Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

Case Study #1

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Case 1

- 19yo male, originally diagnosed with precursor B-ALL at 17yo, neutral cytogenetics, and treated as per AALL1131
- Obese
- Multiple infectious complications during treatment

- During Maintenance, 30 months from original diagnosis, suffers a combined BM/CNS relapse

- Receives 4 weeks of reinduction chemotherapy with VXLD, clears CNS but bone marrow refractory with 75% ALL blasts (CD19+, CD22+)

Case 1: Question 1

- Which of the following is the best *initial* therapy for this situation?

A. Salvage chemotherapy (FLAG, CPM/ETOP, e.g.)
B. Blinatumomab
C. Inotuzumab
D. Tisagenlecleucel

Case 1: Question 2

- The patient receives inotuzumab, and achieves an MRD-negative remission. He proceeds to an allogeneic HSCT. Which of the following transplant-related adverse events is the most significant risk for this patient?

A. Veno-occlusive disease/Sinusoidal obstructive syndrome (VOD/SOS)
B. Graft-vs-host disease (GVHD)
C. Transplant-associated thrombotic microangiopathy (TA-TMA)
D. Hemophagocytic lymphohistiocytosis (HLH)

Case 2

- 19yo male, originally diagnosed with precursor B-ALL at 17yo, neutral cytogenetics, and treated as per AALL1131
- Obese
- Multiple infectious complications during treatment

- During Maintenance, 30 months from original diagnosis, suffers a combined BM/CNS relapse

- Receives 4 weeks of reinduction chemotherapy with VXLD, clears CNS, bone marrow with morphologic remission but 0.13% MRD by flow cytometry (CD19+, CD22+)

Case 2: Question 1

- Which of the following is the best *initial* therapy for this situation?

A. Salvage chemotherapy (FLAG, CPM/ETOP, e.g.)
B. Blinatumomab
C. Inotuzumab
D. Tisagenlecleucel

CHILDREN'S ONCOLOGY GROUP

Case 2: Question 2

- The patient begins blinatumomab; 48 hours into the infusion, he experiences acute delirium, followed by a generalized tonic-clonic seizure. The infusion is held, and the seizure stops with antiepileptics, but the patient remains confused and somnolent. There is no fever or other signs of cytokine release syndrome. Which of the following additional treatments is recommended?

