Contents

- ✓ Epidemiology (screening/adjuvant therapy)
- ✓ Diagnosis (histology/staging)
- ✓ Treatment (medical treatment)
- ✓ ADC

Epidemiology (Worldwide)

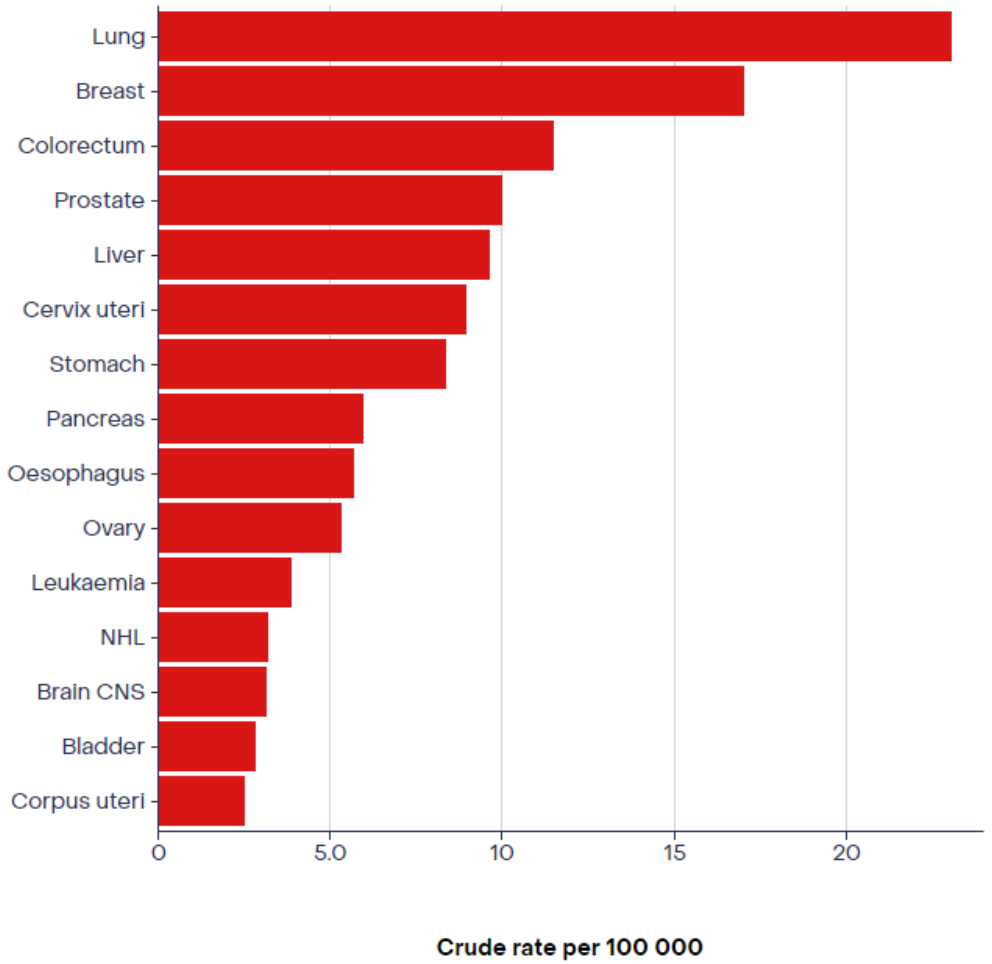
International Agency for Research on Cancer
World Health Organization

Estimated number of new cancer cases in 2022

ICD	Cancer	Number	Crude Rate*
C00-97/C44	All cancers†	18,741,966	237.7
C33-34	Lung	2,480,675	31.5
C50	Breast	2,296,840	58.7
C18-21	Colorectum	1,926,425	24.4
C61	Prostate	1,467,854	37.0
C16	Stomach	968,784	12.3
C22	Liver	866,136	11.0

†exclude non-melanoma skin cancer
*Crude and age-standardized rates per 100,000

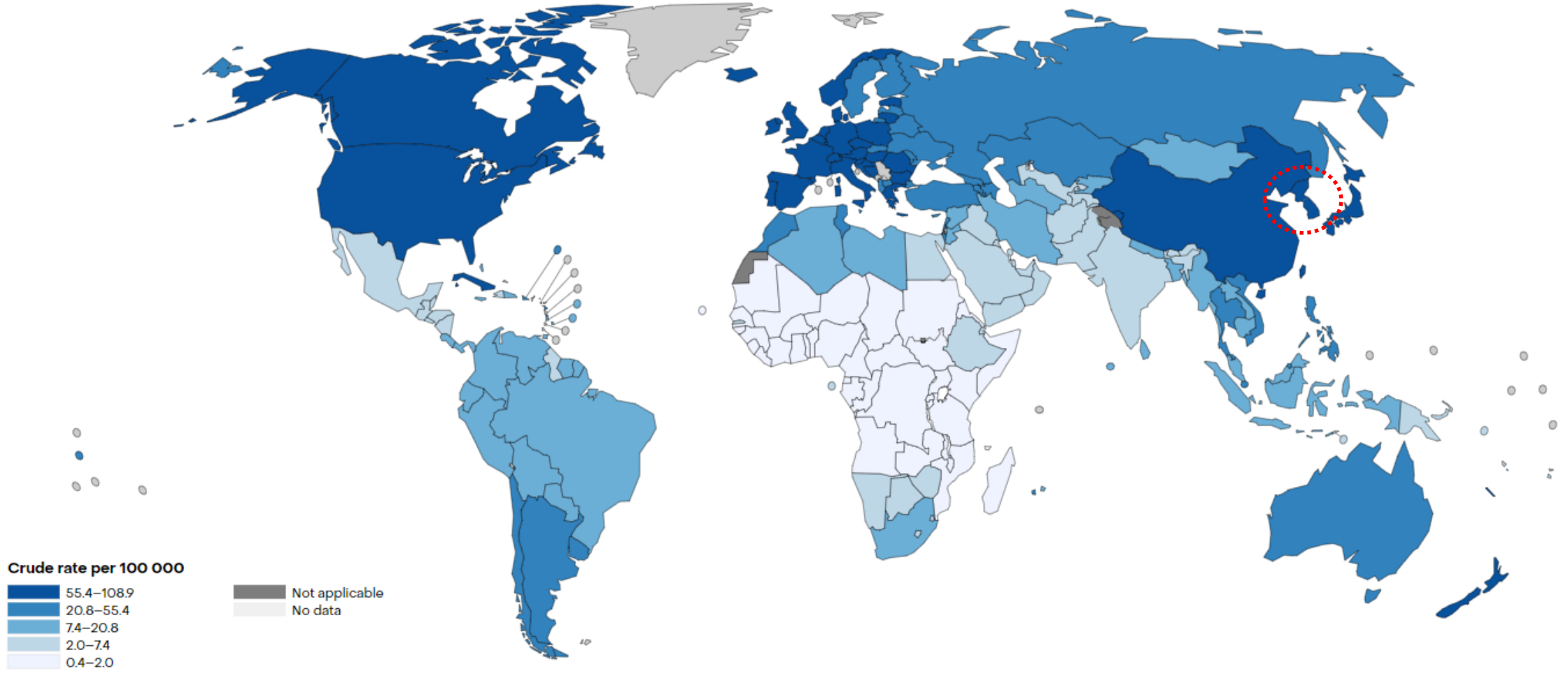
Crude rate per 100 000, Mortality, Both sexes, in 2022



Referred from *https://gco.iarc.fr/today/home*

Crude rate per 100 000, Incidence, Both sexes, in 2022
Trachea, bronchus and lung

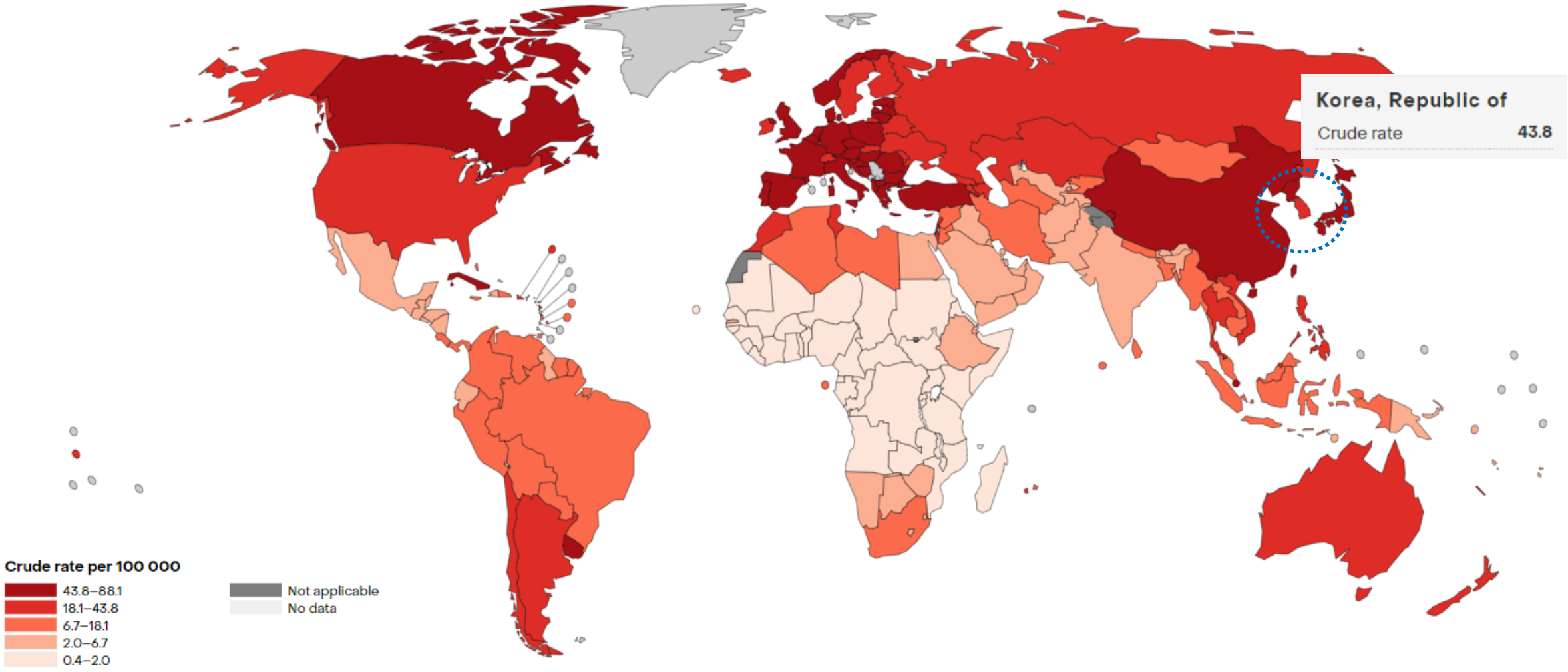
International Agency for Research on Cancer
World Health Organization



Referred from https://gco.iarc.who.int/today/en/dataviz

Crude rate per 100 000, Mortality, Both sexes, in 2022
Trachea, bronchus and lung

International Agency for Research on Cancer
World Health Organization

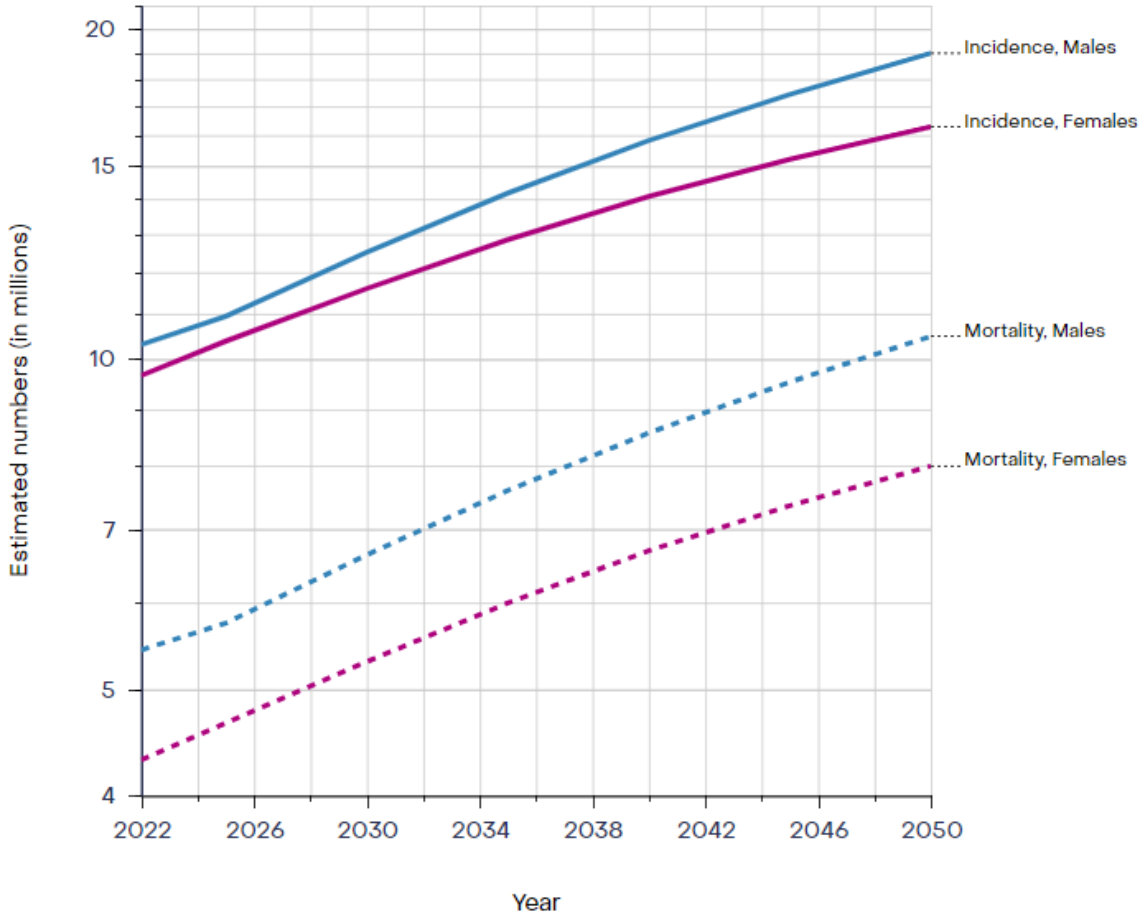


Referred from https://gco.iarc.who.int/today/en/dataviz

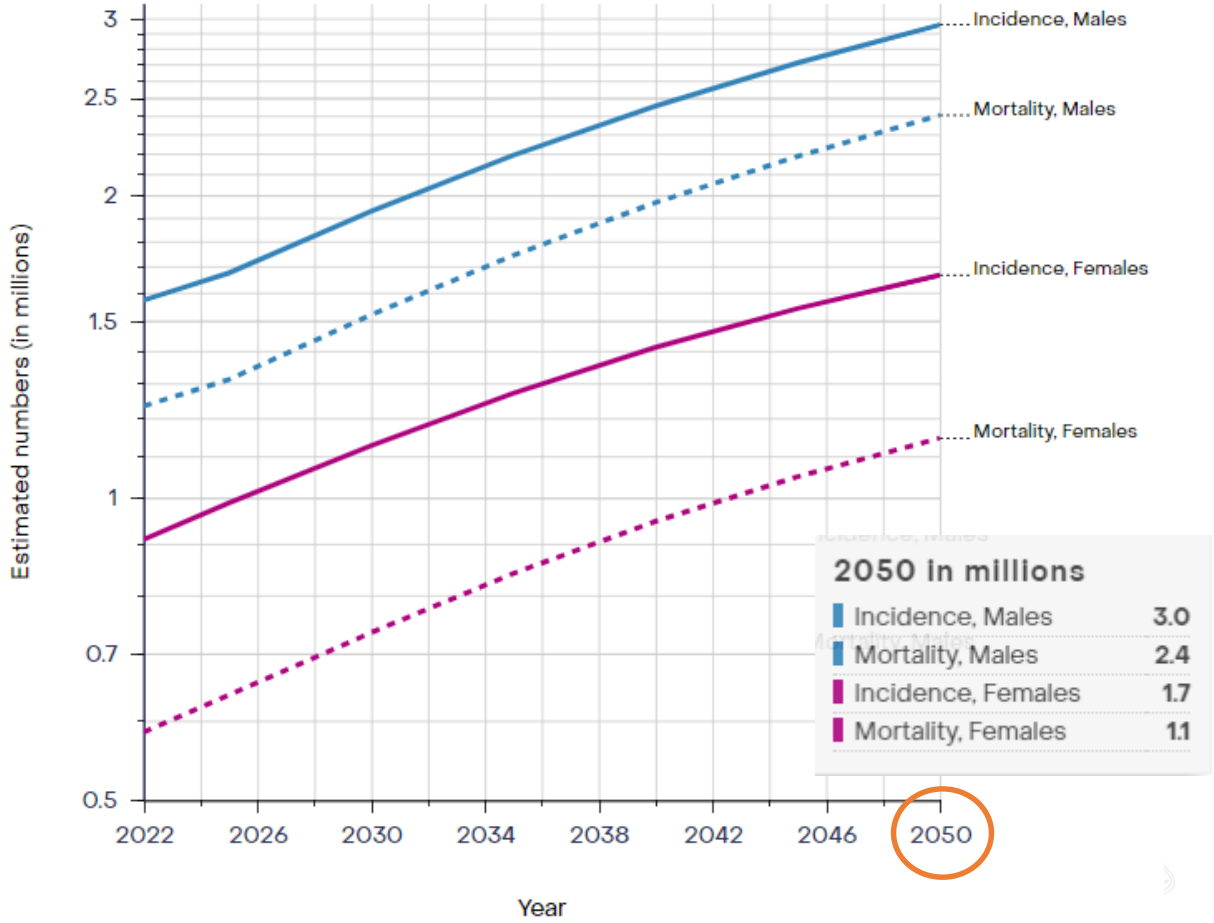
Estimated numbers from 2022 to 2050, Males and Females, age [0-85+]

International Agency for Research on Cancer
World Health Organization

All Cancers



Trachea, bronchus and lung



Referred from https://gco.iarc.who.int/today/en/dataviz

Epidemiology (Korea)

국가암정보센터 National Cancer Information Center

<2021년 주요 암종 발생자수 및 발생분율>

(단위: 명, %, 명/10만명)

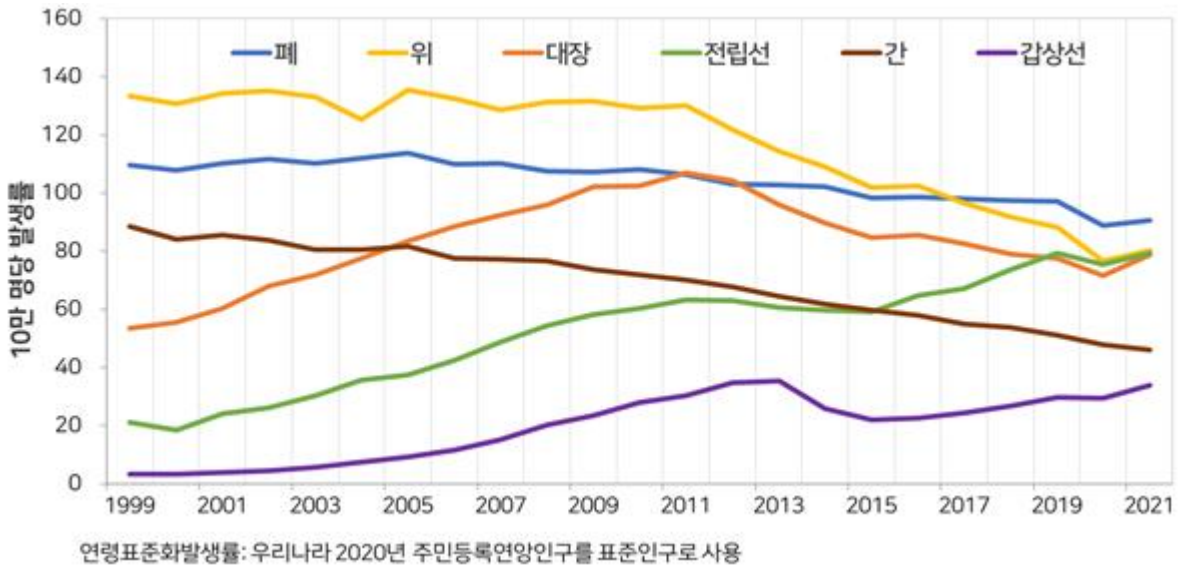
순위	암종(2020년 순위)	발생자수	분율	조발생률	표준화발생률*
	모든 악성암	277,523	100.0	540.6	526.7
	갑상선암 제외	242,220	87.3	471.9	458.1
1	갑상선	35,303	12.7	68.8	68.6
2	대장(3)	32,751	11.8	63.8	61.9
3	폐(2)	31,616	11.4	61.6	59.3
4	위	29,361	10.6	57.2	55.3
5	유방	28,861	10.4	56.2	55.7
6	전립선	18,697	6.7	36.4	35.0
7	간	15,131	5.5	29.5	28.5
8	췌장	8,872	3.2	17.3	16.7
9	담낭 및 기타담도	7,617	2.7	14.8	14.2
10	신장	6,883	2.5	13.4	13.1

(단위: 명, %, 명/10만명)

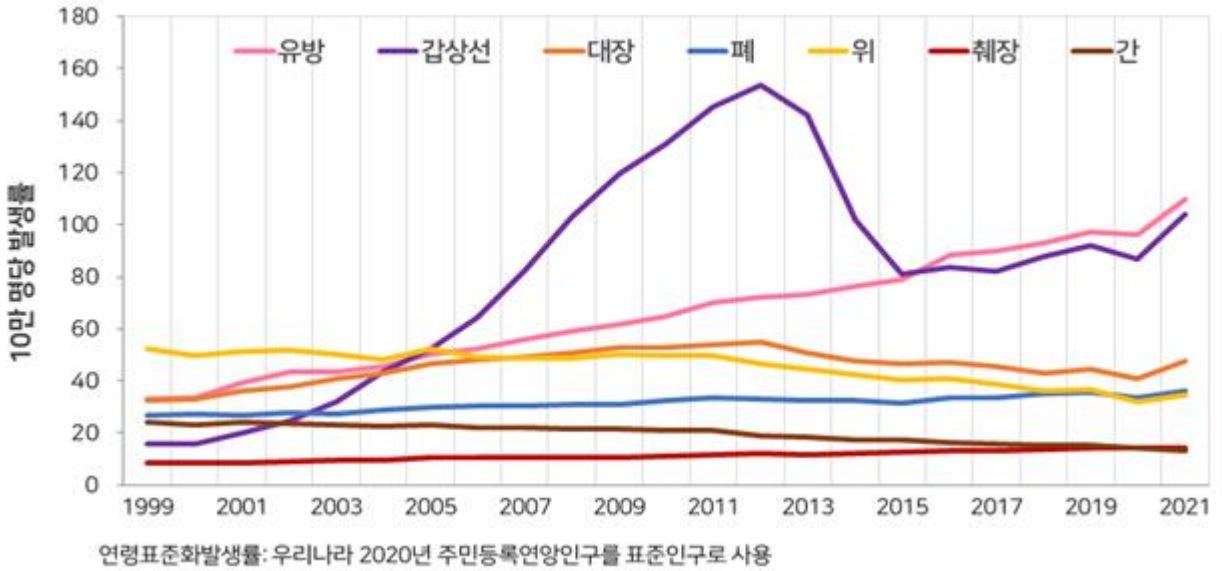
순위	남자					여자				
	암종('20 순위)	발생자수	분율	조 발생률	표준화 발생률*	암종('20 순위)	발생자수	분율	조 발생률	표준화 발생률*
	모든 악성암	143,723	100.0	561.7	596.7	모든 악성암	133,800	100.0	519.7	489.5
	갑상선암 제외	134,952	93.9	527.4	562.9	갑상선암 제외	107,268	80.2	416.7	385.5
1	폐	21,176	14.7	82.8	90.5	유방	28,720	21.5	111.6	109.9
2	위	19,533	13.6	76.3	80.2	갑상선	26,532	19.8	103.1	104.0
3	대장(4)	19,142	13.3	74.8	78.7	대장	13,609	10.2	52.9	47.5
4	전립선(3)	18,697	13.0	73.1	79.3	폐	10,440	7.8	40.6	36.1
5	간	11,207	7.8	43.8	46.1	위	9,828	7.3	38.2	34.5
6	갑상선	8,771	6.1	34.3	33.9	췌장	4,280	3.2	16.6	14.5
7	신장(8)	4,775	3.3	18.7	19.0	간	3,924	2.9	15.2	13.3
8	췌장(7)	4,592	3.2	17.9	19.2	자궁체부	3,749	2.8	14.6	14.3
9	방광(10)	4,201	2.9	16.4	18.3	담낭 및 기타담도	3,532	2.6	13.7	11.5
10	담낭 및 기타담도(9)	4,085	2.8	16.0	17.7	난소(11)	3,221	2.4	12.5	12.1

Referred from https://www.cancer.go.kr

Epidemiology (Korea)



