Difficult Lung Cases From Thailand

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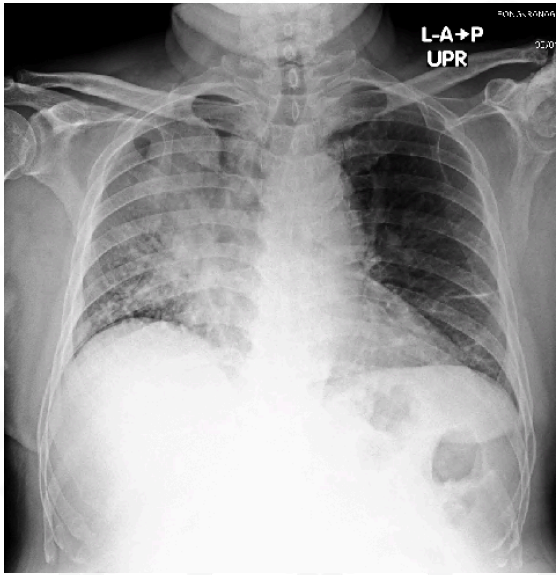
Faculty Disclosure

- Honoraria: Astra Zeneca, Boehringer Ingelheim, Roche
- Research funding: Astra Zeneca, Boehringer Ingelheim, Roche, Novartis, Samsung

Case presentation: 1st case; P-S

- A 83 YO Thai man, presented with dyspnea for 2 months
- Heavy smoke
- PS I
- An old man, looked fatigue, facial swelling, s/p rt. AK amputation
- LN +ve
- Abnormal bronchial and crackles at RUL
- Heart and abdomen: WNL
- Ext: one leg, no clubbing, no edema



FOB

- Month 0
- TBBx
- Right upper, biopsy

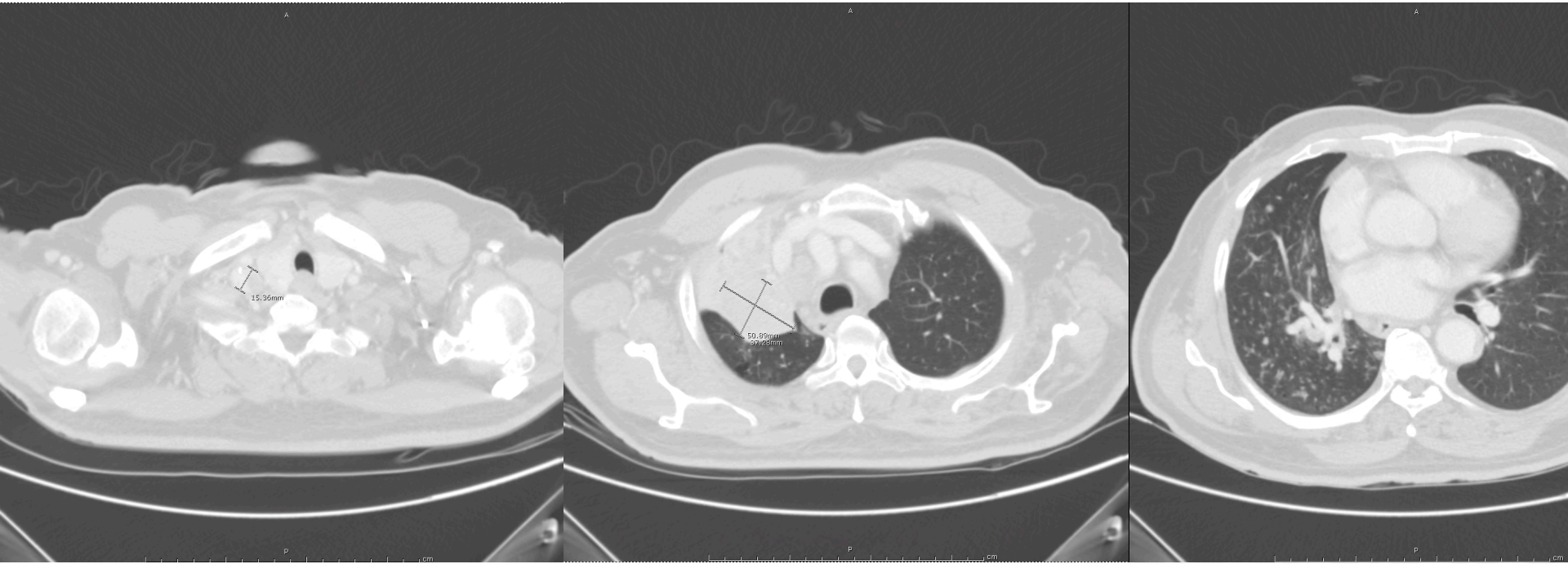
- Adenocarcinoma
- positive for TTF-1
- negative for p63
- positive for mucin

