Lung Cancer 146 (2020) 23–29

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Real world data of durvalumab consolidation after chemoradiotherapy in stage III non-small-cell lung cancer

Hyun Ae Jung[a,1], Jae Myoung Noh[b,1], Jong-Mu Sun[a], Se-Hoon Lee[a], Jin Seok Ahn[a], Myung-Ju Ahn[a], Hongryull Pyo[b], Yong Chan Ahn[b], Keunchil Park[a,*]

[a] Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
[b] Department of Radiation Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Keywords:
Concurrent chemo-radiotherapy
Durvalumab
Consolidation
Non-small-cell lung cancer

ABSTRACT

Objectives: The PACIFIC study demonstrated the benefits of durvalumab consolidation on progression-free survival (PFS) and overall survival (OS) among patients with unresectable locally advanced non-small-cell lung cancer (LA-NSCLC). However, in real-world practice, patients with unresectable LA-NSCLC are heterogeneous with diverse tumor burdens and clinical factors; thus, it is important to examine the effectiveness and side effects of durvalumab when used in real clinical practice.

Materials and methods: We investigated the efficacy of durvalumab consolidation and the incidence of radiation pneumonitis in patients who received concurrent chemo-radiotherapy (CCRT) for unresectable LA-NSCLC in a single institute.

Results: Overall, 55.3 % of patients did not meet the criteria of the PACIFIC study; however, they still received consolidation durvalumab in real-world practice. Durvalumab consolidation was associated with favorable PFS in the total population as well as in the subgroup of patients who did not meet the criteria of the PACIFIC study. However, radiation pneumonitis occurred more frequently in the durvalumab group, especially within 3–6 months after CCRT. The incidence of grade 3 radiation pneumonitis was 14.3 % in the durvalumab group versus 2.5 % in the observation group.

Conclusions: Durvalumab consolidation was associated with favorable PFS in patients with LA-NSCLC in clinical practice. However, careful selection of candidates for durvalumab treatment and active surveillance and appropriate management for radiation pneumonitis are needed.

1. Introduction

Stage III non-small-cell lung cancer (NSCLC) is a heterogeneous set of conditions including potentially resectable disease and unresectable NSCLC. Long-term outcomes are poor with a 5-year overall survival (OS) rate of 15–35 % for stage IIIA and 3–10 % for stage IIIB according to the AJCC 7th edition. Unresectable locally advanced (LA)-NSCLC accounts for about 30–50 % of stage III NSCLC [1]. Randomized phase III trials have shown the superiority of concurrent chemo-radiotherapy (CCRT) compared with sequential chemoradiotherapy in patients with unresectable LA-NSCLC [2,3]. Therefore, CCRT is the standard of care for unresectable LA-NSCLC. However, the overall survival (OS) rate in LA-NSCLC after CCRT treatment remains disappointing with a median progression-free survival (PFS) of 16 months and a median survival of 24 months [4]. At our institution, the median PFS after CCRT treatment in patients with stage III non-squamous cell lung cancer was 8.9–11.8 months [5].

The PACIFIC study was a successful randomized controlled trial (RCT) that demonstrated the efficacy of durvalumab consolidation therapy. In the PACIFIC study [6], in patients with LA-NSCLC, durvalumab administered after CCRT improved median PFS by 16.8 months (95 % confidence interval [CI] 13.0–18.1) compared to placebo (5.6 months, 95 % CI 4.6–7.8). The most common grade 3 or 4 adverse event was pneumonia (4.4 % in the durvalumab group). Radiation pneumonitis also occurred in 33.9 % and 24.8 % of patients administered durvalumab and placebo, respectively. In particular, grade 3 or 4 radiation pneumonitis occurred in 3.4 % and 2.6 % of patients administered durvalumab and placebo, respectively.

* Corresponding author at: Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Republic of Korea.
E-mail address: kpark@skku.edu (K. Park).
[1] These authors contributed equally.

https://doi.org/10.1016/j.lungcan.2020.05.035
Received 24 February 2020; Received in revised form 23 May 2020; Accepted 26 May 2020

