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Recent advances in the evidence-based management of non-small cell lung cancer: Current diagnostic approaches, molecular profiling, precision oncology, systemic therapies, surgical management, radiotherapy, and future therapeutic directions

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***Abstract*---Background:** Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer cases and remains one of the leading causes of cancer-related mortality worldwide. Despite improvements in early detection and multidisciplinary care, many patients are diagnosed with advanced disease, resulting in poor long-term survival. Recent advances in molecular diagnostics, targeted therapies, immunotherapy, minimally invasive surgery, and precision medicine have substantially transformed the management of NSCLC and improved clinical outcomes for selected patient populations. **Aim:** This review aimed to summarize current evidence regarding the diagnosis and evidence-based management of NSCLC, with emphasis on risk factors, conventional treatment modalities, biomarker testing, and recent therapeutic advances that support personalized patient care. **Methods:** A comprehensive narrative review was conducted using published clinical guidelines, randomized controlled trials, systematic reviews, meta-analyses, and landmark studies addressing surgical treatment, chemotherapy, radiotherapy, molecular profiling, targeted therapy, and biomarker-directed management of NSCLC. **Results:** Surgical resection remains the preferred treatment for resectable early-stage disease, while platinum-based chemotherapy and radiotherapy continue to play central roles in locally advanced and metastatic NSCLC. Minimally invasive surgical approaches and stereotactic body radiation therapy have improved local disease control with lower treatment-related morbidity. Molecular profiling has identified actionable biomarkers including EGFR, ALK, KRAS, and BRAF mutations, allowing the implementation of targeted therapies that achieve higher response rates and prolonged progression-free survival compared with conventional chemotherapy. Comprehensive biomarker testing has become essential for selecting individualized treatment strategies and optimizing clinical outcomes. **Conclusion:** Contemporary management of NSCLC has shifted toward precision oncology through integration of molecular diagnostics with multidisciplinary treatment approaches. Personalized therapy based on genomic alterations has significantly improved survival, treatment efficacy, and quality of life, while ongoing research continues to expand therapeutic options and advance individualized cancer care.

***Keywords*---**Non-small cell lung cancer, NSCLC, molecular biomarkers, precision medicine, EGFR, ALK, KRAS, BRAF, chemotherapy, radiotherapy, surgery, targeted therapy.

Introduction

Lung cancer remains one of the most significant global public health challenges and continues to be the leading cause of cancer-related mortality among both men and women worldwide. Despite remarkable advances in diagnostic techniques, molecular biology, surgical management, radiotherapy, targeted therapies, and immunotherapy, lung cancer is still associated with poor long-term survival because many patients present with advanced or metastatic disease at

the time of diagnosis. The disease imposes a substantial clinical, social, and economic burden, accounting for more cancer-related deaths than colorectal, breast, and pancreatic cancers combined (1,2). More than half of patients diagnosed with lung cancer die within the first year following diagnosis, and the overall five-year survival rate remains approximately 17.8%, underscoring the urgent need for improved strategies in early detection, individualized treatment, and disease prevention (3). Lung cancer is broadly classified into two major histological categories: small-cell lung carcinoma (SCLC) and non-small cell lung cancer (NSCLC), which account for approximately 15% and 85% of all newly diagnosed lung cancers, respectively (4). NSCLC represents a heterogeneous group of epithelial malignancies characterized by distinct pathological features, molecular alterations, biological behavior, and therapeutic responses. Owing to its high prevalence and diverse molecular landscape, NSCLC has become the primary focus of extensive clinical research aimed at developing personalized therapeutic approaches that improve patient survival and quality of life.

