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Lung Cancer: A Comprehensive Review of the Etiopathogenesis, Molecular Stratification, and the Paradigm Shift in Precision Oncology

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ABSTRACT

Lung cancer remains the preeminent global oncologic challenge, maintaining its status as the leading cause of cancer-related mortality alongside a significant epidemiological shift toward developing nations. This comprehensive review explores the complex etiopathogenesis of the disease, highlighting the interplay between tobacco-induced epigenetic modifications and chronic inflammation within the tumor microenvironment. The article details the evolution of pathological classification, specifically the transition toward standardized TNM staging for Small Cell Lung Cancer (SCLC) to guide increasingly complex multimodal care.

A major focus is placed on the paradigm shift in Non-Small Cell Lung Cancer (NSCLC), where molecular profiling has transformed from an advanced-stage necessity to an early-stage imperative. The review analyzes the impact of landmark trials, such as ADAURA and ALINA, which established the efficacy of adjuvant targeted therapies. Furthermore, it examines the expanding landscape of actionable genomic drivers-including EGFR, ALK, and the historically undruggable KRAS G12C-and the strategies utilized to overcome acquired resistance. Finally, the author discusses emerging therapeutic frontiers, including the rise of Antibody-Drug Conjugates (ADCs), the potential of Personalized Cancer Vaccines (PCVs) for eliminating minimal residual disease, and the clinical utility of liquid biopsy (ctDNA) for dynamic tumor profiling.

Keywords: Lung Cancer; Precision Oncology; NSCLC (Non-Small Cell Lung Cancer); Immunotherapy; KRAS G12C; Antibody-Drug Conjugates (ADCs); Liquid Biopsy (ctDNA); Personalized Cancer Vaccines

INTRODUCTION

The Evolving Global Epidemiology and Burden of Disease. Lung cancer remains the most significant global oncologic challenge, maintaining its position as the leading cause of cancer-related mortality worldwide [1]. Recent global estimates from the International Agency for Research on Cancer (IARC) highlight the persistent and growing burden of the disease. In 2022, lung cancer accounted for approximately 2.5 million new cases globally, representing 12.4% of total new cancer diagnoses, and was responsible for 1.8 million deaths, comprising 18.7% of all cancer-related fatalities [2].

Despite considerable scientific and clinical progress, the prognosis for lung cancer remains grim compared to other common malignancies. The 5-year survival rate in the United States historically averages only ~23% [1]. This low survival statistic underscores a critical paradox: while revolutionary targeted therapies and immunotherapies have transformed outcomes in advanced settings (as

discussed in subsequent sections), the primary bottlenecks remain centered on inadequate early detection and systemic deficiencies in therapeutic access. The failure to achieve widespread adoption of screening protocols in high-risk populations, coupled with delays in diagnosis, means that a majority of patients still present with advanced, less curable disease (Figure 1).

