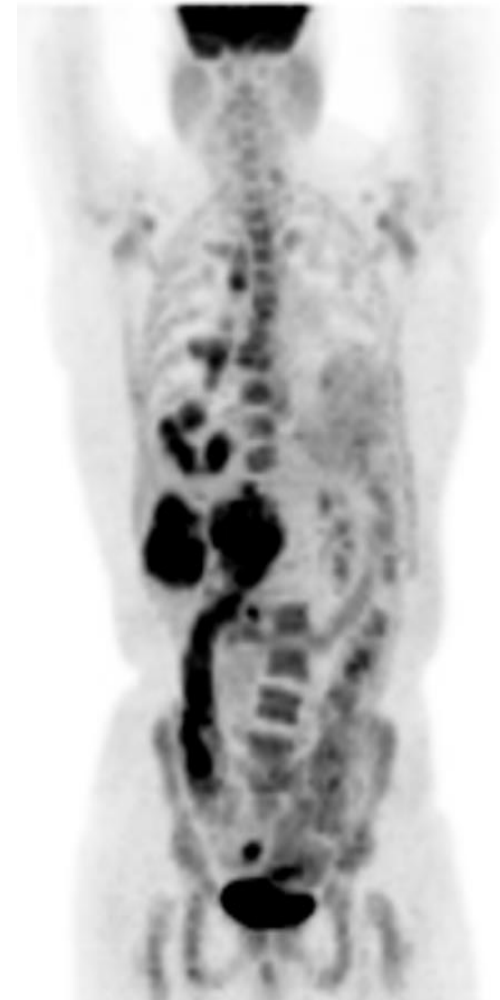
Case 1: Immunotherapy

- 57-year-old woman with cough & increasing SOB & weight loss.
- 30 pack-year tobacco hx. Quit 15 years ago.
- CT chest: RUL primary, mediastinal LNs, bone mets, liver mets.
- Biopsy of liver metastasis positive for NSCLC-adenocarcinoma.
- MRI brain is negative for brain metastasis.
- Zubrod PS is a 1.



Case 1: Immunotherapy

- The patient is motivated for therapy (PS=1).
- Molecular testing: KRAS G12C mutation
- PD-L1 expression by the DAKO 22C3 IHC test is 10%.
- TMB calculated by Foundation One is high (19 mut/MB).

Question 1: For frontline treatment of this patient’s KRAS-mutated stage IV lung adenocarcinoma you recommend:

1. Carboplatin/pemetrexed/pembrolizumab
2. Platinum/pemetrexed
3. Nivolumab
4. Carboplatin/paclitaxel/bevacizumab
5. Pembrolizumab

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Question 2: What influenced your decision for treating a patient with first-line PD-1 antibody in stage IV lung adenocarcinoma assuming EGFR, ALK, and ROS1 are negative?

1. **PD-L1 expression only**
2. **Tumor mutational burden only**
3. **Both 1 and 2 if PD-L1 expression is < 50%**
4. **KRAS mutation positivity**
5. **Nothing. I will just give carboplatin/pemetrexed and pembrolizumab to all stage IV lung adenocarcinomas now.**

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- The patient receives cisplatin and pemetrexed x 4 followed by maintenance pemetrexed with initial response and then progression after 8 cycles. She still has excellent performance status.

Question 3: In this patient with PD-L1 expression of 10% and high tumor mutational burden (TMB) which do you recommend for 2nd-line treatment?

