College of Human Medicine
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# Neoadjuvant Cemiplimab in Cutaneous Squamous Cell Carcinoma: Local Tumor Clearance with Persistent Nodal Metastasis

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## Introduction

- CSCC is the second most common non-melanoma skin cancer (~20% of cases).Rising incidence due to aging population and improved screening. [2]
- 3–5% of cases progress to locally advanced or metastatic disease. [1]
- Cemiplimab, a PD-1 inhibitor, has shown significant efficacy in advanced CSCC. [3]
- CSCC has a high mutational burden and immune checkpoint dysregulation, enhancing response to PD-1 blockade. [4]
- Case demonstrates neoadjuvant cemiplimab use to enable functional preservation while achieving local control.

## Case Summary

A 54-year-old man presented with a slowly growing ulcerated lesion on the dorsum of his left hand, first noted in 2020 but significantly enlarged by 2024.

Biopsy revealed *invasive, well-differentiated squamous cell carcinoma* with positive margins. Patient was also found to have palpable left epitrochlear and axillary lymph nodes that were benign appearing on ultrasound. Given its large size per NCCN guidelines and the low likelihood of achieving margin-negative resection, neoadjuvant cemiplimab was started to avoid amputation.

After four cycles, the lesion markedly regressed and was resected with negative margins. Following completion of neoadjuvant therapy, the patient underwent wide local excision, excision of the palpable epitrochlear node, and sentinel lymph node biopsy.

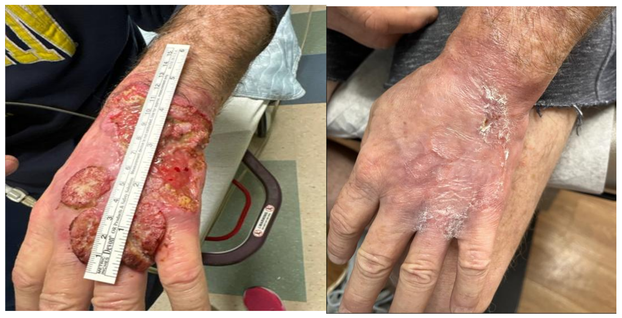
Final surgical pathology demonstrated no residual carcinoma in the primary wide local excision specimen (pathologic complete response at the primary site). However, metastatic squamous cell carcinoma was identified in the excised epitrochlear lymph node and in 2/2 left axillary sentinel lymph nodes.

## Case Summary (continued)

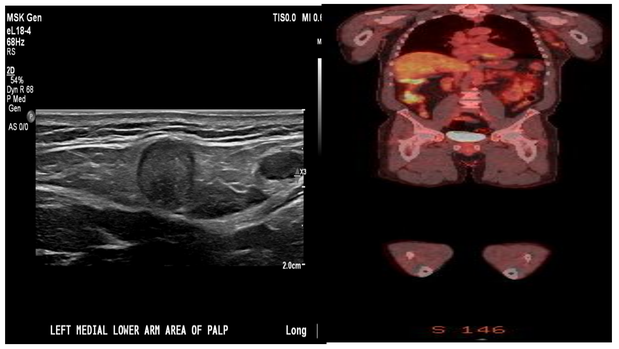
Postoperative PET/CT showed mild FDG uptake in the left axilla compatible with postsurgical change and no distant metastatic disease.

After multidisciplinary team discussion, the patient underwent completion left axillary lymph node dissection coordinated with second-stage split-thickness skin grafting; final pathology showed no additional nodal metastases among the eight additional nodes. The patient recovered with complete graft take and returned to full use and range of motion of the hand. He was restarted on adjuvant cemiplimab with a planned 1-year course and is tolerating therapy well..

**Notable pathological findings:**
Primary lesion PD-L1: 2% expression.
Metastatic lymph node PD-L1: 10% expression — higher than primary, yet metastasis occurred.



Top Left to Right: 1) Ulcerated left hand prior to treatment 2) post-grafting and 4 weeks into adjuvant cemiplimab




Left to Right: 3) US of benign appearing epitrochlear lymph node 4) PET/FDG uptake

## Discussion

- Neoadjuvant benefit: cemiplimab enabled tumor regression that allowed limb-sparing wide excision rather than amputation; consistent with neoadjuvant CSCC data showing substantial pCR rates.
- Systemic failure despite local pCR: nodal progression occurred despite pCR at primary—illustrates that local pathologic response does not guarantee systemic disease control.
- Response patterns to immunotherapy: clinicians must differentiate pseudoprogression (immune infiltration/necrosis), true progression, and hyperprogression (accelerated tumor growth after ICI); management differs substantially
- Neoadjuvant cemiplimab can achieve meaningful tumor downstaging and preserve function in large, high-risk CSCC.
- PD-L1 alone is insufficient as a sole predictive marker; adopt a multi-parameter approach (TMB, IFN-γ signatures, genomic alterations).
- Multidisciplinary care (dermatology, surgical oncology, medical oncology, radiology, pathology, reconstructive surgery) is critical for optimal outcomes.

## References

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