

Management of unresectable stage III NSCLCa



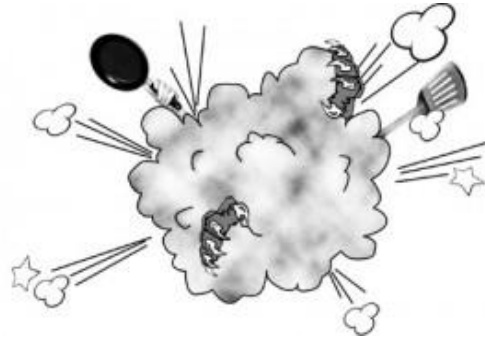
Jae Cheol Lee

Department of Oncology, Asan Medical Center

Controversies in Mx of stage III NSCLCa



Operate !



Radiate !

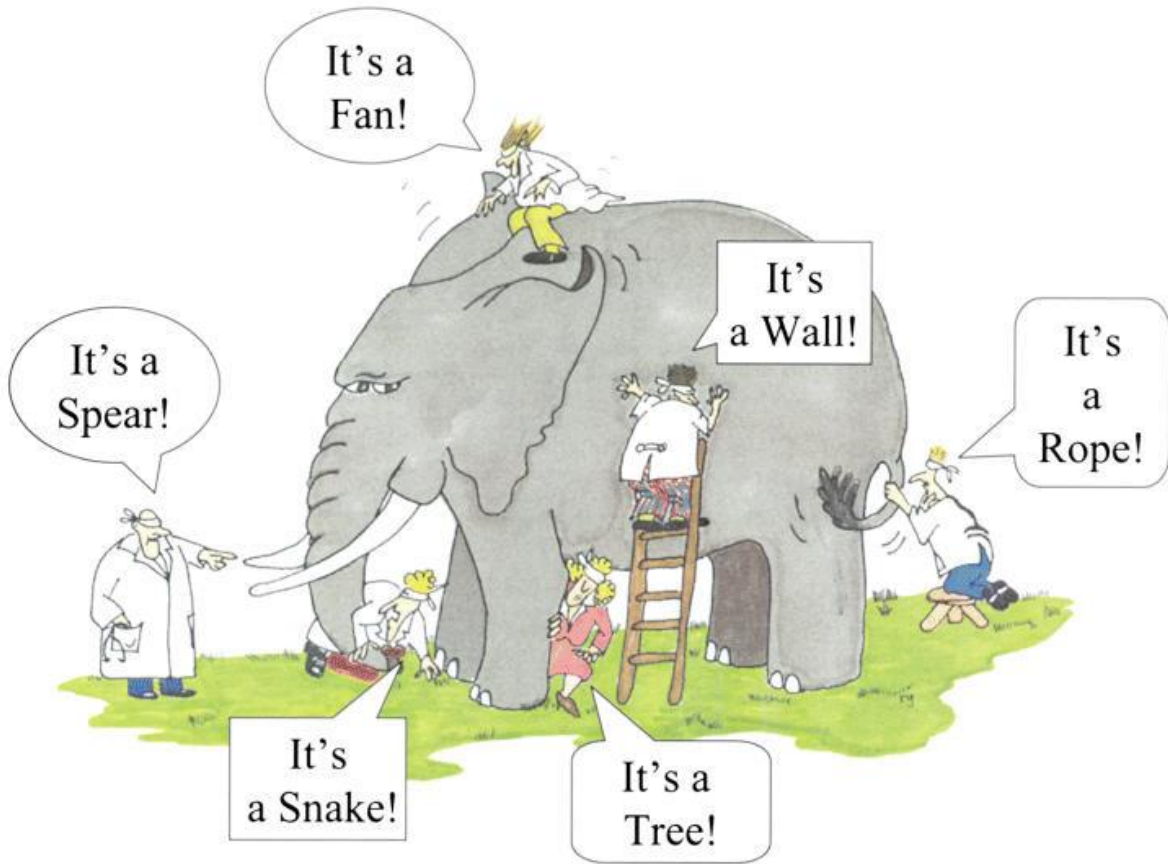


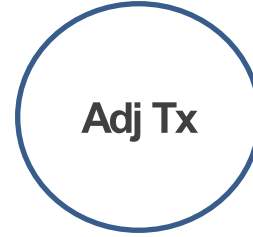
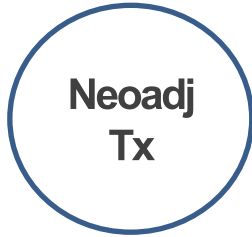
Medicate !

T/M and label	Description	N0	N1	N2	N3
T1					
T1a	≤1 cm	I A1	II B	III A	III B
T1b	>1–2 cm	I A2	II B	III A	III B
T1c	>2–3 cm	I A3	II B	III A	III B
T2					
T2a	Central, visceral and pleura >3–4 m	I B	II B	III A	III B
T2b	>4–5 cm	II A	II B	III A	III B
T3	>5–7 cm Invasive Satellite	II B	III A	III B	III C
T4	>7 cm Invasive Ipsilateral nodes	III A	III A	III B	III C
M1					
M1a	Contralateral nodes Pleura disseminated	IV A	IV A	IV A	IV A
M1b	Single	IV A	IV A	IV A	IV A
M1c	Multi	IV B	IV B	IV B	IV B

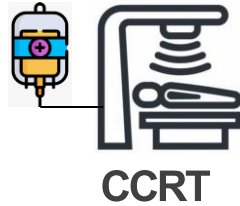
5yr survival rate

	Clinical stage	Pathological stage
I A1	92	90
I A2	83	85
I A3	77	80
I B	68	73
II A	60	65
II B	53	56
III A	36	41
III B	26	24
III C	13	12
IV A	10	
IV B	0	





