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Original Study

Durvalumab After Chemoradiotherapy for Locally Advanced NSCLC: A Real-World Analysis Using a Nationwide Claims Database in Japan

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ABSTRACT

Using a nationwide Japanese claims database, we analyzed 1439 patients who received durvalumab after chemoradiotherapy for locally advanced NSCLC. Median overall survival was 48.4 months and the 12-month cumulative incidence of radiation pneumonitis requiring steroids was 19.4%. Intensity-modulated radiotherapy was associated with reduced pneumonitis risk, and durvalumab rechallenge was administered in 37.5% of pneumonitis cases.

Background: Durvalumab consolidation therapy after chemoradiotherapy (CRT) for locally advanced non-small cell lung cancer (NSCLC) is an established standard of care. However, real-world data from claims databases, which capture a broad clinical landscape, are lacking in Asia. This study aimed to characterize real-world treatment patterns and clinical outcomes using a nationwide claims database in Japan.

Patients and Methods: Patients who received durvalumab after definitive CRT for NSCLC between 2018 and 2024 were identified from the DeSC database. Overall survival (OS) was estimated using the Kaplan–Meier method. Radiation pneumonitis requiring steroid treatment was estimated using the cumulative incidence function with death as a competing risk.

Results: A total of 1439 patients were identified, and the median age was 73.6 years. The median durvalumab treatment duration was 5.3 months, and treatment completion rates (≥ 10 and ≥ 11 months) were 32.2% and 26.3%, respectively. The median OS was 48.4 months (95% CI, 42.1-57.4 months). The 12-month cumulative incidence of pneumonitis requiring steroid treatment was 19.4% (95% CI, 17.3-21.6%). In multivariable analysis, increasing age, shorter CRT-to-durvalumab interval, pre-existing pneumonitis diagnosis, and respiratory motion management fee were associated with increased pneumonitis risk, whereas the use of intensity-modulated radiotherapy was associated with reduced risk. Among 280 patients who developed pneumonitis, durvalumab rechallenge was administered in 37.5%.

Conclusion: In this nationwide claims database study, we characterized the clinical practice of CRT with durvalumab treatment and the clinical outcomes in Japan. These real-world findings from Asia complement existing evidence and may inform treatment optimization for durvalumab after CRT.

Introduction

Durvalumab consolidation therapy after definitive chemoradiotherapy (CRT) for unresectable locally advanced non-small cell lung cancer (NSCLC) has been approved worldwide and established as a standard of care, following the PACIFIC trial, which demonstrated significant improvements in both progression-free survival (PFS) and overall survival (OS).[1-4]

Since the approval of durvalumab, studies evaluating its effectiveness and safety in real-world clinical practice have been reported.[5,6] In Asian populations as well, prospective and retrospective multicenter observational studies have demonstrated similar survival outcomes.[7-10] On the other hand, pneumonitis after CRT has been reported more frequently in the Asian subgroup in the PACIFIC trial population.[11] While the incidence of symptomatic pneumonitis of Grade 2 or higher has been reported as 19%-26% in the western populations,[11-15] data from Japan have reported higher rates of 34%-39%.[7,16-18] However, nation-

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wide characteristics of survival outcomes and pneumonitis incidence in Asian countries, including not only large facilities but also smaller community hospitals, have not been fully revealed.

For the purpose of investigating the nationwide clinical practice and clinical outcomes, studies utilizing electronic health record data and veterans' healthcare databases have been reported from North America.[19,20] These studies have the advantage of reflecting general clinical practice that cannot be fully captured in clinical trials through their large and comprehensive case accrual. However, no study with a similar design has been conducted in Asia. Therefore, in this study, we used a nationwide claims database in Japan to investigate the real-world patterns of durvalumab treatment after CRT, including treatment completion rates, survival outcomes, incidence of radiation pneumonitis, and rechallenge after pneumonitis.

Materials and Methods

Data Source

This study used the DeSC database (DeSC Healthcare, Tokyo, Japan), a commercial claims database in Japan. Japan has a universal health insurance system, in which all citizens are required to enroll in a public health insurance plan. The DeSC database, which contained a cumulative total of 16.6 million registered individuals as of April 2025, is constructed from data provided by multiple insurers, including Health Insurance Societies covering employees and their dependents, the National Health Insurance covering primarily self-employed individuals and retirees, and the Latter-Stage Elderly Healthcare System primarily covering individuals aged 75 years or older. This enables the tracking of all insured medical services and drug prescriptions across a wide range of age groups from younger adults to the elderly. Based on these characteristics, the DeSC database has been reported to provide favorable coverage of population age distribution and disease prevalence.[21] For this study, a dataset containing information from February 2014 to February 2025 was received on September 5, 2025, and used for analysis.

Study Population

To examine patients who received durvalumab after definitive CRT for NSCLC, patients were selected according to the following criteria. Considering the approval date of durvalumab and the available follow-up period, patients who received at least one dose of durvalumab between 2018 and 2024 were extracted, and the date of the first durvalumab administration was defined as day 0. In Japan, durvalumab was first approved in July 2018 as consolidation therapy after definitive CRT for NSCLC, and has since become available for the first-line treatment of extensive-stage small cell lung cancer (ED-SCLC), for advanced or recurrent NSCLC, as well as for biliary tract cancer, hepatocellular carcinoma, and endometrial cancer by the end of 2024. Taking this into account, the following eligibility and exclusion criteria were established to identify cases of durvalumab administration after CRT for NSCLC. The eligibility criteria included a diagnosis of NSCLC (ICD-10 codes: C34 and D022, excluding small cell lung cancer codes) and a history of CRT (defined as 20-40 treatment days of radiotherapy with concurrent chemotherapy administered during that period) within 1 year prior to day 0. The exclusion criteria included any of the following within 1 year prior to day 0: a primary cancer diagnosis other than NSCLC, a diagnosis of distant metastasis, or a record of surgery for lung cancer.

