Module 2 - Developing Treatment Plans for Patients With High-Risk cSCC: Neoadjuvant Therapy

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Case #2: History

History of present illness (HPI)

- A 71-year-old female with a history over several months of a painful right nasal skin lesion
- Biopsy: Squamous cell carcinoma
- Presented to Mohs for resection

Past medical history (PMHx)

- History of prior nonmelanoma skin cancers
- No immunosuppression
- No prior radiation

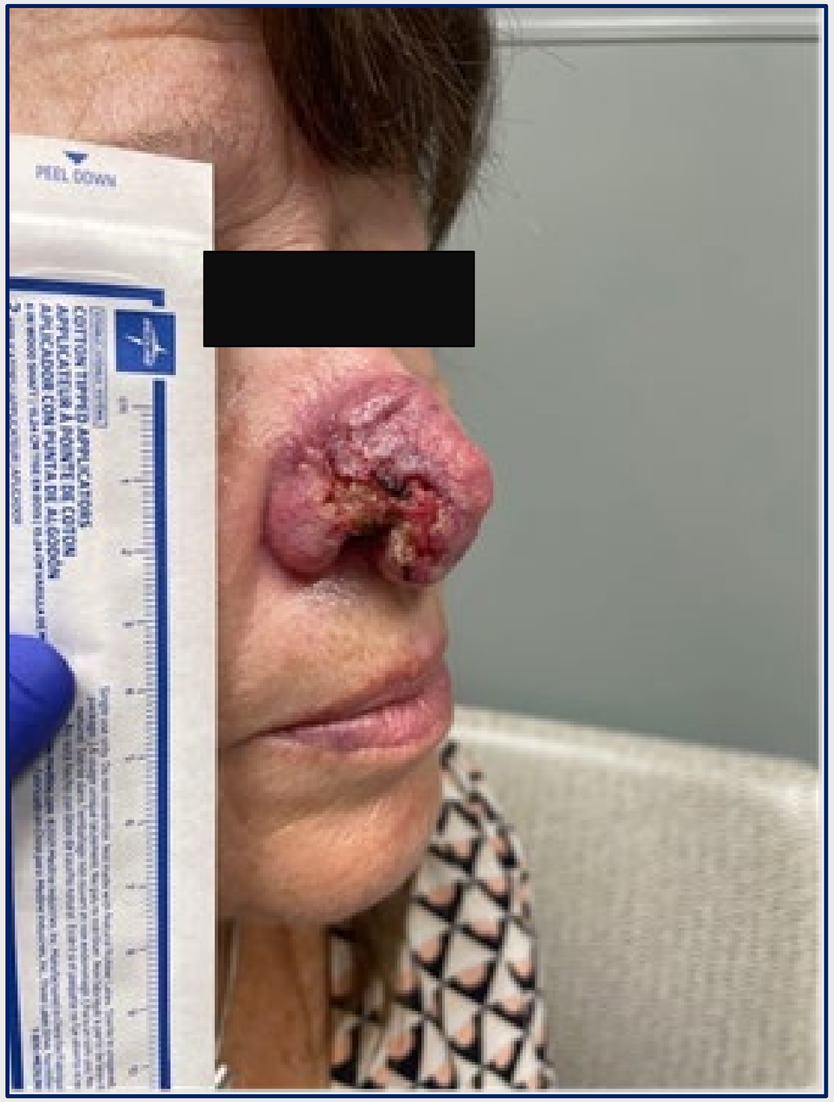


Image courtesy of Neil Gross, MD, FACS

Case #2: Exam

- **General:** No acute distress; normocephalic and atraumatic; tearful
- **Nose:** **Deeply ulcerative mass with full thickness involvement of right nasal ala and nasal tip**
- **Neck:** No adenopathy
- **Neurologic assessment:** Cranial nerves are intact

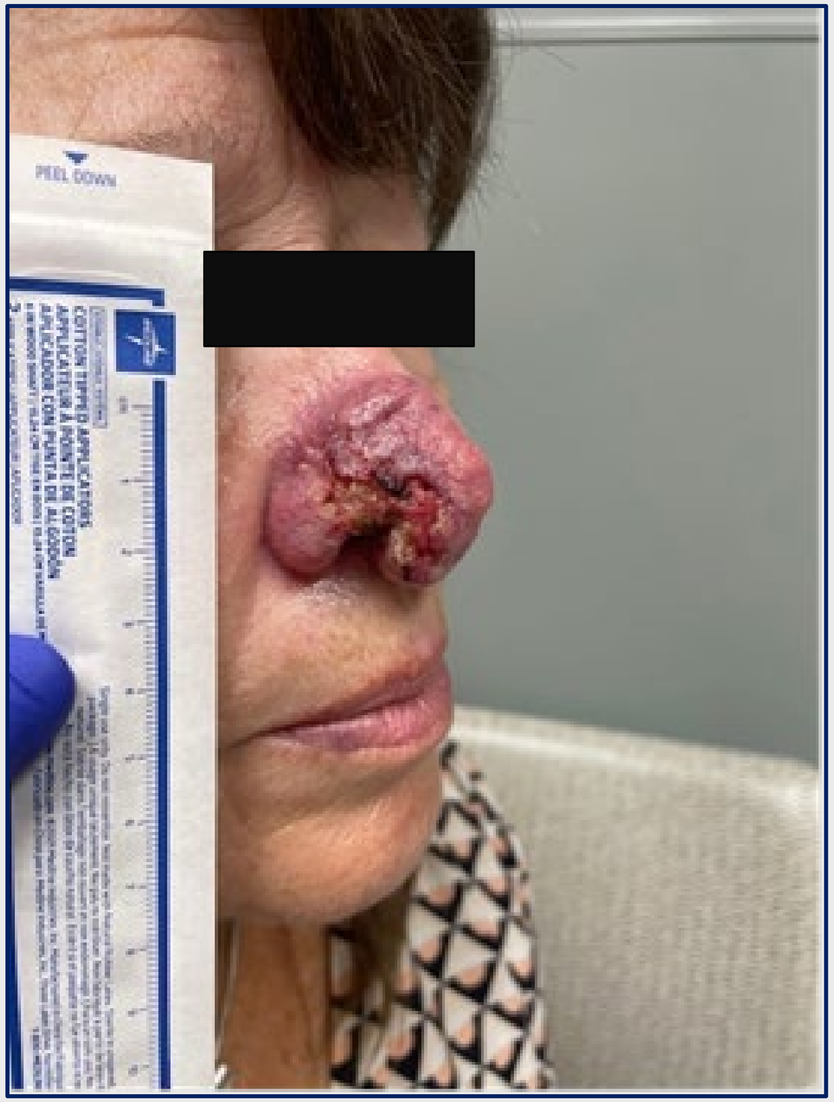


Image courtesy of Neil Gross, MD, FACS

Case #2: Baseline Imaging

- 1.7 x 2.7 x 1.5 cm enhancing lesion of the right nasal ala
- No bone involvement
- No cranial nerve involvement
- No adenopathy

