

Supplementary data

Table S1. Scores based on systemic inflammation/nutritional status in the three cohorts of patients, treated with ICI in monotherapy, ICI+CT, or CT alone.

Continuous scores (ALI, PNI, and SII) were log-transformed in order to obtain a more symmetric distribution.

Scores	Cohort 1 (n=75) ICI Median (P25; P75) or n (%)	Cohort 2 (n=56) ICI+CT Median (P25; P75) or n (%)	Cohort 3 (n=221) CT Median (P25; P75) or n (%)
LIPI			
0	35 (47)	9 (16)	70 (32)
1	25 (33)	29 (52)	95 (43)
2	14 (19)	18 (32)	54 (24)
Missing	1 (1)	0 (0)	2 (1)
mLIPI			
0	12 (16)	5 (9)	36 (16)
1	39 (52)	37 (66)	125 (57)
2	20 (27)	12 (21)	46 (21)
3	3 (4)	2 (4)	12 (5)
Missing	1 (1)	0 (0)	2 (1)
SIPS			
0	34 (45)	20 (36)	36 (16)
1	25 (33)	29 (52)	78 (35)
2	14 (19)	7 (12)	59 (27)
Missing	2 (3)	0 (0)	48 (22)
ALI			
Median (P25; P75)	1.25 (0.99; 1.38)	0.97 (0.80; 1.30)	1.09 (0.77; 1.38)
Missing	2	0	48
EPSILoN			
0	9 (12)	3 (5)	22 (10)
1-2	50 (67)	38 (68)	150 (68)
3-5	15 (20)	15 (27)	41 (19)
Missing	1 (1)	0 (0)	8 (4)
PNI			
Median (P25; P75)	1.63 (1.60; 1.67)	1.66 (1.60; 1.68)	1.62 (1.57; 1.68)
Missing	2	0	48
SII			
Median (P25; P75)	3.16 (2.92; 3.49)	3.53 (3.24; 3.73)	3.29 (2.99; 3.59)
Missing	0	0	0
GRIm			
0	25 (33)	12 (21)	29 (13)
1	22 (29)	23 (41)	72 (33)
2	21 (28)	15 (27)	36 (16)
3	4 (5)	6 (11)	36 (16)
Missing	3 (4)	0 (0)	48 (22)
RMH			
0	27 (36)	21 (38)	37 (17)
1	25 (33)	14 (25)	58 (26)
2	15 (20)	16 (29)	56 (25)
3	5 (7)	5 (9)	22 (10)
Missing	3 (4)	0 (0)	48 (22)
LIPS-3			
0	20 (27)	8 (14)	53 (24)
1	28 (37)	32 (57)	104 (47)

2	22 (29)	13 (23)	43 (19)
3	5 (7)	3 (5)	21 (10)
Missing	0 (0)	0 (0)	0 (0)
LIPS-4			
0	20 (27)	10 (18)	39 (18)
1	22 (29)	18 (32)	92 (42)
2	15 (20)	19 (34)	46 (21)
3	14 (19)	8 (14)	34 (15)
4	3 (4)	1 (2)	8 (4)
Missing	1 (1)	0 (0)	2 (1)
Holtzman			
0	3 (4)	1 (2)	11 (5)
1	15 (20)	8 (14)	44 (20)
2	37 (49)	14 (25)	102 (46)
3	13 (17)	23 (41)	54 (25)
4	7 (9)	10 (18)	9 (4)
Missing	0 (0)	0 (0)	1 (0)
GPS			
0	13 (17)	18 (32)	23 (10)
1	35 (47)	26 (46)	72 (33)
2	24 (32)	12 (21)	79 (36)
Missing	3 (4)	0 (0)	47 (21)

Abbreviations: ALI — Advanced Lung Cancer Inflammation Index [1], CT — chemotherapy alone, EPSILoN [2], GPS — Glasgow Prognostic Score [3], GRIm — Gustave Roussy Immune Score [4], Holtzman — score described by Holtzman et. al [5], ICI — ICI in monotherapy, ICI+CT — ICI in combination with chemotherapy, LIPI — Lung Immune Prognostic Index [6], LIPS-3 — Lung Immuno-oncology Prognostic Score 3 [7], LIPS-4 — Lung Immuno-oncology Prognostic Score 4 [7], mLIPI — Modified Lung Immune Prognostic Index [8], n — number, P — percentile, PNI — Prognostic Nutritional Index [9], RMH — Royal Marsden Hospital Prognostic Score [10], SII — Systemic Immune-Inflammation Index, expressed in 10^9 cells/L [11], and SIPS — Scottish Inflammatory Prognostic Score [12].

