BHIVA
British HIV Association

2023 Spring Conference

Mon 24th – Wed 26th April
Gateshead, UK

Clinical session

Chair: Ashini Fox

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Malignancy – what's new in lung cancer?

Qamar Ghafoor

University Hospitals Birmingham NHS Foundation Trust, UK

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University Hospitals Birmingham

Conflict of Interest

AstraZeneca, Pfizer, Chugai, Roche, Amgen

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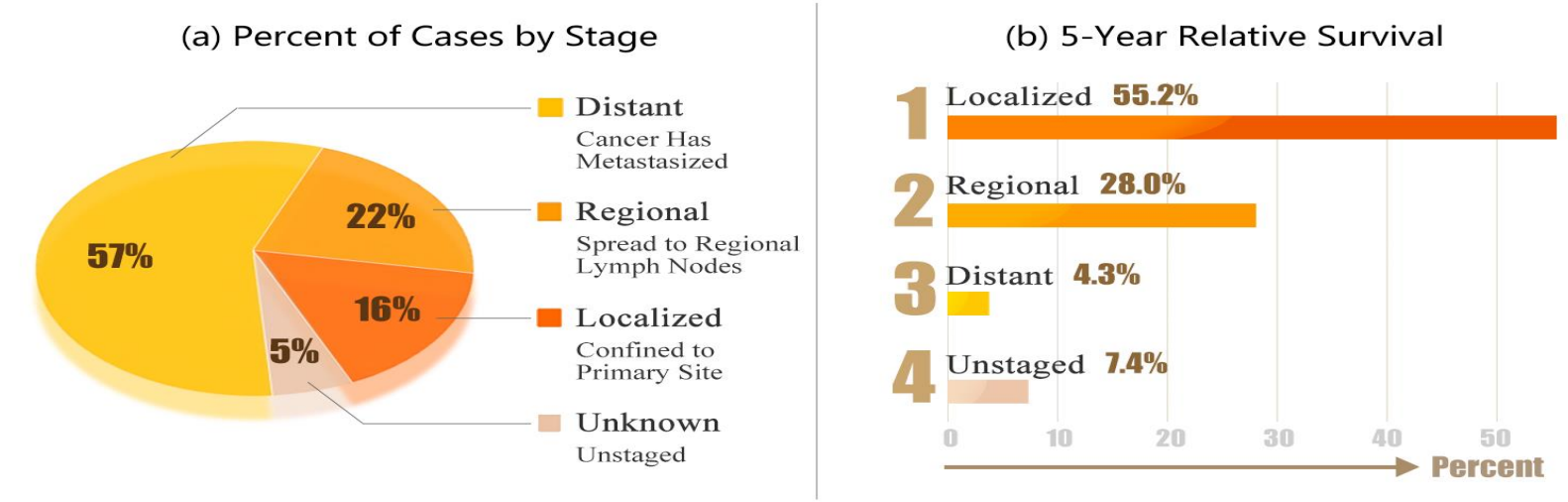
- Lung cancer is the UK's largest cause of cancer deaths (21%)
- Approximately 50,000 new cases per year
- In 2017, data showed only 10% of lung cancer patient survived 10 years
- Despite screening and better treatments, this figure is only slowly improving

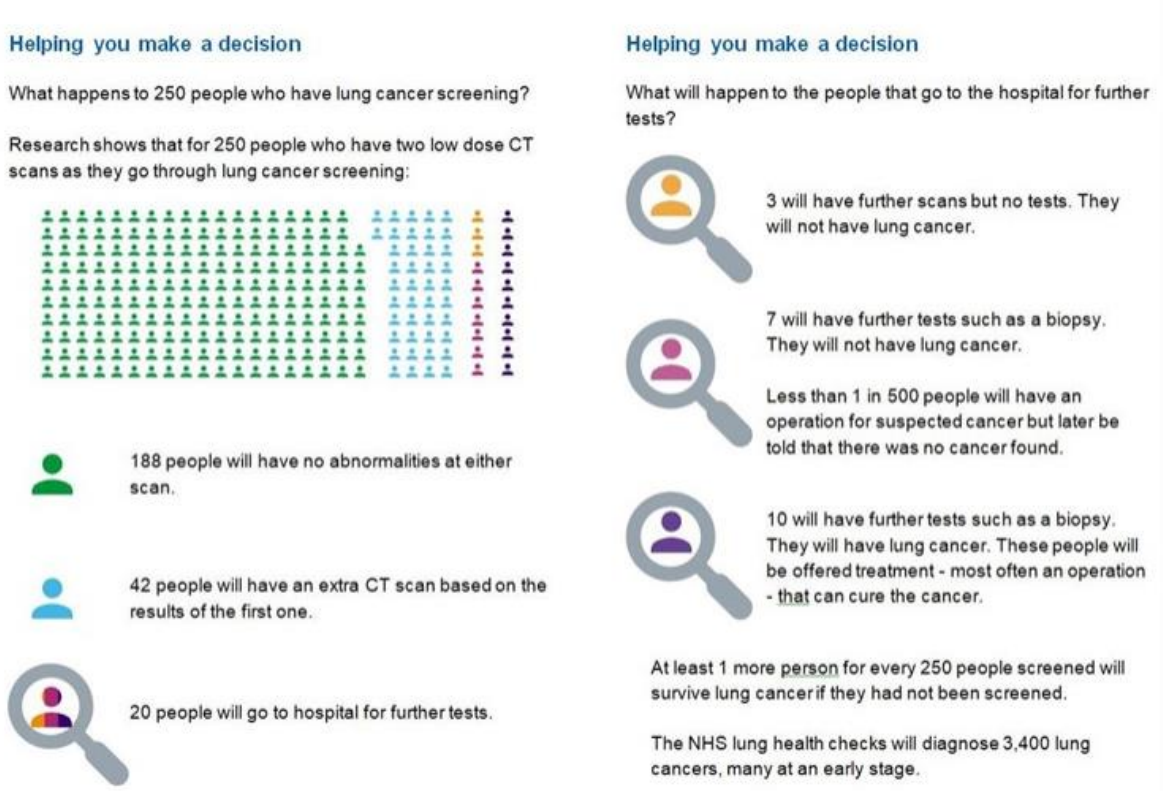
Most lung cancer is diagnosed in the advanced stage

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Lung and Bronchus Cancer



· SEER 18 2006-2012, All Races, Both Sexes by SEER Summary Stage 2000 ·

Screening



Helping you make a decision

What happens to 250 people who have lung cancer screening?

Research shows that for 250 people who have two low dose CT scans as they go through lung cancer screening:

188 people will have no abnormalities at either scan.

42 people will have an extra CT scan based on the results of the first one.

20 people will go to hospital for further tests.

Helping you make a decision

What will happen to the people that go to the hospital for further tests?

3 will have further scans but no tests. They will not have lung cancer.

7 will have further tests such as a biopsy. They will not have lung cancer.

Less than 1 in 500 people will have an operation for suspected cancer but later be told that there was no cancer found.

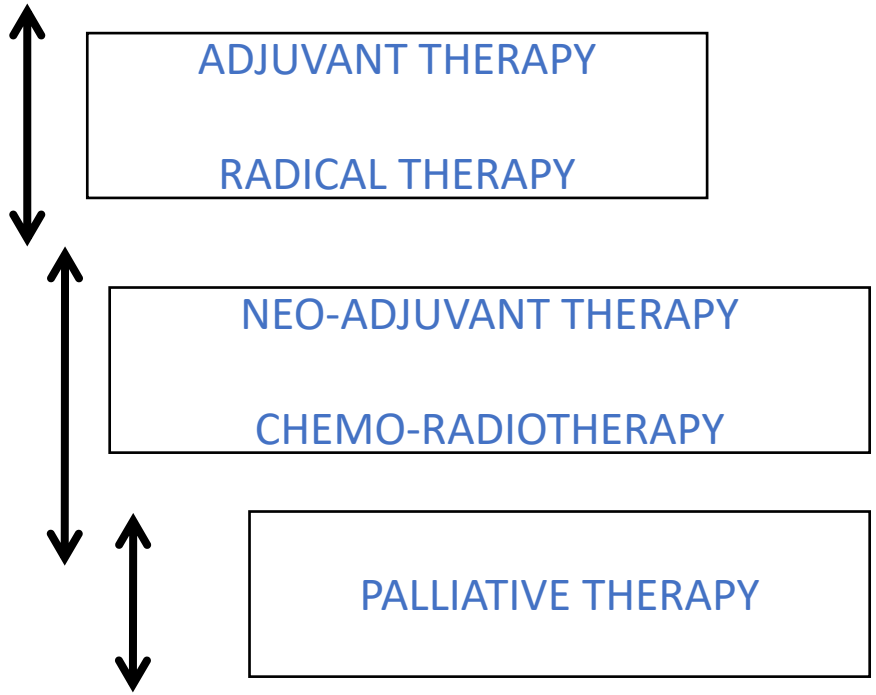
10 will have further tests such as a biopsy. They will have lung cancer. These people will be offered treatment - most often an operation - that can cure the cancer.

