Current Status Of Lung Cancer Research

Abstract:

One of the most common cancers to cause death worldwide is lung cancer. Lung carcinoma, another name for lung cancer, is a malignant lung tumor that is characterized by uncontrolled~~unchecked~~ cell proliferation in lung tissues. This tumor has the potential to metastasize, or expand outside of the lung, into neighboring tissue or other sections of the body~~, if left untreated~~. The majority of primary lung malignancies, ~~also known as cancers that begin in the lung~~, are carcinomas that develop from epithelial cells. Small-cell lung cancer (SCLC) and non-small-cell lung carcinoma are the two main primary kinds (NSCLC). Lung cancer is primarily caused by prolonged cigarette smoke exposure (85% of cases). Approximately 10-15% of occurrences include non-smokers. These situations are frequently brought on by a confluence of genetic predispositions and exposure to asbestos, radon gas, or other environmental pollutants, such as secondhand smoke. This article provides a thorough overview of lung cancer's epidemiology, causes, forms, symptoms, and treatments.

1. Introduction:

Cancer is a condition in which the body's cells proliferateuncontrolled~~unchecked~~. Lung cancer is the name for cancer that first appears in the lungs. ~~In addition to lymph nodes and other body organs including the brain, lung cancer can also start in the lungs.~~ Lung cancer can potentially spread from other organs. Metastases are cancer cells that have spread from one organ to another (Agrawal et al., 2007; Albright et al., 2016; Alder et al., 2008; Sethi, 2002) . Since 98–99% of all lung cancers are carcinomas, lung cancer is also known as lung carcinoma, and it is a malignant lung tumorcharacterized by ~~unchecked~~ uncontrolledcell proliferation in lung tissues. Lung carcinomas develop from epithelial tissues or from epithelial cells that have undergone malignant transformation. Other lung cancers, like the uncommon sarcomas of the lung, are caused by the malignant transformation of connective tissues, which develop from mesenchymal cells and include fat, muscle, and bone. Rarely, lung cancer can also develop from lymphomas and

melanomas (derived from lymphoid and melanocyte cell lineages)~~("<Non-Small-Cell-Lung Cancer Treatment (PDQ®) Patient Version - NCI.pdf>,")~~.One of the biggest causes of cancer-related deaths worldwide is lung cancer. Lung cancer has the highest prevalence among all cancers, ~~and its cases are continuously increasing~~with increasing incidence(Bray et al., 2018). Tumors coming from the bronchi or the lung parenchyma are referred to as bronchiogenic carcinomas or lung cancer. It ranks among the top reasons for cancer-related fatalities in the US. Lung cancer has been the cause of more female fatalities since 1987 than breast cancer (Rebecca L Siegel, Miller, Fuchs, & Jemal, 2022). The sponge-like lungs are located in your chest. They are responsible for supplying the body with oxygen and expelling carbon dioxide. Air enters your lungs through your windpipe when you breathe in (trachea). The trachea separates into bronchi, which are tubes that enter the lungs. These separate into bronchioles, which are smaller branches. The tiny air sacs known as alveoli are located at the end of the bronchioles. Your blood receives oxygen from the air thanks to the alveoli. The blood's carbon dioxide is removed by them. This is expelled from your body as you exhale (exhale). The right lung has three parts (lobes). Two lobes make up your left lung (Alpert et al., 2019; Amor et al., 2020; Anderson et al., 2020; Angelidis et al., 2019; Araya et al., 2013; Armanios et al., 2007; Association, 2010; Group, 1994).L~~l~~ung cancer is a condition marked by unchecked cell proliferation in the lungs. Midway through the 19th century, doctors made the first mention of lung cancer. It was regarded as relatively uncommon at the beginning of the 20th century, but by the end of the century it was the main cause of cancer-related death in males in more than 25 developed nations. The most common cancer-related death worldwide in the twenty-first century was lung cancer. It had eclipsed breast cancer by 2022 and now kills more women from cancer in affluent nations. Though increases in environmental air pollution were considered to have played a role, the rapid rise in the prevalence of lung cancer around the world was mostly attributed to the increased use of cigarettes after World War I (Sasaki et al., 2011; Sayin et al., 2014; Schafer et al., 2017; Schumacker, 2011; Sharma & Goodwin, 2006). Cough is the most prevalent but non-specific sign of lung cancer. Lung cancer is far more likely to occur if there are any associated symptoms, such as hemoptysis or shortness of breath, or systemic symptoms, such as anorexia or weight loss. It is advised to use imaging, refer to a multidisciplinary lung cancer team, and confirm the diagnosis with mediastinoscopy, thoracentesis, fine-needle aspiration, or sputum cytology. Depending on the stage, histology, immunotherapy biomarker testing, and patient health status, if

