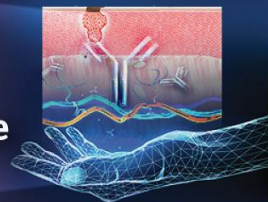


# Navigating Clinical Challenges in cSCC:

## Leveraging AI Tools for Improved Decision-Making Across the Continuum of Care



### Recent and key publications on high-risk cSCC

#### Resources on cSCC Risk Stratification

Resource	Address
Erasmus MC Cancer Institute. Prediction of metastatic risk in patients with cutaneous squamous cell carcinoma (cSCC). cSCC Risk Calculator.	<a href="https://emc-dermatology.shinyapps.io/csc-abs-met-risk/">https://emc-dermatology.shinyapps.io/csc-abs-met-risk/</a>
Gibson FT, Ran NA, Karn EE, et al. Patterns of disease-specific death from cutaneous squamous cell carcinoma: A multicenter retrospective cohort. <i>J Am Acad Dermatol</i> . 2026;2:658-660.	<a href="https://pubmed.ncbi.nlm.nih.gov/41076132/">https://pubmed.ncbi.nlm.nih.gov/41076132/</a>
Granger EE, Ran NA, Groover MK, et al. Most cutaneous squamous cell carcinoma recurrences occur in the first 3 years after diagnosis: A multicenter retrospective cohort study. <i>J Am Acad Dermatol</i> . 2024;91:957-960.	<a href="https://pubmed.ncbi.nlm.nih.gov/38971189/">https://pubmed.ncbi.nlm.nih.gov/38971189/</a>
Gupta N, Weitzman RE, Murad F, et al. Identifying Brigham and Women's Hospital stage T2a cutaneous squamous cell carcinomas at risk of poor outcomes. <i>J Am Acad Dermatol</i> . 2022;86:1301-1308.	<a href="https://pubmed.ncbi.nlm.nih.gov/34864111/">https://pubmed.ncbi.nlm.nih.gov/34864111/</a>
Huis In 't Veld EA, Boere T, Zuur CL, et al. Oncological outcome after lymph node dissection for cutaneous squamous cell carcinoma. <i>Ann Surg Oncol</i> . 202330:5017-5026.	<a href="https://pubmed.ncbi.nlm.nih.gov/36991168/">https://pubmed.ncbi.nlm.nih.gov/36991168/</a>
Jambusaria-Pahlajani A, et al. riSCC: A personalized risk model for the development of poor outcomes in cutaneous squamous cell carcinoma. <i>J Am Acad Dermatol</i> . 2025;93:73-81.	<a href="https://pubmed.ncbi.nlm.nih.gov/40024391/">https://pubmed.ncbi.nlm.nih.gov/40024391/</a>
Jambusaria-Pahlajani A, Kanetsky PA, Karia PS, et al. Evaluation of AJCC tumor staging for cutaneous squamous cell carcinoma and a proposed alternative tumor staging system. <i>JAMA Dermatol</i> . 2013;149:402-410.	<a href="https://pubmed.ncbi.nlm.nih.gov/23325457/">https://pubmed.ncbi.nlm.nih.gov/23325457/</a>
Karia PS, Jambusaria-Pahlajani A, Harrington DP, Murphy GF, Qureshi AA, Schmults CD. Evaluation of American Joint Committee on Cancer, International Union Against Cancer, and Brigham and Women's Hospital tumor staging for cutaneous squamous cell carcinoma. <i>J Clin Oncol</i> . 2014;32:327-334.	<a href="https://pubmed.ncbi.nlm.nih.gov/24366933/">https://pubmed.ncbi.nlm.nih.gov/24366933/</a>
Masarwy R, Shilo S, Carmel Neiderman NN, et al. The prognostic value and clinical utility of the 40-gene expression profile (40-GEP) test in cutaneous squamous cell carcinoma: systematic review and meta-analysis. <i>Cancers (Basel)</i> . 2023;15:2456.	<a href="https://pubmed.ncbi.nlm.nih.gov/37173922/">https://pubmed.ncbi.nlm.nih.gov/37173922/</a>
National Comprehensive Cancer Network®. NCCN Clinical Practice Guidelines in Oncology. Squamous Cell Skin Cancer. Version 1.2026.	<a href="https://www.nccn.org/guidelines/guidelines-detail?category=1&amp;id=1465">https://www.nccn.org/guidelines/guidelines-detail?category=1&amp;id=1465</a>
Porceddu SV, Connolly E, Bressel M, Wratten C, Liu HY, Rischin D. Prognostic subgroups for disease-free survival with cutaneous squamous cell carcinoma of the head and neck: A secondary analysis of a randomized clinical trial. <i>JAMA Otolaryngol Head Neck Surg</i> . 2025;151:938-945.	<a href="https://pubmed.ncbi.nlm.nih.gov/40875250/">https://pubmed.ncbi.nlm.nih.gov/40875250/</a>

