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ORIGINAL RESEARCH ARTICLE

Real-World Data on Subsequent Therapy for First-Line Osimertinib-Induced Pneumonitis: Safety of EGFR-TKI Rechallenge (Osi-risk Study TORG-TG2101)

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Abstract

Background Although osimertinib is a promising therapeutic agent for advanced epidermal growth factor receptor (*EGFR*) mutation-positive lung cancer, the incidence of pneumonitis is particularly high among Japanese patients receiving the drug. Furthermore, the safety and efficacy of subsequent anticancer treatments, including EGFR-tyrosine kinase inhibitor (TKI) rechallenge, which are to be administered after pneumonitis recovery, remain unclear.

Objective This study investigated the safety of EGFR-TKI rechallenge in patients who experienced first-line osimertinib-induced pneumonitis, with a primary focus on recurrent pneumonitis.

Patients and Methods We retrospectively reviewed the data of patients with *EGFR* mutation-positive lung cancer who developed initial pneumonitis following first-line osimertinib treatment across 34 institutions in Japan between August 2018 and September 2020.

Results Among the 124 patients included, 68 (54.8%) patients underwent EGFR-TKI rechallenge. The recurrence rate of pneumonitis following EGFR-TKI rechallenge was 27% (95% confidence interval [CI] 17–39) at 12 months. The cumulative incidence of recurrent pneumonitis was significantly higher in the osimertinib group than in the first- and second-generation EGFR-TKI (conventional EGFR-TKI) groups (hazard ratio [HR] 3.1; 95% CI 1.3–7.5; $p = 0.013$). Multivariate analysis revealed a significant association between EGFR-TKI type (osimertinib or conventional EGFR-TKI) and pneumonitis recurrence, regardless of severity or status of initial pneumonitis (HR 3.29; 95% CI 1.12–9.68; $p = 0.03$).

Conclusions Osimertinib rechallenge after initial pneumonitis was associated with significantly higher recurrence rates than conventional EGFR-TKI rechallenge.

1 Introduction

In patients with advanced non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor (*EGFR*) mutations, compared with first-generation EGFR-tyrosine kinase inhibitors (TKIs), the third-generation EGFR-TKI osimertinib is associated with prolonged progression-free survival (PFS) and overall survival (OS) [1–7]. However, both the FLAURA trial (phase III study

Key Points

About 50% of patients were EGFR-TKI rechallenged after osimertinib-induced pneumonitis.

The recurrence rate of pneumonitis was higher in the osimertinib rechallenge group than in the first- and second-generation EGFR-TKI rechallenge group.

Extended author information available on the last page of the article

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comparing osimertinib with first-generation EGFR-TKIs) and the Osi-fact study (retrospective, real-world analyses of osimertinib) indicated that the incidence of osimertinib-induced pneumonitis is particularly high among Japanese patients (12.3% and 12.8%, respectively) [6–8].

Osimertinib is often discontinued upon pneumonitis diagnosis; however, the anticancer drugs to be administered after recovery have not yet been determined. Successful cases of EGFR-TKI rechallenge after osimertinib-induced pneumonitis have been reported [9–16]. There are reports of transient asymptomatic pulmonary opacity (TAPO), a phenomenon distinct from pneumonitis, with similar imaging features, allowing for continuous osimertinib treatment [17, 18]. However, the incidence of TAPO is unknown and clear clinical criteria are lacking. Furthermore, the safety and efficacy of EGFR-TKI re-administration remain unclear. The present study investigated real-world data on the subsequent treatment of patients with *EGFR*-mutated NSCLC after osimertinib-induced pneumonitis and the safety of EGFR-TKI rechallenge.

2 Materials and Methods

2.1 Patients

The clinical records of patients with *EGFR*-mutated unresectable NSCLC who developed pneumonitis following first-line osimertinib at 34 institutions in Japan were reviewed retrospectively. Records of patients treated between August 2018 and September 2020 were reviewed. The diseases were classified according to the eighth edition of the Union for International Cancer Control TNM classification [19]. The cutoff date for data collection was March 31, 2021. The study was approved by the ethics and institutional review boards of all institutions involved. Informed consent was obtained from patients in the form of an opt-out on each institution's website.