연도별 연령표준화발생률 추이 : 남자



연도별 연령표준화발생률 추이 : 여자

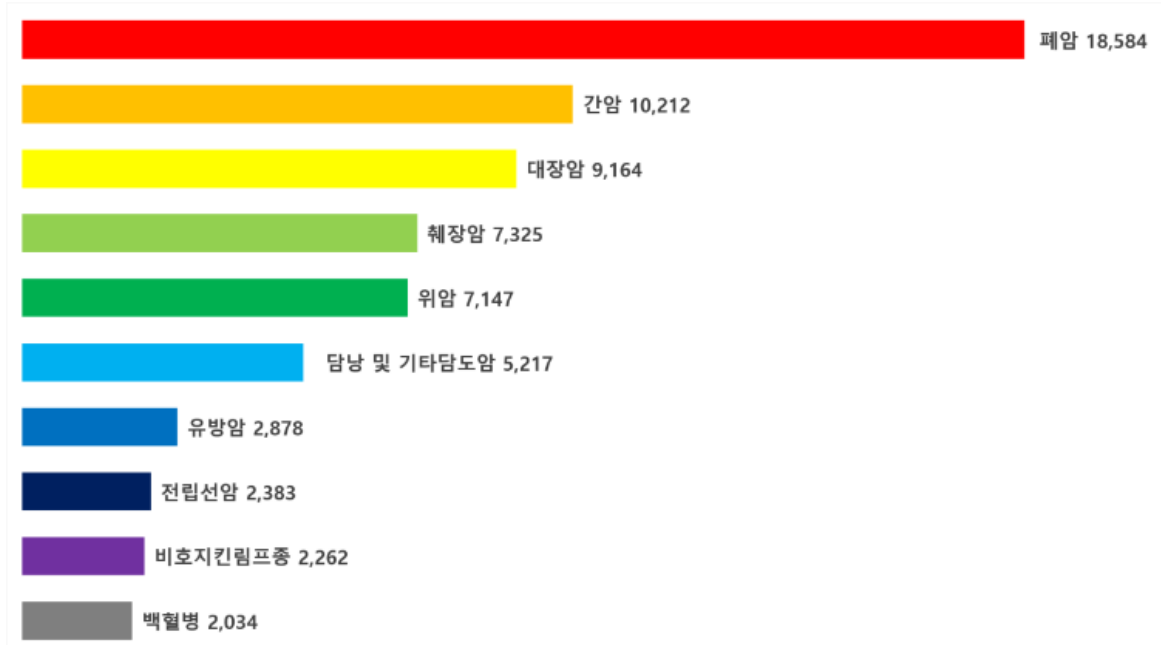
Referred from *https://www.cancer.go.kr*

Epidemiology (Korea)

국가암정보센터
National Cancer Information Center

<2022년 주요 암종별 사망률: 남녀전체 >

암종	국제질병분류(ICD-10)	사망자수	분율(%)
모든 암	C00-C97	83,378	100
폐암	C33-C34	18,584	22.3
간암	C22	10,212	12.2
대장암	C18-C21	9,164	11.0
췌장암	C25	7,325	8.8
위암	C16	7,147	8.6
담낭 및 기타담도암	C23-C24	5,217	6.3
유방암	C50	2,878	3.5
전립선암	C61	2,383	2.9
비호지킨림프종	C82-C86	2,262	2.7
백혈병	C91-C95	2,034	2.4



Referred from https://www.cancer.go.kr

Epidemiology (Korea)

국가암정보센터
National Cancer Information Center

주요 암종 5년 상대 생존율 추이: 남녀전체

(단위 : %,%p)

발생 순위	암종	발생기간							증감*
		'93-'95	'96-'00	'01-'05	'06-'10	'11-'15	'16-'20	'17-'21	
	모든 암	42.9	45.2	54.2	65.5	70.8	71.6	72.1	29.2
1	갑상선	94.5	95.0	98.4	100.0	100.2	100.0	100.1	5.6
2	대장	56.2	58.9	66.9	73.9	76.1	74.3	74.3	18.1
3	폐	12.5	13.7	16.6	20.3	27.6	37.2	38.5	26.0
4	위	43.9	47.3	58.0	68.4	75.9	77.9	77.9	34.0
5	유방	79.2	83.7	88.7	91.2	92.8	93.8	93.8	14.6
6	전립선	59.1	69.4	81.0	92.0	94.2	95.6	96.0	36.9
7	간	11.8	14.1	20.6	28.3	34.5	38.8	39.3	27.5
8	췌장	10.6	8.7	8.4	8.6	11.0	15.1	15.9	5.3
9	담낭 및 기타담도	18.7	20.7	23.1	26.9	28.8	28.7	28.9	10.2
10	신장	64.2	67.0	73.7	78.6	82.6	85.7	86.4	22.2

주요 암종 5년 생존율 국제 비교

암종	한국 (12 - 16)	미국 (08 - 14)	캐나다 (06 - 08)	일본 (06 - 08)
모든 암	70.6	69.2	60.0	62.1
위	76.0	32.1	25.0	64.6
대장	75.9	66.2	64	71.1
갑상선	100.2	98.3	98.0	93.7
폐	28.2	19.9	17.0	31.9
유방	92.7	91.1	87.0	91.1
간	34.6	18.8	19.0	32.6
전립선	93.9	98.9	95.0	97.5
췌장	11.4	9.1	8.0	7.7
자궁경부	79.8	68.9	73.0	73.4

Referred from https://www.cancer.go.kr

Epidemiology (Republic of KOREA)

International Agency for Research on Cancer
World Health Organization

Estimated number of new cancer cases in 2022

ICD	Cancer	Number	Crude Rate*
C00-97/C44	All cancers†	232,963	453.9
C33-34	Lung	31,337	61.1
C18-21	Colorectum	29,560	57.6
C16	Stomach	29,267	57.0
C50	Breast	24,772	96.6
C73	Thyroid	17,642	34.4
C61	Prostate	16,374	63.8

Estimated number of cancer-related deaths in 2022

ICD	Cancer	Number	Crude Rate*
C00-97/C44	All cancers†	97,268	189.5
C33-34	Lung	22,474	43.8
C22	Liver	12,595	24.5
C18-21	Colorectum	11,595	22.6
C16	Stomach	8,517	16.6
C25	Pancreas	7,582	14.8
C50	Breast	2,913	11.4

†exclude non-melanoma skin cancer
*Crude and age-standardized rates per 100,000

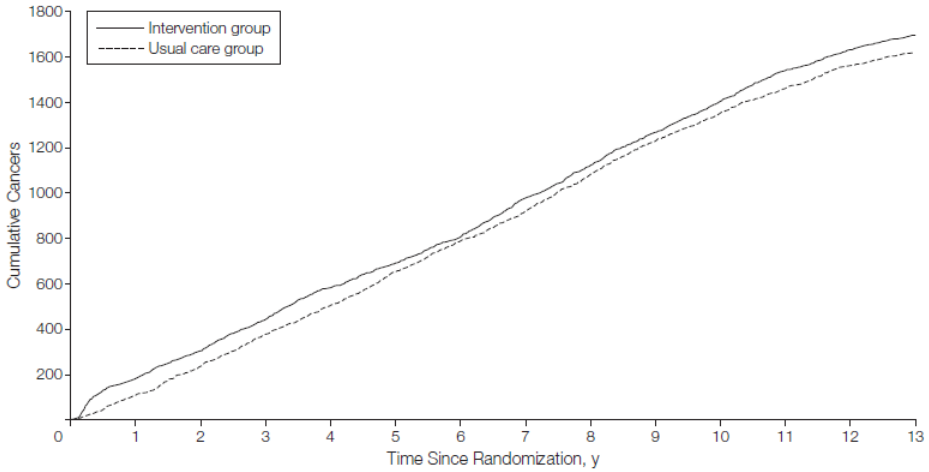
Referred from *https://gco.iarc.fr/today/home*

Early Detection and Screening

Screening by Chest Radiograph and Lung Cancer Mortality

The Prostate, Lung, Colorectal, and Ovarian (PLCO) Randomized Trial

Figure 2. Lung Cancer Incidence by Year



Intervention group													
Cumulative cancers	181	304	441	583	692	808	981	1124	1268	1405	1544	1633	1696
Cumulative person-years	76617	152416	227322	301309	374374	446481	517521	587405	655538	718389	771188	812963	844011
Usual care group													
Cumulative cancers	109	235	377	504	653	790	923	1084	1232	1358	1465	1563	1620
Cumulative person-years	76597	152495	227549	301699	374873	446975	517940	587701	655718	718398	771147	812834	843762

Design, Setting, and Participants Randomized controlled trial that involved 154 901 participants aged 55 through 74 years, 77 445 of whom were assigned to annual screenings and 77 456 to usual care at 1 of 10 screening centers across the United States between November 1993 and July 2001. The data from a subset of eligible participants for the National Lung Screening Trial (NLST), which compared chest radiograph with spiral computed tomographic (CT) screening, were analyzed.

Intervention Participants in the intervention group were offered annual posteroanterior view chest radiograph for 4 years. Diagnostic follow-up of positive screening results was determined by participants and their health care practitioners. Participants in the usual care group were offered no interventions and received their usual medical care. All diagnosed cancers, deaths, and causes of death were ascertained through the earlier of 13 years of follow-up or until December 31, 2009.

Main Outcome Measures Mortality from lung cancer. Secondary outcomes included lung cancer incidence, complications associated with diagnostic procedures, and all-cause mortality.

Results Screening adherence was 86.6% at baseline and 79% to 84% at years 1 through 3; the rate of screening use in the usual care group was 11%. Cumulative lung cancer incidence rates through 13 years of follow-up were 20.1 per 10 000 person-years in the intervention group and 19.2 per 10 000 person-years in the usual care group (rate ratio [RR]; 1.05, 95% CI, 0.98-1.12). A total of 1213 lung cancer deaths were observed in the intervention group compared with 1230 in usual care group through 13 years (mortality RR, 0.99; 95% CI, 0.87-1.22). Stage and histology were similar between the 2 groups. The RR of mortality for the subset of participants eligible for the NLST, over the same 6-year follow-up period, was 0.94 (95% CI, 0.81-1.10).

Conclusion Annual screening with chest radiograph did not reduce lung cancer mortality compared with usual care.

Trial Registration clinicaltrials.gov Identifier: NCT00002540

JAMA. 2011;306(17):1865-1873

Screening (NLST study)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

METHODS

From August 2002 through April 2004, we enrolled 53,454 persons at high risk for lung cancer at 33 U.S. medical centers. Participants were randomly assigned to undergo three annual screenings with either low-dose CT (26,722 participants) or single-view posteroanterior chest radiography (26,732). Data were collected on cases of lung cancer and deaths from lung cancer that occurred through December 31, 2009.

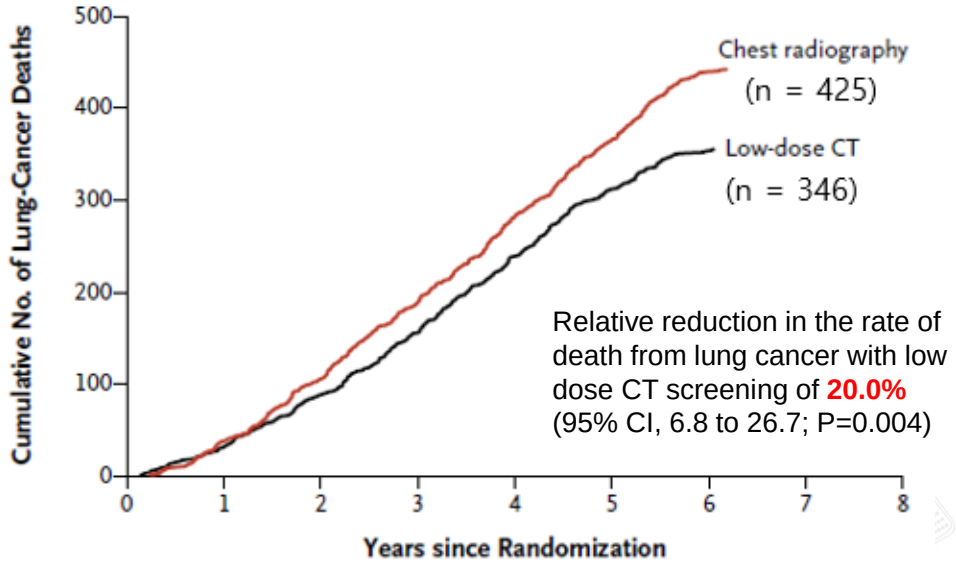
✓ Eligible

1. Between 55 and 74 years of age
2. History of cigarette smoking of at least 30 pack-years. If former-smokers, quit within the previous 15 years

✓ Positive (suspicious for lung cancer)

1. Any non-calcified nodule measuring at least 4mm in CT scan
2. Any non-calcified nodule or mass at radiographic images

Cumulative Numbers of Deaths from Lung Cancer



Relative reduction in the rate of death from lung cancer with low dose CT screening of **20.0%** (95% CI, 6.8 to 26.7; P=0.004)

N Engl J Med 2011;365:395-409.

Screening (NLST study)

Frequency and Positive Predictive Value of Positive Screening Results, According to Study Group

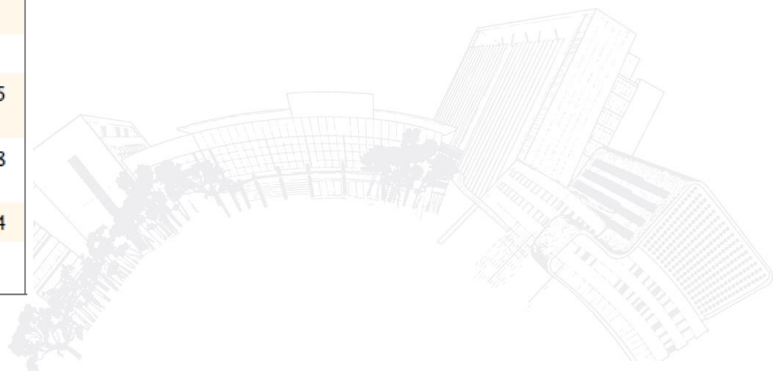
Finding at Initial Screening	Low-Dose CT						Chest Radiography					
	Confirmed Lung Cancer			Total	PPV	PPV Range	Confirmed Lung Cancer			Total	PPV	PPV Range
	yes	no	unknown				yes	no	unknown			
					percent						*percent*	
Patients												
Positive screening	270	6911	10	7191	3.8	3.3–4.2	136	2243	8	2387	5.7	4.8–6.6
With subsequent biopsy	265 (98.1)	236 (3.4)	0	501 (7.0)	52.9	48.4–57.4	132 (97.1)	56 (2.5)	0	188 (7.9)	70.2	64.0–76.8
With noncalcified nodule or mass	267 (98.9)	6765 (97.9)	9 (90.0)	7041 (97.9)	3.8	3.3–4.2	123 (90.4)	1982 (88.4)	7 (87.5)	2112 (88.5)	5.8	4.9–6.9
Size of nodule or mass†												
<4 mm	0	1 (<1)	0	1 (<1)	0.0	0.0–0.0	1 (0.7)	40 (1.8)	1 (12.5)	42 (1.8)	2.4	0.0–7.9
≥4 mm	267 (98.9)	6743 (97.6)	9 (90.0)	7019 (97.6)	3.8	3.4–4.3	115 (84.6)	1807 (80.6)	6 (75.0)	1928 (80.8)	6.0	4.9–7.1
4–6 mm	18 (6.7)	3642 (52.7)	8 (80.0)	3668 (51.0)	0.5	0.3–0.7	5 (3.7)	491 (21.9)	2 (25.0)	498 (20.9)	1.0	0.2–2.0
7–10 mm	35 (13.0)	2079 (30.1)	1 (10.0)	2115 (29.4)	1.7	1.1–2.2	12 (8.8)	692 (30.9)	2 (25.0)	706 (29.6)	1.7	0.8–2.9
11–20 mm	111 (41.1)	821 (11.9)	0	932 (13.0)	11.9	9.8–13.9	38 (27.9)	481 (21.4)	2 (25.0)	521 (21.8)	7.3	5.1–9.7
21–30 mm	58 (21.5)	137 (2.0)	0	195 (2.7)	29.7	23.7–36.4	27 (19.9)	92 (4.1)	0	119 (5.0)	22.7	15.2–30.4
>30 mm	45 (16.7)	64 (0.9)	0	109 (1.5)	41.3	32.1–51.0	33 (24.3)	51 (2.3)	0	84 (3.5)	39.3	28.6–50.6
Unknown	0	21 (0.3)	0	21 (0.3)	0.0	0.0–0.0	7 (5.1)	135 (6.0)	0	142 (5.9)	4.9	1.8–8.7
Other findings												
Atelectasis, segmental or more extensive‡	3 (1.1)	69 (1.0)	0	72 (1.0)	4.2	0.0–9.0	4 (2.9)	24 (1.1)	0	28 (1.2)	14.3	3.4–29.5
Noncalcified hilar or mediastinal adenopathy or mass	51 (18.9)	225 (3.3)	1 (10.0)	277 (3.9)	18.5	14.1–23.4	8 (5.9)	78 (3.5)	0	86 (3.6)	9.3	3.8–15.8
Consolidation‡	7 (2.6)	80 (1.2)	0	87 (1.2)	8.0	2.6–14.4	3 (2.2)	41 (1.8)	1 (12.5)	45 (1.9)	6.8	0.0–14.4
Pleural thickening or effusion	16 (5.9)	439 (6.4)	1 (10.0)	456 (6.3)	3.5	1.9–5.3	10 (7.4)	161 (7.2)	1 (12.5)	172 (7.2)	5.8	2.5–9.4

Several Questions of NLST

Will populations with risk profiles that are different from those of the NLST participants benefit?

For how long should screening continue?

Would the use of **different criteria** for a positive screening result, such as a larger nodule diameter, still result in a benefit?



N Engl J Med 2013;368:1980-91.

Screening in Korea

Pusan National University Yangsan Hospital

Item	Requirement	Quality of the evidence
Population	Healthy subjects	Grade B[a]
	Aged 55-74 yr	
	≥30 pack-year smoking history	
	Current smokers	
	Former smokers have quit within past 15 yr	
Screening tool	LDCT	Grade B[a]
	Chest radiograph	Grade D[a]
	Sputum cytology	Grade D[a]
	Serum tumor marker	Grade D[a]
Frequency	Annually	
Comment	Smoking cessation counseling must be offered to current smokers.	
	Screening should not be viewed as an alternative to smoking cessation.	
	People should be Informed about the potential benefits, limitations, and harms associated with screening for lung cancer with LDCT.	
	LDCT screening should be performed at qualified hospitals.	

검진 권고안과 권고등급

(1) 30갑년 이상의 흡연력이 있는(금연 후 15년이 경과한 과거 흡연자는 제외) 55–74세인 고위험군을 대상으로 저선량 흉부 CT를 이용한 폐암선별검사를 매년 시행할 것을 권고한다(권고등급 B).

(2) 흉부X선, 객담 세포진 검사 및 현재까지 개발된 carcinoembryonic antigen, squamous cell carcinoma anti-gen, CYFRA 21-1, neuron specific enolase 등 혈청 종양표지자를 이용한 폐암 선별검사는 권고하지 않는다(권고등급 D).

J Korean Med Assoc 2015 April; 58(4): 291-301

보도자료

보건복지부 MINISTRY OF HEALTH & WELFARE

제목	55-74세 고위험흡연자 대상 폐암검진 도입		
등록일	2016-09-12[최종수정일 : 2016-09-12]	조회수	3894
담당자	황경원	담당부서	질병정책과

55~74세 고위험흡연자 대상 폐암검진 도입

1. **국가암검진에 신규로 폐암검진 도입을 추진하고 암환자에 대한 의료비 지원을 개선한다.**
   1. 암 중 사망원인 1위인 폐암을 국가암검진으로 추가 도입하여 조기 발견을 통한 폐암의 사망률 감소를 추진한다.
      - 폐암 검진 권고안에 따라 '17년에는 55세 이상 74세 이하의 30갑년* 이상 흡연력이 있는 분을 대상으로 저선량 CT를 통해 시범적으로 검진을 수행할 계획**이다.

        * 갑년(Pack year)은 1년간 하루 한 갑씩 흡연했을 때를 기준으로 한 담배소비량으로, 30갑년은 매일 1갑씩 30년 또는 매일 2갑씩 15년 등 의미

        ** 총 8,000명 대상, 예산 29억원 확보
      - 또한 시범사업 결과를 기반으로 폐암 검진의 대상기준 및 절차를 확정하고 단계적으로 폐암검진을 도입할 예정이다.

Screening in Korea

Pusan National University Yangsan Hospital

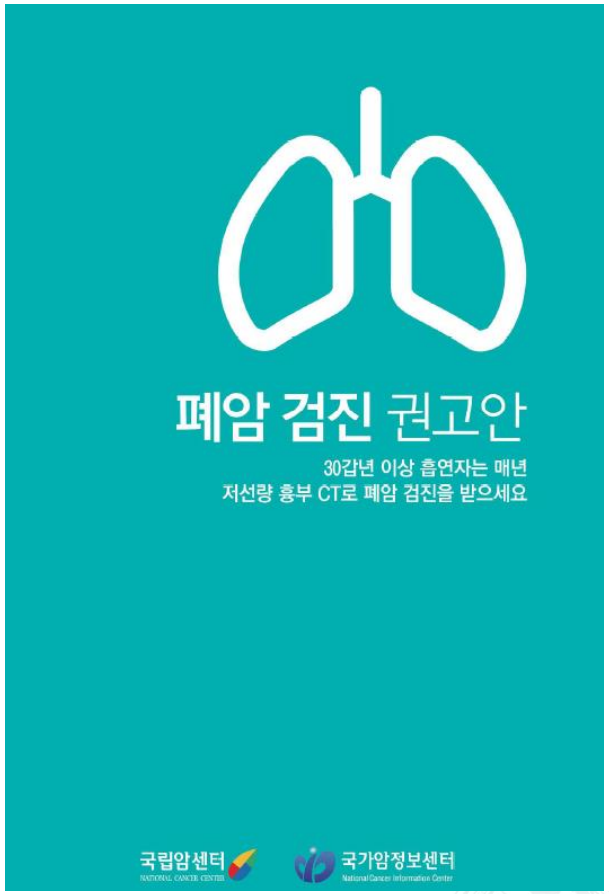
폐암도 국가검진...30년 흡연자 1만원만 내고 검사 받으세요

입력 : 2018.12.26 04:01:03

우선 내년 7월부터 국가 암검진 대상에 폐암이 추가된다. 이로써 국가 암검진 대상이 위암·간암·유방암·대장암·자궁경부암 등 기존 5종에서 6종으로 늘어난다. 만 54~74세 남녀 중 30갑년(매일 1갑씩 30년 또는 2갑씩 15년) 이상 흡연력을 지닌 사람은 2년마다 폐암 검진을 받을 수 있다. 폐암 검진 비용은 1인당 11만원 정도로 이 가운데 10%만 환자 본인이 내면 된다. 또 내년 7월부터 2년간 대장암 검진 시 대변 혈흔 여부를 알아보는 분변잠혈 검사 대신 대장 내시경 검사가 1차 검사로 사용되는 시범사업이 실시된다.

내년부터 바뀌는 보건의료 혜택

항목	시기	내용
폐암 국가 암검진	내년 7월부터	30갑년 이상 흡연력 지닌 사람 2년마다 폐암 검진, 환자 부담 비용은 10%



https://www.mk.co.kr/news/it/view/2018/12/802548/
폐암 검진 권고안 (국립암센터 & 국가암정보센터 발간)

Korea Lung RADS

고형 결절		
크기	발견시기/변화	범주
<6 mm	첫 검진	2
	변화 없음	2
	크기 증가	4A
	새로 발생 (<4 mm)	2
	새로 발생 (4-6 mm)	3
6-8 mm	첫 검진	3
	변화 없음	2
	크기 증가	4A
	새로 발생	4A
8-15 mm	첫 검진	4A
	변화 없음	2
	크기 증가	4B
	새로 발생	4B
≥15 mm	첫 검진	4B
	변화 없음	2
	크기 증가	4B
	새로 발생	4B

부분 고형 결절		
크기	발견시기/변화	범주
<6 mm	첫 검진	2
	변화 없음	2
	크기 증가 (고형<4 mm)	4A
	크기 증가 (고형 4-6 mm)	4B
	새로 발생	3
≥6 mm (고형<6 mm)	첫 검진	3
	변화 없음	2
	크기 증가 (고형<4 mm)	4A
	크기 증가 (고형 4-6 mm)	4B
	새로 발견 (고형<4 mm)	4A
	새로 발견 (고형 4-6 mm)	4B
≥6 mm (고형 6-8 mm)	첫 검진	4A
	변화 없음	2
	크기 증가	4B
	새로 발생	4B
≥8 mm (고형 ≥8 mm)	첫 검진	4B
	변화 없음	2
	크기 증가	4B
	새로 발견	4B

간유리 결절		
크기	발견시기/변화	범주
<20 mm	첫 검진	2
	변화 없음	2
	크기 증가	2
	새로 발견	2
≥20 mm	첫 검진	3
	변화 없음	2
	크기 증가	2
	새로 발생	3

기타 분류 기준	범주
기관지 내 결절	4A
범주 3,4+추가 영상 소견	4X
폐경화, 무기폐, 림프절확대	
기타 (침상변연 등 자유기술)	
결절 외 의미 있는 소견	S
과거 폐암 진단	C

범주	범주 설명	악성 가능성	
0	불완전	평가 불능	이전 흉부 CT 필요 또는 추가 흉부 CT 시행 필요
1	이상 없음	< 1%	**12개월 후** LDCT
2	양성 결절	< 1%	**12개월 후** LDCT [2b: 범주 3,4에 해당하나 양성 가능성이 높은 영상소견]
3	경계선 결절	1-2%	**6개월 후** LDCT
4A	폐암 의심	5-15%	**3개월 후** LDCT 흉부 CT (≥8mm 고형 부분이 있는 경우 PET/CT 시행 가능)
4B, X	폐암 의심	> 15%	**즉시** 흉부 CT, (≥8mm 고형 부분이 있는 경우) PET/CT 및 조직검사

Lung-RADS

: Lung Imaging Reporting And Data System

Korean J Med 2020;95:95-103

Early detection is a cure ??

