LiVDerm
REVOLUTIONIZING DERMATOLOGY EDUCATION

PD-1 Inhibitors (and more) for Advanced BCC and SCC

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INDUSTRY DISCLOSURE

Company/Sponsor	Type
AbbVie	Consulting (Honoraria)/Grant/Research Funding/Speaker Bureau
Aclaris	Grant/Research Funding
Allergan	Consulting (Honoraria)/Advisory Board/Grant/Research Funding
Almirall	Speaker's Bureau/Advisory Board (Honoraria)/Consulting
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AOBiome	Grant/Reasearch Funding
Arcutis Premier Research	Grant/Research Funding
ASLAN	Grant/Research Funding
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Biofrontera AG	Advisory Board (Honoraria)
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Brickell Biotech	Grant/Research Funding
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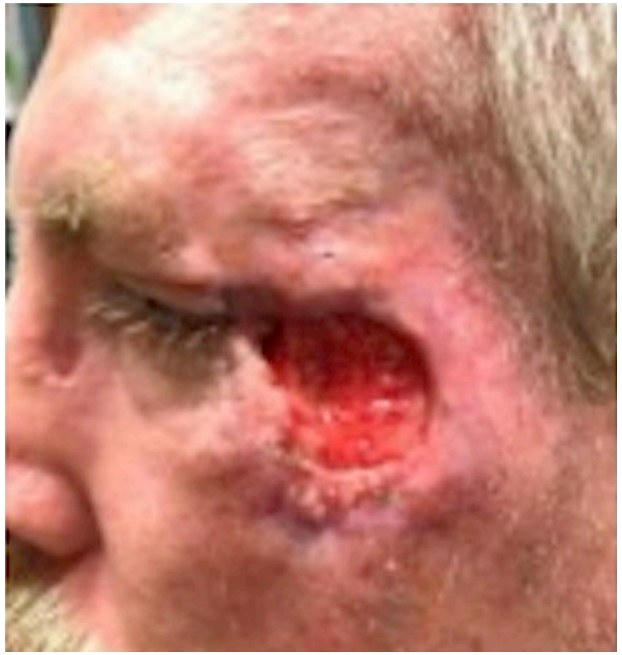
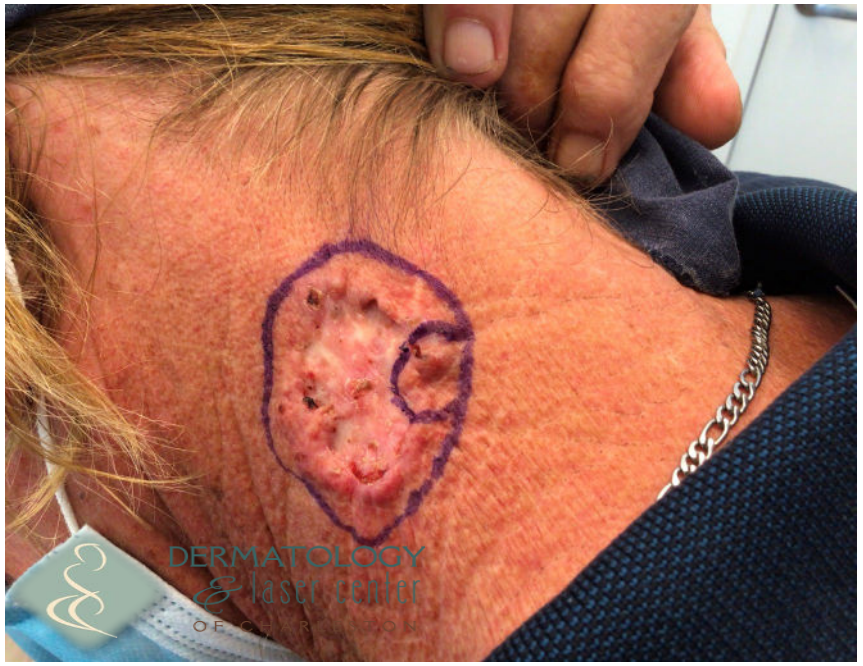
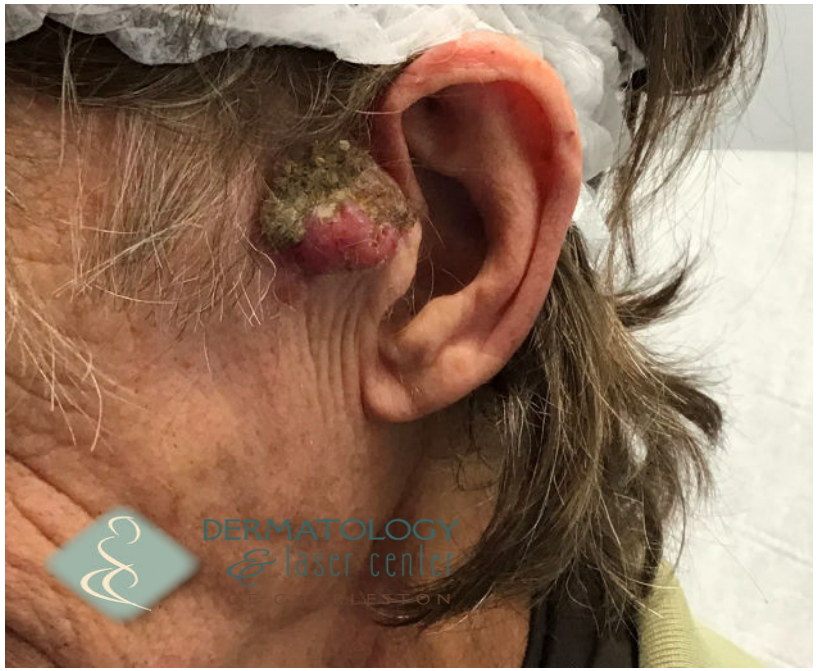
Cara Therapeutics	Grant/Research Funding
Castle BioScience	Grant/Research Funding/Consulting (Honoraria)
Celgene	Grant/Research Funding/Advisory Board
Centocor Ortho Biotech (Now Janssen Biotech)	Grant/Research Funding
ChemoCentryx	Grant/Research Funding
CMS Aesthetics DCME	Consulting
Coherus Biosciences	Grant/Research Funding
Concert Pharmaceutical	Grant/Research Funding
Corrona	Grant/Research Funding
Cutanea Life Sciences	Grant/Research Funding
Dermavant	Grant/Research Funding
Dermira	Grant/Research Funding
DT Pharmacy & DT Collagen (Melasma)	Grant/Research Funding
DUSA/ Sun Pharma	Speaker Bureau
EPI Health	Grant/Research Funding/Consulting (Honoraria)/Speaker's Bureau
Foundation for Research and Education in Dermatology (Fred)	Consulting (Honoraria)
Galderma (Nestle)	Grant/Research Funding/Consulting (Honoraria)
Genetech	Consulting
Greenway Therapeutix	Advisory Board (No Compensation received)
Janssen Pharmaceuticals, Inc	Grant/Research Funding
Kiniksa	Grant/Research Funding
Kintor	Consulting
Leo	Grant/Research Funding/Speaker's Bureau
Lilly	Grant/Research Funding/Consulting (Fees)/Stockholder/Speaker Bureau
MED Learning Group	CME Program (Aug-Oct 2019)
Merz	Grant/Research Funding/Consulting (Honoraria)
MJH Associates	OncLive SCC Insights Filming/Stacy Jaffe
Nestle Skin Health	Grant/Research Funding
Nextphase	Consulting
Nimbus	Grant/Research Funding
Novartis	Grant/Research Funding/Consulting (Honoraria)
Ortho Dermatologics	Consulting, Fees
Pfizer	Grant/Research Funding
Pharmatecture	Consulting
Pierre Fabre	Consulting, Fees
Plasmed	Consulting, Fees
Processa	Grant/Research Funding
Prolacta Bioscience	Consulting
Pulse BioSciences	Grant/Research Funding/Consulting
Regeneron	Grant/Research Funding/Consulting (Fees)/Speaker's Bureau (Honoraria)
Remedly, Inc	Advisory Board (Stock Options)
Sanofi Genzyme	Grant/Research Funding/Speaker's Bureau
Sisaf	Grant/Research Funding
Skinceuticals/L'Oreal	Consulting, Fees
Sun Pharma	Consulting/Speaker's Bureau (Honoraria)
Trevi	Grant/Research Funding
UCB	Consulting
Verrica	Grant/Research Funding/Consulting

HIGH RISK TUMORS







Atlas, Kanos, Symanowski et al. Abstract 10065 ASCO 2020

Major Classes of Approved Treatments for Advanced NMSC

Hedgehog Pathway Inhibitors (FDA Approval Date)

- Vismodegib (30JAN2012) – mBCC or laBCC
  - Dosed 150mg PO daily
- Sonidegib (24JUL2015) – laBCC (mBCC outside USA)
  - Dosed 200mg PO daily (1 hr before or 2 hr after a meal)

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 and expanded to laSCC (06JUL2021)
  - Dosed IV 200mg every 3 weeks

PubMed ▼ Peter Lee and vismodegib

Format: Abstract

Full text links

FULL TEXT JAMA Dermatology

JAMA Dermatol. 2017

JAMA Dermatol 2017:321-322

A Novel Alternate Dosing of Vismodegib for Treatment of Patients With Advanced Basal Cell Carcinomas.

Becker LR[1], Aakhus AE[1], Reich HC[1], Lee PK[1].

"This study evaluates a novel alternate dosing regimen of vismodegib that has led to decreased toxicity and eliminates the need for a loading dose"

SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
	11	12	13	14	15	16
17	18	19	20	21	22	23
24 / 31	25	26	27	28	29	30

A hedgehog inhibitor dosed at 10 days per month is "*optimal maintenance*" for basal cell nevus syndrome (BCNS) patients

- Effects of Sonidegib Following Dose Reduction and Treatment Interruption in Patients with Advanced Basal Cell Carcinoma During 42-Month BOLT Trial.

- Dose interruptions similar between 200- and 800-mg (68.4% vs 65.3%)

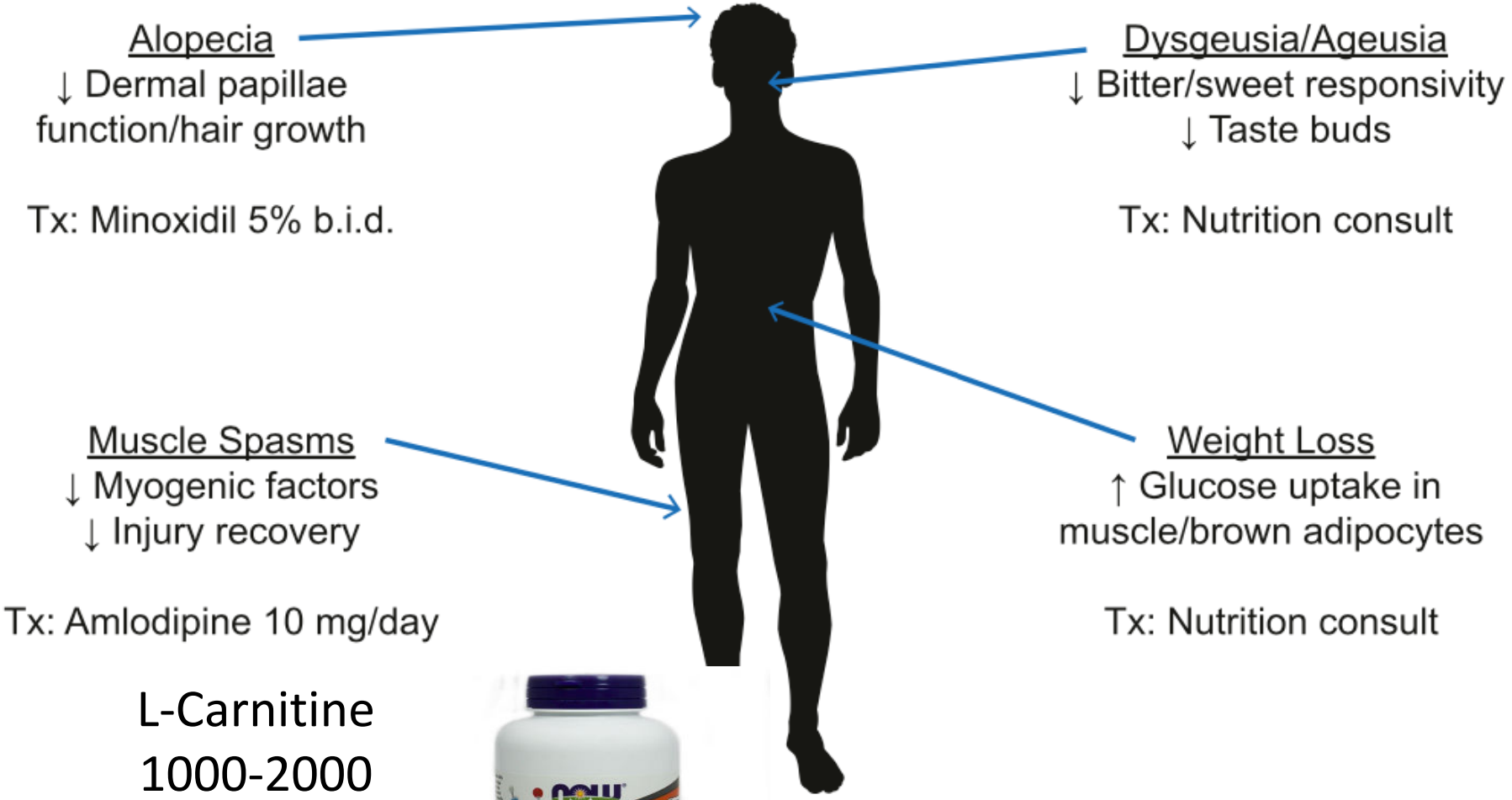
- Dose reductions more frequent in 800 mg (36.7%) than 200 mg (16.5%)

- ORR for 200 mg daily (48.1%) similar to patients without dose reduction or interruption (48.5%).

