

Supplementary Table 1 Detailed information on 47 patients enrolled in the study

ID	Sex	Age	Localization of tumor/s	Synch/metach	Localization of resected tumor	Type of surgery	R	ctDNA	Postoperative state/development
F 120	M	61	Right colon, liver	Synch	Right colon	Right hemicolectomy	R2b	x	Distal metastases present
F 168	F	66	Rectum, liver, lungs	Metach	Liver	Right hemihepatectomy	R0	o	After 6 mo recurrence in liver and lungs
F 202	M	60	Rectosigmoid, liver	Metach	Liver	Metastasectomy (left hepatic lobe)	R2b	x	Distal metastases present (right hepatic lobe)
				Metach	Liver	Metastasectomy	R0	o	15 mo no recurrence
F 203	M	62	Rectum with infiltration into the prostate, liver and lungs	Synch	Rectum	Palliative stomy	R2c	x	Primary tumor and distal metastases present
F 204	M	54	Colon, muscle in the pelvic	Metach	Muscle in the pelvic area	Metastasectomy	R0	o	After 21 mo recurrence in retroperitoneum

			area, retroperitoneum	Metach	retroperitoneum	metastasectomy	R0	o	6 mo no recurrence
F 216	F	76	Splenic flexure, liver	Synch	Splenic flexure, liver	Left hemicolectomy, metastasectomy	R0	o	27 mo no recurrence
F 223	M	58	Sigmoid, liver	Metach	Liver	metastasectomy	R0	o	After 10 mo recurrence in liver
F 243	M	60	Rectosigmoid, liver, lungs, skeleton	synch	Rectosigmoid, liver	Resection of the rectosigmoid, metastasectomy	R0	o	After 4 mo recurrence in liver, lungs, skeleton
F 246	M	76	Cecum, liver	Synch	Cecum	Subtotal colectomy	R2b	x	Distal metastases present
F 276	M	87	Cecum, liver, spleen, lymph nodes in the peritoneum and pelvis	Synch	Cecum	Palliative right hemicolectomy	R2b	x	Distal metastases present
KK 003	M	73	Rectosigmoid, liver	Synch	Liver	Metastasectomy	R2a	x	Primary tumor present

KK 014	M	57	Rectum, liver	Metach	Liver	RFA CT navigated of metastases	R0	no sample	After 10 mo recurrence in liver
				Metach	Liver	Segmentectomy	R0	no sample	After 10 mo recurrence in liver
KK 041	M	66	Hepatic flexure, rectum, liver	Metach	Liver	Metastasectomy	R0	o	after 5 mo recurrence in liver
KK 057	F	32	Right colon, liver	Synch	Right colon, liver	Right hemicolectomy, metastasectomy (left hepatic lobe)	R2b	x	Distal metastases present (right hepatic lobe)
				Synch	Liver	right Hemihepatectomy (in the second stage)	R0	o	29 mo no recurrence
KK 064	M	76	Rectum, liver	Synch	Rectum, liver	Low anterior resection of the rectum, Metastasectomy	R0	o	After 22 mo recurrence in liver
KK 075	M	39	Rectum, liver	Metach	Liver	Metastasectomy	R1	x	After 7 mo recurrence in liver
KK 086	F	85	Right colon, liver	Synch	Right colon, liver	Right hemicolectomy, metastasectomy	R0	x	After 6 mo recurrence in liver

KK 180	F	59	transverse colon, liver, lungs	Synch	transverse colon, liver	Resection of the transverse colon, metastasectomy	R1	o	After 22 mo recurrence in liver and lungs
KK 092	F	42	Rectum, liver, lungs	Synch	Rectum	Low anterior resection of the rectum	R2b	x	Distal metastases present
				Synch	Liver	right hemihepatectomy (in the second stage)	R1	x	After 4 mo recurrence in liver and lungs
KK 224	M	59	Rectum, liver, lungs	Synch	Rectum	Resection of the rectum	R2b	x	Distal metastases present
				Synch	Liver	Metastasectomy and RFA CT navigated (in the second stage)	R0	o	After 7 mo recurrence in lungs
KK 344	F	49	Cecum, liver	synch	Cecum, liver	Right hemicolectomy, metastasectomy (left hepatic lobe)	R2b	x	Distal metastases present (right hepatic lobe)
KK 367	F	69	Rectum, liver, peritoneum	Metach	Liver	Metastasectomy	R1	o	After 7 mo recurrence in liver and peritoneum

				Metach	liver, peritoneum	Metastasectomy and RFA CT navigated	R0	o	3 mo no recurrence
KK 380	M	66	Right colon, liver	Metach	Liver	Metastasectomy	R0	o	no data (postoperative follow-up at the place of residence)
KK 386	M	76	Rectosigmoid, liver	Synch	Rectosigmoid	Resection of the rectosigmoid	R2b	x	distal metastases present
KK 470	F	56	Colon, liver	Synch	Colon, liver	Right hemicolectomy, metastasectomy (left hepatic lobe)	R2b	x	distal metastases present (right hepatic lobe)
				Synch	Liver	right hemihepatectomy	R0	o	after 5 mo recurrence in lungs
KK 473	M	77	Rectosigmoid, liver	Synch ¹	Liver	Segmentectomy and metastasectomy (in the second stage)	R0	o	no data (postoperative follow-up at the place of residence)
KK 492	F	58	Rectum, liver	Synch	Liver	Metastasectomy	R2a	x	primary tumor present

