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Value of local therapy in unresectable non-small cell lung cancer receiving immune checkpoint inhibitor-based treatment: a retrospective study

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Abstract

Background: Immune checkpoint inhibitors (ICIs) have transformed systemic therapy for unresectable epidermal growth factor receptor (EGFR) mutation-negative non-small cell lung cancer (NSCLC). However, the role of complementary radical local therapy (LT) in locally advanced NSCLC (LA-NSCLC) receiving ICI-based therapy remains unclear. We evaluated recurrence patterns, survival outcomes, and subgroups benefiting from LT.

Methods: This retrospective study included 206 patients with unresectable NSCLC receiving ICI-based systemic therapy, divided into radical LT and non-LT groups. Of the 206 patients, 124 received radical LT combined with ICIs and 82 received ICI-based therapy without local intervention. Median follow-up was 40.4 months. Clinicopathological characteristics, recurrence patterns, and survival outcomes were compared. Multivariate Cox regression and subgroup analyses identified prognostic factors and populations benefiting from LT.

Results: Overall recurrence rates were comparable; LT was associated with delayed recurrence, less early locoregional relapse, and more isolated distant metastasis. Median progression-free survival (PFS) and overall survival (OS) were significantly longer in the LT group. Radical LT was an independent favorable prognostic factor for PFS and OS. Benefits were more prominent in patients with squamous cell carcinoma, stage IIIB–IIIC disease, programmed death-ligand 1 (PD-L1) tumor proportion score of 0–49%, initial stable or progressive disease, and fewer ICI cycles.

Conclusions: In summary, radical LT may delay progression and modify recurrence patterns in unresectable NSCLC receiving ICI-based therapy. Histology, PD-L1 expression, disease stage, and initial immunotherapy response may help identify candidates for multimodal therapy.

Keywords

locally advanced non-small cell lung cancer, immune checkpoint inhibitor, local therapy, recurrence patterns, time to recurrence, overall survival

Background

Unresectable epidermal growth factor receptor (EGFR) mutation-negative non-small cell lung cancer (NSCLC) represents a highly heterogeneous disease with diverse tumor burden, metastatic risk and clinical outcomes [1], and its optimal treatment strategy has long been a core focus of thoracic oncology research [2]. Prior to the immunotherapy era, concurrent chemoradiotherapy was the standard of care for unresectable advanced NSCLC [3]. The PACIFIC trial established consolidation durvalumab as the global standard of care after definitive concurrent chemoradiotherapy, increasing the 5-year overall survival (OS) rate from approximately 28% to 42.9% [4]. These findings demonstrate that consolidative immunotherapy following chemoradiotherapy significantly prolongs patient survival. Chemoradiotherapy and immunotherapy are the standard treatment regimens for this population.

Nevertheless, in real-world clinical practice, a considerable subset of patients cannot complete the PACIFIC treatment regimen. Contributing factors include poor physical tolerance, unacceptable chemoradiation-related toxicities, underlying comorbidities, financial constraints, and patient refusal of concurrent chemoradiotherapy, rendering them ineligible for this standard curative strategy. Immune checkpoint inhibitor (ICI)-based systemic therapy is the primary treatment option for these patients.

Against this real-world background, local therapy including thoracic radiotherapy and surgical resection has emerged as a promising complementary intervention for patients receiving ICI-based systemic treatment [5]. Local therapy can eradicate macroscopic intrathoracic lesions and induce immunogenic cell death, which may synergize with ICIs to potentiate systemic antitumor immunity [6]. However, multiple critical knowledge gaps remain. First, most prospective clinical evidence was obtained from PACIFIC trials. It remains uncertain whether local therapy translates into survival benefits for patients who cannot undergo the standard PACIFIC chemoradiotherapy plus consolidation immunotherapy protocol. Second, how local therapy reshapes tumor failure trajectories has not yet been fully clarified, including whether it suppresses locoregional recurrence or modifies the timing of subsequent distant metastases. Third, the survival gains from combined local-ICI therapy were not consistent across all individuals. Sufficient subgroup evidence is lacking to identify optimal candidates, and the modulatory effects of histology, programmed death-ligand 1 (PD-L1) expression, baseline disease stage, and initial immunotherapeutic response require further

validation. Furthermore, the independent prognostic effect of radical local therapy combined with ICI-based treatment warrants confirmation in a real-world cohort.

