

Case Sharing of Afatinib for the Treatment of Patients With Advanced Squamous Cell Lung Cancer

2017 Conversations in Oncology in Shanghai, China

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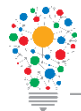
BI Symposium

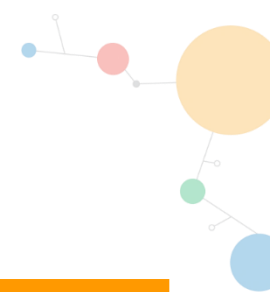
LET'S COLLABORATE
ONCOLOGY FROM BOEHRINGER INGELHEIM



Patient

- Brief Introduction of Medical History
 - 53-year-old male with a history of smoking for 30 years
 - Chief complaints: paroxysmal cough, a small amount of bloody phlegm with asthma after activities for over 10 days
 - ECOG score: 1





Auxiliary Examination and Clinical Diagnosis

- Pathological and Imaging Examinations

Date	Observation
Aug 10, 2012	<ul style="list-style-type: none">• Tracheoscopy indicated papillary neoplasm at opening of the left lower lobe.• Abdominal B-ultrasound was normal
Aug 13, 2012	<ul style="list-style-type: none">• Cranial MRI indicated ischemic foci in bilateral frontal lobes;• TCT examination detected a small amount of cancerous cells and inclination to squamous cell carcinoma
Aug 14, 2012	<ul style="list-style-type: none">• Pathology test indicated squamous cell carcinoma
Aug 16, 2012	<ul style="list-style-type: none">• Enhanced chest CT examination indicated space-occupying lesion in the left lower lobe with obstructive atelectasis, enlarged lymph nodes of hilum of left lung and mediastina, small amount of pleural effusion on the left side

- On August 15, 2012, the whole body radioisotope bone scanning was normal



Therapeutic Regimen

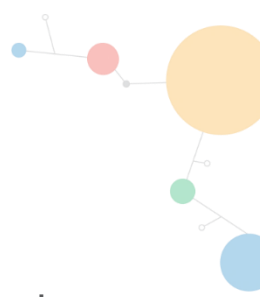
- On August 20, 2012, left pneumonectomy was performed under general anesthesia
- Pathological Diagnosis:
 - **Squamous cell carcinoma** of bronchus at root of left lower lobe, with necrosis, mild-low differentiation, **P-T2bN2M0**, R (-), stage IIIA, PSI, infiltration of bronchial wall, hilar vascular wall invasion, size of lump 6.5*5*3.4 cm
 - Cancer metastases to lymph gland between upper and lower lobes, subcarina, tracheal bronchus, lower pulmonary ligament and hilum, no cancer metastases to lymph gland at incisal edge of left principal bronchus, para-aortic, paraesophageal, orifice of upper lobe; lymph gland under aortic arch was fatty tissue and microscopy of left lower pulmonary nodule detected pulmonary interstitial tissue hyperplasia with foreign body granuloma formation
 - The postoperative recovery was good without special discomfort currently and the patient was admitted into the hospital for further treatment



Therapeutic Regimen

Timing	Cycle	TC Regimen Chemotherapy	Notes
September 2012	1	Paclitaxel 300mg/ Carboplatin 450mg	<ul style="list-style-type: none">WBCmin $2.0 \times 10^9/L$The patient developed generalised rash with pruritus following half-month chemotherapy
October 18, 2012	2	Paclitaxel 300mg/ Carboplatin 450mg	<ul style="list-style-type: none">WBCmin $2.6 \times 10^9/L$, ANCmin $0.6 \times 10^9/L$The rash on the head was obvious following the chemotherapy and now has been improved compared with before
November 16, 2012	3	Paclitaxel 270mg/ Carboplatin 450mg	<ul style="list-style-type: none">WBCmin $2.4 \times 10^9/L$, ANCmin $0.89 \times 10^9/L$.The patient was hospitalized for the third cycle of chemotherapyChemotherapy contraindication was excluded after hospitalization this time
December 13, 2012	4	Paclitaxel 270mg/ Carboplatin 450mg	<ul style="list-style-type: none">It went smoothly without obvious discomfort. Now the general condition was good. The patient was discharged and followed up





Follow Up

- Examination Report
 - Clear consciousness, stable breath; no palpated enlargement of supraclavicular lymph nodes, soft abdomen, liver and spleen untouched under the ribs; clear breath sounds in both lungs, no rale, regular cardiac rhythm, no murmur; nervous system (-)
- Clinical Diagnosis
 - Bronchiogenic carcinoma, primary, central type, left lung, squamous, post pneumonectomy



