First-Line Pembrolizumab Monotherapy for Advanced NSCLC With Programmed Death-Ligand 1 Expression Greater Than or Equal to 50%: Real-World Study Including Older Patients in Japan

Yasushi Goto, MD, PhD, a,* Atsuhisa Tamura, MD, PhD, b Hirotaka Matsumoto, MD, c Kazutoshi Isobe, MD, PhD, d Tomohiro Ozaki, MD, e Melissa L. Santorelli, PhD, MPH, f Kazuko Taniguchi, MS, g Tetsu Kamitani, MD, PhD, g Masato Irisawa, PhD, g Kingo Kanda, MPharm, g Machiko Abe, MS, g Thomas Burke, PharmD, PhD, f Hiroshi Nokihara, MD, PhD h i

aDepartment of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan
bCenter for Pulmonary Diseases, National Hospital Organization Tokyo National Hospital, Tokyo, Japan
cDepartment of Respiratory Medicine, Hyogo Prefectural Amagasaki General Medical Center, Hyogo, Japan
dDepartment of Respiratory Medicine, Toho University School of Medicine, Tokyo, Japan
eDivision of Medical Oncology, Kishiwada City Hospital, Osaka, Japan
fCenter for Observational & Real World Evidence (CORE), Merck & Co., Inc., Rahway, New Jersey
gMSD K.K., Tokyo, Japan
hDepartment of Respiratory Medicine and Rheumatology, Graduate School of Biomedical Sciences, Tokushima University, Tokushima, Japan
iPresent Address: Respiratory Medicine, Center Hospital of the National Center for Global Health and Medicine, Tokyo, Japan

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ABSTRACT

Introduction: Pembrolizumab became available in Japan in February 2017 for first-line monotherapy of unresectable advanced and metastatic NSCLC with programmed death-ligand 1 (PD-L1) tumor proportion score (TPS) greater than or equal to 50%. This retrospective chart review study aimed to describe real-world clinical outcomes of first-line pembrolizumab monotherapy, including for patients 75 years or older, who are under-represented in clinical trials.

Methods: We identified patients (≥20 y old) at 23 sites initiating first-line pembrolizumab monotherapy from July...
In February 2017, pembrolizumab became the first immune checkpoint inhibitor (ICI) approved and reimbursed in Japan for first-line monotherapy of unresectable advanced and metastatic NSCLC with programmed death-ligand 1 (PD-L1) tumor proportion score (TPS) greater than or equal to 50%. This approval was based on the original findings of the KEYNOTE-024 clinical trial (ClinicalTrials.gov identifier: NCT02142738), in which pembrolizumab monotherapy was associated with significantly longer progression-free survival (PFS) and overall survival (OS) as compared with platinum-based chemotherapy for first-line therapy of stage IV NSCLC with PD-L1 TPS greater than or equal to 50% and no EGFR or ALK genomic alterations. In the most recent analysis, with 5 years of follow-up in KEYNOTE-024, median pembrolizumab treatment duration was 7.9 months, and the Kaplan-Meier median OS was 26.3 months (95% confidence interval [CI]: 18.3–40.4), with 5-year OS rate of 31.9%, in the pembrolizumab arm.

Lung cancer is a leading cause of new cancer cases in Japan, number three among both men and women and the number one cause of deaths for both sexes, responsible for 20% of cancer-related deaths in 2020. The burden of lung cancer is notably high among older adults in Japan: the median age at diagnosis is 70 years and approximately 81% of deaths from lung cancer in 2019 were recorded among patients 70 years and older. Nevertheless, older individuals tend to be underrepresented in lung cancer clinical trials, both in Japan and elsewhere, and patients 75 years and older thus constitute a patient population often treated with ICIs in clinical settings but for whom little clinical trial evidence is available. For example, in a pooled analysis of the KEYNOTE-024 and KEYNOTE-042 clinical trials, only 11% (93 of 904) of the patients with advanced NSCLC and PD-L1 TPS greater than or equal to 50% were 75 years or older. The outcomes for the 49 patients in the pembrolizumab arms of these trials who were 75 years or older were largely similar to overall outcomes, and the authors joined others in calling for further study of ICI therapy for larger populations of patients 75 years and older treated in routine oncology practice.

