e- ISSN 0976-0342
Print ISSN 2229-7456

International Journal of Pharmacy & Therapeutics

Journal homepage: www.ijptjournal.com

Research article

NON-SMALL CELL LUNG CANCER (NSCLC)-DIAGNOSTIC AND THERAPEUTIC OPTIONS

Gnana Prasuna G*, Anupama P, Venkatesh M, Prasanna Kumar Naik B

Department of Pharmacy Practice, Saastra College of Pharmaceutical Education and Research, Varigonda, Nellore-524311, Andhra Pradesh, India

ABSTRACT

The lungs play a crucial role in sustaining life by collaborating with the heart and circulatory system to supply essential oxygen to the body. They possess a remarkable reserve capacity, working efficiently even under various conditions. Similarly, the heart and circulatory system have a reserve capacity, enabling cancerous lung tumours to grow over several years without hindering lung function. Additionally, the lungs have fewer nerves for pain transmission, allowing cancer to progress for an extended period without causing noticeable symptoms. Despite being a global health concern, lung cancer is often asymptomatic in its early stages, making it a challenging disease to detect. The prognosis for lung cancer, particularly non-small cell lung cancer (NSCLC), is generally more favourable when diagnosed early. NSCLC is considered a life-threatening condition, and early detection coupled with prompt intervention is crucial. Treatment options such as surgery, radiation therapy, and chemotherapy can significantly contribute to a positive prognosis for individuals with non-small cell lung cancer. Early diagnosis and swift initiation of appropriate therapies are paramount in improving outcomes and increasing the chances of successful treatment.

Key Words:- NSCLC, Cancer Cells, Radiotherapy, Chemotherapy, Invasive Therapies.

Access this article online	
Home page: http://ijptjournal.com/	**Quick Response code**
Received:23.12.2023 **Revised:**28.12.2023	**Accepted:**03.01.2024

Corresponding Author

G.Gnana prasuna

E-mail: Gnana.guru00@gmail.com

INTRODUCTION

Normal cells in the body typically follow a regulated cycle of growth, division, and programmed cell death. In the early years of an individual's life, cells actively grow. Once adulthood is reached, cell division primarily occurs to replace aging or damaged cells and to facilitate tissue repair. Cancer, as outlined by Hanahan et al. (2000), initiates when cells in a specific body part undergo uncontrolled growth. Various types of cancer share a common origin in the unchecked proliferation of abnormal cells. Unlike normal cells, cancer cells defy the natural process of cell death, persistently growing and generating new abnormal cells. Additionally, cancer cells can invade neighbouring tissues, a characteristic absent in normal cells. The transformation of a cell into a cancerous state is attributed to DNA damage. While normal cells typically repair or undergo programmed cell death in response to DNA damage, cancer cells deviate from this norm, continuously producing unnecessary new cells with the same damaged DNA. Factors such as inherited genetic mutations and environmental influences contribute to DNA damage. Smoking, for instance, is a clear contributor to DNA damage in some cases, while in others, the cause remains unclear. Typically, cancer cells form tumours, although exceptions exist, such as in leukaemia, where tumours are rare, and cancer cells circulate in the blood and blood-forming organs.

Not all tumors are cancerous; benign tumors, for example, can cause issues by growing large and pressing on healthy organs but do not invade or metastasize. Lung cancers, as discussed by (Gould *et al.* 2004), may originate in the cells lining the bronchi, bronchioles, or alveoli. Pre-cancerous changes in lung cells may precede cancer development, with initial abnormal cell growth not forming visible masses or causing symptoms. As cancer progresses, cells may release chemicals that promote the formation of blood vessels, supporting tumor growth. Lung cancer, often posing a significant threat (Alberg *et al*., 2005), tends to metastasize before detection through imaging tests like chest x-rays. Lung cancer cells can enter lymphatic vessels and begin to grow in lymph nodes around the bronchi and in the mediastinum (the area between the 2 lungs). Once lung cancer cells have reached the lymph nodes, they are more likely to have spread to other organs of the body as well. The stage (extent) of the cancer and decisions about treatment are based in part on whether or not the cancer has spread to the nearby lymph nodes in the mediastinum.

Types of Lung Cancer

There are 2 major types of lung cancer: Small cell and Non-small cell lung cancer (NSCLC)

Approximately 85% to 90% of lung cancers fall under the category of non-small cell lung cancer (NSCLC). NSCLC comprises three primary subtypes, characterized by variations in cell size, shape, and chemical composition observable under a microscope. Despite these differences, these subtypes are collectively categorized due to the similarity in treatment approaches and prognosis, as emphasized by (Horn *et al*. 2014).

