IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 3, November 2025
Impact Factor: 7.67

Screening on Lung Cancer: Etiology, Pathophysiology, Treatment

Warkhade Kishor K and Pawar Reshma D
Sahakar Maharshi Kisanrao Varal Patil College of Pharmacy, Nighoj

Abstract: *Lung cancer was the most commonly diagnosed cancer in the world as well as the leading cause of cancer death in men globally in 2008.1 Among women, world wide, it was the fourth most commonly diagnosed cancer and the second leading cause of cancer death[29]. Among women, world wide, it was the fourth most commonly diagnosed cancer and the second leading cause of cancer death[30].Lung cancer is one of the most common malignant cancers in most countries and is the leading cause of death among cancer diseases worldwide. Despite constant progress in diagnosis and therapy, survival rates of patients diagnosed with lung cancer remain unsatisfactory.Small-cell lung cancer (SCLC) accounts for roughly 15% of all lung malignancies and is distinguished by a high proliferative rate, a proclivity for early metastasis, and a poor prognosis. Exposure to cigarette carcinogens is highly linked to SCLC. Only one-third of individuals have earlier-stage illness that is responsive to possibly curative multimodality treatment at the time of diagnosis. SCLC genomic analysis revealed a high mutation load and widespread chromosomal rearrangements, nearly usually with functional inactivation of the tumour suppressor genes TP53 and RB1. The relative expression of prominent transcriptional regulators has been used to identify subtypes of illness in both human SCLC and murine models, revealing significant intra-tumoural variation. Tumor development, metastasis, and acquired treatment resistance have been linked to aspects of this heterogeneity. Despite the fact that clinical progress in the treatment of SCLC has been notoriously poor, a greater knowledge of the biology of the disease has revealed new vulnerabilities that might be targeted therapeutically. Immune checkpoint blockade, which was recently introduced into the treatment of SCLC patients, has given benefit to patients, with a small fraction of patients experiencing long term benefits. Strategies to focus tailored therapy to the patients most likely to react and to extend the long-term benefits of successful anti-tumor immunity to a larger number of patients are urgently needed and are now being researched.*

Keywords: etiology, Risk factor, pathophysiology, symptoms, treatment-dignosis.

I. INTRODUCTION

A decade ago, tumor-promoting inflammation and avoiding immune destruction were added to the list of hallmarks of cancer, the group of molecular properties that characterize malignant tumors [2].Lung cancer has been the most common cancer worldwide since 1985, both in terms of incidence and mortality. Globally, lung cancer is the largest contributor to new cancer diagnoses (1,350,000 new cases and 12.4% of total new cancer cases) and to death from cancer[1] . Malignant lung cancer is still a current clinical problem, posing a real threat to the entire world population[8,14,15].

Cancer is characterized by uncontrolled cell growth and acquisition of metastatic properties. In most cases, activation of oncogenes and/or deactivation of tumor suppressor genes lead to uncontrolled cell cycle progression and inactivation of apoptotic mechanisms[4].Lung cancer arises from the cells of the respiratory epithelium and can be divided into two broad categories. Small cell lung cancer (SCLC) is a highly malignant tumor derived from cells exhibiting neuroendocrine characteristics and accounts for 15% of lung cancer cases. Non–small cell lung cancer (NSCLC), which accounts for the remaining 85% of cases, is further divided into 3 major pathologic subtypes: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma[1] .Small-cell lung cancer (SCLC) is a high-grade neuroendocrine carcinoma that mostly affects current or past smokers and has a dismal prognosis[7,11].SCLC accounts for around 15% of all lung cancer cases. SCLC patients typically present with respiratory symptoms such as cough, dyspnea (laboured

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 3, November 2025 Impact Factor: 7.67

breathing), or haemoptysis (blood cough), with imaging revealing a centrally located lung mass and frequently bulky thoracic lymph node involvement; two-thirds of patients have distant metastatic disease at the time of diagnosis[11].The contralateral lung, brain, liver, adrenal glands, and bone are the most common sites of metastasis. The concentration of circulating tumour cells (CTCs) in SCLC is among the highest of any solid tumour, reflecting its strong metastatic proclivity[12].Although more than half of lung cancers are diagnosed at a late stage, when cure is unlikely, the survival of patients diagnosed with Stage I lung cancer is also surprisingly low[6,10].In normal circumstances, malignant cells should be detected and destroyed by the immune system as soon as they appear, in a process called immune surveillance [2] .Lung cancer was the most commonly diagnosed cancer and the leading cause of cancer death in men in 2008 globally.2 For women, lung cancer was the fourth most commonly diagnosed cancer and the second leading cause of cancer death[1] .Surgery and adjuvant platinum-based chemotherapy may be used in the few patients who show with extremely early-stage illness upon diagnosis, but most patients with early-stage or locally progressed disease are treated with concomitant radiation and platinum-based chemotherapy[13].Up to 80% of cancer patients suf fer from a multiorgan, metabolic wasting syndrome known as cancer cachexia, which results in the death of up to one third of these cancer patients[3].

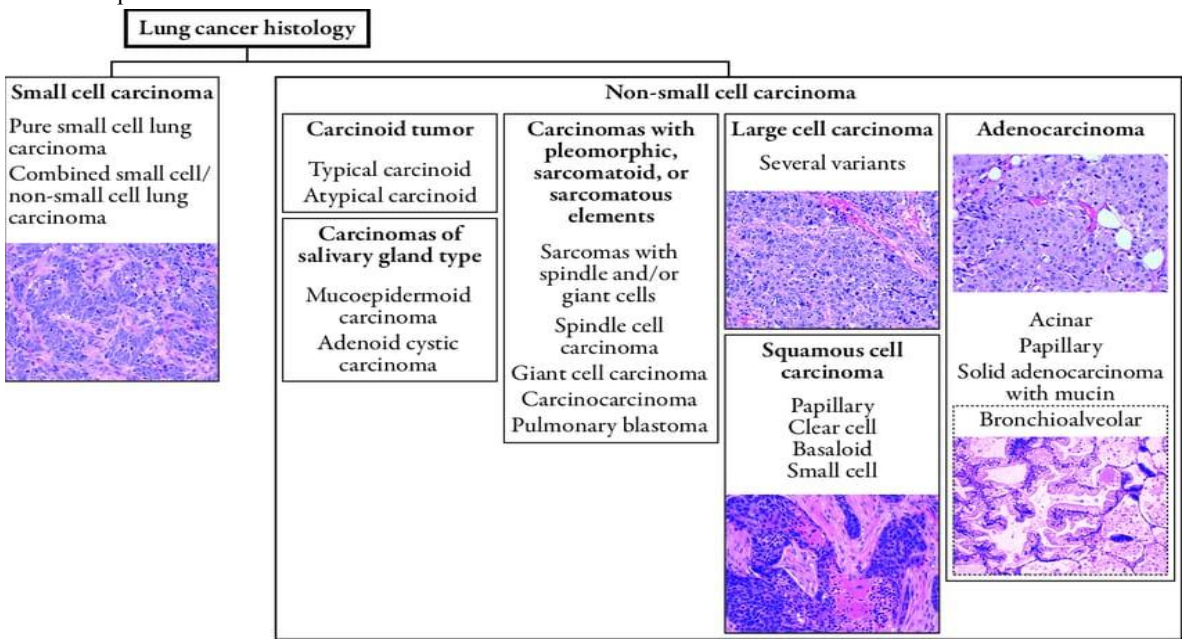

Fig 1: Lung Hiostology

Etiology:

Exogenous noxae have a decisive role in the development of lung cancer—in particular, cigarette smoke inhalation. About 90% of lung cancers may be ascribed to this cause[16]. Other relevant etiological factors are occuptional exposure to asbestos, polycyclic hydrocarbons (in soot and tar), chromates, arsenic, and nickel. Radon, a gaseous radio active decay product of uranium, is naturally present as background radiation that varies in intensity from region to region and is also present in uranium mines[9]. There are several studies that show a relationship between air pollution and radon exposure and SCLC in never-smokers, although the evidence for both is weak[7,17].

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 3, November 2025
Impact Factor: 7.67

Risk Factor:

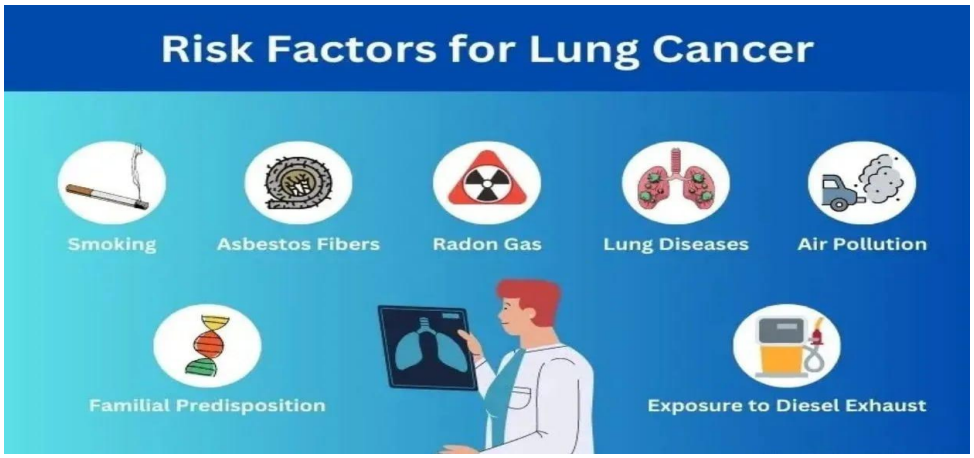

Fig 2: Risk factor

SCLC is one of the malignancies with the strongest epidemiological links to tobacco, and its prevalence tends to lag behind that of smoking by roughly 30 years[18,7]. Only 2% of SCLC cases occur in never-smokers (defined as fewer than 100 cigarettes smoked in their lifetime)[19]. There are several studies that show a relationship between air pollution and radon exposure and SCLC in never-smokers, although the evidence for both is weak. Inherited genetic variables are likely to play a minimal influence in the development of SCLC susceptibility[20,21,22].

Fig 3: Cancerous lung

Pathophysiology:

Lung cancer is the third most frequently diagnosed cancer in Germany in both men and women[23]. Once smoking has stopped, the risk of developing lung cancer reduces over time[10]. Other rel evant etiological factors are occuptional exposure to asbestos, polycyclic hydrocarbons (in soot and tar), chromates, arsenic, and nickel. Radon, a gaseous radioactive decay product of uranium, is naturally present as background radiation that varies in intensity from region to region and is also present in uranium mines[24]. Lung cancer can develop as a consequence of several genetic factors and epigenetic changes (for example, point mutations, amplifications, insertions, deletions and translocations)[25]. The molecular basis of lung cancer should be understood as the accumulation of many genetic and epigenetic changes in the

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 3, November 2025
Impact Factor: 7.67

nucleus of the cell, which occur over a long period of time[26]. The cancer process is initiated when a given cell breaks out of the control of the mechanisms that determine its division and location. Its cell cycle is similar to that of normal cells, with the difference that this cell does not submit to regulatory mechanisms and becomes insensitive to signals from other cells. Disorders in the expression of genes regulating the cell cycle play a key role in any neoplastic transformation. The initiation and progression of the neoplastic process is influenced by the following:

Abnormalities in the regulation of the cell cycle; Mutations in proto-oncogenes and tumor suppressor genes; Disorders of the DNA repair process; Increased expression of growth factors and angiogenesis; Avoidance of apoptosis (mutations of anti- and pro-apoptotic genes);EW Increased telomerase activity; 4 of 31 Tissue invasion and metastasis.[9].