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lung cancer is found, there are various treatment choices. Surgery, immunotherapy, chemotherapy, and/or radiotherapy are all forms of treatment (Hosseini et al., 2022; "<Lung Cancer_ Diagnosis, Treatment Principles, and Screening _ AAFP.pdf>," ; Nijakowski et al., 2022; Utsumi et al., 2023).

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2. Etiology:

Lung cancer is most frequently caused by smoking. 90% of lung cancer cases are thought to be caused by smoking. Male smokers are at the greatest danger. Exposure to additional toxins, such as asbestos, increases the risk. Due to the intricate interactions between smoking, environmental variables, and genetics, there is no connection between the number of packs smoked annually and lung cancer. Passive smoking increases the risk of lung cancer by 20 to 30% (Alberg & Samet, 2003). Radiation for the treatment of cancers other than lung cancer, particularly non-Hodgkins lymphoma and breast cancer is another factor (Cohen et al., 2017; Raaschou-Nielsen et al., 2016). Lung cancer is also linked to exposure to metals like chromium, nickel, arsenic, and polycyclic aromatic hydrocarbons. Independent of smoking, lung conditions like idiopathic pulmonary fibrosis raise the risk of lung cancer(Boyer et al., 2017; Ramo, Liu, & Prochaska, 2012). Additionally known risk factors for lung cancer include radon and asbestos. Lung cancer risk is increased by asbestos exposure, especially occupational exposure, in a dose-dependent way that varies depending on the type of asbestos ~~fibre~~fiber. Risk of asbestos exposure outside of the workplace is less clear. The Environmental Protection Agency (EPA) of the United States has set guidelines for low-level tolerable non-occupational asbestos exposure, asserting that the health risk to building occupants of asbestos that is left undisturbed and free of reparable particles is negligible (Burns, 2000; Lorigan, Radford, Howell, & Thatcher, 2005; Wagner, 1997). Lung cancer risk among uranium miners who were exposed to radon was minimal but considerable. As a byproduct of uranium and radium decay, radon has also been demonstrated to build up in residences. Residential radon poses significant risks, especially for smokers, and is believed to be responsible for about 2% of lung cancer deaths in Europe, according to a meta-analysis of data from that continent(Darby et al., 2005; Grosche, Kreuzer, Kreisheimer, Schnelzer, & Tschense, 2006).

Estimated New Cases

Males				Females		
Prostate	268,490	27%		Breast	287,850	31%
Lung & bronchus	117,910	12%		Lung & bronchus	118,830	13%
Colon & rectum	80,690	8%		Colon & rectum	70,340	8%
Urinary bladder	61,700	6%		Uterine corpus	65,950	7%
Melanoma of the skin	57,180	6%		Melanoma of the skin	42,600	5%
Kidney & renal pelvis	50,290	5%		Non-Hodgkin lymphoma	36,350	4%
Non-Hodgkin lymphoma	44,120	4%		Thyroid	31,940	3%
Oral cavity & pharynx	38,700	4%		Pancreas	29,240	3%
Leukemia	35,810	4%		Kidney & renal pelvis	28,710	3%
Pancreas	32,970	3%		Leukemia	24,840	3%
All Sites	**983,160**	**100%**		**All Sites**	**934,870**	**100%**

