

Depth of Response (DepOR) to Immunotherapy is Associated with Survival Outcomes in Oligoprogressive NSCLC: A Real-World Data Analysis

BACKGROUND

- Oligoprogressive disease (OPD) is a distinct metastatic disease entity, in which a small number of lesions (≤5) progress either during or after systemic therapy in an otherwise stable metastatic disease.¹
- Emerging data supports the use of local ablative therapy (LAT; radiation/surgery) for progressing lesions (PLs), while continuing systemic therapy for non-progressing lesions (NPLs).^{1,2}
- Limited evidence exists on the outcomes of continuing immunotherapy (IO) in patients with OPD.

Objective: This real-world analysis aimed to investigate whether depth of response (DepOR) in NPLs to IO correlates with survival outcomes.

METHODS

- We utilized a longitudinal retrospective real-world dataset of patients with mNSCLC without EGFR/ALK alterations across 10 US and European institutions. Patients receiving 1L IO, comprising of PD-(L)1 inhibitors, between December 2014 and November 2022 were included.³
- Lesion-level measurements were curated from routine CT scans. Patients with OPD during 1L IO treatment were identified as those with 1–5 extracranial PLs and no limit on NPLs.
- Response of NPLs were longitudinally evaluated from the time of OPD until IO discontinuation. RECIST measurements were analyzed to estimate the continued treatment effect attributable to IO post-OPD. PLs were considered potential targets for LAT and were excluded in response evaluation.
- DepOR** = change in SOD from the time of OPD across NPLs (excluding bone lesions).
- Best response** = maximum percent change in DepOR across NPLs.
- OS and TTNT** were analyzed in patients stratified by DepOR from best response.

RESULTS

Patient and tumor characteristics

- Among 586 patients who received 1L IO, 215 (36.7%) developed OPD. Of these, 70 patients continued IO and had ≥1 follow-up scan available. Patient and tumor characteristics are shown in **Table 1**.

Table 1. Patient and tumor characteristics

Characteristics	N=70
Age at IO initiation, median (IQR)	70.5 (62.3–76.8)
Sex, n (%)	
Male	38 (54.3)
Female	32 (45.7)
Race, n (%)	
White	38 (54.3)
Asian	3 (4.3)
Black	1 (1.4)
Unknown	28 (40.0)
Smoking status, n (%)	
Current/former smoker	25 (35.7)
Never smoker	1 (1.4)
Unknown	44 (62.9)
Lesion count at IO initiation, median (IQR)	6.0 (5.0–8.0)
IO regimen type, n (%)	
IO monotherapy	31 (44.3)
IO/chemotherapy combination	39 (55.7)
Histology, n (%)	
Adenocarcinoma	52 (74.3)
Squamous cell carcinoma	9 (12.9)
Other	9 (12.9)
PD-L1 status, n (%)	
High (TPS ≥50%)	38 (54.3)
Low (TPS 1–49%)	16 (22.9)
Negative (TPS <1%)	15 (21.4)
Unknown	1 (1.4)

PLs and NPLs at the time of OPD

- The median (IQR) duration of 1L IO was 2.6 (2.2–3.3) months.
- Of the 70 patients, 55 (78.6%) and 24 (34.3%) had PLs in known metastatic and new sites, respectively (**Table 2**); 9 (12.9%) patients had PLs in both known and new sites.
- The median (IQR) number of NPLs was 4 (2–6).