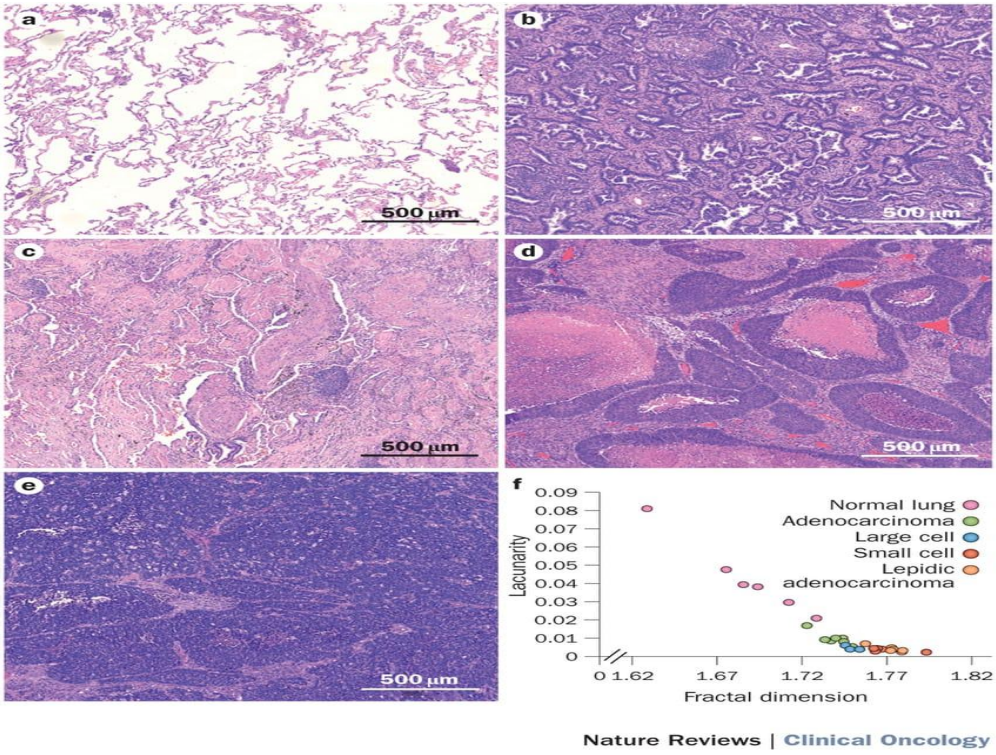

Fig 4: Cancer cell images

Clinical Presentation

Patients with lung cancer are almost always symptomatic at diagnosis [74] Symptoms can be caused by the primary tumor (e.g., cough, hemoptysis); intrathoracic spread (e.g., Horner syndrome, superior vena cava obstruc tion); and distant metastases (e.g., bone pain). These symptoms are a result of ectopic pro duction of hormones from the tumor or the body's reaction to the tumor, and are not directly attributable to the tumor or metas tasis. About 10% of patients with lung can cer present with a paraneoplastic syndrome, and this rate is higher in patients with SCLC[74] . The best treatment for paraneoplas tic syndromes is treatment of the underlying cancer[74] . Digital clubbing is a common para neoplastic syndrome finding that is poorly understood, and it is more common with NSCLC. Most data about symptoms at presenta tion of lung cancer are from referral centers, making extrapolation to the primary care setting difficult [75] Two individual symptoms that significantly increase the likelihood of lung cancer are digital clubbing and hemop tysis[74-77] Other independent predictors of lung cancer include loss of appetite, weight loss, fatigue, dyspnea, chest or rib pain, and an increasing number of visits to evaluate persistent cough[76] .Patients rarely present with only one symptom, and the positive predictive value is higher when two or more symptoms are reported. For example, the combination of weight loss and hemopty sis has a positive predictive value of 9.2% [77]Lung can cer should be highly

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 3, November 2025 Impact Factor: 7.67

suspected in any patient older than 40 years with risk factors and symptoms. However, phy sicians must remember that lung cancer can occur in younger persons and in individuals without known risk factors.

Initial Evaluation

The initial evaluation of a patient with suspected lung cancer begins with a history and physical examination; complete blood count; measurement of alkaline phos phatase, hepatic transaminase, and calcium levels; chem istries (electrolytes, blood urea nitrogen, creatinine); and chest radiography [78] .Normal findings on a chest radio graph do not rule out lung cancer because a small tumor can be hidden within the mediastinum or elsewhere in the chest. If suspicion remains high because a likely alter native diagnosis is not identified on the chest radiograph, contrast-enhanced computed tomography (CT) should be performed, followed by positron emission tomography if necessary [74.76.78] A multidisciplinary team consisting of a pulmonolo gist, medical oncologist, radiation oncologist, patholo gist, radiologist, and thoracic surgeon then plans the diagnostic evaluation, the results of which guide

Symptoms:

Most patients with lung cancer have symptoms at the time they are diagnosed. However, there are no specific early symtoms. The symptoms of lung cancer (Box) may be caused by endobronchial growth, intrathoracic extension, or distant metastases. In addition, systemic signs of cachexia and, occasionally, also symptoms of paraneoplastic syndrome may be encountered[10].

❖ Cough ❖ Dyspnea❖ Hoarseness ❖ Chest pain ❖ Wheezing ❖ Hemoptysis ❖ Nausea/Vomiting ❖ Swelling of face and arms ❖ Anorexia ❖ Weight Loss ❖ Fatigue ❖ Bone pain ❖ Clubbing ❖ Headache ❖ Seizures[5].

Prevention:

All measures that reduce cigarette smoking reduce the incidence of lung cancer[10].

Treatment/dignosis:

Determining the stage of lung cancer includes an assessment of the status of the primary tumor (feature T, tumor), regional lymph nodes (feature N, node) and organs where metastases may be present (feature M, metastasis)[8].

Local therapy modalities are surgery and radiotherapy. For systemic therapy, conventional chemotherapy and increasingly also targeted therapies (i.e. interventions that affect tumor-specific structures at the molecular level) are employed. Chemotherapy is polychemother apy—so long as the patient's condition permits[10]. Treatment for lung cancer is often multimodal. Radiotherapy and chemotherapy can be administered simultaneously as radiochemotherapy. Chemotherapy, radiotherapy, and radiochemotherapy may precede surgery (neoadjuvant therapy) or may follow it (adjuvant therapy)[27].

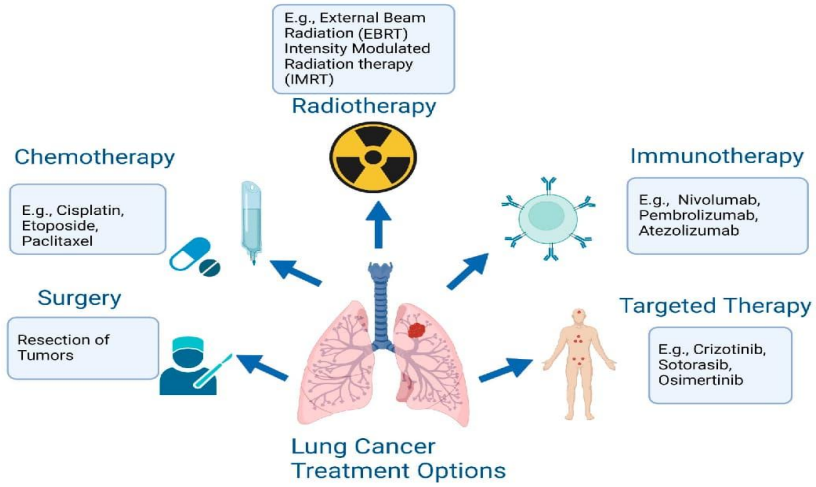

Fig 5: lung cancer treatment

DOI: 10.48175/IJARSCT-29876

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 3, November 2025 Impact Factor: 7.67

MOLECULARALTERATIONSANDTARGETEDTHERAPIES IN LUNG CANCER:

In the past years, with the development of new targeted therapies, tremendous efforts have been direct ed toward identifying potentially druggable molecular alterations, especially against known activating muta tions. Although numerous mutations have been described in lung adenocarcinoma,9 the mutation status remains unknown in more than 50% of cases.10 To date, we can identify therapeutic targets in only 20% of lung [29,10].

