Novedades y Claves en Cáncer de Pulmón 2022

Carcinoma de pulmón microcítico y otros tumores

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Con la colaboración de:

Bristol Myers Squibb™

Janssen Oncology

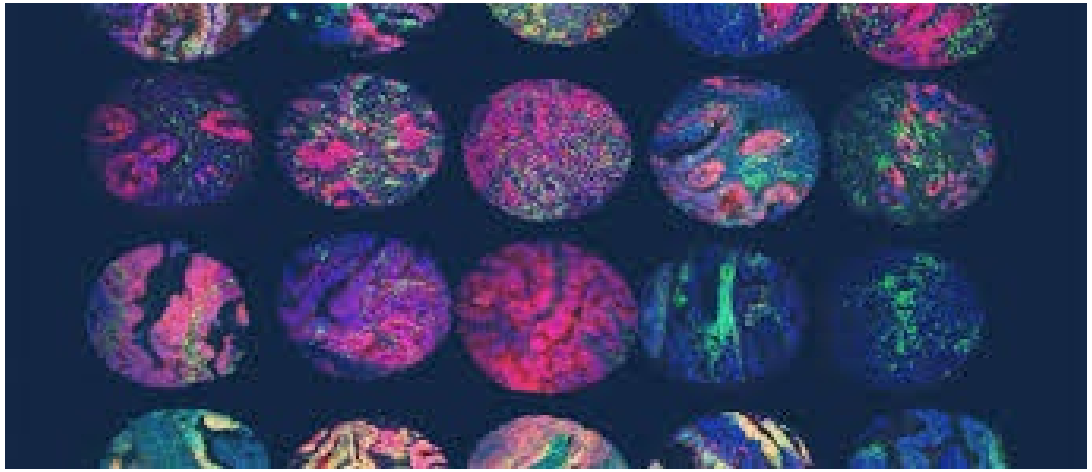
PHARMACEUTICAL COMPANIES OF Johnson&Johnson

Organizado por:

GECP lung cancer research

Potenciales Conflictos de Interés

- Employment: Servicio Madrileño de Salud
- Consultant or advisory board: Amgen, Boehringer
- Research Founding: none
- Travel, accomodation and meeting support: Sanofi, Pierre Fabre
- Speaking: BMS, MSD, Pierre Fabre, Astra Zeneca
- Stock ownership: none

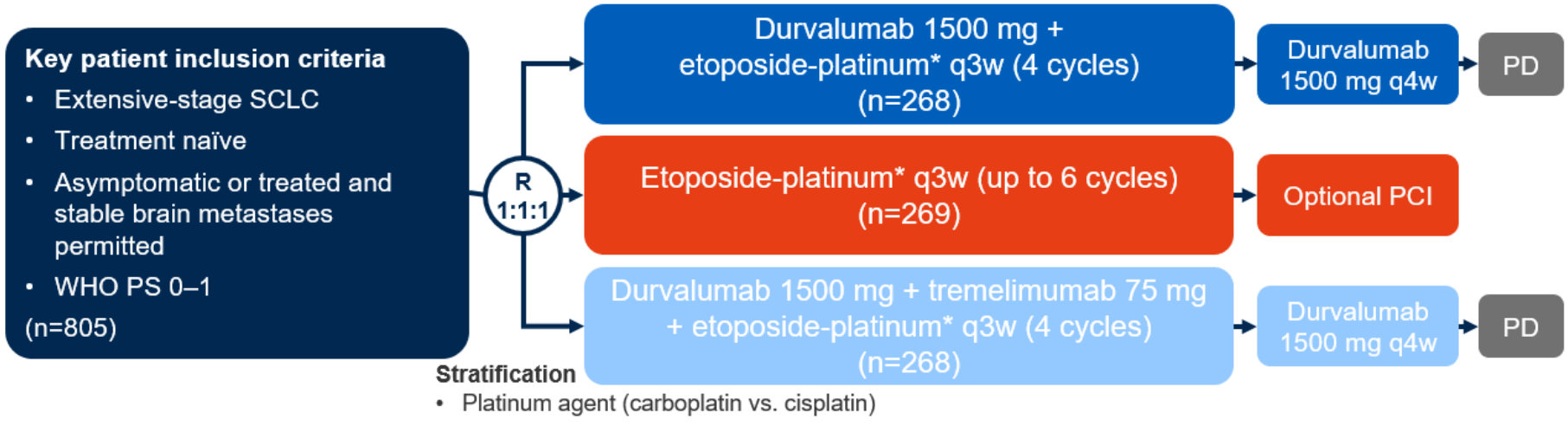


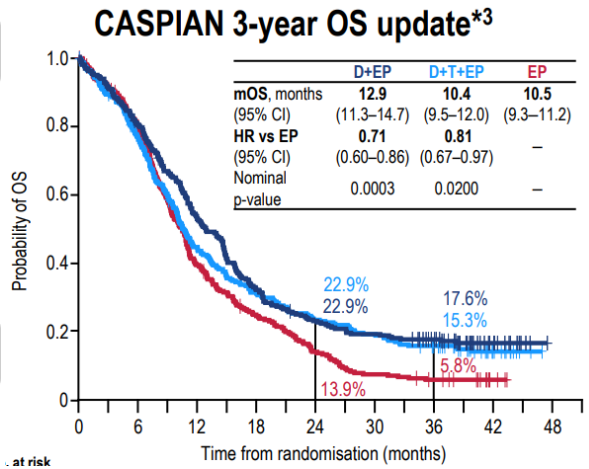
CARCINOMA MICROCÍTICO DE PULMÓN: SUBTIPOS MOLECULARES

Organizado por:

GECP lung cancer research

Durvalumab (D) + platinum-etoposide (EP) in 1L extensive-stage small-cell lung cancer (ES-SCLC): Exploratory analysis of SCLC molecular subtypes in CASPIAN





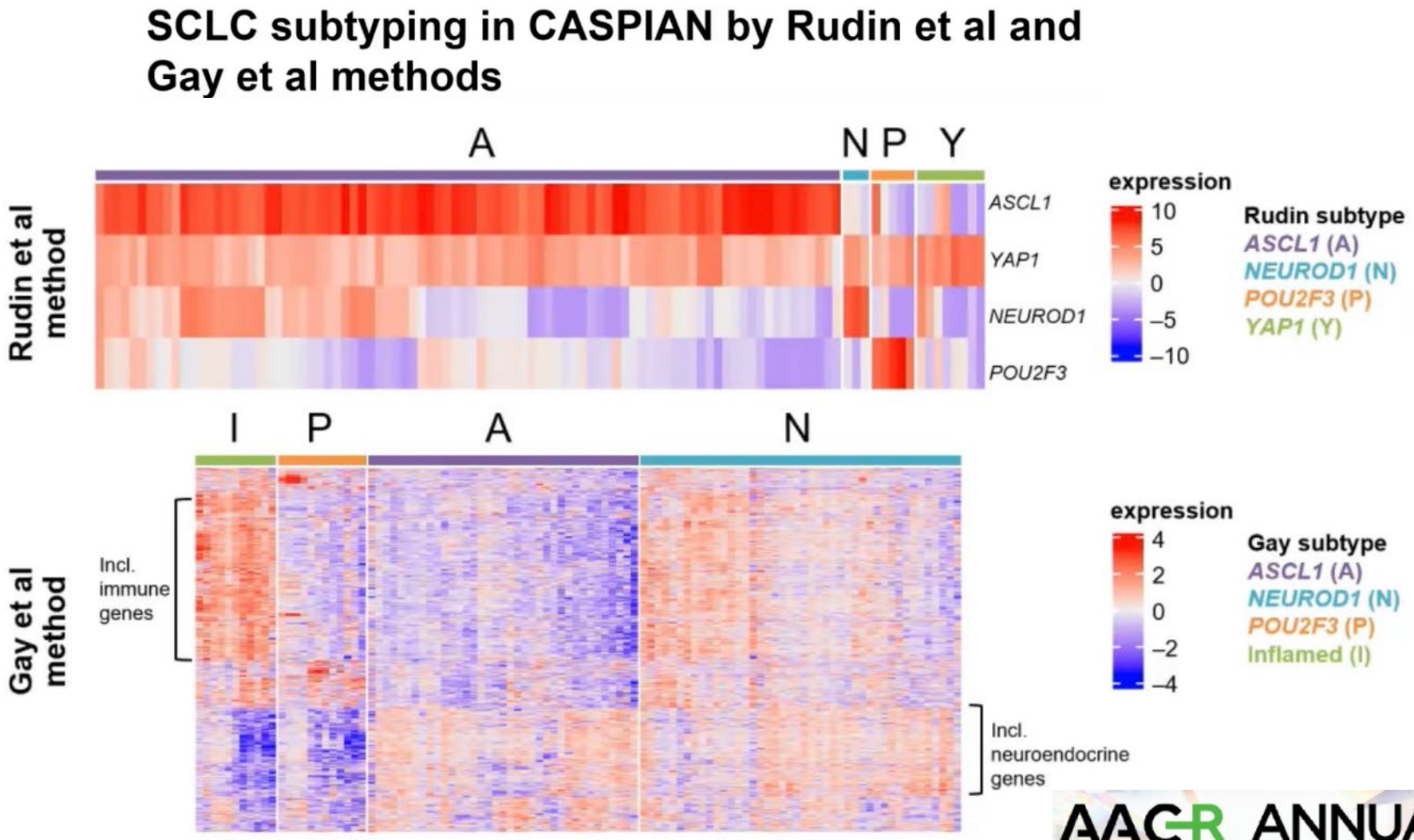
Objetive: To evaluate the concordance between two RNAseq-based methods[1,2] for SCLC subtyping and the association of subtypes on survival in patients with extensive-stage SCLC treated with durvalumab + etoposide-platinum in the CASPIAN study

Xie M, et al. AACR; 2022. Abstract nr CT024

AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

Organizado por: GECP lung cancer research

Durvalumab (D) + platinum-etoposide (EP) in 1L extensive-stage small-cell lung cancer (ES-SCLC): Exploratory analysis of SCLC molecular subtypes in CASPIAN



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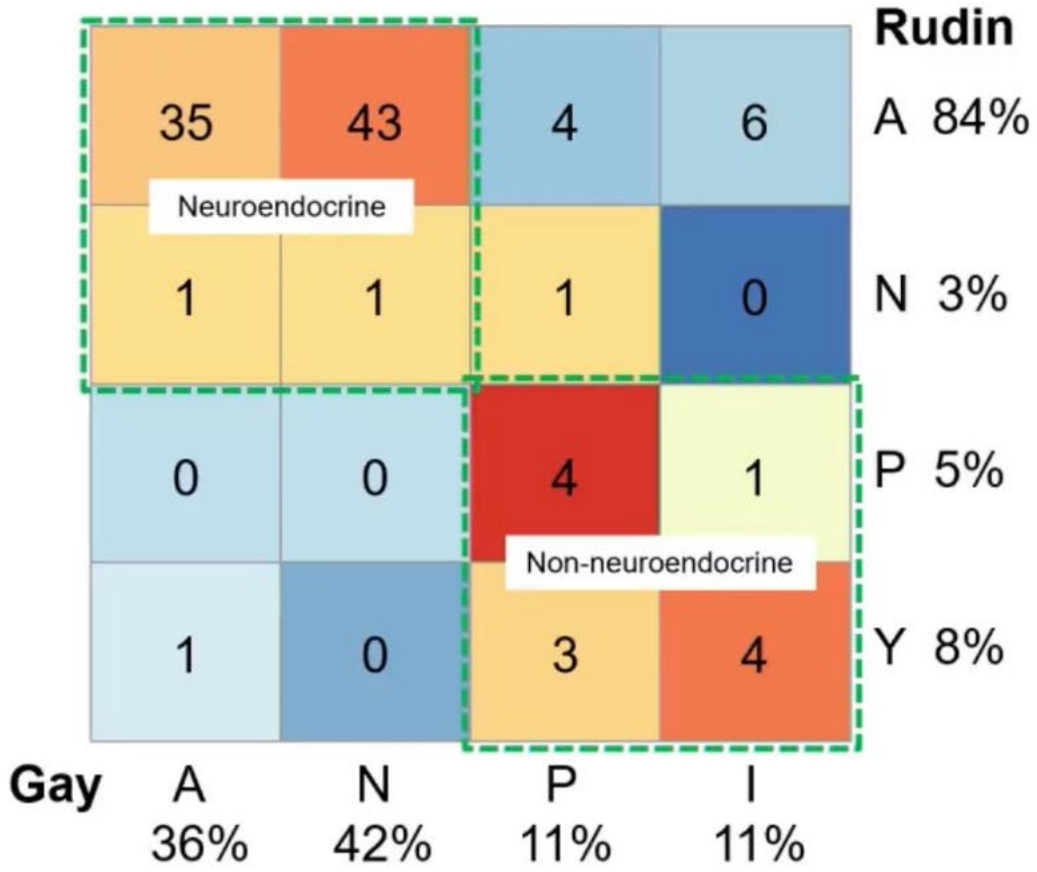
Durvalumab (D) + platinum-etoposide (EP) in 1L extensive-stage small-cell lung cancer (ES-SCLC): Exploratory analysis of SCLC molecular subtypes in CASPIAN

