

18th Multidisciplinary Management of Cancers: A Case-based Approach**2018 Melanoma Panel**

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18th Multidisciplinary Management of Cancers: A Case-based Approach**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

18th Multidisciplinary Management of Cancers: A Case-based Approach**Case 1: 64 year-old male with itchy, bleeding mole**

- 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

18th Multidisciplinary Management of Cancers: A Case-based Approach**Case 1: 64 year-old male with \geq IIC Melanoma**

- Pathology results:
 - Wide local excision: scar/granulation tissue, no residual melanoma
 - 2/2 left axillary sentinel lymph nodes negative for melanoma



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Case 1: 64 year-old male with stage IIC melanoma

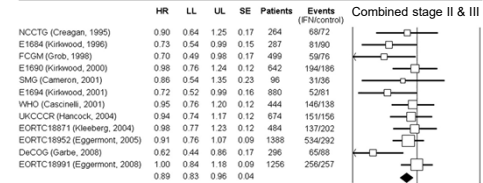
Q1: Next step?

- A. Frequent skin & lymph node exams
- B. Gene-expression profiling for recurrence risk
- C. Surveillance PET scans/nodal US
- D. Interferon



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Adjuvant Interferon Meta-analysis: Overall Survival



OS Subgroup analysis of just stage II pts: 0.70 (0.50 to 0.98)

From: Interferon Alpha Adjuvant Therapy in Patients With High-Risk Melanoma: A Systematic Review and Meta-analysis
 J Natl Cancer Inst. 2010;102(17):1493-501. doi:10.1093/jnci/djq009
 J Natl Cancer Inst | © The Author 2010. Published by Oxford University Press.



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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



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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

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Case 2: 69 year-old female, stage IIIB Melanoma

Q1: What additional tests do you order on the pathologic sample?

- A. PD-L1 immunohistochemistry score
- B. BRAF mutation analysis
- C. Both
- D. Neither

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Case 2: 69 year-old female, stage IIIB Melanoma

Q2: Does this patient need a completion axillary node dissection?

- A. Yes
- B. No
- C. It depends

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Case 2: 69 year-old female, stage IIIB Melanoma

Q3: BRAF V600E mutation found. What is the next step?

- A. Surveillance
- B. Interferon
- C. Ipilimumab
- D. Nivolumab
- E. Dabrafenib + trametinib



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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=0.0006)
- 41% of pts on TKIs had Gr 3-4 AEs
- More permanent discontinuations (26%), dose reductions (38%), and interruptions (66%) on TKI arm

Long GV, et al. N Engl J Med. 2017 Nov 9;377(19):1813-1823.

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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 IIT 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 46%

Weber J, et al. N Engl J Med. 2017 Nov 9;377(19):1824-1835.

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END OF CASE 2

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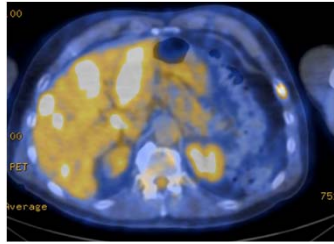
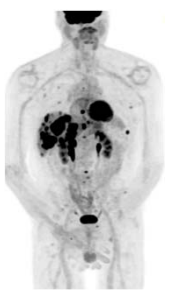
Case 3: 65 year-old male

- 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

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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

18th Multidisciplinary Management of Cancers: A Case-based ApproachCase 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

18th Multidisciplinary Management of Cancers: A Case-based ApproachCase 3: 65 year-old male, metastatic melanoma
- BRAF V600E+, PD-L1 negative

Q1: What do you recommend?

- A. BRAF inhibitor alone
- B. BRAF + MEK inhibition
- C. Nivolumab + Ipilimumab
- D. Nivo or Pembro alone
- E. Ipi Alone

