Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.
eFigure 1. Tumor Markers of the sMPCC Case During Treatment and Follow-up

The dotted line is the normal value of tumor markers.

CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen.
**eTable 1. Differences in MSI/MMR Status Between NGS and IHC in 78 sMPCC Patients**

| Characteristic                          | NGS | IHC |
|----------------------------------------|-----|-----|
| All MSI-H/All dMMR                     | 10  | 12  |
| MSI-H & MSS/dMMR & pMMR                | 7   | 4   |
| All MSS/All pMMR                       | 61  | 62  |

sMPCC, synchronous multiple primary colorectal cancer; MMR, mismatch repair; dMMR, mismatch repair; pMMR, proficient mismatch repair; MSI, microsatellite instability; MSI-H, microsatellite instability-high; MSS, microsatellite stability.
eFigure 2. Mutation Spectrum in All Lesions of the 78 Patients

The mutation spectrum of all samples from sMPCC patients was analyzed and visualized with a heatmap. A deeper red color indicates more enrichment of a specific mutation type.
eFigure 3. Landscape of the Top 20 Most Frequently Mutated Genes and Analyses of Pathway Enrichment Comparison Among Each Group of Among sMPCC and SPCRC Groups Patients

A. The top 20 most frequently mutated genes are shown in the histogram on the right of each group of sMPCC patients (all MSI-H, MSI-H&MSS, all MSS) and SPCRC patients. The number of mutations is illustrated in the upper panel. The types of mutations are colored differentially and labeled.

B. The enriched pathways are shown for each lesion among each group of sMPCC patients (all MSI-H, MSI-H & MSS, all MSS) and SPCRC patients. The fraction of mutated genes involved in each pathway is displayed on the left side of each group of sMPCC patients (all MSI-H, MSI-H & MSS, all MSS) and SPCRC patients. The fraction of samples with mutated genes in each pathway is shown on the right side of each group.
eTable 2. Differences in Pathogenic Germline Variations (PGVs) Between sMPCC and SPCRC Patients

| Characteristic    | sMPCC | SPCRC | P-value |
|-------------------|-------|-------|---------|
| Germline mutations|       |       | 0.40    |
| With PGVs         | 15    | 11    |         |
| Without PGVs      | 63    | 69    |         |

sMPCC, synchronous multiple primary colorectal cancer; SPCRC, single primary colorectal cancer.
eTable 3. Correlation of Pathogenic Germline Variations (PGVs) With Family History in sMPCC Patients

| Characteristic         | With PGVs | Without PGVs | p-value |
|------------------------|-----------|--------------|---------|
| Family history         |           |              | < 0.001 |
| With family history    | 7         | 3            |         |
| Without family history | 8         | 60           |         |

sMPCC, synchronous multiple primary colorectal cancer.
eTable 4. Correlation Between TMB and MSI Status in sMPCC and SPCRC Patients

| Characteristic | sMPCC | | | | SPCRC |
|---|---|---|---|---|---|
| All MSI-H | MSI-H & MSS | All MSS | All MSI-H | MSI-H & MSS | All MSS |
| TMB-H | 10 | 6 | 5 | 11 |
| TMB-L | 0 | 1 | 56 | 100 |

sMPCC, synchronous multiple primary colorectal cancer; SPCRC, single primary colorectal cancer; MSI, microsatellite instability; TMB, tumor mutation burden.
eFigure 4. Kaplan-Meier Analysis of OS and PFS by MMR Status (A) and MSI Status (B) in sMPCC Patients

OS, overall survival; PFS, progression-free survival.