————— **All stage III** —————> **Similar Outcome**

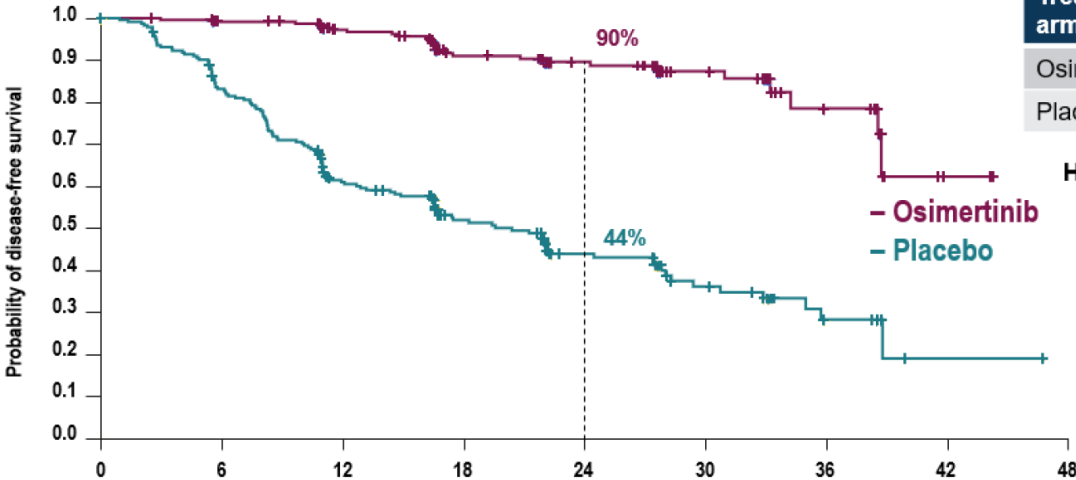


+ adjuvant Tx with durvalumab

Standard of Care

Osimertinib in EGFR-mutant lung cancer

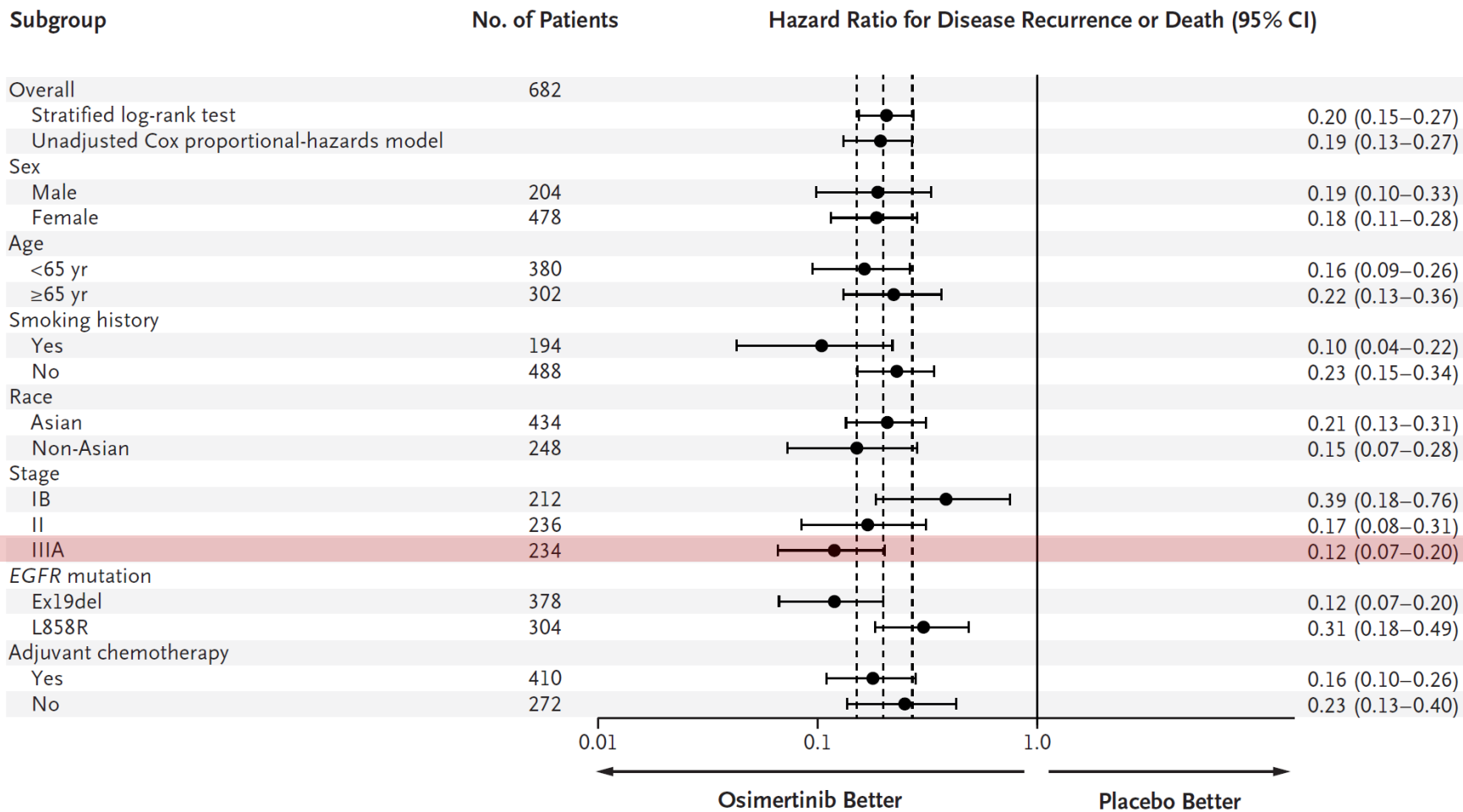
Median follow-up: osimertinib 22.1 months, placebo: 14.9 months



Treatment arms	Median DFS, months (95% CI)
Osimertinib	NR (38.8-NC)
Placebo	19.6 (16.6-24.5)

HR 0.17 (99.06% CI, 0.11-0.26); p<0.001
 Maturity 33%:
 osimertinib 11%, placebo 55%

No. at risk	Time from randomization (months)								
	0	6	12	18	24	30	36	42	48
Osimertinib	233	219	189	137	97	52	18	2	0
Placebo	237	190	127	82	51	27	9	1	0



Neoadjuvant IO ± chemo

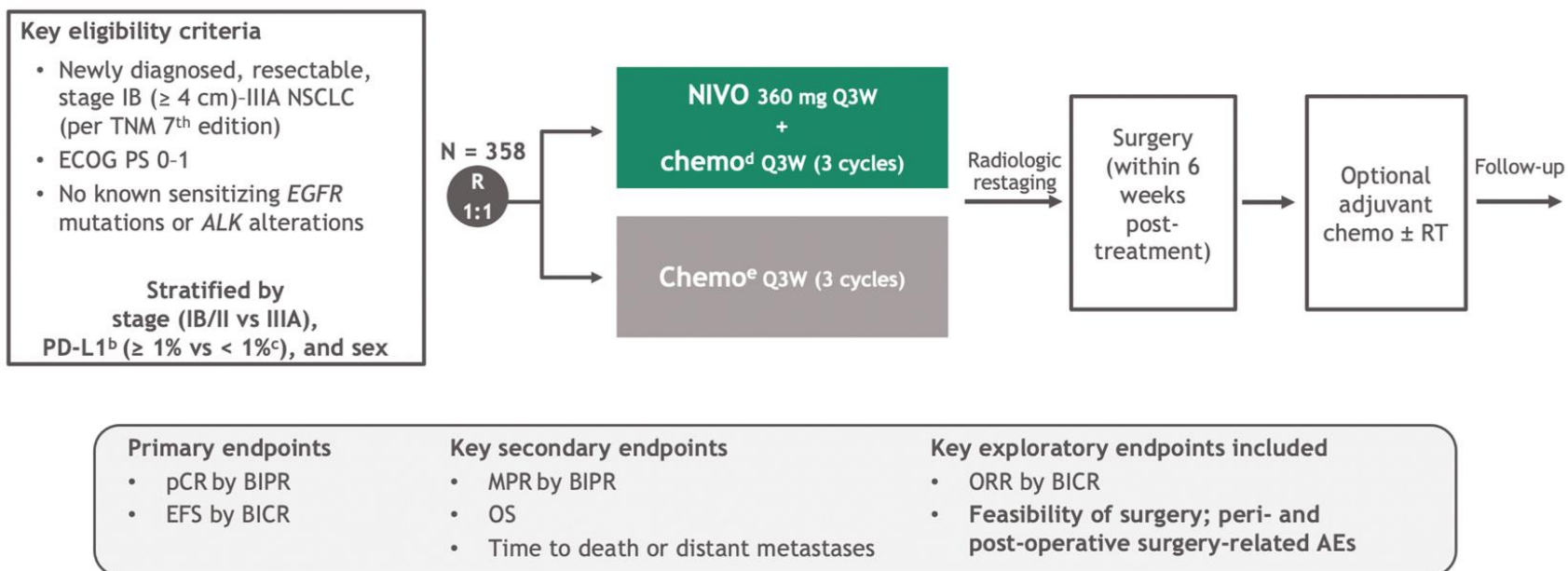
Table 3. Ongoing Clinical Trials With Neoadjuvant Immune Checkpoint Inhibitors With or Without Chemotherapy

Trial	NCT	Drug	Stage	Target Accrual	Phase	End Point
MK3475-223	NCT02938624	Pembrolizumab different dose/ regimens → S	I-II	28	I	Toxicity, MPR
TOP 1501	NCT02818920	Pembrolizumab (200 mg) × 2 cycles → S → pembrolizumab (200 mg) × 4 cycles	IB-III A	32	II	Surgical feasibility
PRICNEPS	NCT02994576	Atezolizumab (1200 mg) × 1 cycle → S	IB-III A (no N2)	60	II	Toxicity
SAKK 16/14	NCT02572843	CT × 3 → durvalumab (750 mg) × 2 cycles → S → durvalumab (750 mg) × 1 y	III A (N2)	68	II	EFS
IONESCO	NCT03030131	Durvalumab (750 mg) Q2W × 3 cycles → S	IB-II	81	II	R0 resection
Columbia University	NCT02716038	CT + atezolizumab (1200 mg) × 4 cycles → S	IB-III A	30	II	MPR
KEYNOTE 617	NCT03425643	CT + pembrolizumab (200 mg)/ placebo × 4 cycles → S → pembrolizumab/placebo × 13 cycles	II-III B (T3-4N2)	786	III	EFS, OS
CheckMate 816 ^a	NCT02998528	CT + nivolumab (360 mg) × 3 cycles → S vs. CT × 3 cycles → S	IB-III A	350	III	EFS, pCR
IMpower 030	NCT03456063	CT + atezolizumab (1200 mg)/ placebo × 4 cycles → S → atezolizumab/placebo × 16 cycles	II-III B (cT3N2)	374	III	MPR, EFS
AEGEAN	NCT03800134	CT + durvalumab (1500 mg)/ placebo × 3 cycles → S → durvalumab/placebo Q4W × 12 cycles	II A-III B	300	III	MPR

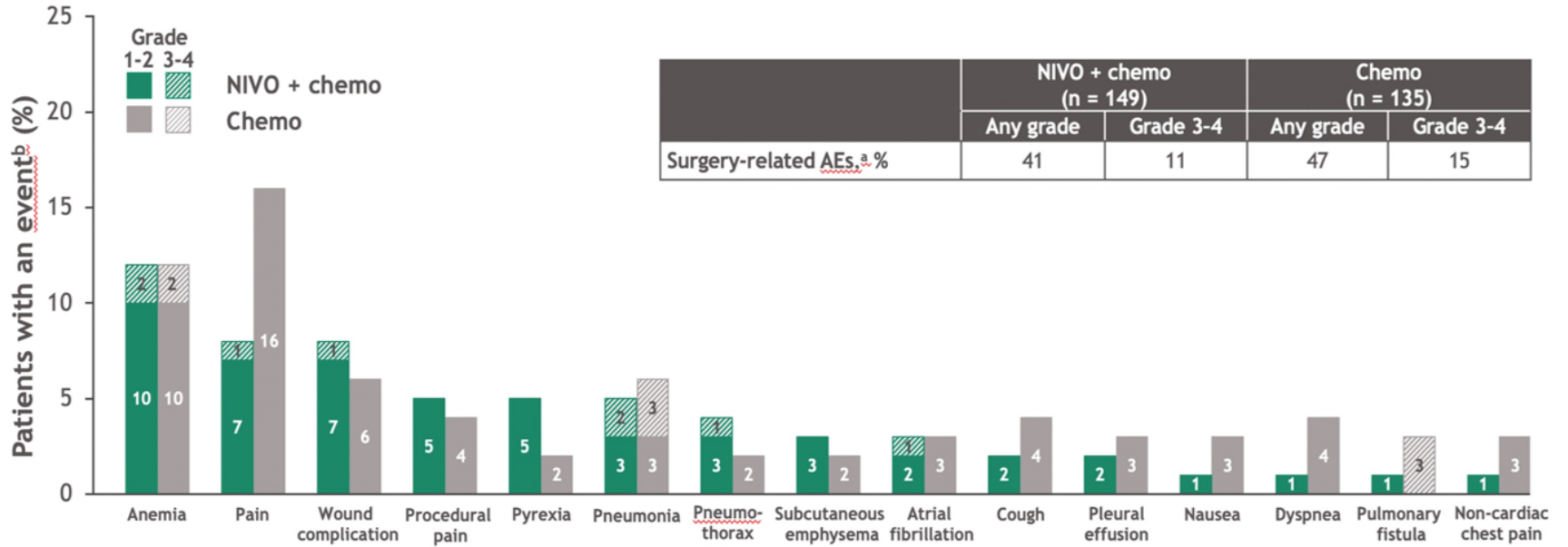
^aThe third arm of the trial, nivolumab plus ipilimumab, was withdrawn after results from NADIM trial.

