Cancer Immunotherapy in Practice

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Disclosures

None relevant to this talk.

Objectives

- Cancer immunotherapy 101
- Key immunotherapy toxicities and management
- Participation in clinical trials

Buckets of cancer treatment

Chemotherapy

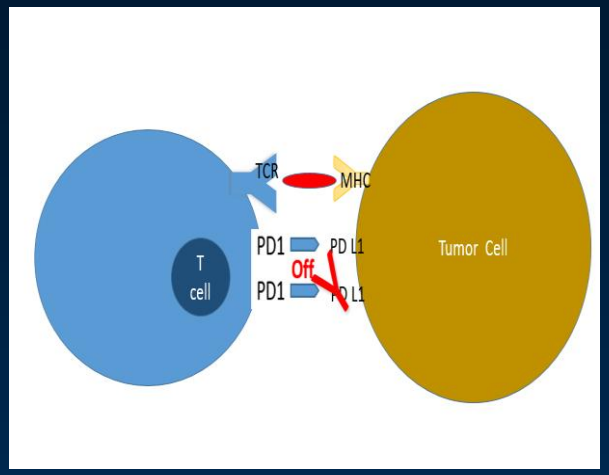
Hormone therapy

Targeted therapy

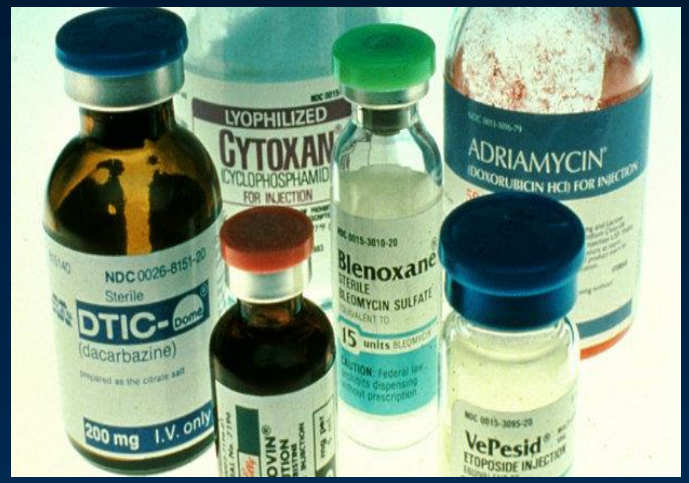
Biologics

Immunotherapy

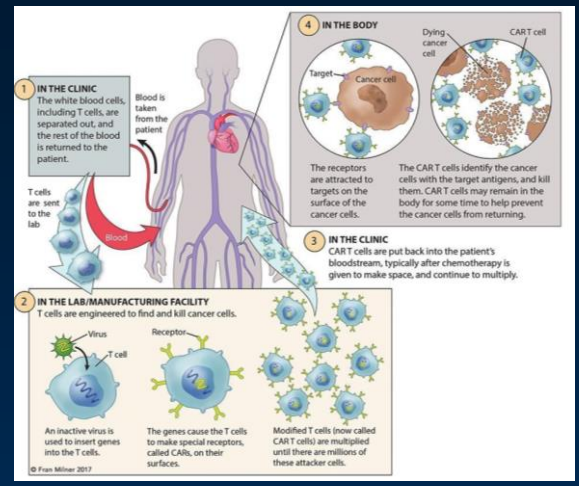
Buckets of immunotherapy



PD1/PDL1



IO+chemo



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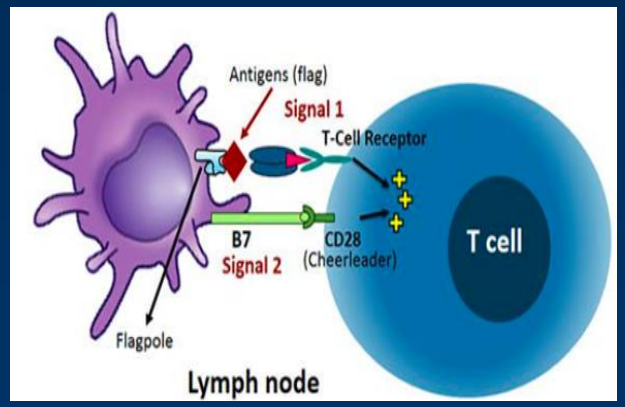
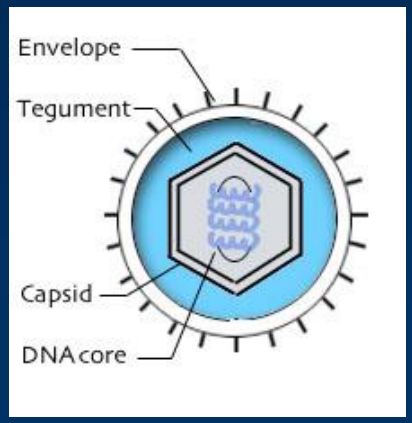
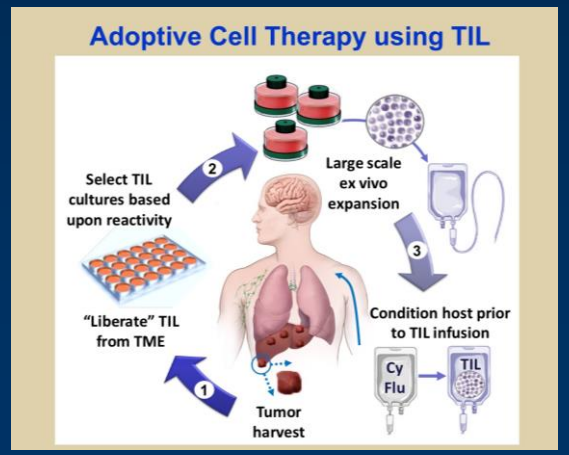


