ESMO Clinical Practice Guidelines

Non-Small-Cell Lung Cancer Case Presentation

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Disclosures

No potential conflicts of interest declared

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Stage IV lung adenocarcinoma

- 58-year old woman, married, no children, works as executive secretary, suffers from back pain since December 2009
- After 2 months of unsuccessful treatment by a chiropractor, her family doctor orders an MRI. A tumor leading to destruction of the first lumbar vertebra is identified and the patient referred to oncology
- The medical history and physical examination are otherwise not contributive. Patient has stopped smoking 30 years ago (15 pack-years)

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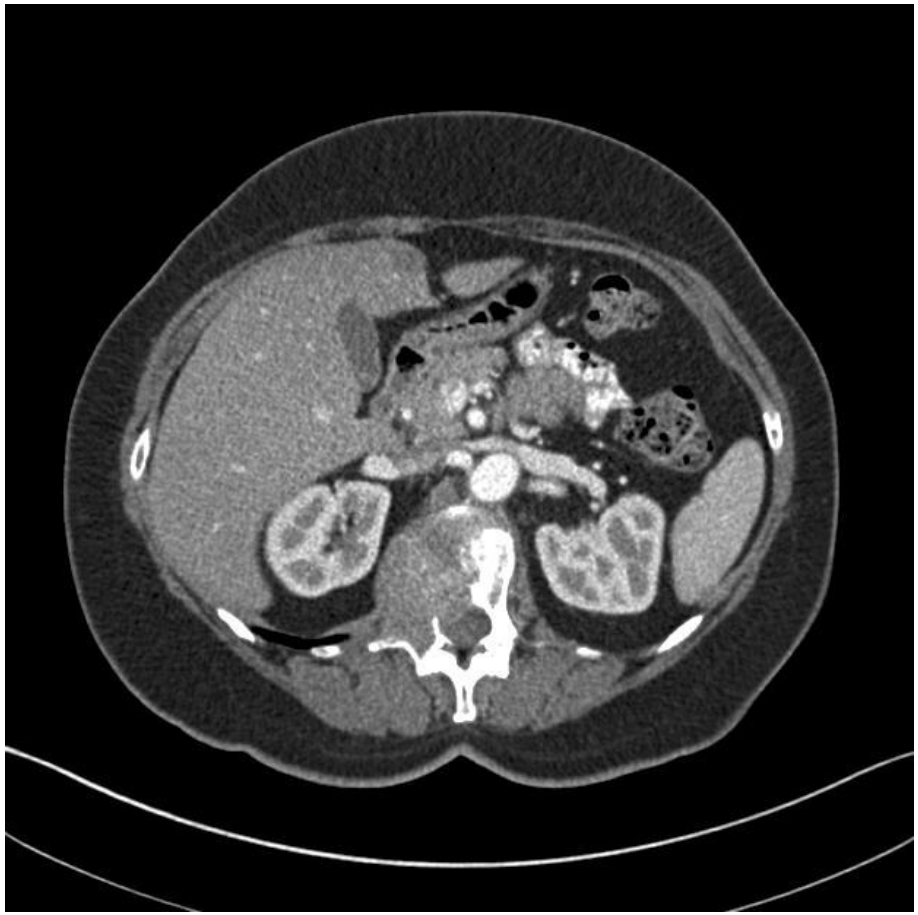
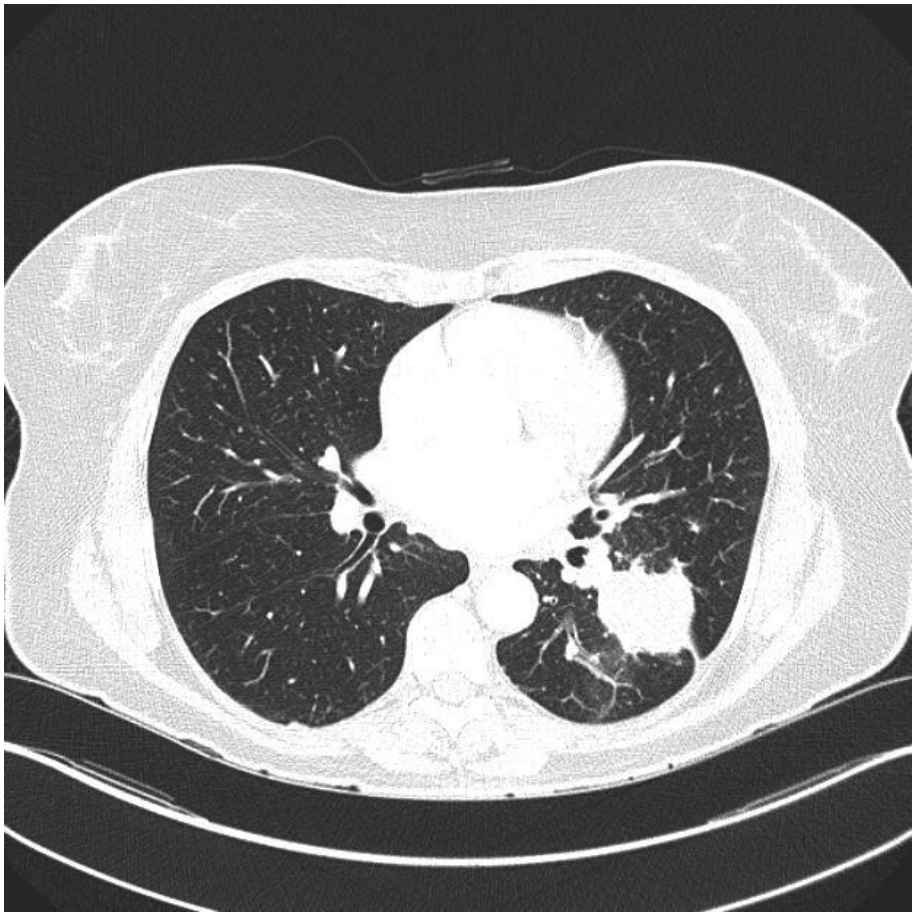
Stage IV lung adenocarcinoma





