# Clinical Case

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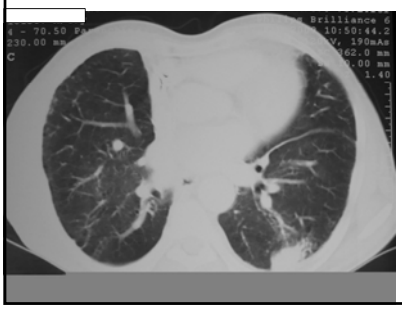
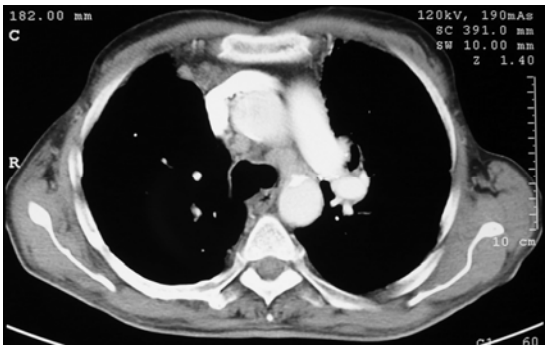
## History

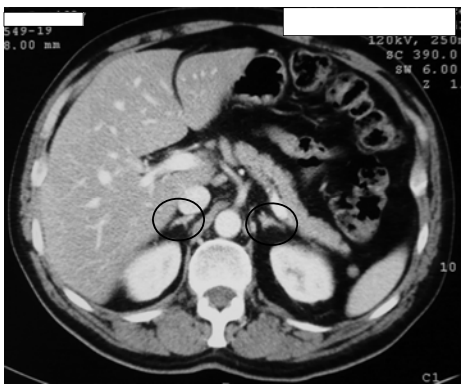
- A 68 year-old man
- Former smoker: 75 pack-years, quit 2 years ago
- Abdominal aortic aneurysm, for which he received annual computed tomography (CT) scans
- Coronary artery disease
- Hyperlipidemia
- ECOG PS=0 (stays active walking his dog)
- No weight loss, no relevant signs/symptoms

## Diagnostic

- Aneurysm on his most recent scan is only 2 cm
- Left lower lobe (LLL) lung mass, prevalently located in the lung periphery was identified plus enlarged mediastinal lymphnode
- In addition a modest bilateral enlargement of the adrenal glands was documented




182.00 mm
C
120kV, 190mAs
SC 391.0 mm
SW 10.00 mm
Z 1.40
R
10 cm


120kV,
SC 390.0
SW 6.00
10

- Based on these results what further procedure would you recommend?

- **Biopsy of the primary lesion through fiberbroncoscopy or transthoracic fine needle aspiration biopsy**
- **Positron Emission Tomography (PET) scan**
- Mediastinoscopy, if negative proceed to lobectomy
- Biopsy followed by definitive radiation (with or without chemotherapy)

PLEASE ANSWER

1: **Biopsy of the primary lesion through fiberbroncoscopy or transthoracic fine needle aspiration biopsy**

- Any patient, unless contraindicated, should be diagnosed
- Any diagnostic attempt should be made to characterize the tumor histologically: cytological diagnosis through sputum cytology, bronchial aspirate or washing or FNA are frequently diagnostic possibilities.
- It is recommended to perform fiberbronchoscopy in a patient with a suspected lung cancer because it contribute to stage properly the tumor and discover synchronous lesions.