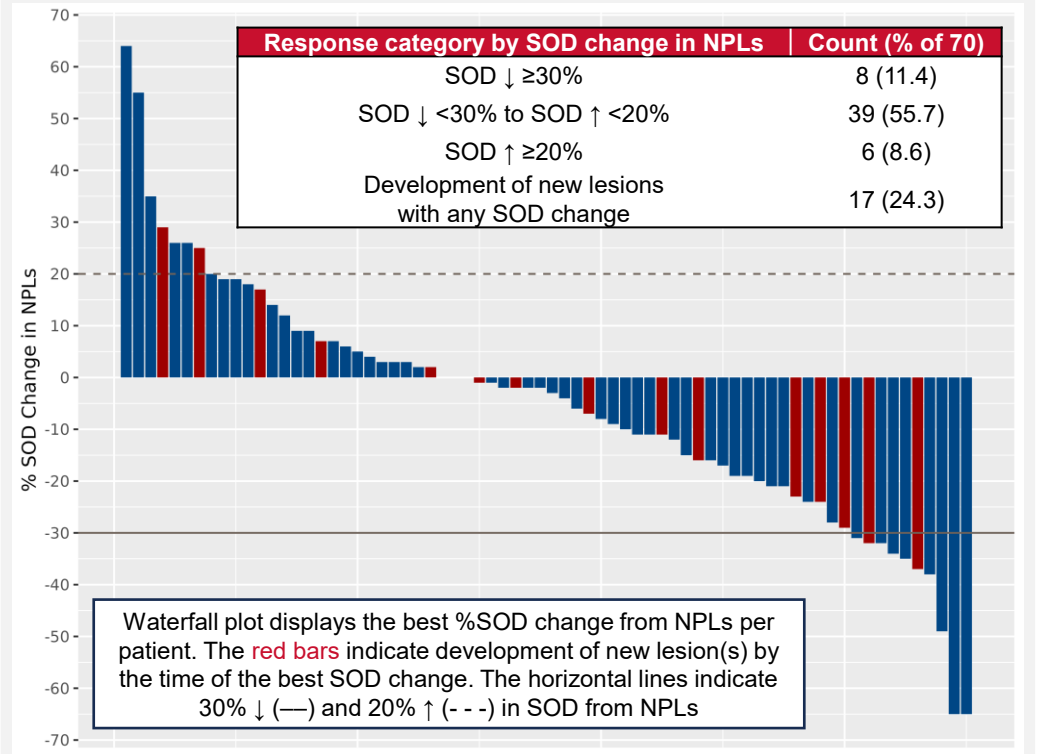
Table 2. Lesion sites for PLs and NPLs at the time of OPD

Lesion site	PLs at OPD			NPLs at OPD
	≥1 lesion, n	≥1 known lesion, n	≥1 new lesion, n	≥1 lesion, n
Lung	33	21	14	65
Lymph node	30	24	9	50
Liver	4	2	2	3
Adrenal	0	0	0	6
Bone	11	11	0	11
Non-target/unspecified	8	6	2	13
Total (% of 70)	70 (100)	55 (78.6)	24 (34.3)	70 (100)

Best response among NPLs in patients with oligoprogressive NSCLC

- At the time of best response (median 3.4 months post-OPD), 32 (45.7%) patients experienced any SOD reduction (↓) in NPLs, including 8 (11.4%; 95% CI=3.98, 18.9%) with ≥30% ↓ (**Figure 1**).
- The remaining 38 (54.3%) patients had SOD increase (↑) or the appearance of new lesion(s) (**Figure 1**).

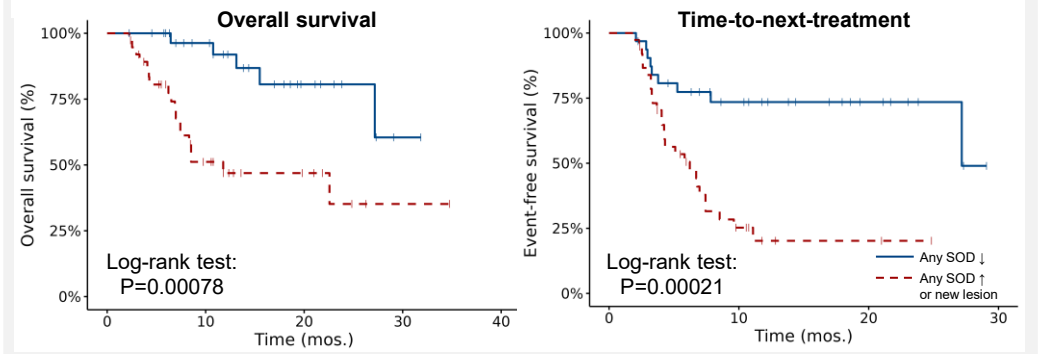
Figure 1. Best response among NPLs in patients with OPD during IO treatment



