

# Treating Aggressive Cutaneous Malignancies in Immunocompromised Patients – A Dermatologist's Perspective



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# Disclosure

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- No relevant financial interests to disclose
- Consent was obtained prior to use of patient images

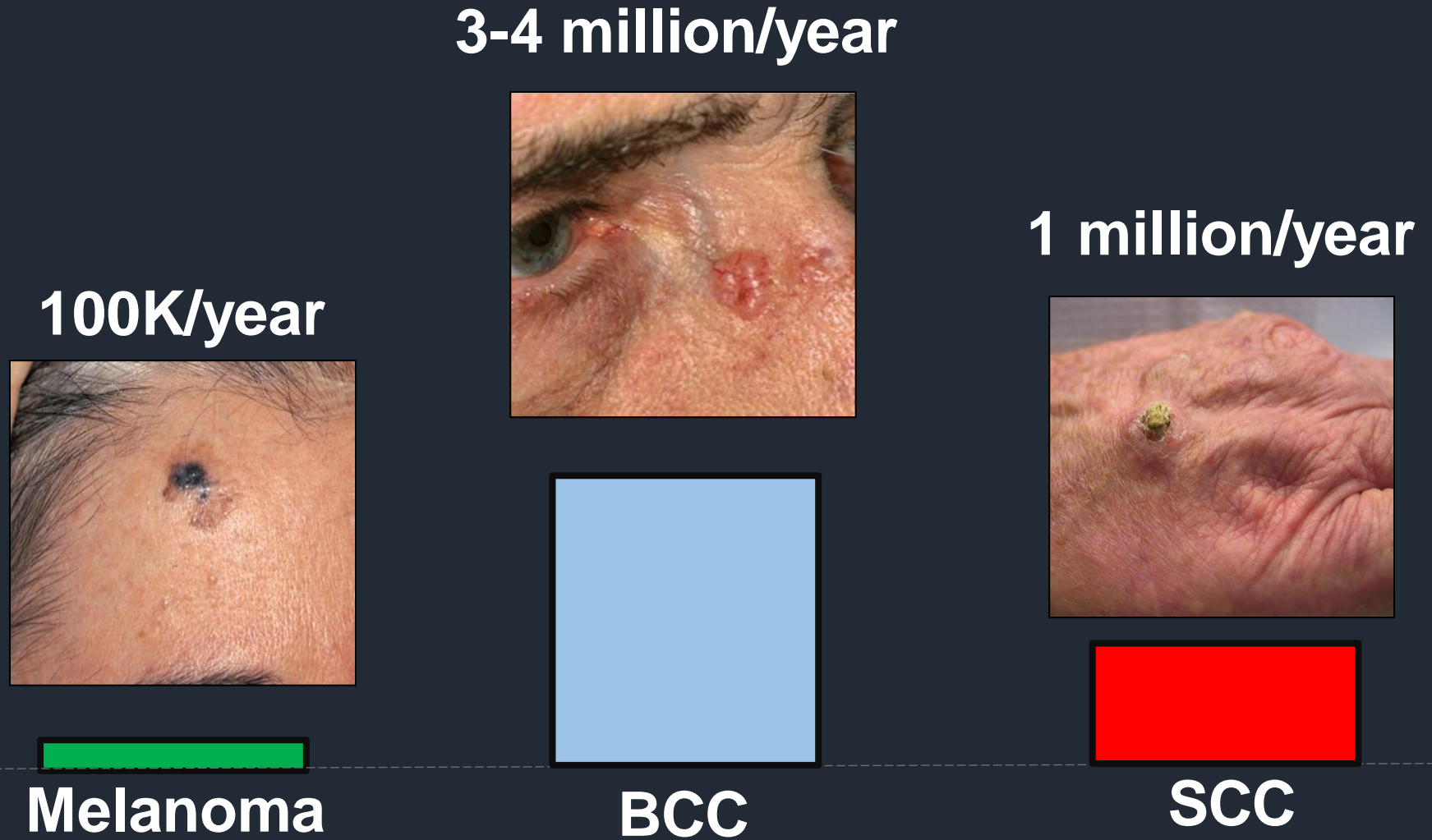
# Learning Objectives

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- Background
- How to Triage?
- How does immunosuppression increase skin cancer risk?
- Review immunosuppressive medications
- Cases

# Skin Cancers in the US

Incidence



# Skin Cancer Mortality

Melanoma Awareness  
Ribbon



8,000



Melanoma

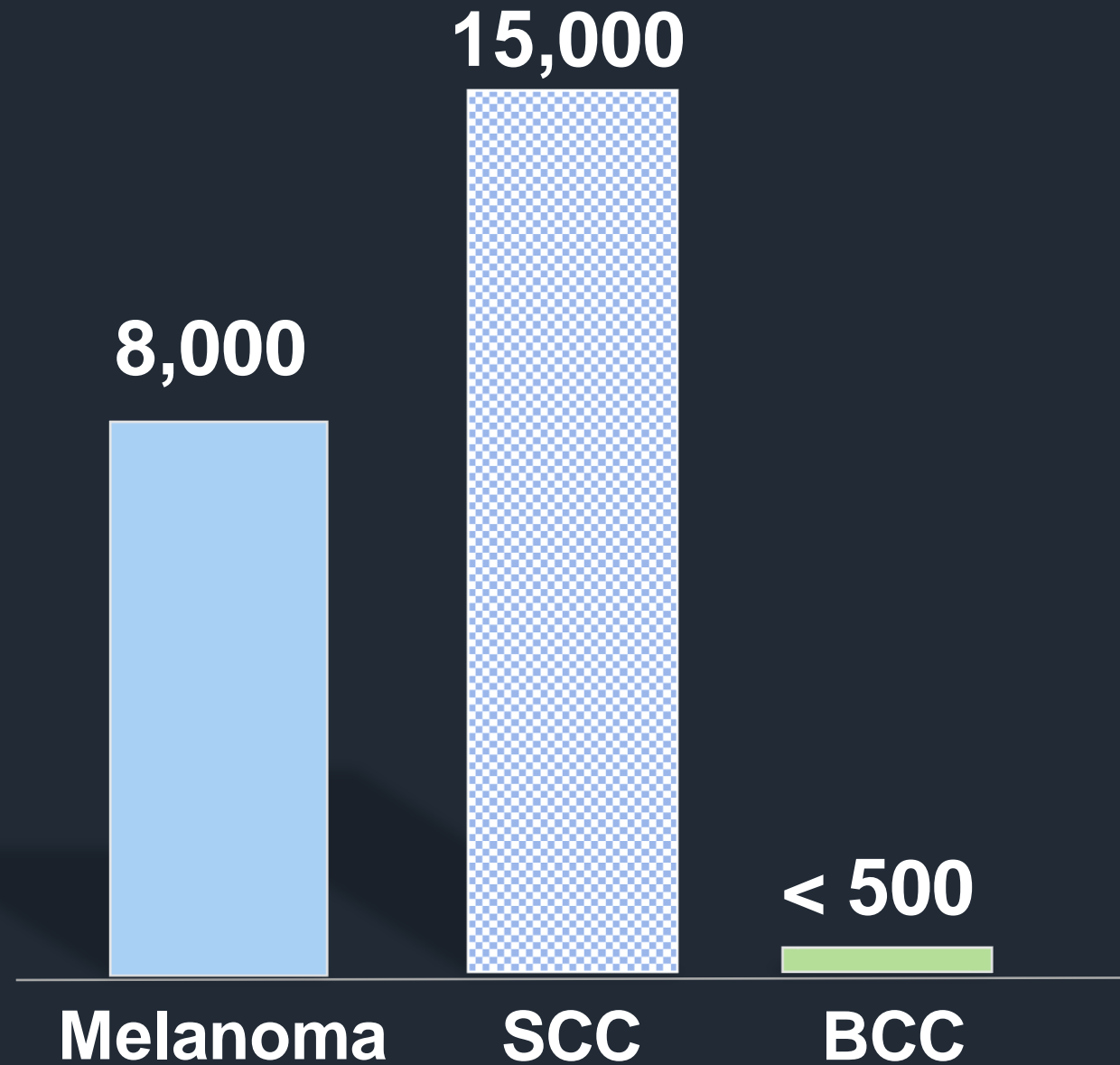
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BCC

