Supplementary material

Supplementary Table 1. Summary of pre-treatment patients' characteristics in the atezolizumab treated cohort of IMvigor211

	Total No. 459
Actual treatment given: Atezolizumab	459 (100%)
Age (years)	67 (59 - 73)
Sex	
Male	351 (76%)
Female	108 (24%)
Race	
White	329 (72%)
Asian	63 (14%)
Other	1 (<1%)
Missing	66 (14%)
Smoking history	
Never	139 (30%)
Previous	262 (57%)
Current	57 (12%)
Missing	1 (<1%)
Primary site	
Bladder	319 (69%)
Other	8 (2%)
Renal pelvis	64 (14%)
Ureter	59 (13%)
Urethra	9 (2%)
Disease Status	
Locally advanced	42 (9%)
Metastatic Disease	417 (91%)
Count of tumour sites	2 (1 - 3)
Bone metastasis	109 (24%)
Liver metastasis	136 (30%)
Lung metastasis	181 (39%)
Visceral metastasis	354 (77%)
Disease Status	
Locally advanced	42 (9%)
Metastatic Disease	417 (91%)
ECOG PS Score	

0	216 (47%)
1	243 (53%)
Hemoglobin (g/dL)	
<10	54 (12%)
≥10	397 (86%)
Missing	8 (2%)
Number of prior systemic therapies in advanced setting	
<1	129 (28%)
≥1	330 (72%)
Time of diagnosis in Months	
<12	97 (21%)
≥12	359 (78%)
Missing	3 (1%)
PD-L1 tumor-infiltrating immune cell expression level	
0	147 (32%)
1	198 (43%)
2	114 (25%)
Lactate Dehydrogenase (U/L)	
Median (IQR)	221 (177 - 330)
Missing	29 (6%)
Neutrophil to lymphocyte ratio (10^9/L)	
Median (IQR)	3.5 (2.5 - 5.5)
Missing	13 (2.8%)
Data are median (IQR) or number of patients (%).	

Supplementary Table 2. Summary of pre-treatment patient-reported outcome values in the atezolizumab treated cohort of IMvigor211

	Total No. 459
Global Health Status	
Low	91 (20%)
Intermediate	190 (41%)
High	158 (34%)
Missing	20 (4%)
Physical Function	
Low	152 (33%)
Intermediate	170 (37%)
High	119 (26%)
Missing	18 (4%)
Role Function	
Low	33 (7%)
High	408 (89%)
Missing	18 (4%)
Emotional Function	
Low	34 (7%)
Intermediate	310 (68%)
High	97 (21%)
Missing	18 (4%)
Cognitive Function	
Intermediate	110 (24%)
High	331 (72%)
Missing	18 (4%)
Social Function	
Low	48 (10%)
High	393 (86%)
Missing	18 (4%)
Fatigue	
Low	112 (24%)
Intermediate	295 (64%)
High	34 (7%)
Missing	18 (4%)
Nausea and Vomiting	

Low	390 (85%)
High	51 (11%)
Missing	18 (4%)
Pain	
Low	298 (65%)
High	143 (31%)
Missing	18 (4%)
Dyspnoea	
Low	259 (56%)
Intermediate	181 (39%)
Missing	19 (4%)
Insomnia	
Low	423 (92%)
High	17 (4%)
Missing	19 (4%)
Appetite loss	
Low/Intermediate	414 (90%)
High	26 (6%)
Missing	19 (4%)
Constipation	
Low	241 (53%)
High	198 (43%)
Missing	20 (4%)
Financial difficulties	
Low	309 (67%)
Intermediate	131 (29%)
Missing	19 (4%)
Data are median (IQR) or number of patients (%).	