Observational studies provide the opportunity to study heterogeneous patient populations treated for advanced NSCLC in real-world settings. In this subanalysis of a large, retrospective, observational study of first-line treatment patterns and clinical outcomes for advanced NSCLC in Japan, we aimed to describe real-world outcomes of first-line pembrolizumab monotherapy since the introduction of this regimen in Japan, and inclusion in Japan Lung Cancer Society Guidelines, for treating advanced NSCLC with PD-L1 TPS greater than or equal to 50% and no actionable genomic alterations. A prespecified exploratory objective was to describe real-world clinical outcomes of first-line pembrolizumab monotherapy also by age (<75, ≥75 y).

**Materials and Methods**

**Patients**

Patient data for this retrospective study were abstracted retrospectively from medical records at 23 hospitals throughout Japan by trained abstractors using electronic case report forms, as previously described in detail. Each patient was assigned a unique number for study identification purposes. The study protocol was approved by the local Ethics Committee at each participating center; informed consent from individual patients was not required by applicable local laws, regulations, and guidelines for noninterventional research.
Patients eligible for the main study were 20 years or older at diagnosis of pathologically confirmed advanced or recurrent NSCLC (unresectable stages IIIb, IIIC, or IV), with a record of PD-L1 test results and no known actionable genomic alterations, as documented before or when they initiated first-line therapy for advanced NSCLC during the index period from July 1, 2017, to December 20, 2018. The four actionable genomic alterations for which patients were excluded were EGFR and BRAF gene mutations and ALK and ROS1 gene rearrangements, as per dates of drug approvals and indications listed by the Japan Pharmaceuticals and Medical Devices Agency.14,19 Enrollment in a first-line clinical trial, an incomplete medical record, or treatment with curative intent by means of surgery or chemoradiation was also cause for study exclusion.

This subanalysis included all patients treated with first-line pembrolizumab monotherapy who had PD-L1 TPS greater than or equal to 50% and Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 to 2, or unknown PS, excluding those with PS of 3 or 4. Patients were followed until data cutoff (September 30, 2019) or study discontinuation for death or other reason. The date of last known activity (last contact date) was defined as the latest date of recorded treatment or other health care resource use.

Assessments

Clinical outcome assessments included OS, real-world PFS (rwPFS), real-world tumor response rate (rwTRR), real-world disease control rate, and real-world duration of response (rwDOR). We defined OS as the time from pembrolizumab initiation to death, with censoring at the last contact date for patients who were still alive. rwPFS was determined from pembrolizumab initiation to the first clinically or radiologically documented disease progression or death, whichever occurred first, with censoring at the start of a new line of therapy or last contact date for those with no new therapy.

The rwTRR was determined as the proportion of patients who had a radiologically documented or clinician-assessed best tumor response of complete response (CR) or partial response (PR), and the real-world disease control rate was defined as the proportion of patients with radiologically documented or clinician-assessed best response of CR, PR, or stable disease. For those patients with best response of CR or PR, we determined the rwDOR from the first CR or PR record to the first date of documented disease progression or death from any cause, with censoring at the start of a new line of therapy for patients with no disease progression or death and at the last contact date for those with no new line of therapy.

We also estimated two treatment-related outcomes, real-world time on treatment (rwToT) and real-world time to next treatment (rwTTNT). The rwToT was determined from first to last pembrolizumab administration dates, as previously described,20 defining pembrolizumab discontinuation at the last dose if patients died, continued to a next line of therapy, or had a gap of greater than or equal to 120 days between their last dose and last known activity; all other patients were censored at their last pembrolizumab administration date. The rwTTNT was defined as the time from pembrolizumab initiation to initiation of a subsequent (second-line) therapy, with censoring at the last clinical contact if no subsequent systemic therapies were administered.

Statistical Analyses

We summarized baseline patient characteristics, reasons for pembrolizumab discontinuation, and subsequent systemic treatment regimens using descriptive statistics for all patients and by age group (<75 and ≥75 y).

