



Área de formación virtual SEOM

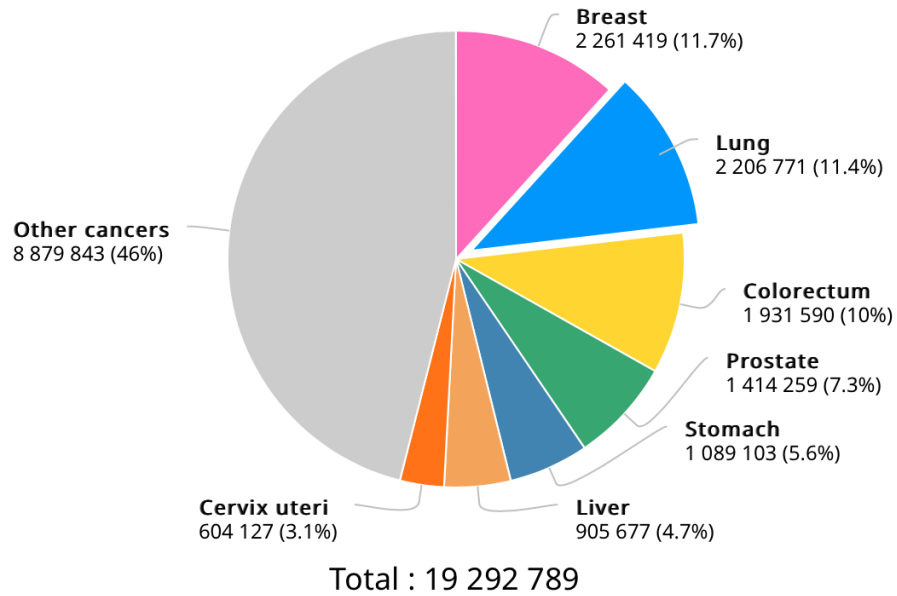
**Pulmón no microcítico.
Enfermedad locorregional resecable e irresecable.**

*Dra. Ivana Sullivan
Instituto Oncológico Dr. Rosell
Hospital de la Santa Creu i Sant Pau
Barcelona*

- Epidemiología
 - Incidencia y supervivencia
- Diagnóstico
 - Estadificación mediastínica
- Enfermedad locorregional
 - Definición y estrategias de tratamiento
- Enfermedad locorregional: nuevos estándares de tratamiento
 - Neoadyuvancia → Cirugía
 - Cirugía → Adyuvancia
 - Tratamiento peroperatorio: Neoadyuvancia → Cirugía → Adyuvancia
 - Enfermedad irresecable
- Conclusiones

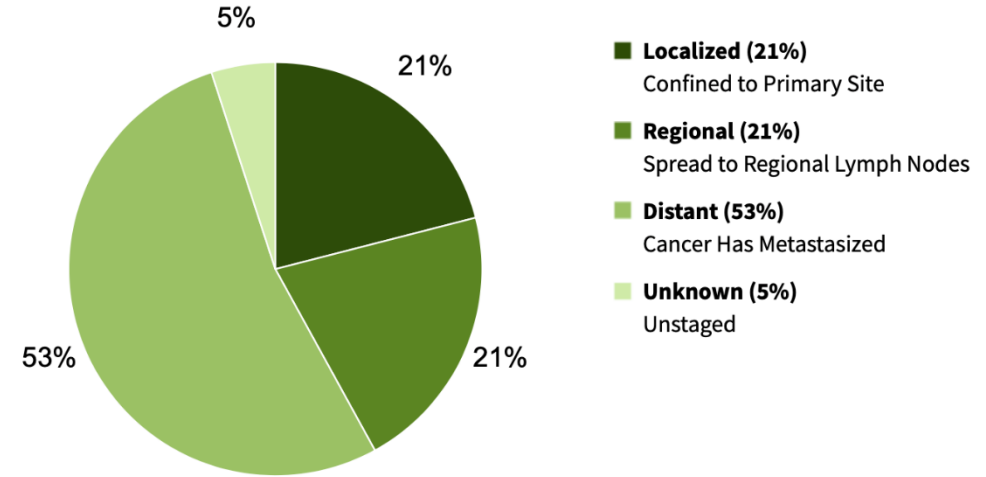
Incidencia

Estimated number of new cases in 2020, World, both sexes, all ages



Data source: GLOBOCAN 2020
 Graph production: Global Cancer Observatory (<http://gco.iarc.fr/>)
 © International Agency for Research on Cancer 2024

