

Supplementary Material

Supplementary Table 1: Characteristics of stage III non-small cell lung cancer patients who received durvalumab after definitive chemoradiation

<u>All Patients (n=45)</u>	Patients without irAE (N=31)	Patients with irAE (N=14)	p-value
Age, median	66.9	67.4	0.78
Sex, male/female	13/13	12/2	0.03
never/light-smokers (<10 py)	0	0	
pack-years, mean	41.5	47.5	0.23
ECOG PS 0 / 1, number	13 / 11	9 / 5	0.5
PD-L1 TPS, mean	38.1	33.4	0.95
NLR, mean	7.0	5.6	0.45

Abbreviations: irAE: immune-related adverse events; ECOG PS: ECOG performance status; NLR: neutrophil-to-lymphocyte ratio.

Supplementary Table 2: Description of irAEs, their severity and management

Affected organs	Patients (N)	Grade ≥ 3 (N)	Steroids (N)
Pneumonitis	7	6	7
Dermatitis	1	0	0
Endocrinological	4	1	2
Hepatitis	2	1	2

Supplementary Table 3: Univariable 12-week landmark analysis of progression-free and overall survival according to occurrence of irAE in NSCLC

The association of irAE and other variables with progression-free (PFS) and overall survival (OS) was analyzed using a univariable Cox regression 12- landmark analysis. Statistically significant results have been highlighted in bold.

PFS with 12-week landmark	HR	P-value	95%-CI
IrAE occurrence	0.68	0.004	0.53-0.88
PD-L1 TPS (<1, 1-49, 50+)	0.70	<0.001	0.59-0.82
NLR (≥ 5 , <5)	1.20	1.20	0.95-1.51
Treatment line	1.11	0.09	0.98-1.26
Treatment type ¹	1.16	0.26	0.90-1.51
ECOG PS	1.13	0.29	0.91-1.40
OS with 12-week landmark	HR	P-value	95%-CI
IrAE occurrence	0.40	<0.001	0.29-0.55
PD-L1 TPS (<1, 1-49, 50+)	0.77	0.001	0.66-0.89
NLR (≥ 5 , <5)	1.52	<0.001	1.21-1.90
Treatment line	1.19	0.001	1.07-1.33
Treatment type ¹	0.75	0.06	0.56-1.01
ECOG PS	1.26	0.03	1.03-1.55

Abbreviations: PFS: progression-free survival; OS: overall survival; HR: hazard ratio; 95% CI: 95% confidence interval; irAE: immune related adverse events; ECOG PS: Eastern Cooperative Oncology Group Performance Status; IO: immunotherapy; PD-L1 TPS: Programmed Death Ligand 1 Tumor Proportion Score (%); NLR: Neutrophil-to-Lymphocyte Ratio.

¹chemoimmunotherapy vs. IO- monotherapy.

Supplementary Table 4: Multivariable 12-week landmark analysis of progression-free and overall survival according to occurrence of irAE in NSCLC

The association of irAE and other variables with progression-free (PFS) and overall survival (OS) was analyzed using a multivariable Cox regression 12-week landmark analysis. Statistically significant results have been highlighted in bold.

PFS with 12-week landmark	HR	P-value	95%-CI
IrAE occurrence	0.68	0.009	0.51-0.90
PD-L1 TPS (<1, 1-49, 50+)	0.71	<0.001	0.59-0.86
NLR (≥ 5 , <5)	1.05	0.73	0.80-1.34
Treatment line	1.14	0.12	0.97-1.33
Treatment type ¹	0.98	0.91	0.70-1.40
ECOG PS	1.16	0.23	0.91-1.45
OS with 12-week landmark	HR	P-value	95%-CI
IrAE occurrence	0.40	<0.001	0.28-0.58
PD-L1 TPS (<1, 1-49, 50+)	0.76	0.003	0.64-0.91
NLR (≥ 5 , <5)	1.45	0.003	1.13-1.86
Treatment line	1.13	0.08	0.99-1.30
Treatment type ¹	0.71	0.07	0.49-1.03
ECOG PS	1.35	0.01	1.07-1.71

Abbreviations: PFS: progression-free survival; OS: overall survival; HR: hazard ratio; 95% CI: 95% confidence interval; irAE: immune related adverse events; ECOG PS: Eastern Cooperative Oncology Group Performance Status; IO: immunotherapy; PD-L1 TPS: Programmed Death Ligand 1 Tumor Proportion Score (%); NLR: Neutrophil-to-Lymphocyte Ratio.

¹ chemoimmunotherapy vs. IO- monotherapy.

Supplementary Table 5: Multivariable time-dependent Cox regression analysis of overall survival

The association of irAE and other variables with overall survival (OS) was analyzed using a multivariable Cox regression with immune-related adverse events (irAE) as a time dependent co-variate. Included were all parameters used in the multivariable analysis of Table 4. Statistically significant results have been highlighted.

¹ OS, multivariable analysis	HR	P-value	95% CI
irAE	0.70	0.03	0.51-0.97
PD-L1 TPS (<1, 1-49, 50+)	0.77	<0.001	0.66-0.89
NLR (≥ 5 , <5)	1.91	<0.001	1.55-2.37
treatment line	1.14	0.01	1.03-1.27
treatment type ¹	0.47	<0.001	0.34-0.64
ECOG PS	1.45	<0.001	1.20-1.75

Abbreviations: PFS, progression-free survival; OS, overall survival, HR, hazard ratio; 95% CI: 95% confidence interval; irAE, immune-related adverse events; ECOG PS, Eastern Cooperative Oncology Group performance status; IO, immunotherapy; PD-L1 TPS, Programmed Death Ligand 1 Tumor Proportion Score (%); NLR: Neutrophil-to-Lymphocyte Ratio.

