

Table S1 Summary of patient characteristics by treatment arm

	Total	Atezolizumab + Bevacizumab + Carboplatin + Paclitaxel	Atezolizumab + Carboplatin + Nab-Paclitaxel	Atezolizumab + Carboplatin + Paclitaxel	Bevacizumab + Carboplatin + Paclitaxel	Carboplatin + Nab-Paclitaxel	P value
	No. 2,892	No. 393	No. 807	No. 732	No. 394	No. 566	
Actual treatment included atezolizumab	1,932 (67%)	393 (100%)	807 (100%)	732 (100%)	0 (0%)	0 (0%)	< 0.001
STUDY							< 0.001
Mpower130	705 (24%)	0 (0%)	473 (59%)	0 (0%)	0 (0%)	232 (41%)	
IMpower131	1,000 (35%)	0 (0%)	334 (41%)	332 (45%)	0 (0%)	334 (59%)	
IMpower150	1,187 (41%)	393 (100%)	0 (0%)	400 (55%)	394 (100%)	0 (0%)	
Age (years)	64 (58–70)	63 (57–70)	64 (58–70)	64 (58–70)	63 (57–69)	65 (58–71)	0.043
Sex							< 0.001
Male	1,929 (67%)	239 (61%)	540 (67%)	511 (70%)	233 (59%)	406 (72%)	
Female	963 (33%)	154 (39%)	267 (33%)	221 (30%)	161 (41%)	160 (28%)	
Race							0.001
White	2,460 (85%)	316 (80%)	699 (87%)	617 (84%)	329 (84%)	499 (88%)	
Asian	276 (10%)	55 (14%)	55 (7%)	80 (11%)	46 (12%)	40 (7%)	
Other	89 (3%)	9 (2%)	30 (4%)	20 (3%)	13 (3%)	17 (3%)	
Missing	67 (2%)	13 (3%)	23 (3%)	15 (2%)	6 (2%)	10 (2%)	
ECOG PS							0.062
0	1,140 (39%)	158 (40%)	316 (39%)	287 (39%)	177 (45%)	202 (36%)	
1	1,743 (60%)	232 (59%)	489 (61%)	445 (61%)	214 (54%)	363 (64%)	
Missing	9 (<1%)	3 (1%)	2 (<1%)	0 (0%)	3 (1%)	1 (<1%)	
Smoking history							< 0.001
Never	401 (14%)	80 (20%)	96 (12%)	107 (15%)	76 (19%)	42 (7%)	
Previous	1,768 (61%)	224 (57%)	514 (64%)	432 (59%)	229 (58%)	369 (65%)	
Current	723 (25%)	89 (23%)	197 (24%)	193 (26%)	89 (23%)	155 (27%)	
Histology							< 0.001
Non-squamous	1,893 (65%)	393 (100%)	473 (59%)	401 (55%)	394 (100%)	232 (41%)	
Squamous	999 (35%)	0 (0%)	334 (41%)	331 (45%)	0 (0%)	334 (59%)	
Liver tumor site at baseline	417 (14%)	49 (12%)	124 (15%)	105 (14%)	55 (14%)	84 (15%)	0.74
PD-L1 highest of TC and IC expression level (official)							0.86
0	1,418 (49%)	187 (48%)	401 (50%)	346 (47%)	196 (50%)	288 (51%)	
1	502 (17%)	68 (17%)	127 (16%)	148 (20%)	67 (17%)	92 (16%)	
2	470 (16%)	64 (16%)	135 (17%)	116 (16%)	59 (15%)	96 (17%)	
3	499 (17%)	74 (19%)	143 (18%)	120 (16%)	72 (18%)	90 (16%)	
Missing	3 (<1%)	0 (0%)	1 (<1%)	2 (<1%)	0 (0%)	0 (0%)	
Comorbidity count	7 (4–11)	6 (4–11)	8 (5–12)	6 (4–10)	6 (4–10)	7 (4–11)	< 0.001

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

Table S2 Summary of pre-treatment patient-reported outcome values by treatment arm

