macrocephalae*), *Fuling* (*Poria*), *Zhigancao* (*Radix et Rhizoma Glycyrrhizae Praeparata cum Melle*), *Shudihuang* (*Radix Rehmanniae Praeparata*), *Baishao* (*Radix Paeoniae Alba*), *Danggui* (*Radix Angelicae Sinensis*), *Gouqizi* (*Fructus Lycii*), *Shanyuou* (*Fructus Corni*), *Jixieteng* (*Caulis Spatholobi*), etc..

Variant formula: ① for dizziness and tinnitus, soreness and weakness of the waist and knees, frequent nocturia, add *Gejie* (*Geckoi*), *Yinyanghuo* (*Fructus Lycii*), *Bajitian* (*Radix Morindae Officinalis*); ② for palpitation and dizziness, insomnia and dreaminess, limbs and body weakness, emaciation, add *Yuanzhi* (*Radix Polygalae*), *Suanzaoren* (*Semen Ziziphi Spinosae*), *Longyanrou* (*Arillus*

Longan), *Shengmuli* (*Concha Ostreae*), *Longgu* (*Os Draconis*); ③ for low fever and sweating, add *Huanglian* (*Rhizoma Coptidis*), *Mudanpi* (*Cortex Moutan*), *Yinchaihu* (*Radix Stellariae*), *Digupi* (*Cortex Lycii*), *Fuxiaomai* (*Fructus Tritici Levis*); ④ for fixed pain refusing to pressure that exaggerated at night, and squamous and dry skin, add *Taoren* (*Semen Persicae*), *Honghua* (*Flos Carthami*), *Xiangfu* (*Rhizoma Cyperi*), *Biejia* (*Carapax Trionycis*), *Paoshanjia* (*Squama Manitis Praeparatum*).

Other treatments: TCM herbal paste formula can effectively reduce the incidence of myelosuppression after chemotherapy and alleviate the degree of myelosuppression. As one of the most distinctive therapeutic tools of TCM, it has four major effects: regulating, nourishing, preventing and treating, and for bone marrow suppression, the main treatment principle is to invigorate spleen, tonify kidney and harmonize qi and blood.

③ Peripheral neurotoxicity

Peripheral neurotoxicity is a common toxic reaction of antineoplastic drugs, which mainly manifests as symmetrical numbness of fingers and toes, abnormal sensation of touch, pain, or in severe cases, decreased or absent tendon reflexes, sensory impairment of extremities, muscle pain or weakness, and movement disorders. Peripheral neurotoxicity after chemotherapy for lung cancer can be classified as "blood paralysis" in TCM. The cause of blood paralysis lies in the weakness of qi and blood, and the evil enters the yin part of the body. Chemotherapeutic drugs are very toxic and their long-term application can damage yang, which may become insufficient to warm blood and meridian and lead to obstructed blood flow; in addition, cold pathogen blocks tendons and meridian and causes stasis and obstruction of vessel and collateral, resulting in numbness at extremities and sensory disorders.^[38]

Treatment: Warming meridians to promote smooth flow of qi, promoting blood circulation for removing blood stasis.

Prescription: Modified Hexue Tongbi

Decoction: *Danggui* (*Radix Angelicae Sinensis*), *Chuanxiong* (*Rhizoma Chuanxiong*), *Aiye* (*Folium Artemisiae Argyi*), *Guizhi* (*Ramulus Cinnamomi*), *Chishao* (*Radix Paeoniae Rubra*), *Danshen* (*Radix et Rhizoma Salviae Miltiorrhizae*), *Mudanpi* (*Cortex Moutan*), *Lulutong* (*Fructus Liquidambaris*), etc..

Variant formula based on the differentiation:

If the pain in the joints is wandering, or accompanied by symptoms such as aversion to wind, headache, fever, etc., add *Fangfeng* (*Radix Saposhnikoviae*), *Qinjiao* (*Radix Gentianae Macrophyllae*), *Mahuang* (*Herba Ephedrae*), etc.; ② If it is accompanied by soreness and weakness of back, waist and knees, add *Duzhong* (*Cortex Eucommiae*), *Sangjisheng* (*Herba Taxilli*), *Yinyanghuo* (*Fructus Lycii*), etc., *Duzhong* (*Cortex Eucommiae*), *Sangjisheng* (*Herba Taxilli*), *Yinyanghuo* (*Fructus Lycii*), *Xuduan* (*Radix Dipsaci*), etc..