KK 509	M	71	Sigmoid, liver	Metach	Liver	right Hemihepatectomy	R0	o	4 mo no recurrence
KK 578	M	56	Rectosigmoid, liver, lungs	Synch	Liver, lungs	metastasectomy	R2b	x	Distal metastases present
KK 596	M	77	Colon, liver	Metach	Liver	Metastasectomy	R1	o	5 mo no recurrence
Mc 001	M	62	Rectum, liver	Metach	Liver	Segmentectomy	R0	No sample	After 12 mo recurrence in liver
				Metach	Liver	Segmentectomy	R0	o	28 mo no recurrence
Mc 002	F	59	Sigmoid, liver	Synch	Sigmoid, liver	Resection of the sigmoid, segmentectomy and metastasectomy	R0	No sample	After 16 mo recurrence in liver
				Metach	Liver	RFA laparotomy	R0	No sample	20 mo no recurrence
Mc 006	M	57	Sigmoid, liver, lymph nodes	Synch ¹	Liver	Metastasectomy RFA CT navigated (in the second stage)	R0	o	After 7 mo recurrence in liver

				Metach	Liver	Metastasectomy RFA CT navigated	R0	x	After 6 mo recurrence in liver
				Metach	Liver	Metastasectomy	R0	o	after 15 mo recurrence in lymph nodes
				Metach	lymph nodes	Lymfadenectomy	R0	o	after 5 mo Recurrence in liver
Mc 007	M	59	Rectum, liver	Synch	Rectum	Resection of the primary tumor (Hartmann's operation)	R2b	x	distal metastases present
				Synch	Liver	Metastasectomy (in the second stage)	R1	x	After 3 mo recurrence in liver
Mc 019	F	32	Right colon, liver, lungs	Synch	Right colon, liver	Right hemicolectomy, left hemihepatectomy	R0	No sample	After 3 mo recurrence in lungs
Mc 021	F	84	Rectosigmoid, liver	Metach	Liver	Segmentectomy	R0	o	24 mo no recurrence
Mc 026	M	73	Sigmoid, liver	Synch ¹	Liver	Segmentectomy (in the second stage)	R1	x	After 3 mo recurrence in liver

Mc 031	M	68	Right colon, liver	Synch ¹	Liver	Left hepatectomy (in the second stage)	R0	No sample	After 9 mo recurrence in liver
Mc 036	M	74	Right colon, liver	Metach	Liver	metastasectomy	R0	o	36 mo no recurrence
Mc 037	M	60	Sigmoid, liver	Metach	Liver	Metastasectomy	R0	o	20 mo no recurrence
Mc 039	M	59	Rectum, liver	Metach	Liver	Segmentectomy	R0	o	After 6 mo recurrence in liver
Mc 040	M	69	Rectum, liver	Synch ¹	Liver	Segmentectomy (in the second stage)	R0	No sample	After 16 mo recurrence in liver
Mc 063	F	52	Rectosigmoid, liver	Synch	Rectosigmoid, liver	Resection of the rectosigmoid, RFA laparotomy	R2b	No sample	Distal metastases present
				Metach	Liver	RFA CT navigated	R0	No sample	After 6 mo recurrence in liver
Mc 068	F	71	Right colon, liver	Synch ¹	Liver	Right hemihepatectomy (in the second stage)	R0	o	After 6 mo recurrence in liver
				Metach	Liver	RFA CT navigated	R0	No sample	After 8 mo recurrence in liver

Mc 070	M	72	Right colon, liver	Synch	Right colon, liver	Right hemicolectomy, metastasectomy	R0	o	After 6 mo recurrence in lungs
Mc 074	M	62	Sigmoid, liver	Synch ¹	Liver	Metastasectomy (in the second stage)	R0	No sample	After 11 mo recurrence in liver
Mc 075	F	71	Right colon, liver	Synch	right colon, liver	Right hemicolectomy, RFA laparotomy	R0	No sample	After 4 mo recurrence in liver

X and o letters indicate ctDNA positivity and negativity after surgery, respectively. ¹Information on the surgical treatment of the primary tumor is not available as these data and samples were not included in the study. ctDNA: Circulating tumor DNA; Metach: Metachronous; R: Radicality; R0: Complete resection with no macroscopic or microscopic tumor residues; R1: Microscopically incomplete resection; R2a: Macroscopic presence of a residue of the primary tumor; R2b: Macroscopic presence of distal metastases; R2c: Macroscopic presence of residues of primary tumor and distal metastases; Synch: Synchronous.