*Dose escalation may be tried for non-responders, but may not improve outcomes.

Lewis K, Dummer R, Farberg AS, Guminski A, Squittieri N, Migden M. Dermatol Ther (Heidelb). 2021;11:2225-2234

MANAGEMENT OF ADVERSE EVENTS HHIS



Screen and Monitor (monthly): Usual labs plus: Creatine kinase (CK) and creatinine. Lipase may ↑

L-Carnitine 1000-2000 mg/day

The Oncologist 2016;21:1218–1229

L-Carnitine Reduces Muscle Cramps in Patients Taking Vismodegib

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[b]Department of Dermatology, University of Tennessee Health Science Center, Memphis, TN
[c]Arkansas Dermatology, Little Rock, AR
[d]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY

ABSTRACT

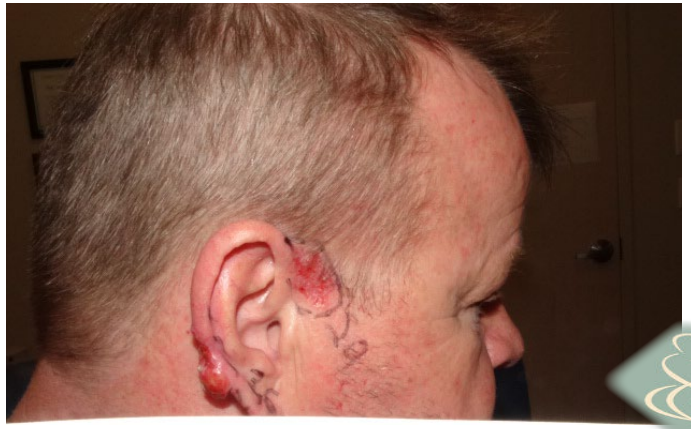
Vismodegib is an oral, small-molecule hedgehog pathway inhibitor (HHI) approved for the treatment of locally advanced and metastatic basal cell carcinoma. While an effective treatment option for these conditions, HHI therapy is associated with muscle cramps in a significant number of patients. This adverse effect negatively impacts patient quality of life and patient adherence to the prescribed treatment regimen.

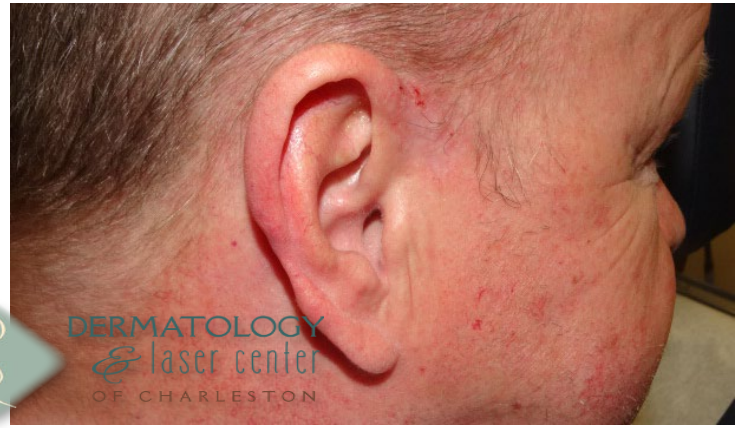
Levocarnitine (L-carnitine) is a trimethylated amino acid known to play a critical role in lipid metabolism. It has antioxidant properties, and several studies have illustrated its effectiveness in lessening the severity of muscle cramps in various disease processes.

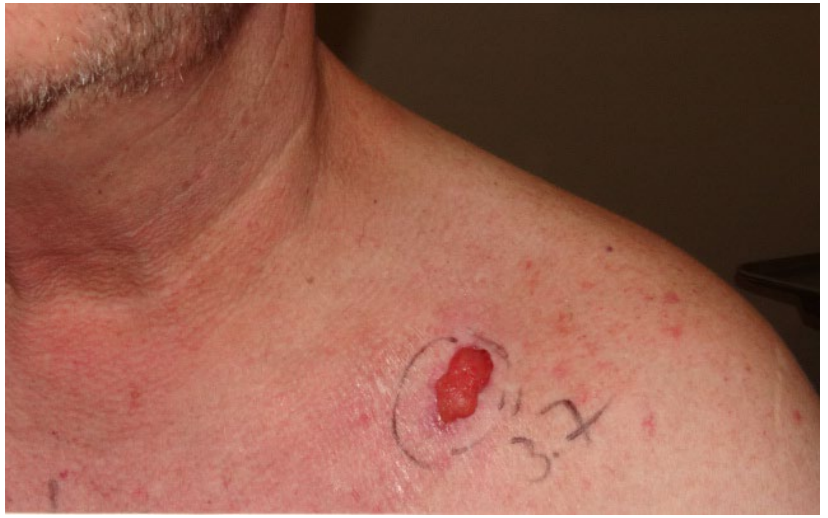
We present three patients who developed muscle cramping associated with vismodegib treatment for basal cell carcinoma. Each was started on L-carnitine therapy, and all three reported a significant decrease in the severity of their muscle cramps to the point that they were able to continue HHI therapy without taking a drug holiday. These cases illustrate a promising treatment option for the most common side effect associated with HHI treatment.