Supplementary Table 3. Univariable and adjusted association between PROs and PFS for patients treated with atezolizumab

	Univariable					Adjusted**			
	n	HR*	95% CI	P-value	c	n	HR*	95% CI	P-value
Physical function	441	0.89	0.85 to 0.93	<0.001	0.57	345	0.89	0.83 to 0.94	<0.001
Pain	441	1.09	1.06 to 1.13	<0.001	0.58	345	1.07	1.02 to 1.12	0.003
Appetite	440	1.07	1.03 to 1.10	<0.001	0.56	345	1.08	1.03 to 1.13	<0.001
Global health	439	0.88	0.84 to 0.92	<0.001	0.58	344	0.88	0.83 to 0.93	<0.001
Fatigue	441	1.10	1.06 to 1.15	<0.001	0.58	345	1.10	1.04 to 1.16	<0.001

CI=confidence interval, HR=hazard ratio.

Supplementary Table 4. Univariable and adjusted association between PROs and objective response for patients treated with atezolizumab

	Univariable					Adjusted**			
	n	OR*	95% CI	P-value	c	n	OR*	95% CI	P-value
Physical function	441	1.17	1.02 to 1.34	0.026	0.59	345	1.07	0.89 to 1.29	0.463
Pain	441	0.83	0.75 to 0.93	<0.001	0.63	345	0.96	0.84 to 1.10	0.528
Appetite	440	0.89	0.80 to 0.98	0.020	0.59	345	0.96	0.84 to 1.09	0.501
Global health	439	1.32	1.16 to 1.51	<0.001	0.66	344	1.29	1.08 to 1.53	0.005
Fatigue	441	0.87	0.77 to 0.97	0.014	0.60	345	0.93	0.80 to 1.09	0.363

CI=confidence interval, HR=hazard ratio.
*HR based on 10-unit increase
**Adjusted for haemoglobin, sex, age, race, smoking history, ECOG performance status, disease status, PD-L1 tumor-infiltrating immune cell expression level, time since diagnosis, number of prior systemic therapies in advanced setting, liver metastasis, bone metastasis, lung metastasis, lactate dehydrogenase and neutrophil to lymphocyte ratio. A total of 120 patients had missing data in the adjustment variables.

Supplementary Table 5. Univariable and adjusted association between PROs and grade ≥ 3 adverse effects for patients treated with atezolizumab

	Univariable					Adjusted**			
	n	HR*	95% CI	P-value	c	n	HR*	95% CI	P-value
Physical function	441	0.93	0.88 to 0.98	0.014	0.56	345	1.03	0.95 to 1.12	0.459
Pain	441	1.08	1.04 to 1.13	<0.001	0.57	345	1.03	0.97 to 1.09	0.391
Appetite	440	1.10	1.06 to 1.15	<0.001	0.57	345	1.06	1.00 to 1.12	0.053
Global health	439	0.95	0.89 to 1.00	0.061	0.54	344	1.00	0.93 to 1.09	0.947
Fatigue	441	1.08	1.03 to 1.14	0.002	0.55	345	1.04	0.97 to 1.11	0.304

CI=confidence interval, HR=hazard ratio.
*HR based on 10-unit increase.
**Adjusted for haemoglobin, sex, age, race, smoking history, ECOG performance status, disease status, PD-L1 tumor-infiltrating immune cell expression level, time since diagnosis, number of prior systemic therapies in advanced setting, liver metastasis, bone metastasis, lung metastasis, lactate dehydrogenase and neutrophil to lymphocyte ratio. A total of 120 patients had missing data in the adjustment variables.

Supplementary Table 6. Univariable and adjusted association between PROs and overall survival for patients treated with chemotherapy

	Univariable					Adjusted**			
	n	HR*	95% CI	P-value	c	n	HR*	95% CI	P-value

	n	HR*	95% CI	P-value	c	n	HR*	95% CI	P-value
Physical function	421	0.87	0.83 to 0.90	<0.001	0.62	322	0.92	0.87 to 0.97	0.002
Pain	421	1.13	1.09 to 1.16	<0.001	0.63	322	1.10	1.05 to 1.15	<0.001
Appetite	421	1.10	1.07 to 1.14	<0.001	0.59	322	1.06	1.02 to 1.11	0.007
Global health	420	0.86	0.82 to 0.90	<0.001	0.61	322	0.89	0.84 to 0.95	<0.001
Fatigue	421	1.17	1.13 to 1.22	<0.001	0.63	322	1.12	1.07 to 1.18	<0.001

