Update on Treatment of Lung Cancer (Focusing on NSCLC)

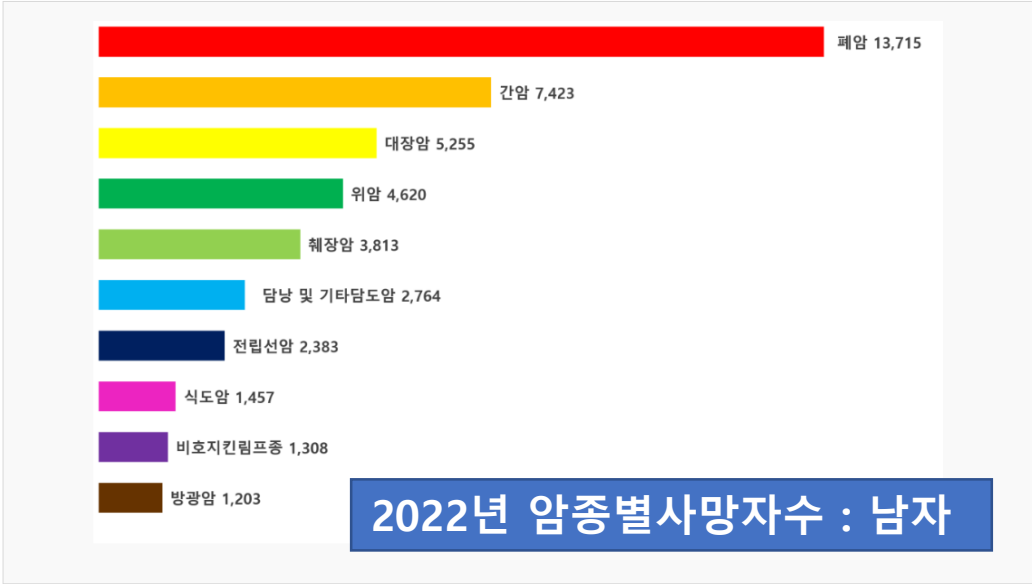
2024.5.25

인제대학교 부산백병원 호흡기.알레르기내과

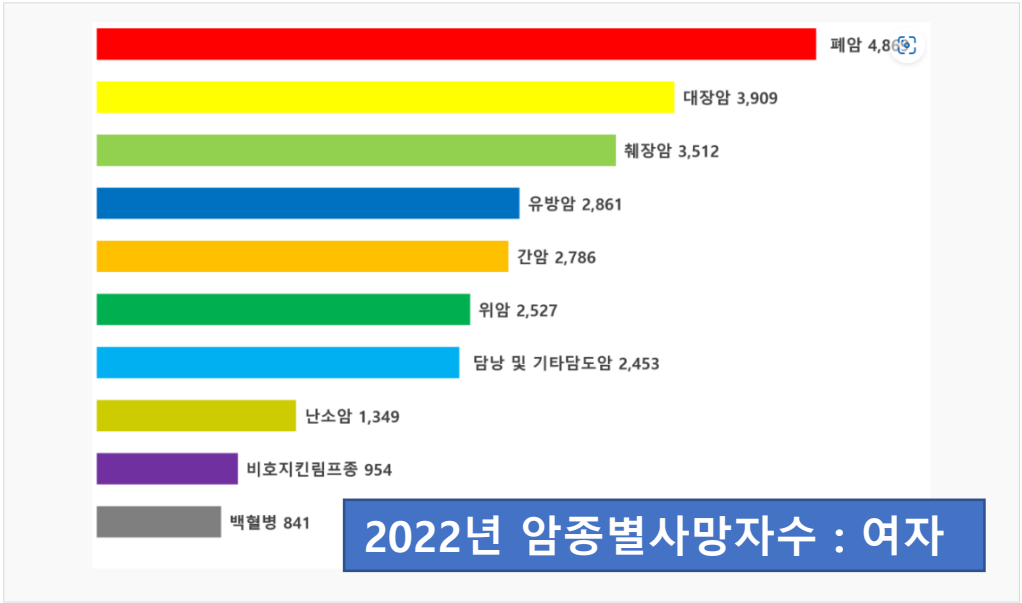
이 현 경

우리나라 폐암의 발생율 및 사망률 통계

성별 10대암 발생율
2020, 국가암 정보센터

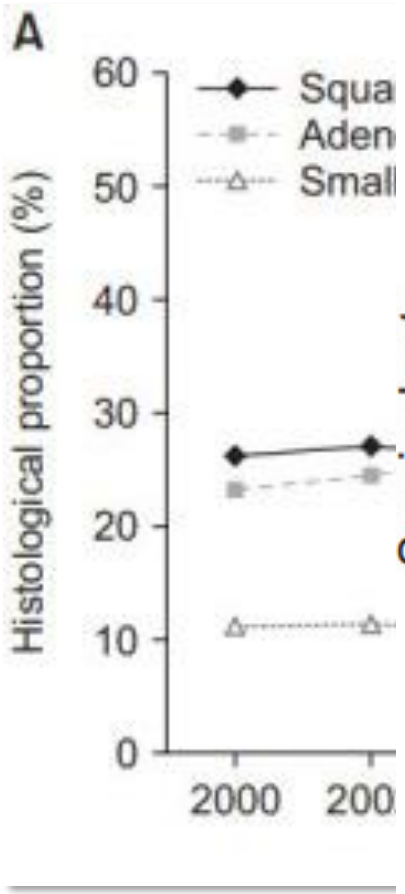


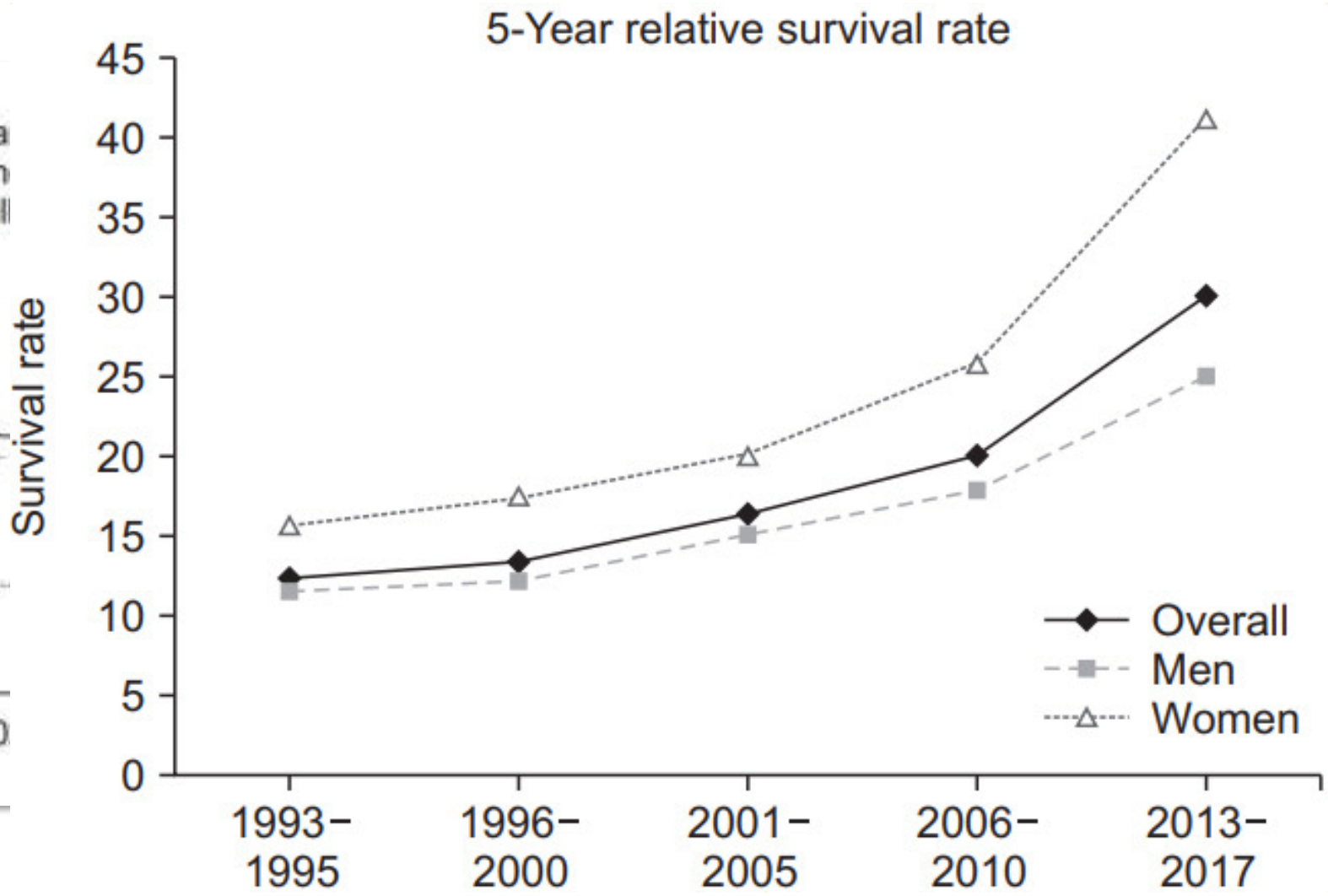
2022년 암종별사망자수 : 남자

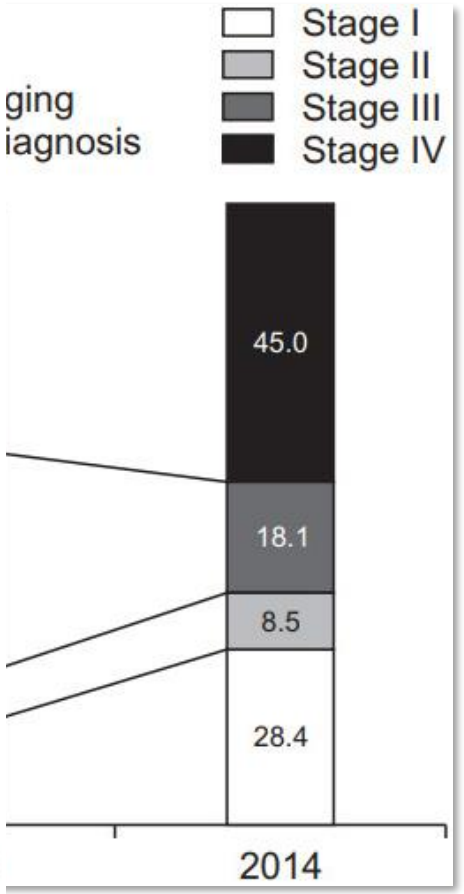


2022년 암종별사망자수 : 여자

우리나라 폐암의 trend (조직형, 병기, 5년 생존율)







Lee JG, et al. Tuberc Respir Dis. 2021;84: 89–95.

강의 목차

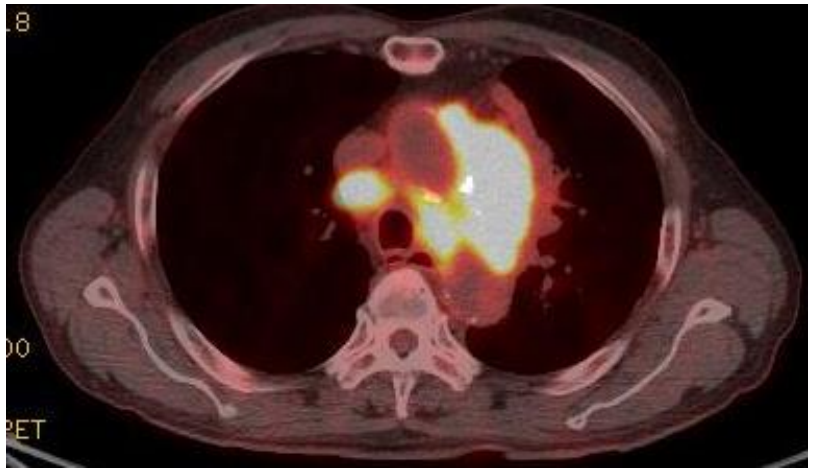
- **폐암관련 기본개념정리**
- 진료지침 정리
  - ✓ 미국종합암네트워크 (NCCN)
  - ✓ 유럽암학회
  - ✓ 대한폐암학회
- 요약

폐암확진을 위해 '조직획득'이 필수과정

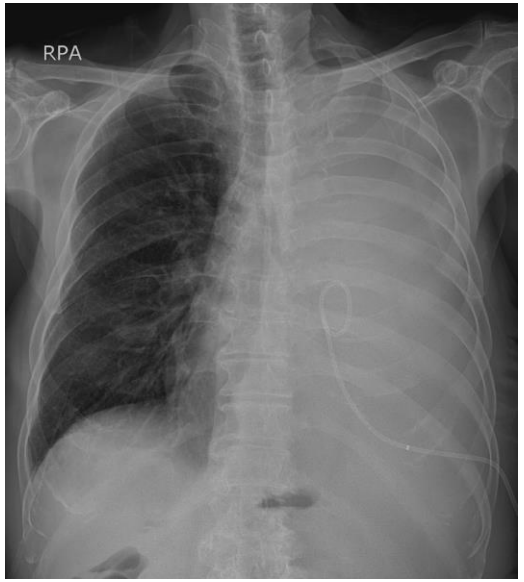
어디서 조직을 얻을 것인가 ?

원발부위 : 폐

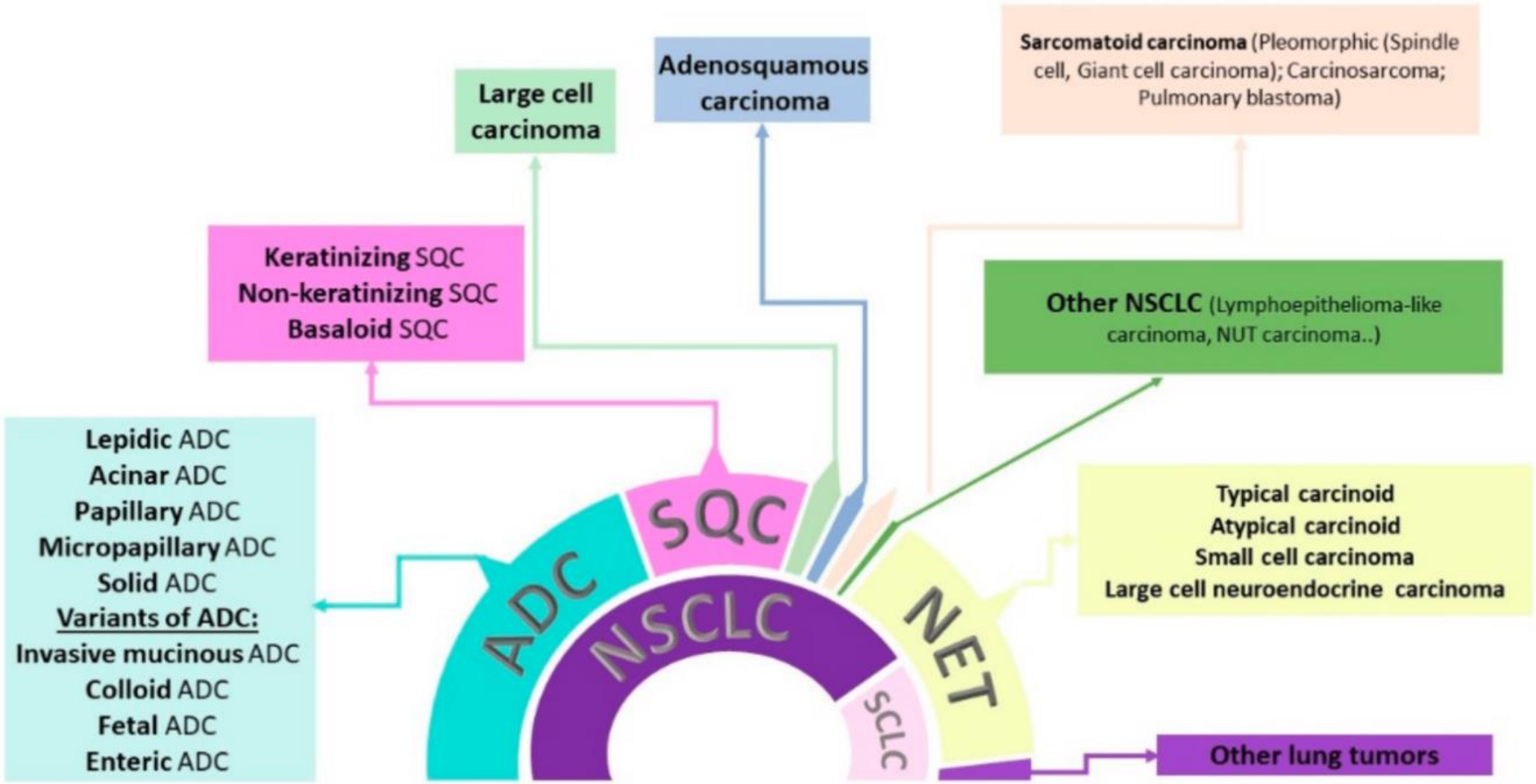
전이부위 : 림프절, 흉수, 기타장기



기관지내시경초음파
(EBUS-TBNA)



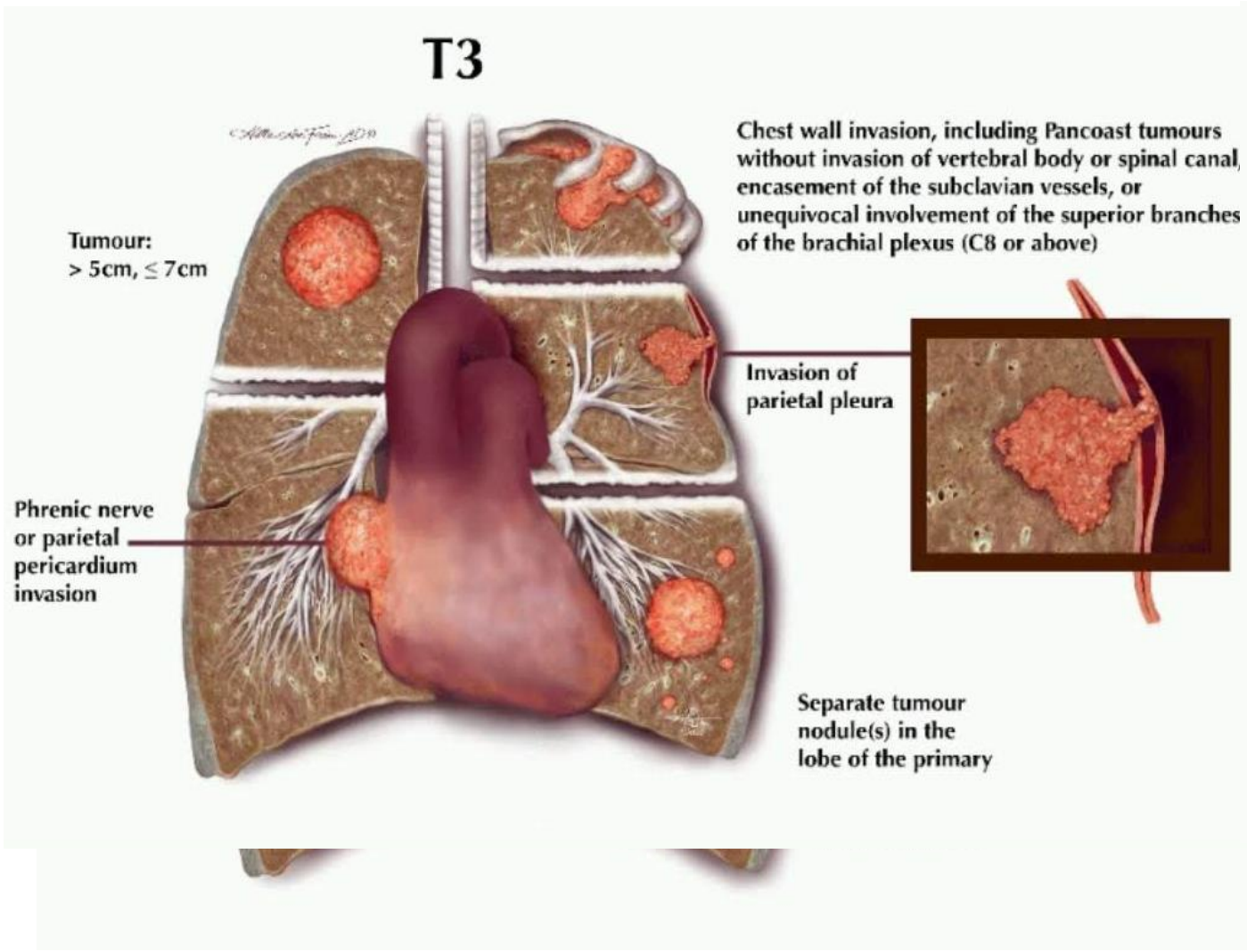
폐암의 조직학적 분류 (2021 WHO 분류)

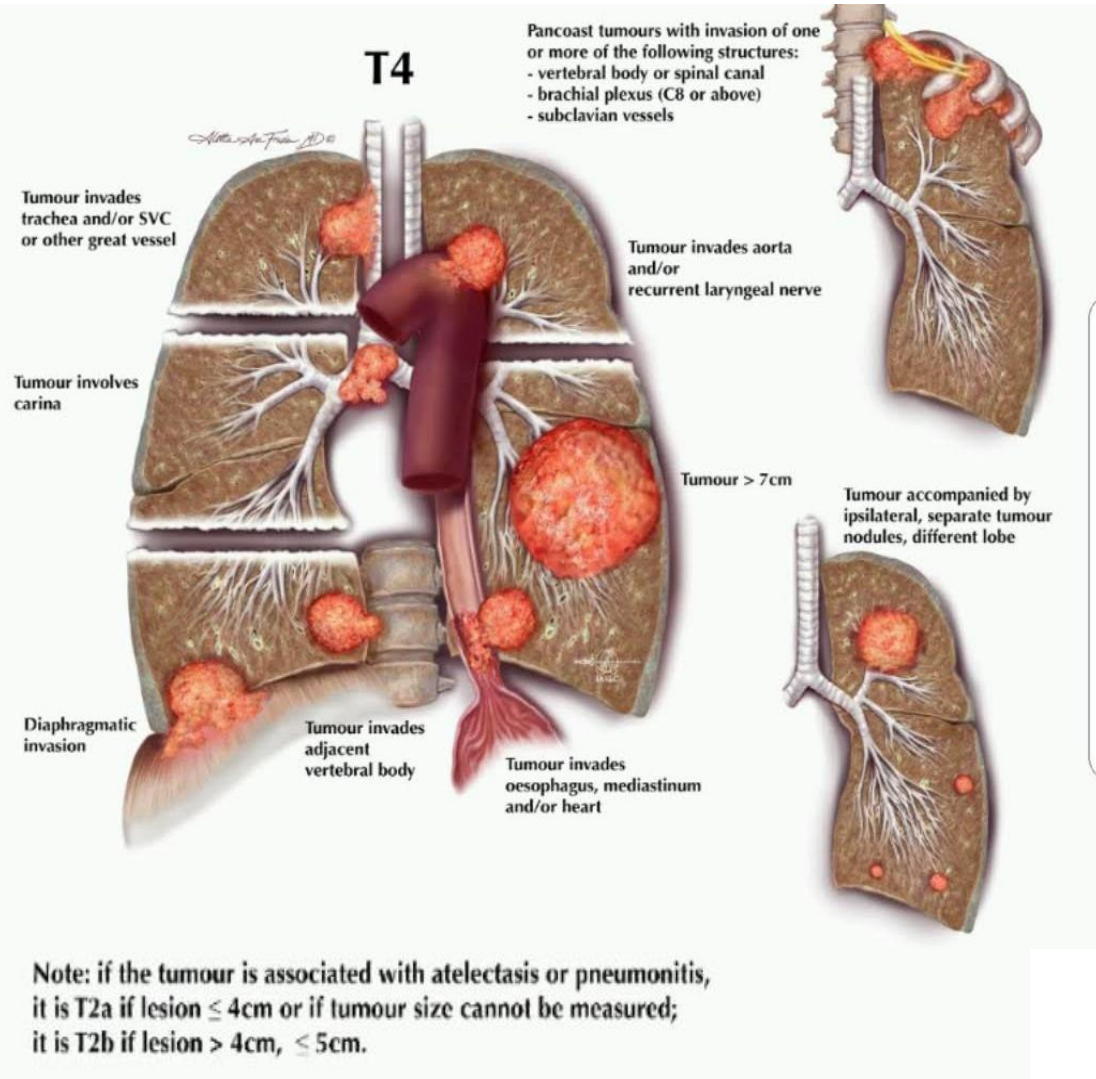


* ADC: adenocarcinoma, SQC: squamous cell carcinoma, NET: neuroendocrine carcinoma

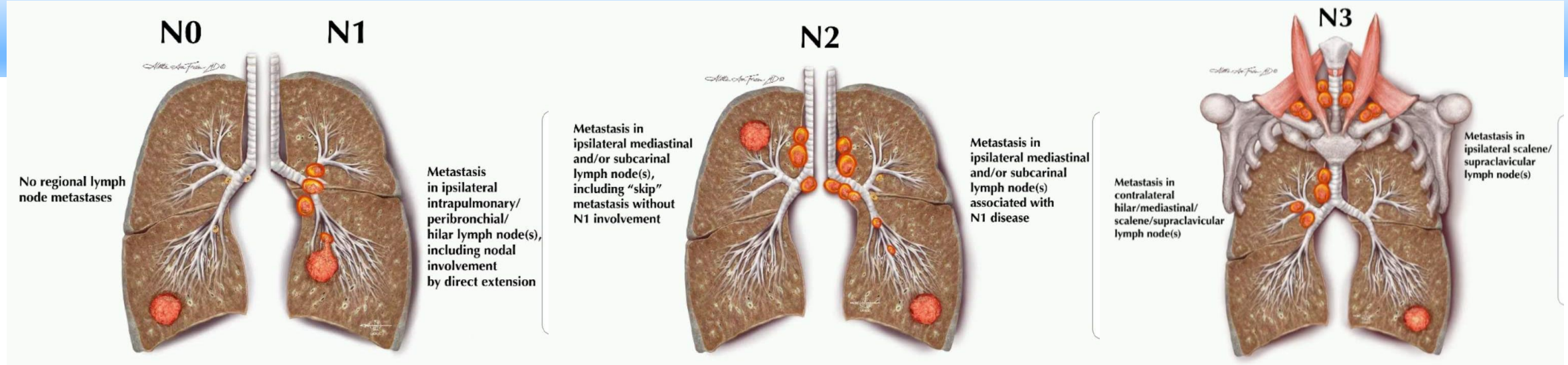
J. Pers. Med. 2021, 11(11), 1102; https://doi.org/10.3390/jpm11111102

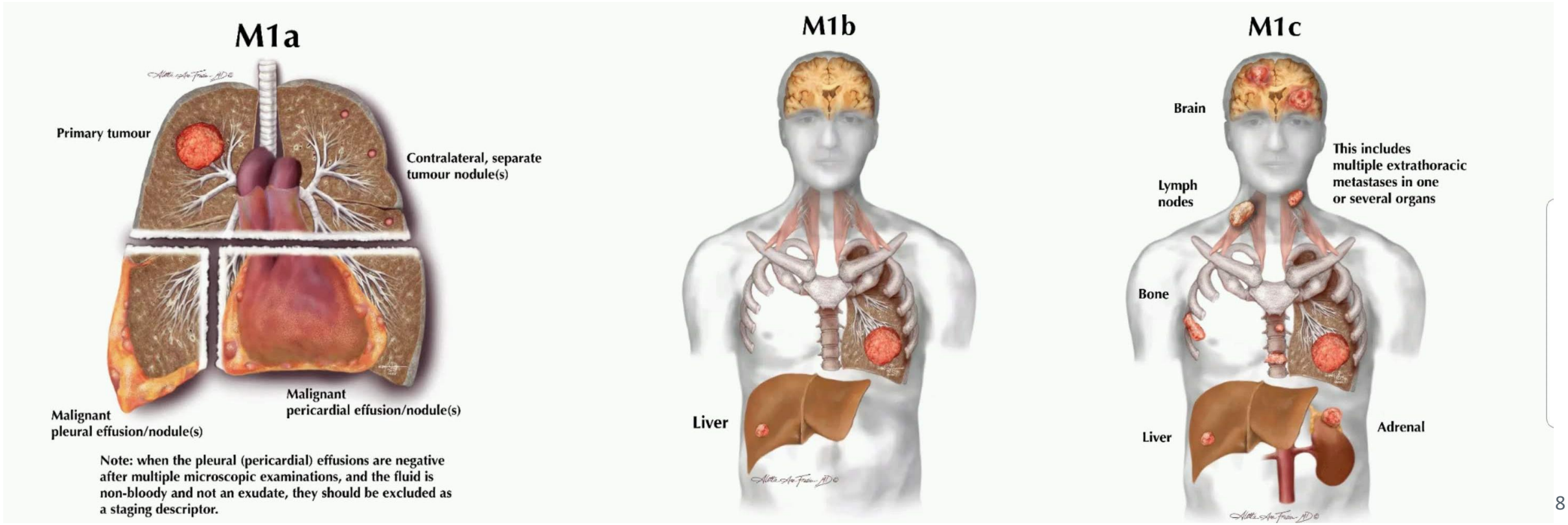
폐암의 치료법 결정 및 예후예측의 핵심은 '병기결정'





Note: if the tumour is associated with atelectasis or pneumonitis, it is T2a if lesion ≤ 4cm or if tumour size cannot be measured; it is T2b if lesion > 4cm, ≤ 5cm.