Staging [month 0]

- The study shows endobronchial lesion, about 1.9 cm in size at right main bronchus. There is large mass, about 3.7x5.1 cm in size in collapsed RUL. It compressed right upper pulmonary artery and SVC. Multiple lung nodules in both lungs are 0.3-0.8 cm in size. Multiple necrotic nodes at right supraclavicular, 4R, 2R, 7 are found.

- T4 N3 M1a

- Stage IV


15.36mm
50.89mm
97.28mm

Management of SVC syndrome ?

A. XRT then systemic Rx
B. XRT with systemic Rx
C. Systemic Rx

Biomarkers Testing ?

A. Sequential: EGFR, if negative then ALK
B. Sequential: ALK, if negative then EGFR
C. Sequential: PD-L1, if negative then EGFR and ALK
D. Concurrent: EGFR and ALK, if all negative then PD-L1
E. Concurrent: EGFR, ALK and PD-L1

Biomarkers Results

- EGFR mutation (COBAS)
  - Mutation detected
  - G719X mutation detected
- ALK by immunohistochemistry (D5F3)
  - Negative
- PD-L1
  - Not tested

Systemic Treatment ? for uncommon G719X mutation

A. Platinum doublets
B. Platinum doublets + bevacizumab
C. First-gen EGFR-TKIs
D. Second-gen EGFR-TKIs
E. Third-gen EGFR-TKIs

Afatinib

- Afatinib (40) 1x1 oral fasting state
- Loperamide (2) prn for diarrhea

  2 cap oral stat

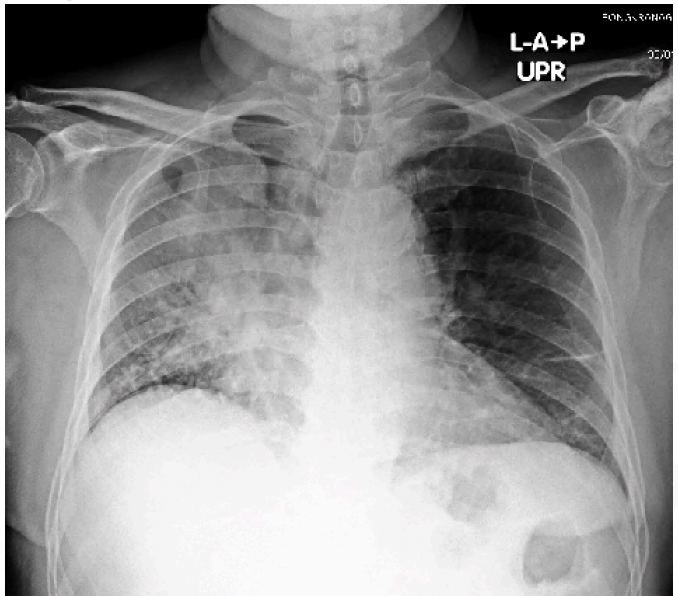
  then 1 cap q 2 hrs until stop diarrhea for 10 hrs

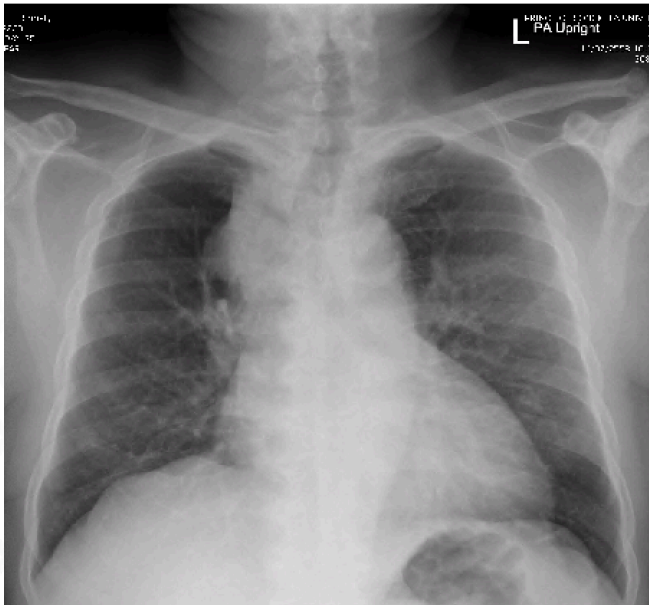
  (during sleep period q 4 hrs)