IASLC

THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

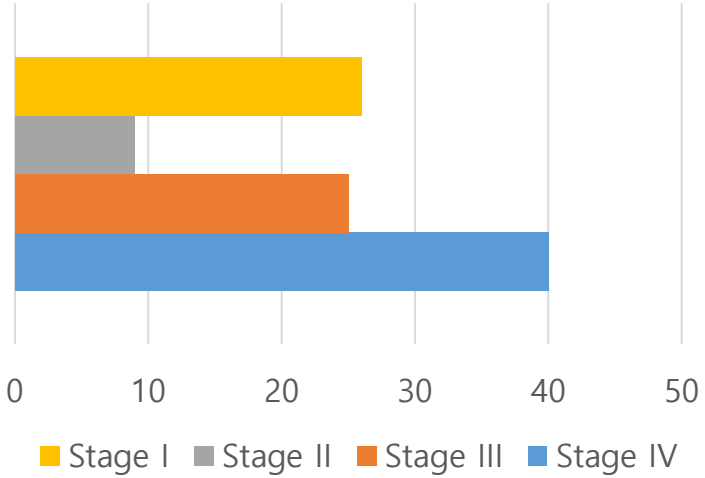
The IASLC is a global multidisciplinary organization dedicated to eradication of all forms of lung cancer. From provision of educational events around the world and virtually to research projects and publications that advance the science of lung cancer, the IASLC's members—consisting of medical, surgical, and radiation oncologists, as well as other thoracic oncology specialists such as nurses, basic scientists, pathologists, radiologists, pulmonologists, statisticians, patient research advocates, patients, and their caregivers—are raising the bar for care of patients with lung cancer.

Not all patients with early stage lung cancer have been completely cured !!

Epidemiology

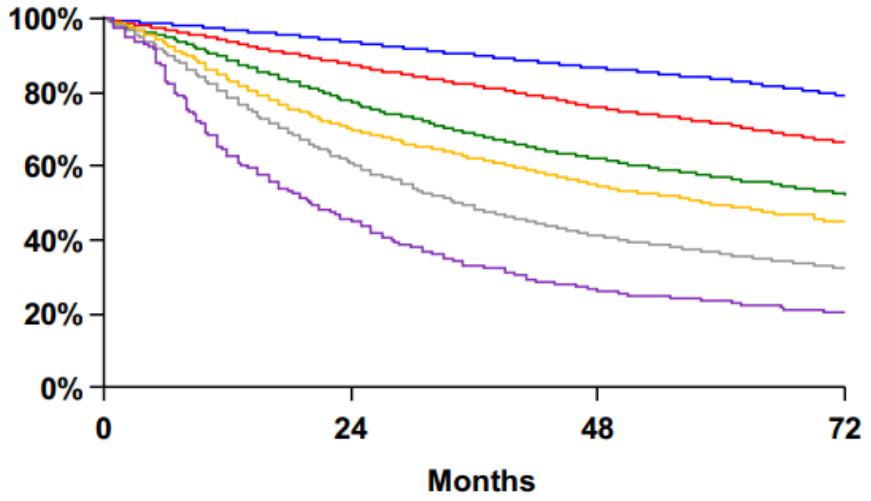
Pusan National University Yangsan Hospital

% at diagnosis



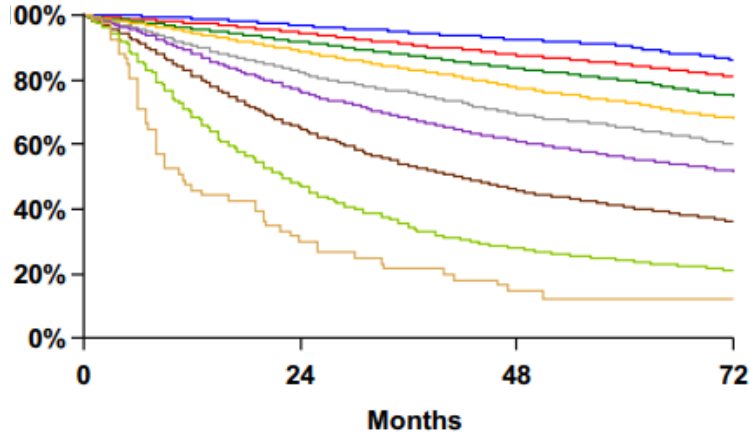
Approximately **30%** of patients with NSCLC present with resectable disease at diagnosis

OS by pathologic stage according to 7th Ed.



7th Ed.	Events / N	MST	24 Month	60 Month
IA	1837 / 11423	NR	94%	83%
IB	2168 / 7711	NR	87%	71%
IIA	1514 / 3702	NR	77%	57%
IIB	1325 / 2776	58.9	70%	49%
IIIA	3467 / 5818	35.0	61%	36%
IIIB	364 / 506	20.0	45%	23%

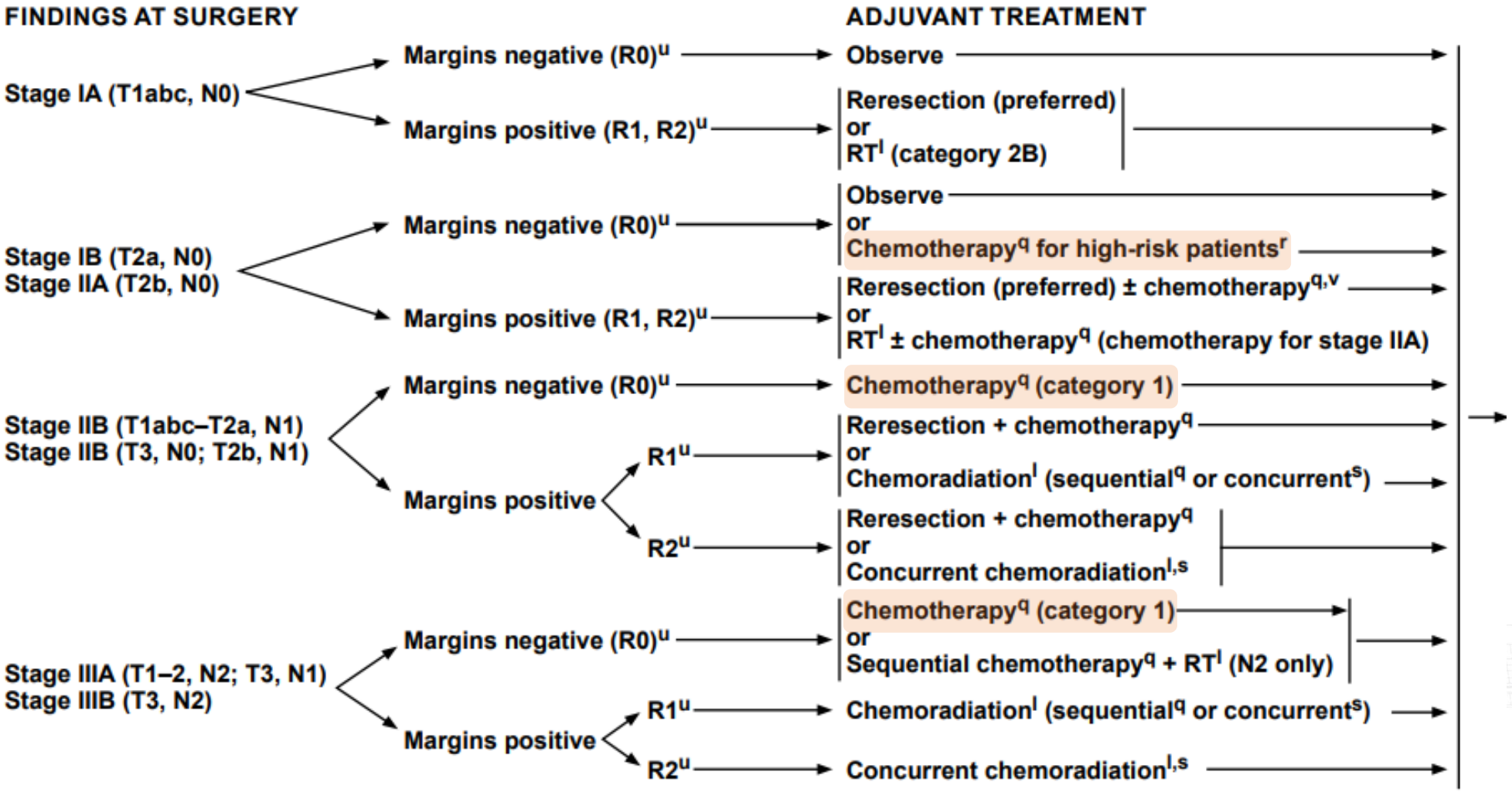
OS by pathologic stage according to 8th Ed.



8th Ed. Proposed	Events / N	MST	24 Month	60 Month
IA1	139 / 1389	NR	97%	90%
IA2	823 / 5633	NR	94%	85%
IA3	875 / 4401	NR	92%	80%
IB	1618 / 6095	NR	89%	73%
IIA	556 / 1638	NR	82%	65%
IIB	2175 / 5226	NR	76%	56%
IIIA	3219 / 5756	41.9	65%	41%
IIIB	1215 / 1729	22.0	47%	24%
IIIC	55 / 69	11.0	30%	12%

Ann Oncol 2010;21:vii196–vii198, *J Thorac Oncol* 2016;11:39-51

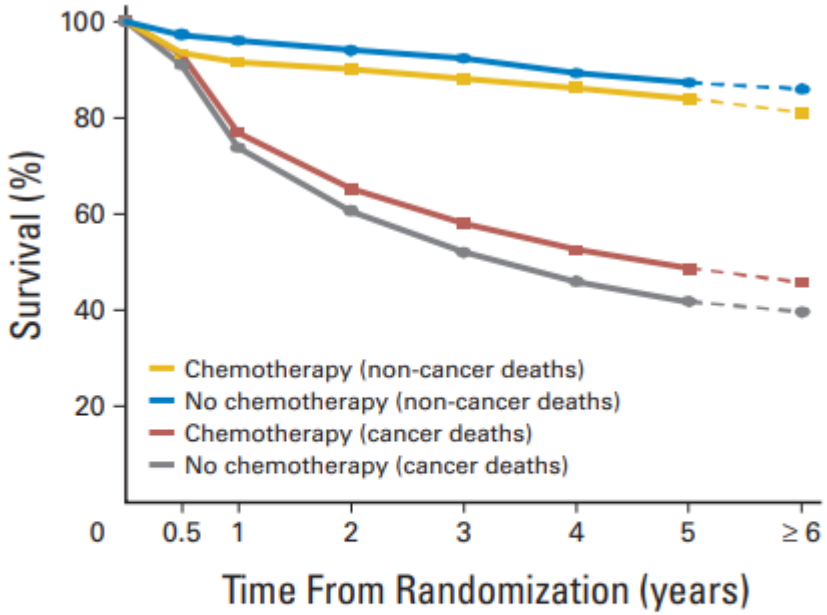
NCCN Guidelines ver 3.2020 (Adjuvant Tx)



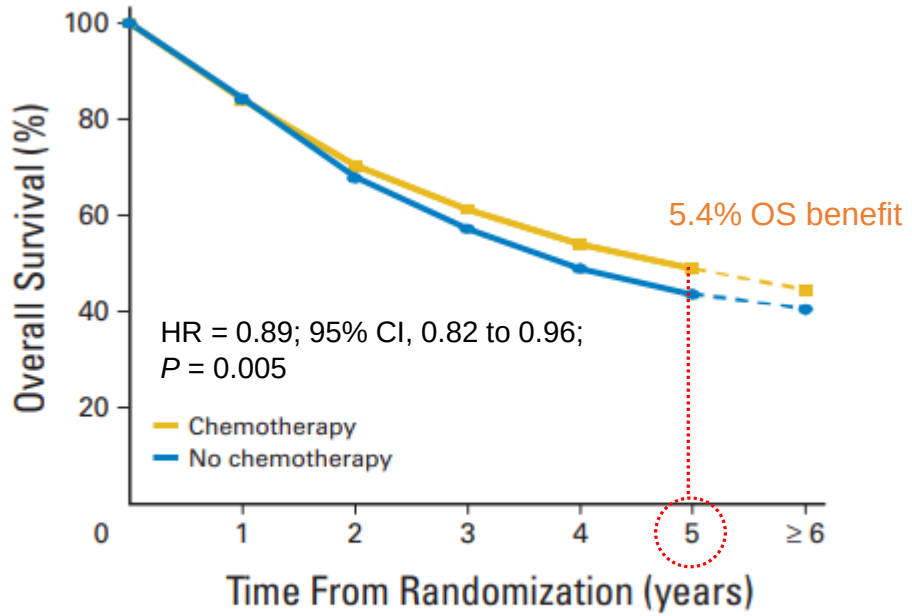
Lung Adjuvant Cisplatin Evaluation

Pooled analysis from the five largest trials (4,584 patients)

The absolute effect of chemotherapy at 5 years was a decrease of 6.9% for lung cancer death and an increase of 1.4% for non-lung cancer death



Non-cancer deaths / person years by period	Years 0-3	Years 4-5	Years ≥ 6
Control	88 / 4,353	42 / 1,399	9 / 611
Chemotherapy	141 / 4,635	38 / 1,611	24 / 708
Cancer deaths by period			
Control	878	197	40
Chemotherapy	716	165	52



Deaths / person years by period	Years 0-3	Years 4-5	Years ≥ 6
Control	966 / 5,155	239 / 1,668	49 / 720
Chemotherapy	857 / 5,181	203 / 1,817	76 / 790

J Clin Oncol 2008;26:3552-3559

ADAURA

ADAURA Phase III double-blind study design

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
- ≥18 years (Japan / Taiwan: ≥20)
- WHO performance status 0 / 1
- Confirmed primary non-squamous NSCLC Ex19del / L858R‡
- Brain imaging, if not completed pre-operatively
- Complete resection with negative margins§
- Max. interval between surgery and randomization:
  - 10 weeks without adjuvant chemotherapy
  - 26 weeks with adjuvant chemotherapy

Stratification by:
stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
race (Asian vs non-Asian)

Randomization 1:1 (N=682)

- Osimertinib 80 mg, once daily
- Placebo, once daily

Planned treatment duration: 3 years

Treatment continues until:
- Disease recurrence
- Treatment completed
- Discontinuation criterion met

Follow up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

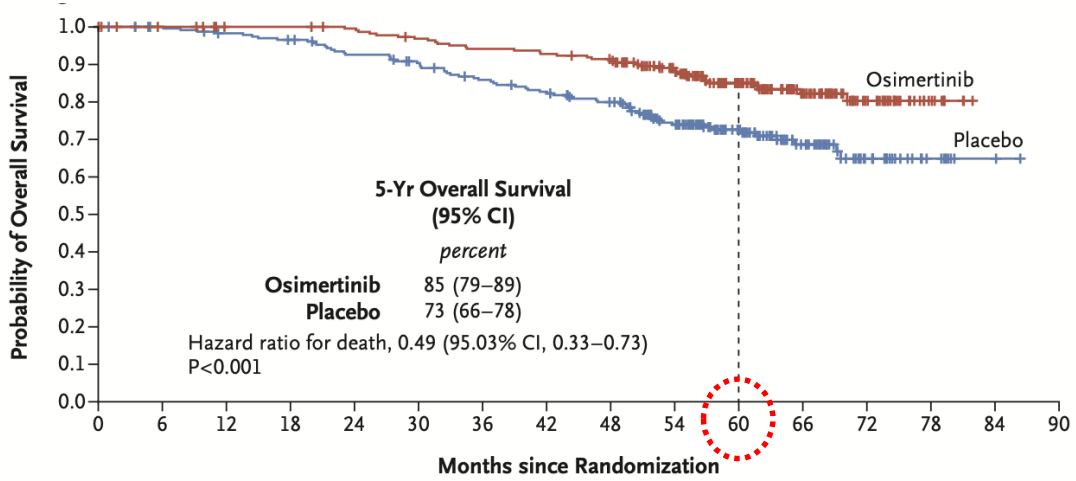
Endpoints

- **Primary**: DFS, by investigator assessment, in stage II/IIIA patients; designed for superiority under the assumed DFS HR of 0.70
- **Secondary**: DFS in the overall population¶, DFS at 2, 3, 4, and 5 years, OS, safety, health-related quality of life

*AJCC 7th edition; postsurgical, pathology-based. †Prior, post, or planned radiotherapy was not allowed. ‡Centrally confirmed in tissue. §Patients received a CT scan after resection and within 28 days prior to treatment. ¶Stage IB/II/IIIA

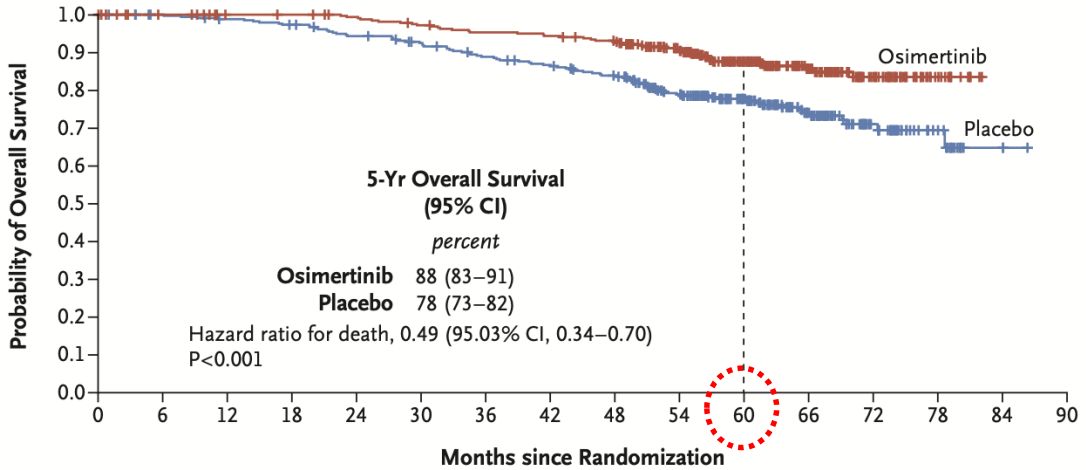
ADAURA: Overall Survival

Patients with Stage II to IIIA Disease



No. at Risk															
Osimertinib	233	229	224	224	221	214	208	205	200	170	115	69	33	9	0
Placebo	237	232	226	221	210	202	190	182	171	138	94	53	25	8	2	0

Patients with Stage IB to IIIA Disease



No. at Risk															
Osimertinib	339	332	325	324	319	311	304	301	294	252	176	108	50	15	0
Placebo	343	338	332	326	314	304	290	281	267	223	164	97	44	17	3	0

N Engl J Med 2023;389:137-47

MADRID 2023 ESMO congress

ALINA: efficacy and safety of adjuvant alectinib versus chemotherapy in patients with early-stage *ALK*+ NSCLC

Benjamin J. Solomon[1], Jin Seok Ahn[2], Rafal Dziadziuszko[3], Fabrice Barlesi[4], Makoto Nishio[5], Dae Ho Lee[6], Jong-Seok Lee[7], Wenzhao Zhong[8], Hidehito Horinouchi[9], Weimin Mao[10], Maximilian Hochmair[11], Filippo de Marinis[12], Maria Rita Migliorino[13], Igor Bondarenko[14], Tania Ochi Lohmann[15], Tingting Xu[16], Andres Cardona[17], Walter Bordogna[18], Thorsten Ruf[19], Yi-Long Wu[8]

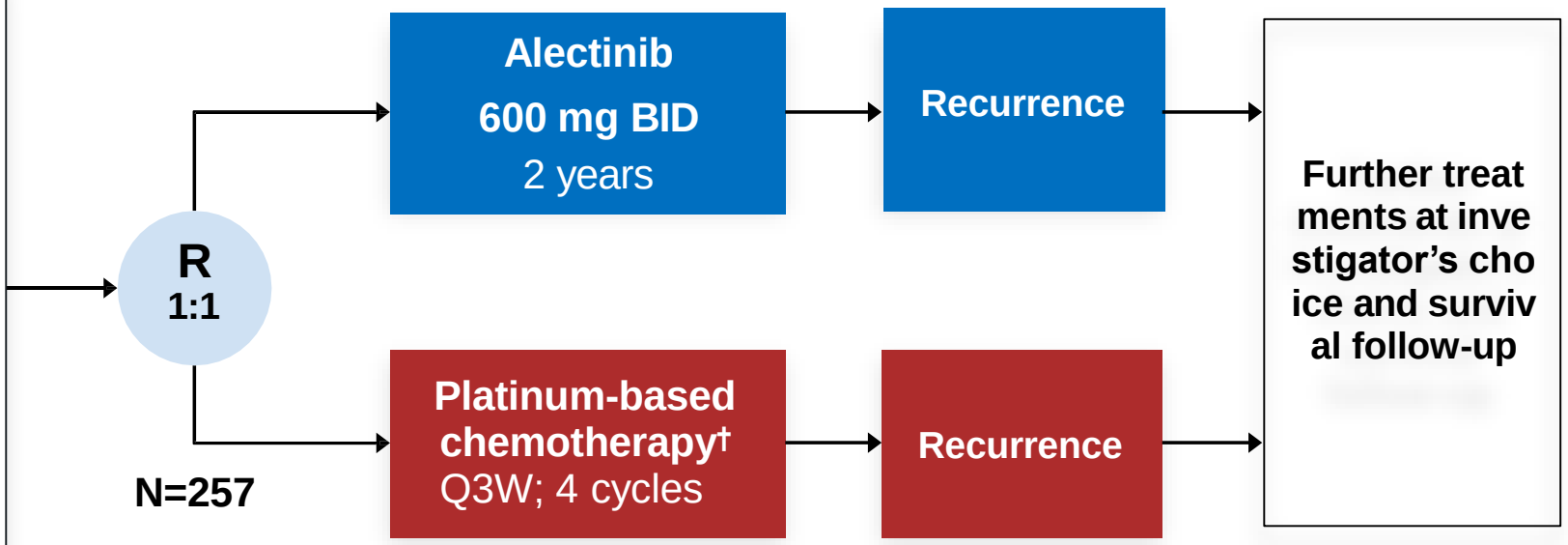
[1]Peter MacCallum Cancer Centre, Melbourne, Australia; [2]Samsung Medical Center, Seoul, Republic of Korea; [3]Medical University of Gdansk, Gdańsk, Poland; [4]International Center for Thoracic Cancers (CICT), France; Paris Saclay University, Faculty of Medicine, France; [5]Cancer Institute Hospital, Japanese Foundation for Cancer Research, Koto, Tokyo, Japan; [6]Asan Medical Center, Seoul, Republic of Korea; [7]Division of Hematology and Medical Oncology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea; [8]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong, China; [9]Department of Thoracic Oncology, National Cancer Center Hospital, Chuo City, Tokyo, Japan; [10]Institute of Basic Medicine and Cancer, Chinese Academy of Sciences, Zhejiang, China; [11]Department of Respiratory & Critical Care Medicine, Karl-Landsteiner-Institute of Lung Research & Pulmonary Oncology, Clinic Floridsdorf; [12]Thoracic Oncology Division, European Institute of Oncology, Via Giuseppe Ripamonti, Milan, Italy; [13]Pneumo-Oncology Unit, San Camillo Forlanini Hospital, Rome, Italy; [14]Dnipropetrovsk Medical Academy, Dnipro, Ukraine; [15]PD Oncology, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]Department of Clinical Science, Roche (China) Shanghai, China; [17]Data and Statistical Sciences, F. Hoffmann-La Roche Ltd, Switzerland; [18]Product Development Medical Affairs, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [19]PD Safety Risk Management, F. Hoffmann-La Roche Ltd, Basel, Switzerland

ALINA study design*

Resected Stage IB (≥4cm)–IIIA *ALK*+ NSCLC
per UICC/AJCC 7th edition

Other key eligibility criteria:
- ECOG PS 0–1
- Eligible to receive platinum-based chemotherapy
- Adequate end-organ function
- No prior systemic cancer therapy

Stratification factors:
- Stage: IB (≥ 4cm) vs II vs IIIA
- Race: Asian vs non-Asian



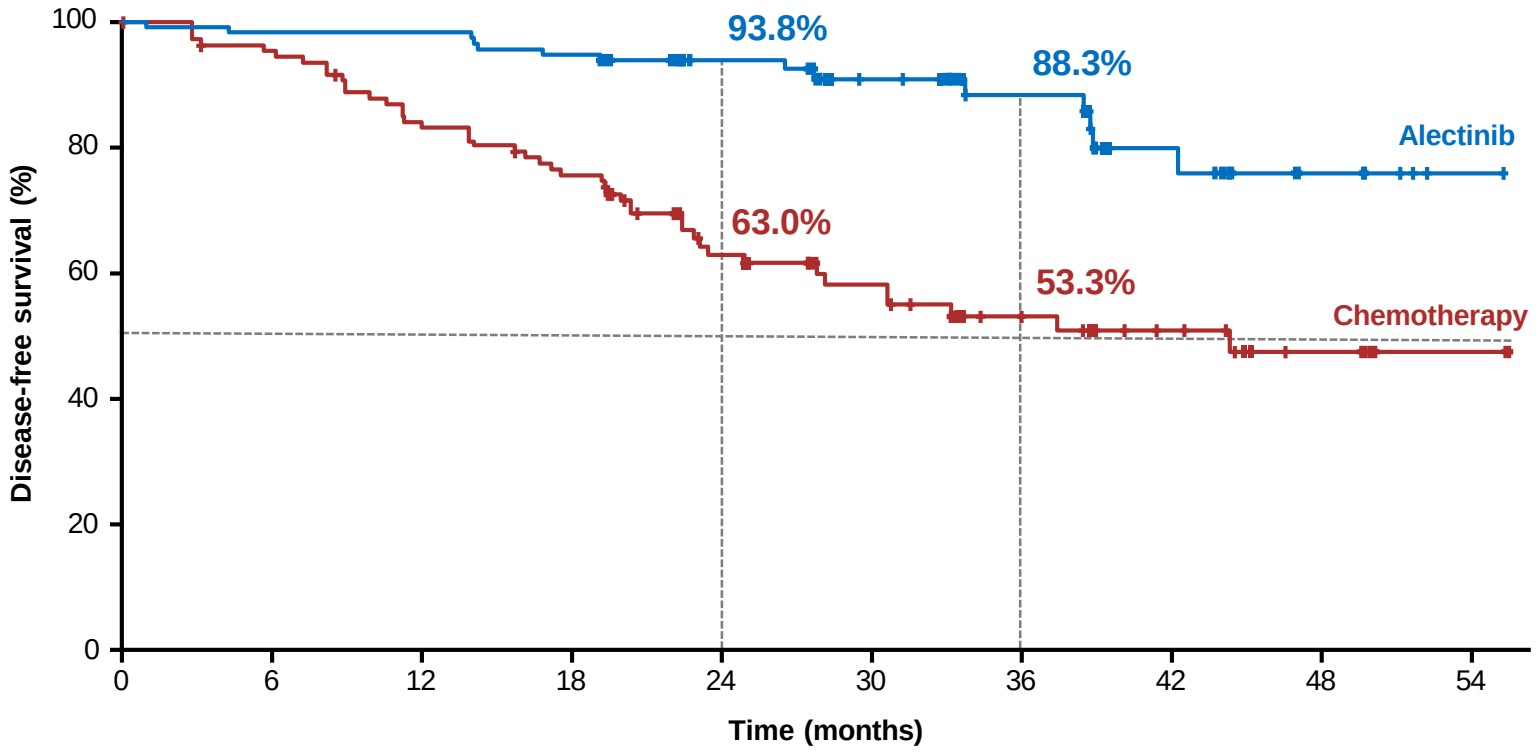
Primary endpoint
- DFS per investigator,‡ tested hierarchically:
  - Stage II–IIIA → ITT (Stage IB–IIIA)

