

Effectiveness and Durable Outcomes with Second-Line Immunotherapy in Advanced NSCLC in Real World Practice in India

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Abstract

Background:

This retrospective real-world study evaluated long-term outcomes and prognostic factors in advanced NSCLC patients who progressed after chemotherapy and received predominantly weight-based immune checkpoint inhibitors (ICIs).

Methods:

This single-centre Indian study included patients with squamous or non-squamous NSCLC, with at least one prior line of platinum-based chemotherapy, had ECOG PS 1–4, and known PD-L1 status. Assessed outcomes included progression-free survival (PFS), overall survival (OS), prognostic factors long-term response, conditional survival at 6- and 12-month landmarks, and safety.

Results:

Among 97 patients (88.7% male; median age 63 years), most received weight-based nivolumab (n = 86). Median follow-up was 54.5 months. Best overall response (BOR) was partial response (20.6%) and stable disease (20.6%), with a disease control rate of 41.2%. Median time to immunotherapy discontinuation was 3.4 months, due to disease progression. Median PFS was 3.6 months. Bone metastases (HR 0.46; $P < 0.001$), mutation, and ECOG PS (HR 0.37; $P = 0.025$) were independent predictors of PFS. Median OS was 10.6 months, with 1-, 2-, and 3-year OS rates of 46%, 31.4%, and 21.8%. ECOG PS (HR 0.33; $P = 0.011$), and extra-thoracic metastatic sites (HR 0.45; $P = 0.027$) were independent predictors of OS. Immune-related AEs (36.1%) were associated with improved OS and PFS. Long-term survival was notable, with 21.6% alive beyond 24 months. Better conditional survival observed at 6 or 12 months landmarks. BOR strongly predicted prolonged survival (HR 0.08; $P < 0.001$).

Conclusion:

This study supports weight-based dosing approach and demonstrates durable long-term survival in patients with advanced NSCLC, supporting pragmatic use of ICIs in resource-constrained settings.

1. Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of cases [1]. Outcomes following progression on the first-line platinum-based chemotherapy remain poor, with median survival rarely exceeding one year. The advent of immune checkpoint inhibitors (ICIs) (PD-1/PD-L1 inhibitors) has transformed the management of advanced NSCLC, even in the second-line setting, demonstrating durable responses and improved

survival as evident in CheckMate 017/057, KEYNOTE-010, and OAK [2–7]. ICIs, including nivolumab, pembrolizumab, and atezolizumab, have largely replaced chemotherapy as standard second-line therapy. These agents have shifted short-lived responses to the potential long-term survival seen in over 15% of patients, highlighting the potential for durable disease control [8]. Long-term follow-up from CheckMate 017/057 or KEYNOTE-010 trials has demonstrated that approximately 13–18% of patients treated with ICIs remain alive at 4–5 years [6, 9].

Despite these advances, ICIs adoption in real-world practice in low- and middle-income countries (LMIC) remains constrained by high costs and limited healthcare resources. Data from Tata Memorial Hospital, India, indicate that only around 2.8% of eligible patients received ICIs, underscoring the profound affordability gap [10]. In this context, optimizing dosing strategies without compromising efficacy is of critical importance.

ICIs like Nivolumab (a key PD-1 inhibitor) were initially approved at a weight-based dose (3 mg/kg) and later replaced by fixed dosing for logistical convenience. However, pharmacokinetic data suggested that fixed dosing may result in drug overexposure, particularly in patients with lower body weight, leading to unnecessary drug utilization and increased costs [9, 11–13].

Revisiting weight-based dosing may offer a pragmatic approach in resource-constrained settings, potentially reducing drug consumption (by aligning drug doses to patient body weight) while maintaining comparable efficacy and safety, and improving access to ICIs. However, real-world data on long-term outcomes with such strategies remain limited.

To address these challenges, we report a real-world analysis of Indian patients with advanced NSCLC treated with second-line ICIs, predominantly weight-based nivolumab (along with pembrolizumab and atezolizumab in fixed doses), following progression on chemotherapy. Building on our previously reported cohort of 64 patients [14], the present study includes extended follow-up and additional endpoints to provide more mature insights into long-term survival, treatment durability, and prognostic factors. We aim to generate context-specific data to support the rational use of immunotherapy in India.

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting checklist [15].

2. Materials and Methods

2.1 Study Design

This was a retrospective, real-world evidence study conducted at a single tertiary cancer centre in India. The data collection period spanned 5 years, with a cut-off date of 31 March 2025. This analysis builds upon our previously published cohort of 64 patients and now includes updated second-line ICIs outcomes with an expanded sample size and extended follow-up. ICIs regimens included nivolumab administered predominantly as weight-based dosing (3 mg/kg every 2 weeks), pembrolizumab (200 mg

every 3 weeks), or atezolizumab (1200 mg every 3 weeks) as per institutional practice. Data was extracted from electronic medical records and hospital information systems.

2.2 Study Population

Patients ≥ 18 years of age, of either sex, with histologically confirmed advanced NSCLC (squamous or non-squamous), who had received at least one prior line of platinum-based chemotherapy before initiation of second-line ICIs were selected for this study. All patients had documented PD-L1 expression; scoring was performed on tumor blocks using the concentrated mouse monoclonal antibody clone 22C3 (Dako) on Ventana benchmark. An Eastern Cooperative Oncology Group (ECOG) performance status (PS) was recorded for all patients and categorized as good PS (ECOG PS – 0,1,2) as PS 1 and poor PS (ECOG PS – 3,4) as PS 2 for subgroup analyses.

2.3 Study Objectives

The primary objective of the study was to evaluate overall survival (OS) and progression-free survival (PFS). The secondary objectives were to identify factors associated with treatment outcomes, assess long-term response, estimate conditional survival at predefined landmark timepoints, and evaluate the safety profile and the impact of subsequent lines of therapy on OS.

The study was approved by the Institutional Review Board (IRB) of Rajiv Gandhi Cancer Institute and Research Centre (RGCIRC), New Delhi, India. As this was a retrospective study using anonymized data, informed consent was waived by this IRB in line with the ICMR guidelines. The study was conducted in accordance with the ethical standards of the Institution and in accordance with the Declaration of Helsinki, and its subsequent amendments.

2.4 Statistical Analysis

Patient demographics and baseline characteristics were summarized using descriptive statistics. Continuous variables were reported as median, standard deviation, minimum, and maximum values. Categorical variables were expressed as counts and percentages. Survival outcomes (OS and PFS) were estimated using Kaplan–Meier methodology. PFS was defined as the duration from initiation of ICIs until documented disease progression or death from any cause, whichever occurred first. OS was defined as the time from initiation of ICIs to death from any cause. Patients alive or progression-free at the time of analysis were censored at the date of last follow-up. Sensitivity analysis was performed for OS. Survival distributions (OS and PFS) within different subgroups were compared using the two-sided log-rank test.

Univariate Cox proportional hazards regression was performed to evaluate the association between individual covariates and survival outcome. It was followed by Multivariate Cox regression, adjusting for all covariates, to estimate hazard ratios (HRs) with 95% confidence intervals (CIs).

Long-term responders were defined as patients with survival time ≥ 24 months. Predictors of long-term response and objective response were assessed using univariate and multivariate logistic regression models, with results presented as odds ratios (ORs).

A landmark analysis of OS was conducted to estimate conditional survival probabilities among patients who remained event-free at predefined time points (6 and 12 months) after initiating ICIs. Subsequent survival was calculated from each respective landmark (e.g., 12-month survival among patients alive at 6 months, and 24-month survival among patients alive at 12 months).

The impact of subsequent lines of systemic therapy on survival was assessed using a time-dependent Multivariate Cox regression model. A two-sided p-value of < 0.05 was considered statistically significant for all analyses. We used AI tool to improve English grammar and writing.