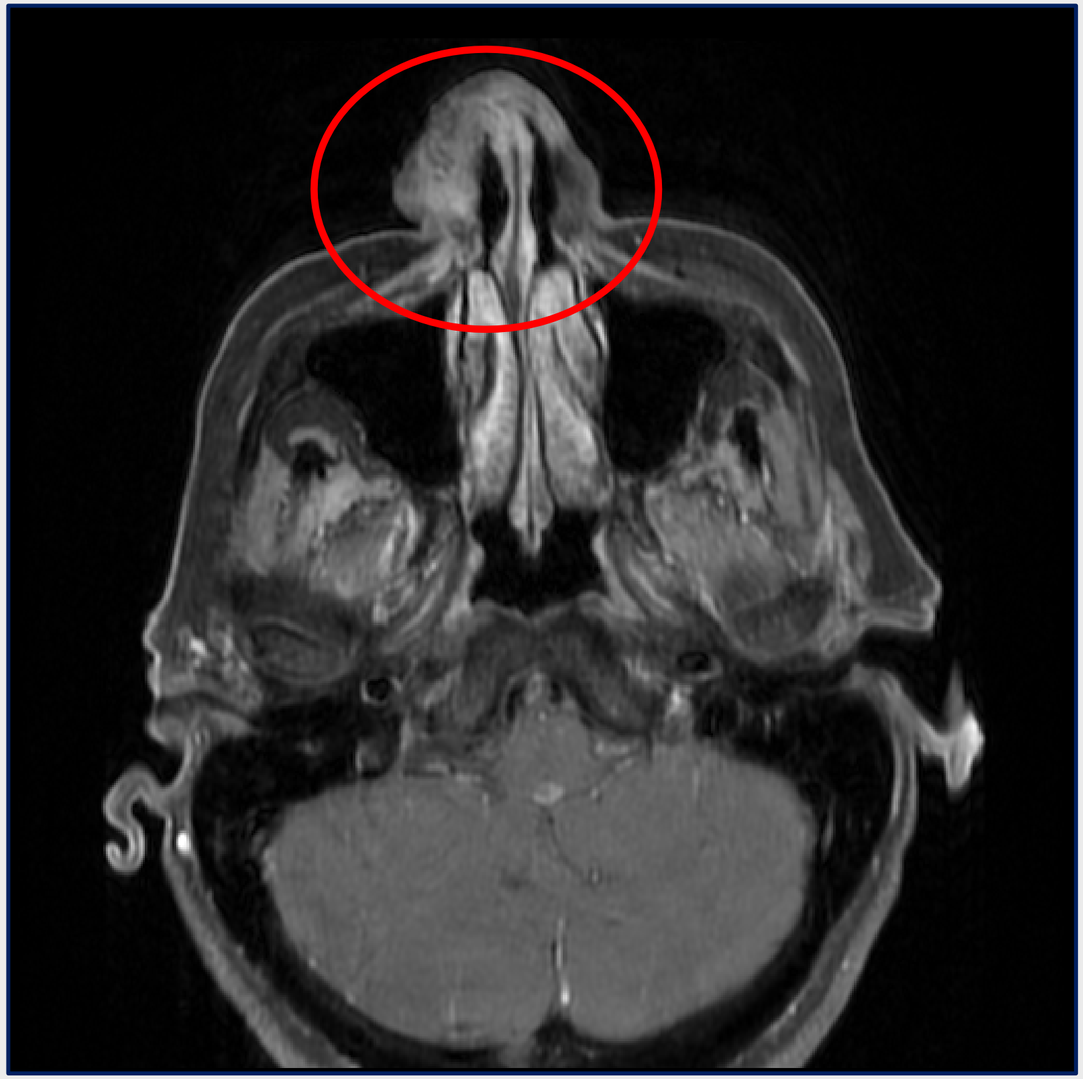


Image courtesy of Neil Gross, MD, FACS

Case #2: Classification

American Joint Committee on Cancer (AJCC) 8: Stage III

- cT3: Tumor larger than 4 cm in maximum dimension or minor bone erosion or perineural invasion or deep invasion*
- cN0: No regional lymph node metastasis
- cM0: No distant metastasis

*Deep invasion is defined as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumor).

What About Adjuvant Therapy?

KEYNOTE-630
NCT03833167

NEWS RELEASE

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

2024-08-29

C-POST
NCT03969004

Adjuvant (cemiplimab) Significantly Improves Disease-Free Survival (DFS) After Surgery in High-Risk Cutaneous Squamous Cell Carcinoma (CSCC) in Phase 3 Trial

