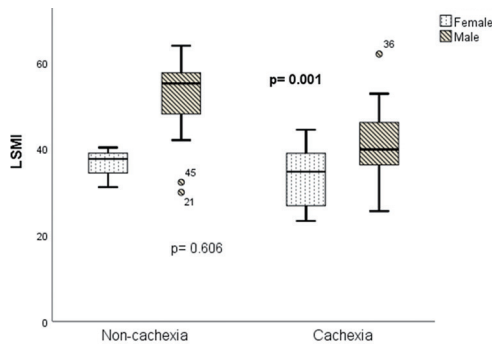
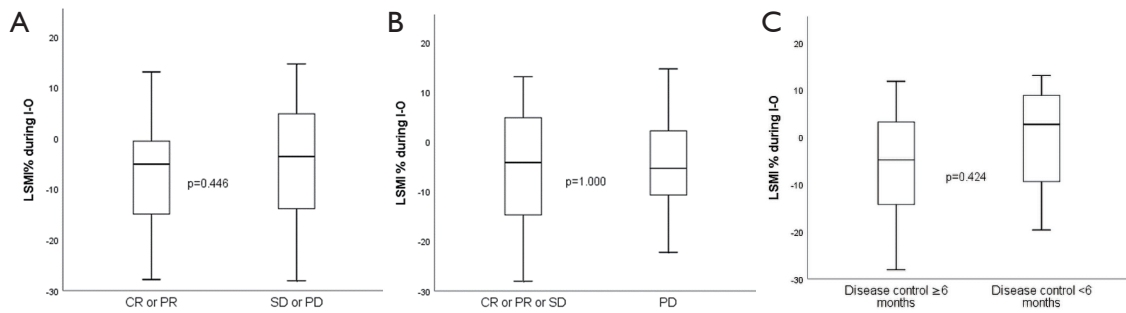


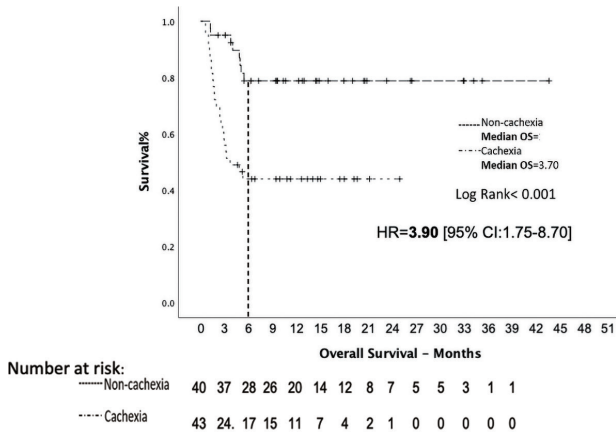
**Figure S1** Flow chart of our study. <sup>\*1</sup>, classification for cachexia was conducted according to the criteria by Fearon *et al.* (18). <sup>\*2</sup>, LSMI: Lumbar Skeletal Muscle Index.



**Figure S2** Kruskal-Wallis test examining potential differences in the distributions of baseline LSMI values between cachectic *vs.* non-cachectic males and cachectic *vs.* non-cachectic females.



**Figure S3** Kruskal-Wallis test investigating any potential difference in the distributions of LSMI change % during I-O. (A) Between patients who had CR or PR *vs.* those who experience SD or PD. (B) Between patients who had CR or PR or PD *vs.* those who experienced PD. (C) Between individuals who achieved prolonged disease control for  $\geq 6$  months *vs.* those who did not.



