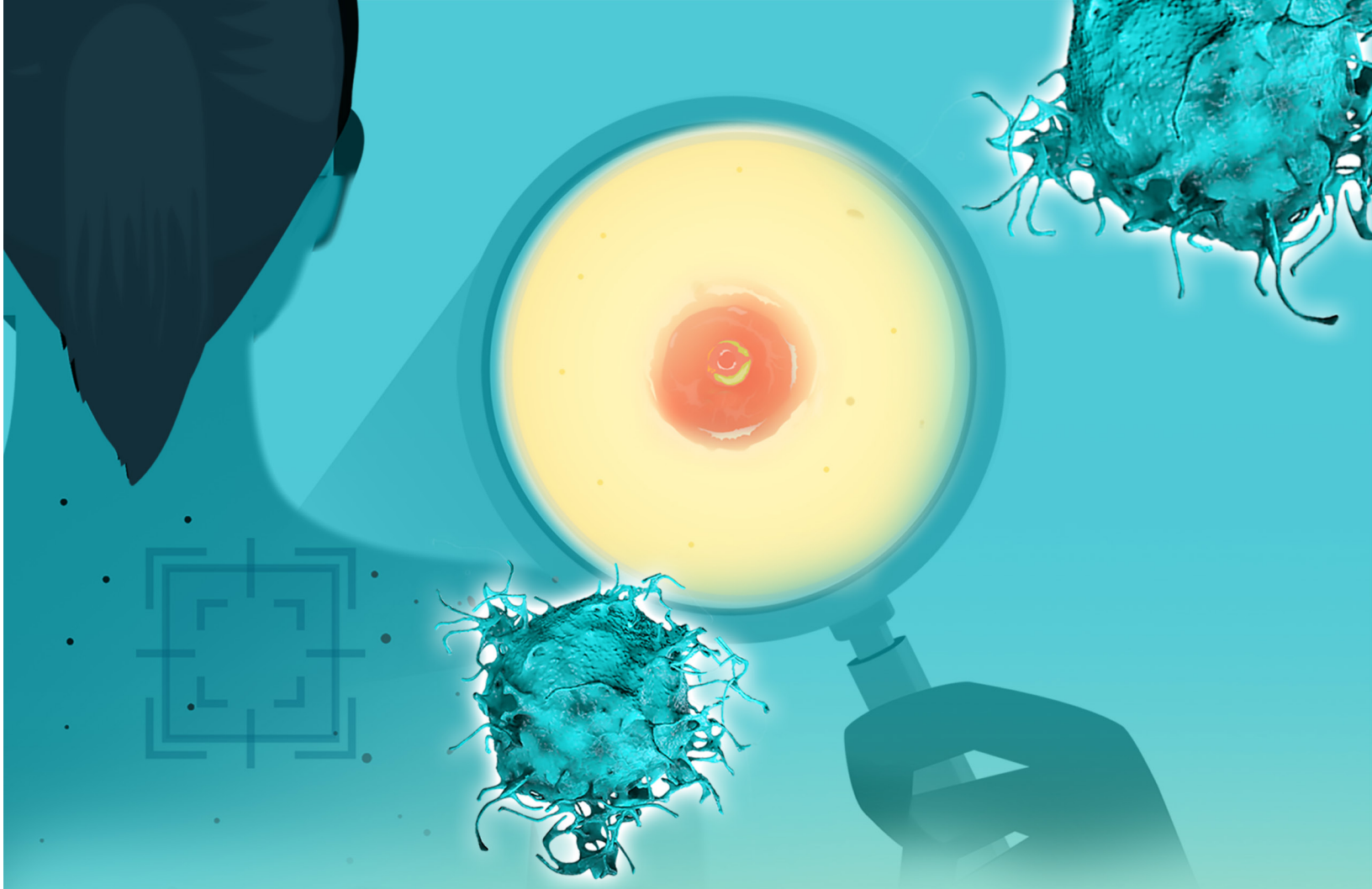

ACMS 2025:

A Tailored Approach to Non-Melanoma Skin Cancers:

Managing the High-Risk Patient With Systemic Immune-Activating Therapy

MED LEARNING GROUP

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This program is supported by an independent educational grant from Regeneron Pharmaceuticals, Inc.

A Tailored Approach to Non-Melanoma Skin Cancers: Managing the High-Risk Patient With Systemic Immune-Activating Therapy

PROGRAM CHAIRS

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Washington, DC

PROGRAM OVERVIEW

This educational activity is designed for surgical dermatologists, Mohs surgeons, dermatologists, and other healthcare professionals who manage patients with advanced or metastatic basal cell carcinoma or cutaneous squamous cell carcinoma. Our goal is to help these clinicians better explain the risk assessment of patients with non-melanoma skin cancers (NMSCs) who may derive optimal benefit with new systemic therapies when compared to Mohs surgery, incorporate patient trials data for systemic immunotherapy into the treatment of both advanced cutaneous squamous cell carcinoma and basal cell carcinoma, and collaborate with other members of the NMSC healthcare team to provide a multidisciplinary approach to the development of treatment plans for individuals with high-risk NMSCs.

TARGET AUDIENCE

This activity is designed to meet the educational needs of surgical dermatologists, Mohs surgeons, dermatologists, and other healthcare practitioners who care for patients with advanced/metastatic basal cell carcinoma or cutaneous squamous cell carcinoma.

LEARNING OBJECTIVES

Upon the completion of this program, attendees should be able to:

- Explain the risk-assessment of patients with non-melanoma skin cancers who may derive optimal benefit with new systemic therapies when compared to Mohs surgery
- Incorporate patient trials data for systemic immunotherapy into the treatment of both advanced cutaneous squamous cell carcinoma and basal cell carcinoma
- Collaborate with other members of the NMSC health care team to provide a multidisciplinary approach to the development of treatment plans for individuals with high risk NMSCs

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David M. Miller, MD, PhD, FAAD	• Consulting fees/advisory board: Almirall, Bristol Myers Squibb, EMD Serono, Merck, Regeneron, Sanofi Genzyme • Contracted research: Regeneron, Kartos Therapeutics, NeoImmuneTech, Inc., Project Data Sphere • Ownership interest: Stock options from Checkpoint Therapeutics and Avstera Therapeutics
Vishal Patel, MD	• Consulting fees: Regeneron, Sun Pharma, Almirall, Biofrontera, Palvella, Replimune • Speakers bureau: Regeneron, Sun Pharma, Almirall • Contracted research: Regeneron, Phio • Ownership interest: Avstera, Thirona

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A Tailored Approach to Non-Melanoma Skin Cancers: Managing the High-Risk Patient With Systemic Immune-Activating Therapy

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Boston, Massachusetts

ACMS American College of Mohs Surgery

57TH ANNUAL MEETING

May 15-18, 2025 • Gaylord Opryland Resort

Disclosures

- **Dr Patel** discloses that he has received consulting fees from Regeneron Pharmaceuticals, Inc., Sun Pharma, Almirall, Biofrontera, Palvella Therapeutics, and Replimune; has served on the speakers' bureau for Regeneron Pharmaceuticals, Inc., Sun Pharma, and Almirall; has received research funds from Regeneron Pharmaceuticals, Inc. and Phio; and has stock options in Avstera Therapeutics and Thirona.
- **Dr Miller** discloses that he has served as consultant/on advisory board for Merck, EMD Serono, Regeneron, Sanofi Genzyme, Almirall, and Bristol Myers Squibb; has conducted contracted research for Regeneron, Kartos Therapeutics, NeoImmune Tech, Inc, Project Data Sphere; and owns stock options in Checkpoint Therapeutics and Avstera Therapeutics
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All relevant financial relationships have been mitigated
This activity is supported by an independent medical education grant from Regeneron Pharmaceuticals, Inc.

Learning Objectives

- Explain the risk assessment of patients with non-melanoma skin cancers (NMSCs) who may derive optimal benefit with new systemic therapies when compared with Mohs surgery
- Incorporate patient trials data for systemic immunotherapy into the treatment of both advanced cutaneous squamous cell carcinoma and basal cell carcinoma
- Collaborate with other members of the NMSC healthcare team to provide a multidisciplinary approach to the development of treatment plans for individuals with high-risk NMSCs

Set the Stage: Definitions

Set the Stage: Definitions

ICI	High-risk
Neoadjuvant	Locally advanced
Adjuvant	Resectable
Definitive treatment	R0/R1/R2 resection

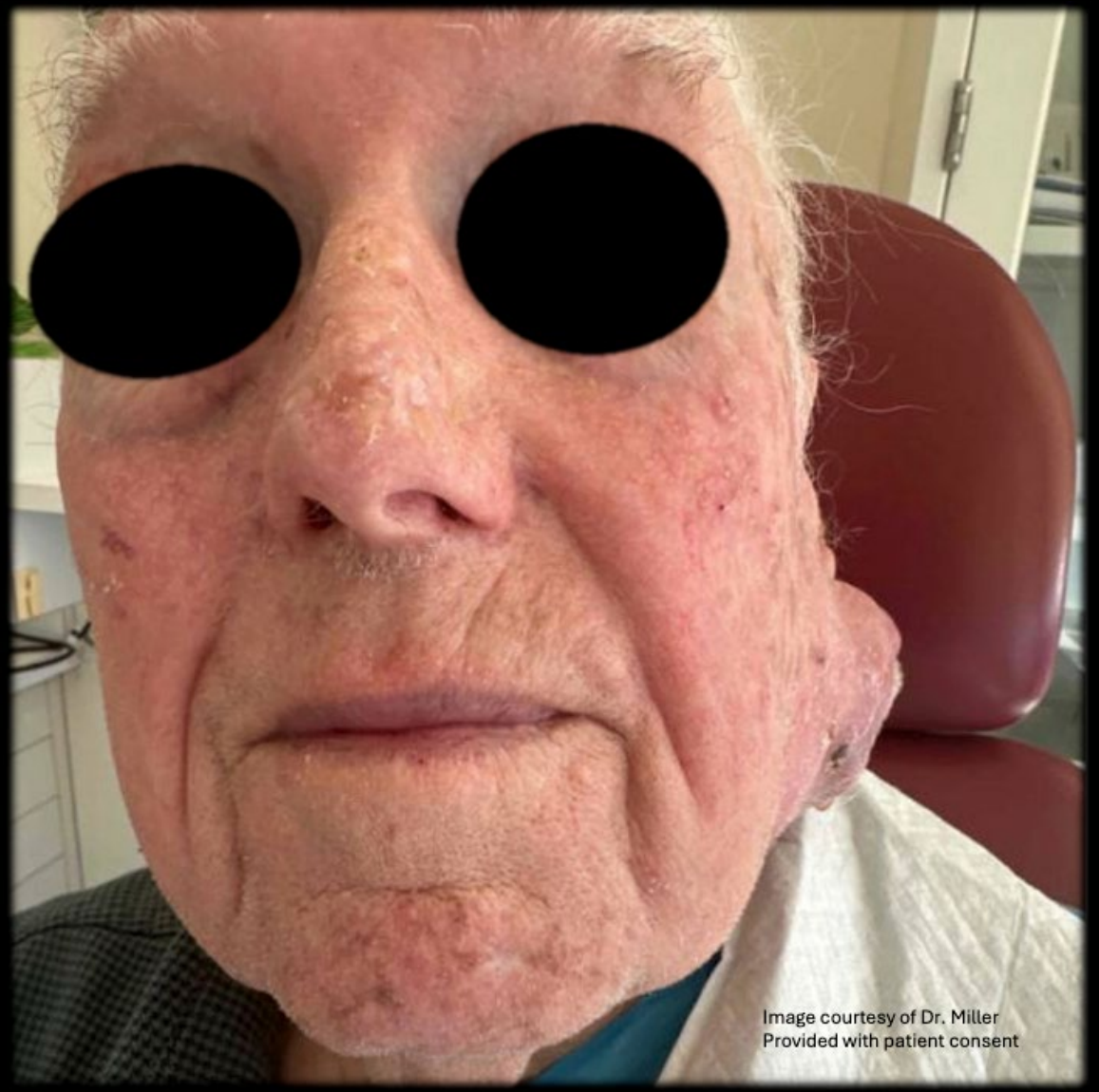
ICI = immune checkpoint inhibitor.

Case 1. Carl

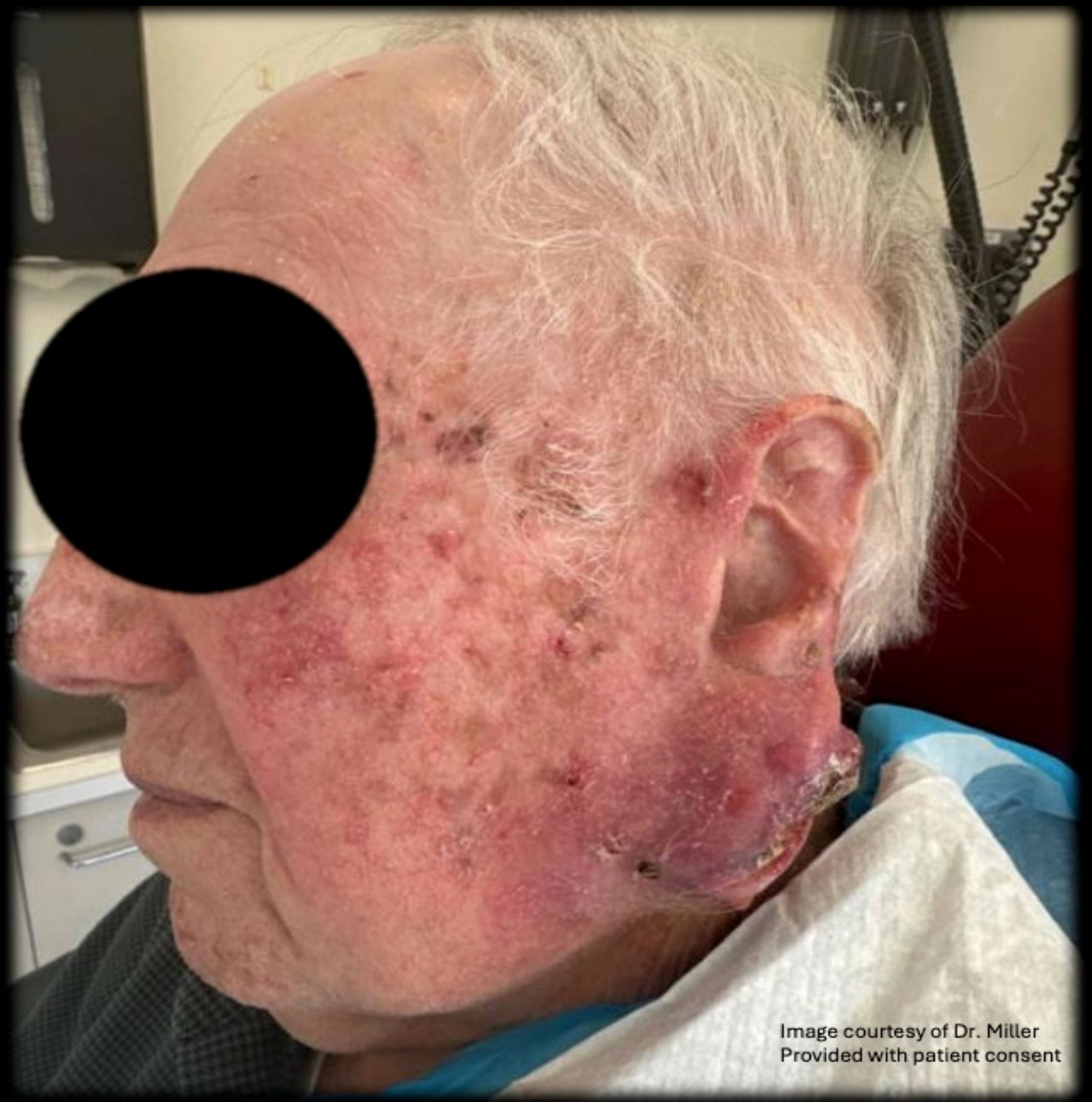
- Carl is a male in the 9th decade of life, with PMH of numerous NMSCs, Afib on coumadin, HTN, CKD, chronic bladder-outlet obstruction
- He presented to our multidisciplinary clinic with a history of several months of a growing left angle-of-jaw mass

Afib = atrial fibrillation; CKD = chronic kidney disease; HTN = hypertension; NMSC = non-melanoma skin cancer; PMH = past medical history.

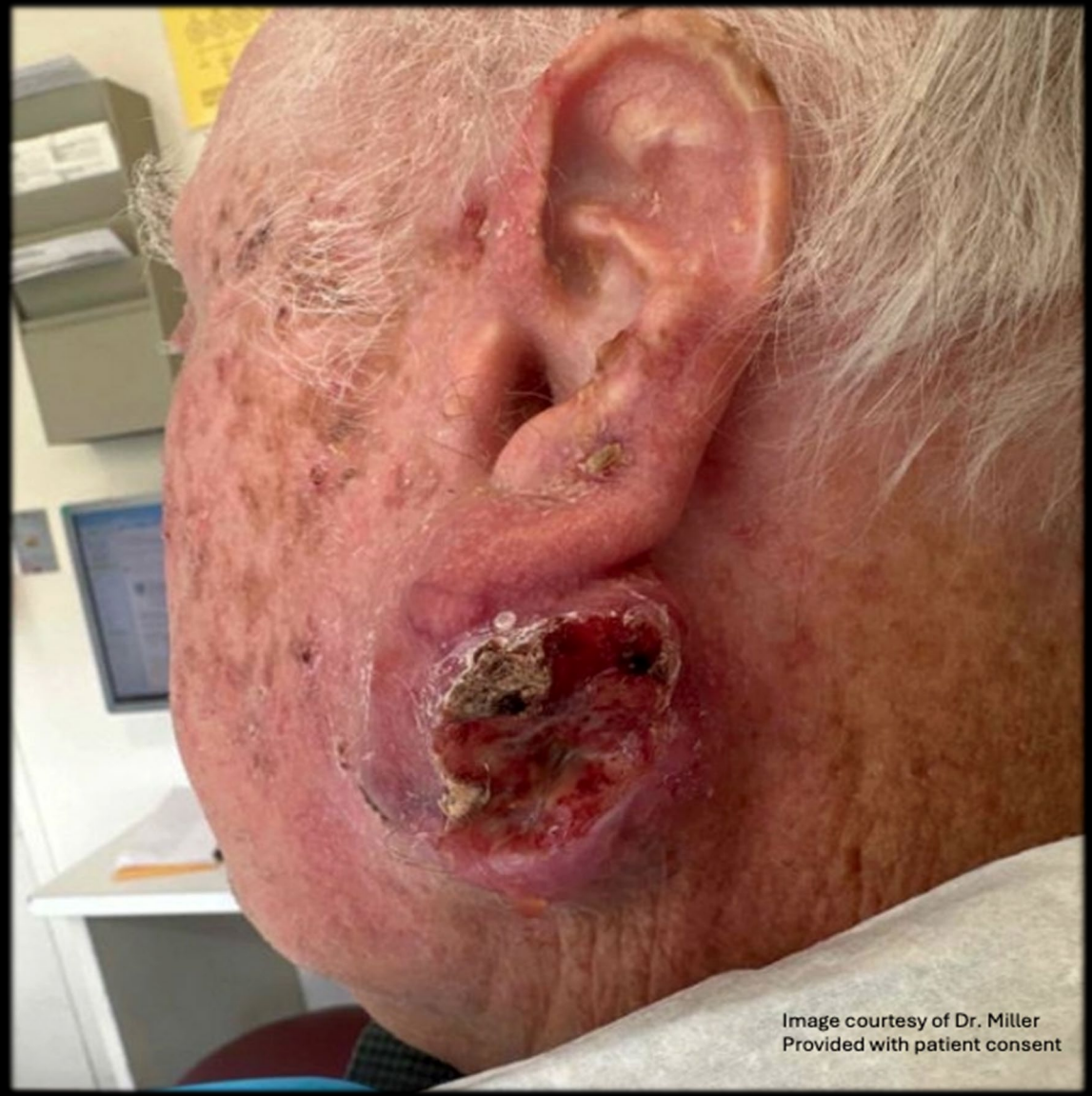
Case 1.
Carl at Presentation



Case 1. Carl at Presentation (continued 1)



Case 1. Carl at Presentation (continued 2)



Case 1. Diagnosis

- Biopsy shows squamous cell carcinoma
- Cross-sectional imaging at the time of Carl's presentation demonstrated…

Case 1. Imaging at Presentation

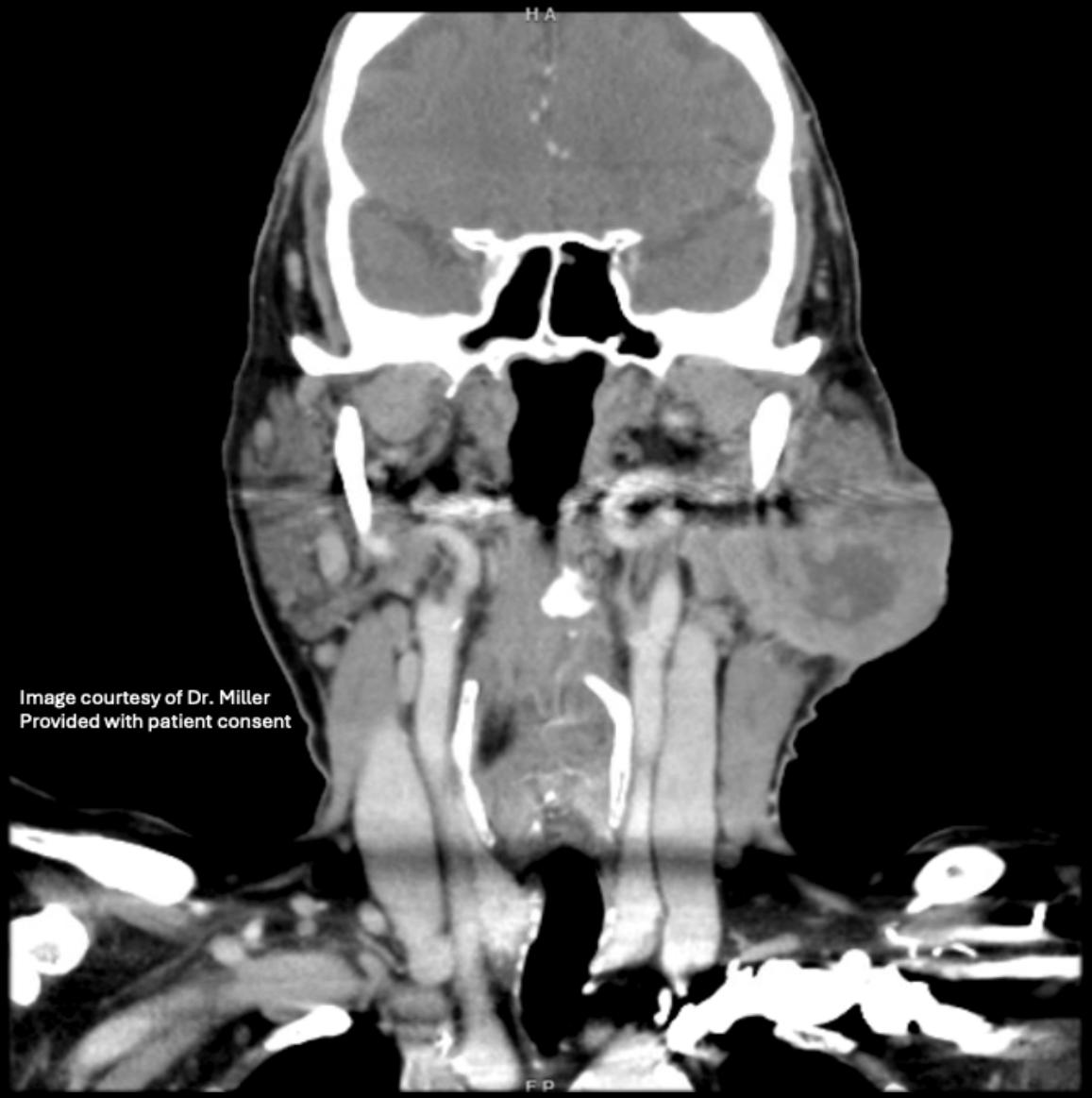


Image courtesy of Dr. Miller
Provided with patient consent

Case 1. Imaging at Presentation (continued)

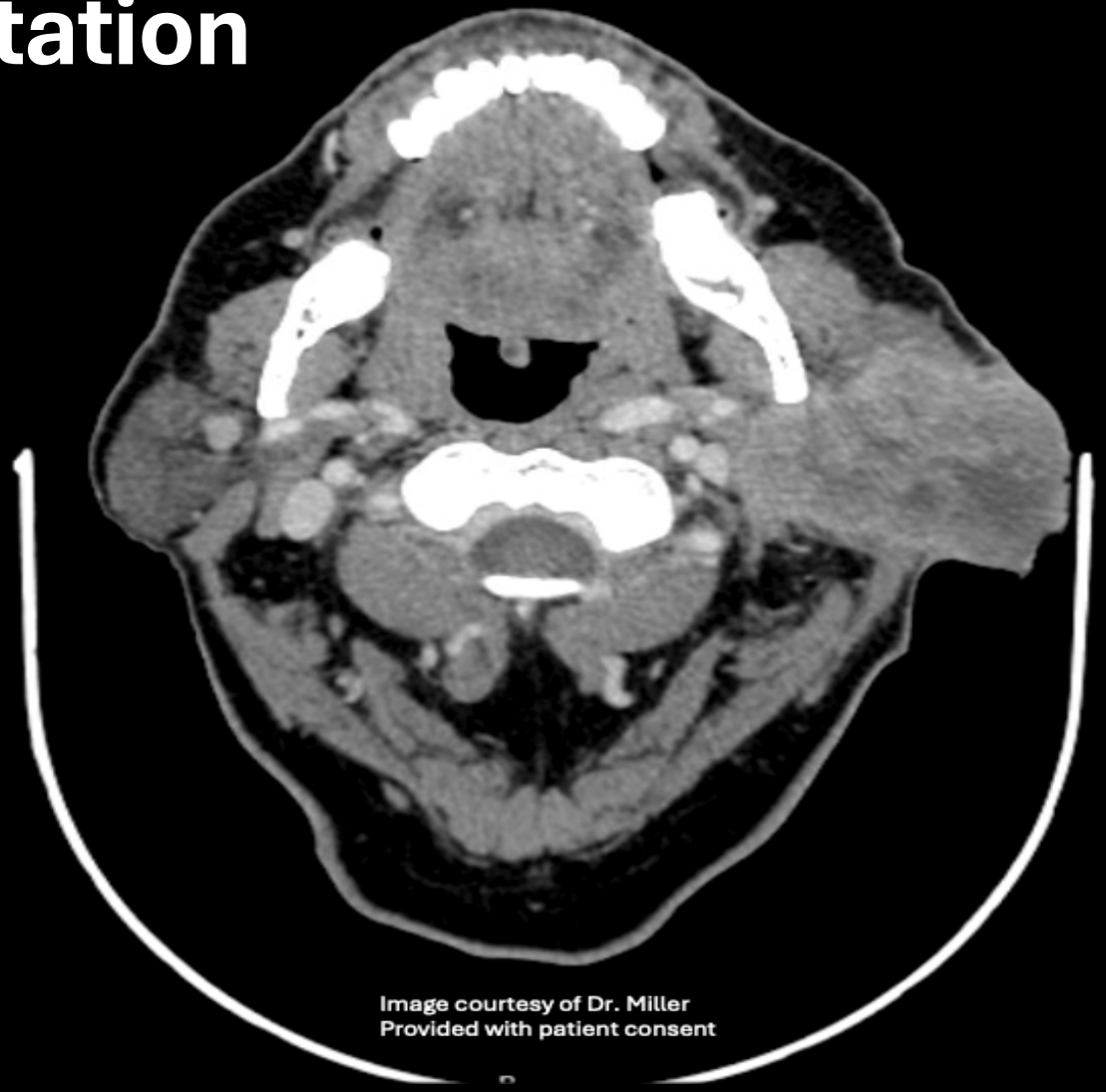


Image courtesy of Dr. Miller
Provided with patient consent

Case 1. Evaluation

There was no evidence of distant metastases

Case 1. Question for Discussion

Which specialists would you bring into the conversation to develop a treatment plan for Carl?

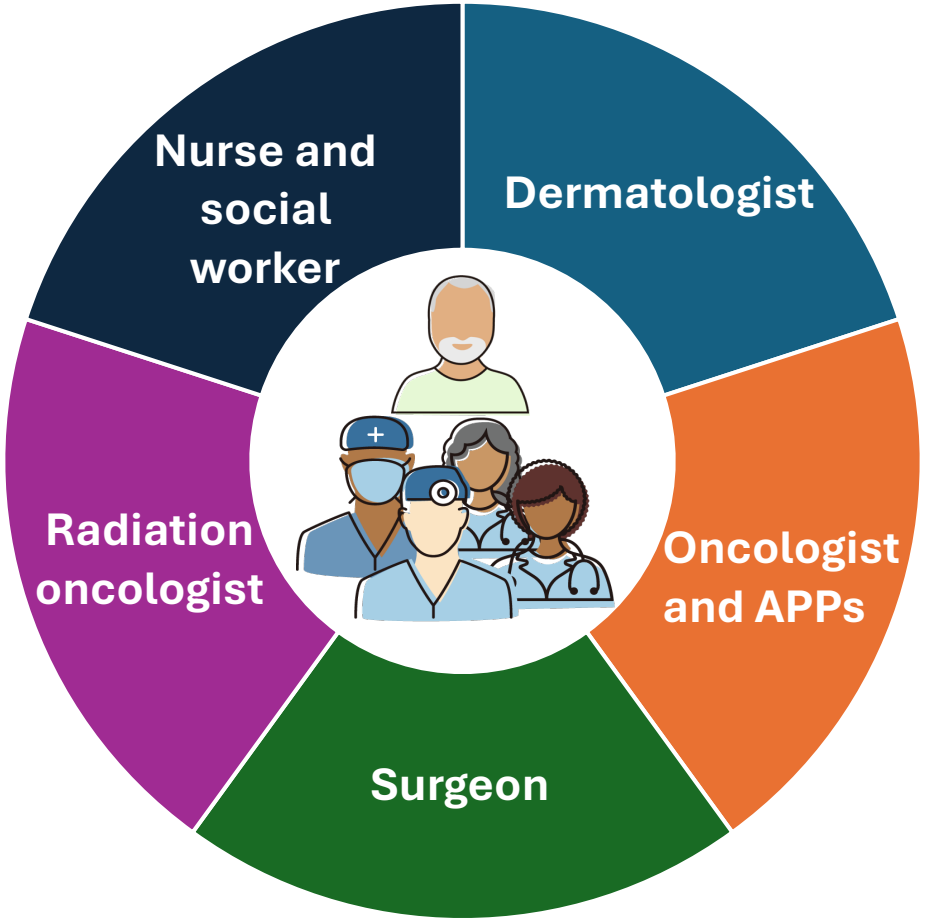
Now let's watch an animation on

Shared Decision-Making in Oncology

https://www.youtube.com/watch?v=LqbnAlWq8C4

Multidisciplinary Care in NMSC

Multidisciplinary care is critical to optimal patient management



- Advanced NMSCs are multifaceted with a wide range of presentations and responses to treatment
- Treatment requires skills and expertise across many subspecialists who need to work in coordination
- Patient perspective is important to ensure that treatment choices match patient goals of therapy

Negbenebor NA. *Cutis*. 2021;107:E22-E23.

