

Evaluation of the correlation between circulating tumor DNA dynamics and lung cancer chemotherapy efficacy

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Background

- ◆ Chemotherapy as one of the most important medical treatment for lung cancer patients is commonly used when patients are not suitable for surgery or relapse after surgery.
- ◆ Response evaluation criteria in solid tumors (RECIST) is a commonly used method to evaluate lung cancer chemotherapy efficacy. However, the RECIST method is expensive, and easily causes radiation damage to patients.
- ◆ Circulating tumor DNA (ctDNA) dynamics refers to the fluctuation of ctDNA over a period of time, and it can be used as an indicator for monitoring the efficacy of chemotherapy through a non-invasive and radiation-free way in some cancers¹. But there are few reports on the application of ctDNA dynamics in monitoring the efficacy of lung cancer chemotherapy.
- ◆ The aim of our study was to assess the consistency between the ctDNA dynamics and efficacy of lung cancer chemotherapy.

Methods

- ◆ The peripheral blood of 238 lung cancer patients who received chemotherapy before each chemotherapy cycle were collected. And the efficacy of chemotherapy was evaluated by the RECIST method.
- ◆ An ultrasensitive and quantitative method named LNA-dPNA PCR clamp was used to monitor the dynamics of *EGFR* L858R in plasma².
- ◆ The consistency between *EGFR* L858R dynamics and the RECIST results were evaluated.

Results and Discussion

- ◆ A total of 238 lung cancer patients requiring chemotherapy were included in our study. Among them, 158 cases were lung adenocarcinoma, accounting for 66.4%; 51 cases were squamous cell carcinoma, accounting for 21.4%. According to the stage of patients, there are 19 cases in stage I, 17 cases in stage II, 37 cases in stage III, and 165 cases in stage IV. The patients requiring chemotherapy are mainly patients with advanced lung cancer, accounting for 84.9%.

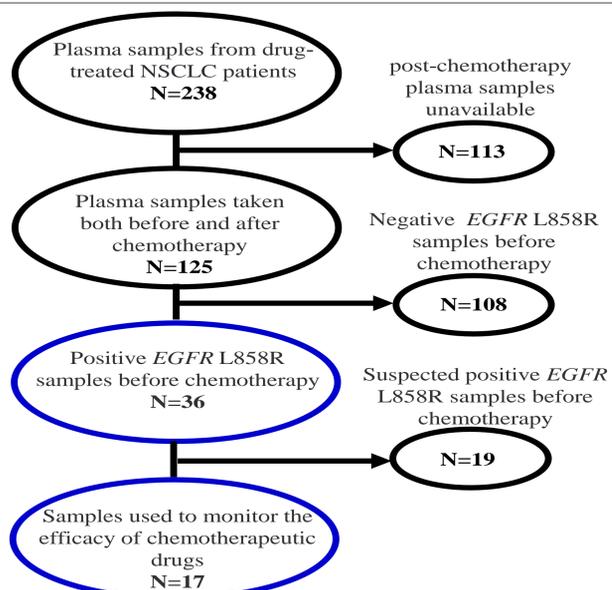


Fig.1 Lung cancer patients used to monitor the dynamics of *EGFR* L858R in plasma

- ◆ Of the 238 patients with lung cancer, 125 patients have collected peripheral bloods for more than two chemotherapy cycles. Dynamics of *EGFR* L858R in plasma were detected from the 125 patients by LNA-dPNA PCR clamp. After evaluation of *EGFR* L858R dynamics, 17 patients were positive for *EGFR* L858R mutations in peripheral blood, with a positive rate of 13.6% (Fig.1).
- ◆ The consistency between the *EGFR* L858R dynamics and efficacy of lung cancer chemotherapy was shown in Fig.2. As shown in Fig.2A, high ctDNA level was found before surgery. And it decrease to almost zero after removing the tumor. And then followed by relapse, the level of ctDNA increased. It showed a good correlation between the changes of ctDNA content in plasma and the efficacy of chemotherapy drugs in this patient.
- ◆ Besides this, we also found the inconsistent between ctDNA changes and the efficacy of chemotherapy drugs. As shown in Fig.2B, the postoperative status is stable, but the ctDNA content increased. Further analysis of its CT revealed that although the size of the original lesion was reduced, there were multiple nodules in other lung lobes, which suggest the possibility of disease metastasis.

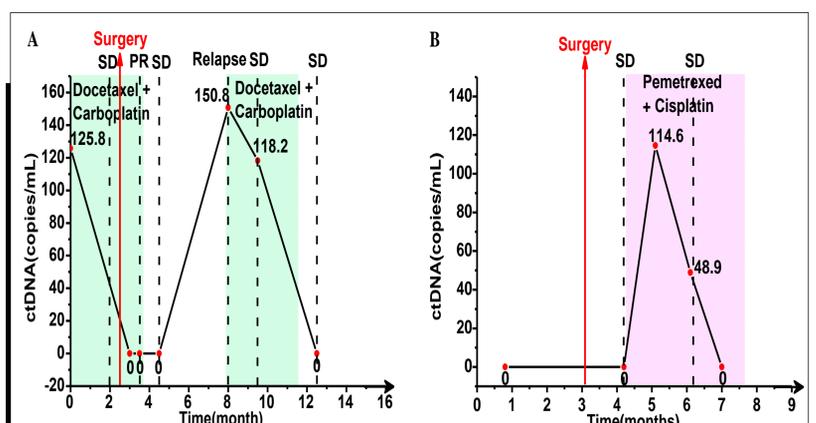


Fig.2. The consistency between the *EGFR* L858R dynamics and efficacy of lung cancer chemotherapy

A Typical result of *EGFR* L858R dynamics consistent with RECIST results;

B. Typical result of *EGFR* L858R dynamics inconsistent with the RECIST results.

- ◆ Of the 17 patients with positive for *EGFR* L858R mutations, there were 11 patients with a consistent tendency of *EGFR* L858R dynamics and RECIST results, with a ratio of 64.7%; and 6 patients with inconsistencies, with a ratio of 35.3%. However, the statistical results of only 17 patients in our study are small, and the sample size needs to be expanded for further verification.

Conclusions

- ◆ This study preliminarily explored the feasibility of using ctDNA dynamics to evaluate the efficacy of lung cancer chemotherapy with a limited sample size; a non-invasive and non-radioactive method, which has a promising prospect to monitor the efficacy of lung cancer chemotherapy in the future.

References

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2. S. Zhang, Z. Chen, C. Huang, etc, *Analyst*, 2019, 144, 1718-1724.