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Molecular triage of lung cancer for targeted therapy

Sir,

The type of lung cancer as per histology is small cell and non-small cell carcinoma which includes adenocarcinoma with variants, squamous carcinoma. Biomolecular testing[1-3] includes tests of genes or proteins required to analyze which can be targeted with therapy to treat the patients. Molecular diagnostics-guided targeted therapies have become a standard treatment for patients with lung cancer. Driver genetic alterations such as epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) rearrangements are currently used as predictive biomarkers for EGFR tyrosine kinase inhibitors and ALK inhibitors, respectively. Targeted therapy with gefitinib, erlotinib, and afatinib used for EGFR-mutated advanced non-small cell lung carcinoma (NSCLC), and the ALK inhibitors crizotinib and ceritinib in ALK positive and for ROS1 rearrangement positive NSCLC crizotinib is used. Bevacizumab (Avastin) is used to treat advanced NSCLC. Ramucirumab (Cyramza) can also be used to treat advanced NSCLC. Patients with lung cancer can get benefits from molecular testing of their tumors regardless of stage. For example, molecular testing can provide accurate information on staging (in case of multiple tumors), prognostic stratification, and prompt treatment in case of recurrence. Since most driver mutations develop in early steps of carcinogenesis, tumor samples from either primary masses or metastatic lesions are equally suitable for mutation testing. In the case of multiple primary lung cancers, each tumor may be tested. This short communication or review stresses on the limitations of performing focused molecular analysis on NSCLC biopsies after diagnostic investigations are complete. The paucity of tissue available, the quality of DNA extracted, and the low frequency of aberrations detected means alternative approaches should be sought as the detection of the molecular and genetic mutations is necessary for targeted therapy as mentioned in Table 1.

Table 1: Depicting the molecules and selective targeted treatment for the adenocarcinomas (NSCLC)

Lung cancer	Patient selection and gene molecule isolated	Treatment
NSCLC	EGFR	Tyrosine kinase inhibitor erlotinib, gefitinib, and afatinib
NSCLC	ALK	Crizotinib
NSCLC	ROS	Crizotinib
NSCLC	RET	Cabozantinib
NSCLC	BRAF	BRAF inhibitors

NSCLC: Non-small cell lung carcinoma, EGFR: Epidermal growth factor receptor, ALK: Anaplastic lymphoma kinase

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