

Successful Use of Cemiplimab in a Very Elderly Patient With Cutaneous Squamous Cell Carcinoma

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Abstract. *Background/Aim:* Cutaneous squamous cell carcinoma (SCC) is a common skin cancer with significant morbidity and mortality, particularly in advanced stages. Treatment options for metastatic cutaneous SCC in very elderly patients are limited due to concerns about treatment tolerability and potential adverse effects. *Case Report:* We report the case of a 90-year-old female patient with metastatic cutaneous SCC who was treated with cemiplimab, a monoclonal antibody (m-Ab) against programmed cell death protein 1 (PD-1), in combination with radiotherapy. The patient received cemiplimab for a limited period, during which time she demonstrated significant clinical improvement without severe adverse events. Radiotherapy was performed as a locoregional treatment with the aim to enhance immunotherapy efficacy. *Discussion:* This case highlights the feasibility and effectiveness of cemiplimab in very elderly patients with metastatic cutaneous SCC. Despite the common apprehensions regarding the use of immunotherapy in this age group, our patient tolerated cemiplimab well, and the combination with radiotherapy proved beneficial. This suggests that even in very elderly patients, short-term use of

cemiplimab, in conjunction with locoregional treatments such as radiotherapy, can be a viable and successful therapeutic approach. *Conclusion:* Cemiplimab, even in combination with radiotherapy, can be effectively and safely administered to very elderly patients with metastatic cutaneous SCC. This case supports the consideration of immunotherapy, even for a limited duration, as a practical option in the management of advanced cutaneous SCC in elderly patients, expanding the potential treatment strategies for this population.

Cutaneous squamous cell carcinoma (SCC) is described to represent around 20% of non-melanomatous skin cancer, with an increasing incidence, particularly in men over the age of 80 years (1). Cutaneous SCC is likely more common in older patients due to cumulative UV-radiation exposure, with rates 5-10 times higher in those aged over 75 years (2). The therapeutic management of advanced or metastatic cutaneous SCC can be challenging, especially in very elderly patients who often have multiple comorbidities and reduced functional reserve. Recently immune checkpoint inhibitors (ICI) such as cemiplimab, a monoclonal antibody (mAb) against programmed death 1 (PD-1), have become the standard of care for the management of patients with advanced cutaneous SCC who cannot be cured with surgery or radiotherapy. However, data on the use of immunotherapy in very elderly patients are limited and sometimes conflicting. The elderly population is often underrepresented in clinical trials, making it difficult to draw definitive conclusions about the efficacy and safety of these therapies in this age group. Additionally, there is widespread concern about the potential deterioration in the overall health status and increased risk of adverse events following immunotherapeutic treatments in very elderly patients (3, 4). This is particularly relevant for advanced cutaneous SCC, with the cemiplimab pivotal study having a median cohort age of 71 years and median ages of 77 and 79 years reported in real-world population studies from France (5) and Italy (6), respectively.

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Key Words: Cutaneous squamous cell carcinoma, immune checkpoint inhibitor, radiotherapy, elderly.

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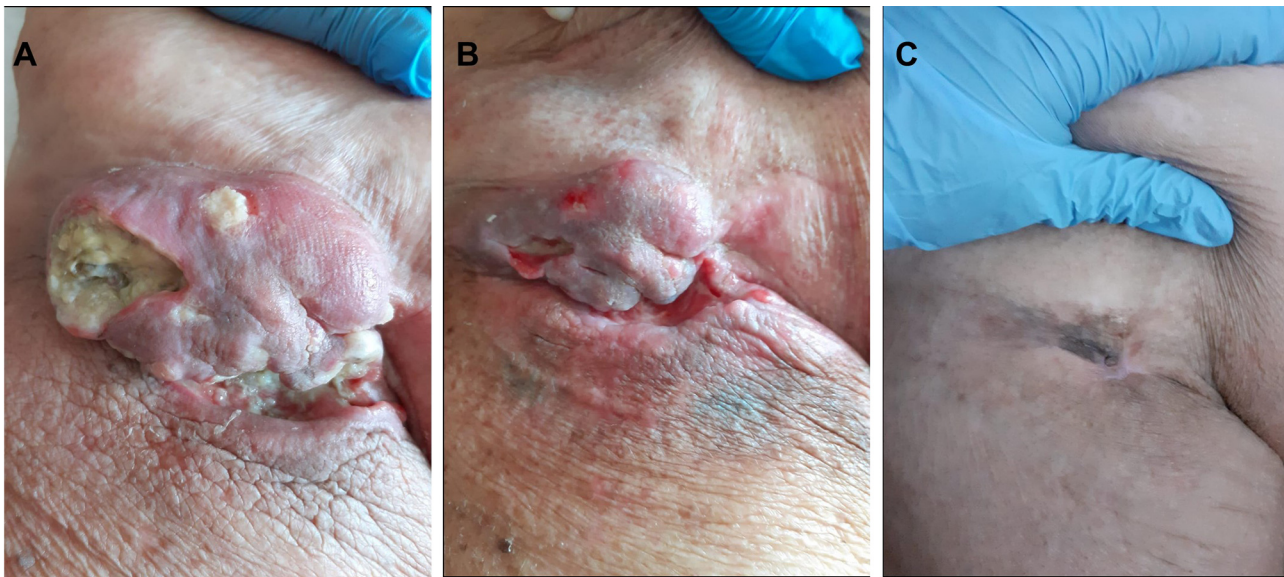


Figure 1. Results of cemiplimab associated with concurrent radiotherapy in a 90-year-old woman with right inguinal lymph node metastasis from cutaneous squamous cell carcinoma of the right thigh. Images taken after five radiotherapy sessions for a total of 25 Gy (A) and after 1 (B) and 3 (C) months of concurrent cemiplimab.