SCLC molecular subtype prevalence in CASPIAN



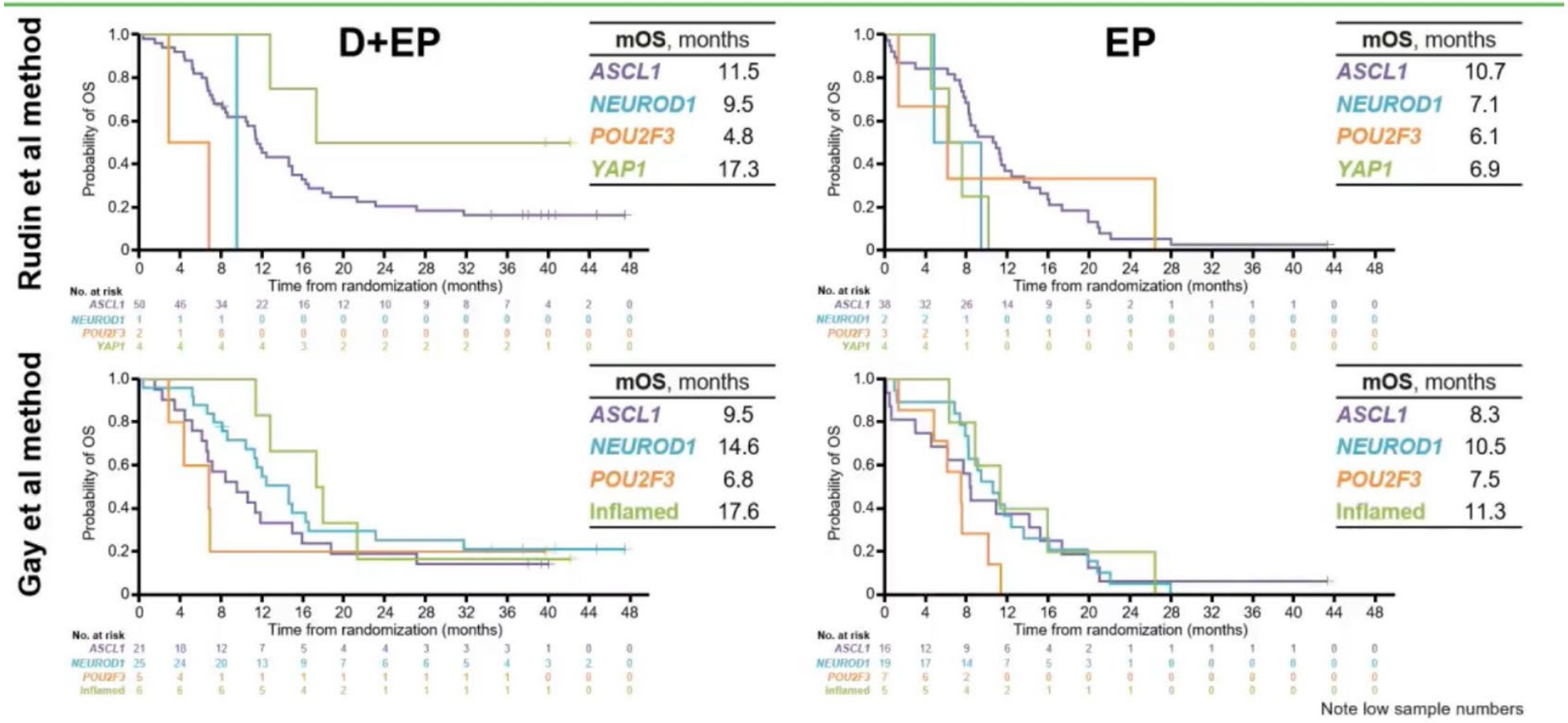
- RNA-based four-subtype classification is method-dependent
- The methods show high agreement in distinguishing neuroendocrine from non-neuroendocrine subtypes
- The methods show highest concordance between non-neuroendocrine subtypes (Rudin and Gay *POU2F3;* Rudin *YAP1* and Gay Inflamed)
  - Prevalence of Rudin *YAP1* = 8%
  - Prevalence of Gay Inflamed = 11%

Xie M, et al. AACR; 2022. Abstract nr CT024

Durvalumab (D) + platinum-etoposide (EP) in 1L extensive-stage small-cell lung cancer (ES-SCLC): Exploratory analysis of SCLC molecular subtypes in CASPIAN

AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

Overall survival by molecular subtype



Xie M, et al. AACR; 2022. Abstract nr CT024

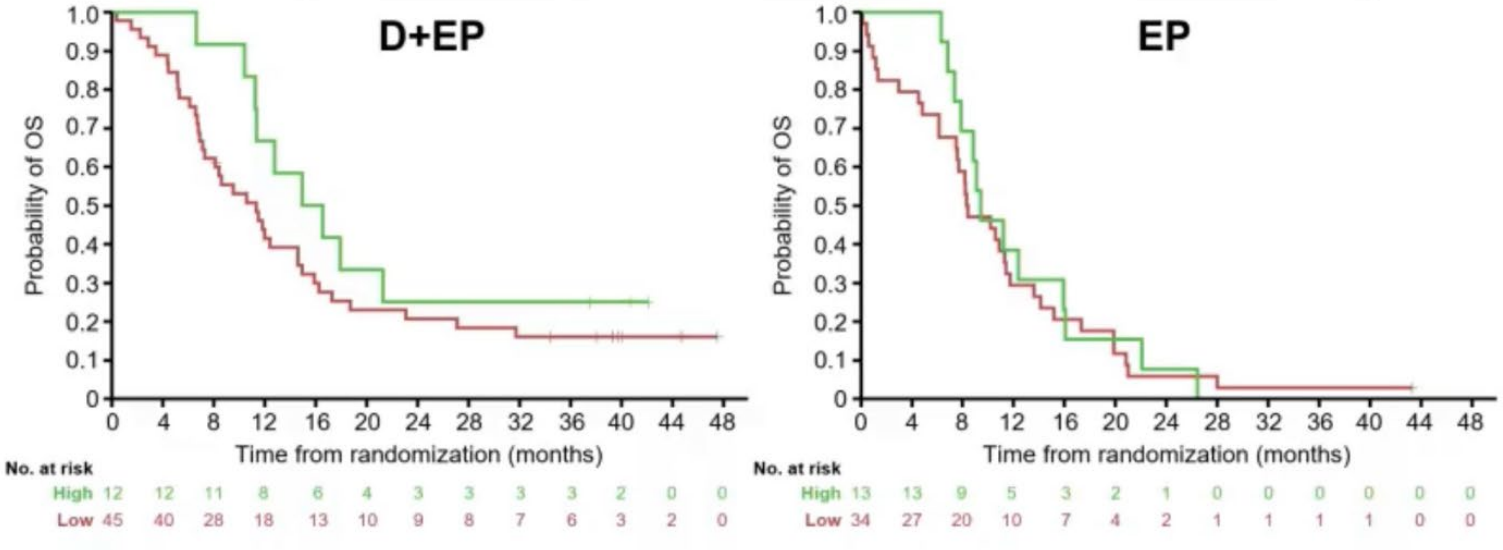
Organizado por: GECP lung cancer research

Durvalumab (D) + platinum-etoposide (EP) in 1L extensive-stage small-cell lung cancer (ES-SCLC): Exploratory analysis of SCLC molecular subtypes in CASPIAN

OS according to T-cell inflamed signature

High = top quartile
Low = rest

	D+EP		EP	
Inflamed signature	High	Low	High	Low
mOS, months (95% CI)	15.8 (10.4–NE)	11.3 (7.1–14.6)	9.4 (7.3–15.9)	8.3 (6.1–11.4)
HR high vs low (95% CI)	0.64 (0.31–1.32)		0.87 (0.45–1.66)	



Conclusions

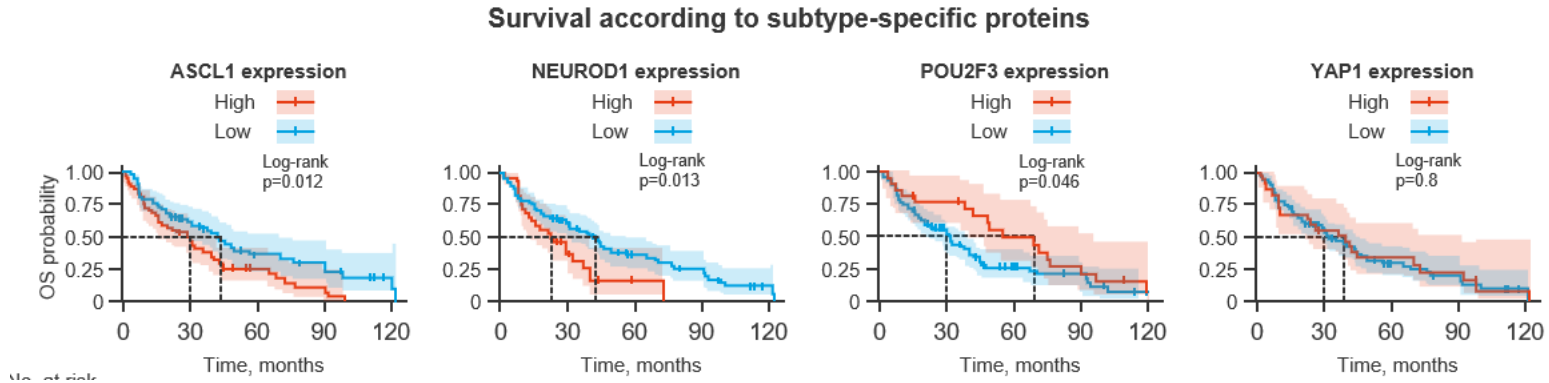
There was greater concordance between the two RNAseq-based methods for differentiating between neuroendocrine and non-neuroendocrine subtypes than for distinguishing the four main subtypes

Patients with inflamed (Gay et al.[1]) or YAP1 (Rudin et al.[2]) subtype had the longest OS in the durvalumab + etoposide-platinum arm

Xie M, et al. AACR; 2022. Abstract nr CT024

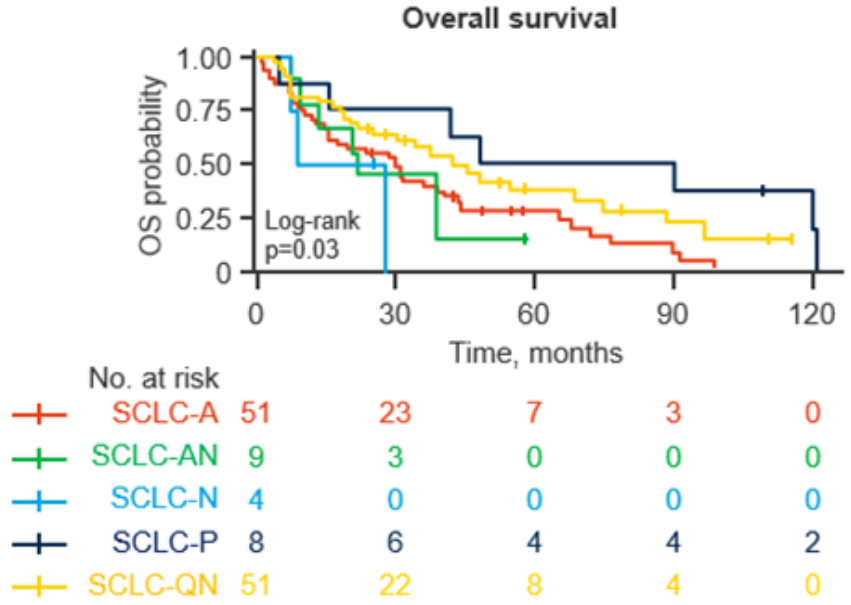
Molecular Subtypes of Surgically Resected Small Cell Lung Cancer: Expression Pattern and Prognostic Relevance

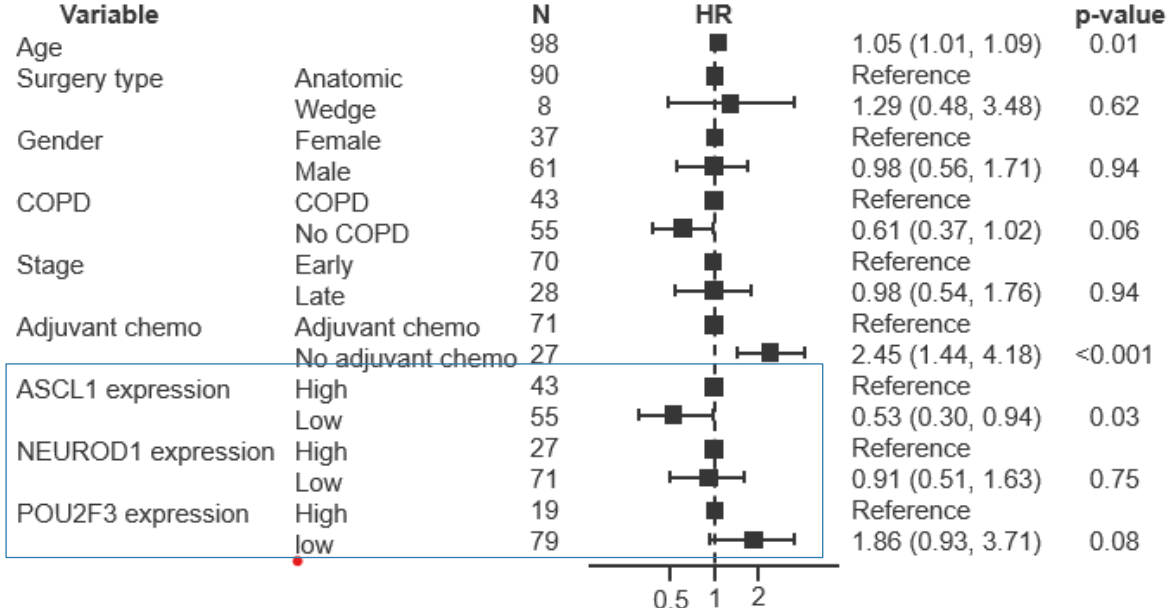
- **Study objective**
  - To evaluate the molecular subtypes of surgically resected SCLC and their impact on survival
- **Methods**
  - IHC analysis was performed on 386 surgically resected SCLC samples to determine expression of subtype-specific transcription factors as well as P53 and RB1 proteins
  - Human SCLC cell lines (n=26) were used to investigate the in vitro efficacy of various therapeutics agents by proteomics and cell viability assays



Megyesfalvi Z, et al. J Thorac Oncol 2022;17(suppl):Abstr MA01.04

Molecular Subtypes of Surgically Resected Small Cell Lung Cancer: Expression Pattern and Prognostic Relevance





In patients with SCLC, differential expression of ASCL1, NEUROD1 and POU2F3 can distinguish different subtypes with high POU2F3 expression being associated with better survival outcomes and ASCL1 expression being associated with poorer survival outcomes.

High POU2F3 and YAP1 protein abundances correlated with sensitivity and resistance to standard-of-care chemotherapeutics, respectively.

