Cutaneous Squamous Cell Carcinoma Updates and Controversies Case Study

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No conflicts of interest

Case Study

- A challenging cutaneous squamous cell carcinoma
  - Multidisciplinary team approach

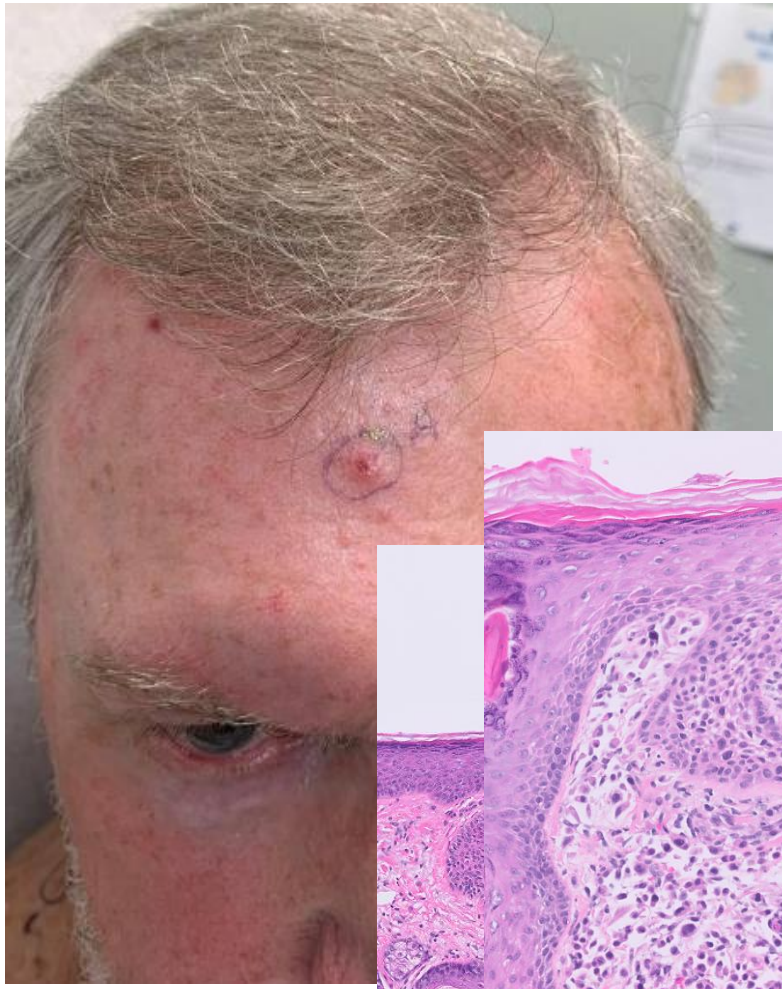
Our patient

70 year-old man, 2 years s/p renal transplant for IgA nephropathy

- Prednisone
- Tacrolimus

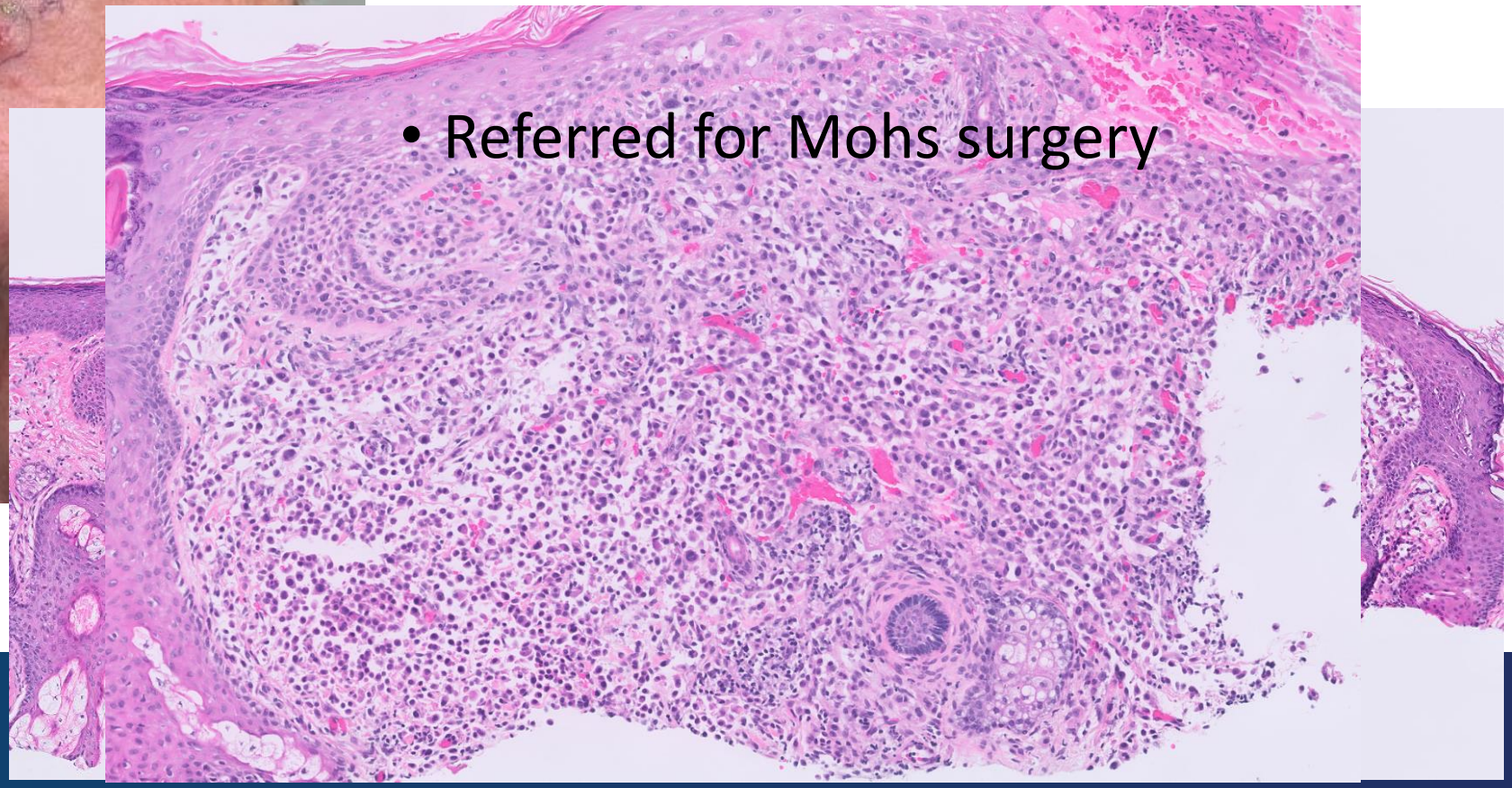
History of 6 non-melanoma skin cancers

- Field therapy with 5-FU
- Several Mohs surgeries



Our patient

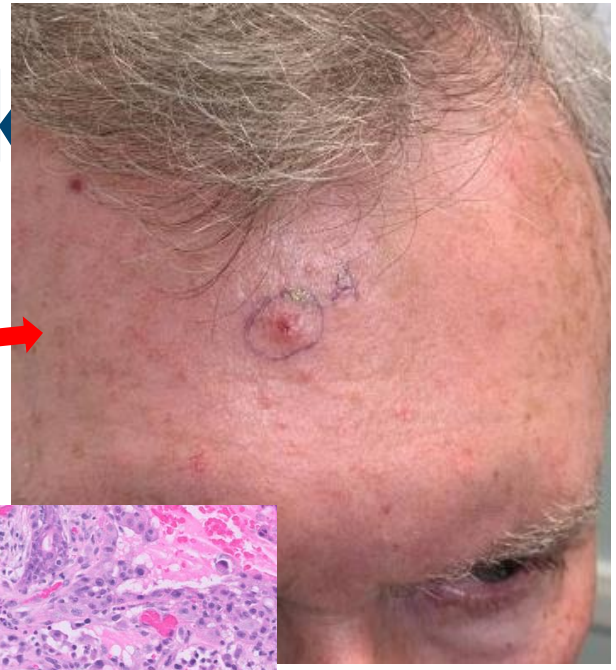
- Squamous cell carcinoma, moderately differentiated and acantholytic

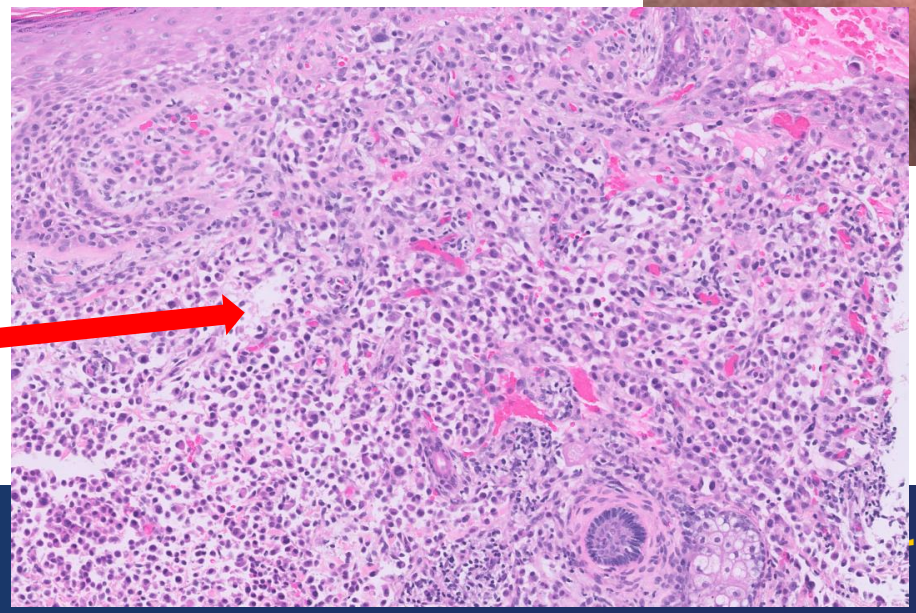


- Referred for Mohs surgery

In the general population, what clinicopathologic criteria are associated with increased risk metastasis?

- Tumors of the head and neck area
- Tumors of increasing size
- Deep tumors
- Histologic grade of the tumor
- Perineural invasion





Are there risk-strati

- YES!

- AJCC 8th edition
- Brigham and Women tumor staging system

- NCCN Squamous Cell 2024

Table I. American Joint Committee on Cancer (AJCC) cutaneous SCC staging system for tumors of the head and neck skin 8th edition

T category	T criteria	N category	N criteria for pathologic N	M category	M criteria
TX	Primary tumor cannot be identified	NX	Regional lymph nodes cannot be assessed	M0	No distant metastasis
Tis	Carcinoma in situ	N0	No regional lymph node metastasis	M1	Distant metastasis