To address these unmet clinical needs, we performed a retrospective cohort study of 206 patients with NSCLC receiving ICI-based systemic therapy, many of whom were not eligible for standard PACIFIC-type treatment. We aimed to compare recurrence-metastasis patterns, progression-free survival (PFS), and OS between patients who received local therapy and those treated with ICI-based systemic treatment. Multivariate Cox regression was applied to identify independent prognostic factors, and stratified subgroup analyses were conducted to explore population-level heterogeneity in survival benefits. This study aimed to provide real-world clinical evidence for multimodal treatment selection and support individualized clinical decision-making for patients receiving immunotherapy.

Methods

Study design and participant details

Patients diagnosed with histologically confirmed unresectable EGFR mutation-negative NSCLC at our institution between January 2021 and January 2023 were retrospectively screened. The inclusion criteria were as follows: (1) no radiologically or pathologically confirmed distant metastasis (M0) prior to initiation of ICI therapy; (2) receipt of at least 2 cycles of PD-1/PD-L1 inhibitor monotherapy or chemoimmunotherapy; and (3) availability of complete baseline clinicopathological, treatment, imaging, and long-term follow-up data. The exclusion criteria were as follows: (1) stage IV metastatic disease at initial diagnosis; (2) incomplete follow-up with loss to follow-up within 12 months of ICI initiation; and (3) concurrent malignant tumors of other organs.

All enrolled patients were categorized into two study groups:

1. Local therapy group (LT group): Received radical pulmonary resection or definitive thoracic radiotherapy targeting the primary lung lesions and metastatic mediastinal/hilar lymph nodes before, during, or after ICI treatment.

2. Non-local therapy group (Non-LT group): Received systemic ICI-based therapy only, without any radical surgical or radiation ablation of the intrathoracic tumor lesions.

institutional review board approved this retrospective observational study, and the requirement for written informed consent was waived owing to the use of de-identified clinical data. This study was conducted in compliance with the principles of the Declaration of Helsinki.

Clinical data collection

The collected baseline variables included patient age, sex, smoking history, Eastern Cooperative Oncology Group (ECOG) performance status, histological subtype (squamous cell carcinoma, adenocarcinoma, and rare NSCLC), clinical TN stage, PD-L1 tumor proportion score (TPS), baseline tumor burden, and ICI treatment regimen (ICI monotherapy or platinum-based chemoimmunotherapy). Treatment-related data included the modality and timing of local intervention, total cycles of immunotherapy, and occurrence of grade 3 immune-related adverse events (irAEs).

Surveillance and Recurrence Definition

Chest and abdominal contrast-enhanced computed tomography (CT) was performed every 3 months for the first 2 years, every 6 months from year 3 to year 5, and annually after 5 years. Routine brain magnetic resonance imaging (MRI) was performed every 6 months during the first 2 years. Positron emission tomography-computed tomography (PET-CT) was performed in patients with elevated tumor markers or suspicious lesions on routine CT/MRI. Tumor recurrence was defined as pathological biopsy confirmation or consistent progressive imaging findings meeting the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria. The time to recurrence (TTR) was calculated from the date of completion of curative ICI-based comprehensive treatment to the first radiological or pathological diagnosis of progressive disease.

Statistical analysis

All statistical analyses were performed using SPSS 26.0 and R 4.2 software. Categorical variables are presented as counts and percentages and were compared using the chi-square test or Fisher's exact test, as appropriate. Kaplan-Meier survival curves were generated for TTR, PFS, and OS, and intergroup survival differences were assessed using the log-rank test. Univariate Cox regression was first performed to screen for potential prognostic factors with $p < 0.1$, and variables with statistical significance were incorporated into multivariate Cox proportional hazards regression models to identify independent prognostic predictors. Two-sided p-values < 0.05 were considered statistically significant.