Squamous cell lung carcinoma

Roughly 25% to 30% of lung cancers belong to the category of squamous cell carcinomas. These cancers originate in the early forms of squamous cells, flat cells lining the interior of the lung airways. Squamous cell carcinomas are frequently associated with a history of smoking and are commonly located in the central regions of the lungs, near bronchi.

Adenocarcinoma of lung

Approximately 40% of lung cancers are classified as adenocarcinomas. These cancers originate in the early versions of cells responsible for secreting substances like mucus. While adenocarcinomas are prevalent among current or former smokers, they are also the most common type of lung cancer observed in non-smokers. This subtype is more frequently diagnosed in women than men, and it has a higher likelihood of occurring in younger individuals compared to other lung cancer types. Adenocarcinomas are typically found in the outer regions of the lung, exhibit a slower growth rate than other variants, and are more likely to be detected before spreading beyond the lung.

Large cell lung carcinoma:

Comprising approximately 10% to 15% of lung cancers, large cell carcinoma is a type that can manifest in any part of the lung. Notably, it tends to exhibit rapid growth and dissemination, posing challenges in its treatment. A specific subtype, known as large cell neuroendocrine carcinoma, shares similarities with small cell lung cancer and is characterized by its fast-paced growth.

Lung carcinoid tumors:

Carcinoid tumors of the lung, constituting fewer than 5% of lung tumors, predominantly fall into the category of typical carcinoid tumors. Most of these tumors exhibit slow growth and can often be effectively treated through surgery, leading to a favorable prognosis. While some typical carcinoid tumors have the potential to spread, their overall outlook is generally more positive compared to both small cell and non-small cell lung cancer. In contrast, atypical carcinoid tumors are less common. Their prognosis falls between that of typical carcinoids and small cell lung cancer, indicating a moderate level of aggressiveness.

DIAGNOSIS

Non-Invasive Methods (Wang *et al.,* 1995).

C-X-Ray

Chest x-rays are typically the initial diagnostic test used to identify any masses, spots, or abnormalities in the lungs. Chest x-rays are a common and widely available imaging tool that can provide a preliminary assessment of lung health. Regular chest x-rays may also be recommended for individuals at high risk for lung cancer, such as heavy smokers, as part of routine screening efforts.

CT Scan

A CT (or CAT) scan is a more advanced imaging technique compared to routine chest x-rays, and it is more likely to detect lung tumors. It provides detailed information about the size, shape, and position of lung tumors, offering a comprehensive view of the affected area. Additionally, CT scans can identify enlarged lymph nodes that might contain cancer that has spread from the lungs. The versatility of CT scans extends beyond the lungs, as they can be used to examine other internal organs for potential signs of cancer spread. This includes the adrenal glands, liver, brain, and more. The CT scan utilizes x-rays to generate detailed cross-sectional images of the body. Unlike traditional x-rays, a CT scanner captures multiple images while rotating around the patient lying on a table. A computer then combines these images to create detailed slices of the body part under examination.

MRI Scan

MRI scans are most commonly employed to investigate the potential spread of lung cancer to the brain or spinal cord (Webb *et al*., 1991). Similar to CT scans, MRI scans provide detailed images of soft tissues within the body. Instead of x-rays, MRI scans use radio waves and strong magnets. The energy from the radio waves is absorbed and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates this pattern into a highly detailed image of parts of the body. Before the scan, a contrast material called gadolinium is often injected into a vein to enhance visibility and provide clearer details (Webb *et al*., 1991).

PET scan

A PET scan is a crucial test, especially for patients suspected of having early-stage lung cancer. This test aids doctors in assessing whether the cancer has spread to nearby lymph nodes or other areas, assisting in the determination of the feasibility of surgery as a treatment option. Additionally, a PET scan is valuable for obtaining a better understanding of whether an abnormal area identified on a chest x-ray or CT scan may be cancerous (Yasufuku *et al*., 2006).PET scans can reveal the spread of cancer (Truong *et al*., 2004) to various locations, including the liver, bones, adrenal glands, or other organs. However, they are not as effective for examining the brain, as all brain cells utilize a significant amount of glucose. In this test, a form of radioactive sugar known as fluorodeoxyglucose or FDG is injected into the bloodstream. The amount of radioactivity used is very low and will pass out of the body over the next day or so. Since cancer cells grow rapidly, they absorb more of the radioactive sugar. Approximately an hour after the injection, the patient is placed on a table within the PET scanner. The patient lies on the table for about 30 minutes while a special camera captures a picture of areas with radioactivity in the body. While the image is not as finely detailed as a CT or MRI scan, it provides valuable information about the entire body (Gross *et al*., 2011).

