

Figure S1 Follow-up from pembrolizumab initiation. Kaplan-Meier estimates of follow-up time using the reverse Kaplan-Meier method. Tick marks indicate censoring of data (patient death). Data in square brackets represent 95% CI. mF, median follow-up; CI, confidence interval.

Table S1 Details of radiation treatment for OP

OP site	RT method	Number of fractions	Dose (gray)	Number of treated sites/total progressive sites		
Adrenal gland	SBRT	5	30	2/4		
		5	35	1/4		
		5	45	1/4		
Bone	SBRT	5	20	2/6		
		5	30	1/6		
		5	35	1/6		
		10	30	2/6		
Bone and pleural	SBRT	5	30	1/2		
	IMRT	10	30	1/2		
Brain	SBRT	1	14	3/13		
		5	33	1/13		
		4	33	1/13		
		3	33	2/13		
		4	20	1/13		
		2	11	1/13		
	IMRT	10	30	2/13		
		5	20	2/13		
		Lung	SBRT	5	50	1/17
				5	62,5	2/17
3	56			1/17		
3	45			1/17		
IMRT	15		45	4/17		
	17		51	6/17		
	10		30	1/17		
33	66	1/17				
Lung and lymph node	IMRT	10	30	1		
Lymph node	SBRT	3	51	1/3		
		3	33	1/3		
		5	30	1/3		
Pleural	IMRT	10	30	1		

OP, oligoprogression; SBRT, stereotactic body radiotherapy; IMRT, intensity-modulated radiotherapy.

Table S2 Univariate and multivariable analysis of features associated with TTNT

Variables	Strata	Number	Median TTNT (95% CI) (months)	Univariate		Multivariate	
				HR (95% CI)	P value	HR (95% CI)	P value
Sex	Female	10	NA (12.2–NA)	Reference	0.41		
	Male	26	19.6 (9.9–NA)	1.59 (0.52–4.86)			
Smoking status	Currently smoking	20	15.3 (9.9–NA)	Reference	0.87		
	Ex-smoker	13	19.6 (12.2–NA)	0.77 (0.28–2.08)			
	Never smoked	2	4.5 (4.5–NA)	0.85 (0.28–2.08)			
Stage at diagnosis	I–III	8	32.4 (8.5–NA)	Reference	0.55		
	IV	28	15.3 (12.2–NA)	1.45 (0.42–5.03)			
Bone metastasis at diagnosis [†]	No	27	32.4 (12.6–NA)	Reference	0.12	Reference	0.05
	Yes	9	9.9 (7.1–NA)	2.2 (0.79–6.13)		2.86 (0.98–8.32)	
Adrenal gland metastasis at diagnosis [†]	No	29	32.4 (12.6–NA)	Reference	0.02	Reference	0.01
	Yes	7	8.4 (3.6–NA)	3.19 (1.17–8.68)		3.95 (1.39–11.2)	
Lung metastasis at diagnosis	No	22	16.1 (9.9–NA)	Reference	0.52		
	Yes	14	NA (12.2–NA)	0.72 (0.25–2.02)			
Node metastasis at diagnosis	No	27	32.4 (9.9–NA)	Reference	0.79		
	Yes	9	19.6 (12.4–NA)	0.87 (0.3–2.48)			
Brain metastasis at diagnosis	No	28	15.3 (12.4–NA)	Reference	0.95		
	Yes	8	19.6 (7.1–NA)	1.04 (0.34–3.2)			
Pleural metastasis at diagnosis	No	33	22.7 (15.3–NA)	Reference	0.43		
	Yes	3	19.1 (17.3–NA)	1.84 (0.4–8.56)			
Other meta sites at diagnosis	No	33	19.6 (12.4–NA)	Reference	0.83		
	Yes	3	NA (7.1–NA)	0.81 (0.11–6.13)			
Number of metastasis sites at first-line	0	5	32.4 (8.5–NA)	Reference	0.3		
	1–2	16	NA (12.4–NA)	0.56 (0.13–2.36)			
	≥3	15	12.6 (8.4–NA)	1.34 (0.13–2.36)			
Tumour histology	Adenocarcinoma	25	19.6 (12.4–NA)	Reference	0.8		
	Squamous cell carcinoma	11	15.3 (9.9–NA)	0.9 (0.32–2.54)			
ECOG category [†]	0–1	30	32.4 (12.4–NA)	Reference	0.02		
	2–4	6	8.5 (4.6–NA)	3.4 (1.16–9.9)			
Age (years)	<70	20	32.4 (12.2–NA)	Reference	0.4		
	≥70	16	12.6 (9–NA)	1.44 (0.56–3.68)			
PD-L1 (%) [†]	0–49	16	12.4 (4.6–NA)	Reference	0.14		
	50–100	20	NA (12.6–NA)	0.5 (0.2–1.27)			
Charlson index (without lung cancer)	0	18	15.3 (9.9–NA)	Reference	0.6		
	1–2	12	32.4 (19.6–NA)	0.77 (0.26–2.32)			
	3–6	6	12.3 (2.5–NA)	1.44 (0.26–2.32)			

[†], variables with a univariate P value <0.2 were used in the stepwise model for multivariable analysis. TTNT, time to next systemic treatment; HR, hazard ratio; CI, confidence interval; NA, not achieved; ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed cell death-ligand 1.

