Module 4 - Multidisciplinary Care of cSCC

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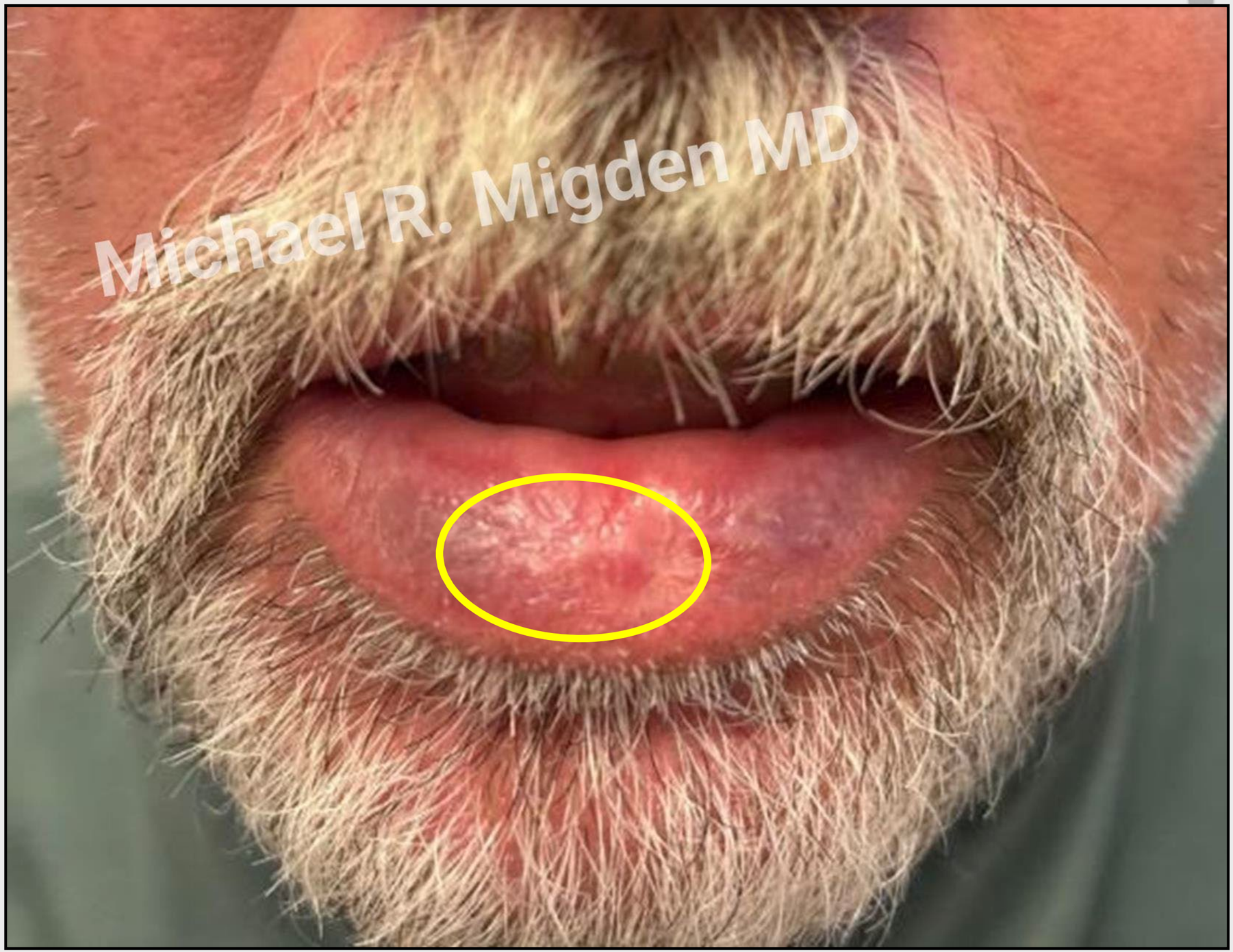
Multidisciplinary Specialists in the Care of Patients With High-Risk cSCC

- Dermatologist
- Head and neck surgeon
- Medical oncologist
- Dermatopathologist
- +/- other specialists as needed regarding toxicities
- Mohs surgeon
- Surgical oncologist
- Radiation oncologist
- Radiologist

When Is Extensive Mohs Appropriate for Aggressive, Larger SCC?

- Patient medically stable and not experiencing “surgical fatigue”
  - Symptom control oral analgesia/anxiolysis adequate: No moderate or deep sedation
- Imaging: Tumor depth achievable (eg, not parotid); resectable in Mohs setting
- Adequate confidence: Precise tumor mapping/probability of obtaining clear margins
- **“Moat” resection** in very large cases; may combine with HNS central en bloc excision
- **With** approved, **effective, systemic treatment (single agent) and NCCN supportive neoadjuvant, the consequences of immediate large surgery** should be weighed against the risks associated with immunotherapy; surgery **at what cost?**

HNS = head and neck surgery. NCCN = National Comprehensive Cancer Network.

