

**Supplementary tables:**

<b>Table A1: Study population characteristics according treatment type</b>			
	<b>All patients</b>	<b>ICIs cohort</b>	<b>TAs cohort</b>
<b>Total, n (%)</b>	799 (100)	518 (64.8)	281 (35.2)
<b>Age years, median (IQR)</b>	59.4 (50.2 - 67.4)	60.1 (50.1 - 68)	58.2 (50.3 - 66.7)
<b>Sex, female</b>	413 (51.7)	243 (46.9%)	170 (60.5%)
<b>Tumor type</b>			
Breast	95 (11.9)	43 (8.3)	52 (18.5)
CRC	134 (16.8)	76 (14.7)	58 (20.6)
Non-CRC gastrointestinal	136 (17)	75 (14.5)	61 (21.7)
Gynaecological	76 (9.5)	42 (8.1)	34 (12.1)
H&N	55 (6.9)	41 (7.9)	14 (5)
Lung	83 (10.4)	67 (12.9)	16 (5.7)
Melanoma	94 (11.8)	83 (16)	11 (3.9)
Others	126 (15.8)	91 (17.6)	35 (12.5)
<b>Treatment</b>			
Monotherapy	430 (53.8)	205 (39.5)	225 (80.0)
Combination	369 (46.1)	313 (60.4)	56 (19.9)
<b>ECOG, 0</b>	315 (39.4)	234 (45.2)	81 (28.9)
<b>No. metastatic sites</b>			
Median (IQR)	3 (2 - 3)	2 (2-3)	3 (2-4)
No. metastatic sites > 2	404 (50.6)	247 (47.7%)	157(55.9%)
<b>Liver metastases</b>	354 (44.3)	205 (39.6%)	149 (53.0%)
<b>Platelet</b>			
Median (IQR)	259 (194 - 325)	263 (203 - 335)	247 (187 - 311)
Platelet > 400	105 (13.2)	78 (15.1)	27 (9.6)
<b>Albumin</b>			
Median (IQR)	4 (3.7 - 4.2)	4 (3.7 - 4.2)	3.9 (3.7 - 4.2)
Albumin < 3.5	106 (13.3)	60 (11.6%)	46 (16.4%)
<b>LDH</b>			
Median (IQR)	442 (349 - 631)	441 (347 - 608)	455 (352 - 648)
LDH > ULN	534 (66.8)	345 (66.6)	189 (67.3)
<b>Lymphocytes</b>			
Median (IQR)	1.3 (1 - 1.7)	1.3 (1 - 1.7)	1.3 (1 - 1.7)
Lymphocytes < 1.2	291 (36.4)	194 (37.5)	97 (34.5)
<b>Leucocytes</b>			
Median (IQR)	6.7 (5.2 - 8.5)	6.7 (5.3 - 8.4)	6.7 (5.0 - 8.7)
Leucocytes > 11	73 (9.1)	49 (9.5)	24 (8.5)
<b>Neutrophils</b>			
Median (IQR)	4.3 (3.3 - 5.9)	4.3 (3.3 - 5.8)	4.3 (3.3 - 6.0)
Neutrophils > 7	115 (14.4)	74 (14.3)	41 (14.6)
<b>Neutrophil/Lymphocyte ratio</b>			
Median (IQR)	3.4 (2.4 - 4.9)	3.4 (2.4 - 5.1)	3.3 (2.4 - 54.7)
neutrophil/lymphocyte> 6	121 (15.1)	76 (14.7)	45 (16.0)
<b>dNLR</b>			
Median (IQR)	2.1 (1.5 - 2.7)	2.1 (1.5 - 2.8)	2.1 (1.6 - 2.6)

dNLR > 3	151 (18.9)	105 (20.3%)	46 (16.4%)
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N, number; IQR, interquartile range; CRC, colorectal, H&N, head and neck; ECOG, performance status; LDH, lactate dehydrogenase; dNLR, derived neutrophils/(leukocytes minus neutrophils) ratio HR.

**Table A2:**

<b>Missing data (n=799)</b>		
	<b>n</b>	<b>%</b>
<b>Age</b>	2	0.3%
<b>Sex</b>	0	0%
<b>ECOG</b>	5	0.6%
<b>No. of metastatic sites</b>	4	0.5%
<b>Liver metastases</b>	4	0.5%
<b>Platelet count</b>	3	0.7%
<b>Albumin</b>	4	0.5%
<b>Drug Regimen</b>	0	0%
<b>LDH</b>	226	28.3%
<b>Lymphocytes</b>	1	0.1%
<b>Leucocytes</b>	1	0.1%
<b>Neutrophils</b>	1	0.1%
<b>Neutrophil/Lymphocyte ratio</b>	1	0.1%
<b>dNLR</b>	1	0.1%

No, number; ECOG, performance status; LDH, lactate dehydrogenase; dNLR, derived neutrophils/(leukocytes minus neutrophils) ratio.

