



Brigham and Women's Hospital

Founding Member, Mass General Brigham

ONCOLOGY BOARD REVIEW

Daniel Roberts, MD

Associate Medical Director for Quality, DFCI Network

DFCI-Foxborough Regional Campus

Lank Center for Genitourinary Oncology



Dan Roberts, MD



Loyola University of Chicago, Stritch School of Medicine
Medicine Residency @BIDMC
Hematology-Oncology Fellowship @BIDMC
MBA Candidate – Isenberg School of Management @UMass

- Clinical focus: GU Oncology, some general heme/onc
- Administrative focus: Quality and Patient safety
- Research Focus: Academic-Community hybrid model of care



DISCLOSURES

I have no financial disclosures



OBJECTIVES

Use Q&A format to:

- Highlight common clinical scenarios and their management in general hematology-oncology
- Review key oncologic concepts for non-oncologists caring for patients with cancer



Question 1

A 63-year-old woman previously completed 5 years of tamoxifen after lumpectomy and RT for a 1.5 cm, ER/PR +, her-2 negative, node negative breast cancer. She presents to your office with new, severe, localized low back pain. Physical examination is normal, including the neurologic exam. The alkaline phosphatase is 330 (elevated), and the remainder of her CMP and CBC are WNL. A bone scan is abnormal in several areas of the thoracic and lumbar spine, as well as in several ribs. The immediate next course of action at this point should be:

- A. Combination chemotherapy
- B. Hormonal therapy +/- CDK inhibitor
- C. MRI scan of the spine
- D. Radiation therapy to areas of localized disease
- E. Systemic staging scans and bone biopsy



Question 1 - Answer

- A. Combination chemotherapy – almost never recommended with metastatic HR+ breast cancer.
- B. Hormonal therapy +/- CDK inhibition – will likely be appropriate initial systemic therapy, but key initial issue is evaluating for cord compression.
- C. MRI scan of the spine – you must rule out or rule in spinal cord compression – and neurologic outcome is best if it is discovered prior to the onset of neurologic findings.
- D. Radiation therapy to areas of localized disease – this might be appropriate at some time for palliation, and urgent RT vs. surgery would be indicated if spinal cord compression is present on MRI.
- E. Systemic staging scans and biopsy will be required, but evaluation of cord compression is most urgent.



Question 2

A 68-year-old male presents with back pain, anemia and fevers. He has no lymphadenopathy or splenomegaly. Laboratory studies are notable for HCT of 34%, total protein of 9.8 gm/dL, albumin 2.8 gm/dL, creatinine of 3.2 mg/dL, and calcium of 12.3 mg/dl. Plain films of the spine show generalized osteoporosis without focal defects. Which one of the following is true:

- A. Fever is a worrisome sign and infection is a life-threatening risk in this disease
- B. Renal failure is likely a reversible consequence of dehydration
- C. The patient should undergo CT scans with IV contrast to evaluate for potential sources of fever
- D. The lack of lytic lesion argues against an underlying diagnosis of myeloma
- E. IgA and IgG paraproteins have similar serum viscosities



Question 2 - Answer

- A. Fever is a worrisome sign and infection is a life-threatening risk for myeloma patients. Infection is the most common cause of disease-related mortality.
- B. Renal failure is a common complication of myeloma due to myeloma kidney (via most commonly cast nephropathy, proximal tubular toxicity, deposition disease), as well as hypercalcemia, and can be acutely and irreversibly worsened by dehydration.
- C. Patients with myeloma should not receive IV CT contrast in the setting of kidney injury, and contrast should be used very judiciously even in patients with normal renal function.
- D. The most common radiographic abnormality seen in patients with myeloma is generalized osteoporosis, not lytic bone lesions. CT, MRI and PET are much more sensitive for bone involvement.
- E. IgA and IgG paraproteins have different serum viscosities – IgA paraproteins have higher viscosity than IgG paraproteins. IgM has highest viscosity, although IgM myeloma is rare.



Question 3

A 46-year-old woman presents to your office for routine health care maintenance. She is concerned about the possibility of developing breast cancer and asks you about her risk factors. Which statement is correct:

- A. A previous history of LCIS does not substantially increase her risk of developing breast cancer
- B. Presence of a BRCA1 germ line mutation will substantially increase her risk of developing breast cancer
- C. A maternal aunt with post-menopausal breast cancer will substantially increase her risk of developing breast cancer
- D. The majority of women with breast cancer have identifiable risk factors for the development of breast cancer
- E. Duration and degree of estrogen (endogenous and exogenous) exposure is not associated with increased of developing breast cancer



Question 3 - Answer

- A. A previous biopsy which revealed LCIS will substantially increase her risk of developing breast cancer – LCIS increases the likelihood of future breast cancer incidence to approximately 1% per year.
- B. BRCA1 (65-79%) and BRCA2 (36-53%) mutations are associated with an increased risk of breast cancer.
- C. First degree relatives and relatives who develop breast cancer at a younger age confer the greatest risk on family members.
- D. 80-85% of patients have no identifiable risk factors other than being a woman.
- E. Increased duration and degree of estrogen (endogenous and exogenous) exposure will increase the risk of developing breast cancer – early menarche, HRT, etc.