	Reference Value*	Atezolizumab + Bevacizumab + Carboplatin + Paclitaxel	Atezolizumab + Carboplatin + Nab-Paclitaxel	Atezolizumab + Carboplatin + Paclitaxel	Bevacizumab + Carboplatin + Paclitaxel	Carboplatin + Nab-Paclitaxel	P-value
	No. 1,313	No. 393	No. 807	No. 732	No. 394	No. 566	
Global Health Status							0.058
Median (IQR)	58.3 (41.7–66.7)	67 (50–83)	62 (50–75)	67 (50–83)	67 (50–83)	58 (50–75)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Physical Function							0.14
Median (IQR)	73.3 (46.7–86.7)	80 (60–93)	80 (60–88)	80 (60–93)	80 (60–93)	80 (60–88)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Role Function							0.18
Median (IQR)	66.7 (33.3–83.3)	67 (50–100)	67 (33–100)	67 (50–100)	67 (50–100)	67 (50–100)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Emotional Function							0.064
Median (IQR)	66.7 (50–83.3)	75 (58–92)	75 (58–92)	75 (67–92)	75 (58–83)	75 (58–92)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Cognitive Function							0.18
Median (IQR)	83.3 (66.7–100)	83 (67–100)	100 (67–100)	100 (67–100)	83 (67–100)	100 (67–100)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Social Function							0.48
Median (IQR)	66.7 (50–100)	83 (67–100)	83 (67–100)	83 (67–100)	83 (67–100)	83 (67–100)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Fatigue							0.053
Median (IQR)	44.4 (22.2–66.7)	33 (22–56)	33 (22–56)	33 (22–56)	33 (22–44)	33 (22–56)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Nausea and Vomiting							0.62
Median (IQR)	0 (0–16.7)	0 (0–0)	0 (0–17)	0 (0–0)	0 (0–17)	0 (0–0)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Pain							0.84
Median (IQR)	33.3 (0–66.7)	17 (0–50)	17 (0–50)	17 (0–50)	33 (0–50)	33 (0–50)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Dyspnoea							0.021
Median (IQR)	33.3 (0–66.7)	33 (0–33)	33 (0–67)	33 (0–67)	33 (0–67)	33 (0–67)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Insomnia							0.1
Median (IQR)	33.3 (0–66.7)	33 (0–67)	33 (0–67)	33 (0–33)	33 (0–67)	33 (0–67)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Appetite Loss							0.29
Median (IQR)	33.3 (0–66.7)	0 (0–33)	33 (0–33)	33 (0–33)	0 (0–33)	33 (0–33)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Constipation							0.008
Median (IQR)	0 (0–33.3)	0 (0–33)	0 (0–33)	0 (0–33)	0 (0–33)	0 (0–33)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Diarrhoea							0.6
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	
Financial Difficulties							0.11
Median (IQR)	0 (0–33.3)	0 (0–33)	0 (0–33)	0 (0–33)	0 (0–33)	0 (0–33)	
Missing		37 (9%)	87 (11%)	67 (9%)	34 (9%)	78 (14%)	

Data are median (IQR) or number of patients (%). P values per Chi-Square test for categorical data and Kruskal-Wallis test for continuous data. *, Reference value according to EORTC QLQ-C30 Tables of Reference Values for Lung cancer: stage III-IV (p. 181).

Table S3 Univariable and multivariable association between PROs and OS for patients treated with atezolizumab

PRO	Univariable					Multivariable [#]			
	n	HR*	95% CI	P	c	n	HR*	95% CI	P
Physical Function	1741	0.84	0.82 to 0.87	<0.001	0.62	1686	0.87	0.84 to 0.89	<0.001
Fatigue	1741	1.15	1.12 to 1.18	<0.001	0.61	1686	1.14	1.11 to 1.17	<0.001
Appetite Loss	1741	1.11	1.09 to 1.13	<0.001	0.6	1686	1.1	1.08 to 1.12	<0.001
Pain	1741	1.12	1.09 to 1.14	<0.001	0.6	1686	1.1	1.08 to 1.13	<0.001
Role Function	1741	0.91	0.89 to 0.93	<0.001	0.6	1686	0.93	0.91 to 0.95	<0.001
Global Health Status	1741	0.88	0.86 to 0.91	<0.001	0.59	1686	0.9	0.87 to 0.93	<0.001
Social Function	1741	0.91	0.89 to 0.93	<0.001	0.58	1686	0.92	0.89 to 0.94	<0.001
Dyspnoea	1741	1.07	1.05 to 1.09	<0.001	0.56	1686	1.06	1.04 to 1.09	<0.001
Constipation	1741	1.09	1.06 to 1.11	<0.001	0.56	1686	1.07	1.05 to 1.10	<0.001
Nausea and Vomiting	1741	1.1	1.06 to 1.14	<0.001	0.55	1686	1.09	1.05 to 1.13	<0.001
Insomnia	1741	1.05	1.03 to 1.07	<0.001	0.54	1686	1.04	1.02 to 1.07	<0.001
Emotional Function	1741	0.95	0.92 to 0.98	<0.001	0.54	1686	0.95	0.92 to 0.98	<0.001
Cognitive Function	1741	0.95	0.92 to 0.98	0.002	0.52	1686	0.96	0.93 to 0.99	0.013
Financial Difficulties	1741	1.03	1.01 to 1.05	0.009	0.52	1686	1.03	1.00 to 1.05	0.035
Diarrhoea	1741	1	0.96 to 1.04	0.997	0.5	1686	1	0.95 to 1.04	0.851