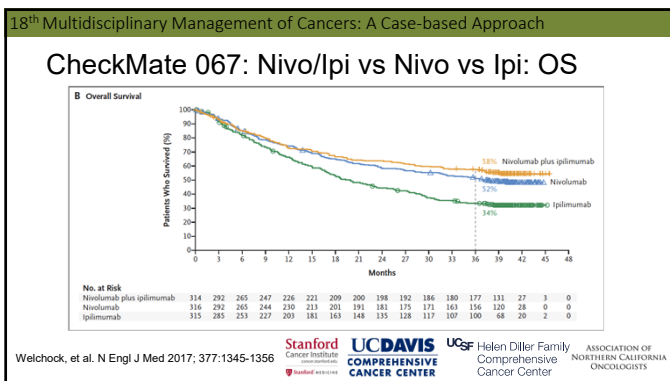
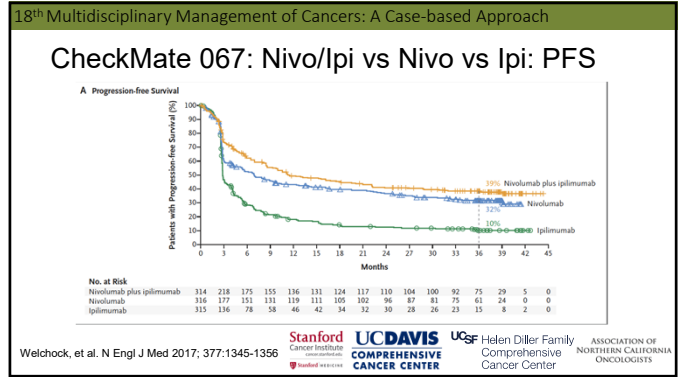
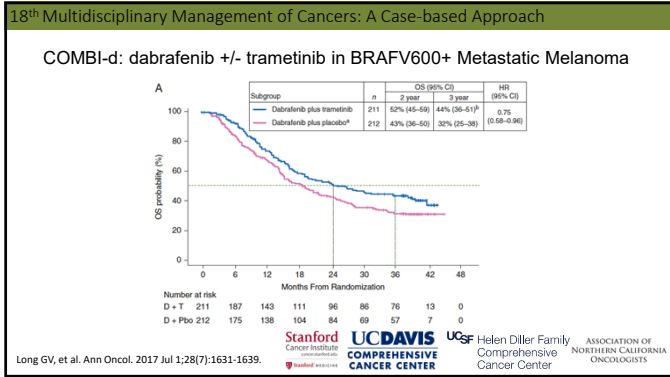
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Case 3: 65 year-old male, BRAF+ metastatic melanoma

- 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 BRAF inhibitor
- C. Restart Vemurafenib only
- D. Switch to immunotherapy



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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

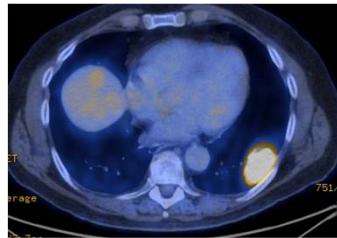
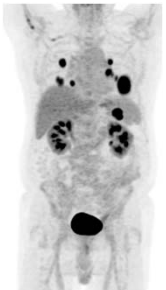
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END OF CASE 3

Case 4: 59 year-old male

- Incidentally discovered pulmonary mass on CT chest angiogram for aortic regurgitation workup
- PMHx of several nonmelanoma skin cancers

Case 4: 59 year-old male



CT-guided
Lung mass Bx:
**Metastatic
melanoma,
BRAF WT**

PD-L1 IHC:
Positive, 50%

Case 4: 59 year-old male, BRAF WT, PD-L1+

Q1: What systemic therapy do you offer?

- Nivolumab + Ipilimumab
- Nivolumab or Pembrolizumab
- Ipilimumab

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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

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

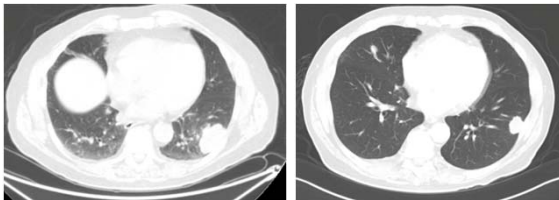
Q2: What do you do?

- Discontinue ipilimumab, continue Nivo q2 weeks
- D/C Nivo & ipi, give prednisone 1-2mg/kg/day

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

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

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Case 4: 59 year-old male, s/p Pneumonitis on Nivo/Ipi

Q3: Next step?

- Observe with surveillance imaging
- Restart Nivolumab monotherapy q2 weeks
- Restart Nivolumab + Ipilimumab

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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

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Case 4: 59 year-old male, CR on Nivolumab 2 years

Q4: Any changes to management?

- Continue nivolumab until intolerance or progression
- Discontinue nivolumab, continue serial imaging

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END OF CASE 4

Thank you!