Question 4

A 67-year-old male smoker presents with headaches, forgetfulness, And poor coordination. Several times over the past few weeks he has had periods of confusion and urinary incontinence. Head CT scan reveals multiple round enhancing lesions. Chest x-ray shows a 2 cm lesion in the right mid lung field. The most likely diagnosis is:

- A. Prostate cancer metastatic to lung and brain
- B. Pneumonia with brain abscesses
- C. Colon cancer with lung and brain metastases
- D. Non-small cell lung cancer with brain metastases
- E. Gastric cancer with lung and brain metastases



Question 4 - Answer

- A. Prostate cancer commonly metastasizes to bone, rarely to lung, and even more rarely to brain.
- B. Pneumonia with brain abscesses – possible, rare, no infectious symptoms in this patient.
- C. Brain metastases are an uncommon complication of colon cancer.
- D. Brain metastases are very common in patients with carcinoma of the lung, both at presentation and later in the course of illness. Brain MRI included in routine staging. NSCLC (80+%) is much more common than SCLC(15-20%), therefore NSCLC is the most likely diagnosis.
- E. Brain metastases are less common with gastric cancer.



Question 5

A 26-year-old woman with stage II Hodgkin lymphoma and bulky mediastinal disease is treated with ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) and radiation to the mediastinum. Which of the following is most true:

- A. She is more likely to die of other causes than HL
- B. Given she is over 20, she is not at increased risk of breast cancer
- C. She should receive bleomycin with every cycle of chemotherapy
- D. She is likely to have difficulty with fertility in the future
- E. She is not at increased risk for heart disease



Question 5 - Answer

- A. HD is highly curable, but there is increased mortality from other diseases, and she is more likely to die of other causes, including treatment-related heart disease and secondary cancers.
- B. She has an increased risk of breast cancer – women under 30 who receive chest radiation have an increased risk of breast cancer and should be screened more aggressively per NCCN guidelines (initiate 8-10 years post-radiation, include MRI and mammography).
- C. If PET CR after 2 cycles of ABVD, bleomycin is frequently omitted given risk of pulmonary toxicity (fibrosis).
- D. She is likely to remain fertile without increased risk of children with birth defects – ABVD and chest radiation do not impair fertility or decrease the likelihood of having a normal child.
- E. She is at increased risk for heart disease – she is at increased risk for cardiomyopathy from doxorubicin and coronary artery disease from radiation.



Question 6

A 46-year-old Japanese-American woman, never smoker, is diagnosed with stage IV adenocarcinoma of the lung, metastatic to liver and bone. Which of the following is correct:

- A. She is potentially curable with intensive modern chemotherapy
- B. The likelihood of responding to an EGFR kinase inhibitor is related to the presence of specific mutations in the kinase region
- C. The likelihood of having a mutation of the kinase region of EGFR is random and not related to gender, smoking history or ethnic background
- D. Cytotoxic chemotherapy combined with immunotherapy is the only potentially beneficial treatment
- E. Development of resistance to kinase inhibitors is rare



Question 6 - Answer

- A. She is incurable and modern therapy has not changed this fact, although average duration of survival is certainly increasing.
- B. The likelihood of responding to an EGFR kinase inhibitor is related to the presence of a mutation in the kinase region. EGFR overexpression alone, without tyrosine kinase mutation, is not associated with response to TKIs.
- C. The likelihood of having a mutation of the kinase region of EGFR is increased in this patient as she is a woman, a non-smoker and of Asian descent.
- D. If her tumor has an EGFR kinase mutation she has a good chance of responding to an inhibitor. Patients with EGFR driver mutations generally do not respond well to IO.
- E. Development of resistance to EGFR kinase inhibitors eventually develops in most patients.