Results

Baseline clinicopathological characteristics

In total, 206 eligible patients with unresectable NSCLC receiving ICI therapy were included in the final analysis with complete follow-up data (Table 1); 124 patients underwent local treatment, including surgery and radiotherapy. The median age of the entire cohort was 65.6 years (range, 35–85 years). Majority of the study population was male (91.3%), and most patients had a history of heavy smoking. Squamous cell carcinoma was the most common histologic type (63.6%). Most baseline covariates, including age, sex, smoking history, histological subtype, PD-L1 expression distribution, clinical American Joint Committee on Cancer (AJCC) stage, median number of immunotherapy cycles, and incidence of irAEs were well balanced between the two cohorts, with all intergroup $p > 0.05$. The only statistically significant baseline disparity was in the category of ICIs administered ($p = 0.012$); all patients without local therapy received PD-1 monotherapy, whereas 7.3% of patients receiving combined local treatment were treated with PD-L1 inhibitors. No obvious imbalance was detected in disease burden or tumor biomarkers, which minimized major baseline bias and supported credible subsequent comparative analyses of recurrence and survival endpoints between the two treatment strategies.

Recurrence and metastatic patterns stratified by local therapy

Follow-up data were evaluated for all 206 enrolled patients. Median follow-up duration for the entire cohort was 40.4 months. The recurrence-related outcomes stratified by radical local therapy are shown in Table

2. Among the 206 patients evaluated, overall recurrence/metastasis rate was 55.3% (114/206). Despite the comparable overall recurrence rates between patients who received local therapy and those who did not (LT group vs. Non-LT group, 64.2% vs. 74.7%), a notable divergence was observed in the failure modes. Stratified by recurrence timing, early relapse (≤6 months) was far less frequent in the LT group (10.1% of all recurrent cases) than in the Non-LT group (28.9%), whereas mid-term recurrence (6–24 months) predominated in the LT group (81.2% vs. 55.6%). Late recurrence (>24 months) accounted for 8.6% of recurrent cases in the LT group and 15.5% in the Non-LT group. In terms of global failure phenotypes, isolated locoregional recurrence (LR-only) was the predominant relapse type in both groups, with a markedly higher proportion in the Non-LT cohort (78.8% vs. 58.0%). The contralateral lung was the most frequent metastatic site in both groups (39 patients with distant lesions). Kaplan–Meier survival analysis demonstrated that the median PFS (19.1 months vs. 12.7 months, $p = 0.03$) and OS (56.8 months vs. 31.8 months, $p = 0.001$) were significantly prolonged in the LT cohort (Fig. 1A, B). Patients with early recurrence had a drastically inferior median OS (10.0 months) compared with those developing mid or late recurrence (45.8 months) (Fig. 1C).

Multivariate analysis of prognostic factors for immunotherapy-treated unresectable NSCLC

Multivariate Cox proportional hazards regression was performed to determine the independent prognostic predictors of OS and PFS in patients with unresectable NSCLC receiving immunotherapy (Fig. 2). After adjusting for confounding clinical covariates, pathological type (hazard ratio [HR] = 0.148, 95% confidence interval [CI] 0.354–0.844, $p = 0.019$), disease stage (HR = 0.380, 95% CI 0.582–0.890, $p = 0.013$), and local treatment (HR = 1.176, 95% CI 1.785–2.707, $p = 0.006$) were independently correlated with OS, whereas irAE subtype, sex, age, immunotherapy cycles, and post-treatment efficacy assessment showed no independent prognostic significance. For PFS, pathological type (HR = 0.228, 95% CI 0.467–0.958, $p = 0.038$), immunotherapy cycles (HR = 1.148, 95% CI 1.625–2.301, $p = 0.006$), and local treatment (HR = 1.184, 95% CI 1.692–2.416, $p = 0.004$) were independent prognostic factors, whereas other variables failed to reach statistical significance. Collectively, our findings underscore the fact that histological characteristics, disease stage, duration of immunotherapy exposure, and administration of local intervention jointly shape clinical prognosis.