However, only a small fraction of the carefully selected patients were enrolled in the RCT, comprising approximately 5% of the population [7]. Lung cancer patients represent only approximately 12.5 % of all cancer clinical trial populations, which demonstrates the underrepresentation of lung cancer in this lethal disease with varied epidemiology [8]. In the PACIFIC study, patients were randomly assigned to groups after CCRT. Key inclusion criteria were unresectable stage III NSCLC, completion of treatment with concurrent chemoradiotherapy, no evidence of disease progression, and a performance status after chemoradiotherapy of 0 − 1. Patients who were enrolled in the PACIFIC study received radiotherapy with a mean dose to the lung (MLD) of less than 20 Gy, a V20 (the volume of lung parenchyma that received 20 Gy or more) of less than 35 %, or both. The time to randomization was up to 42 days. Also, patients with grade 2 or higher pneumonitis after CCRT were excluded. The results of phase 3 clinical studies in an ideal setting may vary from those observed when patients are treated in a real-world setting. In addition, 20 % of the patients enrolled in the PACIFIC study did not complete 12 months of durvalumab treatment, possibly due to side effects or other causes. The median number of infusions received was 20 (range, 1–27) in the durvalumab group and 14 (range, 1–26) in the placebo group. In addition, the PACIFIC study placed restrictions on the radiation dose of enrolled patients and as a result may have selected patients with a low clinical tumor burden, including primary lesions.

Therefore, in the present study, we report the results of durvalumab consolidation treatment in patients with unresectable LA-NSCLC in a real-world setting with a special focus on the occurrence of radiation pneumonitis.

2. Materials and methods

2.1. Study subjects and data collection

This study included patients with unresectable LA-NSCLC treated at Samsung Medical Center between August 2018 and January 2019. Eligible patients had histologically confirmed NSCLC and completed the planned CCRT. Patients enrolled in the durvalumab group met the inclusion criteria of the durvalumab EAP program. Patient demographic and clinical characteristics such as age, sex, smoking history, performance status, and *Epidermal growth factor receptor* (*EGFR*) gene mutation type were reviewed using a lung cancer cohort (ROOT: Realtime autOmatically updated data warehOuse in healThcare for NSCLC). This non-interventional observational study used a novel algorithm for big data analysis of retrospectively collected and assessed anonymized EMRs from a clinical data warehouse. The study was conducted in accordance with the Declaration of Helsinki. Approval for the study protocol was obtained from the independent review board at SMC (SMC IRB 2018-05-130-003).

2.2. Statistical analysis

The cutoff date for all data used in the analyses was September 30, 2019. Primary endpoints were PFS and radiation pneumonitis-free survival (RPFS). PFS was defined as the last date of CCRT until radiographically confirmed progression or death. RPFS was defined as the last date of CCRT until radiographically confirmed radiation pneumonitis or death. G2-RPFS (Grade 2 or higher radiation pneumonitis-free survival) was defined as the last date of CCRT until radiographically confirmed grade 2 or higher radiation pneumonitis or death. The PFS, RFPS, and G2-RPFS were calculated using a Kaplan–Meier estimator and compared using the log rank test. The PFS and RPFS were presented as the median value with two-sided 95 % CIs. A chi-square test was used to compare patient clinical characteristics and dose-volume parameters based on the radiotherapy (RT) techniques used.

The definition of radiation pneumonitis and grading were as follows. Radiation pneumonitis was diagnosed clinically based on the presence of classic symptoms, timing and history of radiation therapy, imaging findings, and exclusion of alternative causes, such as infection, cardiogenic edema, pulmonary embolism, drug-induced pneumonitis, and other causes. Radiation pneumonitis may be graded in several ways. The following is the Common Toxicity Criteria for Adverse Events (Version 4.0)

Grade 1: Asymptomatic, radiographic findings only

Grade 2: Symptomatic, but not interfering with activities of daily living

Grade 3: Symptomatic and interfering with activities of daily living, oxygen indicated

Grade 4: Life threatening, ventilator support is indicated

Grade 5: Death

2.3. Treatment

2.3.1. Concurrent chemoradiotherapy

The concurrent chemotherapeutic regimen was weekly paclitaxel plus cisplatin or carboplatin. The simulation procedure for RT planning and the definitions of target volumes were described previously [5,9]. Proton beam therapy (PBT) was recommended for patients with poor lung function or underlying lung disease. Follow-up chest CT was performed 1 month after CCRT, positron emission tomography (PET)-CT was done 3–4 months after completion of CCRT, and chest CT was repeated every 3 months thereafter in the observation group and every 8 weeks thereafter in the durvalumab maintenance group.

2.3.2. Maintenance treatment

Durvalumab (10 mg/kg) was administered intravenously every 2 weeks until withdrawal of consent, unacceptable toxicity, disease progression at the discretion of the physician, or for 1 year.