CT, chemotherapy; EFS, event-free survival; MPR, major pathologic response; NCT, National Clinical Trial; OS, overall survival; pCR, pathologic complete response; Q4W, every 4 weeks; S, surgery.

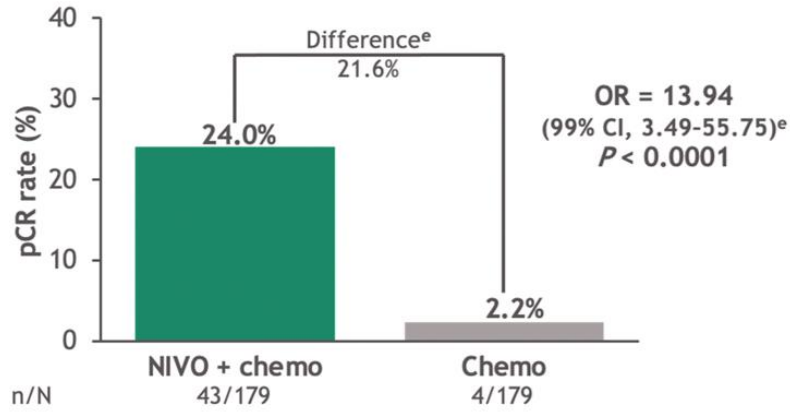
CheckMate 816 study design^{a,1}



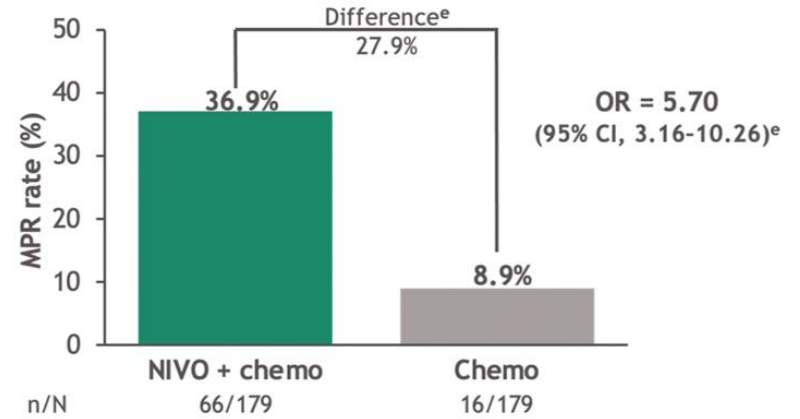
90 days surgery-related complications



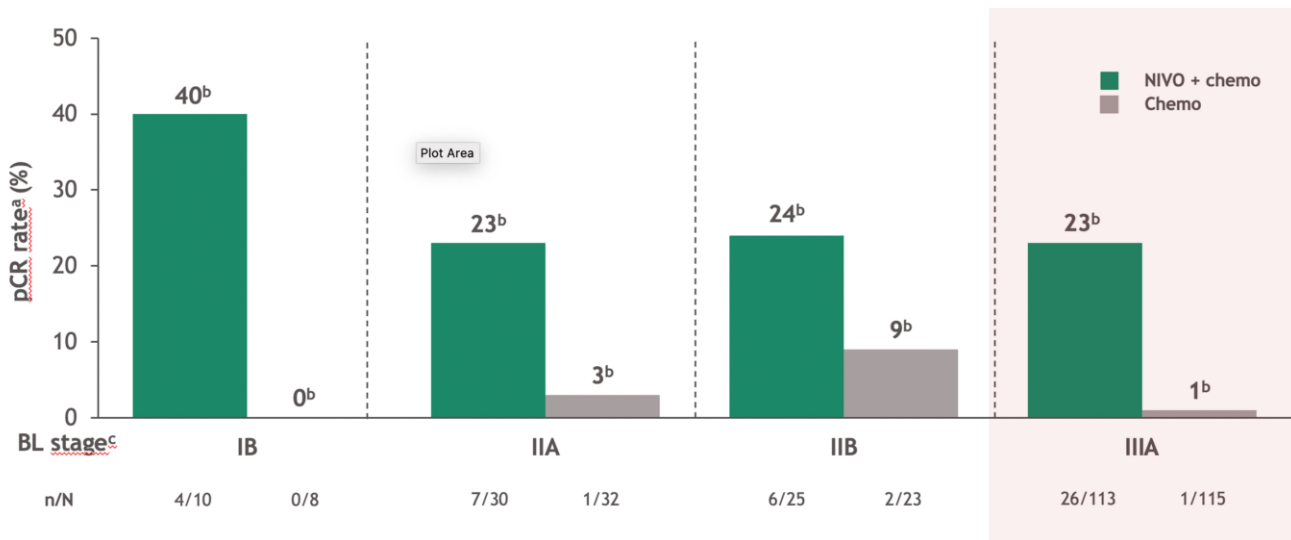
pCR^{b,c} in ITT (ypTON0)^d



MPR^{b,f} in ITT^d



pCR by baseline stage of disease



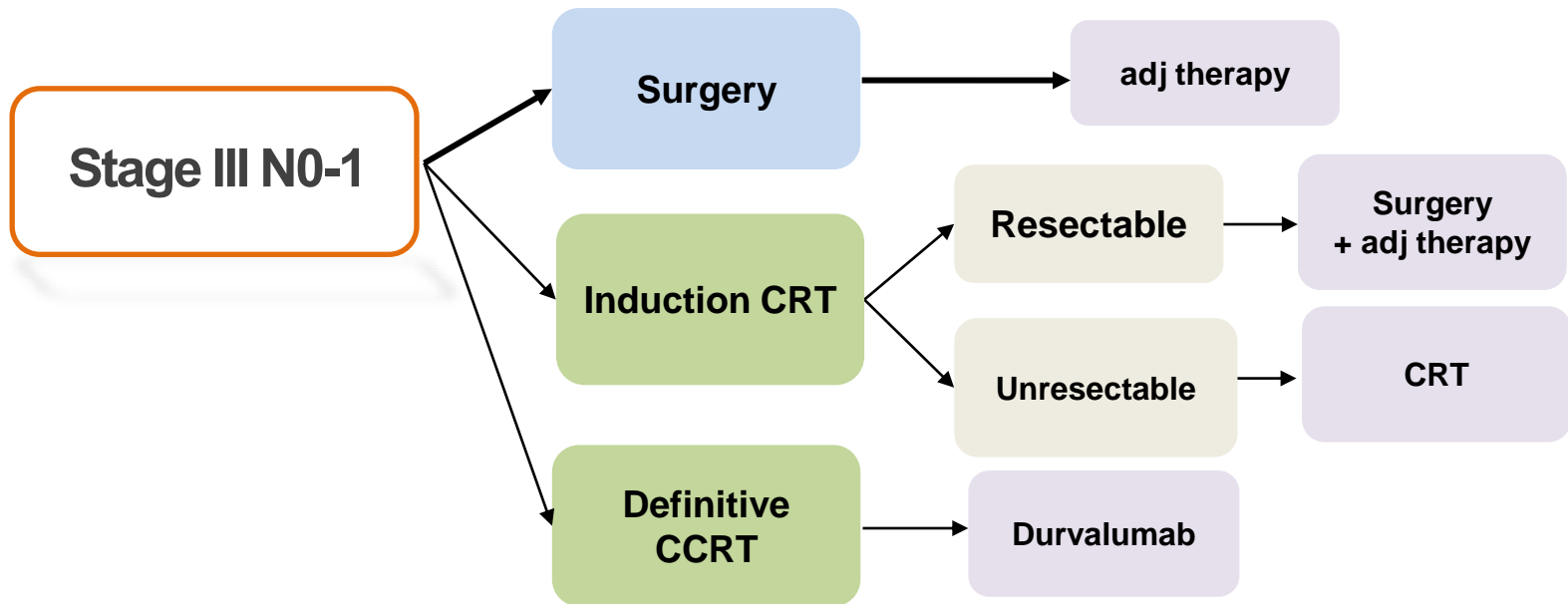
Mx of stage III NSCLCa



Multidisciplinary team (MDT)

