

Advances in Cancer Immunotherapy[™]

Case Study #1: Cutaneous Squamous Cell Carcinoma



85 yr old Caucasian Female, history of "deep" SCC removed from LEFT forearm 'many' years ago.

~ 6/2021 Self palpated a Left axillary mass \rightarrow Increased in size and symptoms

Mammogram negative

Biopsy:

A. Soft tissue, left axilla, biopsy (A1-A3):

KERATINIZING SQUAMOUS CELL CARCINOMA.

B. Soft tissue, left subpectoral, biopsy (B1-B4):

KERATINIZING SQUAMOUS CELL CARCINOMA.









Select Initial Therapeutic strategy

- A. Surgery
- B. Radiation therapy (+)
- C. Cytotoxic chemotherapy.
- D. Systemic immunotherapy.
- E. Neoadjuvant therapy.

Initial treatment : 4 cycles Cemiplimab



Select <u>follow on</u> Therapeutic strategy

- A. Surgery
- B. Radiation therapy (+)
- C. Cytotoxic chemotherapy.
- D. Continue cemiplimab.
- E. Neoadjuvant therapy.

TREATMENT: 3 additional cycles Cemiplimab (7 total)

- Recurrent infections w/tumor ulceration, admitted to ICU for bleeding tumor mass and sepsis.
- Short term pressor support and broad spectrum antibiotics.



Select therapeutic strategy

- A. Surgery
- B. Radiation therapy (+)
- C. Cytotoxic chemotherapy.
- D. Continue cemiplimab.
- E. Neoadjuvant therapy.

TREATMENT:

- Dose-escalated palliative RT 09/23/2021 10/12/2021
 - 37.5/45 Gy in 15 fx
- Required adaptive replan after 8 fractions due to shrinkage











Select post-XRT therapeutic strategy

- A. Surgery
- B. Radiation therapy (+)
- C. Cytotoxic chemotherapy.
- D. Restart cemiplimab.
- E. Neoadjuvant therapy.

Post Radiation Therapy: Effect on target tumor

Pre-XRT

4 month post end of XRT



Can this patient be rendered NED ?

- A. Surgery
- B. Radiation therapy (+)
- C. Cytotoxic chemotherapy.
- D. Restart cemiplimab.
- E. Ablative therapy to oligometastases



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Case Study #2: Merkel Cell Carcinoma



68 yr old Hispanic female.

- 3/2018: painless LEFT elbow lump (mosquito bite). Progressed in size, palpable left axillary lump.
- 4/2018: Ultrasound : multiple enlarged LNs, largest 4.8 cm
 2.4 X 1.2X3 cm subcut Left elbow mass.
 Biopsy = "high grade neuroendocrine carcinoma consistent with merkel cell carcinoma."

Past Medical History Type II Diabetes Workup: disease at elbow and ipsilateral axilla.



CT Chest, Abdomen, Pelvis (excerpt of report): There is extensive adenopathy centered in the left axilla, extending into the infraclavicular and supraclavicular regions.

The adenopathy is worse compared to the outside exam. For example, the node on series 6 image 33 measures 4.8 x 3.7 cm up from 2.7 x 3.1 cm and the node on image 49 measures 3.4 x 2.5 cm up from 1.5 x 1.4 cm.

This adenopathy is encasing the left axillary vessels. The left axillary vein is not well opacified and cannot be assessed for patency. The left axillary artery is patent

Select Initial Therapeutic strategy

- A. Surgery
- B. Radiation therapy
- C. Cytotoxic chemotherapy.
- D. Systemic immunotherapy.
- E. Neoadjuvant therapy.