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Diagnosis and therapy

- 18.2.2010: Surgical decompression and dorsal stabilization
- Histology: Adenocarcinoma, TTF-1 positive, ER negative
- Diagnosis: Adenocarcinoma of the lung with mediastinal and cervical lymph node as well as bone metastasis, cT2a cN3 cM1b, Stage IV

What is your strategy?

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Q 1: Systemic therapy: which of the following would you choose?

1. Ciplatin-pemetrexed ASAP (neurotoxity?)
2. Carboplatin-pemetrexed ASAP
3. Cisplatin-pemetrexed bevacizumab (bevacizumab and spinal cord compression?)
4. Carboplatin-pemetrexed-bevacizumab
5. Wait for mutation testing (> 8 days)

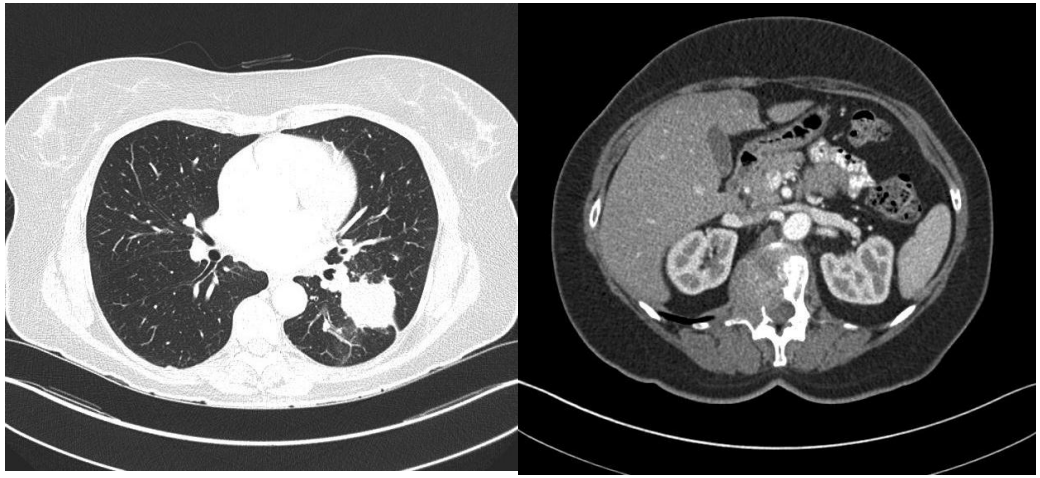
Systemic therapy

- Adjuvant post-operative local radiotherapy started for 10 days
- In absence of threatening lesion, decison is made to wait for EGFR molecular biology results
- 16.3.2010: Complete results of pathology :
  - EGFR genotype (exons 18 bis 21)
  - Deletion in exon 19 (p.746E_750Adel)
  - EGFR-FISH: positive (high-grade polysomy)
  - EGFR-IHC: protein expression score 3+ (DAKO Score 0-3)

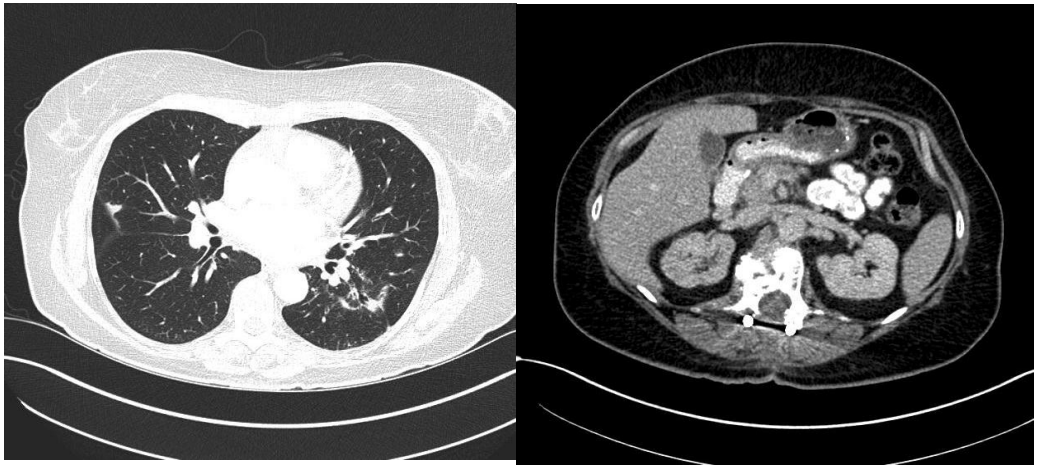
Systemic therapy

- Same day: Initiation of erlotinib 150mg/day (after completion of radiotherapy)

March 10



June 10



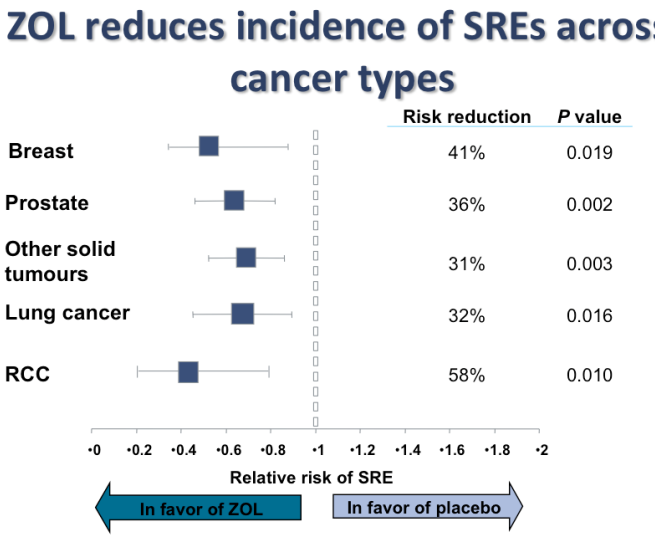
Q 2: Which of the following options would you choose for bone protection?