Bone scanning

A bone scan is a valuable diagnostic test to determine if cancer has spread to the bones. During this procedure, a small amount of low-level radioactive material is injected intravenously (IV) into a vein. This substance gradually settles in areas of bone changes throughout the entire skeleton over a couple of hours. Subsequently, the patient lies on a table for about 30 minutes while a special camera detects the radioactivity. Active bone changes attract the radioactivity, appearing as hot spots on the images. While these hot spots may suggest metastatic cancer, it's important to note that conditions such as arthritis or other bone diseases can also produce similar results. Bone scans, often conducted in patients with non-small cell lung cancer, are particularly useful in determining whether cancer has spread to the bones. These scans are typically performed when there is reason to suspect that the cancer may have metastasized to the bones. They provide crucial information for oncologists to assess the extent of cancer spread and tailor appropriate treatment strategies.

Invasive and Semi-invasive tests

Sputum cytology

Examining a sample of sputum, which is the mucus coughed up from the lungs, under a microscope is a diagnostic method to detect cancer cells. For optimal results, obtaining early morning samples over a period of three consecutive days is recommended.

Thoracentesis

Thoracentesis is a diagnostic procedure performed when there is an accumulation of fluid around the lungs, known as pleural effusion. This procedure aims to determine the cause of the fluid buildup, whether it is related to cancer spreading to the lining of the lungs (pleura) or caused by other conditions such as heart failure or infection. If a malignant pleural effusion is diagnosed, thoracentesis may be repeated to remove additional fluid. The buildup of fluid around the lungs can impede proper air filling, and thoracentesis not only aids in diagnosing the underlying cause but also helps the patient breathe more effectively by alleviating the fluid accumulation.

CT Guided Needle Biopsy

Certainly, a CT scan can be a valuable tool for guiding a biopsy procedure when a suspected area of cancer is located deep within the body. CT-guided biopsy is particularly useful when the suspected cancerous area is not easily accessible through traditional means. It provides a more precise and targeted approach, reducing the need for invasive procedures. The real-time imaging offered by CT scans enhances the accuracy of the biopsy, ensuring that the sample is taken from the intended site

Needle biopsy

Fine needle aspiration (FNA) biopsy and core biopsy are methods used by doctors to obtain small samples from suspicious areas or masses in the lungs for diagnostic purposes.

Procedure: If the suspected tumor is in the outer part of the lungs, either type of biopsy needle can be inserted through the skin on the chest wall.

Guidance: The doctor may use fluoroscopy or CT imaging to guide the needle into the area. The direction of the needle is adjusted based on the imaging results.

Complication: A possible complication is a pneumothorax, where air leaks into the space between the lung and chest wall, causing part of the lung to collapse. This can lead to breathing difficulties, but pneumothorax often improves without treatment. If necessary, a small tube may be inserted to remove air.

FNA Biopsy for Lymph Nodes:

- Transtracheal FNA or Transbronchial FNA: The needle is passed through the wall of the trachea or bronchi during bronchoscopy or end bronchial ultrasound.
- Endoscopic Esophageal Ultrasound: FNA biopsy is done by passing the needle through the wall of the esophagus.

These biopsy techniques are valuable for diagnosing lung cancer and providing crucial information for treatment planning.

Bronchoscopy

Bronchoscopy is a diagnostic procedure that helps identify tumors or blockages in the larger airways of the lungs, often allowing for biopsies during the examination. The process involves using a lighted, flexible fiber-optic tube, known as a bronchoscope, which is inserted through the mouth or nose and directed into the windpipe and bronchi. To enhance patient comfort, the mouth and throat are numbed with a spray, and medication may be administered through an intravenous (IV) line. The bronchoscope is equipped with small instruments for taking tissue samples (biopsies), and the doctor can also collect cells from the airway lining using techniques like bronchial brushing or bronchial washing with sterile saltwater. Subsequently, the obtained tissue and cell samples undergo microscopic examination (Leong *et al*., 2012) to aid in diagnosis.

Bronchial Ultrasound

Ultrasound is an imaging test that utilizes sound waves to generate images of the interior of the body. A transducer, resembling a probe, emits sound waves and captures the resulting echoes as they rebound off bodily tissues. These echoes are translated by a computer into a black-and-white image displayed on a computer screen. In the case of end bronchial ultrasound (Herth et al., 2004), an ultrasound transducer is attached to the tip of a bronchoscope, which is then inserted into the windpipe. This procedure is performed under local anesthesia and light sedation. The transducer can be directed in various orientations to examine structures in the mediastinum (the region between the lungs), including lymph nodes. If suspicious areas, such as enlarged lymph nodes, are identified through ultrasound, a hollow needle can be passed through the bronchoscope and guided into these areas to obtain a biopsy. The collected samples are subsequently sent to a laboratory for microscopic examination (Gu *et al.,* 2009).