Imaging Evaluation (Pre-treatment With Afatinib) on April 25, 2013

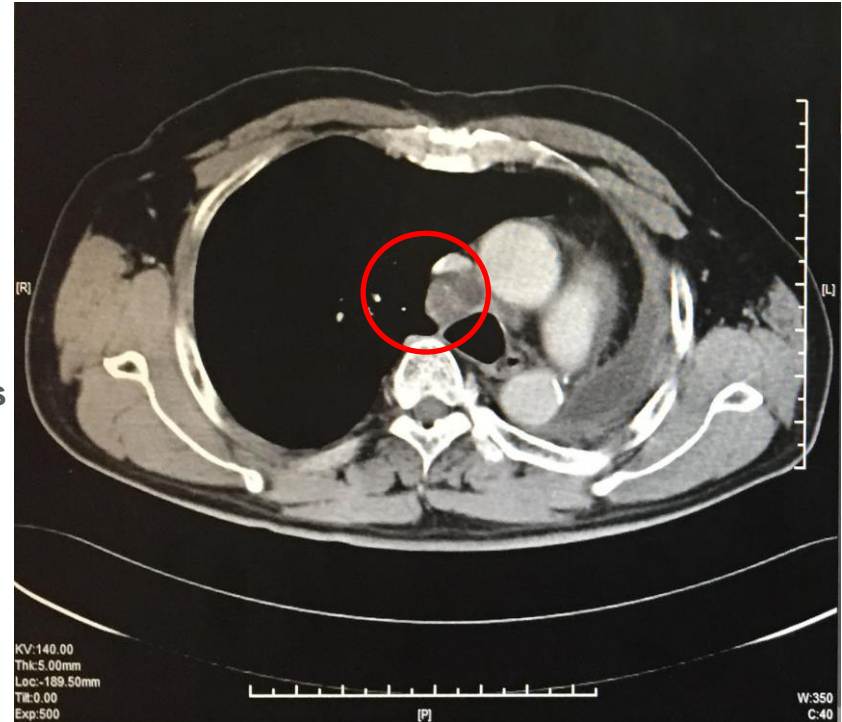
- Examination Report

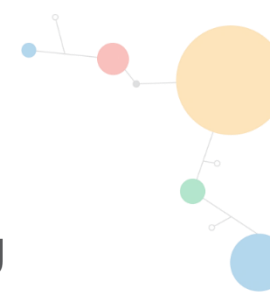
- Examination area: chest
- Examination observation: stenosis in the left thorax, mediastinum deviated to left, left localized pleural thickening with pleural effusion; a few stripes and patchy shadows in the middle lobe of right lung; a small amount of bullous emphysema in the right lung;

enlargement of posterior vena cava lymph nodes (4R group)

- Examination conclusion: postoperative change of left thorax, left pleural thickening with pleural effusion; a few chronic inflammations in the middle lobe of right lung, a small amount of bullous emphysema in the right lung; enlargement of mediastinal lymph nodes.

Please follow up.



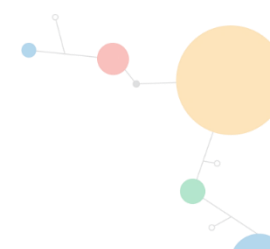


Pre-treatment With Afatinib (April 25, 2013)

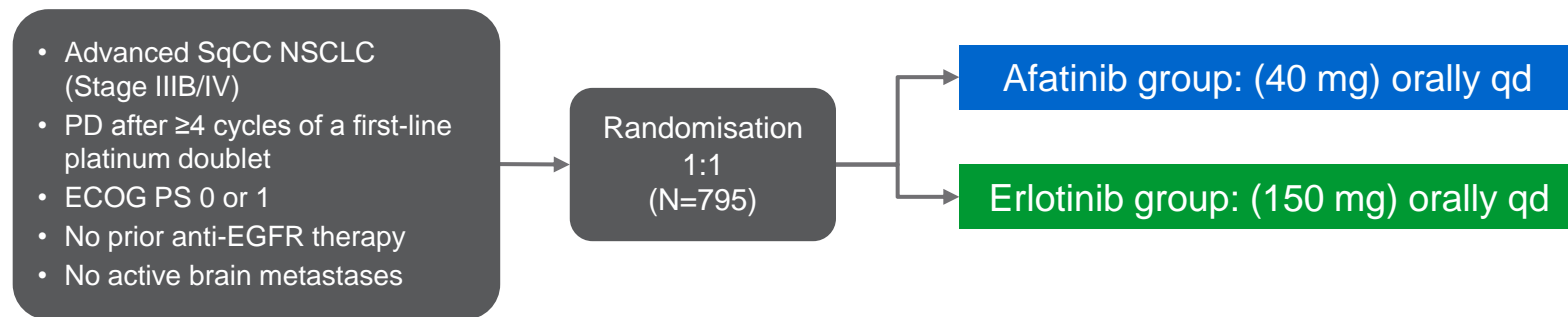
- In case of recurrence or metastasis during or within one year following adjuvant/neoadjuvant chemotherapy, the therapy is considered a failure targeting first-line systemic chemotherapy for progressive disease
- Chemotherapy failure was less than 1 year. The TC regimen was identified as a first-line treatment. **The patient was eligible for LUX-LUNG 8 clinical trial of afatinib vs erlotinib**



