



Title	Preoperative chemotherapy in colorectal cancer patients with synchronous liver metastasis
Author(s)	Ichikawa, Nobuki; Kamiyama, Toshiya; Yokoo, Hideki; Homma, Shigenori; Maeda, Yoshiaki; Shinohara, Toshiki; Tsuruga, Yosuke; Kazui, Keizo; Iijima, Hiroaki; Yoshida, Tadashi; Taketomi, Akinobu
Citation	Molecular and clinical oncology, 12(4), 374-383 <a href="https://doi.org/10.3892/mco.2020.1992">https://doi.org/10.3892/mco.2020.1992</a>
Issue Date	2020-04
Doc URL	<a href="http://hdl.handle.net/2115/79361">http://hdl.handle.net/2115/79361</a>
Type	article
Additional Information	There are other files related to this item in HUSCAP. Check the above URL.
File Information	Supplementary_Data.pdf



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Figure S1. Association between K-RAS status and overall survival in K-RAS available cohort.

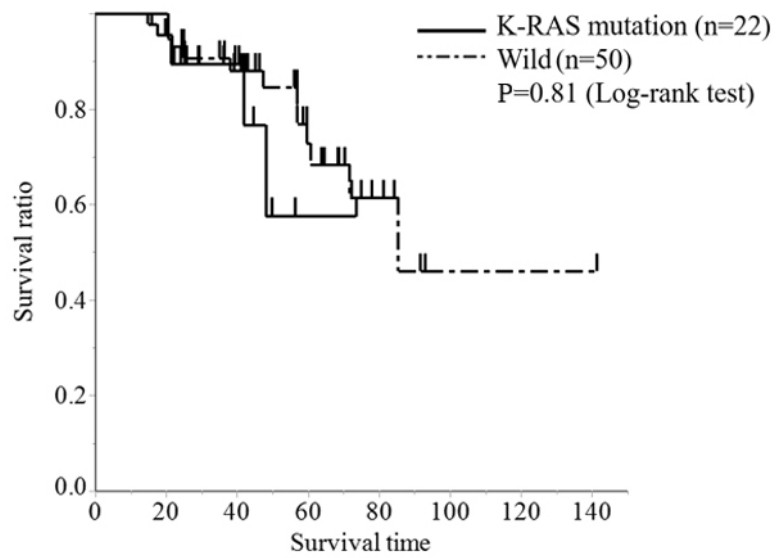


Table SI. Risk factors for shorter survival in NAC group.

Risk factor	Univariate analysis			Multivariate analysis			
	N	HR	95% C.I.	P-value	HR	95% C.I.	P-value
Age							
<50	8	1.00	-				
≥50	56	0.70	0.17-4.64	0.66			
Sex							
Male	26	1.00	-				
Female	38	1.65	0.56-4.88	0.35			
Tumor location							
Left	49	1.00	0				
Right	15	1.35	0.30-4.42	0.65			
Histology							
Well/mod	53	1.00	-				
Other	9	2.30	0.50-8.03	0.25			
Unknown	2	-	-	-			
T							
1-3	46	1.00	-		1.00	-	
4	17	4.12	1.39-12.1	0.01	5.57	1.78-17.8	0.003
Unknown	1	-	-	-	-	-	-
N							
Negative	8	1.00	-				
Positive	49	2.30	0.41-43.7	0.38			
Unknown	7	-	-	-			
H							
1	22	1.00	-				
2	30	1.67	0.45-7.83	0.44			
3	12	2.90	0.63-14.8	0.16			
ly							
Negative	22	1.00	-				
Positive	38	2.95	0.78-19.1	0.11			
Unknown	4	-	-	-			
v							
Negative	9	1.00	-				
Positive	52	2.50	0.49-45.8	0.31			
Unknown	3	-	-	-			
Simultaneous liver resection							
Yes	4	1.00	-				
No	60	0.24	0.06-1.63	0.12			
Procedures							
Partial	35	1.00	-				
Segmentectomy	14	1.88	0.53-6.25	0.43			
Lobectomy	15	0.31	0.01-1.75	0.21			
Adjuvant							
Yes	47	1.00	-				
No	17	0.75	0.20-2.30	0.63			
Historical margin positive							
No	46	1.00	-				
Yes	16	1.41	0.30-5.06	0.62			
Unknown	2	-	-	-			
Adjuvant Oxalipatin							
Yes	20	1.00	-				
No	42	1.41	0.40-6.47	0.59			
Unknown	2	-	-	-			
Adjuvant Bevasizumab							
Yes	11	1.00	-				
No	51	1.16	0.03-7.66	0.84			
Unknown	2	-	-	-			

Table SI. Continued. Risk factors for shorter survival in NAC group.