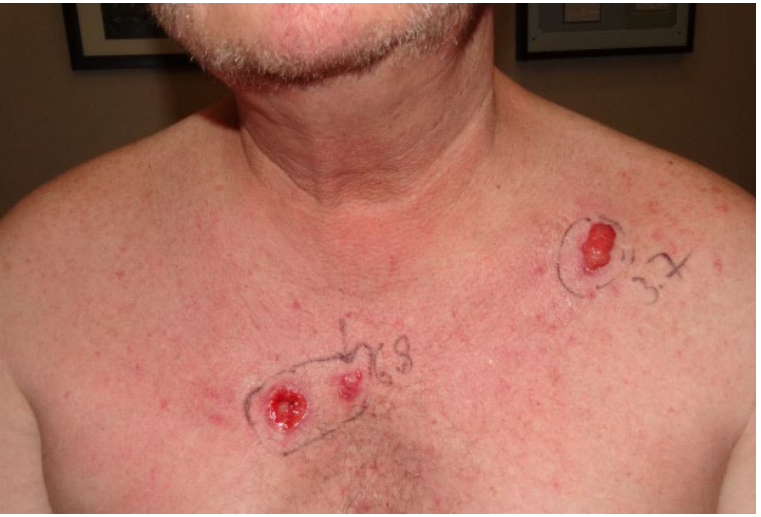
L-CARNITINE

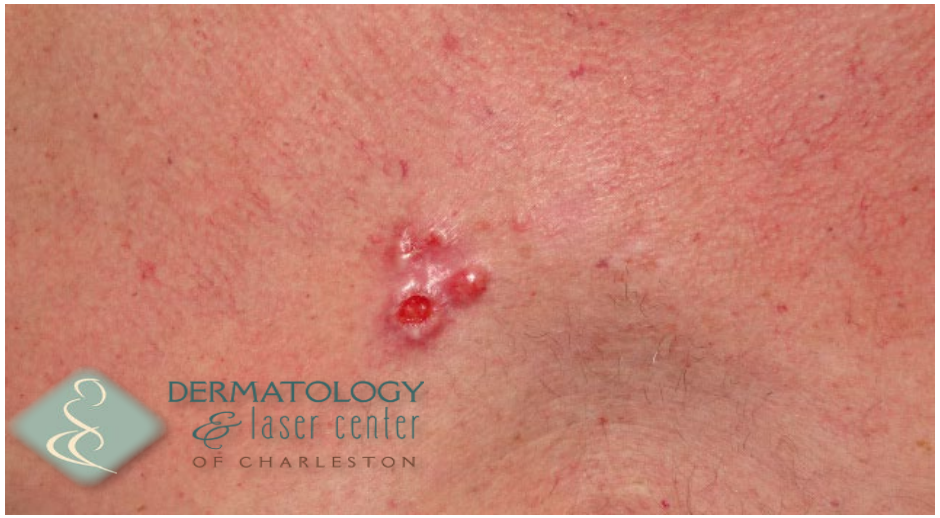
VISMODEGIB RESPONSES OVER 9 MONTHS

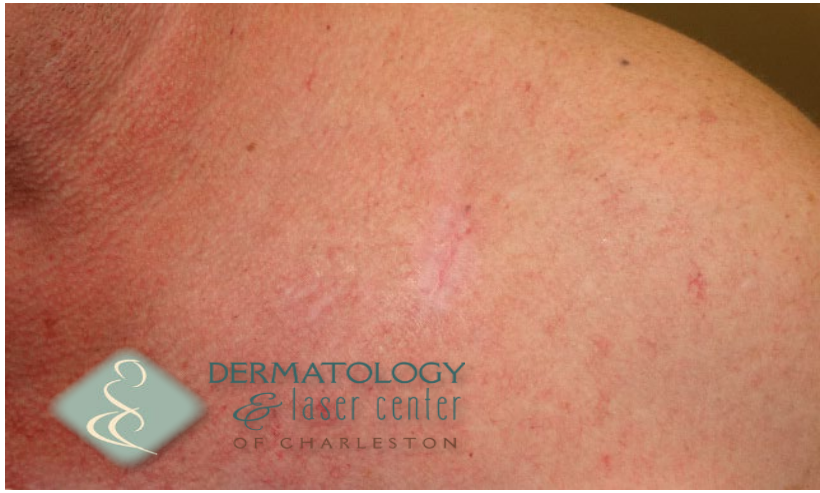




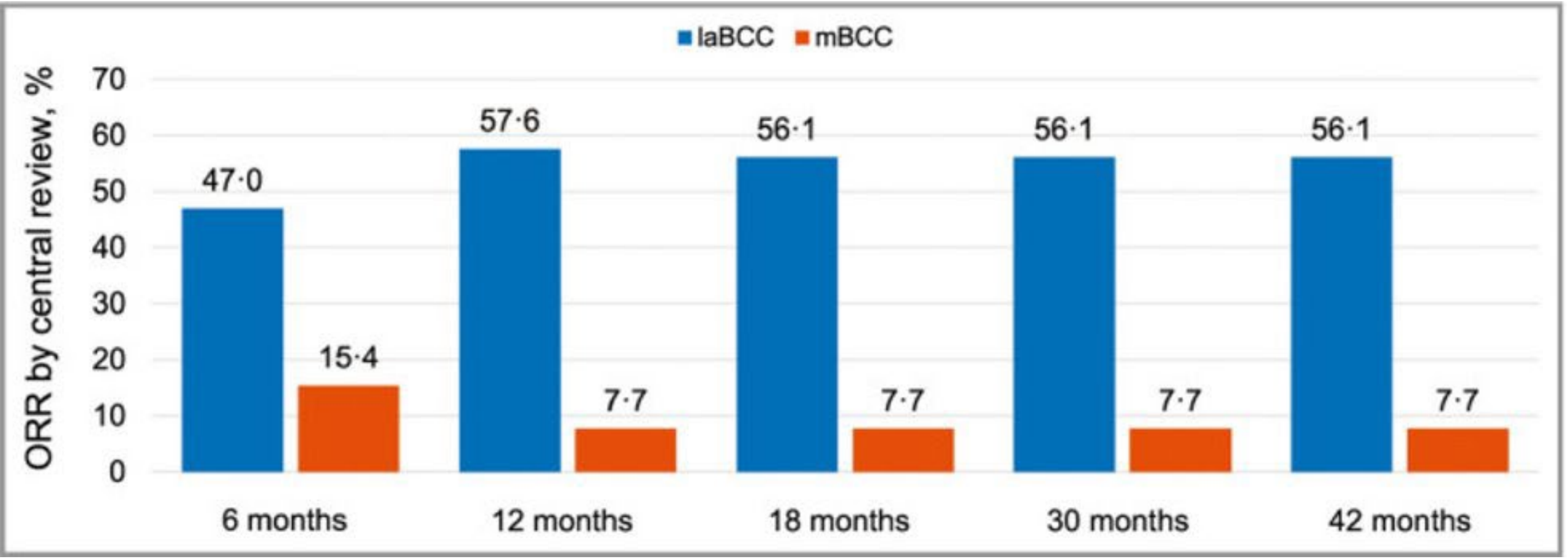




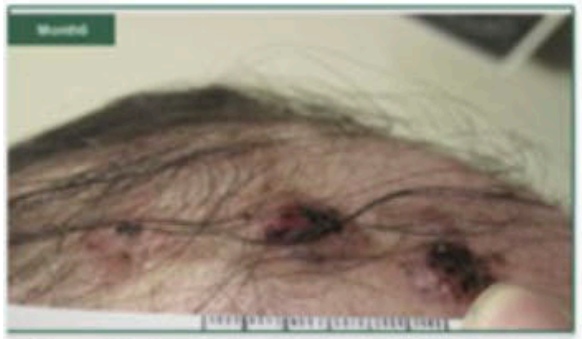




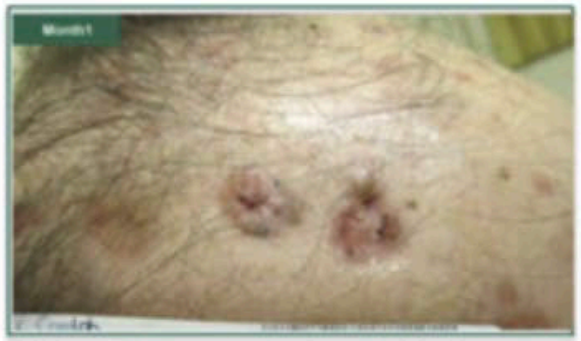
Objective response rates by central review across all BOLT (Basal Cell Carcinoma Outcomes with LDE225 Treatment) analyses in patients receiving sonidegib 200mg/day mg daily.c



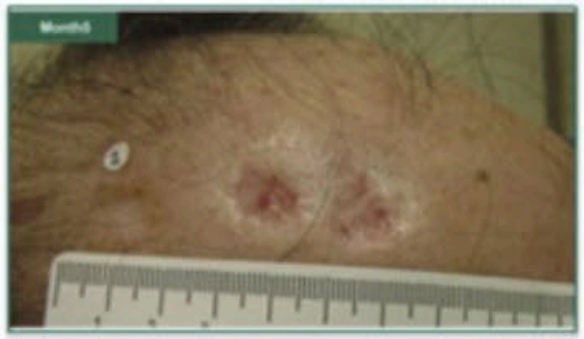
SONIDEGIB RESPONSES OVER 23 MONTHS



Month 0



Month 1



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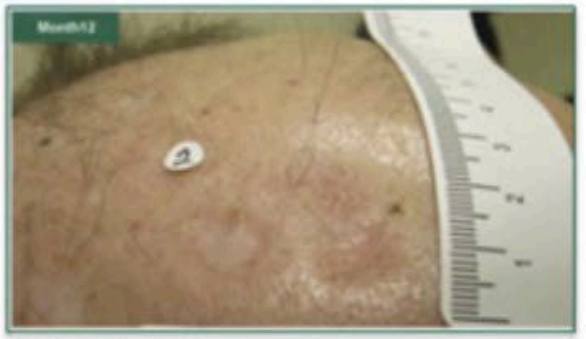
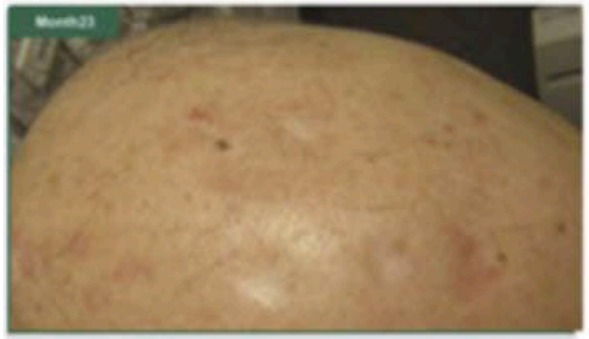


Month 11



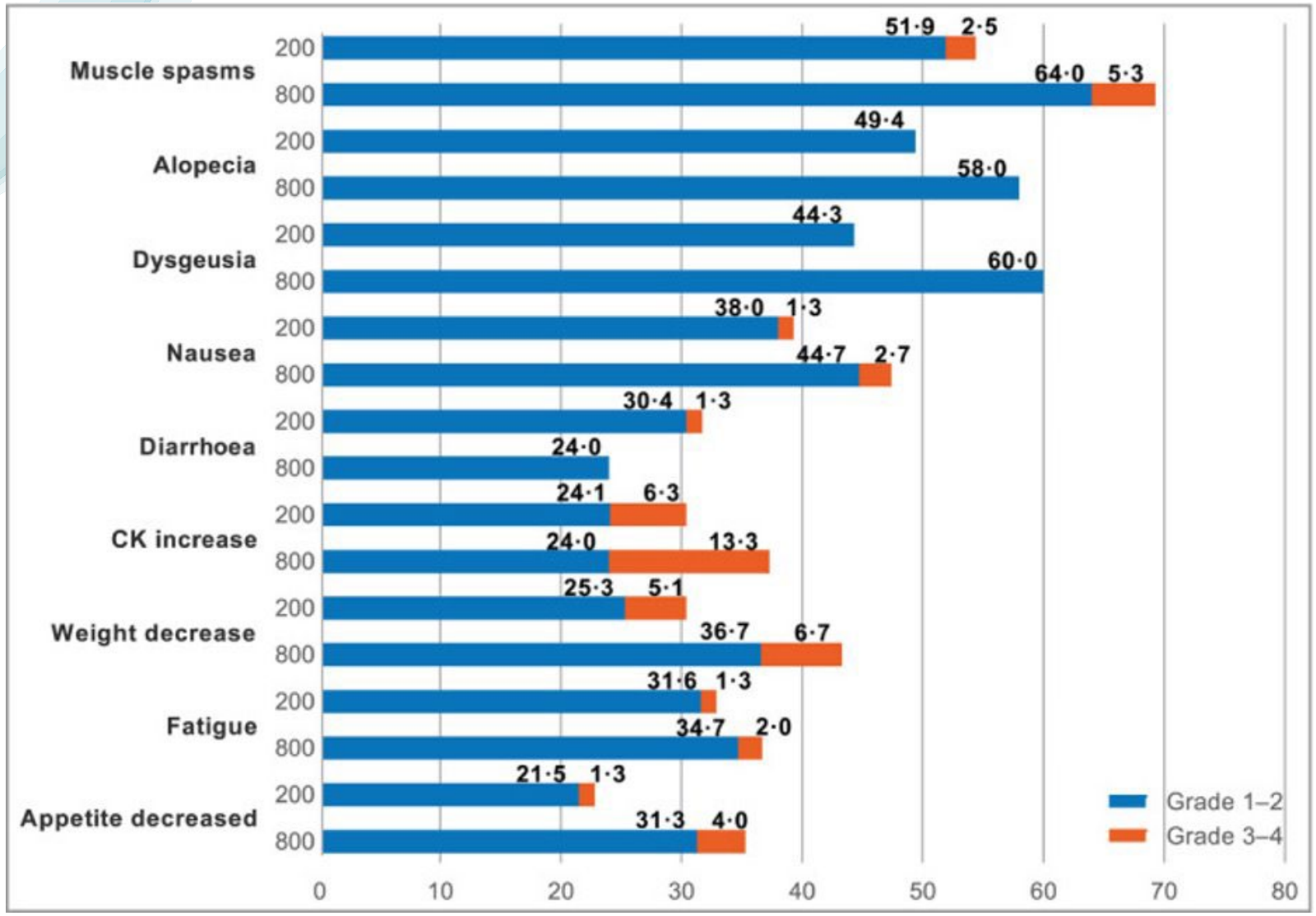
Month 23

COMPARING VISMODEGIB AND SONIDEGIB

	Vismodegib (ERIVANCE study)[19]	Sonidegib (BOLT study)[27]
Indication	Locally advanced BCC that has recurred following surgery, metastatic BCC, and patients who are not candidates for surgery or radiation	Locally advanced BCC that has recurred following surgery, and patients who are not candidates for surgery or radiation
Dose	150 mg once daily	200 mg once daily
Objective response rate (complete or partial response)	43% in locally advanced 30% in metastatic BCC	56% in locally advanced
Median duration of response	7.6 months	26.1 months
Progression-free survival	9.5 months	22.1 months
Common side effects	Muscle spasms, alopecia, dysgeusia, weight loss, fatigue, nausea, decreased appetite, and diarrhea	

- Half-life vismodegib is 4-12 days/sonidegib is 28 days

Wilson et al. J Am Acad Dermatol Volume 86, Number 6



Adverse Effect Profile of sonidegib

Use and Monitoring for HPI - Recommendations

Table 4. Summary of Recommendations[21] for HPI Use

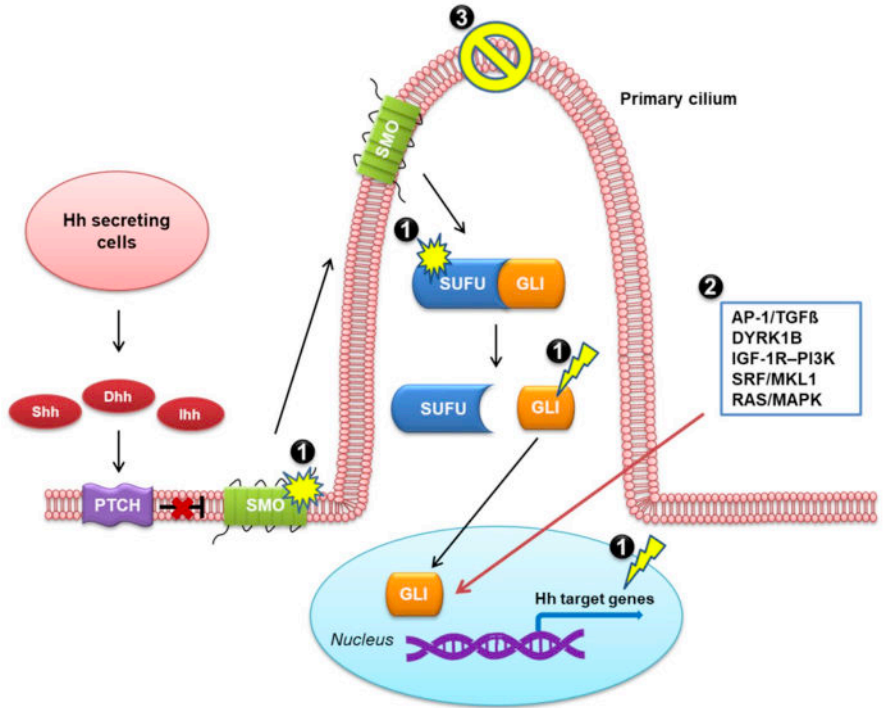
Indication	Recommendation	Grade of Recommendation[a]	Quality of Evidence[b]	Selected References
HPI for laBCC	Strong recommendation	1	A	Basset-Seguin et al[8] Chang et al[6] Migden et al[20] Sekulic et al[12]
HPI for mBCC	Strong recommendation	1	A	Basset-Seguin et al[8] Chang et al[6] Migden et al[20] Sekulic et al[12]
HPI for basal cell nevus syndrome	Recommendation	2A	B	Tang et al[3] Ozgur et al[17]
Use of a drug holiday or pulse dosing to mitigate adverse effects	Weak recommendation	2B	C	Dummer et al[22] Viscusi et al[15] Yang et al[23]
Monitor CPK	Strong recommendation[c]	A	A	Migden et al[20] Ally et al[24]
Monitor LFTS	Weak recommendation	2B	C	Ash et al[25] Ventarola et al[26]
Monitor electrolytes	Weak recommendation	2B	C	Simone et al[14]
Monitor bone density/lipids in premenopausal women	Weak recommendation	2B	C	Strasswimmer et al[27]
Monitor for pregnancy prevention	Strong recommendation	1	A	Kimura et al[28] Lipinski et al[29,30]
Monitor cardiovascular status	Weak recommendation	2B	C	Huizenga[31] Simone et al[14]