LUX-LUNG 8 Project



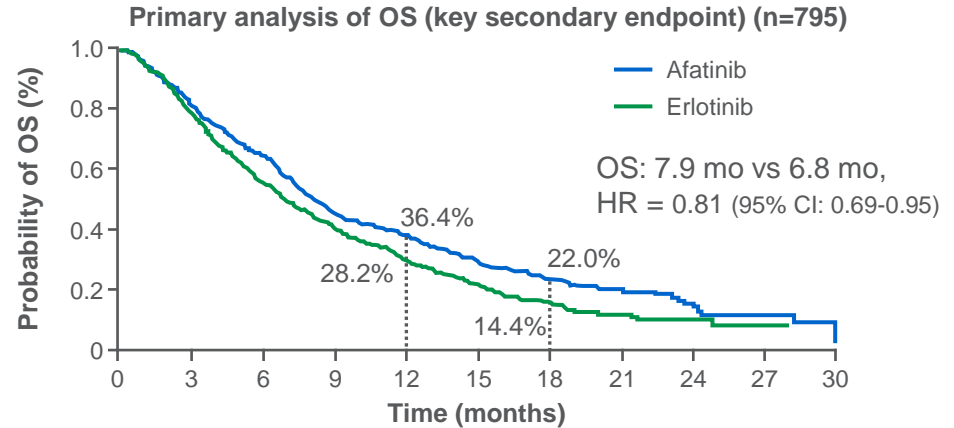
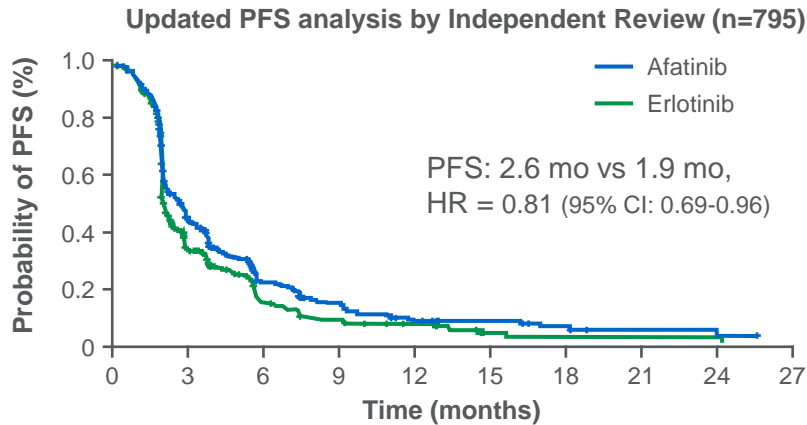
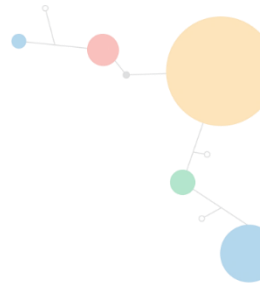
A Global Phase III Clinical Study Comparing Afatinib and Erlotinib for the Second-line Treatment of Advanced Squamous Cell Lung Cancer



Primary endpoint: PFS (independent site evaluation)
Secondary endpoint: OS etc.



