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Efficacy and safety of induction immunochemotherapy followed by radiotherapy for patients with unresectable locally advanced non-small cell lung cancer: A retrospective study

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Abstract

Objectives Immune checkpoint inhibitor (ICI) has displayed considerable advantages in consolidation therapy of locally advanced non-small cell lung cancer (LA-NSCLC) after concurrent chemoradiotherapy (cCRT). However, many patients are considered unsuitable for cCRT owing to concerns with tolerability. In this study, we aimed to assess the efficacy and toxicity of induction immunochemotherapy followed by radiotherapy for unresectable LA-NSCLC who are not capable of receiving cCRT.

Methods From January 2019 and December 2022, LA-NSCLC patients treated with induction immunochemotherapy followed by radiotherapy as initial treatment at our institution were retrospectively reviewed. The short-term efficacy, overall survival (OS), progression free survival (PFS) and tolerability of induction immunochemotherapy followed by radiotherapy were evaluated in these patients.

Results Overall, 24 patients were enrolled (median age 64 years, 33.3% with ECOG performance status score 2, and 62.5% with stage IIIB-IIIC). Median follow-up from the start of induction immunochemotherapy was 30.5 months. Median number of induction immunochemotherapy was 4 cycles. A median radiotherapy dose of 60 Gy was delivered. After radiotherapy, 16 patients (66.6%) received consolidation immunotherapy. The overall response rate in these patients was 87.5%. The 1-year, 2-year and 3-year OS were 91.7%, 74.8% and 57.0%, respectively. The 1-year, 2-year and 3-year PFS were 87.0%, 54.1% and 37.1%, respectively. The incidence of grade ≥ 2 and grade ≥ 3 pneumonitis were 37.5% and 16.7%, respectively. Radiation pneumonitis of any grade occurred in 8 patients (33.3%), and the incidence of grade ≥ 2 and grade ≥ 3 radiation pneumonitis were 16.7% and 12.5%, respectively.

Conclusion Induction immunochemotherapy followed by radiotherapy and consolidated immunotherapy had encouraging efficacy with acceptable toxicity for LA-NSCLC not capable of receiving cCRT.

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Keywords Induction immunochemotherapy, Radiotherapy, Locally advanced non-small cell lung cancer, Efficacy, Safety

Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of lung cancer cases [1, 2]. Locally advanced NSCLC (LA-NSCLC) makes up one third of NSCLC cases with heterogeneous prognosis and evolving treatment paradigms [3]. Definitive-intent radiotherapy has been a standard treatment for unresectable LA-NSCLC either concurrently or sequentially given with systemic therapy or as primary curative therapy. In the immunotherapy era, the standard-of-care for fit unresectable LA-NSCLC is concurrent chemoradiotherapy (cCRT) followed by immune checkpoint inhibitor (ICI) durvalumab [4].

However, patients with advanced age, clinically relevant comorbidities or extensive tumor invasion are not candidates for cCRT. In that case, sCRT represents an effective and valid choice, raising the concern of undertreatment and urgent need for new therapeutic modality [5]. In recent years, neoadjuvant immunotherapies with ICIs have demonstrated remarkable therapeutic efficacy and acceptable safety in resectable NSCLC [6–8]. The two phase III studies Checkmate 816 and Keynote-671 demonstrated neoadjuvant immunochemotherapy could yield longer event-free survival (EFS) and pathological complete response (pCR) than chemotherapy alone for resectable NSCLC (6–7). The addition of ICI to neoadjuvant chemotherapy did not lead to increased issues with tolerability or feasibility of surgery. The promising results of Checkmate 816 and Keynote-671 trial has led to the FDA approval of immunotherapy in the neoadjuvant and adjuvant setting.

Given the potential superior clinical benefit of induction immunochemotherapy over chemotherapy alone, the question of whether induction immunochemotherapy can improve outcome for unresectable LA-NSCLC is of considerable interest. Therefore, our study attempted to evaluate the efficacy and toxicity of induction immunochemotherapy followed by radiotherapy for unresectable LA-NSCLC unable to receive cCRT at our institution.