CTLA-4

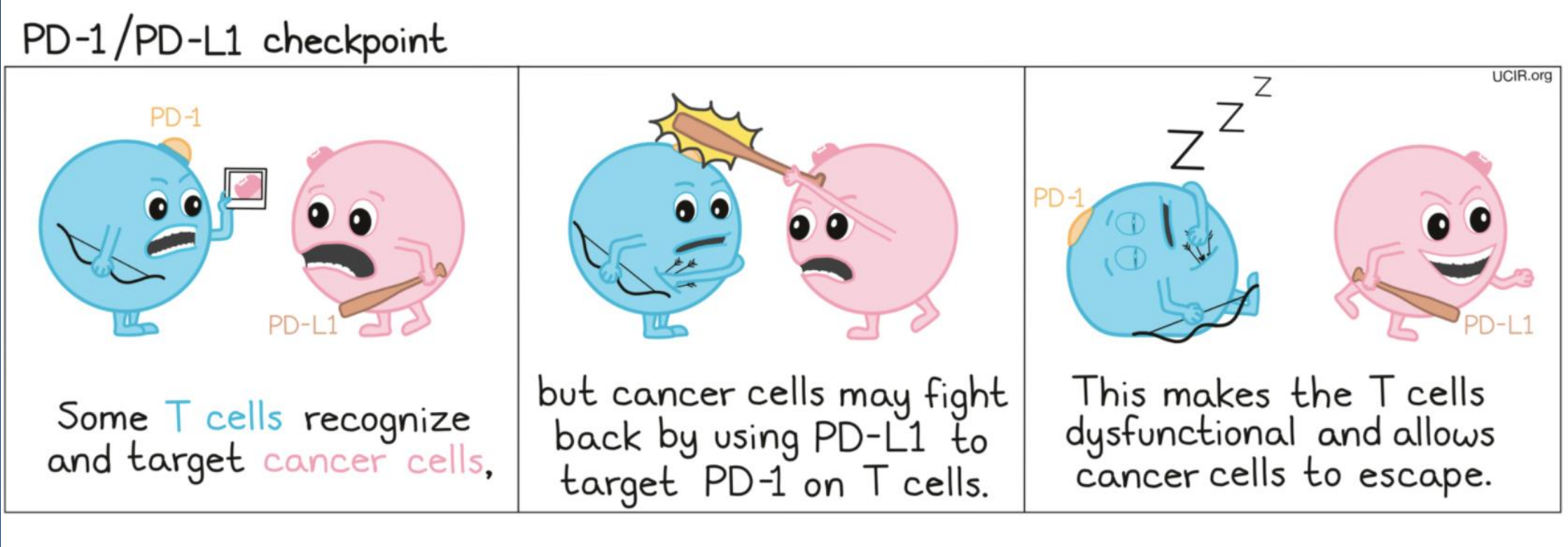


Oncolytic Virus Therapy

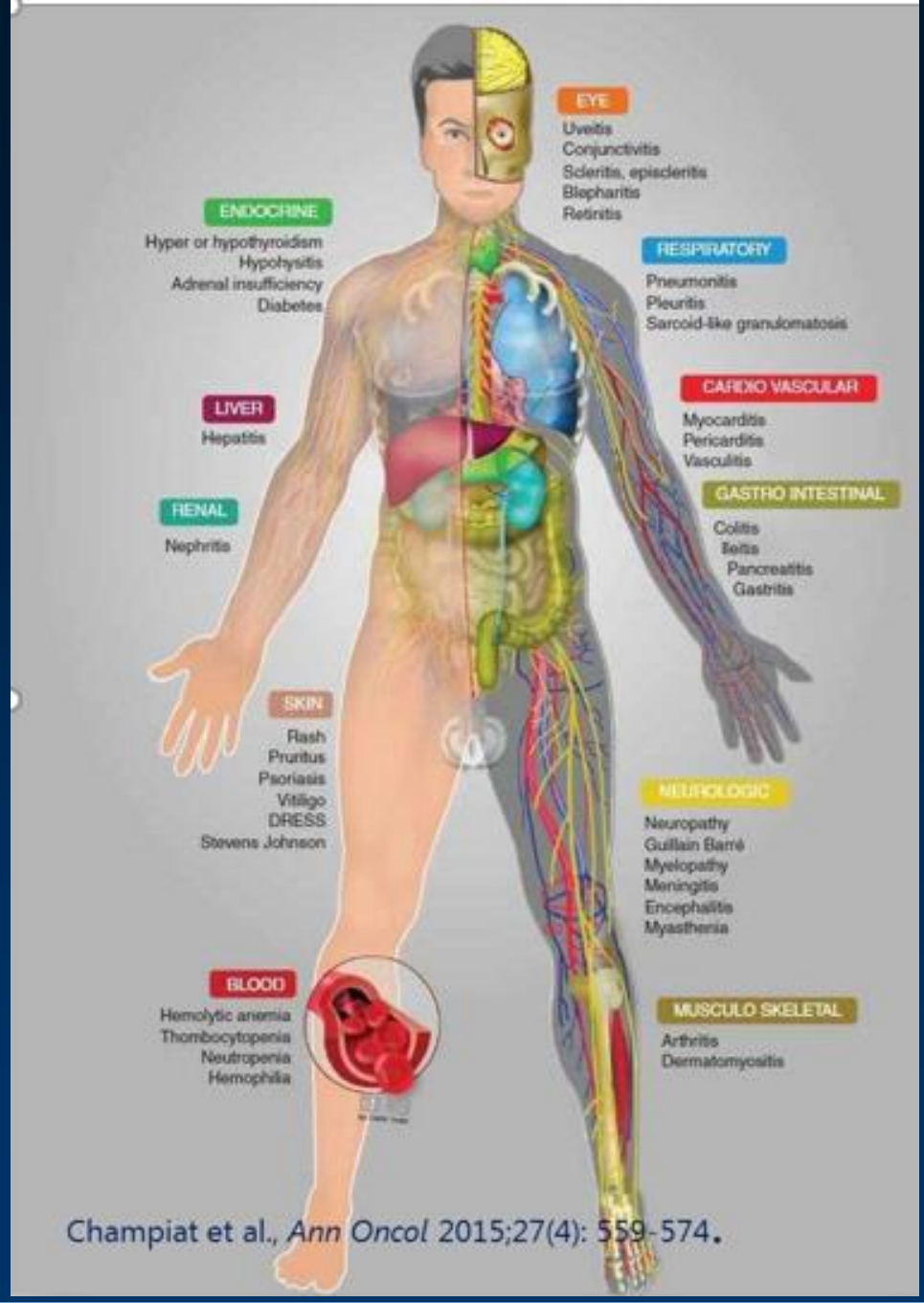


Adoptive T Cell/TILS

Interaction between cancer cells and immune cells



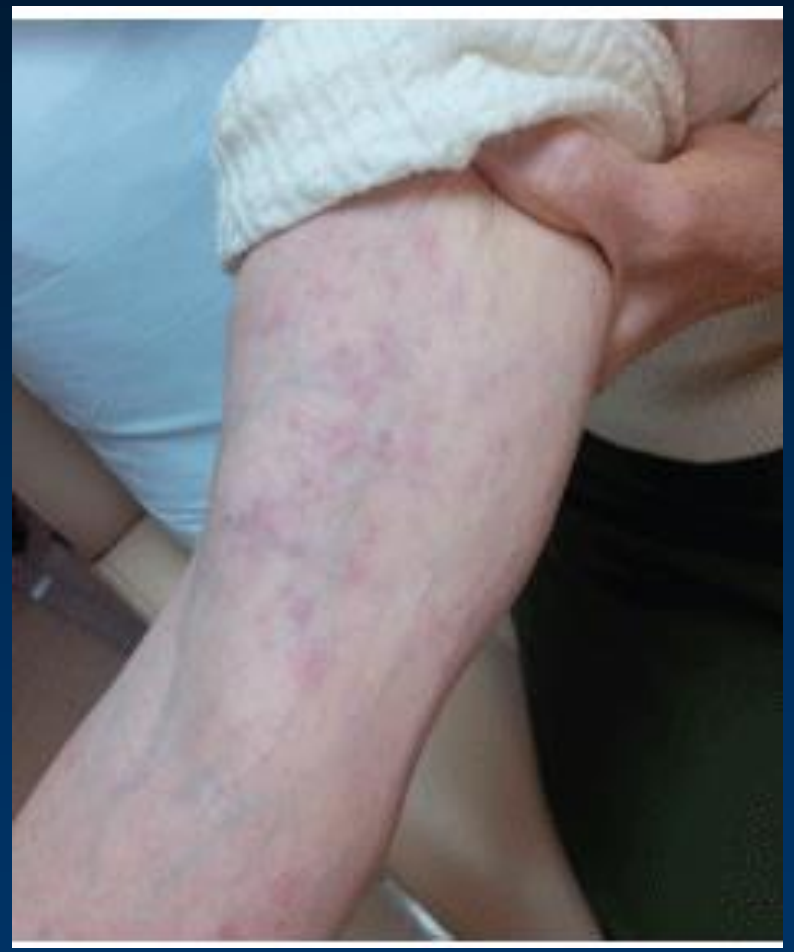
Immune Related AE's



Case 1

A 65 year old on pembrolizumab presents to the clinic for his second cycle of therapy. He has been feeling well. He has a mild macular rash on his forearms. It is not pruritic or painful. Labs are normal.

Can treatment be given today?