A. Dopamine drip

B. Tocilizumab (anti-IL6R antibody)

→ C. Dexamethasone

D. Defibrotide

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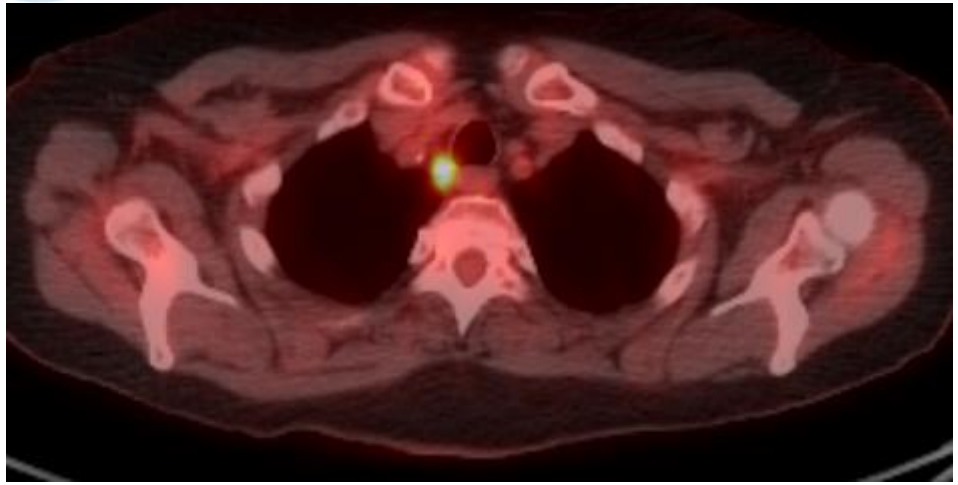
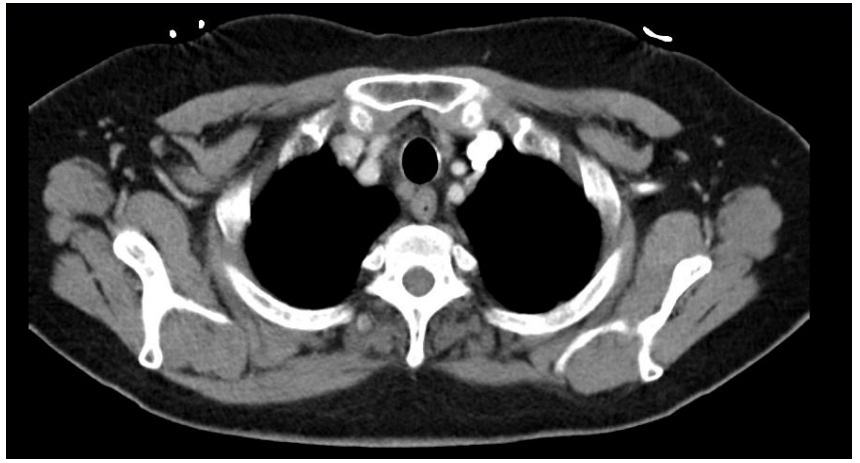
Case 3#
David Ilson, MD, PhD

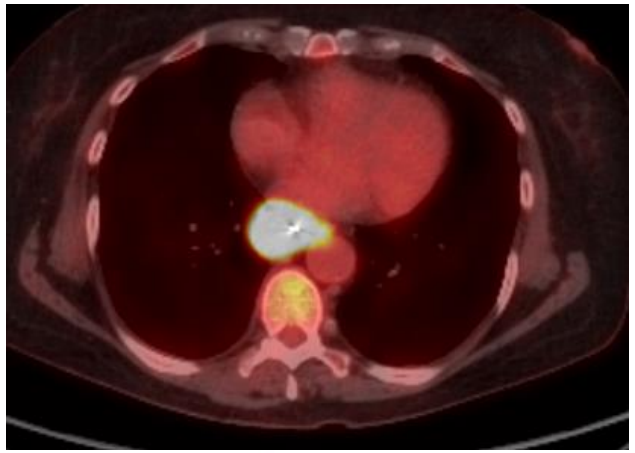
Metastatic HER2+ GEJ Cancer

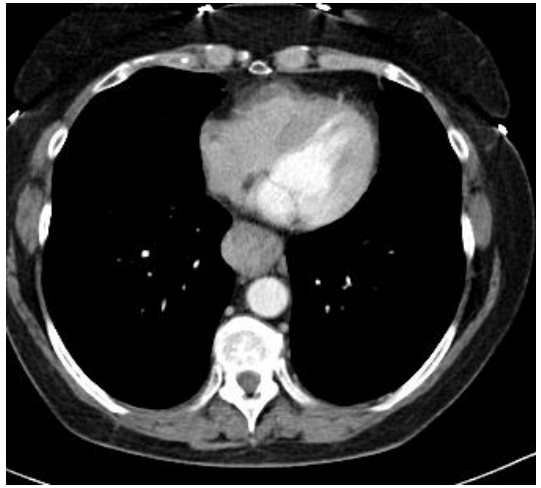
- 72 yo female presents with reflux, dysphagia, belching, early satiety
- PMH: Asthma, HTN, 14 pack year smoking
- EGD: obstructing circumferential mass in the GEJ, Barrett's, biopsy adenocarcinoma
- CT and PET scan: Upper paratracheal, para esophageal, GH nodes, primary, small liver metastases
- Tumor tissue tests + HER2, IHC 3+, PDL-1 CPS 1%
- Genomic profiling is pending

