Lung Cancer UPDATES
WCLC HIGHLIGHTS
06 - 09 SEPTIEMBRE 2025
Barcelona, Spain

Iniciativa científica de:
GECP
lung cancer research

Cáncer de pulmón no microcítico estadio IV (avanzado) SIN driver

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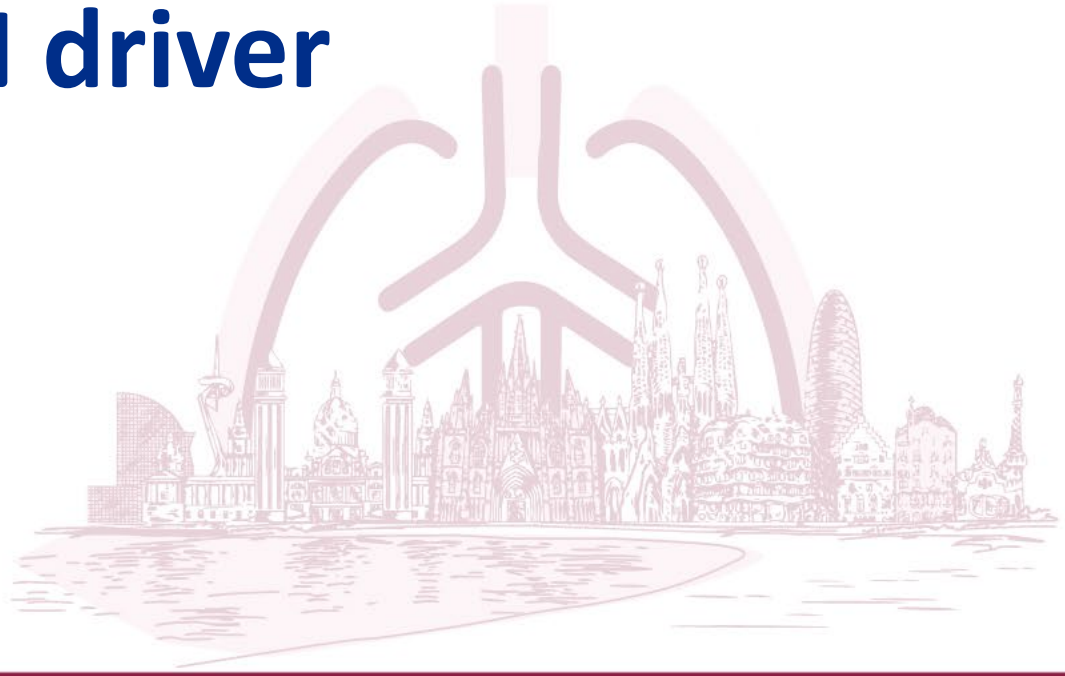


COIs

Consultant or Advisory Role: BMS, MSD, Takeda, Roche, Pfizer, Roche, Ipsen, Astra-Zéneca,

Boehringer, Bayer, Janssen, Recordati

Speaking: GSK, Roche, Ipsen, Lilly, Astellas, Janssen, Novartis, Boehringer, Eisai, Sanofi

Grant or travel support: MSD, Ipsen, Roche, Janssen, Pfizer, Astellas, Takeda

Participation in clinical trials: Merck, Astellas, Pfizer, Ipsen, Roche, AZ, Mirati, PharmaMar, Gilead, Regeneron, Summit Ther

ASTRUM-002

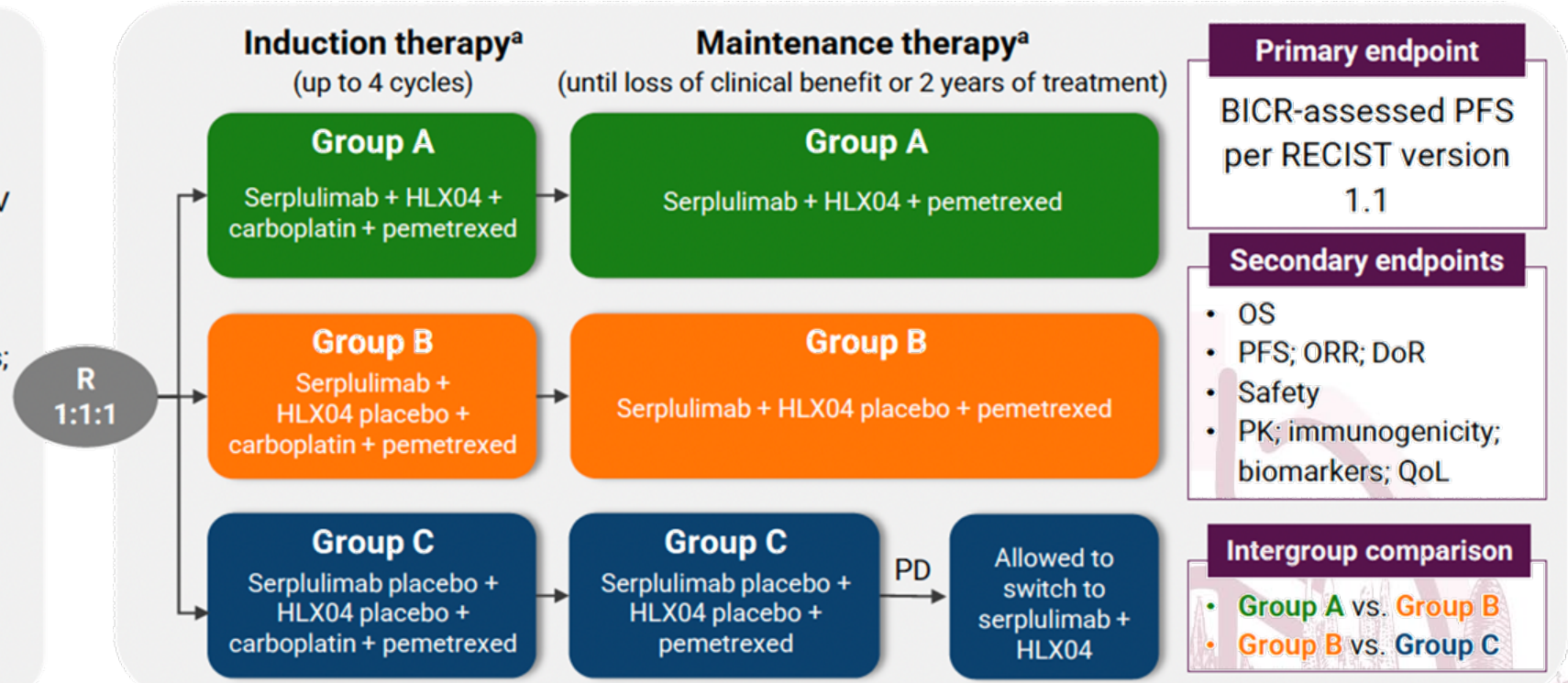
A randomized, double-blind, multicenter phase 3 study (NCT03952403)