Megyesfalvi Z, et al. J Thorac Oncol 2022;17(suppl):Abstr MA01.04

Comparative expression of driver transcription factors in extra-pulmonary small cell carcinoma

Study objective

- To characterize gene expression in extra-pulmonary small cell carcinomas (EPSCC) and to assess its correlation with clinical outcomes

Methods

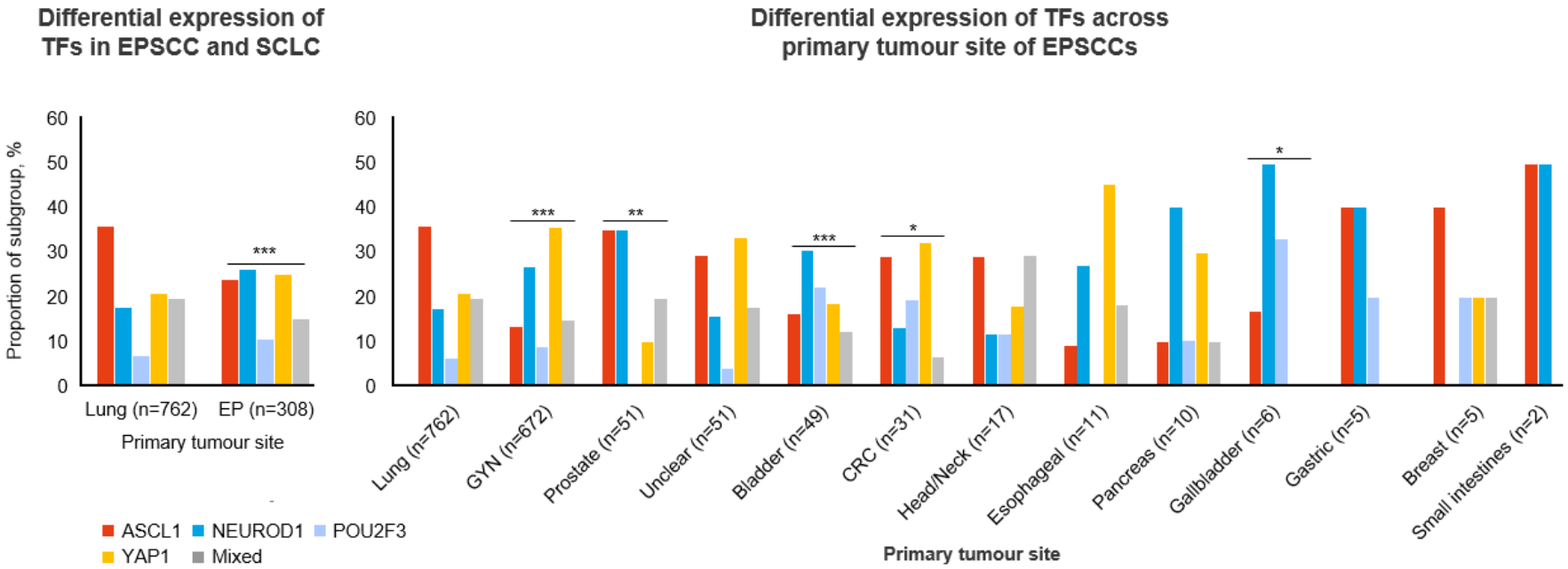
- DNA and RNA sequencing were performed on samples from 1070 patients with SCC
- Following molecular profiling (Caris Life Sciences) samples were stratified into 5 subtypes based on the relative expression of key transcription factors: ASCL1, NEUROD1, YAP1, POU2F3 and mixed
- OS was assessed for 111 patients who received etoposide + platinum-based therapy

Organizado por:

GECP lung cancer research

Liu S, et al. Ann Oncol 2022;33(suppl):Abstr 889MO

Comparative expression of driver transcription factors in extra-pulmonary small cell carcinoma



*p<0.05, **p<0.01, ***p<0.001

Conclusions

The expression of different transcription factors was observed in EPSCC compared with SCLC

A higher expression of NEUROD1 and YAP1 was associated with longer survival regardless of primary site of tumour origin, suggesting that the transcription factor subtypes may be predictive of therapeutic vulnerabilities

Liu S, et al. Ann Oncol 2022;33(suppl):Abstr 889MO

Organizado por:

GECP lung cancer research

The genomic landscape of small cell lung cancer in never smoking patients

Study objective

- To evaluate the genomic landscape of never smokers with SCLC compared with current/former smokers

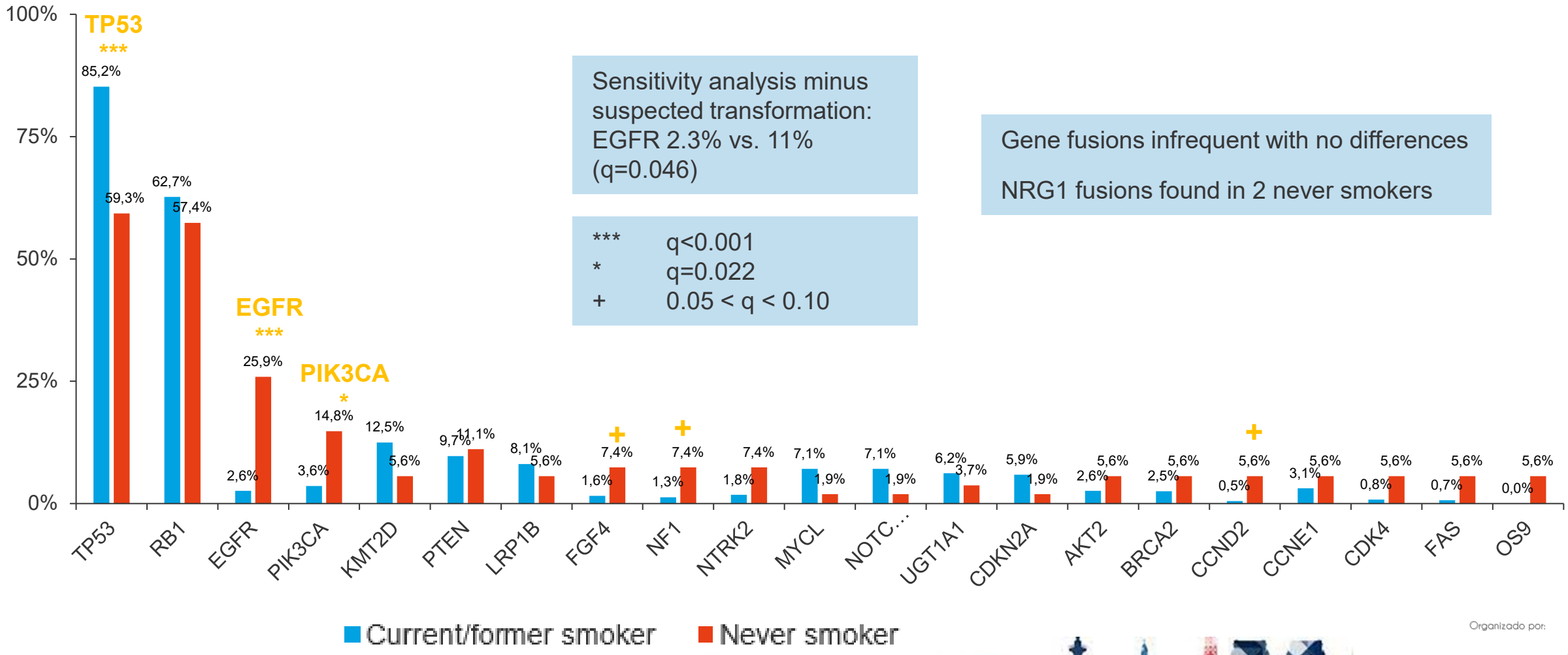
Methods

- Data were collected from 662 patients with SCLC (either current/former smokers or never smokers) in the Tempus database
- Tumours were sequenced with the Tempus xT assay
- Tumour immune cell infiltration was estimated from RNA expression data, and PD-L1 positivity was defined by tumour expression >1% (22C3 pharmDx IHC)

Oh M, et al. Ann Oncol 2022;33(suppl):Abstr 1529MO

The genomic landscape of small cell lung cancer in never smoking patients

Never smokers exhibit unique somatic variant landscape



Sensitivity analysis minus suspected transformation: EGFR 2.3% vs. 11% (q=0.046)

***	q<0.001
*	q=0.022
+	0.05 < q < 0.10

Gene fusions infrequent with no differences

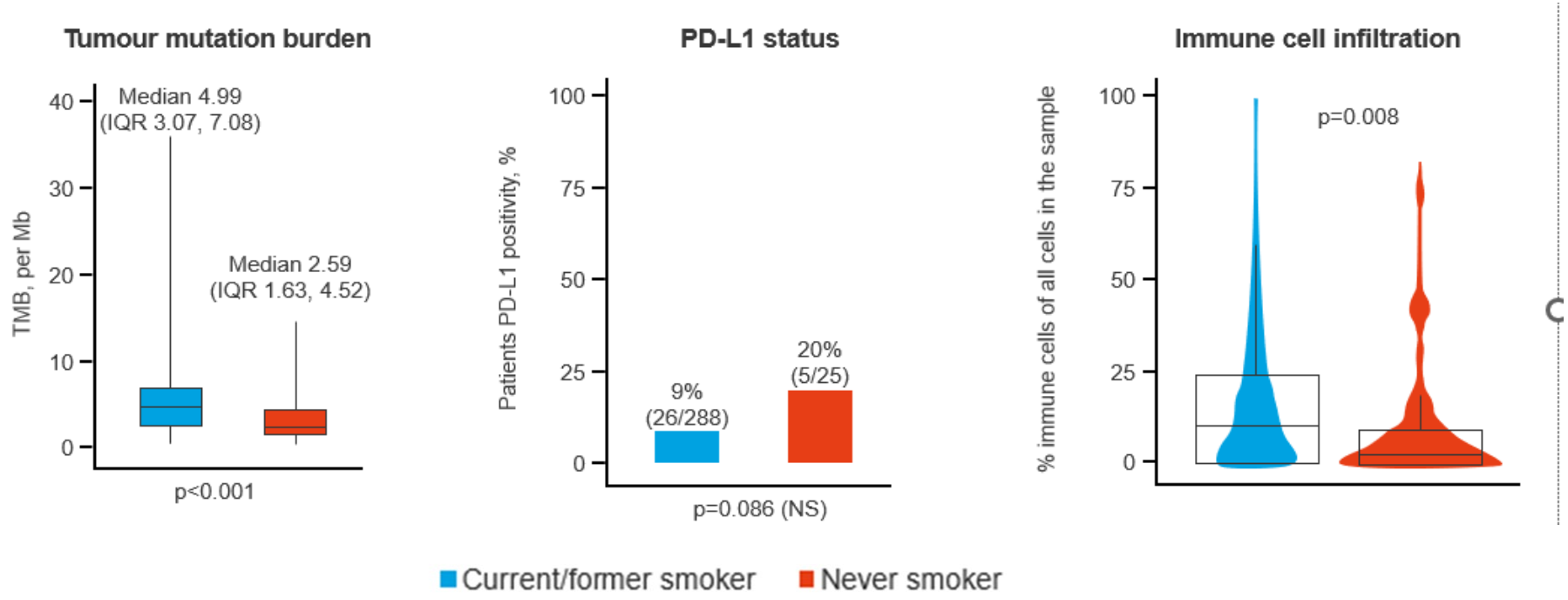
NRG1 fusions found in 2 never smokers

Organizado por:

GECP lung cancer research

Oh M, et al. Ann Oncol 2022;33(suppl):Abstr 1529MO

The genomic landscape of small cell lung cancer in never smoking patients



Conclusions

In never smokers with SCLC, mutations in oncogenic drivers (EGFR, PIK3CA) plus lower TMB and immune cell infiltration were observed compared with current/former smokers, suggesting that this group of patients may have a distinct genomic entity

Oh M, et al. Ann Oncol 2022;33(suppl):Abstr 1529MO

CARCINOMA MICROCÍTICO DE PULMÓN: ENFERMEDAD LIMITADA

Organizado por:

GECP
lung cancer research

Comparison of quality of life in patients randomized to high-dose once daily (QD) thoracic radiotherapy (TRT) with standard twice daily (BID) TRT in limited stage small cell lung cancer (LS-SCLC) on CALGB 30610

- 70Gy QD TRT was not superior to 45Gy BID TRT OS compared to in limited stage small cell lung cancer

Median OS of 30.5 mos (QD) Vs. 28.7 mos (BID); HR 0.94; P = 0.9

No major differences in toxicity between the two arms

CALGB 30610: DOI: 10.1200/JCO.2021.39.15_suppl.8505 *Journal of Clinical Oncology* 39, no. 15_suppl (May 20, 2021) 8505-8505

- Given the equivalence in efficacy, differences in QOL scale measurements may help the clinician choose between the BID Vs. QD TRT routes !?

Patients were administered the FACT-L, FACT Trial Outcome Index-Lung Cancer (FACT-L TOI) and other scales at various points during the TRT

Patients were also asked to assess treatment inconvenience at multiple time points.

2022 ASCO ANNUAL MEETING

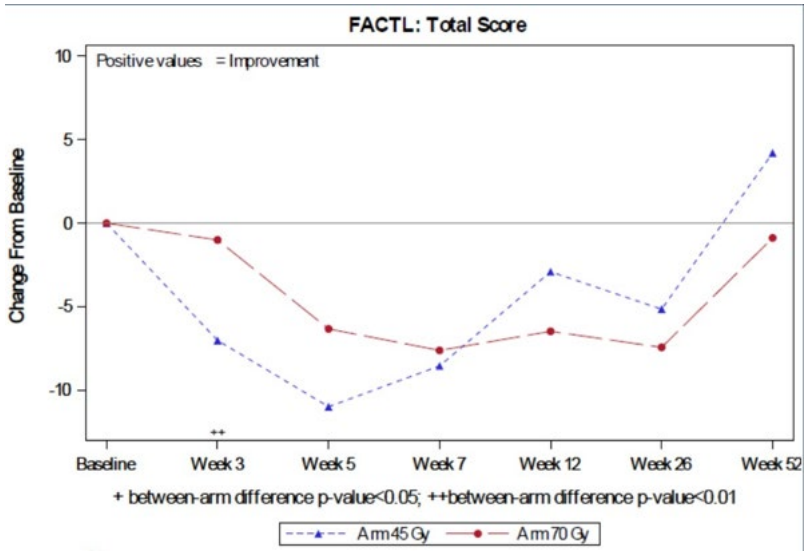
#ASCO22

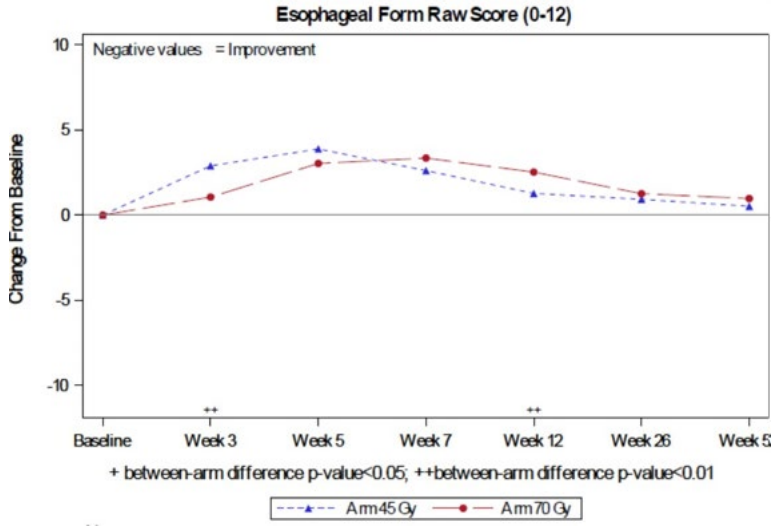
Organizado por:

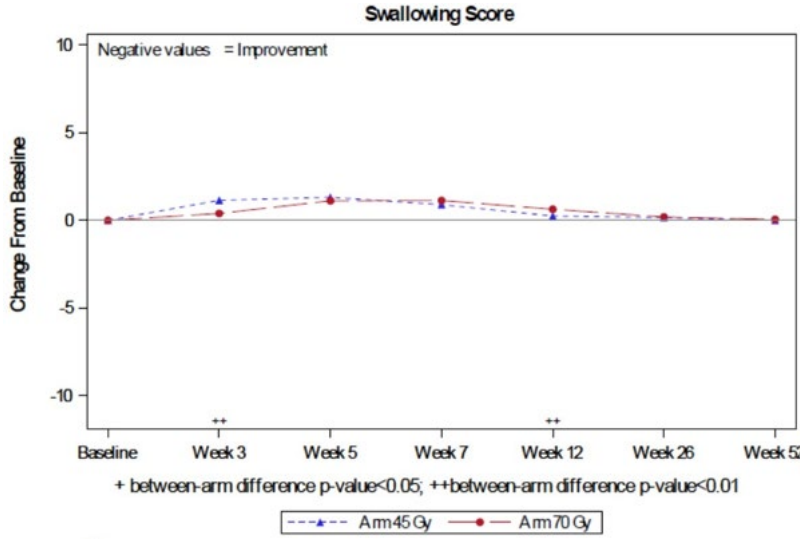
GECP lung cancer research

Apar Kishor Ganti J Clin Oncol 40, 2022 (suppl 16; abstr 8504)

Comparison of quality of life in patients randomized to high-dose once daily (QD) thoracic radiotherapy (TRT) with standard twice daily (BID) TRT in limited stage small cell lung cancer (LS-SCLC) on CALGB 30610





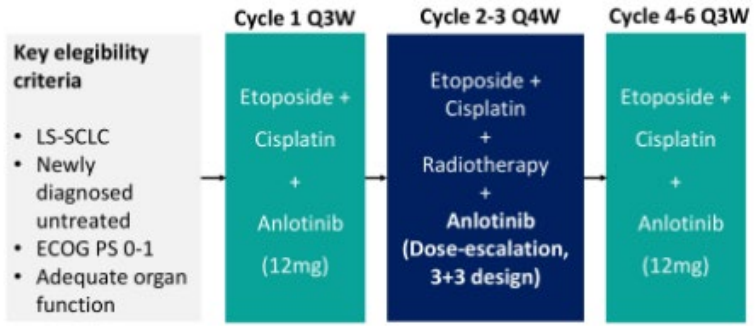


The FACT-L total score mean worsening was significantly less in the QD arm compared to the BID arm at week 3 (-1.0 vs -7.0; P=.003)

Mean increase in the acute esophagitis score (1.06 vs 2.89; P<.001) and difficulty swallowing (0.39 vs 1.14; P<.001) were significantly greater in the BID arm at week 3.

