Case Studies in Immunotherapy for the Treatment of Melanoma SITC CPG Webinar

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Disclosures

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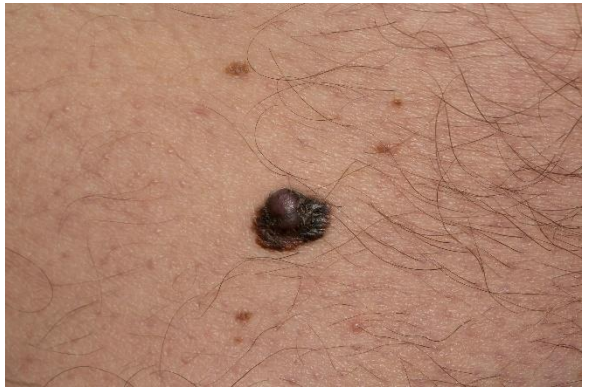
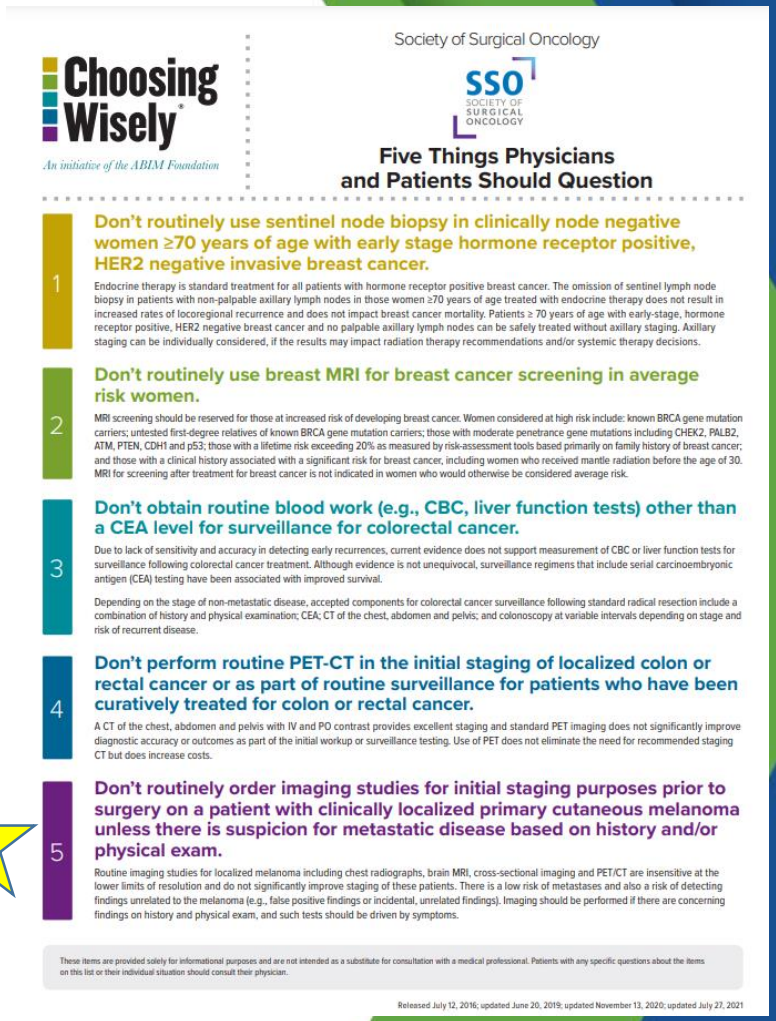
Case #1

- 65 year old RHD male presents with darkening skin lesion left arm
- PMH: Hypertension
- Diagnostic biopsy
  - Superficial spreading melanoma
  - Breslow depth 1.2 mm
  - Clark level IV
  - 2 mit/mm^2
  - No LVI, TILs non-brisk, no regression



Case #1

- Physical exam
  - Healing biopsy site left arm
  - No palpable cervical or axillary adenopathy
- Clinical stage T2a N0
- Recommendation
  - Wide local excision, lymphatic mapping, sentinel lymph node surgery