Other endpoints
- CNS disease-free survival
- OS
- Safety

Disease assessments (including brain MRI)§ were conducted: at baseline, every 12 weeks for year 1–2, every 24 weeks for year 3–5, then annually

Data cut-off: 26 June 2023; CNS, central nervous system; DFS, disease-free survival; ITT, intention to treat
*Superiority trial; †Cisplatin + pemetrexed, cisplatin + vinorelbine or cisplatin + gemcitabine; cisplatin could be switched to carboplatin in case of intolerability; ‡DFS defined as the time from randomisation to the first documented recurrence of disease or new primary NSCLC as determined by the investigator, or death from any cause, whichever occurs first; §Assessment by CT scan where MRI not available; NCT03456076

Disease-free survival: stage II–IIIA*



No. at risk

Alectinib	116	111	111	107	67	49	35	21	10	3
Chemo	115	102	88	79	48	35	23	17	10	2

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

Median survival follow up: alectinib, 27.9 months; chemotherapy, 27.8 months

Data cut-off: 26 June 2023; Time from last patient in to data cut off was ~18 months

*Per UICC/AJCC 7th edition; †Stratified log rank; DFS defined as the time from randomisation to the first documented recurrence of disease or new primary NSCLC as determined by the investigator, or death from any cause, whichever occurs first

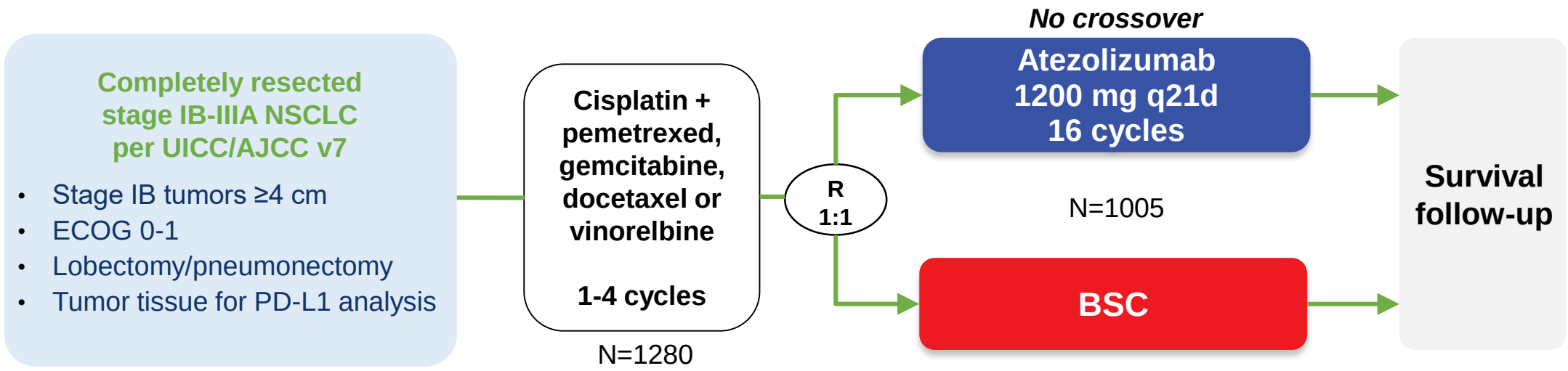
2021 ASCO ANNUAL MEETING

IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC)

Heather A. Wakelee,[1] Nasser Altorki,[2] Caicun Zhou,[3] Tibor Csőszi,[4] Ihor O. Vynnychenko,[5] Oleksandr Goloborodko,[6] Alexander Luft,[7] Andrey Akopov,[8] Alex Martinez-Marti,[9] Hirotsugu Kenmotsu,[10] Yuh-Min Chen,[11] Antonio Chella,[12] Shunichi Sugawara,[13] Fan Wu,[14] Jing Yi,[15] Yu Deng,[15] Mark McCleland,[15] Elizabeth Bennett,[15] Barbara J. Gitlitz,[15] Enriqueta Felip[16]

[1]Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA; [2]New York-Presbyterian Hospital, Weill Cornell Medicine, New York, NY, USA; [3]Tongji University Affiliated Shanghai Pulmonary Hospital, Shanghai, China; [4]Jasz-Nagykun-Szolnok Megyei Hetenyi Geza Korhaz-Rendelointezet, Szolnok, Hungary; [5]Sumy State University, Regional Municipal Institution Sumy Regional Clinical Oncology Dispensary, Sumy, Ukraine; [6]MI Zaporizhzhia Regional Clinical Oncological Dispensary Zaporizhzhia SMU Ch of Oncology, Zaporizhzhya, Ukraine; [7]Leningrad Regional Clinical Hospital, St. Petersburg, Russia; [8]Pavlov State Med Univ, St. Petersburg, Russia; [9]Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; [10]Shizuoka Cancer Center, Shizuoka, Japan; [11]Taipei Veterans General Hospital and National Yang Ming Chiao Tung University, Taipei, Taiwan; [12]Azienda Ospedaliero Universitaria Pisana, Pisa, Italy; [13]Sendai Kousei Hospital, Miyagi, Japan; [14]Roche (China) Holding Ltd, Shanghai, China; [15]Genentech, Inc., South San Francisco, CA, USA; [16]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

IMpower010: study design



Stratification factors

- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints

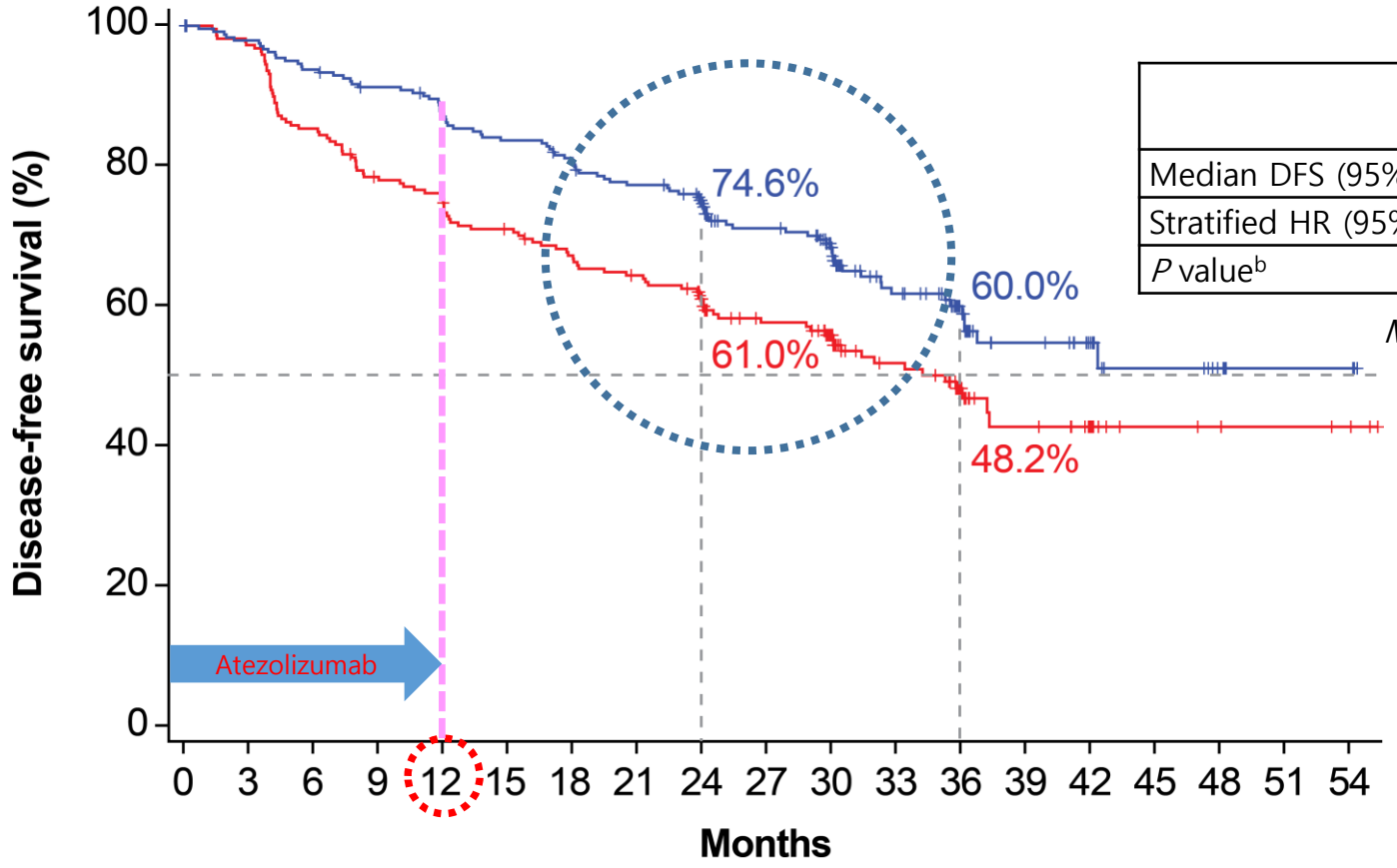
- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Key secondary endpoints

- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

Both arms included observation and regular scans for disease recurrence on the same schedule.
ECOG, Eastern Cooperative Oncology Group; IC, tumor-infiltrating immune cells; ITT, intent to treat; TC, tumor cells. [a] Per SP142 assay.

IMpower010: DFS in the PD-L1 TC ≥1%[a] stage II-IIIA population (primary endpoint)

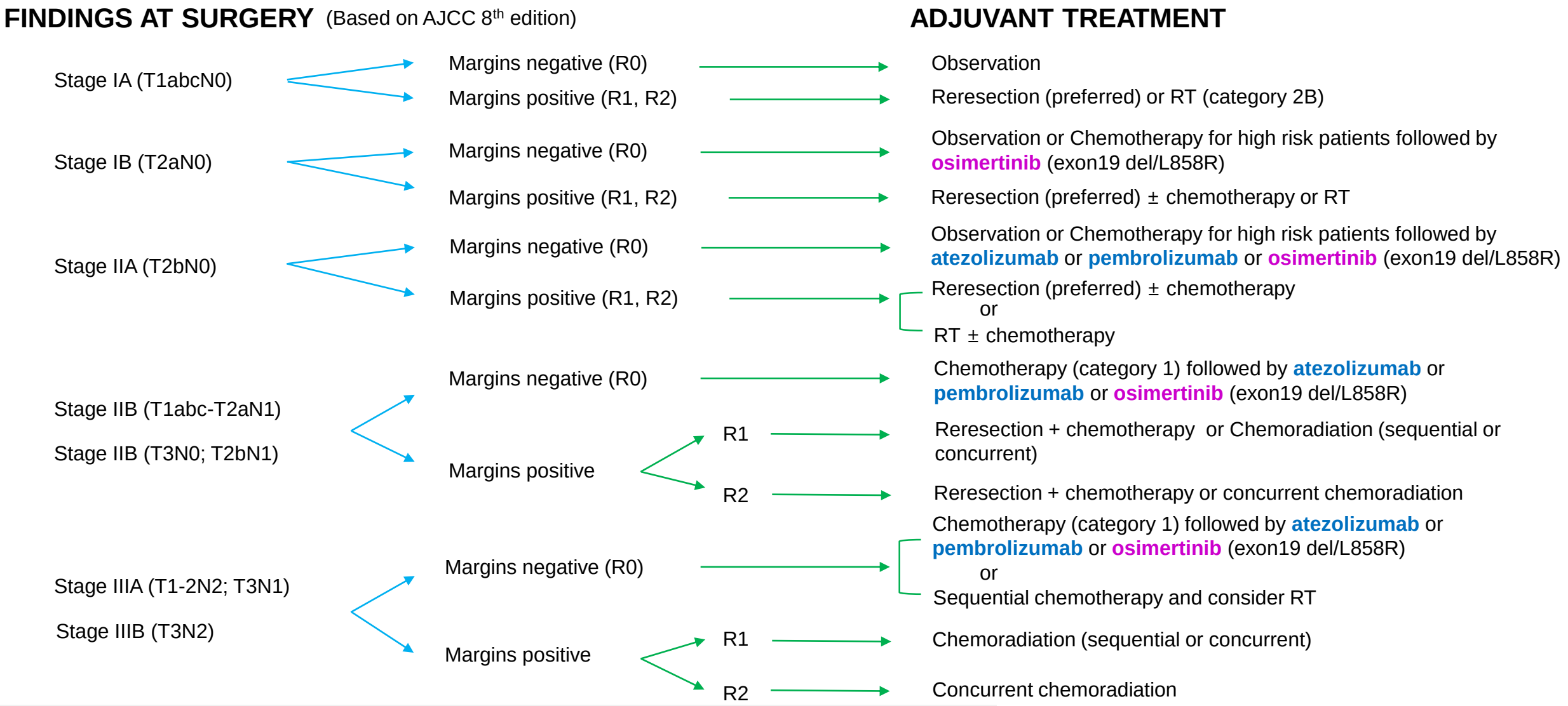


	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	

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

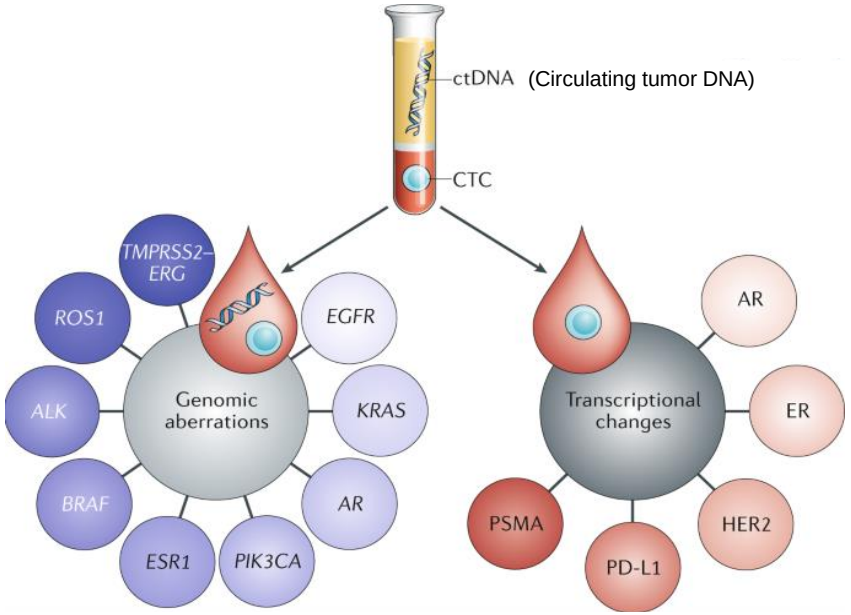
Clinical cutoff: January 21, 2021. CI, confidence interval; HR, hazard ratio; NE, not evaluable. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS.

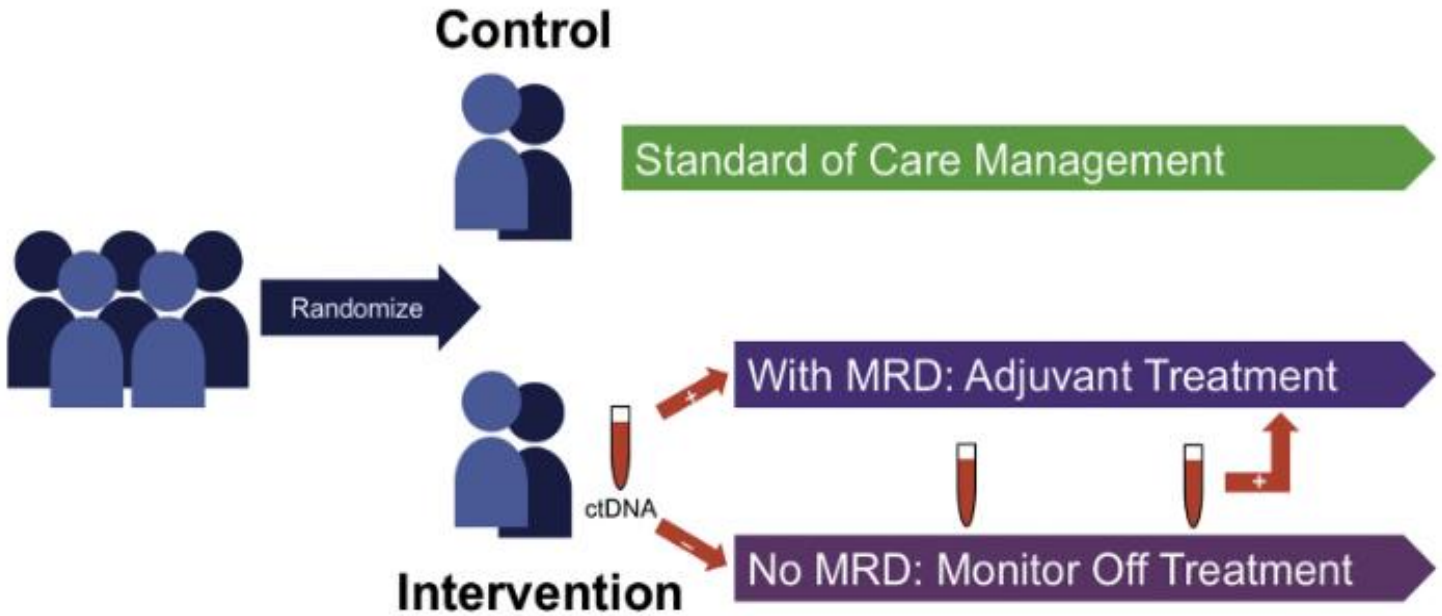
NCCN Guidelines ver 2.2023



Minimal Residual Disease (MRD)

Liquid biopsy (cell free DNA)





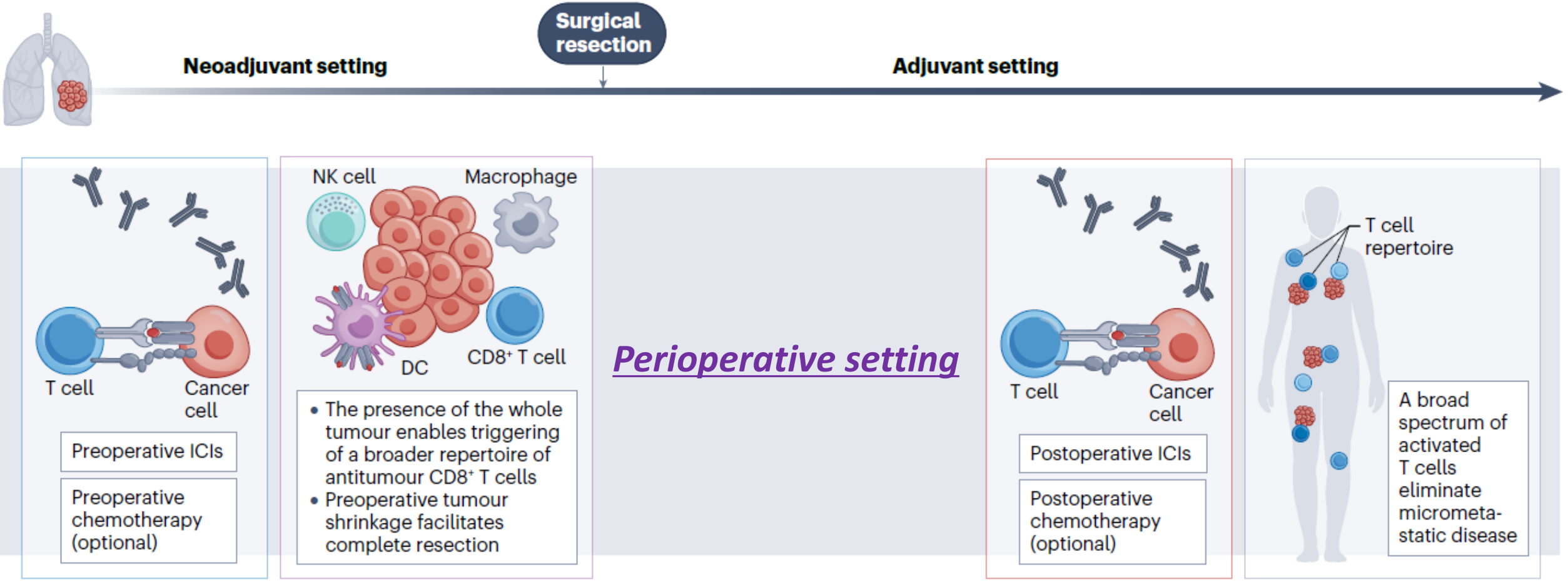
Proposed design for clinical trial evaluating tailored treatment based on the detection of MRD

Limitation of liquid biopsy

1. Sensitivity
2. False positive
3. False negative

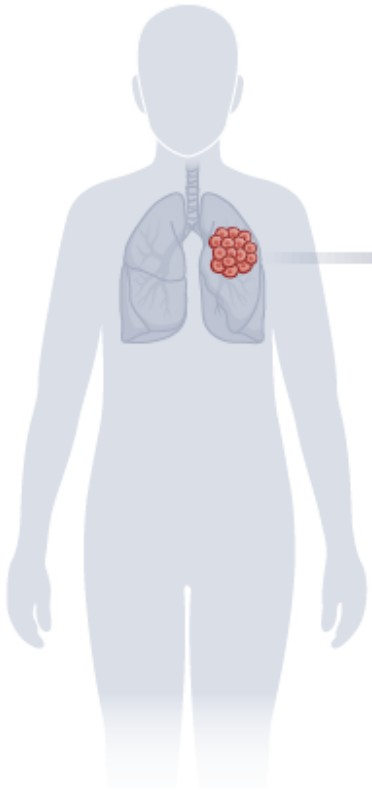
J Thorac Oncol 2019;14(1):16-24, Nat Rev Clin Oncol 2019;16:409-424

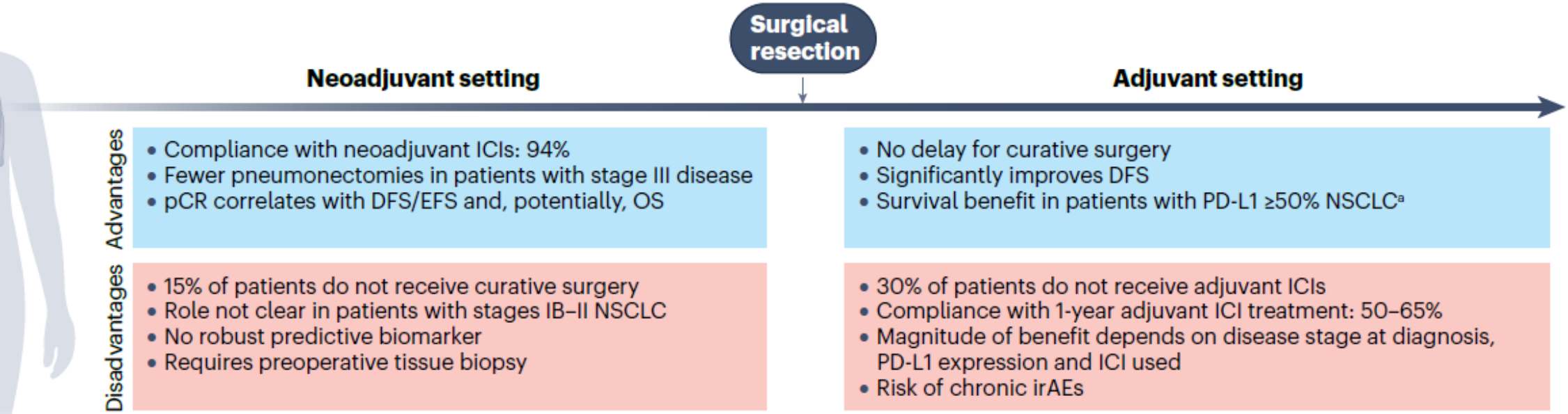
Biological rationale for ICIs in resectable NSCLC



