Abstract 1813

Clinical utility of cerebrospinal fluid (CSF) circulating tumour DNA (ctDNA) next generation sequencing (NGS) for diagnosis and treatment of leptomeningeal metastasis (LM) in patients with non-small cell lung cancer (NSCLC): a multi-centre retrospective study

Type: Abstract

Topic: Precision medicine

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Background

LM is a challenging complication of advanced NSCLC. Firstly, CSF cytology is gold standard for LM diagnosis but has limited sensitivity. Secondly, most systemic treatments are ineffective in treating LM. Studies have reported that CSF in LM are rich in ctDNA that is feasible for genomic sequencing. Clinical utility of CSF ctDNA NGS for diagnosis and treatment of LM remains underexplored.

Methods

This was a multi-centre retrospective study conducted in Hong Kong (Prince of Wales Hospital) and Singapore (Icon Cancer Centre Mount Elizabeth and Curie Oncology – Farrer). Advanced NSCLC patients (pts) with CSF ctDNA NGS done between March 2018 and May 2025 were enrolled. Clinical features, radiology results, CSF cytology and treatment outcomes were collated.

Results

A total of 36 pts were enrolled (age 39-80, 27 female). For baseline mutation: 11 pts had EGFR L858R mutation, 6 had EGFR exon 19 deletion, 5 had uncommon EGFR, 2 had ALK rearrangement, 1 had BRAF V600E, 1 had ERBB and 10 were unknown. Driver oncogenic alterations were detected in CSF ctDNA in 30 pts (83%), and all concordant with baseline mutation. CSF ctDNA NGS revealed new potentially actionable alterations in 13 cases: 2 had EGFR T790M, 3 had C797X, 2 had L718V, 2 had L792X, 1 had G796S, 1 had L838V, and 1 had MET exon 14 skipping.

Among 12 pts with clinical data for analysis, brain imaging, CSF cytology, and CSF ctDNA were positive in 10 (83%), 2 (17%), and 8 (67%) cases, respectively. One pt had LM symptoms but was negative in imaging and cytology found positive CSF ctDNA, which diagnosed LM. One showed acquired MET exon 14 skipping alteration in ctDNA, thus capmatinib was added on top of EGFR targeted therapy. One had known EGFR exon 19 deletion with negative CSF cytology showed T790M mutation in ctDNA and treatment was switched to osimertinib.

Conclusions

In patients with NSCLC and LM symptoms, CSF ctDNA had higher sensitivity compared to cytology in LM diagnosis. CSF ctDNA may also detect actionable resistance mechanisms in guiding treatment. Further research is required to study the role of CSF ctDNA NGS in diagnosis and treatment of LM.

Clinical trial identification

Editorial acknowledgement

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