APP = advanced practice provider.

Shared Decision-Making (SDM) in Cutaneous Malignancies

The Steps of SDM

- Invite **participation** of the patient and any chosen caregiver(s) in decision-making
- Present and discuss **options, risks, and benefits**
- Discuss the **patient's values and preferences**
- Help patients make a **decision that is consistent** with their goals and preferences

Decision aids can:

- Promote involvement in SDM
- Guide clinician/patient conversations
- Elicit patient values and preferences regarding treatment options

THINGS I MIGHT CONSIDER IN MY DECISION:

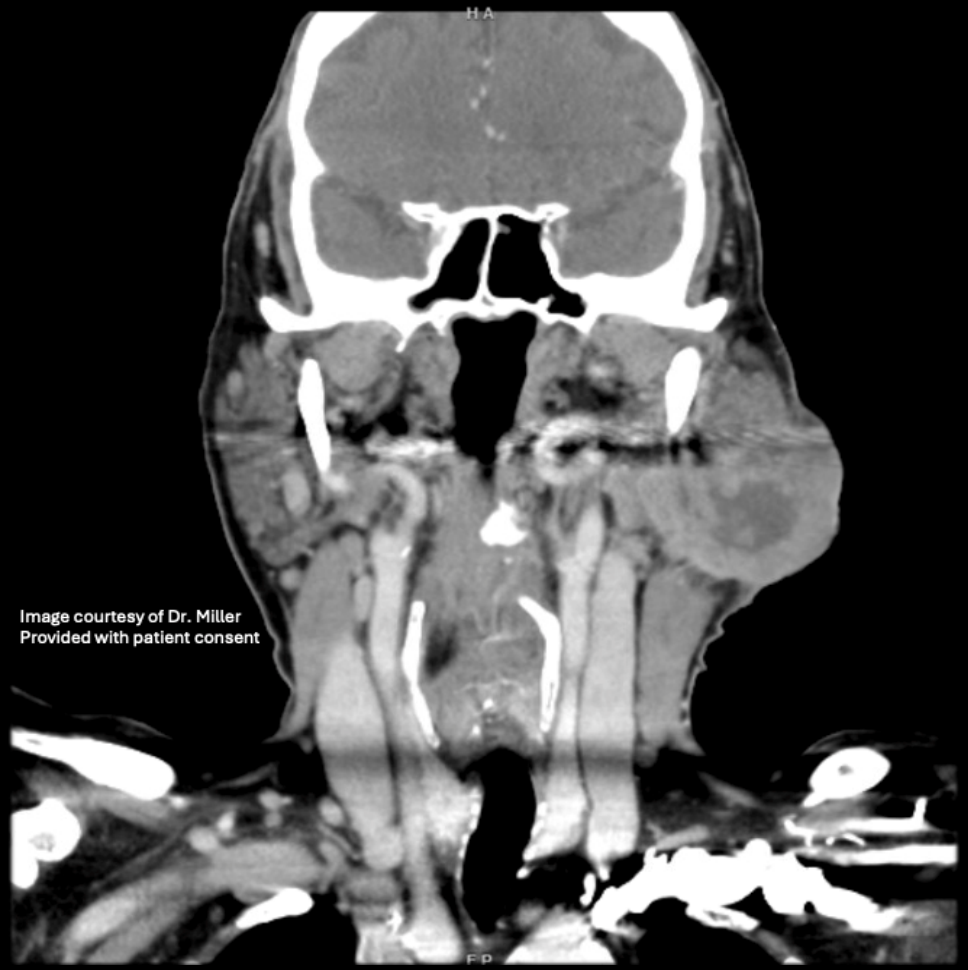
My lifestyle is:	My current health:	My social factors:	My concern for scar:	Concerns or questions about surgery:
☐ Active	☐ Few medical problems	☐ Able to care for myself	☐ Yes	☐ Yes
☐ Sedentary	☐ Many medical problems	☐ Need help caring for myself	☐ No	☐ No

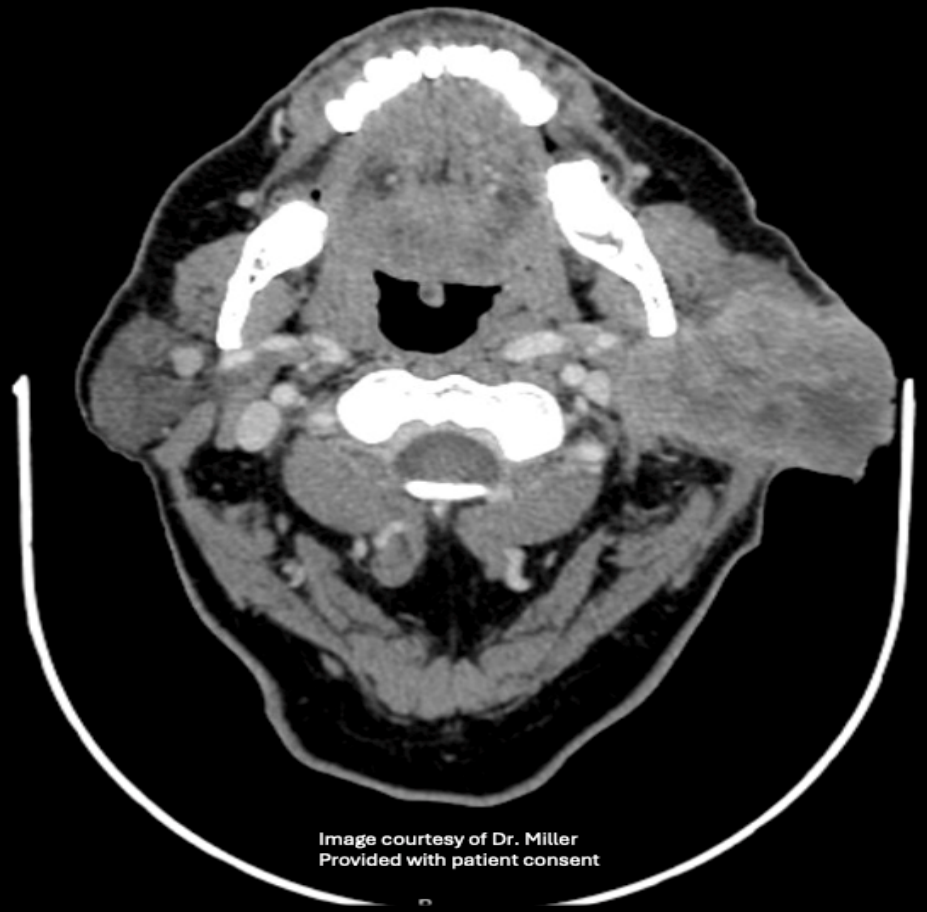
Association of Community Cancer Centers (ACCC). Shared decision-making: Practical implementation for oncology team, 2021 (www.accc-cancer.org/docs/projects/sdm/shared-decision-making-publication_final.pdf?sfvrsn= 994b7f55_0). American Society for Dermatologic Surgery (ASDS). Decision aids for low-risk BCC (www.asds.net/Portals/0/PDF/asdsa/shared-decision-making-tool-bcc.pdf). URLs accessed 4/18/25.

Case 1. Questions for Discussion

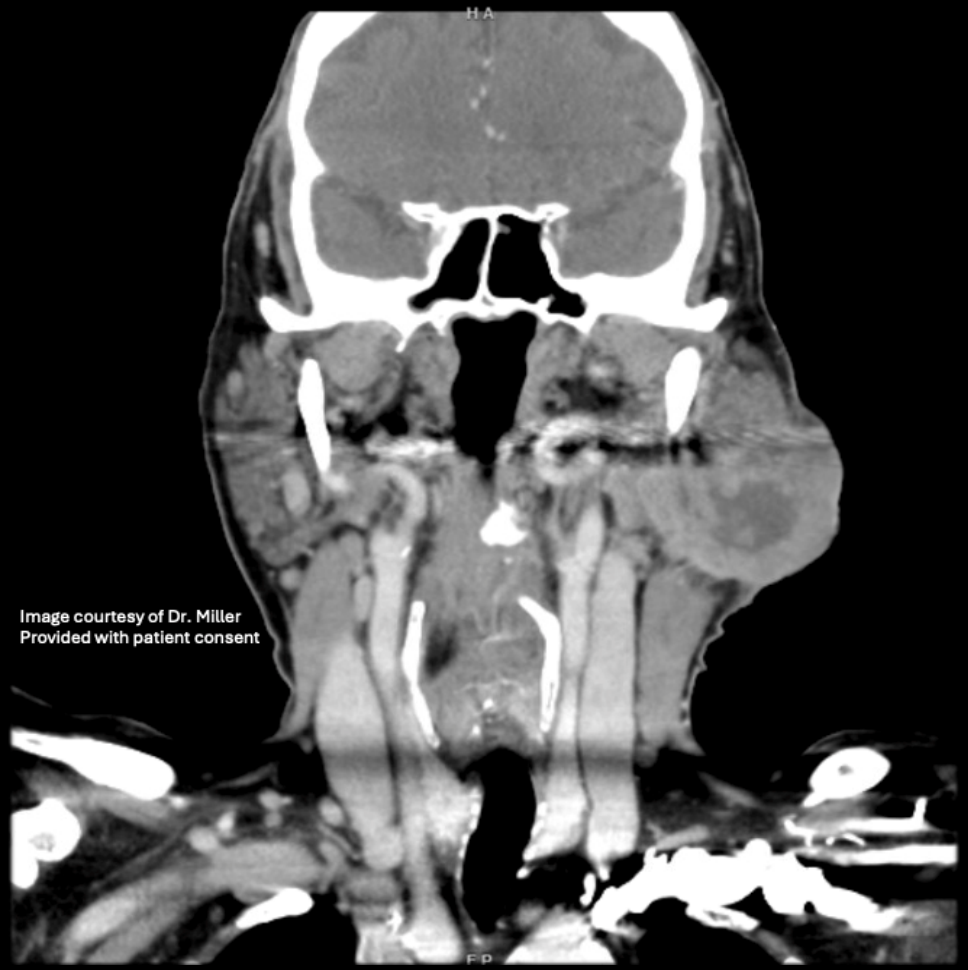
- Which specialists would you bring into the conversation to develop a treatment plan for Carl?
- How do you assess which treatment options are going to be most beneficial to Carl?

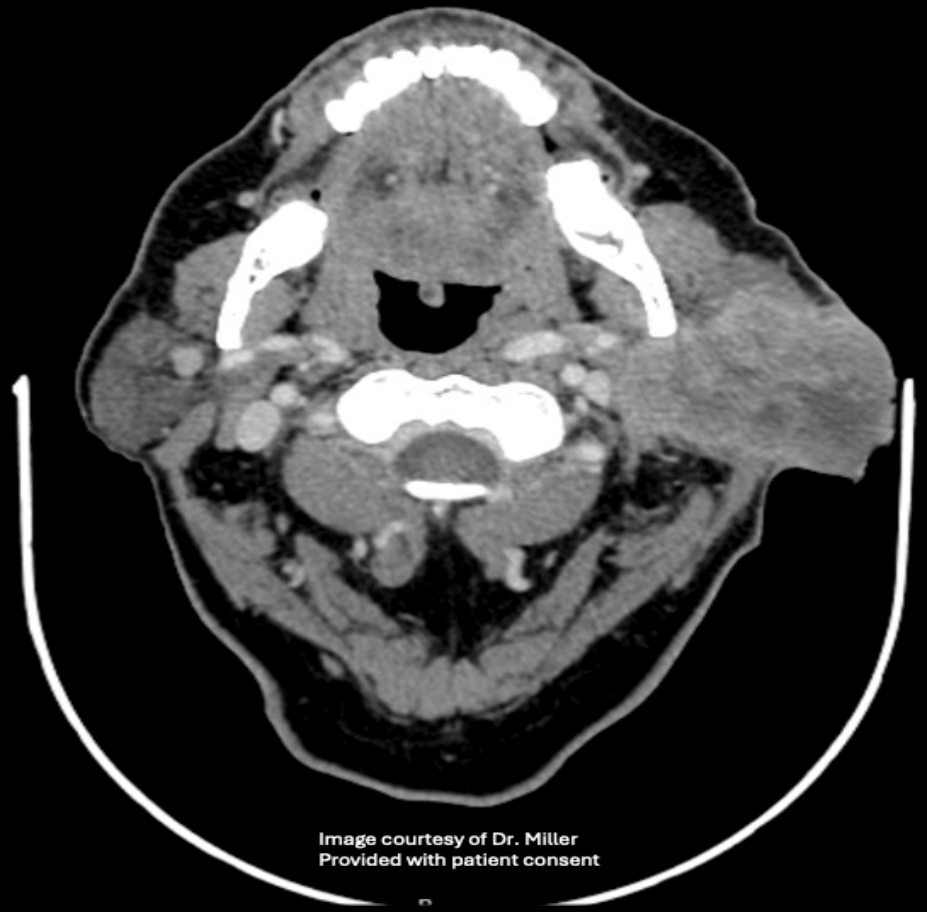
Case 1. Role of Surgery?



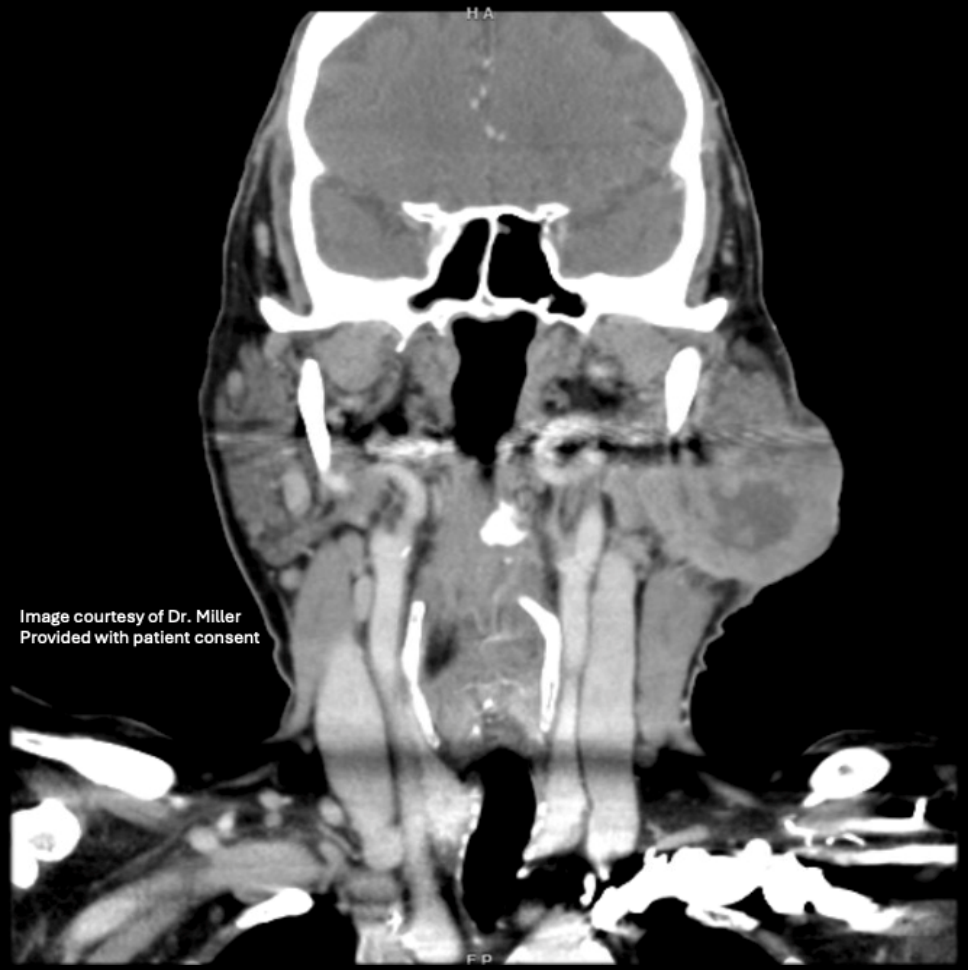


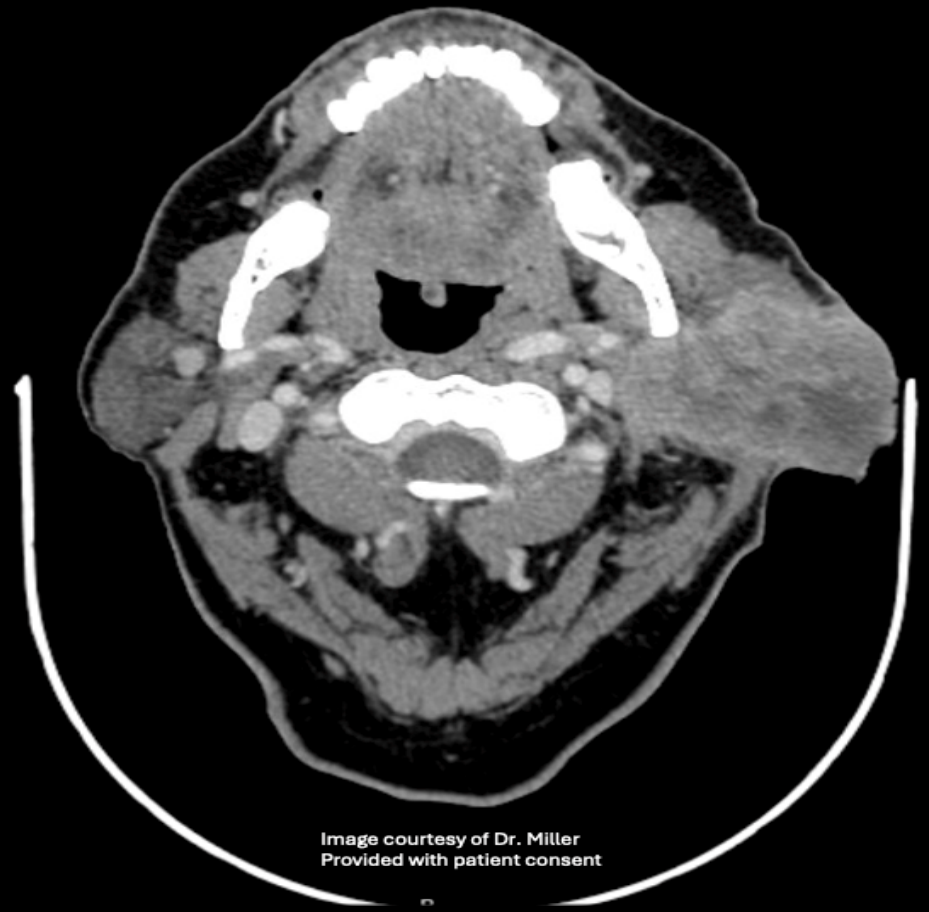
Case 1. Role of Radiation?





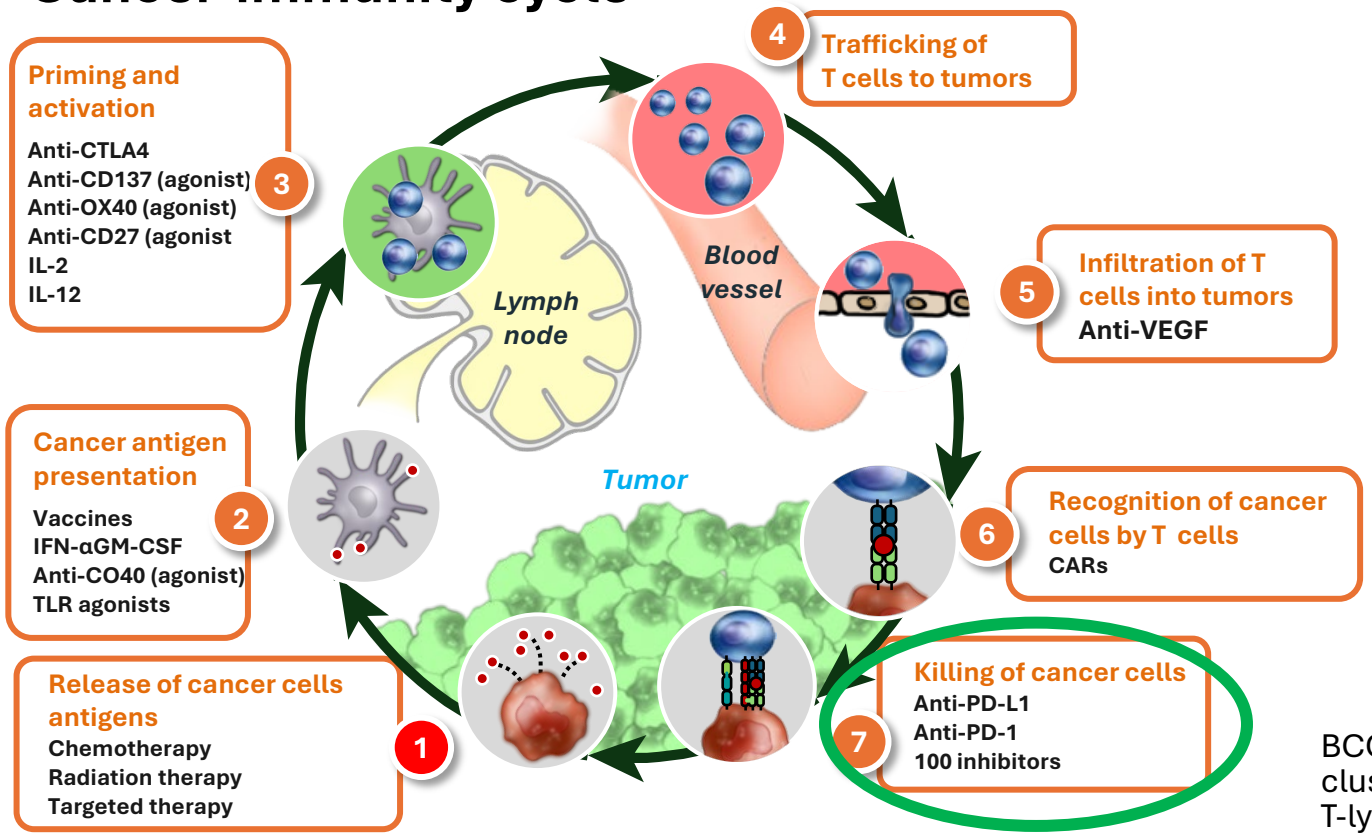
Case 1. Role of Systemic Therapy?





Rationale for PD-1 Inhibition in NMSC

Cancer-immunity cycle[1]



- High TMB in cSCC and BCC[2]
  - Other cancers → high TMB linked to better immunotherapy response
- Degree of PD-L1 expression in cSCC positively correlated to risk of metastasis[3]
- Modification of immune system (especially in solid OTRs) associated with increased risk of cSCC[4]

BCC = basal cell carcinoma; CARs = chimeric antigen receptors; CD = cluster of differentiation; CSF = colony-stimulating factor; CTLA4 = cytotoxic T-lymphocyte associated protein 4; cSCC = cutaneous squamous cell cancer; GM = granulocyte macrophage; IFN = interferon; IL = interleukin; OTR = organ transplant rejection; PD-1 = programmed (cell) death-1; PD-L1 = PD-1 ligand; TLR = toll-like receptor; TMB = tumor mutational burden; VEGF = vascular endothelial growth factor.

1. Modified from Chen DS, Mellman I. *Immunity*. 2013;39:1-10. 2. Boutros A, et al. *Front Oncol*. 2021;11:733917. 3. Slater NA, Googe PB. *J Cutan Pathol*. 2016;43: 663-670. 4. Mittal A, Colegio OR. *Am J Transplant*. 2017;17:2509-2530.

Anti-PD-1 Clinical Trial Data in Locally Advanced/Metastatic CSCC

	Cemiplimab[1–3]	Pembrolizumab[4,5]	Cosibelimab[6]
Phase (design)	2 (3 cohorts: 1 locally advanced and 2 metastatic)	2 (2 cohorts: recurrent/ metastatic and locally advanced)	1 (2 cohorts: metastatic and locally advanced)
Patients, n	193	159	109
Extent of disease	Locally advanced = 40% Metastatic = 60%	Locally advanced = 34% Locoregional only = 30%; Distant only = 16%; Combination = 21%	Locally advanced = 72% Metastatic = 28%
Primary endpoint	ORR	ORR	ORR
Follow-up (median)	22.4 mos	33 mos, 21 mos	33 mos, 21 mos
ORR, %	62	r/m = 35.2, la = 50	met = 47, la = 48
CR, %	22	r/m = 10.5, la = 16.7	met = 8, la = 10
PR, %	40	r/m = 24.8, la = 33.3	met = 10, la = 39

CR = complete response; la = locally advanced; met = metastatic; ORR = objective/overall response rate; PR = partial response; r/m = recurrent/metastatic.

1. Rischin D, et al. *J Clin Oncol*. 2020;38(15 suppl): abstract 10018. 2. Rischin D, et al. *J Immunother Cancer*. 2021;9:e002757. 3. Rischin D, et al. *J Immunother Cancer*. 2024;12:e008325. 4. Grob J-J. *J Clin Oncol*. 2020;38:2916-2925. 5. Hughes BGM, et al. *Ann Oncol*. 2021;32 :1276-1285. 6. FDA. FDA approves cosibelimab-ipdl for metastatic or locally advanced cutaneous squamoud cell carcinoma. (https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-cosibelimab-ipdl-metastatic-or-locally-advanced-cutaneous-squamous-cell-carcinoma). URLs accessed April 29, 2025.

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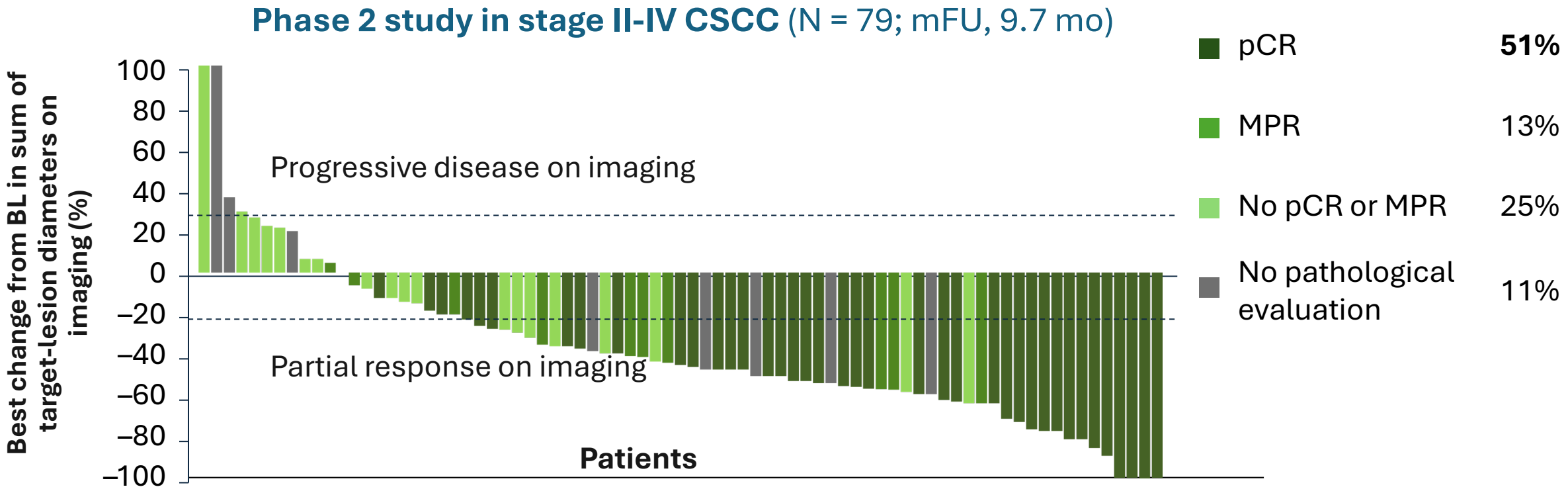
ICIs In the Preoperative Period

Neoadjuvant Immunotherapy for CSCC:
Tumor Response Rate With Cemiplimab

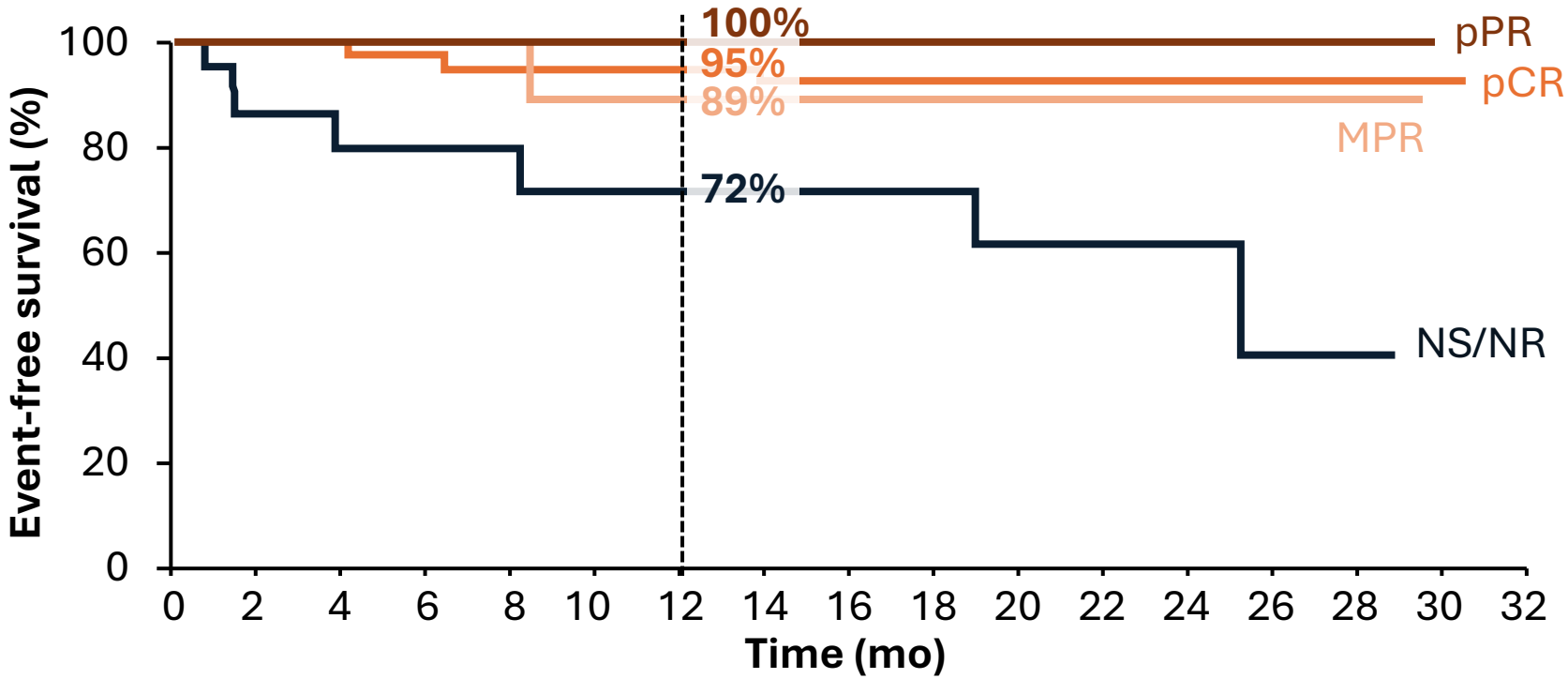


BL = baseline; mFU = median follow-up; MPR = major pathological response (presence of viable tumor cells constituting ≤10% of surgical specimen; pCR = pathological complete response (absence of viable tumor cells in surgical specimen). Cemiplimab is not FDA-approved for this indication.