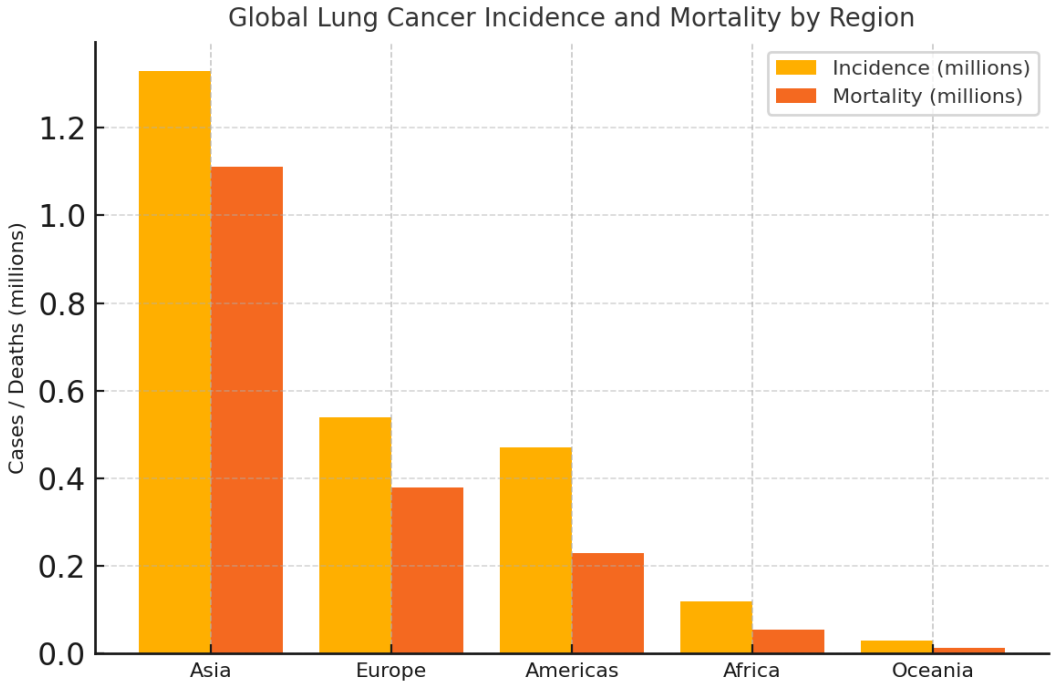

Figure 1: Global lung cancer incidence and mortality by region (2022). Asia bears a disproportionately high burden of new cases and deaths, followed by Europe and the Americas. Effective tobacco control and early detection efforts are needed in high-incidence regions.

LITERATURE REVIEW

Global epidemiological transition

A substantial shift in the epidemiological landscape has been observed over the past four decades. Historically, cancer incidence was concentrated in developed nations; however, current data indicate that approximately half (49.9%) of global lung cancer cases now occur in developing countries [1]. This transition is linked to persistent tobacco use, population growth, and aging demographics in lower- and middle-income nations. This geographical shift has profound implications for global health equity, necessitating intensified resource allocation for cancer management.

According to a World Health Organization (WHO) survey, only 39% of participating countries adequately finance the basics of cancer management as part of their core health benefit packages, highlighting the fragility of health infrastructure in regions now bearing the brunt of the cancer burden [2].

Future projections indicate that the global burden will continue to increase, driven largely by population changes rather than immediate rate increases. The total number of new cancer cases worldwide is predicted to reach 35 million by 2050 [3]. This trajectory mandates that global cancer control strategies focus not only on developing sophisticated treatments but also on implementing scalable prevention programs and standardizing comprehensive diagnostics across diverse resource settings.

Table 1 provides a snapshot of the current global incidence and mortality rankings, reinforcing lung cancer's dominant position in terms of lethality (Table 1).

Table 1: Global Incidence and Mortality of Major Cancers (IARC 2022).

Cancer Type	New Cases (Millions)	Percentage of Total Incidence	Deaths (Millions)	Percentage of Total Mortality
Lung Cancer	2.5	12.4%	1.8	18.7%
Female Breast Cancer	2.3	11.6%	0.67	6.9%
Colorectal Cancer	1.9	9.6%	0.90	9.3%
Prostate Cancer	1.5	7.3%	0.4	~5.6%
Stomach Cancer	0.97	4.9%	0.66	6.8%

DISCUSSION

Etiopathogenesis and underlying molecular mechanisms

The etiology of lung cancer is complex, although tobacco smoking remains the overwhelmingly dominant risk factor. Epidemiological studies consistently demonstrate that smokers are at least three times more likely to develop lung cancer than non-smokers [4]. The molecular pathogenesis involves a multifaceted interaction between inhaled carcinogens, inflammation, and cellular signaling pathways.

The role of tobacco smoke in carcinogenesis

Carcinogenic chemicals found in tobacco smoke induce both direct genetic damage and significant epigenetic modifications [4]. The mechanisms extend beyond simple point mutations, deletions, translocations, and gene recombination to include complex regulation of cellular processes [4].

Epigenetic Modification and Addiction: Smoking leads to the induction of epigenetic alterations in specific genes. For instance, smoking increases the hypermethylation and subsequent inactivation of critical tumor-suppressor miRNAs (miRs). Conversely, it can alter the expression of other miRs, such as miR-504, which is linked to the expression of the Dopamine Receptor gene (DRD1). This link intertwines the molecular mechanisms of cancer progression with the biological mechanisms driving addiction, illustrating the profound and complex systemic effects of tobacco use [4]. The identification of these specific epigenetic signatures suggests a potential avenue for future preventative research aimed at identifying and reversing pre-malignant changes in high-risk individuals before the establishment of invasive disease.