Choosing Wisely
An initiative of the ABIM Foundation

Society of Surgical Oncology
SSO Society of Surgical Oncology

Five Things Physicians and Patients Should Question

1. **Don't routinely use sentinel node biopsy in clinically node negative women ≥70 years of age with early stage hormone receptor positive, HER2 negative invasive breast cancer.**

   Endocrine therapy is standard treatment for all patients with hormone receptor positive breast cancer. The omission of sentinel lymph node biopsy in patients with non-palpable axillary lymph nodes in those women ≥70 years of age treated with endocrine therapy does not result in increased rates of locoregional recurrence and does not impact breast cancer mortality. Patients ≥ 70 years of age with early-stage, hormone receptor positive, HER2 negative breast cancer and no palpable axillary lymph nodes can be safely treated without axillary staging. Axillary staging can be individually considered, if the results may impact radiation therapy recommendations and/or systemic therapy decisions.

2. **Don't routinely use breast MRI for breast cancer screening in average risk women.**

   MRI screening should be reserved for those at increased risk of developing breast cancer. Women considered at high risk include: known BRCA gene mutation carriers; untested first-degree relatives of known BRCA gene mutation carriers; those with moderate penetrance gene mutations including CHEK2, PALB2, ATM, PTEN, CDH1 and p53; those with a lifetime risk exceeding 20% as measured by risk-assessment tools based primarily on family history of breast cancer; and those with a clinical history associated with a significant risk for breast cancer, including women who received mantle radiation before the age of 30. MRI for screening after treatment for breast cancer is not indicated in women who would otherwise be considered average risk.

3. **Don't obtain routine blood work (e.g., CBC, liver function tests) other than a CEA level for surveillance for colorectal cancer.**

   Due to lack of sensitivity and accuracy in detecting early recurrences, current evidence does not support measurement of CBC or liver function tests for surveillance following colorectal cancer treatment. Although evidence is not unequivocal, surveillance regimens that include serial carcinoembryonic antigen (CEA) testing have been associated with improved survival.

   Depending on the stage of non-metastatic disease, accepted components for colorectal cancer surveillance following standard radical resection include a combination of history and physical examination; CEA; CT of the chest, abdomen and pelvis; and colonoscopy at variable intervals depending on stage and risk of recurrent disease.

4. **Don't perform routine PET-CT in the initial staging of localized colon or rectal cancer or as part of routine surveillance for patients who have been curatively treated for colon or rectal cancer.**

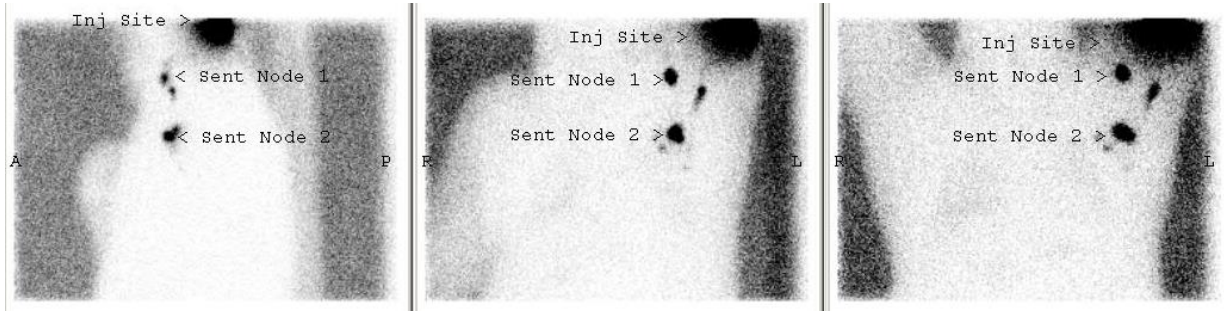
   A CT of the chest, abdomen and pelvis with IV and PO contrast provides excellent staging and standard PET imaging does not significantly improve diagnostic accuracy or outcomes as part of the initial workup or surveillance testing. Use of PET does not eliminate the need for recommended staging CT but does increase costs.