Non-small cell lung cancer is traditionally divided into three principal histological subtypes: squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. Squamous cell carcinoma constitutes approximately 25%–30% of all lung cancer cases and originates from the bronchial epithelial cells lining the central airways. This subtype demonstrates a particularly strong association with long-term cigarette smoking and is commonly located within the proximal bronchi of the lungs (5). Histologically, squamous cell carcinoma is characterized by keratinization and intercellular bridges, features that distinguish it from other NSCLC subtypes. Although advances in smoking cessation programs have contributed to a gradual decline in its incidence, squamous cell carcinoma continues to represent a substantial proportion of smoking-related lung malignancies. Adenocarcinoma is the most common histological subtype of NSCLC, accounting for approximately 40% of all lung cancer cases (6). It originates primarily from type II alveolar epithelial cells and small airway epithelial cells responsible for mucus production and surfactant secretion. Unlike squamous cell carcinoma, adenocarcinoma occurs frequently in both smokers and individuals who have never smoked and affects men and women across all age groups (7). It typically develops in the peripheral regions of the lungs, a distribution that has been partially attributed to changes in cigarette design, particularly the introduction of filters that encourage deeper inhalation of tobacco smoke into distal lung tissue (8,9). Compared with other NSCLC subtypes, adenocarcinoma generally exhibits slower tumor growth, increasing the likelihood of detection before extensive metastatic spread. Furthermore, this subtype is characterized by numerous targetable molecular alterations, including mutations involving epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ROS1, KRAS, BRAF, MET, RET, and other oncogenic drivers, making it particularly amenable to precision medicine and targeted therapy.

Large cell carcinoma represents the least common major subtype of NSCLC, accounting for approximately 5%–10% of lung cancers (10). It is considered an undifferentiated epithelial malignancy because it lacks the morphological characteristics of both squamous and glandular differentiation and is frequently diagnosed after exclusion of other histological subtypes. Large cell carcinoma often demonstrates aggressive biological behavior, rapid tumor growth, and early

metastatic dissemination to regional lymph nodes, the chest wall, and distant organs. Similar to squamous cell carcinoma, this subtype has a strong association with tobacco smoking (11). The increasing understanding of the molecular mechanisms underlying NSCLC has fundamentally transformed its clinical management over the past two decades. Advances in molecular diagnostics, biomarker identification, targeted therapies, immune checkpoint inhibitors, and multidisciplinary treatment strategies have significantly improved survival outcomes for selected patient populations. Nevertheless, NSCLC continues to present considerable diagnostic and therapeutic challenges due to tumor heterogeneity, acquired treatment resistance, and disease recurrence. Consequently, ongoing research continues to focus on optimizing precision medicine approaches, identifying novel therapeutic targets, and developing innovative treatment strategies that improve long-term survival while minimizing treatment-related toxicity.

Risk Factors

The development of non-small cell lung cancer (NSCLC) is influenced by a complex interaction of environmental exposures, occupational hazards, genetic susceptibility, and lifestyle factors. Although considerable progress has been achieved in understanding the molecular mechanisms of lung carcinogenesis, prevention remains the most effective strategy for reducing disease incidence and mortality. Identification of modifiable and nonmodifiable risk factors is therefore essential for implementing targeted prevention programs, promoting early detection, and identifying individuals who may benefit from lung cancer screening. Cigarette smoking remains the single most important risk factor for lung cancer and accounts for the overwhelming majority of cases worldwide. The widespread commercialization of manufactured cigarettes during the twentieth century was accompanied by a dramatic increase in lung cancer incidence, firmly establishing tobacco smoking as the principal etiological factor for the disease (2). Smoking is responsible for approximately 80% of all lung cancer-related deaths, with the risk increasing proportionally according to both the duration of smoking and cumulative tobacco exposure, commonly measured in pack-years (12). Tobacco smoke contains thousands of chemical compounds, including numerous established carcinogens such as polycyclic aromatic hydrocarbons, nitrosamines, benzene, and heavy metals. These carcinogens induce DNA damage, promote genetic mutations, and activate oncogenic signaling pathways that contribute to malignant transformation. The risk of lung cancer decreases after smoking cessation; however, former smokers continue to experience an elevated lifetime risk compared with individuals who have never smoked.

