Chemotherapy Beyond Standard Regimen

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Contents – NSCLC

- Standard regimen
- Second- or Further-lines options
  - (-) Target agents
  - (-) Immune checkpoint inhibitors (ICIs)
- Case study

NSCLC

clinical practice guidelines

Annals of Oncology 27 (Supplement 5): v1–v27, 2016
doi:10.1093/annonc/mdw326

Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

S. Novello[1], F. Barlesi[2], R. Califano[3,4], T. Cufer[5], S. Ekman[6], M. Giaj Levra[7], K. Kerr[8], S. Popat[9], M. Reck[10], S. Senan[11], G. V. Simo[12], J. Vansteenkiste[13] & S. Peters[14] on behalf of the ESMO Guidelines Committee*

Ann Oncol 2016;25(Supplement5):v1-v27

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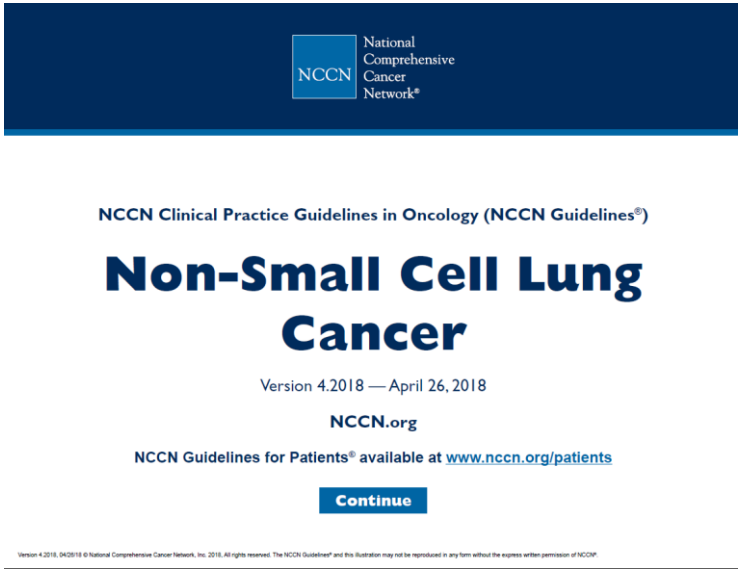
JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Systemic Therapy for Stage IV Non–Small-Cell Lung Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Nasser Hanna, David Johnson, Sarah Temin, Sherman Baker Jr, Julie Brahmer, Peter M. Ellis, Giuseppe Giaccone, Paul J. Hesketh, Ishmael Jaiyesimi, Natasha B. Leighl, Gregory J. Riely, Joan H. Schiller, Bryan J. Schneider, Thomas J. Smith, Joan Tashbar, William A. Biermann, and Gregory Masters

J Clin Oncol 2017;35(30):3484-3515



NCCN 2018 Ver 4

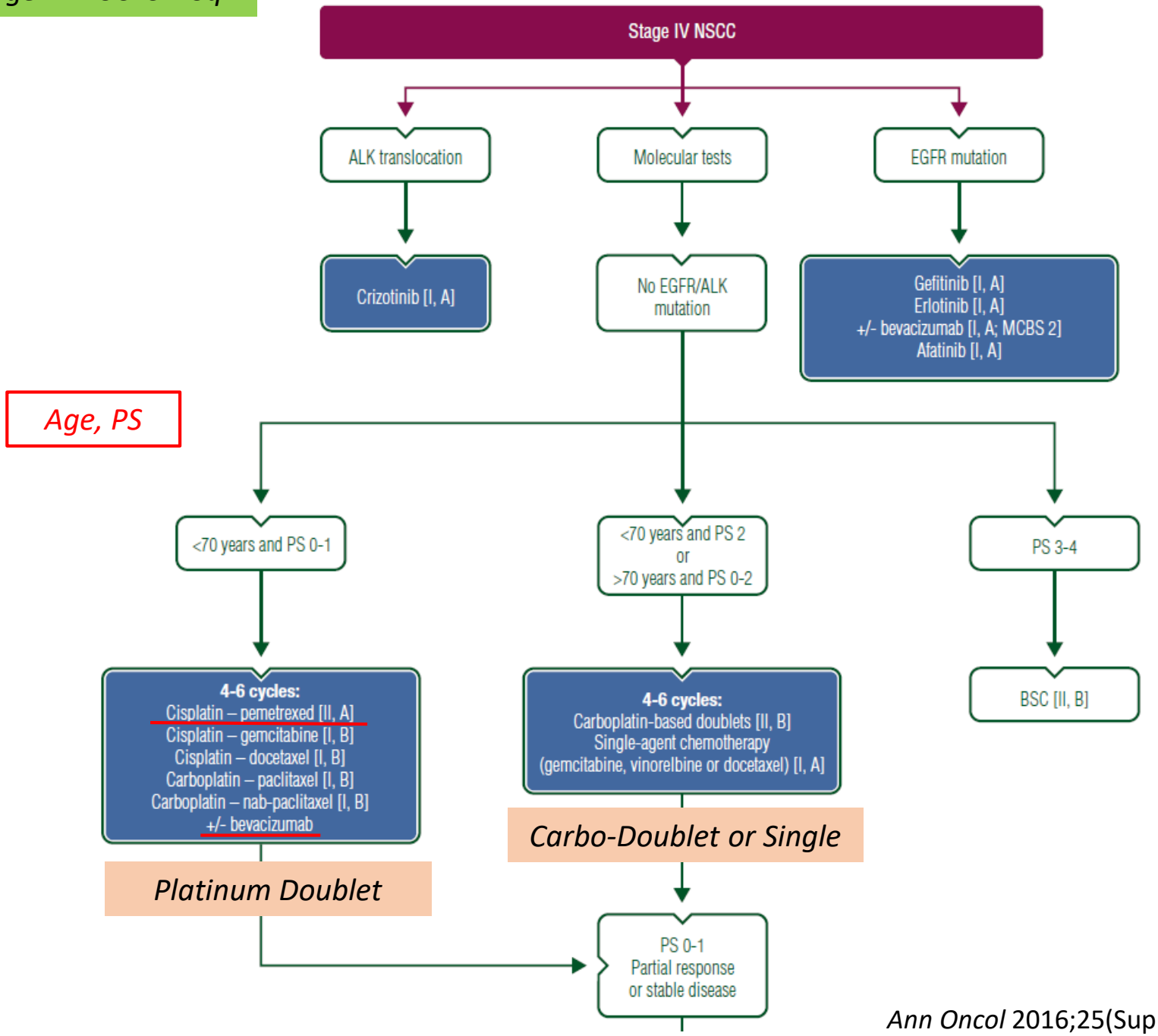
Current Standard of Care in Advanced NSCLC

Sub group	ONCOGENE ADDICTED	OTHERS		HIGHLY SENSITIVE TO IMMUNO
		NON SQUAMOUS	SQUAMOUS	
First Line	EGFR: gefitinib, erlotinib, afatinib, icotinib, dacomitinib, osimertinib, poziotinib (if EGFR exon 20 mut) ALK: crizotinib, ceritinib 750 mg, ceritinib 450 mg (low fat meal), alectinib, lorlatinib, ensartinib BRAF: dabrafenib + trametinib ROS1: crizotinib, ceritinib, entrectinib MET: crizotinib NTRK: larotrectinib, entrectinib	Platinum-CT Pemetrexed is an option Bevacizumab can be added Pembrolizumab + platinum/pemetrexed (US) Nivolumab + Ipilimumab Nivolumab + platinum CT	Platinum-CT Necitumumab can be added Nivolumab + ipilimumab Nivolumab + platinum CT	Pembrolizumab if PDL1 ≥ 50% tumor cells Atezolizumab in TC 2/3 - IC 2/3 tumors Avelumab in PD-L1 ≥ 1% Durvalumab in PD-L1 ≥25% Nivolumab + Ipilimumab Nivolumab + platinum CT Pembrolizumab + platinum/pemetrexed (in non-squamous histology)
Second And Further Line	EGFR: osimertinib if T790M+ EGFR+/ MET+: savolitinib + osimertinib ALK: ceritinib 750 mg, ceritinib 450 mg (low fat meal), alectinib, brigatinib, lorlatinib, ensartinib BRAF: dabrafenib + trametinib RET: vandetanib, LOXO-292 HER2 : TDM-1 ROS1: lorlatinib	Docetaxel +/- nintedanib Docetaxel +/- ramucirumab Bevacizumab + Paclitaxel is an option in non-squamous (if Beva not administered in 1st line). Nivolumab Atezolizumab Avelumab		Platinum CT based on histology (if Pembro in first line). Pembrolizumab in PD-L1 ≥ 1% (if not administered in 1st line). Nivolumab Atezolizumab Durvalumab in PD-L1 ≥25% Avelumab

Phase I-II studies Phase III studies

J Thorac Oncol 2018;13(3):301-22

Stage IV NSCLC-NSq



Ann Oncol 2016;25(Supplement5):v1-v27

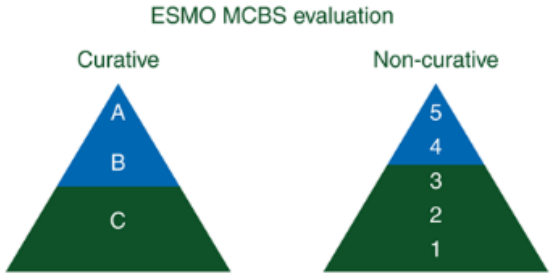
PS 0-1
Partial response
or stable disease

Maintenance treatment:
Pemetrexed (switch) [I, B]
Pemetrexed (continuation) [I, A]
Erlotinib (EGFR-activating mutation) [I, B]
+/- bevacizumab (if given before)

Disease progression → PS 3-4 → BSC

PS 0-2

Pemetrexed [I, B]
Docetaxel [I, B]
Nivolumab [I, B; MCBS 5]
Pembrolizumab if PD-L1 >1%
[I, A; MCBS 3 if PD-L1 >1%; MCBS 5 if PD-L1 >50%]
Ramucirumab – docetaxel [I, B; MCBS 1]
Nintedanib – docetaxel [II, B]
Erlotinib [II, C]



***MCBS**, Magnitude of Clinical Benefit Scale*

Ann Oncol 2016;25(Supplement5):v1-v27

Stage IV NSCLC-NSq without driver mutation

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Non-Small Cell Lung Cancer

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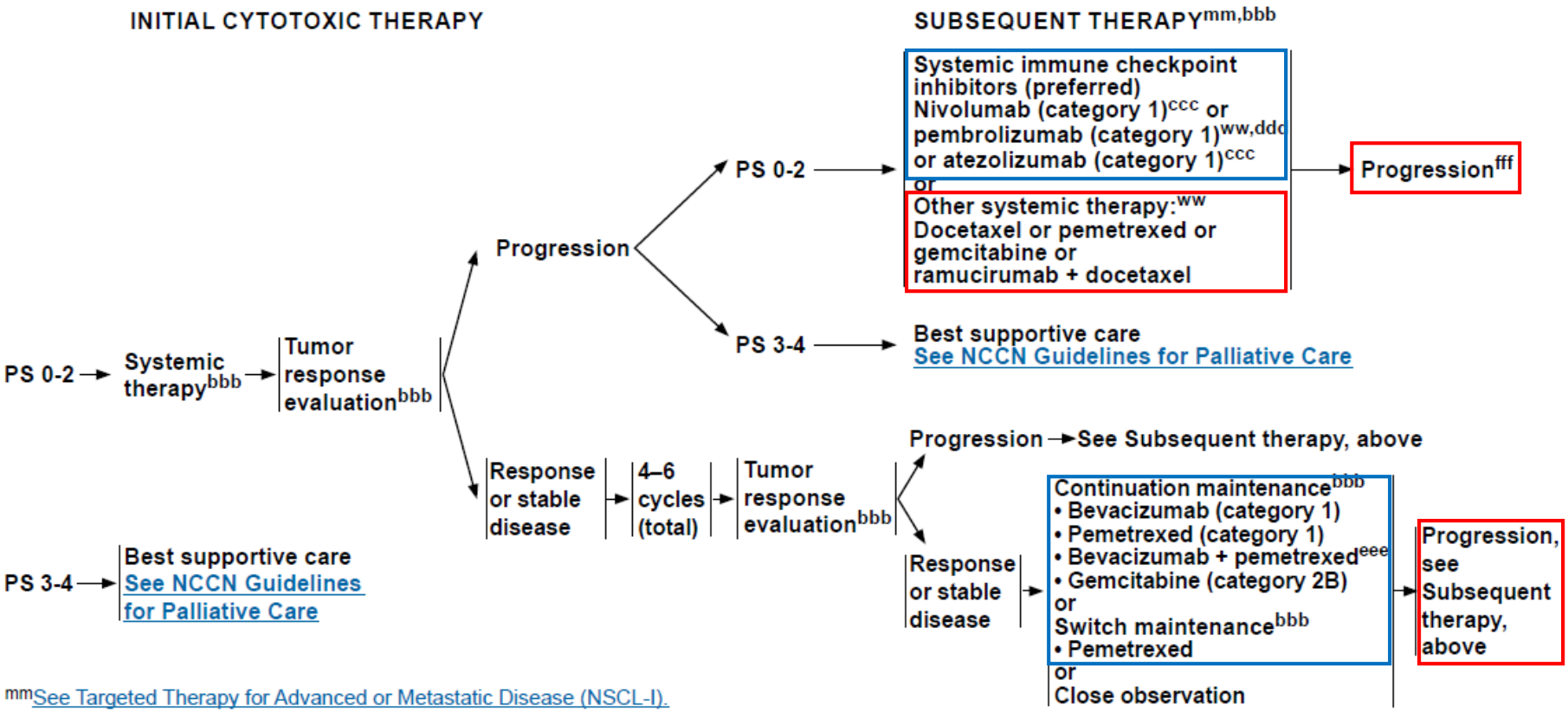
ADENOCARCINOMA, LARGE CELL, NSCLC NOS



[mm] See Targeted Therapy for Advanced or Metastatic Disease (NSCL-I).

[ww] If not previously given.

[bbb] See Systemic Therapy for Advanced or Metastatic Disease (NSCL-J).

[ccc] If pembrolizumab not previously given.

[ddd] Pembrolizumab is approved for patients with NSCLC tumors with PD-L1 expression levels ≥1%, as determined by an FDA-approved test.

[eee] If bevacizumab was used with a first-line pemetrexed/platinum chemotherapy regimen.

[fff] If not already given, options for PS 0-2 include (nivolumab, pembrolizumab, or atezolizumab), docetaxel (category 2B), pemetrexed (category 2B), gemcitabine (category 2B), or ramucirumab + docetaxel (category 2B); options for PS 3-4 include best supportive care. Options for further progression are best supportive care or clinical trial.

Stage IV NSCLC-NSq with sensitizing EGFR mutation

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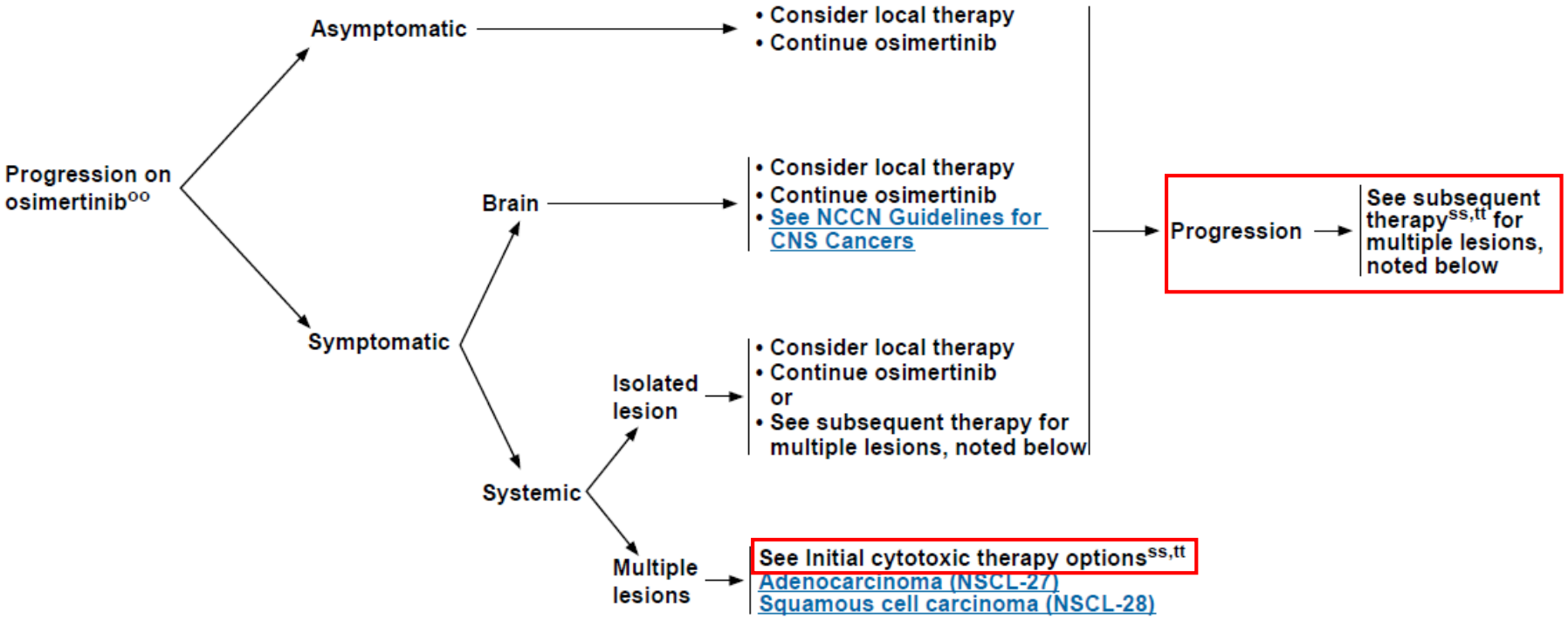
SENSITIZING EGFR MUTATION POSITIVE[hh] | **SUBSEQUENT THERAPY[mm]**



[hh]See Principles of Molecular and Biomarker Analysis (NSCL-G).
[mm]See Targeted Therapy for Advanced or Metastatic Disease (NSCL-I).
[oo]Beware of flare phenomenon in subset of patients who discontinue EGFR TKI. If disease flare occurs, restart EGFR TKI.
[ss]Afatinib + cetuximab may be considered in patients with disease progression on EGFR TKI therapy.
[tt]The data in the second-line setting suggest that immunotherapy is less effective, irrespective of PD-L1 expression, in tumors with an actionable mutation.