Subgroup analyses of survival benefit derived from radical local therapy

Cox regression analyses were performed to identify populations that derived survival benefits from radical local therapy among ICI-treated patients with unresectable NSCLC, with OS and PFS HR and *p*-values summarized in Fig. 3. Histology showed prominent prognostic heterogeneity; patients with squamous cell carcinoma achieved significant OS (HR = 0.5196, $p = 0.0017$) and PFS (HR = 0.5952, $p = 0.0053$) benefits after local intervention, whereas patients with adenocarcinoma had no statistically significant improvement in survival (OS, $p = 0.2239$; PFS, $p = 0.2087$). Age-based analysis indicated that patients younger than 65 years gained both OS ($p = 0.0303$) and PFS ($p = 0.0446$) benefits from local therapy, whereas patients aged ≥65 years obtained a significant OS improvement ($p = 0.0413$) with a borderline PFS benefit ($p = 0.0785$). For ICI cycles, patients receiving fewer than 6 cycles obtained a significant PFS benefit ($p = 0.0389$), with a borderline OS improvement, whereas those receiving ≥6 cycles showed a significant OS advantage ($p = 0.0478$) but nonsignificant PFS prolongation. Stage stratification revealed that patients with stage IIIB/IIIC disease had significant OS ($p = 0.0399$) and PFS ($p = 0.0442$) improvements with local therapy, whereas patients with stage II/IIIA disease showed no survival difference. Patients with initial stable disease/progressive disease (SD/PD) had significant OS ($p = 0.0118$) and PFS ($p < 0.001$) benefits from local ablation; however, patients with complete response/partial response (CR/PR) did not gain additional survival benefit. Patients with a PD-L1 TPS of 0–49% had significantly reduced risks of death and progression after local treatment (OS, $p = 0.005$, PFS, $p = 0.0147$), whereas patients with TPS ≥50% showed no statistically significant survival improvement.

Discussion

The landmark PACIFIC trial established consolidative immunotherapy following concurrent chemoradiotherapy as the standard treatment for unresectable NSCLC [7]. Local therapy (surgery or radiotherapy) combined with ICIs has attracted widespread clinical attention. Radiotherapy and surgical resection can directly debulk macroscopic intrathoracic lesions and induce immunogenic cell death, which may synergistically amplify the antitumor immune response with ICIs [8,9]. However, major clinical controversies persist. First, the survival gain from adding local therapy is not consistent across all patient

populations, and uniform guidelines for candidate screening are lacking. Second, most prospective trials have focused on chemoradiation followed by ICI consolidation, whereas real-world data evaluating upfront ICI combined with sequential radical local intervention remain limited, especially when stratified by histology, PD-L1 expression, and initial treatment response. Third, few studies have systematically characterized how local therapy reshapes recurrence and metastatic failure patterns, thus limiting the mechanistic interpretation of its survival benefits. Against this background, our real-world cohort of 206 ICI-treated patients with unresectable NSCLC stratified by receipt of local therapy, provides complementary evidence for individualized management.

Our cohort demonstrated that, although the aggregate recurrence rate showed no statistically significant difference between the two arms, local therapy profoundly altered the timing and anatomical distribution of disease relapse, which may mechanistically explain the survival benefit associated with local therapy. Patients who did not receive local therapy exhibited a remarkably higher proportion of early recurrence within 6 months, dominated by isolated locoregional relapse originating from uncontrolled bulky primary and nodal lesions. Local treatment effectively eradicated intrathoracic tumors and alleviated local tumor burden, markedly suppressing rapid early regional progression. In contrast, local therapy recipients presented with mid-term recurrence as the primary failure event. This pattern supports the limitation of local treatment in eliminating preexisting occult systemic micrometastases, which eventually progress to distant lesions after the intrathoracic disease is well controlled [10,11]. Notably, once distant dissemination occurred, the spectrum of metastatic organs and single or multi-organ metastatic burden was comparable between the groups, indicating that metastatic organ tropism was predominantly determined by intrinsic tumor biological features rather than prior thoracic local therapy [12]. Consistent with these differences in recurrence, Kaplan–Meier curves demonstrated substantially prolonged median PFS and median OS in the local therapy cohort, whereas early recurrence/metastasis predicted dismal long-term survival, further highlighting the survival benefit of local treatment in combined ICI treatment. Subgroup forest plot analyses demonstrated prominent heterogeneity in the magnitude of survival gain derived from local therapy, offering potential stratification criteria for clinical candidate selection. Most of the advantages in OS and PFS were observed in patients with squamous cell carcinoma. We speculated that this was consistent with the pathological and biological traits of this subtype. Squamous NSCLC is typically characterized by bulky