Case by case decision

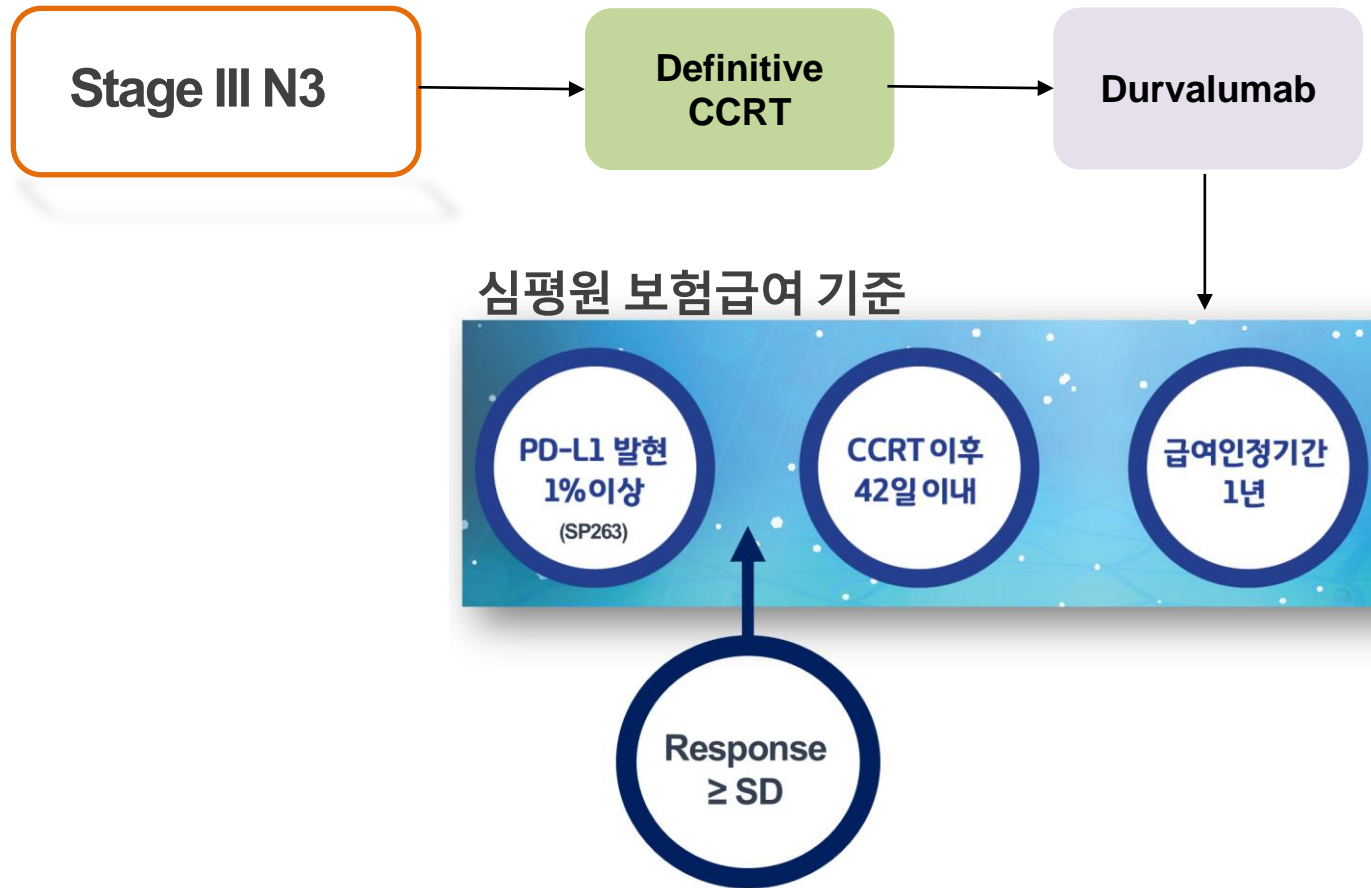
Mx of stage III NSCLCa



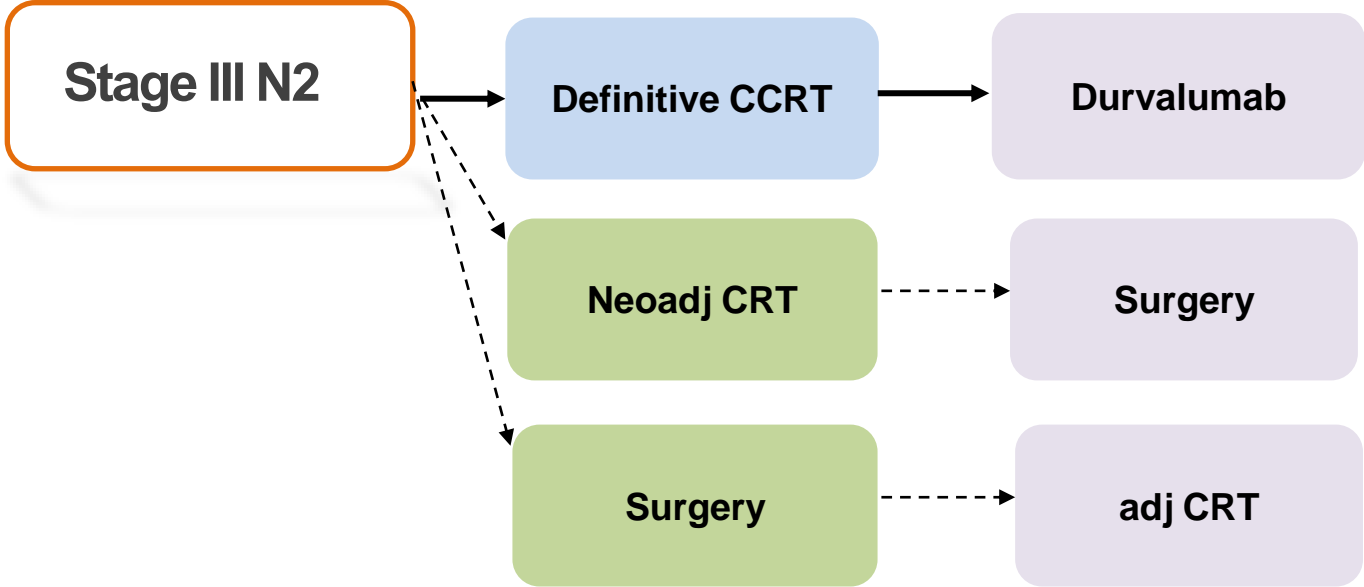
No universally accepted definition of resectability

Case by case decision in MDT with experienced surgeon

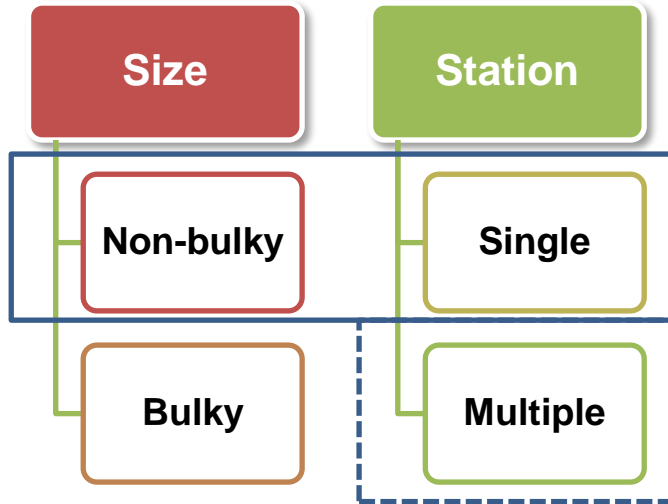
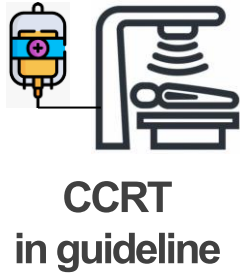
Mx of stage III NSCLCa