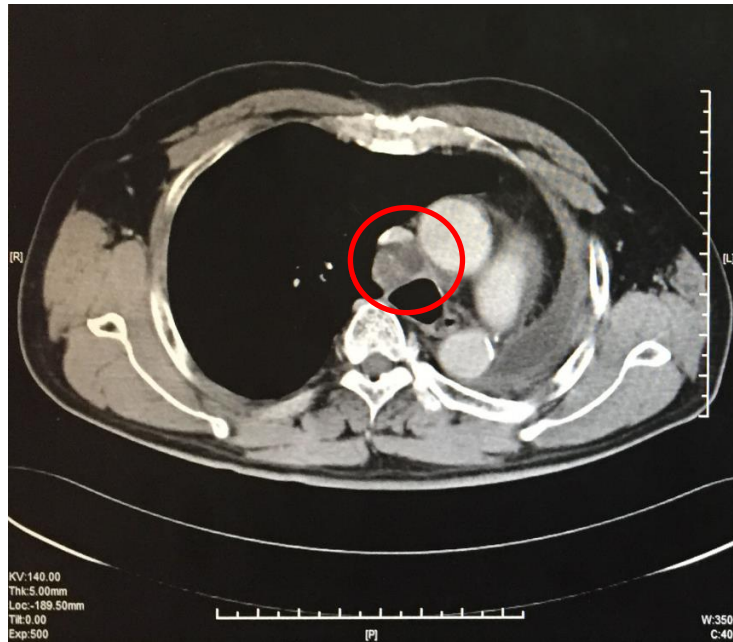
LUX-Lung 8: Significant Improvement in PFS and OS With Afatinib Compared With Erlotinib



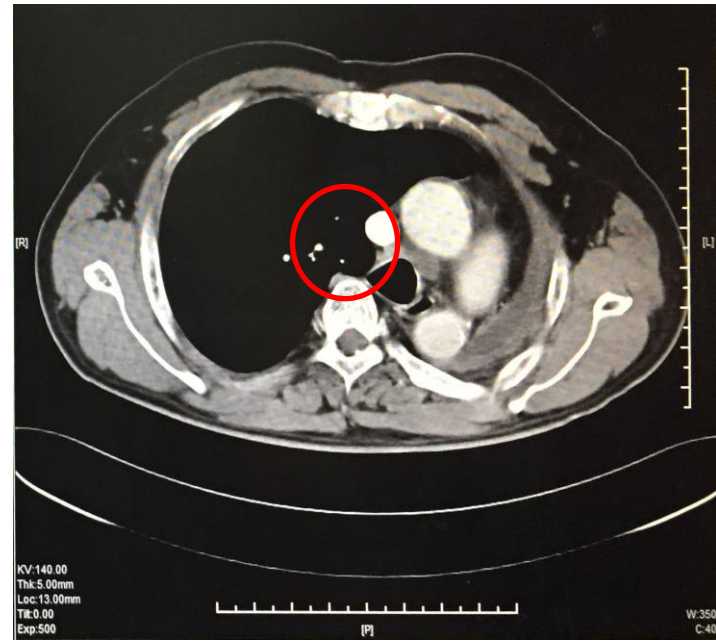
- Afatinib has been approved for the treatment of patients with metastatic lung squamous cell carcinoma with disease progression following platinum-based chemotherapy



Imaging Evaluation (Pre- and Post-treatment With Afatinib) on June 20, 2013



25-Apr-2013

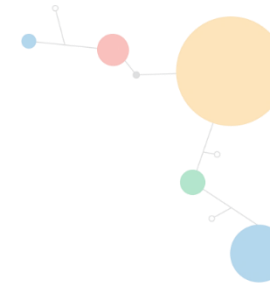


2 months later

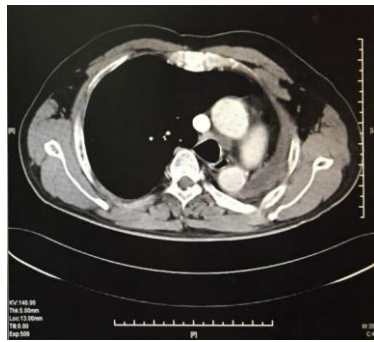
Response Evaluation: PR



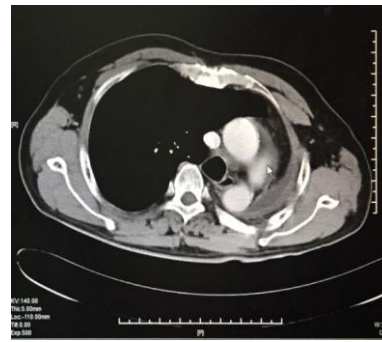
Imaging Evaluation (Pre- and Post-treatment With Afatinib) in 2013



25-Apr-2013



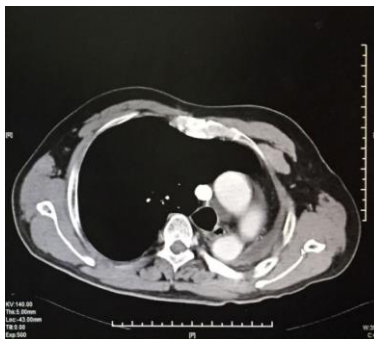
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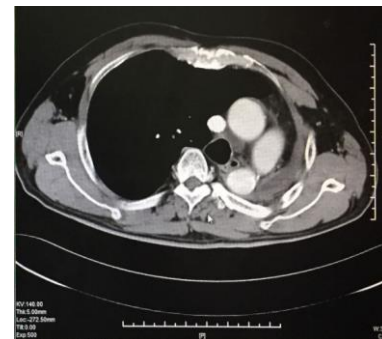
3 months later



