LBA7
Neoadjuvant immune checkpoint inhibition in locally advanced MMR-deficient colon cancer: The NICHE-2 study


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Background
Neoadjuvant immunotherapy has shown promising responses in several cancer types. For colon cancer (CC), NICHE was the first neoadjuvant immunotherapy study to show pathologic responses in 100% of dMMR tumors. Importantly, disease-free survival (DFS) in patients (pts) with stage III dMMR CC is similar to that of pMMR pts, with 3-year recurrence risks of over 40% in high-risk (T4 and/or N2) stage III tumors despite adjuvant chemotherapy. Improving outcome for this patient population is urgently needed.

Methods
In the NICHE-2 study, pts with non-metastatic dMMR CC were treated with one dose of ipilimumab (1mg/kg) and two doses of nivolumab (3mg/kg) and underwent surgery ≤6 weeks of registration. The co-primary endpoints were safety (ITT) and 3-year DFS (PP). Secondary endpoints included major pathologic response (MPR) and complete response (pCR) rates. Pathologic response was defined as ≤50% residual viable tumor (RVT), and MPR as ≤10% RVT. Here we present safety and pathologic response data.

Results
A total of 112 pts were treated. Grade 3-4 immune-related adverse events were observed in 3 (3%) patients and only 3 pts experienced delay in surgery, meeting the safety primary endpoint. In the PP population (n=107), baseline radiologic assessment revealed 89% stage III, 77% high-risk stage III (Table), and 64% T4 tumors. With a median time from first dose to surgery of 5 weeks, pathologic response was observed in 106/107 (99%) pts, consisting of 102/107 (95%) MPR and 4 (4%) PR. PCR was observed in 72/107 (67%) pts. At a median follow-up of 13 months (range 1-57), none of the pts had disease recurrence. Table: 000LBA7

<table>
<thead>
<tr>
<th>Clinical stage</th>
<th>Pathologic response</th>
<th>MPR</th>
<th>pCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>I/II (n = 12)</td>
<td>11 (92%)</td>
<td></td>
<td>9 (75%)</td>
</tr>
<tr>
<td>Low risk IIIa/b (n = 13)</td>
<td>13 (100%)</td>
<td>10 (77%)</td>
<td></td>
</tr>
<tr>
<td>High risk IIIa/b (n = 17)</td>
<td>16 (94%)</td>
<td>10 (59%)</td>
<td></td>
</tr>
<tr>
<td>High risk IIIc (n = 65)</td>
<td>62 (95%)</td>
<td>43 (66%)</td>
<td></td>
</tr>
<tr>
<td>Total (n = 107)</td>
<td>102 (95%)</td>
<td>72 (67%)</td>
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Conclusions
In NICHE-2 we confirm the previously reported pathologic responses to short-term neoadjuvant nivolumab plus ipilimumab in a large cohort of dMMR CC pts, with an MPR rate of 95%, including 67% pCR. The first survival data suggest a strong potential for neoadjuvant immunotherapy to become standard of care and allow further exploration of organ-sparing approaches.

Clinical trial identification
NL58483.031.16, EudraCT 016-002940-17.

Legal entity responsible for the study
Netherlands Cancer Institute.

Funding
Bristol-Myers Squibb.

Disclosure