CI, confidence interval; HR, hazard ratio, *, HR based on 10-unit increase, [#], Adjusted for Age, Sex, Race, ECOG-PS, Smoking history, Histology, Liver tumor site at baseline, PD-L1 highest of TC and IC expression level (official) and comorbidity count.

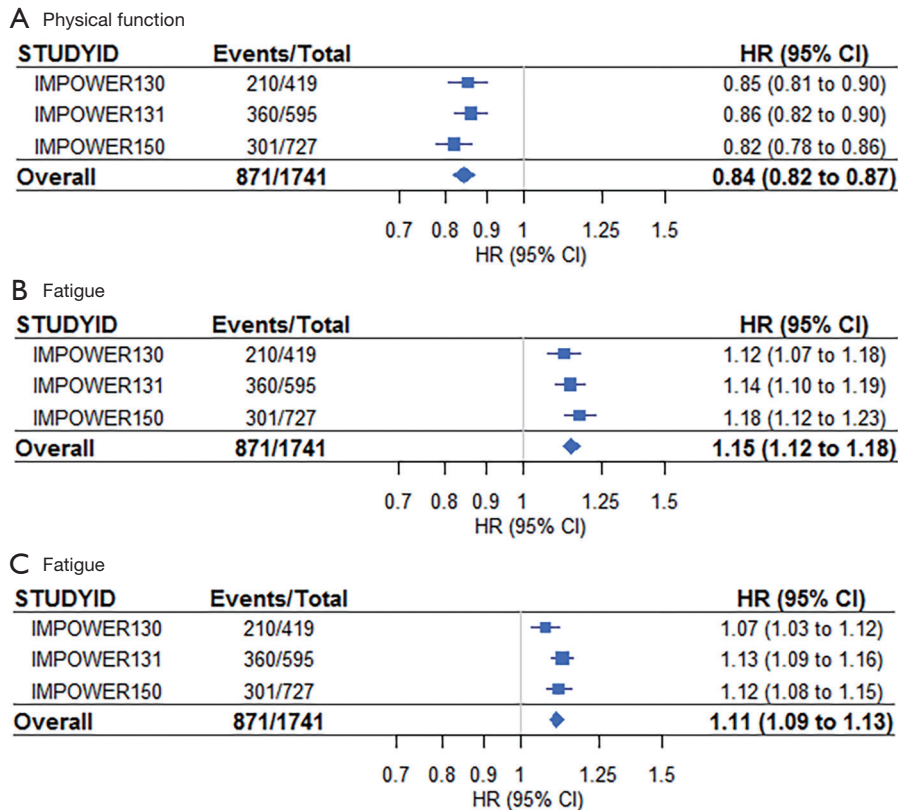


Figure S1 Univariable association between patient-reported physical function, fatigue and appetite loss with OS for patients treated with atezolizumab by study.

Table S4 Univariable and multivariable association between PROs and PFS for patients treated with atezolizumab

PRO	Univariable					Multivariable [#]			
	n	HR*	95% CI	P	c	n	HR*	95% CI	P
Fatigue	1741	1.09	1.07 to 1.11	<0.001	0.57	1686	1.08	1.06 to 1.11	<0.001
Physical Function	1741	0.9	0.88 to 0.93	<0.001	0.57	1686	0.91	0.89 to 0.94	<0.001
Pain	1741	1.08	1.06 to 1.10	<0.001	0.57	1686	1.07	1.05 to 1.09	<0.001
Role Function	1741	0.94	0.92 to 0.95	<0.001	0.56	1686	0.95	0.93 to 0.97	<0.001
Global Health Status	1741	0.92	0.90 to 0.94	<0.001	0.56	1686	0.93	0.91 to 0.96	<0.001
Appetite Loss	1741	1.06	1.04 to 1.08	<0.001	0.56	1686	1.05	1.04 to 1.07	<0.001
Social Function	1741	0.93	0.91 to 0.95	<0.001	0.55	1686	0.94	0.92 to 0.96	<0.001
Dyspnoea	1741	1.04	1.02 to 1.06	<0.001	0.54	1686	1.04	1.02 to 1.06	<0.001
Emotional Function	1741	0.95	0.93 to 0.97	<0.001	0.53	1686	0.95	0.93 to 0.97	<0.001
Constipation	1741	1.05	1.03 to 1.07	<0.001	0.53	1686	1.04	1.02 to 1.06	<0.001
Insomnia	1741	1.02	1.01 to 1.04	0.004	0.53	1686	1.02	1.01 to 1.04	0.011
Nausea and Vomiting	1741	1.06	1.02 to 1.09	<0.001	0.53	1686	1.05	1.02 to 1.09	0.002
Cognitive Function	1741	0.96	0.94 to 0.99	0.003	0.52	1686	0.97	0.94 to 1.00	0.026
Financial Difficulties	1741	1.02	1.00 to 1.04	0.044	0.51	1686	1.01	0.99 to 1.03	0.251
Diarrhoea	1741	1.01	0.98 to 1.05	0.468	0.5	1686	1.01	0.98 to 1.05	0.565