3. Results

3.1 Patient Characteristics

A total of 97 patients were included in this real-world analysis. The median age was 63 years (range, 27–82), with 61% aged ≥ 60 years. The cohort was predominantly male (86%) and smokers (75%), with non-squamous histology observed in 61% of patients. Prior to initiation of ICIs, 69% of patients had received one prior line of chemotherapy, while 31% had received ≥ 2 prior lines of chemotherapy. PD-L1 testing was positive in 56% of patients. Good performance status (PS1) (ECOG 0, 1, 2) was reported in 92% of patients. Extra-thoracic metastasis was present in 71% of patients; bone metastases (43%), liver metastases (12%), and brain metastases (27%). Next-generation sequencing (NGS) data were available for 53% of our patients, and all of them were EGFR, ALK, and ROS negative. Detailed baseline characteristics are presented in Fig. 1.

Of the 97 patients, 86 (89%) received nivolumab, 10 (10%) received atezolizumab, and 1 (1%) received pembrolizumab. 55 patients (57%) initiated ICIs within 9 months of diagnosis, while 42 (43%) received it after 9 months. The median number of immunotherapy cycles administered was 6 (range, 1–90), reflecting considerable variability in treatment duration. By the data cut-off, 95 patients (98%) had discontinued ICIs, with two patients continuing treatment and under follow-up. The median duration of ICIs treatment was 3.4 months (range, 0.6–55.4 months). Among the 95 patients who discontinued ICIs treatment, 50 (53%) received subsequent lines of therapy. The median duration of follow-up from initiation of ICIs to the data cut-off, including the period of further treatment, was 54.5 months (range, 7.2–104.1 months) for these patients.

3.2 Treatment Outcomes

The best overall response (BOR) to immunotherapy was partial response (PR) seen in 20 (20.6%) patients, stable disease (SD) in 20 (20.6%), and progressive disease (PD) in 57 (58.8%) patients, resulting in an objective response of 20.6% and disease control rate (DCR) of 41.2% (PR + SD).

In both univariate and multivariate logistic regression analysis, PD-L1 expression $< 1\%$ was significantly associated with lower odds of achieving an objective response as compared with those with PD-L1 $\geq 50\%$ (univariate OR 0.20, objective response as compared with those with PD-L1 $\geq 50\%$ (univariate OR

0.20; 95% CI: 0.06 to 0.60; $P = 0.003$; multivariate OR 0.15, 95% CI: 0.04 to 0.52; $P = 0.004$). Other subgroup analyses were not statistically significant.

The median PFS for the overall cohort was 3.6 months (95% CI: 2.5–4.6 months). The estimated 1-, 2-, 3-, and 4-year PFS rates were 17.5%, 8%, 4.6%, and 1.5%, respectively (Fig. 2).

Data was divided into different subgroups as given in Table 1. PFS, when compared within these different subgroups using the log-rank test, showed that patients with liver metastases (median, 1.9 vs 3.7 months; $P = 0.013$) and those with bone metastases (median, 2.5 vs 4.3 months; $P = 0.003$) had significantly shorter PFS than patients without involvement of these sites. All other subgroups, including squamous vs. non-squamous histology, PD-L1 categories, smoking history, etc., demonstrated comparable PFS.

On univariate Cox proportional-hazards regression, the absence of liver metastases (HR 0.46; 95% CI: 0.25 to 0.86) and bone metastases (HR 0.53; 95% CI: 0.34 to 0.81) were significantly associated with improved PFS (" $P < 0.05$ ") (Table 1 and Fig. 3).

Table 1
Univariate Cox Proportional Hazards Analysis of Clinical and Disease Characteristics for PFS

Disease Characteristics		Hazard Ratio	95% CI	P-value
Histology	Squamous cell carcinoma vs non-squamous cell carcinoma	0.95	0.63–1.44	0.816
PD-L1 Categories	Negative vs Positive	1.40	0.92–2.13	0.111
PD-L1 Categories (1)	1 to 49 vs 50 or More	1.07	0.61–1.86	0.817
	Less than 1 vs 50 or More	1.46	0.86–2.49	0.166
Smoking	No vs Yes	1.11	0.69–1.78	0.674
Liver Metastases	No vs Yes	0.46	0.25–0.86	0.014*
Brain Metastases	No vs Yes	1.21	0.76–1.93	0.420
Bone Metastases	No vs Yes	0.53	0.34–0.81	0.004*
Time to IO Initiation	Within 9 months vs After 9 months	0.98	0.65–1.48	0.933
Prior Lines of Chemotherapy	1st Line vs $\geq$ 2nd Line	1.23	0.79–1.92	0.358
ECOG	PS1 vs PS2	0.64	0.29–1.39	0.259
Extra-Thoracic Sites	No vs Yes	0.65	0.41–1.03	0.067
Number of Extra-Thoracic Sites	None vs Two or more	0.65	0.39–1.1	0.110
	Single vs Two or more	1.02	0.63–1.65	0.939
Pleural Effusion	No vs Yes	0.70	0.46–1.07	0.098
Mutation	No vs Yes	0.84	0.56–1.28	0.418

PD-L1, programmed death-ligand 1; IO, immunotherapy; ECOG, Eastern Cooperative Oncology Group; PS, performance status; CI, confidence interval.

The multivariate hazards model after adjusting for all relevant covariates, showed that ECOG PS, bone metastases, mutation, and brain metastases remained independent predictors of PFS. Patients without bone metastases had a 54% lower risk of progression (HR 0.46; 95% CI: 0.25 to 0.86; $P < 0.001$), good ECOG, PS 1 conferred a 63% lower risk of progression (HR 0.37; 95% CI: 0.16 to 0.88; $P = 0.025$), and also the patients with no gene mutation had 33% lower risk of progression. Paradoxically, the absence of brain metastases was associated with a higher risk of progression (HR 1.87; 95% CI: 1.08 to 3.24; $P = 0.026$) (Fig. 4).

In this study, the median OS was 10.6 months (95% CI: 7.7–18.4 months) in the overall cohort. The estimated 1-, 2-, 3-, and 4-year OS rates were 46%, 31.4%, 21.8% and 21.8%, respectively. At the data cut-off, deaths were reported in 70 patients, 15 patients were alive, and 12 were lost to follow-up. In a sensitivity analysis, the median OS after considering the worst-case scenario (patients who were lost to follow-up were considered dead instead of censoring) was 8.5 months (95% CI: 6.8–13.3 months) (Fig. 5).

Subgroup analysis by log-rank test showed that patients with liver metastases (median, 4.4 vs 11.1 months; $P = 0.046$) and those with poor ECOG, PS 2 (median, 2.6 vs 11.4 months; $P = 0.026$) had a significantly shorter median OS. All other subgroups demonstrated comparable OS.

In univariate Cox regression analysis, only ECOG PS was a significant predictor of OS, with patients having good ECOG, PS 1 demonstrating improved OS compared with those with poor ECOG, PS 2 (HR 0.41; 95% CI: 0.19 to 0.91; $P = 0.029$) (Table 2 and Fig. 6).