Question 7

A 22-year-old man presents with a left supraclavicular mass and an otherwise normal physical examination. Chest x-ray shows a widened mediastinum. Aspiration cytology of the supraclavicular mass demonstrates undifferentiated carcinoma. The next clinical action should be:

- A. Initiation of multi-agent chemotherapy
- B. MRI scan of the chest
- C. Mediastinoscopy and biopsy of the para-tracheal nodes
- D. Testicular ultrasound
- E. Initiation of radiation therapy to the mediastinum and supraclavicular areas



Question 7 - Answer

- A. Initiation of multi-agent chemotherapy – while likely ultimately indicated, need a firm diagnosis first. FNA often inadequate for precise diagnosis of lymphomas and germ cell tumors. All testicular cancers are potentially curable regardless of stage. Indeed, there is no stage IV for testicular cancer (I-IIIC).
- B. MRI scan of the chest – will not add helpful information as resection is not indicated in this disease.
- C. Mediastinoscopy and biopsy of the para-tracheal nodes – only if negative testicular imaging, and supraclavicular node would be an easier site of excisional/incisional biopsy.
- D. Testicular ultrasound – occult testicular cancers can present with this pattern of spread and they are highly curable and relatively common in this age group – so the burden of proof is on you to find curable diseases. Orchiectomy will provide definitive pathology in most cases of testicular cancer.
- E. Initiation of radiation therapy to the mediastinum and supraclavicular areas – better to know what you are treating – this would be clearly palliative, and there is a high chance of response to multiagent chemotherapy.



Question 8

In which of the following patients would yearly screening with low-dose CT for lung cancer NOT be considered:

- A. 47F with 2 ppd active cigarette use and history of lung cancer in both parents.
- B. 57F with history of 1 ppd cigarette use from ages 15-50.
- C. 70M with asbestos exposure, 50 pyh tobacco use, who quit smoking at age 58.
- D. 75F with active ½ ppd cigarette use since age 30.
- E. 60M with 50 pyh who stopped smoking after an MI at age 50.



Question 8 - Answer

- A. Criteria for screening are varied, but most guidelines include age range of 55-79, at least 20-30 pyh tobacco use, and active tobacco use within the past 15 years. This patient is younger, at 47, than current screening guidelines recommend initiating CT scanning. The remainder of the patients (choices B-E) are appropriate for screening CT as per guidelines above.

Organization	Recommendation	Year
American Association of Thoracic Surgery	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 79 years with ≥ 30 pack-year history of smoking and current smoker or quit within past 15 years; ages 50 to 79 years with ≥ 20 pack-year history and cumulative risk $> 5\%$ over next 5 years; or lung cancer survivors with no incidence of disease for ≥ 4 years).	2012
American Cancer Society	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 74 years with ≥ 30 pack-year history of smoking and current smoker or quit within past 15 years).	2013
American College of Chest Physicians	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 77 years with ≥ 30 pack-year history of smoking and current smoker or quit within past 15 years).	2018
American Society of Clinical Oncology	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 74 years with ≥ 30 pack-year history of smoking and current smoker or quit within past 15 years).	2019
Canadian Task Force on the Periodic Health Examination	Recommends screening asymptomatic adults aged 55 to 74 years with at least a 30 pack-year smoking history who smoke or quit smoking < 15 years ago with low-dose CT every year for 3 consecutive years.	2016
National Comprehensive Cancer Network	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 74 years with ≥ 30 pack-year history of smoking or if no longer smoking, smoking cessation within 15 years, or age ≥ 50 years with a ≥ 20 pack-year history of smoking with 1 additional risk factor*).	2018
US Preventive Services Task Force	Recommends annual low-dose CT scan screening for high-risk individuals (ages 50 to 80 years with a 20 pack-year history of smoking and current smoker or quit within past 15 years). Discontinue when person has not smoked for 15 years or if limited life expectancy.	2021
Centers for Medicare and Medicaid Services	Recommends annual low-dose CT scan screening after completion of a shared decision-making visit for high-risk individuals (ages 55 to 77 years with ≥ 30 pack-year history of smoking and current smoker or quit within the past 15 years).	2015
American Academy of Family Physicians	Concludes that evidence is insufficient to recommend for or against low-dose CT scan screening in persons at high risk for lung cancer based on age and smoking history.	2013



Question 9

An 85 year-old male presents with progressive low back pain and normocytic anemia. Imaging demonstrates multiple bone lesions c/w metastases, alk phos is 542 and PSA is 89. Bone biopsy confirms adenocarcinoma c/w prostate origin. Given his age and symptomatic metastatic disease, androgen deprivation therapy (ADT) with leuprolide +/- additional antiandrogenic therapy is recommended as initial therapy. Which of the following is NOT a well-described potential effect of leuprolide:

- A. Hot flashes
- B. Decreased libido
- C. Depression and/or cognitive changes
- D. Increased bone density
- E. Metabolic syndrome/DM



Question 9 - Answer

- D. Increased bone density. ADT is associated with decreased bone density, and bone density needs to be monitored during treatment.