Gross ND, et al. *N Engl J Med*. 2022;387:1557-1568.

Neoadjuvant Immunotherapy for CSCC:
Event-Free Survival With Cemiplimab

Phase 2 study in stage II-IV CSCC (N = 79; mFU, 18.7 mo)



Post-surgery, 60% of patients with pCR received no adjuvant treatment

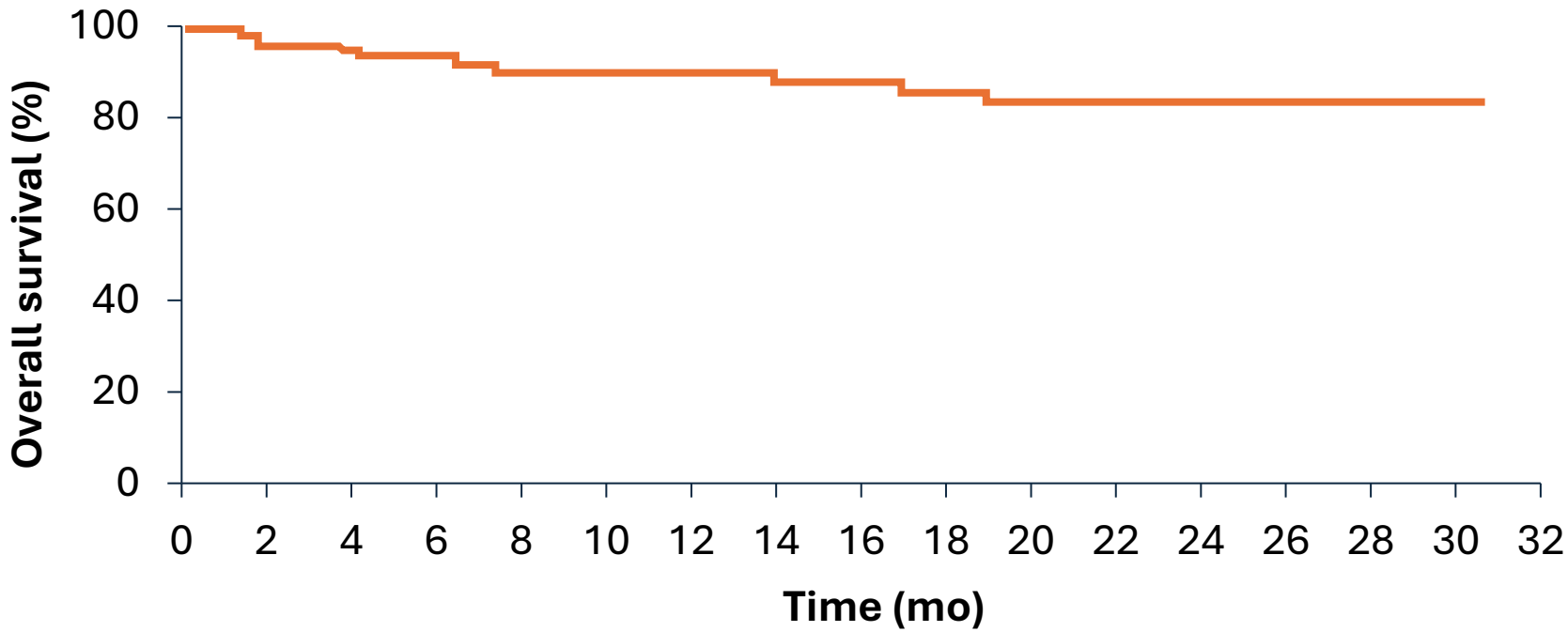
NR = No response; NS = No surgery; pPR: pathologic partial response.
Cemiplimab is not FDA-approved for this indication.

Gross ND, et al. *Lancet Oncol*. 2023;24:1196-1205.

No patients achieving pCR had disease recurrence; 3 patients died.
9 patients had no surgery; 13 patients had no response.

Neoadjuvant Immunotherapy in CSCC:
Overall Survival With Cemiplimab

Phase 2 study in stage II-IV CSCC (N = 79; mFU, 18.7 mo)

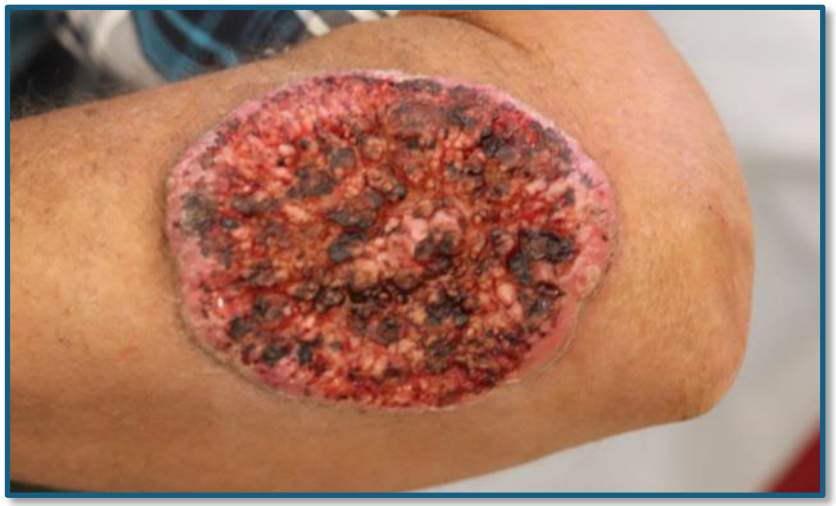


Median survival was not reached

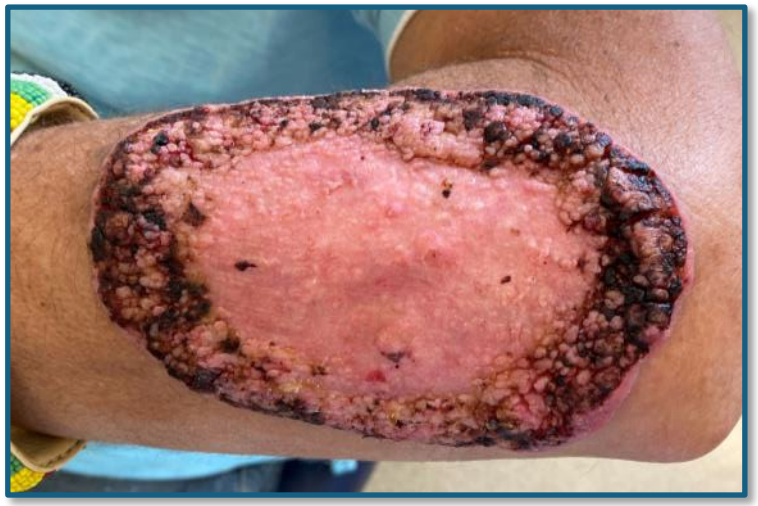
Cemiplimab is not FDA-approved for this indication.

Gross ND, et al. *Lancet Oncol*. 2023;24:1196-1205.

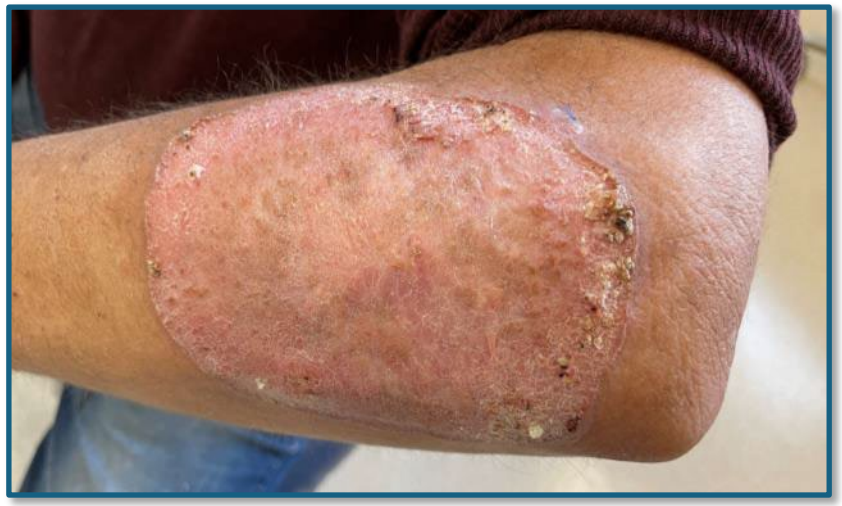
Clinical Trial Example



Baseline



S/p 2 doses of cemiplimab

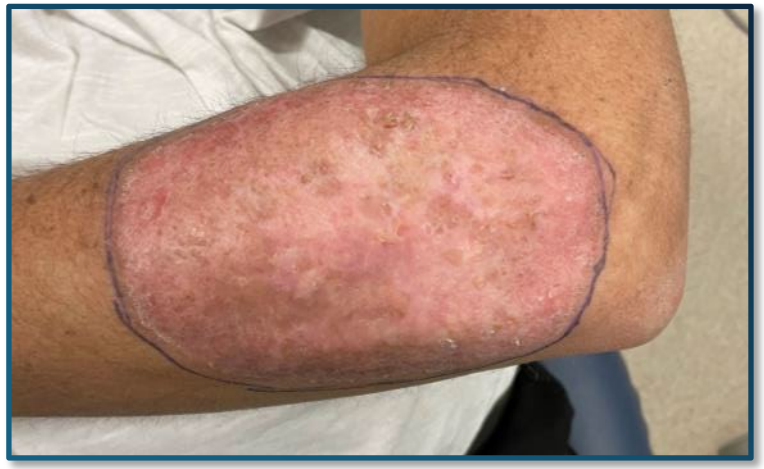


S/p 3 doses of cemiplimab

Cemiplimab is not FDA-approved for this indication.

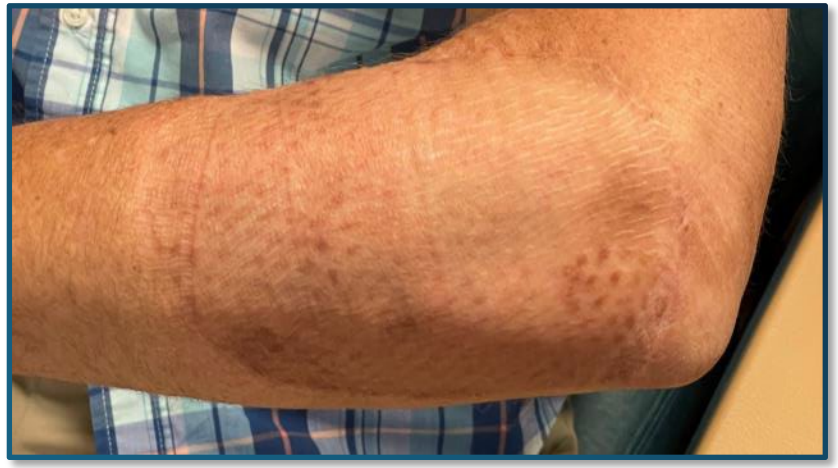
S/p = status post.

Clinical Trial Example
(continued)



S/p 4 doses of cemiplimab

S/p MMS resection



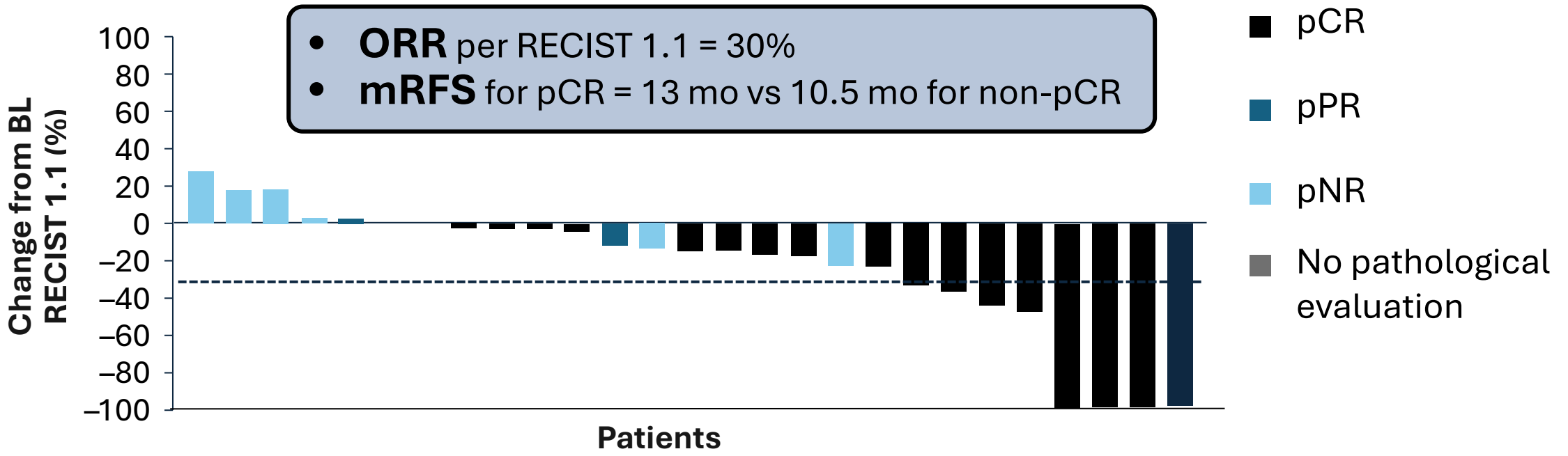
S/p STSG repair

Cemiplimab is not FDA-approved for this indication.

MMS = Mohs micrographic surgery; STSG = split-thickness skin graft.

Neoadjuvant Immunotherapy in CSCC:
Response Rate With Pembrolizumab

Phase 2 study in PD-1 naïve resectable locally advanced CSCC (N = 26

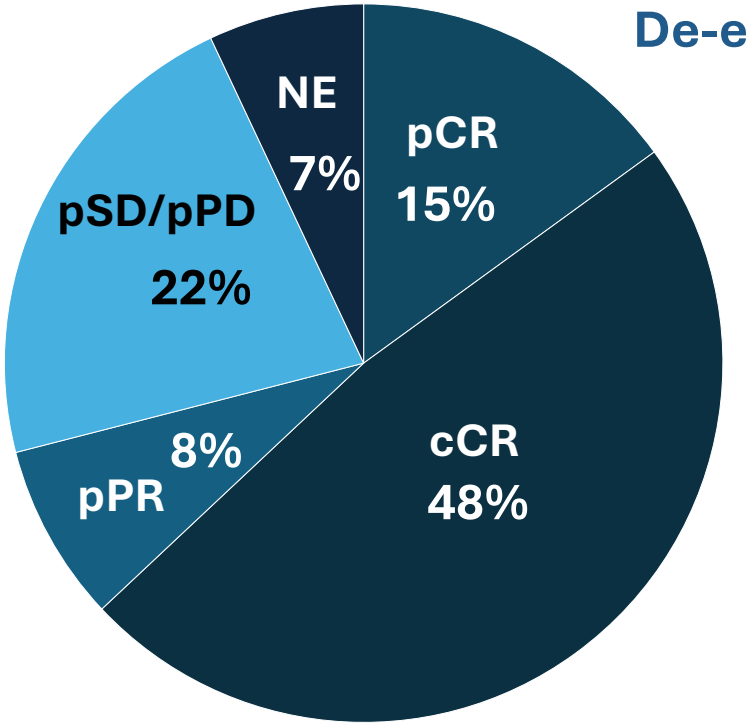


mRFS = median relapse-free survival; pNR = pathological nonresponse; RECIST = Response Evaluation in Solid Tumors. Pembrolizumab is not FDA-approved for this indication.

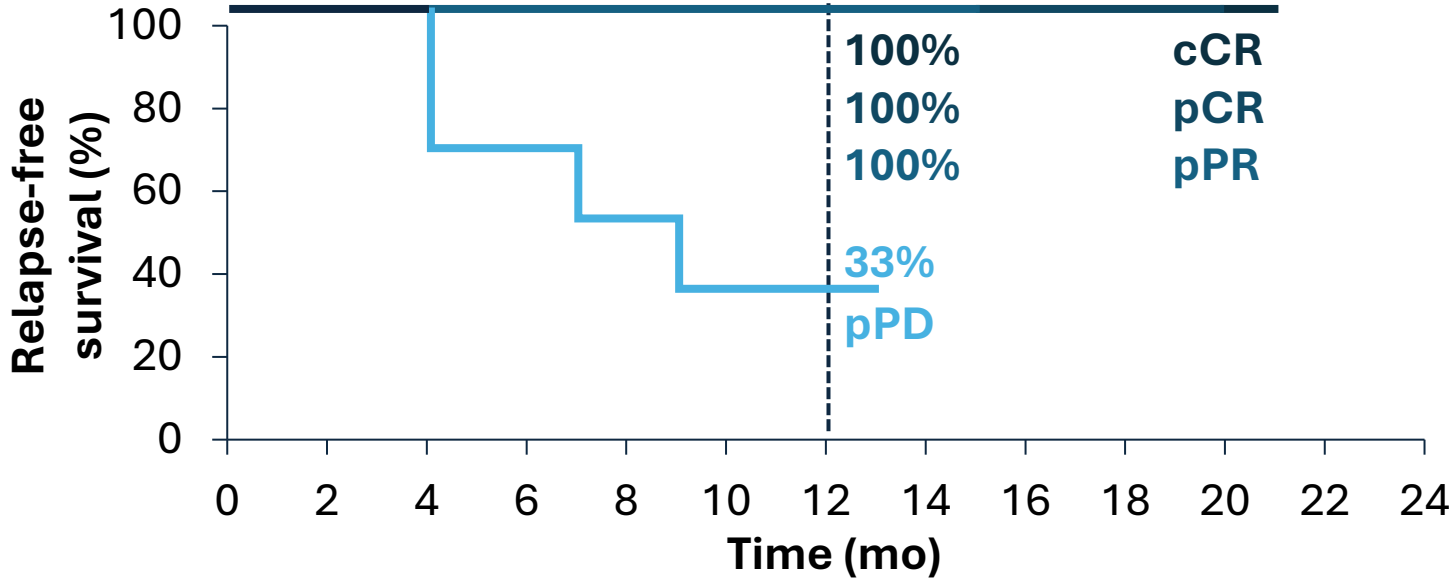
Amatore F, et al. American Society of Clinical Oncology (ASCO) 2024. Poster 9591.

Neoadjuvant Immunotherapy in CSCC:
Relapse-Free Survival With Pembrolizumab

De-Squamate: Phase 2 study in resectable locally advanced CSCC (N = 27; minimum FU = 6 mo)



De-escalation of surgery or radiotherapy in 63%



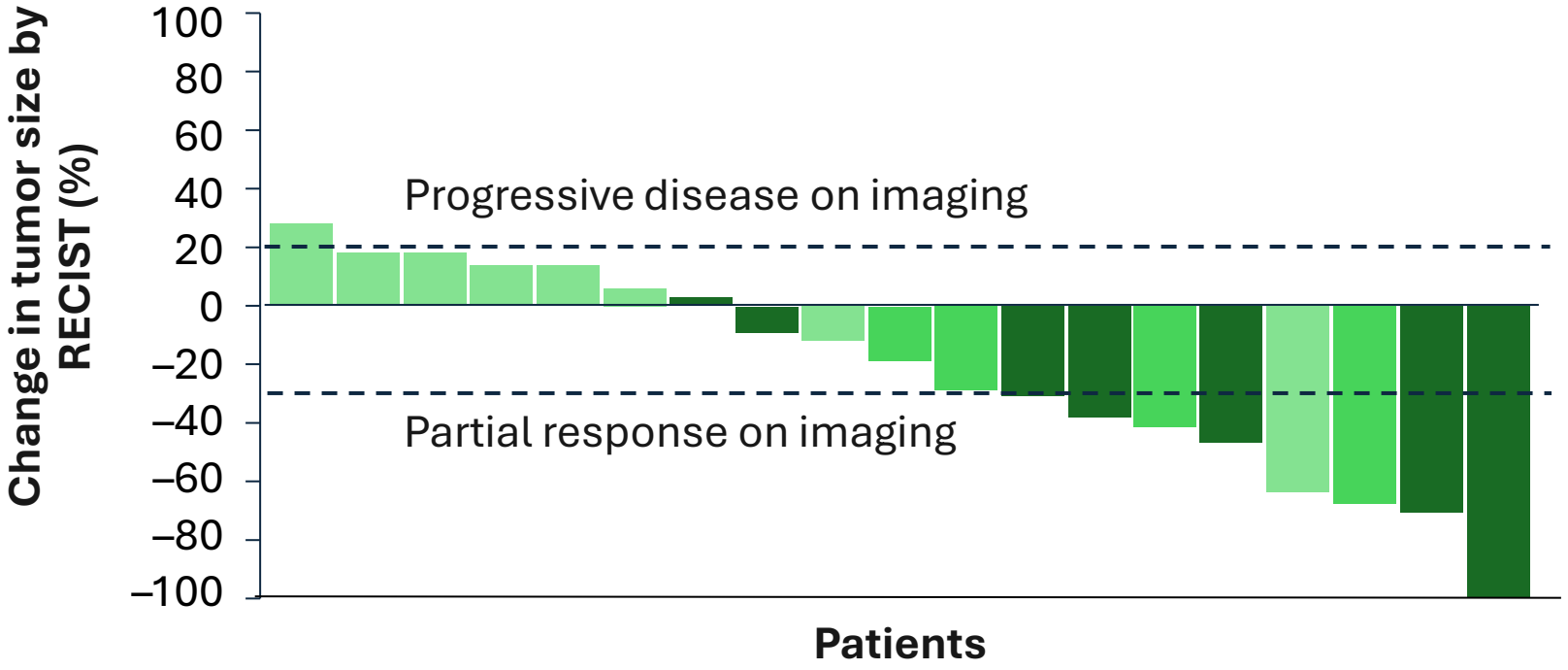
Pembrolizumab is not FDA-approved for this indication.

Ladwa R, et al. *J Clin Oncol*. 42(16 suppl): abstract 9514.

cCR = clinical complete response; NE = not evaluable; pPD = pathologic progressive disease; pSD = pathologic stable disease.

Neoadjuvant Immunotherapy in CSCC:
Efficacy With Atezolizumab

Phase 2 study in resectable stage III-IV CSCC or stage II CSCC for which standard therapy would incur an unacceptable morbidity (N = 20; mFU = 14 mo)



pCR	**35%**
MPR	20%
No pCR or MPR	40%

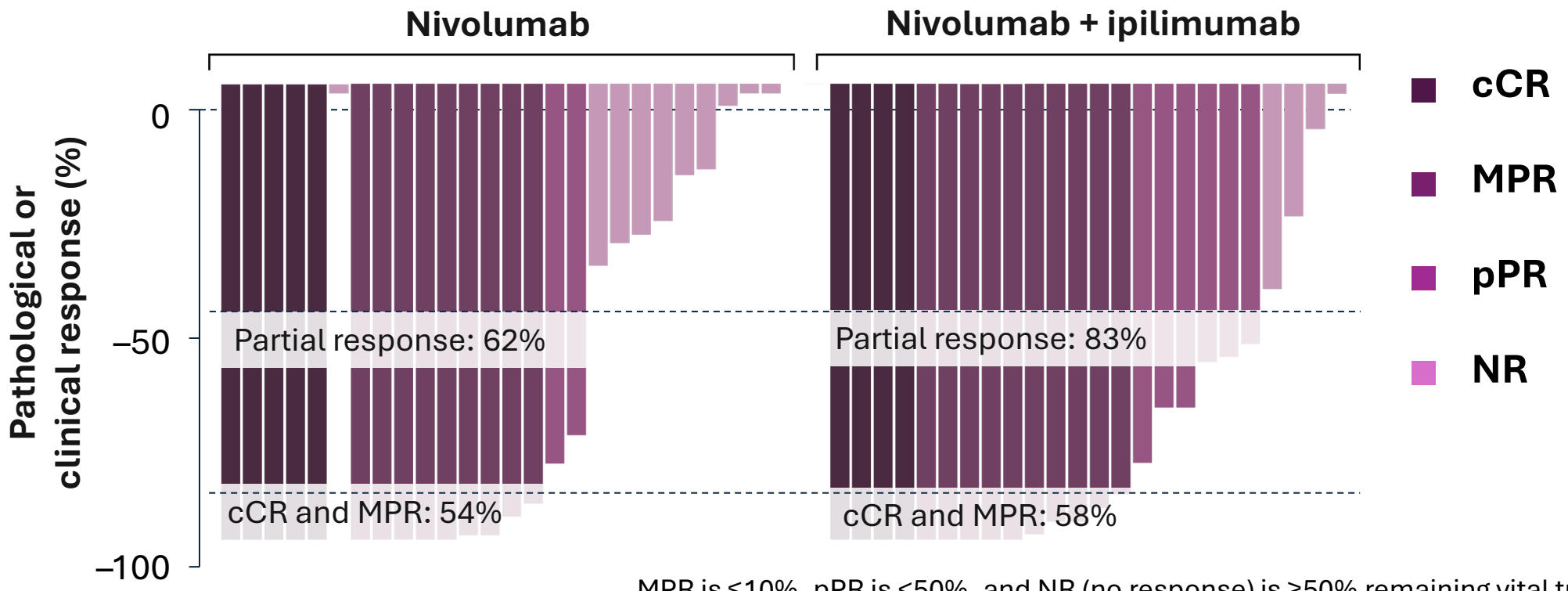
CR in 1 patient (5%)

CR = complete response.

Divi V, et al. *JCO Oncol Adv*. 2024;1:e2400058.