**Figure S4** Log-rank test demonstrating the effect of cancer cachexia syndrome on 6 months survival.

**Table S1** Effect of the studied variables on response rates

Variable	N=83	CR or PR	SD or PD	P value (chi-square test, 95% CI)
<b>Age</b>				
<70 years old	51	12	39	0.385
$\geq 70$ years old	32	5	27	
<b>Gender</b>				
Male	70	14	56	0.801
Female	13	3	10	
<b>Performance status</b>				
0-1	65	14	51	0.650
2	18	3	15	

**Table S1** (continued)

**Table S1** (continued)

Variable	N=83	CR or PR	SD or PD	P value (chi-square test, 95% CI)
<b>Histology</b>				
Non-squamous	51	12	39	0.385
Squamous	32	5	27	
<b>Brain metastases</b>				
Yes	20	4	16	0.951
No	63	13	50	
<b>Liver metastases</b>				
Yes	23	3	20	0.298
No	60	14	46	
<b>Bone metastases</b>				
Yes	29	7	22	0.545
No	54	10	44	
<b>Disease burden*</b>				
High	26	5	21	0.849
Low	57		45	
<b>PD-L1 status</b>				
<1%	14	3	11	0.988
≥1%	37		29	
<b>Baseline albumin levels</b>				
<3.5 g/dL	12	0	12	0.085
≥3.5 g/dL	64	13	51	
<b>BMI</b>				
<25 kg/m <sup>2</sup>	32	3	29	0.047
≥25 kg/m <sup>2</sup>	51	14	37	
<b>Cancer Cachexia</b>				
Yes	43	2	41	<0.01
No	40		25	
<b>Baseline LSMI</b>				
<LNV	39	6	33	0.051
≥LNV	15	6	9	

\*, high disease burden was defined as >2 organs with metastatic spread. LSMI, lumbar skeletal muscle index (at the level of 3<sup>rd</sup> lumbar vertebra), LNV, lower normal value that was set for males =55 cm/m<sup>2</sup> and for females =39 cm/m<sup>2</sup>.

**Table S2** Effect of the studied variables on disease control (CR or PR or SD) rates.

Variable	N=83	CR or PR or SD	PD	P value (chi-square test, 95% CI)
<b>Age</b>				
<70 years old	51	24	27	0.274
≥70 years old	32	19	13	
<b>Gender</b>				
Male	70	38	32	0.294
Female	13	5	8	
<b>Performance status</b>				
0–1	65	37	28	0.076
2	18	6	12	
<b>Histology</b>				
Non-squamous	51	24	27	0.274
Squamous	32	19	13	
<b>Brain metastases</b>				
Yes	20	8	12	0.225
No	63	35	28	
<b>Liver metastases</b>				
Yes	23	8	15	0.055
No	60	35	25	
<b>Bone metastases</b>				
Yes	29	11	18	0.064
No	54	32	22	
<b>Disease burden*</b>				
High	26	9	17	0.034
Low	57	34	23	
<b>PD-L1 status</b>				
<1%	N=51 14	5	9	0.180
≥1%	37	21	16	
<b>Baseline albumin levels</b>				
<3.5 g/dL	N=76 12	4	8	0.174
≥3.5 g/dL	64	35	29	
<b>BMI</b>				
<25 kg/m <sup>2</sup>	32	12	20	0.039
≥25 kg/m <sup>2</sup>	51	31	20	

Table S2 (continued)

**Table S2** (continued)

Variable	N=83	CR or PR or SD	PD	P value (chi-square test, 95% CI)
<b>Cancer Cachexia</b>				
Yes	43	12	31	<0.01
No	40	31	9	
<b>Baseline LSMI</b>				
	N=54			
<LNV	39	13	26	<0.01
≥LNV	15	13	2	

\*, high disease burden was defined as >2 organs with metastatic spread. LSMI, lumbar skeletal muscle index (at the level of 3<sup>rd</sup> lumbar vertebra), LNV, lower normal value that was set for males =55 cm/m<sup>2</sup> and for females =39 cm/m<sup>2</sup>.