2.2 Definition of the EGFR-TKI Rechallenge Period

EGFR-TKI rechallenge was defined as the re-administration of EGFR-TKIs, including osimertinib, as the second-line or subsequent therapy after initial pneumonitis induced by first-line osimertinib treatment. However, if a patient was diagnosed with TAPO and continued osimertinib treatment, the first-line osimertinib period was defined as the duration from starting first-line osimertinib to the onset of TAPO (initial pneumonitis) and the EGFR-TKI rechallenge period was defined as the duration from initial pneumonitis to the last date of osimertinib administration or death.

2.3 Diagnosis and Assessment of Pneumonitis

The diagnosis and onset date of pneumonitis were determined by the treating physician. The radiological characteristics of pneumonitis were analyzed retrospectively using computed tomography (CT) images of the chest of eligible patients from each institution and evaluated by a board-certified radiologist and pulmonologist. Herein, TAPO was identified and evaluated as pneumonitis, as no clear criteria for TAPO are available. The CT phenotypical appearance of EGFR-TKI-induced pneumonitis was classified into: (1) organized pneumonia (OP) pattern (peripheral predominance and multiple plaques), (2) hypersensitivity pneumonitis (HP) pattern, (3) diffuse alveolar damage (DAD) pattern, (4) nonspecific interstitial pneumonia (NSIP) pattern, and (5) not evaluable or undetermined.

2.4 Statistical Analyses

Competing risk models (Fine and Gray) were applied to assess the cumulative incidence of pneumonitis and compare differences in cumulative incidence curves between the osimertinib and the first- and second-generation EGFR-TKI (conventional EGFR-TKI) groups. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using the Cox proportional hazards model. Patients lost to follow-up, those still alive at the cutoff date, or those who died were censored. All p values were based on a two-sided hypothesis testing, with $p < 0.05$ indicating significance. All statistical analyses were performed using EZR for R 2.13.0 (R Foundation for Statistical Computing, Vienna, Austria) [20].

3 Results

3.1 Patient Characteristics

In total, 124 patients were included in the study. Their baseline characteristics are summarized in Table 1. The majority of the patients had an Eastern Cooperative Oncology Group performance status (ECOG-PS) of 0–1 (85.5%) and showed adenocarcinoma histology (98.4%). Approximately 10% of the patients had a PD-L1 tumor percentage score (TPS) ≥50%. The median timing of initial pneumonitis onset was approximately 60 days. In addition, no noticeable difference was found between the EGFR-TKI rechallenge population and total population. None of the patients rechallenged with EGFR-TKI showed grade 4 initial pneumonitis induced by first-line osimertinib.

Table 1 Baseline characteristics of patients included in the study

Characteristic	Total ($N = 124$)	EGFR-TKI rechallenge group ($N = 68$)	p value
Age [y], median (range)	75 (44–90)	72 (44–89)	0.10
Sex (%)			0.88
Men	50 (40.3)	26 (38.2)	
Women	74 (59.7)	42 (61.8)	
ECOG-PS, *n* (%)			0.98
0	46 (37.1)	25 (36.8)	
1	60 (48.4)	35 (51.5)	
2	13 (10.5)	6 (8.8)	
3	5 (4.0)	2 (2.9)	
Smoking status, *n* (%)			0.90
Current or former	56 (45.2)	30 (44.1)	
Never	68 (54.8)	38 (55.9)	
Radiotherapy history before treatment, *n* (%)			0.52
Yes	6 (4.8)	5 (7.4)	
No	118 (95.2)	63 (92.6)	
Histology, *n* (%)			0.62
Adenocarcinoma	122 (98.4)	66 (97.1)	
Non-adenocarcinoma	2 (1.6)	2 (2.9)	
Stage, *n* (%)			0.88
III	3 (2.5)	2 (2.9)	
IV	82 (66.1)	43 (63.2)	
Recurrence	39 (31.4)	23 (33.8)	
EGFR mutation type, *n* (%)			0.70
19 deletion	56 (45.2)	35 (51.5)	
L858R	62 (50.0)	30 (44.1)	
Others	6 (4.8)	3 (4.4)	
PD-L1 tumor proportion score, *n* (%)			0.73
≥ 50%	15 (12.1)	5 (7.4)	
1–49%	30 (24.2)	19 (27.9)	
< 1%	38 (30.6)	23 (33.8)	
Unknown	41 (33.1)	21 (30.9)	
Brain metastasis, *n* (%)			0.74
Present	33 (26.6)	20 (29.4)	
Absent	91 (73.4)	48 (70.6)	
Liver metastasis, *n* (%)			1.00
Present	19 (15.3)	10 (14.7)	
Absent	105 (84.7)	58 (85.3)	
Bone metastasis, *n* (%)			0.29
Present	50 (40.3)	33 (48.5)	
Absent	74 (59.7)	35 (51.5)	
Pleural effusion, *n* (%)			0.55
Present	57 (46.0)	28 (41.2)	
Absent	67 (54.0)	40 (58.8)	
With interstitial lung disease, *n* (%)			0.46
Present	4 (3.2)	4 (5.9)	
Absent	120 (96.8)	64 (94.1)	
With emphysema, *n* (%)			0.81
Present	13 (10.5)	8 (11.8)	
Absent	111 (89.5)	60 (88.2)	

