

Personalized & Evolving Lung Cancer Treatment

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Introduction

This paper highlights the rapid evolution of targeted therapies for Non-Small Cell Lung Cancer (NSCLC), detailing critical molecular drivers such as EGFR mutations, ALK rearrangements, and ROS1 fusions. It extensively covers the notable success of tyrosine kinase inhibitors (TKIs) while also addressing the significant challenges posed by resistance mechanisms, advocating for next-generation inhibitors and combination strategies to advance treatment outcomes [1].

This review chronicles significant advancements in Small Cell Lung Cancer (SCLC) treatment, notably recognizing how immunotherapy, particularly with PD-1/PD-L1 inhibitors combined with chemotherapy, has profoundly reshaped the therapeutic landscape. It further explores novel and promising approaches, including PARP inhibitors and DLL3-targeted therapies, all aimed at improving the prognosis and management of this aggressive disease [2].

This article presents a comprehensive overview of adjuvant therapy in early-stage NSCLC, emphasizing a recent paradigm shift driven by targeted therapies and immunotherapy. It specifically highlights key FDA approvals, such as adjuvant osimertinib for EGFR-mutated disease and atezolizumab for resected PD-L1 positive tumors, thereby establishing new benchmarks for enhancing disease-free survival rates following surgical interventions [3].

This paper concentrates on the evolving therapeutic landscape for malignant pleural mesothelioma, acknowledging it as a particularly aggressive and challenging cancer. It thoroughly examines the emergence of immunotherapy, with a focus on checkpoint inhibitors, as a substantial advancement, coupled with discussions on novel targeted agents and integrated multimodal strategies designed to alleviate the historically poor prognosis associated with this condition [4].

This article delves into the most recent advancements in radiation therapy for lung cancer. It spans from the application of stereotactic body radiation therapy (SBRT) for early-stage disease to its increasingly vital role in both locally advanced and metastatic settings. The discussion underscores significant improvements in treatment precision and personalization, encompassing adaptations based on tumor biology and the strategic combination of radiation with systemic therapies like immunotherapy [5].

This review meticulously examines the intricate issue of resistance to immune checkpoint inhibitors (ICIs) in NSCLC. It clearly differentiates between primary and acquired resistance mechanisms, pinpointing crucial factors such as PD-L1 expression dynamics, T-cell dysfunction, various genomic alterations, and the multifaceted role of the tumor microenvironment. A profound understanding of these underlying mechanisms is presented as essential for devising effective strategies to overcome resistance and ultimately improve patient outcomes [6].

This article investigates the highly dynamic field of biomarkers in NSCLC, which are fundamentally important for guiding individualized treatment strategies. It comprehensively covers well-established markers, including EGFR mutations, ALK rearrangements, and PD-L1 expression. Furthermore, it discusses promising emerging biomarkers and sophisticated liquid biopsy techniques, which collectively offer the potential for earlier detection, more accurate prognostication, and significantly more precise treatment selection [7].

This article reviews the continuous advancements in surgical approaches for early-stage lung cancer. It prominently highlights the growing adoption of minimally invasive techniques, specifically Video-Assisted Thoracoscopic Surgery (VATS) and Robotic-Assisted Thoracoscopic Surgery (RATS). The review emphasizes how these sophisticated methods contribute significantly to improved patient recovery, a reduction in complications, and the sustained maintenance of oncologic efficacy, thereby leading to superior overall patient outcomes [8].

This paper explores groundbreaking innovative therapeutic strategies that extend beyond the currently established targeted therapies and immunotherapies for advanced NSCLC. It delves into several highly promising areas, such as antibody-drug conjugates (ADCs), bispecific antibodies, and various cell-based therapies. The discussion meticulously outlines their respective mechanisms of action and their considerable potential to surmount existing treatment resistance and enhance patient responses, especially in particularly challenging clinical scenarios [9].

This article reviews the current status of lung cancer screening through low-dose computed tomography (LDCT), underscoring the established guidelines and identifying the specific populations that derive the most benefit from such screening programs. It also thoughtfully addresses future directions, discussing strategic approaches to enhance screening uptake, refine risk stratification models, and seamlessly integrate novel technologies for the purpose of earlier and more accurate detection of lung cancer [10].

Description

Significant progress marks the therapeutic landscape for Non-Small Cell Lung Cancer (NSCLC). Targeted therapies continue their rapid evolution, zeroing in on critical molecular drivers such as EGFR mutations, ALK rearrangements, and ROS1 fusions [1]. The success of Tyrosine Kinase Inhibitors (TKIs) is undeniable, yet the emergence of resistance mechanisms continually pushes research towards next-generation inhibitors and strategic combination therapies to forge improved paths forward [1]. In early-stage NSCLC, adjuvant therapy has seen a transformative shift. Recent FDA approvals for adjuvant osimertinib in EGFR-mutated disease and atezolizumab for resected PD-L1 positive tumors are setting new benchmarks for enhancing disease-free survival after surgery [3]. Beyond established targeted

treatments and immunotherapies, a suite of novel therapeutic strategies is emerging for advanced NSCLC. These promising areas include antibody-drug conjugates (ADCs), bispecific antibodies, and various cell-based therapies, all explored for their potential to circumvent treatment resistance and improve patient responses in complex cases [9].