For swollen limb joints, inhibited sinew movement, and white and greasy tongue fur, *Huangqi* (*Radix Astragali*), *Yiyiren* (*Semen Coix*), *Cangzhu* (*Rhizoma Atractylodis*), etc. are added; ④ for localized skin coldness and pain when exposed to cold, *Fuzhi* (*Radix Aconiti Lateralis Praeparata*), *Chuanwu* (*Radix Aconiti*), *Xixin* (*Radix et Rhizoma Asari*), etc. are added; ⑤ for dim complexion, subcutaneous induratum and ecchymosis, dark purple tongue and stringy and hesitant pulse, *Taoren* (*Semen Persicae*), *Honghua* (*Flos Carthami*), *Sanqi* (*Radix et Rhizoma Notoginseng*), *Dilong* (*Pheretima*), etc..

Other treatments:

External cleansing: use *Guizhi* (*Ramulus Cinnamomi*) 10 g, *Chishao* (*Radix Paeoniae Rubra*) 15 g, *Chuanxiong* (*Rhizoma Chuanxiong*) 20 g, *Danshen* (*Radix et Rhizoma Salviae Miltiorrhizae*) 30 g, *Weilingxian* (*Radix et Rhizoma Clematidis*) 30 g, *Xuchangqing* (*Radix et Rhizoma Cynanchi Paniculati*) 30 g of herbal decoction for external washing and soaking of hands and feet. The decoction should be warm, apply once a day for 30 minutes.

Acupuncture: *Quchi* (LI 11), *Neiguan* (PC 6), *Hegu* (LI 4), *Xuehai* (SP 10), *Zusanli* (ST 36), and

Sanyinjiao (SP 6) are selected as the main acupoints and can be Modified according to the patient's clinical symptoms. For numbness of fingertips or toe tips, add Shixuan (EX-UE11) and Qiduan (EX-LE12) for local bloodletting; for motor dysfunction or muscle atrophy, add Yanglingquan (GB 34) and acupuncture points of the Yangming meridian of the hands and feet; for phlegm-damp, add Fenglong (ST 40). Neiguan (PC 6) and Hegu (LI 4) are used for direct acupuncture of 0.5-0.8 inch, and the methods of lifting and twisting, and even reinforcing-reducing method are applied; Quchi (LI 11) and Xuehai (SP 10), Zusanli (ST 36), and Sanyinjiao (SP 6) were directly acupunctured 1 to 1.2 inches, and the tonic method was applied using the method of lifting and twisting. The treatment is performed once a day, 6 times a week. (evidence type D)

④ Cancer-caused fatigue

Cancer-related fatigue (CRF) occurs in 50% to 90% of patients as lung cancer disease progresses or during antineoplastic therapy. Cancer-related fatigue is defined as an unusual, persistent, subjective feeling of exertion that disrupts normal body function. It is characterized by rapid development, high intensity, high energy expenditure, and long duration (usually greater than or equal to 6 months), which cannot be relieved by rest and sleep, and can significantly reduce the quality of life of cancer patients and affect their treatment and recovery. The main symptoms of cancer-related fatigue are tiredness, anorexia, abdominal distension after eating, fatigue, mental fatigue and laziness to speak, yellowish complexion, nausea and vomiting, oppression in chest, etc.. According to TCM, this disease can be classified as "consumptive disease", with the main pathogenesis being the decline of the zang-fu viscera and the depletion of qi, blood, yin and yang, and the deficiency being the main cause and deficiency and excess intermingling. The disease is mainly located in spleen and kidney, with pathological factors such as qi stagnation, phlegm and dampness, blood stasis, etc..

Treatment principle: invigorating spleen and benefiting qi, nourishing blood to generate marrow. Formula: Modified Bazhen Decoction plus Jingui

Shenwi Decoction: *Shudihuang* (*Radix Rehmanniae Praeparata*), *Danggui* (*Radix Angelicae Sinensis*), *Chuanxiong* (*Rhizoma Chuanxiong*), *Baishao* (*Radix Paeoniae Alba*), *Renshen* (*Radix et Rhizoma Ginseng*), *Baizhu* (*Rhizoma Atractylodis Macrocephalae*), *Fuling* (*Poria*), *Gancao* (*Radix et Rhizoma Glycyrrhizae*), *Shufuzhi* (*Radix Aconiti Lateralis Praeparata*), *Rougui* (*Cortex Cinnamomi*), *Shanyurou* (*Fructus Corni*), *Shanyao* (*Rhizoma Dioscoreae*), etc.