All of the other choices are potential adverse effects of ADT. Additional potential risks include fatigue, increased fat mass/decreased muscle mass, erectile dysfunction, and possibly increased risk of cardiovascular events.

Of note, GnRH antagonists (degarelix) appear to have a lower risk of cardiovascular events as compared to GnRH agonists (leuprolide)



Question 10

A 77-year-old woman with stage IV NSCLC has been doing well for several months on maintenance pembrolizumab + pemetrexed. She then presents to the ER with rapidly progressive dyspnea over the past week accompanied by dry cough. She has not had fevers or sick contacts. In the ER, O2 sat on RA is 82%, RR 22. CXR is unremarkable, ECG shows tachycardia. PECT is without clot, shows stable R hilar mass, and new diffuse GGOs and areas of mildly increased interstitial markings. BNP is 200 (normal) and recent echocardiogram showed nl PASP and EF.

Along with admission to the hospital, which one of the following interventions is most urgently indicated:

- A. Pip-tazo/vanco for healthcare-associated pneumonia
- B. Enoxaparin for suspected small vessel thromboembolic disease
- C. Steroids at a minimum dose of 1 mg/kg prednisone or IV equivalent
- D. Etanercept
- E. Furosemide



Question 10 - Answer

- A. Atypical pneumonia may present this way and antibiotics are often given with the initial presentation of pneumonitis, but this presentation is more consistent with ICI (immune checkpoint inhibitor)-induced pneumonitis.
- B. There is no evidence of chronic thromboembolic disease by recent echo or current CT imaging.
- C. Early initiation of steroids is critical for ICI-induced pneumonitis, which is the most likely diagnosis in this patient without significant evidence of infection or CHF and new symptoms and radiographic findings suggestive of pneumonitis. Often a dose of 2 mg/kg/day solumedrol is initiated with hypoxemia-inducing pneumonitis, but a minimum of 1 mg/kg prednisone or equivalent is recommended in all current ICI toxicity guidelines.
- D. Etanercept may be indicated for steroid-refractory ICI pneumonitis, but is not recommended as frontline therapy.
- E. Diuresis may be considered, but the clinical evidence is most supportive of pneumonitis and not CHF as primary driver of hypoxemic respiratory distress.



Question 11

46-year-old woman with epithelial ovarian cancer is found at the time of surgical debulking to have bilateral ovarian masses with multiple peritoneal and omental nodules, 3/17 lymph nodes involved with disease, as well as ascitic fluid. All tumor that can be removed is removed, but tumor masses of up to 2-3 cm remain. There is no evidence of disease outside of the peritoneal cavity. Postoperatively, the patient is treated with paclitaxel and carboplatin for 6 cycles.

Which of the following is true regarding patients with non-optimally debulked stage 3 ovarian cancer:

- A. A very low chance of response to chemotherapy and a very low chance of cure.
- B. A high chance of complete clinical response, but a low chance for cure.
- C. A high chance of response and a high chance for cure.
- D. She will need radiation therapy delivered to the whole abdomen.
- E. She will need localized radiation therapy to the pelvis.



Question 11 - Answer

- A. Ovarian cancer is a tumor that responds to many chemotherapy and targeted agents but has a high recurrence and death rate.
- B. A high chance of complete clinical response, but a low chance for cure – as above.
- C. As in “B”
- D. Whole abdominal radiation is very toxic, limits the ability to give chemotherapy, and does not improve outcome.
- E. Localized radiation therapy to the pelvis limits the ability to give chemotherapy and does not improve outcome.



Question 12

A 72-year-old man presents with hematuria. Cystoscopy reveals multiple bladder nodules which are biopsied and reveal urothelial cell carcinoma. The likelihood of developing metastatic bladder cancer is most closely related to:

- A. The size of the tumors in the bladder
- B. The number of tumors in the bladder
- C. History of smoking
- D. Family history of bladder cancer
- E. Bladder wall muscle invasion by the tumor



Question 12 - Answer

- A. Tumors without muscle invasion can be large and still have a low risk for developing metastases.
- B. A large number of tumors in the bladder can be technically challenging to remove and treat, but this does not affect survival if adequate resection is achieved.
- C. History of smoking – this is a risk factor for developing bladder cancer, but does not determine likelihood of developing metastases.
- D. Family history – weak risk factor for developing bladder cancer, but does not affect risk of metastases.
- E. Bladder wall muscle invasion by the tumor – this is the most important risk factor for the development of metastases. *If no muscle present in biopsy, re-biopsy!*