3. Results

3.1. Patient characteristics

This analysis included 61 patients who received CCRT for LA-NSCLC from August 2018 to January 2019 at Samsung Medical Center. Among them, 21 patients received durvalumab consolidation followed by CCRT and 40 patients underwent regular follow-up after CCRT. The durvalumab and observation groups were treated with CCRT during the same period. In the durvalumab group, patients met the inclusion criteria for the durvalumab EAP program and provided written informed consent. Reasons for exclusion of the 40 patients not treated with durvalumab were follows: Three patients had grade 2 or higher radiation pneumonitis, three patients died, one patient had poor performance, one patient exhibited disease progression, seven patients received a total dose > 66 Gy, and 25 patients did not assign informed consent (13 of 25 patients had poor lung function and received PBT). Seven (14.3 %) patients with EGFR-mutant NSCLC were included. Squamous histology was present in 60.7 % of patients. In all, 24 (29.3 %), 10 (16.4 %) and 27 (44.3 %) patients had stage IIIA, stage IIIB and stage IIIC, respectively, according to AJCC 8th edition (Table 1).

Supplementary Table 1 shows the radiation method, total radiation dose and mean organ radiation dose. We used various radiation methods including proton radiotherapy (n = 13). Of the patients enrolled in this study, 17 (27.9 %) had a MLD of 20 Gy or more. Nine received durvalumab consolidation treatment. There were 21 patients (50.9 %) who had V20 of more than 35 % and 10 of these patients received durvalumab consolidation treatment. Eight patients had a mean esophagus dose of more than 34 Gy, three of whom received durvalumab.

Thirty-three (55.7 %) patients did not meet the criteria of the original PACIFIC protocol. Twenty-eight patients did not meet the radiation dose criteria of the original PACIFIC protocol. This included the following details: total lung dose > 66 Gy, n = 7; mean lung dose > 20

Table 1
Baseline characteristics.

		Treatment based group			Overall
		Durvalumab (N = 21)	Observation (N = 40)	*p*-value	N = 61
Age	Median (range), years	65.9 (35.7 − 76.5)	67.2 (49.7 − 77.0)	1.00	66.2 (35.7 − 81.7)
	65 − 74 years	11	13		24
	≥75 years	1	10		11
Sex	Male	19	36	1.00	55
	Female	2	4		6
ECOG	0	4	11	0.69	15
	1	17	28		45
	2–3	0	1		1
Smoking	Never smoker	5	6	0.72	11
	Ex-smoker	8	18		26
	Current smoker	8	16		24
Histology	Squamous	15	22	0.43	37
	Non-Squamous	6	13		19
	Others		5		5
Location	Upper lobe	12	22	0.64	34
	Middle lobe	0	3		3
	Lower lobe	6	12		18
	Overlapping	3	3		6
Stage	IIIA	6	18	0.45	24
	IIIB	4	6		10
	IIIC	11	16		27
EGFR status	Mutation test (N = 50)	19	30	0.24	49
	MT	2	5		7
	WT	17	25		42
ALK status	IHC (N = 48)	18	30	NA	48
	0–1	18	30		48
PD-L1 expression	PD-L1(22C3) (N = 50)	19	31	NA	50
	<1%	5	16		21
	1–9%	5	5		10
	10–49 %	4	1		5
	>50 %	5	9		14
	SP263 assay (N = 49)	19	30		49
	<1%	7	16		23
	1–9%	4	4		8
	10–49 %	3	5		8
	>50 %	5	5		10

ECOG, Eastern Cooperative Oncology Group; EGFR, Epidermal growth factor receptor; MT, mutation positive; WT, wild type; ALK, Anaplastic lymphoma kinase.

Gy (n = 17); V20 ≥ 35 %, n = 21; and mean esophagus dose ≥34 Gy, n = 8. Among the 28 patients who did not meet the organ-specific radiation dose criteria of the original PACIFIC protocol, 12 patients received durvalumab treatment through the EAP program

With respect to clinical criteria, 8 patients did not meet the criteria of the original PACIFIC protocol. Three patients had grade 2 or higher-grade radiation pneumonitis within 42 days after CCRT. Two patients died due to pneumonia and one from other reasons. One patient was ineligible because of poor performance, whereas one patient was ineligible because of early progression after CCRT.

