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ADVANCED NON SMALL CELL LUNG CANCER

Disclosures

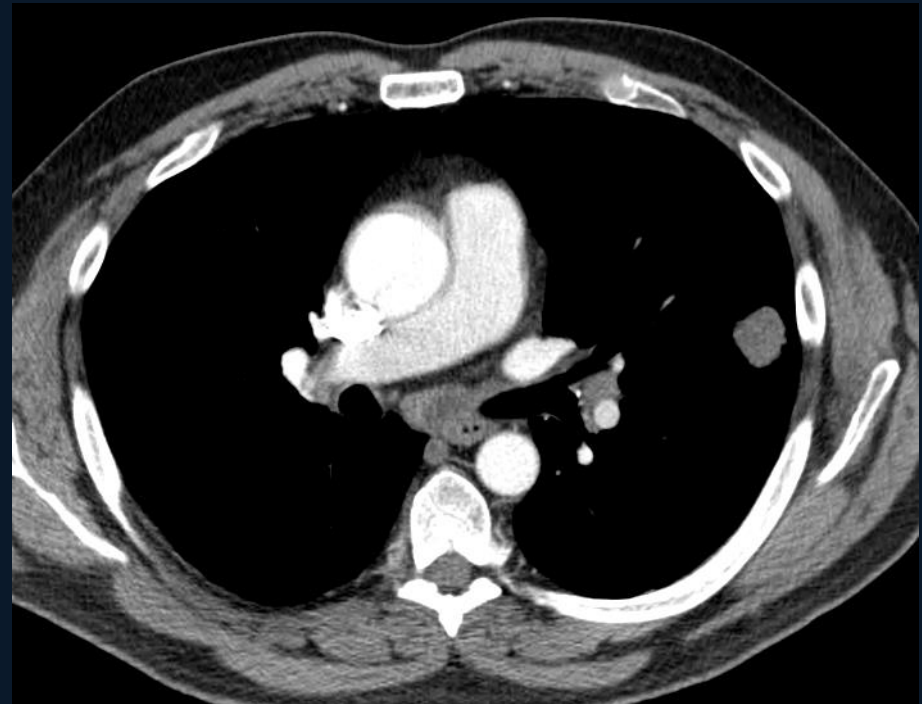
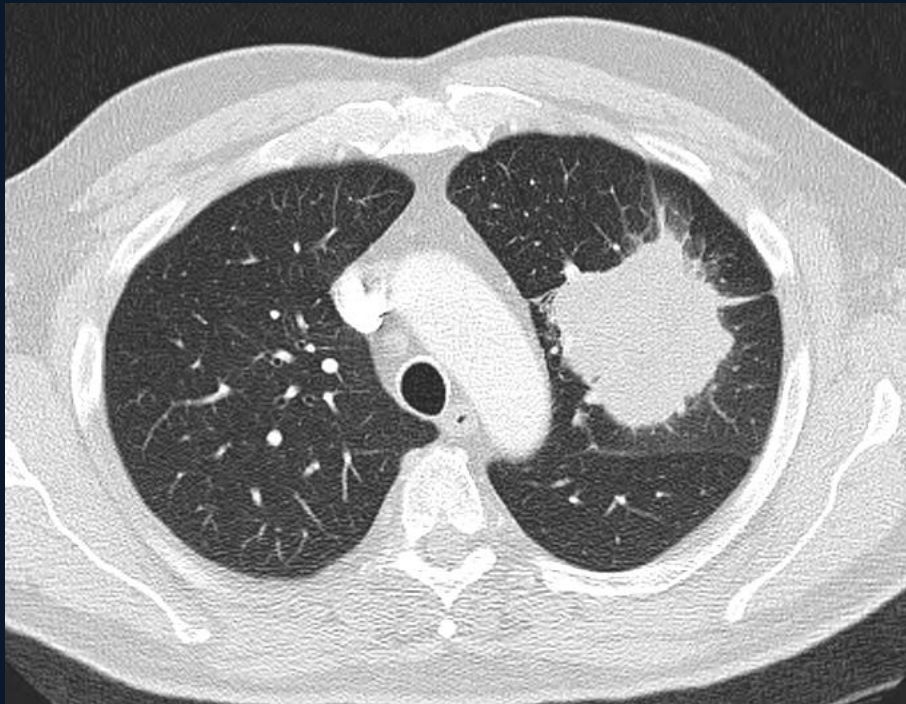
- Consultancy / Advisory Board
 - Merck, Roche, Lilly
- Educational presentation / Speaker
 - Lilly, Pfizer
- Travel and accommodation grants
 - Roche, Amgen
- Conflict of interest
 - None

