South Beach Symposium
medical + aesthetic dermatology
CELEBRATING 20 YEARS
OF PREMIER MEDICAL & AESTHETIC DERMATOLOGY EDUCATION

REIMAGINING
MEDICAL AND
AESTHETIC
DERMATOLOGY

Clinical Update on PD-1 Inhibitors for c-SCC

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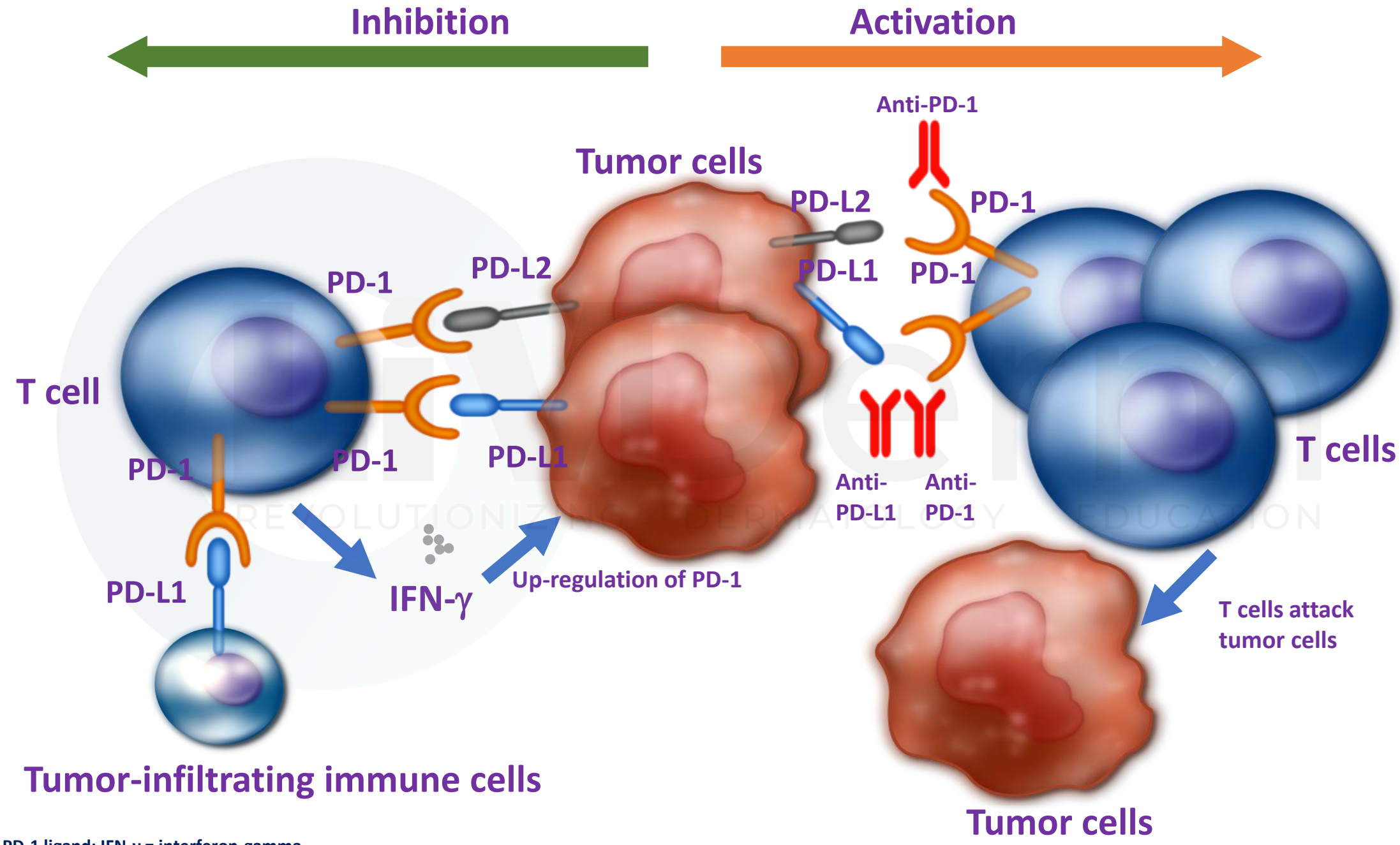
Clinical Instructor, Edward Via College of Osteopathic Medicine

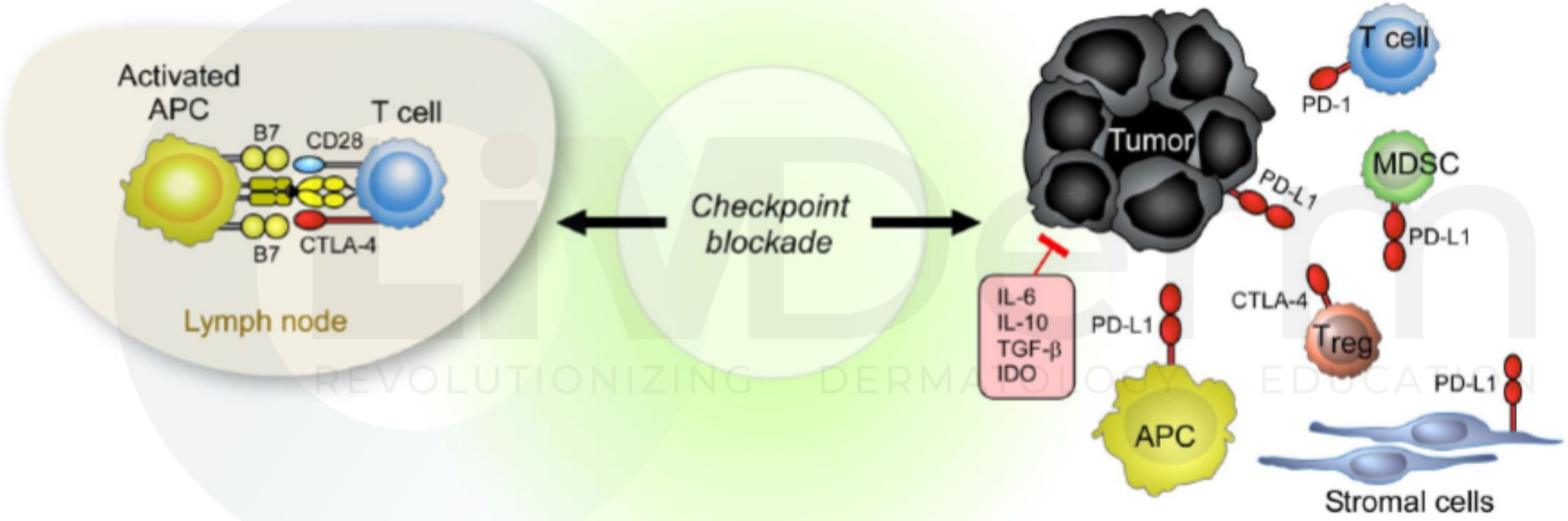
Major Classes of Approved Treatments for Advanced NMSC

- PD-1 Inhibitors
  - Cemiplimab
    - (28SEP2018) – laCSCC or mCSCC
    - (09FEB2021) - laBCC and mBCC - previously treated with HHI or not appropriate for HHI
    - Dosed IV 350mg every 3 weeks
  - Pembrolizumab (24JUN2020) – recurrent or mCSCC
    - Dosed IV 200mg every 3 weeks



PD-L1 = PD-1 ligand; IFN-γ = interferon-gamma

Where Does Checkpoint Blockade Function?



CTLA-4 in the Lymph Node

PD-1 in the Tumor

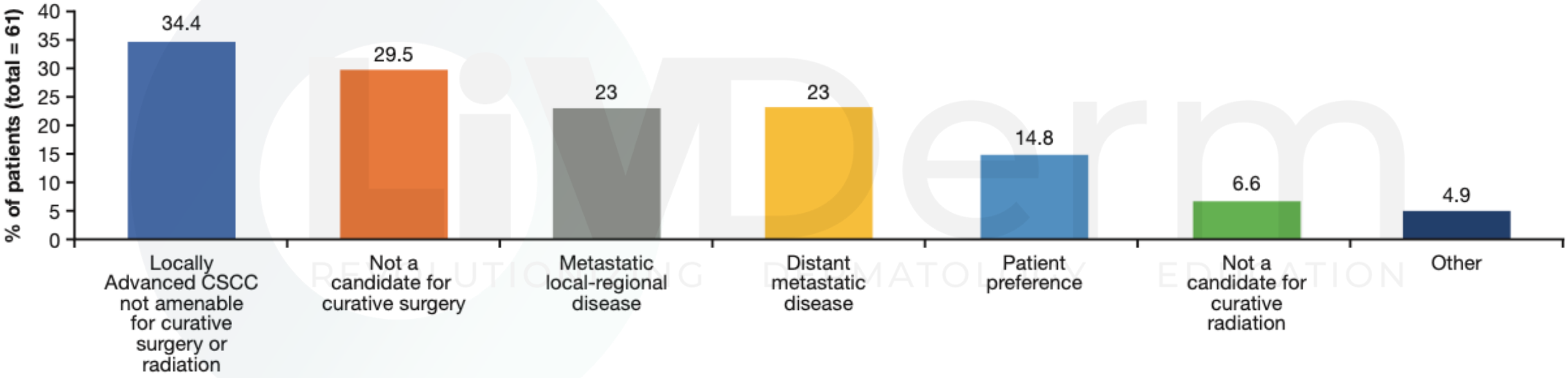
PD-L1 Expression

	TMB (median mutations/Mb)	PD-L1 expression (Tumor)	PD-L1 expression (TILs)
BCC	47.3	22%-89%	82-94%
cSCC (immunocompetent)	45.2	25-41%	60%
MCC (non-virus associated)	53.9	0%	25%
MCC (MPyV-associated)	1.2	50%	56%
Cutaneous melanoma	13.5	30%-35%	50%

- PD-L1 expression varies in NMSC
  - 25-41% in cSCC
- PD-L1 expression also varies in tumor infiltrating lymphocytes (TIL's) related to specific tumor types
- Potential for increased PD-L1 expression in previously treated NMSC's

Stonesifer CJ, Djavid AR, Grimes JM, Khaleel AE, Soliman YS, Maisel-Campbell A, Garcia-Saleem TJ, Geskin LJ, Carvajal RD. Immune Checkpoint Inhibition in Non-Melanoma Skin Cancer: A Review of Current Evidence. Front Oncol. 2021 Dec 20;11:734354. doi: 10.3389/fonc.2021.734354. PMID: 34988009; PMCID: PMC8720968.

Why do clinicians initiate cemiplimab (CSCC)?



