Targeting METex14 in NSCLC: Clinical Advances and Unmet Needs

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Educational background

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Professional experience

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MET exon 14 skipping (METex14) alterations have been established as a distinct oncogenic driver in a subset of non-small cell lung cancer (NSCLC), occurring in approximately 3-4% of patients. The development of highly selective MET tyrosine kinase inhibitors (TKIs), such as tepotinib and capmatinib and, has fundamentally transformed the treatment strategy for this patient population, shifting the paradigm from conventional chemotherapy to targeted molecular therapy.

This presentation will first review the significant clinical advances achieved with MET TKIs. We will delve into the pivotal clinical trial data that led to their regulatory approval, highlighting the impressive objective response rates and durable clinical benefits observed in both treatment-naïve and previously treated patients. Special attention will be given to the efficacy of these agents in challenging clinical scenarios, including patients with brain metastases.

Despite these successes, significant unmet needs persist. The presentation will then critically address the key challenges in managing METex14-mutated NSCLC. These include the emergence of on-target and off-target acquired resistance mechanisms, the optimal sequencing of therapies, and the management of treatment-related adverse events such as peripheral edema. Furthermore, we will explore the ongoing research into next-generation MET inhibitors and rational combination strategies designed to overcome resistance and prolong patient survival. This talk aims to provide a comprehensive overview of the current landscape and future directions for targeting METex14, offering insights for optimizing patient care in this molecularly defined subgroup of NSCLC.