At least 1 more person for every 250 people screened will survive lung cancer if they had not been screened.

The NHS lung health checks will diagnose 3,400 lung cancers, many at an early stage.

Stage Specific Treatment

ANATOMIC STAGE/PROGNOSTIC GROUPS			
Occult Carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
Stage IV	Any T	Any N	M1a
	Any T	Any N	M1b



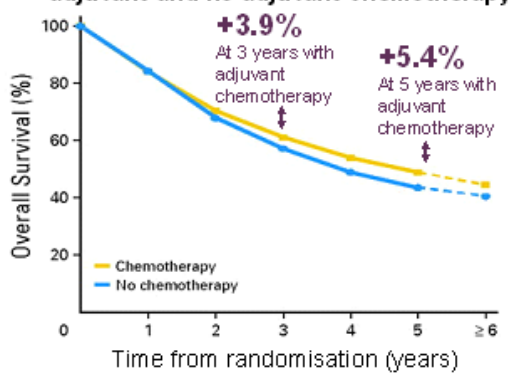
Adjuvant Therapy

- IALT, ANITA, JBR 10, CALGB 9633, ALPI.
- For a subset of stage 1B (> 4cm) or beyond (any node positivity).
- 4 to 10% improvement in 5 year survival.
- 4 cycles of cisplatin doublet chemotherapy.

Adjuvant chemotherapy results in an absolute survival benefit of 4?5% at 5 years compared to no chemotherapy in stage IA–III NSCLC patients[1]

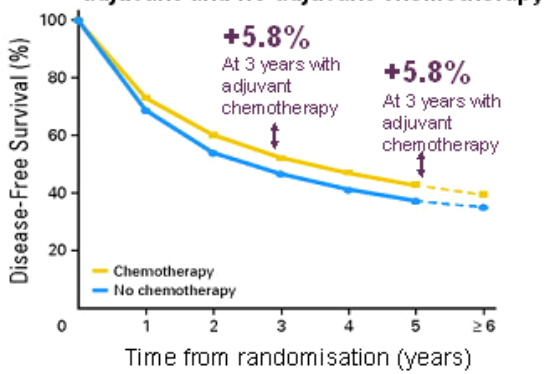
A pooled analysis from the 5 largest trials (4,584 patients) of cisplatin-based chemotherapy in completely resected patients

OS in stage IA?III NSCLC patients given adjuvant and no adjuvant chemotherapy



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

DFS in stage IA?III NSCLC patients given adjuvant and no adjuvant chemotherapy



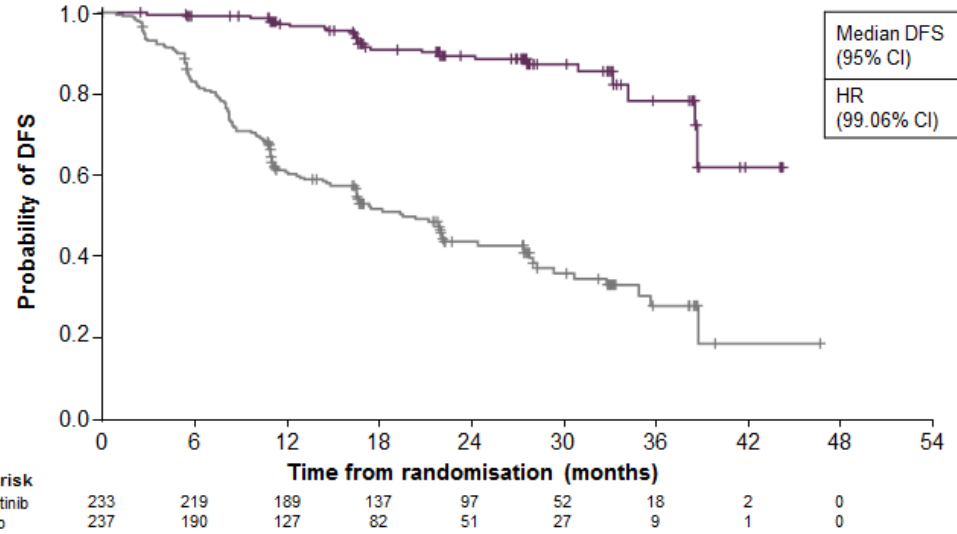
Events / person years by period	Years 0-3	Years 4-5	Years ≥ 6
Control	1,222 / 4,341	163 / 1,396	35 / 610
Chemotherapy	1,047 / 4,627	159 / 1,606	59 / 708

DFS, disease-free survival; NSCLC, non-small cell lung cancer; OS, overall survival.

1. Pignon JP et al. J Clin Oncol. 2008;26(21):3552?9.

Osimertinib resulted in a statistically significant and clinically meaningful improvement in median DFS by investigator assessment over placebo[1]

Primary Endpoint: DFS in Patients With Stage II–IIIA Disease



	OSIMERTINIB	PLACEBO
Median DFS (95% CI)	NR (38.8–NC)	19.6 (16.6–24.5)
HR (99.06% CI)	0.17 (0.11–0.26)	

Data maturity 33% (osimertinib 11%, placebo 55%)
P<0.001

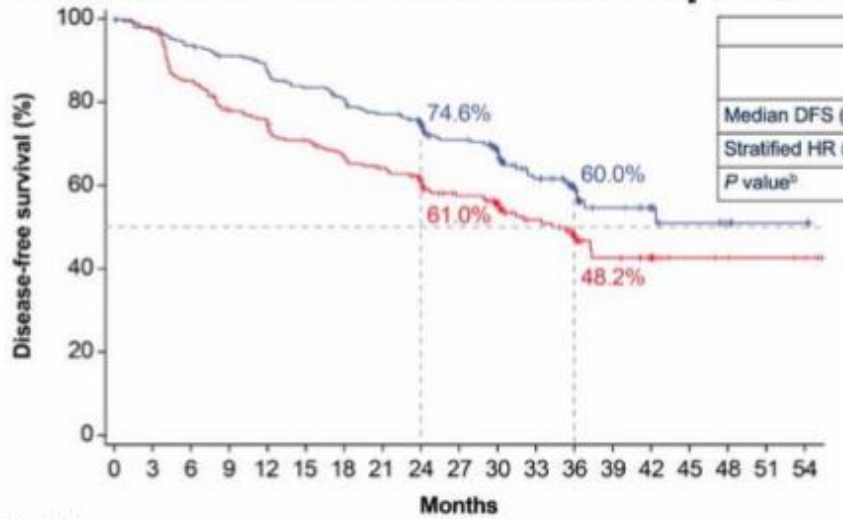
This corresponds to an 83% reduction in risk of recurrence or death

ADAURA data cut-off: January 17th, 2020.

CI, confidence interval; DFS, disease-free survival; HR, hazard ratio; NC, not calculable; NR, not reached.

