Nama : dr. Elisna Syahruddin, PhD, SpP(K)

Tempat Tanggal Lahir :

EDUCATIONS

1980 Senior High School II Bukittinggi

1986 Medical Doctor, Faculty of Medicine, Universitas Sumatera Utara, Medan

1999 Ph.D, Postgraduate School of Medical Science, Hiroshima University, Jepang

2000 Pulmonologist, Faculty of Medicine Universitas Indonesia, Jakarta

2007 Consultant Thoracic Oncology (collegiums, Indonesian Society of Respiratory)

2017 General Palliative Care (Singapore International Foundation)

POSITIONS

1. Members, National Cancer Center Committee, Ministry of Health Republic Indonesia
2. Lecturer, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia, Persahabatan National Respiratory Referral Hospital, Jakarta
3. Medical staff, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia. Persahabatan National Respiratory Referral Hospital, Jakarta
4. Head of Division of Thoracic Oncology, Department of Pulmonology and Respiratory Medicine,
5. Faculty of Medicine, Universitas Indonesia, Persahabatan National Respiratory Referral Hospital, Jakarta
6. Members, Research Methodology Module. Faculty of Medicine, Universitas Indonesia, Jakarta
7. Members, Team of Lecturer Credit Point Assessor, Faculty of Medicine, Universitas Indonesia, Jakarta
8. *Reviewer*, e-Jurnal Kedokteran Indonesia, Faculty of Medicine, Universitas Indonesia, Jakarta
9. Head of Oncology Team, Persahabatan National Respiratory Referral Hospital, Jakarta
10. Head of Palliative Team, Persahabatan National Respiratory Referral Hospital, Jakarta
11. Head of SubCommittee Reasearch , Persahabatan National Respiratory Referral Hospital, Jakarta
12. Secretary of Health Research Ethics Committee, Persahabatan National Respiratory Referral Hospital, Jakarta
13. Secreatry of Human Cancer Research Center-Indonesian Medical Education and Research Institute (HCRC- IMERI)
14. Organizations: International Association for the study on lung cancer (IASLC), Indonesian Cancer Foundation, Indonesian Society of Oncology, Indonesian Association for the Study on Thoracic Oncology (IASTO).

UP DATE ON MANAGEMENT OF LUNG CANCER AND LUNG METASTASIS

MANADO , 27 JANUARY 2018

dr. Elisna Syahruddin, PhD, Sp.P(K)

Department of Pulmonology and Respiratory Medicine

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Curriculum Vitae
dr. Elisna Syahruddin, PhD, Sp.P(K)

EDUCATIONS

1986 Doctor , Faculty of Medicine Universitas Sumatera Utara, Medan
1999 PhD, Hiroshima University, Japan
2000 Pulmonologist, Faculty of Medicine Universitas Indonesia, Jakarta
2007 Consultan of Thoracic Ongology , Indonesian Society of Respiratory
2017 General Paliative Care

POSITIONS

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Head of Division of Thoracic Oncology, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Indonesia.
Research Metodology Modul, Faculty of Medicine Universitas Indonesia.
Reviewer, e-Jurnal Kedokteran Indonesia
Medical staff, Department of Pulmonology and Respiratory Medicine, Persahabatan National Respiratory Refferal Hospital, Jakarta
Head of Oncology Team/Board, Persahabatan National Respiratory Refferal Hospital, Jakarta
Head of Palliative Care, Persahabatan National Respiratory Refferal Hospital, Jakarta
Head of Subcommittee of Reserach, Persahabatan National Respiratory Refferal Hospital, Jakarta
Secretary of Ethical Committee on Health Research

ORGANIZATIONS

PDPI, Indonesian Society of Respiratory
YKI, Indonesian Cancer Foundation
POI, Indonesian Society of Oncology
IASTO, Indonesian Assocition for the Study of Thoracic Oncology

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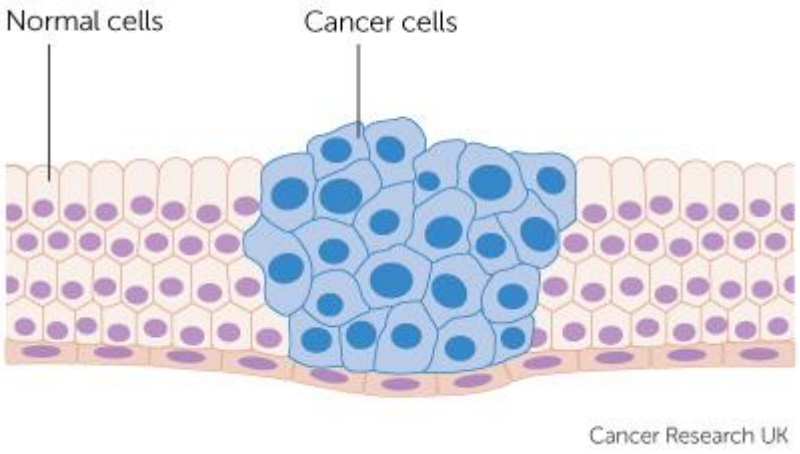
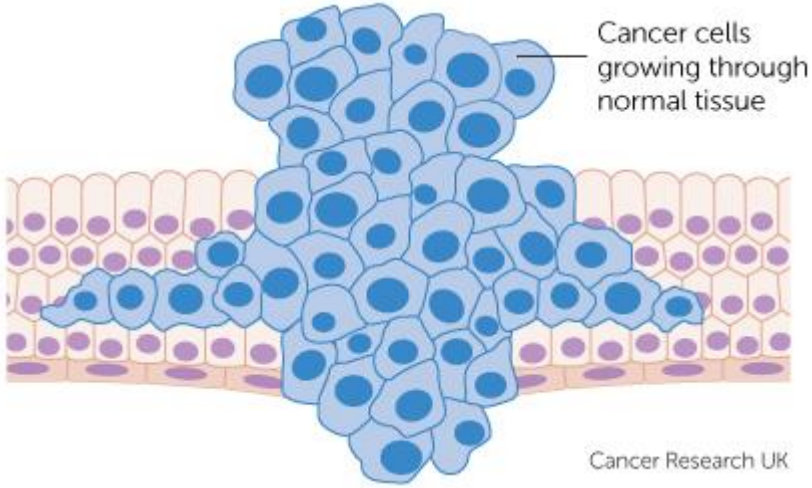
What is cancer?

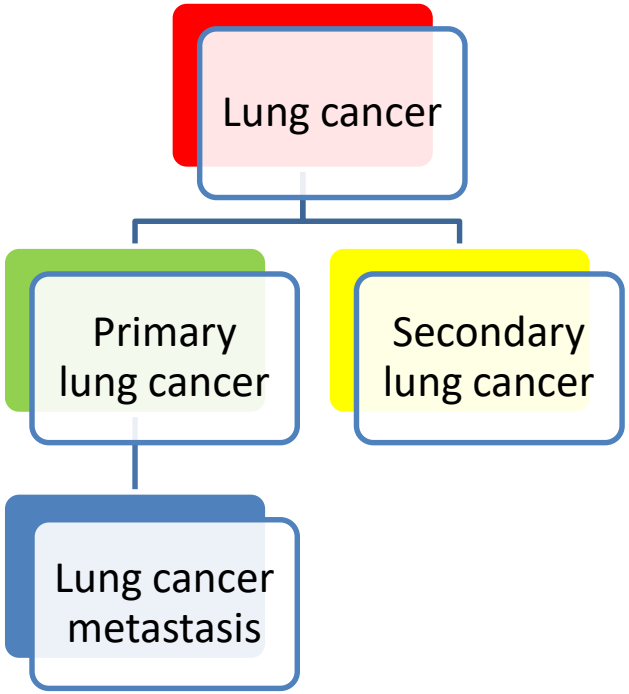




Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body.[Not all tumors are cancerous; benign tumors do not spread to other parts of the body. (Defining cancer. *National Cancer Institute*. Archived from the original on 25 June 2014. Retrieved 10 June 2014.)

Cancer starts when cell schange abnormality . Cancer is when abnormal cells divide in an uncontrolled way. Cancer starts when gene changes make one cell or a few cells begin to grow and multiply too much (http://www.cancerresearchuk.org/about-cancer/what-is-

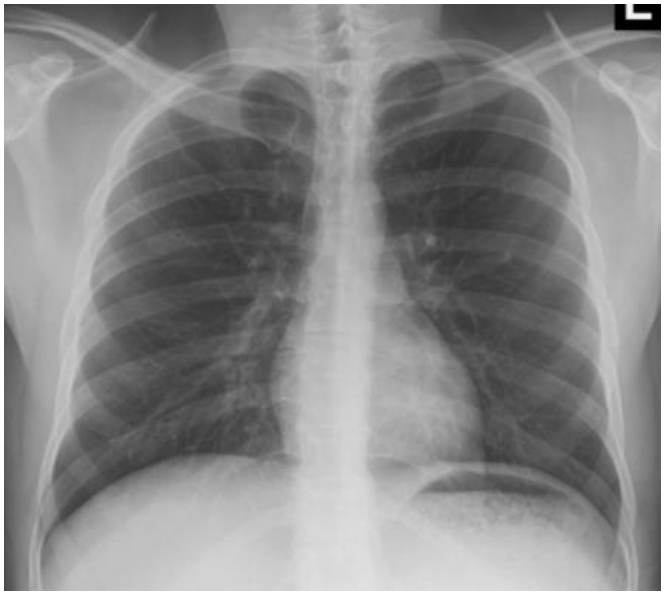
What is lung cancer cancer?

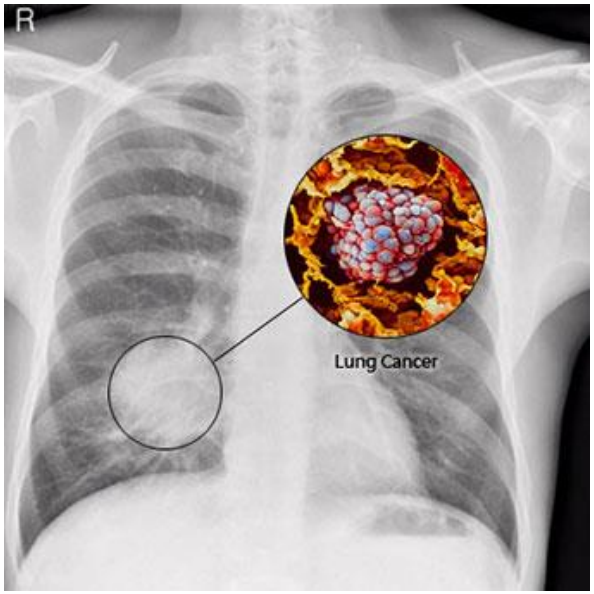


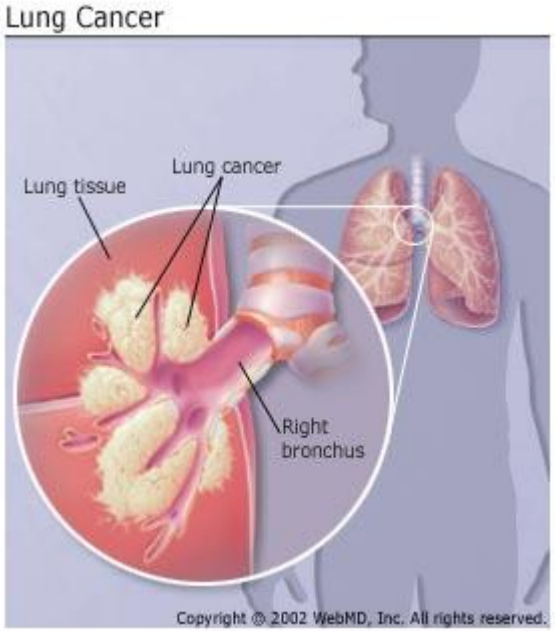
Primary lung cancer is lung cancer originating from the bronchial epithelium.

Secondary lung cancer or lung metastatis is cancer that started in another part of the body and spread to the

What is primary lung cancer?



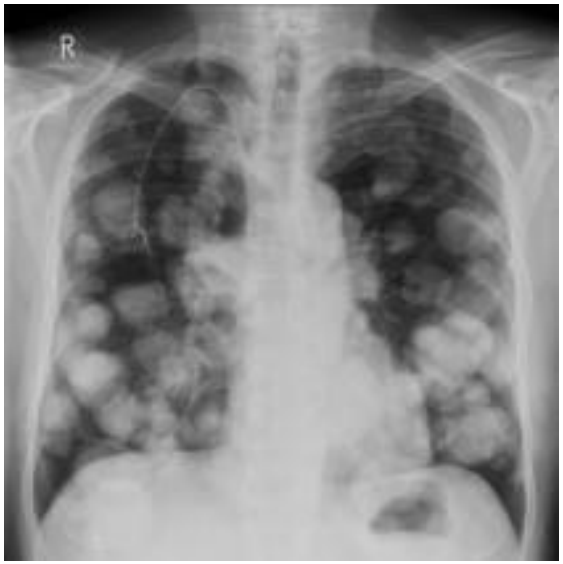


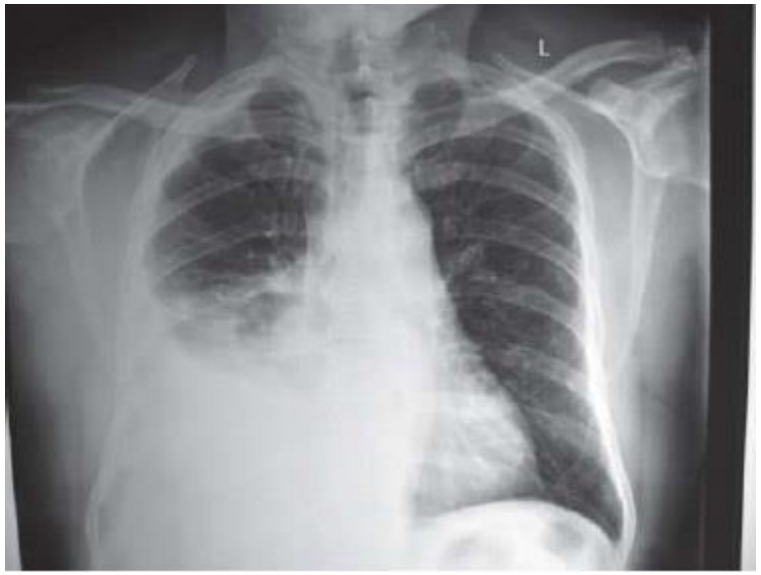


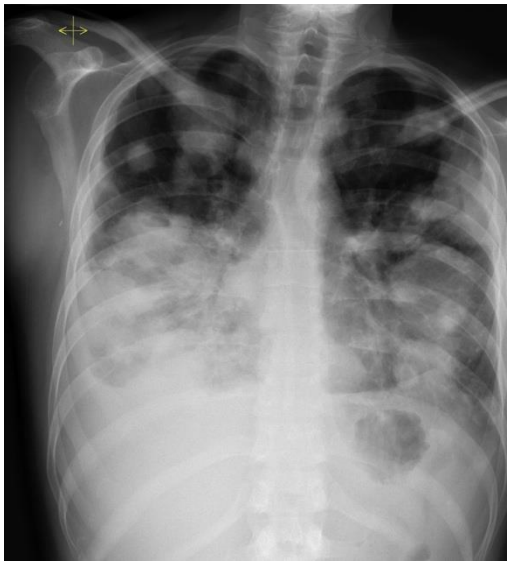
Primary lung cancer is lung cancer originating from the bronchial epithelium.

Lung cancer can **spread (metastasis) to** nearly any region of the body, but the most common areas are the lymph nodes, brain, plural, lung, bones, liver and adrenal glands

What is lung metastasis?







Almost any cancer has the ability to spread to the lungs, but the tumors that most commonly do so include bladder cancer, colon cancer, breast cancer, prostate cancer, sarcoma, Wilms tumor, Thyroid, and

Lung Cancer

Lung cancer accounts for about 27 percent of all cancer deaths and is by far the leading cause of cancer death among both men and women.

Each year, more people die of lung cancer than of colon, breast, and prostate cancers combined.

Cigarette smoking is the cause of 80-90% of all lung cancer deaths.

What is the Problems of Lung Cancer ?