Study Outcomes and Analyses

This was a retrospective cohort study. The following outcomes were examined to characterize the real-world treatment patterns and clinical outcomes of durvalumab consolidation therapy after CRT for NSCLC.

Patient baseline characteristics and treatment details were summarized descriptively. Continuous variables were reported as medians with interquartile ranges (IQR), and categorical variables as frequencies and proportions. The duration of durvalumab treatment was defined as the period from the first to the last administration. As surrogate indicators of treatment completion, the proportions of patients with treatment durations of $\geq$ 10 months and $\geq$ 11 months were examined. As an exploratory analysis, the proportion of IMRT use was cross-tabulated by treatment year and urban facility classification, with temporal trends assessed using the Cochran–Armitage trend test and between-group differences using the chi-squared test.

The observation period for each patient was determined by the insurer-reported observation end date. The date of the last medical service within the observation end month was used as the date of censoring or, for patients with a death flag in the database, as the date of death. Overall survival (OS) was defined as the time from the first durvalumab administration (day 0) to death from any cause. Time to first subsequent therapy or death (TFST) was defined as the time from day 0 to the first occurrence of surgery, administration of chemotherapy other than durvalumab, radiotherapy, or death. OS and TFST were estimated using the Kaplan–Meier method. Factors associated with OS were evaluated using the Cox proportional hazards model, and hazard ratios (HR) with 95% confidence intervals (CI) were calculated.

The radiation pneumonitis event was defined as the co-occurrence of a radiation pneumonitis diagnosis and administration of oral or intravenous corticosteroids within the same month after day 0. As sensitivity analyses, the following analyses were conducted: (1) alternative event definition using only the occurrence of a radiation pneumonitis diagnosis regardless of steroid administration, and (2) the day when the radiotherapy course was completed was set as day 0. The cumulative incidence of radiation pneumonitis events was estimated using the cumulative incidence function (CIF), with death treated as a competing risk. Factors associated with radiation pneumonitis were evaluated using the Fine–Gray subdistribution hazard model, and subdistribution hazard ratios (sHR) with 95% CI were calculated.

Among patients who developed radiation pneumonitis requiring steroid treatment, subsequent rechallenge with durvalumab was examined. The proportion of patients who received rechallenge was reported, and the cumulative incidence was additionally estimated using the CIF with death as a competing risk. Histograms of total durvalumab treatment duration were described by rechallenge status among patients with pneumonitis events. For patients who underwent rechallenge, baseline characteristics were compared between those with total treatment durations of $<$ 10 months and $\geq$ 10 months using the Mann–Whitney U test and the Pearson chi-squared test.

Statistical significance was set at a 2-sided $P < .05$. Data extraction and processing were performed using Python version 3.9.6 (Python Software Foundation, Wilmington, DE, USA) with the DuckDB library version 1.4.1 (DuckDB Labs, Amsterdam, Netherlands). Statistical analyses were conducted using R version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

Covariates

Patient baseline characteristics included the year of durvalumab initiation, age, sex, and a history of interstitial pneumonia diagnosis before day 0. The Charlson Comorbidity Index (CCI)[22] was calculated based on ICD-10 diagnosis codes recorded in the 12 months prior to treatment initiation, using the updated coding algorithm by Quan et al.[23] Tumor-related components (any malignancy, metastatic solid tumor, leukemia, and lymphoma) were excluded from the index to avoid conflation with the index cancer diagnosis, consistent with the approach used in cancer-specific comorbidity assessment.[24] CCI scores were categorized as 0, 1, 2, and 3 or higher. Radiotherapy-related variables included whether the treatment facility was classified as urban (defined as located in one of the 23 special wards of Tokyo or a government-designated city), the number of radiotherapy fractions and treatment duration, use of intensity-modulated radiotherapy (IMRT) and respiratory motion

Table 1
Patient Characteristics and Treatment Details (N = 1439).

Characteristic	Value
Year of durvalumab initiation, n (%)	
2018	82 (5.7%)
2019	245 (17.0%)
2020	281 (19.5%)
2021	284 (19.7%)
2022	321 (22.3%)
2023	179 (12.4%)
2024	47 (3.3%)
Age, years, median [IQR]	73.6 [69.1-77.4]
Female sex, n (%)	313 (21.8%)
History of interstitial pneumonia, n (%)	81 (5.6%)
Charlson Comorbidity Index, n (%)	
0	515 (35.8%)
1	440 (30.6%)
2	191 (13.3%)
3+	293 (20.4%)
Urban treatment facility, n (%)	800 (55.6%)
Number of RT fractions, median [IQR]	30 [30-30]
Number of RT fractions, n (%)	
20-29	170 (11.8%)
30	1157 (80.4%)
31-40	112 (7.8%)
RT duration, days, median [IQR]	44 [43-46]
IMRT use, n (%)	470 (32.7%)
Respiratory motion management fee, n (%)	97 (6.7%)
Taxane-based chemotherapy, n (%)	1017 (70.7%)
Interval from CRT to durvalumab, days, median [IQR]	16 [12-27]
Radiation pneumonitis before durvalumab, n (%)	33 (2.3%)

Abbreviations: CCI = Charlson Comorbidity Index; CRT = chemoradiotherapy; IMRT = intensity-modulated radiotherapy; IQR = interquartile range; RT = radiotherapy.

management fee during the treatment period, and the presence of a radiation pneumonitis diagnosis between the start of radiotherapy and the day before day 0. The respiratory motion management fee is a reimbursement add-on available when tumor respiratory motion exceeding 10 mm is managed to 5 mm or less, typically through breath-hold techniques for lower-lobe tumors. Drug therapy-related variables included the use of taxane-based chemotherapy, which has been previously suggested as a potential factor associated with pneumonitis, and the interval from the end of CRT to the first durvalumab administration.