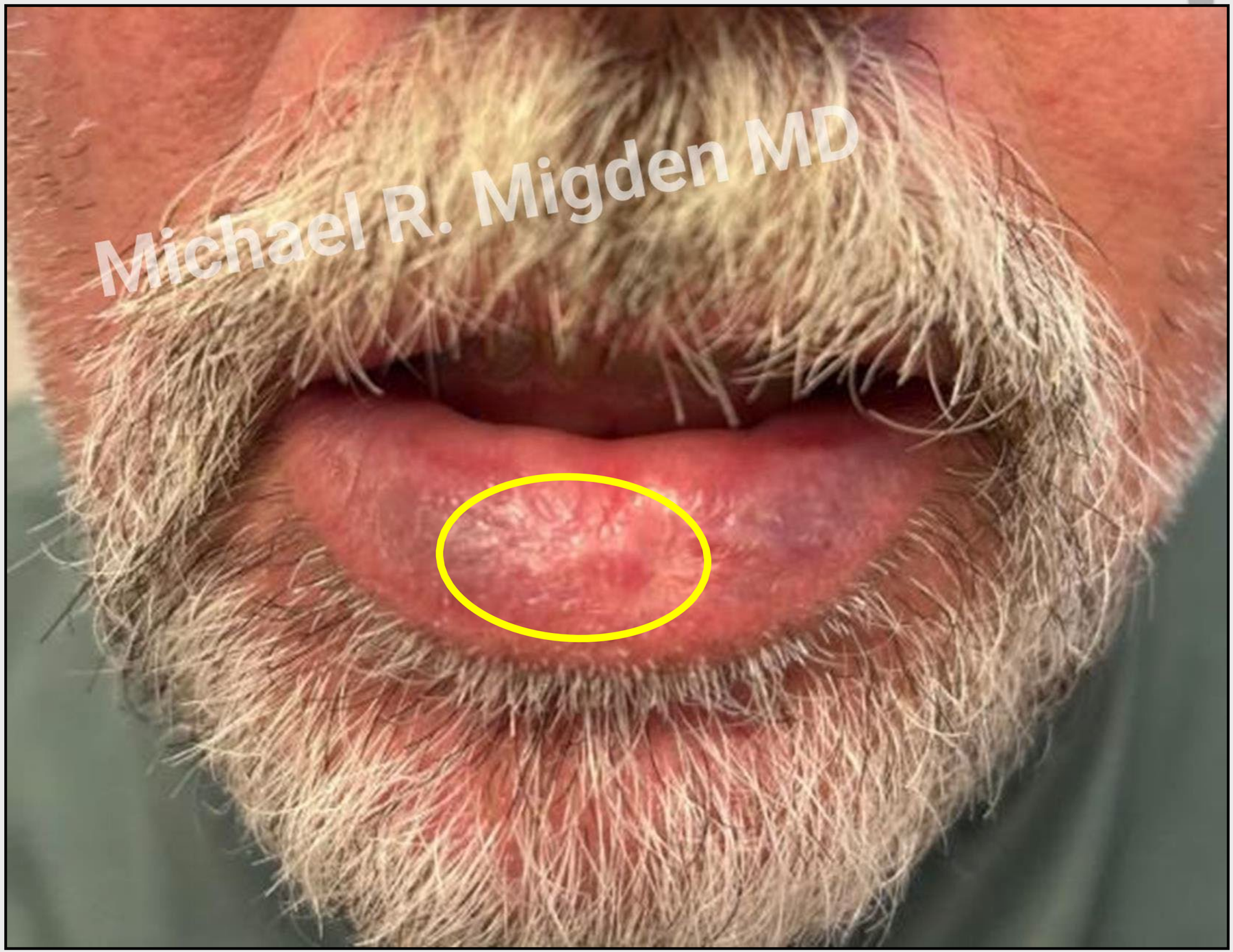


Case #4 - Introduction

- A 59-year-old male with 1.5 x 1.4 cSCC lower dry lip vermillion
- Ill-defined after biopsy
- Outside path: Well-differentiated cSCC

Image courtesy of Michael R. Migden, MD

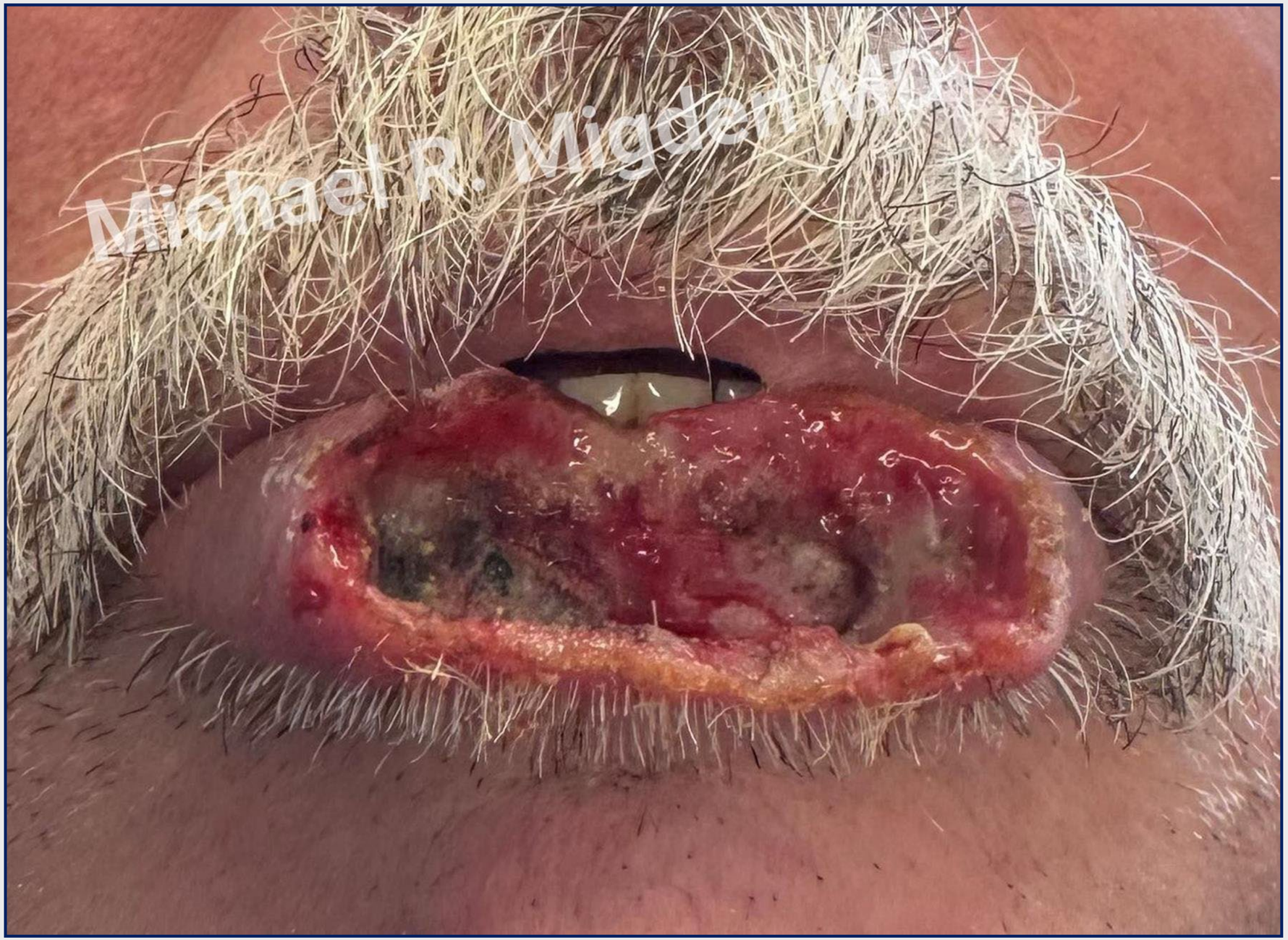
cSCC = cutaneous squamous cell carcinoma.