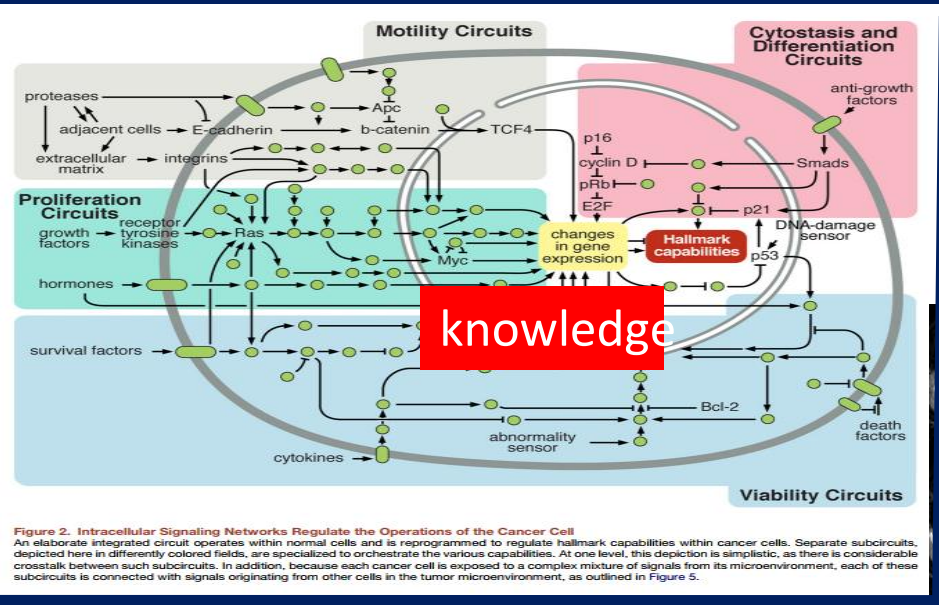
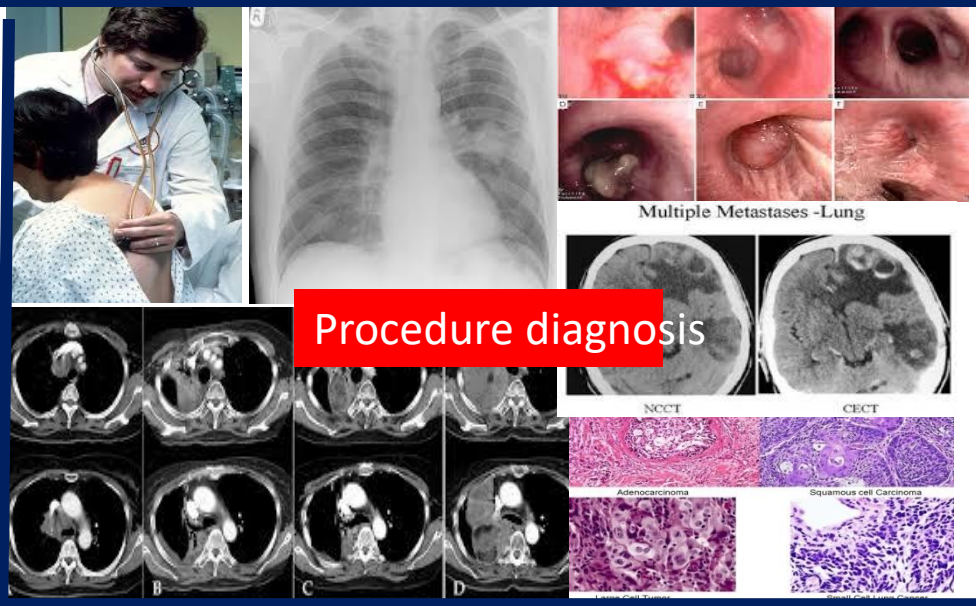


Figure 2. Intracellular Signaling Networks Regulate the Operations of the Cancer Cell
An elaborate integrated circuit operates within normal cells and is reprogrammed to regulate hallmark capabilities within cancer cells. Separate subcircuits, depicted here in differently colored fields, are specialized to orchestrate the various capabilities. At one level, this depiction is simplistic, as there is considerable crosstalk between such subcircuits. In addition, because each cancer cell is exposed to a complex mixture of signals from its microenvironment, each of these subcircuits is connected with signals originating from other cells in the tumor microenvironment, as outlined in Figure 5.

knowledge



Procedure diagnosis

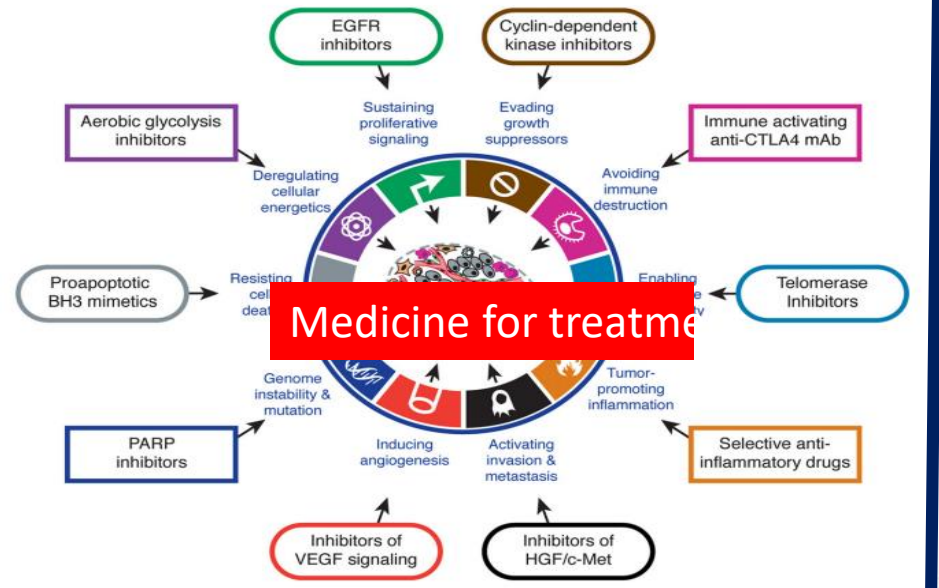
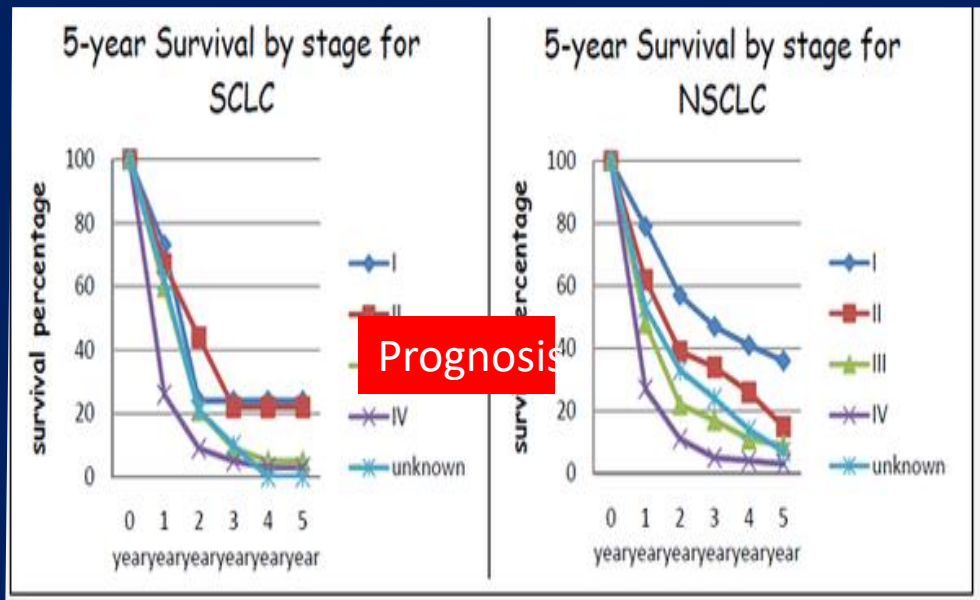


Figure 6. Therapeutic Targeting of the Hallmarks of Cancer
Drugs that interfere with each of the acquired capabilities necessary for tumor growth and progression have been developed and are in clinical trials or in some cases approved for clinical use in treating certain forms of human cancer. Additionally, the investigational drugs are being developed to target each of the enabling characteristics and emerging hallmarks depicted in Figure 3, which also hold promise as cancer therapeutics. The drugs listed are but illustrative examples; there is a deep pipeline of candidate drugs with different molecular targets and modes of action in development for most of these hallmarks.

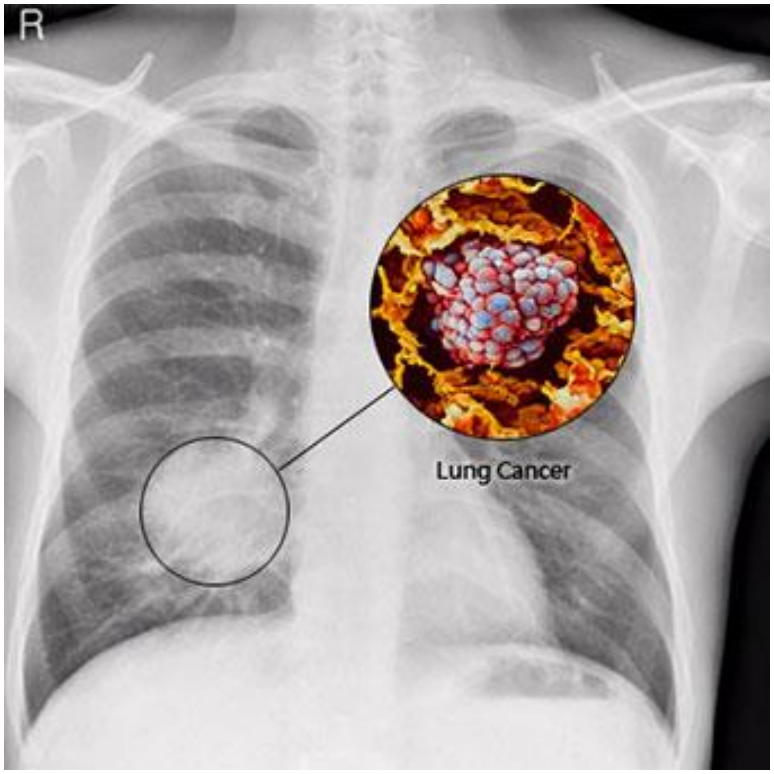
Medicine for treatme



Prognosis

Table 3 (left). 5-year Survival from SCLC by stage. Table 4 (right). 5-year Survival from NSCLC by stage. Data is compiled from CHH Registry from 1995-2010.

MANAGEMENT OF LUNG CANCER



- ❑ Preventive
- ❑ Screening and early detection
- ❑ Diagnosis
- ❑ Treatment

MANAGEMENT OF LUNG CANCER

Preventive

Screening and early detection

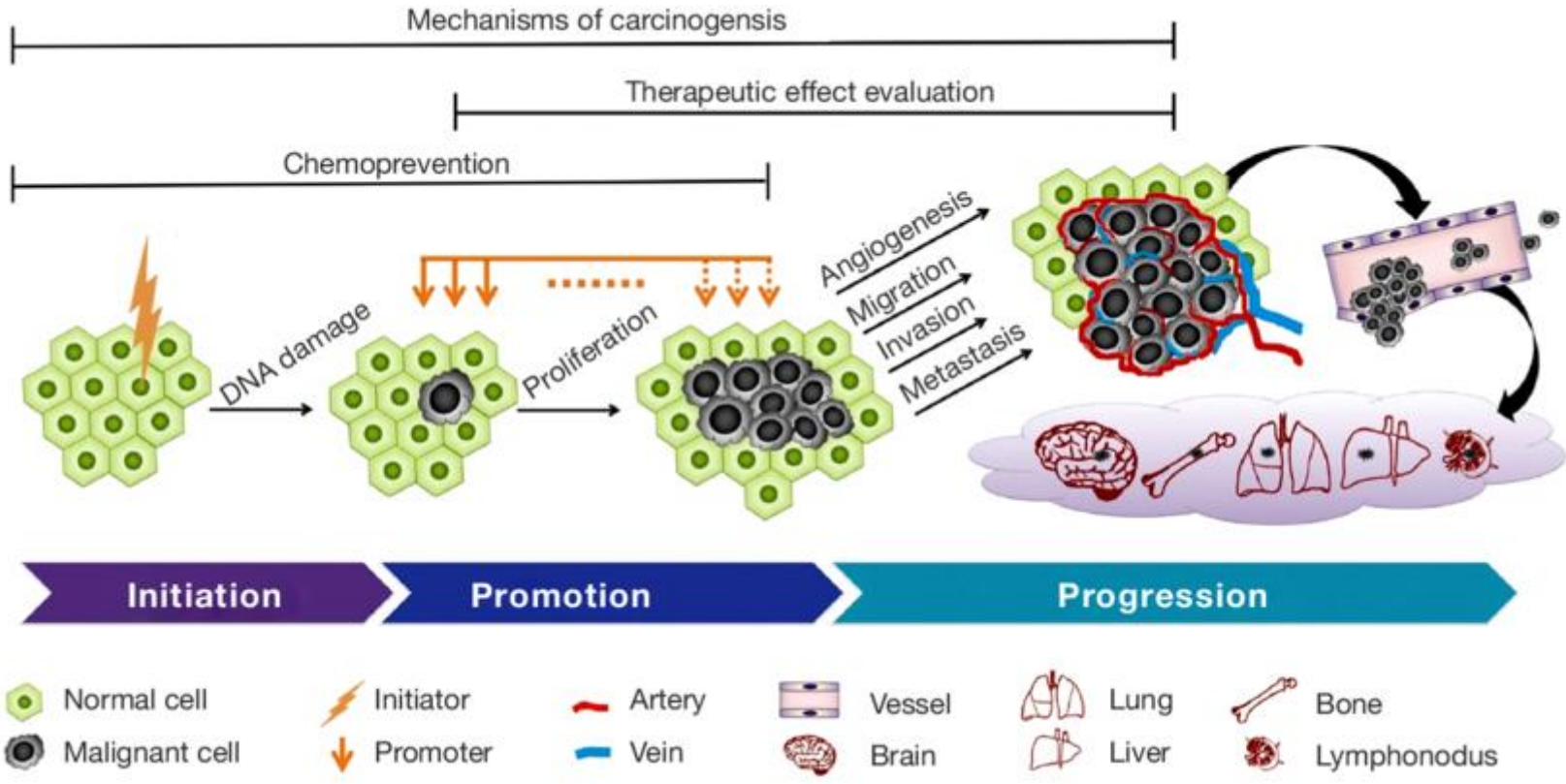
Diagnosis

Treatment

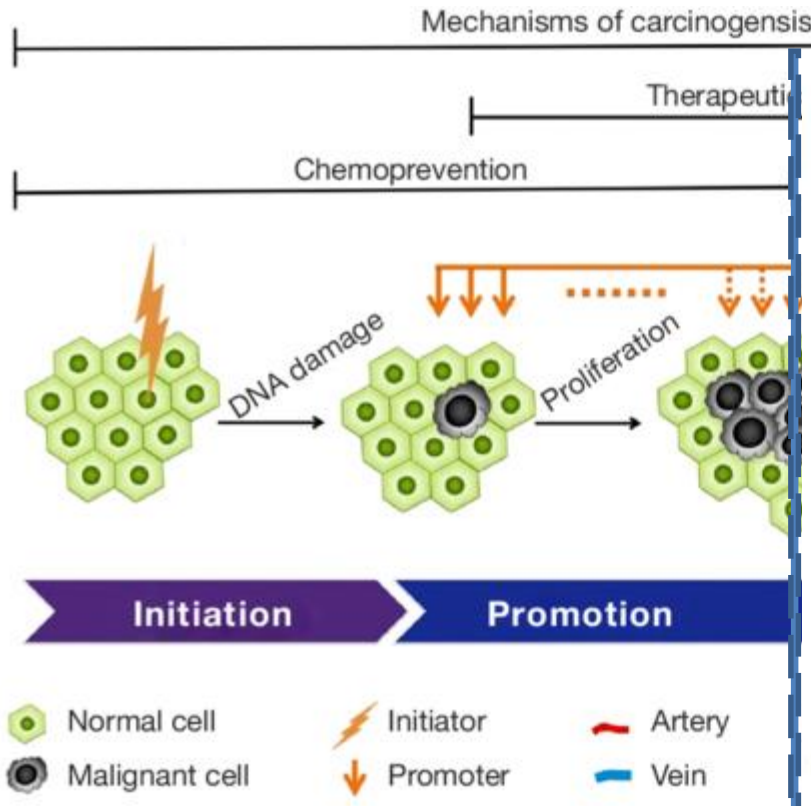
Morbidity (Incidence)

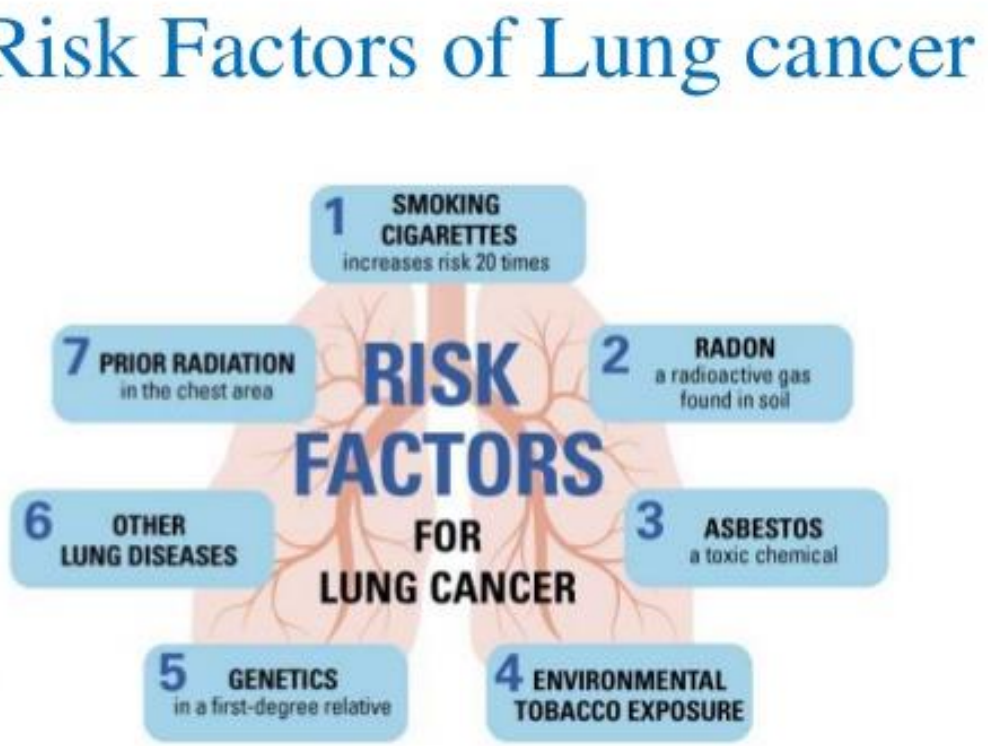
Mortality (survival)