Estimated Deaths

Males				Females		
Lung & bronchus	68,820	21%		Lung & bronchus	61,360	21%
Prostate	34,500	11%		Breast	43,250	15%
Colon & rectum	28,400	9%		Colon & rectum	24,180	8%
Pancreas	25,970	8%		Pancreas	23,860	8%
Liver & intrahepatic bile duct	20,420	6%		Ovary	12,810	4%
Leukemia	14,020	4%		Uterine corpus	12,550	4%
Esophagus	13,250	4%		Liver & intrahepatic bile duct	10,100	4%
Urinary bladder	12,120	4%		Leukemia	9,980	3%
Non-Hodgkin lymphoma	11,700	4%		Non-Hodgkin lymphoma	8,550	3%
Brain & other nervous system	10,710	3%		Brain & other nervous system	7,570	3%
All Sites	**322,090**	**100%**		**All Sites**	**287,270**	**100%**

Figure 1 Lung Cancer Statistics 2022(Rebecca L Siegel et al., 2022) – Permission taken? Or just scheme your own figure.

3. Epidemiology:

Lung cancer is the second most prevalent cancer worldwide and the leading cause of cancer death. Lung cancer was responsible for 1.8 million new cases of death in 2020, or 18% of all cancer-related deaths(Hyuna Sung et al., 2021). Compared to other major malignancies, lung cancer had a substantially poorer 5-year survival rate (7%–25%)(Weiss, Stephenson, Edwards, Rigney, & Copeland, 2014). Due to lung cancer's high death rate, which produced a significant worldwide burden of disease, the distribution of mortality was extremely comparable to that of its incidence (Howlader et al., 2020; Jemal et al., 2008). Treatment developments in some high-income nations, such as the United States, the United Kingdom, Australia, and New Zealand, have recently improved lung cancer mortality (Luo et al., 2018; Torre, Siegel, & Jemal, 2016).

The majority of cancer diagnoses globally (12.4% of all cancer diagnoses worldwide) are lung cancer cases, which also account for the majority of cancer-related deaths. According to the American Cancer Society, there are over 154,000 lung cancer-related fatalities and over 234,000

new instances of lung cancer in the country every year. With a projected 1.8 million deaths, lung cancer continued to be the most common type of cancer death worldwide, according to the Global Cancer Statistics report from 2020(R. L. Siegel, Miller, & Jemal, 2017; H. Sung et al., 2021).

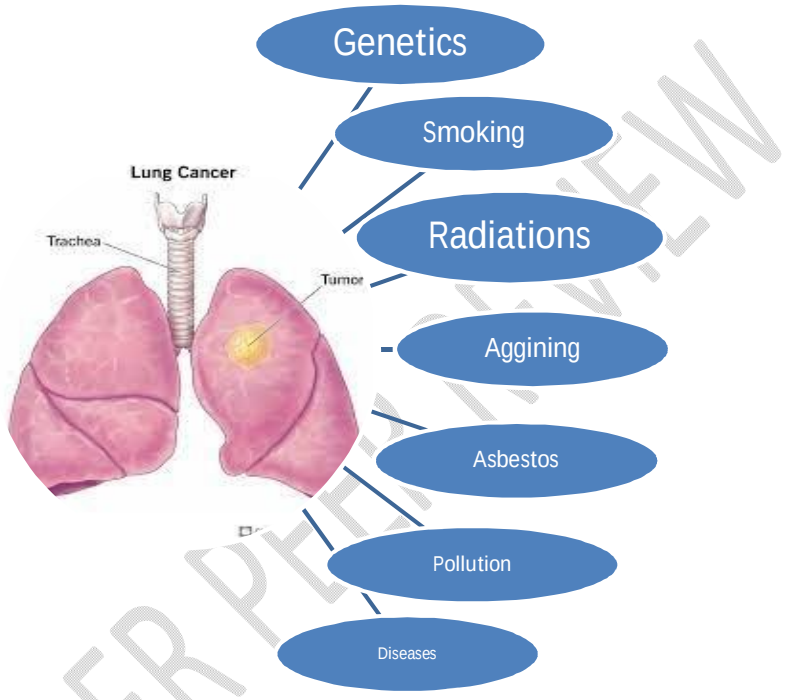

Figure 2Different Causes Of lung Cancer – Is it original figure or copied and need perimission? Aging spelling – make all same font and size.

