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Open Access Case Report

Sustained Clinical and Metabolic Response to Pembrolizumab-Based Therapy for Suspected Persistent or Recurrent Oral Tongue Squamous Cell Carcinoma After Salvage Surgery: A Case Report

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Review began 07/22/2026
Review ended 10/22/2026
Published 11/02/2026

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DOI: 10.7759/cureus.118992

Abstract

Recurrent oral tongue squamous cell carcinoma (OTSCC) is associated with poor prognosis despite multimodal treatment, and durable responses to immune checkpoint inhibitors remain uncommon. We report the case of a 73-year-old man with a history of pT1N0 moderately differentiated tongue squamous cell carcinoma treated with surgery and adjuvant radiotherapy in 2014 who developed biopsy-confirmed locoregional recurrence after a 10-year disease-free interval. He underwent salvage right partial glossectomy, right selective neck dissection (levels I-IV), and radial forearm free-flap reconstruction. Postoperative clinical and radiological findings raised concern for suspected persistent or recurrent disease, prompting initiation of palliative systemic therapy with pembrolizumab, paclitaxel, and carboplatin. Following an initial partial response, treatment was subsequently continued with pembrolizumab-based therapy, with the addition of low-dose cyclophosphamide from cycle 8 onward. Serial PET/CT imaging demonstrated progressive disease regression, culminating in sustained absence of clinically evident disease and near-complete radiological response after more than 23 cycles of pembrolizumab-based therapy, with no evidence of locoregional or distant disease progression on follow-up. During treatment, the patient developed hypothyroidism requiring gradual escalation of levothyroxine replacement, which was successfully managed without interruption of immunotherapy. This case highlights the potential for sustained disease control with pembrolizumab-based therapy in selected patients with suspected persistent or recurrent OTSCC, despite palliative treatment intent, while emphasising the importance of vigilant recognition and management of endocrine adverse events during extended immunotherapy.

Categories: Radiology, Oncology, Internal Medicine
Keywords: durable complete response, immune checkpoint inhibitor, immune-related hypothyroidism, maintenance therapy, oral immunotherapy, oral tongue squamous cell carcinoma, pembrolizumab, recurrent or metastatic squamous cell carcinoma of the head and neck, salvage surgery

Introduction

Head and neck squamous cell carcinomas (HNSCCs) are a heterogeneous group of malignancies arising from the mucosal epithelium of the oral cavity, pharynx, and larynx. Globally, head and neck cancers continue to represent a substantial public health burden, particularly in low- and middle-income countries, where oral cavity cancers account for a significant proportion of cancer incidence and mortality. In the Indian subcontinent, oral cancer remains one of the most frequently diagnosed malignancies among men and a leading cause of cancer-related death [1].

Oral tongue squamous cell carcinoma (OTSCC) is the most common malignancy of the oral cavity and is characterised by aggressive local invasion, a high risk of locoregional recurrence, and significant functional morbidity affecting speech and swallowing [2]. Although surgery with or without adjuvant radiotherapy remains the cornerstone of treatment for localised disease, management of recurrent OTSCC remains challenging, particularly in patients previously treated with multimodality therapy.

Recent advances in immunotherapy have transformed the treatment landscape of recurrent or metastatic HNSCC. Programmed cell death protein-1 (PD-1) inhibitors, including pembrolizumab, have demonstrated clinically meaningful survival benefits and are now established therapeutic options in recurrent or unresectable disease [3]. Nevertheless, durable complete responses remain uncommon in routine clinical practice, and optimal treatment duration and predictors of long-term benefit remain incompletely understood.

Herein, we report the clinical course of a 73-year-old man with a history of OTSCC who demonstrated sustained clinical improvement and near-complete radiological response on serial ^{18}F-FDG PET/CT following salvage surgery and prolonged pembrolizumab-based systemic therapy exceeding 23 treatment cycles. This case additionally highlights the development and management of treatment-associated hypothyroidism during long-term immunotherapy. The postoperative suspicion of persistent or recurrent disease was not histopathologically confirmed, and the observed response is therefore described in terms of clinical improvement and sustained metabolic disease control rather than a formally established complete response.