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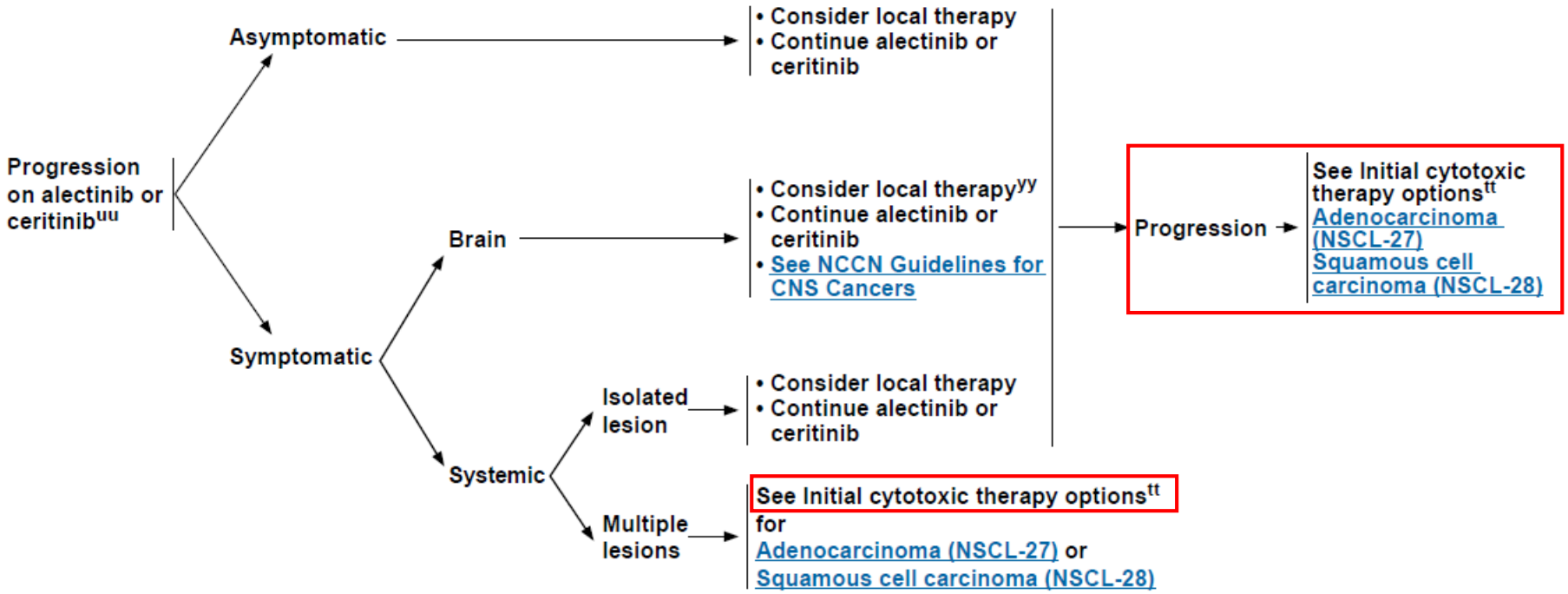
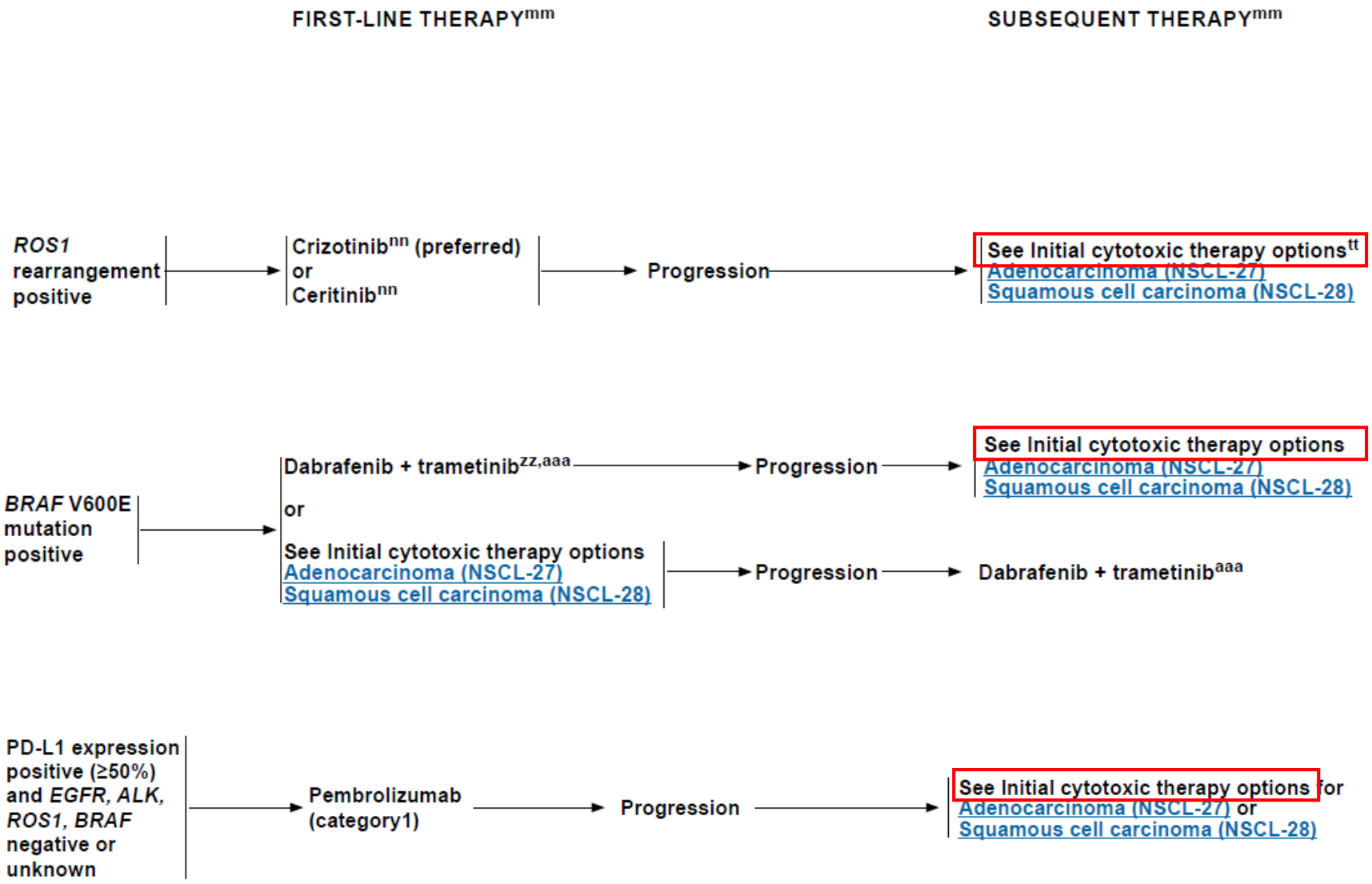
ALK REARRANGEMENT POSITIVE[hh]

SUBSEQUENT THERAPY[mm,rr]



[hh] See Principles of Molecular and Biomarker Analysis (NSCL-G).
[mm] See Targeted Therapy for Advanced or Metastatic Disease (NSCL-I).
[rr] For rapid radiologic progression or threatened organ function, alternate therapy should be instituted.
[tt] The data in the second-line setting suggest that immunotherapy is less effective, irrespective of PD-L1 expression, in tumors with an actionable mutation.
[uu] Beware of flare phenomenon in subset of patients who discontinue ALK inhibitor. If disease flare occurs, restart ALK inhibitor.
[yy] If considering WBRT, consider switching ALK inhibitor before using WBRT.

Stage IV NSCLC-NSq with ROS1, BRAF, PD-L1



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SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE*,**

Initial Cytotoxic Therapy Options

Adenocarcinoma, Large Cell, NSCLC NOS (PS 0-1)

- Bevacizumab/carboplatin/paclitaxel (category 1)[1,†,‡,#]
- Bevacizumab/carboplatin/pemetrexed[2,†,‡,#]
- Bevacizumab/cisplatin/pemetrexed[3,†,‡,#]
- Carboplatin/albumin-bound paclitaxel (category 1)[4]
- Carboplatin/docetaxel (category 1)[5]
- Carboplatin/etoposide (category 1)[6,7]
- Carboplatin/gemcitabine (category 1)[8]
- Carboplatin/paclitaxel (category 1)[9]
- Carboplatin/pemetrexed (category 1)[10]
- Cisplatin/docetaxel (category 1)[5]
- Cisplatin/etoposide (category 1)[11]
- Cisplatin/gemcitabine (category 1)[9,12]
- Cisplatin/paclitaxel (category 1)[13]
- Cisplatin/pemetrexed (category 1)[12]
- Gemcitabine/docetaxel (category 1)[14]
- Gemcitabine/vinorelbine (category 1)[15]
- Pembrolizumab/carboplatin/pemetrexed[16,17,¶]
- Pembrolizumab/cisplatin/pemetrexed[17,¶]

Adenocarcinoma, Large Cell, NSCLC NOS (PS 2)

- Albumin-bound paclitaxel[18]
- Carboplatin/albumin-bound paclitaxel[19,20]
- Carboplatin/docetaxel[5]
- Carboplatin/etoposide[6,7]
- Carboplatin/gemcitabine[8]
- Carboplatin/paclitaxel[9]
- Carboplatin/pemetrexed[10]
- Docetaxel[21,22]
- Gemcitabine[23-25]
- Gemcitabine/docetaxel[14]
- Gemcitabine/vinorelbine[15]
- Paclitaxel[26-28]
- Pemetrexed[29]

*Albumin-bound paclitaxel may be substituted for either paclitaxel or docetaxel in patients who have experienced hypersensitivity reactions after receiving paclitaxel or docetaxel despite premedication, or for patients where the standard premedications (ie, dexamethasone, H2 blockers, H1 blockers) are contraindicated.

**Carboplatin-based regimens are often used for patients with comorbidities or those who cannot tolerate cisplatin.

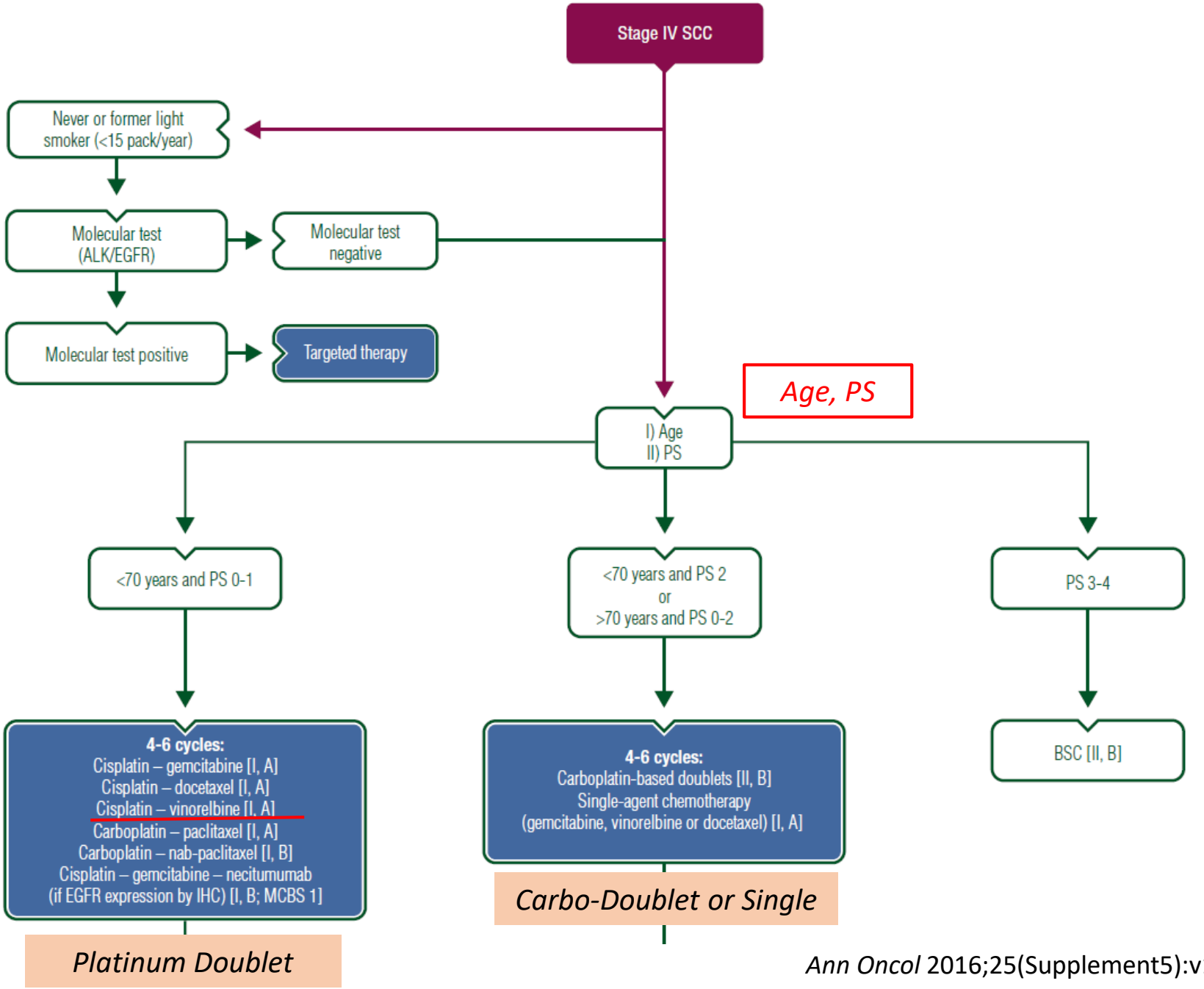
†Bevacizumab should be given until progression.

‡Any regimen with a high risk of thrombocytopenia and the potential risk of bleeding should be used with caution in combination with bevacizumab.

#Criteria for treatment with bevacizumab: non-squamous NSCLC, and no recent history of hemoptysis. Bevacizumab should not be given as a single agent, unless as maintenance if initially used with chemotherapy.

¶If pembrolizumab not previously given.

Stage IV NSCLC-Sq



Ann Oncol 2016;25(Supplement5):v1-v27

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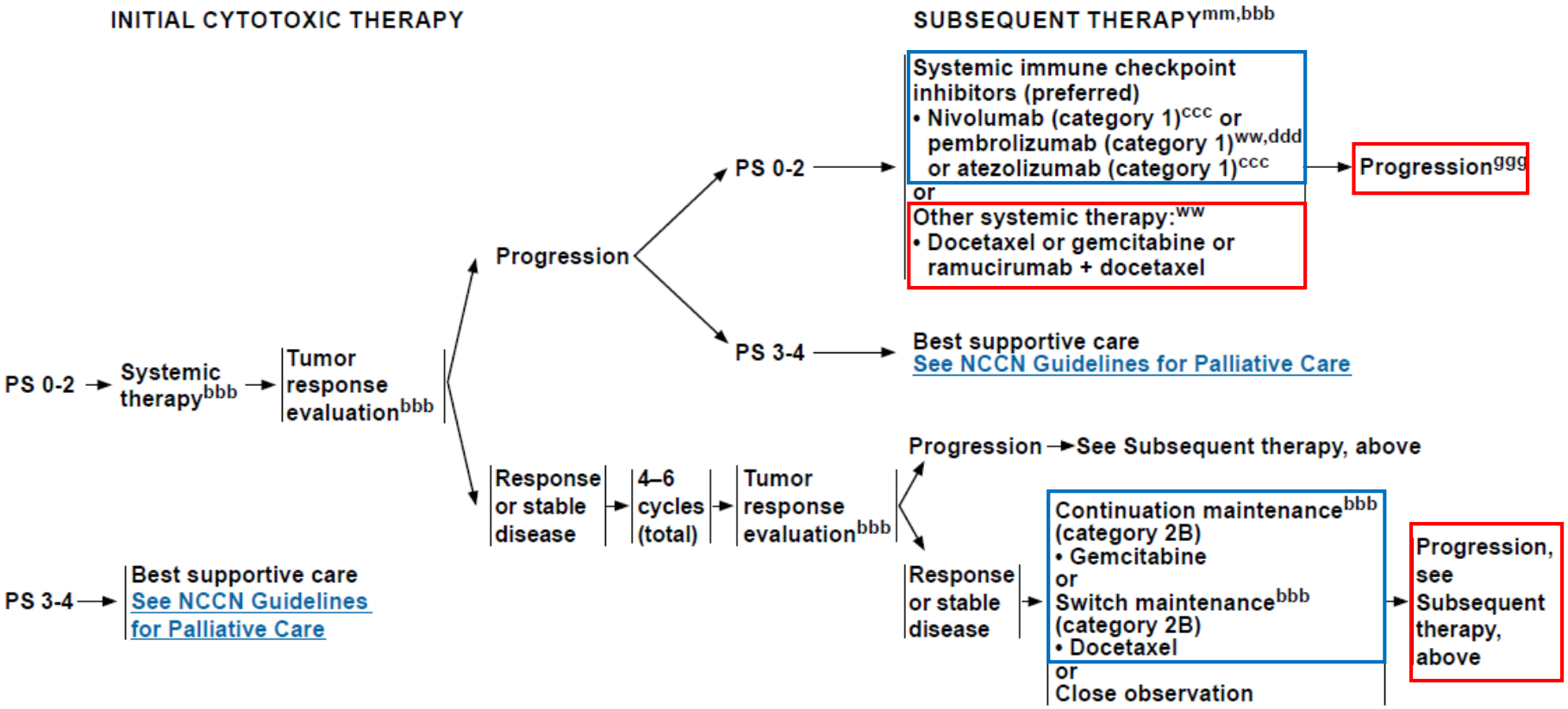
SQUAMOUS CELL CARCINOMA



[mm] See Targeted Therapy for Advanced or Metastatic Disease (NSCL-I).
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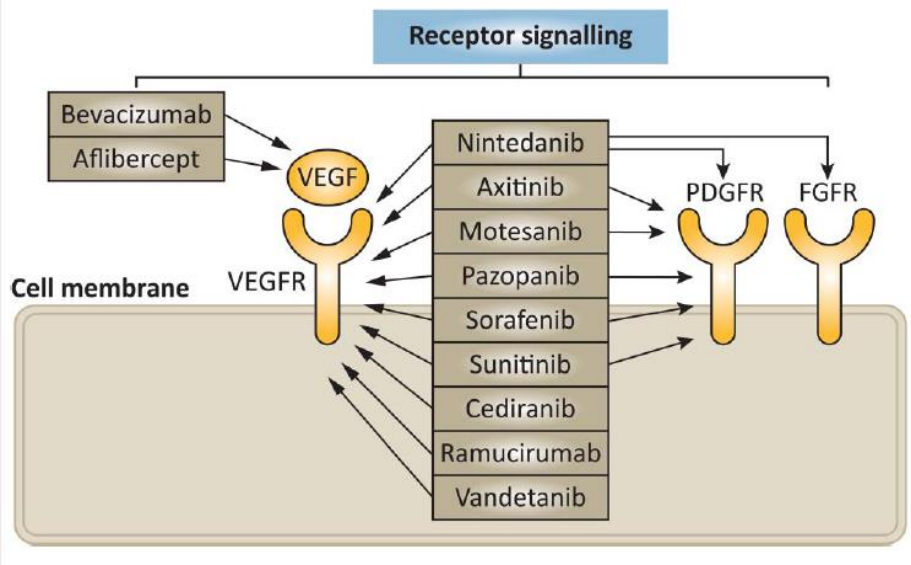
[bbb] See Systemic Therapy for Advanced or Metastatic Disease (NSCL-J).
[ccc] If pembrolizumab not previously given.
[ddd] Pembrolizumab is approved for patients with NSCLC tumors with PD-L1 expression levels ≥1%, as determined by an FDA-approved test.
[ggg] If not already given, options for PS 0-2 include (nivolumab, pembrolizumab, or atezolizumab), docetaxel (category 2B), gemcitabine (category 2B), or ramucirumab + docetaxel (category 2B); options for PS 3-4 include best supportive care. Options for further progression are best supportive care or clinical trial.