Genotype-Phenotype Correlations in Lung Cancer:

Adenocarcinoma is the most frequent cell type of lung cancer, accounting for more than 50% of cancers in the most recent series. To date, most validated and investiga tional predictive biomarkers have been identified in adenocarcinoma, as compared to other cell types, and a new subtype classification of adenocarcinoma has been proposed by the International Association for the Study of Lung Cancer, American Thoracic Society, and the Euro pean Respiratory Society, which takes into account the molecular pathology of these tumors. The current classy fication of lung adenocarcinoma by the World Health Organization recognizes several distinct morphologic subtypes of adenocarcinoma: papillary, acinar, solid, and lepidic. Most lung adenocarcinomas exhibit combine tions of morphologic patterns[32-34]. While the biologic basis for the histologic subtypes remains an area of active investigation, there is evidence that some subtypes may be associated with specific molecular alterations[35-37] or a better outcome[38,39,40].

Targeted Therapies in Lung Cancers With Epidermal Growth Factor Receptor Abnormalities:

Epidermal Growth Factor Receptor.—Recognized mechanisms of epidermal growth factor receptor (EGFR) gain of function in non–small cell lung carcinoma (NSCLC) include somatic activating mutations in the exons encoding the tyrosine kinase domain and EGFR gene amplification[40,41,42].The EGFR mutation status is best determined by gene sequencing abnormalities of EGFR; status may also be observed with gene copy number determined by fluorescence in situ hybridization (FISH) or chromogenic in situ hybridization and with protein expression determined by immunohistochemistry with mutation-specific antibodies. Several mutations have been recently described in the tyrosine kinase domain of EGFR[41-42]. Epidermal growth factor receptor is expressed in 50% of NSCLCs, and its expression is correlated with poor prognosis.These 2 factors make EGFR and its family members prime candidates for the development of targeted therapeutics.27 EGFR kinase domain mutations target 4 exons [39-41]which encode part of the tyrosine kinase domain (the entire kinase domain is encoded by exons 18–24) and are clustered around the adenosine triphosphate–binding pocket of the enzyme. EGFR gene amplification is detected in some EGFR mutation–positive patients as well, and it is reported to be associated with disease progression. A subset of lung adenocarcinomas shows activation of growth factor re ceptor (EGFR) by mutations and/or amplification but the interaction between them is complex and unclear. Us ing novel techniques, including EGFR mutation–specific immunohistochemistry, Sholl et a studied a unique cohort known to have a high prevalence of EGFR muta tions; the authors showed that EGFR-amplified lung adenocarcinomas have distinct genetic alterations, unique clinic pathologic features, and worsened prognosis. Fur thermoses, EGFR amplification and EGFR mutations are heterogeneously distributed within any given tumor. These are novel and important findings with implications for the efficacy of treatment with tyrosine kinase inhibitors for patients with EGFR-mutant lung adenocarcinoma[43].

Recent discoveries have described EGFR mutation–specific antibodies that could help in the rapid screening of lung cancers with EGFR mutations [44]. Mutations in the tyrosine kinase domain of the epidermal growth factor receptor have prognostic signify cancel, since patients with EGFR-mutant NSCLC have prolonged disease-free survival, compared with those with wild-type disease, regardless of the treatment received[45,45]. Although EGFR mutations are predictive of response to EGFR tyrosine kinase inhibitor (TKI) therapy, they do not appear to be predictive of a differential effect on survival[46].

Targeted Agents Against Lung Cancer With EGFR Mutations.

—The 2 TKI agents currently approved for use in lung cancer, which target lung cancer with EGFR mutations, are gefitinib (2002) and erlotinib (2003). EGFR mutation is a specific target for therapy by TKIs and is a validated biomarker of treatment response. The clinical utility of this biomarker is supported by prospective clinical trials that

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 3, November 2025 Impact Factor: 7.67

have demonstrated a progression-free survival benefit of TKI as first-line therapy in EGFR mutant patients. Based on current data, predictive biomarker tests for EGFR should involve mutational analysis. Mutation-specific antibodies for EGFR can be used for screening, but negative immunohistochemistry findings will require mutation analysis to exclude uncommon EGFR mutations that are not detected by these antibodies. EGFR FISH testing is less predictive of TKI response rate than mutation testing in clinical studies, and currently should not be used as a method for EGFR TKI treatment selection. Resistance to TKI therapy is associated with KRAS mutation and specific acquired EGFR mutations such as T790M. These molecular events, as well as other genetic alterations in c-Met (amplification), ERBB3 (overexerts soon), and epiregulin (autocrine loop activation), account for approximately 50% of cases of TKI resistance [47-49].

Genotype-Phenotype Correlations:

For patients with lung adenocarcinoma treated with erlotinib and befit nib, favorable responses were associated with adenocar cinoma with lepidic patterns.18 This finding led to trials of gefitinib and erlotinib that showed that 17% to 22% of patients had a response to gefitinib [50,51].The relationship of EGFR mutation status with adenocarcinoma subtype is a matter of intense debate[52,53]. Genetic abnormalities can be seen in different histologic subtypes, although with various frequency. One characteristic correlation is that mucinous adenocarcinoma (Figure 2) may be exclude lively thyroid transcription factor 1 (TTF1) negative and EGFR-mutation negative, but it may have Ras mutation and expresses CDX2, possibly because of its presumed derivation from bronchiolar mucinous goblet cells[54].

Targeted Therapies With Angiogenesis Inhibitors in Nonsquamous NSCLC :

Recent studies show that NSCLCs with histologic profiles other than squamous cell carcinoma appear to be more strongly associated with response to treatment with bevacizumab. Bevacizumab (Avastin, Genentech/ Roche, South San Francisco, California) is a monoclonal antibody with high affinity for vascular endothelial growth factor (VEGF). Despite the potential benefit of bevacizumab for some patients with previously untreat ed advanced NSCLC[55,56] .the appropriate clinical setting for the use of this antiangiogenic agent is stringent, owing to safety issues raised in patients with lung squamous cell carcinoma (SCC), and requires an accurate diagnosis of the pretreatment biopsy specimens. The clinical activity of bevacizumab in inoperable, locally advanced, metastatic, or recurrent NSCLC was first shown in chemotherapy-naive patients.48 Patients with non-squamous NSCLC histology are the only patients who benefit from treatment with bevacizumab in combination with chemotherapy[55]. Bevacizumab is currently contraindicated in patients with SCC on the basis of the result so far ecently published phase II trial[48]. in which 31% of patients with SCC histology developed a life-threatening or fatal hemoptysis associated with bevacizumab, although it is still not clear whether histology alone is the reason for increased bleeding risk. Excluding patients with SCC appeared to markedly limit the risk of life-threatening bleeding complications associated with bevacizumab.