Case Presentation

A 73-year-old man from Haryana, India, with a history of OTSCC, presented with locoregional recurrence after previous definitive treatment. His initial diagnosis was made in 2014, when he was found to have a moderately differentiated squamous cell carcinoma of the tongue staged as pT1N0. He underwent surgical resection followed by adjuvant radiotherapy and remained disease-free on follow-up for approximately 10 years. In May 2024, surveillance evaluation raised suspicion of disease recurrence. An ^{18}F-FDG PET/CT scan demonstrated increased metabolic activity in the right tongue, with associated cervical lymph nodal uptake. Subsequent biopsy confirmed recurrent moderately differentiated squamous cell carcinoma of the tongue.

The patient underwent salvage surgery on 31 May 2024 consisting of right partial glossectomy, right selective neck dissection (levels I-IV), and radial artery forearm flap reconstruction. During postoperative follow-up, clinical examination demonstrated induration at the junction of the flap and native tongue with a suspicious submucosal lesion. The neck showed no evidence of disease. Contrast-enhanced magnetic resonance imaging demonstrated diffuse enhancement involving the parapharyngeal space, vallecula, and residual tongue medial to the flap. These findings raised concern for recurrent disease versus postoperative inflammatory changes.

However, histopathological confirmation of postoperative persistent or recurrent disease was not obtained. Serial whole-body ^{18}F-FDG PET maximum intensity projection images demonstrate progressive reduction in metabolic activity from baseline (December 2024) to June and November 2025, with resolution of previously identified cervical nodal uptake and only low-grade residual uptake in the operative bed on subsequent imaging (Figure *1*). Figure *2* illustrates serial fused ^{18}F-FDG PET/CT images of the right oral tongue/parapharyngeal operative bed at baseline (December 2024) and during follow-up (June and November 2025), demonstrating a marked reduction in FDG uptake with treatment and persistent low-grade residual uptake on subsequent imaging. A pretreatment ^{18}F-FDG PET/CT performed in December 2024 demonstrated FDG-avid findings in the right oral tongue/ parapharyngeal operative bed with cervical nodal uptake, serving as the baseline for subsequent response assessment (Figure *1A*; Figure *2A*, *2D*, *2G*). Following multidisciplinary evaluation, the patient and family were counselled regarding the guarded prognosis and palliative treatment intent. Systemic treatment was initiated on December 30, 2024 with pembrolizumab, paclitaxel, and carboplatin administered every three weeks. Given concerns regarding persistent or recurrent disease after salvage surgery and the limited likelihood of cure, palliative systemic therapy was pursued after detailed discussions regarding prognosis, life expectancy, and treatment goals. A

How to cite this article
Chaudhary Y, Mishra A, Khare S, et al. (November 02, 2026) Sustained Clinical and Metabolic Response to Pembrolizumab-Based Therapy for Suspected Persistent or Recurrent Oral Tongue Squamous Cell Carcinoma After Salvage Surgery: A Case Report. Cureus 18(11): e118992. DOI 10.7759/cureus.118992

partial clinical and radiological response was documented on February 10, 2025, following the initial treatment cycles.

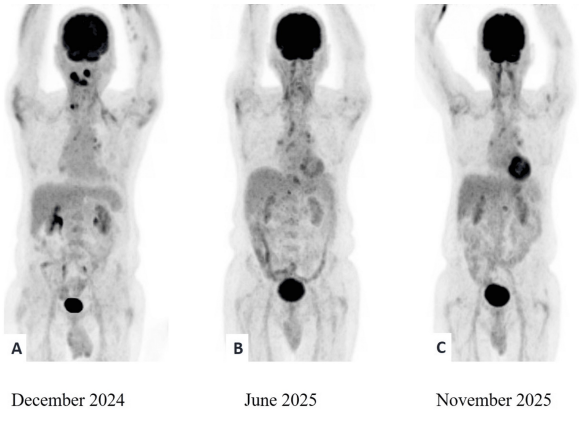


FIGURE 1: Serial whole-body ^{18}F-FDG PET MIP images showing sustained near-complete radiological response

Whole-body ^{18}F-fluorodeoxyglucose (FDG) PET maximum intensity projection (MIP) images. (A) Baseline (December 2024, pre-treatment): FDG-avid disease in the right oral tongue/parapharyngeal operative bed with cervical nodal uptake. (B) June 2025: marked response with resolution of cervical nodal uptake. (C) November 2025: near-complete response, only low-grade residual operative-bed uptake; left upper-abdominal focus is the gastrostomy tube (inflammatory).