intrathoracic locoregional lesions with a low propensity for early distant spread compared with other types [13]. Local therapy renders these patients highly susceptible to regional recurrence and thus may provide the greatest benefit through local thoracic debulking. Conversely, adenocarcinoma exhibited no statistically significant survival improvement with additional local therapy, which may be attributed to its inherent tendency toward early distant micrometastasis [14], diminishing the value of intrathoracic treatment. Notably, this study has a longer median follow-up (40.4 months) than the PACIFIC trial (median follow-up, 34.2 months). Furthermore, the median PFS (19.1 months, $p = 0.03$) and median OS (56.8 months, $p = 0.001$) in the LT cohort are similar to those in the durvalumab cohort of the PACIFIC trial (47.5 and 16.9 months, respectively), confirming that radical local intervention could attain long-term survival benefits similar to those of standard immunotherapy consolidation.

Furthermore, patients with intermediate PD-L1 expression (TPS 0–49%) obtained prominent reductions in the risks of death and progression after local therapy, whereas no significant benefit was detected in the TPS ≥50% subgroups. There is evidence that high PD-L1 tumors are intrinsically sensitive to ICIs [15], which sufficiently control both primary lesions and occult micrometastases without additional local intervention; low- or intermediate-PD-L1 tumors show limited immunotherapy efficacy, and local therapy may compensate for insufficient systemic disease control. In addition, patients with stage IIIB–IIIC disease, limited ICI cycles (<6 cycles), and initial SD/PD with immunotherapy gained significant survival benefits from local therapy, likely because well-controlled baseline tumor burden or systemic immunotherapy weakens the synergistic antitumor effect of local therapy. Collectively, these subgroup data established potential predictive markers for identifying optimal candidates for local treatment during immunotherapy.

Our real-world cohort study provides evidence of the recurrence patterns, independent prognostic value, and subgroup heterogeneity of radical local therapy in ICI-treated locally advanced NSCLC (LA-NSCLC). In clinical practice, we suggest considering prioritizing local treatment plus ICI regimens for patients with squamous histology, PD-L1 TPS 0–49%, stage IIIB–IIIC disease, and those failing to achieve CR/PR with initial immunotherapy.

This study has some limitations. First, this was a single-center retrospective analysis with a moderate sample size, and a notable proportion of patients lacked complete PD-L1 testing data, which may have

introduced information bias. Second, we did not stratify the local therapy modalities (surgery vs. radiotherapy) or radiation dose/fractionation schedules, we could not compare the differential efficacy of distinct locoregional approaches. Third, no external validation cohort was included to verify the predictive ability of the subgroups. Future large-scale prospective multicenter trials are required to validate our stratified benefit findings, explore the optimal sequencing of ICI and local therapy, and develop predictive biomarkers to precisely identify the patients most likely to derive survival benefits from combined multimodal treatment.

Conclusions

Within the ICI treatment paradigm for LA-NSCLC, complementary radical local therapy (surgery or thoracic radiotherapy) is an important component of comprehensive curative management. Local treatment reduces baseline intrathoracic tumor burden, significantly lowers the risk of early tumor recurrence within 6 months after treatment, prolongs the time to first progression, and independently improves long-term overall survival. Local treatment should be considered for patients with squamous histology, PD-L1 TPS 0–49%, stage IIIB–IIIC disease, and those failing to achieve CR/PR with initial immunotherapy to optimize antitumor efficacy and long-term prognostic outcomes.

List of abbreviations

ICI, immune checkpoint inhibitor; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; LT, local therapy; LA-NSCLC, locally advanced NSCLC; PFS, progression-free survival; OS, overall survival; PD-L1, programmed death-ligand 1; ECOG, Eastern Cooperative Oncology Group; TPS, tumor proportion score; irAEs, immune-related adverse events; CT, computed tomography; MRI, magnetic resonance imaging; PET-CT, positron emission tomography-computed tomography; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to recurrence; AJCC, American Joint Committee on Cancer; HR, hazard ratio; CI, confidence interval; SD/PD, stable disease/progressive disease; CR/PR, complete response/partial response.

