

Introduction

Immune checkpoint inhibition (ICI) with or without chemotherapy has significantly improved survival in patients (pts) with metastatic non-small cell lung cancer (NSCLC) (1-2). While ICI duration is commonly limited to two years, the optimal duration of ICI, and post-progression treatment outcomes in pts who received at least two years of ICI are largely unknown.

Methods

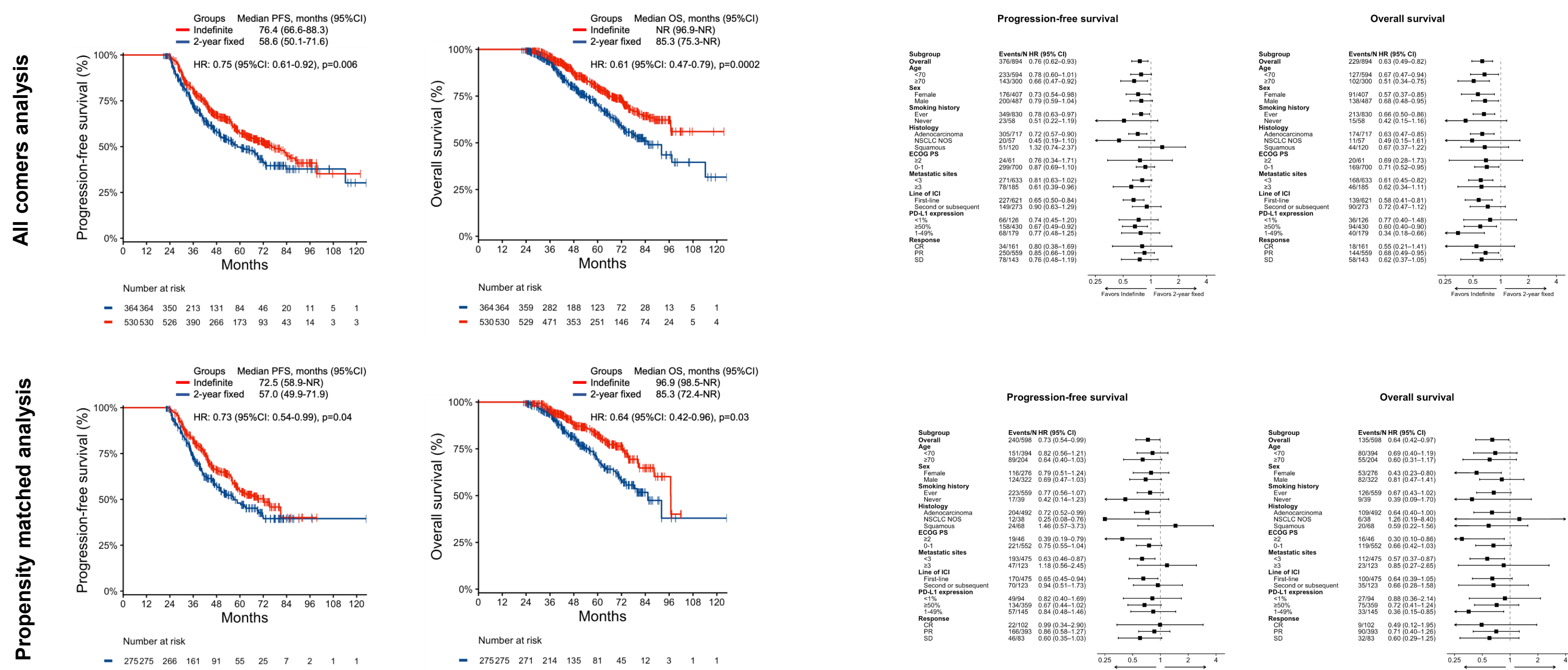
We conducted an international, multi-center study of pts with metastatic NSCLC treated with ICI for at least two years to characterize clinical outcomes and post-progression treatment patterns. Log-rank tests were used to test for differences in event-time distributions, and Cox proportional hazards models were used to estimate HR.