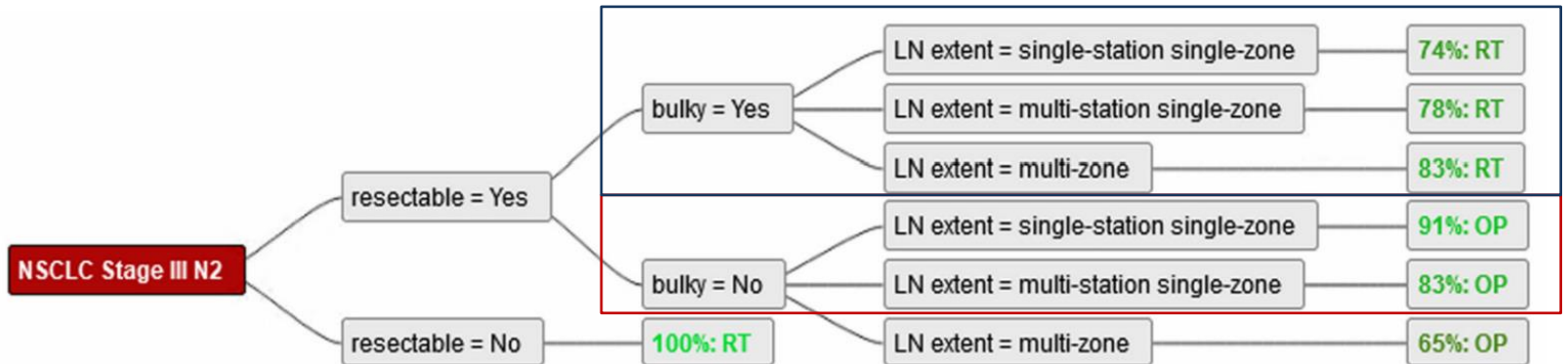
Debates on stage III N2



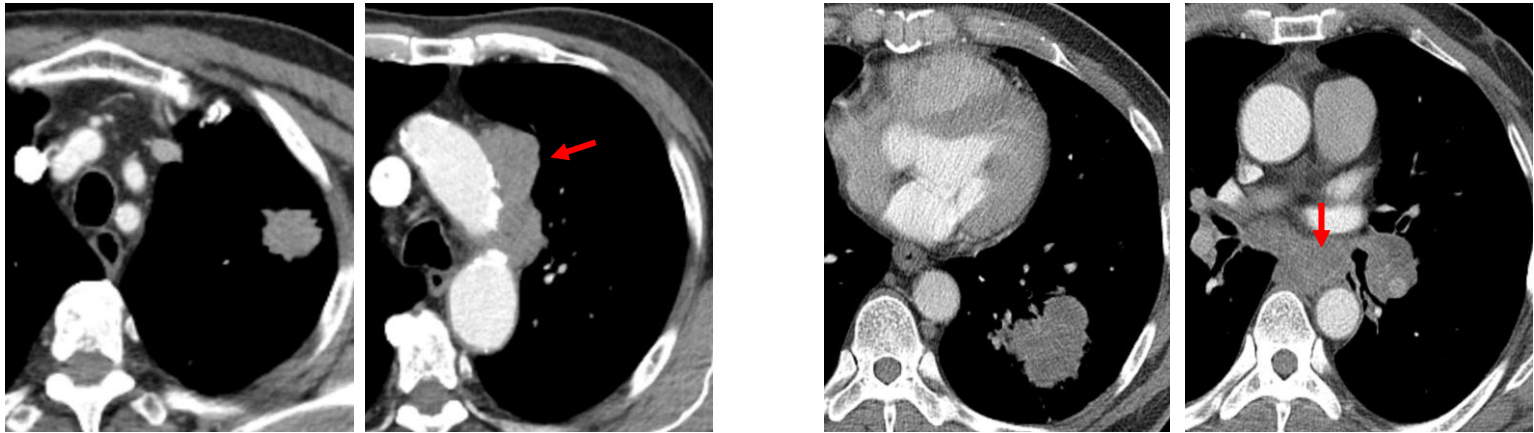
Heterogeneity of N2 status



Favor surgery
in RW practice



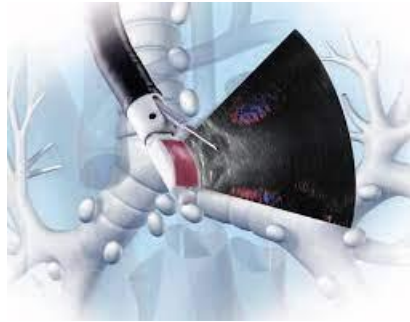
Bulky N2



Possible extracapsular spread

Difficult R0 resection

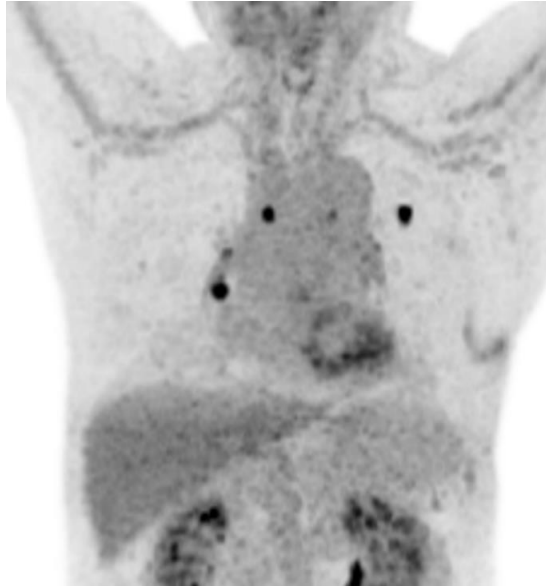
Accurate nodal staging



[Lymph node (EBUS guided needle biopsy)(Des)[Histochemistry],Tissue]

DIAGNOSIS :

- A) Lymph node, (B; 11L), EBUS transbronchial needle aspiration biopsy:
 - Anthracofibrosis, negative for malignancy
- B) Lymph node, (C; 4L), EBUS transbronchial needle aspiration biopsy:
 - Anthracofibrosis, negative for malignancy
- C) Lymph node, (D; 7), EBUS transbronchial needle aspiration biopsy:
 - Anthracofibrosis, negative for malignancy
- D) Lymph node, (E: 4R), EBUS transbronchial needle aspiration biopsy:
 - Anthracofibrosis, negative for malignancy
- E) Lymph node, (F: 11R), EBUS transbronchial needle aspiration biopsy:
 - Anthracofibrosis, negative for malignancy



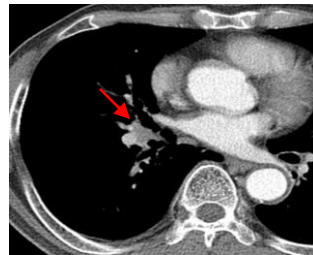
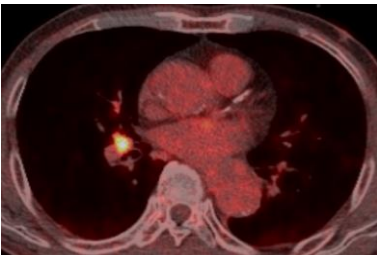
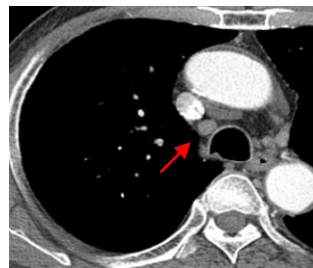
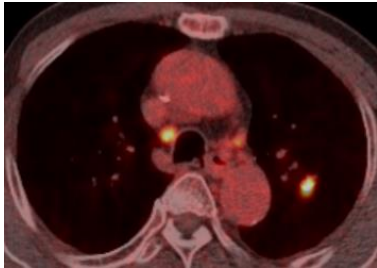
[Lymph node (EBUS guided TBNA)]

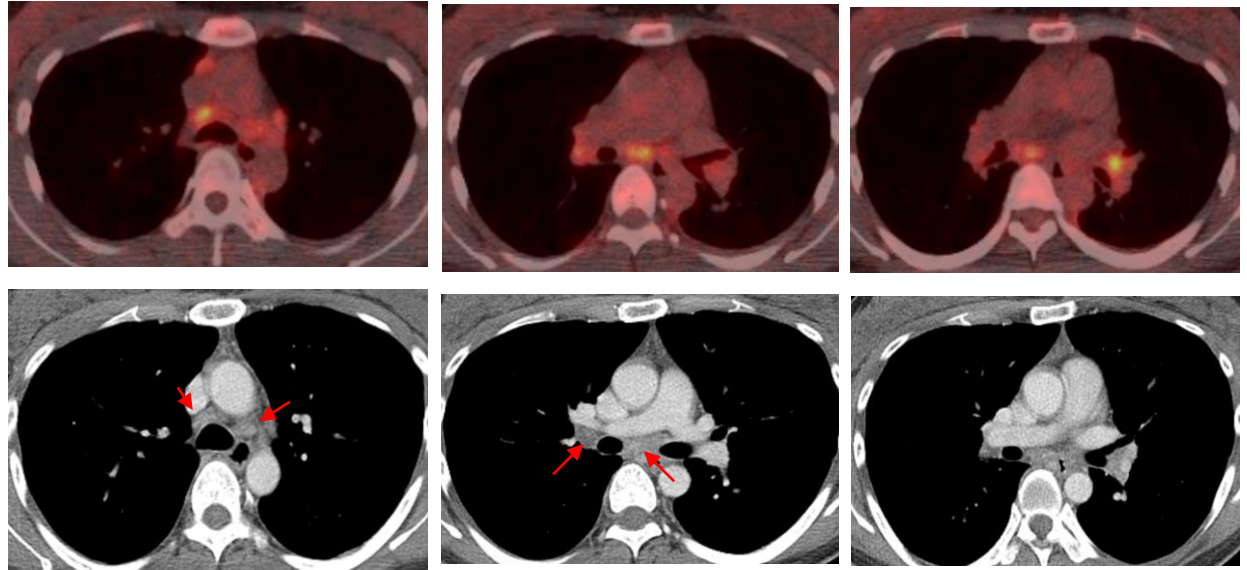
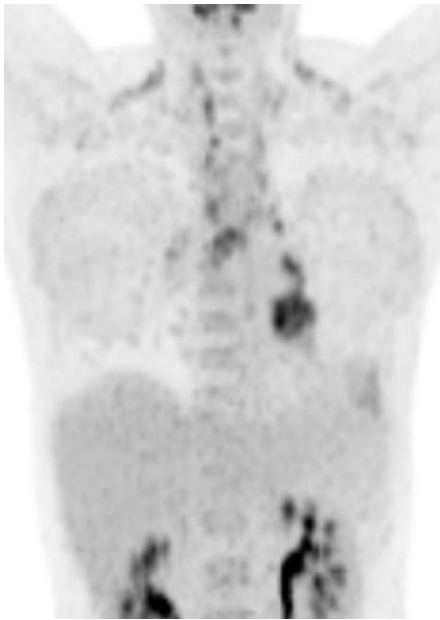
A) Lymph node, (A;11R), EBUS guided TBNA :
- Negative for malignant cells