Neoadjuvant Immunotherapy in CSCC:
Responses With Nivolumab ± Ipilimumab

MATISSE: Phase 2 study in stage I-IVa CSCC (N = 50; mFU, 14 mo)

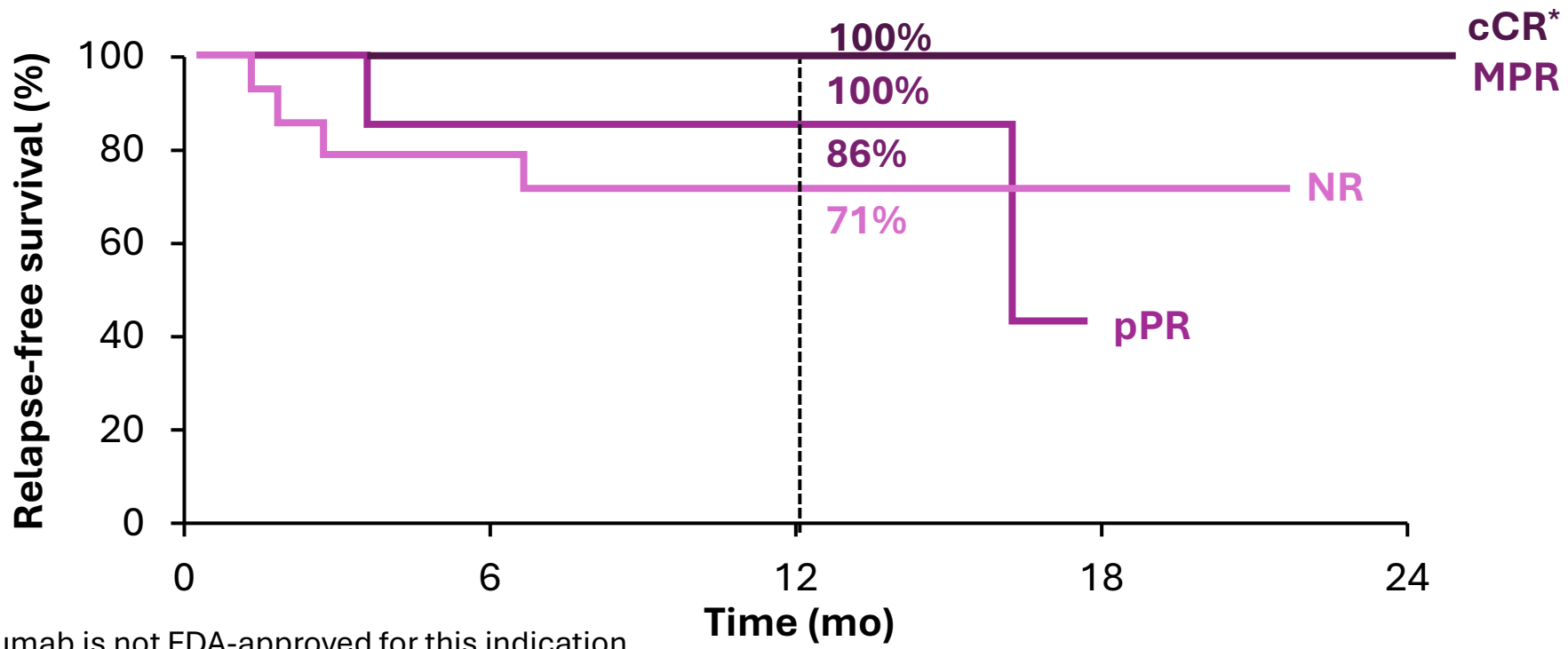


MPR is ≤10%, pPR is <50%, and NR (no response) is ≥50% remaining vital tumor cells in surgical resection specimen. Nivolumab ± ipilimumab is not FDA-approved for this indication.

Zuur CL, et al. *J Clin Oncol.* 2023;41(16 suppl): abstract 9507.

Neoadjuvant Immunotherapy in CSCC:
RFS With Nivolumab ± Ipilimumab

MATISSE: Phase 2 study in stage I-IVa CSCC (N = 50; mFU, 14 mo)



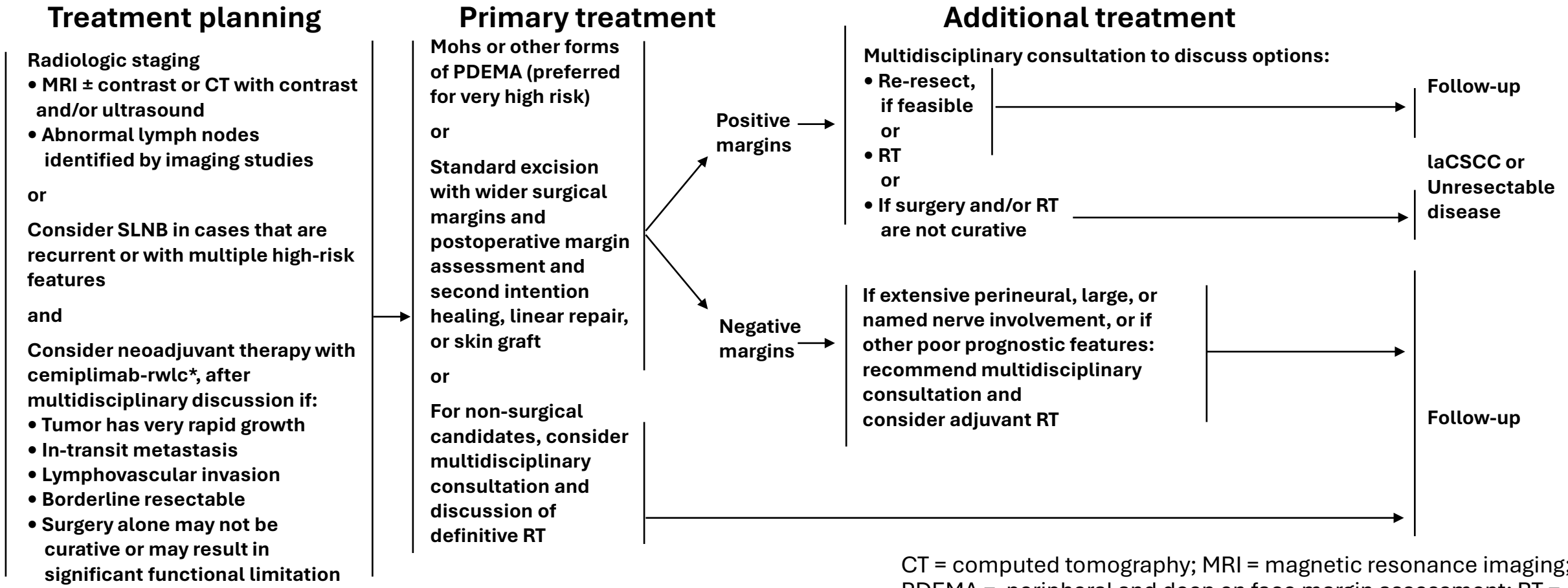
Nivolumab ± ipilimumab is not FDA-approved for this indication.

Zuur CL, et al. *J Clin Oncol.* 2023;41(16 suppl): abstract 9507.

*18-month follow-up; others are 13-month follow-up.

What does this all mean?

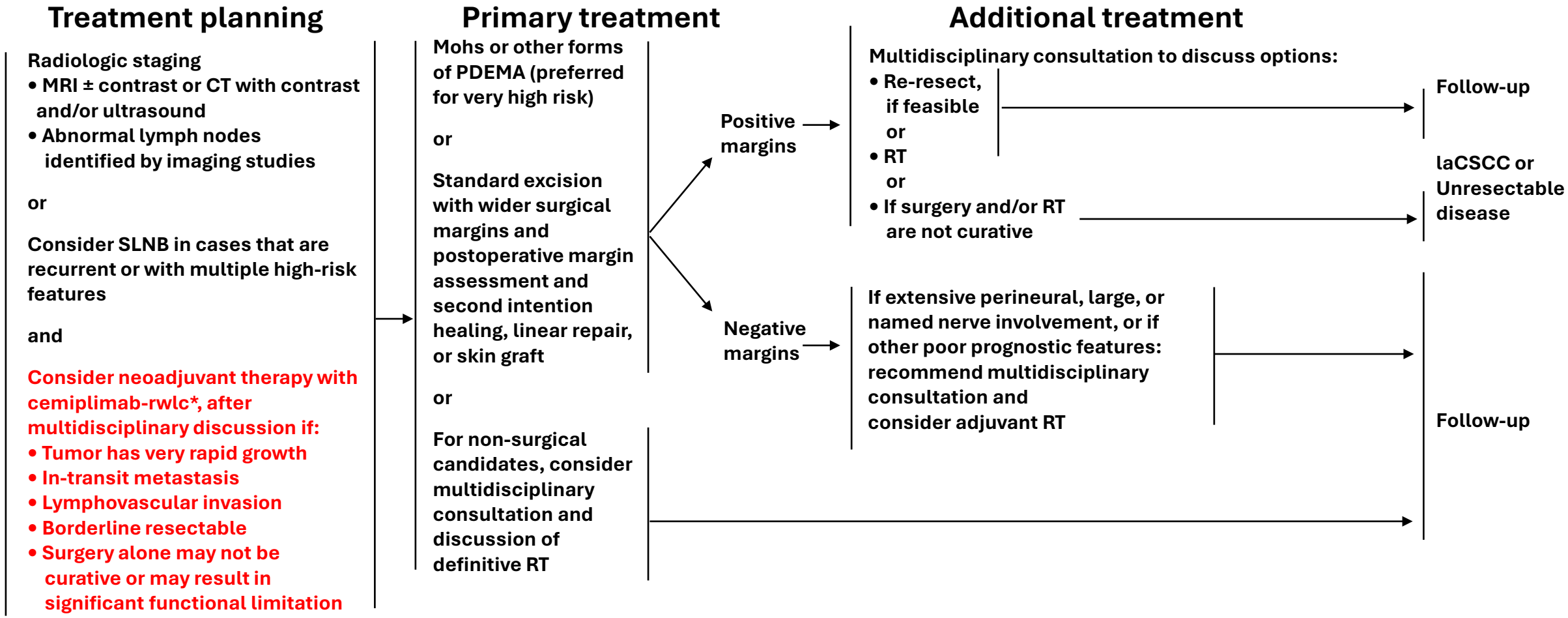
Guidelines for Very-High-Risk CSCC



Modified from National Comprehensive Cancer Network (NCCN). Squamous cell skin cancer. Ver 2.2025 (www.nccn.org/professionals/physician_gls/pdf/squamous.pdf). Accessed 4/18/25.

CT = computed tomography; MRI = magnetic resonance imaging; PDEMA = peripheral and deep en face margin assessment; RT = radiation therapy; SLNB = sentinel lymph node biopsy.
*Cemiplimab is not FDA-approved for this indication.

Guidelines for Very-High-Risk CSCC (continued 1)



Modified from National Comprehensive Cancer Network (NCCN). Squamous cell skin cancer. Ver 2.2025

*Cemiplimab is not FDA-approved for this indication.

Guidelines for Very-High-Risk CSCC (continued 2)

Consider neoadjuvant therapy with cemiplimab-rwlc, after multidisciplinary discussion if:

- Tumor has very rapid growth
- In-transit metastasis
- Lymphovascular invasion
- Borderline resectable
- Surgery alone may not be curative or may result in significant functional limitation

NCCN. Squamous cell skin cancer. Version 2.2025

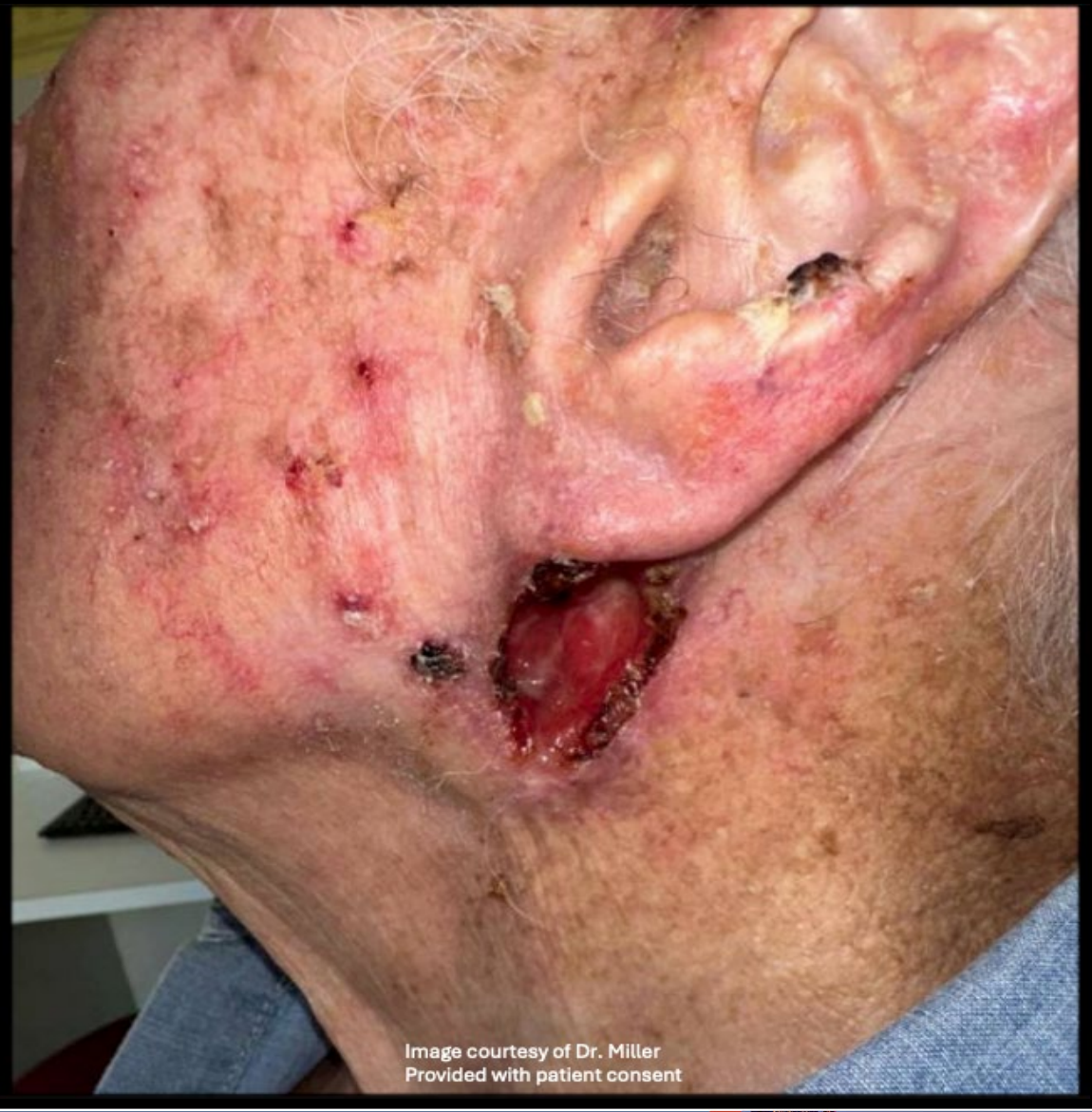
Return to Our First Case

Case 1. Immunotherapy

- Carl started on anti-PD-1 immunotherapy
- After 2 doses, he presents to multidisciplinary clinic

Case 1. After 2 Doses of Anti-PD-1 Immunotherapy

Case 1. After 2 Doses of Anti-PD-1 Immunotherapy (continued 1)



Case 1. After 2 Doses of Anti-PD-1 Immunotherapy (continued 2)

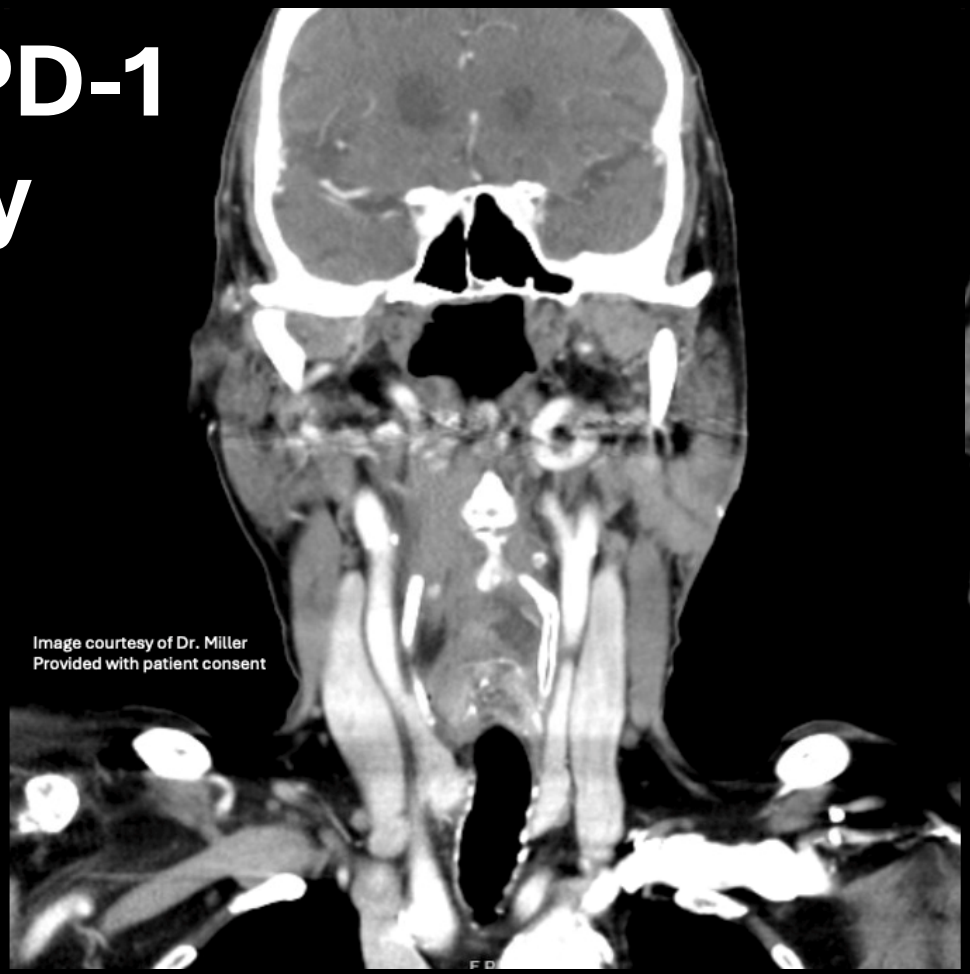


Image courtesy of Dr. Miller
Provided with patient consent

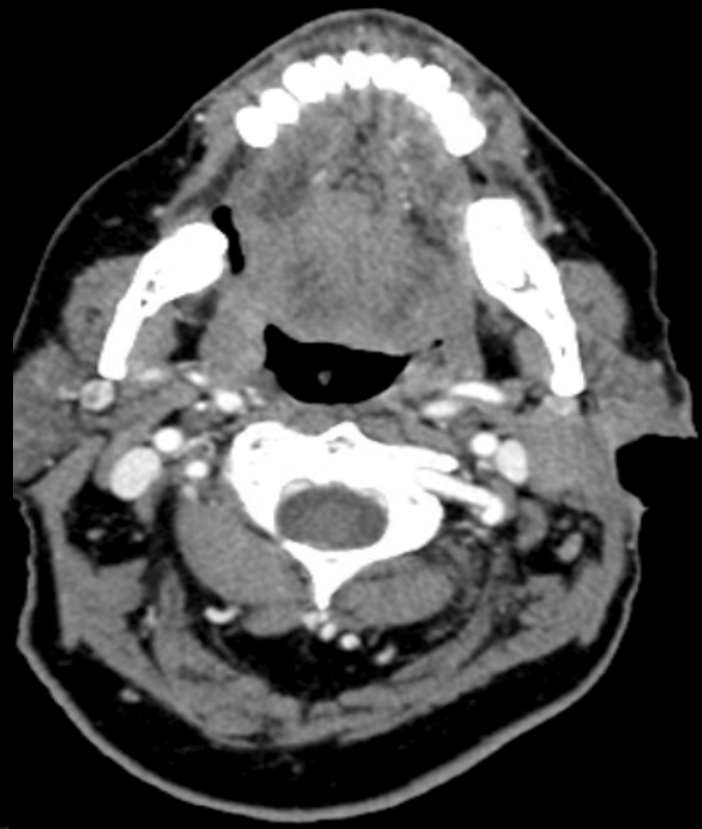


Image courtesy of Dr. Miller
Provided with patient consent

Role of Surgery?

Safety of ICI in the preoperative setting?

Case 1. Follow-Up on Immunotherapy

- At the MDC visit, Carl reports that he has been experiencing worsening anorexia in the last 3 weeks:

  “All I’ve been eating are popsicles the last three weeks”

- He also reports increased frequency of loose watery bowel movements (4x per day)
- Carl also mentions right knee pain

MDC = multidisciplinary care.

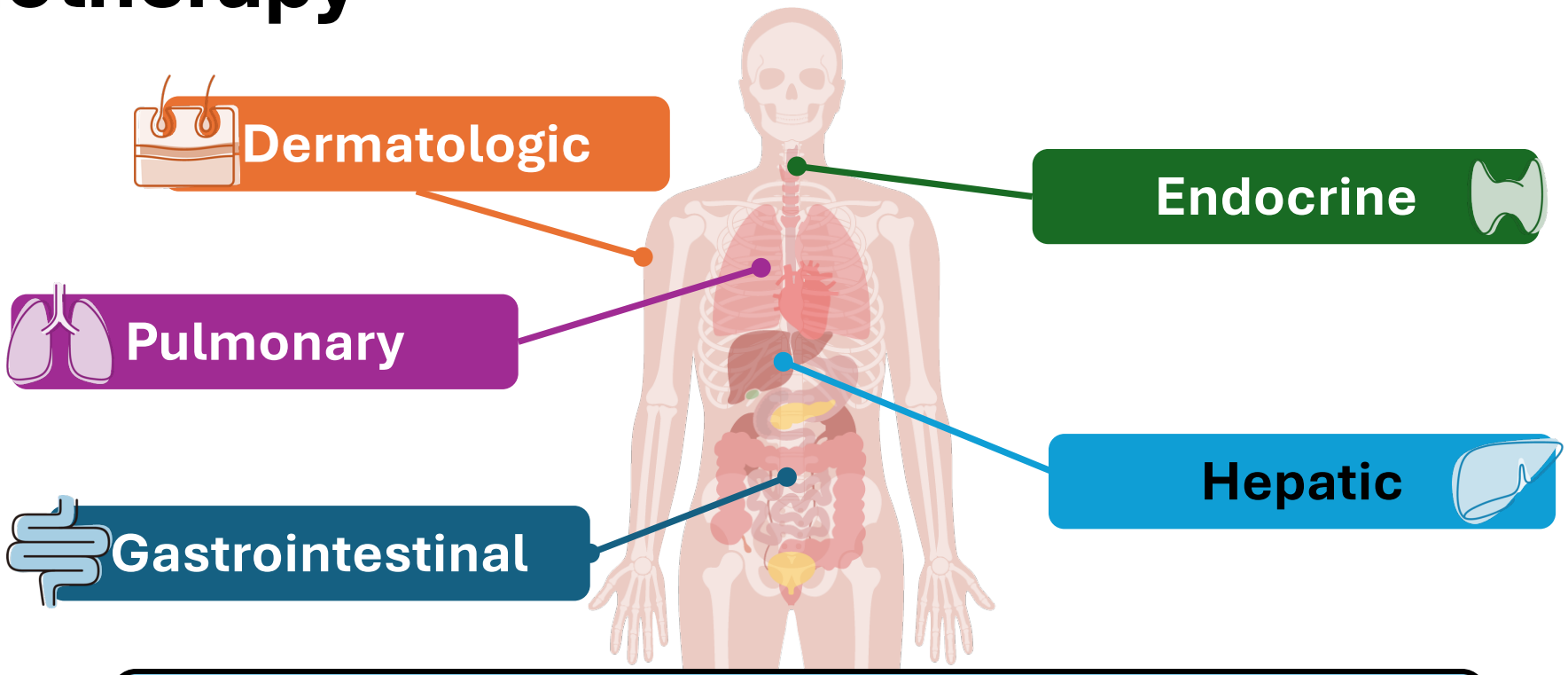
Case 1. Laboratory Results

Carl's labs are remarkable for:

- WBC = 20.08 k/uL (baseline WNL)
- Sodium = 126 mmol/L (baseline 140 mg/dL)
- Creatinine = 2.81 mg/dL (baseline 1.40 mg/dL)
- NT-proBNP = 6699 pg/mL (no baseline)

NT-proBNP = N-terminal pro B-type natriuretic peptide; WBC = white blood (cell) count; WNL = within normal limits.

Recognizing Key Organ Systems Affected by Immunotherapy



Patients can experience multiple immune-related AEs over the duration of treatment and even after discontinuation

Schneider BJ, et al. *J Clin Oncol*. 2021;39:4073-4126. Darnell EP, et al. *Curr Oncol Rep*. 2020;22:39.

AE = adverse event.

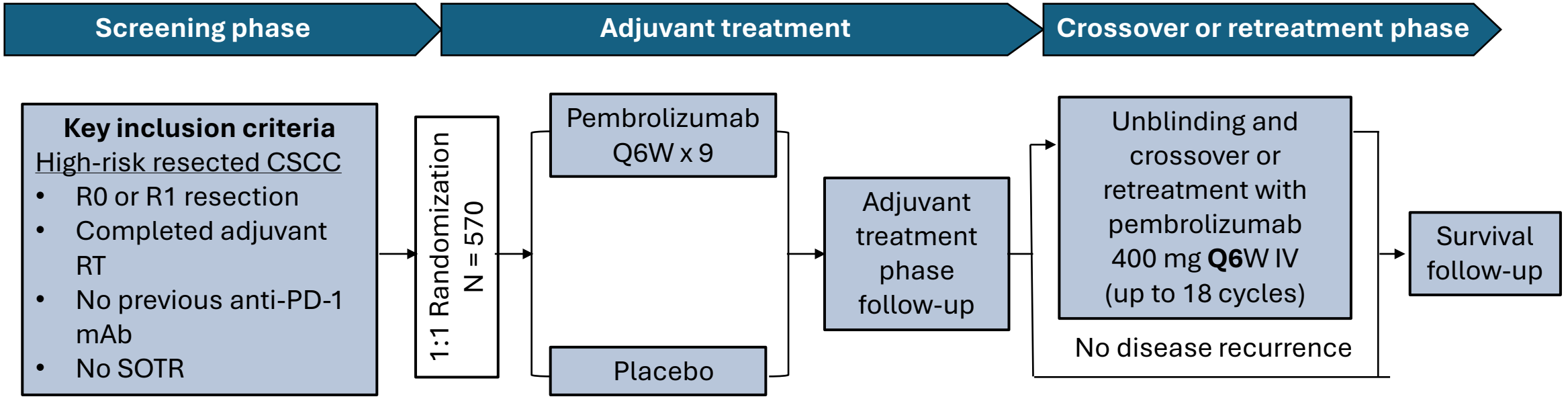
Management of Immune-Related Adverse Events

Grade 1	Grade 2	Grade 3	Grade 4
Continue, monitor closely; exceptions for some neuro, blood, and heart issues	**Suspend**, resume if symptoms improve. Consider low-dose corticosteroids	**Suspend**, start high-dose corticosteroids, taper over 4–6 weeks. Use additional immunosuppressants if needed	**Discontinue**, except for endocrinopathies and potentially cutaneous. Hospitalize and treat

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

What Is the Role of ICI in the Postoperative Period?

KEYNOTE 630: Adjuvant Pembrolizumab in CSCC



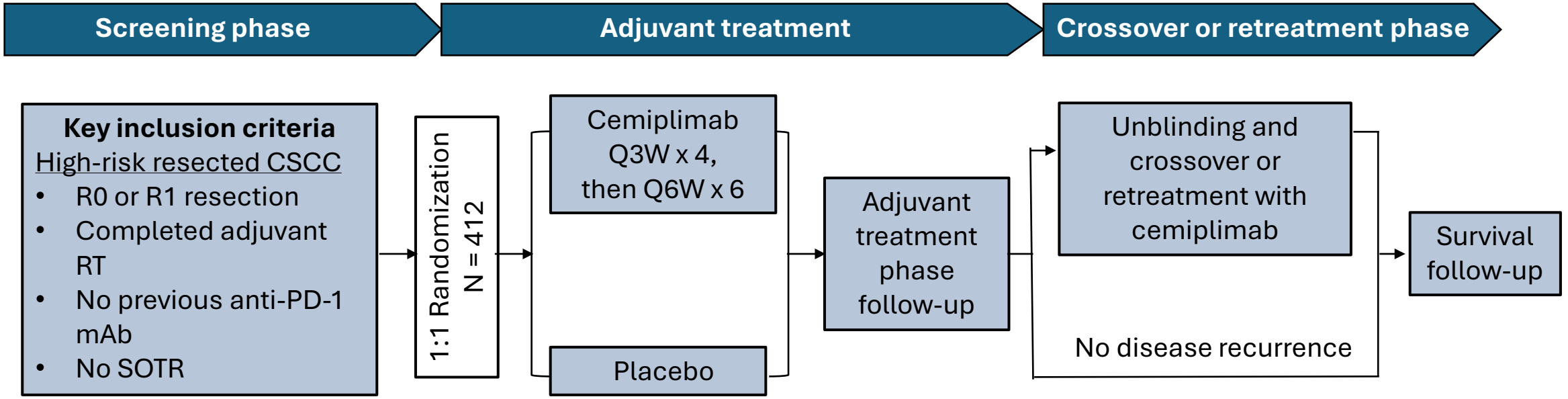
- **Primary endpoint:** Recurrence-free survival
- **Secondary endpoint:** Change from baseline in QoL

Pembrolizumab is not FDA-approved for this indication.

IV = intravenous; mAb = monoclonal antibody; Q6W = every 6 weeks; SOTR = solid organ transplant recipient.

KEYNOTE 630 (https://clinicaltrials.gov/study/NCT03833167). Accessed 4/18/25.

R2810-ONC-1788: Adjuvant Cemiplimab in CSCC



- **Primary endpoint:** Disease-free survival
- **Secondary endpoints:** OS, FFLRR, FFDR

Cemiplimab is not FDA-approved for this indication.

FFDR = freedom from distance recurrence; FFLRR = freedom from locoregional recurrence; OS = overall survival; Q3W = every 3 weeks.

NCT03969004 (https://clinicaltrials.gov/study/NCT03969004). Accessed 4/18/25.

KEYNOTE 630: Adjuvant Pembrolizumab in CSCC

News release

Merck Provides Update on Phase 3 KEYNOTE-867 and KEYNOTE 630 Trials

2024-08-29

Merck is also discontinuing the Phase 3 KEYNOTE-630 trial evaluating KEYTRUDA for the adjuvant treatment of patients with high-risk locally advanced cutaneous squamous cell carcinoma (cSCC) following surgery and radiation based on the recommendation of an independent DMC. The DMC recommended that the study should be stopped for futility as the risk/benefit profile did not support continuing the trial. Data from a pre-planned analysis showed that KEYTRUDA did not cross the boundary for statistical significance in recurrence-free survival (RFS), the study's primary endpoint. The study's key secondary endpoint, OS, was not formally tested, but at the time of the analysis, the results did not favor KEYTRUDA compared to placebo. The safety profile of KEYTRUDA in this trial was consistent with the established safety profile of KEYTRUDA.