Signaling Pathway Modulation: Carcinogenic compounds in cigarette smoke are known to activate or inactivate numerous intracellular signaling pathways [4]. This modulation grants malignant cells the capacity for uncontrolled proliferation and evasion of apoptosis, two hallmarks of cancer progression.

The tumor microenvironment and chronic inflammation

A thorough understanding of lung cancer pathogenesis requires acknowledging the critical role of the Tumor Microenvironment (TME) [5]. The TME in tobacco-induced lung cancer is characterized by a unique, chronic inflammatory cellular network. This inflammation is driven by structural, stromal, and inflammatory cells of the lung, which act in complicity to promote carcinogenesis [5].

This prominent role of chronic inflammation in the TME provides a direct mechanistic explanation for the observed efficacy of Immune Checkpoint Inhibitors (ICIs) in many smokers. High levels of chronic inflammation often correlate with a Higher Tumor Mutational Burden (TMB) and an increased presence of T-cells and immune checkpoints within the TME, effectively priming the tumor site for immune-mediated destruction upon checkpoint blockade. Targeting the TME's inflammatory components thus represents a key therapeutic axis, especially in non-oncogene-driven disease.

Pathological classification and staging

The histological classification of lung malignancies is fundamentally divided into two major entities: Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC).

Non-Small Cell Lung Cancer (NSCLC) staging

NSCLC encompasses several subtypes, including adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Treatment decisions are predominantly governed by the American Joint

Committee on Cancer (AJCC) TNM staging system, which utilizes three key parameters[6]:

- ***T (Tumor):*** The size and extent of the primary tumor, including local invasion into adjacent structures.
- ***N (Nodes):*** The presence and extent of regional lymph node spread.
- ***M (Metastasis):*** The presence of distant metastasis (e.g., to the brain, bones, liver, or adrenal glands) [6].

NSCLC stages are grouped from Stage 0 (carcinoma in situ, CIS) through Stage IV (metastatic disease). Furthermore, staging is categorized as either clinical (based on imaging, physical exam, and initial biopsy findings) or pathologic (determined by comprehensive examination of tissue removed during surgical resection), with the latter providing the most precise prognostic information and guiding crucial adjuvant therapy decisions [6].

Small Cell Lung Cancer (SCLC) staging evolution

SCLC, historically defined by its aggressive behavior and neuroendocrine features, has traditionally been classified using a simpler two-tiered system: limited stage (confined to one hemithorax and regional lymph nodes) or extensive stage (spread beyond this boundary) [7].

There is a noticeable clinical trend toward adopting the standardized AJCC TNM numbering system for SCLC [7]. This shift from a broad pathological dichotomy to a granular numerical system is significant, reflecting the increasing complexity of SCLC management. The simple limited/extensive classification is increasingly insufficient for contemporary care pathways that must incorporate novel systemic therapies (e.g., immunotherapy combinations) and increasingly aggressive local control measures (e.g., surgical resection and precise radiation delivery) for early-stage or localized disease. Utilizing TNM allows for more precise prognostic stratification and informed integration of multimodality treatment.

Foundational treatment strategies: a stage-based approach

Contemporary lung cancer management relies on multidisciplinary care guided by standardized protocols such as those produced by the National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO) [8]. Treatment selection is based on cancer type, stage, patient performance status, and molecular characteristics.

Early and locally advanced disease

For early-stage (Stages I-II) NSCLC, curative intent is typically achieved through surgical resection or definitive Stereotactic Body Radiation Therapy (SBRT).

The transformation of adjuvant therapy: A paradigm shift has occurred with the successful integration of systemic targeted therapy into the adjuvant (post-surgery) setting. Landmark Phase 3 clinical trials, such as ADAURA (evaluating osimertinib) and ALINA (evaluating alectinib), demonstrated practice-changing benefits for patients with specific oncogene-driven early-stage NSCLC, resulting in significantly improved clinical outcomes [9].

The success of these trials transforms molecular profiling from an advanced-stage necessity into an early-stage imperative [9]. Comprehensive molecular testing is now mandatory for all newly diagnosed NSCLC patients, regardless of clinical stage, to identify candidates for potentially curative targeted adjuvant therapy.