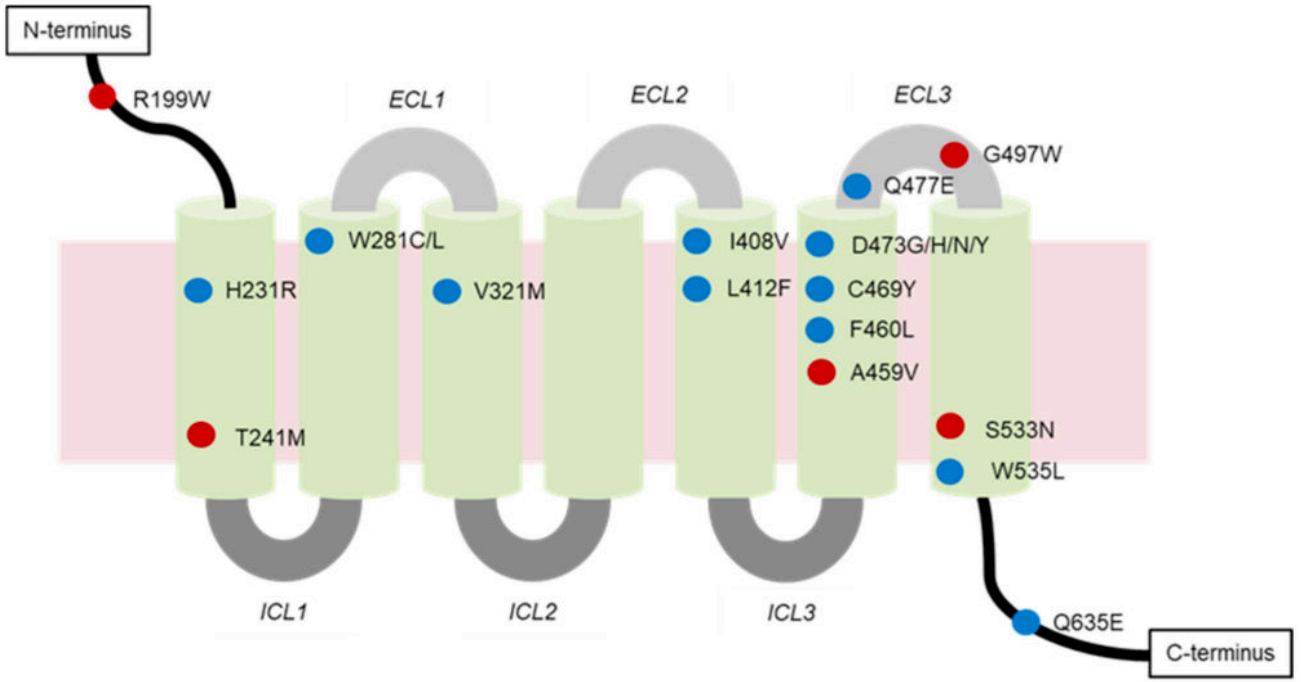
Overcoming drug resistance HPI

Develop novel and potent 2nd generation SMO inhibitors

Target downstream components of SMO in the Hh pathway or signaling molecules

Genetic pre-screening

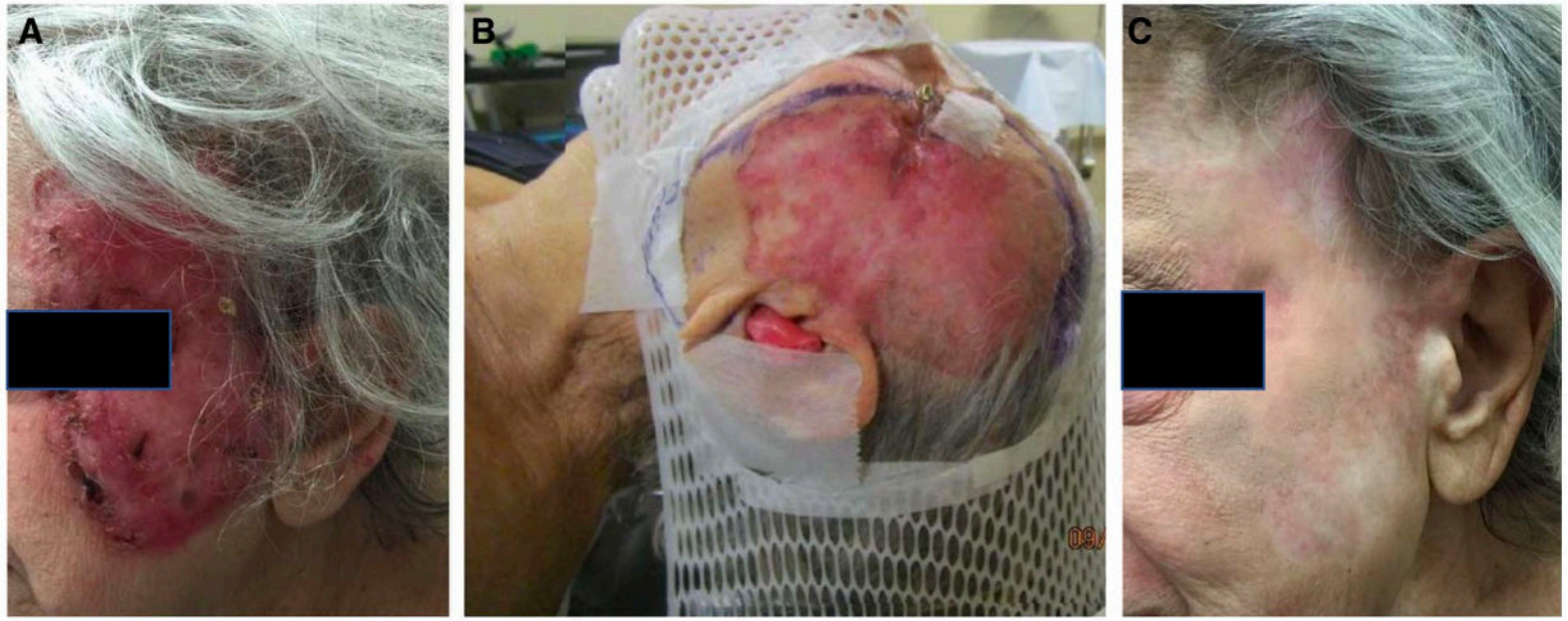




Int. J. Mol. Sci. **2022**, *23*, 1733

X HHI + XRT

- Case series n=12
- CR 100%/PFS 88.8% at 40 mos/16.6% relapse
- HHI may increase XRT induced cytotoxicity
- Induction with HHI may improve XRT response and durability with modest toxicity



Baseline 2.5 months 52 months

Melanoma and Cutaneous Malignancies

The Oncologist®

Hedgehog Inhibitor Induction with Addition of Concurrent Superficial Radiotherapy in Patients with Locally Advanced Basal Cell Carcinoma: A Case Series

Joshua P. Weissman,[a,b] Wolfram Samlowski,[b,c,d] Raul Meoz[b,c,d]

[a]Feinberg School of Medicine, Northwestern University, Evanston, Illinois, USA; [b]Comprehensive Cancer Centers of Nevada, Las Vegas, Nevada, USA; [c]School of Medicine, University of Nevada, Las Vegas, Las Vegas, Nevada; [d]University of Nevada School of Medicine, Reno, Nevada, USA

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Non-melanoma skin cancer • Keratinocyte carcinoma • Sonidegib • Vismodegib

The Oncologist 2021;26:e2247–e2253

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  - Dosed IV 350mg every 3 weeks
- Pembrolizumab (24JUN2020) – recurrent or mCSCC
  - Dosed IV 200mg every 3 weeks

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

- 22-89% in BCC
- 25-41% in cSCC

PD-L1 expression also varies in tumor infiltrating lymphocytes (TIL's) related to specific tumor types

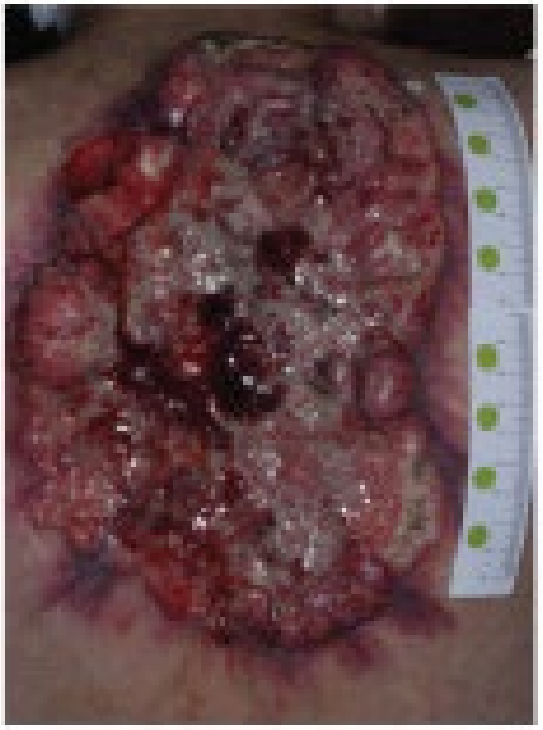
Potential for increased PD-L1 expression in previously treated NMSC's

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.

