Chemotherapy, targeted therapy and immunotherapy: How to assess response?

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Post chemotherapy

RECIST 1.1 Criteria (based on morphologic changes):

- Baseline CT scan within 4 weeks before treatment starts and slice thickness $\leqslant$ 5 mm and i.v. contrast are mandatory.
- Assess response after at least 4 weeks, optimal is 6-8 weeks.
- Axial plane used for measurement.
- MRI can also be used, and FDG-PET/CT is complimentary.

Target lesions

- Tumour ≥ 10 mm
- Lymph nodes ≥ 15 mm
- 2 per organ, max 5

- Mention series and image number in report

Non-target lesions

- Pleural effusion, ascites
- Lymphangitic spread
- Leptomeningeal disease
- Bone lesions without a soft tissue component
- Any non-measurable lesion/node
- Lymph node 10-15 mm in SAD is pathological but non-target

Progressive disease criteria

- Reference : Smallest sum of longest diameter on the study.
- ≥ 20% increase
- Absolute increase of at least 5 mm
- New lesion, be it measurable or non-measurable
- Unequivocal progression of non-target lesions

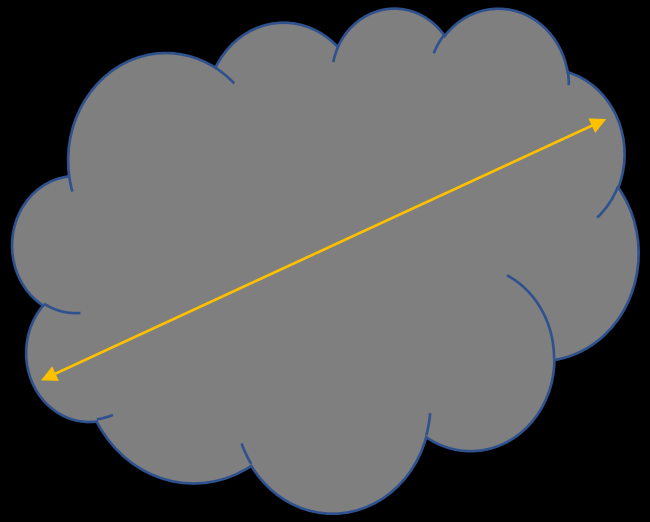
Partial response, stable disease, and complete response

- ≥ 30 % decrease is PR
- Not fitting into PR or PD is SD
- Resolution of all the lesions is CR

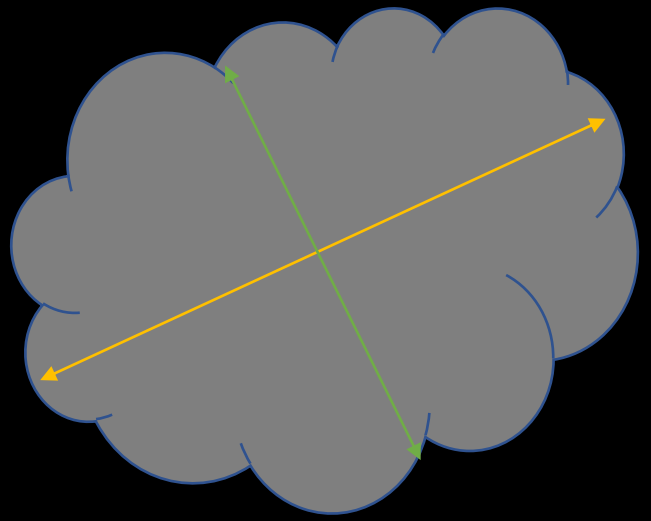
Addressing the dilemma

- Lesions on a follow up scan at a location not scanned at baseline, to be regarded as a “new lesion”.
- Default value of 5 mm if a previously seen target lesion is not visualised on a follow up scan.
- Even if SAD of a lymph node below 15 mm on follow up, it needs to be measured if it was a target lesion before.
- Cavitation needs to be documented, though longest diameter still measured.