Esophageal endoscopy adjuvant with ultrasound

This procedure is akin to end bronchial ultrasound, but it involves the insertion of an endoscope (a lighted, flexible scope) through the throat and into the esophagus (the tube connecting the throat to the stomach). Conducted under local anesthesia and light sedation, this procedure allows the doctor to explore the esophagus, which lies just behind the windpipe and is in close proximity to certain lymph nodes within the chest that may be susceptible to the spread of lung cancer. Similar to end bronchial ultrasound, the transducer can be maneuvered in different directions to examine lymph nodes and other chest structures that might harbor lung cancer. If enlarged lymph nodes are identified on the ultrasound, a hollow needle can be passed through the endoscope to obtain biopsy samples, which are then sent to a laboratory for microscopic analysis.

Mediastinoscopy and mediastinotomy

These procedures are conducted to directly examine and obtain samples from the structures in the mediastinum (the region between the lungs). They are performed in an operating room with patients under general anesthesia, ensuring they are in a deep sleep throughout the procedure. The primary distinction between the two procedures lies in the location and size of the incision. In the first method, a small incision is made in the front of the neck, and a thin, hollow, illuminated tube is inserted behind the sternum (breastbone) and in front of the windpipe to inspect the area. Instruments can be passed through this tube to collect tissue samples from the lymph nodes along the windpipe and the major bronchial tube areas. Examining these samples under a microscope can reveal the presence of cancer cells. The second method involves a slightly larger incision, typically around 2 inches long, made between the left second and third ribs next to the breastbone. This allows the surgeon to access certain lymph nodes that cannot be reached through mediastinoscopy.

Thoracoscopy

Thoracoscopy is a surgical procedure conducted to investigate whether cancer has spread to the spaces between the lungs and the chest wall or to the linings of these spaces. Additionally, it can be employed to sample tumors located on the outer parts of the lungs, adjacent lymph nodes, and fluid, while also assessing whether a tumor is infiltrating nearby tissues or organs. Typically, this procedure is not performed solely for diagnosing lung cancer, unless other diagnostic tests like needle biopsies fail to yield sufficient samples. Thoracoscopy is carried out in the operating room under general anesthesia, ensuring the patient is in a deep sleep. A small incision is made in the side of the chest wall, and a thin, illuminated tube with a small video camera at its end is inserted through the incision. This enables the doctor to visualize the space between the lungs and the chest wall. Using the camera, potential cancer deposits on the lining of the lung or chest wall can be identified, and small pieces of tissue can be removed for microscopic examination. In some cases, a larger incision in the chest wall, known as a thoracotomy, may be necessary. Thoracoscopy can also be a component of the treatment plan, particularly in early-stage lung cancers, where part of a lung is removed in a procedure known as video-assisted thoracic surgery (VATS).

Immunohistochemistry

In this test, very thin slices of the sample are affixed to glass microscope slides. These samples undergo treatment with specific proteins known as antibodies, which are tailored to bind exclusively to a particular substance present in certain cancer cells. If the cells contain that specific substance, the antibody will bind to them. Subsequently, chemicals are introduced to facilitate a color change in the antibodies attached to the cells. The examining doctor, observing the sample under a microscope, can detect this color change.

Molecular tests Blood tests

Blood tests are not employed for the direct diagnosis of lung cancer. However, they can be utilized to assess overall health, particularly to determine if an individual is suitable for surgery. A complete blood count (CBC) is conducted to ascertain the normalcy of various cell types in the blood. This includes identifying conditions such as anemia (characterized by a low count of red blood cells), potential bleeding issues (indicated by a low count of blood platelets), or an elevated risk of infections (associated with a low count of white blood cells). In cases where chemotherapy is administered, this test is regularly repeated as these drugs can impact the blood-forming cells in the bone marrow. Additionally, blood chemistry tests are conducted to assess the functioning of organs like the liver or kidneys. Abnormal levels of certain chemicals in the blood, such as an increased level of lactate dehydrogenase (LDH), may indicate the spread of cancer to organs like the liver and bones.