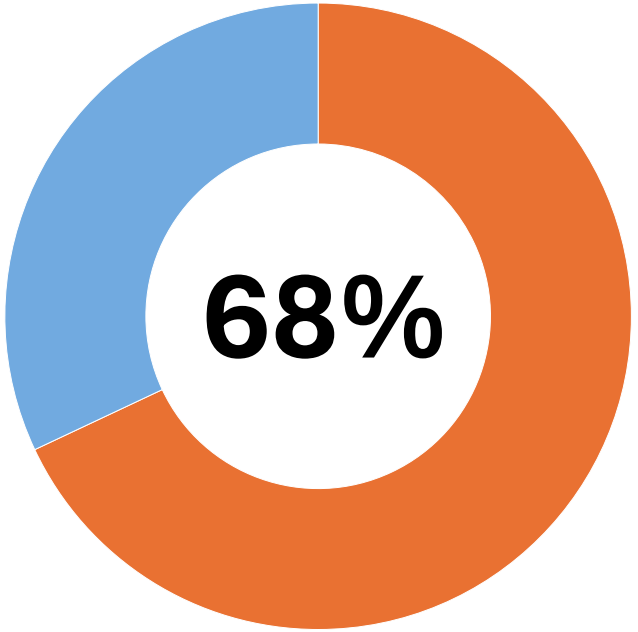
Pembrolizumab is not FDA-approved for this indication.

Merck press release, 8/29/24 (www.merck.com/news/merck-provides-update-on-phase-3-keynote-867-and-keynote-630-trials/). Accessed 4/18/25.

R2810-ONC-1788: Adjuvant Cemiplimab in CSCC

Press Release January 13, 2025

Adjuvant cemiplimab was associated with:



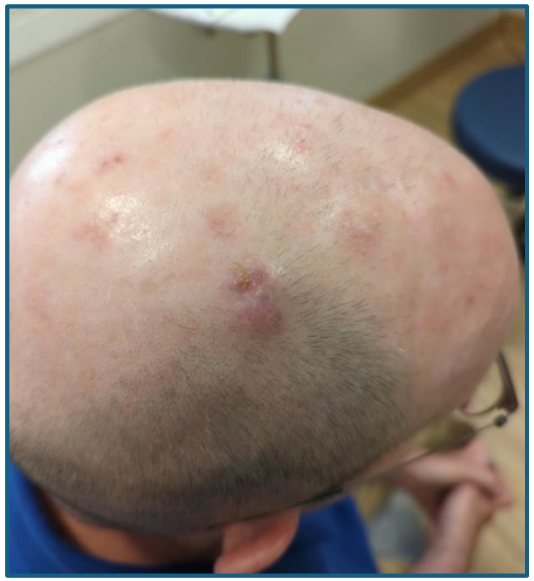
reduction in **DFS** vs placebo
(HR = 0.32; 95% CI, 0.20–0.51;
P < .0001)

Cemiplimab is not FDA-approved for this indication.

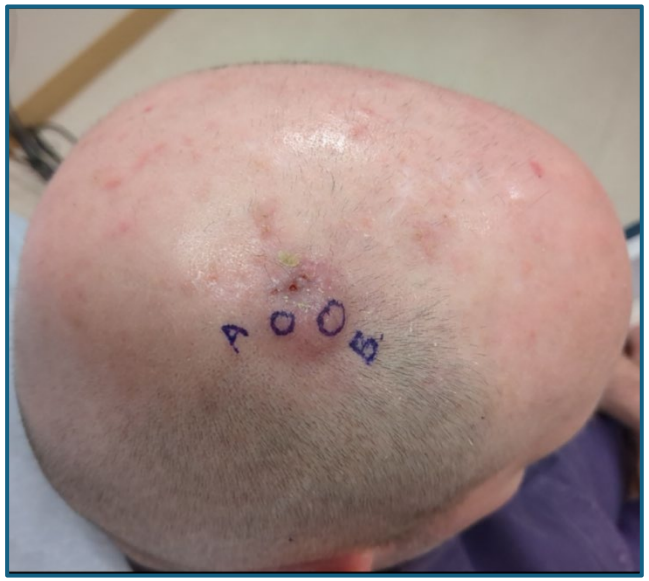
CI = confidence interval; DFS = disease-free survival; HR = hazard ratio.

Regeneron press release, 1/13/2025 (https://investor.regeneron.com/node/30621/pdf). Accessed 4/18/25.

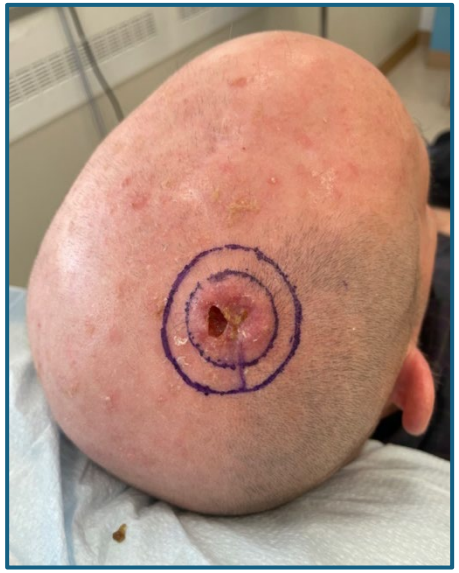
Clinical Trial Example



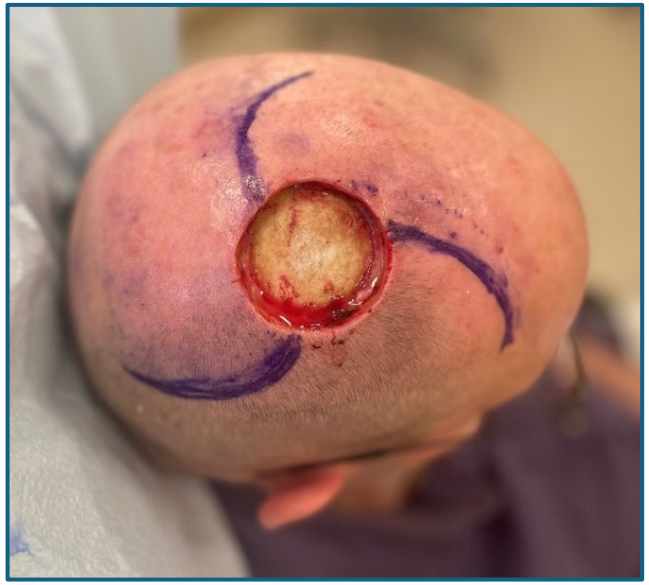
Sept 2023



Oct 2023



Nov 2023
Preoperative



Nov 2023
Postoperative

High-risk features: ITM, multifocal PNI, invasion to bone

ITM = in transit metastases; PNI = perineural invasion. Cemiplimab is not FDA-approved for this indication.

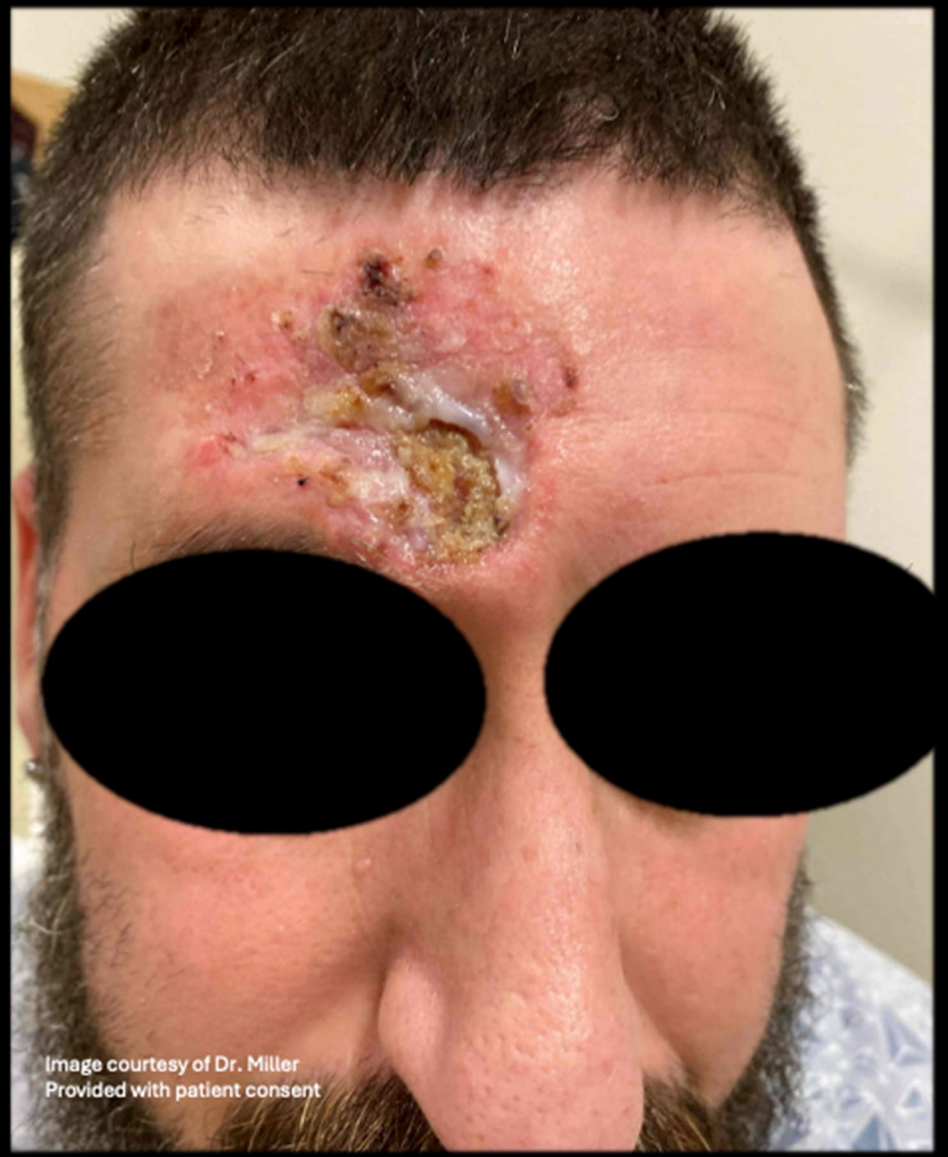
Management of Advanced CSCC: Summary Statement

Management of Advanced BCC

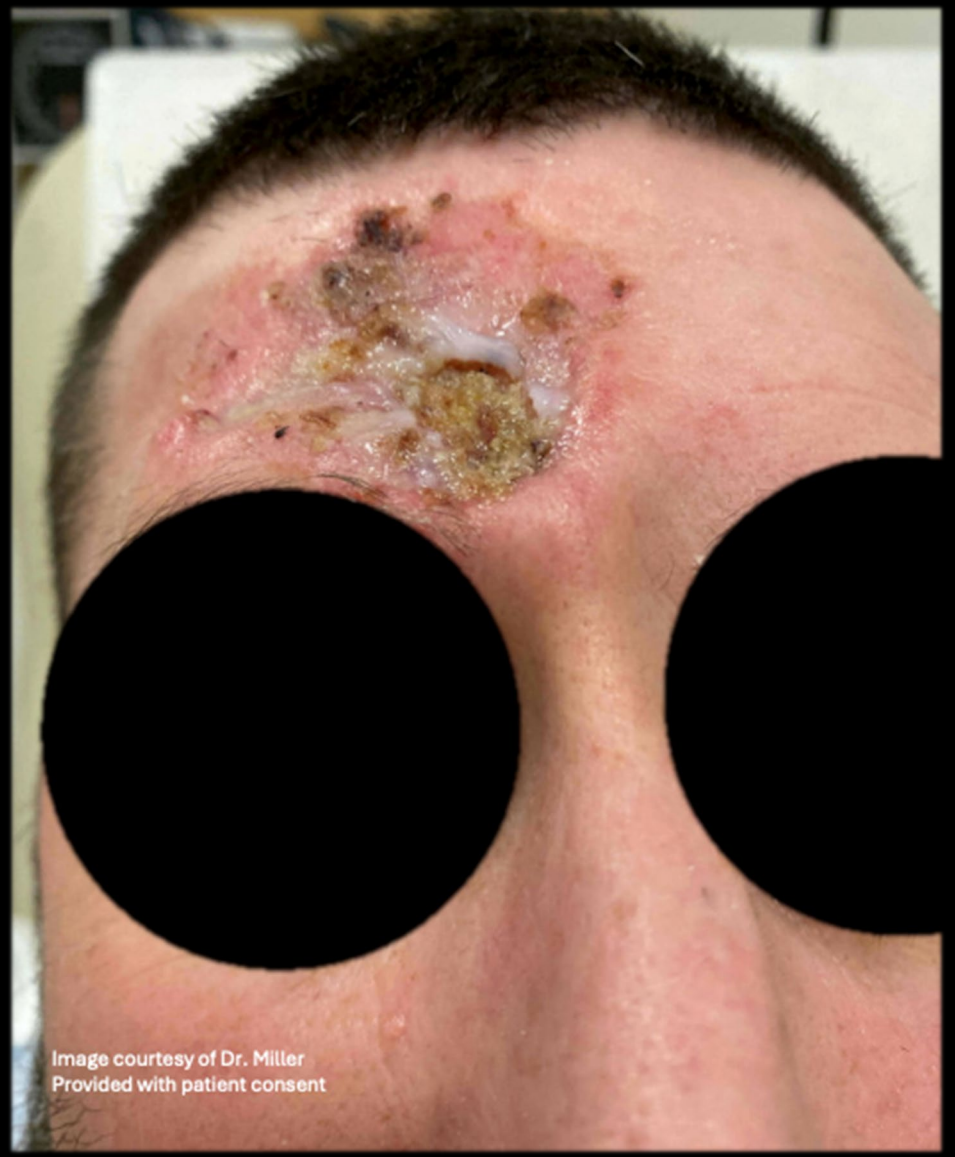
Case 2. Jack

- Jack is a male in the 4th decade of life, with no significant PMH
- He presented to our multidisciplinary clinic with a several-year history of a growing lesion on his right forehead
- Jack reports that for the last few months he has lost the feeling in the skin above his eyebrow and extending to his hairline

Case 2. Jack at Presentation



Case 2. Jack at Presentation (continued)



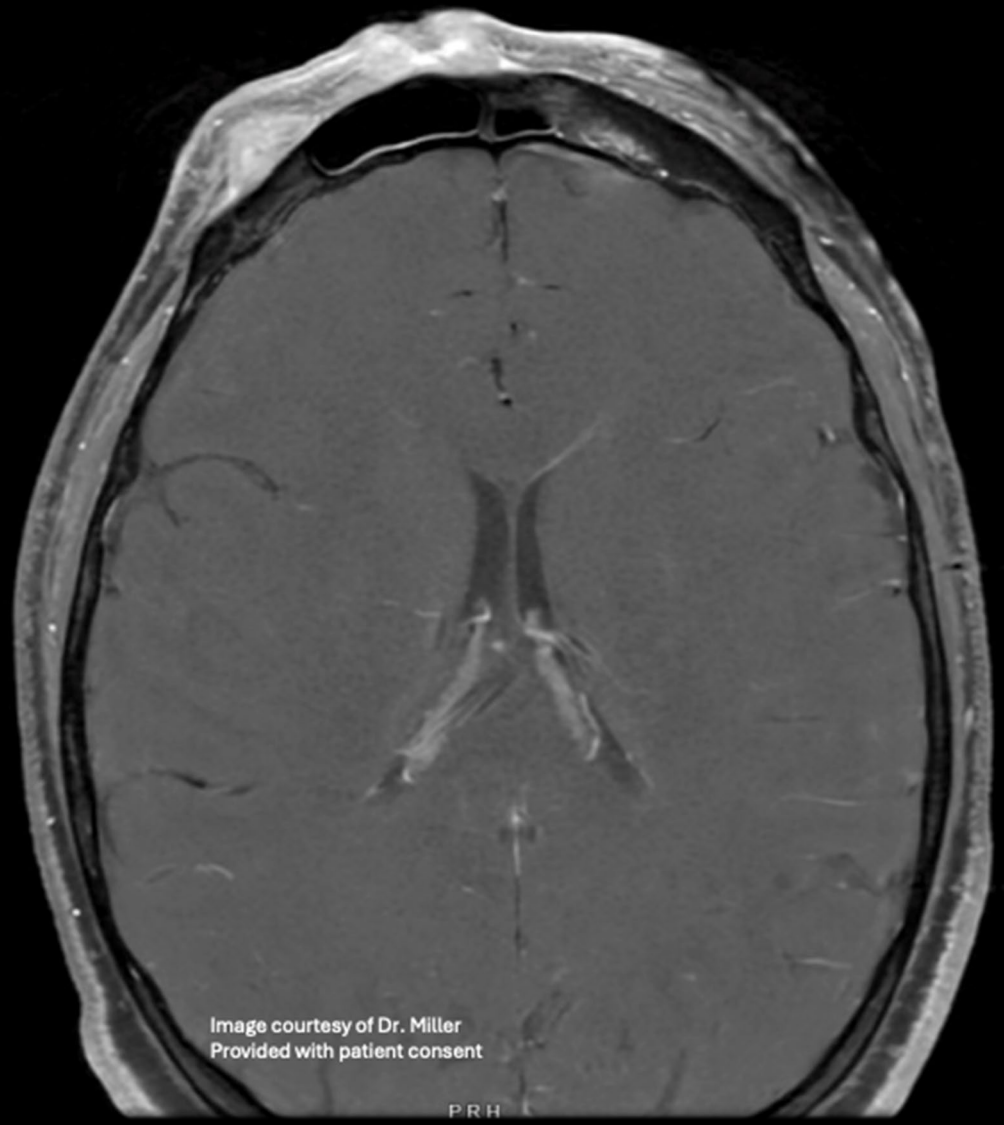
Case 2. Diagnosis

Jack’s biopsy shows basal cell carcinoma

Case 2. Question for Discussion

What would be your next steps in Jack’s treatment?

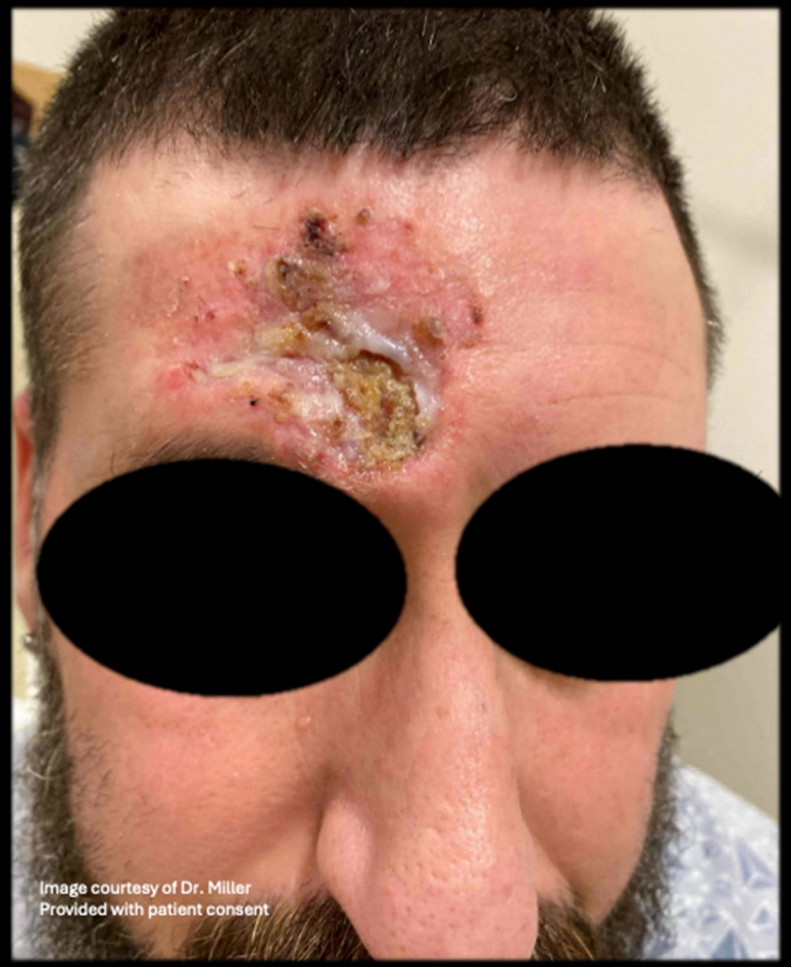
Case 2. Imaging at Presentation

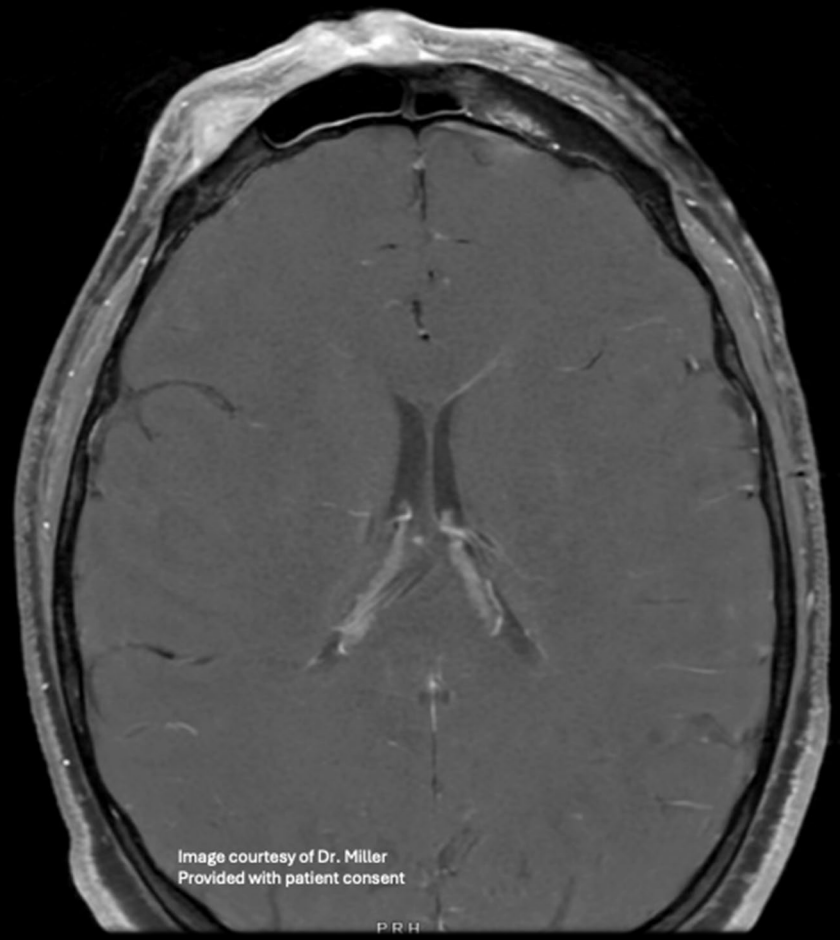


Case 2. Questions for Discussion

- What would be your next steps in Jack's treatment?
- Which treatment options are going to be most beneficial to Jack?

Case 2. Role of Surgery?





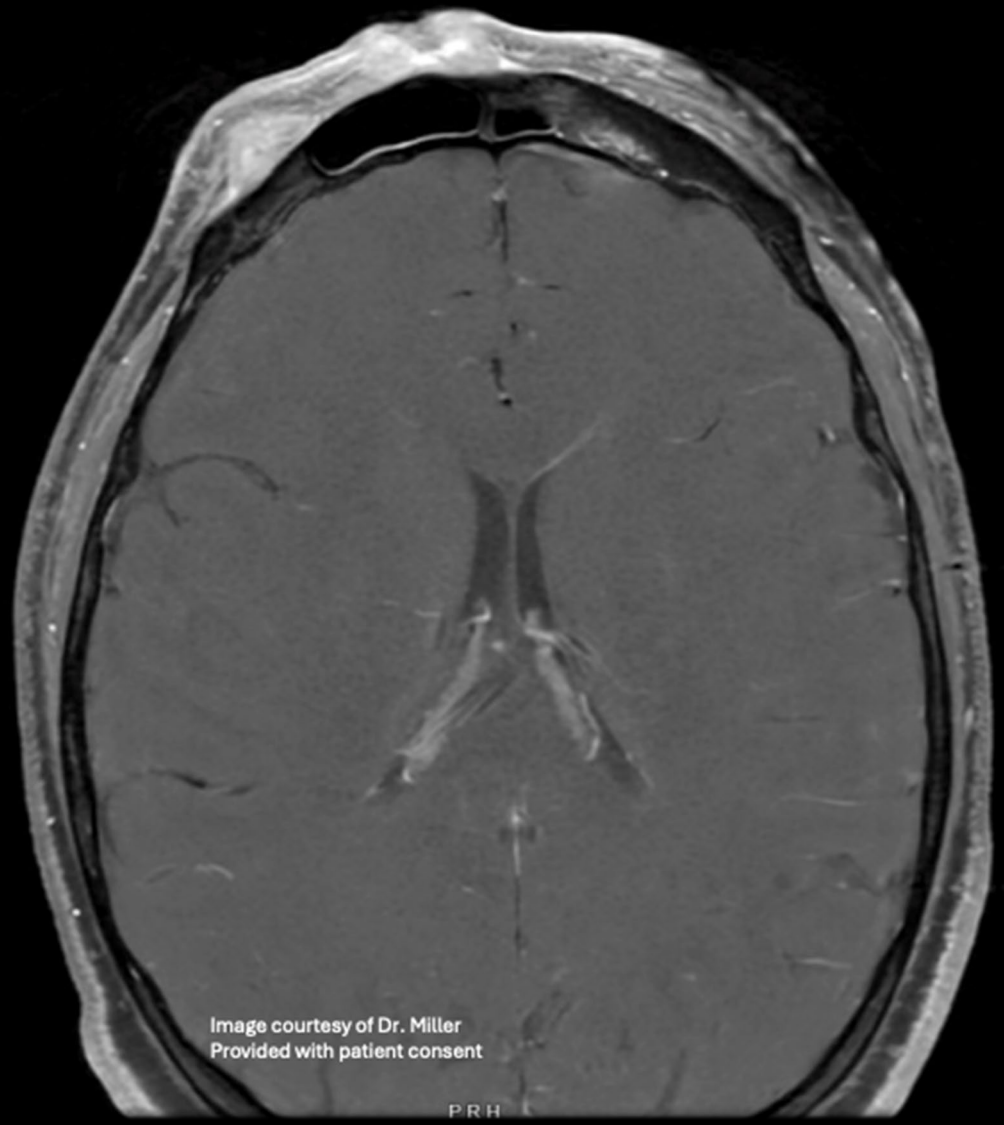
A Practitioner's Casebook:
Defining Candidates for Surgical Management

Risk	Stage	Surgical outcome
Easy to treat, low risk of recurrence	I	Recurrences only from blind treatments or insufficient surgical margins
Common BCC	IIA	Good results and low recurrence expected with surgery
	IIB	Surgery possible but complexity increases due to multiplicity
Advanced BCC	IIIA	Curable without expected functional mutilations
	IIIB	Curable with surgery, but functional impairment/mutilation inevitable
	IIIC	Cure not expected by surgery regardless of extent
Metastatic BCC	IV	Cure not expected; metastatic disease

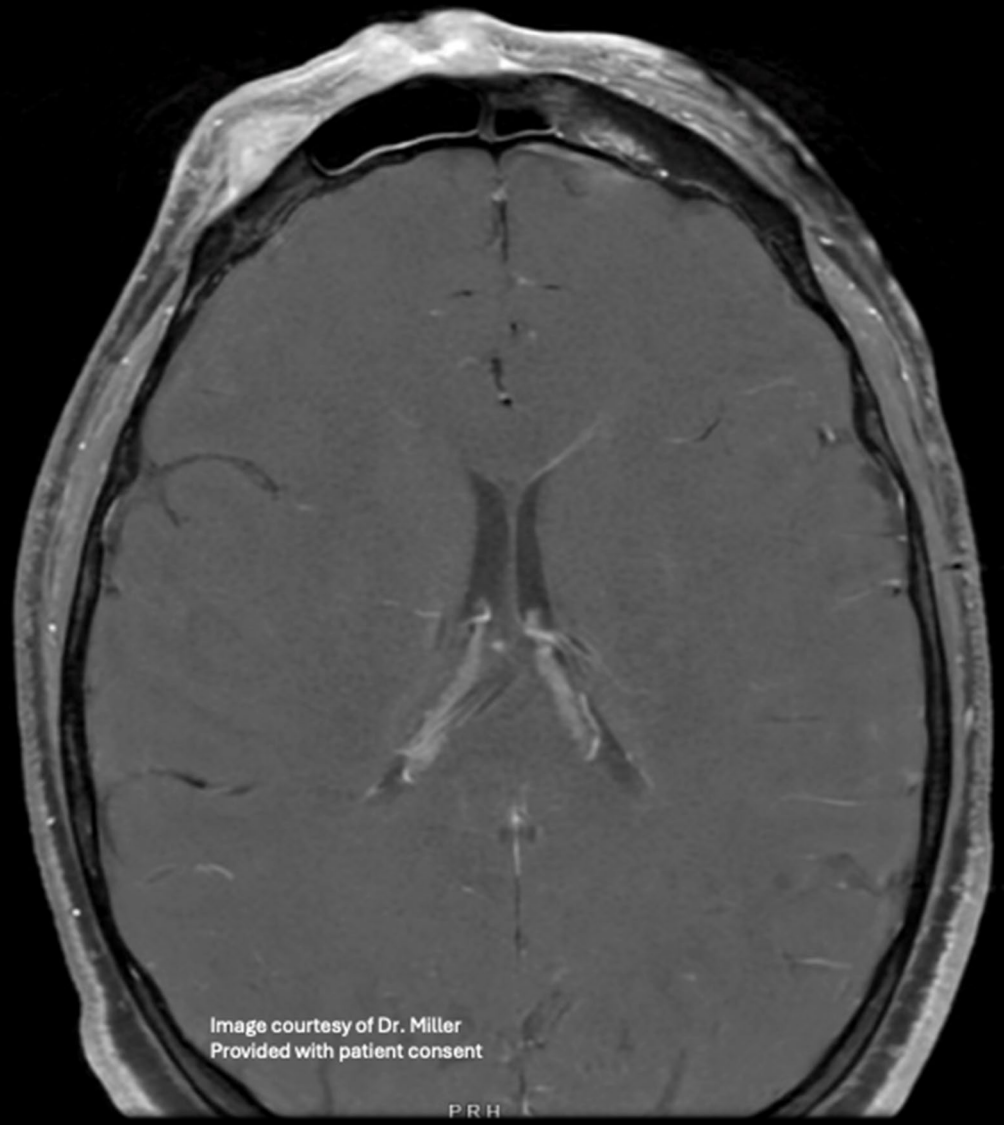
Should we be staging disease in such a way in practice?