Stage IV lung adenocarcinoma

- 62-y/o male reports progressive dry cough, mild fatigue, new onset left sided chest pain, and a 2kg weight loss within the last 3 months. Mild aphasia developed over last 3 days; no further neurological impairment. ECOG PS 0.
- The medical history includes hypertension and an appendectomy. Medications include codeine and candesartan. Patient is right-handed, married, works as a sales manager, drinks alcohol in moderation, and has never smoked. His children are healthy; there is no family history of cancer.

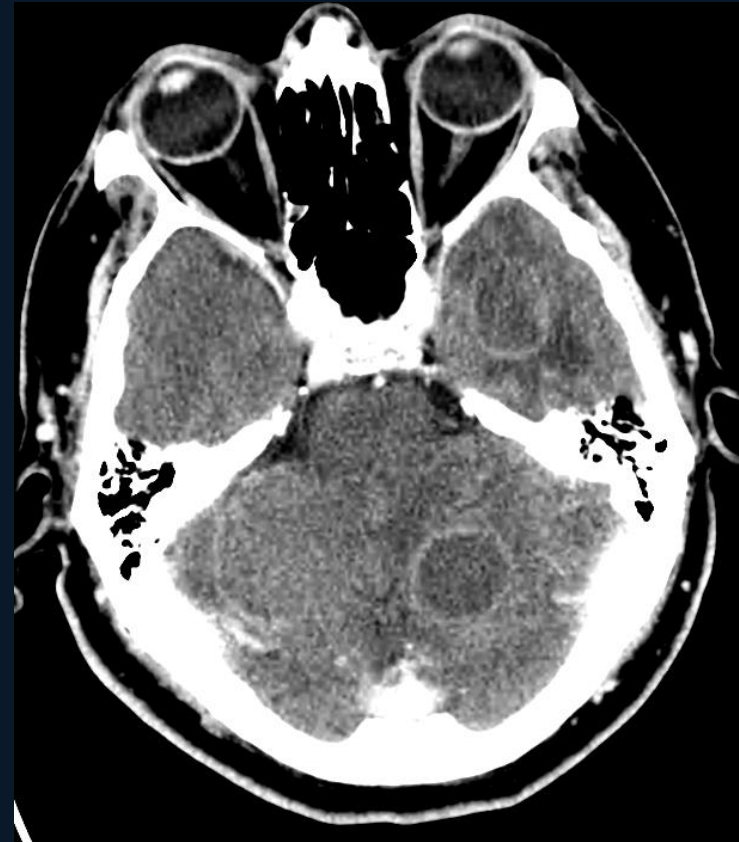
Stage IV lung adenocarcinoma

Chest CT scan shows a mass in the left upper lobe extending to the left hilum, a peripheral mass in the left upper lobe, and lymphadenopathy in stations 10L, 11L, 4L, 6 and 7.



Stage IV lung adenocarcinoma

Brain CT scan shows multiple left hemispheric and bilateral cerebellar lesions



Diagnosis

- Bronchoscopy and EBUS-guided FNA
- Histology: morphology: adenocarcinoma, IHC:TTF-1 positive
- Diagnosis: Adenocarcinoma of the lung with ipsilateral mediastinal lymph node and brain metastases, cT3 cN2 cM1b, stage IV

What is your strategy ?

Q 1: What is the recommended initial therapy?

- 1) Whole-brain radiotherapy
- 2) Platinum-based doublet chemotherapy
- 3) Wait for mutation testing (≥ 8 working days)

Diagnosis (2)

- *EGFR* genotyping (exons 18, 19, 20 and 21)
- Point mutation in exon 21 (L858R)

What is your choice of systemic therapy?

