

Table S1 ICD-10 codes for the Charlson comorbidity index

Disease	Score	ICD-10 codes
Myocardial infarction	1	I21; I22; I23; I25.2; I25.3
Congestive heart failure	1	I50; I11.0; I13.0; I13.2; I25.5
Peripheral vascular disease	1	I70-I74; I731; I738; I739; I77; I771; I790; I792; K551; K558; K559; Z958; Z959; R02; K55.003; K55.004; K55.010
Cerebrovascular disease	1	I60-I63; I65; I66; G450-G452; G458; G459; G46; I64; G454; I670; I671; I672; I674; I675; I676; I677; I678; I679; I681; I682; I688; I69; I60-I69; G45; G46
Dementia	1	F00; F01; F02; F03; F051; G30; G311
Chronic pulmonary disease	1	J40-J47; J67; J60-J66; I278; I279; J684; J701; J703; J84.1; J92.0; J96.1; J98.2; J98.3; J84.9
Connective tissue disease	1	M30-M36; M332; M331; M053; M058-M060; M063; M069; M050-M052; M353; M05; M06; M315; M351; M360; M08; M09; D86
Ulcer disease	1	K25-K28; K22.1
Mild liver disease	1	B18; K700-K703; K709; K713; K715; K717; K73; K74; K760; K762-K764; K768; K769; Z944; K71.0; K71.6; K71.9; K75; K76.103; B16.9; B19.9
Diabetes mellitus	1	E109-E111; E119; E139; E101; E131; E141; E135; E100; E11.600; E120; E121; E126; E128-E131; E136; E138-E141; E146; E148; E149; E11.701
Hemiplegia	2	G81; G041; G820-G822; G114; G801; G802; G82; G830; G831-G834; G839; G838
Moderate/severe renal disease	2	N03; N052; N053; N054; N055; N056; N072; N073; N074; N01; N18; N19; N25; I120; I131; N057; Z490; Z491; Z492; Z940; Z992/I12; I13; N00-N05; N07; N11; N14; N17; Q61
Diabetes mellitus with chronic complications	2	E102; E112; E132; E142; E103; E113; E133; E143; E104; E114; E134; E144; E105; E107; E115; E122-E125; E127; E135; E137; E145; E147; E10.6; E10.8; E11.601; E11.8; E11.6; E14.5
Any tumor	2	C00-C76
Leukemia	2	C91-C95; C91.001; C95.902
Lymphoma	2	C81-C85; C88; C90; C96
Moderate/severe liver disease	3	K729; K76-K767; K721; I850; I859; I864; I982; K704; K711; B15.0; B15.9; B16.0; B16.2; B19.0; K72; I85; Z944
Metastatic solid tumor	6	C77-C80
AIDS	6	B20; B21; B22; B23; B24

ICD-10, 10th revision of the International Statistical Classification of Diseases and Related Health Problems; AIDS, acquired immune deficiency syndrome.

Table S2 Risk factors associated with all-cause mortality (including smoking history)

