

## Supplementary material

**Table S1.** Spearman correlation table of the mean of CD3<sup>+</sup> and CD8<sup>+</sup> density and PD-1 and PD-L1 expression in pulmonary metastases and primary CRC

		met PD1 (TC)	met PD1 (IM)	met PDL1 (TCe)	met PDL1 (IC)
Median of metastases T-cell density	Correlation Coefficient	<b>0.631**</b>	<b>0.697**</b>	0.061	<b>0.405**</b>
	Sig. (2-tailed)	<0.001	<0.001	0.627	0.001
	N	67	63	67	66
		prim PD1 (TC)	prim PD1 (IM)	prim PDL1 (TCe)	prim PDL1 (IC)
Median of primary tumour T-cell density	Correlation Coefficient	<b>0.449**</b>	<b>0.595**</b>	0.221	<b>0.361**</b>
	Sig. (2-tailed)	<0.001	<0.001	0.096	0.005
	N	59	59	58	58

\*\* . Correlation is significant at the 0.01 level (2-tailed).

\* . Correlation is significant at the 0.05 level (2-tailed).

**Table S2.** Baseline characteristics of pulmonary metastasectomy patients according to ICS of primary colorectal tumour (n=61)

	ICS 0	ICS 1	ICS 2	p-value
	n (%)	n (%)	n (%)	
	13	35	14	
<b>Sex</b>				0.614
Female	5 (38.5%)	18 (52.9%)	8 (57.1%)	
Male	8 (61.5%)	16 (47.1%)	6 (42.9%)	
<b>Age (M;SD)</b>	67.2 (9.3)	66.9 (9.2)	71.7 (10.1)	0.368
<b>CCI</b>				0.481
1	9 (69.2%)	20 (58.8%)	8 (57.1%)	
2	4 (30.8%)	7 (20.6%)	3 (21.4%)	
≥3	0 (0.0%)	7 (20.6%)	3 (21.4%)	
<b>CRC stage</b>				0.223
1-2	3 (23.1%)	15 (44.1%)	2 (14.3%)	
3	7 (53.8%)	10 (29.4%)	8 (57.1%)	
4	3 (23.1%)	9 (26.5%)	4 (28.6%)	
<b>CRC location</b>				0.941
Colon	7 (53.8%)	17 (50.0%)	8 (57.1%)	
Rectum	6 (46.2%)	17 (50.0%)	6 (42.9%)	
<b>Neoadjuvant CRC</b>				0.876
No	8 (61.5%)	23 (67.6%)	9 (69.2%)	
Radiotherapy	1 (7.7%)	4 (11.8%)	2 (15.4%)	
Chemotherapy	1 (7.7%)	1 (2.9%)	1 (7.7%)	
Radio-chemotherapy	3 (23.1%)	6 (17.6%)	1 (7.7%)	
<b>DFI (d; MD; IQR)</b>	750 (67-1004)	364 (0-745)	193 (0-762)	0.222
<b>Synchronicity</b>				0.101
Synchronous	1 (7.7%)	4 (11.8%)	5 (35.7%)	
Metachronous	12 (92.3%)	30 (88.2%)	9 (64.3%)	
<b>No of pulmonary metastases</b>				0.209
1	6 (46.2%)	23 (67.6%)	11 (78.6%)	
≥1	7 (53.8%)	11 (32.4%)	3 (21.4%)	
<b>Size of largest PM (cm; MD; IQR)</b>	1.5 (1.2-2.2)	2.1 (1.2-3.5)	3.5 (2.5-3.6)	0.170
<b>Laterality of metastasis</b>				0.256
Unilateral	9 (69.2%)	29 (85.3%)	13 (92.9%)	
Bilateral	4 (30.8%)	5 (14.7%)	1 (7.1%)	
<b>BRAF</b>				>0.999