N0
N1
No regional lymph node metastases
Metastasis in ipsilateral intrapulmonary/ peribronchial/ hilar lymph node(s), including nodal involvement by direct extension
N2
Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s), including "skip" metastasis without N1 involvement
Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s) associated with N1 disease
N3
Metastasis in contralateral hilar/mediastinal/ scalene/supraclavicular lymph node(s)
Metastasis in ipsilateral scalene/ supraclavicular lymph node(s)

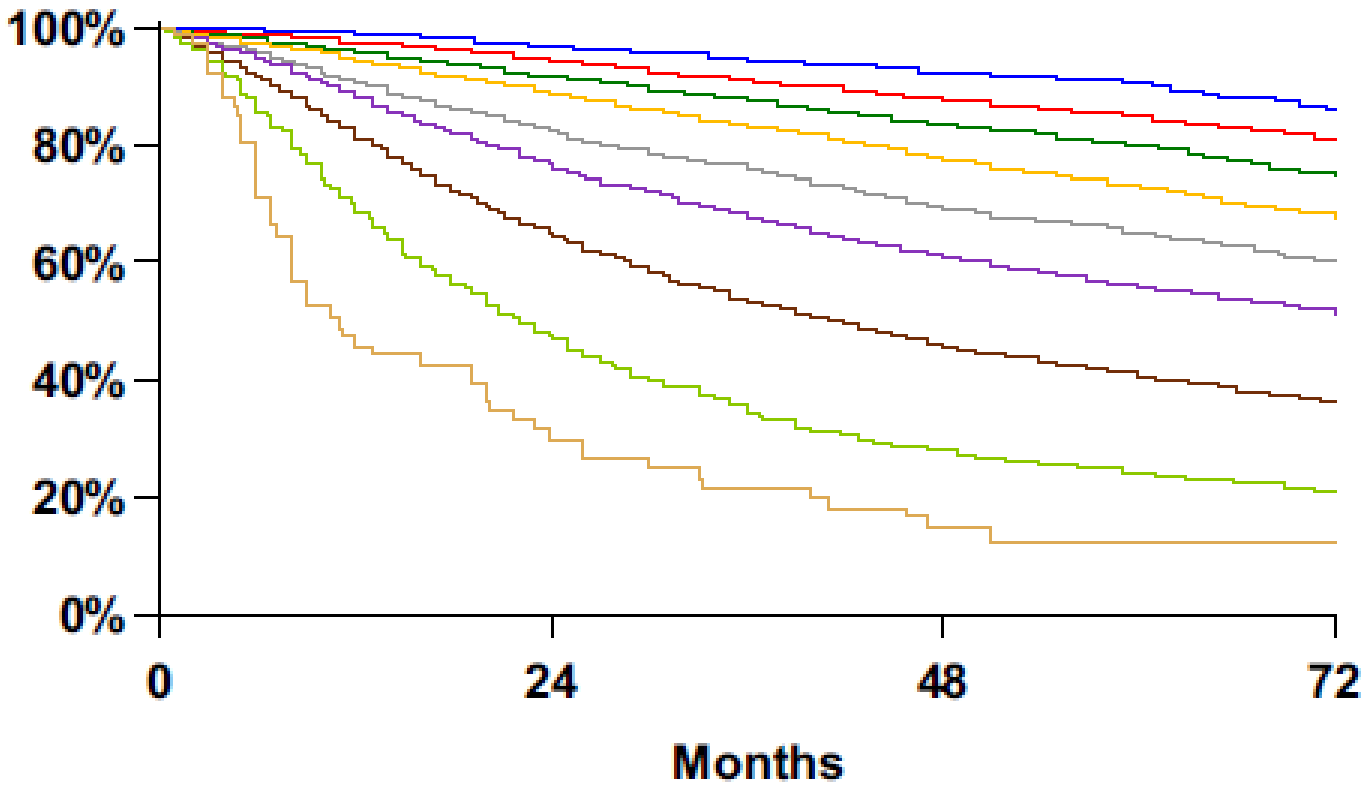

M1a
Primary tumour
Contralateral, separate tumour nodule(s)
Malignant pericardial effusion/nodule(s)
Malignant pleural effusion/nodule(s)
Note: when the pleural (pericardial) effusions are negative after multiple microscopic examinations, and the fluid is non-bloody and not an exudate, they should be excluded as a staging descriptor.
M1b
Liver
M1c
Brain
This includes multiple extrathoracic metastases in one or several organs
Lymph nodes
Bone
Liver
Adrenal

TNM 병기결정 챠트 (8th edition)

STAGE	T	N	M
Occult carcinoma	TX	N0	M0
0	Tis	N0	M0
IA1	T1mi	N0	M0
	T1a	N0	M0
IA2	T1b	N0	M0
IA3	T1c	N0	M0
IB	T2a	N0	M0
IIA	T2b	N0	M0
IIB	T1a	N1	M0
	T1b	N1	M0
	T1c	N1	M0
	T2a	N1	M0
	T2b	N1	M0
	T3	N0	M0
IIIA	T1a	N2	M0
	T1b	N2	M0
	T1c	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
IIIB	T1a	N3	M0
	T1b	N3	M0
	T1c	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N2	M0
	T4	N2	M0
IIIC	T3	N3	M0
	T4	N3	M0
IVA	Any T	Any N	M1a
	Any T	Any N	M1b
IVB	Any T	Any N	M1c

병기에 따른 폐암의 예후 (병리적으로 확진된 경우)

8th Edition



Proposed	Events / N	MST	24 Month	60 Month
IA1	139 / 1389	NR	97%	90%
IA2	823 / 5633	NR	94%	85%
IA3	875 / 4401	NR	92%	80%
IB	1618 / 6095	NR	89%	73%
IIA	556 / 1638	NR	82%	65%
IIB	2175 / 5226	NR	76%	56%
IIIA	3219 / 5756	41.9	65%	41%
IIIB	1215 / 1729	22.0	47%	24%
IIIC	55 / 69	11.0	30%	12%

J Thorac Oncol 2015;11(1): 39-51

환자의 활동도 평가 (Eastern Cooperative Oncology Group)

ECOG Performance Status

점수	정 의
0	완전히 문제없이 활동할 수 있다 발병전과 같은 일상생활을 제한없이 할 수 있다
1	육체적으로 격한 활동은 제하되지만, 보행가능하고, 가벼운 작업이나 앉아서의 작업을 할 수 있다. (예, 가벼운 가사, 사무작업)
2	보행가능으로, 스스로 신변의 일은 모두 가능하지만, 작업은 할 수 없다. 하루 중 50%이상은 침대밖에서 지낸다.
3	자신의 신변의 일을 한정적으로 할 수 없다. 하루 중 50%이상을 침대나 의자에서 지낸다.
4	전혀 움직일 수 없다. 자신의 신변 일은 전혀 할 수 없다. 완전히 침대나 의자에서 지낸다.

https://blog.naver.com/ranman/221604644741

항암치료의 종류 및 목적

Neoadjuvant Chemotherapy (선행보조항암)

- When: Usually before surgery
- Purpose: to reduce the size of the tumor, making it simpler to remove

수술적 폐절제

Adjuvant Chemotherapy (보조항암)

- When: Usually after surgery
- Purpose: to eradicate any cancer cells that might remain following therapy

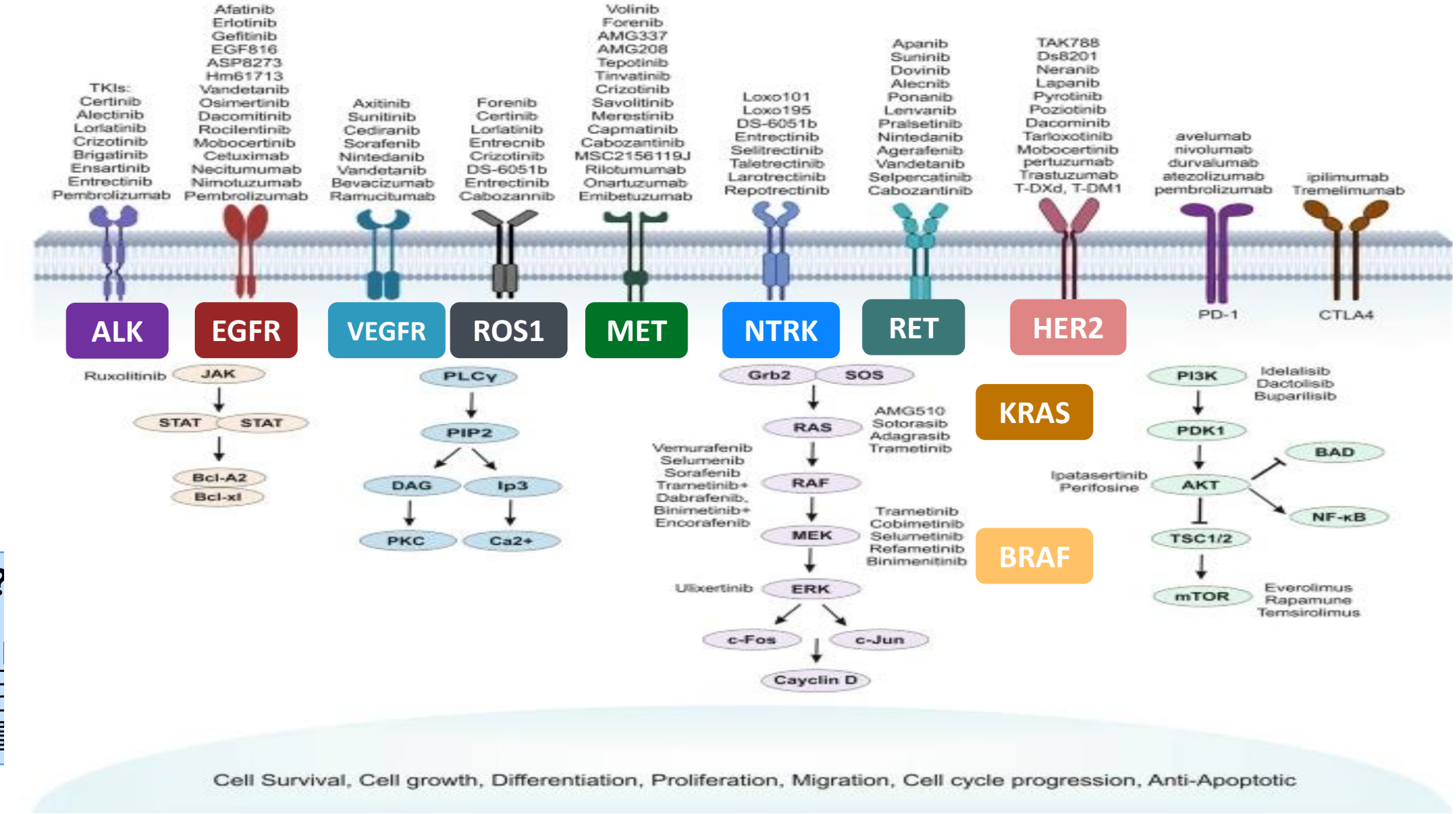
Palliative Chemotherapy (고식적항암)

- When: when cancer has spread and there is no cure.
- Purpose: to reduce symptoms and enhance quality of life

폐암절제의 수준 평가 (R0~R2)

R0	Complete resection, No residual tumor
R1	**Microscopic** residual tumor
R2	**Macroscopic** residual tumor

폐암표적치료제 (Targeted therapy)

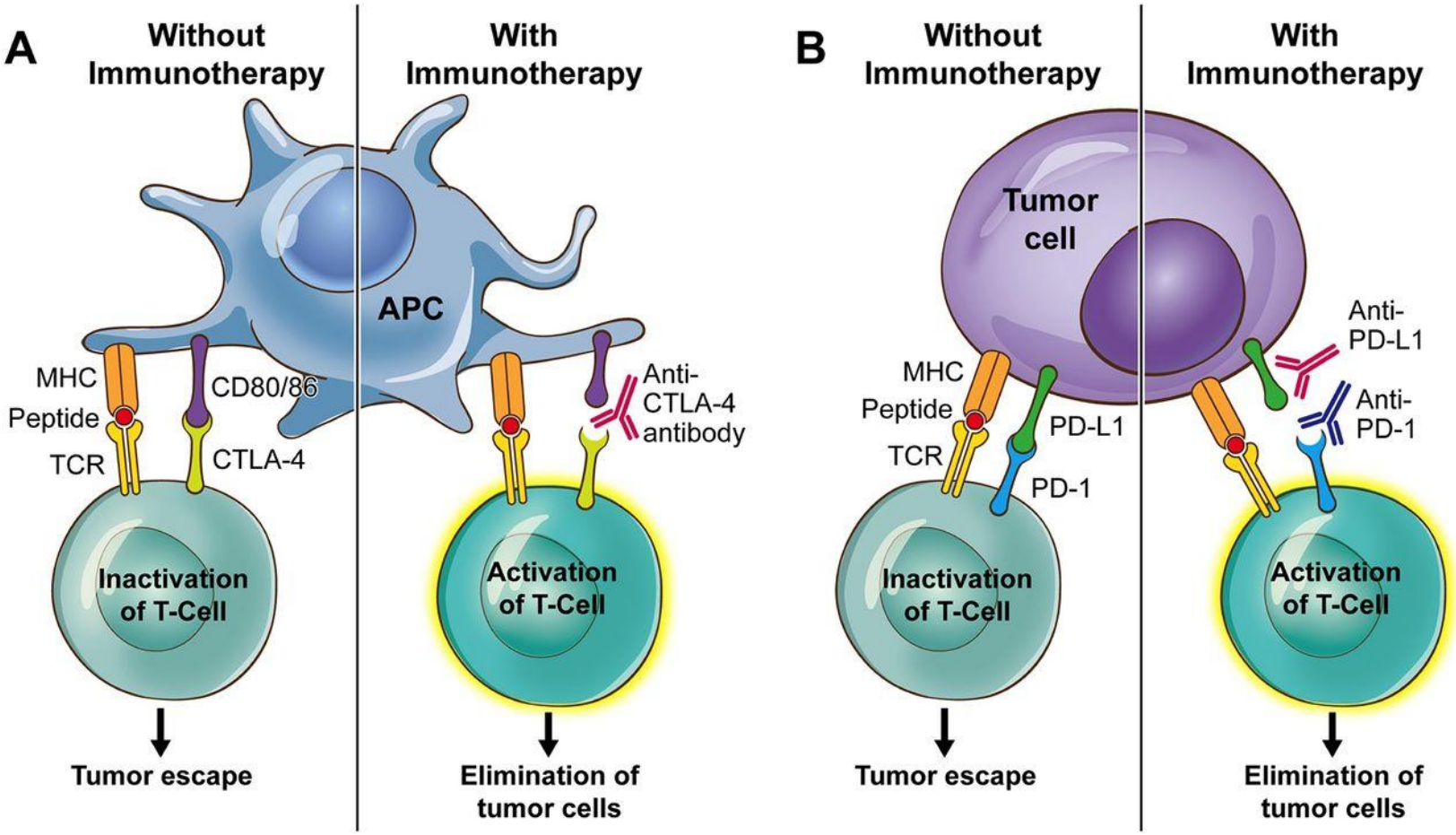


표적치료제란 ?

암의 생존과 확산
특별한 유전자, 단
으로 하는 약제를

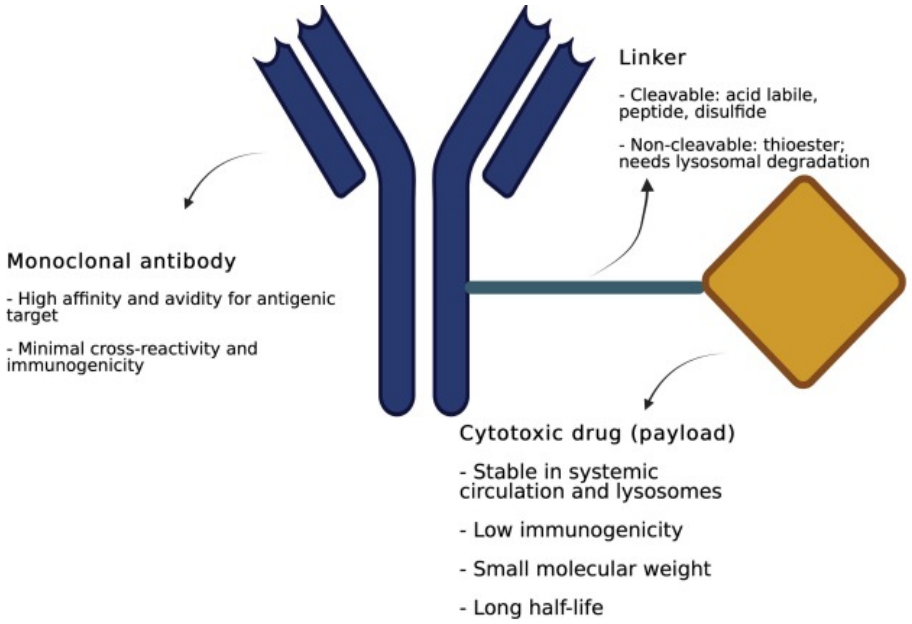
M. Araghi, et al. Cancer cell International. 2023; 23

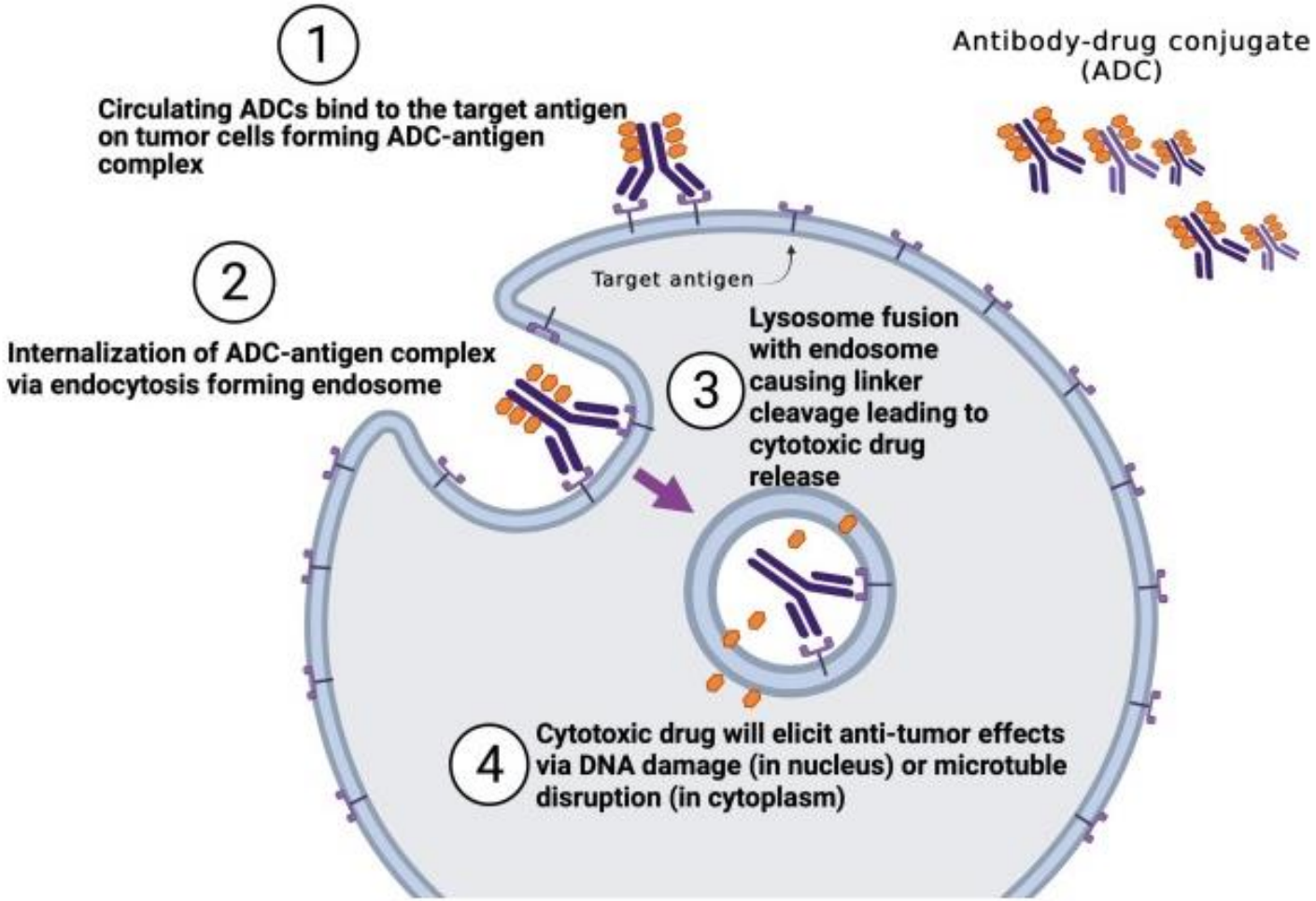
면역관문억제제 (Immune Check Point Inhibitor : ICI)의 기전



Soularue E. Gut 2018

항체약물중합체 (Antibody-drug conjugate)

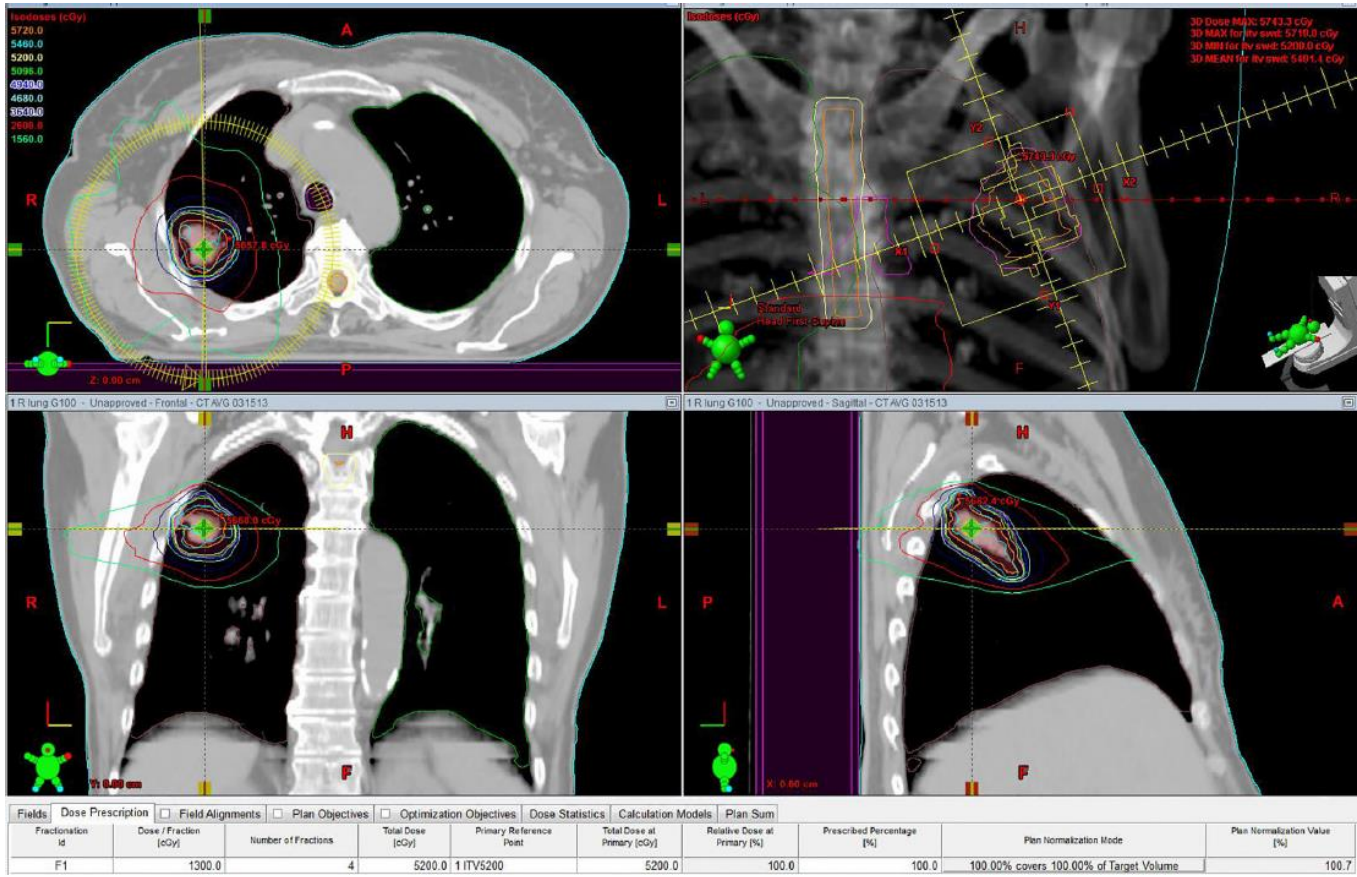




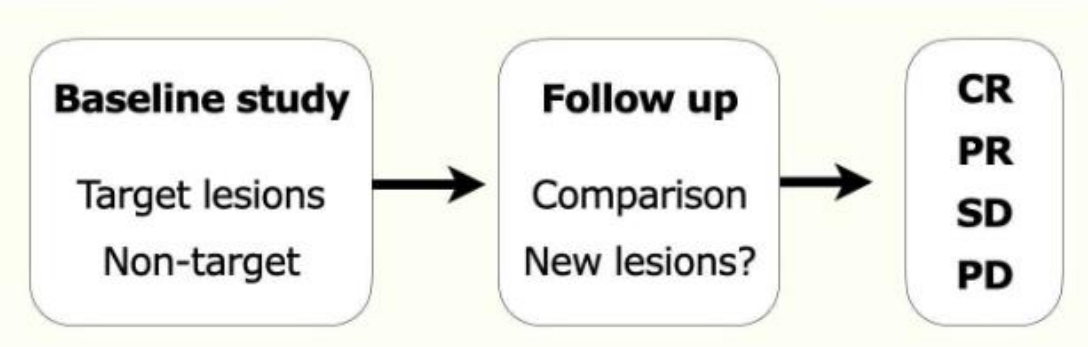
https://www.sciencedirect.com/science/article/pii/S0305737222000573

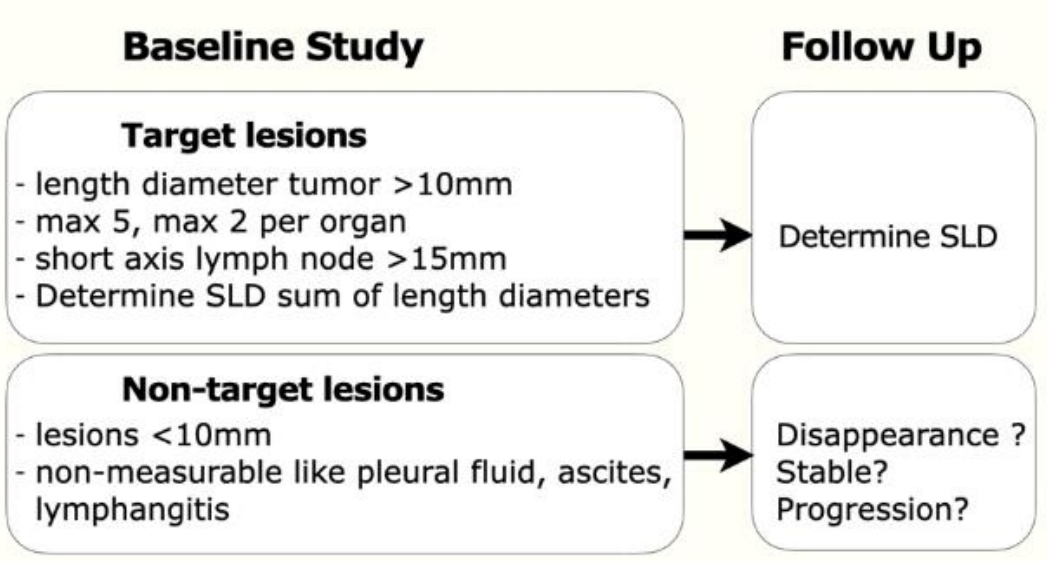
정위적방사선요법 : Stereotactic Body Irradiation Therapy (SBRT)

- 사이버나이프
- 감마나이프
- 노발리스



폐암치료반응 평가관련 개념/용어정리 : RECIST 1.1





Criteria for target lesions

Tumours

CT scan: long axis ≥ 10mm
Chest X-ray: long axis ≥ 20mm

Malignant lymph nodes

Short axis diameter ≥ 15mm

CR Disappearance of all lesions and pathologic lymph nodes

PR ≥ 30% decrease SLD (병변 장축의 총 합을 의미)
no new lesions
no progression of non-target lesions

SD no PR - no PD

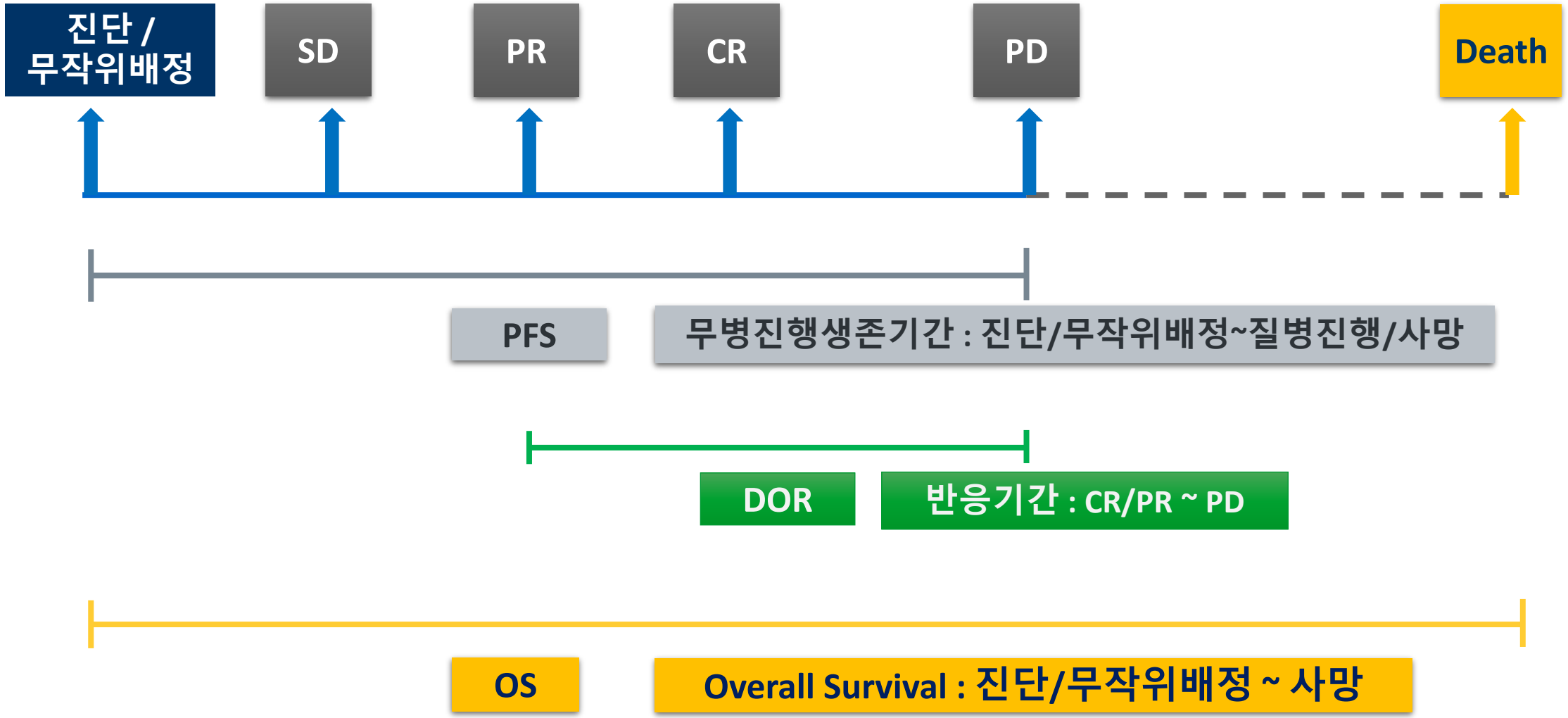
PD ≥ 20% increase SLD* compared to smallest SLD in study
or progression of non-target lesions
or new lesions

*SD: stable disease, PR: partial remission, CR: complete remission, PD: progressive disease

*** SLD : sum of longest diameter**

https://radiologyassistant.nl/more/recist-1-1/recist-1-1-1

폐암관련 기본개념/ 용어 정리 : 효과평가 도구들



*SD: stable disease, PR: partial remission, CR: complete remission, PD: progressive disease

강의 목차

- 폐암관련 기본개념정리
- 진료지침 정리
  - ✓ **미국종합암네트워크 (NCCN)**
  - ✓ 유럽암학회
  - ✓ 대한폐암학회
- 요약

NCCN National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Non-Small Cell Lung Cancer

Version 5.2024 — April 23, 2024 **2024.4**

NCCN.org

NCCN Guidelines for Patients® available at www.nccn.org/patients

Continue

폐암 진료지침 3판

Guidelines for Treatment of Lung Cancer

2023.11

KALC 대한폐암학회

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

L. E. Hendriks[1], K. M. Kerr[2], J. Menis[3], T. S. Mok[4], U. Nestle[5,6], A. Passaro[7], S. Peters[8], D. Planchard[9], E. F. Smit[10,11], B. J. Solomon[12], G. Veronesi[13,14] & M. Reck[15], on behalf of the ESMO Guidelines Committee*

[1]Department of Pulmonology, GROW School for Oncology and Reproduction, Maastricht University Medical Center, Maastricht, The Netherlands; [2]Aberdeen Royal Infirmary, Aberdeen University Medical School, Aberdeen, UK; [3]Medical Oncology Department, University and Hospital Trust of Verona, Verona, Italy; [4]Department of Clinical Oncology, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China; [5]Department of Radiation Oncology, University Hospital Freiburg, Freiburg; [6]Department of Radiation Oncology, Kliniken Maria Hilf, Moenchengladbach, Germany; [7]Division of Thoracic Oncology, European Institute of Oncology IRCCS, Milan, Italy; [8]Department of Oncology, Centre Hospitalier Universitaire Vaudois, Lausanne University, Lausanne, Switzerland; [9]Department of Medical Oncology, Thoracic Group, Gustave-Roussy, Villejuif, France; [10]Thoracic Oncology Service, Netherlands Cancer Institute, Amsterdam; [11]Department of Pulmonary Diseases, Leiden University Medical Center, Leiden, The Netherlands; [12]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; [13]Faculty of Medicine and Surgery-Vita-Salute San Raffaele University, Milan; [14]Division of Thoracic Surgery, IRCCS San Raffaele Scientific Institute, Milan, Italy; [15]Department of Thoracic Oncology, Airway Research Center North, German Center for Lung Research, Lung Clinic, Grosshansdorf, Germany

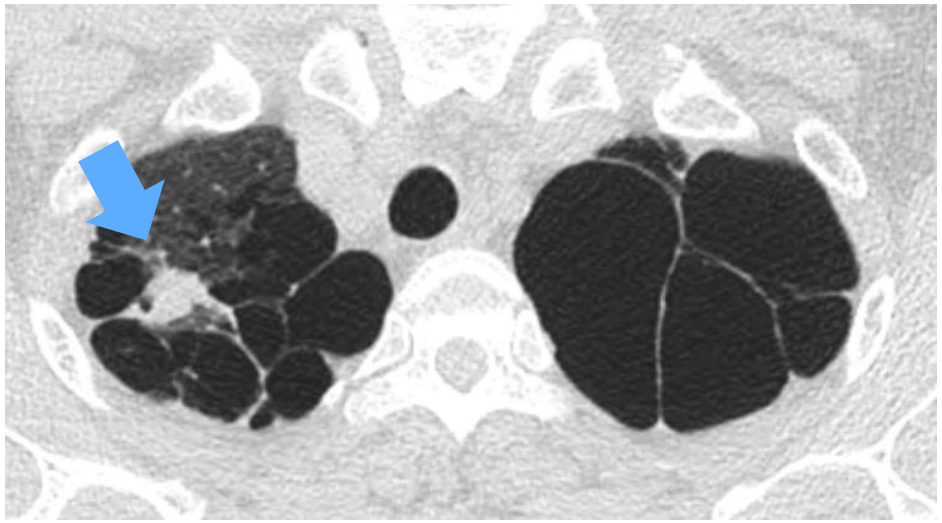
Available online 23 January 2023 **2023.1**

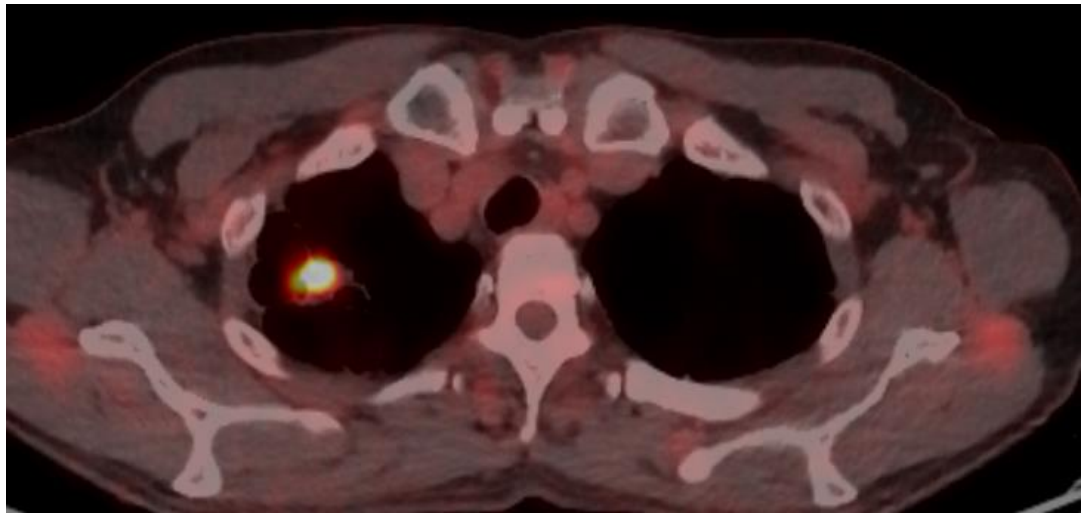
진 단 (1)

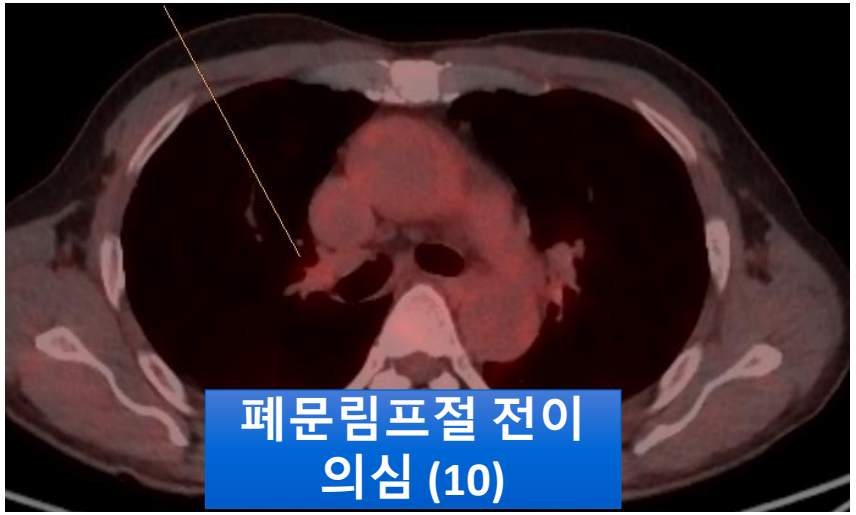
- Stage IA 폐암의 가능성이 매우 높은 경우 (위험인자 및 영상소견 등)
  수술 전 조직검사가 필요하지 않다
- 수술 전 조직검사의 시도가 권장되는 경우는 ? (appropriate)
  - 폐암 << 염증성 병변 (육아종성 결절 등)
  - Stage IB 또는 그 이상일 가능성이 높아 수술 전 전신치료가 필요할 가능성이 있는 경우
  - Stereotactic ablative radiotherapy (SABR)전 진단이 필요한 경우
- **다학제평가**에서 조직검사가 위험성이 높거나 어려운 경우에는 임상적으로 폐암을 진단하는 것이 적합하고, 치료를 진행하는 것이 정당하다.

