**Supplementary method**

***MSI/MMR and RAS/BRAF status***

Microsatellite instability (MSI) status (five mononucleotide repeat markers: BAT-25, BAT-26, NR-21, NR-24, and MONO-27) was determined using the Promega MSI kit (Promega, Madison, WI, USA).MMR status was assessed by IHC using monoclonal antibodies for anti-mutL homolog 1 (MLH1, ES05), anti-mutS homolog 2 (MSH2, FE11), anti-postmeiotic segregation increased 2 (PMS2, EP51), and anti-mutS homolog 6 (MSH6, EP49) (Agilent Technologies, Santa Clara, CA), and tumors that lacked either MLH1, MSH2, PMS2, or MSH6 expression were considered MMR-deficient (MMR-D), whereas those that maintained the expression of MLH1, MSH2, PMS2, and MSH6 were considered MMR-proficient (MMR-P). *RAS* or *BRAF* status was investigated by approved testing such as RASKET (Medical& Biological Laboratories (MBL), Nagoya, Japan) and investigating *KRAS* exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), exon 4 (codons 117 and 146), *NRAS* exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), exon 4 (codons 117 and 146), and *BRAF* codon 600.

***RNA sequencing***

Total RNA was extracted from fresh frozen (FF) samples with an RNeasy Mini Kit (Qiagen, Hilden, Germany) according to the manufacturer’s instructions. Total RNA was extracted from FFPE samples using an RNeasy FFPE Kit (Qiagen) and was then treated with DNase I (Thermo Fisher Scientific). Complementary DNA (cDNA) was prepared from the polyA-selected RNA using the NEBNext Ultra Directional RNA Library Prep Kit (FF, New England BioLabs, Ipswich, MA), or from the ribosome RNA depeleted RNA using the NEBNext Ultra RNA Library Prep Kit (FFPE, New England BioLabs). The prepared RNA-seq libraries underwent next-generation sequencing of 125 bp from both ends (paired-end reads) with a HiSeq2500 platform (Illumina, San Diego, CA). For expression profiling with the RNA-seq data, paired-end reads were aligned to the hg38 human genome assembly using TopHat2 (https://ccb.jhu.edu/software/tophat/index.shtml) (Kim et al., 2013). The expression level of each RefSeq gene was calculated from the mapped read counts using Cufflinks (http://cufflinks.cbcb.umd.edu) (Trapnell et al., 2012).

**Whole exon sequencing (WES) and mutational analysis**

DNA was extracted from FF samples with the QIAmp DNA Mini Kit (QIAGEN) according to the manufacturer’s instructions. Genomic DNA was isolated from FFPE samples using GeneRead DNA FFPE Kits (Qiagen) Sequencing libraries were prepared for WES with the NEBNext Ultra DNA Library Prep Kit (FF, New England BioLabs) or KAPA Hyper Prep Kit for Illumina (FFPE, Roche), according to the manufacturer’s instructions. The amplified DNA fragments underwent enrichment of the exonic fragments using the SureSelect Human All Exon Kit v6 (Agilent Technologies). Massively parallel sequencing of the isolated fragments was performed with a HiSeq2500 platform (Illumina). Paired-end WES reads were independently aligned to the human reference genome (hg38) using BWA (Li and Durbin, 2009), Bowtie2 (http://bowtie-bio.sourceforge.net/bowtie2/index.shtml), and NovoAlign (http://www.novocraft.com/products/novoalign/). Somatic mutations were called using MuTect (http://www.broadinstitute.org/cancer/cga/mutect), SomaticIndelDetector (http://www.broadinstitute.org/cancer/cga/node/87), and VarScan (http://varscan.sourceforge.net). Mutations were discarded if (I) the read depth was < 20 or the variant allele frequency (VAF) was < 0.1, (II) they were supported by only one strand of the genome, or (III) they were present in the normal human genomes in either the 1000 Genomes Project dataset (http://www.internationalgenome.org/) or our in-house database. Gene mutations were annotated by SnpEff (http://snpeff.sourceforge.net).

**Figure Legends**

**Figure S1.** Consort diagram

**Figure S2.** Computed tomography during the study treatment of the 4 patients with objective response in cohort B

**Figure S3.** (A) Kaplan–Meier plots of progression-free survival in cohort A. (B) Progression-free survival in cohort B. (C) Overall survival in cohort A. (D) Overall survival in cohort B.