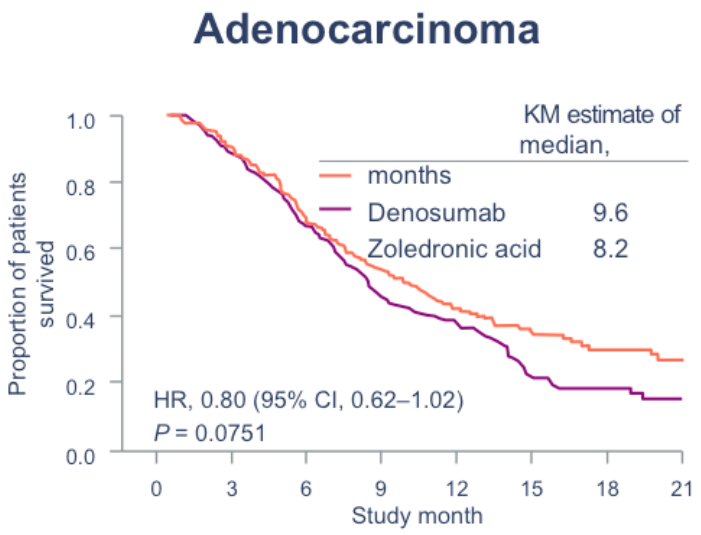
1. Zoledronic acid
2. Denosumab
3. Calcium and Vitamin D3 only
4. No bone protective drug in NSCLC
5. Denosumab and Calcium + Vitamin D3

Bone targeted agent?

Primary Cancer Site Evaluated by Trial	Time to First SRE: Median (months)	HR	95% CI	*P*	OS	Summary of AEs of Interest (trends and statistically significant; unadjusted)
Solid tumors (not breast or prostate) and myeloma[11]	20.6 *v* 16.3	0.84	0.71 to 0.98	< .001 (noninferiority) .06 adjusted (superiority)	No difference in overall population NSCLC: HR, 0.79; 95% CI, 0.66 to 0.95	Zoledronic acid: more acute phase reaction symptoms, renal AEs Denosumab: more hypocalcemia

NSCLC: HR of 0.84 for NSCLC (95% CI: 0.64–1.10; p = 0.20)





Denosumab monthly

Henry JCO 2011, Rosen JCO 2003, Scagliotti WCLC 2011

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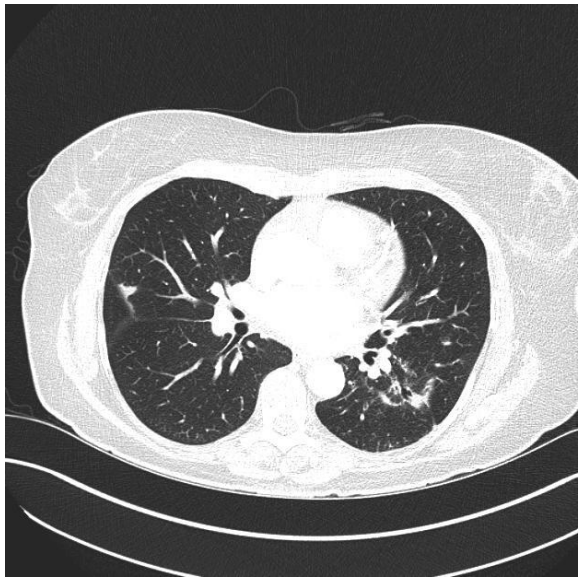
Follow-up on TKI



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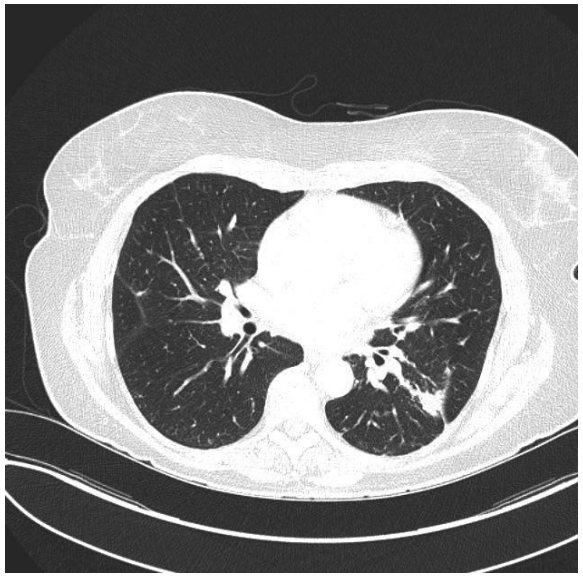
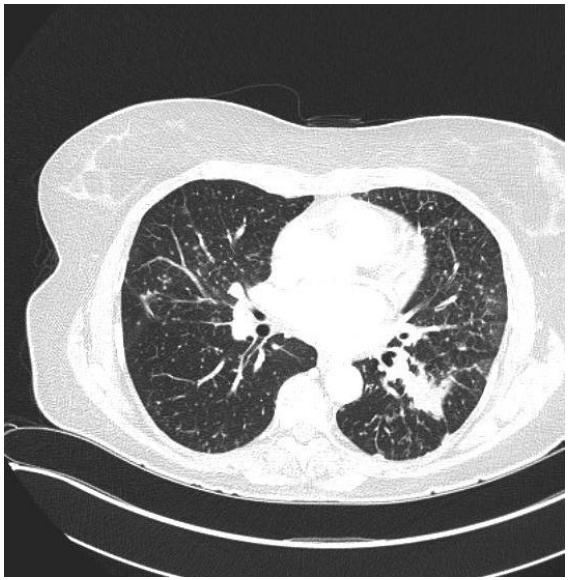