Patients who received PBT had poorer lung function than patients who received X-ray treatment. The diffusing capacity for carbon monoxide (DLCO) was 50.9 % and 78.3 % for PBT and X-ray therapy, respectively (P < 0.001). FEV1 was 1.78 L and 2.41 L for PBT and X-ray therapy, respectively (<0.001). In patients who received PBT, MLD, LV5, and LV20 were lower than in the group that received X-ray therapy (Supplementary Table 2)

3.2. Radiation pneumonitis

Most (81.0 %) patients in the durvalumab group developed any-grade radiation pneumonitis. Among patients in the observation group, 37.5 % experienced any-grade radiation pneumonitis. Grade 2 or higher radiation pneumonitis occurred in 42.9 % (9) and 20 % (8) of patients in the durvalumab and observation groups, respectively (grade 3: 14.3 % in the durvalumab group versus 2.5 % in the observation group). Among the 9 patients in the durvalumab group who had grade 2 or higher radiation pneumonitis, 7 patients recovered to grade 1 or were symptom-free within 2 weeks; however, 2 of these 7 experienced worsening lung function due to recurring radiation pneumonitis after restarting durvalumab and discontinued treatment. The remaining 2 of the 9 patients with grade 2 or higher radiation pneumonitis discontinued durvalumab treatment early because lung function did not recover despite initial steroid treatment for radiation pneumonitis. Among the 8 patients in the observation group with radiation pneumonitis, 7 patients recovered from radiation pneumonitis without recurrence. Patients who experienced grade 2 or higher radiation pneumonitis discontinued durvalumab treatment and were started on prednisolone 1 mg/kg per oral or the equivalent methylprednisolone dose administered intravenously for 2 weeks followed by a slow taper over 3–12 weeks. Supportive care with anti-tussive therapy and supplemental oxygen was provided. The risk factors for radiation pneumonitis were high MLD (≥20 Gy), V20 35 % and above and durvalumab consolidation treatment. These parameters were associated with grade 2 or higher-grade radiation pneumonitis (Table 2). Table 3 shows the results of multivariable Cox proportional hazard regression analysis for radiation pneumonitis. Before multivariate analysis, we checked the variance inflation factor (VIF) of MLD and LV20 to confirm the possibility of multicollinearity. The VIF was 3.79, so we included MLD, LV20, and durvalumab in multivariate analysis. For any grade radiation pneumonitis, durvalumab consolidation was independently associated with a higher incidence of radiation pneumonitis (hazard ratio [HR] 6.13, 95 % CI 1.68 − 22.46; p = 0.006). For grade 2 or higher radiation pneumonitis, durvalumab consolidation treatment was marginally correlated with incidence of grade 2 or higher radiation pneumonitis (HR 3.58, 95 % CI 0.94 − 13.68; p = 0.06).

Table 2
Relationship between radiation dosage, consolidation treatment and RT pneumonitis by chi-square.

Parameter		No. of patient	RT pneumonitis	*p* value	RT Pneumonitis ≥ Grade 2	*p* value
MLD	< 20 Gy	44	19(43.2 %)	0.024	7(15.9 %)	< 0.001
	≥ 20 Gy	17	13(76.5 %)		12(70.6 %)	
Lung V20	< 35 %	40	17(42.5 %)	0.058	6(15.0 %)	< 0.001
	≥ 35 %	21	15(71.4 %)		13(61.9 %)	
Consolidation	Observation	40	15(37.5 %)	0.001	8(20.0 %)	0.018
	Durvalumab	21	17(81.0 %)		11(50.0 %)	

RT, radiation; MLD, Mean lung dose; Lung V20, the volume of lung parenchyma that received 20 Gy or more.

Grade 2 or higher radiation pneumonitis occurred in 33.3 % (16/48) and 23.1 % (3/13) of patients in the radiotherapy (three-dimensional conformal radiotherapy (3D-CRT) or intensity-modulated radiotherapy (IMRT)) and PBT groups, respectively.

3.3. Radiation pneumonitis-free survival

In univariate analysis, high MLD (≥ 20 Gy), V20 (≥ 35 %) and durvalumab consolidation treatment were related to poor RPFS. However, in multivariate analysis, only durvalumab consolidation was significantly associated with decreased RPFS (HR, 2,23, 95 % CI 1.12 − 4.44; p = 0.023) (Table 4).

Median RPFS was 8.2 months (95 % CI 1.1–15.7) for the observation group and 3.1 months (95 % CI 2.6–3.5) for the durvalumab maintenance group (p = 0.004) (Fig. 1-1). Median G2PFS was not reached in the observation group and was 3.4 months in the durvalumab group (95 % CI 2.5–4.3) (p value = 0.081, Fig. 1-2).