Table 1 (continued)

Characteristic	Total ($N = 124$)	EGFR-TKI rechallenge group ($N = 68$)	p value
Time to occurrence of initial pneumonitis caused by first-line osimertinib treatment [days], median (range)	60 (3–434)	56.5 (5–434)	0.74
CTCAE grade of initial pneumonitis, *n* (%)			0.09
1	40 (32.3)	30 (44.1)	
2	42 (33.9)	24 (35.3)	
3	32 (25.8)	14 (20.6)	
4	2 (1.6)	0	
5	8 (6.4)	0	

CTCAE Common Terminology Criteria for Adverse Events, *ECOG-PS* Eastern Cooperative Oncology Group performance status, *EGFR* epidermal growth factor receptor, *PD-1* programmed death-1, *PD-L1* programmed cell death protein ligand 1, *TKI* tyrosine kinase inhibitor

3.2 Anticancer Therapy After Initial Pneumonitis

Out of the 124 patients who developed initial pneumonitis after first-line osimertinib, 87, 46, and 41 patients received second-line treatment, EGFR-TKI rechallenge, and chemotherapy, respectively (Fig. 1). The most common second-line EGFR-TKI and chemotherapy regimen were osimertinib ($n = 19$, 41.3%) and carboplatin + pemetrexed ($n = 12$, 29.3%), respectively (Table 2). Among the patients receiving second-line chemotherapy, 22 eventually received EGFR-TKI rechallenge after the second-line treatment (Fig. 1). Combined with those receiving second-line EGFR-TKI, a total of 68 patients received EGFR-TKIs (Fig. 1).

3.3 Risk of Pneumonitis Recurrence Following EGFR-TKI Rechallenge

During the study, the estimated median recurrence time was not achieved (range 18.8 months to not available [NA]) and the pneumonitis recurrence rates were 21% (95% CI 12–32), 25% (95% CI 15–37), and 27% (95% CI 17–39) at 3, 6, and 12 months, respectively (Fig. 2a). When patients in the EGFR-TKI rechallenge group were divided into those re-administered osimertinib (osimertinib group) versus those administered first- and second-generation EGFR-TKIs (conventional EGFR-TKI group), the median times to recurrence were 9.2 months (range 2.2 months to NA) months and NA (range NA to NA), respectively. The incidence of

