Lung Cancer UPDATES
ASCO HIGHLIGTHS
03-07 JUNIO 2022
Chicago, IL

CHICAGO

Iniciativa científica de:
GECP lung cancer research

¿Qué hay de nuevo en ASCO 22?

NSCLA locorregional

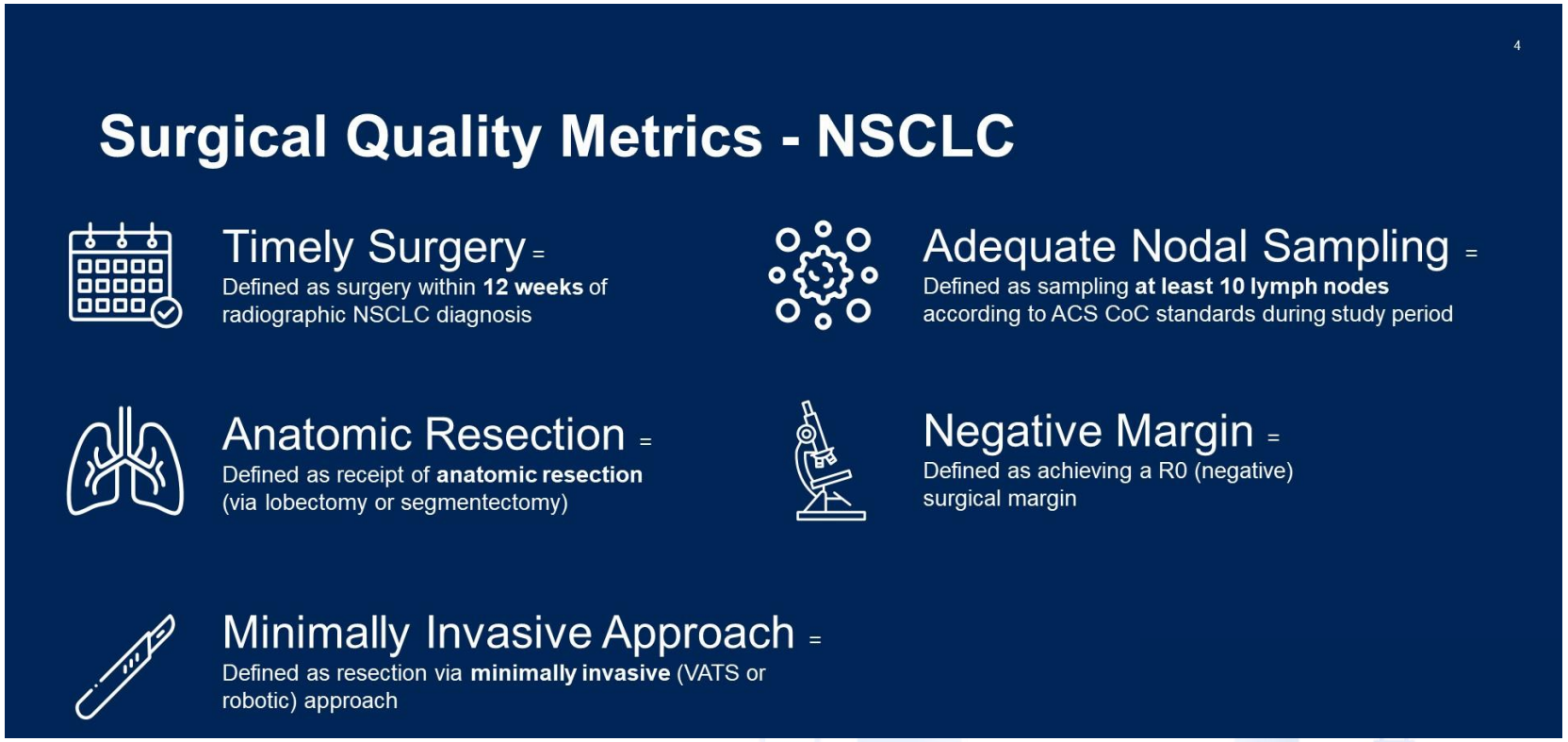
SCLC

Otros tumores torácicos

Martín Lázaro Quintela
Hospital Álvaro Cunqueiro
Área Sanitaria de Vigo

NSCLC *early*

Métricas intraoperatorias y supervivencia



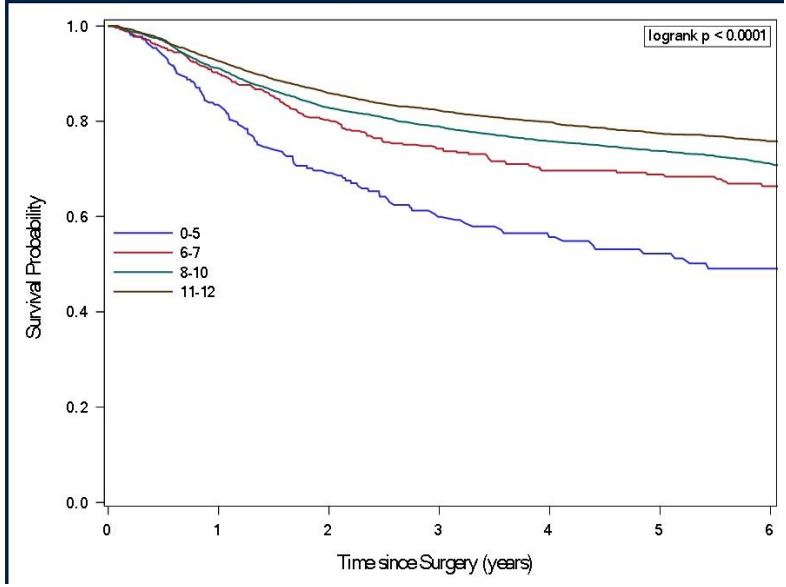
- 9628 pacientes con estadio I resecados
- VHA

Eiden. ASCO 22.

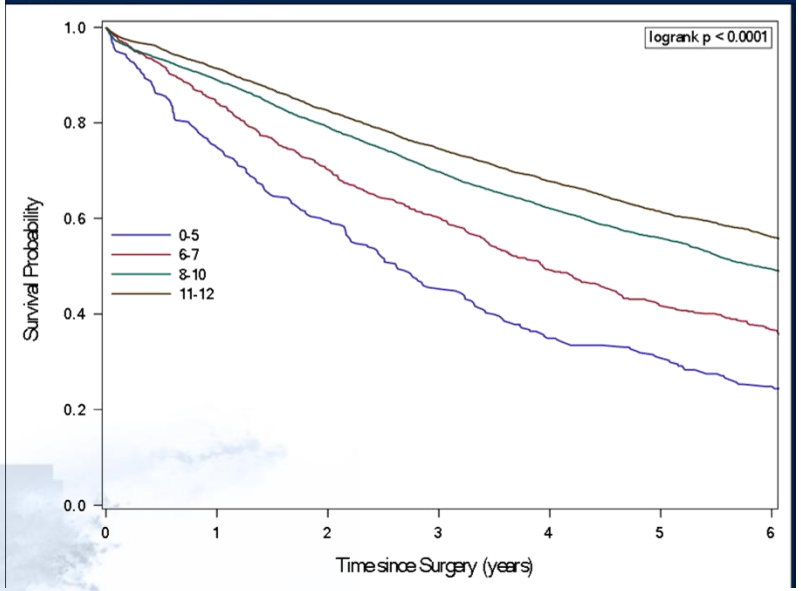
Score development

Variable[a]	aHR, 95% CI	β	p-value	Points
Delayed surgery				
>12 weeks	[1 ref]	-	-	0
≤12 weeks	0.895 (0.845-0.948)	-0.11	<0.001	1
Surgical approach				
Open	[1 ref]	-	-	0
Minimally invasive	0.907 (0.855-0.962)	-0.10	0.001	1
Extent of resection				
Wedge	[1 ref]	-	-	0
Lobectomy	0.837 (0.776-0.903)	-0.18	<0.001	2
Segmentectomy	0.835 (0.729-0.956)	-0.18	0.009	2
Pneumonectomy[b]	1.255 (1.012-1.555)	0.23	0.04	0
Nodal sampling adequacy				
0 LN	[1 ref]	-	-	0
1-4 LN	0.887 (0.802-0.980)	-0.12	0.02	1
5-9 LN	0.829 (0.747-0.920)	-0.19	<0.001	2
≥10 LN	0.822 (0.740-0.914)	-0.20	<0.001	2
Surgical margin				
R1+	[1 ref]	-	-	0
R0	0.552 (0.481-0.634)	-0.59	<0.001	6

(B) Recurrence-free Survival

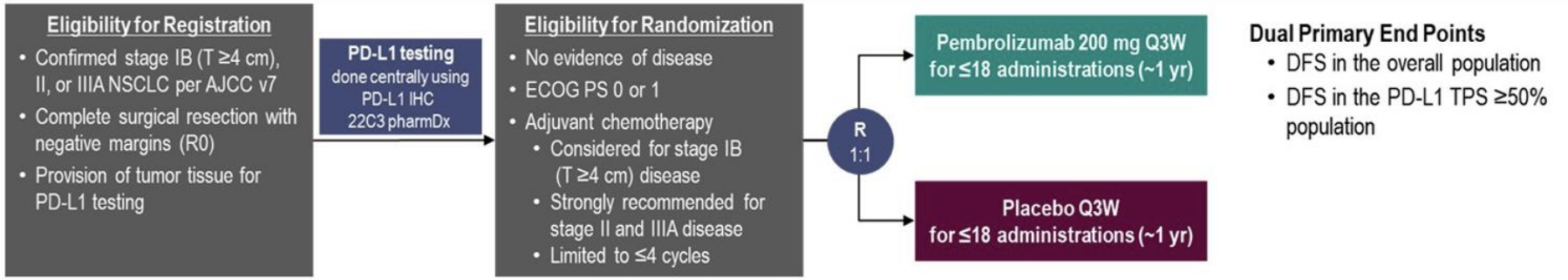


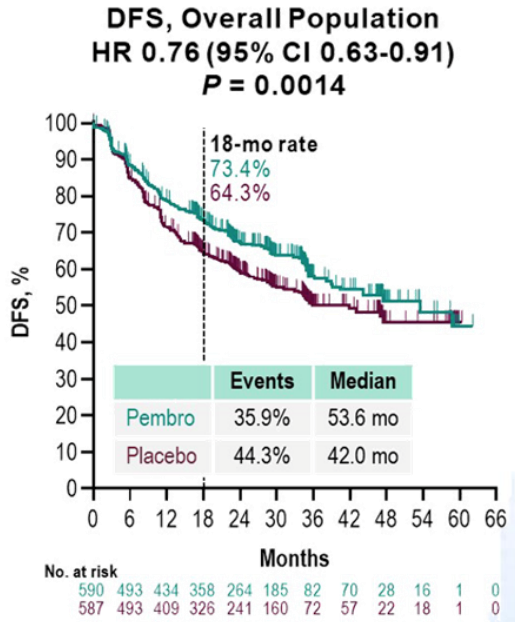
(A) Overall Survival

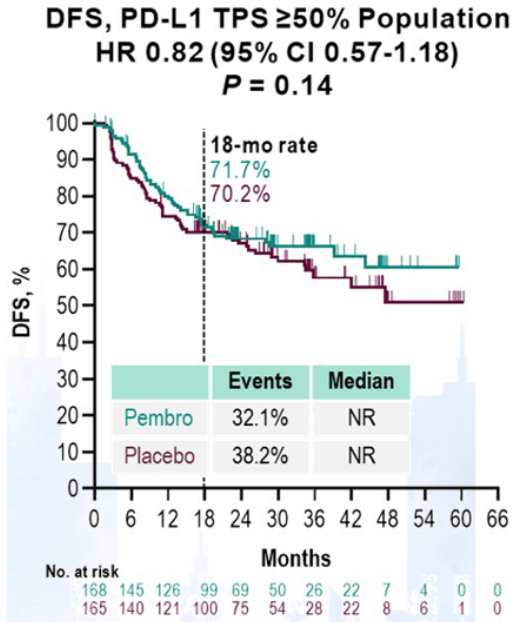


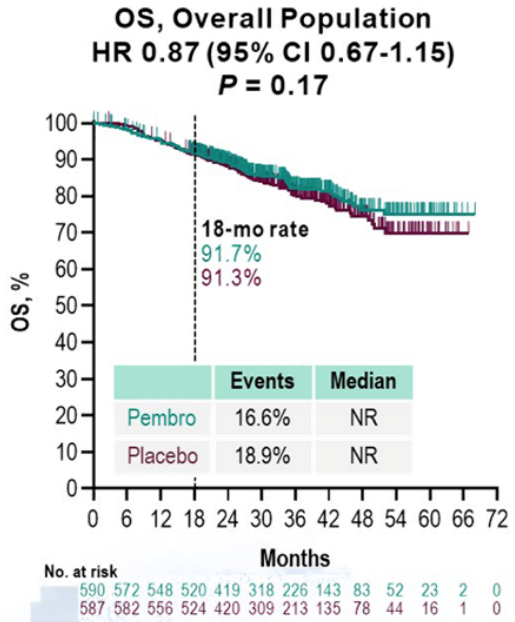
Eiden. ASCO 22.