Key inclusion criteria:

- Aged 18–75 years;
- ECOG PS of 0 or 1;
- Histologically/cytologically diagnosed with stage IIIB, IIIC, or IV nsqNSCLC that cannot be treated with surgery or radiotherapy;
- No *EGFR* sensitizing mutations or *ALK* or *ROS1* gene rearrangements;
- No prior systemic treatment for nsqNSCLC.

Stratification factors:

- PD-L1 expression level (negative vs. positive vs. not evaluable);
- Smoking history (yes vs. no);
- Brain metastasis (yes vs. no).

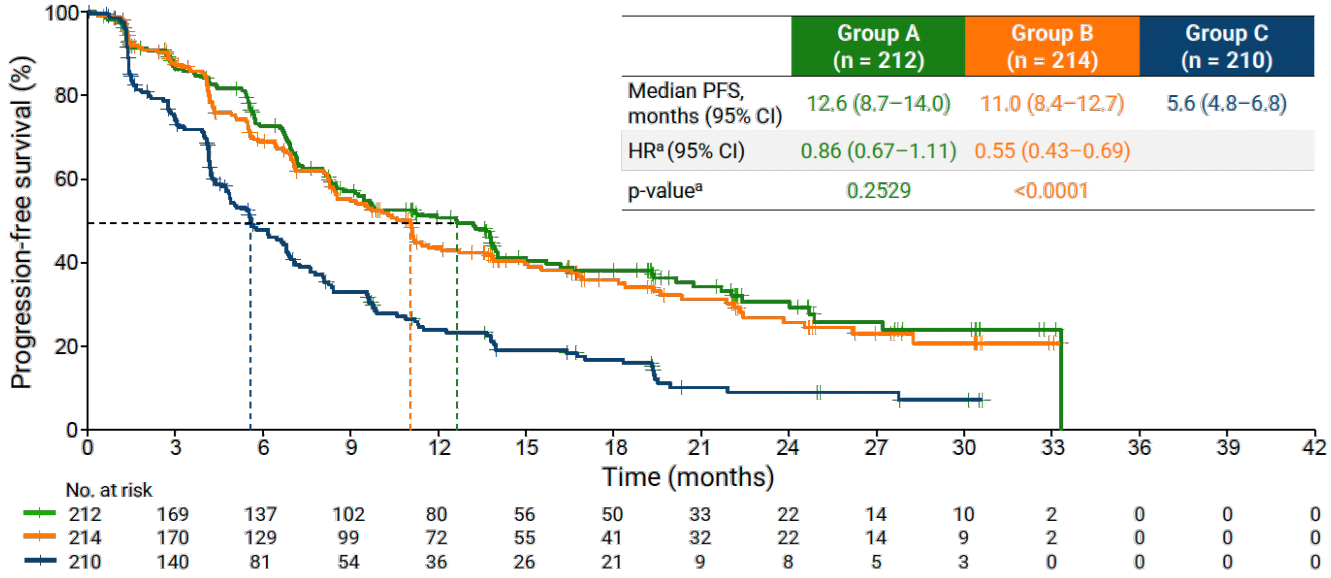


Shi. WCLC 2025

ASTRUM-002

Primary endpoint: BICR-assessed PFS

Improved PFS upon adding serplulimab to chemotherapy



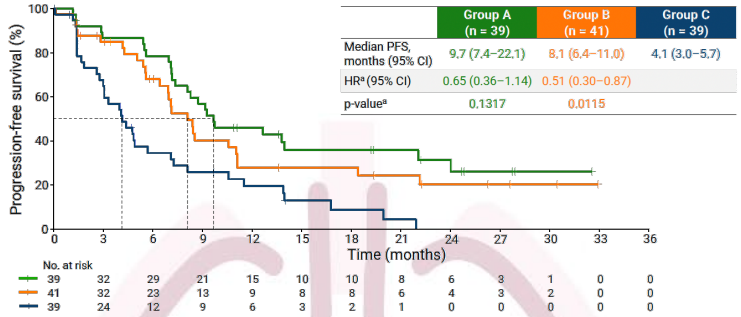
	Group A (n = 212)	Group B (n = 214)	Group C (n = 210)
Median PFS, months (95% CI)	12.6 (8.7–14.0)	11.0 (8.4–12.7)	5.6 (4.8–6.8)
HR[a] (95% CI)	0.86 (0.67–1.11)	0.55 (0.43–0.69)	
p-value[a]	0.2529	<0.0001	

[a] Group B was statistically compared to Group C, while Group A was compared to Group B.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; No., number; PFS, progression-free survival.

Patients with brain metastasis

Improved PFS upon adding serplulimab to chemotherapy



	Group A (n = 39)	Group B (n = 41)	Group C (n = 39)
Median PFS, months (95% CI)	9.7 (7.4–22.1)	8.1 (6.4–11.0)	4.1 (3.0–5.7)
HR[a] (95% CI)	0.65 (0.36–1.14)	0.51 (0.30–0.87)	
p-value[a]	0.1317	0.0115	

Shi. WCLC 2025

ZEAL-1L

Study design

- Phase 3, multicenter, randomized, double-blind study

Inclusion

- Histologically or cytologically confirmed diagnosis of NSCLC without known targetable driver alteration (squamous or non-squamous; mixed histology allowed)
- Advanced (Stage IIIB not amenable to definitive chemoradiotherapy) or metastatic (Stage IV) NSCLC
- Completed 4–6 cycles of pembrolizumab + platinum-based 1L induction chemo and achieved SD, PR, or CR
- ECOG score of 0 to 1; adequate organ function
- Asymptomatic brain metastases permitted