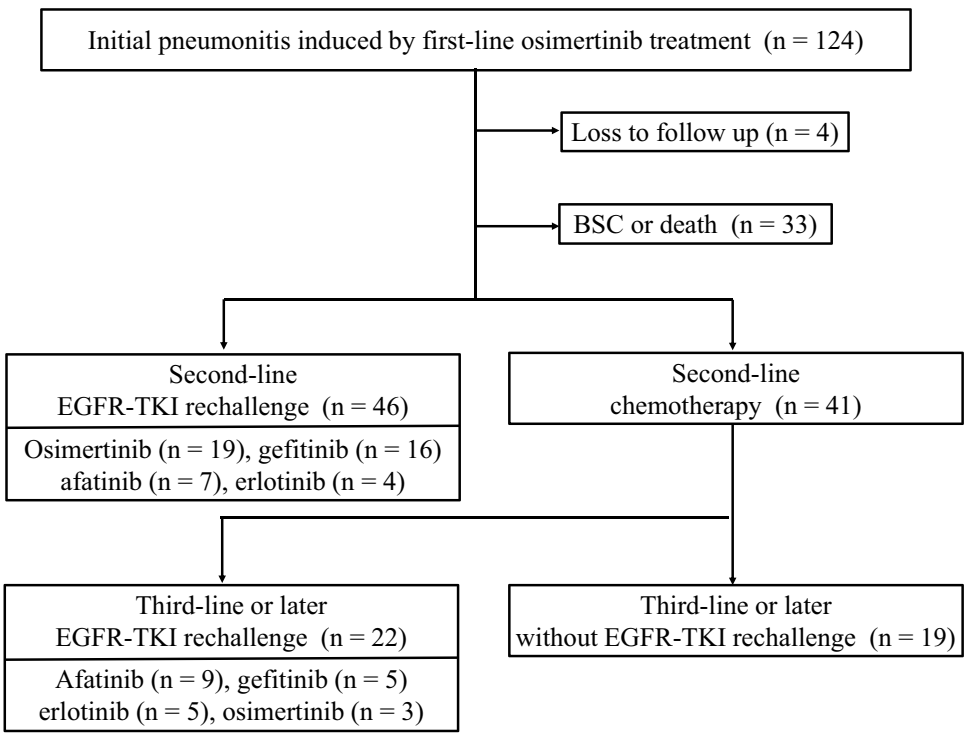

Fig. 1 Flow diagram representing patient treatment procedures. One hundred and twenty-four patients were included in this study; among them, four could not be followed up owing to issues at the patient's end. Thirty-three patients were in supportive care or died because of initial pneumonitis. As second-line treatment, EGFR-TKI rechallenge was administered to 46 patients and chemotherapy to 41 patients. Among the patients who received chemotherapy, 22 eventually received EGFR-TKI rechallenge after the second-line treatment, whereas 19 did not. *EGFR* epidermal growth factor receptor, *TKI* tyrosine kinase inhibitor

Table 2 Second-line treatment after initial pneumonitis with osimertinib

Second-line treatment ($n = 87$)			
EGFR-TKI rechallenge ($n = 46$)		Chemotherapy ($n = 41$)	
EGFR-TKI regimen	*n*	Chemotherapy regimen	*n*
Osimertinib	19	Carboplatin + Pemetrexed	12
Gefitinib	16	Carboplatin + nab-Paclitaxel	8
Afatinib	7	Cisplatin + Pemetrexed	5
Erlotinib	4	Carboplatin + Paclitaxel + Bevacizumab	4
		Carboplatin + Pemetrexed + Bevacizumab	3
		Pemetrexed	3
		Carboplatin + nab-Paclitaxel + Pembrolizumab	1
		Cisplatin + Pemetrexed + Bevacizumab	1
		Pemetrexed + Bevacizumab	1
		Vinorelbine	1
		Atezolizumab	1
		S-1	1
		EGFR-TKI rechallenge following 2nd-line chemotherapy ($n = 22$)	
		Afatinib	9
		Gefitinib	5
		Erlotinib (including Erlotinib + Bevacizumab)	5
		Osimertinib	3