B) Lymph node, (B;4R), EBUS guided TBNA :
- Negative for malignant cells

D) Lymph node, (D;11L), EBUS guided TBNA :
- Negative for malignant cells

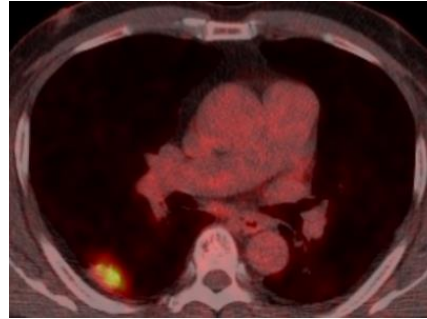
C) Lymph node, (C;4L), EBUS guided TBNA :
- Negative for malignant cells





Lymph node (EBUS guided needle biopsy)

- A) Lymph node, (A; 11R), EBUS TBNA:
 - METASTATIC ADENOCARCINOMA
- B) Lymph node, (B; 4R), EBUS TBNA:
 - METASTATIC ADENOCARCINOMA
- C) Lymph node, (C; 7), EBUS TBNA:
 - METASTATIC ADENOCARCINOMA
- D) Lymph node, (D; 4L), EBUS TBNA:
 - Negative for malignancy
- E) Lymph node, (E; 11L), EBUS TBNA:
 - METASTATIC ADENOCARCINOMA



[Lung,Right (Ectomy)(Des)[Histochemistry],Tissue]

Lung, (right lower lobe), lobectomy:- INVASIVE ADENOCARCINOMA, IASLC GRADE 3 (POORLY DIFFERENTIATED)

ACINAR, SINGLE, 2.8 x 2.3 x 1.5 cm, RIGHT LOWER LOBE,

1) tumor focality: unifocal

2) pleural invasion: visceral elastic

3) lymphovascular invasion: not identified

4) perineural invasion: not identified

5) bronchial margin: clear

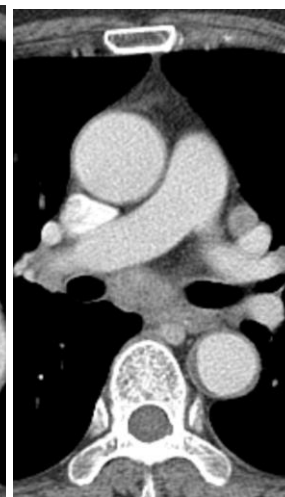
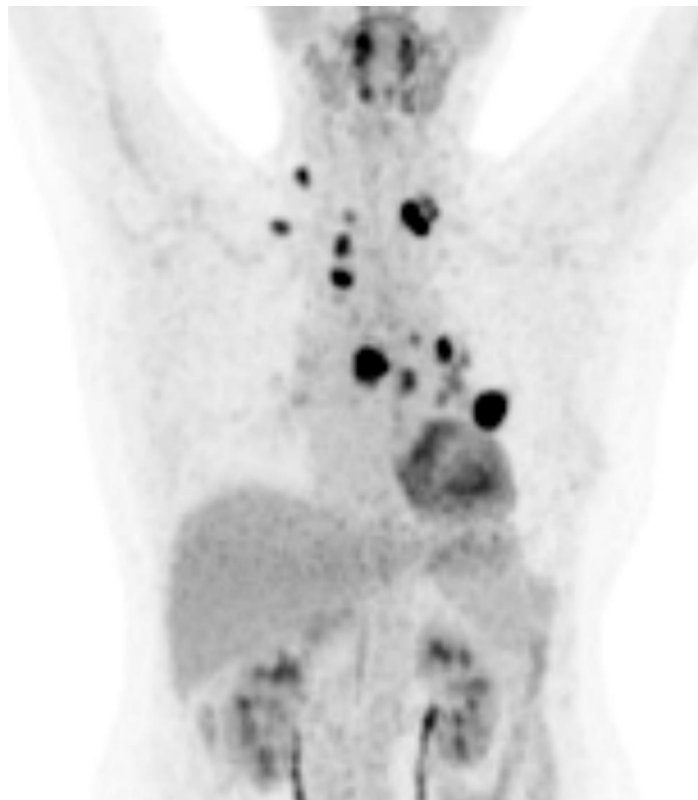
6) vascular margin: clear

(distance of invasive carcinoma from closest margin: 5.8 cm)

7) **metastasis in 2 of 13 lymph nodes (2/13)**

(peribronchial LN, 0/1; LN #2R, 0/0; LN #4R, 0/1; **LN #7, 1/4; LN #10, 1/3;** LN #11, 0/4)

Q. M/72 ADC PD-L1+



→ **CCRT + durvalumab**

LN biopsy

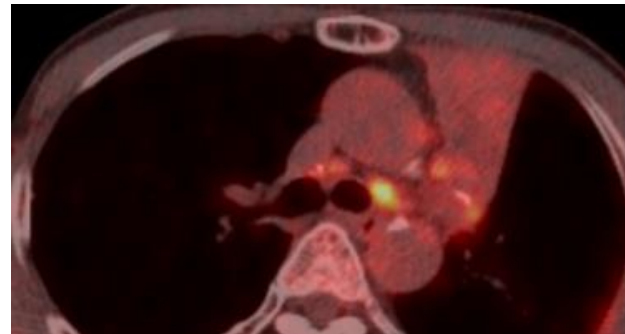
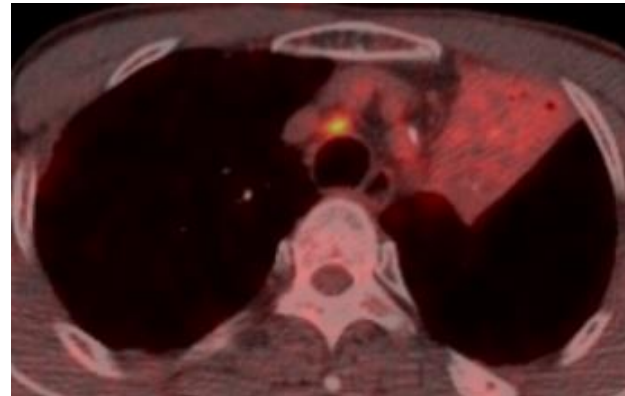
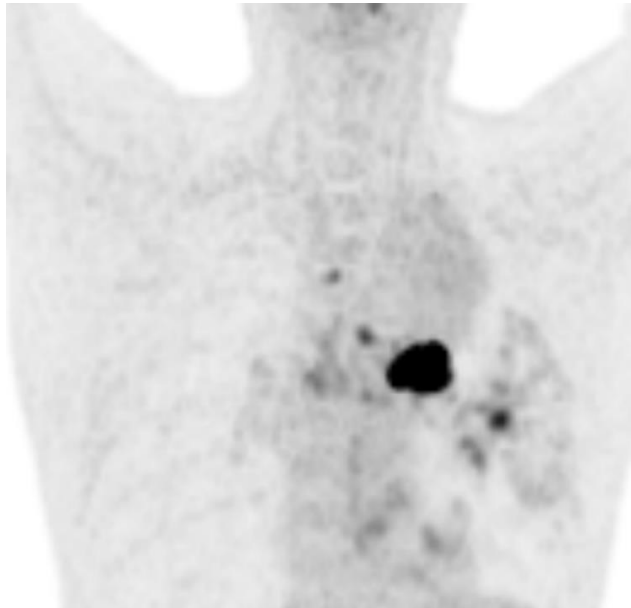
Lt SCN+

