

Table S2.

Patient	Sex	Age	Biopsy type*	Molecular pathology genetic testing of tumour tissue**	Treatment prior to tissue collection for organoid generation? ***	Treatment post tissue collection?	Medium throughput drug screening of organoid?	Organoid and germline DNA WES?	Tumour tissue RNAseq?
1	F	71	Operative	Primary tumor: <i>KRAS</i> ND, CRPM:NA.	5FU monotherapy FOLFOX	FOLFIRI+ EGFRi FOLFOX Vandetinib	pan-cancer 87 drug library	Yes	Yes
2	F	47	Operative	CRPM: <i>KRAS</i> ND, <i>NRAS</i> ND, <i>BRAF</i> ND.	CAPOX/FOLFOX,	FOLFIRI + EGFRi Gemcitabine	pan-cancer 87 drug library	Yes	Yes
3	F	60	Laparoscopy	CRPM: <i>KRAS</i> ND, <i>NRAS</i> ND, <i>BRAF</i> ND.	FOLFIRI + VEGFRi	FOLFOX +EGFRi Regorafenib	pan-cancer 87 drug library	Yes	Yes
4	M	78	Operative	CRPM: <i>KRAS</i> ND, <i>NRAS</i> ND, <i>BRAF</i> ND.	5-FU+chemo-radiation		pan-cancer 87 drug library	Yes	Yes
5	M	80	Operative	CRPM: <i>KRAS</i> p.Gly13Asp/c.38G>A, <i>NRAS</i> ND, <i>BRAF</i> ND.	FOLFOX + VEGFRi, FOLFIRI + VEGFRi, 5-FU with radiation	Nil	pan-cancer 87 drug library	Yes	Yes
6C#	F	69	Operative	NA.	Chemo Naive	FOLFOX	targeted 35 drug library	Yes	Yes
6P#							targeted 35 drug library		
7C#	F	60	Operative	CRPM: <i>KRAS</i> ND, <i>NRAS</i> ND, <i>BRAF</i> ND.	Chemo Naïve	FOLFOX	targeted 35 drug library	Yes	Yes
7P#							targeted 35 drug library		
8	F	34	Operative ^{##}	Primary tumor: <i>KRAS</i> p.Gly13Asp/c.38 G>A, <i>NRAS</i> ND, <i>BRAF</i> ND. CRPM: NA.	5-FU+ radiation	FOLFOX	targeted 35 drug library	Yes	Yes
9	F	34	Percutaneous	CRPM: <i>KRAS</i> ND, <i>NRAS</i> ND, <i>BRAF</i> ND.	FOLFOX, FOLFOX + VEGFRi, FOLFIRI + EGFRi, CAR-T cell trial, Lonsurf	Lonsurf	targeted 35 drug library	Yes	NA
10	F	59	Operative	CRPM: <i>KRAS</i> ND, <i>NRAS</i> MUT, <i>BRAF</i> ND.	FOLFOX	FOLFOX, FOLFIRI CAR-T cell trial	targeted 35 drug library	Yes	Yes
11	M		Operative	NA.	Oxaliplatin based	FOLFIRI	targeted 35 drug library	Yes	NA
12	F	57	Laparoscopy	CRPM: <i>KRAS</i> ND, <i>NRAS</i> ND, <i>BRAF</i> ND.	FOLFOX	FOLFOX+ EGFRi	targeted 35 drug library	Yes	Yes
13	F	35	Operative	NA.	Chemo naïve	FOLFOX+VEGFRi	NA	Tissue WES	Yes C & P
14	F	67	Operative	CRPM: <i>KRAS</i> ND, <i>NRAS</i> ND, <i>BRAF</i> ND	CAPOX	FOLFOX+EGFRi	targeted 35 drug library	Yes	NA
15	F	52	Operative	NA.	CAPOX, FOLFOX	FOLFOX	targeted 35 drug library	NA	NA
16	F	63	Operative	NA.	FOLFOX, CAPOX, FOLFIRI + EGFRi	FOLFIRI	NA	NA	Yes
17	F	83	Operative	NA.	CAPOX	Capecitabine	NA	NA	Yes
18	F	50	Operative	NA.	FOLFOX + VEGFRi, CAPOX		targeted 35 drug library	NA	Yes
19	M	71	Laparoscopy	CRPM: <i>KRAS</i> p.Gly12Ala	FOLFOX	FOLFOX	NA	NA	NA

Table S2. Patient characteristics & analyses.

#: Synchronous resection of primary tumour along with peritoneal metastases. C: colonic primary, P: peritoneal metastases

* Operative: at time of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy;

Laparoscopy: at time of staging laparoscopy to evaluate disease burden;

##Operative: operative specimen when surgery performed with palliative intent only; Percutaneous: needle biopsy guided by ultrasound/computed tomography.

**Genetic testing in an independent lab.

***Patient chemotherapy regimens prior to establishment of organoids:

FOLFOX: 5FU/Leucovorin+ Oxaliplatin; FOLFIRI: 5FU/leucovorin + irinotecan; EGFRi: monoclonal antibody inhibitor of epidermal growth factor receptor (cetuximab); CAPOX: capecitabine + Oxaliplatin; VEGFRi: Vascular endothelial growth factor receptor inhibitor (bevacizumab);

Lonsurf: Trifluridine and tipiracil

ND, genetic variant not detected in gene, MUT, genetic variant detected. CRPM, colorectal cancer peritoneal metastasis.

WES, whole exome sequencing. Numerous previous publications report the excellent concordance between genetic variants found in patient tumour samples and organoids derived from those same specimens. In particular the pivotal early metastatic colorectal cancer study (Weeber et al 2015 PNAS 112:13308-13311) noted 90% concordance in genetic alterations between tumour organoids and the source tissue, and that any discrepancies were never in driver mutations or in actionable drug targets. As such we undertook whole exome sequencing of patient-derived tumoroids and peritonoids only, not the source tissue. Molecular pathology testing of n=9 patient tissue samples for *KRAS*, *BRAF* and *NRAS* variants was undertaken in an independent pathology laboratory and is 100% concordant with our WES data from peritonoids.

RNAseq, mRNA sequencing.

NA, not available.