Preventive : Lung Carcinogenesis

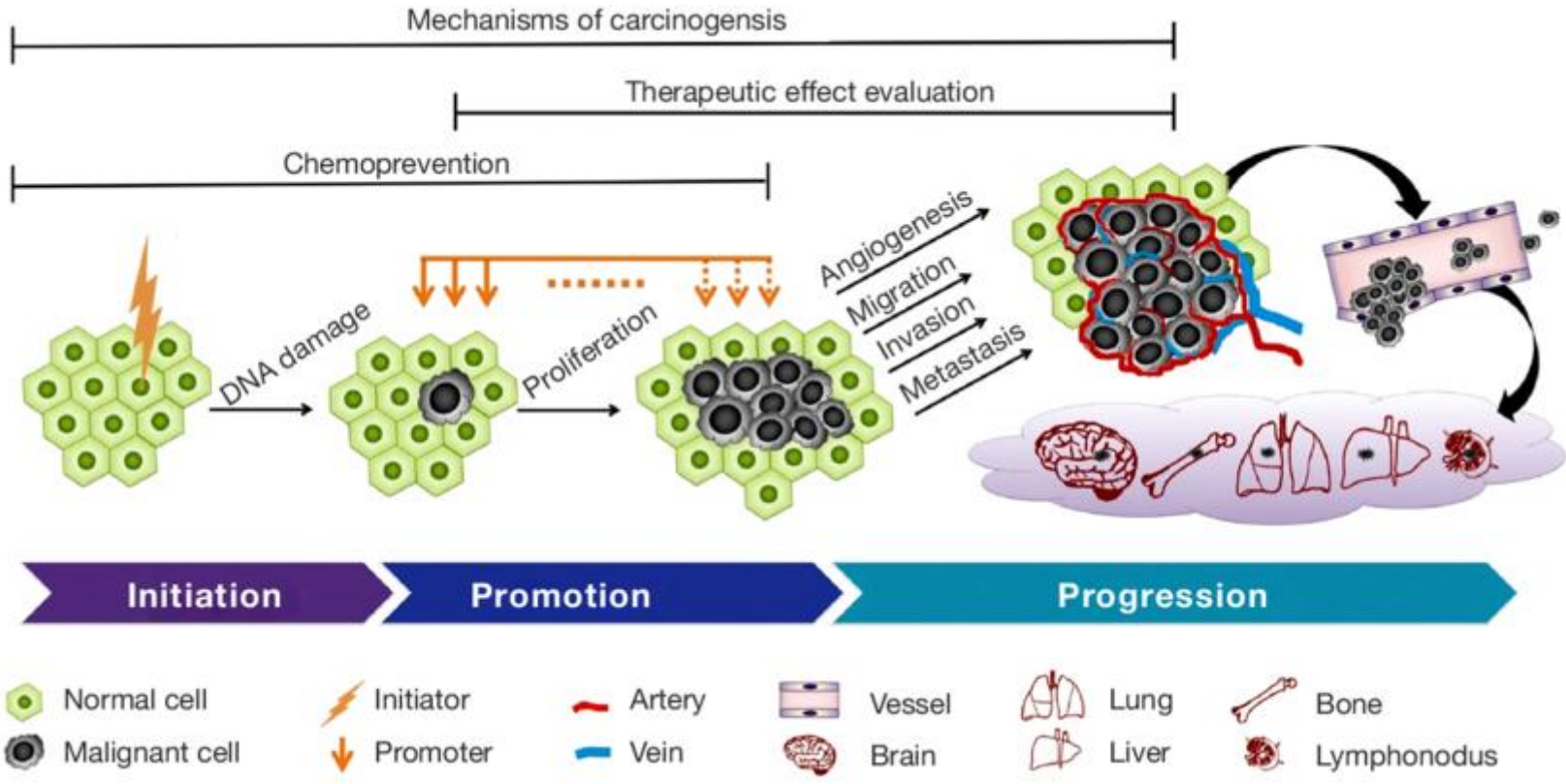


Preventive : Lung Carcinogenesis





Screening : Lung Carcinogenesis



Screening : Lung Carcinogenesis and Risk

Lung Cancer: Screening

Release Date: December 2013

Recommendation Summary

Summary of Recommendation and Evidence

Population	Recommendation	Grade (What's This?)
Adults Aged 55-80, with a History of Smoking	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lung-can

Screening : Lung Carcinogenesis and Risk

TABLE 2 Selection criteria, number of enrolled individuals and the rate of diagnosed lung cancer of major randomised controlled trials

Study	Selection criteria		Patients screened n (follow-up)	Lung cancer diagnosed at initial screening (total in follow-up)
	Age years	Tobacco smoking (delay since weaning)		
DLCST	50–70	⩾20 pack-years (0–9 years)	2052 (58 months)	0.8% (3.4%)
DANTE	60–74 (only men)	⩾20 pack-years (0–9 years)	1276 (34 months)	2.2% (4.7%)
ITALUNG	55–69	⩾20 pack-years (active or former)	1406 (36 months)	1.5% (2.8%)
MILD	⩾49	⩾20 pack-years (0–9 years)	1190# (120 months) 1186¶ (53 months)	0.8% (2.4%)
NELSON	50–75	⩾15 pack-years* (0–9 years)	7907 (60 months)	0.9% (2.6%)
NLST	55–74	⩾30 pack-years (0–15 years)	26722 (78 months)	1.1% (2.4%)

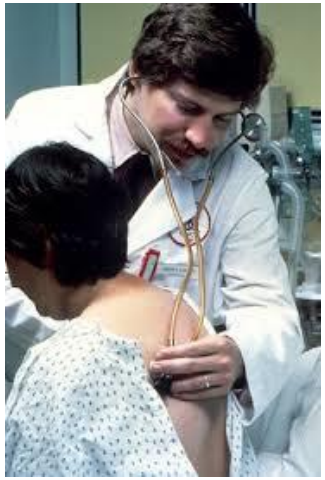
#: annual computed tomography; ¶: biannual computed tomography; *: NELSON inclusion criteria: number of cigarettes smoked is ⩾ 15 per day for 25 years OR ⩾10 cigarettes per day for 30 years AND still smoking or have quit <10 years ago.

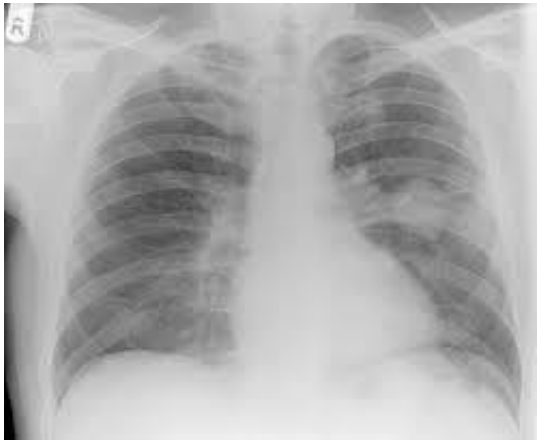
Conclusion

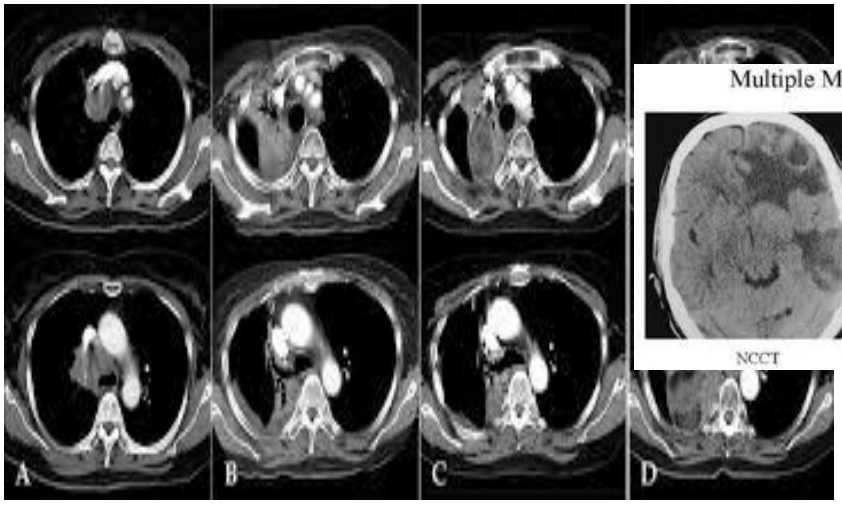
Lung cancer is a devastating disease with poor survival once the disease is advanced. As the main risk factor for lung cancer is smoking, there is an urgent need to advocate against smoking and encourage cessation. There are accumulated data supporting the survival benefit for screening of individuals at high risk for early detection of lung cancer using LDCT. Based on the available evidence, we summarised the key elements necessary for a comprehensive lung cancer screening programme in Europe including minimum requirements and recommended refinements. These should be adjusted to the national infrastructure and healthcare system in order to exactly define eligibility using a risk model, nodule management and quality assurance plan. The establishment of a central registry, including a biobank and an image bank, preferably on a European level, is strongly encouraged.

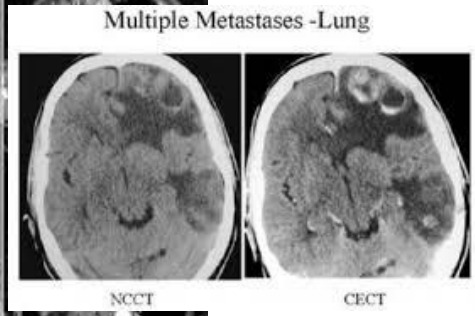
ESR/ERS white paper on lung cancer screening.

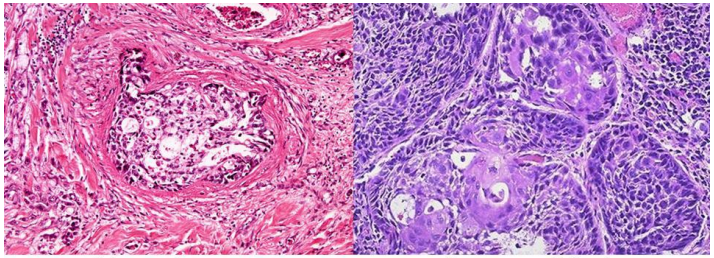
Diagnosis : Lung Cancer

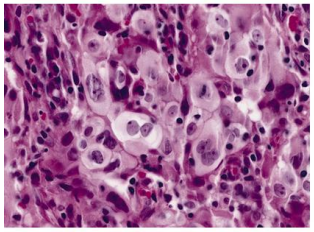


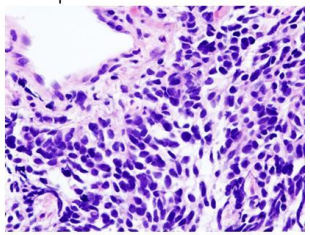




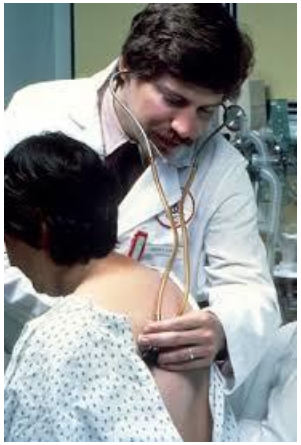


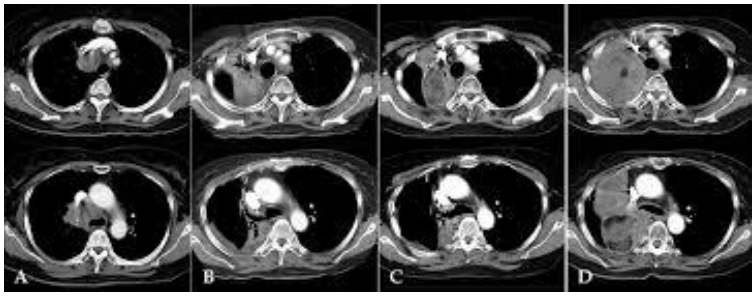


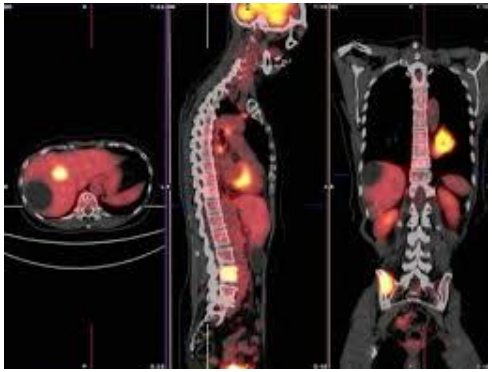


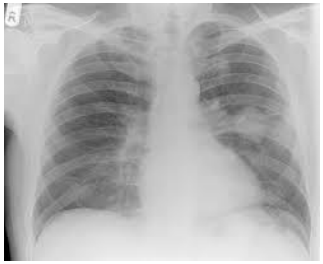


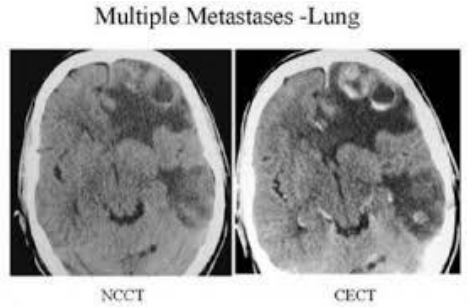
Diagnosis : Lung Cancer

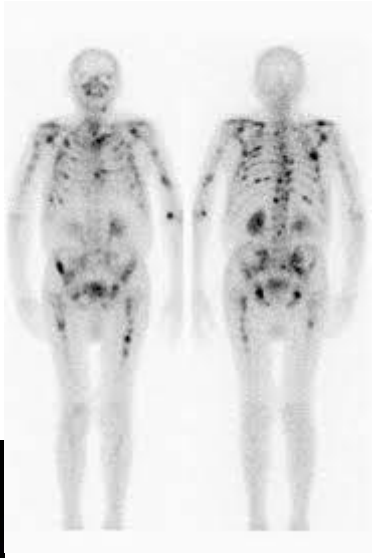












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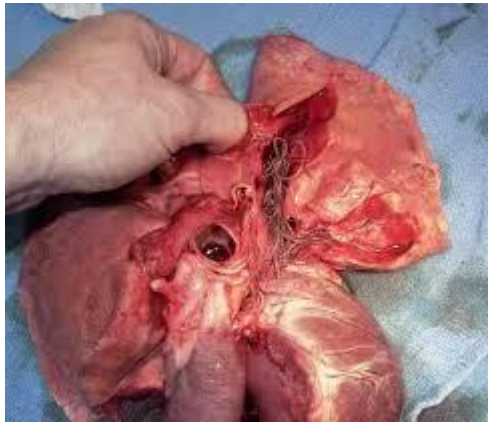
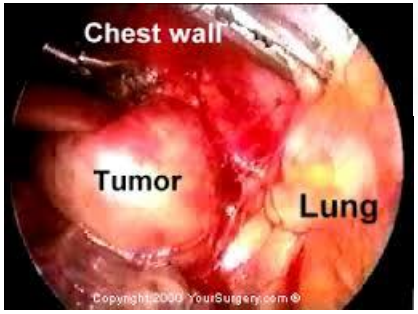
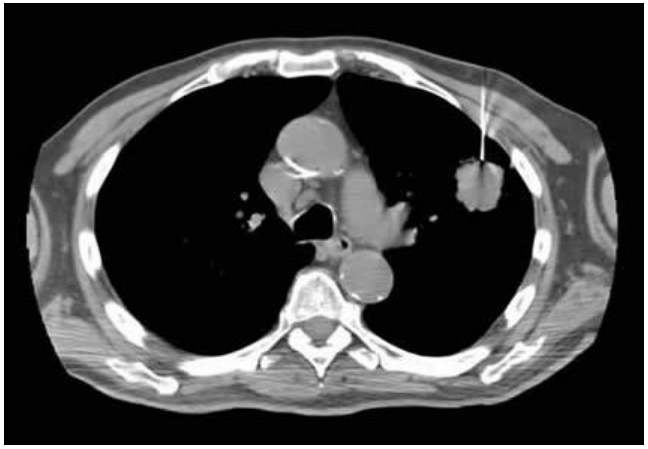