Table 2
Univariate Cox Proportional Hazards Analysis of Clinical and Disease Characteristics for OS

Disease Characteristics		Hazard Ratio	95% CI	P-value
Histology	Squamous cell carcinoma vs non-squamous cell carcinoma	1.32	0.82–2.12	0.255
PD-L1 Categories	Negative vs Positive	1.20	0.74–1.94	0.466
PD-L1 Categories (1)	1 to 49 vs 50 or More	1.00	0.52–1.9	0.990
	Less than 1 vs 50 or More	1.19	0.65–2.19	0.570
Smoking	No vs Yes	1.24	0.72–2.12	0.441
Liver Metastases	No vs Yes	0.51	0.26–1	0.051
Brain Metastases	No vs Yes	1.36	0.77–2.38	0.290
Bone Metastases	No vs Yes	0.67	0.41–1.09	0.107
Time to IO Initiation	Within 9 months vs After 9 months	1.22	0.76–1.97	0.413
Prior Lines of chemotherapy	1st Line vs ≥ 2nd Line	1.36	0.8–2.31	0.255
ECOG	PS1 vs PS2	0.41	0.19–0.91	0.029*
Extra-Thoracic Sites	No vs Yes	0.59	0.34–1.02	0.060
Number of Extra-Thoracic Sites	None vs Two or more	0.62	0.33–1.15	0.129
	Single vs Two or more	1.09	0.63–1.89	0.753
Pleural Effusion	No vs Yes	0.70	0.43–1.14	0.154
Mutation	No vs Yes	1.45	0.88–2.39	0.143

PD-L1, programmed death-ligand 1; IO, immunotherapy; ECOG, Eastern Cooperative Oncology Group; PS, performance status; CI, confidence interval.

On multivariate analysis, ECOG PS, extra-thoracic metastases, and brain metastases were independent predictors of overall survival. Good ECOG, PS 1 was associated with a 67% lower risk of death (HR 0.33; 95% CI: 0.14 to 0.77; P = 0.011), and absence of extra-thoracic metastases reduced the risk of mortality by 55% (HR 0.45; 95% CI: 0.23 to 0.91; P = 0.027). Consistent with PFS, the absence of brain metastases was paradoxically associated with a higher risk of death (HR 2.29; 95% CI: 1.17 to 4.46; P = 0.015).

3.2.1 Long Term Survivors

A total of 21.6% of patients survived for 24 months or longer following initiation of ICIs. In both the univariate and multivariate logistic regression analysis, the absence of bone metastases was significantly associated with long-term survival, conferring approximately a three-fold higher likelihood of being a long-term survivor compared with patients who had bone metastases (ORs 3.04 -univariate and 3.77-multivariate analyses).

3.2.2 Landmark Analysis

Conditional survival analysis highlighted that early disease control strongly correlated with long-term survival outcomes. At 6 months, 60 patients (62%) were alive, and at 12 months, 39 patients (40%) remained alive. Among patients alive at 6 months, the probability of surviving an additional 12, 24, and 30 months was 57.6%, 37.5%, and 32.7%, respectively. Among those alive at 12 months, the probability of surviving an additional 12, 18, and 24 months was 68.2%, 54.5%, and 47.5%, respectively. Conditional survival probabilities improved markedly for patients' event-free at both 6- and 12-month landmarks (Fig. 7).

3.2.3 Impact of Subsequent Systemic Therapy

Among the 50 patients (53%) who received further systemic therapy after ICIs discontinuation, SD/PR was achieved in 58%, while PD occurred in 42%. Univariate analysis indicated that receipt of further systemic therapy after ICIs discontinuation did not significantly affect OS (HR 1.49; 95% CI: 0.86 to 2.55; P = 0.147). A time-dependent multivariate cox regression after adjusting for all other covariates showed that the further treatment had a 28% lower hazard of death compared to those who did not receive it, although this was not statistically significant (HR 0.72; 95% CI: 0.37 to 1.39; P = 0.336). The BOR to ICIs was a strong predictor of survival. Patients achieving PR or SD on ICIs had significantly lower risk of death (improved OS) compared with those with PD (HR 0.08; 95% CI: 0.03 to 0.19; P < 0.001) (Fig. 8).

3.2.4 Safety Profile

In this study, overall, 36.1% of patients experienced at least one immune-related adverse event (irAE), with endocrine and dermatologic toxicities being the most frequent. The majority of events were grade 1–2 in severity, while severe irAEs ($\geq$ grade 3) were seen in 11 patients (11.3%). No new safety signals were identified. Subgroup analyses demonstrated that the incidence of irAEs was comparable across age groups and sex, indicating consistent tolerability across patient subsets. irAEs were generally

manageable, with no treatment-related deaths reported, and most events resolved with standard immunosuppressive therapy. Thirteen patients (27.6%) required oral corticosteroids, and one patient required intravenous steroids for management.

When stratified by irAEs occurrence, it was observed that patients who developed any irAE demonstrated significantly improved outcomes, with a longer median PFS and OS compared to those who did not experience irAEs (log-rank “P < 0.05” for both comparisons) (Table 3). In univariate Cox regression, the presence of irAEs was associated with a reduced risk of disease progression and death (Fig. 9).

Table 3
Progression- Free Survival and Overall Survival by irAEs

PFS	irAEs	n	Events	Median (months) (SE)	95% CI	P-value
	Yes	35	34 (97.1%)	7.7 (2.37)	3.8–13.1	0.005*
	No	62	61 (98.4%)	2.7 (0.854)	2.1– 4.2	-
OS	Yes	35	26 (74.3%)	20.0 (11.73)	10.9–56.9	0.01*
	No	62	44 (71.0%)	8.2 (2.07)	5.2–13.3	-

PFS, progression free survival; OS, overall survival; irAE, immune-related adverse events; CI, confidence interval.

4. Discussion

This retrospective real-world study of 97 patients, with approximately five years of follow-up provides valuable insights into the use of ICIs in routine clinical practice. Our findings demonstrate clinically meaningful long-term survival outcomes, response durability, and key prognostic factors that may guide clinical decision-making in routine practice. In lieu of the fact that very few patients from India were a part of clinical trials and even fewer were able to receive immunotherapy, our findings emphasize the value of RWE in complementing the clinical trial data and address the unmet needs in diverse populations.

An important aspect of this study is the evaluation of weight-based dosing in a real-world setting in routine clinical practice in India, where average body weight is typically lower than that in Western populations, fixed dosing may lead to unnecessary drug utilization and increased treatment costs. Nivolumab, which constituted the majority of our treatment group, was administered at a dose of 3 mg/kg every 2 weeks. This approach provided adequate exposure with optimal efficacy and tolerability, particularly in patients with lower body weight.

Consistent with prior pivotal studies (CheckMate 017 and CheckMate 057 trials), our findings suggest that revisiting weight-based dosing can achieve comparable clinical outcomes while offering the

potential for significant cost savings. This approach may improve affordability and expand access to ICIs in resource-constrained settings without compromising efficacy [4, 5].

The survival outcomes (median PFS of 3.6 months and OS of 10.6 months) in our study are broadly consistent with those reported in pivotal phase III clinical trials such as CheckMate 017, CheckMate 057, and OAK [4, 5, 7].

Specifically, long term survival achieved at a 4-year was 15.5% [11] in the OAK trial and at 5 years was 13.4% in the pooled Checkmate 017/057 population [9]. These findings align with the “long tail” survival phenomenon seen in the long-term follow-up.

Being a real-world setting, our study included a broader, less-selected population than the pivotal trials – 8% of patients had poor ECOG, PS 2, 27% had brain metastases, and 31% had received ≥ 2 prior chemotherapy lines – groups often excluded from clinical trials. Despite these adverse baseline characteristics, survival outcomes were consistent with phase III studies, supporting the real-world effectiveness and generalizability of immunotherapy in this setting.

Several real-world studies, both global and from India, have evaluated the use of ICIs in NSCLC. Large registry studies such as the French CLINIVO cohort (n = 902) reported 5 years PFS and OS rates as 4% and 10%, respectively [12] corroborating the durability and feasibility of ICIs in routine practice. In the study by Aydin et al., the median PFS was 4.7 months, and factors such as ECOG performance status, PD-L1 expression $> 1\%$, were identified as significant prognostic indicators, similar findings we observed in our study also [13].