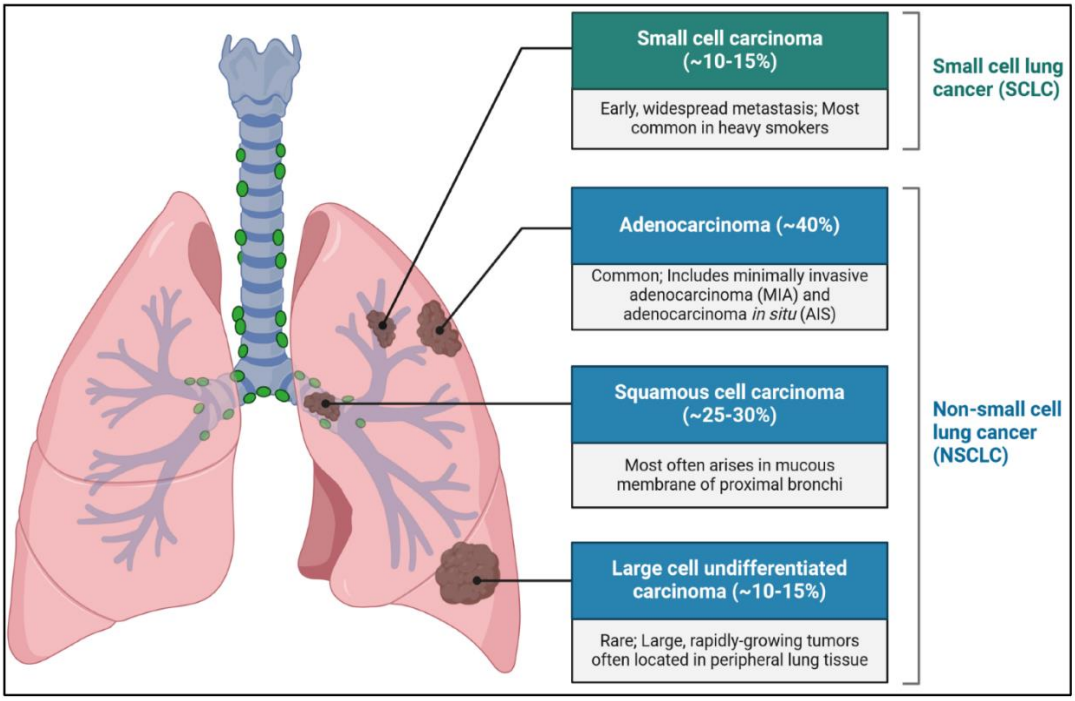

Figure 1: Lung Cancers

Exposure to secondhand or passive tobacco smoke also represents a significant and well-established risk factor for lung cancer. Individuals who have never actively smoked but are chronically exposed to environmental tobacco smoke, particularly within households or workplaces, demonstrate a substantially increased risk of developing lung cancer. A comprehensive meta-analysis reported relative risks ranging from 1.14 to 5.20 among lifelong nonsmokers living with smokers (13). Similarly, the United States Surgeon General has estimated that chronic household exposure to tobacco smoke increases the risk of lung cancer among nonsmokers by approximately 20% to 30% (14). These findings emphasize the importance of comprehensive smoke-free policies and public health interventions designed to minimize involuntary exposure to tobacco smoke. Radon exposure constitutes the second leading cause of lung cancer and the leading cause among individuals who have never smoked. Radon is a naturally occurring radioactive gas generated from the decay of uranium present in soil and rock. Approximately 21,000 lung cancer deaths annually in the United States have been attributed to radon exposure (15). Although historically associated with underground mining, increasing attention has focused on residential radon accumulation, particularly in basements and poorly ventilated buildings constructed over uranium-rich geological formations. Large case-control studies conducted across North America, Europe, and China have consistently demonstrated increased lung cancer incidence among individuals exposed to residential radon concentrations as low as 2.7 picocuries per liter (pCi/L) (16–18). The carcinogenic effects of radon are further amplified in smokers, illustrating the synergistic interaction between environmental and behavioral risk factors.