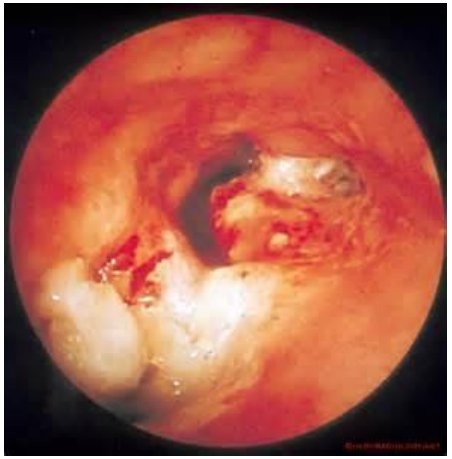
BRONCHOSCOPY

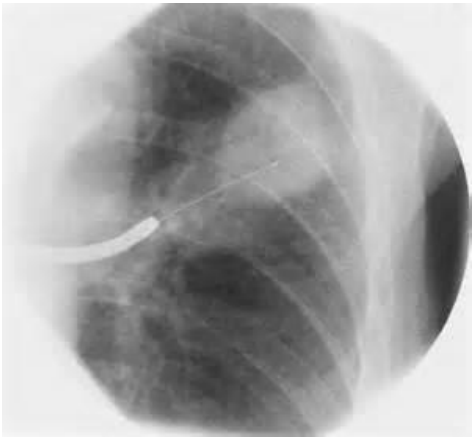
PLEUROSCOPY

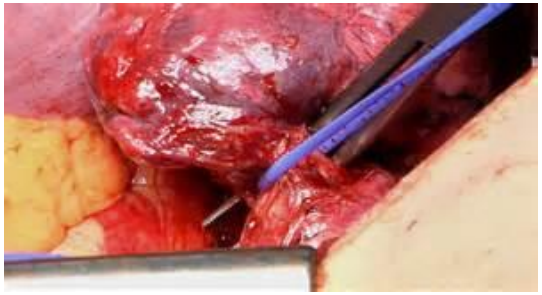


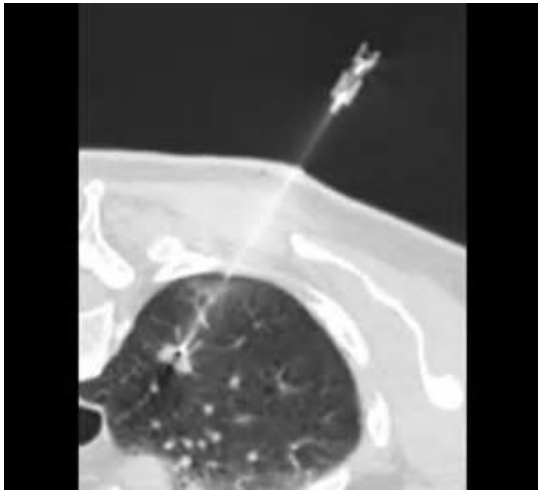
Diagnosis : Lung Cancer

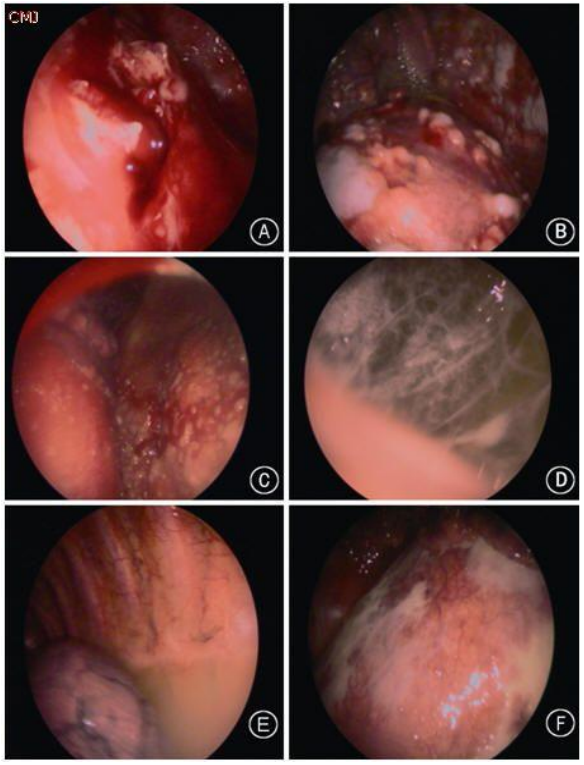


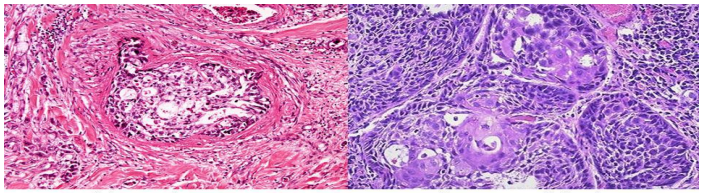


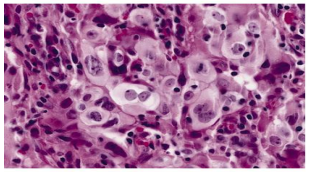


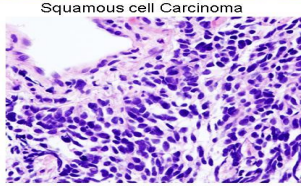


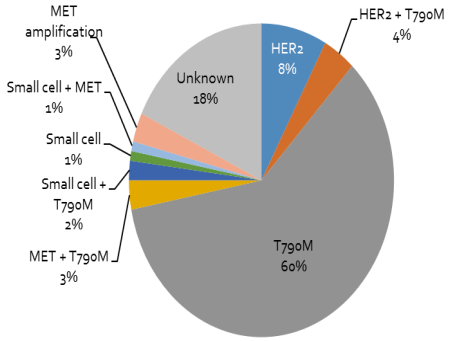




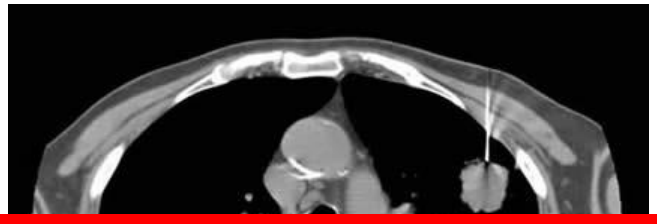


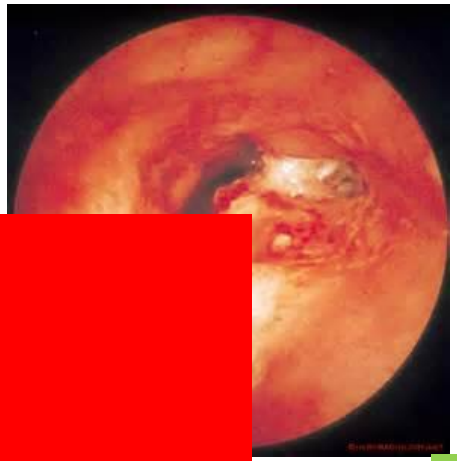


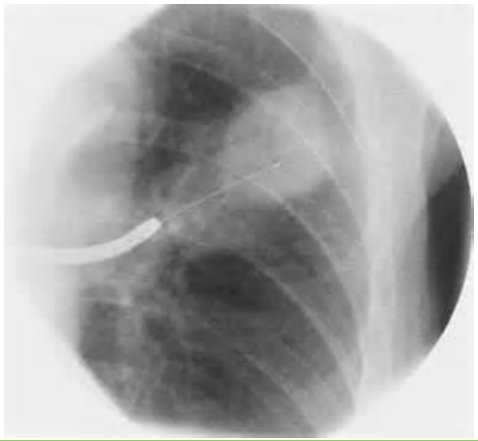




Diagnosis : Lung Cancer





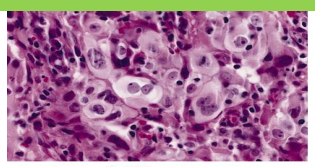


Cell cancer

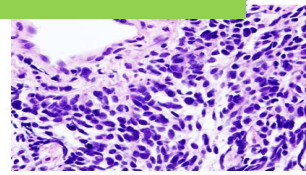
Stage of the disease

Molecular marker

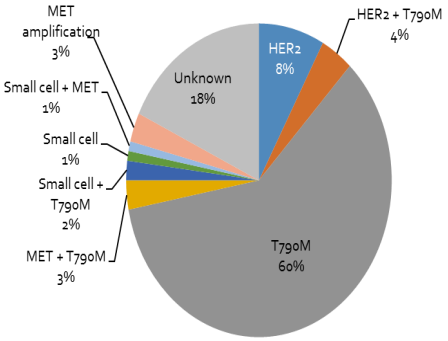
Treatment

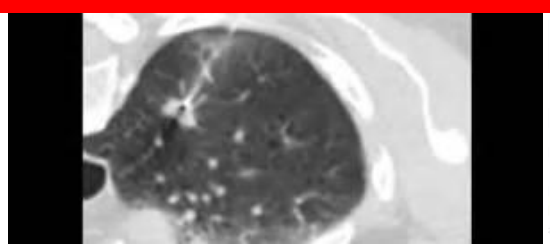


Large Cell Tumor



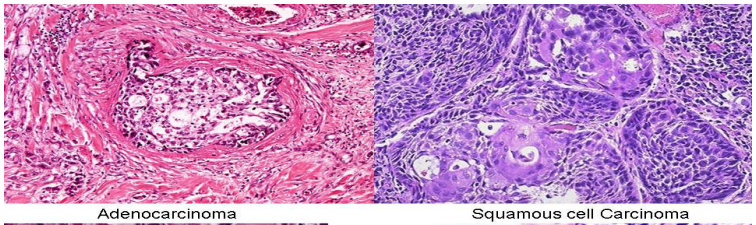
Small Cell Lung Cancer

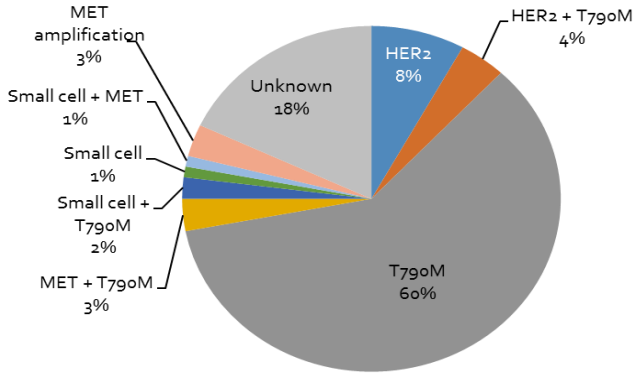




Diagnosis : Lung Cancer

- Lung Cancer
  - SCLC
    - LD-SCLC
    - ED-SCLC
  - NSCLC
    - Stage I/II
    - Stage IIIA
    - Stage IIIB-IV





Treatment : Lung Cancer

Modalities Therapy for Lung Cancer

- Curable
- Local control

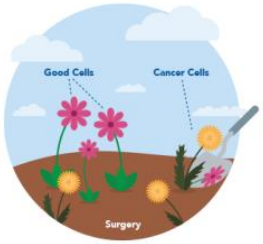
surgery

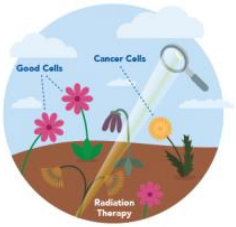
Radiotherapy

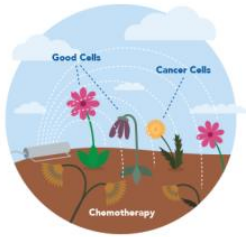
- Local control

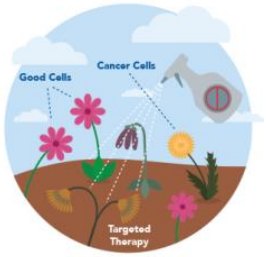
- chemotherapy
- Targeted therapy
- Immunotherapy

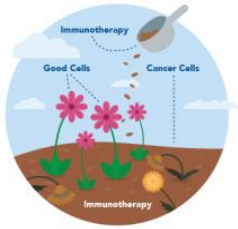
Systemic therapy



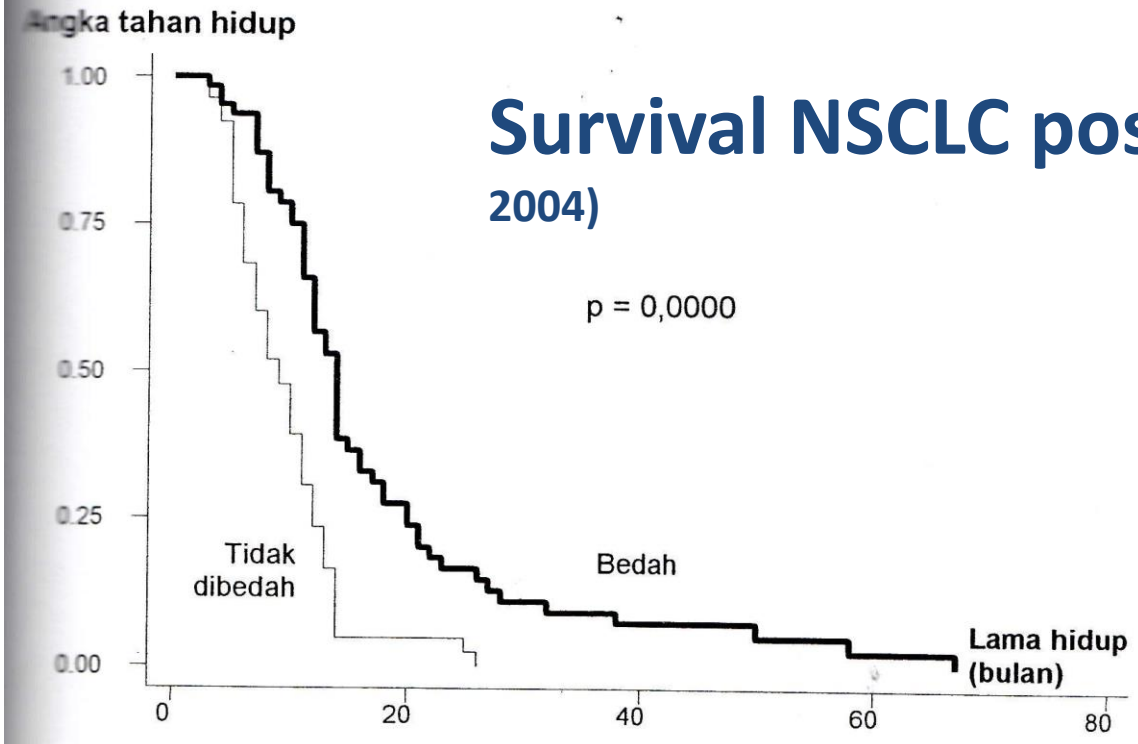








Treatment Lung Cancer (surgery)



Survival NSCLC post Surgery (Burhan E, 2004)

p = 0,0000

Gambar 13. Kurva Kaplan-Meier membandingkan tindakan bedah dan tanpa bedah

Tabel 13. Perbandingan *hazzard ratio* kelompok pembedahan saja dengan neoadjuvan dan adjuvan

Tindakan	HR	Standard Error	p	95% CI	
Pembedahan saja	0,4797657	0,1485433	0,018	0,261507	0,8801872
Neoadjuvan	0,2939657	0,104224	0,001	0,1467262	0,5889598
Adjuvan	0,416561	0,1031338	0,000	0,2564099	0,676741

Treatment Lung Cancer (surgery)

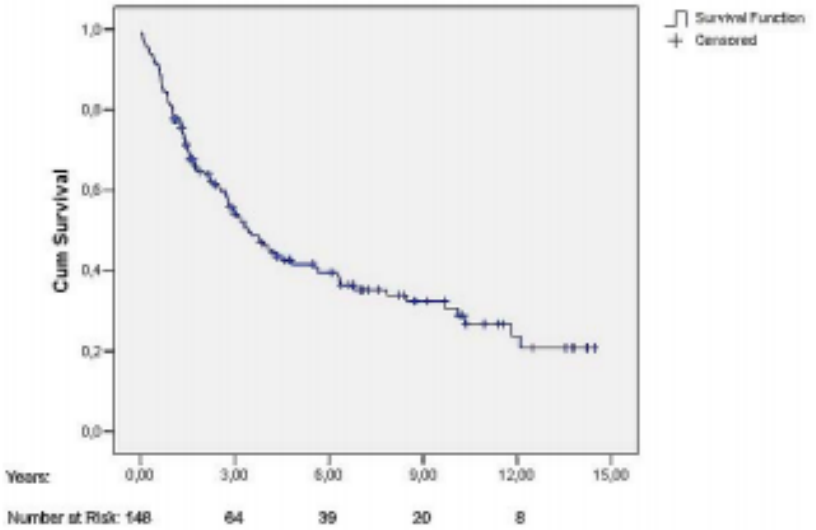


Figure 1
Postoperative survival curve (Kaplan-Meier plot) for all patients.

