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Review on Ret-Gene Fusion Positive Non-Small Cell Lung Cancer

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Abstract: RET (rearranged during transfection) gene fusion–positive non–small cell lung cancer (NSCLC) represents a distinct molecular subtype, occurring in approximately 1–2% of NSCLC cases, predominantly among younger, non-smoking patients with adenocarcinoma histology. RET fusions result in constitutive activation of RET tyrosine kinase signaling, driving tumorigenesis. Accurate detection through next-generation sequencing (NGS) or RNA-based assays is essential for guiding targeted therapy. The development of selective RET inhibitors, such as selpercatinib and pralsetinib, has revolutionized treatment, demonstrating high response rates, durable disease control, and favorable safety profiles compared with traditional chemotherapy or multikinase inhibitors. Despite these advances, acquired resistance and central nervous system progression remain significant challenges. RET fusion–positive NSCLC exemplifies the success of precision oncology, highlighting the importance of comprehensive molecular profiling and continued research into next-generation inhibitors and combination treatment strategies to further improve patient outcomes.

Keywords: RET gene fusion (NSCLC), Tyrosine kinase inhibitors, Next-generation sequencing, Chemotherapy

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