Results

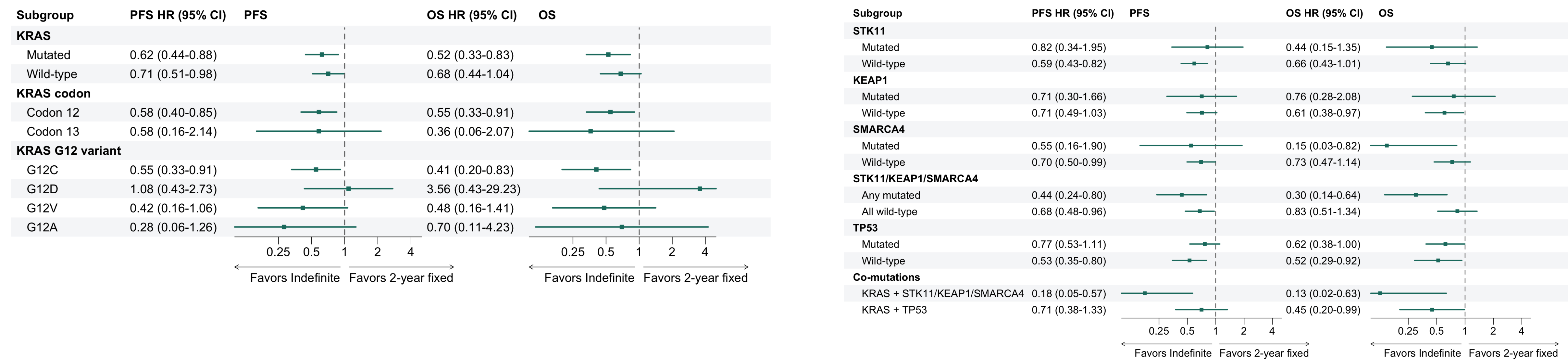
Patient characteristics

	Overall (N=694)
Age	
<70	594 (86.4%)
≥70	300 (33.6%)
Sex	
Female	407 (45.5%)
Male	487 (54.5%)
Smoking history	
Ever	530 (92.8%)
Never	58 (6.5%)
Missing	6 (0.7%)
ECOG PS	
2	61 (6.8%)
0-1	700 (78.3%)
Missing	133 (14.9%)
Histology	
Adenocarcinoma	717 (80.2%)
NSCLC NOS	57 (6.4%)
Squamous	120 (13.4%)
PD-L1 categories	
<1%	126 (14.1%)
≥50%	430 (48.1%)
1-49%	179 (20.0%)
Missing	159 (17.8%)
Driver alterations	
ALK fusion	1 (0.1%)
BRAF	28 (3.1%)
EGFR	14 (1.6%)
HER2	5 (0.6%)
KRAS	297 (33.2%)
MET	10 (1.1%)
None identified	276 (30.9%)
NRG1 fusion	1 (0.1%)
NTRK1 fusion	1 (0.1%)
RET fusion	1 (0.1%)
ROS1 fusion	1 (0.1%)
Missing	259 (29.0%)
Line of ICI	
First-line	621 (69.5%)
Second or subsequent	273 (30.5%)
Immunotherapy received	
PD-(L)1 + CTLA-4 blockade +/- chemotherapy	15 (1.7%)
PD-(L)1 blockade + chemotherapy	252 (28.2%)
PD-(L)1 monotherapy	627 (70.1%)
Immunotherapy duration	
Fixed	364 (40.7%)
Indefinite	530 (59.3%)

PFS and OS with 2-year fixed versus indefinite immunotherapy



PFS and OS with 2-year fixed versus indefinite immunotherapy according to KRAS, STK11, KEAP1, SMARCA4 and TP53 mutations