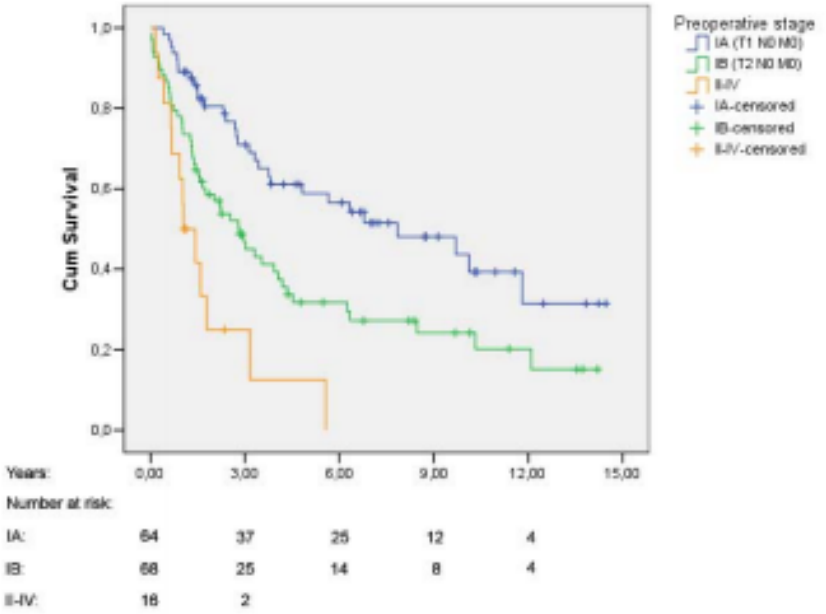
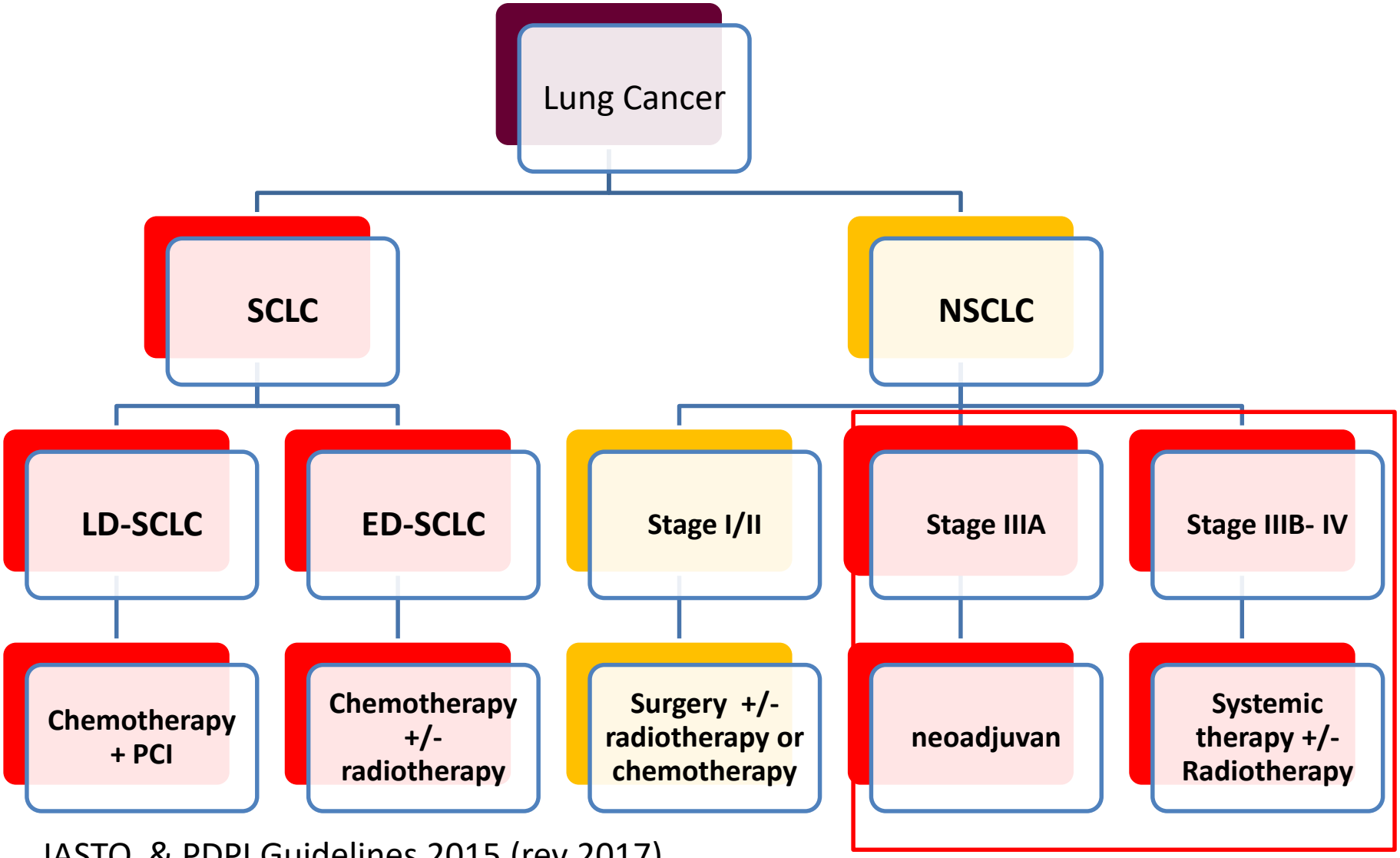


Figure 3
Kaplan-Meier plot for overall survival stratified by preoperative stage.

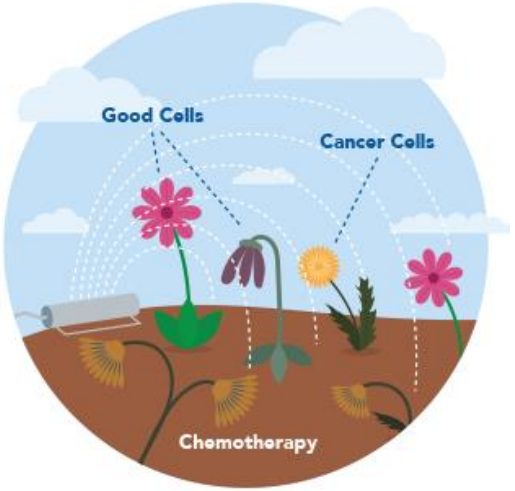
Kjetil Roth et al. BMC Pulmonary Medicine 2008, 8:22 doi:10.1186/1471-2466-8-22

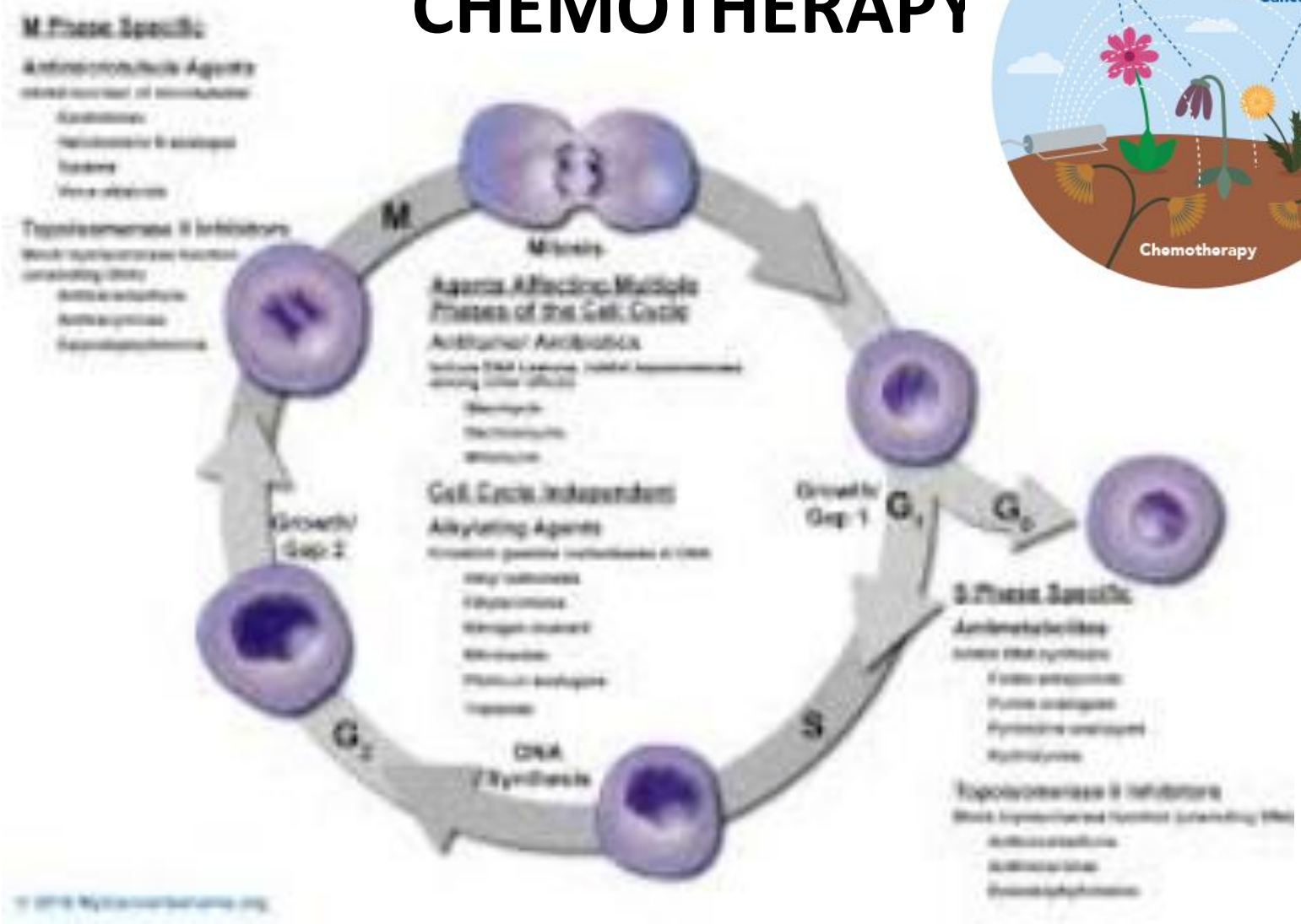
Treatment Lung Cancer (advanced stage)



IASTO & PDPI Guidelines 2015 (rev 2017)

CHEMOTHERAPY





Treatment Lung Cancer (Chemotherapy)

ANTI NEOPLASTIC FOR CHEMOTHERAPY OF LUNG CANCER

	doses	
carboplatin	AUC-5	Day 1
cisplatin	60 mg/BSA	Day 1
gemcitabine	1.250 mg / BSA	Day 1 and 8
paclitaxel	175 mg/ BSA	Day 1
etoposide	100 mg/BSA	Day 1,2 and 3
Vinoralbine	25 mg/BSA	Day 1and 8
docetaxel	75 mg/BSA	Day 1
pemetrexat	500 mg/BSA	Day 1 (for non -SCC only)

REGIMEN : Platinum based, doubled , three

Treatment Lung Cancer (Chemotherapy)

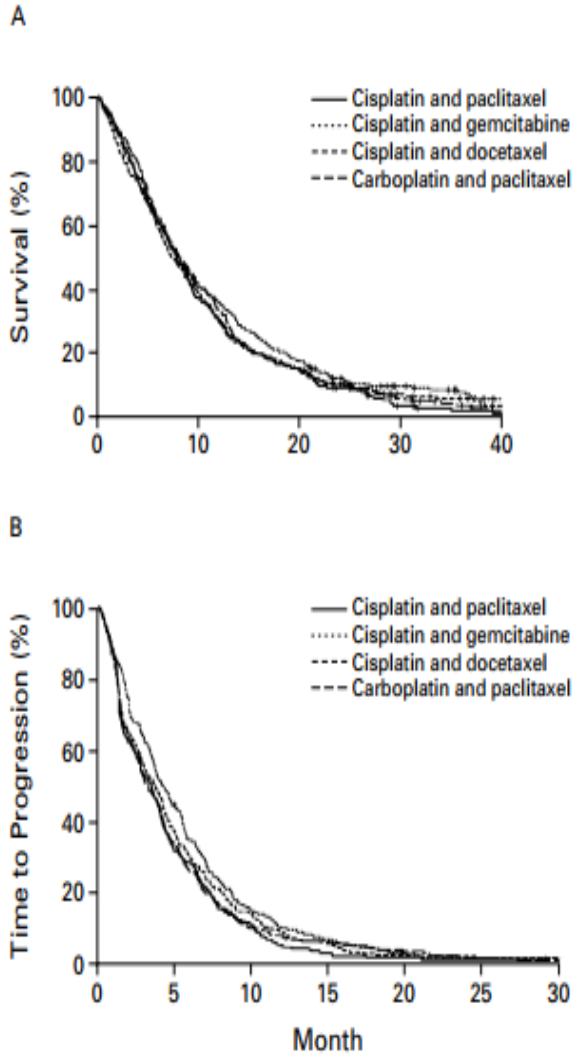


Figure 2. Kaplan–Meier Estimates of Overall Survival (Panel A) and the Time to Progression of Disease (Panel B) in the Study Patients, According to the Assigned Treatment.

COMPARISON OF FOUR CHEMOTHERAPY REGIMENS FOR ADVANCED NON–SMALL-CELL LUNG CANCER

N Eng J Med 2002: : 3.46: 92 - 8:

Treatment Lung Cancer (Chemotherapy)

Table 1. Comparison of two-drug combinations

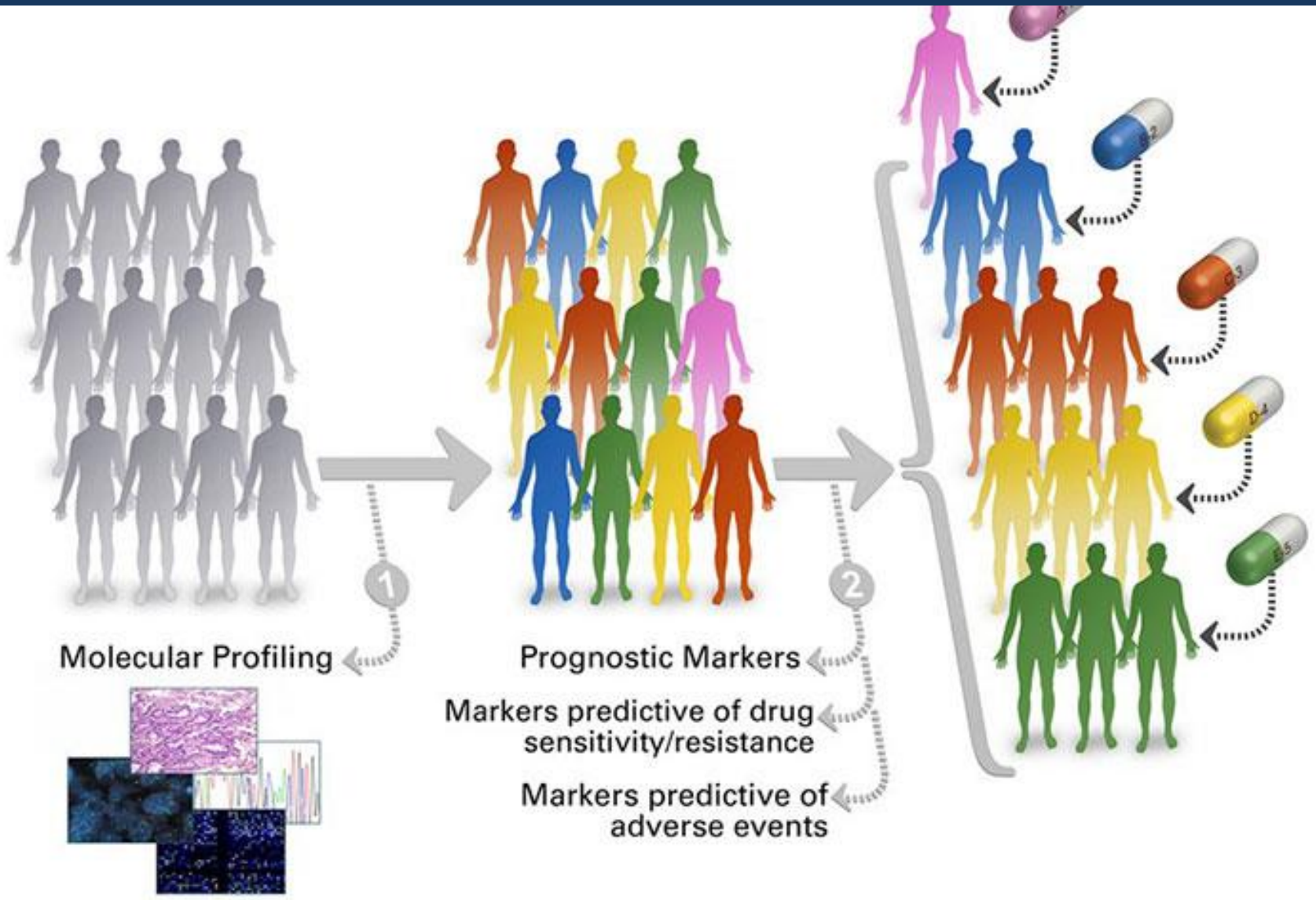
Study	Regimen	Response rate	Median survival (months)	1-Year survival
Belani et al. [41], $n = 369$	Cisplatin + etoposide	15%	9.0	37%
	Carboplatin + paclitaxel	23%	7.8	32%
Schiller et al. [10], ECOG 1594, $n =$ 1,155	Cisplatin + paclitaxel	21%	7.8	31%
	Cisplatin + gemcitabine	21%	8.1	36%
	Cisplatin + docetaxel	17%	7.4	31%
	Carboplatin + paclitaxel	16%	8.1	34%
Fossella et al. [22], TAX 326, $n = 1,218$	Cisplatin + vinorelbine	25%	10.1	41%
	Cisplatin + docetaxel	32%[a]	11.3	46%
	Carboplatin + docetaxel	24%	9.4	38%
Kelly et al. [11], SWOG 9509, $n = 408$	Cisplatin+ vinorelbine	28%	8.1	36%
	Carboplatin + paclitaxel	24%	8.6	38%

[a] $p = .029$.