Crucially, the ALINA trial results extended beyond survival metrics to address quality of life (QoL). Data demonstrated that patients receiving adjuvant alectinib reported better QoL compared to those receiving standard adjuvant chemotherapy [10]. This finding signals an evolution in clinical trial design, where the highest standard of care is defined by maximizing survival durability while simultaneously minimizing treatment toxicity and preserving patient functionality.

For locally advanced (Stage III) NSCLC, standard care often involves definitive chemoradiation followed by consolidation immunotherapy, such as Durvalumab, a strategy strongly recommended by ASCO guidelines [11].

Advanced disease management

NSCLC Immunotherapy: For advanced NSCLC, Immunotherapy (ICIs) has become a mainstay of treatment. In patients with high Programmed Death-Ligand 1 (PD-L1) expression (\geq 50%), monotherapy with Pembrolizumab is strongly recommended [11]. ICIs like Nivolumab and Atezolizumab are broadly utilized across various advanced squamous and non-squamous NSCLC subtypes, often without selection based on PD-L1 levels in combination regimens [11] (Figure 2).

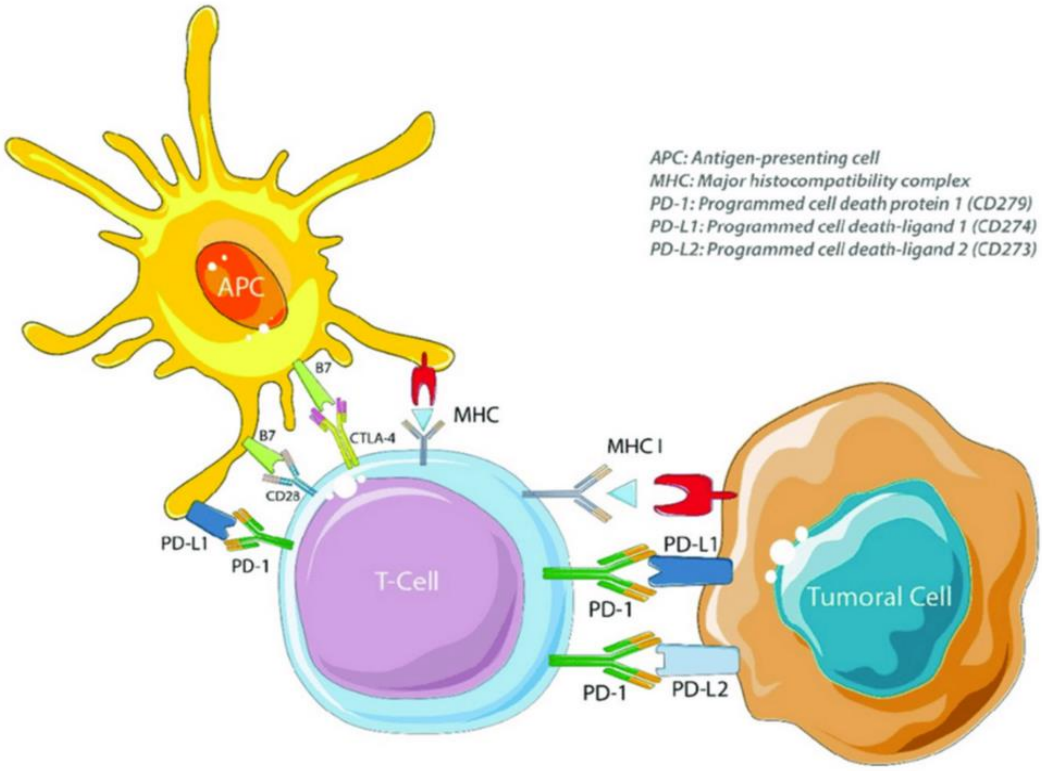

Figure 2: The PD-1/PD-L1 immune checkpoint and its inhibition. Tumor cells can overexpress PD-L1, which binds to PD-1 receptors on T-cells, delivering an "off" signal that dampens the immune response. This allows tumors to evade immune surveillance. Immune checkpoint inhibitors (anti-PD-1 or anti-PD-L1 antibodies) block this interaction, thereby restoring T-cell activity against cancer cells. In NSCLC, blockade of the PD-1/PD-L1 pathway has led to improved survival in subsets of patients, particularly those with high PD-L1 expression or high tumor mutational burden.

