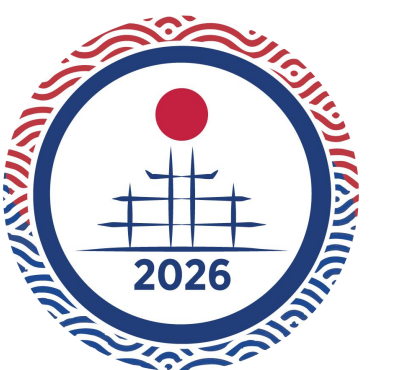




ID1416: Combined EGFR-TKI, BRAF and MEK inhibitors treatment for advanced non-small-cell lung cancer patients with an acquired BRAF V600E mutation, report of 5cases

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INTRODUCTION

Although EGFR-tyrosine kinase inhibitors (EGFR-TKIs) initially show promising antitumor activity, most patients with advanced non-small cell lung cancer (NSCLC) eventually develop resistance. The BRAF V600E mutation, a rare genetic alteration, is an important mechanism of acquired resistance to EGFR-TKIs. While BRAF plus MEK inhibition is effective and safe in patients with primary BRAF V600E/K-mutant metastatic NSCLC, the optimal treatment strategy for BRAF V600E-mediated EGFR-TKI resistance remains unclear

DISCUSSION

Two cucessful cases with a PFS longer than 6months after the progression on osimertinib are both with young age and good PS. Dual-targeted therapy demonstrates favorable efficacy in patients with primary BRAF-mutant tumors, whereas similar promising outcomes are not consistently observed in those with secondary BRAF mutations. This discrepancy highlights the need for further investigation into the underlying mechanisms of resistance, which may involve distinct clonal evolution, concurrent genomic alterations, and alternative pathway activation. In addition, triple-targeted regimens are associated with higher toxicity compared with dual-targeted combinations. Given the increased incidence and severity of adverse events, it remains clinically relevant to explore whether dose adjustments, such as dose reduction or intermittent administration, are necessary to optimize the safety and tolerability of triple-targeted therapy without compromising antitumor activity

CONCLUSION

Combined EGFR and BRAF-targeted tyrosine kinase inhibitor (TKI) therapy demonstrates non-inferior efficacy compared with conventional chemotherapy. Dual EGFR/BRAF inhibition further enhances antitumor activity, though it is associated with a significantly higher incidence and severity of adverse events. Given this risk-benefit trade-off, such treatment strategies require further clinical investigation to optimize safety, tolerability, and long-term outcomes

REFERENCES & ACKNOWLEDGEMENTS

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Case Description

Six patients with EGFR-mutant non-small cell lung cancer (NSCLC) were found to harbor the BRAF V600E mutation by next-generation sequencing (NGS) after disease progression on EGFR-TKI therapy. Among them, five patients were treated with furmonertinib, dabrafenib, and trametinib. Two patients achieved progression-free survival (PFS) of 7 and 8 months after full-dose treatment. Two other patients required dose reduction of dabrafenib and trametinib due to treatment-related toxicity, with clinical benefit lasting only 2 months. The remaining patient received full-dose therapy but experienced disease progression in the lung and brain, resulting in a clinical benefit of only 2 months