## 2. Positron Emission Tomography (PET) scan

- CT scanning provides anatomic detail that better identifies the location of the tumor, its proximity to local structures, and whether or not lymph nodes in the mediastinum are enlarged.
- FDG-PET reveals higher sensitivity and specificity than chest CT scanning, for staging lung cancer in the mediastinum and even if it contribute to detect unsuspected metastatic lesions
- FDG-PET is not an exam to make diagnosis of lung cancer: remember false positive (granulomatous diseases, chronic infections) and false negative results (BAC, carcinoids)

## 3. Mediastinoscopy, if negative proceed to lobectomy

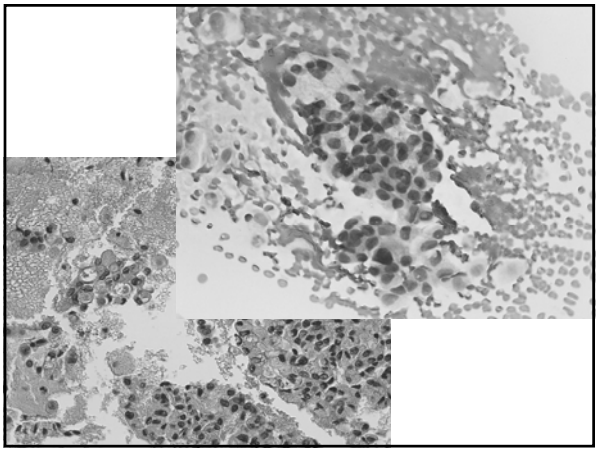
- If performed at this stage mediastinoscopy may be absolutely useless and it will expose the patient to potential unnecessary morbidity (and mortality) if additional examinations will confirm/reveal extrathoracic metastases.
- In addition to mediastinoscopy a variety of less invasive staging tests are available to investigate the mediastinal involvement by the tumor , including thoracoscopy (video-assisted thoracoscopic surgery), transbronchial needle aspiration (TBNA), transthoracic needle aspiration (TTNA), and endoscopic ultrasound with fine needle aspiration (EUS-NA).

## 4. Biopsy followed by definitive radiation (with or without chemotherapy)

- Again, a lack of information at this point about the extension of the neoplastic disease is making this choice totally wrong.

## Diagnostic

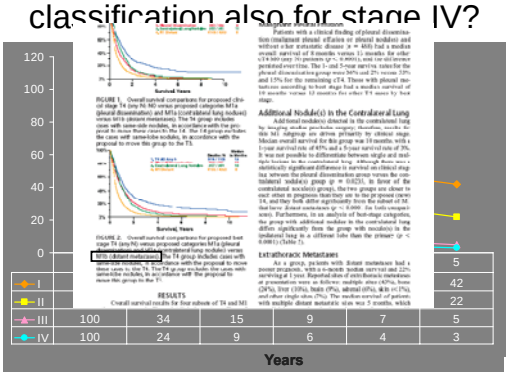
- **Pt was submitted to FBS which did not revealed any endobronchial lesion and the bronchial aspirate was negative for neoplastic cells.**
- **In the subsequent days he was submitted to a FNA biopsy of the primary tumor with a diagnosis of adenocarcinoma.**



## Diagnostic

- **As a part of a staging work up the patient received a FDG-PET scan that was positive in the LLL mass and the mediastinal LN seen on CT scan.**
- **It was also revealed an hot spot (SUVMax 4.5) on the right adrenal gland documented previously modestly enlarged to the CT scan.**
- **He was clinically classified as stage IV.**

There is a proposal for a new classification also for stage IV?