Coalescence

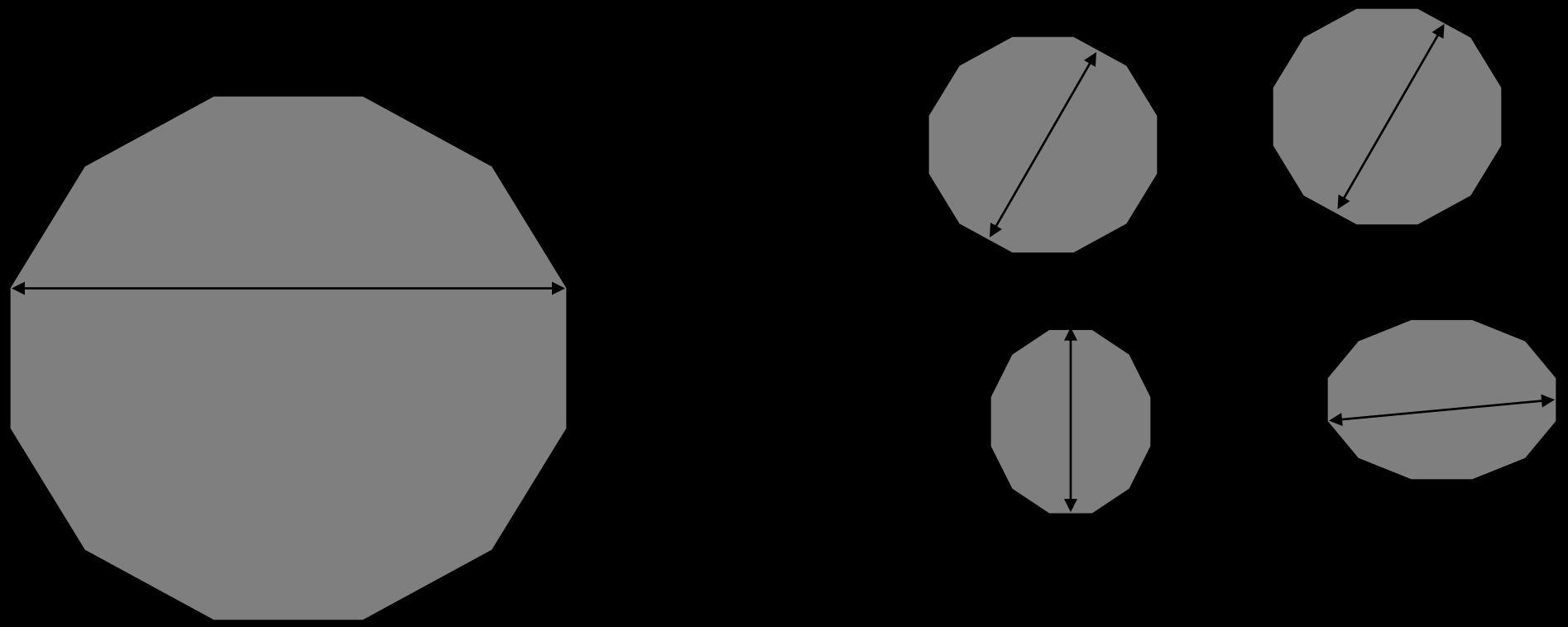


Coalesced tumour



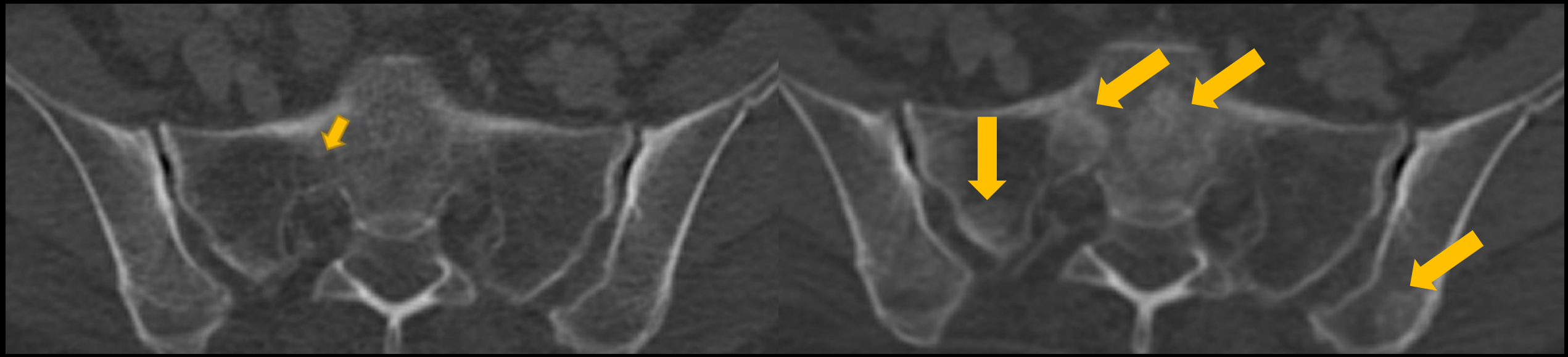
Coalesced lymph nodes

Fragmentation



Bone lesions

- New onset sclerotic bone lesion suggests response not PD.
- Both lytic and sclerotic bone lesions are non-measurable.
- Soft tissue component associated with lytic bone lesion is measurable if fulfils criteria of target lesion by RECIST 1.1.