Pulmonary function tests

Pulmonary function tests (PFTs) are frequently conducted post-diagnosis of lung cancer to evaluate the functionality of a patient's lungs, especially when surgery is being considered as a treatment option. Surgery to remove lung cancer may involve the removal of part or the entirety of a lung, impacting respiratory function. For individuals with compromised lung function, it's essential to determine whether there is sufficient lung reserve to tolerate the removal of a portion of the lung. Various types of PFTs exist, but the fundamental principle involves breathing in and out through a tube connected to a machine that measures airflow. In some cases, PFTs are combined with arterial blood gas testing, where blood is drawn from an artery to assess its oxygen and carbon dioxide levels, providing crucial information for surgical considerations.

TREATMENT OF NON-SMALL CELL LUNG CANCER

Depending on the stage of the disease and other factors, the main treatment options for people with non-small cell lung cancer (NSCLC) can include:

- Surgery
- Radiofrequency ablation
- Radiation therapy
- Chemotherapy
- Targeted therapies
- Palliative procedures can also be used to help with symptoms.

Types of lung surgery (Posther *et al.,* 2006)

These operations require general anesthesia

1. **Pneumonectomy:**
   an entire lung is removed in this surgery.

2. **Lobectomy:**
   an entire section (lobe) of a lung is removed in this surgery.

3. **Segmentectomy:**
   part of a lobe is removed in this surgery.

Another surgical approach for treating certain cancers in the large airways of the lungs is known as a sleeve resection. The specific operation recommended by your doctor depends on factors such as the size and location of the tumor and the overall functioning of your lungs.

4. **Video-assisted thoracic surgery (VATS):**

In some cases of early-stage lung cancers located near the outer part of the lung, doctors may opt for a procedure known as video-assisted thoracic surgery (VATS). This minimally invasive approach involves smaller incisions compared to a thoracotomy. During VATS, a thin, rigid tube with a small video camera at the end is inserted through a small cut in the side of the chest, allowing the surgeon to visualize the chest on a TV monitor. One or two additional small incisions are made, and long instruments are passed through them to perform the necessary operation, which would typically be done using an open approach (thoracotomy). If a lobectomy or pneumonectomy is performed, one of the incisions may be enlarged to facilitate specimen removal. Due to the use of smaller incisions, patients often experience less postoperative pain and a shorter hospital stay, usually lasting 4 to 5 days.

5. Radiofrequency ablation (RFA):

For certain small lung tumors located near the outer edge of the lungs, a technique called radiofrequency ablation (RFA) might be considered as a treatment option. RFA employs high-energy radio waves to heat the tumor and destroy cancer cells. During RFA, a thin, needle-like probe is inserted through the skin and carefully guided into the tumor with the assistance of CT scans. Once the probe is correctly positioned, an electric current is passed through it, generating heat within the tumor and causing the destruction of cancer cells. This procedure is typically conducted on an outpatient basis, using local anesthesia to numb the area where the probe is inserted. While major complications are infrequent, potential issues may include the partial collapse of a lung (often resolving on its own) or bleeding into the lung.

Radiation therapy

1. External beam radiation:

External Beam Radiation Therapy (EBRT) is a treatment modality that directs radiation from outside the body onto the cancerous tissue. This approach is commonly employed to treat primary lung cancer or instances where the cancer has spread to other organs. Before initiating the treatment, the radiation team conducts precise measurements to determine the correct angles for directing the radiation beams and the appropriate radiation dose. The treatment process resembles receiving an x-ray, but with a stronger dose of radiation. While the procedure itself is painless, the setup time to position the patient for treatment is usually longer. Typically, radiation treatments for lung cancer are administered five days a week over a span of 5 to 7 weeks, although the duration may vary based on individual circumstances.

2. 3-D conformal radiation therapy (3D- CRT):

Three-Dimensional Conformal Radiation Therapy (3D-CRT) employs specialized computers to precisely map the location of tumors. This advanced technique shapes and directs radiation beams at the tumors from multiple angles, reducing the risk of damage to surrounding healthy tissues. The precise mapping and targeted delivery of radiation enhance the effectiveness of the treatment while minimizing adverse effects on normal tissues.

3. Intensity modulated radiation therapy (IMRT):

Intensity-Modulated Radiation Therapy (IMRT) represents an advanced iteration of 3D therapy. In IMRT, a computer-driven machine dynamically moves around the patient while delivering radiation. This technology not only shapes and directs beams at the tumor from various angles but also allows for the adjustment of beam intensity. This capability enables the limitation of radiation doses reaching the most sensitive normal tissues, making IMRT particularly valuable when tumors are in proximity to critical structures such as the spinal cord. Many leading hospitals and cancer centers have adopted IMRT for its precision and efficacy.