Table S3 Univariate and multivariable analysis of features associated with OS

Variables	Strata	Number	Median OS (95% CI) (months)	Univariate		Multivariate	
				HR (95% CI)	P value	HR (95% CI)	P value
Sex	Female	10	NA (29.9–NA)	Reference	0.78		
	Male	26	NA (36.5–NA)	1.21 (0.32–4.6)			
Smoking status	Currently smoking	20	40.1 (29.9–NA)	Reference	0.43		
	Ex-smoker	13	NA (NA–NA)	0.45 (0.09–2.12)			
	Never smoked	2	12.7 (12.7–NA)	1.37 (0.09–2.12)			
Stage at diagnosis	I–III	8	NA (NA–NA)	Reference	0.32		
	IV	28	NA (36.5–NA)	3.36 (0.43–26.32)			
Pleural metastasis at diagnosis	No	33	NA (36.5–NA)	Reference	0.84		
	Yes	3	25.4 (25.4–NA)	1.64 (0.2–13.61)			
Bone metastasis at diagnosis [†]	No	27	NA (NA–NA)	Reference	0.02	Reference	0.01
	Yes	9	28 (12.7–NA)	3.83 (1.15–12.8)		5.82 (1.48–22.9)	
Adrenal gland metastasis at diagnosis [†]	No	29	NA (40.1–NA)	Reference	0.006	Reference	0.008
	Yes	7	25.4 (17.9–NA)	5.77 (1.4–23.74)		8.12 (1.73–38.1)	
Lung metastasis at diagnosis	No	22	NA (29.9–NA)	Reference	0.70		
	Yes	14	NA (40.1–NA)	0.68 (0.18–2.56)			
Node metastasis at diagnosis	No	27	NA (29.9–NA)	Reference	0.73		
	Yes	9	NA (22.5–NA)	0.97 (0.26–3.68)			
Brain metastasis at diagnosis	No	28	NA (36.5–NA)	Reference	0.65		
	Yes	8	NA (22.5–NA)	0.9 (0.19–4.18)			
Other meta sites at diagnosis	No	33	NA (24–NA)	Reference	0.52		
	Yes	3	NA (7.2 –NA)	1.62 (0.33–8.02)			
Number of metastasis sites at first-line	0	5	NA (29.9–NA)	Reference	0.62		
	1–2	16	NA (28–NA)	1.7 (0.19–15.27)			
	≥3	15	40.1 (36.5–NA)	3.07 (0.19–15.27)			
Tumour histology	Adenocarcinoma	25	NA (29.9–NA)	Reference	0.66		
	Squamous cell carcinoma	11	40.1 (36.5–NA)	1.34 (0.39–4.59)			
ECOG category [†]	0–1	30	NA (40.1–NA)	Reference	0.13	–	–
	2–4	6	29.9 (29.9–NA)	2.72 (0.7–10.6)			
Age (years) [†]	<70	20	NA (NA–NA)	Reference	0.04	–	–
	≥70	16	40.1 (25.4–NA)	3.66 (0.97–13.81)			
PD-L1 (%)	0–49	16	29.9 (28–NA)	Reference	0.69		
	50–100	20	NA (40.1–NA)	0.65 (0.19–2.17)			
Charlson index (without lung cancer)	0	18	NA (40.1–NA)	Reference	0.71		
	1–2	12	NA (29.9–NA)	1.13 (0.27–4.75)			
	3–6	6	28 (22.5–NA)	2.05 (0.27–4.75)			

[†], variables with a univariate P value <0.2 were used in the stepwise model for multivariable analysis. OS, overall survival; HR, hazard ratio; CI, confidence interval; NA, not achieved; ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed cell death-ligand 1.