Ethical Considerations

This was an observational study using an anonymized database, and informed consent from patients was waived. This study was approved by the Ethics Committee of Tohoku University Graduate School of Medicine (approval number: 2025-1-452).

Results

Patient Characteristics

Based on the eligibility and exclusion criteria, 1439 patients were selected. Patient characteristics and treatment details are shown in Table 1. Overall, 80.4% of patients received 30 fractions of radiotherapy, and IMRT was used in 32.7% of cases. In an exploratory analysis, IMRT use was more frequent in urban than non-urban facilities (37.5% vs. 26.6%) and increased over time from 12.6% in 2018 to 41.9% in 2024 (both $P < .01$, Supplementary Table 1). Respiratory motion management fee was present in 6.7% of cases. The CCI was 0 in 35.8%, 1 in 30.6%, 2 in 13.3%, and 3 or higher in 20.4% of patients. Taxane-based chemotherapy was administered in 70.7% of cases. The median interval from the end of CRT to the first durvalumab administration was 16 days, and 2.3% of patients had a radiation pneumonitis diagnosis recorded before the initiation of durvalumab. The median follow-up

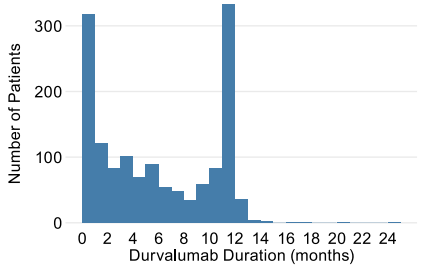

Figure 1. Histogram of durvalumab treatment duration.

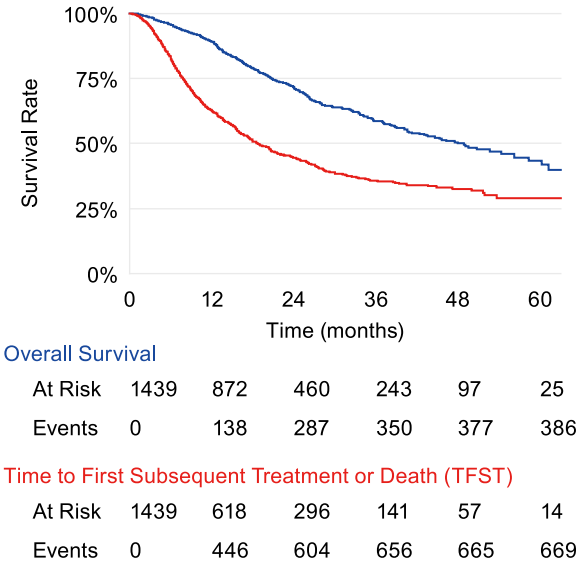

Figure 2. Kaplan–Meier plots of overall survival and time to first subsequent treatment or death.

was 11.6 months (IQR: 3.3-24.2 months), and 387 deaths (26.9%) were observed during the study period.

Duration of Durvalumab Treatment

The histogram of treatment duration is shown in Figure 1. The median treatment duration for the entire cohort was 5.3 months (IQR: 1.4-11.1 months). The proportions of patients who received treatment for 10 months or longer and 11 months or longer in the entire study period between 2018 and 2024, used as surrogate indicators of treatment completion, were 32.2% and 26.3%, respectively. In an additional exploratory analysis restricted to patients treated between 2018 and 2022, the proportions of patients with treatment durations of 10 months or longer and 11 months or longer were 36.5% and 30.0%, respectively.

Survival Analysis

OS and TFST are shown in Figure 2. The median OS was 48.4 months (95% CI, 42.1-57.4 months). The 2-year and 5-year OS rates were 70.4% (95% CI, 67.5-73.5%) and 42.1% (95% CI, 36.1-49.0%), respectively. The median TFST was 18.5 months (95% CI, 16.8-20.7 months). The 2-year and 5-year TFST rates were 44.2% (95% CI, 41.2-47.5%) and 28.0% (95% CI, 23.7-33.2%), respectively.

The results of multivariable Cox regression analysis for factors associated with OS are shown in Table 2. Older age (HR per 10 years: 1.87, 95% CI, 1.58-2.21, $P < .001$), female sex (HR: 0.60, 95% CI, 0.45-0.80, $P < .001$), respiratory motion management fee (HR: 1.89, 95% CI, 1.25-2.84, $P = .002$), and CCI of 3 or higher (HR: 1.33, 95% CI, 1.00-1.75, $P = .048$) were significantly associated with OS.

Table 2
Multivariable Cox Regression Analysis for Overall Survival.

Variable	HR	95% CI	*P*-Value
Year of durvalumab initiation	1.05	0.96-1.14	.31
Age (per 10 y)	1.87	1.58-2.21	< .001
Female sex	0.60	0.45-0.80	< .001
History of interstitial pneumonia	1.30	0.88-1.93	.19
CCI (ref: 0)			
1	1.21	0.93-1.57	.16
2	1.07	0.76-1.50	.72
3+	1.33	1.00-1.75	.048
Urban treatment facility	1.07	0.87-1.32	.54
Number of RT fractions (ref: 30)			
20-29	1.23	0.89-1.69	.20
31-40	0.75	0.49-1.14	.17
IMRT use	0.84	0.66-1.07	.16
Respiratory motion management fee	1.89	1.25-2.84	.002
Taxane-based chemotherapy	0.97	0.78-1.21	.79
Interval from CRT to durvalumab (per wk)	1.02	0.98-1.07	.39
Radiation pneumonitis before durvalumab	0.96	0.49-1.91	.92

Abbreviations: CCI = Charlson Comorbidity Index; CI = confidence interval; CRT = chemoradiotherapy; HR = hazard ratio; IMRT = intensity-modulated radiotherapy; RT = radiotherapy.

