

# Metastatic cutaneous squamous cell carcinoma responsive to cemiplimab in a patient with multiple myeloma



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**Key words:** cemiplimab; metastatic squamous cell carcinoma; multiple myeloma.

## INTRODUCTION

Cutaneous squamous cell carcinoma (cSCC) is the second most common malignancy worldwide, with more than 700,000 cases per year in the United States.<sup>1</sup> Cemiplimab, a programmed cell death (PD)-1 inhibitor, was approved by the US Food and Drug Administration in 2018 as the first drug specifically to treat patients with locally advanced or metastatic cSCC who are not candidates for curative surgery or curative radiation. Phase 1 (n = 26) and phase 2 (n = 59) open-label, multicenter clinical trials showed a 50% overall response rate in advanced cSCC, with median duration of response exceeding 6 months.<sup>2</sup> However, these studies excluded participants with comorbid conditions affecting the immune system such as multiple myeloma (MM). Because MM patients have 2.44 times higher incidence of cSCC than patients without MM,<sup>3</sup> exploring the potential benefits and risks of PD-1 inhibitors for advanced cSCC in MM patients is clinically important. The effectiveness and safety of PD-1 inhibitors for cSCC in patients with MM is not well known, and it is possible that T-cell responses necessary for PD-1 inhibitor effectiveness are not sufficient in MM patients. Here we report a case of clinically complete response of metastatic cSCC on cemiplimab in a patient with known MM.

### Abbreviations used:

ALP:	alkaline phosphatase
ALT:	alanine aminotransferase
AST:	aspartate aminotransferase
cSCC:	cutaneous squamous cell carcinoma
CT:	computed tomography
MM:	multiple melanoma
PD-1:	programmed cell death protein 1
PET-CT:	positron emission tomography/ computed tomography

## CASE REPORT

A man in his 60s with a 16-year history of IgG MM managed with multiple medications presented to the dermatology clinic with a forehead lesion found by biopsy to be a desmoplastic cSCC with perineural and subcutaneous invasion. The patient's MM had previously involved his pelvic bone and had been treated with radiation, then revlimid with dexamethasone 12 years ago, with resolution of his M spike and normalization of activity on positron emission tomography/computed tomography (PET-CT) imaging (Fig 1, A). His MM remained quiescent until 2 years before presentation, when his  $\kappa$ -free light chain levels started to increase, and he was started on combination therapy consisting of daratumumab and dexamethasone with improvement.

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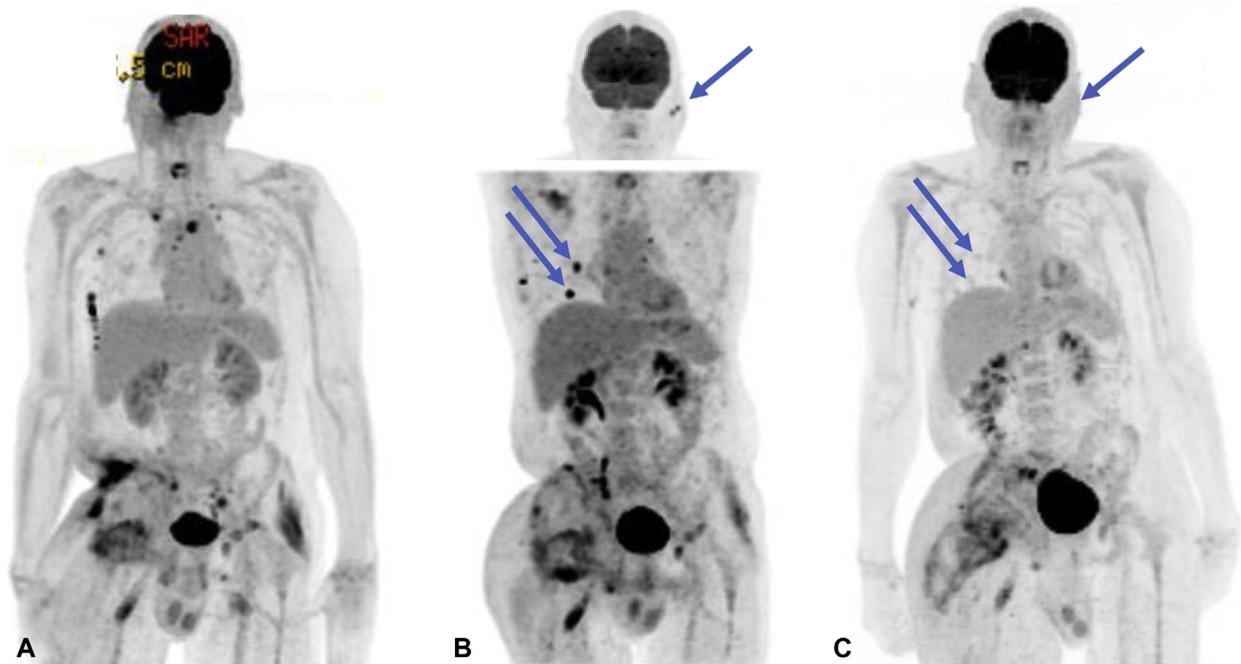
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**Fig 1.** PET-CT scans of the case patient. **A**, Patient with multiple areas of MM involvement prior to his cSCC diagnosis. **B**, Seven months after the previous PET-CT in (**A**), new areas of uptake in the preauricular region and lungs (*blue arrows*) were detected, indicative of metastatic cSCC. **C**, Three month after starting cemiplimab, PET-CT found clinically complete response of preauricular and pulmonary cSCCs, with sustained response 12 months after cemiplimab start.