The Kaplan-Meier method was used to estimate time-to-event outcomes, including OS, rwPFS, rwDOR, rwToT, and rwTTNT. These clinical and treatment-related outcomes were determined overall and by age group (<75 and ≥75 y) and baseline PS (0–1 and 2). The Clopper-Pearson exact method was used to calculate 95% CIs for prevalence, and a Poisson distribution was used to calculate 95% CIs for incidence.

Analyses were prespecified before database lock in the final statistical analysis plan. Sample size calculations were not performed as the main study and this sub-analysis (hereafter referred to as this study) were descriptive with no hypothesis testing. Statistical analyses were performed using SAS software, version 9.4 or later (SAS Institute, Cary, NC).

Results

Patients

We identified 441 eligible patients (see Supplementary Fig. 1 depicting patient identification), of whom 346 (78%) were men (Table 1). Their median age was 70 years, including 303 patients (69%) who were younger than 75 years and 138 (31%) who were 75 years or older. Approximately 53% of those younger than 75 years and 56% of those 75 years or older had ECOG PS of 0 or 1, and 8% in each age group had ECOG PS of 2. Most patients in each age group had non-squamous NSCLC (67% and 56%, respectively), and 12% and 20% had a history of lung surgery, most often lobectomy (77% and 96%, respectively). Other baseline characteristics are summarized overall and by age group in Table 1. As previously reported, PD-L1 testing was
conducted using the pembrolizumab companion diagnostic (PD-L1 IHC 22C3 pharmDx, Agilent Technologies Japan Ltd., Hachioji, Tokyo, Japan) for more than 99% of the patients.17

The median patient follow-up time was 13.5 months (range: 0.1 to 26.9 mo) from pembrolizumab initiation to date of death, end of patient follow-up, or data cutoff (September 30, 2019), whichever occurred first. The 441 patients received a median of seven pembrolizumab doses (range: 1–38).

Clinical Outcomes

The median OS was not reached (NR) among all 441 patients, for whom the Kaplan-Meier estimated OS rates at 12 and 24 months were 72% and 58%, respectively (Table 2). Median rwPFS was 10.0 months (95% CI: 8.2–11.8).

Outcomes for patient subgroups younger than 75 years and 75 years or older and ECOG PS 0 to 1 and 2 are depicted in Figure 1. The median OS was NR for those younger than 75 years, and median OS was 23.5 months (95% CI: 16.2–NR) for those 75 years or older (Fig. 1A). The 12-month OS rates were 74% and 67%, respectively, and 24-month OS rates were 62% and 48%, respectively. Median rwPFS was 10.1 months (95% CI: 7.7–12.9) and 9.5 months (95% CI: 6.2–14.2), respectively (Fig. 1C). For the 240 patients with PS 0 to 1, the median OS was NR (Fig. 1B) and the median rwPFS was 10.0 months (95% CI: 7.2–14.0) (Fig. 1D), whereas for the 36 patients with PS of 2, median OS was 11.8 months (95% CI: 4.2–NR) and median rwPFS was 3.7 months (95% CI: 1.7–5.2).

A total of 166 patients had best tumor response of CR or PR, for a rwTRR of 37.6% (95% CI: 33.1–42.3) (Table 3).

Treatment and Patient Disposition

The median rwToT with pembrolizumab was 5.6 months (95% CI: 4.4–6.7) overall (Table 2) and 5.7 and 5.6 months for those younger than 75 years and 75 years or older, respectively (Fig. 2A). At 12 months, 26% of patients remained on pembrolizumab therapy, including 27% and 22% of those younger than 75 years and 75 years or older, respectively (Fig. 2A), and 26% and 11% of those with PS 0 to 1 and 2, respectively (Fig. 2B). At data cutoff, 24 patients (5%) were censored for rwToT, and 417 patients (95%) met the criteria for treatment discontinuation as defined analytically.