SCLC systemic therapy: Standard management for extensive stage SCLC involves platinum-based chemotherapy combined with immunotherapy. For patients whose SCLC relapses relatively early (within six months of primary treatment), NCCN guidelines recommend the combination of Nivolumab \pm Ipilimumab as a second-line option [11].

Precision oncology: Targeting actionable genomic drivers

The field of NSCLC treatment has been revolutionized by the identification of molecularly actionable targets, enabling a precision medicine approach. Molecular testing is fundamental for treatment selection, particularly in advanced disease settings [9,12].

Established and emerging target pathways

The landscape of targetable genomic alterations is constantly expanding, including established drivers like EGFR, ALK, ROS1, RET, ERBB2 (HER2), BRAF, and MET exon 14 skipping (METex14) [9]. The therapeutic standard for these pathways involves specific generations of Tyrosine Kinase Inhibitors (TKIs). For instance, third-generation TKIs such as Osimertinib are used for EGFR-mutated disease (Table 2) (Figure 3).

Table 2: Actionable Oncogenic Drivers in NSCLC and Associated First-Line Therapies.

Genomic Alteration	Prevalence (NSCLC)	Oncogenic Mechanism	First-Line Targeted Agents (Examples)
EGFR (Exon 19 del, L858R)	15–30%	Constitutive kinase activation	Osimertinib (3rd-gen EGFR TKI)
ALK Rearrangement	3–7%	Fusion protein (TK activation)	Alectinib, Brigatinib (ALK TKIs)
KRAS G12C Mutation	~13%	Aberrant GTPase (MAPK activation)	Sotorasib, Adagrasib (covalent KRAS^G12C^ inhibitors)

ROS1 Rearrangement	1–2%	Fusion tyrosine kinase	Crizotinib, Entrectinib
RET Rearrangement	1–2%	Fusion tyrosine kinase	Selpercatinib, Pralsetinib
MET Exon 14 Skipping	3–4%	Impaired tyrosine kinase degradation	Capmatinib, Tepotinib
ERBB2 (HER2) Mutation	~2–3%	Constitutive kinase activation	Trastuzumab deruxtecan (HER2 ADC)
BRAF^V600E^ Mutation	~1%	Constitutive MAPK activation	Dabrafenib + Trametinib (BRAF/MEK inhibitors)

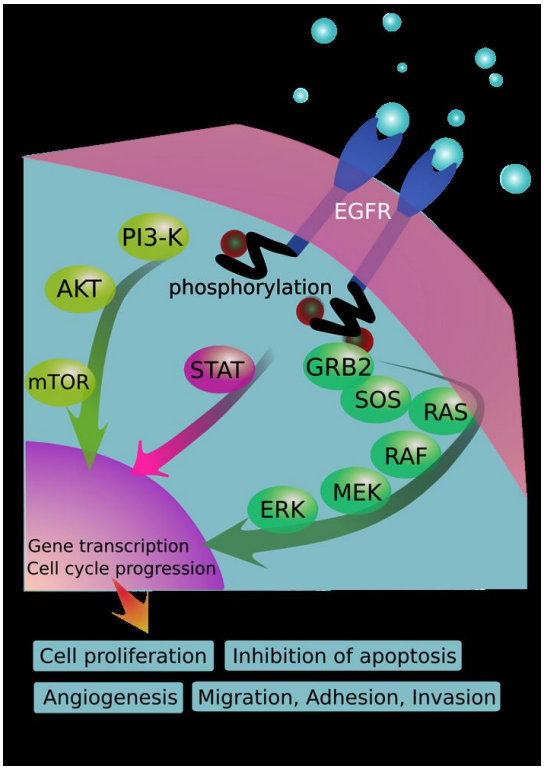

Figure 3: Schematic of EGFR and RAS signaling pathways and targeted therapies. Activation of EGFR triggers downstream RAS–RAF–MEK–ERK and PI3K–AKT pathways, driving cell proliferation and survival. Key oncogenic mutations (e.g., EGFR L858R, KRAS G12C) hyperactivate these cascades. Targeted inhibitors, such as EGFR tyrosine kinase inhibitors and covalent KRAS G12C inhibitors, block critical nodes in these pathways to suppress tumor growth.