T1	Tumor <2 cm in greatest dimension	N1	Metastasis in a single ipsilateral lymph node, ≤3 cm in greatest dimension and ENE⁻*		
T2	Tumor ≥2 cm but <4 cm in greatest dimension	N2	Metastasis in a single ipsilateral lymph node ≤3 cm in greatest dimension and ENE⁺; or >3 cm but not >6 cm in greatest dimension and ENE⁻; or metastases in multiple ipsilateral lymph nodes, none >6 cm in greatest dimension and ENE⁻; or in bilateral or contralateral lymph nodes, none >6 cm in greatest dimension and ENE⁻		
T3	Tumor ≥4 cm in clinical diameter OR minor bone erosion OR perineural invasion OR deep invasion†	N2a	Metastasis in single ipsilateral or contralateral node ≤3 cm in greatest dimension and ENE⁺; or in a single ipsilateral node >3 cm but not >6 cm in greatest dimension and ENE⁻		
T4	Tumor with gross cortical bone/marrow, skull base invasion, and/or skull base foramen invasion	N2b	Metastasis in multiple ipsilateral nodes, none >6 cm in greatest dimension and ENE⁻		
T4a	Tumor with gross cortical bone/marrow invasion	N2c	Metastasis in bilateral or contralateral lymph nodes, none >6 cm in greatest dimension and ENE⁻		
T4b	Tumor with skull base invasion and/or skull base foramen involvement	N3	Metastasis in a lymph node >6 cm in greatest dimension and ENE⁻; or in a single ipsilateral node >3 cm in greatest dimension and ENE⁺; or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE⁺		
		N3a	Metastasis in a lymph node >6 cm in greatest dimension and ENE⁻		
		N3b	Metastasis in a single ipsilateral node >3 cm in greatest dimension and ENE⁺; or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE⁺		