Declarations

Ethics approval and consent to participate

This study was conducted in compliance with the principles of the Declaration of Helsinki. The institutional review board approved this retrospective observational study, and the requirement for written informed consent was waived owing to the use of de-identified clinical data. Ethics approval was obtained by the Ethics Committee of Hubei Cancer Hospital (No. LLHBCH2026YN-117)

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Conceptualization, Y.P.; methodology, L,S.; software, Y,X.; data curation, F,L and C,L.; writing—original draft preparation, L,S.; writing—review and editing, Y,X.; funding acquisition, Y,P. All authors have read and agreed to the published version of the manuscript.

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Figure legends

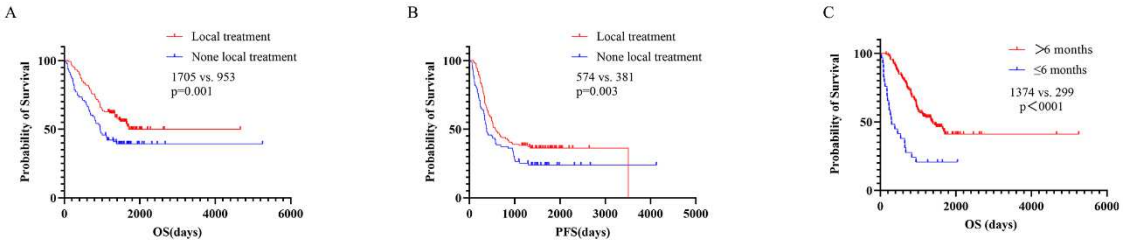


Fig. 1 Kaplan–Meier survival analysis of patients with unresectable NSCLC receiving ICI-based therapy. (A) OS in patients who received radical local therapy versus those who did not. (B) OS in patients who received radical local therapy versus those who did not. (C) OS stratified by time to recurrence: patients with recurrence >6 months versus those with recurrence ≤6 months. ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; OS, overall survival.

