Melanoma/Cutaneous Oncology

Panelists:
Sunil Reddy (Chair)       Katy Tsai
Susan Swetter            David Minor
Scott Christensen        Thach-Giao Truong
Amanda Kirane            Kevin Kim
Adil Daud                Evan Hall (Fellow)

Case #1

• 64 yo previously healthy F with a history of stage I melanoma diagnosed in 2011 on her R shoulder - pathology showed lentigo maligna, 0.38 mm depth, no ulceration
• 2017 – Patient developed increasing mild-moderate abdominal pain and bloating
• CT CAP w contrast showed a 9 cm necrotic appearing liver mass, mild-moderate ascites, and abdominal lymphadenopathy measuring up to 1.7 cm

• PET/CT showed: 1) the liver mass was FDG-avid, 2) abdominal lymphadenopathy had low-grade FDG-avid metabolism, and 3) development of moderate R pleural effusion also noted to have low-grade FDG avidity
• CT guided biopsy of the liver confirmed metastatic melanoma (+SOX-10+, -AE1/AE3, -Melan-A, -HMB-45)
• BRAF testing: wild-type
• MRI Brain: no evidence of intracranial metastases
• ECOG 1
What would you recommend for initial treatment in this case?

A. Single-agent PD-1 antibody (e.g. pembrolizumab or nivolumab)
B. CTLA-4/PD-1 combination antibody therapy (ipilimumab/nivolumab)
C. Other

If a BRAF V600E mutation had been identified, what would be your first line systemic therapy of choice?

A. Single-agent PD-1 antibody (e.g. pembrolizumab or nivolumab)
B. CTLA-4/PD-1 combination antibody therapy (ipilimumab/nivolumab)
C. BRAF/MEK inhibitor combination (e.g. dabrafenib/trametinib, vemurafenib/cobimetinib, or encorafenib/binimetinib)
D. Other

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Case #1, continued:

• The patient began therapy with ipilimumab and nivolumab
• Within two cycles, she began to feel improvement in her abdominal distention and bloating symptoms.
• Shortly after cycle #3, she developed progressive weakness and difficulty walking over a period of several days. She had one mechanical fall without LOC, but was now unable to climb stairs. She denied back pain, numbness, tingling, vertigo, diplopia, dysphagia or other symptoms.
Case #1, continued:

Clinical Exam:

Lower extremities with reduced strength, particularly in proximal muscles (3+ to 4/5 with hip flexion, leg extension/flexion and quadriceps, R>L)
Normal strength in upper extremities
Normal sensation
Normal Babinski
Diminished reflexes in lower extremities.
New intention tremor in upper extremities

MRI Complete Spine: no abnormal cord signal or enhancement to suggest myelopathy or metastasis.

MRI Brain: no evidence of metastatic disease

LP:
WBC 15 (H) (87% lymphs), RBC 13; protein 167 (H), glucose 69 (nl); cytology negative for malignant cells

Viral serologies: negative

EMG/NCS: motor polyradiculopathy, with features of demyelination noted

Diagnosis felt to be most consistent with Guillain-Barre like syndrome 2/2 immune checkpoint inhibitor therapy

She was treated with corticosteroids (1 mg/kg prednisone) with a prolonged taper. She experienced rapid improvement in her symptoms, which ended up resolving within 3-4 weeks after initiation of steroids.

PET/CT shortly after completion of steroids (after three cycles of ipilimumab/nivolumab) showed complete metabolic response and decreased size of liver lesion (now 5 cm – previously 9 cm).