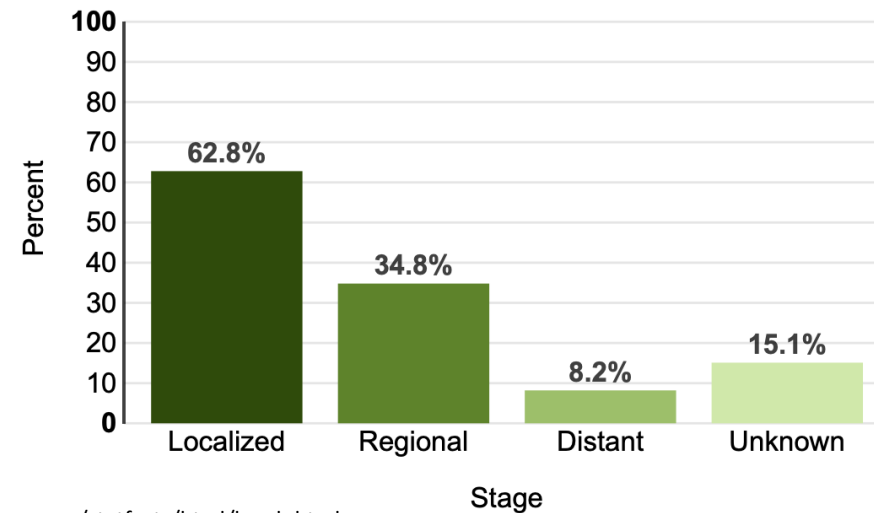
Percent of Cases by Stage



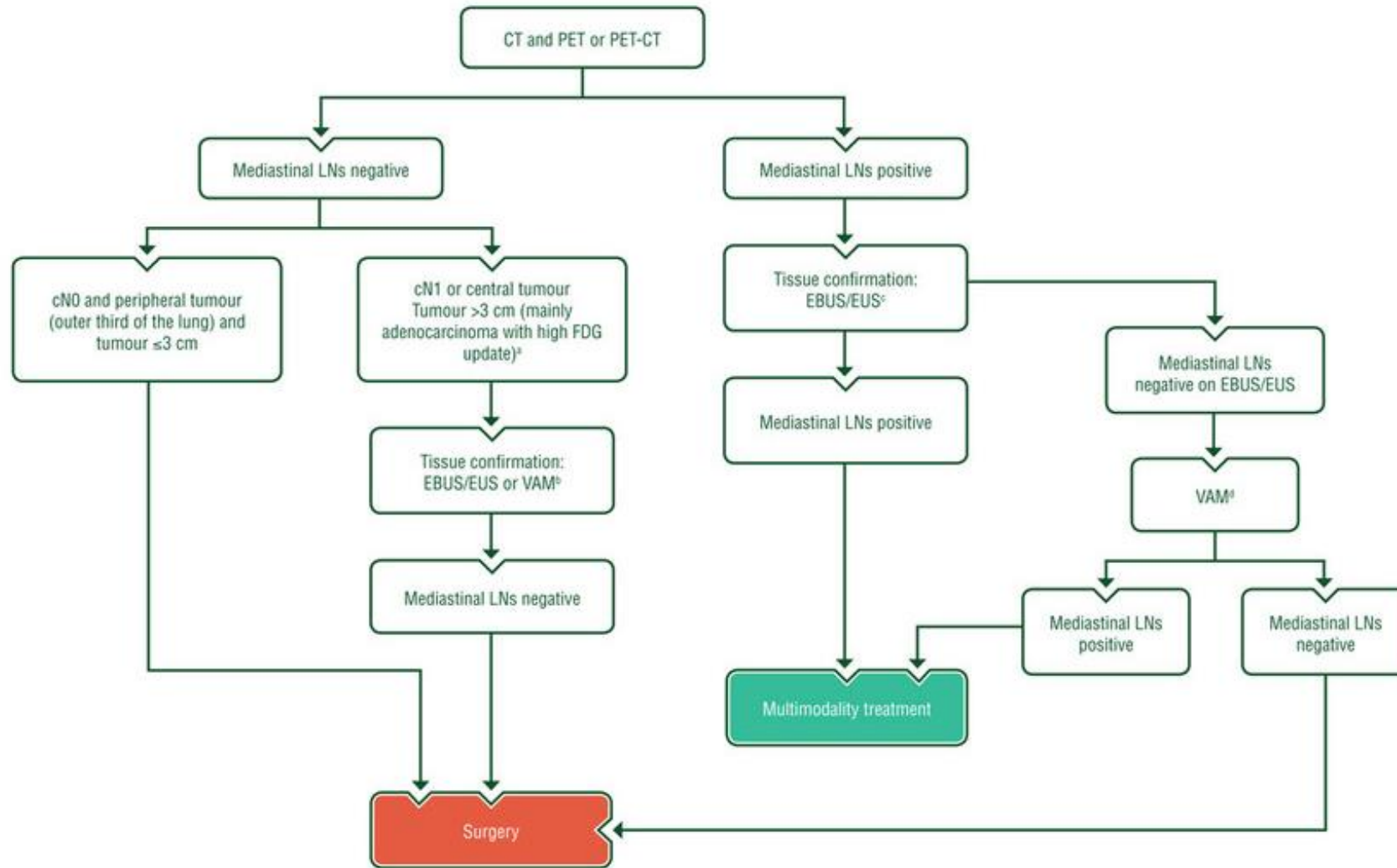
- **Localized (21%)**
Confined to Primary Site
- **Regional (21%)**
Spread to Regional Lymph Nodes
- **Distant (53%)**
Cancer Has Metastasized
- **Unknown (5%)**
Unstaged

Supervivencia

5-Year Relative Survival



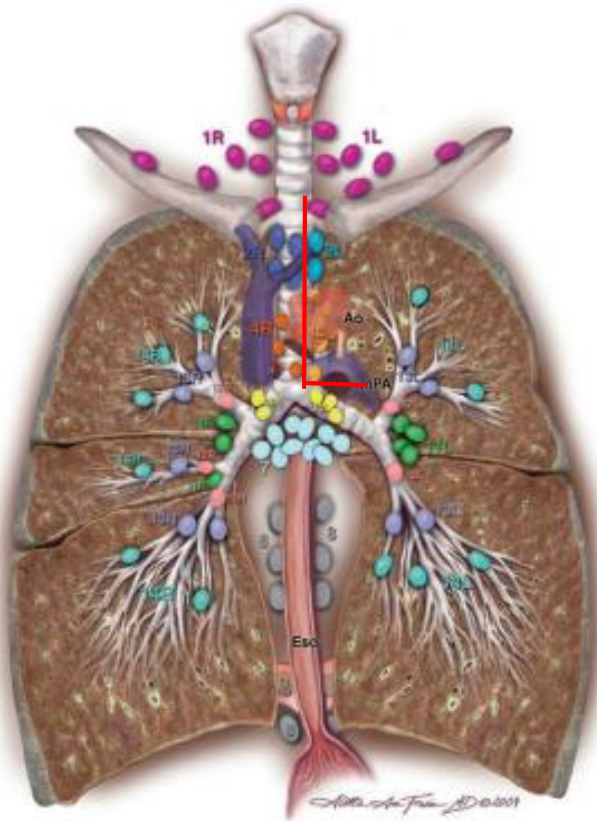
<https://seer.cancer.gov/statfacts/html/lungb.html>



Diagnóstico

Estadificación mediastínica

- LN MAP



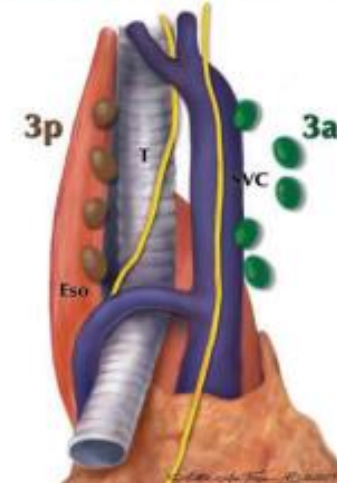
Supraclavicular zone
1 Low cervical, supraclavicular, and sternal notch nodes

Superior mediastinal nodes
Upper zone
2R Upper paratracheal (right)
2L Upper paratracheal (left)
3a Prevascular
3p Retrotracheal
4R Lower paratracheal (right)
4L Lower paratracheal (left)

Aortic nodes
AP zone
5 Subaortic
6 Para-aortic (ascending aorta or phrenic)



Inferior mediastinal nodes
Subcarinal zone
7 Subcarinal
Lower zone
8 Paraesophageal (below carina)
9 Pulmonary ligament



N1 nodes
Hilar/interlobar zone
10 Hilar
11 Interlobar
Peripheral zone
12 Lobar
13 Segmental
14 Subsegmental

The IASLC lung cancer staging project. A proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. J Thorac Oncol 2009;4:568-77.

