ALK融合基因阳性的晚期非小细胞肺癌靶向治疗进展

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Title: The targeted therapy progress of advanced non-small cell lung cancer with ALK fusion gene positive

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摘要: 近十年来，晚期非小细胞肺癌（non-small cell lung cancer，NSCLC）在治疗方面出现重大的模式转变。关键致癌性突变（如驱动基因突变和染色体重排）的存在，使得靶向治疗相比传统的细胞毒性化学疗法显示出更高的敏感性。2007年间变性淋巴瘤激酶（anaplastic lymphoma kinase，ALK）基因与棘皮动物微管相关蛋白样-4（echinoderm microtubule-associated protein-4，EML4）基因融合突变首次在NSCLC患者中被发现。随后研究证实，ALK-EML4融合突变阳性的NSCLC（ALK+NSCLC）显示出对克唑替尼治疗的敏感性。随着后续一系列靶向治疗新药的研发，将ALK+NSCLC靶向治疗推向高潮。本综述回顾ALK+NSCLC的分子生物学发病机制、流行病学特征及检测方法，汇总其抑制剂的重要临床试验结果，并解读ALK+NSCLC抑制剂耐药机制及合并脑转移的最新研究进展。

Abstract: In the past decade，there has been a major pattern transformation in the treatment of advanced non-small cell lung cancer(NSCLC).The presence of key oncogenic mutations（such as driving gene mutations and chromosomal rearrangements） has made that targeted therapies have a higher sensitivity compared with traditional cytotoxic chemotherapy.Fusion mutations in the anaplastic lymphoma kinase（ALK） gene and the echinoderm microtubule-associated protein-4(EML4)gene were first discovered in patients with NSCLC in 2007.Subsequent studies confirmed that the ALK-EML4 fusion mutation positive non-small-cell lung cancer(ALK+NSCLC) showed sensitivity to crizotinib treatment.With the subsequent development of a series of targeted therapeutic new drugs，the ALK+ NSCLC targeted therapy was pushed to the top.This review summarizes the molecular biology pathogenesis，epidemiological characteristics，and detection methods of ALK+NSCLC，summarizing the results of important clinical trials of inhibitors and reviewing the latest advances in ALK+NSCLC inhibitor resistance mechanisms and brain metastases.

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