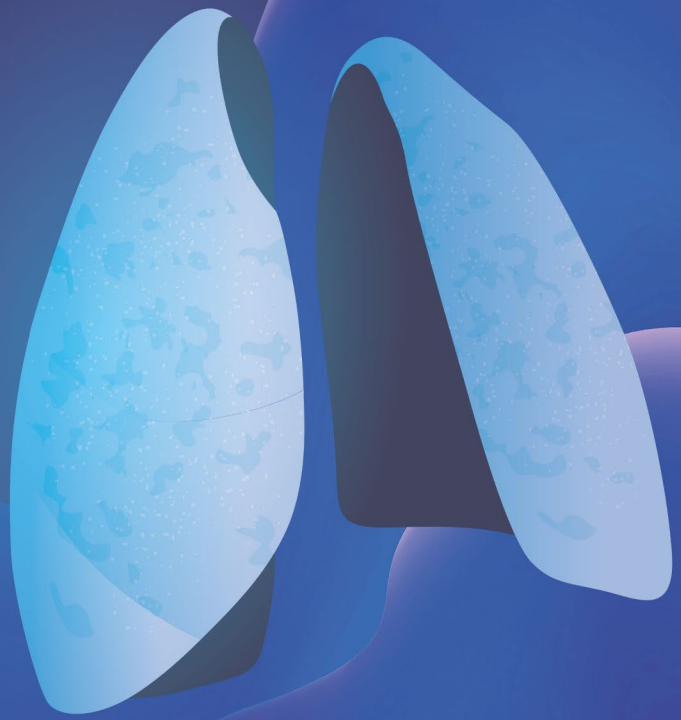

Novedades & Claves en CÁNCER de PULMÓN 2024

Introducción

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Organizado por:

GECP lung cancer research

Patrocinado por:

Bristol Myers Squibb™

Johnson&Johnson

Disclosures of Financial Relationships

✓Honoraria
- ✓ MSD Oncology, Pfizer, Astellas Pharma, Roche, Novartis, Janssen-Cilag, Bristol-Myers Squibb, Astra Zeneca

✓Consulting of Advisory Role
- ✓ Janssen-Cilag, MSD Oncology, Bristol-Myers Squibb, Boehringer Ingelheim, Beigene

✓Speaker´s Bureau
- ✓ MSD Oncology, Astra Zeneca

✓Research Funding
- ✓ Miratti Therapeutics, Astra Zeneca, Bayer, OncoMed, Astellas Pharma, Janssen-Cilag, Roche, Abbvie, Boehringer-Ingelheim, Pfizer, PharmaMar, Bristol-Myers Squibb, Novartis, Celgene, Ignyta

✓Travel, Accomodations, Expenses
- ✓ Bristol-Myers Squibb, Janssen-Cilag, Takeda, Pfizer, MSD Oncology, Roche, Merck

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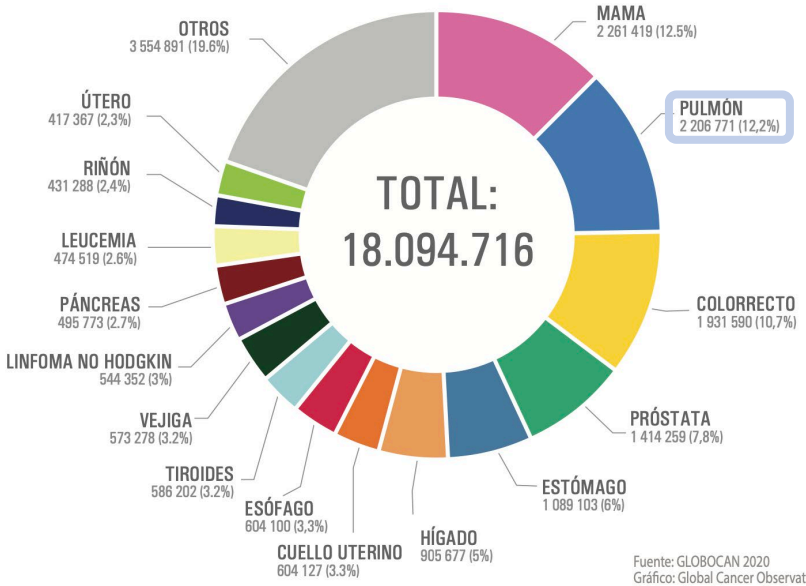

Fuente: GLOBOCAN 2020
Gráfico: Global Cancer Observatory (http://gco.iarc.fr/)
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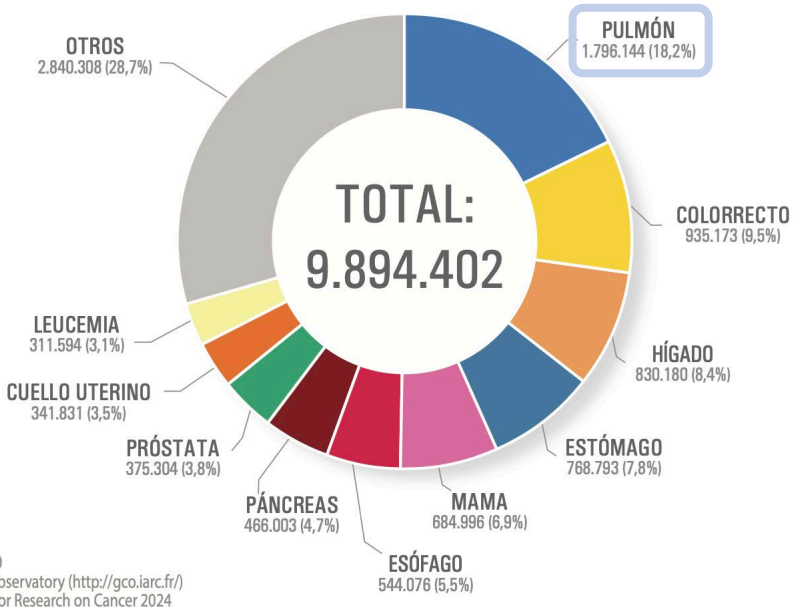

uente: GLOBOCAN 2020
ráfico: Global Cancer Observatory (http://gco.iarc.fr/)
International Agency for Research on Cancer 2024

Lung Cancer Is the Most Commonly Diagnosed Cancer and the Leading Cause of Cancer Death Worldwide

Estimated Age-Standardized Rates in 2020
Lung, Both Sexes, All Ages[a]

	Incidence	Mortality
Northern America	32.6	19.3
Europe	29.4	22.6
Oceania	24.0	16.1
Asia	22.9	19.3
Latin American and Caribbean	12.0	10.5
Africa	6.2	5.6

In 2020, lung cancer accounted for **11.4% of total cancer cases** and contributes to **18% of total cancer deaths**[b]

World Health Organization. International Agency for Research on Cancer; 2018. Accessed June 5, 2023. https://gco.iarc.fr; b. Sung H, et al. CA Cancer J Clin. 2021;71:209-249.

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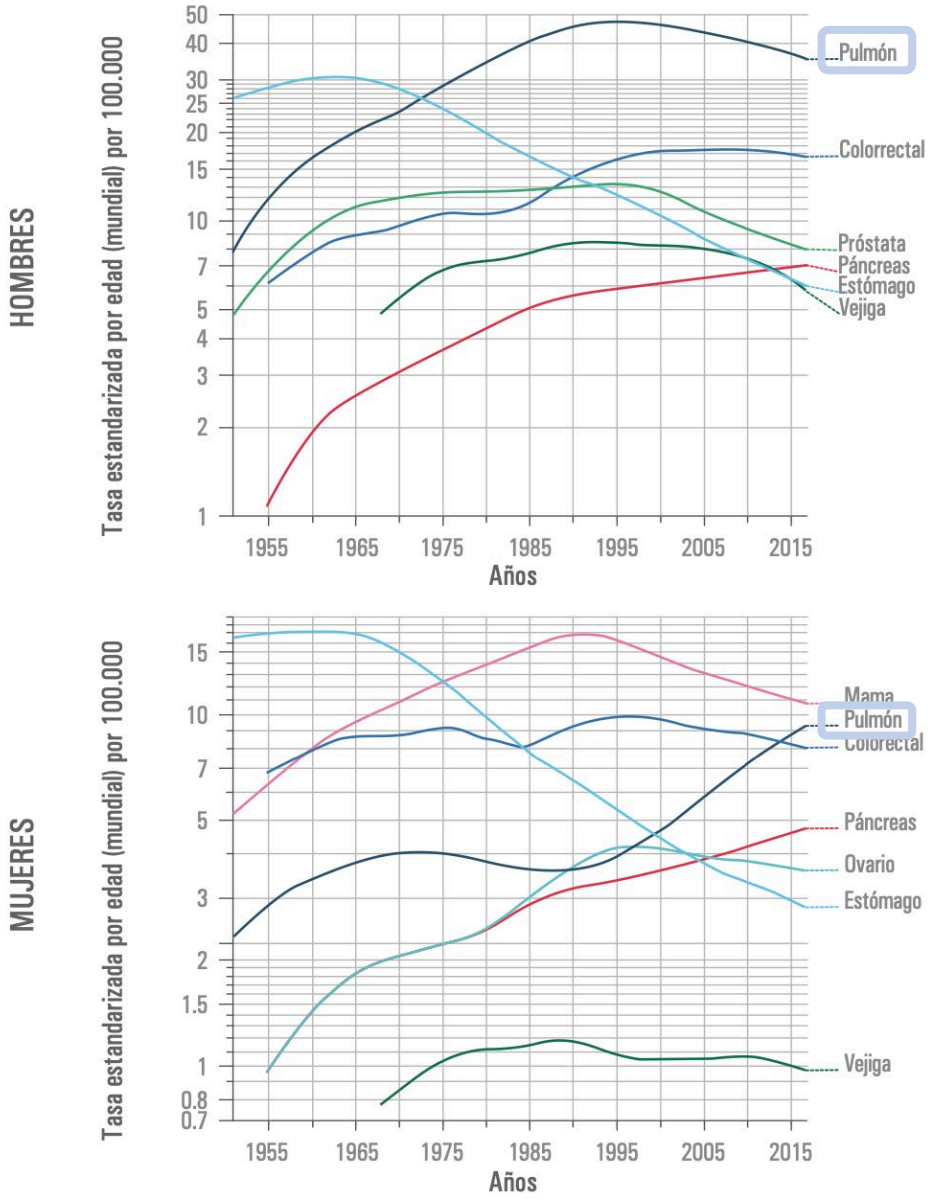
TIPO TUMORAL	N
Cavidad oral y faringe	7.603
Esófago	2.269
Estómago	6.868
Colon	29.648
Recto	14.646
Hígado	6.856
Vesícula biliar	2.358
Páncreas	9.986
Laringe	3.181
Pulmón	32.768
Melanoma de piel	7.881
Mama	36.395
Cérvix uterino	2.259
Cuerpo uterino	7.305
Ovario	3.716
Próstata	30.316
Testículo	1.549
Riñón (sin pelvis)	9.208
Vejiga urinaria	22.097
Encéfalo y sistema nervioso	4.419
Tiroides	6.345
Linfoma de Hodgkin	1.673
Linfomas no hodgkinianos	10.706
Mieloma	3.313
Leucemias	5.861
Otros	17.440
Todos excepto piel no melanoma	286.664

Fuente: Red Española de Registros de Cáncer (REDECAN).



Fuente: GLOBOCAN 2020 Gráfico: Global Cancer Observatory (http://gco.iarc.fr/) © International Agency for Research on Cancer 2024 v 1.0

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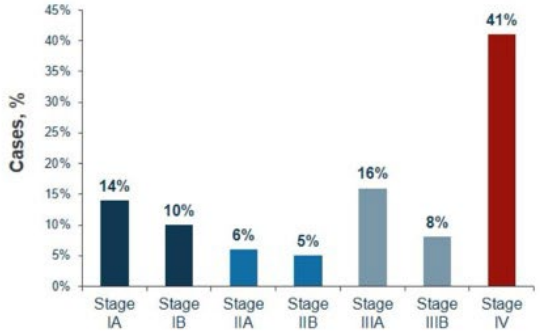
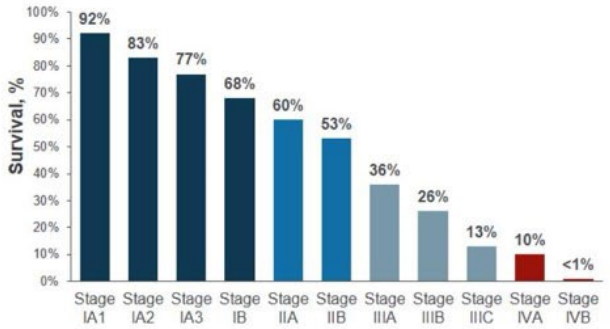
Lung Cancer Is Commonly Diagnosed at an Advanced Stage and Is Associated With a Poor Prognosis

Diagnosed Cases of NSCLC by Stage[a]



5-Year Survival for Patients with NSCLC[b]*



*Based on the clinical staging of the 8th edition IASLC.
IASLC, International Association for the Study of Lung Cancer; NSCLC, non-small cell lung cancer.
a. Heist RS, et al. Cancer Cell. 2012;21:448.e2; b. Goldstraw P, et al. J Thorac Oncol. 2016;11:39-51.