CI=confidence interval, HR=hazard ratio, *, HR based on 10-unit increase, [#], Adjusted for Age, Sex, Race, ECOG-PS, Smoking history, Histology, Liver tumor site at baseline and PD-L1 highest of TC and IC expression level (official).

Table S5 Summary of patient-reported physical function raw scores by physician- assessed ECOG-PS in patients treated with atezolizumab

	Total No. 1,927	0 No. 761	1+ No. 1,166	P-value
Physical function				< 0.001
High	456 (24%)	247 (32%)	209 (18%)	
Intermediate	1,010 (52%)	379 (50%)	631 (54%)	
Low	270 (14%)	45 (6%)	225 (19%)	
Missing	191 (10%)	90 (12%)	101 (9%)	
Trouble doing strenuous activities				< 0.001
1	351 (18%)	181 (24%)	170 (15%)	
2	540 (28%)	222 (29%)	318 (27%)	
3	318 (17%)	101 (13%)	217 (19%)	
4	193 (10%)	39 (5%)	154 (13%)	
Missing	525 (27%)	218 (29%)	307 (26%)	
Trouble taking a long walk				< 0.001
1	373 (19%)	196 (26%)	177 (15%)	
2	496 (26%)	195 (26%)	301 (26%)	
3	310 (16%)	105 (14%)	205 (18%)	
4	223 (12%)	47 (6%)	176 (15%)	
Missing	525 (27%)	218 (29%)	307 (26%)	
Trouble taking a short walk				< 0.001
1	869 (45%)	394 (52%)	475 (41%)	
2	357 (19%)	120 (16%)	237 (20%)	
3	126 (7%)	25 (3%)	101 (9%)	
4	50 (3%)	4 (1%)	46 (4%)	
Missing	525 (27%)	218 (29%)	307 (26%)	
Stay in bed or chair during the day				< 0.001
1	774 (40%)	377 (50%)	397 (34%)	
2	392 (20%)	127 (17%)	265 (23%)	
3	182 (9%)	26 (3%)	156 (13%)	
4	54 (3%)	13 (2%)	41 (4%)	
Missing	525 (27%)	218 (29%)	307 (26%)	
Need help eating, dressing, washing				< 0.001
1	1,261 (65%)	522 (69%)	739 (63%)	
2	101 (5%)	16 (2%)	85 (7%)	
3	29 (2%)	4 (1%)	25 (2%)	
4	11 (1%)	1 (<1%)	10 (1%)	
Missing	525 (27%)	218 (29%)	307 (26%)	

Data are median (IQR) or number of patients (%). P values per Chi-Square test for categorical data and Kruskal-Wallis test for continuous data. 1 = Not at All, 2 = A Little, 3 = Quite a bit, 4 = Very much.

Table S6 Associations between patient-reported physical function and ECOG-PS with PFS for patients treated with atezolizumab

	Univariable				Multivariable [#]		
	n	HR [95% CI]	P	c	n	HR [95% CI]	P
Physical function			<0.001	0.56			<0.001
Low	270	1.86 [1.57 to 2.21]			270	1.71 [1.43 to 2.04]	
Intermediate	1013	1.34 [1.18 to 1.53]			1010	1.30 [1.14 to 1.49]	
High	458	1			456	1	
ECOG-PS	1927		<0.001	0.55			<0.001
0	761	1			671		
1+	1166	1.44 [1.30 to 1.60]			1065	1.32 [1.17 to 1.48]	

[#], Model includes pre-treatment physical function and ECOG-PS. CI, confidence interval; HR, hazard ratio.