4. Stereotactic body radiation therapy (SBRT):

Stereotactic Body Radiotherapy (SBRT), also known as stereotactic ablative radiotherapy (SABR), is occasionally employed as a treatment strategy, especially for individuals who may not be suitable candidates for surgery. In contrast to the conventional approach of administering small doses of radiation daily over several weeks, SBRT employs highly focused beams of high-dose radiation delivered in a condensed treatment schedule, typically spanning 1 to 5 sessions. Multiple beams are precisely directed at the tumor from various angles, enhancing the precision and effectiveness of the treatment.

5. Stereotactic radiosurgery (SRS):

Stereotactic Radiosurgery (SRS) is a form of stereotactic radiation therapy administered in a single session. It is sometimes utilized as an alternative to or in conjunction with surgery, particularly for solitary tumors that have metastasized to the brain. One approach involves the use of a Gamma Knife®, a machine that concentrates approximately 200 radiation beams on the tumor from diverse angles over a duration ranging from minutes to hours. The patient's head is securely positioned within a rigid frame to maintain stability. Another version employs a linear accelerator, a computer-controlled device generating radiation, which orbits around the patient's head to deliver radiation from numerous angles. These treatments can be repeated if necessary.

6. Brachytherapy (internal radiation therapy)

In individuals diagnosed with lung cancer, brachytherapy is occasionally employed to reduce tumors within the airways, aiming to alleviate associated symptoms. However, its utilization is less common for lung cancer compared to other cancers such as those affecting the head and neck. In this treatment approach, the physician introduces a small source of radioactive material, often in the form of tiny pellets, directly into the cancerous site or into the airway adjacent to the cancer. This procedure is typically conducted through a bronchoscope, although it may also be performed during surgery. The radiation emitted has a limited range, minimizing its impact on surrounding healthy tissues. In most cases, the radioactive source is removed after a brief duration. Alternatively, on rare occasions, small radioactive seeds may be left in place permanently, with the radiation gradually diminishing over several weeks (Wender *et al.*, 2013)**.**

Chemotherapy (Quoix *et al.,* 2011)

Chemotherapy (chemo) is a treatment involving anti-cancer drugs administered either through injection into a vein or taken orally. These drugs circulate throughout the bloodstream, making them effective against cancer anywhere in the body. In the context of non-small cell lung cancer (NSCLC), chemotherapy may be employed in different situations:

- Neoadjuvant Therapy: Given before surgery, sometimes in combination with radiation therapy, to shrink a tumor.
- Adjuvant Therapy: Administered after surgery, sometimes alongside radiation therapy, to eliminate any remaining cancer cells.
- Main Treatment: Used as the primary treatment, sometimes in conjunction with radiation therapy, for more advanced cancers or specific cases.

Chemo is typically administered in cycles, with a treatment period (usually 1 to 3 days) followed by a rest period to allow the body to recover. Some drugs are given daily. The cycles generally last about 3 to 4 weeks. While chemo may not be recommended for patients in poor health, advanced age alone is not a barrier to receiving this treatment. Common chemo drugs for NSCLC include cisplatin, carboplatin, paclitaxel (Taxol®), albumin-bound paclitaxel (nab-paclitaxel, Abraxane®), docetaxel (Taxotere®), gemcitabine (Gemzar®), vinorelbine (Navelbine®), irinotecan (Camptosar®), etoposide (VP-16®), vinblastine, and pemetrexed (Alimta®). NSCLC treatment often involves a combination of two chemo drugs, with studies indicating that combinations are more effective, although they may cause more side effects. Single-drug chemo is an option for those who may not tolerate combination chemotherapy well, such as individuals in poor overall health or the elderly. Common combinations include cisplatin or carboplatin with another drug, while alternatives may include gemcitabine with vinorelbine or paclitaxel.

Drugs that target angiogenesis

Tumors require new blood vessels for nourishment, a process known as angiogenesis. Certain targeted drugs, called angiogenesis inhibitors, work by blocking the formation of these new blood vessels. Bevacizumab (Avastin®) is an angiogenesis inhibitor used in the treatment of advanced non-small cell lung cancer. It is a monoclonal antibody, a synthetic version of a specific immune system protein, that targets vascular endothelial growth factor (VEGF), a protein crucial for the formation of new blood vessels. Bevacizumab is often combined with chemotherapy for a period. If the cancer responds positively, chemotherapy may be discontinued, and bevacizumab is administered as a standalone treatment until the cancer resumes growth. It's important to note that the potential side effects of bevacizumab differ from those of chemotherapy drugs. One notable side effect is the risk of serious bleeding, which can limit its use. As a precaution, bevacizumab is not employed in patients who are experiencing coughing up blood.