Exclusion

- Mixed small cell lung cancer or sarcomatoid variant NSCLC
- Receipt of prior PARP inhibitor(s) in prior lines of treatment
- Known history of MDS or AML or active tuberculosis
- Systolic BP >140 mmHg and/or diastolic BP >90 mmHg

Experimental: Niraparib + Pembrolizumab

Comparator: Placebo + Pembrolizumab

Stratification

- Histology Squamous vs. Non-SQ
- Response SD vs CR/PR
- PD-L1 Status TPS <1% vs >=1%

Dosing

- **Niraparib**: 100-mg tablets or matched placebo orally QD, continuously (200 or 300 mg starting dose)
- **Pembrolizumab**: 200 mg IV Q3W

Endpoints

Primary:

1. PFS by BICR in the CR/PR population

Key Secondary/Other:

2. PFS by BICR in the ITT population
3. OS in the CR/PR population
4. OS in the ITT population
5. Time to progression in the CNS (assessed by BICR using RANO-BM)
- Safety

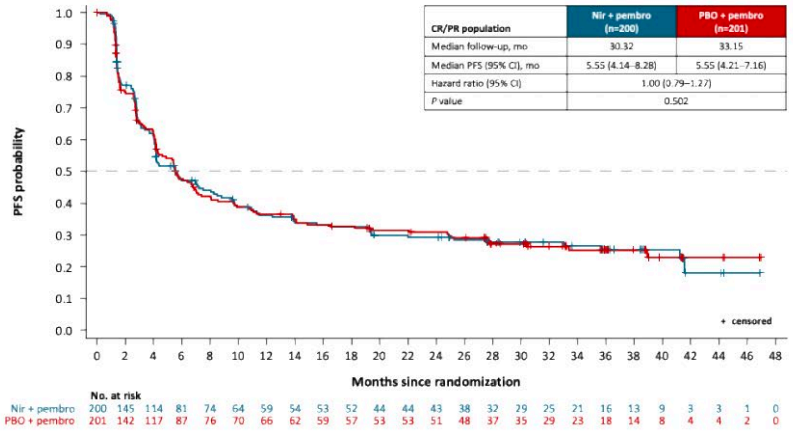
Hierarchical Testing

- The 5 efficacy endpoints will be tested in the pre-specified sequential order.
- If any endpoint fails to reach statistical significance, formal testing will stop and all subsequent endpoints will not be formally tested.

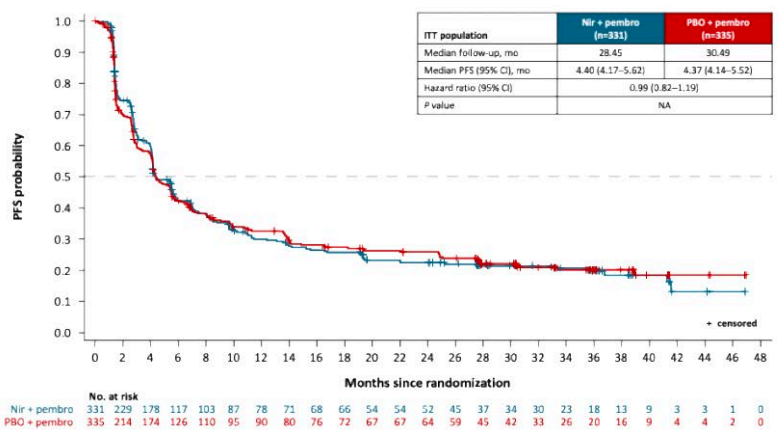
ZEAL-1L

PFS in the CR/PR or ITT population

CR/PR



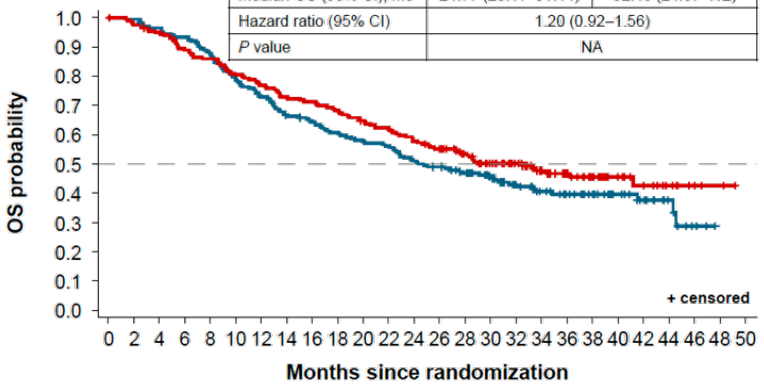
ITT



Key secondary endpoint: Overall Survival

CR/PR population

CR/PR population	Nir + pembro (n=200)	PBO + pembro (n=201)
Median follow-up, mo	34.66	34.43
Median OS (95% CI), mo	24.77 (20.11–31.44)	32.49 (24.67–NE)
Hazard ratio (95% CI)	1.20 (0.92–1.56)	
P value	NA	

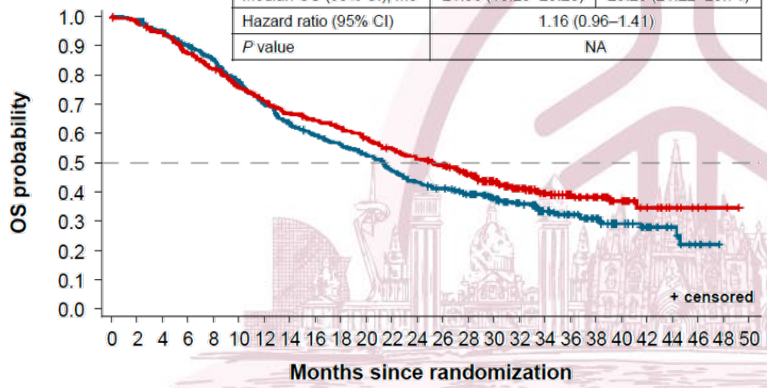


No. at risk

Nir + pembro	200	199	192	186	175	157	145	132	126	119	113	110	100	95	86	74	56	46	38	32	23	16	9	3	0
PBO + pembro	201	195	189	177	171	160	153	145	142	136	128	122	114	108	95	80	68	53	41	32	21	14	8	3	2	0

ITT population

ITT population	Nir + pembro (n=331)	PBO + pembro (n=335)
Median follow-up, mo	34.30	33.45
Median OS (95% CI), mo	21.36 (18.23–23.23)	25.26 (21.22–28.71)
Hazard ratio (95% CI)	1.16 (0.96–1.41)	
P value	NA	