Mountzios G, et al. *Nat Rev Clin Oncol*. 2023 Jul 24

Neoadjuvant vs Adjuvant treatment





[a]Data from the IMpower 010 trial

Mountzios G, et al. *Nat Rev Clin Oncol*. 2023 Jul 24

Perioperative Phase 3 Trials

Pusan National University Yangsan Hospital

	KEYNOTE-671[1–4] (Merck Sharp & Dohme Corp.)	IMpower030[5,6] (Genentech/Roche)	CheckMate 77T[7,8] (Bristol Myers Squibb)	AEGEAN[9–13] (AstraZeneca)	Neotorch[14–16] (Shanghai Junshi Biosciences Co.)
Treatment Arms	Pembrolizumab + cisplatin + gemcitabine/pemetrexed (neoadjuvant) + pembrolizumab (adjuvant) vs placebo + cisplatin + gemcitabine/pemetrexed (neoadjuvant) + placebo (adjuvant)	Atezolizumab + chemotherapy (neoadjuvant) + atezolizumab monotherapy (adjuvant) vs placebo + chemotherapy (neoadjuvant) + BSC (adjuvant)	Nivolumab + histology-based platinum doublet chemotherapy (neoadjuvant) + nivolumab (adjuvant) vs placebo + histology-based platinum doublet chemotherapy (neoadjuvant) + placebo (adjuvant)	Durvalumab + chemotherapy (neoadjuvant) + durvalumab monotherapy (adjuvant) vs placebo + chemotherapy (neoadjuvant) + placebo (adjuvant)	Toripalimab + platinum doublet chemotherapy vs placebo + platinum doublet chemotherapy
Study Type	Double-blind, randomized, parallel group	Double-blind, randomized, parallel group	Double-blind, randomized, parallel group	Double-blind, randomized, parallel group	Double-blind, randomized, parallel group
Population	**N≈786** Untreated, resectable, stage II–IIIB (N2), SQ or NSQ NSCLC	**N=453** Resectable, stage II–IIIB (T3N2 only), SQ or NSQ NSCLC	**N≈452** Untreated, resectable, stage IIA (>4 cm)–IIIB (T3N2), SQ or NSQ NSCLC	**N=802** Untreated, resectable, stage IIA–IIIB (N2), SQ or NSQ NSCLC	**N=404** Untreated, resectable, stage II–IIIB (N2), SQ or NSQ NSCLC
Stratification	Stage (II vs III), PD-L1 expression (<50% vs ≥50%), histology (SQ vs NSQ), region (East Asia vs non–East Asia)	Not specified	Not specified	Stage (II vs III), PD-L1 expression (<1% vs ≥1%)	Disease stage (II vs IIIA vs IIIB), pathological type (SQ vs NSQ), PD-L1 status (≥1% vs <1% or NE), planned surgical operation (pneumonectomy vs lobectomy)
Primary End Points	• EFS *(dual primary end point met per press release[4])* • OS	EFS by IRF	EFS	• pCR • EFS	• EFS in stage III and stage II-III (EFS end point met per press release[5]) • MPR in stage III and stage II-III
Secondary End Points/ Safety	• MPR • pCR • HRQoL • Perioperative complications • Safety	• pCR, MPR • ORR, DFS • OS • EFS by investigator • 2- and 3-year EFS, 2- and 3-year OS • HRQoL • PK, immunogenicity • Surgical delays and cancellations • (Post)operative complications • Safety	• OS • pCR • MPR • Safety	• MPR • DFS • OS • HRQoL • PK, immunogenicity • pCR, MPR, EFS, DS, OS in PD-L1 ≥1% • Safety	• pCR in stage III and stage II-III • EFS in stage III and stage II-III • DFS in stage III and stage II-III • OS at 2 and 3 years, and up to 5 years • Safety
	2023 ASCO ANNUAL MEETING	Data Not Yet Reported	MADRID 2023 ESMO congress	AACR ANNUAL MEETING 2023	2023 ASCO ANNUAL MEETING

1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03425643. Accessed April 14, 2023. 2. Fernando HC et al. Presented at ASCO 2018. Abstract TPS8583. 3. Tsuboi M et al. Presented at EMSO 2020. Abstract 1235TiP. 4. Merck [press release]. https://www.merck.com/news/merck-announces-phase-3-keynote-671-trial-met-primary-endpoint-of-event-free-survival-efs-in-patients-with-resectable-stage-ii-iiia-or-iiib-non-small-cell-lung-cancer/. Accessed March 8, 2023. 5. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03456063. Accessed April 14, 2023. 6. Peters S, et al. *Ann Oncol*. 2019;30(suppl_2):II26-II30. 7. ClinicalTrials.gov. https://www.clinicaltrials.gov/ct2/show/NCT04025879. Accessed April 14, 2023. 8. Cascone T et al. Presented at ASCO 2020. Abstract TPS9076. 9. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03800134. Accessed April 14, 2023. 10. Heymach J et al. Presented at WCLC 2019. Abstract P1.18-02. 11. Heymach JV et al. *Clin Lung Cancer*. 2021;S1525-7304(21)00265-5. 12. Heymach JV et al. *Clin Lung Cancer*. 2022;23(3):e247-e251. 13. Heymach JV et al. Presented at AACR 2023. Abstract CT005. 14. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04158440. Accessed April 14, 2023. 15. Junshi Biosciences [press release]. Junshi Biosciences Announces Toripalimab as Perioperative (globenewswire.com). Accessed February 8, 2023. 16. Lu S. Presented at ASCO Plenary Series Program April 2023. Abstract 425126.

NCCN Guidelins ver 4.2024

Neoadjuvant Systemic Therapy in Patients Who Are Candidates for Immune Checkpoint Inhibitors

- **Nivolumab 360 mg and platinum-doublet chemotherapy every 3 weeks for 3 cycles[1]**
  - **Platinum-doublet chemotherapy options include:**
    - **Carboplatin AUC 5 or AUC 6 day 1, paclitaxel 175 mg/m² or 200 mg/m² day 1 (any histology)**
    - **Cisplatin 75 mg/m² day 1, pemetrexed 500 mg/m² day 1 (nonsquamous histology)**
    - **Cisplatin 75 mg/m² day 1, gemcitabine 1000 mg/m² or 1250 mg/m² days 1 and 8 (squamous histology)**
    - **Cisplatin 75 mg/m² day 1, paclitaxel 175 mg/m² or 200 mg/m² day 1 (any histology)**
  - **Chemotherapy regimens for patients who are not candidates for cisplatin-based therapy**
    - **Carboplatin AUC 5 or AUC 6 day 1, pemetrexed 500 mg/m² day 1 (nonsquamous histology)**
    - **Carboplatin AUC 5 or AUC 6 day 1, gemcitabine 1000 mg/m² or 1250 mg/m² days 1 and 8 (squamous histology)**
- **Pembrolizumab 200 mg and cisplatin-based doublet therapy every 3 weeks for 4 cycles and then continued as single-agent pembrolizumab as adjuvant treatment after surgery (category 1); Systemic Therapy Following Previous Neoadjuvant or Adjuvant Systemic Therapy[2]**
  - **Cisplatin 75 mg/m² day 1, gemcitabine 1000 mg/m² days 1 and 8 (squamous histology)**
  - **Cisplatin 75 mg/m² day 1, pemetrexed 500 mg/m² day 1 (nonsquamous histology)**

[a] Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents; some oncogenic drivers (ie, *EGFR* exon 19 deletion or exon 21 L858R, *ALK* rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

DIAGNOSIS

양산부산대학교병원
Pusan National University Yangsan Hospital

Staging

- CT(chest/abdomen/neck)/PET-CT/MRI (brain/liver/spine)

Clinical Stage (C-stage)

Pathologic Stage (P-stage)

TNM staging

T: Extent of primary tumor

Tx: Primary tumor cannot be assessed
T0: No evidence of primary tumor
Tis: Carcinoma in situ
T1-4: Increasing size and/or local extent of primary tumor

N: Absence of presence and extent of regional lymph node metastasis

Nx: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastasis
N1-3: Increasing involvement of regional lymph nodes

M: Absence of presence of distant metastasis

M0: No distant metastasis
M1: Distant metastasis

Staging system

IASLC
INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

- **2009** – 7th TNM classification
- **2016** – 8th TNM classification

uicc
global cancer control
A MEMBERSHIP ORGANISATION
FIGHTING CANCER TOGETHER

AJCC
American Joint Committee on Cancer
Validating science. Improving patient care.

Editions of the AJCC *Cancer Staging Manual*

The publication dates and effective dates for past editions of the AJCC Cancer

Edition	Publication Year	Effective Year
1	1977	1978
2	1983	1984
3	1988	1989
4	1992	1993
5	1997	1998
6	2002	2003
7	2009	2010
8	2016	2018

Manual for Staging of Cancer 1977

AMERICAN JOINT COMMITTEE
FOR
CANCER STAGING AND END-RESULTS REPORTING

DEFINITIONS

TNM CLASSIFICATION

Primary Tumor (T)

- TX Tumor proven by the presence of malignant cells in bronchopulmonary secretions but not visualized roentgenographically or bronchoscopically, or any tumor that cannot be assessed
- T0 No evidence of primary tumor
- TIS Carcinoma in situ
- T1 Tumor 3.0 cm or less in greatest diameter, surrounded by lung or visceral pleura, and without evidence of invasion proximal to a lobar bronchus at bronchoscopy
- T2 Tumor more than 3.0 cm in greatest diameter, or a tumor of any size that either invades the visceral pleura or has associated atelectasis or obstructive pneumonitis extending to the hilar region. At bronchoscopy, the proximal extent of demonstrable tumor must be within a lobar bronchus or at least 2.0 cm distal to the carina. Any associated atelectasis or obstructive pneumonitis must involve less than an entire lung and there must be no pleural effusion
- T3 Tumor of any size with direct extension into an adjacent structure such as the parietal pleura or the chest wall, the diaphragm, or the mediastinum and its contents; or a tumor demonstrable bronchoscopically to involve a main bronchus less than 2.0 cm distal to the carina; or any tumor associated with atelectasis or obstructive pneumonitis of an entire lung or pleural effusion

Nodal Involvement (N)

- N0 No demonstrable metastasis to regional lymph nodes
- N1 Metastasis to lymph nodes in the peribronchial or the ipsilateral hilar region, or both, including direct extension
- N2 Metastasis to lymph nodes in the mediastinum

Distant Metastasis (M)

- MX Not assessed
- M0 No (known) distant metastasis
- M1 Distant metastasis present

STAGE GROUPING

Occult stage	TX N0 M0	Occult carcinoma with bronchopulmonary secretions containing malignant cells but without other evidence of the primary tumor or evidence of metastasis to the regional lymph nodes or distant metastasis
Stage I	TIS N0 M0	Carcinoma in situ
	T1 N0 M0 T1 N1 M0 T2 N0 M0	Tumor that can be classified T1 without any metastasis or with metastasis to the lymph nodes in the peribronchial and/or ipsilateral hilar region only or a tumor that can be classified T2 without any metastasis to nodes or distant metastasis *NOTE: TX N1 M0 and T0 N1 M0 are also theoretically possible, but such a clinical diagnosis would be difficult if not impossible to make. If such a diagnosis is made, it should be included under stage I*
Stage II	T2 N1 M0	Tumor classified as T2 with metastasis to the lymph nodes in the peribronchial and/or ipsilateral hilar region only
Stage III	T3 with any N or M N2 with any T or M M1 with any T or N	Any tumor more extensive than T2, or any tumor with metastasis to the lymph nodes in the mediastinum, or any tumor with distant metastasis

TNM 8th edition

T (primary tumor)	
T0	No primary tumor
Tis	Carcinoma in situ (squamous or adenocarcinoma)
T1	Tumor ≤3 cm
T1mi	Minimally invasive adenocarcinoma
T1a	Superficial spreading tumor in central airways*
T1a	Tumor ≤1 cm
T1b	Tumor >1 but ≤2 cm
T1c	Tumor >2 but ≤3 cm
T2	Tumor >3 but ≤5 cm or tumor involving: visceral pleura,† main bronchus (not carina), atelectasis to hilum†
T2a	Tumor >3 but ≤4 cm
T2b	Tumor >4 but ≤5 cm
T3	Tumor >5 but ≤7 cm or invading chest wall, pericardium, phrenic nerve; or separate tumor nodule(s) in the same lobe
T4	Tumor >7 cm or tumor invading: mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, esophagus, spine; or tumor nodule(s) in a different ipsilateral lobe
N (regional lymph nodes)	
N0	No regional node metastasis
N1	Metastasis in ipsilateral pulmonary or hilar nodes
N2	Metastasis in ipsilateral mediastinal or subcarinal nodes
N3	Metastasis in contralateral mediastinal, hilar, or supraclavicular nodes
M (distant metastasis)	
M0	No distant metastasis
M1a	Malignant pleural or pericardial effusion‡ or pleural or pericardial nodules or separate tumor nodule(s) in a contralateral lobe
M1b	Single extrathoracic metastasis
M1c	Multiple extrathoracic metastases (1 or >1 organ)

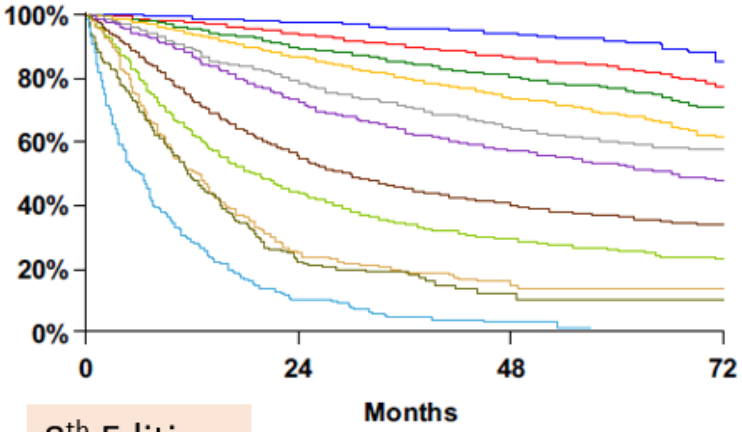
*Superficial spreading tumor of any size but confined to the tracheal or bronchial wall. †Atelectasis or obstructive pneumonitis extending to hilum; such tumors are classified as T2a if >3 and ≤4 cm, T2b if >4 and ≤5 cm. ‡Pleural effusions are excluded that are cytologically negative, nonbloody, transudative, and clinically judged not to be due to cancer.

Definitions for TNM descriptors

J Thorac Cardiovasc Surg 2018;155:356-9

TNM 8th edition

T/M	Subcategory	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIB	IIIC
T4	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB



8th Edition

Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%

J Thorac Oncol 2015;11(1): 39-51, *J Thorac Cardiovasc Surg* 2018;155:356-9

Diagnosis Flow

Pusan National University Yangsan Hospital

15.3 ds

Hospital Visit

Present Illness

★

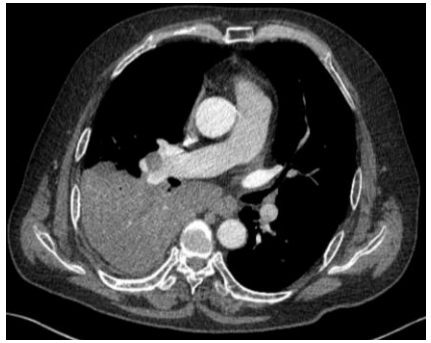
incidentally detected lung mass 로 내원함

통증

★

☐ 없음 ☐ 있음(점수) ☐ Wong-ba

CT chest



Pathologic confirmation

Modality decision

1. Bronchoscopy
2. Radial GS-EBUS
3. ENB
4. EBUS-TBNA
5. EUS
6. CT-guided PCNBx
7. Bone biopsy
8. Brain surgery
9. Thoracoscopic pleural Bx
10. VATS-lung Bx

Pathology Report

< 병리검사 결과 >
GROSS:
The number of the specimens: 2
1. Labeled as: "RLL1"
    Specimen: Fragments of yellow white soft tissue (0.3cc)
    Block 1 in toto
2. Labeled as: "RLL2"
    Specimen: Fragments of yellow white soft tissue (0.3cc)
    Block 2 in toto

DIAGNOSIS:
Lung, lower lobe, [#1, #2], right, bronchoscopic biopsy:
 Squamous cell carcinoma.

#. Immunohistochemistry
 CK5/6, p40 : positive
 TTF-1 : negative

 ALK (D5F3, CDx) : Negative

 PD-L1 SP263 (Ventana) Tumor Expression: 0 %

Staging w/u

1. PET/CT
2. MR brain
3. Bone scan (option)

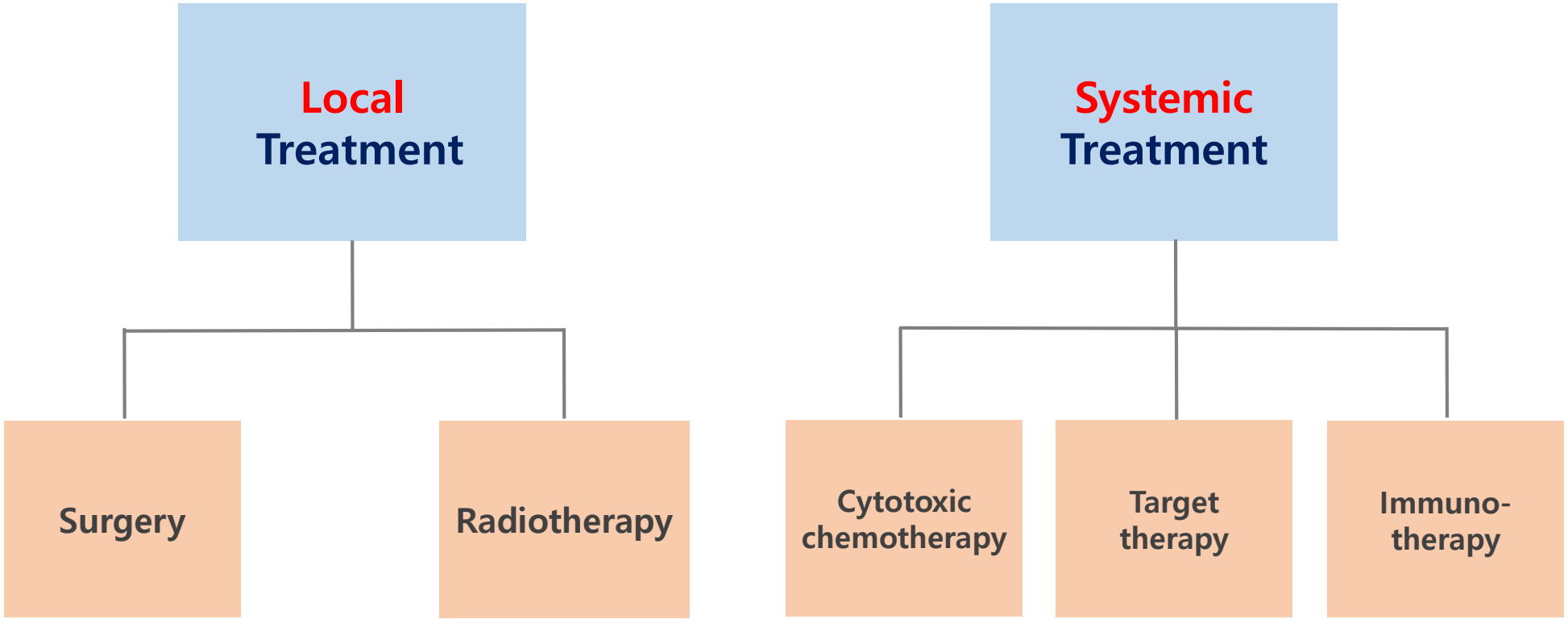
Treatment

양산부산대학교병원
Pusan National University Yangsan Hospital

Outline of Lung Cancer Treatment

T/M	Subcategory	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIB	IIIC
T4	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB

Outline of Lung Cancer Treatment



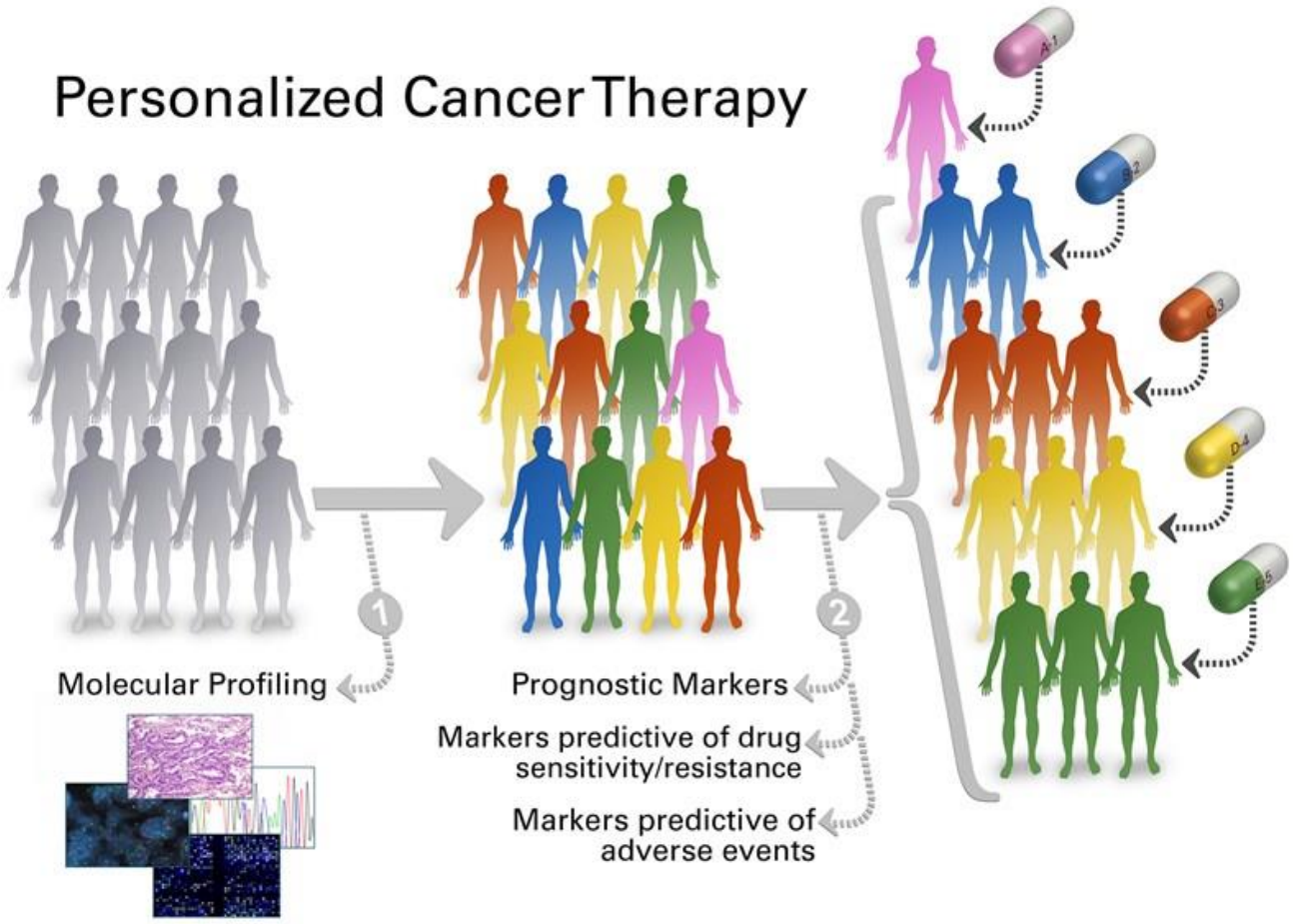
Targeted Therapy

PRECISION MEDICINE INITIATIVE

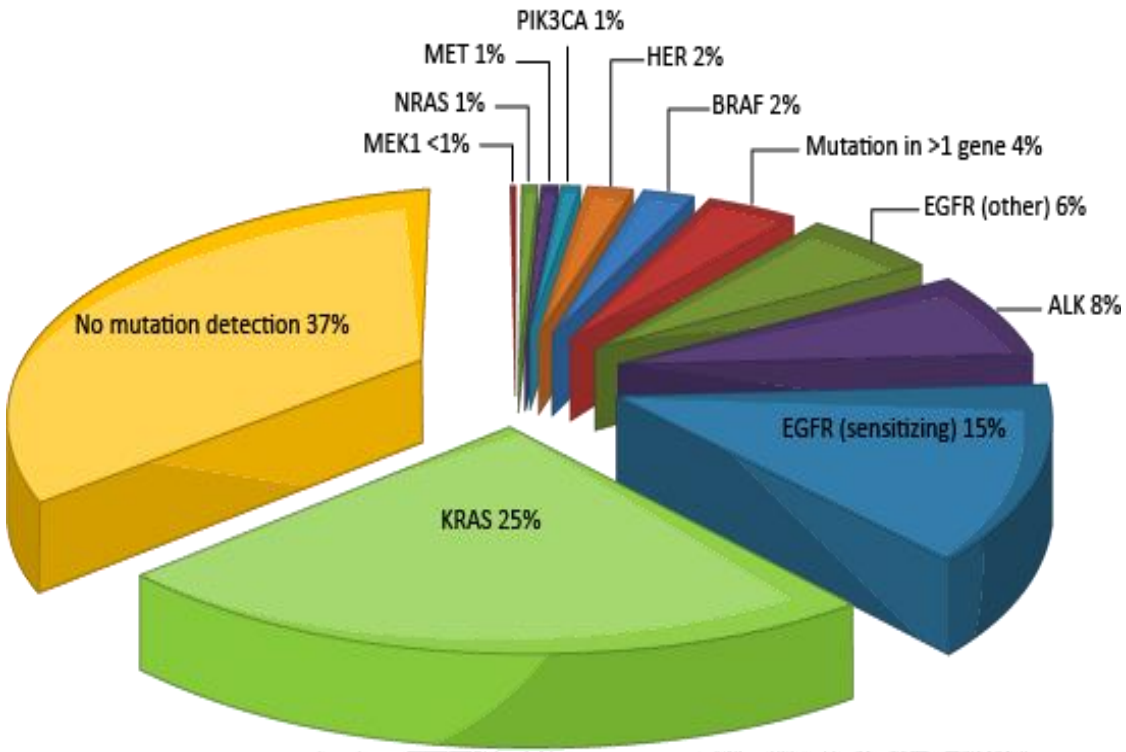
"Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals. You can match a blood transfusion to a blood type — that was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature?"