CI=confidence interval, HR=hazard ratio.
*HR based on 10-unit increase
**Adjusted for haemoglobin, sex, age, race, smoking history, ECOG performance status, disease status, PD-L1 tumor-infiltrating immune cell expression level, time since diagnosis, number of prior systemic therapies in advanced setting, liver metastasis, bone metastasis, lung metastasis, lactate dehydrogenase and neutrophil to lymphocyte ratio. A total of 120 patients had missing data in the adjustment variables.

Supplementary Table 7. Univariable and adjusted association between PROs and PFS for patients treated with chemotherapy

	Univariable					Adjusted**			
	n	HR*	95% CI	P-value	c	n	HR*	95% CI	P-value
Physical function	421	0.92	0.89 to 0.96	<0.001	0.59	322	0.95	0.90 to 1.00	0.056
Pain	421	1.09	1.06 to 1.12	<0.001	0.61	322	1.06	1.02 to 1.10	0.005
Appetite	421	1.06	1.03 to 1.10	<0.001	0.56	322	1.04	1.00 to 1.09	0.036
Global health	420	0.91	0.87 to 0.95	<0.001	0.57	322	0.93	0.88 to 0.99	0.026
Fatigue	421	1.11	1.07 to 1.15	<0.001	0.6	322	1.07	1.03 to 1.13	0.003

CI=confidence interval, HR=hazard ratio.
*HR based on 10-unit increase
**Adjusted for haemoglobin, sex, age, race, smoking history, ECOG performance status, disease status, PD-L1 tumor-infiltrating immune cell expression level, time since diagnosis, number of prior systemic therapies in advanced setting, liver metastasis, bone metastasis, lung metastasis, lactate dehydrogenase and neutrophil to lymphocyte ratio. A total of 120 patients had missing data in the adjustment variables.

Supplementary Table 8. Summary of patient characteristics by patient-reported physical function in the atezolizumab treated cohort of IMvigor211

	Total No. 441	Low No. 152	Intermediate No. 170	High No. 119	P-value
Age (years)	67 (59 - 73)	68 (59 - 74)	67 (59 - 72)	66 (60 - 71)	0.23
Sex					0.23
Male	335 (76%)	109 (72%)	130 (76%)	96 (81%)	
Female	106 (24%)	43 (28%)	40 (24%)	23 (19%)	
Race					0.65
White	314 (71%)	113 (74%)	115 (68%)	86 (72%)	
Asian	63 (14%)	25 (16%)	24 (14%)	14 (12%)	
Other	1 (<1%)	0 (0%)	1 (1%)	0 (0%)	
Missing	63 (14%)	14 (9%)	30 (18%)	19 (16%)	
Smoking history					0.070
Never	133 (30%)	45 (30%)	53 (31%)	35 (29%)	
Previous	253 (57%)	79 (52%)	100 (59%)	74 (62%)	
Current	54 (12%)	28 (18%)	16 (9%)	10 (8%)	
Missing	1 (<1%)	0 (0%)	1 (1%)	0 (0%)	
Primary site					0.53
Bladder	304 (69%)	103 (68%)	113 (66%)	88 (74%)	
Other	8 (2%)	4 (3%)	2 (1%)	2 (2%)	
Renal pelvis	63 (14%)	25 (16%)	26 (15%)	12 (10%)	
Ureter	57 (13%)	19 (12%)	23 (14%)	15 (13%)	
Urethra	9 (2%)	1 (1%)	6 (4%)	2 (2%)	
Disease Status					0.63
Locally advanced	39 (9%)	15 (10%)	16 (9%)	8 (7%)	
Metastatic Disease	402 (91%)	137 (90%)	154 (91%)	111 (93%)	
Count of tumour sites	2 (1 - 3)	2 (1 - 3)	2 (1 - 3)	2 (1 - 2)	< 0.001
Bone metastasis	105 (24%)	47 (31%)	39 (23%)	19 (16%)	0.015
Liver metastasis	130 (29%)	52 (34%)	46 (27%)	32 (27%)	0.29
Lung metastasis	173 (39%)	56 (37%)	74 (44%)	43 (36%)	0.34