Demographics, Prior Therapies and Reasons for Cemiplimab Treatment: Prospective

CemiplimAb-rwlc Survivorship and Epidemiology (C.A.S.E.) Study in Patients with

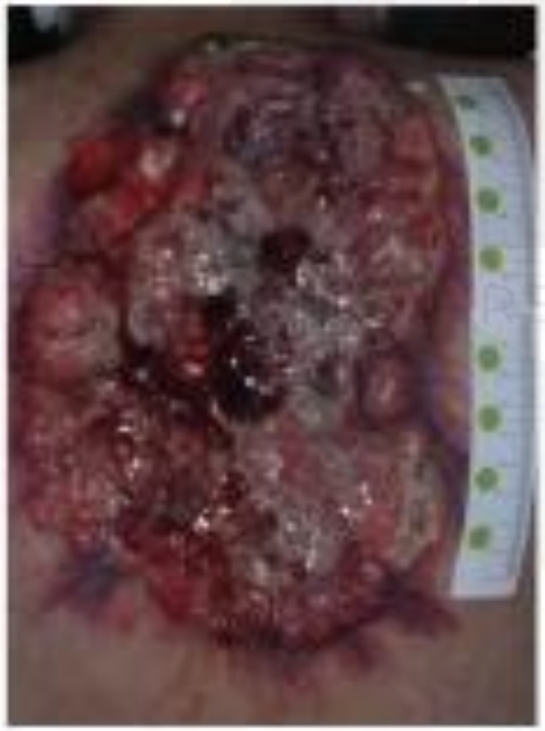
Advanced Cutaneous Squamous Cell Carcinoma

Guilherme Rabinowits,1 Jade Homsi,2 Mina Nikanjam,3 Rhonda Gentry,4 John Strasswimmer,5 Suraj Venna,6 Michael R. Migden,7 Sunandana Chandra,8 Emily Ruiz,9 Haixin R. Zhang,10 Jennifer McGinniss,10 Alex Seluzhytsky,11 Jigar Desai10

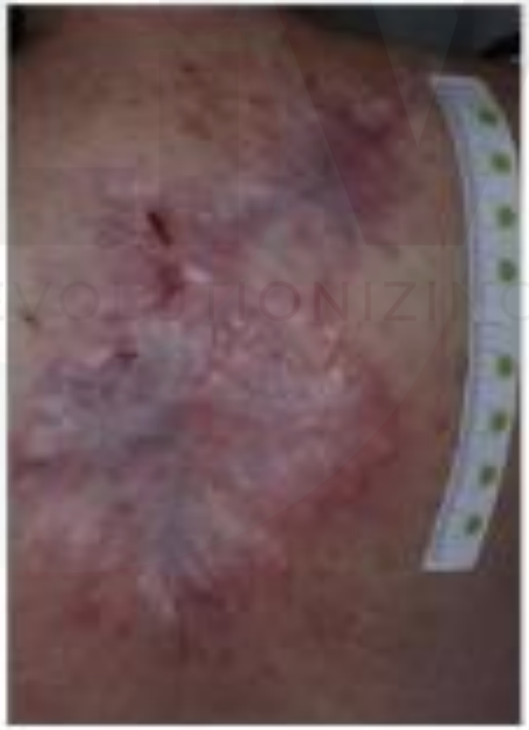
Examples of Outcomes CSCC

A 70-year-old female with a large CSCC tumor of the left back

Baseline

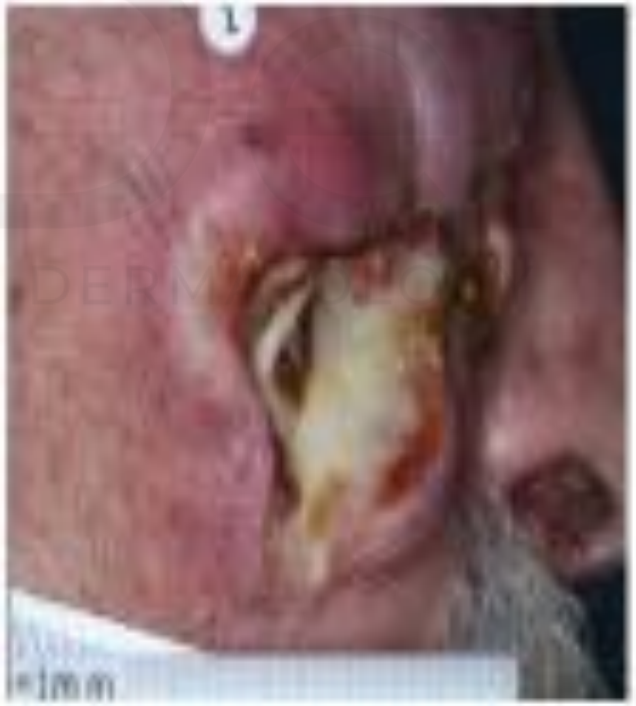


Week 48



A 70-year-old male with a large CSCC tumor of the right face

Baseline



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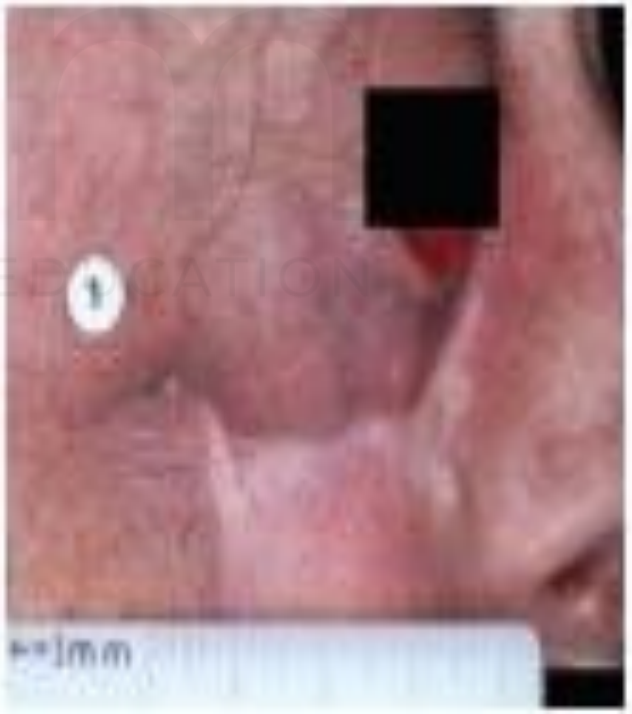
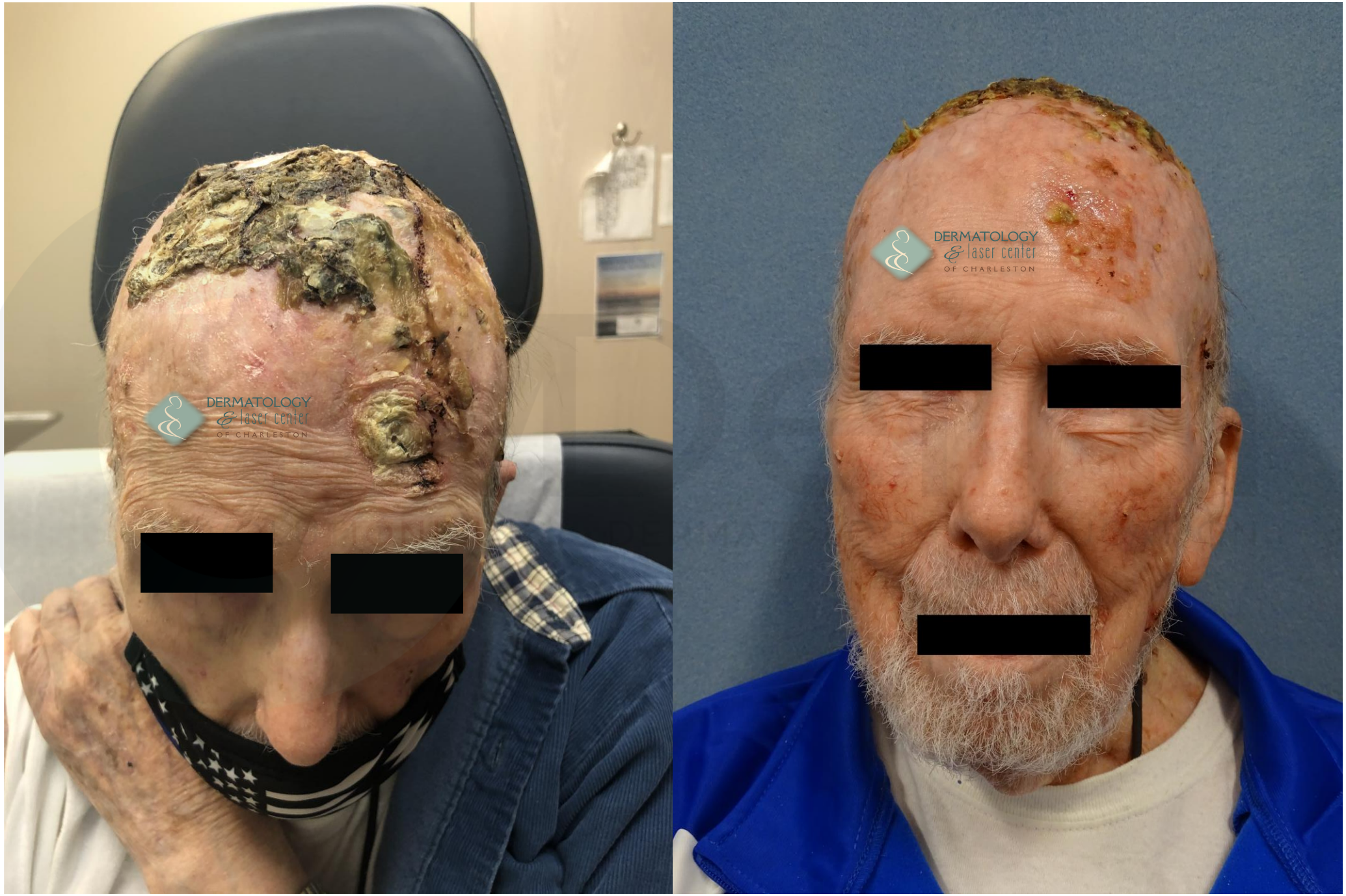


J Clin Oncol 37, 2019 (suppl; abstr 6015)


DERMATOLOGY
& laser center
OF CHARLESTON
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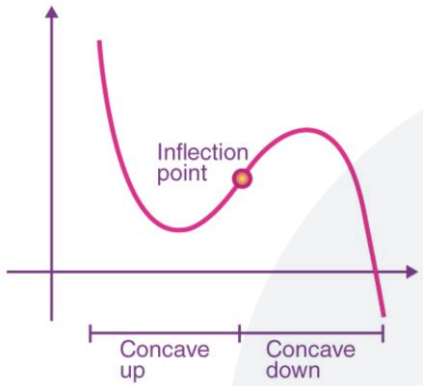
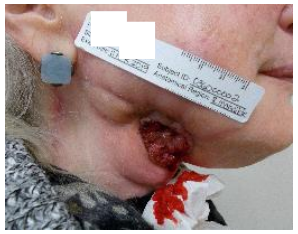


Involve MDT

A



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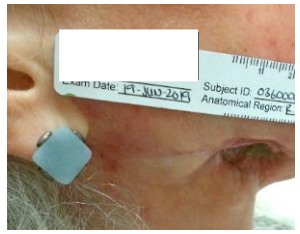
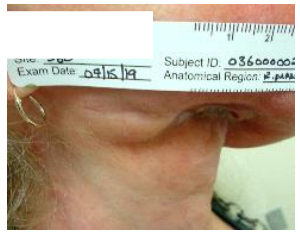
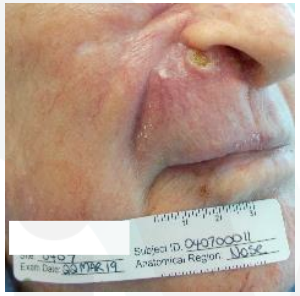


Week 8



Week 12

B



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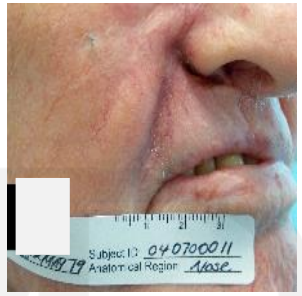
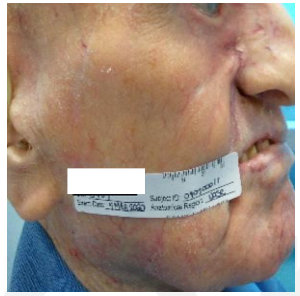


Week 6



Week 48

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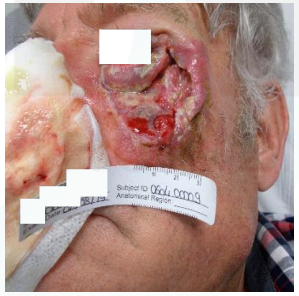

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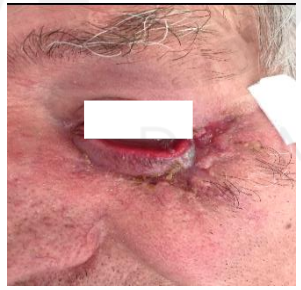
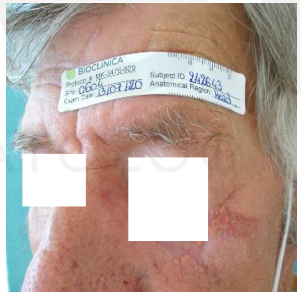


Week 6



Week 48

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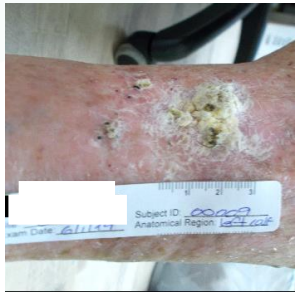
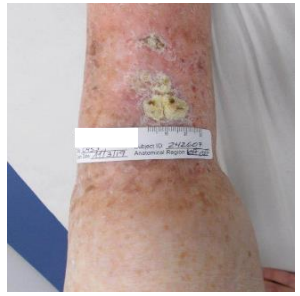
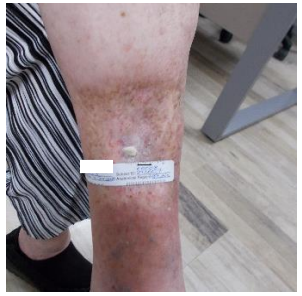


Baseline



Week 6



Week 72

Pembrolizumab 2IA

Hughes BGM, Munoz-Couselo E, Mortier L, Bratland Å, Gutzmer R, Roshdy O, González Mendoza R, Schachter J, Arance A, Grange F, Meyer N, Joshi A, Billan S, Zhang P, Gumuscu B, Swaby RF, Grob JJ. Pembrolizumab for locally advanced and recurrent/metastatic cutaneous squamous cell carcinoma (KEYNOTE-629 study): an open-label, nonrandomized, multicenter, phase II trial. Ann Oncol. 2021 Oct;32(10):1276-1285. doi: 10.1016/j.annonc.2021.07.008. Epub 2021 Jul 20. PMID: 34293460.