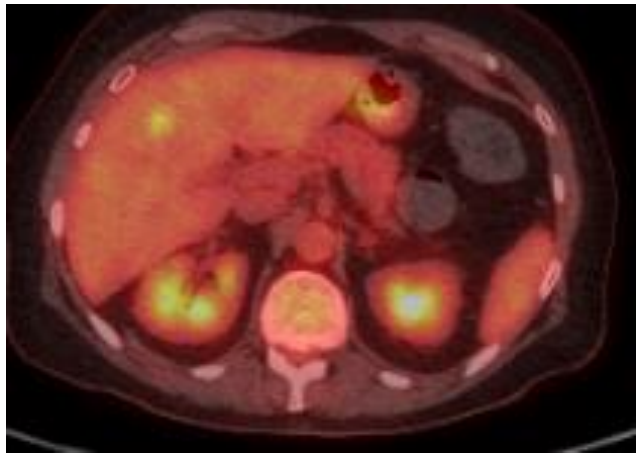
Metastatic HER2+ GEJ Cancer

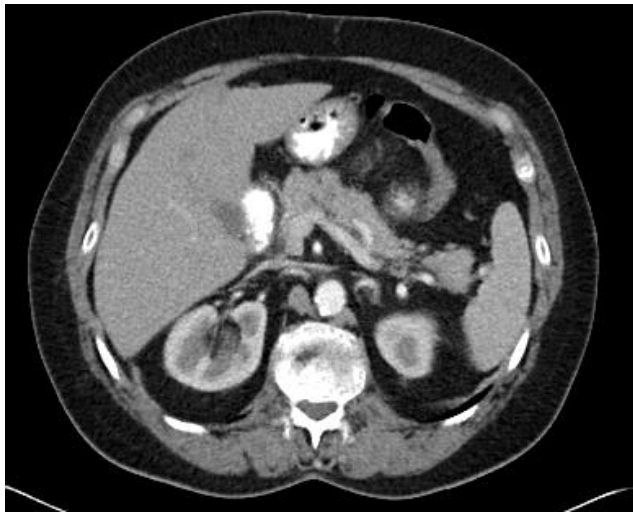












Metastatic HER2+ GEJ Cancer

- Your next step is
- 1) Wait for FISH confirmation of HER2 status
- 2) Initiate chemo with FOLFOX, trastuzumab
- 3) Initiate chemo with FOLFOX, trastuzumab, and pembrolizumab
- 4) Initiate chemo with FLOT + trastuzumab
- 5) Wait for genomic profiling for MSI status

