

CHAPTER 6: TREATMENT FOR SMALL CELL LUNG CANCER

INTRODUCTION

This chapter provides an overview of treatment for small cell lung cancer (SCLC). Treatment options are presented based on the extent of disease. As you read this chapter, keep in mind that each person's treatment plan is unique to his or her situation. This chapter provides information to help you discuss your treatment options with your cancer care team. However, it will not provide you with treatment recommendations. Many factors unique to your situation must be taken into account to make these crucial decisions. Only your cancer care team can make treatment recommendations.

Ongoing clinical trials are evaluating how best to treat SCLC. This chapter presents current treatment standards at the time of its writing. However, state of the art lung cancer care is constantly evolving. Ask your cancer team about new treatment options and clinical trials you may want to consider. You may want to seek the advice of more than one expert before deciding on a treatment plan.

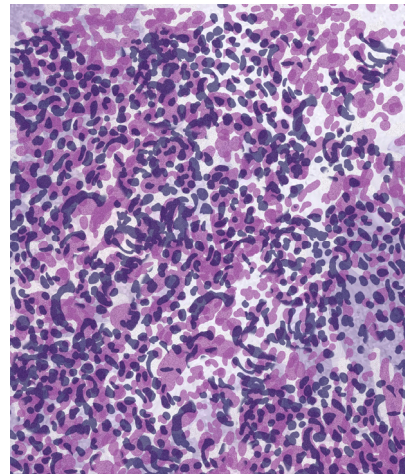
Chemotherapy and radiation treatments are the mainstays of treatment for SCLC. A *medical oncologist* is an expert in the chemotherapeutic treatment of cancer. A *radiation oncologist* is the professional to consult about *radiotherapy*. In special circumstances, surgery may be used to treat SCLC. If surgery is a possibility for you, consult with a *thoracic surgeon*, a surgeon who specializes in chest surgery.

Your cancer care team will provide you with information about your treatment options, but all treatment decisions are ultimately up to you. No one is more qualified than you are to make decisions about what treatments best suit your goals and preferences. Seek information and expert advice, and then decide what is best for you.

OVERVIEW OF SMALL CELL LUNG CANCER

Lung cancer arises from abnormal *epithelial cells* in the airways of the lungs. Epithelial *cells* cover all free surfaces in the body including the airways. Lung cancer is divided into two main types based on how it looks under the microscope: small cell lung cancer and non-small cell lung cancer (NSCLC). As the name implies, the cancerous epithelial cells of SCLC are abnormally small. This appearance led to the term *oat cell carcinoma* to describe SCLC because the cells resemble oat grains (see Figure 1). SCLC is sometimes called small cell undifferentiated carcinoma. In the United States, approximately 20% of lung cancers are SCLC.

SCLC and NSCLC differ in the sites of their genetic damage and their patterns of growth and spread. SCLC typically grows more quickly than NSCLC does. SCLC generally spreads to *lymph nodes* and *metastasizes* earlier in the course of the disease than does NSCLC. Overall, SCLC is initially much more responsive to chemotherapy and radiotherapy than NSCLC is.



*Figure 1: Microscopic View of Small Cell Lung Cancer**

Characteristic features of SCLC include:

- There is a strong relationship between SCLC and tobacco smoking. Only about 1% of SCLC occurs in people who have never smoked.
- SCLC often occurs in one of the larger airways. Therefore, SCLC tumors are often located near the center of the lung.
- Most people with SCLC have metastases or spread of the disease beyond the original tumor at the time of diagnosis.
- Combined small cell carcinoma is a variant of SCLC.

See *Chapter 3: Lung Cancer Overview* for additional information about lung cancer development, growth, and spread.

BEFORE TREATMENT

SCLC Staging

Accurate staging of SCLC is critical because treatment options depend on the extent of your disease. Most health care providers categorize SCLC as either limited or extensive based on a system created by the Veterans Administration Lung Cancer Study Group. SCLC is staged according to the spread of disease in the chest. People whose disease is confined to one lung, the *mediastinum*, and/or the *regional lymph nodes* have limited stage SCLC. Limited stage disease can be treated in a single radiotherapy field. Approximately 30% of people with SCLC have limited stage disease at diagnosis. Limited stage SCLC corresponds to stages I through IIIB of the TNM staging system. See *Chapter 4: Lung Cancer Diagnosis and Staging* for information about the TNM staging system.