Methods and materials

Eligibility

We retrospectively reviewed the clinical records of LA-NSCLC patients treated with induction immunochemotherapy followed by radiotherapy as initial treatment at our institution between January 2019 and December 2022. The criteria for inclusion were as follows: [1] histologically or cytologically proven NSCLC; [2] clinically diagnosed as stage III, unresectable disease according to the International Association for the Study of Lung Cancer staging manual (8th edition); [3] patients not eligible for receiving standard cCRT due to compromised performance status, advanced age, comorbidities or large tumor volume; [4] patients completed induction immunochemotherapy consisting of at least two cycles of chemotherapy and ICI; [5] patients treated with curative thoracic radiotherapy no less than 50 Gy. Patients with prior thoracic radiotherapy or surgery were excluded. The study was approved by local institutional review board (2022BJYYEC-190-02). Informed consent was exempted by the board due to the retrospective nature of the study.

Evaluation and follow-up

Pre-treatment evaluation consisted of patient medical history and physical examination, laboratory investigation, contrast enhanced chest and abdominal computed tomography (CT), brain MRI/CT, bronchoscopy, and radionuclide bone scanning. Positron emission tomography (PET)-CT was recommended but not mandatory. All patients underwent complete blood cell counts (CBCs) and blood chemistry examinations once a week during the treatment period. The follow-up evaluation included patient history, physical examination, hematological tests, contrast enhanced chest and abdominal CT at the following timepoints: 1 month after completion of radiotherapy, then every 3 months during and after consolidation ICI therapy for 2 years, then 6 months for the following 3 years and annually thereafter. Other imaging examinations were obtained when recurrence was suspected.

The treatment response evaluation was evaluated in accordance with the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 [9]. The objective response rate (ORR) was defined as complete response (CR) and partial response (PR) by RECIST 1.1. ORR was assessed after radical radiotherapy. Treatment-related adverse events (AEs) were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Radiation pneumonitis (RP) and checkpoint inhibitor pneumonitis (CIP) were assessed by medical records and follow-up chest CT by multidisciplinary team including a medical oncologist, a radiation oncologist and a radiologist. The differentiation of CIP and RP was mostly based on the timing and CT characteristics of pneumonitis. RP usually occurred in less than 6 months after TRT within or at the edge of the radiation field, but CIP had a broader range of CT manifestations and longer time window [9]. Overall survival (OS) was calculated from the beginning of initial treatment to the time

Table 1 Baseline demographic and clinical characteristics of patients

	Overall (*n* = 24)
Age (median, range), years	64 (47–79)
Gender	
Male	24(100%)
Female	0
ECOG	
0	1 (4.2%)
1	15 (62.5%)
2	8 (33.3%)
Smoking	
Never	1 (4.2%)
Former/current	23 (95.8%)
ACCI	
≤2	7 (29.2%)
>2	17 (70.8%)
WHO histology	
Squamous cell carcinoma	20 (83.3%)
Non-squamous cell carcinoma	4 (16.7%)
Stage	
IIIA	9 (37.5%)
IIIB	7 (29.2%)
IIIC	8 (33.3%)
PD-L1 TPS	
<1%	5 (20.8%)
≥1%	11 (45.8%)
NA	8 (33.3%)
Driver gene status	
Mutated	0
Wild type	19 (79.2%)
NA	5 (20.8%)
Induction immunochemotherapy cycle (median, range)	4 (2–6)
The interval between immunochemotherapy and radiotherapy (median, range), days	35 (16–98)
Radiation dose	
<56 Gy	3 (12.5%)
≥56 Gy	21 (87.5%)
Mean lung dose (median, range), Gy	11.9 (8.1–15.2)
Lung V5 (median, range), %	47.4 (35.9–58.9)
Lung V20 (median, range), %	24.4 (14.6–31.0)
Consolidation ICI	
No	8 (33.4%)
Yes	16 (66.6%)
Time of ICIs post RT	
≤42	12 (75.0%)
>42	4 (25.0%)

ECOG, Eastern Cooperative Oncology Group; ACCI: age-adjusted Charlson comorbidity index; TPS, tumor proportion score; NA, not available; MLD, mean lung dose; V5, percentage of lung volume exceeding 5 Gy; V20, percentage of lung volume exceeding 20 Gy; ICI, immune checkpoint inhibitor

of death or last follow-up. Progression free survival (PFS) was calculated from the beginning of initial treatment to the time of tumor progression, death from any cause, or last follow-up. The parameters of radiation dose to lung assessed included percentage of lung volume exceeding 20 Gy (V20), percentage of lung volume exceeding 5 Gy (V5), and mean lung dose (MLD).