# Skin Cancer Mortality

Melanoma Awareness  
Ribbon



# Increased Risk in SOTR

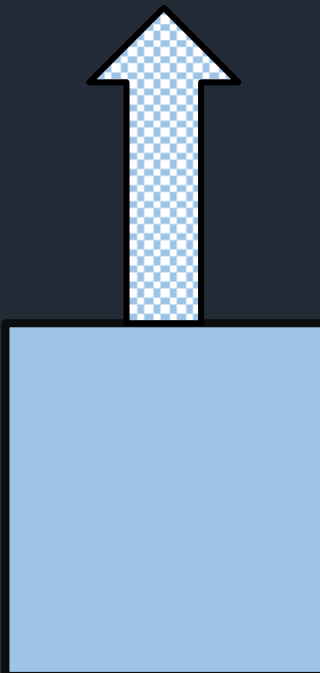
Incidence

3x Risk



Melanoma

10x Risk



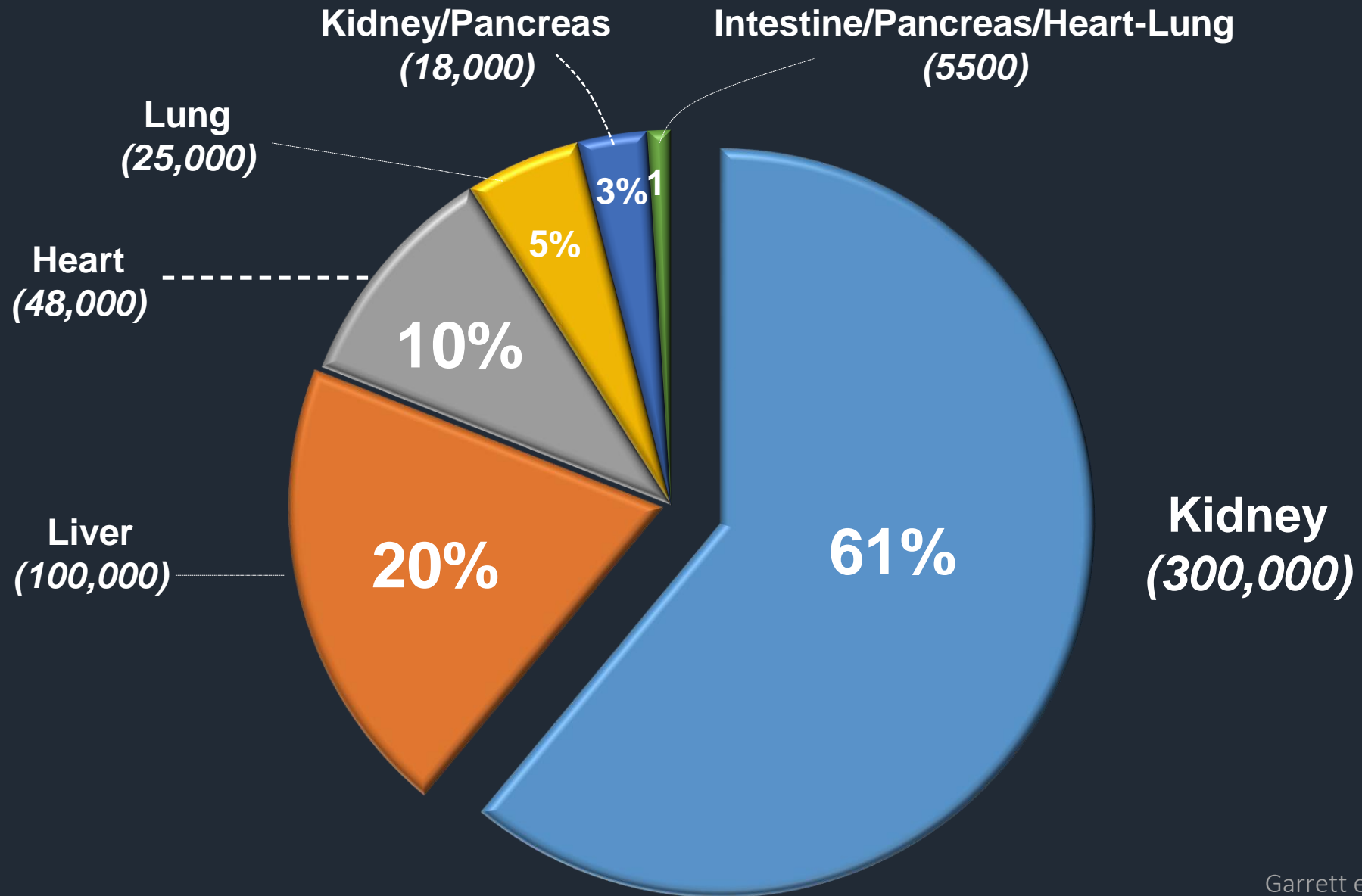
BCC

65-250x  
Risk



SCC

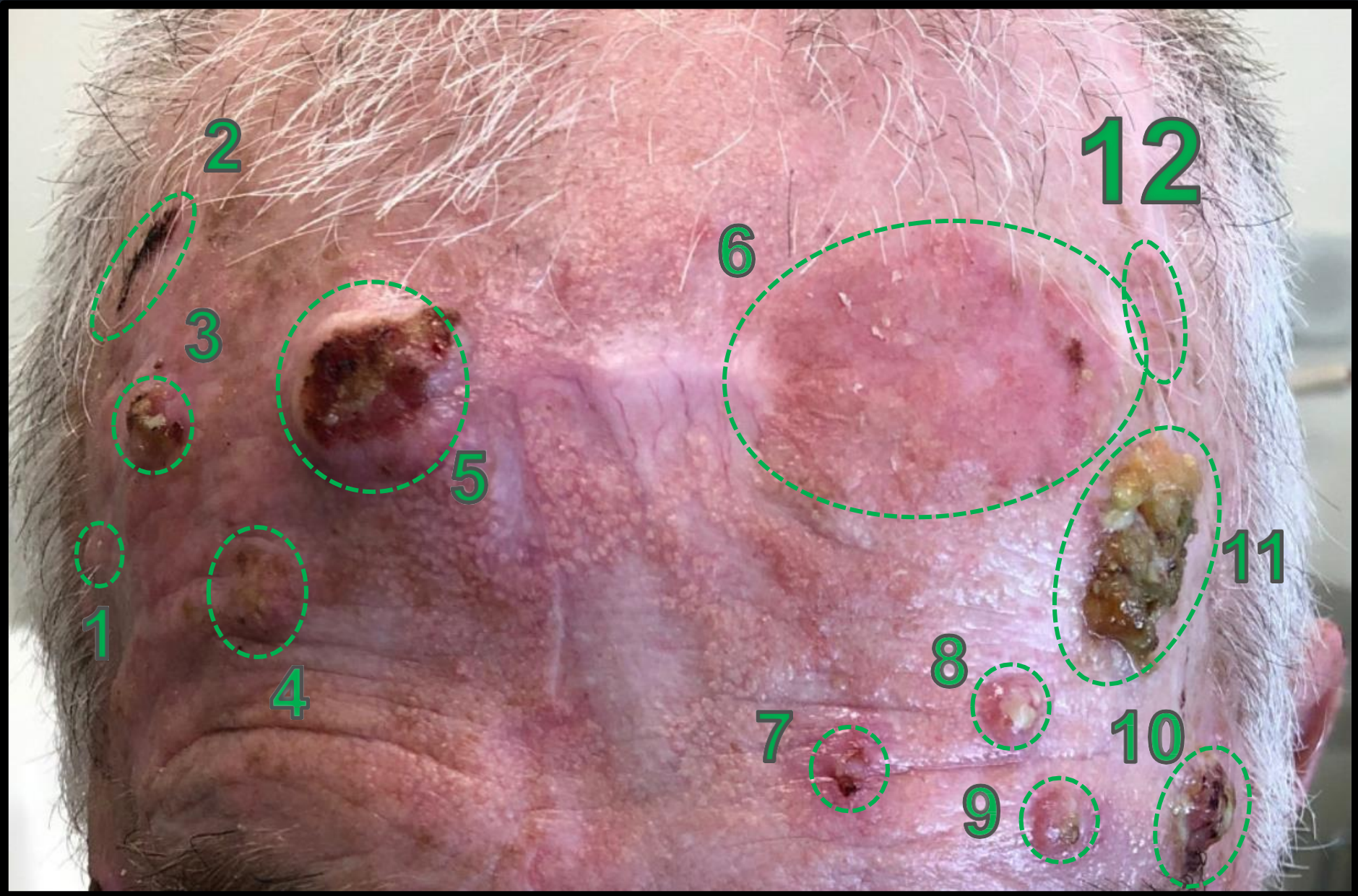
# Solid Organ Transplantation in the US





Triage





# Clinical Outcomes in High Risk cSCC

<u>Outcome</u>	T1	T2a	T2b	T3
Local Recurrence	0.6%	5%	21%	67%
Nodal Metastases	0.1%	3-7%	21-29%	50-67%
Mortality	0%	1%	10%	100%

**T1 – 0 factors**

**T2a – 1 factor**

**T2b – 2-3 factors**

**T3 – 4 factors or bone invasion**

## High Risk Features:

- Diameter > 2cm
- Poor differentiation
- Perineural invasion
- Invasion beyond fat

# Triage

## Clinical Features

- ✓ Location