No. at risk

Nir + pembro	331	327	313	298	281	255	231	207	193	183	172	154	141	132	119	103	83	63	50	38	26	18	10	4	0
PBO + pembro	335	327	314	290	272	251	235	221	212	204	191	178	167	158	135	112	88	67	51	40	24	14	8	3	2	0

Ramalingam WCLC 2025

NIVIPI-Brain

Treatment naïve patients with stage IV NSCLC with untreated brain metastases not amenable for SRS, *EGFR/ALK/ROS1* negative, any PD-L1, ECOG PS 0-1, measurable systemic and brain lesions

COHORT A (n=44)
Asymptomatic brain metastases and not receiving steroids
COHORT B (n=27)
Olygosymptomatic brain metastases controlled with low dose steroids (dexa ≤ 4mg qd)

Tumor evaluation by body CT scan and brain MRI
Q6W until the 12th week and thereafter Q9W until disease progression

NIVO 360mg Q3W + IPI 1mg/kg Q6W
+
Chemotherapy Q3W (2 cycles)*

Until disease progression#, unacceptable toxicity or a maximum of 2 years

*Non-squamous: CDDP or CBDCA + pemetrexed; squamous:CBDCA + paclitaxel

Primary endpoint:
Intracranial disease control rate (icDCR): percentage of patients without progression for at least 6 months, as asssessed by RANO-BM

Secondary endpoints:
- Intracranial and systemic ORR & PFS by RANO-BM and by RECIST v1.1 respectively
- Safety by CTCAE v5.0
- Overall Survival
- Time to brain RT and quality of life

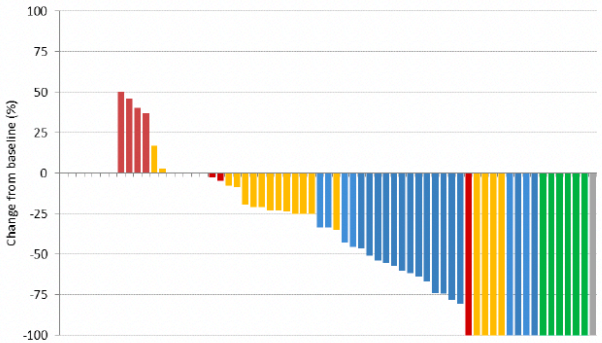
#Patients with exclusive CNS PD were allowed to continue within the study after brain RT

CBDCA: carboplatin; CDDP: cisplatin; CT: computerized tomography; CTCAE: common toxicity criteria for adverse events; IPI: ipilimumab; MRI: magnetic resonance imaging; NIVO: nivolumab; ORR: overall response rate; PD: progression disease; RANO-BM: response assessment in neuro-oncology brain metastases; RECIST: response evaluation criteria in solid tumors; RT: radiotherapy

NIVIPI-Brain

CNS Best ORR (by RANO-BM)

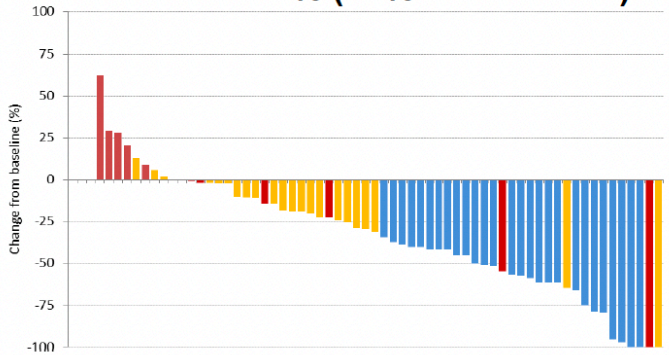
ORR = 41.5% (95% CI 24.9-54-4)



Clinical Benefit Rate (CBR) = 73.8%
6 CR, 21 RP and 21 SD

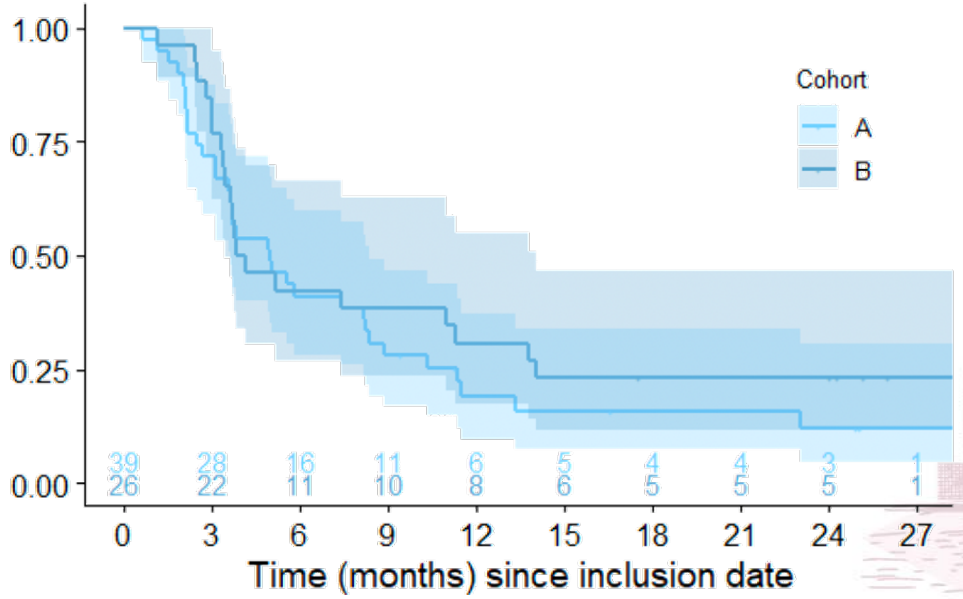
Systemic Best ORR (by RECIST)

ORR = 41.5% (95% CI 24.9-54-4)



Clinical Benefit Rate (CBR) = 78.4%
27 RP and 24 SD

Primary Endpoint: Intracranial DCR (by RANO-BM)