PEARLS/KEYNOTE-091: actualización IA2





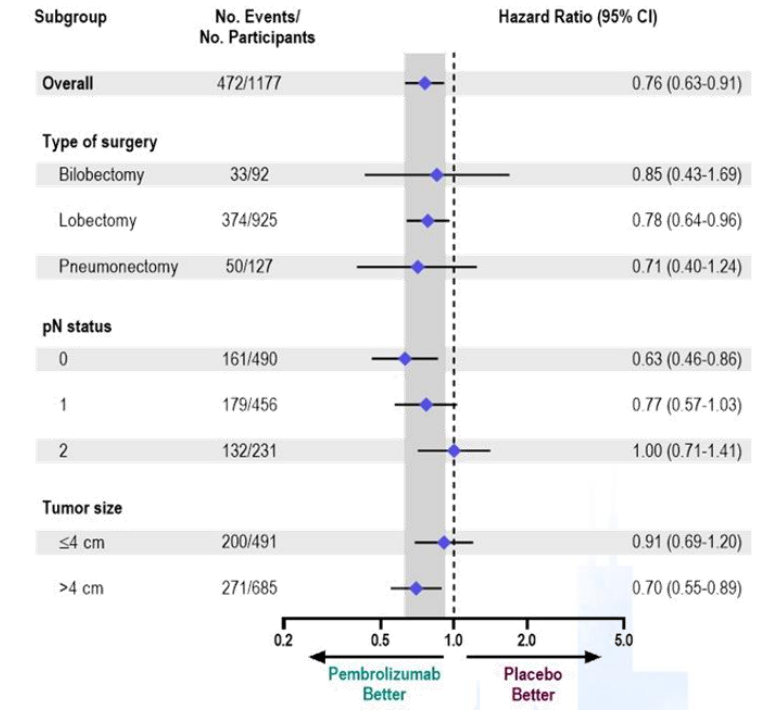


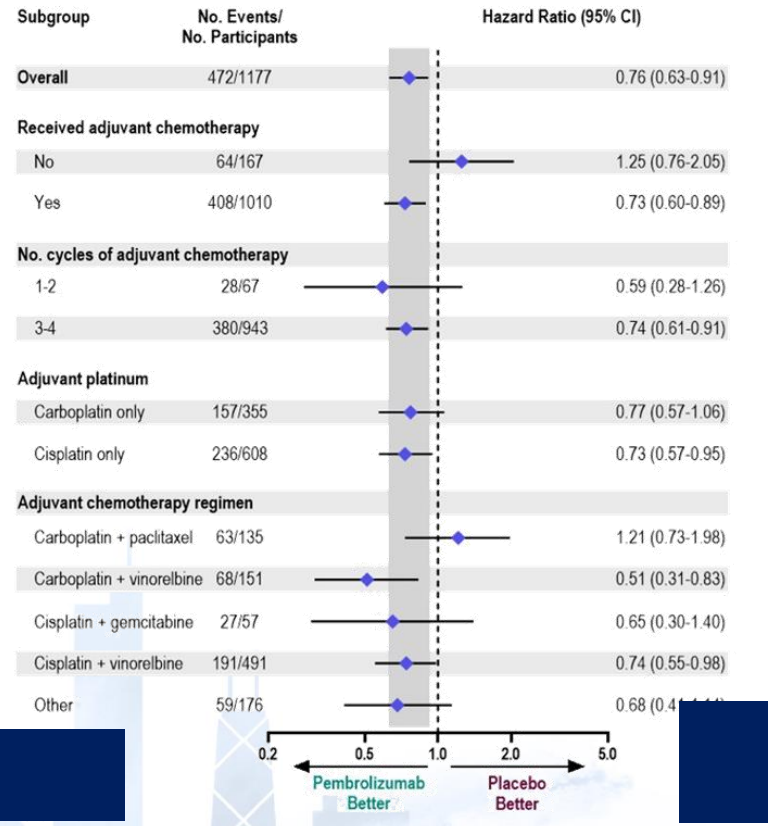


O'Brien. ASCO 22

PEARLS/KEYNOTE-091: actualización IA2

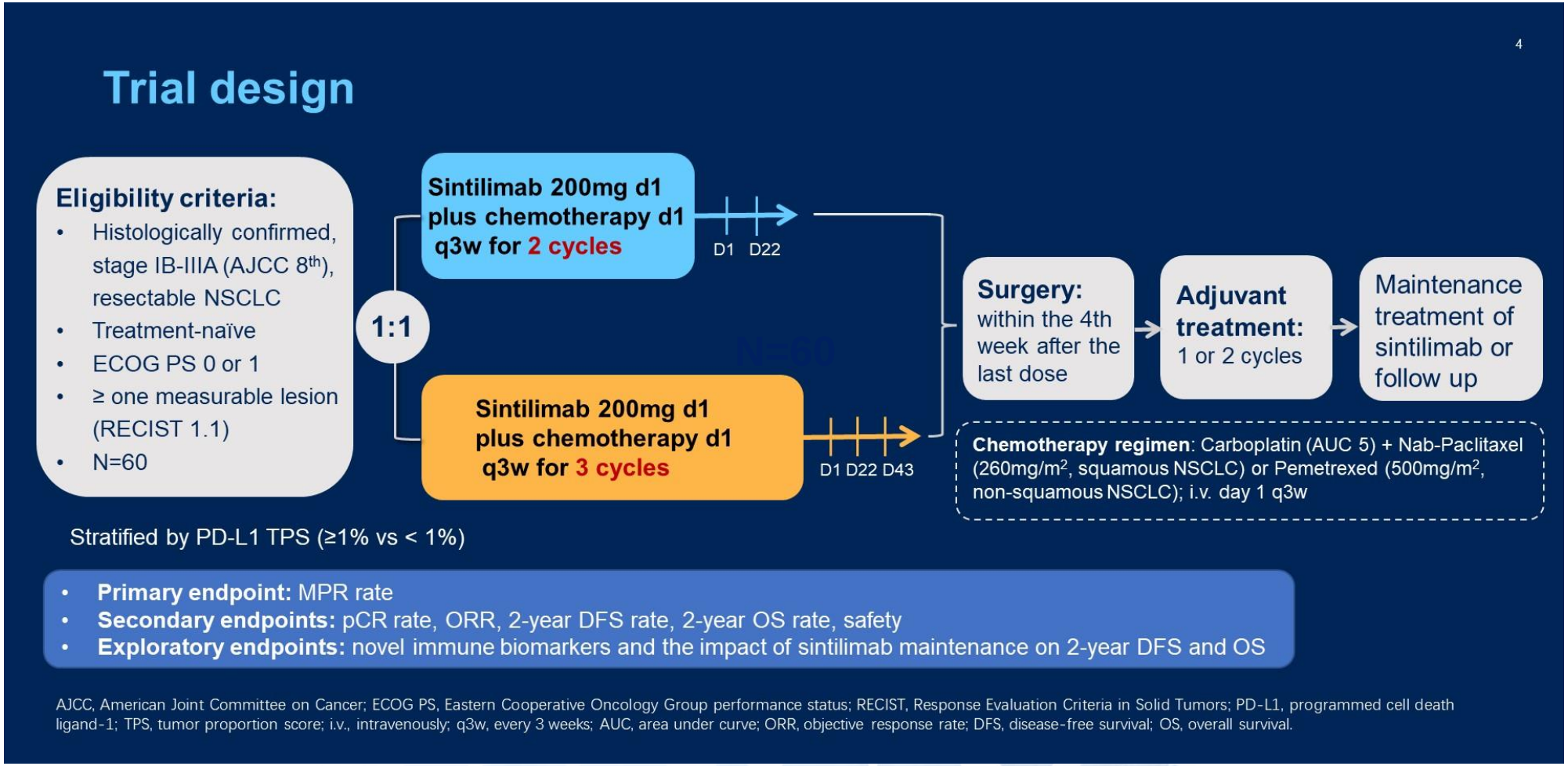
Análisis según cirugía, tamaño tumoral y tipo de quimioterapia adyuvante





O'Brien. ASCO 22

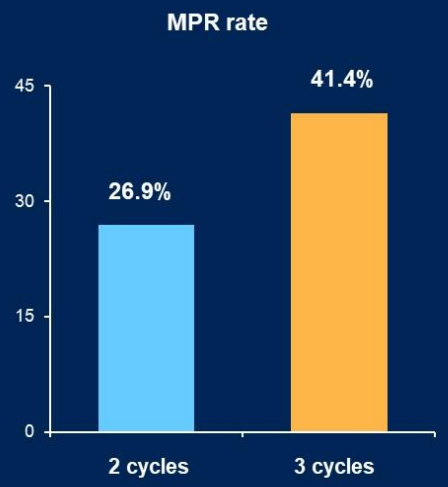
neoSCORE: fase II



Qiu. ASCO 22

neoSCORE: fase II

Primary endpoint



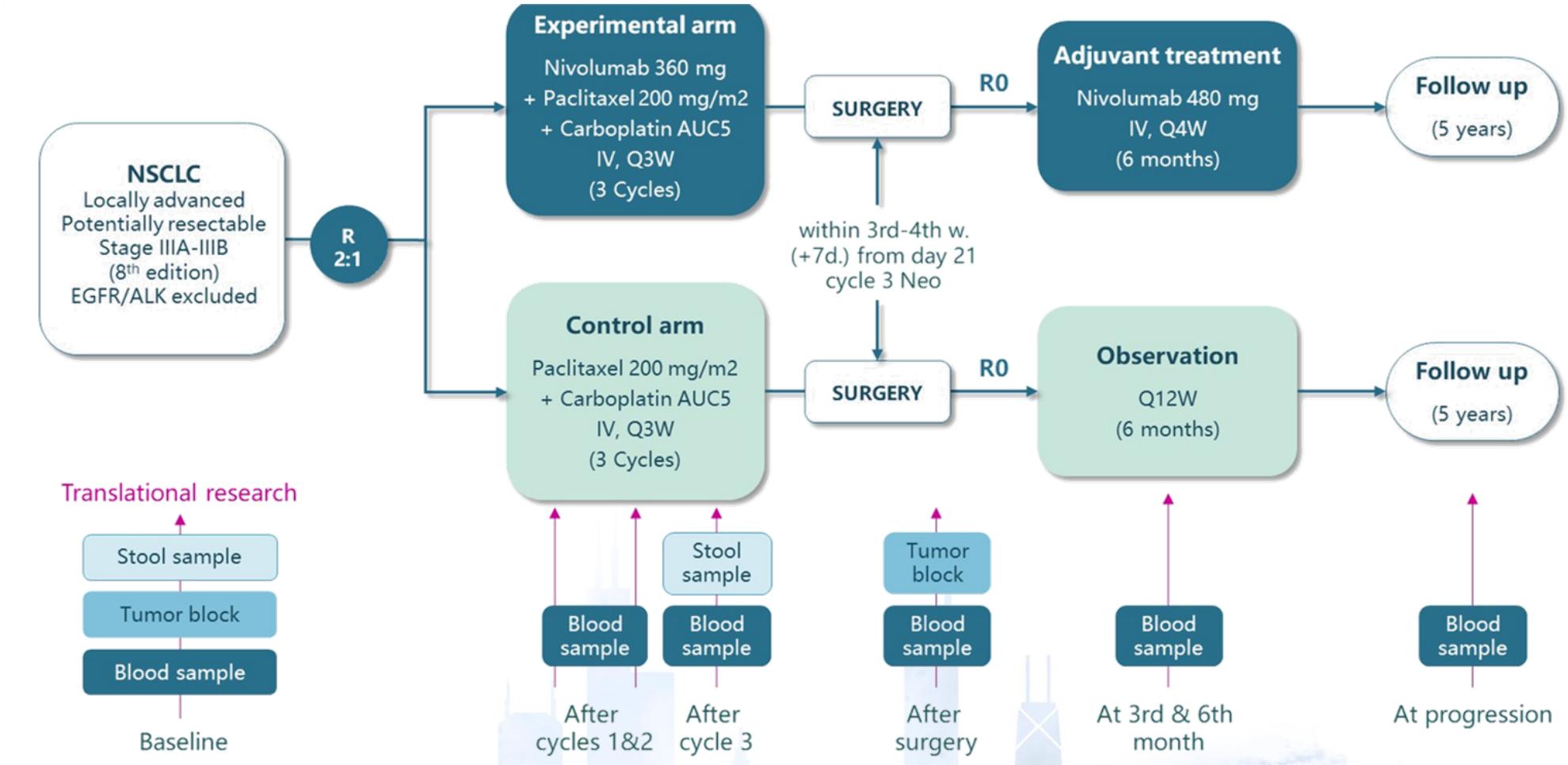
- Three cycles treatment presented a **14.5%** increase in MPR rate in comparison to two cycles

Pathological response, n(%)	Total, n=55	2 cycles, n=26	3 cycles, n=29	*P* value*
MPR	19（34.5%） (95% CI：22.2-48.6%)	7（26.9%） (95% CI：11.6-47.8%)	12（41.4%） (95% CI：23.5-61.1%)	0.260

- Narrow cycle difference of treatment
- Small sample size

*, the two-sided *P* value was from the χ2 test, the exact two-sided 95% CIs were calculated by use of the Clopper-Pearson method.

