Received: 8 February 2023 | Revised: 24 October 2023 | Accepted: 4 November 2023

DOI: 10.1002/ccr3.8219

CASE REPORT

Clinical Case Reports Open Access WILEY

# Successful treatment with nivolumab in a patient with unresectable oral squamous cell carcinoma following ineffective chemoradiotherapy

**Katsuhisa Sekido**[1,2] | **Shuichi Imaue**[1] | **Hidetake Tachinami**[1] | **Kei Tomihara**[3] | **Norihito Naruto**[4] | **Kentaro Yamagishi**[4] | **Atsushi Ikeda**[1] | **Kumiko Fujiwara**[5] | **Makoto Noguchi**[1]

[1]Department of Oral and Maxillofacial Surgery, Faculty of Medicine, Academic Assembly, University of Toyama 2630 Sugitani, Toyama City, Japan

[2]Department of Oral and Maxillofacial Surgery, Toyama Red Cross Hospital, Toyama City, Japan

[3]Divisions of Oral and Maxillofacial Surgery, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

[4]Department of Radiology, Faculty of Medicine, Academic Assembly, University of Toyama, Toyama City, Japan

[5]Department of Dentistry and Oral Surgery, Division of Medicine for Function and Morphology of Sensory Organs, Faculty of Medicine, Osaka Medical and Pharmaceutical University, Takatsuki, Japan

**Correspondence**
Shuichi Imaue, Department of Oral and Maxillofacial Surgery, Faculty of Medicine, Academic Assembly, University of Toyama 2630 Sugitani, Toyama City, Toyama 930-0194, Japan.
Email: simaue@med.u-toyama.ac.jp

**Key clinical message**

Nivolumab has been clinically successful in prolonging the overall survival of patients with recurrent and metastatic head and neck cancer, complete remission is rare. Synergistic combinations of immunotherapy and conventional cancer treatments, such as radiotherapy or chemotherapy, are likely to be the most viable strategies for improving patient responses.

**Abstract**

Immune checkpoint inhibitors have revolutionized recurrent, metastatic oral cancer treatment; however complete remission in advanced stages is unusual. We present a case of complete remission of advanced oral squamous cell carcinoma for >4 years in a 64-year-old Japanese woman, that responded poorly to chemoradiotherapy but well to subsequent nivolumab treatment.

**KEYWORDS**

chemoradiotherapy, complete remission, immune checkpoint inhibitor, nivolumab, oral squamous cell carcinoma

## 1 | INTRODUCTION

Oral cancer is one of the most common malignant tumors occurring worldwide, ranking eighth among men and 14th among women.[1] Treatment for oral squamous cell carcinoma (OSCC) includes a single-modality therapy of surgery, radiotherapy, or various combinations of these modalities, with or without systemic

chemotherapy.[2] Recent advances in treatment options and diagnostic techniques have significantly improved patient outcomes.[3] The treatment selection for OSCC should be based on various factors, including tumor resectability, disease control probability, or the patient's general condition. However, despite recent advances in reconstructive surgery, surgical treatment of oral cancer patients with locally advanced tumors remains a clinical challenge because functional or cosmetic deficits following surgical treatment are still unsatisfactory.[4] For patients with inoperable tumors or when surgery is anticipated to result in poor functional or cosmetic outcomes, patients may be candidates for curative chemoradiotherapy (CRT) or palliative radiotherapy (RT), considering their quality of life.[4] However, the treatment benefit of CRT or RT for advanced oral cancers, especially those classified as T4 disease, is still dismal; therefore, therapeutic intervention with a novel strategy is desired to enhance treatment benefits markedly.

Recently, cancer immunotherapy based on the blockade of immune checkpoint molecules such as programmed cell death protein 1 (PD-1), cytotoxic T lymphocyte-associated antigen-4, and programmed death-ligand 1 (PD-L1) has offered novel insights into the treatment of recurrent or metastatic cancers refractory to other therapies.[5–7] Nivolumab, a human monoclonal immunoglobulin G4 antibody targeting PD-1 on T-cells, was approved in Japan in 2017 and has been used to treat platinum-refractory recurrent and metastatic head and neck cancer. Although nivolumab has been clinically successful in prolonging the overall survival of patients with recurrent and metastatic head and neck cancer, complete remission is rare.[8] Here, we present the case of a patient with locally advanced OSCC who underwent chemoradiotherapy and was subsequently treated with nivolumab, after which the patient experienced complete remission.

## 2 | CASE STORY/EXAMINATION

A 64-year-old Japanese woman was referred to our hospital in 2017 with a complaint of painful, extensive tumor formation on the right side of her mandible. She had been aware of tumor formation for approximately 1 year, which gradually increased in size and pain. However, she had no opportunity to visit the hospital because she was busy caring for her husband, who was bedridden with chronic kidney disease. Subsequently, as her intraoral tumor proliferated and spread to the facial skin, causing difficulty in eating and drinking, she consulted the Department of Oral and Maxillofacial Surgery at a local hospital. The patient was referred to our department with a suspected diagnosis of a malignant oral tumor.