Question 13

A 32-year-old man presents with fevers, petechiae and fatigue and is found to have acute myelogenous leukemia. Allogeneic bone marrow transplantation will most likely be recommended (presuming a suitable donor can be found) if:

- A. His initial blast count is $> 100,000/\text{mm}^3$
- B. He is septic at presentation
- C. He has acute promyelocytic leukemia and is in active DIC
- D. His leukemic blasts have a 7q chromosomal deletion
- E. His leukemic blasts have a t(8;21) chromosomal translocation



Question 13 - Answer

- A. His initial blast count of $> 100,000/\text{mm}^3$ does not affect prognosis in AML.
- B. Being septic at presentation affects initial mortality but not ultimate response to chemotherapy.
- C. Acute promyelocytic leukemia with DIC affects initial mortality but not ultimate response to systemic therapy, and in fact many of these patients ultimately have a good prognosis with ATRA/arsenic alone.
- D. Leukemic blasts with a 7q- chromosomal deletion portend a poor prognosis with standard chemotherapy. Cytogenetics/molecular features are the most important factors in determining prognosis/need for HSCT.
- E. Patients whose leukemic blasts have a core binding factor (t(8;21) or inversion 16) chromosomal translocation have a better prognosis than average and HSCT is not recommended in first remission.



Question 14

You are evaluating a 52-year-old man with newly diagnosed non small-cell carcinoma of the right lung. In which of the following scenarios is the patient **potentially resectable** with goal of cure?

- A. Contralateral (N3) mediastinal adenopathy.
- B. Enlarged (4 cm) left adrenal gland.
- C. Ipsilateral pleural effusion.
- D. Ipsilateral (N2) mediastinal adenopathy.
- E. Ipsilateral supraclavicular adenopathy



Question 14 - Answer

- A. Patients with contralateral (N3) mediastinal adenopathy are not considered resectable (Stage IIIB). Chemoradiation followed by immunotherapy is the standard of care.
- B. 25% of patients with NSCLC will have adrenal metastases early on, and these pts are not helped by resection – and an adrenal mass of this size is more likely malignant than representing a benign adenoma. If adrenal is only site of metastasis and diagnosis is unclear, biopsy to absolutely confirm if metastatic disease should be pursued, if possible.
- C. Presence of a malignant pleural effusion is stage IV disease and considered incurable.
- D. Patients with ipsilateral (N2) mediastinal adenopathy are potentially resectable, and potentially curable, particularly after preoperative chemotherapy and radiation. (Stage IIIA)
- E. Enlarged ipsilateral or contralateral supraclavicular lymph nodes (N3) are indicative of stage IIIB or IIIC disease (B vs C depends on primary tumor characteristics), and these patients are not helped by resection. Chemoradiation followed by immunotherapy is the standard of care.



Question 15

A 42-year-old pre-menopausal comes to you to discuss interventions that may reduce her risk of breast cancer. She has a family history of breast cancer in her mother and one sister. At age 38 she underwent a breast biopsy which was benign, and she recently had another biopsy which demonstrated ADH (atypical ductal hyperplasia) but no evidence of malignancy. Onset of menses was at age 13, and she does not have children. You calculate her 5 year risk of developing breast cancer with the Gail model (<https://bcrisktool.cancer.gov/calculator.html>). Her result is significantly higher than twice that of women with average risk. You discuss chemoprophylaxis with a SERM (selective estrogen receptor modulator) for 5 years and she is interested in pursuing therapy.

Which of the following is true regarding tamoxifen and raloxifene?

- A. Raloxifene is a bone strengthening agent but tamoxifen is not
- B. Both increase the risk of endometrial cancer.
- C. Both decrease the risk of developing a future breast cancer
- D. Tamoxifen increases risk of hot flashes, but raloxifene does not
- E. Tamoxifen increases the risk of VTE, but raloxifene does not



Question 15 - Answer

- A. Both increase bone density (primary use of raloxifene, which is only approved post-menopause; tamoxifen is approved for all patients).
- B. Tamoxifen increases the risk of endometrial cancer, but raloxifene does not (raloxifene does not act as estrogen on endometrial tissue).
- C. Both decrease the risk developing breast cancer. Tamoxifen by approximately 50%, raloxifene by approximately 40%. However, there is no documented improvement in breast cancer-specific mortality.
- D. Both increase the likelihood of hot flashes.
- E. Both increase the risk of VTE.