  not more than 10 cap/day
- Sun screen SPF 15 - 30
- Avoid spicy food

Afatinib 40 mg [Baseline] [month 1]

- 1 weeks: mucositis gr II
- Afatinib 30 mg





Afatinib 20 mg [month 3]

- Afatinib 20 mg [month 3 – month 28]
- CT: PD [new tiny lesion] without s/s
- What's next?
  - A. Switch to CMTs
  - B. Switch to Osimertinib
  - C. Treatment beyond RECIST PD
  - D. Re-biopsy for EGFR testing
  - E. Blood based EGFR testing

Afatinib 20 mg [month 3]

- Afatinib 20 mg [month 3 – month 28]
- CT: PD [new tiny lesion] without s/s

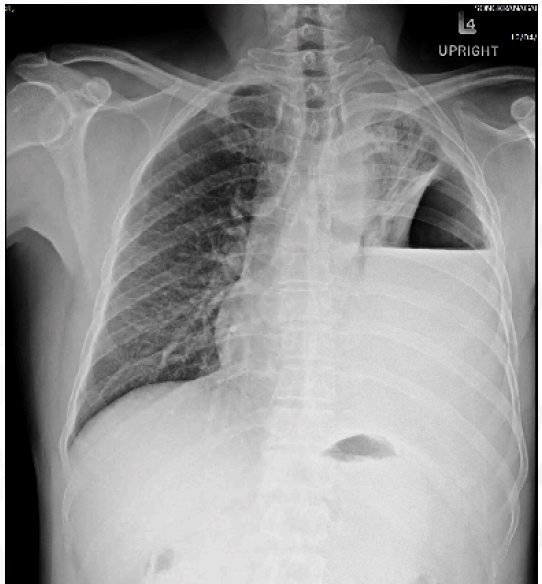
- Retest for EGFR
  - EGFR mutation using Therascreen kit
  - Exon 18 = mutation detected