Pathology Report of Resection Materials

TUMOR SIZE: 65.0 x 45.0 MM (AS PER GROSS DESCRIPTION) TUMOR THICKNESS: 45.0 MM MITOTIC COUNT: 66/MM2 PATTERN OF GROWTH: INFILTRATIVE LYMPHOCYTIC INFILTRATE: NON-BRISK VASCULAR INVASION: PRESENT INVASION BEYOND SUBCUTANEOUS TISSUE (BONE, MUSCLE, FASCIA, OR CARTILAGE): NOT IDENTIFIED Margins: Free of malignancy

A. LEFT AXILLA, LEVEL III MARGIN, EXCISION:

Fibroconnective tissue, negative for carcinoma.

B. LEFT AXILLARY CONTENTS, LEVEL I, II, III, LYMPH NODE DISSECTION:

Sixteen lymph nodes, negative for viable metastatic carcinoma on H&E sections See comment.

B. Most of the grossly appearing lymph nodes reveal almost/complete replacement of the nodal parenchyma by fibrosis and extensive histiocytic infiltrate, and therefore lymph node count may not be completely accurate. Foci of tumor necrosis are present in some of the sections (B6, B20); **no viable tumor is readily identified** on H&E sections. These changes are consistent with treatment effect

Select Follow on Therapeutic strategy

- A. Radiation therapy
- B. Cytotoxic chemotherapy.
- C. Systemic Adjuvant immunotherapy.
- D. Surveillance only

Follow on Therapeutic strategy

- A. Radiation therapy
- B. Cytotoxic chemotherapy.
- C. Systemic Adjuvant immunotherapy.

D. Surveillance only

Neoadjuvant then Adjuvant Avelumab : 5/25/18-10/25/19 Complicated by Shingles at Cycle 12. Delayed and then continued to completion.



12/22/2020: Routine Surveillance CT CAP:

- 2.8 x 1.9 cm left adrenal lesion is new and is suspicious for metastases.
- Postsurgical and postradiation changes are noted in the thorax as described above, unchanged.

BIOPSY of Adrenal gland, left:

METASTATIC NEUROENDOCRINE CARCINOMA, CONSISTENT WITH METASTASIS FROM THE KNOWN MERKEL CELL CARCINOMA

Select <u>Salvage</u> Therapeutic strategy

- A. Surgery
- B. Radiation therapy
- C. Ablative therapy
- D. Cytotoxic chemotherapy.
- E. Systemic immunotherapy (Avelumab?)

Avelumab rechallenge: re-initiated 1/15/2021 12/22/2020 09/03/2021



Solitary Site of MCC Metastases

Can this woman be rendered free of disease (NED status) ?

Select <u>NED</u> Therapeutic strategy

- A. Surgery
- B. Radiation therapy
- C. Ablative therapy
- D. Cytotoxic chemotherapy.
- E. Long term immunotherapy (Avelumab?)



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Case Study #3



32 yo F, otherwise healthy

- Mole on right flank
- Followed by dermatology, but stable since childhood
- Bleed spontaneously 2-3 weeks prior to seeking medical attention
- Biopsy 5 mm thick, ulcerated, nodular melanoma, 2 mit/mm2



32 yo F, otherwise healthy

- Brain MRI
 - NED
- PET/CT scan
 - FDG-avid, SQ nodule noted (yellow arrow)



32 yo F with bleeding more and malignant nodule

- Wide local excision
- Sentinel lymph node (no positive nodes)
- Resection of palpable nodule
- T4B
- N1C
- M0

Molecular profiling shows: BRAFV600E

	Me	AJ lanor	CC E na St	ighth age I	Editi II Sul	ion ogrou	ps		
N Category	T Category								
	Т0	T1a	T1b	T2a	T2b	T3a	T3b	T4a	T4b
N1a	N/A	A	A	A	в	в	C	С	C
N1b	в	в	в	в	в	в	C	C	С
N1c	в	в	в	в	в	в	С	С	C
N2a	N/A	Α	Α	А	в	в	C	С	С
N2b	С	в	в	в	в	в	С	C	С
N2c	С	С	С	С	С	С	С	С	С
N3a	N/A	С	С	С	С	С	С	С	D
N3b	С	С	С	С	с	c	С	¢	D
N3c	C	С	С	C	С	C	С	С	D
Instruction	ns						L	egen	d
 Select patient's N category at left of chart. Select patient's T category at top of chart. 							A	Stage IIIA	
 (3) Note letter at the intersection of T&N on grid. (4) Determine patient's AJCC stage using legend. 						в	Stage IIIB		
							С	Stage IIIC	
N/A=Not assigned, please see manual for details.4							D	Stag	e IIID