The most significant recent breakthrough involves the KRAS G12C mutation, historically deemed "undruggable." The development of covalent inhibitors, such as Sotorasib and Adagrasib, has successfully transformed this mutation into a viable therapeutic target [13]. Ongoing Phase 3 trials, such as the comparison of Divarasib against existing KRAS G12C inhibitors, aim to refine the optimal sequencing and combination strategies for this patient population [13].

Overcoming acquired resistance

The major clinical bottleneck in TKI-based therapy remains the inevitability of acquired resistance, where the tumor evolves mechanisms to bypass the initial drug blockade. This challenge drives continuous research into novel agents and therapeutic combinations designed to circumvent or delay resistance mechanisms [9].

Consequently, there is a strong emerging trend toward utilizing combination therapies in the first-line setting. This proactive strategy involves combining multiple therapeutic modalities (e.g., TKI + TKI, TKI + Chemotherapy, or TKI +

Immunotherapy) to simultaneously target multiple pathways or suppress the growth of pre-existing resistant clones, thereby delaying the time to progression and enhancing treatment durability [9].

The rapid pace of discovery has introduced several new potential therapeutic targets beyond the established drivers, including KRAS non-G12C variants, HER3, Nectin-4, ITGB6, PRMT5, and folate receptor alpha [14]. This dynamic expansion of the molecular landscape emphasizes the necessity for academic and regulatory bodies to produce rapid and continuous updates to clinical guidelines and validates the reliance on broad, next-generation sequencing panels to capture all therapeutically relevant information [8].

Emerging therapeutic frontiers

The most recent advances in lung cancer therapy focus on utilizing innovative drug classes and optimizing drug delivery methods.

Antibody-Drug Conjugates (ADCs)

Antibody-Drug Conjugates (ADCs) represent a promising novel class of agents designed to overcome the limitations of standard targeted therapy and chemotherapy [9]. ADCs utilize an antibody to specifically target antigens expressed on the tumor cell surface (providing precision), coupled to a potent cytotoxic payload (providing cell-killing mechanism). This dual-action mechanism allows ADCs to exert a targeted cytotoxic effect, often bypassing typical TKI resistance pathways [9].

A significant advantage of this platform is the promising activity observed within the Central Nervous System (CNS), which is a common site of metastasis in lung cancer that often represents an unmet clinical need [9]. Initial reports demonstrating CNS efficacy with ADCs suggest they could fundamentally change the management of brain metastases. Furthermore, the ability of ADCs to target emerging antigens such as HER3 and Nectin-4 positions them as crucial components in the future therapeutic arsenal [14].

Optimized combination and delivery strategies

In the KRAS-positive setting, researchers are actively investigating combinations of targeted agents and immunotherapy. One such strategy involves combining Olomorasib (a second-generation KRAS G12C-targeted TKI) with Pembrolizumab (an ICI), with early data suggesting promise despite manageable side effects [10]. This approach aims to maximize the initial response depth and delay acquired resistance by addressing both the oncogene addiction and the inflammatory TME simultaneously.

In a landmark Phase 3 trial, researchers also focused on optimizing patient convenience and quality of life through novel drug delivery methods [10]. The study demonstrated that subcutaneous injections of complex biologics, such as Amivantamab (a bispecific antibody targeting EGFR and MET), were non-inferior—and in some cases provided better clinical outcomes—compared to traditional Intravenous (IV) infusions [10]. This finding has significant operational implications, suggesting that advanced care can be increasingly decentralized and delivered in more convenient settings, potentially including at-home administration, thereby reducing the burden on infusion centers and enhancing patient adherence.

Experimental treatments and future projections

Beyond currently approved agents, experimental research is converging on highly personalized, immune-based strategies and non-invasive detection methods.

Personalized Cancer Vaccines (PCVs)

Personalized Cancer Vaccines (PCVs) represent a promising frontier in immunotherapy [15]. These vaccines are meticulously tailored to the unique genetic profile of a patient's tumor. The process involves sequencing tumor DNA and RNA to identify unique neoantigens (mutations not present in normal tissue) that can be used to train the patient's immune system [15].