Wild-type	13 (100.0%)	31 (93.9%)	14 (100.0%)	
Mutant	0 (0.0%)	2 (6.1%)	0 (0.0%)	
<b>met PD-1 (TC)</b>				0.016
Low	5 (38.5%)	25 (73.5%)	5 (35.7%)	
High	8 (61.5%)	9 (26.5%)	9 (64.3%)	
<b>met PD-1 (IM)</b>				0.080
Low	8 (61.5%)	19 (63.3%)	4 (28.6%)	
High	5 (38.5%)	11 (36.7%)	10 (71.4%)	
<b>met PD-L1 (TCe)</b>				0.443
Low	13 (100.0%)	34 (100.0%)	13 (92.9%)	
High	0 (0.0%)	0 (0.0%)	1 (7.1%)	
<b>met PD-L1 (IC)</b>				0.082
Low	4 (30.8%)	5 (14.7%)	0 (0.0%)	
High	9 (69.2%)	29 (85.3%)	13 (100.0%)	
<b>prim PD-1 (TC)</b>				0.031*
Low	9 (69.2%)	19 (55.9%)	3 (21.4%)	
High	4 (30.8%)	15 (44.1%)	11 (78.6%)	
<b>prim PD-1 (IM)</b>				<0.001*
Low	12 (92.3%)	17 (51.5%)	2 (14.3%)	
High	1 (7.7%)	16 (48.5%)	12 (85.7%)	
<b>prim PD-L1 (TCe)</b>				0.702
Low	13 (100.0%)	32 (97.0%)	13 (92.9%)	
High	0 (0.0%)	1 (3.0%)	1 (7.1%)	
<b>prim PD-L1 (IC)</b>				0.002*
Low	12 (92.3%)	26 (78.8%)	5 (35.7%)	
High	1 (7.7%)	7 (21.2%)	9 (64.3%)	
<b>ICS of metastases</b>				0.074
Low	4 (30.8%)	5 (14.7%)	0 (0.0%)	
Intermediate	5 (38.5%)	23 (67.6%)	8 (57.1%)	
High	4 (30.8%)	6 (17.6%)	6 (42.9%)	

\*Statistically significant at the 0.05 level

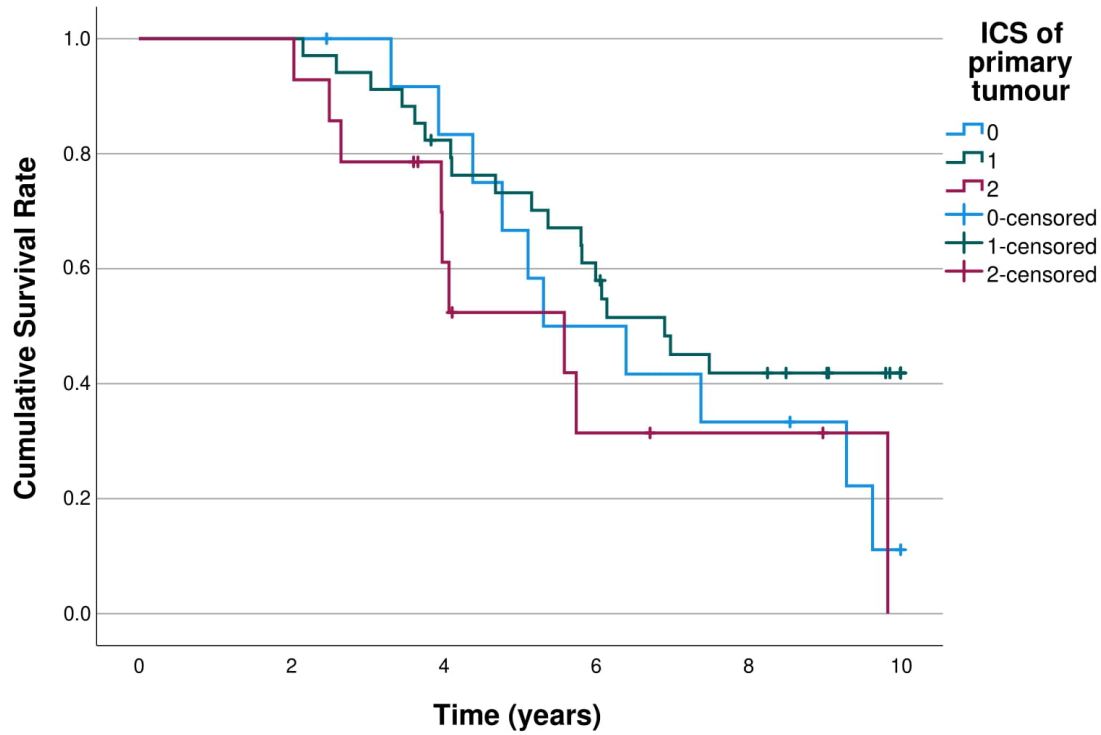
**Table S3.** Spearman correlation table of CD3+ and CD8+ densities between primary tumour and first pulmonary metastases.