Visceral metastasis	340 (77%)	123 (81%)	131 (77%)	86 (72%)	0.24
Disease Status					0.63
Locally advanced	39 (9%)	15 (10%)	16 (9%)	8 (7%)	
Metastatic Disease	402 (91%)	137 (90%)	154 (91%)	111 (93%)	
ECOG performance status					< 0.001
0	207 (47%)	38 (25%)	91 (54%)	78 (66%)	
1	234 (53%)	114 (75%)	79 (46%)	41 (34%)	
Hemoglobin (g/dL)					0.001
<10	53 (12%)	27 (18%)	22 (13%)	4 (3%)	
≥10	381 (86%)	122 (80%)	145 (85%)	114 (96%)	
Missing	7 (2%)	3 (2%)	3 (2%)	1 (1%)	
Number of prior systemic therapies in advanced setting					0.70
<1	122 (28%)	39 (26%)	47 (28%)	36 (30%)	
≥1	319 (72%)	113 (74%)	123 (72%)	83 (70%)	
Time since diagnosis (months)					0.39
<12	93 (21%)	35 (23%)	38 (22%)	20 (17%)	
≥12	346 (78%)	116 (76%)	131 (77%)	99 (83%)	
Missing	2 (<1%)	1 (1%)	1 (1%)	0 (0%)	
PD-L1 tumor-infiltrating immune cell expression level					0.72
0	142 (32%)	49 (32%)	58 (34%)	35 (29%)	
1	189 (43%)	67 (44%)	70 (41%)	52 (44%)	
2	110 (25%)	36 (24%)	42 (25%)	32 (27%)	
Lactate Dehydrogenase (U/L)					0.16
Median (IQR)	222 (179 - 330)	231 (186 - 366)	221 (176 - 316)	214 (174 - 304)	
Missing	27 (6%)	10 (7%)	12 (7%)	5 (4%)	
Neutrophil to lymphocyte ratio					< 0.001
Median (IQR)	3.5 (2.5 - 5.5)	4.5 (3.1 - 6.8)	3.3 (2.4 - 4.7)	3.0 (2.2 - 4.5)	
Missing	12 (2.7%)	3 (2.0%)	5 (2.9%)	4 (3.4%)	

Data are median (IQR) or number of patients (%). P values per Chi-Square test for categorical data and Kruskal-Wallis test for continuous data.

Supplementary Table 9. Univariable and multivariable association between patient-reported physical function and ECOG-PS with overall survival for chemotherapy patient cohort within IMvigor211

	Univariable					Multivariable model**			
	n	HR*	95% CI	P-value	c	n	HR*	95% CI	P-value
Physical function status				<0.001	0.60				<0.001
High	120	1.00					1.00		
Intermediate	169	1.57	1.17 to 2.12				1.40	1.02 to 1.91	
Low	132	2.34	1.77 to 3.09				2.04	1.51 to 2.75	
ECOG PS Score				<0.001	0.56				0.019
0	197	1.00					1.00		
1	246	1.70	1.36 to 2.11				1.34	1.05 to 1.71	