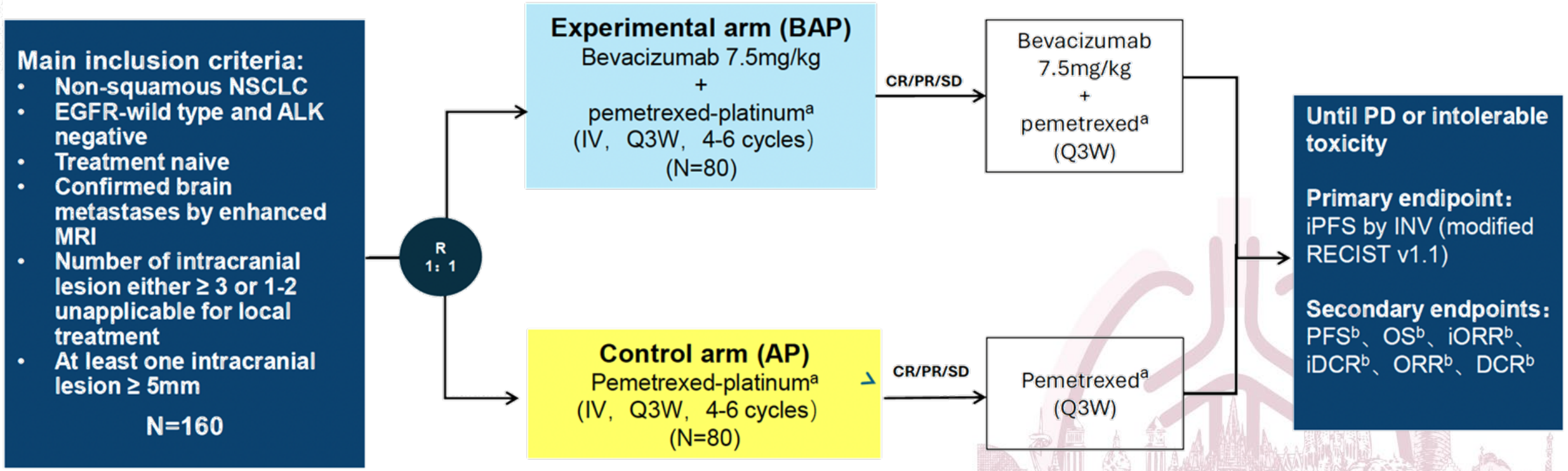
Cohort	Intracranial DCR
A	At 6 months 41% (95% CI 28-60)
B	At 5 months 46% (95% 31-79)

As the intracranial DCR is below 50%, the study did not achieve the expected efficacy

Nadal WCLC 2025

BAP BRAIN

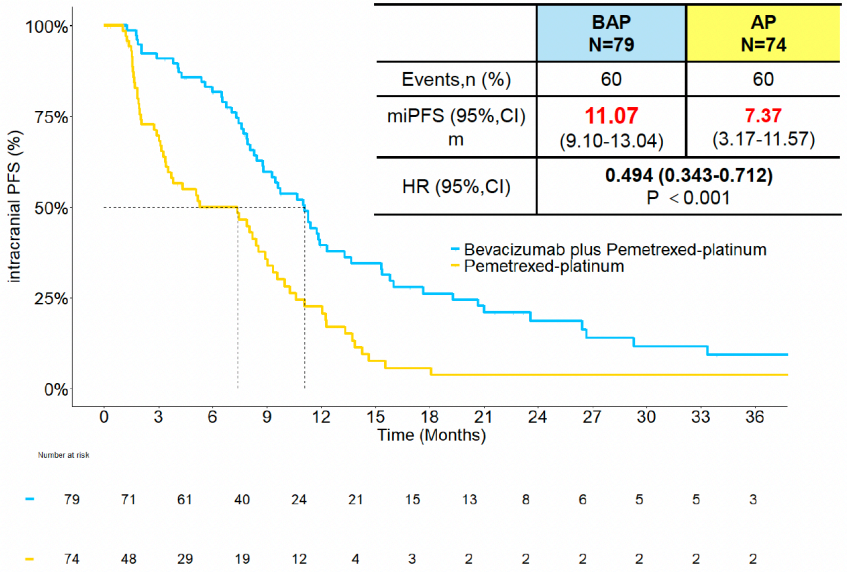
➢ Randomized, multi-center phase 3 study conducted across 11 centers in China (NCT01951482)



Chen WCLC 2025

BAP BRAIN

Primary Endpoint：iPFS

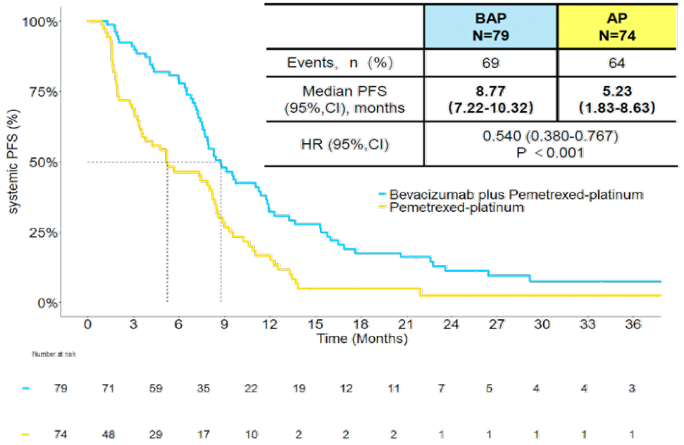


	BAP N=79	AP N=74
Events,n (%)	60	60
miPFS (95%,CI) m	11.07 (9.10-13.04)	7.37 (3.17-11.57)
HR (95%,CI)	0.494 (0.343-0.712) P ＜0.001	

Data cutoff：January 31, 2025 Median Folow-up：16.7months (range 7.4-32.0 mo)

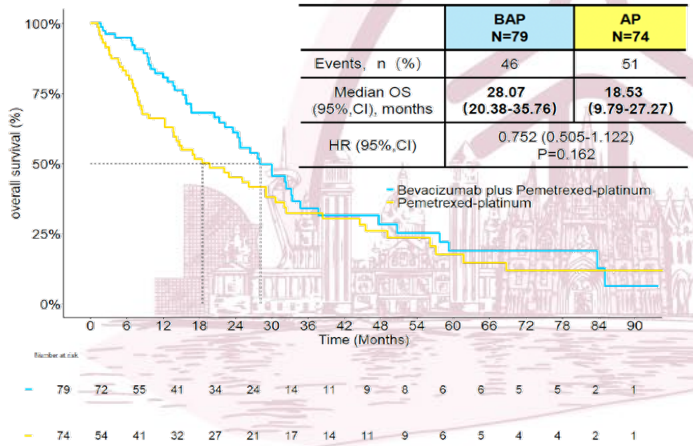
Secondary Endpoints：

PFS



	BAP N=79	AP N=74
Events，n (%)	69	64
Median PFS (95%,CI), months	8.77 (7.22-10.32)	5.23 (1.83-8.63)
HR (95%,CI)	0.540 (0.380-0.767) P ＜0.001	