1. Wu Y et al. N Engl J Med 2020:383:1711–23.

Atezolizumab following surgery and chemotherapy reduced the risk of disease recurrence or death by 34% in people with stage II-IIIA NSCLC whose tumors express ≥1% PD-L1[a]



	PD-L1 TC ≥1% stage II-IIIA	
	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)

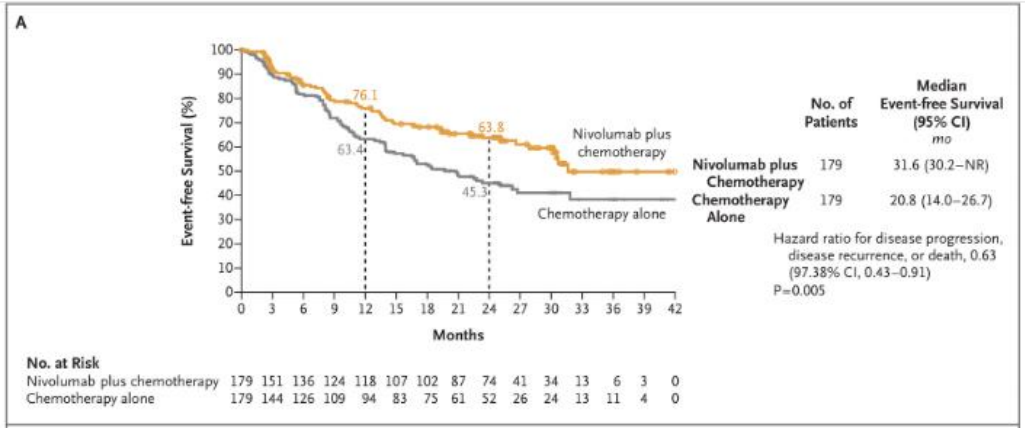
Clinical cutoff: January 21, 2021. CI, confidence interval; HR, hazard ratio; NE, not evaluable. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS.

Source: Dr Heather Wakelee & Asco.

Neo-Adjuvant Therapy

- The aim is to downstage and improve operability success.
  Allows earlier control of micro-metastases.

- Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer
- Pathological Complete Response - 24%
- NHS approved – March 2023



Chemo-Radiotherapy

- Option for inoperable N2 and select N3 patients.
- Aim for good long term control.
- Some long term survivors / patients cured.
- Sequential vs Concurrent.

IMFINZI™ ▼ (durvalumab) for unresectable stage III NSCLC: PACIFIC

The pivotal phase III, randomised, double-blind, placebo-controlled, multi-centre global study for IMFINZI™ vs placebo was designed to be representative of the variation in stage III NSCLC clinical practice[1]

Treatments of patients with stage III unresectable NSCLC who have not progressed following platinum-based concurrent chemoradiotherapy
Patients randomised = 713

Randomisation 2:1
1–42 days post-cCRT

Stratification factors

1. Age at randomisation (<65 vs ≥65 years of age)
2. Sex (male vs female)
3. Smoking history (smoker vs non-smoker)

IMFINZI™ IV 10 mg/kg q2w up to 12 months (N=476)

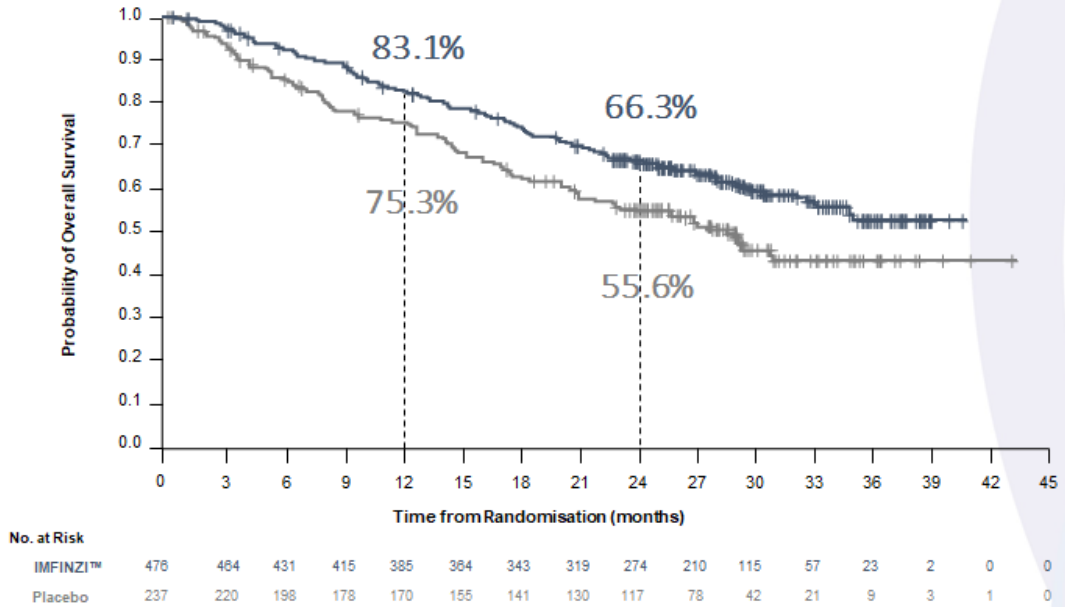
Placebo IV q2w (N=237)

Co-primary Endpoints	Secondary Endpoints	
• OS • PFS*	• OS24 • DoR (per BICR) • ORR (per BICR) • APF12 and APF18	• TTDM • Safety and tolerability • Health-related QoL • PK and immunogenicity

* Response Evaluation Criteria In Solid Tumours v1.1

Overall Survival* (ITT)

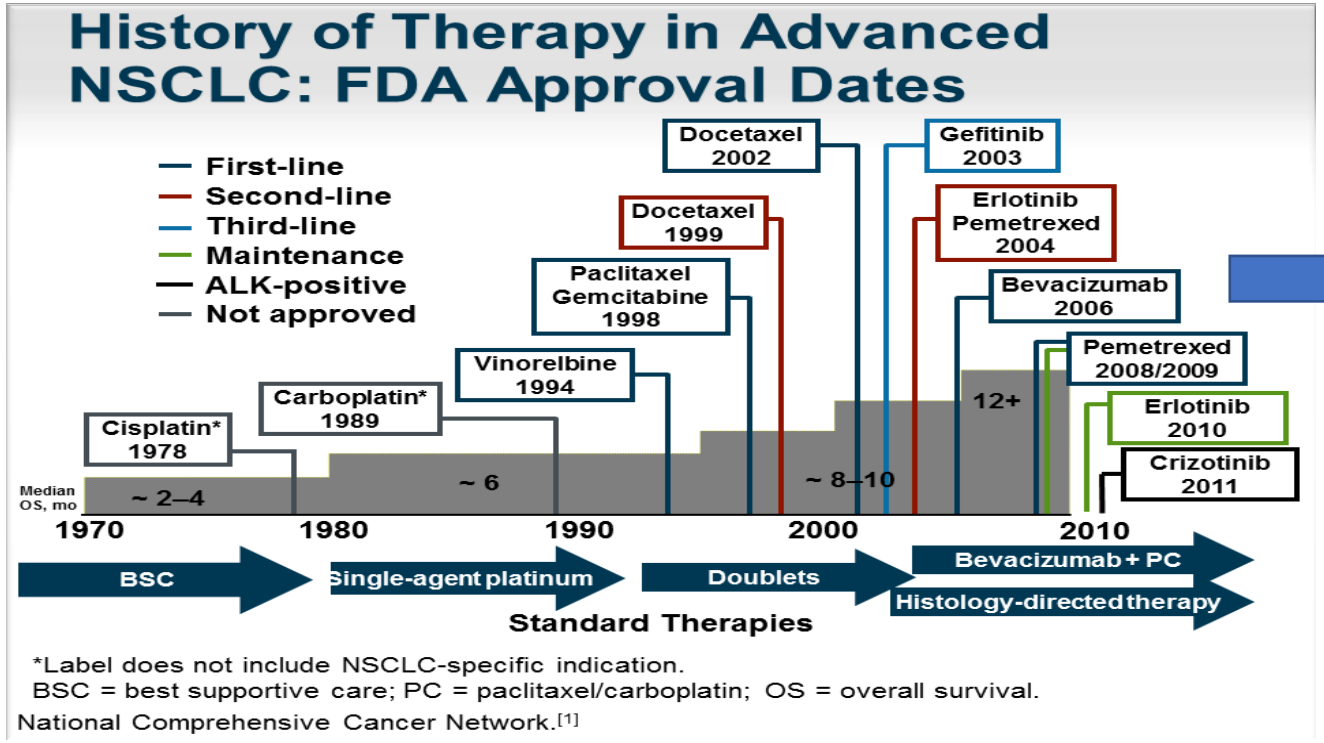
In the ITT population, IMFINZI™ demonstrated a 32% reduction in the risk of death vs placebo (HR: 0.68; 95% CI, 0.53-0.87)[1]