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NCCN Guidelines Version 1.2024
Squamous Cell Skin Cancer

NCCN Guidelines Index
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Discussion

STRATIFICATION TO DETERMINE TREATMENT OPTIONS AND FOLLOW-UP FOR LOCAL CSCC BASED ON RISK FACTORS FOR LOCAL RECURRENCE, METASTASES, OR DEATH FROM DISEASE

Risk Group[a]	Low Risk	High Risk	Very High Risk
Treatment options	SCC-3	SCC-4	SCC-4 and SCC-5
H&P			
Location/size[b]	Trunk, extremities ≤2 cm	Trunk, extremities >2 cm – ≤4 cm	>4 cm (any location)
		Head, neck, hands, feet, pretibia, and anogenital (any size)[e]	
Clinical extent	Well-defined	Poorly defined	
Primary vs. recurrent	Primary	Recurrent	
Immunosuppression	(-)	(+)	
Site of prior RT or chronic inflammatory process	(-)	(+)	
Rapidly growing tumor	(-)	(+)	
Neurologic symptoms	(-)	(+)	
Pathology (SCC-A)			
Degree of differentiation	Well or moderately differentiated		Poor differentiation
Histologic features: Acantholytic (adenoid), adenosquamous (showing mucin production), or metaplastic (carcinosarcomatous) subtypes	(-)	(+)	Desmoplastic SCC
Depth[c,d]: Thickness or level of invasion	<2 mm thick and no invasion beyond subcutaneous fat	2–6 mm depth	>6 mm or invasion beyond subcutaneous fat
Perineural involvement	(-)	(+)	Tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring ≥0.1 mm
Lymphatic or vascular involvement	(-)	(-)	(+)

Is our patient higher risk?

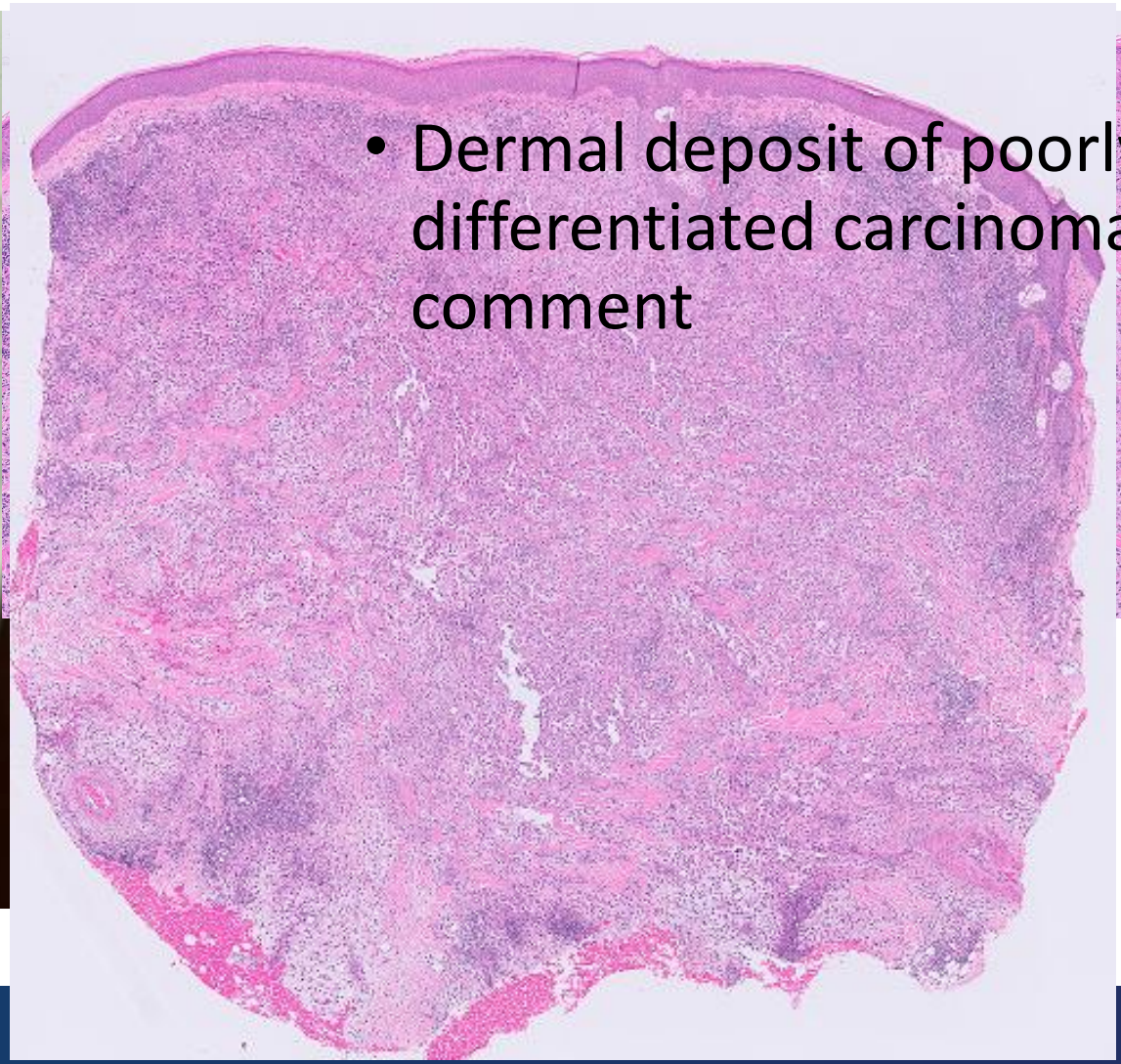
Cumulative incidence and risk factors for cutaneous squamous cell carcinoma metastases in organ transplant recipients: The Skin Care in Organ Transplant Patients in Europe-International Transplant Skin Cancer Collaborative metastases study, a prospective multicenter study

