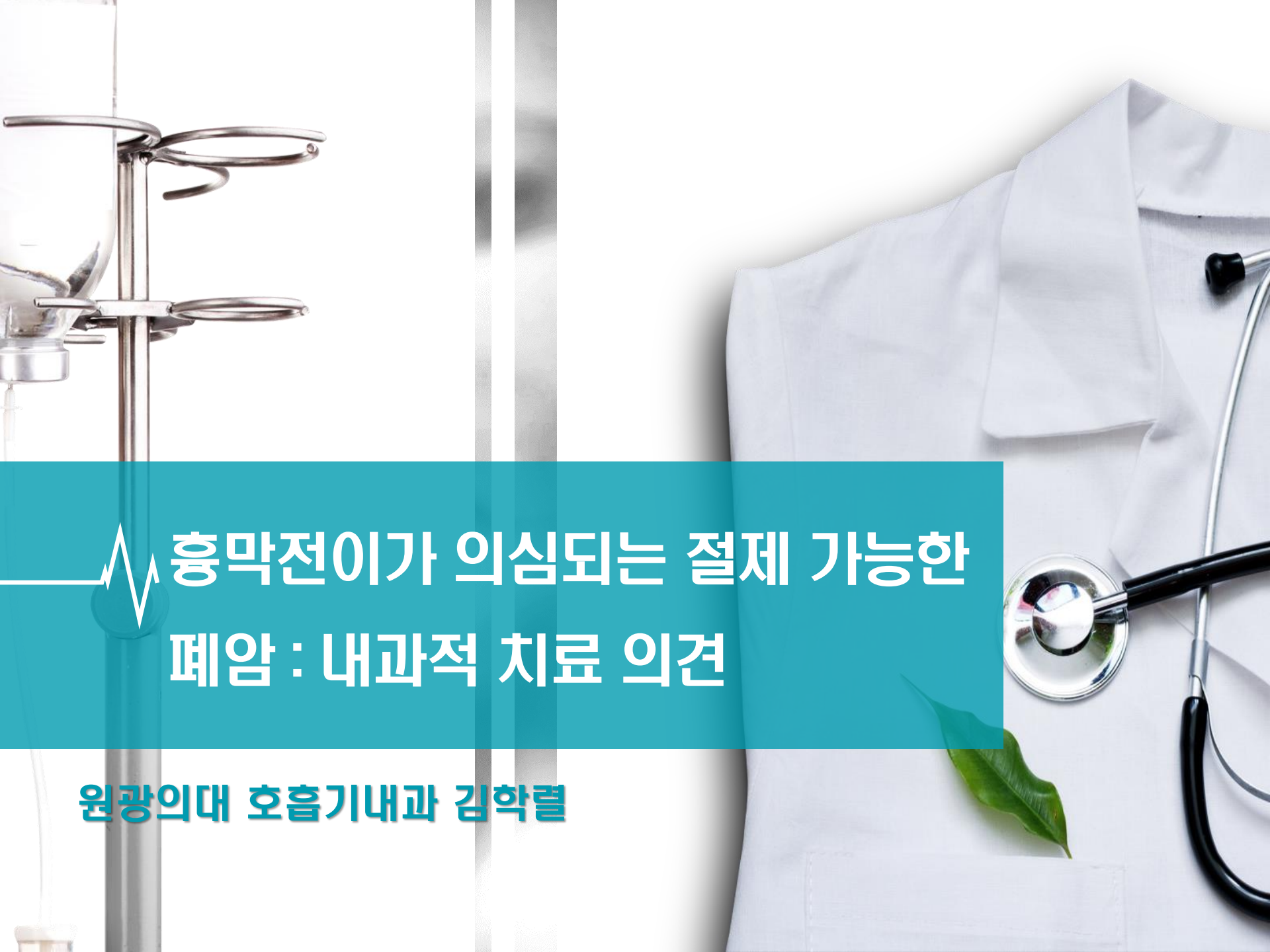


흉막전이가 의심되는 절제 가능한 폐암 : 내과적 치료 의견

원광의대 호흡기내과 김학렬

2018 KBO 프로야구 홈그라운드 승률:
445승 301패 승률 60% !!!!

Contents

01 M1a의 근거

IASLC 8th

NCCN가이드라인

7 th TNM staging of Lung Cancer

TABLE 1. Innovations Introduced in the seventh Edition of the Tumor, Node, and Metastases Classification of Lung Cancer

Descriptor/TNM	Category/Stage in the sixth Edition	Category/Stage in the seventh Edition
Tumor size ≤ 2 cm	T1	T1a
Tumor size > 2 cm but ≤ 3 cm	T1	T1b
Tumor size > 3 cm but ≤ 5 cm	T2	T2a
Tumor size > 5 cm but ≤ 7 cm	T2	T2b
Tumor size > 7 cm	T2	T3
Additional tumor nodule(s) in the same lobe of the primary tumor	T4	T3
Additional tumor nodule(s) in another ipsilateral lobe	M1	T4
Pleural dissemination (malignant pleural effusion and separated pleural nodules)	T4	M1a
Pericardial dissemination (malignant pericardial effusion and separated pericardial nodules)	N/A	M1a
Intrathoracic metastases	M1	M1a
Extrathoracic metastases	M1	M1b
T2b N0 M0	IB	IIA
T2a N1 M0	IIB	IIA
T4 N0-1 M0	IIIB	IIIA

Pleural dissemination (malignant pleural effusion and separated pleural nodules) **T4 → M1a**

- **First staging system proposed by IASLC**
- **Since 2010**
- **Analyzed 81,495 patients between1990 to 2000**
- **New lymph node map (IASLC lymph node map)**
- **New definition of pleural invasion**

Rami-Porta et al. JTO 2014

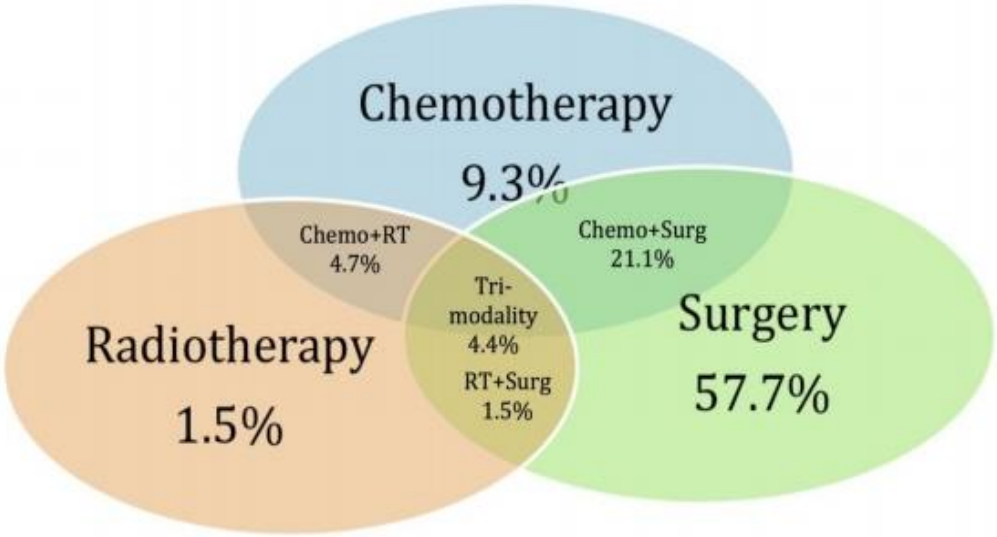
Dataset for 8th edition

From 1999-2010 (2009-2013)

77,156 patients

- Initially 94,708 patients, excluded 17,752 patients
- NSCLC 70,967 / SCLC 6,189
- From Europe (49%), Asia (44%), North America (5%), Australia and South America

Treatment modalities



Rami-Porta et al. JTO 2015

Recommendation for M descriptors

M1a (intrathoracic)

- As it is; pleural / pericardial effusion, contralateral/bilateral tumor nodules, pleural / pericardial nodules and multiple M1a descriptors

M1b (single extrathoracic)

- Single metastasis in a single organ
- Brain, liver, bone, distant LN / skin / peritoneum and adrenal gland
- Categorization of individual organs prospectively

M1c (multiple extrathoracic)

- Multiple metastases in a single organ or in several organs
- Recommend to register in detail about number of metastatic lesions and the number of involved organs

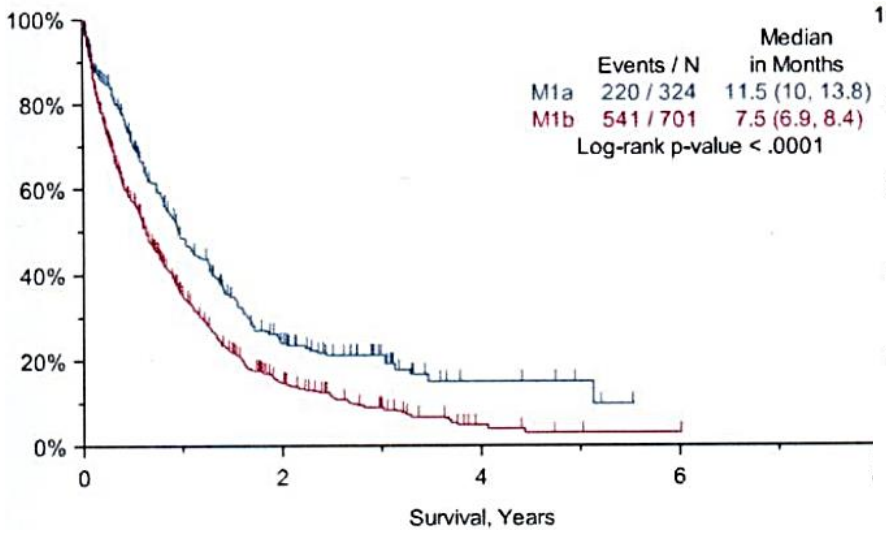
Eberhardt et al. JTO 2015

M descriptors

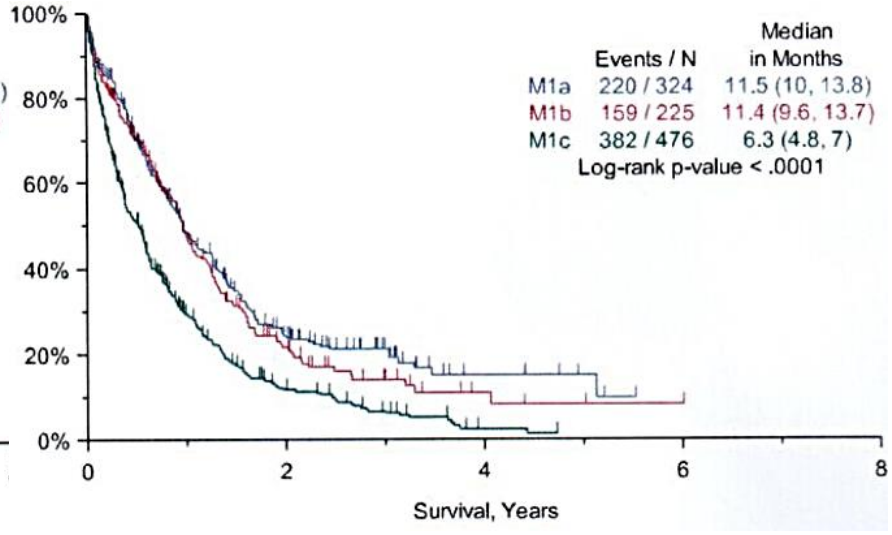
Prognostic Impact of Single and Multiple Metastatic Lesions in a Single Organ vs Multiple Metastatic Sites

Proposed Category	Variable	Overall Survival		
		n/N (%)	HR (95% CI)	*P* Value
M1a	M1a	324/1025 (32)	Reference level	
M1b	M1b, single organ/lesion	225/1025 (22)	1.11 (0.91, 1.36)	0.308
M1c	M1b, single organ/multiple lesions	229/1025 (22)	1.63 (1.34, 1.99)	<0.001
	M1b, multiple organs	247/1025 (24)	1.85 (1.52, 2.24)	<0.001

P value from score χ^2 test in Cox regression.
HR, hazard ratio; 95% CI, 95% confidence interval.



7th edition and proposed 8th editiion M caegories

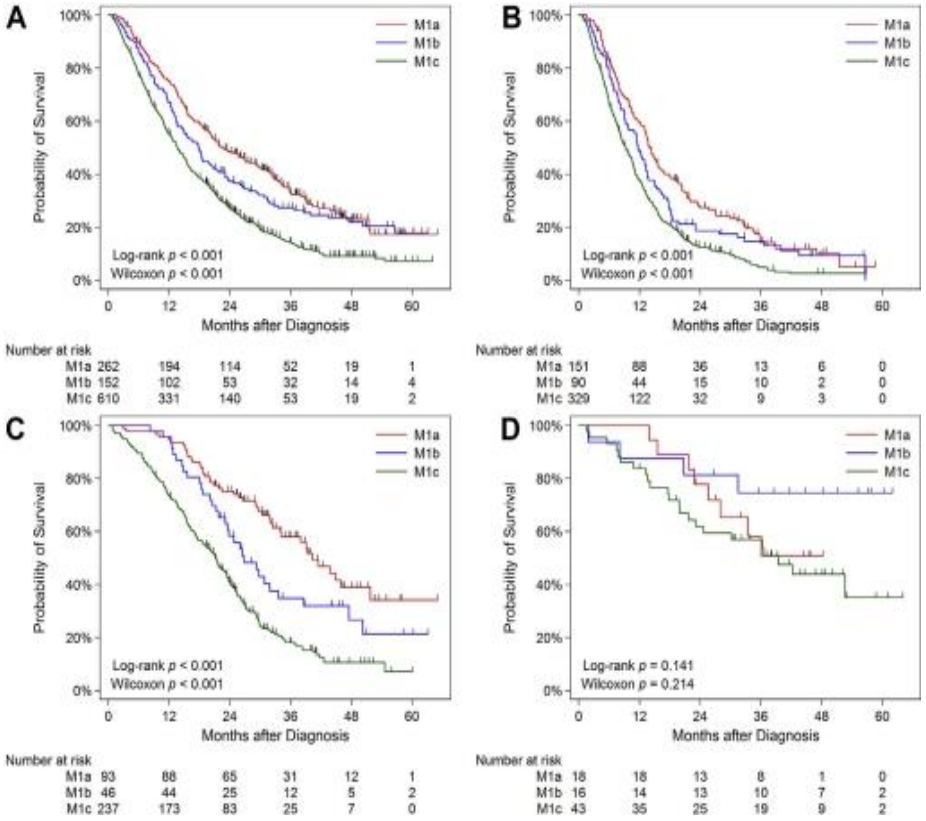


New M1b showed similar survival with M1a

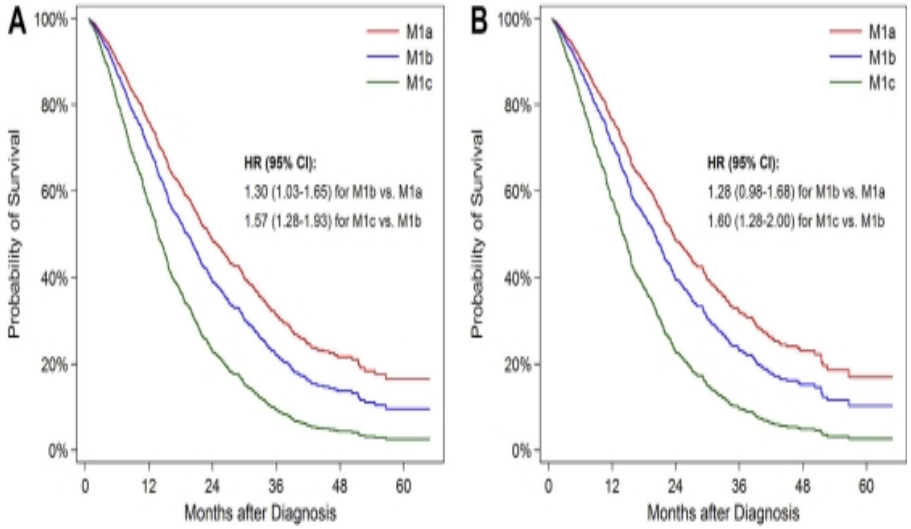
Eberhardt WEI et al. JTO 2015

Prognostic Impact of Newly Proposed M Descriptors in TNM Classification of NSCLC

1024 stage IV NSCLC pts in 2011-2014



< Type별 Kaplan-Meier 생존곡선 >
A) Negative B) EGFR-mutated C) ALK-translocated D) Cohort



