


# Cemiplimab for Locally Advanced Cutaneous Squamous Cell Carcinoma: A Case Series of 3 Unique Scenarios

Journal of Investigative Medicine High Impact Case Reports  
Volume 10: 1–4  
© 2022 American Federation for Medical Research  
DOI: 10.1177/23247096221121408  
journals.sagepub.com/home/hic  


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## Abstract

Cemiplimab, a monoclonal antibody directed against programmed death receptor 1 (PD-1), has shown promising results in cutaneous squamous cell carcinoma (cSCC). In a nonrandomized trial where cemiplimab 3 mg/kg was given every 2 weeks for up to 96 weeks, a 44% response rate was noted. This case series discusses 3 unique scenarios of patients with advanced cSCC treated with cemiplimab. The first case is of an end stage kidney disease (ESKD) patient with failed living donor kidney transplant who had developed recurrent cSCC despite several excisions and topical 5-fluorouracil and acitretin therapy. He received 8 cycles of cemiplimab leading to resolution. This case serves as an example of the safety and efficacy of cemiplimab in a complex patient who is a kidney transplant recipient on hemodialysis. The second case describes an elderly gentleman with inoperable cSCC initially treated with radiotherapy who later received 9 cycles of cemiplimab for recurrent metastatic disease with excellent response. This case supports the safe and effective use of cemiplimab in an elderly patient. In the third case, cSCC presented itself as a large fungating mass that would have otherwise necessitated limb amputation and was successfully treated with 18 cycles of cemiplimab. This case highlights the dramatic response to cemiplimab obviating the need for surgical intervention and resulting in limb salvage.

## Keywords

cemiplimab, cutaneous squamous cell carcinoma, cSCC, programmed death receptor 1, PD-1, immunotherapy

## Introduction

Cutaneous squamous cell carcinoma (cSCC) accounts for approximately 20% of nonmelanoma skin cancers and is the second most common type of skin malignancy in the United States, after basal cell carcinoma (BCC).<sup>1-3</sup> The incidence of cSCC has increased over the past 20 years in the United States, although no clear cause for this rise has been suggested. Some proposed reasons are increase in tanning bed use, aging population, and higher levels of exposure to the sun. Another common cause for cSCC is long-term immunosuppression, for example, HIV infection, long-term steroid use, and solid organ transplantation.<sup>4,5</sup> The incidence of cSCC is known to increase with duration and degree of immunosuppression and sun exposure preceding or following solid organ transplantation. Due to increased surveillance, high-risk lesions are identified more frequently, for which surgery is typically the standard of care. When surgical intervention is not possible or contraindicated, radiation therapy and systemic therapy such as cisplatin and epidermal growth factor receptor inhibitors like cetuximab are used often with poor outcomes.<sup>6</sup>

Recently, the role of cemiplimab, a monoclonal antibody directed against programmed death receptor 1 (PD-1), has been investigated. An open label, multicenter, phase 1 study of cemiplimab for expansion cohorts of patients with locally advanced or metastatic cSCC as well as a nonrandomized, global phase 2 study for a cohort of patients with metastatic disease demonstrated that cemiplimab (3 mg/kg of body weight, administered over 30 minutes every 2 weeks with duration of treatment up to 96 weeks or until the patient had disease progression or unacceptable toxic effects) induced a response in approximately half the patients.<sup>7</sup> These results were pivotal as no uniformly accepted standard of care for nonsurgical management of cSCC was available prior to

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Received June 6, 2022. Revised July 23, 2022. Accepted August 7, 2022.

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cemiplimab. We present a case series involving 3 unique patients with advanced cSCC treated with cemiplimab.

## Case Series

The first patient is a 54-year-old male with end stage kidney disease (ESKD) who received a living donor kidney transplant in his adolescent years, which eventually failed necessitating hemodialysis (HD) 3 times a week. He developed cSCC with diffuse involvement of hands, arms, and scalp, while receiving immunosuppressive therapy. He was initially treated with local excisions and topical 5-fluorouracil and acitretin. He had multiple recurrences despite local therapy and discontinuation of immunosuppressive agents. He was deemed a poor candidate for further surgical excisions or radiotherapy due to the extensive nature of his lesions. He was referred to medical oncology for consideration of systemic therapy. After explaining potential benefits and risks of cemiplimab, he was started on full-dose (350 mg every 3 weeks). After 3 cycles, he developed significant fatigue. Hence, subsequent cycles were dose reduced to 280 mg every 3 weeks. He tolerated the new dose extremely well with excellent response and resolution of his lesions after 8 cycles of cemiplimab. He has been on surveillance since then with plans of resuming treatment should there be a recurrence.