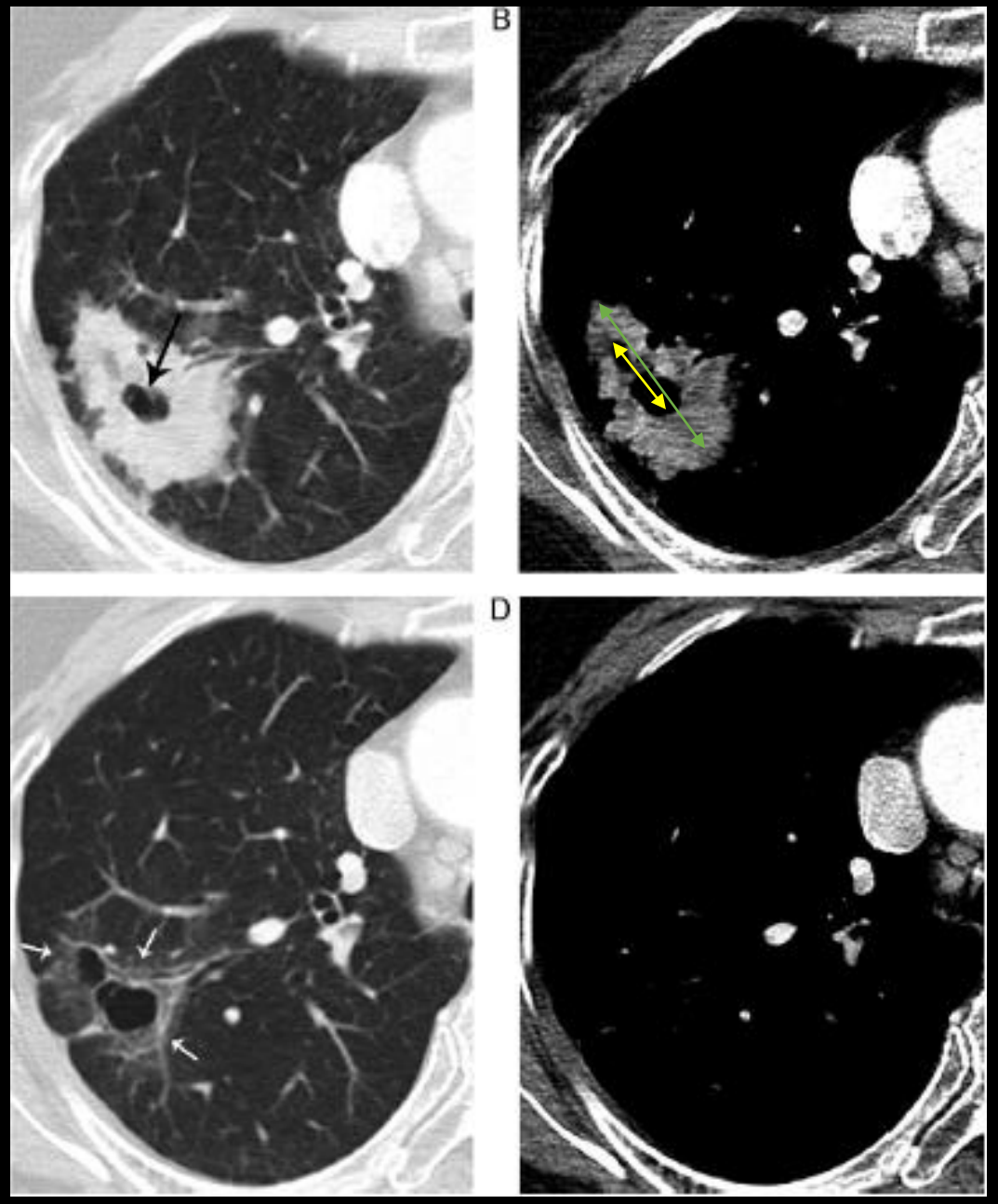


Post molecular targeted therapy

- *Limitations of RECIST 1.1*
- Decrease in tumour attenuation
- Intratumoral cavitation

- *Proposed alternatives:*
- CT tumour volume using segmentation software
- CT tumour perfusion
- Dual energy CT
- DW MRI
- FDG-PET/CT