Targeted Therapies in Lung Cancers With Anaplastic Lymphoma Kinase Abnormalities:

On August 26, 2011, the US Food and Drug Administration approved crizotinib for the treatment of patients with locally advanced or metastatic NSCLC that is positive for anaplastic lymphoma kinase (ALK) by FISH (Figure 3). Anaplastic large cell lymphoma kinase gene (ALK) was originally identified through cloning of the t(2;5)(p23;35) translocation found in a subset of anaplastic large cell lymphomas (ALCLs), a tumor of T-cell line age [57,58] .ALK encodes a tyrosine kinase receptor that is normally expressed only in select neuronal cell types. In ALK-rearranged ALCLs, the intracytoplasmic portion of ALK is fused to the N-terminal portion of nucleophosmin (NPM), resulting in a chimeric protein with constitu tive kinase activity. Several other balanced translocations involving ALK have been discovered in ALCLs; however, the various resulting chimeric proteins all retain the ALK kinase domain [59].The importance of the kinase activity is exemplified by ALK-rearranged ALCL cell lines, which are dependent upon ALK enzymatic activity for growth and survival. Recently, ALK rearrangements were identified in rare NSCLC cell lines and in isolated primary adenocarcino mas from Japanese and Chinese populations [60.61]Most ALK rearrangements within NSCLCs derive from an interstitial deletion and inversion in chromosome arm 2p and result in the EML4-ALK fusion gene product [60,61] Murine tumors ,human celllines, and recently published clinical trial have shown that lung

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 3, November 2025 Impact Factor: 7.67

cancers expressing EML-ALK are sensitive to inhibitors of ALK kinase activity [62-64] Thus, it is critical to efficiently and accurately identify those lung adenocarcinomas that harbor ALK rearrangements in routine practice in order to guide the appropriate clinical therapy. None of the ALK-rearranged adenocarcinomas showed coexistent mutations in EGFR. Recently published studies show that ALK-rearranged adenocarcinomas are more likely to present in younger patients with a history of never-smoking, and at higher stage, relative to those without ALK rearrangements(ALKgermline).Most ALK rearranged adenocarcinomas had a distinct histologic appearance represented by solid tumor growth and frequent signet ring cells with abundant intracellular mucin (Figure 4)[65]The developing evidence-based guideline recommendations of the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology for the molecular testing of lung cancers will likely conclude that (1) ALK rearrangements should be typically assessed by molecular cytogenetic techniques such as FISH and (2) the currently commercially available ALK monoclonal anti bodies may potentially help in screening lung cancers for ALK rearrangements. However, some antibodies have poor performance in identifying ALK-rearranged lung cancers; some antibodies are very good, but not commercially available; and some hold promise, but the published data and the number of cases test edare limited. Therefore, it is premature to make recommendations stating that immune histochemistry is useful in identifying cases with ALK rearrangements. In the meantime, FISH is the recommended test for ALK.

Other Molecular Abnormalities That Show Promise for Targeted Therapies in Lung Cancer :

Human Epidermal Growth Factor Receptor 2.—

Unlike the other members of the human epidermal growth factor receptor (HER) family, HER2/neu is not strictly a receptor tyrosine kinase because no high-affinity endogenous ligand has been identified. HER2/neu acts as a signaling network coordinator and amplifier when it forms hetero dimers with other HER family members. HER2/neu mutations occur in 2% of NSCLCs [66,67} .These are in-frame insertions in exon 20 that target the corresponding tyrosine kinase domain region, as in EGFR-insertion mutations. These mutations occur in the same subpopulation as that with EGFR mutations (adenocarcinoma, never-smoker, East Asian, and women).AlthoughHER2/ neu mutations occur in only 2% of patients, HER2/neu is frequently over expressed (to some degree) in NSCLC and appears to be associated with drug resistance, increased metastatic potential, increased production of VEGF, and poor prognosis.60 HER2/neu-mediated resistance to DNA damaging agents requires the activation of Akt, which phosphorylates murine double minute 2 (MDM2) and therefore enhances MDM2-mediated ubiquitination and degradation of p53. Blocking the Akt pathway mediated by HER2-neu increases the cytotoxic effect of DNA damaging drugs in tumor cells with wild-type TP53. Furthermore, recent studies have shown that the G/G genotype of the MDM2 polymorphism is associated with worse overall survival among patients with early-stage NSCLC, particularly those whose tumors have squamous cell histology[68]. Trastuzumab is a chimerized monoclonal antibody against HER2/neu. Combinations of trastuzumab and chemotherapy are well tolerated, with response rates of 21% to 40%[69]. One trial showed that patients whose tumors highly overexpressed HER2/neu (3+) by immu nohistochemistry or showed evidence of amplification by FISH had a good response. It appears that highly overexpressing HER2/neu cases of NSCLC (3+ by immu nohistochemistry), although relatively infrequent (3% 9%), may show benefit with treatment with trastuzumab. MET Proto-oncogene.— MET can be activated by mutations, autocrine/paracrine growth, over expression by gene amplification, or decreased degradation.63 Germ line and somatic MET gene mutations have been reported in hereditary and sporadic papillary renal cell cancers[70] In other cancers, MET gene mutations and amplifications have been reported to be predictors of response to therapy.65 Expression of MET and phospho-MET has been studied in lungcancer; recently, 40% of lung cancer tissues were shown to over express MET [71,72,73].Recent studies have shown that survival for patients with NSCLC who have 5 or more copies/cell is worse than for those who have less than 5 copies/cell; moreover, MET gene amplification leads to EGFR tyrosine kinase resistance in EGFR-mutant patients. Anti-hepatocyte growth factor antibodies, anti MET antibodies, and small-molecule MET TKI inhibitors are all in various stages of development, and elucidation of predictive biomarkers for MET inhibitors will be important for future trials and treatment decisions [70].