- ✓ Pain
- ✓ Recurrence
- ✓ Nodularity
- ✓ Ulceration



# Triage



Location - Back

*Histology - Squamous cell carcinoma, moderately to poorly differentiated, keratinizing*

Size: 1.2 cm

Histologic grade: 2/4

Depth - Anatomic level: IV

Depth - Thickness: 0.8 mm

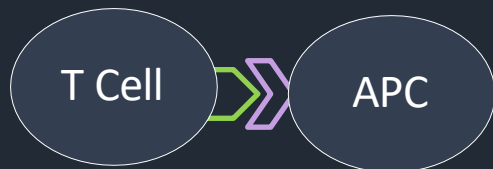
Perineural invasion: None

Margins: Extends to base

# Medications That Increase Risk

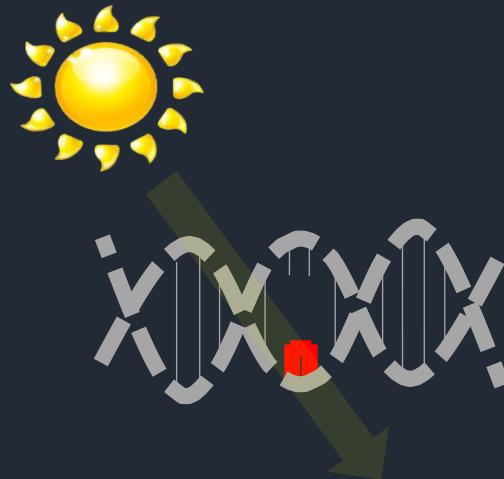
## Immune Suppression

- +++ Cyclosporine A
- +++ Azathioprine
- ++ Tacrolimus
- ++ Mycophenolate
- + Methotrexate
- + TNF- $\alpha$  inhibitors



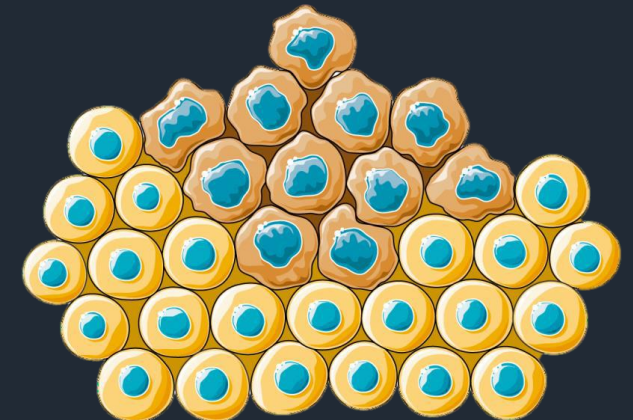
## Phototoxicity

- +++ Psoralen
- +++ Azathioprine
- +++ Voriconazole
- + Fluoroquinolone
- + HCTZ