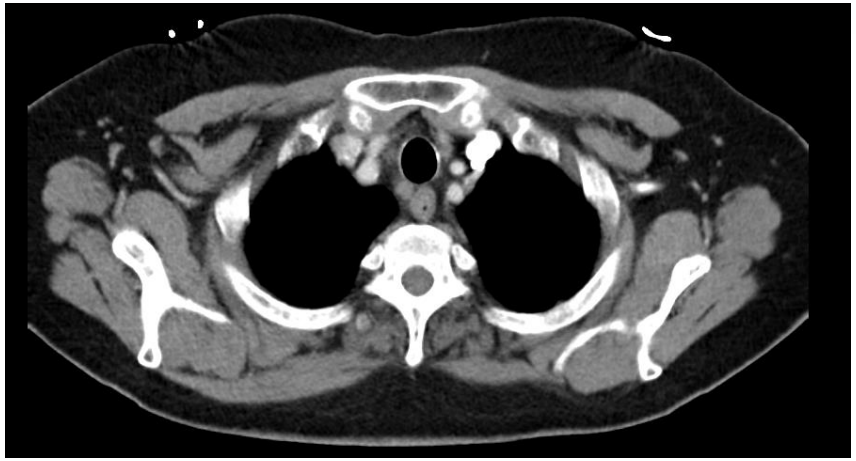
Metastatic HER2+ GEJ Cancer

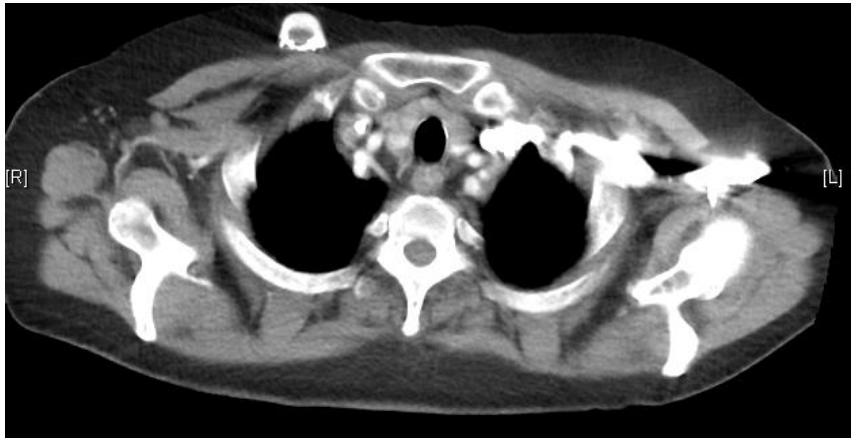
- Your next step is
- 1) Wait for FISH confirmation of HER2 status
- 2) Initiate chemo with FOLFOX, trastuzumab
- 3) Initiate chemo with FOLFOX, trastuzumab, and pembrolizumab*
- 4) Initiate chemo with FLOT + trastuzumab
- 5) Wait for genomic profiling for MSI status

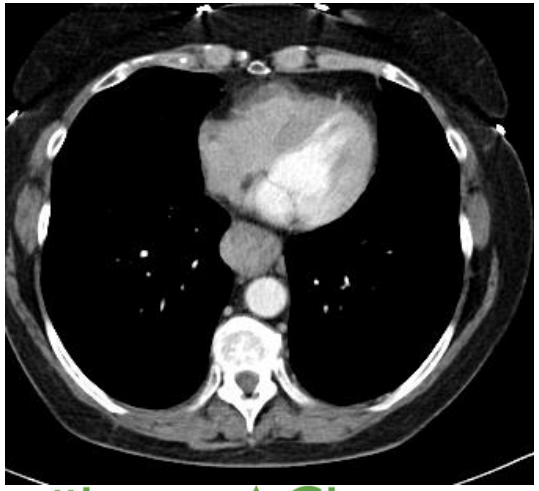
Metastatic HER2+ GEJ Cancer

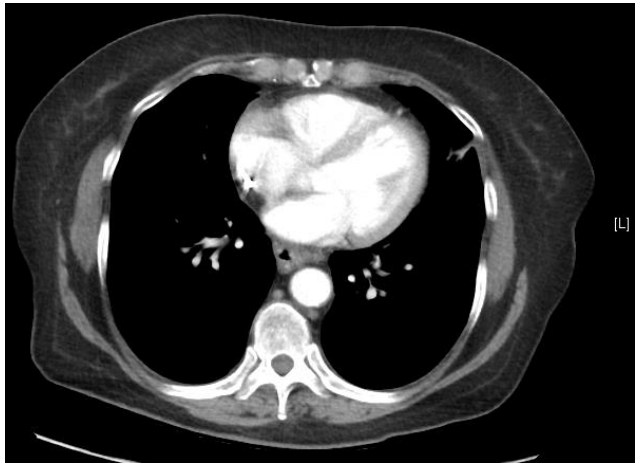
- The patient is treated on trial with 5-FU, oxaliplatin, trastuzumab, and pembrolizumab
- Genomic profiling: MSS, amplification of HER2 (8.4), p53 mutation, mutations in ARID1A and B, ERBB3, Cyclin D, ALK, CSF1R, PREX2, PIK3R1 deletion, and RARA, loss TGFBR2
- Infusional 5-FU is dose reduced for mucositis
- Reflux and dysphagia improve
- Serial CT imaging shows a response in the liver and other disease sites
- Oxaliplatin and 5-FU discontinued due to toxicity

