Predictive value of C-reactive protein (CRP) in microsatellite-stable (MSS) metastatic colorectal cancer (CRC) patients given first-line alternating short-course oxaliplatin-based chemotherapy (FLOX) and nivolumab

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Background
- Tumour-associated systemic inflammation impedes immune checkpoint blockade (ICB) efficacy.
- We explored whether the initial 2 FLOX cycles of alternating short-course FLOX and nivolumab may affect circulating CRP and outcome (progression-free survival; PFS) in first-line treatment of metastatic MSS-CRC.

Methods

<table>
<thead>
<tr>
<th>Week</th>
<th>Control arm</th>
<th>Experimental arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>FLOX</td>
<td>FLOX</td>
</tr>
<tr>
<td>1</td>
<td>Nivolumab</td>
<td>Nivolumab</td>
</tr>
<tr>
<td>3</td>
<td>FLOX</td>
<td>Nivolumab</td>
</tr>
<tr>
<td>5</td>
<td>Nivolumab</td>
<td>FLOX</td>
</tr>
<tr>
<td>7</td>
<td>Nivolumab</td>
<td>Nivolumab</td>
</tr>
</tbody>
</table>

Withdrawal of consent (n = 4)

Patients randomly assigned (n = 76)

Sequence 1
 allocated to FLOX only (n = 38)

Sequence 2
 allocated to FLOX and nivolumab (n = 38)

Control arm
 reached Visit 3 (n = 37)

Experimental arm
 reached Visit 3 (n = 36)

Control arm
 reached Visit 3 (n = 37)

Patients randomly assigned (n = 76)

Results
- For the entire cohort, CRP was median 13.0 mg/L (range, 0.7-112.0) at baseline (Visit 1; n=76) and median 6.0 mg/L (range, 0.5-60.0) after 2 FLOX cycles (Visit 3; n=73); *p = 0.014 (Mann-Whitney U-test).

Conclusions
- In metastatic MSS-CRC patients receiving first-line therapy, CRP <5.0 mg/L after the initial 2 FLOX cycles identifies patients responding to the sequential nivolumab with improved PFS compared to patients continuing FLOX.
- As a rapid, cost-effective analysis, and if early oxaliplatin-based chemotherapy counteracts tumour-associated systemic inflammation, CRP may predict ICB efficacy in metastatic MSS-CRC.