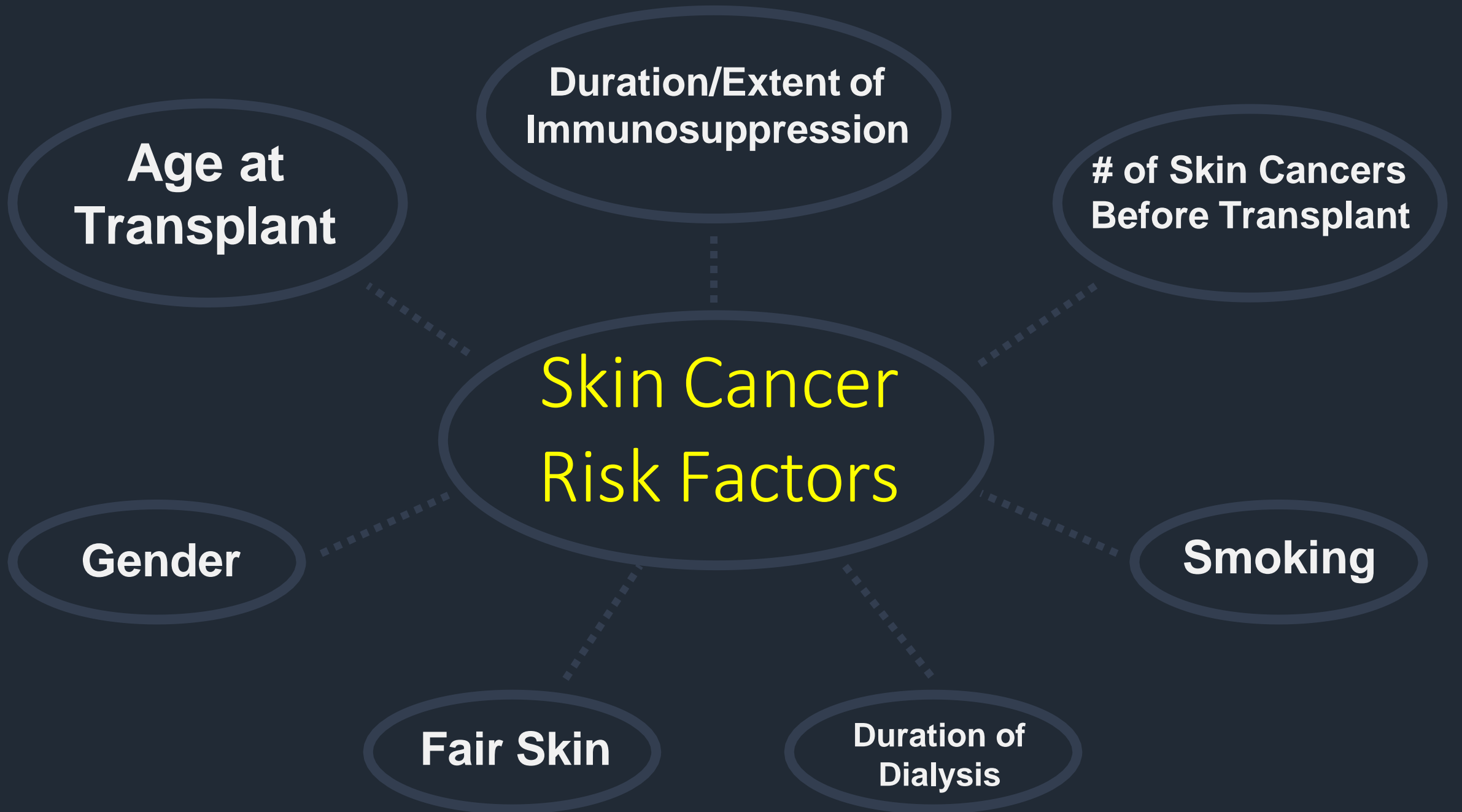
## Increased Cell Proliferation

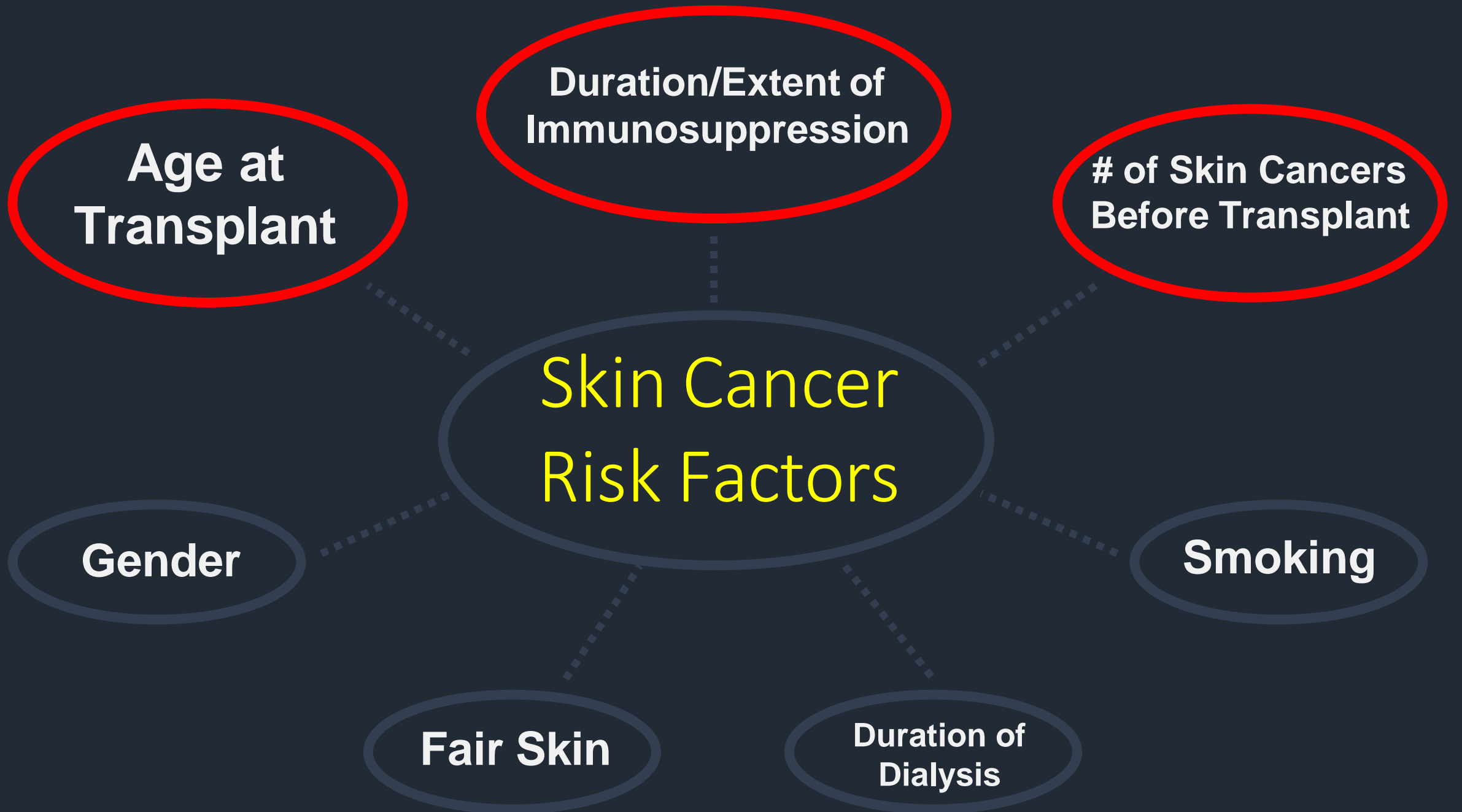
- ++ B-raf (Vemurafenib)
- ++ JAKi (Ruxolitinib)
- ++ Hydroxyurea
- ++ Sorafenib
- + Vismodegib



# NMSC in Immunosuppressed Patients









2016



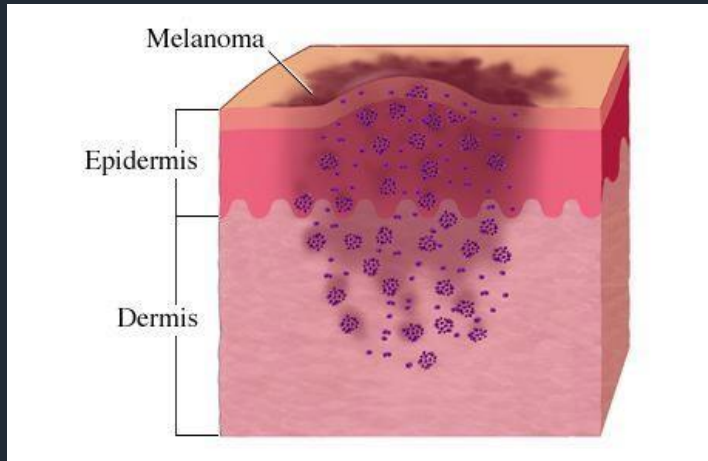
2021



2024



# Voriconazole



- 3<sup>rd</sup> Gen Triazole antifungal (approved in 2002) with activity against *Aspergillus*, *Coccidiomycosis*, *Candida*, *Fusarium*
- likely promotes *phototoxicity* and has been shown to promote *aggressive SCC* and *melanoma*
- ~ 10% of patients on voriconazole develop skin CA
- Avg time to develop ~ 25 months