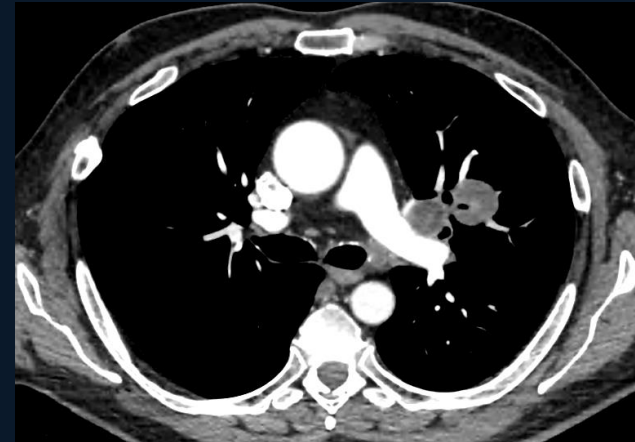
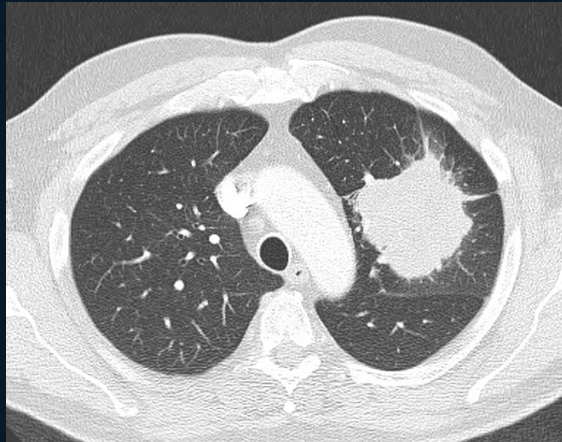
Q2: What is the recommended first-line systemic therapy?

- 1) Platinum-based doublet chemotherapy
- 2) Choice of erlotinib, gefitinib or afatinib
- 3) Afatinib
- 4) EGFR TKI intercalated with chemotherapy

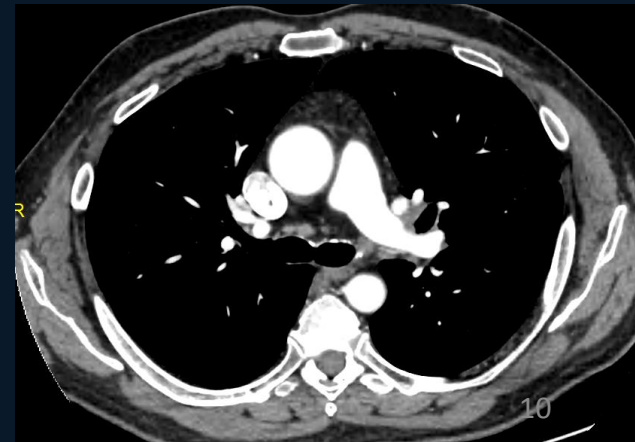
First-line systemic therapy

Initiation of gefitinib 250mg/day after completion of brain radiotherapy

Baseline



5 M



Follow-up on TKI



2 M



5 M



9 M

Activation of other receptor tyrosine kinases?
(eg, *ERBB2* amplification)

FAS/NFκB activation?

Epithelial-mesenchymal transition?
(AXL, Slug activation?)

Loss or spliced variant of BIM?

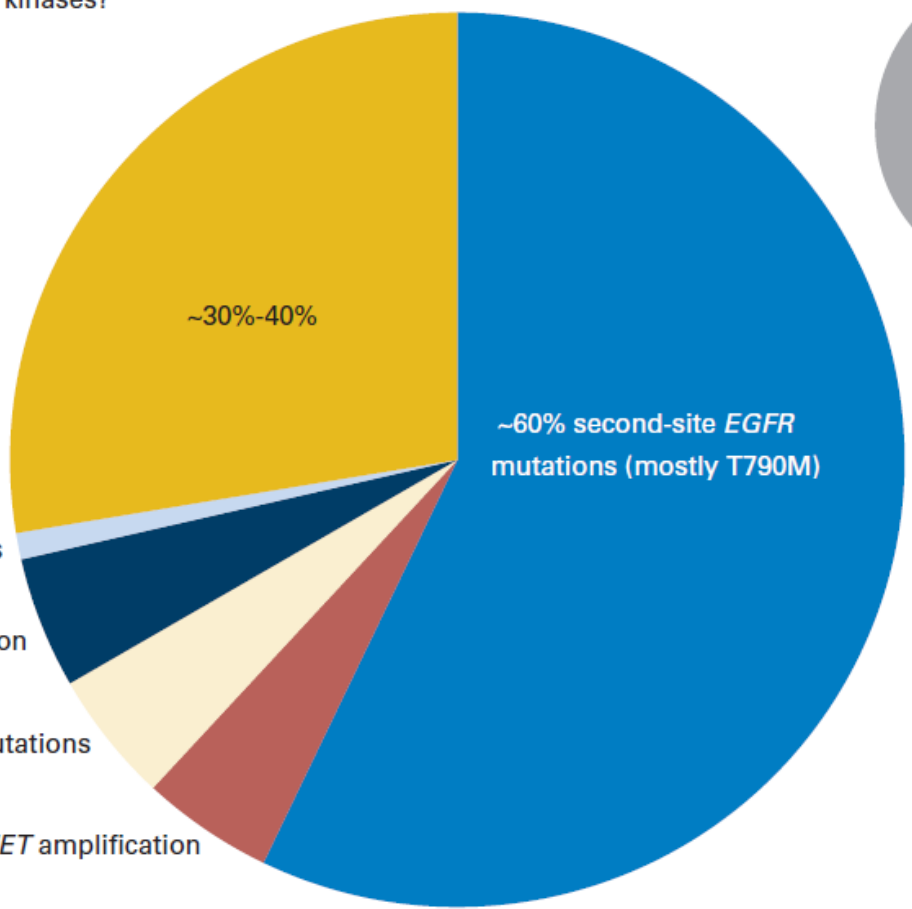
Other? (eg, *CRKL* or *ERK*
amplification)