PCVs are being investigated for two primary applications:

- ***Therapeutic use:*** To stimulate the immune system to recognize and attack existing cancer cells.
- ***Preventative application:*** To prevent recurrence after conventional therapies have eradicated bulk disease, or ambitiously, to prevent primary onset in high-risk populations [15].

By stimulating the immune system post-treatment, PCVs aim to eliminate Minimal Residual Disease (MRD), which is the underlying cause of clinical relapse [15]. The concept of utilizing highly personalized neoantigen targeting to stop disease before its clinical manifestation moves precision medicine into the realm of population-level

prevention, offering a potential path to profoundly impact future lung cancer epidemiology (Figure 4)

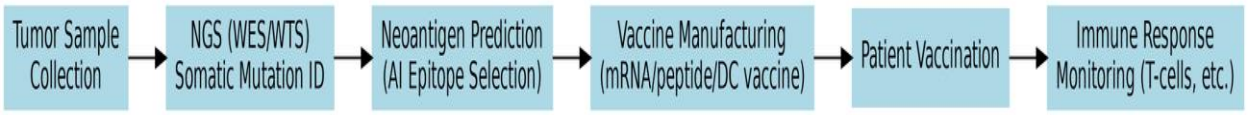

Figure 4: Personalized neoantigen vaccine development workflow. Tumor DNA/RNA from a patient's resected lung cancer is sequenced to identify somatic mutations. Predicted immunogenic neoantigen peptides (red stars) are selected using bioinformatics and AI algorithms. A personalized vaccine (such as an mRNA vaccine encoding selected neoantigens) is manufactured and administered to the patient. The vaccine is intended to elicit T-cell responses against tumor cells harboring those mutations. Immune monitoring (e.g., measuring neoantigen-specific T-cells in blood) follows vaccination to assess response.

Liquid biopsy and dynamic tumor profiling

Circulating tumor DNA (ctDNA), obtained *via* liquid biopsy, has become an invaluable, minimally invasive tool for dynamic tumor profiling [16]. This method allows researchers and clinicians to capture tumor evolution in real-time, offering substantial advantages over traditional, invasive tissue re-biopsy [16].

Clinical Utility: ctDNA is essential for the rapid and non-invasive detection of acquired resistance mechanisms during TKI treatment, guiding subsequent therapeutic lines [16]. Beyond resistance monitoring, the use of ctDNA for surveillance of minimal residual disease is rapidly expanding. Monitoring MRD not only provides an early warning for relapse but also offers a potential tool for clinical de-escalation, allowing clinicians to identify select patients who may be eligible to safely de-escalate or cease adjuvant therapies without compromising long-term outcomes, thereby maximizing quality of life [17-19] (Figure 5).

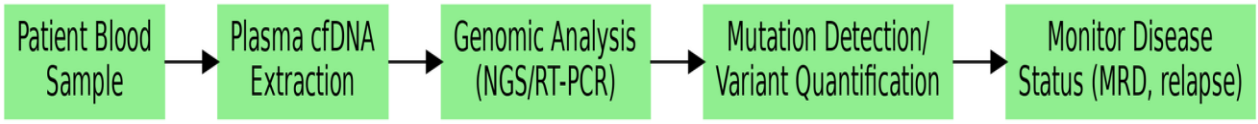

Figure 5: Flowchart of circulating tumor DNA (ctDNA) monitoring in lung cancer. Blood samples are collected from the patient and processed to isolate plasma. Circulating tumor DNA is extracted and analyzed using high-sensitivity methods (digital PCR or ultra-deep sequencing) to detect tumor-specific mutations. The presence and quantity of ctDNA variants are used to monitor disease status: declining ctDNA levels often indicate response to therapy, whereas rising ctDNA can signal residual disease or early relapse prior to clinical or radiographic progression.

