


CASE REPORT

Anti-PD-1 therapy using cemiplimab for advanced cutaneous squamous cell carcinoma in HIV patient: A case report

Abdurahman Alloghbi¹  | James Ninia² | Bayan Alshare¹ | Jeffrey Hotaling³ | Syed Raza³ | Ammar Sukari¹

¹Department of Oncology, Karmanos Cancer Institute, Wayne State University, Detroit, Michigan, USA

²School of Medicine, Wayne State University, Detroit, Michigan, USA

³Department of Surgical Oncology, Karmanos Cancer Institute, Detroit, Michigan, USA

Correspondence

Abdurahman Alloghbi, Department of Oncology, Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA.

Email: alloghba@karmanos.org

Funding information

This case report received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Abstract

This is a case of a 60-year-old man living with HIV who presented with advanced cutaneous squamous cell carcinoma. After workup, medical and surgical treatment, and disease recurrence, he achieved a complete response with no unexpected toxicities after immunotherapy with cemiplimab.

KEYWORDS

advanced cutaneous squamous cell carcinoma, cemiplimab, immunotherapy, skin cancer, squamous cell carcinoma

1 | INTRODUCTION

Over the past few years, there have been significant advances in cancer immunotherapy.¹ Many of the cancer immunotherapy agents currently approved for use are immune checkpoint inhibitors (ICIs) that target the programmed cell death-1/programmed cell death ligand pathway (PD-1/PD-L1), expressed on T cells and different tissue normal cells, consecutively. One such immunotherapy agent is cemiplimab, a monoclonal antibody targeting PD-1, which is significant as the first FDA-approved systemic therapy for advanced cutaneous squamous cell

carcinoma (CSCC).² Prospective data supported the use of cemiplimab in CSCC patients, including one study across two open-label clinical trials which found that the objective response rate of cemiplimab therapy in patients with metastatic or locally advanced CSCC was 47%.² However, data supporting the use of cemiplimab and similar agents in cancer patients with concomitant human immunodeficiency virus (HIV) infection are scant, as cancer patients living with HIV are often excluded from prospective clinical trials due to concerns about the safety of these novel agents in patients with HIV. Here, we report a case of CSCC in a patient with HIV, controlled with highly active

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2021 The Authors. *Clinical Case Reports* published by John Wiley & Sons Ltd.

antiretroviral therapy (HAART), who tolerated and responded to systemic therapy with cemiplimab. Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy on the title page of the manuscript.

2 | CASE REPORT

We report the case of a 60-year-old man with CSCC, and a past medical history of HIV diagnosed ten years prior to cancer diagnosis and controlled with HAART.

He first presented in early 2018 with a right-sided neck mass. At the time, he was diagnosed with cutaneous squamous cell carcinoma of the neck and was treated with Mohs surgery with subsequent reconstruction in February 2018. A few months later, the patient noticed swelling in his right neck at the median surgical margin. As the swelling progressed, the patient underwent a CT scan of the head and neck in June 2018, which revealed a right-sided cervical heterogeneous mass measuring approximately $4 \times 2.5 \times 2$ cm.

On June 30, 2018, the patient underwent wide local excision of the lesion, modified radical neck dissection, right superficial parotidectomy, and left anterolateral thigh-free flap reconstruction. Pathology demonstrated seven out of 34 lymph nodes were positive for metastatic SCC. The largest node was at level 2b and measured 10 mm with extracapsular extension. Due to the extracapsular extension, at this juncture the patient went on to receive treatment with chemoradiation.

The patient started one cycle of cisplatin on August 14, 2018, with concurrent radiotherapy (CRT) at a dose of 6600cGy in 33 fractions. Due to acute kidney injury, cisplatin was replaced with carboplatin. He received a total of 3 cycles of platinum-based CRT, which concluded on September 24, 2018. In May 2019, the patient presented with a mid-neck subcutaneous mass. FNA biopsy showed SCC, consist with dermal metastasis of CSCC. In light of these findings, he was started on cemiplimab on July 2, 2019.

The patient has since received all 33 total planned cycles of cemiplimab. Cycle 14 of cemiplimab was delayed due to the start of the COVID-19 pandemic, but immunotherapy was resumed promptly thereafter. The final cycle of cemiplimab was administered in June 2021. Clinically, he has had a complete response (CR) with no radiologic evidence of disease first reported on neck MRI and CT scans in late August 2019 (NI-RADS 1). An MRI of the neck and a CT scan of the thorax from June 2021 both revealed no evidence of recurrent CSCC or suspicious lymph nodes, along with expected postsurgical and post-radiation changes.