Grading IRAE's using CTCAE

Determining *degree* of toxicity is key to management

Grade 1: Mild, asymptomatic, no intervention required

Grade 2: Moderate, local or non-invasive intervention required

Grade 3: Severe or medically significant, but not life-threatening.

Grade 4: Life-threatening consequences; urgent intervention required

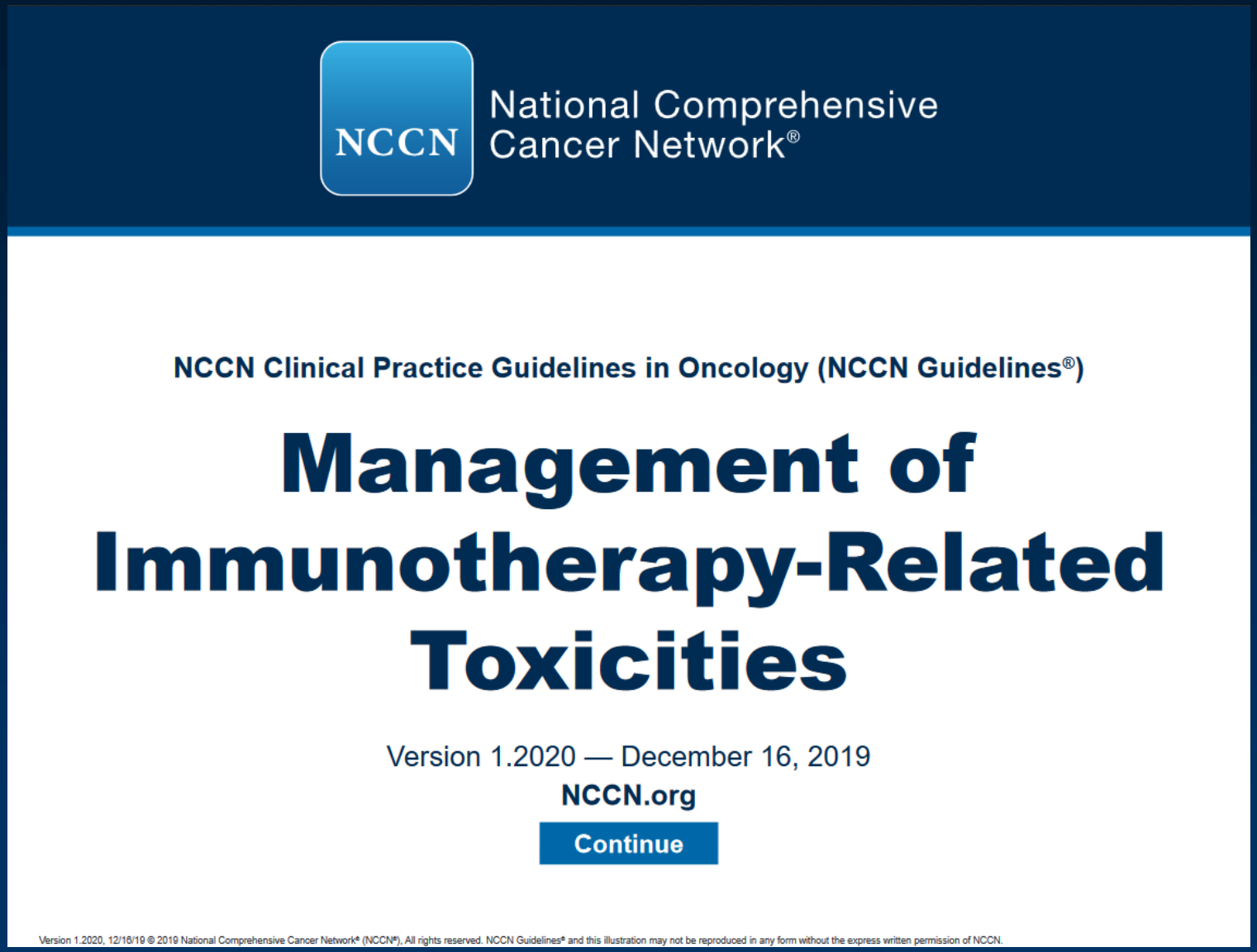
Grade 5: Death related to AE

Electronic version is available at
https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm

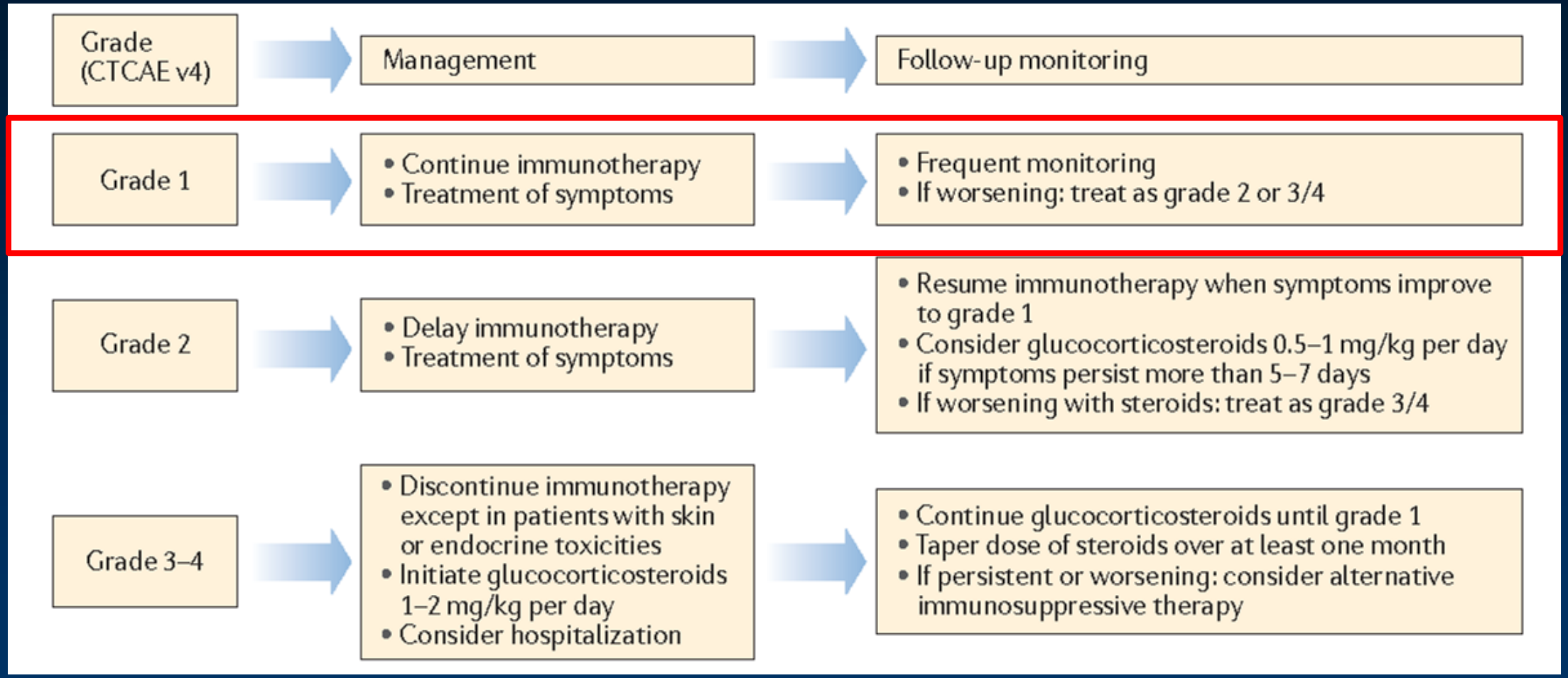
Case 1: Grading the Skin Rash

Skin and subcutaneous tissue disorders					
CTCAE Term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Purpura	Combined area of lesions covering <10% BSA	Combined area of lesions covering 10 - 30% BSA; bleeding with trauma	Combined area of lesions covering >30% BSA; spontaneous bleeding	-	-
Definition: A disorder characterized by hemorrhagic areas of the skin and mucous membrane. Newer lesions appear reddish in color. Older lesions are usually a darker purple color and eventually become a brownish-yellow color. **Navigational Note:** -					
Rash acneiform	Papules and/or pustules covering <10% BSA, which may or may not be associated with symptoms of pruritus or tenderness	Papules and/or pustules covering 10 - 30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; associated with psychosocial impact; limiting instrumental ADL; papules and/or pustules covering > 30% BSA with or without mild symptoms	Papules and/or pustules covering >30% BSA with moderate or severe symptoms; limiting self-care ADL; associated with local superinfection with oral antibiotics indicated	Life-threatening consequences; papules and/or pustules covering any % BSA, which may or may not be associated with symptoms of pruritus or tenderness and are associated with extensive superinfection with IV antibiotics indicated	Death
Definition: A disorder characterized by an eruption of papules and pustules, typically appearing in face, scalp, upper chest and back. **Navigational Note:** -					
Rash maculo-papular	Macules/papules covering <10% BSA with or without symptoms (e.g., pruritus, burning, tightness)	Macules/papules covering 10 - 30% BSA with or without symptoms (e.g., pruritus, burning, tightness); limiting instrumental ADL; rash covering > 30% BSA with or without mild symptoms	Macules/papules covering >30% BSA with moderate or severe symptoms; limiting self care ADL	-	-
Definition: A disorder characterized by the presence of macules (flat) and papules (elevated). Also known as morbilliform rash, it is one of the most common cutaneous adverse events, frequently affecting the upper trunk, spreading centripetally and associated with pruritis.					

Managing IRAE's with NCCN Practice Guidelines



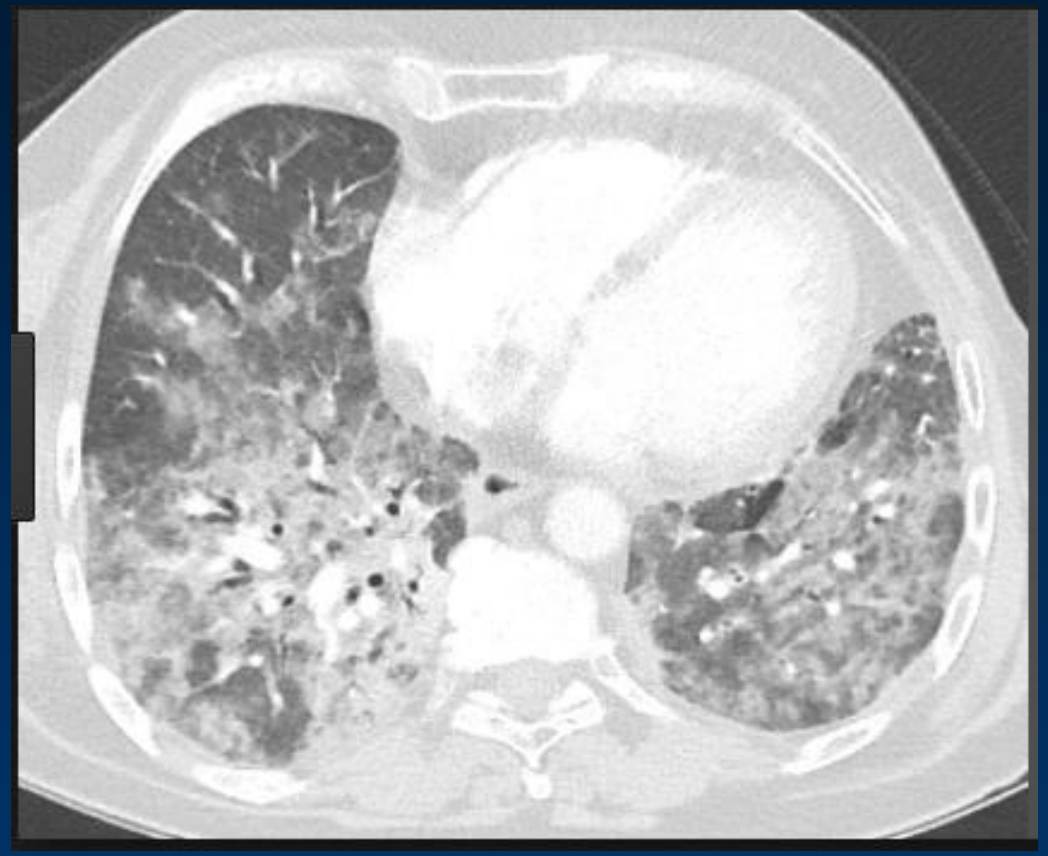
General Principles of Management of IRAE's