In India, available experiences, though very limited, are broadly supportive. The multicentric CRSF 2020-01 study, which included 26% NSCLC cases, reported a pooled response rate of 24% and median OS of 10 months [16]. Noronha *et al.* described outcomes in 76 NSCLC patients treated with ICIs, highlighting evolving PD-L1 testing practices and the use of both flat and weight-based nivolumab dosing [17]. A study from a single centre in Northern India, focused on the safety profile of immunotherapy in a second-line setting [18]. Building on these studies, our study provides a focused evaluation of second-line ICIs exclusively in advanced NSCLC with long term extended follow-up.

One of the key observations of our study is the substantial proportion of long-term survivors, with over 21.6% of patients surviving beyond 24 months, a result similar to long-term survival rates (23–29%) reported in pivotal CheckMate trials of nivolumab. Our conditional survival analysis further demonstrated that patients who survived the initial 6–12 months had significantly improved survival probabilities at subsequent time points, highlighting the importance of early disease control by ICIs in predicting long-term benefit.

Our analysis also identified key prognostic factors that influence outcomes. Poor performance status (ECOG PS 2), and the presence of bone and liver metastases were associated with inferior PFS and OS. These findings are consistent with literature [9, 16, 17], indicating that disease burden and functional

status are critical determinants of immunotherapy outcomes. One interesting but paradoxical observation from our analysis is that patients with CNS metastases did not fare as poorly as anticipated. This may be attributable to the use of cranial radiotherapy (whole-brain radiotherapy or stereotactic radiosurgery), which, in combination with ICIs, may have mitigated the adverse prognostic impact of brain metastases. Traditionally, brain involvement in NSCLC has been associated with dismal outcomes; [19] however, our findings suggest that effective use of advanced local therapies in combination may reduce the adverse prognostic impact of brain metastases.

Furthermore, PD-L1 expression retained its predictive role in response, with higher expression associated with improved response rates. This finding is similar to those observed in KEYNOTE-010 and other global studies, which confirm the correlation between PD-L1 positivity and immunotherapy efficacy [6, 20–22]. Notably, numerically favourable outcomes were also observed in PD-L1–negative (TPS 0%) and low-expressing (TPS 1–49%) subgroups, although the statistical significance was not observed for PFS and OS. This suggest that PD-L1 negativity alone should not preclude immunotherapy in appropriate patients.

irAEs were documented in 36% of patients, which were predominantly Grade 1–2 endocrine and dermatologic toxicities. This safety profile was consistent with established data, were manageable, and with no new safety signals. Notably, the occurrence of irAEs was associated with improved PFS and OS, suggesting that immune activation underlying these events may reflect enhanced antitumor efficacy. This association has been consistently demonstrated across tumor types and real-world cohorts [23–25].

The study has several limitations inherent to its retrospective and real-world design. Being a single-centre study, our findings may not be fully generalizable to the broader Indian NSCLC population. As with most retrospective datasets, unmeasured confounders and heterogeneity in prior lines of therapy may have impacted the outcomes. The relatively modest sample size and lack of comparative arm may have restricted the ability to detect small differences in subgroup analyses.

Despite these limitations, the study provides one of the most comprehensive real-world datasets from India, with over 5 years of follow-up, evaluation of weight-based dosing regimen and long-term safety of ICIs, offering valuable insights directly relevant to clinical practice.

5. Conclusion

To conclude, this real-world study reinforces that the use of second-line ICIs is both effective and feasible in Indian patients with advanced NSCLC. This study further supports weight-based dosing approach and demonstrates durable long-term survival benefits, which are particularly relevant in resource-constrained settings. Our findings support the continued integration of ICIs into treatment strategies and highlight the importance of using tailored context-specific approaches to optimize outcomes and improve access in India and other resource-constrained settings. Together, these data

contribute to the growing body of evidence supporting immunotherapy as a transformative standard of care in the real-world scenario outside of trial populations.

Declarations

Ethics Approval and Accordance Statement

The study was approved by the Institutional Review Board of Rajiv Gandhi Cancer Institute and Research Centre (RGCIRC), New Delhi, India and was conducted in accordance with the ethical standards of the Institution and in accordance with the Declaration of Helsinki and its subsequent amendments (IRB approval number- RES/SCM/68/2025/44).

Consent to Participate

Since anonymized data was extracted retrospectively from electronic medical records and hospital information systems for analysis and publication, the requirement for informed consent was not required and was waived by the Institutional Review Board (IRB) of Rajiv Gandhi Cancer Institute and Research Centre (RGCIRC), New Delhi, India, in line with the ICMR guidelines.

Consent to Publish

Not applicable.

Accordance Statement

The study was conducted in accordance with the ethical standards of the Institution and in accordance with the Declaration of Helsinki and its amendments.

Competing Interests

The authors declare no competing interests.

Funding

No funding was received for this study.

Author Contribution

U.B., M.B. and M.I. contributed to the conception and design of the study. U.B. provided administrative support. U.B., S.C., S.N., A.P., A.M., K.C., and L.D. provided study materials or patients. B.A., M.B., M.S.,

A.D., R.S., S.C., S.N., A.P., K.C., and L.D. collected and assembled data. M.B., M.I., and A.M. analyzed and interpreted the data. All authors contributed to writing the manuscript and approved the final version.

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Data Availability

The data will be shared upon reasonable requests after institutional ethics committee approval.