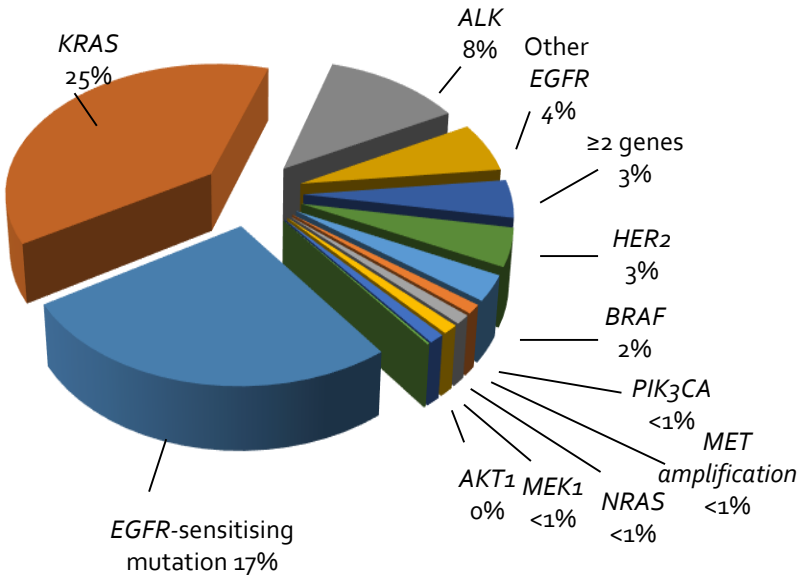
Systemic Chemotherapy for Advanced Non-Small Cell Lung Cancer: Recent Advances and Future Directions

Ramalingam S, et al.
The Oncologist 2008;13(suppl 1):5–13

Treatment Lung Cancer (Targeted Therapy)



Oncogenic drivers associated with lung cancer[1]



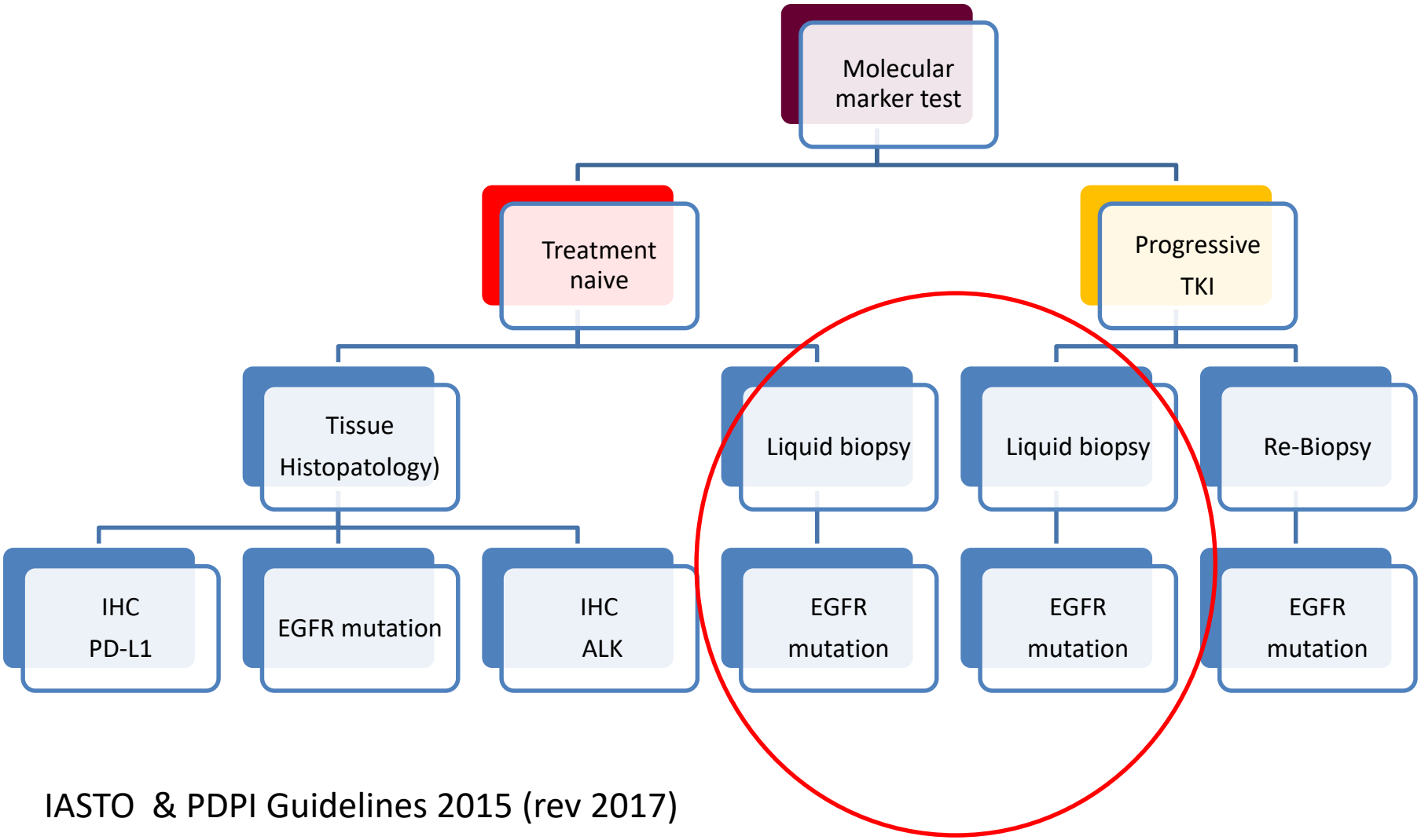
- Several oncogenic drivers have been identified that are associated with the development of lung cancer, including EGFR-sensitising activating mutations[1]
- EGFR tyrosine kinase activation indirectly inhibits apoptosis and promotes tumour cell survival through signal transduction pathways[2]

Tumours from 733 patients were tested for 10 oncogenic drivers; 64% of patients were positive for one or more genes as detailed in the pie chart

NB: the frequency of the different genetic aberrations varies based on patients characte
e.g. smoking status, gender, race.

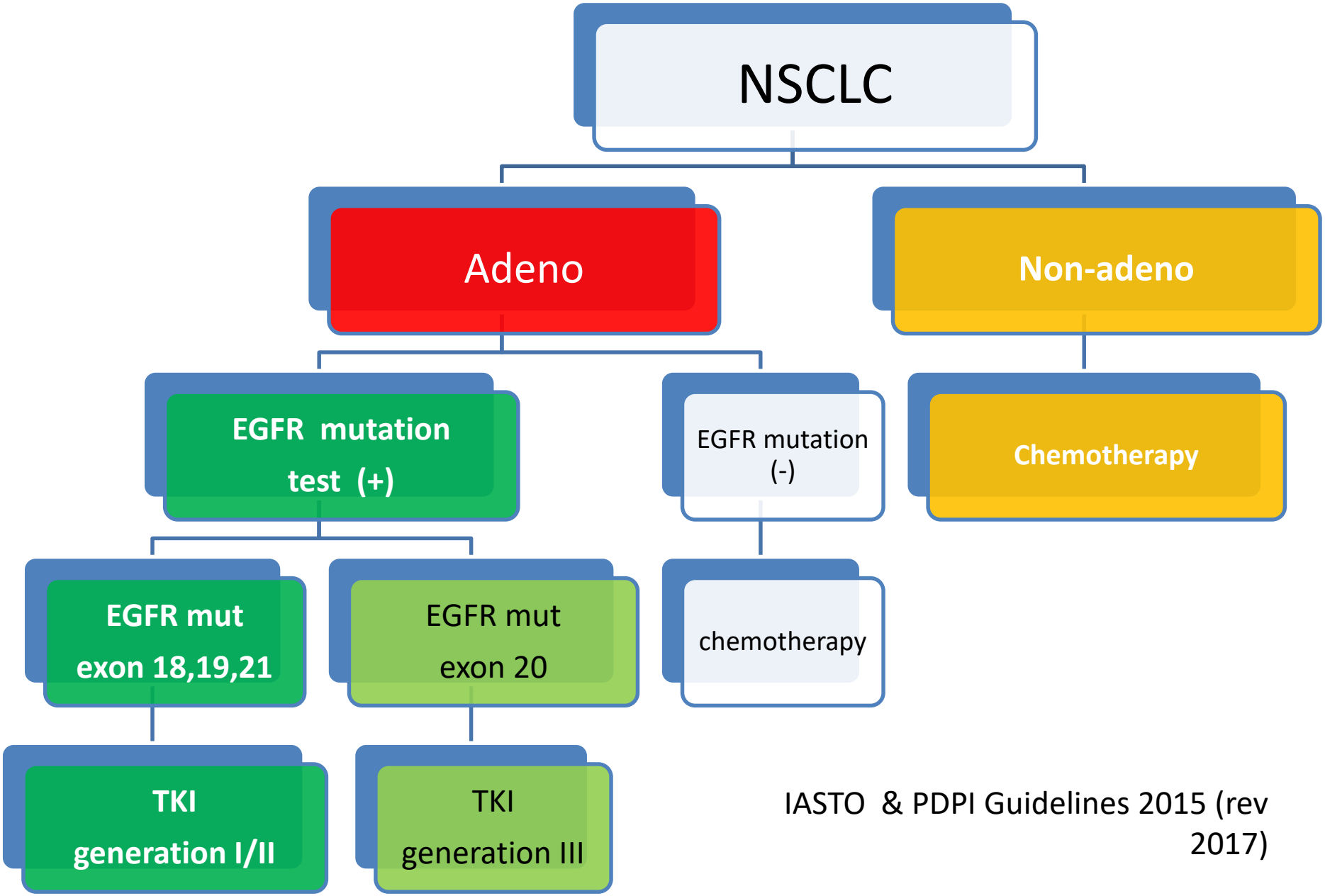
1. Kris MG, et al. JAMA 2014;311:1998–2006;
2. Herbst RS & Bunn Jr, PA. Clin Cancer Res 2003;9:5813–5824.

Molecular Markers Test for Lung



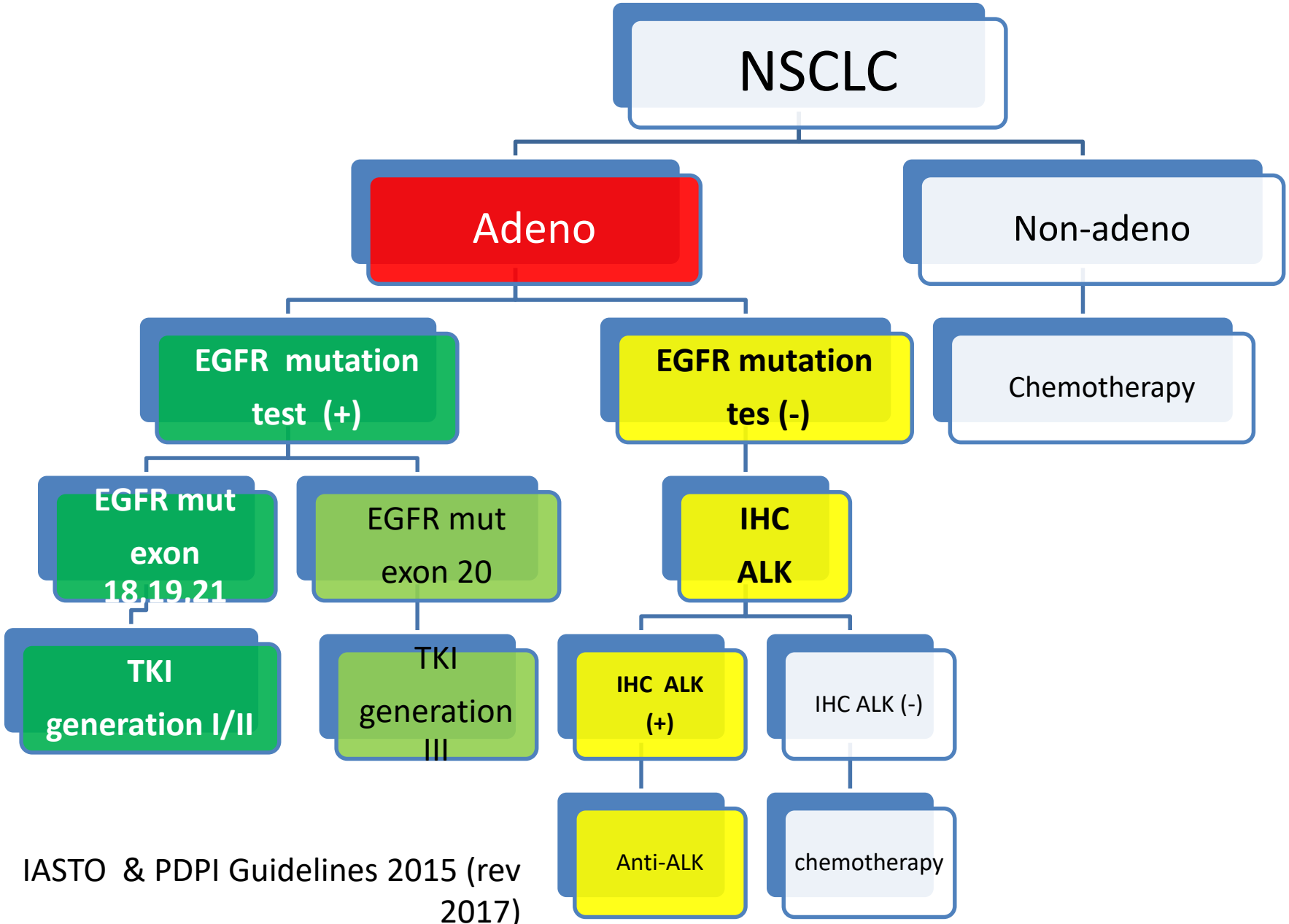
IASTO & PDPI Guidelines 2015 (rev 2017)

Treatment Lung Cancer



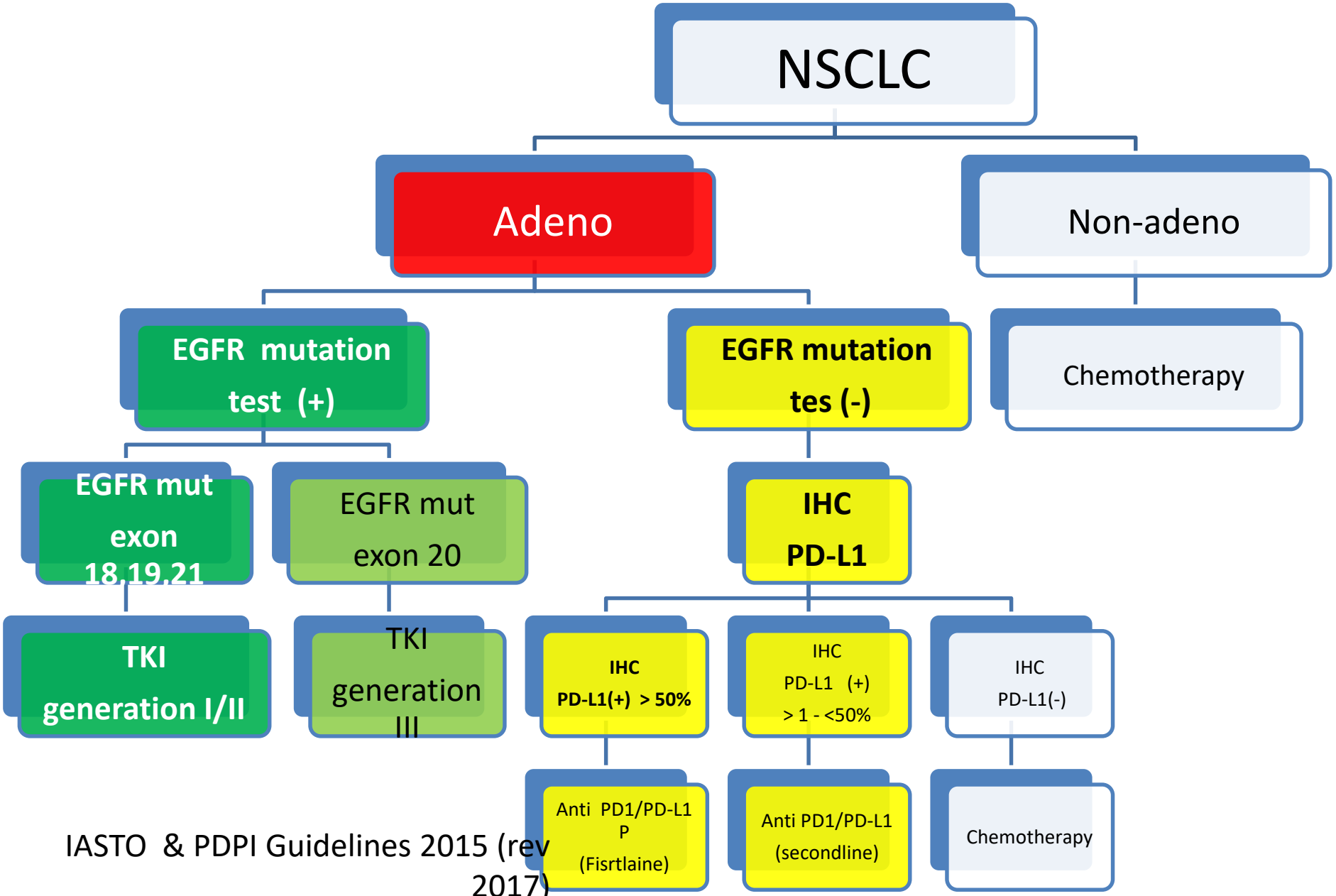
IASTO & PDPI Guidelines 2015 (rev 2017)

Treatment Lung Cancer



IASTO & PDPI Guidelines 2015 (rev 2017)