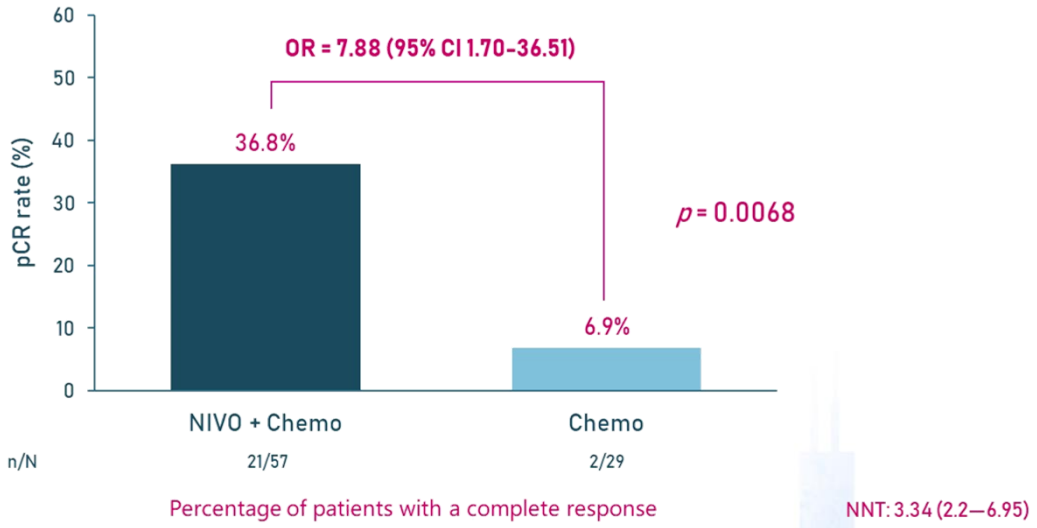
NADIM II



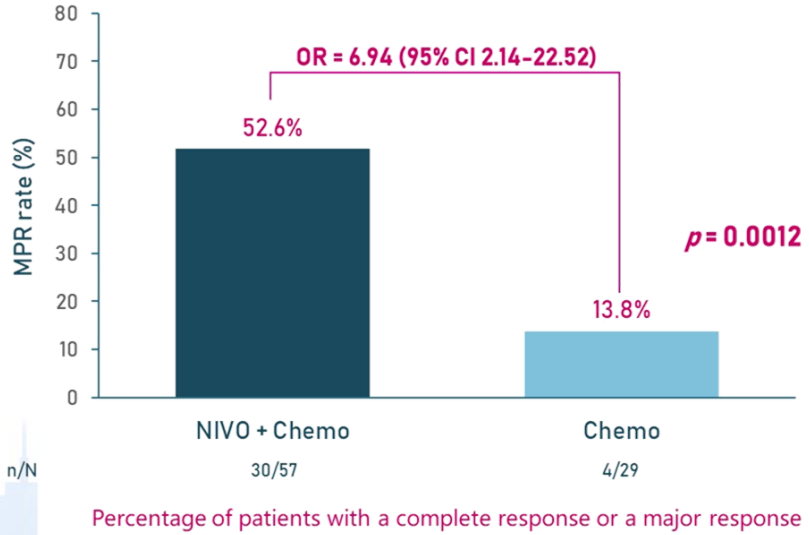
Objetivo principal: Respuestas completas patológicas
O. secundarios: MPR, RR, OS, PFS, seguridad, biomarcadores

NADIM II: pCR y MPR

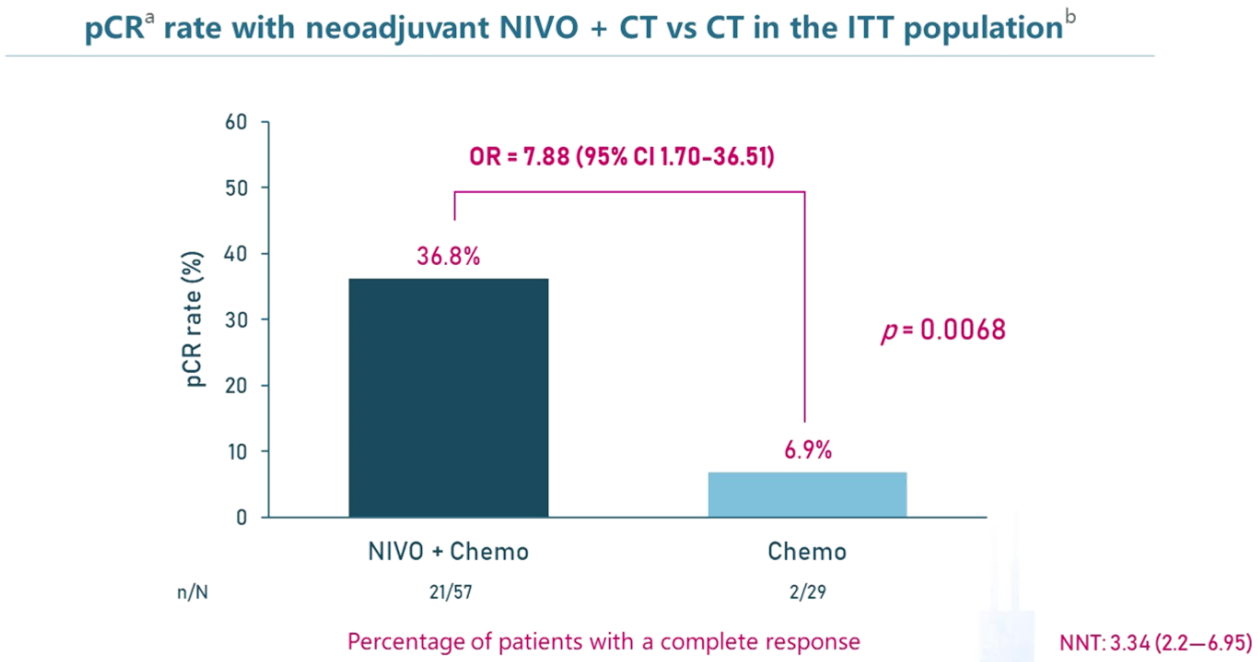
pCR[a] rate with neoadjuvant NIVO + CT vs CT in the ITT population[b]



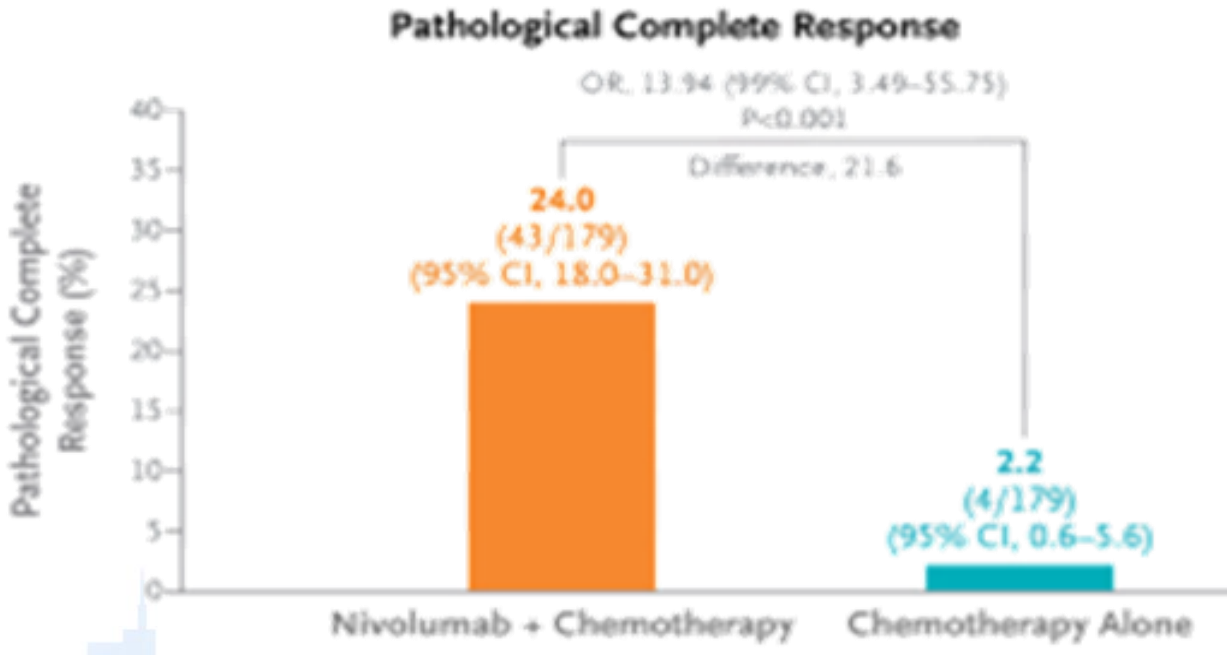
MPR[a] rate with neoadjuvant NIVO + CT vs CT in the ITT population[b]



NADIM II y CM-816



Provencio. ASCO 22

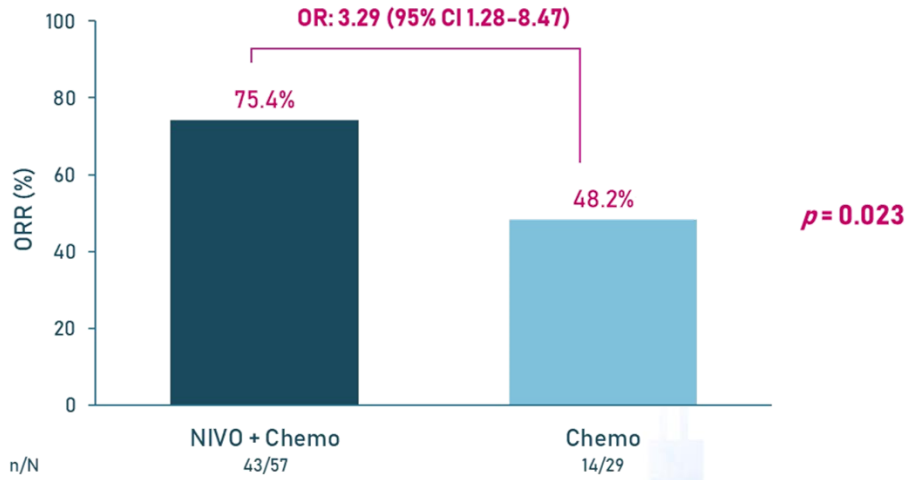


Forde NEJM 2022;386:1973-84

Primary endpointe: EFS y pCR

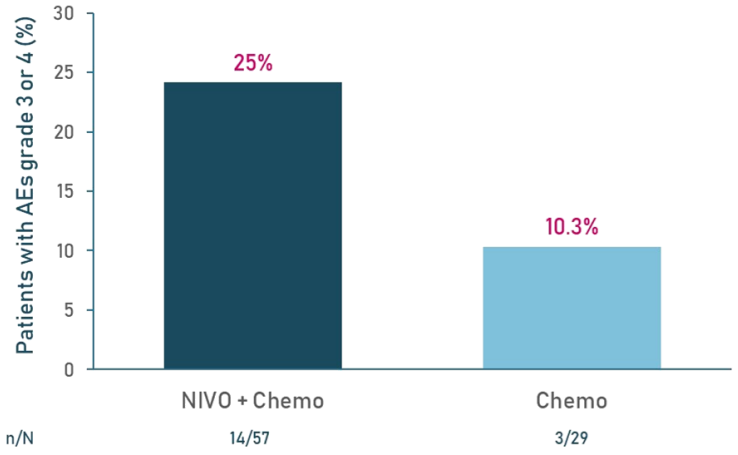
NADIM II: ORR y seguridad

ORR[a] with neoadjuvant NIVO + Chemo vs Chemo in the ITT population [b]



Percentage of patients with a complete response or a partial response

Adverse events G 3-4 summary (ITT population)