Statistical analysis

The OS and PFS were estimated using the Kaplan–Meier method. The log-rank test was applied to compare the differences of OS and PFS between subgroups for factors including grade ≥ 2 pneumonitis and consolidation immunotherapy. Fisher's exact tests and Mann-Whitney U tests were adopted for comparing categorical variables and continuous variables between patients with or without pneumonitis. All tests were two-sided, and $p \le 0.05$ was considered statistically significant. All the analyses were performed using the SPSS software package (version 22.0, SPSS, Inc.)

Results

Baseline characteristics and treatment

Between January 2019 and December 2022, we identified 33 consecutive stage III unresectable NSCLC patients who received induction immunochemotherapy consisting of at least two cycles. We excluded 5 patients who refused radiotherapy and 4 patients who received radical surgery after tumor shrinkage; thus, a total of 24 patients were enrolled in this study. In terms of the reason for not receiving cCRT, 8 patients had Eastern Cooperative Oncology Group performance status (ECOG PS) 2, 6 patients were older than 70 years, 5 patients were due to comorbidities and 5 patients were due to extensive tumor invasion. Table 1 lists the characteristics of the study cohort. Median age was 64 years (range: 47–79). All patients were male sex. The majority of patients had ECOG PS of 0 or 1 (66.7%), smoking history (95.8%), and squamous cell carcinoma histologic type (83.3%). About three quarters of patients (70.8%) had age-adjusted Charlson comorbidity index > 2 at baseline, including 8 patients (33.3%) had history of chronic obstructive pulmonary disease (COPD). There were 37.5%, 29.2% and 33.3% of patients at stage IIIA, IIIB and IIIC, respectively. 8 patients (33.3%) had unknown PD-L1 expression status, 5 patients (20.8%) had PD-L1 tumor proportion score (TPS) < 1% and 11 patients (45.8%) had PD-L1 TPS ≥ 1%. Among the 19 patients with molecular testing results, 6 patients used DNA based next generation sequencing and the rest 13 patients used real-time polymerase chain reaction (PCR). As for driver gene status, 4 patients with lung adenocarcinoma were all wild-type.

All the induction immunochemotherapy regimen consisted of platinum-based doublet chemotherapy with

anti-PD-1 monoclonal antibody and median number of induction immunochemotherapy cycles was 4 (range: 2–6). The majority patients (95.8%) remained unresectable and 1 patient refused surgery after induction immunochemotherapy. The median time between completion of induction immunochemotherapy and radiotherapy was 35 days (range: 16–98). All patients received intensity-modulated definitive radiotherapy with median dose at 60 Gy (range: 50–64). 16 patients (66.6%) were treated with anti-PD-1 monoclonal antibody consolidation. Covid-19 ($n = 2$; 8.3%) and unresolved adverse event (AE) ($n = 6$; 25%) were the most common reasons for discontinuing consolidation ICI treatment. The median time between radiotherapy termination and consolidation ICI initiation was 38 days (range: 27–72).

Efficacy

The median follow-up from the initiation of induction treatment in this study was 30.5 months. After induction immunochemotherapy, 16 patients (66.6%) achieved PR, 7 patients (29.2%) had stable disease (SD) and one patient (4.2%) had progressive disease (PD). The ORR after radiotherapy in these patients was 87.5% with 21 patients achieving PR (Fig. 1). At the last follow up, a total of 11 patients (45.8%) experienced progression, including 4 patients had local relapse, 4 patients had distant metastasis, and 3 had both. At last follow up, 6 patients had died of cancer and 1 patient died of pneumonitis. As shown in Fig. 2A, the 1-year, 2-year and 3-year OS were 91.7%, 74.8% and 57.0%, respectively. Median OS was not reached (NR). The 1-year, 2-year and 3-year PFS were 87.0%, 54.1% and 37.1%, respectively (Fig. 2B). Median PFS was 24.0 months.