Occupational exposure to carcinogenic substances is another major contributor to lung cancer development. Lung cancer remains one of the most common occupational malignancies worldwide. Among occupational carcinogens, asbestos has been extensively studied and is strongly associated with both malignant mesothelioma and lung cancer (19,20). Research has demonstrated that asbestos fiber dimensions significantly influence carcinogenic potential and lung cancer mortality, with certain fiber types exhibiting greater pathogenicity than others (21). Recognition of these hazards has prompted substantial regulatory efforts to restrict asbestos use in commercial and industrial settings. In addition to asbestos, numerous other occupational agents have been implicated in lung carcinogenesis, including arsenic and its compounds, beryllium, cadmium, crystalline silica, vinyl chloride, nickel compounds, chromium compounds, coal-derived products, chloromethyl ethers, mustard gas, and diesel engine exhaust (22,23). Workers employed in mining, construction, manufacturing, metallurgy, transportation, and chemical industries therefore require appropriate occupational safety measures and exposure monitoring to reduce cancer risk. Environmental air pollution has emerged as an increasingly important risk factor, particularly in urban populations. Chronic exposure to traffic-related air pollutants, industrial emissions, and fine particulate matter containing polycyclic aromatic hydrocarbons contributes to persistent pulmonary inflammation, oxidative stress, and DNA damage that promote carcinogenesis (24). Epidemiological studies have demonstrated that prolonged exposure to ambient air pollution is associated with approximately an 8% increase in lung cancer mortality, highlighting the importance of environmental policies aimed at improving air quality and reducing population-level exposure to airborne carcinogens (25).

Genetic predisposition also contributes substantially to lung cancer susceptibility. Individuals with a personal history of lung cancer or a first-degree relative diagnosed with the disease exhibit an increased lifetime risk of developing lung malignancies, suggesting an inherited component of disease susceptibility (26). Advances in molecular genetics have identified several inherited genetic variants associated with increased lung cancer risk. Among these, germline mutations in the TP53 tumor suppressor gene significantly increase susceptibility, particularly among smokers. Individuals carrying TP53 germline sequence variants who smoke have been reported to possess more than a threefold greater risk of developing lung cancer compared with nonsmoking carriers (27). Furthermore, multiple independent genome-wide association studies have identified susceptibility loci on chromosome 15 containing genes encoding subunits of the nicotinic acetylcholine receptor (28–30). These receptor variants influence nicotine dependence and may directly affect cellular proliferation following nicotine binding. Individuals carrying one copy of the susceptibility allele exhibit an approximately 30% increased risk of lung cancer, whereas those carrying two copies demonstrate an estimated 70% to 80% higher risk than individuals without the genetic variant (28–30). Overall, the pathogenesis of NSCLC results from the cumulative effects of tobacco exposure, environmental and occupational carcinogens, inherited genetic susceptibility, and other host-related factors. Understanding these risk factors remains fundamental for developing effective prevention strategies, implementing targeted screening programs, and reducing

the global burden of lung cancer through comprehensive public health interventions and individualized risk assessment.

Current Treatment Options

The management of non-small cell lung cancer (NSCLC) has evolved substantially over recent decades owing to advances in surgical techniques, systemic therapies, radiation oncology, molecular diagnostics, and multidisciplinary cancer care. Selection of the most appropriate treatment strategy depends on several factors, including tumor stage, histological subtype, molecular profile, anatomical resectability, patient age, performance status, cardiopulmonary reserve, comorbidities, and patient preferences. Contemporary treatment aims not only to prolong overall survival but also to preserve pulmonary function, minimize treatment-related toxicity, improve quality of life, and reduce disease recurrence. Optimal management requires close collaboration among thoracic surgeons, medical oncologists, radiation oncologists, pulmonologists, radiologists, pathologists, and supportive care specialists to develop individualized treatment plans based on current evidence and international clinical guidelines.