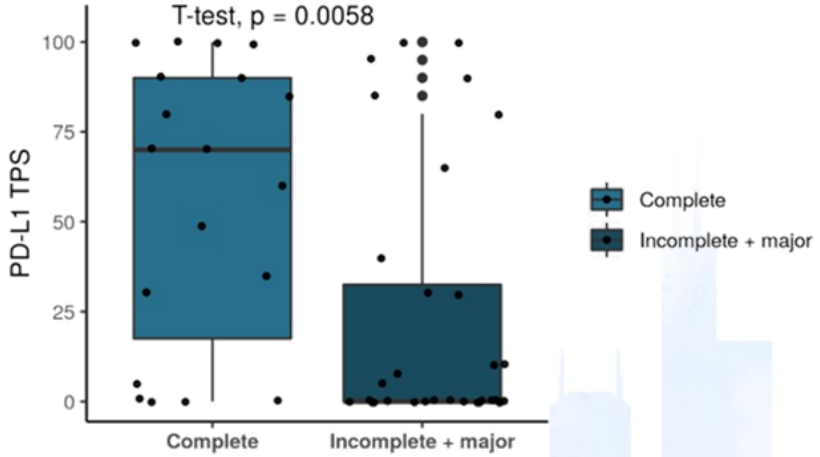


No grade 5 treatment-related adverse events were observed

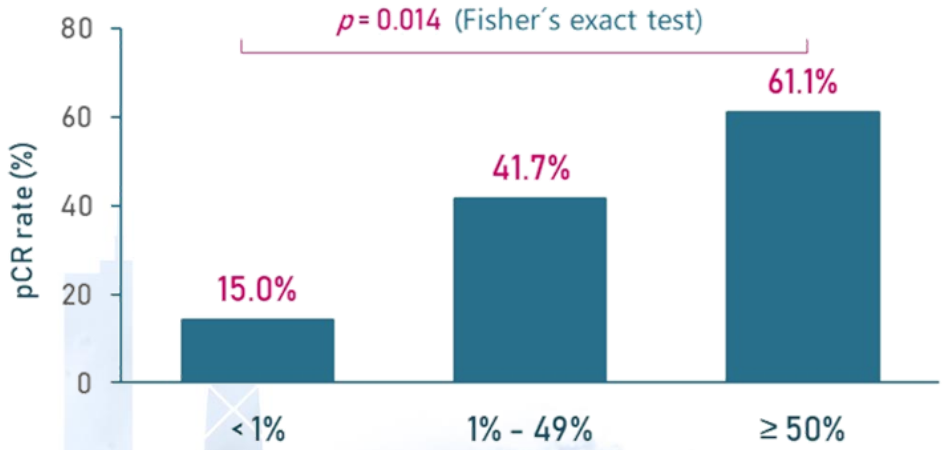
NADIM II: biomarcadores

Predictive biomarkers of response (pCR)[a] to neoadjuvant NIVO + CT (ITT population)[b]

- Patients who achieved pCR had higher PD-L1 expression than patients who did not
- pCR rate raised across increasing categories of PD-L1 TPS
- Predictive value of PD-L1 TPS for pCR was AUC 0.728 (95% CI 0.58-0.87; p = 0.001)
- **OR** for pCR in the PD-L1 positive group (**≥1%**): **16.0** (95% CI 1.86-137.61; ***p* = 0.007**)



Pathological response



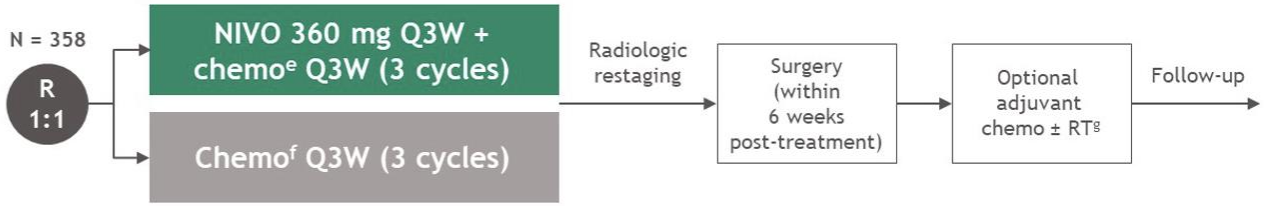
PD-L1 Tumor Proportion Score

CM-816

Key eligibility criteria

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

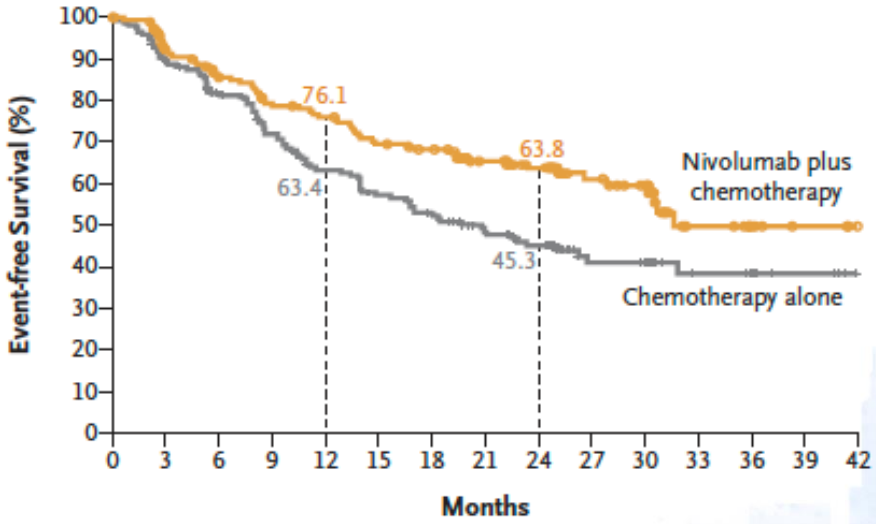
Stratified by stage (IB-II vs IIIA), PD-L1[c] (≥ 1% vs < 1%[d]), and sex



Primary endpoints
- pCR by BIPR
- EFS by BICR

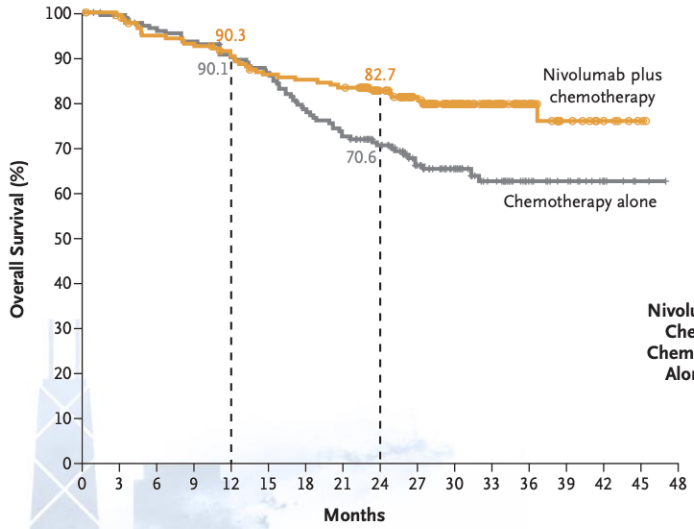
Secondary endpoints
- MPR by BIPR
- OS
- Time to death or distant metastases

Key exploratory analyses
- EFS by pathological regression



	No. of Patients	Median Event-free Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	31.6 (30.2–NR)
Chemotherapy Alone	179	20.8 (14.0–26.7)

Hazard ratio for disease progression, disease recurrence, or death, 0.63 (97.38% CI, 0.43–0.91)
P=0.005



	No. of Patients	Median Overall Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	NR (NR–NR)
Chemotherapy Alone	179	NR (NR–NR)

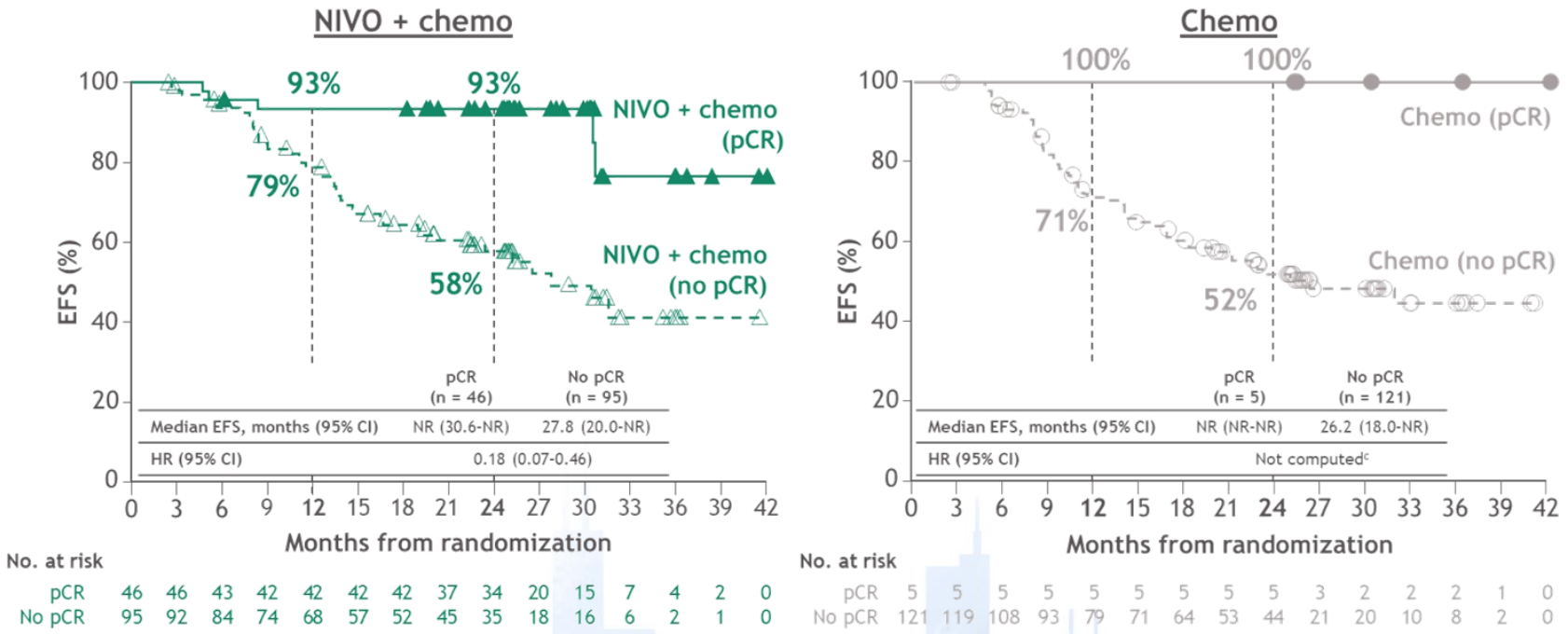
Hazard ratio for death, 0.57 (99.67% CI, 0.30–1.07)
P=0.008

Forde NEJM 2022;386:1973-84

CM-816: asociación de regresión patológica con EFS

CheckMate 816 neoadjuvant NIVO + chemo in resectable NSCLC: EFS by pathological regression

EFS by pCR status[a] (primary tumor) in the path-evaluable patient population



- EFS was also improved in patients with MPR[b] in the primary tumor compared with those without; HR (95% CI) was 0.26 (0.14–0.50) for NIVO + chemo and 0.48 (0.22–1.05) for chemo, respectively

Minimum follow-up: 21 months; median follow-up: 29.5 months.

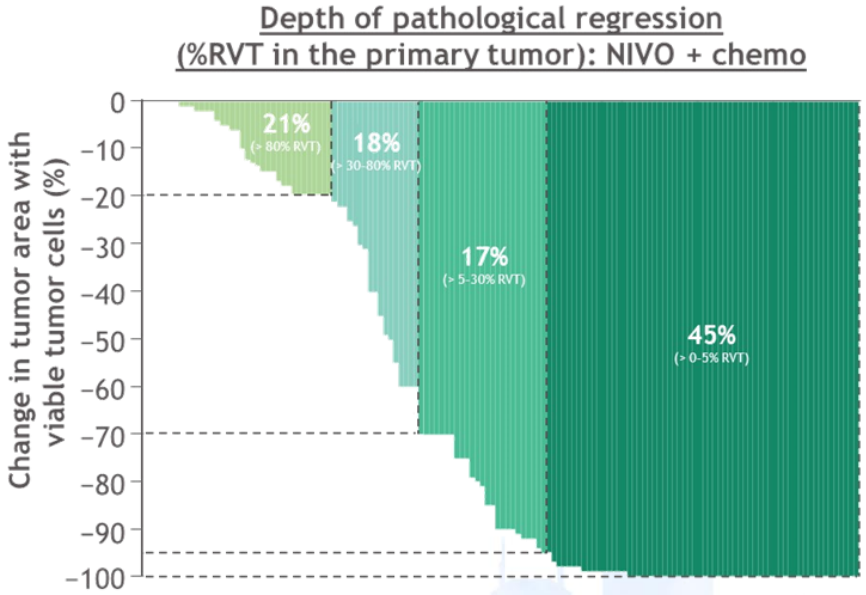
[a]pCR: 0% RVT cells in the primary tumor in the path-evaluable patient population (patients who underwent surgery and had pathologically evaluable samples); [b]MPR: ≤ 10% RVT cells in the primary tumor in the path-evaluable patient population; [c]HR was not computed for the chemo arm due to only 5 patients having a pCR.