Table 3
Multivariable Analysis for Radiation Pneumonitis Requiring Steroid Treatment.

Variable	sHR	95% CI	*P*-Value
Year of durvalumab initiation	1.05	0.97-1.14	.21
Age (per 10 y)	1.54	1.30-1.84	< .001
Female sex	0.94	0.70-1.26	.69
History of interstitial pneumonia	1.07	0.67-1.70	.79
CCI (ref: 0)			
1	1.20	0.90-1.61	.21
2	1.09	0.74-1.61	.67
3+	1.13	0.81-1.59	.47
Urban treatment facility	0.86	0.68-1.10	.24
Number of RT fractions (ref: 30)			
20-29	1.22	0.86-1.73	.27
31-40	0.97	0.62-1.52	.90
IMRT use	0.74	0.56-0.98	.036
Respiratory motion management fee	1.54	1.01-2.34	.046
Taxane-based chemotherapy	1.27	0.97-1.67	.084
Interval from CRT to durvalumab (per wk)	0.93	0.89-0.97	.002
Radiation pneumonitis before durvalumab	8.73	5.96-12.78	< .001

Abbreviations: CCI = Charlson Comorbidity Index; CI = confidence interval; CRT = chemoradiotherapy; IMRT = intensity-modulated radiotherapy; RT = radiotherapy; sHR = subdistribution hazard ratio.

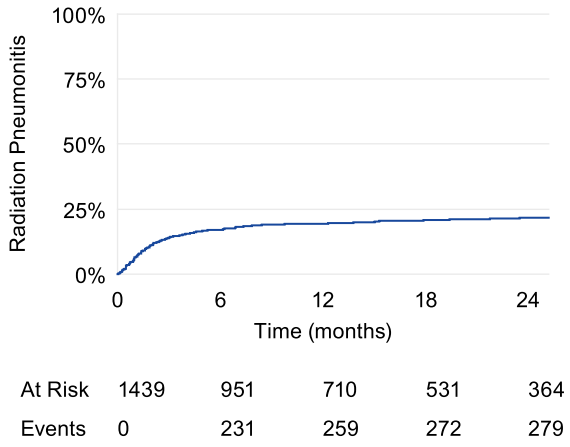

Figure 3. Cumulative incidence of radiation pneumonitis events requiring steroid treatment.

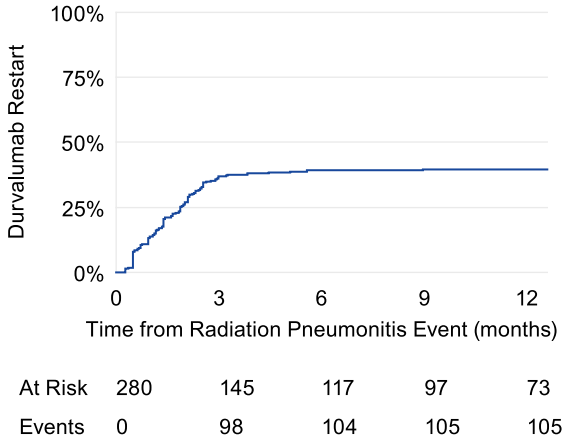

Figure 4. Cumulative incidence of durvalumab rechallenge among patients with radiation pneumonitis events requiring steroid treatment.

Incidence of Radiation Pneumonitis Events

The cumulative incidence curve of radiation pneumonitis events requiring steroid treatment is shown in Figure 3. The cumulative incidence at 12 months was 19.4% (95% CI, 17.3-21.6%). The results of multivariable analysis for factors associated with radiation pneumonitis events requiring steroid treatment are shown in Table 3. Age (sHR per 10 years: 1.54, 95% CI, 1.30-1.84, $P < .001$), IMRT use (sHR: 0.74, 95% CI, 0.56-0.98, $P = .036$), respiratory motion management fee (sHR: 1.54, 95% CI, 1.01-2.34, $P = .046$), interval from CRT completion to durvalumab initiation (sHR per week: 0.93, 95% CI, 0.89-0.97, $P = .002$), and the presence of a pneumonitis diagnosis before durvalumab initiation (sHR: 8.73, 95% CI, 5.96-12.78, $P < .001$) were significantly associated with the occurrence of radiation pneumonitis events. A sensitivity analysis using radiation pneumonitis diagnosis regardless of steroid treatment as the event was also performed (Supplementary Table 2). In this analysis, age, IMRT use, respiratory motion management fee, taxane-based chemotherapy, interval from CRT completion to durvalumab initiation, and the presence of a pneumonitis diagnosis before durvalumab initiation were identified as significant factors. In another sensitivity analysis using the day when the radiotherapy course was completed as day 0, the interval from CRT completion to durvalumab initiation was not statistically significant (sHR per week: 0.99, 95% CI, 0.93-1.05, $P = .72$, Supplementary Table 3).

Durvalumab Rechallenge After Radiation Pneumonitis

The cumulative incidence curve of durvalumab rechallenge among the 280 patients with recorded radiation pneumonitis events requiring steroid treatment is shown in Figure 4. Rechallenge was administered in 105 patients (37.5%, 95% CI, 31.9-43.5%). Most rechallenges occurred within 3 months, after which the cumulative incidence largely plateaued. Histograms of total durvalumab treatment duration by rechallenge status are shown in Supplementary Figure 1. Among the 105 rechallenge patients, 51 (48.6%) and 42 (40.0%) achieved total treatment durations of ≥ 10 and ≥ 11 months, respectively, although these durations included the interruption period due to pneumonitis. When rechallenge patients were compared by total treatment duration (Supplementary Table 4), those with <10 months had a shorter interval from durvalumab initiation to pneumonitis onset than those with ≥ 10 months (4.7 vs. 7.3 weeks, $P = .019$).