Supplementary Table 2 Overview of the patient samples and detected mutations

ID	Detected mutations			Number of plasma samples		
	Primary tumor	Node	Metastasis/es	Pre	Post	Follow-up
F 120	KRAS ex 2, APC ex 15	No sample	no sample	1	1	2
F 168	o	No sample	APC ex 15 ¹	1	1	4
F 202	APC ex 15, TP53 ex 5	o	APC ex 15, TP53 ex 5	1	1	11
F 203	KRAS ex 2, APC ex 15, TP53 ex 8, PIK3CA ex 9	No sample	KRAS ex 2, TP53 ex 8, PIK3CA ex 9	1	1	4
F 204	APC ex 15, TP53 ex 8	No sample	APC ex 15, TP53 ex 8	1	1	9
F 216	KRAS ex 2, APC ex 15	KRAS ex 2, APC ex 15	KRAS ex 2, APC ex 15	1	1	5
F 223	No sample	No sample	TP53 ex 6, BRAF ex 15, APC ex 15	1	1	No sample
F 243	KRAS ex 2, APC ex 15	o	o	1	1	3
F 246	KRAS ex 2, APC ex 15, PIK3CA ex 9	KRAS ex 2, PIK3CA ex 9	KRAS ex 2, PIK3CA ex 9	1	1	No sample
F 276	APC ex 15, PIK3CA ex 9	APC ex 15, PIK3CA ex 9	APC ex 15, PIK3CA ex 9	1	1	No sample
KK 003	No sample	No sample	APC ex 15	1	1	No sample
KK 014	No sample	No sample	TP53 ex 8, PIK3CA ex 9 ¹	1	No sample	3
KK 017	No sample	No sample	KRAS ex 2	1	No sample	3
KK 041	No sample	No sample	KRAS ex 2	1	1	No sample

KK 057	No sample	No sample	KRAS ex 2, TP53 ex 8 ¹	1	1	2
KK 064	KRAS ex 2, TP53 ex 8, PIK3CA ex 9	No sample	KRAS ex 2, TP53 ex 8, PIK3CA ex 9	1	1	1
KK 075	No sample	No sample	TP53 ex 6, APC ex 15	1	1	1
KK 086	KRAS ex 3, PIK3CA ex 9	No sample	KRAS ex 3, PIK3CA ex 9	1	1	2
KK 092	KRAS ex 3	No sample	TP53 ex 5, APC ex 15	1	1	3
KK 180	TP53 ex 8, PIK3CA ex 9 ¹	No sample	TP53 ex 8, PIK3CA ex 9	1	1	1
KK 224	KRAS ex 2	No sample	KRAS ex 2	1	1	3
KK 344	No sample	No sample	KRAS ex 2	1	1	No sample
KK 367	TP53 ex 5	No sample	TP53 ex 5	1	1	3
KK 380	No sample	No sample	KRAS ex 2	1	1	No sample
KK 386	KRAS ex 2	No sample	no sample	1	1	No sample
KK 470	KRAS ex 2, TP53 ex 8 ¹	No sample	KRAS ex 2, TP53 ex 8	1	1	3
KK 473	KRAS ex 2	No sample	no sample	1	1	No sample
KK 492	No sample	No sample	APC ex 15	1	1	No sample
KK 509	PIK3CA ex 9 ¹	No sample	no sample	1	1	2
KK 578	No sample	No sample	TP53 ex 5, TP53 ex 6	1	1	No sample
KK 596	No sample	No sample	KRAS ex 2	1	1	No sample
Mc 001	KRAS ex 2	No sample	KRAS ex 2 ¹	1	1	4
Mc 002	No sample	No sample	KRAS ex 2, CTNNB1 ex 3 ¹	1	No sample	1

Mc 006	No sample	KRAS ex 2, PIK3CA ex 20	KRAS ex 2, PIK3CA ex 20	1	1	14
Mc 007	KRAS ex 2	No sample	no sample	1	1	7
Mc 019	No sample	No sample	TP53 ex 8, APC ex 15	1	No sample	1
Mc 021	No sample	No sample	KRAS ex 2, PIK3CA ex 9	1	1	No sample
Mc 026	No sample	No sample	APC ex 15	1	1	No sample
Mc 031	No sample	No sample	KRAS ex 2, CTNNB1 ex 3	1	No sample	1
Mc 036	No sample	No sample	KRAS ex 2, APC ex 15	1	1	5
Mc 037	No sample	No sample	TP53 ex 5, TP53 ex 8	1	1	No sample
Mc 039	No sample	No sample	KRAS ex 2, TP53 ex 7, APC ex 15	1	1	No sample
Mc 040	No sample	No sample	TP53 ex 6	1	No sample	No sample
Mc 063	No sample	No sample	KRAS ex 2, TP53 ex 6	2	No sample	3
Mc 068	No sample	No sample	KRAS ex 2, PIK3CA ex 9	2	1	6
Mc 070	KRAS ex 2, TP53 ex 7	No sample	KRAS ex 2, PIK3CA ex 9	2	1	No sample
Mc 074	No sample	No sample	KRAS ex 2	1	No sample	4
Mc 075	No sample	No sample	KRAS ex 2, PIK3CA ex 9	1	No sample	1

In total, 79 tumor tissue samples and 202 plasma samples were collected in the course of the study. The letter 'o' indicates negative results of mutation analysis. ¹Two metastase samples. Ex: Exon; Post: Postoperative; Pre: Preoperative.