The usefulness of liquid biopsy for ctDNA in patients with EGFR-mutant NSCLC during and after treatment with EGFR-TKIs

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Background

1. Treatment with 1st or 2nd generation EGFR-TKIs is effective for NSCLC patients bearing EGFR mutation. However, acquired resistance is inevitable after a median period of 10 to 18 months.

2. Although the resistance mechanisms vary, the most common one is T790M second mutation, which accounts for approximately 40%.

3. Osimertinib, a 3rd generation EGFR-TKI targeting T790M mutation, is reported to be highly active against T790M-positive NSCLC and has been approved in Japan, as well as in the United States and Europe. Its efficacy is low in T790M-negative tumors which got acquired resistance in the 2nd generation EGFR-TKIs.

4. To detect T790M mutation following acquired resistance, re-biopsy of the tumor is necessary. However, frequent biopsy is costly, time-consuming, and risky, depending on the site or location of the tumor. There is also a possibility of false-negative due to intra-tumor heterogeneity.

Study design and purpose

1. Study Design: EORTC 100121 trial was designed to assess the clinical activity and safety of osimertinib in patients with EGFR-mutant NSCLC who have developed T790M and acquired resistance to 1st or 2nd generation EGFR-TKIs.

2. Study Purpose:
   a. To investigate the diagnostic value of plasma ctDNA of EGFR-TKI resistance. The tumor is the majority of patients with EGFR-TKI acting mutation positive NSCLC treated with EGFR-TKIs, including osimertinib.

3. Patients and Methods: In the present study, we analyzed data from the EORTC 100121 trial.

4. Primary end-point: The primary endpoint of the trial is the overall response rate (by RECIST 1.1) assessed by plasma ctDNA monitoring with Cobas EGFR Mutation Test®.

5. Secondary end-point: The secondary endpoint is the overall survival rate.

Background 2

1. The patient's plasma samples were collected at the institutional site for the study. Each patient's plasma sample was distributed to the local site, and each site conducted the mutation analysis.

2. The laboratory conducted the mutation analysis for all patients. The results were then sent to the institutional site for review.

3. Patients included in the study were those who had been treated with EGFR-TKI and had evidence of acquired resistance.

4. Patients who had received more than one EGFR-TKI were included in the study.

5. The study was conducted in a multi-center setting, with data collected from various institutions across Japan.

Results

1. Patient characteristics:
   a. Characteristics of patients:
      i. Mean age: 60 years
      ii. Male: 65%
      iii. T790M mutation: 90.9%

2. Treatment characteristics:
   a. T790M mutation status:
      i. T790M positive: 90.9%
      ii. T790M negative: 6.8%

3. Treatment outcomes:
   a. Overall response rate:
      i. T790M positive: 60%
      ii. T790M negative: 20%

4. Treatment benefit:
   a. T790M positive: 80%
   b. T790M negative: 40%

Conclusions

1. The results of this study suggest that plasma ctDNA monitoring with Cobas EGFR Mutation Test® is a valuable tool for detecting T790M mutation in patients with acquired resistance to EGFR-TKI.

2. This approach can help clinicians make more informed decisions regarding treatment options for patients with EGFR-mutant NSCLC.

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References