Evaluation of liquid biopsies for molecular profiling and monitoring in advanced non-small cell lung cancer (NSCLC) patients

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BACKGROUND

A prospective study was performed:
- To assess the molecular alterations in ctDNA of advanced NSCLC patients in whom the initial molecular profile was unknown due to insufficient cellularity in biopsy.
- To assess correlation of dynamic ctDNA with those in the tissue (if available) in this lung cancer population.
- To assess the concordance of molecular abnormalities in ctDNA with those in the tissue (if available) in this lung cancer population.
- To assess the dynamic marker of chemotherapy efficacy.
- Circulating tumor DNA (ctDNA) can be used as a non-invasive liquid biopsy for the detection, and quantification of molecular abnormalities.

OBJECTIVES

- Sensitivity and specificity of ctDNA varies across the different methods and its evolution during chemotherapy is unknown.
- To assess the molecular alterations in ctDNA before chemotherapy initiation, and then on day 2, 21 and 42 at the first radiological evaluation.
- To assess the correlation of dynamic ctDNA with radiological response by RECIST 1.1 criteria.
- To measure the distribution of ctDNA allele fraction by responder cohorts (RECIST 1.1) at D42
- To assess concordance of molecular altertions in ctDNA and tissue in 8 out of 9 patients (89% concordance).
- To assess correlation of dynamic ctDNA with platinum-based chemotherapy or concomitant chemotherapy-radiotherapy in 8 out of 9 patients (89% concordance).
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METHODS

- Blood tests were performed day 1 before chemotherapy initiation, and then on day 2, 21 and 42 at the first radiological evaluation.
- A prospective study was performed:
- To assess the molecular alterations in ctDNA before chemotherapy initiation, and then on day 2, 21 and 42 at the first radiological evaluation.
- To assess the correlation of dynamic ctDNA with radiological response by RECIST 1.1 criteria.
- To assess the concordance of molecular abnormalities in ctDNA with those in the tissue (if available) in this lung cancer population.
- To assess the dynamic marker of chemotherapy efficacy.

RESULTS

- 30 advanced NSCLC patients, all adenocarcinoma subtype and treated with platinum-based chemotherapy or concomitant chemotherapy-radiotherapy were recruited. Main patients’ clinical characteristics are reported in Table 1.
- Molecular profile on tissue was performed in 27 patients. Among 4 of the 27 (15%) there was insufficient cellularity in biopsy. In 9 out of 23 (39%), a molecular alteration was reported.
- Liquid biopsy detected at least one molecular alteration in 70% of patients (21/30).
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CONCLUSIONS

- Of 17 patients with repeated liquid biopsy testing (D1, D21, D42) and at least one molecular alteration, the dynamic ctDNA profiles at D21 and D42 correlate with radiological response by RECIST 1.1 at D42 (p < 0.01).

METHODS cont.

- Clinical Characteristics

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<tr>
<td>Former</td>
<td>6 (20)</td>
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</tbody>
</table>

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RESULTS cont.

- Early evolution (D2) of ctDNA analysis identified alterations in 10 genes (KRAS, EGFR, ERBB2, MET, BRAF, TP53, PTEN, STK11, PIK3CA, U2AF1).

Early ctdNA changes

- Early evolution (D2) of ctDNA by responder cohorts (RECIST 1.1) was analyzed (Figure 2).
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Graphs and tables are displayed in the document.