Case #4

- A 59-year-old male with 1.5 x 1.4 cSCC lower dry lip vermillion
- Ill-defined after biopsy
- Outside path: Well-differentiated cSCC
- **Path Re-read academic center: Moderate to poor differentiated cSCC**

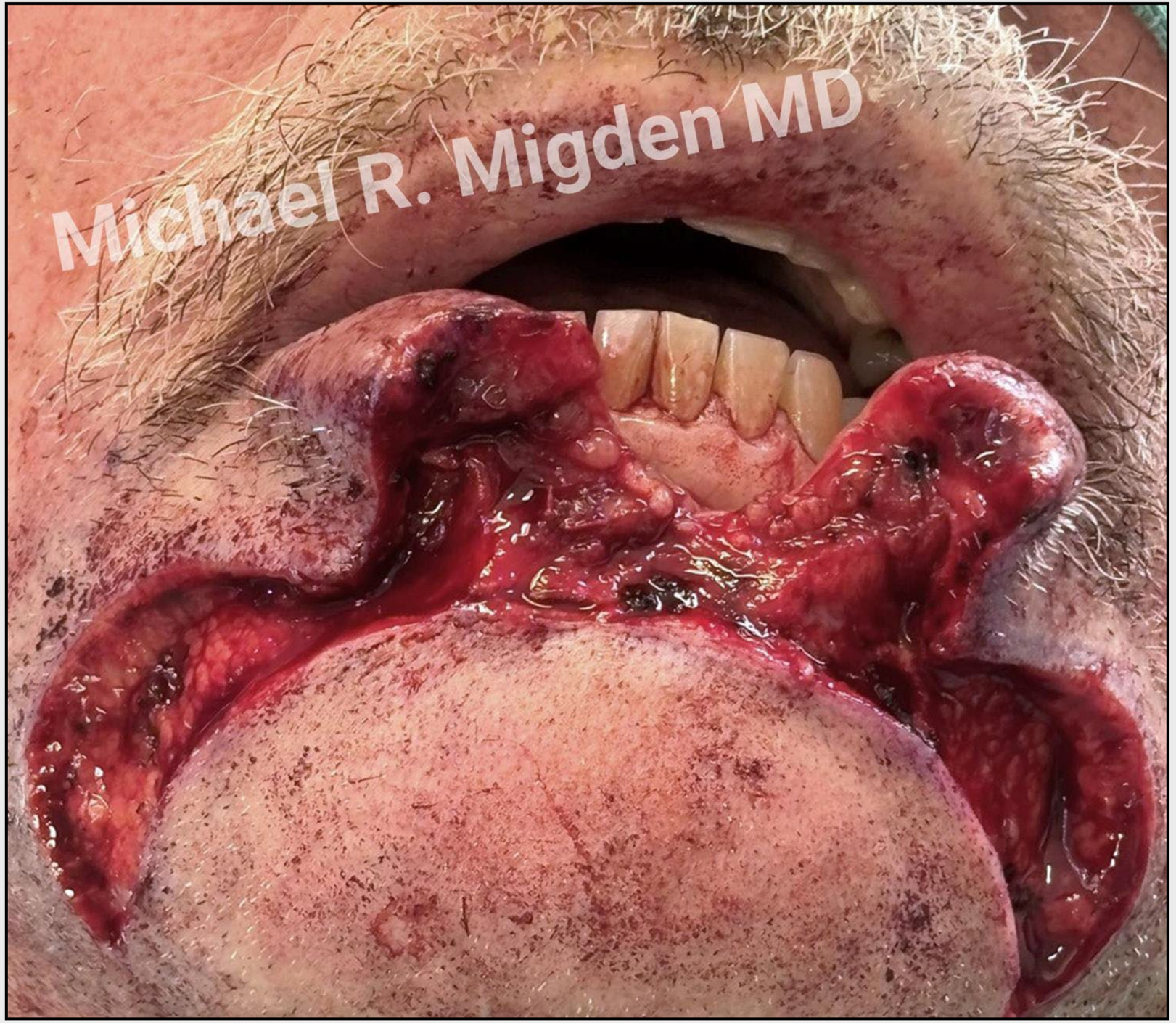
Image courtesy of Michael R. Migden, MD



Case #4

- Mohs clear in 2 stages
- En face stage IHC #1 beyond Mohs read: Minute foci poorly differentiated cSCC with perineural invasion 0.2 mm caliber
- En face stage IHC #2 read: **Positive single cells**, small clusters, **poorly differentiated cSCC**