2R+

4R+

7+

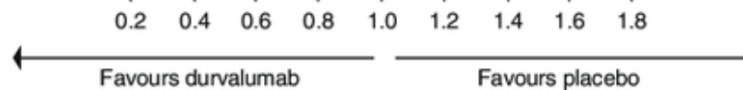
Q. M/63 Sq PD-L1-



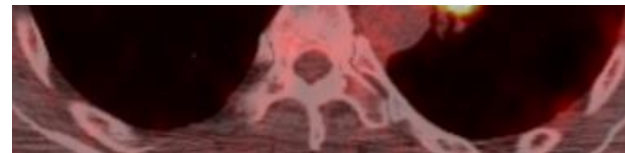
LN biopsy
2R+
4L+

PD-L1 status

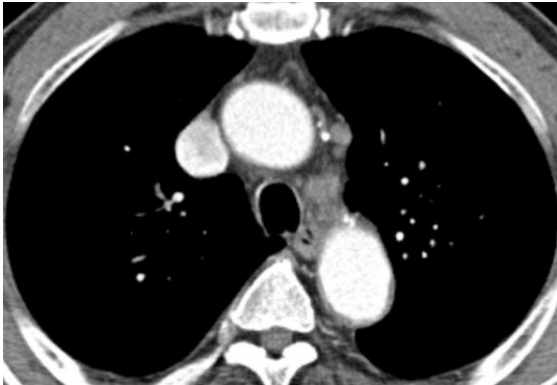
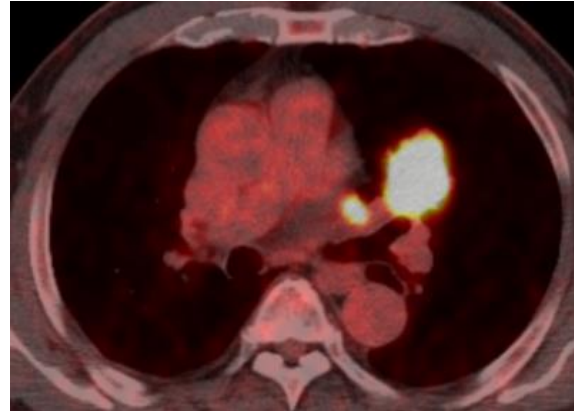
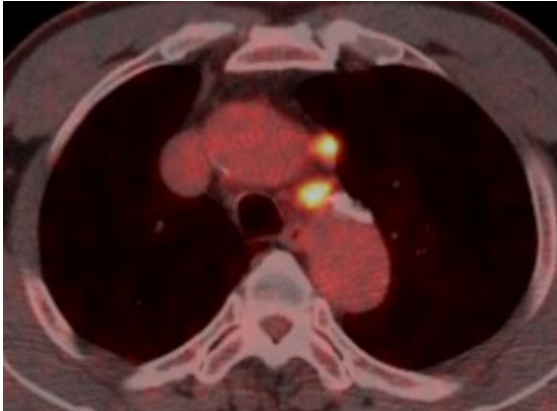
≥25%	41/115 (35.7)	23/44 (52.3)		0.50 (0.30-0.83)
<25%	90/187 (48.1)	53/105 (50.5)		0.89 (0.63-1.25)
Unknown	79/174 (45.4)	58/88 (65.9)		0.60 (0.43-0.84)
1-24% (posthoc analysis)	43/97 (44.3)	26/47 (55.3)		0.67 (0.41-1.10)
≥1% (posthoc analysis)	84/212 (39.6)	49/91 (53.8)		0.59 (0.41-0.83)
<1% (posthoc analysis)	47/90 (52.2)	27/58 (46.6)		1.14 (0.71-1.84)



→ **CCRT**



Q. M/69 Sq PD-L1+



LN biopsy

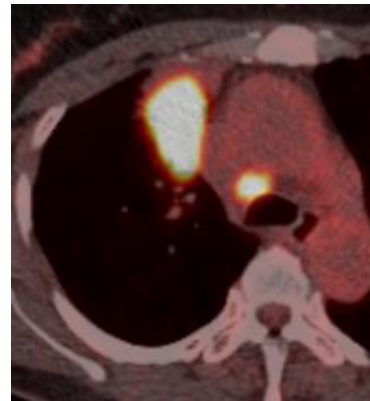
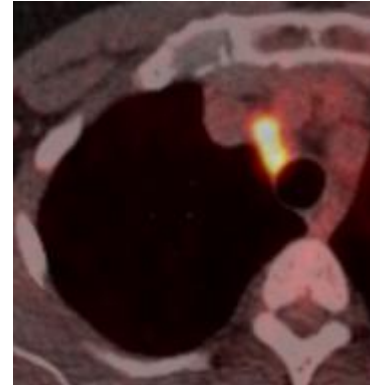
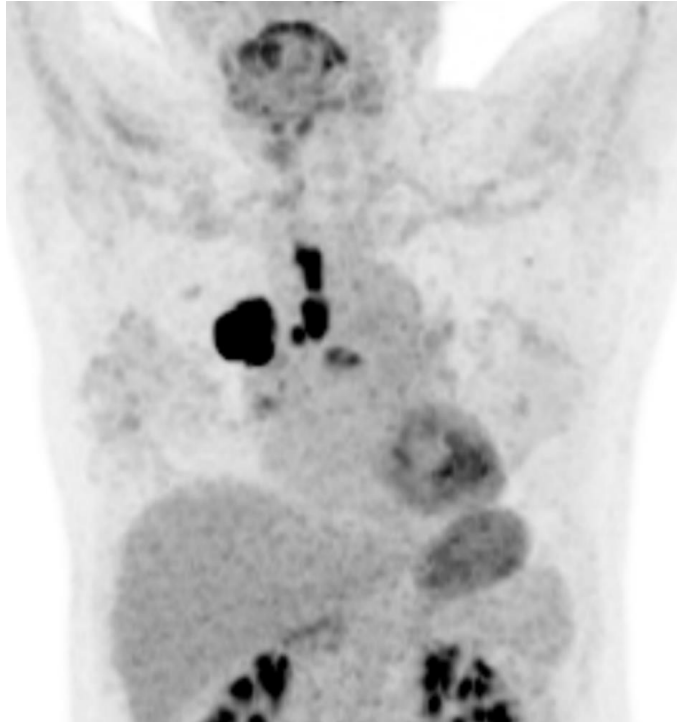
5+

6?

10L+

→ CCRT + durvalumab

Q. F/60 ADC PD-L1+



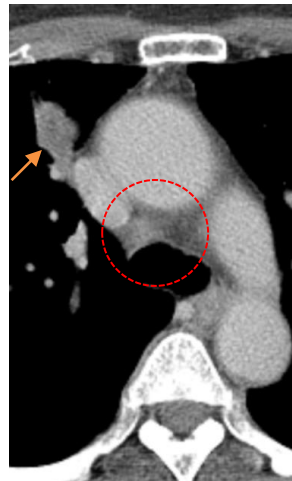
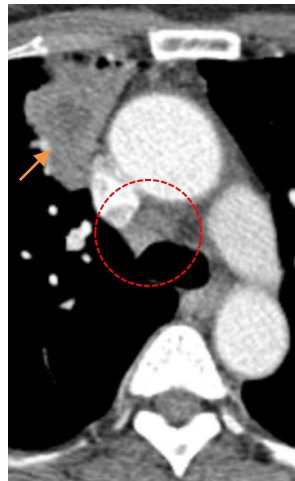
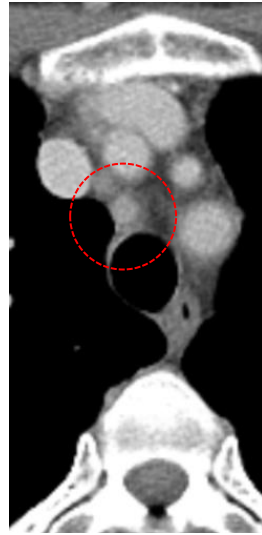
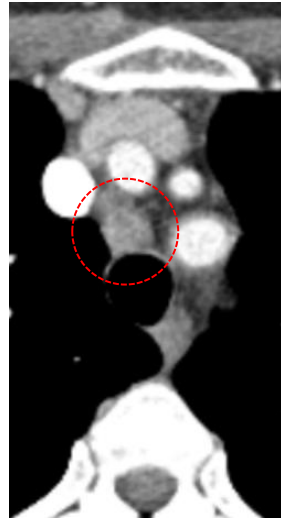
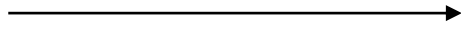
LN biopsy

2R+

4R+

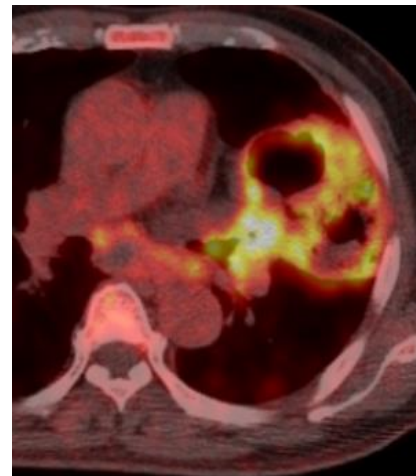
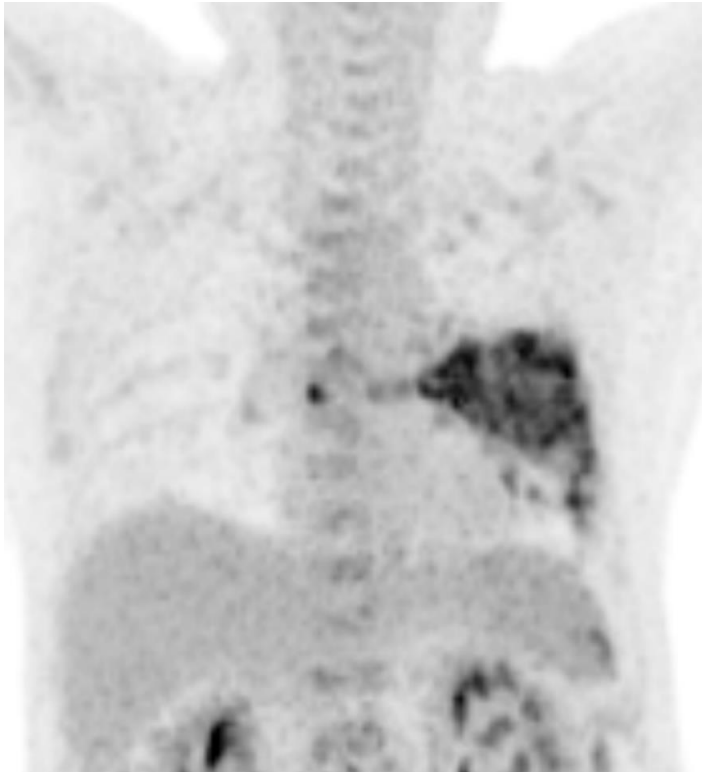
→ **CCRT + durvalumab ?**