Treatment beyond RECIST PD: Uncommon mutation

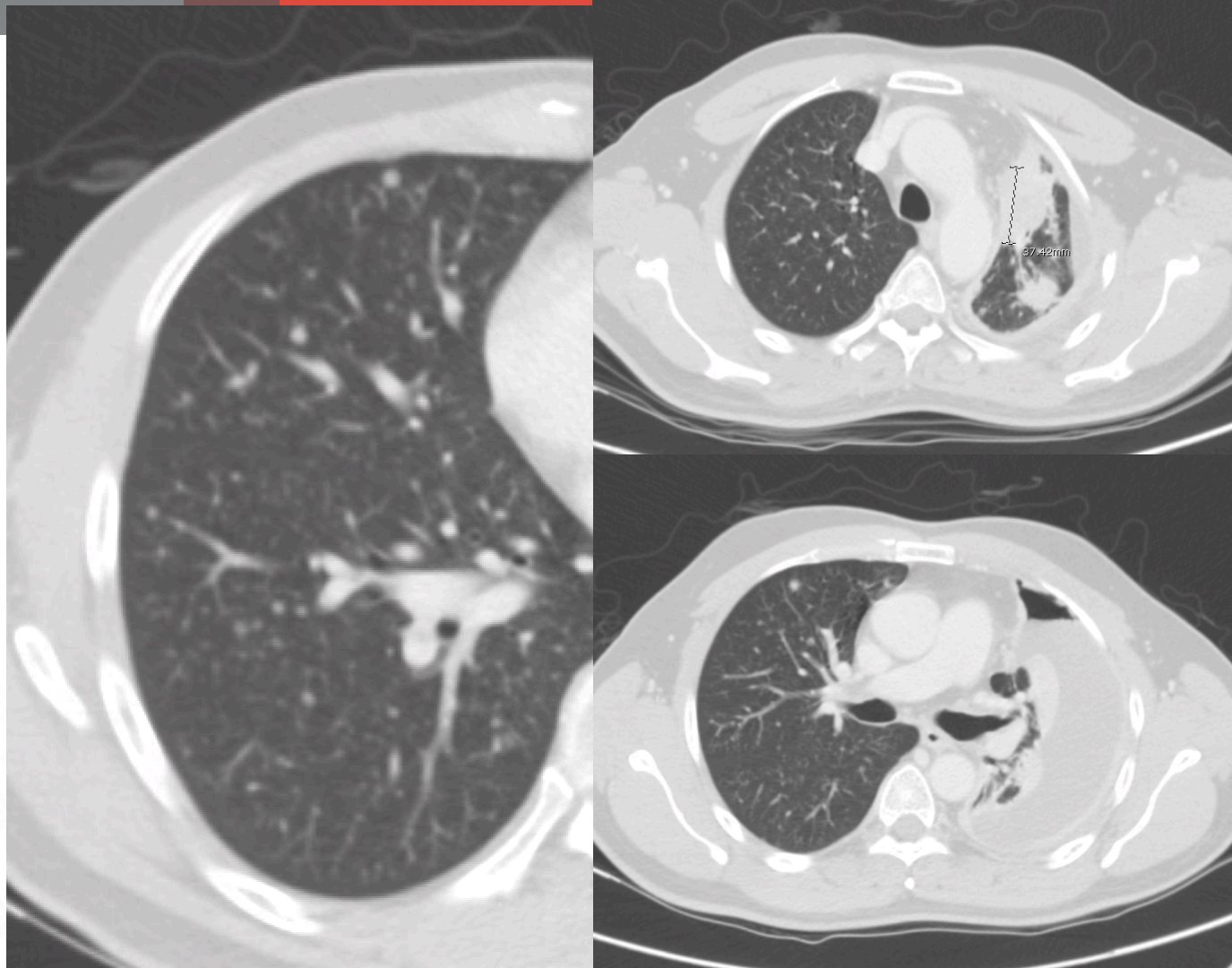
- Afatinib (20) until last visit on 21 Mar 2019
  - Start afatinib on 16 Jun 2015
  - First RECIST PD on 31 Aug 2017 (26 months after started afatinib)
  - Still on afatinib without second PD until previous visit on 21 Mar 2019 (45 months ++)

Case presentation: 2nd case; T-J

- A 58 YO Thai man, presented with dyspnea for 3 months
- occasional smoked
- PS I
- A middle-age man, looked fatigue
- Decrease breath sound at left lung
- Heart and abdomen: WNL
- Ext:, no clubbing, no edema



28 Apr 2015



Biomarkers Results

- EGFR mutation (COBAS)
  - Mutation detected
    - Del 19
- ALK by immunohistochemistry (D5F3)
  - Positive
- PD-L1
  - Not tested

Which target; stage IV with (possible) dual mutations?

- A. start with ALK TKIs
  - Crizotinib, ceritinib, alectinib
- B. start with EGFR TKIs
  - Gefitinib, erlotinib, afatinib, osimertinib
- C. Start with EGFR-TKIs plus ALK-TKIs
- D. Retest for FISH assay
- E. Start with IO + CMT

ALK-TKIs

- 27 May 2015 Crizotinib (250) 1x2

- 13 Jun 2015 AE: abnormal sensation both arm
- 16 Jun 2015 non-massive hemoptysis

- 18 Jun 2015 CT: Progressive disease, new lung nodules. Improve acute pulmonary embolism in left lower lobar artery

EGFR-TKIs

- 24 Jun 2015 started Gefitinib
  - Best response: stable disease (SD)
- Still need intermittent pleural fluid release.
- RECIST: PD on 05 Jan 2018 (31 months of Gefitinib)