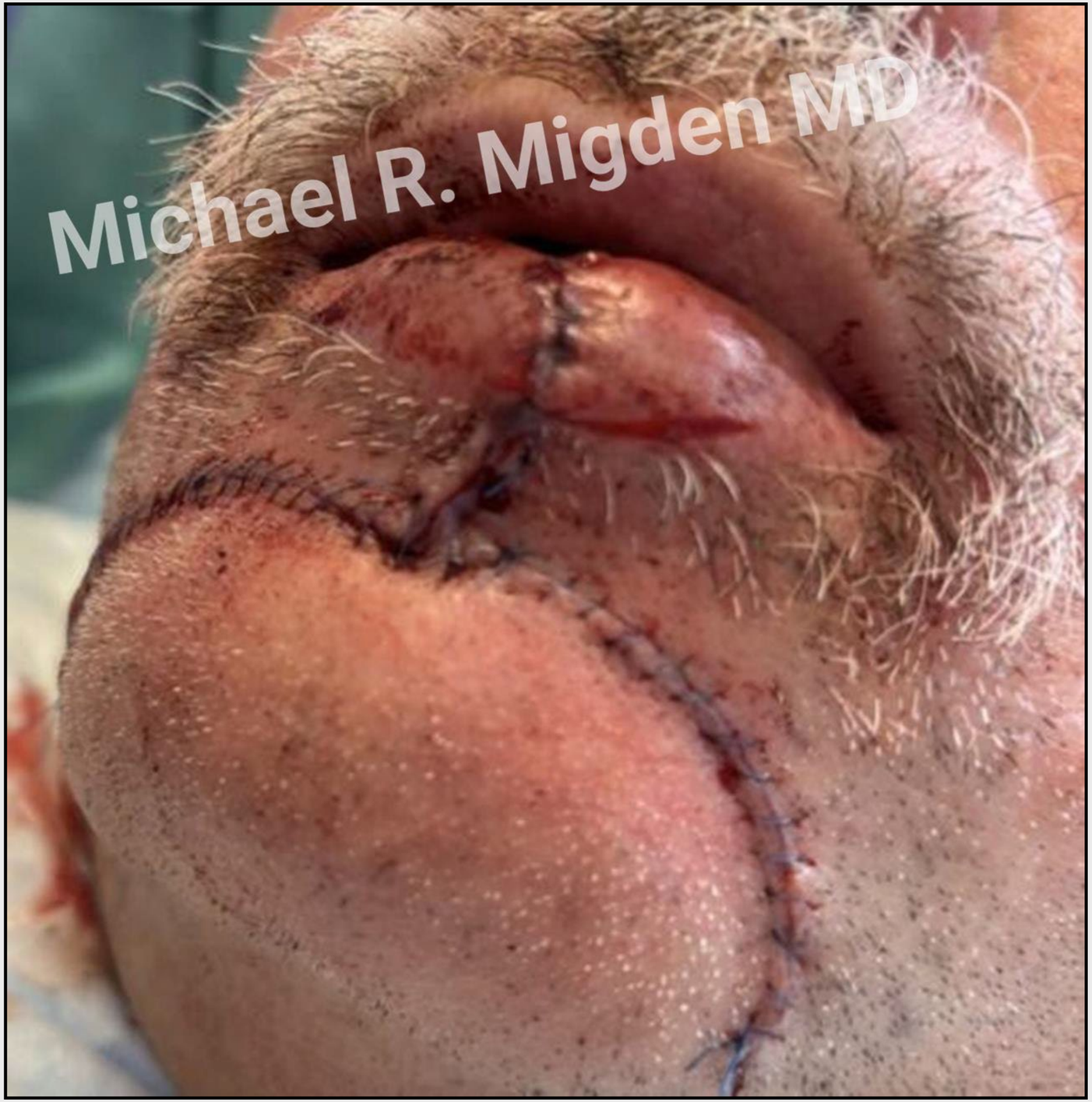
Image courtesy of Michael R. Migden, MD



Case #4

- Central en face biopsy IHC #3: Unequivocal carcinoma not identified
- Bilateral crescentic advancement flap local anesthesia + symptom control prescription