Grade (CTCAE v4)	Management	Follow-up monitoring
Grade 1	• Continue immunotherapy • Treatment of symptoms	• Frequent monitoring • If worsening: treat as grade 2 or 3/4
Grade 2	• Delay immunotherapy • Treatment of symptoms	• Resume immunotherapy when symptoms improve to grade 1 • Consider glucocorticosteroids 0.5–1 mg/kg per day if symptoms persist more than 5–7 days • If worsening with steroids: treat as grade 3/4
Grade 3–4	• Discontinue immunotherapy except in patients with skin or endocrine toxicities • Initiate glucocorticosteroids 1–2 mg/kg per day • Consider hospitalization	• Continue glucocorticosteroids until grade 1 • Taper dose of steroids over at least one month • If persistent or worsening: consider alternative immunosuppressive therapy

Case 2

A 48 year old woman with COPD and metastatic HNSCC to the lungs is admitted with “pneumonia”. Her cancer was diagnosed 6 months ago, and treated with pembrolizumab + chemotherapy. Three months into the treatment, scans showed stable disease. On presentation she has a room air 02 Sat of 85%, BP of 135/80 and Temp 99. CT scan is shown.



Case 2: What is the differential diagnosis?

A. Disease progression

B. COVID

C. ARDS

D. Pneumonitis

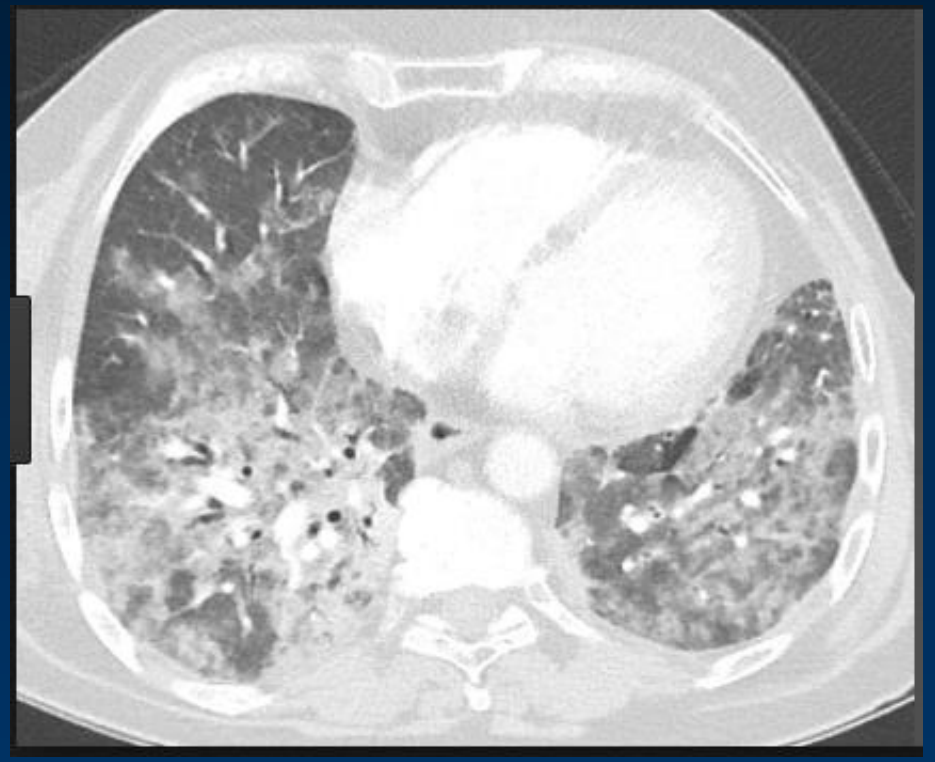
Case 2: Pneumonitis

Diagnostic work up:

- CXR and /or CT scan
- Radiographic findings of ground glass lesions and /or disseminated nodular infiltrates
- Bronchoscopy
- PFTs
- Blood gas

Management:

- IV Steroids (Grade 3)
- Albuterol Nebulizers
- Oxygen
- Prophylactic antibiotics and antifungals for patients on high dose steroids
- Add mycophenolate, cyclophosphamide, IVIG, or infliximab if the patient does not improve



Steroids have an important role for IRAEs

- Patients who benefit from corticosteroids usually do so in a few days
- If symptoms do not improve in a few days, particularly after IV steroids, consider further immunosuppression

Combination IO therapies are more toxic

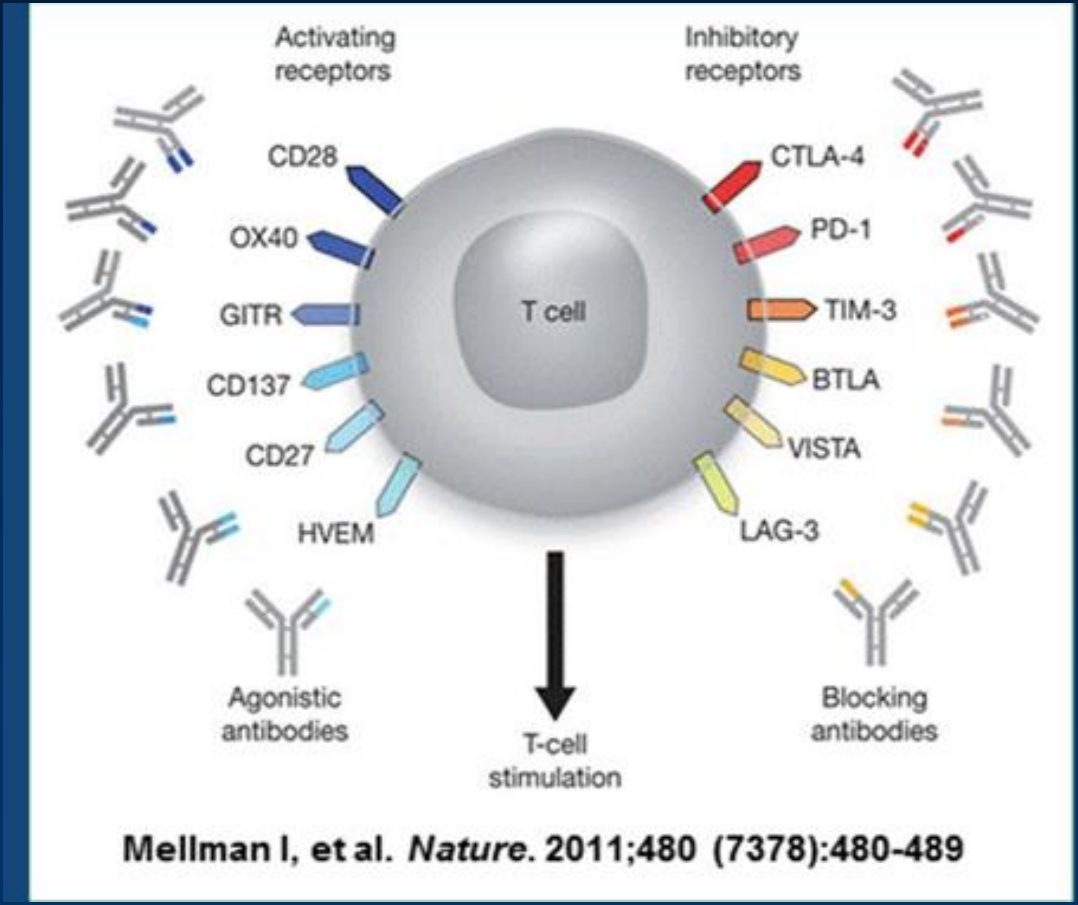
Incidence of serious irAEs (Grade ≥3)

