ESMO-JSMO joint symposium: how to integrate genome sequencing data in oncology

NEW INSIGHTS FOR SEQUENCING DATA IN LUNG CANCER

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Cases of non-small-cell lung cancer (NSCC) carrying EGFR mutations have been shown to be hyperresponsive to EGFR tyrosine kinase inhibitors. Chromosomal translocations and corresponding gene fusions play an important role in initiating tumorigenesis. Association of ALK, ROS1 and RET fusion transcripts and its potential as lung tumor predictive biomarkers for respective kinase inhibitors has increased the need of technology that could detect these biomarkers starting from limited amount of FFPE material for precision medicine with molecular targeted agents. We have set up the MassArray Lung Cancer Panel and Lung Fusion Panel (Sequenom) to analyze the FFPE biopsy samples of lung cancer and examined its feasibility. Deep sequencing technologies as well as liquid biopsy are powerful tools for this strategy. The OncoNetwork Consortium and Life Technologies collaborated for the development of lung fusion panel based on Ion AmpliSeq™ RNA chemistry to: 1) Detect all variants of ALK, ROS1, or RET fusion transcripts described in COSMIC in a single reaction using 10 ng of total RNA; 2) Include 5' and 3' ALK, ROS1, RET gene expression assays as an indicator of translocation at this gene; 3) Include endogenous RNA assay controls to determine if the quality of the results could be affected by RNA quality; 4) Provide similar results on archived FFPE samples tested by FISH. Monitoring of the acquired resistance to EGFR-TKI and ALK inhibitors is another important issue for the development of the next generation therapeutics. Rebiopsy is essential to detect secondary mutations of EGFR (T790M) that causes the resistance to EGFR-TKI. However tissue availability limits the genotyping of EGFR in a clinical setting. We have developed the several sensitive assays (Scorpion-Arms, Cobas(R) EGFR mutation test, SABER and droplet-digital PCR (ddPCR) system e.g.) to detect EGFR mutations and fusion genes from tumor-derived DNA in tissue and blood of lung cancer patients. We have monitored the EGFR mutation status during anti-EGFR treatment. We have now concluded that ddPCR system, e.g., is a suitable technology for liquid biopsies. In collaboration with the West Japan Oncology Group (WJOG), we have established a prescreening system to detect marker-positive population using these deep sequencing technologies and ddPCR for the clinical studies.

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