3.4. Progression-free survival

Fig. 2-1 suggests that durvalumab maintenance followed by CCRT in LA-NSCLC led to superior PFS compared to the observation group (not reached versus 9.6 months; 95 % CI 4.5–14.8, p = 0.060). Even in patients who did not meet the criteria of the PACIFIC study, durvalumab consolidation treatment was associated with favorable PFS (Fig. 2-2, p = 0.073, not reached in the durvalumab consolidation group versus 6.4 months [95 % CI: 4.3–8.4] in the observation group).

3.5. Next line of treatment

Among 27 patients who experienced disease progression, 11 patients received a next line of treatment (platinum-containing doublet chemotherapy in 5, single-agent chemotherapy in 1, EGFR-TKIs in 3, salvage CCRT in 2). In the durvalumab group, 6 patients experienced disease progression. One patient experienced local disease progression and underwent salvage CCRT for that. Among the other 5 patients, who experienced systemic disease progression, 2 patients received platinum-containing doublet chemotherapy, 1 patient received EGFR-TKIs, and 2 patients did not receive further treatment). In the observation group, 21 patients experienced disease progression. Among the 9 patients who experienced local disease progression, 1 patient received salvage CCRT, 1 patient received single-agent chemotherapy, 1 patient received platinum-containing doublet chemotherapy, and 6 patients did not receive further treatment. Among the 12 patients who experienced systemic disease progression, 1 patient received platinum-containing doublet chemotherapy, 1 patient received platinum-containing doublet chemotherapy plus immune-check point inhibitor, 2 patients received EGFR-TKI, and 8 patients did not receive further treatment. Median OS was not reached at the time of data collection. However, patients who received durvalumab showed a favorable OS trend compared to those in the observation group (Supplementary Fig. 2).

4. Discussion

The PACIFIC study was a practice-changing study in the management of unresectable LA-NSCLC. In our study, durvalumab consolidation showed superior PFS compared to the observation group in a real-world setting.

The criteria for clinical trial enrollment are strict, leading to discrepancies between outcomes in clinical practice compared to the ideal setting of clinical trials. In a study by Al-Baimani et al., in real-world practice, 73 % of patients were excluded by clinical trial criteria. However, 46 % of ineligible patients actually received therapy and experienced survival rates similar to the eligible treated patients [10]. In a Japanese study, among 98 patients with stage III NSCLC, 35 (35.7 %) patients did not meet the criteria of the PACIFIC study. Sixteen (16.3 %) patients were not eligible before CCRT because of their poor performance. Nineteen (19.4 %) patients were not eligible after CCRT because of disease progression within 42 days of radiation therapy termination, grade 2 pneumonitis, poor performance or higher dosage of organ-specific radiation, especially V20 [11]. In another Japanese study, 30.1 % of unresectable LA-NSCLC did not meet the criteria of the PACIFIC study due to grade 2 or higher radiation pneumonia (16.4 %), other pneumonia (2.7 %), poor performance (9.6 %) or disease progression after CCRT (4.1 %) [12]. The incidence of radiation pneumonia of any grade was 73.9 %.

In our real-world data, 55 % of patients with unresectable LA-NSCLC did not meet the criteria of the PACIFIC study for various reasons, including radiation dosage and clinical parameters. Patients enrolled in the PACIFIC study had a total radiation dose of 60 Gy ± 10 %. The mean organ radiation dose for the radiation site was also limited. The mean lung dose was < 20 Gy and/or a V20 of < 35 %, and the mean esophagus dose was < 34 Gy, whereas V45 was < 35 % and V30 was < 30 %.

Nevertheless, the efficacy of durvalumab consolidation was demonstrated in our real-world data. Even in patients who were ineligible

Table 3
Multivariable cox proportional hazards regression analysis for radiation pneumonitis.

		RT pneumonitis			RT pneumonitis ≥ Grade 2		
		HR	95 % CI	*p* value	HR	95 % CI	*p* value
MLD	≥ 20	2.33	0.21 − 26.04	0.49	5.88	0.45 − 78.04	0.18
Lung V20	≥ 35 %	1.49	0.17 − 13.46	0.72	2.05	0.17 − 26.27	0.58
Consolidation	Durvalumab	6.13	1.68 − 22.46	0.006	3.58	0.94 − 13.68	0.06

HR, Hazard ratio; CI, Confidence interval; RT, radiation; MLD, Mean lung dose; Lung V20, the volume of lung parenchyma that received 20 Gy or more.

Table 4
Univariate and multivariate analysis for RPFS.