Anti-CTLA-4	Anti-PD-1	Anti-PD-L1
Ipilimumab	Pembrolizumab	Atezolizumab
	Nivolumab	Avelumab
	Cemiplimab	Durvalumab
34%	14%	

Combination: ipilimumab + nivolumab 55%

Arnaud-Coffin et al (2019) Int Jrnl of CA

New IO combination therapies may change the side effect profile



PD1 therapy plus:

1. Chemotherapy
2. Targeted Therapy
   a) Cetuximab
   b) VEGF inhibitors
3. Other immunotherapies
4. Radiation Therapy
5. Oncolytic Viral Therapy

Case 3

A 56 year old woman with recurrent HNSCC presents to discuss treatment options. She is healthy overall and her history is significant only for mild psoriasis. She is not actively on any medications for her psoriasis and stopped she her dermatologist “years ago”.

How do you counsel the patient about her risks of exacerbating her psoriasis with immunotherapy?

Case 3: History of Autoimmune Disease

- Underlying auto immune disease is worse 1/3 of the time
- Increased risk of high grade irAEs in 2/3s
- Weigh the benefit versus the risk

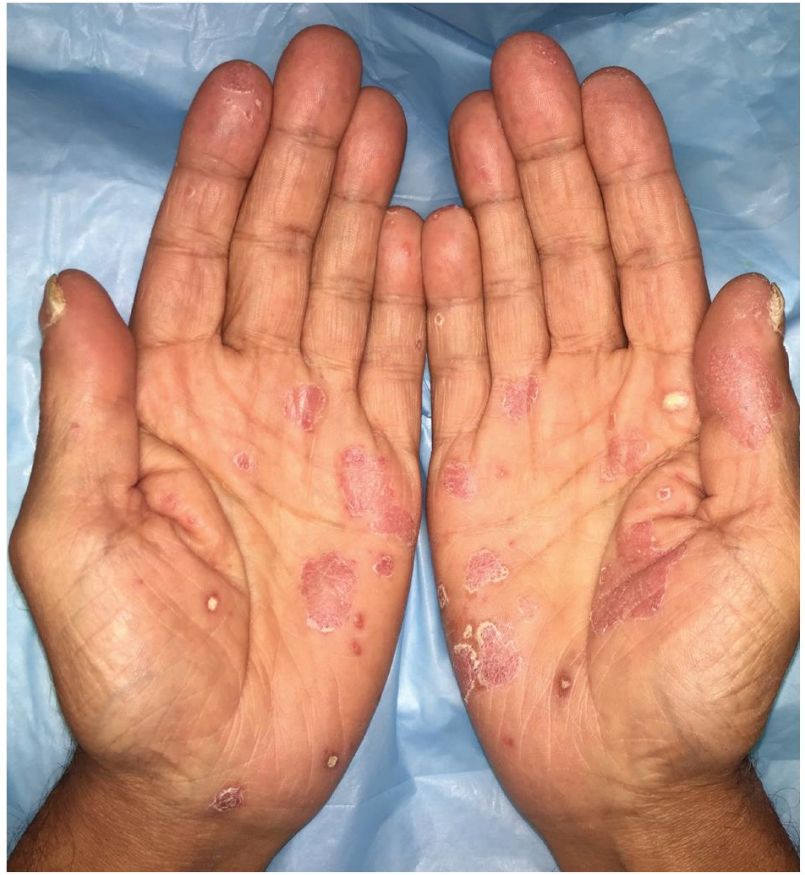
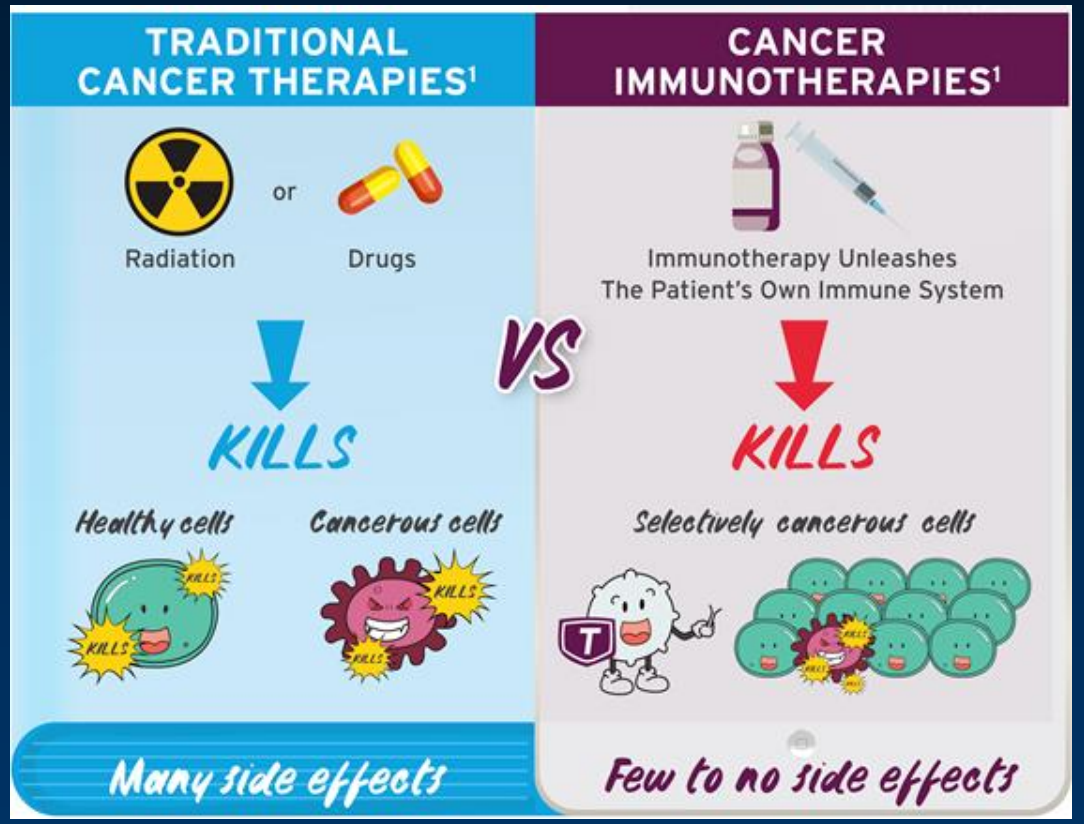


FIGURE 1 Numerous erythematous, circular to oval well-circumscribed, scaly plaques on the bilateral palms.