ESMO Open 2017;2:e000118

Table 1 Targeted agents influencing angiogenesis evaluated in NSCLC

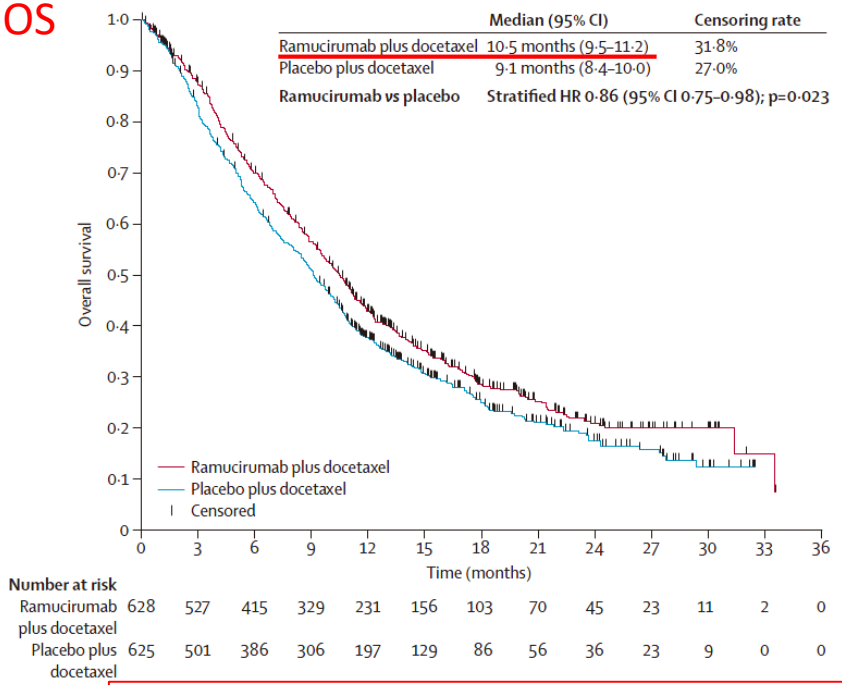
Agent	Description	Target
Bevacizumab	MAb	VEGF-A
Ramucirumab	MAb	VEGFR-2
Anlotinib	TKI	VEGFR-2–3
Apatinib	TKI	VEGFR-2
Axitinib	TKI	VEGFR-1–3, PDGFR, c-kit
Cediranib	TKI	VEGF-1–3
Fruquintinib	TKI	VEGFR-1–3
Lenvatinib	TKI	VEGFR-1–3, PDGFR-α, FGFR-1–4, RET and c-kit
Motesanib	TKI	VEGFR-1–3, PDGFR, kit, RET
Nintedanib	TKI	VEGFR-1–3, FGFR-1–3, PDGFR-α/β
Pazopanib	TKI	VEGFR, PDGFR and c-kit
Sorafenib	TKI	VEGFR-1–3, RET, PDGFR, Flt-3, c-kit
Sunitinib	TKI	VEGFR-1/2, PDGFR-α/β, Flt-3 and c-kit
Vandetanib	TKI	VEGFR, EGFR, RET
Aflibercept	Decoy receptor	All VEGF-A isoforms, VEGF-B, PIGF
Endostar	Recombinant human endostatin	VEGF-induced phosphorylation of VEGFR-2, FGF-2

Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): a multicentre, double-blind, randomised phase 3 trial

Edward B Garon, Tudor-Eliade Ciuleanu, Oscar Arrieta, Kumar Prabhash, Konstantinos N Syrigos, Tuncay Goksel, Keunchil Park, Vera Gorbunova, Ruben Dario Kowalyszyn, Joanna Pikiel, Grzegorz Czyzewicz, Sergey V Orlov, Conrad R Lewanski, Michael Thomas, Paolo Bidoli, Shaker Dakhil, Steven Gans, Joo-Hang Kim, Alexandru Grigorescu, Nina Karaseva, Martin Reck, Federico Cappuzzo, Ekaterine Alexandris, Andreas Sashegyi, Sergey Yurasov, Maurice Pérol

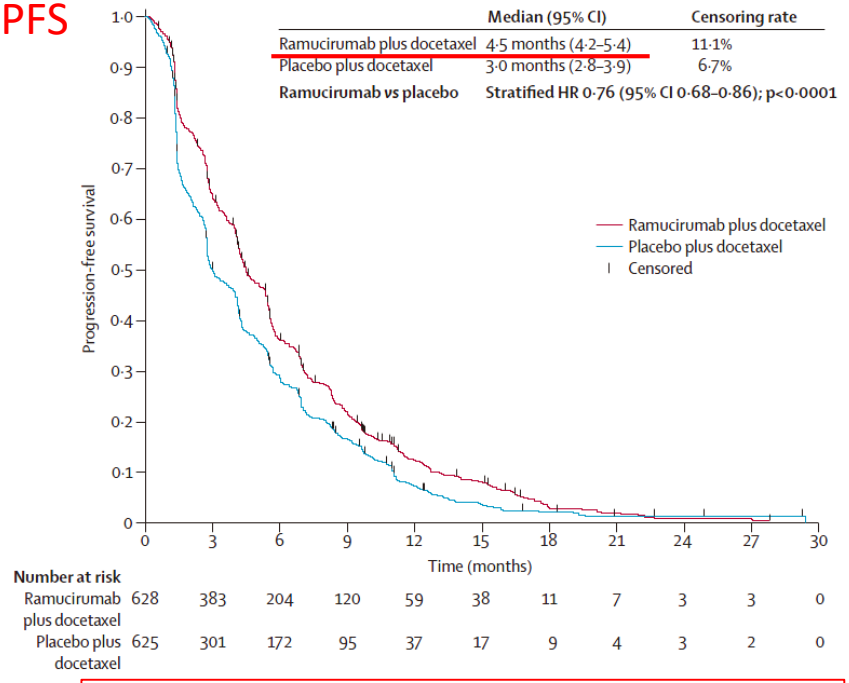
Ramucirumab (Cyramza®) : human IgG1 mAb to extracellular domain of VEGFR-2

OS



NSq : 11.1m (HR 0.83, 95% CI 0.71-0.97, p=0.02)
Sq : 9.5m (HR 0.88, 95% CI 0.69-1.13, p=0.32)

PFS



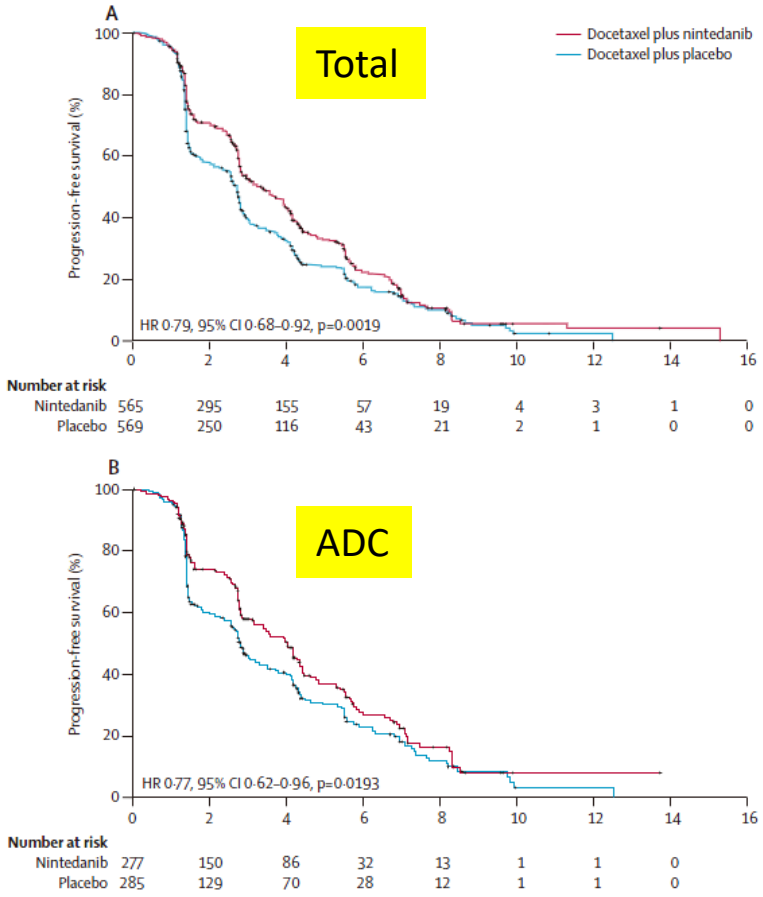
NSq : 4.6m (HR 0.77, 95% CI 0.67-0.88, p<0.001)
Sq : 4.2m (HR 0.76, 95% CI 0.61-0.96, p=0.02)

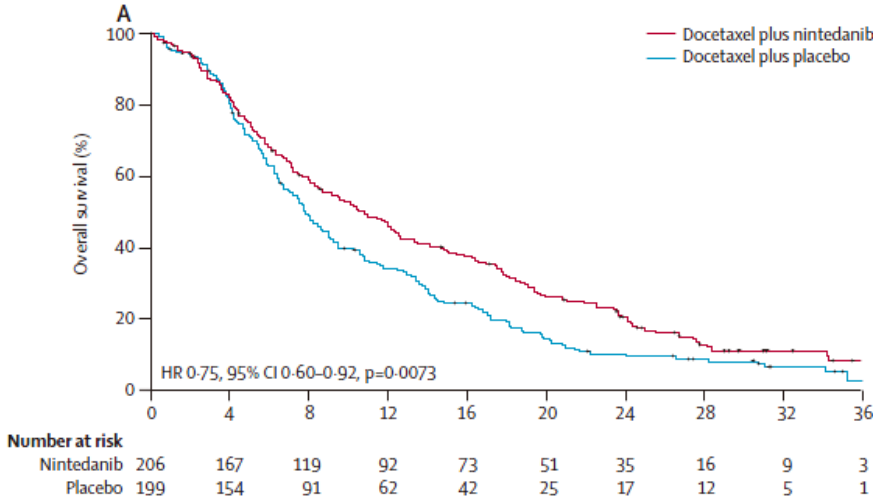
Lancet 2014;384:665-73

Docetaxel plus nintedanib versus docetaxel plus placebo in patients with previously treated non-small-cell lung cancer (LUME-Lung 1): a phase 3, double-blind, randomised controlled trial

Martin Reck, Rolf Kaiser, Anders Mellemgaard, Jean-Yves Douillard, Sergey Orlov, Maciej Krzakowski, Joachim von Pawel, Maya Gottfried, Igor Bondarenko, Meilin Liao, Claudia-Nanette Gann, José Barrueco, Birgit Gaschler-Markefski, Silvia Novello, for the LUME-Lung 1 Study Group

Nintedanib (Ofev®, Vargatef®) : angiokinase inhibitor to VEGFR1-3, FGFR1-3, PDGFRαβ





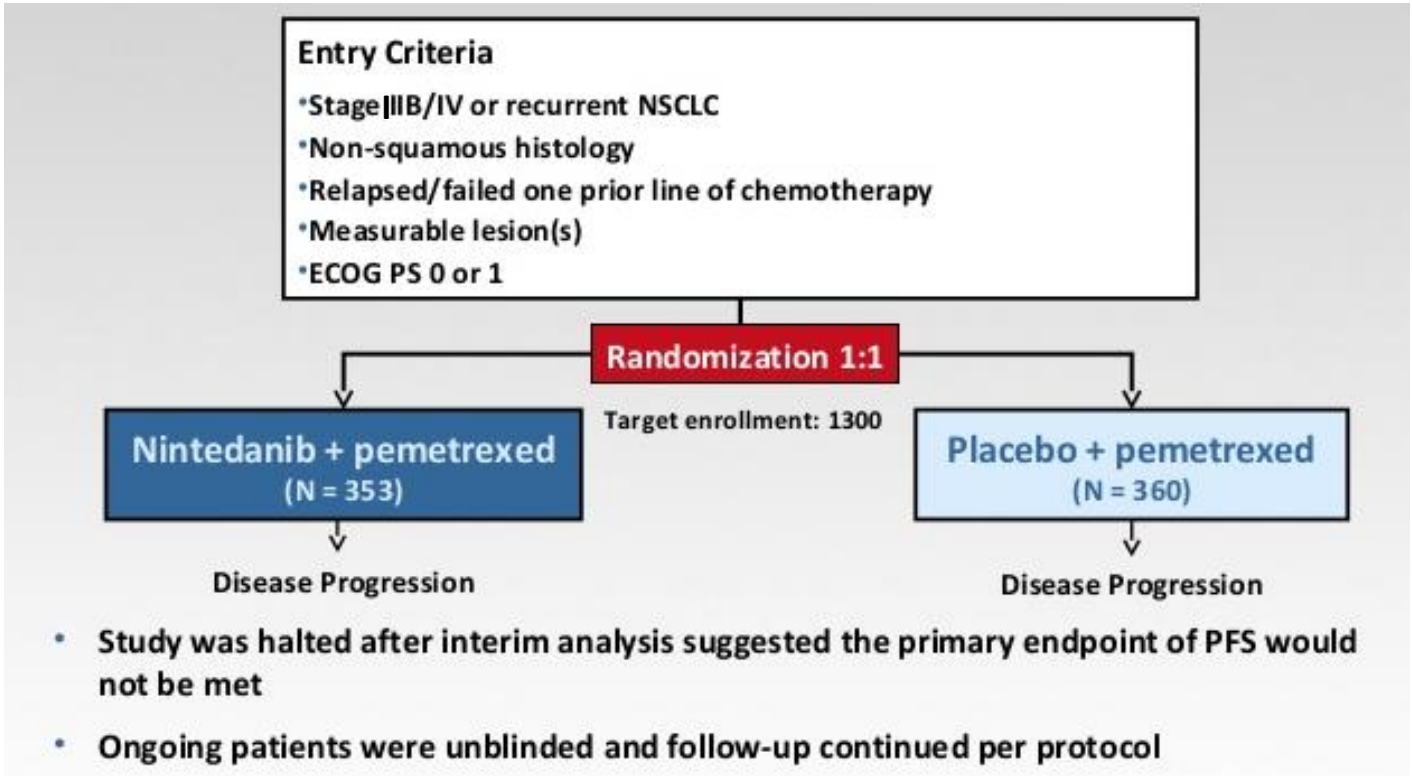
ADC since start of 1st line Tx < 9mon

Lancet Oncol 2014;15:143-55

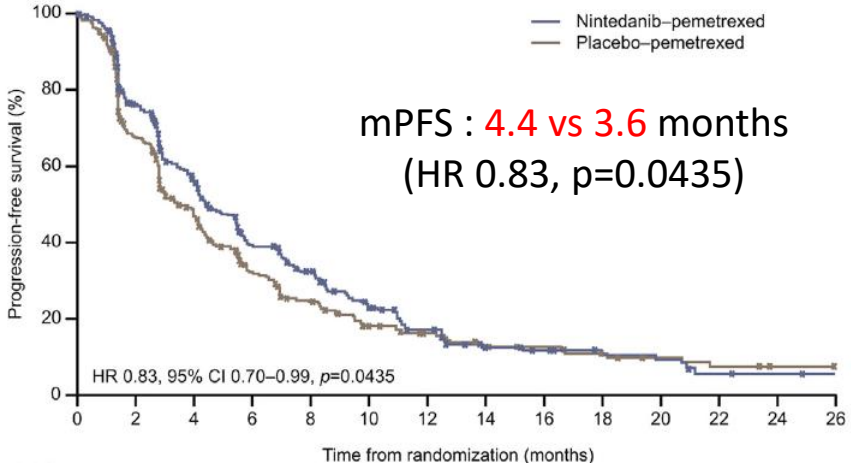
Original research article

Nintedanib plus pemetrexed versus placebo plus pemetrexed in patients with relapsed or refractory, advanced non-small cell lung cancer (LUME-Lung 2): A randomized, double-blind, phase III trial

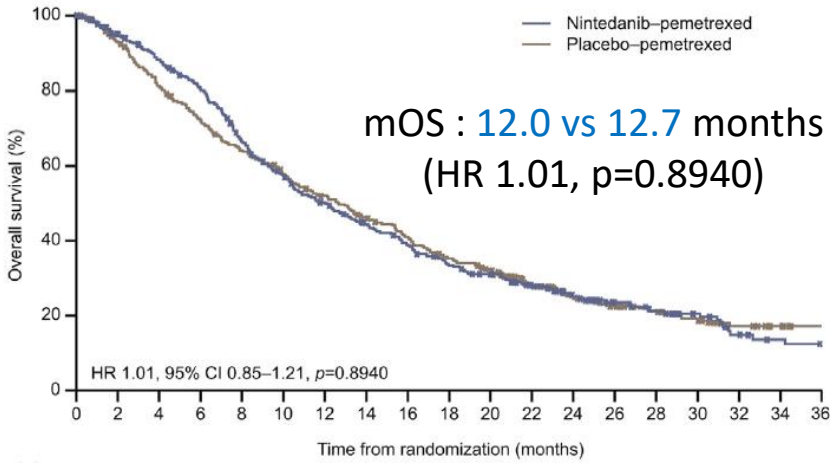
Nasser H. Hanna[a,*,1], Rolf Kaiser[b,c,1], Richard N. Sullivan[d], Osvaldo Rudy Aren[e], Myung-Ju Ahn[f], Beatrice Tiangco[g], Isabelle Voccia[h], Joachim von Pawel[i], Vladimir Kovcin[j], Jason Agulnik[k], Birgit Gaschler-Markefski[b], José Barrueco[l], Patricia Sikken[b], Charles Schloss[l], Joo-Hang Kim[m], for the LUME-Lung 2 Study group



Lung Cancer 2016;102:65-73



mPFS : 4.4 vs 3.6 months
(HR 0.83, p=0.0435)



mOS : 12.0 vs 12.7 months
(HR 1.01, p=0.8940)

Table 3
Overview of AEs (≥10% incidence in either group), classified by CTCAE v3.0.