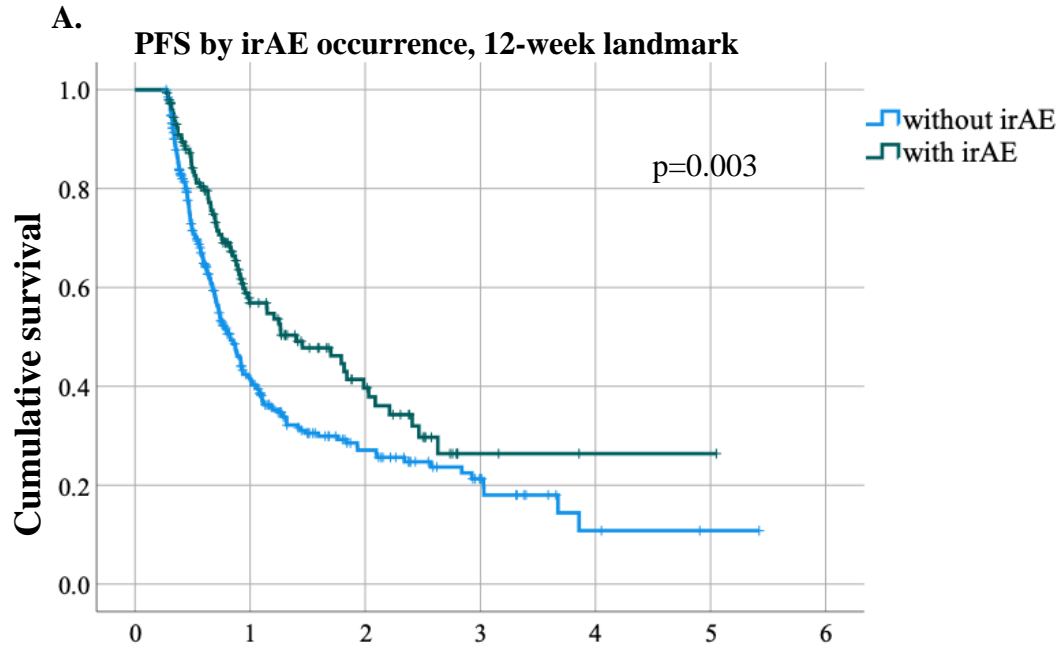
¹ chemoimmunotherapy vs. IO- monotherapy

Supplementary Figure 1. Progression-free and overall survival by occurrence of irAE in a 12-week landmark analysis

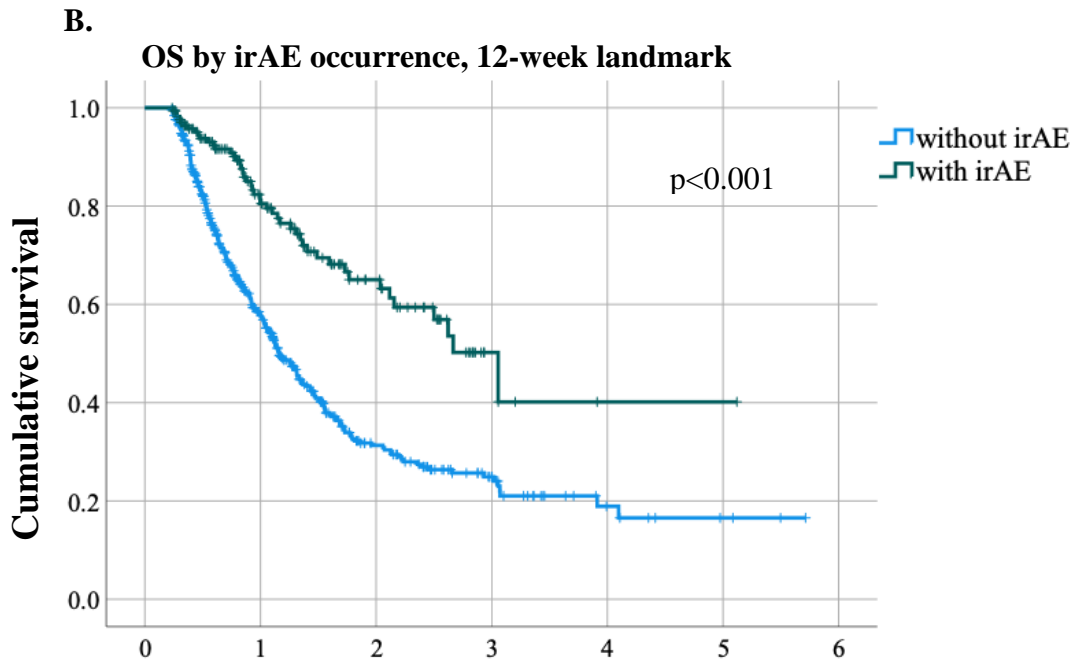
(A) The median progression-free survival under immunotherapy (PFS) was 9 months (95% confidence interval [CI] 8.1-10.4) for patients without immune-related adverse events (irAE) vs. 15 months (8.2-22.1, logrank p=0.003) for patients with irAE in a 12-week landmark analysis.

(B) The median overall survival from immunotherapy start (OS) was 14 months (12.4-15.6) for patients without irAE vs. 37 months (28.5-44.8, logrank p<0.001) for patients with irAE in a 12-week landmark analysis.

Supplementary Figure 1



No. at risk:	PFS (years)						
	0	1	2	3	4	5	6
with irAE:	156	56	23	3	1	1	0
without irAE:	350	98	37	15	3	1	0



No. at risk:	OS (years)						
	0	1	2	3	4	5	6
with irAE:	171	86	36	5	1	1	0
without irAE:	503	208	66	28	7	3	0