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 5, Issue 3, November 2025 Impact Factor: 7.67

OTHER TARGETED MOLECULAR THERAPIES:

There has been tremendous research and investment in the development of small molecules that target key proteins in cell signaling pathways that are aberrantly altered in disease, particularly in carcinogenesis. For instance, receptor tyrosine kinases (RTKs) serve as potential therapeutic targets in several solid tumors, including lung cancer. The RTK c-KIT is highly expressed in small cell lung carcinomas (although it is not mutated), and this has led to clinical trials with the specific c-KIT inhibitor STI571 (Gleevec [imatinib], Novartis, East Han over, New Jersey), alone and in combination therapy. However, these trials have failed to show a meaningful benefit from the imatinib treatment. Antibodies against the angiogenic factor VEGF and small molecules against VEGF receptors, such as SU5416 (an inhibitor of Flk-1 receptor), are being tested in NSCLC and other tumor types. More recently, modification of gene expression with small interfering RNAs has the promise of being the most powerful tool yet[69].

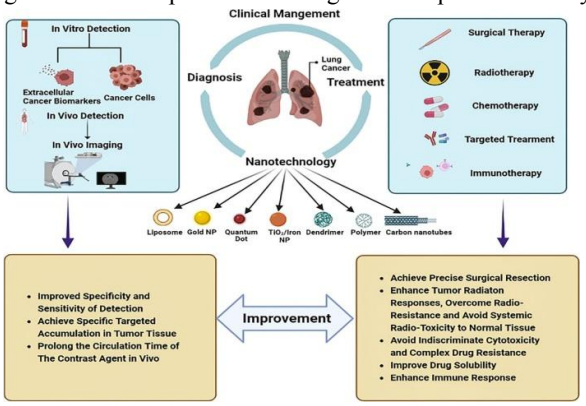

Fig6:Clinical Managment of lung cancer

II. CONCLUSION

Risk factors for lung cancer have been mostly understood and well characterized. Primary prevention of this disease therefore seems to be easy to implement by eliminating environmental hazards and smoking. Despite this, lung cancer remains the leading cause of death among malignant cancers in all highly developed countries. The causes of this phenomenon should be sought in the growing problem of environmental pollution, but above all in the difficulty of eliminating the addiction to smoking. In the prevention of lung cancer, the basic factor is not smoking. Tobacco smoke is the most common cause of lung cancer. It is worth noting that electronic cigarettes are also not recommended in the context of prevention. The lack of proper education means that young people continue to reach for nicotine-containing products, first e-cigarettes and then traditional cigarettes. However, nicotine addiction is extremely strong in many people, and eliminating the addiction using traditional methods (psychotherapy, nicotine replacement therapy, pharmacotherapy) turns out to be impossible. In such cases, reducing the health risk associated with smoking cigarettes can be achieved by replacing them with smokeless products containing nicotine. Many scientific studies have shown that aerosols from e-cigarettes and tobacco heating devices contain over 90% less carcinogenic substances than cigarette smoke[28]. The clinical application of molecular diagnostic techniques has allowed a more precise and rapid assessment of lung cancer and will help to triage the patient to ‘‘personalized’’ therapies that will have the highest success rates for eradicating the tumor. Our knowledge about lung cancer has changed radically in the past decade, and progress mainly depends on identifying new predictive biomarkers. We need to better understand both the tumor and the host biology that underlies tumor sensitivity and resistance in order to provide a rationale for specific targeted therapy. Since many targets can be evaluated by multiple laboratory methods, such as sequence analysis, in situ hybridization, and immune histochemistry, it is critical that efforts focus on standardiz ing methodologies for biomarker testing

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 3, November 2025
Impact Factor: 7.67

REFERENCES

[1]. Cruz CS, Tanoue LT, Matthay RA. Lung cancer: epidemiology, etiology, and prevention. Clinics in chest medicine. 2011 Dec;32(4):10-16.

[2]. Pęczek P, Gajda M, Rutkowski K, Fudalej M, Deptała A, Badowska-Kozakiewicz AM. Cancer-associated inflammation: pathophysiology and clinical significance. Journal of cancer research and clinical oncology. 2023 Jun;149(6):2657-72.

[3]. Tichy L, Parry TL. The pathophysiology of cancer-mediated cardiac cachexia and novel treatment strategies: A narrative review. Cancer medicine. 2023 Sep;12(17):17706-17.

[4]. Sarkar S, Horn G, Moulton K, Oza A, Byler S, Kokolus S, Longacre M. Cancer development, progression, and therapy: an epigenetic overview. International journal of molecular sciences. 2013 Oct 21;14(10):21087-113.

[5]. Yoder LH. An overview of lung cancer symptoms, pathophysiology, and treatment. Medsurg Nursing. 2006 Aug 1;15(4):231.

[6]. Granville CA, Dennis PA. An overview of lung cancer genomics and proteomics. American journal of respiratory cell and molecular biology. 2005 Mar;32(3):169-76.

[7]. Alam MS, Malik G, Tanwar P, Naagar M, Singh T, Singh O, Maity MK. A Review on Small-Cell Lung Cancer: Epidemiology, Pathophysiology, RiskFactors, Diagnosis, Clinical Management and Treatment Modalities. International Journal of Current Science Research and Review (ijcsrr). 1969;6(01):129-51.

[8]. Smolarz B, Łukasiewicz H, Samulak D, Piekarska E, Kołaciński R, Romanowicz H. Lung Cancer—Epidemiology, Pathogenesis, Treatment and Molecular Aspect (Review of Literature). International Journal of Molecular Sciences. 2025 Feb 26;26(5):2049.

[9]. Hammerschmidt S, Wirtz H. Lung cancer: current diagnosis and treatment. Deutsches Ärzteblatt International. 2009 Dec 4;106(49):809.

[10]. Fry WA, Phillips JL, Menck HR. Ten-year survey of lung cancer treat ment and survival in hospitals in the United States: a national cancer data base report. Cancer 1999;86:1867–1876.

[11]. Hann CL, Wu MA, Rekhtman N &Rudin CM in Cancer Principles & Practice of Oncology Ch. 49 (edsDeVita VT, Lawrence TS & Rosenberg SA) 671–700 (Wolters Kluwer, 2019).

[12]. Hou JM et al. Clinical significance and molecular characteristics of circulating tumor cells and circulating tumor microemboli in patients with small-cell lung cancer. J. Clin. Oncol 30, 525–532 (2012).

[13]. Kalemkerian GP et al. NCCN guidelines insights: small cell lung cancer, version 2.2018. J. NatlCompr. CancNetw 16, 1171–1182 (2018).

[14]. Vicidomini, G. Current Challenges and Future Advances in Lung Cancer: Genetics, Instrumental Diagnosis and Treatment. Cancers 2023, 15, 3710.

[15]. Rina, A.; Maffeo, D.; Minnai, F.; Esposito, M.; Palmieri, M.; Serio, V.B.; Rosati, D.; Mari, F.; Frullanti, E.; Colombo, F. The Genetic Analysis and Clinical Therapy in Lung Cancer: Current Advances and Future Directions. Cancers 2024, 16, 2882.