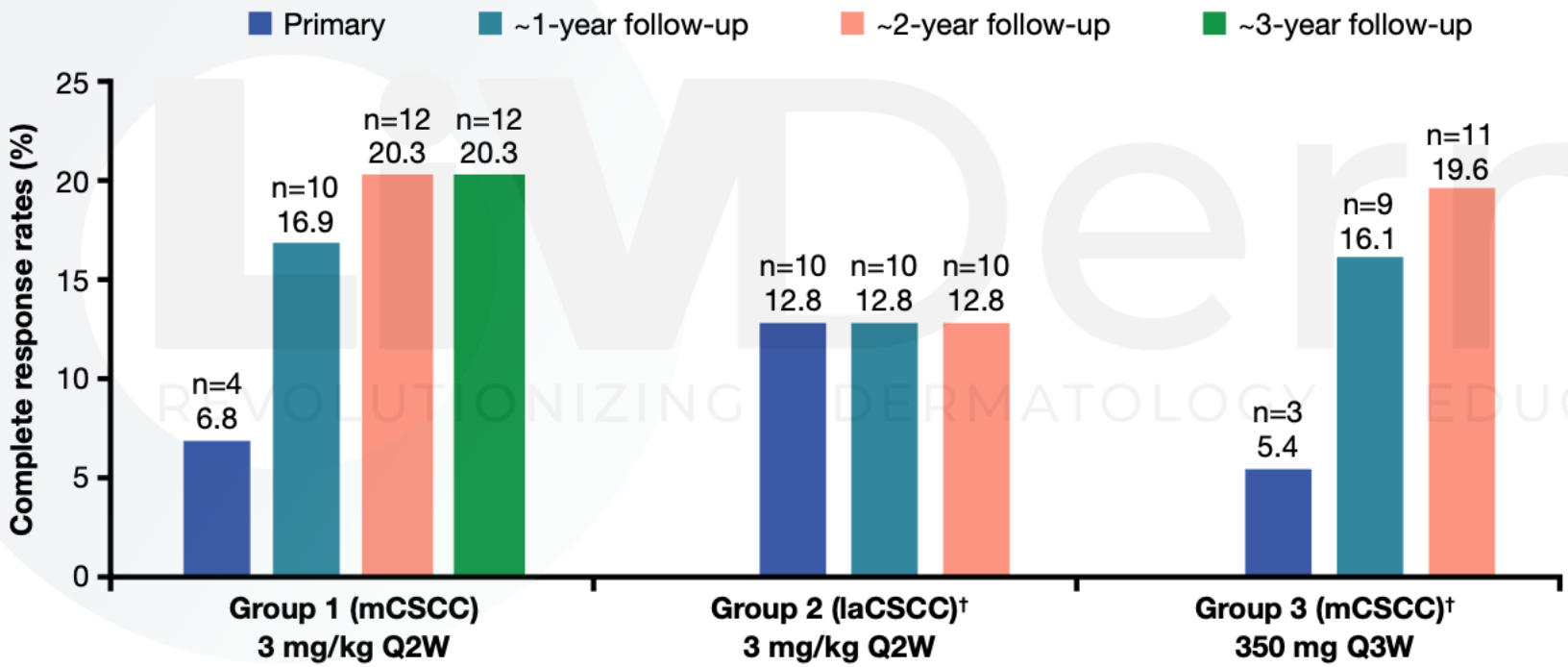
What Data Do We Have/CSCC?

- Pembrolizumab
  - CARSKIN – 1L la/mCSCC 22.4 mos
    - ORR_{W15} 41%, mPFS 8.4m
      - PD-L1+ 55% vs PD-L1- 17%
  - KEYNOTE-629 – la 14.9/rmCSCC 27.2 mos
    - N=159
    - ORR 40.3%
    - ORR la 50.0% (16.7% CR, 33.3% PR)
    - ORR r/m 35.2% (10.5% CR, 24.8% PR)
    - <u>Subgroups:</u>
    - PD-L1 status – ORR increase observed
- Cemiplimab
  - EMPOWER – 1L/2L la/mCSCC 43 mos
    - N=193
    - Group 1 mCSCC 50.8%
      - 20.3% CR, 30.5% PR
    - Group 2 laCSCC 44.9%
      - 12.8% CR, 32.1% PR
    - Group 3 mCSCC 46.4%
      - 19.6% CR, 26.8% PR
    - Total 47.2% ORR
    - <u>Subgroup:</u>
    - Age <65, 65-<75 and >75 similar outcome

Comparison data: response rates with monotherapy agents such as EGFR are in 11-31% range

Maubec E, Boubaya M, Petrow P, et al: Pembrolizumab as first-line therapy in patients with unresectable cutaneous squamous cell carcinoma (cSCC): Phase 2 results from CARSKIN. J Clin Oncol 37, 2019 (suppl; abstr 9547)
J Clin Oncol 38:2916-2925. © 2020 by American Society of Clinical Oncology
Rischin et al: *Presented at 10th World Congress of Melanoma in conjunction with 17th European Association of Dermato Oncology Congress 2021, April 15–17, Virtual Scientific Meeting*

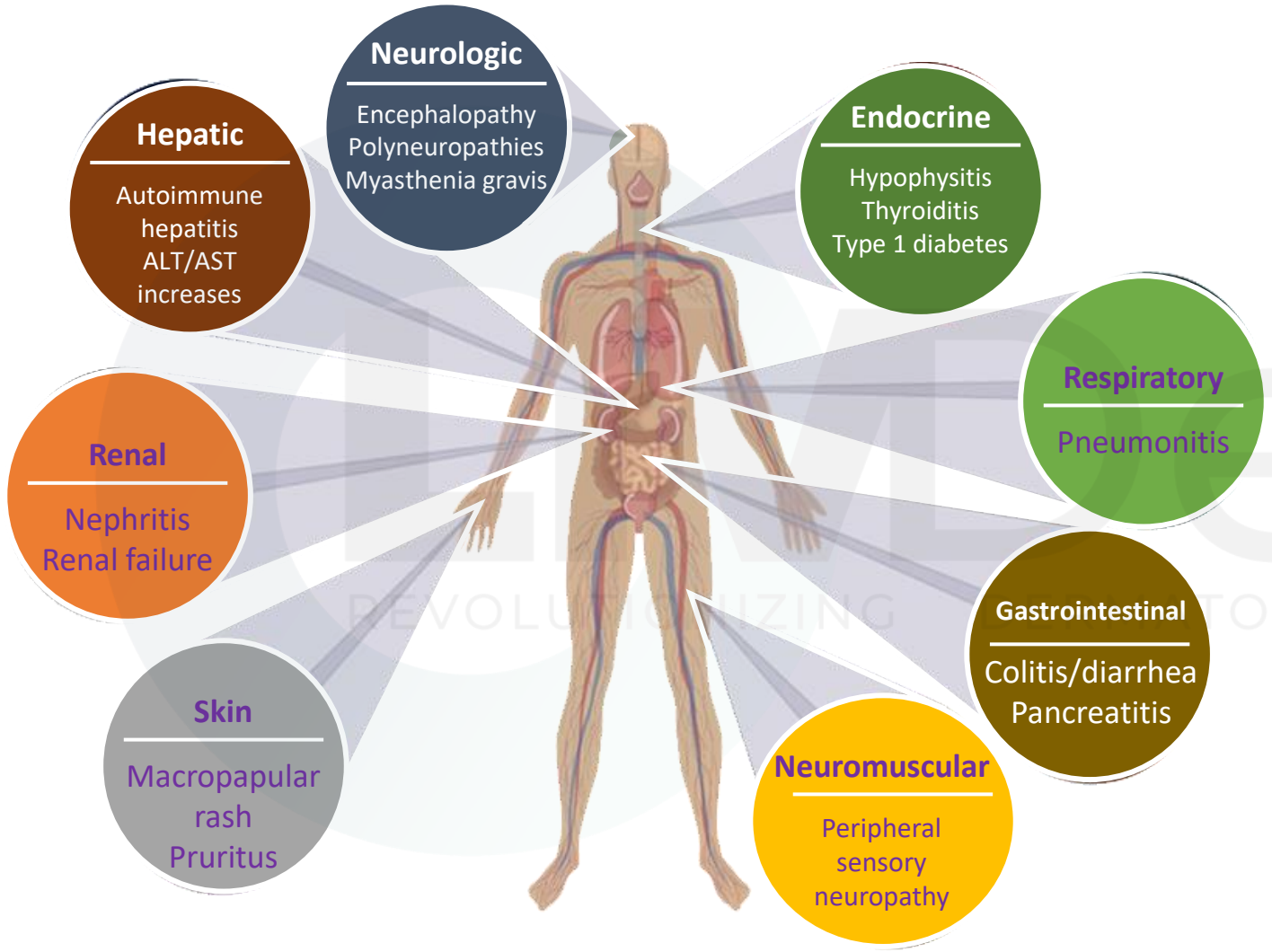
Figure 2. Complete response rates per ICR



†The timepoint for the primary analyses for Groups 2 and 3 data were approximately 1 year after the Group 1 primary analysis.

Rischin et al P-236 Presented at the 10th World Congress of Melanoma in conjunction with 17th European Association of Dermato Oncology Congress 2021, April 15–17, Virtual Scientific Meeting.

