

Case Report

Successful Treatment of Refractory Squamous Cell Cancer of the Head and Neck with Nivolumab and Ipilimumab

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Keywords

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Abstract

Treatment options for patients with platinum-refractory, recurrent, metastatic head and neck squamous cell carcinoma (HNSCC) are limited, and prognosis is poor. Nivolumab (Opdivo) has been approved by the US Food and Drug Administration (FDA) for the treatment of patients with recurrent or metastatic HNSCC who have disease progression on or after platinum-based therapy. Recently, in patients with metastatic malignant melanoma a significant improvement of outcome and response was achieved with the combination of ipilimumab (CTLA4 antibody) and the programmed death (PD)-1 inhibitor nivolumab compared with monotherapy. Based on these results, the combination of nivolumab and ipilimumab has been approved by the FDA for the treatment of patients with unresectable or metastatic melanoma. So far, there have been no data concerning the combination of nivolumab and ipilimumab in squamous cell head and neck cancer. We here present the case of a 46-year-old male with refractory squamous cell head and neck cancer, who was successfully treated with the PD-1 inhibitor nivolumab in combination with the anti-CTLA4 antibody ipilimumab.

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Introduction

Squamous cell carcinoma of the head and neck accounts for 90% of all cases of carcinoma of the head and neck [1].

Treatment options for patients with platinum-refractory, recurrent, metastatic head and neck squamous cell carcinoma (HNSCC) are limited, and prognosis is poor. The recent CheckMate 141 clinical trial demonstrated that nivolumab, an anti-programmed cell death protein 1 monoclonal antibody, was efficacious in extending the median overall survival in this patient population compared with standard therapies [2]. Based on these data, nivolumab (Opdivo) has been approved by the US Food and Drug Administration (FDA) for the treatment of patients with recurrent or metastatic HNSCC who have disease progression on or after platinum-based therapy [3]. Recently, data of the checkmate 069 study have shown significant improvements in objective response and prolonged progression-free survival with the combination of nivolumab plus ipilimumab compared with ipilimumab alone in patients with metastatic malignant melanoma [4].

Based on these results, the combination of nivolumab and ipilimumab has been approved by the FDA for the treatment of patients with unresectable or metastatic melanoma. So far, there have been no data concerning the combination of nivolumab and ipilimumab in squamous cell head and neck cancer.

Case Report

We present the case of a 46-year-old male with refractory squamous cell head and neck cancer, who was successfully treated with the programmed death (PD)-1 inhibitor nivolumab in combination with the anti-CTLA4 antibody ipilimumab. In December 2016, a low differentiated squamous cancer of the tongue pT1,pN2b, L1,V0, G3 was diagnosed. There was no sign of human papilloma virus infection. After R0 resection and neck dissection, he underwent adjuvant radiochemotherapy with cisplatin 35 mg/m² weekly.

In April 2016, a CT scan of the neck showed significant cervical lymph node enlargement. A biopsy confirmed a lymph node metastasis of a squamous cell carcinoma due to the previous cancer. There were no signs of further metastases. The tumor was surgically not resectable, so the intensification of systemic chemotherapy was performed with 5-FU, cisplatin, and cetuximab. A CT scan after two cycles revealed an unsatisfying response with stable disease (Fig. 1a).

The tumor was positive for PD ligand 1 (PD-L1) expression and due to the lack of other treatment options, a therapy with nivolumab (3 mg/kg body weight every 2 weeks) and ipilimumab (1 mg/kg every 6 weeks) was initiated in July 2016. Of note, the patient had a long history of juvenile idiopathic polyarthritis accompanied by unclassified autoimmune hepatitis. Ten days after start of therapy, an increase in rheumatoid factor and liver enzymes was detected. The MRI of the liver showed no pathologic findings, and the hepatitis serology was negative.