**Table A3:**

Cox models for overall survival in the training ICI set (n=362, 255 events)						
	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age (10-years increase)	0.9	0.81 - 0.99	0.02	-	-	-
Sex (male vs female)	0.91	0.71 - 1.16	0.45	-	-	-
<b>ECOG</b>	1.72	1.32 - 2.24	<b>&lt;0.001</b>	1.37	1.04 - 1.80	<b>0.02</b>
<b>No. of metastatic sites</b>	1.43	1.28 - 1.59	<b>&lt;0.001</b>	1.29	1.15 - 1.45	<b>&lt;0.001</b>
<b>Liver metastases (yes vs. no)</b>	1.74	1.35 - 2.24	<b>&lt;0.001</b>	1.37	1.05 - 1.79	<b>0.02</b>
<b>Platelet count (100-unit increase)</b>	1.39	1.25 - 1.54	<b>&lt;0.001</b>	-	-	-
<b>Albumin</b>	0.35	0.27 - 0.47	<b>&lt;0.001</b>	0.56	0.41 - 0.77	<b>&lt;0.001</b>
<b>LDH (100-unit increase)</b>	1.07	1.03 - 1.1	<b>&lt;0.001</b>	1.05	1.02 - 1.09	<b>0.001</b>
<b>Lymphocytes</b>	0.85	0.69 - 1.04	0.11	-	-	-
<b>Leucocytes</b>	1.09	1.05 - 1.14	<b>&lt;0.001</b>	-	-	-
<b>Neutrophils</b>	1.13	1.08 - 1.19	<b>&lt;0.001</b>	-	-	-
<b>Neutrophil/Lymphocyte ratio</b>	1.14	1.09 - 1.19	<b>&lt;0.001</b>	-	-	-
<b>dNLR</b>	1.39	1.25 - 1.54	<b>&lt;0.001</b>	1.19	1.05 - 1.35	<b>0.008</b>

ICI, immune checkpoint inhibitor; ECOG, performance status; LDH, lactate dehydrogenase; dNLR, derived neutrophils/(leukocytes minus neutrophils) ratio; HR, hazard ratio; CI, confidential interval.

Cox models for overall survival in the training TA set (n=196, 171 events)						
	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age (10-years increase)	1	0.88 - 1.14	0.92	-	-	-
Sex (male vs female)	1.47	1.08 - 1.99	0.01	-	-	-
<b>ECOG</b>	1.39	1 - 1.93	<b>0.05</b>	1.32	0.93 - 1.86	0.11
<b>No. of metastatic sites</b>	1.45	1.27 - 1.66	<b>&lt;0.001</b>	1.29	1.12 - 1.49	<b>&lt;0.001</b>
<b>Liver metastases (yes vs. no)</b>	1.7	1.25 - 2.30	<b>&lt;0.001</b>	1.6	1.14 - 2.25	<b>0.006</b>
<b>Platelet count (100-unit increase)</b>	1.28	1.11 - 1.49	<b>0.001</b>	-	-	-
<b>Albumin</b>	0.31	0.20 - 0.47	<b>&lt;0.001</b>	0.42	0.27 - 0.64	<b>&lt;0.001</b>
<b>LDH (100-unit increase)</b>	1.05	1.01 - 1.08	<b>0.005</b>	1.04	1.01 - 1.07	<b>0.04</b>
<b>Lymphocytes</b>	0.85	0.70 - 1.04	0.11	-	-	-
<b>Leucocytes</b>	1.05	1.03 - 1.07	<b>&lt;0.001</b>	-	-	-
<b>Neutrophils</b>	1.05	1.03 - 1.07	<b>&lt;0.001</b>	-	-	-
<b>Neutrophil/Lymphocyte ratio</b>	1.13	1.08 - 1.18	<b>&lt;0.001</b>	-	-	-
<b>dNLR</b>	1.29	1.15 - 1.43	<b>&lt;0.001</b>	1.19	1.05 - 1.35	<b>0.008</b>

TA, target agents; ECOG, performance status; LDH, lactate dehydrogenase; dNLR, derived neutrophils/(leukocytes minus neutrophils) ratio; HR, hazard ratio; CI, confidential interval.

**Table A4**

<b>Final Cox multivariate model for overall survival in the pooled cohort using cubic restricted splines (n=799, 513 events)</b>			
<b>Variable</b>	<b>Coef</b>	<b>S.E.</b>	<b>Hazard ratio</b>
ECOG (1+ vs 0)	0.31	0.099	1.363
Liver metastasis (yes vs no)	0.404	0.096	1.498
No. of metastatic sites (= 2)	0.245	0.149	1.278
No. of metastatic sites (= 3)	0.475	0.153	1.608
No. of metastatic sites (= 4)	0.591	0.173	1.806
No. of metastatic sites (= +5)	1.066	0.193	2.904
LDH	-0.001	0.001	0.999
LDH'	0.025	0.018	1.025
LDH''	-0.057	0.043	0.945
Albumin	-0.802	0.276	0.448
Albumin'	0.839	0.712	2.314
Albumin''	-6.394	4.297	0.002
dNLR	-0.105	0.244	0.9
dNLR'	1.782	1.299	5.942
dNLR''	-4.501	3.258	0.011

ECOG, performance status; LDH, lactate dehydrogenase; dNLR, derived neutrophils/(leukocytes minus neutrophils) ratio; S.E., ; Coef, coefficient.