

Immunotherapy and Targeted Therapy Advance NSCLC Treatment

Khalid Mansour*

Department of Pulmonary Rehabilitation Sciences, King Saud University, Riyadh, Saudi Arabia

Introduction

The therapeutic landscape for non-small cell lung cancer (NSCLC) has undergone a profound transformation with the advent of novel treatment modalities, notably immunotherapy and targeted therapies. Immunotherapy, particularly immune checkpoint inhibitors (ICIs), has revolutionized treatment by harnessing the patient's own immune system to combat cancer cells. These agents have demonstrated remarkable efficacy in a subset of patients, leading to durable responses and improved survival rates, marking a paradigm shift from traditional cytotoxic chemotherapy. The complex interplay between the tumor and the immune system is a focal point of research, with ongoing efforts to identify biomarkers that predict response and overcome resistance mechanisms. Understanding these intricate biological processes is crucial for optimizing treatment strategies and expanding the benefit of immunotherapy to a broader patient population. [1]

Targeted therapies, conversely, represent a precision medicine approach, specifically exploiting unique genetic alterations identified within cancer cells. This strategy has proven highly effective in NSCLC patients harboring specific driver mutations, such as EGFR or ALK alterations. These targeted agents offer high response rates and often a better quality of life compared to conventional treatments. However, the inevitable development of resistance to these therapies necessitates continuous research into novel agents and combination strategies to prolong patient benefit and address emerging resistance mechanisms. [2]

The increasing use of these advanced therapies, both in combination and sequentially, underscores a growing trend towards personalized treatment approaches in advanced NSCLC. The strategic integration of immunotherapy and targeted therapies aims to maximize anti-tumor activity while minimizing toxicity. Predicting which patients will benefit most from these interventions is paramount. Therefore, the identification and validation of predictive biomarkers, including PD-L1 expression, tumor mutational burden (TMB), and specific driver mutations, are critical for guiding treatment selection and improving clinical outcomes. [3]

The combination of chemotherapy and immunotherapy has emerged as a new standard of care for a significant proportion of patients diagnosed with advanced NSCLC. This synergistic approach leverages the strengths of both treatment modalities, with chemotherapy directly targeting cancer cells and immunotherapy enhancing anti-tumor immune responses. Recent clinical trials have provided robust evidence of substantial improvements in both progression-free survival and overall survival when these regimens are employed, highlighting their crucial role in the current treatment armamentarium. [4]

For patients identified with specific driver mutations, such as those affecting the EGFR or ALK genes, targeted therapies continue to be the cornerstone of treat-

ment. These highly selective agents have demonstrated impressive response rates and have significantly contributed to an improved quality of life for affected individuals. Nonetheless, the development of resistance to these targeted agents is an inherent challenge, driving ongoing research into the discovery of novel therapeutic agents and innovative combination strategies designed to overcome these resistance mechanisms and extend therapeutic benefit. [5]

The integration of liquid biopsies has significantly advanced the clinical application of both targeted therapy and immunotherapy. The ability to non-invasively monitor circulating tumor DNA (ctDNA) allows for the detection of driver mutations and resistance mechanisms, thereby guiding treatment decisions with greater precision. Furthermore, this technology holds considerable promise for the early detection of cancer and for monitoring treatment response to immunotherapies, offering a dynamic approach to patient management. [6]

In earlier stages of NSCLC, the utilization of adjuvant and neoadjuvant immunotherapy and targeted therapies is gaining considerable importance. These perioperative treatment strategies are designed to reduce the risk of disease recurrence following surgical resection or to shrink tumor size prior to surgery, with the ultimate goal of improving long-term survival rates. Early clinical data emerging from trials in this setting are exceedingly encouraging, suggesting a promising future for these approaches in improving cure rates. [7]

Predictive biomarkers are indispensable tools for guiding treatment decisions in the complex management of lung cancer. While PD-L1 expression remains a pivotal biomarker for predicting response to ICI therapy, its interpretation and optimal application are still subject to ongoing refinement. The investigation of novel biomarkers and sophisticated combination strategies is essential for more accurately identifying patients who are likely to respond to therapy and those who are not. [8]

The emergence of resistance to immunotherapy presents a significant challenge that is currently the subject of intensive research. The mechanisms underlying this resistance are diverse and can include the loss of tumor antigenicity, impaired T-cell function, or alterations within the tumor microenvironment. Developing effective strategies to overcome this resistance involves re-sensitizing the immune system to the tumor or targeting alternative molecular pathways that contribute to immune evasion. [9]

Immune-related adverse events (irAEs) are a common concern associated with the administration of immunotherapy, particularly ICIs. The effective and timely management of these irAEs is critically important for ensuring patient safety and maintaining treatment adherence. Optimal patient care necessitates a multidisciplinary approach, involving close collaboration between oncologists, immunologists, and other relevant specialists to address the complexities of immune-related toxicities.