- **Are you confident with the diagnosis of adrenal metastasis by PET?**

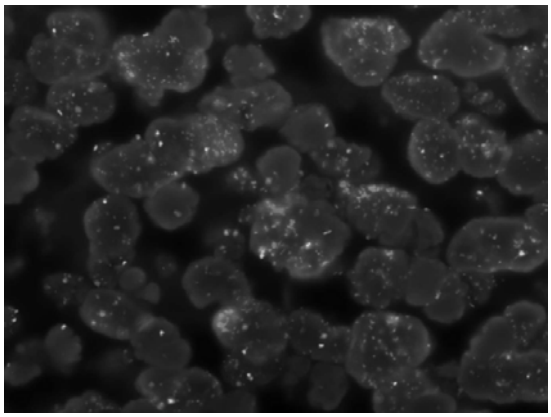
  **1)Yes**

  **2)No**

  **PLEASE ANSWER**

## Yes

- Possibility of false positive adrenal enlargements

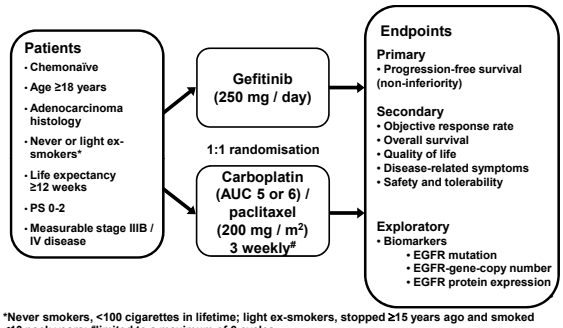


- **What kind of therapeutic approach would you recommend**

- 1. Anti EGFRi mono-therapy
- 2. Carboplatin/paclitaxel + bevacizumab
- 3. Cisplatin-based chemotherapy
- 4. Cisplatin-vinorelbine plus cetuximab
- 5. Cisplatin-pemetrexed
- 6. A non platinum doublet

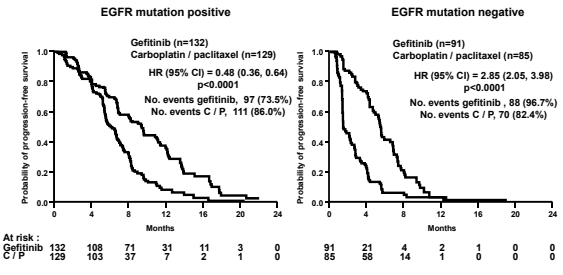
**PLEASE ANSWER**

## 1: Anti EGFRi mono-therapy
## This could be a correct answer…..**BUT**




*Never smokers, <100 cigarettes in lifetime; light ex-smokers, stopped ≥15 years ago and smoked ≤10 pack years; #limited to a maximum of 6 cycles
Carboplatin / paclitaxel was offered to gefitinib patients upon progression
PS, performance status; EGFR, epidermal growth factor receptor

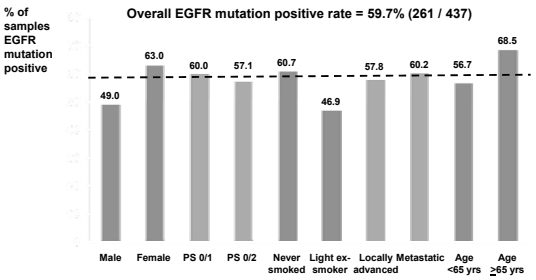
## Progression-free Survival in EGFR Mutation Positive and Negative Patients