Extensive stage SCLC has spread to the *contralateral* lung (the lung opposite the one with the original tumor), is associated with a malignant *pleural effusion*, and/or is accompanied by distant metastasis. Approximately 70% of people with SCLC have extensive stage disease at the time of diagnosis. Extensive stage SCLC corresponds to stage IIIB with pleural effusion, and stage IV of the TNM staging system.

Staging must be accomplished before treatment options can be considered. The National Comprehensive Cancer Network (NCCN) has published practice guidelines for the treatment of SCLC.¹ According to these guidelines, SCLC staging should include the following tests and activities:

- medical history and complete physical examination
- chest x-ray
- *CT scan* of the chest, liver, and adrenal glands
- *MRI* or *CT scan* of the head (brain)
- *bone scan*
- blood tests including a complete blood count (CBC), platelet count, liver function tests, calcium, lactate dehydrogenase (LDH), blood urea nitrogen (BUN), and creatinine

Your doctor may order additional tests based on the results of these tests.

Positron emission tomography (PET) scanning is being studied as a staging tool for people with SCLC. Results from early studies indicate PET scans may be useful for detecting unsuspected metastasis.^{2,3} While results from early studies are promising, PET scans are not currently recommended for routine SCLC staging.⁴

Long-term survival is more likely for people with limited stage SCLC than for people with extensive disease. Median survival time among people treated for limited SCLC is 16-24 months.⁵⁻⁷ Five-year survival is approximately 10-20%.⁸⁻¹⁰ Median survival among people treated for extensive SCLC is 6-12 months. Long-term survival with extensive SCLC is uncommon. However, no one can predict your personal chance of survival. There are always people who beat the odds; you may be one of them. While the statistics for SCLC are rather discouraging, remember, there are survivors!

Treatment Preparations

Researchers have found a person's *performance status* affects his or her SCLC *prognosis*.⁹ Performance status is a measure of how well a person is able to perform ordinary tasks and carry out daily activities. As you prepare for treatment, you may want to assess your lifestyle and health habits. Does your lifestyle enhance your overall health?

If you are a smoker, it would be best to stop smoking. Some people believe that once they have been diagnosed with lung cancer, it does not matter if they continue to smoke. This is not true. Studies have shown that people with limited SCLC who continue to smoke have a less favorable prognosis than those who stop smoking.¹¹ Although surgery is an option for only a small percentage of people with SCLC, thoracic surgeons strongly encourage people to stop smoking before surgery. Smoking can worsen many of *symptoms* of lung cancer and its treatment including mouth sores, shortness of breath, and *peripheral neuropathy*.

Smoking damages your health. Stopping smoking will greatly enhance your overall health. Smoking cessation is difficult because nicotine addiction is very powerful. Talk with your cancer care providers about smoking cessation programs, nicotine replacement therapy, and use of the drug bupropion (Zyban[®]) to help you successfully stop smoking.

Lung cancer treatment is hard on the body. You need to take in enough calories to meet the energy demands treatment places on your body. If you are losing weight or are having problems with your appetite, you may want to talk with a nutritionist or dietician before beginning treatment. He or she can advise you about the number of calories you need and give you tips to ensure you are getting adequate nutrition.

Exercise is an important factor in your overall health. Continue your current program if you already exercise regularly. You may need to modify your routine if the energy demands of treatment cause *fatigue*. If you are not currently exercising, talk with your health care providers about beginning a gentle exercise program. All forms of exercise are helpful and there are many choices. Anything that gets you up and moving is exercise including walking, biking, gardening, golfing, dancing, yoga, swimming, and many other activities. Be sure to discuss your exercise program with your health care providers to ensure it is safe for you.

Urgent dental work should be done before beginning treatment. Mouth sores and problems with the teeth are common side effects of chemotherapy and some forms of radiotherapy. Healthy gums and teeth help prevent or reduce the severity of these problems.