The estimated median rwTTNT was 18.3 months (95% CI: 14.3–NR) overall, 17.5 months among patients younger than 75 years and 18.3 months among those 75 years or older (Fig. 2C). At 24 months, the percentages of

| Characteristics | All Patients | Age < 75 y | Age ≥ 75 y |
|-----------------|-------------|------------|------------|
| Characteristics | (N = 441) | (n = 303) | (n = 138) |
| Age, median (range) | 70 (30-89) | 67 (30-74) | 79 (75-89) |
| Men | 346 (78.5) | 240 (79.2) | 106 (76.8) |
| Smoking status known, n | 436 | 300 | 136 |
| Current smoker | 65 (14.9) | 53 (17.7) | 12 (8.8) |
| Former smoker | 323 (74.1) | 223 (74.3) | 100 (73.5) |
| Never smoker | 48 (11.0) | 24 (8.0) | 24 (17.6) |
| ECOG performance status | | | |
| 0 | 85 (19.3) | 64 (21.1) | 21 (15.2) |
| 1 | 155 (35.1) | 98 (32.3) | 57 (41.3) |
| 2 | 36 (8.2) | 25 (8.3) | 11 (8.0) |
| Unknown | 165 (37.4) | 116 (38.3) | 49 (35.5) |
| NSCLC histologic diagnosis known, n | 420 | 289 | 131 |
| Nonsquamous | 267 (63.6) | 194 (67.1) | 73 (55.7) |
| Squamous | 123 (29.3) | 74 (25.6) | 49 (37.4) |
| Other | 30 (7.1) | 21 (7.3) | 9 (6.9) |
| No metastasis at index date | 85 (19.3) | 50 (16.5) | 35 (25.4) |
| Brain metastasis at index date | 92 (20.9) | 68 (22.4) | 24 (17.4) |
| Pretreated | 66 (71.7) | 52 (76.5) | 14 (58.3) |
| Liver metastasis at index date | 34 (7.7) | 25 (8.3) | 9 (6.5) |
| Bone metastasis at index date | 118 (26.8) | 89 (29.4) | 29 (21.0) |
| History of lung surgery | 62 (14.1) | 35 (11.6) | 27 (19.6) |
| Previous radiation therapy | 39 (8.8) | 20 (6.6) | 19 (13.8) |
| Previous chemoradiation | 14 (3.2) | 9 (3.0) | 5 (3.6) |

Note: Data are n (%) unless otherwise noted. Percentages may not total 100 because of rounding.

Percentages for smoking and NSCLC histologic diagnosis are of known totals.

Brain metastases treated before initiation of first-line therapy.

ECOG, Eastern Cooperative Oncology Group.
patients who had not received subsequent systemic therapy were 47% overall, including 46% of those younger than 75 years and 50% of those 75 years or older (Table 2 and Fig. 2) and 48% of those with PS of 0 to 1 (Fig. 2D).

The reasons for pembrolizumab discontinuation are summarized in Supplementary Table 1. The most common reason, both overall and by age group, was radiologically documented disease progression, recorded for 183 patients (51% of 356 patients with a reported reason), including 125 (51%) and 58 (52%) who were younger than 75 years and 75 years or older, respectively. Toxicity was the second most common reason (79; 22%), reported for 61 (25%) and 18 (16%) patients younger than 75 years and 75 years or older, respectively.

Overall, 161 patients (37%) continued to second-line therapy and 74 (17%) continued to third-line therapy (Table 4). Platinum-doublet therapy was the most common second-line therapy (122; 76%), and a nonplatinum cytotoxic regimen was the most common third-line therapy (50; 68%). In both second and third lines, the most common platinum-doublet regimens administered were carboplatin plus nab-paclitaxel and carboplatin plus pemetrexed, and the most common nonplatinum cytotoxic agent was docetaxel (data not shown).

The choice of subsequent systemic therapy regimen differed substantially between age groups, with nonplatinum cytotoxic regimens administered more frequently than platinum doublets to those 75 years or older (Table 4).

**Discussion**

We identified 441 patients with highly PD-L1–expressing advanced NSCLC, with no known EGFR, ALK, ROSI, or BRAF genomic alterations, who initiated first-line pembrolizumab monotherapy soon after this regimen became available in Japan. With a median patient follow-up time of 13.5 months, the median OS was NR; and the estimated survival rate for all patients at 24 months was 57.9%. We observed that median OS was also NR for patients younger than 75 years old and for patients with good performance status (ECOG PS 0–1). The median OS was shorter for the 138 patients who were 75 years or older (23.5 mo; 95% CI: 16.2–NR), whereas median PFS was similar in the two age groups (10.1 versus 9.5 mo for those <75 versus ≥75 y, respectively). Estimated 24-month OS was 62% among those younger than 75 years and 48% among those 75 years or older.