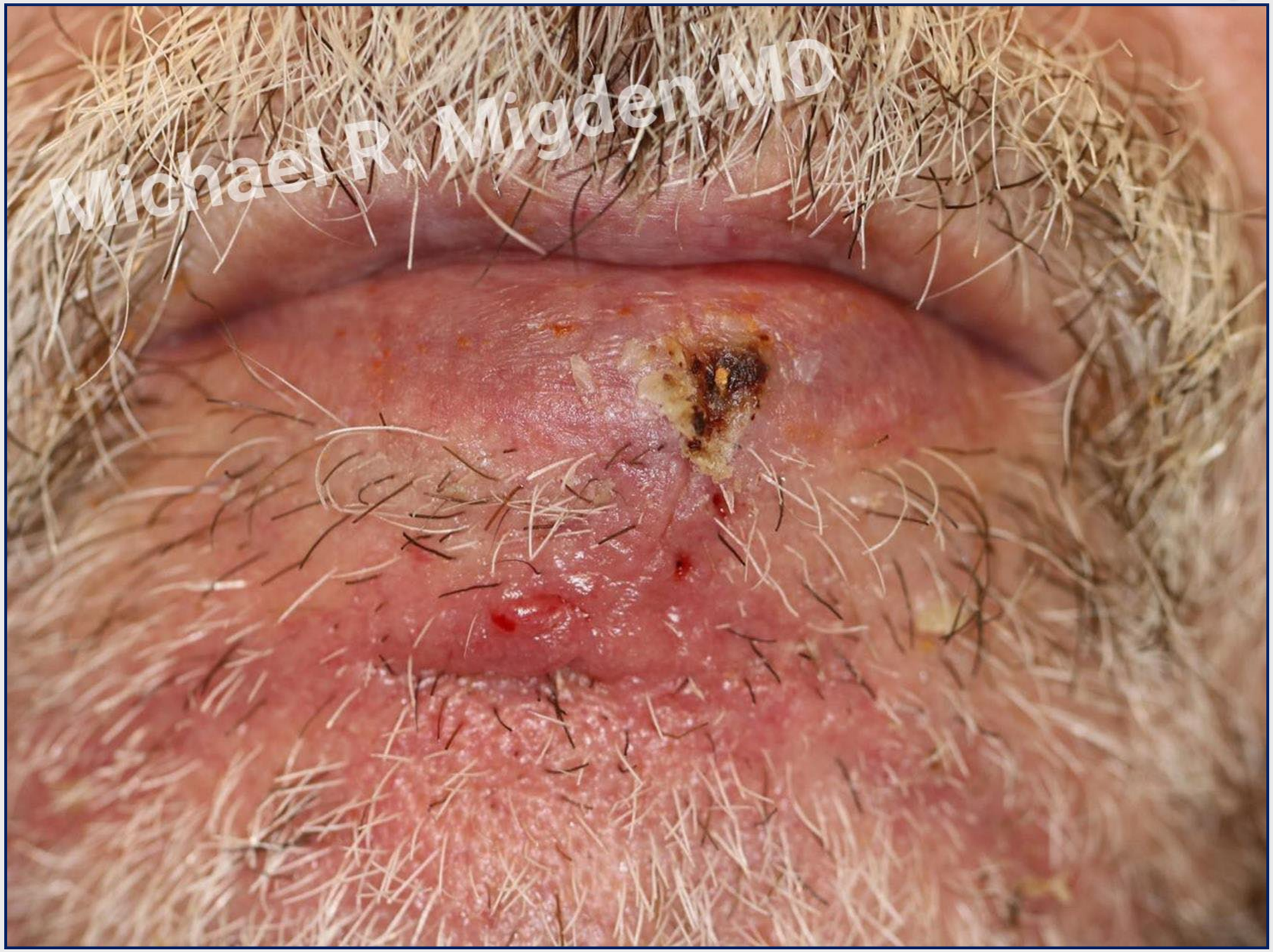
Image courtesy of Michael R. Migden, MD



Case #4

- Bilateral crescentic advancement flaps using local anesthesia

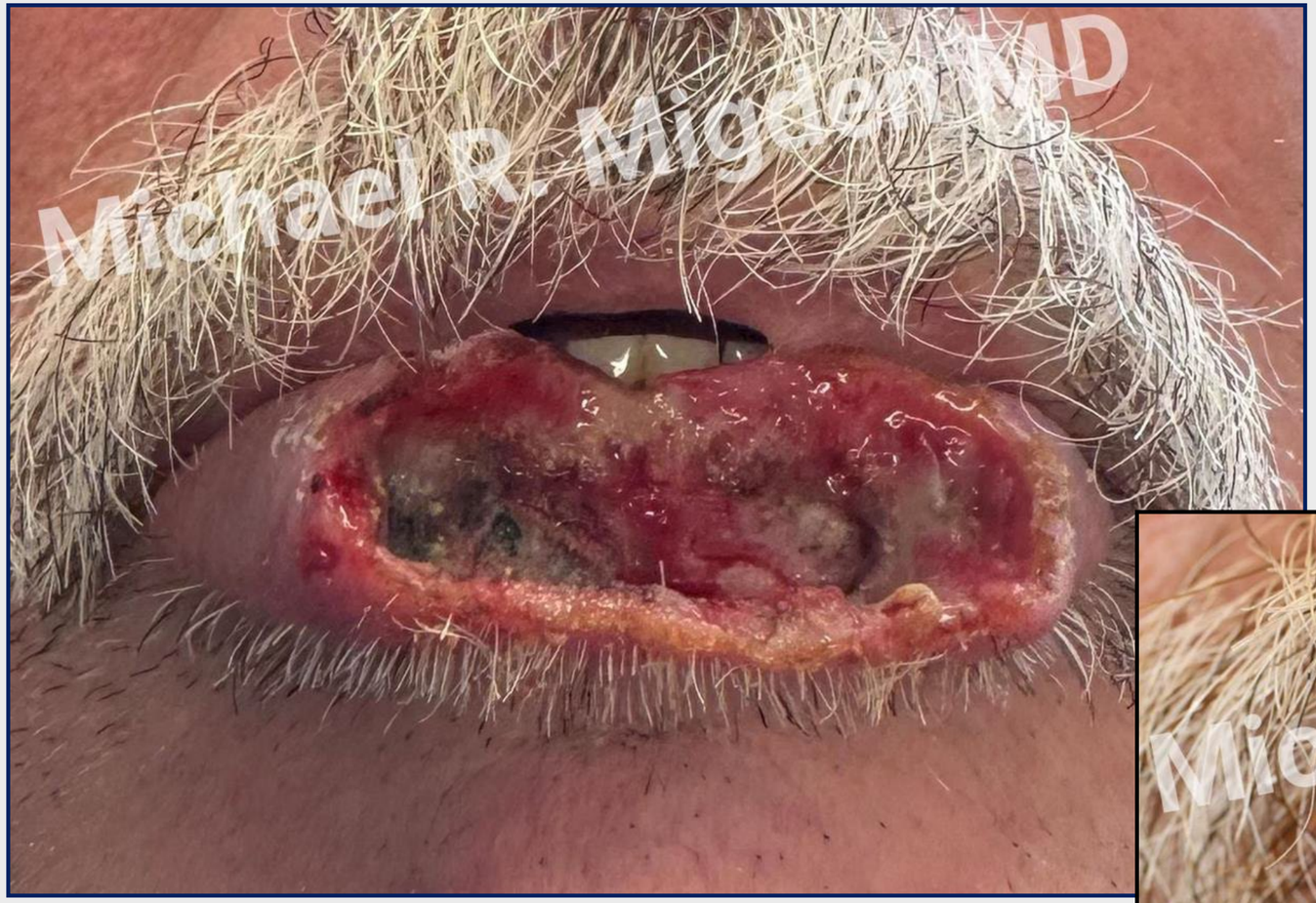
Image courtesy of Michael R. Migden, MD



Case #4

- Postoperative stereotactic radiosurgery (SR) 11 days out from reconstruction
- Patient undergoing RT