– President Obama, January 30, 2015

Targeted Therapy



Driver mutations (actionable mutations)



J Clin Oncol. 2013;31(suppl; abstr 8019)

Targeted Therapy

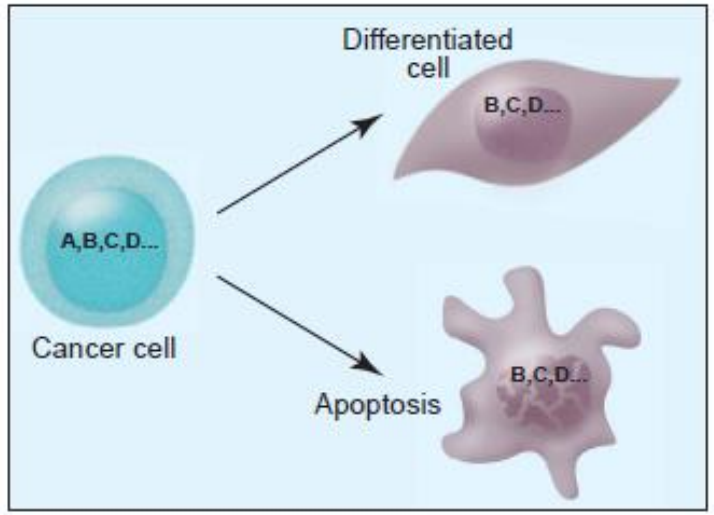
Science
AAAS

Addiction to Oncogenes--the Achilles Heal of Cancer
I. Bernard Weinstein
Science **297**, 63 (2002);
DOI: 10.1126/science.1073096

PERSPECTIVES: CANCER

Addiction to Oncogenes—the Achilles Heal of Cancer

I. Bernard Weinstein



It is likely that administering a single drug will lead to the emergence of **drug-resistant mutations** or of cell variants whose circuitry is no longer addicted to a specific oncogene or sensitive to a specific tumor suppressor

Actionable Target in HIRA (reimbursement)

- ***EGFR*** gene mutation
- ***ALK*** rearrangement
- ***ROS1*** rearrangement
- ***BRAF*** gene mutation (V600E)
- ***NTRK*** rearrangement

Actionable Rare mutations

- *EGFR* exon 20 insertions
- *KRAS* G12C mutations
- *RET* fusions
- *MET* 14 skipping mutations
- *NTRK* fusions

Driver Mutations

		Detection Methods	TAT	Treatment
♣ *EGFR* mutations (activate) ♣ *ALK* fusions ♣ *ROS1* fusions ♣ *BRAF* mutation (*V600E*)	Reflex	PCR/IHC (NGS)	Short (<7ds)	Reimbursed (1st line)
♣ *KRAS* mutation (*G12C*) ♣ *EGFR* exon 20 insertion ♣ *RET* fusions ♣ *MET* skipping mutations ♣ *HER2* mutations ♣ *NTRK* fusions*	Optional	NGS (PCR)	Long (>3wks)	Not-reimbursed (later line)

* reimbursed

What do guidelines recommend on biomarker testing in advanced NSCLC ?

Pusan National University Yangsan Hospital

Predictive biomarkers	ESMO guidelines (updated 2023)[1]	NCCN guidelines (updated 2023)[2]	CAP/IASLC/AMP guidelines (updated 2018)[3,4]	ASCO guidelines (updated 2018)[5]	Pan-Asian guidelines (updated 2019)[6]
EGFR	●	●	●	●	●
ALK	●	●	●	●	●
ROS1	●	●	●	●	●
BRAF	●	●	●	●	●
PD-L1	●	●	●	●	●
NTRK	●	●	●	●	●
KRAS	●	●	●	●	●
MET	●	●	●	●	●
RET	●	●	●	●	●
HER2	●	●	●	●	●

● Testing recommended

● Expanded panel testing recommended

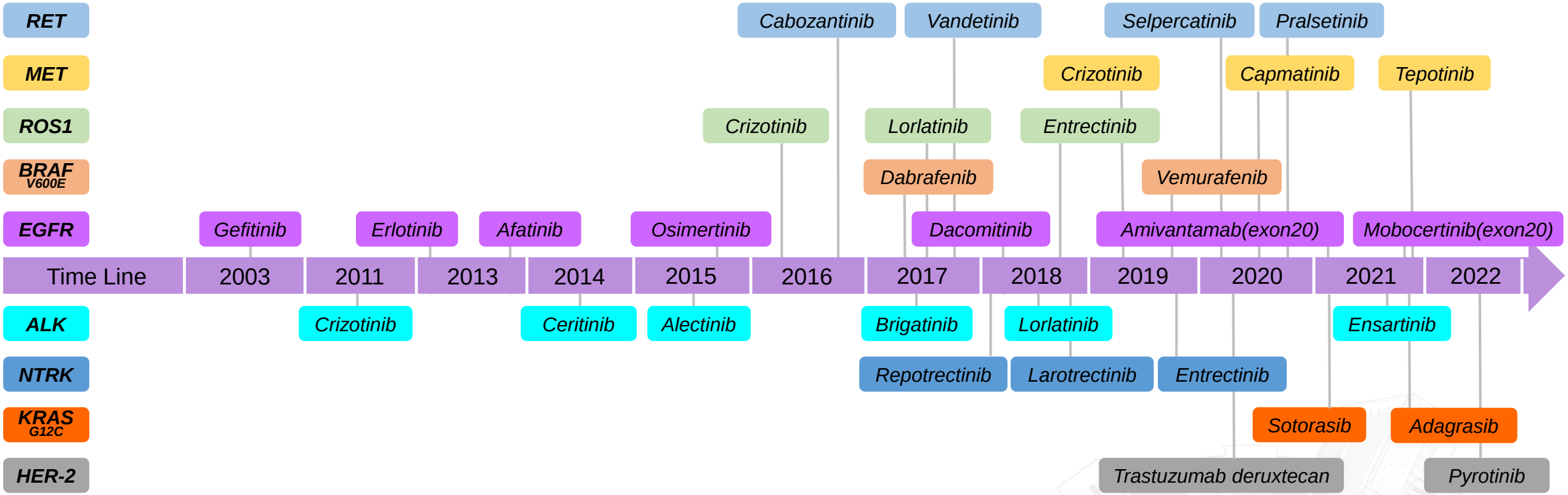
● Single gene or expanded panel testing recommended

● No guideline recommendations to date

AMP, Association for Molecular Pathology; ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; ESMO, European Society for Medical Oncology; IASLC, International Association for the Study of Lung Cancer; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; PD-L1, programmed cell death-ligand 1.

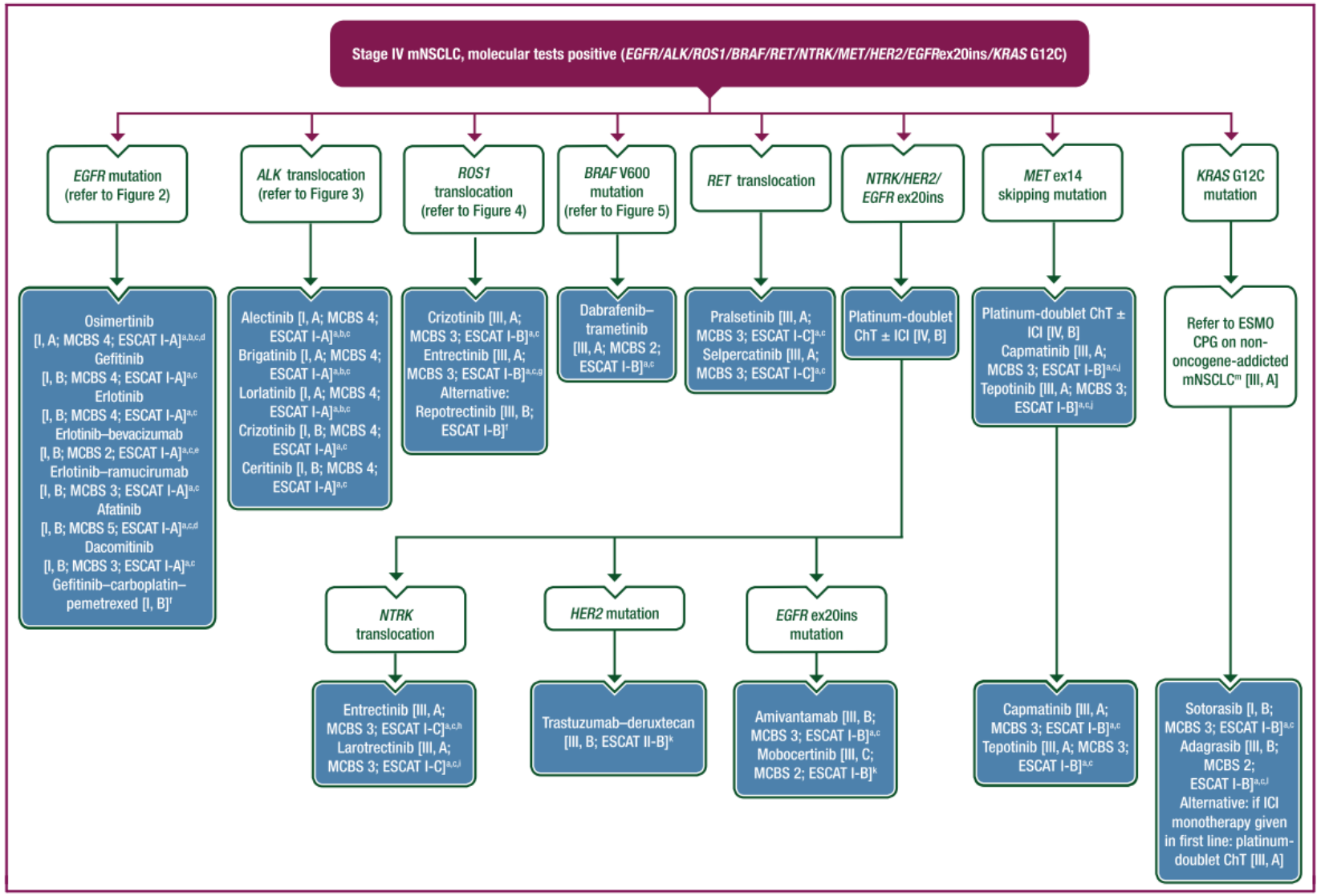
Figure adapted from et al. Lung Cancer 1. Hendriks LE, et al. Ann Oncol. 2023; 2. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Version 1.2023; 3. Lindeman NI, et al. J Thorac Oncol 2018;13:323–358; 4. Leighl NB, et al. J Clin Oncol 2014;32:3673–3679; 5. Kalemkerian GP, et al. J Clin Oncol 2018;36:911–919; 6. Wu YL, et al. Ann Oncol 2019;30:171–210.

Timeline of FDA approved target therapies



Guo H, et al. Cells. 2022;11

Targeted Therapy Algorithm in advanced NSCLC

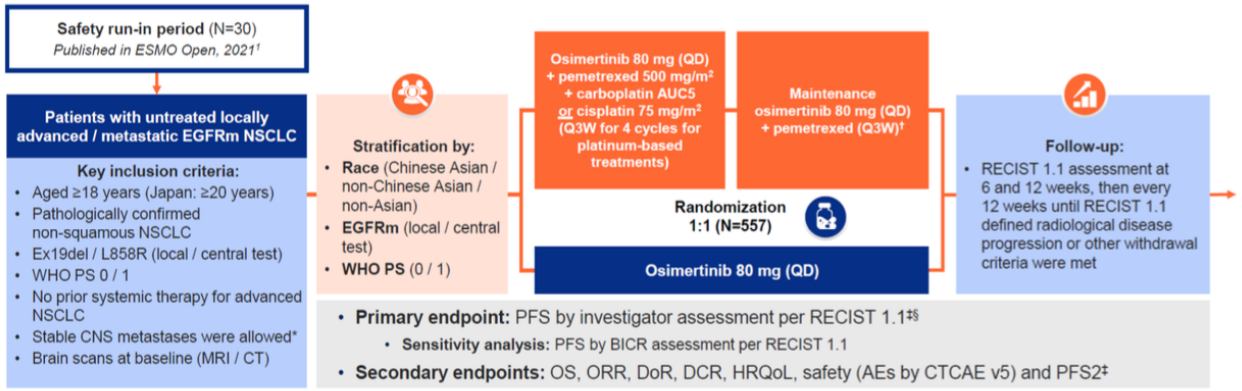


Hendriks LE, et al. Ann Oncol 2023; doi: https://doi.org/10.1016/j.annonc.2022.12.009.

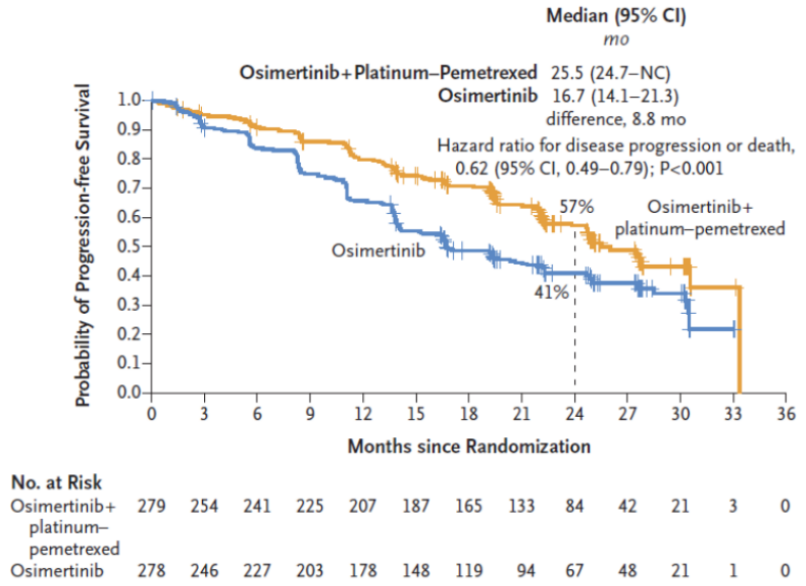
[Reference] Osimertinib with or without Chemo in EGFRm NSCLC

- Osimertinib plus chemotherapy significantly improved PFS compared to osimertinib monotherapy (HR 0.62; 95% CI 0.49, 0.79; p<0.0001; **51% maturity**). **Investigator-assessed mPFS was improved by approximately 8.8 months with osimertinib plus platinum-pemetrexed compared to osimertinib monotherapy (25.5 months vs. 16.7 months)**.
- Median total duration of osimertinib exposure was 22.3 months in the osimertinib plus platinum-pemetrexed arm and 19.3 months in the osimertinib monotherapy arm. **In the combination arm patients received a median of 12 cycles of pemetrexed (range 1-48) and 211 patients (76%) completed 4 cycles of platinum-based chemotherapy**.
- **The incidence of grade 3 or higher adverse events from any cause was higher with the combination than with monotherapy** - a finding driven by known chemotherapy-related adverse events.
- In conclusion, **Osimertinib plus chemotherapy demonstrated a statistically significant and clinically meaningful PFS benefit over osimertinib monotherapy, with a manageable safety and tolerability profile.**

[Study Design]

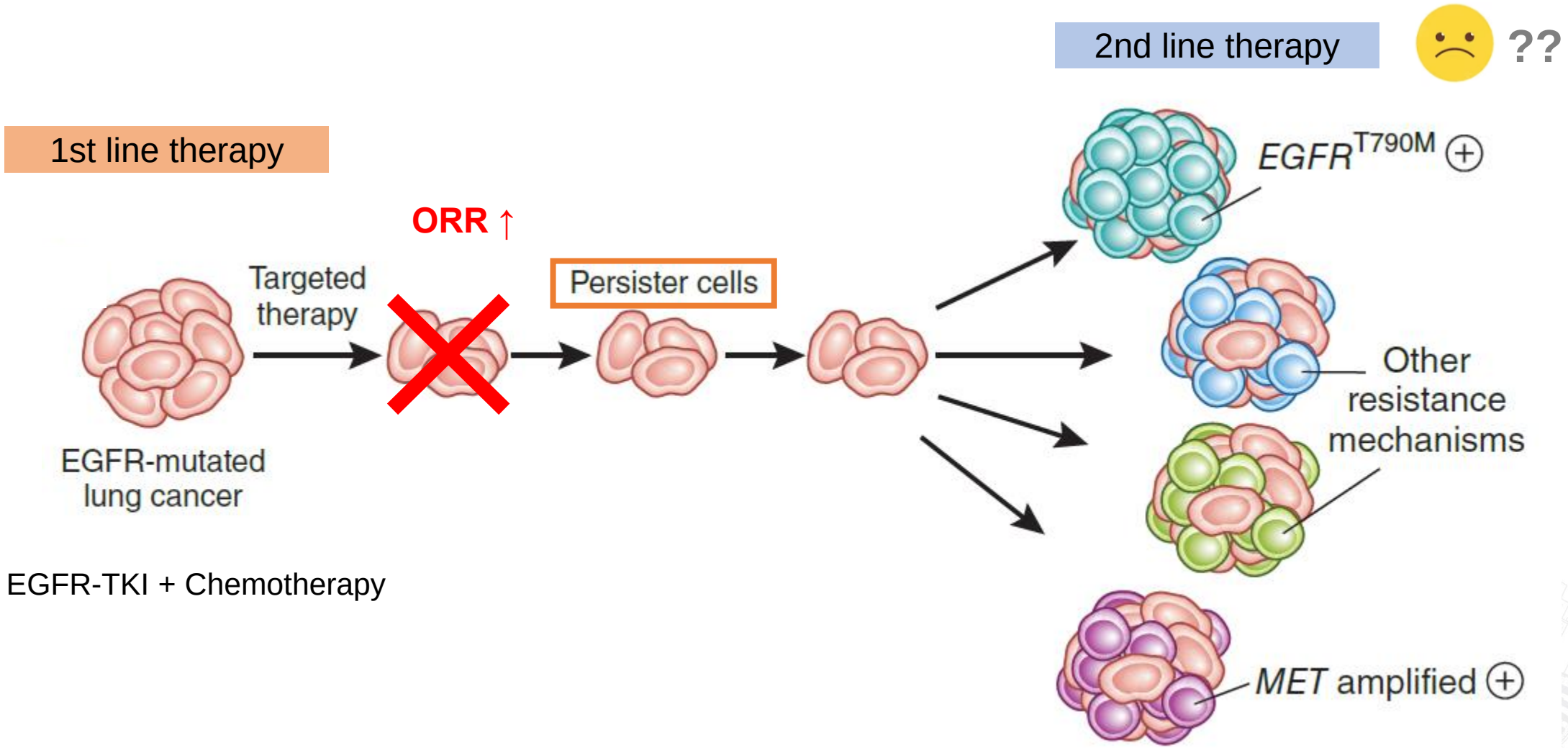


[Primary Endpoint: PFS According to Investigator assessment]



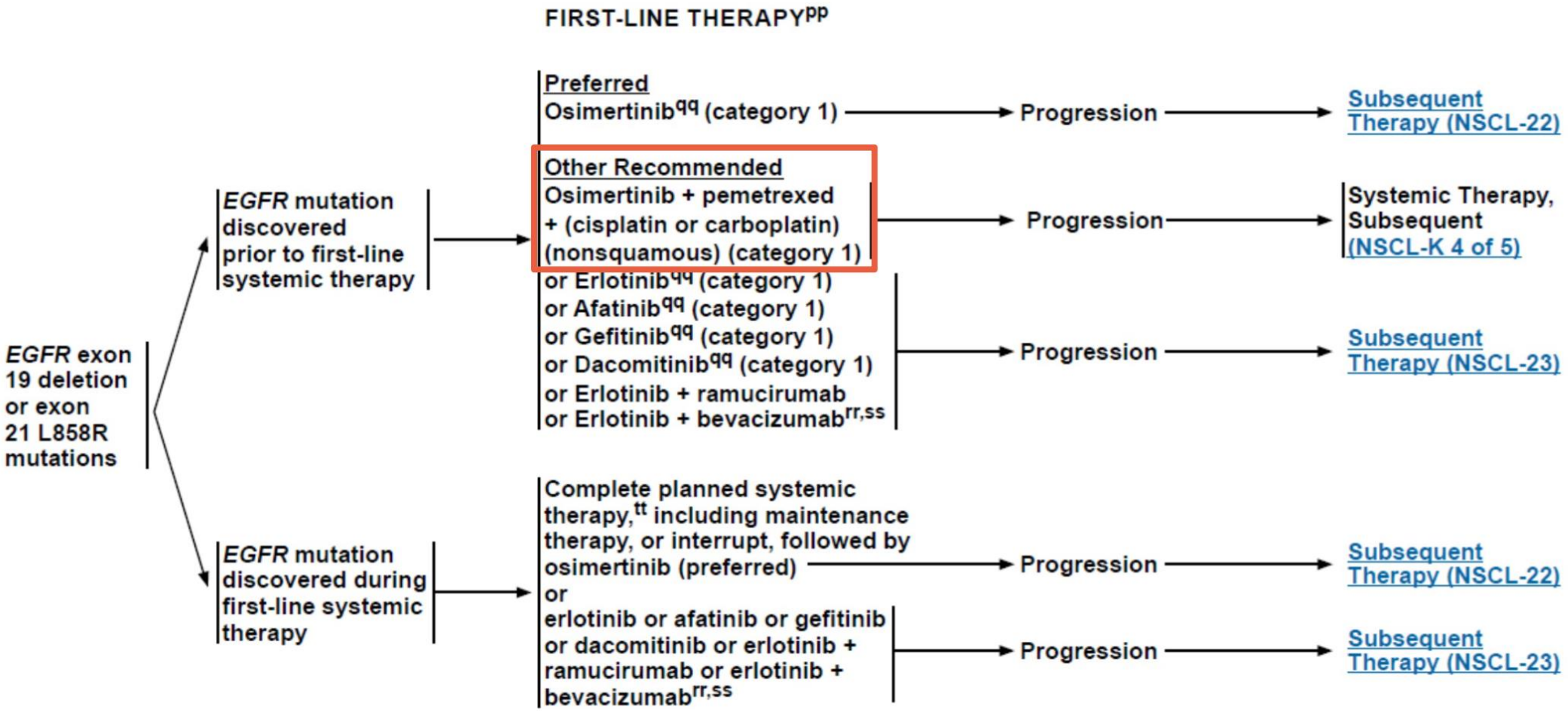
1. D Planchard et al. N Engl J Med . 2023 Nov 23;389(21):1935-1948. 2. P. Janne et al. WCLC2023. PL03.13

Combination Treatment Rationale



✕ EGFR-TKI + Chemotherapy

NCCN Guidelines ver1. 2024



mm Principles of Molecular and Biomarker Analysis (NSCL-H); pp Molecular or Biomarker-Directed Therapy for Advanced or Metastatic Disease (NSCL-J). ; qq For performance status 0–4.
rr Criteria for treatment with bevacizumab: nonsquamous NSCLC, and no recent history of hemoptysis.; ss An FDA-approved biosimilar is an appropriate substitute for bevacizumab.
tt If systemic therapy regimen contains an immune checkpoint inhibitor, physicians should be aware of the long half-life of such drugs and data reporting adverse events when using osimertinib in combination with or following checkpoint inhibitors. The rate of side effects (pneumonitis) is higher within 3 months.
Schoenfeld AJ, et al. Ann Oncol 2019;30:839-844; Oshima Y, et al. JAMA Oncol 2018;4:1112-1115; Oxnard GR, et al. Ann Oncol 2020;31:507-516; Gettinger S, et al. J Thorac Oncol 2018;13:1363-1372.

NCCN Guideline. Non-Small Cell Lung Cancer Version 1. 2024: December 21, 2023

NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer, Version 1.2024

타그리소-항암화학 병용요법, 폐암 적응증 확대

EGFR 변이 비편평 비소세포폐암 1차 치료 적응증 획득
병용요법, 임상서 타그리소 단독요법 대비 PFS 더 길게 나타나

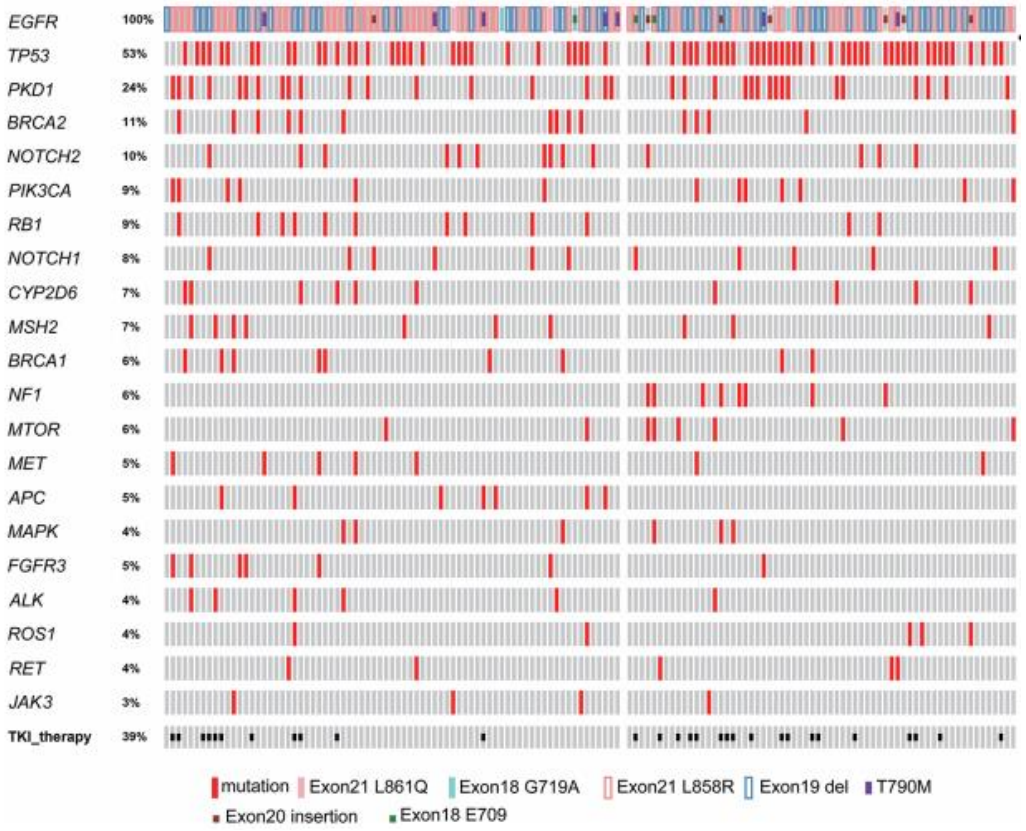
한국아스트라제네카 '타그리소정' 제품이미지.