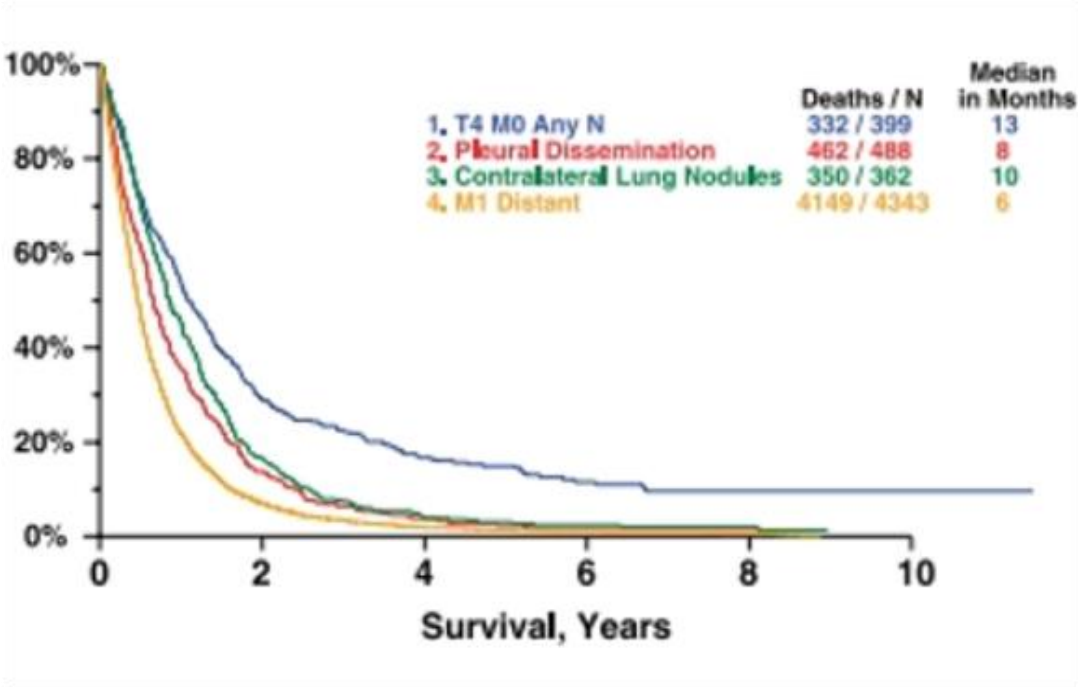
< 전체 Kaplan-Meier 생존곡선 >

중간생존률:
M1a 22.5 M, M1b 17.8 M, M1c 13.6 M

Shin J et al. J Thorac Oncol 2017;12:520

같은 M1a라도 생존율의 차이가 있다!!

	흉막전이 ± 악성흉수	반대편 폐전이
중간생존기간	8M	10M
1년생존율	36%	45%
5년생존율	2%	3%



Postmus PE et al. J Thorac Oncol 2007;2:686

NCCN Guidelines Version 1.2019
Non-Small Cell Lung Cancer

NCCN Guidelines Index
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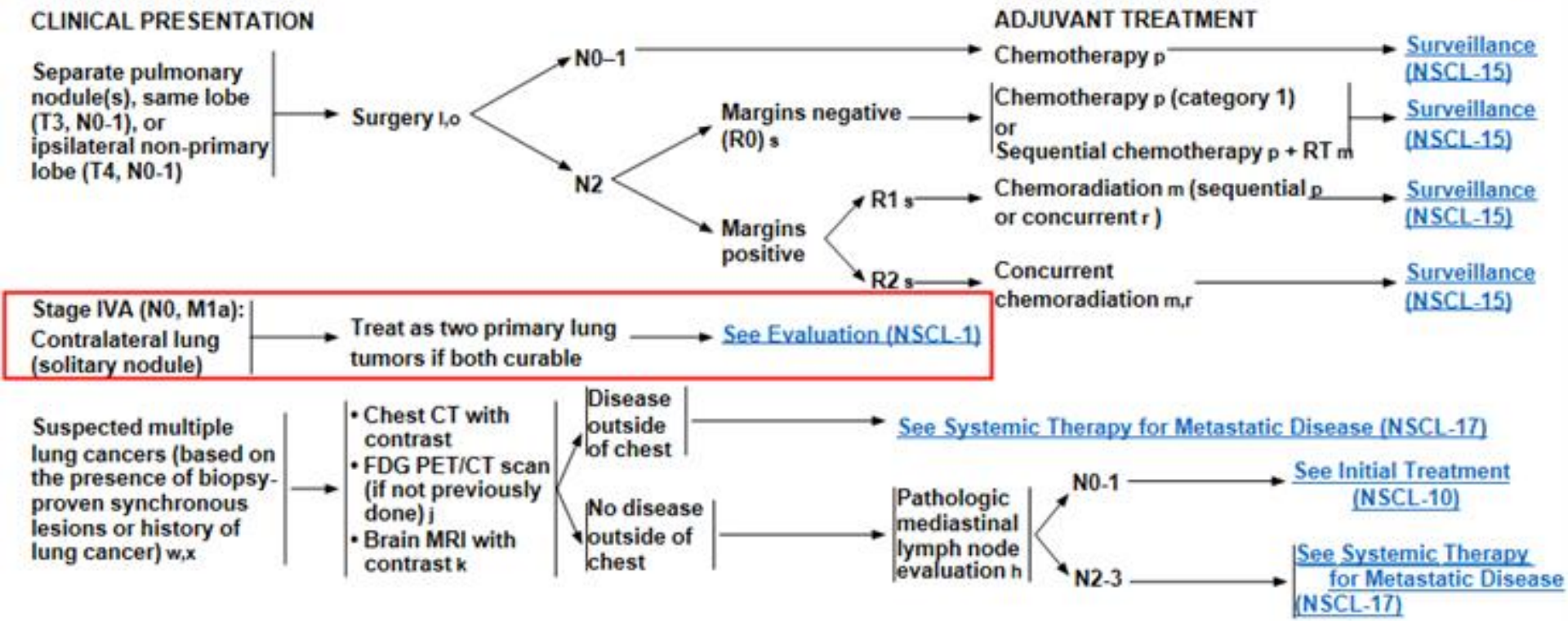


h Methods for evaluation include mediastinoscopy, mediastinotomy, EBUS, EUS, and CT-guided biopsy.

j PET/CT performed skull base to knees or whole body. Positive PET/CT scan findings for distant disease need pathologic or other radiologic confirmation. If PET/CT scan is positive in the mediastinum, lymph node status needs pathologic confirmation.

k If MRI is not possible, CT of head with contrast.

l See Principles of Surgical Therapy (NSCL-B).

m See Principles of Radiation Therapy (NSCL-C).

o After surgical evaluation, patients likely to receive adjuvant chemotherapy may be treated with induction chemotherapy as an alternative.

p See Chemotherapy Regimens for Neoadjuvant and Adjuvant Therapy (NSCL-D).

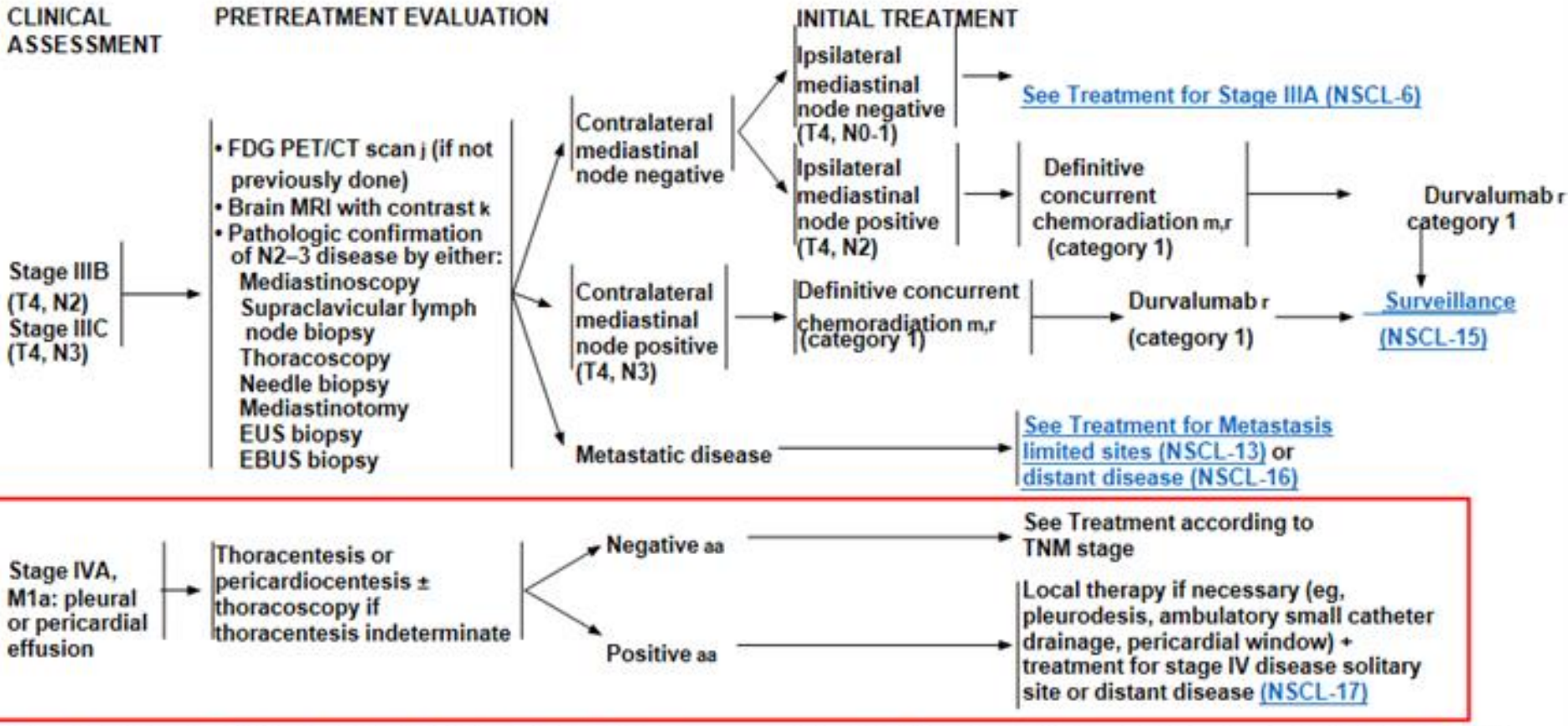
r See Chemotherapy Regimens Used with Radiation Therapy (NSCL-E).

s R0 = no residual tumor, R1 = microscopic residual tumor, R2 = macroscopic residual tumor.

w Lesions with different cell types (eg, squamous cell carcinoma, adenocarcinoma) may be different primary tumors. This analysis may be limited by small biopsy samples. However, lesions of the same cell type are not necessarily metastases.

x For guidance regarding the evaluation, workup, and management of subsolid pulmonary nodules, please see the diagnostic evaluation of a nodule suspicious for lung cancer (DIAG-1).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



j PET/CT performed skull base to knees or whole body. Positive PET/CT scan findings for distant disease need pathologic or other radiologic confirmation. If PET/CT scan is positive in the mediastinum, lymph node status needs pathologic confirmation.

k If MRI is not possible, CT of head with contrast.

m See Principles of Radiation Therapy (NSCL-C).

r See Chemotherapy Regimens Used with Radiation Therapy (NSCL-E).

aa Most pleural (pericardial) effusions with lung cancer are a result of the tumor. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumor, and fluid is non-bloody and not an exudate. If these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging descriptor.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

02 폐암의 흉막전이에 대한 수술적 치료

Positive data

Negative data

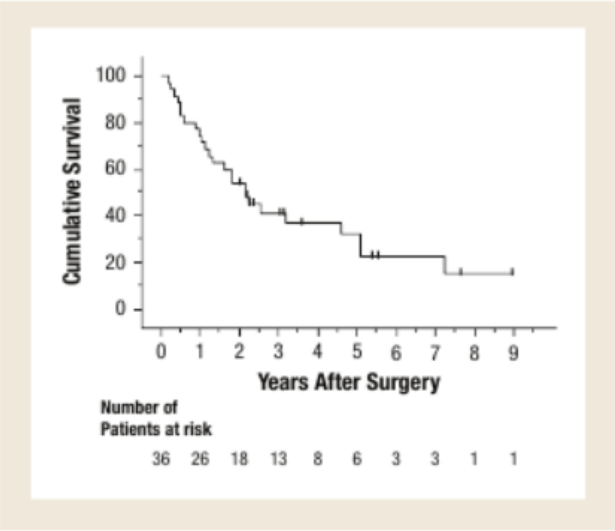
예후 및 예측인자

Characteristics of studies of NSCLC Pleural Metastases Managed with surgery

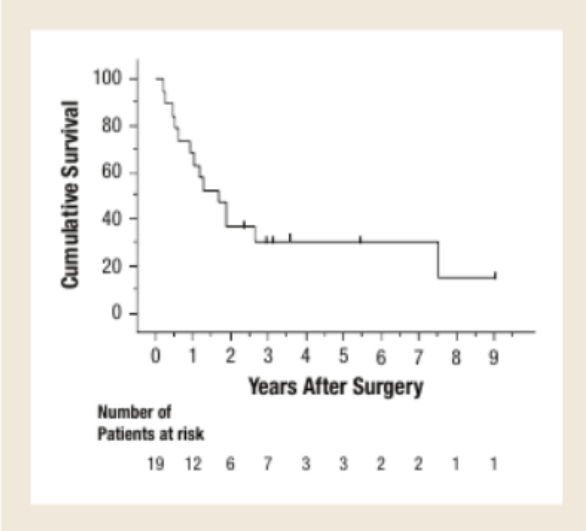
Author, Year of publication	N	Age	Performance Status (ECOG)	Operative Procedures	Perioperative outcomes	Significant Factors on Multivariate Analysis	Survival
Hanagiri, 2012	17	65.8	0-1	Anatomic and non-anatomic resection	NR	NR	25.1%, 5-year
Fukuse, 2001	49	62.3	NR	Explaratory thoracotomy anatomic and non-anatomic resection intraoperative chemotherapy	NR	Tumor size, pleural dissemination	26.7% 3-year
Ichinose, 2001	100	63	NR	Anatomic and non-anatomic resection intraoperative chemotherapy (n=47)	NR	Gender, Clinical and pathologic Nodal status, Intrapleural treatment, Intrapleural and Adjuvant treatment	31.8%, 3-year 22.8%, 5-year
Liu, 2015	80	58	NR	Anatomic and non-anatomic resection	NR	Smoking status and Adjuvant treatment	31%, 5-year
Okamoto, 2012	100	62.7	NR	Anatomic and non-anatomic resection intraoperative chemotherapy (n=37)	NR	Pathologic nodal status, pneumonectomy	41.4%, 3-year 23.7%, 5-year
Mordant, 2011	32 study croup, 38 control	59	NR	Pneumonectomy or Lobectomy VS Exploratory Thoracotomy	Study:5 Death:11 complications: control : 0 Deaths, 0 complications	No significant factors	Study: 16%, 5-year Control :0, 5-year
Kimura, 2010	19	67.9	NR	Anatomic and non-anatomic resection intraoperative chemotherapy (n=12)	NR	NR	MST 28.5 month
Yamaguchi, 2015	11	55	0-1	Induction chemoradiation followed by Extrapleural pneumonectomy	NR	NR	33.3% 3-year 22.2% 5-year