Her medical history included appendicitis in her teenage years and no smoking or alcohol consumption. On initial assessment, she complained of slight fatigue, fever, and persistent pain in the right side of her mandible. Extraoral findings revealed a large indurated facial tumor on the right side of the mandible, with partial necrosis and bleeding (Figure 1A). Blood examination revealed mild anemia (hemoglobin:10.6 g/dL) and undernutrition (albumin:3.7 g/dL), but no other abnormalities. Her general condition was maintained, and the Eastern Cooperative Oncology Group (ECOG) performance status was 0. Intraoral findings revealed a tumor on the right side of the mandibular gingiva that extended anteriorly to the mandibular incisor gingiva and lower lip, posteriorly to the retromolar area, lingually to the floor of the mouth, and laterally to the buccal mucosa (Figure 1B). Moreover, intraoral gingival tumors perforated through the mandibular bone and muscles surrounding the facial skin. Panoramic radiography revealed ill-defined destructive bone resorption, with a pathological fracture on the right side of the mandible (Figure 2). Computed tomography

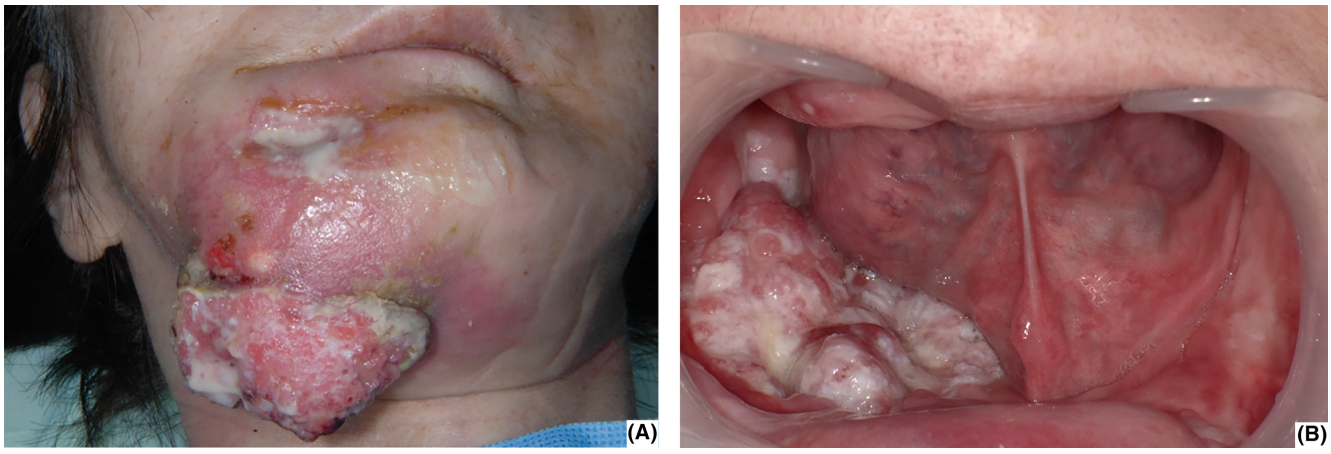


FIGURE 1 Photographs during the patient's first visit, showing the patient's (A) extraorally spreading tumor and (B) an intraoral tumor.

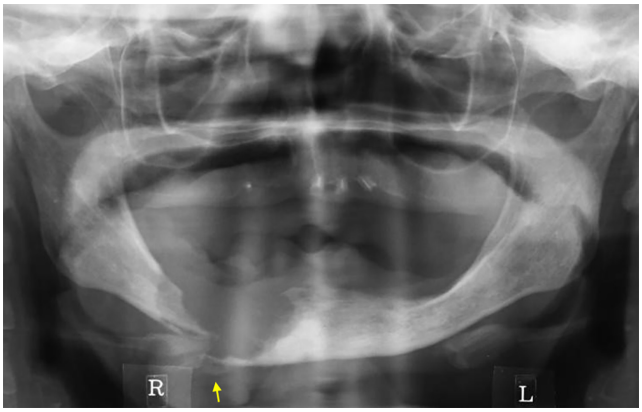


**FIGURE 2** Panoramic radiograph showing ill-defined destructive bone resorption, accompanied by fracture on the right side of the mandible (arrow).

(CT) and magnetic resonance imaging (MRI) revealed a large enhancing lesion (59×55mm) on the right side of the mandible spreading from the oral cavity to the facial skin (Figure 3). CT of the neck revealed several enlarged and unilateral lymph nodes at Levels I and II, suggesting the presence of lymph node metastases. No other specific findings were observed on CT of the abdominal or thoracic region. Biopsy findings revealed the features of invasive squamous cell carcinoma(Figure 4). The tumor of the right mandible was classified as clinically malignant Stage IV (T4bN2bM0) based on the Union for International Cancer Control TNM classification criteria (8th edition) for oral cancer.

She was initially treated with induction chemotherapy using intra-arterial cisplatin (CDDP) infusion and concurrent peroral S-1 (a prodrug of fluorouracil, gimeracil, and oteracil potassium as modulators). S-1 (100 mg/body/day) was administered for 2 weeks, followed by a rest period of two cycles, and CDDP (80 mg/m$^2$) was infused biweekly for three cycles. A tumor reduction rate of 24% was achieved (45×42mm). She was subsequently treated with super-selective intra-arterial CDDP infusion concurrent with intensity-modulated radiation therapy (CCRT) at 70 Gy/35 fr, with weekly CDDP (80 mg/m$^2$) for five cycles. She tolerated CCRT well, except for the emergence of Grade 2 dermatitis and Grade 2 oral mucositis, which was treated with a topical steroid. However, a residual tumor was suspected macroscopically, and the reduction rate was only 5% on CT (43×35mm), 2 weeks after irradiation (Figure 5). Subsequently, the patient, agreed to receive immunotherapy with nivolumab and treatment was started immediately. The patient's clinical condition at pretreatment with nivolumab was good (Eastern ECOG performance status, 0), and PD-L1 expression in the tumor was 5% on immunohistochemistry (Figure 6).