October 10



March 11

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Q 3: Second line treatment – how would you proceed?

1. Ciplatin-pemetrexed carboplatin-pemetrexed
2. Cisplatin-pemetrexed bevacizumab
3. Carboplatin-pemetrexed-bevacizumab
4. Second line standard chemotherapy docetaxel
5. Second line standard chemotherapy pemetrexed

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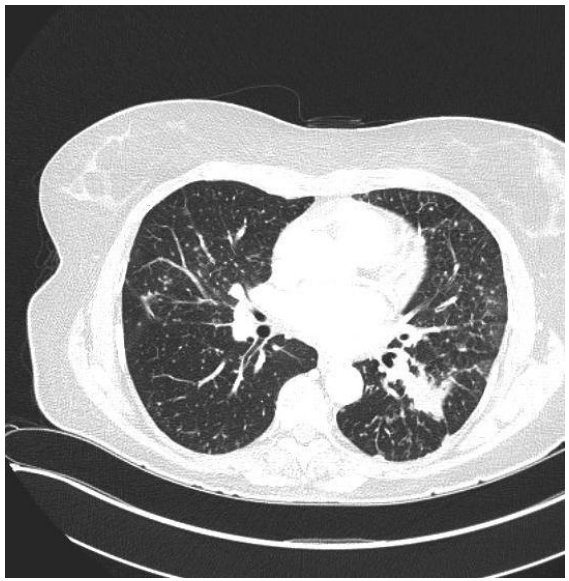
Second line treatment with cis-pem



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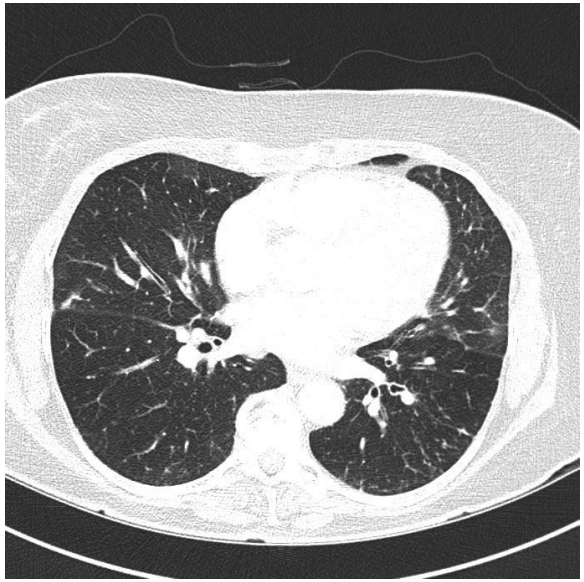
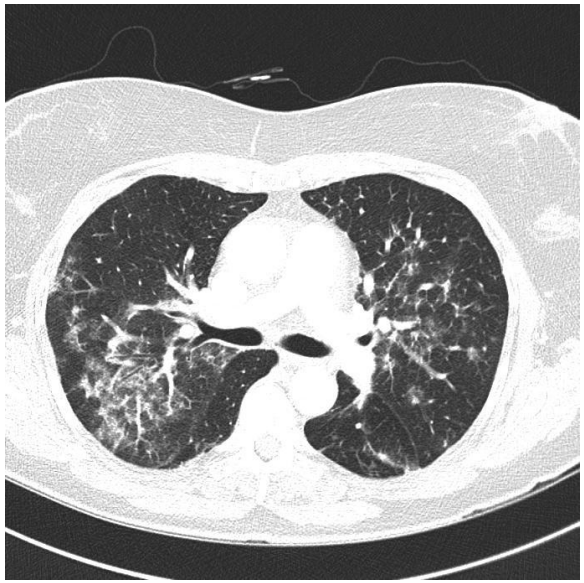


