translational research

MUTATIONAL ANALYSIS OF CIRCULATING DNA AND CELLS IN PATIENTS WITH METASTATIC COLORECTAL CANCER

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Aim: The circulating tumor cells present morphological and genetic alterations. Our study is based on the association between the presence of KRAS mutations in circulating free cell DNA (ccfDNA) and the determination of genetically abnormal circulating cells (GACC), selecting these by size and the genetic alterations detected by FISH in patients who have undergone various treatments with metastatic colorectal cancer (CRCm).

Methods: CTCs were quantified by means an automated fluorescence method (MetaFer-MetaCyte of MetaSystem), allowing selection of cells by size and genetic alterations. We analyzed mutation in plasma from KRAS gene by Pyrosequencing. Finally, we studied the association between KRAS mutation detected and the presence of 19 KRAS mutations in codons 12, 13, and 61 in FFPET CRC specimens.

Results: Only 31 cells >7 micra were found in the controls out of the 36400 cells analyzed (0.08%). In the case of the patients, 389 cells were found (1.15%), the difference becoming statistically relevant after the MWW-test (p=0.001). None of the controls presented cells with two or more genetic alterations and over 7 micra in size, whereas 50% of the patients presented these characteristics despite having received treatment. 6 patients had a detectable plasma KRAS mutation in ccfDNA not previously found in the tumor. We found a connection between the presence of KRAS mutations in ccfDNA and the presence of GACC (p=0.048) Concordance between tumor-tissue analysis, ccfDNA analysis and GACC.

Conclusions: In our study we found KRAS mutations in ccfDNA of multitreated metastatic colorectal cancer patients which is related to the presence of morphogenetically altered cells.

Disclosure: All authors have declared no conflicts of interest.

Table: 1619P

<table>
<thead>
<tr>
<th>KRAS</th>
<th>GACC</th>
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<tbody>
<tr>
<td>Mutant</td>
<td>WT</td>
</tr>
<tr>
<td>ccfDNA</td>
<td>11</td>
</tr>
<tr>
<td>WT</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
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