~1% *BRAF* mutations

~5% small-cell cancer transformation

~5% *PIK3CA* mutations

5-10% *MET* amplification



± Pharmacokinetic failure

± Exogenous factors
eg, HGF, IL-6

Diagnosis (3)

- Rebiopsy upon progression with *EGFR* genotyping (exons 18, 19, 20 and 21)
- Point mutation in exon 20 (T790M) and exon 21 (L858R)

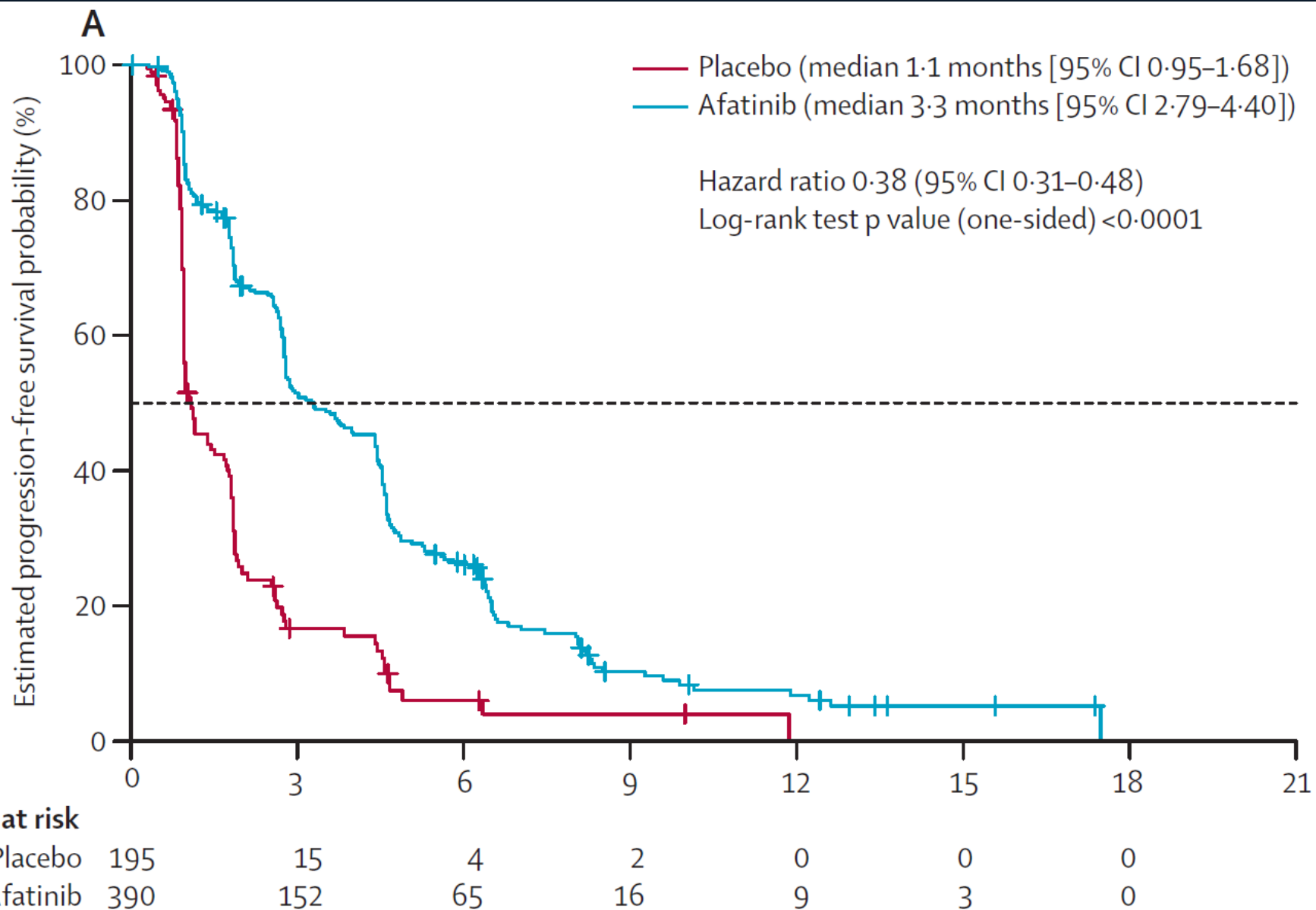
What is your choice of systemic therapy?