- Lung Cancer Screening
- Diagnosis in Early Stages
- Multidisciplinary Tumor Committee
- Biomarkers
- New Approaches and Drugs

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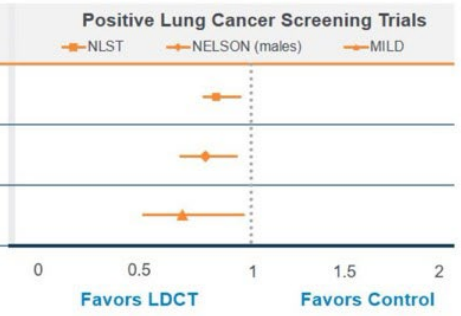
Impact of Lung Cancer Screening on staging and mortality

Lung Cancer Screening Significantly Reduces Lung Cancer Mortality
3 Large Randomized Trials

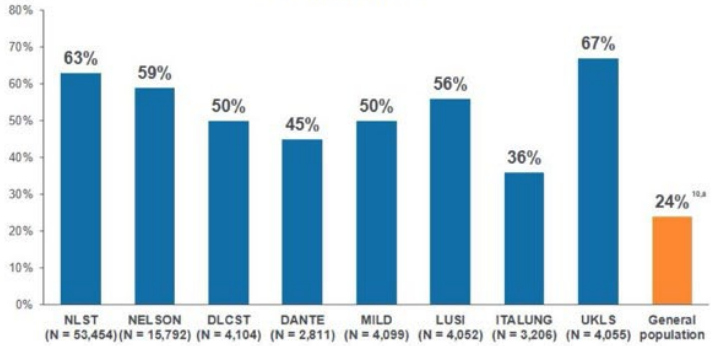
	N, LDCT arm	N, control arm	RR or HR (95% CI)
NLST (2011)[a,b]	26,722	26,732	RR: 0.8 (0.73, 0.93)
NELSON (2018)[c] (males*)	6583	6612	RR: 0.76 (0.61, 0.94)
MILD (2019)[d]	2376	1723	HR: 0.61 (0.39, 0.95)



*Among male participants. Among female participants, RR = 0.67 (95% CI: 0.38, 1.14).
HR, hazard ratio; MILD, Multicentric Italian Lung Detection Trial; NELSON, Dutch-Belgian Randomized Lung Cancer Screening Trial; NLST, National Lung Screening Trial; RR, rate ratio.
a. The National Lung Screening Trial Research Team. N Engl J Med. 2011;365:395-409; b. National Lung Screening Trial Research Team. J Thorac Oncol. 2019;14:1732-1742; c. de Koning HJ, et al. N Engl J Med. 2020;382:503-513; d. Pastorino U, et al. Ann Oncol. 2019;30:1162-1169.

Low-Dose CT Screening
Stage Shift

Percent of Stage I Cases Detected in Lung Cancer Screening RCTs[a-k]



- **The majority of cases detected through LDCT screening are stage I where curative resection is likely[a-i,k]**
- Among patients in the International ELCAP study (N = 31,567), 73% with stage I disease who underwent surgical resection within 1 month after diagnosis had an estimated 10-year survival rate of 92%[k]

[a]Includes Stages IA and IB; estimated from SEER validation set of proposed 7th edition IASLC staging.
CT, computed tomography; ELCAP, Early Lung Cancer Action Program; LDCT, low-dose computed tomography; RCT, randomized clinical trial.
a. National Lung Screening Trial Research Team. N Engl J Med. 2011;365:395-409; b. de Koning HJ, et al. N Engl J Med. 2020;382:503-513; c. Wille MM, et al. Am J Respir Crit Care Med. 2016;193:542-551; d. Infante M, et al. Am J Respir Crit Care Med. 2015;191:1166-1175; e. Pastorino U, et al. Ann Oncol. 2019;30:1162-1169; f. Becker N, et al. Int J Cancer. 2020;146:1503-1513; g. Lopes Pegna A, et al. J Thorac Oncol. 2013;8:866-875; h. Paci E, et al. Thorax. 2017;72:825-831; i. Field JK, et al. Health Technol Assess. 2016;20:1-146; j. Heist RS, et al. Cancer Cell. 2012;21:448.e2; k. Henschke CI, et al. N Engl J Med. 2006;355:1763-1771.

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Molecular Biomarkers

Biomarkers with a recommended first-line targeted treatment option:	Biomarkers with targeted options for second-line or later:	Emerging biomarkers
• *EGFR* exon 19 del, L858R, S768I, L861Q, G719X, Exon 20 insertion • *ALK* rearrangement • *ROS1* rearrangement • *BRAF* V600E • *NTRK* rearrangement • *MET* exon 14 skipping • *RET* rearrangement • PD-L1 positive (negative for other actionable molecular biomarkers)	• *KRAS* G12C • *ERBB2*	• High-level MET amplification ▫ Definition of high-level amplification is still evolving ○ NGS assays will give a value dependent on bioinformatics and enrichment of starting material (blood or tissue) ○ Cellular assays (ie, FISH) have different workflow but may be more consistent ▫ Capmatinib, crizotinib, or tepotinib may be used (not FDA approved for this indication in NSCLC) • Many other predictive biomarkers (eg, NRG1, RIT1, NF1, PIK3CA) are currently under evaluation in clinical trials for treatment of advanced/metastatic NSCLC

Gene or protein	Alteration	NCCN preferred therapy	Other recommended therapies
EGFR[a]	Exon 19 del or L858R	Osimertinib*	Osimertinib + pemetrexed + (cisplatin or carboplatin) (for nonsqamous)*, erlotinib*, afatinib*, gefitinib*, dacomitinib*, erlotinib + ramucirumab, or erlotinib + bevacizumab
	S768I, L861Q, G719X	Afatinib or osimertinib	Erlotinib, gefitinib, or dacomitinib
	Exon 20 insertion	Amivantamab + carboplatin + pemetrexed (non-squamous)* or systemic therapy	
KRAS	G12C	Systemic therapy based on PD-L1	
ALK	Rearrangement	Alectinib*, brigatinib*, or lorlatinib*	Ceritinib* In certain circumstances: crizotinib*
ROS1	Rearrangement	Entrectinib, crizotinib, or reprotrectinib	Ceritinib
BRAF	V600E	Dabrafenib + trametinib or encorafenib + binimetinib	In certain circumstances: vemurafenib or dabrafenib Or systemic therapy
NTRK1/2/3	Rearrangement	Larotrectinib or entrectinib	In certain circumstances: systemic therapy
MET	Exon 14 skipping	Capmatinib or tepotinib	In certain circumstances: crizotinib or systemic therapy
RET	Rearrangement	Selpercatinib or pralsetinib	In certain circumstances: cabozantinib or systemic therapy
***ERBB2* (HER2)**	Mutation	Systemic therapy	
PD-L1	≥50% and negative for actionable molecular biomarkers[b]	Systemic therapy, please see NCCN guidelines for the most up to date list	
	≥1%–49% and negative for actionable molecular biomarkers[b]		
	<1% and negative for actionable molecular biomarkers[b]		

*NCCN Category 1 recommendation; [a]the most common resistance mutation to first- and second-generation EGFR TKIs is EGFR T790M; [b]see NCCN NSCLC guidelines for recommended therapies for patients with contraindications to PD-1 or PD-L1 inhibitors

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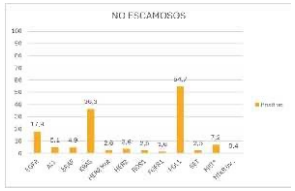
RTT – 36.000 pts

TASA DE ANALISIS DE MARCADORES (%)

EL 81,2% DE LOS PACIENTES DE LA COHORTE TIENEN ANALIZADO AL MENOS 1 MARCADOR



81% pts have at least one

ATLAS PROJECT

RATIONALE

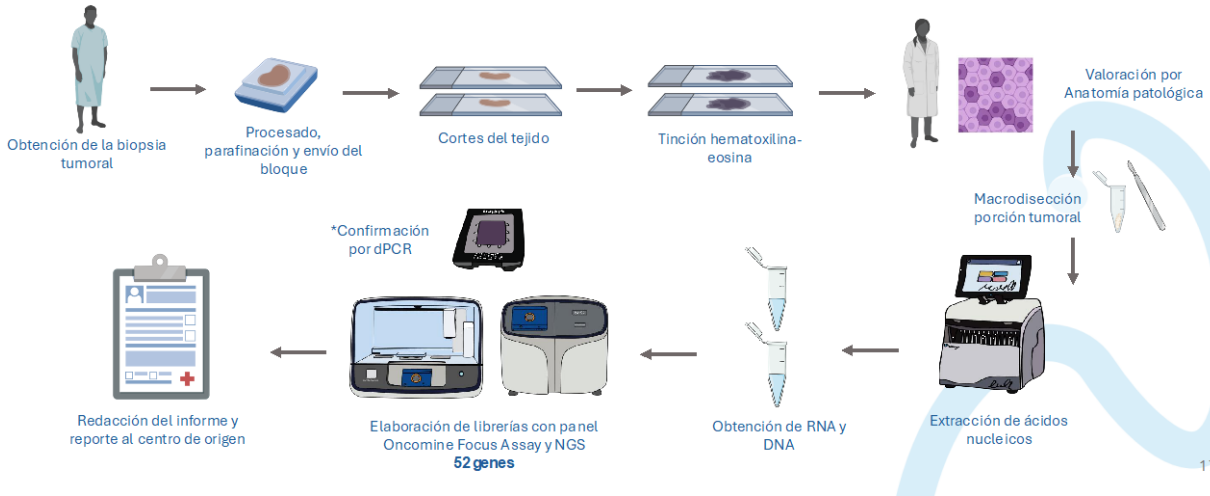
Testing Situation in Spain:

- No national plan exists for molecular biomarker analysis in Spain
- TTR showed some differences across spanish regions.
- Molecular testing is not accesible for all centers.
- An increase in the number of markers is expected in the next years
- Cost effectiveness of decentralized testing?

A centralized network with a technical ability and a competitive attitude is needed to support the weight of precision medicine.

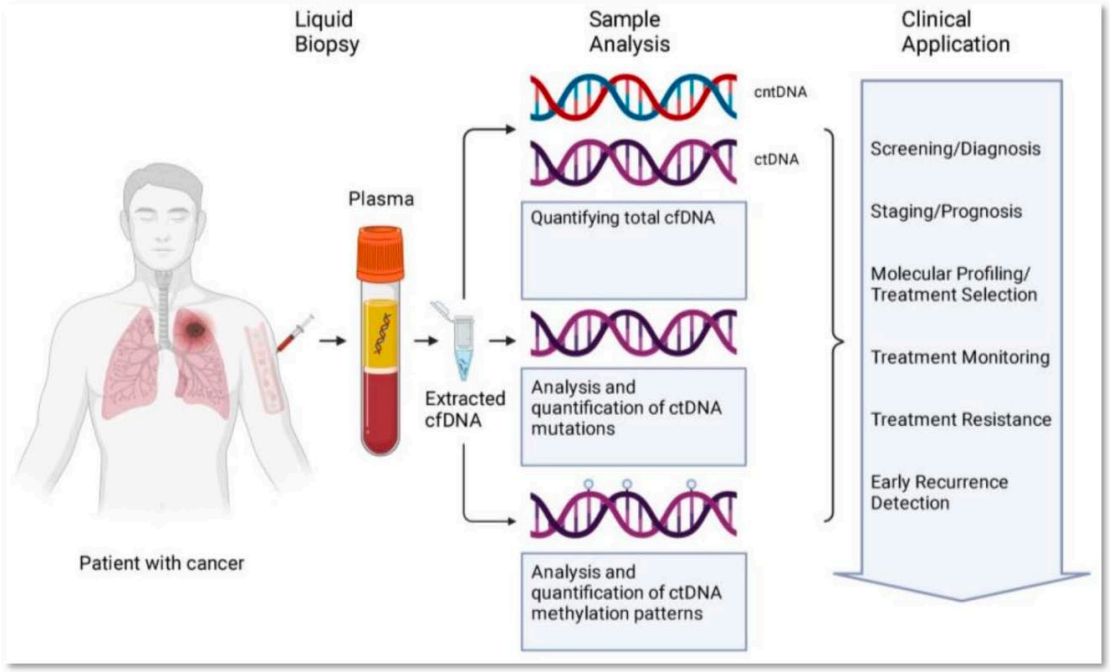
→ **ATLAS Proyect** ←

Proyecto ATLAS: procesamiento de muestras



We hope for rapid integration into daily clinical practice

ctDNA Analysis & Clinical Applications



Dao et al. 2023 Int J Mol Sci

- Early detection/screening
- Identification actionable genomic alterations
- Disease monitoring (e.g. MRD)
- Acquired resistance variants

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Importance of the MDT in Patient-Centered Care

MDT, multidisciplinary team.