Table S4 Univariate and multivariable analysis of features associated with PFS

Variables	Strata	Number	Median PFS (95% CI) (months)	Univariate		Multivariate	
				HR (95% CI)	P value	HR (95% CI)	P value
Tumour histology	Adenocarcinoma	33	12.6 (5.8–NA)	Reference	0.49		
	Squamous cell carcinoma	14	9.5 (6.1–NA)	1.31 (0.6–2.85)			
Number of OP	1	36	11.9 (6.1–NA)	Reference	0.87		
	2	9	10.3 (3.8–NA)	1.28 (0.51–3.2)			
	3	2	3.1 (3.1–NA)	0.98 (0.51–3.2)			
New lesion at OP	No	27	12.6 (7.6–NA)	Reference	0.27		
	Yes	20	8.5 (3.8–NA)	1.52 (0.72–3.21)			
Adrenal gland OP	No	43	9.7 (5.8–NA)	Reference	0.17		
	Yes	4	NA (11.3–NA)	0.27 (0.04–1.98)			
Pleural OP [†]	No	44	11.9 (7.6–NA)	Reference	0.004	–	–
	Yes	3	2.5 (2–NA)	5.09 (1.48–17.52)			
Bone OP [†]	No	39	12.6 (9.2–NA)	Reference	0.004	Reference	0.004
	Yes	8	3.9 (3–NA)	3.21 (1.39–7.42)		3.21 (1.39–7.42)	
Lung OP [†]	No	29	8.5 (4–NA)	Reference	0.04	–	–
	Yes	18	NA (9.2–NA)	0.44 (0.19–0.99)			
Brain OP	No	34	11.9 (8.5–NA)	Reference	0.52		
	Yes	12	8.2 (3.2–NA)	1.34 (0.56–3.21)			
Lymph node OP	No	43	10.3 (6.1–NA)	Reference	0.73		
	Yes	4	12.6 (3–NA)	1.24 (0.37–4.11)			
RT method	Conformational	21	8.5 (5.8–NA)	Reference	0.31		
	Stereotaxy	26	12.6 (6.1–NA)	0.69 (0.32–1.48)			
Concomitant corticoids	No	34	10.3 (7.6–NA)	Reference	0.68		
	Yes	13	15 (3.2–NA)	1.19 (0.52–2.7)			

[†], variables with a univariate P value <0.2 were used in the stepwise model for multivariable analysis. PFS, progression-free survival; HR, hazard ratio; CI, confidence interval; OP, oligoprogression; NA, not achieved; RT, radiotherapy.

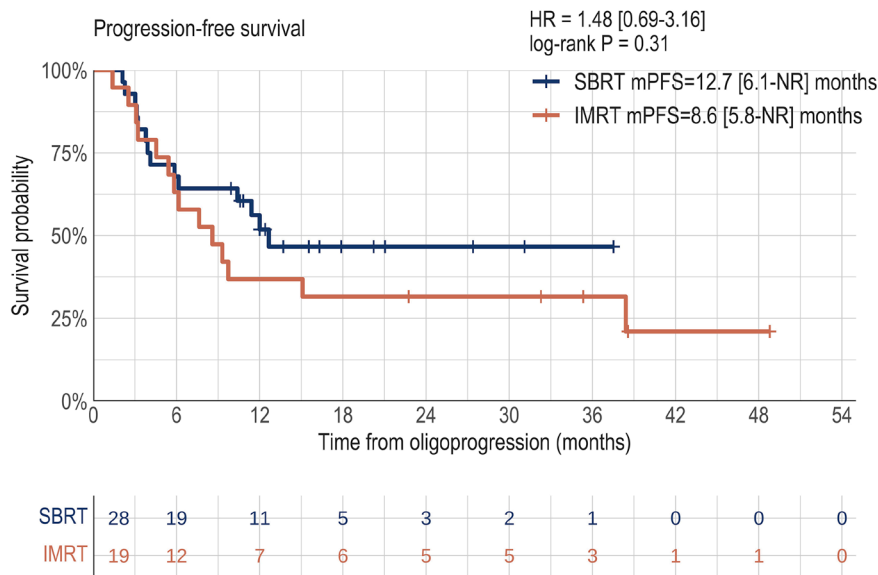


Figure S2 Kaplan-Meier estimates of PFS according to RT technique group. PFS was defined as the duration between the date of the first OP and the date of disease progression (RECIST or not-RECIST progressive disease) or death. Tick marks indicate censored data. Data in square brackets represent 95% CI. HR, hazard ratio; SBRT, stereotactic body radiotherapy; mPFS, median progression-free survival; NR, not reached; IMRT, intensity-modulated radiotherapy; PFS, progression-free survival; RT, radiotherapy; OP, oligoprogression; RECIST, Response Evaluation Criteria in Solid Tumors.

Table S5 Best radiological response of oligoprogressive lesions treated with RT according to RECIST 1.1 criteria

Response pattern	OPs (n=47)
Complete response	5 (10.6)
Partial response	28 (59.6)
Stable disease	10 (21.3)
Progressive disease	2 (4.3)
Not available	2 (4.3)

Data are presented as n (%). A total of 47 OPs among the 36 patients. RT, radiotherapy; RECIST, Response Evaluation Criteria in Solid Tumors; OP, oligoprogression.