OS



	BAP N=79	AP N=74
Events，n (%)	46	51
Median OS (95%,CI), months	28.07 (20.38-35.76)	18.53 (9.79-27.27)
HR (95%,CI)	0.752 (0.505-1.122) P=0.162	

Chen WCLC 2025

TROPION-Lung01

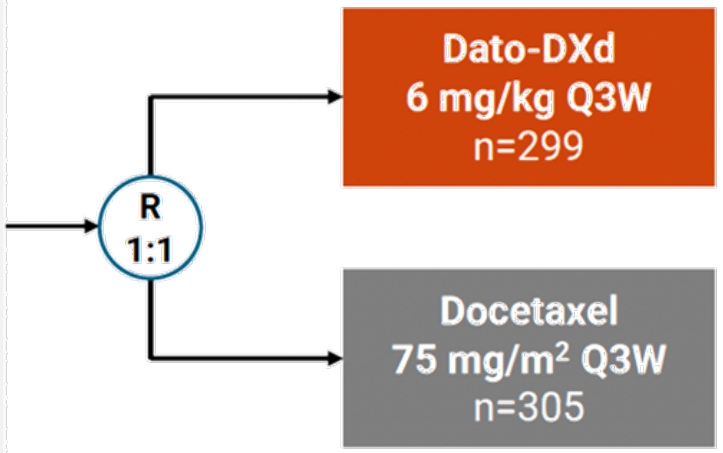
Phase 3, Randomized, Open-Label Study (NCT04656652)

Key eligibility criteria

- NSCLC (stage IIIB, IIIC, or IV)
- ECOG PS 0 or 1
- No prior docetaxel
- **Patients with clinically inactive, asymptomatic brain metastases were eligible**

Without actionable genomic alterations:[a]
- 1–2 prior lines, including Pt-CT and anti–PD-(L)1 mAb therapy

With actionable genomic alterations:
- Positive for *EGFR*, *ALK*, *NTRK*, *BRAF*, *ROS1*, *MET* exon 14 skipping, or *RET*
- 1–2 prior approved targeted therapies + Pt-CT and ≤1 anti–PD-(L)1 mAb



Stratified by: histology;[b] actionable genomic alteration;[c] anti–PD-(L)1 mAb included in most recent prior therapy;[d] and region[e]

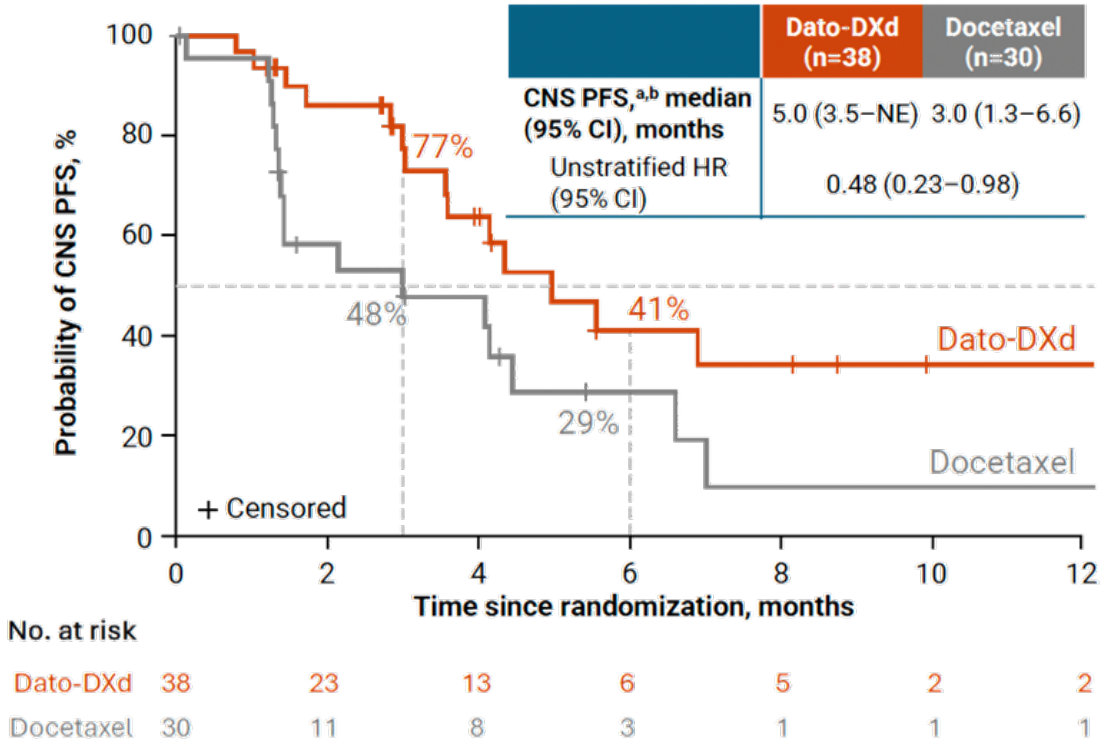
Dual primary end points:
- PFS by BICR per RECIST 1.1
- OS

Post hoc analysis (intracranial activity):
- CNS ORR, DCR, and PFS, assessed by CNS BICR per CNS RECIST
- Percentage change from baseline in SOD in measurable brain metastases

TROPION-Lung01

CNS PFS

All Patients With Untreated BM or Progression After RT

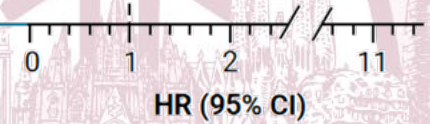


	Dato-DXd (n=38)	Docetaxel (n=30)
CNS PFS,[a,b] median (95% CI), months	5.0 (3.5–NE)	3.0 (1.3–6.6)
Unstratified HR (95% CI)	0.48 (0.23–0.98)	