3 | DISCUSSION

To our knowledge, this is the first reported case of a CSCC patient with HIV responding to anti-PD-1 treatment with cemiplimab and tolerating it with no severe adverse effect (SAE). He achieved a complete remission (CR) and has had a significant duration of response with no evidence of disease on regular follow-up imaging. A CR was achieved by only 4 out of the 85 participants in the aforementioned study of cemiplimab in patients with metastatic or locally advanced CSCC.²

However, robust prospective data supporting the use of cemiplimab in CSCC patients with HIV do not exist. In fact, prospective data supporting the use of any ICI against PD-1/PD-L1 as cancer immunotherapy in any cancer patients living with HIV are scant.³ This is especially significant when one considers the fact that cancer is a leading cause of morbidity and mortality for the approximately 38 million people living with HIV around the globe.⁴⁻⁷ A recent small open-label phase one trial of pembrolizumab in HIV patients with different malignancies found it safe to be used in cancer patients with HIV (NCT02595866); however, the generalizability of this study is limited by its small sample size and lack of randomization.⁸ There is a clear need for future prospective trials to assess both the safety and efficacy of ICIs in cancer patients living with HIV.

However, this case report can be added to a growing body of retrospective studies and case reports, suggesting that ICIs such as cemiplimab and pembrolizumab may be both safe and effective for HIV-positive cancer patients. Due to the mechanism of action of anti-PD-1 antibodies like cemiplimab, it has been theorized that treatment with these agents in cancer patients living with HIV may enhance both the anti-tumor and anti-viral activities of their immune system.⁹ Immune checkpoints like PD-1 function as inhibitory receptors. Their immunosuppressive effects are mediated by binding to ligands such as PD-L1, a ligand expressed on healthy human cells but that is sometimes upregulated by cancer cells.¹⁰⁻¹³ The interaction of PD-1 with its ligand is an important immune checkpoint in healthy individuals, preventing persistent immune activation by native tissues and therefore autoimmune disease. However, in patients with chronic viral infections like HIV or in patients with cancer, the upregulation of checkpoint inhibitors including PD-1 on T cells or its ligand on cancer cells inhibits the physiologic anti-tumor and anti-viral responses of the human immune system.¹³⁻¹⁵ While the anti-tumoral activity of anti-PD-1 antibodies is a well-studied phenomenon, data on the potential anti-viral effects of these biologics are scarcer. We found another case report of an HIV-positive patient with non-small cell lung carcinoma whose HIV viral reservoir decreased while receiving treatment with an anti-PD-1 antibody called nivolumab.¹⁶

Over the past several years, ICIs targeting PD-1/PD-L1 have accumulated many FDA approvals as a treatment option for advanced solid tumors, with data supporting their use in various malignancies including non-small cell lung cancer^{17,18} and Merkel cell carcinoma.¹⁹ The recent approval of cemiplimab for advanced CSCC represents another novel oncologic application of anti-PD-1 therapy.²

Moreover, existing data, while limited, appear to indicate that cancer patients living with HIV similarly tolerate treatment with PD-1 blockade when compared to cancer patients without HIV. The patient presented herein experienced no unexpected toxicities. Additionally, the patient who received nivolumab in the aforementioned case report also experienced no unexpected toxicities.¹⁶ Moreover, the previously discussed prospective study assessing the safety of pembrolizumab in this population (NCT02595866) found an acceptable safety profile in cancer patients living with HIV who were being treated with antiretroviral therapy and who had CD4+ T-cell counts over 100 cells/ μ l.⁸ In the future, similar prospective studies with other anti-PD-1 antibodies such as nivolumab and cemiplimab would be welcome additions to the safety literature surrounding this class of biologics.

4 | CONCLUSION

This case provides additional evidence that PD-1 blockade may be a promising avenue worth pursuing in the management of certain malignancies in cancer patients living with HIV. Further prospective studies are required to evaluate the safety and efficacy of cemiplimab, and other anti-PD-1 antibodies, in cancer patients living with HIV.

ACKNOWLEDGMENT

None.

CONFLICTS OF INTEREST

None.

AUTHOR CONTRIBUTION

A.A, J.N, B.A, J.H, S.R, and A.S involved in report conception and design, analysis and interpretation of results, and draft manuscript preparation. A.A and J.N collected the data. All authors reviewed the results and approved the final version of the manuscript.

ETHICS APPROVAL

Not applicable.

CONSENT

Published with written consent of the patient.

DATA AVAILABILITY STATEMENT

All data underlying the results are available as part of the article, and no additional source data are required.