[16]. Alberg AJ, Ford JG, Samet JM: Epidemiology of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007; 132: 29–55.

[17]. Rodriguez-Martinez A, Torres-Duran M, Barros-Dios JM &Ruano-RavinaA Residential radon and small cell lung cancer. A systematic review. Cancer Lett 426, 57–62 (2018).

[18]. Huang R et al. Associated links among smoking, chronic obstructive pulmonary disease, and small cell lung cancer: a pooled analysis in the International Lung Cancer Consortium. EBioMedicine 2, 1677–1685 (2015).

[19]. Varghese AM et al. Small-cell lung cancers in patients who never smoked cigarettes. J. Thorac. Oncol 9, 892–896 (2014).

[20]. Rodriguez-Martinez A, Torres-Duran M, Barros-Dios JM &Ruano-RavinaA Residential radon and small cell lung cancer. A systematic review. Cancer Lett 426, 57–62 (2018).

[21]. Wang J et al. Genetic predisposition to lung cancer: comprehensive literature integration, meta-analysis, and multiple evidence assessment of candidate-gene association studies. Sci. Rep 7, 8371 (2017).

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 3, November 2025
Impact Factor: 7.67

[22]. Lamichhane DK et al. Lung cancer risk and residential exposure to air pollution: a korean population-based case-control study. Yonsei Med. J 58, 1111–1118 (2017).

[23]. Batzler WU, Giersiepen K, Hentschel S, et al.: Cancer in Germany, 2003–2004. Incidence and Trends. In: Robert Koch Institut, V. Gde KiDe, (eds.): Contributions to Federal Health Reporting. Berlin: Mer cedes Druck, 2008.

[24]. . Alberg AJ, Ford JG, Samet JM: Epidemiology of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007; 132: 29–55.

[25]. Cooper, W.A.; Lam, D.C.; O'Toole, S.A.; Minna, J.D. Molecular biology of lung cancer. J. Thorac. Dis. 2013, 5 (Suppl. S5), S479–S490

[26]. Massion, P.P.; Carbone, D.P. The molecular basis of lung cancer: Molecular abnormalities and therapeutic implications. Respir.

[27]. McCrory DC, Lewis SZ, Heitzer J, Colice G, Alberts WM: Meth- odology for lung cancer evidence review and guideline develop ment: ACCP evidence-based clinical practice guidelines (2nd Edition). Chest 2007; 132: 23–28.

[28]. Sahu, R.; Shah, K.; Malviya, R.; Paliwal, D.; Sagar, S.; Singh, S.; Prajapati, B.G.; Bhattacharya, S. E-Cigarettes and Associated Health Risks: An Update on Cancer Potential. Adv. Respir. Med. 2023, 91, 516–531

[29]. Cagle PT, Chirieac LR. Advances in treatment of lung cancer with targeted therapy. Archives of pathology & laboratory medicine. 2012 May 1;136(5):504-9.

[30]. Sato M, Shames DS, Gazdar AF, Minna JD. A translational view of the molecular pathogenesis of lung cancer. J Thorac Oncol. 2007;2(4):327–343.

[31]. Herbst RS, Heymach JV, Lippman SM. Lung cancer. N Engl J Med. 2008; 359(13):1367–1380.

[32]. Travis WD, Brambilla E, Muller-Hermelink HK, Harris CC, eds. Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart. Lyon, France: IARC Press; 2004. World Health Organization Classification of Tumours; vol 10.

[33]. Barletta JA, Perner S, Iafrate AJ, et al. Clinical significance of TTF-1 protein expression and TTF-1 gene amplification in lung adenocarcinoma. J Cell Mol Med. 2009;13(8B):1977–986.

[34]. Motoi N, Szoke J, Riely GJ, et al. Lung adenocarcinoma: modification of the 2004 WHO mixed subtype to include the major histologic subtype suggests correlations between papillary and micropapillary adenocarcinoma subtypes, EGFRmutations and gene expression analysis. Am J Surg Pathol. 2008;32(6):810 827.

[35]. Finberg KE, Sequist LV, Joshi VA, et al. Mucinous differentiation correlates with absence of EGFR mutation and presence of KRAS mutation in lung adenocarcinomas with bronchioloalveolar features. J Mol Diagn. 2007;9(3):320 326.

[36]. Haneda H, Sasaki H, Shimizu S, et al. Epidermal growth factor receptor gene mutation defines distinct subsets among small adenocarcinomas of the lung. Lung Cancer. 2006;52(1):47–52.

[37]. Hsieh RK, Lim KH, Kuo HT, Tzen CY, Huang MJ. Female sex and bronchioloalveolar pathologic subtype predict EGFR mutations in non-small cell lung cancer. Chest. 2005;128(1):317–321.

[38]. Jackman DM, Chirieac LR, Janne PA. Bronchioloalveolar carcinoma: a review of the epidemiology, pathology, and treatment. Semin Respir Crit Care Med. 2005;26(3):342–352.

[39]. Noguchi M, Morikawa A, Kawasaki M, et al. Small adenocarcinoma of the lung: histologic characteristics and prognosis. Cancer. 1995;75(12):2844–2852.

[40]. Sakao Y, Miyamoto H, Sakuraba M, et al. Prognostic significance of a histologic subtype in small adenocarcinoma of the lung: the impact of nonbronchioloalveolar carcinoma components. Ann Thorac Surg. 2007;83(1): 209–214.

[41]. Lynch TJ, Bell DW, Sordella R, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib. N Engl J Med. 2004;350(21):2129–2139.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 3, November 2025
Impact Factor: 7.67

[42]. Testa JR, Siegfried JM. Chromosome abnormalities in human non-small cell lung cancer. Cancer Res. 1992;52(9 suppl):2702s–2706s.

[43]. Sholl LM, Yeap BY, Iafrate AJ, et al. Lung adenocarcinoma with EGFR amplification has distinct clinic pathologic and molecular features in never smokers. Cancer Res. 2009;69(21):8341–8348.

[44]. Yu J, Kane S, Wu J, et al. Mutation-specific antibodies for the detection of EGFR mutations in non-small-cell lung cancer. Clin Cancer Res. 2009;15(9): 3023–3028.

[45]. Sasaki H, Shimizu S, Endo K, et al. EGFR and erbB2 mutation status in Japanese lung cancer patients. Int J Cancer. 2006;118(1):180–184.

[46]. 36. Mok TS, Wu YL, Thongprasert S, et al. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. N Engl J Med. 2009;361(10):947–957.