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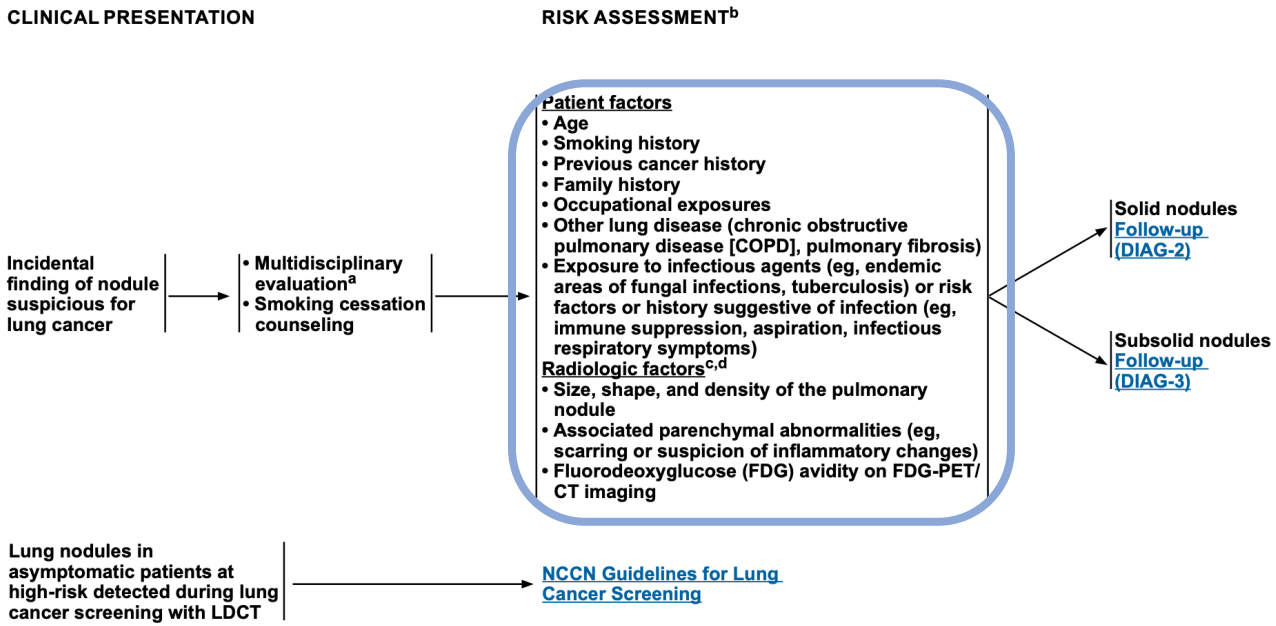
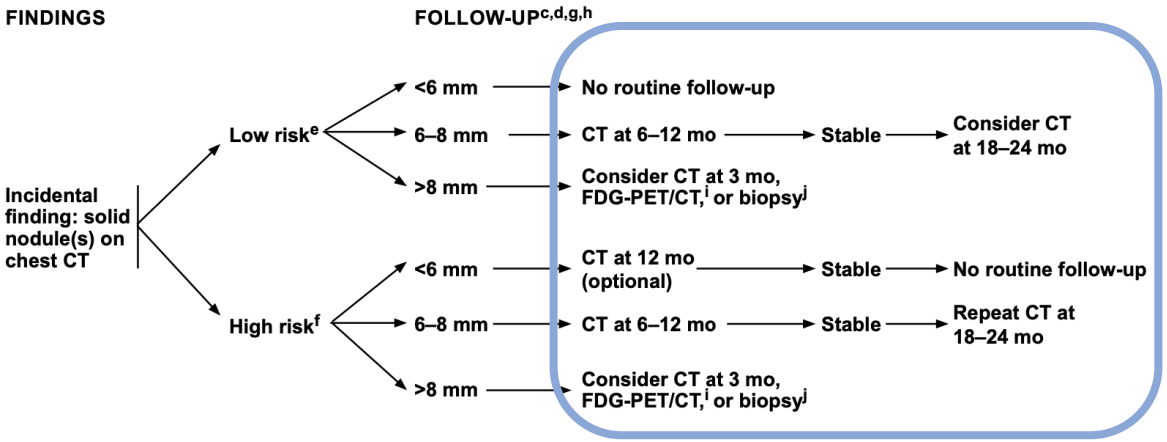
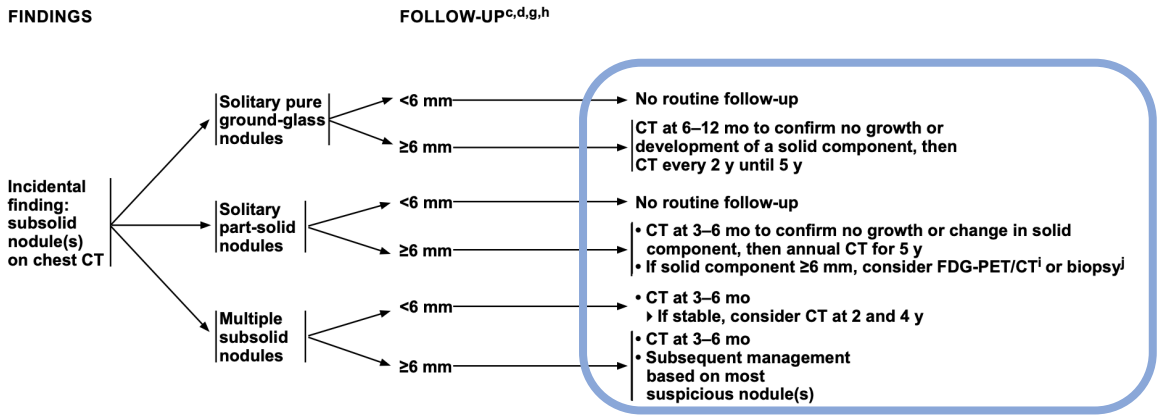
Incidental Nodules







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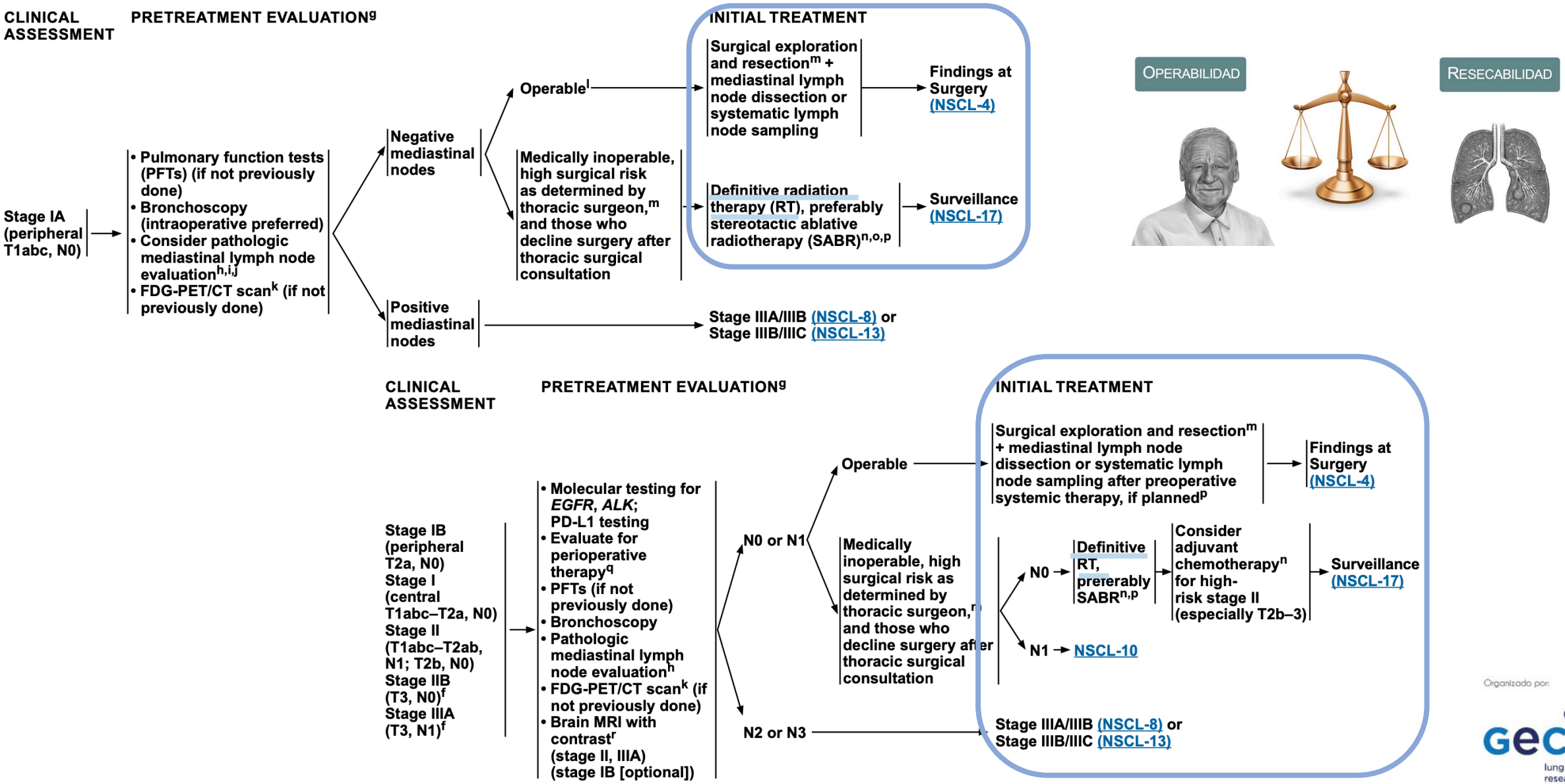
Early Stages NSCLC



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Adjuvant Treatment

ADJUVANT IMMUNOTHERAPY TRIALS

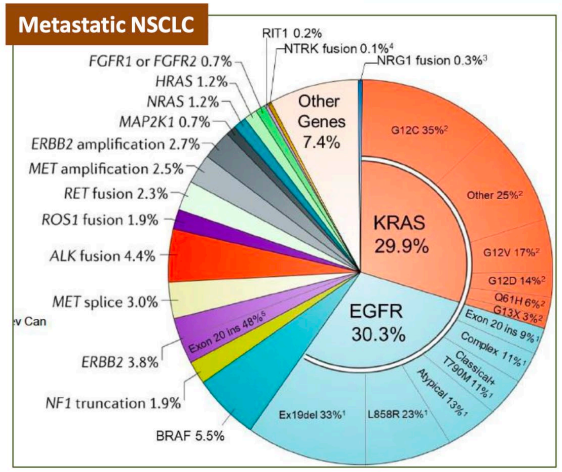
Study	Registry No.	Stage	No. of Patients	Experimental Arm	Control Arm	Prior Adjuvant Therapy	Primary Endpoint
ANVIL	NCT02595944	IB (> 4 cm), II, IIIA (AJCC 7th edition)	903	Nivolumab (1 y)	Observation	CT and/or RT allowed	DFS, OS in ITT DFS, OS in PD-L1 ≥ 1%
PEARLS/ KEYNOTE-091[49]	NCT02504372	IB (> 4 cm), II, IIIA (AJCC 7th edition)	1,177	Pembrolizumab (1 y)	Placebo	CT allowed; No RT allowed	DFS
IMpower010[48]	NCT02486718	IB (> 4 cm), II, IIIA (AJCC 7th edition)	1,280	Atezolizumab (16 cycles)	Observation (BSC)	CT required (CDDP)	DFS in PD-L1 TC ≥ 1% stage II-IIIA DFS in all stage II-IIIA DFS in ITT
BR-31 (IFCT1401)	NCT02273375	IB (> 4 cm), II, IIIA (AJCC 7th edition)	1,360	Durvalumab (1 y)	Placebo	CT recommended; RT allowed (N2 disease)	DFS in PD-L1 ≥ 25% and in all randomly assigned
CANOPY-A	NCT03447769	II-IIIB (N2) (AJCC 8th edition)	1,500	Canakinumab	Placebo	CT required; RT allowed	DFS
MERMAID-1	NCT04385368	II-III (AJCC 8th edition)	332	Durvalumab + CT	Placebo + CT	—	DFS in MRD+
MERMAID-2	NCT04642469	II-III (AJCC 8th edition)	284 (MRD+)	Durvalumab	Placebo	CT and/or RT allowed	DFS in PD-L1 ≥ 1%
NADIM ADJUVANT	NCT04564157	IB (> 4 cm), II, IIIA (AJCC 8th edition)	210	Nivolumab + CT	CT	Not allowed	DFS

