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Targeted therapies in lung cancer: Progress, challenges, and future prospects.

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Introduction

Lung cancer remains a leading cause of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of cases. Over the past two decades, a revolution in cancer treatment has occurred with the development of targeted therapies—drugs designed to interfere with specific molecular pathways essential for tumor growth and survival. These therapies have transformed lung cancer from a uniformly grim diagnosis to a condition that, in many cases, can be managed with precision and hope [1].

The foundation of targeted therapy lies in molecular profiling of tumors. Genetic mutations, rearrangements, and amplifications in oncogenes such as epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ROS1, BRAF, and MET have been identified as key drivers in subsets of NSCLC. Identifying these alterations allows clinicians to select therapies that specifically inhibit these abnormal proteins, thereby suppressing tumor growth while sparing normal cells [2].

One of the earliest breakthroughs came with the discovery of EGFR mutations, particularly in non-smoking Asian women with adenocarcinoma. First-generation EGFR tyrosine kinase inhibitors (TKIs) such as erlotinib and gefitinib showed remarkable efficacy in this group. Subsequent generations of TKIs, like afatinib and osimertinib, have improved outcomes further by overcoming resistance mutations like T790M and offering better central nervous system penetration [3].

Similarly, ALK rearrangements, present in about 5% of NSCLC cases, responded well to crizotinib, a first-in-class ALK inhibitor. However, resistance and progression necessitated the development of second- and third-generation agents such as alectinib, brigatinib, and lorlatinib, which offer prolonged progression-free survival and improved outcomes in brain metastases. These advances underscore the dynamic nature of targeted therapy development [4].

ROS1, RET, and NTRK rearrangements, though rare, have also been successfully targeted. Drugs like entrectinib and larotrectinib for NTRK fusions, and selpercatinib for RET fusions, have received regulatory approvals based on compelling clinical trial data. The emerging landscape of MET exon 14 skipping mutations and HER2 alterations is being addressed with new agents like capmatinib and trastuzumab-deruxtecan, broadening the spectrum of personalized lung cancer treatment [5].

Conclusion

In conclusion, targeted therapies have dramatically improved the prognosis and quality of life for many lung cancer patients. By focusing on the molecular drivers of disease, these treatments offer personalized, more effective, and less toxic alternatives to conventional chemotherapy. Continued innovation, coupled with efforts to enhance global access and affordability, will be crucial in realizing the full potential of targeted therapies and reshaping the future of lung cancer care.

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