Drugs that target EGFR

Epidermal Growth Factor Receptor (EGFR) is a protein located on the surface of cells, playing a role in cell growth and division. In some cases of non-small cell lung cancer (NSCLC), certain cells have an overabundance of EGFR, leading to accelerated growth. Targeted drugs designed to address EGFR in the treatment of NSCLC include Erlotinib (Tarceva®) and Afatinib (Gilotrif®). Erlotinib and afatinib function by inhibiting the signal from EGFR that instructs cells to grow. These drugs can be administered on their own, without chemotherapy, as the initial treatment for advanced NSCLCs that possess specific mutations in the EGFR gene. Erlotinib is also employed in the treatment of advanced NSCLC. Both erlotinib and afatinib are available in pill form. Common side effects include skin problems, diarrhea, mouth sores, and loss of appetite. Skin problems may manifest as an acne-like rash on the face and chest, potentially leading to skin infections in some cases.

Drugs that target the ALK gene

Approximately 5% of non-small cell lung cancers (NSCLCs) exhibit a rearrangement in a gene known as ALK (Anaplastic Lymphoma Kinase). This alteration is frequently observed in non-smokers or light smokers who have the adenocarcinoma subtype of NSCLC. The rearrangement in the ALK gene results in the production of an abnormal ALK protein that stimulates the growth and spread of cancer cells. Targeted drugs that focus on ALK, such as Crizotinib, are capable of addressing the abnormal ALK protein, leading to tumor shrinkage in patients with the ALK gene rearrangement in their lung cancers. These drugs are often used instead of chemotherapy, especially in individuals with cancers featuring the ALK gene rearrangement, and they can be beneficial even after chemotherapy has ceased. Crizotinib and other ALK inhibitors are administered in pill form. Common side effects of these drugs include nausea and vomiting, diarrhea, constipation, fatigue, and changes in vision. Some side effects can be severe, including low white blood cell counts, lung inflammation, liver damage, and heart rhythm problems. Regular monitoring and communication with healthcare providers are crucial to managing these potential side effects.

Maintenance chemotherapy:

In the management of advanced lung cancers, particularly for individuals who can tolerate chemotherapy, healthcare providers often administer combinations of two chemotherapy drugs over approximately 4 to 6 cycles. Recent studies have indicated that for cancers that have not progressed, continuing treatment beyond the initial 4 to 6 cycles with a single chemotherapy drug like pemetrexed or a targeted drug such as erlotinib may provide some individuals with a longer life expectancy. This approach is referred to as maintenance therapy. However, it's essential to consider that prolonged treatment may mean individuals do not get a break from the side effects associated with chemotherapy. The decision to pursue maintenance therapy should be carefully weighed against the potential benefits and drawbacks, taking into account the individual's overall health and preferences.

Targeted Immune Therapies

Researchers are hoping to develop drugs that can the cancer.

PD-1 and PD-L1 blockers:

Cancer cells can employ natural pathways in the body to evade detection and destruction by the immune system, such as having the protein PD-L1 on their surface. New drugs designed to block the PD-L1 protein or its corresponding PD-1 protein on immune cells, known as T cells, have shown promise in helping the immune system recognize and attack cancer cells. In early studies, an anti-PD-1 drug like nivolumab demonstrated the ability to shrink tumors in approximately 1 out of 5 people with non-small cell lung cancer (NSCLC). Another drug targeting PD-L1, known as BMS-936559, showed tumor-shrinking effects in about 1 out of 10 people. Many of these tumor responses have been observed to be long-lasting. Additionally, drugs like pembrolizumab, MPDL3280A, and MEDI4736 have shown the ability to shrink tumors in patients with lung cancer. Larger studies are underway to further investigate the efficacy of these novel drugs.

Vaccines:

Clinical trials are underway to test vaccines that stimulate the immune response against lung cancer cells. Unlike traditional vaccines for infectious diseases like measles or mumps, these vaccines are designed to treat, rather than prevent, lung cancer. These treatments appear to have limited side effects. The vaccines are composed of lung cancer cells grown in the laboratory or cell components, such as parts of proteins commonly found on cancer cells. For example, the MUC1 protein found on some lung cancer cells is targeted by the TG4010 vaccine, which induces an immune response against that protein. A recent study compared combining TG4010 with chemotherapy to treatment with chemotherapy alone in patients with advanced lung cancer. The group receiving the vaccine showed a higher likelihood of tumor shrinkage or growth cessation compared to the chemotherapy-only group. Further studies are planned to assess if the vaccine can extend patients' survival. Another vaccine, L-BLP25 (tecemotide), also targets the MUC1 protein. It consists of the protein (MUC1) enclosed in a liposome (fat droplet) to potentially enhance its effectiveness. A small study in patients with advanced non-small cell lung cancer (NSCLC) suggested that it might improve survival time. However, recent results from a larger study did not find a significant improvement in overall survival. This vaccine is currently being studied in patients with stage III disease after treatment with chemotherapy and radiation, aiming to enhance the cure rate.