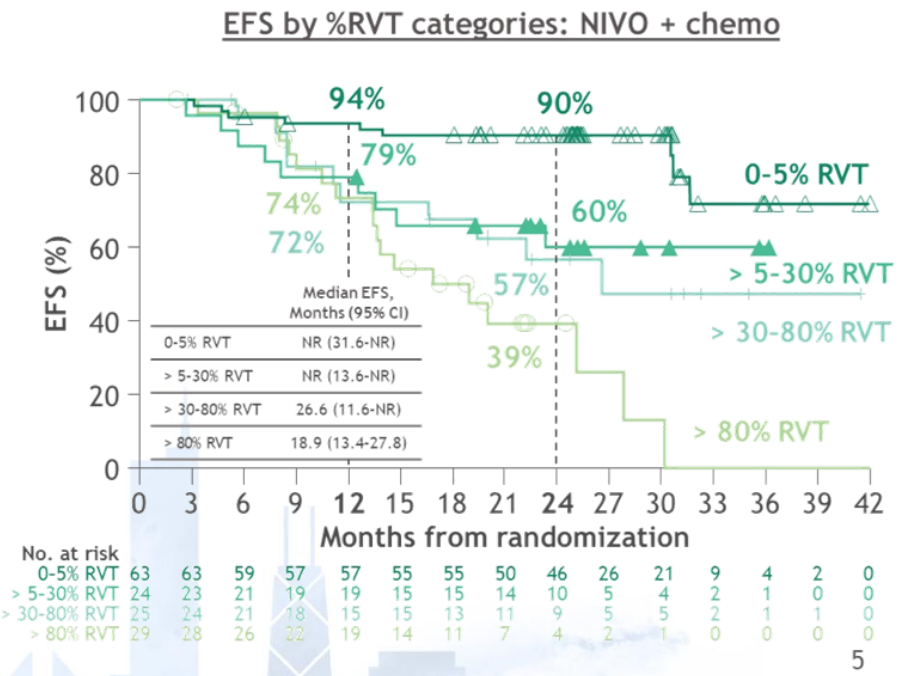
CM-816: asociación de regresión patológica con EFS

CheckMate 816 neoadjuvant NIVO + chemo in resectable NSCLC: EFS by pathological regression

EFS by depth of pathological regression (primary tumor)[a]: NIVO + chemo

- Based on a ROC curve analysis, depth of pathological regression (measured by %RVT) as a continuous variable in the primary tumor appeared to be predictive of EFS at 2 years for NIVO + chemo (AUC = 0.74), but not for chemo (AUC = 0.54)





Minimum follow-up: 21 months; median follow-up: 29.5 months.

[a]Path-evaluable patient population.

Quimioterapia vs quimio-radioterapia neoadyuvante en estadio III-N2 resecados

SEER database 2004-15

O. principal: OS y CSS

1175 pacientes

(799 QRT, 376 QT)

No encuentran diferencias en

OS ni en CSS

Survival	OS	CRT	CT
OS			
1-year		84.7%	83.2%
3-year		57.3%	57.3%
5-year		47.1%	44.1%
Median		51 months	47 months

Survival	CSS	CRT	CT
CSS			
1-year		86.6%	85.5%
3-year		62.3%	61.8%
5-year		53.8%	48.9%
Median		75 months	59 months

Microcítico

2

ASTRUM-005: Serplulimab

Study Design

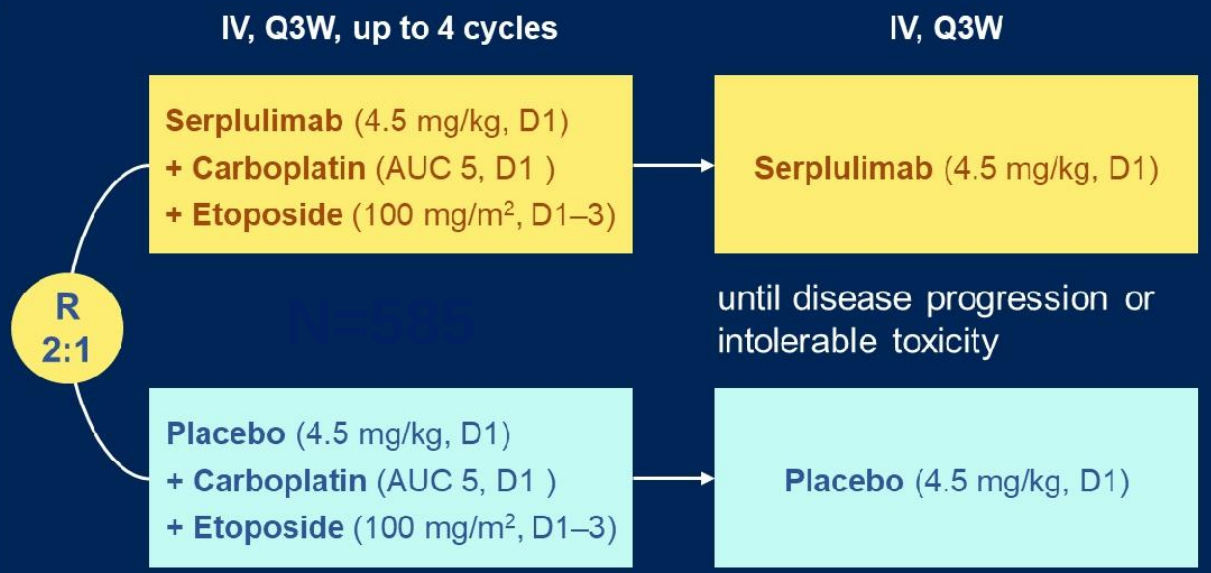
A randomized, double-blind, multicenter, placebo-controlled, phase 3 trial (NCT04063163)

Main inclusion criteria

- Histologically/cytologically diagnosed with ES-SCLC
- No prior systemic therapy for ES-SCLC
- At least one measurable lesion
- ECOG PS 0/1

Stratification factors

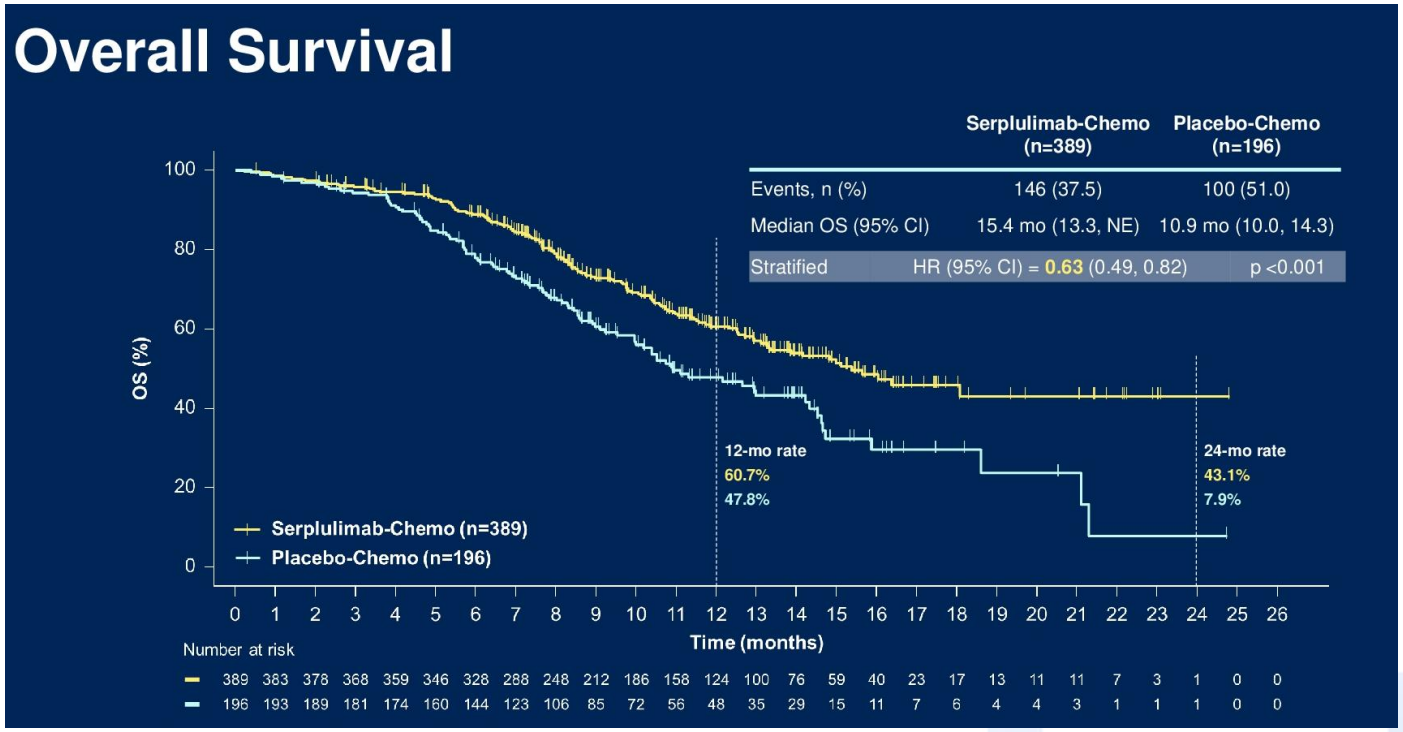
- PD-L1 expression levels (negative: TPS <1%, positive: TPS ≥1%, or NA)
- Brain metastases (Yes vs No)
- Age (<65 vs ≥65)

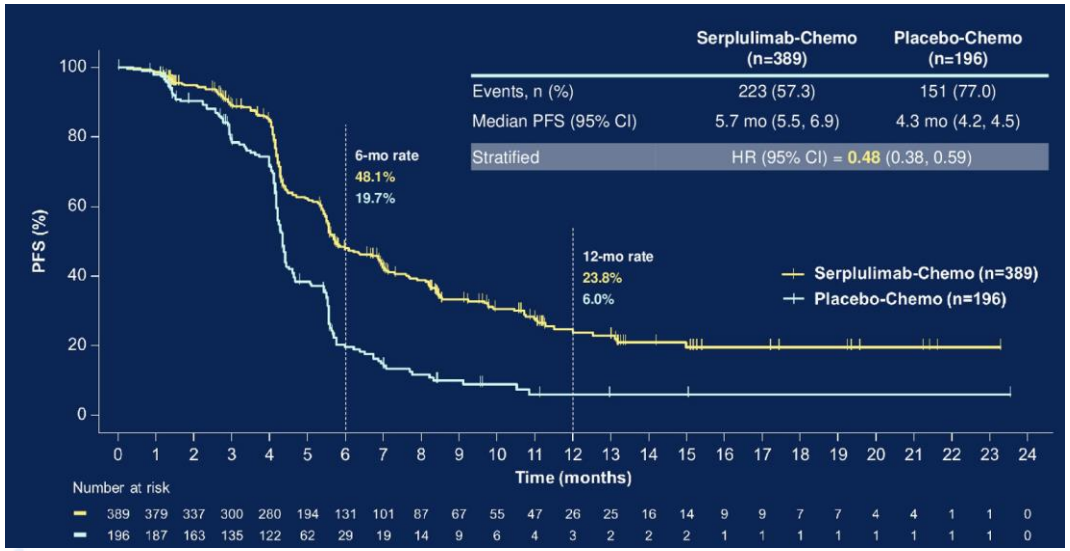


Primary endpoint: OS

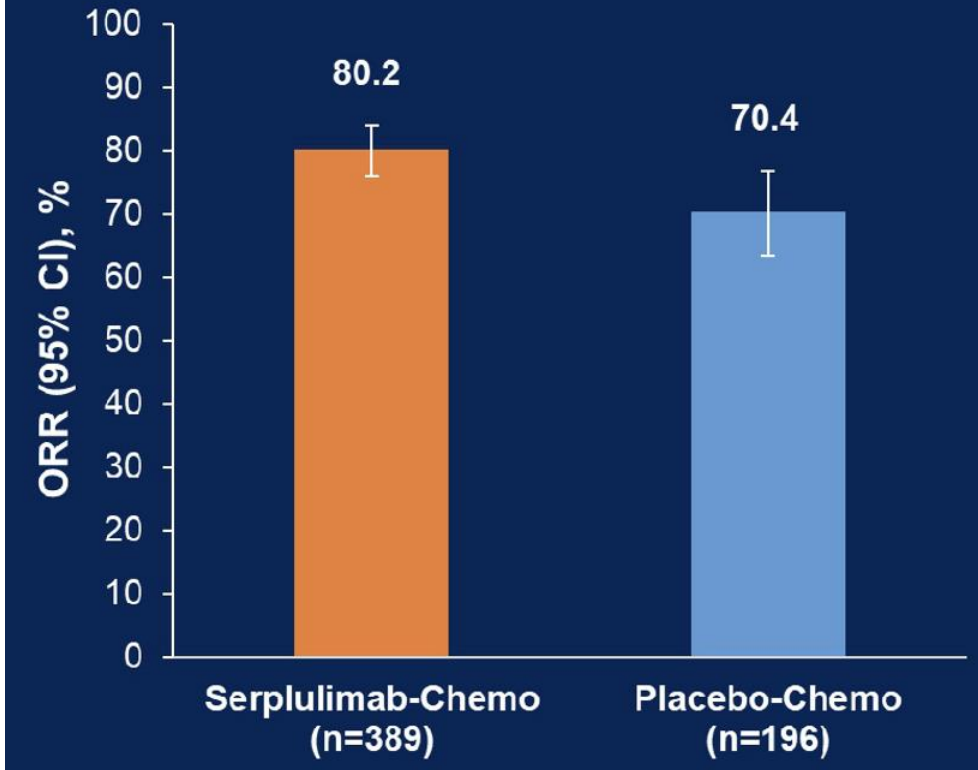
Secondary endpoints: PFS, ORR, DOR, Safety and immunogenicity