Virtually Any Organ Can Be Subject to Autoimmunity

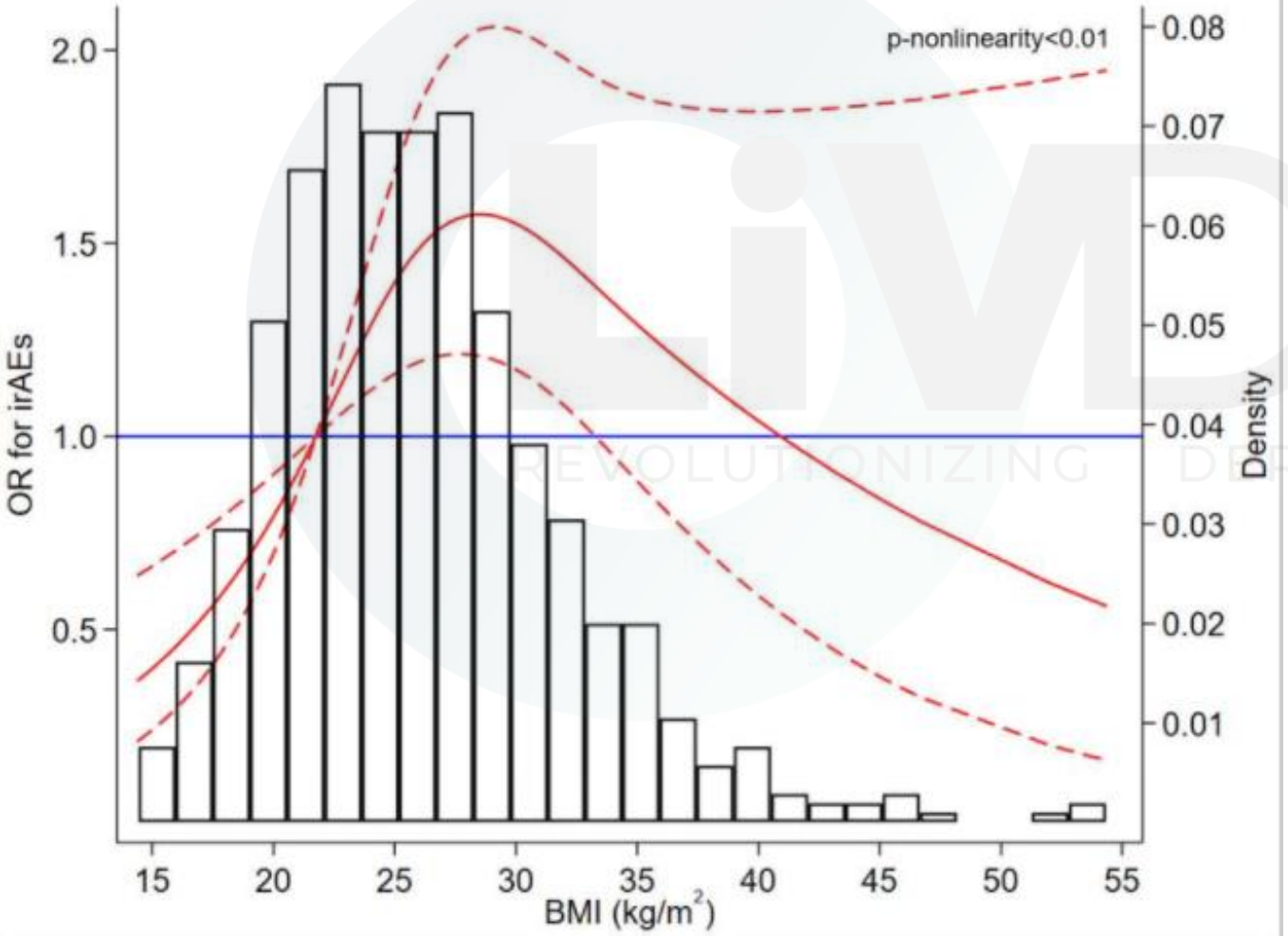


- Most common irAEs are dermatological and gastrointestinal
- Other possible irAEs
  - Hematologic (hemolytic anemia, thrombocytopenia)
  - Cardiovascular (myocarditis, pericarditis, vasculitis)
  - Ocular (blepharitis, conjunctivitis, iritis, scleritis, uveitis)
- Most common AEs
  - Fatigue, nausea, diarrhea, pruritus
  - Vary by trial and medication

irAE = immune-related adverse event; ALT = alanine aminotransferase; AST = aspartate aminotransferase.

Teply BA, Lipson EJ. *Oncology (Williston Park).* 2014;28(suppl 3):30-38. Hodi FS, et al. *N Engl J Med.* 2010;363:711-723. Topalian SL, et al. *N Engl J Med.* 2012;366:2443-2454. Mellati M, et al. *Diabetes Care.* 2015;38:e137-e138. Forde PM, et al. *Anticancer Res.* 2012;32:4607-4608. Hottinger AF. *Curr Opin Neurol.* 2016;29:806-812. Brahmer JR, et al. *J Clin Oncol.* 2018;36:1714-1768.

Association between BMI and irAE's?



- Recent study suggests potential correlation between BMI and increased irAE's with *Pembrolizumab*
  - Multiple ICI's examined, though only Pembrolizumab applicable to skin cancer
- Non-linear association between pre-treatment BMI and irAE's
- No statistical significance in patients ≥ 65 y.o. and/or BMI ≥34
- Stronger association of BMI in younger, healthier patients (no multimorbidity)

Zhang, D., Shah, N. J., Cook, M., Blackburn, M., Serzan, M. T., Advani, S., Potosky, A. L., Atkins, M. B., & Braithwaite, D. (2021). Association between Body Mass Index and Immune-Related Adverse Events (irAEs) among Advanced-Stage Cancer Patients Receiving Immune Checkpoint Inhibitors: A Pan-Cancer Analysis. *Cancers*, *13*(23), 6109. https://doi.org/10.3390/cancers13236109

PRINCIPLES OF ROUTINE MONITORING FOR IMMUNE-CHECKPOINT INHIBITORS

Pre-Therapy Assessment[a]	Monitoring Frequency[b]	Evaluation for Abnormal Findings/Symptoms
Clinical • Physical examination • Patient and relevant family history of any autoimmune/organ-specific disease, endocrinopathy, or infectious disease. • Neurologic examination • Bowel habits (typical frequency/ consistency) • Infectious disease screening (HIV; hepatitis A, B, C) as indicated	Clinical examination at each visit with adverse event (AE) symptom assessment	Follow-up testing based on findings, symptoms
Imaging • Cross-sectional imaging • Brain MRI if indicated	Periodic imaging as indicated	Follow-up testing as indicated based on imaging findings
General bloodwork • Complete blood count (CBC) (with differential if indicated) • Comprehensive metabolic panel (CMP)	Repeat prior to each treatment or every 4 weeks during immunotherapy, then in 6–12 weeks or as indicated	HbA1c for elevated glucose
Dermatologic (ICI_DERM-1) • Examination of skin and mucosa if history of immune-related skin disorder	Conduct/repeat as needed based on symptoms	Consider dermatology referral. Monitor affected skin and lesion type; photographic documentation. Skin biopsy if indicated.
Pancreatic (ICI_ENDO-1) • Baseline testing is not required	No routine monitoring needed if asymptomatic	Amylase, lipase, and consider abdominal CT with contrast or MRCP for suspected pancreatitis.
Thyroid (ICI_ENDO-2) • Thyroid-stimulating hormone (TSH), free thyroxine (T4)	Every 4–6 weeks during immunotherapy, then follow-up every 12 weeks as indicated	See ICI_ENDO-2 and ICI_ENDO-3
Pituitary/Adrenal (ICI_ENDO-4) • Consider serum cortisol (morning preferred) and thyroid function as above	Consider repeating every 4–6 weeks during immunotherapy (IO only regimens[c]), then follow-up every12 weeks as indicated	Luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (males), estradiol (females), adrenocorticotropic hormone (ACTH), and serum cortisol. Cosyntropin stimulation test as indicated.
Pulmonary (ICI_PULM-1) • Oxygen saturation (resting and with ambulation) • Consider pulmonary function tests (PFTs) with diffusion capacity for high-risk patients (eg, interstitial lung disease on imaging, COPD, previous suspected treatment-related lung toxicity)	Repeat oxygen saturation tests based on symptoms	Chest CT with contrast to evaluate for pneumonitis, biopsy, or bronchoscopy with bronchoalveolar lavage (BAL) if needed to exclude other causes.
Cardiovascular (ICI_CARDIO-1) • Consider baseline electrocardiogram (ECG) • Individualized assessment in consultation with cardiology as indicated	Consider periodic testing for those with abnormal baseline or symptoms	Individualized follow-up in consultation with cardiology as indicated
Musculoskeletal (ICI_MS-1) • Joint examination/functional assessment as needed for patients with pre-existing disease	No routine monitoring needed if asymptomatic	Consider rheumatology referral. Depending on clinical situation, consider C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), or creatine kinase (CK)

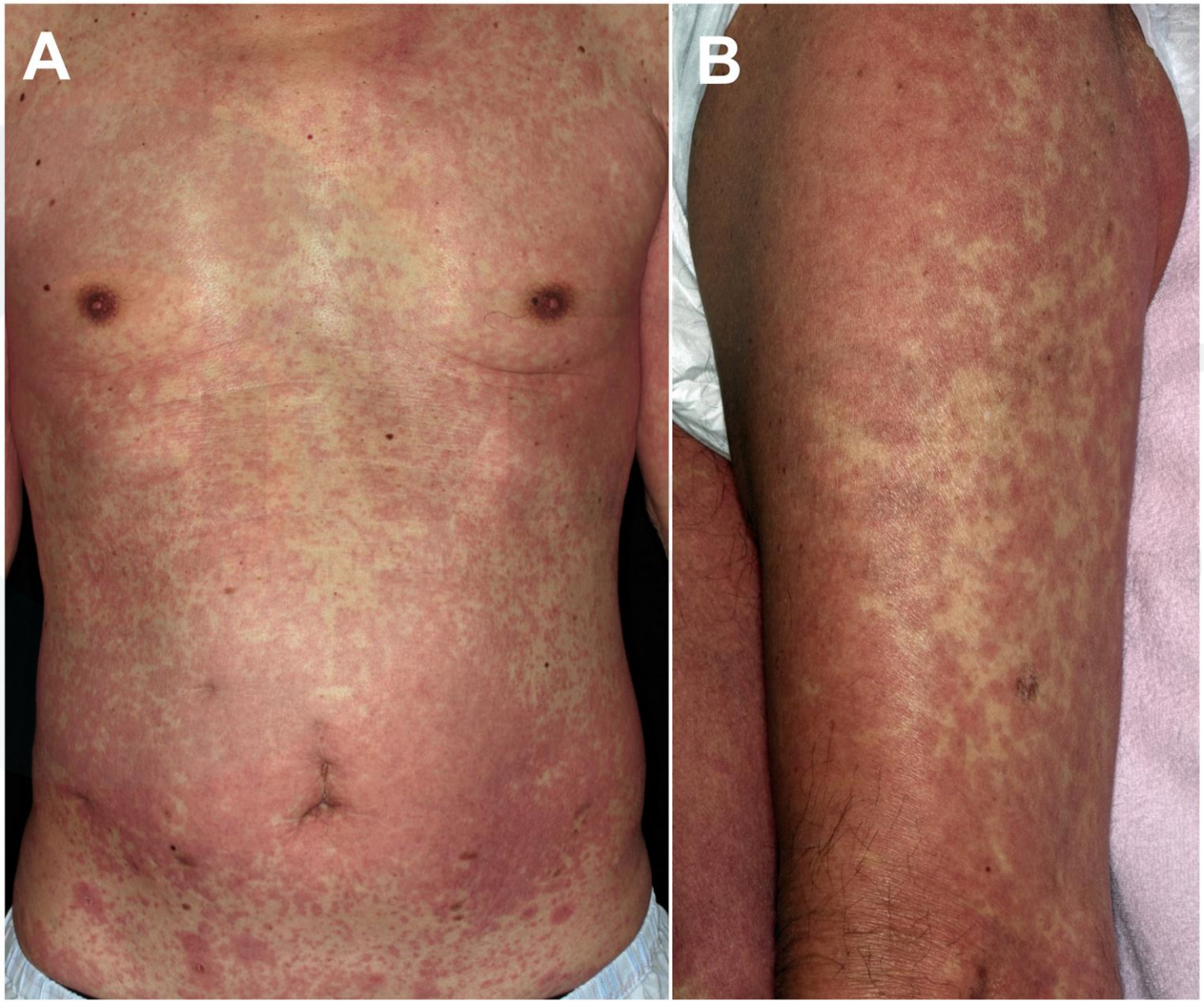
Routine Monitoring of Immune Checkpoint Inhibitors