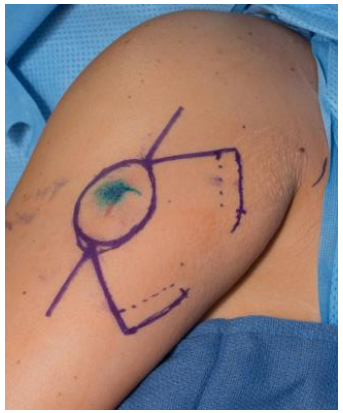
5. **Don't routinely order imaging studies for initial staging purposes prior to surgery on a patient with clinically localized primary cutaneous melanoma unless there is suspicion for metastatic disease based on history and/or physical exam.**

   Routine imaging studies for localized melanoma including chest radiographs, brain MRI, cross-sectional imaging and PET/CT are insensitive at the lower limits of resolution and do not significantly improve staging of these patients. There is a low risk of metastases and also a risk of detecting findings unrelated to the melanoma (e.g., false positive findings or incidental, unrelated findings). Imaging should be performed if there are concerning findings on history and physical exam, and such tests should be driven by symptoms.

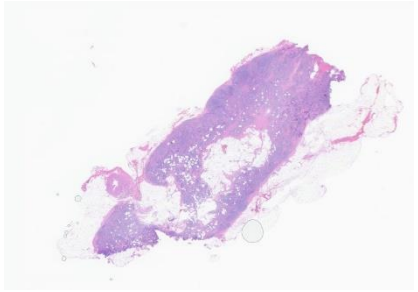
Released July 12, 2016; updated June 20, 2019; updated November 13, 2020; updated July 27, 2021