Image courtesy of Michael R. Migden, MD



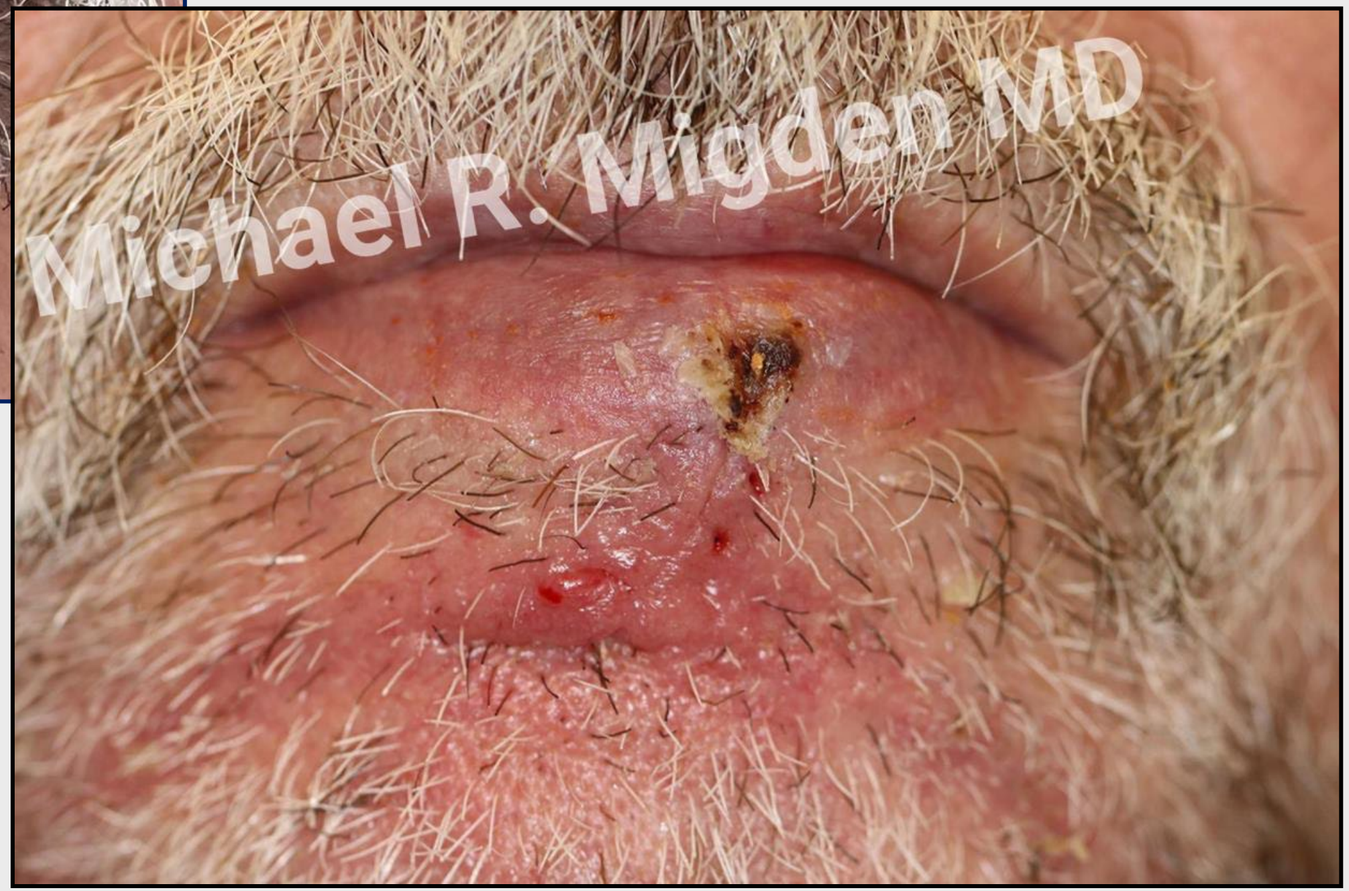


Image courtesy of Michael R. Migden, MD

C-POST Methods: High-Risk Criteria

Nodal and **non-nodal** high-risk criteria*

Nodal disease	In-transit metastases	Perineural invasion	T4 lesions	Recurrent cSCC
ECE with ≥1 node ≥20 mm[1] OR ≥3 nodes regardless of ECE	Skin or subcutaneous metastases >20 mm from the primary lesion but not beyond the regional nodal basin	Clinical and/or radiologic involvement of named nerves	Invasion of cortical bone or skull base	cSCC that arises within the area of previously resected tumor plus ≥1 additional feature ▪ ≥N2b disease associated with the recurrent lesion ▪ Nominal ≥T3 ▪ Poorly differentiated histology and recurrent lesion ≥20 mm diameter

*High-risk cSCC with both nodal and nonnodal features was categorized as high-risk nodal disease.

ECE = extracapsular extension.

Connolly E, et al. European SocieTy for Radiotherapy and Oncology (ESTRO) 2025; Abstract E25-1045.

Adjuvant Treatment of cSCC at High Risk of Recurrence

C-POST study

The safety of cemiplimab-rwlc was evaluated in patients with cSCC at high risk of recurrence after surgery and radiation in the C-POST study (see Clinical Studies [14.1]).

Patients were assigned to receive

- Cemiplimab-rwlc 350 mg (n = 140) or placebo (n = 140) intravenously every 3 weeks for 12 weeks, followed by 700 mg cemiplimab-rwlc or placebo intravenously every 6 weeks for an additional 36 weeks, or
- Cemiplimab-rwlc 350 mg every 3 weeks (n= 65) or placebo (n = 64) for up to 48 weeks

Treatment continued until disease recurrence, unacceptable toxicity, or up to 48 weeks.

The median duration of exposure was 48 weeks (range: 3 weeks to 52 weeks) in cemiplimab-rwlc-treated patients.

- Serious adverse reactions occurred in 18% of patients who received cemiplimab-rwlc; serious adverse reactions that occurred in >1% of patients in the cemiplimab-rwlc arm were pneumonia (1.5%), rash (1.5%), diarrhea (1.5%), adrenal insufficiency (1%), and arrhythmia (1%)
- Permanent discontinuation due to an adverse reaction occurred in 10% of patients who received cemiplimab-rwlc; adverse reactions resulting in permanent discontinuation in >1% of patients were alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, and adrenal insufficiency
- Dosage interruptions due to an adverse reaction occurred in 22% of patients who received cemiplimab-rwlc; adverse reactions leading to interruptions in >1% of patients included COVID-19, diarrhea, alanine aminotransferase increased, urinary tract infection, upper respiratory tract infection, aspartate aminotransferase increased, edema, dyspnea, pneumonitis. pneumonia. and rash

Cemiplimab-rwlc (Libtayo®) prescribing information (PI) 2025 (https://www.libtayohcp.com/). Accessed 12/8/2025.

High/Very-High-Risk cSCC Sent for Mohs Surgery

Clinical/radiographic extent?

Is tumor well-defined?

Symptom control during procedure?