When To Begin Treatment

Lung cancer grows for many years it is large enough to be detected. Once you have been diagnosed, you may be anxious to begin treatment right away. However, unless your doctor tells you otherwise, you may benefit from taking a few days to organize your thoughts and make plans before starting treatment. You may want to use the time to arrange time off from your job, plan for household help, or collect information about your disease. Planning can help reduce your stress, which can make it easier to cope with the challenges of treatment. You may want some quiet time with loved ones and friends to gather your physical and emotional strength before treatment begins.

While taking a few days before beginning treatment will not affect your prognosis, lengthy treatment delays should be avoided. A long delay could give your cancer time to grow and/or spread.

I did a lot of research [before beginning treatment]. Mind you, this was before the Internet, so it took some effort. I also got a second opinion. Even though I had confidence in my doctor, I needed that extra verification. Once I got a second opinion and it concurred with my doctor, I felt secure. I was comfortable when I started treatment because I researched my treatment options and got a second opinion. Doing this it put me in control of the situation. I did not feel like a victim.
– Elaine, diagnosed with limited stage SCLC in 1989 at age 58

Talk with your cancer care providers about any symptoms you are experiencing. Initiating treatment of disease-related symptoms before therapy begins can make cancer treatments easier to tolerate. *Supportive care* treatments can begin while you and your cancer care team are developing your treatment strategy.

It is up to you what treatments you want to receive. Discuss the purpose, potential side effects, and expected results of each treatment option with your cancer care team. Use your cancer care providers as consultants to aid you in making decisions. Alternatively, you may decide to give your primary cancer doctor permission to choose the treatment he or she believes to be the best option for you. This is as valid a decision as any other you might make. You are the most qualified person to decide how you want to manage your cancer care.

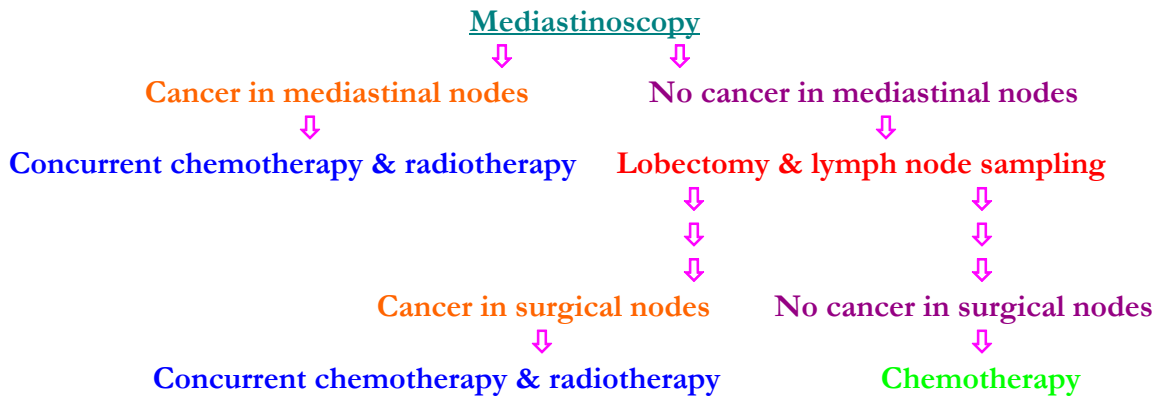
LIMITED STAGE SMALL CELL LUNG CANCER TREATMENT

Single SCLC Tumor Without Evidence of Spread

Most experts recommend a *mediastinoscopy* for people with limited stage SCLC who have a single tumor and no evidence of spread on their initial *staging* workup. A mediastinoscopy is a surgical procedure in which a rigid instrument called an *endoscope* is inserted through a small incision at the base of the neck or near the breastbone into the central area of chest called the mediastinum. The mediastinum contains the heart and the large blood vessels entering and leaving it, the *trachea*, the *esophagus*, and the *mediastinal lymph nodes*. A mediastinoscopy is performed to examine the mediastinal structures and take tissue samples from local lymph nodes. Lymph node samples are examined under a microscope to determine if there are lung cancer cells present. Mediastinoscopy is performed under general anesthesia and usually requires an overnight hospital stay.