The real-world clinical outcomes with first-line pembrolizumab monotherapy in this study were consistent with results reported in clinical trials. For example, the Kaplan-Meier 12-month OS rate for patients in this study was 72.2% overall and the 12-month OS rates for corresponding patient populations (with PD-L1 TPS ≥ 50%) in the pembrolizumab arms of clinical trials were 70.3%, 63.5%, and 67.9% in KEYNOTE-024, KEYNOTE-042, and KEYNOTE-598, respectively. We identified 441 patients with highly PD-L1–expressing advanced NSCLC, with no known EGFR, ALK, ROSI, or BRAF genomic alterations, who initiated first-line pembrolizumab monotherapy in this study were consistent with those in the main study. With 5 years of follow-up in KEYNOTE-024, median OS was 26.3 months. Nevertheless, we note that our real-world population differed from KEYNOTE-024 and KEYNOTE-598 by including patients with stage III NSCLC (19% of patients in the present study had no recorded metastasis at the index date), and it differed from all three clinical trials by including patients with ECOG PS of 2, who represented 8% of the patients.
For the 138 patients who were 75 years or older treated with pembrolizumab in this study, 11 (8%) of whom had ECOG PS of 2 and 49 (36%) of whom had unknown ECOG PS, the 12-month OS rate was 67.2%. The corresponding 12-month OS rate for 49 patients 75 years or older (all with ECOG PS of 0 or 1) treated with pembrolizumab in KEYNOTE-024 and KEYNOTE-042 (pooled analyses) was 60.7%, with median OS of 27.4 months (95% CI: 10.6–NR), not dissimilar to that in the present study (23.5 mo; 95% CI: 16.2–NR). These findings suggest that, despite the paucity of clinical trial results for older adults (≥75 y), pembrolizumab can be considered an appropriate first-line therapy for those with highly PD-L1–expressing advanced NSCLC, particularly as an alternative to platinum-doublet therapy that was frequently administered to older individuals in 2013, as reported in a large study by Noda-Narita et al. Further support for this inference is provided by a recent large, retrospective study...
conducted in the United States and Europe, which found that ICI monotherapy may be effective and was generally well-tolerated among patients 80 years or older with cancer (no Japanese centers were included in the latter study).

In Japan, Tambo et al. studied a similar but smaller patient population than that in the present study (n = 95, median age 72 y, 75% men), also treated with first-line pembrolizumab monotherapy for advanced or recurrent NSCLC. In their study, median OS was NR and

Figure 2. Kaplan-Meier estimates of (A) rwToT by age and (B) by ECOG performance status and (C) rwTTNT by age and (D) by ECOG performance status. CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; rwToT, real-world time on treatment; NA, not assessable; NR, not reached; rwToT, real-world time to next treatment.

Table 4. Distribution of Subsequent Systemic Therapy Regimens by Treatment Line

| Subsequent Systemic Therapy          | All Patients (N = 441) | Age < 75 y (n = 303) | Age ≥ 75 y (n = 138) |
|--------------------------------------|-----------------------|----------------------|----------------------|
| Second-line regimen                  |                       |                      |                      |
| Platinum doublet                     | 161 (36.5)            | 116 (38.3)           | 45 (32.6)            |
| ICI monotherapy                      | 122 (75.8)            | 103 (88.8)           | 19 (42.2)            |
| ICI + chemotherapy                   | 3 (1.9)               | 2 (1.7)              | 1 (2.2)              |
| Nonplatinum cytotoxic agent          | 34 (21.1)             | 9 (7.8)              | 25 (55.6)            |
| Other                                | 1 (0.6)               | 1 (0.9)              | 0                    |
| Third-line regimen                   | 74 (16.8)             | 51 (16.8)            | 23 (16.7)            |
| Platinum doublet                     | 7 (9.5)               | 7 (13.7)             | 0                    |
| ICI monotherapy                      | 14 (18.9)             | 8 (15.7)             | 6 (26.1)             |
| Nonplatinum cytotoxic agent          | 50 (67.6)             | 33 (64.7)            | 17 (73.9)            |
| Tyrosine kinase inhibitor            | 2 (2.7)               | 2 (3.9)              | 0                    |
| Other                                | 1 (1.4)               | 1 (2.0)              | 0                    |