Variables	Overall survival			P value
	Adjusted HR	95% CI		
		Low	High	
ICI use	0.80	0.74	0.85	<0.0001
Age (years)				
<40	Ref.	-	-	
40-49	0.82	0.54	1.25	0.350
50-59	1.03	0.69	1.52	0.898
60-69	1.18	0.80	1.74	0.410
≥70	1.39	0.94	2.06	0.099
Sex				
Male	1.30	1.16	1.44	<0.0001
Female	Ref.	-	-	
Income level				
Medical-aid	1.15	0.94	1.41	0.165
1Q	1.08	0.98	1.18	0.115
2Q	1.11	1.01	1.21	0.031
3Q	1.10	1.01	1.20	0.025
4Q (richest)	Ref.	-	-	
Type of hospital				
Secondary hospital	1.03	0.96	1.10	0.452
Tertiary hospital	Ref.	-	-	
Comorbidity				
Hypertension	0.97	0.91	1.05	0.469
Diabetes	1.03	0.97	1.11	0.339
COPD	1.05	0.97	1.14	0.205
CKD	1.09	0.87	1.38	0.452
CHF	0.99	0.90	1.10	0.876
CVD	1.03	0.95	1.12	0.428
CCI				
6	1.00	-	-	
7	0.99	0.83	1.18	0.929
≥8	0.95	0.81	1.11	0.530
Cancer stage				
Stage IIIB	Ref.	-	-	
Stage IV	1.22	1.04	1.43	0.016
Brain mvetastasis	0.99	0.75	1.32	0.964
Smoking status				
Never-smoker	Ref.	-	-	
Ex-smoker (<10 pack-year)	0.91	0.77	1.08	0.263
Ex-smoker (≥10 pack-year)	1.07	0.97	1.18	0.180
Current smoker (<10 pack-year)	1.06	0.89	1.27	0.489
Current smoker (≥10 pack-year)	1.07	0.97	1.17	0.184

HR, hazard ratio; CI, confidence interval; ICI, immune-check point inhibitor; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CHF, congestive heart failure; CVD, cerebrovascular disease; CCI, Charlson comorbidity index; 1Q, first quintile; 2Q, second quintile; 3Q, third quintile; 4Q, fourth quintile (richest).

Table S3 Risk factors associated with disease progression (including smoking history)

Variables	Disease progression			P value
	Adjusted HR	95% CI		
		Low	High	
ICI use	0.93	0.85	1.02	0.127
Age (years)				
<40	Ref.	-	-	-
40-49	1.09	0.66	1.79	0.736
50-59	1.07	0.66	1.72	0.790
60-69	0.98	0.61	1.56	0.916
≥70	0.79	0.49	1.28	0.339
Sex				
Male	1.09	0.94	1.25	0.250
Female	Ref.	-	-	
Income level				
Medical-aid	1.47	1.13	1.91	0.004
1Q	0.99	0.88	1.13	0.924
2Q	1.08	0.96	1.22	0.203
3Q	1.00	0.90	1.12	0.955
4Q (richest)	Ref.	-	-	
Type of hospital				
Secondary hospital	1.01	0.92	1.10	0.894
Tertiary hospital	Ref.	-	-	
Comorbidity				
Hypertension	1.01	0.92	1.11	0.816
Diabetes	0.99	0.91	1.09	0.899
COPD	0.91	0.81	1.01	0.087
CKD	0.82	0.57	1.18	0.284
CHF	0.90	0.78	1.04	0.139
CVD	1.02	0.91	1.15	0.730
CCI				
6	Ref.	-	-	
7	1.09	0.87	1.36	0.454
≥8	0.98	0.81	1.20	0.867
Cancer stage				
Stage IIIB	Ref.	-	-	
Stage IV	0.84	0.70	1.02	0.071
Brain metastasis	0.83	0.56	1.22	0.332
Smoking status				
Never-smoker	Ref.	-	-	-
Ex-smoker (<10 pack-year)	0.97	0.78	1.21	0.779
Ex-smoker (≥10 pack-year)	0.97	0.84	1.11	0.662
Current smoker (<10 pack-year)	0.94	0.75	1.18	0.575
Current smoker (≥10 pack-year)	0.95	0.84	1.09	0.482

HR, hazard ratio; CI, confidence interval; ICI, immune-check point inhibitor; 1Q, first quintile; 2Q, second quintile; 3Q, third quintile; 4Q, fourth quintile (richest); COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CHF, congestive heart failure; CVD, cerebrovascular disease; CCI, Charlson comorbidity index.