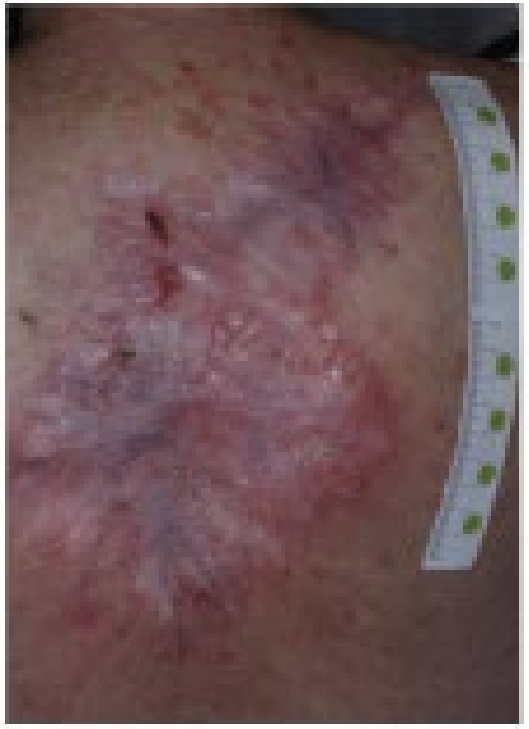
EXAMPLES OF OUTCOMES CSCC

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

Baseline

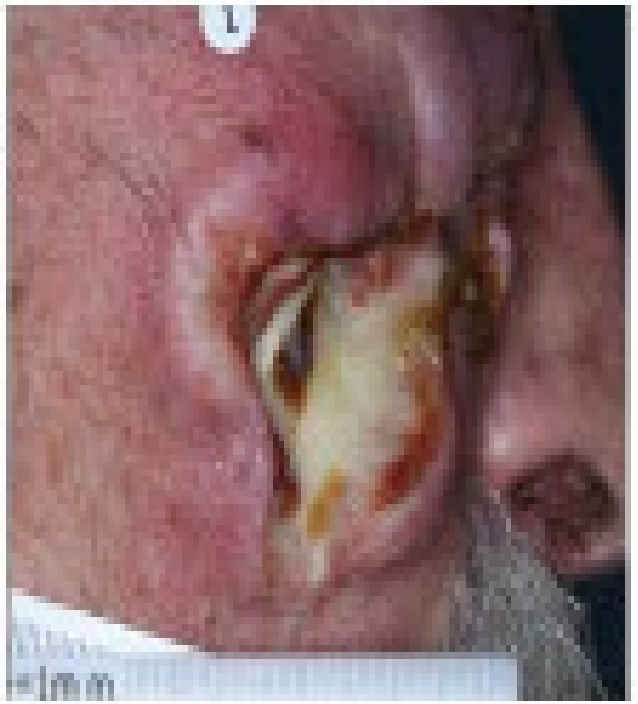


Week 48

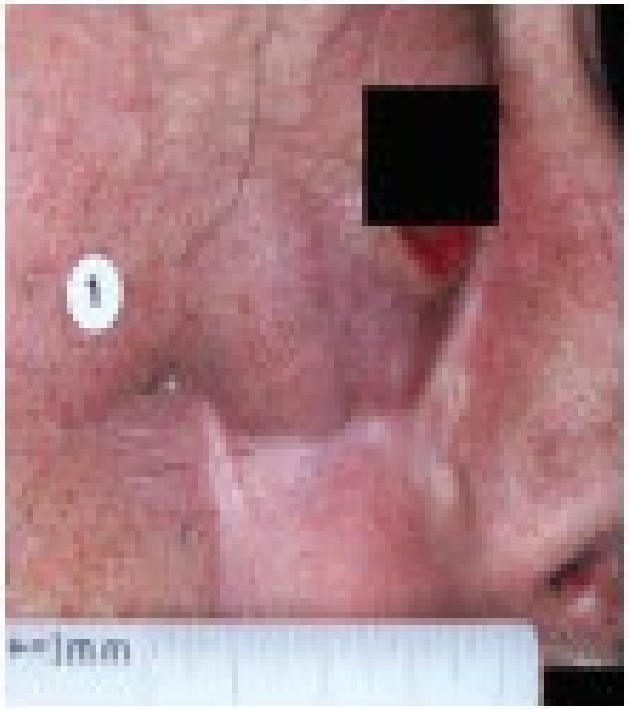


A 70-year-old male with a large CSCC tumor of the right face

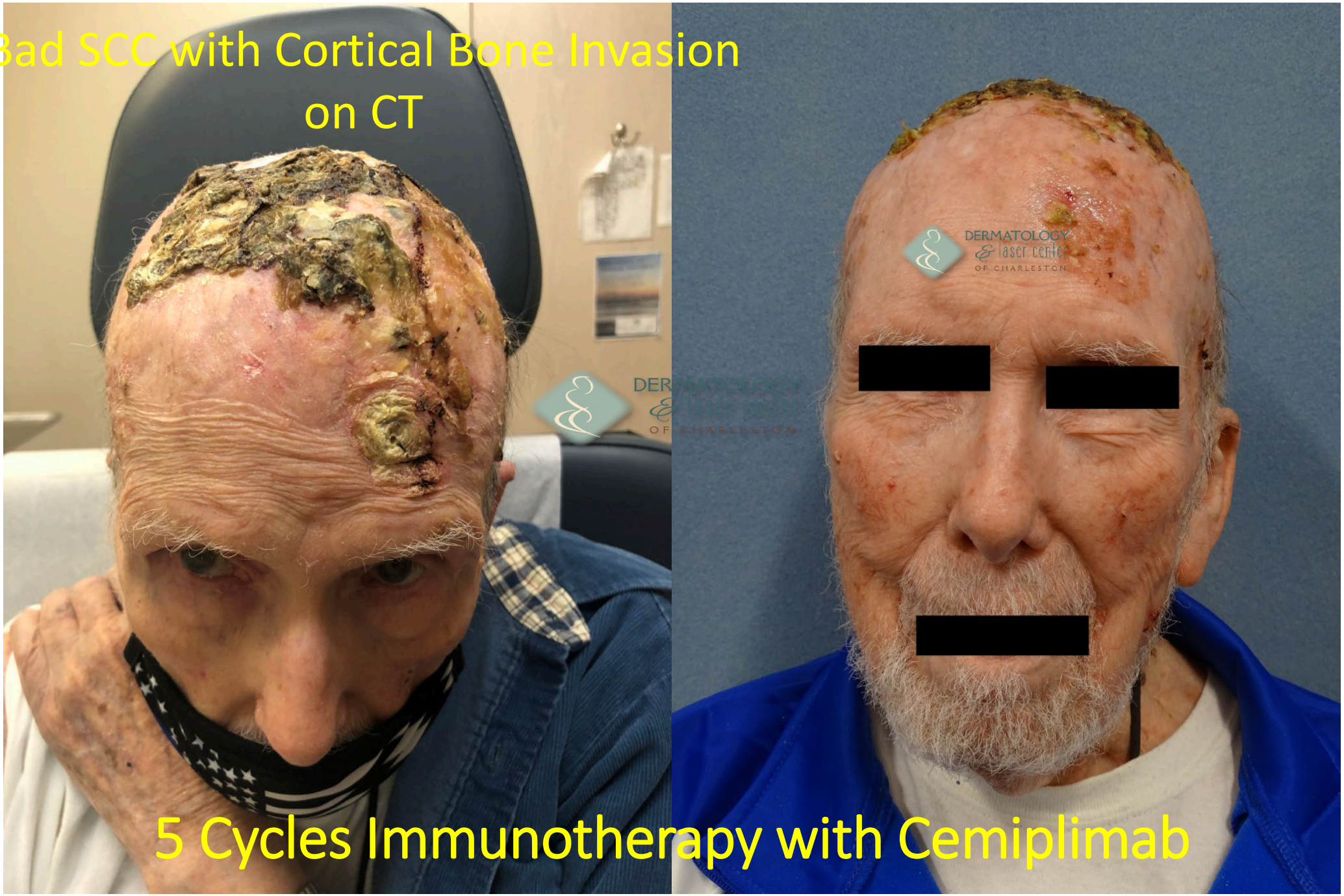
Baseline

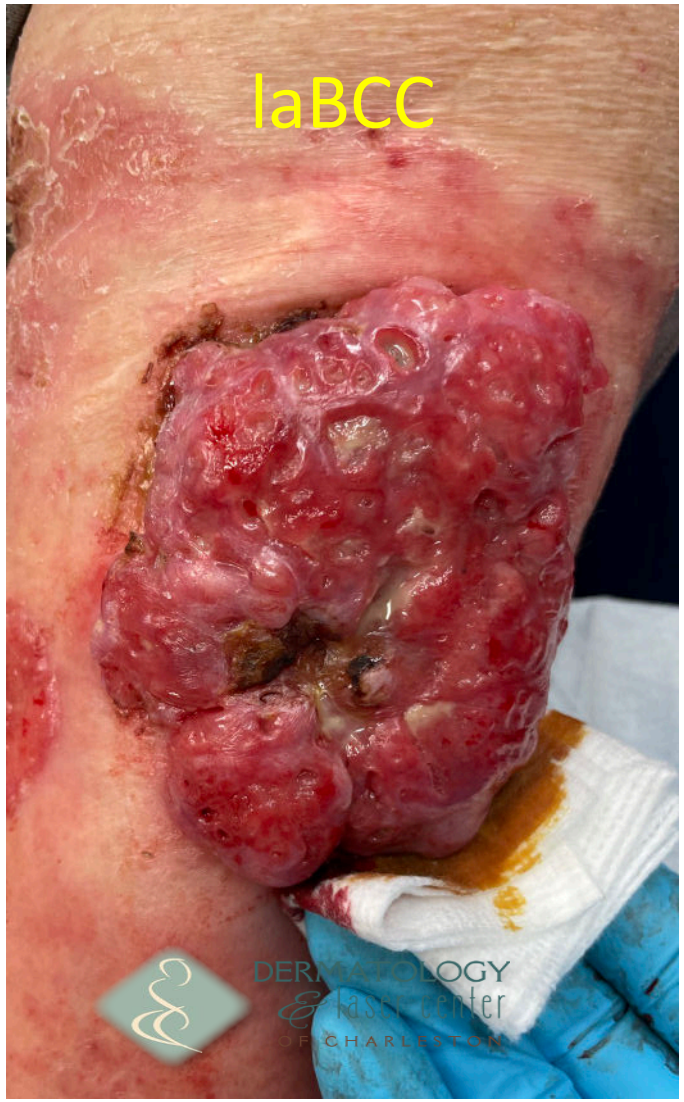


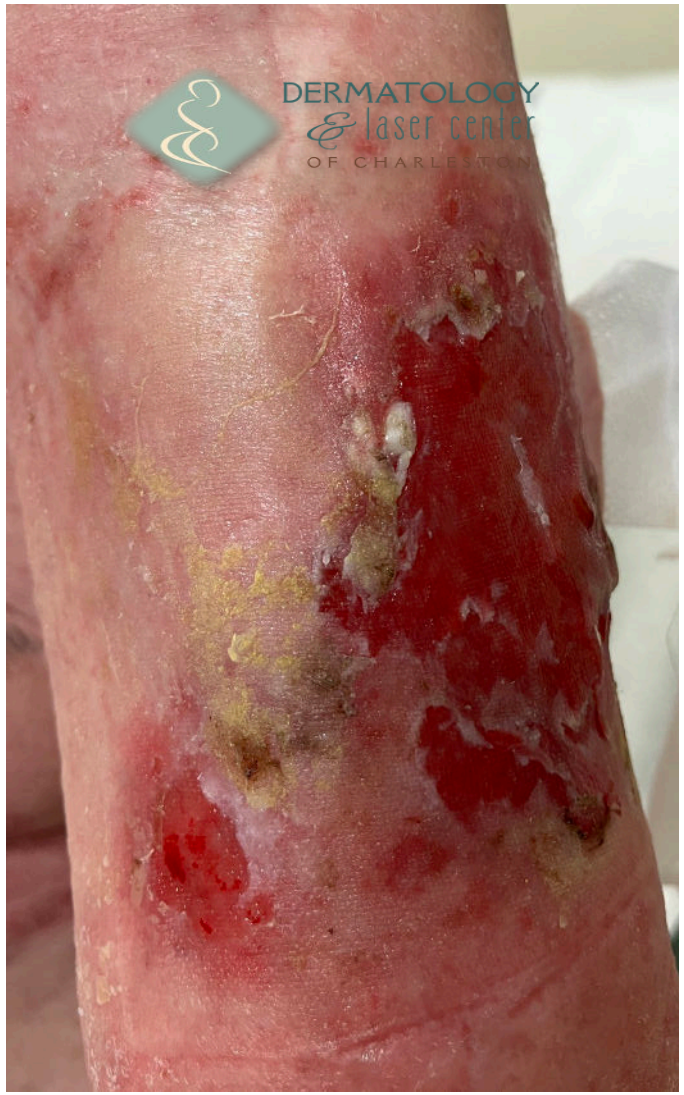
Week 18

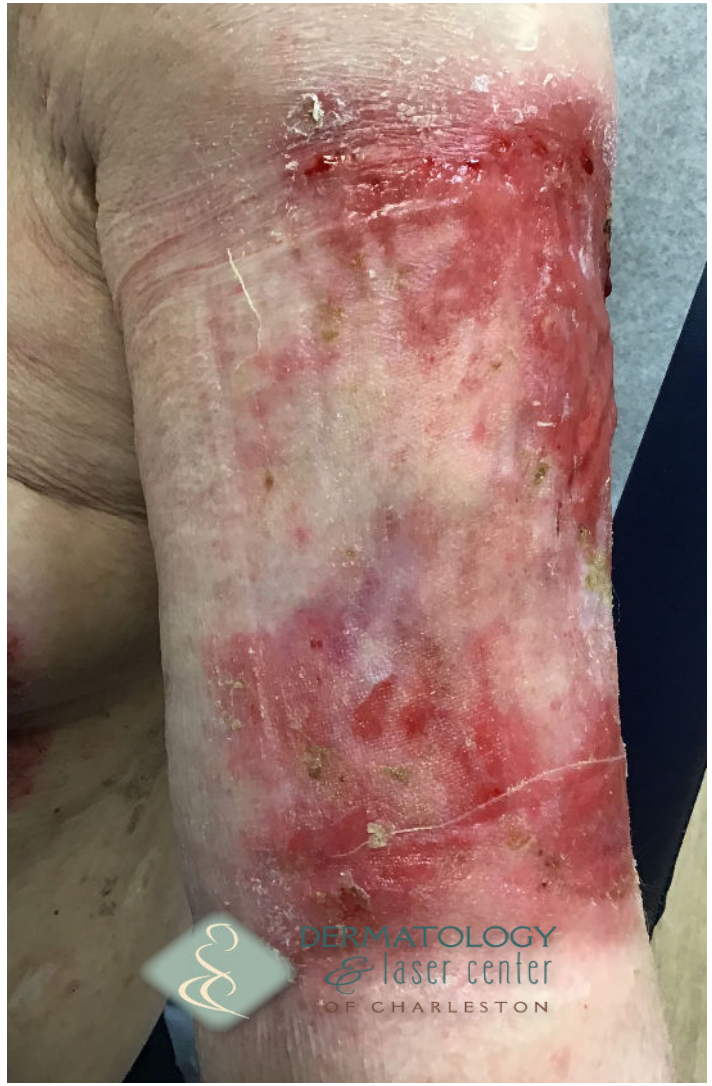


J Clin Oncol 37, 2019 (suppl; abstr 6015)