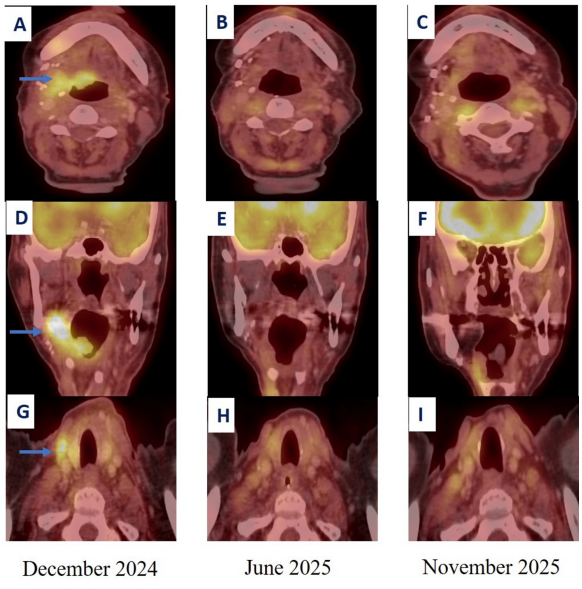


FIGURE 2: Serial fused ^{18}F-FDG PET/CT images of the operative bed showing sustained near-complete radiological response

Fused axial (A–C, G–I) and coronal (D–F) ^{18}F-FDG PET/CT of the right oral tongue/parapharyngeal operative bed: December 2024 (A, D, G), June 2025 (B, E, H), and November 2025 (C, F, I). Baseline: intense operative-bed uptake (blue arrows). June 2025: marked reduction after pembrolizumab-based therapy. November 2025: only low-grade residual uptake, favoured inflammatory, consistent with near-complete response.

During cycle 4, paclitaxel and carboplatin were administered without pembrolizumab. Pembrolizumab was administered in combination with paclitaxel and carboplatin during cycles 5-7. Given the favourable response, treatment was transitioned to maintenance pembrolizumab (200 mg every three weeks) in combination with low-dose cyclophosphamide from cycle 8 onward. The recorded date of cyclophosphamide initiation was May 24, 2025.

PET/CT performed in June 2025 (post-cycle 9) demonstrated interval resolution of previously metabolically active cervical lymph nodes. Mild residual FDG uptake persisted within the operative bed involving the right parapharyngeal space and residual tongue medial to the flap (SUVmax 1.8; delayed SUVmax 4.2), interpreted as post-treatment inflammatory change rather than active malignancy (Figure *1B*; Figures *2B*, *2E*, *2H*). No new metabolically active lesions were identified on response assessment imaging.
The residual uptake was considered potentially attributable to postoperative or post-treatment inflammatory changes; however, active malignancy could not be definitively excluded by imaging alone. Follow-up PET/CT in November 2025 demonstrated stable low-level uptake within the operative bed (SUVmax 2.5) without evidence of new metabolically active locoregional or distant disease. The residual uptake remained low grade and was interpreted as postoperative inflammatory change rather than recurrent malignancy, consistent with sustained complete clinical and near-complete radiological response (Figure *1C*; Figures *2C*, *2F*, *2I*). No abnormal metabolically active disease was identified elsewhere in the body. These findings were consistent with continued disease control and absence of radiologically evident disease progression.

Follow-up PET/CT on November 22, 2025, demonstrated stable low-level uptake within the operative bed (SUVmax 2.5), without evidence of new metabolically active locoregional or distant disease (Figure *1C*; Figures *2C*, *2F*, *2I*). The residual uptake was favoured to represent postoperative or post-treatment inflammatory change, although this interpretation was not histopathologically confirmed. Overall, serial imaging demonstrated sustained metabolic disease control and a near-complete radiological response rather than a formally established complete response, as standardised RECIST-based response measurements were

unavailable. No new metabolically active disease was identified elsewhere in the body.