- No T790M detected on ddPCR

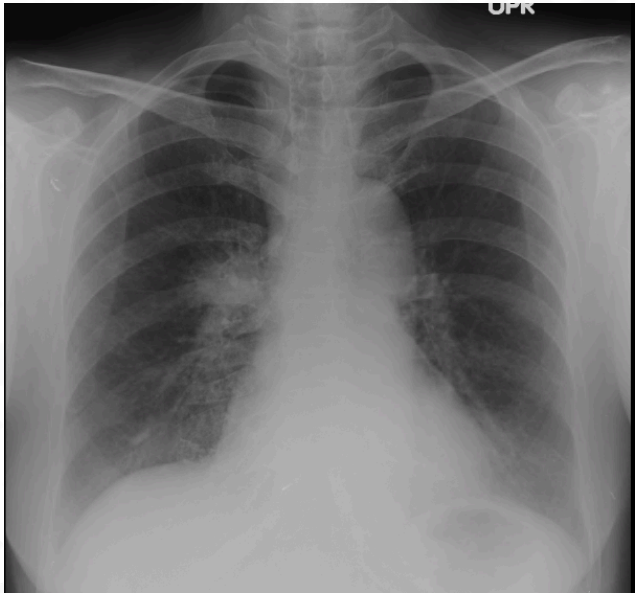
ALK +ve and EGFR +ve

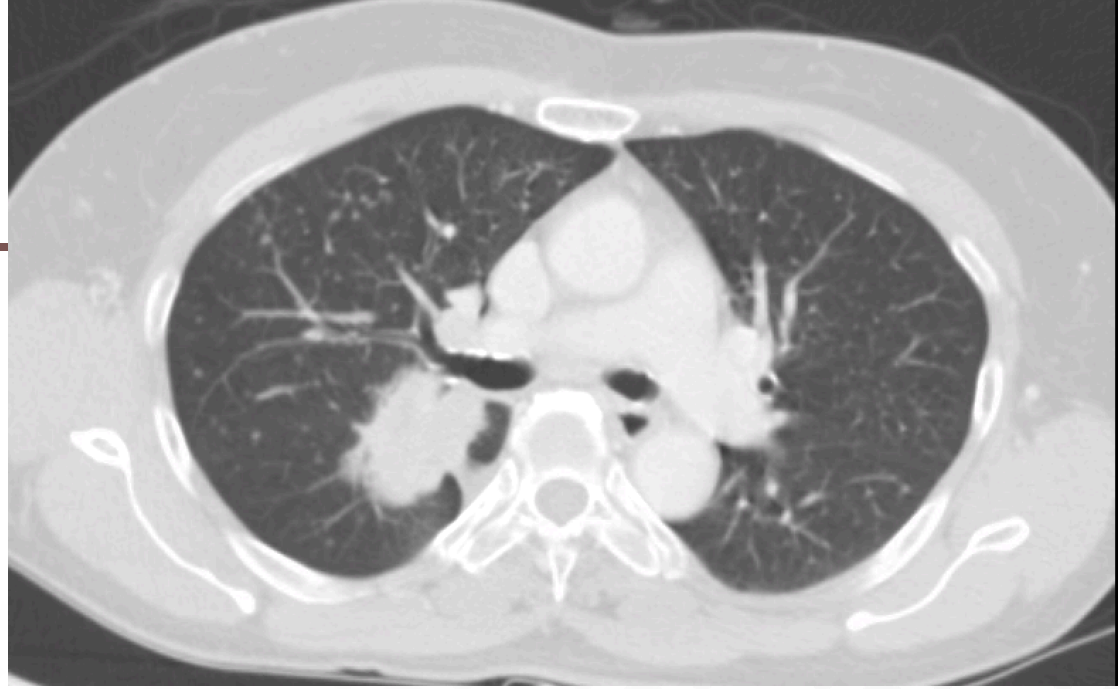
- 22 Mar 2018 – 02 Aug 2018 Paclitaxel-carboplatin
  - Best response: PD

- Passed away on 27 Oct 2018 (42 months after Dx)

Case presentation: 3rd case; P-M

- A 61 YO Thai female, presented with dyspnea for 3 months
- Never smoke
- PS I
- An old female, looked healthy
- Normal breath sound both lungs
- Heart and abdomen: WNL
- Ext: no clubbing, no edema