June 11



July 11

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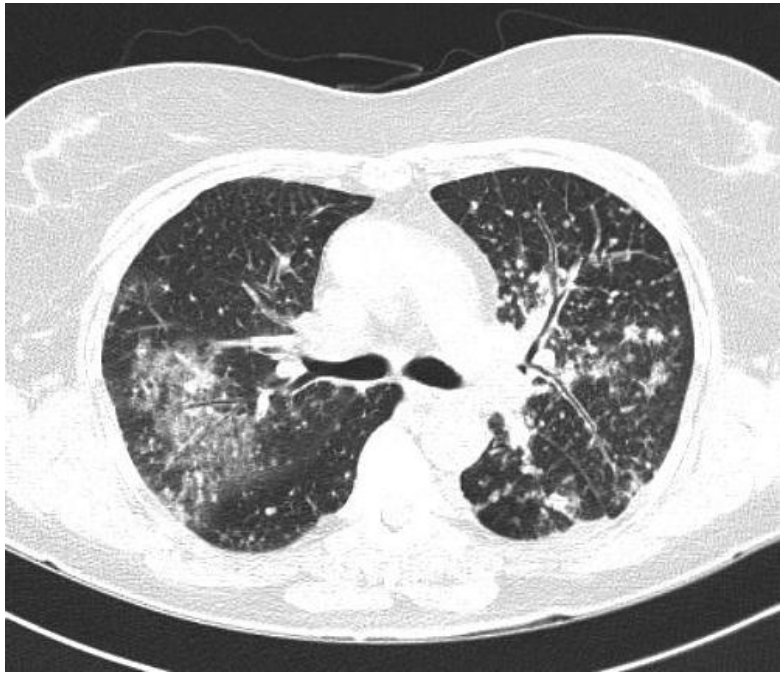
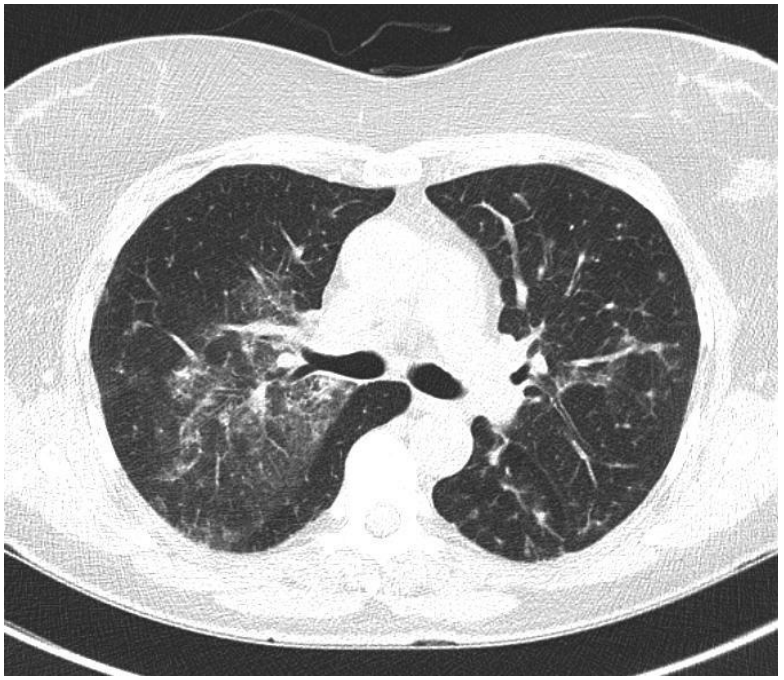
Re-treatment with EGFR TKI as third line