Nivolumab was administered at 240 mg every 2 weeks. After five cycles of nivolumab administration, the patient developed hypothyroidism as a thyroid immune-related adverse event (irAE), for which she received levothyroxine; however, the nivolumab treatment regimen remained unaltered. After nine cycles of nivolumab, QTc interval prolongation was observed, and a cardiologist closely followed up with the patient. The interruption of nivolumab treatment improved her cardiac symptoms, and treatment was restarted after 2 months. Clinical findings and CT after 13 cycles of nivolumab administration revealed complete tumor remission (Figure 7). After 40 cycles, blood examination revealed pancytopenia (white blood cell count,1170/μL; hemoglobin:8.6 g/dL; platelets,2.3×10$^4$/μL). She was diagnosed with megaloblastic anemia as a hematological irAE and received methylcobalamin, during which the nivolumab treatment regimen remained unaltered. To date, she has been under treatment with nivolumab and has been in remission for more than 4 years after the initiation of nivolumab treatment (Figure 8).

## 3 | DISCUSSION

Here, we present a case of complete remission of advanced OSCC following immunotherapy with nivolumab after chemoradiotherapy. As the oral cavity is an easily accessible site for inspection, oral cancer can be diagnosed relatively early. If detected at an early stage, the outcome of patients with oral cancer is better. However, treating patients presenting with oral cancer at an advanced stage is difficult, and more than 50% of oral cancers are still detected at an advanced stage.[9] Although continuous advancements in multimodal therapies have revealed improvements in the control of oral cancer, the optimal therapy is largely unknown, especially in cases where surgical resection is not feasible.[3]

Recently, the emerging role of immunotherapy in cancer and its potential as a novel alternative for cancer treatment have received increasing attention. In particular, the emergence of immune checkpoint inhibitors (ICIs) has revolutionized the treatment of recurrent or metastatic oral cancer, resulting in better overall survival than that achieved using conventional therapies.[5–7] However, the overall response rate to ICIs among patients with advanced oral cancer is <20%, with numerous patients displaying primary or acquired resistance.[8] Hence, prognostic indicators for patients receiving ICIs need to be urgently identified, along with the causes of this resistance and strategies to overcome them.

Various mechanisms underlying impaired antigen presentation and T-cell activation have been suggested

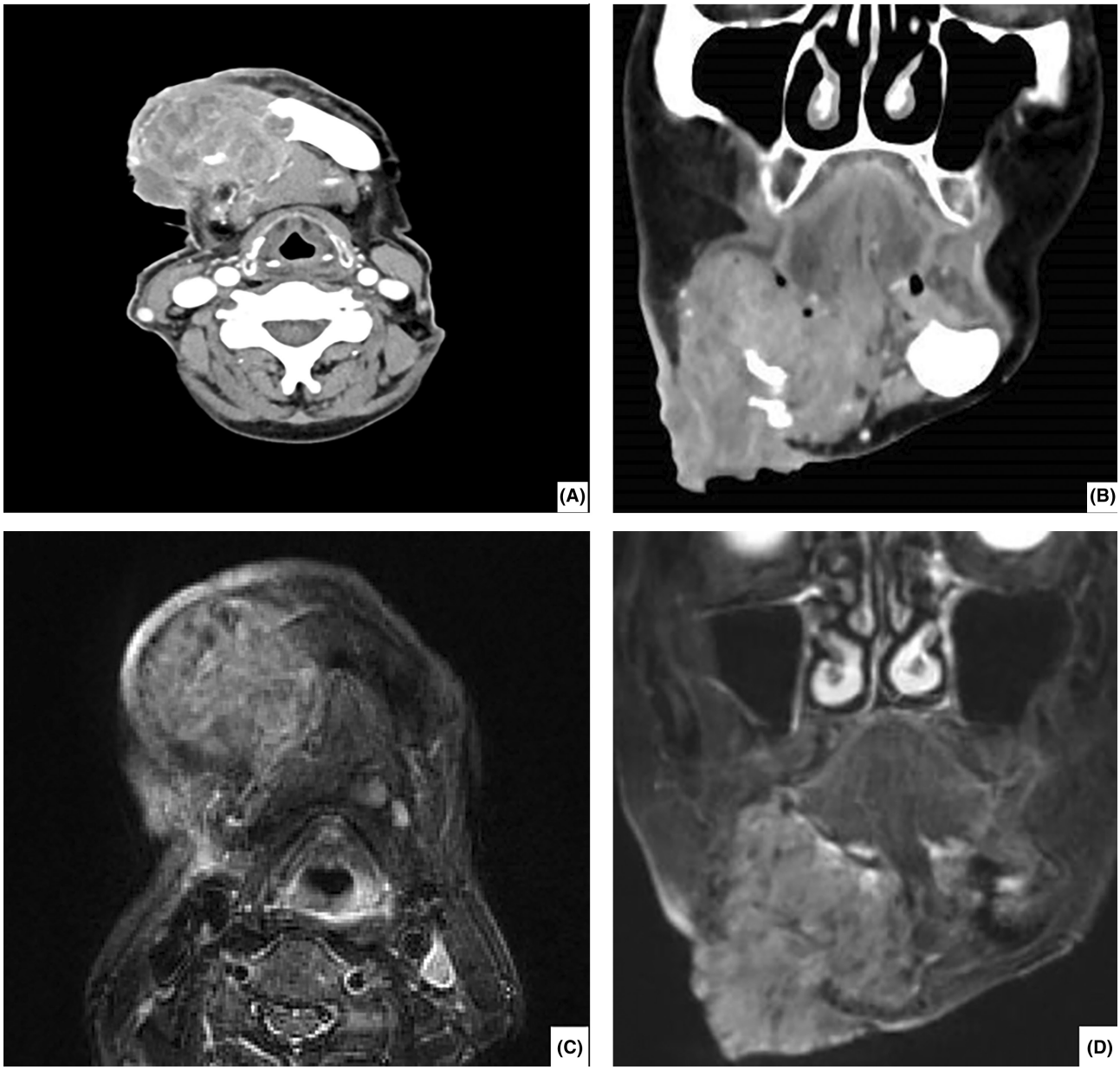


**FIGURE 3** CT and MRI showing a homogeneous mass on the right side of the mandible (A) contrast-enhanced axial CT image (B) contrast enhanced coronal CT image (C) axial short inversion time inversion recovery (STIR) image (D) coronal STIR image.