CONCLUSION AND OUTLOOK

This review highlights how an improved understanding of lung cancer biology has catalyzed a paradigm shift in management-from one-size-fits-all approaches toward precision oncology. The global burden of lung cancer continues to rise, particularly in developing regions, largely driven by entrenched tobacco use and demographic changes. Strengthening tobacco control remains the cornerstone of primary prevention. Smoking is still estimated to cause ~85% of lung cancer cases, reinforcing the critical importance of smoking cessation and prevention efforts worldwide. In addition, reducing exposure to other risk factors (air pollution, occupational carcinogens like asbestos, and radon in homes) is essential, especially as a sizable fraction of lung cancers in never-smokers becomes more apparent in certain populations (e.g., East Asian women)

On the diagnostic front, the evolution of pathological and molecular classification has enabled clinicians to match patients with the most effective therapies. The implementation of comprehensive molecular testing in NSCLC has ensured that targetable oncogenic drivers are identified at the earliest opportunity. The success of targeted therapies against EGFR mutations and ALK fusions paved the way for tackling previously untargetable mutations. The development of KRAS-G12C inhibitors, validated by clinical trial data, is a triumph of modern drug design and exemplifies the value of persistent scientific investment in lung cancer. These advances have incrementally improved survival in advanced NSCLC and, when applied in the adjuvant setting (e.g., osimertinib in ADAURA, alectinib in ALINA), are moving the needle in early-stage disease as well.

Immunotherapy has dramatically altered the trajectory of metastatic lung cancer for a subset of patients, and the challenge moving forward is to extend these benefits to a larger proportion of patients. Combination strategies (chemo-immunotherapy, dual checkpoint blockade, or novel immune modulators) and biomarker-driven patient selection are active areas of investigation. Additionally, mitigating and managing immune-related toxicities is crucial as these treatments are used more broadly and in earlier-stage disease.

The emerging modalities discussed-ADCs, personalized vaccines, and liquid biopsies-represent the next wave of innovation. ADCs offer a way to overcome the lack of "druggability" for certain targets by delivering cytotoxics directly to cancer cells expressing specific antigens. The impressive results of trastuzumab deruxtecan in HER2-mutant NSCLC have opened new avenues for patients who historically had limited options. Ongoing trials of ADCs (targeting TROP2, CEACAM5, EGFR, and others) will determine how broadly this modality can be applied in lung cancer and whether they should be combined with other therapies for maximal effect.

Personalized cancer vaccines are an exciting yet challenging frontier. The recent success of an mRNA neoantigen vaccine in melanoma (KEYNOTE-942) demonstrating improved recurrence-free survival when added to immunotherapy provides a strong rationale to test similar approaches in lung cancer, which often has abundant neoantigens (especially in smokers). If technical and logistical hurdles can be overcome, PCVs could become a highly individualized adjunct to therapy, essentially "mopping up" residual microscopic disease by stimulating the patient's immune system to recognize and destroy tumor cells bearing patient-specific mutations.

Liquid biopsy and ctDNA analysis stand to revolutionize both our research and clinical practice by offering a window into tumor genetics in real time. The ability to detect emerging resistance mutations via plasma (for example, EGFR C797S after osimertinib, or MET amplifications after KRAS inhibitors) allows for nimble changes in therapy without needing an invasive tissue biopsy. Moreover, ctDNA-based minimal residual disease detection could risk-stratify patients after surgery or definitive chemoradiation and identify who might benefit from additional therapy versus who could be spared. As assays become more standardized, it is conceivable that in the near future, routine follow-up of lung cancer patients will include periodic blood tests for ctDNA to enable early intervention upon molecular relapse.

In conclusion, the management of lung cancer is rapidly evolving on multiple fronts: epidemiologically, with a need for stronger prevention in high-burden regions; diagnostically, with increasingly refined pathology and molecular testing; and therapeutically, with an expanding arsenal of targeted drugs, immunotherapies, and novel treatment modalities. Multidisciplinary care-including thoracic surgery, medical oncology, radiation oncology, pulmonology, and palliative care-remains essential to optimize outcomes, particularly as new treatments are integrated across disease stages. Precision medicine approaches have begun to erode the historically poor prognosis of lung cancer, but continued research and equitable implementation of advances worldwide will be key to achieving further gains. The paradigm shift toward precision oncology in lung cancer serves as a model for other malignancies and offers hope that even the most challenging cancers can become manageable, if not curable, diseases in the foreseeable future.

DECLARATION

Conflict of interest

Abhit Singh serves as Chief Medical Advisor for the WeHeal Foundation.

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Authors' contribution

The author solely contributed to the conception, design, analysis, and writing of this manuscript and approved the final version for publication.

Ethical approval

This article does not contain any studies with human participants or animals performed by the author. Ethical approval was not required for this study.

Consent for publication

Not applicable.

Data availability

Not applicable.

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