Conclusions: Both radiation regimens were well tolerated. However, the QD arm had better quality of life scores at week 3 and was perceived to be less inconvenient.

A phase I study of anlotinib with concurrent chemoradiotherapy for limited-stage small cell lung cancer



- Chemotherapy
  - Cycle 1/4/5/6: etoposide, 100 mg/m^2, d1-3, q3w and cisplatin, 25 mg/m^2, d1-3, q3w.
  - Cycle 2/3: etoposide, 50 mg/m^2, d1-5, q4w and cisplatin, 25 mg/m^2, d1-3, q4w.
- Radiotherapy
  - 60 Gy in 30 daily 2-Gy fractions starting on day 1 of cycle 2.

	Grade 1	Grade 2	Grade 3	Grade 4	All grades
Lymphocyte count decreased	2 (17%)	3 (25%)	6 (50%)	0 (0%)	11 (92%)
Anemia	5 (42%)	6 (50%)	0 (0%)	0 (0%)	11 (92%)
Neutrophil count decreased	1 (8%)	3 (25%)	5 (42%)	1 (8%)	10 (83%)
White blood cell count decreased	0 (0%)	6 (50%)	5 (42%)	0 (0%)	11 (92%)
Platelet count decreased	5 (42%)	3 (25%)	0 (0%)	0 (0%)	8 (67%)
Hypertension	0 (0%)	5 (42%)	2 (17%)	0 (0%)	7 (58%)
Nausea	2 (17%)	4 (33%)	0 (0%)	0 (0%)	6 (50%)
Constipation	4 (33%)	0 (0%)	0 (0%)	0 (0%)	4 (33%)
Hypertriglyceridemia	4 (33%)	0 (0%)	0 (0%)	0 (0%)	4 (33%)
Expectoration	0 (0%)	3 (25%)	0 (0%)	0 (0%)	3 (25%)
Cough	1 (8%)	2 (17%)	0 (0%)	0 (0%)	3 (25%)
Hypercholesteremia	3 (25%)	0 (0%)	0 (0%)	0 (0%)	3 (25%)
Decreased appetite	3 (25%)	0 (0%)	0 (0%)	0 (0%)	3 (25%)
Hyponatraemia	1 (8%)	1 (8%)	0 (0%)	0 (0%)	2 (17%)
Radiation esophagitis	1 (8%)	1 (8%)	0 (0%)	0 (0%)	2 (17%)
Upper respiratory tract infection	1 (8%)	1 (8%)	0 (0%)	0 (0%)	2 (17%)
Bloody sputum	1 (8%)	1 (8%)	0 (0%)	0 (0%)	2 (17%)
Increased ALT	2 (17%)	0 (0%)	0 (0%)	0 (0%)	2 (17%)
Hypoproteinemia	2 (17%)	0 (0%)	0 (0%)	0 (0%)	2 (17%)
Red blood cell count decreased	2 (17%)	0 (0%)	0 (0%)	0 (0%)	2 (17%)
Hypoparathyroidism	2 (17%)	0 (0%)	0 (0%)	0 (0%)	2 (17%)
Hands trembling	2 (17%)	0 (0%)	0 (0%)	0 (0%)	2 (17%)
Albumin decreased	0 (0%)	0 (0%)	1 (8%)	0 (0%)	1 (8%)
pulmonary embolism	0 (0%)	0 (0%)	1 (8%)	0 (0%)	1 (8%)

Conclusion: Combined treatment with anlotinib and CCRT for limited-stage small cell lung cancer is well tolerated and further clinical investigation is warranted

Journal of Clinical Oncology 40, no. 16_suppl (June 01, 2022) 8579-8579.

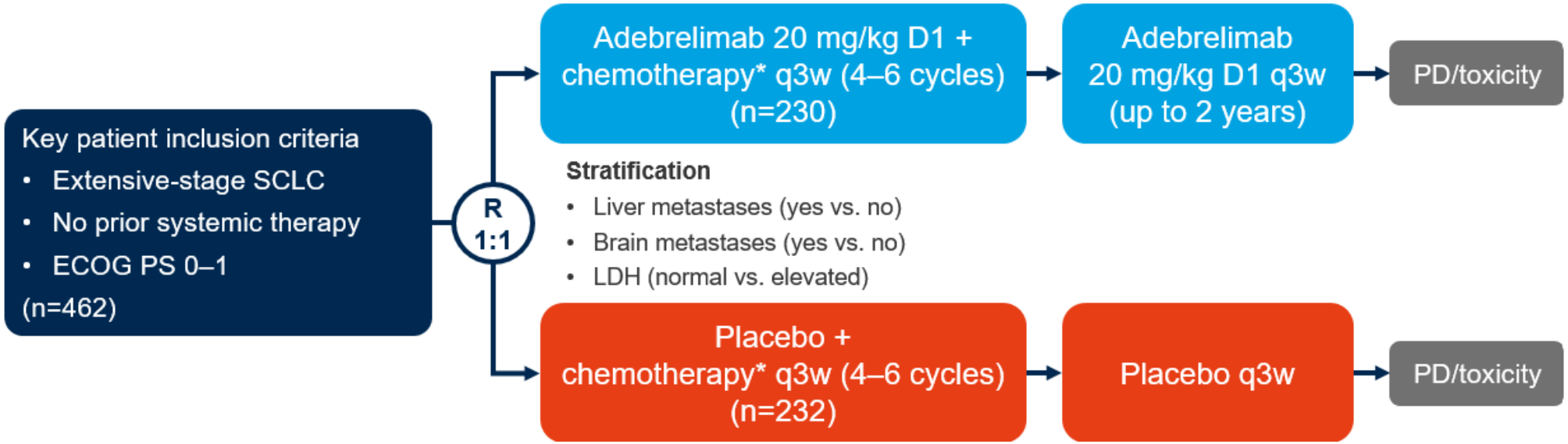
CARCINOMA MICROCÍTICO DE PULMÓN: ENFERMEDAD EXTENDIDA

Organizado por:

GECP lung cancer research

Adebrelimab or placebo plus carboplatin and etoposide as first-line treatment for extensive-stage SCLC: A phase 3 trial(CAPSTONE-1)

- **Study objective**
  - To evaluate the efficacy and safety of 1L adebrelimab (a fully humanized IgG4 anti-PD-L1 monoclonal antibody) + chemotherapy in patients with extensive-stage SCLC



- *Carboplatin AUC5 D1 + etoposide 100 mg/m^2 D1–3

Primary endpoint

- OS

Secondary endpoints

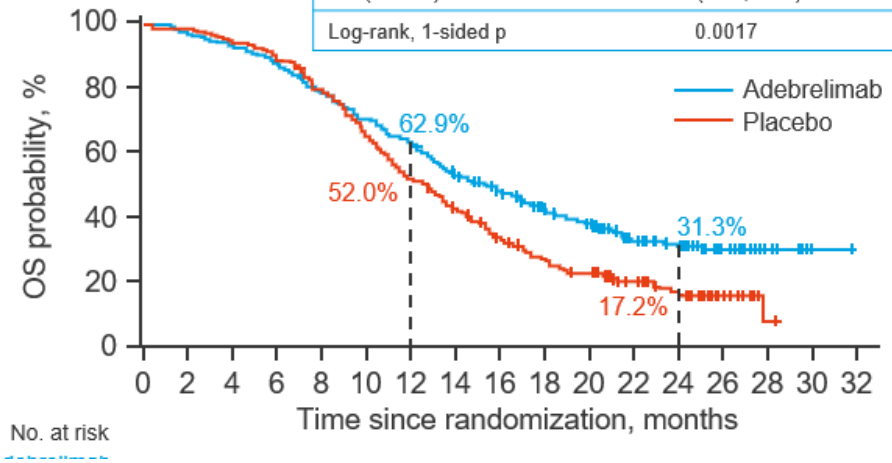
- PFS, ORR, DoR, DCR, safety

Cheng Y, et al. AACR; 2022. Abstract nr CT038

Adebrelimab or placebo plus carboplatin and etoposide as first-line treatment for extensive-stage SCLC: A phase 3 trial

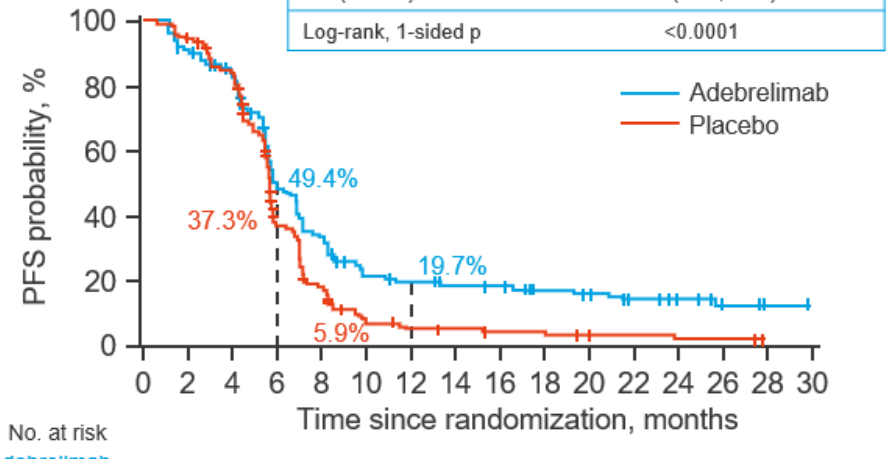
Overall survival

	Adebrelimab + chemotherapy	Placebo + chemotherapy
mOS, mo (95%CI)	15.3 (13.2, 17.5)	12.8 (11.3, 13.7)
HR (95%CI)	0.72 (0.58, 0.90)	
Log-rank, 1-sided p	0.0017	



Progression-free survival

	Adebrelimab + chemotherapy	Placebo + chemotherapy
mPFS, mo (95%CI)	5.8 (5.6, 6.9)	5.6 (5.5, 5.7)
HR (95%CI)	0.67 (0.54, 0.83)	
Log-rank, 1-sided p	<0.0001	



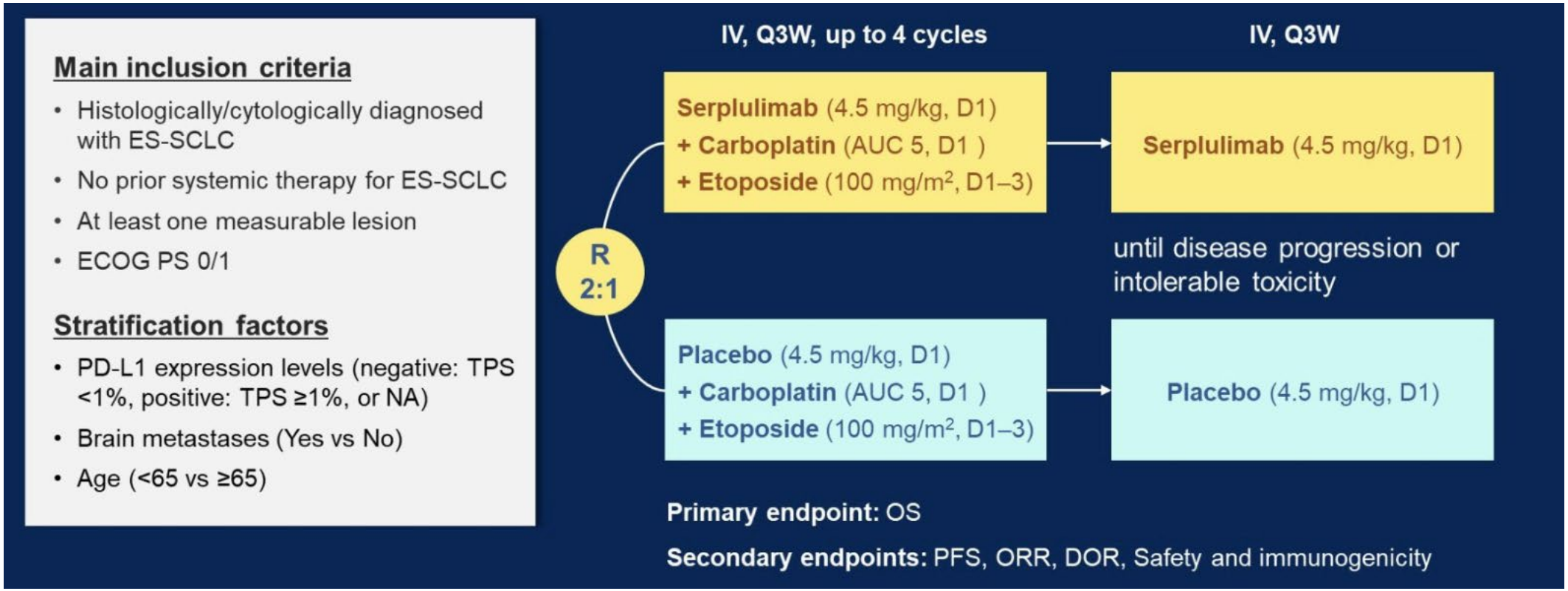
Conclusions

In patients with extensive-stage SCLC, adebrelimab + chemotherapy demonstrated significant improvement in survival compared with chemotherapy alone and had a manageable safety profile