January 13, 2025 at 6:15 AM EST

PDF Version

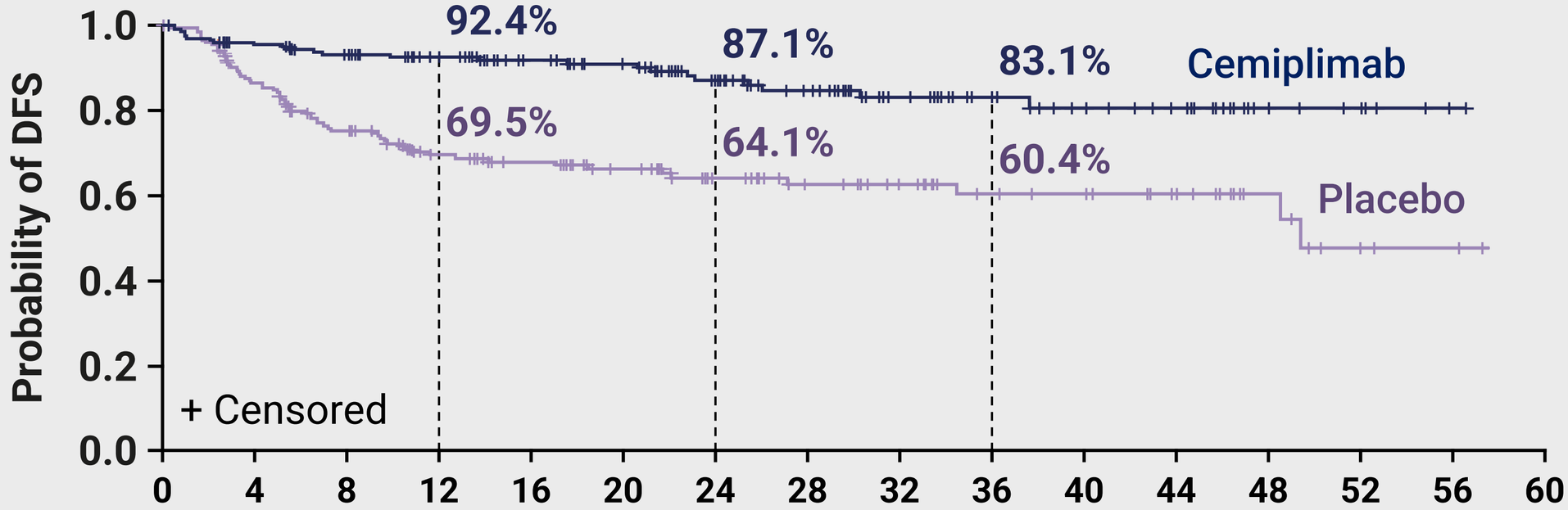
Primary endpoint of DFS met at first prespecified interim analysis, showing a 68% reduction in the risk of disease recurrence or death in patients with high-risk CSCC after surgery compared to placebo

Koyfman SA, et al. American Society of Clinical Oncology (ASCO) 2025; Abstract 6000. Rischin D, et al. ASCO 2025: Abstract 6001.

Adjuvant Cemiplimab in High Risk cSCC

C-POST Trial

	# of events	Median disease-free survival (months)
Cemiplimab	24	NR (NE–NE)
Placebo	65	49.4 (48.5–NE)
HR for disease recurrence or death	0.32 (95% CI, 0.20–0.51) $p < .001$	



Patients at risk

Cemiplimab	209	172	157	132	116	104	83	66	47	33	27	22	9	6	1	0
Placebo	206	161	130	94	82	69	53	42	36	26	24	18	10	4	2	0

CI = confidence interval; cSCC = cutaneous squamous cell carcinoma; DFS = disease-free survival; HR = hazard ratio; NE = not evaluable; NR = not reached.

Rischin D, et al. *New Engl J Med.* 2025;393:774-785.

What About Neoadjuvant Therapy?

Neoadjuvant Cemiplimab

Phase 2 nonrandomized, multicentre study (Australia, Germany, United States)

Primary endpoint

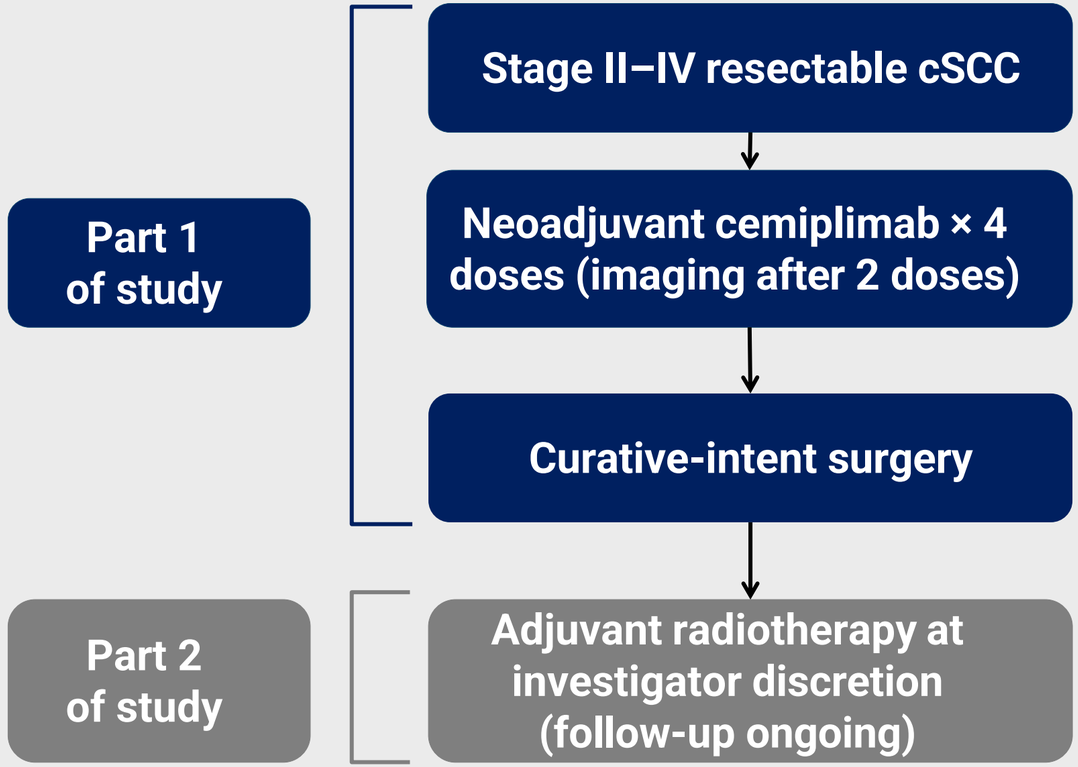
- pCR (0% viable tumor) rate per ICPR
  - Null hypothesis: pCR rate = 25%

Secondary endpoints

- MPR (>0% but ≤10% viable tumor) rate per ICPR
- pCR and MPR rates per local pathology review
- Radiological ORR per RECIST 1.1
- Safety and tolerability