Surgery

Surgical resection remains the cornerstone of curative treatment for patients with early-stage and selected locally advanced NSCLC. Patients diagnosed with stage I, stage II, and carefully selected stage IIIA disease are generally considered candidates for surgery when complete tumor removal is technically feasible and the patient possesses sufficient cardiopulmonary reserve to tolerate the procedure. Before surgery, comprehensive staging is performed using high-resolution computed tomography (CT), positron emission tomography-computed tomography (PET-CT), mediastinal lymph node assessment, bronchoscopy, and tissue biopsy to determine tumor extent, nodal involvement, and the presence of distant metastases. Equally important is the assessment of pulmonary function, cardiovascular status, and other comorbidities to determine surgical operability. The primary objective of surgery is complete anatomical resection with negative surgical margins while preserving as much healthy lung tissue as possible. Lobectomy with systematic mediastinal lymph node dissection or sampling remains the standard surgical procedure for most resectable tumors because it offers superior long-term survival and lower recurrence rates compared with more limited resections. Segmentectomy or wedge resection may be considered for selected patients with small peripheral tumors or those with limited pulmonary reserve. More extensive procedures, including pneumonectomy, may occasionally be required for centrally located tumors involving major bronchi or pulmonary vessels. Minimally invasive surgical techniques have transformed thoracic surgery over the past two decades. Video-assisted thoracoscopic surgery (VATS) has become widely adopted because it enables surgeons to perform anatomical lung resections through several small thoracic incisions rather than a traditional thoracotomy. During VATS, a thoracoscope equipped with a high-definition camera provides excellent visualization of the operative field while specialized instruments allow precise tumor removal. Compared with conventional open thoracotomy, VATS is associated with reduced postoperative pain, lower blood loss, fewer pulmonary complications, shorter hospitalization, faster recovery,

improved postoperative pulmonary function, and earlier initiation of adjuvant therapy without compromising oncological outcomes (31). More recently, robotic-assisted thoracic surgery has further expanded minimally invasive surgical options by enhancing surgical precision, dexterity, and visualization.

Adjuvant Therapy

Despite complete surgical resection, microscopic residual disease may persist and contribute to disease recurrence. Consequently, adjuvant therapy plays an essential role in reducing relapse risk and improving long-term survival among patients with resected NSCLC who possess high-risk pathological features. The choice of adjuvant treatment depends on pathological stage, lymph node involvement, surgical margins, molecular alterations, and overall patient fitness. Patients with stage IIA, stage IIB, and stage IIIA NSCLC generally receive platinum-based adjuvant chemotherapy following complete tumor resection because multiple randomized clinical trials have demonstrated improvements in disease-free survival and overall survival through eradication of residual microscopic disease (32). Depending on pathological findings, postoperative radiotherapy may also be indicated in selected patients with positive surgical margins or extensive mediastinal lymph node involvement. In recent years, advances in molecular profiling have expanded the role of adjuvant targeted therapies and immunotherapies for patients harboring actionable genetic alterations or expressing predictive biomarkers, further improving recurrence-free survival in appropriately selected populations.

Chemotherapy

Approximately 40% of patients with NSCLC present with stage IV metastatic disease at initial diagnosis, precluding curative surgical intervention. In these patients, systemic therapy represents the principal treatment modality, with therapeutic goals focused on prolonging survival, controlling tumor progression, alleviating symptoms, preserving organ function, and maintaining quality of life (33). Although targeted therapies and immunotherapy have transformed treatment for biomarker-selected patients, cytotoxic chemotherapy continues to play an important role, particularly among patients without actionable molecular alterations. For patients with advanced NSCLC and good functional status, defined as an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, platinum-based combination chemotherapy remains a standard first-line treatment option. According to recommendations from the American Society of Clinical Oncology, treatment generally consists of cisplatin or carboplatin combined with a third-generation cytotoxic agent, including paclitaxel, gemcitabine, docetaxel, vinorelbine, irinotecan, or pemetrexed (34). Multiple large multicenter randomized clinical trials comparing these combinations have demonstrated broadly similar therapeutic efficacy, with median overall survival ranging from approximately 8 to 10 months and no single regimen consistently outperforming the others (35–38). Therefore, treatment selection is primarily guided by anticipated toxicity profiles, patient comorbidities, histological subtype, renal function, and individual treatment preferences.

Histological classification significantly influences chemotherapy selection. Patients with nonsquamous histology, particularly adenocarcinoma, derive greater benefit from pemetrexed-containing regimens because of superior efficacy and a more favorable toxicity profile in this subgroup. Cisplatin generally provides slightly greater antitumor activity than carboplatin; however, it is associated with higher rates of nephrotoxicity, ototoxicity, neurotoxicity, nausea, and vomiting. Carboplatin is therefore frequently preferred for older adults and patients with significant comorbid conditions because of its improved tolerability. Performance status remains one of the strongest predictors of treatment tolerance and survival. Patients with an ECOG performance status of 2 may benefit from less intensive treatment, often involving single-agent chemotherapy rather than platinum-based combinations (39). Treatment response should be evaluated regularly using clinical assessment and radiological imaging. Significant toxicity, disease progression, or failure to achieve meaningful tumor reduction after approximately four treatment cycles generally necessitates modification or discontinuation of chemotherapy (40,41). Patients with poor performance status (ECOG 3 or higher) rarely benefit from aggressive cytotoxic therapy because treatment-related toxicity frequently outweighs potential clinical benefit. In these individuals, supportive and palliative care aimed at symptom control and quality-of-life improvement is usually the preferred management strategy.