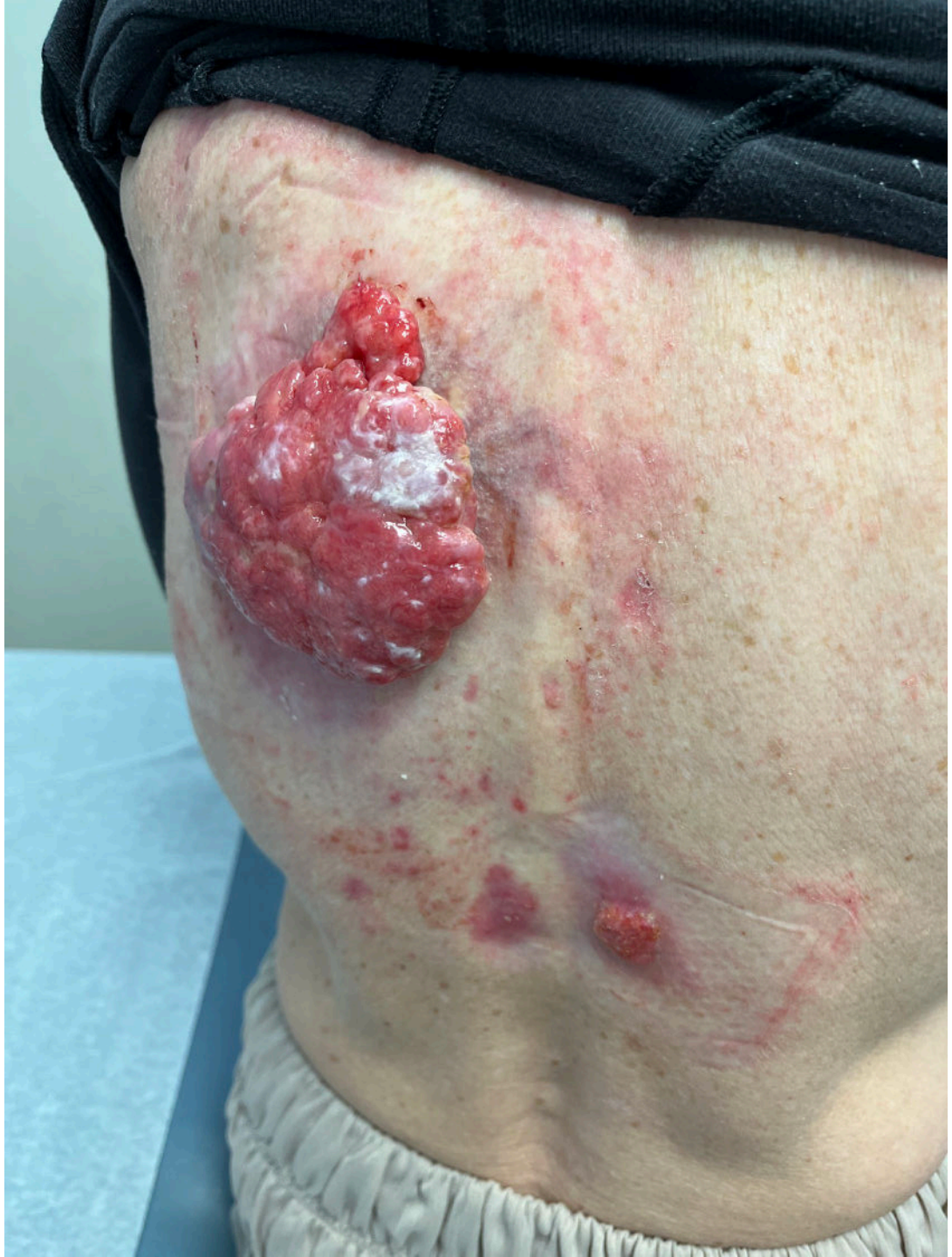

Bad SCC with Cortical Bone Invasion on CT
5 Cycles Immunotherapy with Cemiplimab
DERMATOLOGY & laser center OF CHARLESTON

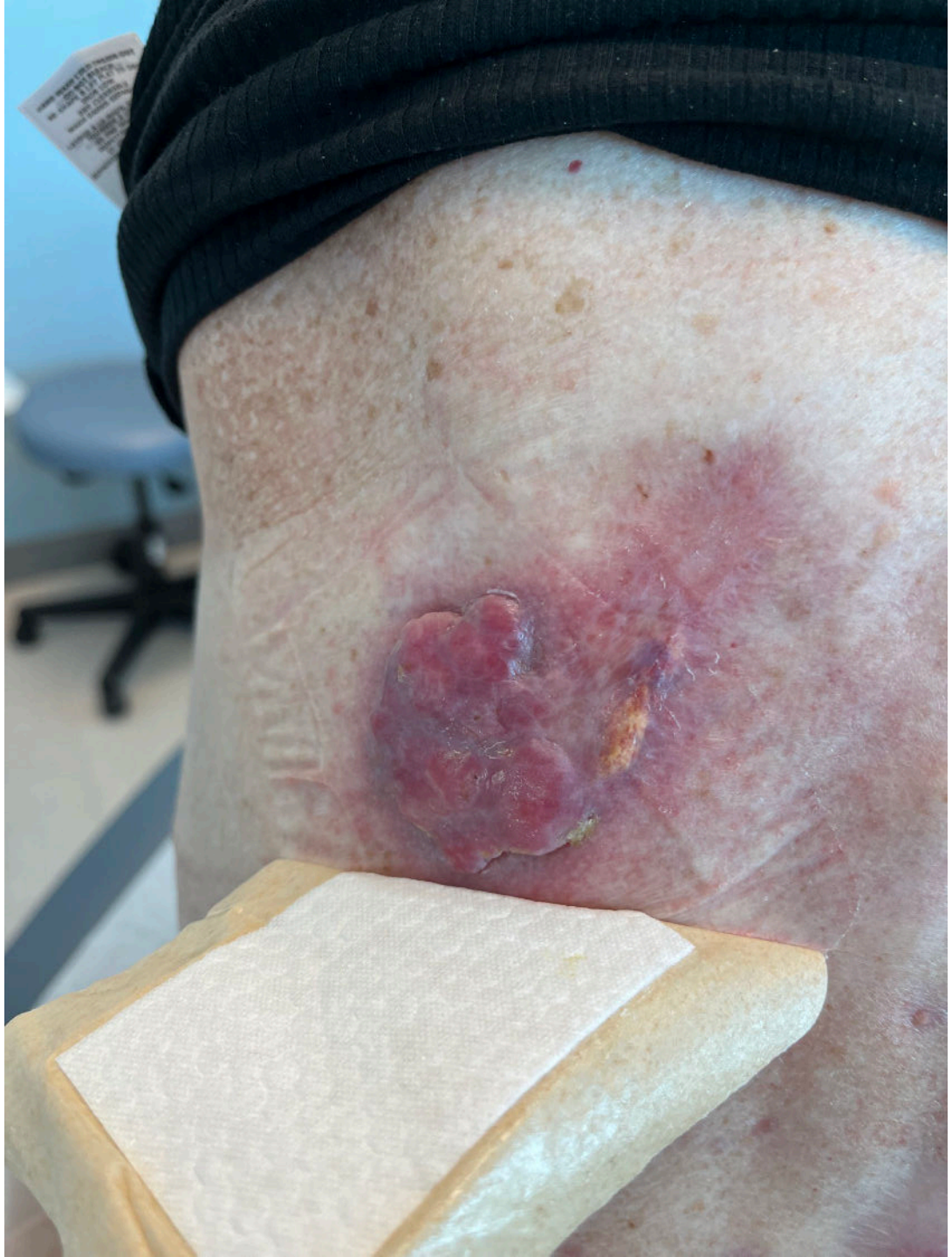




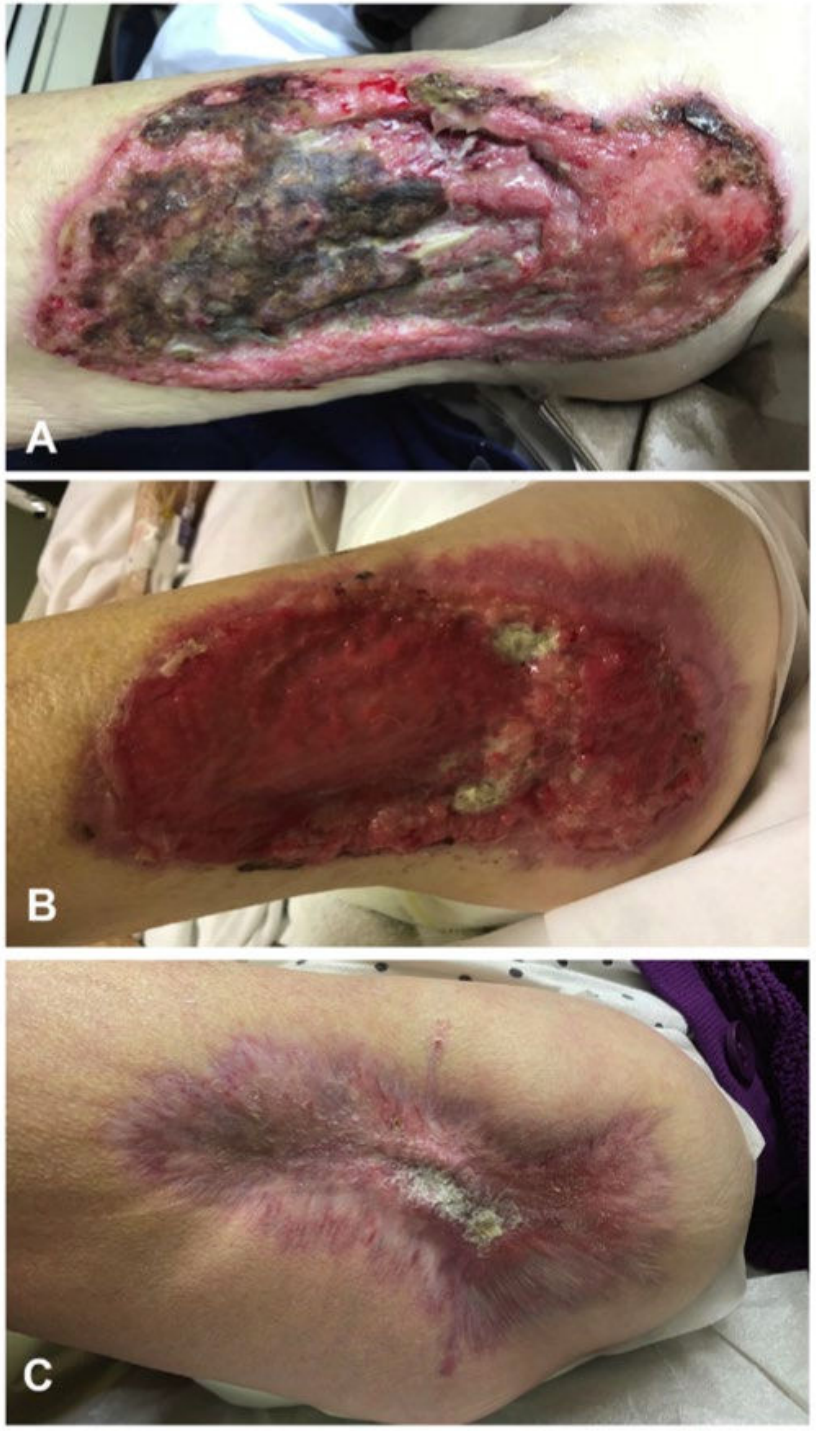


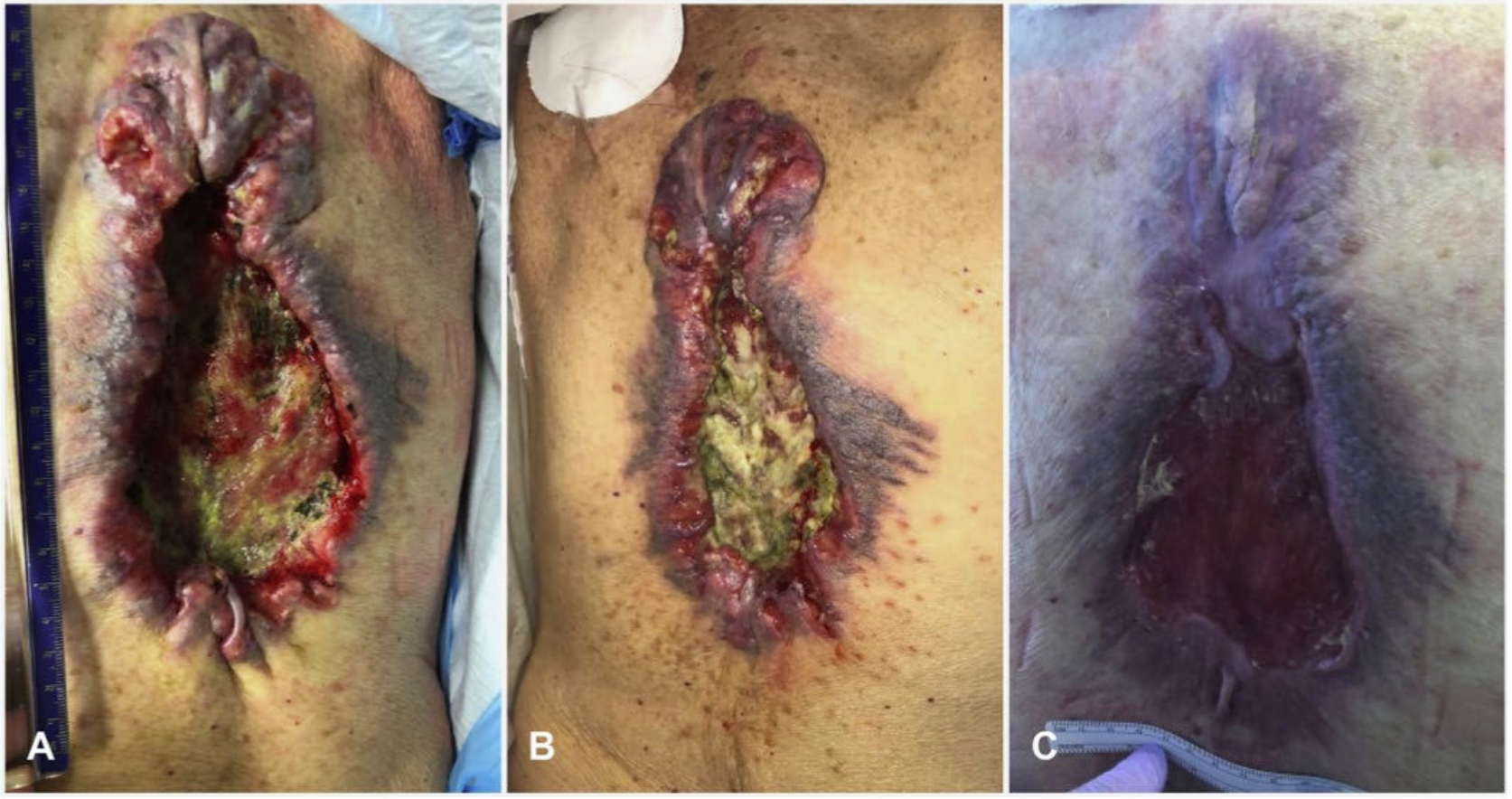
3 then 6 Cycles Immunotherapy with Cemiplimab