Correlative analyses

- Exploration of TMB and PD-L1 expression with treatment response

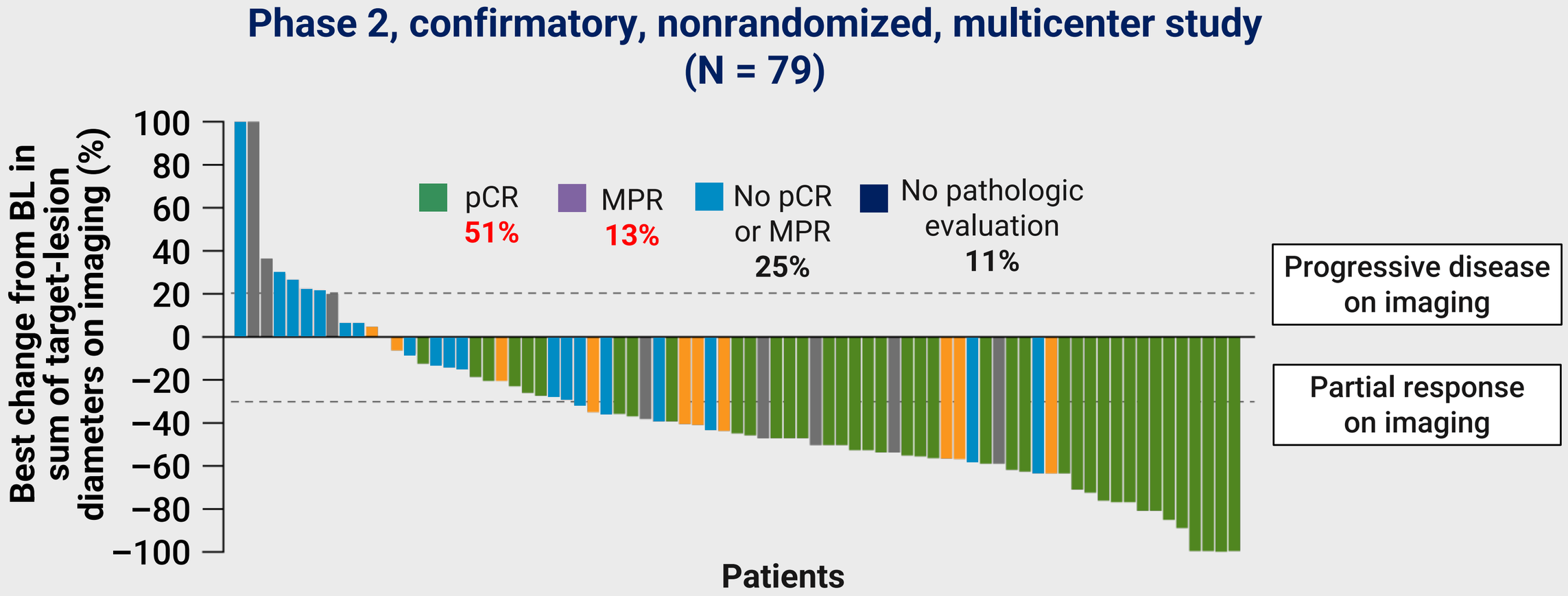


ICPR = independent central pathologic review; MPR = major pathological response; ORR = objective response rate; pCR = pathologic complete response; PD-L1 = programmed cell death-ligand 1; RECIST = Response Evaluation Criteria in Solid Tumours; TMB = tumor mutational burden.

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

Phase 2 Neoadjuvant Cemiplimab for Stage II to IV cSCC

Results

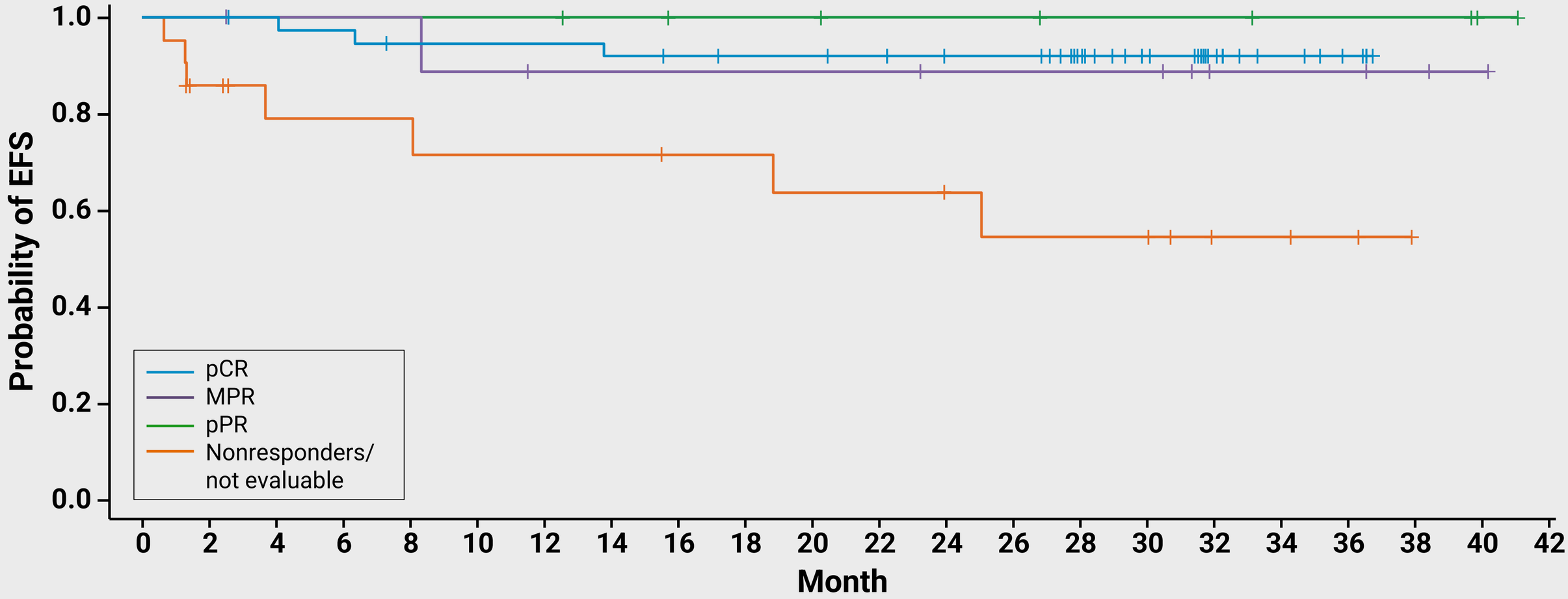


BL = baseline; pCR = pathologic complete response (absence of viable tumor cells in surgical specimen); MPR = major pathological response (presence of viable tumor cells that constitute ≤10% of surgical specimen).