Variant formula: ① for dry mouth and throat, poor appetite, dry stools, dry tongue with little fur, add *Shashen* (*Radix Adenophorae seu Glehniae*), *Maidong* (*Radix Ophiopogonis*), *Xuanshen* (*Radix Scrophulariae*), *Shenqu* (*Massa Medicata Fermentata*), *Sangjisheng* (*Herba Taxilli*), *Sangshenzi* (*Semen Fructus Mori*); ② For vertigo and tinnitus, dysphoria with feverish sensation in chest and night sweating, add *Nvzhenzi* (*Fructus Ligustri Lucidi*), *Hanliancao* (*Herba Ecliptae*), *Biejiajiao* (*Carapax Trionycis Platri*), *Guibanjiao* (*Colla Testudinis Platri*), *Fuxiaomai* (*Fructus Tritici Levis*); (3) for soreness and weakness of waist and knees, aversion to cold, cold extremities, diarrhea with undigested food, daybreak diarrhea, and white and pale complexion, add *Lujiaojiao* (*Colla Cornus Cervi*), *Gejie* (*Geckoi*), *Buguzhi* (*Fructus Psoraleae*).

Other treatments

Chinese patent medicine: herbal preparations such as *Shenling Baizhu Powder*, *Shenqi Fuzheng Injection* (evidence type C), *Zhengyuan Capsule*, and *Compound Ejiao Syrup* can relieve cancer-caused deficient fatigue.

Moxibustion: Shenque (RN 8), Guanyuan (RN 4), Qihai (RN 6), and Zhongwan (RN 12) are selected as the main acupoints, and moxibustion was applied for 20 minutes at each point. (evidence type C)

Acupuncture: Baihui (DU 20), Shenmen (HT 7), Guanyuan (RN 4), Sanyinjiao (SP 6), Zusanli (ST 36), Xuehai (SP 10), and Hegu (LI 4) are selected as the main acupuncture points, and conventional acupuncture was performed combined with Ashi points according to the patient's clinical symptoms.

It can be combined with electro-acupuncture. (evidence type D)

(2) Toxic and side reactions due to targeted drugs

① Targeted drug-associated rash

Rash is the most common adverse reaction in targeted lung cancer therapy, with a 60% to 80% incidence during treatment with EGFR-TKI analogs. The most prominent manifestation is acneiform rash, also known as papular rash, which appears as red papules and/or pustules on the face, scalp, chest, back, abdomen or thighs.

According to TCM, the rash caused by targeted therapy belongs to "drug eruption" and "lung-wind acne", and its general etiology and pathogenesis are yin deficiency and blood dryness inside, and the accumulation of toxin outside. The drug pathogen invades the stria and intersitital space, fire-toxin burns the blood and nutrient-blood, so that stagnated heat of lung channel cannot be discharged, and then the rash develops on the skin; the toxin enters the interior and turns into heat, burning yin and fluid, and lead to malnutrition of skin. The application of oral and topical herbal treatment can not only relieve the rash and itching, but will not reduce the anti-tumor efficacy of molecular targeting drugs.^[40,41]

Treatment principle: resolving superficialities syndrome with pungent and cool natured drugs, nourishing yin and moisten dryness. Formula: Jingfen Siwu Decoction with addition and subtraction, composed of *Jingjie* (*Herba Schizonepetae*), *Fangfeng* (*Radix Saposhnikoviae*), *Shengdihuang* (*Radix Rehmanniae*), *Chishao* (*Radix Paeoniae Rubra*), *Danggui* (*Radix Angelicae Sinensis*), *Chuanxiong* (*Rhizoma Chuanxiong*), *Baixianpi* (*Cortex Dictamni*), *Zicao* (*Radix Arnebiae*), *Chantui* (*Periostracum Cicadae*), etc..

Variant Formula based on the differentiation:

(1) for erythematous rash, papular, blistering, skin swelling, skin lesions, or even oozing, add *Bixie* (*Rhizoma Dioscoreae Hypoglaucae*), *Kushen* (*Radix Sophorae Flavescentis*), *Xuchangqing* (*Radix et Rhizoma Cynanchi Paniculati*), *Zicao* (*Radix Arnebiae*); (2) for flushed lesions, papules,