CI=confidence interval, HR=hazard ratio.
*HR based on 10-unit increase
**Multivariable model testing if there is independent information from both patient reported physical function and ECOG PS.
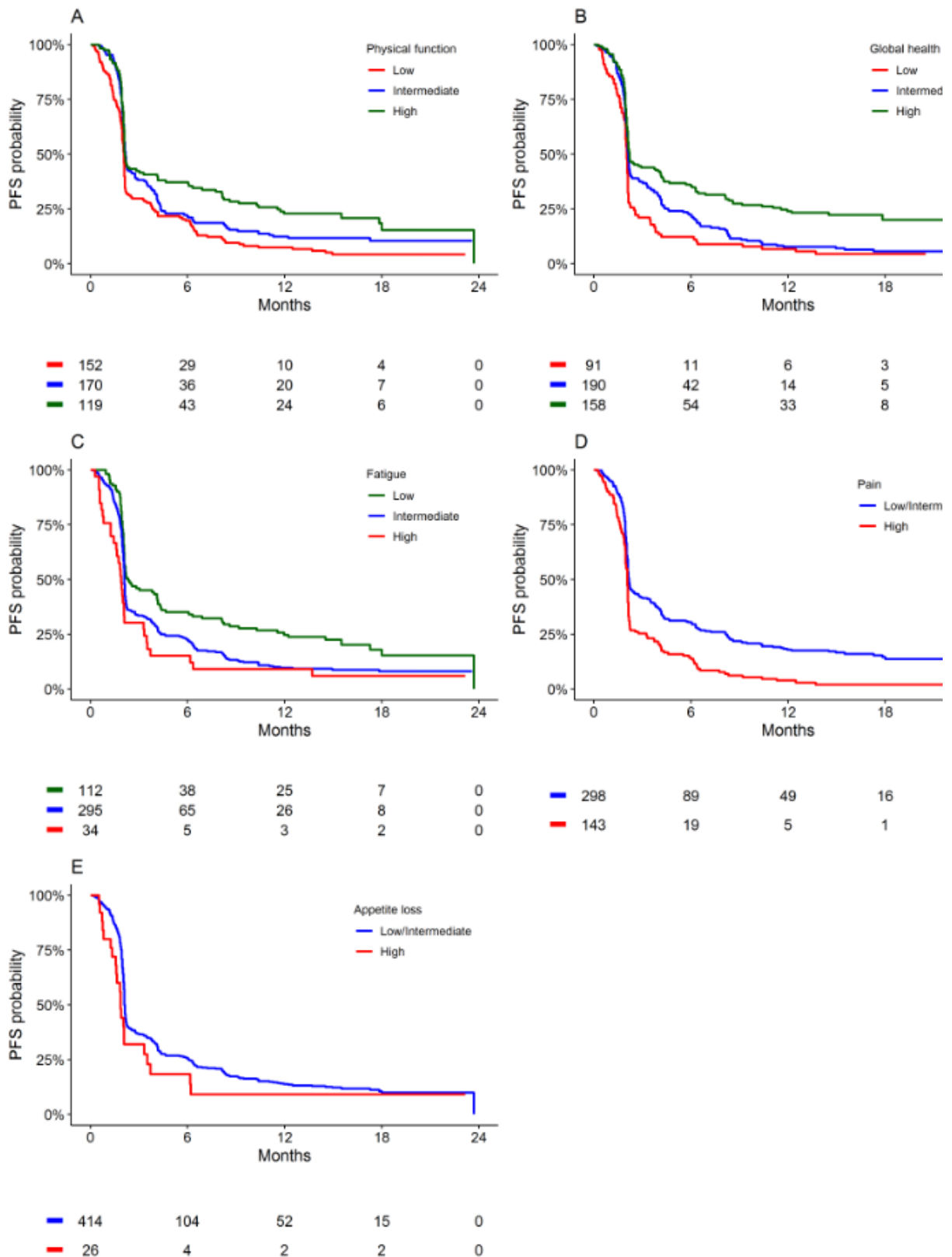
Supplementary Figure 1. Kaplan-Meier estimates of progression free survival (PFS) by patient-reported physical function, fatigue, appetite, global health, and pain symptoms for patients treated with atezolizumab.