J Am Acad Dermatol
June 2024

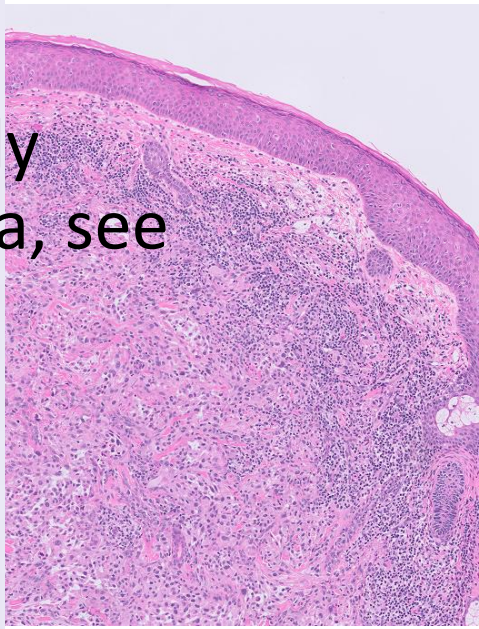
- Solid organ transplant recipients have **50 – 100-fold increased risk** of cSCC compared with immunocompetent patients
- More likely to develop **multiple cSCC**
- **Metastasis in up to 10%**
  - Develop within 2 years of primary SCC