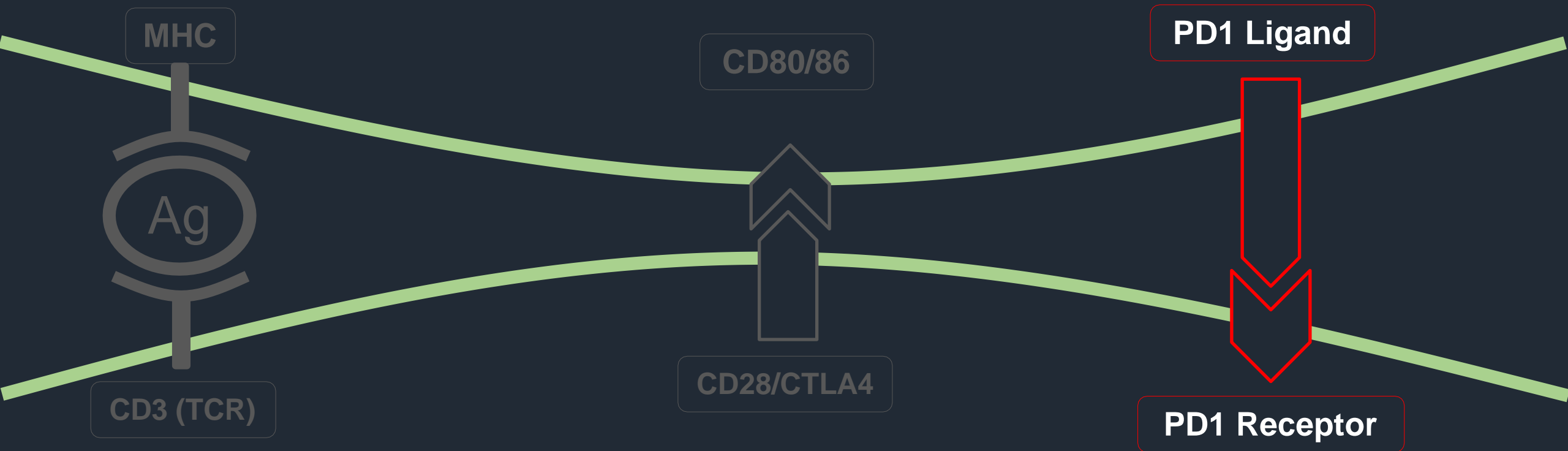
# Progression of SCC after Voriconazole



1 year

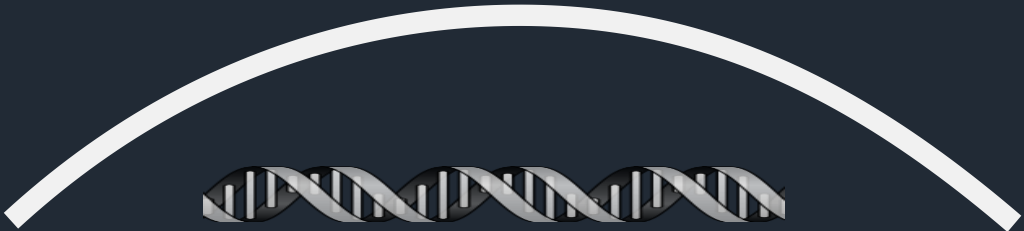
Immunotherapy?

# Antigen Presenting Cell

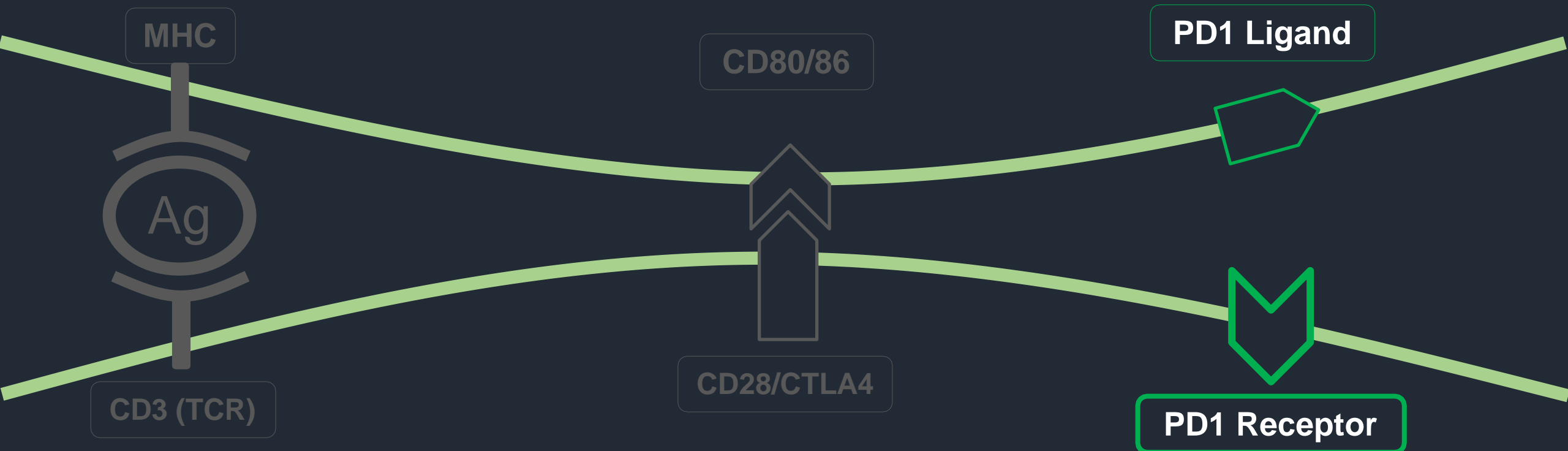


**Immune Suppression**

# T Cell



# Antigen Presenting Cell



PD1 Ligand

CD80/86

MHC

Ag

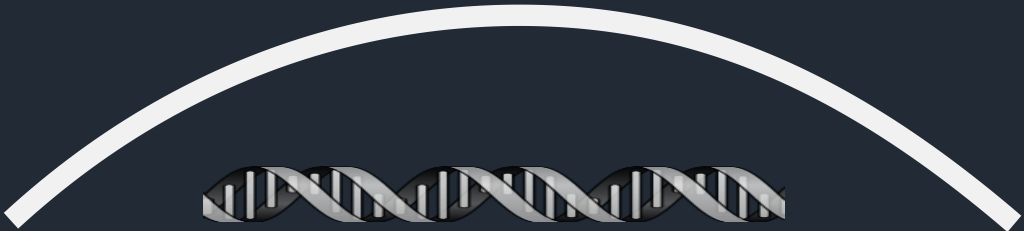
CD3 (TCR)