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Figures

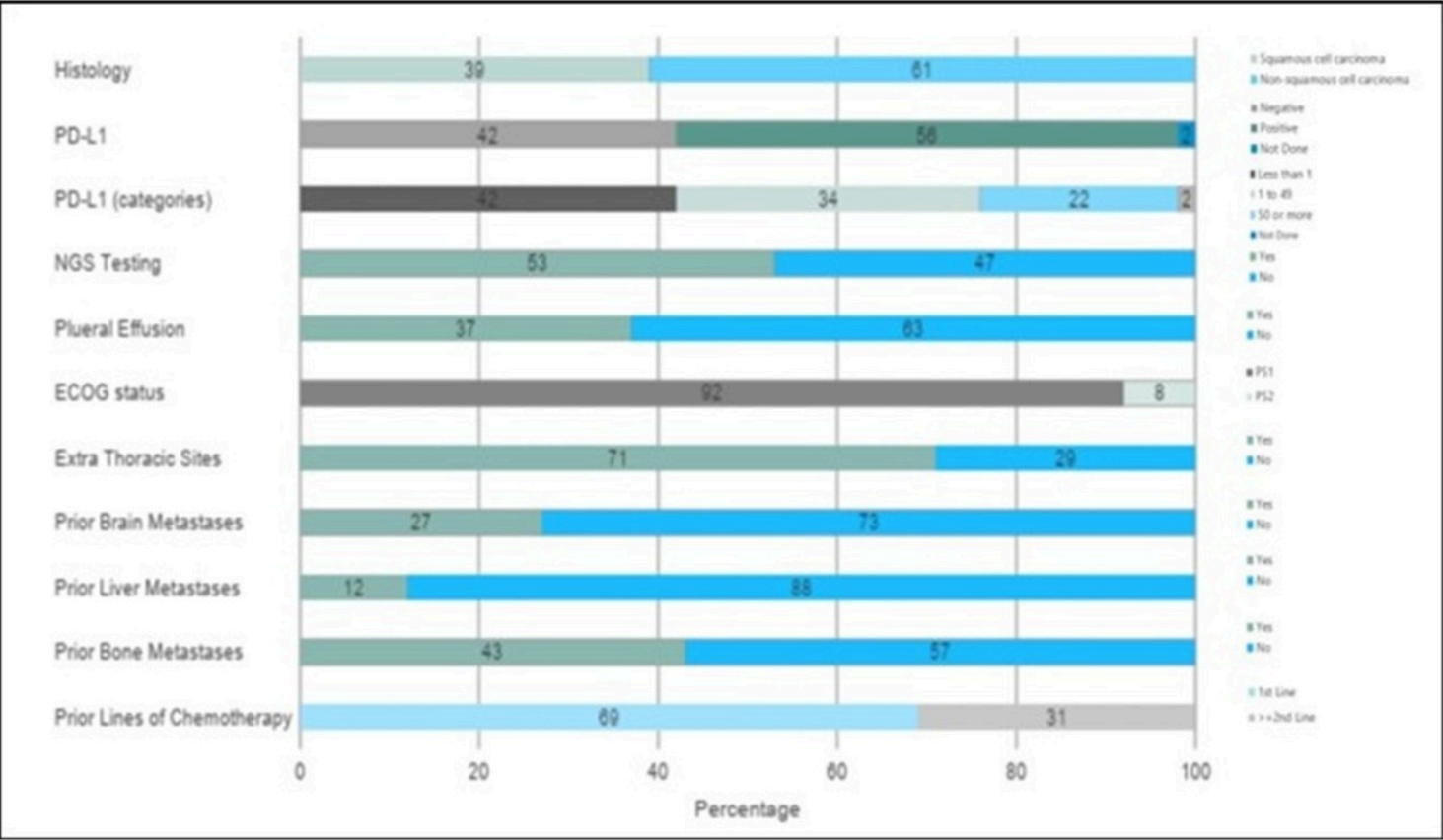


Figure 1

Baseline Clinical Characteristics of Patients. PD-L1, programmed death-ligand 1; NGS, Next-generation sequencing; ECOG, Eastern Cooperative Oncology Group; PS, performance status.

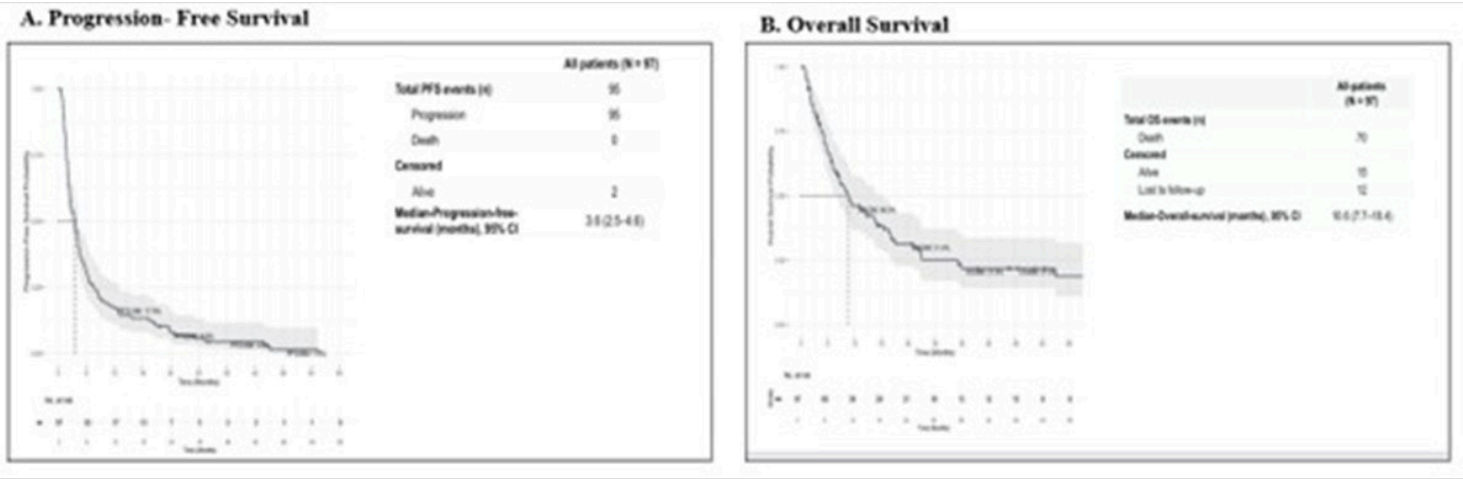


Figure 2

Kaplan–Meier Curve for Progression-Free Survival. Median PFS of 3.6 months. Shaded areas represent 95% confidence intervals, and numbers at risk are displayed below the x-axis. PFS, progression-free survival; CI, confidence interval.

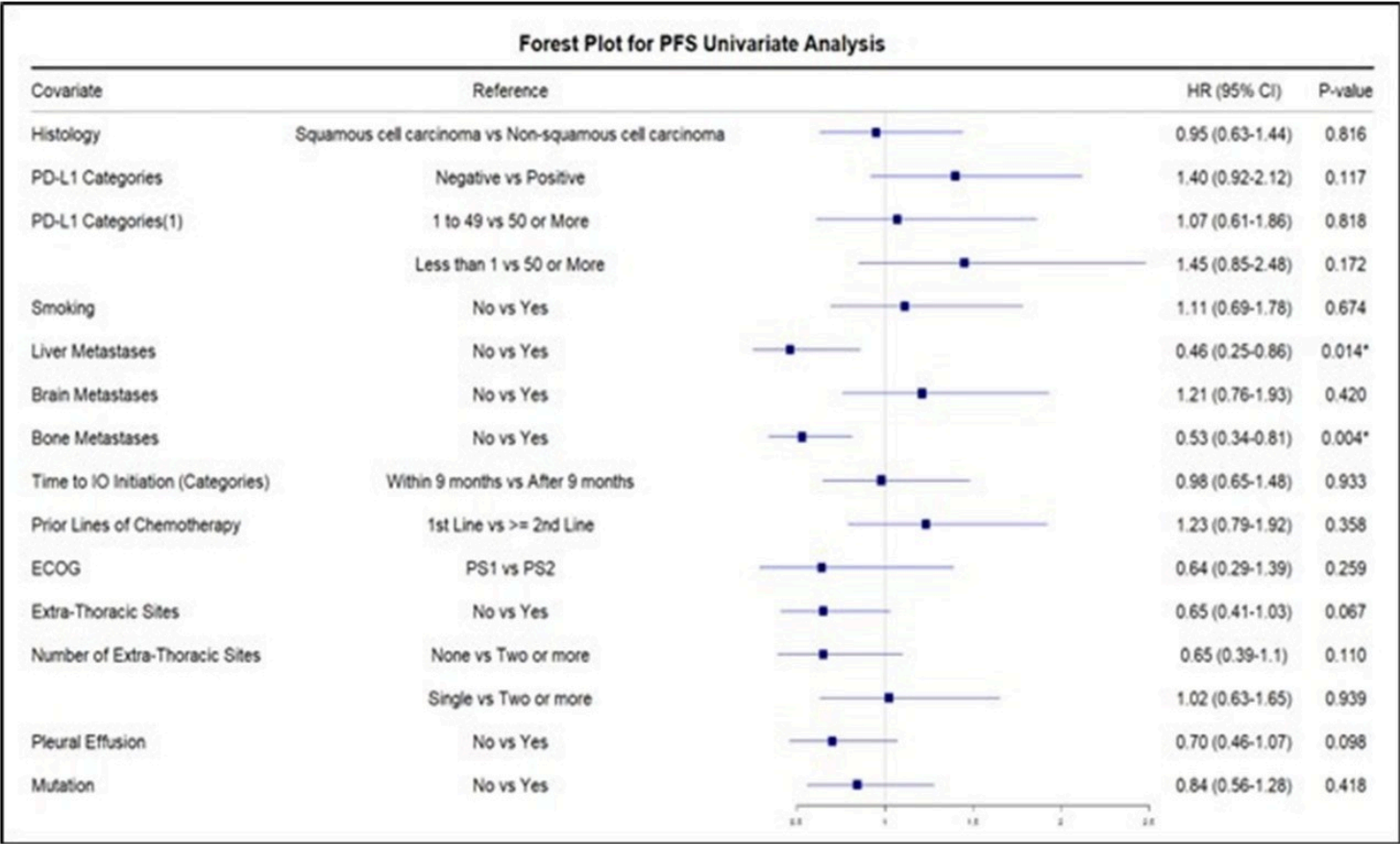


Figure 3

Forest Plot for Univariate Analysis of Progression- Free Survival. PD-L1, programmed death-ligand 1; IO, immunotherapy; ECOG, Eastern Cooperative Oncology Group; PS, performance status; HR, hazard ratio; CI, confidence interval.