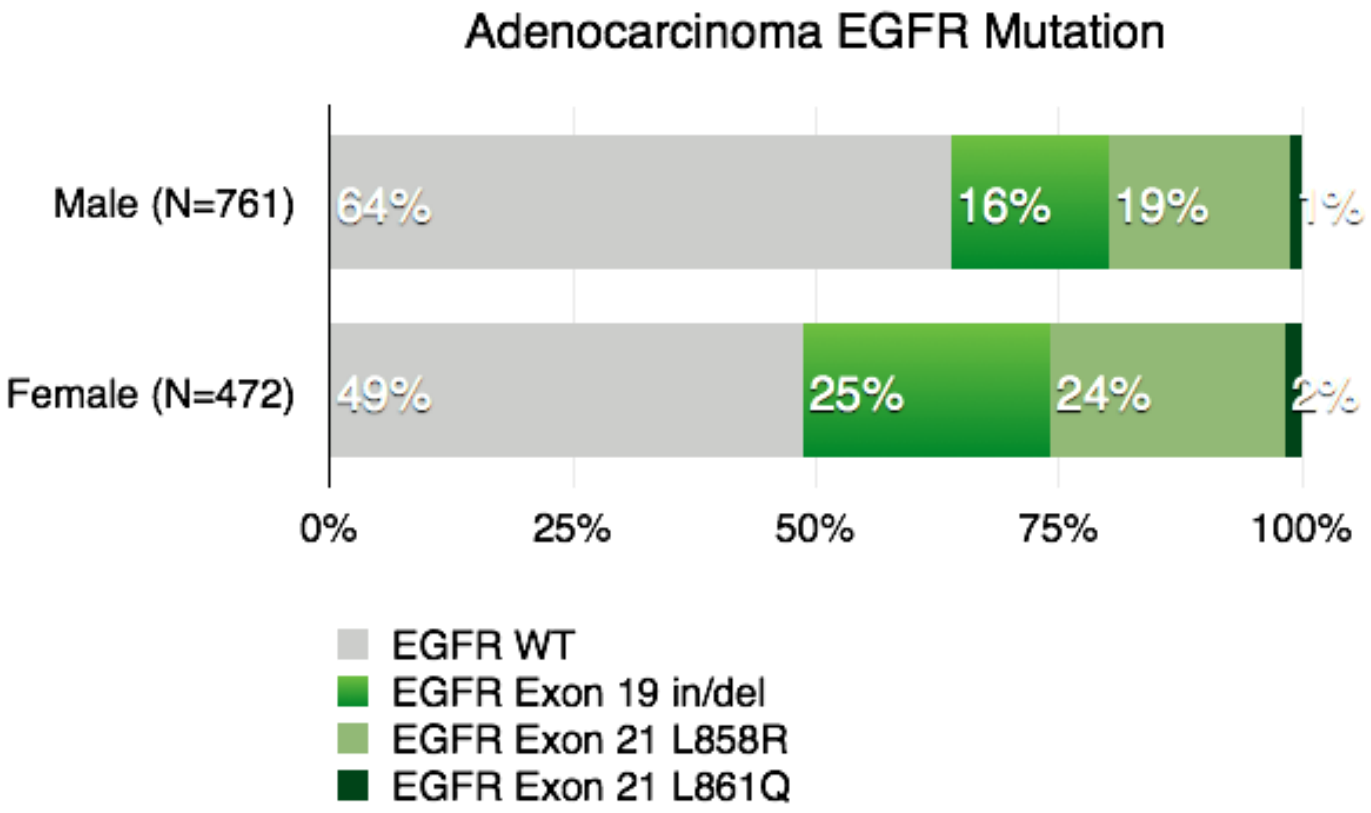
Treatment Lung Cancer



IASTO & PDPI Guidelines 2015 (rev 2017)

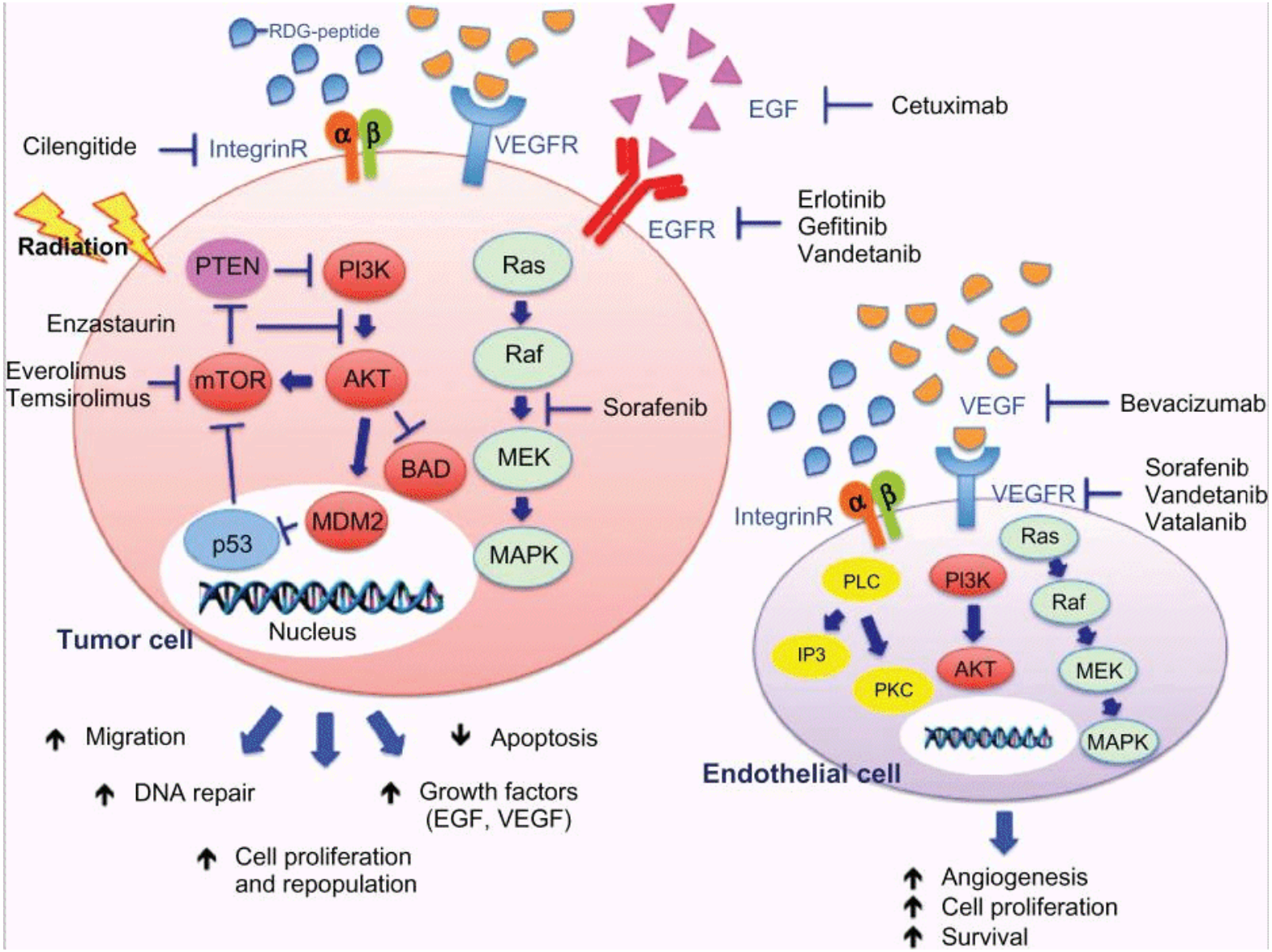
Molecular Markers Test for Lung

Adenocarcinoma EGFR Mutation Rate , Referred by Indonesia Pulmonologist
January 2010 – August 2014 (n = 1235)



Indonesian Society of Respirology (unpublished data)

Treatment Lung Cancer (Targeted Therapy)



Treatment Lung Cancer (Targeted Therapy)

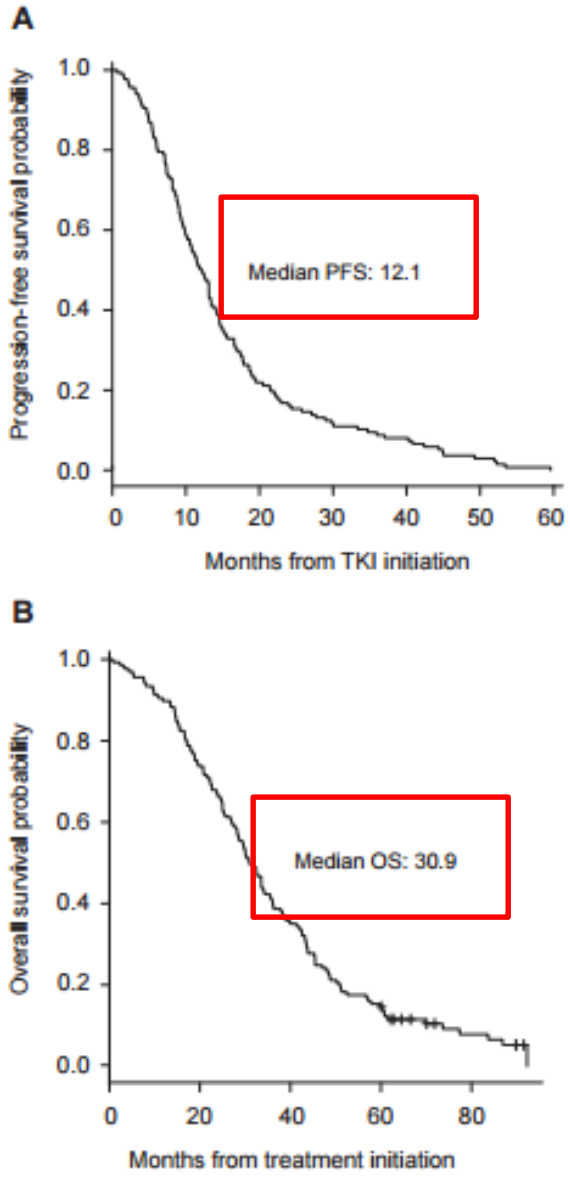


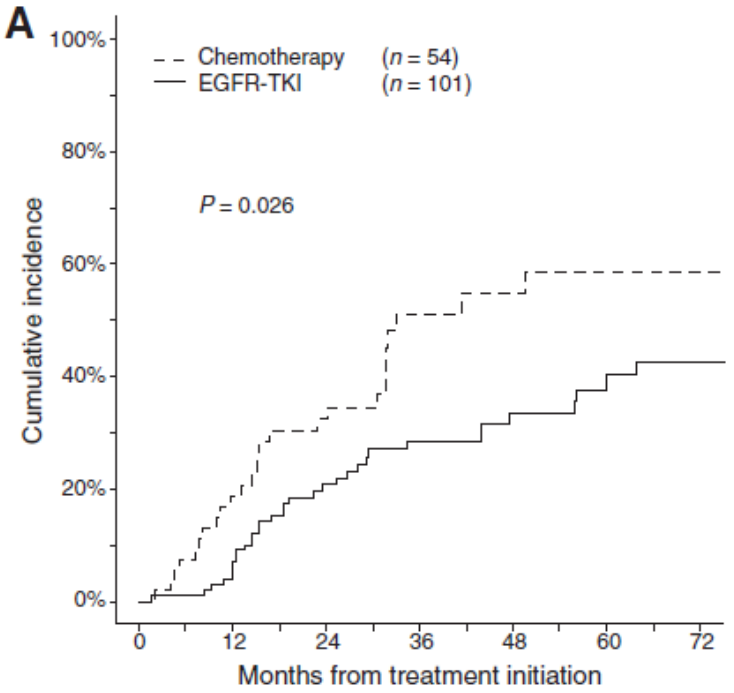
Figure 1. Kaplan-Meier plot of progression-free survival (*A*) and overall survival (*B*) for all patients in the study cohort. Median survival rates are annotated in months.

Five-Year Survival in EGFR-Mutant Metastatic Lung Adenocarcinoma Treated with EGFR-TKIs .

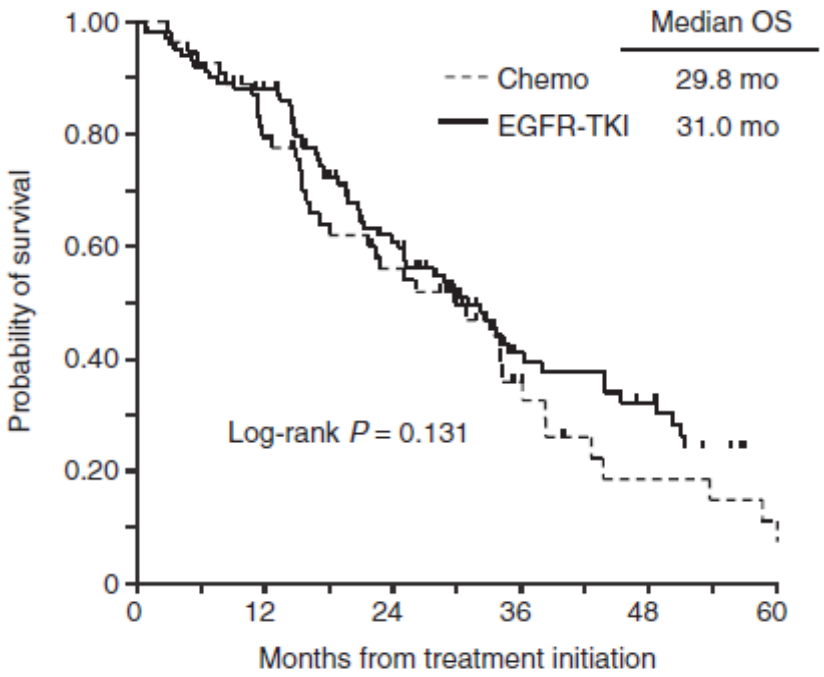
Jessica J. Lin, et al
Journal of Thoracic Oncology
2016; Vol. 11 No. 4: 556-565