		<b>met CD3<sup>+</sup> (TC)</b>	<b>met CD3<sup>+</sup> (IM)</b>	<b>met CD8<sup>+</sup> (TC)</b>	<b>met CD8<sup>+</sup> (IM)</b>
<b>met CD3<sup>+</sup> (TC)</b>	Correlation Coefficient	1.000	<b>0.670**</b>	<b>0.856**</b>	<b>0.654**</b>
	Sig. (2-tailed)		<0.001	<0.001	<0.001
	N	67	65	67	65
<b>met CD3<sup>+</sup> (IM)</b>	Correlation Coefficient	<b>,670**</b>	1.000	<b>,613**</b>	<b>,798**</b>
	Sig. (2-tailed)	<0.001		<0.001	<0.001
	N	65	65	65	65
<b>met CD8<sup>+</sup> (TC)</b>	Correlation Coefficient	<b>,856**</b>	<b>,613**</b>	1.000	<b>,774**</b>
	Sig. (2-tailed)	<0.001	<0.001		<0.001
	N	67	65	67	65
<b>met CD8<sup>+</sup> (IM)</b>	Correlation Coefficient	<b>,654**</b>	<b>,798**</b>	<b>,774**</b>	1.000
	Sig. (2-tailed)	<0.001	<0.001	<0.001	
	N	65	65	65	65
<b>prim CD3<sup>+</sup> (TC)</b>	Correlation Coefficient	0.004	0.189	0.103	<b>.290*</b>
	Sig. (2-tailed)	0.977	0.153	0.428	0.026
	N	61	59	61	59
<b>prim CD3<sup>+</sup> (IM)</b>	Correlation Coefficient	0.061	0.209	0.162	0.192
	Sig. (2-tailed)	0.644	0.115	0.218	0.149
	N	60	58	60	58
<b>prim CD8<sup>+</sup> (TC)</b>	Correlation Coefficient	0.234	0.229	<b>0.259*</b>	<b>0.350**</b>
	Sig. (2-tailed)	0.070	0.081	0.044	0.007
	N	61	59	61	59
<b>prim CD8<sup>+</sup> (IM)</b>	Correlation Coefficient	<b>0.354**</b>	<b>0.350**</b>	<b>0.362**</b>	<b>0.406**</b>
	Sig. (2-tailed)	0.006	0.008	0.005	0.002