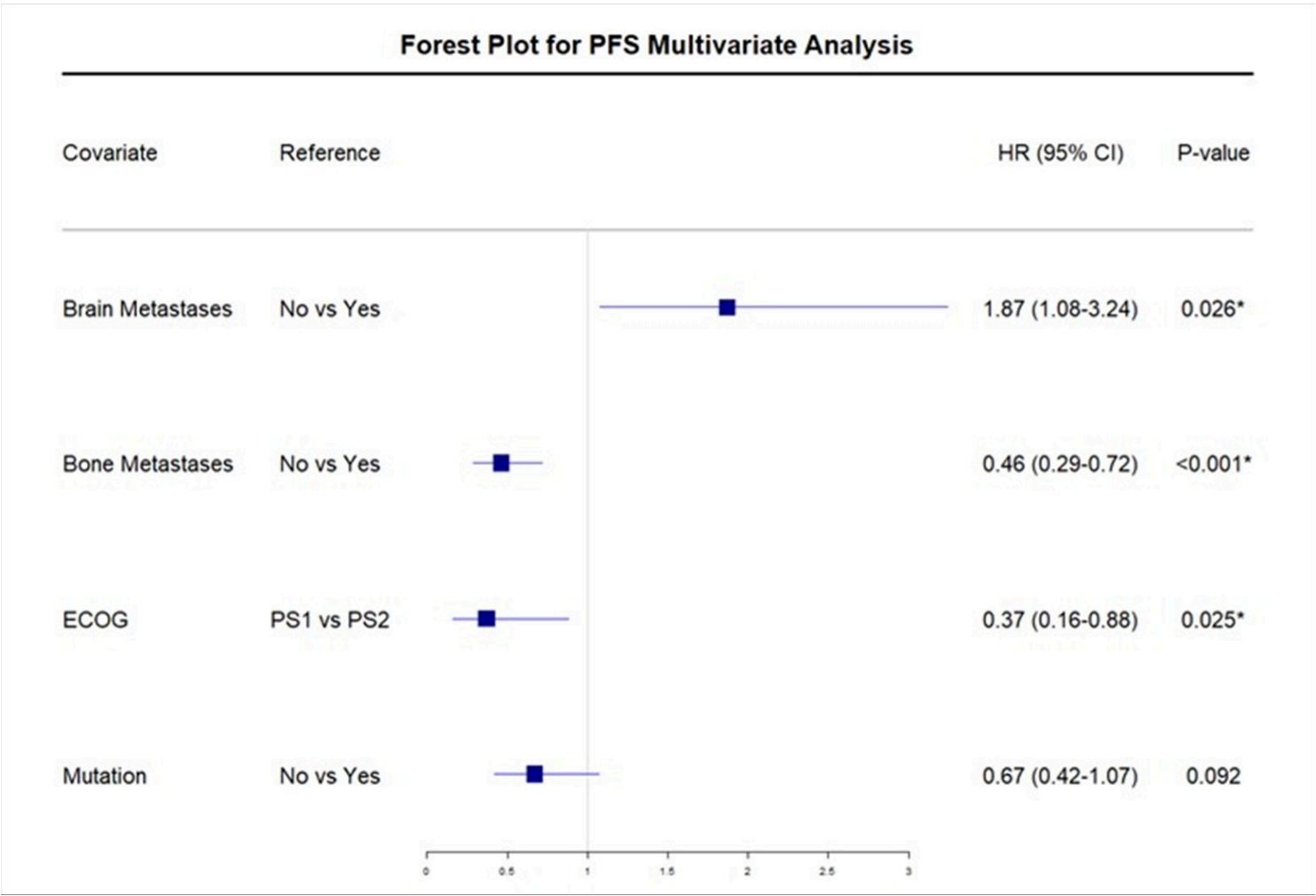


Figure 4

Forest Plot for Multivariate Analysis of Progression Free Survival. Hazard ratios (HRs) with 95% confidence intervals (CIs) are shown for covariates identified as independent predictors of PFS. Bone metastases and ECOG PS (PS1 vs PS2) were significantly associated with improved PFS, while absence of brain metastases was associated with worse PFS; mutation status was not statistically significant. PFS, progression-free survival; ECOG, Eastern Cooperative Oncology Group; PS, performance status; HR, hazard ratio; CI, confidence interval.

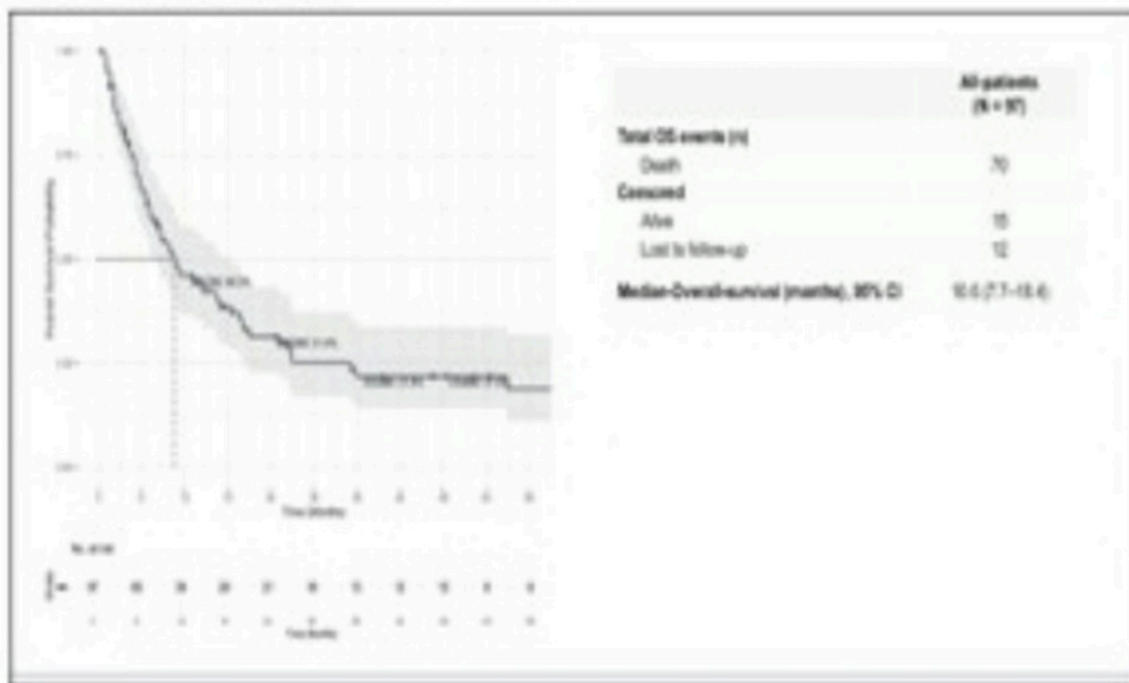


Figure 5

Kaplan–Meier Curve for Overall Survival. Median OS of 10.6 months. Shaded areas represent 95% confidence intervals, and numbers at risk are displayed below the x-axis. OS, overall survival; CI, confidence interval.