Results of a surgical resection for pts with stage IV NSCLC

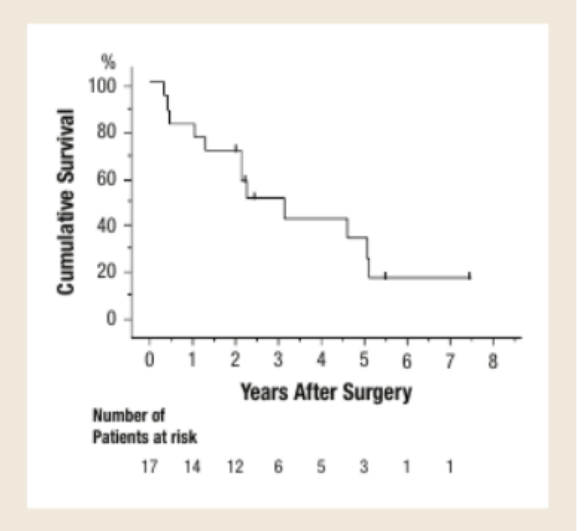
흉막전이가 있는 환자는 수술 후 생존율이 더 낮다



Stage IV NSCLC post OP 5-yr survival rate : 26.8%



NSCLC pts with distant metastasis post-OP 5-yr survival rate : 30.1%



NSCLC pts with pleural dissemination post-OP 5-yr survival rate : 25.1%

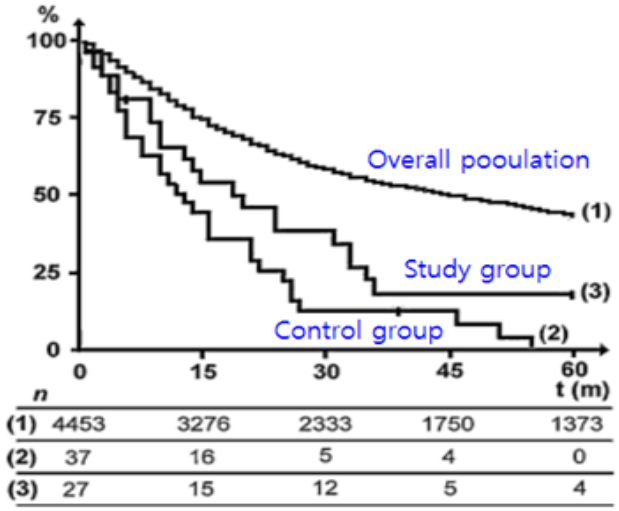
- 36 pts who underwent surgical resection for stage IV NSCLC between 1999 and 2008
- All pts had either synchronous distant metastasis, or pleural dissemination
- 17 pts had ipsilateral pleural dissemination

Hanagiri T et al. Clin Lung Cancer 2012;13:220

Surgery for metastatic pleural extension of NSCLC

흉막전이를 수술적 절제를 하면 생존율의 이득이 있다

- Overall population : Population undergoing pulmonary resection in a curative attempt (n=4668)
- Control group : Exploratory thoracotomy in case of unexpected disseminated carcinomatous pleuritis (n=38)
- Study group : Undiagnosed pleural malignant disease (M1a) discovered during thoracotomy
  (n=32, When feasible, patients underwent complete surgical resection)
  Lobectomy (n=23), Pneumonectomy (n=9)



OS established with the K-M method (Y axis : overall survival %, X axis : time (months)

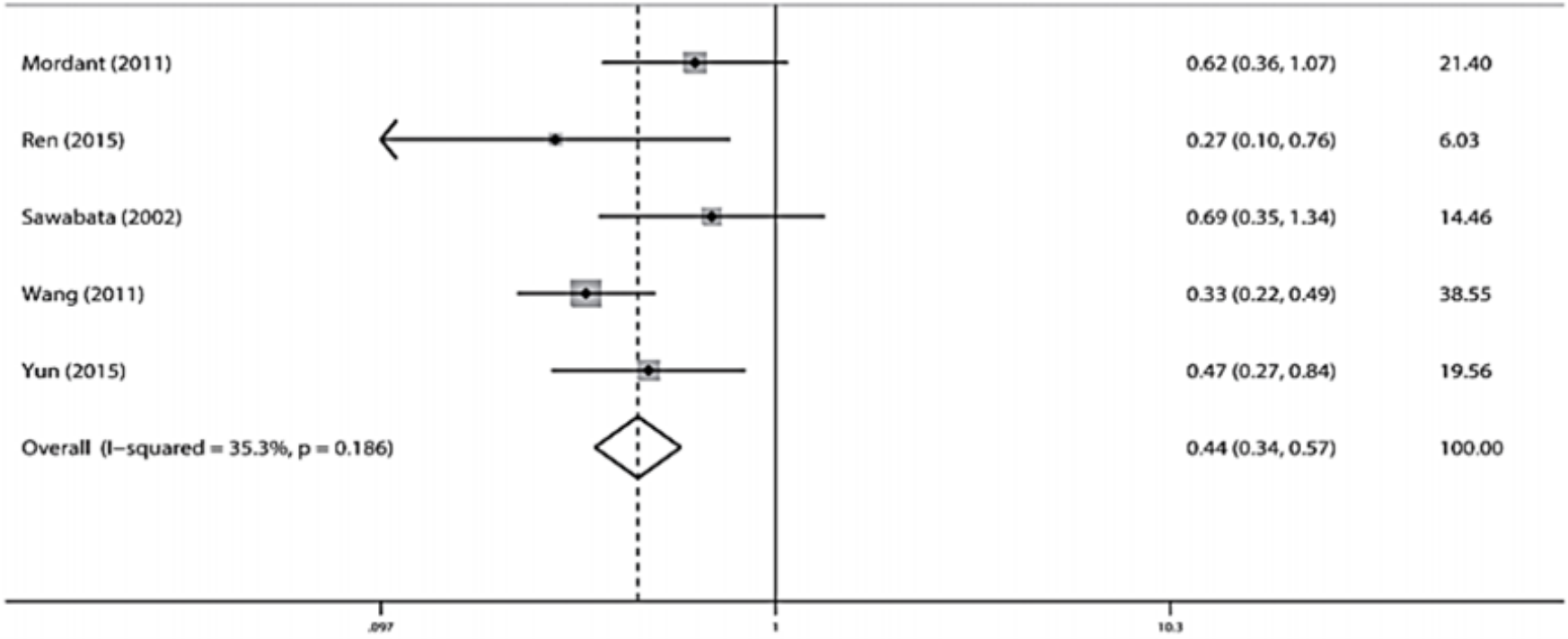
	Overall population (n=4668)	Control group (n=38)	Study group (n=32)
Death from cancer	1525 (52.9%)	26 (93%)	16 (57%)
Death from other cause	815 (28%)	1 (4%)	7 (15%)
Cause of death unknown	542 (18.8%)	1 (4%)	5 (16%)
5-year survival rate	44.1%	0%	16%
Median (months)	47	13	15

Mordant et al. Eur J Cardiothorac Surg 2011;40:1444

Should primary tumor be resected for NSCLC with malignant pleural disease unexpectedly found during operation?—a systemic review and meta-analysis

흉막전이의 수술적 절제에 대한 메타분석결과

- Nine articles with a total number of 861 pts
- Five of them compared the survival benefit between exploration and resection
- Four studies investigated the prognostic factors in these pts



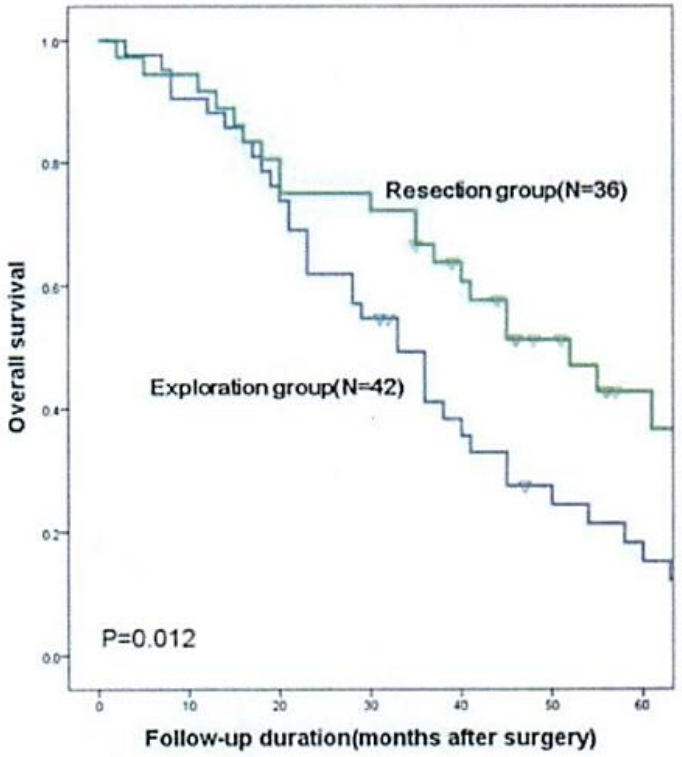
Xu Y et al. J Thorac Dis 2016;8:2843

Surgical Outcomes after Pulmonary Resection for Non-Small Cell Lung Cancer with Localized Pleural Seeding First Detected during Surgery

흉막전이의 수술적 절제에 대한 국내보고

- A retrospective analysis - 3,975 pts who underwent surgery for NSCLC from 2000 to 2011.
- 78 (2.0%) pts - unexpected pleural seeding detected during surgery
- Exploration with pleural biopsy - 42 pts (exploration-only group)
- Pulmonary resection, including for the main tumor
  - 36 pts (resection group; sublobar resection in 12, lobectomy in 21, and pneumonectomy in 3 pts) 1

	Exploration G	Resection G
3-yr survival rate	41.1%	66.7%
5-yr survival rate	15.2%	42.7%
Median survival time	33 M	52 M
		P=0.012



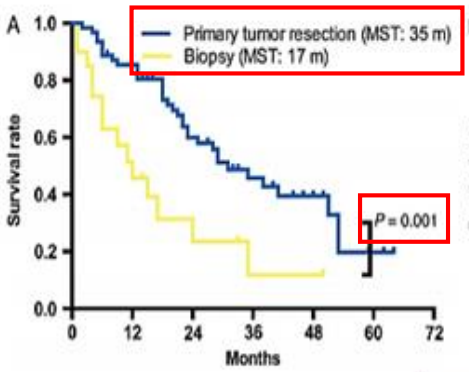
Yun JK et al. Thorac Cardiovasc Surg 2018;66:142

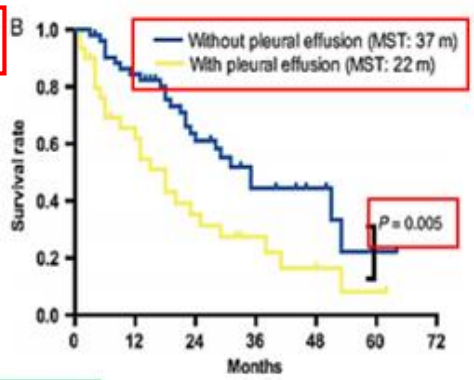
흉막전이의 수술적 제거- 어떤 환자에 이득이 있는가?

Primary tumour resection showed survival benefits for NSCLC with unexpected malignant pleural dissemination

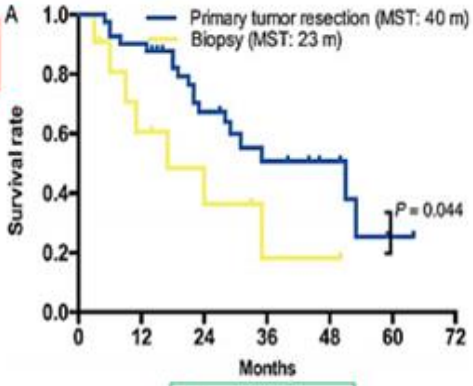
수술 중 예기치 않게 발견된 흉수가 없는 흉막전이

- No consensus concerning on-site operative decisions for unexpected, intraoperatively encountered malignant pleural disseminations
- 9576 NSCLC → 83 cases (0.9%)
- No PE 52 cases, minimal PE (<300ml) 31 cases

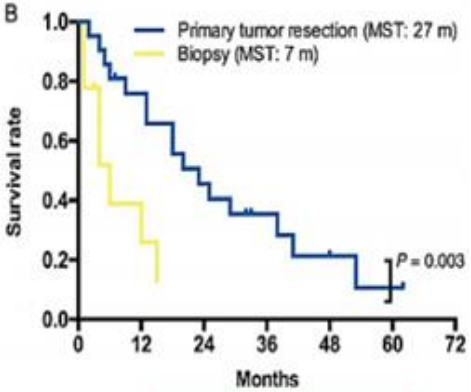




83 cases



No PE cases



Minimal PE cases

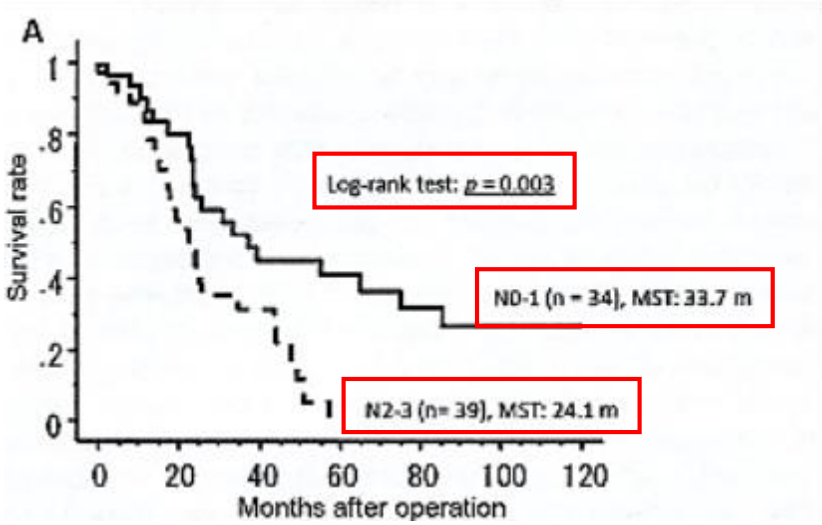
- Pts with MPN but without PE had better survival compared with PE
- Primary tumour resection had survival benefits for pts with unexpected intraoperatively proven MPN
- Pulmonary resection including the main tumor - increase long-term survival for NSCLC pts with localized pleural seeding first detected during surgery, without a significant increase in hospital mortality or morbidity

Ren YJ et al. Interact Cardovasc Thorac Surg 2016;22:321

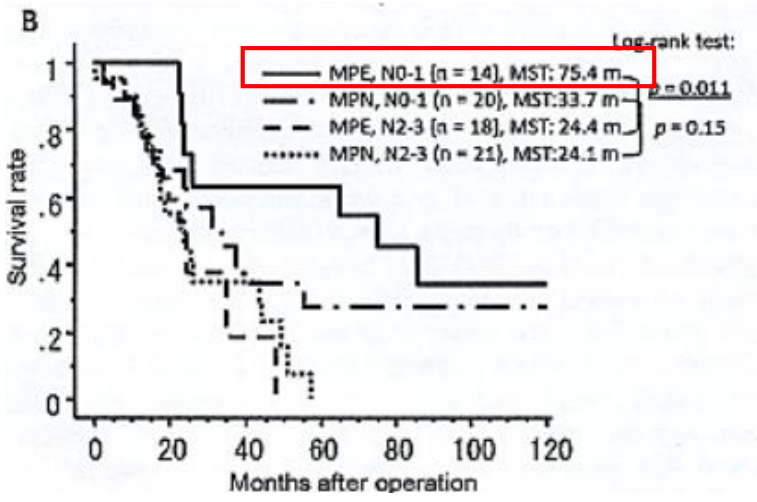
Pulmonary resection for lung cancer with MPD first detected at thoracotomy

N0-1 악성흉수에서 수술적 제거한 경우 생존율의 이득

- 1623 NSCLC pts, who underwent surgery, retrospectively reviewed.
- A hundred patients (6.2%) were classified with pathological stage IV.
- 73 pts with MPD, which included 32 with effusion without nodules (MPE) and 41 with nodules with or without effusion (MPN)
- Intra-or postop pleural chemotherapy was administered to 37 MPD pts



A. Postop OS of pts with MPD according to N status



B. Postop OS of pts with MPE, MPN stratified by N status

Okamoto et al. Eur J Cardiothorac Surg 2012;41:25

Pulmonary resection for lung cancer with MPD first detected at thoracotomy

N0-1 흉막전이 폐암환자에서 수술적 제거한 경우 생존율의 이득

Table 3: Multivariate analysis for prognostic factors in patients with malignant pleural disease

		HR	95% CI	*p*-Value
Age (y)	<65	1		
	>65	0.92	0.51–1.66	0.79
Gender	Male	1		
	Female	1.1	0.59–2.05	0.77
Nodal status	N0–1	1		
	N2–3	2.39	1.21–4.74	0.01
Procedure	Others	1		
	Pneumonectomy	5.29	1.48–18.9	0.013
Pleural disease	MPE	1		
	MPN	1.29	0.71–2.32	0.4

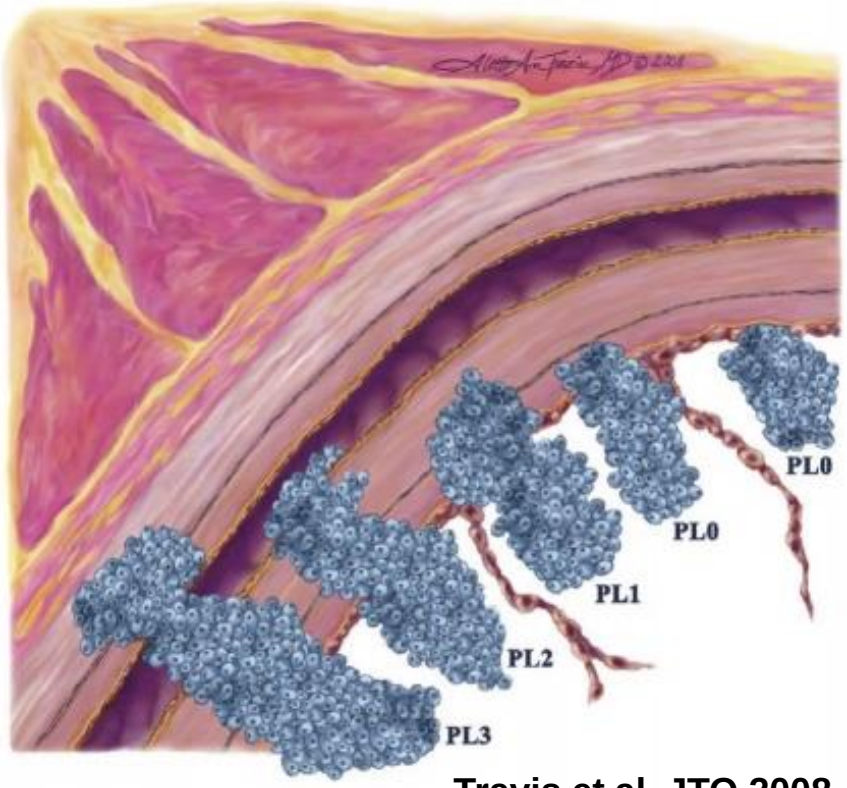
CI = confidence interval, HR = hazard ratio, MST = median survival time, MPE = malignant pleural effusion without nodules, MPN = malignant pleural nodules with or without effusion.