	Nintedanib–pemetrexed (*n* = 347)		Placebo–pemetrexed (*n* = 357)	
	All grades	Grade ≥3	All grades	Grade ≥3
Patients with any adverse event[a]	331 (95.4%)	237 (68.3%)	336 (94.1%)	194 (54.3%)
Increased ALT	149 (42.9%)	81 (23.3%)	87 (24.4%)	26 (7.3%)
Increased AST	129 (37.2%)	42 (12.1%)	68 (19.0%)	6 (1.7%)
Nausea	128 (36.9%)	10 (2.9%)	119 (33.3%)	5 (1.4%)
Diarrhea	121 (34.9%)	12 (3.5%)	55 (15.4%)	4 (1.1%)
Fatigue	117 (33.7%)	21 (6.1%)	130 (36.4%)	24 (6.7%)
Decreased appetite	98 (28.2%)	4 (1.2%)	90 (25.2%)	7 (2.0%)
Vomiting	86 (24.8%)	6 (1.7%)	72 (20.2%)	10 (2.8%)
Decreased neutrophils	75 (21.6%)	43 (12.4%)	48 (13.4%)	26 (7.3%)
Decreased WBC count	57 (16.4%)	15 (4.3%)	38 (10.6%)	19 (5.3%)
Cough	55 (15.9%)	1 (0.3%)	60 (16.8%)	8 (2.2%)
Dyspnea	54 (15.6%)	15 (4.3%)	79 (22.1%)	15 (4.2%)
Constipation	50 (14.4%)	1 (0.3%)	65 (18.2%)	2 (0.6%)
Headache	44 (12.7%)	1 (0.3%)	48 (13.4%)	1 (0.3%)
Abdominal pain	43 (12.4%)	2 (0.6%)	29 (8.1%)	3 (0.8%)
Decreased hemoglobin	41 (11.8%)	11 (3.2%)	44 (12.3%)	5 (1.4%)
Pyrexia	38 (11.0%)	1 (0.3%)	46 (12.9%)	2 (0.6%)
Back pain	37 (10.7%)	1 (0.3%)	40 (11.2%)	7 (2.0%)
Dizziness	31 (8.9%)	1 (0.3%)	39 (10.9%)	1 (0.3%)
Insomnia	29 (8.4%)	1 (0.3%)	37 (10.4%)	1 (0.3%)

Lung Cancer 2016;102:65-73

REVIEW ARTICLE

Current and Emergent Therapy Options for Advanced Squamous Cell Lung Cancer

Mark A. Socinski, MD,[a,*] Coleman Obasaju, MD, PhD,[b] David Gandara, MD,[c] Fred R. Hirsch, MD,[d] Philip Bonomi, MD,[e] Paul A. Bunn Jr, MD,[d] Edward S. Kim, MD,[f] Corey J. Langer, MD,[g] Ronald B. Natale, MD,[h] Silvia Novello, MD, PhD,[i] Luis Paz-Ares, MD,[j] Maurice Pérol, MD,[k] Martin Reck, MD,[l] Suresh S. Ramalingam, MD,[m] Craig H. Reynolds, MD,[n] David R. Spigel, MD,[o] Heather Wakelee, MD,[p] Nick Thatcher, MB, BChir[q]

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J Thorac Oncol 2018;13(2):165-83

Relapsed or Refractory NSCLC

ASCO Guideline (2017)

Third-Line Treatment

- In patients without a tumor EGFR-sensitizing mutation or ALK or ROS1 gene rearrangement and with non–squamous cell carcinoma and PS of 0 or 1 (and appropriate PS of 2), who received chemotherapy with or without bevacizumab and immune checkpoint therapy, single-agent pemetrexed or docetaxel are options (Type: informal consensus; Evidence quality: low; Strength of recommendation: strong).
- In patients with tumor EGFR-sensitizing mutation(s) who have received at least one first-line EGFR-TKI and prior platinum-based chemotherapy, there are insufficient data to recommend immunotherapy in preference to chemotherapy (pemetrexed or docetaxel [Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: weak]).

Fourth-Line Treatment

- Patients and clinicians should consider and discuss experimental treatment, clinical trials, and continued best supportive (palliative) care.

J Clin Oncol 2017;35(30):3484-3515

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2018
Non-Small Cell Lung Cancer

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Discussion

SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE*,**,§

Initial Cytotoxic Therapy Options

Squamous Cell Carcinoma (PS 0-1)

- Carboplatin/albumin-bound paclitaxel (category 1)[4]
- Carboplatin/docetaxel (category 1)[5]
- Carboplatin/gemcitabine (category 1)[8]
- Carboplatin/paclitaxel (category 1)[9]
- Cisplatin/docetaxel (category 1)[5]
- Cisplatin/etoposide (category 1)[11]
- Cisplatin/gemcitabine (category 1)[9,12]
- Cisplatin/paclitaxel (category 1)[13]
- Gemcitabine/docetaxel (category 1)[14]
- Gemcitabine/vinorelbine (category 1)[15]

Squamous Cell Carcinoma (PS 2)

- Albumin-bound paclitaxel[18]
- Carboplatin/albumin-bound paclitaxel[19,20]
- Carboplatin/docetaxel[5]
- Carboplatin/etoposide[6,7]
- Carboplatin/gemcitabine[8]
- Carboplatin/paclitaxel[9]
- Docetaxel[21,22]
- Gemcitabine[23-25]
- Gemcitabine/docetaxel[14]
- Gemcitabine/vinorelbine[15]
- Paclitaxel[26-28]

*Albumin-bound paclitaxel may be substituted for either paclitaxel or docetaxel in patients who have experienced hypersensitivity reactions after receiving paclitaxel or docetaxel despite premedication, or for patients where the standard premedications (ie, dexamethasone, H2 blockers, H1 blockers) are contraindicated.

**Carboplatin-based regimens are often used for patients with comorbidities or those who cannot tolerate cisplatin.

§Cisplatin/gemcitabine/necitumumab in the first-line setting and afatinib in the second-line setting are not used at NCCN Member Institutions for these indications related to the efficacy and safety of these agents compared to the efficacy and safety of other available agents.

Increased Response Rates to Salvage Chemotherapy Administered after PD-1/PD-L1 Inhibitors in Patients with Non-Small Cell Lung Cancer

Song Ee Park, MD, Se Hoon Lee, MD, PhD, Jin Seok Ahn, MD, PhD, Myung-Ju Ahn, MD, PhD, Keunchil Park, MD, PhD, Jong-Mu Sun, MD, PhD*

* LCBI : last chemotherapy administered before immunotherapy
* SCAI : salvage chemotherapy administered after immunotherapy

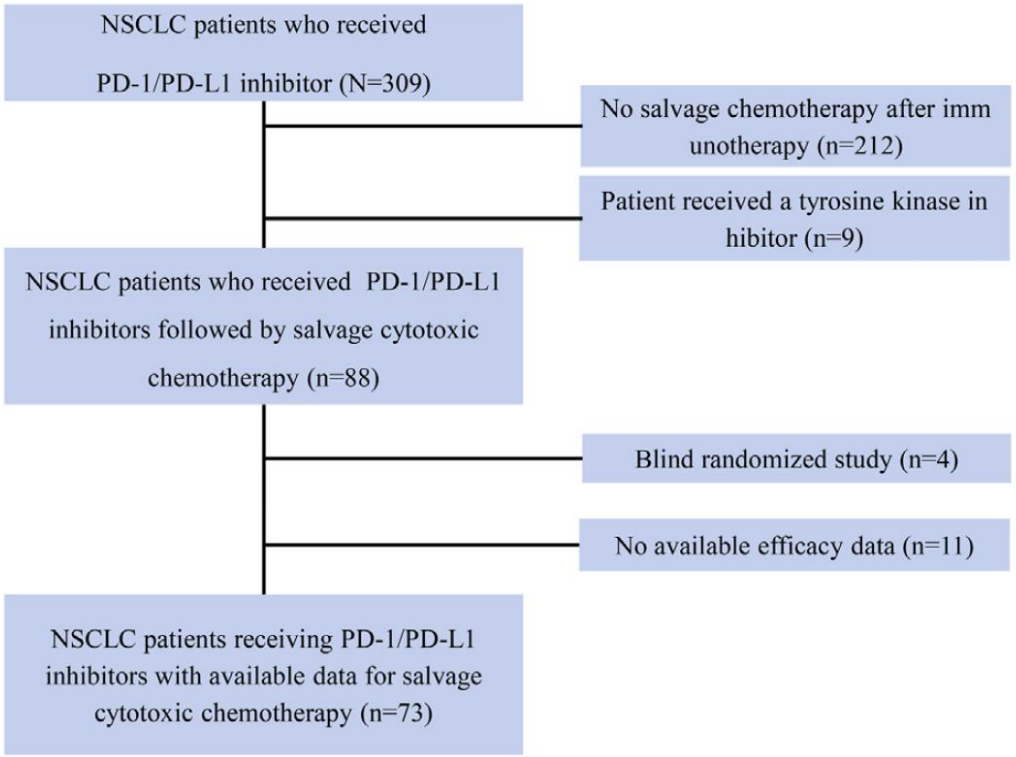


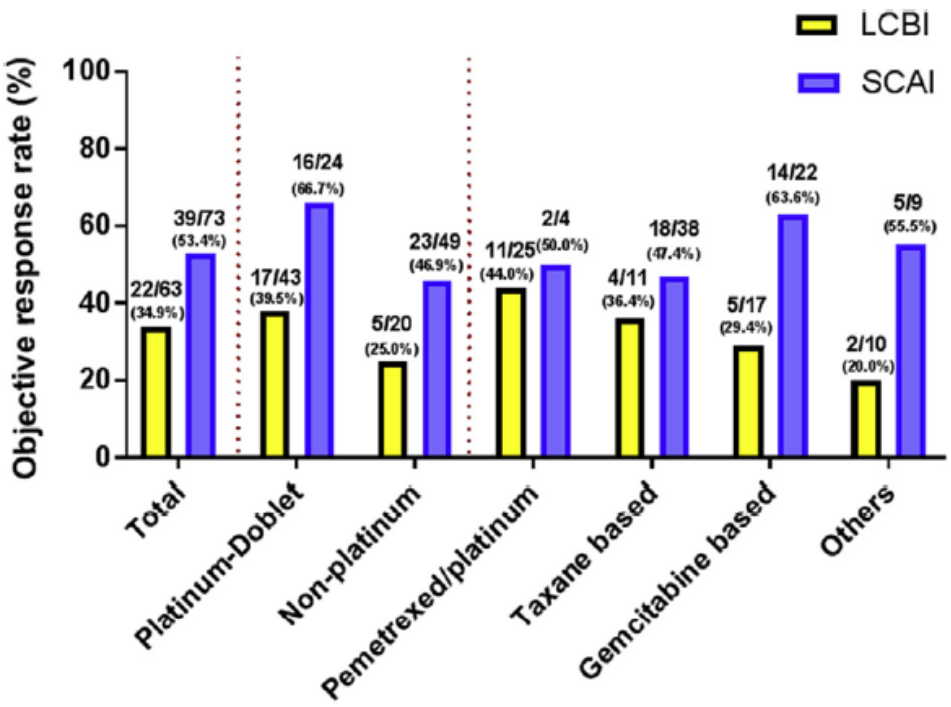
Table 1. Patient Baseline Characteristics

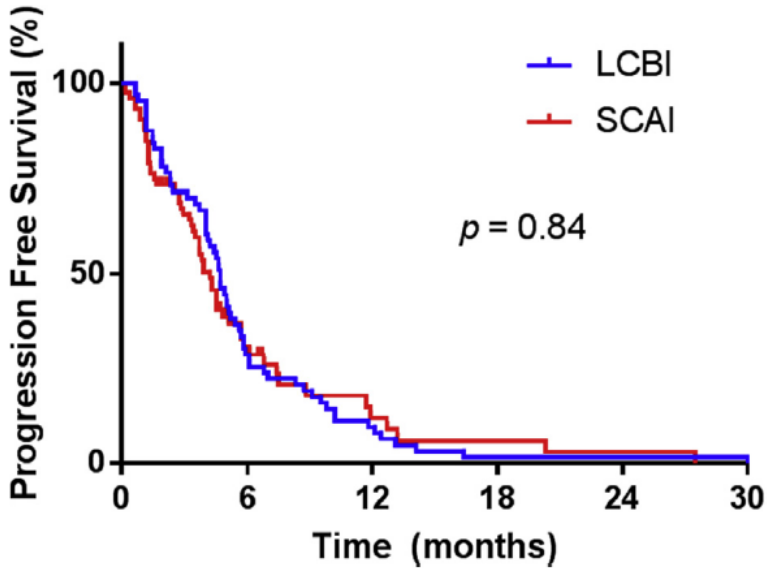
Characteristics	Total (N = 73)
Median age (range), y	60 (35-83)
Sex, n (%)	
Male	50 (68.5%)
Female	23 (31.5%)
ECOG performance status, n (%)	
0	1 (1.4%)
1	58 (79.5%)
2	14 (19.2%)
Smoking status, n (%)	
Former or current	42 (57.5.9%)
Never	31 (42.5%)
Histologic subtype, n (%)	
Squamous cell carcinoma	25 (34.7%)
Adenocarcinoma	44 (60.3%)
Other	4 (5.5%)
EGFR mutation, n (%)	
Wild type	49 (67.1%)
Mutant	8 (11.0%)
Unknown	16 (21.9%)
ALK, n (%)	
Wild type	55 (75.3%)
Mutant	3 (4.1%)
Unknown	15 (20.5%)
Immunotherapy, n (%)	
Nivolumab	34 (46.5%)
Pembrolizumab	30 (41.1%)
Durvalumab	4 (5.5%)
Avelumab	3 (4.1%)
Durvalumab plus tremelimumab	1 (1.4%)
Atezolizumab	1 (1.4%)
Salvage chemotherapy after immunotherapy, n (%)	
Second-line	10 (13.7%)
Third-line	38 (52.1%)
Fourth-line	10 (13.7%)
Fifth-line	8 (11.0%)
Sixth-line or more	7 (9.5%)

J Thorac Oncol 2018;13(1):106-111

Table 2. Comparison of Clinical Outcomes between LCBI and SCAI

Clinical Outcomes	All			Platinum-Based Doublet			Nonplatinum		
	LCBI (n = 63)	SCAI (n = 73)	*p* Value	LCBI (n = 43)	SCAI (n = 24)	*p* Value	LCBI (n = 20)	SCAI (n = 49)	*p* Value
ORR, n (%)	22 (34.9%)	39 (53.4%)	0.03	17 (39.5%)	16 (66.7%)	0.03	5 (25.0%)	23 (46.9%)	0.09
Median PFS, mo	4.7	4.2	0.84	4.7	4.5	0.86	3.5	3.8	0.56





J Thorac Oncol 2018;13(1):106-111

Considerations for Drug selection

- Age
- Performance
- Compliance of a patient
- Drug-specific complication
- Schedule or Interval of drug administration (Residence)
- Cost, Economic state, Support from caregivers

……

Drug-specific complications (A → Z)

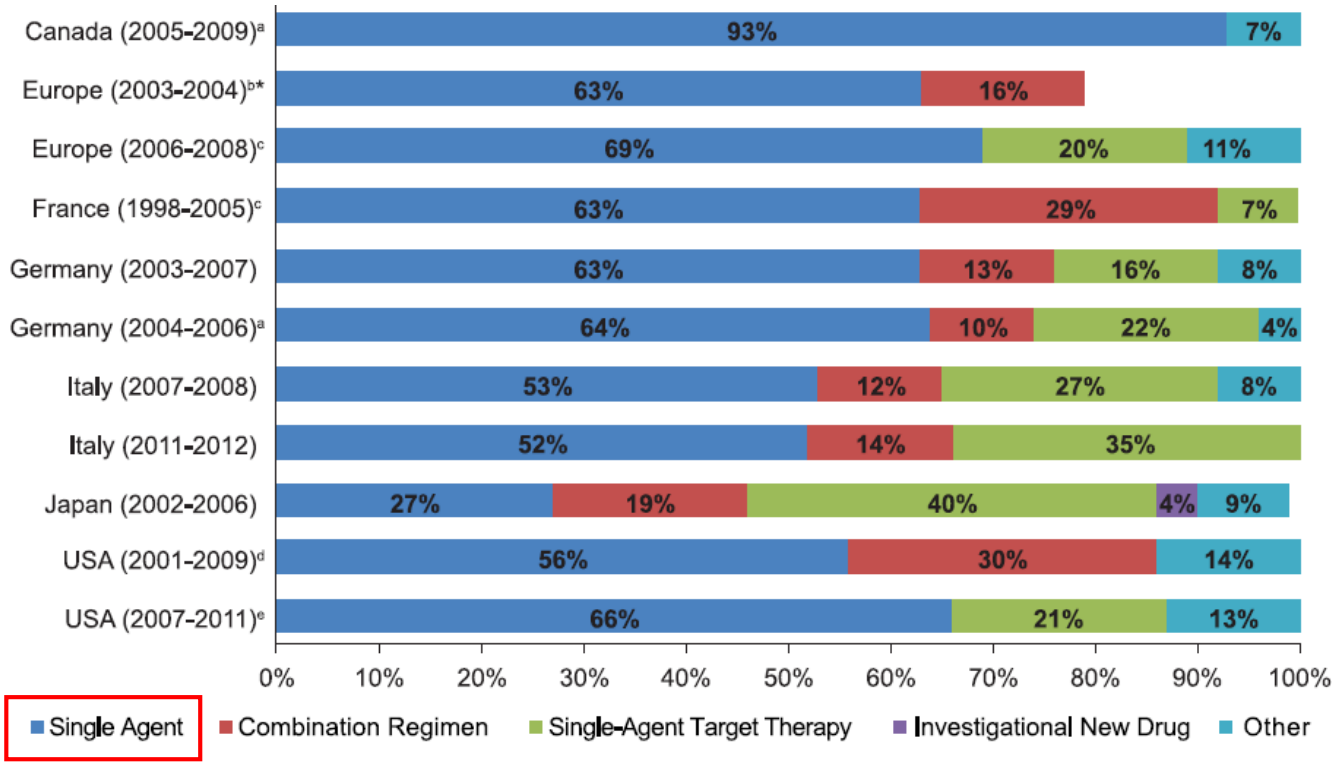
- Belotecan : Myelosuppression
- Docetaxel : Mucositis, Extravasation, Hypersensitivity
- Etoposide : Myelosuppression
- Gemcitabine : Anemia, Transaminitis
- Irinotecan : Diarrhea, Nausea, Vomiting
- Paclitaxel : Neuropathy, Hypersensitivity
- Pemetrexed : Anemia
- Topotecan : Myelosuppression
- Vinorelbine : Neuropathy, Extravasation

PLOS ONE

RESEARCH ARTICLE

Real-world treatment patterns for patients receiving second-line and third-line treatment for advanced non-small cell lung cancer: A systematic review of recently published studies

Second-Line systemic regimen composition



PLoS One 2017;12(4):e0175679

Table 2. Summary of second-line treatment patterns.