Case #1

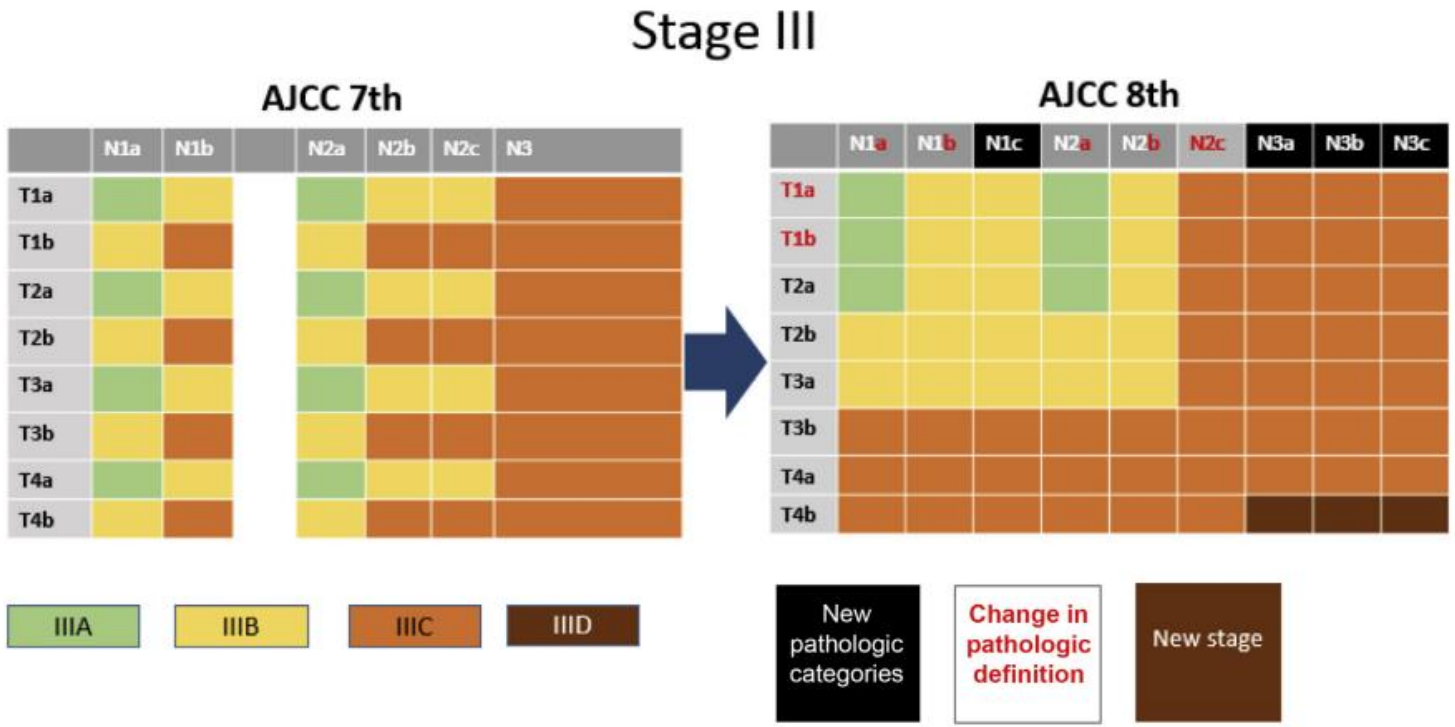




- Surgical pathology
  - WLE: Breslow depth 4.2mm
  - SLN: 1 of 2 SLNs with 8 mm metastasis, without extranodal extension
  - T4a, N1a
- AJCC 8 pathologic stage IIIC



Case #1



AJCC 7th to 8th Edition Change

Case #1

- Next steps:
  - Equipoise for patients with cN0 disease with respect to MSS for nodal observation vs CLND per MSLT-2
- Medical oncology consultation
  - BRAF testing?
  - Imaging studies?
- Discussion
- Treatment recommendations

Panel Recommendations

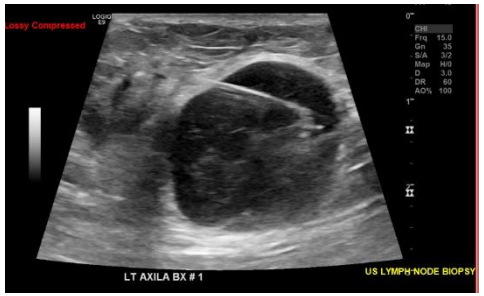
- For patients with resected IIIA melanoma, adjuvant therapy with either anti-PD-1 IC (LE:2) or BRAF-targeted therapy (BRAFm disease) should be considered
- For patients with resected stage III BRAFm melanoma both ICI and targeted therapies have shown similar RFS benefit, but no head to head prospective comparison data, therefore consider toxicity profile of either vs absolute benefit

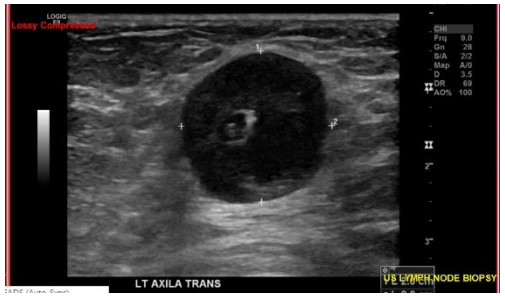
Case #2

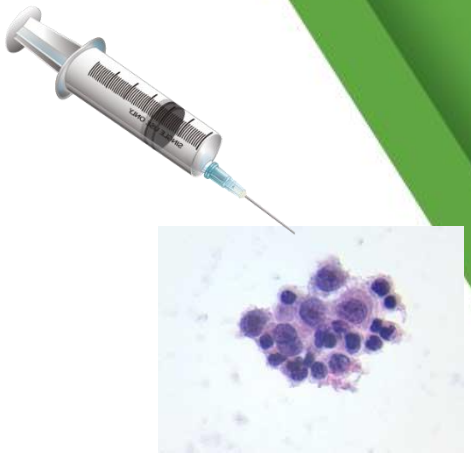
- 50 yo RHD healthy female
- Right axillary mass, enlarging over past 2 months
- PMH: Negative for trauma, infection; no prior cancer
- Physical exam by PCP shows 5 cm right axillary mass
- Imaging
  - Negative mammogram
  - Axillary ultrasound