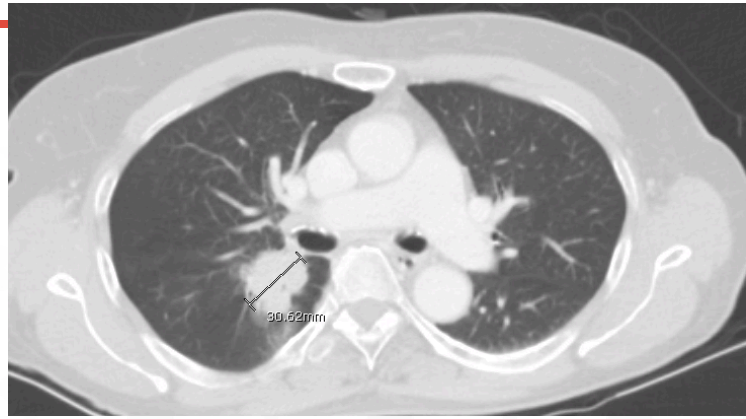
T2N3M1 multiple small lung nodules

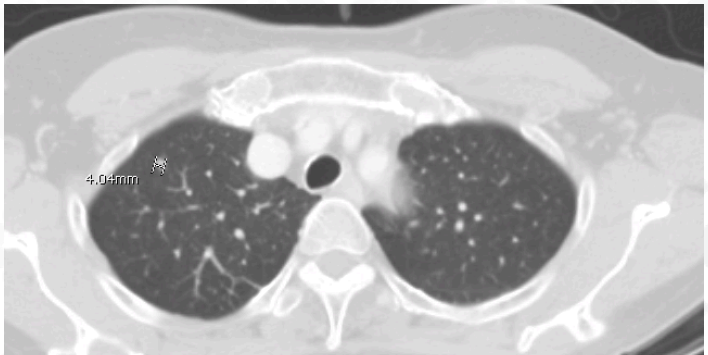
- FOB: adenocarcinoma, TTF1+, mucin +ve
- *EGFR:* L858R mutation

- Afatinib (40) in clinical trial

  During 20 Sep 2011 until 04 Feb 2013

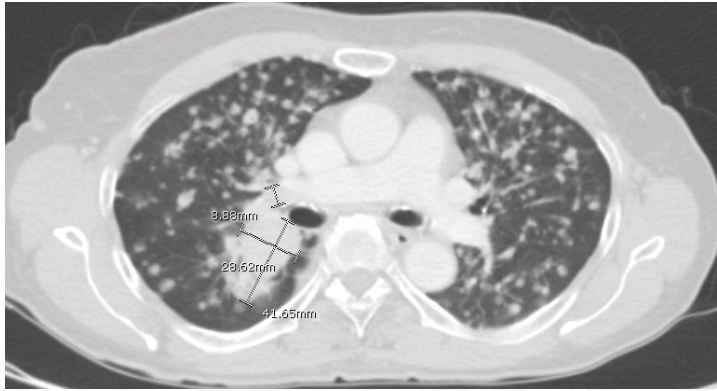
- Then PD





- Afatinib (40) in clinical trial 20 Sep 2011 – 04 Feb 2013
- Paclitaxel carboplatin 05 Feb 2013 – 13 Jun 2013
- Docetaxel 11 Jul 2013 – 07 Nov 2013
- CT 31 Jul 14 → PD

- What's next ?



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- Paclitaxel carboplatin 05 Feb 2013 – 13 Jun 2013
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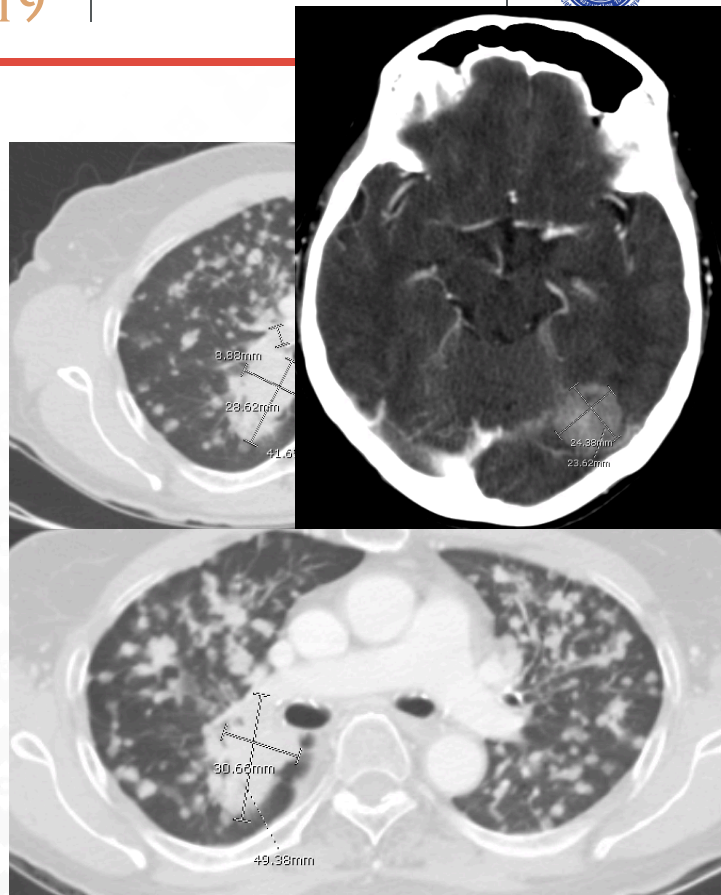
- Pemetrexed 05 Feb 2015 – 21 May 2015
- CT 01 Oct 2016 → PD