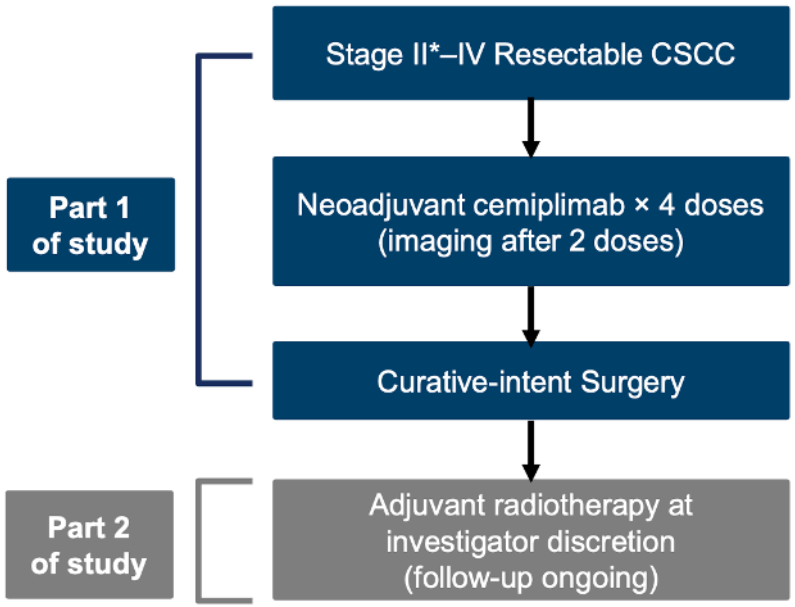
Neoadjuvant PD-L1 therapy in laBCC





JAAD Case Reports 2020;6:628-33.

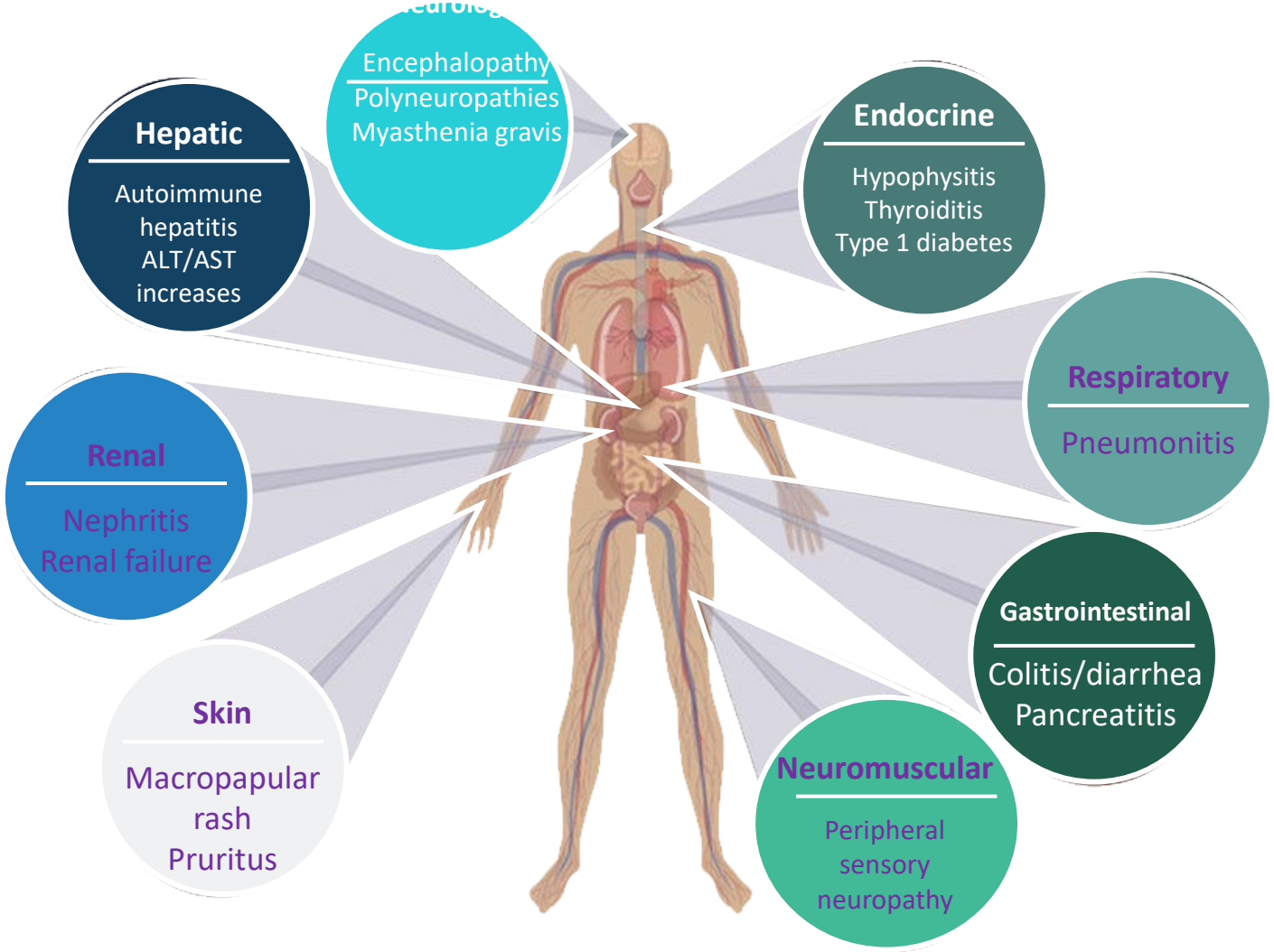
Neoadjuvant Use of PD-1i in cSCC



	Neoadjuvant cemiplimab (N=79)	
Pathologic response	**ICPR N (%) [95% CI]**	**Local pathology review N (%) [95% CI]**
pCR (0% viable tumor cells)	**40 (50.6) [39.1–62.1]**	42 (53.2) [41.6–64.5]
MPR (>0% and ≤10% viable tumor cells)	10 (12.7) [6.2–22.0]	10 (12.7) [6.2–22.0]
Combined pathologic response (pCR + MPR)	50 (63.3) [51.7–73.9]	52 (65.8) [54.3–76.1]
Non-pCR/MPR	20 (25.3)	NA*
Not evaluable (no surgery)	9 (11.4)	9 (11.4)
Radiological response		**Local imaging review N (%) [95% CI]**
Objective response rate (ORR), RECIST 1.1		54 (68.4) [56.9–78.4]
Best overall response		
Complete response		5 (6.3)
Partial response		49 (62.0)
Stable disease		16 (20.3)
Progressive disease		8 (10.1)
Not evaluable		1 (1.3)

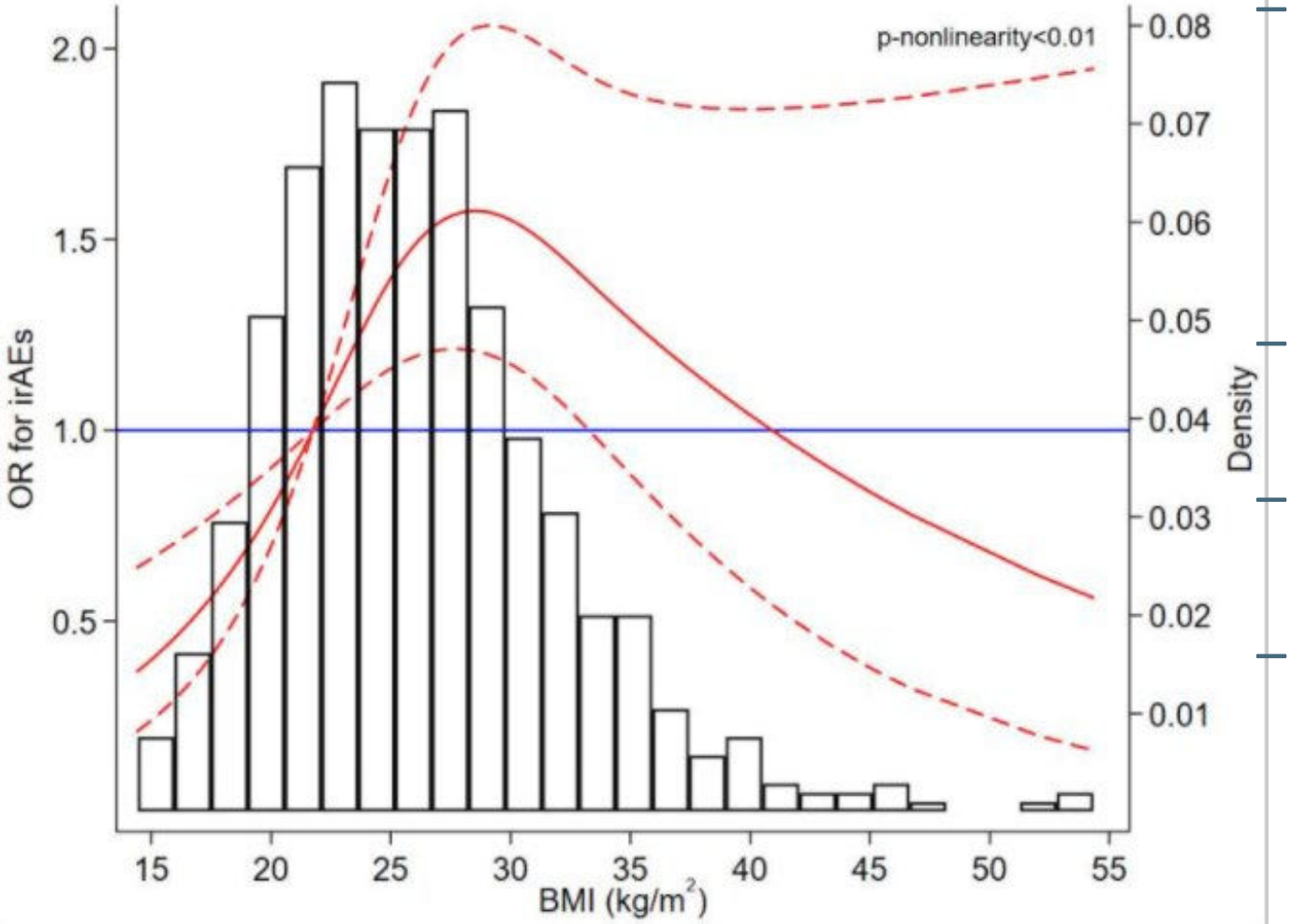
Gross et al. Poster at ESMO Congress 2022