NCCN NSCLC, V5, 2024

M/55, RUL nodule with severe emphysema







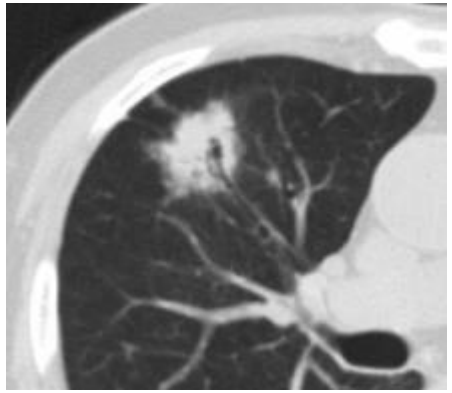
수술로
진단

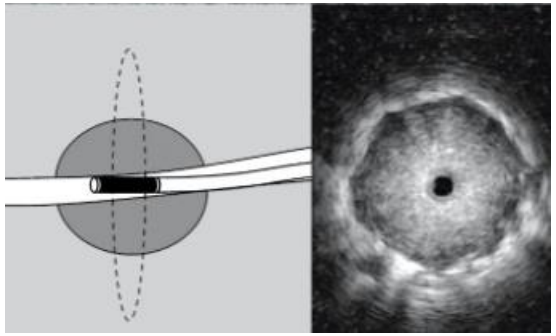
장쪽 흉막침범

pT2aN1M0 (IIB)

진 단 (2)

- **조직검사 site의 결정** : 가장 높은 병기를 결정해 줄 수 있는 위치의 조직을 얻는 것이 바람직하다 (전이병변, 종격동 림프절 > 폐 병변).
- Advanced stage 가능성이 높은 경우는 조직검사 위치 결정에 PET/CT가 자주 효과적으로 이용된다.
- 폐결절의 조직검사 : radial-EBUS, navigational bronchoscope, 경흉부세침흡인 등을 이용할 수 있다 (폐 바깥쪽 1/3 이라는 단어 삭제됨)





Tuberculosis and Respiratory Diseases 2019;82(4):319-327.

https://mforum.com.au/endobronchial-ultrasound/

NCCN NSCLC, V5, 2024

진 단 (3)

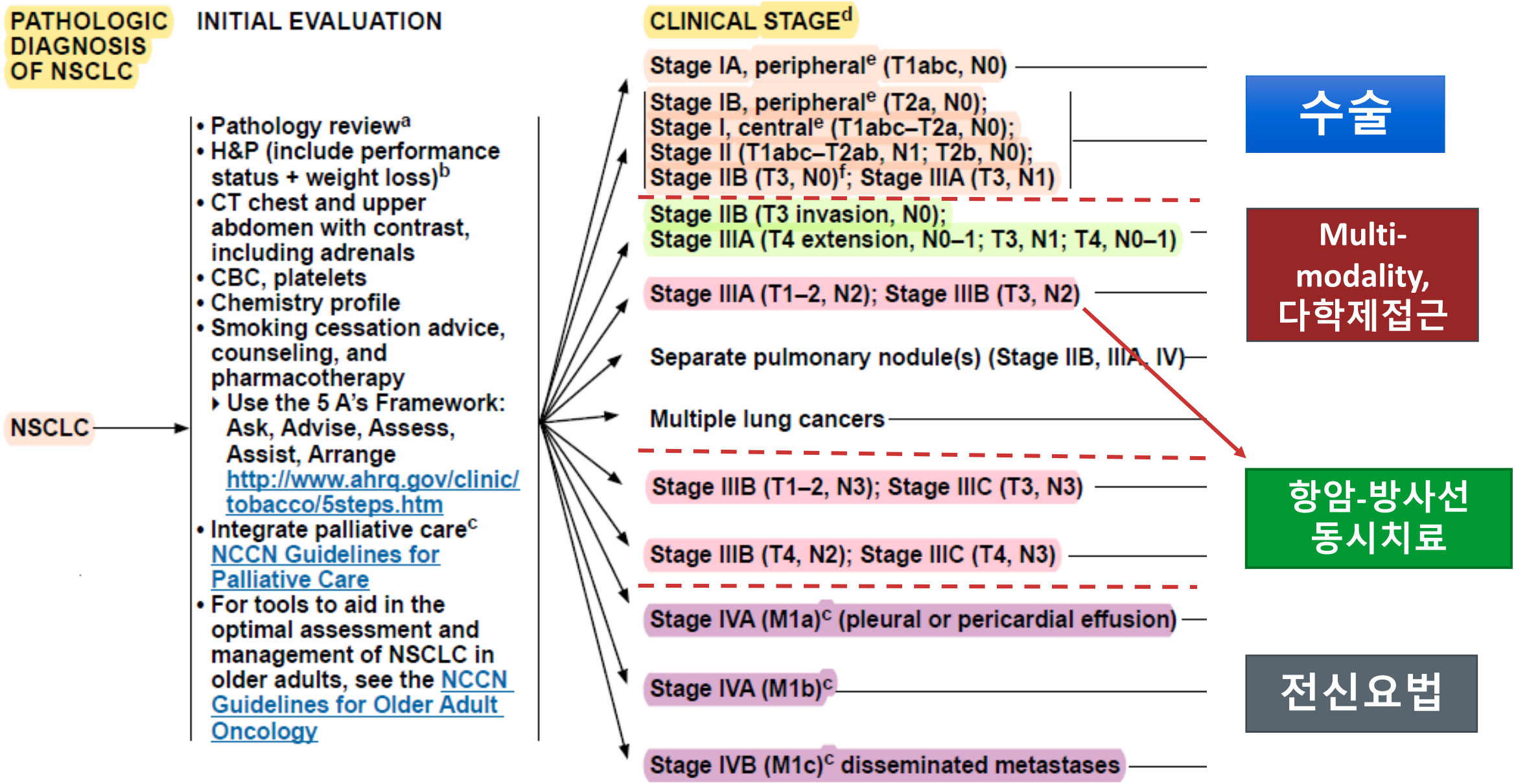
- PET/CT and/or CT에서 폐암양성 림프절로 의심되나 EBUS-TBNA 음성인 경우는 수술적 절제 전 mediastinoscopy를 해야 한다.
- 흉수가 동반된 폐암의 접근법
  - 흉부세포검사가 음성이어도 흉막침범을 배제할 수 없다.
  - 림프구가 우세한 흉수일 경우, 세포검사 음성이어도, 완치목적의 치료를 개시하기 전에 흉강경 검사를 반드시 고려해야 한다.

치료방침 결정시 중요한 고려요소들

- **종격동 림프절**에 대한 병리적 진단이 필수적이다 (EBUS, EUS, CT-guided biopsy, mediastinoscopy)
- **절제가능성**은 어떠한 치료가 시작되기 **전에** 흉부외과의사가 결정해야 한다.
- 수술 전 후 전신치료 (**perioperative treatment**) (항암, 항암+면역항암, 표적항암 등)를 고려할 상황에 대해 숙지하고 있어야 한다.

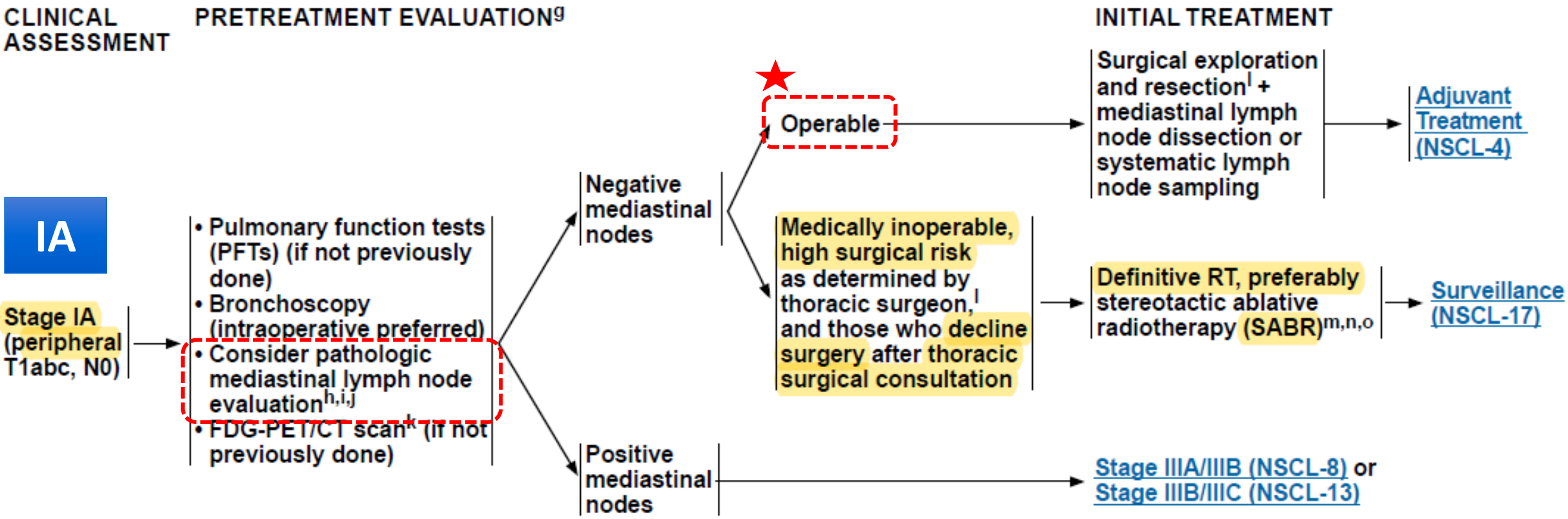
NCCN NSCLC, V5, 2024

폐암병기에 따른 치료 : overview



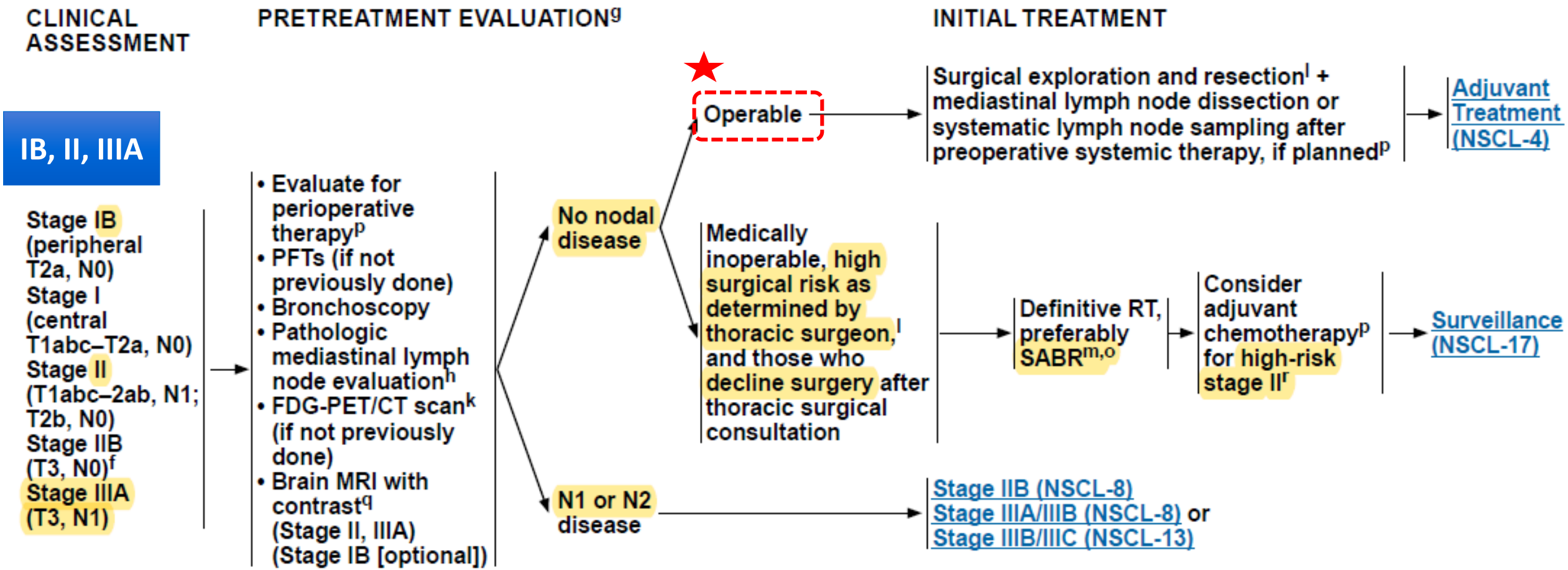
NCCN NSCLC, V5, 2024

Early stage (1)

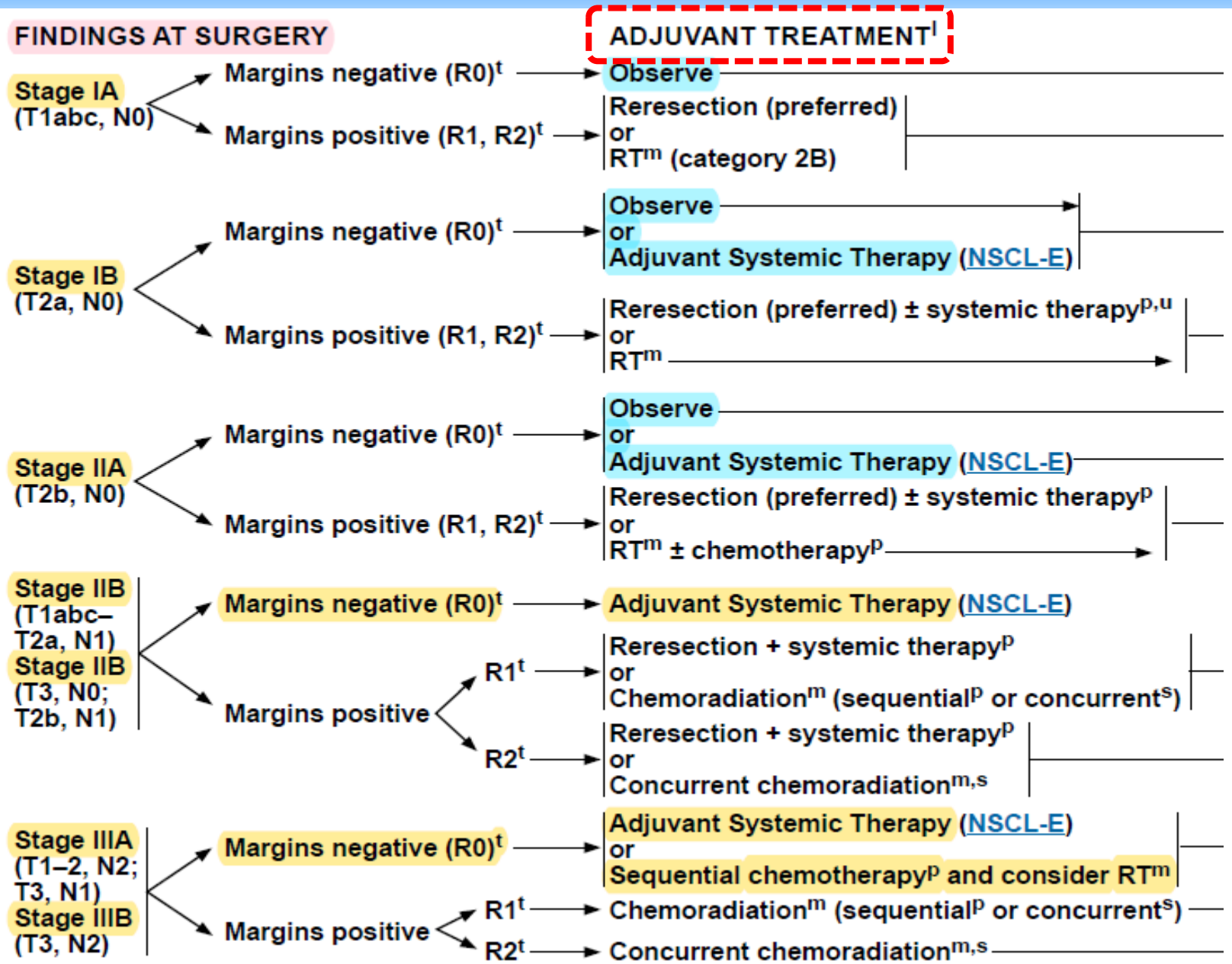


* There is low likelihood of positive mediastinal lymph nodes when these nodes are CT and FDG-PET/CT negative in peripheral tumors (outer third of lung) ≤3 cm

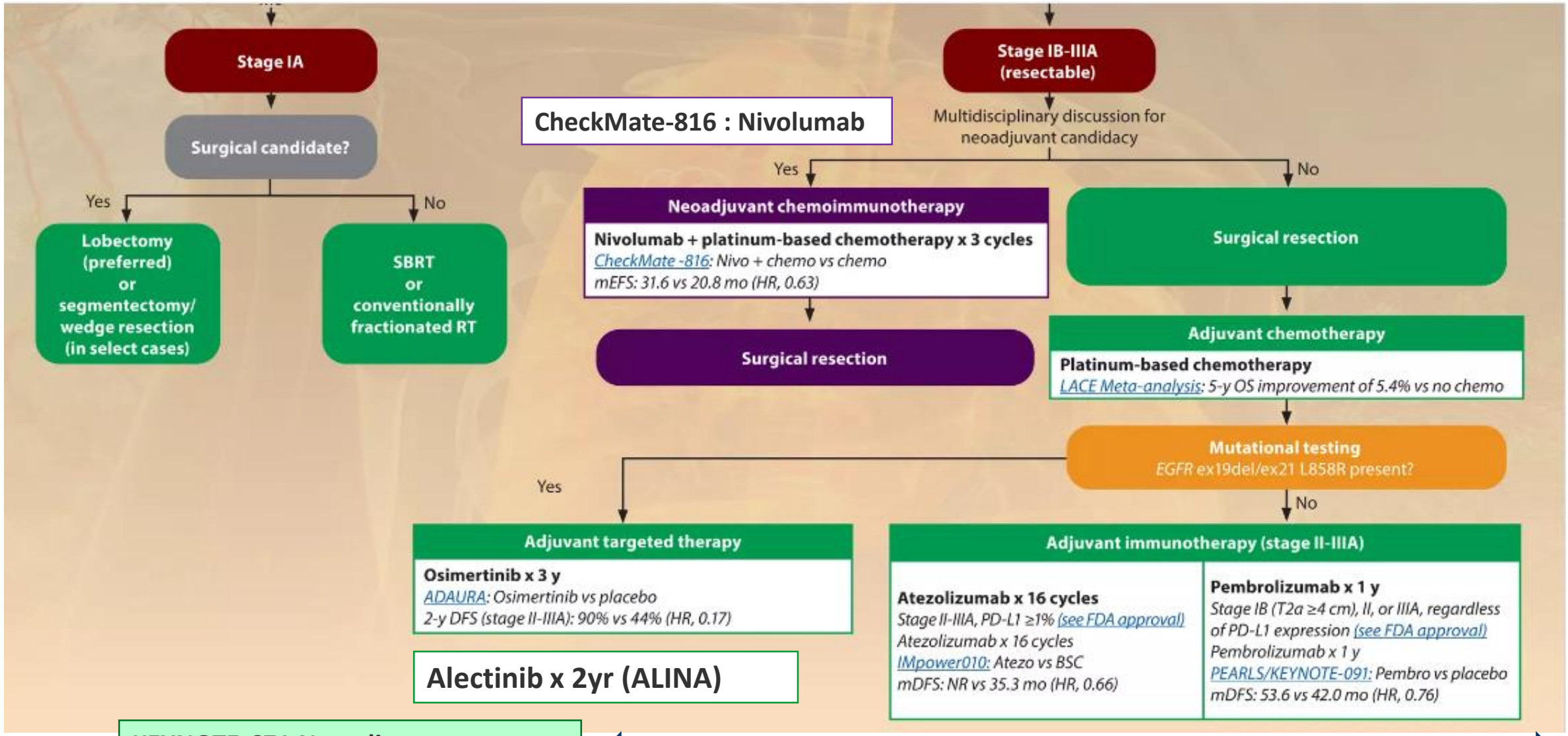
Early stage (2)



Early stage (3) : 수술 후 치료



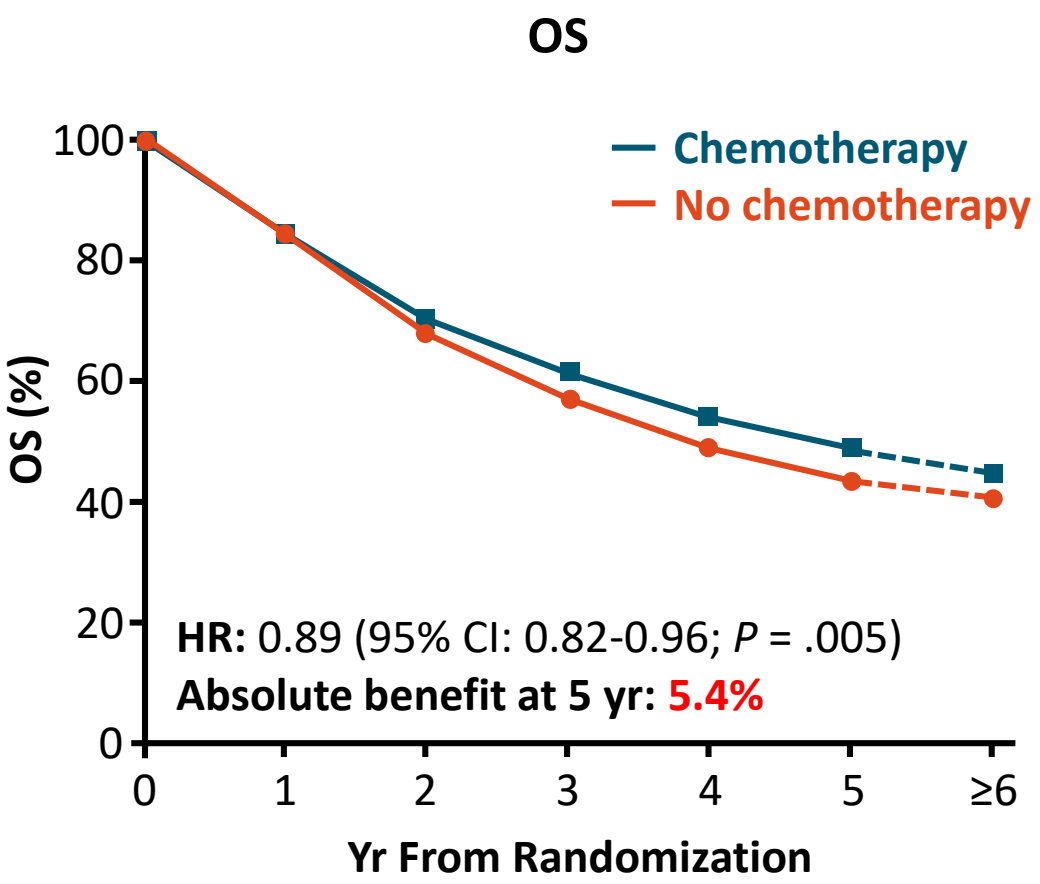
수술 전 후 전신치료 (Perioperative systemic therapies)



KEYNOTE-671 Neoadjuvant Chemo+Pembro -> adjuvant Pembro

Meta-analysis: Lung Adjuvant Cisplatin Evaluation

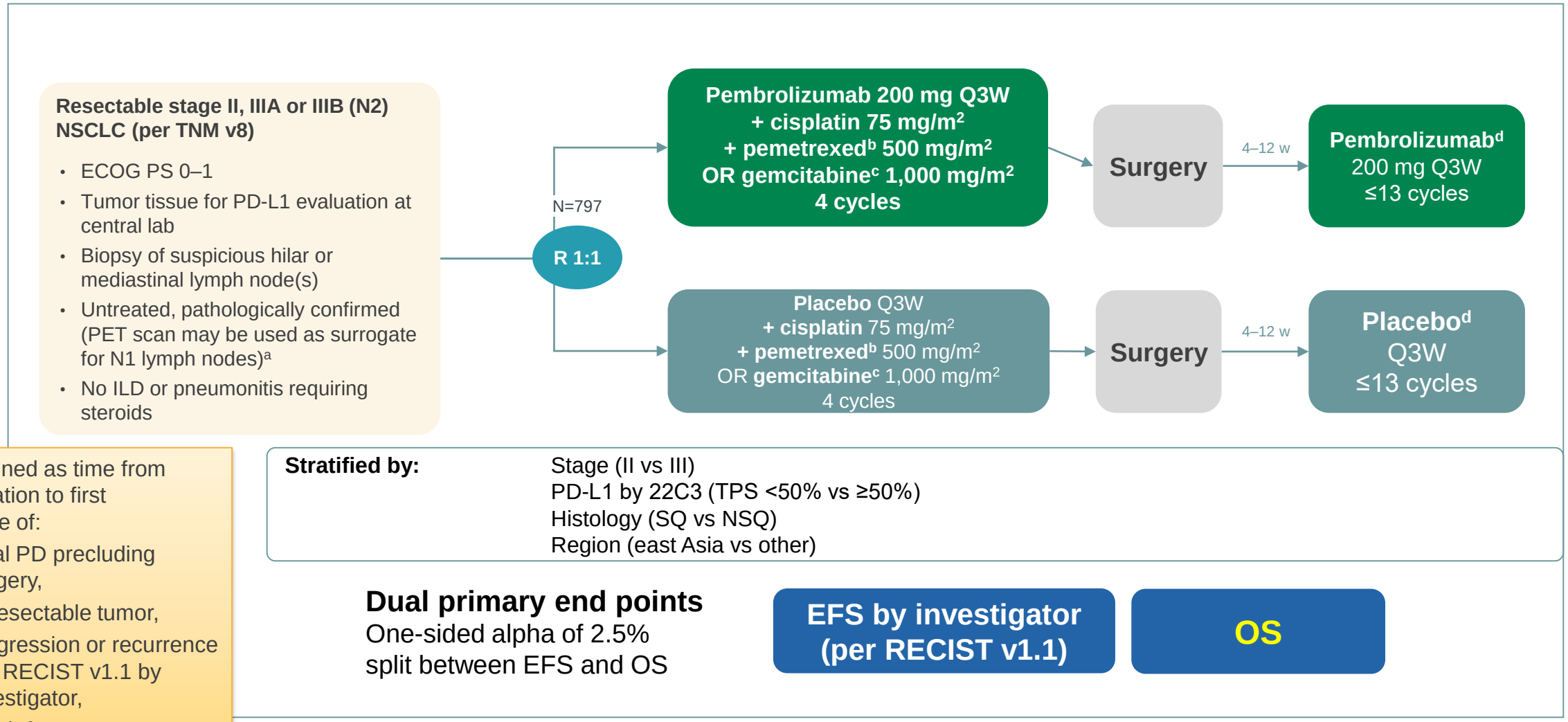
- Pooled individual patient data from 5 studies of adjuvant cisplatin-based chemotherapy for completely resected early-stage NSCLC conducted after 1995 (N = 4584)
  - Studies: ALPI, ANITA, BLT, IALT, JBR10
- Chemotherapy at Yr 5
  - ↓ **6.9%** lung cancer death
  - ↑ **1.4%** noncancer death



Pignon. JCO. 2016;26:3552.

Slide credit: clinicaloptions.com

KEYNOTE-671 : Study Design



*EFS : Event free survival

Event-Free Survival (IA2) : Primary endpoint

KEYNOTE-671

	Pts w/ Event	Median (95% CI), mo
Pembro arm	43.8%	47.2 (32.9-NR)
Placebo arm	62.0%	18.3 (14.8-22.1)

Almost 2.5x

HR 0.59 (95% CI, 0.48-0.72)

KEYNOTE-671의 1차 중간 분석 결과 키트루다군은 위약군 대비 개선된 EFS와 OS 결과를 보였습니다. [키트루다군 vs. 위약군 : 2-year EFS (62.4% vs. 40.6%), 2-year OS (80.9% vs. 77.6%),; Data cutoff date: July 29, 2022 with median follow-up 25.2 months][2]

EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause.

Data cutoff date : July 10, 2023 with median follow-up was 36.6 months (range, 18.8-62.0)

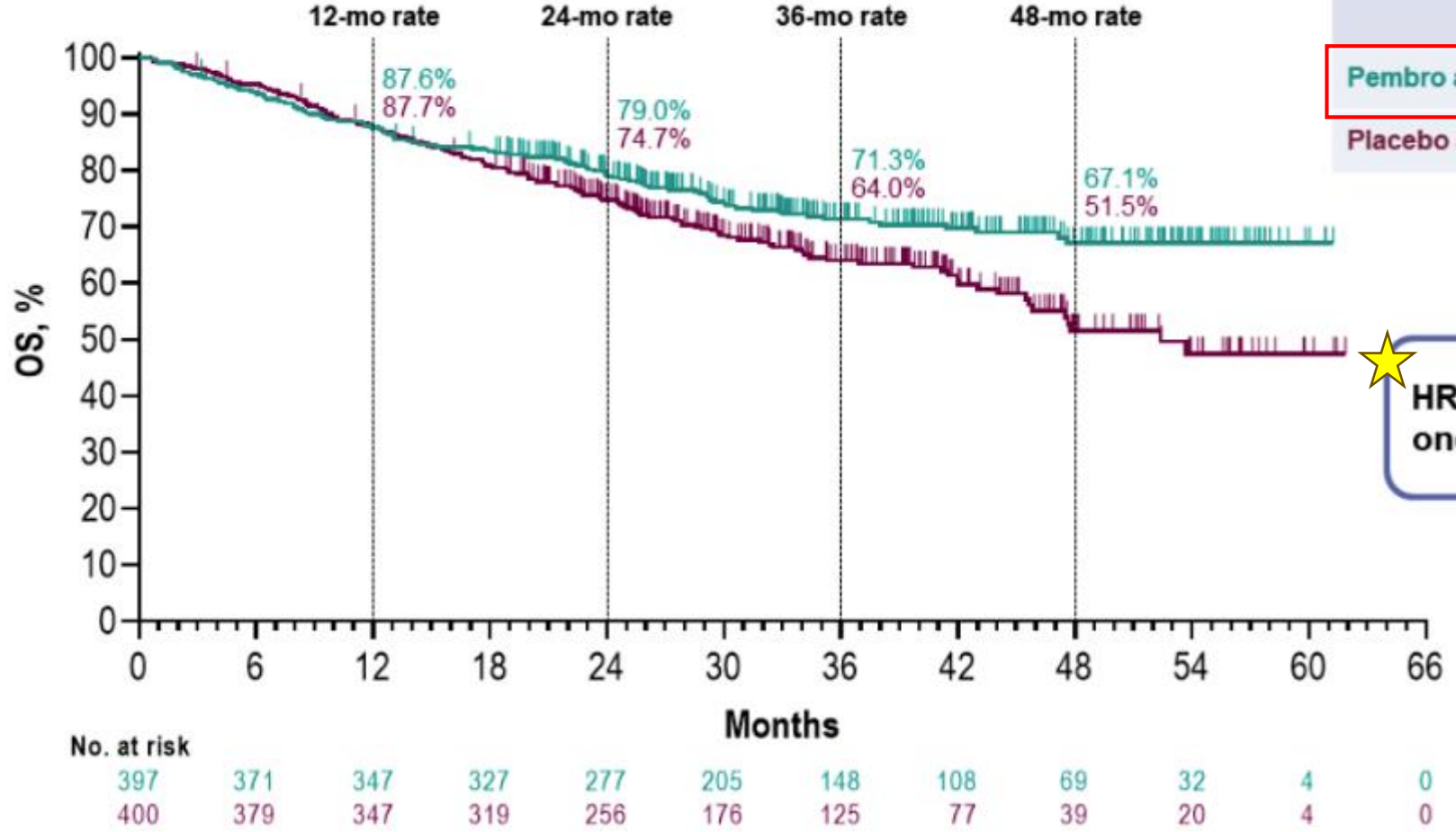
※ 최신 정보 전달을 위해 ESMO 2023 학회 자료를 바탕으로 제작되었습니다. (As of 11/2023) 추후 공인된 학술지에 발표되는 Full Data를 확인해주시길 바랍니다.