**Table S3** Univariate and multivariate logistic regression on the odds ratio (OR) of the analyzed covariates on the probability of developing disease progression (PD) as response to treatment with ICIs

Variable	Univariate			Multivariate		
	OR (95% CI)	P value	AUC (95% CI)	OR (95% CI)	P value	AUC (95% CI)
Age ≥70 years old	0.61 (0.25–1.49)	0.276	0.558 (0.434–0.682)			
PS=2	2.64 (0.88–7.91)	0.082	0.580 (0.456–0.704)			
Female gender	1.90 (0.56–6.39)	0.299	0.542 (0.417–0.667)			
Squamous histology	0.61 (0.25–1.49)	0.276	0.558 (0.434–0.682)			
Bone metastases	2.38 (0.94–6.01)	0.066	0.597 (0.474–0.720)			
Liver metastases	2.63 (0.97–7.13)	0.059	0.594 (0.471–0.718)			
Brain metastases	1.88 (0.67–5.22)	0.229	0.557 (0.432–0.681)			
PD-L1 <1%	2.36 (0.66–8.40)	0.185	0.584 (0.426–0.742)			
ICIs administered as 2 <sup>nd</sup> or later line of treatment	1.43 (0.49–4.20)	0.517	0.529 (0.404–0.653)			
Albumin <3.5 g/dL	2.41 (0.66–8.83)	0.183	0.557 (0.427–0.687)			
BMI <25 kg/m <sup>2</sup>	2.58 (1.04–6.19)	0.041	0.610 (0.488–0.733)	1.94 (0.69–5.44)	0.209	
Baseline cancer cachexia	8.89 (3.28–24.12)	<0.001	0.748 (0.640–0.856)	8.11 (2.95–22.94)	<0.001	
Overall						0.748 (0.640–0.856)

OR, Odds Ratio; AUC, Area under the curve; PS, Performance status.

**Table S4** Log-rank test on the effect of the studied variables on PFS and OS (n=83)

Variable	Median PFS (Months)	P value (log-rank test)	Median OS (Months)	P value (log-rank test)
<b>Age</b>				
<70 years old	4.00	0.803	9.47	0.957
≥70 years old	7.17		12.70	
<b>Gender</b>				
Male	4.80	0.253	10.33	0.531
Female	2.10		9.43	
<b>Performance Status</b>				
0–1	5.77	0.217	12.60	0.008
2	2.40		3.17	
<b>Histology</b>				
Squamous	5.77	0.580	9.57	0.572
Non-squamous	3.00		9.90	
<b>BMI</b>				
<25 kg/m <sup>2</sup>	2.53	0.153	4.00	0.273
≥25 kg/m <sup>2</sup>	6.20		10.33	
<b>Line of treatment of ICI administration</b>				
1 <sup>st</sup> line	13.80	0.019	Not reached	0.002
2 <sup>nd</sup> or later lines	4.40		9.43	
<b>Brain metastases</b>				
Yes	2.17	0.203	6.77	0.299
No	4.93		10.80	
<b>Bone metastases</b>				
Yes	4.80	0.674	7.23	0.198
No	3.23		12.70	
<b>Liver metastases</b>				
Yes	2.10	0.056	6.77	0.405
No	5.77		10.80	
<b>Disease burden*</b>				
High	2.53	0.057	4.83	0.038
Low	4.93		13.37	
<b>Baseline albumin levels</b>				
<3.5 g/dL	1.77	0.008	2.40	0.017
≥3.5 g/dL	5.77		11.23	

**Table S4** (continued)

**Table S4** (continued)

Variable	Median PFS (Months)	P value (log-rank test)	Median OS (Months)	P value (log-rank test)
PD-L1 levels				
<1%	2.57	0.880	7.23	0.184
≥1%	4.80		12.60	
Baseline Cancer Cachexia				
Yes	2.37		3.70	
No	7.33	<0.001	17.93	<0.001
Baseline LSMI				
<LNV	2.97	0.032	5.43	0.006
≥LNV	7.97		Not reached	
LSMI reduction % during ICI treatment				
<-5%	7.97	0.193	19.20	0.400
≥-5%	7.33		14.03	

\*, high disease burden was defined as > 2 organs with metastatic spread. ICI, Immune checkpoint inhibitor; LSMI, lumbar skeletal muscle index (at the level of 3<sup>rd</sup> lumbar vertebra); LNV, lower normal value that was set for males =55 cm/m<sup>2</sup> and for females =39 cm/m<sup>2</sup>.