Discussion

This study used a nationwide claims database in Japan to characterize the real-world treatment patterns of 1439 NSCLC patients who received durvalumab consolidation therapy after CRT. A strength of this study is its inclusion of patients from both large academic centers and community hospitals, reflecting a broad real-world clinical landscape.

To our knowledge, this is the first study from Asia to employ a claims database-based design of this kind.

The median age of the study population was 73.6 years, which was approximately 10 years older than the 64 years in the PACIFIC trial [1] and 66 years in PACIFIC-R,[5] and approximately 5 years older than the 69 years reported in the AYAME study from Japan.[9] This finding likely reflects the aging demographic of the Japanese patient population and the inclusion of elderly patients in rural areas who may not have been included in previous multicenter studies. Despite this elderly population, the median OS of 48.4 months in the present study was generally comparable to the 47.5 months reported in the PACIFIC trial[3] and the 44.6 months in the Canadian RELEVANCE study.[25] Studies from Korea and Japan examining elderly patients have reported that, although patients aged 70 or 75 years and older may experience increased rates of adverse events and shorter OS, their PFS remains comparable to that of younger patients, supporting the administration of durvalumab in older patients.[26,27] Our results are consistent with these findings and suggest that favorable survival outcomes can be achieved even in real-world data that include rural areas, smaller facilities, and a higher mean age population.

In the Cox regression analysis for OS, older age (HR per 10 years: 1.87, $P < .001$), female sex (HR: 0.60, $P < .001$), respiratory motion management fee (HR: 1.89, $P = .002$), and CCI of 3 or higher (HR: 1.33, $P = .048$) were identified as significant factors. Most of these are established prognostic factors in the cancer population and are consistent with previous reports.[26-29] Notably, the present study showed an association between respiratory motion management fee and worse OS. This may reflect tumor location in the lower lobe, which has been reported as an adverse prognostic factor in lung cancer.[30] IMRT use did not reach statistical significance for OS (HR: 0.84, $P = .16$) despite its significant association with reduced pneumonitis risk. It should also be noted that the absence of ECOG PS, histology, and PD-L1 expression in this claims database, which are among the strongest known prognostic factors in locally advanced NSCLC, limits the interpretability of the OS regression results.[25,27,29,31]

Despite the favorable overall survival, the treatment completion rates defined as durvalumab administration for 10 months or longer and 11 months or longer were only 32.2% and 26.3%, respectively. Even in an exploratory analysis restricted to patients treated in an earlier period between 2018 and 2022 to account for potentially insufficient follow-up in the claims database, these rates were 36.5% and 30.0%, respectively. These values were lower than the completion rates of 40%-47% reported in previous studies.[8,9,25] A study analyzing US community data reported that the proportions of patients who received 10 and 11 months of treatment were 39% and 28%, respectively, somewhat closer to our results, suggesting modestly lower completion rates in real-world clinical practice.[19] In our study, while the median interval from CRT to durvalumab initiation was short at 16 days, approximately 25% of patients discontinued within the first month, suggesting the existence of cases in which durvalumab was promptly initiated after CRT completion but proved to be insufficiently tolerable. Additionally, as a claims database study, the present analysis likely included smaller facilities with less experience in adverse event management, which may have contributed to lower completion rates.

The 12-month cumulative incidence of radiation pneumonitis requiring steroid treatment in this study was 19.4%. It should be noted that the event definition in this study, based on the co-occurrence of a radiation pneumonitis diagnosis and corticosteroid prescription within the same month, approximates but does not directly correspond to the CTCAE Grade 2 definition (symptomatic; medical intervention indicated; limiting instrumental ADL). Because the original CTCAE Grade 2 can include mild symptomatic pneumonitis not requiring steroid treatment, the event rate in this study likely represents an underestimate compared with Grade 2 or higher. With this caveat, the event rate in our study was roughly comparable to the 19.8% Grade 2 or higher pneumonitis rate reported in the PACIFIC trial,[11] suggesting that the actual incidence of Grade 2 or higher pneumonitis was likely higher than in the PACIFIC trial. Japanese multicenter data have reported a Grade 2 or higher pneumonitis rate of 34.4%, and it has been suggested that pneumonitis may be more frequent in Asian populations and elderly cohorts.[11,16] The true incidence of Grade 2 or higher pneumonitis in our study was presumably similar.

In the multivariable analysis of pneumonitis occurrence, increasing age, shorter interval from CRT to durvalumab initiation, the presence of a radiation pneumonitis diagnosis before durvalumab initiation, and respiratory motion management fee were significantly associated with increased pneumonitis risk, whereas IMRT use was significantly associated with decreased risk. These results were largely consistent in the sensitivity analysis using any pneumonitis diagnosis as the event regardless of steroid treatment, suggesting robustness of the findings. The positive association between age and pneumonitis risk is consistent with reports from Japan and Korea analyzing elderly patient data, and may reflect the decline in pulmonary reserve associated with aging.[26,27]

The use of IMRT was significantly associated with a reduction in pneumonitis risk (sHR 0.74, $P = .036$). This finding represents one of the clinically important observations in this study. IMRT offers superior dose conformity to the target and the potential to reduce the volume receiving 20 Gy or higher (V20) and mean lung dose (MLD), which are established risk factors for pneumonitis in previous reports, compared with 3D conformal radiotherapy (3D-CRT).[13,32,33] On the other hand, IMRT has also been noted to increase the low-dose region including V5, reported as an independent predictor of symptomatic pneumonitis.[34] Despite the issue of low-dose scatter with IMRT, our results indicate that, at the population level, IMRT appears to be net protective. However, individual DVH parameters (V20, V5, MLD, etc.) were not available in the current study, and direct comparison of dose-volume indices between IMRT and 3D-CRT was not possible. In exploratory analyses, IMRT utilization increased over time, reaching 41.9% in the most recent year, whereas facilities in non-urban areas had lower utilization rates than urban facilities (26.6% vs. 37.5%, $P < .001$). These findings suggest that the use of advanced radiotherapy techniques may be influenced not only by individual patient-based decision-making but also by disparities in technology adoption across institutions.