Safety

During induction immunochemotherapy, the most common AE were hematological toxicities. AE of grade ≥ 2 included 5 (20.8%) leukopenia, 1 (4.2%) anemia, 1 (4.2%) thrombocytopenia and 1 (4.2%) fatigue. Treatment-related toxicities of the whole treatment course are shown in Table 2. The most common AE was leukopenia, with grade 3–4 leukopenia observed in 12.5% of enrolled patients. The incidence of grade ≥ 2 and grade ≥ 3 pneumonitis was 37.5% and 16.7%, respectively. Radiation pneumonitis of any grade occurred in 8 patients (33.3%), and the incidence of grade ≥ 2 and grade ≥ 3 radiation pneumonitis was 16.7% and 12.5% respectively. One patient died due to radiation pneumonitis complicated by Pneumocystis carinii. This patient had chronic obstructive pulmonary disease and diabetes history. The radiation dose was 68 Gy with lung V5 and V20 at 55% and 31%, respectively. He was diagnosed grade 3 radiation pneumonitis one month after completion of radiotherapy and received steroid treatment. However, his symptoms

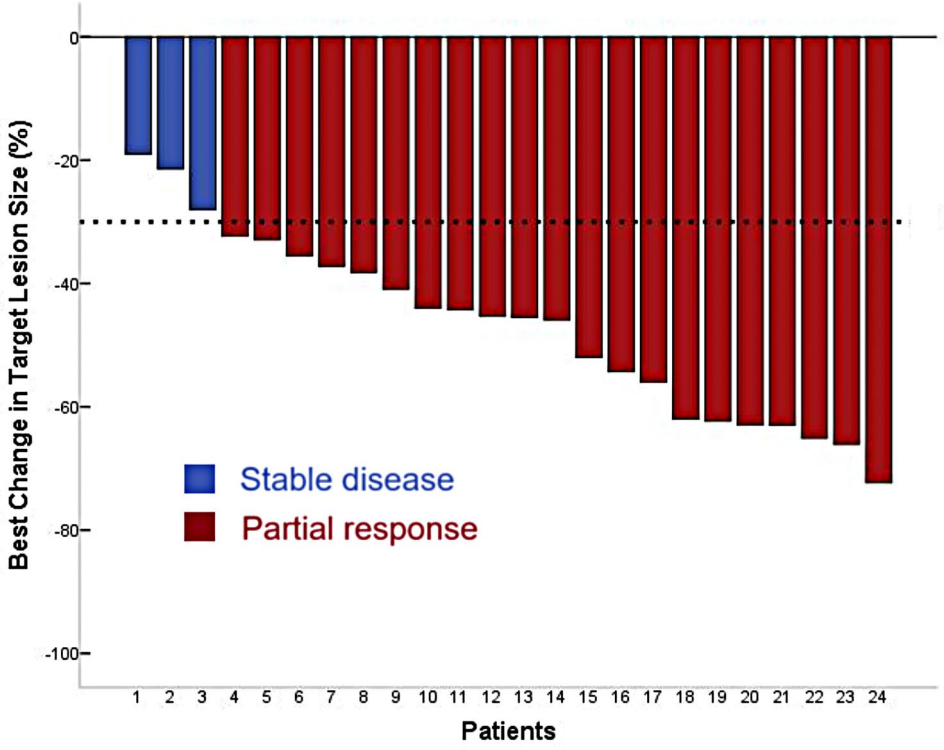

Fig. 1 The best response evaluated after induction immunochemotherapy and radical radiotherapy. The dashed line corresponds to 30% reduction in target lesion size assessed by RECIST 1.1 criteria