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

Phase 2 Neoadjuvant Cemiplimab for Stage II to IV cSCC

Results



Median follow-up = 29.4 months (range: 1.3–41.3)

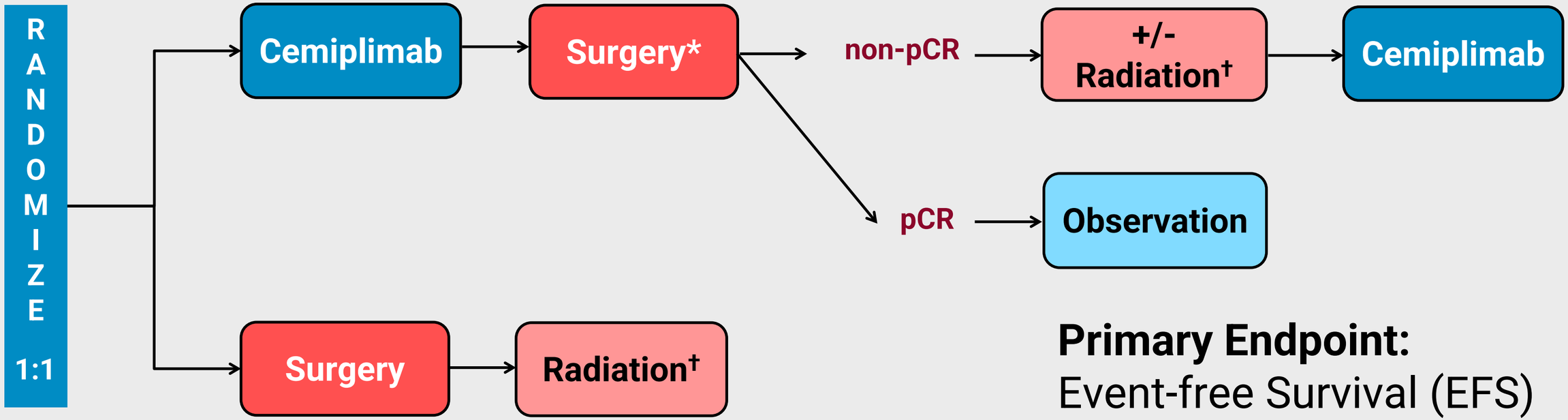
EFS = event-free survival.

Gross ND, et al. *Lancet Oncol.* 2023;24:1196-1205. Rischin D, et al. European Society for Medical Oncology (ESMO) 2024.

NRG-HN014 Schema

Randomized Phase 3 Trial

N = 420



Primary Endpoint:
Event-free Survival (EFS)

* Response-adapted oncologic surgery
†As indicated per protocol
pCR = pathologic complete response.

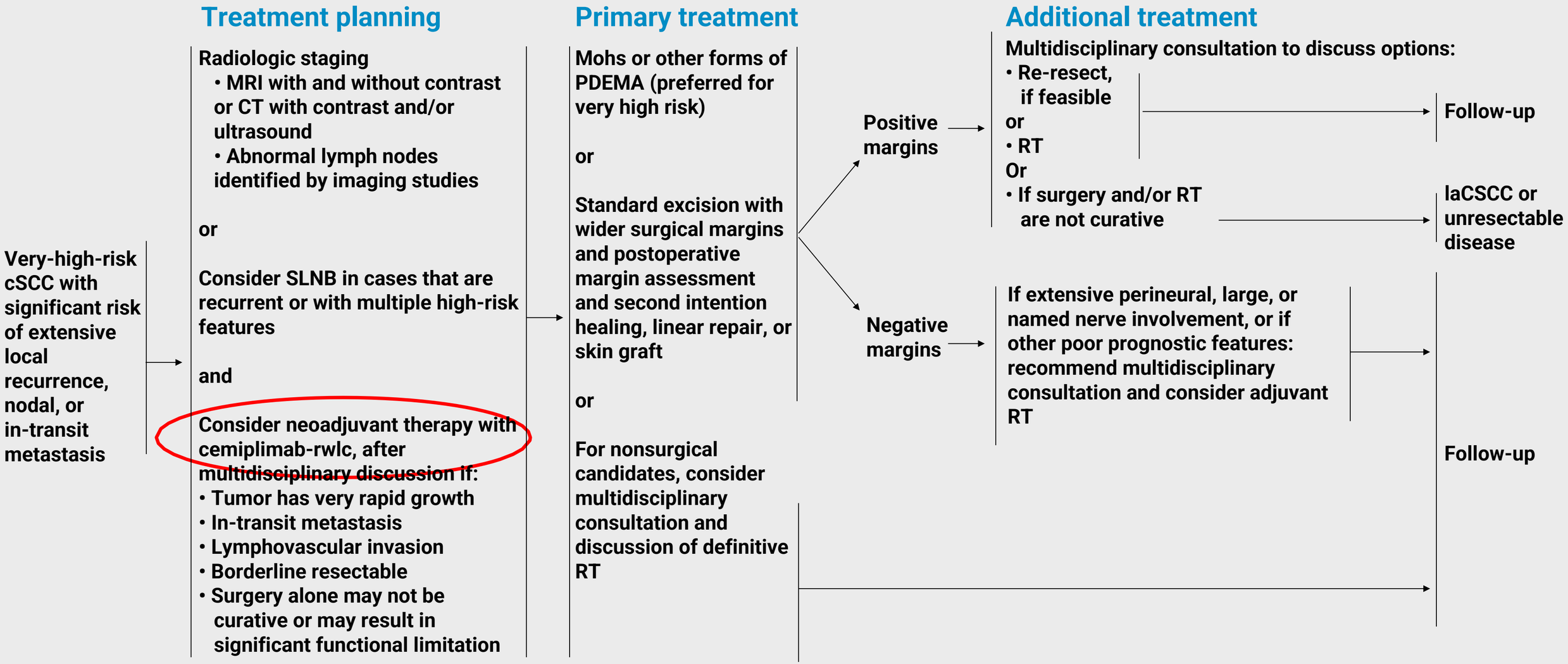
ClincalTrials.gov: NCT06568172

CCTG TROG CANCER RESEARCH NRG ONCOLOGY
Advancing Research. Improving Lives.

When to Consider Neoadjuvant Therapy?