EGFR epidermal growth factor receptor, *TKI* tyrosine kinase inhibitor

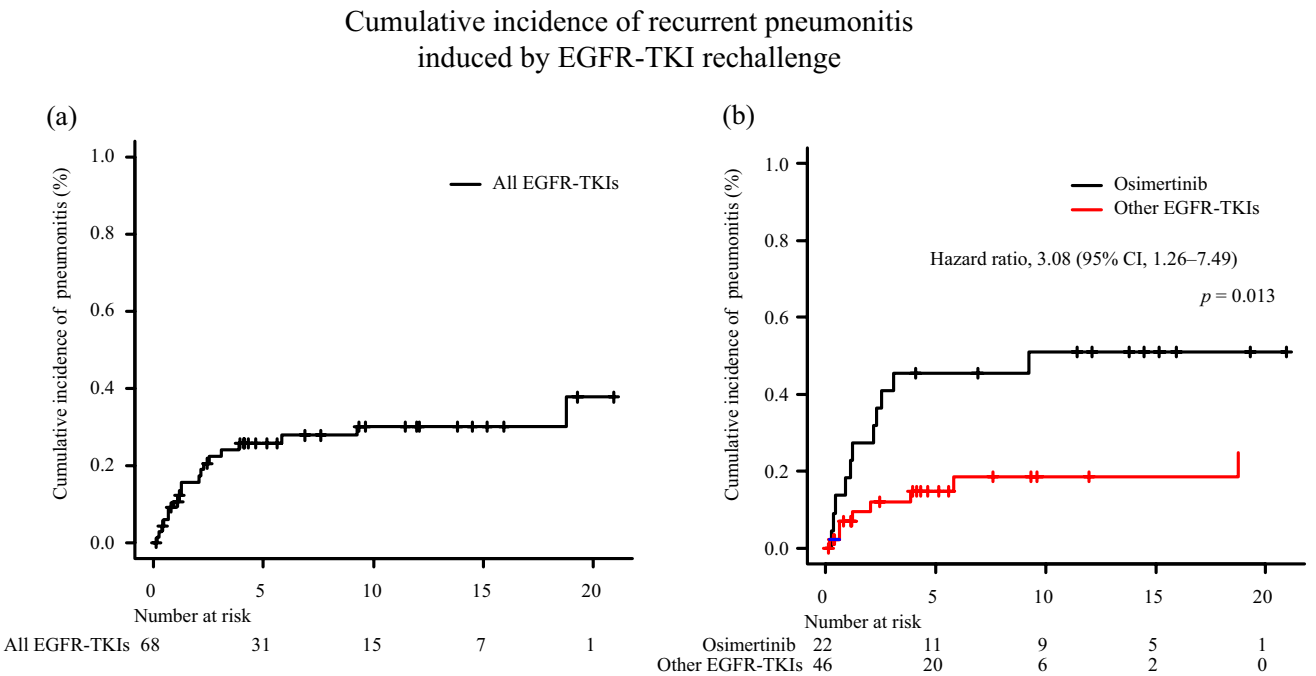

Fig. 2 Cumulative incidence of recurrent pneumonitis induced in all patients who received EGFR-TKI rechallenge is shown in (**a**), and the cumulative incidence of pneumonitis recurrence in the EGFR-TKI-rechallenged population divided into those receiving osimertinib and conventional EGFR-TKIs is shown in (**b**). Patients who were lost to follow-up, those still alive at the cutoff date, or those with tumor progression were excluded. *EGFR* epidermal growth factor receptor, *TKI* tyrosine kinase inhibitor

pneumonitis at 6 months was 46% (95% CI 24–68) with osimertinib rechallenge and 15% (95% CI 6.3–29) with conventional EGFR-TKI rechallenge, reaching 50% (95% CI 28–72) and 15% (95% CI 6.3–29) at 12 months, respectively. The cumulative incidence of recurrent pneumonitis was significantly higher in the osimertinib group than in the conventional EGFR-TKI group (HR 3.1; 95% CI 1.3–7.5; $p = 0.013$) (Fig. 2b). According to multivariate analysis, both the type of EGFR-TKI and the occurrence of initial pneumonitis within 60 days after the initial osimertinib administration were significantly associated with the incidence of pneumonitis induced by EGFR-TKI rechallenge (Table 3).

In addition, we compared the cumulative incidence of recurrent pneumonitis following EGFR-TKI rechallenge between patients who developed initial Common Terminology Criteria for Adverse Events (CTCAE) grade 1 or 2 pneumonitis and those who developed grade 3 pneumonitis and observed no significant difference between the two groups (HR 1.1; 95% CI 0.4–2.8; $p = 0.92$) (Supplementary Fig. S1, see electronic supplementary material [ESM]).