Risk factor	Univariate analysis			Multivariate analysis			
	N	HR	95% C.I.	P-value	HR	95% C.I.	P-value
Adjuvant Irinotecan							
Yes	15	1.00	-				
No	47	0.57	0.16-2.20	0.39			
Unknown	2	-	-	-			
H stage after NAC							
1	27	1.00	-		1.00	-	
2	28	4.44	1.14-29.1	0.02	5.71	1.45-38.2	0.01
3	8	8.45	0.99-72.1	0.05	10.9	1.20-102	0.03
0	1	-	-	-	-	-	-
Noadjuvant Oxaliplatin							
Yes	54	1.00	-				
No	10	1.14	0.25-3.69	0.83			
Noadjuvant Bevasizumab							
Yes	35	1.00	-				
No	29	0.59	0.17-1.75	0.35			
Noadjuvant Irinotecan							
Yes	20	1.00	-				
No	44	0.84	0.28-2.58	0.75			
Noadjuvant P/Cmab							
Yes	21	1.00	-				
No	43	1.97	0.60-8.81	0.27			

The variables with  $P < 0.1$  in the univariate Cox proportional hazard regression analysis were used as components for the multivariate Cox regression analysis. P/Cmab, Cetuximab/Panitumumab; Cases with unknown data were excluded in each analyze. T indicates invasion depth of the primary tumor; N, Lymph node metastasis; H, liver metastasis; H0, patients with no visible liver metastasis; H1, patients with fewer than 3 liver metastases with a maximum diameter  $< 5$  cm; H3, patients with more than 4 metastases with a maximum diameter  $> 5$  cm; H2, patients excluded from subgroups H1 and H3; ly, lymph vessel invasion of the primary tumor; v, venous invasion of the primary tumor NAC, neoadjuvant chemotherapy.

Table SII. Risk factors for shorter survival in Non-NAC group.

Risk factor	Univariate analysis			Multivariate analysis			
	N	HR	95% C.I.	P-value	HR	95% C.I.	P-value
Age							
<50	5	1.00	-				
≥50	37	3.70	0.70-68.5	0.13			
Sex							
Male	23	1.00	-		1.00	-	
Female	19	2.29	1.00-9.73	0.049	4.09	1.17-17.1	0.02
Tumor location							
Left	31	1.00	-				
Right	11	2.32	0.69-6.91	0.15			
Histology							
Well/mod	35	1.00	-				
Other	6	3.04	0.68-9.83	0.12			
Unknown	1	-	-	-			
T							
1-3	34	1.00	-				
4	8	0.63	0.09-2.33	0.52			
N							
Negative	4	1.00	-				
Positive	34	0.53	0.14-3.44	0.44			
Unknown	4	-	-	-			
H							
1	31	1.00	-	0.35			
2	9	1.81	0.47-5.93	0.21			
3	2	2.29	0.44-12.8				
ly							
Negative	12	1.00	-		1.00	-	
Positive	28	8.01	1.57-146	0.008	10.5	1.88-199	0.004
Unknown	2	-	-	-	-	-	-
v							
Negative	7	1.00	-				
Positive	33	0.90	0.27-3.99	0.87			
Unknown	2	-	-	-			
Simultaneous liver resection							
Yes	21	1.00	-				
No	21	0.81	0.26-2.35	0.70			
Procedures							
Partial	25	1.00	-				
Segmentectomy	9	1.66	0.43-5.56	0.43			
Lobectomy	8	1.74	0.35-6.80	0.45			
Adjuvant							
Yes	25	1.00	-		1.00	-	
No	17	2.42	0.81-7.15	0.10	6.42	1.76-26.8	0.004
Historical margin positive							
No	33	1.00	-				
Yes	7	1.04	0.16-3.96	0.95			
Unknown	2	-	-	-			
Adjuvant Oxalipatin							
Yes	13	1.00	-	0.06			
No	29	3.00	0.92-13.4				
Adjuvant Bevasizumab							
Yes	1	1.00	-	0.44			
No	41	0.40	0.07-7.51				

The variables with P<0.1 in the univariate Cox proportional hazard regression analysis were used as components for the multivariate Cox regression analysis. Cases with unknown data were excluded in each analyze. T indicates invasion depth of the primary tumor; N, Lymph node metastasis; H, liver metastasis; H0, patients with no visible liver metastasis; H1, patients with fewer than 3 liver metastases with a maximum diameter <5 cm; H3, patients with more than 4 metastases with a maximum diameter >5 cm; H2, patients excluded from subgroups H1 and H3; ly, lymph vessel invasion of the primary tumor; v, venous invasion of the primary tumor NAC, neoadjuvant chemotherapy.