to be associated with resistance to ICIs. Lower levels of tumor mutation burden and neoantigens, which are associated with insufficient tumor immunogenicity, predict a poor response to ICIs in different cancers, indicating that tumor mutation burden is a crucial biomarker for predicting response to ICIs.[10,11] The expression of PD-L1 in tumors has also been widely used as a predictive biomarker in the clinical setting for ICI treatment of different cancers. Higher PD-L1 expression has been suggestively associated with better outcomes for ICI treatment in various cancers, including head and neck.[8,12] Moreover, systemic inflammatory markers, such as the neutrophil-to-lymphocyte ratio (NLR), considered a key marker of inflammation, have also been suggested as potential indicators for predicting responses to ICIs in different cancers.[13,14] Significant correlations between lower NLR and better response to ICIs have been reported in several cancers; specifically, a cut off value of <5 has been reportedly associated with more prolonged overall survival in patients receiving ICIs.[13] Even with initially high NLR values, overall survival was prolonged in patients with a decrease in NLR during ICI treatment.[15] Consistently, the NLR value in this patient was relatively high at 14.3 on the initiation of nivolumab treatment, which markedly decreased to 3.5 after the first infusion of nivolumab.

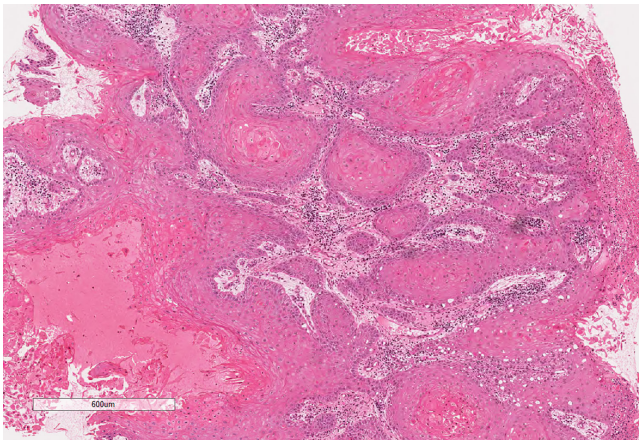


**FIGURE 4** Well differentiated squamous cell carcinoma invading and forming small and large cell groups, with only a small lymphocytic infiltrate.

The emergence of irAEs, which are often distinctly different from conventional chemotherapy-induced toxicity, is potentially fatal, and early recognition and appropriate management are required during ICI therapy.[16] Various irAEs have been recognized, including dermatologic, endocrine, pulmonary, gastrointestinal, hepatic, and ocular origin, which exhibit different clinical manifestations.[5,6] Hypothyroidism, QTc prolongation, and megaloblastic anemia were observed after 5, 9, and 42 cycles of nivolumab administration, respectively. Hypothyroidism was treated with levothyroxine, megaloblastic anemia was treated with methylcobalamin, and nivolumab was resumed. Although QTc prolongation was suspected of myocarditis due to irAEs, no increase in creatine kinase MB, B-type natriuretic peptide, or troponin T levels was observed. Cardiovascular irAEs are relatively rare, with