3.4 Comparing Pneumonitis Recurrence in Second-Line Treatment: Chemotherapy versus EGFR-TKI Rechallenge

Of the 87 patients who received second-line treatment, 19 received osimertinib rechallenge, 27 received conventional EGFR-TKI rechallenge, and 41 received chemotherapy. The incidence of pneumonitis at 12 months of the second-line treatment period was 47.4% (95% CI 24.4–71.1) in the osimertinib group, 15% (95% CI 6.3–29) in the conventional EGFR-TKI group, and 7.3% (95% CI 1.5–20) in the chemotherapy group. The cumulative incidence of recurrent pneumonitis was significantly higher in the osimertinib group than in the chemotherapy group (HR 5.85; 95% CI 1.88–18.2; $p = 0.002$) (Supplementary Fig. S2, see ESM). On the other hand, there was no significant difference between the conventional EGFR-TKI and chemotherapy groups (HR 1.31; 95% CI 0.67–2.54; $p = 0.43$).

3.5 Impact of Initial Pneumonitis on Recurrence

Initial pneumonitis imaging patterns in all 124 patients were evaluated (Fig. 3). The OP pattern was the most frequent ($n = 57$, 46.0%), followed by the HP ($n = 25$, 20.2%), DAD ($n = 24$, 19.2%), and NSIP patterns ($n = 7$, 5.6%). Similarly, OP ($n = 10$, 52.6%) was the most frequent pattern during recurrence after rechallenge, followed by HP ($n = 5$, 26.3%), DAD ($n = 2$, 10.5%), and NSIP ($n = 1$, 5.3%). There was no difference based on the CTCAE grade, steroid treatment, and radiological imaging pattern of initial pneumonitis between patients with and those without pneumonitis after the rechallenge. Among patients with recurrent pneumonitis due to EGFR-TKI rechallenge, approximately 10% had CTCAE grade 3 or higher disease (Table 4).

4 Discussion

To the best of our knowledge, this study is the first to evaluate the safety and efficacy of EGFR-TKI rechallenge in patients who developed pneumonitis after first-line osimertinib treatment. Herein, the frequency of pneumonitis after EGFR-TKI rechallenge is reported, and the results

Table 3 Risk factors for pneumonitis after EGFR-TKI rechallenge

Risk factor for pneumonitis	Crude HR	95% CI	*p* value	Adjusted HR[a]	95% CI	*p* value
Type of EGFR-TKI (osimertinib vs 1st- or 2nd-generation EGFR-TKI)	3.08	1.26–7.49	0.013	3.93	1.58–9.80	0.003
Duration from the initial administration of osimertinib to the onset of initial pneumonitis (within 60 days vs more than 60 days)	4.10	1.39–12.1	0.01	4.58	1.57–13.34	0.005
Smoking history (current or former vs never)	1.48	0.61–3.60	0.39			
Treatment line (second-line vs third-line or later)	0.92	0.36–2.37	0.87			
CTCAE Grade of initial pneumonitis (grade 1 vs grade 2 or higher)	1.63	0.67–3.98	0.28			
PD-L1 expression (TPS ≥ 50% vs < 50% or unknown)	1.02	0.15–7.20	0.98			
ECOG-PS at EGFR-TKI rechallenge (PS 0, 1 vs PS 2 or higher)	3.72	0.54–25.4	0.18			
Radiological imaging patterns of initial pneumonitis (OP pattern vs other imaging patterns)	1.06	0.44–2.58	0.89			

CI confidence interval, *CTCAE* Common Terminology Criteria for Adverse Events, *ECOG-PS* Eastern Cooperative Oncology Group performance status, *EGFR* epidermal growth factor receptor, *HR* hazard ratio, *OP* organizing pneumonitis, *OS* overall survival, *PD-L1* programmed cell death ligand 1, *TKI* tyrosine kinase inhibitor, *TPS* tumor percentage score

[a]HR for type of EGFR-TKI was adjusted for treatment line, ECOG-PS at EGFR-TKI rechallenge, and duration from the initial administration of osimertinib to the onset of initial pneumonitis

