Background As highly sensitive liquid biopsy assays have been developed, minimal residual disease (MRD) has emerged as a novel tool to predict the prognosis of cancer patients.\(^1\) Monitoring MRD during post-curative-intent treatment can help detect relapse of disease many months earlier compared to radiological imaging evaluation.\(^1,2,5\) Recurrence remains a challenge among early-stage non-small cell lung cancer (NSCLC) patients who are treated with curative intent.\(^3\) Some patients with seemingly successful treatment of early-stage cancer can have occult micrometastases or MRD that persists after the initial therapy which can be a potential source of subsequent metastatic relapse at distant sites.\(^4\) This study compares longitudinal changes in tissue-based ctDNA levels of thirty NSCLC patients.

Methods Thirty patients included in this study were treated with concurrent chemoradiotherapy or surgery and/or neoadjuvant or adjuvant chemotherapy for stage I-IV lung cancer. The patients underwent a multiplex polymerase chain reaction (mPCR) assay for detection of ctDNA in plasma, where 16 individual-specific mutation signatures were identified by upfront tissue sampling. These were matched to normal whole-exome sequencing to identify progression or relapse of disease (SignateraTM, Natera, Austin, Texas). Patients who were MRD-positive at any time point after curative treatment were defined as ‘MRD positive (MP)’. Among patients who were monitored for two or more times, patients whose MRD was persistently detected in blood were classified as ‘MRD persistently positive (MPP)’.

Results ctDNA was evaluated one time in fifteen patients (42.9\%) and two or more times in twenty patients (57.1\%). MRD was detectable among nine patients (25.7\%) after curative treatment at a median of 4 months (range 0–41 months). Among nine MP patients, six experienced progressions. In twenty-nine patients with NSCLC who did not relapse after surgery, the assay confirmed MRD negativity at 71 of 73-time points. Three patients were MPP, ctDNA was continuously detectable in three out of twenty patients, and all of them showed progression, including one patient who died (figure 1). MRD positive patients had marginally worse overall survival (OS) and progression-free survival (PFS) (p=0.092 and p=0.04, respectively). However, persistent MRD positivity showed a stronger correlation with poor OS and PFS (p=0.037 and p < 0.001, respectively) (figure 2).

Conclusions This is the first report of real-world data on tissue-based ctDNA MRD assay among NSCLC patients treated curatively. The results indicate that post-curative-intent treatment ctDNA MRD monitoring can be predictive of clinical prognosis including OS or PFS.

REFERENCES