No. at risk

Dato-DXd	38	23	13	6	5	2	2
Docetaxel	30	11	8	3	1	1	1

Subgroup	Events, n / N: Dato-DXd (n=38)	Events, n / N: Docetaxel (n=30)	HR (95% CI)
Histology			
Nonsquamous (n=56)	11 / 31	13 / 25	0.37 (0.16–0.83)
Squamous (n=12)	3 / 7	3 / 5	1.81 (0.30–11.02)
***EGFR*m**			
Absent (n=46)	9 / 27	10 / 19	0.51 (0.21–1.27)
Present (n=22)	5 / 11	6 / 11	0.33 (0.09–1.20)

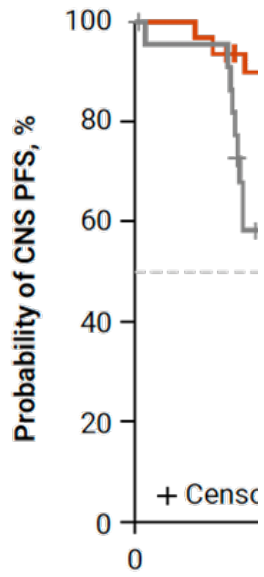


Post-Tostivint WCLC 2025

TROPION-Lung01

CNS PFS

All Patien



	Dato-DXd (n=16)	Docetaxel (n=11)
CNS confirmed ORR,[a] % (95% CI)	38 (15–65)	0 (0–29)
CNS confirmed BOR,[a] n (%)		
CR	1 (6)	0
PR	5 (31)	0
SD	8 (50)	4 (36)
PD	0	2 (18)
NE	2 (13)	5 (46)
CNS confirmed DCR,[a] % (95% CI)	88 (62–98)	36 (11–69)

(95% CI)

(0.16–0.83)

.81 (0.30–11.02)

.51 (0.21–1.27)

33 (0.09–1.20)

No. at risk

Dato-DXd	38	23	13	6	5	2	2
Docetaxel	30	11	8	3	1	1	1

0 1 2 11

HR (95% CI)

SUPER BRAIN

Study Design (NCT05807893)

Study Design

Inclusion Criteria

- 18 to 75 years;
- Stage IV non-squamous NSCLC with untreated BMs confirmed by histopathology or cytology;
- MRI-confirmed brain parenchymal metastasis with ≥3 lesions; or 1-2 lesions unsuitable for or refused local treatment;
- ≥ 1 measurable lesion with a diameter ≥5mm in the brain;
- No EFGR sensitive gene mutation, no ALK/ROS1 gene fusion;
- ECOG PS score is 0-1;
- …

Until PD, unacceptable toxicity, or death, for up to 2 years

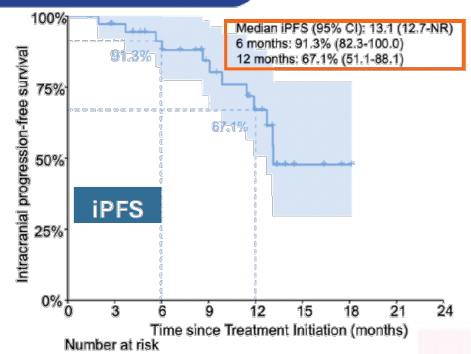
Patients accessed for eligibility → **40 enrolled** → **First line treatment** **serplulimab** combined with **bevacizumab**, **pemetrexed**, and **carboplatin** → 4-6 cycles → **maintenance therapy** **serplulimab** plus **bevacizumab** and **pemetrexed**

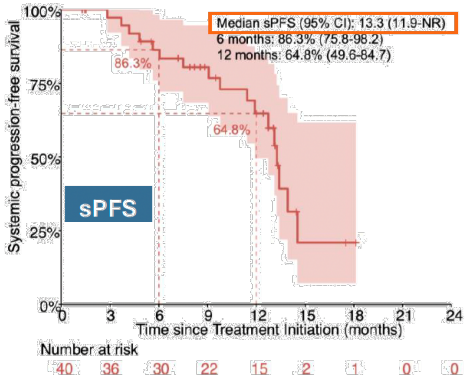
Primary endpoint intracranial progression-free survival (iPFS)

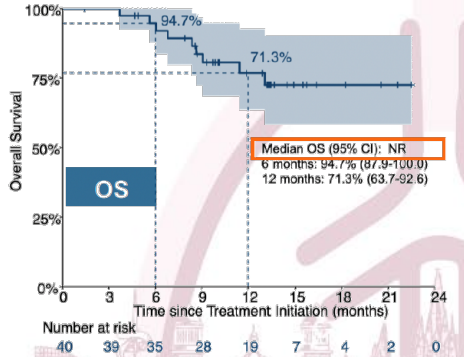
Secondary endpoint PFS, OS, ORR, Safety

median follow-up time: 13.3 months (95% CI: 13.0–13.5) 17 February 2025

Survival







- **PFS** The median iPFS was 13.1 months, with 6-month and 12-month iPFS rates of 91.3 % and 67.1% respectively. The median sPFS was 13.3 months.
- **OS** Nine patients (22.5%) died due to PD, and the 12-month OS rate was 71.3%.

ORR intracraneal: 84%
ORR extracraneal: 64%

Yu WCLC 2025

First-line atezolizumab plus chemotherapy in elderly patients with advanced NSCLC
IFCT-1805 ELDERLY: a randomized, multicenter, open-label, phase 3 trial

Key eligility criteria
NSCLC
Stage IIIB, IIIC non irradiable or IV (8th classification)
Age 70 - 89
PS 0 -1
MMS ≥ 24
EGFR, ALK wild type

R 2:1
N=510

Carboplatin Q4W - weekly paclitaxel (4 cycles) + Atezolizumab Q3W (max 2 years) (CT + ATZ arm)
until progression or unacceptable toxicity