Ran NA, Granger EE, Brodland DG, et al. Risk factor number and recurrence, metastasis, and disease-related death in cutaneous squamous cell carcinoma. <i>JAMA Dermatol.</i> 2025;161:597-604.	<a href="https://pubmed.ncbi.nlm.nih.gov/40105853/">https://pubmed.ncbi.nlm.nih.gov/40105853/</a>
Rentiroia-Pacheco B, Tokez S, Bramer EM, et al. Personalised decision making to predict absolute metastatic risk in cutaneous squamous cell carcinoma: Development and validation of a clinico-pathological model. <i>EClinicalMedicine.</i> 2023;63:102150.	<a href="https://pubmed.ncbi.nlm.nih.gov/37662519/">https://pubmed.ncbi.nlm.nih.gov/37662519/</a>
Ruiz ES, Karia PS, Besaw R, Schmults CD. Performance of the American Joint Committee on Cancer Staging Manual, 8th Edition vs the Brigham and Women's Hospital Tumor Classification System for Cutaneous Squamous Cell Carcinoma. <i>JAMA Dermatol.</i> 2019;155:819-825.	<a href="https://pubmed.ncbi.nlm.nih.gov/30969315/">https://pubmed.ncbi.nlm.nih.gov/30969315/</a>
Ruiz ES, Karia PS, Morgan FC, Schmults CD. The positive impact of radiologic imaging on high-stage cutaneous squamous cell carcinoma management. <i>J Am Acad Dermatol.</i> 2017;76:217-225.	<a href="https://pubmed.ncbi.nlm.nih.gov/27707594/">https://pubmed.ncbi.nlm.nih.gov/27707594/</a>
Sahovaler A, Krishnan RJ, Yeh DH, et al. Outcomes of cutaneous squamous cell carcinoma in the head and neck region with regional lymph node metastasis: A systematic review and meta-analysis. <i>JAMA Otolaryngol Head Neck Surg.</i> 2019;145:352-360.	<a href="https://pubmed.ncbi.nlm.nih.gov/30844021/">https://pubmed.ncbi.nlm.nih.gov/30844021/</a>
Skin Cancer Outcomes Consortium (SCOUT). Data-Driven Risk Stratification for CSCC. 2025.	<a href="https://www.scoutconsortium.org/app-landing-page">https://www.scoutconsortium.org/app-landing-page</a>
Steijlen OFM, Pozza L, Traets JJH, et al. Enhanced metastatic risk stratification for cutaneous squamous cell carcinoma by combining clinical guidelines with the Erasmus MC model: Results from 2 nationwide nested case-control studies. <i>J Am Acad Dermatol.</i> 2025;93:699-706.	<a href="https://pubmed.ncbi.nlm.nih.gov/40383274/">https://pubmed.ncbi.nlm.nih.gov/40383274/</a>
Wysong A. Squamous-cell carcinoma of the skin. <i>N Engl J Med.</i> 2023;388:2262-2273.	<a href="https://pubmed.ncbi.nlm.nih.gov/37314707/">https://pubmed.ncbi.nlm.nih.gov/37314707/</a>