Note: Data are n (%), with drug regimens presented as percentage of the relevant treatment line. Percentages may not add up to 100 because of rounding. ICI, immune checkpoint inhibitor of programmed death 1 or programmed death-ligand 1.
median PFS was 6.1 months; there was no significant difference in OS by age (<70 versus ≥70 y) in univariable analyses (p = 0.838). In a second multicenter, observational study in Japan, for the 47 patients 75 years or older who received first-line pembrolizumab monotherapy for advanced NSCLC, median OS was NR (95% CI: 10.3–NR). Other previous retrospective studies of patients with advanced NSCLC treated with ICI therapy in Japan differed in patient population or study design, thus precluding comparisons with our findings.

The median rwToT with pembrolizumab in this study was 5.6 months (95% CI: 4.4–6.7), and this estimate did not vary appreciably by age group, suggesting a similar duration of pembrolizumab monotherapy for older patients relative to younger patients in real-world settings in Japan. For context, the median pembrolizumab treatment duration was 7.9 months (95% CI: 6.2–11.7) in the KEYNOTE-024 clinical trial and 6.6 months (95% CI: 4.9–8.5) in the KEYNOTE-042 clinical trial subset of patients with PD-L1 TPS greater than or equal to 50%. The somewhat shorter rwToT estimate for the first-line pembrolizumab-treated population in the current study relative to those two KEYNOTE trials could be related to either patient characteristics or operational factors unique to the clinical or real-world setting in Japan. For patients with PS 0 or 1 in our study, the median rwToT estimate was 5.7 months (95% CI: 4.2–6.7), somewhat shorter than the median rwToT of 6.9 months (95% CI: 5.6–8.3) reported in a recent database study in the United States of patients with PS 0 or 1 treated with first-line pembrolizumab monotherapy for metastatic NSCLC (stage IV) with PD-L1 expression greater than or equal to 50%. Other estimates of pembrolizumab treatment duration for Japanese patients in either clinical trial or real-world settings are currently unavailable for comparison.

Our study did not include safety or safety-related outcomes; therefore, we cannot draw conclusions around pembrolizumab safety from the current study. Nevertheless, it should be noted that toxicity was abstracted as the reason for pembrolizumab discontinuation for 22% of patients (25% and 16% of patients aged <75 y and ≥75 y, respectively). Although additional details regarding these patient outcomes (e.g., observed or anticipated toxicity, toxicity type, or severity) are not available in the present study owing to the retrospective design, Yamamoto et al. recently described 52-week safety data collected in a post-marketing surveillance study of 2740 patients with NSCLC who were treated with first-line or second-line and later pembrolizumab from December 2016 to June 2019 at 717 centers across Japan. The 1179 patients who received first-line pembrolizumab monotherapy had unresectable advanced or recurrent NSCLC with PD-L1 TPS of greater than or equal to 50%, similar to the present study and in accordance with regulatory approvals during that time period. Overall, the most common adverse events (AEs) were pyrexia and rash, whereas the most common AE of special interest (as designated in the Japanese risk management plan) was interstitial lung disease. Grade 5 treatment-related AEs were experienced by 70 (6%), and grade 5 pembrolizumab-induced AEs of special interest were experienced by 23 (2%) of the 1179 patients. The authors note that the incidence of AEs of special interest was similar between patients younger than 75 years and those 75 years or older.

Strengths of this study include the large, well-characterized patient population treated in real-world settings in Japan. We evaluated clinical outcomes by age group and performance status, and the study included 138 patients 75 years or older, a larger number than in most previous studies, in addition to the 36 patients with ECOG PS of 2 who would have been excluded from clinical trials.