Lee et al. proposed a CT response criteria based on the presence of cavitation, necrosis, and attenuation changes for response assessment in NSCLC patients who underwent epidermal growth factor receptor(EGFR) tyrosine kinase inhibitor (TKI) therapy.



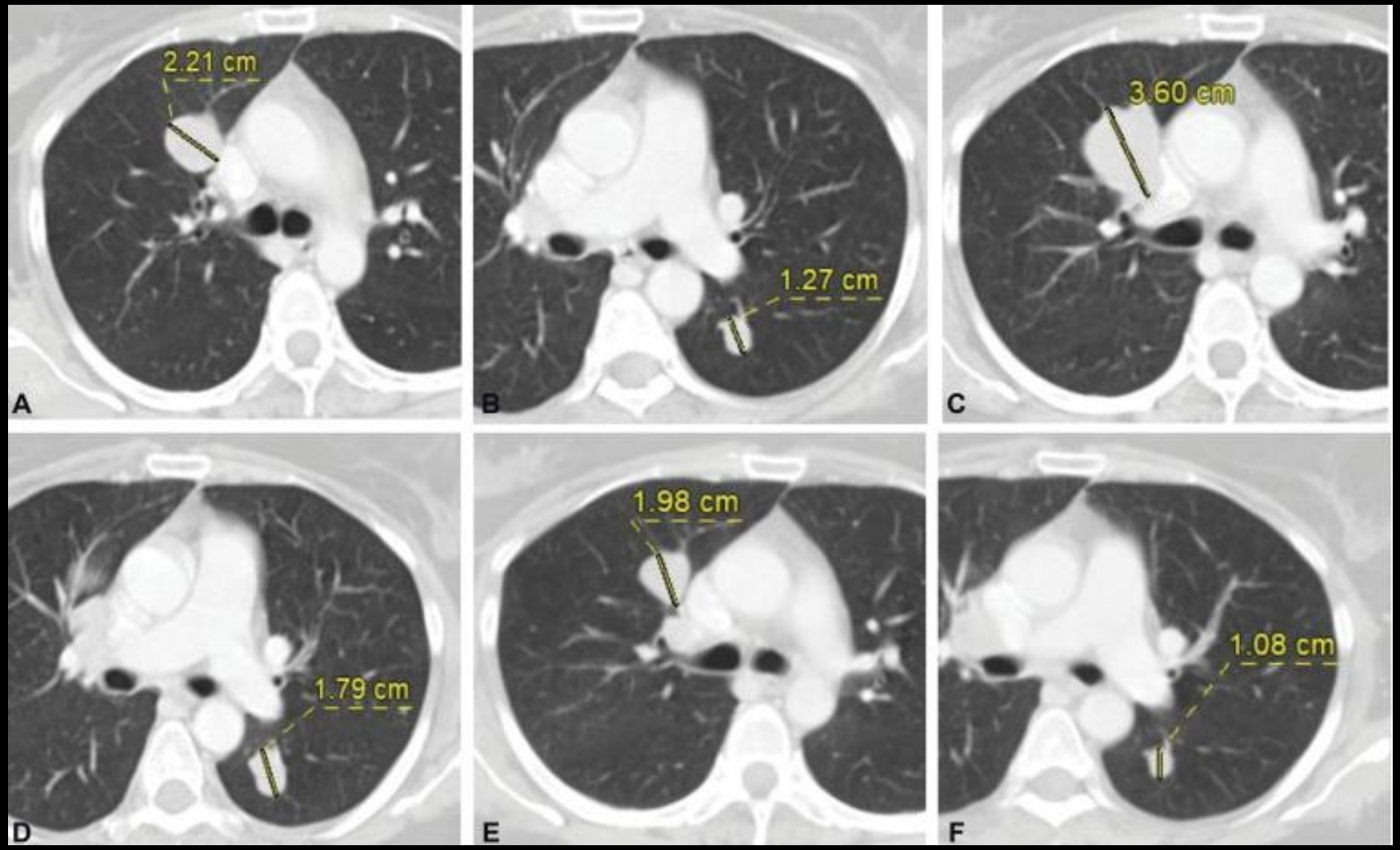
H.Y. Lee et al. / Lung Cancer 73 (2011) 63–69