Question 16

A 42-year-old premenopausal woman presents with a 3 cm, poorly differentiated, ER/PR-negative, HER-2-positive invasive ductal cancer with 5 involved axillary lymph nodes. Which of the following is true:

- A. The presence of HER-2 on breast cancer cells does not affect prognosis
- B. Adjuvant chemotherapy is not effective in reducing the subsequent development of metastatic breast cancer
- C. Her-2 directed therapy (trastuzumab, pertuzumab), when added to chemotherapy, substantially reduces the risk of developing metastatic disease in the future
- D. Letrozole, an aromatase inhibitor, would further improve the cure rate for this patient
- E. The addition of trastuzumab to chemotherapy is safe, without short and long-term complications



Question 16 - Answer

- A. Tumors which overexpress HER2 are more likely to metastasize than HR+/HER2 negative tumors, in the absence of HER2-directed therapy.
- B. Adjuvant chemotherapy substantially reduces the risk of subsequently developing metastatic breast cancer for both HER2-positive and negative tumors.
- C. Trastuzumab +/- pertuzumab, when added to chemotherapy, further reduces the risk of developing metastatic disease in the future.
- D. Letrozole, an aromatase inhibitor, is not effective for pts with hormone receptor-negative tumors, or in premenopausal women with HR-positive tumors.
- E. Trastuzumab, when administered after doxorubicin, is associated with an increased risk of cardiomyopathy compared to trastuzumab without prior anthracycline. Q12 week echocardiograms are recommended to monitor for an asymptomatic drop in EF.



Question 17

A 56-year-old man with a history of a primary melanoma on the right forearm 3 years ago presents with hepatomegaly and is found to have metastatic melanoma in the liver, braf wild-type. PET CT and brain MRI show no other sites of disease. He is in otherwise good health and engages in moderate physical activity 3-5 days per week.

Which of the following is the best treatment option:

- A. Dacarbazine plus tamoxifen
- B. No therapy is effective or warranted and the patient should be placed in hospice care
- C. Checkpoint inhibitor therapy with either nivolumab plus ipilimumab, or single agent pembrolizumab or nivolumab.
- D. Prophylactic brain irradiation
- D. Dabrafenib/trametinib



Question 17 - Answer

- A. Dacarbazine plus tamoxifen was a treatment option in the past, but tamoxifen was subsequently shown to be ineffective, and the benefit from dacarbazine is marginal. Chemotherapy is not commonly used for melanoma in the age of immuno- and targeted therapy.
- B. Metastatic melanoma has been transformed with immune checkpoint inhibitor (ICI) therapy, with substantial increases in overall survival compared with chemotherapy and radiation alone.
- C. ICI therapy has been shown to be highly active in this disease, either dual CTLA-4 (ipi)/PD-1 (nivo), or single agent PD-1 (pembro, nivo) inhibition are acceptable options. Higher response rates with dual inhibitions are also accompanied by higher immune toxicity incidence and severity. In general, dual inhibition is preferred in non-elderly patients with an adequate performance status.
- D. Patients with metastatic melanoma do frequently develop brain metastases, but prophylactic brain irradiation has not been shown to improve outcomes.
- D. BRAF-directed therapy can be highly effective in patients with sensitive mutations (V600E most common), but this patient is BRAF wild type and targeted therapy would not be expected to be effective.



Question 18

A 64-year-old woman has a routine CBC showing a WBC of 14,500/mm³ with 75% mature-appearing lymphocytes, Hct 41%, and plt of 180,000/mm³. She has no adenopathy or splenomegaly on physical exam and feels well in general.

Which of the following is true:

- A. The diagnosis of CLL can only be made on a bone marrow aspirate and biopsy
- B. She is at increased risk for infection
- C. She is in need of urgent chemotherapy
- D. She is likely to die of CLL before her 70th birthday
- E. Splenomegaly is rare in patients with this disease



Question 18 - Answer

- A. The diagnosis of CLL can be made by testing of the peripheral blood with flow cytometry, looking for the co-expression of CD20 and CD5 and absence of Cyclin D1 translocations (which implies mantle cell lymphoma).
- B. She is at increased risk for infection due to decreased antibody production in response to infection and dysregulated immune function, and infection is the leading cause of disease-related death for patients with CLL.
- C. Many people with CLL are without indications for therapy for years following diagnosis. Reasons to initiate treatment include non-immune cytopenias, bulky adenopathy, systemic B symptoms, or Richter's transformation. She has none of these clinical features.
- D. Statistically she is likely to be alive at age 75.
- E. Splenomegaly is a common finding in patients with CLL.