	No. of events / No. of patients (%)	Median OS (95% CI) months
IMFINZI™	183/476 (38.4)	NR (34.7–NR)
Placebo	116/237 (48.9)	28.7 (22.9–NR)

OS HR = 0.68
99.73% CI, 0.469–0.997†
P=0.00251

- Evolution of Lung cancer



EGFR

Afatinib
Osimertinib
Dacomitinb

ROS1

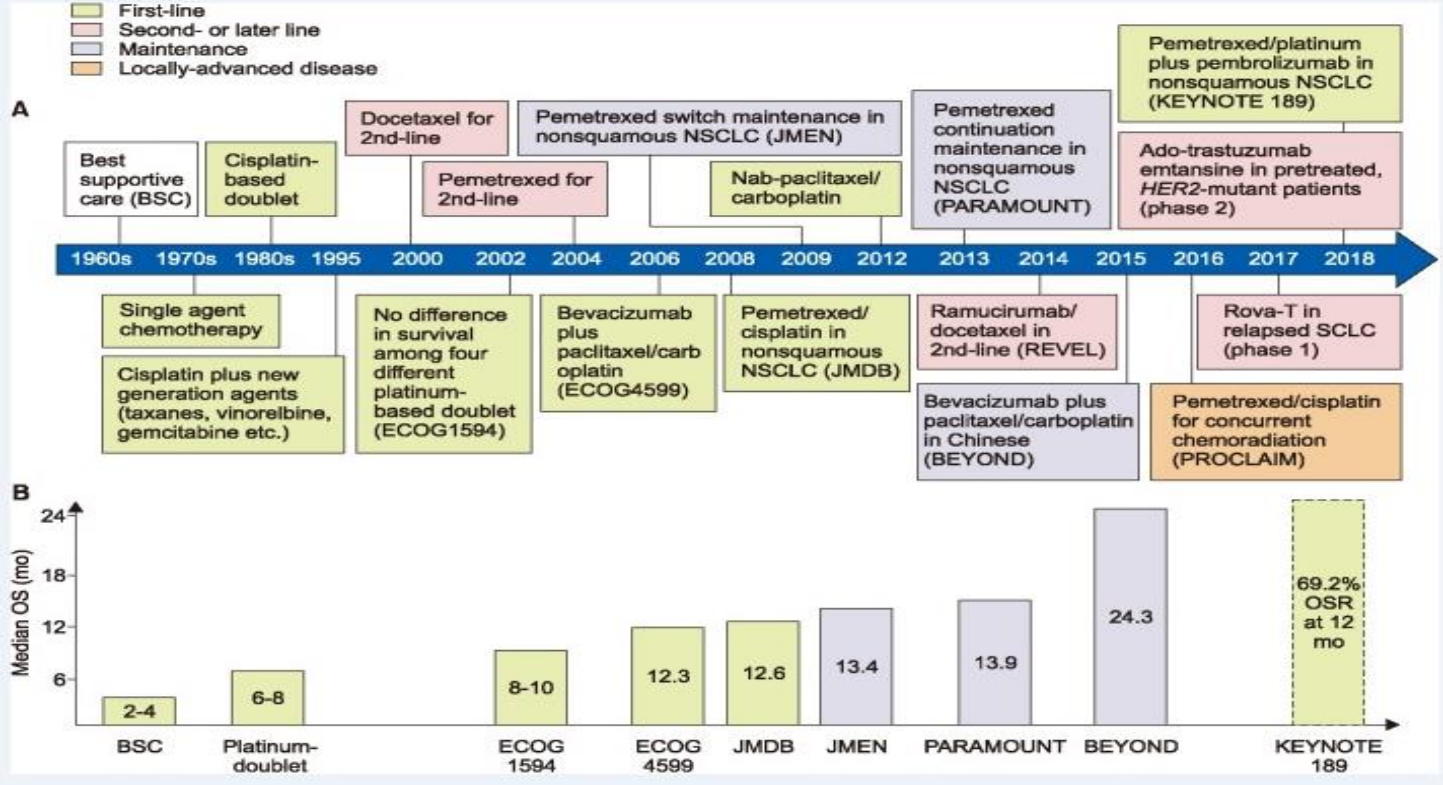
Crizotinib
Entrectinib

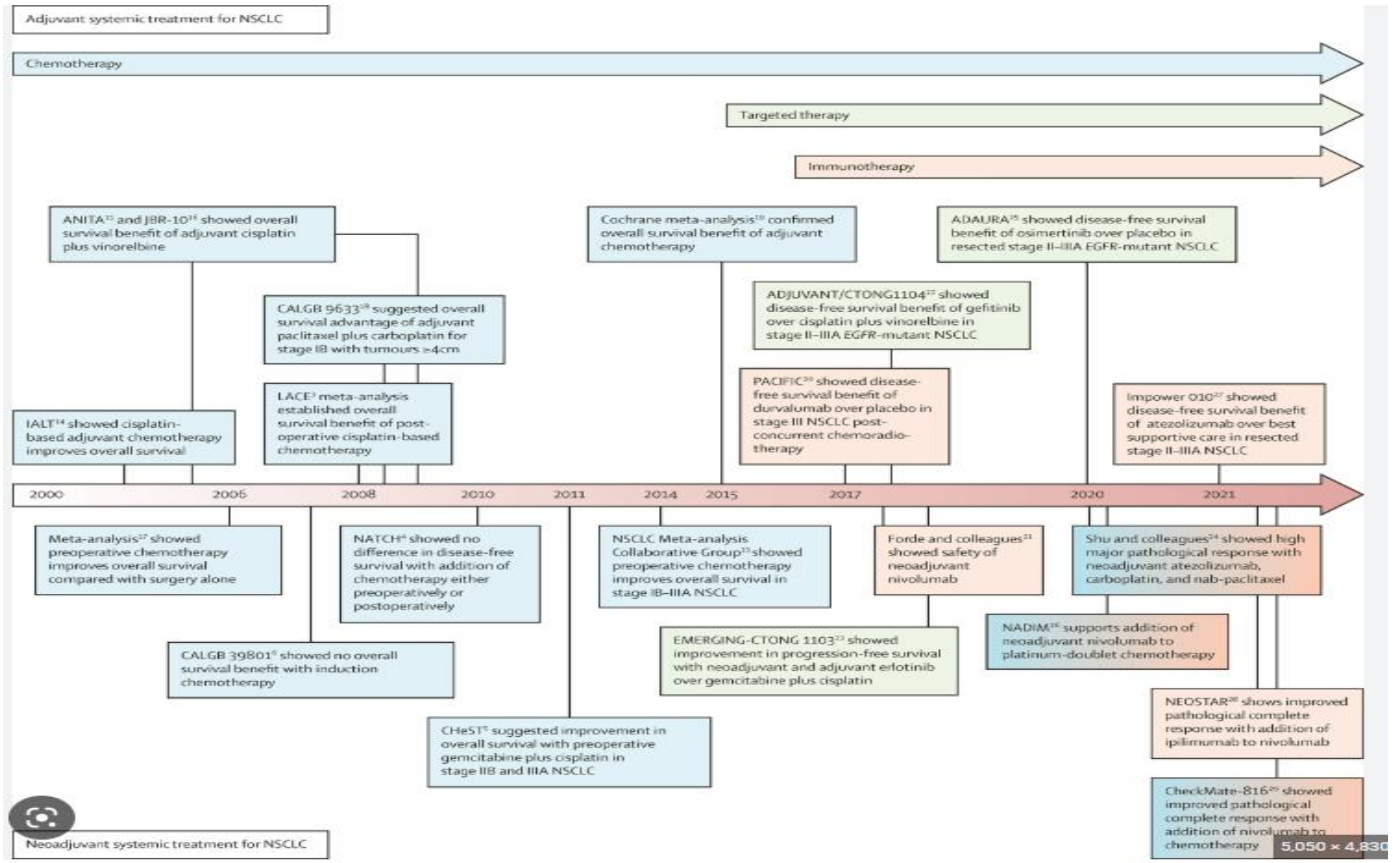
ALK

Ceritinib
Alectinib
Brigatinib
Lorlatinib

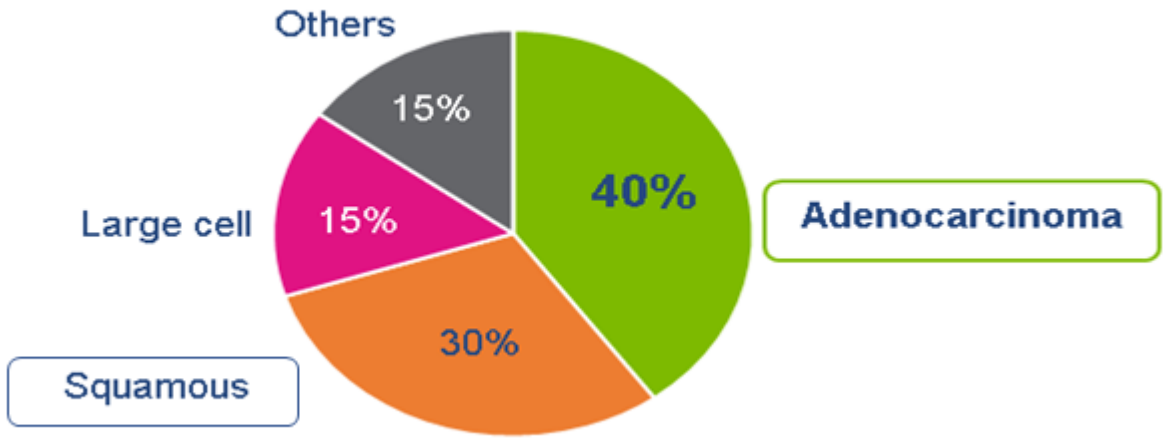
Check Point Inhibitors

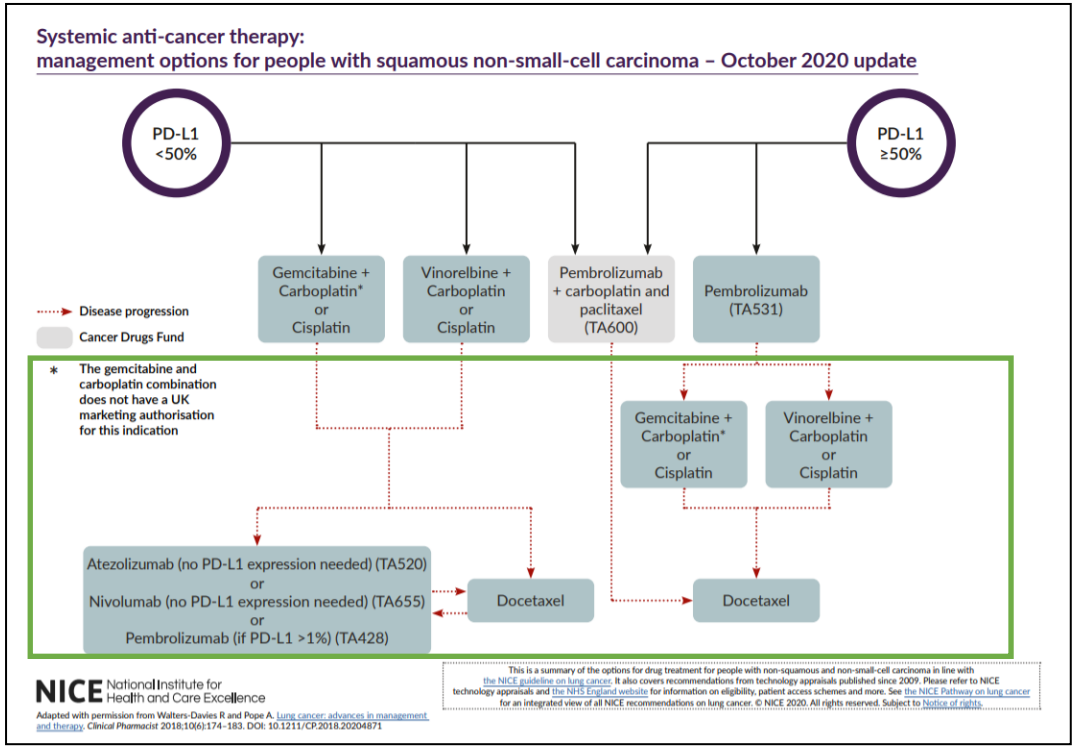
Nivolumab
Pembrolizumab
Atezolizumab
Durvalumab
Avelumab


First-line
Second- or later line
Maintenance
Locally-advanced disease
A
Best supportive care (BSC)
Cisplatin-based doublet
Docetaxel for 2nd-line
Pemetrexed for 2nd-line
Pemetrexed switch maintenance in nonsquamous NSCLC (JMEN)
Nab-paclitaxel/ carboplatin
Pemetrexed continuation maintenance in nonsquamous NSCLC (PARAMOUNT)