Adjuvant Treatment

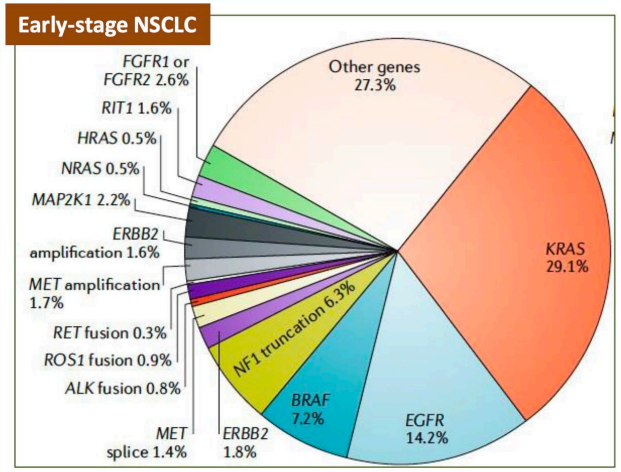
ADJUVANT TKIs

- TKIs in NSCLC with actionable genomic alterations (AGA) have improved the outcome in metastatic setting
- These strategies have also been tested in patients with resectable early-stage NSCLC

Metastatic NSCLC



Early-stage NSCLC



ADAURA: 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§
- Maximum 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**

43% of patients with progressive disease received osimertinib as a subsequent treatment

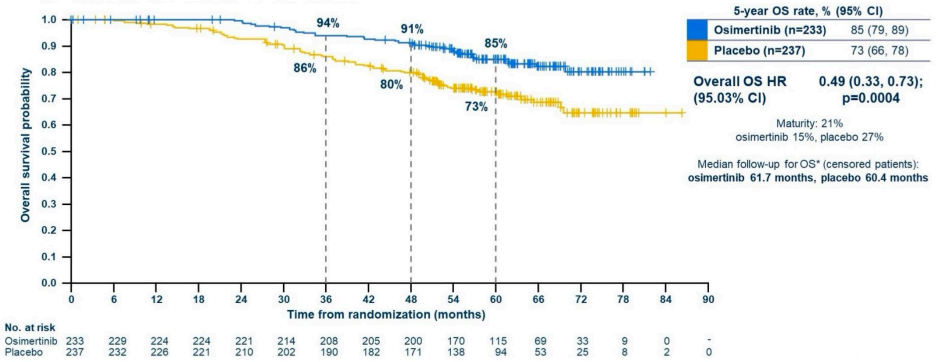
Planned treatment duration: 3 years

Treatment continued until:
- Disease recurrence
- Treatment completion
- Discontinuation criterion met

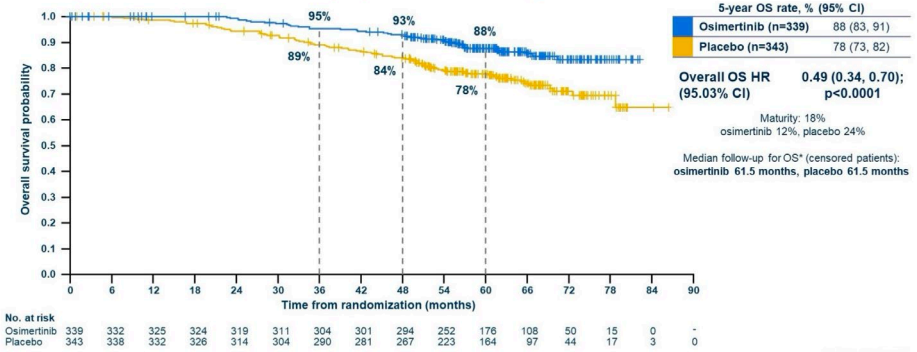
Follow-up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

Endpoints
- **Primary 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

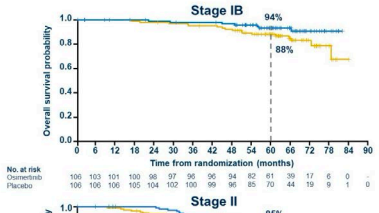
ADAURA: adjuvant osimertinib has demonstrated significant improvement in OS vs placebo in the primary population of stage II-IIIA disease

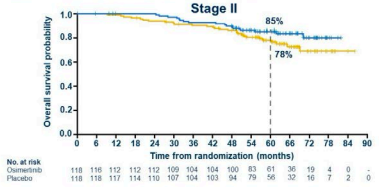


ADAURA: adjuvant osimertinib has demonstrated significant improvement in OS vs placebo in the overall population of stage IB-IIIA disease



ADAURA: overall survival by disease stage





	Stage IB	Stage II	Stage IIIA
5 year OS rate, % (95% CI)			
Osimertinib	94 (86, 97)	85 (77, 91)	85 (76, 91)
Placebo	88 (80, 93)	78 (69, 85)	67 (57, 75)
Overall HR (95% CI)	0.44 (0.17, 1.02)	0.63 (0.34, 1.12)	0.37 (0.20, 0.64)

The benefit in OS was more pronounced with higher disease stages

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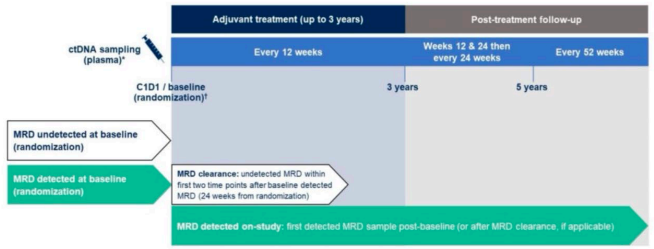
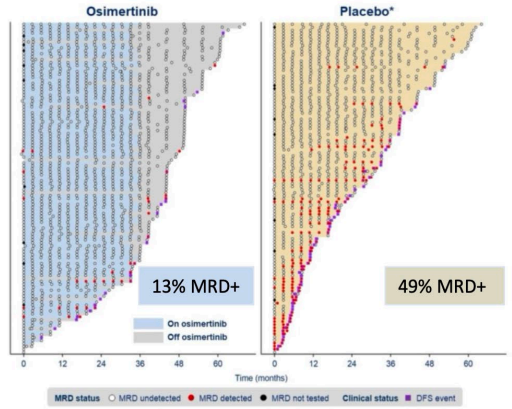
Adjuvant Treatment

ADAURA: molecular residual disease (MRD)

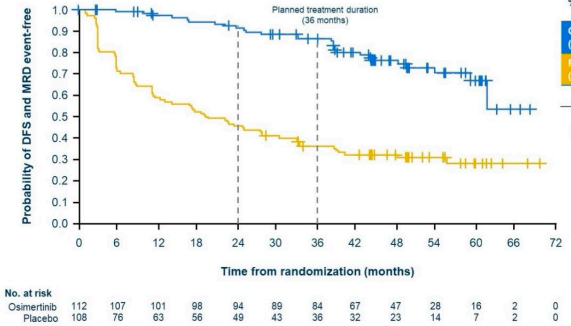




MRD events were detected more frequently with placebo vs osimertinib

John T, ASCO 2024

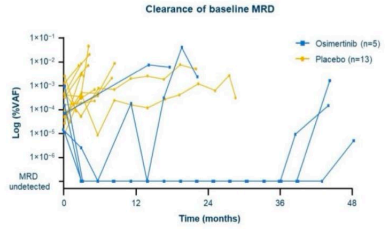
ADAURA: molecular residual disease (MRD)



% (95% CI)	DFS and MRD event-free rate	
	24 months	36 months
Osimertinib (n=112)	91 (84, 95)	86 (78, 92)
Placebo (n=108)	46 (36, 55)	36 (27, 45)

HR (95% CI) 0.23 (0.15, 0.36)†

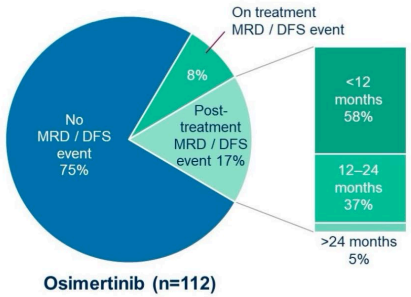
Median follow-up time, months (95% CI):
osimertinib 44.2 (42.4, 49.1), placebo 19.1 (11.1, 28.3)

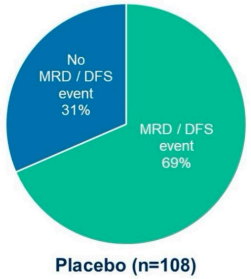


- Detected MRD at baseline was associated with poor outcomes
- Patients receiving osimertinib were more likely to be DFS and MRD event free vs placebo
  - Of 18 patients with detected MRD at baseline
    - 4 / 5 patients receiving osimertinib cleared MRD
    - 0 / 13 patients receiving placebo cleared MRD

John T, ASCO 2024

ADAURA: molecular residual disease (MRD)





- DFS and MRD event-free status was maintained for most patients during osimertinib treatment
- At 24 months post-osimertinib treatment, the DFS and MRD event-free rate was 66%

% (95% CI)	DFS and MRD event-free rate in the post-treatment follow-up period	
	12 months post-osimertinib discontinuation	24 months post-osimertinib discontinuation
Osimertinib (n=112)	80 (71, 87)	66 (53, 77)

John T, ASCO 2024

Organizado por:
GECP lung cancer research

Adjuvant Treatment

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

R 1:1

N=257

Alectinib 600 mg BID 2 years → **Recurrence**

Platinum-based chemotherapy† Q3W; 4 cycles → **Recurrence**

Further treatments at investigator's choice and survival follow-up

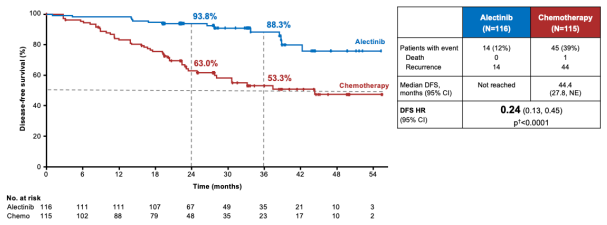
Primary endpoint
- DFS per investigator,‡ tested hierarchically:
  - Stage II–IIIA → ITT (Stage IB–IIIA)

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

Solomon BJ, et al. ESMO 2023; Wu YL, et al. N Engl J Med 2024;390(14):1265-76.

ALINA: disease-free survival (DFS)

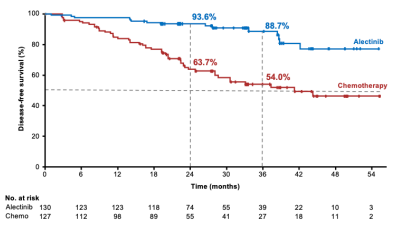
DFS stage II-IIIA



	Alectinib (N=116)	Chemotherapy (N=115)
Patients with event	14 (12%)	45 (39%)
Death	0	1
Recurrence	14	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	

DFS stage II-IIIA NSCLC: HR 0.24 (95% CI 0.13-0.45; p<0.001)
2-year DFS of 93.8% (alectinib)and 63.0% (CT)

DFS ITT stage IB-IIIA



	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	

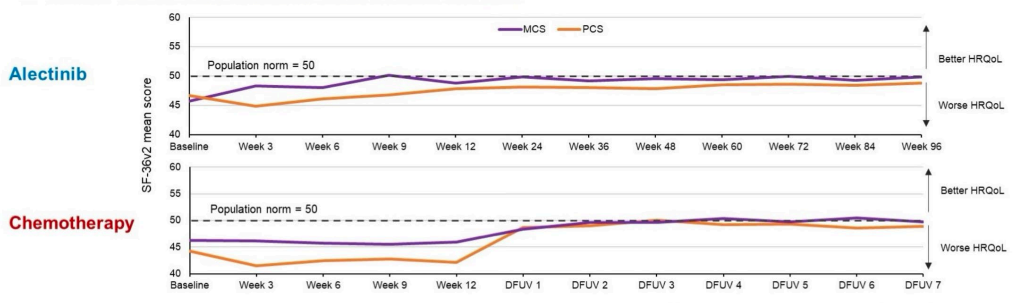
At the data cutoff date, **OS data were immature** with only 6 (2.3%) OS events reported‡

DFS stage II-IIIA NSCLC: HR 0.24 (95% CI 0.13-0.43; p<0.001)
2-year DFS of 93.6% (alectinib)and 63.7% (CT)

Solomon BJ, et al. ESMO 2023; Wu YL, et al. N Engl J Med 2024;390(14):1265-76.