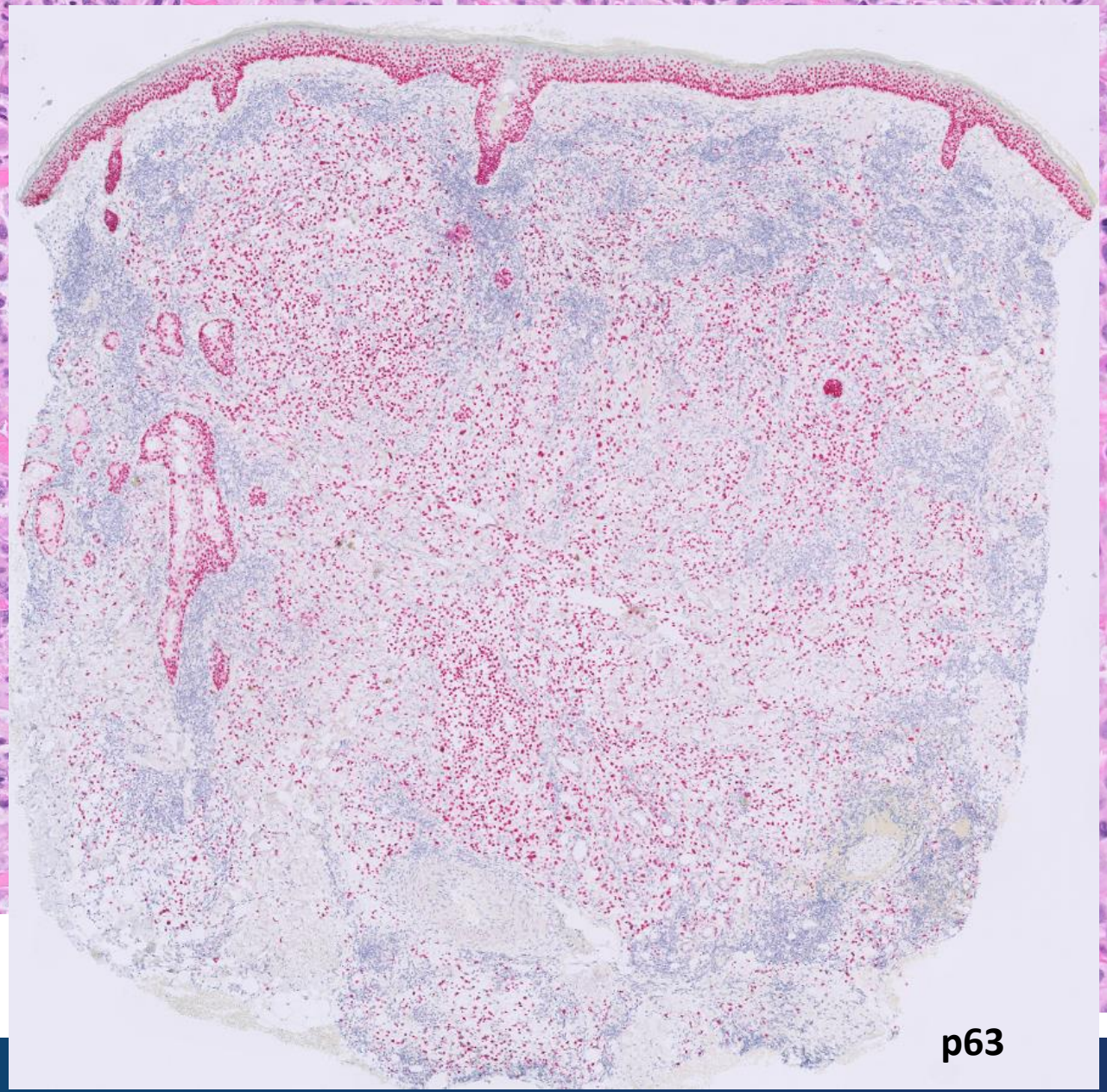
3 months later

- 2 new lesions of concern



- Dermal deposit of poorly differentiated carcinoma, see comment

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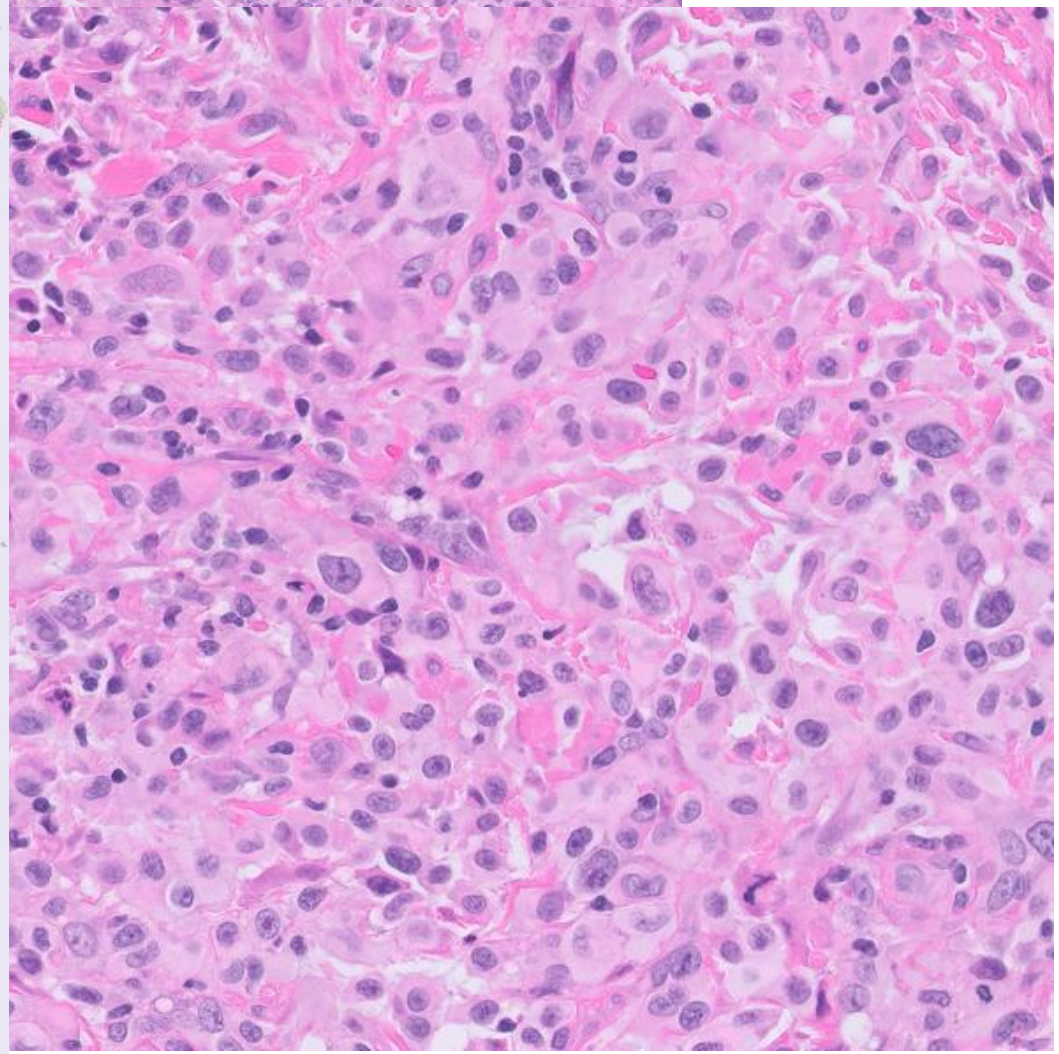
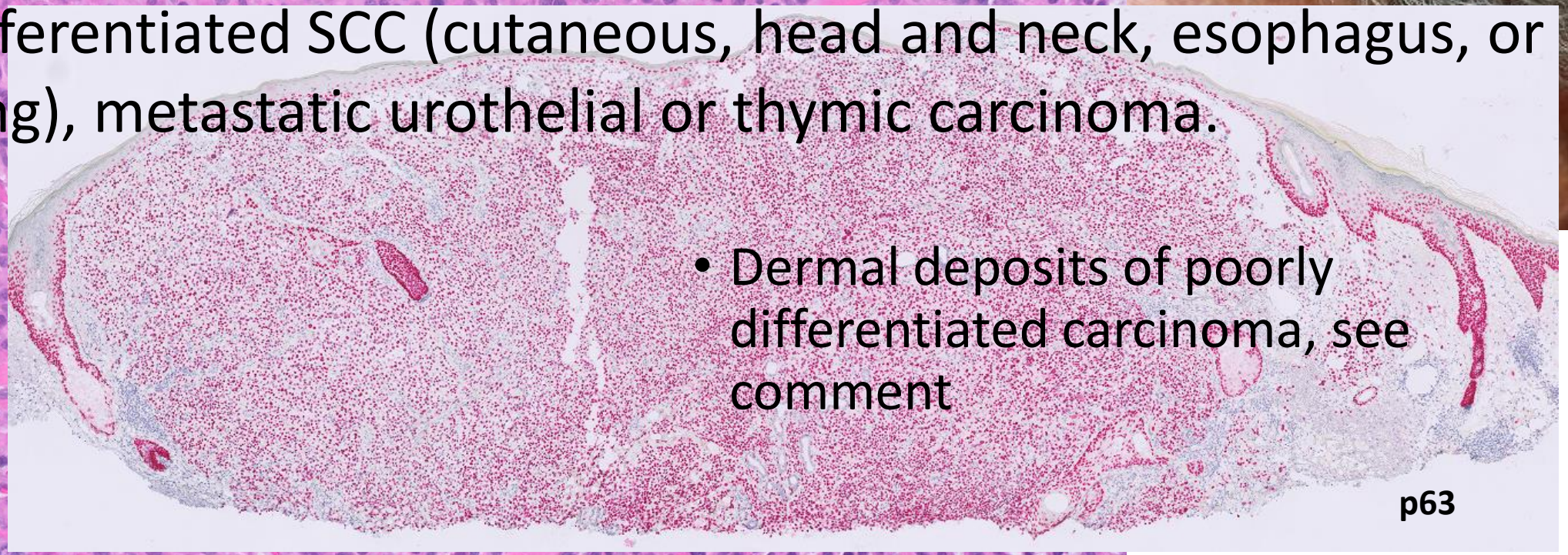