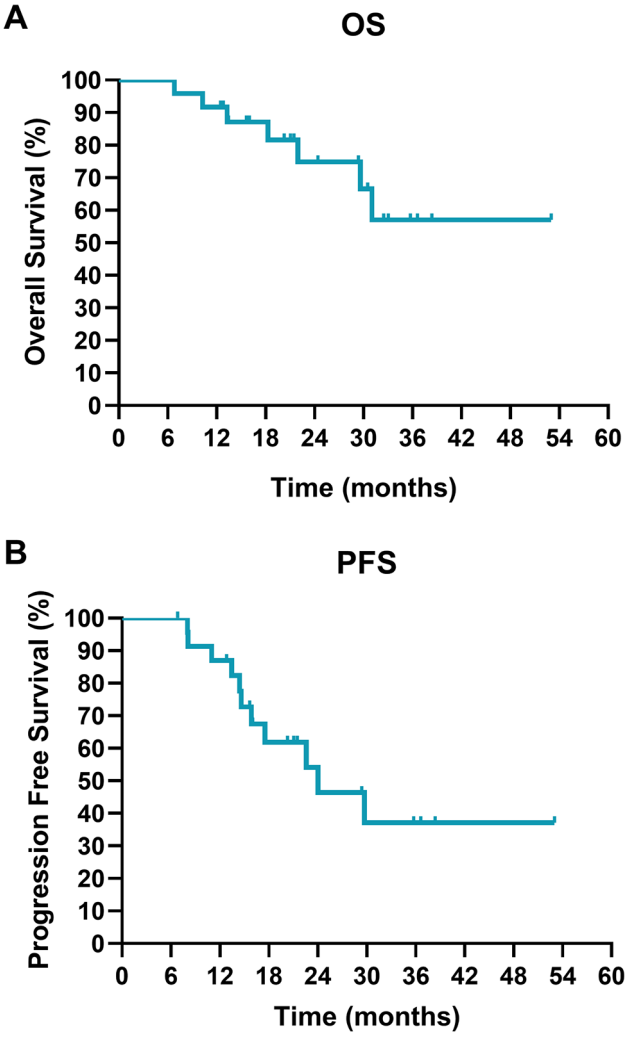

Fig. 2 Kaplan-Meier curves for overall survival (**A**) and progression free survival (**B**)

didn't respond well to steroid therapy and bronchoalveolar lavage fluid test indicated infection of Pneumocystis carinii. The patient was treated in intensive care unit and died one month after development of pneumonitis.

In terms of predictors for pneumonitis, the presence of COPD increased risk of grade ≥ 3 pneumonitis (37.5% vs. 0%, $p = 0.028$). No significant difference of grade ≥ 2 or grade ≥ 3 pneumonitis was observed between patients with ≥ 4 cycles of induction treatment and patients with < 4 cycles of induction treatment (grade ≥ 2: 36.8% vs. 20.0%, $p = 0.631$; grade ≥ 3: 10.5% vs. 20.0%, $p = 0.521$). The lung V20 ($p = 0.118$), V5 ($p = 0.342$), and mean dose ($p = 0.098$) were all not statistically different between patients with grade ≥ 2 RP and patients with grade < 2 RP. And the lung V20 ($p = 0.132$), V5 ($p = 0.108$), and mean dose ($p = 0.160$) were also not statistically different between patients with or without high grade (≥ 3) RP.

Subgroup analysis

In subgroup analysis, the median OS and PFS for patients experiencing grade ≥ 2 pneumonitis were significantly inferior (median OS, 23.7 months vs. 49.9 months, $p = 0.006$, Fig. 3A; median PFS, 19.0 months vs. 39.4 months, $p = 0.019$, Fig. 3B). Regarding consolidation immunotherapy, patients with consolidation immunotherapy achieved significantly better OS (median OS, 44.8 months vs. 21.6 months; $p = 0.011$; Fig. 3C) compared with patients without consolidation immunotherapy. Though the PFS for patients receiving consolidation immunotherapy was numerically higher than those without consolidation immunotherapy, the difference did not reach statistical significance (median PFS, 33.6 months vs. 19.7 months; $p = 0.394$; Fig. 3D).

Discussion

LA-NSCLC comprises a heterogeneous group of patients and accounts for approximately one-third of NSCLC cases. The PACIFIC trial [5] has established cCRT followed by consolidation immunotherapy as standard of care for LA-NSCLC with median PFS and OS at 18 months and 36 months, respectively. However, real-world studies revealed that more than half of patients were not eligible for cCRT [10, 11]. For patients receiving sCRT, results of GEMSTONE-301 revealed consolidation immunotherapy could further improve outcome compared with sCRT alone [12]. Of note, approximately 25 -50% of LA-NSCLC patients who receive CRT are not eligible for adjuvant immunotherapy phase because of severe toxicity, impaired performance status or early disease progression [13–15]. Furthermore, the efficacy of immunotherapy may be attenuated in the adjuvant setting because of immunocompromised status of patients and non-prevalent tumor antigens [5]. For patients unfit for cCRT, or not eligible of adjuvant immunotherapy, new treatment diagrams are urgently needed.