CD28/CTLA4

PD1 Receptor

Immune Activation

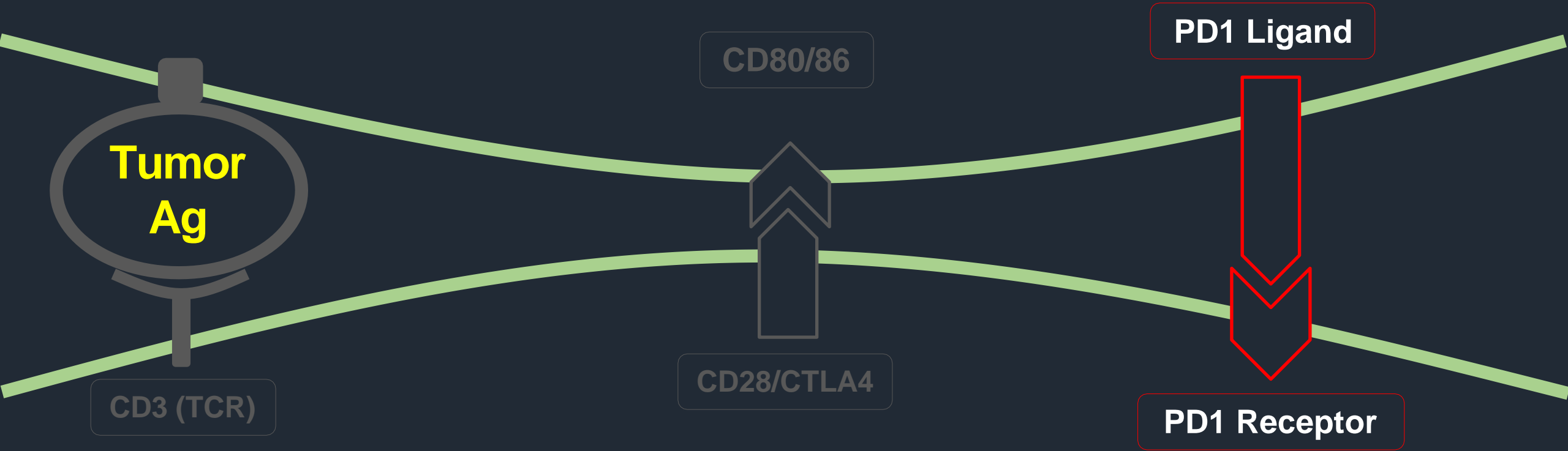
T Cell





# Tumor Cell

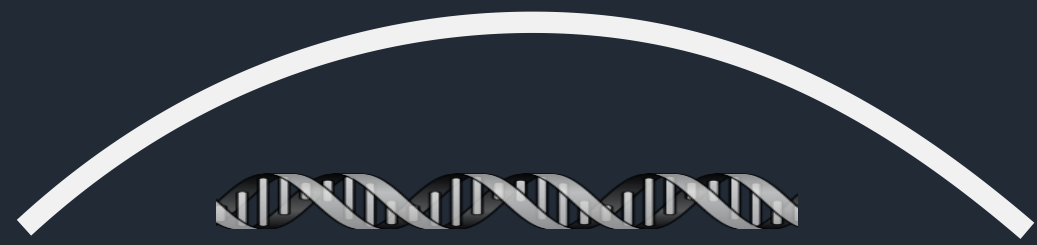
# Tumor Growth



**PD1 Receptor**

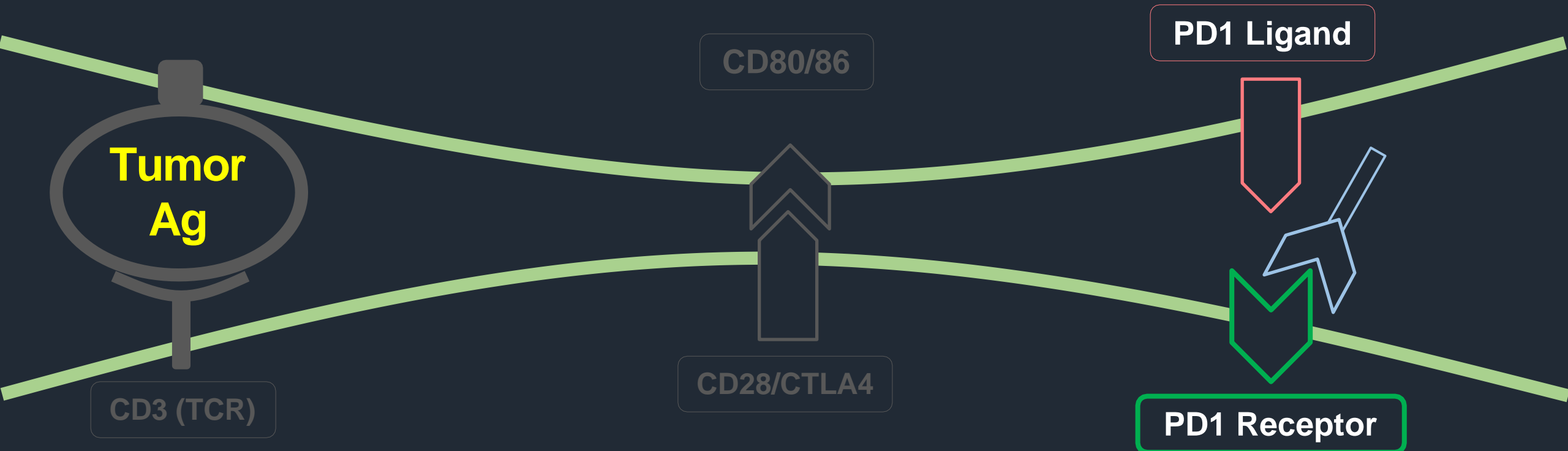
**Immune Suppression**

# T Cell



# Tumor Cell

# Tumor Death



CD3 (TCR)

CD80/86

PD1 Ligand

Tumor Ag

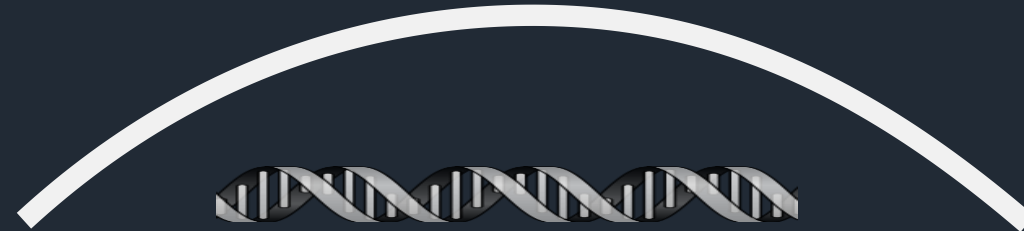
CD28/CTLA4

PD1 Receptor

**~ 46% ORR in SCC**

**Immune Activation**

T Cell



# PD1 Inhibitors in Transplant Patients

Small study showing safety of PD1 inhibitors for SCC in Kidney Transplant Patients:

7 patients with advanced SCC

**3/7 with overall response**

3/7 progressed

1/7 stable disease

**1/7 rejected kidney**

Other studies have shown rejection rate between **40-50%** in all types of tumors with response rate of ~15%

Less likely to experience rejection: - long duration since transplant, single agent immunosuppression, use of mTor inhibitors

Aggressive Squamoproliferative Disease



Increase rate of formation of aggressive SCC

Development of aggressive porocarcinoma

# Dermal Metastasis

**2023** – Poorly differentiated SCC on the scalp

**1/24** – Recurrent poorly differentiated SCC on the scalp

**2/24** – Dermal, in-transit metastasis

**54% 1-year mortality rate** for in-transit metastatic SCC

**3/24** - Started Cemiplimab and had Mohs to clear dermal metastasis



# Skin Changes During Immunotherapy



**2017** – presented with back pain. MRI showed diffuse bony mets. BM biopsy showed *IgA Kappa plasma cell myeloma*. Treated with daratumumab + lenalidomide (2018-2020).

