NEOADJUVANT IMMUNOTHERAPY IN STAGE III COLON CANCER WITH DEFICIENT MISMATCH REPAIR: A SINGLE-CENTRE EXPERIENCE

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Introduction

High microsatellite instability (MSI-H) or deficient mismatch repair (dMMR) colon cancer occurs in approximately 10% to 15% of all colorectal cancer cases.

Recent trials, including NICHE and NICHE-2, have demonstrated remarkable efficacy of neoadjuvant immunotherapy in dMMR colon cancer, reporting high pathological complete response (pCR) rates. This case series presents real-world, single-centre data on neoadjuvant treatment with nivolumab and ipilimumab in patients with locally advanced, resectable stage III dMMR colon cancer, focusing on safety and pathological response outcomes.

Methods

Between December 2022 and August 2025 eight patients with dMMR colon carcinoma (clinical stage cT2-cT4, cN+) received neoadjuvant immunotherapy following the NICHE-2 protocol:

- Ipilimumab 1 mg/kg (single dose) and
- Nivolumab 3 mg/kg (two doses, two weeks apart).

All patients underwent surgery within six weeks after the last nivolumab infusion. Immune-related adverse events (IRAEs) were monitored throughout treatment and follow-up.

Patients (n=8)	
Median age (range) – yr	67 (34-88)
Female – no. (%)	4 (50)
Tumor stage – no. (%)	
• cT3	6 (75)
• cT4	2 (25)
Nodal status – no. (%)	
• cN1	5 (62.5)
• cN2	3 (37.5)
Primary tumour location – no. (%)	
• Right	6 (75)
• Left	2 (25)
Pathological response – no. (%)	
• MR	1 (12.5)
• PR	2 (25)
• NCR	1 (12.5)
• CR	4 (50)
Surgery delayed – no. (%)	0 (0)
irAE > grade 1 – no. (%)	1 (12.5)

Table1: Summary of patient and disease characteristics, pathological responses, surgery schedule and irAEs

Note: MR: Minimal Response; PR: Partial Response; NCR: Near Complete Response; CR: Complete Response; irAE: Immune-Related Adverse Event

Results

All eight patients completed treatment and surgery as scheduled. A pathological response was observed in seven of eight patients (87.5%), including four (50%) who achieved complete pathological remission. One pCR case was confirmed to have Lynch syndrome, while another is undergoing genetic evaluation for hereditary predisposition. Three patients showed major pathological response, while one patient demonstrated no pathological regression. Overall, therapy was well-tolerated. One patient developed immune-related diarrhoea requiring steroids and subsequent biological therapy with a monoclonal antibody. No other patient experienced > grade 1 irAEs, and no ongoing adverse events were reported at last follow-up.

Conclusions

Neoadjuvant combination immunotherapy with nivolumab and ipilimumab is highly effective, safe and feasible in patients with locally advanced dMMR colon cancer, yielding high complete and major pathological response rates consistent with those reported in the NICHE-2 trial. Treatment and surgery could be completed as scheduled. No new safety concerns were identified.

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