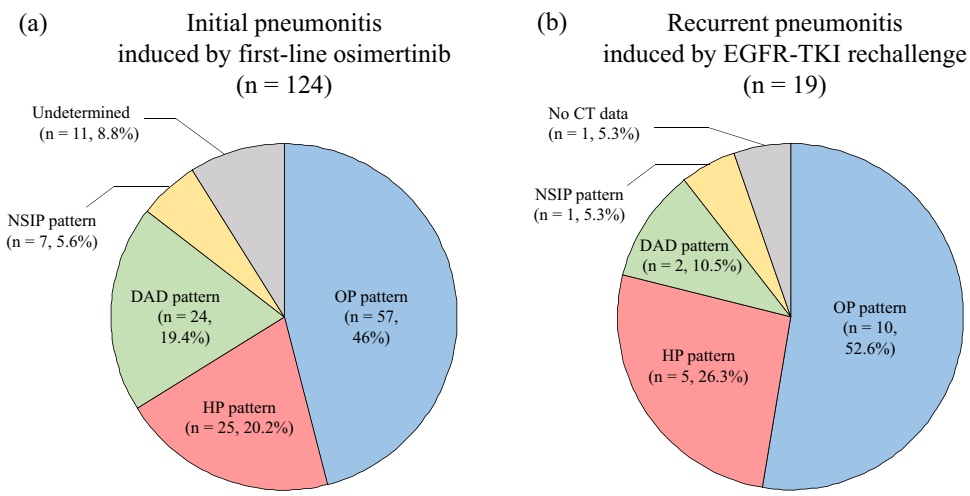

Fig. 3 Pneumonitis imaging patterns at the time of initial pneumonitis induced by first-line osimertinib (**a**) and the EGFR-TKI rechallenge-induced recurrent pneumonitis (**b**). *DAD* diffuse alveolar damage, *EGFR* epidermal growth factor receptor, *HP* hypersensitivity pneumonitis, *NSIP* nonspecific interstitial pneumonia, *OP* organized pneumonia, *TKI* tyrosine kinase inhibitor

Table 4 Comparison between patients with and without recurrent pneumonitis due to EGFR-TKI rechallenge

	Recurrent pneumonitis ($N = 19$)	Without recurrent pneumonitis ($N = 49$)	p value
CTCAE grade of initial pneumonitis			0.60
1	10 (52.6)	20 (40.8)	
2	5 (26.3)	19 (38.8)	
3	4 (21.1)	10 (20.4)	
4	0	0	
Steroid treatment for initial pneumonitis			0.79
Yes	9 (47.4)	26 (53.1)	
No	10 (52.6)	23 (46.9)	
Radiological imaging pattern of initial pneumonitis			0.74
OP pattern	9 (47.4)	25 (51.0)	
HP pattern	7 (36.8)	11 (22.4)	
DAD pattern	1 (5.3)	5 (10.2)	
NSIP pattern	1 (5.3)	2 (4.1)	
Undetermined pattern	1 (5.3)	6 (12.2)	
CTCAE grade of recurrent pneumonitis induced by EGFR-TKI rechallenge			
1	9 (47.4)		
2	8 (42.1)		
3	2 (10.5)		
4	0		
5	0		

CTCAE Common Terminology Criteria for Adverse Events, DAD, diffuse alveolar damage; EGFR, epidermal growth factor receptor; HP, hypersensitivity pneumonia; NSIP, nonspecific interstitial pneumonia; OP, organizing pneumonia, *TKI* tyrosine kinase inhibitor

suggest that pneumonitis risk was significantly higher after osimertinib rechallenge than after conventional EGFR-TKI administration.

Approximately 50% of the patients re-treated with osimertinib developed recurrent pneumonitis, suggesting that conventional EGFR-TKI rechallenge led to a lower pneumonitis frequency. Pneumonitis frequency after the re-administration of conventional EGFR-TKIs was approximately 15%, similar to that with first-line osimertinib treatment in Japanese patients, suggesting that rechallenge with EGFR-TKIs other than osimertinib may be acceptable. However, the frequency of 15% is clearly higher than the frequency of pneumonitis in the group administered conventional EGFR-TKIs in first-line treatment [21–23].