itching, vesicles and oozing after scratching, add *Baixianpi* (*Cortex Dictamni*), *Cangzhu* (*Rhizoma Atractylodis*), *Fuling* (*Poria*); (3) if the disease has been prolonged, recurrent, with dark lesions, rough, flaky and chap skin and intolerable itching, add *Chantui* (*Periostracum Cicadae*), *Danshen* (*Radix et Rhizoma Salviae Miltiorrhizae*), *Danggui* (*Radix Angelicae Sinensis*), *Wuzhishan* (*Radix Saposhnikoviae*), *Fangfeng* (*Radix Saposhnikoviae*); ④ for numbness of limbs, add *Haifengteng* (*Caulis Piperis Kadsurae*), for numbness in the limbs, add *Haifengteng* (*Caulis Piperis Kadsurae*), *Chishao* (*Radix Paeoniae Rubra*), *Lulutong* (*Fructus Liquidambaris*), *Sanleng* (*Rhizoma Sparganii*); ⑤ for fire scorching lung-gold, dry mouth and throat, add *Maidong* (*Radix Ophiopogonis*), *Baihe* (*Bulbus Lilii*) to nourish yin and moisten the lung; (6) For obvious skin redness, swelling and heat pain, add *Jinyinhua* (*Flos Lonicerae Japonicae*), *Pugongying* (*Herba Taraxaci*).

Other treatments

External treatment: *Jinyinhua* (*Flos Lonicerae Japonicae*), *Pugongying* (*Herba Taraxaci*), *Difuzi* (*Fructus Kochiae*), *Guanhuangbai* (*Cortex Phellodendri Amurensis*) (*Herba Violae*), *Baixianpi* (*Cortex Dictamni*), *Bingpian* (*Borneolum Syntheticum*) and other herbs or "Zhiyang Pingfu Lotion [composed of *Huangqin* (*Radix Scutellariae*), *Radix Scutellariae*], *Kushen* (*Radix Sophorae Flavescentis*), *Baixianpi* (*Cortex Dictamni*), *Machixian* (*Herba Portulacae*), etc.] can be applied externally to the rash twice daily.

Dietetic therapy: dietetic therapy is used according to the clinical manifestations of patients as a supplement. For papules or pustules, *Shengdi Oujie Lvdou* Soup [*Shengdi* (*Radix Rehmanniae*) *Oujie* (*Nodus Nelumbinis Rhizomatis*) (*Shengdihuang* (*Radix Rehmanniae*) 30 g, *Oujie* (*Nodus Nelumbinis Rhizomatis*) 300 g, *Lvdou* (*Semen Phaseoli Radiati*) 100 g, appropriate amount of honey] can be given to clear heat and cool blood, nourish yin and generate fluid; for rash with redness, swelling, heat and pain or ulceration and oozing all over the body, *Wushe Yimi* Soup [*Wushaoshegan* (*Zaocys*) 20 g, *Yiyiren* (*Semen Coix*) 50 g, *Pork Back Bones* 300 g] to clear heat and detoxify toxins, nourish yin and

dispel dampness; for skin rashes, pustules with dry mouth and yellow urine, *Yinhua Maogen Zhuzhe* Drink [*Jinyinhua* (*Flos Lonicerae Japonicae*) 30 g, *Xianbaimaogen* (*Rhizoma Imperatae Recens*) 200 g, *Chinese Sugar Cane* 400 g] to clear heat and removing toxicity substance, ventilating lung qi and inducing diuresis.

②Diarrhea due to targeted drugs

Diarrhea is one of the common adverse reactions of targeted drug therapy for lung cancer, which mainly manifests as increased frequency of bowel movements, thin stools with increased water content, and is often accompanied by fever, weakness and dehydration. This disease belongs to the category of "diarrhea" in TCM, and the general pathogenesis are the deficiency of spleen and stomach and the blockage of dampness and turbidity. The spleen belongs to yang-earth in five elements, which likes dryness and hates dampness. If spleen is deficient and unable to transform and transport water, then dampness will be generated internally; when dampness traps spleen, diarrhea will be caused.

Treatment principle: Regulating qi, resolving dampness, warming spleen and relieving diarrhea. Formula: Modified *Huoxiang Zhengqi* Powder plus *Pingwei* Powder *Huoxiang* (*Herba Agastachis*), *Dafupi* (*Pericarpium Arecae*), *Fabanxia* (*Rhizoma Pinelliae Praeparatum*), *Baizhi* (*Radix Angelicae Dahuricae*), *Zisuye* (*Folium Perillae*), *Fuling* (*Poria*), *Cangzhu* (*Rhizoma Atractylodis*), *Houpo* (*Cortex Magnoliae Officinalis*), *Chenpi* (*Pericarpium Citri Reticulatae*), *Zhigancao* (*Radix et Rhizoma Glycyrrhizae Praeparata cum Melle*), etc.. Variant formula: ① For those with mental fatigue and weakness, abdominal distension and poor appetite, panting and laziness to speak and pale white tongue fur, add *Dangshen* (*Radix Codonopsis*), *Baibian dou* (*Semen Lablab Album*), *Lianzi* (*Semen Nelumbinis*), *Renshen* (*Radix et Rhizoma Ginseng*), *Shanyao* (*Rhizoma Dioscoreae*), *Yiyiren* (*Semen Coix*), etc.; ② for food stagnation injuring stomach, foul belching and acid regurgitation, sour and foul-smelling excretion, thick and greasy tongue fur, slippery or deep pulse, add *Shanzha* (*Fructus Crataegi*), *Sharen* (*Fructus Amomi*), *Jineijin* (*Endothelium*