Country	Reference	Number of Patients Enrolled	Patients With First-Line Treatment, n (%)[a]	Patients With Second-Line Treatment, n (%)[a]	Overall Second-Line Treatment Regimen Distribution, n (%)[b]	Distribution of Single-Agent Treatments, n (%)[b]	Distribution of Combination Regimens, n (%)[b]	Distribution of Targeted Therapy, n (%)[b]
Brazil[c]	Younes et al, 2011	2673	1548 (58%)	625 (40.4%)	Non-platinum based 95% Platinum based 5%	NR	NR	NR
Canada[c]	Sacher et al, 2015	8113	1944 (24%)	609 (31.3%)	Single agent 93% Other 7%	Docetaxel 52% Pemetrexed 41%	NR	NR
Europe[d]	Bischoff et al, 2010	975	975 (100%)	285 (29.2%)	Single agent 63% Combination regimen 16%	Taxane 120 (42%) Vinorelbine 31 (11%) Gemcitabine 29 (10%)	NR	NR
Europe[e]	Moro-Sibilot et al, 2010; Vergnenegre et al, 2012 (SELECTTIONN)	1013	1013 (100%)	1013 (100%)	Single agent 700 (69%) Targeted therapy 206 (20%) Other regimens 106 (11%)	Pemetrexed 468 (46%) Docetaxel 232 (23%)	NR	Erlotinib 207 (20%)
France[f]	Carpentier, 2016	1,047	863 (82%)	431 (41.2%)	Single agent 273 (64%) Combination regimen 126 (29%) Targeted therapy 32 (7%)	Docetaxel 100 (23%) Pemetrexed 17 (4%) Other 156 (36%)	Cisplatin based: 48 (11%) Carboplatin based: 78 (18%)	Erlotinib or gefitinib 32 (7%)
Germany	Zietemann, 2011; Zietemann, 2010	406	406 (100%)	213 (52.5%)	Single agent 134 (63%) Combination regimen 28 (13%) Targeted therapy 35 (16%) Other regimen 16 (8%)	Docetaxel 66 (31%) Gemcitabine 31 (15%) Vinorelbine 24 (11%) Pemetrexed 13 (6%)	Gemcitabine + mitomycin 10 (5%) Carboplatin + paclitaxel 7 (3%) Carboplatin + vinorelbine 5 (2%) Carboplatin + gemcitabine 3 (1%) Carboplatin + docetaxel 3 (1%)	Erlotinib 20 (9%) Gefitinib 15 (7%)
Germany[c]	Reinmuth et al, 2013	493	352 (71%)	183 (52%)	Single agent 117 (64%) Combination regimen 18 (10%) Targeted therapy 41 (22%) Other 7 (4%)	NR	Platinum based 18 (10%)	EGFR-TKI 41 (22%)
Italy	De Marinis et al, 2014; Gridelli et al, 2014 (LIFE)	541	541 (100%)	464 (85.8%)	Single agent 241 (52%) Combination regimen 63 (14%) Targeted therapy 163 (35%)	Docetaxel 118 (25%) Pemetrexed 68 (15%) Gemcitabine 26 (6%) Vinorelbine 23 (5%) Carboplatin 2 (<1%) Cisplatin 2 (<1%) Paclitaxel 2 (<1%)	Carboplatin + gemcitabine 15 (3%) Cisplatin + pemetrexed 14 (3%) Docetaxel + gemcitabine 9 (2%) Carboplatin + paclitaxel 8 (2%) Carboplatin + pemetrexed 7 (2%) Cisplatin + gemcitabine 5 (1%) Other 5 (1%)	Erlotinib 149 (32%) Gefitinib 9 (2%) Bevacizumab combination 3 (1%) Crizotinib 2 (<1%)

PLoS One 2017;12(4):e0175679

Country	Reference	Number of Patients Enrolled	Patients With First-Line Treatment, n (%)[a]	Patients With Second-Line Treatment, n (%)[a]	Overall Second-Line Treatment Regimen Distribution, n (%)[b]	Distribution of Single-Agent Treatments, n (%)[b]	Distribution of Combination Regimens, n (%)[b]	Distribution of Targeted Therapy, n (%)[b]
Italy	Gridelli et al, 2011	987	790 (80%)	275 (35%)	Single agent 146 (53%) Combination regimen 34 (12%) Targeted therapy 73 (27%) Clinical trial 22 (8%)	Pemetrexed 56 (20%) Docetaxel 46 (17%) Gemcitabine 19 (7%) Vinorelbine 19 (7%) Cisplatin or carboplatin 3 (1%) Other 3 (1%)	Carboplatin + vinorelbine 6 (2%) Carboplatin + pemetrexed 6 (2%) Carboplatin + gemcitabine 4 (1%) Docetaxel + vinorelbine 2 (1%) Carboplatin + paclitaxel 2 (1%) Cisplatin + docetaxel 2 (1%) Cisplatin + gemcitabine 1 (<1%) Other 6 (2%)	Erlotinib 73 (27%)
Japan	Asahina et al, 2012	599	599 (100%)	415 (69%)	Single agent 114 (27%) Combination regimen 80 (19%) Targeted therapy 167 (40%) Investigational new drug 15 (4%) Other 39 (9%)	Docetaxel 114 (27%)	Carboplatin + paclitaxel 64 (15%) Carboplatin + gemcitabine 16 (4%)	Gefitinib 167 (40%)
United States[g]	Pan et al, 2013	1168	1168 (100%)	1168 (100%)	Single agent 781 (66%) Targeted therapy 241 (21%) Other 146 (13%)	Pemetrexed 635 (54%) Docetaxel 117 (10%) Gemcitabine 29 (2%)	NR	Erlotinib 205 (18%) Bevacizumab combination 36 (3%)
United States[h]	Davis et al, 2015	17,133	7029 (41%)	3405 (20%)	Single agent 1916 (56%) Combination regimen 1012 (30%) Other 477 (14%)	Gemcitabine 550 (16%) Docetaxel 459 (14%) Pemetrexed 376 (11%) Vinorelbine 207 (6%) Paclitaxel 206 (6%) Carboplatin 118 (3%)	Carboplatin + paclitaxel 458 (14%) Carboplatin + gemcitabine 299 (9%) Carboplatin + docetaxel 181 (5%) Gemcitabine + vinorelbine 74 (2%)	NR

PLoS One 2017;12(4):e0175679

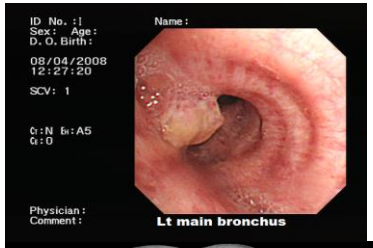
Table 3. Summary of survival outcomes by definition of survival time.

Region/ Country	Source	Number of Patients	Study Setting	Study Period	Median OS, months (first line)	Median OS, months (second line)	Median OS, months (third line)	Median OS (BSC only)	OS Definition
Time from start of each chemotherapy line until death/study end									
Japan	Asahina et al, 2012	599	Single institution	2002–2006	15.3 (13.8–16.5)	12.8 (10.7–14.5)	12.0 (9.3–14.2)		Time from first day of each chemotherapy line until death or last day of follow-up period
Germany	Reinmuth et al, 2013	493	Single institution	2004–2006	7.6 (6.8–8.5)	6.2 (5.0–7.4)	5.2 (3.5–7.0)		Time from the beginning of the respective line of systemic therapy
Europe (Germany)	Zietemann, 2010 and 2011	405	Single institution	2003–2008	8.9 (8.2–10.1)	4.6 (3.8–5.7)	3.8 (2.6–5.4)		Time from first day of each chemotherapy line until death or last day of follow-up period; OS given in days in study and converted to months (days/30)
Time from start of second-line chemotherapy until death/study end									
Europe (multiple)	SELECTTION study—2010, 2012	1013	Provider based	2006–2008		ACA: 8.1 (6.9–9.0) other NSCLC: 6.2 (5.5–6.8)			Time from start of second-line chemotherapy until death or date of last contact
United States	Pan et al, 2013	1168	Provider based	2007–2011		7.5 (6.6–8.4)			Time from start of second-line chemotherapy until death or date of last follow-up visit (K-M)
Time from the start of third-line chemotherapy until death/study end									
France	Carpentier et al, 2016	226	Population based	1998–2005			TKI: 5.9 (4.2–10.1)		Time from initiation of third line treatment to date of death, vital status, or end of study period (K-M)

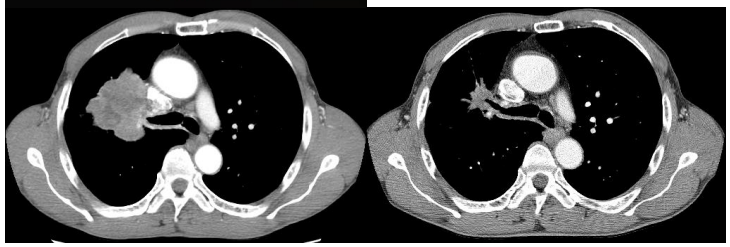
PLoS One 2017;12(4):e0175679

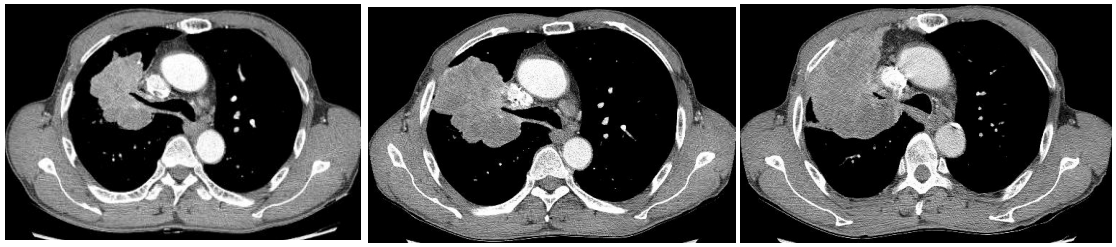
Case 1 M/70

SQC, RUL (08.8.4), IV (cT4N2M1a : Lt.main bronchus)

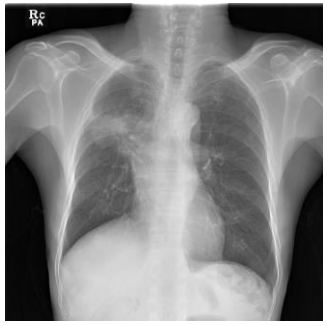


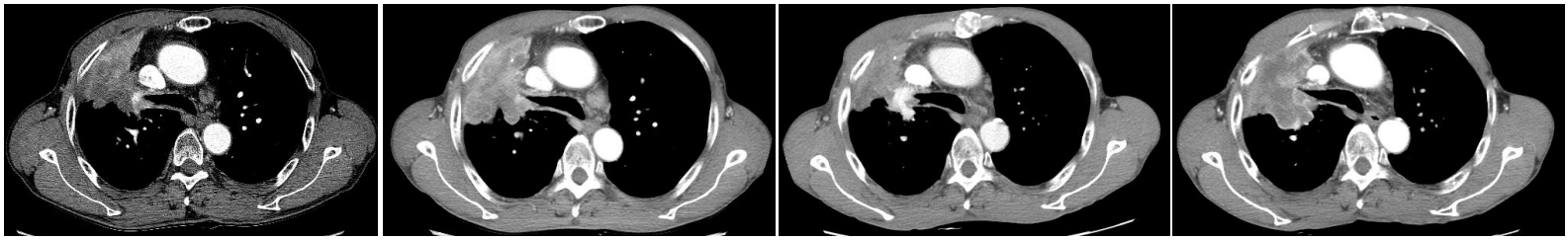
- **G**-Gemcitabine, **D**-Docetaxel(**wD**-weakly), **N**-Vinorelbine, **I**-Irinotecan, **E**-Etoposide(**OE**-oral), **Pdx**-Paclitaxel, **UFT**-Tegafur/uracil, **A**-Pemetrexed
- **H**-Topotecan, **Cb**-Belotecan
- **P**-Cisplatin, **C**-Carboplatin





1-GP#6 (08.8.27 ~ 12.23)	2-wD#2 (09.3.16 ~ 4.20)	3-Tarceva#2 (09.4.30 ~ 6.15)	4-N#2 (09.6.16 ~ 7.14)	5-I#4 (09.7.27 ~ 10.7)

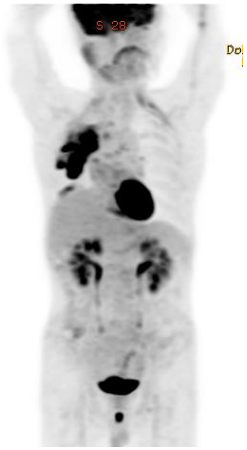


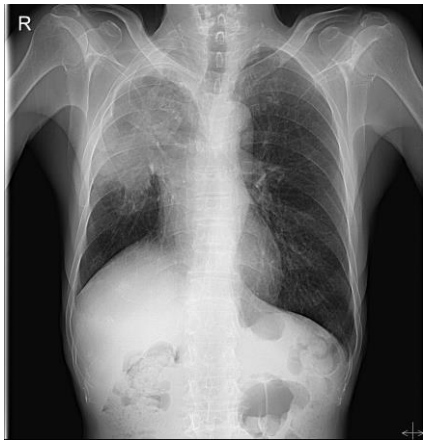


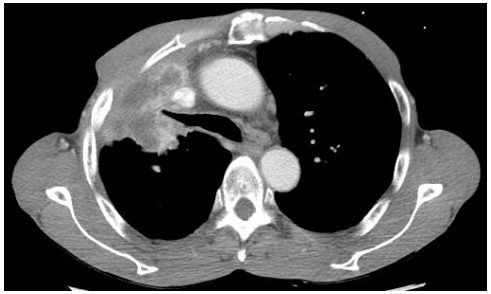
pRT to RUL (09.10.29 ~ 11.13)	6-EC#4 (10.3.8 ~ 6.14)	7-Pdx#1 (10.8.11)	2”pRT to RUL (10.9.9 ~ 9.24)	8-UFT6# (10.10.11 ~ 11.4.21)	3”pRT to RUL (11.5.12 ~ 5.25)

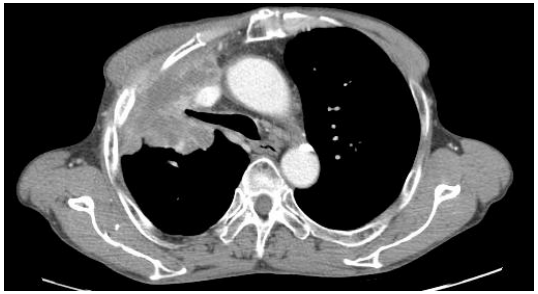
Case 1 M/70

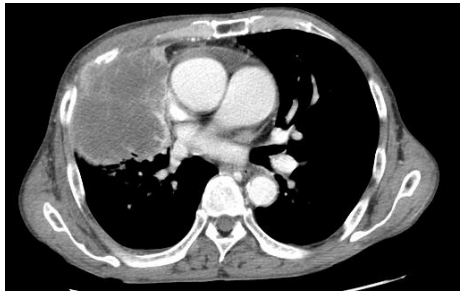
SQC, RUL (08.8.4), IV (cT4N2M1a : Lt.main bronchus)











9-GC#4 (11.8.29 ~ 11.7)	10-OE#3 (12.1.2 ~ 2.25)	Chemo-Off

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Non-Small Cell Lung Cancer

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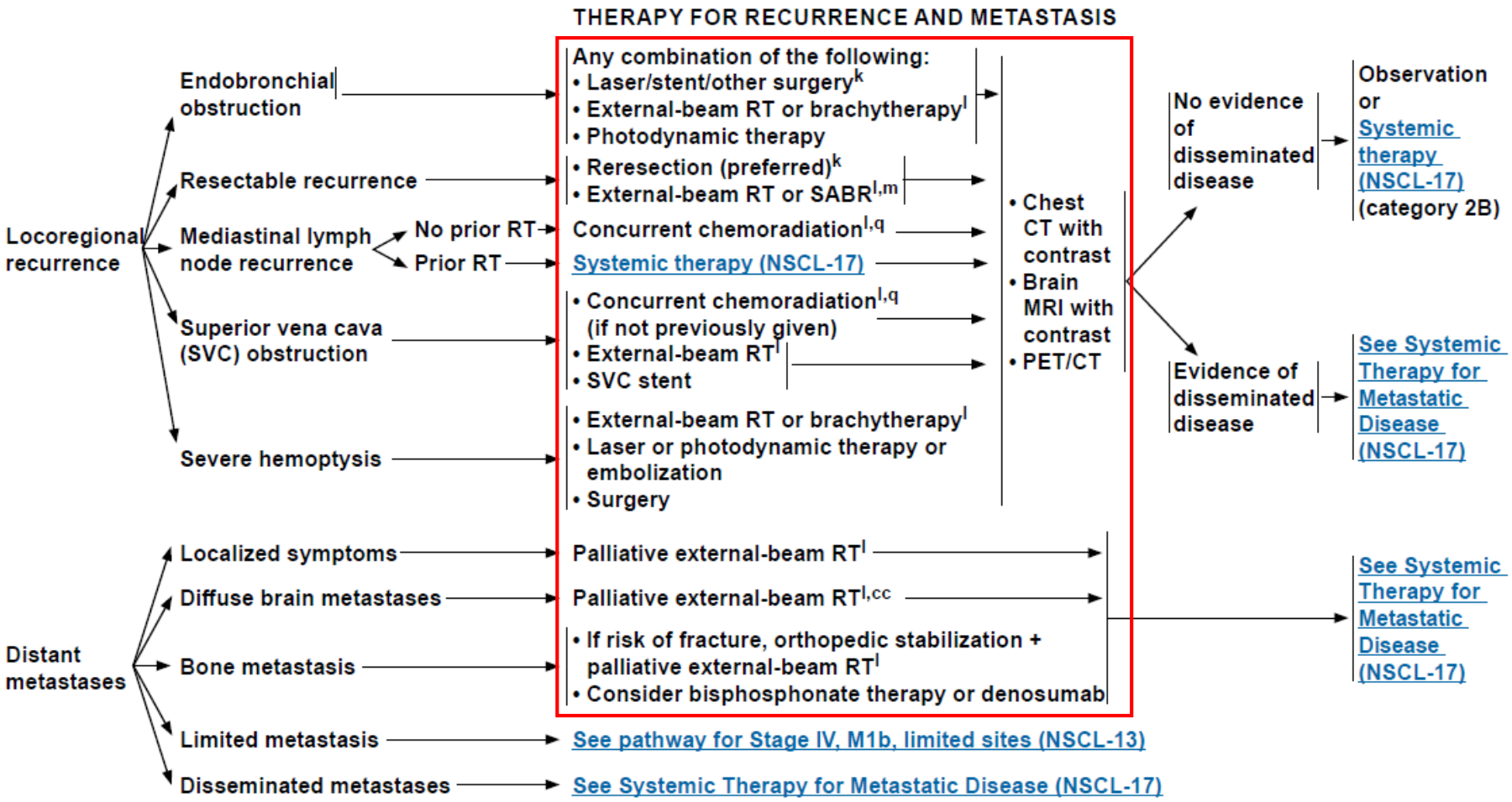
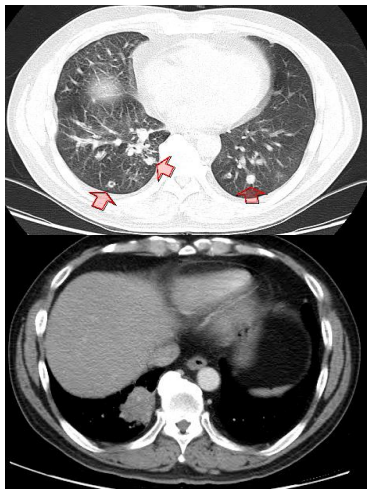
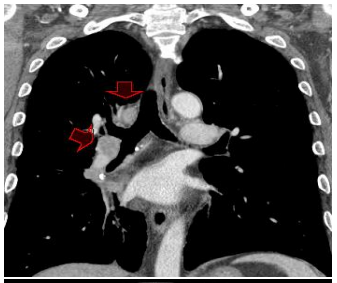


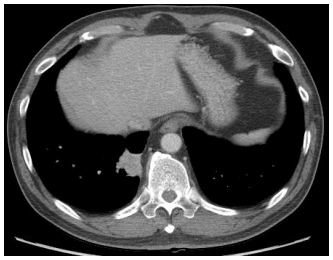
[k] See Principles of Surgical Therapy (NSCL-B).
[l] See Principles of Radiation Therapy (NSCL-C).
[m] Interventional radiology ablation is an option for selected patients.
[q] See Chemotherapy Regimens Used with Radiation Therapy (NSCL-E).
[cc] See NCCN Guidelines for Central Nervous System Cancers.