Our second patient is an elderly gentleman, 91 years old, with a history of BCC and cSCC who was evaluated for a right parotid mass with overlying ulceration and drainage. Imaging revealed a solid mass that was inseparable from the posterior aspect of the parotid gland with ipsilateral cervical lymphadenopathy, concerning for metastatic disease. Surgical pathology confirmed invasive moderately differentiated cSCC. The tumor was inoperable due to the size and location of the lesion that would increase the likelihood of significant morbidity and loss of function from a surgical intervention. He completed 6 weeks of radiation therapy with significant improvement in the extent of the lesion. Follow-up positron emission tomography (PET) scan revealed decreased activity at the tumor site and reduced size and activity of all but one affected cervical lymph node. Unfortunately, a repeat PET scan in the following year showed increased size and activity of right cervical lymph nodes; new involvement of supraclavicular, mediastinal, and hilar lymph nodes; and diffuse bony metastases. He was started on cemiplimab infusions of 350 mg every 3 weeks. Following the first cycle, he reported poor oral intake, nausea, emesis, and fatigue. The dose was reduced to 280 mg resulting in abatement of all adverse effects but mild fatigue. He responded favorably to 4 cycles of cemiplimab with significant improvements in mediastinal, hilar, and supraclavicular lymphadenopathy as confirmed by imaging. He received 5 additional cycles of cemiplimab therapy for a total of 9 infusions, without new adverse effects. Imaging reaffirmed continued response. Due to favorable response, it was agreed up on to take a treatment break. Unfortunately, he

passed away 3 months after cessation of therapy due to natural causes.

The third patient developed locally advanced, recurrent cSCC precluding any surgical intervention due to high odds of severe disability and deformity. A 63-year-old male with a history of pityriasis rubra pilaris (PRP) and recurrent cSCC treated with local excisions presented with a large, fungating mass on his left forearm. The mass started as a small, erythematous lesion which progressed slowly over 18 months followed by an accelerated phase of growth leading to significant morbidity and hospitalization. Imaging revealed a large fungating mass extending from the left elbow to mid-forearm without any bony involvement. Staging computed tomography (CT) scans revealed no distant metastases. A biopsy of the mass confirmed cSCC. He was offered surgical intervention involving either an above the elbow amputation or a wide resection with limb-sparing approach with an uncertain outcome. He declined both options. He was then initiated on full-dose (350 mg every 3 weeks) cemiplimab therapy with neoadjuvant intent. He tolerated the treatments extremely well with the exception of a mild infusion reaction to the first cycle that did not require any treatment interruption or dose reduction. He had a dramatic response to treatment such that his forearm mass sloughed off by the fourth cycle of cemiplimab. After 13 cycles of cemiplimab, he was reevaluated for surgical intervention. However, with the lack of any discrete masses on imaging obviating the need for such, systemic treatment was continued. Of note, he had an exacerbation of PRP after the fourth cycle that was managed with topical clindamycin, without interruption of cemiplimab therapy. He completed 18 cycles of treatment with no immunotherapy-related adverse events.

## Discussion

The cases discussed above pose 3 distinct scenarios of cSCC all involving a rather dramatic response to cemiplimab, without overt therapy-related side effects. Given the sharp rise in incidence in cSCC from 50% to 200% in the past 2 decades, this treatment option is invaluable.<sup>2</sup> Reported adverse effects of cemiplimab include diarrhea, fatigue, nausea, and rash. While some of these adverse effects were experienced by our patients, they were not severe enough to warrant treatment interruption.