		Univariate analysis			Multivariate analysis		
		Median RPFS	95 % CI	*p*-value	HR	95 % CI	*p*-value
MLD	= > 20	2.6	2.01 – 3.19	0.023	1.51	0.42 – 5.38	0.527
	< 20	5.8	NA		1		
Lung V20	> = 35 %	3.1	1.35 – 4.85	0.021	1.41	0.41 – 4.79	0.584
	< 35 %	8.2	NA		1		
Consolidation	Durvalumab	3.1	2.88 – 3.32	0.009	2.23	1.12 – 4.44	0.023
	Observation	8.2	NA		1		

MLD, Mean lung dose; RPFS, Radiation pneumonitis free survival; Lung V20, the volume of lung parenchyma that received 20 Gy or more.

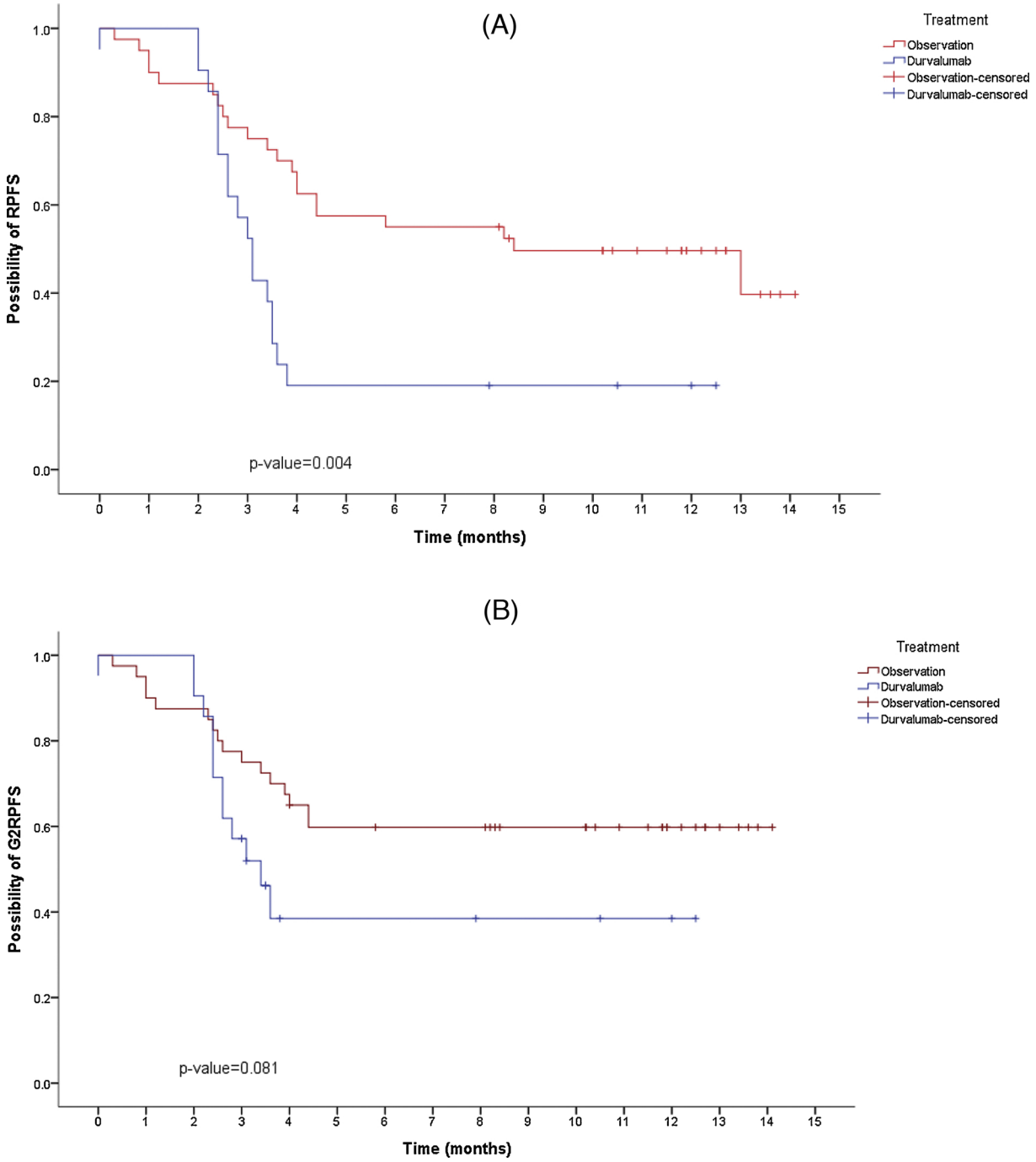

Fig. 1. (A) Radiation pneumonitis-free survival (RPFS). **(B)** Grade 2-3 radiation pneumonitis-free survival.