In the era of immunotherapy, numerous studies indicated the combination of ICI with chemotherapy or radiotherapy could further improve pathological response and prognosis for stage III NSCLC [5, 6, 16, 17]. However, whether induction immunochemotherapy plus radiotherapy is superior to conventional sCRT for unresectable LA-NSCLC remain unclear. This study presents real-world data with relatively long follow up on induction immunochemotherapy followed by radiotherapy for unresectable LA-NSCLC in a single-center setting. In this study, induction immunochemotherapy plus RT achieved encouraging efficacy with a manageable safety profile. The phase II PACIFIC-6 study reported the efficacy of durvalumab after sCRT for in a frailer unresectable LA-NSCLC population compared with PACIFIC [18]. In the PACIFIC-6 trial, the median PFS and 12-month PFS were 10.9 months and 49.6%, respectively.

Table 2 Treatment related adverse events

Adverse event, *n* (%)	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Pneumonitis	17 (70.8)	8 (33.3)	5 (20.8)	3 (12.5)	0	1 (4.2)
RP	9 (37.5)	5 (20.8)	1 (4.2)	2 (8.3)	0	1 (4.2)
CIP	8 (33.3)	3 (12.5)	4 (16.6)	1 (4.2)	0	0
Leukopenia	17 (70.8)	10 (41.7)	4 (16.7)	2 (8.3)	1 (4.2)	0
Anemia	11 (45.8)	9 (37.5)	2 (8.3)	0	0	0
Thrombocytopenia	10 (41.7)	9 (37.5)	1 (4.2)	0	0	0
Esophagitis	15 (62.5)	5 (20.8)	10 (41.6)	0	0	0
Radiation dermatitis	4 (16.7)	4 (16.7)	0	0	0	0
Fatigue	6 (25.0)	5 (20.8)	1 (4.2)	0	0	0
Pyrexia	3 (12.5)	3 (12.5)	0	0	0	0
Elevated ALT	4 (16.7)	3 (12.5)	1 (4.2)	0	0	0
Nausea	5 (20.8)	5 (20.8)	0	0	0	0
Diarrhea	2 (8.3)	2 (8.3)	0	0	0	0
Pruritus	2 (8.3)	2 (8.3)	0	0	0	0
Rash	3 (12.5)	3 (12.5)	0	0	0	0
Thyroid dysfunction	3 (12.5)	3 (12.5)	0	0	0	0
Musculoskeletal pain	1 (4.2)	1 (4.2)	0	0	0	0
Cough	1 (4.2)	1 (4.2)	0	0	0	0
Peripheral neuropathy	1 (4.2)	1 (4.2)	0	0	0	0
Adrenal insufficiency	1 (4.2)	1 (4.2)	0	0	0	0

RP: radiation pneumonitis; CIP: checkpoint inhibitor pneumonitis; ALT: alanine aminotransferase