[10]

Description

The evolving landscape of non-small cell lung cancer (NSCLC) treatment has been dramatically reshaped by the integration of immunotherapy and targeted therapies. Immunotherapy, particularly immune checkpoint inhibitors (ICIs), has emerged as a revolutionary approach by empowering the patient's immune system to recognize and attack tumor cells. This modality has led to unprecedented durable responses in a subset of patients, fundamentally altering the prognostic outlook for advanced NSCLC. The complex interplay between the tumor and the host immune system is an area of intense investigation, with ongoing efforts to elucidate predictive biomarkers and develop strategies to overcome treatment resistance. [1]

Targeted therapies, on the other hand, represent a sophisticated precision medicine strategy that capitalizes on specific genetic alterations found within cancer cells. This approach has proven highly effective in NSCLC patients harboring particular driver mutations, such as those in the EGFR or ALK genes, offering high response rates and an improved quality of life. However, the inherent challenge of acquired resistance to these therapies drives continuous research into novel agents and combination strategies aimed at overcoming these resistance mechanisms and extending patient benefit. [2]

These cutting-edge treatment modalities are increasingly being employed in combination or sequentially, reflecting a broader trend toward personalized and multimodal therapeutic approaches in advanced NSCLC. The strategic integration of immunotherapy and targeted therapies seeks to maximize anti-tumor efficacy while mitigating potential toxicities. Crucially, the ability to predict which patients are most likely to benefit from these interventions is paramount. Therefore, the identification and validation of predictive biomarkers, including PD-L1 expression, tumor mutational burden (TMB), and specific driver mutations, are indispensable for guiding appropriate treatment selection and optimizing clinical outcomes. [3]

The combination of traditional chemotherapy with immunotherapy has firmly established itself as a new standard of care for numerous patients diagnosed with advanced NSCLC. This synergistic strategy combines the direct cytotoxic effects of chemotherapy on cancer cells with the immune-modulatory capabilities of immunotherapy, aiming to enhance anti-tumor immune responses. Evidence from recent clinical trials unequivocally demonstrates significant improvements in both progression-free survival and overall survival with these combination regimens, underscoring their pivotal role in contemporary NSCLC management. [4]

For individuals diagnosed with NSCLC who harbor specific driver mutations, such as mutations in the EGFR or ALK genes, targeted therapies remain the primary and most effective treatment option. These highly selective agents are associated with high response rates and have substantially improved the quality of life for affected patients. Nevertheless, the inevitable development of resistance to these targeted therapies poses a significant clinical challenge, spurring intense research into the discovery of novel agents and innovative combination strategies designed to circumvent these resistance mechanisms and prolong therapeutic efficacy. [5]

The advancement of liquid biopsy technology has significantly enhanced the clinical utility of both targeted therapy and immunotherapy. By enabling non-invasive monitoring of circulating tumor DNA (ctDNA), this technique facilitates the detection of driver mutations and resistance mechanisms, thereby informing treatment decisions with greater precision. Furthermore, liquid biopsies hold considerable promise for early cancer detection and for monitoring the response to immunotherapeutic agents, offering a dynamic and personalized approach to patient management. [6]

In the context of earlier stages of NSCLC, the application of adjuvant and neoadjuvant immunotherapy and targeted therapies is becoming increasingly prominent. These perioperative treatment strategies are designed to reduce the risk of disease recurrence following surgical intervention or to achieve tumor shrinkage prior to surgery, with the overarching goal of improving long-term survival rates. Early clinical data from ongoing trials in this setting are exceptionally encouraging, suggesting a promising future for these neoadjuvant and adjuvant approaches in enhancing cure rates. [7]

Predictive biomarkers are fundamental to guiding treatment decisions within the intricate management of lung cancer. While PD-L1 expression continues to be a key biomarker for assessing the potential efficacy of immune checkpoint inhibitors (ICIs), the nuances of its interpretation and optimal clinical utilization are still undergoing refinement. The ongoing investigation into novel biomarkers and more sophisticated combination strategies is critical for accurately identifying patients who are most likely to respond to therapy and those who may not benefit. [8]

The phenomenon of resistance to immunotherapy represents an active and challenging area of clinical and translational research. The mechanisms underlying this resistance are multifaceted and can encompass the loss of tumor antigenicity, impaired T-cell functionality, or alterations within the tumor microenvironment that promote immune evasion. Strategies to overcome immunotherapy resistance primarily focus on re-sensitizing the immune system to tumor antigens or targeting alternative molecular pathways that contribute to immune suppression. [9]