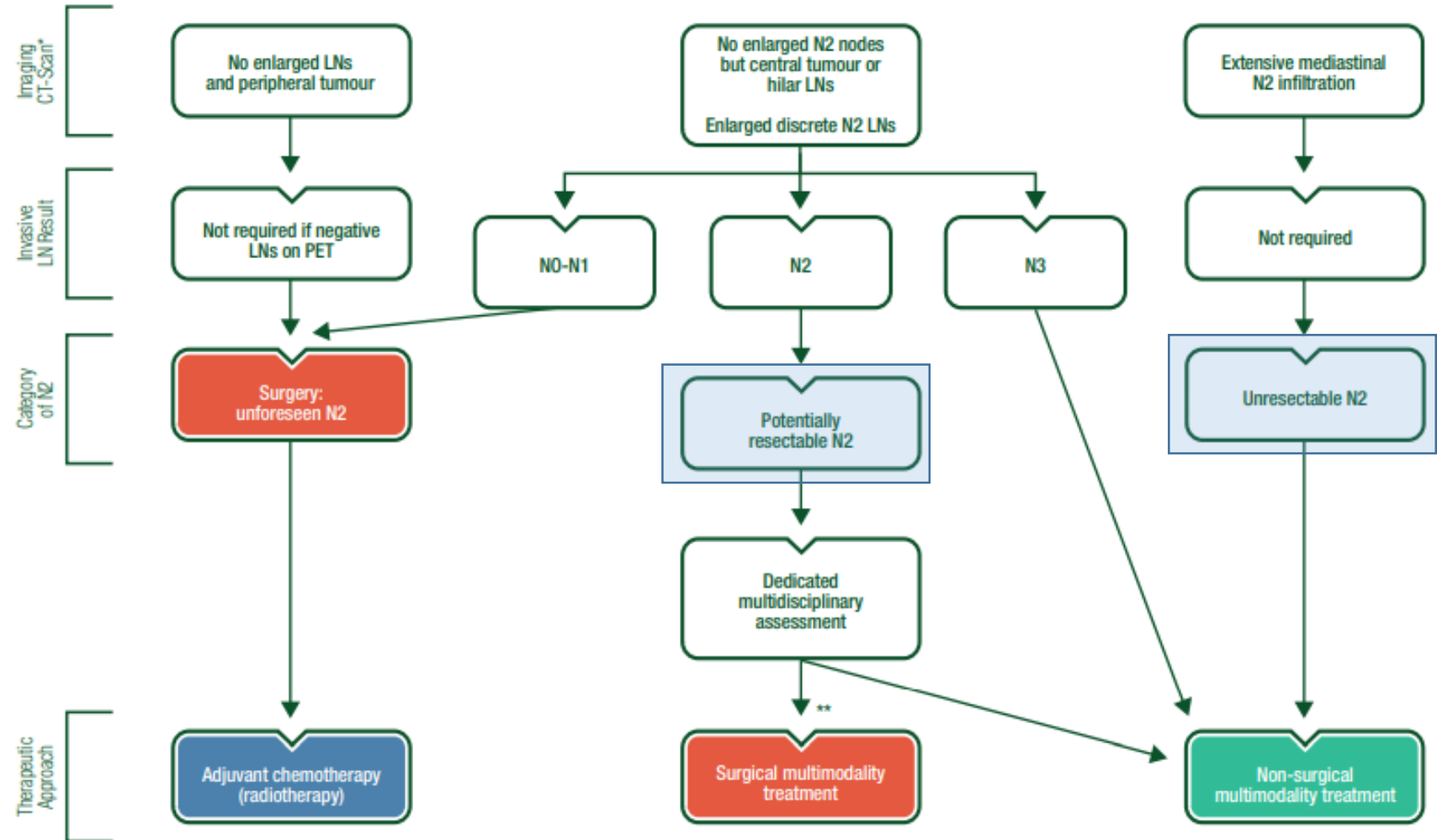
Diagnóstico

Estadificación mediastínica

Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[†]

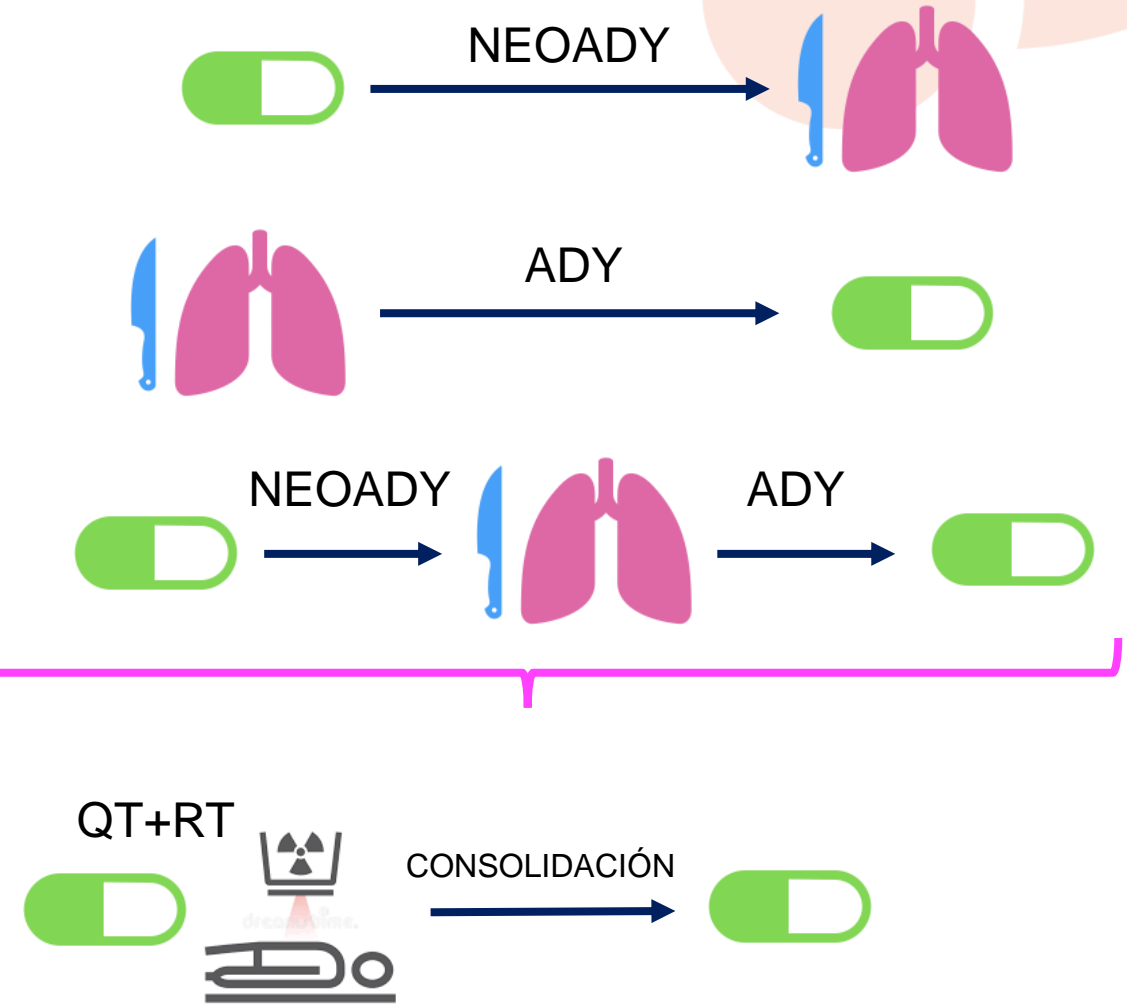
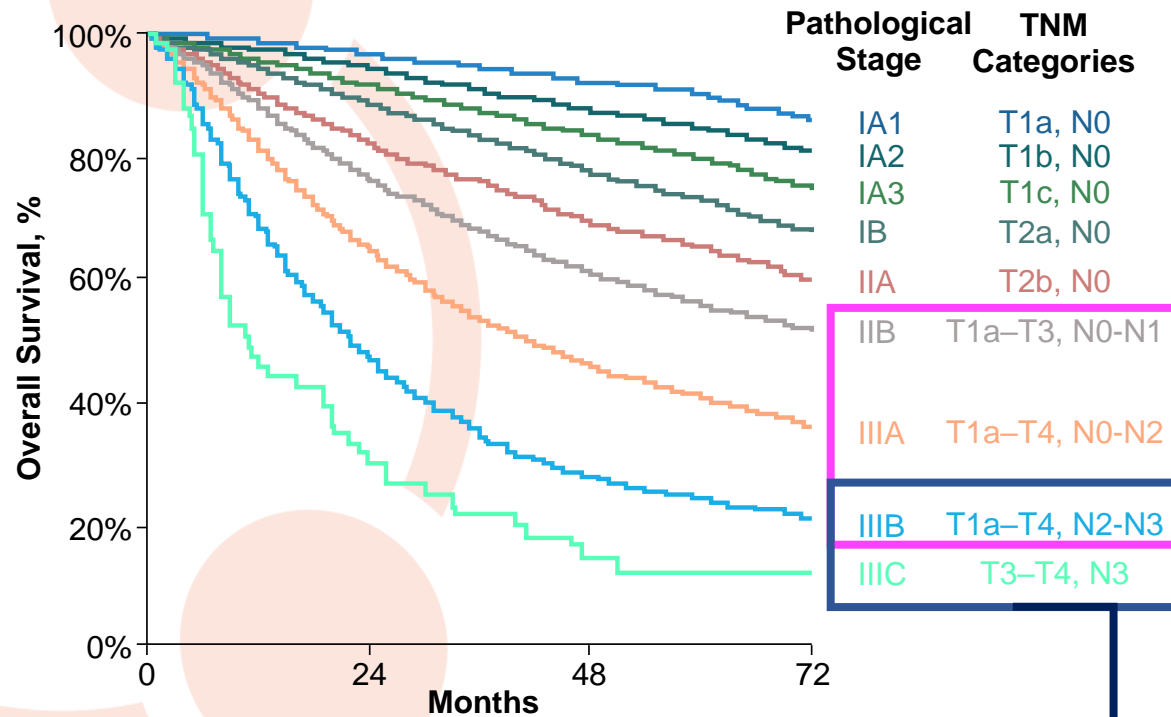
P. E. Postmus¹, K. M. Kerr², M. Oudkerk³, S. Senan⁴, D. A. Waller⁵, J. Vansteenkiste⁶, C. Escriu¹ & S. Peters⁷, on behalf of the ESMO Guidelines Committee*