Reference 1. Spicer J, et al. Overall Survival in the KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC. Slide deck presented at: ESMO 2023. **2.** Wakelee H, et al. Perioperative Pembrolizumab for Early-Stage Non-Small-Cell Lung Cancer. N Engl J Med. 2023 Aug 10;389(6):491-503.

KR-KEY-01736 06/2024

Overall Survial (IA2) : Primary endpoint

KEYNOTE-671



	Pts w/ Event	Median (95% CI), mo
Pembro arm	27.7%	NR (NR-NR)
Placebo arm	36.0%	52.4 (45.7-NR)

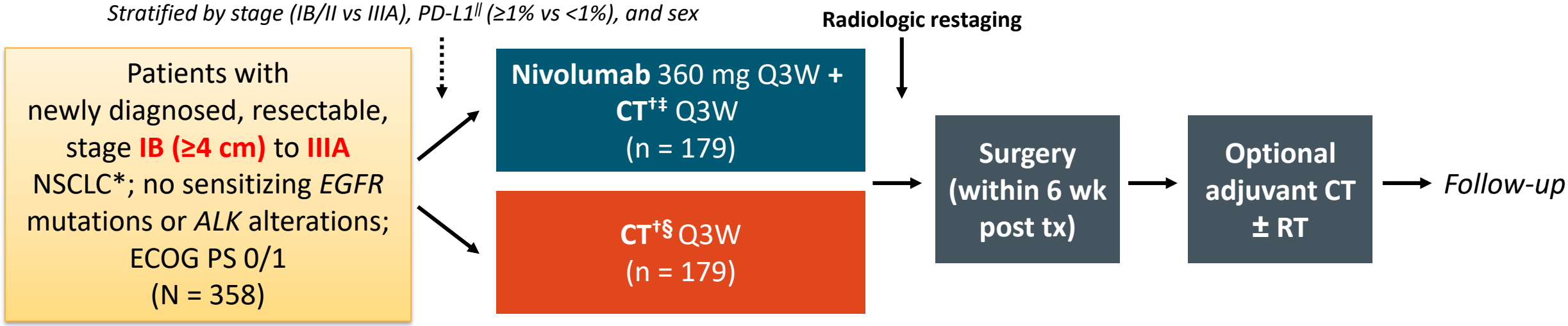
HR 0.72 (95% CI, 0.56-0.93)
one-sided *P* = 0.00517[a]

OS defined as time from randomization to death from any cause. a. Significance boundary at IA2, one-sided *P*=0.00543.
Data cutoff date : July 10, 2023 with median follow-up was 36.6 months (range, 18.8-62.0)
※ 최신 정보 전달을 위해 ESMO 2023 학회 자료를 바탕으로 제작되었습니다. (As of 11/2023) 추후 공인된 학술지에 발표되는 Full Data를 확인해주시길 바랍니다.
Reference 1. Spicer J, et al. Overall Survival in the KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC. Slide deck presented at: ESMO 2023.

KR-KEY-01736 06/2024

CheckMate 816: Neoadjuvant Nivolumab + Platinum Chemotherapy for Resectable Stage IB-IIIA NSCLC

- Randomized, open-label phase III trial (data cutoff: September 16, 2020; min f/u: 7.6 mo)



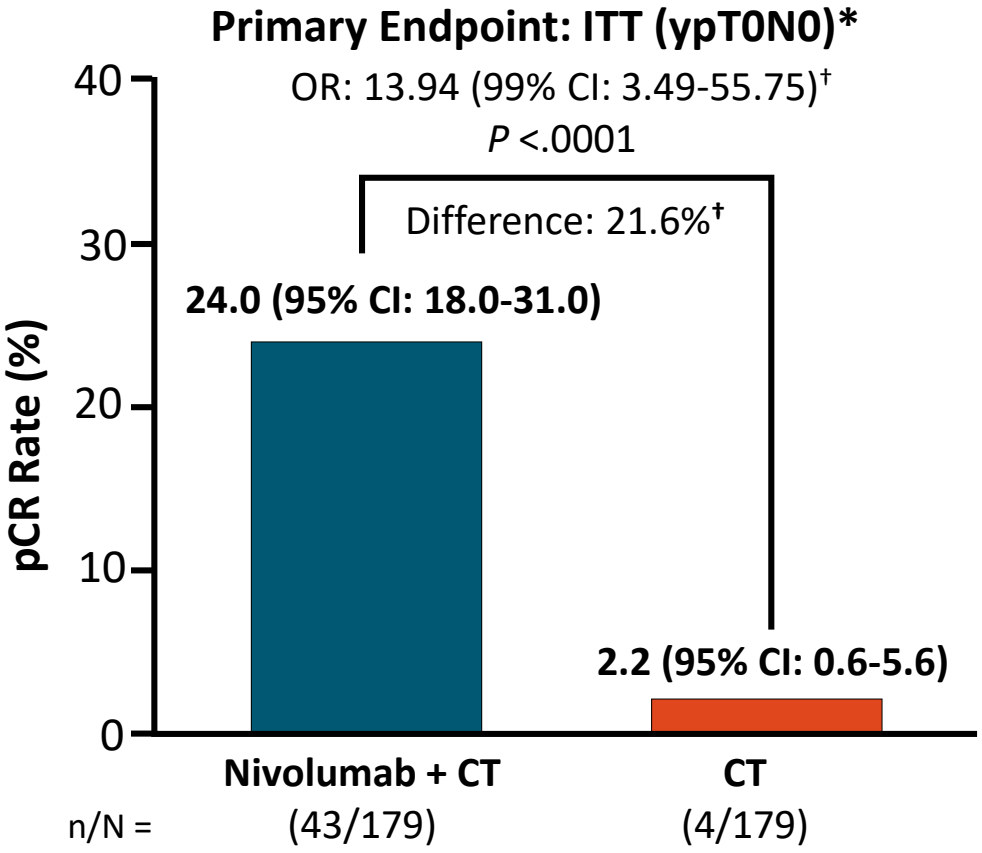
***By TNM 7th edition**. †3 cycles. ‡NSQ: cisplatin/pemetrexed or carboplatin/paclitaxel; SQ: cisplatin/gemcitabine or carboplatin/paclitaxel. §NSQ: cisplatin/pemetrexed; SQ: cisplatin/vinorelbine, cisplatin/docetaxel, cisplatin/gemcitabine; both: carboplatin/paclitaxel. ‖PD-L1 28-8 pharmDx IHC assay.

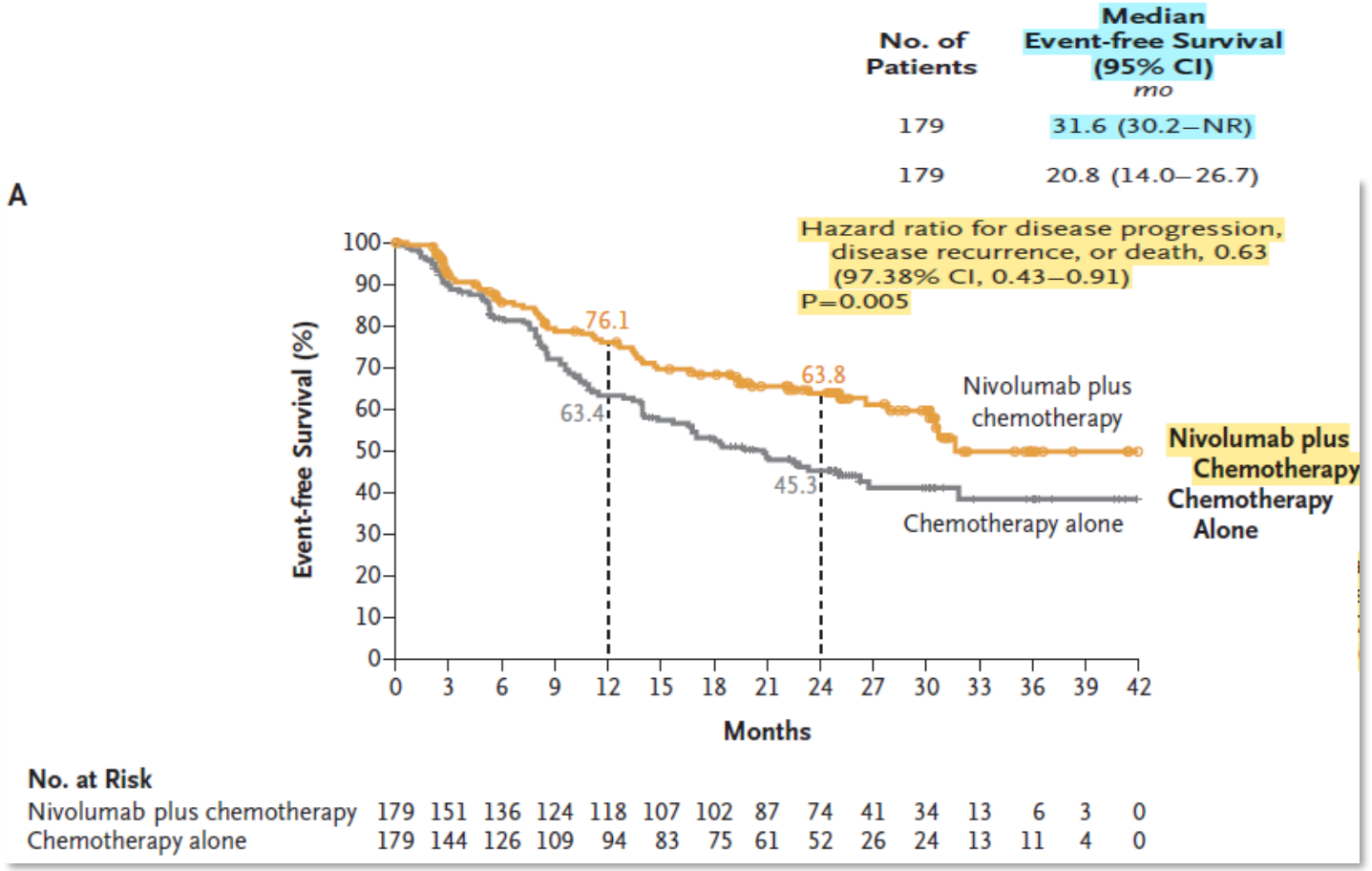
- **Primary endpoints:** pCR (by BIPR) and EFS (by BICR)
- **Key secondary endpoints:** OS, mPR (by BIPR), time to death or distant metastasis
- **Key exploratory endpoints:** ORR (by BICR), feasibility of surgery, peri- and postoperative surgery related AEs

Forde. AACR 2021. Abstr CT003. Spicer. ASCO 2021. Abstr 8503. NCT02998528.

Slide credit: clinicaloptions.com

CheckMate 816: Primary End Point (pCR and EFS)





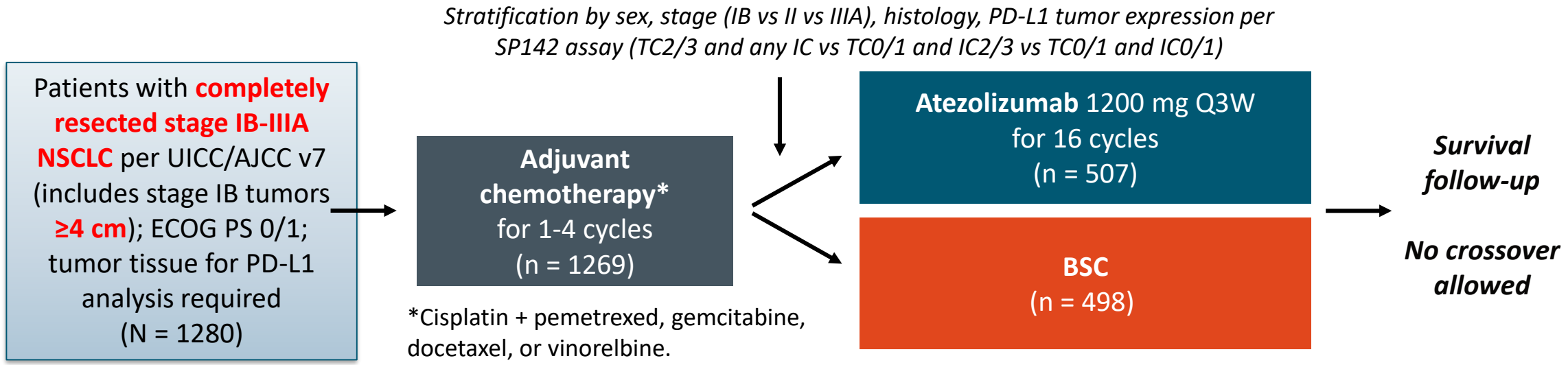
pCR defined as 0% residual viable tumor cells in primary lung tumor and sampled LNs. *In ITT population, those who did not undergo surgery categorized as nonresponders in primary analysis. †Calculated using stratified Cochran–Mantel–Haenszel method. ‡Patients who underwent definitive surgery with evaluable pathology sample.

Forde. AACR 2021. Abstr CT003.

Slide credit: clinicaloptions.com

IMpower010: Study Design (adjuvant atezolizumab)

- **Randomized, open-label phase III trial (data cutoff for interim analysis: January 21, 2021)**



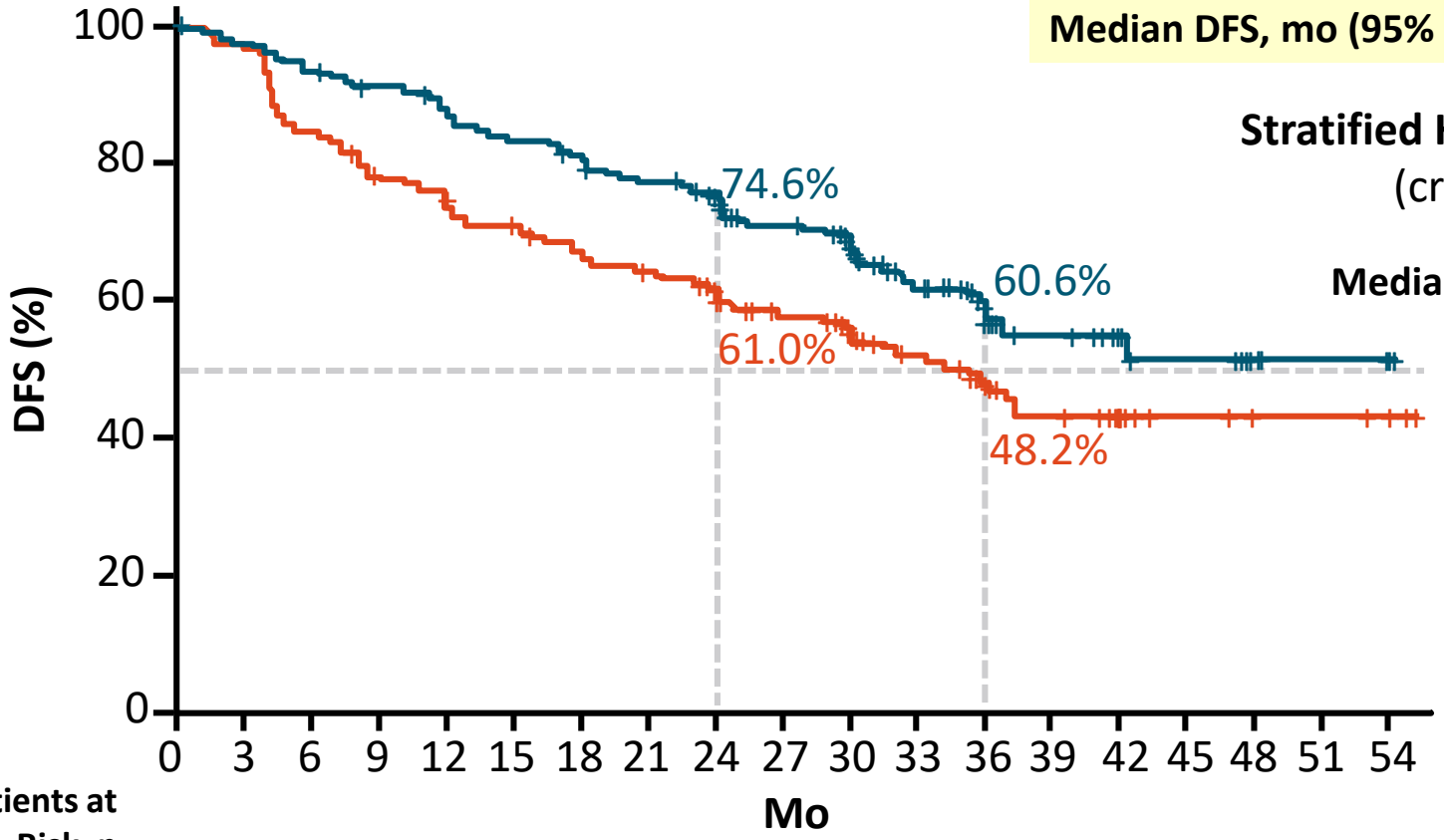
- **Primary endpoint**: hierarchical evaluation of investigator-assessed **DFS** in 3 populations
  - Stage II-IIIA with PD-L1 TC ≥1% (by PD-L1 SP264 IHC assay) → all randomized stage II-IIIA → ITT population (stage IB-IIIA)
- Key secondary endpoints: OS (ITT); DFS in stage II-IIIA with PD-L1 TC ≥50 (by PD-L1 SP263 IHC assay); 3-yr and 5-yr DFS in all 3 populations; safety

Wakelee. ASCO 2021. Abstr 8500.

Slide credit: clinicaloptions.com

IMpower010: DFS in Stage II-IIIA NSCLC With PD-L1 TC ≥1% (Primary Endpoint)

	Atezolizumab (n = 248)	BSC (n = 228)
Median DFS, mo (95% CI)	NE (36.1-NE)	35.3 (29.0-NE)



Stratified HR: 0.66 (95% CI: 0.50-0.88; *P* = .004)
(crossed significance boundary)

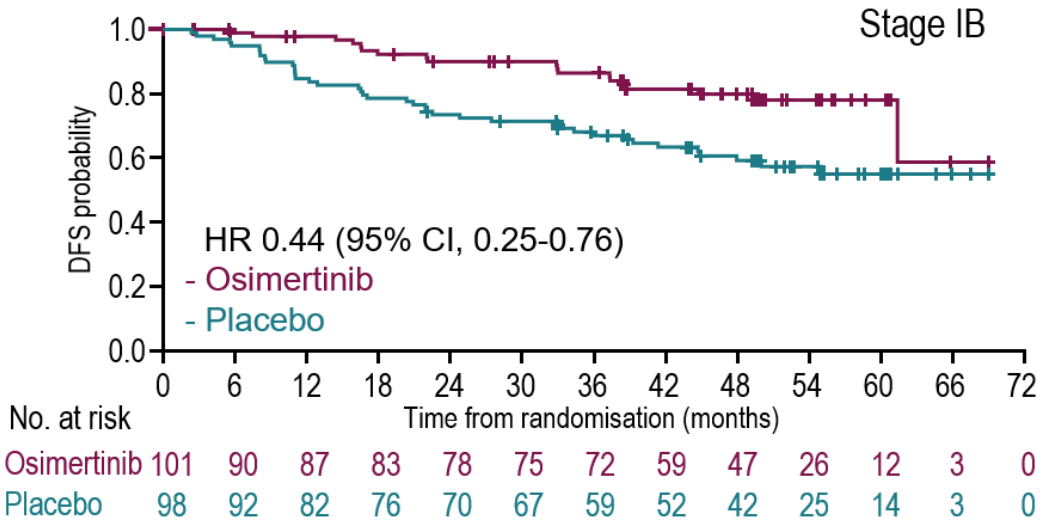
Median follow up: 32.8 mo (range: 0.1-57.5)

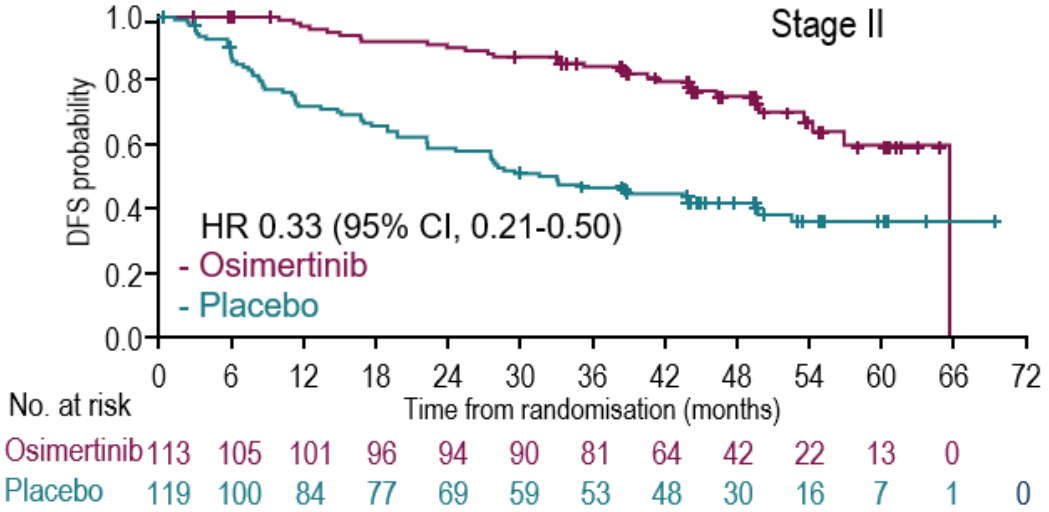
* DFS : disease free survival

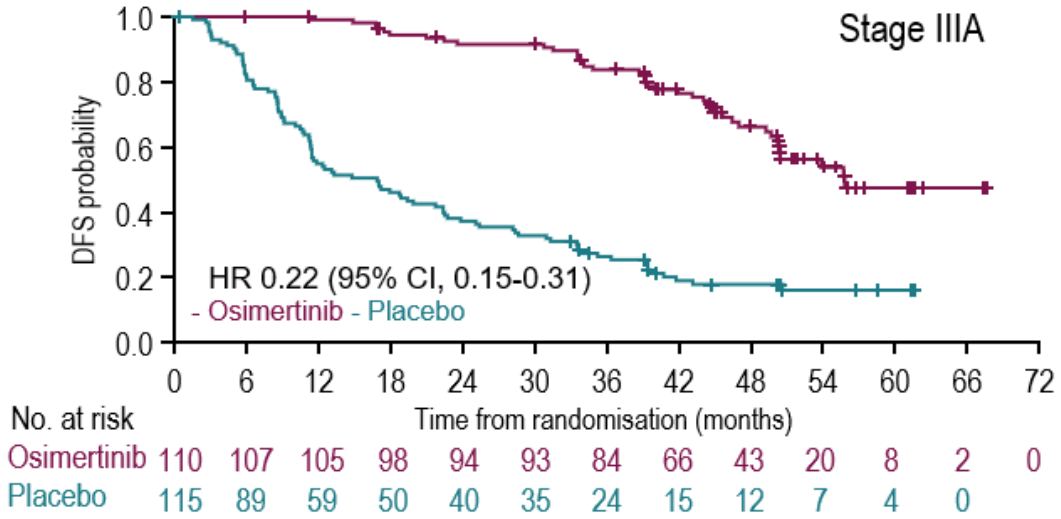
Patients at Risk, n																		
Atezolizumab	248	235	225	217	206	198	190	181	159	134	111	76	54	31	22	12	8	3	3
BSC	228	212	186	169	160	151	142	135	117	97	80	59	38	21	14	7	6	4	3

PD-L1 expression by SP263 assay.

수술 후 보조요법 : EGFR (+) with Osimertinib for 3yrs vs placebo







Treatment Arm	Stage IB	Stage II	Stage IIIA
4-year DFS rate, % (95% CI)			
Osimertinib	80 (69-87)	75 (65-83)	66 (55-75)
Placebo	60 (49-69)	43 (34-52)	16 (10-24)
Overall HR (95% CI)	0.44 (0.25-0.76)	0.33 (0.21-0.50)	0.22 (0.15-0.31)

Data cut-off: April 11, 2022.

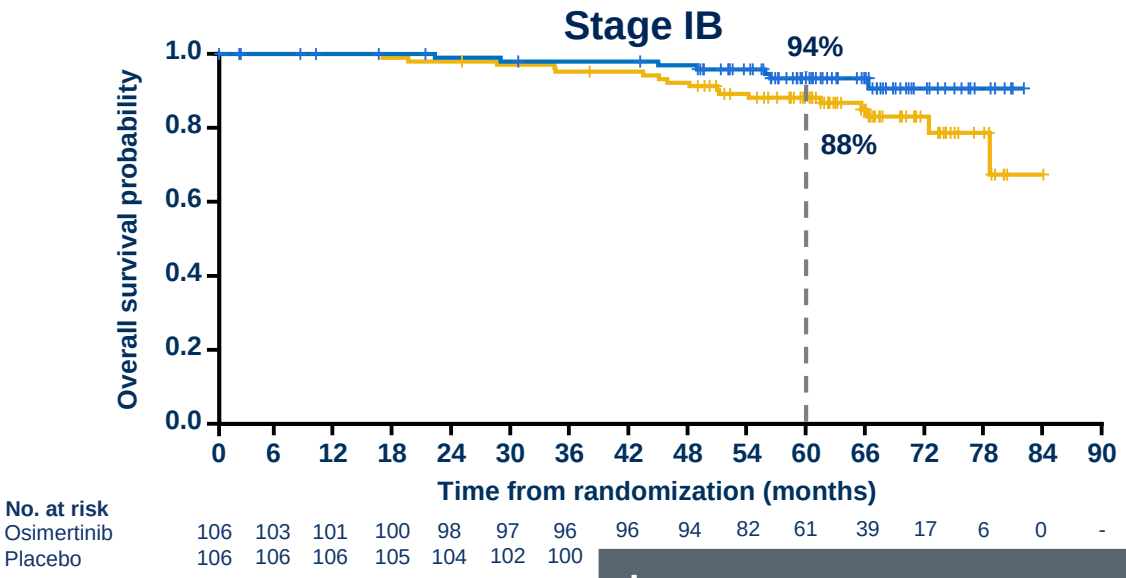
[a]Re-staging based on data captured in the Pathology at Dagnosis AJCC 8th edition manual, per investigator assessment conducted before the primary analys

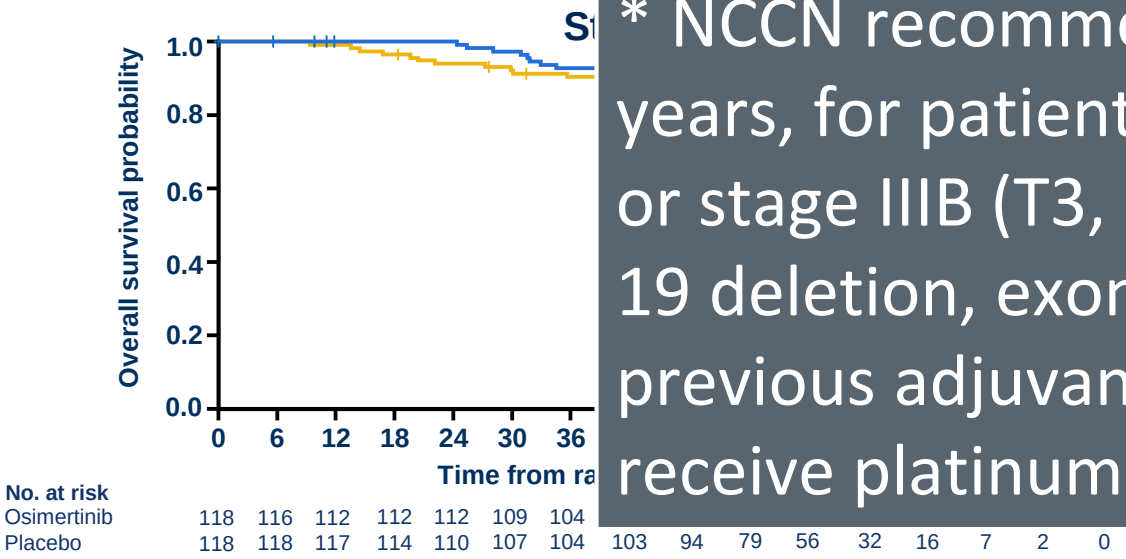
Herbst RS, Tsuboi M, John J, et al. J Clin Oncol on January 31,2023: DOI https://doi. org/10.1200/JCO.22.02186

ADAURA

병기에 따른 생존분석 (overall survival)

ADAURA





	Stage IB	Stage II	Stage IIIA
5 year OS rate, % (95% CI)			
Osimertinib	94 (86, 97)	85 (77, 91)	85 (76, 91)
Placebo	88 (80, 93)	78 (69, 85)	67 (57, 75)
Overall HR (95% CI)	**0.44 (0.17, 1.02)**	**0.63 (0.34, 1.12)**	**0.37 (0.20, 0.64)**

* NCCN recommendation : Osimertinib 80 mg daily for 3 years, for patients with completely resected stage IB–IIIA or stage IIIB (T3, N2) NSCLC and positive for EGFR (exon 19 deletion, exon 21 L858R) mutations who received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy

Placebo 119 114 109 107 100 95 86 79 77 59 38 21 9 1 0

Data cut-off: January 27, 2023. Tick marks indicate censored data.