Questions 19-23

Match mechanism of action to antineoplastic agent:

- A. Bevacizumab**
- B. Cyclophosphamide**
- C. Lenalidomide**
- D. Trastuzumab**
- E. Ipilimumab**

- 19. Immunomodulation/enhancement of cell-mediated immunity via multiple mechanisms
- 20. Inhibition of HER2
- 21. Inhibition of VEGF
- 22. Alkylation of DNA
- 23. Decreased T cell inactivation by tumor



Questions 19-23 - Answers

- A. Bevacizumab - 21**
- B. Cyclophosphamide - 22**
- C. Lenalidomide - 19**
- D. Trastuzumab - 20**
- E. Ipilimumab- 23**

- 19. Immunomodulation/enhancement of cell-mediated immunity via multiple mechanisms
- 20. Inhibition of HER2
- 21. Inhibition of VEGF
- 22. Alkylation of DNA
- 23. Increased T cell response versus tumor (via blocking tumor-induced T cell downregulation)



Questions 24-28

Match toxicity to the most appropriate antineoplastic agent:

- A. Bevacizumab**
- B. Cyclophosphamide**
- C. Lenalidomide**
- D. Trastuzumab**
- E. Pembrolizumab**

- 24. Congestive heart failure
- 25. Hypertension; bleeding and clotting
- 26. Colitis, pneumonitis, hypophysitis
- 27. Rash, VTE, teratogenicity
- 28. Hematuria; secondary malignancies (MDS, AML)



Questions 24-28 - Answers

- A. Bevacizumab - 25**
- B. Cyclophosphamide - 28**
- C. Lenalidomide - 27**
- D. Trastuzumab - 24**
- E. Pembrolizumab - 26**

- 24. Congestive heart failure
- 25. Hypertension; bleeding and clotting
- 26. Colitis, pneumonitis, hypophysitis
- 27. Rash, VTE, teratogenicity
- 28. Hematuria; secondary malignancies (MDS, AML)



Question 29

A 49-year-old man with metastatic melanoma is receiving combined checkpoint inhibitor blockade with ipilimumab and nivolumab. During the course of treatment he develops multiple immune-related adverse reactions (irAEs).

Which of the following is least likely to reverse:

- A. Rash
- B. Hypothyroidism
- C. Colitis
- D. Pneumonitis
- E. Hepatitis



Question 29 - Answer

- A. Rash
- B. Hypothyroidism. Checkpoint inhibitor-induced endocrinopathies are in general permanent, and patients will require life-long supplementation. If severe enough, other toxicities may potentially lead to permanent injury or even death, but are more frequently reversible.
- C. Colitis
- D. Pneumonitis
- E. Hepatitis



Question 30

Which of the following is true regarding patients with active cancers and VTE:

- A. Patients with stage IV solid tumor malignancies who develop VTE on treatment should be considered for indefinite anticoagulation for secondary VTE prevention.
- B. Patients with stage IV high-grade lymphomas who developed VTE on treatment should remain on indefinite anticoagulation for secondary VTE prevention.
- C. Patients with cancer who are diagnosed with VTE should receive LMWH preferentially over DOACs for VTE treatment.
- D. Patients who develop VTE despite being anticoagulated should undergo IVC filter placement.
- E. Patients with severe thrombocytopenia ($\text{plt} < 10$) do not develop VTE.



Question 30 - Answer

- A. Patients with stage IV solid tumor malignancies who develop VTE on treatment are at high risk of developing recurrent VTE and should be considered for indefinite anticoagulation unless contraindicated by risk of bleeding.
- B. Patients with stage IV high-grade lymphomas who developed VTE on treatment should be treated for a minimum of the recommend length of AC for primary treatment, but if in remission/treatment complete can be considered for time-limited VTE treatment.
- C. Multiple studies have demonstrated DOACs to be non-inferior to LMWH. However, there is evidence of increased risk of bleeding with DOACs in patients with luminal GI tumors.
- D. IVC filters should be avoided when possible due to the risk of long-term complications. If placed, they should ideally be removed within 14 days.
- E. Although it is less common, patients with severe thrombocytopenia (plt<10) can indeed develop VTE, including life-threatening clots.



Question 31

A 79-year-old man presents with an unintentional 20# weight loss, disequilibrium and hemoptysis. Other medical conditions include COPD on 3LNC, ESRD on HD, and severe PVD with a history of R BKA. He is wheelchair-bound at baseline and spends most of his waking hours in bed or resting in a recliner. Imaging demonstrates a large R hilar mass, multiple liver lesions and a solitary 4 cm cerebellar lesion with surrounding edema.