A subsequent PET/CT was performed on July 25, 2026. The findings of this scan should be incorporated into the description of the most recent imaging assessment to estal

The patient continued pembrolizumab-based treatment and received more than 23 cycles. Serial oncology assessments documented ongoing disease control throughout treatment, and response assessment following 16 cycles reported a sustained near-complete response on PET/CT evaluation. At the most recent documented imaging assessment, the disease status should be described according to the July 25, 2026 PET/CT findings. The date of the most recent clinical assessment, its findings, and the corresponding disease status should be specified where documented.

During treatment, the patient developed hypothyroidism requiring progressive escalation of levothyroxine replacement therapy. The daily dose increased from 50 µg to 75 up. Thyroid hormone replacement was continued with ongoing clinical and biochemical monitoring. Despite this endocrine toxicity, treatment was not interrupted, and sustained clinical disease control was documented during the available follow-up.

Discussion

This case describes a 73-year-old man with a history of OTSCC who demonstrated sustained clinical improvement and near-complete radiological response on serial PET/CT following salvage surgery and pembrolizumab-based systemic therapy. Although postoperative findings raised concern for persistent or recurrent disease, histopathological confirmation was not obtained. The observed outcome is therefore best described as sustained clinical and metabolic disease control rather than a definitively established complete response. The patient continued treatment for more than 23 cycles, with ongoing disease control documented during follow-up.

OTSCC is the most common malignancy of the oral cavity and is associated with a significant risk of locoregional recurrence despite definitive treatment [2]. Management of recurrent disease remains challenging, particularly in patients who have previously undergone surgery and radiotherapy. Although salvage surgery remains an important treatment modality for resectable recurrence, long-term disease control is often difficult to achieve.

Immune checkpoint inhibitors targeting the PD-1 pathway have become established therapeutic options in recurrent or metastatic HNSCC [3]. The clinical benefit of PD-1 inhibition in recurrent HNSCC has been demonstrated in landmark phase III trials. In the KEYNOTE-040 study, pembrolizumab improved overall survival compared with investigator's choice chemotherapy in previously treated recurrent or metastatic HNSCC, while also demonstrating a favourable safety profile [4]. Similarly, the CheckMate-141 trial demonstrated a significant overall survival benefit with nivolumab in patients with platinum-refractory recurrent or metastatic HNSCC [5]. The subsequent KEYNOTE-048 trial further established pembrolizumab, either as monotherapy or in combination with platinum-based chemotherapy and fluorouracil, as a standard first-line treatment option for recurrent or metastatic HNSCC and contributed to its incorporation into international treatment guidelines [6]. However, the chemotherapy regimen used in the present case differed from the pembrolizumab-platinum-fluorouracil regimen evaluated in KEYNOTE-048, as this patient received paclitaxel and carboplatin with pembrolizumab during most of the induction phase. Accordingly, evidence from KEYNOTE-048 should not be regarded as direct evidence for the exact regimen administered in this case.

Pembrolizumab restores antitumour immune activity by blocking PD-1-mediated inhibition of T lymphocytes, thereby enhancing immune recognition of malignant cells. In the present case, pembrolizumab was administered with paclitaxel and carboplatin during the initial treatment phase, with pembrolizumab omitted during cycle 4 and administered again with chemotherapy during cycles 5-7. A partial clinical and radiological response was documented on February 10, 2025. From cycle 8 onward, treatment consisted of pembrolizumab with low-dose cyclophosphamide. Subsequent PET/CT examinations demonstrated resolution of previously metabolically active cervical lymph nodes and persistent low-grade uptake in the operative bed, without new metabolically active lesions at the reported assessment time points. The optimal duration of PD-1 inhibitor therapy in HNSCC remains uncertain. Although treatment duration in clinical trials is generally protocol-defined, decisions regarding continuation in routine practice are individualized according to response, toxicity, and patient preference. The duration of treatment in this case should be interpreted in context: more than 23 cycles administered at three-week intervals corresponds to approximately 16 months, and treatment duration alone does not establish an exceptional outcome. The more relevant observation is the sustained clinical and metabolic disease control documented during follow-up.