The presence of respiratory motion management fee was associated with increased pneumonitis risk (sHR 1.54, $P = .046$). Respiratory motion management techniques are primarily applied to lower-lobe lesions near the diaphragm; thus, this factor can be interpreted as a surrogate marker for lower-lobe tumor location and larger respiratory diaphragmatic motion, which can increase the dose to normal lung. Gao et al. reported an association between lower-lobe lesions and increased pneumonitis at the level of univariate analysis.[13] Particularly in this study, where lung dose parameters were unavailable, this factor may have been detected as significant because it encompasses lung dose information.

The interval from CRT completion to durvalumab initiation showed an sHR of 0.93 per week in the main analysis ($P = .002$), indicating that a longer interval was associated with a lower pneumonitis risk. A post hoc analysis of the PACIFIC trial showed that initiating durvalumab within 14 days was associated with improved PFS,[3] supporting the benefit of early initiation. Our results present the seemingly contradictory finding that a shorter interval increases pneumonitis risk. However, in an additional sensitivity landmark analysis using the CRT completion date as the origin, the significance of the interval was lost (sHR per week: 0.99, $P = .72$). Taken together, the association between a longer interval and lower pneumonitis risk likely reflects the passage of time through the peak-risk period after radiotherapy rather than a true effect. In other words, our findings do not provide support for intentionally delaying durvalumab initiation to reduce pneumonitis risk.

Taxane-based chemotherapy showed only a trend toward significance in the primary analysis (sHR 1.27, $P = .084$) and reached significance in the sensitivity analysis using any pneumonitis diagnosis as the event (sHR 1.30, $P = .044$). Among the existing studies, Saito et al. examined the association between taxane-based chemotherapy and pneu-

monitis in a multicenter retrospective study and demonstrated no significant difference (HR 1.44, $P = .14$).[7] Our results also cannot exclude the possibility that taxane-based agents have some influence on pneumonitis risk; however, the association was inconsistent, and no definitive conclusion could be drawn.

Among the 280 patients who developed pneumonitis requiring steroid treatment, rechallenge with durvalumab was observed in 37.5%, which is comparable to a previous report.[7] The majority of rechallenges occurred within 3 months, with minimal increase beyond this point. Previous reports have shown that Grade 2 or higher pneumonitis is associated with worse OS in durvalumab treatment[17]; however, Kakiuchi et al. compared patients who underwent rechallenge after Grade 2 pneumonitis with those who did not, reporting that PFS was 32.0 months in the rechallenge group compared with 5.3 months in the non-rechallenge group, suggesting a benefit of rechallenge when feasible.[35] In our analysis, 48.6% of rechallenge patients achieved a total treatment duration of ≥ 10 months, suggesting that treatment continuation and completion is feasible in a substantial proportion of patients. Patients who achieved ≥ 10 months of total treatment had a longer interval from durvalumab initiation to pneumonitis onset than those who did not. This suggests that patients who develop pneumonitis early after durvalumab initiation may be less likely to achieve successful rechallenge. In practice, decisions regarding durvalumab rechallenge after pneumonitis require individualized and careful assessment of pneumonitis severity and recovery status; however, the data from this study reflect current real-world treatment patterns.

This study has several limitations. First, as with previous claims database-based studies, the accuracy and validity of variable and event identification in this study have inherent limitations. Second, the claims database did not contain clinical information such as stage classification, PD-L1 expression and EGFR mutation status, histology, ECOG PS, and smoking status, nor DVH parameters such as V20, V5, or MLD, precluding adjustment for these established risk and prognostic factors. Although a Cox regression analysis for OS was performed, the absence of these key covariates limits the interpretability of the OS prognostic analysis. Moreover, the lack of EGFR mutation data precluded confirmatory analyses regarding the favorable OS and higher pneumonitis rates that have been suggested in this population. Third, it was not possible to distinguish the reasons for delayed durvalumab initiation (whether due to post-CRT adverse events or institutional treatment policies) in individual cases. Fourth, systematic identification of a control group treated with CRT alone was not feasible in this database, and direct comparison with patients who did not receive durvalumab was not possible. Despite these limitations, this study using a nationwide claims database provides insights that reflect real-world clinical practice across Japan and complements the existing evidence.

Conclusion

In conclusion, this study analyzed 1439 patients using a nationwide claims database in Japan and characterized the real-world patterns of durvalumab treatment after CRT. Despite the elderly study population with a median age of 73.6 years, a favorable median OS of 48.4 months was observed. The 12-month cumulative incidence of pneumonitis requiring steroid treatment was 19.4%, and IMRT use was significantly associated with reduced pneumonitis risk. Durvalumab rechallenge after a pneumonitis event was administered in 37.5% of patients. These findings provide fundamental data from real-world clinical practice in Asia that may contribute to optimizing treatment strategies for durvalumab after CRT.