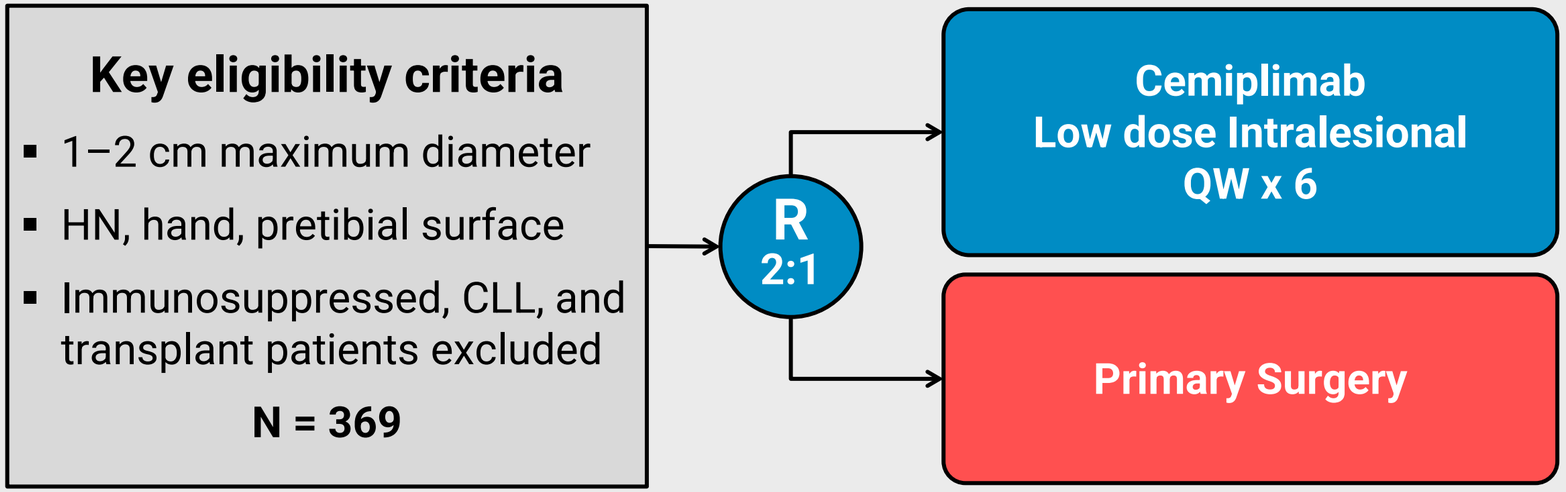
Opportunities for multidisciplinary collaboration?

“Intervene earlier and, where possible, locally”

Society for Immunotherapy of Cancer (SITC) 2023 plenary session panel consensus

Phase 3 Trial of Intralesional Cemiplimab in Patients with Early-Stage CSCC (NCT06585410): Study Design

Randomized, Open-label Study



Primary Endpoints

- EFS (both arms): 1 year and 3 year from randomization, per investigator assessment

Secondary Endpoints

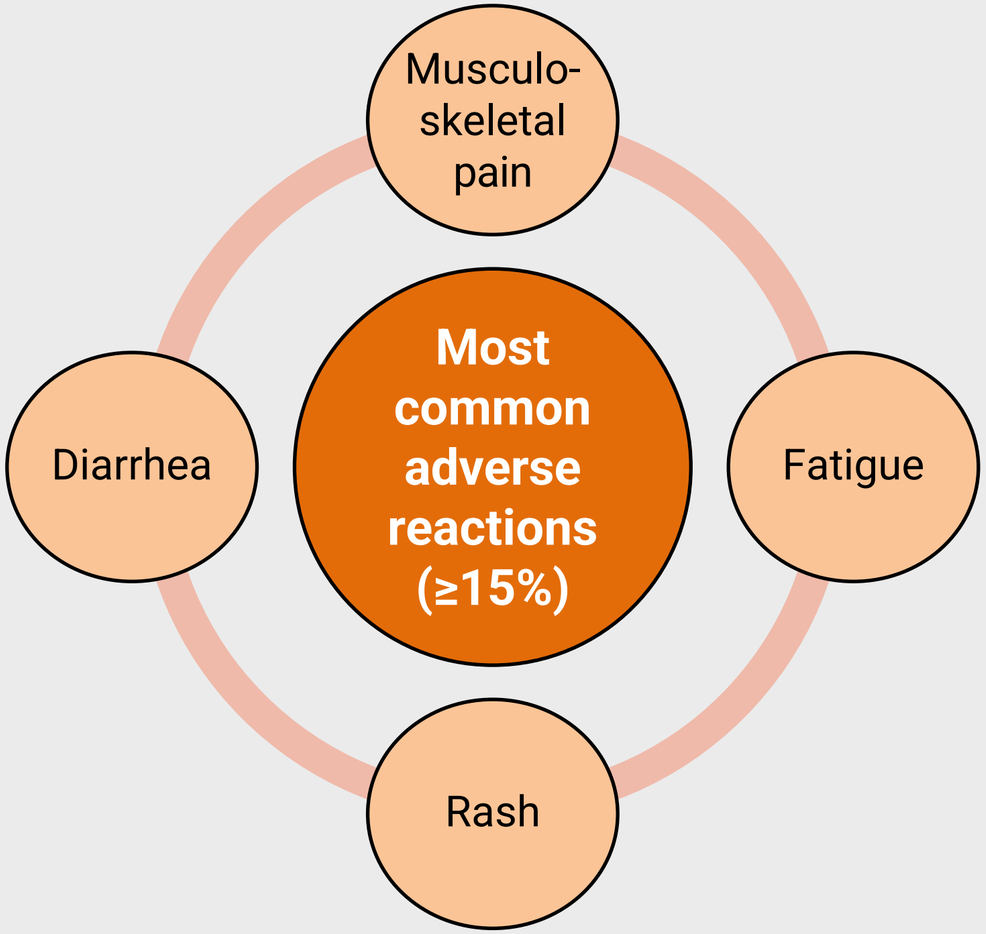
- CCR (experimental arm)
- Non-target lesions in region of TLs (experimental arm)
- Size of surgical defect
- Size of biopsy defect
- Safety and tolerability

CCR = composite complete response; CLL = chronic lymphocytic leukemia; CSCC = cutaneous squamous cell carcinoma; EFS = evainee survival; HN = head and neck; R = randomized; TL = target lesion.

ClinicalTrials.gov identifier: NCT06585410. Accessed December 10, 2025.

AEs Associated With Immunotherapy

Management requires a coordinated multidisciplinary approach



irAEs Can Occur In Any Organ System or Tissue

- Pneumonitis
- Colitis
- Hepatitis
- Endocrinopathies
- Dermatologic reactions
- Nephritis and kidney dysfunction
- Solid organ transplant rejection

AEs = adverse events; irAE = immune-related adverse event.

Cemiplimab-rwlc (Libtayo®) PI 2025 (https://www.libtayohcp.com/). Pembrolizumab (Kaytruda®) PI 2025 (https://www.keytruda.com/). URLs accessed 12/8/2025.