If there is no evidence of cancer in the mediastinal lymph nodes, surgery is usually performed to remove the lobe of the lung containing the tumor. This procedure is called a *lobectomy*. Area lymph nodes are sampled during surgery. Tissue samples are sent to the laboratory to check for cancer cells.

Figure 2: Treatment for Single SCLC Tumor Without Evidence of Spread



After recovery from surgery, chemotherapy is given to people whose surgical lymph node samples show no evidence of cancer. Chemotherapy is given to eliminate undetected cancer cells that may still be present in the body. If cancer cells are detected in the surgical lymph node samples, chemotherapy is given along with radiotherapy to the mediastinum. This combined approach is called *concurrent* treatment, meaning both treatments are given at the same time. Radiotherapy is added to boost the chances of controlling cancer cells that may be present in the remaining mediastinal lymph nodes.

Limited SCLC Beyond The Original Lung Tumor

Your overall health is a factor in choosing the best treatment if you have limited stage SCLC that has spread beyond the original lung tumor. Oncologists use very specific criteria to assess your overall health and performance status. The ECOG and Karnofsky scales are commonly used to gauge performance status (see Tables 1 and 2).

Table 1: ECOG Performance Status Scale¹²

Grade	ECOG Performance Status
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair

Table 2: Karnofsky Performance Status Scale*

Descriptor	Score
Normal health	100%
Minor symptoms	90%
Normal activity with some effort	80%
Unable to carry on normal activity but able to care for oneself	70%
Requires occasional help with personal needs	60%
Disabled	50%
Requires considerable assistance and medical care	40%
Severely disabled, in hospital	30%
Very sick, active support needed	20%
Moribund	10%

*originally developed by Drs. David Karnofsky and Joseph Burchenal

Most experts recommend concurrent chemotherapy and radiotherapy for people with good performance status who do not have underlying lung disease. Investigators have found the addition of early radiotherapy to chemotherapy improves survival with limited SCLC. The decision whether to include radiotherapy along with chemotherapy for people whose performance status is compromised by other illnesses is made on a case-by-case basis.

EXTENSIVE STAGE SMALL CELL LUNG CANCER TREATMENT

Chemotherapy is the primary form of treatment for extensive stage SCLC. SCLC is usually very responsive to *first line* chemotherapy. Lung cancer management guidelines compiled by the American College of Chest Physicians recommend a platinum-based chemotherapy

regimen for people with extensive SCLC.⁴ This involves use of either cisplatin or carboplatin (platinum containing chemotherapy drugs) plus one or more additional chemotherapy agents.

Radiation therapy is often used to control metastatic disease symptoms. Areas commonly treated include bone lesions and the brain. See *Chapter 5: Lung Cancer Treatment Overview* for information about radiation treatments for brain metastasis.

CHEMOTHERAPY OPTIONS FOR SMALL CELL LUNG CANCER

Chemotherapy is the cornerstone of treatment for SCLC. SCLC is typically very responsive to first line chemotherapy. Reported response rates range from 80-100% for limited disease and 60-89% for extensive disease.¹³ Many chemotherapy agents are active against SCLC (see Table 3). Chemotherapy for SCLC is usually combination therapy, meaning two or more drugs are used. This approach has proven more effective than single drug therapy for SCLC.¹⁴⁻¹⁶ Four to six cycles of treatment are typically administered.

Table 3: Chemotherapy Drugs Active Against Small Cell Lung Cancer^{1,17}

Generic Name	Trade Name
— Established Agents —	
carboplatin	Paraplatin [®]
cisplatin	Platinol [®]
cyclophosphamide	Cytoxan [®] , Neosar [®]
doxorubicin	Adriamycin [®]
etoposide	VePesid [®] , Etopophos [®] , Toposar [®]
ifosfamide	Ifex [®]
methotrexate	Amethopterin [®] , Folex [®] , Mexate [®] , MTX
teniposide	Vumon [®]
vincristine	Oncovin [®] , Vincasar PFS [®] , Vincrex [®]
— Newer Agents —	
docetaxel	Taxotere [®]
gemcitabine	Gemzar [®]
irinotecan	Camptosar [®]
paclitaxel	Taxol [®]
topotecan	Hycamtin [®]
vinorelbine	Navelbine [®]