Annals of Oncology 28 (Supplement 4): iv1–iv21, 2017
doi:10.1093/annonc/mdx222



Enfermedad locorregional

Definición y estrategias de tratamiento

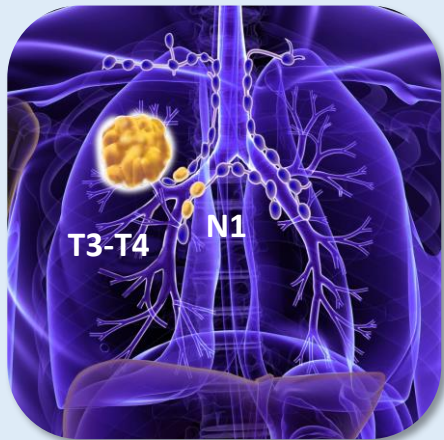


IASLC=International Association for the Study of Lung cancer; TNM=tumor, node, metastasis. Goldstraw P et al. *J Thorac Oncol.* 2015;11(1):39-51; Canadian Cancer Society. Prognosis and survival for lung cancer. Updated January 2022. <https://cancer.ca/en/cancer-information/cancer-types/lung/prognosis-and-survival.ca>

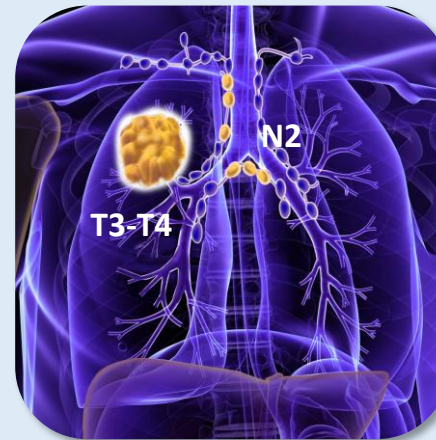
Enfermedad locorregional

Estadio III: enfermedad heterogénea que requiere de un abordaje homogéneo

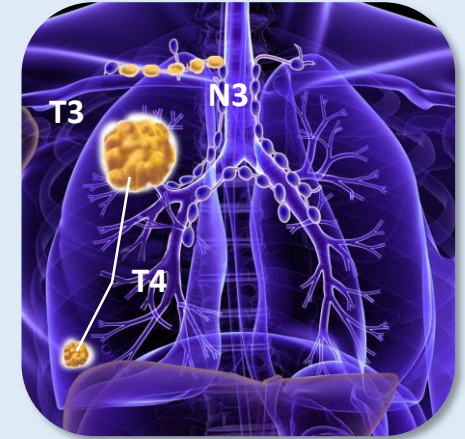
STAGE IIIA



STAGE IIIB



STAGE IIIC



Enfermedad locorregional: nuevos estándares de tratamiento

Cirugía → Adyuvancia

IMpower 010

Completely resected stage IB-IIIa NSCLC per UICC/AJCC v7

- Stage IB tumors ≥4 cm
- ECOG 0-1
- Lobectomy/pneumonectomy
- Tumor tissue for PD-L1 analysis

Cisplatin + pemetrexed, gemcitabine, docetaxel or vinorelbine
1-4 cycles
N=1280

R
1:1

No crossover

Atezolizumab
1200 mg q21d
16 cycles
N=1005

BSC
N=1005

Survival follow-up

12% stage I, ~50% stage II, 40% stage III
55% PD-L1+; ~15% known driver alteration

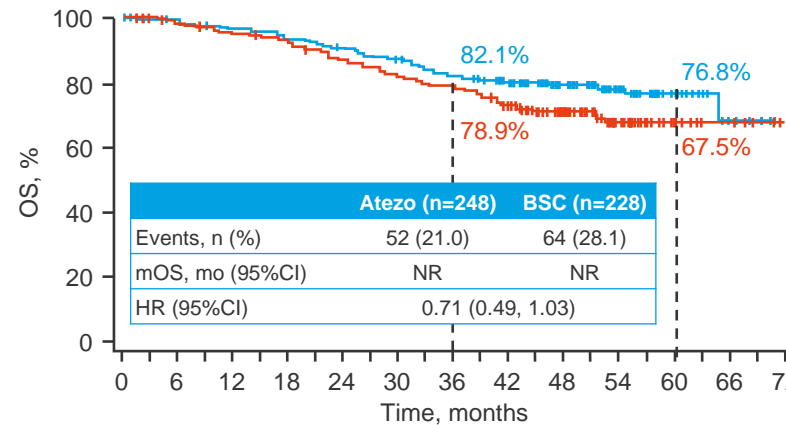
Primary endpoints

- Investigator-assessed DFS tested hierarchically:
 1. PD-L1 TC ≥1% (per SP263) Stage II-IIIa population
 2. All-randomised Stage II-IIIa population
 3. ITT population (Stage IB-IIIa)

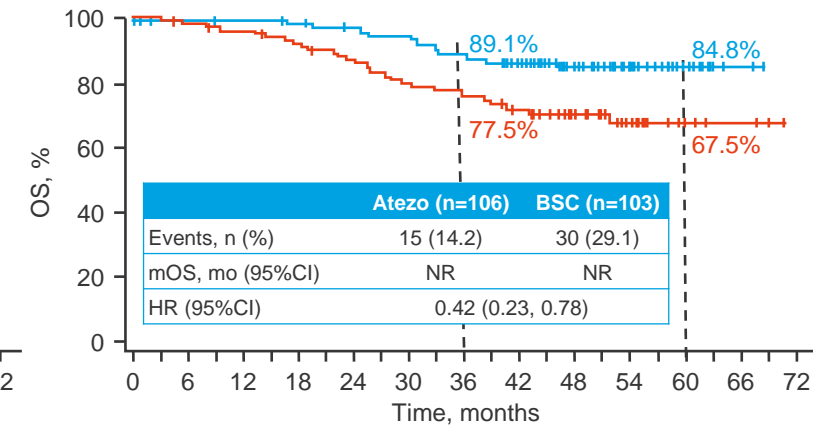
Julio 2023 aprobación de atezolizumab en estadios II-IIIa operados + QT adyuvante basada en platino PD-L1 ≥ 50%