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

ASSOCIATION BETWEEN BMI AND IRAE'S

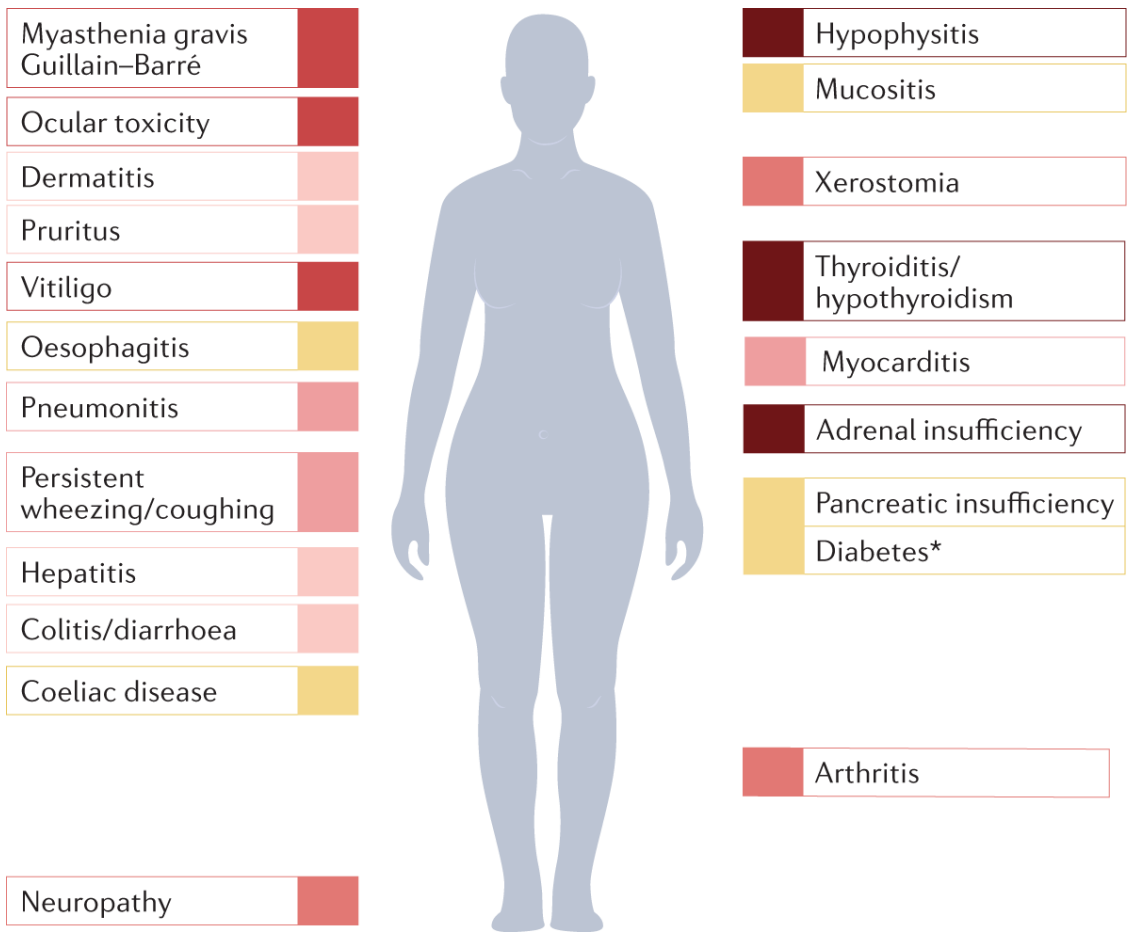


- Recent study suggests potential correlation between BMI and increased irAE's with *Pembrolizumab*
  - Multiple ICI's examined, though only Pembrolizumab applicable to skin cancer
- Non-linear association between pre-treatment BMI and irAE's
- No statistical significance in patients ≥ 65 y.o. and/or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

Chronic Immune Related AE's

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



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

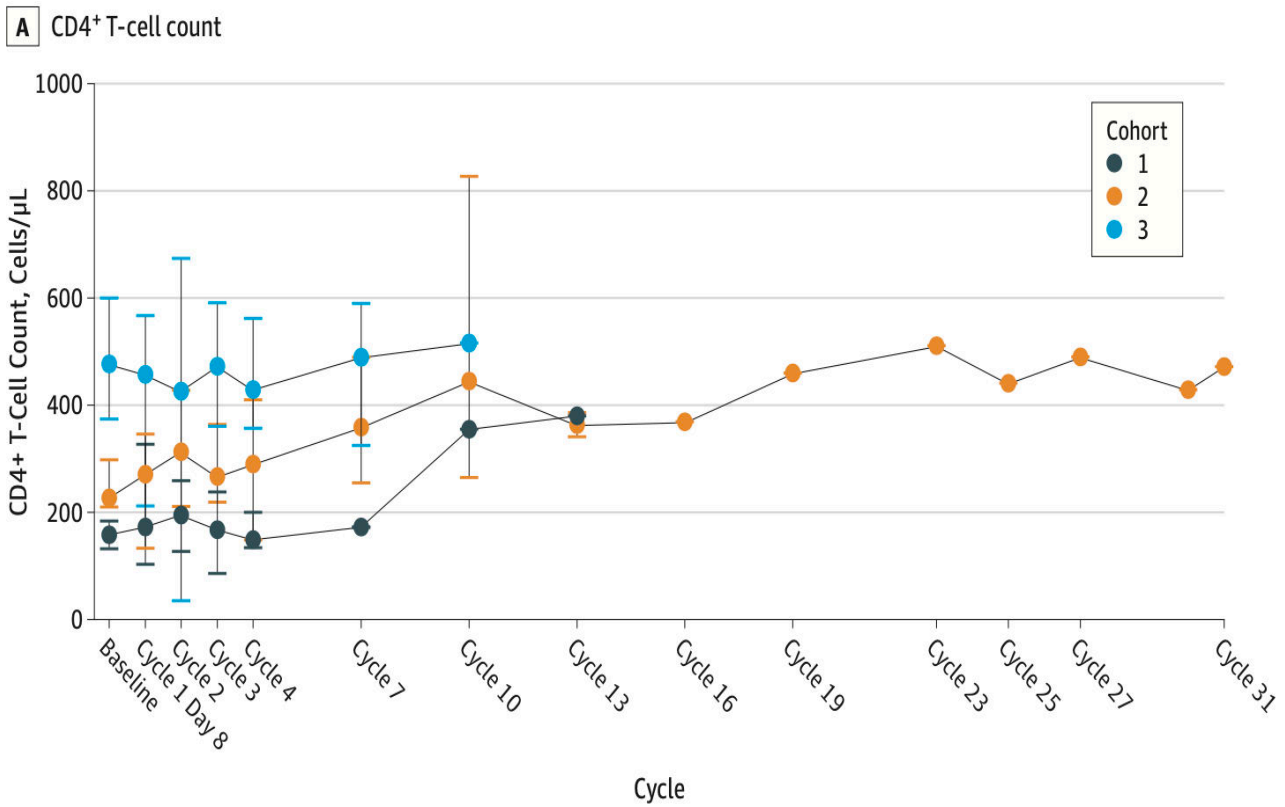
Special Populations

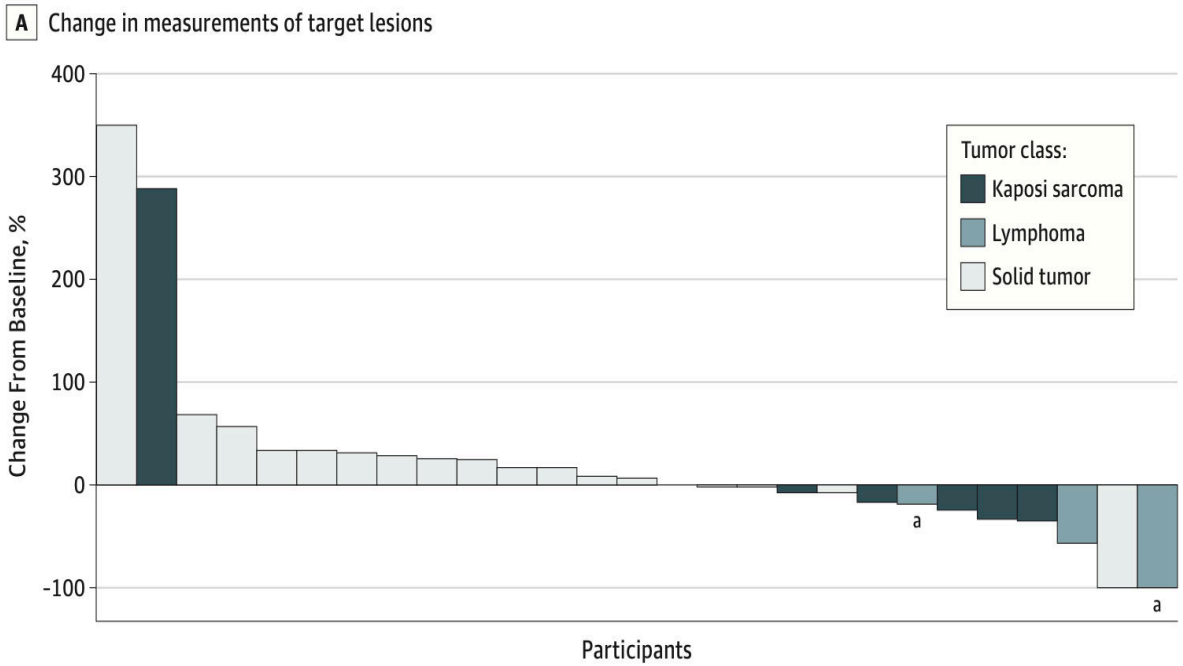
- HIV+ on Antiretroviral Treatment
- Solid Organ Transplant
- PD-L1 Tumor Status
- Treatment Beyond Progression
- First Line (1L) vs. 2nd Line (2L)

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.

Pembrolizumab induces HIV latency reversal in people living with HIV and cancer on antiretroviral therapy

THOMAS S. ULDRICK, SCOTT V. ADAMS, REMI FROMENTIN, MICHAEL ROCHE, STEVEN P. FLING, PRISCILA H. GONÇALVES, KATHRYN LURAIN, RAMYA RAMASWAMI, CHIA-CHING JACKIE WANG, [...] SHARON R. LEWIN +15 authors Authors Info & Affiliations

SCIENCE TRANSLATIONAL MEDICINE • 26 Jan 2022 • Vol 14, Issue 629 • DOI: 10.1126/scitranslmed.abl3836

- Potential for anti-PD1 mAb to increase CD4+ T cells with inducible virus in latent HIV infection
  - Better immune recognition and decreased ability for HIV to remain latent
- Limitations to the study, but important potential benefit to be aware of when prescribing

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)

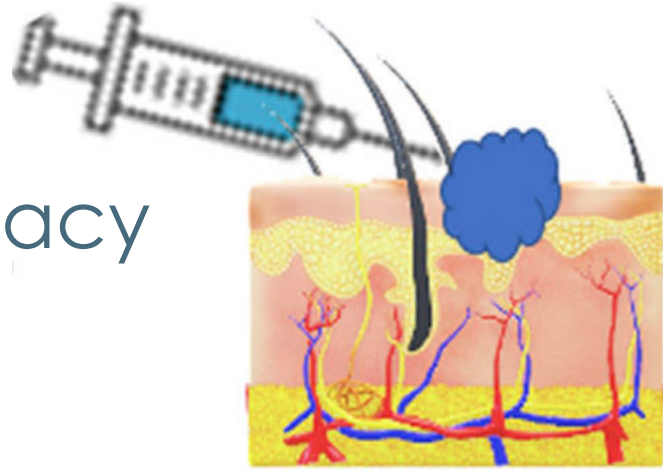
Immune Checkpoint Inhibitor Use in Solid Organ Transplant Recipients: A Systematic Review

Andrew J. Portuguese, MD[1,2]; Scott S. Tykodi, MD, PhD[1,2]; Christopher D. Blosser, MD[1,3]; Ted A. Gooley, PhD[2]; John A. Thompson, MD[1,2]; and Evan T. Hall, MD, MPhil[1,2]

- The most frequent cancer in SOT-recipients is cSCC
- However cSCC also had the best response rate to ICIs with an ORR of 68.2%
- May decrease likelihood of transplant rejection with modification of immunosuppressive regimen
  - Induction steroid taper
  - Possible decreased rejection with Tacrolimus or mTOR inhibitors

WHAT'S T-VEC (TALIMOGENE LAHERPAREPVEC)

- It's an HSV-1 oncolytic virus modified by gene deletion and insertion
- Approved (2015) for Stage IIIB-IV melanoma
- It's an **intratumoral** injection
- Causes tumor cell lysis via improved antigen presentation of infected tumor cells
- Induces a systemic immune response via GM-CSF insertion to virus
- It's being studied for NMSC (especially refractory) and has demonstrated efficacy



Kaufman HL, Shalhout SZ and Iodice G (2022) Talimogene Laherparepvec: Moving From First-In- Class to Best-In-Class. Front. Mol. Biosci. 9:834841.

Hedgehog Inhibitor Advantages

- Works quickly
- Its a pill, not an injection or an infusion
- Adverse events are unlikely to result in hospitalization or death
- Adverse events can be controlled by intermittent dosing and L-carnitine
- Can be given by dermatologist or dermatology provider
- Works better than advertised

Hedgehog Inhibitor Disadvantages

- Almost all patients get some adverse events
- Not sure when to discontinue
- Sometimes difficult to get to durable remission
  - Implies drug resistance

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 usually given by oncologist

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 HHIs and PD-L1s are multisystemic and warrant close attention

T-VEC is a new class of cancer therapy with proven effectiveness in melanoma and ongoing study for other indications

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

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THANK YOU!

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