Pemetrexed/platinum plus pembrolizumab in nonsquamous NSCLC (KEYNOTE 189)
Ado-trastuzumab emtansine in pretreated, HER2-mutant patients (phase 2)
1960s 1970s 1980s 1995 2000 2002 2004 2006 2008 2009 2012 2013 2014 2015 2016 2017 2018
Single agent chemotherapy
Cisplatin plus new generation agents (taxanes, vinorelbine, gemcitabine etc.)
No difference in survival among four different platinum-based doublet (ECOG1594)
Bevacizumab plus paclitaxel/carboplatin (ECOG4599)
Pemetrexed/ cisplatin in nonsquamous NSCLC (JMDB)
Ramucirumab/ docetaxel in 2nd-line (REVEL)
Bevacizumab plus paclitaxel/carboplatin in Chinese (BEYOND)
Rova-T in relapsed SCLC (phase 1)
Pemetrexed/cisplatin for concurrent chemoradiation (PROCLAIM)
B
Median OS (mo)
24
18
12
6
2-4
6-8
8-10
12.3
12.6
13.4
13.9
24.3
69.2% OSR at 12 mo
BSC
Platinum-doublet
ECOG 1594
ECOG 4599
JMDB
JMEN
PARAMOUNT
BEYOND
KEYNOTE 189