Table S4 Baseline characteristics of the total study population (grouped by specific drugs)

Variables	Total (N=7,297)	Non-ICI therapy		ICI therapy		P value
		Targeted therapy (N=1,147)	Cytotoxic chemotherapy (N=3,665)	Nivolumab (N=961)	Pembrolizumab (N=1,524)	
Age (mean ± SD)		64.8±10.9	65.2±9.1	67.4±9.2	66.4±9.6	<0.0001
<40	83 (1.1)	26 (2.2)	37 (1.0)	4 (0.4)	16 (1.0)	<0.0001
40-49	338 (4.6)	84 (7.3)	156 (4.2)	30 (3.1)	68 (4.4)	
50-59	1,346 (18.4)	234 (20.4)	712 (19.4)	148 (15.4)	252 (16.5)	
60-69	2,789 (38.2)	366 (31.9)	1,515 (41.3)	345 (35.9)	563 (36.9)	
≥ 70	2,741 (37.6)	437 (38.1)	1,245 (33.9)	434 (45.1)	625 (41.0)	
Sex						
Men	5,931 (81.3)	718 (62.6)	3,109 (84.8)	808 (84.0)	1,296 (85.0)	0.857
Women	1,366 (18.7)	429 (37.4)	556 (15.1)	153 (15.9)	228 (14.9)	
Income level						
Medical-aid	394 (5.4)	60 (5.2)	193 (5.2)	63 (6.5)	78 (5.1)	0.118
1Q	1,340 (18.4)	224 (19.5)	667 (18.2)	173 (18.2)	276 (18.1)	
2Q	1,447 (19.8)	218 (19.0)	750 (20.4)	192 (19.9)	287 (18.8)	
3Q	1,819 (24.9)	284 (24.7)	917 (25.0)	230 (23.9)	388 (25.4)	
4Q (richest)	2,297 (31.5)	361 (31.4)	1,138 (31.0)	303 (31.5)	495 (32.4)	
Level of care						
Secondary hospital	2,388 (32.7)	391 (34.0)	1,156 (31.5)	313 (32.5)	528 (34.6)	0.118
Tertiary hospital	4,909 (67.3)	756 (65.9)	2,509 (68.4)	648 (67.4)	996 (65.3)	
Comorbidity						
Hypertension	3,910 (53.5)	589 (51.3)	1,977 (53.9)	533 (55.4)	811 (53.2)	0.268
Diabetes	3,139 (43.0)	445 (38.8)	1,593 (43.4)	428 (44.5)	673 (44.1)	0.015
COPD	1,553 (21.2)	177 (15.4)	842 (22.9)	229 (23.8)	305 (20.0)	<0.0001
CKD	153 (2.0)	19 (1.6)	67 (1.8)	25 (2.6)	42 (2.7)	0.078
CHF	870 (11.9)	116 (10.1)	436 (11.9)	126 (13.1)	192 (12.6)	0.136
CVD	1,337 (18.3)	192 (16.7)	681 (18.5)	197 (20.5)	267 (17.5)	0.122
CCI						
6	449 (6.1)	96 (8.3)	199 (5.4)	51 (5.3)	103 (6.7)	<0.0001
7	783 (10.7)	147 (12.8)	367 (10.0)	100 (10.4)	169 (11.0)	
≥8	6,065 (83.1)	904 (78.8)	3,099 (84.5)	810 (84.2)	1,252 (82.1)	
Cancer stage						
Stage IIIB	295 (4.0)	33 (2.8)	218 (5.9)	16 (1.6)	28 (1.8)	<0.0001
Stage IV	7,002 (95.9)	1,114 (97.1)	3,447 (94.0)	945 (98.3)	1,496 (98.1)	
Brain metastasis	106 (1.4)	15 (1.3)	53 (1.4)	11 (1.1)	27 (1.7)	0.595

ICI, immune-check point inhibitor; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CHF, congestive heart failure; CVD, cerebrovascular disease; CCI, Charlson comorbidity index; 1Q, first quintile; 2Q, second quintile; 3Q, third quintile; 4Q, fourth quintile (richest).