Overall survival

PD-L1 TC ≥1% (stage II-IIIa)



PD-L1 TC ≥50% (stage II-IIIa) excluding EGFR/ALK+



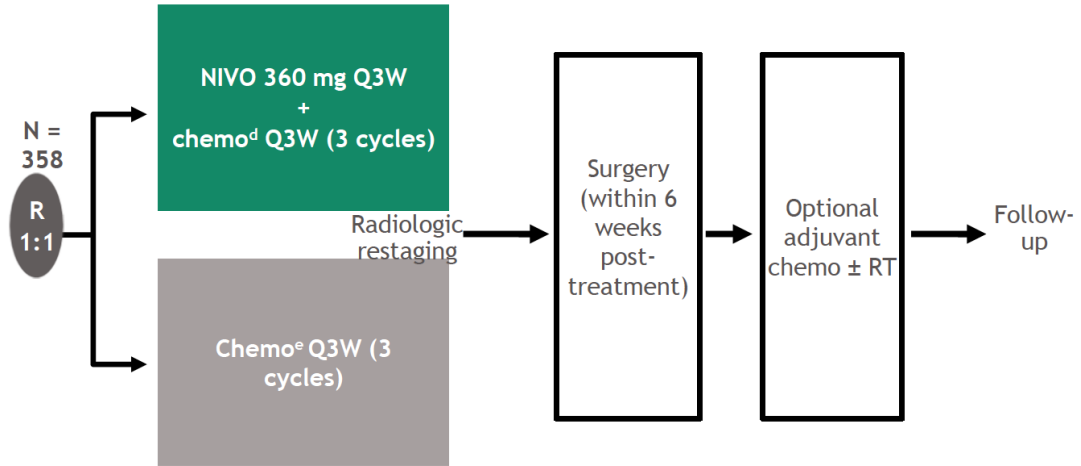
Enfermedad locorregional: nuevos estándares de tratamiento

Neoadyuvancia → Cirugía

Key eligibility criteria

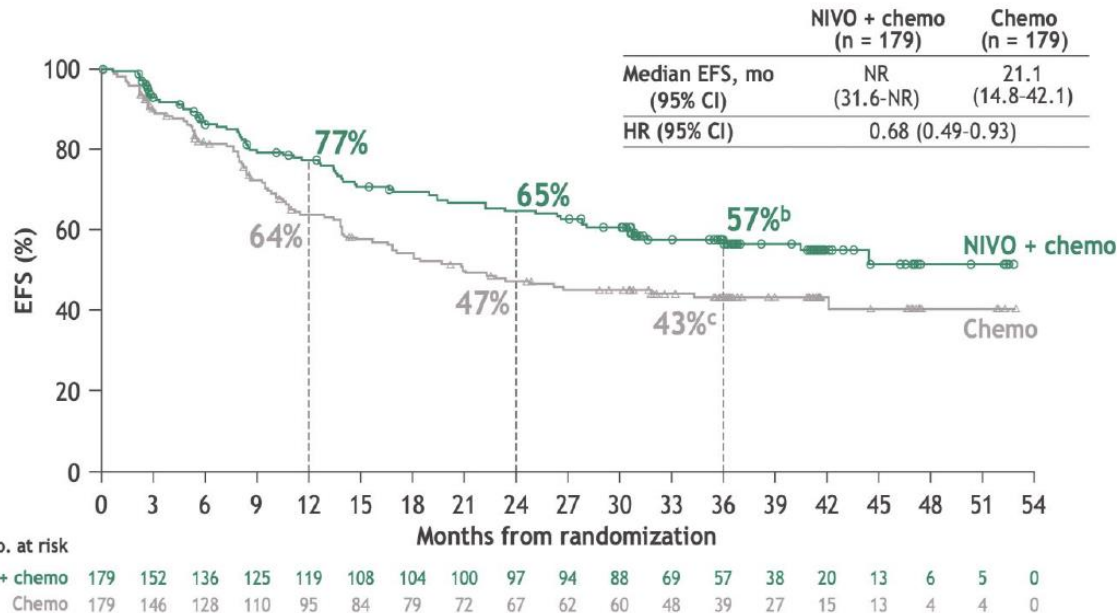
- Newly diagnosed, resectable, stage IB (≥ 4 cm)-IIIA NSCLC (per TNM 7th edition)
- ECOG PS 0-1
- No known sensitizing *EGFR* mutations or *ALK* alterations

