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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

		Pathologic response	
		MPR	pCR
Clinical stage	I/II (*n* = 12)	11 (92%)	9 (75%)
Low risk IIIa/b (*n* = 13)	13 (100%)	10 (77%)	
High risk IIIa/b (*n* = 17)	16 (94%)	10 (59%)	
High risk IIIc (*n* = 65)	62 (95%)	43 (66%)	
Total (*n* = 107)	102 (95%)	72 (67%)	

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

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