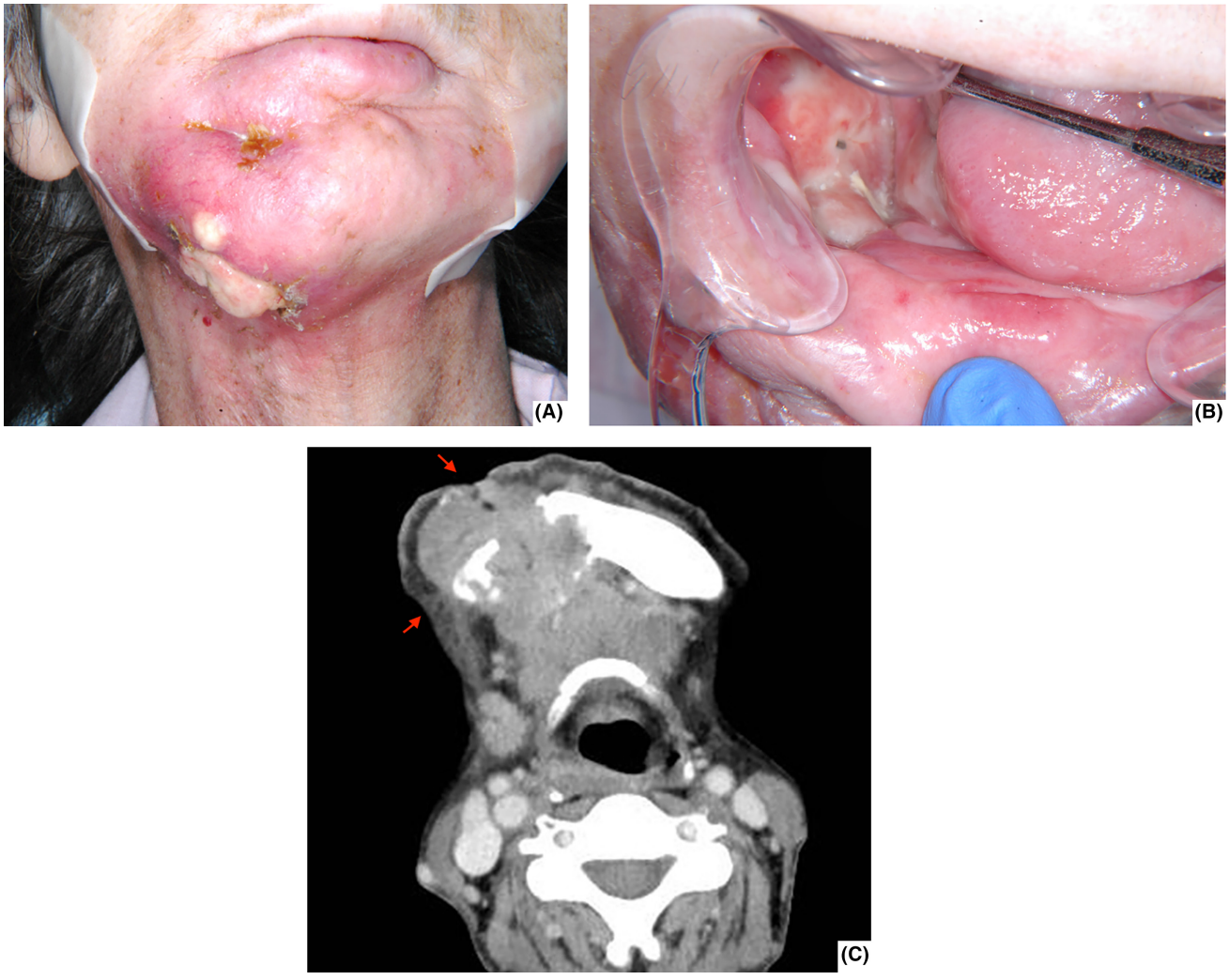


**FIGURE 5** (A, B) A photograph showing the patient's extra- and intraoral appearance after super-selective intra-arterial cisplatin infusion concurrent with intensity-modulated radiation therapy (C) contrast-enhanced axial CT showing residual tumor in the mandible (arrows) after concurrent chemoradiotherapy.

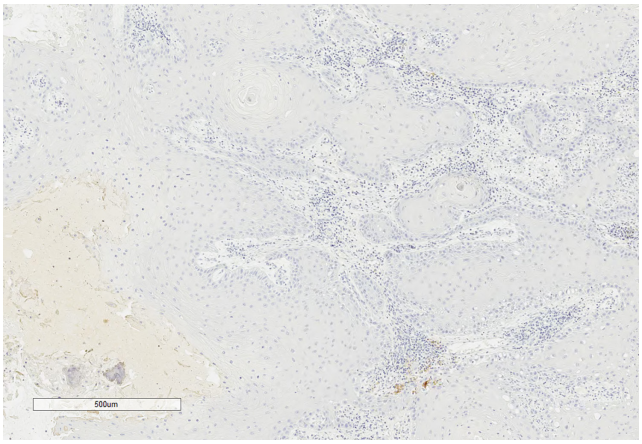


FIGURE 6 In the biopsy specimen, PD-L1 expression in the tumor is 5% on immunohistochemistry.

an incidence of 0.27%–1.14%.[17] However, significant vigilance is recommended because cardiovascular irAEs can be life-threatening.[17,18] It was unclear whether QTc prolongation was an irAE of myocarditis; nevertheless, we interrupted nivolumab treatment. Subsequently, the QTc prolongation resolved spontaneously. Thus, we resumed nivolumab treatment, and QTc prolongation was not observed. Recent studies have also shown that the emergence of irAEs is reportedly associated with better outcomes for ICI treatment in several cancers.[19–21] However, the association between the types of irAEs and the response to ICIs in different cancer types remains unclear.

In our case, ICI treatment was administered 2 weeks after chemoradiotherapy. Generally, radiotherapy kills cancer cells by damaging their DNA; therefore, it takes