CHECKMATE 816



37% stage IB/II; 63% stage IIIA
50% PD-L1 >1%
No *EGFR/ALK*

pCR 24%
 mPR 37%

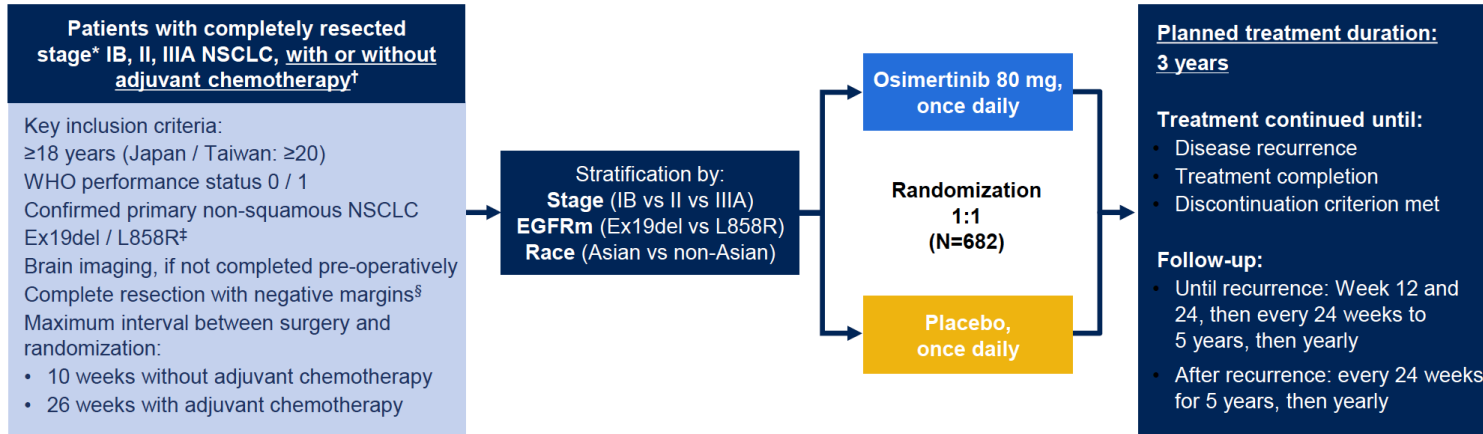


Diciembre 2023 aprobación de quimioterapia + nivolumab neoadyuvante PD-L1 ≥ 1%

Enfermedad locorregional: nuevos estándares de tratamiento

Cirugía → Adyuvancia en CPCNP EGFR mutado

ADAURA

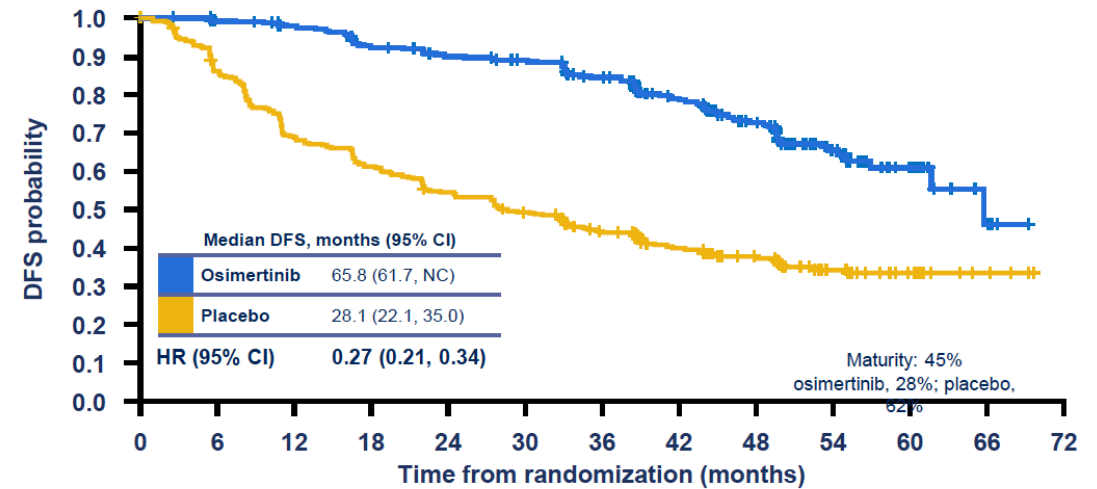


31% stage IB, ~35% stage II, 34% stage III
 100% known EGFRmut (Del19/L858R ex21)

Endpoints

- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

• Diciembre 2022 aprobación de osimertinib en estadios IB-IIIa tras cirugía



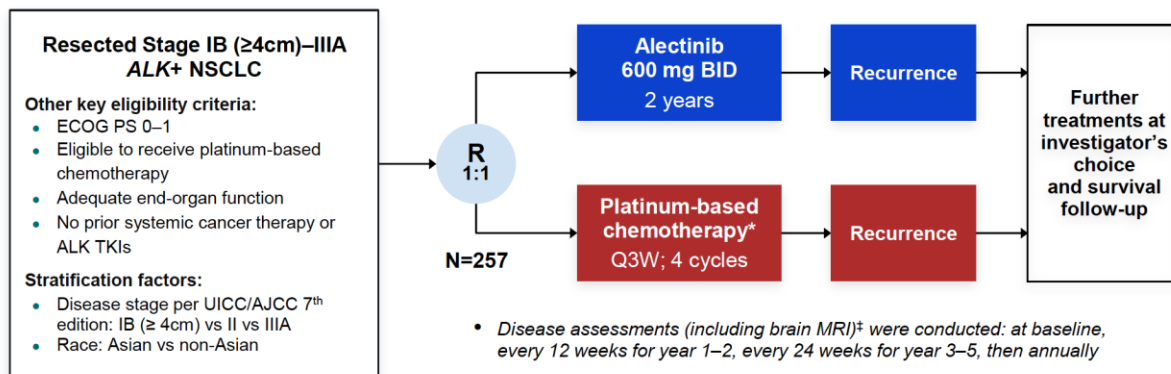
No. at risk	0	6	12	18	24	30	36	42	48	54	60	66	72
Osimertinib	339	316	307	289	278	270	249	201	139	73	33	5	0
Placebo	343	288	230	205	181	162	137	115	84	48	25	4	0

Tsuboi et al. NEJM 2023

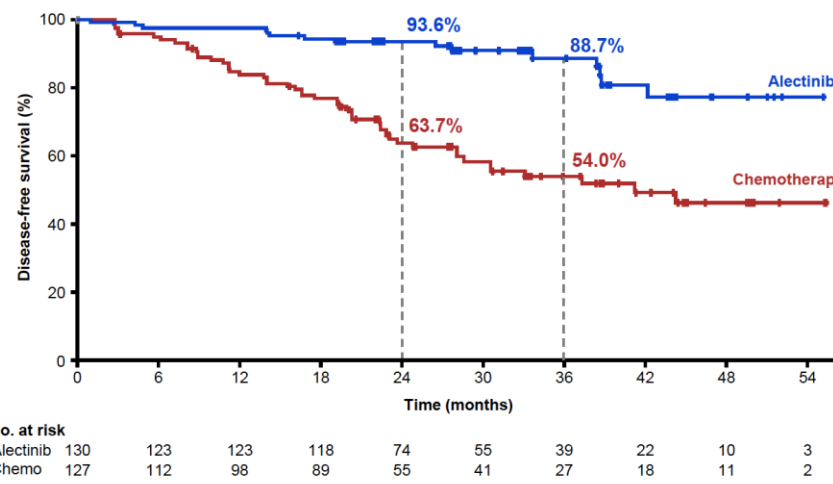
Enfermedad locorregional: nuevos estándares de tratamiento

Cirugía → Adyuvancia en CPCNP ALK translocado

ALINA



- Primary endpoint**
- DFS per investigator,[§] tested hierarchically:
 - Stage II-III A → ITT (Stage IB-III A)
- Other endpoints**
- CNS disease-free survival
 - OS
 - Safety



	Alectinib (N=130)	Chemotherapy (N=127)
Patients with event	15 (12%)	50 (39%)
Death	0	1
Recurrence	15	49
Median DFS, months (95% CI)	Not reached	41.3 (28.5, NE)
DFS HR (95% CI)	0.24 (0.13, 0.43) p†<0.0001	