- **MPD status (MPE or MPN) was not significant**
- **N status (N0-1 VS N2-3)**
- **Type of surgical procedure (Pneumonectomy vs other procedure) were found to be significant prognostic factors**

Okamoto et al. Eur J Cardiothorac Surg 2012;41:25

Level of pleural invasion effects on prognosis in lung cancer

Visceral pleural invasion (-)수술한 경우 생존율의 이득



Travis et al. JTO 2008

- **Modified Hammar Classification**
  - PL0; within the subpleural lung parenchyme
  - PL1; invades beyond the elastic layer
  - PL2; invades the pleural surface
  - PL3; invades the any components of parietal pleura

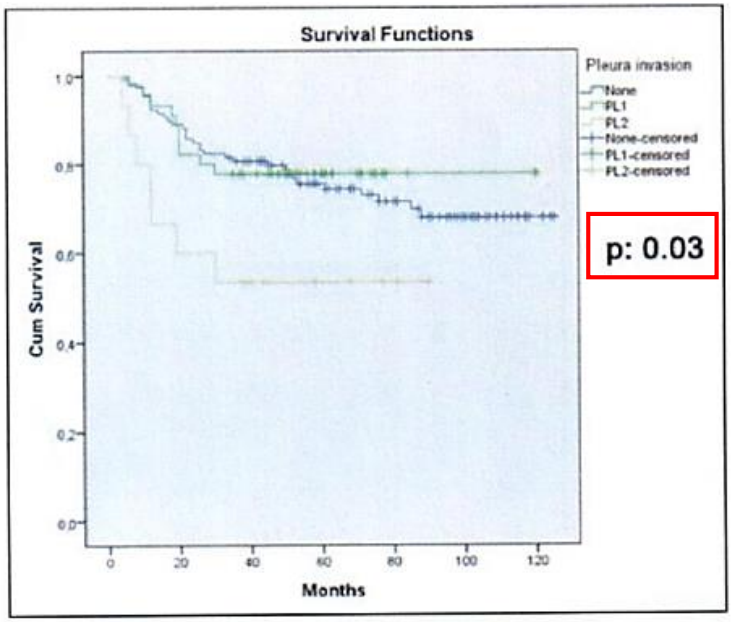
Tanju S et al. Tumori 2018; Aug 30. Epub ahead of print

Level of pleural invasion effects on prognosis in lung cancer

Visceral pleural invasion (-)수술한 경우 생존율의 이득

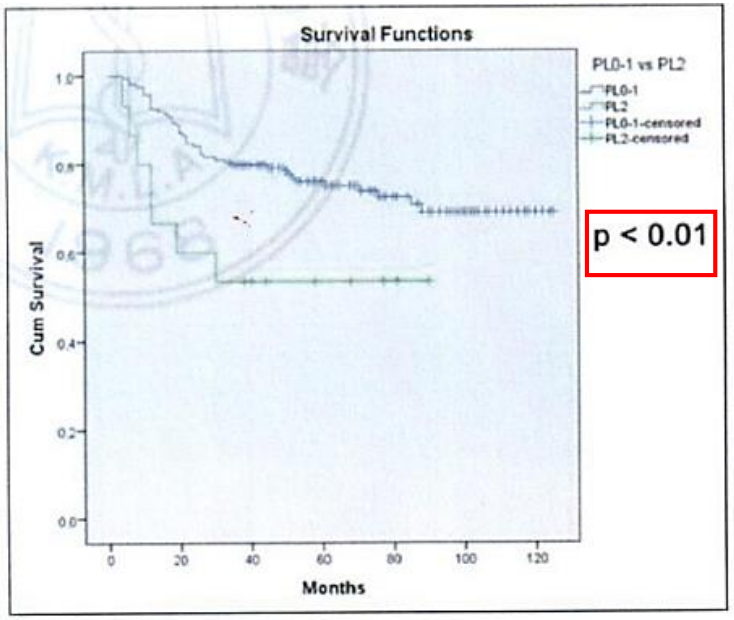
- 233 pts underwent lung resection
- Median F/U – 59 M (range 4-126)
- VPI extent - PL0 in 119 (65.7%) pts, PL1 in 47 (26%) pts, PL2 in 15 (8%) pts

Fig 2.



5-yr OS - 74.7%:PL0, 77.8%:PL1, 53.3%:PL2
P=0.03

Fig 4.



Subgroup analysis,
Significant in PL0 vs PL2 (p=0.02) and PL1 vs PL2 (p=0.04)

Tanju S et al. Tumori 2018; Aug 30. Epub ahead of print

Survival of M1a NSCLC Treated Surgically: A Retrospective Single-Center Study

흉막전이의 수술적방법은?

- **Type of lung resection performed for primary tumor (80** pts**)**

  : **Complete resection** (**43** pts)

  Limited resection (**37** pts)

- **Four to six cycles of cisplatin-based adjuvant chemotherapy**

  were used as standard of care in pts

Site of metastasis	
Pleural nodules metastasis	51
Pleural effusion	7
Contralateral lung	9
Diaphragm nodules metastasis	5
Pericardium nodules metastasis	8
Histology	
Adenocarcinoma/squamous carcinoma/large cell/others	55/16/5/4
Surgical procedure	
Complete resection/limited resection	43/37
Adjuvant therapy,[b] Yes/No	66/14

Table 2 Prognostic factors: univariate analysis

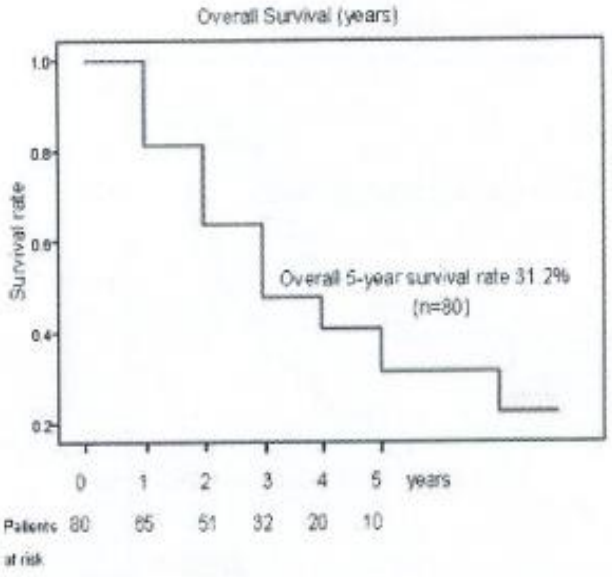
Variable	5-y survival rate	*p*
Total	31.2%	
Gender (female/male)	37.6%/28.0%	0.41
Age		
<60 y/60 y or older	26.6%/34.9%	0.513
Smoking Index (<400/≥400)	18.6%/40.3%	0.006
Current drinker/nondrinker	21.4%/34.8%	0.343
p-N		
pN1–2/pN0	42.4%/20%	0.155
pN0–1/pN2	29.2%/41.7%	0.348
Site of metastasis		
Pleural effusion/others	12.5%/36.8%	0.069
Histology		
Adenocarcinoma/others	32.3%/25.4%	0.074
Surgical procedure		
Complete resection/ limited resection	16.3%/31.4%	0.067
Adjuvant therapy		
Yes/no	47%/23.1%	0.013

Liu et al. Thorac Cardiovasc Surg 2015;63:577

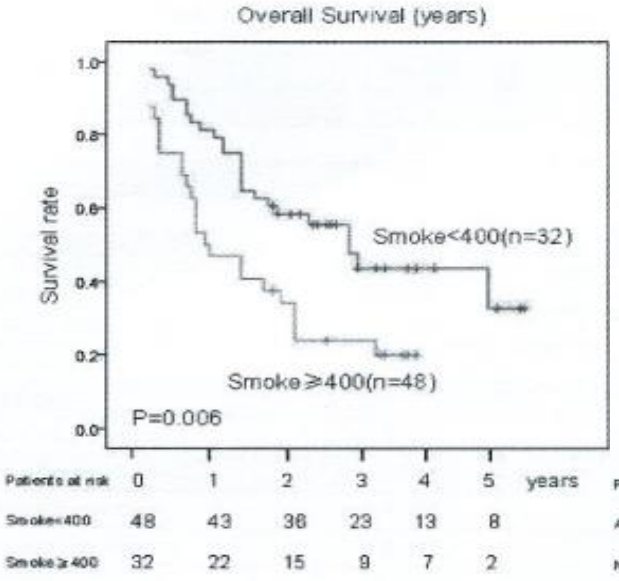
Survival of M1a NSCLC Treated Surgically: A Retrospective Single-Center Study

흉막전이의 수술적방법은?

Overall 5-yr survival rate
31.2% (median 34.3 M)

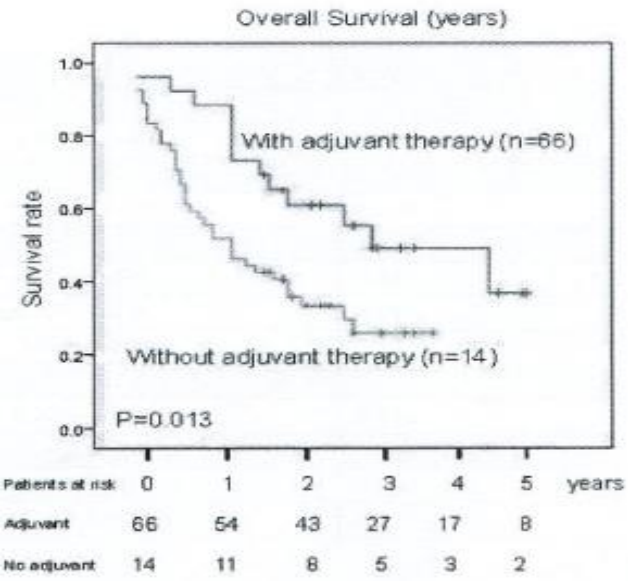


Postoperative survival according to smoking index



≥400 5-yr survival rate 18.6%
<400 5-yr survival rate 40.3%

The Kaplan-Meier survival analysis based on multimodality therapy (with and without postoperative adjuvant therapy)



Adjuvant Tx - improved 5-yr survival (47.0% vs 23.1%)

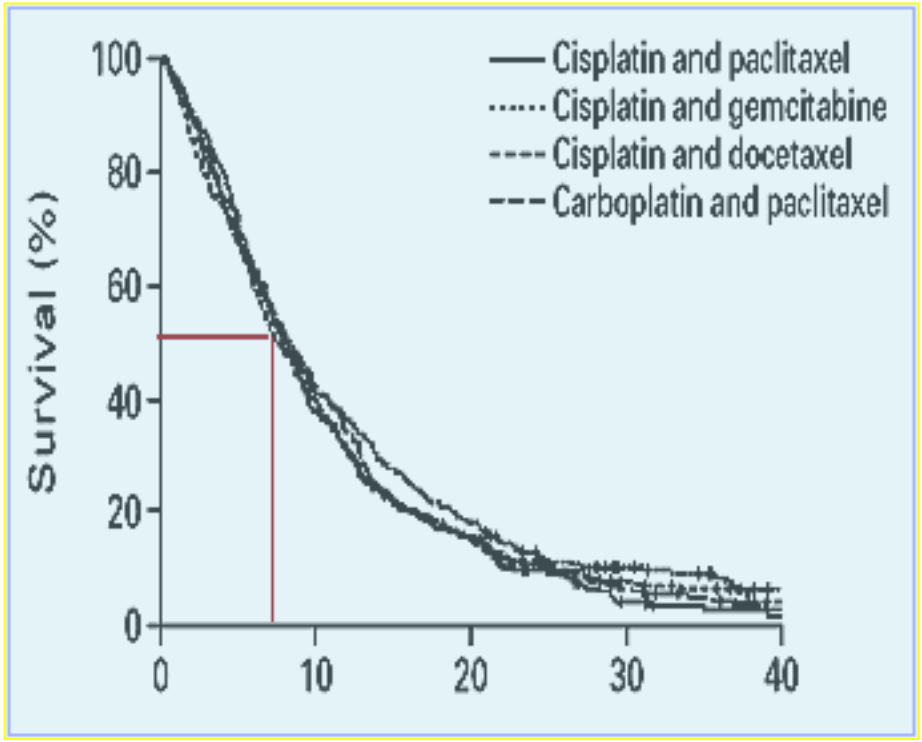
Liu et al. Thorac Cardiovasc Surg 2015;63:577

03 폐암의 흉막전이에 대한 내과적 치료

Target 치료제

면역항암제

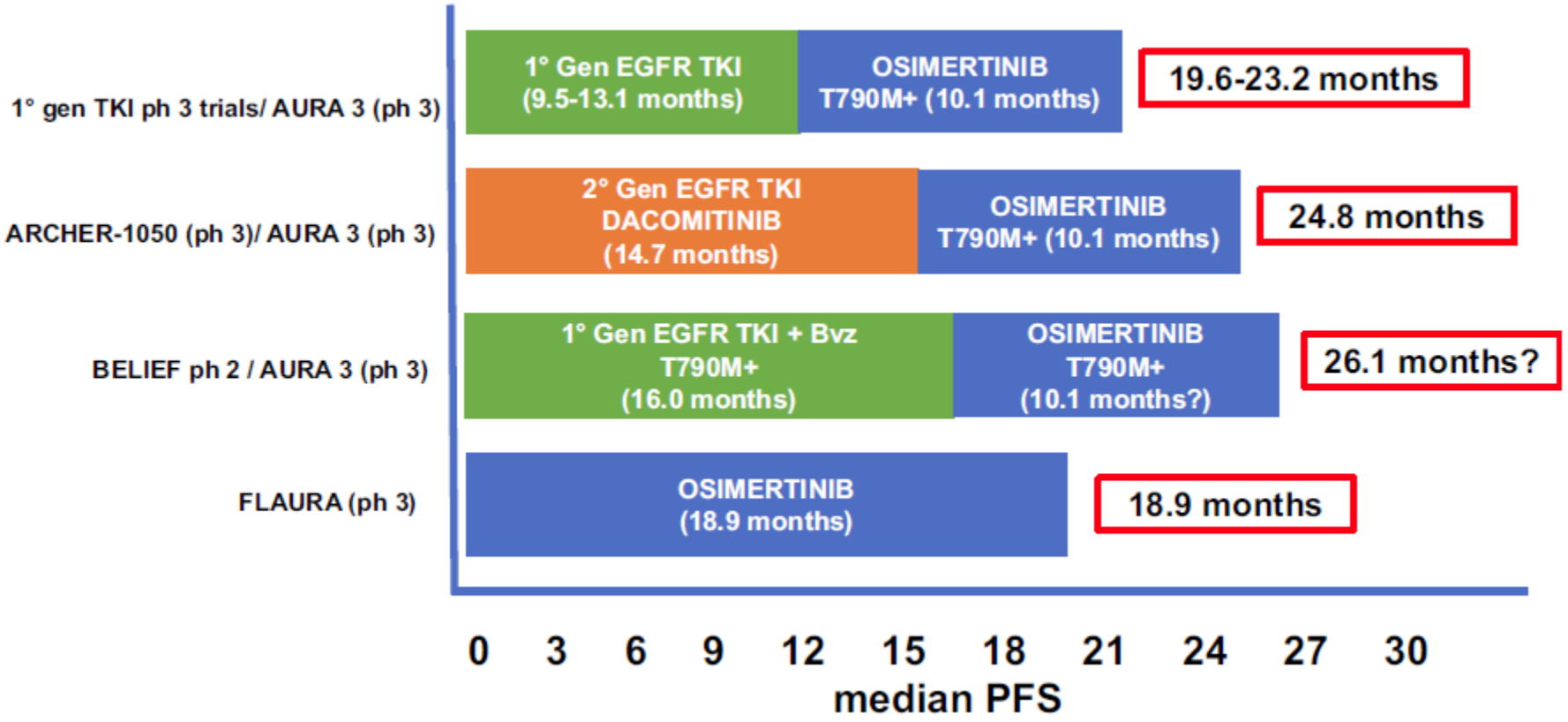
Platinum + Paclitaxel, Docetaxel, Gemcitabine or Vinorelbine