ORCID

Abdurahman Alloghbi  <https://orcid.org/0000-0002-1620-7853>

REFERENCES

- Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. *Nat Rev Cancer*. 2012;12(4):252-264. doi:10.1038/nrc3239
- Migden MR, Rischin D, Schmults CD, et al. PD-1 Blockade with cemiplimab in advanced cutaneous squamous-cell carcinoma. *N Engl J Med*. 2018;379(4):341-351. doi:10.1056/nejmoa1805131
- Haanen JBAG, Robert C. Immune checkpoint inhibitors. *Prog Tumor Res*. 2015. doi:10.1159/000437178
- Morlat P, Roussillon C, Henard S, et al. Causes of death among HIV-infected patients in France in 2010 (national survey): trends since 2000. *Aids*. 2014;28(8):1181-1191. doi:10.1097/QAD.0000000000000222
- Reddy KP, Kong CY, Hyle EP, et al. Lung cancer mortality associated with smoking and smoking cessation among people living with HIV in the United States. *JAMA Intern Med*. 2017;177(11):1613-1621. doi:10.1001/jamainternmed.2017.4349
- Bonnet F, Burty C, Lewden C, et al. Changes in cancer mortality among HIV-infected patients: the Mortalité 2005 survey. *Clin Infect Dis*. 2009;48(5):633-639. doi:10.1086/596766
- Vandenhende M-A, Roussillon C, Henard S, et al. Cancer-related causes of death among HIV-infected patients in France in 2010: evolution since 2000. *PLoS One*. 2015;10(6):1-12. doi:10.1371/journal.pone.0129550
- Uldrick TS, Gonçalves PH, Abdul-Hay M, et al. Assessment of the safety of pembrolizumab in patients with HIV and advanced cancer—a phase 1 study. *JAMA Oncol*. 2019;5(9):1332-1339. doi:10.1001/jamaoncol.2019.2244
- Wykes MN, Lewin SR. Immune checkpoint blockade in infectious diseases. *Nat Rev Immunol*. 2018;18(2):91-104. doi:10.1038/nri.2017.112
- Wherry EJ, Kurachi M. Molecular and cellular insights into T cell exhaustion. *Nat Rev Immunol*. 2015;15(8):486-499. doi:10.1038/nri3862
- Vlahopoulos SA. Aberrant control of NF- κ B in cancer permits transcriptional and phenotypic plasticity, to curtail dependence on host tissue: molecular mode. *Cancer Biol Med*. 2017;14(3):254-270. doi:10.20892/j.issn.2095-3941.2017.0029
- Jian H, Fangrong S, Haitao H, Chunhua L, Guangbo Z. Th1high in tumor microenvironment is an indicator of poor prognosis for patients with NSCLC. *Oncotarget*. 2017;8(8):13116-13125. doi:10.18632/oncotarget.14471
- Chen S, Crabill GA, Pritchard TS, et al. Mechanisms regulating PD-L1 expression on tumor and immune cells. *J Immunother Cancer*. 2019;7(1):1-12. doi:10.1186/s40425-019-0770-2
- Barber DL, Wherry EJ, Masopust D, et al. Restoring function in exhausted CD8 T cells during chronic viral infection. *Nature*. 2006;439(7077):682-687. doi:10.1038/nature04444

15. Moskophidis D, Lechner F, Pircher H, Zinkernagel RM. Virus persistence in acutely infected immunocompetent mice by exhaustion of antiviral cytotoxic effector T cells. *Nature*. 1993;362(6422):758-761. doi:10.1038/362758a0
16. Guihot A, Marcelin A-G, Massiani M-A, et al. Drastic decrease of the HIV reservoir in a patient treated with nivolumab for lung cancer. *Ann Oncol*. 2018;29(2):517-518. doi:10.1093/annonc/mdx696
17. Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus chemotherapy for PD-L1-Positive non-small-cell lung cancer. *N Engl J Med*. 2016;375(19):1823-1833. doi:10.1056/nejmoa1606774
18. Herbst RS, Baas P, Kim D-W, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet*. 2016;387(10027):1540-1550. doi:10.1016/S0140-6736(15)01281-7
19. Nghiem PT, Bhatia S, Lipson EJ, et al. PD-1 blockade with pembrolizumab in advanced Merkel-cell carcinoma. *N Engl J Med*. 2016;374(26):2542-2552. doi:10.1056/nejmoa1603702

How to cite this article: Alloghbi A, Ninia J, Alshare B, Hotaling J, Raza S, Sukari A. Anti-PD-1 therapy using cemiplimab for advanced cutaneous squamous cell carcinoma in HIV patient: A case report. *Clin Case Rep*. 2021;9:e05228. doi:[10.1002/ccr3.5228](https://doi.org/10.1002/ccr3.5228)