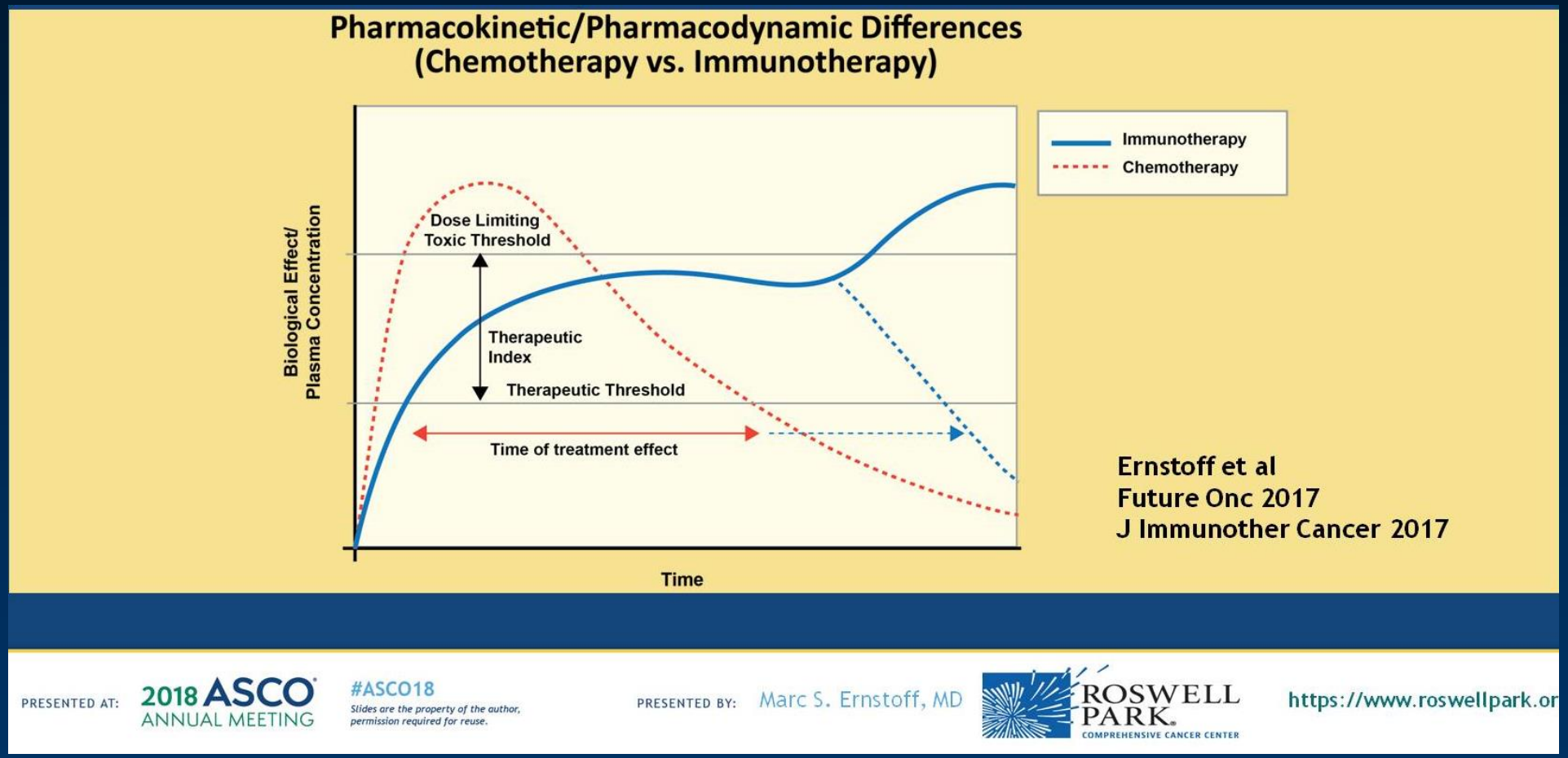
Case 4

A 79 year old man with metastatic HNSCC to the lung, bone, and liver has been deciding between immunotherapy vs. immunotherapy + chemotherapy. He wants to be treated aggressively but is concerned about side effects given his other medical problems.

Your patients wants to understand the differences in the side effect profile of immunotherapy vs. chemotherapy.



Case 4: Chemo vs. IO



- Chemotherapy side effects can be severe, but are more predictable than IO
- IO side effects can be unpredictable, persistent, recurrent

Key Takeaways about irAEs

- CTCAE (Common Toxicity Criteria for Adverse Events) is useful to grade toxicity
- Management of irAE using reliable source such as NCCN.org.
- Patients usually respond to steroids in a few days; if they don’t, move to more aggressive management
- Good PS treated with PD1 therapies have a low risk of grade 3-5 toxicity
- Toxicity risk depends on sequence, combinations, pre-existing autoimmune disease
- Rare but important irAEs are possible (CNS and heart)
- IrAES can be permanent, and delayed even long after the treatment is done

Participation in Clinical Trials

What is a clinical trial?