- Response Rate 20%
- Median Survival 8 months
- 1-Year Survival 35%
- 2-Year Survival 10%

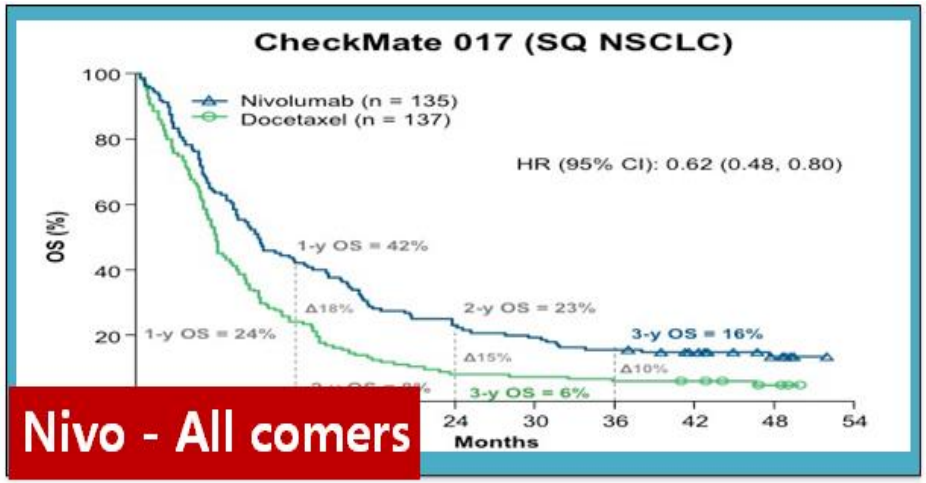
N Engl J Med 2002

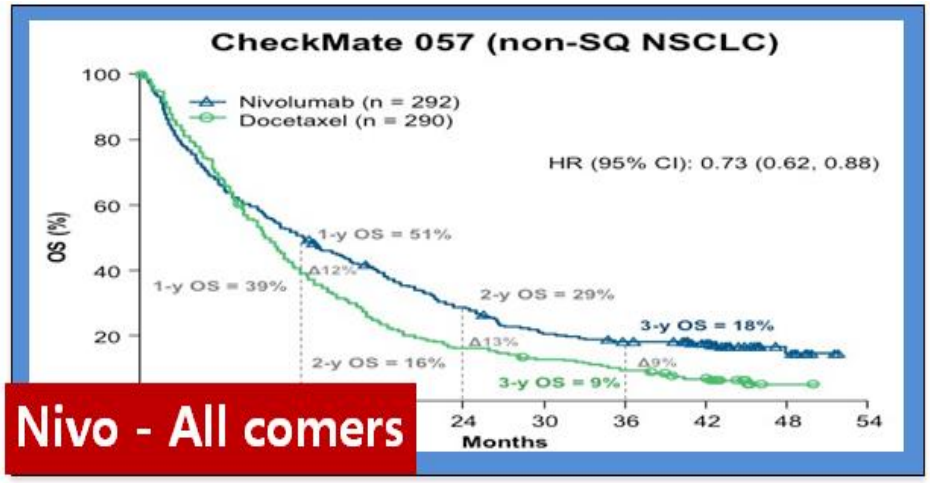
Sequential treatment strategies for EGFR

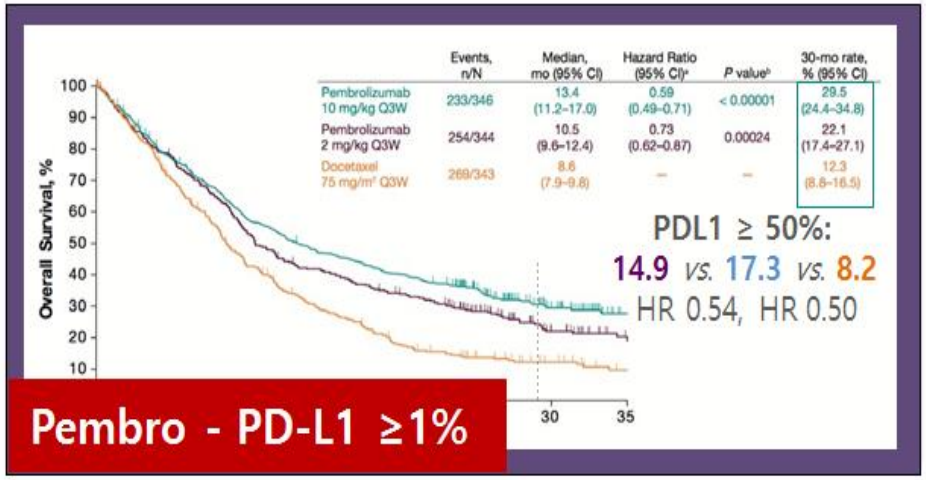


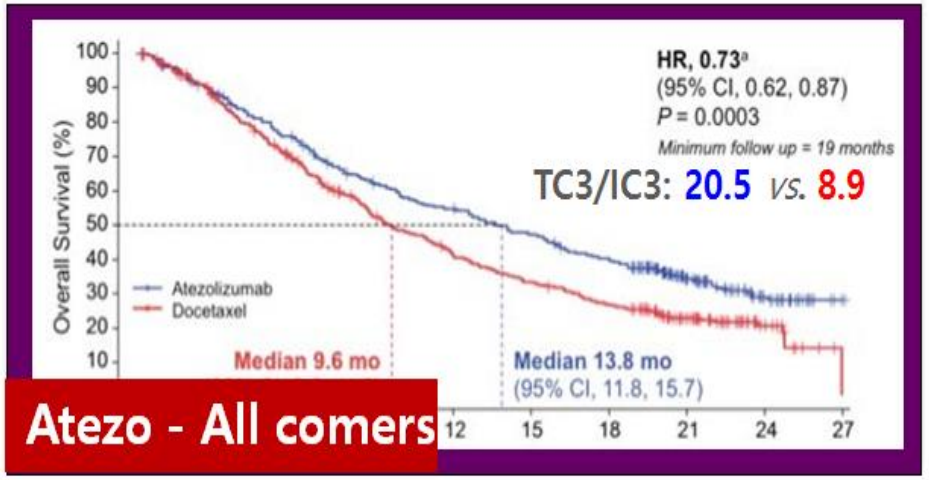
J Thorac Oncol 2018;13:301-322

Second-Line IO



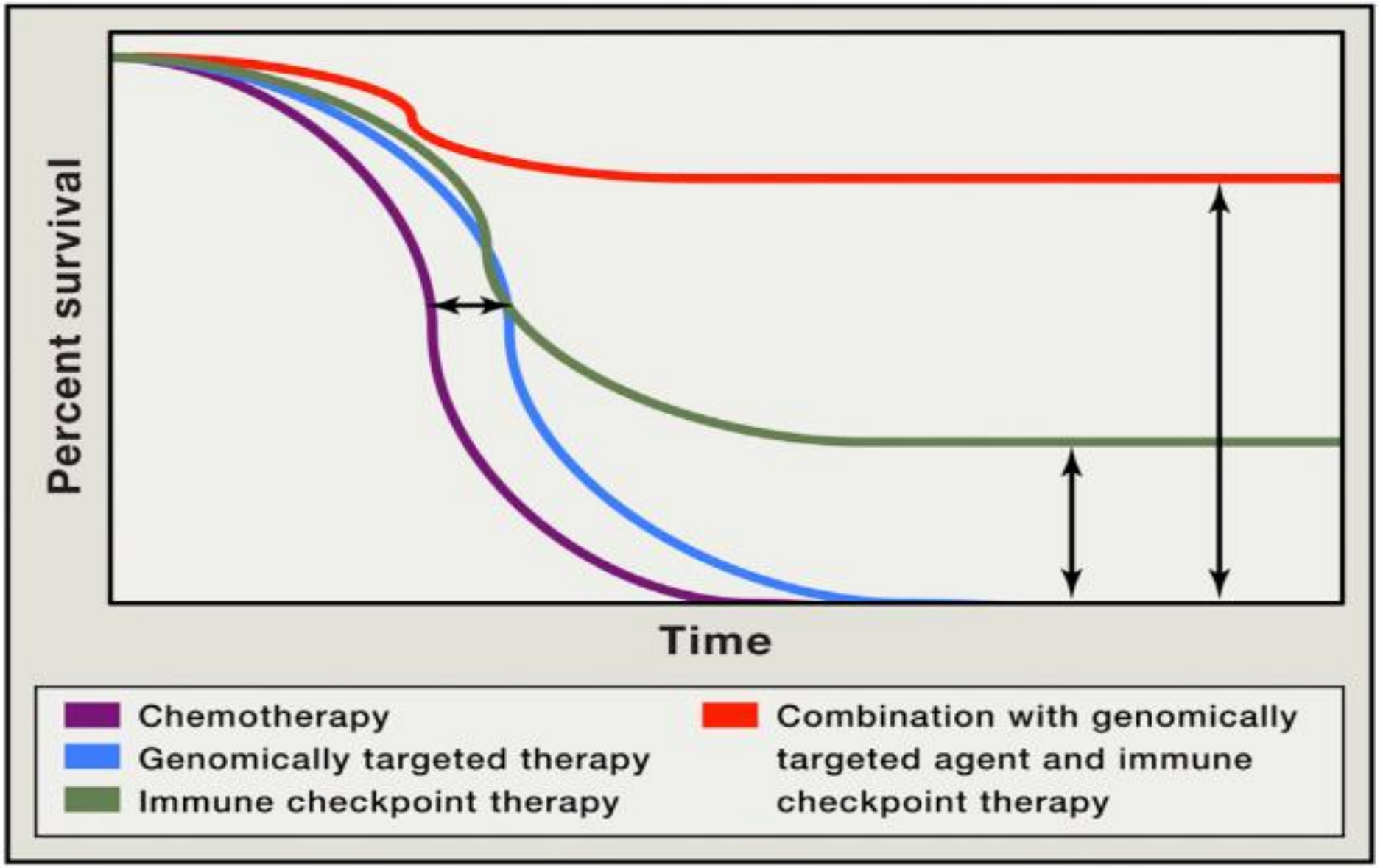






Courtesy of J. Remon Brahmer J, et al. N Engl J Med. 2015;373(2):123-135. Borghaei H, et al. N Engl J Med. 2015;373(17):1627-1639. Felip E, et al. Ann Oncol. 2017;28(Suppl 5): Abstract 1301PD. Herbst R, et al. Lancet. 2016;387(10027):1540-1550. Herbst R, et al. Ann Oncol. 2016;27(Suppl 6): Abstract LBA48. Herbst R, et al. J Clin Oncol. 2017;35(suppl):9090. Rittmeyer A, et al. Lancet. 2017;389(10066):255-265

폐암치료의 미래

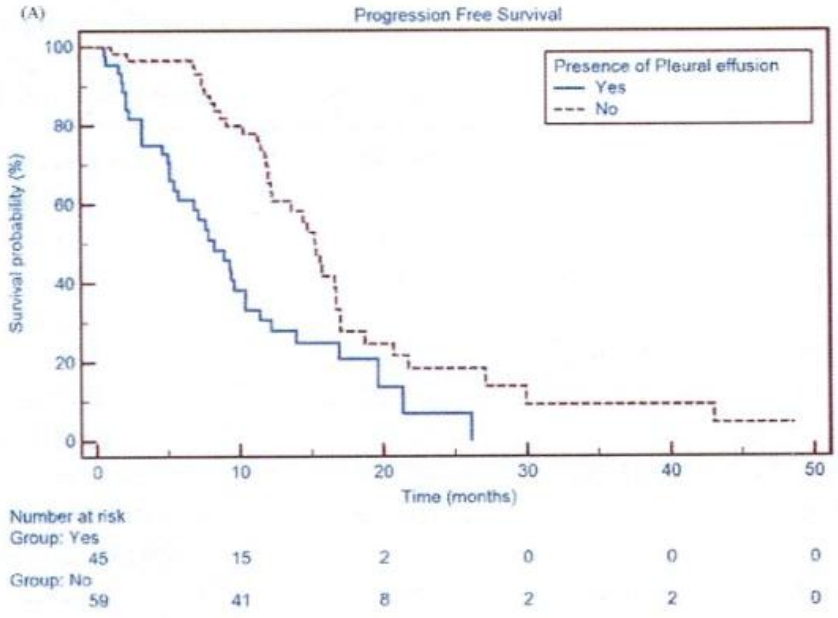

Percent survival
Time
Chemotherapy
Genomically targeted therapy
Immune checkpoint therapy
Combination with genomically targeted agent and immune checkpoint therapy

타깃치료 – EGFR-TKI

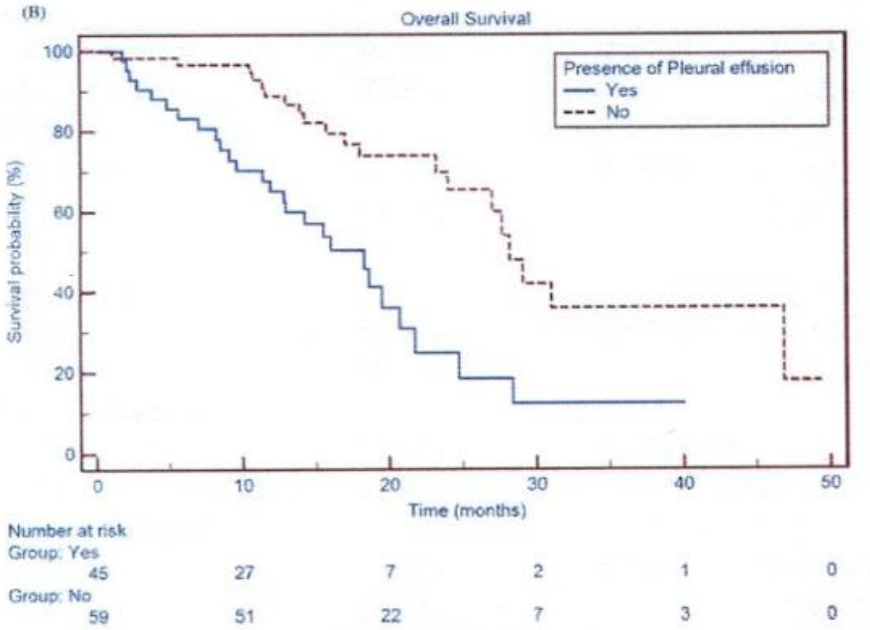
Presence of PE is associated with a poor Px in pts with EGFR-mutated lung cancer receiving TK inhibitors as first-line Tx

악성흉수의 존재는 EGFR-TKI 치료제 환자의 불량한 예후인자이다

104 pts - With MPE (45pts) : without MPE (59pts)



median PFS - 8.2M : 15.3M P=0.0004



OS - 16.3M : 28.2M P=0.0003

The presence of PE predicts poor PFS and OS in lung caner pts receiving TKIs as the first-line Tx

Wang TF et al. Asia Pac J Clin Oncol 2017;13:304

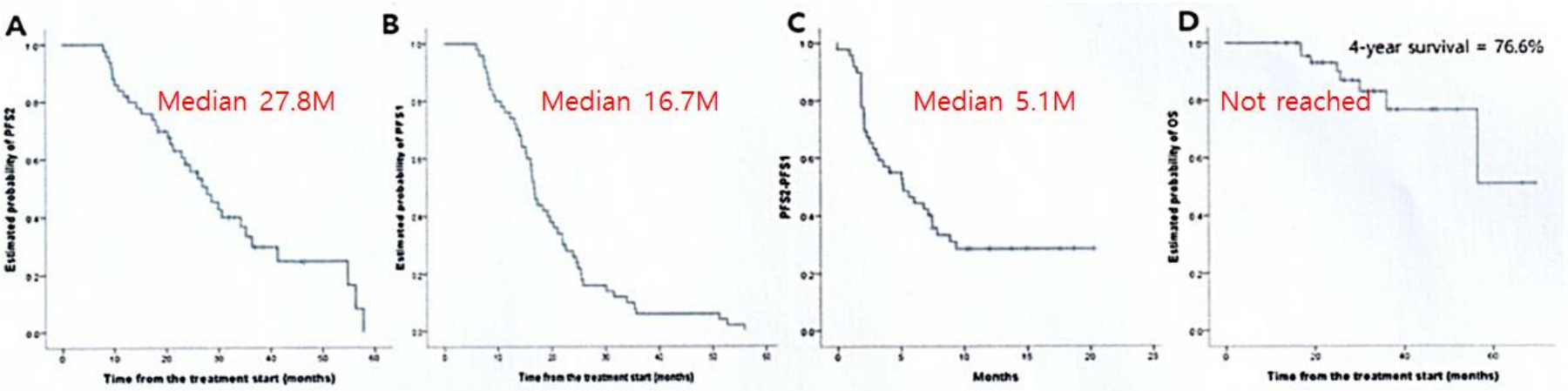
Continuation of gefitinib beyond progression in pts with EGFR mutation-positive NSCLC: A phase II single-arm trial

Gefitinib beyond progression 환자에서 gefitinib 치료지속의 예측인자 분석

50 pts with EGFR-mutant NSCLC who progressed during gefitinib Tx

1st endpoint - PFS2 (time from first gefitinib dose to off-gefitinib progression).