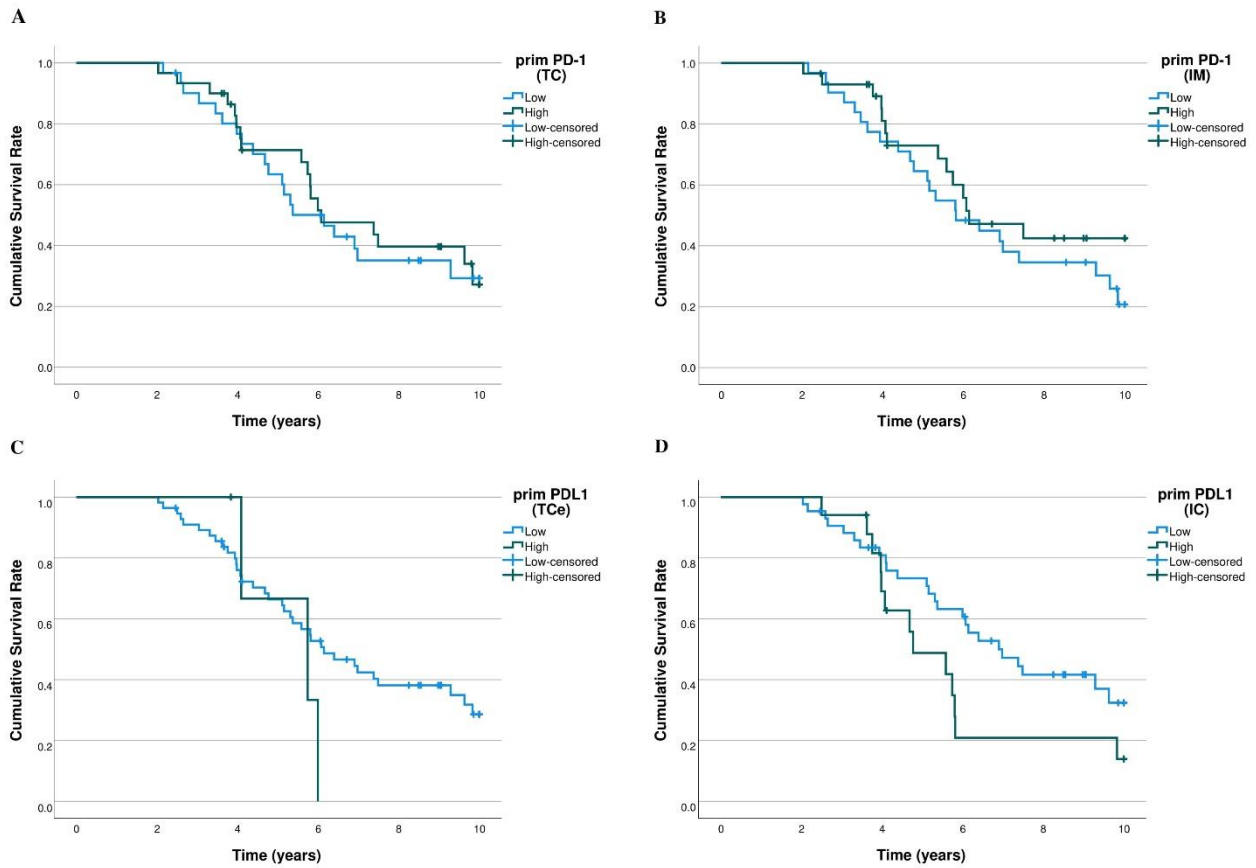
	N	59	57	59	57
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\*\*, Correlation is significant at the 0.01 level (2-tailed).