Modified from Peris K, et al. *Eur J Cancer*. 2023;192:113254.

Case 2.
Role of Radiotherapy?

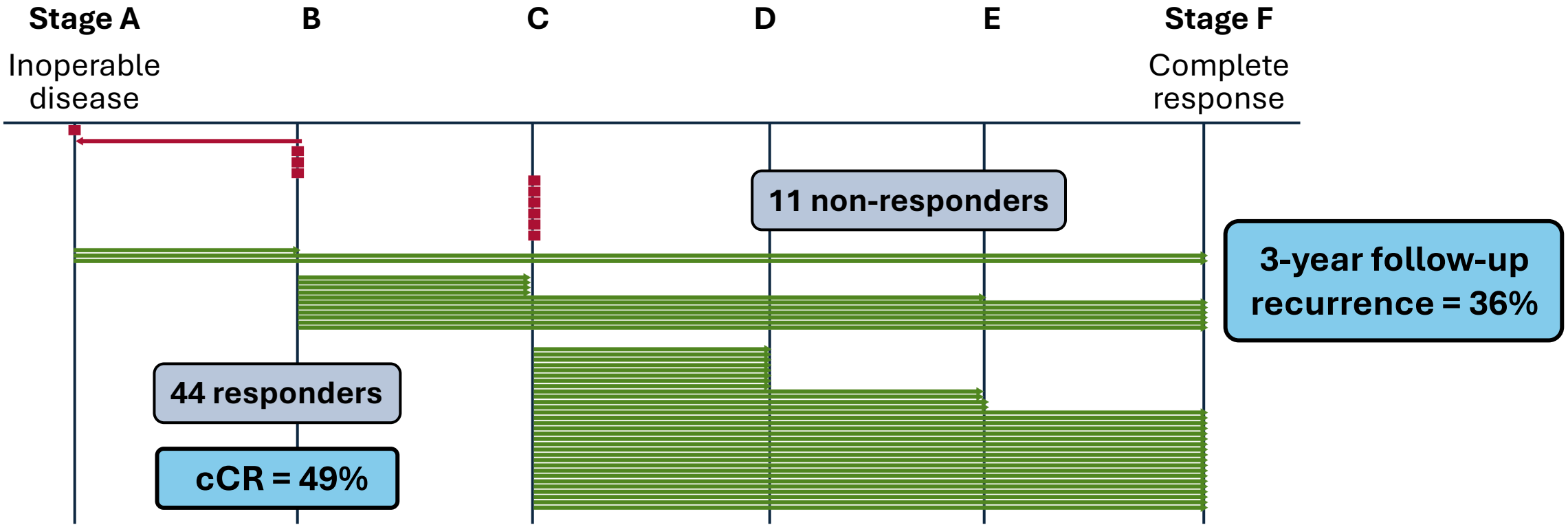


Case 2.
Role of Systemic Therapy?



Neoadjuvant HHIs in BCC: Responses With Vismodegib

VISMONEO: Phase 2 study evaluating neoadjuvant vismodegib in confirmed facial BCC (N = 55; mean treatment duration = 6.0 mo)

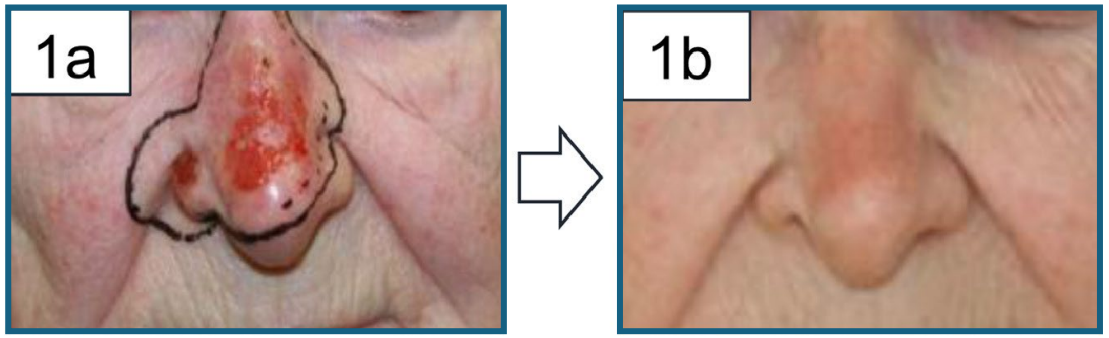


Bertrand N, et al. *EClinicalMedicine*. 2021;35:100844.

HHI = hedgehog (pathway) inhibitor. Vismodegib is not FDA-approved for this indication.

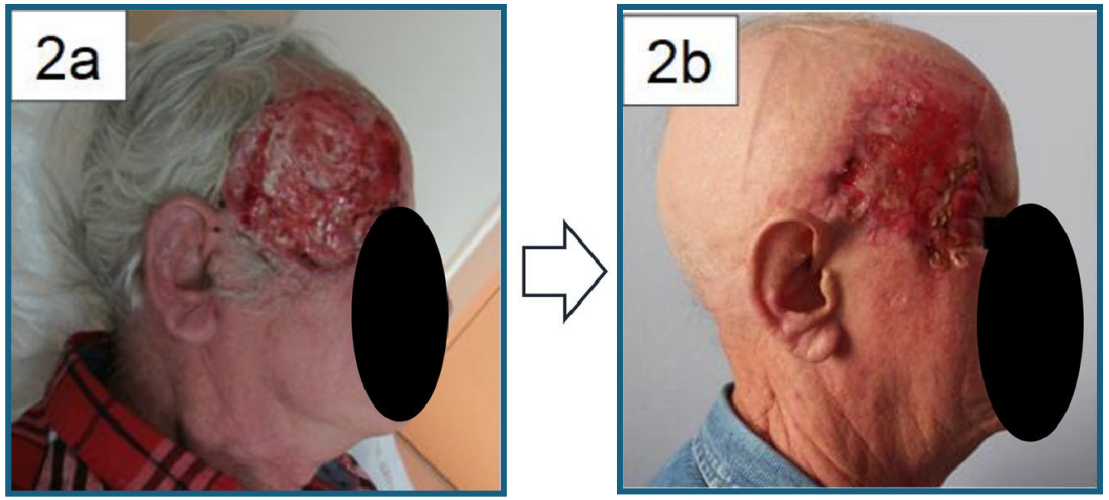
Exploring Patients' Clinical Journeys on Neoadjuvant HHIs

Baseline



After 7 months of vismodegib

Baseline



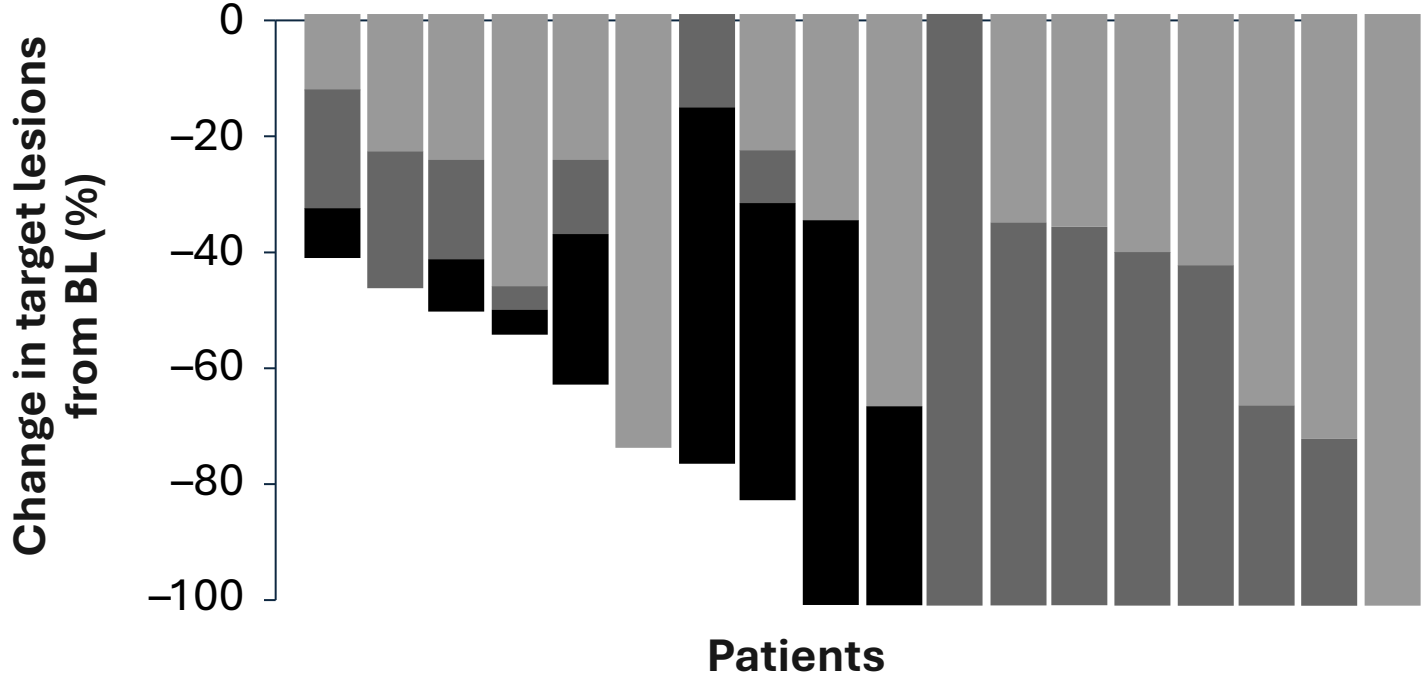
After 10 months of vismodegib

Images from Bertrand N, et al. *EClinicalMedicine*. 2021;35:100844.

Vismodegib is not FDA-approved for this indication.

Neoadjuvant HHIs in BCC:
Responses With Vismodegib and Radiation Therapy

Phase 2 study evaluating induction vismodegib followed by 7 wk of concurrent vismodegib and RT in unresectable locally advanced BCC (N = 24; mFU = 5.7 years)



- Response 1 year after 7 wk of concurrent vismodegib and RT
- Response 3 mo after 7 wks of concurrent vismodegib and RT
- Response after 12–14 wk of induction vismodegib

LRC at 12 mo = 91%

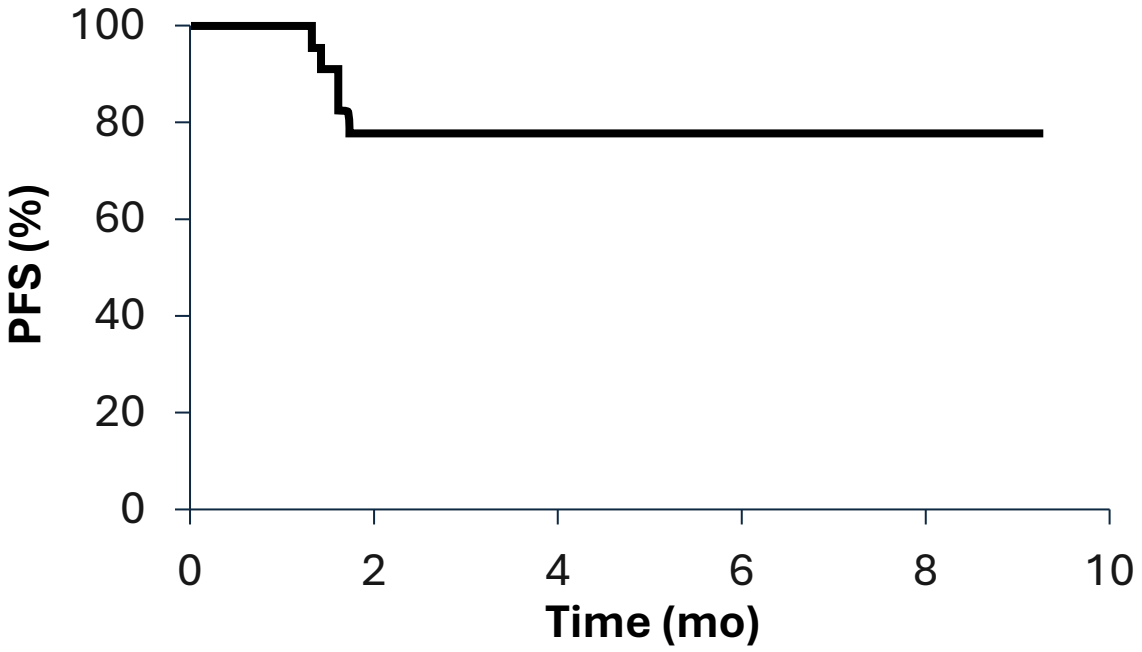
Barker CA, et al. *J Clin Oncol*. 2024;42:2327-2335.

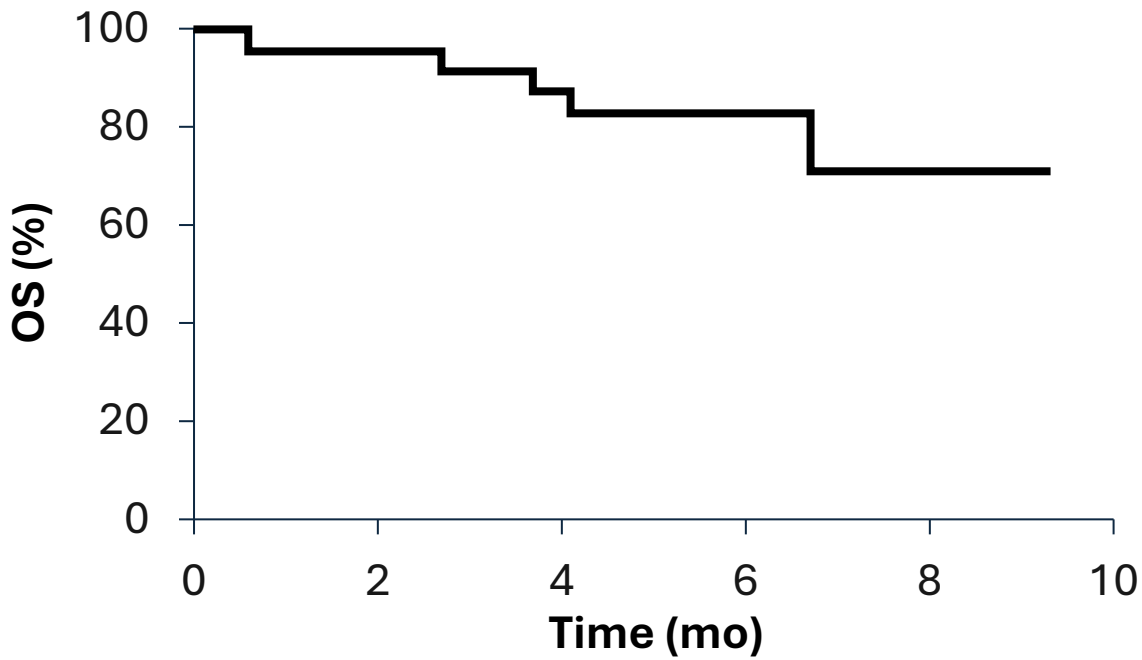
LRC = locoregional control. Vismodegib is not FDA-approved for this indication.

Neoadjuvant HHIs in BCC:

Survival With Vismodegib and Radiation Therapy

Phase 2 study evaluating induction vismodegib followed by 7 wk of concurrent vismodegib and RT in unresectable locally advanced BCC (N = 24; mFU = 5.7 years)





Barker CA, et al. *J Clin Oncol*. 2024;42:2327-2335.

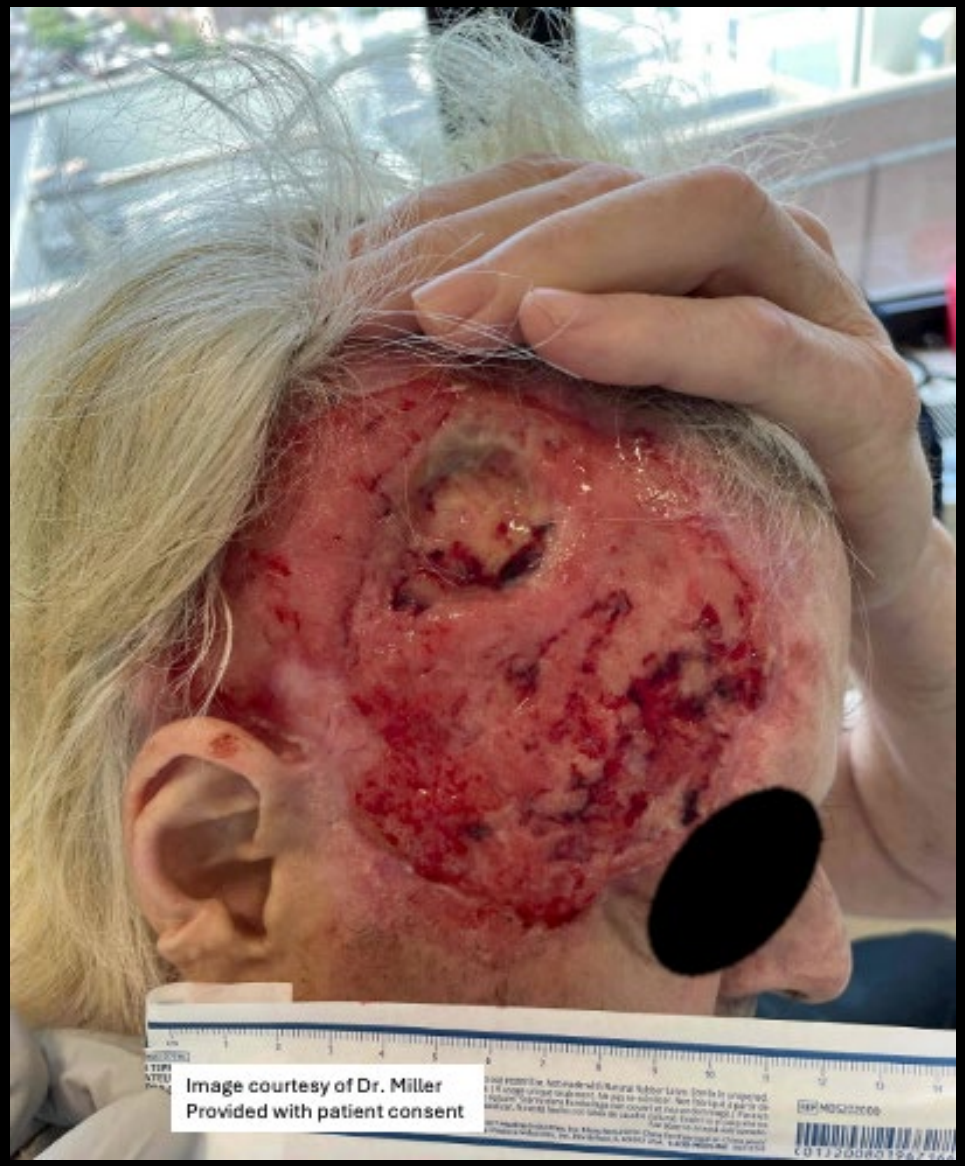
PFS = progression-free survival. Vismodegib is not FDA-approved for this indication.

Reference(s): Barker CA et al. *J Clin Oncol*. 2024;42:2327-2335.

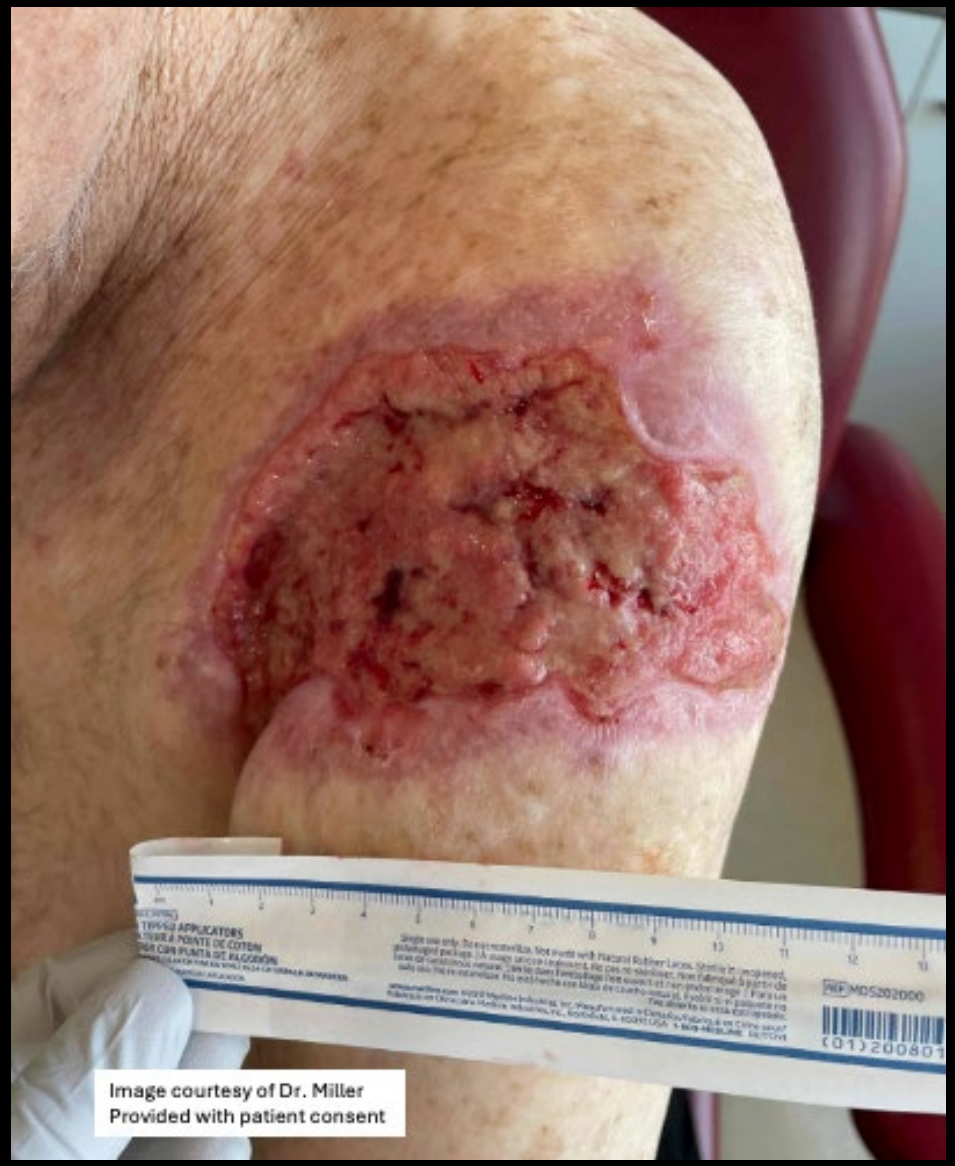
Case 3. Bill

- Bill is a male in the 7th decade of life, with no significant PMH
- He presented to our multidisciplinary clinic with a several-year history of growing lesions on his right scalp and left upper arm/shoulder

Case 3.
Bill at Presentation



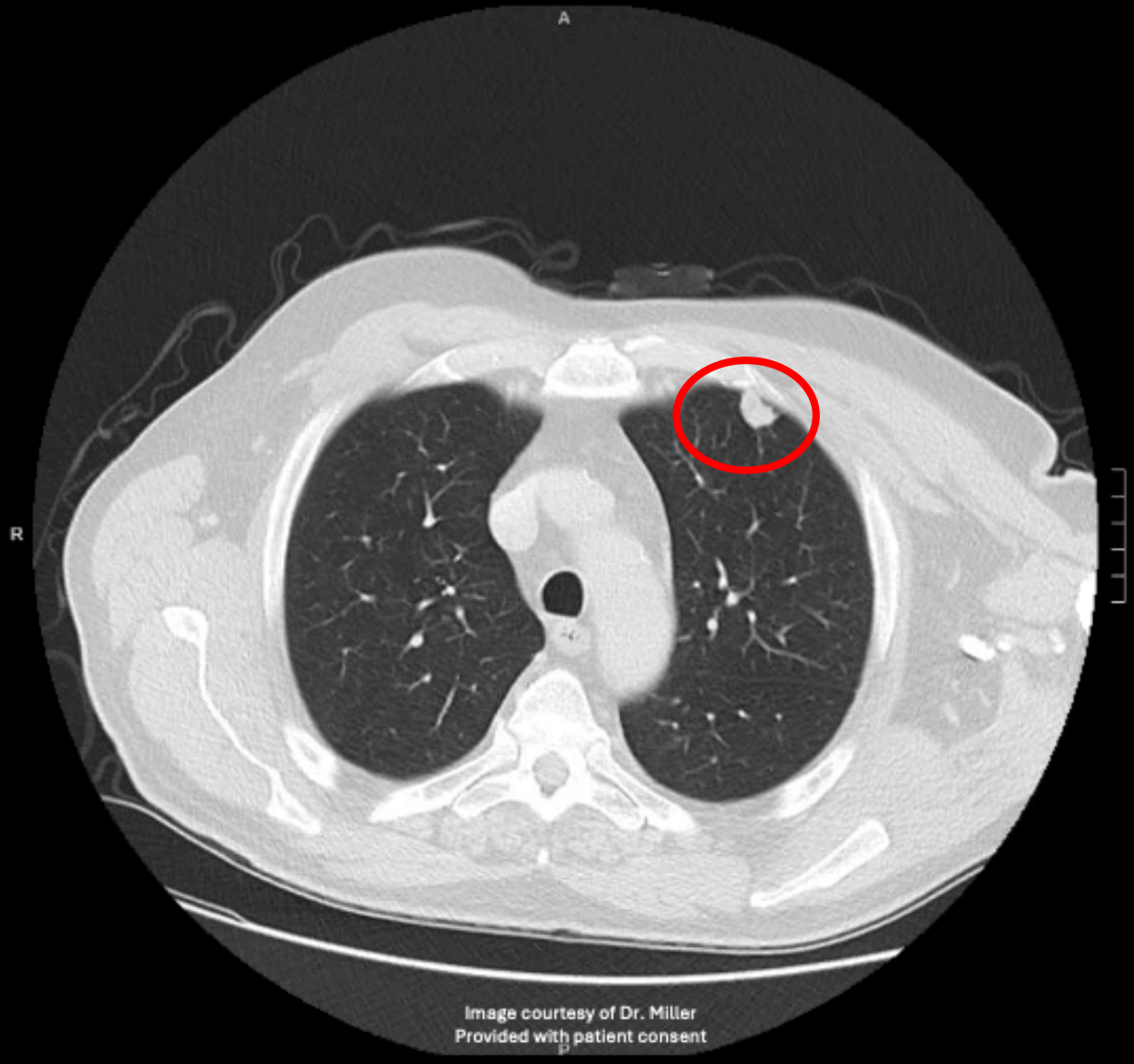
Case 3. Bill at Presentation (continued)