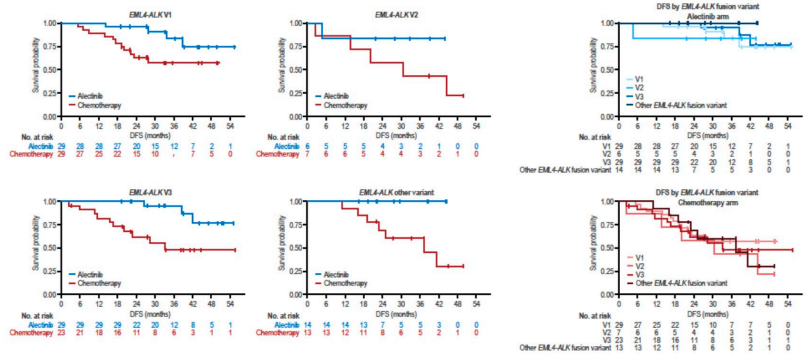
ALINA: long-term HRQoL outcomes

- During active treatment with alectinib, MCS (mental component summary) and PCS (physical component summary) generally improved through to week 96 and were similar to the general population
- With CT, MCS and PCS improved after treatment was completed
- Similar trends were observed across health domains



Nishio M, et al. ASCO 2024

ALINA: DFS by EML4-ALK fusion variant



- Alectinib showed DFS benefit vs chemotherapy regardless of *EML4-ALK* fusion variant
- Alectinib and chemotherapy showed comparable DFS in all *EML4-ALK* fusion variants

Solomon BJ, et al. ESMO 2024

Organizado por:
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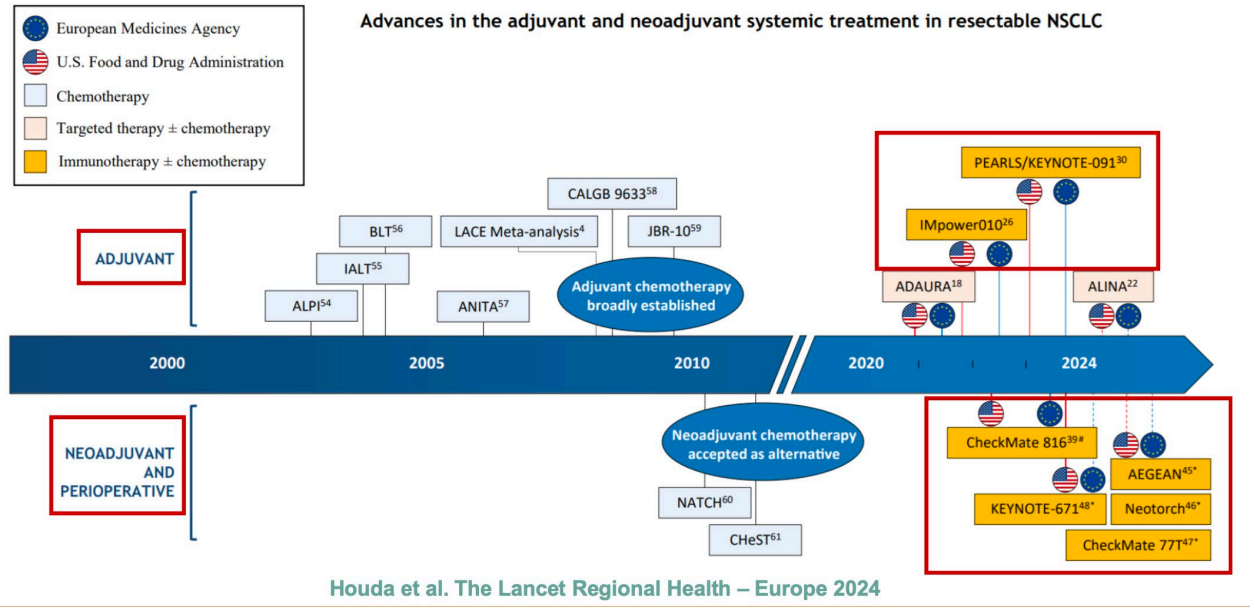
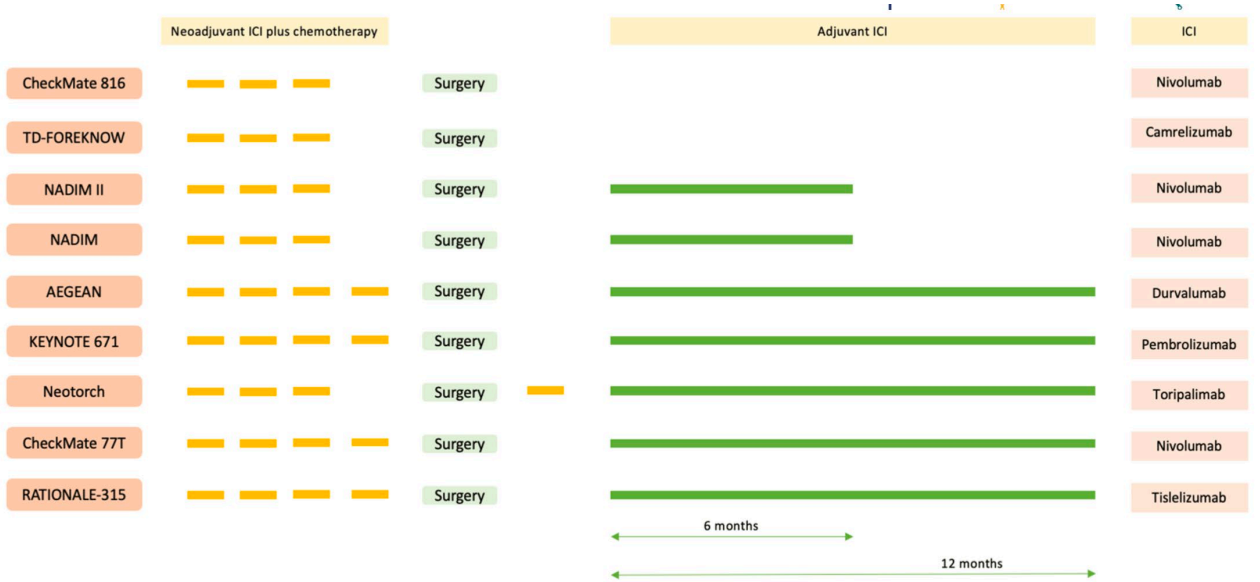
Locally Advanced NSCLC



Houda et al. The Lancet Regional Health – Europe 2024

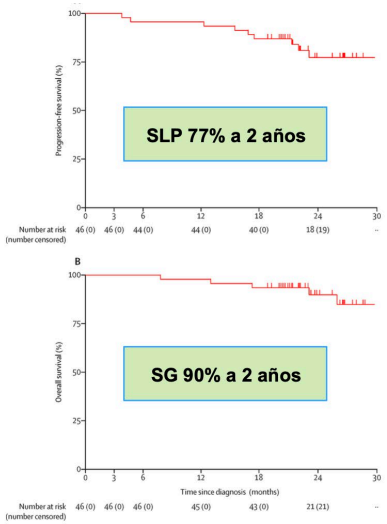


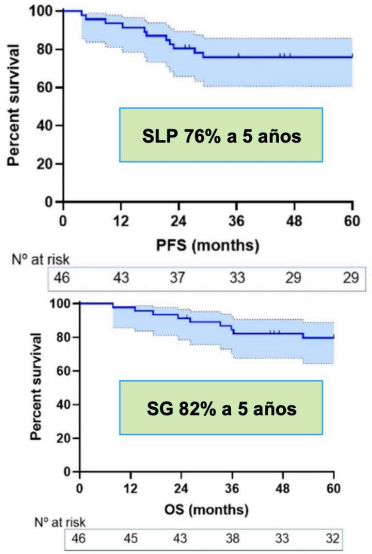
Verma et al. Cancers, 2024

Organizado por:
GECP lung cancer research

Locally Advanced NSCLC

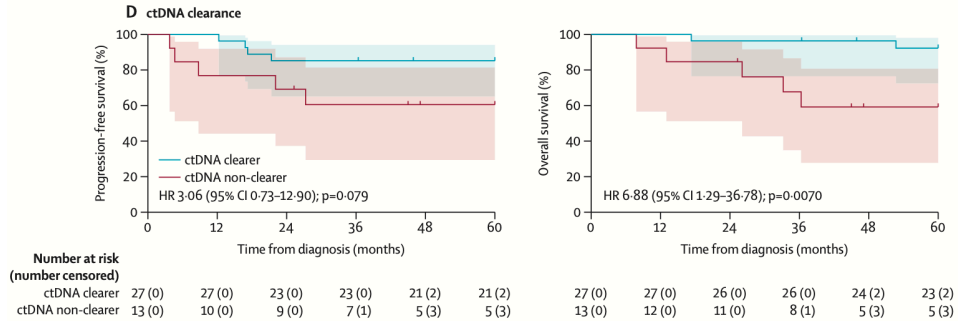
Patient baseline characteristics	N=46 (ITT)
Age (median, range)	63(41-77)
Male, N (%)	34 (74 %)
ECOG PS 0 N (%) 1 N (%)	 25 (54%) 21 (46%)
Smoking status, N (%) Former/current	 46 (100%)
Adenocarcinoma, N (%)	28 (61)
Co-morbidities, N (%)	43 (93,5)
N2	**33 (89.2)**
Multiple station	**25 (75.8)**

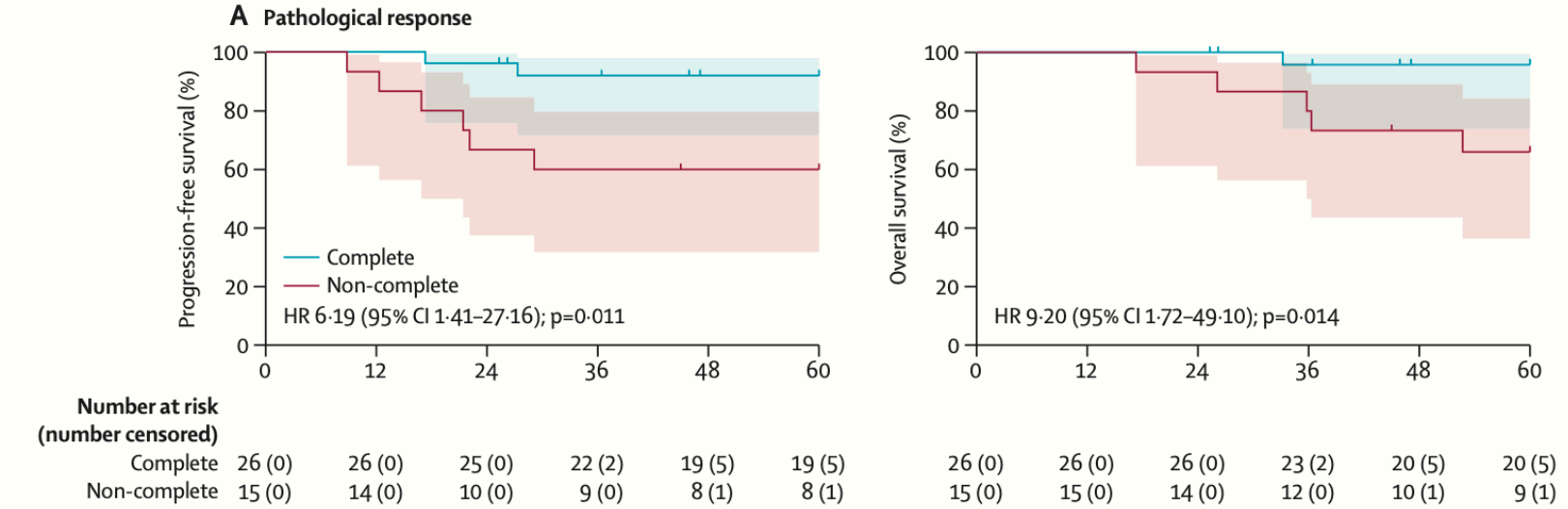




Provencio et al. Lancet Oncol, 2020; Provencio et al. WCLC 2024

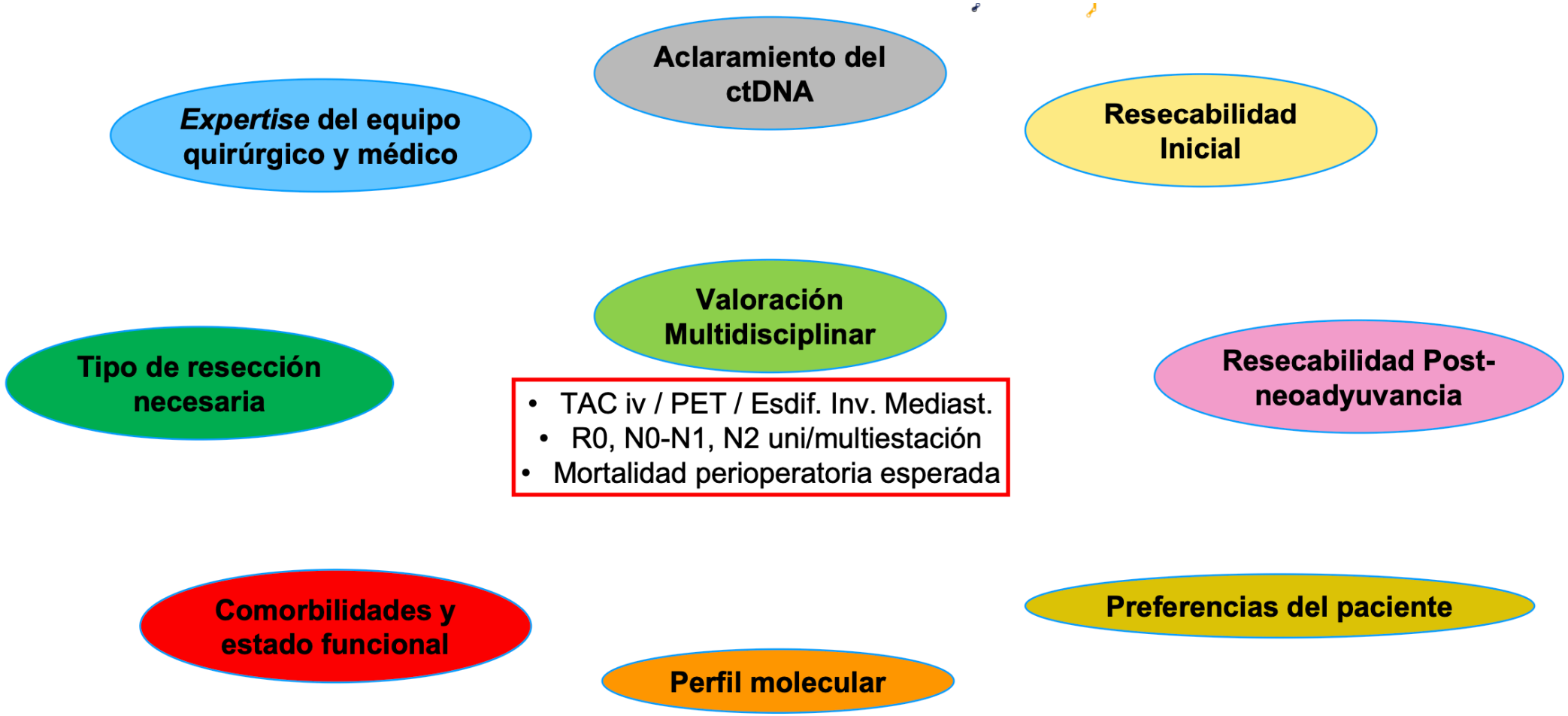
Perioperative chemotherapy and nivolumab in non-small-cell lung cancer (NADIM): 5-year clinical outcomes from a multicentre, single-arm, phase 2 trial