Q 3: What is the recommended second-line treatment?

- 1) Chemotherapy
- 2) Gefitinib beyond RECIST progression
- 3) Chemotherapy + EGFR TKI
- 4) Afatinib
- 5) Afatinib + cetuximab
- 6) 3rd generation EGFR TKI (AZD9291, CO-1686, HM61713, through clinical trial)

Q 4: If chemotherapy, which treatment would you recommend?

- 1) Cisplatin / pemetrexed
- 2) Cisplatin / pemetrexed / bevacizumab
- 3) Carboplatin / pemetrexed
- 4) Carboplatin / pemetrexed / bevacizumab
- 5) Docetaxel
- 6) Pemetrexed
- 7) Carboplatin / paclitaxel / bevacizumab



Second-line systemic therapy

Initiation of afatinib (!) 40mg/day



10 M



13 M



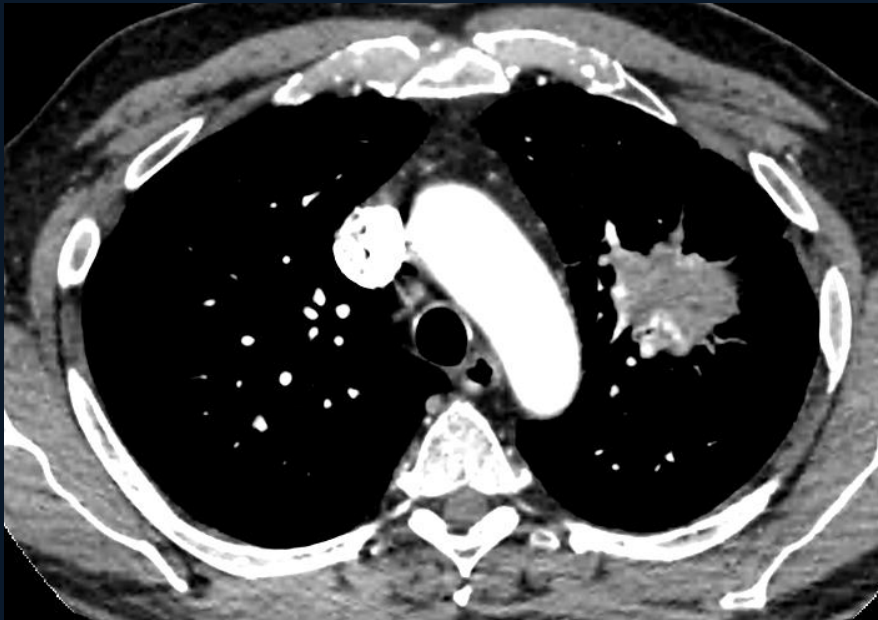
16 M

Q 5: Which treatment would you recommend for third-line therapy?