National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Management of Immune Checkpoint Inhibitor-Related Toxicities

Version 1.2026 — October 23, 2025

NCCN Guidelines for Patients®

NCCN recognizes the importance of clinical trials and encourages participation when applicable and available. Trials should be designed to maximize inclusiveness and broad representative enrollment.

ASCO special articles

Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update

Bryan J. Schneider, MD[1]; Jarushka Naidoo, MD[2,3]; Bianca D. Santomasso, MD, PhD[4]; Christina Lacchetti, MHSc[5]; Sherry Adkins, MS[6]; Milan Anadkat, MD[7]; Michael B. Atkins, MD[8]; Kelly J. Brassil, PhD[6]; Jeffrey M. Caterino, MD, MPH[9]; Ian Chau, MD[10]; Marianne J. Davies, DNP[11]; Marc S. Ernstoff, MD[12]; Leslie Fecher, MD[1]; Monalisa Ghosh, MD[13]; Ishmael Jaiyesimi, DO, MS[14]; Jennifer S. Mammen, MD, PhD[15]; Aung Naing, MD[6], Loretta J. Nastoupil, MD[6]; Tanyanika Phillips, MD[16]; Laura D. Porter, MD[17]; Cristina A. Reichner, MD[18]; Carole Seigel, MBA[19], Jung-Min Song, MSN, RN, CNS[20]; Alexander Spira, MD, PhD[21]; Maria Suarez-Almazor, MD[6]; Umang Swami, MD[22]; John A. Thompson, MD[23]; Praveen Vikas, MD[24]; Yinghong Wang, MD[6]; Jeffrey S. Weber, MD, PhD[25]; Pauline Funchain, MD[20]; and Kathryn Bollin, MD[26]

abstract

PURPOSE To increase awareness, outline strategies, and offer guidance on the recommended management of immune-related adverse events (irAEs) in patients treated with immune checkpoint inhibitor (ICPi) therapy.

METHODS A multidisciplinary panel of medical oncology, dermatology, gastroenterology, rheumatology, pulmonology, endocrinology, neurology, hematology, emergency medicine, nursing, trialists, and advocacy experts was convened to update the guideline. Guideline development involved a systematic literature review and an informal consensus process. The systematic review focused on evidence published from 2017 through 2021.

RESULTS A total of 175 studies met the eligibility criteria of the systematic review and were pertinent to the development of the recommendations. Because of the paucity of high-quality evidence, recommendations are based on expert consensus.

RECOMMENDATIONS Recommendations for specific organ system–based toxicity diagnosis and management are presented. While management varies according to the organ system affected, in general, ICPi therapy should be continued with close monitoring for grade 1 toxicities, except for some neurologic, hematologic, and cardiac toxicities. ICPi therapy may be suspended for most grade 2 toxicities, with consideration of resuming when symptoms revert ≤ grade 1. Corticosteroids may be administered. Grade 3 toxicities generally warrant suspension of ICPis and the initiation of high-dose corticosteroids. Corticosteroids should be tapered over the course of at least 4-6 weeks. Some refractory cases may require other immunosuppressive therapy. In general, permanent discontinuation of ICPis is recommended with grade 4 toxicities, except for endocrinopathies that have been controlled by hormone replacement. Additional information is available at www.asco.org/supportive-care-guidelines.

J Clin Oncol 39:4073-4126.

Table 3: Lung Toxicities

Management of immune-related adverse events for ICP: Update

3.1 Pneumonitis	
Workup and evaluation Should include the following: Pulse oximetry and CT chest!? Preferably with contrast if concerned for other etiologies such as pulmonary embolus. For grade 2 or higher, may include the following infectious workup: Nasal swab, sputum culture, and sensitivity, blood culture and sensitivity, urine culture, and sensitivity. COVID-19 evaluation—per institutional guidelines where relevant.	
Grading	**Management**
Grade 1: Asymptomatic; confined to one lobe of the lung or <25% of lung parenchyma; clinical or diagnostic observations only	Hold ICP inhibitor or proceed with close monitoring. Monitor patients weekly with history and physical examination, pulse oximetry; may also offer chest imaging (CXR, CT) if uncertain diagnosis and/or to follow progress. Repeat chest imaging in 3-4 weeks or sooner if patient becomes symptomatic. In patients who have had baseline testing, may offer a repeat spirometry or DLCO in 3-4 weeks. May resume ICP inhibitor with radiographic evidence of improvement or resolution if held. If no improvement, should treat as grade 2.
Grade 2: Symptomatic; Involves more than one lobe of the lung or 25% to 50% of lung parenchyma; medical intervention indicated; limiting instrumental ADL	Hold ICP inhibitor until clinical improvement to = Grade 1. Prednisone 1-2 mg/kg/d and taper over 4 to 6 weeks. Consider bronchoscopy with BAL = transbronchial biopsy. Consider empiric antibiotics if infection remains in the differential diagnosis after workup. Monitor at least once per week with history and physical examination, pulse oximetry, consider radiologic imaging; if no clinical improvement after 48 to 72 hours of prednisone, treat as grade 3. Pulmonary and infectious disease consults if necessary.
Grade 3: Severe symptoms; Hospitalization required: Involves all lung lobes or >50% of lung parenchyma; limiting self-care ADL; oxygen indicated.	Permanently discontinue ICP. Empiric antibiotics may be considered. Methylprednisolone IV 1 to 2 mg/kg/d. If no improvement after 48 hours, may add immunosuppressive agent. Options include infliximab or mycophenolate mofetil IV or IVIG or cyclophosphamide (See Table A2 for dosing). Taper corticosteroids over 4 to 6 weeks? Pulmonary and infectious disease consults if necessary. May consider bronchoscopy with BAL + transbronchial biopsy if patient can tolerate.
Grade 4: Life-threatening respiratory compromise; urgent intervention indicated (intubation)	

ADL = activity of daily living; BAL = bronchoalveolar lavage; CT = computed tomography; CXR = chest x-ray; DLCO = diffusing capacity of lung for carbon monoxide; ICP = immune checkpoint; IV = intravenous; IVIG = intravenous immune globulin.

[a]Subset of patients may develop chronic pneumonitis and may require longer taper. Chronic pneumonitis is a described phenomenon where the incidence is not known but <2%.

Schneider BJ, et al. *J Clin Oncol.* 2021;39(36):4073-4126.