August 11



February 12

Rechallenge with TKI

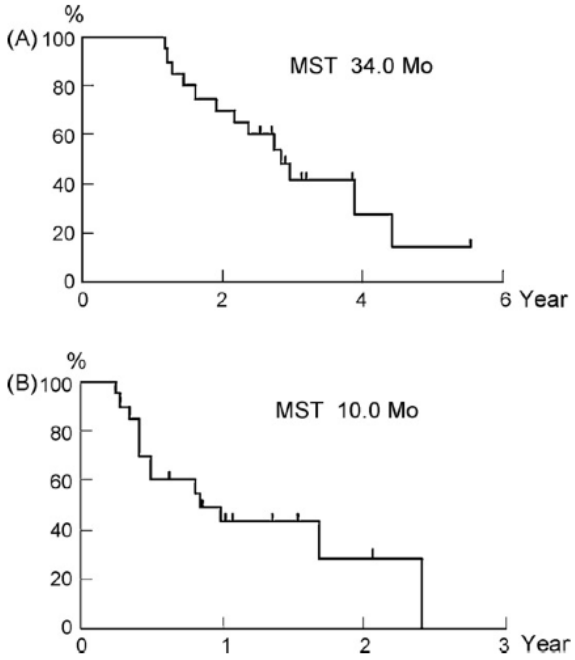
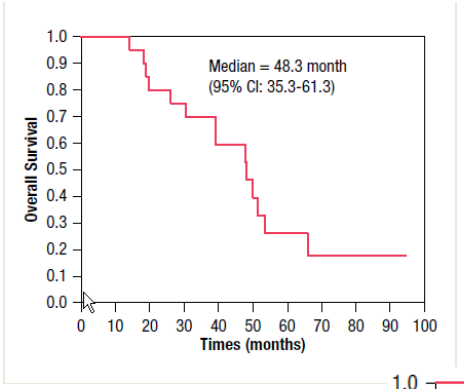


Fig. 1. Kaplan–Meier curve of survival from the start of the initial gefitinib (A) and the start of re-administration of gefitinib (B).

Response to re-administration of gefitinib.

Response	Response to initial gefitinib	
	PR	SD
PR	5	0
SD	4	4
PD	7	0

Response rate was 25%, disease control rate (PR + SD) was 65%.



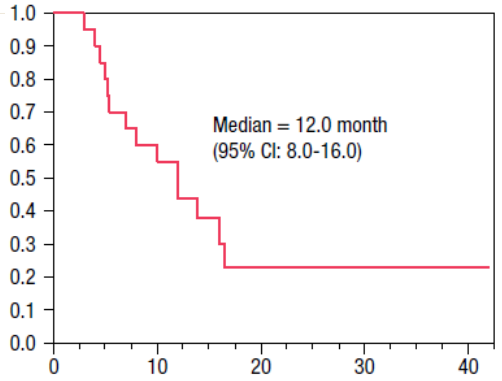


Table 3 Response to Gefitinib Readministration[a]

Response	No. Patients
Complete Response	0
Partial Response	3
Stable Disease	6
Progressive Disease	11

[a] Response rate 15% (95% CI, 3.%-37.9%); disease control rate 45% (95% CI, 23.1%-68.5%).