She continues in a CR by PET presently.
Updated results from CHECKMATE-067: Ipi/Nivo vs Nivo vs Ipi in Stage IV Melanoma


- **Any Grade 3 Treatment Related AE:**
  - 48% Ipi/Nivo vs 17% Nivo
- **Any Grade 4 Treatment Related AE:**
  - 11% Ipi/Nivo vs 5% Nivo
- **Grade 3 Colitis:**
  - 8% Ipi/Nivo vs 1% Nivo


Neurologic Immune-Related Adverse Events:

- Review of >3,700 pts treated on trials with nivolumab +/- ipilimumab:
  - 35 patients (0.93%) had serious neurological IRAEs
    - 22 Neuropathy
    - 6 Encephalitis
    - 5 Non-infective meningitis
    - 3 Neuromuscular disorders


COLUMBUS TRIAL: Encorafenib/binimetinib vs vemurafenib vs encorafenib in BRAF Mutant Melanoma

Case #2

- 58 yo otherwise healthy male noted to have a hyperpigmented lesion of his back
- Biopsy showed invasive melanoma, nodular type, Breslow depth at least 3.7 mm, mitotic index 10/mm², without ulceration. He had no clinically detectable lymph nodes.

He underwent wide local excision with sentinel lymph node biopsy. Pathology showed uninvolved surgical margins with 1/8 total involved lymph nodes (four sampled in R axilla, four in L axilla), with melanoma in lymph node measuring 1.1 mm in greatest dimension. Final pathologic staging was pT3apN1a (stage IIIB by AJCC 8th edition)

Post-operatively, PET/CT did not reveal evidence of metastatic disease.

BRAF testing was positive for V600E mutation.

Which of the following would you recommend for further treatment at this time?

A. No further treatment recommended
B. Radiation to the involved lymph node basin
C. Adjuvant PD-1 (nivolumab) for one year
D. Adjuvant BRAF/MEK inhibition (dabrafenib/trametinib) for one year

The patient began therapy with adjuvant nivolumab, and has been tolerating it well without evidence of recurrent disease thus far (approx. 7 months into his course).
Case #3

- 66 year old female with a history of Merkel cell carcinoma:
  - 2014 – Underwent surgical resection of R scalp Merkel cell carcinoma, followed by adjuvant radiation therapy
  - 2016 – Surveillance imaging detected an FDG-avid pulmonary nodule, which was removed by lobectomy with pathology showing metastatic Merkel cell carcinoma
  - 2017 – CT chest showed mildly enlarged subcarinal lymph adenopathy and a new R lung nodule measuring 1.5 cm. The lung nodule was biopsied and found to represent metastatic Merkel cell carcinoma.
What strategy for systemic therapy would you recommend?

A. Cytotoxic chemotherapy (e.g. platinum/etoposide)
B. Immunotherapy (PD-1 antibody) (such as avelumab or pembrolizumab)
C. Other

Case # 3 continued:

- The patient began pembrolizumab with subsequent imaging showing stable disease for several months.
- Late 2018 – She began to feel increasing fatigue and was noted to have increase in number and FDG avidity of pulmonary nodules (largest 1.7 cm), new FDG avid lesion in her L gluteus muscle (biopsy proven metastatic MCC).

Avelumab in 2nd Line Advanced Merkel Cell Carcinoma: JAVELIN-200 Trial

Kaufman et al, JITC, 2018, 6:7

Pembrolizumab in 1st Line for Advanced Merkel Cell Carcinoma: KEYNOTE-017

Nghiem et al, NEJM, 2016, 374:2542-2552
Case #4

- 57 yo previously healthy M with progressive vision loss of the L eye
- August 2018 – He was found to have a large mass in the ciliary body concerning for uveal melanoma.
- CT CAP showed no evidence of metastatic disease

Case #4, continued

- Patient underwent enucleation with orbital implant. Pathology showed “choroidal melanoma” with basal diameter 14 mm, thickness 10 mm, size category 3. There were negative surgical margins. Staging was pT3a, G2, pNX, pMX.
- Gene expression profiling was obtained (Castle Biosciences) and showed GEP class 2 (high risk) and elevated expression of PRAME (+PRAME).

The patient was recommended to undergo a plan of surveillance imaging (alternating CT CAP every 6 months with MRI Liver with Eovist every six months)

- MRI Liver showed >20 new liver lesions (largest 1.1 x 1.1 cm) concerning for metastatic disease
- Biopsy confirmed metastatic melanoma.
Thank you to the panelists for their participation and expertise and to the audience for your attention!