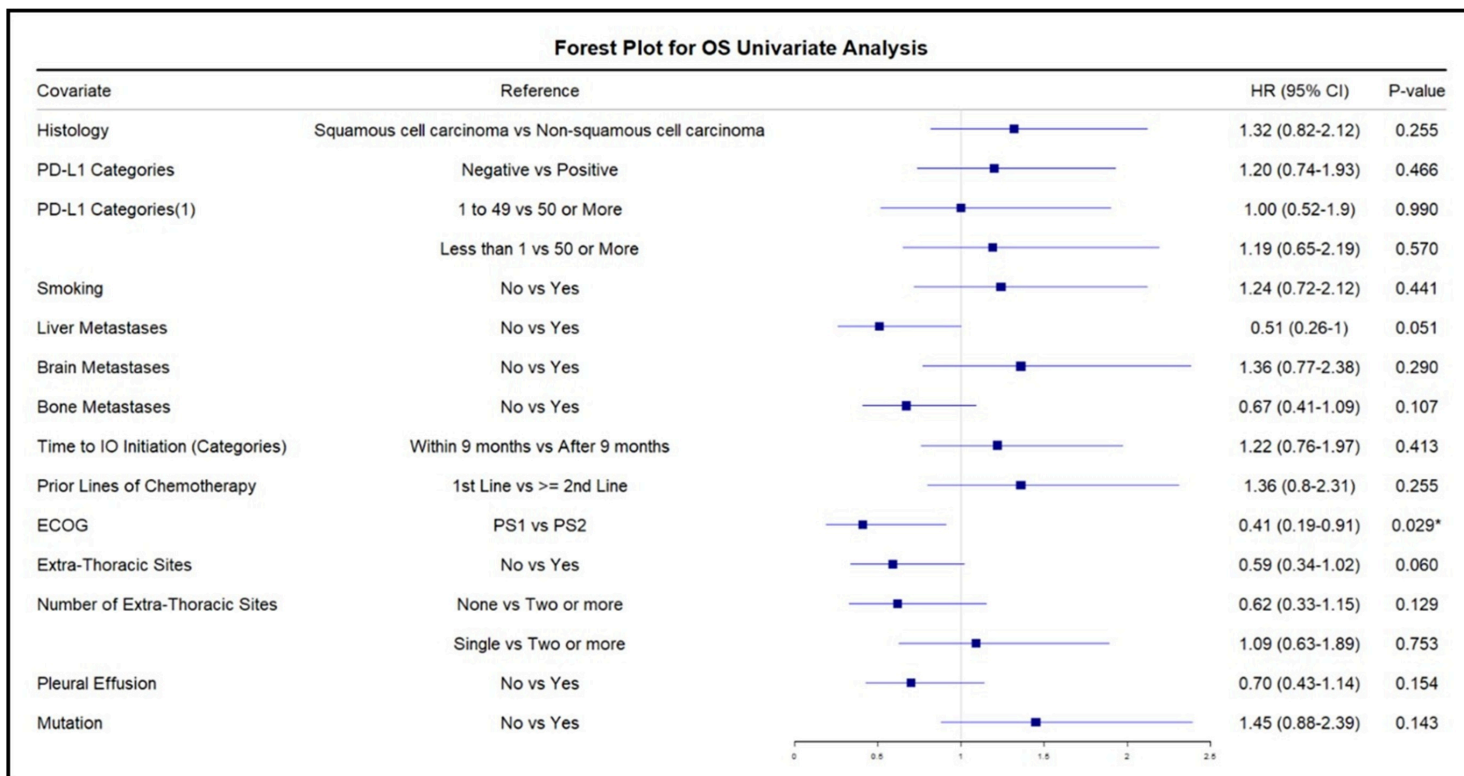


Figure 6

Forest Plot for Univariate Analysis of Overall Survival. Hazard ratios with 95% confidence intervals are shown for various covariates. ECOG performance status (PS1 vs PS2) was significantly associated with OS. PD-L1, programmed death-ligand 1; IO, immunotherapy; ECOG, Eastern Cooperative Oncology Group; PS, performance status, HR, hazard ratio; CI, confidence interval.

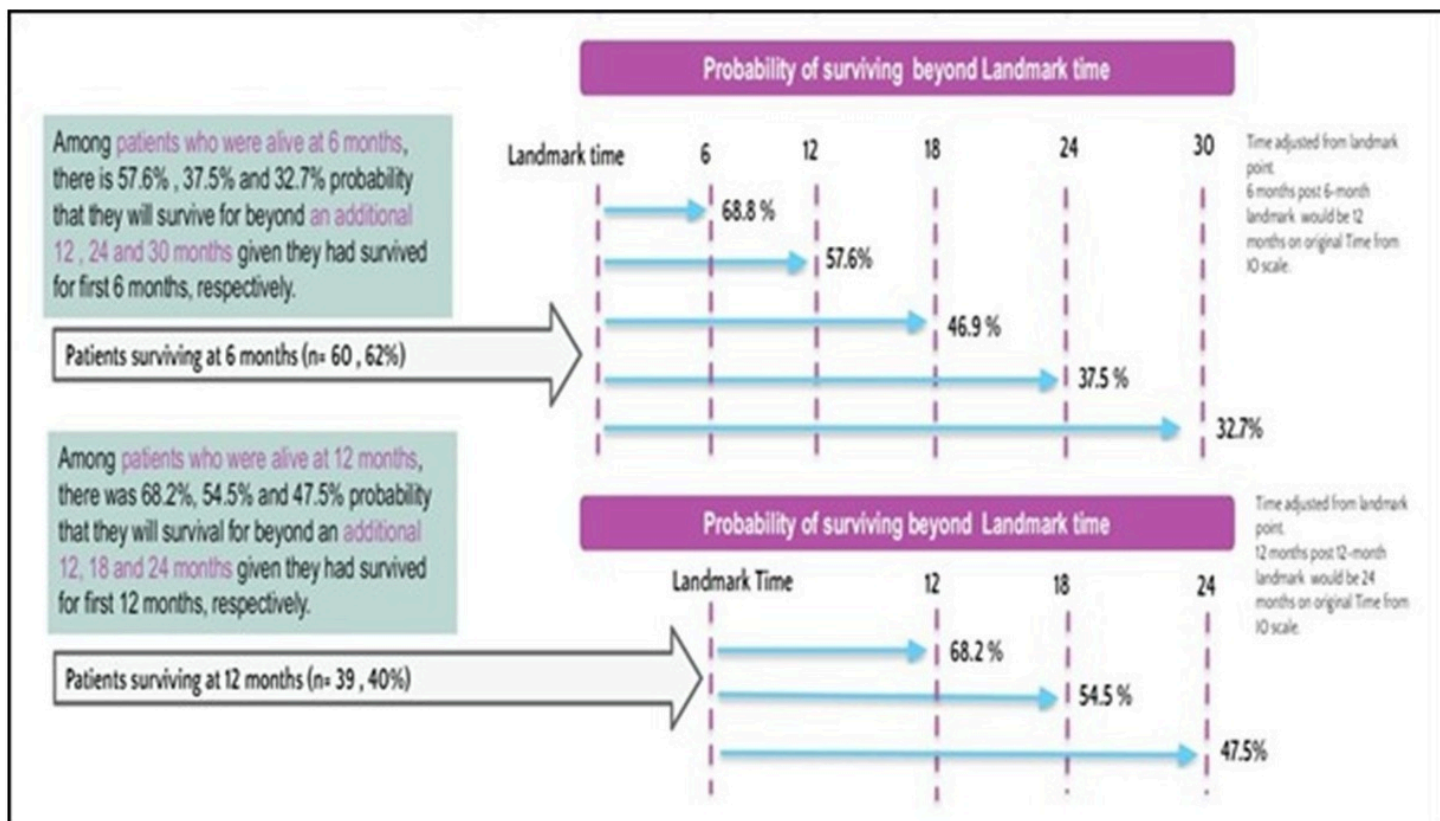


Figure 7

Landmark Analysis. Analysis shows probabilities of surviving beyond the landmark time of 6 and 12 months. IO, immunotherapy.