ASTRUM-005: Serplulimab

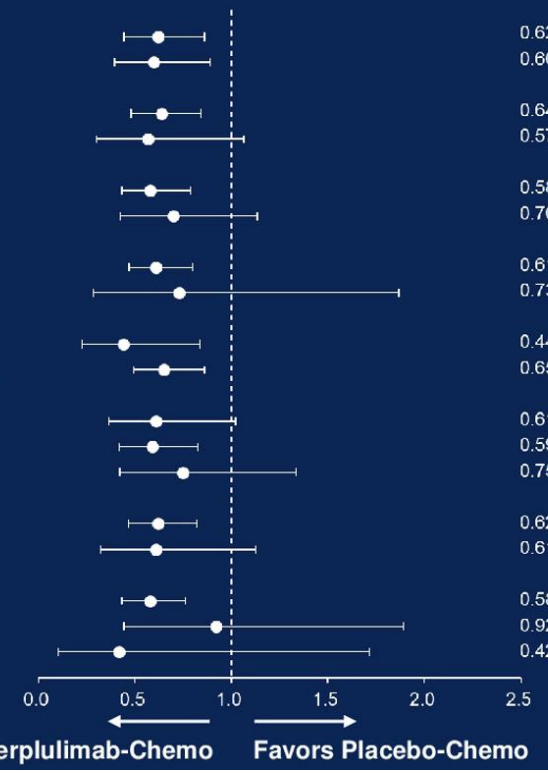




Cheng. ASCO 22



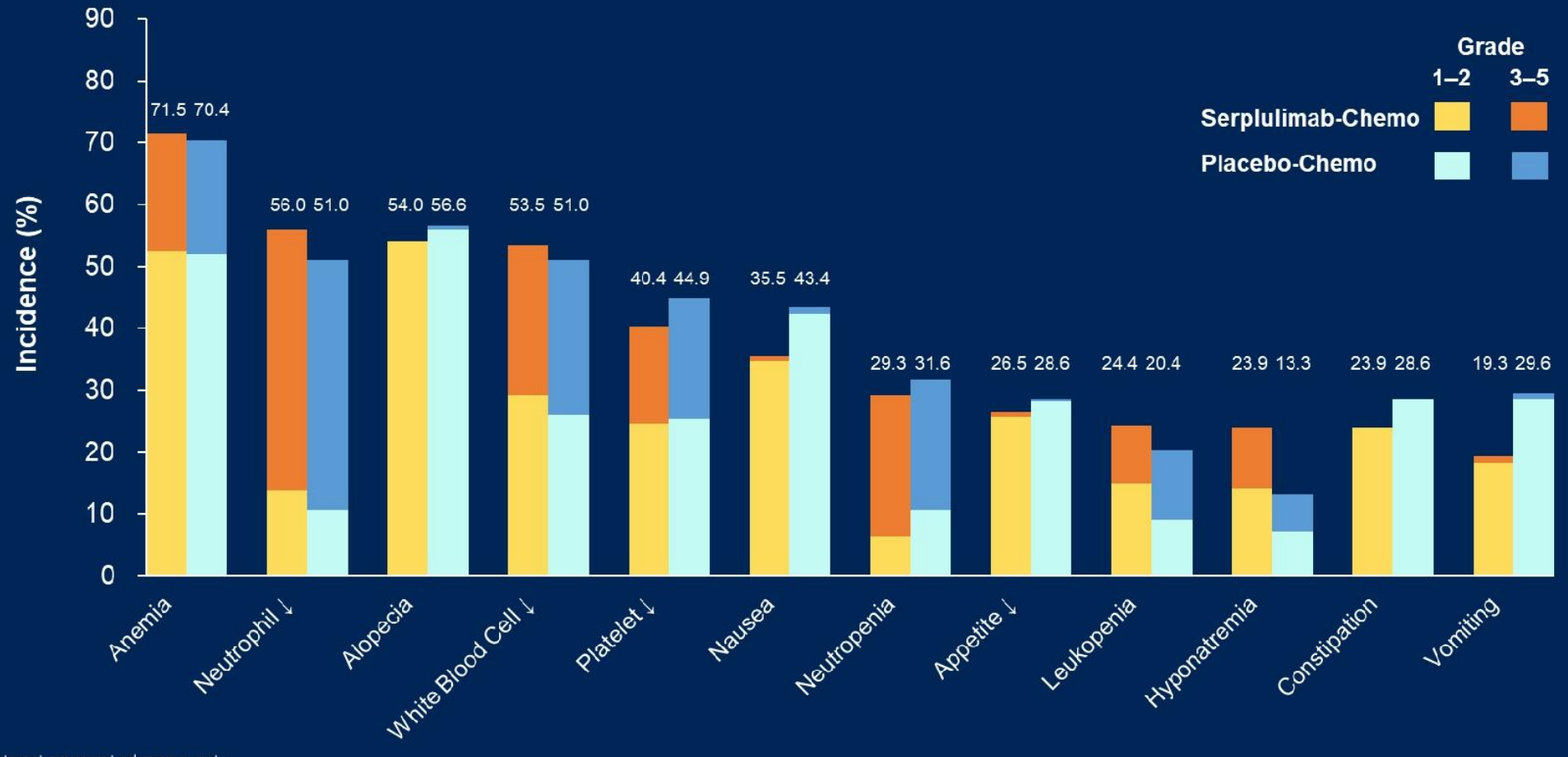
Subgroups	Serplulimab-Chemo (n=389)	Placebo-Chemo (n=196)	HR (95% CI)
Age			
< 65 years	89/235 (37.9)	60/119 (50.4)	0.62 (0.45, 0.86)
≥ 65 years	57/154 (37.0)	40/77 (51.9)	0.60 (0.40, 0.89)
Sex			
Male	121/317 (38.2)	84/164 (51.2)	0.64 (0.48, 0.84)
Female	25/72 (34.7)	16/32 (50.0)	0.57 (0.30, 1.06)
Race			
Asian	103/262 (39.3)	74/139 (53.2)	0.58 (0.43, 0.79)
Non-Asian	43/127 (33.9)	26/57 (45.6)	0.70 (0.43, 1.13)
Ethnicity			
Non-Hispanic or Latino	134/366 (36.6)	92/184 (50.0)	0.61 (0.47, 0.80)
Other	12/23 (52.2)	8/12 (66.7)	0.73 (0.29, 1.87)
ECOG PS			
0	21/71 (29.6)	16/32 (50.0)	0.44 (0.23, 0.84)
1	125/318 (39.3)	84/164 (51.2)	0.65 (0.49, 0.86)
Smoker status			
Current	37/102 (36.3)	24/48 (50.0)	0.61 (0.36, 1.02)
Former	75/206 (36.4)	58/113 (51.3)	0.59 (0.42, 0.83)
Never	34/81 (42.0)	18/35 (51.4)	0.75 (0.42, 1.33)
Brain metastases			
No	123/339 (36.3)	82/168 (48.8)	0.62 (0.47, 0.82)
Yes	23/50 (46.0)	18/28 (64.3)	0.61 (0.33, 1.13)
PD-L1 expression levels			
TPS < 1%	121/317 (38.2)	83/152 (54.6)	0.58 (0.44, 0.76)
TPS ≥ 1%	22/62 (35.5)	11/34 (32.4)	0.92 (0.44, 1.89)
Not available	3/10 (30.0)	6/10 (60.0)	0.42 (0.10, 1.72)



azard ratio; *PD-L1*, programmed death ligand-1;

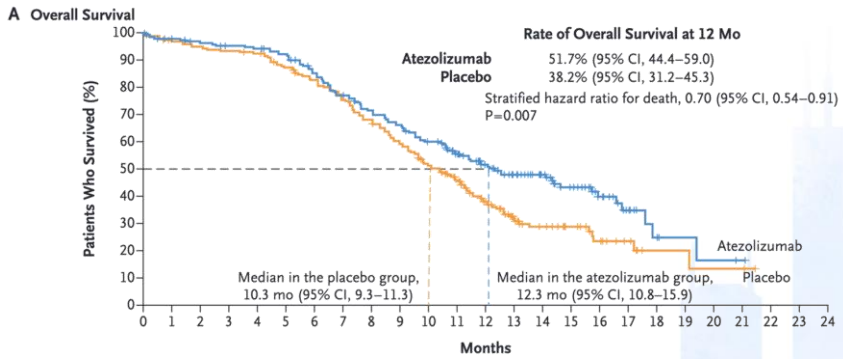
Cheng. ASCO 22

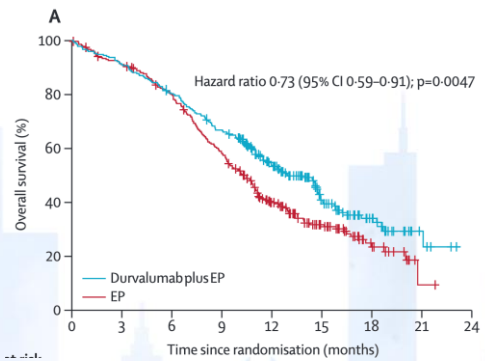
Most Common TEAEs

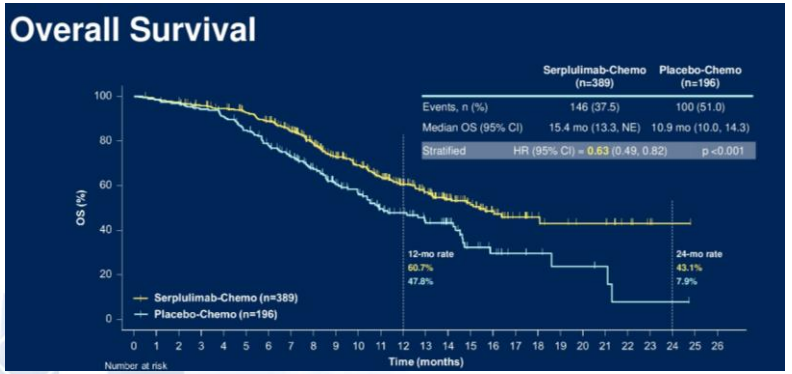


TEAE, treatment-emergent adverse event;

Estudio	n	Supervivencia global, m	HR	p-value	Mediana de seguim, m
ImPower 133[1]	403 1.1	12.3 / 10.3	0.76	0.0154	22.9
CASPIAN[2]	805 1:1	12.9 / 10.5	0.71	0.003	39.4
ASTRUM-005[3]	585 2:1	15.4 / 10.9	0.63	<0.001	12.3







1. Horn; N Eng J Med 2018;379:2220-9. 2. Paz-Ares. *The Lancet* **394**, 1929–1939 (2019). 3. Cheng; ASCO 2022

SKYSCRAPER-2

1L ES-SCLC

- ECOG PS 0–1
- Measurable disease
- No prior systemic treatment for ES disease
- Patients with treated or untreated asymptomatic brain metastases eligible

N=490

R 1:1

Induction (4 x 21 day cycles)

Tiragolumab 600 mg IV Q3W + Atezolizumab 1200 mg IV Q3W + Carboplatin + Etoposide (CE)*

Placebo IV Q3W + Atezolizumab 1200 mg IV Q3W + Carboplatin + Etoposide (CE)*

Maintenance

Tiragolumab + Atezolizumab

Placebo + Atezolizumab

Treat until progression, loss of clinical benefit, or unacceptable toxicity

No crossover

Stratification Factors:

- **ECOG PS** (0 vs. 1)
- **Brain metastases** (Yes vs. No)
- **LDH** (≤ ULN vs > ULN)

Co-Primary Endpoints:

- Investigator-assessed OS and PFS in **Primary Analysis Set** (all randomized patients without presence or history of brain metastases at baseline)

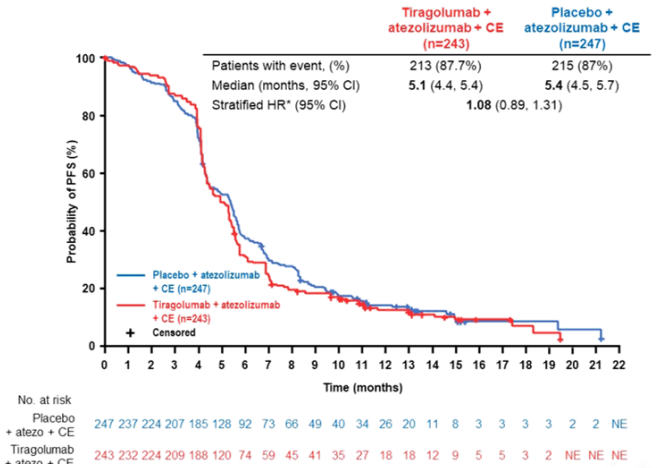
Secondary Endpoints:

PFS and OS in **Full Analysis Set** (all randomized patients)
Confirmed ORR
Duration of response
Safety
Pharmacokinetics