Table SIII. Risk factors for shorter survival in K-RAS available cohort.

Risk factor	Univariate analysis			Multivariate analysis			
	N	HR	95% C.I.	P-value	HR	95% C.I.	P-value
Age							
<50	8	1.00	-				
≥50	64	2.09	0.41-37.9	0.42			
Sex							
Male	43	1.00	-				
Female	29	1.27	0.45-3.45	0.63			
Tumor location							
Left	55	1.00	-				
Right	17	3.21	0.83-10.4	0.08			
Histology							
Well/mod	61	1.00	-				
Other	9	1.29	0.20-4.88	0.74			
Unknown	2	-	-	-			
T							
1-3	54	1.00	-				
4	17	2.30	0.71-6.52	0.15			
Unknown	1	-	-	-			
N							
0	7	1.00	-	0.83			
1	57	1.17	0.30-7.81	-			
Unknown	8	-	-	-			
H							
1	29	1.00	-	0.41	1.00	-	0.54
2	30	1.67	0.47-6.59	0.03	1.50	0.39-6.16	0.04
3	13	3.75	1.06-14.7		3.56	1.01-14.0	
ly							
Negative	27	1.00	-				
Positive	42	2.02	0.63-8.91	0.24			
Unknown	3	-	-	-			
v							
Negative	10	1.00	-				
Positive	59	1.82	0.35-33.4	0.52			
Unknown	3	-	-	-			
Simultaneous liver resection							
Yes	9	1.00	-	0.22			
No	63	0.41	0.12-1.86				
Procedures							
0	34	1.00	-	0.43			
1,s	19	2.17	0.63-6.71	0.67			
2	19	0.72	0.10-3.00				
Adjuvant							
Yes	46	1.00	-	0.37			
No	26	1.57	0.55-4.27				
Historical margin positive							
No	51	1.00	-				
Yes	19	1.64	0.44-4.99	0.42			
Unknown	2	-	-	-			
Adjuvant oxalipatin							
Yes	21	1.00	-		1.00		
No	49	3.60	0.99-23.0	0.05	3.29	0.89-21.2	0.07
Unknown	2	-	-	-	-	-	-
Adjuvant bevasizumab							
Yes	11	1.00	-				
No	59	1.25	0.34-8.07	0.76			
Unknown	2	-	-	-			

Table SIII. Continued. Risk factors for shorter survival in K-RAS available cohort.

Risk factor	Univariate analysis			Multivariate analysis			
	N	HR	95% C.I.	P-value	HR	95% C.I.	P-value
Adjuvant irinotecan							
Yes	13	1.00	-				
No	57	0.46	0.14-1.71	0.22			
Unknown	2	-	-	-			
Adjuvant P/Cmab							
Yes	1						
No	69	-	-	-			
Unknown	2	-	-	-			
K-RAS							
Wild	50	1.00	-	0.41			
Mutation	22	1.67	0.44-5.30				
NAC							
Yes	55	1.00	-	0.51			
No	17	1.43	0.44-3.96				
Noadjuvant Oxaliplatin							
Yes	48	1.00	-	0.36			
No	24	1.59	0.56-4.32				
Noadjuvant Bevasizumab							
Yes	29	1.00	-	0.93			
No	43	1.04	0.38-2.92				
Noadjuvant Irinotecan							
Yes	17	1.00	-	0.67			
No	55	0.79	0.28-2.42				
Noadjuvant P/Cmab							
Yes	20	1.00	-	0.15			
No	52	2.34	0.73-10.3				

The variables with  $P < 0.1$  in the univariate Cox proportional hazard regression analysis were used as components for the multivariate Cox regression analysis. Cases with unknown data were excluded in each analyze. P/Cmab, Cetuximab/Panitumumab. T indicates invasion depth of the primary tumor; N, Lymph node metastasis; H, liver metastasis; H0, patients with no visible liver metastasis; H1, patients with fewer than 3 liver metastases with a maximum diameter  $< 5$  cm; H3, patients with more than 4 metastases with a maximum diameter  $> 5$  cm; H2, patients excluded from subgroups H1 and H3; ly, lymph vessel invasion of the primary tumor; v, venous invasion of the primary tumor NAC, neoadjuvant chemotherapy.