Organizado por:
GECP lung cancer research

Locally Advanced NSCLC



Organizado por:
GECP
lung cancer research

Unresectable NSCLC

LAURA

Patients with locally advanced, unresectable stage III[a] EGFRm NSCLC with no progression during / following definitive CRT[†] treatment

Key inclusion criteria:
- ≥18 years (Japan: ≥20)
- WHO PS 0 / 1
- Confirmed locally advanced, unresectable stage III* NSCLC
- Ex19del / L858R[‡]
- Maximum interval between last dose of CRT and randomization: 6 weeks

Osimertinib 80 mg, once daily

Randomization 2:1 (N=216)

Stratification by:
Concurrent vs sequential CRT
Stage IIIA vs stage IIIB/IIIC
China vs non-China

Placebo, once daily

Treatment duration until BICR-assessed progression (per RECIST v1.1), toxicity, or other discontinuation criteria

Open-label osimertinib after BICR-confirmed progression offered to both treatment arms[§]

Tumor assessments:
- Chest CT / MRI and brain MRI
- At baseline, every 8 weeks to Week 48, then every 12 weeks until BICR-assessed progression

Endpoints
- **Primary endpoint:** PFS assessed by BICR per RECIST v1.1 (sensitivity analysis: PFS by investigator assessment)
- **Secondary endpoints included:** OS, CNS PFS, safety

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

1–42 days post-cCRT

R

Durvalumab 10 mg/kg q2w for up to 12 months N=476

2:1 randomisation, stratified by age, sex, and smoking history

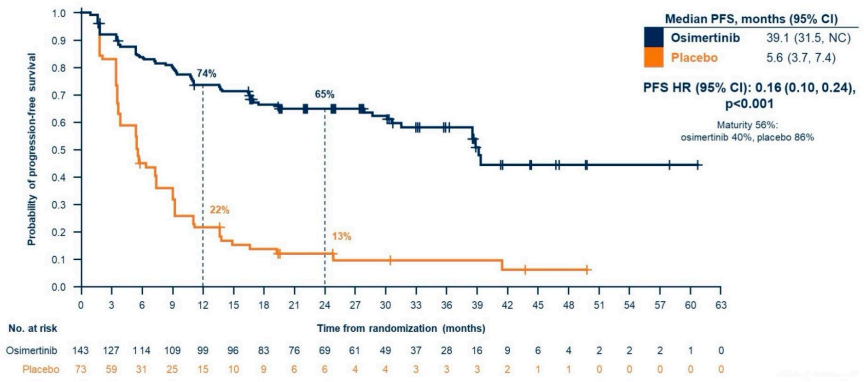
Placebo q2w for up to 12 months N=237

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

LAURA

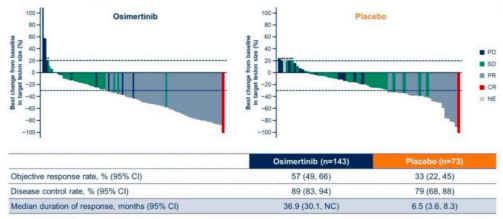
Progression-free survival by BICR



Ramalingam SS, et al. ASCO 2024; Lu S, et al. N Engl J Med 2024;391(7):585-97

LAURA

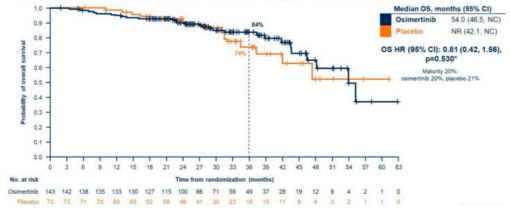
Tumor response by BICR



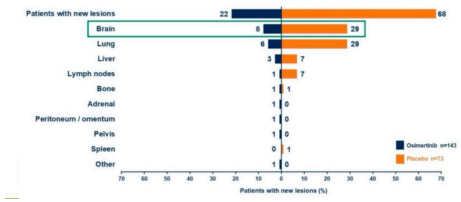
	Osimertinib (n=143)	Placebo (n=73)
Objective response rate, % (95% CI)	57 (49, 66)	33 (22, 45)
Disease control rate, % (95% CI)	89 (83, 94)	79 (68, 88)
Median duration of response, months (95% CI)	36.9 (30.1, NC)	6.5 (3.6, 8.3)

Interim analysis of overall survival

- In the placebo arm, 81% of patients with BICR-confirmed progression crossed over to osimertinib



Sites of new lesions by BICR



- ORR 57% vs 33%: DCR 89% vs 79%; mDoR 36.9 vs 6.5m
- Patients with new brain lesions: 8% vs 29%
- Interim data OS showed a positive trend in favor of osimertinib, despite a high proportion of patients crossing over to osimertinib in the placebo arm (81%)

Ramalingam SS, et al. ASCO 2024; Lu S, et al. N Engl J Med 2024;391(7):585-97

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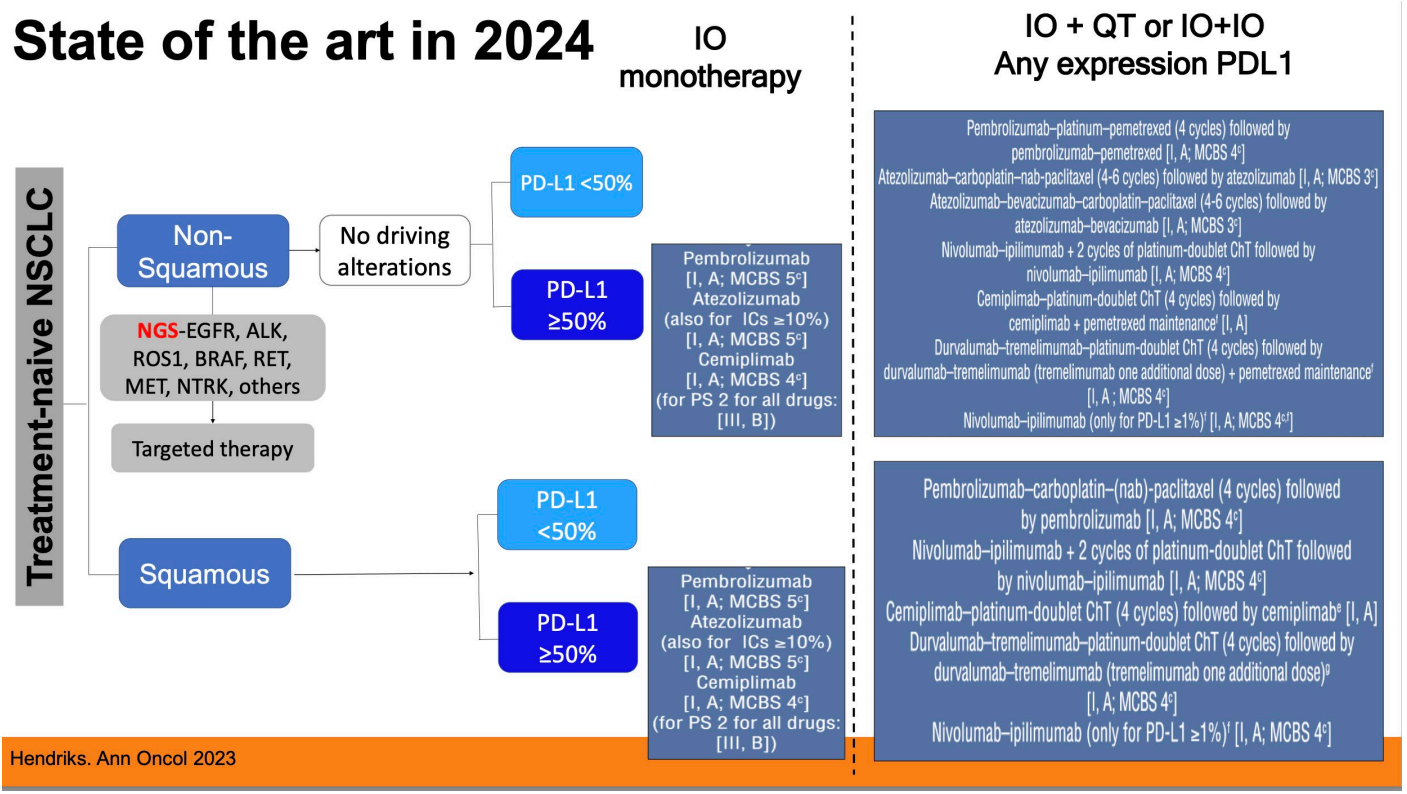
Advanced Non-targeted NSCLC



News combinations

News CkP´I

ADC

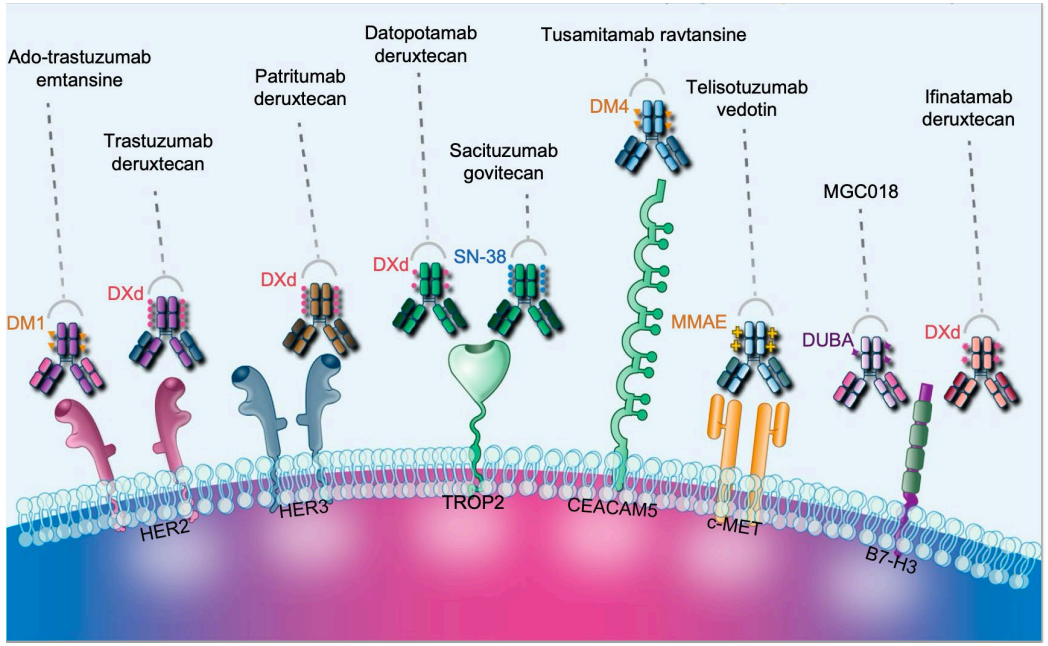
Bispecfic drugs

First line

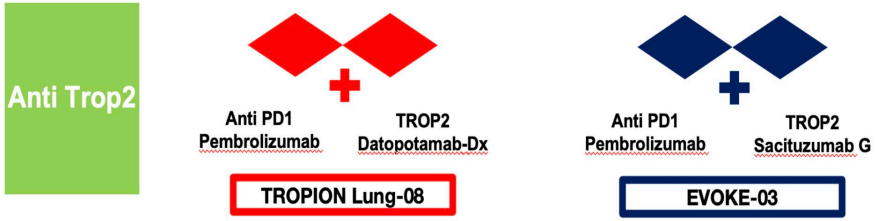
Other lines

Organizado por:
GECP lung cancer research

Advanced Non-targeted NSCLC



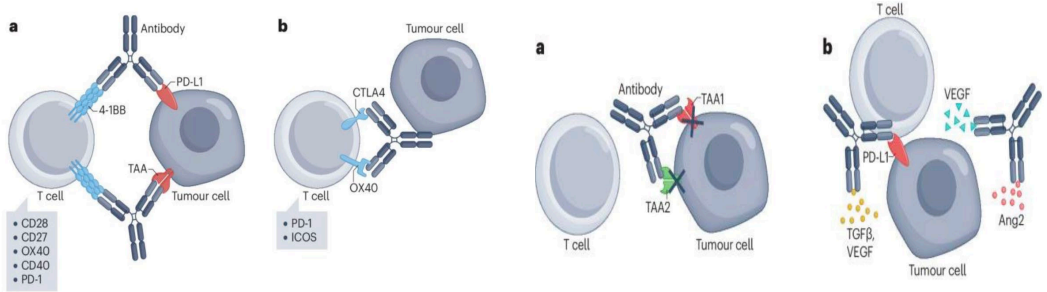
Trials with TROP2 in 1L and PDL1>50%



Trials with TROP2 combinations in 1L all comers

TROPION-Lung02	IB	Dato-DXd + pembro + pembro + platinum	1L/2L	NCT04526691
TROPION-Lung04	IB	Dato-DXd + durva + durva + platinum	1L/2L	NCT04612751
TROPION-Lung07	III	Dato-DXd + pembro + platinum Dato-DXd + pembro Pembro + pemetrexed + platinum	1L PDL1 < 50%	NCT05555732
TROPION-Lung08	III	Dato-DXd + pembro Pembro	1L PDL1 ≥ 50%	NCT05215340
AVANZAR	III	Dato-DXd + durva + carboplatin Pembro + histology-specific platinum doublet	1L	NCT05687266
EVOKE-03	III	Sacituzumab + pembro Pembro	1L PDL1 ≥ 50%	NCT05609968
EVOKE-02	II	Sacituzumab + pembro Sacituzumab + pembro + platinum	1L	NCT05186974