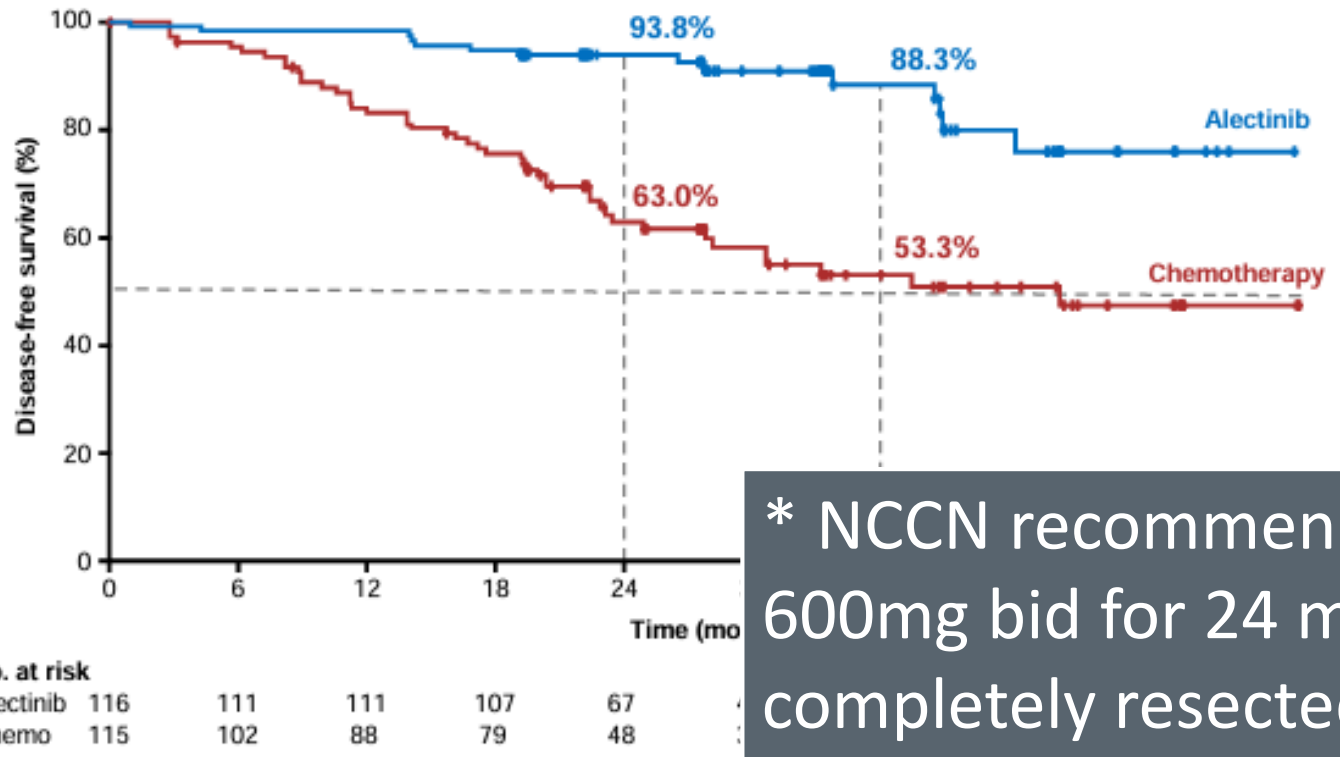
1.Tsuboi M, Herbst RS et al. N Engl J Med. 2023 Jun 4. doi: 10.1056/NEJMoa2304594

CI, confidence interval; HR, hazard ratio; OS, overall survival

수술 후 보조요법 : ALK(+) with Alectinib for 2yrs vs chemotherapy

Disease-free survival: stage II–IIIA*

ALINA



Median survival follow

	Alectinib (N=116)	Chemotherapy (N=115)
Patients with event Death Recurrence	14 (12%) 0 14	45 (39%) 1 44
Median DFS, months (95% CI)	Not reached	44.4 (27.8, NE)
DFS HR (95% CI)	**0.24** (0.13, 0.45) p†<0.0001	

* NCCN recommendation : Alectinib 600mg bid for 24 months for patients with completely resected **stage II–IIIA or stage IIIB** (T3, N2) NSCLC and positive for ALK rearrangements

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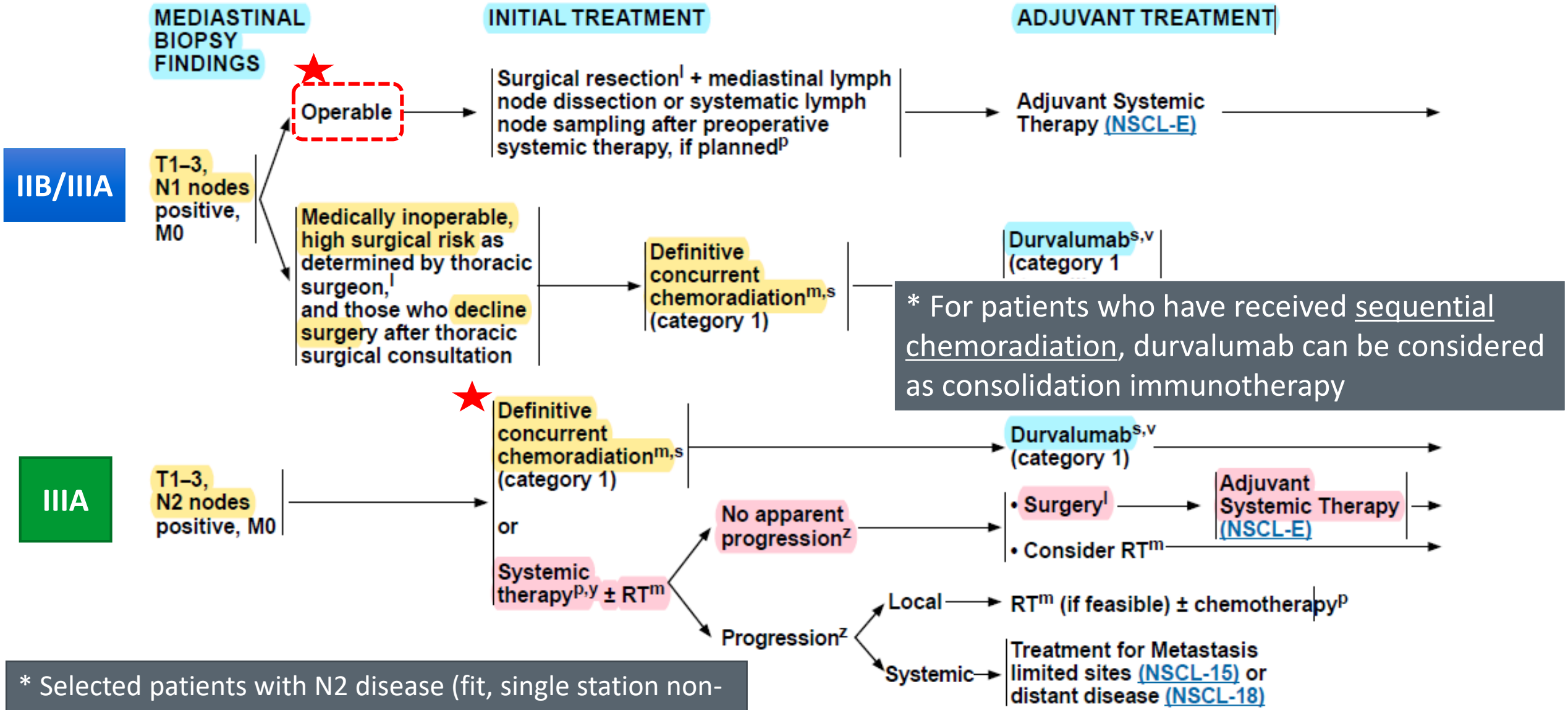
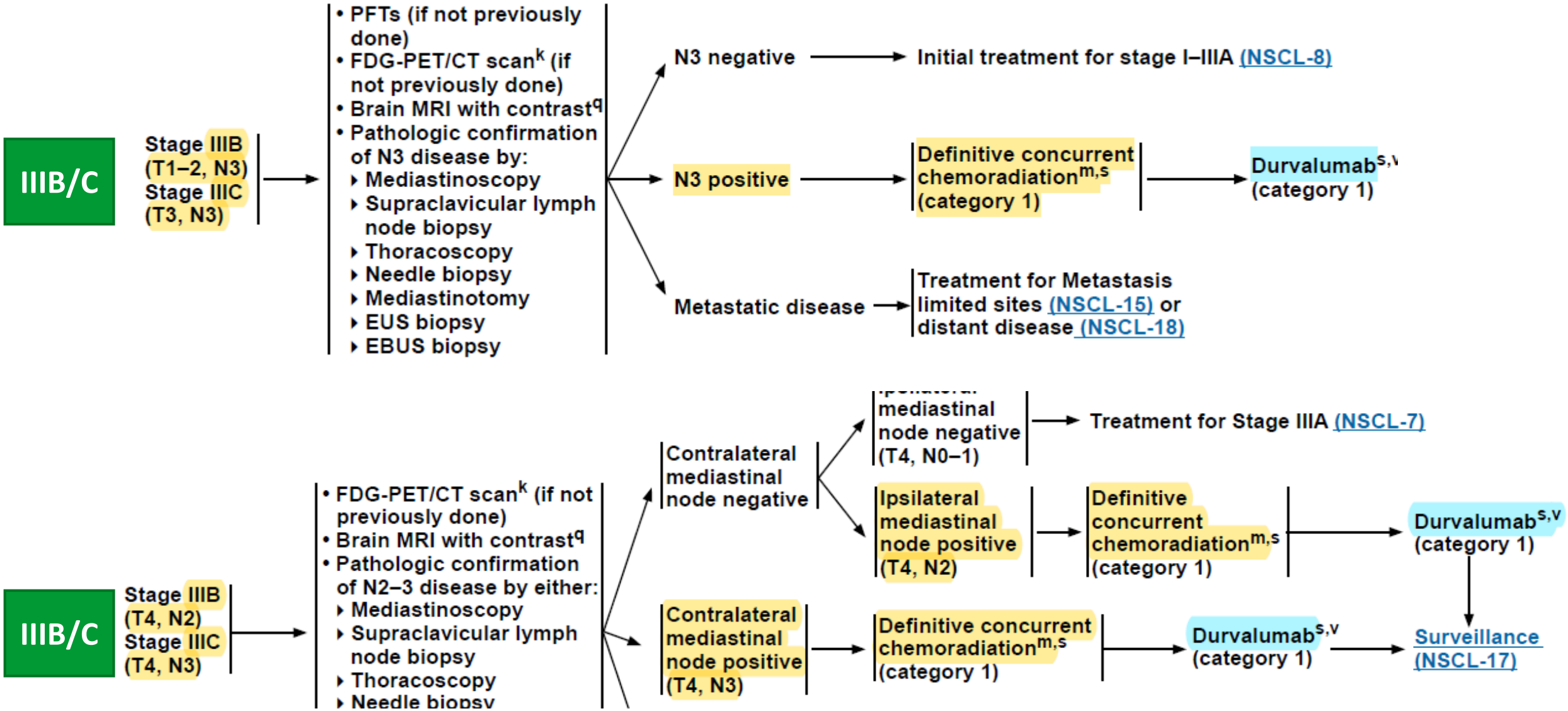
국소진행 (locally advanced IIB/IIIA)



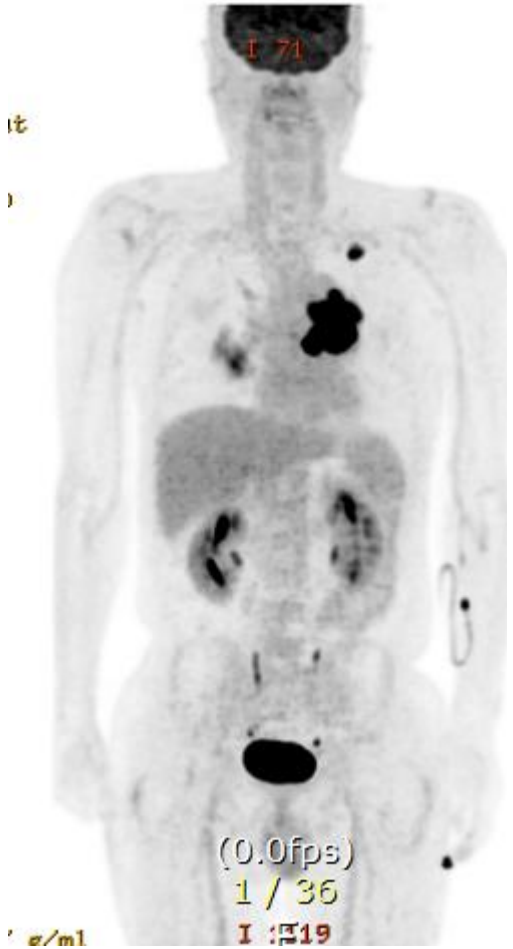
* Selected patients with N2 disease (fit, single station non-bulky N2, requiring only lobectomy) may be considered for systemic therapy followed by surgery.

치 료 : 국소진행 (locally advanced IIIB/C)

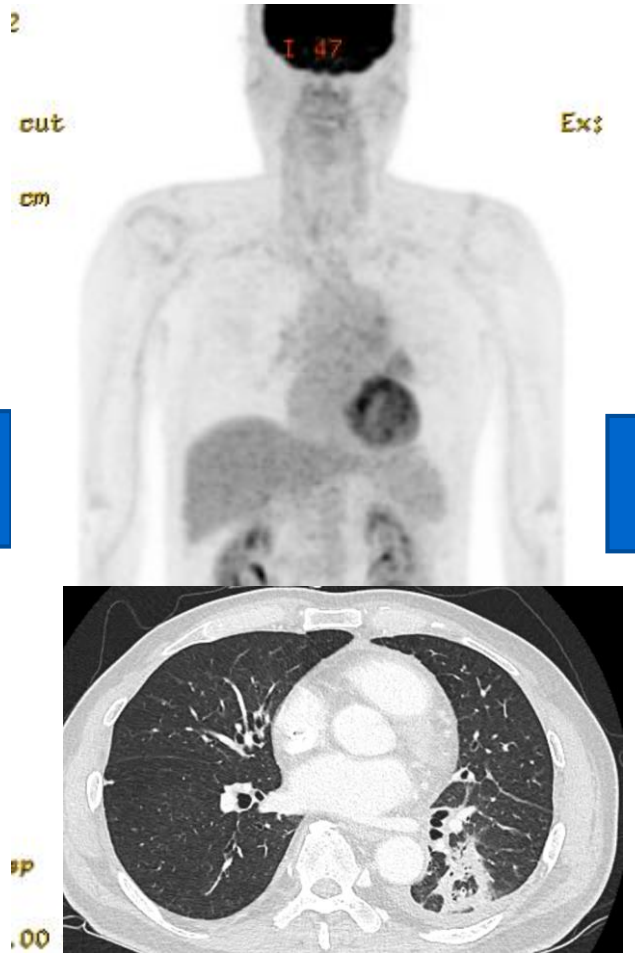


69/M, cT4N2M0 (IIIB), Adenocarcinoma (no EGFR, ALK)

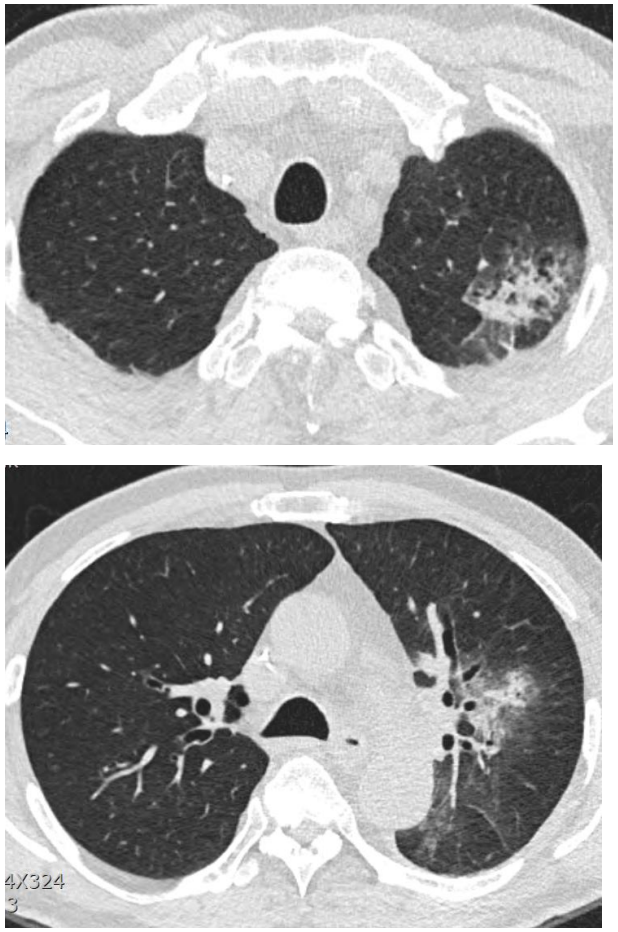
*** 방사선 폐렴 vs ILD by Durvalumab ??**



Pemetrexed + cisplatin + RT



Durvalumab #2



치 료 : 국소진행 (T3 invasion, T4 extension)

CLINICAL ASSESSMENT

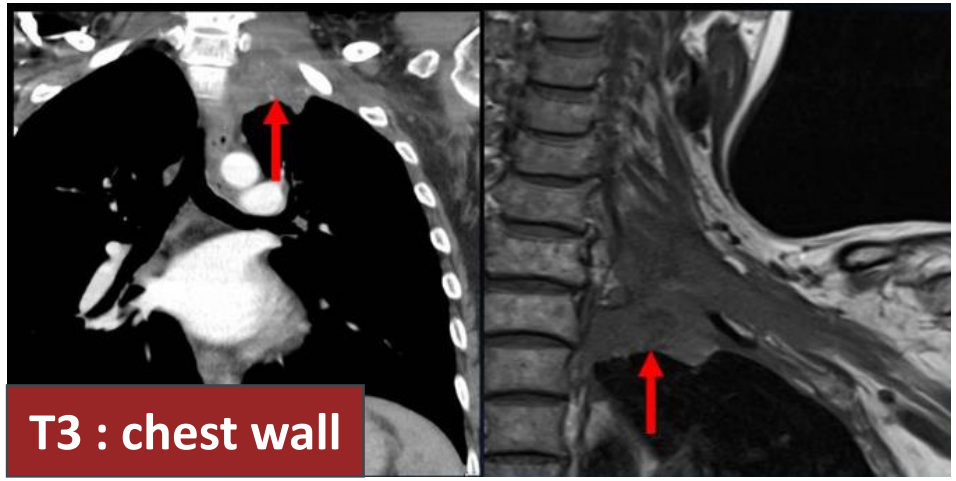
PRETREATMENT EVALUATION

CLINICAL EVALUATION

Stage IIB (T3 invasion, N0)
Stage IIIA (T4 extension, N0–1; T3, N1; T4, N0–1)

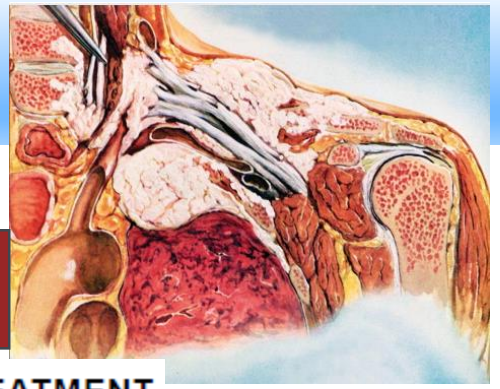
- Evaluate for perioperative therapy[p]
- PFTs (if not previously done)
- Bronchoscopy
- Pathologic mediastinal lymph node evaluation[h]
- Brain MRI with contrast[q]
- MRI with contrast of spine + thoracic inlet for superior sulcus lesions abutting the spine, subclavian vessels, or brachial plexus
- FDG-PET/CT scan[k] (if not previously done)

- Superior sulcus tumor
- Chest wall
- Trachea/carina or mediastinum
- Stage IIIA (T4, N0–1)
- Unresectable disease
- Positive mediastinal nodes
- Metastatic disease



T3 : chest wall

치료 : Superior sulcus tumor



T4: brachial plexus, subclavian v, ribs

IIB/IIIA

CLINICAL PRESENTATION → INITIAL TREATMENT → ADJUVANT TREATMENT

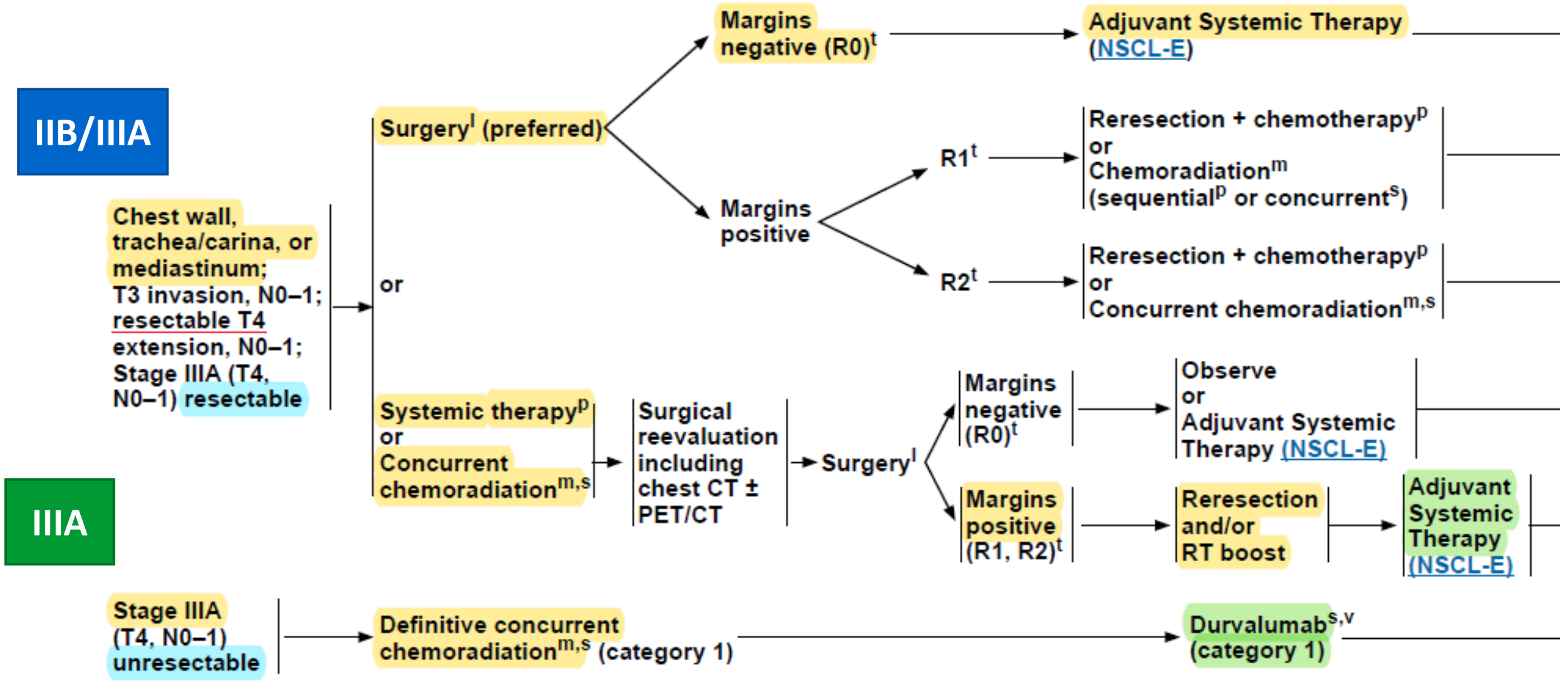
Superior sulcus tumor (T3 invasion, N0–1) → Preoperative concurrent chemoradiation[m,s] → Surgery[l] + Adjuvant Systemic Therapy (NSCL-E)

IIIA

Superior sulcus tumor (T4 extension, N0–1)

- Possibly resectable[l] → Preoperative concurrent chemoradiation[m,s] → Surgical reevaluation including chest CT with or without contrast ± FDG-PET/CT[w]
  - Resectable → Surgery[l] + Adjuvant Systemic Therapy (NSCL-E)
  - Unresectable → Complete definitive chemoradiation[m,s] → Durvalumab[s,v] (category 1)
- Unresectable[l] → Definitive concurrent chemoradiation[m,s] → Durvalumab[s,v] (category 1)

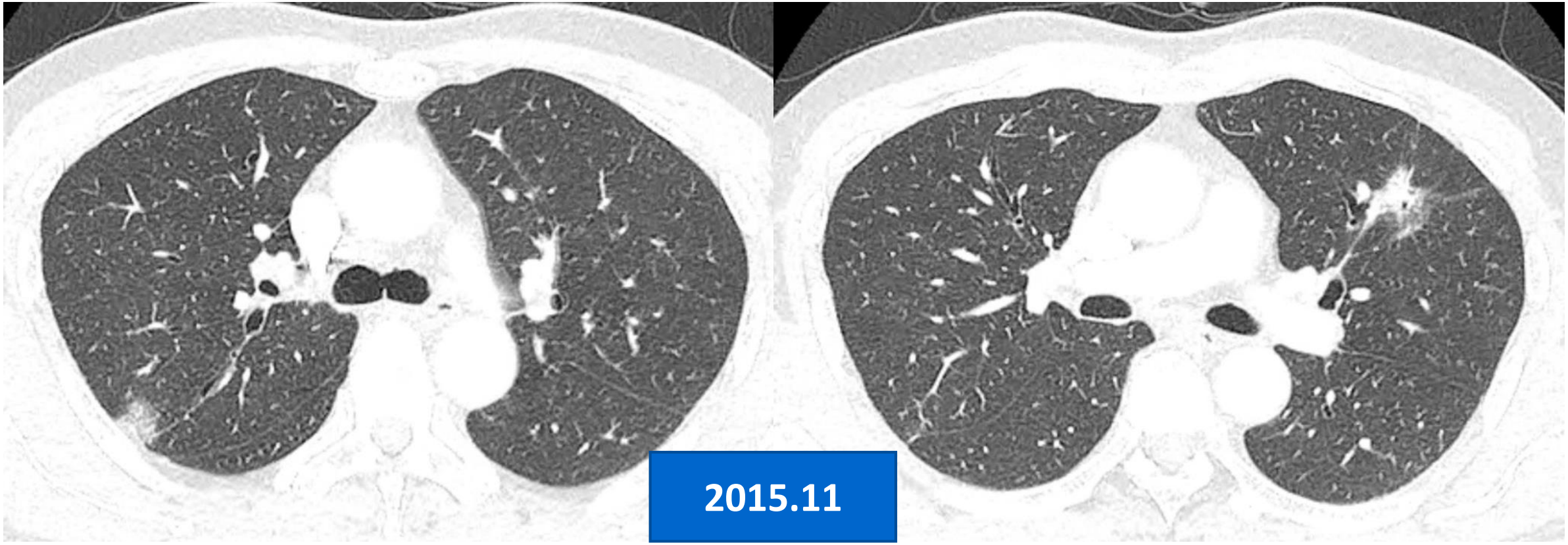
치료 : Chest wall, trachea/carina or mediastinum



Stage IVA (N0, M1a): contralateral lung (solitary lung nodule)

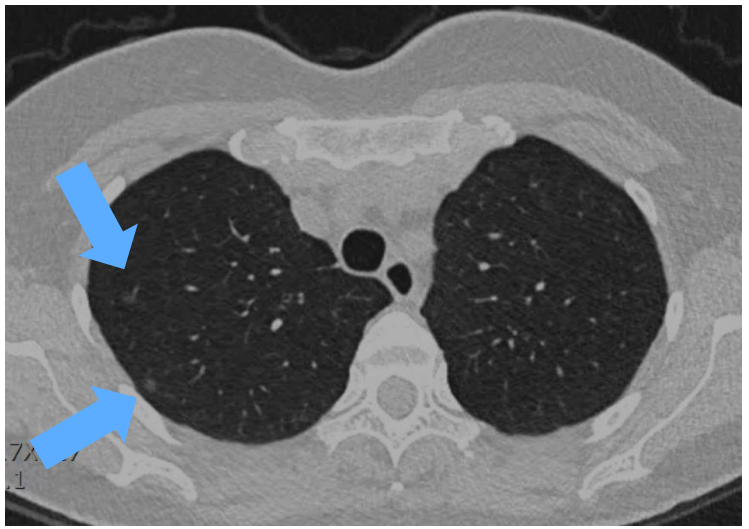
* Treat as two primary lung tumors if both curable.

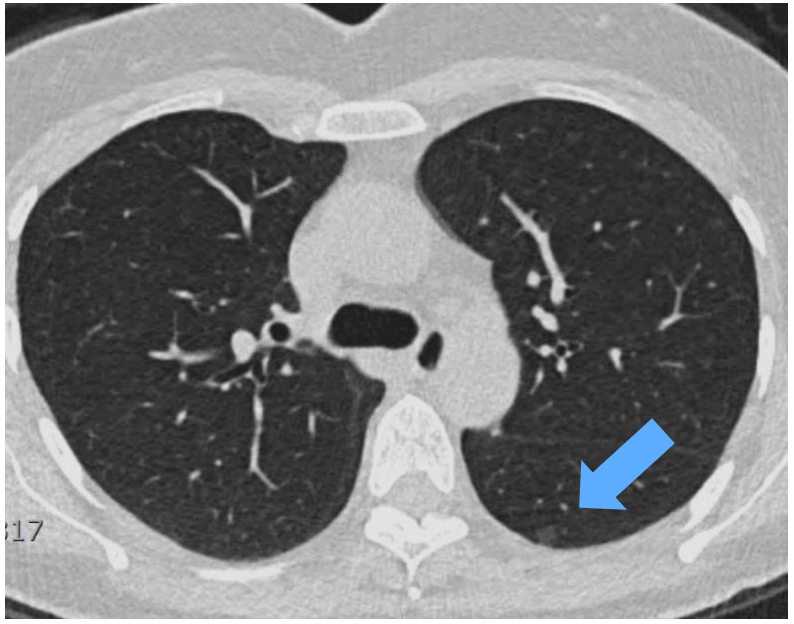
2015.11.20 LULectomy (pT1bN0M0)
2016.3.8 RULectomy (pTaN0M0)
Adenocarcinoma, No EGFR, ALK

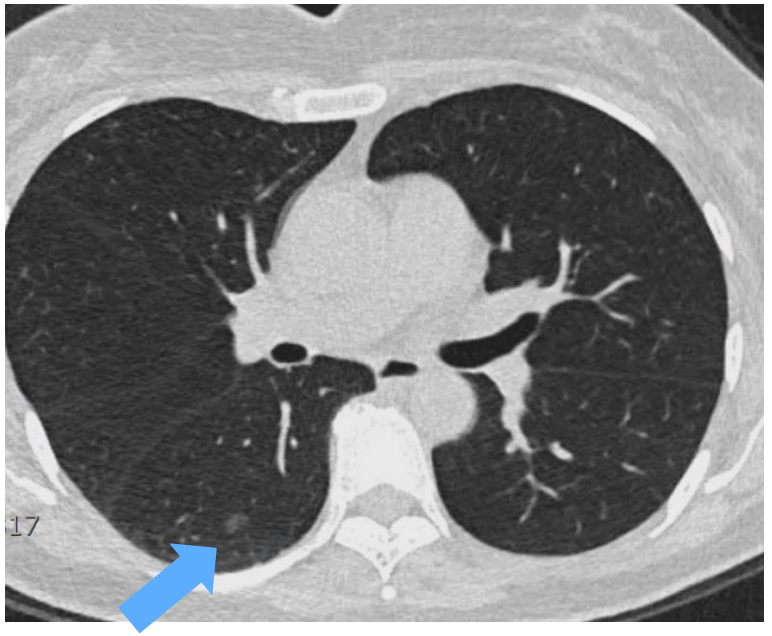


2015.11

Stage IVA (N0, M1a): Multiple lung cancers





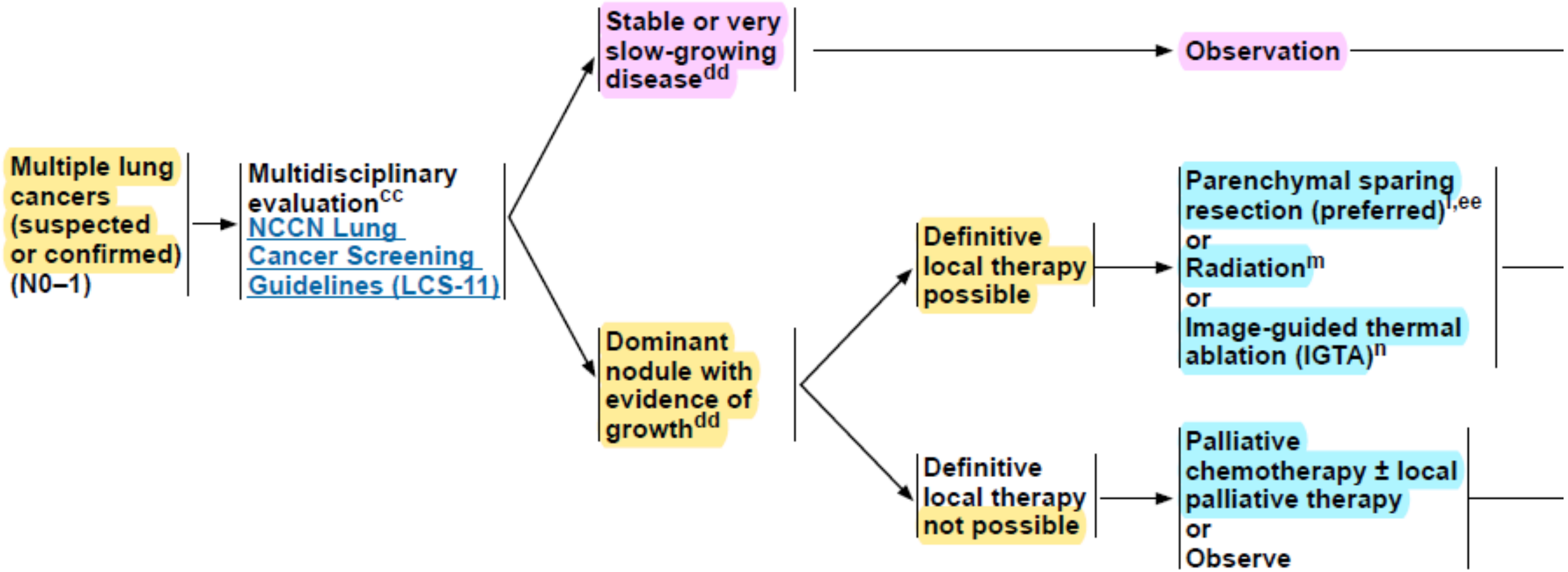


* 23.5
우상엽쐐기절제술

* NGS : 유전자이상 발견되지 않음

53/F

Stage IVA (N0, M1a): Multiple lung cancers



* IGTA therapy (eg, cryotherapy, microwave, radiofrequency) may be an option for select patients

확실한 치료(definitive therapy)를 완료한 뒤 추적방법

No evidence of clinical/radiographic disease

- Stage I–II (primary treatment included surgery ± chemotherapy)
  - H&P and chest CT[jj] ± contrast every 6 mo for 2–3 y, then H&P and a low-dose non–contrast-enhanced chest CT annually
- Stage I–II (primary treatment included RT) or stage III or stage IV (oligometastatic with all sites treated with definitive intent)
  - H&P and chest CT[jj] ± contrast every 3–6 mo for 3 y, then H&P and chest CT ± contrast every 6 mo for 2 y, then H&P and a low-dose non–contrast-enhanced chest CT annually
    - ◊ Residual or new radiographic abnormalities may require more frequent imaging
- Smoking cessation advice, counseling, and pharmacotherapy
- FDG-PET/CT[kk] or brain MRI is not routinely indicated
- Cancer Survivorship Care (NSCL-G)

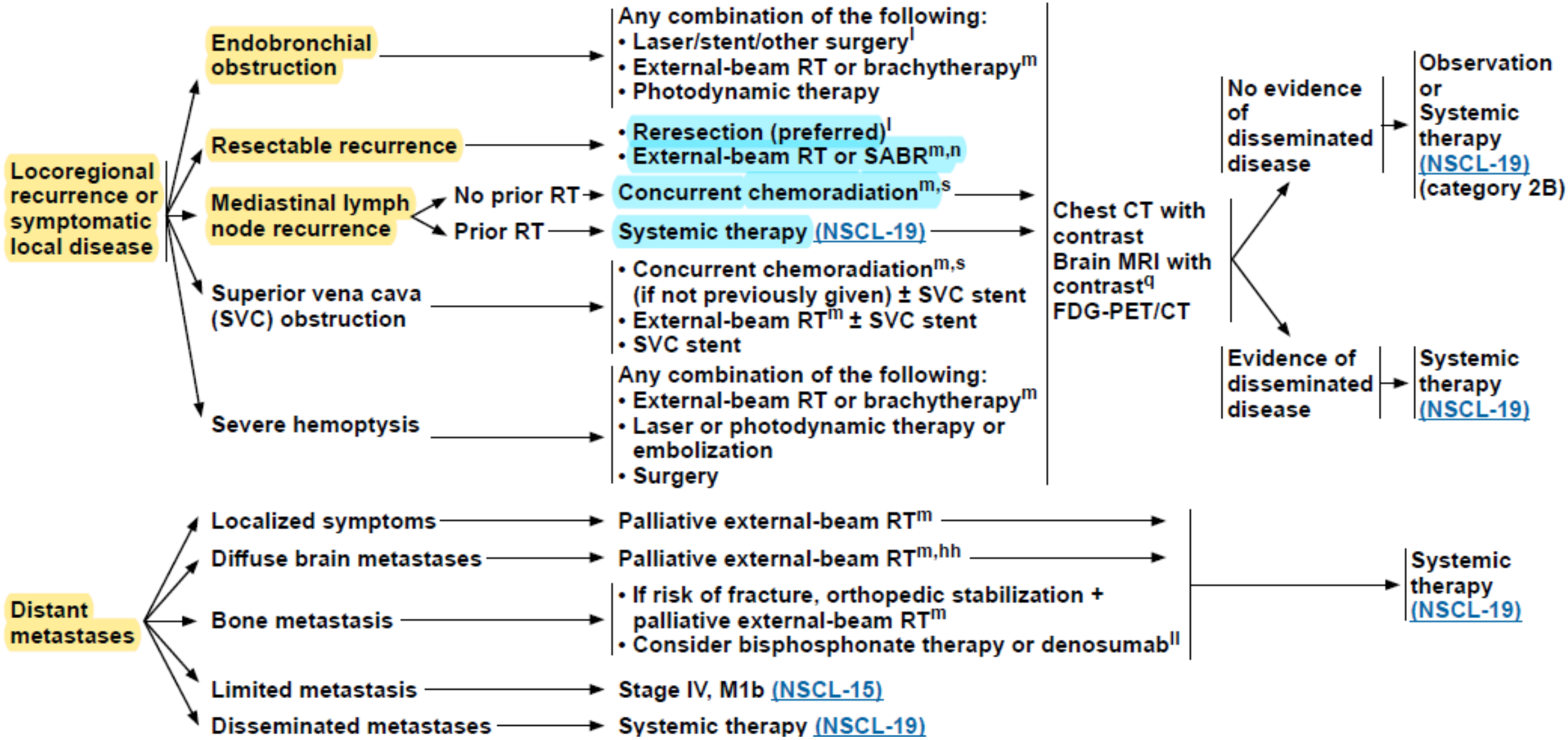
→ Recurrence →

- FDG-PET/CT
- Brain MRI with contrast[q]