Cheng Y, et al. AACR; 2022. Abstract nr CT038

Organizado por:

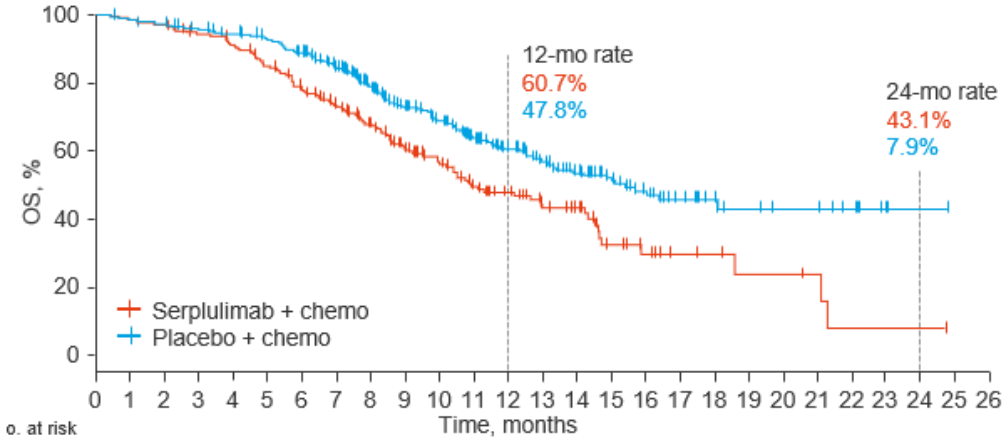
Serplulimab, a novel anti-PD-1 antibody, plus chemotherapy versus chemotherapy alone as first-line treatment for extensive-stage small-cell lung cancer: An international randomized phase 3 study



Cheng Y, et al. J Clin Oncol 2022;40(suppl):Abstr 8505

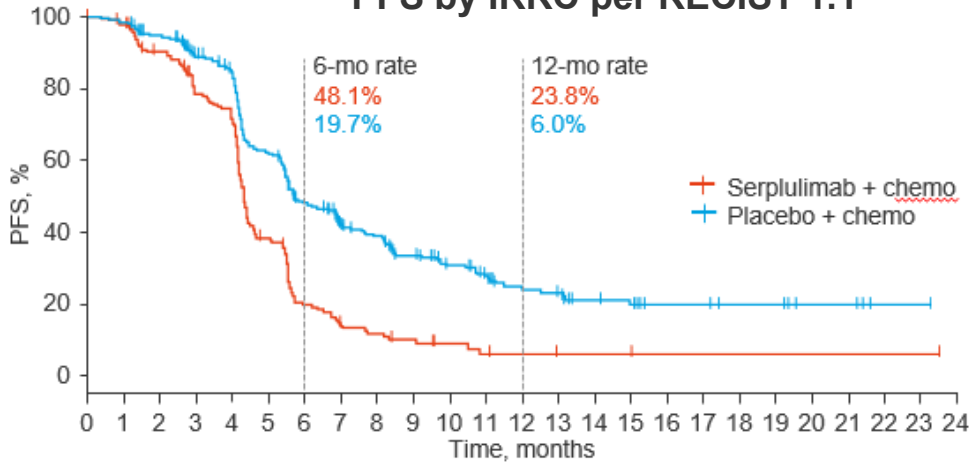
Serplulimab, a novel anti-PD-1 antibody, plus chemotherapy versus chemotherapy alone as first-line treatment for extensive-stage small-cell lung cancer: An international randomized phase 3 study

Overall survival



	Serplulimab + chemo (n=389)	Placebo + chemo (n=196)
Events, n (%)	146 (37.5)	100 (51.0)
mOS, mo (95%CI)	15.4 (13.3, NE)	10.9 (10.0, 14.3)
HR (95%CI); p-value	0.63 (0.49, 0.82); <0.001	

PFS by IRRC per RECIST 1.1



	Serplulimab + chemo (n=389)	Placebo + chemo (n=196)
Events, n (%)	223 (57.3)	151 (77.0)
mPFS, mo (95%CI)	5.7 (5.5, 6.9)	4.3 (4.2, 4.5)
HR (95%CI)	0.48 (0.38, 0.59)	

In patients with extensive-stage SCLC, serplulimab + CT demonstrated superior survival to SoC at this planned interim analysis and had a manageable safety profile

Cheng Y, et al. J Clin Oncol 2022;40(suppl):Abstr 8505

Primary Results from IMfirst, a Phase IIIb Open Label Safety Study of Atezolizumab Plus Carboplatin/Cisplatin and Etoposide in an Interventional Real World Clinical Setting of Extensive-Stage Small Cell Lung Cancer (ES-SCLC) in Spain

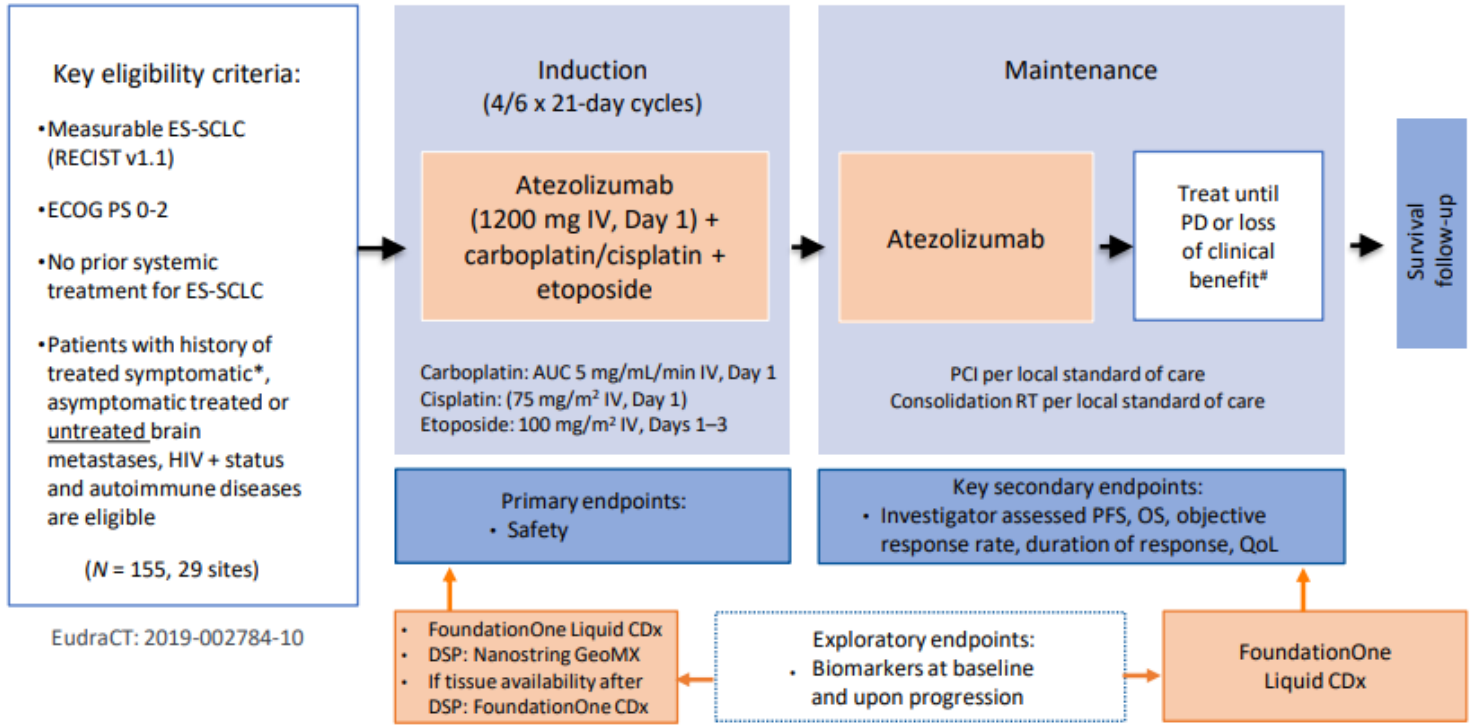


Table 1. Demographic and baseline characteristics

n (%)	All patients (*N* = 155)
Age	
≤65 years	82 (52.9)
>65 years	73 (47.1)
Gender	
Male	112 (72.3)
Female	43 (27.7)
Smoking history	
Never	2 (1.3)
Current	87 (56.1)
Former	66 (42.6)
ECOG PS	
0	38 (24.5)
1	100 (64.5)
2	17 (11.0)
CNS metastases at baseline	27 (17.4)
Autoimmune disease	2 (1.3)
Comorbidities*	110 (80.0)
LDH > ULN at baseline	88 (56.8)
High tumor burden#	130 (83.9)
Concomitant steroid treatment at baseline	34 (21.9)
Prior radiotherapy at baseline	27 (17.4)

García Campelo, Annals Oncol, 22, VOLUME 33, SUPPLEMENT 7, S1246-S1247

Primary Results from IMfirst, a Phase IIIb Open Label Safety Study of Atezolizumab Plus Carboplatin/Cisplatin and Etoposide in an Interventional Real World Clinical Setting of Extensive-Stage Small Cell Lung Cancer (ES-SCLC) in Spain

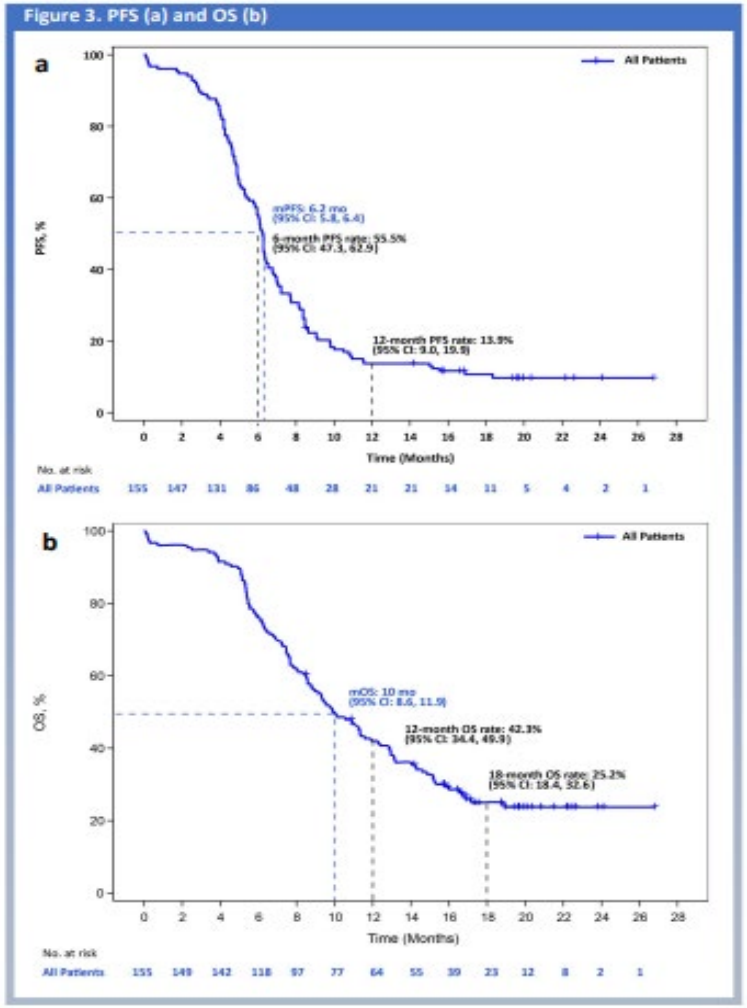


Table 3. Efficacy summary

	All patients (*N* = 155)
ORR, *n* (%)*	107 (69.0)
Best overall response, *n* (%)	
Complete response	1 (0.67)
Partial response	106 (68.4)
Stable disease	31 (20)
Progressive disease	5 (3.2)
Not evaluable[#]	12 (7.7)
mDOR, months (95% CI)	5.1 (4.8, 5.8)
Progression-free survival (PFS)[¥]	
mPFS (95% CI), months	6.2 (5.8, 6.4)
6-month PFS rate, % (95% CI)	55.5 (47.3, 62.9)
12-month PFS rate, % (95% CI)	13.9 (9.0, 19.9)
Overall survival (OS)	
mOS (95% CI), months	10.0 (8.6, 11.9)
12-month OS rate, % (95% CI)	42.3 (34.4, 49.9)
18-month OS rate, % (95% CI)	25.2 (18.4, 32.6)

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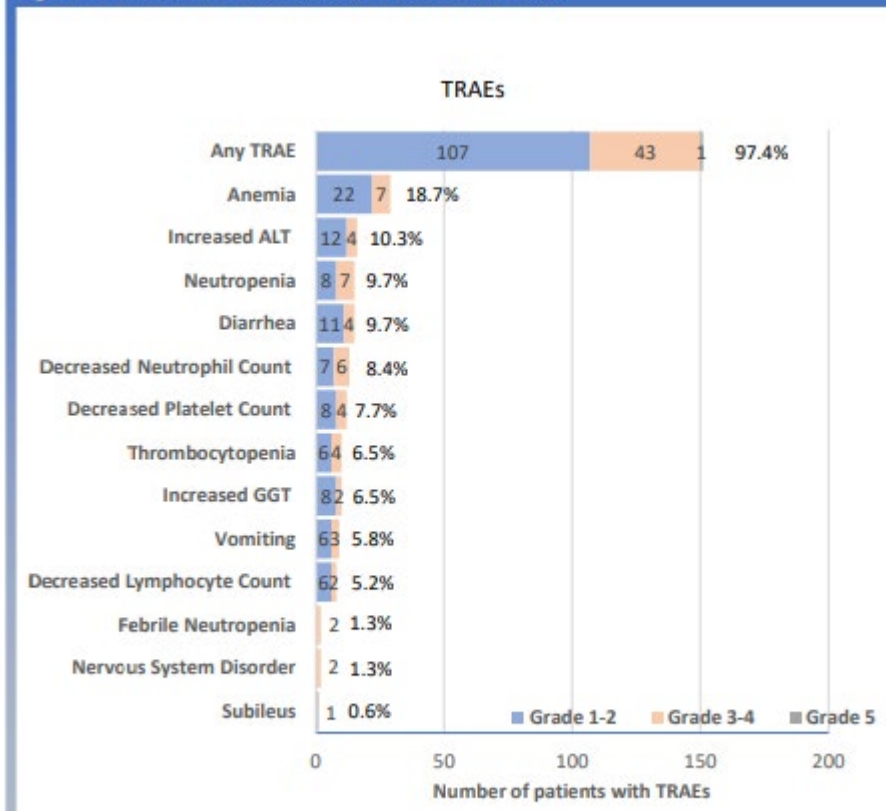
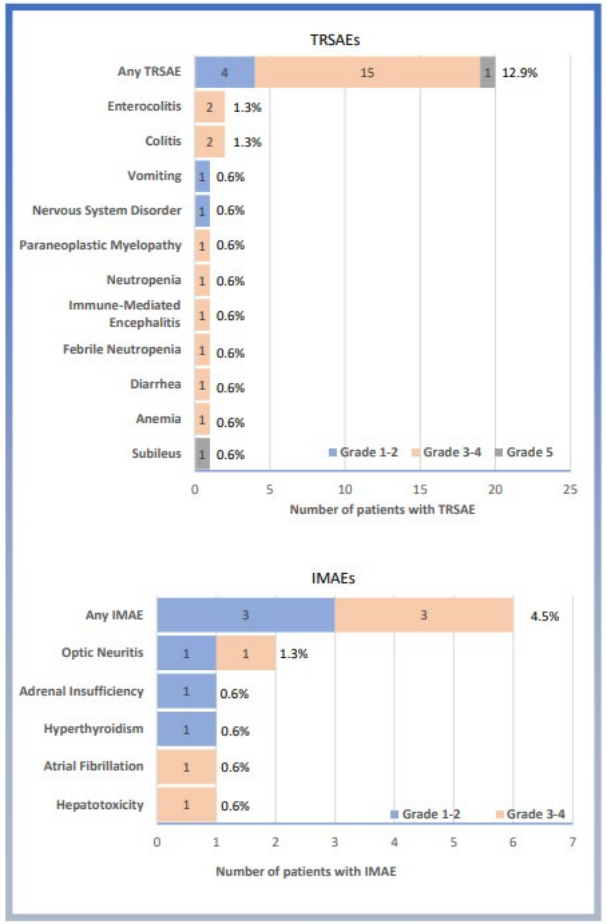
García Campelo, Annals Oncol, 22, VOLUME 33, SUPPLEMENT 7, S1246-S1247