Bispecific and multispecific antibody



Bring immune cells close to tumor cells

Blocking multiple signals

Maria-Elisabeth Goebeleret al. 2024 nature reviews clinical oncology

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Advanced targeted NSCLC

Contextualizing the Data: Amivantamab (IV) Indications and Clinical Trials in Advanced NSCLC

Clinical Trial	Amivantamab Regimen	Phase	Patient Population	Status
CHRYSALIS NCT02609776	Amivantamab	I	Cohorts for EGFR and MET	FDA, EMA, NICE approval for EGFR ex20ins, post-platinum
PAPILLON NCT04538664	Amivantamab + Carboplatin/pemetrexed	III	EGFR ex20ins, 1L	FDA approval
MARIPOSA NCT04487080	Amivantamab + Lazertinib	III	EGFR ex19del/L858R, 1L	Under FDA review
MARIPOSA-2 NCT04988295	Amivantamab + Carboplatin/pemetrexed +/- Lazertinib	III	EGFR ex19del/L858R, 2L	Under FDA review
CHRYSALIS-2 NCT04077463	Amivantamab + Lazertinib	I/Ib	EGFR ex19del/L858R, 2L	Clinical trial ongoing
METalmark NCT05488314	Amivantamab + Capmatinib	I/II	MET ex14 skipping, MET amplified	Clinical trial ongoing
PolyDamas NCT05908734	Amivantamab + Cetrelimab	I/II	No genotype restriction	Clinical trial ongoing

Amivantamab Plus Chemotherapy vs Chemotherapy as First-Line Treatment in *EGFR* Exon 20 Insertion–mutated Advanced NSCLC: Analysis of Post-Progression Endpoints From PAPILLON

Enriqueta Felip,[1] Catherine Shu,[2] Andres Aguilar,[3] Ke-Jing Tang,[4] Maria Del Rosario Garcia Campelo,[5] Kang-yun Lee,[6] Angelo Delmonte,[7] Joshua K. Sabari,[8] Nicolas Girard,[9] Aaron S. Mansfield,[10] Keunchil Park,[11,12] Caicun Zhou,[13] Karen Xia,[14] Archan Bhattacharya,[15] Mark Wade,[14] Mahadi Baig,[16] Trishala Agrawal,[14] Parthiv Mahadevia,[16] Roland E. Knoblauch,[14] Rachel E. Sanborn[17]

[1]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [2]Columbia University Medical Center, New York, NY, USA; [3]Hospital Universitario Quiron-Dexeus, Barcelona, Spain; [4]The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [5]Hospital Universitario A Coruña, Coruña, Spain; [6]Taipei Medical University Shuang Ho Hospital, Taipei, Taiwan; [7]IRCCS Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori" (IRST), Meldola, Italy; [8]Langone Health at NYU School of Medicine, New York, NY, USA; [9]Institut Curie, Institut du Thorax Curie-Montsouris, Paris, France, and Paris-Saclay University, UVSQ, Versailles, France; [10]Mayo Clinic, Rochester, MN, USA; [11]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [12]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [13]Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China; [14]Janssen Research & Development, Spring House, PA, USA; [15]Janssen Research & Development, High Wycombe, UK; [16]Janssen Research & Development, Raritan, NJ, USA; [17]Earle A. Chiles Research Institute, Providence Cancer Institute of Oregon, Portland, OR, USA.

Amivantamab Plus Chemotherapy vs Chemotherapy in *EGFR*–mutant Advanced NSCLC After Progression on Osimertinib: A Post-progression Analysis of MARIPOSA-2

Ryan D. Gentzler,[1] Alexander I. Spira,[2] Barbara Melosky,[3] Scott Owen,[4] Timothy F. Burns,[5] Erminia Massarelli,[6] Misako Nagasaka,[7] Bruno Fang,[8] Rachel E. Sanborn,[9] Oscar Arrieta,[10] Cynthia Card,[11] Federico Cappuzzo,[12] Karen Xia,[13] Pei-Ling Chu,[14] Sujay Shah,[13] Brooke Diorio,[15] Angela Girvin,[13] Parthiv Mahadevia,[14] Joshua M. Bauml,[13] Karen L. Reckamp[16]

[1]Hematology/Oncology, University of Virginia Cancer Center, Charlottesville, VA, USA; [2]Virginia Cancer Specialists, Fairfax, VA, USA; [3]British Columbia Cancer Agency, Vancouver, British Columbia, Canada; [4]McGill University Health Centre (MUHC), Montreal, Quebec, Canada; [5]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [6]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [7]University of California Irvine School of Medicine, Orange, CA, USA; [8]Astera Cancer Care, East Brunswick, NJ, USA; [9]Earle A. Chiles Research Institute, Providence Cancer Institute of Oregon, Portland, OR, USA; [10]Instituto Nacional de Cancerologia, Mexico City, Mexico; [11]Amie Charbonneau Cancer Institute, Calgary, Alberta, Canada; [12]IRCCS Regina Elena National Cancer Institute, Rome, Italy; [13]Janssen Research & Development, Spring House, PA, USA; [14]Janssen Research & Development, Raritan, NJ, USA; [15]Janssen Research & Development, Titusville, NJ, USA; [16]Cedars Sinai Medical Center, Los Angeles, CA, USA.

Amivantamab plus lazertinib in atypical *EGFR*-mutated advanced non-small cell lung cancer (NSCLC): Results from CHRYSALIS-2

Byoung Chul Cho[1], Yongsheng Wang[2], Enriqueta Felip[3], Jiuwei Cui[4], Alexander I Spira[5], Joel W Neal[6], Christina Baik[7], Melina E Marmarelis[8], Eiki Ichihara[9], Jong-Seok Lee[10], Se-Hoon Lee[11], James Chih-Hsin Yang[12], Sebastian Michels[13], Zacharias Anastasiou[14], Joshua C Curtin[15], Xuesong Lyu[16], Levon Demirdjian[17], Isabelle Leconte[18], Leonardo Trani[15], Mahadi Baig[19], Joshua M Bauml[15], Pascale Tomasini[20]

[1]Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [2]Department of Oncology, West China Hospital, Sichuan University, Chengdu, China; [3]Medical Oncology Service, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron Barcelona Hospital Campus, Universitat Autónoma de Barcelona, Barcelona, Spain; [4]The First Hospital of Jilin University, Changchun, China; [5]Virginia Cancer Specialists, Fairfax, VA, USA; [6]Stanford Cancer Institute, Stanford University, Stanford, CA, USA; [7]University of Washington Fred Hutchinson Cancer Center, Seattle, WA, USA; [8]Division of Hematology and Oncology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [9]Okayama University Hospital, Okayama, Japan; [10]Seoul National University Bundang Hospital, Seongnam, Republic of Korea; [11]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [12]Department of Medical Oncology, National Taiwan University Cancer Center, Taipei, Taiwan; [13]Univeristy of Cologne, Faculty of Medicine, and University Hospital Cologne, Cologne, Germany; [14]Janssen-Cilag Pharmaceutical, Pefki, Greece; [15]Janssen Research & Development, Spring House, PA, USA; [16]Janssen Research & Development, Shanghai, China; [17]Janssen Research & Development, San Diego, CA, USA; [18]Janssen Research & Development, Allschwil, Switzerland; [19]Janssen Research & Development, Raritan, NJ, USA; [20]Multidisciplinary Oncology & Therapeutic Innovations Department, Assistance Publique - Hôpitaux de Marseille, Aix-Marseille University, CNRS, INSERM, CRCM, APHM, Marseille, France.

PALOMA-3: Phase III Noninferiority Trial of SC Amivantamab vs IV Amivantamab Each With Lazertinib in Progressive Advanced *EGFR*-Mutated NSCLC

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Amivantamab plus lazertinib vs osimertinib in first-line *EGFR*-mutant advanced non-small cell lung cancer (NSCLC) with biomarkers of high-risk disease: A secondary analysis from the phase 3 MARIPOSA study

Enriqueta Felip[1], Byoung Chul Cho[2], Vanesa Gutiérrez[3], Adlinda Alip[4], Benjamin Besse[5], Shun Lu[6], Alexander I Spira[7], Nicolas Girard[8], Raffaele Califano[9], Shirish M Gadgeel[10], James Chih-Hsin Yang[11], Naoyuki Nogami[12], Koichi Azuma[13], Joshua C Curtin[14], Jiarui Zhang[14], Anesh Panchal[15], Mariah Ennis[14], Seema Sethi[14], Joshua M Bauml[14], Se-Hoon Lee[16]

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Organizado por:

GECP lung cancer research

Advanced targeted NSCLC

FLAURA2 Phase III study design (NCT04035486)

Patients with untreated locally advanced / metastatic EGFRm NSCLC

Key inclusion criteria:

- Aged ≥18 years (Japan: ≥20 years)
- Pathologically confirmed non-squamous NSCLC
- Ex19del / L858R (local / central test)
- WHO PS 0 / 1
- No prior systemic therapy for advanced NSCLC
- Stable CNS metastases were allowed*
- Brain scans at baseline (MRI / CT)

Osimertinib 80 mg (QD) + pemetrexed 500 mg/m² + carboplatin AUC5 or cisplatin 75 mg/m² (Q3W for 4 cycles)

Maintenance osimertinib 80 mg (QD) + pemetrexed 500 mg/m² (Q3W)†

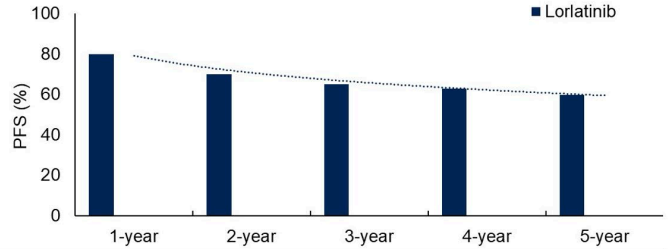
Follow-up: RECIST v1.1 assessment at 6 and 12 weeks, then Q12W until RECIST v1.1 defined radiological disease progression or other withdrawal criteria were met

Randomization 1:1 (N=557)
Stratification by: race (Chinese Asian / non-Chinese Asian / non-Asian); **EGFR test** (local / central); **WHO PS** (0 / 1)

Osimertinib 80 mg (QD)

- **Primary endpoint:** PFS by investigator assessment per RECIST v1.1‡§
- **Secondary endpoints include:** OS, ORR, DoR, DCR, HRQoL and safety (AEs by CTCAE v5) and PFS2‡

Evaluating CROWN in the Context of ALK Treatment Landscape: Systemic Efficacy

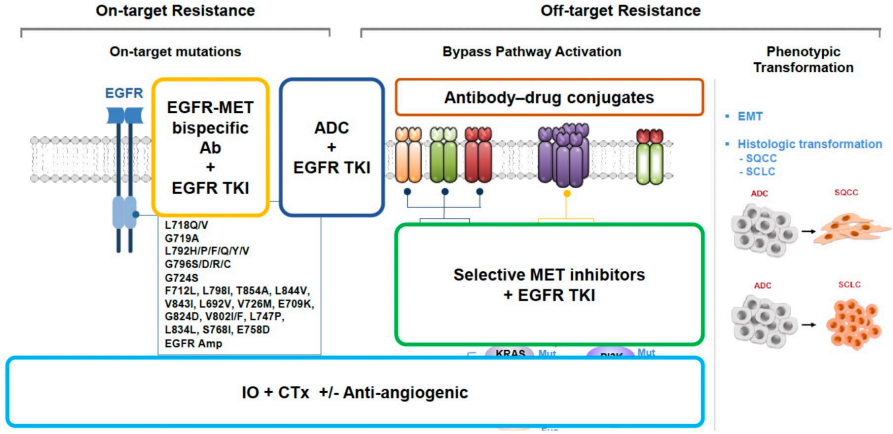


	Median PFS	1-year PFS (%)	2-year PFS (%)	3-year PFS (%)	4-year PFS (%)	5-year PFS (%)
Lorlatinib[1-3]	Not reached at 60.2 mos	80	70	63	63	60