4. Pathop Physiology of Lung Cancer:

Lung cancer's pathophysiology is extremely complicated and still not fully understood. It is believed that regular exposure to toxins like cigarette smoke causes lung epithelial dysplasia. If the exposure is sustained, genetic alterations and changes in protein synthesis result. In turn, this disturbs the cell cycle and encourages the development of cancer. MYC, BCL2, and p53 for small cell lung cancer (SCLC) and EGFR, KRAS, and p16 for non-small cell lung cancer are the genetic mutations most frequently linked to the development of lung cancer (NSCLC) (Cagle,

Allen, & Olsen, 2013; Lindeman et al., 2018; Lindeman et al., 2013). Lung cancers are classified histopathologically based on cellular and molecular subtypes, which is a crucial step in the diagnosis and treatment of lung malignancies. Lung malignancies are divided into the following categories.

Table 1 :Categories of Lung malignancies

Lung cancer type	Location in the lung	Features	References
Adenosquamous Carcinoma	**Pperipheral lung**	• uncommon • highly aggressive lung tumor	(Filosso et al., 2011)
Adenocarcinoma	**Peripheral lung**	• Most prevalent type of lung cancer in non-smokers and more prevalent in women; • develops from type II alveolar and small airway epithelial cells; • should be tested for the EGFR mutation for potential targeted therapy; • occasionally appears at the site of scarring; • tends to form glands and secrete mucin;	(Kadota et al., 2014)
Squamous cell carcinoma	**⅔ central ⅓ peripheral**	• **Clearly connected to cigarette smoking** • **Develops from**	**(Aisner et al., 1990; Chute et al., 1985; Rajdev et al., 2018; Sahn, 1998)**

		proximal big airway epithelial cells • **Have a tendency to produce blockage and distal atelectasis.** • **The greatest prognosis is due to intrathoracic spread rather than distant metastasis**	
Small-cell lung carcinoma (SCLC)	**Central**	• Most potent link to smoking • Is produced by the same pulmonary neuroendocrine cells that produce neurotransmitters, growth factors, and vasoactive chemicals. • Commonly secretes ADH (SIADH) or ACTH and causes paraneoplastic syndrome (ectopic Cushing syndrome) • The worst prognosis is caused by rapid growth and early distant metastases (brain, liver, bone).	(Kadota et al., 2014)
Large cell carcinoma	**Peripheral**	• behaving similarly to adenocarcinomas but	(Kadota et al., 2014)

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		with slightly larger lesions	

5. Symptoms:

Lung cancer typically first appears in patients between the ages ~~of 5 and 6~~??????. At the time of presentation, about three-fourths of patients exhibit clinical symptoms, the most prevalent of which are cough (50-75%), hemoptysis (25-50%), dyspnea (25%), and chest discomfort (20%). It's possible to experience generalized symptoms like anorexia, weight loss, or weariness that are connected to the malignancy's systemic manifestations. The occurrence of regional or distant metastases, the presence of paraneoplastic syndromes, and the local consequences of the main tumor all affect the clinical symptoms. The symptoms of lung cancer may be brought on by the release of hormones or bioactive compounds, or they may be brought on by immune-mediated destruction of neural tissue brought on by antibody or cell-mediated immune responses. The most prevalent of these paraneoplastic syndromes, which affect 10–20% of lung cancer patients, are connected to the release of antidiuretic and adrenocorticotropin hormones. These hormones can cause serum hypoosmolarity and hyponatremia as well as Cushing's syndrome (central obesity, hypertension, glucose intolerance, plethora, and hirsutism), ~~respectively~~ ???(Chao & Zhang, 2012; Hasegawa et al., 2000; Kakinuma et al., 2004; Ost, Jim Yeung, Tanoue, & Gould, 2013; Prenzel et al., 2003; Steinert, 2011).