## Neoadjuvant Therapy For High-Risk cSCC

Resource	Address
A Study of (Neo)Adjuvant Intismeran Autogene (V940) and Pembrolizumab in Cutaneous Squamous Cell Carcinoma (V940-007) (INTERpath-007). ClinicalTrials.gov identifier NCT06295809. Last updated December 9, 2025.	<a href="https://clinicaltrials.gov/study/NCT06295809">https://clinicaltrials.gov/study/NCT06295809</a>
Amatore F, Sridharan S, Karunamurthy A, et al Pathologic response rates to neoadjuvant pembrolizumab in locally advanced (LA) resectable cutaneous squamous cell carcinoma (cSCC). <i>J Clin Oncol.</i> 2024;42(16_suppl):9591.	<a href="https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.9591">https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.9591</a>
ClinicalTrials.gov. Deep sequencing in Cutaneous Squamous Cell caRciNomias (DISCERN). ClinicalTrials.gov identifier NCT05878288. Last updated November 21, 2024.	<a href="https://clinicaltrials.gov/study/NCT05878288">https://clinicaltrials.gov/study/NCT05878288</a>
Gross ND, Miller DM, Khushalani NI, et al. Neoadjuvant cemiplimab and surgery for stage II-IV cutaneous squamous-cell carcinoma: Follow-up and survival outcomes of a single-arm, multicentre, phase 2 study. <i>Lancet Oncol.</i> 2023;24:1196-1205.	<a href="https://pubmed.ncbi.nlm.nih.gov/37875144/">https://pubmed.ncbi.nlm.nih.gov/37875144/</a>
Gross ND, Miller DM, Khushalani NI, et al. Neoadjuvant cemiplimab for stage II to IV cutaneous squamous-cell carcinoma. <i>N Engl J Med.</i> 2022;387:1557-1568.	<a href="https://pubmed.ncbi.nlm.nih.gov/36094839/">https://pubmed.ncbi.nlm.nih.gov/36094839/</a>

Ladwa R, Lee JHJ, Porceddu SV, et al. A phase 2 study of de-escalation in resectable, locally advanced cutaneous squamous cell carcinoma (cSCC) with the use of neoadjuvant pembrolizumab: De-Squamate. <i>J Clin Oncol</i> . 2024;42:9514.	<a href="https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.9514">https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.9514</a>
Neoadjuvant Cemiplimab in Newly Diagnosed or Recurrent Stage I-II Merkel Cell Carcinoma and Locoregionally Advanced Cutaneous Squamous Cell Carcinoma. ClinicalTrials.gov identifier NCT04975152. Last updated December 5, 2025.	<a href="https://clinicaltrials.gov/study/NCT04975152">https://clinicaltrials.gov/study/NCT04975152</a>
Neoadjuvant Study of PD-1 Inhibitor Pembrolizumab in PD-1 Naive Cutaneous Squamous Cell Carcinoma (cSCC). ClinicalTrials.gov identifier NCT04808999. Last updated May 29, 2025.	<a href="https://clinicaltrials.gov/study/NCT04808999">https://clinicaltrials.gov/study/NCT04808999</a>
Rischin D, Miller DM, Khushalani NI, et al. Neoadjuvant cemiplimab for stage II–IV cutaneous squamous cell carcinoma: 2-year follow-up and biomarker analyses. <i>EJC Skin Cancer</i> . 2025;3(suppl 1):100702.	<a href="https://www.ejcskn.com/article/S2772-6118(25)00423-9/fulltext">https://www.ejcskn.com/article/S2772-6118(25)00423-9/fulltext</a>
Spadafora M, Paganelli A, Raucci M, et al. Neoadjuvant immunotherapy in cutaneous squamous cell carcinoma: Systematic literature review and state of the art. <i>Cancers (Basel)</i> . 2025;17:637.	<a href="https://pmc.ncbi.nlm.nih.gov/articles/PMC11852655/">https://pmc.ncbi.nlm.nih.gov/articles/PMC11852655/</a>
Study of Cemiplimab in Patients With Type of Skin Cancer Stage II to IV Cutaneous Squamous Cell Carcinoma. ClinicalTrials.gov identifier NCT04154943. Last updated December 23, 2025.	<a href="https://clinicaltrials.gov/study/NCT04154943">https://clinicaltrials.gov/study/NCT04154943</a>
Testing the Addition of an Immunotherapy Drug, Cemiplimab (REGN2810), Plus Surgery to the Usual Surgery Alone for Treating Advanced Skin Cancer. ClinicalTrials.gov identifier NCT 06568172. Last updated January 21, 2026.	<a href="https://www.clinicaltrials.gov/study/NCT06568172">https://www.clinicaltrials.gov/study/NCT06568172</a>