OS and TTNT stratified by DepOR in NPLs

- Patients with any SOD ↓ in NPLs had significantly improved OS and TTNT (**Figure 2**).
- Patient and tumor characteristics in subgroups stratified by DepOR are shown in **Table 3**.

Figure 2. Kaplan–Meier curves for OS and TTNT stratified by DepOR in NPLs



DepOR category; N=70	N	mOS (95% CI), months	mTTNT (95% CI), months
Any SOD ↓	32	NR (27.2, NR)	27.2 (27.2, NR)
Any SOD ↑ or new lesion	38	11.8 (7.43, NR)	6.22 (4.24, 8.52)

Note: TTNT event defined as initiation of next treatment or death.

Table 3. Patient and tumor characteristics stratified by DepOR in NPLs post-OPD

Characteristics	Any SOD ↓ N=32	Any SOD ↑ or New Lesion N=38
Age at IO initiation, median (IQR)	71.0 (65.0–80.0)	69.5 (62.0–76.0)
Sex, n (%)		
Male	17 (53.1)	21 (55.3)
Female	15 (46.9)	17 (44.7)
Race, n (%)		
White	19 (59.4)	19 (50.0)
Asian	1 (3.1)	2 (5.3)
Black	1 (3.1)	0 (0)
Unknown	11 (34.4)	17 (44.7)
Smoking status, n (%)		
Current/former smoker	14 (43.8)	11 (28.9)
Never smoker	1 (3.1)	0 (0)
Unknown	17 (53.1)	27 (71.1)
Lesion count at IO initiation, median (IQR)	6.5 (5.0–8.0)	6.0 (4.0–8.0)
IO regimen type, n (%)		
IO monotherapy	19 (59.4)	12 (31.6)
IO/chemotherapy combination	13 (40.6)	26 (68.4)
Histology, n (%)		
Adenocarcinoma	26 (81.3)	26 (68.4)
Squamous cell carcinoma	2 (6.3)	7 (18.4)
Other	4 (12.5)	5 (13.2)
PD-L1 status, n (%)		
High (TPS ≥50%)	24 (75.0)	14 (36.8)
Low (TPS 1–49%)	5 (15.6)	11 (28.9)
Negative (TPS <1%)	3 (9.4)	12 (31.6)
Unknown	0 (0)	1 (2.6)
Months of treatment prior to OPD, median (IQR)	2.7 (2.1–3.0)	2.6 (2.2–3.7)

CONCLUSION: In this real-world cohort of patients continuing IO for oligoprogressive NSCLC, continued response in NPLs was associated with improved survival. This finding has clinical implications for monitoring DepOR in NPLs and optimizing interventions, particularly through novel IO combinations.

ABBREVIATIONS: 1L, first-line; CT, computed tomography; DepOR, depth of response; ECOG, Eastern Cooperative Oncology Group; EGFR/ALK, epidermal growth factor receptor/anaplastic lymphoma kinase; IO, immunotherapy; IQR, interquartile range; LAT, local ablative therapy; mNSCLC, metastatic non-small cell lung cancer; OPD, oligoprogressive disease; OS, overall survival; NPL, non-progressing lesion; NR, not reached; NSCLC, non-small cell lung cancer; PD-L1, programmed death ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors; SOD, sum of diameter; TPS, tumor proportion score; TTNT, time-to-next-treatment; US, United States.

REFERENCES:
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