- What's next?

- Afatinib (40) in clinical trial 20 Sep 2011 – 04 Feb 2013
- Paclitaxel carboplatin 05 Feb 2013 – 13 Jun 2013
- Docetaxel 11 Jul 2013 – 07 Nov 2013
- CT 31 Jul 14 → PD
- Pemetrexed 05 Feb 2015 – 21 May 2015
- CT 01 Oct 2016 → PD
- Gemcitabine cisplatin 15 Oct 2015 – 31 Mar 2016
- CT 06 May 2016 → PD



What's next?

- A. Reassure and best supportive care
- B. Palliative brain XRT
- C. Palliative brain XRT and test for T790M
- D. Palliative brain XRT and then IO

Re-biopsy for biomarker testing

- EGFR
  - Exon 18: no mutation
  - Exon 19: positive for mutation; c 2249C>T p.(A750V)
  - Exon 20: positive for mutation; c 2369C>T p.(T790M)
  - Exon 21: positive for mutation; c 2573T>G p.(L858R)

Re-biopsy for biomarker testing

- EGFR
  - Exon 18: no mutation
  - Exon 19: positive for mutation; c 2249C>T p.(A750V)
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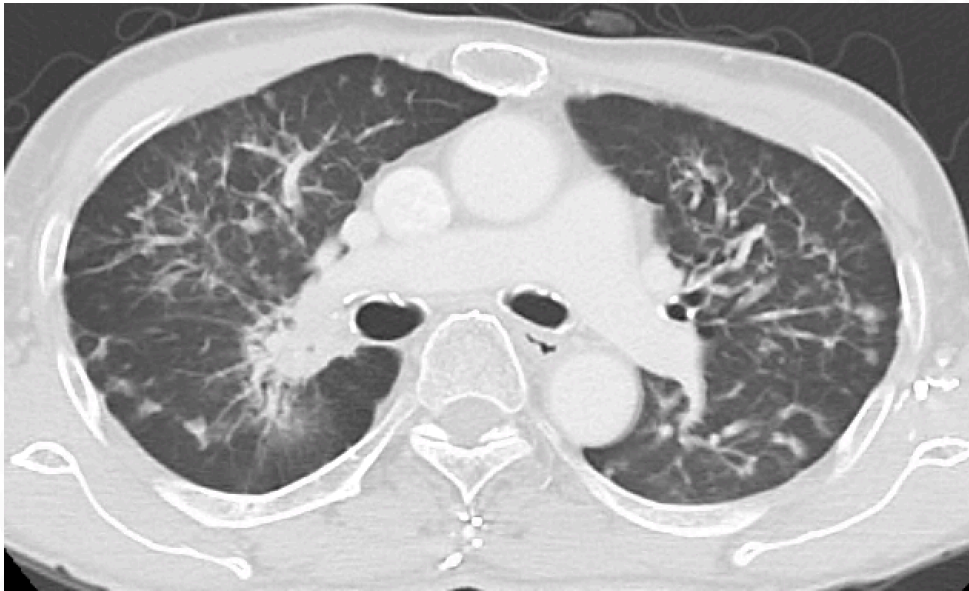
- Palliative brain XRT

02 Feb 2019



- Osimertinib 26 Aug 2016 – now
- Dx 23 Aug 2011 – now

Summary

- Case 1- Uncommon EGFR with durable response
- Case 2- EGFR and ALK
- Case 3- EGFR with multiple mutations (and multiple lines of treatment)

Any Questions?

Thank you for attention ☺

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