7 months later



6 months later

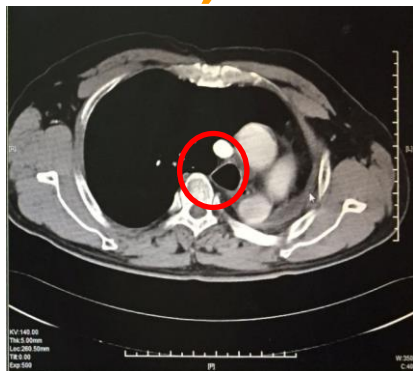
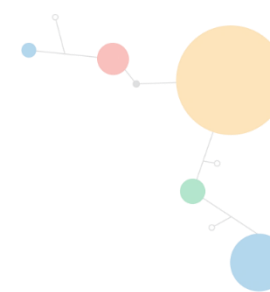


4 months later

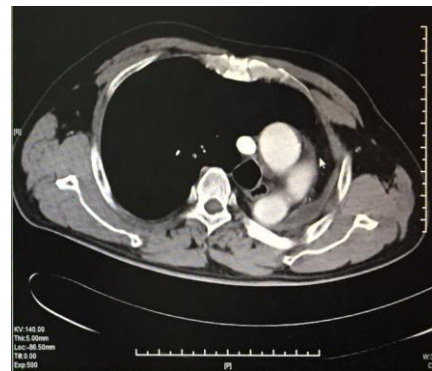


Response Evaluation: PR

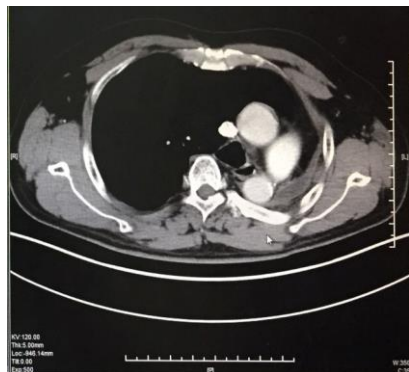
Imaging Evaluation (Pre- and Post-treatment With Afatinib) in 2014