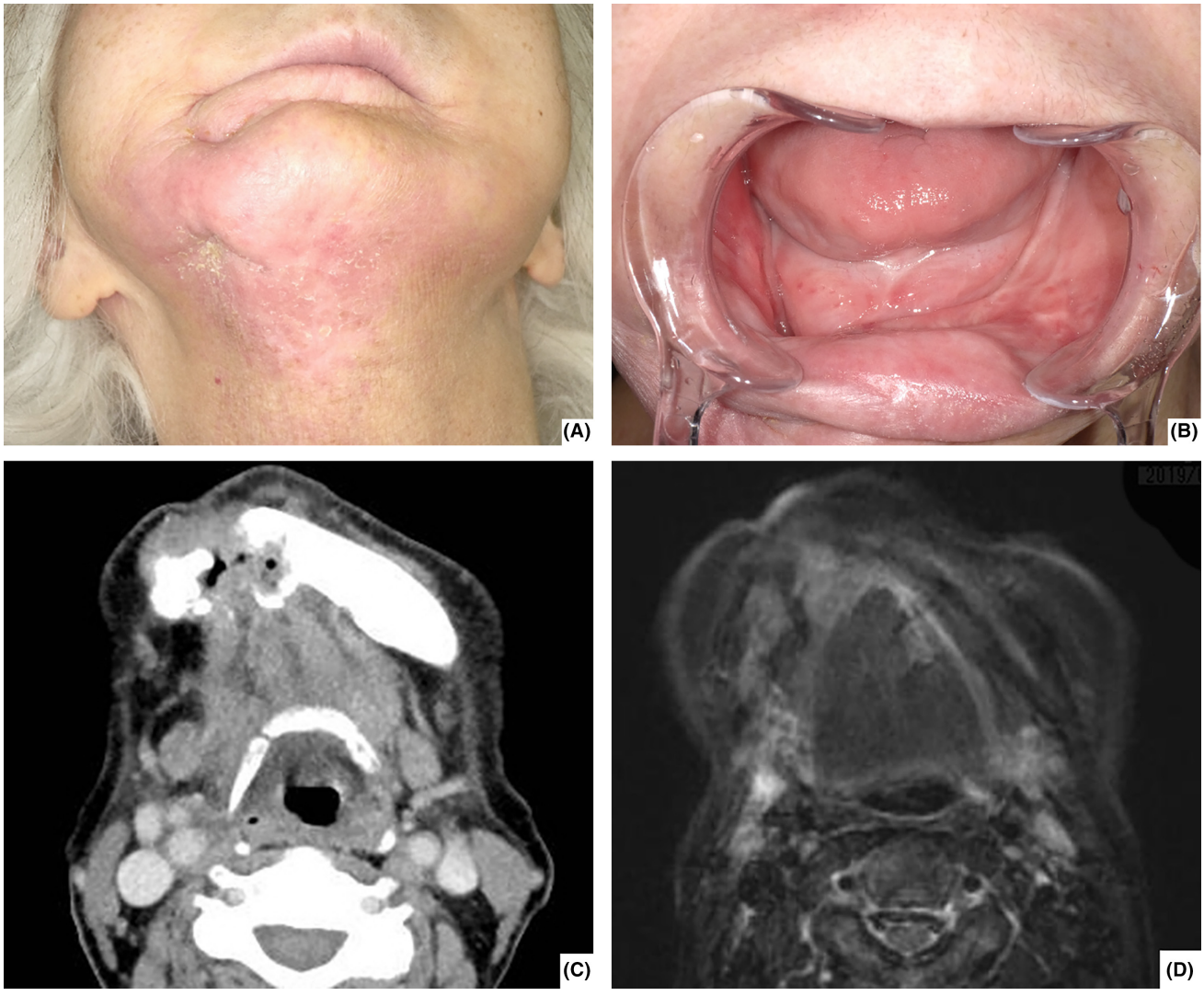


FIGURE 7 (A, B) A photograph showing the patient's intra- and extraoral appearance after 13 cycles of nivolumab treatment (C, D) Contrast-enhanced CT and STIR image showing no residual tumor in the mandible.

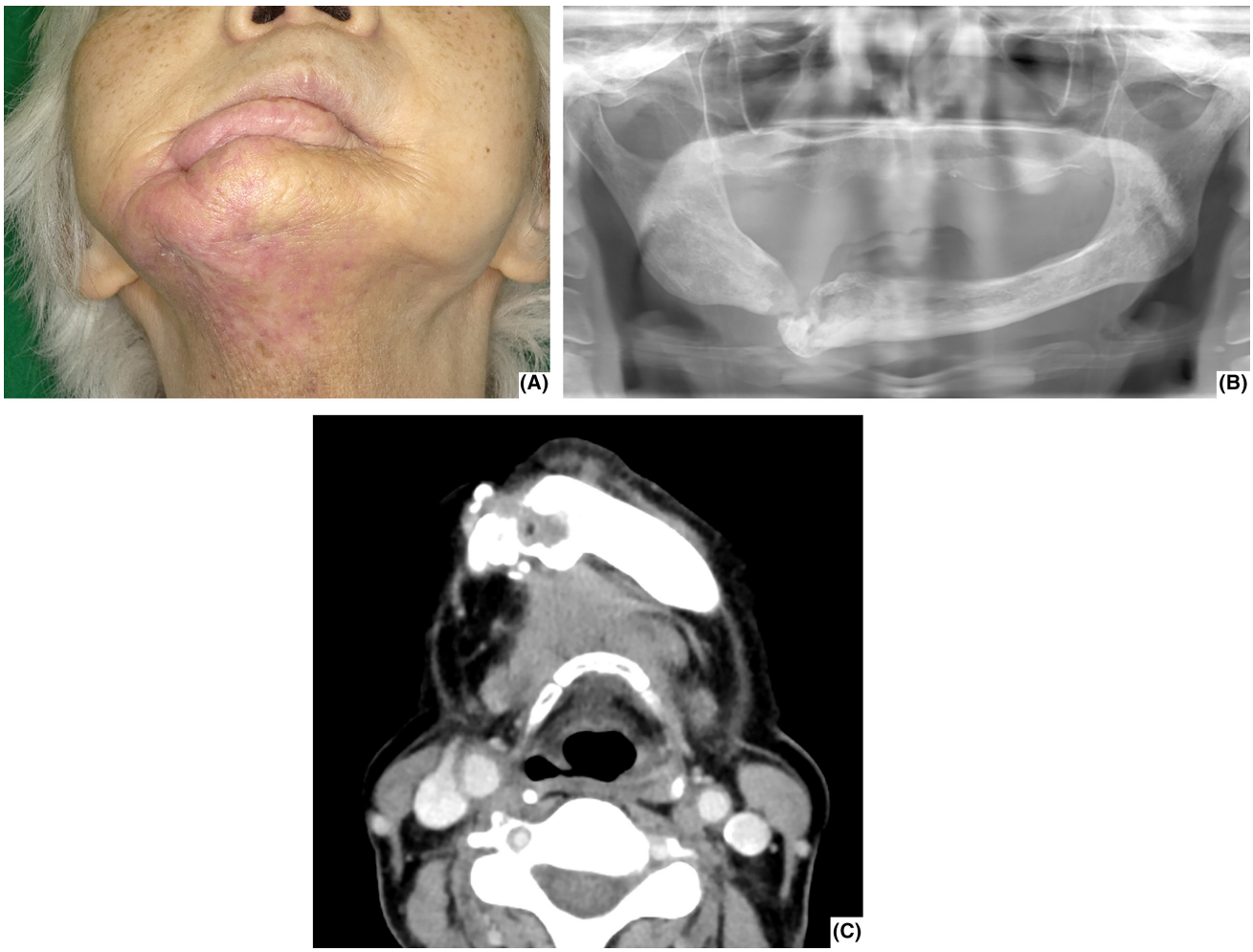


**FIGURE 8** A photograph showing the patient's (A) extraoral appearance, (B) panoramic radiograph, (C) contrast-enhanced axial CT image 4 years after the initiation of nivolumab treatment.