Highlights

- Clinical exam at each visit for AE
- Bloodwork:
  - CBC (+/- with diff) + CMP prior to each treatment or every 4 weeks during treatment, then 6-12 weeks after discontinuation of treatment
  - TSH + free T4 every 4-6 weeks during tx, f/u every 12 weeks after discontinuation
  - Consider serum cortisol (morning) every 4-6 weeks during tx, f/u every 12 weeks after discontinuation
- Consider baseline PFT's for high risk patients (lung dz, previous treatment related lung toxicity)
  - Follow up testing based on AE's and/or abnormal baseline testing
- Baseline cardiology assessment + consider baseline ECG
  - Follow up testing based on AE's and/or abnormal baseline testing

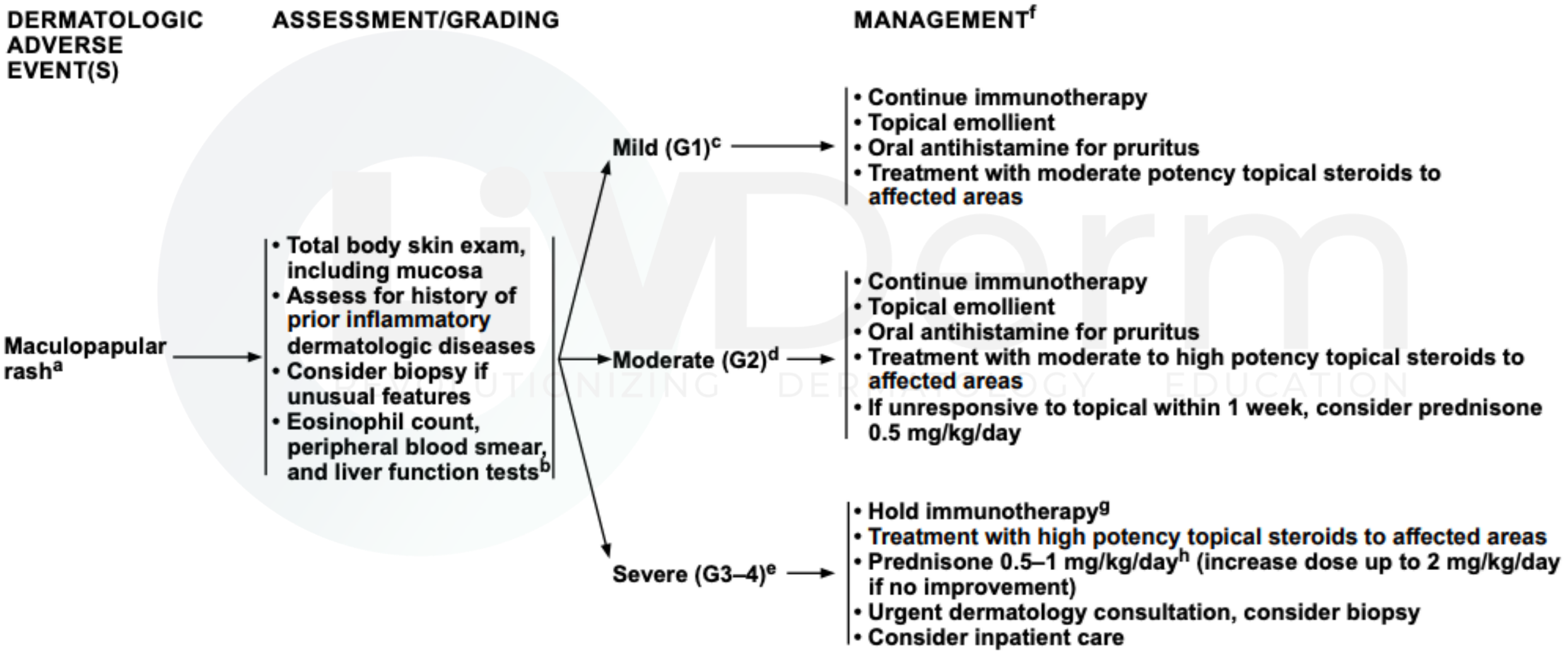
Management of Adverse Events: RASH

Maculopapular rash

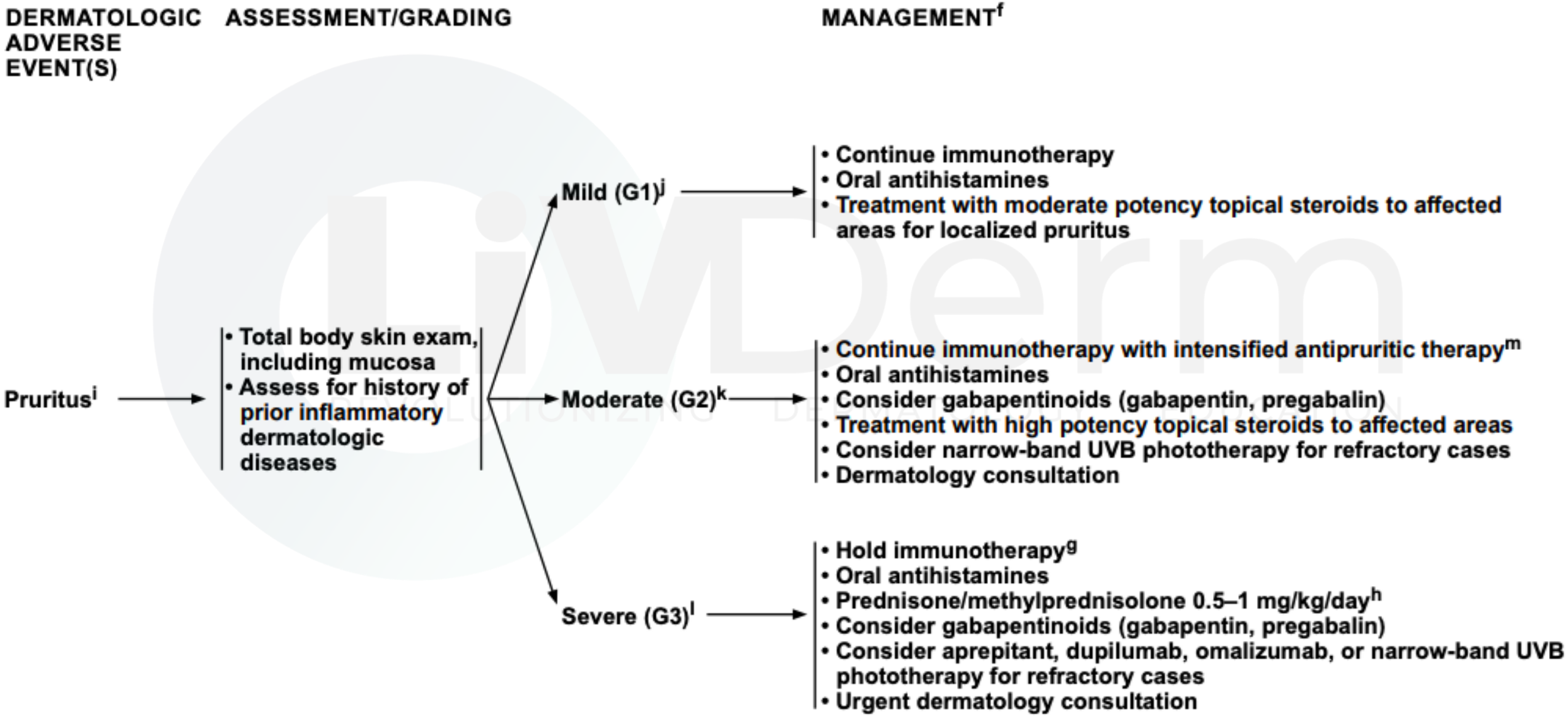


Okiyama N, Tanaka R. Immune-related adverse events in various organs caused by immune checkpoint inhibitors. Allergol Int. 2022 Jan 28:S1323-8930(22)00002-8. doi: 10.1016/j.alit.2022.01.001. Epub ahead of print. PMID: 35101349.

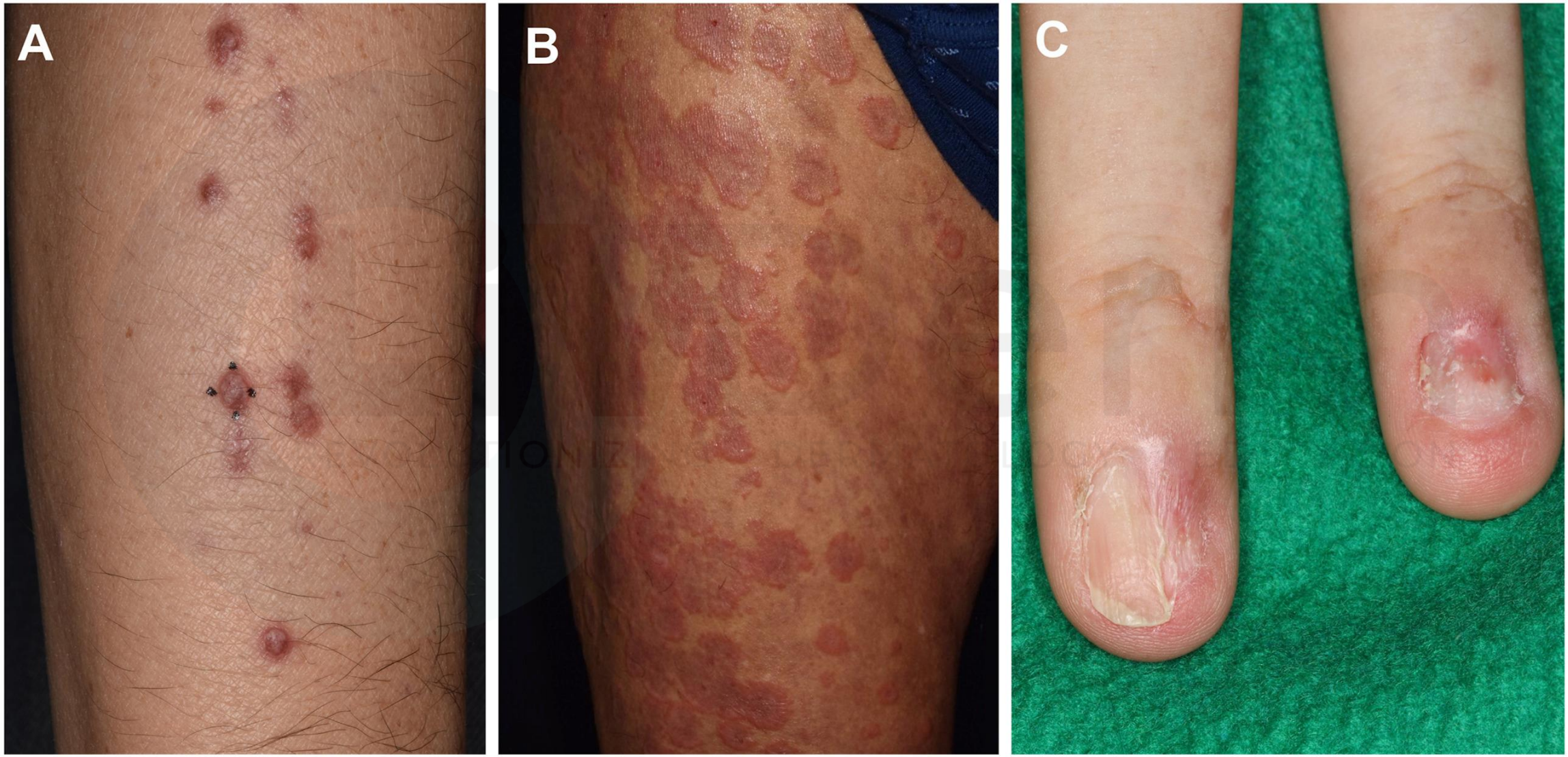
Management of Adverse Events: RASH



Management of Adverse Events: PRURITUS

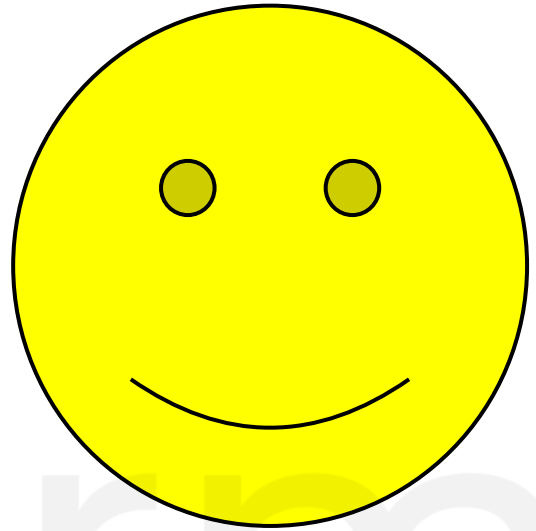


cirAE's – Lichen Planus

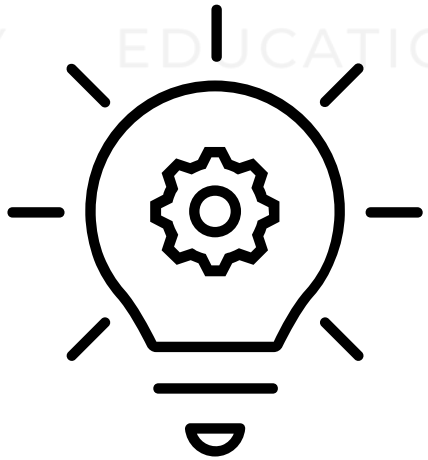


Okiyama N, Tanaka R. Immune-related adverse events in various organs caused by immune checkpoint inhibitors. Allergol Int. 2022 Jan 28:S1323-8930(22)00002-8. doi: 10.1016/j.alit.2022.01.001. Epub ahead of print. PMID: 35101349.