Durable complete responses to immune checkpoint inhibitors in HNSCC remain relatively uncommon. Adibi et al. reported a durable radiological and molecular complete response following nivolumab therapy in a patient with recurrent HNSCC, highlighting the potential for sustained disease control in selected individuals receiving immunotherapy [7]. The present case similarly illustrates sustained disease control during pembrolizumab-based treatment; however, direct comparison with a formally documented complete response is limited because postoperative persistent or recurrent disease was not histopathologically confirmed and formal RECIST-based response measurements were unavailable. Although conclusions cannot be drawn from individual cases, these observations support the possibility that a subset of patients may derive long-term benefit from immune checkpoint inhibition.

Long-term follow-up of the CheckMate-141 trial further demonstrated that a subset of patients experienced durable survival beyond two years, supporting the concept that prolonged disease control can occur in selected responders receiving immune checkpoint blockade [8]. In our patient, serial PET/CT demonstrated a sustained near-complete radiological response, with residual low-grade operative-bed uptake and no new metabolically active disease at the reported assessment time points. These findings support continued metabolic disease control but do not establish complete tumour eradication. The contribution of low-dose cyclophosphamide to the observed outcome cannot be determined from this single case. Although cyclophosphamide has been investigated as an immunomodulatory agent capable of influencing regulatory T-cell activity, this biological rationale does not establish clinical efficacy for pembrolizumab-cyclophosphamide maintenance in HNSCC. The relative contributions of salvage surgery, chemotherapy, pembrolizumab, and cyclophosphamide to the patient's favourable outcome cannot be independently assessed [9].

Immune-related endocrine adverse events are increasingly recognised during anti-PD-1 therapy. During treatment, our patient developed hypothyroidism requiring progressive escalation of levothyroxine replacement therapy. Thyroid dysfunction represents a recognised endocrine toxicity associated with pembrolizumab therapy [10,11]. Early recognition and appropriate hormone replacement are important because these adverse events can often be managed without discontinuation of treatment. In the present case, hypothyroidism was managed with thyroid hormone replacement, allowing systemic treatment to continue. However, baseline thyroid function, serial thyroid hormone measurements, and the precise onset of dysfunction were unavailable; therefore, a definitive causal attribution to pembrolizumab cannot be established from the available information. Emerging evidence has suggested a potential association between immune-related endocrine adverse events and improved oncological outcomes in patients receiving immune checkpoint inhibitors; however, this relationship remains incompletely understood and cannot be established from an individual case [12]. Evidence derived from other tumour types should not be interpreted as demonstrating that hypothyroidism predicts a favourable response in OTSCC.

Several limitations should be acknowledged. This report describes a single patient and therefore cannot establish treatment efficacy or generalisability. PD-L1 expression status and other predictive biomarkers were unavailable, limiting assessment of factors potentially associated with response. Formal RECIST-based response measurements were not available, preventing standardized categorization of the observed radiological response. In addition, although postoperative clinical and radiological findings raised concern for persistent or recurrent disease and prompted systemic treatment, histopathological confirmation of postoperative persistent or recurrent disease was not obtained. The low-grade residual operative-bed uptake was considered potentially inflammatory, but this interpretation was not histopathologically confirmed. Furthermore, the individual contributions of salvage surgery, chemotherapy, pembrolizumab, and

cyclophosphamide cannot be separated. These limitations should be considered when interpreting the observed clinical outcome. This case illustrates sustained clinical improvement and metabolic disease control during pembrolizumab-based systemic therapy, together with the management of hypothyroidism during continued treatment. Further studies are required to better define predictors of durable response and optimal treatment duration in patients receiving immune checkpoint inhibitors for recurrent HNSCC.

Conclusions

This case illustrates a favourable and sustained clinical and metabolic response in a patient with suspected persistent or recurrent OTSCC after salvage surgery who received pembrolizumab-based systemic therapy. The observed outcome should be interpreted cautiously because postoperative persistent or recurrent disease was not histopathologically confirmed, formal RECIST-based response measurements were unavailable, and the individual contributions of surgery, chemotherapy, pembrolizumab, and cyclophosphamide cannot be separated. The case highlights the potential for sustained disease control in selected patients and the importance of monitoring and managing treatment-related endocrine dysfunction during immunotherapy.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

The authors sincerely acknowledge Yashika Batra for her constant encouragement, patience, and unwavering support throughout the preparation of this manuscript. Her motivation and belief in this work were deeply appreciated.

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