2nd endpoints - PFS1 (time from first gefitinib dose to progression); the difference between PFS2 and PFS1 (PFS2-PFS1); overall survival (OS)

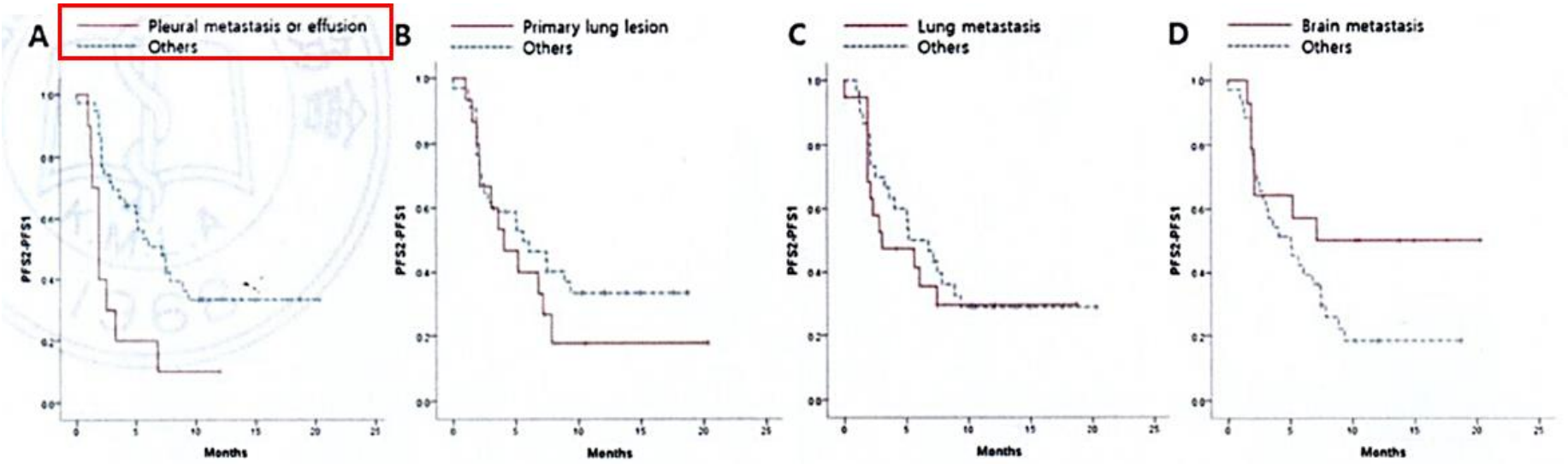


PFS2 PFS1 PFS2-PFS1 OS

Lim SW et al. Lung Cancer 2018;124:293

Continuation of gefitinib beyond progression in pts with EGFR mutation-positive NSCLC: A phase II single-arm trial

흉막전이나 악성흉수를 가진 환자군이 다른 진행군보다 **PFS2-PFS1**이 의미 있게 짧았다



P=0.005 (1.8 vs 7.1M)

P=0.308 (4.0 vs 5.6M)

P=0.652 (3.0 vs 5.1M)

P=0.111 (7.1 vs 5.0M)

- 12 pts (24.4%) continued gefitinib Tx for 14M (7.2-20.3) after progression
- PFS2-PFS1 was significantly shorter in pts with pleural metastasis or pleural effusion compared with the other types of progression (1.8M vs. 7.1M, p=0.005)

Lim SW et al. Lung Cancer 2018;124:293

Impact of Pleural Effusion on Outcomes of Pts Receiving Osimertinib for NSCLC Harboring EGFR T790M

Osimertinib 치료환자에서 악성 흉수는 치료실패의 예측인자

- **23 pts (7 pts with PE) treated with osimertinib**

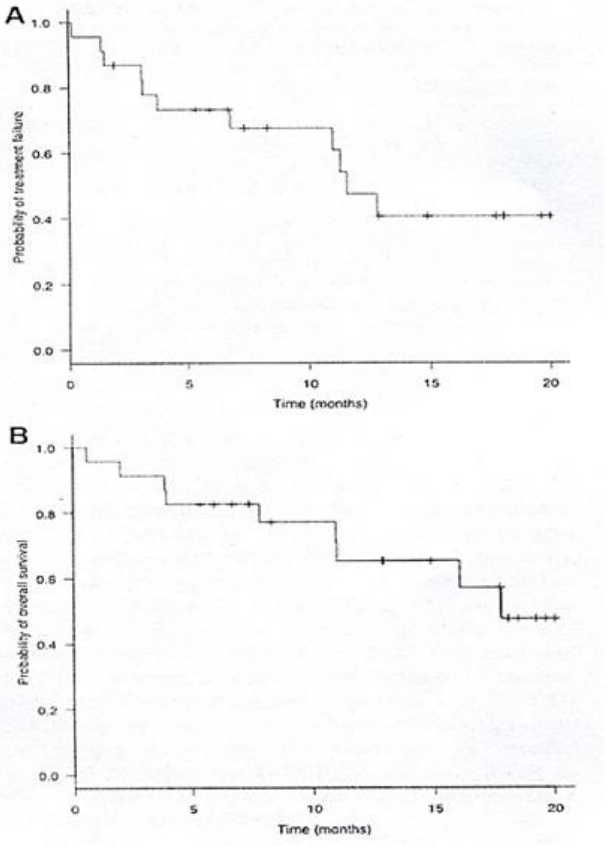
Factor	Time to treatment failure (months)		
	HR	95% CI	*p*-Value
Age ≥75 years	1.36	0.41-4.5	0.61
Female	1.87	0.24-14.7	0.55
Exon 21 L858R*	2.16	0.60-7.7	0.24
ECOG performance status≥2	1.06	0.28-4.0	0.93
Pleural effusion	3.81	1.1-12.8	0.021
Brain metastases	1.84	0.5-6.3	0.33
Bone metastases	1.29	0.4-4.2	0.67
Liver metastases	2.63	0.7-10.0	0.14

<Prognostic factors associated with time to Tx failure>

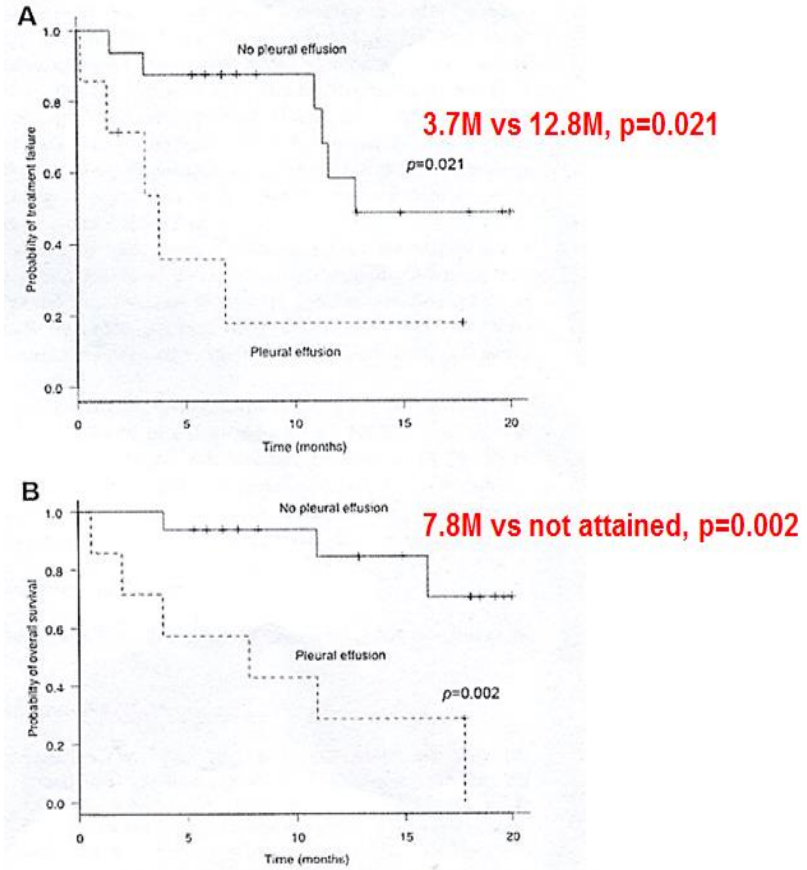
Masuhiro K et al. Anticancer Res 2018;38:3567

Impact of Pleural Effusion on Outcomes of Pts Receiving Osimertinib for NSCLC Harboring EGFR T790M

Osimertinib 치료환자에서 악성 흉수는 치료실패의 예측인자



<전체환자 A. Time to Tx failure B. OS>



<PE유무에 따른 A. Time to Tx failure B. OS>

- Brain, bone, liver metastasis – no significant

Masuhiro K et al. Anticancer Res 2018;38:3567

원광대 병원 **Case**

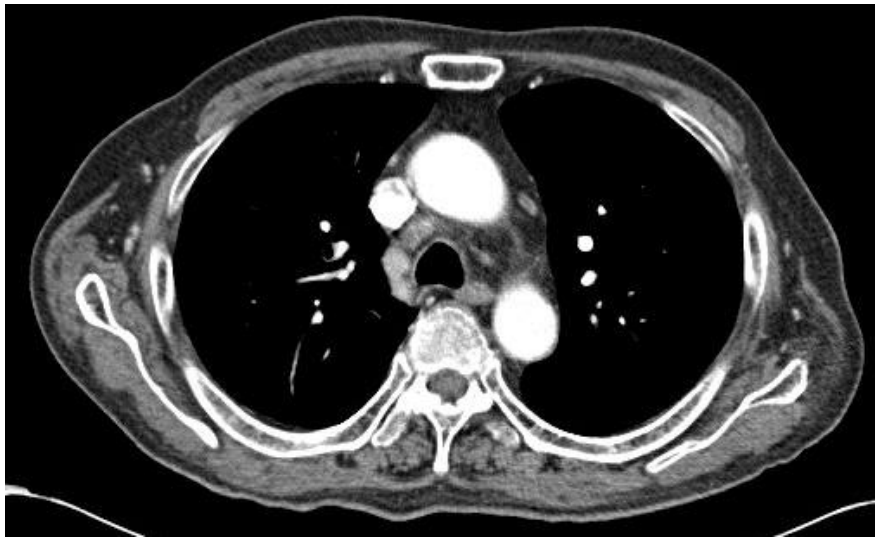
- **Age/Sex** 73/M
- **Chief Complaint** Dyspnea
- **Present Illness**

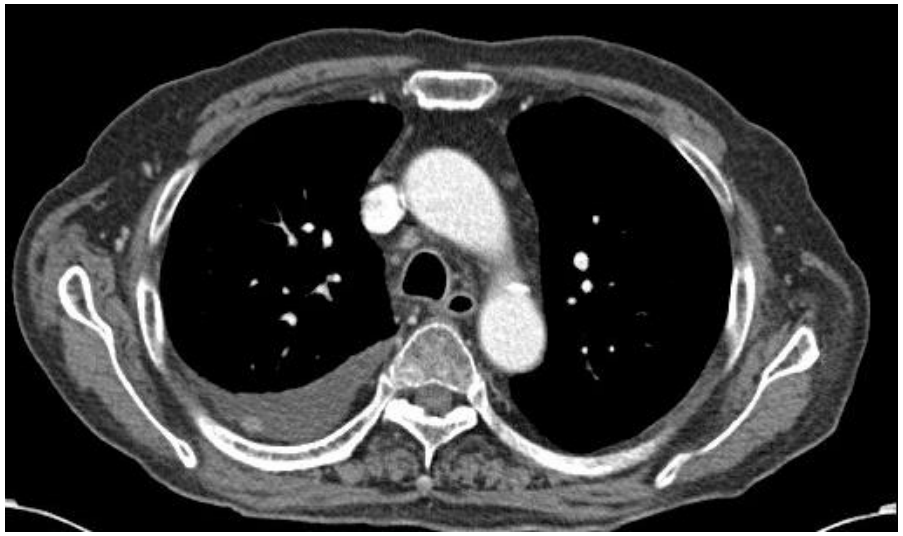
  Lung cancer로 폐선암 4기 환자로 EGFR exon 19 del으로 Gefitinib 사용 후 Stable disease 소견 보여 경과관찰 하던 환자분으로 내원 4일 전부터 dyspnea 악화 보여 내원함

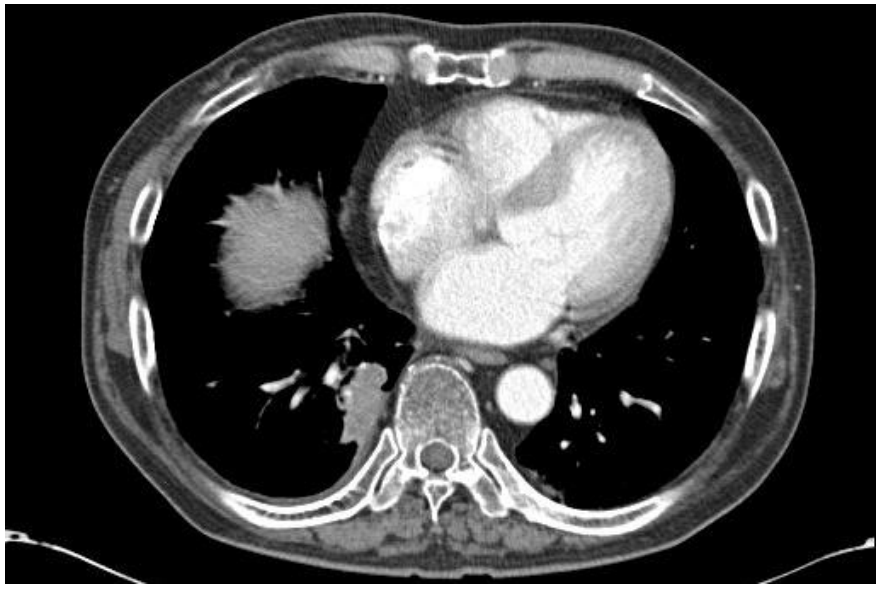
- Adenocarcinoma, stage 4 (T3N3M1a, EGFR exon 19 del, ALK (-))