Table SIV. Risk factors for shorter progression free survival in NAC group.

Risk factors	Univariate analysis			Multivariate analysis			
	N	HR	95% C.I.	P-value	HR	95% C.I.	P-value
Age							
<50	7	1.00	-	0.15			
≥50	53	0.50	0.22-1.33				
Sex							
Male	25	1.00	-	0.79			
Female	35	0.92	0.49-1.67				
Tumor location							
Left	47	1.00	-	0.52			
Right	13	1.26	0.58-2.47				
Histology							
Well/mod	50	1.00	-	0.15			
Other	8	1.90	0.76-4.16				
Unknown	2	-	-				
T							
1-3	43	1.00	-	0.002	1.00	-	0.001
4	16	2.90	1.49-5.46		3.78	1.68-8.28	
Unknown	1	-	-		-	-	
N							
Negative	8	1.00	-	0.06	1.00	-	0.08
Positive	44	2.24	0.94-6.59		2.24	0.90-6.80	
Unknown	8	-	-		-	-	
H							
1	21	1.00	-	0.89			
2	29	0.95	0.49-1.88		0.48		
3	10	1.34	0.56-3.00				
ly							
Negative	22	1.00	-	0.09	1.00	-	0.09
Positive	36	1.71	0.91-3.38		1.85	0.89-4.09	
Unknown	2	-	-		-	-	
v							
Negative	9	1.00	-	0.11			
Positive	49	2.01	0.86-5.91		0.11		
Unknown	2	-	-		-	-	
Simultaneous liver resection							
Yes	4	1.00	-	0.59			
No	56	1.44	0.44-8.88				
Procedures							
0	29	1.00	-	0.14			
1,s	19	1.68	0.83-3.31		0.79		
2	12	0.89	0.37-1.93				
Adjuvant							
Yes	39	1.00	-	0.83			
No	21	0.93	0.48-1.72				
Historical margin positive							
No	44	1.00	-	0.08	1.00	-	0.04
Yes	14	1.89	0.93-3.61		2.30	1.03-4.84	
Unknown	3	-	-		-	-	
Adjuvant Oxalipatin							
Yes	20	1.00	-	0.72			
No	40	0.89	0.48-1.69				
Adjuvant Bevasizumab							
Yes	9	1.00	-	0.31			
No	51	1.49	0.70-3.67				
Adjuvant Irinotecan							
Yes	13	1.00	-	0.95			
No	47	0.98	0.53-1.88				



Table SIV. Continued. Risk factors for shorter progression free survival in NAC group.

Risk factors	Univariate analysis			Multivariate analysis			
	N	HR	95% C.I.	P-value	HR	95% C.I.	P-value
Adjuvant P/Cmab							
Yes	1	-	-	-			
No	59						
H stage after NAC							
1	27	1.00	-	-			
2	27	1.46	0.77-2.76	0.23			
3	5	2.18	0.62-5.89	0.19			
0	1	-	-	-			
Noadjuvant Oxalipratin							
Yes	50	1.00	-				
No	10	1.16	0.52-3.32	0.69			
Noadjuvant Bevasizumab							
Yes	33	1.00	-				
No	27	0.97	0.53-1.75	0.35			
Noadjuvant Irinotcan							
Yes	19	1.00	-				
No	41	0.98	0.53-1.88	0.95			
Noadjuvant P/Cmab							
Yes	20	1.00	-				
No	40	0.96	0.52-1.88	0.92			

The variables with  $P < 0.1$  in the univariate Cox proportional hazard regression analysis were used as components for the multivariate Cox regression analysis. Cases with unknown data were excluded in each analyze. P/Cmab, Cetuximab/Panitumumab; T indicates invasion depth of the primary tumor; N, Lymph node metastasis; H, liver metastasis; H0, patients with no visible liver metastasis; H1, patients with fewer than 3 liver metastases with a maximum diameter  $< 5$  cm; H3, patients with more than 4 metastases with a maximum diameter  $> 5$  cm; H2, patients excluded from subgroups H1 and H3; ly, lymph vessel invasion of the primary tumor; v, venous invasion of the primary tumor NAC, neoadjuvant chemotherapy.