Educate your staff!

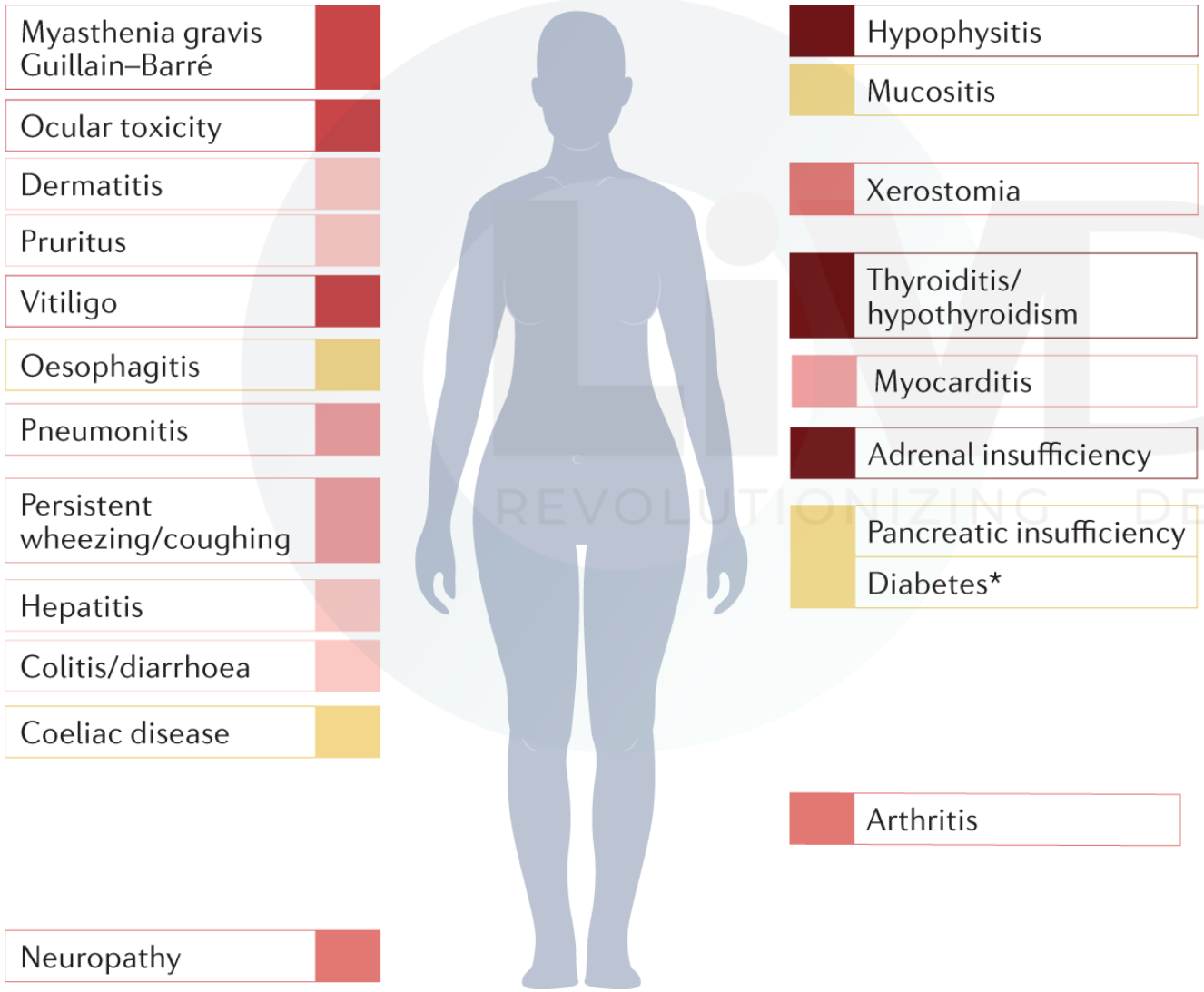


Even if patients are being seen by an oncologist/other physician, they may call your office for rashes, etc. that may actually be serious AE's related to treatment!!



CONDITIONS	SIGNS AND SYMPTOMS (MAY INCLUDE 1 or MORE)
CARDIO: Myocarditis	Chest pain, shortness of breath, fatigue, irregular heart beat (arrhythmia), syncope
DERM: Bullous dermatitis	Inflammation of the skin and the presence of bullae, which are filled with fluid. The most common immune-related bullous dermatitis is bullous pemphigoid. May be intense or widespread; intermittent; skin changes from scratching (eg, edema, papulation, excoriations, lichenification, oozing/crusts); limiting instrumental activities of daily living (iADLs).
DERM: Maculopapular rash (morbilliform rash)	Macules (flat) and papules (elevated)
DERM: Pruritis	Itching sensation, with or without rash
DERM: Stevens-Johnson syndrome (SJS) and toxic epidermal necrosis (TEN)	SJS, overlapping SJS/TEN, and TEN are characterized by separation of the dermis involving <10%, 10%–30%, and >30% BSA, respectively
ENDO: Hyperglycemia-related diabetic ketoacidosis (DKA)	Excessive thirst, frequent urination, general weakness, vomiting, confusion, abdominal pain, dry skin, dry mouth, increased heart rate, and fruity odor on the breath
ENDO: Asymptomatic/ subclinical hypothyroidism	Elevated TSH with normal free T4. Usually asymptomatic, may consider with increased fatigue
ENDO: Clinical (overt) primary hypothyroidism	Fatigue, lethargy, sensation of being cold, possible constipation
ENDO: Thyrotoxicosis due to thyroiditis	Most patients with thyrotoxicosis due to thyroiditis have minimal, if any symptoms. If symptoms do arise, may include uncommonly, tachycardia, tremor, anxiety, enlarged and tender thyroid gland (rarely).
ENDO: Hypophysitis	Acute onset headache, photophobia, nausea/emesis, fatigue, muscle weakness, may have low blood pressure
ENDO: Primary adrenal insufficiency	High ACTH with low morning cortisol, abnormal cosyntropin stimulation test. This is a rare diagnosis not usually associated with checkpoint immunotherapy.
GI: Colitis	Watery diarrhea, cramping, urgency, abdominal pain, blood and mucus in the stool, fever, nocturnal bowel movements. Blood in the stool and/or fever should prompt a more thorough workup for infection and for other causes of GI bleeding, including peptic ulcer disease (PUD) and malignant bleeding.
GI: Transaminitis	Elevated alanine transaminase (ALT) and aspartate transaminase (AST)
GI: Pancreatitis	Acute pancreatitis: epigastric pain, nausea, possible vomiting Chronic pancreatitis: chronic abdominal pain, deficiency in pancreatic enzyme production with possible malabsorption

Chronic Immune Related AE's



- >12 weeks after discontinuation of treatment
  - Much more common than previously thought – up to 43%
- Most commonly endocrinopathies

Johnson, D.B., Nebhan, C.A., Moslehi, J.J. *et al.* Immune-checkpoint inhibitors: long-term implications of toxicity. *Nat Rev Clin Oncol* **19,** 254–267 (2022). https://doi.org/10.1038/s41571-022-00600-w

Cutaneous immune-related effects predicts efficacy?

- Cutaneous immune-related adverse events (cirAEs) most common – 20-40%
  - Pruritus, drug eruption, xerosis, nonspecific rash, eczematous dermatitis, bullous pemphigoid, Grover's Disease
- 7008 patients with one of 4 cancers: lung, digestive organs, melanoma, urinary tract (+ 7008 controlled/matched patients)
- Results suggest cirAE's are strongly associated with ICI response and patient survival

Tang K, Seo J, Tiu BC, et al. Association of Cutaneous Immune-Related Adverse Events With Increased Survival in Patients Treated With Anti–Programmed Cell Death 1 and Anti–Programmed Cell Death Ligand 1 Therapy. *JAMA Dermatol.* 2022;158(2):189–193. doi:10.1001/jamadermatol.2021.5476

Table 2. Association Between Cutaneous Eruptions and Survival Among Patients Treated With Anti–PD-1 or Anti–PD-L1 Therapy

Cutaneous diagnosis[a]	No.	Hazard ratio	*P* value[b]
Hyperhidrosis	281	1.381	.08
Mucositis	563	1.161	.21
Dermatomyositis	105	0.93	.79
Maculopapular eruption	230	0.845	.36
Erythroderma	247	0.769	.17
Drug eruption and nonspecific drug reaction	1075	0.755	.001
Hyperkeratosis	39	0.707	.49
Rash and other nonspecific eruption	3163	0.704	<.001
Psoriasis	299	0.703	.05
Pruritus	1694	0.695	<.001
Xerostomia	163	0.671	.13
Xerosis	441	0.626	.001
Eczema and atopic dermatitis	72	0.612	.15
Vitiligo	100	0.534	.09
Bullous pemphigoid	32	0.524	.33
Lichen planus	97	0.511	.03
Grover disease	18	0.468	.28
Any cutaneous diagnosis	7008	0.778	<.001

Abbreviations: PD-1, programmed cell death 1; PD-L1, programmed cell death ligand 1.

[a] Cutaneous diagnoses were identified based on published literature and expert opinion; each row represents a separate Cox proportional hazards model adjusted for demographic characteristics, cancer type, and cancer stage.

[b] Benjamini-Hochberg *P* value of significance = .001.