CONCLUSION

The improved life expectancy for non-small cell lung cancer patients is a positive development, thanks to the availability of effective treatment options. However, the presence of persistent chronic pain, often originating from the oncologic aspects, remains a significant challenge, affecting the quality of life for survivors in advanced stages of lung cancer post-treatment. While there are various diagnostic and adjuvant medications available to manage pain, these treatments may come with associated side effects. There is a recognized need for more effective approaches to manage lung cancer treatments, especially in addressing chronic pain with minimal side effects. Further studies and research are essential to explore novel therapies and agents that can provide rapid and adequate relief for patients, ensuring an improved quality of life during and after treatment. The goal is to discover interventions that not only enhance the efficacy of treatment but also minimize the adverse effects associated with current pain management strategies.

REFERENCES

Alberg AJ, Brock MV, Stuart JM. Epidemiology of lung cancer: Looking to the future. *J Clin Oncol*, 23, 2005, 3175-3185.

American Joint Committee on Cancer. Lung. *AJCC Cancer Staging Manual*. 7th ed. New York: Springer, 2010, 253-266.

Gould MK, Silvestri GA, Detterbeck F.Multidisciplinary management of lung cancer. *N Engl J Med* 350(19), 2004, 2008-10.

Gu P, Zhao YZ, Jiang LY, Zhang W, Xin Y, Han BH. Endobronchial ultrasound-guided transbronchial needle aspiration for staging of lung cancer: a systematic review and meta-analysis. *Eur J Cancer*.45(8), 2009, 1389 96.

Gross BH, Brown RK, Kalemkerian GP. Optimal anatomic coverage for CT in staging lung cancer: lessons from PET-CT correlation. *Lung Cancer*. 73(1), 2011, 59-62.
Hanahan D, Weinberg RA. The hallmarks of cancer. *Cell* 100, 2000, 57-70.
Herth FJ, Becker HD, Ernst A. Ultrasound-guided transbronchial needle aspiration: an experience in 242 patients. *Chest.* 123(2),2003, 604-7.
Herth F, Becker HD, Ernst A. Conventional vs endobronchial ultrasound- guided transbronchial needle aspiration: a randomized trial. *Chest.*125(1), 2004, 322-25.
Leong S, Ju H, Marshall H, Bowman R, Yang I, Ree AM, Saxon C, Fong KM.Electromagnetic navigation bronchoscopy: A descriptive analysis. *J Thorac Dis*. 4(2), 2012, 173-85.
Posther KE, Harpole DH. The surgical management of lung cancer. *Cancer Investigation.* 24, 2006, 56-67.
Quoix E, Ramlau R, Westeel V,. Therapeutic vaccination with TG4010 and first-line chemotherapy in advanced non-small-cell lung cancer: A controlled phase 2B trial.*Lancet Oncol*. 12, 2011, 1125-33.
Truong MT, Munden RF, Movsas B. Imaging to optimally stage lung cancer: conventional modalities and PET/CT. *J Am Coll Radiol.* 1(12), 2004, 957-64
Webb WR, Gatsonis C, Zerhouni EA, Heelan RT, Glazer GM, Francis IR, CT and MR imaging in staging non-small cell bronchogenic carcinoma: report of the Radiologic Diagnostic Oncology Group. *Radiology*. 178(3), 1991, 705-13.
Wender R, Fontham E, Barrera E,. American Cancer Society lung cancer screening guidelines. *CA Cancer J Clin*. 63, 2013, 106-117.
Wang KP. Transbronchial needle aspiration and percutaneous needle aspiration for staging and diagnosis of lung cancer. *Clin Chest Med*. 16(3), 1995, 535-52.
Yasufuku K, Nakajima T, Motoori K, Sekine Y, Shibuya K, Hiroshima K, Comparison of end bronchial ultrasound, positron emission tomography, and CT for lymph node staging of lung cancer. *Chest*. 130(3), 2006, 710-18.

Cite this article:
Gnana Prasuna G, Anupama P, Venkatesh M, Prasanna Kumar Naik B. Non-small cell lung cancer (nsclc)-diagnostic and therapeutic options. *International Journal of Pharmacy & Therapeutics*, 15(1), 2024, 7-15.