The most appropriate next step is:

- A. Referral to neurosurgery for diagnostic and therapeutic cerebellar resection
- B. Bronchoscopic biopsy for tissue confirmation and molecular testing
- C. Referral to radiation oncology for whole brain radiation
- D. Referral to palliative care and ultimate transition to hospice
- E. Peripheral blood circulating tumor DNA (ctDNA) testing to assess for potential targeted therapeutic options



Question 31 - Answer

- A. Cerebellar resection is an aggressive approach with potential significant morbidity and should be avoided in this chronically ill, and now terminally ill, patient
- B. Diagnostic interventions that present potential risks without affecting management should be avoided. This patient is not a candidate for systemic therapy.
- C. WBRT can have significant short-term (nausea/vomiting, fatigue, headache, dizziness, hearing loss), as well as long-term (cognitive), toxicity. Any potential benefit in this setting is outweighed by risks of short-term toxicity and logistical barriers.
- D. Patients with a poor performance status (ECOG 3 or greater, KPS 50 or less) and/or very limited life expectancy should be referred for palliative care/hospice rather than disease-directed evaluations and interventions. This is particularly true in patients where comorbid conditions lead to poor performance status.
- E. As above, diagnostic studies that will not alter therapeutic management should be avoided.



Question 32

In which of the following malignancies are some cases potentially vaccine preventable?

- A. Squamous cell carcinoma of the cervix
- B. Hepatocellular carcinoma
- C. Endemic Burkitt lymphoma
- D. Squamous cell carcinoma of the oropharynx
- E. Squamous cell carcinoma of the anus



Question 32 - Answer

Which of the following malignancies is not potentially vaccine-preventable?

- A. Squamous cell carcinoma of the cervix – HPV vaccine. All HPV-associated cancers are further potentiated by concomitant HIV infection, and all patients with such cancers should be tested for HIV.
- B. Hepatocellular carcinoma – HBV vaccine. Lifetime risk in chronic HBV carriers of developing cirrhosis and/or HCC ranges from 15-40%. HCV is associated with both HCC as well as some types of NHL (in particular splenic marginal zone).
- C. Burkitt lymphoma – EBV. EBV is associated with multiple types of lymphoma (Hodgkin as well as non-Hodgkin), as well as nasopharyngeal carcinoma.
- D. Squamous cell carcinoma of the oropharynx – HPV vaccine
- E. Squamous cell carcinoma of the anus – HPV vaccine

Additional potential viral-associated neoplasms include:

HHV8: Kaposi sarcoma, primary effusion lymphoma, multicentric Castleman's

Merkel cell polyomavirus: Merkel cell carcinoma

HTLV-1: Adult T-cell leukemia/lymphoma



Question 33

60 year old male with relapsed Diffuse large B Cell lymphoma is treated with epicortimab (a CD3- CD20 bispecific antibody). Within 24 hours, he developed fever and was sent to the emergency department. He was found to have a temperature of 102.1 F, BP of 90/62, HR 116, and O2 saturation of 93%. What is the most likely diagnosis? Labs show a leukocytosis to 12,000, CRP 182 mg/L, and fibrinogen of 172 mg/dL.

- A. Sepsis from bacteremia
- B. Hemophagocytic Lymphohistiocytosis (LHL)/Macrophage Activation Syndrome (MAS)
- C. Progression of disease
- D. Cytokine Release Syndrome
- E. Pulmonary Embolism



Question 33 - Answer

60 year old male with relapsed Diffuse large B Cell lymphoma is treated with epicortimab (a CD3- CD20 bispecific antibody). Within 24 hours, he developed fever and was sent to the emergency department. He was found to have a temperature of 102.1 F, BP of 90/62, HR 116, and O2 saturation of 93%. What is the most likely diagnosis? Labs show a leukocytosis to 12,000, CRP 182 mg/L, and fibrinogen of 172 mg/dL.

- A. Sepsis from bacteremia
- B. Hemophagocytic Lymphohistiocytosis (LHL)/Macrophage Activation Syndrome (MAS)
- C. Progression of disease
- D. Cytokine Release Syndrome
- E. Pulmonary Embolism



Question 34

The same 60 year old is admitted to the hospital. What is the best management for severe or grade 3 Cytokine Release Syndrome?

- A. 1 Igram IV methylprednisolone
- B. Dexamethasone 10 mg initially followed by 4 mg q 6 hours
- C. Tocilizumab 8 mg/kg monotherapy
- D. Steroids + tocilizumab 8 mg/kg
- E. Antibiotics plus NSAIDs.



Question 34 - Answer

The same 60 year old is admitted to the hospital. What is the best management for severe or grade 3 Cytokine Release Syndrome?

- A. 1 Igram IV methylprednisolone
- B. Dexamethasone 10 mg initially followed by 4 mg q 6 hours
- C. Tocilizumab 8 mg/kg monotherapy
- D. Steroids + tocilizumab 8 mg/kg
- E. Antibiotics plus NSAIDs.



ONCOLOGY BOARD REVIEW

QUESTIONS??

Daniel_Roberts@DFCI.harvard.edu