Treatment with TKI vs Chemotherapy

Cumulative incidence of BM in advanced EGFR+ NSCLC

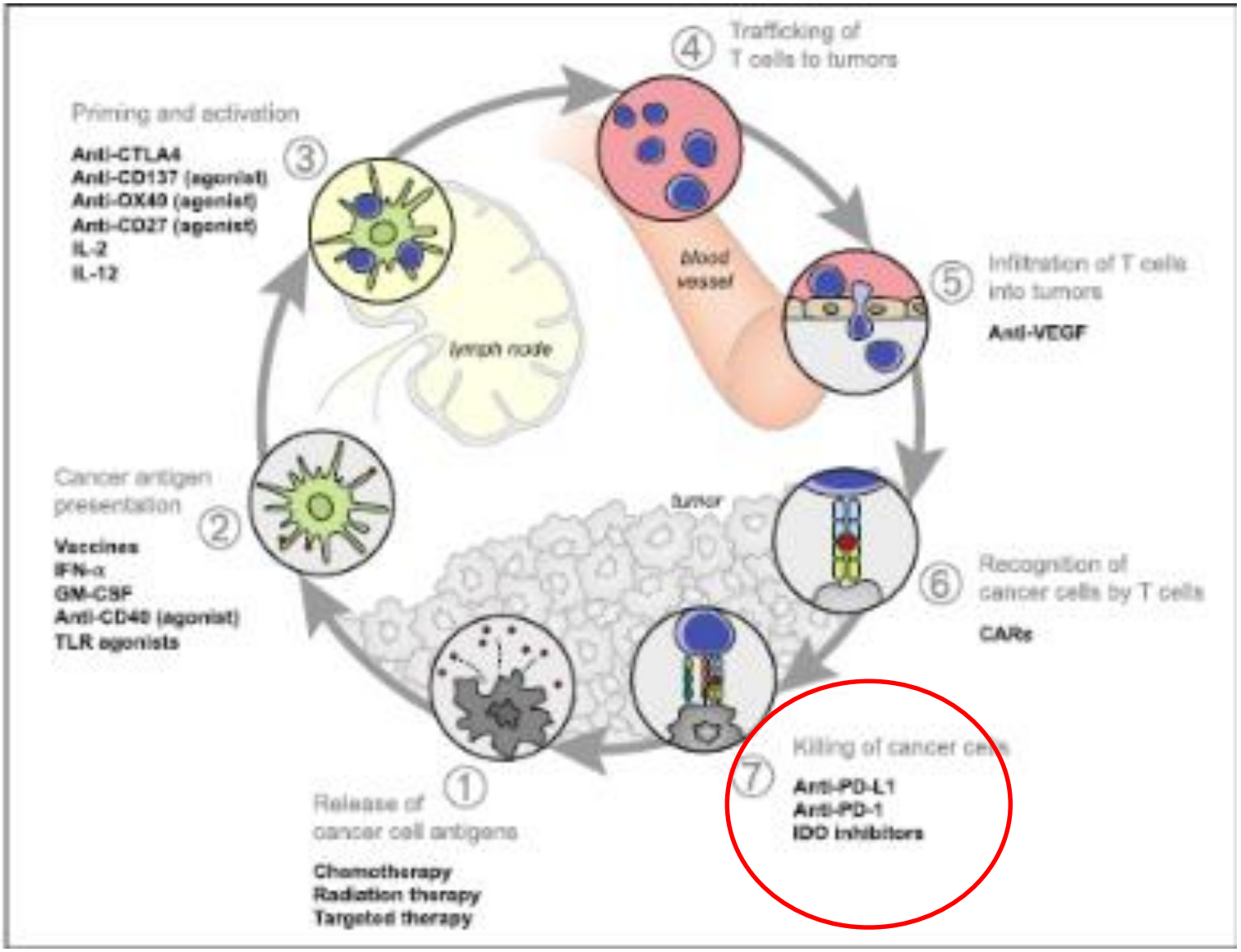


Overall survival in all eligible patients



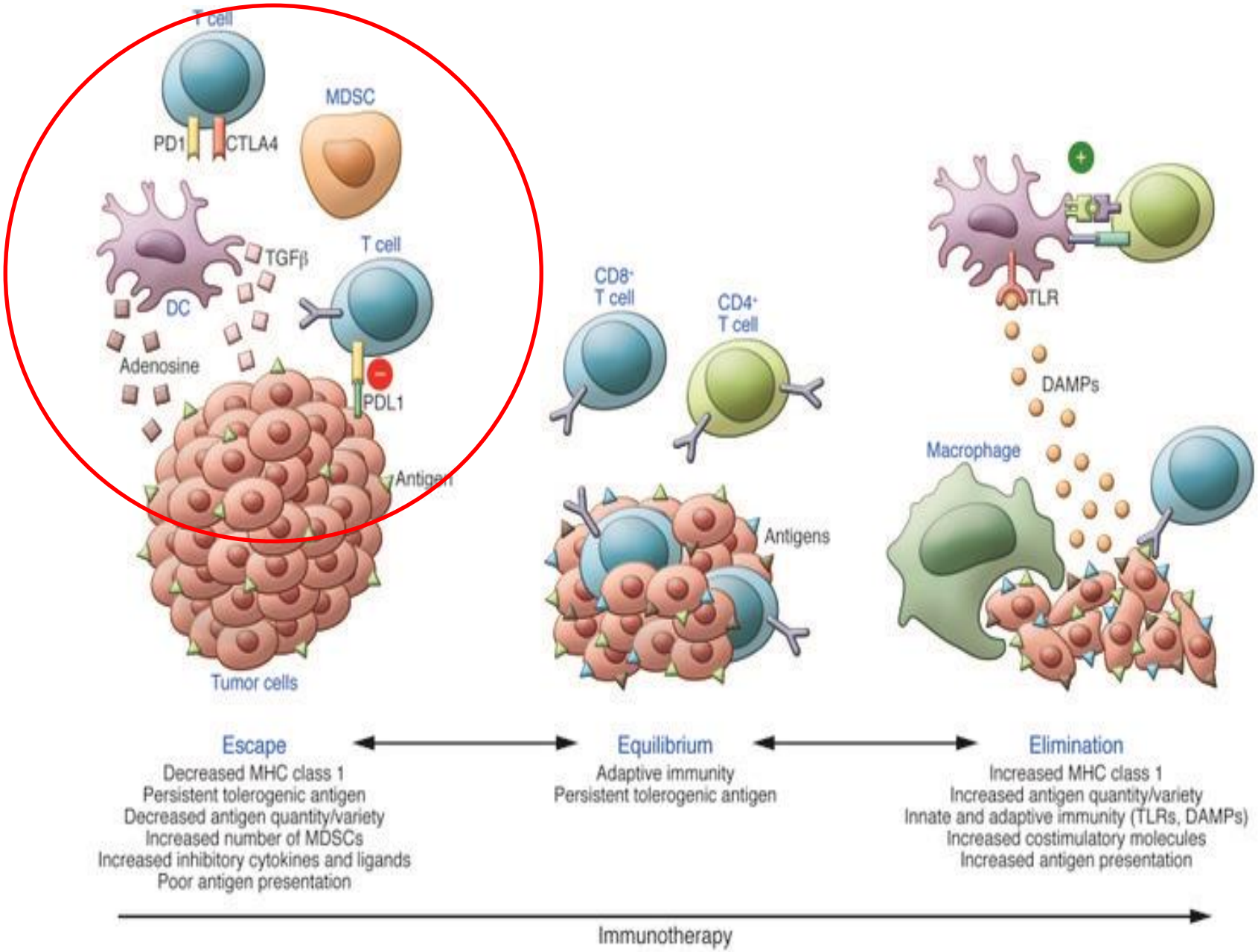
Stephanie Heon, et al. Clin Cancer Res; 18(16); 4406–14.

Treatment Lung Cancer (Immunotherapy = I-



Chen DS, et al. Oncology meets immunology: The cancer immunity cycles. Immunity

Treatment Lung Cancer (Immunotherapy = I-



Programmed cell death ligand-1 (PD-L1) expression by immunohistochemistry (IHC)

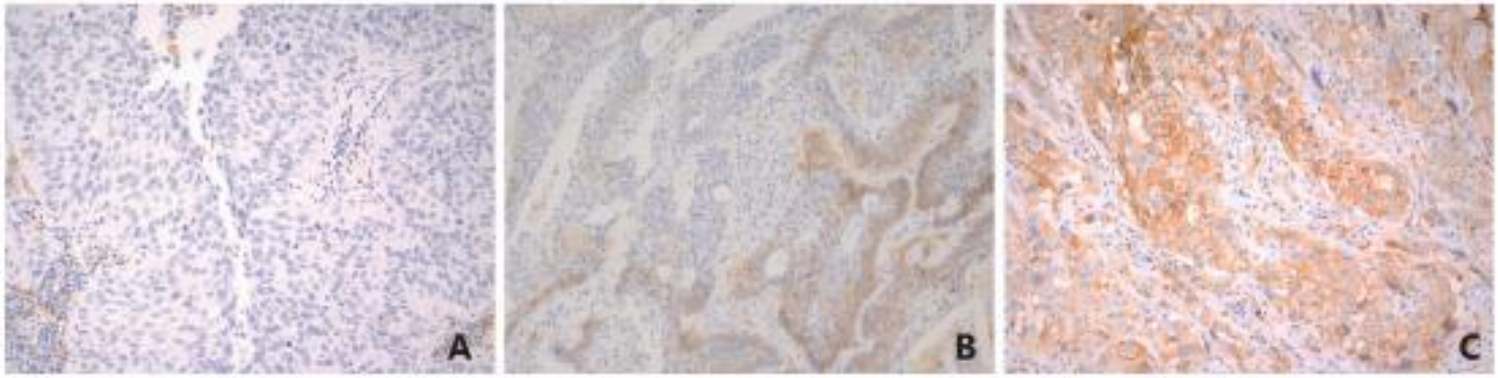


Figure 1 Representative images of PD-L1 immunostaining in lung squamous cell carcinoma. (A) No positive staining in the tumor cells.(B) 30% of the tumor cells with positive membranous staining. (C) The vast majority of the tumor cells with positive membranous staining.

Mino-Kenudson M. Programmed cell detah ligand-1 (PD-L1 expression by immunohistochemistry: could it be predictive and/or prognostic in non-small cell lung cancer. Cancer Biol Med. 2016; 13: 157-70

PD-L1 expression in lung cancer and its correlation with driver mutations: a meta-analysis

Minghui Zhang[1], Guoliang Li[2], Yanbo Wang[3], Yan Wang[4], Shu Zhao[1], Pu Haihong[1], Hongli Zhao[1] & Yan Wang[1]

Although many studies have addressed the prognostic value of programmed cell death-ligand 1 (PD-L1) expression in lung cancer, the results remain controversial. A systematic search of the PubMed, EMBASE, and Cochrane Library databases was performed to identify the correlation between PD-L1 expression and driver mutations and overall survival (OS). This meta-analysis enrolled a total of 11,444 patients for 47 studies, and the pooled results showed that increased PD-L1 expression was associated with poor prognosis (HR = 1.40, 95% CI: 1.19–1.65, $P < 0.001$). In subgroup analysis stratified according to histology types, the pooled results demonstrated that increased PD-L1 expression was an unfavorable prognostic factor for non-small cell lung cancer (NSCLC) (HR = 1.26, 95% CI: 1.05–1.52, $P = 0.01$) and pulmonary lymphoepithelioma-like carcinoma (LELC) (HR = 3.04, 95% CI: 1.19–7.77, $P = 0.02$), rather than small cell lung cancer (SCLC) (HR = 0.62, 95% CI: 0.27–1.39, $P = 0.24$). The pooled ORs indicated that PD-L1 expression was associated with gender, smoking status, histology, differentiation, tumour size, lymph nodal metastasis, TNM stage and EGFR mutation. However, PD-L1 expression was not correlated with ALK rearrangement and KRAS mutations.

https://www.nature.com/ published online 31 Augustus 2017

Expert Opin Biol Ther. 2016;16(3):397-406. doi: 10.1517/14712598.2016.1145652.

Pembrolizumab for the treatment of non-small cell lung cancer.

Lim SH[1], Sun JM[1], Lee SH[1], Ahn JS[1], Park K[1], Ahn MJ[1].

Author information

Abstract

INTRODUCTION: Immune checkpoint inhibitors targeting programmed death protein 1 (PD-1) receptor and its ligand, PD-L1, have recently led to significant and durable improvements in the clinical outcomes of some types of cancers including lung cancer.

AREAS COVERED: Pembrolizumab was approved by the US FDA for the treatment of advanced or metastatic NSCLC whose disease has progressed after other treatments and with tumors that express PD-L1. In the phase I KEYNOTE-001 trial, the overall response rate (ORR) was 19.4%, the median progression-free survival (PFS) and overall survival (OS) were 3.7 months and 12.0 months for 495 unselected NSCLC patients. Strong PD-L1 expression (≥ 50%) was associated with higher ORR, longer PFS, and longer OS. The phase II/III randomized KEYNOTE-010 trial demonstrated that pembrolizumab improved OS versus docetaxel in patients with previously treated NSCLC.

EXPERT OPINION: Pembrolizumab, demonstrated durable response and prolonged OS especially in NSCLC patients with high expression of PD-1, thereby suggests a new treatment paradigm. However, many issues remain to be explored, including the identification of other robust biomarkers that can accurately predict the immune-responsiveness of tumors. Along with the identification of predictive biomarkers, further understanding of the tumor microenvironment is necessary to improve treatment outcomes through combinations of immunotherapy or combined with other targeted therapies.

Ann Oncol. 2017 Apr 1;28(4):874-881. doi: 10.1093/annonc/mdx008.

Pembrolizumab as first-line therapy for patients with PD-L1-positive advanced non-small cell lung cancer: a phase 1 trial.

Hui R[1], Garon EB[2], Goldman JW[2], Leighl NB[3], Hellmann MD[4], Patnaik A[5], Gandhi L[6], Eder JP[7], Ahn MJ[8], Horn L[9], Felip E[10], Carcereny E[11], Rangwala R[12], Lubiniecki GM[12], Zhang J[12], Emancipator K[12], Roach C[13], Rizvi NA[14].

Author information

Abstract

BACKGROUND: Pembrolizumab improved survival as first- and second-line therapy compared with chemotherapy in patients with highly programmed death ligand 1 (PD-L1) expressing advanced non-small cell lung cancer (NSCLC). We report the long-term safety and clinical activity of pembrolizumab as first-line therapy for patients with advanced NSCLC and the correlation between PD-L1 expression and efficacy.

PATIENTS AND METHODS: In the open-label phase 1b KEYNOTE-001 trial, treatment-naive patients with advanced NSCLC whose tumors expressed PD-L1 (≥1% staining, assessed using a prototype assay) were randomly assigned to intravenous pembrolizumab 2 or 10 mg/kg every 3 (Q3W) or 2 (Q2W) weeks. Response was assessed per central RECIST v1.1 every 9 weeks in all patients who received ≥1 pembrolizumab dose. Using pre-treatment tumor tissue, a clinical assay quantified the percentage of tumor cells expressing PD-L1 as tumor proportion score (TPS).

RESULTS: Between 1 March 2013 and 18 September 2015, 101 patients received pembrolizumab 2 mg/kg Q3W (n = 6), 10 mg/kg Q3W (n = 49), or 10 mg/kg Q2W (n = 46). Of these, 27 (26.7%) had TPS ≥50%, 52 (51.5%) had TPS 1%-49%, and 12 (11.9%) had TPS <1%. The objective response rate (ORR) was 27% (27/101, 95% CI 18-37) and median overall survival was 22.1 months (95% CI 17.1-27.2). In patients with PD-L1 TPS ≥50%, ORR, 12-month PFS, and 12-month OS were higher [14/27 (51.9%; 95% CI 32%-71%), 54%, and 85%, respectively] than the overall population [27/101 (26.7%; 95% CI 18.4%-36.5%), 35%, 71%]. Pembrolizumab was well tolerated, with only 12 (11.9%) patients experiencing grade 3/4 treatment-related adverse events and no treatment-related deaths.

CONCLUSIONS: Pembrolizumab provides promising long-term OS benefit with a manageable safety profile for PD-L1-expressing treatment-naive advanced NSCLC, with greatest efficacy observed in patients with TPS ≥50%.

CLINICAL TRIAL NAME AND NUMBER: KEYNOTE-001 (ClinicalTrials.gov, NCT01295827).

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TABLE III: Antitumor Activity by PD-L1 Status in Patients in the ≥2L NSCLC Expansion Cohort.[6]

	Durvalumab 10 mg/kg q2w							
	High PD-L1 Expression[a]		Low/Negative PD-L1 Expression[b]		PD-L1 Expression Unknown		Total	
Confirmed ORR, % (95% CI)	BICR	IA	BICR	IA	BICR	IA	BICR	IA
All patients	n=115 20.0 (13.1–28.5)	n=115 24.3 (16.8–33.2)	n=108 2.8 (0.6–7.9)	n=107 5.6 (2.1–11.8)	n=17 11.8 (1.5–36.4)	n=16 18.8 (4.0–45.6)	N=240 11.7 (7.9–16.4)	N=238 15.5 (11.2–20.8)
Patients with squamous histology	n=76 18.4 (10.5–29.0)	n=76 27.6 (18.0–39.1)	n=44 2.3 (0.1–12.0)	n=44 6.8 (1.4–18.7)	n=7 0 (0.0–41.0)	n=7 14.3 (0.4–57.9)	N=127 11.8 (6.8–18.7)	N=127 19.7 (13.2–27.7)
Patients with non-squamous histology	n=39 23.1 (11.1–39.3)	n=39 17.9 (7.5–33.5)	n=64 3.1 (0.4–10.8)	n=63 4.8 (1.0–13.3)	n=10 20.0 (2.5–55.6)	n=9 22.2 (2.8–60.0)	N=113 11.5 (6.3–18.9)	N=111 10.8 (5.7–18.1)

2L = second line; BICR = blinded independent central review; IA = investigator assessment; NSCLC = non-small cell lung cancer; ORR = objective response rate; PD-L1 = programmed cell death ligand-1; q2w = every 2 weeks. [a]PD-L1 high is defined as staining in ≥25% of tumor cells; [b]PD-L1 low is defined as staining in <25% tumor cells.

Dose 10-20 mg/kg, q2w

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TABLE IV: Overall Survival in ≥2L NSCLC Population by PD-L1 Status and Histology.[6]

	High PD-L1 Expression[a]	Low/Negative PD-L1 Expression[b]	Total
Overall ≥2L Population	**(n=115)**	**(n=108)**	**(N=240)**
Median OS, months (95% CI)	15.4 (9.8–22.4)	7.6 (5.4–10.0)	10.2 (8.2–14.0)
12-month OS, % (95% CI)	56 (46–66)	37 (28–47)	47 (40–54)
Median PFS, months (95% CI)	2.2 (1.4–3.6)	1.4 (1.3–1.5)	1.5 (1.4–2.2)
12-month PFS, % (95% CI)	14 (8–22)	2 (0–8)	9 (6–14)
≥2L Patients With Squamous Histology	**(n=76)**	**(n=44)**	**(N=127)**
Median OS, months (95% CI)	15.4 (11.3–25.3)	7.8 (4.1–10.2)	13.4 (9.0–16.8)
12-month OS, % (95% CI)	61 (48–72)	33 (17–49)	52 (41–61)
Median PFS, months (95% CI)	2.3 (1.4–3.6)	1.4 (1.2–1.9)	1.5 (1.4–2.6)
12-month PFS, % (95% CI)	13 (6–23)	0 (NE–NE)	10 (5–17)
≥2L Patients With Non-squamous Histology	**(n=39)**	**(n=64)**	**(N=113)**
Median OS, months (95% CI)	11.0 (2.8–23.0)	7.6 (4.3–13.8)	8.2 (4.9–14.0)
12-month OS, % (95% CI)	47 (30–63)	40 (27–52)	43 (33–52)
Median PFS, months (95% CI)	1.9 (1.2–5.5)	1.4 (1.3–2.5)	1.4 (1.3–2.5)
12-month PFS, % (95% CI)	16 (6–31)	2 (0–10)	9 (4–16)

2L = second line; OS = overall survival; PD-L1 = programmed cell death ligand-1; PFS = progression free survival. [a]PD-L1 high is defined as staining in ≥25% of tumor cells; [b]PD-L1 low is defined as staining in <25% tumor cells.

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Articles

Activity and safety of nivolumab, an anti-PD-1 immune checkpoint inhibitor, for patients with advanced, refractory squamous non-small-cell lung cancer (CheckMate 063): a

Methods

We did this phase 2, single-arm trial at 27 sites (academic, hospital, and private cancer centres) in France, Germany, Italy, and USA. Patients who had received two or more previous treatments received intravenous nivolumab (3 mg/kg) every 2 weeks until progression or unacceptable toxic effects. The primary endpoint was the proportion of patients with a confirmed objective response as assessed by an independent radiology review committee. We included all treated patients in the analyses. This study is registered with ClinicalTrials.gov, number NCT01721759.

Findings

Between Nov 16, 2012, and July 22, 2013, we enrolled and treated 117 patients. 17 (14·5%, 95% CI 8·7–22·2) of 117 patients had an objective response as assessed by an independent radiology review committee. Median time to response was 3·3 months (IQR 2·2–4·8), and median duration of response was not reached (95% CI 8·31–not applicable); 13 (77%) of 17 of responses were ongoing at the time of analysis. 30 (26%) of 117 patients had stable disease (median duration 6·0 months, 95% CI 4·7–10·9). 20 (17%) of 117 patients reported grade 3–4 treatment-related adverse events, including: fatigue (five [4%] of 117 patients), pneumonitis (four [3%]), and diarrhoea (three [3%]). There were two treatment-associated deaths caused by pneumonia and ischaemic stroke that occurred in patients with multiple comorbidities in the setting of progressive disease.

Interpretation

Nivolumab has clinically meaningful activity and a manageable safety profile in previously treated patients with advanced, refractory, squamous non-small cell lung cancer. These data support the assessment of nivolumab in randomised, controlled, phase 3 studies of first-line and second-line treatment.

Make the most noise ever for Lung Cancer Awareness Month this November – and throughout the year. Whether you are an individual, healthcare provider or company we make it super easy for you to add your voice to our national movement for lung cancer