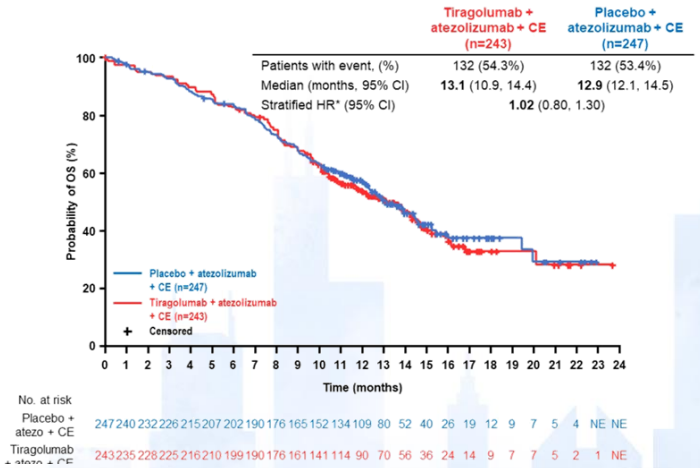
Primary analysis

- Cut-off date of 6 Feb 2022
- Median follow-up of 14.3 months (Primary Analysis Set)

PFS in the Full Analysis Set

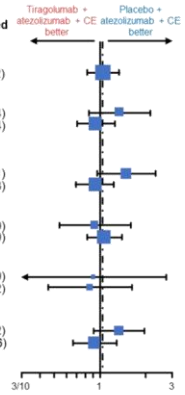


Interim OS in the Full Analysis Set



Subgroup analysis of OS: Full Analysis Set

Baseline risk factors	Total n	Placebo + atezolizumab + CE (n=247) n	Events	Median (months)	Tiragolumab + atezolizumab + CE (n=243) n	Events	Median (months)	Unstratified hazard ratio	Unstratified 95% CI
All patients	490	247	132	12.9	243	132	13.1	1.04	(0.82, 1.32)
Baseline ECOG									
0	168	82	31	NE	86	41	14.9	1.34	(0.84, 2.14)
1	321	165	101	12.0	156	90	11.7	0.93	(0.70, 1.24)
LDH									
≤ULN	199	94	34	19.4	105	48	14.8	1.48	(0.95, 2.31)
>ULN	291	153	98	9.9	138	84	10.3	0.92	(0.68, 1.23)
Brain metastasis									
Yes	93	46	27	10.6	47	25	11.7	0.92	(0.53, 1.59)
No	397	201	105	13.6	196	107	13.6	1.06	(0.81, 1.39)
Brain metastasis: Yes									
Treated	33	19	9	16.0	14	5	NE	0.89	(0.29, 2.69)
Untreated	60	27	18	10.2	33	20	11.7	0.85	(0.45, 1.62)
Liver metastasis at enrollment									
Yes	183	94	54	12.3	89	57	9.9	1.32	(0.91, 1.92)
No	307	153	78	13.8	154	75	14.2	0.92	(0.67, 1.26)

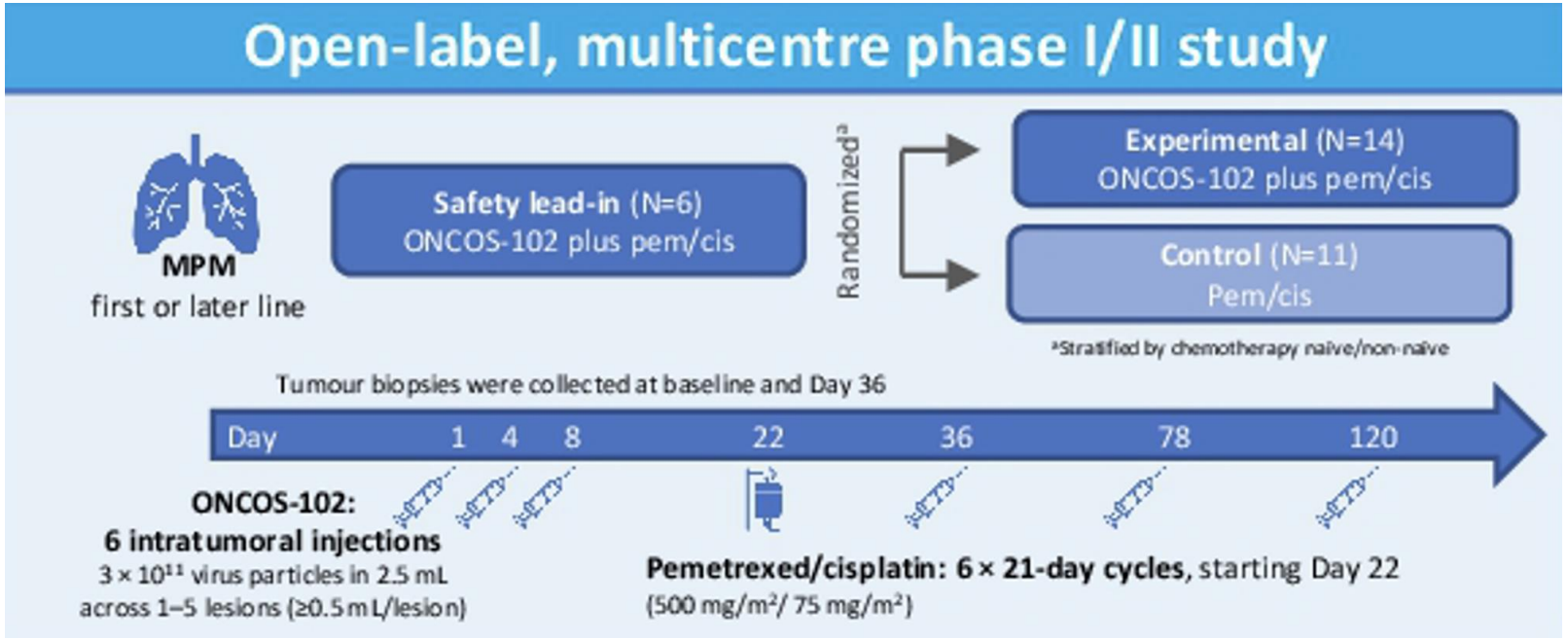


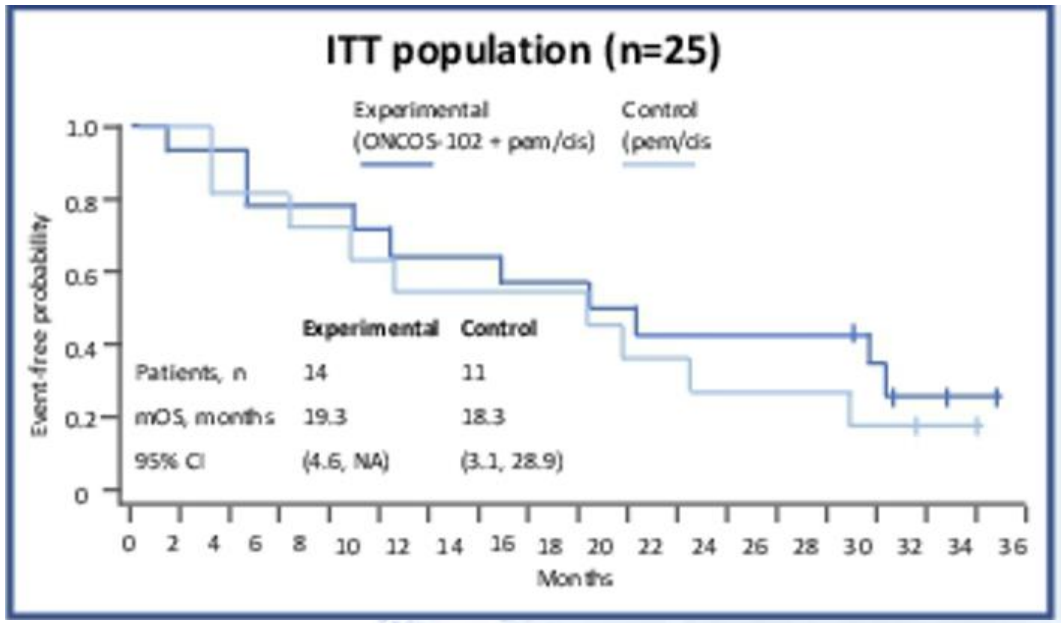
Rudin. ASCO 2022

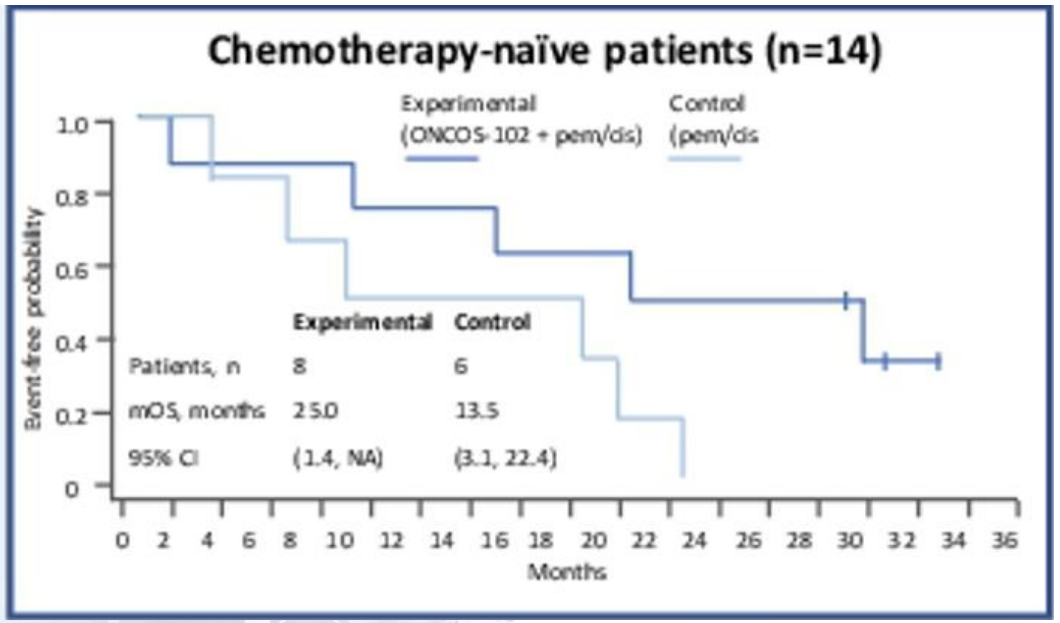
Otros tumores

3

Mesotelioma Análisis final con ONCOS-102







Ponce. ASCO 2022

Lenvatinib for the treatment of Thymic Epithelial Tumors (TETs): a real-life multicenter experience

Benitez JC[1], Florez-Arango J[1], Dansin E[2], Giaccone G[3], Basse C[4], Mazieres J[5], Pierret T[6], Giaj-Levra M[6], Pons-Tostivint E[7], Arrondeau J[8], Aldea M[1], Aboubakar F[9], Pascale M[10], Molina T[11], Girard N[3,12], Besse B[1,13]

[1]Cancer Medicine Department Gustave Roussy, Villejuif, France; [2]Department of pneumology, Oscar Lambret, Lille, France ; [3]Cancer Medicine Department, Weill Cornell Medicine and New York-Presbyterian Hospital, New York City, United States of America; [4]Thoracic Oncology Service, Thorax Institute Curie Montsouris, Institut Curie, Paris; [5]Department of pneumology, University Hospital of Toulouse, Toulouse, France; [6]Department of pneumology, University Hospital of Grenoble-Alpes, Grenoble, France; [7]Department of medical oncology, University Hospital of Nantes, Nantes, France ; [8]Cochin Hospital, Paris, France; [9]French Group of thoracic oncology, [10]French Group of thoracic oncology; [11]Necker's et Enfants University Hospital, Paris, France; [12]Saint Quentin en Yvelines University of Versailles, Paris-Saclay Campus, Versailles, France; [13]Paris-Saclay University, Orsay, France.

2022 ASCO ANNUAL MEETING #Poster 211

Background

- TETs are rare malignancies of the anterior mediastinum being thymoma (T) B3 and thymic carcinoma (TC) the most aggressive subtypes.
- There is no standard treatment after platinum-based chemotherapy in refractory or metastatic setting.
- A phase 2 trial has reported clinical benefit for Lenvatinib 24mg (objective response rate [ORR] of 38%).
- Lenvatinib is a a novel multi-targeted inhibitor of VEGFR, FGFR, RET, c-Kit, and other kinases; significant toxicity grade 3 hypertension was 64%.
- No real-life data exists.

Methods

- We selected patients (pts) under Lenvatinib as a second-line or beyond for refractory TETs from 9 International centers from France (belonging to the nationwide network RYTHMIC), Belgium and United States.
- We analyzed epidemiologic, clinical and pathological characteristics of patients with TET's.
- The toxicity was evaluated according to CTCAE v4, with a local evaluation of efficacy and we assessed toxicity profile and survival outcomes.