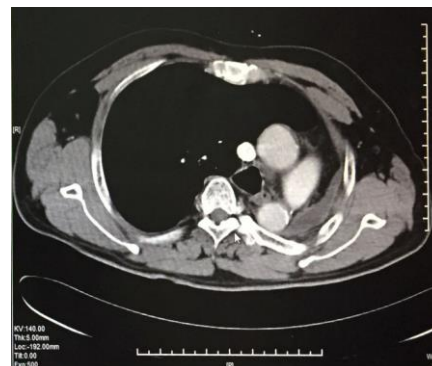
7 months later



9 months later



13 months later

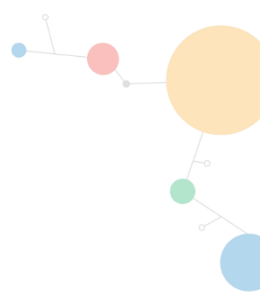


11 months later



Response Evaluation: PR



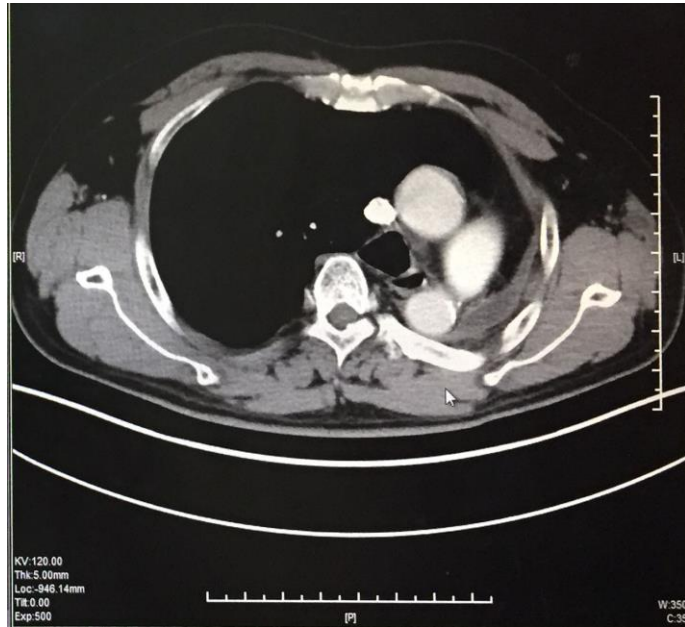


Examination Condition on May 22, 2014

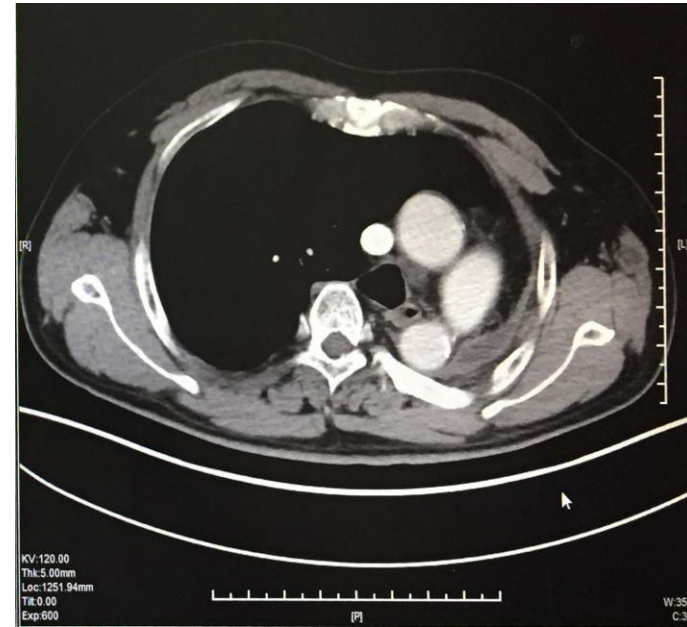
- Examination Report
 - Examination area: chest
 - Examination observation: stenosis in the left thorax and lung, mediastinum deviated to left, left localized pleural thickening with pleural effusion; a few scattered stripes and patchy shadows in the right lung; a small amount of bullous emphysema in the right lung; no speciality of mediastinum and hilus of both lungs, slight pleural thickening on the right side, without pleural effusion; Calcification shadow of aortic wall and coronary.
 - Examination conclusion: postoperative change of left thorax, left pleural thickening with pleural effusion; a few chronic inflammations scattered in the right lung, a small amount of bullous emphysema in the right lung. Please follow up.



Imaging Evaluation (Post-treatment With Afatinib) on July 17, 2014



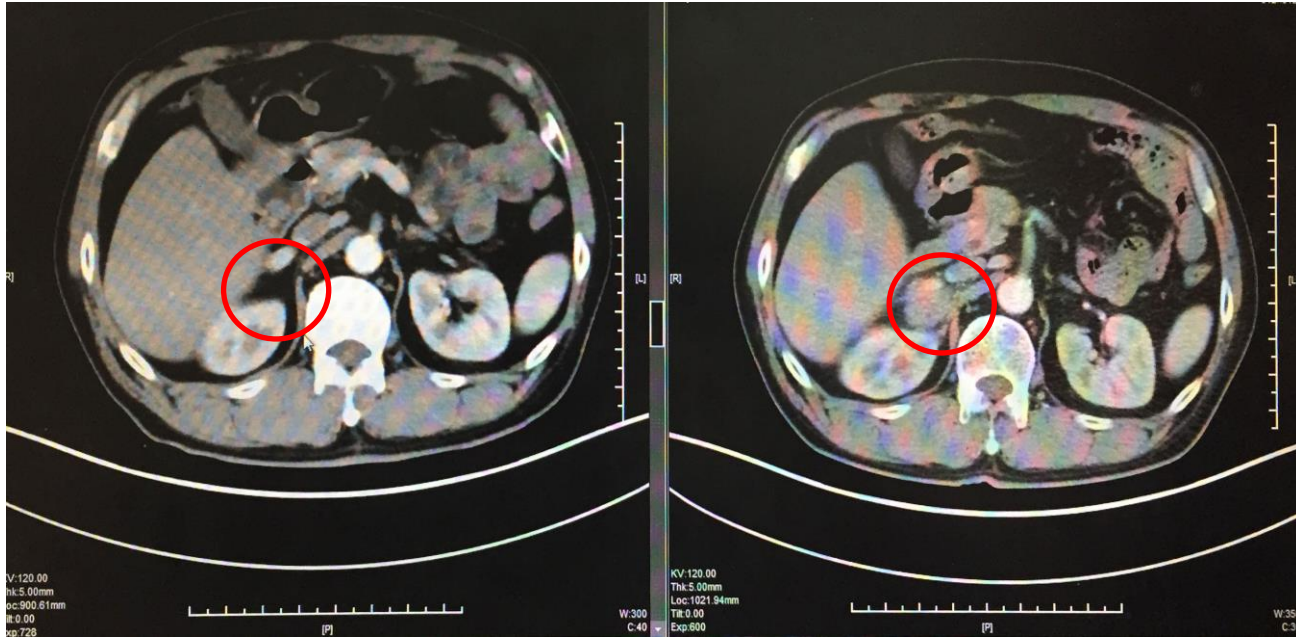
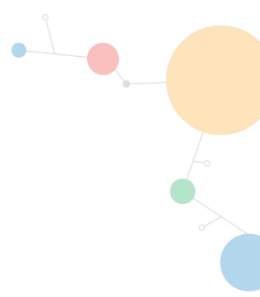
13 months later