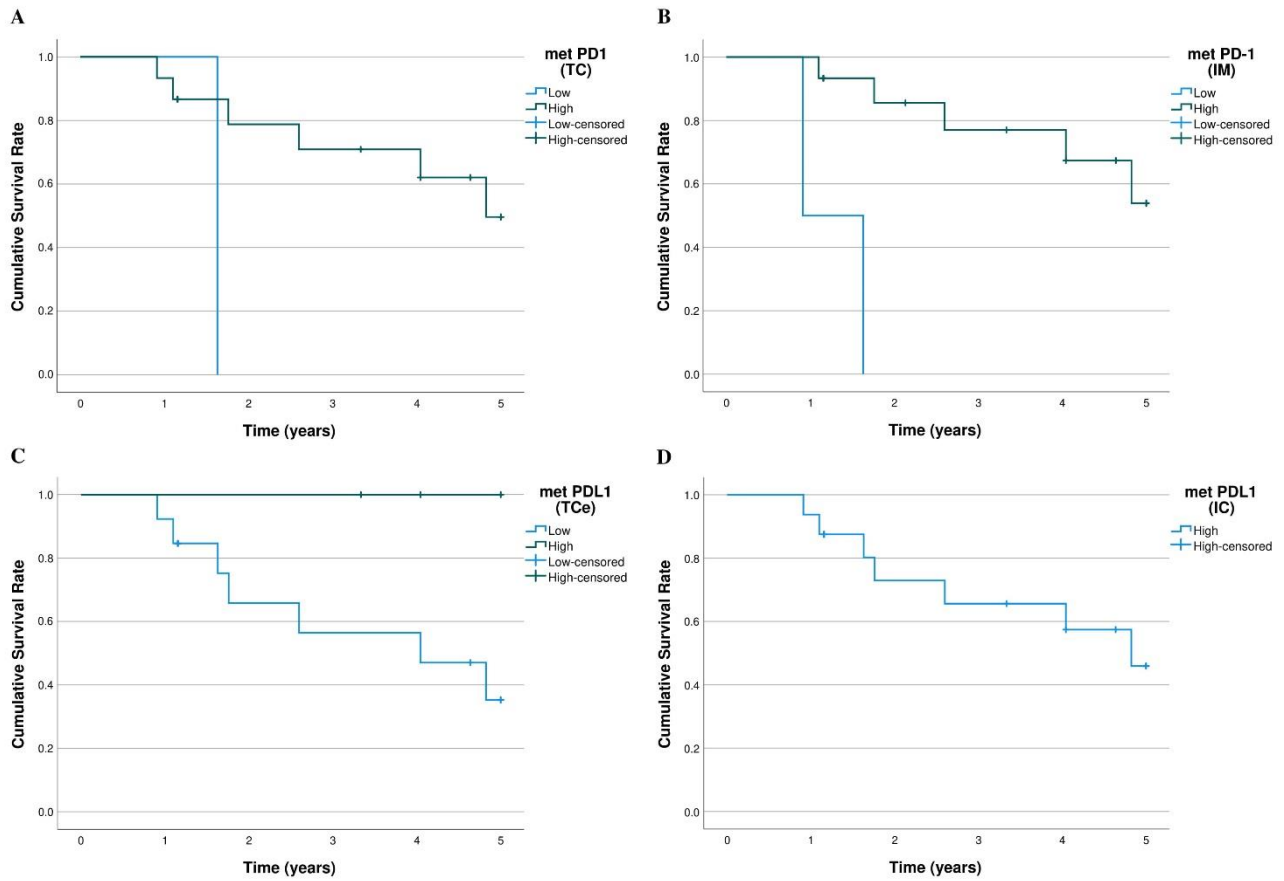
\*, Correlation is significant at the 0.05 level (2-tailed).



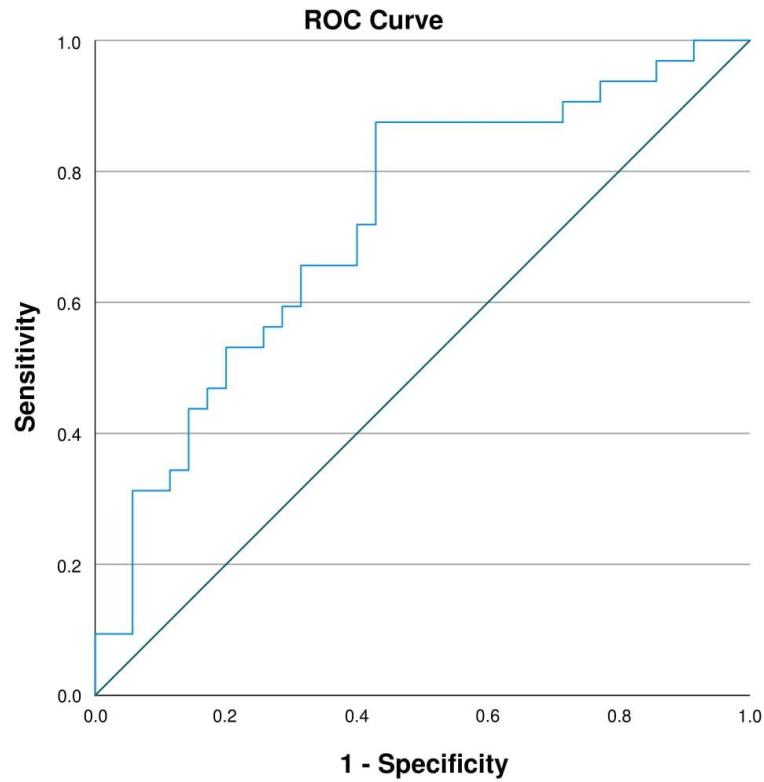
**Figure S1.** K-M curves of 10-year survival stratified by the ICS of the primary tumour. Log rank  $p=0.152$ .



