

- 48yo Caucasian F, non-smoker presents with increasing dyspnea
- Physical exam reveals decreased breath sounds over lower ½ left lung field
- Chest x-ray reveals large L pleural effusion
- CT reveals large L pleural effusion with L pleural implants, L hilar and mediastinal LAD, LUL 2.5cm
- PET/CT confirms these are avid, no distant disease



What is your next diagnostic step?

- 1. Drainage of fluid with cytology and cell button
- 2. Liquid biopsy
- 3. EBUS for FNA of nodes
- 4. CT guided biopsy of LUL lesion



- Pleural cytology reveals adenocarcinoma, TTF1+, Napsin A+, p63-, PD-L1 22C3 75%, but "scant remaining tissue precludes molecular diagnostics"
- Liquid biopsy reveals TP53 mutation and some variants of unknown significance

- 1. Pembrolizumab
- 2. Carboplatin/pemetrexed
- 3. Carboplatin/pemetrexed + bevacizumab
- 4. Carboplatin/pemetrexed + pembrolizumab
- 5. Further diagnostics



- CT guided core biopsy of primary lesion confirms adenocarcinoma
- Molecular testing reveals an EML4/ALK rearrangement
- PD-L1 testing by 22C3 80%
- MRI brain reveals 2 lesions: 2mm R frontal, 3mm L parietal, both without edema or mass effect (patient asymptomatic)



- 1. Radiation consult for stereotactic radiosurgery, then crizotinib
- 2. Radiation consult for stereotactic radiosurgery, then alectinib
- 3. Radiation consult for stereotactic radiosurgery, then pembro
- 4. Crizotinib, close f/u of brain
- 5. Alectinib, close f/u of brain
- 6. Pembro, close f/u of brain





- She goes on alectinib
- Imaging at 6 weeks reveals significant reduction in 2 brain mets, and in primary mass, LAD and pleural fluid
- Imaging q2-3 months shows ongoing PR until 12 months later when primary lesion increases from 1 to 3cm with new L lung nodules ranging from 1-2cm, 2 new R lung nodules, 1-2cm, new R adrenal mass 2.5cm, and reaccumulation of pleural fluid



- 1. Change to chemotherapy
- 2. Change to immunotherapy
- 3. Change to chemotherapy + immunotherapy
- 4. Change to ceritinib
- 5. Biopsy

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 - Answer different if
 - Brain-only progression in 1 or 2 spots?
 - Oligoprogression to adrenal, otherwise stable?





- Biopsy reveals adenocarcinoma
- PD-L1 by 22C3 85%
- EML4/ALK detected, no ALK resistance mutations
- MRI brain remains stable

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