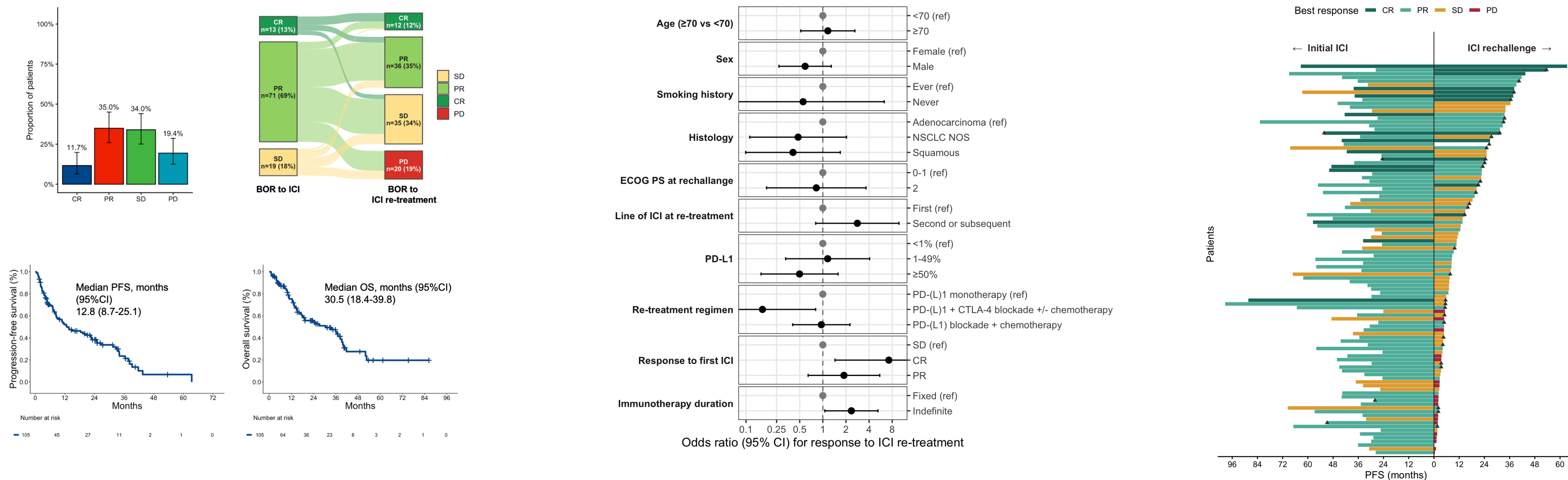


Multivariable Cox regression

Variable	N	Hazard ratio	p
Immunotherapy duration	Fixed 276	Reference	
	Indefinite 327	0.75 (0.58, 0.96)	0.02
Age	<70 397	Reference	
	≥70 206	1.28 (0.98, 1.67)	0.07
Sex	Female 277	Reference	
	Male 326	0.94 (0.73, 1.21)	0.63
PD-L1 categories	<1% 94	Reference	
	≥50% 363	0.65 (0.47, 0.90)	0.01
	1-49% 146	0.80 (0.55, 1.18)	0.27
Histology	Adenocarcinoma 493	Reference	
	NSCLC NOS 38	0.68 (0.38, 1.22)	0.20
	Squamous 72	0.83 (0.54, 1.29)	0.41
ECOG PS	≥2 50	Reference	
	0-1 553	0.96 (0.60, 1.55)	0.88
Smoking history	Ever 563	Reference	
	Never 40	1.20 (0.73, 1.94)	0.47
Metastatic sites	<3 479	Reference	
	≥3 124	0.96 (0.70, 1.32)	0.81

Variable	N	Hazard ratio	p
Immunotherapy duration	Fixed 276	Reference	
	Indefinite 327	0.56 (0.40, 0.79)	0.001
Age	<70 397	Reference	
	≥70 206	1.67 (1.17, 2.39)	0.004
Sex	Female 277	Reference	
	Male 326	1.43 (1.00, 2.03)	0.049
PD-L1 categories	<1% 94	Reference	
	≥50% 363	0.61 (0.39, 0.96)	0.031
	1-49% 146	0.81 (0.48, 1.35)	0.418
Histology	Adenocarcinoma 493	Reference	
	NSCLC NOS 38	0.61 (0.27, 1.40)	0.243
	Squamous 72	1.25 (0.77, 2.04)	0.367
ECOG PS	≥2 50	Reference	
	0-1 553	0.53 (0.32, 0.90)	0.020
Smoking history	Ever 563	Reference	
	Never 40	1.35 (0.70, 2.61)	0.373
Metastatic sites	<3 479	Reference	
	≥3 124	0.89 (0.57, 1.40)	0.621

Clinical outcomes and predictors of immunotherapy retreatment efficacy



Conclusion

Continuation of ICI beyond 2 years was associated with longer PFS and OS compared with fixed-duration treatment. These findings argue against assuming equivalence between treatment strategies and support prospective randomized evaluation of ICI duration.

References

- Reck M, et al. Five-Year Outcomes With Pembrolizumab Versus Chemotherapy for Metastatic Non-Small-Cell Lung Cancer With PD-L1 Tumor Proportion Score ≥ 50. *J Clin Oncol*.
- de Castro G Jr, et al. Five-Year Outcomes With Pembrolizumab Versus Chemotherapy as First-Line Therapy in Patients With Non-Small-Cell Lung Cancer and Programmed Death Ligand-1 Tumor Proportion Score ≥ 1% in the KEYNOTE-042 Study. *J Clin Oncol*.