Tomizawa, Lung Cancer 2010; Koizumi, Clin Lung Cancer 2012, Heon ASCO 2012

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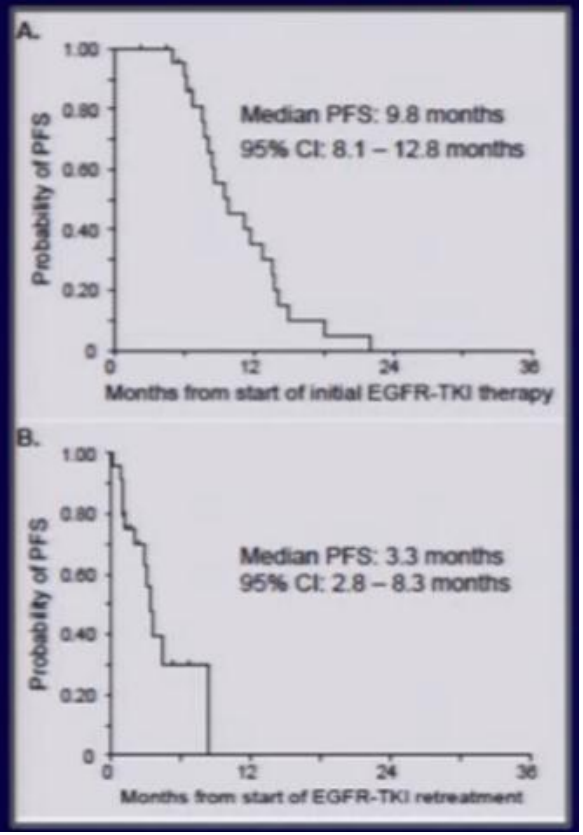
Rechallenge with TKI

EGFR TKI Re-treatment after Acquired Resistance: DFCI/MGH Experience

- Retrospective, 24 pts (over 9.5 yrs) with activating EGFR mutation after AR to gefitinib (30%) or erlotinib (70%)
- RR 4%, SD 63%
- Median interval off EGFR TKI 5 mo (range 2-46 mo)
- Greater benefit w/longer interval of EGFR TKI (PFS 4.4 vs. 1.9 mo for 6 mo interval off EGFR TKI)

Heon, ASCO 2012, A#7525



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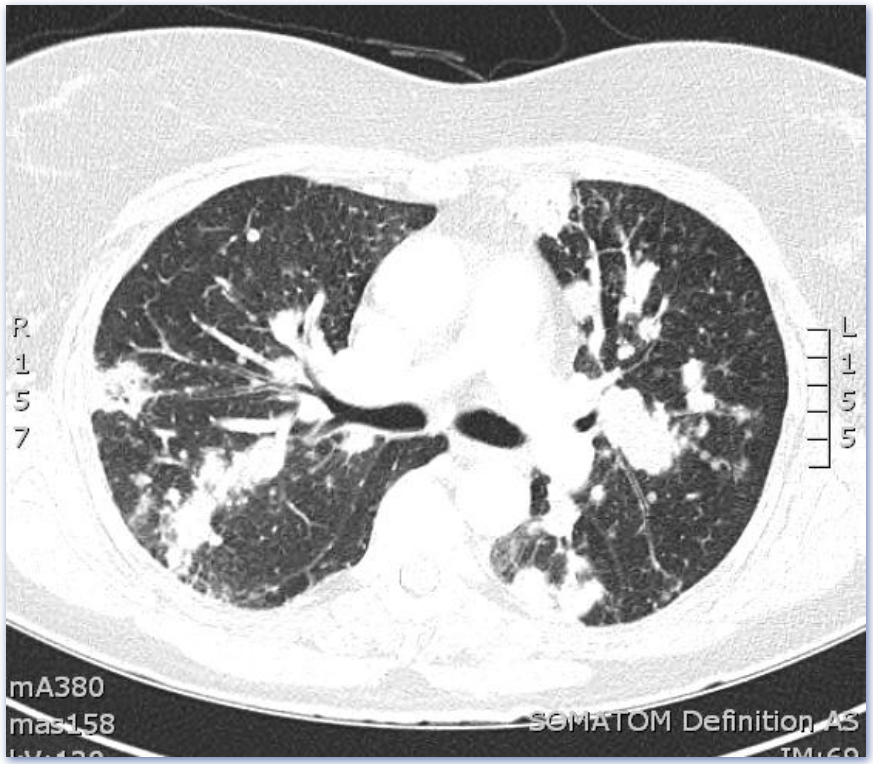
Symptomatic progression



March 12

Q 4: Fourth line treatment: how to continue?

1. Docetaxel
2. Pemetrexed again
3. Carboplatin-pemetrexed
4. Other cisplatin or carboplatin-based doublet
5. Rebiopsy (SCLC unknown at that time, for T790M and afatinib/customized trial? Exon 19 persistence proof?)

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Fourth line treatment

Fourth line carboplatin-pemetrexed

PR AFTER 4 CYCLES