Radiotherapy

Radiotherapy represents another essential component of multidisciplinary NSCLC management and may be administered with curative, definitive, adjuvant, neoadjuvant, or palliative intent. Ionizing radiation induces irreparable DNA damage within malignant cells, resulting in apoptosis and inhibition of tumor proliferation. Patients with localized disease who are medically inoperable because of advanced age, impaired pulmonary function, or significant comorbidities may receive definitive radiotherapy as an alternative to surgical resection. Radiotherapy also provides substantial symptomatic relief in patients with metastatic disease by reducing pain, controlling hemoptysis, relieving airway obstruction, and improving neurological symptoms associated with brain or spinal metastases (42). Technological advances have significantly improved radiation precision while minimizing exposure of surrounding healthy tissues. Stereotactic body radiation therapy (SBRT) has emerged as the preferred treatment for medically inoperable patients with early-stage NSCLC presenting with small peripheral tumors and no evidence of regional lymph node involvement. SBRT utilizes advanced image-guided localization systems to deliver highly focused, ablative doses of radiation with submillimeter accuracy over a limited number of treatment sessions. This approach achieves excellent local tumor control while substantially reducing radiation exposure to adjacent normal lung tissue. Clinical evidence strongly supports the effectiveness of SBRT in appropriately selected patients. A meta-analysis comparing photon-, proton-, and carbon ion-based radiotherapy demonstrated that SBRT provided superior two-year overall survival, lower healthcare costs, and greater patient convenience than alternative radiation modalities (43). A prospective phase II study with 50-month follow-up involving 70 medically inoperable patients with stage I NSCLC reported excellent local tumor control following SBRT, confirming its durability and effectiveness in patients unable to undergo surgery (44). Similarly, a multicenter

phase III trial evaluating medically inoperable early-stage NSCLC found a three-year overall survival rate of 55.8% with acceptable treatment-related toxicity among patients treated with SBRT (45). Subsequent investigations have consistently demonstrated that SBRT achieves local control rates approaching those obtained with surgical resection while producing considerably lower treatment-related morbidity, making it the standard of care for medically inoperable early-stage disease (46,47).

Biomarker Testing

Biomarker testing has become a fundamental component of the modern management of non-small cell lung cancer (NSCLC), enabling the transition from conventional chemotherapy to precision medicine. Advances in molecular diagnostics have demonstrated that NSCLC comprises multiple genetically distinct diseases characterized by specific oncogenic driver mutations that influence tumor behavior and therapeutic response. Identification of these molecular alterations allows clinicians to select targeted therapies that improve survival, increase response rates, and reduce treatment-related toxicity compared with traditional cytotoxic chemotherapy (48). In addition to the well-established therapeutic targets involving epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) rearrangements, genomic profiling has identified several additional actionable alterations, including ROS1 and RET gene rearrangements, MET amplification, and mutations involving BRAF, HER2, and KRAS, many of which continue to expand the therapeutic landscape of NSCLC. Among currently established biomarkers, mutations of the epidermal growth factor receptor (EGFR) gene represent one of the most clinically important molecular abnormalities. EGFR encodes a transmembrane receptor tyrosine kinase that regulates cellular proliferation, survival, differentiation, and migration through activation of intracellular signaling pathways. Activating mutations result in continuous receptor stimulation and uncontrolled cellular proliferation. EGFR mutations occur in approximately 10%–15% of lung adenocarcinomas, particularly among patients of Asian or European ancestry, women, individuals with adenocarcinoma histology, and those who have never smoked (49–51). Most clinically significant mutations occur within exons 18–21 of the tyrosine kinase domain, with exon 19 deletions and the exon 21 L858R substitution accounting for nearly 90% of cases. These alterations confer high sensitivity to EGFR tyrosine kinase inhibitors such as erlotinib and gefitinib, producing objective response rates approaching 70% in appropriately selected patients (52). Consequently, routine EGFR mutation testing is recommended before initiating first-line systemic therapy in patients with advanced nonsquamous NSCLC.