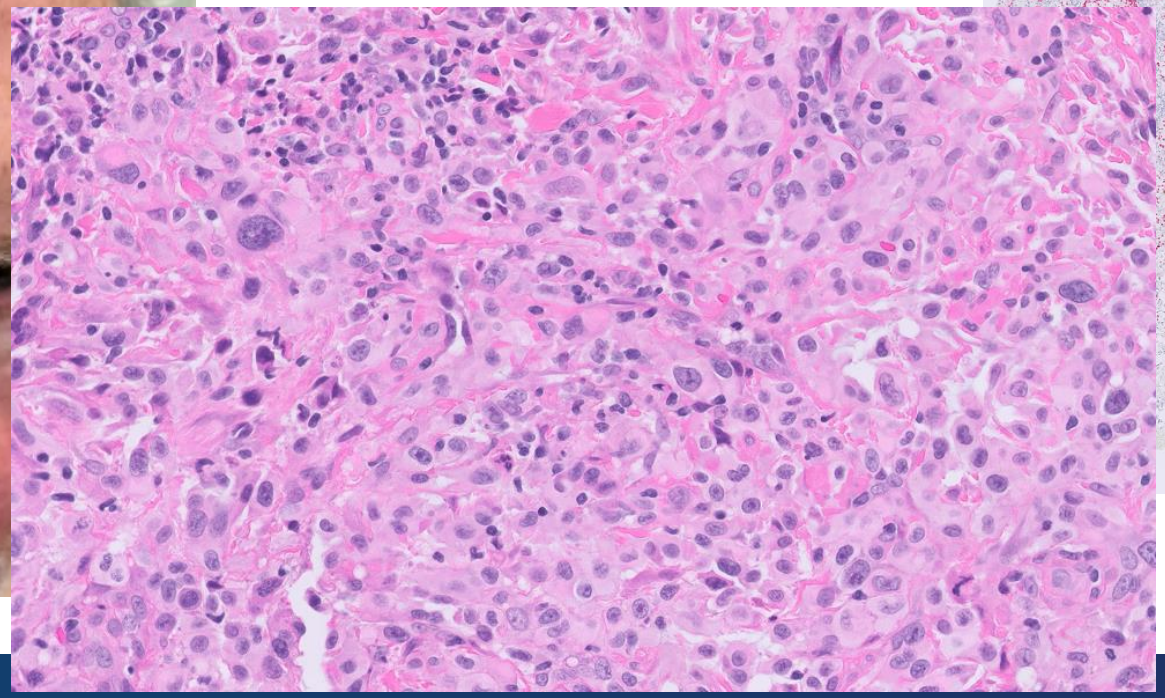
Comment: The morphology of specimens are similar.
A metastatic process if favored. Considerations include a poorly differentiated SCC (cutaneous, head and neck, esophagus, or lung), metastatic urothelial or thymic carcinoma.

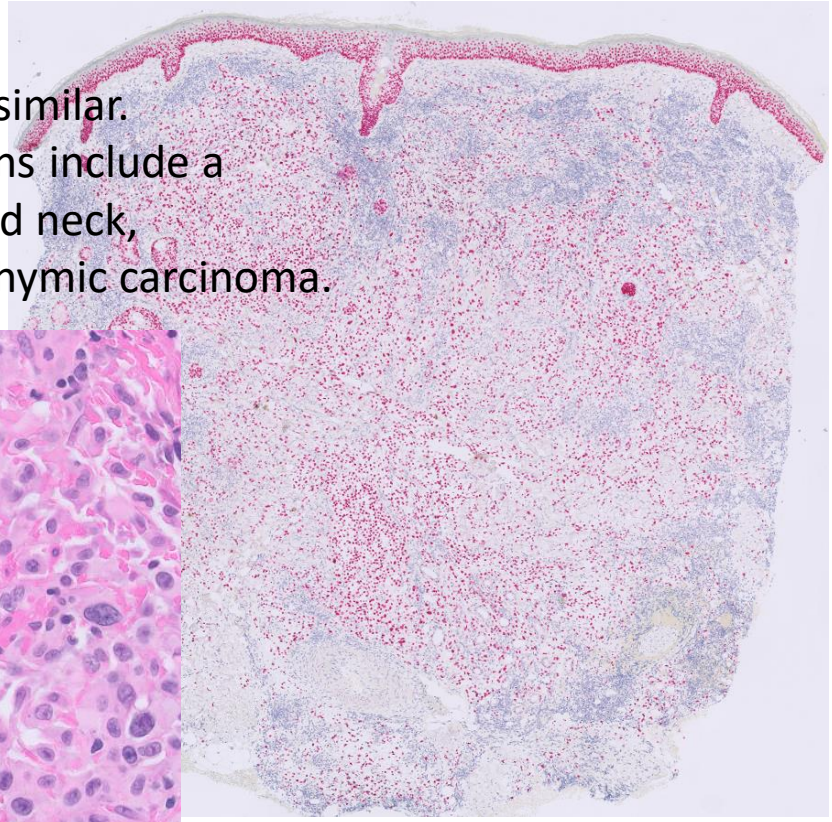


- Dermal deposits of poorly differentiated carcinoma, see comment

What would you do next?