Neoadj CRT



→ Op

Q. M/74 SQ PD-L1+

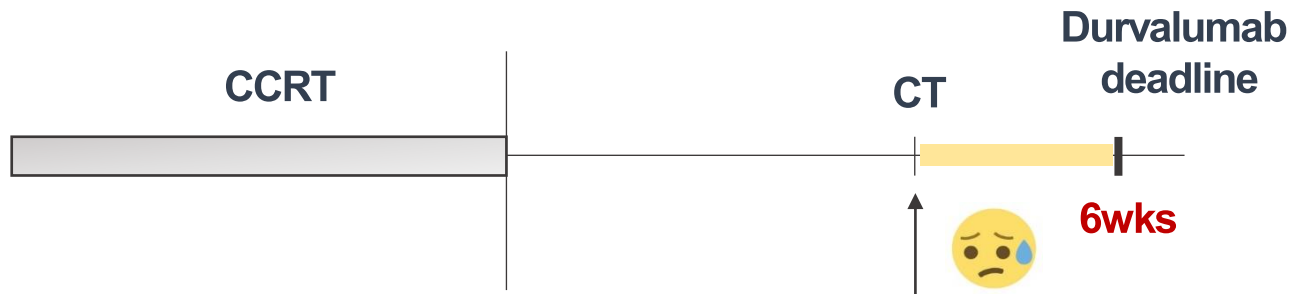


LN biopsy

7+

11L+

→ CCRT + durvalumab



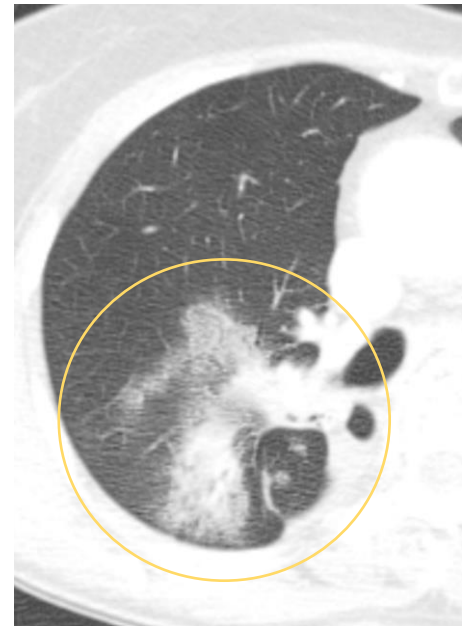
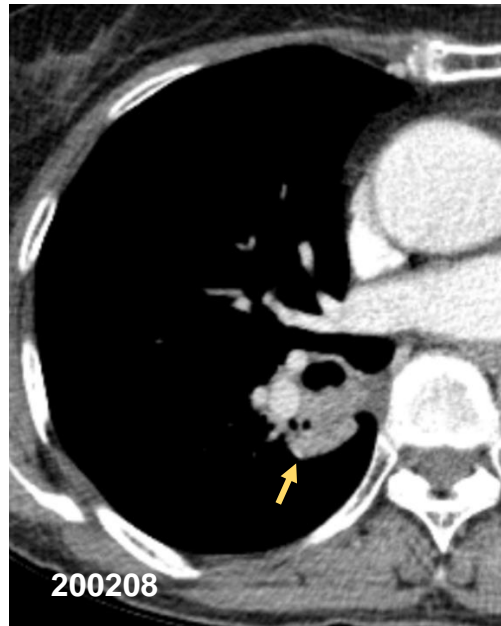
If RT pneumonitis

Sometimes difficult to be on time!

F/60s, NSCLCa, ADC, T4N1M0
PD-L1+
CCRT (191127 - 200120)

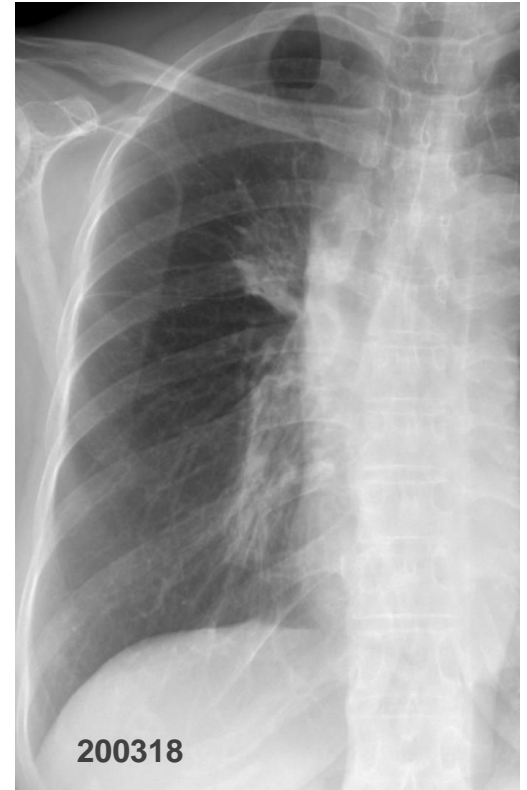
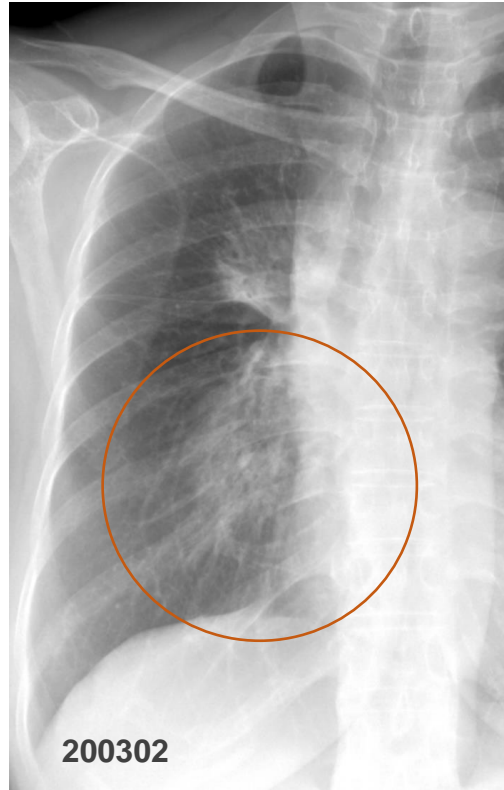
200218 OPD

Cough, mild dyspnea since 2wks ago → gradually improving
Observation for 2wks without steroid

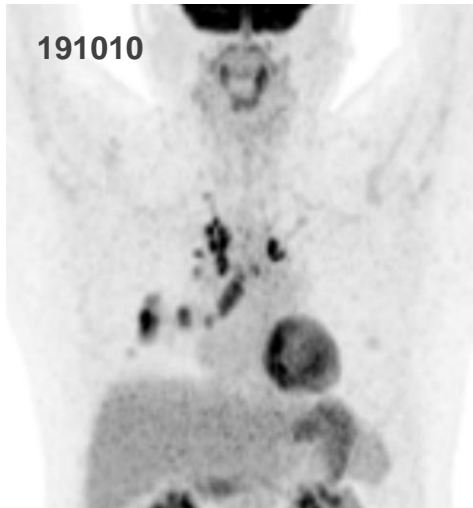


↑ cough, dyspnea without fever
Pd 40mg 1wk & 20mg 1wk

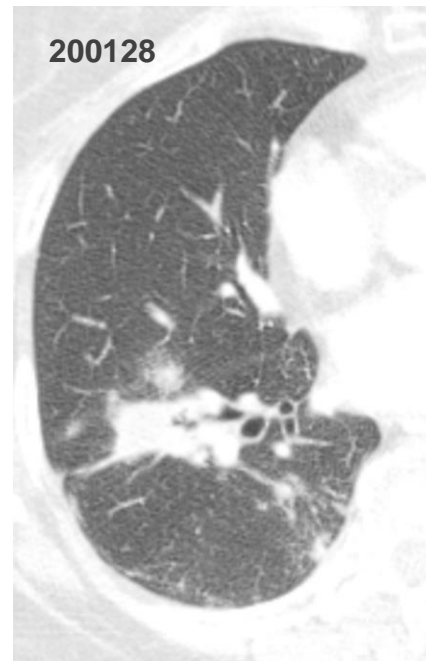
Sx improved
Durvalumab start



F/60s, NSCLCa, ADC, T1N3M0
PD-L1+
CCRT (191105 - 191218)



200128 OPD
No specific Sx → Durvalumab start



No CPA

200212 OPD

Cough, dyspnea

Durvalumab hold, Pd 40mg 2wks → 30mg 1wk → 15mg 2wks





200318 OPD

Sx improved

Durvalumab restart



Mx of unresectable stage III NSCLCa

-  **Accurate nodal staging**
-  **Case by case decision at MDT**



thank you!