Corneum Gigeriae Galli), etc.; ③ for those with liver qi stagnation, belching and acid regurgitation, and frequent sighing, add *Chaihu* (*Radix Bupleuri*), *Yujin* (*Radix Curcumae*), *Chuanlianzi* (*Fructus Toosendan*), etc.; ④ for kidney yang deficiency, with symptoms of mental fatigue and weakness, cold pain in the back, chronic diarrhea, pale and enlarged tongue with white fur, and deep, weak and slow pulse, add *Sishen Pill* [*Roudoukou* (*Semen Myristicae*), *Buguzhi* (*Fructus Psoraleae*), *Maidong* (*Fructus Schisandrae Chinensis*), *Wuzhuyu* (*Fructus Evodiae*)], etc.; ⑤ For prolonged diarrhea and rectal prolapse, add *Huangqi* (*Radix Astragali*), *Shengma* (*Rhizoma Cimicifugae*), *Ganjiang* (*Rhizoma Zingiberis*), etc.; ⑥ for heat due to depression, with symptoms of irritability, panting, vomiting, bitterness in the mouth, red tongue with yellow fur, and stringy pulse, add *Huanglian* (*Rhizoma Coptidis*), *Zhizi* (*Fructus Gardeniae*), etc..

Other treatments

Local application of medicinals on acupuncture points: make *Dingxiang* (*Flos Caryophylli*), *Shengbanxia* (*Rhizoma Pinelliae*), *Wuzhuyu* (*Fructus Evodiae*), *Paofupian* (*Radix Aconiti Lateralis Praeparata*), *Rougui* (*Cortex Cinnamomi*) into powder and mix with ginger juice to make a paste. The paste can be applied to *Zhongwan* (RN 12), *Neiguan* (PC 6) and *Shenque* (RN 8) for 3-5 days, 6 hours a day.

Ginger moxibustion: place a 3-4mm fresh ginger slice on the *Shenque* (RN 8) and pierce several small holes in it, light the moxa column on the ginger slices once a day for 3 days.

③ Oral mucositis due to targeted drugs

Oral mucositis is one of the common adverse reactions of targeted drugs, which is characterized by ulceration of oral mucosa and localized severe pain, usually in the soft palate, tongue, gingiva, floor of mouth, buccal mucosa, and even pharynx. This disease belongs to "mouth sores" in TCM, and its main pathogenesis include the accumulation of heat in the heart and spleen and the deficiency of yin and fire. The mouth is the organ of the spleen and the tongue is the seedling of the heart. Due to accumulation of heat in heart and spleen, deficiency

of kidney yin and lack of control of ministerial fire, fire-heat inflames mouth and tongue, resulting in oral mucositis.