Clinical Practice Points

- Durvalumab consolidation after chemoradiotherapy is the standard of care for unresectable stage III NSCLC, but real-world nationwide data from Asia, including community hospitals and elderly patients, have been limited.
- In this nationwide Japanese claims-database analysis of 1439 patients (median age 73.6 years), median overall survival was 48.4 months and the 12-month cumulative incidence of radiation pneumonitis requiring steroids was 19.4%, supporting durvalumab efficacy in older real-world cohorts.
- Intensity-modulated radiotherapy was independently associated with a lower pneumonitis risk (sHR 0.74), whereas older age, preexisting pneumonitis diagnosis, respiratory motion management fee, and a shorter CRT-to-durvalumab interval were associated with higher pneumonitis risk.
- Durvalumab rechallenge after pneumonitis was administered in 37.5% of patients, mostly within 3 months, indicating that rechallenge is feasible in selected patients in real-world practice.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work the author(s) used ChatGPT, Gemini, Claude, and Cursor in order to draft analysis code and assist with manuscript preparation. After using these tools/services, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

Data Availability Statement

The data that support the findings of this study are not publicly available due to contractual restrictions with the data provider (DeSC Healthcare).

Disclosure

NT reports a relationship with Elekta KK that includes speaking and lecture fees and travel reimbursement. KJ reports relationships with Elekta KK that include funding grants and with Varian Medical Systems Inc that include consulting or advisory. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Kazuya Takeda: Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Takaya Yamamoto:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Rei Umezawa:** Writing – review & editing, Supervision, Methodology. **Noriyoshi Takahashi:** Writing – review & editing, Supervision, Methodology. **Shinsaku Okuda:** Software, Methodology, Formal analysis. **Keiichi Jingu:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cllc.2026.05.010.