Tang K, Seo J, Tiu BC, et al. Association of Cutaneous Immune-Related Adverse Events With Increased Survival in Patients Treated With Anti–Programmed Cell Death 1 and Anti–Programmed Cell Death Ligand 1 Therapy. *JAMA Dermatol.* 2022;158(2):189–193. doi:10.1001/jamadermatol.2021.5476

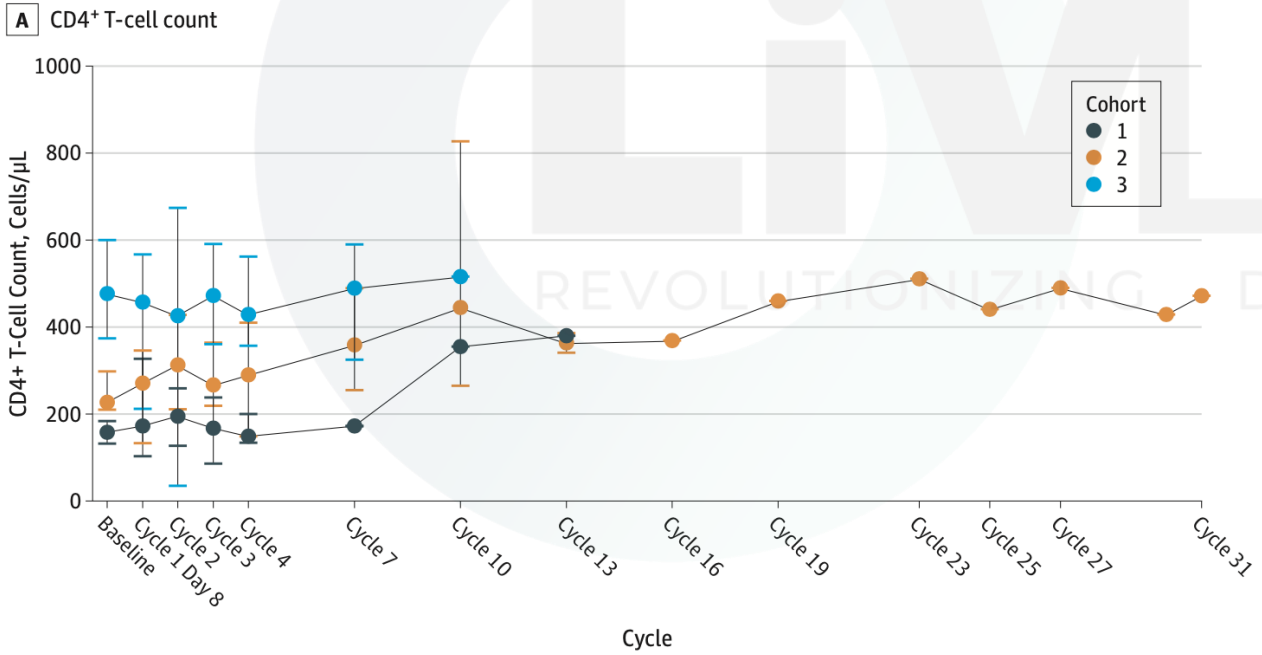
Special Populations

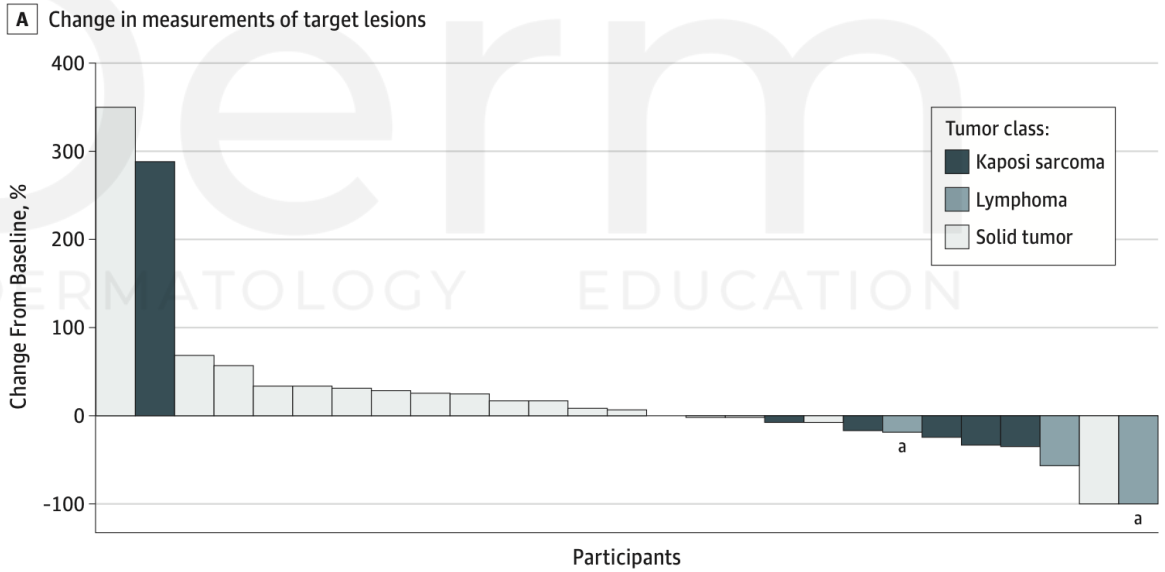
- HIV+ on Antiretroviral Treatment
- Solid Organ Transplant
- PD-L1 Tumor Status
- Treatment Beyond Progression
- First Line (1L) vs. 2nd Line (2L)

JAMA Oncology | Original Investigation

Assessment of the Safety of Pembrolizumab in Patients With HIV and Advanced Cancer—A Phase 1 Study

Thomas S. Uldrick, MD, MS; Priscila H. Gonçalves, MD; Maher Abdul-Hay, MD; Alisa J. Claeys, MSW; Brinda Emu, MD; Marc S. Ernstoff, MD; Steven P. Fling, PhD; Lawrence Fong, MD; Judith C. Kaiser, MBA, BSN, RN; Andreanne M. Lacroix, BSc; Steve Y. Lee, MD; Lisa M. Lundgren, MS, RPh; Kathryn Lurain, MD, MPH; Christopher H. Parsons, MD, PhD; Sharavi Peeramsetti, MSc; Ramya Ramaswami, MBBS; Elad Sharon, MD, MPH; Mario Sznol, MD; Chia-Ching (Jackie) Wang, MD; Robert Yarchoan, MD; Martin A. Cheever, MD; for the Cancer Immunotherapy Trials Network (CITN)-12 Study Team





JAMA Oncol. 2019;5(9):1332-1339. doi:10.1001/jamaoncol.2019.2244 Published online June 2, 2019.

Immune checkpoint inhibitor therapy in solid organ transplant recipients: A patient-centered systematic review

Juliya Fisher, MD,[a] Nathalie Zeitouni, MDCM, FRCPC,[b] Weijia Fan, MS,[c] and Faramarz H. Samie, MD, PhD[a]
New York, New York; and Phoenix, Arizona

Table V. Overall response rates and rates of progression and death

Immunotherapy	Total no. cases	Overall response, n (%)	Progression or death secondary to disease, n (%)	Death secondary to rejection, n (%)
Ipilimumab	12	3 (25)	9 (75)	0 (0)
Nivolumab	23*	7 (30)	10 (43)	5 (22)
Pembrolizumab	15	6 (40)	6 (40)	3 (20)
Ipilimumab followed by nivolumab	3	1 (33)	2 (67)	0 (0)
Ipilimumab followed by pembrolizumab	3*	1 (50)	1 (50)	0 (0)
Pembrolizumab followed by ipilimumab	1	0 (0)	1 (100)	0 (0)

*The clinical outcome of 1 patient was not reported in the original case report.

Table III. Rate of rejection by organ type

Transplant type	Rejection, n (%)	Death secondary to rejection, n (%)
Kidney, n = 32	13 (41)	2 (6)
Liver, n = 20	7 (35)	6 (30)
Cardiac, n = 5	1 (20)	0 (0)

Evidence-Based Consensus Recommendations for the Evolving Treatment of Patients with High-Risk and Advanced Cutaneous Squamous Cell Carcinoma

Guilherme Rabinowits,[1,*] Michael R. Migden,[2,3] Todd E. Schlesinger,[4] Robert L. Ferris,[5,6,7,8] Morganna Freeman,[9] Valerie Guild,[10] Shlomo Koyfman,[11] Anna C. Pavlick,[12] Neil Swanson,[13] Gregory T. Wolf,[14] and Scott M. Dinehart[15]

1. Determine if advanced SCC (laSCC or mSCC)

2. Determine if eligible for surgery

- **MULTIDISCIPLINARY APPROACH!!**
- Surgeons experienced in the field should consult with team/other physicians
- Weigh benefits of surgery with potential risks
  - I.e. likelihood of clearance vs considerable functional and/or cosmetic deficits

3. Weigh benefits/risks of radiation therapy vs systemic therapy

- Radiation may be considered with uncertain recurrent tumors, uncertain surgical margins (multifocal or large-caliber nerve invasion or lymphovascular invasion), used as adjuvant therapy with microscopically residual disease that cannot be resected

Rabinowits, G., Migden, M. R., Schlesinger, T. E., Ferris, R. L., Freeman, M., Guild, V., Koyfman, S., Pavlick, A. C., Swanson, N., Wolf, G. T., & Dinehart, S. M. (2021). Evidence-Based Consensus Recommendations for the Evolving Treatment of Patients with High-Risk and Advanced Cutaneous Squamous Cell Carcinoma. *JID innovations : skin science from molecules to population health*, *1*(4), 100045. https://doi.org/10.1016/j.xjidi.2021.100045

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4. Cemiplimab should be considered first line therapy in those with laSCC or mSCC

- Highly encouraged to enroll patients in clinical trials for immunotherapy as neoadjuvant!

5. Chemotherapy/targeted therapy can be considered next in patients who are not candidates for or were unsuccessful with immunotherapy

- Lower response rates, higher/more serious adverse events

6. Follow up with treating physician for at least 2 years following tx

- 3-6 months for surgical/radiation therapy
- 3-4 months for systemic therapy

Rabinowits, G., Migden, M. R., Schlesinger, T. E., Ferris, R. L., Freeman, M., Guild, V., Koyfman, S., Pavlick, A. C., Swanson, N., Wolf, G. T., & Dinehart, S. M. (2021). Evidence-Based Consensus Recommendations for the Evolving Treatment of Patients with High-Risk and Advanced Cutaneous Squamous Cell Carcinoma. *JID innovations : skin science from molecules to population health*, *1*(4), 100045. https://doi.org/10.1016/j.xjidi.2021.100045

IS/IC Patients in CASE Real World Evidence Study

- As of March 2021, 138 patients receiving cemiplimab in a real-world setting were enrolled in the CASE study
- 30 patients were IS/IC based on clinical-reported co-morbidities and/or medication use
- IS/IC patients were identified as having one or more of the following diagnoses in medical history:
  - Allogenic bone marrow transplant or solid organ transplant
  - HIV
  - Inflammatory bowel disease
  - Leukemia
  - Lupus
  - Lymphoma
  - Multiple myeloma
  - Multiple sclerosis
  - Psoriasis
  - Psoriatic arthritis
  - Rheumatoid arthritis
  - Myeloproliferative disorder
  - Polycythemia vera
  - COPD with prednisone

