# Liquid biopsies for identification of EGFR mutations and prediction of recurrence

July 25 2016

Three manuscripts published in the recent issue of the *Journal of Thoracic Oncology*, the official journal of the International Association for the Study of Lung Cancer (IASLC), explored the versatility of liquid biopsies by identifying EGFR mutations using circulating tumor DNA (ctDNA) in urine and plasma and examining circulating tumor cells (CTCs) in plasma to predict the risk of lung cancer recurrence after surgical resection. Collectively, these findings illustrate the potential and reach of liquid biopsies in both identifying patients suitable for targeted treatment as well as predicting cancer recurrence.

Lung cancer is the most common type of cancer with the highest cancer-related mortality worldwide. Non-small cell lung cancer (NSCLC) accounts for roughly 85% of lung cancer and most patients present with advanced disease at diagnosis. Surgical resection is the preferred treatment option for patients with medically operable tumors. However, disease recurrence occurs in approximately 50% of cases. Patients with advanced disease are often not candidates for surgical resection and commonly harbor driver mutations that can be targeted by drugs. A major challenge for assessing driver mutations, such as epidermal growth factor receptor (EGFR) mutations, in advanced disease is the scarcity of suitable biopsy tissue for molecular testing. A minimally invasive alternative to invasive tissue biopsy is the use of liquid biopsy, which analyzes ctDNA or CTCs in a liquid biological sample (i.e. urine, blood, or serum).

The first manuscript entitled, Circulating Free Tumor-derived DNA

(ctDNA) Determination of EGFR Mutation Status in Real-World European and Japanese Patients with Advanced NSCLC: the ASSESS Study, used samples from the large ASSESS study to evaluate EGFR mutation status by analyzing ctDNA from blood plasma. The results of the study demonstrated that analyzing ctDNA from plasma is feasible for the identification of EGFR mutations with mutation status concordance in 1,162 matched samples of 89% (sensitivity 46%; specificity 97%; positive predictive value [PPV] 78%; negative PV 90%). The authors comment that, "Accurate and accessible ctDNA mutation testing to address the unmet need in patients without an available/evaluable tumor sample will be important to enable more patients to receive therapies personalized to the mutation status of their tumor."

The second manuscript entitled, A Highly Sensitive and Quantitative Test Platform for Detection of NSCLC EGFR Mutations in Urine and Plasma, analyzed samples from patients enrolled in TIGER-X, a phase 1/2 clinical study of rociletinib in previously treated patients with EGFR mutant-positive advanced NSCLC, to interrogate EGFR activating mutations and the T790M resistance mutation by analyzing ctDNA from urine or blood plasma. The results from the study show that ctDNA derived from NSCLC tumors can be detected with high sensitivity in urine and plasma, sensitivity 93% for T790M, 80% L858R, and 83% exon 19 deletions and sensitivity 93% for T790M, 100% L858R, and 87% exon 19 deletions, respectively. The authors comment that, "In conclusion, our data demonstrates that urine testing using mutation enrichment NGS method successfully identifies EGFR mutations in patients with metastatic NSCLC and has a high concordance with tumor and plasma, suggesting that EGFR mutation detection from urine or plasma should be considered as a viable approach for assessing EGFR mutation status."

Finally, a third manuscript on liquid biopsies entitled, Circulating

tumour cells detected in the tumour-draining pulmonary vein are associated with disease recurrence after surgical resection of non-small cell lung cancer, used blood and tumor-draining pulmonary vein samples from patients pre-surgical resection and intra-operatively to analyze CTCs and circulating tumor microemboli (CTM, clusters). The investigators reported that combining CTC/CTM enumeration in tumor-draining pulmonary veins and peripheral blood at the time of curative-intent surgical resection of NSCLC better identifies those patients at higher risk of lung cancer recurrence than peripheral CTC/CTM numbers alone. "In addition to the potential role of CTCs as a prognostic/predictive biomarker, isolation and genetic analysis of individual CTCs from liquid biopsies may shed light on tumor biology and the metastatic process," said Phil AJ Crosbie, MD, PhD, first author of the article.

Provided by International Association for the Study of Lung Cancer