However, there is growing literature showing that ICI can be effectively and safely administered to older patients (7). In this case report, we present the case of a very elderly patient with cutaneous SCC successfully treated with cemiplimab. Notably, we also integrated the treatment with locoregional radiotherapy, achieving a synergistic and excellent outcome. This case emphasizes the role of radiotherapy in conjunction with immunotherapy in locally advanced cutaneous SCC, including scenarios of oligoprogression during immunotherapy. Our objective is to highlight the fact that immunotherapy can not only be effective but also safe in this population, without compromising overall health status and without a significant increase in adverse events. This case report aims to help bridge the existing data gap, supporting the use of immunotherapy even in very elderly patients.

Case Report

A 90-year-old female was diagnosed in April 2019 with a cutaneous SCC of the right thigh. She presented an Eastern Cooperative Oncology Group performance status (ECOG PS) score of 2, with Geriatric 8 (G8) score (8) of 15, Lee's prognostic index of 13 and Charlson comorbidity index of 6. In subsequent years the patient underwent regular dermatological follow-up. In May 2022, due to biopsy findings of right inguinal lymphadenopathy, the patient underwent instrumental investigations. A whole-body computed tomography (CT) scan showed multiple inguinal

and iliac lymphadenopathies, indicating the patient was not suitable for curative locoregional treatment. A confirmatory excisional biopsy of right inguinal adenopathy was performed, reporting metastasis of SCC. Thus, in August 2022, first-line therapy with cemiplimab at 350 mg intravenously every 3 weeks was started. After an initial partial response at the CT scan performed in December 2022, she experienced objective and radiological progressive disease at the radiological tumor assessment performed in March 2023, with enlargement and ulceration of right inguinal adenopathy (Figure 1). After multidisciplinary discussion, continuation of cemiplimab and radiotherapy to the site of right inguinal lymph node progression were prescribed. In April 2023, the patient received external beam radiotherapy (five radiotherapy sessions for a total of 25 Gy) to the right inguinal lymph node and continued cemiplimab, achieving rapid objective improvement (Figure 1). This was confirmed at whole-body CT scan performed in July 2023, not only of the irradiated right inguinal site, but also of the iliac lymphadenopathy. Unfortunately, the patient's ECOG PS score declined during cemiplimab and radiotherapy administration with a final ECOG PS of 3. Furthermore, the nutritional state worsened, and the patient lost weight. Thus, in August 2023, after 1 year of treatment and due to the objective complete response, cemiplimab was permanently discontinued, with rapid clinical improvement of the patient. The latest whole-body CT scan and clinical evaluation performed in April 2024 confirmed complete response, with ECOG PS of 1.

Ethical considerations. Written informed consent for publication of clinical details and clinical images was obtained from the patient.

Discussion

Updated 2023 European guidelines now recommend the use of anti-PD1 agents as a first-line treatment in patients with advanced cutaneous SCC who are not candidates for curative surgery or radiation (9) based on several pivotal clinical trials that have paved a busy road leading to improved clinical management of patients with SCC (9, 10). However, although elderly and frail patients with ECOG PS ≥ 2 are particularly affected by advanced cutaneous SCC, the proportion of this specific population enrolled in clinical studies is limited, likely due to investigators' worries about the drug safety profile in this frail population, but also in light of the widespread concept that immunotherapy is less effective due to the senescence of the immune system with ageing (11).

Nevertheless, multicenter retrospective studies, aiming to assess the risk/benefit ratio of immunotherapy for advanced cutaneous SCC in elderly patients, confirmed the efficacy of anti-PD1 agents in treating these populations in a real-life setting with no significant loss of efficiency compared to younger patients (4-6, 12, 13). Intriguingly, one retrospective report even had the unexpected finding that elderly patients with metastatic melanoma actually fared better on immune checkpoint inhibitors, with a reported progression-free survival (PFS) on treatment with PD-1 inhibitors greater than expected (13).

In light of this evidence, age should no longer be a limiting factor when prescribing immunotherapy. However, adverse events, including weight loss, may have major consequences in these frail patients and must be closely monitored, particularly using specific geriatric evaluation tools at baseline and regularly throughout the course of treatment to ensure that it remains beneficial (14-16). Interestingly, our patient experienced an objective response not only of the irradiated right inguinal lymph node, but also of the iliac adenopathy, suggesting a potential abscopal effect of radiotherapy when combined with immunotherapy (17-22). The use of concurrent radiotherapy will hopefully undergo closer evaluation in larger studies.

Intriguingly, our patient received cemiplimab therapy for only 1 year, achieving a significant objective response. This suggests that a shorter duration of treatment may be sufficient to reach the necessary efficacy in this category of patients. Recent studies have reported the administration of cemiplimab for a limited period, supporting this observation (23). However, the shortened duration of cemiplimab treatment requires further prospective studies to validate these findings.

Our case report, confirming immunotherapy as an effective strategy to fight cancer, reflects the trend that more and more patients with cutaneous cancer, even if elderly, can successfully receive this type of treatment. Thus, the inclusion of elderly patients in clinical trials seems to be imperative and systematic reporting of subgroup analyses by age may shed light on their optimal management.

Conflicts of Interest

The Authors declare that the research was conducted in the absence of commercial or financial relationships that could be construed as a potential conflict of interest.

Authors' Contributions

All the Authors contributed to the preparation of this work and read and approved the final article. EG, GV, AG, IAV and LD were responsible for collecting the data and drafting the first copy. EG, ID, and LD were responsible for editing the article. LA, EG, and SP were responsible for the final editing and preparation of the article for submission.

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Received May 26, 2024

Revised June 21, 2024

Accepted July 26, 2024