### Adjuvant Therapy for High-Risk cSCC

Resource	Address
Koyfman SA, Lee JHJ, Mortier L, et al. Phase 3 randomized trial (KEYNOTE-630) of adjuvant pembrolizumab (pembro) versus placebo (pbo) for high-risk locally advanced cutaneous squamous cell carcinoma (LA cSCC) following surgery and radiation (RT). <i>J Clin Oncol</i> . 2025;43(16_suppl):6000.	<a href="https://ascopubs.org/doi/10.1200/JCO.2025.43.16_suppl.6000">https://ascopubs.org/doi/10.1200/JCO.2025.43.16_suppl.6000</a>
Lim AM, et al. Impact of Adjuvant Cemiplimab in High-Risk Cutaneous Squamous Cell Carcinoma. <i>Curr Oncol</i> . 2025;32:459.	<a href="https://pubmed.ncbi.nlm.nih.gov/40862828/">https://pubmed.ncbi.nlm.nih.gov/40862828/</a>
Lim AML, Porceddu SV, Day F, et al. Patient-reported outcomes (PROs) in the C-POST trial of adjuvant cemiplimab (cemi) vs placebo (pbo) for high-risk cutaneous squamous cell carcinoma (CSCC). <i>J Clin Oncol</i> . 2025;43(16_suppl):6065.	<a href="https://ascopubs.org/doi/10.1200/JCO.2025.43.16_suppl.6065">https://ascopubs.org/doi/10.1200/JCO.2025.43.16_suppl.6065</a>
Pembrolizumab (MK-3475) Versus Placebo Following Surgery and Radiation in Participants With Locally Advanced Cutaneous Squamous Cell Carcinoma (MK-3475-630/KEYNOTE-630). ClinicalTrials.gov identifier NCT03833167. Last updated December 24, 2025.	<a href="https://clinicaltrials.gov/study/NCT03833167">https://clinicaltrials.gov/study/NCT03833167</a>
Rischin D, Porceddu S, Day F, et al. Adjuvant cemiplimab or placebo in high-risk cutaneous squamous-cell carcinoma. <i>N Engl J Med</i> . 2025;393:774-785.	<a href="https://pubmed.ncbi.nlm.nih.gov/40454639/">https://pubmed.ncbi.nlm.nih.gov/40454639/</a>
Rischin D, Porceddu SV, Day F, et al. 1603MO Analysis of second primary cutaneous squamous cell carcinoma (CSCC) tumors (SPTs) reported during the C-POST trial, a randomized phase III study of adjuvant cemiplimab vs placebo (pbo) for high-risk CSCC. <i>Ann Oncol</i> . 2025;36(suppl 2):S884.	<a href="https://www.annalsofoncology.org/article/S0923-7534(25)03151-5/fulltext">https://www.annalsofoncology.org/article/S0923-7534(25)03151-5/fulltext</a>

Rischin D, Porceddu SV, Day F, et al. 1660P Adjuvant cemiplimab for high-risk cutaneous squamous cell carcinoma: Evaluating dosing intervals in a phase III trial. <i>Ann Oncol</i> . 2025;36(suppl 2):S919.	<a href="https://www.annalsofoncology.org/article/S0923-7534(25)03208-9/fulltext">https://www.annalsofoncology.org/article/S0923-7534(25)03208-9/fulltext</a>
Study of Adjuvant Cemiplimab Versus Placebo After Surgery and Radiation Therapy in Patients With High Risk Cutaneous Squamous Cell Carcinoma. ClinicalTrials.gov identifier NCT03969004. Last updated September 19, 2025.	<a href="https://clinicaltrials.gov/study/NCT03969004">https://clinicaltrials.gov/study/NCT03969004</a>

### Management of Immunotherapy-Related Adverse Events

Resource	Address
National Comprehensive Cancer Network®. NCCN Clinical Practice Guidelines in Oncology. Management of Immunotherapy-Related Toxicities.	<a href="https://www.nccn.org/guidelines/guidelines-detail?category=3&amp;id=1486">https://www.nccn.org/guidelines/guidelines-detail?category=3&amp;id=1486</a>
Schneider BJ, Porceddu S, Rischin D, et al. Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: ASCO guideline update. <i>J Clin Oncol</i> . 2021;39:4073-4126.	<a href="https://pubmed.ncbi.nlm.nih.gov/34724392/">https://pubmed.ncbi.nlm.nih.gov/34724392/</a>