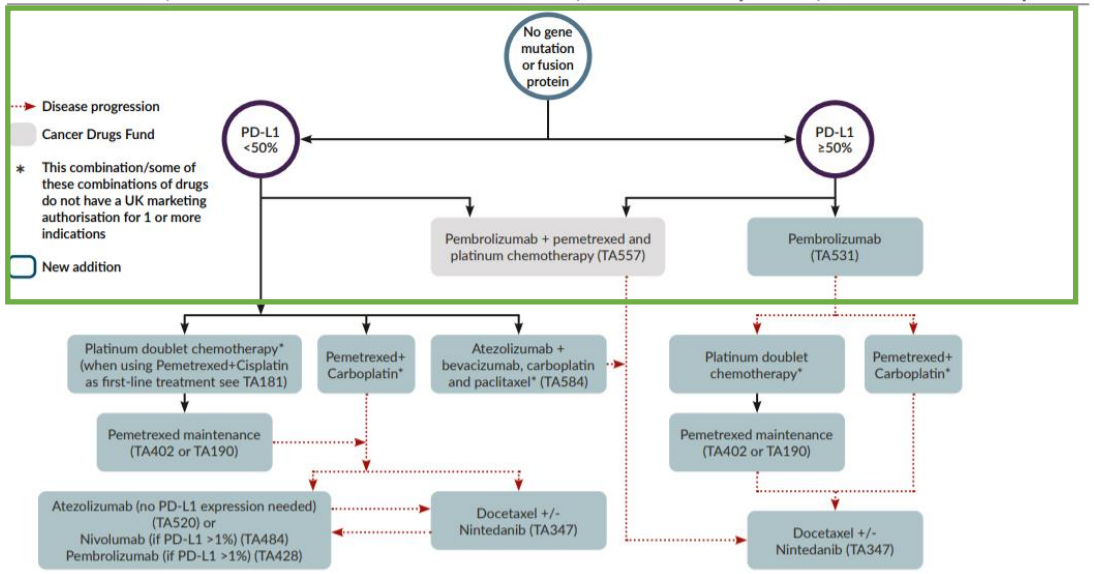

Adjuvant systemic treatment for NSCLC
Chemotherapy
Targeted therapy
Immunotherapy
ANITA[15] and JBR-10[16] showed overall survival benefit of adjuvant cisplatin plus vinorelbine
CALGB 9633[18] suggested overall survival advantage of adjuvant paclitaxel plus carboplatin for stage IB with tumours >4cm
IALT[14] showed cisplatin-based adjuvant chemotherapy improves overall survival
LACE[3] meta-analysis established overall survival benefit of post-operative cisplatin-based chemotherapy
Cochrane meta-analysis[19] confirmed overall survival benefit of adjuvant chemotherapy
ADAURA[25] showed disease-free survival benefit of osimertinib over placebo in resected stage II–IIIA EGFR-mutant NSCLC
ADJUVANT/CTONG1104[22] showed disease-free survival benefit of gefitinib over cisplatin plus vinorelbine in stage II–IIIA EGFR-mutant NSCLC
PACIFIC[20] showed disease-free survival benefit of durvalumab over placebo in stage III NSCLC post-concurrent chemoradiotherapy
Impower 010[27] showed disease-free survival benefit of atezolizumab over best supportive care in resected stage II–IIIA NSCLC
2000
2006
2008
2010
2011
2014
2015
2017
2020
2021
Meta-analysis[17] showed preoperative chemotherapy improves overall survival compared with surgery alone
NATCH[4] showed no difference in disease-free survival with addition of chemotherapy either preoperatively or postoperatively
CALGB 39801[6] showed no overall survival benefit with induction chemotherapy
NSCLC Meta-analysis Collaborative Group[13] showed preoperative chemotherapy improves overall survival in stage IB–IIIA NSCLC
CHeST[5] suggested improvement in overall survival with preoperative gemcitabine plus cisplatin in stage IIB and IIIA NSCLC
EMERGING-CTONG 1103[23] showed improvement in progression-free survival with neoadjuvant and adjuvant erlotinib over gemcitabine plus cisplatin
Forde and colleagues[21] showed safety of neoadjuvant nivolumab
Shu and colleagues[24] showed high major pathological response with neoadjuvant atezolizumab, carboplatin, and nab-paclitaxel
NADIM[26] supports addition of neoadjuvant nivolumab to platinum-doublet chemotherapy
NEOSTAR[28] shows improved pathological complete response with addition of ipilimumab to nivolumab
CheckMate-816[29] showed improved pathological complete response with addition of nivolumab to chemotherapy
Neoadjuvant systemic treatment for NSCLC
5,050 × 4,830

NSCLC can further be divided by histology:




Systemic anti-cancer therapy:
management options for people with squamous non-small-cell carcinoma – October 2020 update
PD-L1 <50%
PD-L1 ≥50%
Gemcitabine + Carboplatin* or Cisplatin
Vinorelbine + Carboplatin or Cisplatin
Pembrolizumab + carboplatin and paclitaxel (TA600)
Pembrolizumab (TA531)
Disease progression
Cancer Drugs Fund
* The gemcitabine and carboplatin combination does not have a UK marketing authorisation for this indication
Gemcitabine + Carboplatin* or Cisplatin
Vinorelbine + Carboplatin or Cisplatin
Atezolizumab (no PD-L1 expression needed) (TA520)
or
Nivolumab (no PD-L1 expression needed) (TA655)
or
Pembrolizumab (if PD-L1 >1%) (TA428)
Docetaxel
Docetaxel
NICE National Institute for Health and Care Excellence
This is a summary of the options for drug treatment for people with non-squamous and non-small-cell carcinoma in line with the NICE guideline on lung cancer. It also covers recommendations from technology appraisals published since 2009. Please refer to NICE technology appraisals and the NHS England website for information on eligibility, patient access schemes and more. See the NICE Pathway on lung cancer for an integrated view of all NICE recommendations on lung cancer. © NICE 2020. All rights reserved. Subject to Notice of rights.
Adapted with permission from Walters-Davies R and Pope A. Lung cancer: advances in management and therapy. Clinical Pharmacist 2018;10(6):174–183. DOI: 10.1211/CP.2018.20204871

Systemic anti-cancer therapy: management options for people with non-squamous (adenocarcinoma, large cell undifferentiated) carcinoma and non-small-cell carcinoma (non-otherwise specified) – December 2020 update



NICE National Institute for Health and Care Excellence

This is page 2 of a 2-page summary of drug treatment options for people with non-squamous and non-small-cell carcinoma in line with the NICE guideline on lung cancer. It also covers recommendations from technology appraisals published since 2009. Please refer to NICE technology appraisals and the NHS England website for information on eligibility, patient access schemes and more. See the NICE Pathway on lung cancer for an integrated view of all NICE recommendations on lung cancer.

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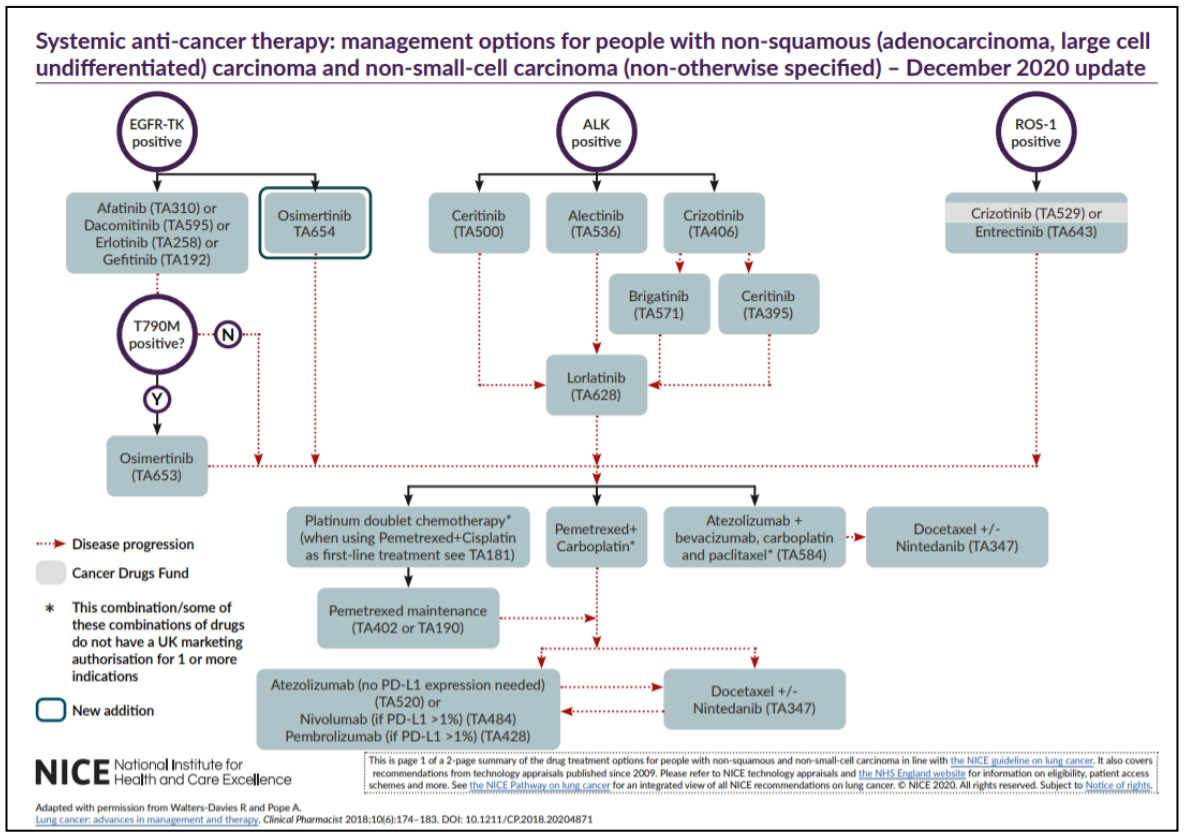
Lung cancer: advances in management and therapy. *Clinical Pharmacist* 2018;10(6):174–183. DOI: 10.1211/CP.2018.20204871