**2/20** - SCCis biopsied from L-occipital scalp

3/20 – during Mohs found to have iSCC

4/20 – inferior to Mohs site, developed 2 new nodules referred for XRT (6 weeks)

5/20 – new nodule immediately outside XRT site (mod diff SCC)

6/20 – Mohs cleared this nodule

9/20 – 2 new nodules on L-parietal/occipital scalp (*poorly diff SCC*)

**10/20** – Referred to UNC Derm. Repeat biopsies performed that confirmed dermal metastases (poorly diff SCC). Referred to UNC Oncology.

**11/20** – Daratumumab/lenalidomide D/C'd and starts Cemiplimab





12/3/20



12/24/20

**3/21** – Cemiplimab discontinued due to patient fatigue and improvement in clinical lesions

**4/21** – MRI shows enhancing soft tissue throughout scalp – malignancy vs treatment. Skin biopsy of scalp shows granulation tissue. Pt does develop BCC on nose which is treated/cleared by Mohs

**9/21** – 4/5 scouting biopsies of scalp show granulation tissue. 1/5 shows iSCC (R-vertex) – treated/cleared by Mohs







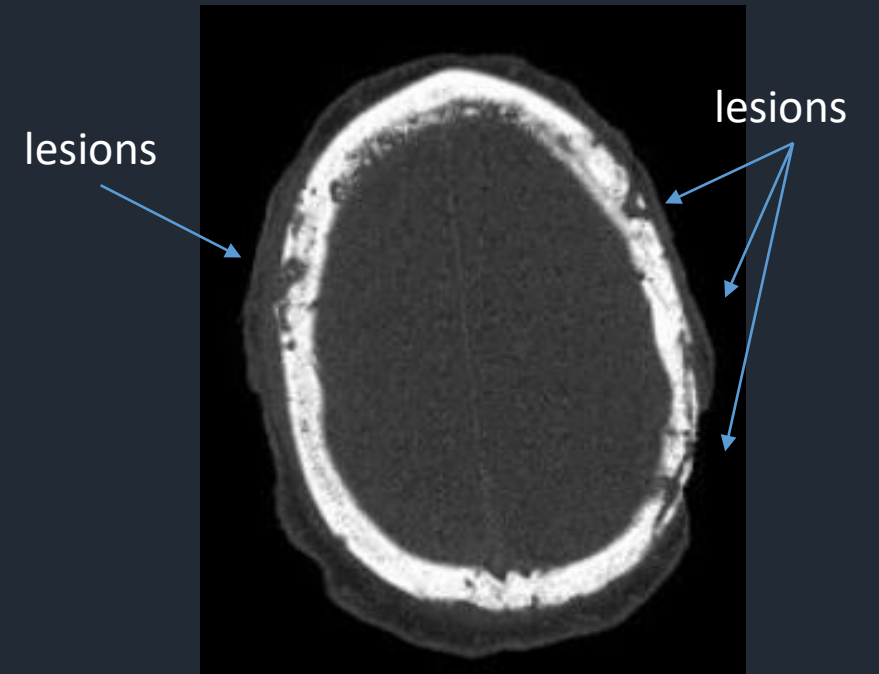
1/22



4/22

**2/22** – new onset low back pain leads to work-up including PET-CT that show enhancing lesions on the scalp. Scans show numerous lesions concerning for metastatic disease

**4/22** Fibrinopurulent exudate, granulation and fibrous tissue with acute and chronic inflammation, negative for malignancy.





4/24



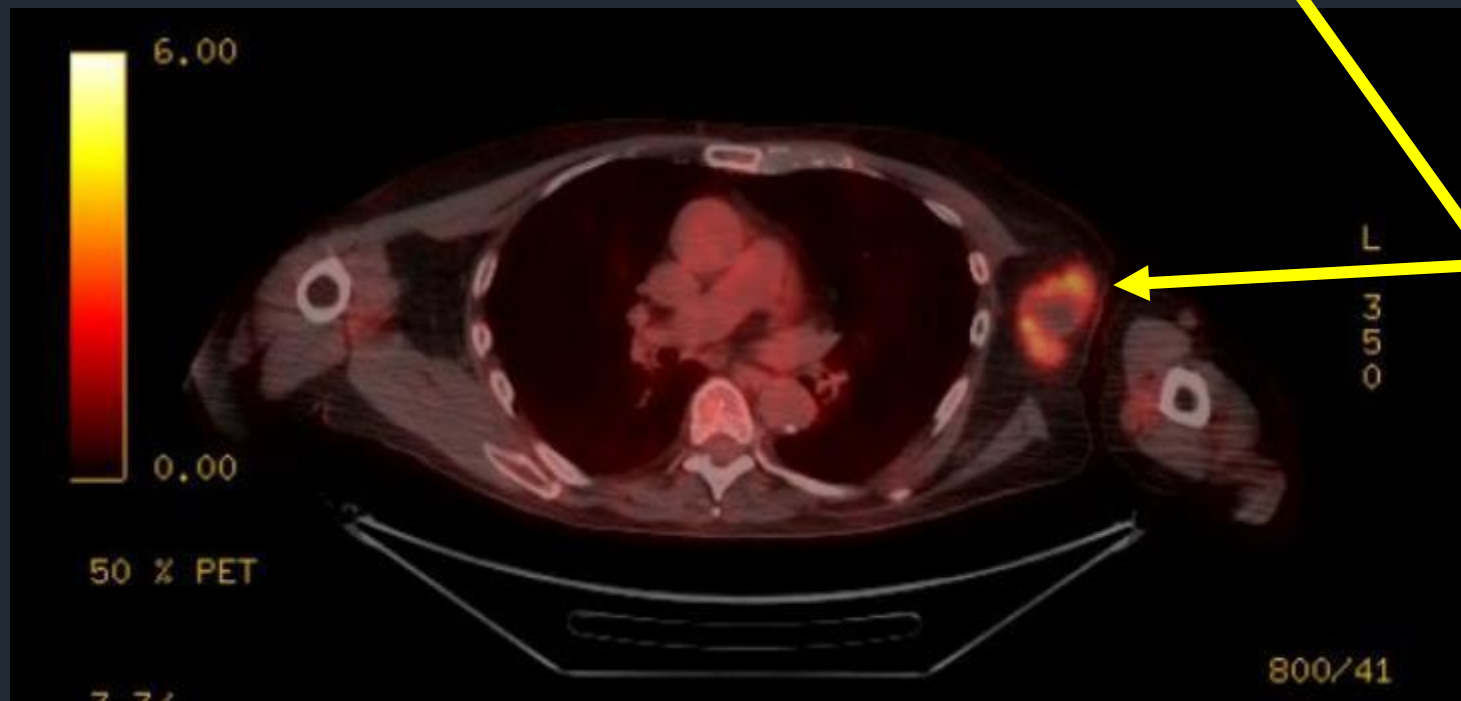
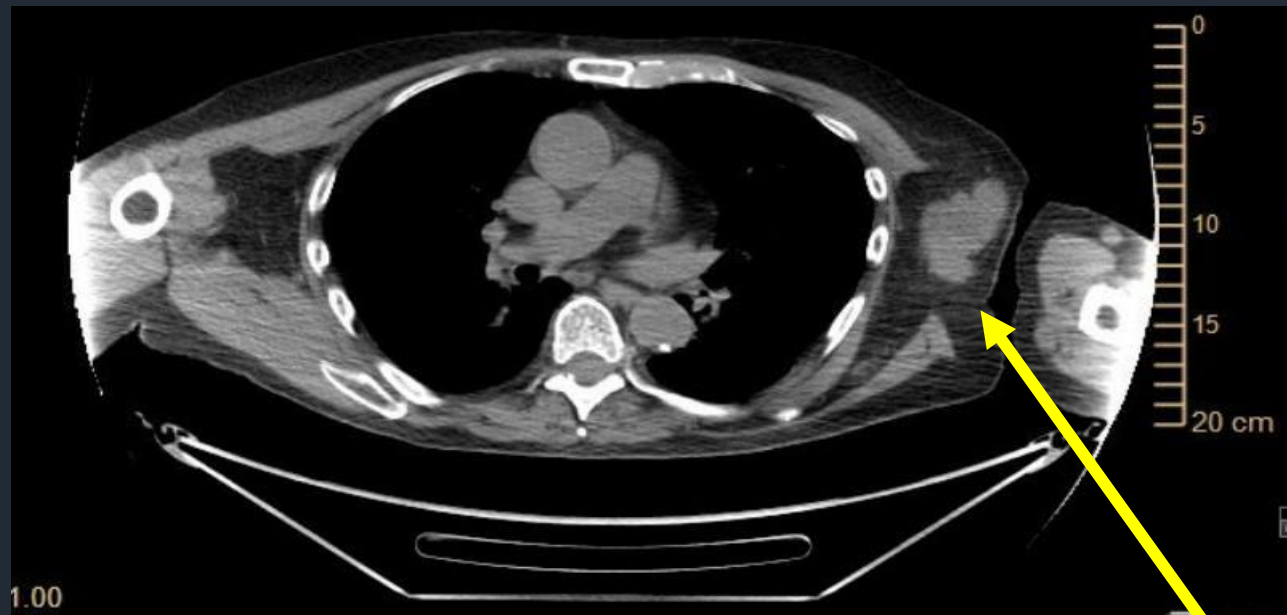