Gershenwald et al. CA Cancer J Clin 2017

32 yo F, otherwise healthy

- Completed 12 months of therapy
- Had mild intermittent fevers, nausea managed with periodic dose holds and
- Remains NED

How should we monitor?

32 yo F, otherwise healthy

- Followed with quarterly visits and CT chest abdomen and pelvis, yearly brain MRI with no evidence of disease for 21 months
- Approximately two years after last dose of dabrafenib and trametinib, imaging showed multiple new pulmonary nodules; slowly growing over time



 Ultimately RLL nodule was big enough to safely biopsy, and path was consistent with recurrent melanoma; o/w NED outside lungs Now 36-year-old woman with recurrent and metastatic, BRAF^{V600E} melanoma s/p 1 year of adjuvant dabrafenib and trametinib that completed nearly two and a half years prior to biopsy-proven

Now what?



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Case Study #4





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68 y.o. female with a history of 1.1 mm ulcerated melanoma without sentinel lymph node involvement who presented to PMD with unremitting cough. CXR showed upper lung mass. Biopsy consistent with melanoma. CT body showed lung and liver masses. MRI negative.

What are appropriate next steps in care?

- A) Send tissue for Next Generation Sequencing
- B) Obtain expert second opinion consult
- C) Begin first line therapy with an approved regimen
- D) Clinical trials as a first line option consult
- E) All of the above





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The patient above is treated and unfortunately needs to change therapy.

What is the appropriate prior to next line of therapy?

- A) Review of initial NGS
- B) Return to eval by outside consultant
- C) Clinical trial evaluation
- D) Approved second line therapy
- E) All of the above





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Case Study #5





MG is a 63 yo man who works full time as a busy lawyer who is technology savvy, he was diagnosed with a right upper arm cutaneous melanoma 5.5 mm in thickness with 2 microsatellite nodules and 1/5 right axillary sentinel nodes positive for metastatic melanoma, followed by 2 short interval satellite lesions being resected ->Stage IIID (pT4b, pN3c, cM0), NRAS positive. Adjuvant therapy was discussed, pt did not qualify for a relevant clinical trial, therefore Nivolumab was discussed. Patient received 1-1 education with the medical oncologist, reinforced by the Nurse Practitioner & infusion RN & education was reinforced with every visit as well as a consistent systematic comprehensive exam.





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Patient presented for cycle 3 Nivolumab, MG called by phone on 7/1/21 to report several days of soft loose stool to liquid diarrhea consistency 3-4 x per day, mild cramping but no urgency, bloating or blood, a methylprednisolone dose pack was prescribed & a modified diet of low fiber & low residue was reviewed as well as foods to avoid & Imodium as needed for this grade 2. 7/2/21 & 7/3/21 follow up by phone & the EMR "my chart" app in attempt to follow up with patient for a status update. MG admits during his 7/13/21 appointment that diarrhea episodes started ~ 6/24/21 and persisted for ~ 7 days before reporting, he had not taken the methylprednisolone dose pack or imodium as advised but he did modify his diet. MG reported that he was very busy with work, he "didn't have time to call" and stated, "it's[diarrhea] is annoying and I had a few incidences I didn't think I would make it through court but I didn't think overall it was that bad, I could handle it".

This is an example of:

- A) A patient not having an immunotherapy wallet card
- B) Lack of knowledge in the use of communication tools, phone, EMR portal
- C) Gap in personal health literacy
- D) A need for referral to an endocrinologist

#LearnA