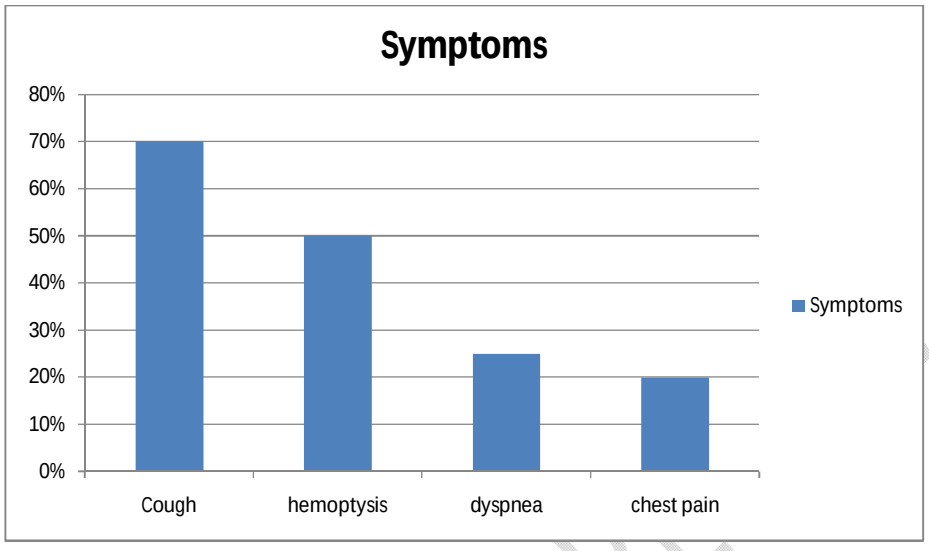

Figure 3 Common Symptoms of Lung cancer– label y axis – remove symptoms on Rt. - reference

6. Stages Of Lung Cancer:

The prognosis and treatment options for lung cancer are influenced by its stage. The stage describes the size of the tumor, its location inside the lung, whether it has moved to other parts of your body or not, and whether it has invaded other tissue.

Table 2 :Pprognosis and treatment options for lung cancer

Stages	Description
Occult stage	Cean find cancer cells in the mucus patient cough up. Neither a biopsy nor imaging scans can reveal tumor. Another name for it is concealed cancer(Elia, Loprete, De Stefano, & Hardavella, 2019; Soneji, Yang, Tanner, &

	Silvestri, 2020; Visentin, Mantovani, Kalinke, Boller, & Sarquis, 2018).
Stage 0	The tumor is quite little. deeper lung tissues or the outside of lungs are free of cancerous cells(D'Angelo et al., 2012; Sculier, Chansky, Crowley, Van Meerbeeck, & Goldstraw, 2008; Tammemägi et al., 2014).
Stage I	Lymph nodes do not have cancer, only the tissues of lungs do(Bugalho, de Santis, Slubowski, Rozman, & Eberhardt, 2017; Créquit et al., 2017; Hoang, Xu, Schiller, Bonomi, & Johnson, 2005; Lizama et al., 2018).
Stage II	Llymph nodes close to lungs may have become infected(Heineman et al., 2018; Mulvenna et al., 2016; Ramos-Esquivel, van der Laat, Rojas-Vigott, Juárez, & Corrales-Rodríguez, 2017).
Stage III	The lymph nodes and the centre of chest have been further affected by its spread(Fréchet, Kazakov, Thiffault, Ferraro, & Liberman, 2018; Labarca, Caviedes, Folch, Majid, & Fernández-Bussy, 2017).
Stage IV	Tthe body is covered widely with cancer. The brain, bones, or liver may have been affected(Ilias et al., 2005).