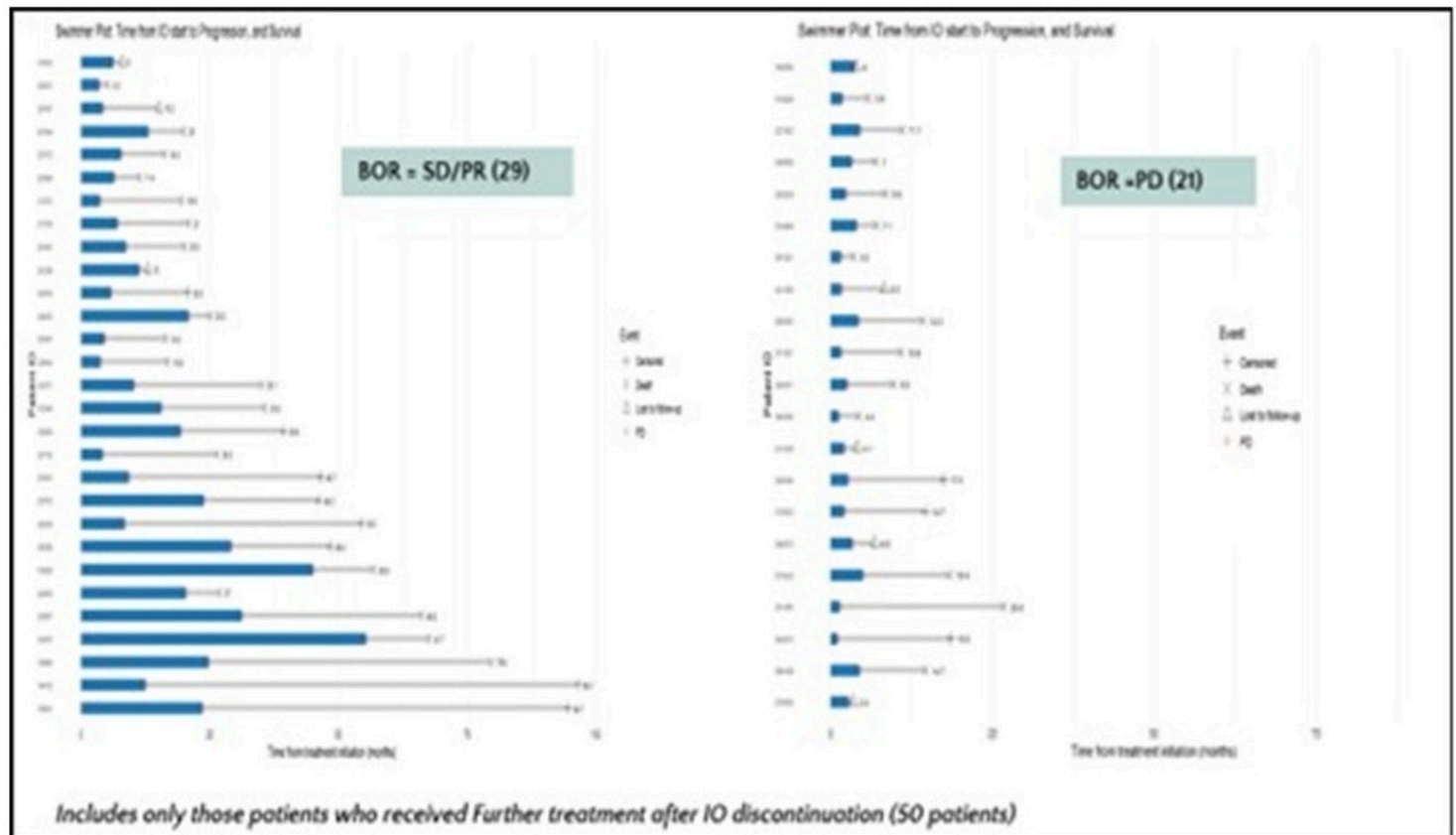


Figure 8

Swimmers Plot: Time from IO start to Progression and Survival. IO, immunotherapy; BOR, best observed response; SD, stable disease; PD, progressive disease; PR, partial response.

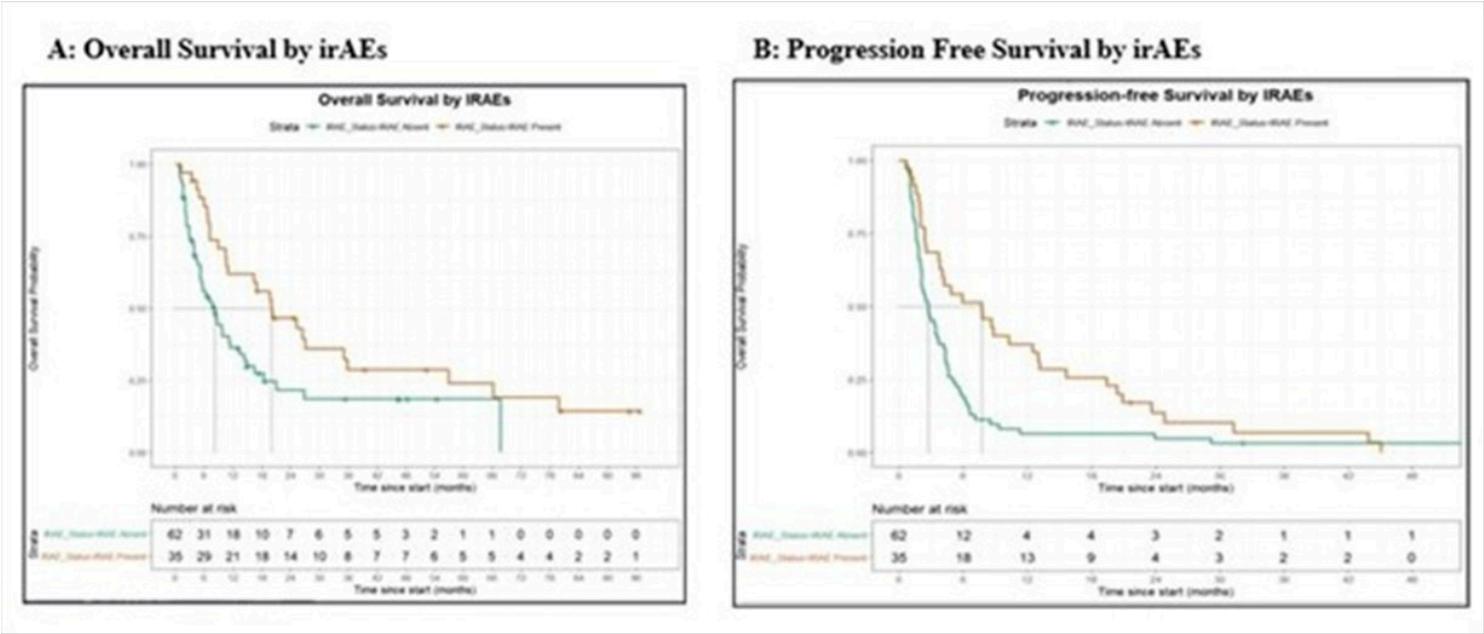


Figure 9

Overall Survival and Progression- Free Survival by irAEs. irAEs, immune-related adverse event.