Case 1: 64 year-old male

- Worsening itchy, bleeding, pigmented lesion on left upper back for 3-4 months
- Has not seen an MD in years
- National park groundskeeper, +++ sun exposure

Local excision: Invasive melanoma, 5.8mm deep, Clark IV, + ulceration, & 10 mitoses/mm²

= pT4b = at least stage IIC

Referred to academic center, undergoes wide local excision & sentinel lymph node biopsy

Pathology results:

- Wide local excision: scar/granulation tissue, no residual melanoma
- 2/2 left axillary sentinel lymph nodes negative for melanoma
Case 1: 64 year-old male with stage IIC melanoma

Q1: Next step?
A. Frequent skin & lymph node exams
B. Gene-expression profiling for recurrence risk
C. Surveillance PET scans/nodal US
D. Interferon
E. Nivolumab

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END OF CASE 1

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Case 2: 69 year-old female

- Evolving mole on right back, diagnosed with 0.9mm melanoma with 2 mitoses per mm2 and ulceration, no vascular invasion
- Underwent WLE & Sentinel node biopsy:
  - some residual melanoma on reexcision (with clear margins)
  - 0.2cm focus of melanoma in sentinel axillary lymph node
- Referred to Medical Oncology for pT1bN1a (stage IIIB) disease
Case 2: 69 year-old female, stage IIIB Melanoma

- PMHx Depression/anxiety, Obesity, & DM2 on insulin
- Exam shows healing axillary wound from node Bx, otherwise NAD
- ECOG PS 0
- Labs unremarkable

Q1: What additional tests do you order on the pathologic sample?
A. PD-L1 immunohistochemistry score
B. BRAF mutation analysis
C. Both
D. Neither

Q2: Does this patient need a completion axillary node dissection?
A. Yes
B. No
C. It depends

Q3: BRAF V600E mutation found. What is the next step?
A. Surveillance
B. Interferon
C. Ipilimumab
D. Nivolumab
E. Dabrafenib + trametinib
ESMO 2017 (Sept)
COMBI-aD: International, phase III randomized, double-blind
- Adjuvant dabrafenib + trametinib vs placebo in BRAF V600 mutated resected stage III with >1mm of nodal disease (1yr Tx)
- Est 3-yr RFS 58% vs 39% (HR 0.47, P=0.001)
- 3yr OS 86% vs 77% (HR 0.57, P=0.008)
- 41% of pts on TKIs had Gr 3-4 AEs
- More permanent discontinuations (20%), dose reductions (38%), and interruptions (69%) on TKI arm

RFS
OS

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Checkmate-238: International, phase III randomized, double-blind
- Resected stage IIIB, IIIC or IV
- Nivolumab vs ipilimumab (1yr Tx)
- ~1:1 BRAF mutated & unmutated
- Prespecified interim analysis: RFS in IT pop
- 1-yr RFS: Nivo 70% vs Ipi 60% (HR 0.65, P<0.001), OS not mature
- TRAEs Gr 3-4: Nivo 14% vs Ipi 48%


END OF CASE 2

Case 3: 65 year-old male
- PMHx of MI/CAD s/p PCI, HTN and stage IIIB melanoma 1 year ago, 1/4 nodes positive, 0.9cm with extracapsular extension, BRAF V600E+
- Deferred adjuvant systemic therapy and completion nodal dissection required for clinical trial, received RT to axilla
- Followed with axillary US and PET scan surveillance
Case 3: 65 year-old male, Hx stage III melanoma

Negative PET 6 months prior
Negative Axillary US 3 months prior
Liver biopsy confirms metastatic melanoma: PD-L1 negative

Case 3: 65 year-old male, metastatic melanoma
- BRAF V600E+, PD-L1 negative

- Very fit, but slight RUQ discomfort, anorexia, ECOG 1
- Repeat Cardiac evaluation reassuring, LVEF 65%
- Lives close to infusion center

Q1: What do you recommend?
A. BRAF inhibitor alone
B. BRAF + MEK inhibition
C. Nivolumab + Ipilimumab
D. Nivo or Pembro alone
E. Ipi Alone

Case 3: 65 year-old male, BRAF+ metastatic melanoma
- Pt starts on vemurafenib + cobimetinib and week 2 develops fever Tm 102.5F, rigors, and dehydration requiring IV fluids. Infectious workup negative. Meds held for 3 days with resolution of symptoms.

Q2: What do you do?
A. Restart both at same dose, with ibuprofen/APAP PRN
B. Restart both with reduced dose
C. Restart Vemurafenib only
D. Switch to immunotherapy
COMBI-d: dabrafenib +/- trametinib in BRAFV600+ Metastatic Melanoma

Overall Survival

CheckMate 067: Nivo/Ipi vs Nivo vs Ipi: PFS

CheckMate 067: Nivo/Ipi vs Nivo vs Ipi: OS

Now recruiting: NCI/Cooperative group trial

EA6134 – A Randomized Phase III Trial of Dabrafenib + Trametinib followed by Ipilimumab + Nivolumab at Progression vs. Ipilimumab + Nivolumab followed by Dabrafenib + Trametinib at Progression in Patients with Advanced BRAFV600 Mutant Melanoma
Case 4: 59 year-old male

- Incidentally discovered pulmonary mass on CT chest angiogram for aortic regurgitation workup
- PMHx of several nonmelanoma skin cancers
- Otherwise healthy, ECOG 0

CT-guided Lung mass Bx: Metastatic melanoma, BRAF WT
PD-L1 IHC: Positive, 50%

Q1: What systemic therapy do you offer?
A. Nivolumab + Ipilimumab
B. Nivolumab or Pembrolizumab alone
C. Ipilimumab
Case 4: 59 year-old male, BRAF WT, PD-L1+

- Starts Nivolumab + ipilimumab q3wks
- After 3 cycles, Develops grade 2 pneumonitis
  = Symptomatic; limits instrumental ADL;
  no hospitalization required

Q2: What do you do?
A. Discontinue ipilimumab,
   continue Nivo q2 weeks
B. D/C Nivo & ipi, give prednisone
   1-2mg/kg/day

Case 4: 59 year-old male, Gr 2 Pneumonitis on Nivo/Ipi

Pt recovers from pneumonitis, completely resolves
Repeat PET shows partial response

Q3: Next step?
A. Observe with surveillance imaging
B. Restart Nivolumab monotherapy q2 weeks
C. Restart Nivolumab + ipilimumab
Case 4: 59 year-old male, s/p Pneumonitis on Nivo/Ipi

- Pt rechallenged with nivolumab alone
- Continues q2 weeks for 58 cycles (over 2 years)
- Tolerating therapy well, continued response
- Achieves CR by 7 months, no recurrence

Q4: Any changes to management?

A. Continue nivolumab until intolerance or progression
B. Discontinue nivolumab, continue serial imaging

END OF CASE 4

Thank you!