Treatment principle: nourishing yin and clearing heat, clearing heart-heat and discharging fire. Formula: Modified Qingwei Powder: *Shengdi* (*Radix Rehmanniae*) *Huang*, *Danggui* (*Radix Angelicae Sinensis*), *Mudanpi* (*Cortex Moutan*), *Huanglian* (*Rhizoma Coptidis*), *Dengxincao* (*Medulla Junci*), *Sangye* (*Folium Mori*), *Shengma* (*Rhizoma Cimicifugae*). Variant formula: ① For excessive heat injuring yin, add *Zhimu* (*Rhizoma Anemarrhenae*), *Huangbai* (*Cortex Phellodendri Chinensis*), *Xuanshen* (*Radix Scrophulariae*), *Tianhuafen* (*Radix Trichosanthis*), *Pugongying* (*Herba Taraxaci*), *Lianqiao* (*Fructus Forsythiae*); for constipation, add *Dahuang* (*Radix et Rhizoma Rhei*), *Mangxiao* (*Natrii Sulfas*), *Xuanshen* (*Radix Scrophulariae*); for dysphoria and insomnia, add *Zhizi* (*Fructus Gardeniae*), *Zhuye* (*Folium Phyllostachydis Henonis*), *Maidong* (*Radix Ophiopogonis*); for feverishness in palms and soles, insomnia and dreaminess, night sweats, red tongue with little fur, and possible fissured tongue, add *Biejia* (*Carapax Trionycis*), *Guiban* (*Plastrum Testudinis*), *Beishashen* (*Radix Glehniae*); if the pain in the oral mucosa is not obvious, with a pale color and prolonged recovery period, accompanied by lethargy and weakness, pale complexion, soreness and cold of waist and knees, loose stools and clear and long urine, remove *Huanglian* (*Rhizoma Coptidis*), *Dengxincao* (*Medulla Junci*), *Sangye* (*Folium Mori*) from the formula, and add *Huangqi* (*Radix Astragali*), *Dangshen* (*Radix Codonopsis*), *Baizhu* (*Rhizoma Atractylodis Macrocephalae*), *Fuling* (*Poria*), *Ganjiang* (*Rhizoma Zingiberis*), *Shufuzhi* (*Radix Aconiti Lateralis Praeparata*).

Other treatments

① Chinese herbal medicine gargle method: *Daqingye* (*Folium Isatidis*) 15 g, *Xuanshen* (*Radix Scrophulariae*) 15 g, *Gancao* (*Radix et Rhizoma Glycyrrhizae*) 5 g, decocted into 500 mL gargle solution, use it 3 times a day.

② Life care: Patients with oral mucositis during the medication period should actively prevent and

care for oral mucositis in daily life, such as paying attention to oral hygiene, brushing teeth in the morning and evening, and rinsing the mouth after meals; avoid eating hard objects to prevent damage to the oral mucosa; for those who wear a denture, they should avoid the mechanical stimulation of the denture from injuring the mucosa. For patients who have developed mouth ulcers, they should pay more attention to their diet, such as avoiding spicy and pungent food, rich meals, and avoiding cold and raw food for those with deficient fire. Do not overwork and avoid straining or staying up late, in case damaging vital qi.

(3) Toxic and side reactions due to radiotherapy

① Radiation pneumonia

In modern Chinese medicine, radiation therapy is defined as the pathogen of "heat-toxicity". The pathogen of heat-toxicity attacks lung directly, burning lung yin and causing abnormal moistening, resulting in impaired diffusion and downbearing of lung, obstruction of qi flow and abnormal distribution of fluids. Together they cause cough, fever, oppression in chest, shortness of breath, and other symptoms. The main treatment for radiation pneumonia in TCM is to nourish yin, clear heat and remove toxicity.

Treatment principle: Benefiting qi and nourish Yin, clear heat and remove toxicity. Formula: Modified Qingfei Jiuzao Decoction: *Sangye* (*Folium Mori*), *Shigao* (*Gypsum Fibrosum*), *Gancao* (*Radix et Rhizoma Glycyrrhizae*), *Humaren* (*Fructus Cannabis*), *Ejiao* (*Colla Corii Asini*), *Pipaye* (*Folium Eriobotryae*), *Renshen* (*Radix et Rhizoma Ginseng*), *Maimendong* (*Succus Ophiopogonis*), *Xingren* (*Semen Armeniacae Amarum*).

Variant formula: ① for obvious cough, add *Zhebeimu* (*Bulbus Fritillariae Thunbergii*), *Juhong* (*Exocarpium Citri Rubrum*), *Jiegeng* (*Radix Platycodonis*), etc.; ② for coughing yellow thick phlegm with chest pain, add *Gualou* (*Fructus Trichosanthis*), *Jiegeng* (*Radix Platycodonis*), *Zhimu* (*Rhizoma Anemarrhenae*), etc.; ③ for tidal fever in the afternoon, add *Yinchaihu* (*Radix Stellariae*), *Qinghao* (*Herba Artemisiae Annuae*), *Biejia* (*Carapax Trionycis*), etc..

Other treatments

TCM directional permeation therapeutic instrument: the herbal tablet [*Beishashen (Radix Glehniae)*, *Maidong (Radix Ophiopogonis)*, *Xuanshen (Radix Scrophulariae)*, *Baihe (Bulbus Lilii)*, *Jinyinhua (Flos Lonicerae Japonicae)*, *Shengdihuang (Radix Rehmanniae)*, *Zhigancao (Radix et Rhizoma Glycyrrhizae Praeparata cum Melle)*, etc.] is attached to 2 electrode plates, and the patient is placed in a sitting or prone position. The electrodes were attached to the left and right Feishu (BL 13) acupoints, the required parameters were adjusted according to the patient's tolerance level, and the treatment was started by turning on the power. After the treatment, the tablet is fixed on the acupuncture points for 2-4 h to ensure that the drug was fully absorbed through the skin. 1 time/day, 30 min/time, 7 days as a course of treatment, 3-4 courses of treatment in total.

