ESMO Clinical Practice Guidelines

Lung Cancer
Clinical Case Presentation

Prof Keith M Kerr
Aberdeen University Medical School
Aberdeen Royal Infirmay
Foresterhill, Aberdeen, UK

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Disclosures: Keith Kerr

- I have acted as consultant/advisor for Roche Genentech, Astra Zeneca, Pfizer, Eli Lilly, Novartis, Boehringer Ingelheim, Clovis, Bristol Myers Squibb, Merck Sharp Dohme

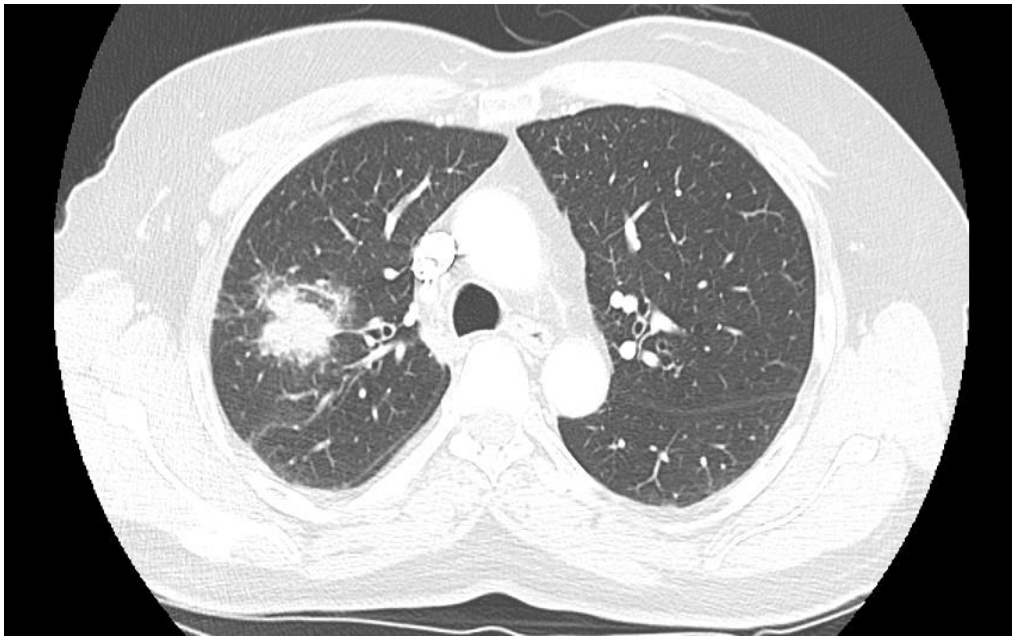
- I have received honoraria for speaker bureau from Roche Genentech, Astra Zeneca, Pfizer, Eli Lilly, Novartis, Boehringer Ingelheim, Bristol Myers Squibb

Introduction

- This 64 year old Caucasian male with a 30 pack/year history of tobacco smoking presented with increasing cough and lethargy

