

**Supplementary Table 1. The clinical characteristics of patients with CRLM in this study.**

<b>Characteristics</b>	<b>(n = 91)</b>
Age at liver resection (years)	Median 59 (34 - 66)
Gender	
Male	47 (51.6%)
Female	44 (48.4%)
Primary tumor location	
Right-sided	18 (19.8%)
Left-sided	73 (80.2%)
Nodal involvement of primary tumor	
N1-2	59 (64.8%)
N0	32 (35.2%)
Time between primary tumor and liver metastases	
Synchronous	71 (78.0%)
Metachronous	20 (22.0%)
Preoperative CEA (ng/mL)	
≤ 5	20 (22.0%)
> 5	71 (78.0%)
Preoperative chemotherapy	
Chemotherapy alone	47 (51.6%)
Chemotherapy + Cetuximab	23 (25.3%)
Chemotherapy + Bevacizumab	14 (15.4%)
No preoperative chemotherapy	7 (7.7%)
Best Response before surgery	
PR	43 (47.3%)
SD	41(45.1%)
NA	7 (7.7%)

Postoperative chemotherapy	
Chemotherapy alone	65 (71.4%)
Chemotherapy + Cetuximab	15 (16.5%)
Chemotherapy +Bevacizumab	3 (3.3%)
No postoperative chemotherapy	8 (8.8%)
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Concomitant ablation	
Yes	27 (29.7%)
No	64 (70.3%)
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Number of liver metastasis	
= 1	25 (27.5%)
> 1	66 (72.5%)
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Extent of liver metastases	
Unilateral	40 (44.0%)
Bilateral	51 (56.0%)
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Diameter of the largest liver metastasis (cm)	Median 4.3 (1.0 – 15.7)
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CRS	
Low risk (Score 0-2)	33 (36.3%)
High risk (Score 3-5)	58 (63.7%)

CRLM, colorectal liver metastasis

CEA, carcinoembryonic antigen

PR, partial response

SD, stable disease

CRS, clinical risk score

**Supplementary Table 2. The clinical characteristics of patients with CRLM at four time points.**

<b>Characteristics</b>	<b>Baseline ctDNA (n = 53)</b>	<b>Pre-operation ctDNA (n = 65)</b>	<b>Post-operation ctDNA (n = 82)</b>	<b>Post-ACT ctDNA (n = 49)</b>
Age at liver resection (years)	Median 56 (20 - 73)	Median 56 (20 - 73)	Median 56 (20 - 75)	Median 56 (20 - 73)
<b>Gender</b>				
Male	32 (60.4%)	43 (66.2%)	53 (64.6%)	30 (61.2%)
Female	21 (39.6%)	22 (33.8%)	29 (35.4%)	19 (38.8%)
<b>Primary tumor location</b>				
Right-sided	9 (17.0%)	11 (16.9%)	16 (19.5%)	9 (18.4%)
Left-sided	44 (83.0%)	54 (83.1%)	66 (80.5%)	40 (81.6%)
<b>Nodal involvement of primary tumor</b>				
N1-2	34 (64.2%)	43 (66.2%)	57 (69.5%)	32 (65.3%)
N0	19 (35.8%)	22 (33.8%)	25 (30.5%)	17 (34.7%)
<b>Prior resection of the primary tumor</b>				
No	33 (62.3%)	36 (55.4%)	49 (59.8%)	31 (63.3%)
Yes	20 (37.7%)	29 (44.6%)	33 (40.2%)	18 (36.7%)
<b>Time between primary tumor and liver metastases</b>				
Synchronous	42 (79.2%)	53 (81.5%)	66 (80.5%)	41 (83.7%)
Metachronous	11 (20.8%)	12 (18.5%)	16 (19.5%)	8 (16.3%)
<b>Preoperative CEA (ng/mL)</b>				
≤ 5	22 (41.5%)	27 (41.5%)	32 (39.0%)	22 (44.9%)
> 5	31 (58.5%)	38 (58.5%)	50 (61.0%)	27 (55.1%)
<b>Preoperative chemotherapy</b>				
Yes	51 (96.2%)	64 (98.5%)	76 (92.7%)	44 (89.8%)
No	2 (3.8%)	1 (1.5%)	6 (7.3%)	5 (10.2%)
<b>Extend of liver metastases</b>				
Solitary	18 (34.0%)	18 (27.7%)	23 (28.0%)	11 (22.4%)
Multifocal	35 (66.0%)	47 (72.3%)	59 (72.0%)	38 (77.6%)
Unilateral	27 (50.9%)	28 (43.1%)	36 (43.9%)	20 (40.8%)