15 months later



Imaging Evaluation (Post-treatment With Afatinib) on July 17, 2014

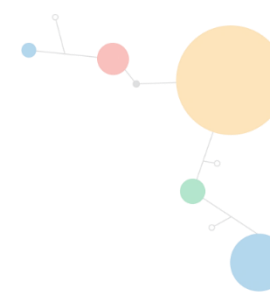


13 months later

15 months later

Response Evaluation: PD

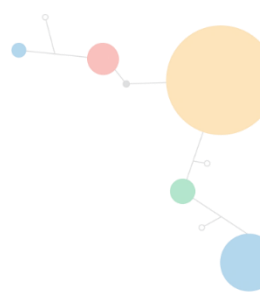




Examination Condition on July 17, 2014

- Examination Report
 - Examination area: chest
 - Examination observation: stenosis in the left thorax, mediastinum deviated to left, left localized pleural thickening with pleural effusion; a few scattered stripes and patchy shadows in the right lung; a small amount of bullous emphysema in the right lung; No speciality of mediastinum and hilus of both lungs, slight pleural thickening on the right side, without pleural effusion; enlargement of right supraclavicular lymph nodes; calcification shadow of aortic wall and coronary. Attachment: New nodules shadow in the right adrenal gland
 - Examination conclusion: postoperative change of left thorax, left pleural thickening with pleural effusion; a few chronic inflammations scattered in the right lung, a small amount of bullous emphysema in the right lung; enlargement of right supraclavicular lymph nodes. Please follow up.
 - Attachment: New nodules in the right adrenal gland

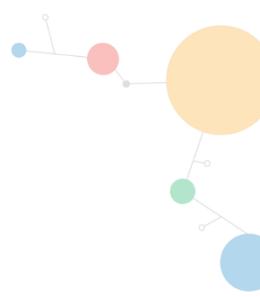




Patient Outcome

- Since April 25, 2013, the patient has taken Afatinib **over 16 months**.
- Response evaluation during the treatment period has always been as: **PR**





Adverse Reaction

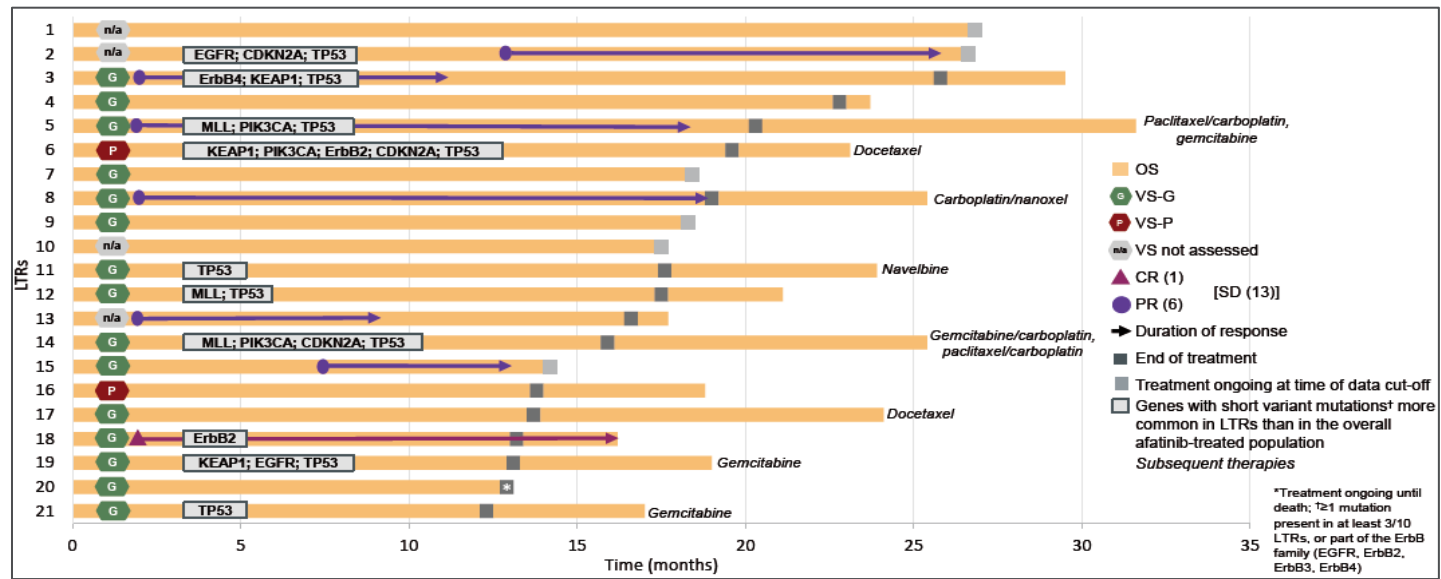
- Main adverse reactions: Grade 2 diarrhoea, Grade 3 rash, Grade 2 paronychia
- After dose reduction for two times, the final dose was 20 mg
- The side effects decreased significantly after dose reduction and mostly were Grade 1 ~ Grade 2



