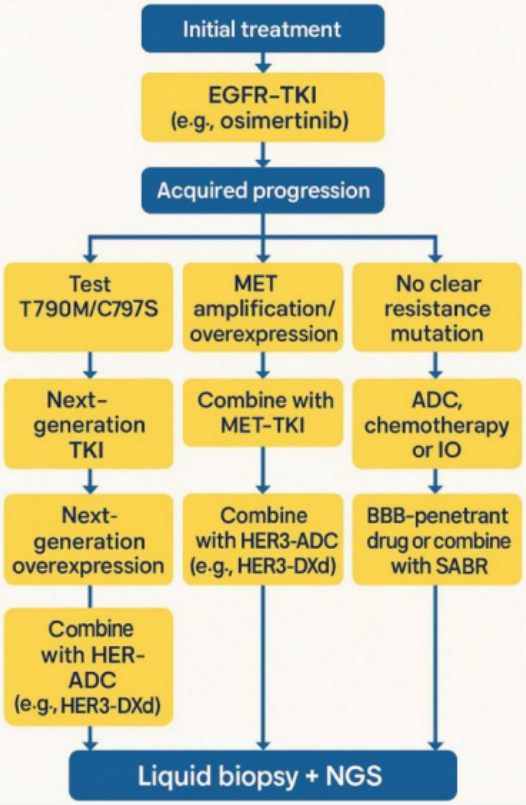
New horizons in NSCLC targeted therapy: advancements and challenges

FAYETTEVILLE, GA, UNITED STATES, December 16, 2025 /EINPresswire.com/ -- Recent advances in the treatment of non-small cell lung cancer (NSCLC) have led to improved patient outcomes, particularly for those with actionable gene mutations. Tyrosine kinase inhibitors (TKIs) targeting mutations in genes such as EGFR, ALK, and KRAS have shown effectiveness across various patient groups.



Sequential therapy strategies in oncogene-driven NSCLC.

Lung cancer is the leading cause of cancer-related deaths worldwide, with non-small cell lung cancer (NSCLC) being the most common type. The identification of driver mutations in genes such as EGFR, ALK, and KRAS has led to the development of targeted therapies, including tyrosine kinase inhibitors (TKIs). These therapies have shown significant promise, offering improved outcomes, particularly for patients with specific mutations. Despite these advances, acquired resistance remains a key challenge, often due to secondary mutations or activation of alternative signaling pathways. Ongoing research is focused on overcoming these resistance mechanisms and improving treatment strategies, with an emphasis on combination therapies and next-generation TKIs.

This review, published (DOI: 10.20892/j.issn.2095-3941.2025.0153) in Cancer Biology & Medicine (2025), provides an overview of recent developments in the treatment of NSCLC driven by oncogene mutations. It explores the effectiveness of TKIs and discusses strategies to address acquired resistance. The study, conducted by researchers from Tianjin Medical University General Hospital, including the Department of Lung Cancer Surgery and the Tianjin Key Laboratory of Lung Cancer Metastasis and Tumor Microenvironment, underscores the need for personalized treatment approaches and the exploration of new therapeutic combinations to improve clinical outcomes for NSCLC patients.

Over the past two decades, targeted therapies for NSCLC have shown considerable progress,

particularly with the use of TKIs for mutations in EGFR, ALK, and KRAS. These therapies have significantly improved patient outcomes, especially in early-stage disease. However, acquired resistance to these therapies remains a major obstacle. Resistance mechanisms can be both EGFR-dependent, such as the T790M mutation, and EGFR-independent, such as MET amplification.

To address these challenges, new-generation TKIs and combination therapies are being developed. For example, osimertinib, a third-generation EGFR-TKI, is effective against T790M resistance but struggles with mutations like C797S. Research into combining EGFR-TKIs with MET inhibitors has shown promise in overcoming resistance. Additionally, bispecific antibodies, like amivantamab, which target both EGFR and MET, are emerging as potential strategies. Clinical trials such as ORCHARD and SAVANNAH are essential in assessing these approaches. Early data suggest that these therapies could help overcome resistance and provide improved progression-free survival, offering a more durable treatment option for NSCLC patients.

Dr. Song Xu, a leading researcher in NSCLC treatment, noted, "While targeted therapies have improved outcomes for many patients with NSCLC, resistance to treatment remains a significant challenge. The development of next-generation inhibitors and combination therapies represents an important step toward overcoming these challenges. It is crucial that we continue to focus on personalized treatment approaches that can adapt to the changing nature of tumors, offering more effective and lasting treatment options for patients."

The advancements in NSCLC treatment discussed in this review have important implications for patient care. The use of targeted therapies, such as EGFR-TKIs and ALK inhibitors, has already improved survival rates for many patients. However, overcoming resistance remains a priority. The introduction of new therapies, including bispecific antibodies and combination regimens, offers the potential for more effective, long-term treatment options. Future research should continue to focus on identifying resistance mechanisms and developing personalized treatment strategies to further improve patient outcomes. These efforts in precision oncology will help provide more tailored and effective therapies for NSCLC patients.

References

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