Primary Results from IMfirst, a Phase IIIb Open Label Safety Study of Atezolizumab Plus Carboplatin/Cisplatin and Etoposide in an Interventional Real World Clinical Setting of Extensive-Stage Small Cell Lung Cancer (ES-SCLC) in Spain

Figure 2. Most common TRAEs, TRSAEs and IMAEs





García Campelo, Annals Oncol, 22, VOLUME 33, SUPPLEMENT 7, S1246-S1247

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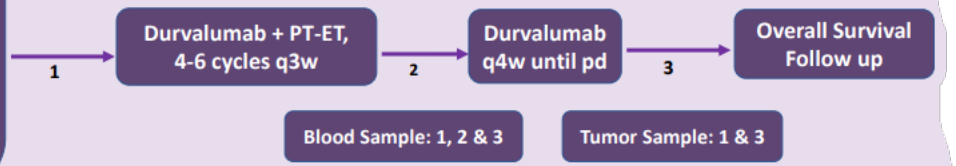
Phase IIIb study of durvalumab plus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CANTABRICO): Treatment patterns of chemotherapy combination phase with durvalumab

elcc European Lung Cancer Congress

Objective: to assess safety and effectiveness of D plus EP in a real world ES-SCLC population

- Treatment naive ES-SCLC, including progressive disease after at least 6 months without treatment for LS-SCLC
- WHO PS 0-2
- Eligible to receive platinum-based 1L therapy
- Patients with either asymptomatic or treated and stable brain metastases are permitted
- Adequate hematologic and organ function
- Life expectancy >12 weeks
- Body weight >30 kg



Primary endpoint:
Safety (incidence of Grade ≥3 AE, imAE)
Secondary endpoints:
PFS, OS, ORR, DOR, 6/12m PFS, 6/12/18m OS, 12m DOR, TTD, safety and tolerability, PRO & health care resources use.

ADVERSE EVENTS		
AEs* (N, %)	All	Grade 3-4
Asthenia	61 (60)	4 (4)
Anaemia	47 (47)	22 (22)
Neutropenia	33 (33)	20 (20)
Dyspnea	28 (28)	3 (3)
Constipation	25 (25)	1 (1)
Alopecia	24 (24)	-
Diarrhoea	20 (20)	-
Cough	15 (15)	-
Thrombocytopenia	14 (14)	9 (9)
Back pain	14 (14)	-
Pyrexia	14 (14)	1 (1)
Nausea	14 (14)	-
Arthralgia	12 (12)	-
Hypothyroidism	11 (11)	-
Vomiting	11 (11)	2 (2)
Decreased appetite	11 (11)	1 (1)

BEST RESPONSE	CANTABRICO*,# N (%)	CASPIAN N (%)
Complete response	4 (4)	6 (2)
Partial response	48 (48)	176 (66)
Stable disease$	33 (33)	20 (7)
Progressive disease	8 (8)	32 (12)
Not evaluable	8 (8)	3 (1)
Objective response	52 (52)	182 (68)
Unconfirmed Objective response	72 (71)	213 (79)
Clinical benefit rate	85 (84)	196 (83)

IMMUNE MEDIATED ADVERSE EVENTS		
IMAE (N, %)	All	Grade 3-5
Hypothyroidism	10 (10)	-
Pneumonitis	4 (4)	3 (3)
Hyperthyroidism	2 (2)	-
Rash	1 (1)	1 (1)
Hypophysitis	1 (1)	-
Nephritis	1 (1)	-
Neurological disorder	1 (1)	1 (1)
Paraneoplastic neurological syndr.	1 (1)	1 (1)

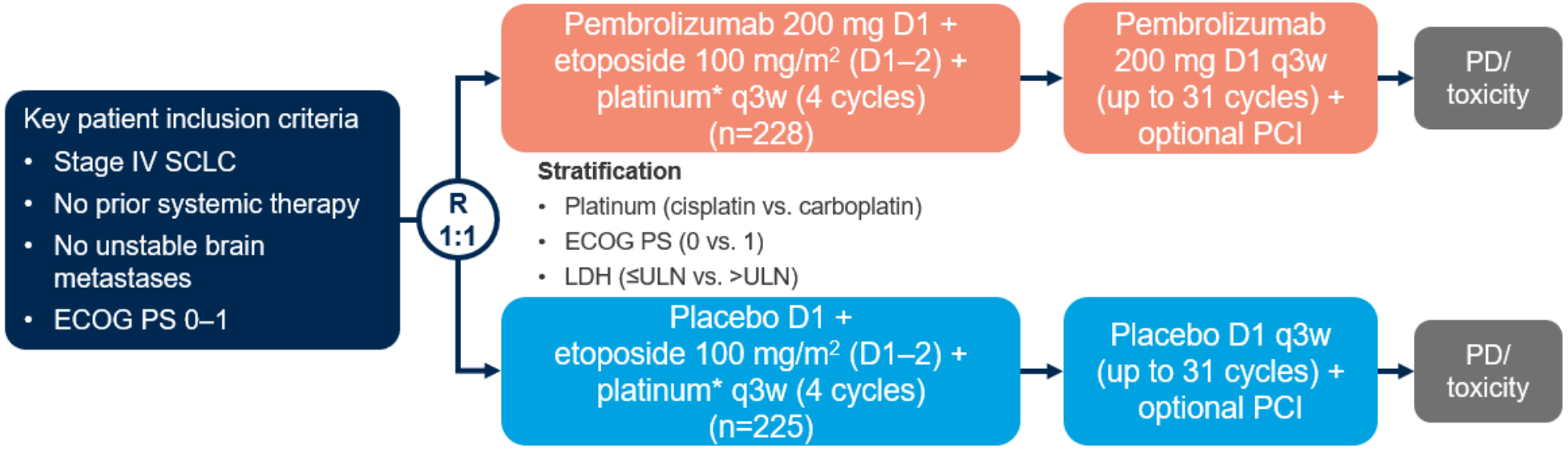
Conclusion: the safety profile and clinical benefit of durvalumab was consistent with CASPIAN.

Organizado por: GECP lung cancer research

D. Isla.Annals of Oncology (2022) 33 (suppl_2): S97-S104

First-Line Pembrolizumab or Placebo Combined With Etoposide and Platinum for ES-SCLC: KEYNOTE-604 Long-Term Follow-Up Results

- **Study objective**
  - To evaluate the long-term efficacy and safety of 1L pembrolizumab + etoposide + platinum in patients with extensive-stage SCLC in the KEYNOTE-604 study



Primary endpoints
- PFS (BICR), OS

Secondary endpoints
- ORR, DoR, safety

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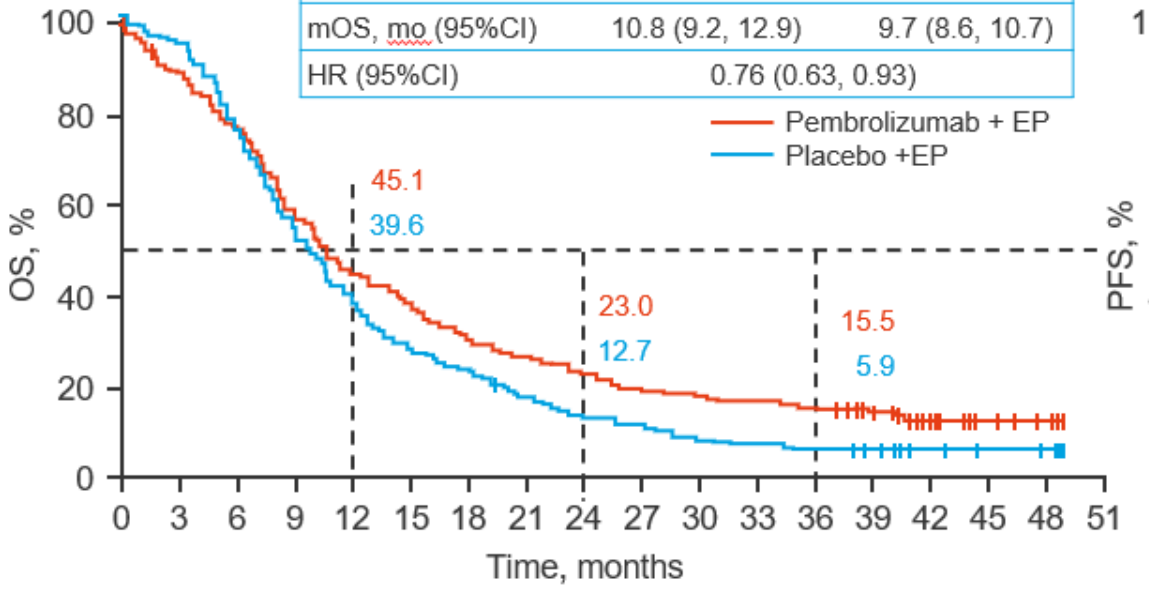
Rudin CM, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.06

First-Line Pembrolizumab or Placebo Combined With Etoposide and Platinum for ES-SCLC: KEYNOTE-604 Long-Term Follow-Up Results

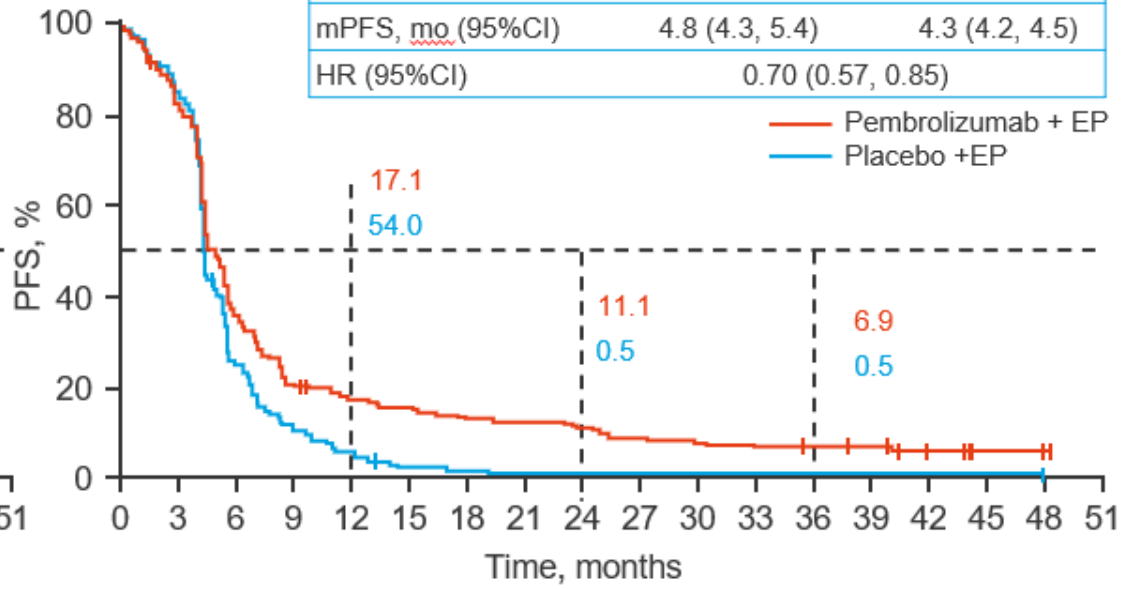
Overall survival

	Pembrolizumab + EP (n=228)	Placebo + EP (n=225)
Events, n (%)	197 (86.4)	211 (93.8)
mOS, mo (95%CI)	10.8 (9.2, 12.9)	9.7 (8.6, 10.7)
HR (95%CI)	0.76 (0.63, 0.93)	



Progression-free survival

	Pembrolizumab + EP (n=228)	Placebo + EP (n=225)
Events, n (%)	210 (92.1)	221 (98.2)
mPFS, mo (95%CI)	4.8 (4.3, 5.4)	4.3 (4.2, 4.5)
HR (95%CI)	0.70 (0.57, 0.85)	



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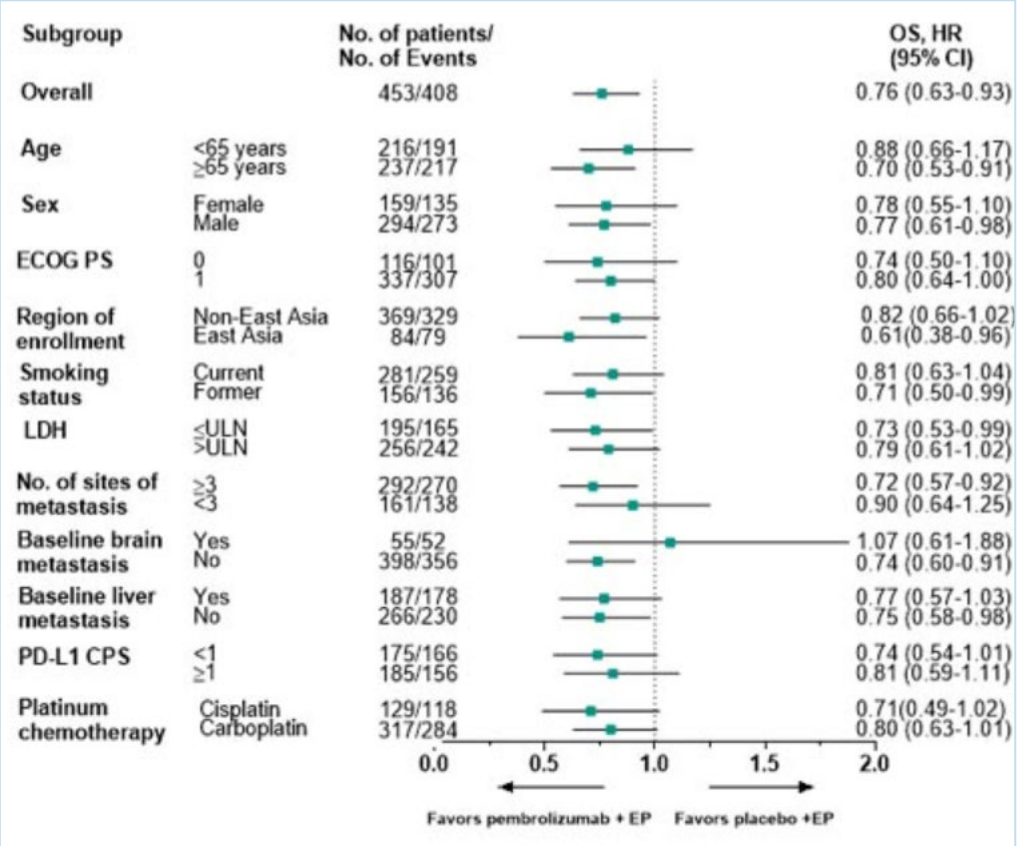
First-Line Pembrolizumab or Placebo Combined With Etoposide and Platinum for ES-SCLC: KEYNOTE-604 Long-Term Follow-Up Results



