Aim: Although epidermal growth factor receptor (EGFR) mutation analysis has been important to decide treatment of advanced non-small cell lung cancer patients (NSCLC), this analysis requires a tumor tissue, which may not be available in certain situations. About 50% of resistance mechanisms to EGFR tyrosine kinase inhibitors (TKIs) in NSCLC patients is reported to be attributed to the T790M mutation in exon 20. Although there are some reports to detect EGFR gene mutation using cell-free DNA (cf DNA) from plasma including digital PCR, there is no methods established in clinical studies. We conducted a prospective study to evaluate plasma EGFR gene mutations for advanced NSCLC patients using RNase H-dependent PCR method and Blocking oligo dependent PCR, which can method with high sensitivity and low price, in Shizuoka Cancer Center.

Methods: Patients included were as follows: advanced or recurrent NSCLC patients; harboring EGFR mutations (exon 19 deletion or L858R in exon 21) in tumor tissues confirmed by Scorpion ARMS method; pre-treatment or post-progression treatment with EGFR-TKI; written informed consent. Cf DNAs were extracted from plasma by QIAamp Circulating Nucleic Acid Kit (QIAGEN®). L858R and T790M were analyzed by the rhPCR and Luminex Technology®. The Blocking oligo dependent PCR and Luminex Technology® were used for detecting exon 19 deletion.

Results: Forty-nine patients, including 22 pre-treatment and 27 post-progression of EGFR-TKI were enrolled in this study. Thirty four patients had exon 19 deletion and 15 had L858R in exon21. In those with exon 19 deletion and L858R in exon 21, the sensitivities of detection of EGFR mutation were 59% (20/34) and 67% (10/15), respectively. 37 % of patients with post-progression of EGFR-TKI showed T790M in exon 20 from their plasma samples, and none of those with pre-treatment did. T790M mutation was detected in 2 re-biopsy tissue samples, and T790M was also detected in their plasma samples.

Conclusions: These results suggested that the RNase H-dependent PCR and Blocking oligo dependent PCR methods may be acceptable to evaluate and have a potential as an alternative method to detect EGFR mutations of cf using DNA from plasma. In future, these methods should be validated for large population in multi-institutional studies. Larger study should be conducted to validate these results.

Disclosure: Y. Fukuda, K. Yamasaki and R. Umehara: Employee of G and G science. All other authors have declared no conflicts of interest.