Because the patient had high-risk cSCC, magnetic resonance imaging of the orbits was performed, which did not show any perineural spread or osseous invasion. The patient underwent Mohs micrographic surgery with plan for local adjuvant radiation. However, during radiation planning, computed tomography (CT) imaging showed 10 pulmonary nodules in the lungs, with CT-guided biopsy of a 9-mm nodule in the right lower lung confirming metastatic cSCC. PET-CT at this time also found new hypermetabolic preauricular lymphadenopathy (*Fig 1, B*).

Although the effects of cemiplimab are not known in cSCC patients with MM, multidisciplinary consultation including medical oncology and hematology suggested no clear contraindication. Of note, the patient's medical history from 3 years prior included 2 brief mild elevations of aspartate aminotransferase (AST) (with the highest to 76 U/L) and alanine aminotransferase (ALT) (to 128 U/L), which were felt to not be clinically significant as they had spontaneously resolved before cemiplimab initiation. However, at the time of cemiplimab initiation, the patient did have persistent mild elevation of alkaline phosphatase (ALP) (with highest value to 272 U/L), thought to be caused by his MM.

The patient was started on cemiplimab, 350 mg intravenously every 3 weeks. A PET-CT 3 months, 6 months, and 12 months after cemiplimab initiation found clinical complete resolution of both the lung nodules and the preauricular lymphadenopathy (*Fig 1, C*). He reported no side effects from the cemiplimab.

However, 3 months after cemiplimab initiation, moderate elevations of AST (to peak 126 U/L), and ALT (to peak 69 U/L) became more persistent, and ALP levels increased (to peak 1,003 U/L), with  $\gamma$ -glutamyl transpeptidase elevation confirming the liver source of the ALP. During this time, concomitant medications that could contribute to hepatotoxicity including fluconazole and ampicillin were discontinued, with partial improvements in the liver function tests. Liver ultrasound scan found cirrhosis; esophagogastroduodenoscopy with portal hypertensive gastropathy supported this diagnosis. The hepatologist felt the cirrhosis was chronic and caused by alcoholic steatohepatitis (from a 20-year history of alcohol usage) and nonalcoholic steatohepatitis (from MM and mitral stenosis). Cemiplimab was discontinued 1 year after initiation with normalization of his AST and ALT, suggesting a mild component of immune-related hepatitis. ALP improved to 368 U/L.

Eleven months after starting cemiplimab, the patient had an increasing M spike and worsening anemia, and carfilzomib was added to daratumumab and dexamethasone for his MM, with improvement in laboratory parameters. Unfortunately, the patient died about 15 months after starting cemiplimab from multiorgan failure in the setting of liver cirrhosis, which contributed to anasarca with pleural effusions and hepatorenal syndrome with kidney failure.

## DISCUSSION

This case is instructive in that the MM patient's duration of response for metastatic cSCC exceeded the meaningful duration of response (105 days) as defined in previous trials for cemiplimab.<sup>1</sup> To date, there is a paucity of systematic studies on the effectiveness of PD-1 inhibition in cSCC patients with altered immune systems, and it is unclear which patients with immunodeficiency can respond to PD-1 inhibition. Our case indicates that a durable response is possible in MM.

Despite the effectiveness of PD-1 inhibitors against several types of solid cancers, including cSCC, the utility of this drug class against hematologic neoplasms is less clear (except for treatment of classic Hodgkin lymphoma).<sup>4-9</sup> Although our patient had a clinical response of cSCC to cemiplimab, he did experience eventual progression of his MM with increase in M spike 11 months after starting PD-1 inhibition, necessitating addition of carfilzomib to his MM treatment regimen.

It is unclear whether the PD-1 inhibition played a significant role in accelerating his hepatic cirrhosis or progression of his MM. Hepatitis is a well-known immune-related adverse event from PD-1 inhibitors, and the presence of MM can make the detection of

PD-1 inhibitor–related hepatitis more challenging, as both can lead to abnormalities in liver function tests. Although our case showed therapeutic benefit of PD-1 inhibition against cSCC, additional systematic studies are needed to assess the risks and benefits of treating advanced cSCC with PD-1 inhibition in MM patients, and the effect of PD-1 inhibition on the course of MM.

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