NCCN guidelines version 1.2026 squamous cell skin cancer

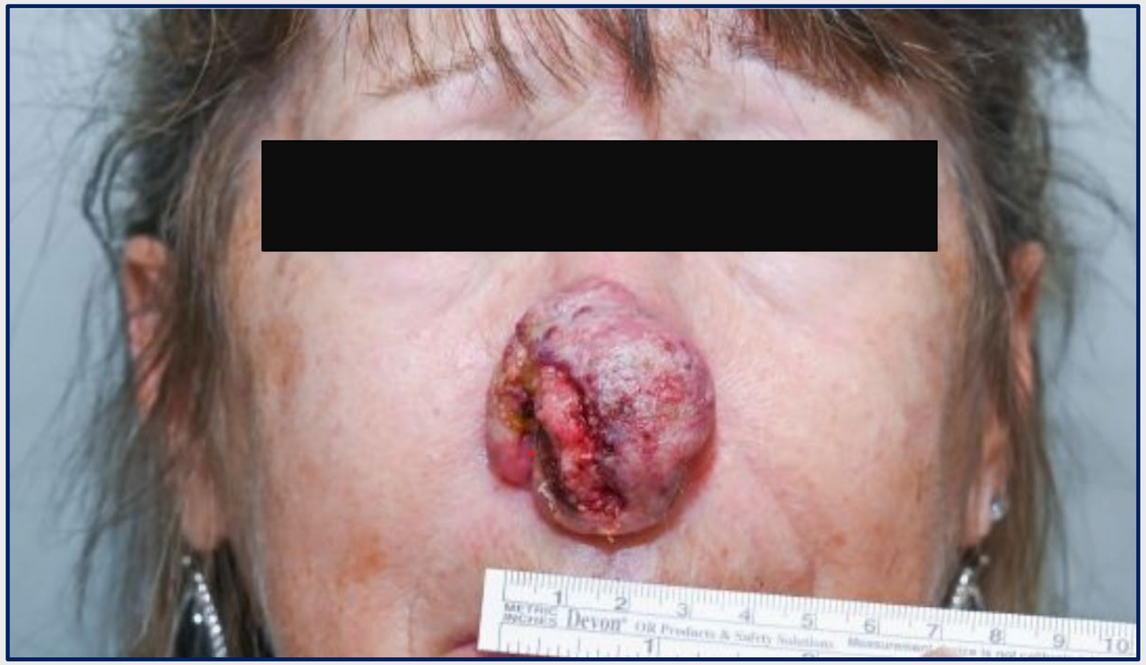
Very-high-risk cSCC

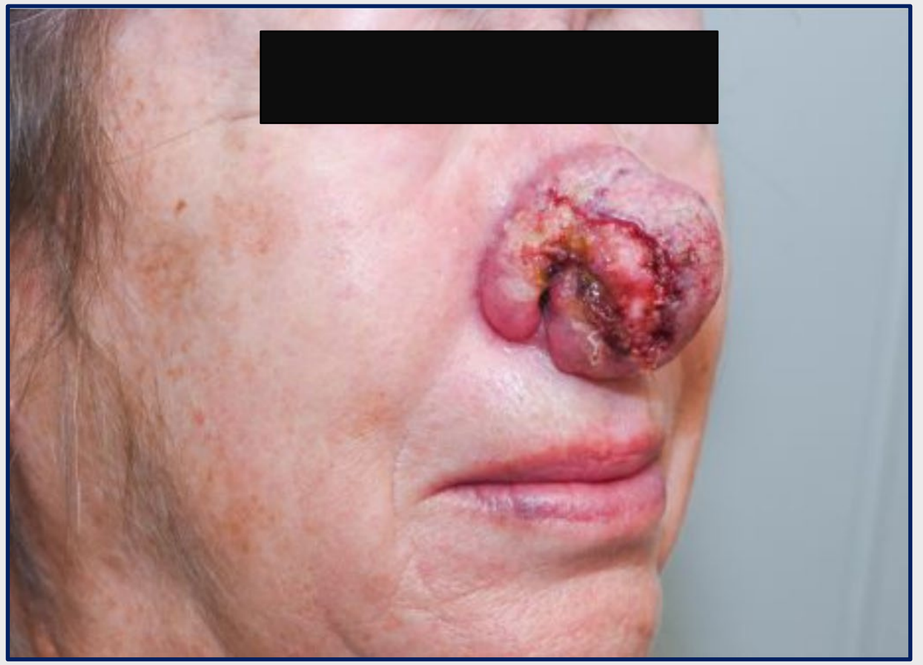


National Comprehensive Cancer Network (NCCN). Guidelines for squamous cell skin cancer, V1.2026 (www.nccn.org/professionals/physician_gls/pdf/squamous.pdf). Accessed 12/5/2025.