한국아스트라제네카의 '타그리소(성분명 오시머티닙)'가 EGFR 변이 비편평 비소세포폐암 1차 치료로 적응증을 확대했다.

식품의약품안전처는 지난 15일 타그리소-페메트렉시드와 백금기반 항암화학요법 병용요법을 EGFR 엑손 19 결손 또는 엑손 21(L858R) 치환 변이된 국소 진행성 또는 전이성 EGFR 변이 비편평 비소세포폐암 1차 치료제로 허가했다.

How to add precision to precision?

Heterogeneity of EGFR mutant tumor by genetic profiling



Precision medicine based solution

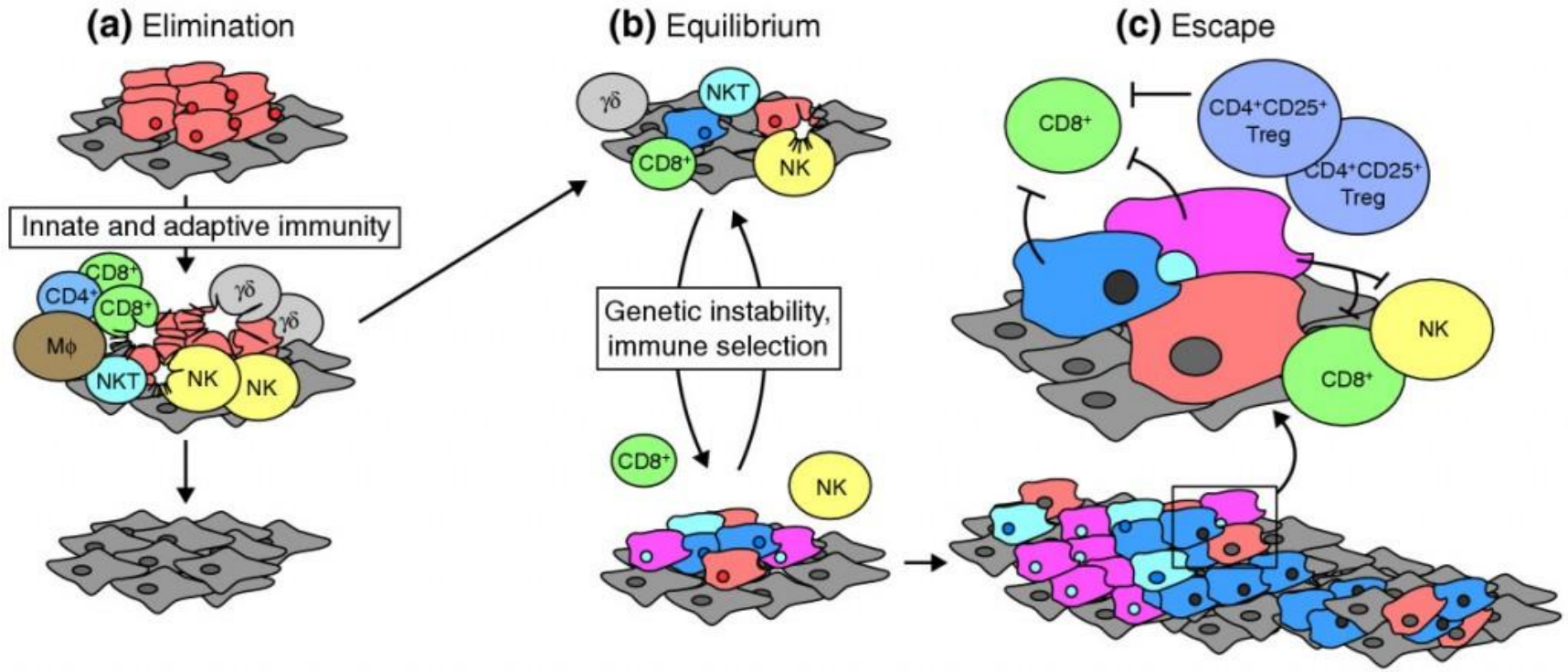
- ✓ EGFR-TKI monotherapy
- ✓ EGFR-TKI + targeted therapy
- ✓ EGFR-TKI + chemotherapy
- ✓ EGFR TKI + IO

The Oncologist 2019;24:1368–1374


CANCER
IMMUNOTHERAPY

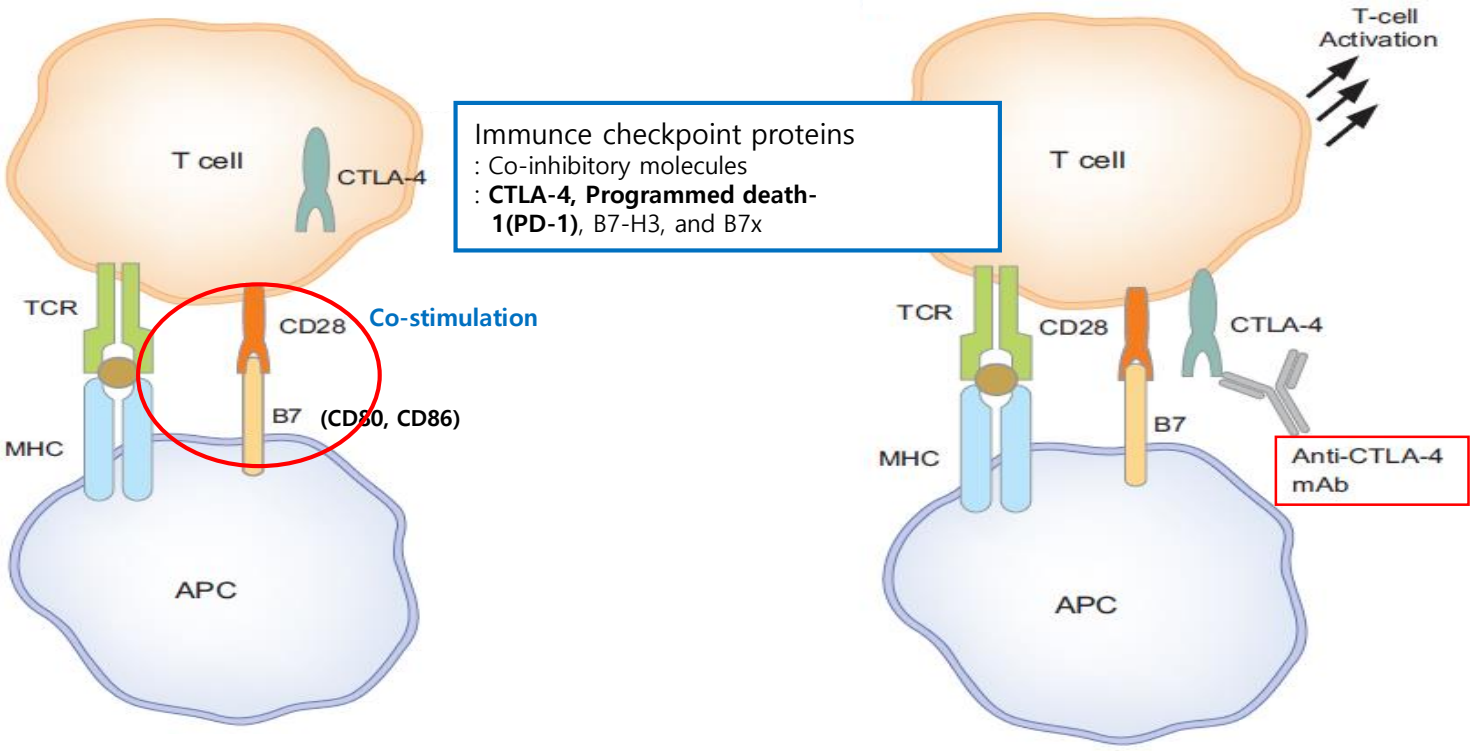
The Three E's

Elimination, Equilibrium, and Escape

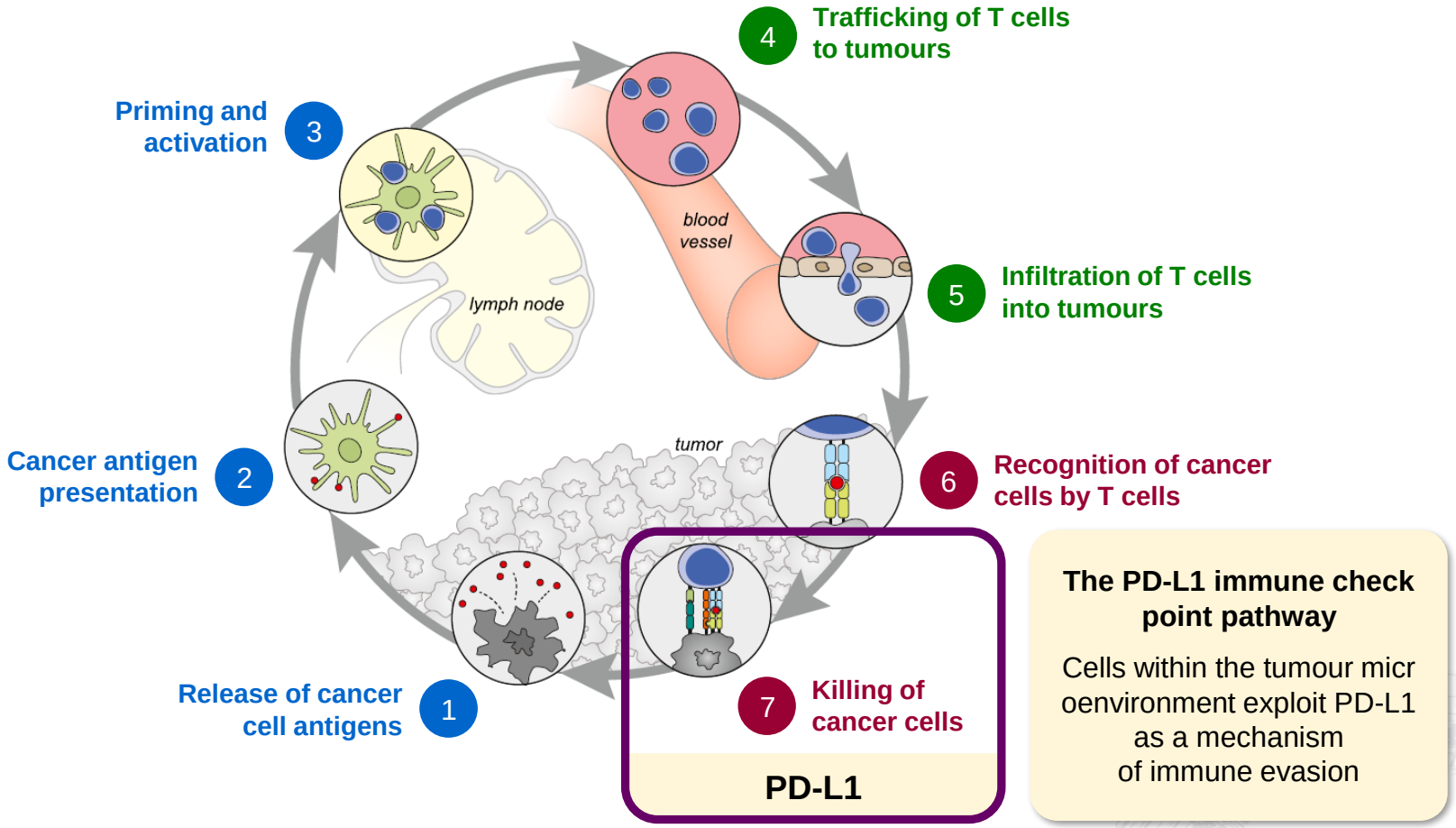


Genome Biol. (2005) 6:211

Immune Checkpoint Protein



Cancer Immune Cycle

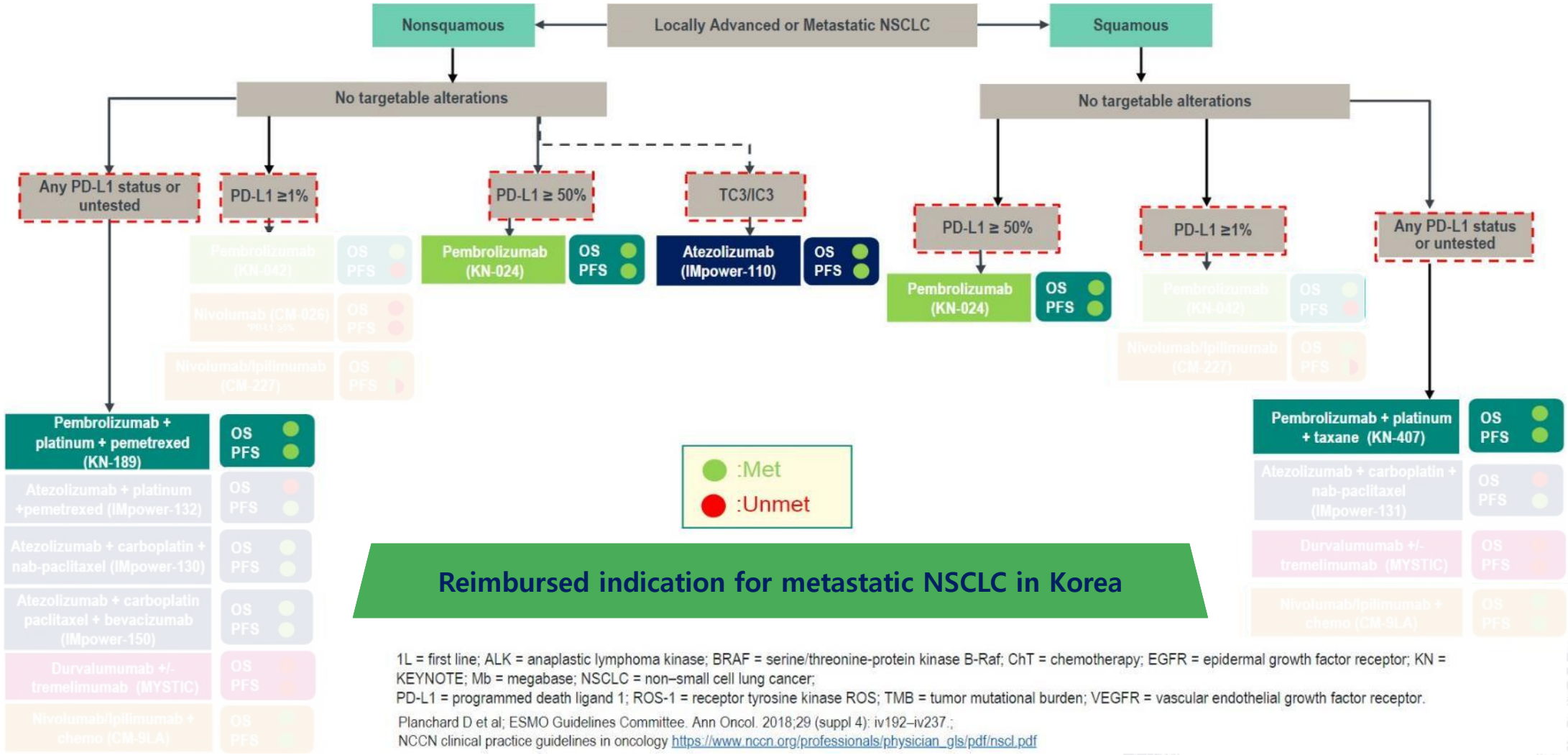


The PD-L1 immune check point pathway

Cells within the tumour micr oenvironment exploit PD-L1 as a mechanism of immune evasion

Chen, et al. Clin Cancer Res 2012

Dynamic First-Line Treatment Landscape in NSCLC

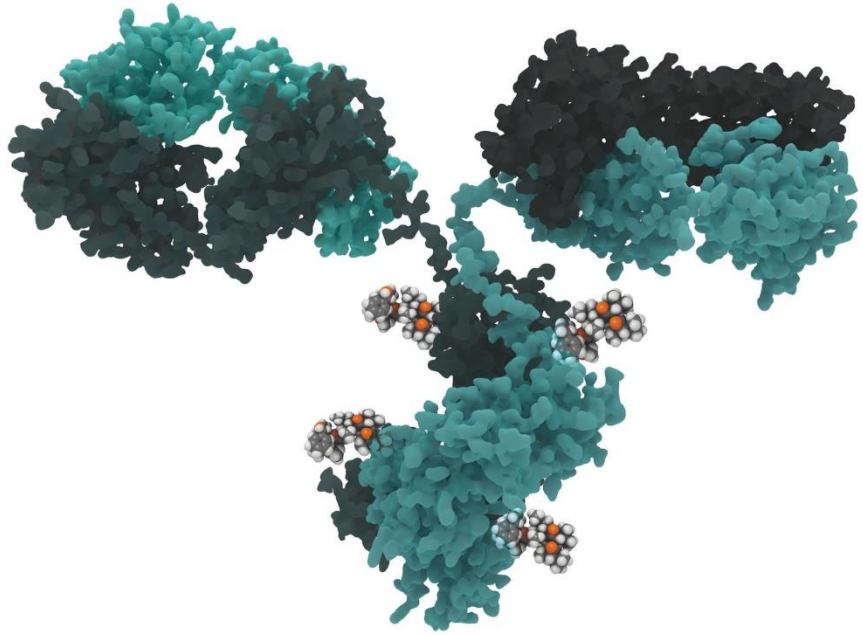


Reimbursed indication for metastatic NSCLC in Korea

1L = first line; ALK = anaplastic lymphoma kinase; BRAF = serine/threonine-protein kinase B-Raf; ChT = chemotherapy; EGFR = epidermal growth factor receptor; KN = KEYNOTE; Mb = megabase; NSCLC = non–small cell lung cancer;
PD-L1 = programmed death ligand 1; ROS-1 = receptor tyrosine kinase ROS; TMB = tumor mutational burden; VEGFR = vascular endothelial growth factor receptor.

Planchard D et al; ESMO Guidelines Committee. Ann Oncol. 2018;29 (suppl 4): iv192–iv237.;
NCCN clinical practice guidelines in oncology https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

Antibody Drug Conjugate

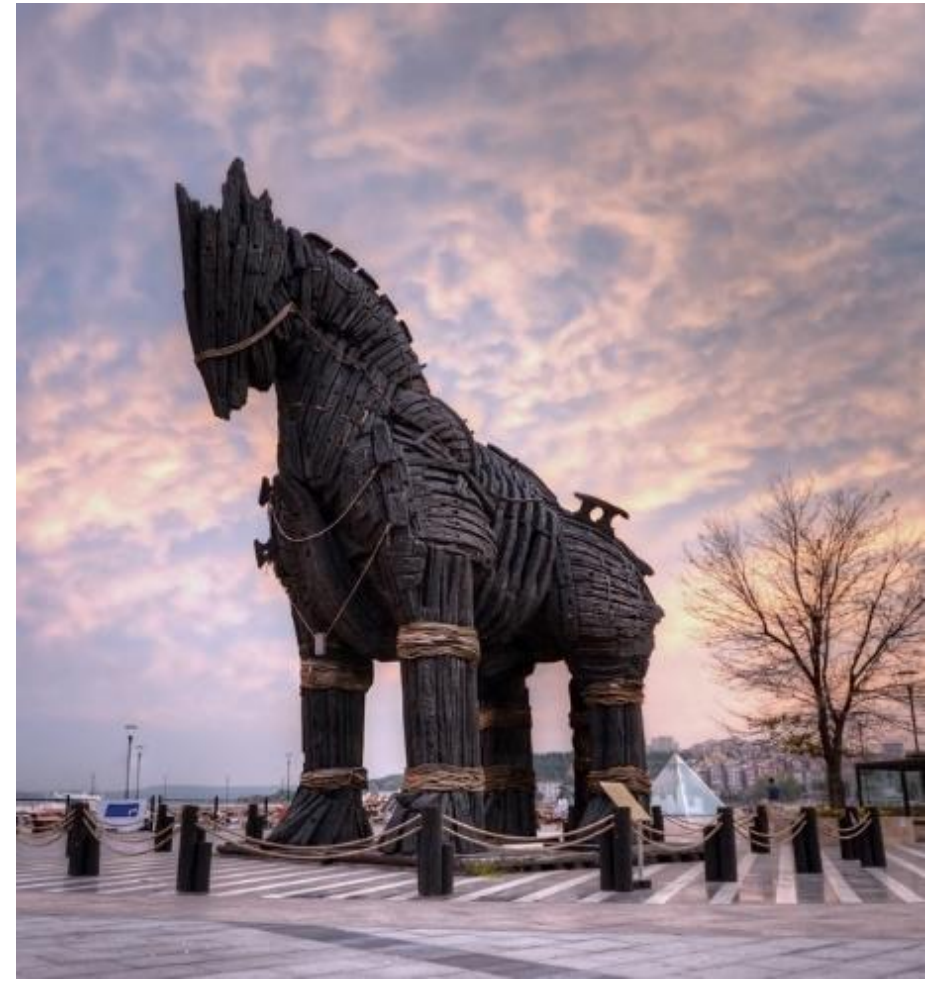


유방암 신약 '엔허투' 8300만원→417만원… 4월부터 급여

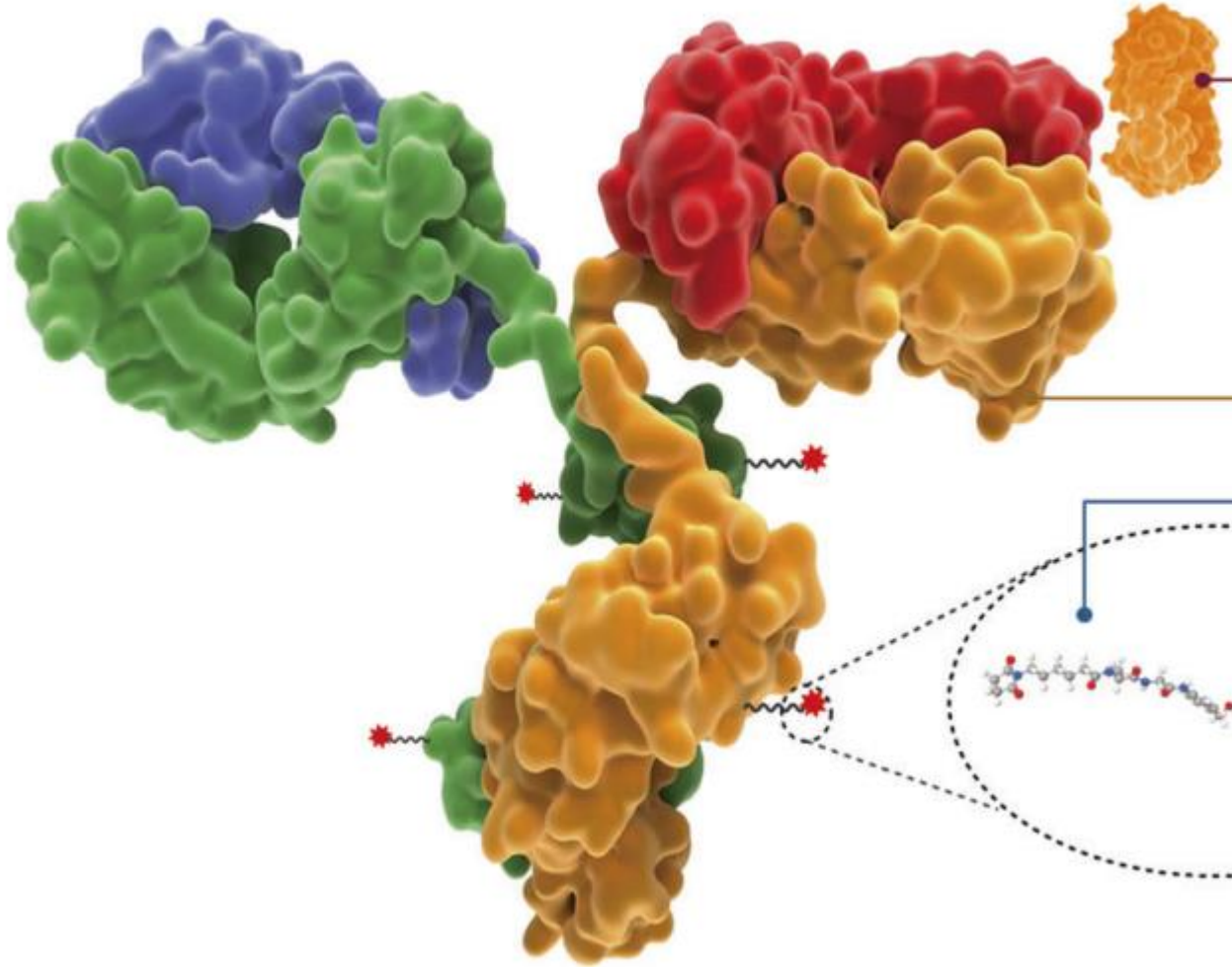
입력 2024.03.28 19:00

4월부터 HER2 양성인 유방암·위암에 엔허투를 보험으로 사용할 수 있다. 다이이찌산쿄 제공

마침내 올해 4월부터 유방암·위암 신약 '엔허투'를 국내 환자들도 치료비 부담 없이 사용할 수 있게 됐다.



Antibody Drug Conjugate ??