Comment: The morphology of specimens are similar.
A metastatic process if favored. Considerations include a poorly differentiated SCC (cutaneous, head and neck, esophagus, or lung), metastatic urothelial or thymic carcinoma.





Our patient

- **ENT oncology** for complete staging
  - PET/CT
- **Transplant team**
  - Discuss immunosuppression
    - Change or reduction ?

Interventions After First Post-Transplant Cutaneous Squamous Cell Carcinoma: A Proposed Decision Framework

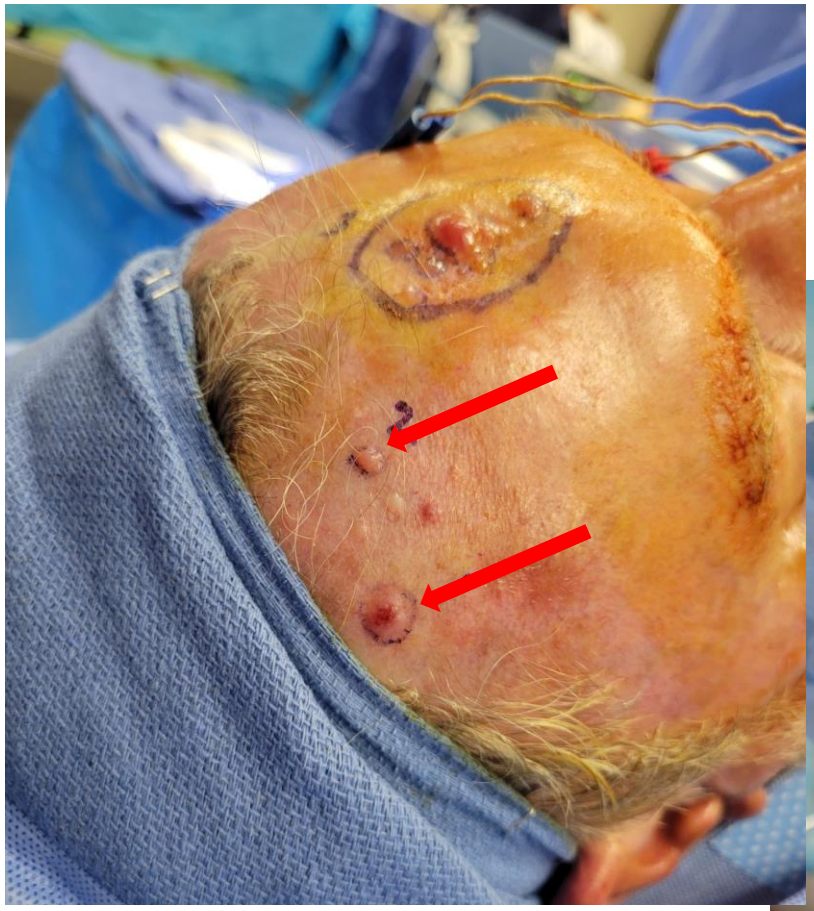
Matthew J. Bottomley[1,2], Paul R. Massey[3], Raj Thuraisingham[4], Alden Doyle[5], Swati Rao[5], Kristin P. Bibee[6], Jan Nico Bouwes Bavinck[7], Anokhi Jambusaria-Pahlajani[8†] and Catherine A. Harwood[9†]*

POINT OF VIEW
published: 22 November 2022
doi: 10.3389/ti.2022.10880

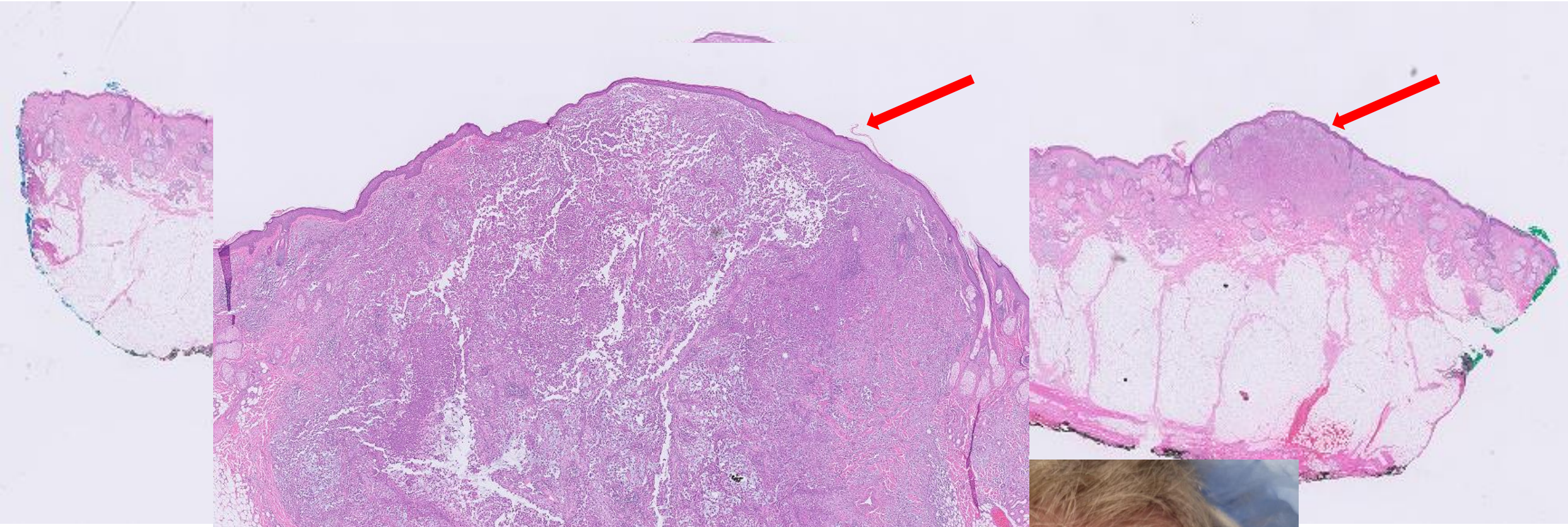
Our patient

- PET/CT prior to surgery with ENT
  - **Multiple areas of hypermetabolic cutaneous activity** most notable along the forehead and left cheek
  - No suspicious hypermetabolic metastatic lymphadenopathy or distant metastatic disease
- **Tacrolimus decreased**