VeriStrat Status and Biomarkers More Commonly Observed in LTRs

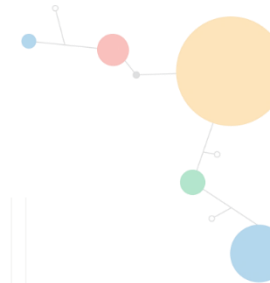


- 15/17 (88%) LTRs with samples evaluated by VeriStrat were VeriStrat-Good (VS-G)
- Overall, 207/336 (62%) afatinib-related patients with samples evaluated were VS-G

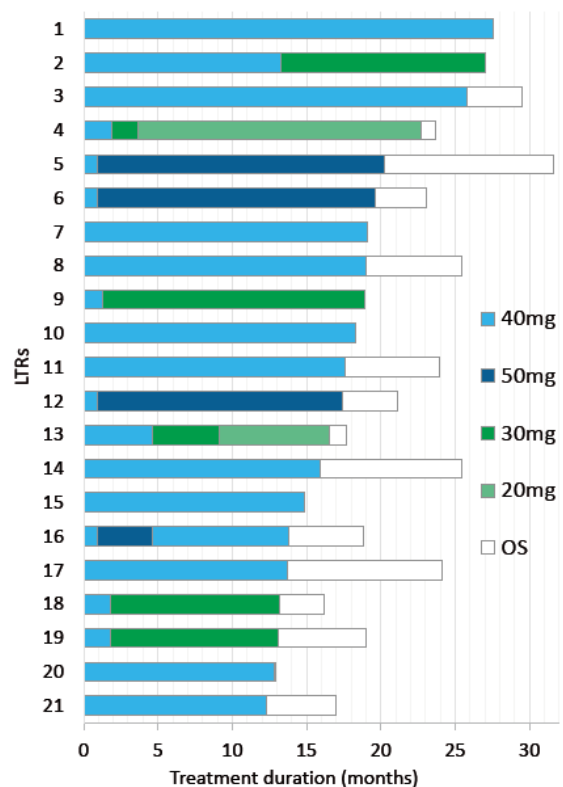


*Stable disease unless noted otherwise (patient 2 was classified as non-evaluable); †Patients were ordered and numbered by treatment duration, with patient 1 being on treatment longest; ‡First observed response at time of tumour measurement; §Last observed response at time of tumour measurement; ¶Treatment ongoing until death; ¶Received ≥1 line of chemotherapy after afatinib; CR = complete response; PR = partial response.

Common Treatment-related AEs and Tolerability-Guided Dose Adjustments



- The frequency of drug-related AEs in LTRs was similar to the overall afatinib-treated population
- Tolerability-guided dose adjustments are shown in the figure on the right:
 - The afatinib 40 mg/day starting dose was maintained in 11/21 and escalated to 50 mg in 4/21 patients
 - 6/21 dose-reduced to 30 mg; two further to 20 mg
- No AE-related treatment discontinuations occurred in LTRs





Results and Conclusion

- The patient relapsed quickly after surgery, had a long term response to afatinib, with significant benefit, but finally experienced progression in external thoracic lesion
- AE was manageable with dose reduction
- In patients with lung squamous cell carcinoma, afatinib should be considered as the preferred TKI in second-line therapy





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