

Study analyzes mutations in cerebrospinal fluid in lung cancer with brain metastases

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Researchers have explored the analysis of mutations in cerebrospinal fluid of lung cancer patients with brain metastases in a study presented at the ESMO Asia 2017 Congress.

Tumour tissue from brain metastasis is difficult to obtain and therefore less invasive methods are needed to identify and monitor the presence of known actionable mutations.

Brain metastases are a frequent complication of non-small cell [lung cancer](#) (NSCLC), especially in [patients](#) with lung adenocarcinoma. Patients with epidermal growth factor receptor (EGFR) [mutations](#) benefit from EGFR tyrosine kinase inhibitors (TKIs), but most relapse within one or two years, many with brain metastases.

"The gold standard for determining EGFR mutation status is DNA sequencing of the tumour, but this is challenging with brain tissue," said lead author Dr Yang Sen, medical oncologist, The Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China. "Tumour-derived DNA from brain metastases may be secreted into cerebrospinal fluid, but not the blood due to the blood-brain barrier."

This study compared EGFR mutation status in blood and cerebrospinal fluid and their relationship to [neurological symptoms](#) and leptomeningeal metastases. The study included 41 lung adenocarcinoma patients with EGFR mutations and [brain metastases](#). EGFR mutation status was analysed in the blood of 37 patients and cerebrospinal fluid of all patients. The presence of leptomeningeal metastases was assessed with magnetic resonance imaging (MRI).

In the entire study population, the rate of EGFR mutations in blood (65%) was significantly higher than in cerebrospinal fluid (37%) ($p=0.013$). Eleven patients had leptomeningeal metastases detected by MRI. The rate of EGFR mutations in cerebrospinal fluid was significantly higher in

patients with leptomeningeal metastases (73%) than in those without leptomeningeal metastases (23%) ($p=0.003$).

Neurological symptoms were present in 27 patients. The rate of EGFR mutations in cerebrospinal fluid was significantly higher in patients with neurological symptoms (48%) than in those without symptoms (14%) ($p=0.033$).

Sen said: "Neurological symptoms and leptomeningeal metastases were closely related with EGFR mutation status in cerebrospinal fluid."

Commenting on the results, Yi-Long Wu, Tenured Professor of Guangdong Lung Cancer Institute, Guangdong General Hospital, and Past President of the Chinese Society of Clinical Oncology (CSCO), said: "Mutation information is needed for patients with lung cancer to make decisions on targeted treatment but tissue biopsies can be difficult to obtain if the tumour is very small or is close to the aorta or heart. There is now a consensus among global experts that liquid biopsy using blood samples should be used to test for T790M and EGFR mutations in patients with NSCLC when tumor tissue is not available."

"The current study using cerebrospinal fluid is too small to reach strong conclusions," continued Wu. "Further developments are needed to increase the sensitivity of genetic testing from liquid biopsies. A clinical trial would help to clarify how liquid biopsies should be used in clinical practice."

Dr Stefan Zimmermann, Senior Consultant, Medical Oncology Department, Lausanne University Hospital, Lausanne, Switzerland, said: "Genotyping of cell-free DNA using droplet digital polymerase chain reaction (PCR) in [cerebrospinal fluid](#) as a less invasive modality to identify and monitor the presence of known actionable mutations is certainly interesting, as [tumour tissue](#) from [brain metastasis](#) is difficult to obtain. However, the sensitivity in the

present study is low, either because of false-negative assays due to an absence of DNA shedding, or analytical issues. Further research is needed before useful insight into the biology of central nervous system metastases is obtained via spinal taps."

Provided by European Society for Medical Oncology

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