Pendiente de aprobaciones

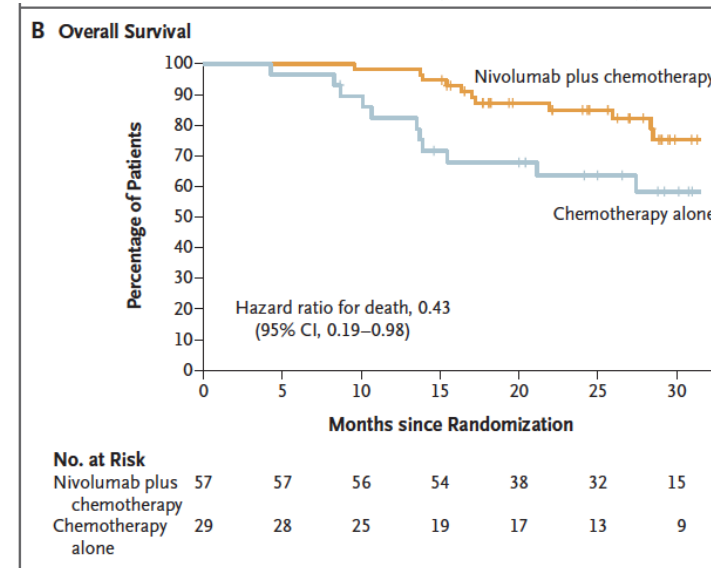
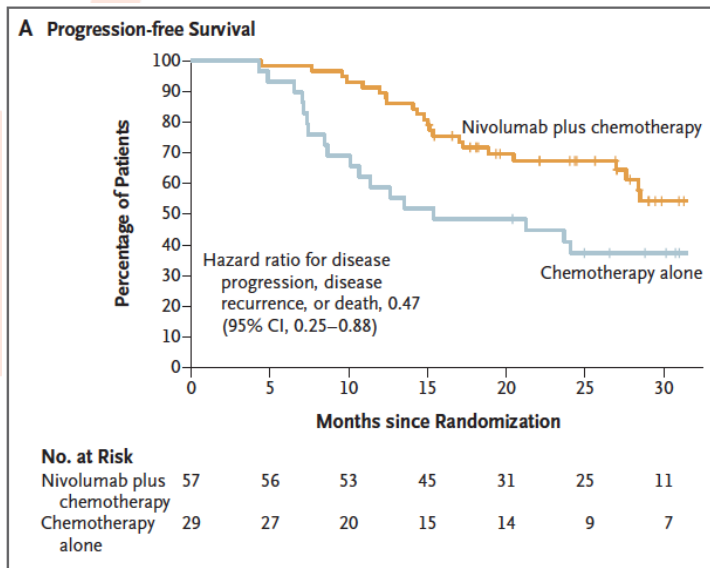
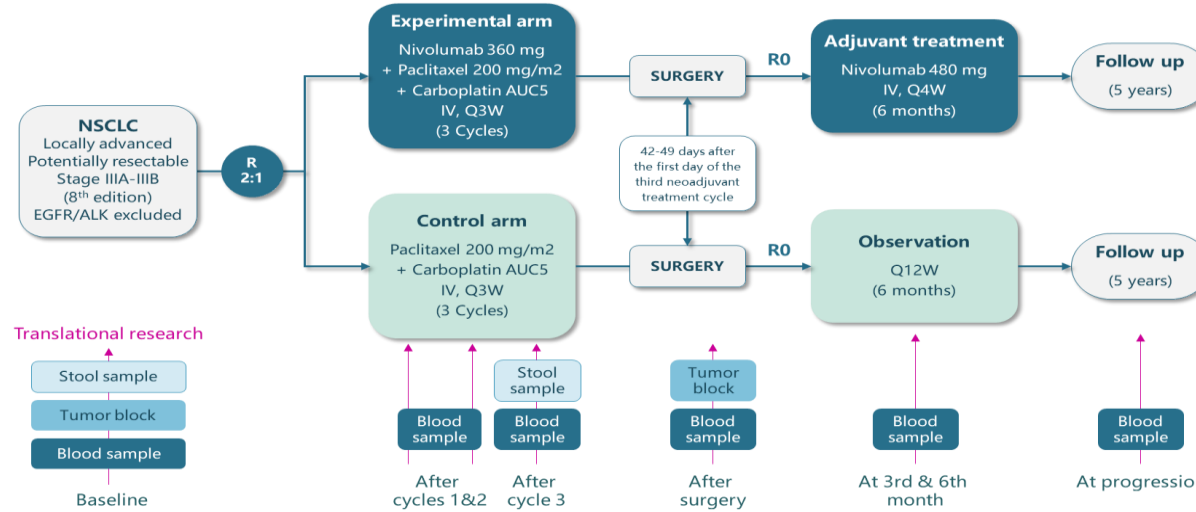
At the data cutoff date, OS data were immature with only 6 (2.3%) OS events reported[§]

Median survival follow up: alectinib, 27.8 months; chemotherapy, 28.4 months

Enfermedad locorregional: nuevos estándares de tratamiento

Neoadyuvancia → Cirugía → Adyuvancia

NADIM II - GRUPO ESPAÑOL DE CÁNCER DE PULMÓN



Enfermedad locorregional: nuevos estándares de tratamiento

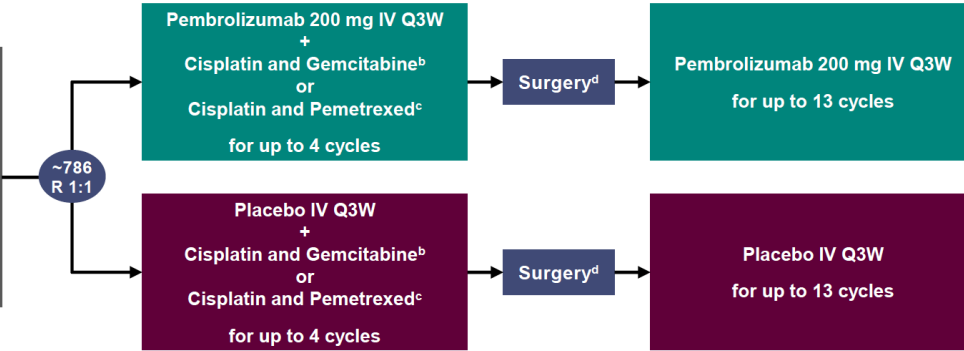
Neoadyuvancia → Cirugía → Adyuvancia

OTROS ENSAYOS CLÍNICOS

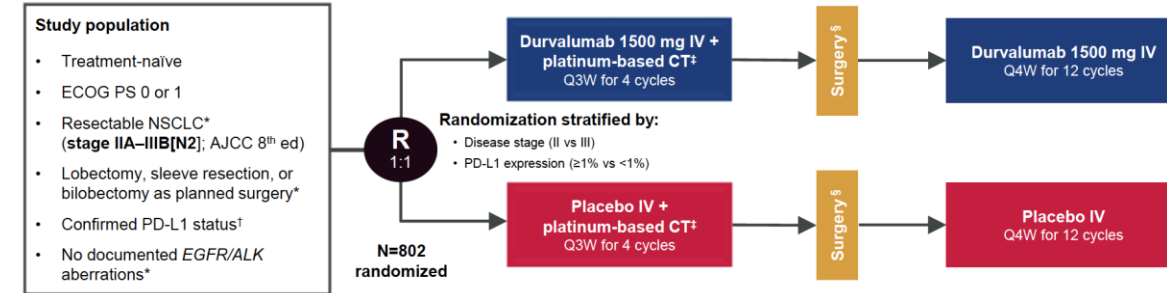
KEYNOTE-671



- Key Eligibility Criteria**
- Pathologically confirmed, resectable stage II, IIIA, or IIIB (N2) NSCLC per AJCC v8
 - No prior therapy
 - Able to undergo surgery
 - Provision of tumor sample for PD-L1 evaluation^a
 - ECOG PS 0 or 1