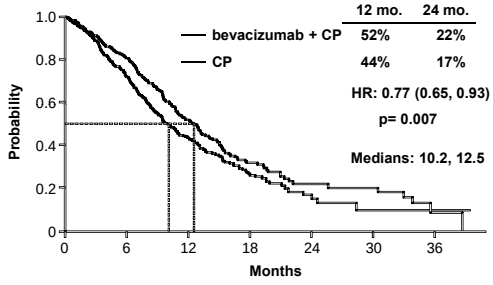

Treatment by subgroup interaction test, p<0.0001

ITT population
Cox analysis with covariates

## EGFR Mutation Positive Status and Clinical Characteristics

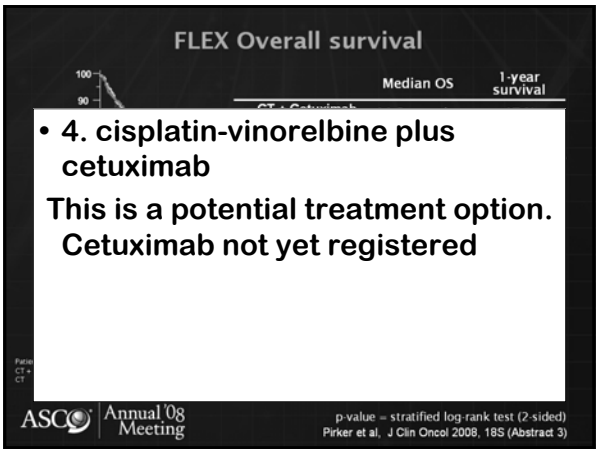



## 2: carboplatin/paclitaxel + bevacizumab
## This is a potential treatment option

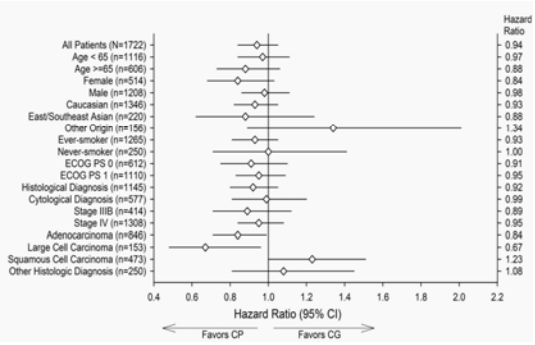



Sandler A, NEJM 2006

- **3: cisplatin-based chemotherapy**
  **This is not the best treatment option**




**5: cisplatin-pemetrexed**
**This is a preferred treatment options among ciplatin-based doublets**




- **6: a non platinum doublet**
  **This is <u>not</u> a treatment option**

***BMJ, 1995***

Consider your answer to the previous question. Is there a biomarker that select by itself the treatment choice?

i.e.: K Ras mutation, EGFR mutations, TS, ERCC1, RRM1, other….

Currently the answer is NO

**How long would you continue initial treatment in this patient?**

1) 4-6 courses
- This is the right answer

2) 8 courses PLEASE ANSWER
- This is not a correct answer

3) Until progression
- This is not the correct answer

## ASCO Guidelines 2003 (&2008)

- " Duration of Therapy: in stage IV NSCLC : first-line platinum-based chemotherapy should be stopped at four cycles in patients who are not responding to treatment. First-line chemotherapy should be administered for no more than six cycles in pts with stage IV NSCLC."

*Pfister et al. ASCO GUIDELINES Update 2003 JCO 2004; 22: 330-353*

these statements were predominantly based on the randomized trials by *Socinski et al* and *Smith et al*

## Would you offer maintenance therapy to this patient?

- Yes, bevacizumab
- Yes, pemetrexed
- No

## Pemetrexed vs Placebo Maintenance

**Double-blind, Placebo-controlled, Multicenter, Phase III Trial**

- Stage IIIB/IV NSCLC
- PS 0-1
- **4 prior cycles of gem, doc, or tax + cis or carb, with CR, PR, or SD**

Randomization factors:
- gender
- PS
- stage
- best tumor response to induction
- non-platinum induction drug
- brain mets

**2:1 Randomization**

→ **Pemetrexed 500 mg/m$^2$ (d1,q21d) + BSC (N=441)***

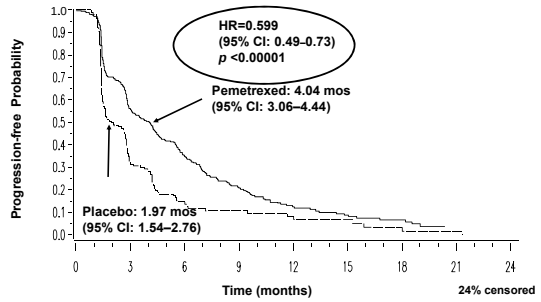
→ **Placebo (d1, q21d) + BSC (N=222)***

**Primary Endpoint = PFS**

*$B_{12}$, folate, and dexamethasone given in both arms

*Ciuleanu et al, J Clin Oncol 2008; 26: 8011*

## Pemetrexed vs Placebo Maintenance Study Progression-free Survival (N=581)




*Ciuleanu et al, J Clin Oncol 2008; 26: 8011*