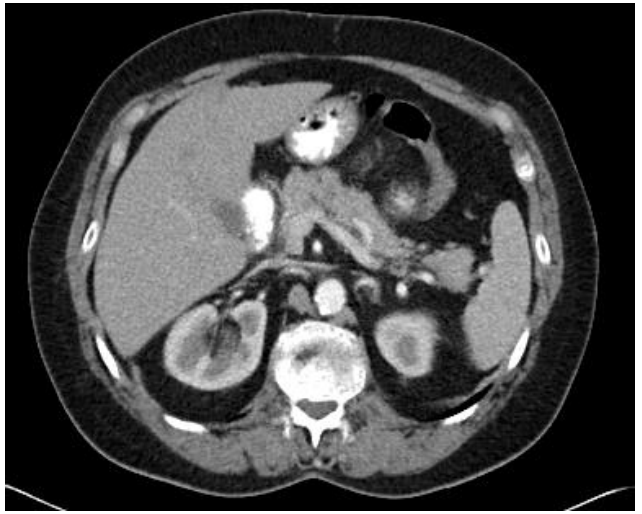
Metastatic HER2+ GEJ Cancer

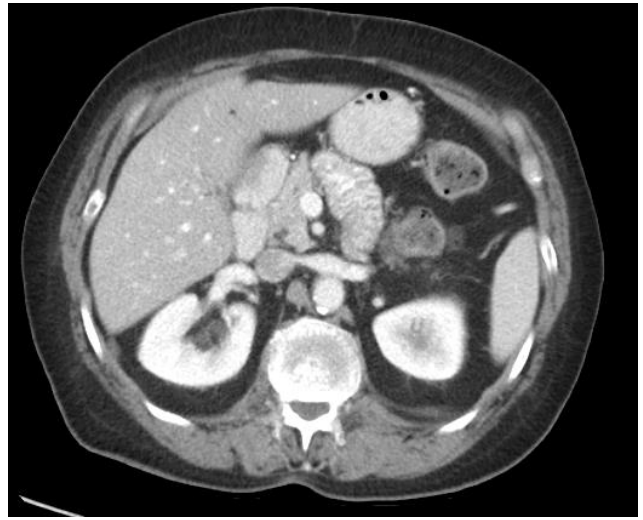








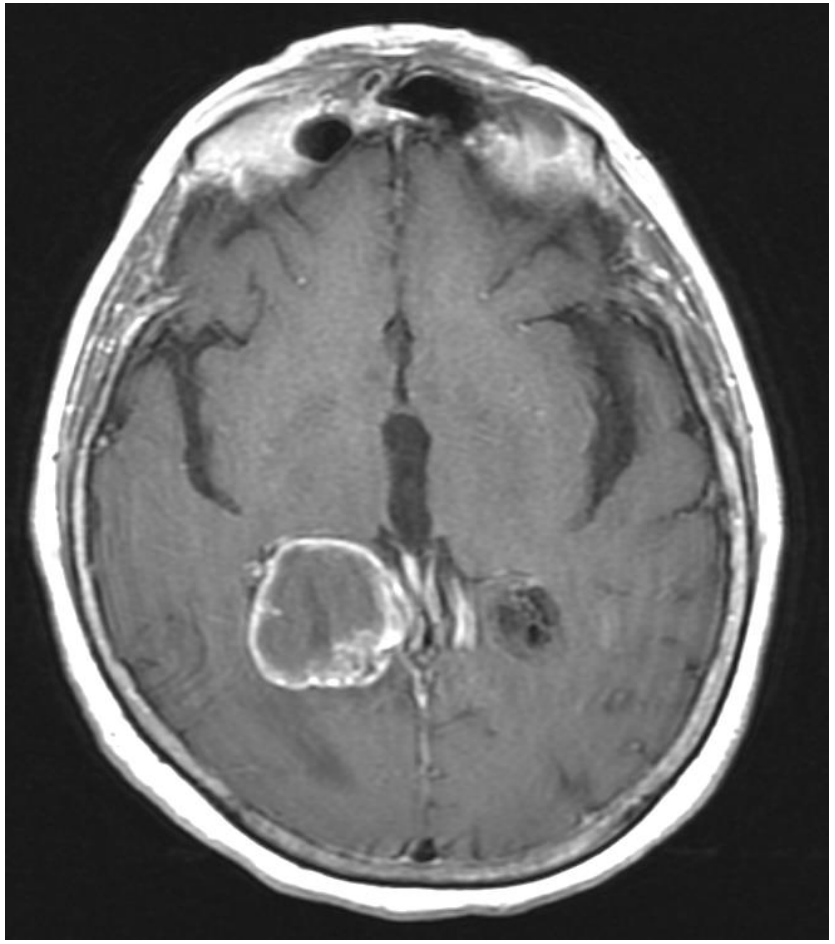


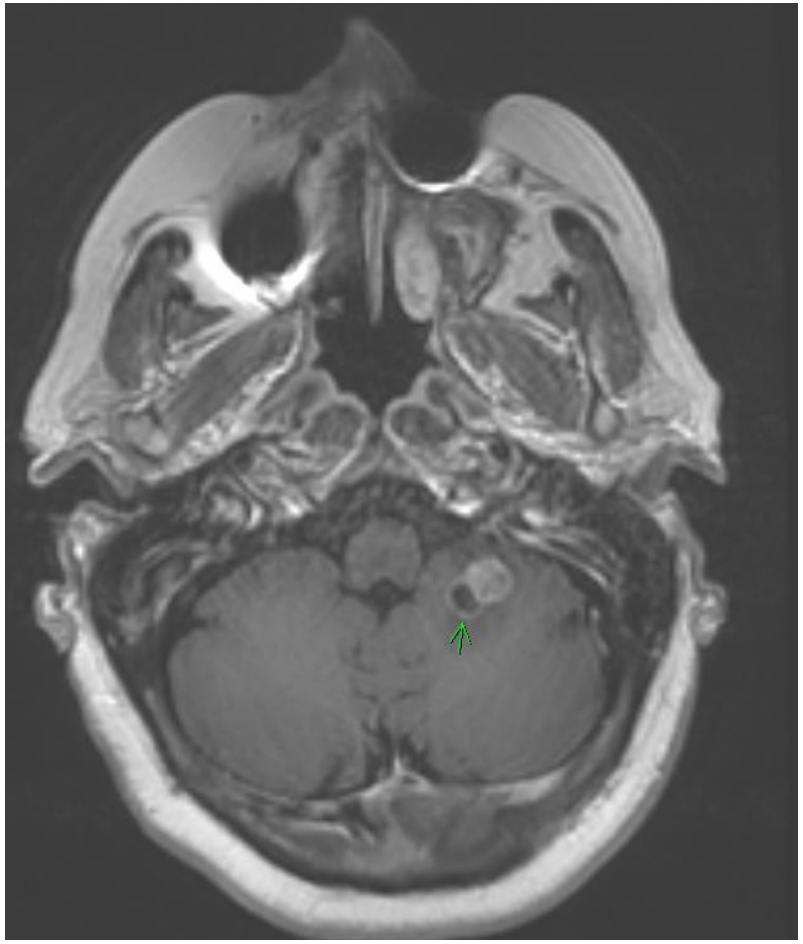


Metastatic HER2+ GEJ Cancer

- CT scans show ongoing response at 8 months, no visible liver lesions
- Maintenance Trastuzumab and pembrolizumab, develops nephritis requiring steroids
- Trastuzumab maintenance therapy continued
- 17 months into therapy she develops idiopathic nausea, fevers, and a possible seizure
- MRI of the brain indicates a right tempero-occipital and left cerebellar metastasis