1. Shaw AT et al., N Engl J Med 2020;383:2018-29
2. Solomon BJ et al., Lancet Respir Med 2023;11(4):354-66
3. Solomon BJ et al., ASCO 2024

Beyond Osi Progression

TREATMENT STRATEGIES based on the resistance mechanism



Organizado por:
GECP lung cancer research

Advanced targeted NSCLC

KRAS G12C

RET

MET ex14

ROS 1

NTRK1,2,3

HER 2, 3

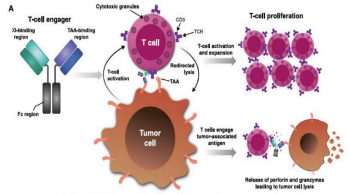
BRAF

Organizado por:

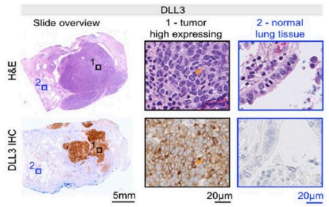
GECP lung cancer research

Other thoracic tumors

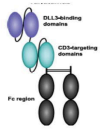
SCLC



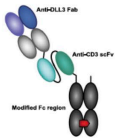
DLL-3 T-cell-mediated engaging



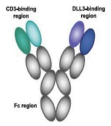
Tarlatamab
Bispecific mAb
Amgen
(Phase 2-3)



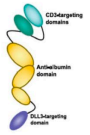
QLS31904
Bispecific mAb
Qilu Pharmaceuticals
(Phase 1)



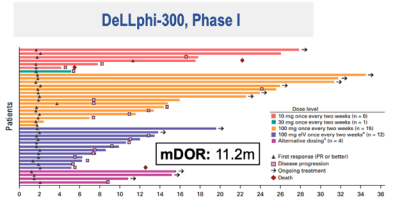
Obrixtamig
(BI 764532)
Bispecific mAb
Boehringer Ingelheim
(Phase 1-2)

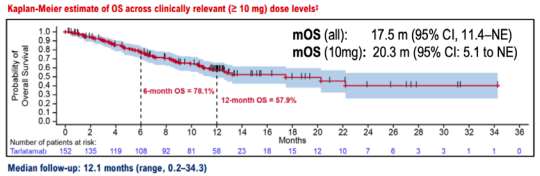


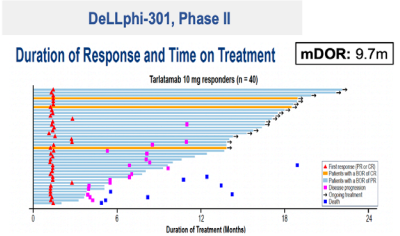
HPN328 or MK-6070
Trispecific mAb
Daiichi/ Merck/Harpoon
(Phase 1/2)

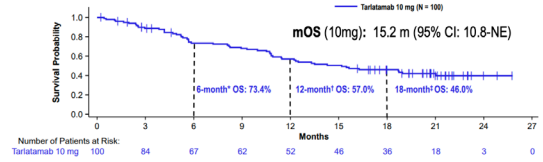


- Others: RO7616789 (Roche/Chugai)

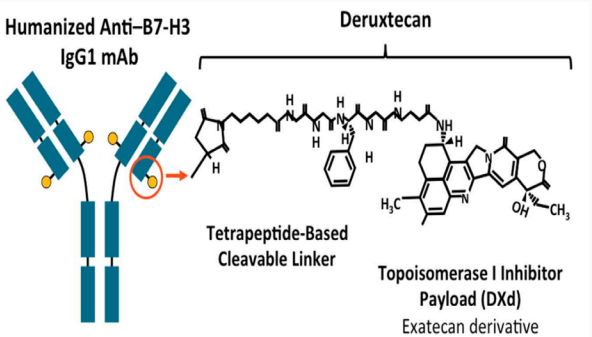






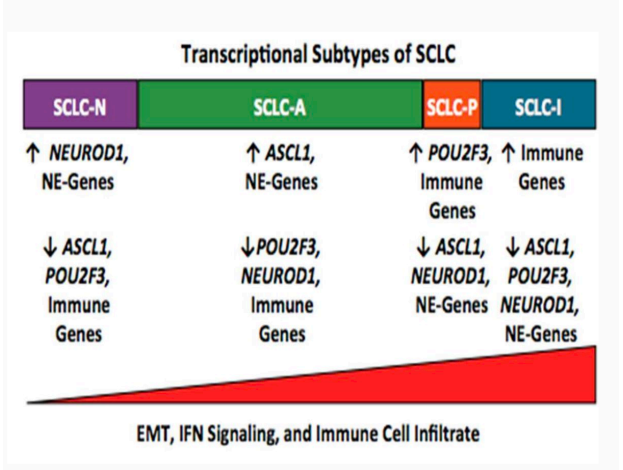


1.- Paz-Ares J Clin Oncol 2023; 2.- Hummel, ELCC 2024, 3.- Dowlati JCO 2024, 4.- Ahn MJ, NEJM 2023 , 5,-Sands J. WCLC 2024



- ✓ High potency, membrane payload with short systemic half-life
- ✓ Optimized DAR 4:1
- ✓ Stability of the linker payload
- ✓ Tumor-selectable cleavable linker
- ✓ Bystander killing effect

IFINATAMAB DERUXTECAN



Organizado por:
GECP lung cancer research

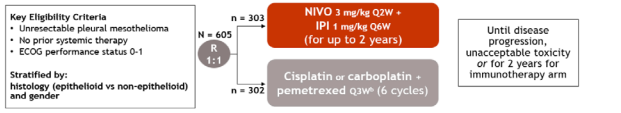
Other thoracic tumors

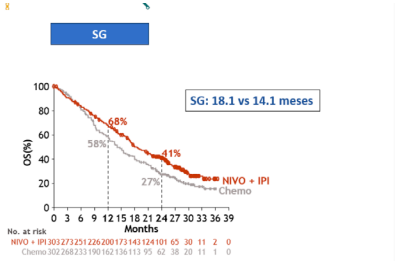
Mesothelioma

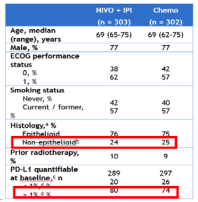
Primer estudio randomizado que compara QT frente a inmunoterapia

No mejoría en PFS ni ORR, sí en SG

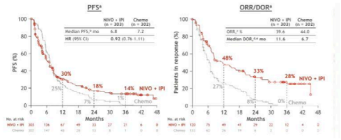
Estudio positivo, aprobado por **FDA y EMA**

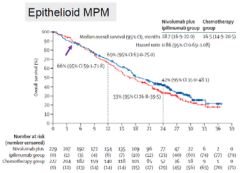


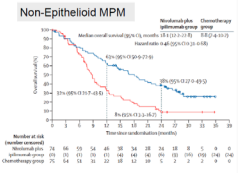




	NIVO + IPI (n = 303)	Chemo (n = 302)
Age, median (range), years	69 (65-75)	69 (62-75)
Male, %	77	77
ECOG performance status		
0, %	38	42
1, %	62	57
Smoking status		
Never, %	42	40
Current / former, %	57	57
Histology,* %		
Epithelioid	76	75
Non-epithelioid	24	25
Prior radiotherapy, %	10	9
PD-L1 quantifiable at baseline,† n	289	297
≥ 1%	209	223
≥ 5%	80	74

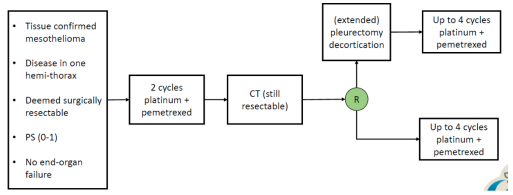


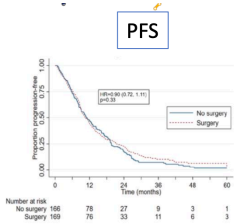


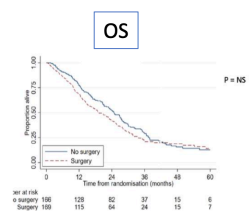


CHECK MATE 473

MARS 2







Objetivo primario supervivencia:

19.3 m cirugía

24.8 m quimioterapia

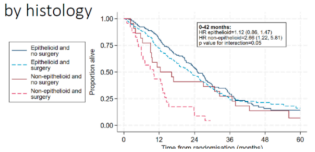
4.5% de los pacientes no recibieron el tto asignado y 7.5% se retiraron después de randomizacion

Incluyó 12% de pacientes con tumores no-epitelioides

Estadiaje por TAC

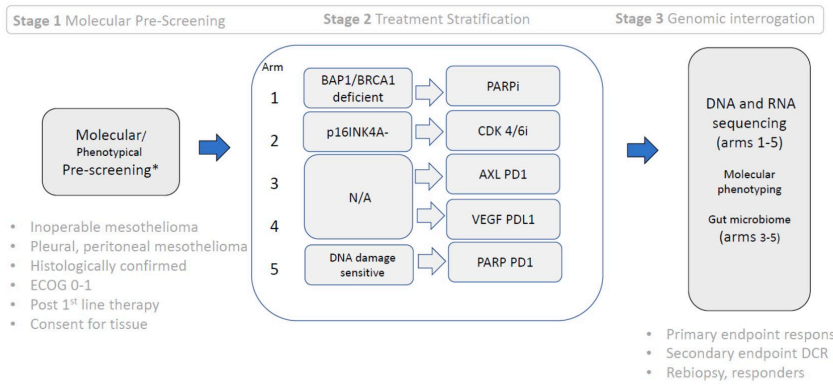
Survival by histology

Completeness of resection	
R0 (no residual tumour)	5/157 (3.2%)
R1 (microscopic residual tumour)	127/157 (80.9%)
R2 (macroscopic residual tumour)	25/157 (15.9%)
Length of hospital stay (days) §	13 (12, 14)
In-hospital mortality	6/157 (3.8%)
30 day mortality	6/157 (3.8%)
90 day mortality	14/157 (8.9%)

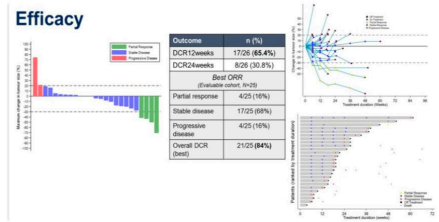


Mesothelioma Stratified Therapy (MiST) study design

Trials.gov ID NCT03654833



- Inoperable mesothelioma
- Pleural, peritoneal mesothelioma
- Histologically confirmed
- ECOG 0-1
- Post 1st line therapy
- Consent for tissue



Outcome	n (%)
DCR12weeks	17/26 (65.4%)
DCR24weeks	8/26 (30.8%)
Best ORR (Evaluable cohort, N=29)	
Partial response	4/25 (16%)
Stable disease	17/25 (68%)
Progressive disease	4/25 (16%)
Overall DCR (best)	21/25 (84%)

- Primary endpoint response
- Secondary endpoint DCR
- Rebiopsy, responders

FENNELL. ASCO 2024

Organizado por:

GECP lung cancer research

Novedades & Claves en CÁNCER de PULMÓN 2024

Añade esta fecha a tu calendario

21 Enero 2025
16:00h-18:00h

FORMATO **VIRTUAL**

ACCEDER

Programa científico

16:00 - 16:10	Introducción Dr. Jose Luís González Larriba Hospital Clínico San Carlos, Madrid
16:10 - 16:30	Biomarcadores pronósticos Dra. Ana Cardeña Hospital Univ. Nuestra Señora de Candelaria, Santa Cruz de Tenerife
16:30 - 16:50	Estadios iniciales y enfermedad localmente avanzada Dr. Eider Akcona Hospital Univ. de Cruces, Baracaldo, Vizcaya
16:50 - 17:10	Enfermedad metastática (incluyendo inmunoterapia) Dra. Noelia Vilariño ICO, Hospital Duran i Reynals, L´Hospitalet de Llobregat, Barcelona
17:10 - 17:30	Cáncer de pulmón microcítico y otros tumores Dr. Juan Luis Martí Hospital General Univ. Dr. Balmis, Alicante
17:30 - 17:45	Debate
17:45 - 18:00	Conclusiones Dr. Jose Luís González Larriba Hospital Clínico San Carlos, Madrid

Organizado por:

GECP lung cancer research

Patrocinado por:

Bristol Myers Squibb™

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