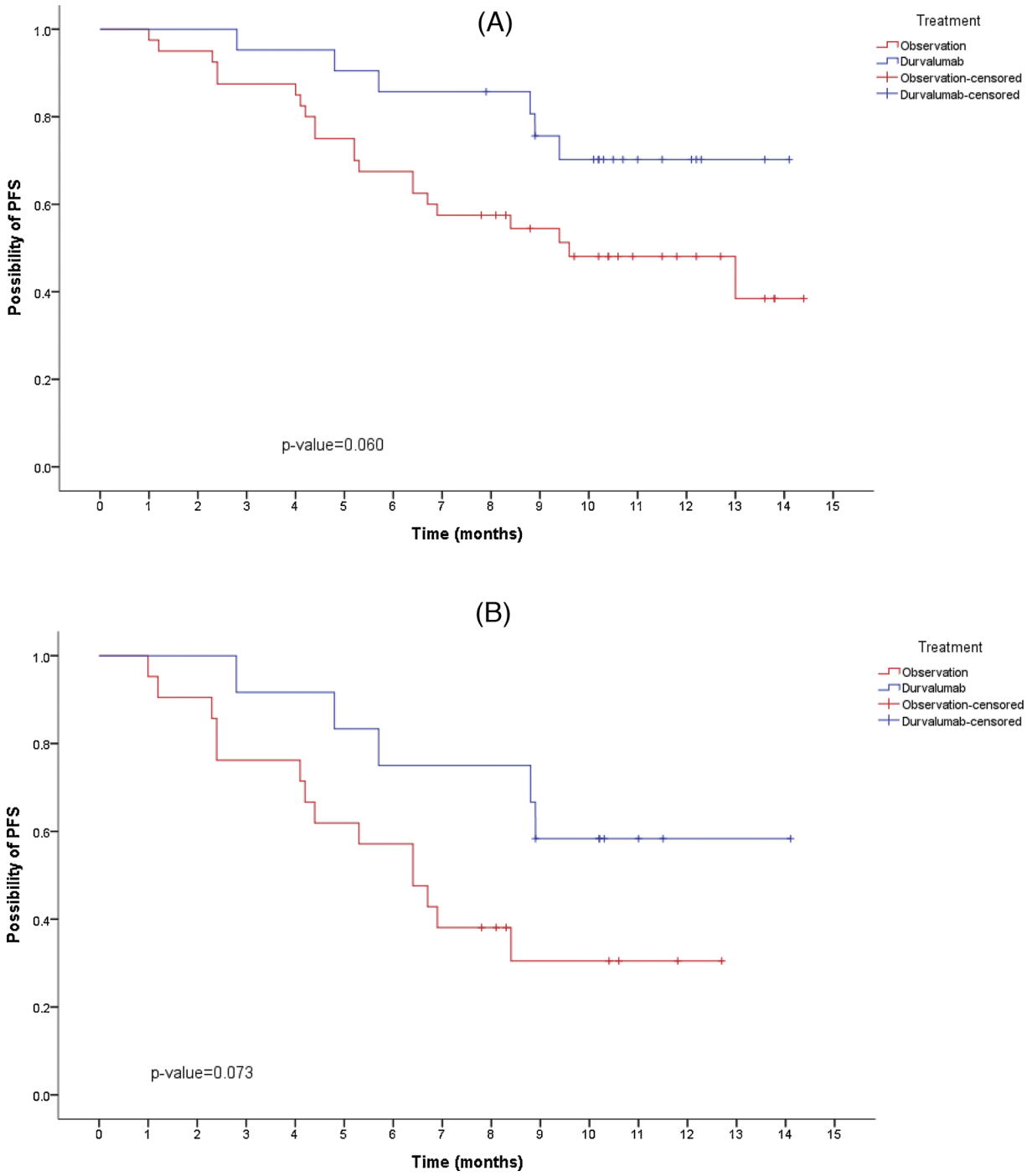

Fig. 2. (A) Kaplan-Meier survival curves (PFS) for stage III NSCLC patients with CCRT followed by durvalumab maintenance or observation. **(B)** Kaplan-Meier survival curves (PFS) for stage III NSCLC patients with CCRT followed by durvalumab maintenance or observation who were ineligible based on the criteria of the PACIFIC study.

for PACIFIC treatment, durvalumab consolidation treatment was associated favorable PFS.