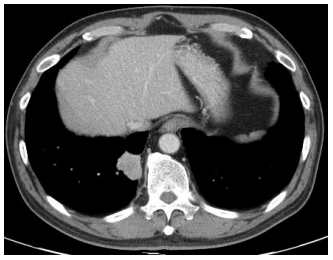
Case 2 M/64

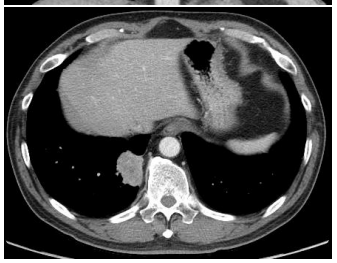
ADC, RLL (10.7.6 TTNB), IV (M1a : lung to lung)
- EGFR wild, ALK-FISH(-)

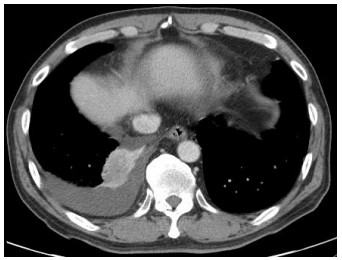










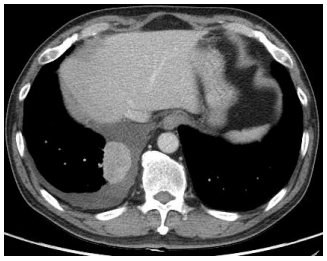


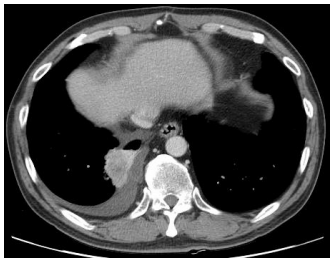
1-AP#6
(10.7.23 ~ 11.9)

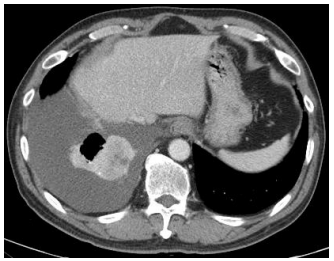
2-Iressa#2
(11.2.8 ~ 3.29)

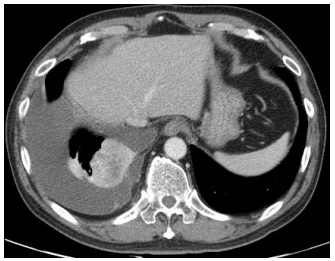
3-wD#6
(11.4.14 ~ 8.25)

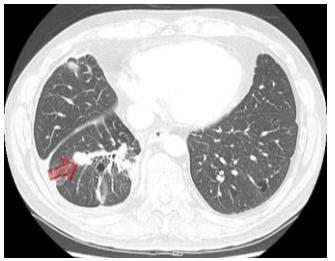
4-G#4
(11.11.24 ~ 12.2.2)











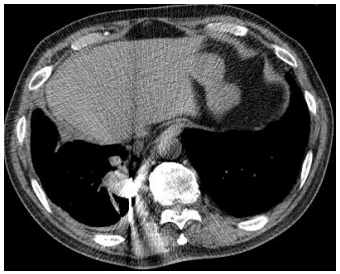
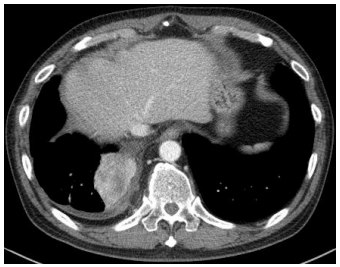
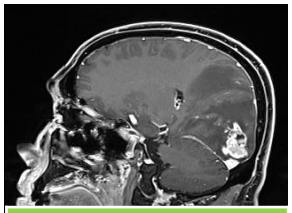
5-N#13
(12.2.16 ~ 13.4.18)

6-Pdx#6
(13.5.16 ~ 13.10.10)

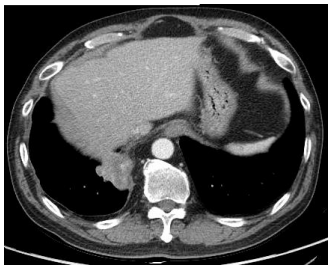
7-N#6
(14.1.2 ~ 9.11)

Case 2 M/64

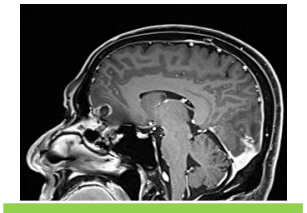
ADC, RLL (10.7.6 TTNB), IV (M1a : lung to lung)
- EGFR wild, ALK-FISH(-), PD-L1(+) HER2(-) MET E14m(+)

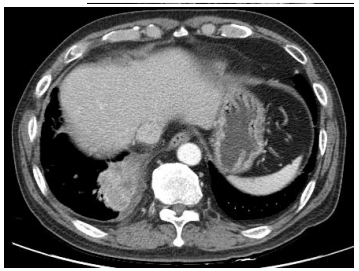
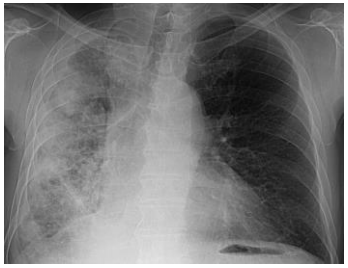
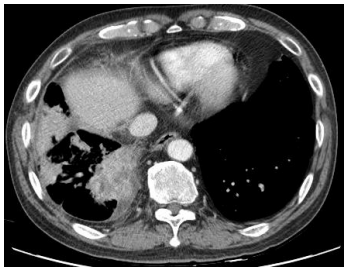
GKS (15.2.12)



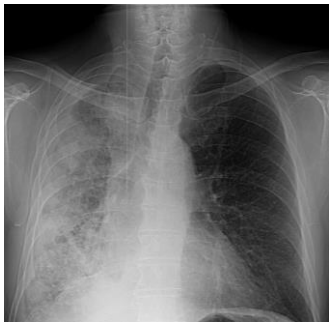
8-Durvalumab (ATLANTIC)
(14.10.23 ~ 15.10.8, 1Yr)

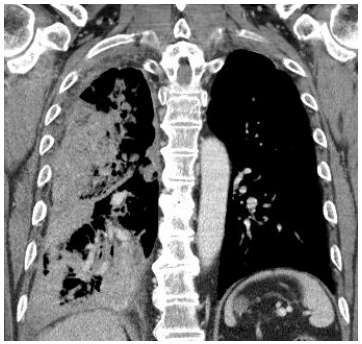
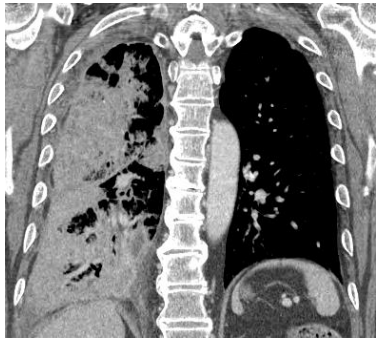


2"GKS (15.12.28)

9-Xalkori#1
(16.3.31 ~ 4.13)



10-N#4
(16.4.14 ~ 8.11)

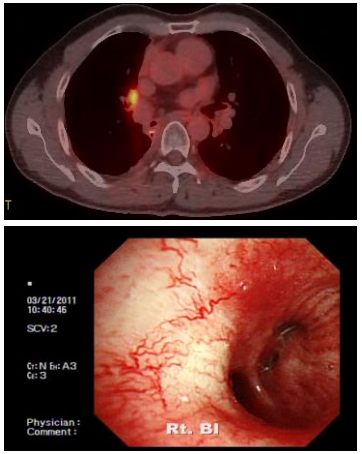
Expired
(16.9.13)

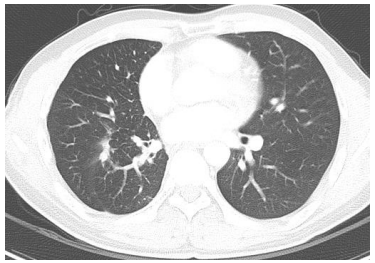
Case 3 M/51

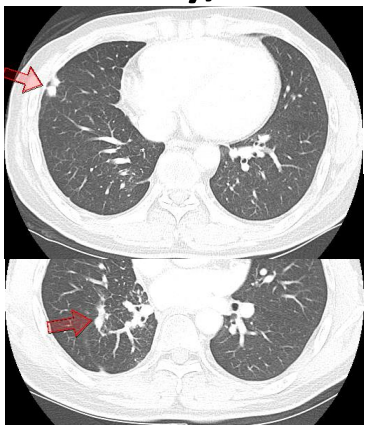
ADC, RLL, IIIA (pT2N2M0), s/p RLL lobectomy c MLND (08.9.25)

- EGFR d-seq : wild

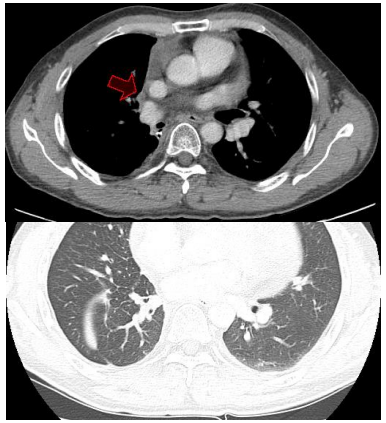
- aTP#4 (08.11.11 ~ 09.1.14), PORT (09.2.3 ~ 3.12, 28fx, 5750cGy)

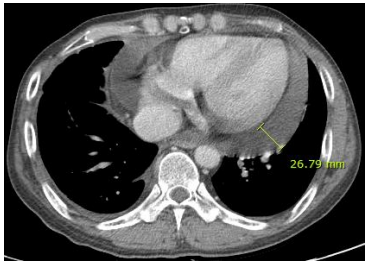




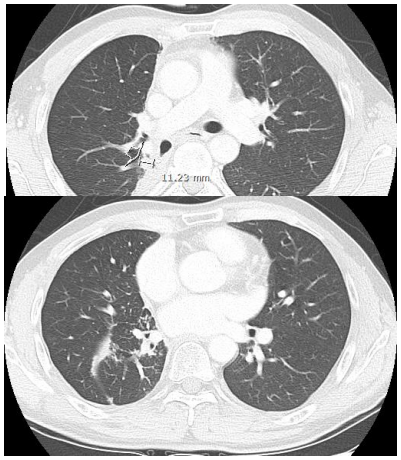


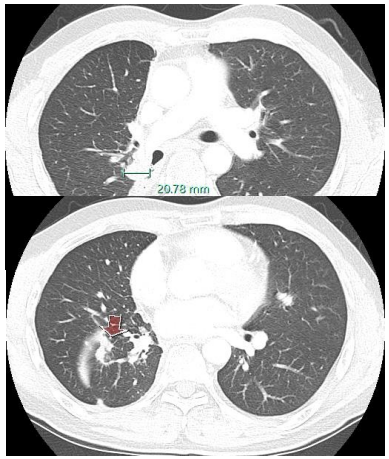
1-AP#6
(11.4.6 ~ 7.20)



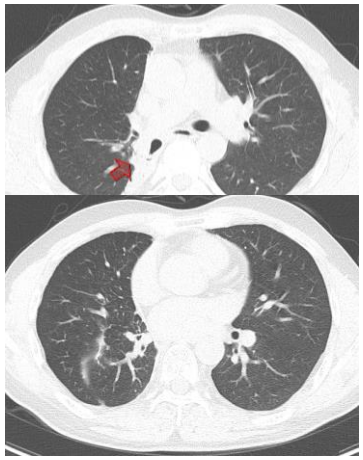


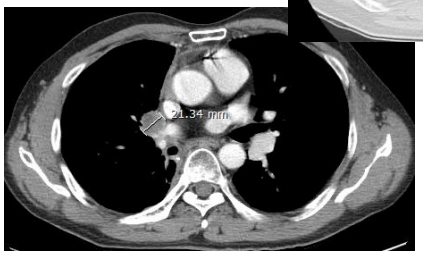
2-Tarceva + CS7017#12
(11.10.26 ~ 12.9.5)

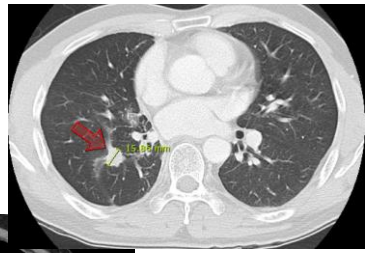




3-D#4
(12.12.5 ~ 13.2.13)







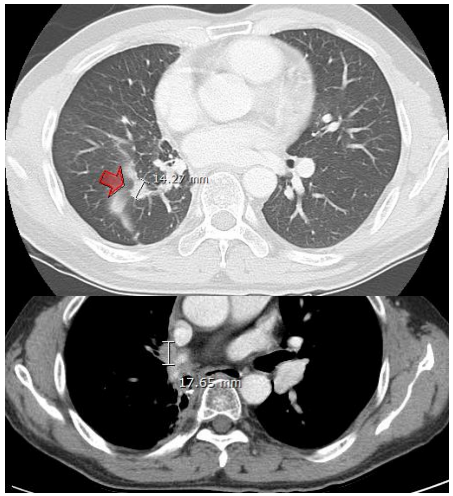
4-Tarceva#24
(13.5.22 ~ 15.5.7)

Case 3 M/51

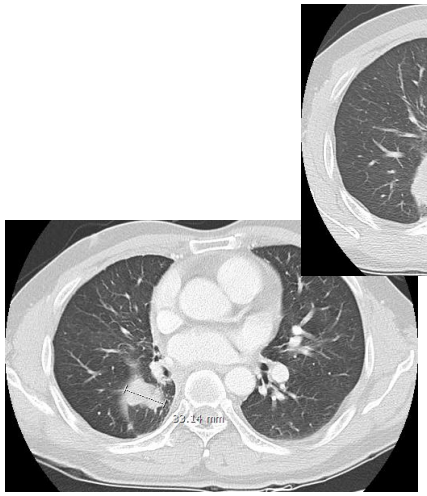
ADC, RLL, IIIA (pT2N2M0), s/p RLL lobectomy c MLND (08.9.25)

- EGFR d-seq : wild PD-L1(-) , EGFR-PNA : E19del(+)

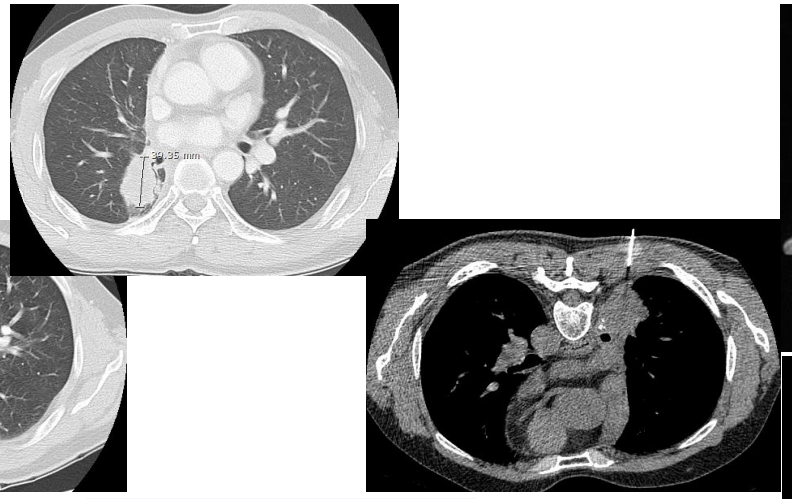
- aTP#4 (08.11.11 ~ 09.1.14), PORT (09.2.3 ~ 3.12, 28fx, 5750cGy)



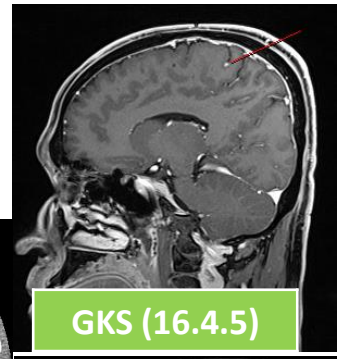
5-GC#6 (15.5.21 ~ 10.12)