KRAS mutations represent another important molecular subtype of NSCLC and are among the most frequently encountered oncogenic alterations in lung adenocarcinoma. These activating mutations primarily involve amino acid substitutions at codons 12, 13, and 61, with G12 and G13 mutations occurring most commonly. KRAS mutations are identified in approximately 10%–25% of lung adenocarcinomas and are more frequently observed in smokers, Caucasian populations, and patients with adenocarcinoma histology (53,54). Unlike EGFR and ALK alterations, KRAS mutations generally occur independently of other major oncogenic drivers, defining a distinct molecular subset of NSCLC (48,52).

Although KRAS mutations have historically been associated with limited predictive value for response to EGFR inhibitors or conventional chemotherapy, recent advances have led to the development of mutation-specific inhibitors targeting KRAS G12C. These agents selectively inhibit the mutant protein without affecting normal KRAS function, providing promising targeted treatment options for this previously difficult-to-treat subgroup (55). Anaplastic lymphoma kinase (ALK) rearrangements constitute another clinically significant therapeutic target, occurring in approximately 3%–7% of NSCLC cases (56–58). These alterations are most frequently identified in younger patients, individuals who have never smoked or have minimal smoking history, and those with adenocarcinoma containing acinar or signet-ring cell features (59–61). The most common rearrangement involves fusion of the EML4 gene with ALK on chromosome 2, resulting in constitutive activation of ALK signaling pathways that promote malignant cell proliferation. ALK rearrangements rarely coexist with EGFR or KRAS mutations, making them a distinct molecular subtype of NSCLC (61,62). Patients with ALK-positive tumors generally derive little benefit from EGFR-targeted therapies; instead, they respond remarkably well to ALK inhibitors. Crizotinib, the first FDA-approved ALK inhibitor, demonstrated objective response rates of 50%–61% in patients with advanced ALK-positive NSCLC. In a pivotal randomized clinical trial, crizotinib significantly prolonged progression-free survival compared with platinum-based chemotherapy (10.9 versus 7 months) while also improving overall response rates (74% versus 45%), establishing it as the standard first-line treatment for advanced ALK-rearranged NSCLC (64).

Mutations involving the BRAF proto-oncogene represent a less common but clinically relevant molecular alteration, occurring in approximately 1%–4% of NSCLC cases, predominantly among patients with adenocarcinoma and those with a history of smoking (54,66–70). BRAF encodes a serine/threonine protein kinase that regulates cell proliferation through the MAPK signaling pathway. The most frequently identified mutation is V600E, although other variants such as G469A and D594G have also been described (69). Similar to EGFR and ALK, BRAF mutations generally occur independently of other major oncogenic drivers, reinforcing the molecular heterogeneity of NSCLC and supporting the need for comprehensive genomic profiling to guide individualized treatment selection.

Conclusion

Non-small cell lung cancer continues to represent a major global health challenge because of its high incidence, biological heterogeneity, and substantial mortality. Nevertheless, significant advances in molecular biology, diagnostic technologies, surgical techniques, radiation oncology, targeted therapy, and multidisciplinary cancer care have fundamentally changed the treatment landscape. Early-stage disease can often be managed successfully with surgery and appropriate adjuvant therapy, whereas advanced disease increasingly benefits from biomarker-guided targeted treatments that improve response rates and prolong survival. Comprehensive molecular profiling has become an essential component of clinical decision-making, enabling individualized therapeutic strategies based on specific genomic alterations. Continued integration of precision medicine, novel targeted agents, immunotherapeutic approaches, and comprehensive supportive care is expected to further improve patient outcomes. Future research should focus on

overcoming treatment resistance, identifying new predictive biomarkers, expanding personalized therapeutic options, and enhancing early detection strategies to reduce the global burden of NSCLC and improve long-term survival.

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