Post immunotherapy

- Immune response evaluation criteria in solid tumour (iRECIST)
- About 5% incidence of pseudoprogression in advanced non-small cell lung cancer (NSCLC).
- iUPD: 20% increase in tumour size from baseline or new-onset target or non-target lesions, then unconfirmed progressive disease.
- If a repeat scan after 4 to 8 weeks shows further progression (>5mm increase in the target or new lesions or increase in the non-target lesion), then confirmed progressive disease should be given on imaging.

- If findings remain stable on follow-up scan, then the term iUPD should be continued till it is confirmed to be true progression or there is a response on further follow-up imaging.

- The term “iUPD” is given to account for pseudoprogression so that the ongoing immunotherapeutic drug is continued and not prematurely withdrawn unless the PD is confirmed on successive imaging or there is a clinical deterioration of the patient.



(A) Metastatic right upper lobe perihilar nodule and (B) left lower lobe nodule at baseline CT. (C and D) Increase in size of these nodules
after immunotherapy and decrease in size on follow-up scan (E and F).

Chakrabarty, N., Mahajan, A., Baheti, A., et al. A Radiologist's Perspective on Treatment-Related Pseudoprogression:

Clues and Hues. Indian Journal of Medical and Paediatric Oncology, 2022;43(01).

- “Hyperprogression” : More than two-fold increase in the pace of tumour progression after starting immunotherapy, associated with worse outcomes.
- Pseudoprogression: Associated with increased survival.
- So, clinical condition of the patient is important in differentiating pseudoprogression from hyperprogression.

Brain metastases

Response assessment in neuro-oncology brain metastases (RANO-BM) criteria:

- CEMRI preferred: Slice thickness 5 mm or less with 0 mm skip, ideally ≤1.5 mm thickness with 0 mm skip.
- Measurable disease: Contrast-enhancing lesion that is at least 10 mm in longest diameter, visible on two or more axial slices, and at least 5 mm in diameter perpendicular to the longest diameter.
- Non-measurable disease: Less than 10 mm, non-reproducible borders, dural metastases, bony metastases, leptomeningeal metastases, and purely cystic lesions.
- Up to 5 target lesions

Thank you