Table S5 Risk factors associated with all-cause mortality (grouped by specific drugs)

Variables	Overall survival			P-value
	Adjusted OR	95% CI		
		Low	High	
Type of chemotherapeutics				
Cytotoxic chemotherapy	Ref.	-	-	
Targeted therapy	0.78	0.73	0.85	<0.0001
Nivolumab	0.84	0.78	0.91	<0.0001
Pembrolizumab	0.70	0.65	0.75	<0.0001
Age (years)				
<40	Ref.	-	-	
40-49	0.95	0.73	1.25	0.740
50-59	1.07	0.83	1.37	0.572
60-69	1.23	0.96	1.57	0.098
≥70	1.42	1.11	1.82	0.004
Sex				
Men	1.22	1.14	1.307	<0.0001
Women	Ref.	-	-	
Income level				
Medical-aid	1.10	0.98	1.24	0.085
1Q	1.07	0.99	1.15	0.073
2Q	1.04	0.96	1.12	0.279
3Q	1.04	0.97	1.11	0.193
4Q (richest)	Ref.	-	-	
Type of hospital				
Secondary hospital	1.01	0.96	1.07	0.583
Tertiary hospital	Ref.	-	-	
Comorbidity				
Hypertension	1.01	0.96	1.07	0.580
Diabetes	1.03	0.97	1.08	0.305
COPD	1.01	0.95	1.08	0.639
CKD	1.16	0.97	1.38	0.086
CHF	1.00	0.92	1.08	0.911
CVD	1.00	0.94	1.07	0.807
CCI				
6	Ref.	-	-	
7	0.98	0.86	1.11	0.765
≥8	0.97	0.86	1.08	0.615
Cancer stage				
Stage IIIB	Ref.	-	-	
Stage IV	1.30	1.14	1.48	<0.0001
Brain metastasis	0.96	0.77	1.19	0.727

COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CHF, congestive heart failure; CVD, cerebrovascular disease; CCI, Charlson comorbidity index; 1Q, first quintile; 2Q, second quintile; 3Q, third quintile; 4Q, fourth quintile (richest).

Table S6 Risk factors associated with disease progression (grouped by specific drugs)

Variables	Disease progression			P-value
	Adjusted OR	95% CI		
		Low	High	
Type of chemotherapeutics				
Cytotoxic chemotherapy	Ref.	-	-	
Targeted therapy	0.81	0.73	0.89	<0.0001
Nivolumab	0.99	0.89	1.10	0.926
Pembrolizumab	0.81	0.74	0.89	<0.0001
Age (years)				
<40	Ref.	-	-	
40-49	1.01	0.74	1.38	0.914
50-59	0.98	0.73	1.30	0.891
60-69	0.88	0.66	1.17	0.393
≥70	0.72	0.54	0.96	0.029
Sex				
Men	0.97	0.89	1.06	0.601
Women	Ref.	-	-	
Income level				
Medical-aid	1.04	0.87	1.23	0.650
1Q	1.00	0.90	1.10	0.975
2Q	1.05	0.95	1.16	0.263
3Q	1.01	0.92	1.10	0.826
4Q (richest)	Ref.	-	-	
Type of hospital				
Secondary hospital	0.96	0.89	1.03	0.353
Tertiary hospital	1.00	-	-	
Comorbidity				
Hypertension	1.04	0.96	1.12	0.260
Diabetes	0.96	0.88	1.03	0.306
COPD	0.89	0.81	0.97	0.015
CKD	0.95	0.72	1.24	0.715
CHF	0.95	0.85	1.07	0.442
CVD	0.95	0.86	1.04	0.313
CCI				
6	Ref.	-	-	
7	0.98	0.83	1.15	0.832
≥8	0.93	0.80	1.07	0.315
Cancer stage				
Stage IIIB	1.00	-	-	
Stage IV	0.85	0.73	0.99	0.036
Brain metastasis	0.89	0.67	1.18	0.434

COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CHF, congestive heart failure; CVD, cerebrovascular disease; CCI, Charlson comorbidity index; 1Q, first quintile; 2Q, second quintile; 3Q, third quintile; 4Q, fourth quintile (richest)