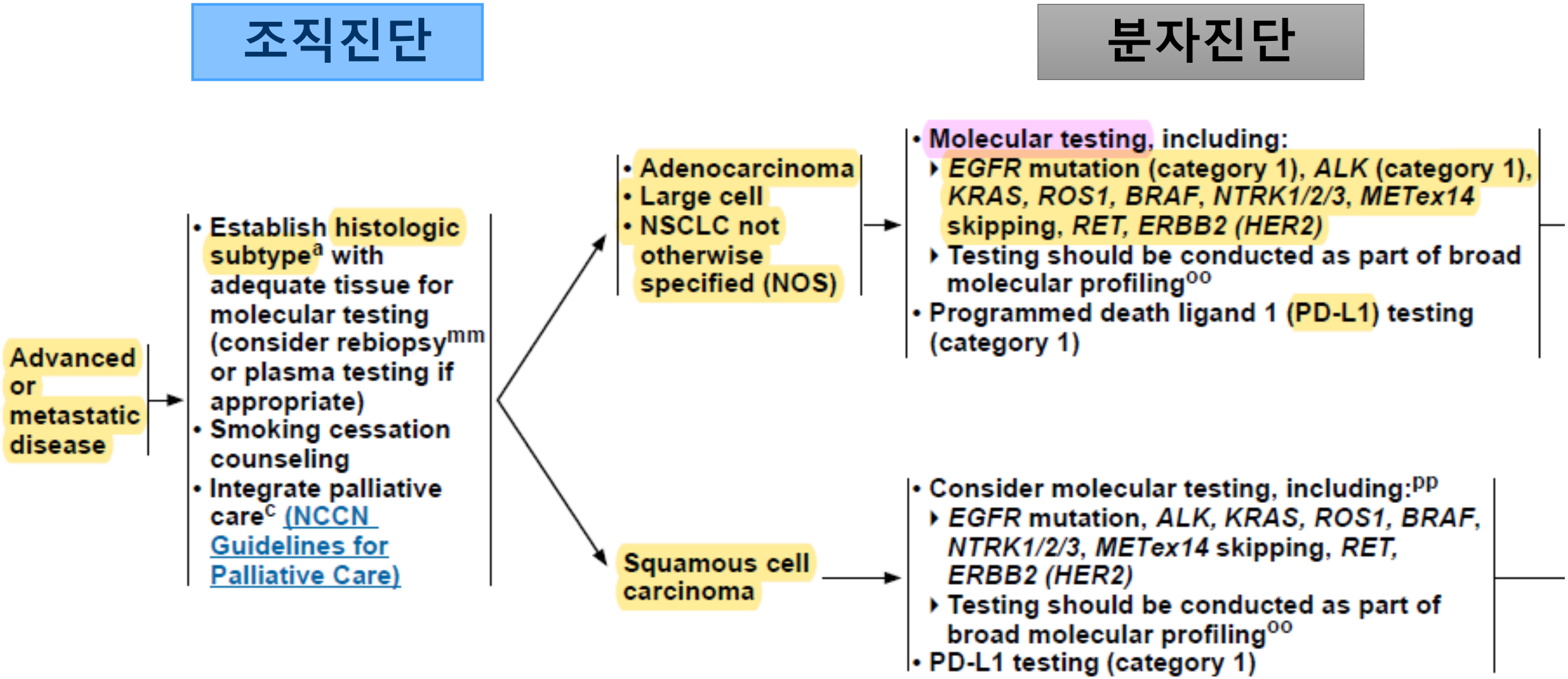
→ Locoregional recurrence

→ Distant metastases

재발한 경우의 치료


Locoregional recurrence or symptomatic local disease
Endobronchial obstruction
Any combination of the following:
• Laser/stent/other surgery[l]
• External-beam RT or brachytherapy[m]
• Photodynamic therapy
Resectable recurrence
• Reresection (preferred)[l]
• External-beam RT or SABR[m,n]
Mediastinal lymph node recurrence
No prior RT
Concurrent chemoradiation[m,s]
Prior RT
Systemic therapy (NSCL-19)
Superior vena cava (SVC) obstruction
• Concurrent chemoradiation[m,s] (if not previously given) ± SVC stent
• External-beam RT[m] ± SVC stent
• SVC stent
Severe hemoptysis
Any combination of the following:
• External-beam RT or brachytherapy[m]
• Laser or photodynamic therapy or embolization
• Surgery
Chest CT with contrast
Brain MRI with contrast[q]
FDG-PET/CT
No evidence of disseminated disease
Observation or Systemic therapy (NSCL-19) (category 2B)
Evidence of disseminated disease
Systemic therapy (NSCL-19)
Distant metastases
Localized symptoms
Palliative external-beam RT[m]
Diffuse brain metastases
Palliative external-beam RT[m,hh]
Bone metastasis
• If risk of fracture, orthopedic stabilization + palliative external-beam RT[m]
• Consider bisphosphonate therapy or denosumab[ll]
Systemic therapy (NSCL-19)
Limited metastasis
Stage IV, M1b (NSCL-15)
Disseminated metastases
Systemic therapy (NSCL-19)

진행성, 전이성 폐암의 치료

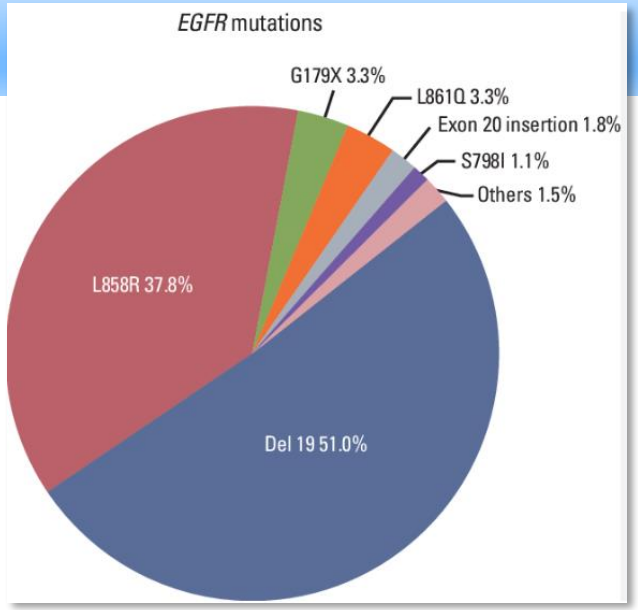


4기, 전이성 폐암치료의 치료결정의 첫걸음 : 분자진단, PD-L1

EGFR exon 19 deletion or exon 21 L858R mutation positive
EGFR S768I, L861Q, and/or G719X mutation positive
EGFR exon 20 insertion mutation positive
KRAS G12C mutation positive
ALK rearrangement positive
ROS1 rearrangement positive
BRAF V600E mutation positive
NTRK1/2/3 gene fusion positive
METex14 skipping mutation positive
RET rearrangement positive
ERBB2 (HER2) mutation positive
PD-L1 ≥1% and negative for actionable molecular biomarkers above
PD-L1 <1% and negative for actionable molecular biomarkers above

NCCN NSCLC, V5, 2024

EGFR (흔한 돌연변이 19del or L858R)



EGFR EXON 19 DELETION OR EXON 21 L858R MUTATIONS[nn]

FIRST-LINE THERAPY[qq]

Lasertinib

EGFR exon 19 deletion or exon 21 L858R mutations

EGFR mutation discovered prior to first-line systemic therapy

- **Preferred**
  - Osimertinib[rr] (category 1) → Progression
- **Other Recommended**
  - Osimertinib + pemetrexed + (cisplatin or carboplatin) (nonsquamous) (category 1) → Progression
  - or Erlotinib[rr] (category 1)
  - or Afatinib[rr] (category 1)
  - or Gefitinib[rr] (category 1)
  - or Dacomitinib[rr] (category 1)
  - or Erlotinib + ramucirumab
  - or Erlotinib + bevacizumab[ss,tt] → Progression

EGFR mutation discovered during first-line systemic therapy

- Complete planned systemic therapy,[uu] including maintenance therapy, or interrupt, followed by osimertinib (preferred) → Progression
- or
- erlotinib or afatinib or gefitinib or dacomitinib or erlotinib + ramucirumab or erlotinib + bevacizumab[ss,tt] → Progression

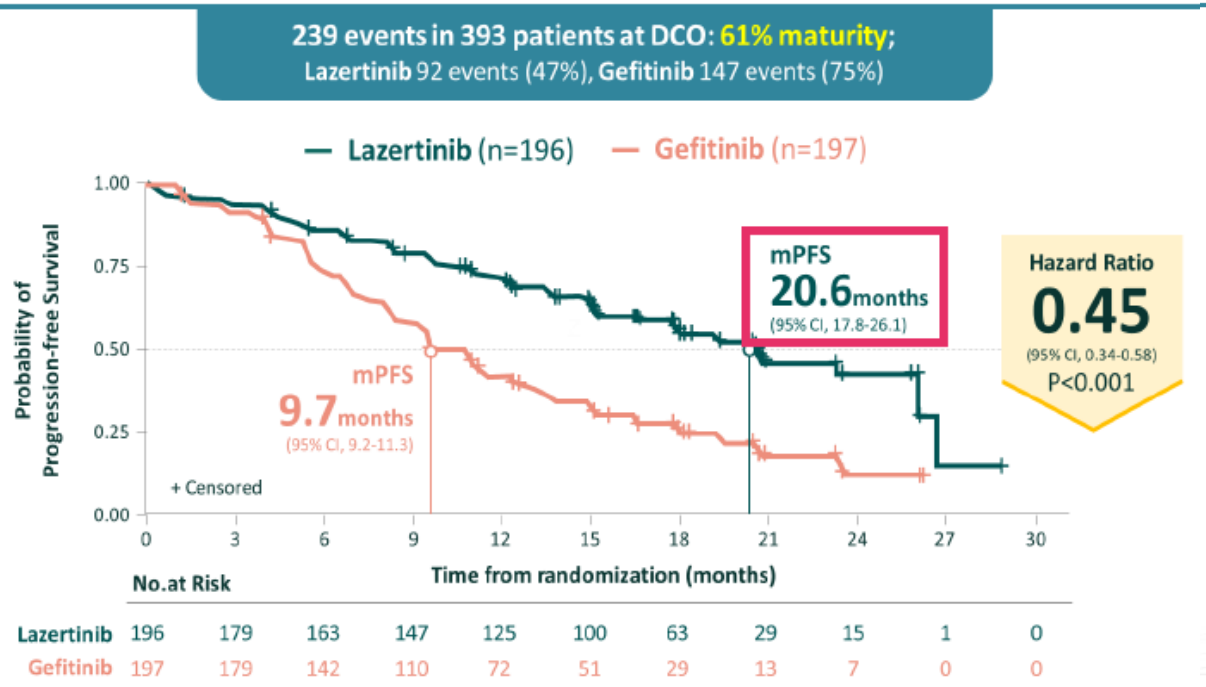
NCCN NSCLC, V5, 2024

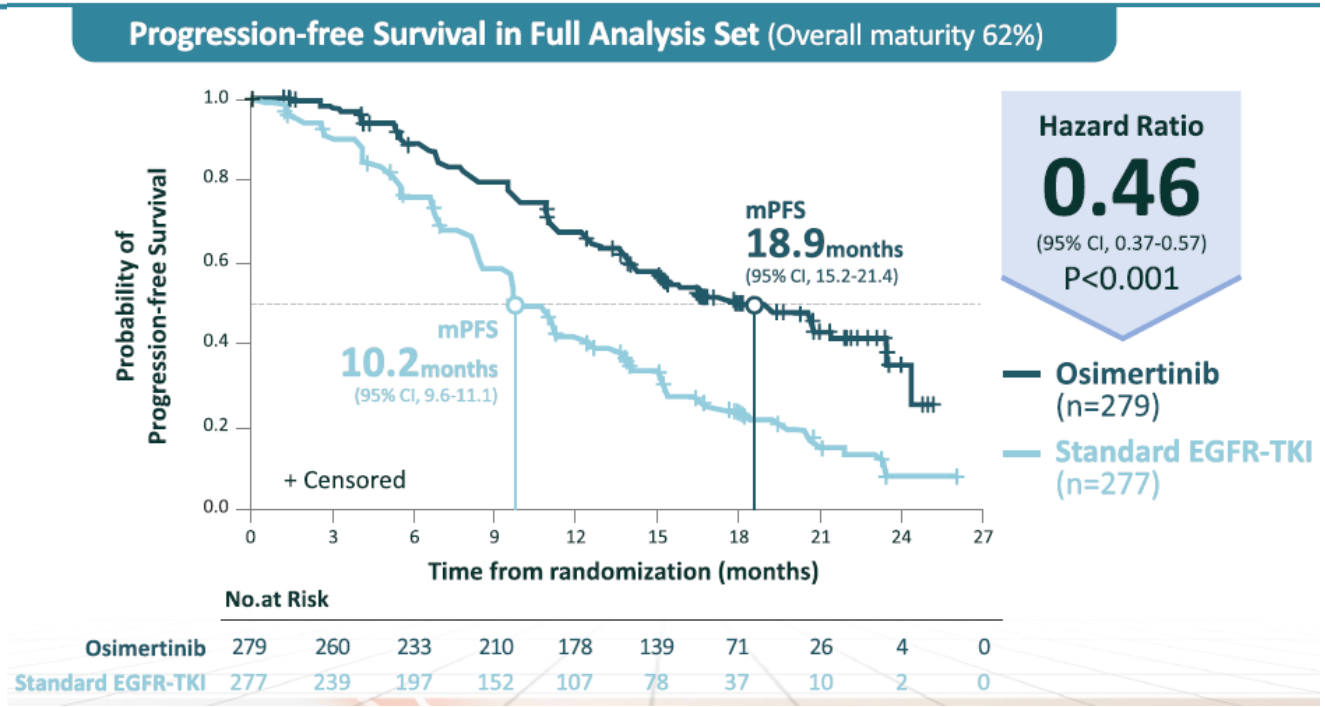
LASER 301: 1st line Lasertinib vs Gefitnib in Ex19del / L858R mutation

Primary End Point : PFS by Investigator Assessment

[Overall population]

FLAURA : 1st line Osimertinib





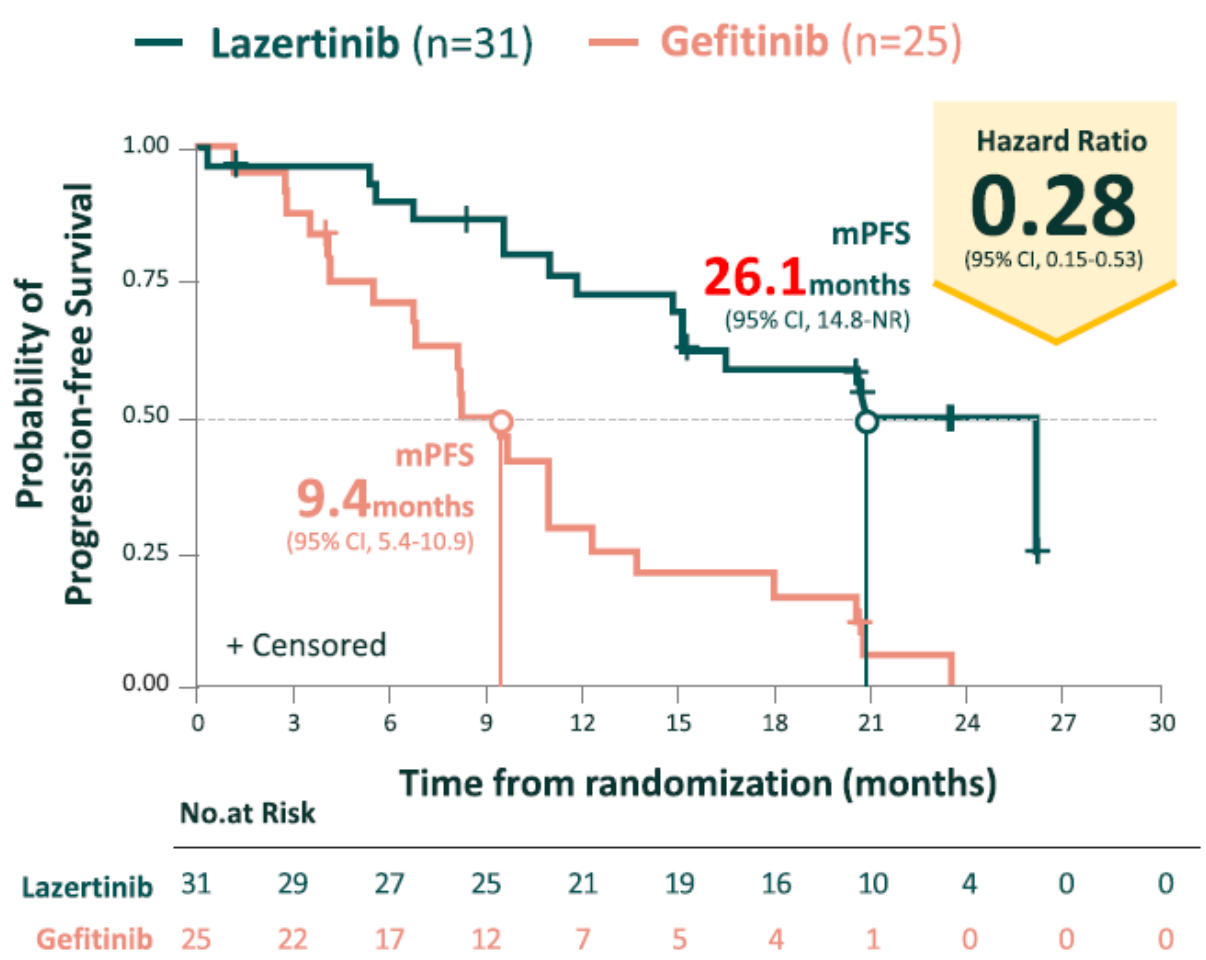
1. BC Cho et al. ESMO Asia 2022. Oral presentation. 2. JH Kang et al. CRT 2023 (https://doi.org/10.4143/crt.2023.453)

LASER 301: 1st line Lasertinib vs Gefitnib in Ex19del / L858R mutation

PFS in patients with Brain metastasis

Korean subset

WITH CNS metastases

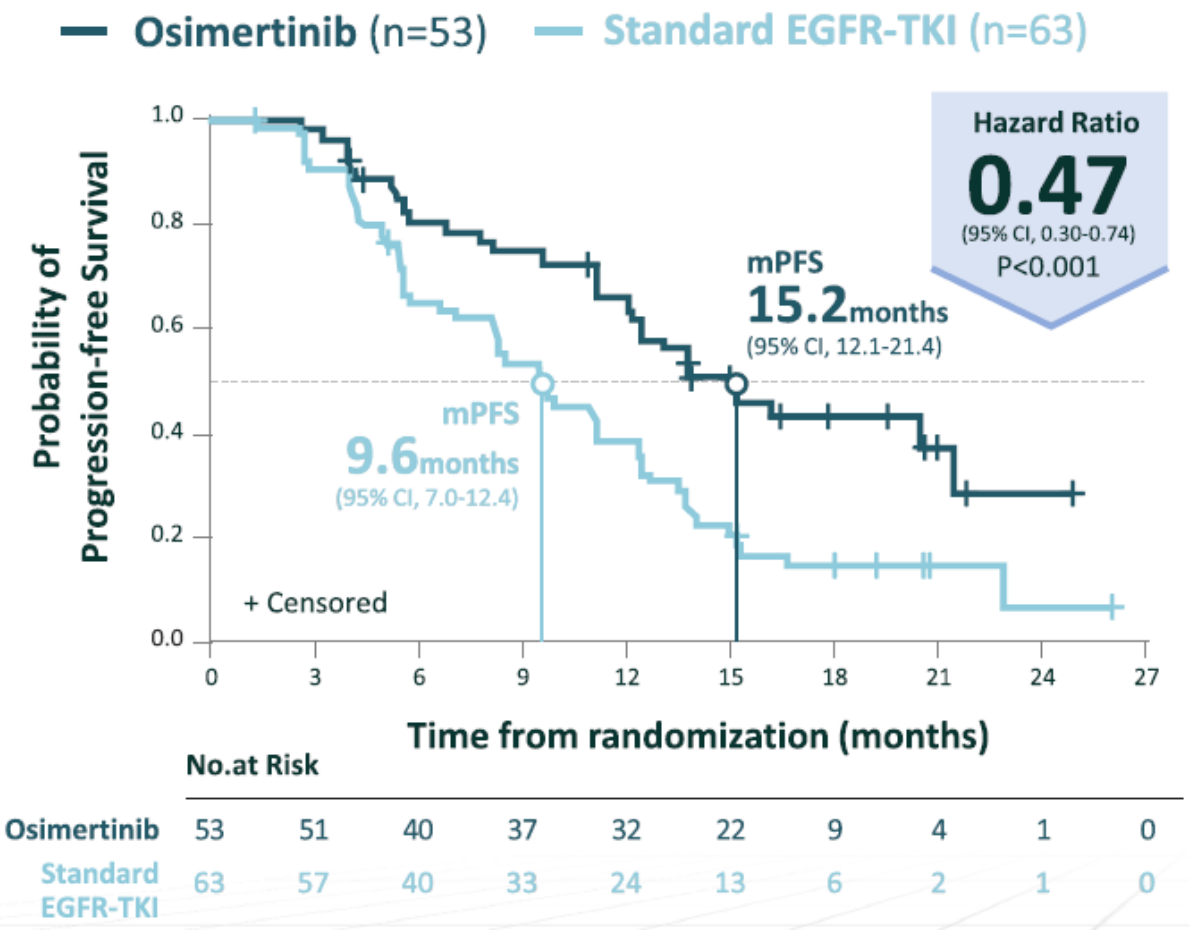


No.at Risk

Lazertinib	31	29	27	25	21	19	16	10	4	0	0
Gefitinib	25	22	17	12	7	5	4	1	0	0	0

FLAURA : 1st line Osimertinib

WITH CNS metastases



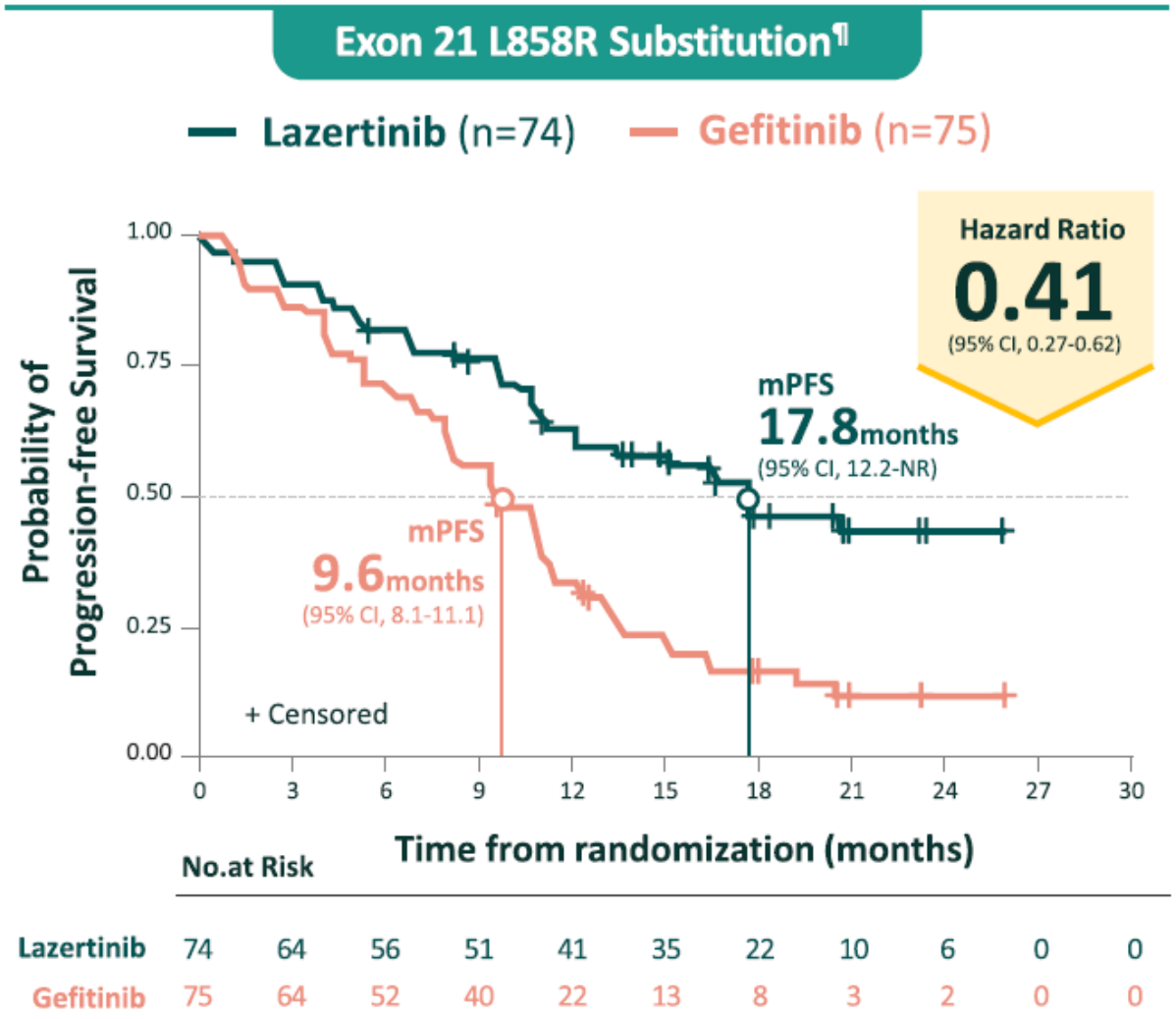
No.at Risk

Osimertinib	53	51	40	37	32	22	9	4	1	0
Standard EGFR-TKI	63	57	40	33	24	13	6	2	1	0

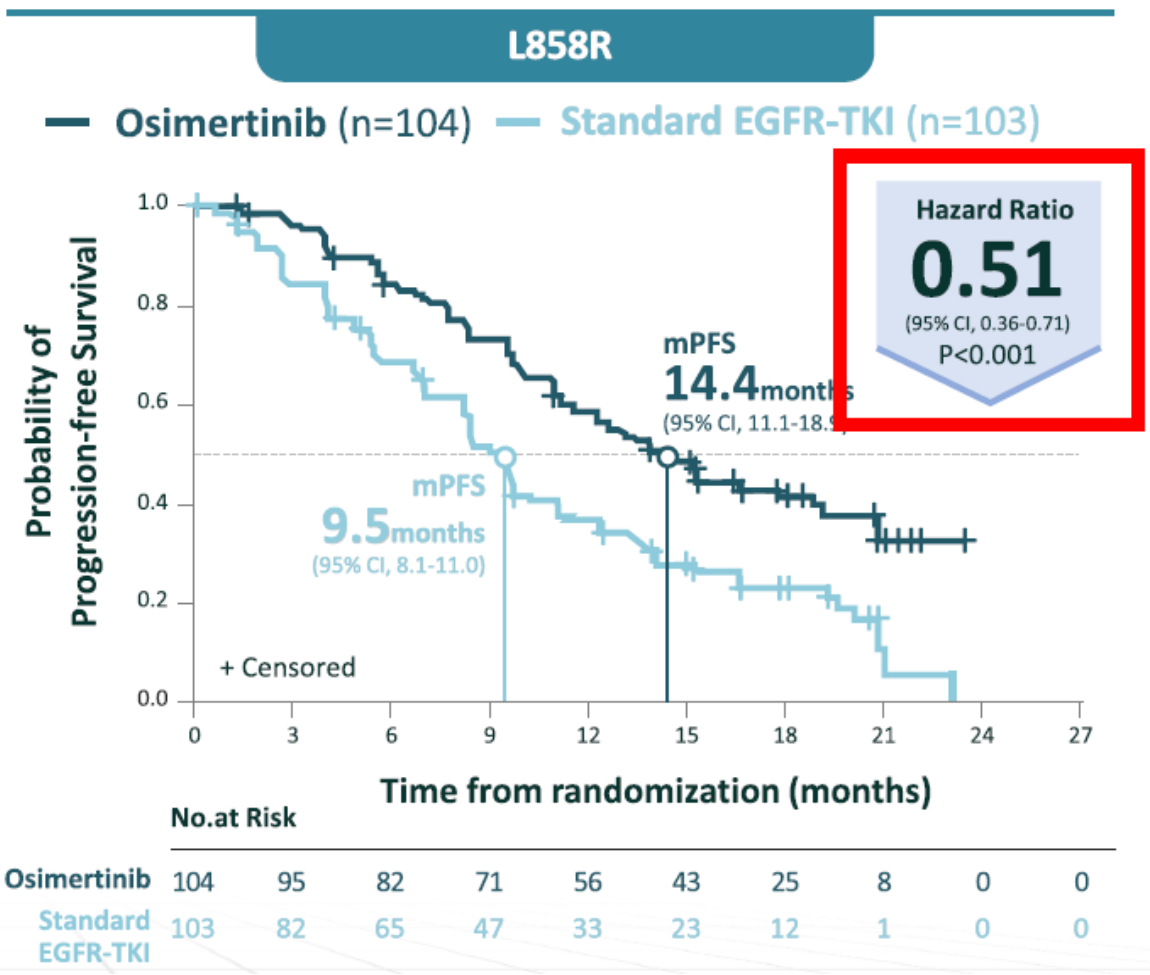
1. BC Cho et al. ESMO Asia 2022. Oral presentation. 2. JH Kang et al. CRT 2023 (https://doi.org/10.4143/crt.2023.453)

LASER 301: 1st line Lasertinib vs Gefitnib in Ex19del / L858R mutation

PFS in patients with L858R mutation

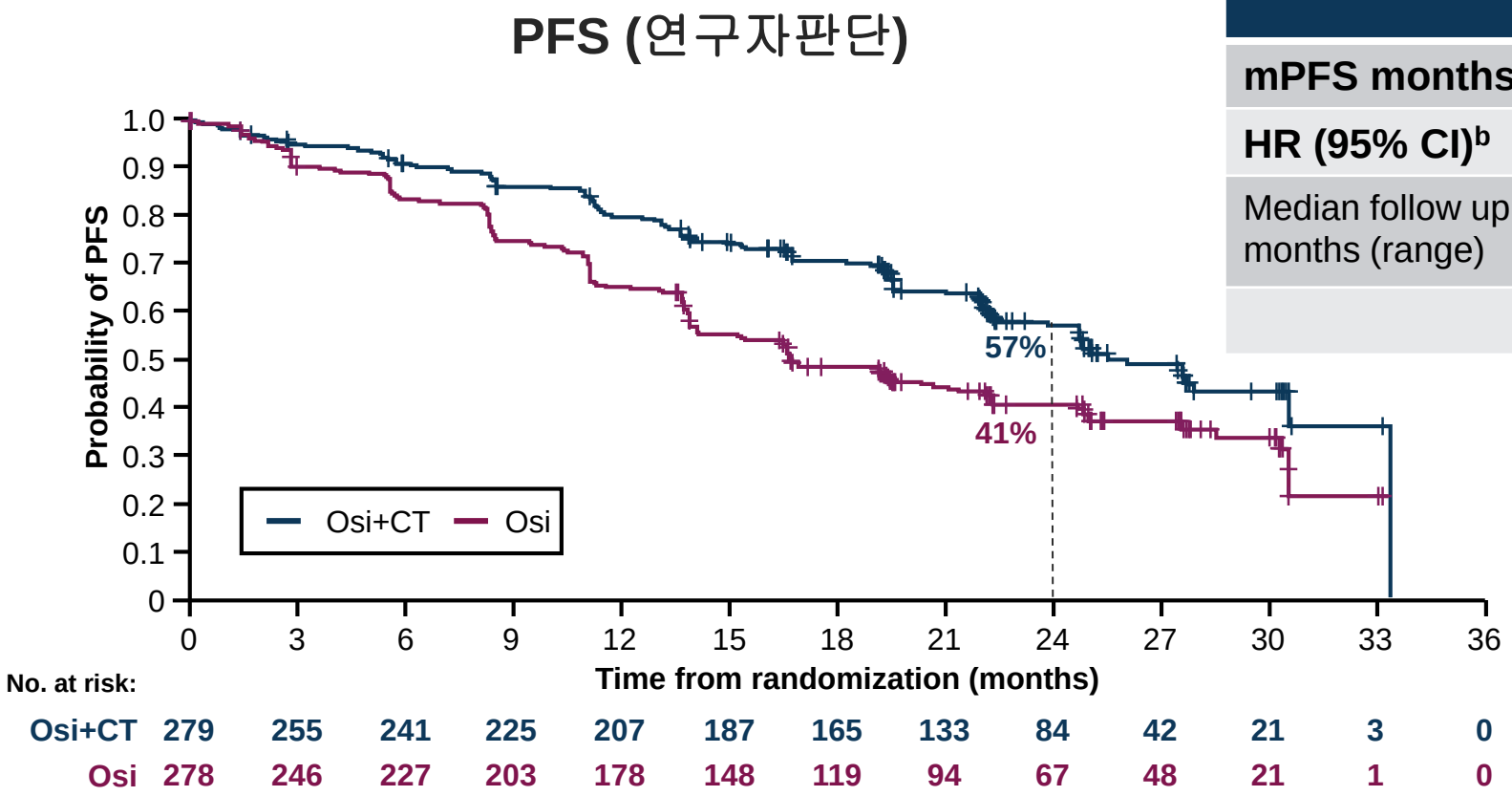


FLAURA : 1st line Osimertinib



1. BC Cho et al. ESMO Asia 2022. Oral presentation. 2. JH Kang et al. CRT 2023 (https://doi.org/10.4143/crt.2023.453)

1L Osimertinib + Platinum-Pemetrexed vs. Osimertinib Monotherapy in *EGFR*m Advanced NSQ NSCLC (per Investigator)



Efficacy	Osimertinib + platinum-pemetrexed[a] (n=279)	Osimertinib (n=278)
mPFS months (95% CI)	**25.5** (24.7-NC)	**16.7** (14.1-21.3)
HR (95% CI)[b]	0.62 (0.49-0.79); p<0.0001	
Median follow up for PFS[a], months (range)	19.5 (0–33.3)	16.5 (0–33.1)
Overall maturity: 51%		

PFS
25.5 vs 16.7

FLUARA 2

DCO: April 03, 2023. **Note:** CT therapy includes cisplatin or carboplatin with pemetrexed. [a]In all patients.