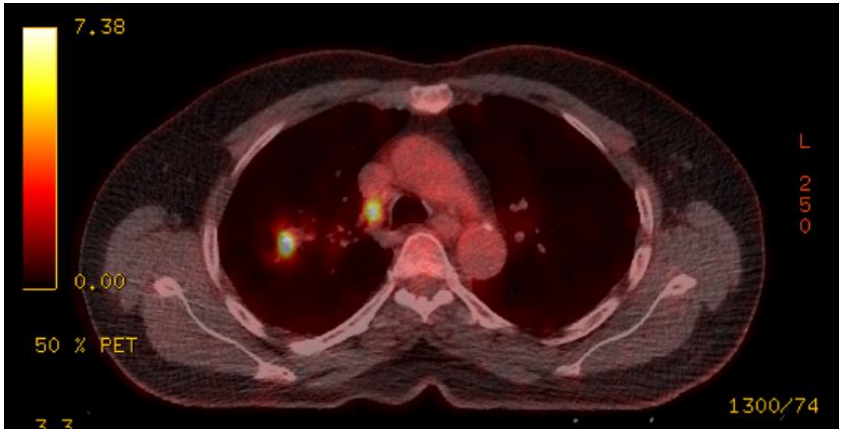
Introduction

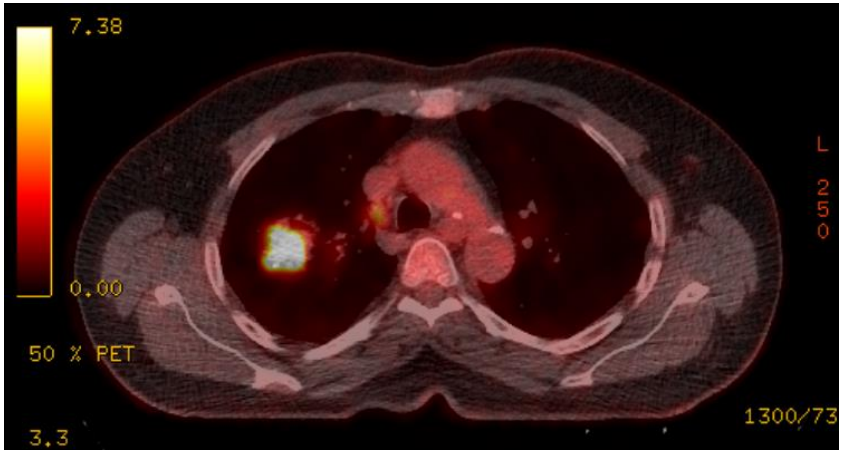
- CT scan revealed a peripheral right upper lobe mass with hilar lymphadenopathy. Discrete nodes visible – non-bulky disease.



Introduction

- PET scan confirmed high SUV in the mass, in R10 hilar nodes but also in station R4. Other stations were clear on PET
- No evidence of extra-thoracic disease





Introduction

- PS0
- No significant past medical history relevant to planned treatment
- Cardiovascular and pulmonary function were good
  - FEV1 2.4l

Introduction

- Bronchoscopy revealed no abnormality
- EBUS fine needle aspiration of R10 and R4 node stations reveal NSCLC which was TTF1/CK7 positive on immunohistochemistry. Station 7 was benign.

Q1: What would be the most appropriate initial treatment?

1. Platinum doublet chemotherapy
2. Radical radiotherapy
3. Concurrent chemoradiotherapy
4. Induction chemotherapy then lobectomy
5. Induction chemoradiotherapy then lobectomy
6. Right upper lobectomy with mediastinal lymph node dissection

Treatment

Right upper lobectomy and mediastinal lymph node dissection

- Stage IIIA
- Micropapillary predominant adenocarcinoma
- pT2a
- pN2 – Stations R4 and 7 positive, R2, 5/6 & R9 negative
- Surgical margins clear
- Patient recovered well from surgery

Q2: Should the patient receive adjuvant therapy?

1. No
2. Yes – Cisplatin & Vinorelbine
3. Yes – Cisplatin & Pemetrexed
4. EGFR tyrosine kinase inhibitor

Cisplatin-Pemetrexed adjuvant therapy – 4 cycles completed

Progression

15 months later the patient represented

- Weight loss, tiredness, breathless and pain in left hip – PS1
- Investigations reveal low serum albumin, anaemia
- Imaging revealed probable mediastinal nodal disease, liver metastases and lytic lesion in left ischium
- Multidisciplinary team meeting requested molecular pathology testing

Q3: Should the patient's tumour have been tested (molecular testing) at the time of initial diagnosis?

1. No
2. Yes – as a routine for non-squamous tumours
3. Yes – only if instructed by MDT
4. Yes – Only when pathology of resected tumour is 'high grade'
5. Unsure

Molecular testing outcomes

- ALK immunohistochemistry negative
- No evidence of *KRAS* or *BRAF* mutation

- EGFR mutation positive by direct sequencing and fragment length analysis
  - 15 base pair Exon 19 deletion mutation

Q4: What would be the appropriate therapy?

1. Cisplatin & Pemetrexed
2. Cisplatin & Gemcitabine
3. Gefitinib
4. Erlotinib
5. Afatinib
6. Other

Treatment at relapse

Patient received afatinib

- Liver metastases showed significant response
- Pain in left hip resolved
- Patients general condition improved
  - Less breathless
  - Gained weight
  - Hb increased

Progression on treatment

14 months after beginning afatinib therapy

- Patient complained of dizziness and headaches
- CT brain scan revealed multiple metastases
- Liver ultrasound scan showed increase in number of hepatic lesions
- PS1 on dexamethaszone

Q5: What is the next appropriate course of action?

1. Whole brain radiotherapy and platinum doublet chemotherapy
2. Switch to erlotinib or gefitinib
3. Immunomodulatory agent
4. Biopsy liver: if T790M positive, 3rd generation TKI
5. Biopsy liver: if T790M negative, chemotherapy +/- whole brain radiotherapy
6. Best supportive care

Treatment at progression

EGFR T790M mutation present in liver biopsy

- Patient is currently receiving AZ9291 (osimertinib)
  - Stable clinical condition
  - Brain and liver metastases show evidence of response