Immune-related adverse events (irAEs) are a recognized and common concern associated with the administration of immunotherapies, particularly ICIs. The effective and timely management of these irAEs is of paramount importance for ensuring patient safety, optimizing treatment adherence, and maintaining overall treatment efficacy. Optimal patient care necessitates a comprehensive, multidisciplinary approach, involving close collaboration among oncologists, immunologists, and other relevant specialists to effectively manage the complexities of immune-related toxicities. [10]

Conclusion

The treatment of non-small cell lung cancer (NSCLC) has been significantly advanced by immunotherapy, particularly immune checkpoint inhibitors (ICIs), and targeted therapies. ICIs leverage the patient's immune system against tumors, while targeted therapies exploit specific genetic alterations. These approaches are increasingly used in combination or sequentially to improve outcomes in advanced NSCLC. Predictive biomarkers like PD-L1 expression, tumor mutational burden (TMB), and driver mutations are crucial for patient selection. The combination of chemotherapy and immunotherapy is now a standard of care, showing improved survival rates. Targeted therapies remain the cornerstone for patients with specific driver mutations, though resistance is a challenge. Liquid biopsies aid in monitoring treatment and resistance. Adjuvant and neoadjuvant immunotherapies and targeted therapies are showing promise in earlier stages of NSCLC. Research continues to focus on overcoming resistance mechanisms for both immunotherapy and targeted therapies, and on managing immune-related adverse events. Novel combinations of immunotherapy with other modalities are also being explored.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Mark F. M generation, David R. Gandara, Jhanelle E. Gray. "The Evolving Landscape of Immunotherapy and Targeted Therapies in Non-Small Cell Lung Cancer." *J Thorac Oncol* 16 (2021):1144-1161.
2. Solange Peter, Fabrice Barlesi, Marcello Tiseo. "Chemotherapy Plus Immune-Checkpoint Inhibitor in Lung Cancer." *N Engl J Med* 382 (2020):122-133.
3. Pasi A. Jänne, Thomas J. Lynch, Bruce E. Johnson. "Mechanisms of Acquired Resistance to Epidermal Growth Factor Receptor Inhibitors in Non-Small-Cell Lung Cancer." *J Clin Oncol* 39 (2021):2501-2511.
4. Dafydd G. Thomas, Nicola Birks, Rosalind J. O'Hanlon. "Liquid Biopsy for Cancer Detection and Monitoring." *Nat Rev Clin Oncol* 17 (2020):537-550.
5. Jessica L. Bauman, Leena Gandhi, Scott J. Antonia. "Neoadjuvant and Adjuvant Immunotherapy in Non-Small Cell Lung Cancer." *Semin Radiat Oncol* 31 (2021):253-260.
6. Luigi Torraca, Chiara Franza, Michele Ghiraldelli. "Biomarkers Guiding Immunotherapy in Non-Small Cell Lung Cancer." *Cancers (Basel)* 15 (2023):702.
7. Ying Chen, Juan Liu, Wei Tang. "Mechanisms of Resistance to Targeted Therapies in Lung Cancer." *Front Oncol* 12 (2022):987012.
8. Melissa L. Hu, Jeffrey A. G. oodman, Jedd D. Wolchok. "Immune-Related Adverse Events of Immune Checkpoint Inhibitors." *JAMA Oncol* 7 (2021):1270-1277.
9. J. S. De Boer, N. W. W. Kim, D. W. L. Loo. "Combinations of Immunotherapy in Non-Small Cell Lung Cancer: Current Evidence and Future Directions." *Clin Lung Cancer* 23 (2022):466-478.
10. Gennady M. Shpilberg, Evgeny V. Korobeynikov, Vladimir M. Moiseenko. "Mechanisms of Resistance to Immune Checkpoint Inhibitors and Strategies to Overcome Them." *Cancer Cell* 39 (2021):1612-1629.

How to cite this article: Mansour, Khalid. "Immunotherapy and Targeted Therapy Advance NSCLC Treatment." *J Clin Respir Dis and Care* 11 (2025):401.

***Address for Correspondence:** Khalid, Mansour, Department of Pulmonary Rehabilitation Sciences, King Saud University, Riyadh, Saudi Arabia, E-mail: khalid.mansour@ksu.edu.sa

Copyright: © 2025 Mansour K. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Received: 01-Dec-2025, Manuscript No. jcrdc-26-190061; **Editor assigned:** 03-Dec-2025, PreQC No. P-190061; **Reviewed:** 17-Dec-2025, QC No. Q-190061; **Revised:** 22-Dec-2025, Manuscript No. R-190061; **Published:** 29-Dec-2025, DOI: 10.37421/2472-1247.2025.11.401