There is no single chemotherapy combination or *protocol* recommended for all people with SCLC. Several active chemotherapy combinations are in use. The choice of chemotherapy drugs used is individualized according to each person's unique needs and circumstances. Drug choices are influenced by your overall health and other illnesses or conditions you may have. Examples of commonly used SCLC chemotherapy combinations are reviewed in this section. Keep in mind, there are many other regimens that are both active and appropriate in specific circumstances.

Etoposide + Cisplatin

This is the most common chemotherapy regimen used for SCLC. The National Comprehensive Cancer Network practice guidelines for the treatment of SCLC name this regimen as the treatment of choice to be used concurrently with radiotherapy for the treatment of limited stage SCLC.¹ This regimen is also frequently used in people with extensive stage disease.

Etoposide + Carboplatin

The substitution of carboplatin for cisplatin is sometimes made to reduce the risks of nausea, vomiting, and peripheral neuropathy. However, this substitution has been associated with increased risk of *myelosuppression* (*anemia*, low white blood cells, and low platelets).¹⁸

Cisplatin + Doxorubicin or Epirubicin + Ifosfamide or Cyclophosphamide

The National Comprehensive Cancer Network treatment guidelines state these combinations may provide a slight survival advantage for people with extensive stage disease based on the results of a few clinical trials. However, there may also be increased toxicity making the trade-off a matter for careful consideration.¹⁹⁻²¹

Cyclophosphamide + Doxorubicin + Vincristine

The use of this chemotherapy combination is well established for SCLC. It can be used alone or concurrently with radiotherapy.

Many ongoing clinical trials are examining the effectiveness of different chemotherapy combinations using newer chemotherapy agents (see Table 4).

Table 4: Chemotherapy Combinations Being Studied for Small Cell Lung Cancer⁴

Platinum Based Regimens
cisplatin-docetaxel (Platinol [®] /Taxotere [®])
cisplatin-irinotecan (Platinol [®] /Camptosar [®])
cisplatin-paclitaxel (Platinol [®] /Taxol [®])
cisplatin-paclitaxel-topotecan (Platinol [®] /Taxol [®] /Hycamtin [®])
cisplatin-etoposide-carboplatin (Platinol [®] /Toposar [®] /Paraplatin [®])
cisplatin-vinblastine-mitomycin C (Platinol [®] /Velban [®] /Mitomycin C)
carboplatin-paclitaxel (Paraplatin [®] /Taxol [®])
Non-Platinum Based Regimens
etoposide-irinotecan (Toposar [®] /Camptosar [®])
etoposide-paclitaxel-epirubicin (Toposar [®] /Taxol [®] /epirubicin)
paclitaxel-doxorubicin (Taxol [®] /Adriamycin [®])
paclitaxel-topotecan (Taxol [®] / Hycamtin [®])

Use the examples of chemotherapy regimens presented here as talking points for your treatment discussions with your oncologist. However, do not consider the above examples as your only options, or even as the preferable options. There is no single chemotherapy regimen that is effective for every person with SCLC. The best chemotherapy choice must take into account many factors specific to you. An oncologist who has all your medical information and test results can discuss the potential advantages and disadvantages of various chemotherapy regimens in terms of your unique situation.

I am a nurse by trade, so as soon as I found out I had lung cancer I was pulling strings, researching, and talking to anyone who could provide information. I do have to say that being a nurse can be a double-edged sword. All the clinical information I received became overwhelming. I just had to sift through the information and only take what I needed. When I think back on how I felt at that time, all I can say is that it was complicated. I was very focused on getting the information – fast – and setting up another appointment with my doctor as soon as possible to start treatment. To be honest, during that initial diagnosis stage, it never occurred to me that the treatments might not work. I just had to go through chemo and radiation and that was that.

