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Metastatic adenocarcinoma of lung: mutational analysis from pleural fluid cytology and it’s therapeutic implication
Baseline presentation

- 65-year old lady, home maker
- Co-morbidity of rheumatoid arthritis x 10 years (on treatment), hypertensive x 3 years (on therapy)
- Presented with dry cough and shortness of breath for 1 wk duration
- On examination: ECOG PS 2, no pallor/icterus/SCLN
- Respiratory system: diminished breath sound on left lower lung. Other S/E- wnl
Investigation

- **CXR-PA view** (07/07/15): prominent interstitial lung marking, mild to moderate left pleural effusion
- **CT chest** (14/07/15): left pleural effusion with patchy consolidation in left inferior lingular segment and an enlarged mediastinal lymph node. Multiple well defined pulmonary nodules
- **Pleural fluid analysis**: glucose 83 mg/dl, protein 4.1 gm/dl, LDH 1342 u/l and ADA 13.2 u/l.
- **Pleural fluid cytology**: metastatic adenocarcinoma. IHC showed tumor cells to be positive for TTF-1 and negative for Calretinin. ALK (ventana IHC): negative
- **EGFR mutation analysis** (from cell block): Positive for deletion mutation in exon 19, (c.2240_2254del TAAGAGAAGCAACAT p.(Leu747_Thr751del))
- **Staging work-up**: No other sites of metastasis
Treatment

- **Impression**: metastatic adenocarcinoma of lung with activating EGFR mutation of exon 19 (deletion)

- She was started on oral Gefitinib 250 mg – once daily

- Patient tolerated well, became PS_1

- CT chest showed: *very good response*

- Now she is doing well on last follow-up (17/11/16)- 18 month f/up
Pre-treatment

Current CT (post Tx-13 months)
Point to discuss

- Molecular testing can be easily done from body fluid in cancer diagnosis- precision oncology - ?Liquid biopsy
- If she has been diagnosed now – what treatment?
  - Gefitinib + pemetrexed vs gefitinib alone
- What next if progressed?
- Options:
  - 2\textsuperscript{nd} like TKI (erlotinib, afatinib)
  - Immunotherapy (PD1 or PDL1 blocker) – not much effective
  - chemotherapy
2\textsuperscript{nd} case

- 42 year /M, never smoker
- 7 months h/o- cough with worsening breathlessness, wt loss
- PS_3
- \textit{CT chest}: left LL lung mass with consolidation with lymphangitis carcinomatosis with b/l multiple lung nodules with left mediastinal and hilar LAP

- \textit{Staging evaluation}: multiple liver & bone metastases

- \textit{Biopsy}: PD mucin producing adenocarcinoma, EGFR-wild type, ALK: strong IHC+ve (ventana)
Treatment

- Patient managed with supportive measures for symptom control
- Started on crizotinib 250 mg –BD, with
- Monthly zoledronic acid

Response

- Had dramatic symptomatic improvement over next 2-wks
- Tolerated crizotinib well – no toxicity so far
- Post 3 months- almost PS _0, resumed his duty
- Response assessment with whole body PET-CT s/o- complete metabolic response
Post 3-months of Crizotinib
What next on progression?

- Site of progression – important:
  - Only brain (sanctuary site)
  - Other systemic single site
  - Multiple site progression
- 2nd line ?- Ceritinib or v other TKIs
- Chemotherapy
- Immunotherapy - ? Not much effective