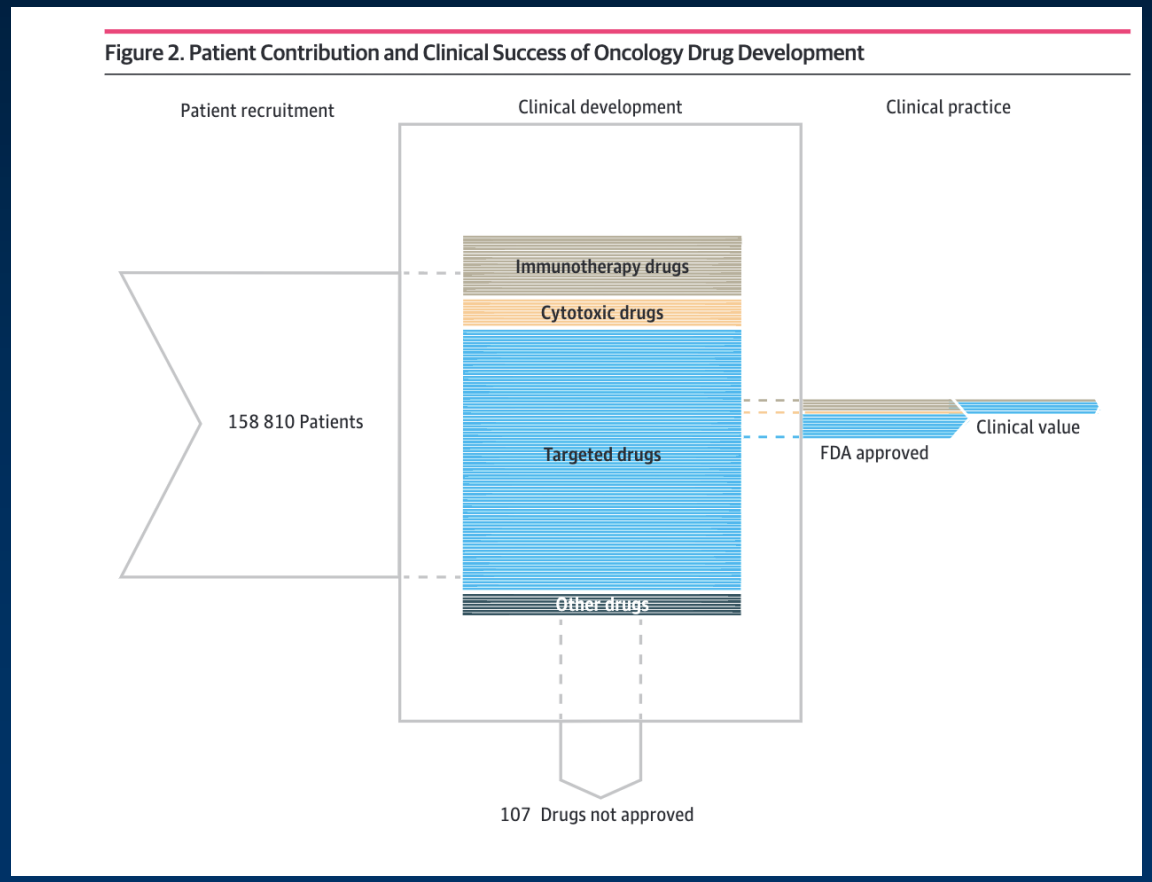
- A **clinical trial** is a research study done in people that helps health care providers understand the best approach to prevent, diagnose, treat, or manage symptoms of diseases, including cancer

- Clinical trials can be used to evaluate a wide range of biomedical (e.g., treatment) and behavioral (e.g., exercise and diet) interventions

- Clinical trials are the cornerstone of creating new cancer interventions and improving patient outcomes.

Why clinical trials are important?

- For ~100 drugs evaluated in phase 1 oncology trial, <10 drugs receive regulatory approval
- A median of 2316 patients per FDA approval of a precision medicine oncology drug



- 158,810 patients enrolled in oncology clinical trials
- Clinical development of 120 oncology drugs 13 oncology drugs gained US FDA approval
- Only 4 approved drugs deemed of intermediate or substantial clinical value by the ASCO Value Framework

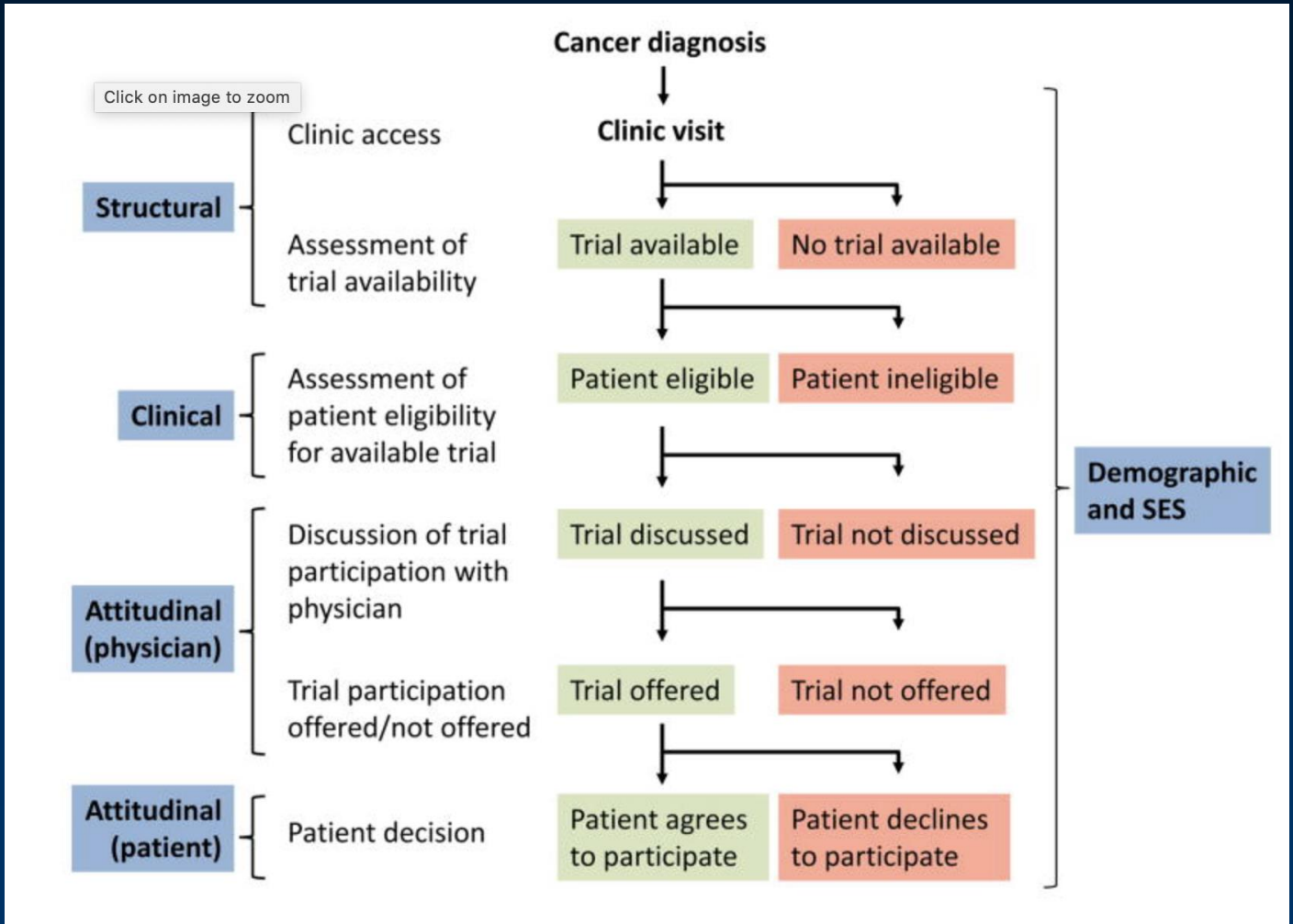
Barriers to clinical trial participation

Common barriers: structural, clinical, attitudinal

An NCI-funded study led by researchers at Fred Hutchinson Cancer Research Center examined why people with cancer do not participate in clinical trials:

- The researchers looked at trial availability, patient eligibility, and physical barriers
- Results: 3 out 4 patients could not enroll in a clinical trial because none were available in the area OR the patient was ineligible to enroll
- Limited enrollment is not due to patient unwillingness

Pathway to improve clinical trial barriers



Unger JM et al. Am Soc Clin Onc. 2018. PMID 27249699

Thank you!

Questions?

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