Lung cancer: Screening, genomics, targeted therapy.

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Introduction

Lung cancer screening programs effectively reduce mortality, particularly with low-dose CT scans. Ongoing research aims to refine screening criteria, integrate risk prediction models, and explore biomarkers to enhance efficiency and reduce false positives, ensuring that benefits outweigh potential harms for high-risk individuals. This proactive approach to patient care is vital for early detection and improved prognoses, demonstrating a clear commitment to public health [1].

Osimertinib demonstrates significant efficacy as adjuvant therapy for resected EGFR-mutated non-small-cell lung cancer, improving disease-free survival. This targeted approach has become a standard of care, highlighting the importance of molecular profiling in guiding treatment decisions post-surgery to prevent recurrence. The implementation of such targeted therapies signifies a major advancement, moving beyond conventional treatments towards precision medicine tailored to individual genetic profiles [2].

Circulating tumor DNA (ctDNA) analysis is revolutionizing non-small-cell lung cancer management, offering a less invasive way to identify actionable mutations, monitor treatment response, and detect minimal residual disease. A consensus statement provides critical guidance for its clinical application, emphasizing standardization and integration into practice. This non-invasive diagnostic tool offers unparalleled flexibility and insight, representing a paradigm shift in how clinicians manage lung cancer throughout its various stages [3].

Entrectinib, a targeted therapy, shows promising and durable efficacy in patients with ROS1 fusion-positive non-small-cell lung cancer. Updated data from clinical trials confirm its role as an effective option for this molecularly defined subset, providing improved outcomes and highlighting the importance of comprehensive genomic profiling. The sustained effectiveness of therapies like Entrectinib reinforces the necessity of comprehensive genetic analysis, which guides the most appropriate and beneficial treatment pathways for patients [4].

Blood-based biomarkers hold significant potential for improving lung cancer screening. Reviews indicate that various markers like ctDNA, microRNAs, and proteins could complement or enhance low-dose CT, aiming for earlier detection, better risk stratification, and reduced invasive procedures. Integrating these innovative biomarkers alongside established screening methods promises a more sensitive and specific detection process, ultimately leading to earlier intervention and better patient management [5].

Liquid biopsy is emerging as a game-changer in lung cancer screening. Its non-invasive nature and ability to detect early disease-associated changes, such as circulating tumor cells or ctDNA, offer promising avenues for enhancing current screening protocols and identifying high-risk individuals more effectively. This revolutionary method allows for the identification of disease much earlier than traditional techniques, offering a new frontier in preventative care and individualized risk assessment [6].

Resistance to EGFR-tyrosine kinase inhibitors (TKIs) remains a significant challenge in NSCLC. Understanding the diverse mechanisms of acquired resistance, including secondary mutations, bypass signaling, and phenotypic changes, is crucial for developing novel strategies and combination therapies to overcome these barriers. Addressing these resistance mechanisms is paramount for extending patient survival and improving quality of life, driving continuous innovation in drug development [7].

Artificial Intelligence (AI) is rapidly transforming lung cancer screening by enhancing nodule detection, characterization, and risk prediction in CT scans. AI-powered tools promise to improve screening accuracy, reduce radiologist workload, and facilitate personalized screening recommendations, marking a significant leap forward in early diagnosis. By automating and refining the diagnostic workflow, AI not only increases efficiency but also enhances the consistency and reliability of screening interpretations across healthcare settings [8].

Identifying reliable biomarkers for immunotherapy selection in NSCLC is critical for personalized treatment. PD-L1 expression, tumor mutational burden (TMB), and other emerging markers are crucial for predicting response to immune checkpoint inhibitors, guiding treatment decisions, and optimizing patient outcomes. A deeper understanding of these predictive markers ensures that patients receive the most effective immunotherapies, minimizing un-

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necessary treatments and maximizing therapeutic benefits [9].

The landscape of liquid biopsy biomarkers for lung cancer is rapidly evolving. Beyond ctDNA, emerging markers like exosomes, circulating tumor cells, and microRNAs are being explored for their potential in early detection, prognosis, and treatment monitoring, promising more comprehensive insights into tumor biology. The ongoing exploration of these diverse markers enriches our understanding of tumor biology, paving the way for more refined diagnostic and prognostic tools that can significantly impact patient care trajectories [10].

Conclusion

Lung cancer screening programs, especially those utilizing low-dose CT scans, effectively reduce mortality. Current research focuses on refining screening criteria, integrating risk prediction, and exploring biomarkers to enhance efficiency and minimize false positives, ensuring optimal benefit for high-risk individuals. Targeted therapies, such as Osimertinib, have become standard for resected EGFR-mutated non-small-cell lung cancer (NSCLC), significantly improving disease-free survival by preventing recurrence through molecular profiling. Similarly, Entrectinib shows durable efficacy for ROS1 fusion-positive NSCLC, underscoring the value of comprehensive genomic profiling. Circulating tumor DNA (ctDNA) analysis is transforming NSCLC management. It offers a less invasive method to identify actionable mutations, monitor treatment response, and detect minimal residual disease. Consensus statements provide vital guidance for its clinical application, emphasizing standardization. Blood-based biomarkers, including ctDNA, microRNAs, and proteins, show potential to complement low-dose CT for earlier detection and better risk stratification, reducing invasive procedures. Liquid biopsy, leveraging circulating tumor cells or ctDNA, is proving to be a game-changer in screening, detecting early disease changes and identifying high-risk individuals. Artificial Intelligence (AI) is enhancing lung cancer screening by improving nodule detection, characterization, and risk prediction in CT scans, promising greater accuracy and personalized recommendations. However, resistance to EGFR-tyrosine kinase inhibitors (TKIs) in NSCLC remains a challenge. Understanding resistance mechanisms like secondary mutations and bypass signaling is key for developing new combination therapies. Identifying reliable biomarkers for immunotherapy selection, such as PD-L1 expression and tumor mutational burden (TMB), is also crucial for guiding personalized treatment and improving patient outcomes. The broader landscape of liquid biopsy biomarkers, including exosomes and circulating tumor cells, continues to evolve, offering comprehensive insights into tumor biology for early detection and treatment monitoring.

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