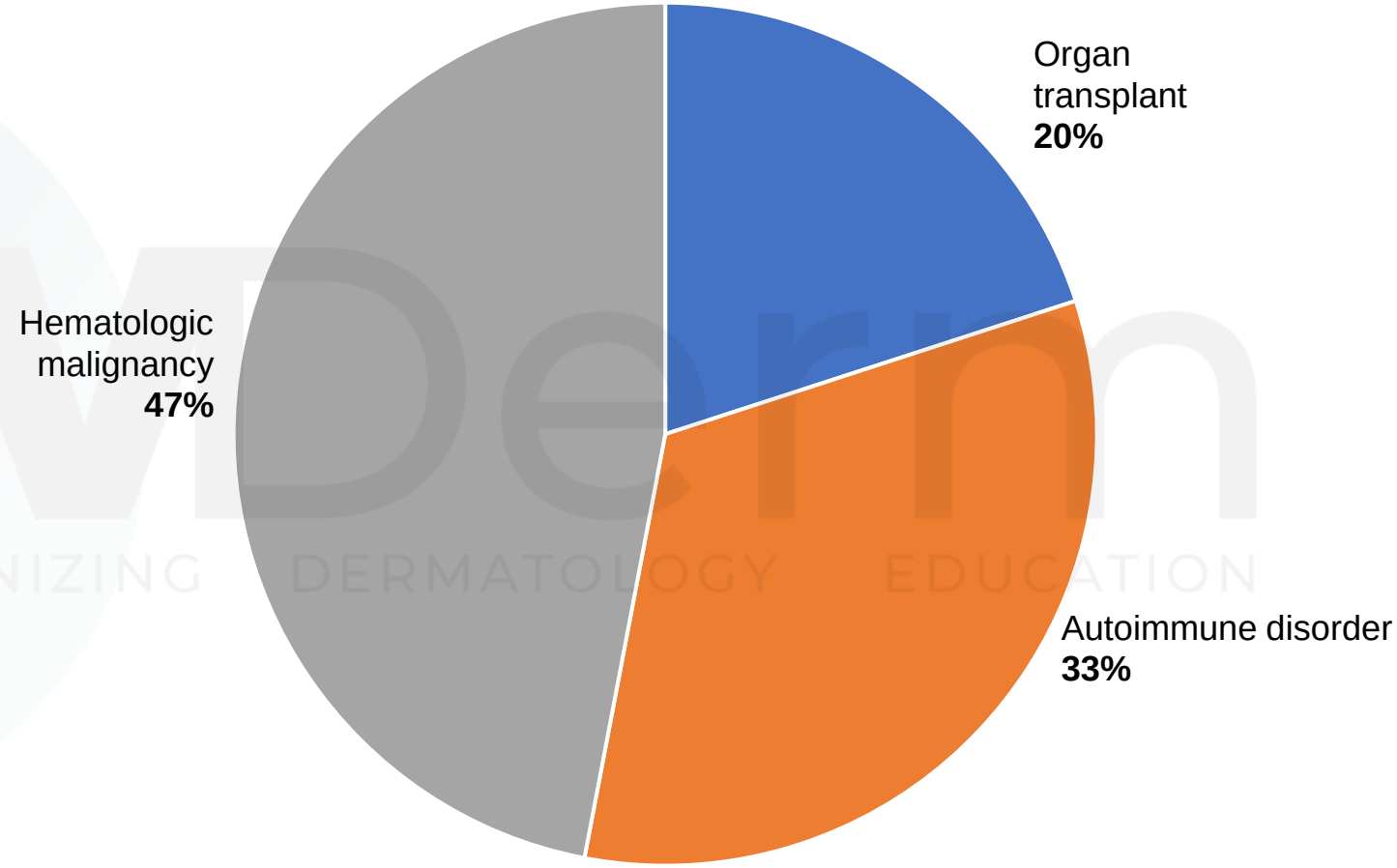
CASE, CemplimAb Survivorship Epidemiology; COPD=chronic obstructive pulmonary disease; CSCC, cutaneous squamous cell carcinoma; HIV, human immunodeficiency virus; IS/IC, immunosuppressed and/or immunocompromised.

Rabinowits G, et al. American Society of Clinical Oncology (ASCO) 2021 Virtual Scientific Meeting, June 4–8, 2021 (abstract 9547).

Overview of Patient IS/IC Status in CASE

Patients were IS/IC due to a history of:

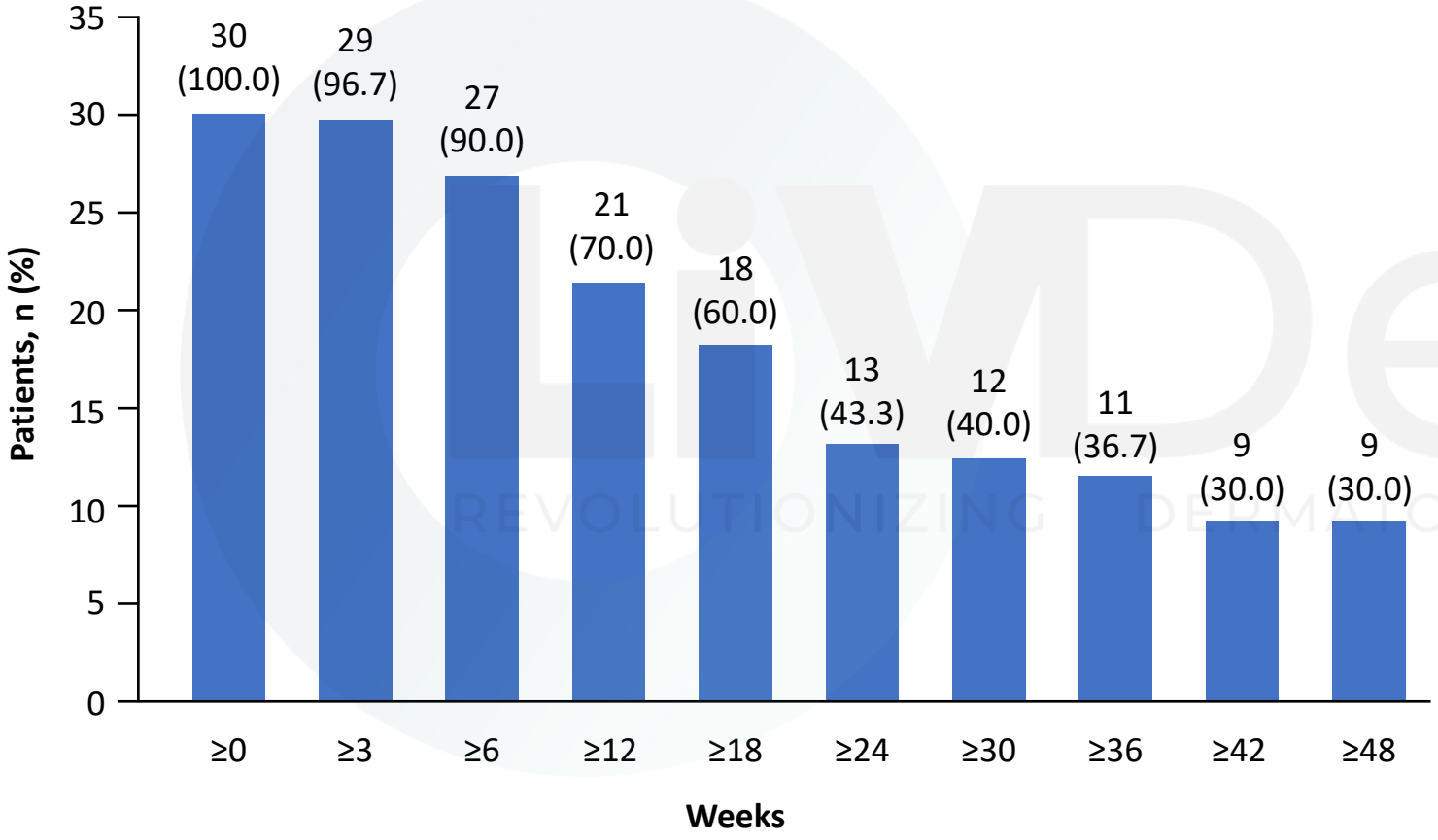
- Solid organ transplant (n=6)
- Hematologic malignancy (n=14)
- Autoimmune disorder (n=10)



CASE, CemplimAb Survivorship Epidemiology; IS/IC, immunosuppressed and/or immunocompromised.

Rabinowits G, et al. American Society of Clinical Oncology (ASCO) 2021 Virtual Scientific Meeting, June 4–8, 2021 (abstract 9547).

IS/IC Patients in CASE: Treatment Duration and Cycles



Cycles	IS/IC patients (N=30)
Mean (SD)	8.2 (6.5)
Median	6.5
Q1:Q3	4.0:10.0
Min:Max	1:25

- Nine patients had a duration of exposure ≥48 weeks
- Median duration of cemiplimab exposure was 21.6 weeks (IQR: 9.9–48.1, range: 0–83)

CASE, CemplimAb Survivorship Epidemiology; IQR, interquartile range; IS/IC, immunosuppressed and/or immunocompromised; Q, quarter; SD, standard deviation.

Rabinowits G, et al. American Society of Clinical Oncology (ASCO) 2021 Virtual Scientific Meeting, June 4–8, 2021 (abstract 9547).

IS/IC Patients in CASE: Discontinuation of Cemiplimab

n (%)	IS/IC patients (N=30)
Treatment ongoing	22 (73.3%)
Treatment discontinued	8 (26.7%)
Primary reason for treatment discontinuation, n/N1 (%)	
Adverse event	1/8 (12.5%)
Patient decision	2/8 (25.0%)
Physician decision	2/8 (25.0%)
Progressive disease	2/8 (25.0%)
Other	1/8 (12.5%)
Primary reason for follow-up discontinuation, n/N2 (%)	
Death	4/5 (80.0%)
Withdrawal by subject	1/5 (20.0%)

- Eight patients discontinued treatment due to any reason (including death or withdrawal from the study)
- One patient discontinued treatment due to an adverse event (elevated liver function tests)
- Four deaths were reported; none were deemed related or attributable to cemiplimab by the investigator (one death was due to sepsis, one due to hypoxia, one due to pneumonia, and one due to an unknown cause)

CASE, CemplimAb Survivorship Epidemiology; IS/IC, immunosuppressed and/or immunocompromised; N1, total number of patients who discontinued treatment; N2, total number of patients who discontinued follow-up

Rabinowits G, et al. American Society of Clinical Oncology (ASCO) 2021 Virtual Scientific Meeting, June 4–8, 2021 (abstract 9547).

Immunotherapy Advantages

- Infusion every 3 weeks
- Works for BCC and SCC
- Most patients have minimal adverse events
- Can be combined with other treatments (XRT)
- Works better clinically than advertised

Immunotherapy Disadvantages

- 1-2% have severe reactions that can precipitate hospitalization or death
- Works slower for BCC than HHI
- Sometimes difficult to get to durable remission
- Infusion given by oncologist

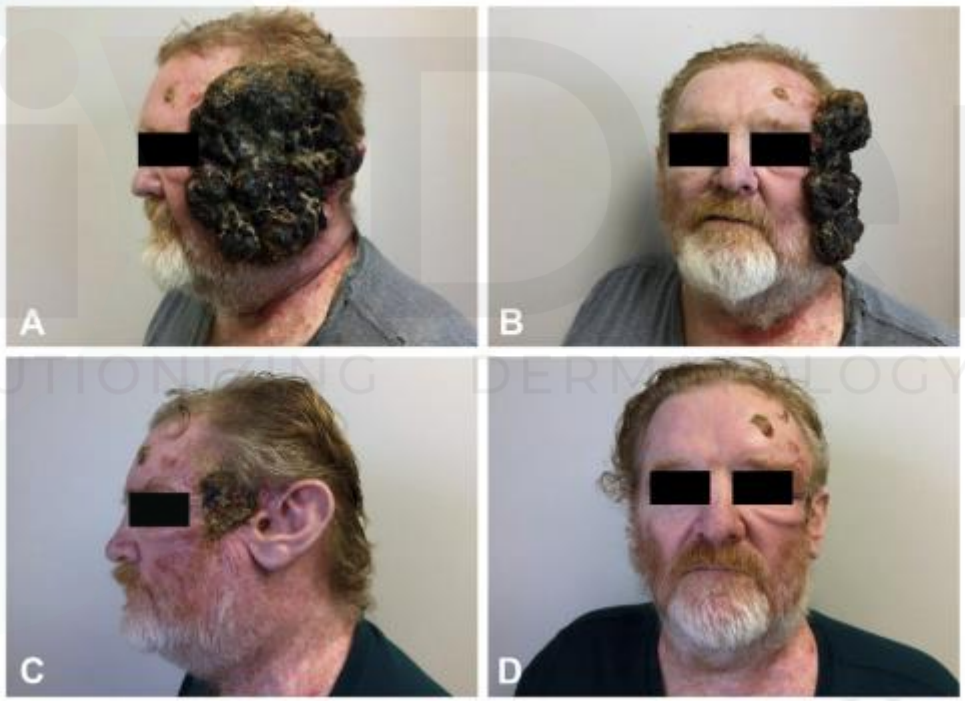
CASE REPORT

Rapid response to cemiplimab for advanced cutaneous squamous cell carcinoma

Hanieh Zargham, MD,[a] and John Strasswimmer, MD, PhD[b]
Vancouver, British Columbia, Canada and Delray Beach, Florida

Initial presentation

6 month progression



After 1 treatment

After 4 treatments

CONCLUSIONS

Emerging treatments for NMSC have advanced the paradigm for treatment from local to systemic

Inhibiting immune tolerance can result in tumor infiltration and shrinkage

Adverse effects of Immune Checkpoint Inhibitors are multisystemic and warrant close attention

Multidisciplinary team should be involved in major decisions involving treatment of advanced skin cancer

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