How can we prevent the following?

9/19



9/19

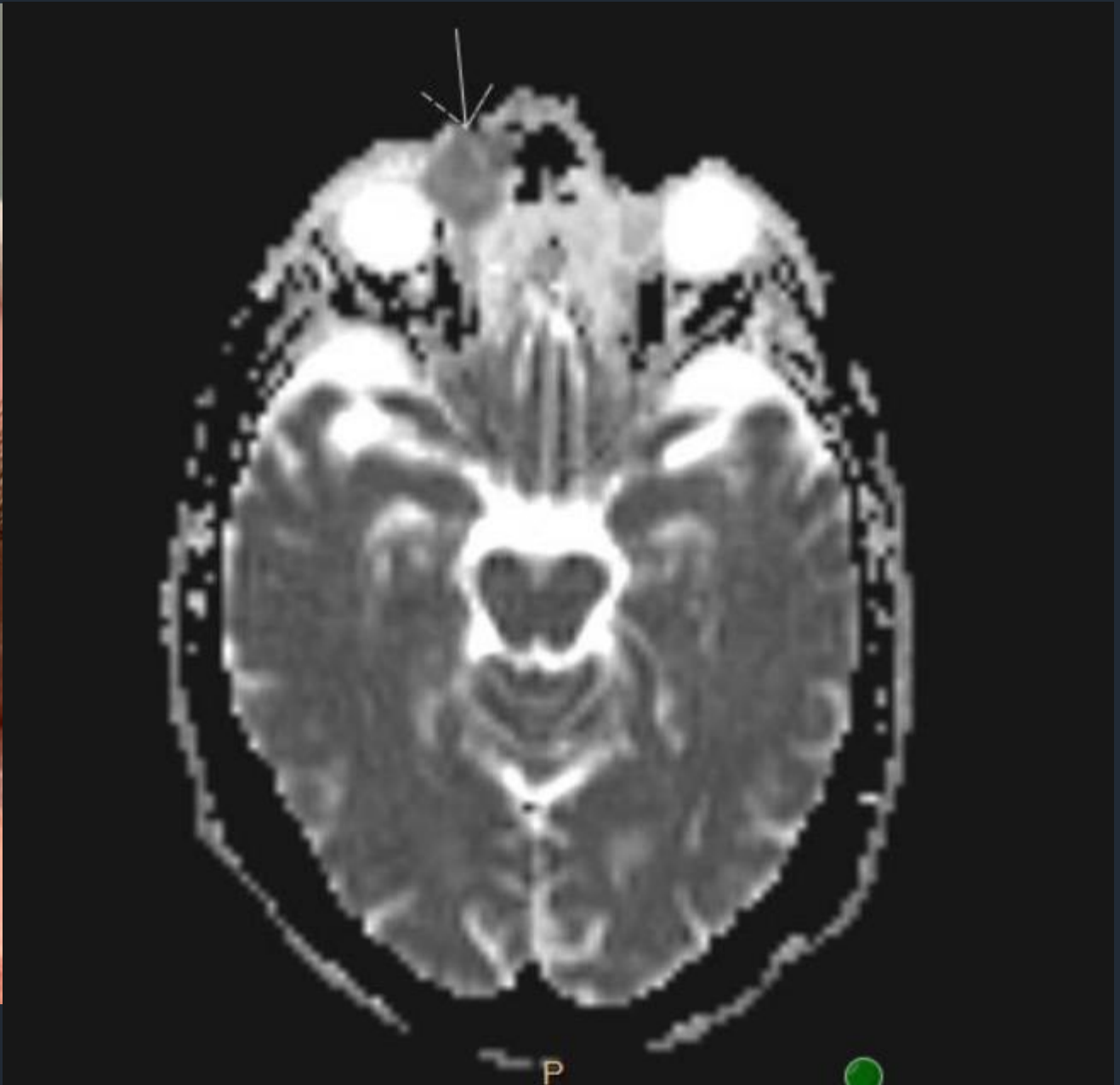


3/20



11/20





4/21



# Revision of Immunosuppression

## Indication

1. Metastatic SCC
2. > than 5-10 iSCC/year
3. New case of Merkel Cell Carcinoma

*T2b (>2cm, perineural, lesion within a year, poor differentiation) lesions in the context of field damage*

## Strategy

- Try to lower dose
- Move from triple drug to double drug
- Switch calcineurin inhib to *mTOR inhib or CTLA4*
- Retinoid
- Hemodialysis (renal Tx)
  - PD1 inhibitor?



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Thank you for your attention!

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