The length of follow-up was adequate for determining median rwPFS but was insufficient to determine median OS, which was NR despite a minimum of 9 months’ potential follow-up and the actual median follow-up of 13.5 months from first-line pembrolizumab initiation. Moreover, this was an observational study that was designed to be descriptive in nature, thus limiting our ability to make comparisons between subgroups that may have differed in the distribution of prognostic factors. For example, age-specific outcomes may have been influenced by the distribution of baseline metastasis, as 25% of patients 75 years or older treated with pembrolizumab monotherapy had no metastasis whereas the corresponding percentage was 17% for patients younger than 75 years. Real-world tumor response information was gleaned from radiologic documentation and clinicians’ notes, as it was not possible to retrospectively apply the Response Evaluation Criteria in Solid Tumors version 1.1 and immune Response Evaluation Criteria in Solid Tumors that are used in prospective clinical trials. Chart abstractors were advised to sequentially identify eligible patients working backward from the first index date and to make every effort to confirm study eligibility in the same sequence so as to minimize selection bias; however, we cannot exclude the potential for bias from unidentified factors. Other study limitations include the potential for errors in medical records or in abstraction to the electronic case report forms. Finally, although study centers were geographically dispersed throughout Japan, our findings may not represent the entire patient population or treatment practices in Japan.

More information about treatment duration in real-world settings in Japan would be of interest. We
observed a shorter duration of first-line pembrolizumab monotherapy than that recorded in clinical trials and U.S. real-world settings but were not able to compare this with other real-world studies conducted in Japan. Further study of real-world patient populations and treatment patterns with long follow-up is needed. It would be helpful to have 5 years of follow-up, similar to that reported recently by Reck et al.\(^2\) from KEYNOTE-024, to observe long-term outcomes. Moreover, studies of real-world effectiveness for other NSCLC pembrolizumab indications (expanded monotherapy and in combination) that became available after the index period of this study would be of interest, including prospective studies to evaluate patient-reported outcomes associated with pembrolizumab therapy.

In conclusion, the results of this noninterventional study complement KEYNOTE clinical trial findings and provide real-world evidence supporting the benefits of first-line pembrolizumab monotherapy for treating advanced NSCLC with PD-L1 TPS greater than or equal to 50% and no actionable genomic alterations, including for patients who are 75 years and older.

**CRediT Authorship Contribution**

**Yasushi Goto:** Methodology, Investigation, Resources, Writing—review and editing, Visualization.

**Atsuhisa Tamura:** Investigation, Resources, Writing—review and editing.

**Hirotaka Matsumoto:** Investigation, Resources, Writing—review and editing.

**Kazutoshi Isobe:** Investigation, Resources, Writing—review and editing.

**Tomohiro Ozaki:** Investigation, Resources, Writing—review and editing.

**Melissa L. Santorelli:** Conceptualization, Methodology, Resources, Data curation, Writing—original draft, Writing—review and editing, Visualization, Supervision, Project administration.

**Kazuko Taniguchi:** Conceptualization, Methodology, Resources, Data curation, Writing—review and editing, Visualization, Supervision, Project administration.

**Tetsu Kamitani:** Conceptualization, Resources, Writing—review and editing, Visualization, Project administration.

**Masato Irisawa:** Resources, Writing—review and editing, Visualization, Project administration.

**Kingo Kanda:** Resources, Writing—review and editing, Visualization, Project administration.

**Machiko Abe:** Conceptualization, Resources, Writing—review and editing, Visualization, Project administration, Funding acquisition.

**Thomas Burke:** Conceptualization, Methodology, Resources, Writing—original draft, Writing—review and editing, Visualization, Supervision, Project administration, Funding acquisition.

**Hiroshi Nokihara:** Methodology, Investigation, Resources, Writing—review and editing, Visualization.

**Supplementary Data**

Note: To access the supplementary material accompanying this article, visit the online version of the *JTO Clinical and Research Reports* at [www.jtocrr.com](http://www.jtocrr.com) and at [https://doi.org/10.1016/j.jtocrr.2022.100397](https://doi.org/10.1016/j.jtocrr.2022.100397).

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