References

1. Antonia SJ, Villegas A, Daniel D, et al. Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. *N Engl J Med*. 2017;377:1919–1929. doi:10.1056/NEJMoa1709937.
2. Antonia SJ, Villegas A, Daniel D, et al. Overall survival with durvalumab after chemoradiotherapy in stage III NSCLC. *N Engl J Med*. 2018;379:2342–2350. doi:10.1056/NEJMoa1809697.
3. Faivre-Finn C, Vicente D, Kurata T, et al. Four-year survival with durvalumab after chemoradiotherapy in stage III NSCLC—an update from the PACIFIC trial. *J Thorac Oncol*. 2021;16:860–867. doi:10.1016/j.jtho.2020.12.015.
4. Spigel DR, Faivre-Finn C, Gray JE, et al. Five-year survival outcomes from the PACIFIC trial: durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. *J Clin Oncol*. 2022;40:1301–1311. doi:10.1200/JCO.21.01308.
5. Girard N, Bar J, Garrido P, et al. Treatment characteristics and real-world progression-free survival in patients with unresectable stage III NSCLC who received durvalumab after chemoradiotherapy: findings from the PACIFIC-R study. *J Thorac Oncol*. 2023;18:181–193. doi:10.1016/j.jtho.2022.10.003.
6. Filippi AR, Bar J, Chouaid C, et al. Real-world outcomes with durvalumab after chemoradiotherapy in patients with unresectable stage III NSCLC: interim analysis of overall survival from PACIFIC-R. *ESMO Open*. 2024;9:103464. doi:10.1016/j.esmoop.2024.103464.
7. Saito G, Oya Y, Taniguchi Y, et al. Real-world survey of pneumonitis and its impact on durvalumab consolidation therapy in patients with non-small cell lung cancer who received chemoradiotherapy after durvalumab approval (HOPE-005/CRIMSON). *Lung Cancer*. 2021;161:86–93. doi:10.1016/j.lungcan.2021.08.019.
8. Park CK, Oh HJ, Kim YC, et al. Korean real-world data on patients with unresectable stage III NSCLC treated with durvalumab after chemoradiotherapy: PACIFIC-KR. *J Thorac Oncol*. 2023;18:1042–1054. doi:10.1016/j.jtho.2023.04.008.
9. Kenmotsu H, Saito Y, Ninomiya K, et al. Long-term safety and effectiveness of durvalumab in unresectable stage III NSCLC in Japan: a multicenter prospective study (AYAME). *J Thorac Oncol*. 2026;21:160–173. doi:10.1016/j.jtho.2025.08.010.
10. Sitthideatphaiboon P, Reungwetwattana T, Jaruhathai S, et al. Durvalumab following definitive chemoradiotherapy among patients with stage III NSCLC in the Thai population: a real-world, multicenter observational study. *Front Oncol*. 2025;15:1647385. doi:10.3389/fonc.2025.1647385.
11. Vansteenkiste JF, Naidoo J, Faivre-Finn C, et al. Symptomatic pneumonitis with durvalumab after concurrent chemoradiotherapy in unresectable stage III NSCLC. *JTO Clin Res Rep*. 2024;5:100638. doi:10.1016/j.jtocrr.2024.100638.
12. Desilets A, Blanc-Durand F, Lau S, et al. Durvalumab therapy following chemoradiation compared with a historical cohort treated with chemoradiation alone in patients with stage III non-small cell lung cancer: a real-world multicentre study. *Eur J Cancer*. 2021;142:83–91. doi:10.1016/j.ejca.2020.10.008.
13. Gao RW, Day CN, Yu NY, et al. Dosimetric predictors of pneumonitis in locally advanced non-small cell lung cancer patients treated with chemoradiation followed by durvalumab. *Lung Cancer*. 2022;170:58–64. doi:10.1016/j.lungcan.2022.06.003.
14. Akkad N, Thomas TS, Luo S, Knoche E, Sanfilippo KM, Keller JW. A real-world study of pneumonitis in non-small cell lung cancer patients receiving durvalumab following concurrent chemoradiation. *J Thorac Dis*. 2023;15:6427–6435. doi:10.21037/jtd-22-1604.
15. Appel S, Wilk L, Saad A, et al. Pneumonitis after chemoradiation followed by durvalumab for locally advanced lung cancer: predictors and effect on survival. *Br J Radiol*. 2025;98:1436–1445. doi:10.1093/bjr/tqaf133.
16. Shintani T, Kishi N, Matsuo Y, et al. Incidence and risk factors of symptomatic radiation pneumonitis in non-small-cell lung cancer patients treated with concurrent chemoradiotherapy and consolidation durvalumab. *Clin Lung Cancer*. 2021;22:401–410. doi:10.1016/j.cllc.2021.01.017.
17. Kinehara Y, Shiroyama T, Tamiya A, et al. Pneumonitis during durvalumab consolidation therapy affects survival in stage III NSCLC. *JTO Clin Res Rep*. 2023;4:100586. doi:10.1016/j.jtocrr.2023.100586.
18. Tsuji K, Mizugaki H, Yokoo K, et al. Durvalumab after chemoradiotherapy in non-small cell lung cancer with EGFR mutation: a real-world study (HOT2101). *Cancer Sci*. 2024;115:1273–1282. doi:10.1111/cas.16094.
19. Waterhouse D, Yong C, Frankart A, et al. Durvalumab real-world treatment patterns and outcomes in patients with stage III non-small-cell lung cancer treated in a US community setting. *Future Oncol*. 2023;19:1905–1916. doi:10.2217/fon-2023-0117.
20. Ohaegbulam K, Anderson C, Thompson RF, Mitin T. Common medical comorbidities influence pneumonitis risk after chemoradiotherapy and durvalumab maintenance in stage III non-small cell lung cancer. *Clin Lung Cancer*. 2025;26:e382–e390.e2. doi:10.1016/j.cllc.2025.04.012.
21. Okada A, Yasunaga H. Prevalence of noncommunicable diseases in Japan using a newly developed administrative claims database covering young, middle-aged, and elderly people. *JMA J*. 2022;5(2):190–198. doi:10.31662/jmaj.2021-0189.
22. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–383. doi:10.1016/0021-9681(87)90171-8.
23. Quan H, Li B, Couris CM, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol*. 2011;173:676–682. doi:10.1093/aje/kwq433.
24. Klabunde CN, Legler JM, Warren JL, Baldwin LM, Schrag D. A refined comorbidity measurement algorithm for claims-based studies of breast, prostate, colorectal, and lung cancer patients. *Ann Epidemiol*. 2007;17:584–590. doi:10.1016/j.annepidem.2007.03.011.
25. Wheatley-Price P, Navani V, Pabani A, et al. Real-world survival outcomes, treatment patterns, and impact of PD-L1 expression among patients with unresectable, stage III NSCLC treated with CRT → durvalumab in Canada: the RELEVANCE study. *Lung Cancer*. 2025;204:108583. doi:10.1016/j.lungcan.2025.108583.
26. Park JE, Hong KS, Choi SH, et al. Durvalumab consolidation after chemoradiotherapy in elderly patients with unresectable stage III NSCLC: a real-world multicenter study. *Clin Lung Cancer*. 2024;25:354–364. doi:10.1016/j.cllc.2024.02.006.
27. Kakiuchi Y, Saruwatari K, Murotani K, et al. Real-world efficacy and safety of durvalumab administration following chemoradiotherapy in elderly patients with unresectable locally advanced non-small cell lung cancer: a multicenter, retrospective study. *Clin Lung Cancer*. 2024;25:661–671.e7. doi:10.1016/j.cllc.2024.07.001.
28. Stevens S, Nindra U, Shahnam A, et al. Real world efficacy and toxicity of consolidation durvalumab following chemoradiotherapy in older Australian patients with unresectable stage III non-small cell lung cancer. *J Geriatr Oncol*. 2024;15:101705. doi:10.1016/j.jgo.2024.101705.
29. Müller JA, Buchberger J, Schmidt-Riese E, et al. Real-world outcomes of chemoradiotherapy in patients with stage II/III non-small-cell lung cancer in the durvalumab era: an observational study. *Cancers*. 2025;17:2498. doi:10.3390/cancers17152498.
30. Liu F, Yuan X, Jiang J, Zhang P, Chen Y, Chu Q. Lower lobe origin is related to unfavorable outcomes in patients with stage I-III lung cancer treated with radical chemoradiotherapy. *Tumori*. 2021;107:400–406. doi:10.1177/0300891620971359.
31. Kashihara T, Nakayama Y, Okuma K, et al. Impact of interstitial lung abnormality on survival after adjuvant durvalumab with chemoradiotherapy for locally advanced non-small cell lung cancer. *Radiother Oncol*. 2023;180:109454. doi:10.1016/j.radonc.2022.109454.
32. Diamond BH, Belani N, Masel R, et al. Predictors of pneumonitis in patients with locally advanced non-small cell lung cancer treated with definitive chemoradiation followed by consolidative durvalumab. *Adv Radiat Oncol*. 2023;8:101130. doi:10.1016/j.adro.2022.101130.
33. Katsui K, Ogata T, Watanabe K, et al. Radiation pneumonitis after definitive concurrent chemoradiotherapy with cisplatin/docetaxel for non-small cell lung cancer: analysis of dose-volume parameters. *Cancer Med*. 2020;9:4540–4549. doi:10.1002/cam4.3093.
34. Tsukita Y, Yamamoto T, Mayahara H, et al. Intensity-modulated radiation therapy with concurrent chemotherapy followed by durvalumab for stage III non-small cell lung cancer: a multi-center retrospective study. *Radiother Oncol*. 2021;160:266–272. doi:10.1016/j.radonc.2021.05.016.
35. Kakiuchi Y, Saruwatari K, Tokito T, et al. Impact of durvalumab re-administration after moderate symptomatic pneumonitis in locally advanced non-small cell lung cancer. *Lung Cancer*. 2025;204:108578. doi:10.1016/j.lungcan.2025.108578.