Responses	Pembrolizumab + EP (n=228)	Placebo + EP (n=225)
ORR, % (95%CI)	70.6 (64.2, 76.4)	61.8 (55.1, 68.2)
BOR, n (%)		
CR	2 (2.2)	2 (0.9)
PR	156 (68.4)	137 (60.9)
SD	40 (17.5)	56 (24.9)
PD	8 (3.5)	12 (5.3)
mDoR, mo (range)	4.2 (1.0+ to 47.2+)	3.7 (1.4+ to 46.8+)
DoR≥12m %	20,7	3,3
DoR≥36m %	11,5	0,8

Conclusions

In patients with extensive-stage SCLC, 1L pembrolizumab + etoposide + platinum continued to demonstrate clinically meaningful improvements in survival with a manageable safety profile

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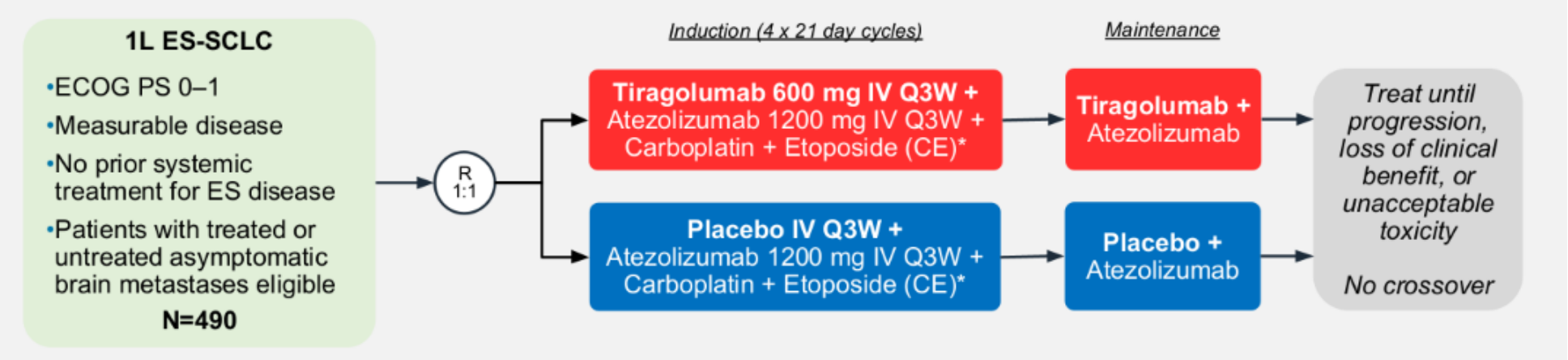
SKYSCRAPER-02: Primary results of a phase III, randomized, double-blind, placebo-controlled study of atezolizumab (atezo) + carboplatin + etoposide (CE) with or without tiragolumab (tira) in patients (pts) with untreated extensive-stage small cell lung cancer (ES-SCLC)

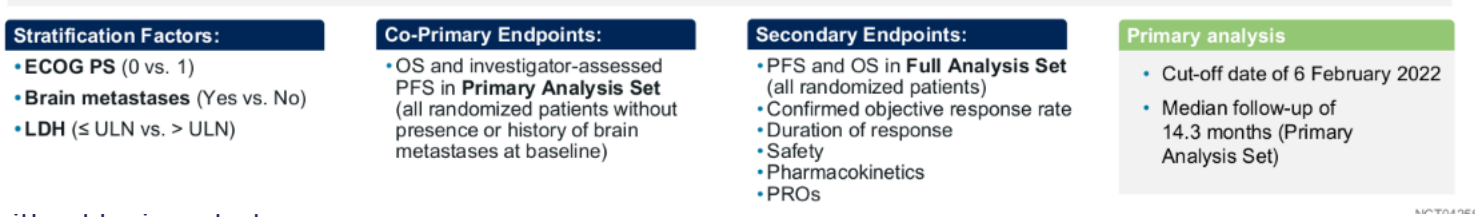


Co-primary endpoints

- OS, PFS (primary analysis set)

Secondary endpoints

- OS, PFS (full analysis set) ORR, DoR, safety



- Primary analysis set included all patients without brain metastases; full analysis set included all enrolled patients

Rudin CM, et al. J Clin Oncol 2022;40(suppl):Abstr LBA8507

SKYSCRAPER-02: Primary results of a phase III, randomized, double-blind, placebo-controlled study of atezolizumab (atezo) + carboplatin + etoposide (CE) with or without tiragolumab (tira) in patients (pts) with untreated extensive-stage small cell lung cancer (ES-SCLC)

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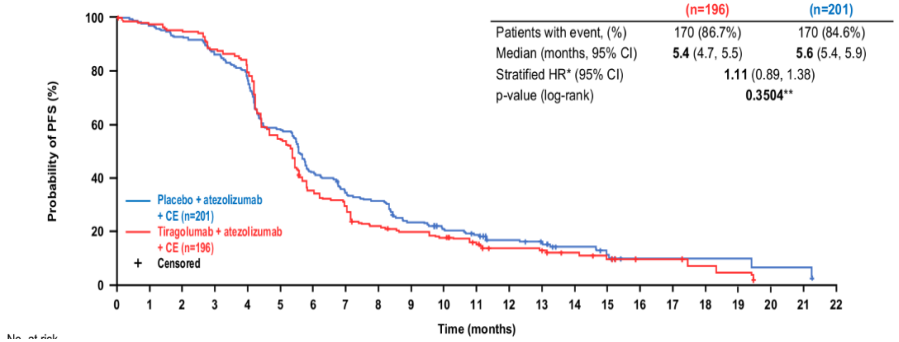
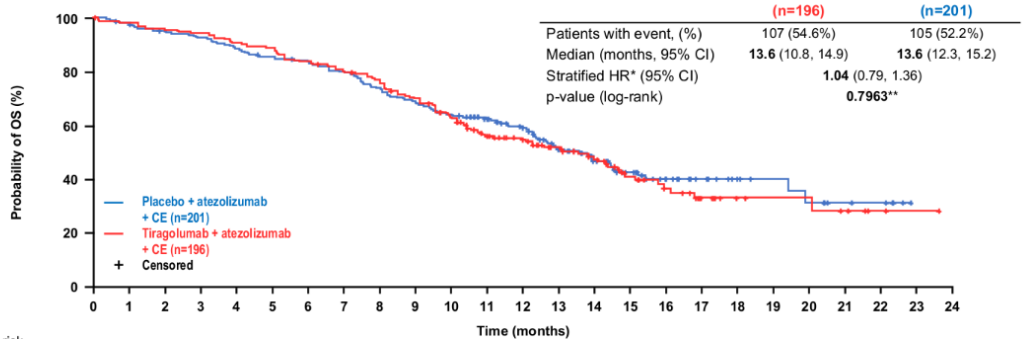
PFS: Primary Analysis Set

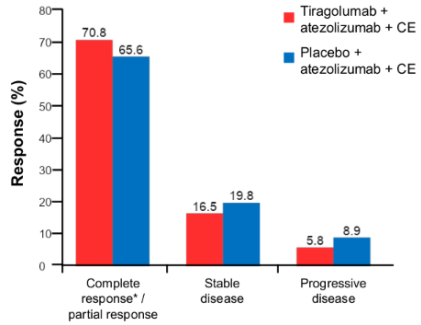


	Tiragolumab + atezolizumab + CE (n=196)	Placebo + atezolizumab + CE (n=201)
Patients with event, (%)	170 (86.7%)	170 (84.6%)
Median (months, 95% CI)	**5.4** (4.7, 5.5)	**5.6** (5.4, 5.9)
Stratified HR* (95% CI)	**1.11** (0.89, 1.38)	
p-value (log-rank)	**0.3504****	

Interim OS: Primary Analysis Set



	Tiragolumab + atezolizumab + CE (n=196)	Placebo + atezolizumab + CE (n=201)
Patients with event, (%)	107 (54.6%)	105 (52.2%)
Median (months, 95% CI)	**13.6** (10.8, 14.9)	**13.6** (12.3, 15.2)
Stratified HR* (95% CI)	**1.04** (0.79, 1.36)	
p-value (log-rank)	**0.7963****	



	Tiragolumab + atezolizumab + CE (n=243)	Placebo + atezolizumab + CE (n=247)
Objective response rate, % (95% CI)	**70.8** (64.6, 76.3)	**65.6** (59.3, 71.4)
Duration of response		
Responders, n	172	162
With subsequent event, n (%)	147 (85.5)	135 (83.3)
Median, months (95% CI)	**4.2** (4.1, 4.4)	**5.1** (4.4, 5.8)

Organizado por: GECP lung cancer research

Rudin CM, et al. J Clin Oncol 2022;40(suppl):Abstr LBA8507

SKYSCRAPER-02: Primary results of a phase III, randomized, double-blind, placebo-controlled study of atezolizumab (atezo) + carboplatin + etoposide (CE) with or without tiragolumab (tira) in patients (pts) with untreated extensive-stage small cell lung cancer (ES-SCLC)

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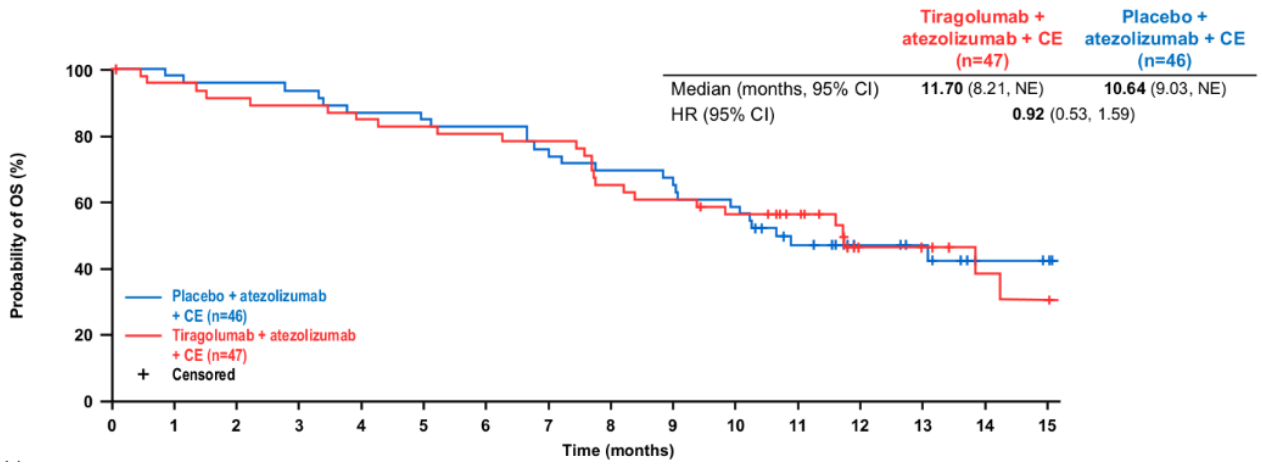
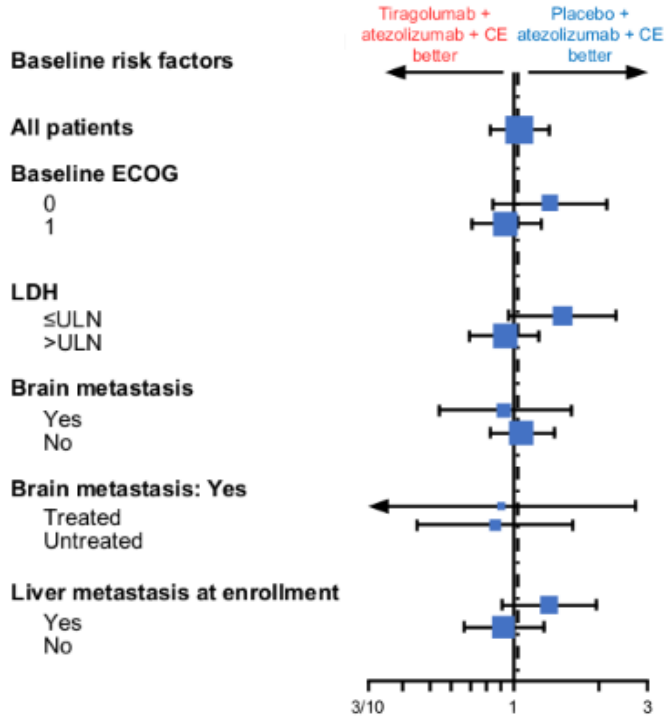
Subgroup OS: patients with brain metastases





Combining tiragolumab with 1L SoC did not demonstrate any additional the survival benefit compared with atezolizumab + CT alone, either in those with or without brain metastases, while atezolizumab +CT showed efficacy in those with untreated brain metastases

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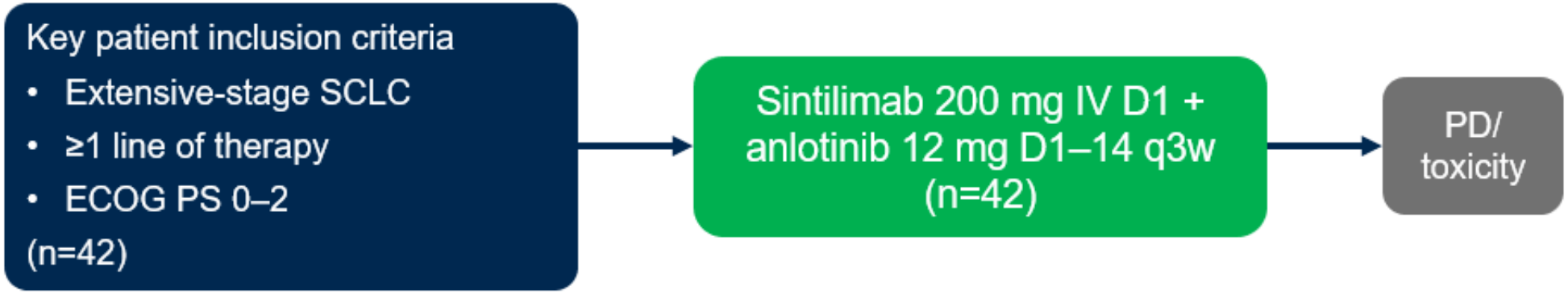
Rudin CM, et al. J Clin Oncol 2022;40(suppl):Abstr LBA8507