Our first case describes a patient on HD who had complete tumor response to cemiplimab given at full-dose of 3 mg/kg every 2 weeks for 8 cycles. There are no reports of using the drug in ESKD patients. In the aforementioned study on cemiplimab in cSCC, only those patients with serum creatinine less than 1.5 times the upper limit of normal were included. Also, there are no clear guidelines on dose modification of cemiplimab from the manufacturer. The CANcer and DialYsis (CANDY) study on patients requiring routine dialysis found that 82% of anticancer drugs required drug administration after HD.<sup>8</sup> Cemiplimab has a molecular weight of 146 kDa which is comparable to that of

pembrolizumab (149 kDa). It is known that molecules in similar size range are not cleared with dialysis. Several reviews showed similar incidence of immune-related adverse events in patients with ESKD receiving dialysis as compared with the general population suggesting that immune checkpoint inhibitors can be safely administered in ESKD without dose adjustments.<sup>9,10</sup> Furthermore, a case series highlighted the efficacy of pembrolizumab for 2 cSCC patients on dialysis for ESKD.<sup>11</sup> It is safe to extrapolate then that cemiplimab would not be removed during HD and therefore could be administered without dose adjustments and regardless of the timing of dialysis. We contacted the manufacturer who also confirmed the same.

Per the National Comprehensive Cancer Network (NCCN) guidelines, cemiplimab is currently indicated for patients with locally advanced or metastatic cSCC, who are not eligible for curative surgical resection or radiotherapy.<sup>12</sup> Migden et al<sup>12</sup> have undertaken the most extensive cemiplimab study to date. However, only patients with adequate organ function have been considered as potential candidates, making it difficult to assess the therapeutic effect of cemiplimab in patients with poor renal function. Furthermore, cemiplimab has been used in transplant recipients with healthy graft function with encouraging outcomes thus far. Ali et al<sup>13</sup> describe a case of successful cemiplimab administration in a patient with a history of renal transplantation who developed metastatic squamous cell carcinoma (SCC) that progressed despite treatment with capecitabine, radiation, and later inguinal node resection followed by cetuximab. The patient received 10 cycles of cemiplimab therapy, developed no evidence of toxicity, and had no progression of his disease. Importantly, renal graft function appeared unaltered by treatment with immunotherapy. That said, literature regarding cemiplimab use in patients with inadequate organ function is lacking. Our first patient in this case series represents an example of safety and efficacy of cemiplimab in a transplant recipient receiving HD due to graft rejection. The patient responded positively to treatment with 20% dose reduction, and the timing of HD had minimal impact on the effectiveness of cemiplimab, likely due to its larger molecular weight making it nondialyzable.

Another important aspect of the use of immunotherapy is understanding how the geriatric population responds to it, as aging is associated with higher rates of cancer incidence. The age-specific incidence of SCC in individuals over the age of 75 years is approximately 1000 to 1500 per 100,000.<sup>2</sup> Interestingly, in a retrospective analysis, patients with metastatic melanoma treated with anti-PD1 monoclonal antibodies (nivolumab and pembrolizumab) had comparable outcomes (progression free survival and overall survival) and safety profiles regardless of patient age.<sup>14</sup> Similarly, an Italian study demonstrated antitumor activity and safety of cemiplimab in elderly patients with cSCC comparable to those in trials with selected patients. The second patient we described here has an age higher than most patients described in these studies. Furthermore, the fact that the adverse effects

he experienced after his first dose resolved with dose reduction and he ultimately enjoyed significant treatment response nevertheless supports the safe and effective use of cemiplimab regardless of advanced age.

Finally, Migden et al<sup>15</sup> reported that patients treated with cemiplimab alone had twice the response compared to those who had 2 or more surgical resections prior to cemiplimab. Based on this finding, an argument can be made that it may be wise to use cemiplimab as a treatment option earlier in the course of the disease. Our final case lends credence to this approach as we had effectually used cemiplimab in neoadjuvant setting for an extensive recurrence of a locally advanced cSCC leading to a dramatic response, negating the need for any surgical intervention.

## Conclusion

This case series highlights the safety and efficacy of cemiplimab in 3 patients with advanced cSCC, who belongs to demographic cohorts that are not well represented in the available literature on cemiplimab—one with a posttransplant patient receiving HD, another with an elderly male with metastatic disease, and a third with extensive locally advanced disease—all of whom had an impressive response to treatment without major adverse events. Further studies are required in larger cohorts.

## Authors' Note

Prior Presentation of Abstract Statement: No prior presentations.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

## Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

## Informed Consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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