Furthermore, patients do not always fully recover from pneumonitis caused by EGFR-TKIs other than osimertinib [21, 22]. Therefore, we suggest that patients be fully informed of the risk of EGFR-TKI re-administration. If EGFR-TKI rechallenge therapy is selected, relatively close intervals between outpatient visits, CT imaging evaluation, and confirmation of respiratory status are considered necessary.

In contrast to the findings of the present study, Imaji et al. suggested that osimertinib rechallenge after osimertinib-induced pneumonitis holds promise in terms of safety and efficacy [24]. In their study, only 5 out of 33 patients in the osimertinib rechallenge group had recurrent pneumonitis, with prolonged PFS, highlighting osimertinib rechallenge as a useful treatment option. However, in their study, patients who continued osimertinib without interrupting treatment after pneumonitis occurrence were also defined as those who were re-administered osimertinib after pneumonitis. Therefore, over a half of the patients in their study only developed grade 1 pneumonitis, with a few cases of grade 2 or higher disease. It is possible that a majority of the grade 1 pneumonitis cases in the present study were cases of TAPO, an osimertinib-specific phenomenon. In this case, it is likely that treatment would be continued, as frosted shadows in the lungs often diminish with continued osimertinib administration. However, not all cases of grade 1 pneumonitis are clinically TAPO cases, and distinguishing TAPO from pneumonitis is difficult. Therefore, osimertinib rechallenge may not always be safe and effective. On the other hand, a separate study reported a median onset of TAPO 24 weeks after the initiation of osimertinib therapy [18]. Furthermore, in the present study, pneumonitis frequently recurred within 60 days after the start of osimertinib treatment, suggesting a potential association, especially when pneumonitis developed after the initial 60 days. If this relation holds true, retreatment with osimertinib may be beneficial, particularly in cases in which pneumonitis occurs after the initial 60 days of osimertinib therapy.

With regard to the radiological characteristics of pneumonitis, Sato et al. reported real-world data on initial osimertinib-induced pneumonitis in the same Japanese population. They reported OP, simple pulmonary eosinophilia, HP, and DAD in 38%, 26%, 23%, and 11% of the patients, respectively [25]. In our study, 46%, 20.2%, and 19.4% of the patients developed OP, HP, and DAD, respectively, indicating that osimertinib-induced initial pneumonitis tends to be associated with a relatively high rate of OP and HP (Fig. 3a). Furthermore, the present study revealed that recurrent pneumonitis after EGFR-TKI rechallenge shows radiological characteristics similar to those of initial pneumonitis, with OP, HP, and DAD rates of 52.6%, 26.3%, and 10.5%, respectively (Fig. 3b). Differences in initial pneumonitis status were also evaluated between the groups in which EGFR-TKI rechallenge did or did not induce recurrent pneumonitis, with regard to CTCAE grade of pneumonia, steroid use, and imaging characteristics (Table 4). However, no differences in patient characteristics were observed between the groups. Imaji et al. also compared CTCAE grade and smoking history during initial pneumonitis between patients in whom EGFR-TKI rechallenge did or did not induce recurrent pneumonitis but found no clear difference [24].

The present study has limitations. First, its retrospective nature may give rise to certain biases. However, ethical considerations limit a prospective study of EGFR-TKI rechallenge after EGFR-TKI-induced pneumonitis, with this work representing the largest study on EGFR-TKI rechallenge after pneumonitis. Second, the follow-up period for EGFR-TKI rechallenge was short, and a longer follow-up period may yield different results.

5 Conclusions

The safety of EGFR-TKI rechallenge in patients with first-line osimertinib-induced pneumonitis were evaluated, and we found that EGFR-TKI rechallenge, especially osimertinib rechallenge, necessitates careful attention to pneumonitis recurrence.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11523-024-01048-x.

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Declarations

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Ethics approval The study was approved by the ethics and institutional review boards of all institutions involved.

Consent to participate Informed consent was obtained from patients in the form of an opt-out on each institution's website.

Consent to publish Not applicable.

Availability of data and materials The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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