Case #2: Neoadjuvant Immunotherapy

- Clinical progression after 1 cycle of cemiplimab

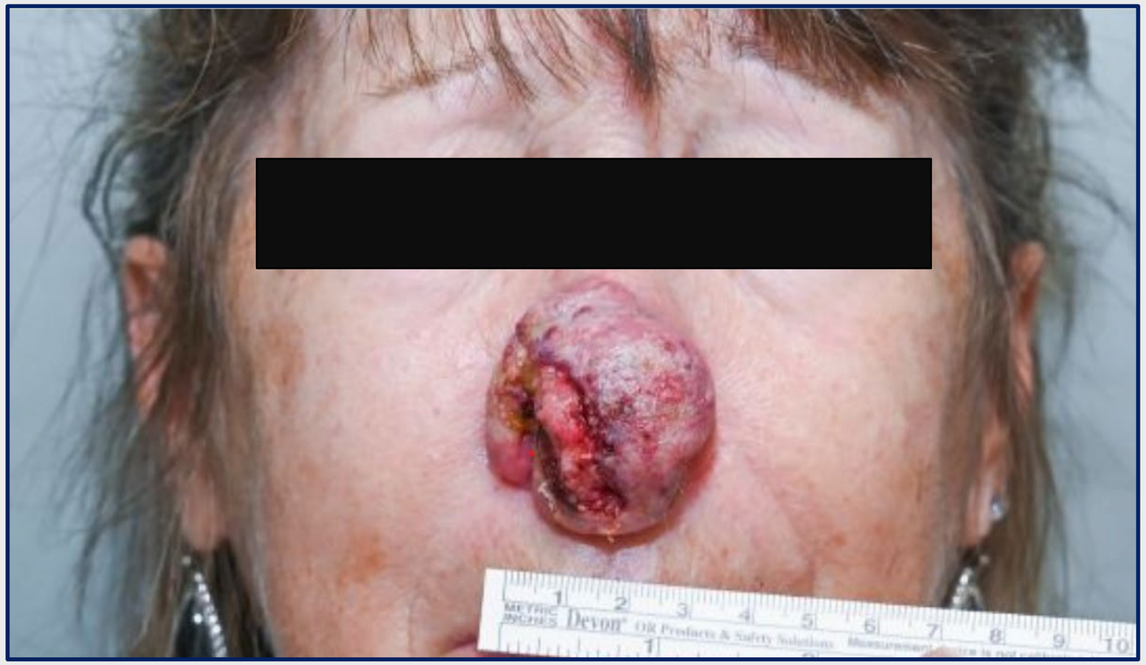




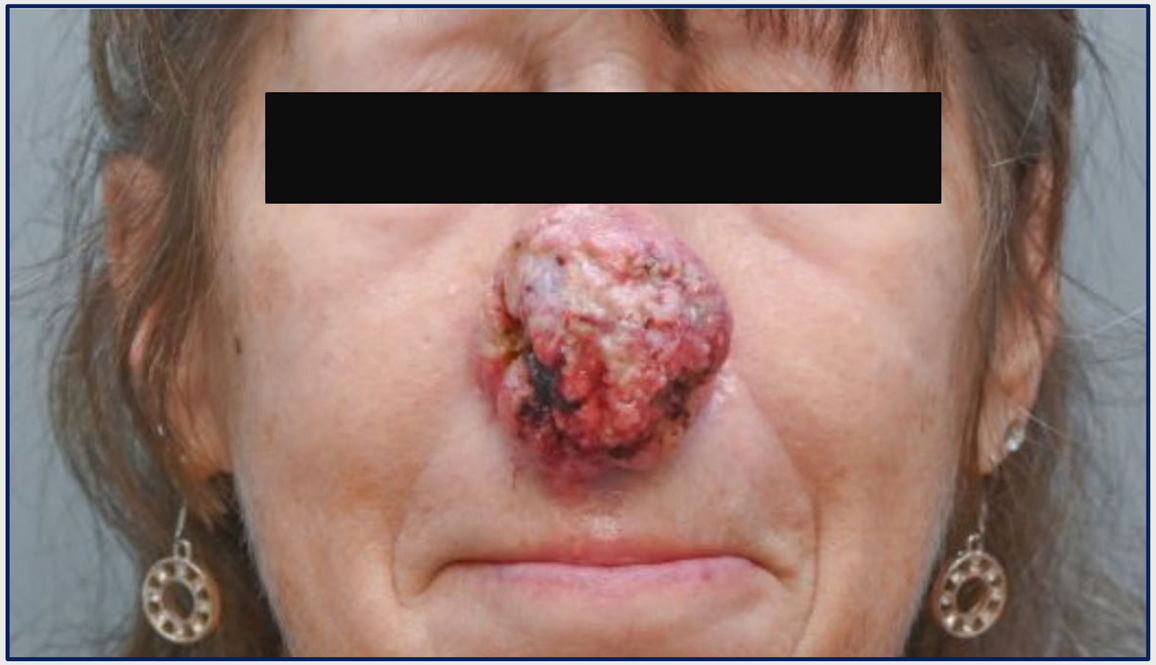
Images courtesy of Neil Gross, MD, FACS

Case #2: Neoadjuvant Immunotherapy

- Clinical progression after 2 cycles of cemiplimab



POST Cycle 1

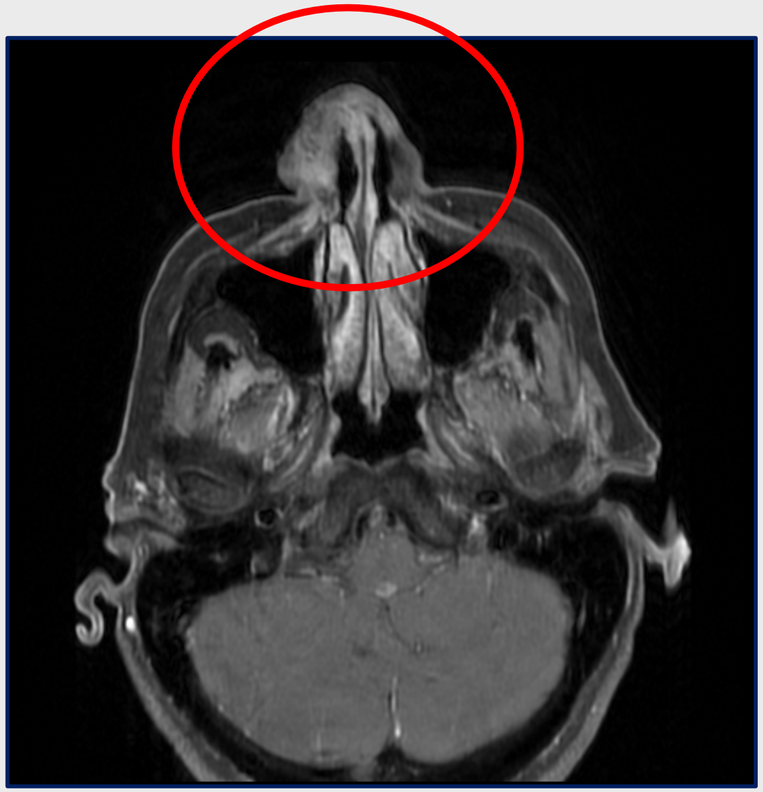


POST Cycle 2

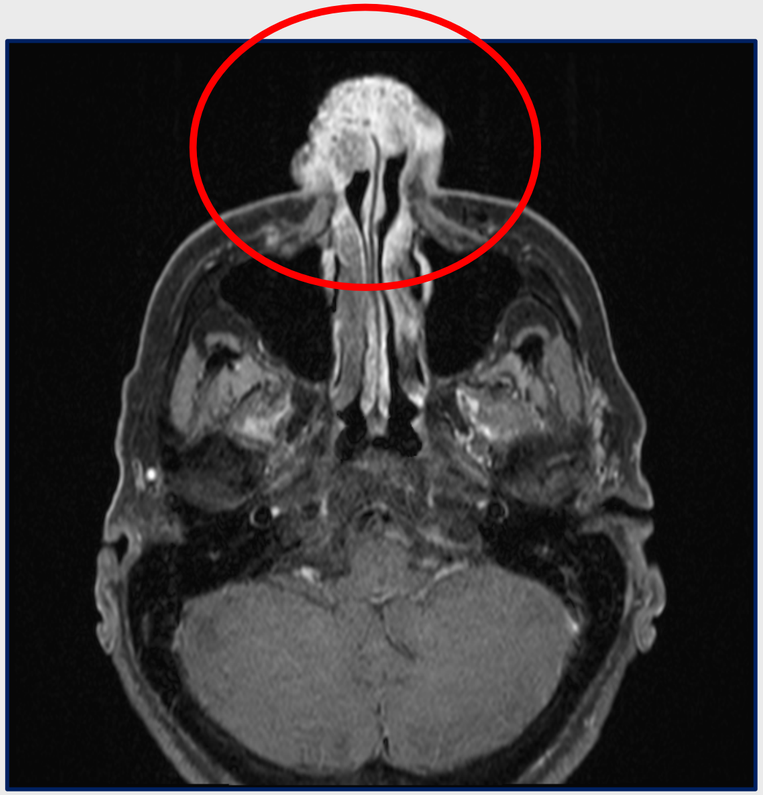