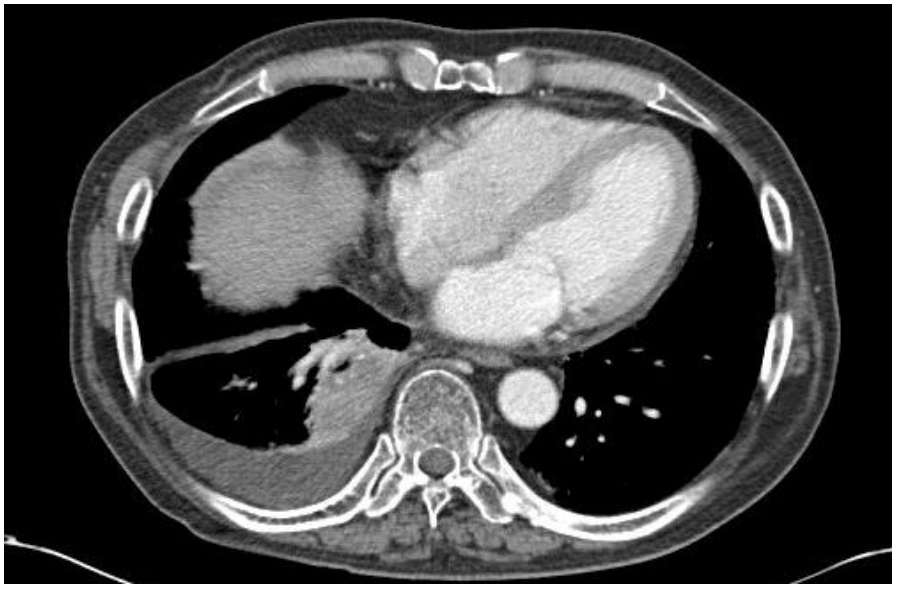
- Gefitinib : 2017.2.22 ~

원광대 병원 Case









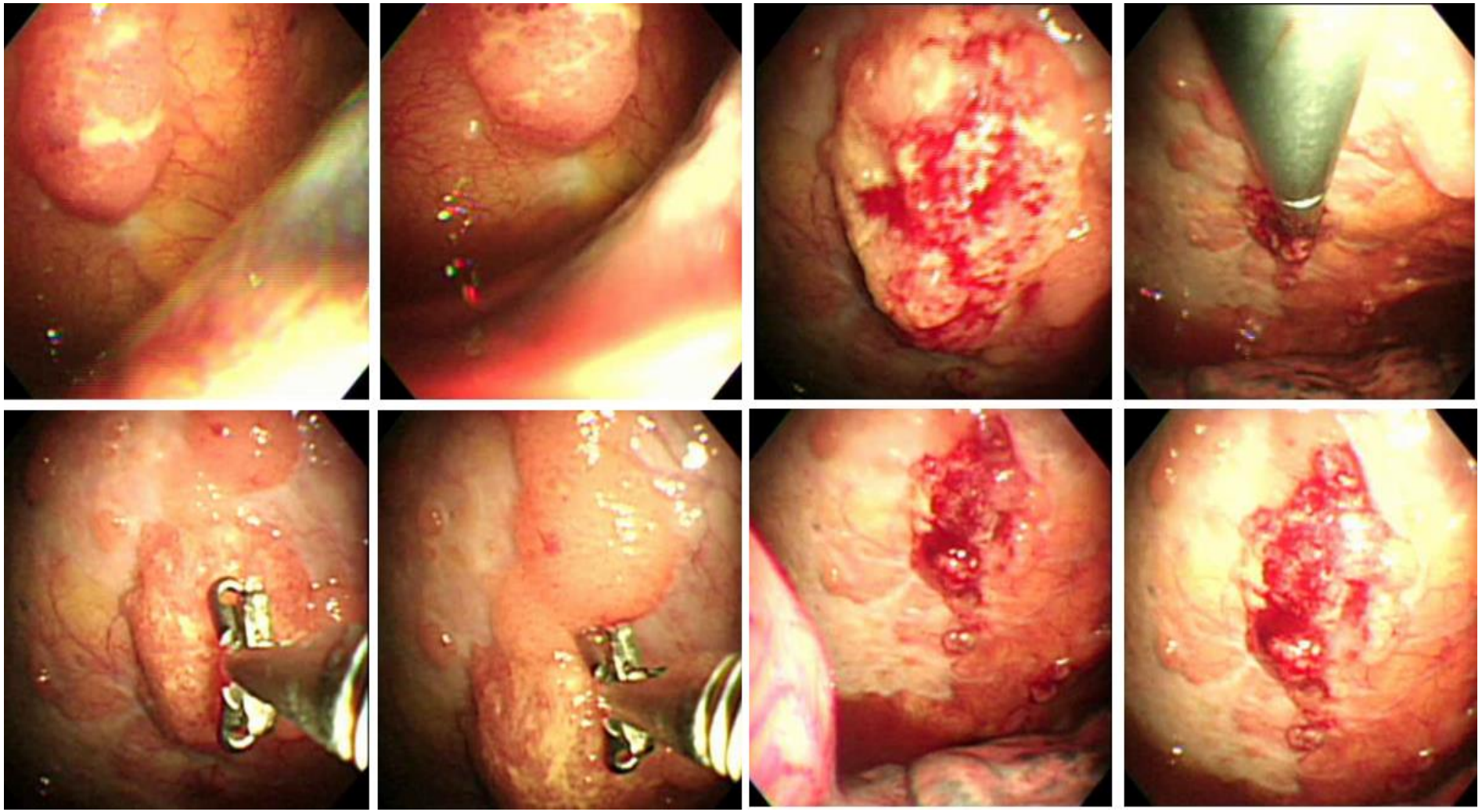
2017.6.20

2017.12.12

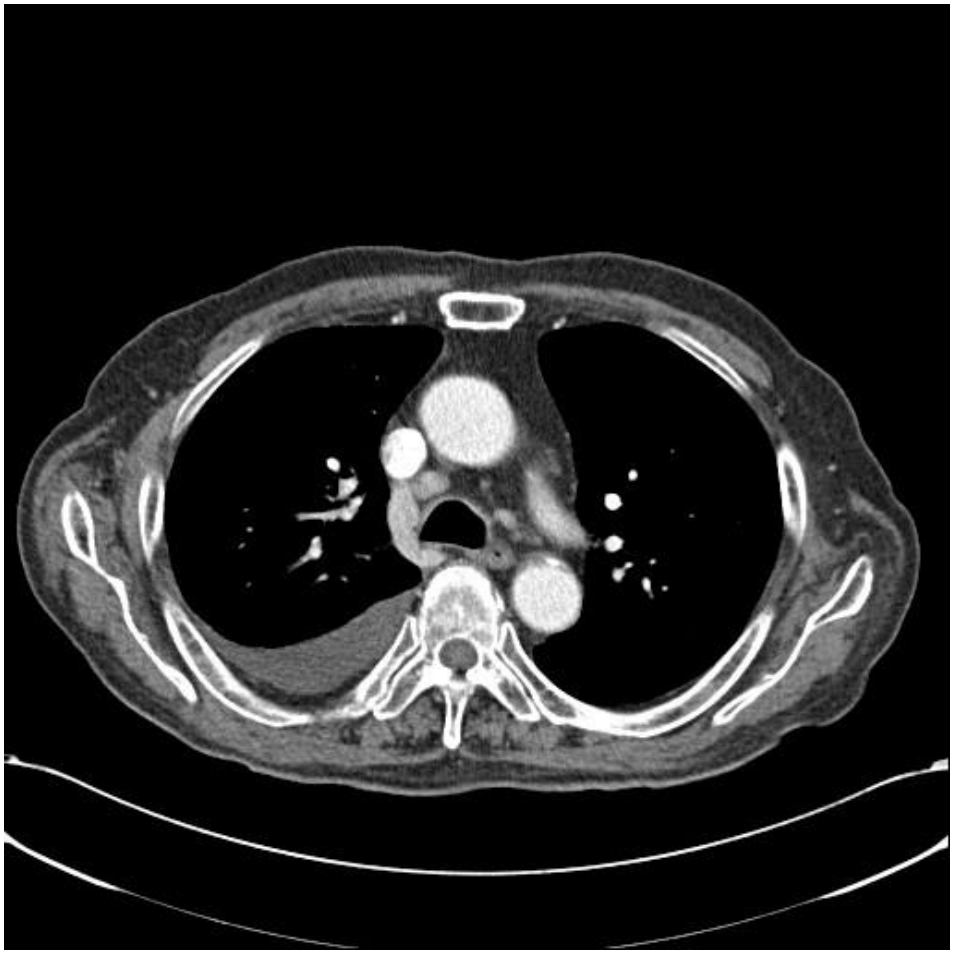
원광대 병원 Case

Medical Thoracoscopy

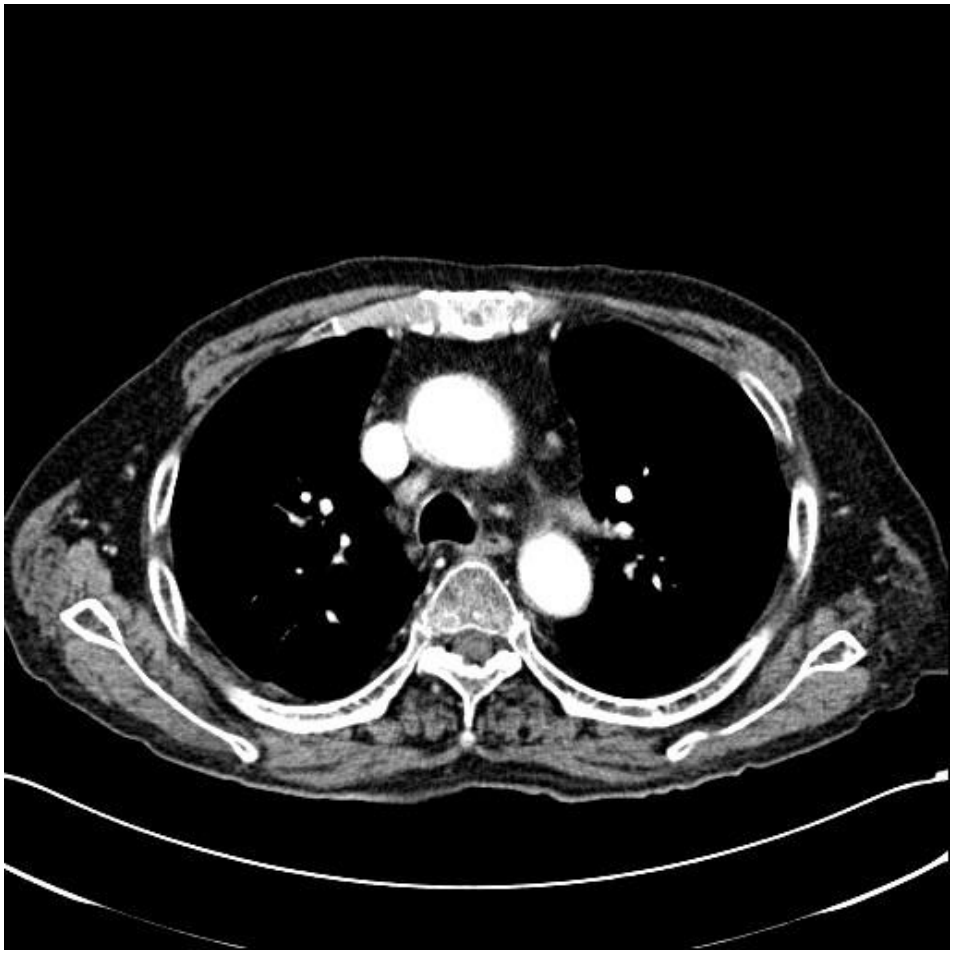
Medical Thoracoscopy



F/U Chest CT



2017.12.12



2018.3.16

면역항암제

Pleural or pericardial metastasis: A significant factor affecting efficacy and adverse events in lung cancer pts treated with PD-1/PD-L1 inhibitors

흉막/심장막 전이는 면역항암제에 대한 반응률이 떨어지고 부작용도 많다

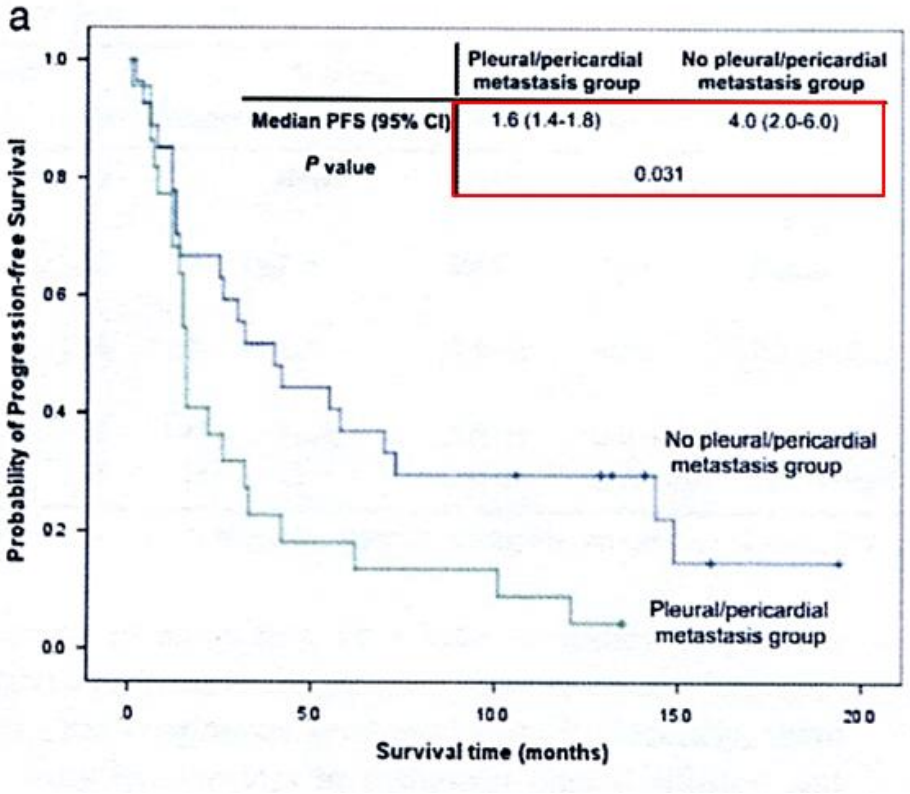
- 51 pts c NSCLC who received PD-1/PD-L1 inhibitors
- Pleural or pericardial metastasis 23 pts
  Response rate - 4.3% vs. 35.7% P=0.007