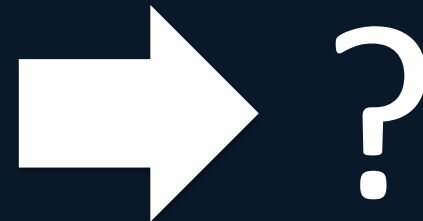
- 1) Cisplatin / pemetrexed
- 2) Cisplatin / pemetrexed / bevacizumab
- 3) Carboplatin / pemetrexed
- 4) Carboplatin / pemetrexed / bevacizumab
- 5) Docetaxel
- 6) Pemetrexed
- 7) Carboplatin / paclitaxel / bevacizumab

Third-line systemic therapy

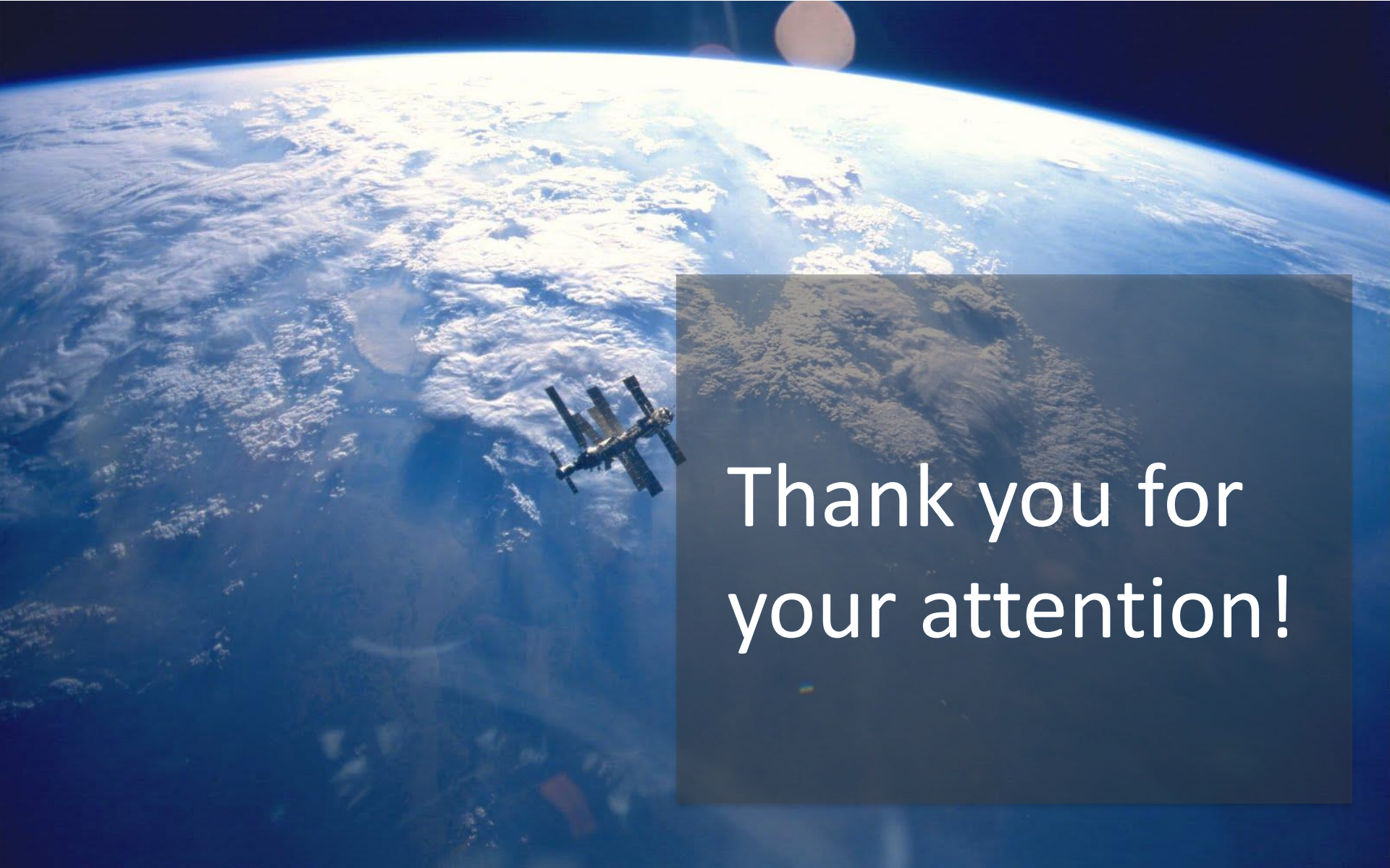
Initiation of cisplatin / pemetrexed chemotherapy



16 M



ESMO Clinical Practice Guidelines



Thank you for
your attention!