Images courtesy of Neil Gross, MD, FACS

Case #2: Neoadjuvant Immunotherapy

- Radiographic progression after 2 cycles of cemiplimab



Baseline

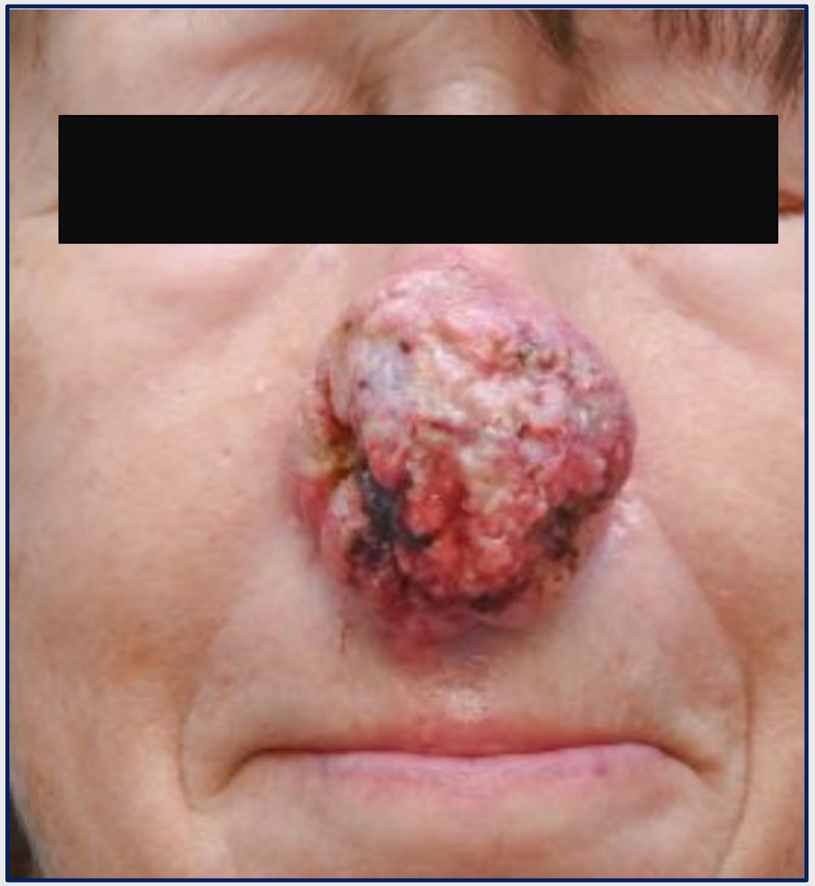


POST Cycle 2

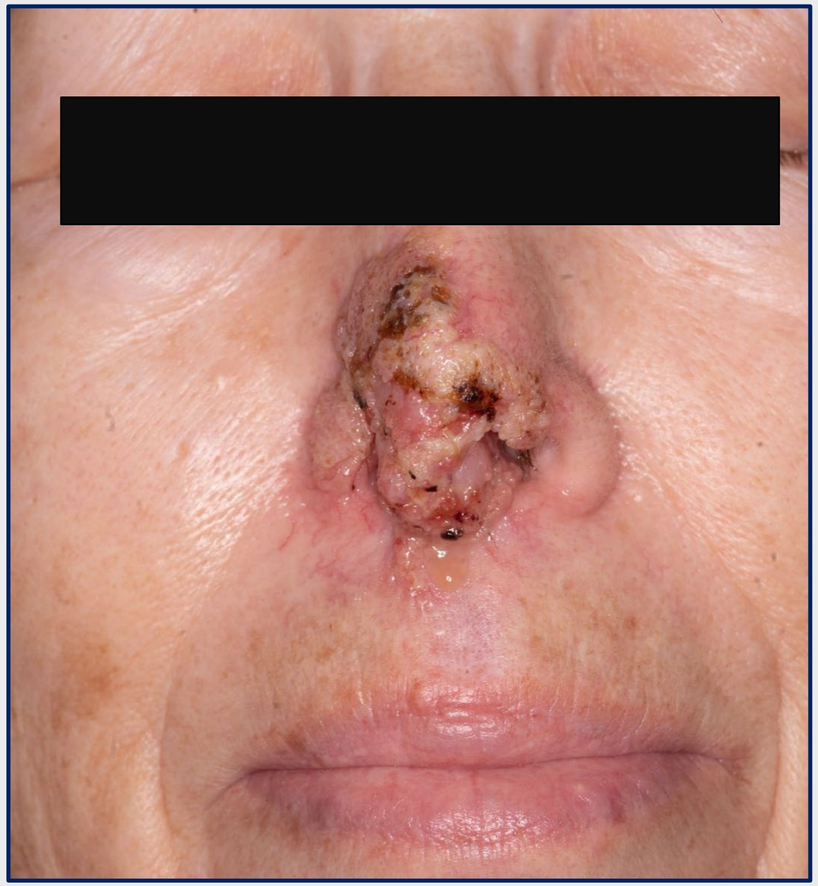
Images courtesy of Neil Gross, MD, FACS

Case #2: Neoadjuvant Chemotherapy

- Switched to carboplatin/paclitaxel



Post immunotherapy



Post chemotherapy

Images courtesy of Neil Gross, MD, FACS