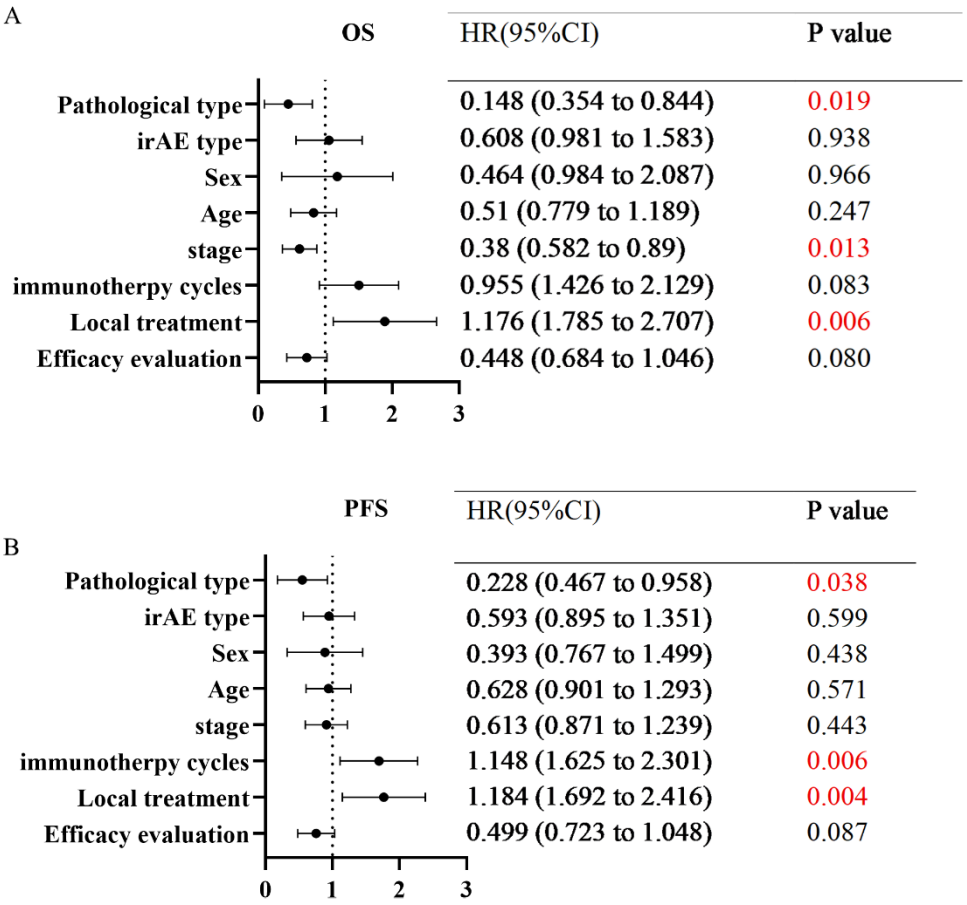


Fig. 2 Multivariate Cox regression analysis was conducted to identify independent prognostic factors for OS and PFS.

(A) HRs and 95% CIs for OS. (B) HRs and 95% CIs for PFS. Significant P-values are marked in red. CIs, confidence intervals; HRs, hazard ratios; OS, overall survival; PFS, progression-free survival.

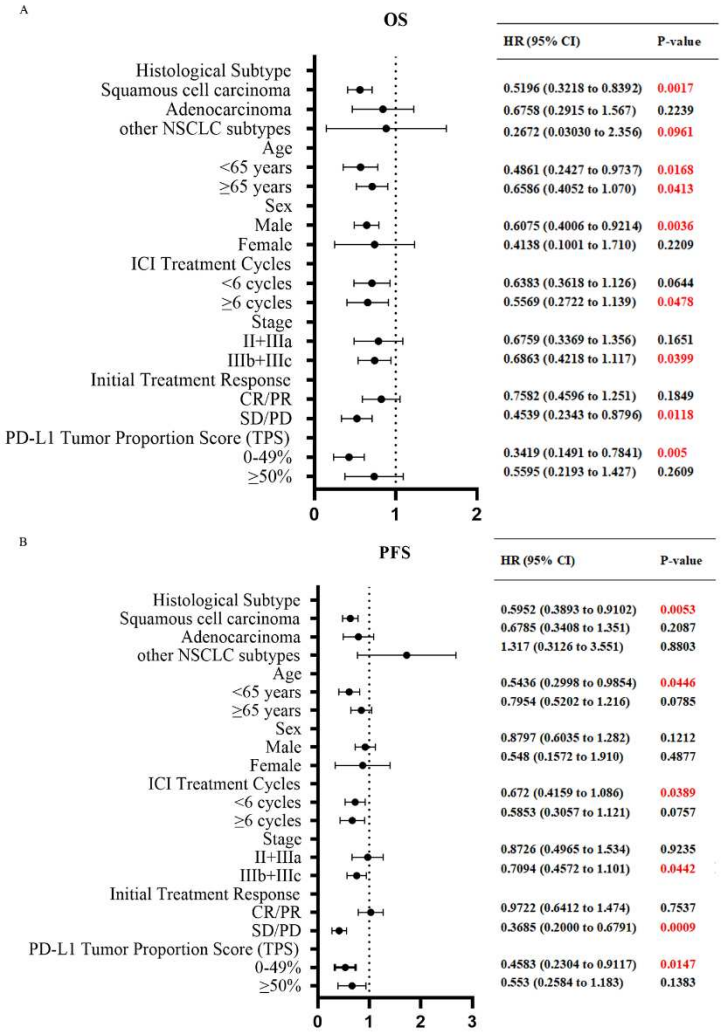


Fig. 3 Forest plots showing subgroup analyses of OS (A) and PFS (B).

HRs and 95% CIs were estimated in subgroups stratified by histological subtype, age, sex, ICI cycles, disease stage, initial treatment response, and PD-L1 TPS. Significant P-values are marked in red. CIs, confidence intervals; HRs, hazard ratios; ICI, immune checkpoint inhibitor; OS, overall survival; PFS, progression-free survival; TPS, tumor proportion score.