② Oral mucositis due to radiotherapy

For details, please refer to the chapter of "oral mucositis due to targeted drugs". Apart from that, radiotherapy is heat-toxicity in TCM, so attention should be paid to nourishing yin and clearing heat, discharging fire and removing toxicity when making syndrome differentiation.

③ Myelosuppression due to radiotherapy

For details, please refer to the chapter on "bone marrow suppression due to chemotherapy". Radiotherapy can consume qi and injure yin, so attention should be paid to nourishing liver and kidney, protecting yin fluid, nourishing yin and clearing heat when making syndrome differentiation.

6 Integrated Chinese and Western Medical Aftercare of Lung Cancer

6.1 Life care

(1) Quit smoking: Smoking is the main risk factor of lung cancer and 85% of lung cancer deaths can be attributed to smoking. Active smoking and passive smoking can both increase the risk of lung cancer.

(2) Weight control: Nutrition and exercise guidelines for oncology patients recommend that oncology patients maintain a healthy weight and

maintain a BMI of 18.5 to 25 kg/m².

(3) Respiratory function exercise: Respiratory function exercise is an effective method to improve the lung function of lung cancer patients as well as to increase the tolerance of comprehensive treatment. Through systematic respiratory function exercise, the respiratory muscle groups can be stimulated, muscle strength can be gradually strengthened, lung compliance can be increased, and effective ventilation can be guaranteed.

(4) Improve environmental hygiene: Maintain the relative humidity of the room in which you live to reduce the interference of dry air with the patient's respiratory tract, and also keep the air clean to avoid the stimulation of smoke and raised dust. Patients with dry cough or little phlegm can inhale by steam or spray to moisten the airway and reduce stimulation. Excessive phlegm that cannot be easily excreted should be dissolved or aspirated by routine nebulization, turning, back patting and aspiration to keep the airway open.

(5) Traditional health care qigong: Baduanjin, Taijiquan, etc. can dredge the meridians, improve qi and blood, relieve anxiety, strengthen the body and accelerate the recovery of patients' zang-fu organs.

(6) Five elements music therapy: five elements music as a characteristic Chinese medicine care method, emphasizing the interrelationship between the five organs, five elements and five musical tuning characteristics. It can influence the qi of the body through different tunes and acoustic vibrations, coordinate qi and blood and maintain the stable function of zang-fu organs. Therefore, patients may maintain a calm and peaceful state of mind, relax the spirit, cultivate the emotions, relieve cancer-caused fatigue, so as to calm the heart and nourish the body.

6.2 Diet care

Patients with lung cancer should take balanced diet and regular physical activities. The diet should be nutritious and varied, mainly plant food like vegetables and fruits. Pay attention to dietetic hygiene. Take more protein and avoid high-fat,

low vitamin and low-fiber meals, and excessively smoked or fried foods. More intake of fruits and vegetables is beneficial to the prognosis of lung cancer patients. Cruciferous vegetables like Chinese cabbage, white radish, and cabbage can help improve lung cancer-related survival rates. Patients in the treatment phase and early recovery phase eat smaller and more frequent meals and choose foods that are easy to swallow. Patients who have lost weight may take high-energy nutritional supplement preparations. Nutritional preparations supplemented with specific micronutrients or minerals may be an option when the ingested diet does not meet the nutritional needs of the patient.

TCM dietetic therapy is based on the theory of zang-fu organs and meridians as well as the theory of the four nature and five flavors of drugs and food, and emphasizes the differentiation of food according to the individual and the evidence. It is important to avoid misusing the so-called "health care" or "cancer prevention" products. Proper dietetic therapy can not only ensure sufficient nutrition for tumor patients, but also adjust the balance of yin and yang and improve the physical condition of patients, and therefore, relieve symptoms and improve survival quality. Dietetic therapy should be applied according to the stage and syndrome differentiation of lung cancer: for example, during lung cancer radiotherapy, patients are susceptible to heat-toxin injuring yin, so foods with the effect of clearing heat and promoting fluid production, cooling blood and removing toxicity can be used, such as ginkgo seed and olive sugar water, Chinese water chestnut and lotus sugar drink, etc.; postoperative patients, whose primordial qi is damaged, mostly manifest as fatigue, weakness of limbs, unquiet sleep and anorexia, so foods with the effect of nourishing blood and tonifying qi can be used; Lung cancer patients receiving chemotherapy mainly manifest clinically as the toxic and side reactions of digestive system, such as loss of appetite, nausea and vomiting, oppression in chest and pain in stomach, stagnant stools, etc.. The pork tripe stewed with villous amomum fruit and porridge of ginkgo seed and Chinese yam are recommended to increase appetite and enliven spleen. For patients receiving bone marrow suppression treatment with symptoms like anemia or significantly decreased