Systemic anti-cancer therapy: management options for people with non-squamous (adenocarcinoma, large cell undifferentiated) carcinoma and non-small-cell carcinoma (non-otherwise specified) – December 2020 update
EGFR-TK positive
Afatinib (TA310) or Dacomitinib (TA595) or Erlotinib (TA258) or Gefitinib (TA192)
Osimertinib TA654
T790M positive?
N
Y
Osimertinib (TA653)
ALK positive
Ceritinib (TA500)
Alectinib (TA536)
Crizotinib (TA406)
Brigatinib (TA571)
Ceritinib (TA395)
Lorlatinib (TA628)
ROS-1 positive
Crizotinib (TA529) or Entrectinib (TA643)
Platinum doublet chemotherapy* (when using Pemetrexed+Cisplatin as first-line treatment see TA181)
Pemetrexed+ Carboplatin*
Atezolizumab + bevacizumab, carboplatin and paclitaxel* (TA584)
Docetaxel +/- Nintedanib (TA347)
Pemetrexed maintenance (TA402 or TA190)
Atezolizumab (no PD-L1 expression needed) (TA520) or Nivolumab (if PD-L1 >1%) (TA484) Pembrolizumab (if PD-L1 >1%) (TA428)
Docetaxel +/- Nintedanib (TA347)
Disease progression
Cancer Drugs Fund
* This combination/some of these combinations of drugs do not have a UK marketing authorisation for 1 or more indications
New addition
NICE National Institute for Health and Care Excellence
This is page 1 of a 2-page summary of the drug treatment options for people with non-squamous and non-small-cell carcinoma in line with the NICE guideline on lung cancer. It also covers recommendations from technology appraisals published since 2009. Please refer to NICE technology appraisals and the NHS England website for information on eligibility, patient access schemes and more. See the NICE Pathway on lung cancer for an integrated view of all NICE recommendations on lung cancer. © NICE 2020. All rights reserved. Subject to Notice of rights.
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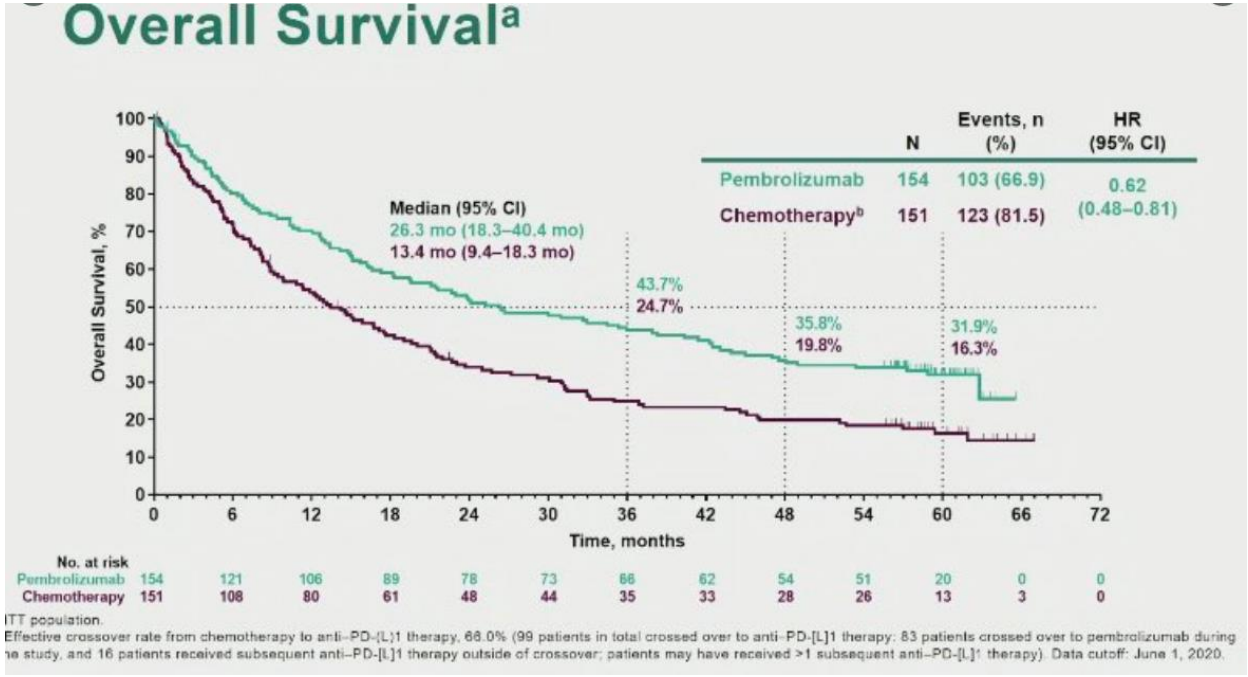
Lung cancer: advances in management and therapy. Clinical Pharmacist 2018;10(6):174–183. DOI: 10.1211/CP.2018.20204871