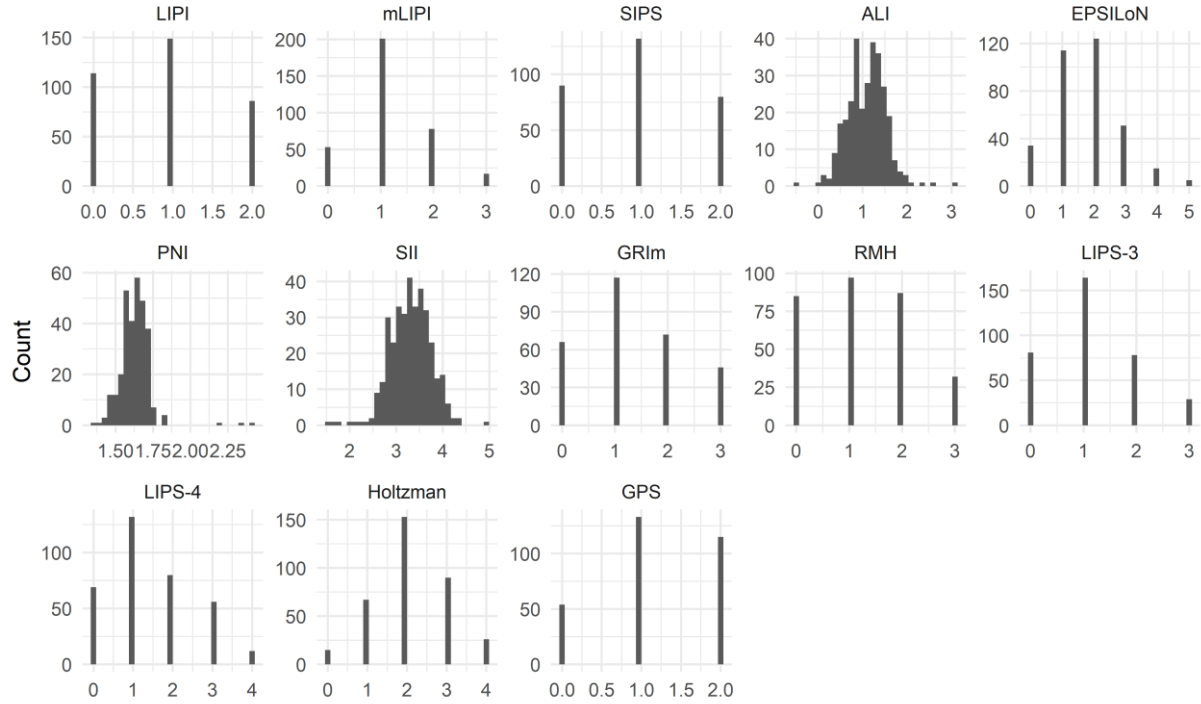


Figure S1. Distribution of the scores based on systemic inflammation/nutritional status. Continuous scores (ALI, PNI, and SII) were log-transformed in order to obtain a more symmetric distribution. Abbreviations: ALI — Advanced Lung cancer Inflammation Index [1], EPSILoN [2], GPS — Glasgow Prognostic Score [3], GRIm — Gustave Roussy Immune Score [4], Holtzman — score described by Holtzman et. al [5], LIPI — Lung Immune Prognostic Index [6], LIPS-3 — Lung Immuno-oncology Prognostic Score 3 [7], LIPS-4 — Lung Immuno-oncology Prognostic Score 4 [7], mLIPI — Modified Lung Immune Prognostic Index [8], PNI — Prognostic Nutritional Index [9], RMH — Royal Marsden Hospital Prognostic Score [10], SII — Systemic Immune-Inflammation Index [11], and SIPS — Scottish Inflammatory Prognostic Score [12].

Table S2. Sensitivity analysis for the concordance index (c-index) for overall survival and progression-free survival using dichotomized scores.

Scores	Imputation	Complete	Balanced	Non-squamous
LIPI				
OS	0.58	0.58	0.58	0.60
PFS	0.57	0.56	0.56	0.59
mLIPI				
OS	0.63	0.63	0.64	0.63
PFS	0.60	0.60	0.61	0.61
SIPS				
OS	0.59	0.60	0.59	0.60
PFS	0.57	0.58	0.57	0.58
ALI				
OS	0.60	0.60	0.59	0.60
PFS	0.57	0.57	0.56	0.57
EPSILoN				
OS	0.59	0.59	0.60	0.59
PFS	0.57	0.57	0.57	0.57
PNI				
OS	0.60	0.61	0.62	0.61
PFS	0.59	0.59	0.61	0.59
SII				
OS	0.57	0.57	0.58	0.58
PFS	0.54	0.54	0.55	0.55
GRIm				
OS	0.62	0.62	0.62	0.62
PFS	0.59	0.59	0.59	0.60
RMH				
OS	0.63	0.64	0.64	0.64
PFS	0.60	0.61	0.61	0.62
LIPS-3				
OS	0.62	0.62	0.64	0.62
PFS	0.59	0.59	0.60	0.59
LIPS-4				
OS	0.63	0.63	0.64	0.64
PFS	0.60	0.60	0.60	0.60
Holtzman				
OS	0.49	0.49	0.50	0.52
PFS	0.50	0.50	0.51	0.50
GPS				
OS	0.61	0.62	0.62	0.62
PFS	0.58	0.59	0.59	0.60