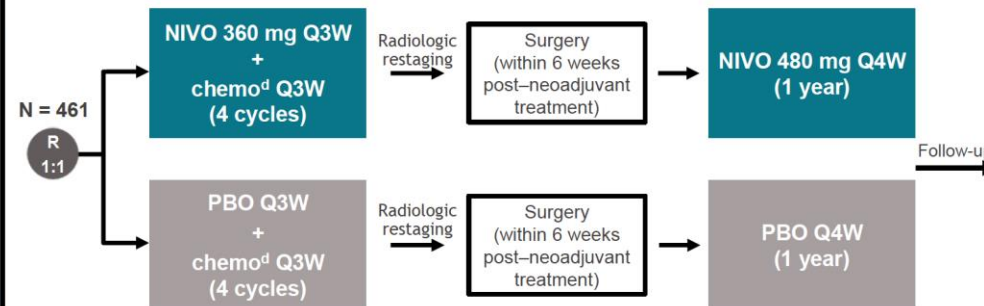


AEGEAN

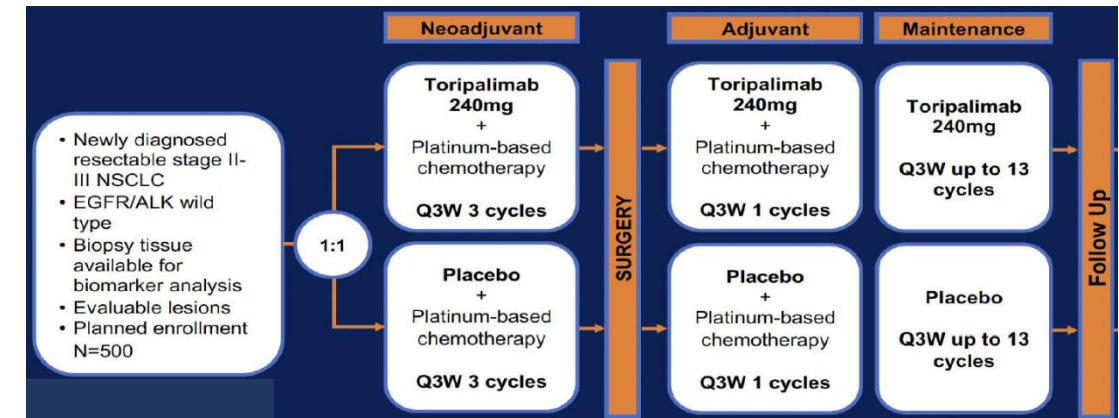


CHECKMATE-77T

- Key eligibility criteria**
- Resectable, stage IIA (> 4 cm)–IIIB (N2) NSCLC (per AJCC 8th edition)
 - No prior systemic anti-cancer treatment
 - ECOG PS 0–1
 - No EGFR mutation/known ALK alterations^b
- Stratified by** histology (NSQ vs SQ) disease stage (II vs III), and tumor PD-L1^c (≥ 1% vs < 1% vs not evaluable/indeterminate)



NEOTORCH



Enfermedad locorregional “irreseccable”

Quimiorradioterapia

RT vs sequential
chemoradiotherapy

OS HR: 0.88 (95% CI, 0.81-0.96)

RT vs concomitant
chemoradiotherapy

OS HR: 0.89 (95% CI, 0.81-0.98)

Sequential vs concurrent
chemoradiotherapy

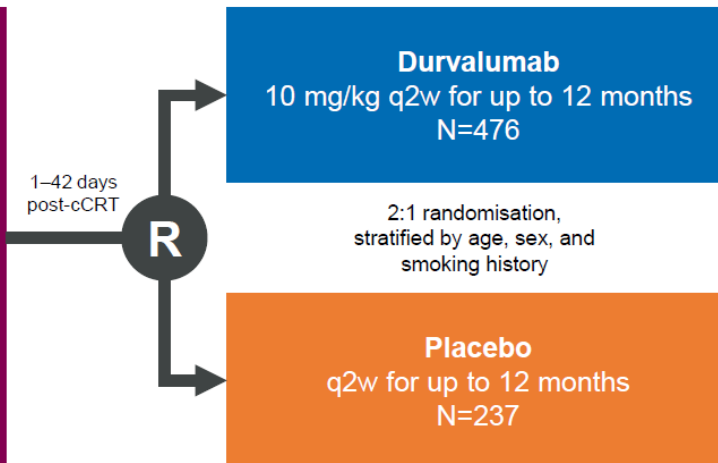
OS HR: 0.84 (95% CI, 0.74-0.95)

Enfermedad locorregional: nuevos estándares de tratamiento

Irresecable: quimiorradioterapia → durvalumab

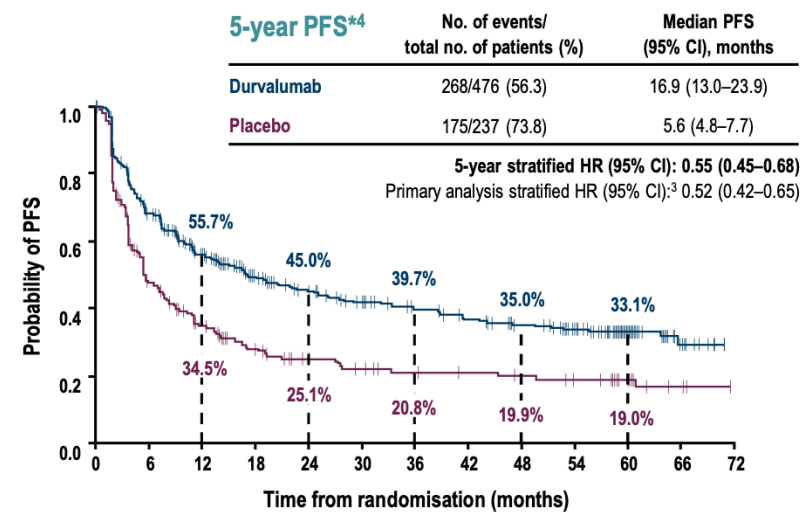
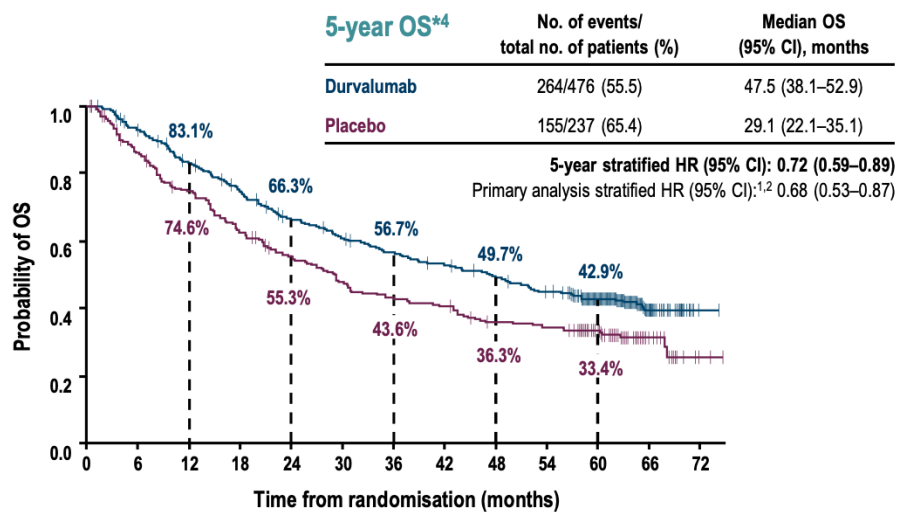
PACIFIC

- Unresectable Stage III NSCLC without progression after definitive platinum-based cCRT* (≥2 cycles)
 - 18 years or older
 - WHO PS score 0 or 1
 - If available, archived pre-cCRT tumour tissue for PD-L1 testing†
- All-comers population (i.e. irrespective of PD-L1 status)**
N=713 randomised



- Primary endpoints**
- PFS by BICR using RECIST v1.1†
 - OS
- Key secondary endpoints**
- ORR, DoR, and TTDM by BICR using RECIST v1.1
 - Safety
 - PROs

Enero 2020 aprobación de durvalumab tras QRT concomitante
PD-L1 1%



- El cáncer de pulmón es la primera causa de muerte por cáncer
- El abordaje del cáncer de pulmón tiene que ser multidisciplinar
- Testado molecular y PD-L1 previo a una neoadyuvancia con quimio + inmunoterapia
 - Si drivers accionables, no indicado
 - Sólo si PD-L1 \geq 1%
- Testado molecular tras cirugía: *EGFR*, *ALK*, otros... Tener presente las características de los pacientes
 - Atezolizumab en estadios II-III A, sólo si PD-L1 \geq 50%
 - Osimertinib en estadios IB-III A EGFR Del19/L858R
- Estadio III: heterogéneo. Se requiere homogeneidad a la hora de abordarlo
- Quimiorradioterapia concomitante \rightarrow Durvalumab en estadio III irresecable y PD-L1 \geq 1%
- Los biomarcadores siguen siendo tarea pendiente
- Tener siempre presente la opción de ensayo clínico



Muchas gracias
por vuestra atención