

# Lenvatinib Can Overcome Immune Resistance in Head and Neck Cancer and Achieve Durable Remission

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South Asian J Cancer



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Squamous cell carcinoma head and neck is the sixth most common cancer worldwide and.<sup>1</sup> Multimodality therapies have been advocated for locoregional relapse or metastatic disease.<sup>2</sup> Combination therapy with lenvatinib has been considered to overcome resistance and improve the efficacy.<sup>3</sup> In a recent study of lenvatinib and pembrolizumab conducted in heavily pretreated recurrent and metastatic head and neck cancer, the median overall survival OS was 6.2 months, and the median progression-free survival (PFS) was 4.6 months.<sup>4</sup>

This combination is currently undergoing study in LEAP-010.<sup>5</sup> Herein, we report a case of heavily pretreated metastatic head and neck cancer in a patient who was treated with a combination of lenvatinib with pembrolizumab.

## Case

A 59-year-old male patient was diagnosed with metastatic carcinoma larynx in 2018. Initial clinical stage was T4aN1M1, poorly differentiated squamous cell carcinoma larynx, p16

**Table 1** List of systemic therapies undergone by the patient with best response and progression-free survival

Duration	Line of therapy	Protocol	Best response (RECIST)	Progression-free survival
December 2018-September 2019	1st line	Paclitaxel + cisplatin + cetuximab followed by cetuximab maintenance	SD	9 Months
September-November 2019	2nd line	Pembrolizumab 200 MG I/V Q 3 weekly	PD	3 Months
November 2019-February 2020	3rd line	Erlotinib + celecoxib + methotrexate	PD	3 Months
February 2020-June 2020	4th line	Capecitabine + carboplatin followed by capecitabine maintenance	PR	5 Months
August 2020-March 2021	Rechallenge	Nanoparticle paclitaxel Q 3 weekly	Mixed response	8 Months
April 2021-June 2021	5th line	Gemcitabine + cetuximab	PD	3 Months
July 2021-October 2021	6th line	Afatinib	PD	4 Months
November 2021-August 2022	7th line	Lenvatinib + pembrolizumab	PR	10 Months

Abbreviations: PD, progressive disease; PR, partial response; SD, stable disease.

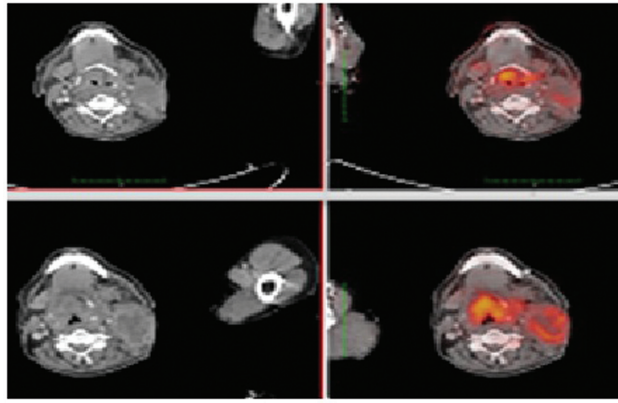
DOI <https://doi.org/10.1055/s-0043-1762939> ISSN 2278-330X

**How to cite this article:** Suri O, Gupta VG. Lenvatinib Can Overcome Immune Resistance in Head and Neck Cancer and Achieve Durable Remission. South Asian J Cancer 2023;00(00):00-00.

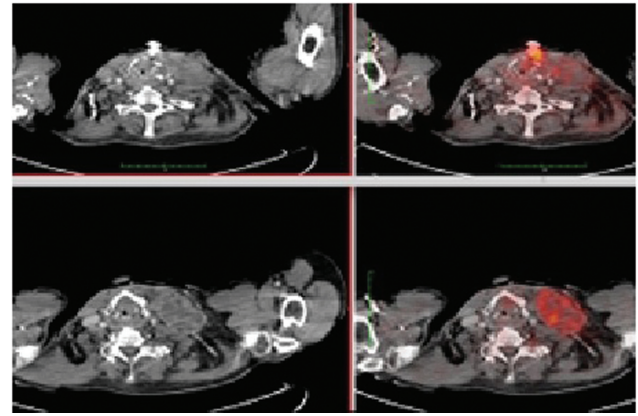
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**Fig. 1** Before lenvatinib + pembrolizumab combination therapy.



**Fig. 2** Ten months after lenvatinib + pembrolizumab combination therapy.

negative. PET-CT was suggestive of metastatic disease. He received multiple lines of therapy as mentioned in **Table 1**. Notably, the patient received second-line therapy with single-agent pembrolizumab to which the disease was refractory, followed by multiple lines of therapy. In view of no clinical trials in India, the patient was started on pembrolizumab 200 mg every 3 weeks in combination with lenvatinib 10 mg daily (PD-L1 testing was not done). The major treatment-related adverse events included Grade II hand foot skin reactions. Post 6 weeks, the patient showed clinical response. PET-CT images of the tumor before and after treatment are shown in **Figs. 1** and **2**. The patient remained in clinical remission until September 2022.

## Discussion

In this case report, we provide strong evidence assuring significant responses of pembrolizumab/lenvatinib combination therapy in heavily pretreated recurrent/metastatic HNSCC even after progression on previous anti-PD-1 therapy. This represents a non-toxic and convenient combination for the management of heavily pretreated recurrent/metastatic HNSCC and the patients who had failed anti-PD-1 therapy. This combination deserves further exploration in prospective studies.

## Conflict of Interest

None declared.

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