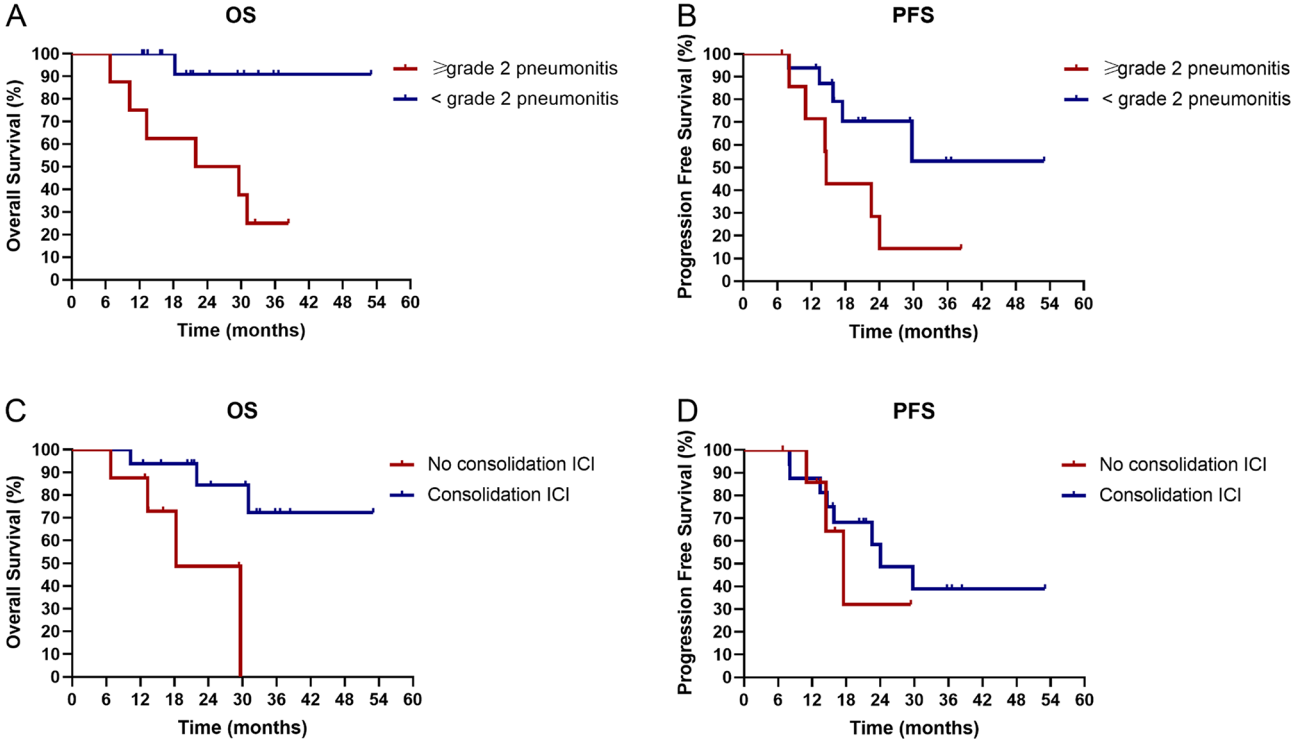

Fig. 3 Kaplan-Meier curves for overall survival (**A**) and progression free survival (**B**) between patients with and without grade ≥ 2 pneumonitis; Kaplan-Meier curves for overall survival (**C**) and progression free survival (**D**) between patients with and without consolidation immunotherapy

The 12-month and 24-month OS were 84.1% and 69.8%, respectively. Although calculated from the start of treatment, the 24 months of median PFS and 74.8% of 2-year OS in our study were superior to PACIFIC 6, suggesting that induction immunochemotherapy before radiotherapy may achieve better outcome to sCRT in the immunotherapy era. The encouraging outcomes of induction immunochemotherapy plus RT observed in our study

are reinforced by the finding of other real-world studies [19, 20]. However, it should be noted that prognosis is typically overestimated in real-world studies due to less frequent use of radiological assessment. Cross-trial comparisons should be interpreted with caution. Prospective studies are needed to confirm the above findings.