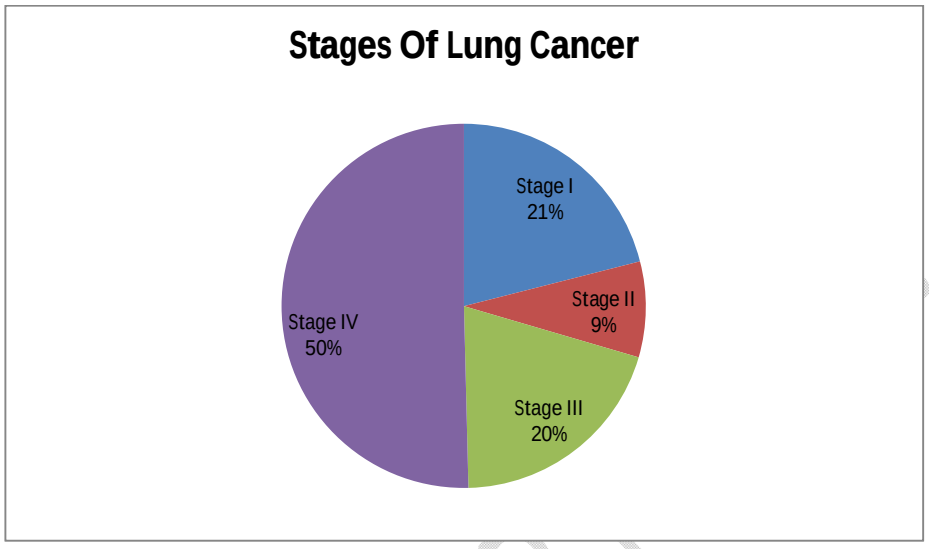

Figure 4 % Distribution of Lung cancer By stages ("<Lung Cancer Canada - Lung Cancer Canada.pdf>,") – what is each color denote for?

7. Diagnosis:

During tests for other diseases, lung tumors are frequently found. Sputum may contain cancer cells, a lung biopsy may be performed to remove a sample of lung tissue for examination, or a bronchoscope may be used to look directly for cancer in the big airways of the lungs (bronchi). X-rays, computerized axial tomography (CAT) scans, positron emission tomography (PET) scans, and magnetic resonance imaging are examples of noninvasive techniques (MRI). Additionally, a number of blood tests can be used to look for proteins and other elements linked to lung cancer.For instance, aberrant variations in parathormone serum levels, the presence of the protein cytokeratin 19 fragment in the blood, or compounds known as carcinogenic antigens may be signs of malignant lung disease. Blood tests to identify DNA released by cells ~~harbouring~~harboring genetic abnormalities linked to lung cancer are also being developed by researchers; this raises the possibility of finding lung ~~tumours~~tumors before they turn malignant.(Kim, Lee, & Huang, 2022; Latimer, 2018).

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8. Current Treatment Options:

Surgery, chemotherapy, and radiation are all used to treat lung cancer, as they are applicable for the majority of cancers. The type of cancer, the stage or severity of the disease, and the patient's general condition all influence the treatment option. The results of genetic testing, which can spot changes that make some lung tumors receptive to particular medications, may also influence the sort of treatment a patient receives (Berrington de González, Kim, & Berg, 2008; Friedman et al., 2010; Gray, Read, McGale, & Darby, 2009; Lemjabbar-Alaoui, Hassan, Yang, & Buchanan, 2015; Straif et al., 2009).

During surgery, a lung lobe, a portion of the lung, or the entire lung may be removed if it is malignant (pneumonectomy). Surgery on the lungs is risky and might result in side effects including bleeding or pneumonia. Even though the removal of the complete lung does not prevent generally healthy individuals from eventually returning to their normal activities, the pre-existing bad state of many patients' lungs causes long-term breathing difficulties after surgery (Cao et al., 2011; Hales, Blakely, & Woodward, 2012; Katanoda et al., 2011).

Radiation can be used on its own or in combination with surgery, either before the operation to reduce tumor size or after the operation to eradicate small pockets of malignant tissue. Radiation therapy can be delivered using external beams or through the surgical implantation of radioactive pellets (brachytherapy). Vomiting, ~~diarrhoea~~diarrhea, exhaustion, or worse lungs damage are examples of side effects. Chemotherapy employs chemicals to kill malignant cells, but these chemicals also, to variable degrees, damage healthy cells, leading to side effects akin to those of radiation therapy. Microwave ablation, an experimental technique that uses heat produced by microwave energy to kill cancer cells, has showed promise in the treatment of lung cancer. Microwave ablation has been shown in preliminary research to decrease and maybe even remove some lung tumors in small subsets of patients (Burdett & Stewart, 2005; Chansky et al., 2017; Howington, Blum, Chang, Balekian, & Murthy, 2013; Pignon et al., 2008; Timmerman et al., 2010; van den Berg, Klinkenberg, Groen, & Widder, 2015).