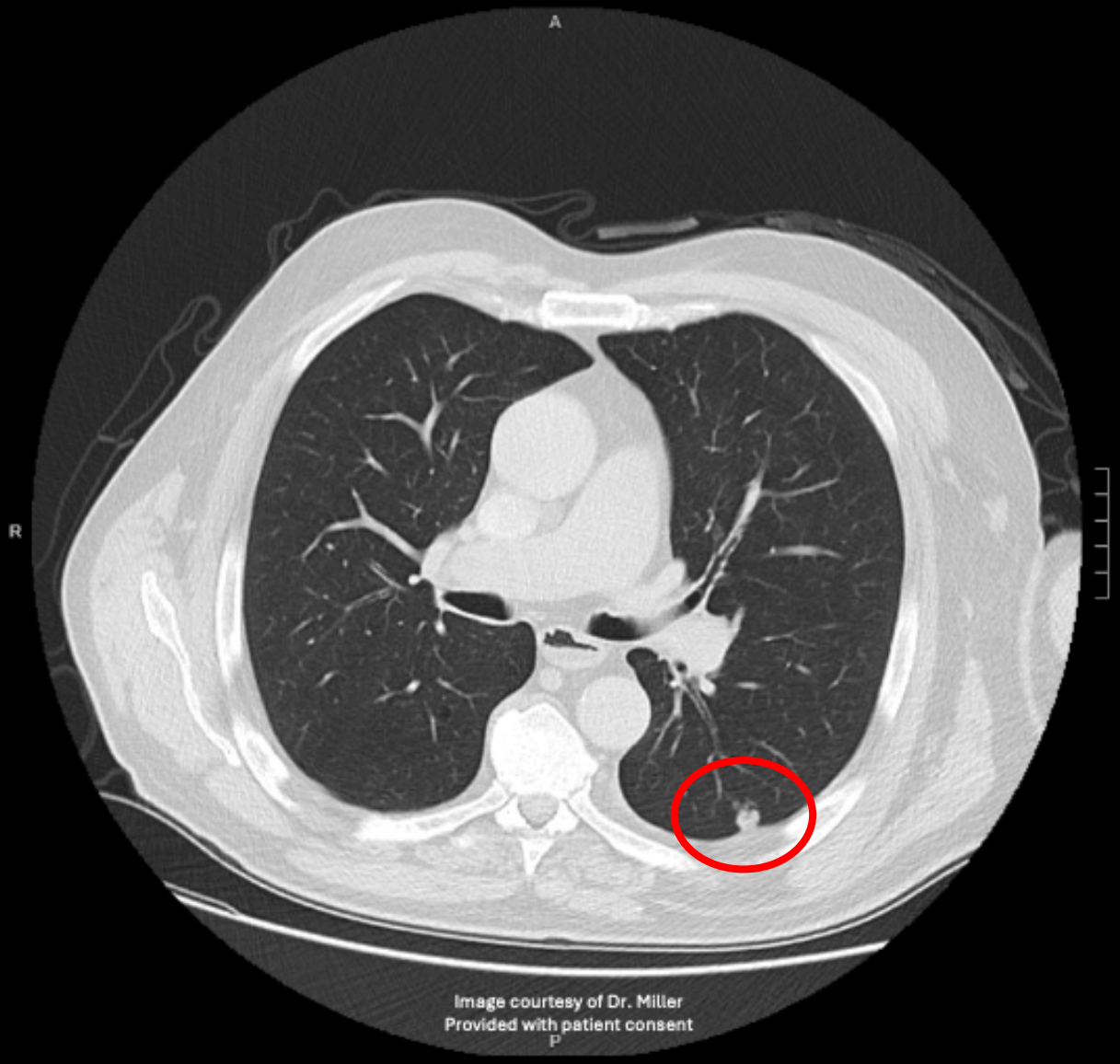
Case 3. Diagnosis

Bill’s skin biopsy demonstrated that he has basal cell carcinoma

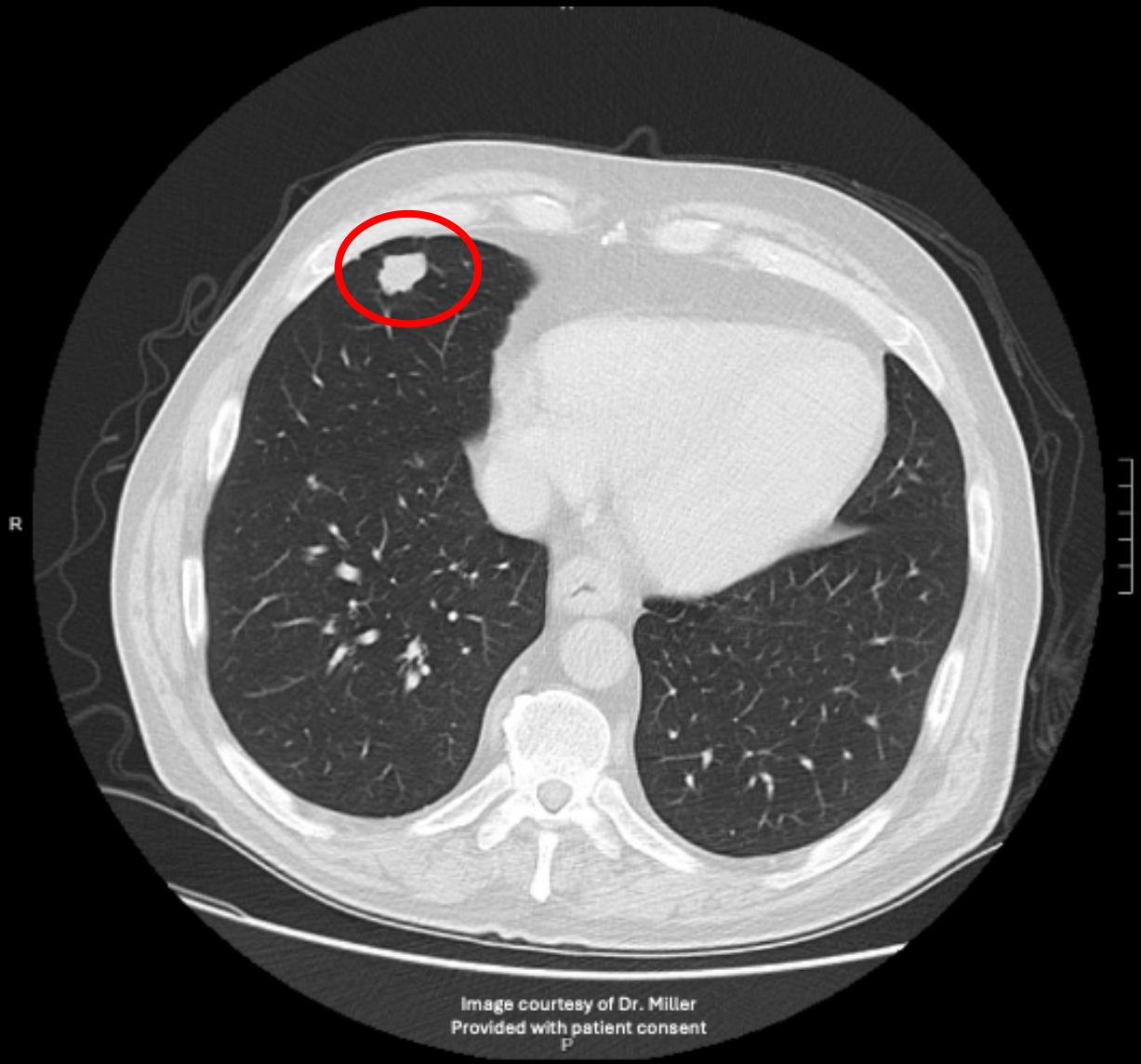
Case 3.
Imaging at Presentation



Case 3. Imaging at Presentation (continued 1)



Case 3. Imaging at Presentation (continued 2)



Case 3. Biopsy

Bill’s lung biopsy demonstrated basal cell carcinoma

Case 3. Question for Discussion

Which treatment options are going to be most beneficial to Bill?

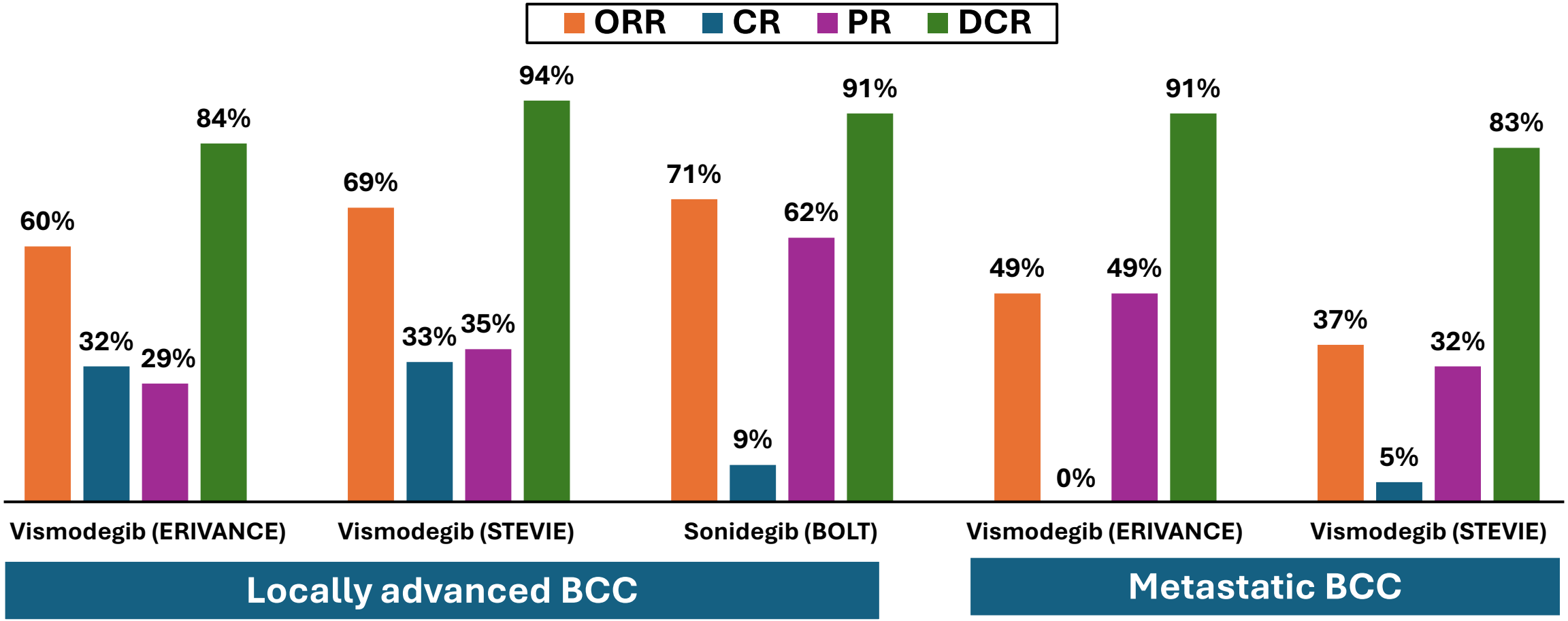
Guidelines for Systemic Therapy for Advanced BCC

	Preferred regimens	Other recommended regimens	Useful in certain circumstances
Locally advanced disease–neoadjuvant	None	*Vismodegib (category 2b)	**Cemiplimab-rwlc (category 2b)
Locally advanced disease	None	• Vismodegib • Sonidegib	Cemiplimab-rwlc
Nodal disease	None	• Vismodegib • Sonidegib (category 2B)	Cemiplimab-rwlc
Metastatic disease	None	Vismodegib	Cemiplimab-rwlc

* Vismodegib is not FDA-approved for this indication.
**Cemiplimab is not FDA-approved for this indication.

NCCN. Basal cell skin cancer. Version 2.2025 (www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf). Accessed 4/18/25.

Tumor Response to SMO Inhibitors



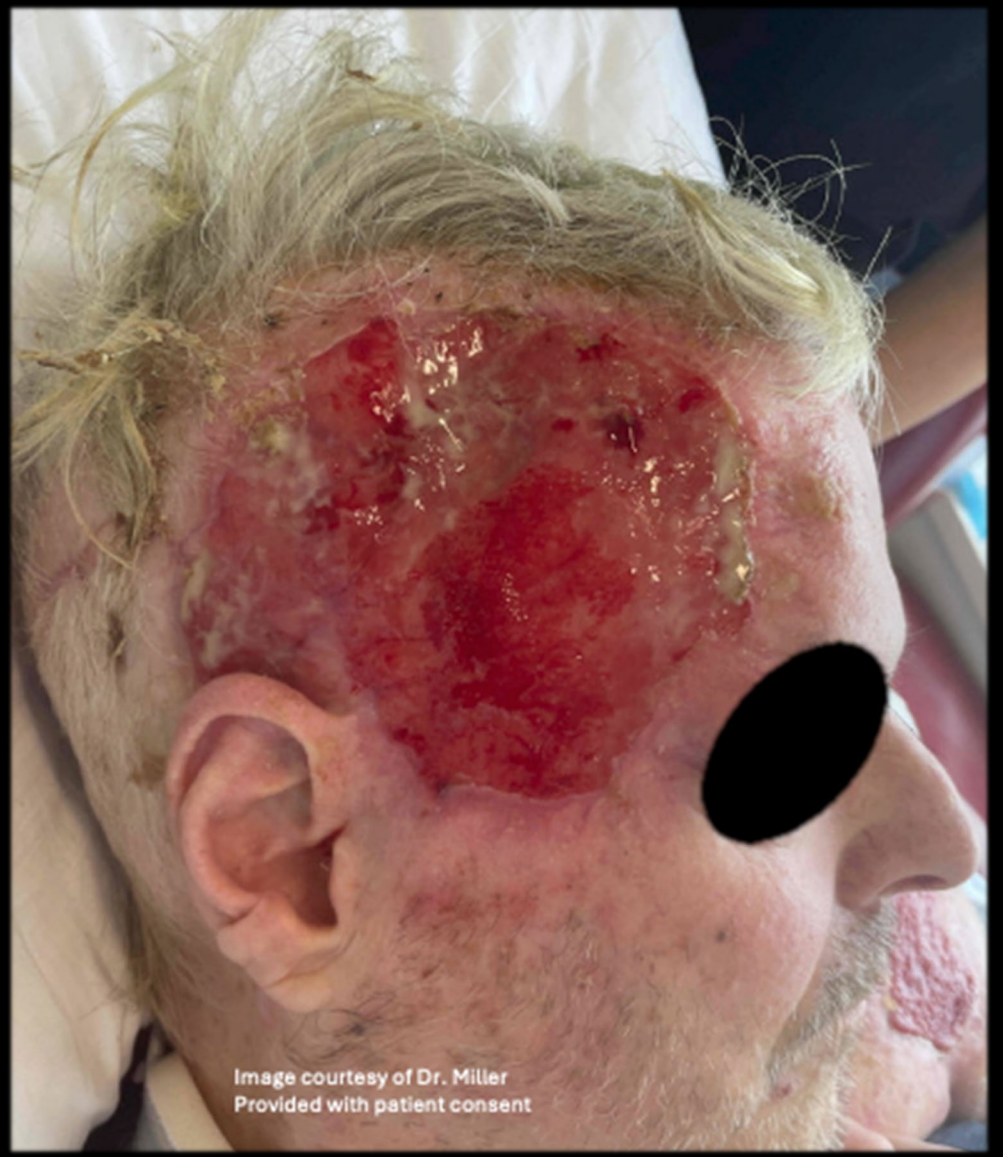
Migden M, et al. *J Drugs Dermatol*. 2021;20:156-165. Sekulic A, et al. *BMC Cancer*. 2017;17:332. Basset-Séguin N, et al. *Eur J Cancer*. 2017;86:334-348. Dummer R, et al. *Br J Dermatol*. 2020;182:1369-1378. Lear JT, Migden MR, Lewis KD, et al. *J Eur Acad Dermatol Venereol*. 2018;32(3):372-381.

DCR = disease control rate; SMO = smoothened.

Case 3. Treatment

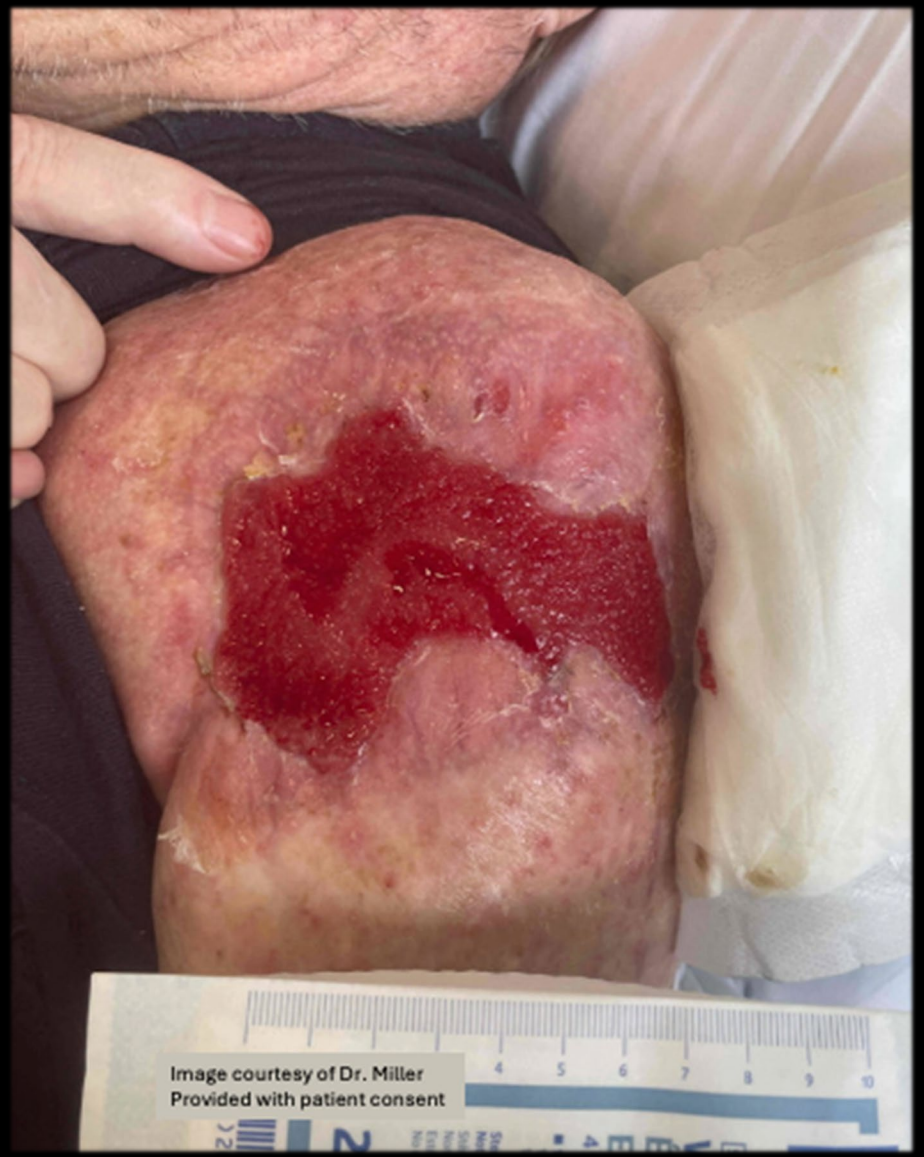
- Bill started on a smoothened inhibitor, dosing daily for 3 months
- At the next follow up visit…

Case 3. Status Post 3 months of SMOi

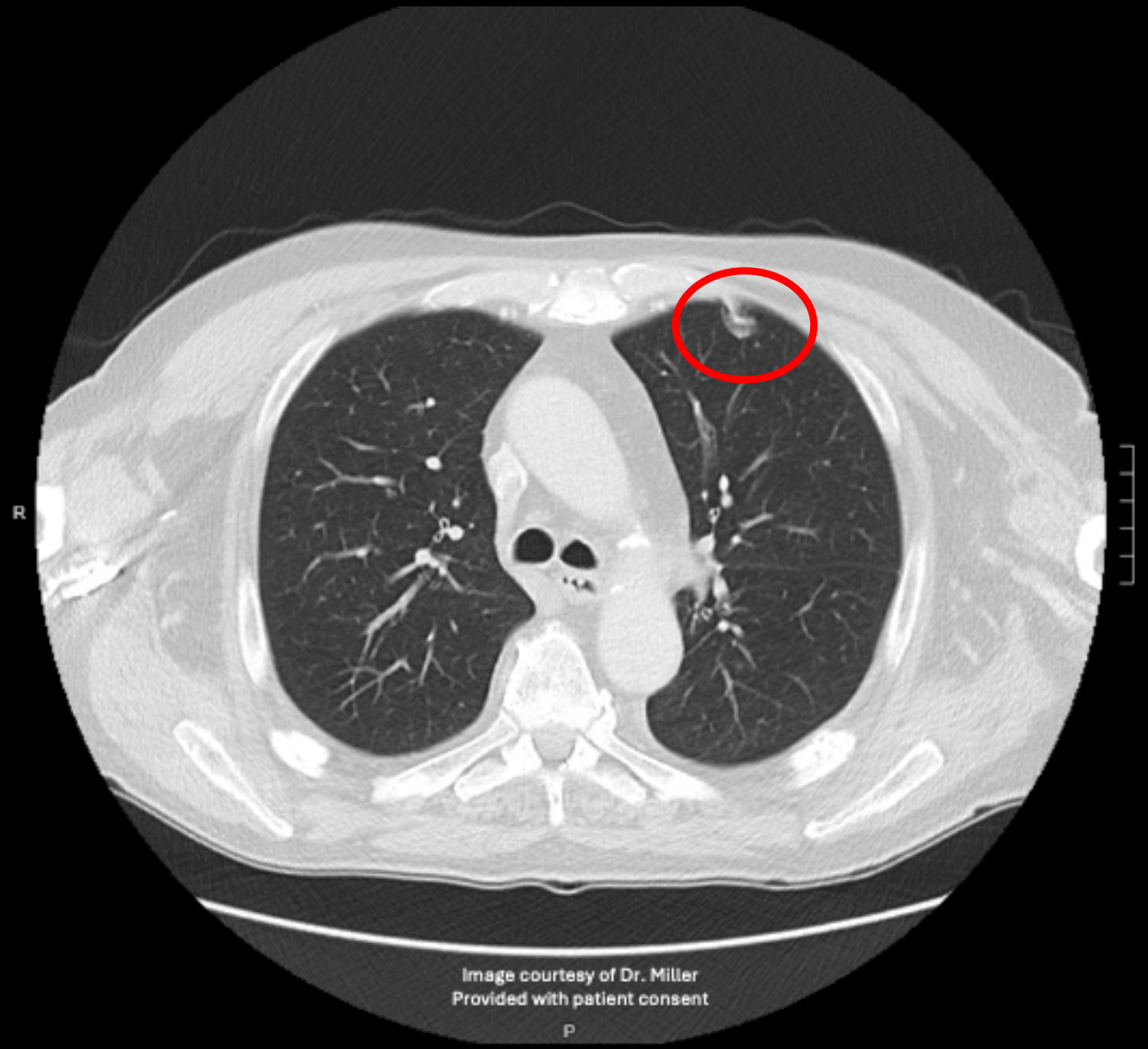


SMOi = smoothened inhibitor.

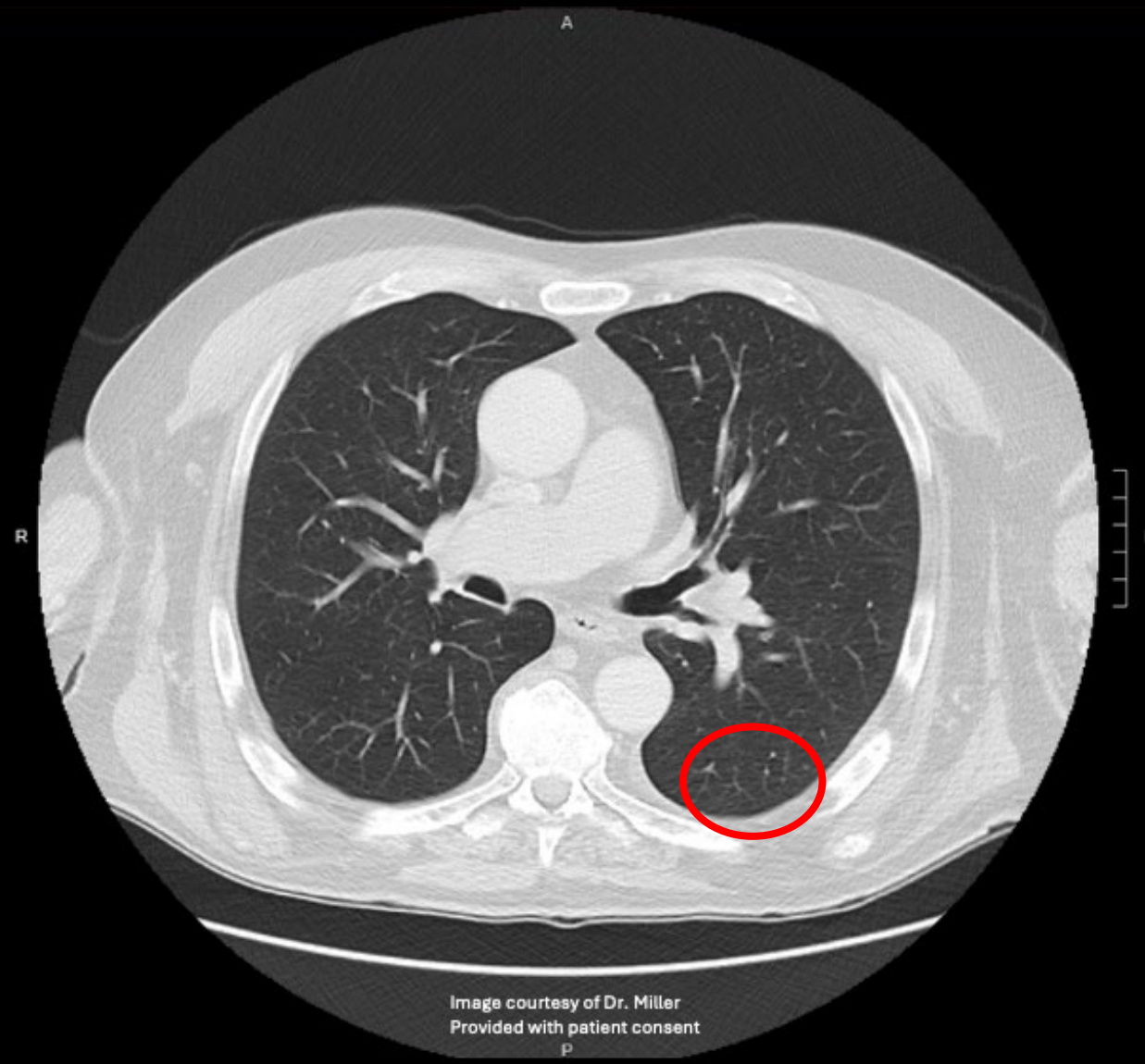
Case 3. Status Post 3 months of SMOi (continued 1)



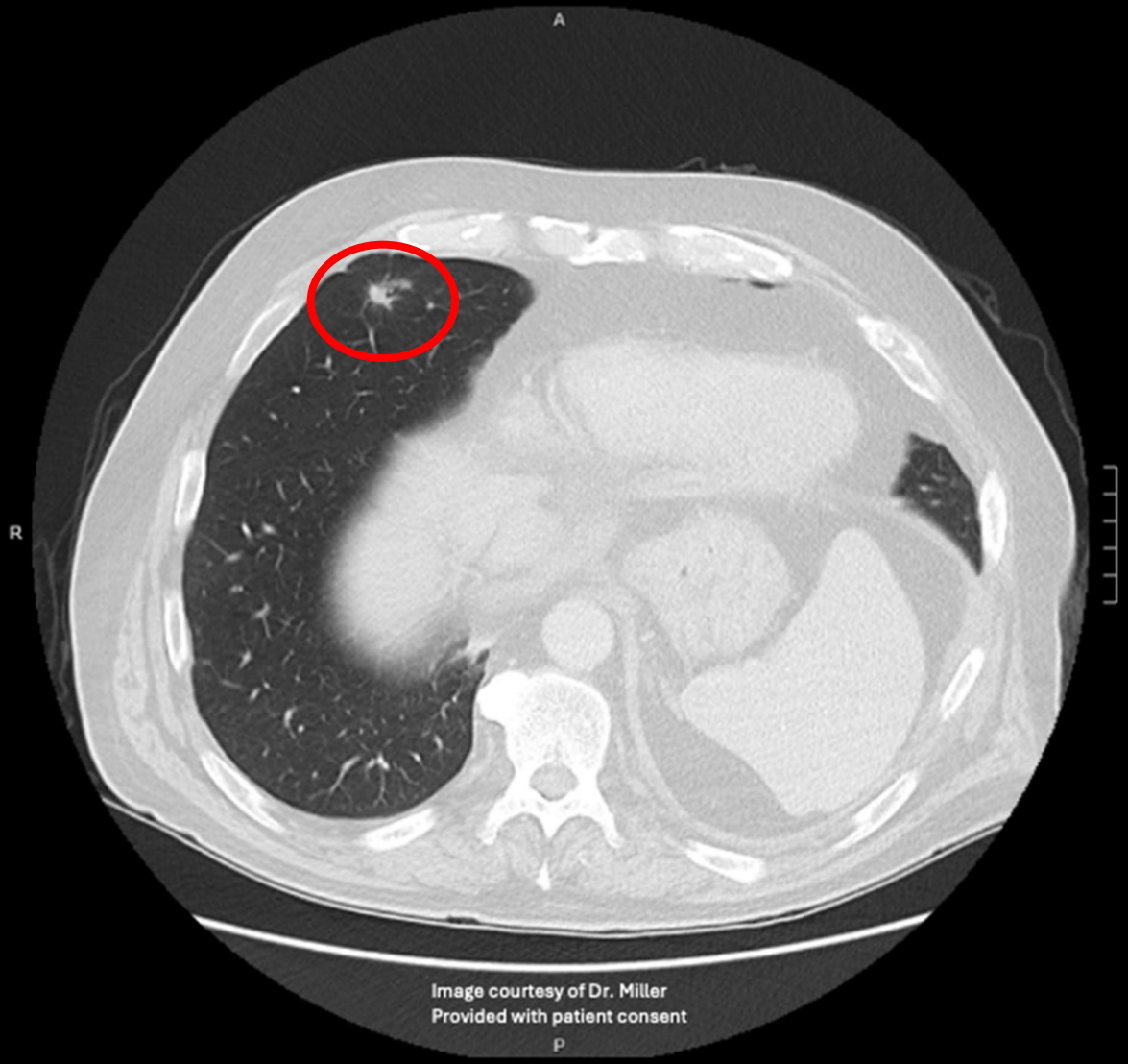
Case 3. Status Post 3 months of SMOi (continued 2)