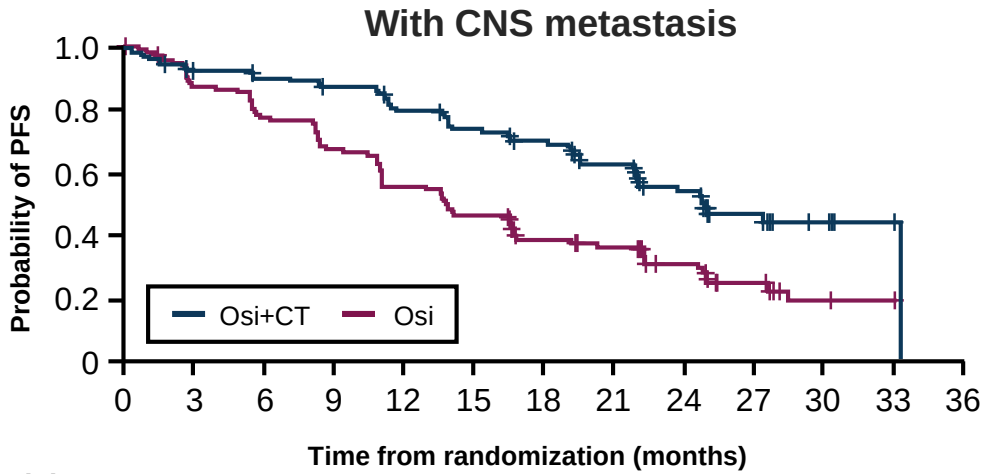
CI = confidence interval; CT = chemotherapy; DCO = data cut-off; *EGFR*m = epidermal growth factor receptor mutation-positive; HR = hazard ration; mPFS = median progression-free survival; NC = not calculable.; NSCLC = non-small cell lung cancer; PFS = progression-free survival. NSQ=non squamous

Planchard D et al. *N Engl J Med*. 2023;389(21):1935-1948.

1L Osimertinib + Platinum-Pemetrexed vs. Osimertinib Monotherapy : PFS and Brain metastasis

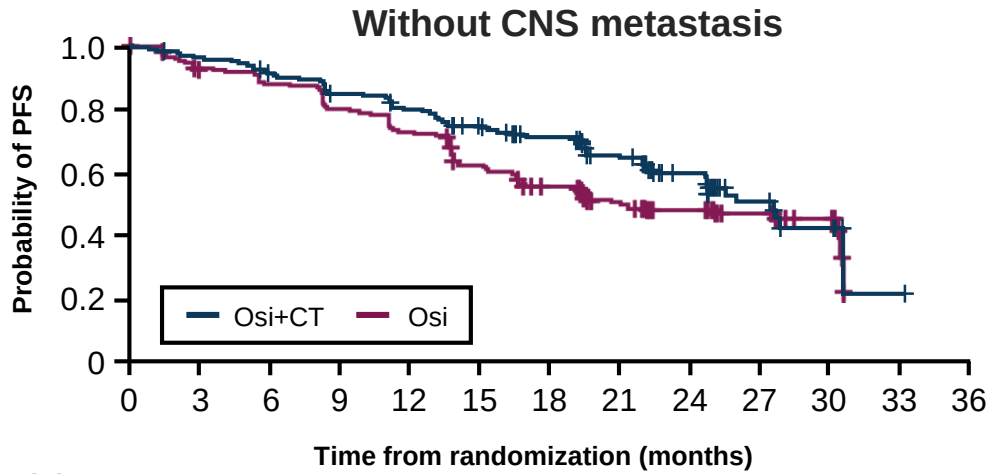
FLUARA 2

- The risk of progression or death was decreased by osimertinib + platinum-pemetrexed vs. osimertinib monotherapy in patients with and without CNS metastases at baseline.



No. at risk:

Osi+CT	116	101	98	93	84	77	70	58	34	19	8	2	0
Osi	110	95	74	73	60	50	37	32	21	13	5	1	0



No. at risk:

Osi+CT	163	153	143	132	123	110	95	75	50	23	13	1	0
Osi	168	151	143	130	118	98	82	62	46	35	16	0	0

Efficacy with CNS metastases	Osimertinib + platinum-pemetrexed (n=116)	Osimertinib (n=110)
mPFS, months (95% CI)	24.9 (22.0-NC)	13.8 (11.0-16.7)
HR (95% CI)	0.47 (0.33-0.66)	

Efficacy without CNS metastases	Osimertinib + platinum-pemetrexed (n=163)	Osimertinib (n=168)
mPFS, months (95% CI)	27.6 (24.7-NC)	21.0 (16.7-30.5)
HR (95% CI)	0.75 (0.55-1.03)	

DCO: April 03, 2023. **Note:** CT include cisplatin or carboplatin with pemetrexed. [a]Investigator assessed.

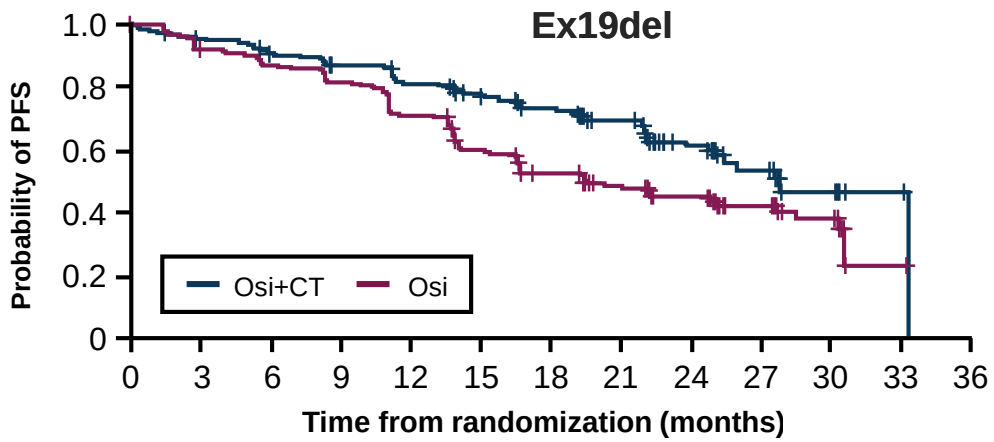
CI = confidence interval; CNS = central nervous system; CT = chemotherapy; DCO = data cut-off; HR = hazard ratio; NC = non calculable; PFS = progression-free survival.

Planchard D et al. *N Engl J Med*. 2023;389(21):1935-1948.

1L Osimertinib + Platinum-Pemetrexed vs. Osimertinib Monotherapy : PFS and EGFR types

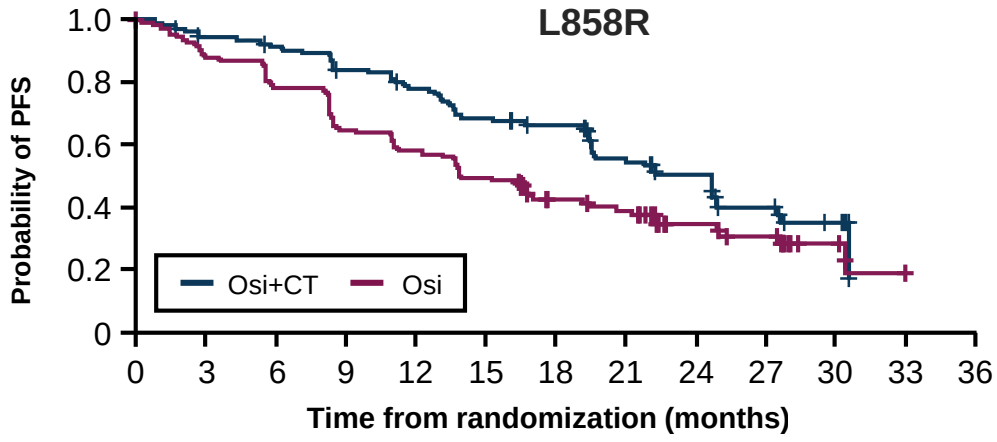
FLUARA 2

- Osimertinib + platinum-pemetrexed was beneficial in patients irrespective of type of *EGFR*m (Ex19del/L858R) with longer PFS compared to osimertinib monotherapy



No. at risk:

Osi+CT	172	159	150	142	131	120	103	86	53	23	9	3	0
Osi	169	152	144	135	117	96	79	63	48	33	16	1	0



No. at risk:

Osi+CT	106	95	91	83	76	67	62	47	31	19	12	0	0
Osi	107	92	82	68	61	52	40	31	19	15	5	0	0

Efficacy in Ex19del	Osimertinib + platinum-pemetrexed (n=172)	Osimertinib (n=169)
mPFS, months (95% CI)	27.9 (25.1-NC)	19.4 (16.5-27.6)
HR (95% CI)	0.60 (0.44-0.83)	

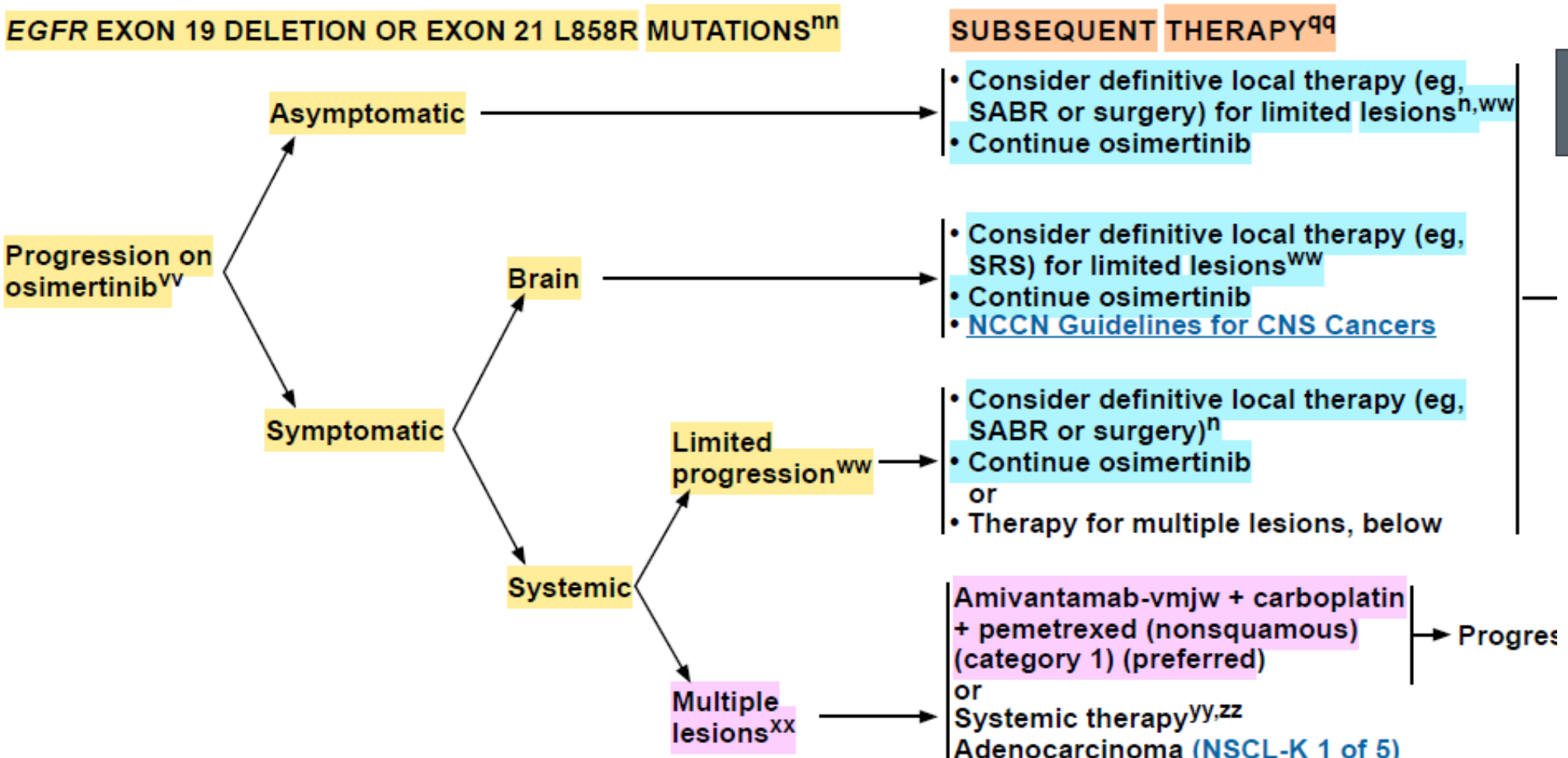
Efficacy in L858R	Osimertinib + platinum-pemetrexed (n=106)	Osimertinib (n=107)
mPFS, months (95% CI)	24.7 (19.5-27.4)	13.9 (11.1-19.4)
HR (95% CI)	0.63 (0.44-0.90)	

DCO: April 03, 2023. **Note:** CT includes cisplatin or carboplatin with pemetrexed. [a]Investigator assessed.

CI = confidence interval; CT = chemotherapy; DCO = data cut-off; *EGFR*m = epidermal growth factor receptor mutation-positive; Ex19del = exon 19 deletion; HR = hazard ratio; mPFS = median progression-free survival; NC = non calculable; PFS = progression-free survival.

Planchard D et al. *N Engl J Med*. 2023;389(21):1935-1948.

EGFR (흔한 돌연변이 19del or L858R) : Post Osimertinib



* Limited lesion : generally 3-5 sites

* Consider biopsy at progression : SCLC transformation, other mechanisms of resistance

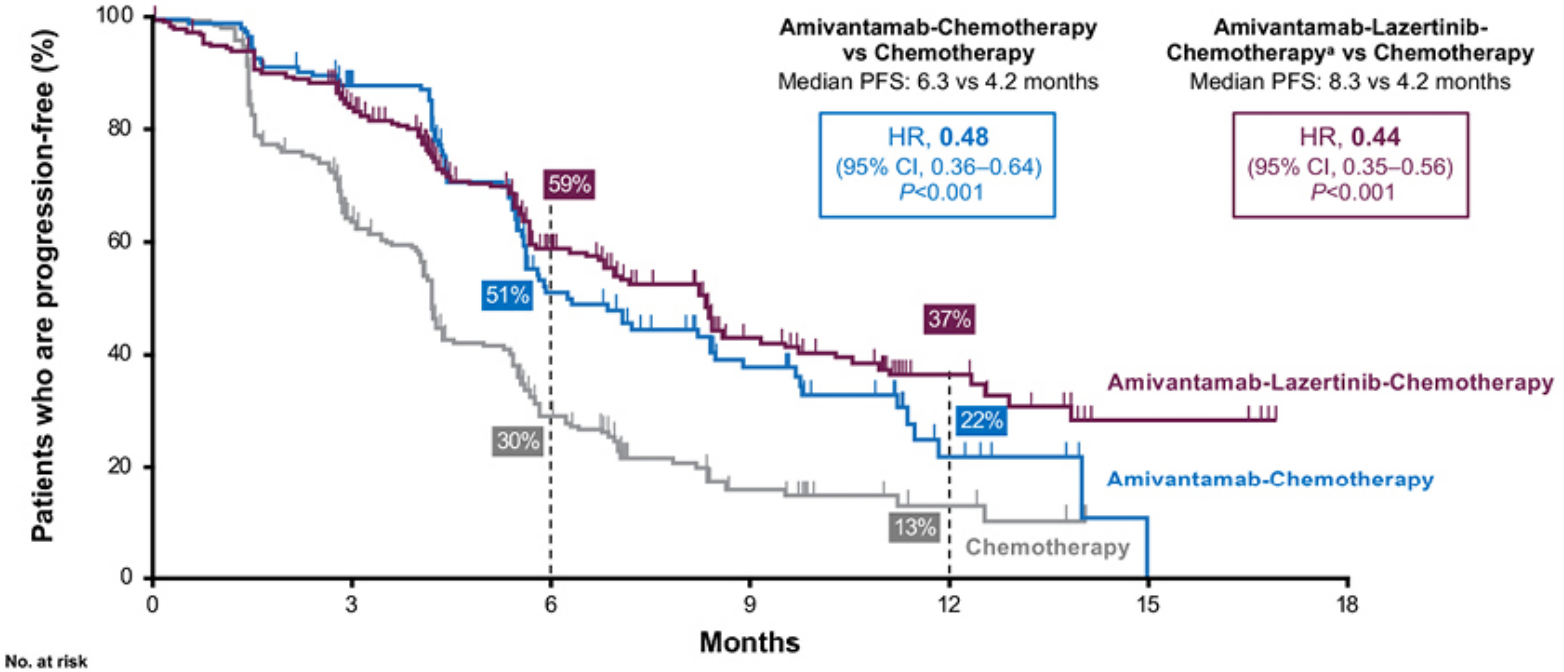
NCCN NSCLC, V5, 2024

Post Osimertinib (2nd line Amivantamab-chemotherapy combination)

MARIPOSA-2

Primary Endpoint: Progression-free Survival by BICR

At a median follow-up of 8.7 months, amivantamab-chemotherapy and amivantamab-lazertinib-chemotherapy reduced the risk of progression or death by 52% and 56%, respectively



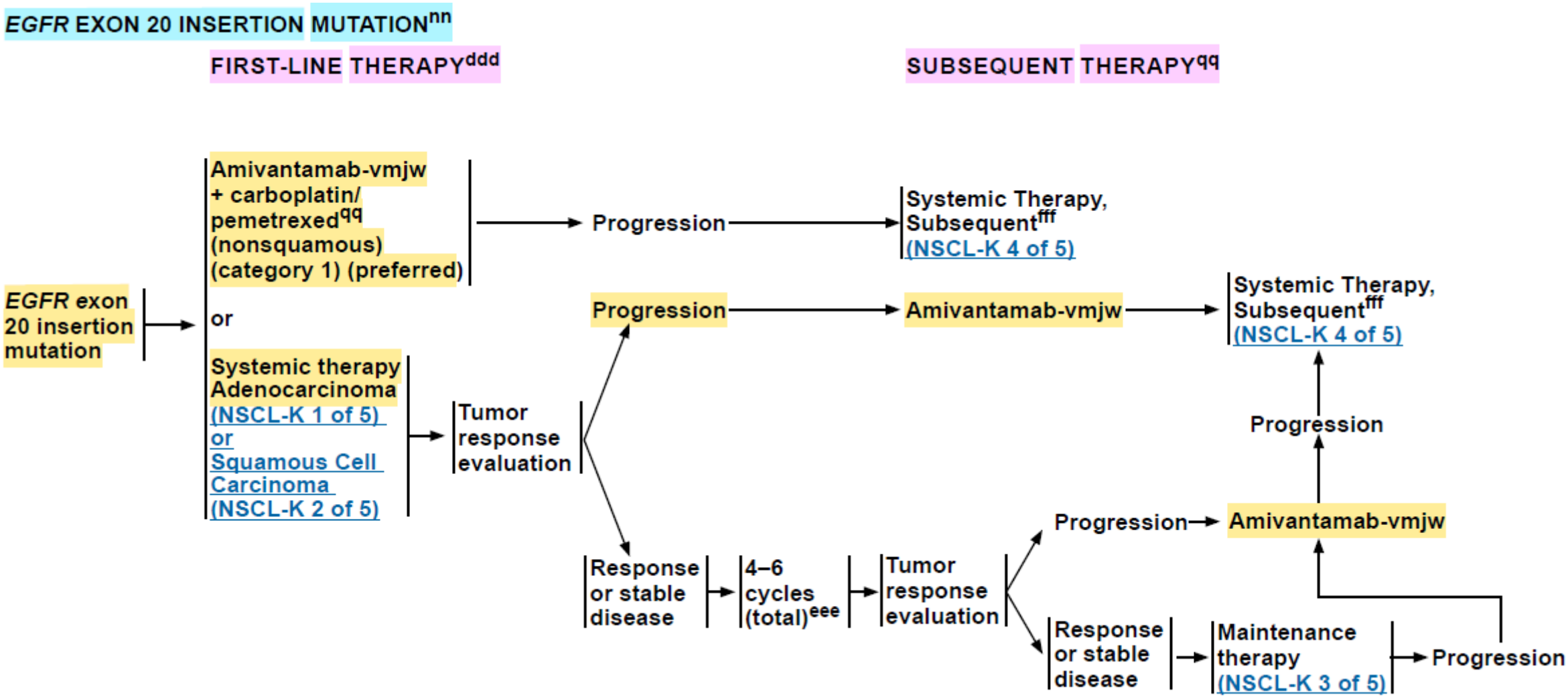
No. at risk							
Amivantamab-Chemotherapy	131	99	49	27	7	0	0
Amivantamab-Lazertinib-Chemotherapy	263	194	104	52	21	4	0
Chemotherapy	263	135	49	17	6	0	0

Consistent PFS benefit by investigator: HR, 0.41 (8.2 vs 4.2 mo; P<0.001[b]) & HR, 0.38 (8.3 vs 4.2 mo; P<0.001[b])

[a]Amivantamab-lazertinib-chemotherapy arm includes all patients regardless of the dosing regimen received. [b]Nominal *P*-value; endpoint not part of hierarchical hypothesis testing.
BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

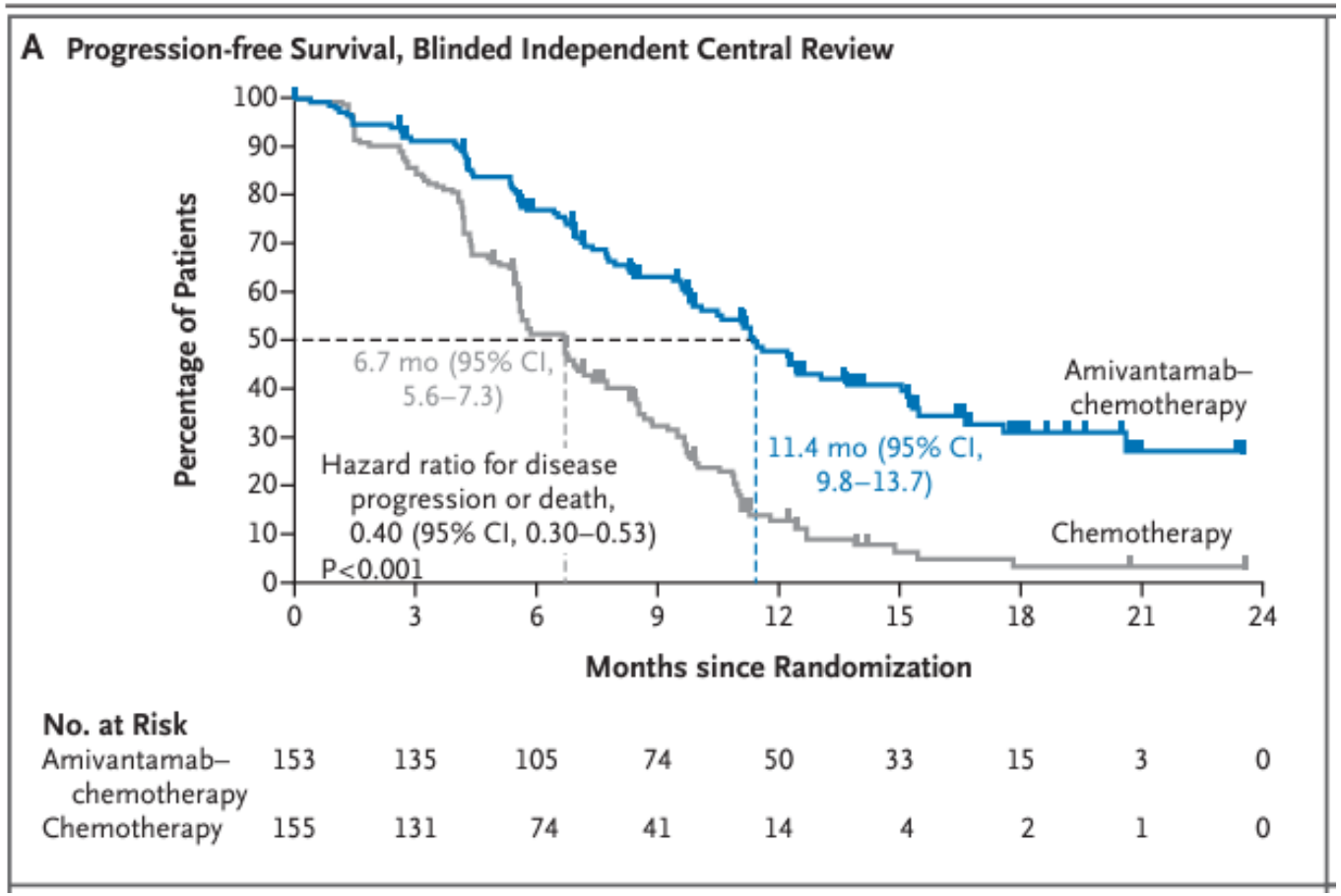
Passaro A, et al. Mariposa-2 at ESMO 2023

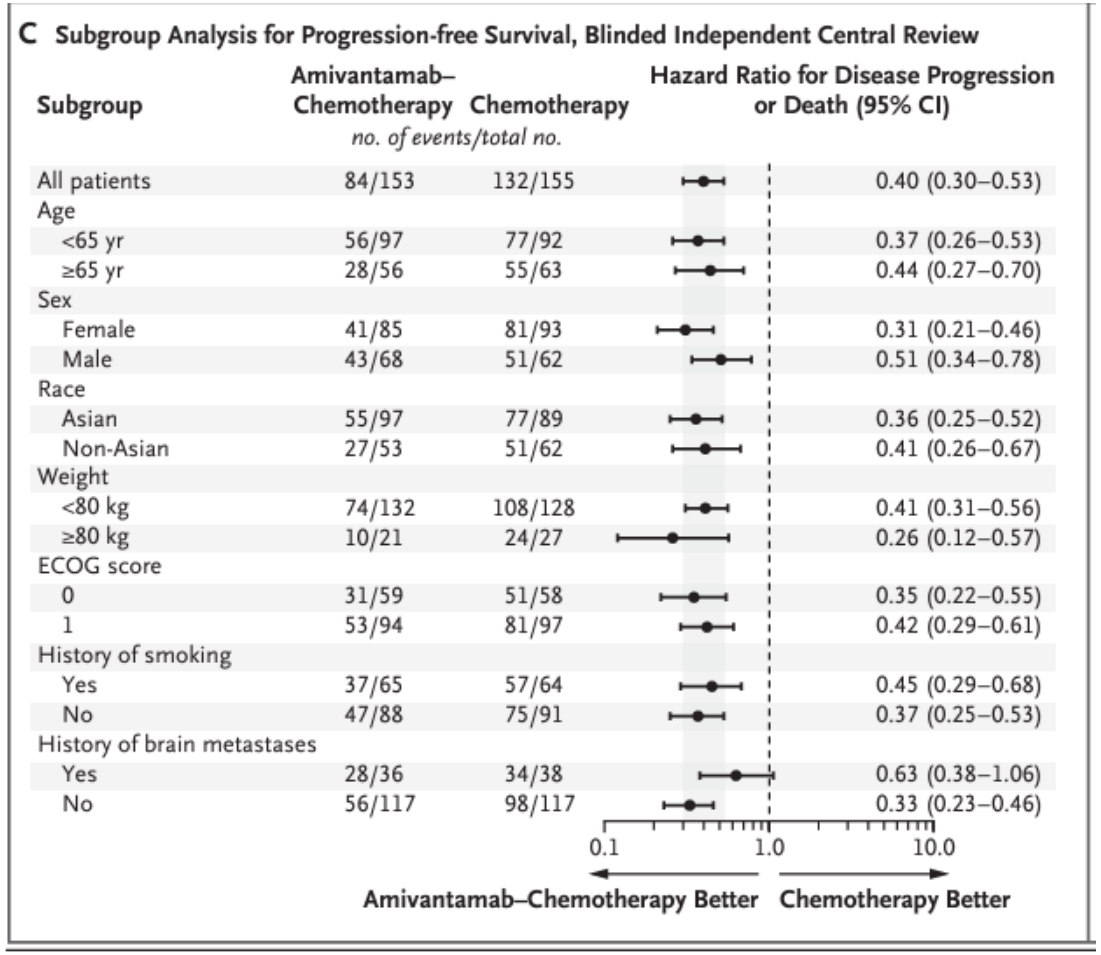
EGFR Exon 20 Insertion Mutation



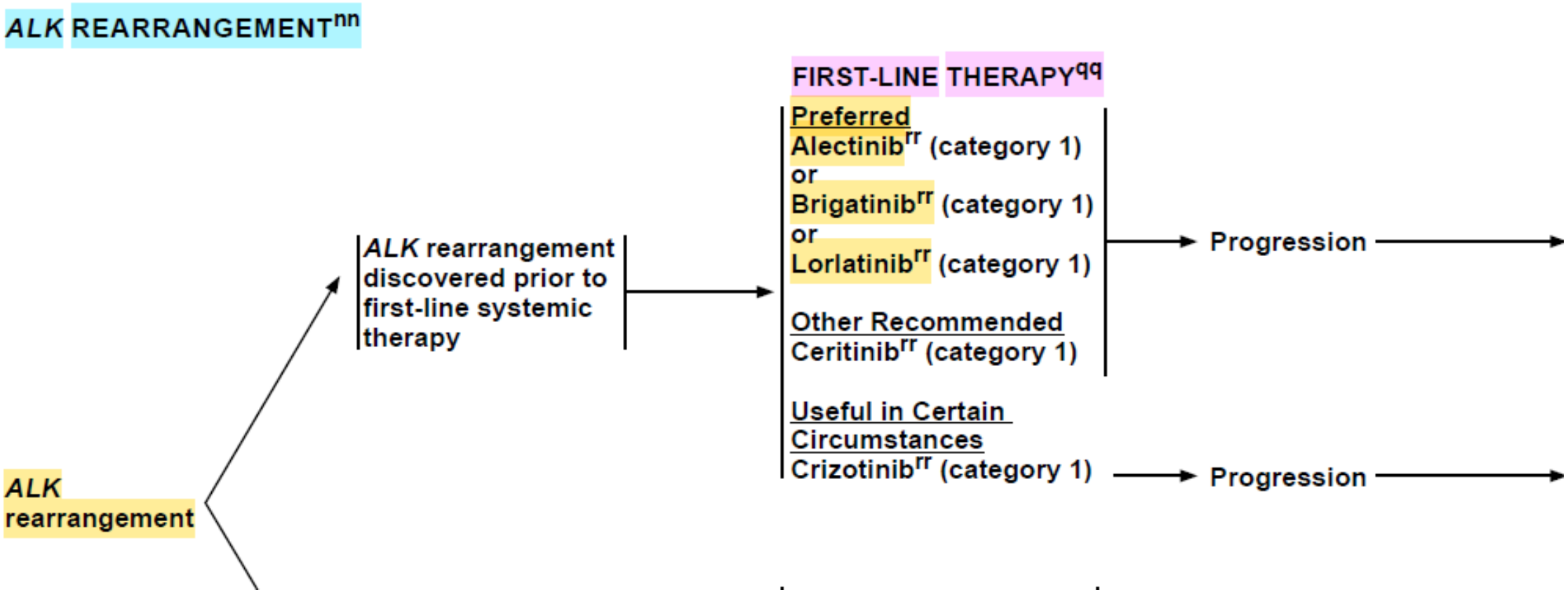
EGFR Exon 20 Insertion Mutation : Amivantamab+chemotherapy

PAPILLON





ALK Rearrangement



ROS1 Rearrangement

FIRST-LINE THERAPY[qq]