The evolution of medication resistance, which is unavoidable, is the major barrier to targeted cancer therapy. Different strategies are used by tumor cells to fend off the targeting agent. Secondary resistance mutations on the target kinase domain most frequently appear in EGFR-

mutant non-small cell lung cancer and reduce the binding affinity of first- and second-generation drugs. The activation of parallel bypass pathways and phenotypic change are additional resistance defense mechanisms. Sequential monotherapies promise to temporarily address the issue of acquired drug resistance, but it is clear that their effectiveness is constrained by the tumor cells' capacity to adapt and develop novel resistance mechanisms in order to survive in the drug environment (Dearden et al., 2017; Jenkins et al., 2017; Karlovich et al., 2016; Marchetti et al., 2015; Wu et al., 2015).

The minimal residual disease cells, a small subpopulation of cells that can withstand the drug and eventually develop additional mutations that allow them to regrow and become the dominant population in the therapy-resistant tumor, have been nominated as a model of drug resistance and tumor progression under targeted therapy in recent studies. This subgroup of cells appears to have undergone a subclonal event, giving rise to driver mutations distinct from the one that causes tumors in the most common ancestor. In order to identify the resistance drivers that emerge from branching development, it is crucial to comprehend intratumoral heterogeneity, which is what causes minimal residual illness.(Bozic et al., 2013; Buder, Tomuta, & Filipits, 2016; Diaz & Bardelli, 2014; Kibirova, Mattes, Smolkin, & Ma, 2019; Zhang et al., 2017).

Over the past ten years, numerous technical, pharmaceutical, and service advancements have been made in the staging and treatment of lung cancer, but doubts about how to most effectively use these advancements and their cost-effectiveness persist. To determine whether newer radiation methods, such SABR, are similar to surgery for lung cancer in its early stages, more research is required. The cost-effectiveness of the more recent targeted medicines is still a hot topic, as is the question of whether investing more money on early supportive care would be wise. Even if there are novel therapies available, access to them is uneven, and more thought needs to be given to resource commissioning to address the hub and spoke effect.

8.1. A New Strategy For Current Lung Cancer Treatment:

For patients with NSCLC, targeted treatments and immunotherapies have become realistic therapy choices, while therapeutic advances for SCLC have not yet been made. Although the majority of SCLC patients initially benefit from frontline cytotoxic therapy, recurrence is all but guaranteed. There are typically few therapeutic choices available for patients because the

ensuing disease is frequently severe and resistant to additional therapy(Ardizzoni et al., 1997; Farago & Keane, 2018; George et al., 2015; Owonikoko et al., 2012; Peifer et al., 2012; Rudin et al., 2012).

SCLC exhibits increased expression of the DNA damage repair enzyme poly (ADP-ribose) polymerase (PARP), making it a possible therapeutic target for this particular tumor type. The inclusion of DNA-damaging drugs has been shown to synergize with PARP inhibitors, providing a promising method for the treatment of recurrent SCLC tumors, whereas the inhibition of PARP alone has demonstrated little to no benefit in this situation(Farago et al., 2019).

The researchers carried out a co-clinical trial in patient-derived xenograft (PDX) models taken from 22 patients to clarify potential biomarkers that could predict responsiveness to this exploratory treatment regimen. They discovered that a molecular signature made up of four genes involved in the inflammatory response could differentiate between sensitive and resistant models, and that low basal expression of these genes was associated with resistance to both the treatment combination under study and platinum etoposide, the standard first-line chemotherapy for SCLC patients(Farago et al., 2019).

Conclusions:

Lung cancer is one of the most frequent malignancies that results in death globally. Lung cancer, also known as lung carcinoma, is a malignant lung ~~tumour~~tumor that is ~~characterised~~characterized by unrestrained cell proliferation in the lung tissues. If untreated, this ~~tumour~~tumor has the potential to metastasis, or grow outside of the lung, into nearby tissue or other parts of the body. The majority of primary lung malignancies, sometimes referred to as cancers that start in the lung, are epithelial cell carcinomas. The two principal types of lung cancer are non-small-cell lung carcinoma and small-cell lung carcinoma (NSCLC). More research is needed to evaluate whether more recent radiation techniques, including SABR, are comparable to surgery for treating lung cancer in its early stages. The question of whether spending more money on early supportive care would be prudent is still a heated topic, as is the cost-effectiveness of the more recent targeted medications. Even if novel medicines are available, there is uneven access to them, and resource commissioning needs to be given more consideration to overcome the hub and spoke effect.

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