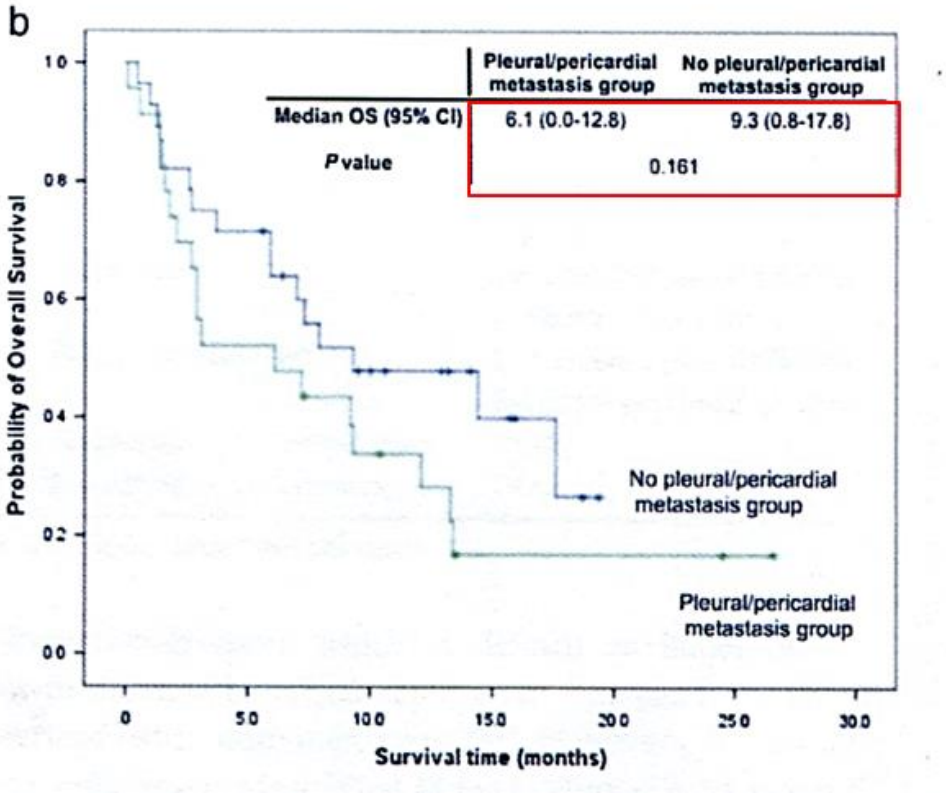
Variable	Pleural or pericardial metastasis (n = 23)	No pleural or pericardial metastasis (n = 28)	P
Age (years)	61.70 ± 12.60	65.71 ± 9.39	0.198
Male gender	15 (65.2)	22 (78.6)	0.454
Smoking status			
Never	10 (43.5)	7 (25.0)	0.054
Former	9 (39.1)	7 (25.0)	
Current	4 (17.4)	14 (50.0)	
EGFR			
Mutant	3 (13.0)	2 (7.1)	0.647
Wild type	20 (87.0)	26 (92.9)	
PD-L1 expression			
Unknown/< 1%	7 (30.4)	10 (35.7)	0.257
Low (1–49%)	3 (13.0)	8 (28.6)	
High (> 50%)	13 (56.5)	10 (35.7)	
Histology			
Squamous	9 (39.1)	17 (60.7)	0.215
Adenocarcinoma	9 (39.1)	9 (32.1)	
Other	5 (21.7)	2 (7.1)	
Number of prior regimens			
0	2 (8.7)	2 (7.1)	0.913
1	11 (47.8)	12 (42.9)	
≥ 2	10 (43.5)	14 (50.0)	
ECOG			
0	3 (13.0)	5 (17.9)	0.838
1	15 (65.2)	19 (67.9)	
2	5 (21.7)	4 (14.3)	
Agent			
Atezolizumab	1 (4.3)	5 (17.9)	0.326
Nivolumab	9 (39.1)	11 (39.3)	
Pembrolizumab	13 (56.5)	12 (42.9)	
Number of distant metastases			
0	8 (34.8)	10 (35.7)	1.000
1	6 (26.1)	7 (25.0)	
≥ 2	9 (39.1)	11 (39.3)	
Number of cycles of immunotherapy	4.52 ± 3.54	6.64 ± 5.84	0.117
AEs			
Any grade	21 (91.3)	14 (50.0)	0.002
Grade 3–5	12 (52.2)	7 (25.0)	0.046
Response			
Cannot be evaluated	4 (17.4)	2 (7.1)	0.037
PR	1 (4.3)	10 (35.7)	
SD	6 (26.1)	7 (25.0)	
PD	12 (52.2)	9 (32.1)	

Kang DH et al. Thorac Cancer 2018 Sep 25. Epub ahead

Pleural or pericardial metastasis: A significant factor affecting efficacy and adverse events in lung cancer pts treated with PD-1/PD-L1 inhibitors

흉막/심장막 전이는 면역항암제에 대한 Median PFS와 OS에 불량한 예측





Kang DH et al. Thorac Cancer 2018 Sep 25. Epub ahead

Metastatic site as a predictor of nivolumab efficacy in pts with advanced NSCLC : A retrospective multicenter trial

Nivolumab 효과의 예측인자로서의 전이부위차이

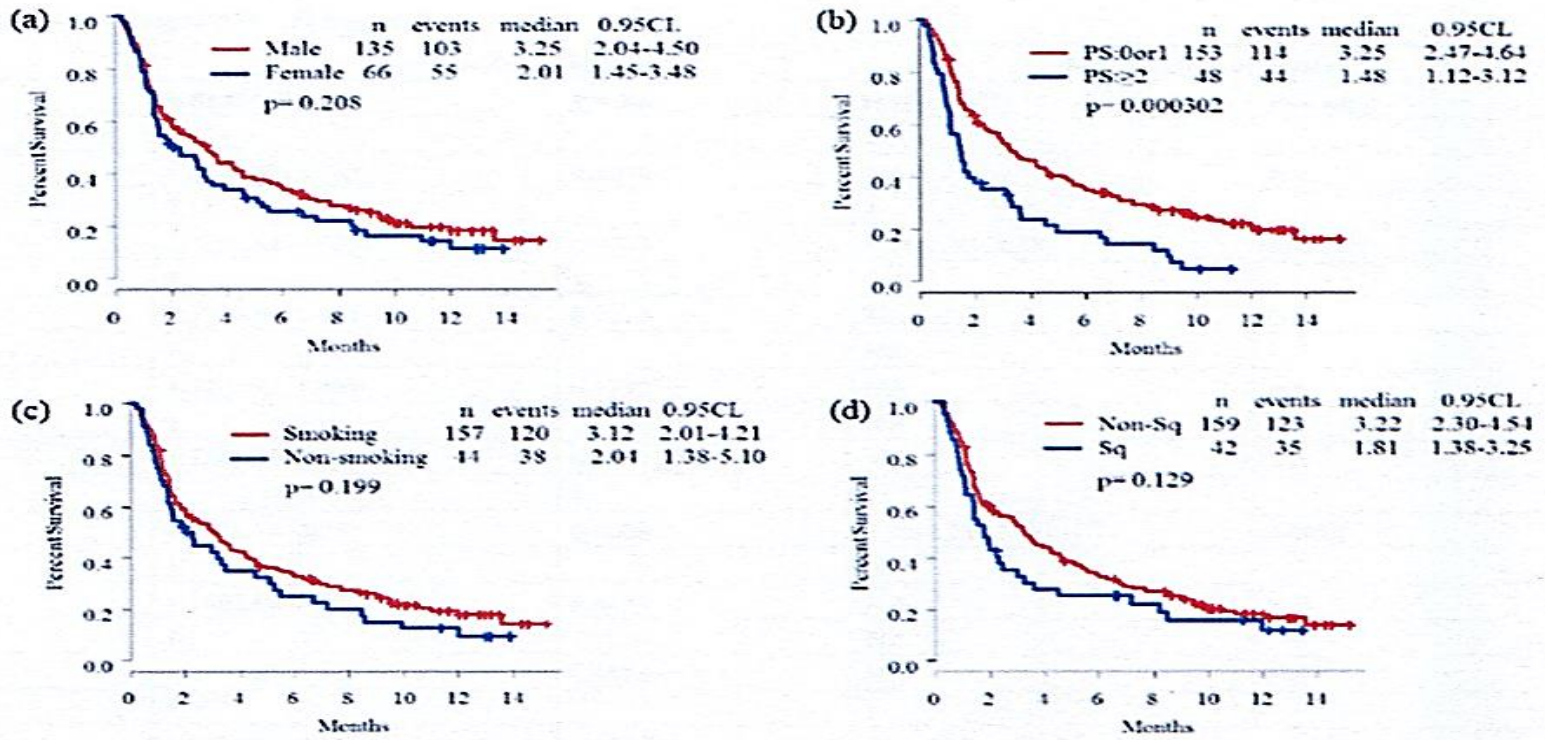


Fig 2. Kaplan-Meier curves of progression-free survival according to (a) sex, (b) Eastern Cooperative Oncology Group performance status (PS), (c) smoking status, and (d) squamous cell (SQ) subtype.

- 201 pts
- PS ≥2 (HR: 1.54, $p < 0.05$)

⇒ correlated with a significantly shorter PFS in nivolumab-treated pts

Tamiya M et al. PLoS One 2018;13:e0192227

Metastatic site as a predictor of nivolumab efficacy in pts with advanced NSCLC : A retrospective multicenter trial

악성흉수의 유무에 따른 Nivolumab 효과의 차이는 없다

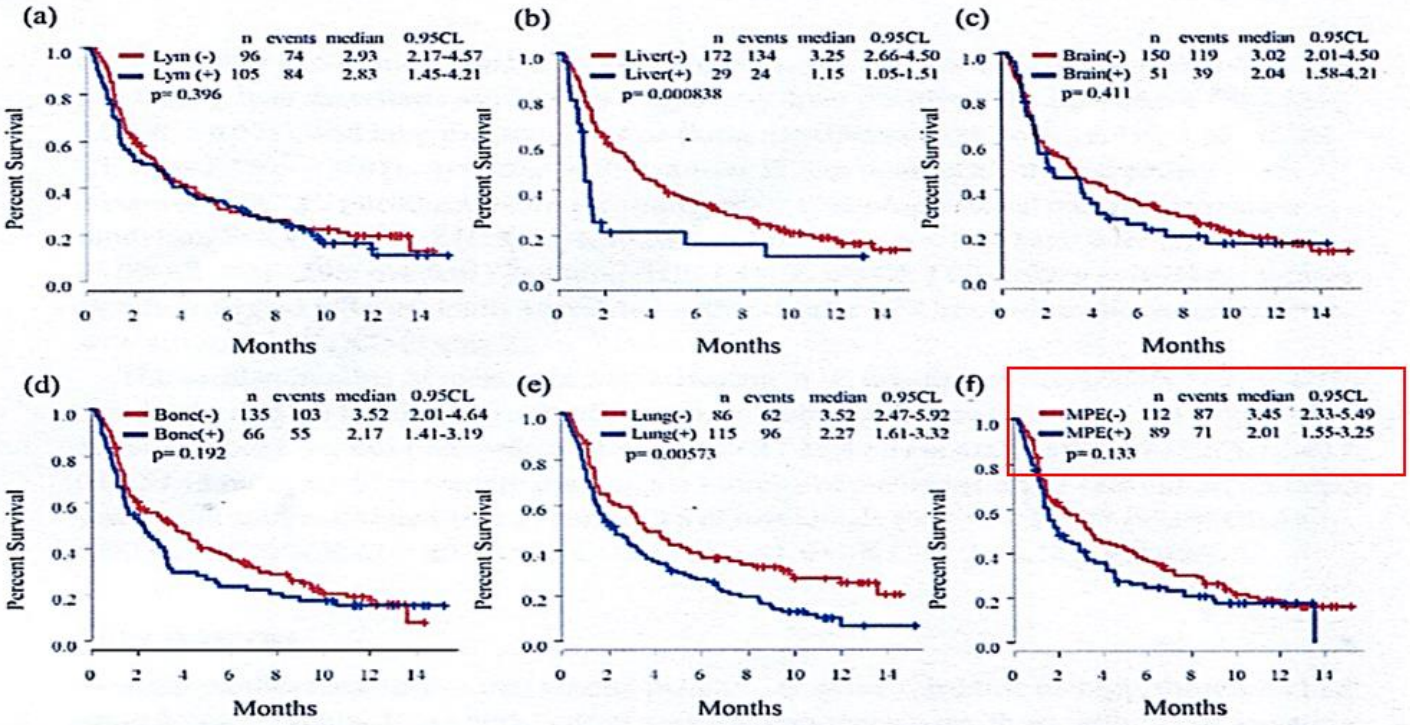


Fig 3. Kaplan-Meier curves of progression-free survival according to metastatic site: (a) thoracic lymph nodes, (b) liver, (c) brain, (d) bone, (e) Lung (intrapulmonary metastasis), and (f) MPE (malignant pleural effusion).

- liver (HR: 1.90, $p < 0.01$) metastases
- lung (HR: 1.41, $p < 0.05$) metastases

$\Rightarrow$ correlated with a significantly shorter PFS in nivolumab-treated pts

Tamiya M et al. PLoS One 2018;13:e0192227

Short course pembrolizumab in complete responders with advanced NSCLC

흉막전이환자도 pembrolizumab 치료에 CR이 올 수 있다

46 pts treated with pembrolizumab; evaluated after cycle 4

- 4 out of 46 pts – complete CR

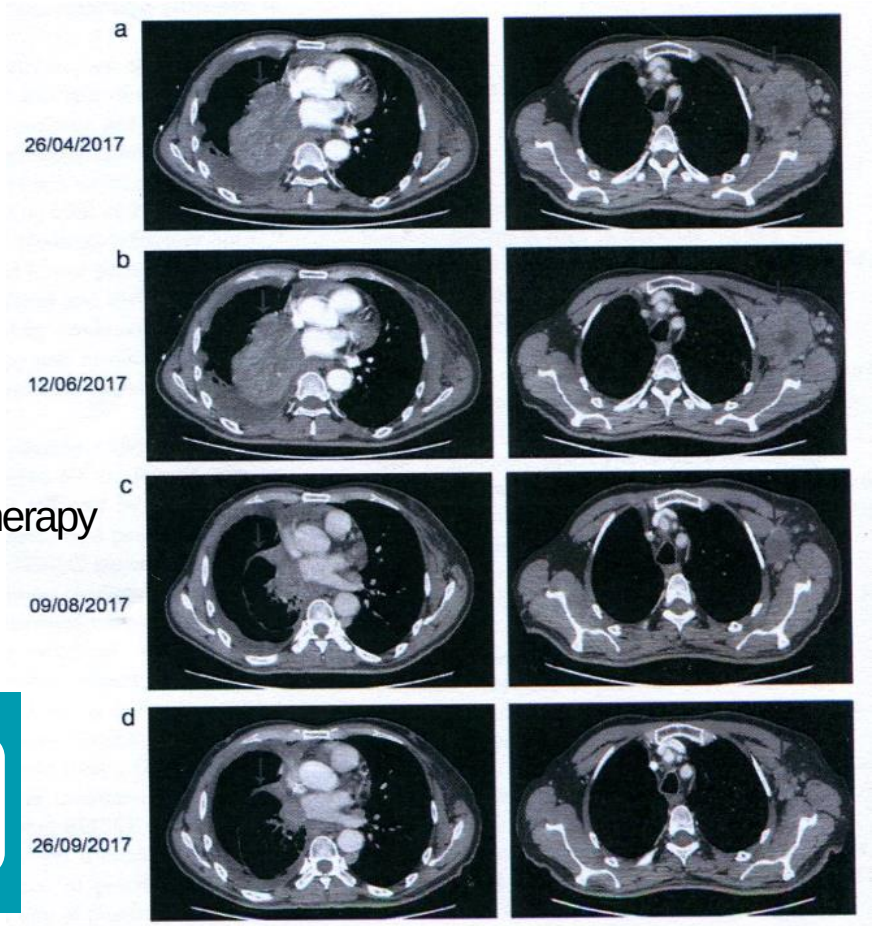
Patient	Baseline PS	Histology	Sites of metastases	Duration of CR (months)	Side effect
#1	4	Adenocarcinoma (EGFR/ALK WT)	Brain, lung, intra-thoracic lymph nodes	12	Nil
#2	2	Adenocarcinoma (EGFR/ALK WT)	Pleural effusion and Pleural nodules	6	G2 rash
#3	1	Adenocarcinoma (EGFR Exon 19 del)	Bilateral lungs	9	Nil
#4	1	Squamous cell carcinoma	Right lung	15	G2 rash

2017 ASCO e20537

Well-controlled pleural effusion indicated pseudoprogression after immunotherapy in lung cancer

악성흉수의 조기 제어는 폐암의 면역치료 후 pseudoprogression의 예측인자?

- 47yr heavy smoker with advanced SqCC
- PE was well controlled with nivolumab
- however with deterioration of PS and tumor progression
- Nivolumab maintained
- PR and rapid improvement PS
- Early control of PE as an indicator for pseudoprogression might be helpful to identify pseudoprogression for immunotherapy



(a) 내원 당시 (b) nivolumab 3 cyle후
(c,d) nivolumab + nab-paclitaxel 2 and 4 cycle후

Liu G et al. Thorac Cancer 2018;9:1190

요 약

1. **IASLC TNM staging – 흉막전이 T4 -> M1a로 재 분류**

2. **흉막전이에 대한 수술적 치료에 대한 생존율의 이득 보고**
   - 대부분 소규모연구, 후향적, 수술 전후의 결과보고가 미흡
   - 수술 시점이나 범위가 아직까지 불명확하고 정립되지 않음

3. **수술적 치료가 고려될 수 있는 상황**
   - 첫 수술시 우연히 발견된 악성흉수가 없는 흉막전이
   - N staging 0-1
   - Visceral pleural invasion (VPI) 음성 환자

4. **흉막전이에 대한 내과적 치료**
   1) 타깃치료제
      진단시 흉막전이 존재하거나 gefitinib beyond Px에 대한 불량한 예후
      3세대 TKI제제에도 효과가 떨어지는 요소
   2) 면역항암제
      진단시 흉막전이 존재시 치료효과 감소
      반대로, 상관없거나 CR 증례보고
      Pseudoprogression의 예측인자가능성

5. **폐암환자에서 흉막전이 subgroup 분석미흡**
   치료반응에 대한 예측/예후인자에 대한 바이오마커 발굴 필요

Thank you

For your attention