3 weeks later



- Intraoperatively, local metastasis/in-transit disease noted



- Multiple dermal deposits of poorly differentiated carcinoma with foci suspicious for lymphovascular invasion

2 months after surgery

2 ½ months after surgery

Our patient

- Radiation oncology
  - Planned radiation after graft healing
- Transplant team
  - Increased prednisone
  - Transition from tacrolimus to sirolimus
- Hematology/oncology team

Multiple dermal deposits of poorly differentiated carcinoma with foci suspicious for lymphovascular invasion

Our patient

- Palliative injections of **intralesional 5FU and triamcinolone**
- Started **acitretin**

- New lymph node enlarged on preauricular cheek

Thoughts on chemoprevention?

- Dermatologist may consider **oral chemoprevention** for patients at high risk for subsequent cSCC
  - **Nicotinamide**
  - **Oral retinoids (acitretin)**

- Acitretin is effective in up to 42% reduction in rates of cSCC in kidney transplant patients
  - **BUT** discontinuation in 19-39% (due to SE of xerosis, alopecia)
  - **Rebound** cSCC's common…

Bavinck JN, Tieben LM, Van der Woude FJ, Tegzess AM, Hermans J, ter Schegget J, et al. Prevention of Skin Cancer and Reduction of Keratotic Skin Lesions during Acitretin Therapy in Renal Transplant Recipients: a Double-Blind, Placebo-Controlled Study. *J Clin Oncol* (1995) 13(8):1933–8. doi:10.

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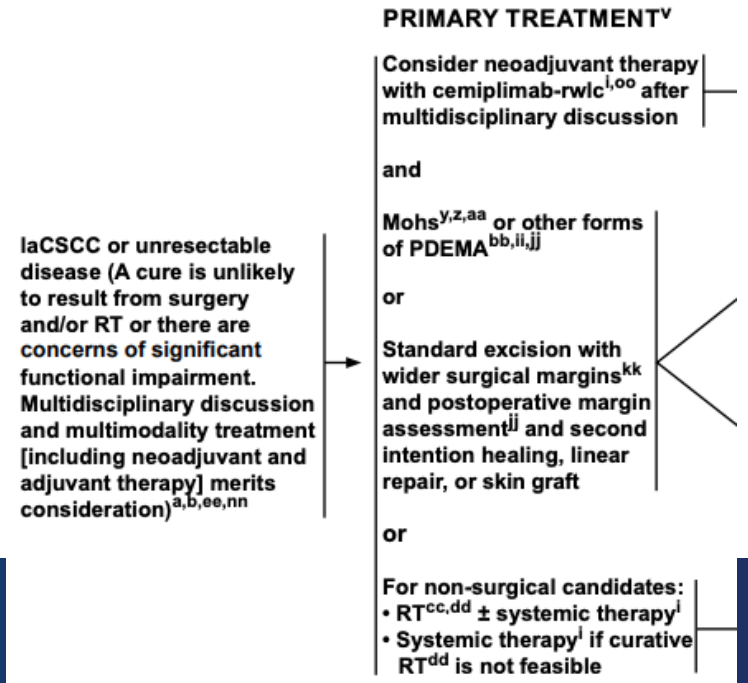
Patient continues to progress. What would you do next?

- New lymph node on preauricular cheek
- Rapidly progressing local (dermal) metastasis
- No response to immunosuppression change
- No improvement with acitretin
- Poor graft healing after 3 months

Role for immunotherapy?

- “Consider neoadjuvant therapy with cemiplimab, after multidisciplinary discussion, if the tumor has very rapid growth, in-transit metastasis, lymphovascular invasion, is borderline resectable, or surgery alone may be not be curative or may result in significant functional limitation.”
  - NCCN 2024



Role for immunotherapy?

- Immune checkpoint inhibitors targeting PD-1 are widely used to treat

Cemiplimab for Kidney Transplant Recipients With Advanced Cutaneous Squamous Cell Carcinoma

Glenn J. Hanna, MD[1]; Harita Dharanesswaran, BS[2]; Anita Giobbie-Hurder, MS[3]; John J. Harran, RN[2]; Zixi Liao, RN[2]; Lori Pai, MD[4]; Vatche Tchekmedyian, MD[5]; Emily S. Ruiz, MD[2]; Abigail H. Waldman, MD[2]; Chrysalyne D. Schmults, MD[2]; Leonardo V. Riella, MD, PhD[6]; Patrick Lizotte, PhD[7]; Cloud P. Paweletz, PhD[7]; Anil K. Chandraker, MD, MBCHB[8]; Naoka Murakami, MD, PhD[8]; and Ann W. Silk, MD[2]

DOI https://doi.org/10.1200/JCO.23.01498

- Kidney allograft rejection rates approaching 50% among nonmelanoma skin cancer patients treated with immunotherapy

- **Prospective trials limited**
  - Cemiplimab + mTor inhibitor + pulsed dose corticosteroids to treat advanced metastatic cSCC

4 months after surgery

- Initiated cemiplimab infusions

5 months after surgery

- 2 cycles of cemiplimab
- Complicated graft rejection
- Resumed dialysis
  - Cessation of immunosuppression
- Complete response clinically and radiographically

Summary

ENT

Radiation oncology

Pathology

Medical oncology

It takes a team…

ENT plastics

Pharmacy

Dermatology

Transplant medicine

Primary care

Urology

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- https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf?ref=theplasticsfella.com

Thank you!

- Questions?

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