a while for the disappearance of cancer cells to be confirmed clinically. CT, MRI, and positron emission tomography (PET) are recommended to evaluate treatment effects.[2] However, owing to the severe local inflammation and edematous changes that occur after radiotherapy, the sensitivity and specificity of early evaluation are known to be inferior to those performed after 3 months of treatment, especially on PET.[22] Therefore, it is essential to take the time to precisely evaluate the effectiveness of treatment to avoid unnecessary treatment. However, in our case, the residual tumor was suspected macroscopically, and the complete disappearance of tumor cells with CRT was considered unlikely. Additional treatment for persistent disease ineffective to CRT can be either with re-irradiation with or without systemic therapy or systemic therapy alone.[2] In recent years, systemic therapy for head and neck cancer has been remarkably developed. For many years, CDDP plus 5FU (PF) is the standard systemic therapy, but the addition of cetuximab, an anti-EGFR antibody, to PF prolongs survival (EXTREME trial).[23] Furthermore, PD-1 antibody pembrolizumab outperformed cetuximab in the Keynote 048 trial, and PF plus pembrolizumab is now the standard systemic therapy for recurrent/metastatic head and neck cancer.[24] Nivolumab has become the standard treatment for platinum-refractory recurrent/metastatic head and neck cancer after Phase III trials showed prolonged survival compared to single-agent systemic therapy such as docetaxel and cetuximab (Checkmate 141 trial).[8] Although not statistically significant, the efficacy of nivolumab tended to be greater in patients with high PD-L1 expression (tumor proportion score: TPS≥1%) than in those with low PD-L1 expression (TPS<1%).[8] In the present case, nivolumab was selected because the patient was platinum-refractory, had a TPS of 5% for PD-L1 expression, had no hematologic toxicity, and could be started relatively early after CRT. The next important question is whether combining immunotherapy with radiotherapy has the potential to

improve patient response and outcome. Unfortunately, a Phase III trial in 2021 did not show any additional effect of another PD-L1 antibody, avelumab, to CRT.[25] However, combining radiotherapy and ICIs could achieve an abscopal effect, a phenomenon in which tumor-specific lymphocytes and systemic antitumor immunity are activated.[26,27] Nevertheless, it remains unknown whether a similar effect in which ICI was started early after radiotherapy was achieved in the present case, which therefore requires further study.

Although the optimal therapy in patients with locally advanced oral cancer is still debatable, an improved understanding of our immune system's ability to eliminate cancer, along with recent remarkable clinical achievements of immunotherapy in multiple cancers, has generated significant interest in this therapeutic modality.[28] However, the response rate remains low, and patient selection using predictive indicators of response to immunotherapy remains an issue. Synergistic combinations of immunotherapy and conventional cancer treatments, such as radiotherapy or chemotherapy, are likely to be the most viable strategies for improving patient responses and outcomes. The appropriate management of irAEs is required during long-term ICI therapy.

## AUTHOR CONTRIBUTIONS

**Katsuhisa Sekido:** Conceptualization; writing – original draft. **Shuichi Imaue:** Conceptualization; writing – original draft. **Hidetake Tachinami:** Writing – review and editing. **Kei Tomihara:** Conceptualization; writing – original draft. **Norihito Naruto:** Supervision. **Kentaro Yamagishi:** Supervision. **Atsushi Ikeda:** Supervision. **KUMIKO FUJIWARA:** Supervision. **Makoto Noguchi:** Project administration; supervision.

## FUNDING INFORMATION

This research did not receive specific grants from public, commercial, or not-for-profit funding agencies.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy reasons.

## ETHICS STATEMENT

This study was approved by the Institutional Review Board for Human Studies of the University of Toyama Hospital (R2019037).

## CONSENT

All the patients provided written informed consent for participation.

## ORCID

*Katsuhisa Sekido* https://orcid.org/0000-0002-9858-5961
*Hidetake Tachinami* https://orcid.org/0000-0001-9255-6863
*Kei Tomihara* https://orcid.org/0000-0002-8147-6603
*Kumiko Fujiwara* https://orcid.org/0000-0001-9158-4141

## REFERENCES

1. de Camargo Cancela M, Voti L, Guerra-Yi M, Chapuis F, Mazuir M, Curado MP. Oral cavity cancer in developed and in developing countries: population-based incidence. *Head Neck*. 2010;32:357-367. doi:10.1002/hed.21193
2. NCCN guidelines head and neck cancers. version 1.2024; 2023. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf
3. Ong W, Zhao R, Lui B, et al. Prognostic significance of lymph node density in squamous cell carcinoma of the tongue. *Head Neck*. 2016;38(Suppl 1):E859-E866. doi:10.1002/hed.24113
4. Brana I, Siu LL. 2012. Locally advanced head and neck squamous cell cancer: treatment choice based on risk factors and optimizing drug prescription. *Ann Oncol*. 2012;23(Suppl 10):x178-x185. doi:10.1093/annonc/mds322
5. Topalian SL, Hodi FS, Brahmer JR, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. *N Engl J Med*. 2012;366:2443-2454. doi:10.1056/NEJMoa1200690
6. Brahmer JR, Tykodi SS, Chow LQM, et al. Safety and activity of anti-PD-L1 antibody in patients with advanced cancer. *N Engl J Med*. 2012;366:2455-2465. doi:10.1056/NEJMoa1200694
7. Wolchok JD, Kluger H, Callahan MK, et al. Nivolumab plus ipilimumab in advanced melanoma. *N Engl J Med*. 2013;369:122-133. doi:10.1056/NEJMoa1302369
8. Ferris RL, Blumenschein G Jr, Fayette J, et al. Nivolumab for recurrent squamous-cell carcinoma of the head and neck. *N Engl J Med*. 2016;375:1856-1867. doi:10.1056/NEJMoa1602252
9. Güneri P, Epstein JB. Late stage diagnosis of oral cancer: components and possible solutions. *Oral Oncol*. 2014;50:1131-1136. doi:10.1016/j.oraloncology.2014.09.005
10. Snyder A, Makarov V, Merghoub T, et al. Genetic basis for clinical response to CTLA-4 blockade in melanoma. *N Engl J Med*. 2014;371:2189-2199. doi:10.1056/NEJMoa1406498
11. Hellmann MD, Ciuleanu TE, Pluzanski A, et al. Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden. *N Engl J Med*. 2018;378:2093-2104. doi:10.1056/NEJMoa1801946
12. Teng MWL, Ngiow SF, Ribas A, Smyth MJ. Classifying cancers based on T-cell infiltration and PD-L1. *Cancer Res*. 2015;75:2139-2145. doi:10.1158/0008-5472.CAN-15-0255
13. Yasumatsu R, Wakasaki T, Hashimoto K, et al. Monitoring the neutrophil-to-lymphocyte ratio may be useful for predicting the anticancer effect of nivolumab in recurrent or metastatic head and neck cancer. *Head Neck*. 2019;41:2610-2618. doi:10.1002/hed.25737
14. Ferrucci PF, Ascierto PA, Pigozzo J, et al. Baseline neutrophils and derived neutrophil-to-lymphocyte ratio: prognostic