ROS1 rearrangement

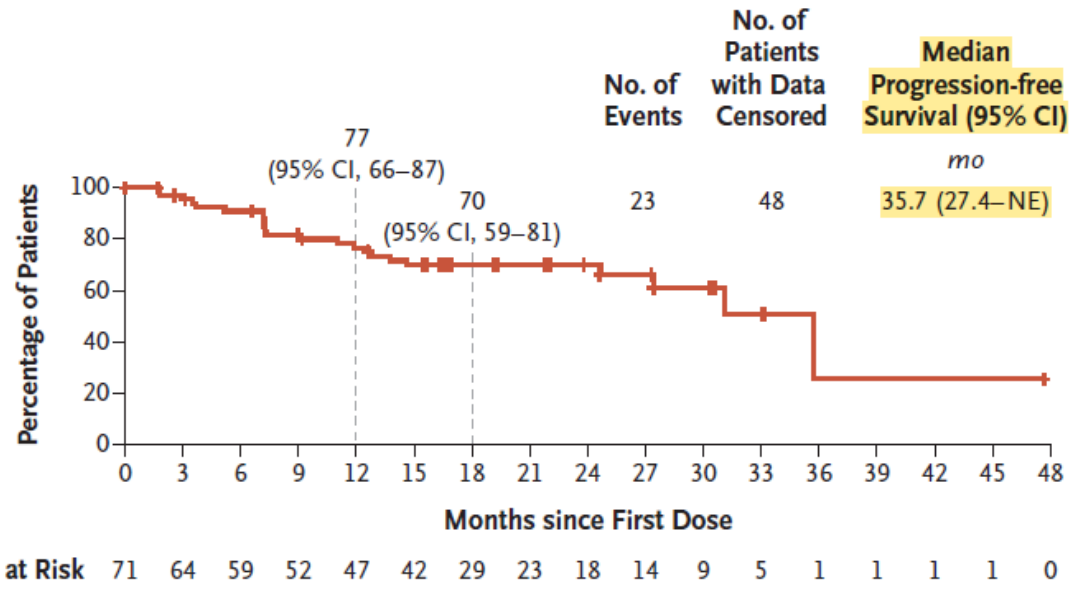
ROS1 rearrangement discovered prior to first-line systemic therapy

→ **Preferred**
Entrectinib[rr,jjj]
or
Crizotinib[rr]
or
Repotrectinib[rr,jjj]
or
Other Recommended
Ceritinib[rr]

→ Progression[vv] →

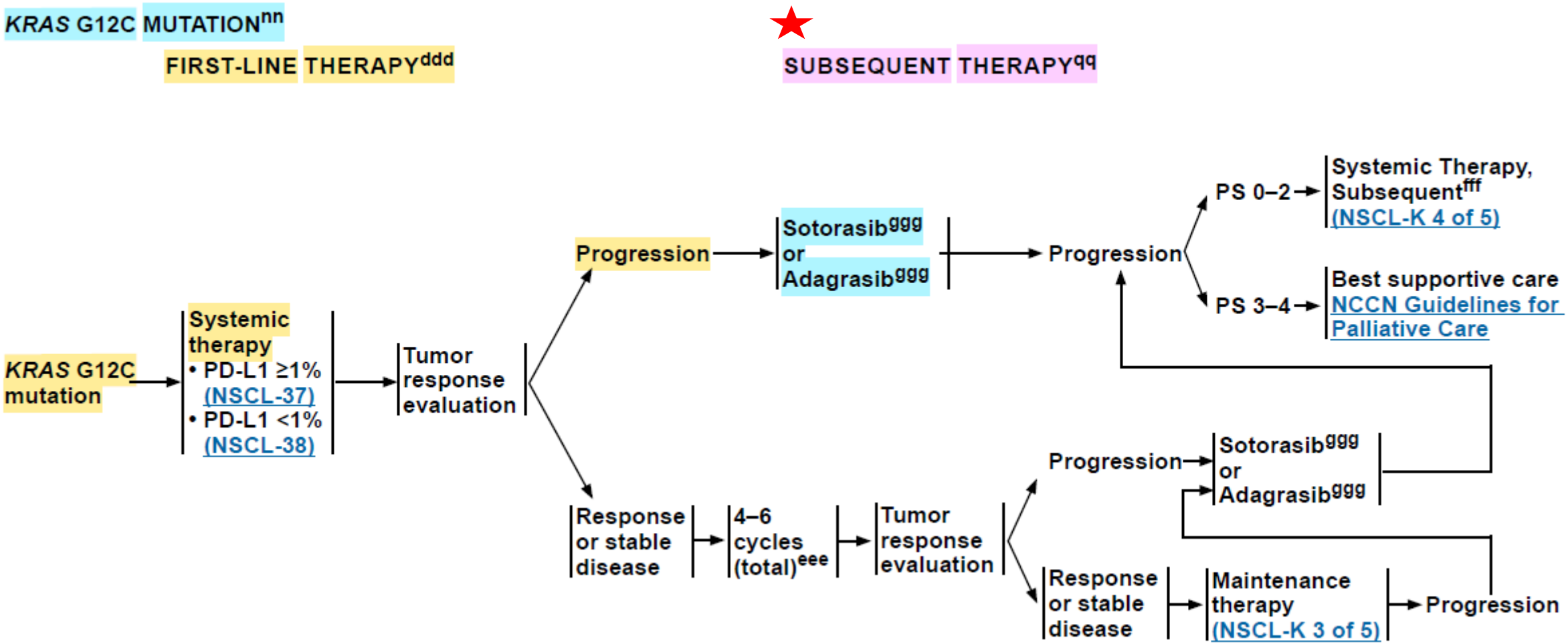
TRIDENT-1

B Progression-free Survival in Cohort with No Previous ROS1 TKI Therapy (N=71)



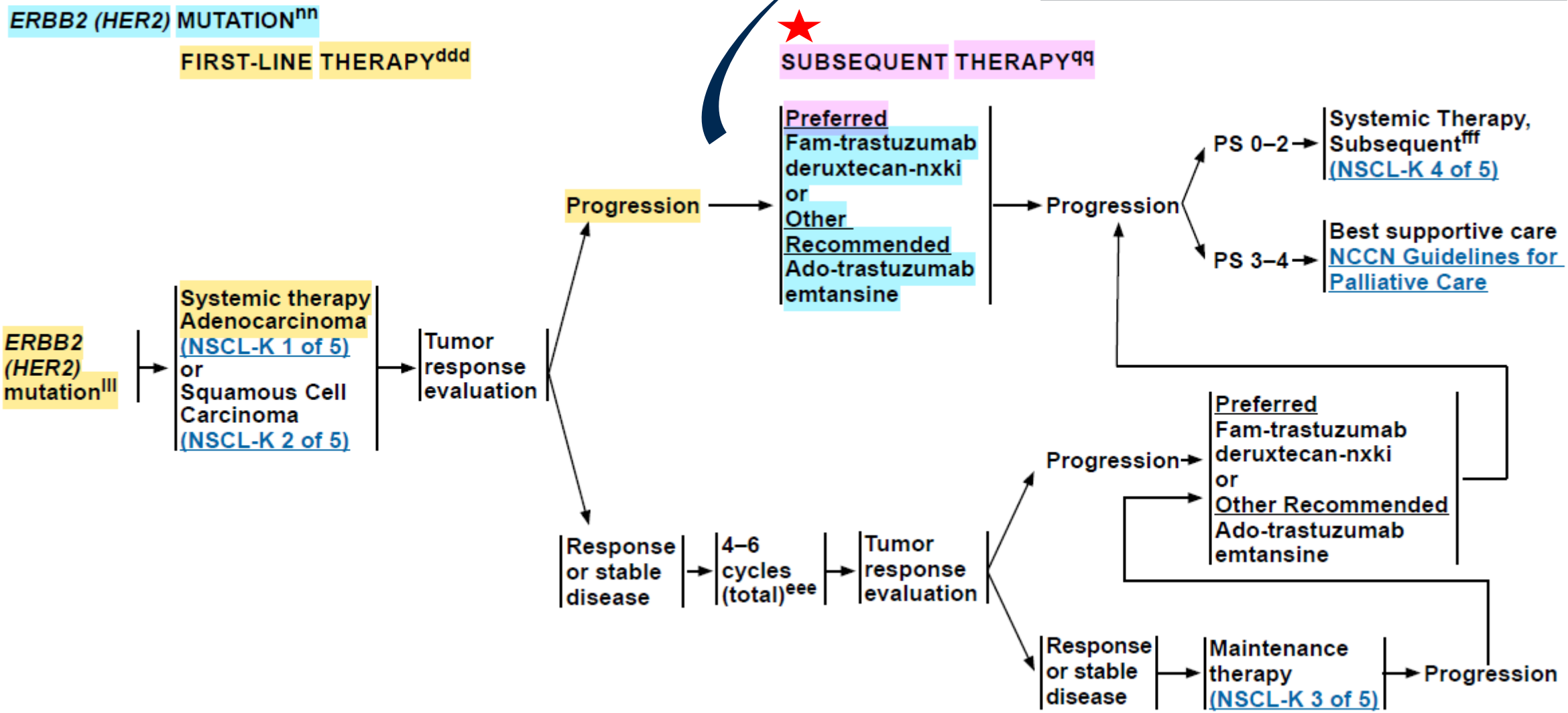
* Entrectinib or repotrectinib may be better for patients with **brain metastases**

KRAS G12C Mutation



ERBB2 (HER2) Mutation

* 항체-약물중합체 치료제
(Antibody-Drug Conjugate; ADC)



Molecular Biomarker-Directed Therapy (진행성, 전이성 폐암)

EGFR Exon 19 Deletion or Exon 21 L858R
- First-line therapy
  - Afatinib[1]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6]
  - Osimertinib + pemetrexed + (cisplatin or carboplatin) (nonsquamous)[7]
  - Erlotinib + ramucirumab[8]
  - Erlotinib + bevacizumab[c] (nonsquamous)[9]
- Subsequent therapy
  - Osimertinib[10]
  - Amivantamab-vmjw + carboplatin + pemetrexed (nonsquamous)[11]

EGFR S768I, L861Q, and/or G719X
- First-line therapy
  - Afatinib[1,12]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6,13]
- Subsequent therapy
  - Osimertinib[10]
  - Amivantamab-vmjw + carboplatin + pemetrexed (nonsquamous)[11]

EGFR Exon 20 Insertion Mutation
- First-line therapy
  - Amivantamab-vmjw + carboplatin + pemetrexed (nonsquamous)[14]
- Subsequent therapy
  - Amivantamab-vmjw[15]

KRAS G12C Mutation[d]
- Subsequent therapy
  - Sotorasib[16]
  - Adagrasib[17]

ALK Rearrangement
- First-line therapy
  - Alectinib[18,19]
  - Brigatinib[20]
  - Ceritinib[21]
  - Crizotinib[18,22]
  - Lorlatinib[23]
- Subsequent therapy
  - Alectinib[24,25]
  - Brigatinib[26]
  - Ceritinib[27]
  - Lorlatinib[28]

ROS1 Rearrangement
- First-line therapy
  - Ceritinib[29]
  - Crizotinib[30]
  - Entrectinib[31]
  - Repotrectinib[32]
- Subsequent therapy
  - Lorlatinib[33]
  - Entrectinib[31]
  - Repotrectinib[32]

BRAF V600E Mutation
- First-line therapy
  - Dabrafenib/trametinib[34]
  - Encorafenib/binimetinib[35]
  - Dabrafenib[36]
  - Vemurafenib
- Subsequent therapy
  - Dabrafenib/trametinib[36,37]
  - Encorafenib/binimetinib[35]

NTRK1/2/3 Gene Fusion
- First-line/Subsequent therapy
  - Larotrectinib[38]
  - Entrectinib[39]

MET Exon 14 Skipping Mutation[d]
- First-line therapy/Subsequent therapy
  - Capmatinib[40]
  - Crizotinib[41]
  - Tepotinib[42]

RET Rearrangement[d]
- First-line therapy/Subsequent therapy
  - Selpercatinib[43]
  - Pralsetinib[44]
  - Cabozantinib[45,46]

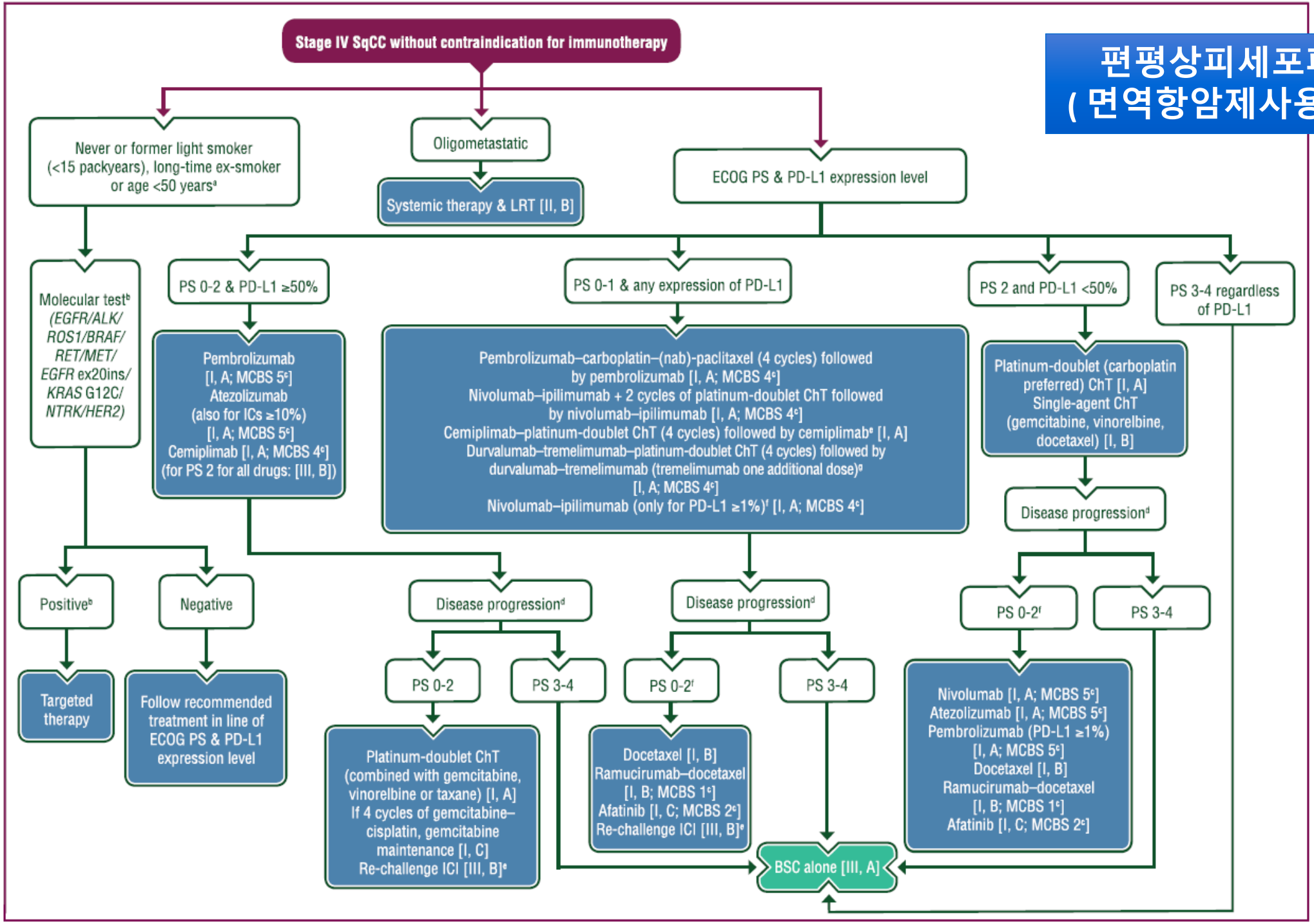
ERBB2 (HER2) Mutation[d]
- Subsequent therapy
  - Fam-trastuzumab deruxtecan-nxki[47]
  - Ado-trastuzumab emtansine[48]

PD-L1 ≥50% First-line Therapy

PD-L1 ≥1%–49% First-line Therapy

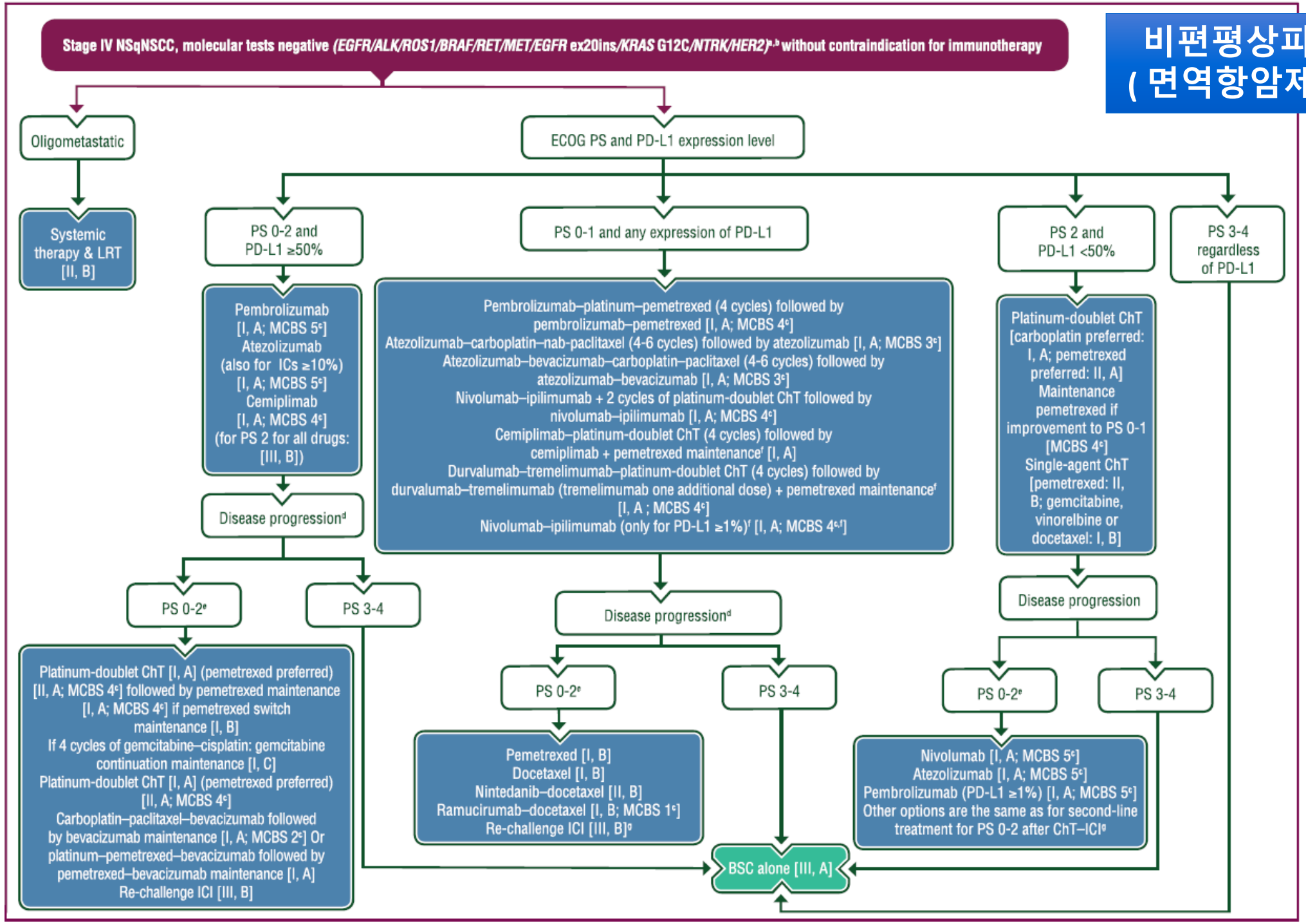
유전자 이상이 발견되지 않은 진행성, 전이성 폐암의 치료

편평상피세포폐암 (면역항암제사용가능)



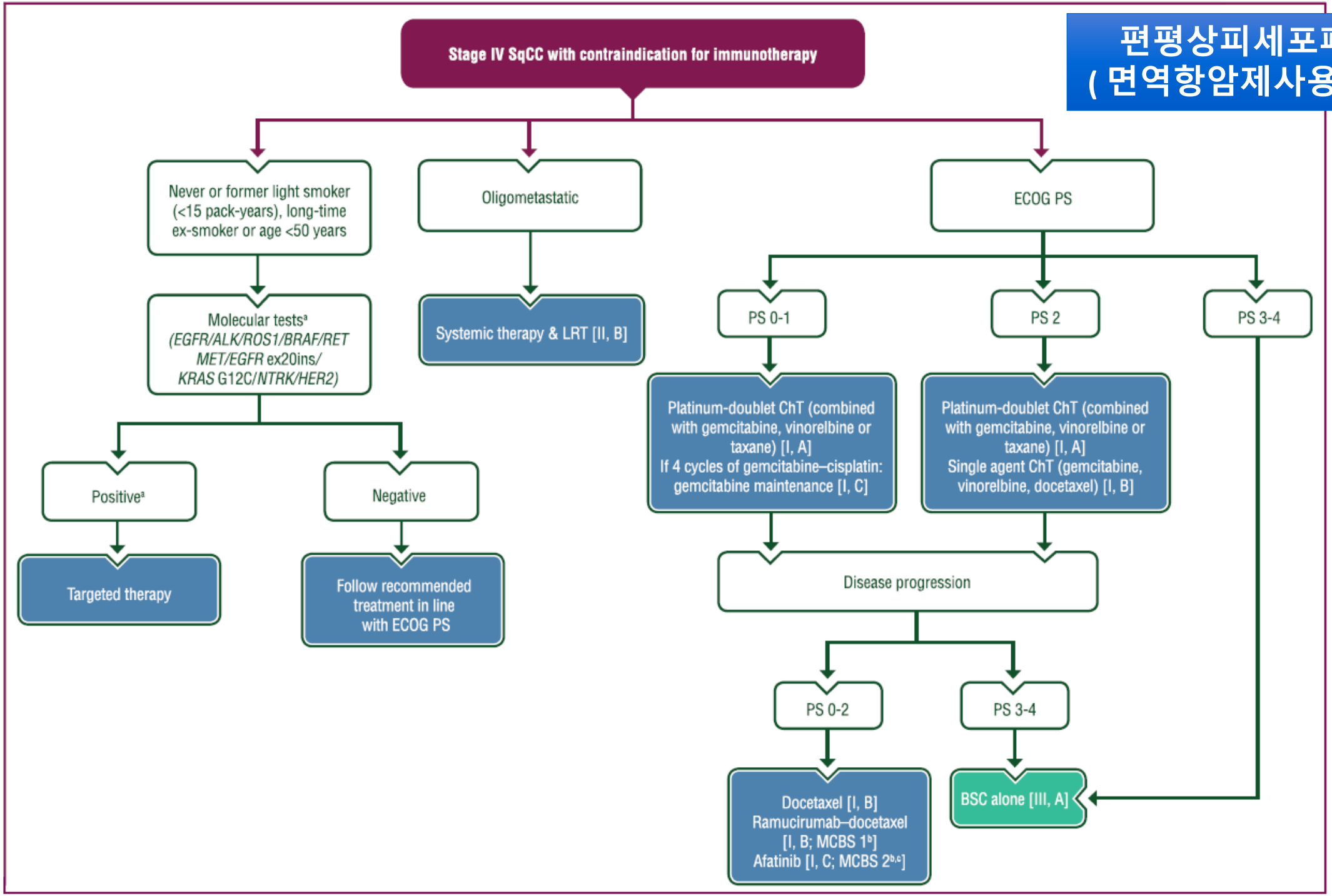
ESMO 2023

비편평상피세포폐암 (면역항암제사용가능)



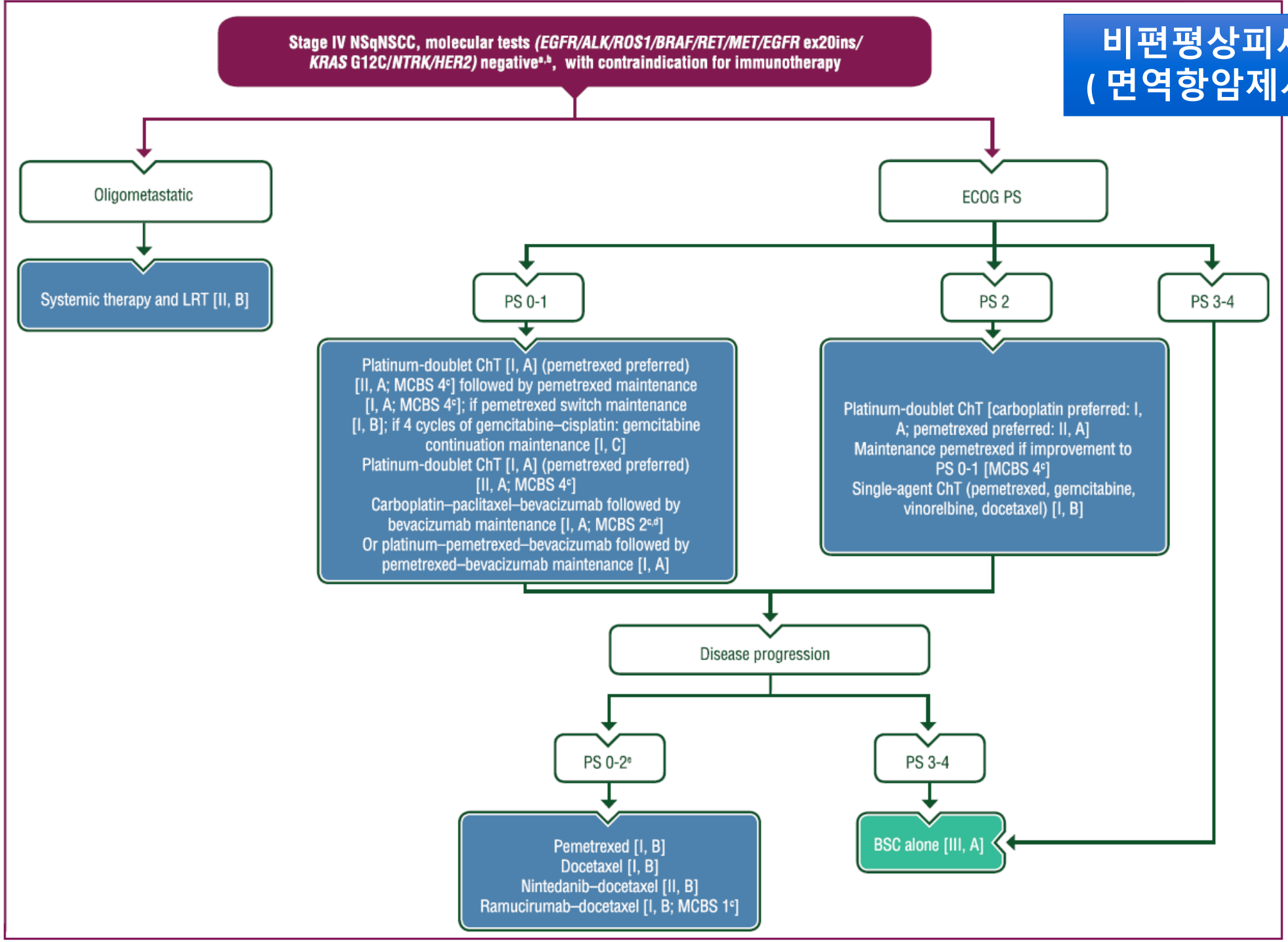
ESMO 2023

편평상피세포폐암 (면역항암제사용불가)



2023

비편평상피세포폐암 (면역항암제사용불가)



SMO 2023

PREVENTION / Early DETECTION

- 유해물질 노출 줄이기 : 담배연기, 미세먼지 등
- 폐암조기검진 : 고위험군 대상

EARLY STAGE

- Perioperative Treatment

  Chemo+IO -> Surgery -> IO / Surgery->IO

  Surgery->(Chemo)->TKI

  Neoadjuvant target therapy (on trial)
- Inoperable cases : radiation (SABR), IGTA

- 다학제 접근, Multi-modality treatment
- Resectability 결정
- Definitive CCRT –> Durvalumab
- Definitive CCRT –> EGFR TKI (LAURA trial)

LOCALLY ADVANCED STAGE

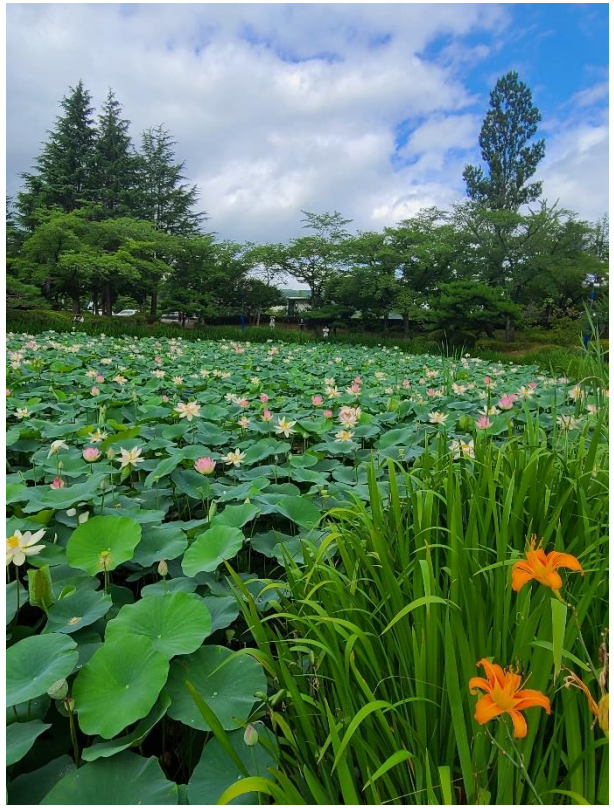
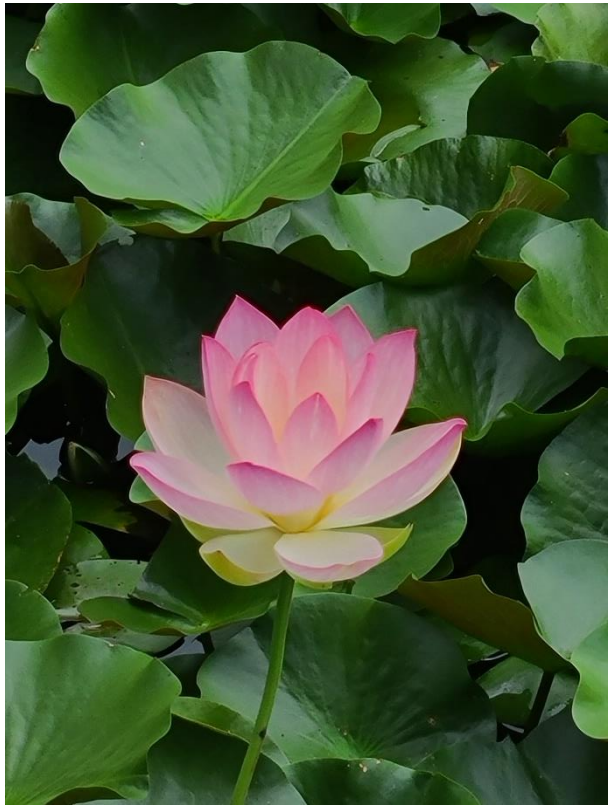
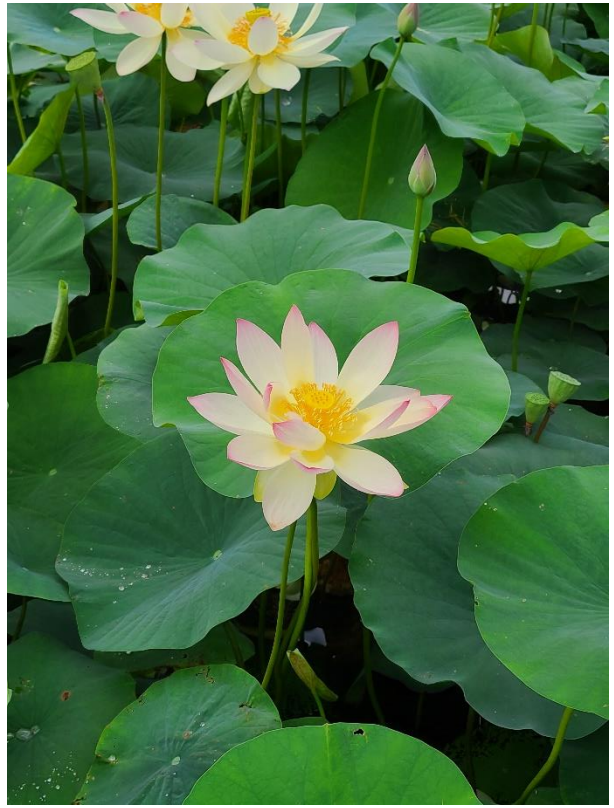
- 분자진단에 의한 치료결정
- 표적치료 ± 세포독성항암/

  면역+세포독성 항암
- 항체-약물 중합체
- Oligometastasis -> 적극적 국소치료

ADVANCED STAGE

요 약

- 폐암진단 및 치료의 발달로 최근 20년간 5년 생존율이 향상 되었음.
- 그러나 더 많은 향상이 필요하고 기대됨.
  - 금연 및 조기발견 (폐암검진 활성화, 특히 고위험군대상)
  - 수술 전 후 치료 (perioperative management) : 면역항암, 표적항암 and/or chemotherapy
  - 4기 전이성폐암 : 표적항암, 면역+세포독성항암 병합
  - 표적의 발견 및 표적에 대한 활발한 약제개발
  - 신개념의 치료 : 항체약물중합체 (antibody-drug conjugate)
  - 국소제거치료 (SABR, IGAT 등)
  - Oligometastasis에 대한 적극적인 치료


Thank you for your kind attention.