– Toni, diagnosed with limited stage SCLC in 1992 at age 39

RESPONSE TO THERAPY

Evaluation During Treatment

Your doctors will initially rely on physical signs and symptoms to gauge your response to therapy. While this not always completely accurate, stable or improving signs and symptoms

are a reasonably reliable indicator that your disease is also probably stable or responding to treatment.

After three or more cycles of therapy, your doctor may order a chest x-ray or CT scan to check tumor size. Therapy will probably be continued if the tumor size is unchanged or reduced and there is no evidence of disease progression. Tumor growth or other symptoms of disease progression indicate the treatment is not active against your cancer. In this situation, treatment should be stopped. Your doctor may recommend trying another treatment regimen.

PET (positron emission tomography) scans are being investigated as a tool to determine response to treatment. PET scans detect changes in the activity of cells rather than measuring tumor size. As a result, PET scans may be capable of identifying changes in cancer cell activity earlier in the course of therapy than CT scans or x-rays. PET scanning to monitor response to therapy is being studied in clinical trials. Because of its experimental status, many insurance companies do not cover the cost of PET scans used for this purpose.

Evaluation After Completion of Treatment

Upon completion of your initial therapy, you will be thoroughly re-evaluated to check your response to treatment. The assessment of treatment response usually includes:

- chest x-ray
- CT scan of the chest, liver, and adrenal glands
- imaging tests to check areas known to have cancerous spread before treatment; the tests used depend on the site of the cancer
- blood tests including a complete blood count, liver function tests, and possibly others

People who have had a complete response to therapy (the disappearance of all signs of cancer) are candidates for prophylactic cranial irradiation or PCI. A prophylactic treatment is one used to act against or prevent a condition. PCI is a series of radiation treatments to

the brain intended to kill undetected cancer cells that may be present. PCI is often used with SCLC because:

- SCLC is known to metastasize early in the disease process.
- The brain is a common site of SCLC metastasis.
- Chemotherapy drugs used to treat SCLC do not get into the brain in high enough concentrations to kill cancer cells that may be present.
- Small areas of metastases (*micrometastasis*) may be present in the brain but are too small to be detected with imaging tests.

PCI is strongly recommended by many cancer experts for people with limited SCLC who have had a complete response to therapy. People with extensive disease who have had a complete response to initial therapy are usually also given the option of PCI. While PCI has been shown to reduce the risk of brain metastases, it is not without potentially harmful side effects. Research has shown that long-term SCLC survivors who have had PCI are at risk for impairments in their mental functions.²² The severity of these impairments is highly variable. It is important to discuss this risk with your doctor before making a decision about whether to have PCI.

RECURRENT DISEASE

Many people who partially or completely respond to initial treatment for SCLC have a relapse. In complete responders, this means the disease comes back either at the site of the original cancer or at another location. For partial responders, this means the disease begins to grow and/or spread after having been stable for a time.

The National Comprehensive Cancer Network guidelines¹ recommend the following monitoring for people who had a complete response to initial treatment:

- Visit your oncologist every two months for the first year, every three months for the second year, and every six months after that.
- At each visit, you should have a physical examination, chest x-ray, and blood tests.

A significant number of people who relapse respond to second line chemotherapy (also called *salvage therapy*). However, the response rates are not nearly as high for salvage therapy as they are for first line treatment. The choice of second line chemotherapy depends on the drugs used for first line treatment, the response to that therapy, and the time to disease progression after initial treatment.

SUMMARY

Varieties of treatments are available for SCLC. Chemotherapy is the cornerstone for the treatment of SCLC. In limited stage disease, chemotherapy and radiotherapy are often used together. Limited stage disease consisting of an isolated tumor may be treated surgically. Extensive stage disease is treated primarily with combination chemotherapy. Radiation therapy is often used to treat disease-related symptoms. Many SCLC clinical trials are available. You may want to consider participating in a clinical trial when evaluating your treatment options.

The choice of treatment will depend on the stage of your disease, your overall health, personal preferences, and other factors. No single approach can be used effectively for all cases of SCLC. Your treatment plan must be individualized to meet your specific situation, needs, and preferences.

Asking your cancer care team questions can help you better understand your treatment options and feel more comfortable with your decisions. Additional sources of information can be found in the ***Resource Directory***.