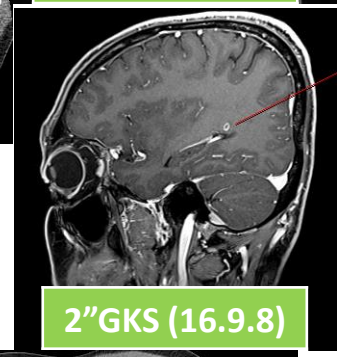
6-N#1 (15.11.5)



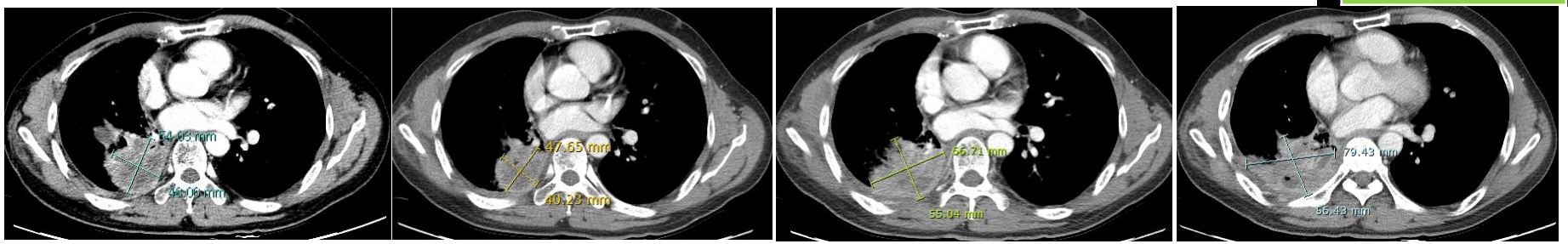
7-EC#2 (15.12.25 ~ 16.1.17)



GKS (16.4.5)



2”GKS (16.9.8)



8-Rociletinib#4 (TIGER-3) (16.5.11 ~ 9.4)

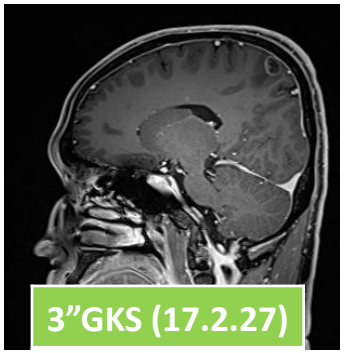
9-I#3 (16.9.22 ~ 11.30)

Case 3 M/51

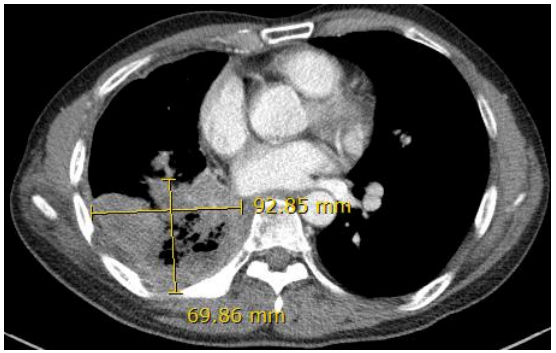
ADC, RLL, IIIA (pT2N2M0), s/p RLL lobectomy c MLND (08.9.25)

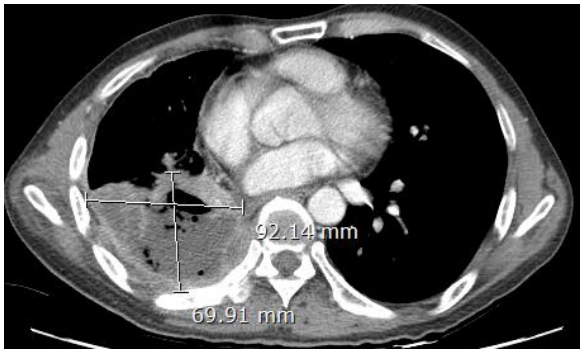
- EGFR d-seq : wild PD-L1(-) , EGFR-PNA : E19del(+)

- aTP#4 (08.11.11 ~ 09.1.14), PORT (09.2.3 ~ 3.12, 28fx, 5750cGy)



3”GKS (17.2.27)





10-Tarceva#1 (17.3.2 ~ 4.10)

11-Opdivo rec) : Refuse

Expired (17.4.24)

Contents – SCLC

- Standard regimen
- Second- or Further-lines options

  (-) Immune checkpoint inhibitors (ICIs)

- Case study

SCLC

clinical practice guidelines

Annals of Oncology 24 (Supplement 6): vi99–vi105, 2013
doi:10.1093/annonc/mdt178
Published online 27 June 2013

Small-cell lung cancer (SCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

M. Früh[1], D. De Ruysscher[2], S. Popat[3], L. Crinò[4], S. Peters[5] & E. Felip[6], on behalf of the ESMO Guidelines Working Group*

Ann Oncol 2013;24(Supplement6):vi99-vi105

VOLUME 33 · NUMBER 34 · DECEMBER 1 2015

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Treatment of Small-Cell Lung Cancer: American Society of Clinical Oncology Endorsement of the American College of Chest Physicians Guideline

Charles M. Rudin, Nofisat Ismaila, Christine L. Hann, Narinder Malhotra, Benjamin Movsas, Kim Norris, M. Catherine Pietanza, Suresh S. Ramalingam, Andrew T. Turrisi III, and Giuseppe Giaccone

J Clin Oncol 2015;33(34):4106-4111

NCCN National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Small Cell Lung Cancer

Version 2.2018 — January 17, 2018

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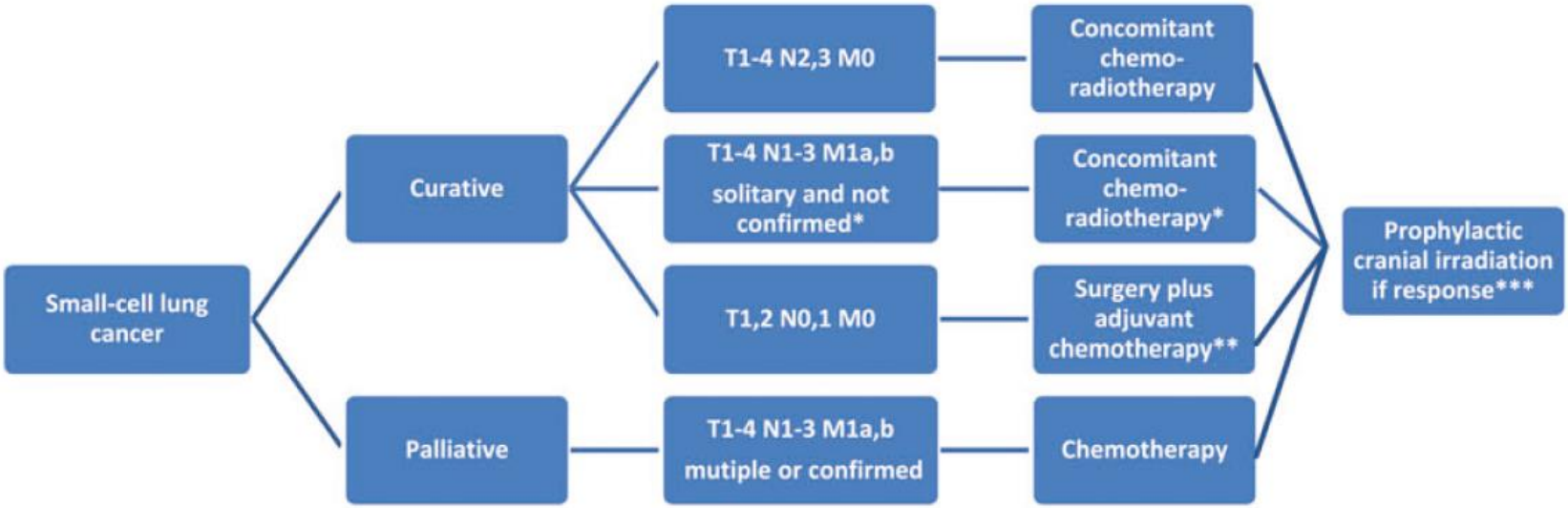
NCCN 2018 Ver 2



***if no confirmation of solitary metastasis is obtained, radiotherapy may be added after first response evaluation and is omitted in case of obvious metastatic involvement**
**** concomitant chemoradiotherapy as an alternative option**
***** or stable disease in case of localised disease**

Ann Oncol 2013;24(Supplement6):vi99-vi105

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NCCN Guidelines Version 2.2018
Small Cell Lung Cancer

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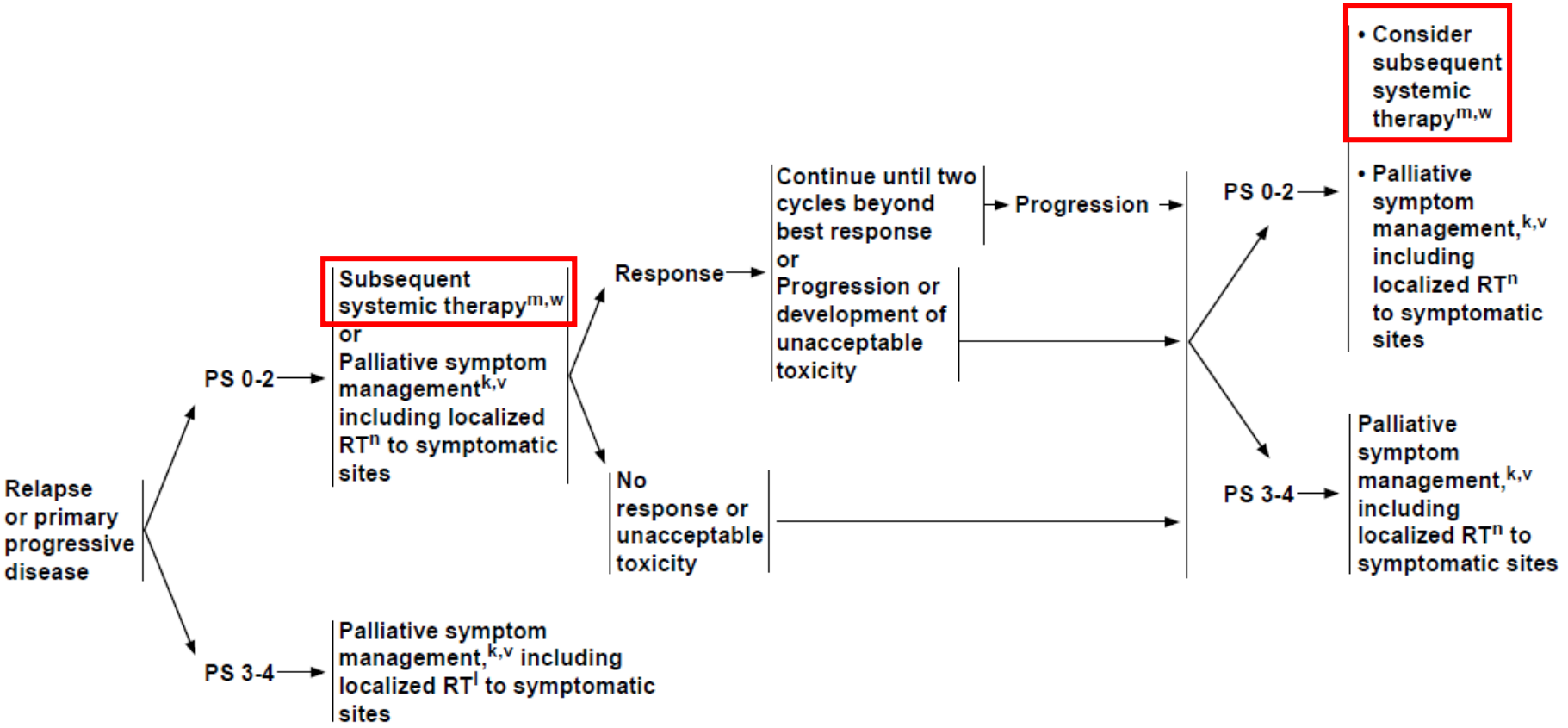
PROGRESSIVE DISEASE **SUBSEQUENT THERAPY/PALLIATIVE THERAPY**



Relapsed or Refractory SCLC

ESMO Guideline (2013)

- For refractory patients and resistant patients with early relapse (<6 weeks), participation in a clinical trial or best supportive care is recommended [II, C]
- Oral or i.v. topotecan are recommended for patients having resistant or sensitive relapse with CAV being an alternative option [II, B]
- Patients with sensitive relapse may derive benefit from reintroduction of the first-line regimen (usually platinum–etoposide) [V, C]

Ann Oncol 2013;24(Supplement6):vi99-vi105

ASCO Guideline (2015)

- In patients with relapsed or refractory SCLC, the administration of second-line, single-agent chemotherapy is recommended (grade 1B).
- Enrollment onto a clinical trial is encouraged.
- Single-agent topotecan has US Food and Drug Administration approval in this context.

J Clin Oncol 2015;33(34):4106-4111

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Small Cell Lung Cancer

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PRINCIPLES OF SYSTEMIC THERAPY* (1 of 3)

Systemic therapy as primary or adjuvant therapy:

- **Limited stage (maximum of 4–6 cycles):**
  - Cisplatin 60 mg/m² day 1 and etoposide 120 mg/m² days 1, 2, 3[1]
  - Cisplatin 80 mg/m² day 1 and etoposide 100 mg/m² days 1, 2, 3[2]
  - Carboplatin AUC 5–6 day 1 and etoposide 100 mg/m² days 1, 2, 3[3]
  - During systemic therapy + RT, cisplatin/etoposide is recommended (category 1).
  - The use of myeloid growth factors is not recommended during concurrent systemic therapy plus radiotherapy (category 1 for not using GM-CSF).[4]

- **Extensive stage (maximum of 4–6 cycles):†**
  - Carboplatin AUC 5–6 day 1 and etoposide 100 mg/m² days 1, 2, 3[5]
  - Cisplatin 75 mg/m² day 1 and etoposide 100 mg/m² days 1, 2, 3[6]
  - Cisplatin 80 mg/m² day 1 and etoposide 80 mg/m² days 1, 2, 3[7]
  - Cisplatin 25 mg/m² days 1, 2, 3 and etoposide 100 mg/m² days 1, 2, 3[8]
  - Carboplatin AUC 5 day 1 and irinotecan 50 mg/m² days 1, 8, 15[9]
  - Cisplatin 60 mg/m² day 1 and irinotecan 60 mg/m² days 1, 8, 15[10]
  - Cisplatin 30 mg/m² days 1, 8 and irinotecan 65 mg/m² days 1, 8[11]

Subsequent systemic therapy:‡

- Clinical trial preferred.

- Relapse ≤6 mo, PS 0-2:
  - Topotecan PO or IV[12-14]
  - Irinotecan[15]
  - Paclitaxel[16,17]
  - Docetaxel[18]
  - Temozolomide[19,20]
  - Nivolumab ± ipilimumab[21,22]
  - Vinorelbine[23,24]
  - Oral etoposide[25,26]
  - Gemcitabine[27,28]
  - Cyclophosphamide/doxorubicin/vincristine (CAV)[12]
  - Bendamustine (category 2B)[29]

- Relapse >6 mo: original regimen[30,31] → Sensitive relapse

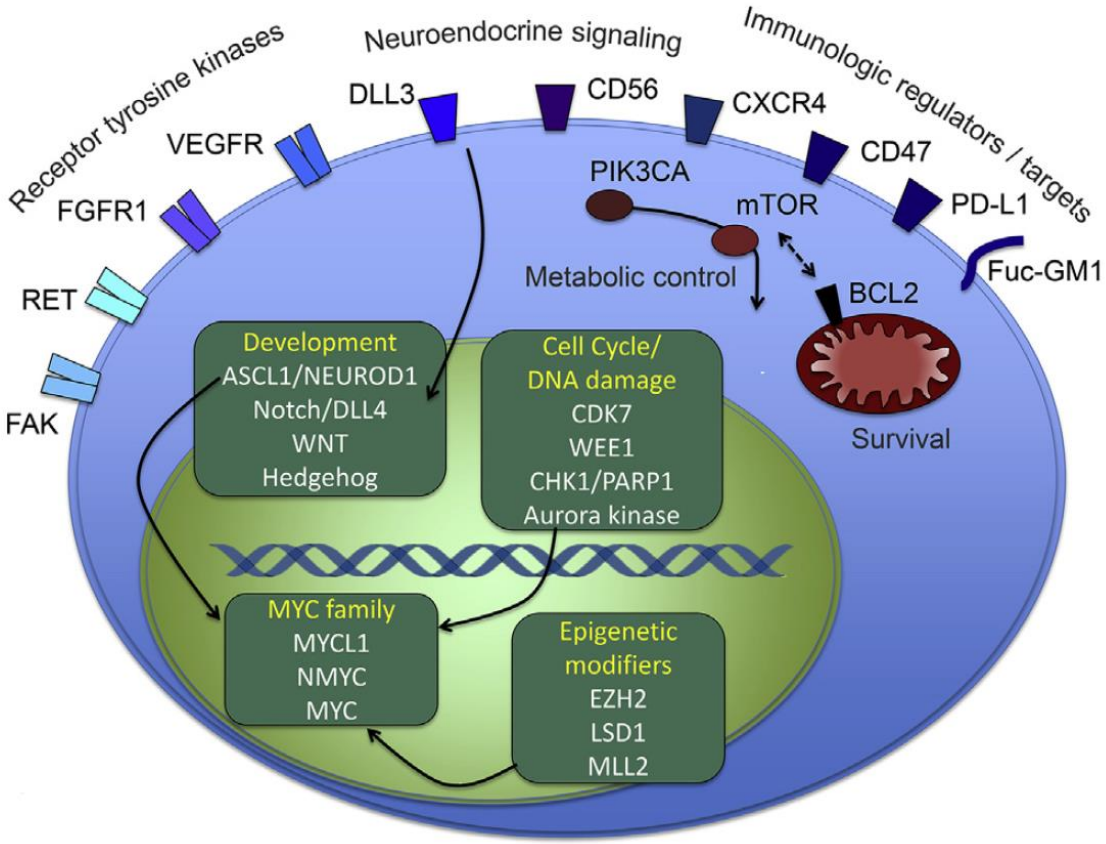
Consider dose reduction or growth factor support for patients with PS 2

Response Assessment SCL-E 2 of 3

References on SCL-E 3 of 3

*The regimens included are representative of the more commonly used regimens for small cell lung cancer. Other regimens may be acceptable.
†If not used as original regimen, may be used as therapy for primary progressive disease.
‡Subsequent systemic therapy refers to second-line and beyond therapy.

Small Cell Lung Cancer: Can Recent Advances in Biology and Molecular Biology Be Translated into Improved Outcomes?



