Review of the current status of RAS mutation testing in patients with metastatic colorectal cancer (mCRC): Flash-RAS study

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**Study objectives**

**Primary objective:**
- To assess the rate of prescribing and conduct of RAS gene mutation tests (KRAS and NRAS exons 2, 3 and 4) in patients recently diagnosed with metastatic colorectal cancer (mCRC).

**Secondary objectives:**
- To describe the change in the rate of prescribing the KRAS gene mutation tests (exons 2, 3 and 4) between 2011 and 2014;
- To describe the reasons for prescribing and non-prescribing these tests depending on the characteristics of the doctors and the patients;
- To analyse the impact of the availability of the KRAS (exons 2, 3 and 4) and NRAS (exons 2, 3 and 4) tests in anatomical pathology laboratories, the impact of their results, the BRAF result, on the therapeutic choice of the doctor or its modification;
- To describe and analyse the time taken to obtain the results of the KRAS and NRAS tests the circuit (who made the request and when) and the therapeutic approach adopted during this period.

**Methods**

National multicenter retrospective observational study

To prevent a selection bias, each participating physician had to screen all patients seen as part of a routine normal clinic visit, during the "Enrolment Period" and who had to meet all the following inclusion criteria:

- Metastatic colorectal cancer histologically-confirmed after March 2014 (launch of NRAS tests in French centers);
- Seen by the physician between 15 June 2014 and 30 September 2014;
- First-line therapy of metastatic disease initiated between 1 March 2014 and 30 June 2014

Exclusion criteria:

- <18 years
- Refused to participate
- Active participation in an interventional study.

**Results**

**Table 1: patients characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=375</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex Male / Female</td>
<td>578 / 42.2</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>67 (31 – 92)</td>
</tr>
<tr>
<td>Synchronous metastases</td>
<td>270 (73.6)</td>
</tr>
<tr>
<td>Primary tumour: colon / rectum / colorectal</td>
<td>762 / 23.2 / 0.5</td>
</tr>
<tr>
<td>Interval to diagnosis of the first metastases – L1 treatment (months)</td>
<td>Median: 1.0 (0.0 ; 3.6)</td>
</tr>
</tbody>
</table>

**L1 chemotherapy:**

- FOLFOX / XELOX: 49.6
- FOLFIRI / XELIRI: 30.7
- 5 FU / Xeloda: 10.7
- Others: 1.3
- FOLFOXINOX: 6.4
- Missing data: 0

**Conclusion**

In 2014, RAS genotyping has become routine practice for the management of patients recently diagnosed with mCRC. The percentage of requests for genotyping in 2014 (80.1%) has increased since 2011 (81.1%).

For a large majority of patients (75.5%), the request for genotyping is done before or not later than one month after the diagnosis of the first metastases. However, for 24.5% of patients, the date of the request for genotyping, more than one month after the diagnosis, does not seem to be compatible with a fully informed decision on 1st line treatment.

The median time to complete the tests was stable between 2011 (19 days) and 2014 (20 days), despite the increase in the number of mutations tested (1 exon versus 6). A narrower standard deviation of the mean confirms a trend for the times to become more uniform. This shows the great reactivity of each stakeholder involved in mCRC patient management in implementing these new tests.

New techniques for the assessment of RAS status currently being tested will probably reduce and homogenize the time required to obtain RAS status.

**Disclosure/Acknowledgment**

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