Bilateral	26 (49.1%)	37 (56.9%)	46 (56.1%)	29 (59.2%)
Concomitant ablation				
Yes	39 (73.6%)	20 (30.8%)	25 (30.5%)	11 (22.4)
No	14 (26.4%)	45 (69.2%)	57 (69.5%)	38 (77.6%)
Postoperative chemotherapy				
Yes	47 (88.7%)	58 (89.2%)	76 (92.7%)	47 (95.9%)
No	6 (11.3%)	7 (10.8%)	6 (7.3%)	2 (4.1%)
CRS				
Low risk (Score 0-2)	21 (39.6%)	18 (27.7%)	30 (36.6%)	21 (42.9%)
High risk (Score 3-5)	32 (60.4%)	47 (72.3%)	52 (63.4%)	28 (57.1%)

CRLM, colorectal liver metastases

CEA, carcinoembryonic antigen

CRS, clinical risk score

Supplementary Table 3. Relationship of ctDNA status and clinical characteristics of CRLM.

Variables	Baseline ctDNA (n = 53)			Pre-operation ctDNA (n = 65)			Post-operation ctDNA (n = 82)			Post-ACT ctDNA (n = 49)		
	Low level (n = 26)	High level (n = 27)	<i>P</i>	Negative (n = 28)	Positive (n = 37)	<i>P</i>	Negative (n = 48)	Positive (n = 34)	<i>P</i>	Negative (n = 27)	Positive (n = 22)	<i>P</i>
Age at liver resection (years)			0.928			0.156			0.443			0.553
< 60	18	19		22	23		33	26		19	18	
≥ 60	8	8		6	14		15	8		8	4	
Gender			0.340			0.420			0.631			0.386
Female	12	9		11	11		18	11		9	10	
Male	14	18		17	26		30	23		18	12	
Primary tumor location			0.409			0.318			0.191			0.598
Right-sided	21	24		26	30		42	26		22	20	
Left-sided	5	3		2	7		6	8		5	2	
Nodal involvement of primary tumor			<b>0.013</b>			0.182			0.249			0.325
No	5	14		12	10		17	8		11	6	
Yes	21	13		16	27		31	26		16	16	
Disease free interval (DFI, months)			0.947			0.861			0.476			0.943
> 12	5	5		5	6		7	7		5	3	
< 12	21	22		23	31		41	27		22	19	
Diameter of the largest LM (cm)			<b>&lt;0.001</b>			0.388			0.354			0.586
< 5	23	9		16	25		33	20		19	17	
≥ 5	3	18		12	12		15	14		8	5	
CEA level (ng/mL)			0.280			0.246			0.272			0.390
< 5	3	1		3	8		7	8		3	5	
≥ 5	23	26		25	29		41	25		24	15	
Number of liver metastasis			0.497			0.700			0.443			0.207

< 2	10	8	8	9	15	8	9	3
≥ 2	16	19	20	28	33	26	18	19
CRS		<b>0.008</b>		0.069		0.503		0.407
0-2	15	6	11	7	19	11	13	8
3-5	11	21	17	30	29	23	14	14
Recurrence		0.132		0.122		< <b>0.001</b>		<b>0.010</b>
No	11	17	16	14	28	7	16	5
Yes	15	10	12	23	20	27	11	17

Low level and high level respectively represented lower-than-median and higher-than-median VAF of baseline ctDNA.