Metastatic HER2+ GEJ Cancer





Metastatic HER2+ GEJ Cancer

- Resection of the larger, SRS of the smaller lesion
- Genomic profiling of the brain lesion: similar to the primary, HER2 15 fold amplified
- Trastuzumab maintenance resumed
- Follow up Brain MRI scans every 3-4 months show disease control
- At 3 years, for progressive dysphagia: EGD + persistent primary
  - Treated with capecitabine/RT with good response, continues trastuzumab
- At 4 years, local progression treatment with Trastuzumab Deruxtecan
- Further local progressive disease
- Treatment with paclitaxel ramucirumab with further local progression
- Transitioned to supportive care at 4.5 years

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Case Study #4

Aditya Bardia, MD, MPH

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43F with metastatic PD-L1 positive triple negative breast cancer had disease progression on 1st line therapy with chemotherapy and pembrolizumab, and is being considered for treatment with sacituzumab govitecan. As you counsel the patient on potential adverse effects, which of the following adverse effect is not seen sacituzumab govitecan, a trop-2 antibody drug conjugate with topoisomerase-1 payload (SN-38):

A. Diarrhea

B. Neutropenia

C. Nausea

D. Peripheral Neuropathy

Correct answer: D

D. Peripheral Neuropathy

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Case Study #5
Aaron Logan, MD, PhD

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Patient case: Leukemia

- 65M presents with fatigue and dyspnea on exertion
- CBC shows:
  - WBC 35,000, absolute blast count 23,000
  - Hgb 6.7
  - Platelets 12,000
- BMBx shows:
  - 90% cellularity with 70% blasts
  - Flow cytometry immunophenotype: CD34+, HLA-DR+, CD13+, CD33+, MPO+
- Rapid FISH shows monosomy 7, negative for t(15;18), t(8;21), inv 16

Patient case: Leukemia

- Diagnosis: AML with likely adverse karyotype; ultimately cytogenetics show:
- Which of the following antibody therapies is appropriate during induction therapy:

A) Magrolimab
B) Gemtuzumab ozogamicin
C) Inotuzumab ozogamicin
D) Nivolumab
E) None of the above

Patient case: Lymphoma

- 32F presents with fatigue and dyspnea on exertion
- CBC shows:
  - WBC 11,000, ANC 8,900, ALC 1,200
  - Hgb 11.1
  - Platelets 221,000
- Palpable lymphadenopathy in bilateral cervical regions and left axilla
- Left axillary LN biopsy c/w classical Hodgkin lymphoma
- PET-CT shows cervical, axillary, and mediastinal FDG avidity, mediastinal mass 8x9cm
- BMBx shows low level involvement

Patient case: Lymphoma

- 32F with stage IV classical Hodgkin lymphoma
- Received initial treatment with ABVD, has persistent cervical and mediastinal LN FDG avidity (Deauville 4 in mediastinum, mass 3x5cm) after 6 cycles, biopsy again shows cHL
- Salvage therapy with brentuximab vedotin x 2 cycles with persistent mediastinal mass (2x5cm with Deauville 3) followed by augmented ICE x 2 cycles achieving metabolic remission
- Proceeds to autologous SCT -> persistent complete metabolic remission
- Elects against BV maintenance
- 27 months after autoSCT, experiences dyspnea on exertion

Patient case: Lymphoma

- Chest CT shows 4x6cm mediastinal mass, biopsy shows cHL
- 32F with multiply relapsed classical Hodgkin lymphoma
- Which of the following antibody therapies is most appropriate for this patient:

A) Magrolimab
B) Inotuzumab ozogamicin
C) Nivolumab
D) Brentuximab + Nivolumab
E) None of the above