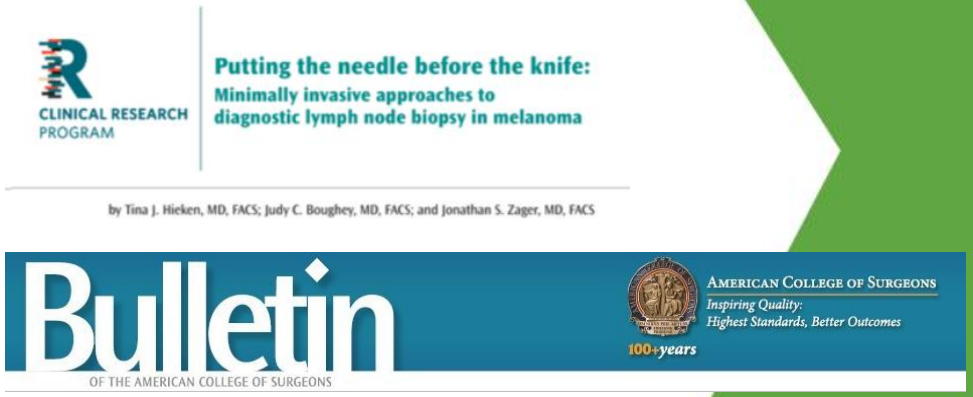
Case #2

- Percutaneous needle biopsy right axilla
  - Metastatic melanoma

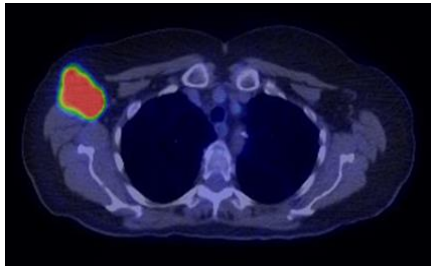








- PET-CT
  - No distant disease
  - Dominant matted nodal mass right axilla



Case #2

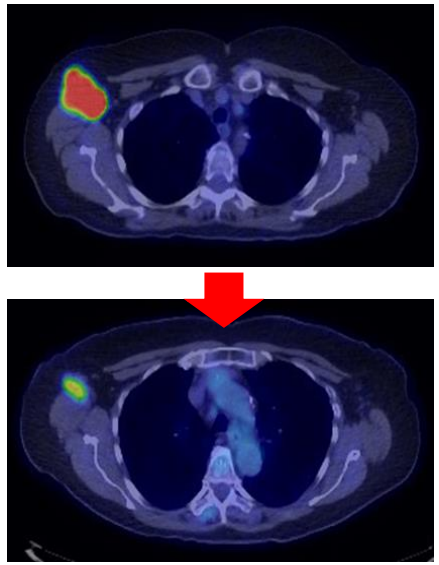
- Multidisciplinary discussion
- Patient enrolled on clinical trial, NeoACTIVATE, NCT03554083, Arm C
- Other options?

Panel Recommendations

- For patients with resectable stage IIIB to IV (without brain metastases) melanoma, while there were no approved neoadjuvant therapies at the time of manuscript publication, neoadjuvant pembrolizumab continued into the adjuvant setting demonstrated improved EFS compared with adjuvant therapy alone in a randomized, phase II trial (LE:2). Neoadjuvant approaches may be considered after multidisciplinary discussion for patients with high-risk stage III and resectable stage IV melanoma. Consideration for clinical trial enrollment is still preferred for eligible patients with high-risk stage III disease.

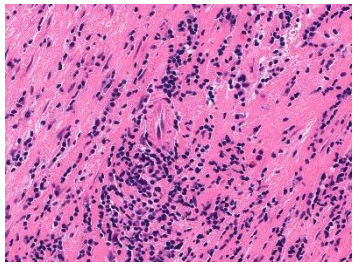
Case #2

- Patient completed 4 cycles of neoadjuvant atezolizumab + tiragolumab
- Physical exam showed marked improvement in matted axillary adenopathy
- Re-staging PET-CT showed iPR

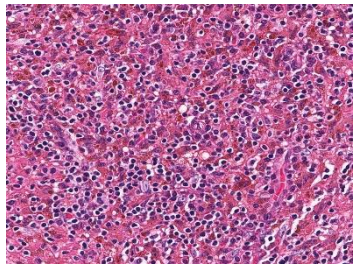


Case #2

- Right axillary lymph node dissection
- Pathology showed pCR (necrosis and fibrosis without viable melanoma with treatment effect)



Area of fibroinflammatory response



No viable tumor cells, macrophages with hemosiderin and melanin

- Adjuvant therapy – per protocol 6 months atezolizumab

Case #2

- <u>Unanswered questions re: neoadjuvant therapy</u>
  - Selection of regimen
    - Immunotherapy over targeted therapy ☑
    - Doublet vs monotherapy
  - When is adjuvant therapy need after neoadjuvant therapy?
  - Should it be response directed?
  - Can extent of operation be response directed?