relevance in metastatic melanoma patients receiving ipilimumab. *Ann Oncol*. 2016;27:732-738. doi:10.1093/annonc/mdw016
15. Lorente D, Mateo J, Templeton AJ, et al. Baseline neutrophil–lymphocyte ratio (NLR) is associated with survival and response to treatment with second-line chemotherapy for advanced prostate cancer independent of baseline steroid use. *Ann Oncol*. 2015;26:750-755. doi:10.1093/annonc/mdu587
16. Ramos-Casals M, Brahmer JR, Callahan MK, et al. Immune-related adverse events of checkpoint inhibitors. *Nat Rev Dis Primers*. 2020;6:38. doi:10.1038/s41572-020-0160-6
17. Lyon AR, Yousaf N, Battisti NML, Moslehi J, Larkin J. Immune checkpoint inhibitors and cardiovascular toxicity. *Lancet Oncol*. 2018;19:e447-e458. doi:10.1016/S1470-2045(18)30457-1
18. Ball S, Ghosh RK, Wongsaengsak S, et al. Cardiovascular toxicities of immune checkpoint inhibitors: JACC review topic of the week. *J Am Coll Cardiol*. 2019;74:1714-1727. doi:10.1016/j.jacc.2019.07.079
19. Freeman-Keller M, Kim Y, Cronin H, Richards A, Gibney G, Weber JS. Nivolumab in resected and unresectable metastatic melanoma: characteristics of immune-related adverse events and association with outcomes. *Clin Cancer Res*. 2016;22:886-894. doi:10.1158/1078-0432.CCR-15-1136
20. Cortellini A, Chiari R, Ricciuti B, et al. Correlations between the immune-related adverse events spectrum and efficacy of anti-PD1 immunotherapy in NSCLC patients. *Clin Lung Cancer*. 2019;20:237-247.e1. doi:10.1016/j.cllc.2019.02.006
21. Yatsuda Y, Hirose S, Ito Y, et al. A durable response after the discontinuation of nivolumab in an advanced gastric cancer patient. *Intern Med*. 2021;60:1011-1017. doi:10.2169/internalmedicine.5893-20
22. Wong ET, Dmytriw AA, Yu E, et al. 18 F-FDG PET/CT for locoregional surveillance following definitive treatment of head and neck cancer: a meta-analysis of reported studies. *Head Neck*. 2019;41:551-561. doi:10.1002/hed.25513
23. Vermorken JB, Mesia R, Rivera F, et al. Platinumbased chemotherapy plus cetuximab in head and neck cancer. *N Engl J Med*. 2008;359:1116-1127.
24. Burtness B, Harrington KJ, Greil R, et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. *Lancet*. 2019;394:1915-1928. doi:10.1016/S0140-6736(19)32591-7
25. Lee NY, Ferris RL, Psyrri A, et al. Avelumab plus standard-of-care chemoradiotherapy versus chemoradiotherapy alone in patients with locally advanced squamous cell carcinoma of the head and neck: a randomised, double-blind, placebo-controlled, multicentre, phase 3 trial. *Lancet Oncol*. 2021;22:450-462.
26. McBride SM, Sherman EJ, Tsai CJ, et al. A phase II randomized trial of nivolumab with stereotactic body radiotherapy (SBRT) versus nivolumab alone in metastatic (M1) head and neck squamous cell carcinoma (HNSCC). *J Clin Oncol*. 2018;36:6009. doi:10.1200/JCO.2018.36.15_suppl.6009
27. Lauber K, Dunn L. Immunotherapy mythbusters in head and neck cancer: the abscopal effect and pseudoprogression. *Am Soc Clin Oncol Educ Book*. 2019;39:352-363. doi:10.1200/EDBK_238339
28. Ferris RL, Blumenschein G, Fayette J, et al. Nivolumab vs investigator's choice in recurrent or metastatic squamous cell carcinoma of the head and neck: 2-year long-term survival update of CheckMate 141 with analyses by tumor PD-L1 expression. *Oral Oncol*. 2018;81:45-51. doi:10.1016/j.oraloncology.2018.04.008

**How to cite this article:** Sekido K, Imaue S, Tachinami H, et al. Successful treatment with nivolumab in a patient with unresectable oral squamous cell carcinoma following ineffective chemoradiotherapy. *Clin Case Rep*. 2023;11:e8219. doi:10.1002/ccr3.8219