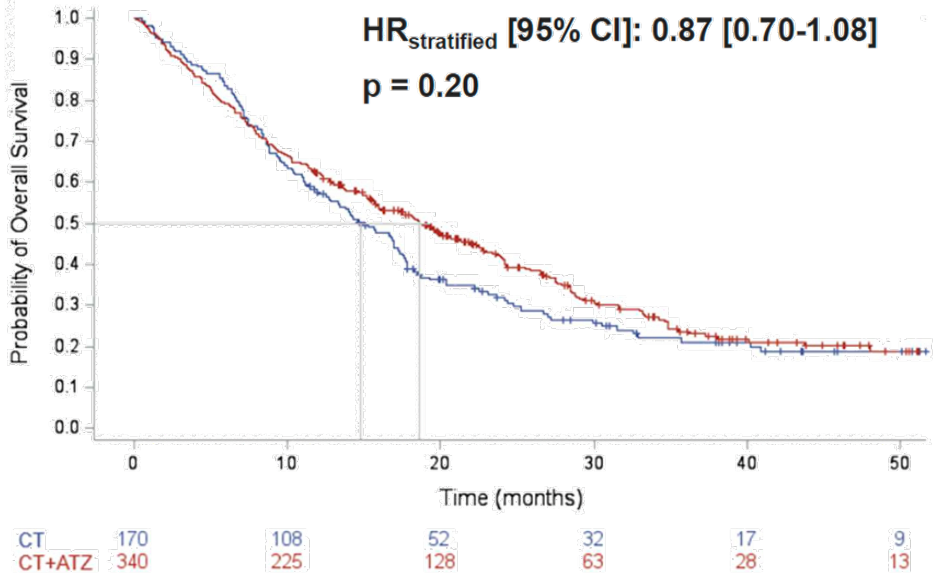
Carboplatin Q4W - weekly paclitaxel (4 cycles) (CT arm)
until progression or unacceptable toxicity

Stratification factors
- histology (squamous vs non squamous),
- age (70-79 vs 80-89),
- expression of PDL1 (0 vs ≥ 1 vs unknown)

Primary endpoint	Overall survival (OS)*
Secondary endpoints	Progression-Free Survival (PFS)* Best response rate* Duration of response* Safety**

First-line atezolizumab plus chemotherapy in elderly patients with advanced NSCLC IFCT-1805 ELDERLY: a randomized, multicenter, open-label, phase 3 trial

Overall survival



	CT (N=170)	CT+ ATZ (N=340)
Median OS: months [95% CI]	15.0 [11.8-17.5]	18.6 [15.5-22.4]
6-m OS: % [95% CI]	83.5 [77-88.3]	79.1 [74.4-83.1]
12-m OS: % [95% CI]	57.6 [49.8-64.7]	62.3 [57-67.3]

Median FU: 38.0 months (IC95%: [33.6; 39.4])

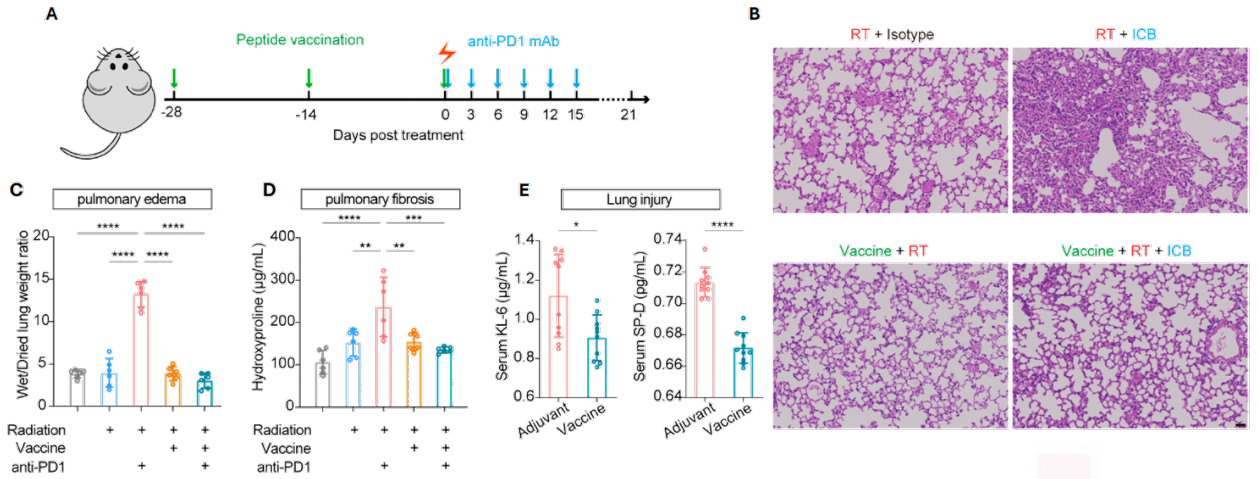
27 november 2024

The addition of ATZ to CT significantly improved PFS, ORR, DOR, independently of PDL1 expression.

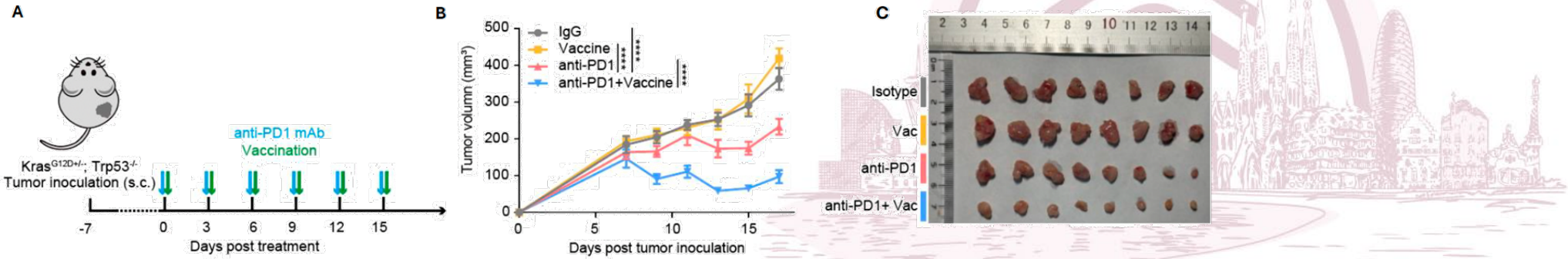
A significantly higher toxicity was seen with the addition of ATZ to CT for elderly patients.

TNFSF8-Targeting CpG Peptide Vaccine Reduces ICB Pneumonitis While Boosting Cancer Immunotherapy Efficacy

Reduced ICB Pneumonitis



Enhanced ICB Efficacy



Rong WCLC 2025


¿Qué sería de la vida si no tuviéramos el valor de intentar algo nuevo?
V. van Gogh