In terms of pulmonary toxicity, previous studies have indicated that combined administration of immunotherapy and radiation result in increased incidence of pneumonitis [21, 22]. The trial KEYNOTE 799 was designed to assess the treatment outcomes of induction immunochemotherapy followed by cCRT plus concurrent and consolidative pembrolizumab [23]. Though cCRT increases incidence of pneumonitis compared with sCRT, the incidence of grade 3 or higher pneumonitis in KEYNOTE 799 was lower than that in our study (5.6% vs. 16.7%). The possible reasons are as follows: Firstly, race may affect the susceptibility of treatment related pneumonitis. A real world meta-analysis reported that Asian patients were prone to develop pneumonitis of all grade than non-Asian patients receiving cCRT followed by immunotherapy (62% vs. 22%, $p = 0.017$) [24]. The percentage of Asian patients in our study were 10 times of that in KEYNOTE 799 (100% vs. 10%). Second, the inclusion and exclusion criteria were stricter in KEYNOTE 799 than our real-word study. KEYNOTE 799 enrolled patients with good performance status (ECOG 0–1) and adequate lung function. Furthermore, patients whose radiation treatment plan not adhering to the restraints of normal lung volume receiving more than 20 Gy (V20) < 31% were excluded in KEYNOTE 799. The high selectivity of patients may explain the higher real-world incidence of pulmonary toxicity than that in clinical trials. It is worth noting that the occurrence of grade ≥ 2 pneumonitis was associated with inferior prognosis in our study. In subgroup analysis, the median OS and PFS for patients experiencing grade ≥ 2 pneumonitis were almost half of that in patients with grade 0–1 pneumonitis (median OS, 23.7 months vs. 49.9 months, $p = 0.006$; median PFS, 19.0 months vs. 39.4 months, $p = 0.019$). Our result was consistent with previous studies suggesting that symptomatic pneumonitis is associated with increased mortality significantly for LA-NSCLC receiving curative intent CRT-ICI [25, 26]. Despite the fact most cases pneumonitis were manageable, few patients were re-challenged with immunotherapy after developing pneumonitis, which potentially resulted in poor prognosis due to early tumor recurrence. Reducing the risk of grade 2 or higher RP would be beneficial.

The PACIFIC-R study assessed the real-world effectiveness of consolidation durvalumab in unresectable stage III NSCLC [16]. The favorable real-world outcomes achieved in the sCRT subset suggested consolidation immunotherapy as a reasonable treatment strategy. The survival outcomes observed in sCRT group of GEMSTONE-301 trial complement the findings from PACIFIC-R. Though all patients in our study received induction immunotherapy, subgroup analysis still demonstrated the superiority of consolidation immunotherapy, indicating the beneficial effect of longer use of immunotherapy. Nevertheless, it should be acknowledged that the choice of observation over consolidation immunotherapy may correlate with other factors such as unrecovered toxicity, tumor progression or economic concern which could influence survival outcomes. Prospective randomized controlled trials are needed to answer whether consolidation immunotherapy is beneficial in this setting.

There are several limitations in the present study. Firstly, this study was a retrospective single institution study which may limit the generalizability of the results. Secondly, due to the small sample size, multivariate analysis was not performed and there will be selection bias. Still, under the circumstance that there is no recognized standard of care for LA-NSCLC unfit for cCRT, our analysis can provide real world evidence of efficacy and safety for the clinical trial design, as well as clinical practice.

Conclusions

This retrospective study demonstrated that induction immunochemotherapy followed by radiotherapy provided encouraging preliminary efficacy with manageable safety profile in a frailer LA-NSCLC patient population. This suggests that induction immunochemotherapy followed by radiotherapy may be a reasonable alternative treatment strategy for LA-NSCLC who are considered unsuitable for cCRT.

Abbreviations

AE	Adverse event
CBC	Complete blood cell count
CIP	Checkpoint inhibitor pneumonitis
CR	Complete response
cCRT	Concurrent chemoradiotherapy
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
EFS	Event-free survival
ECOG PS	Eastern Cooperative Oncology Group performance status
ICI	Immune checkpoint inhibitor
LA-NSCLC	Locally advanced non-small cell lung cancer
MLD	Mean lung dose
NSCLC	Non-small cell lung cancer
ORR	Objective response rate
OS	Overall survival
PCR	Polymerase chain reaction
pCR	Pathological complete response
PD	Progressive disease
PET-CT	Positron emission tomography computed tomography
PFS	Progression-free survival
PR	Partial response
RP	Radiation pneumonitis
sCRT	Sequential chemoradiotherapy
SD	Stable disease
TPS	Tumor proportion score

V5	Percentage of lung volume exceeding 5 Gy
V20	Percentage of lung volume exceeding 20 Gy

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Author contributions
L.L. contributed to the acquisition of the data, analysis and interpretation of the data, and drafting of the manuscript. C.G., Y.Y., M.T., T.Z., D.C., J.J., Y.X. and G.L. collected the data and performed the statistical analyses. Q.Z. conceived of the study, participated in its design and revised the final manuscript. All authors reviewed and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Beijing Hospital, National Center of Gerontology; Institute of Geriatric Medicine, Chinese Academy of Medical Sciences. Informed consent was waived by our Institutional Review Board because of the retrospective nature of our study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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