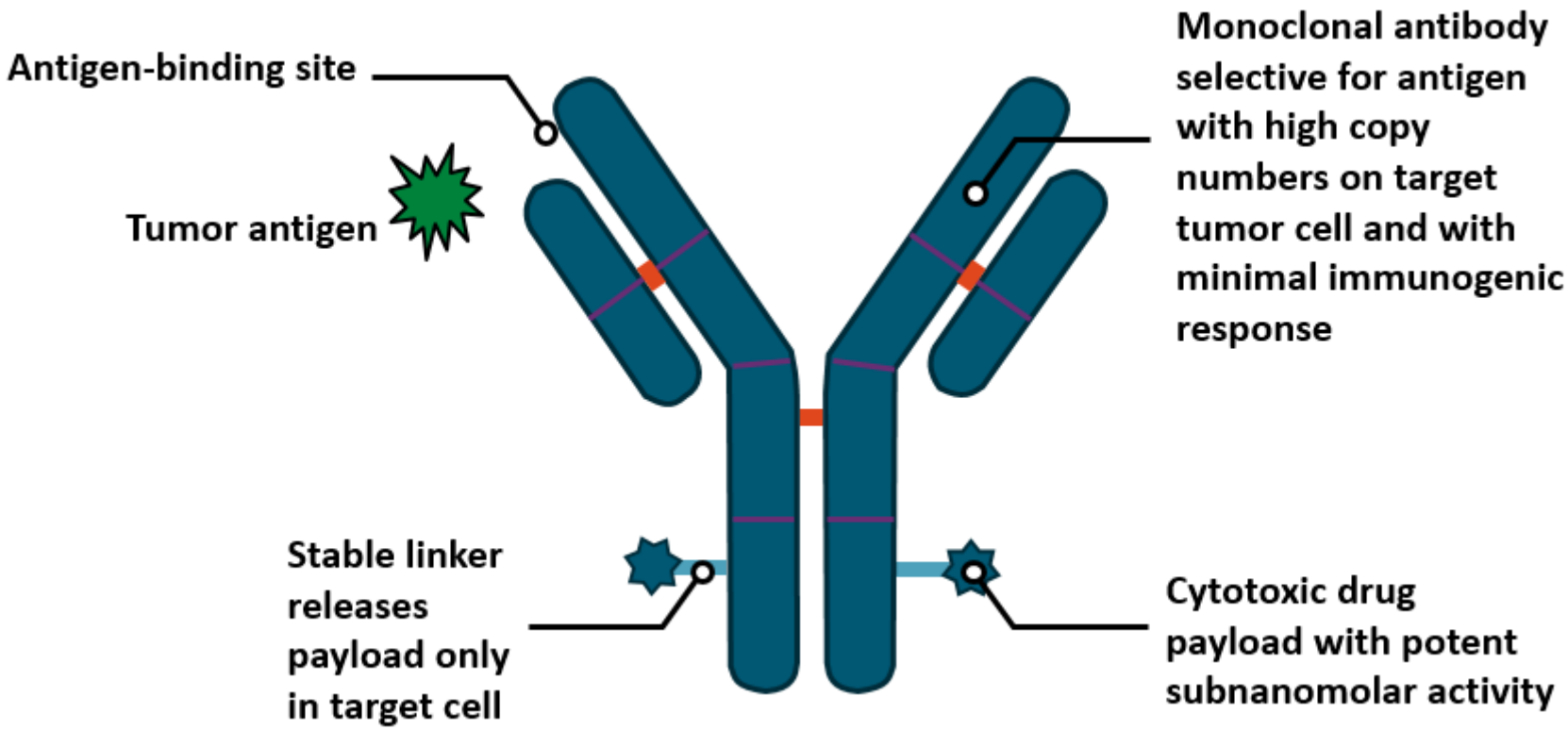


Key functions

Target antigen	Recognition of target cancer cells
Antibody	Guidance system for cytotoxic drugs
Linker	Bridge between antibody and drugs and to control the release of drugs inside cancer cells
Cytotoxic drug	Warhead for destroying cancer cells

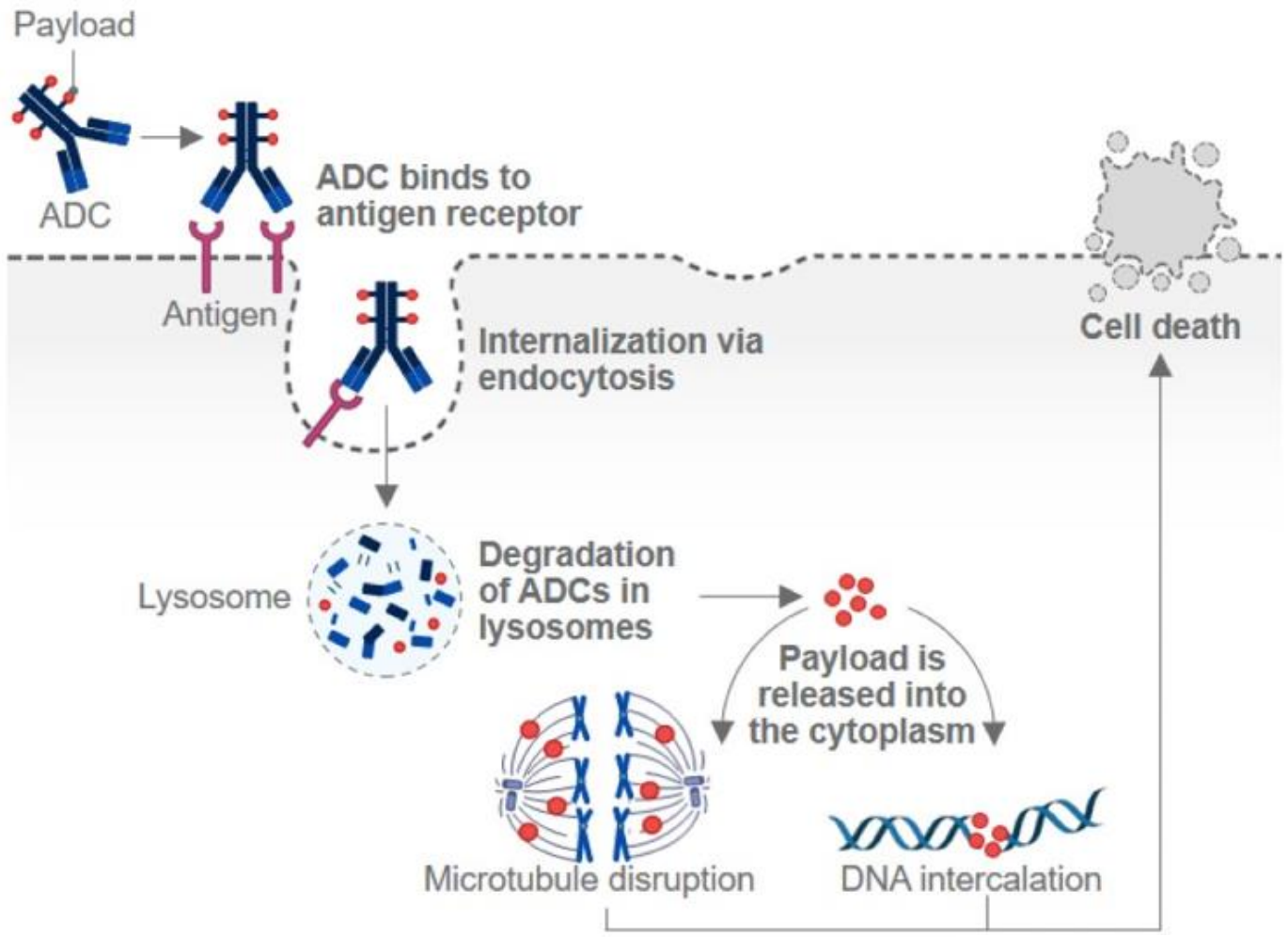
What are Antibody-Drug Conjugates ?

Monoclonal antibody linked to a cytotoxic drug designed to widen the therapeutic window by focusing delivery to specific cells



Drago. Nat Rev Clin Oncol. 2021;18:327.

Mechanism of Action



Antibody

- Provides targeted delivery
- Antigen should be effectively internalized by receptor-mediated endocytosis
- Optimal target antigen should have high expression on the surface of the tumor cells and limited or no expression in healthy tissues

Payload

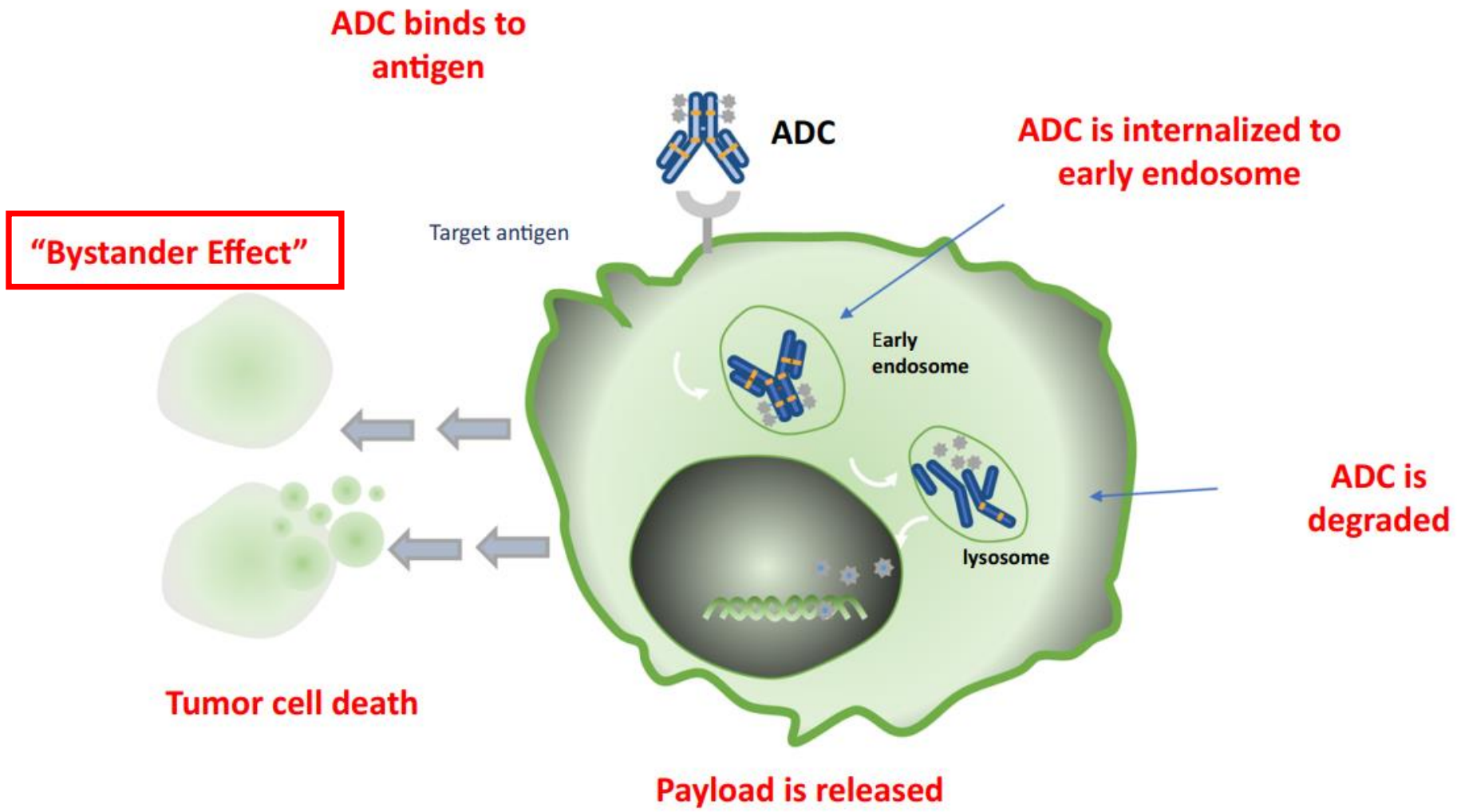
- Most cytotoxic payloads used for ADCs are approximately 100 to 1000 times more potent than small molecule chemotherapeutic agents on their own

Linker

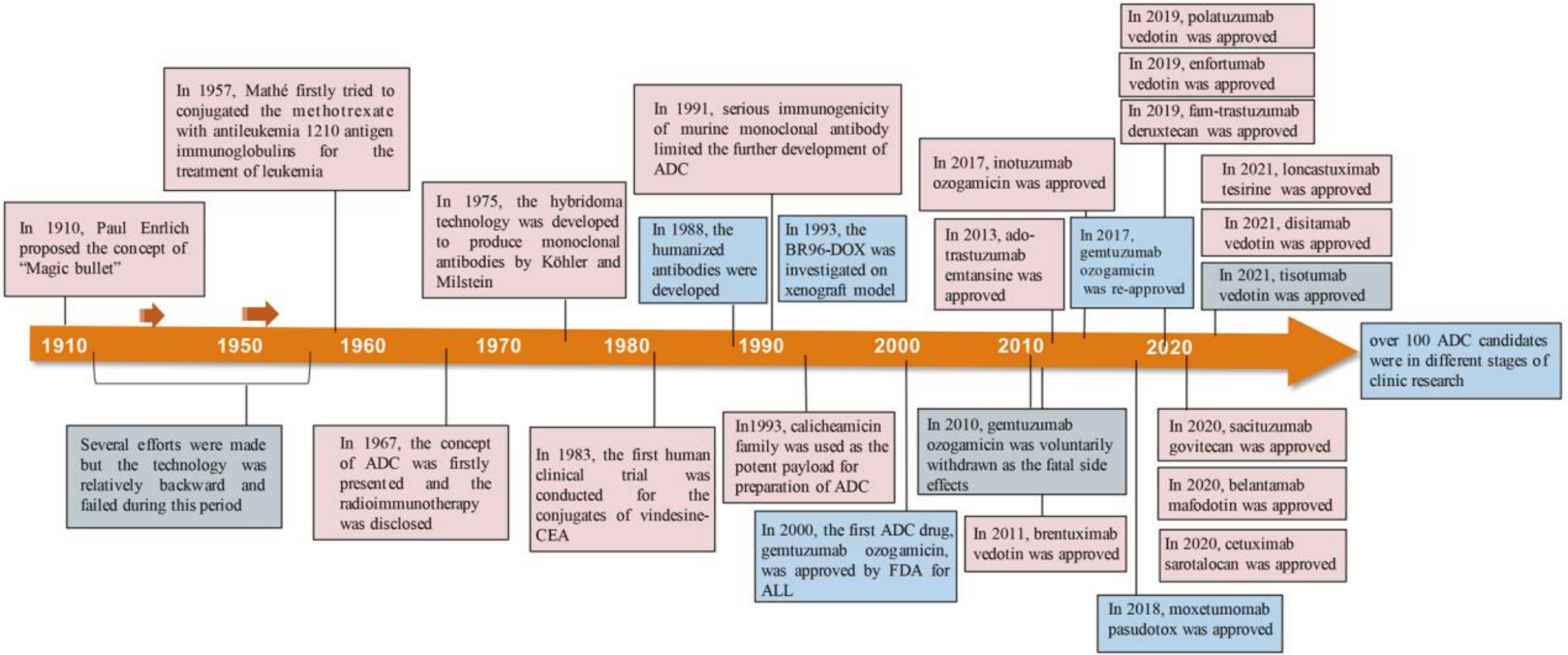
- An ideal linker is highly stable in circulation, meaning it will not release the payload before delivery to the target

Tolcher A, et al. Cancer Treat Rev. 2023;116:102546

Bystander effect ??



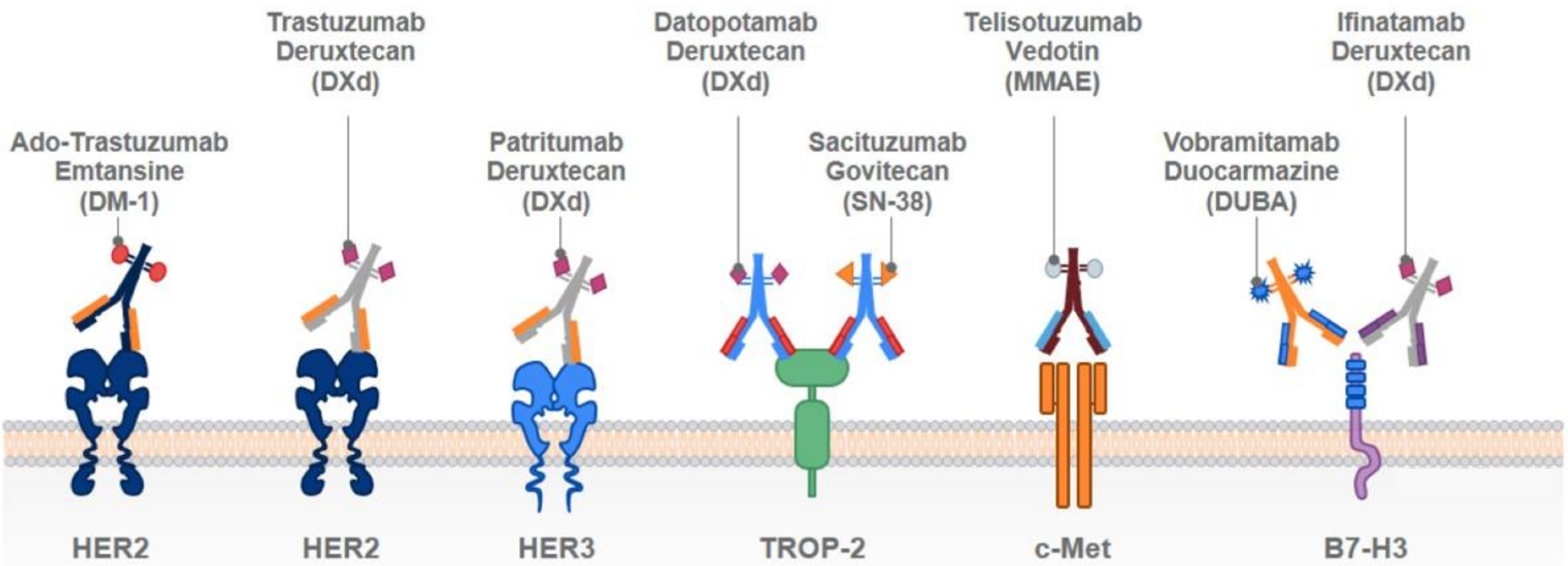
Timeline in the development and approval of ADC drugs



Evolution of the ADC drug development

	First-generation ADC	Second-generation ADC	Third-generation ADC
Antibodies	Mouse-original or chimeric humanized antibodies	Humanized antibodies	Fully humanized antibodies or Fabs
Linkers	Unstable	Improved stability: cleavable and non-cleavable linkers;	Stable in circulation; precise control drugs release into tumor sites
Payloads	Low potency, including calicheamicin, duocarmycin and doxorubicin	Potency, such as auristatins and mytansinoids	High potency, such as PBDs, and tubulysin, and novel payloads like immunomodulators
Conjugation methods	Random lysines	Random lysines and reduced interchain cysteines	Site-specific conjugation
DAR	Uncontrollable (0–8)	4–8	2–4
Representative drugs	Gemtuzumab ozogamicin and inotuzumab ozogamicin	Brentuximab vedotin and ado-trastuzumab emtansine	Polatuzumab vedotin, enfortumab vedotin, and fam-trastuzumab deruxtecan
Advantages	• Specific targeting • Increase therapeutic window to some extent	• Improved targeting ability • More potent payloads • Lower immunogenicity	• Higher efficacy though in cancer cells with low antigen; • Improved DAR along with improved stability and PK/PD; • More potent payloads; • Less off-target toxicity
Disadvantages	• Heterogeneity; • Lack of efficacy; • Narrow therapeutic index; • Off-target toxicity as premature drug loss; • High immunogenicity	• Heterogeneity; • Fast clearance for high DARs; • Off-target toxicity as premature drug loss; • Drug resistance	• Possible toxicity due to highly potent payloads; • Catabolism may be different across species • Drug resistance

ADCs Approved and in Development for NSCLC



B7-H3, B7 homolog 3; CEACAM5, carcinoembryonic antigen-related cell adhesion molecule 5; DM1, emtansine; DM4, maytansine derivative; DUBA, duocarmycin hydroxybenzamide azaindole; DXd, deruxtecan; HER2, human epidermal growth factor receptor 2; HER3, human epidermal growth factor receptor 3; Met, mesenchymal epithelial transition factor; MMAE, monomethyl auristatin E; NSCLC, non-small cell lung cancer; TROP2, trophoblast cell surface antigen 2.
Adapted from Desai A, et al. Lung Cancer. 2022;163:96-106.

Summary of current key ADC clinical data in mNCLC

Trastuzumab deruxtecan (NCT03505710) in HER2-mutant tumors

Linker type - cleavable tetrapeptide-based linker
Antibody subclass - IgG1

FDA-approval - August 11 2022 On August 11, 2022, for NSCLC patients with activating human HER2 mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy.

Outcome	Trastuzumab deruxtecan ($n = 91$)
ORR (95% CI)	55% (44-65)
CR	1 (1%)
PR	49 (54%)
SD	34 (37%)
PD	3 (3%)
Median DOR, months (95% CI)	9.3 months (5.7–14.7)
Median PFS, months (95% CI)	8.2 (6.0–11.9)
Median OS, months (95% CI)	17.8 (13.8–22.1)
Median time to response, months (range)	1.5 (1.2–9.3)

Datopotamab-deruxtecan (NCT03401385)

Antibody subclass–IgG1
Linker type - cleavable tetrapeptide-based linker

Outcome	4 mg/kg ($n = 40$)	6 mg/kg ($n = 39$)	8 mg/kg ($n = 80$)
ORR (95% CI)	23% ($n = 9$)	21% ($n = 8$)	25% ($n = 20$)
Confirmed CR/ PR	$n = 7$	$n = 6$	$n = 19$
PD	15%	21%	9%
DCR	73%	67%	80%

Telisotuzumab vedotin (NCT03539536)

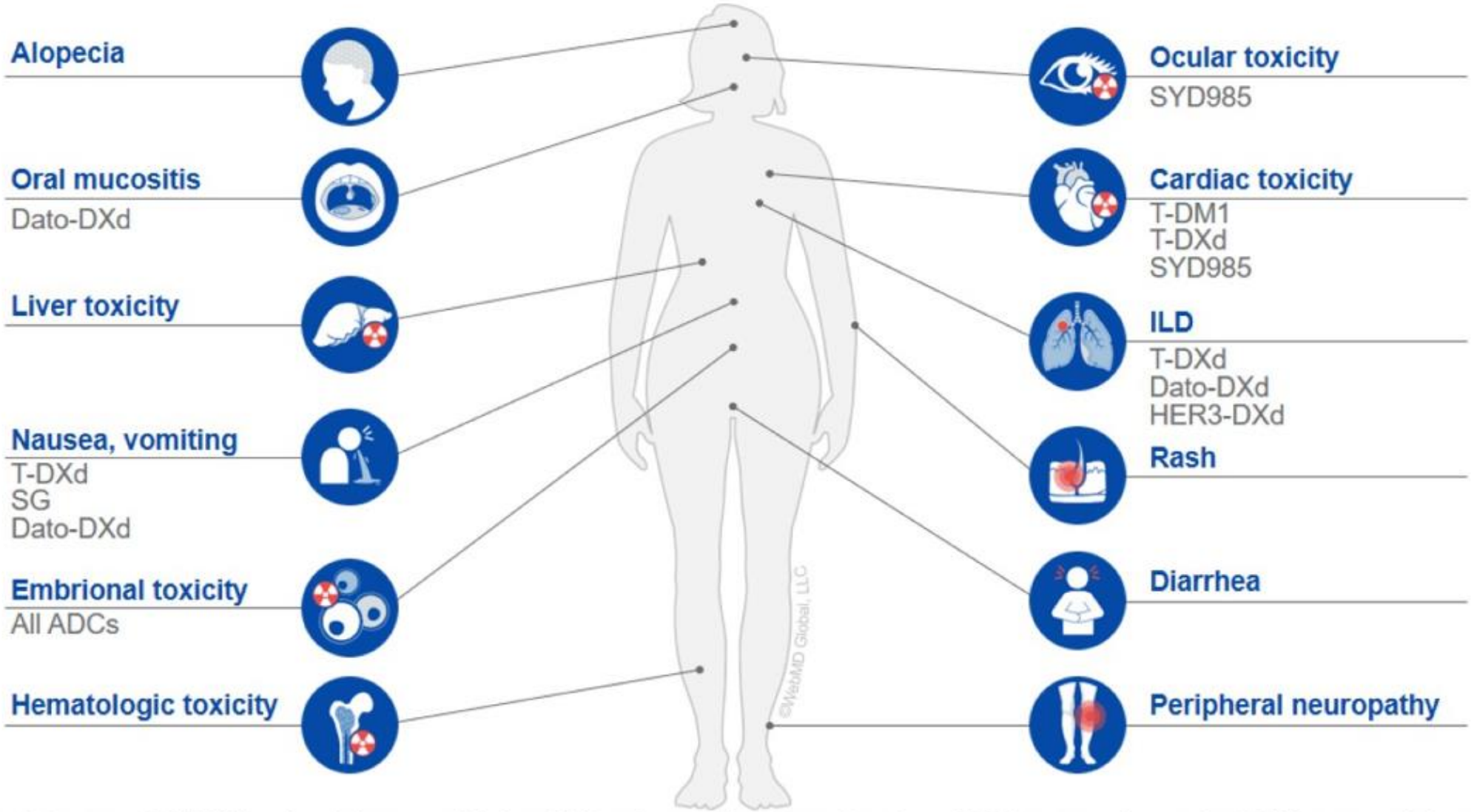
Antibody subclass–IgG1
Linker type - Cleavable dipeptide

Outcome	EGFR mutant ($n = 37$)	Non-squamous EGFR WT cohort ($n = 37$)	c-Met–intermediate ($n = 13$)	c-Met–high ($n = 13$)
ORR (95% CI)	13.3% (3.8–30.7)	35.1% (20.2–52.5)	25% (9.8–46.7)	53.8% (25.1–80.8)

Toxicity of ADCs

- Premature release of the ADC payload in circulation
- ADC binding to non-cancerous expressor cells of the target antigen
- Immune response induced by the antibody part of ADC

Toxicities of ADCs



Dato-DXd, datopotamab deruxtecan; HER3-DXd, patritumab deruxtecan; ILD, interstitial lung disease; SG, sacituzumab govitecan; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
D'Arienzo A, et al. EClinicalMedicine. 2023;62:102113.

양산부산대학교병원
Pusan National University Yangsan Hospital

환자 내몸

Thank you for your attention!!


누리마루APEC하우스
제1전시장
제2전시장
컨벤션홀
오디토리움