Abbreviations: ALI — Advanced Lung cancer Inflammation Index [1], Balanced — population with the three cohorts balanced in sample size (c-index and HR were the median value of 200 analyses on balanced data), Complete — population with complete data only (removing patients with missing data), EPSILoN [2], GPS — Glasgow Prognostic Score [3], GRIm — Gustave Roussy Immune Score [4], Holtzman — score described by Holtzman et. al [5], Imputation — whole population, including patients with missing scores imputed by the MICE algorithm [13] (main analysis), LIPI — Lung Immune Prognostic Index [6], LIPS-3 — Lung Immuno-oncology Prognostic Score 3 [7], LIPS-4 — Lung Immuno-oncology Prognostic Score 4 [7], mLIPI — Modified Lung Immune Prognostic Index [8], Non-squamous — patients with non-squamous NSCLC, OS — overall survival, PFS — progression-free survival, PNI — Prognostic Nutritional Index [9], RMH — Royal Marsden Hospital Prognostic Score [10], SII — Systemic Immune-Inflammation Index [11], and SIPS — Scottish Inflammatory Prognostic Score [12].

Table S3. Sensitivity analysis for the hazard ratio of the interactions for the difference between cohort 1 and cohort 2 for overall survival and progression-free survival.

Scores	Imputation	Complete	Balanced	Non-squamous
LIPI				
OS	0.98	0.98	0.98	0.82
PFS	0.72	0.71	0.69	0.74
mLIPI				
OS	0.61	0.62	0.62	0.43
PFS	0.60	0.60	0.59	0.53
SIPS				
OS	0.24	0.27	0.23	0.25
PFS	0.20	0.22	0.20	0.21
ALI				
OS	1.35	1.31	1.38	1.76
PFS	1.26	1.24	1.24	1.66
EPSILoN				
OS	1.31	1.31	1.27	1.65
PFS	1.02	1.01	0.94	1.34
PNI				
OS	1.21	1.13	1.22	1.12
PFS	1.07	1.03	1.09	1.28
SII				
OS	0.74	0.74	0.72	0.85
PFS	1.22	1.22	1.18	1.25
GRIIm				
OS	1.03	1.09	1.03	0.87
PFS	0.94	0.95	0.93	0.93
RMH				
OS	1.52	1.60	1.49	1.53
PFS	1.39	1.40	1.35	1.49
LIPS-3				
OS	0.46	0.46	0.46	0.28
PFS	0.42	0.42	0.41	0.30
LIPS-4				
OS	1.02	1.04	1.03	0.68
PFS	0.81	0.80	0.79	0.68
Holtzman				
OS	0.60	0.60	0.61	0.71
PFS	0.55	0.55	0.56	0.51
GPS				
OS	0.50	0.53	0.51	0.29
PFS	0.62	0.62	0.61	0.36

Abbreviations: ALI — Advanced Lung cancer Inflammation Index [1], Balanced — population with the three cohorts balanced in sample size (c-index and HR were the median value of 200 analyses on balanced data), Complete — population with complete data only (removing patients with missing data), EPSILoN [2], GPS — Glasgow Prognostic Score [3], GRIIm — Gustave Roussy Immune Score [4], Holtzman — score described by Holtzman et. al [5], Imputation — whole population, including patients with missing scores imputed by the MICE algorithm [13] (main analysis), LIPI — Lung Immune Prognostic Index [6], LIPS-3 — Lung Immunology Prognostic Score 3 [7], LIPS-4 — Lung Immunology Prognostic Score 4 [7], mLIPI — Modified Lung Immune Prognostic Index [8], Non-squamous — patients with non-squamous NSCLC, OS — overall survival, PFS — progression-free survival, PNI — Prognostic Nutritional Index [9], RMH — Royal Marsden Hospital Prognostic Score [10], SII — Systemic Immune-Inflammation Index [11], and SIPS — Scottish Inflammatory Prognostic Score [12].

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