Tables

Table 1. Baseline clinical characteristics of locally advanced NSCLC patients stratified by receipt of local therapy

Variable	Total cohort (N=206)	Local treatment (N=123)	None local treament (N=83)	P Value
Median age, years (range)	65.6 (35–85)	65.0 (35–85)	67.2 (49–83)	0.341
Sex, n (%)				0.899
Male	188 (91.3)	112 (91.1)	76 (91.6)	
Female	18 (8.7)	11 (9,9)	7 (9.2)	
Smoking status, n (%)				0.389
Never-smoker	53(24.9)	29 (23.6)	24 (28.9)	
Former/current smoker	163 (75.1)	94 (76.4)	59 (71.1)	
Tumor pathology & biomarkers				
Histology, n (%)				0.503
Adenocarcinoma	53 (24.4)	30 (24.4)	23 (27.7)	
Squamous cell carcinoma	138 (63.6)	82 (66.7)	56 (67.4)	
Rare subtypes	15 (6.9)	11 (8.9)	4 (4.8)	
PD-L1 TPS, n (%)				
<1%	24 (11.1)	15 (12.2)	9 (10.8)	0.260
1–49%	34 (15.7)	22 (17.9)	12 (14.5)	
≥50%	43 (19.8)	30 (24.4)	13 (15.7)	
Unkown	105(43.5)	56(45.5)	49(59.0)	

AJCC 8th clinical stage, n (%)				
Stage IIA	3 (1.4)	2 (1.6)	1 (1.2)	0.859
Stage IIB	7(3.2)	5(4.1)	2(1.6)	
Stage IIIB	63(29.0)	38(30.1)	25(20.3)	
Stage IIIB	82 (37.8)	48 (39)	34 (27.6)	
Stage IIIC	33 (15.2)	17 (13.8)	16 (13.0)	
Treatment characteristics				
Immunotherapy agent type, n (%)				
PD-1 inhibitor	198 (91.2)	114(92.6)	83(100)	0.012
PD-L1 inhibitor	9 (8.8)	9(7.3)	0 (0)	
Median IO treatment cycles	8 (1–56)	8 (1–56)	7.1(1–56)	0.354
irAEs, n (%)	46 (22.3)	27 (22.0)	19 (22.9)	0.378

Abbreviations: NSCLC = non-small cell lung cancer; IO = immunotherapy; cCRT = concurrent chemoradiotherapy; irAEs = immune-related adverse events; Significant P-values are marked in red.

Table 2. Recurrence and metastatic characteristics stratified by receipt of local therapy

Recurrence and metastatic Characteristics	**Total** (n=**206**)	Local therapy (n=**123**)	None local therapy (n=**83**)	P value
Patients with any recurrence or metastatic, n (%)	114	69(64.2)	45(74.7)	0.79
Early recurrence (≤6 months) , n (%)	20	7(10.1)	13(28.9)	0.01

Mid-term recurrence (6–24 months) , n (%)	81	56(81.2)	25(55.6)	
Late recurrence (>24 months) , n (%)	13	6(8.6)	7(15.5)	
Global recurrence pattern classification, n (%) (of 114 recurrent or metastate patients)				
Isolated locoregional recurrence (LR only)	76	40(58.0)	36(80.0)	0.0457
Isolated distant metastasis (DM only)	24	19(27.5)	5(11.1)	
Synchronous LR + distant recurrence	14	10(14.5)	4(8.9)	
Recurrence distribution, n (%) (of 89 recurrent patients)				
Primary focus	44	21(42.0)	23(59.0)	0.197
Lymph node	15	11(22.0)	4(10.3)	
Lymph node+ Primary focus	30	18(36.0)	12(30.8)	
metastatic organ distribution, n (%) (of 39 recurrent patients)				
Brain	5	3	2	0.646
Contralateral lung	19	15	5	
Bone	9	5	4	
Adrenal gland	2	2	0	
Other extrathoracic organs	5	4	1	
metastatic organ distribution, n (%) (of 39 recurrent patients)				

Single organ metastasis	25	9	0.797
Multiple organ metastasis	2	1	

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375 Significant P-values are marked in red.

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