Immunotherapy

Keynote 024 - 5 year overall OS

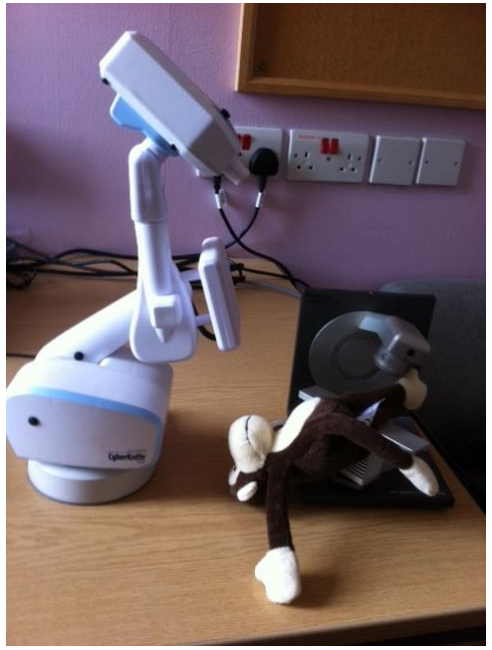


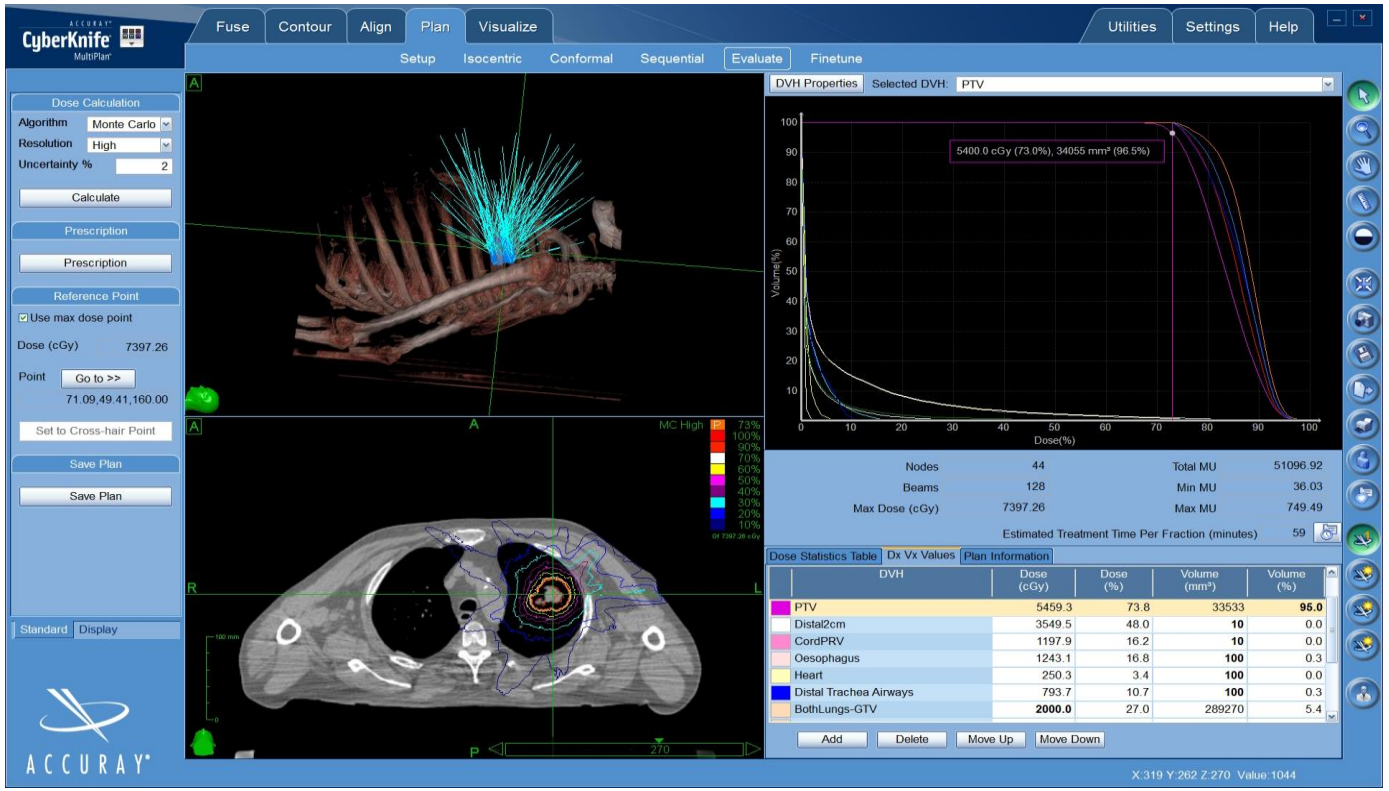
First-line, first- and second-generation EGFR-TKI therapy versus chemotherapy for advanced EGFR+ NSCLC

Study name	Study type	Study population	Patients with EGFRm tumours	Response rate (%)	Median PFS (months)	Median OS (months)
IPASS[1,2] (gefitinib)	Retrospective sub-group analysis	East Asian	261	71.2 vs. 47.3	9.5 vs. 6.3	21.6 vs. 21.9
First-SIGNAL[1,3] (gefitinib)	Retrospective sub-group analysis	Korean	42	55.4 vs. 46.0	5.8 vs. 6.4	22.3 vs. 22.9
NEJGSG 002[1,4] (gefitinib)	Prospective selection	Japanese	230	73.7 vs. 30.7	10.8 vs. 5.4	27.7 vs. 26.6
WJTOG 3405[1,5] (gefitinib)	Prospective selection	Japanese	172	62.1 vs. 32.2	9.2 vs. 6.3	36.0 vs. 39.0
OPTIMAL[1,6,7] (erlotinib)	Prospective selection	Chinese	154	83.0 vs. 36.0	13.1 vs. 4.6	22.8 vs. 27.8
EURTAC[1,8] (erlotinib)	Prospective selection	French, Italian, Spanish	173	64.0 vs. 18.0	9.7 vs. 5.2	19.3 vs. 19.5
LUX-Lung 3[1,9] (afatinib)	Prospective selection	Asian, European, North American, South American, Australian	345	56.1 vs. 22.6	11.1 vs. 6.9	28.2 vs. 28.2

EGFRm, epidermal growth factor receptor mutation; OS, overall survival; PFS, progression-free survival.

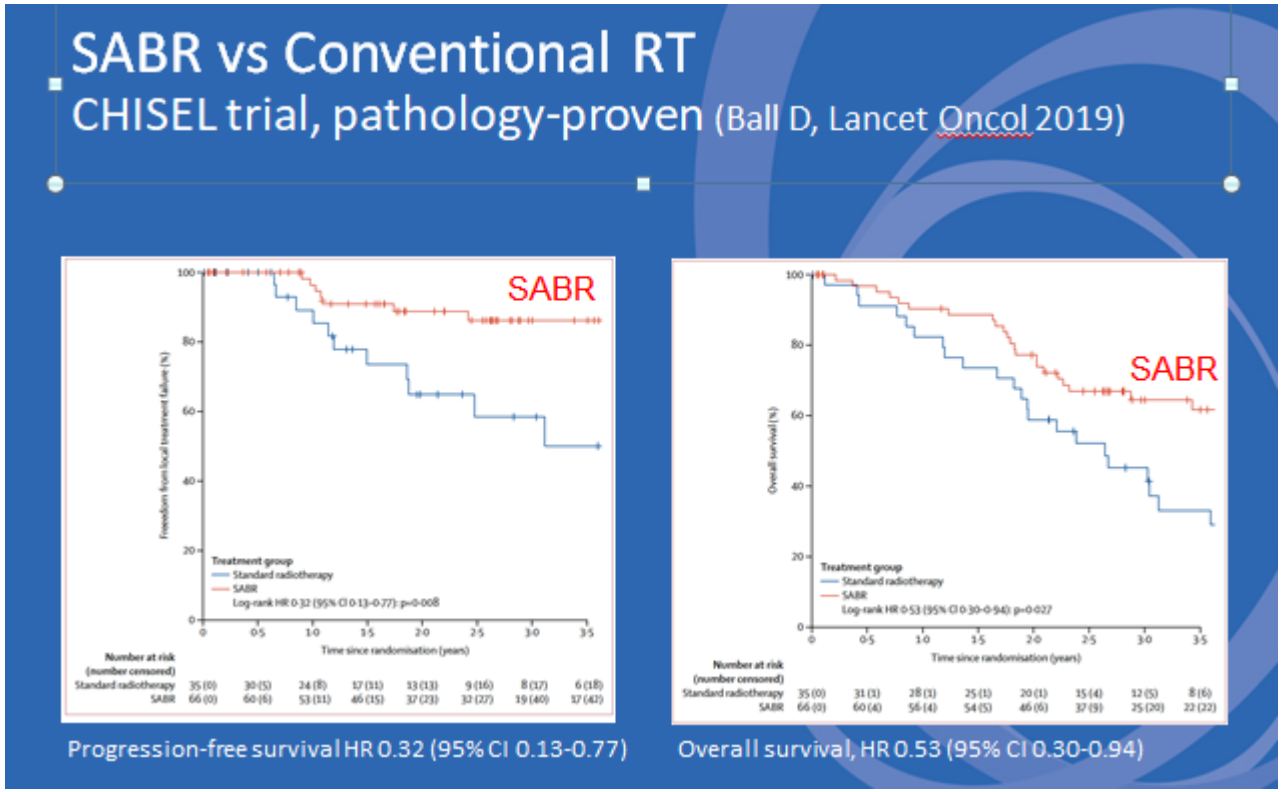
Radiotherapy





SABR – Stereotactic Ablative Body Radiotherapy

- Time-honoured gold standard for the treatment of Stage I lung cancer is surgical resection
- Associated with five-year overall survival rates in the range of 60-70%
- Conventional radiotherapy alone:
  - 5 year survival 10-30%
  - 5 year local control 30-70%



HIV and Lung Cancer

- People living with HIV have a higher risk of developing lung cancer and several other cancers compared with the general population.
- HIV-positive people also appear to get cancer at younger ages.
- People with HIV are more likely to smoke than the general population, but the risk is elevated even for non-smokers.
- HIV treatment itself does not cause lung cancer.

HIV and Lung Cancer

- Most clinical trials of newer targeted therapies and immunotherapies have not enrolled HIV-positive people

HIV and Lung Cancer

- Collaborative, Holistic working
  - Clinicians, Pharmacy, CNS
- Liverpool HIV Interactions (hiv-druginteractions.org)
- https://cancer-druginteractions.org/checker

BHIVA
British HIV Association

2023 Spring Conference

Mon 24th – Wed 26th April
Gateshead, UK