J Thorac Oncol 2016;11(4):452-74

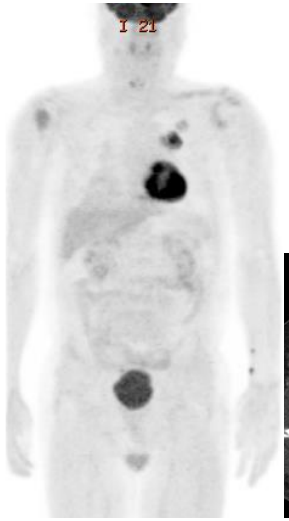
Table 1. Therapeutic Agents and Targets in Small Cell Lung Cancer

Agent	Target	Trial Phase	References
Erismodegib, sonidegib (LDE225)	Smoothened (hedgehog antagonist)	Preclinical, I	57
Vismodegib (GDC-0449)	Smoothened (hedgehog antagonist)	Preclinical, I, II	58
ABT-737	Bcl-2, Bcl-xL	Preclinical	65, 69
Navitoclax (ABT-263)	Bcl-2, Bcl-xL, Bcl-w	Preclinical, I, II[a]	66, 67, 68
Silvestrol	EIF4E	Preclinical	70, 71
PHA-680632	Aurora kinases	Preclinical	74
Alisertib (MLN8237)	Aurora A kinase	Preclinical, I, II	74, 76
Barasertib (AZD1152)	Aurora B kinase	Preclinical, I[a]	75
MEDI0639	DLL4	Preclinical, I	77
Tarextumab (OMP-59R5)	Notch 2/3	Preclinical, I, II	78
Demcizumab (OMP-21M18)	DLL4	Preclinical, I, II (NSCLC)	79
Ponatinib (AP24534)	FGFR1, PDGFRa, VEGFR2	Preclinical, I, II	80, 81
Lucitanib (E-3810)	FGFR1-3, PDGFRα/β, VEGFR1-3	Preclinical, I, II	82
VS-5584	mTOR/PI3K	Preclinical, I	84
AZD8055	mTOR	Preclinical, I[a]	67
Ponatinib, vandetinib, alectinib, cabozaninib	RET	Preclinical, I, II	85
THZ1	CDK7	Preclinical	86
Ruxolitinib (INCB1824)	JAK1/2	Preclinical, I, II (NSCLC)	90
Tofacitinib (CP-690550)	JAK3	Preclinical	89
AZD1480	JAK2	Preclinical, I[a]	91
Amrubicin	Topoisomerase II	Preclinical, I, II, III, Marketed	92, 93, 94
Palifosfamide	Alkylation	Preclinical, I, II, III	
Aldoxorubicin	Anthracycline	Preclinical, I, II	95
Defactinib (VS 6063)	FAK	Preclinical, I, II (NSCLC, Meso)	97, 98
LY2510924	CXCR4	Preclinical, I, II	103
Olaparib (AZD2281)	PARP1/2	Preclinical, I, II	41, 106
Rucaparib (AG-014699,PF-01367338)	PARP1	Preclinical, I, II	41
Talazoparib (BMN-673)	PARP1/2	Preclinical, I, II	42, 43
Veliparib (ABT-888)	PARP1/2	Preclinical, I, II	105, 107
Lorvotuzumab mertansine	CD56	Preclinical, I, II[a]	110, 111
Rovalpituzumab tesirine (SC16LD6.5)	DLL3	Preclinical, I, II	112, 113
GSK126	EZH2	Preclinical	115, 116
Sorafenib	RAF1, BRAF, PDGFRβ, VEGFR2	Preclinical, I, II[a]	117
Bevacizumab	VEGF	Preclinical, I, II, III[a]	118, 121
Thalidomide	Angiogenesis	Preclinical, I, II, III	119, 120
Cediranib (AZD2171)	VEGFR1-3, FLT1/4, cKit, PDGFRβ, FGFR1	Preclinical, I, II[a]	122
Vandetanib	VEGFR2	Preclinical, I, II	123
Aflibercept	VEGF trap	Preclinical, I, II	124
Sunitinib	VEGFR1-3, PDGFRβ, c-KIT, FLT3, RET	Preclinical, I, II	125, 126
Imatinib	PDGFR, c-Kit	Preclinical, I, II[a]	127, 128
Rilotumumab (AMG 102)	HGF	Preclinical, I, II[a]	129
Ganitumab (AMG 479)	IGF-1R	Preclinical, I, II	130
Everolimus	mTOR	Preclinical, I, II	131, 132
Temsirolimus	mTOR	Preclinical, I, II	133
AZD1775 (MK-1775)	WEE1	Preclinical, I, II	134
Ipilimumab	CTLA-4	Preclinical, I, II, III	151, 152
Nivolumab	PD-1	Preclinical, I, II, III	152
Pembrolizumab	PD-1	Preclinical, I, II	153
BMS-986012	Fucosyl-GM1	Preclinical, I, II	158
CAR T cells	CD56	Preclinical	159, 160
Anti CD47 antibodies	CD47	Preclinical, I	165

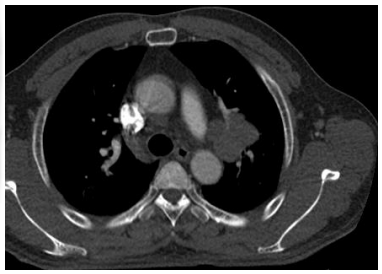
J Thorac Oncol 2016;11(4):452-74

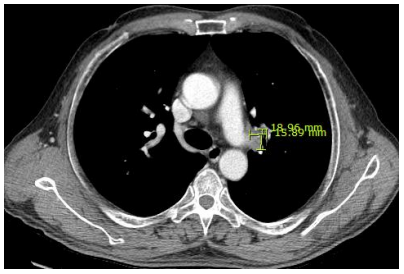
Case 4 M/58

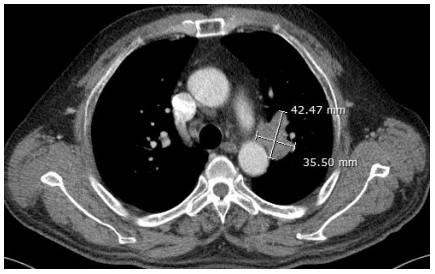
SCLC, LUL (14.9.16), ES (cT2aN2M1b : Lt.2nd rib, Rt.humerus)

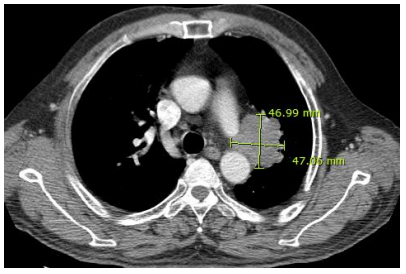


pRT to Rt.humerus & Lt.rib
(14.9.24 ~ 10.8)





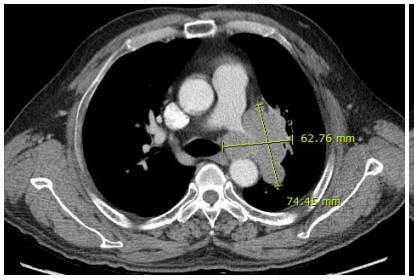


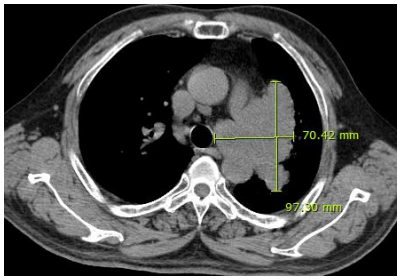


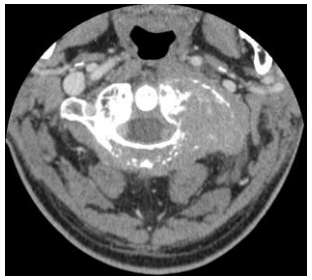
1-EP#6
(14.9.23 ~ 15.1.21)

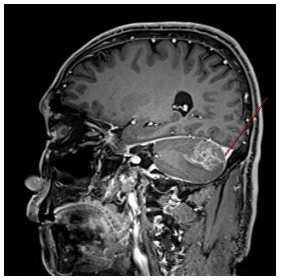
2-Cb#4
(15.5.11 ~ 8.28)

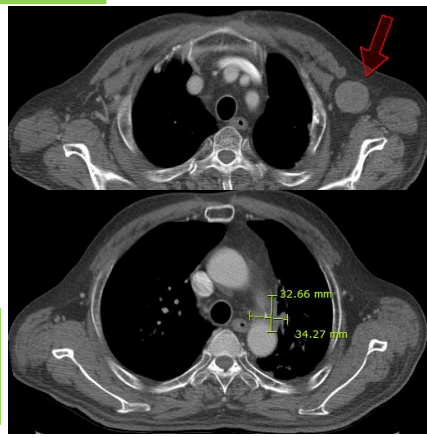
NN-guided Rt.SOC & T.R.
(16.7.13) : Small cell ca











3-EC#4
(15.9.14~ 12.9)

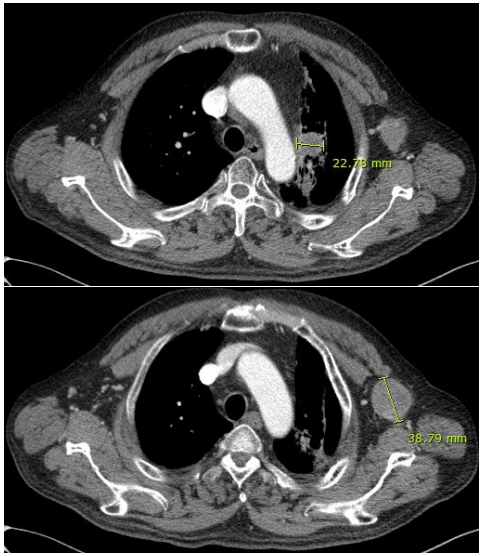
pRT to LUL
(16.2.3 ~ 2.19)

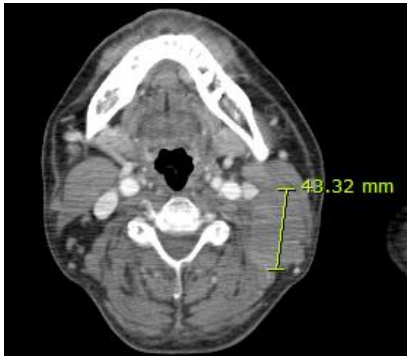
pRT to C1
(16.3.22 ~ 4.1)

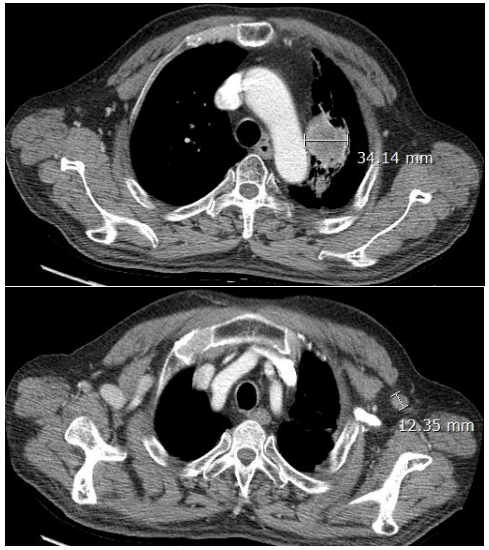
WBRT
(16.8.3 ~ 8.17)

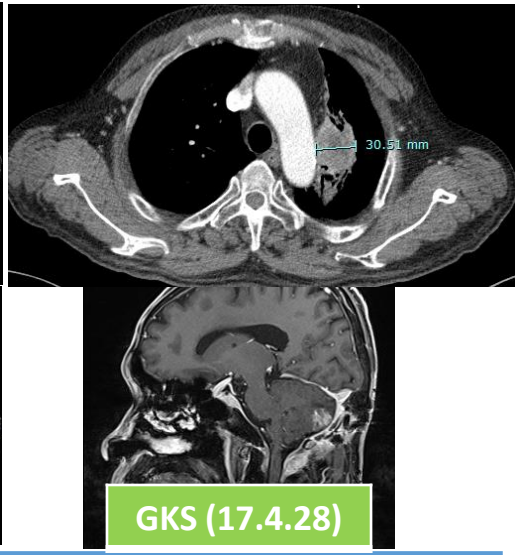
Case 4 M/58

SCLC, LUL (14.9.16), ES (cT2aN2M1b : Lt.2nd rib, Rt.humerus)







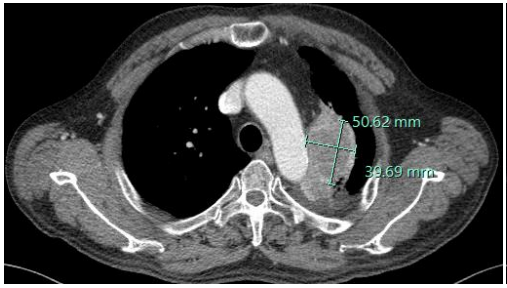


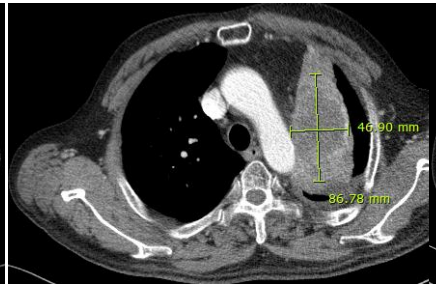
GKS (17.4.28)

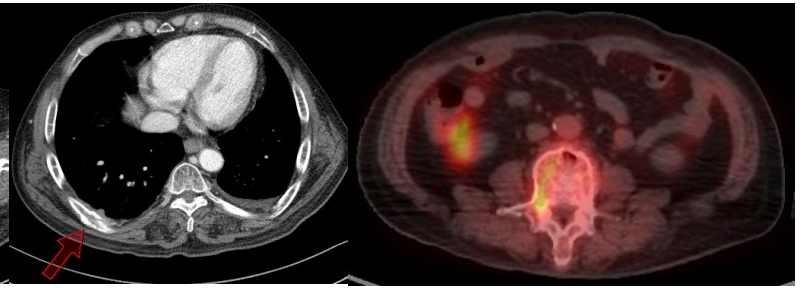
4-EP#4
(16.8.29 ~ 11.18)

pRT to Lt.neck & axilla
(17.1.3 ~ 1.16)

5-Pdx#6
(17.4.3 ~ 9.18)







6-EC#4
(17.10.16 ~ 18.1.16)

pRT to Rt.8th rib
(18.3.6 ~ 3.13)

pRT to L2-S1
(18.3.23 ~ 3.30)

Hospice
(18.4.9)

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018
Small Cell Lung Cancer

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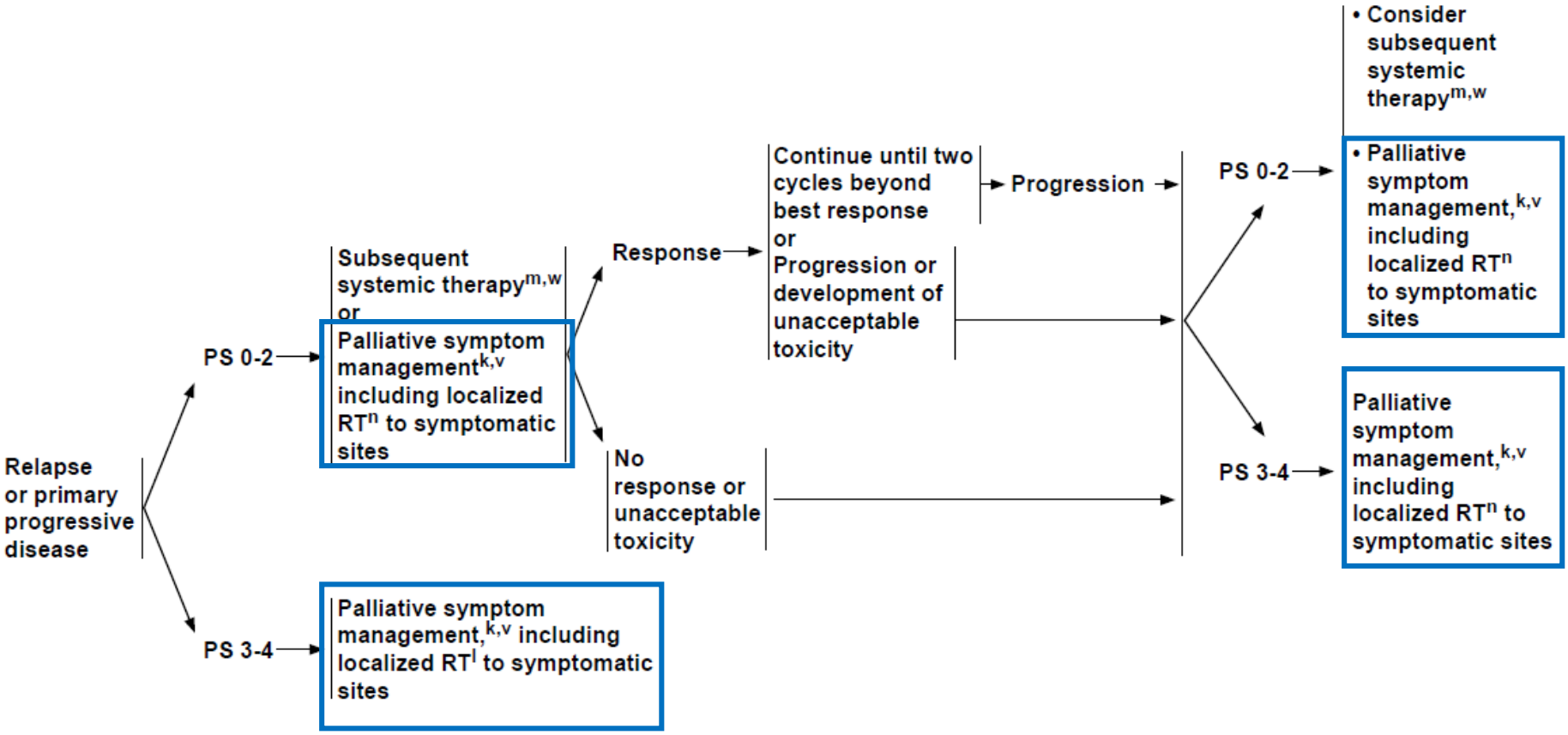
PROGRESSIVE DISEASE **SUBSEQUENT THERAPY/PALLIATIVE THERAPY**



Take Home Messages – Subsequent chemotherapy

- Purpose of chemotherapy in advanced lung cancer

  = Palliation, not Cure

  ➔ Consider patients' factors : Age, PS, Support from caregivers…

- Proper application of Radiotherapy btw chemotherapy

  = Palliative localized RT including SBRT, GKS(Brain)

- Flexible use of chemotherapeutic agents

  = Retreatment, Exchangable

- Keep an eye on Rare mutation and/or Clinical trials

  = Rebiopsy, NGS, etc


Don’t forget
about your
old friend,
of when
you make a
new friend.

Thank You for Your Attention !!

ckpark214@jnu.ac.kr