[47]. Tang Z, Du R, Jiang S, et al. Dual MET-EGFR combinatorial inhibition against T790M-EGFR-mediated erlotinib-resistant lung cancer. Br J Cancer. 2008; 99(6):911–922.

[48]. Cappuzzo F, Janne PA, Skokan M, et al. MET increased gene copy number and primary resistance to gefitinib therapy in non-small-cell lung cancer patients. Ann Oncol. 2009;20(2):298–304.

[49]. Engelman JA, Zejnullahu K, Mitsudomi T, et al. MET amplification leads to gefitinib resistance in lung cancer by activating ERBB3 signaling. Science. 2007; 316(5827):1039–1043.

[50]. West HL, Franklin WA, McCoy J, et al. Gefitinib therapy in advanced bronchioloalveolar carcinoma: Southwest Oncology Group Study S0126. J Clin Oncol. 2006;24(12):1807–1813.

[51]. Miller VA, Riely GJ, Zakowski MF, et al. Molecular characteristics of bronchioloalveolar carcinoma and adenocarcinoma, bronchioloalveolar carci noma subtype, predict response to erlotinib. J Clin Oncol. 2008;26(9):1472 1478.

[52]. Marchetti A, Martella C, Felicioni L, et al. EGFR mutations in non-small cell lung cancer: analysis of a large series of cases and development of a rapid and sensitive method for diagnostic screening with potential implications on pharmacologic treatment. J Clin Oncol. 2005;23(4):857–865.

[53]. Shigematsu H, Lin L, Takahashi T, et al. Clinical and biological features associated with epidermal growth factor receptor gene mutations in lung cancers. J Natl Cancer Inst. 2005;97(5):339–346.

[54]. Finberg KE, Sequist LV, Joshi VA, et al. Mucinous differentiation correlates with absence of EGFR mutation and presence of KRAS mutation in lung adenocarcinomas with bronchioloalveolar features. J Mol Diagn. 2007;9(3):320 326.

[55]. Sandler A, Gray R, Perry MC, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. N Engl J Med. 2006;355(24):2542 2550.

[56]. West H, Harpole D, Travis W. Histologic considerations for individualized systemic therapy approaches for the management of non-small cell lung cancer. Chest. 2009;136(4):1112–1118.

[57]. Lamant L, Meggetto F, al Saati T, et al. High incidence of the t(2;5)(p23;q35) translocation in anaplastic large cell lymphoma and its lack of detection in Hodgkin's disease: comparison of cytogenetic analysis, reverse transcriptase-polymerase chain reaction, and P-80 immunostaining. Blood. 1996; 87(1):284–291.

[58]. . Morris SW, Kirstein MN, Valentine MB, et al. Fusion of a kinase gene, ALK, to a nucleolar protein gene, NPM, in non-Hodgkin's lymphoma. Science. 1994; 263(5151):1281–1284.

[59]. Swerdlow SH, Campo E, Harris, NL, et al, eds. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon, France: IARC Press; 2008. World Health Organization Classification of Tumours; vol 2.

[60]. Soda M, Choi YL, Enomoto M, et al. Identification of the transforming EML4-ALK fusion gene in non-small-cell lung cancer. Nature. 2007;448(7153): 561–566.

[61]. Rikova K, Guo A, Zeng Q, et al. Global survey of phosphotyrosine signaling identifies oncogenic kinases in lung cancer. Cell. 2007;131(6):1190 1203.

[62]. Soda M, Takada S, Takeuchi K, et al. A mouse model for EML4-ALK positive lung cancer. Proc Natl Acad Sci U S A. 2008;105(50):19893–19897.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 3, November 2025
Impact Factor: 7.67

[63]. Koivunen JP, Mermel C, Zejnullahu K, et al. EML4-ALK fusion gene and efficacy of an ALK kinase inhibitor in lung cancer. Clin Cancer Res. 2008;14(13): 4275–4283.

[64]. .Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. N Engl J Med. 2010;363(18):1693 1703.

[65]. Rodig SJ, Mino-Kenudson M, Dacic S, et al. Unique clinic pathologic features characterize ALK-rearranged lung adenocarcinoma in the western population. Clin Cancer Res. 2009;15(16):5216–5223

[66]. Shigematsu H, Takahashi T, Nomura M, et al. Somatic mutations of the HER2 kinase domain in lung adenocarcinomas. Cancer Res. 2005;65(5):1642 1646

[67]. Stephens P, Hunter C, Bignell G, et al. Lung cancer: intragenic ERBB2 kinase mutations in tumours. Nature. 2004;431(7008):525–526.

[68]. Heist RS, Zhou W, Chirieac LR, et al. MDM2 polymorphism, survival, and histology in early-stage non-small-cell lung cancer. J Clin Oncol. 2007;25(16): 2243–2247.

[69]. Azzoli CG, Krug LM, Miller VA, Kris MG, Mass R. Trastuzumab in the treatment of non-small cell lung cancer. Semin Oncol. 2002;29(1 suppl 4):59–65.

[70]. Lindor NM, Dechet CB, Greene MH, et al. Papillary renal cell carcinoma: analysis of germline mutations in the MET proto-oncogene in a clinic-based population. Genet Test. 2001;5(2):101–106.

[71]. Ma PC, Tretiakova MS, MacKinnon AC, et al. Expression and mutational analysis of MET in human solid cancers. Genes Chromosomes Cancer. 2008; 47(12):1025–1037.

[72]. Benedettini E, Sholl LM, Peyton M, et al. Met activation in non-small cell lung cancer is associated with de novo resistance to EGFR inhibitors and the development of brain metastasis. Am J Pathol. 2010;177(1):415–423.

[73]. Yoshida T, Okamoto I, Okamoto W, et al. Effects of Src inhibitors on cell growth and epidermal growth factor receptor and MET signaling in gefitinib resistant non-small cell lung cancer cells with acquired MET amplification. Cancer Sci. 2010;101(1):167–172.

[74]. Beckles MA, Spiro SG, Colice GL, Rudd RM. Initial evaluation of the patient with lung cancer. Chest. 2003;123(1 suppl):97S-104S.

[75]. Hamilton W, Sharp D. Diagnosis of lung cancer in primary care: a struc tured review. Fam Pract. 2004;21(6):605-611

[76]. Shim J, Brindle L, Simon M, George S. A systematic review of symptom atic diagnosis of lung cancer. Fam Pract. 2014;31(2):137-148.

[77]. Shapley M, Mansell G, Jordan JL, Jordan KP. Positive predictive values of 35% in primary care for cancer: systematic review. Br J Gen Pract. 2010; 60(578): e366-e377.

[78]. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: diagnosis and management of lung cancer, 3rd ed.: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143(5 suppl):e142-165S