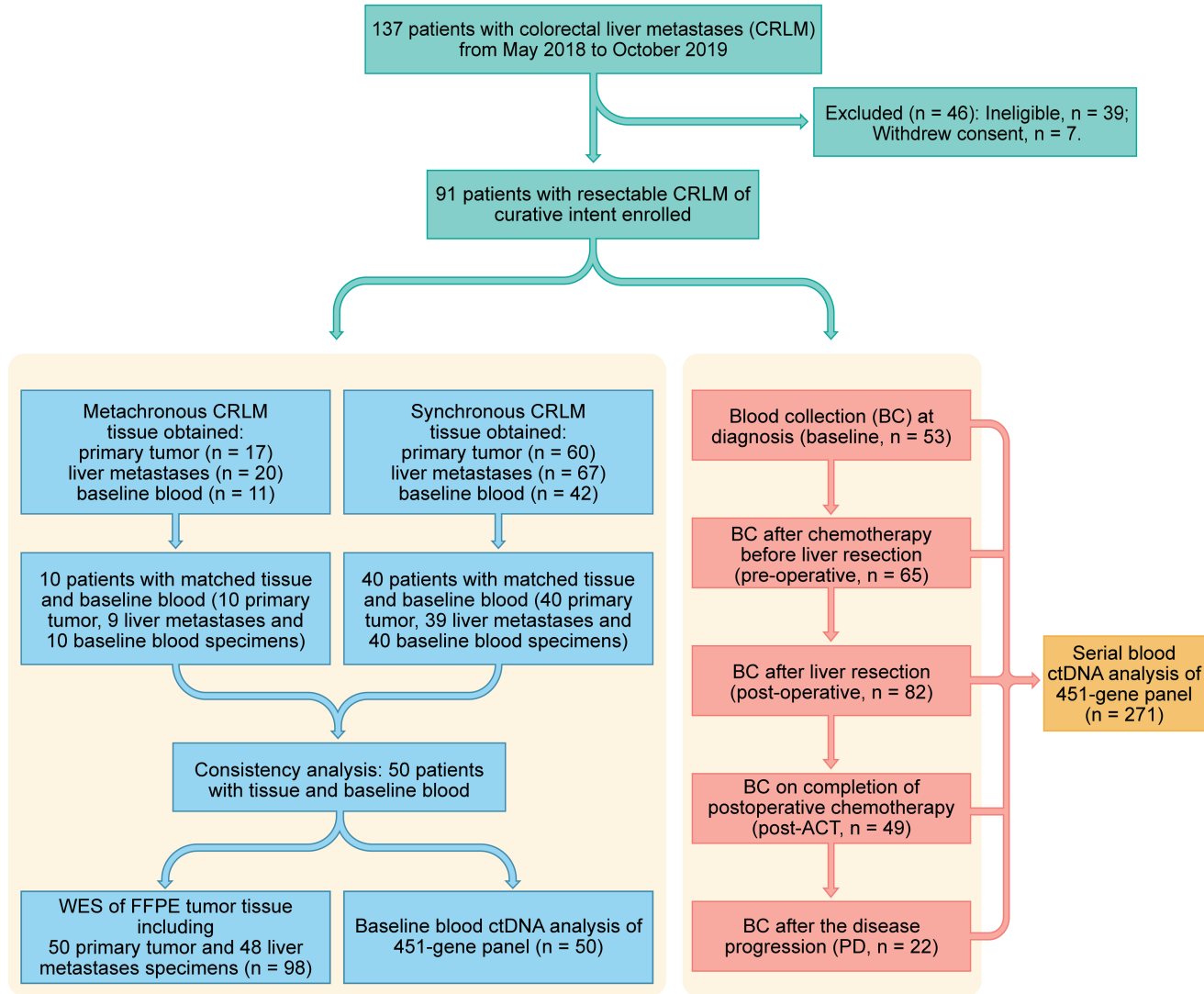
ctDNA, circulating tumor DNA

CRLM, colorectal liver metastasis

LM, liver metastasis

CEA, carcinoembryonic antigen

CRS, clinical risk score



**Supplemental Figure 1. Flow chart of patients enrolled and sample collection at different time points for analysis.**