Because of a suspected underlying immuno-induced hepatitis, therapy with prednisolone was initiated (100 mg/day), and liver parameters decreased significantly. Nevertheless, administration of ipilimumab and nivolumab was continued, and 3 weeks after the second administration of ipilimumab, rheumatoid factor and liver enzymes increased but decreased again after restart of prednisolone 100 mg/day. A CT scan 8 weeks after start of therapy

showed a significant regression of tumor size, and 4 months after start of therapy in November 2016 (Fig. 1b), a nearly complete remission was achieved (Fig. 1c).

In January 2017, MRI showed signs of local relapse. Histology confirmed an infiltration of the known carcinoma. Thus, therapy with heavy ion radiation was initiated, and nivolumab monotherapy was continued. Follow-up with MRI in June 2017 showed stable disease.

Soluble PD-L1 and PD-L2 serum levels were evaluated before and during the treatment using a commercially available ELISA (R&D Systems), showing a significant decrease in serum PD-L1 due to the response to the therapy, followed by an increase at the time of progression. There was no change in PD-L2 serum levels corresponding to response or progression to therapy.

Considering tumor biopsies, there was no change in PD-L1 or HLA class I expression during therapy. Of note, during therapy, no significant changes in white blood cells, B/T cells, T-helper cells, cytotoxic and regulatory T lymphocytes, NK cells, as well as myeloid-derived suppressor cells were detected.

Discussion

To our knowledge, this is the first case report showing a clinically meaningful response to nivolumab in combination with ipilimumab of a refractory metastatic squamous cancer of the head and neck. However, the above strategy, due to very high toxicity, has limitations for use in all patients [5, 6]. In our patient, despite the history of autoimmune hepatitis and juvenile polyarthritis, the treatment-induced elevation of liver enzymes was reversible under corticosteroids, and other side effects were moderate.

We observed that soluble PD-L1 serum levels decreased under response to therapy and increased at time of progression under treatment, while soluble PD-L2 serum levels stayed stable. Further studies are required to examine the value of soluble PD-L1 serum levels as a predictive marker of the response to immunotherapy.

In our patient treated with the combination of nivolumab and ipilimumab, a complete remission after 4 months of therapy was achieved with moderate and reversible side effects. So, the combination of nivolumab and ipilimumab could be a promising option in refractory metastatic squamous cell cancer of the head and neck [7]. There are several trials underway comparing the efficacy of immuno-oncology approaches with standard chemotherapy, and we are eagerly awaiting the results.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

None.

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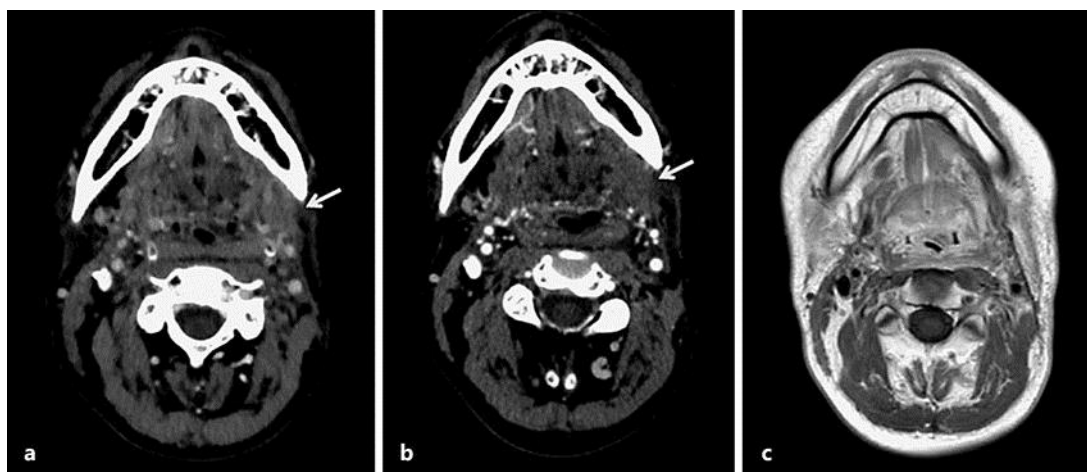


Fig. 1. CT before therapy (a), CT after 8 weeks of therapy (b), and MRI 4 months after start of therapy (c). Arrows show tumor manifestation.