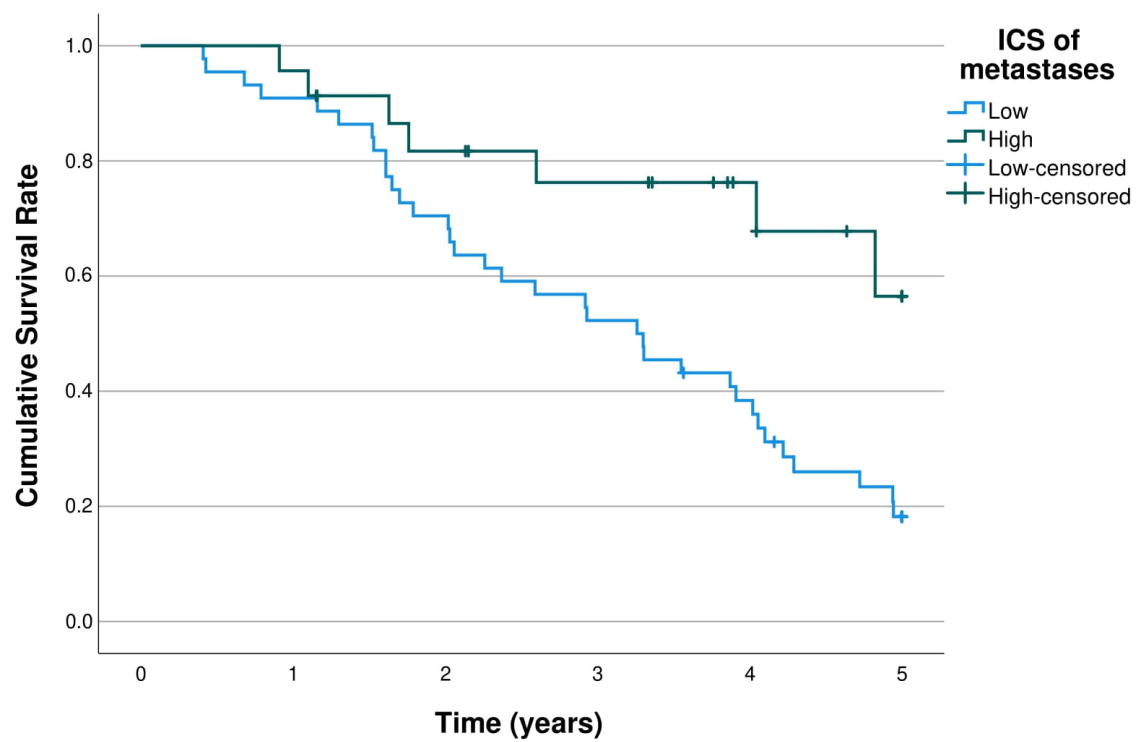
**Figure S2.** K-M 10-year overall survival curves of PD-1/PD-L1 expression of the primary tumour. **(A)** PD-1 expression (low vs. high) in the tumour centre ( $p=0.726$ ). **(B)** PD-1 expression (low vs. high) in the invasive margin ( $p=0.328$ ). **(C)** PD-L1 expression (low vs. high) in the tumour cells ( $p=0.504$ ). **(D)** PD-L1 expression (low vs. high) in the tumour infiltrating immune cells ( $p=0.086$ ).



**Figure S3.** The K-M curves of 5-year overall survival of pulmonary metastasectomy in ICS-high pulmonary metastases (n=17) stratified by **(A)** PD-1 in the tumour centre ( $p=0.076$ ), **(B)** PD-1 in the invasive margin ( $p<0.001$ ), **(C)** PD-L1 in the tumour cells ( $p=0.138$ ) and, **(D)** PD-L1 in the immune cells. Log rank tests were applied.



**Figure S4.** Receiver operating characteristics (ROC) curve of the mean percentile score of the immune cell densities in the invasive margin and tumour centre of the pulmonary metastases.



**Figure S5.** The K-M curves of 5-year overall survival stratified by the ICS of pulmonary metastases according to the cut-off value (65%) selected from ROC-curve (n=67). Log rank  $p=0.009$ .