For Small Cell Lung Cancer (SCLC), a highly aggressive disease, immunotherapy has remarkably altered the treatment landscape. Notably, the combination of PD-1/PD-L1 inhibitors with chemotherapy has become a cornerstone, while novel approaches like PARP inhibitors and DLL3-targeted therapies are actively being investigated to improve patient outcomes [2]. Separately, the therapeutic horizon for malignant pleural mesothelioma, another challenging cancer, has brightened with the advent of immunotherapy, specifically checkpoint inhibitors. This represents a significant leap forward, complemented by ongoing discussions about novel targeted agents and multimodal strategies aimed at mitigating the historically poor prognosis of this condition [4].

Advancements in traditional treatment modalities also play a crucial role across lung cancers. Radiation therapy is increasingly precise and personalized. Stereotactic Body Radiation Therapy (SBRT) is widely used for early-stage disease, and its role is expanding into locally advanced and metastatic settings, often combined with systemic therapies like immunotherapy [5]. Similarly, surgical approaches for early-stage lung cancer have benefited from a growing adoption of minimally invasive techniques. Video-Assisted Thoracoscopic Surgery (VATS) and Robotic-Assisted Thoracoscopic Surgery (RATS) are highlighted for improving patient recovery, reducing complications, and maintaining strong oncologic efficacy, contributing to superior overall patient outcomes [8].

The dynamic field of biomarkers in NSCLC is pivotal for guiding personalized treatment strategies. Well-established markers include EGFR mutations, ALK rearrangements, and PD-L1 expression. However, the landscape is rapidly evolving with emerging biomarkers and sophisticated liquid biopsy techniques. These innovations promise earlier disease detection, more accurate prognostication, and ultimately, more precise treatment selection [7]. Despite these advancements, resistance to immune checkpoint inhibitors (ICIs) in NSCLC remains a complex challenge. Understanding primary and acquired resistance mechanisms, which involve PD-L1 expression dynamics, T-cell dysfunction, genomic alterations, and the tumor microenvironment, is crucial for developing strategies to overcome resistance and enhance patient responses [6].

On the diagnostic front, lung cancer screening using low-dose computed tomography (LDCT) is continually refined. Current guidelines identify populations that benefit most from screening, and future efforts focus on improving screening uptake, enhancing risk stratification, and integrating novel technologies for earlier and more accurate detection of lung cancer [10].

Conclusion

Recent advancements across lung cancer treatment reflect a dynamic shift toward personalized and multimodal strategies. For Non-Small Cell Lung Cancer (NSCLC), targeted therapies have seen rapid evolution, focusing on molecular drivers like EGFR, ALK, and ROS1 mutations. Tyrosine Kinase Inhibitors (TKIs) show significant success, though resistance mechanisms remain a challenge, pushing research into next-generation inhibitors and combination approaches. Adjuvant therapy in early-stage NSCLC has also advanced, with FDA approvals for osimertinib in EGFR-mutated disease and atezolizumab for PD-L1 positive tumors, improving disease-free survival post-surgery. Beyond established methods, novel therapeutic strategies for advanced NSCLC include antibody-drug conjugates (ADCs), bispecific antibodies, and cell-based therapies, aiming to over-

come resistance. Small Cell Lung Cancer (SCLC) treatment has been transformed by immunotherapy, particularly PD-1/PD-L1 inhibitors combined with chemotherapy. Innovative approaches like PARP inhibitors and DLL3-targeted therapies are also under investigation to improve outcomes for this aggressive cancer. Malignant pleural mesothelioma, another challenging cancer, has seen immunotherapy, specifically checkpoint inhibitors, emerge as a significant advancement, alongside novel targeted agents. Radiation therapy for lung cancer has become more precise and personalized, utilizing stereotactic body radiation therapy (SBRT) for early stages and integrating with systemic therapies like immunotherapy. Surgical management for early-stage lung cancer benefits from minimally invasive techniques such as Video-Assisted Thoracoscopic Surgery (VATS) and Robotic-Assisted Thoracoscopic Surgery (RATS), enhancing patient recovery and maintaining oncologic efficacy. The field of biomarkers in NSCLC is rapidly evolving, with established markers like EGFR, ALK, and PD-L1 guiding treatment. Emerging biomarkers and liquid biopsy techniques promise earlier detection and more precise treatment selection. However, resistance to immune checkpoint inhibitors (ICIs) in NSCLC is a complex issue, with mechanisms including PD-L1 dynamics, T-cell dysfunction, and genomic alterations being actively studied to develop strategies to overcome them. Finally, lung cancer screening with low-dose computed tomography (LDCT) continues to refine guidelines for at-risk populations. Future directions aim to improve screening uptake, enhance risk stratification, and integrate new technologies for earlier, more accurate detection. The overall landscape demonstrates a concerted effort to improve prognoses and treatment outcomes across various lung malignancies.

Acknowledgement

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Conflict of Interest

None.

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