1. Nivolumab
2. Pembrolizumab
3. Atezolizumab
4. Docetaxel and Ramucirumab
5. Docetaxel alone

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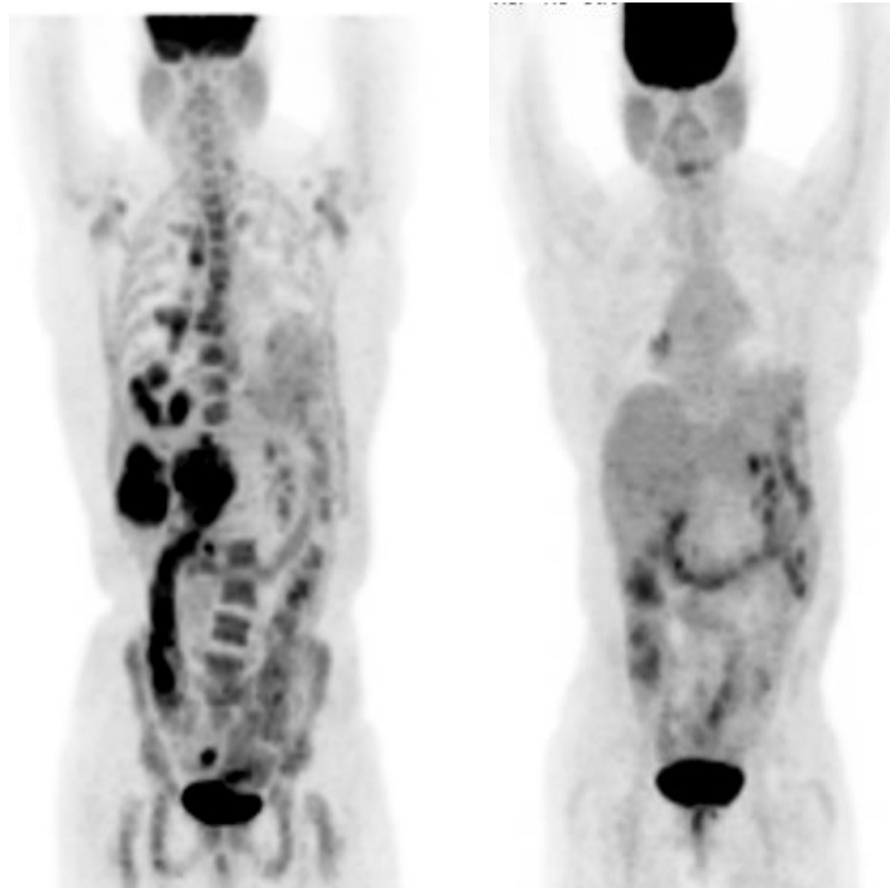
- The patient is started on Atezolizumab & achieves a near complete response



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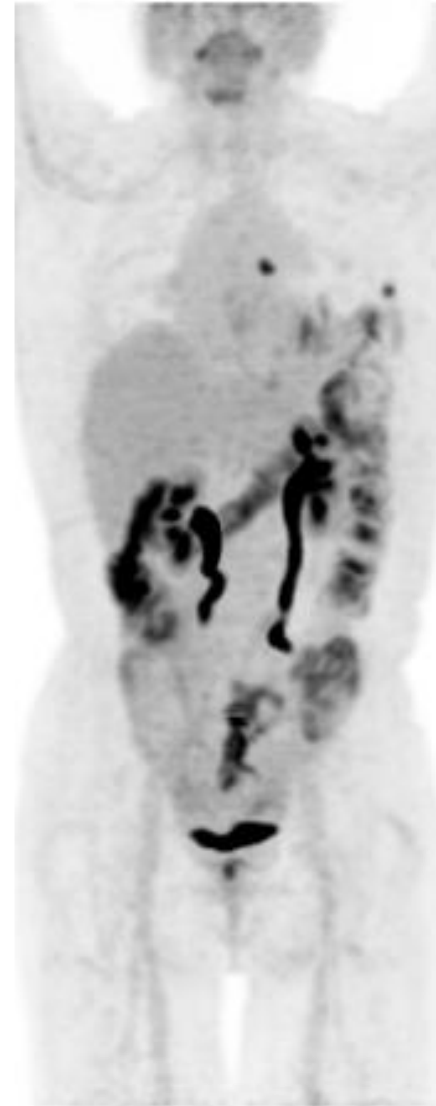
- Four months after near complete response, the patient develops worsening bone pain. PS is still good (PS=1).
- Repeat PET-CT shows progression of disease in 2 areas: a new rib and a new hip metastasis



Case 1: Immunotherapy

- This patient with advanced adenocarcinoma now has new rib and hip metastasis.

Question 4: What would you do next?

1. Radiation to painful bone lesions and continue Atezolizumab
2. Switch to Ipilimumab plus Nivolumab
3. Change from Atezolizumab to Durvalumab
4. This represents “pseudoprogression” so continue Atezolizumab alone
5. Switch to non-Immuotherapy regimen such as Docetaxel plus Ramucirumab