Results

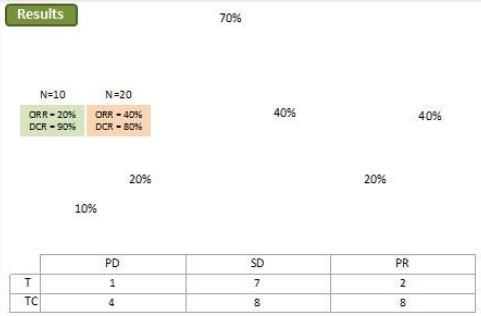
- From March 2020 to April 2022, 30 pts were enrolled. Median age at diagnosis was 49 (24-71), 50% were women, 7/30 (23%) reported auto-immune disorders (AIDs).
- TC was the most frequent subtype (n=20, 66.7%), followed by B3 (n=6, 20%) and B2 (n=4, 13.3%).
- Lenvatinib was used as a second line for 53% of pts, mainly starting from 14 mg/daily (n=20, 69%) and one pts with concomitant pembrolizumab.

josecarlos.benitez-montanez@gustaveroussy.fr

@JcbenitezMD

*First author declare no conflict of interest.

Results



	PD	SD	PR
T	1	7	2
TC	4	8	8

Figure 1. *Bar plot representing response for both thymoma (T) and thymic carcinoma (TC).* The ORR was 33% (p = 0.3) and DCR 80% (p=0.27). PR= Progression disease, SD= Stable disease, PR= Partial response.

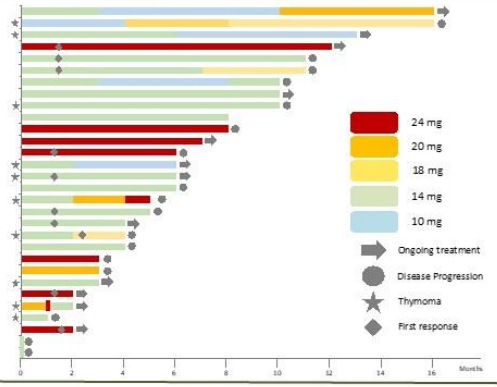


Table 1. *Swimmer plot showing response regarding Lenvatinib dose.* Lenvatinib was used as a second line treatment in 14 (47%) pts and ≥3 in 16 pts (53%). Response was similar along all Lenvatinib doses. Partial response was observed with the dose of 24mg in 3 pts (37.5%) and 14mg in 5 pts (31.3%). Dose de-escalations were needed in 30% of pts.

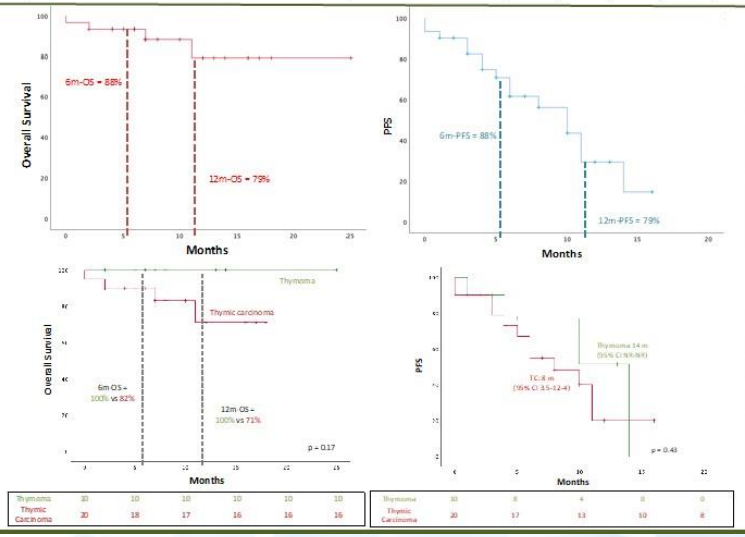


Figure 4. *Kaplan Meier curve of median OS and PFS to Lenvatinib treatment.* with a median follow-up period of 8 months (95%CI 6.3-9.6), Median PFS of 10 months (95%CI 6.4-13.5) and median OS not reached. PFS at 6 and 12 m was 55% and 19%, respectively. OS at 6 and 12 m was 88% and 79%, respectively.

Figure 5. *Kaplan Meier curve of median OS and PFS to Lenvatinib treatment comparing thymoma and TC.* Median PFS was 14 and 8 months for T and TC respectively. T showed 100% OS at 6 and 12 months, however, at 6 and 12 months 82% and 71% of TC were alive, respectively.

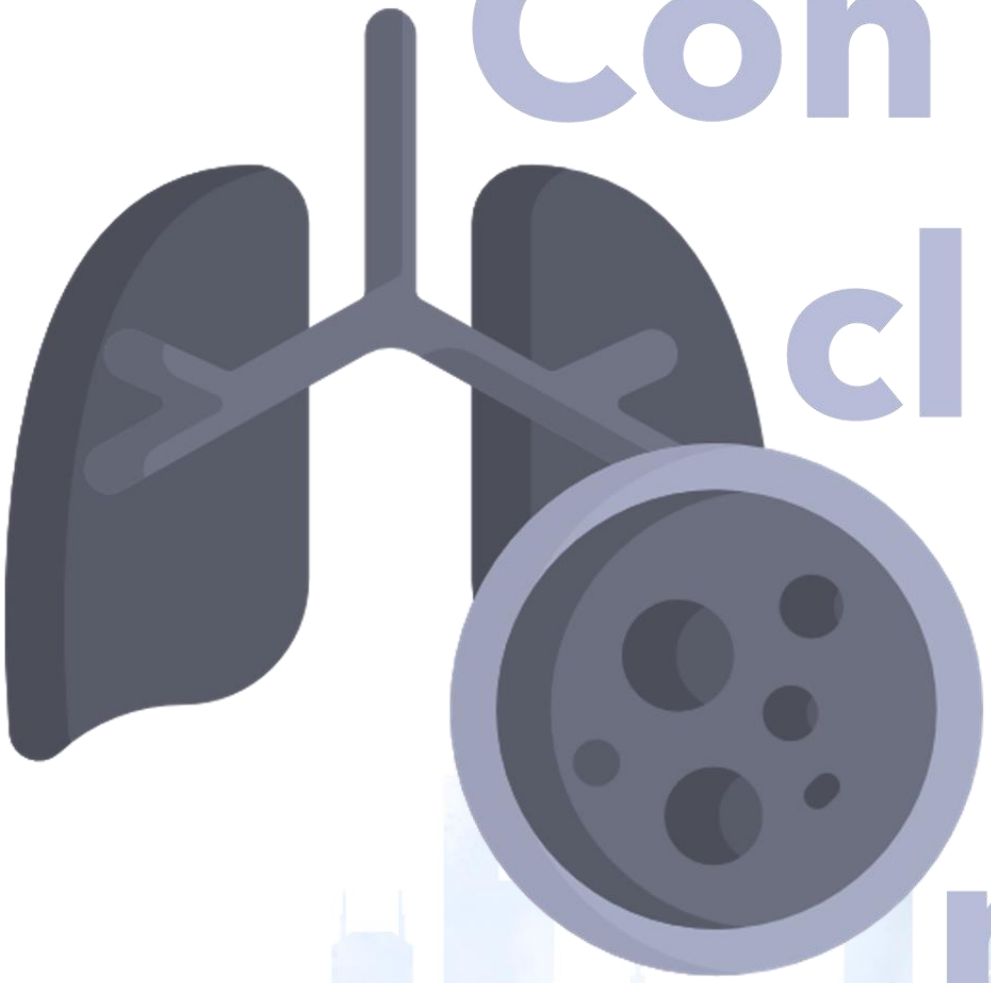
	TOXICITY			
Syndrome	All grades	%	Grade ≥3	%
High blood presure	12	41,3	0	0
Asthenia	7	24,2	1	3,4
Mucositis	6	20	1	3,4
Diarrhea	4	13,7	2	6,9
Hypotiroidism	3	10,3	0	0
Liver toxicity	2	6,9	2	6,9
Abdominal pain	2	6,9	0	0
Neuropathy	2	6,9	0	0
Palmo-plantar SD	1	3,4	0	0
Anemia	2	6,9	0	0
Trombopenia	1	3,4	0	0
Neutropenia	1	3,4	0	0
Headache	1	3,4	0	0
Aedema	1	3,4	0	0
Fever	1	3,4	0	0
Alopecia	1	3,4	0	0

Table 2 : *Toxicity profile of the cohort under Lenvatinib.* Discontinuation rate was 10%. Main toxicity was high blood pleasure, nonetheless all patients showed low AE grade. Of note, 13 pts (43%) were treated with an antihypertensive treatment to avoid high grade toxicity with an OR = 13 (p < 0.0001) in favor to amlodipine and/or bisoprolol.

Conclusions

- We confirm the activity of Lenvatinib in pts with advanced or metastatic T and TC, despite the use of lower doses than the phase 2 study.
- The ORR was 33% with a control of the disease of 90% in thymoma subtypes (20% of RR).
- Lenvatinib did not arise mayor toxicities. Preventive treatment with antihypertensives may avoid high grade of blood pressure adverse events.

Conclusiones



Enfermedad locorregional:

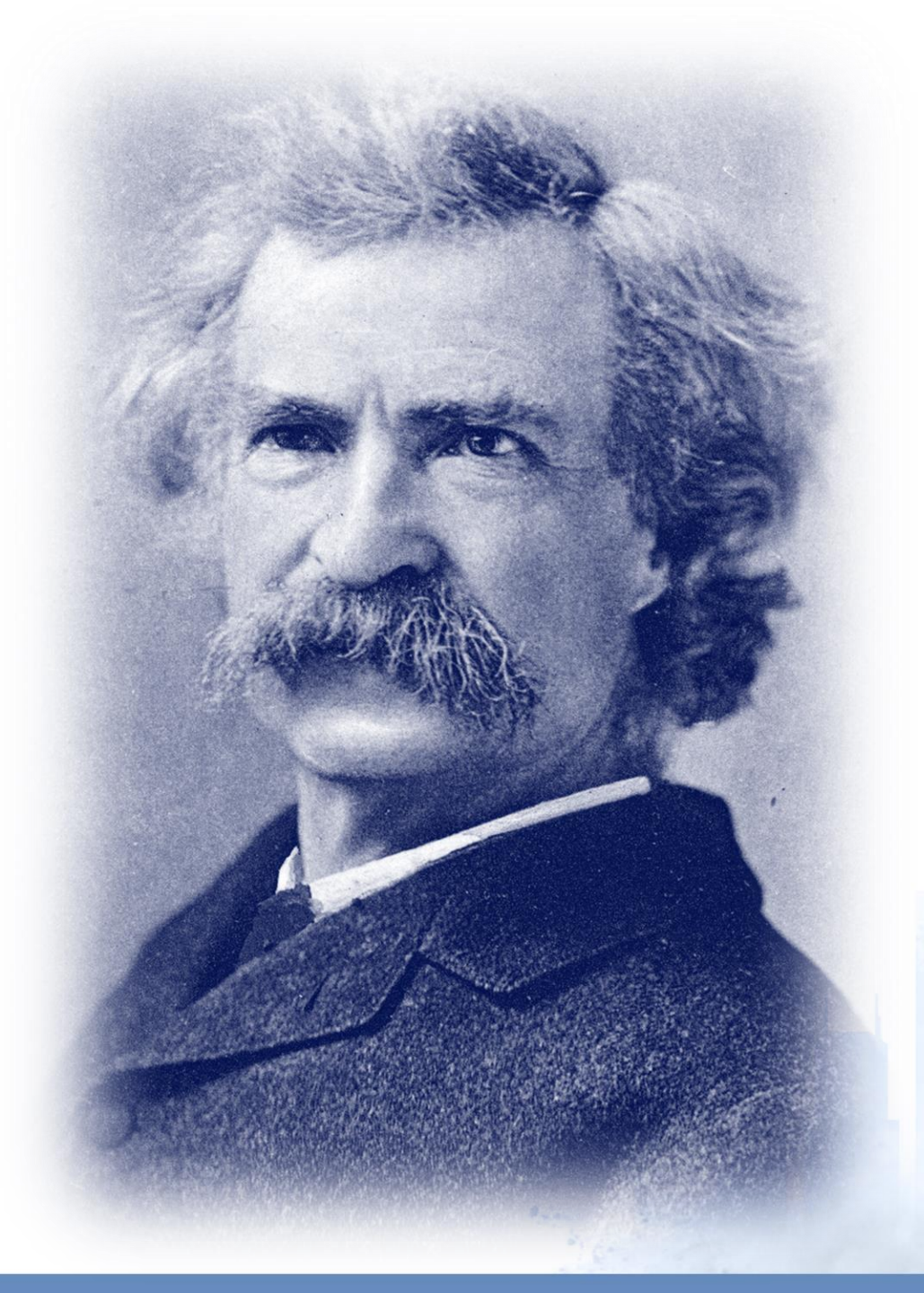
- NADIM II
- Quimio-radio no superior a quimio neoadyuvante

Carcinoma microcítico:

- Serplulimab: beneficio de añadir IO a la QMT
- Tiragolumab no añade beneficio

Otros tumores

- Resultados prometedores ONC-102 en mesotelioma
- Lenvatinib: actividad en tumores epiteliales tímicos



“El hombre que propone una idea nueva es un chiflado, hasta que se comprueba que la idea era excelente”

Mark Twain