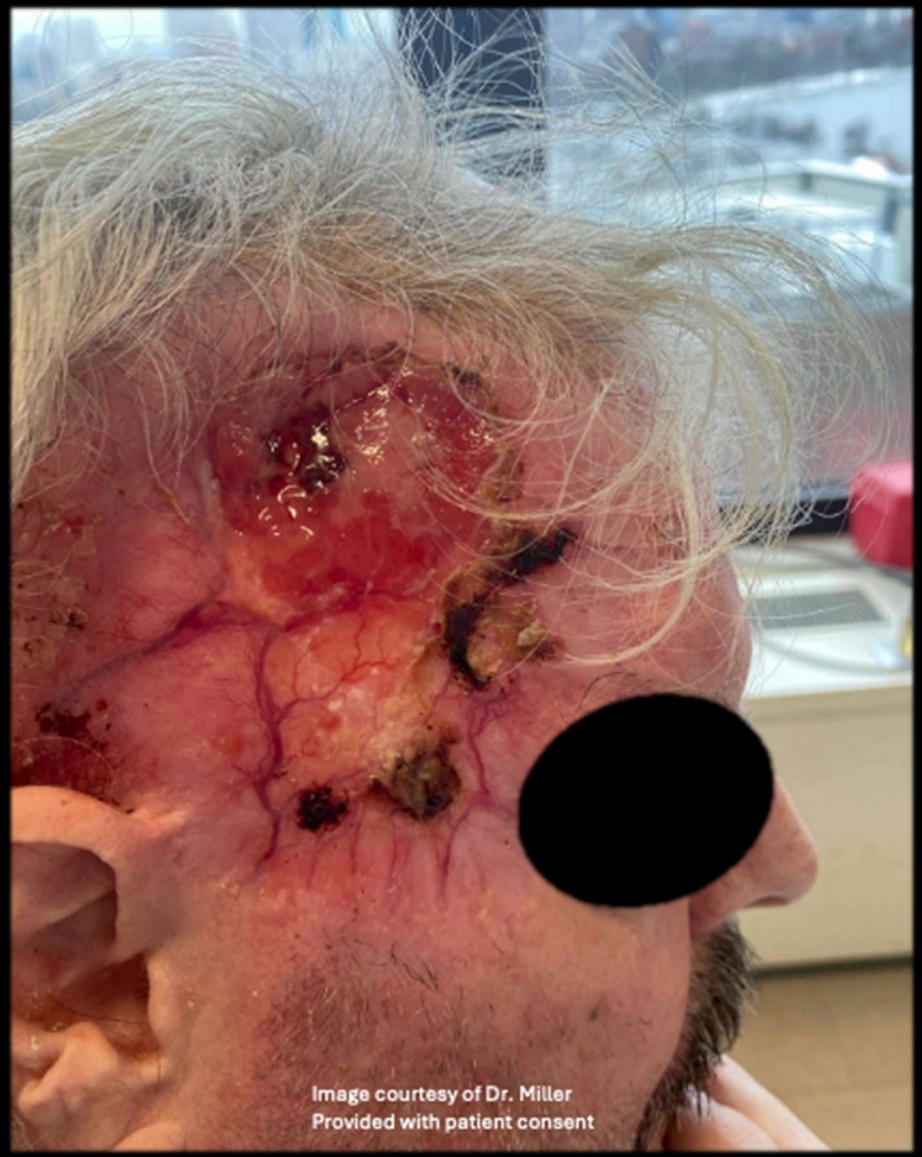
Case 3. Status Post 3 months of SMOi (continued 3)



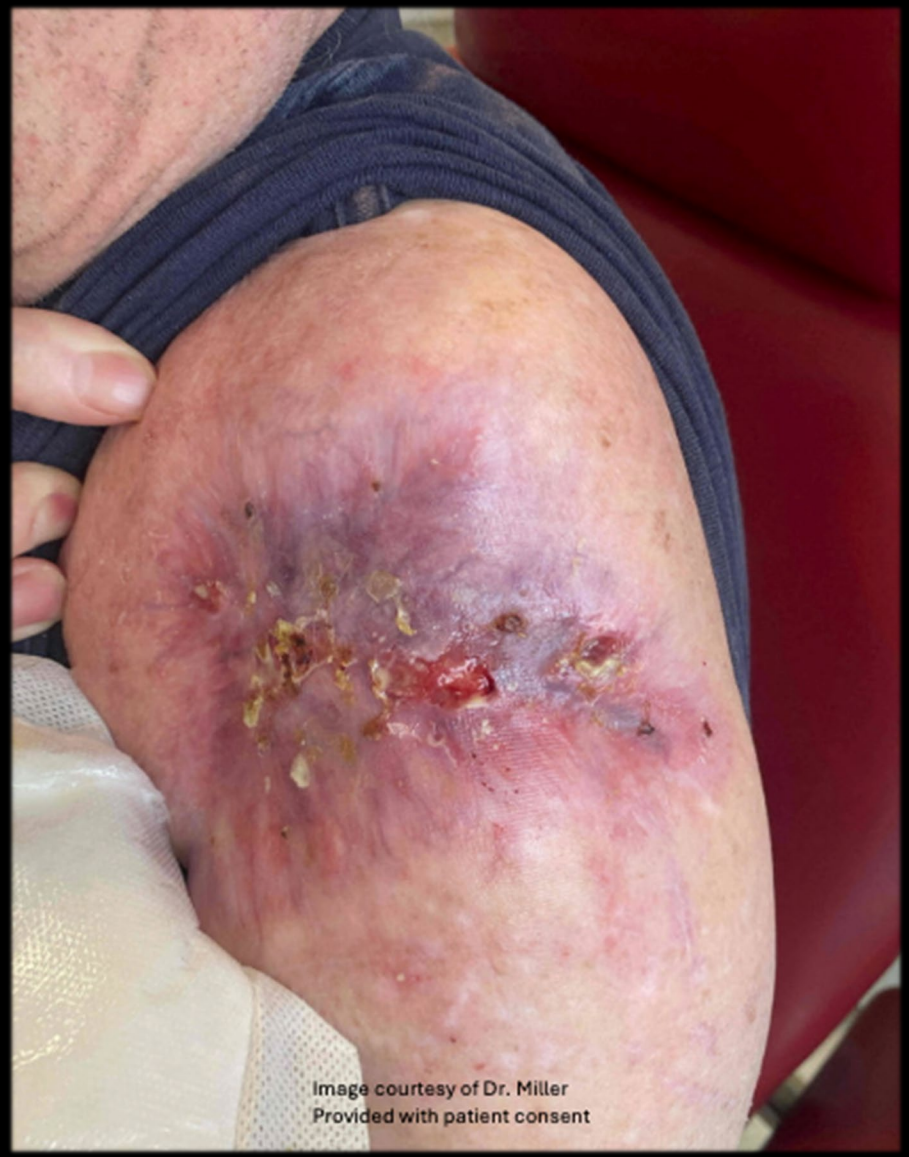
Case 3. Status Post 3 months of SMOi (continued 4)



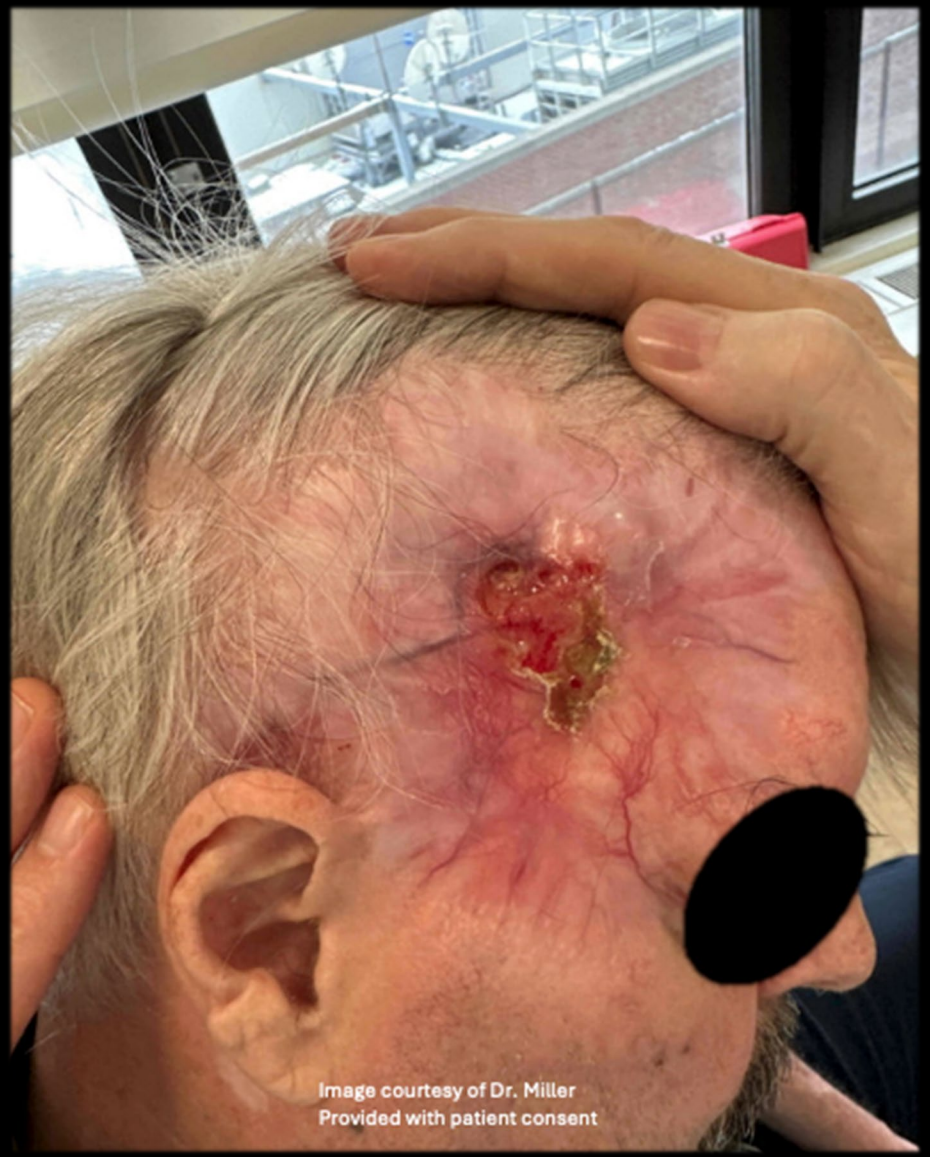
Case 3. Status Post 8 months of SMOi



Case 3. Status Post 8 months of SMOi (continued)



Case 3. Status Post 20 months of SMOi



Case 3. Status Post 20 months of SMOi (continued 1)

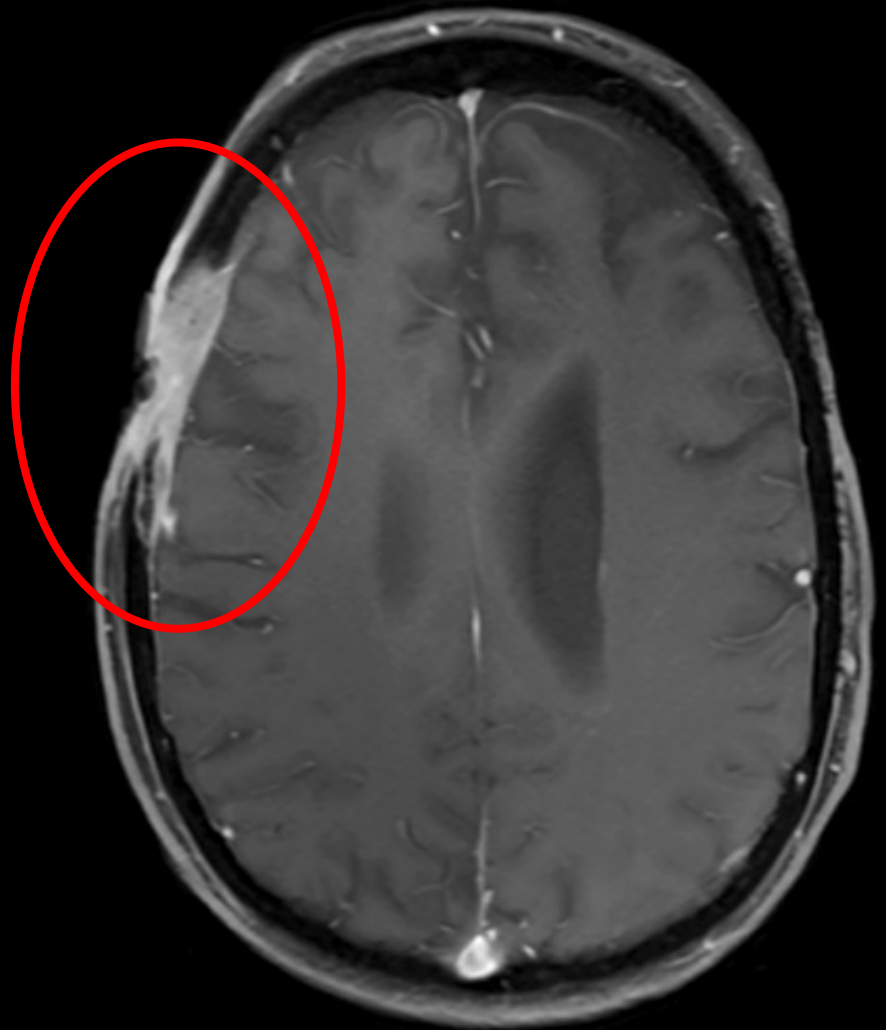
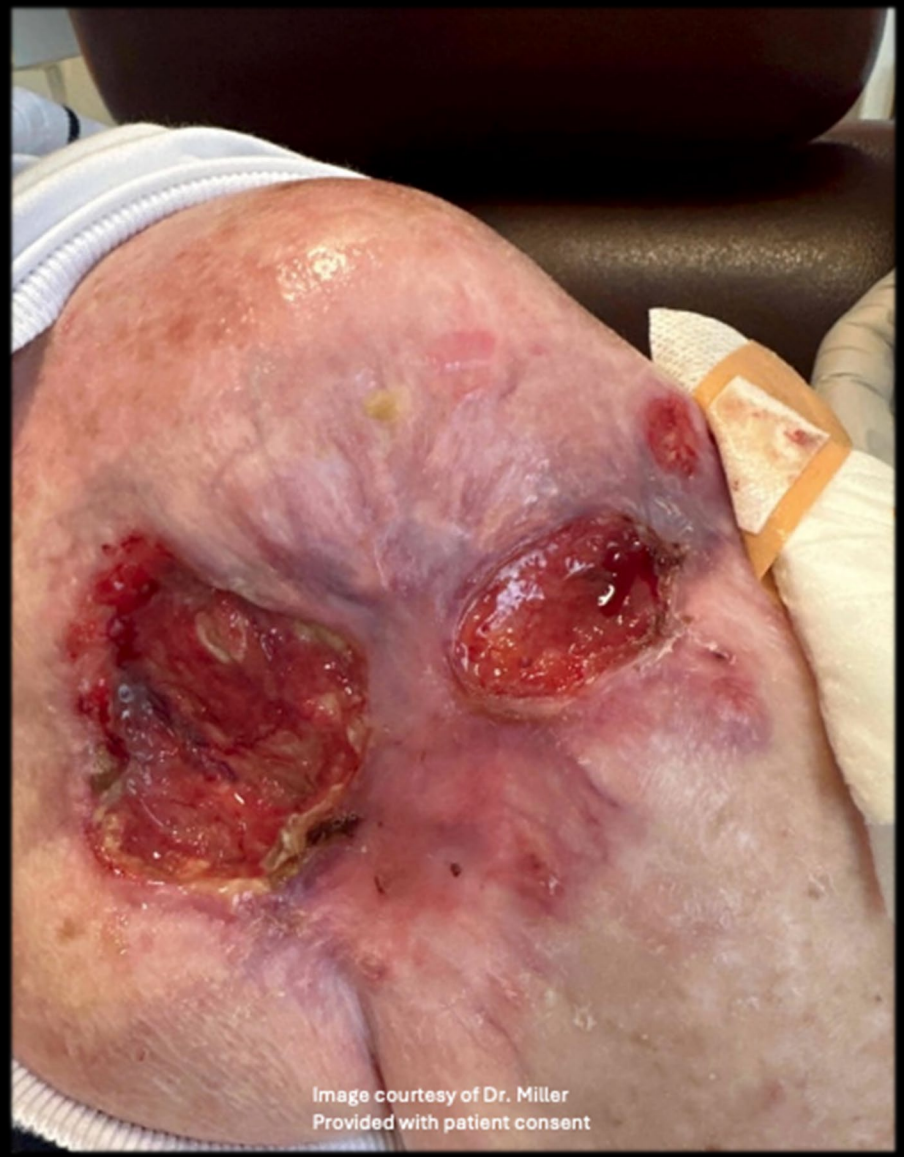
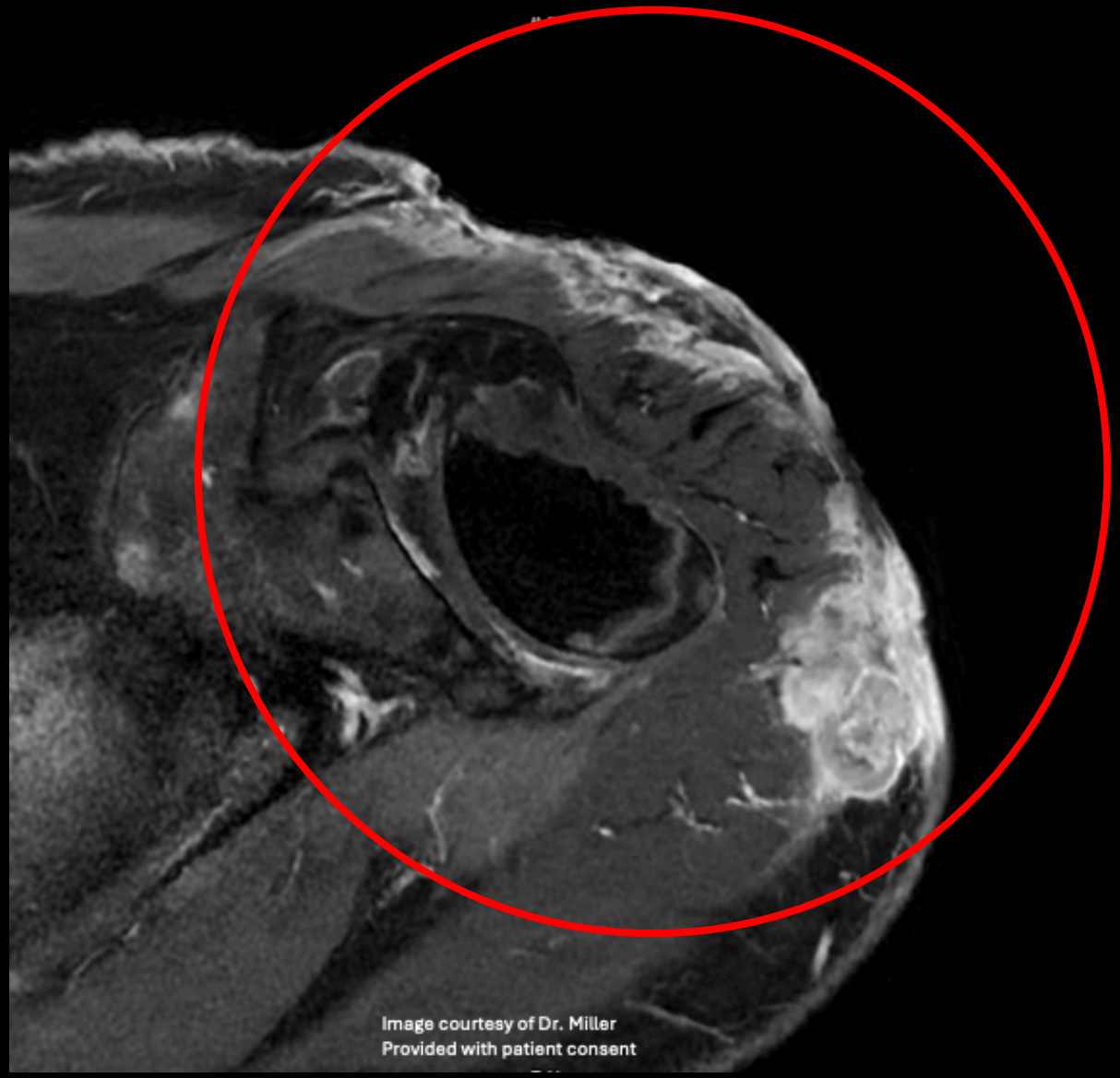


Image courtesy of Dr. Miller
Provided with patient consent

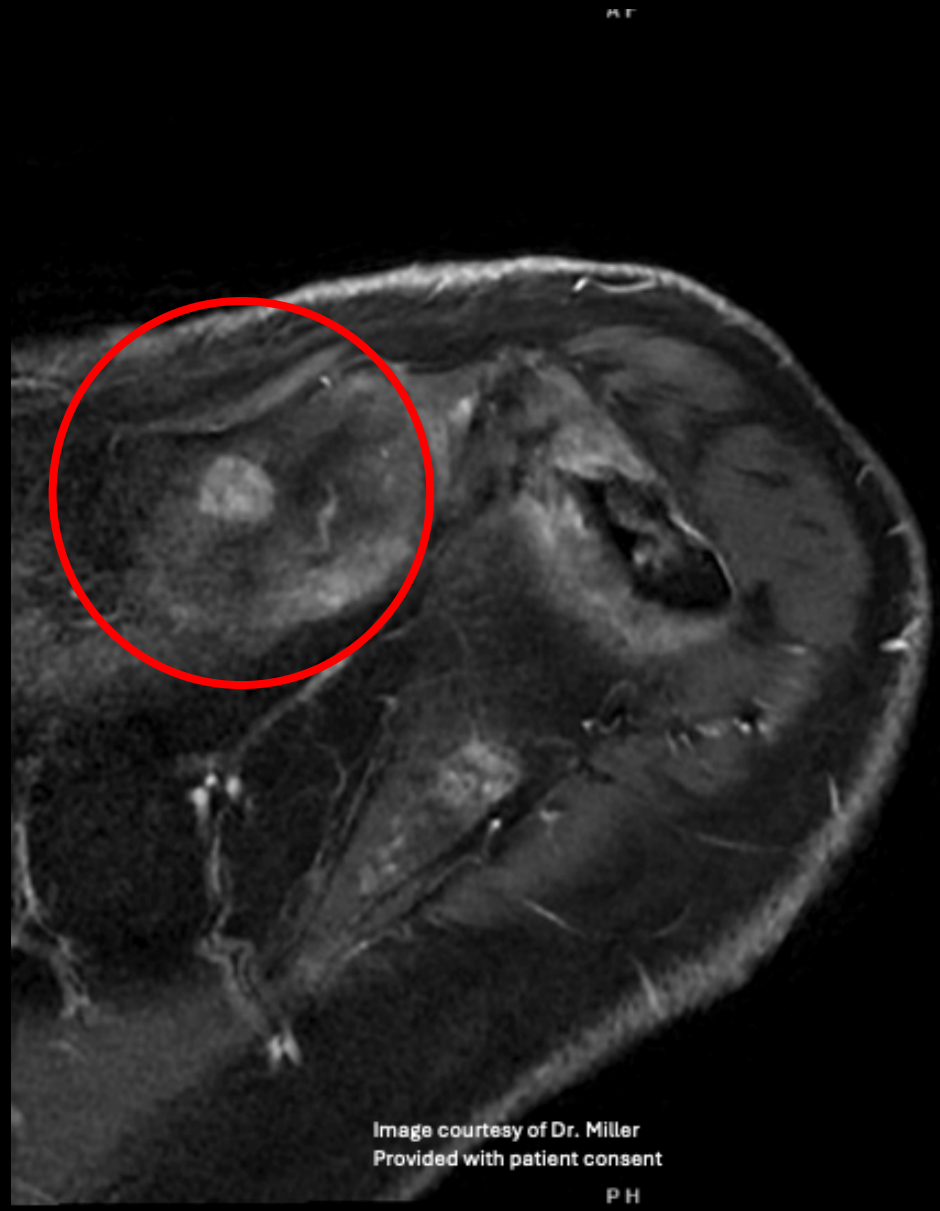
Case 3. Status Post 20 months of SMOi (continued 2)



Case 3. Status Post 20 months of SMOi (continued 3)

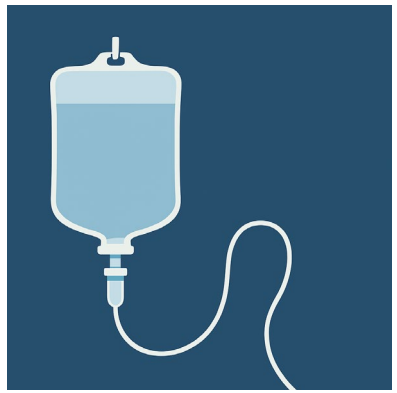


Case 3. Status Post 20 months of SMOi (continued 4)



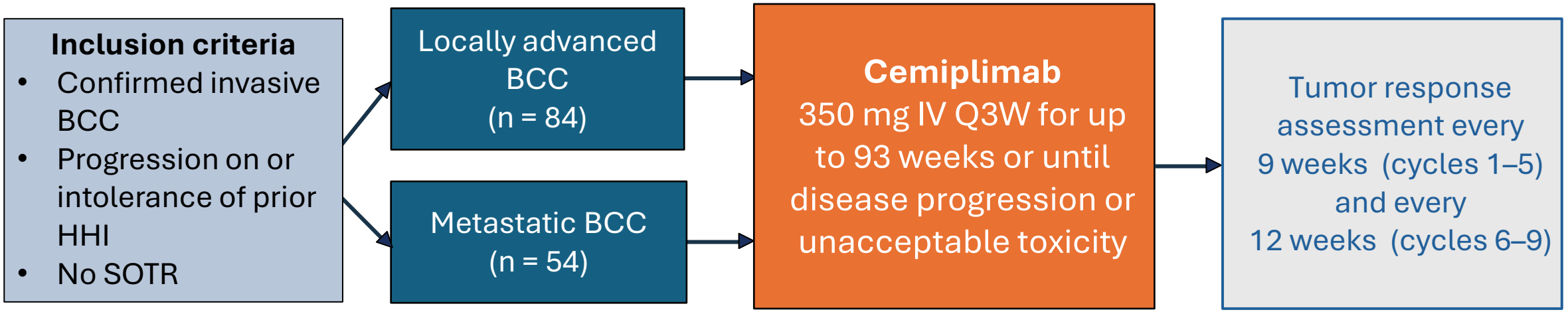
Question for Discussion

Which treatment options are going to be most beneficial to Bill?



Study 1620: Cemiplimab for Advanced BCC

Phase 2, Open-Label, Single Arm Trial



Primary endpoint: confirmed ORR, assessed by independent central review

Secondary endpoints: ORR (investigator assessed), DoR, CR, PFS, OS, QoL, safety

DoR = duration of response.

Cemiplimab-rwlc (Libtayo®) prescribing information, 4/2024 (www.Regeneron.com/downloads/libtayo_fpi.pdf). NCT03132636 (https://clinicaltrials.gov/study/NCT03132636). URLs accessed 4/18/25.

Cemiplimab for Advanced BCC

- Approval by US FDA on February 9, 2021
- First FDA-approved immunotherapy for BCC (locally advanced/metastatic cases previously treated with HHI or for whom HHI is not appropriate)

Cemiplimab in patients not tolerating or progressing on HHI		
	mBCC (n=54)	laBCC (n=84)
ORR, %	22	32
CR, %	1.9	7
PR, %	20	25
DoR, mo (95% CI)	16.7 (9.0–25.8+)	Not reached (2.1–36.8+)

FDA = Food and Drug Administration; US = United States.

Cemiplimab-rwlc (Libtayo®) prescribing information, 4/2024 (www.Regeneron.com/downloads/libtayo_fpi.pdf). FDA approval for cemiplimab in laBCC and mBCC (www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-cemiplimab-rwlc-locally-advanced-and-metastatic-basal-cell-carcinoma). Accessed 4/18/25/

Combination Therapy for Advanced BCC

Pembrolizumab ± Vismodegib for Advanced BCC

- No life-threatening AEs or deaths during study
- 3 grade 3 AEs occurred out of 98 AEs from 16 participants (1 case of hyponatremia attributed to pembrolizumab)
- 23 irAEs; grade 1/2 dermatitis and fatigue most common

	All participants (N = 16)	Pembrolizumab* (n = 9)	Pembrolizumab* + vismodegib (n = 7)
ORR	38%	44%	29%
Probability			
1-year PFS	70%	62%	83%
1-year OS	94%	89%	100%

irAE = immune-related AE.

Chang ALS, et al. *J Am Acad Dermatol*. 2019;80:564-566.

*Pembrolizumab is not currently FDA-approved for BCC.

Phase 2 Study of NIVO ± RELA or IPI for Patients With Advanced Treatment-Naive or Treatment-Refractory BCC

Inclusion criteria

- Adults with histologically confirmed BCC considered by investigator to be metastatic unresectable
- ECOG PS 0 or 1
- No concurrent systemic immunosuppressive therapy

N = 24 enrolled
laBCC = 19
mBCC = 5
Treatment naïve = 10

NIVO
Treatment-naïve or HHI-refractory

NIVO + RELA
aBCC refractory* to anti-PD-(L)1

NIVO + IPI
aBCC refractory* to NIVO + RELA

- **Primary endpoint:** ORR per RECIST 1.1
- **Secondary endpoints:** PFS, DoR, OS

aBCC = advanced BCC; ECOG = Eastern Cooperative Oncology Group; IPI = ipilimumab; NIVO = nivolumab; PD-(L)1 = PD-1 and/or PD-L1; PS = performance status; RELA = relatlimab. Nivolumab ± Ipilimumab and Nivolumab ± relatlamab are not FDA-approved for this indication.

Schenk KM, et al. *Ann Oncol*. 2022;33(suppl 7):S922 (abstract 820P). NCT03521830. (https://clinicaltrials.gov/study/NCT03521830). Accessed 4/18/25.

*Refractory: SD at 36 wk or PD during treatment or within 16 wk of treatment discontinuation.
Schenk KM, et al. *Ann Oncol*. 2022;33(suppl 7):S922 (abstract 820P).

NIVO ± RELA or IPI for Treatment-Naïve or -Refractory aBCC: Efficacy and Safety

Best overall response of patients with aBCC to NIVO and NIVO + RELA			
Best response per RECIST 1.1	**NIVO**		**NIVO + RELA (n = 6)**
	All Evaluable (n = 15)	**Treatment Naive (n = 10)**	
CR/PR, no. (%)	6 (40)	5 (50)	1 (17)*
SD, no. (%)	9 (60)	5 (50)	4 (67)

- 0/5 patients with metastatic disease had a response, regardless of cohort
- Toxicities associated with each regimen were consistent with previous experience

Nivolumab ± ipilimumab and Nivolumab ± relatlamab are not FDA-approved for this indication.

Schenk KM, et al. *Ann Oncol*. 2022;33(suppl 7):S922 (abstract 820P).

*Patient who experienced PR to NIVO + RELA previously experienced SD on NIVO lasting >48 weeks.

Concluding Thoughts…

Visit this link for educational resources:
https://linktr.ee/NMSC_ACMS25

- CREATE a free personalized office poster
- DOWNLOAD mixed reality animations
- VIEW supplemental tools and resources

Thank you!