white blood cells, fatigue and other symptoms, it is recommended to supplement the kidneys and marrow by taking water boiled duck stewed with plantworms, lean meat porridge boiled with wolfberry and sea cucumber, etc. For patients with phlegm-damp who mostly manifest as obesity, fatness and fullness in abdomen, oppression in chest, phlegm, fatigue and heavy body, it is recommended to invigorate the spleen and diffuse dampness and harmonize the stomach and resolve food stagnation by taking porridge of lotus fruit and Chinese yam and fish soup stewed with longan and coix seed.

6.3 Psychological counselling

Tumor patients are prone to pessimism, despair, fear, anger, fantasy, selfishness, anxiety, loneliness, denial and other psychological problems. These are related to the concept of "emotion" in TCM. In treating tumor patients, medical and nursing staff should carry out emotional and spiritual care according to the "seven emotions" theory of TCM to the specific conditions of patients, including using emotion to overcome emotion, language influence, psychological guidance, and diversion of attention.

7 Prospect

A Pilot Project of Chinese and Western Medicine Clinical Collaboration for Major Difficult Diseases-Integrated Chinese and Western Medicine Treatment for Lung Cancer shows the exploration and practice of integrated Chinese and Western medicine treatment of lung cancer in China, and to a certain extent represents the latest achievements of integrated Chinese and Western medicine treatment of lung cancer. However, lung cancer, as the cancer with the highest mortality rate, has witnessed rapid research development in recent years due to the large amount of human, material and financial resources invested in research both at home and abroad, including the pathogenesis new drug development and drug resistance mechanism. Lung cancer is becoming more of a "chronic disease" than an "incurable disease". Evidence shows that the 5-year survival rate of EGFR-positive patients with advanced non-small cell lung cancer is now more than 30%, and the 5-year survival rate of patients with negative driver genes and high PD-L1 expression is also more than 30%. Moreover,

continuously incorporation the latest research results is required to refine and improve this consensus.

At the same time, the rapidly changing status of lung cancer research also poses a challenge on how to integrate Chinese and Western medicine in the current situation. For example, the TCM pathogenesis of lung cancer involves various factors such as qi stagnation, blood stasis, phlegm coagulation, and toxin aggregation, which affect the function of internal organs. It is consistent with the modern medical concept that tumor is a systemic disease, but the correlation and regularity between the TCM pathogenesis and modern medicine need further scientific interpretation; also, there is a shortage of objectification, quantification, and standardization in the TCM syndrome differentiation of lung cancer; and the correlation between the syndrome differentiation of lung cancer in TCM and the imaging, pathology and staging techniques of modern medicine still needs a lot of research work to identify from clinical and diagnostic aspects with the help of modern technology and methods; meanwhile, more evidence-based medical research are required to support the integrated Chinese and Western medicine treatment standard for lung cancer. With the integration of various concepts of Chinese and Western medicine and the continuous development of methods and treatments, improving survival while taking into account safety and quality of life becomes the common goal of Chinese medicine and Western medicine in treating lung cancer. TCM needs to give full play to the advantages of its individualized treatment and effectiveness with low toxicity, lay equal emphasis on evidence-based medical researches and treatment with syndrome differentiation, and complement and learn from modern medicine, so as to form a more comprehensive and better integrated Chinese and Western medical treatment plan.

A Pilot Project of Chinese and Western Medicine Clinical Collaboration for Major Difficult Diseases-Integrated Chinese and Western Medicine Treatment for Lung Cancer is compiled under the joint efforts of Chinese and Western medicine oncologists in their clinical practice over the past 3 years. We'll appreciate it if both TCM and Western

medicine practitioners can study this consensus and give their valuable opinions. We believe that this consensus will contribute to the cause of integrating Chinese and Western medicine in China for the benefit of lung cancer patients.

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