Radiation pneumonitis is diagnosed clinically based on the presence of classic symptoms, timing and history of radiation therapy, appropriate imaging findings, and exclusion of other causes, such as infection and cardiogenic edema. Symptoms of radiation pneumonitis start typically within 3–12 weeks after completion of radiotherapy [13]. However, symptoms may arise later within the first year after radiation. Radiation pneumonitis is poorly understood. In a meta-analysis, the overall rate of symptomatic pneumonitis was 29.8 %, with fatal pneumonitis occurring in 1.9 % of patients undergoing CCRT for NSCLC. Predictive factors of radiation pneumonitis included V20, paclitaxel and carboplatin chemotherapy, and old age [14]. V20 also predicts the development of grade 2 or higher pneumonitis. The incidence of grade 2 or higher pneumonitis 24 months after CCRT is 0% for V20 less than 22 %, 7% for V20 of 22–31 %, 13 % for V20 of 32–40 % and 36 % for V20 greater than 40 %. Moreover, V20 is strongly correlated with the severity of pneumonitis [15]. Major restrictions of PACIFIC study enrollment included the total radiation dose and organ-specific dose. Programmed cell death 1 (PD-1) inhibitors block the PD-1/PD-L2 interaction between macrophages and T-cells, which could increase autoimmune adverse events such as pneumonitis [16,17]. The PACIFIC

and LUN 14–179 (phase II trial of concurrent chemoradiation with consolidation pembrolizumab in patients with unresectable stage III non-small cell lung cancer: Hoosier Cancer Research Network), which evaluated checkpoint-inhibitor use as consolidation therapy following CCRT, showed similar numerically lower rates of grade 3 or greater pneumonitis for the PD-L1 inhibitor durvalumab compared to the PD-1 inhibitor pembrolizumab (3.4 % versus 6.5 %). However, in our study, radiation pneumonitis of grade 3 or higher occurred in 18.2 % of the durvalumab group and 2.5 % of the observation group. In the PACFIC study, the frequency of radiation pneumonitis of grade 3 or higher was mentioned, but this study investigated factors related to radiation pneumonia-free survival of grade 2 or higher, and not factors related to grade 3. This is because clinical grade 2 requires active management including steroids. In our study, the incidence of radiation pneumonitis was higher in the durvalumab consolidation group than the observation group after adjusting for mean lung volume and V20 of radiotherapy, unlike the PACIFIC study. The higher rate of radiation pneumonitis in our study compared to the PACIFIC study may be explained by the organ specific radiation dose (LV20, MLD) as well as underlying lung function and clinical tumor burden of lung cancer.

In addition, we considered the influence of PBT, which could spare normal lung tissue. In patients who underwent PBT, organ-specific doses of radiotherapy were lower than the group that received x-ray therapy. They experienced grade ≥ 2 radiation pneumonitis less frequently. However, in our study, there were no patients who received PBT followed by durvalumab consolidation. Therefore, further investigation of the effects of PBT on radiation pneumonitis following durvalumab consolidation is warranted. However, considering the overall trend, durvalumab is associated with radiation pneumonitis above grade 2. Therefore, the financial and toxicity problems of radiation pneumonitis and the effects on follow-up should also be considered. In particular, most radiation pneumonitis occurred within 3–6 months after CCRT, so there is a need to actively manage radiation pneumonitis through frequent follow-up. In patients who received higher organ-specific doses of radiotherapy than those in the original PACIFIC study, symptom and chest x-ray monitoring should be performed at every visit within 3 months after CCRT.

In conclusion, durvalumab consolidation was associated with favorable PFS. However, in real-world practice, a broader group of patients are likely to be eligible for treatment, including those who do not meet the PACIFIC study's eligibility criteria, and thus careful selection and monitoring of patients undergoing durvalumab consolidation.

Funding

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Ministry of Science and ICT (No. NRF-2017M2A2A7A02018569).

Credit author statement

Keunchil Park designed this study. Hyun Ae, Jae Myoung Noh, Se-Hoon Lee, Jin Seok Ahn, Myung-Ju Ahn, Hongryull Pyo, Yong Chan Ahn and Keunchil Park performed the study and analyzed the data. Hyun Ae Jung and Jae Myoung Noh wrote the manuscript. All authors reviewed the manuscript.

Declaration of Competing Interest

Keunchil Park has an advisor role in this study and received research funding from Astra Zeneca outside of this study.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.lungcan.2020.05.035.

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