Sintilimab plus anlotinib as second or further-line therapy for small cell lung cancer: An objective performance trial



Primary endpoint

- PFS

Secondary endpoints

- ORR, DCR, OS, safety

Ma S, et al. J Clin Oncol 2022;40(suppl):Abstr 8516

Sintilimab plus anlotinib as second or further-line therapy for small cell lung cancer: An objective performance trial

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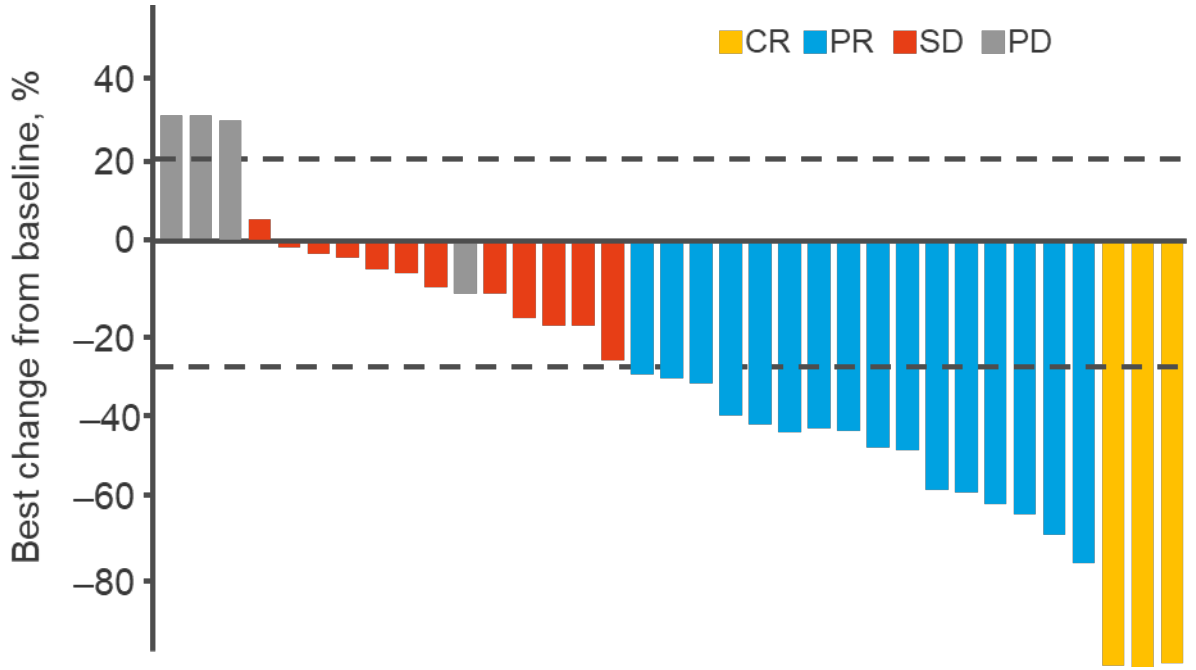
Summary of clinical activity	Sintilimab (n=39)
mPFS, mo (95%CI)	6.0 (4.8, 7.2)
6-mo PFS rate, %	50.5
12-mo PFS rate, %	27.8
mOS, mo (95%CI)	NR
ORR, n (%)	19 (48.7)
DCR, n (%)	31 (79.5)



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Ma S, et al. J Clin Oncol 2022;40(suppl):Abstr 8516

Sintilimab plus anlotinib as second or further-line therapy for small cell lung cancer: An objective performance trial

TRAEs, n (%)	Sintilimab (n=42)
Any	40 (95.2)
Most common (≥10% of patients)	
Hypothyroidism	19 (45.2)
Hypoproteinemia	17 (40.5)
GGT increased	16 (38.1)
Grade 3–4	22 (52.4)
Elevated GGT	5 (11.9)
Elevated bilirubin	3 (7.1)
Elevated ALT	2 (4.8)
Led to discontinuation	3 (11.5)

In patients with extensive-stage SCLC, sintilimab + anlotinib showed encouraging antitumor activity with a manageable safety profile

Ma S, et al. J Clin Oncol 2022;40(suppl):Abstr 8516

Phase 2 Study Analysis of Talazoparib (TALA) Plus Temozolomide (TMZ) for Extensive-Stage Small Cell Lung Cancer (ES-SCLC)

- **Study objective**
  - To evaluate the efficacy and safety of talazoparib + temozolomide in patients with extensive-stage SCLC

Key patient inclusion criteria
- Extensive-stage SCLC
- Relapsed or refractory

(n=28*)

→ Talazoparib 0.75 mg/day + temozolomide 37.5 mg/m^2 D1–5 q4w

Primary endpoint
- ORR

Secondary endpoints
- PFS, OS, DoR, TTR, safety

Response	Talazoparib + temozolomide (n=28)
PR, n (%)	11 (39.3)
mTTR, mo	1.8
mDoR, mo	4.3
mPFS, mo	4.3
mOS, mo	11.9

Goldman J, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.03

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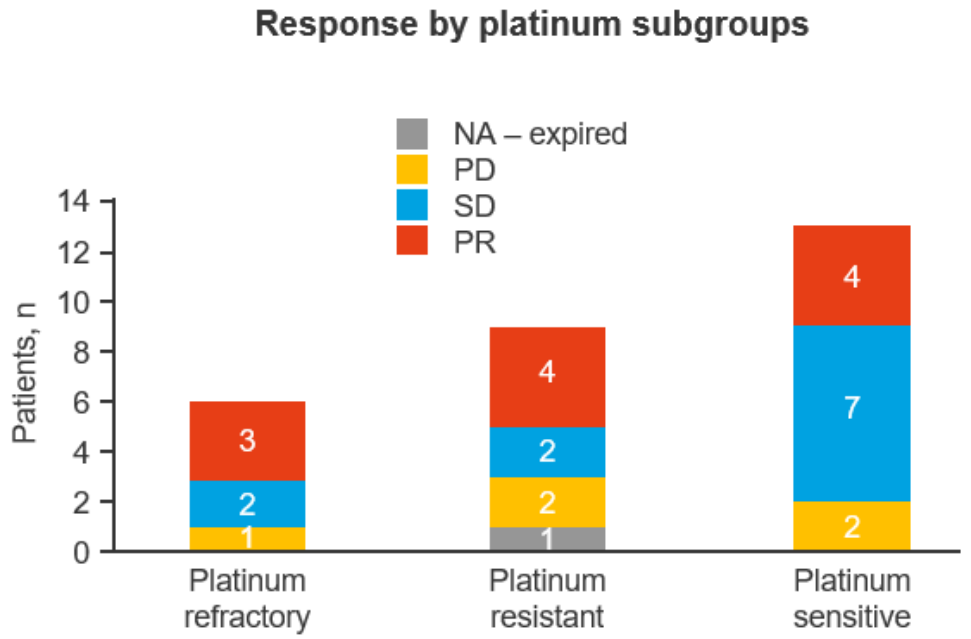
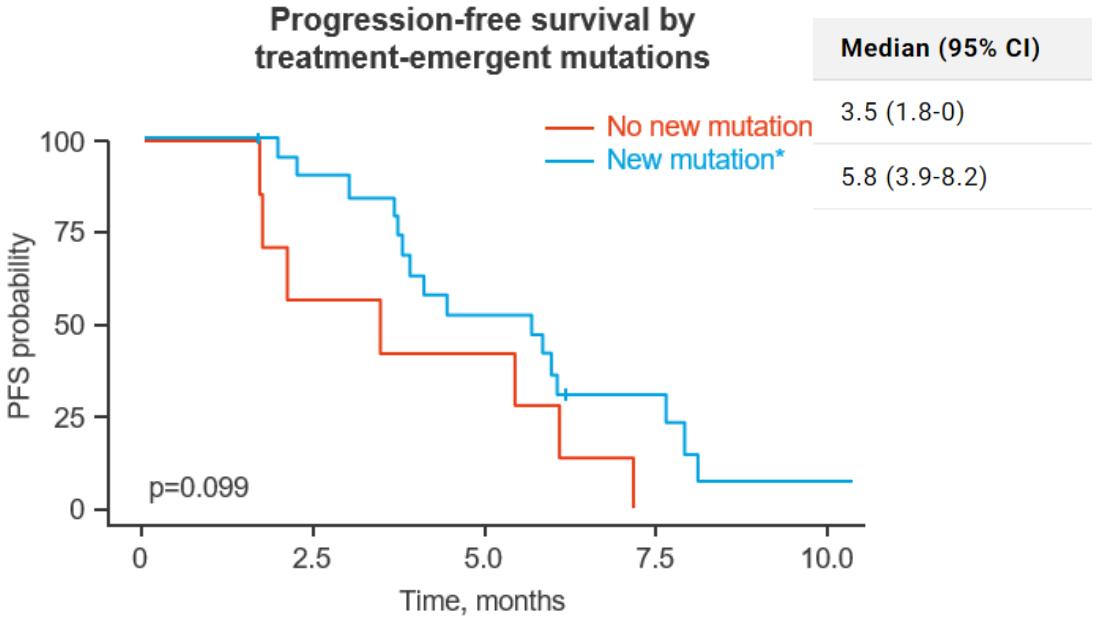
Phase 2 Study Analysis of Talazoparib (TALA) Plus Temozolomide (TMZ) for Extensive-Stage Small Cell Lung Cancer (ES-SCLC)

Response	Talazoparib + temozolomide (n=28)
PR, n (%)	11 (39.3)
mTTR, mo	1.8
mDoR, mo	4.3
mPFS, mo	4.3
mOS, mo	11.9



Goldman J, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.03

Phase 2 Study Analysis of Talazoparib (TALA) Plus Temozolomide (TMZ) for Extensive-Stage Small Cell Lung Cancer (ES-SCLC)



Median (95% CI)
3.5 (1.8-0)
5.8 (3.9-8.2)

Grade 3–4 AEs, %	Talazoparib + temozolomide (n=28)
Platelet count decreased	60.7
Anemia	53.6
Neutrophil count decreased	32.1
WBC count decreased	17.9
Atypical pneumonia	3.6

Conclusions

In patients with extensive-stage SCLC, talazoparib + temozolomide demonstrated promising clinical activity with a manageable safety profile

Goldman J, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.03

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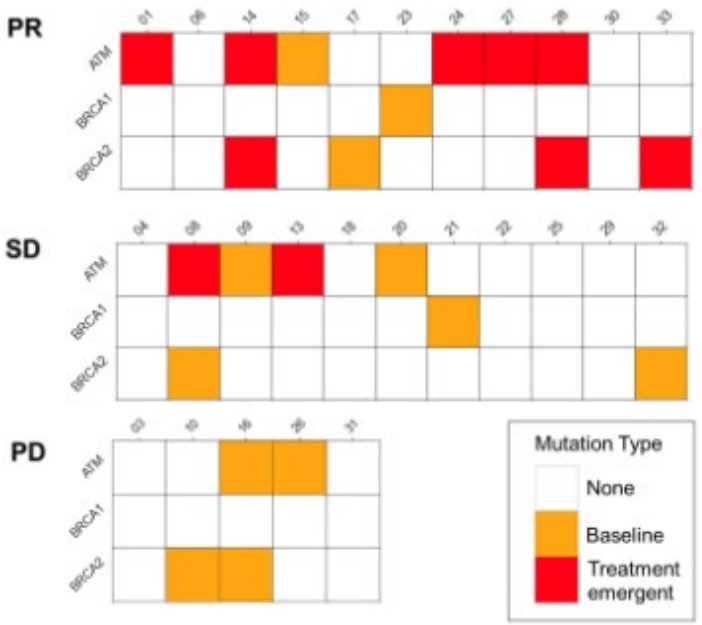
Circulating tumor DNA (ctDNA) mutations associate with response in patients with extensive-stage small cell lung cancer (ES-SCLC) treated with talazoparib and temozolomide (TMZ)

Maria A Velez[1], Amy Lauren Cummings[1], Matthew C Mulroy[2], Edward B. Garon[1], Dennis J. Slamon[1], Jonathan W. Goldman[1]

David Geffen School of Medicine at UCLA, Los Angeles, , CA; UCLA Medical Center, Los Angeles, CA

Figure 1. DDR mutation characterization by best response



ctDNA was collected and assessed based on allele frequency and plasma copy number at baseline and every 8 weeks during treatment with the Guardant360 assay

DDR status was defined as a mutation known or likely to result in aberrant expression of *ATM* or *BRCA1/2*

Conclusions: Mutations in DDR genes occur on treatment with TALA and TMZ and may associate with disease control. Validation is needed

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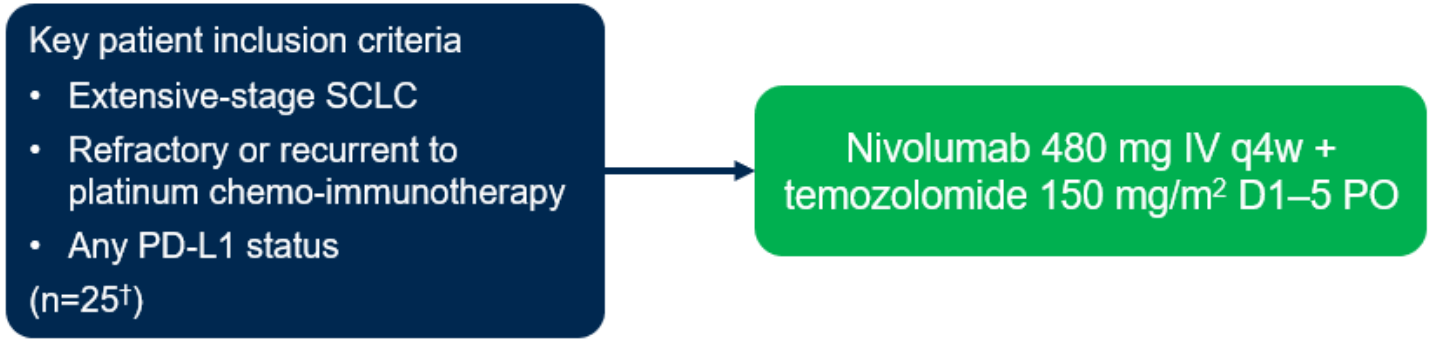
Efficacy of Nivolumab and Temozolomide in Extensive Stage Small Cell Lung Cancer after Chemo-Immunotherapy: A Phase 2 Trial

- **Study objective**
  - To evaluate the efficacy and safety of nivolumab + temozolomide in a cohort of patients with extensive-stage SCLC*



Primary endpoint

- ORR (RECIST v1.1)

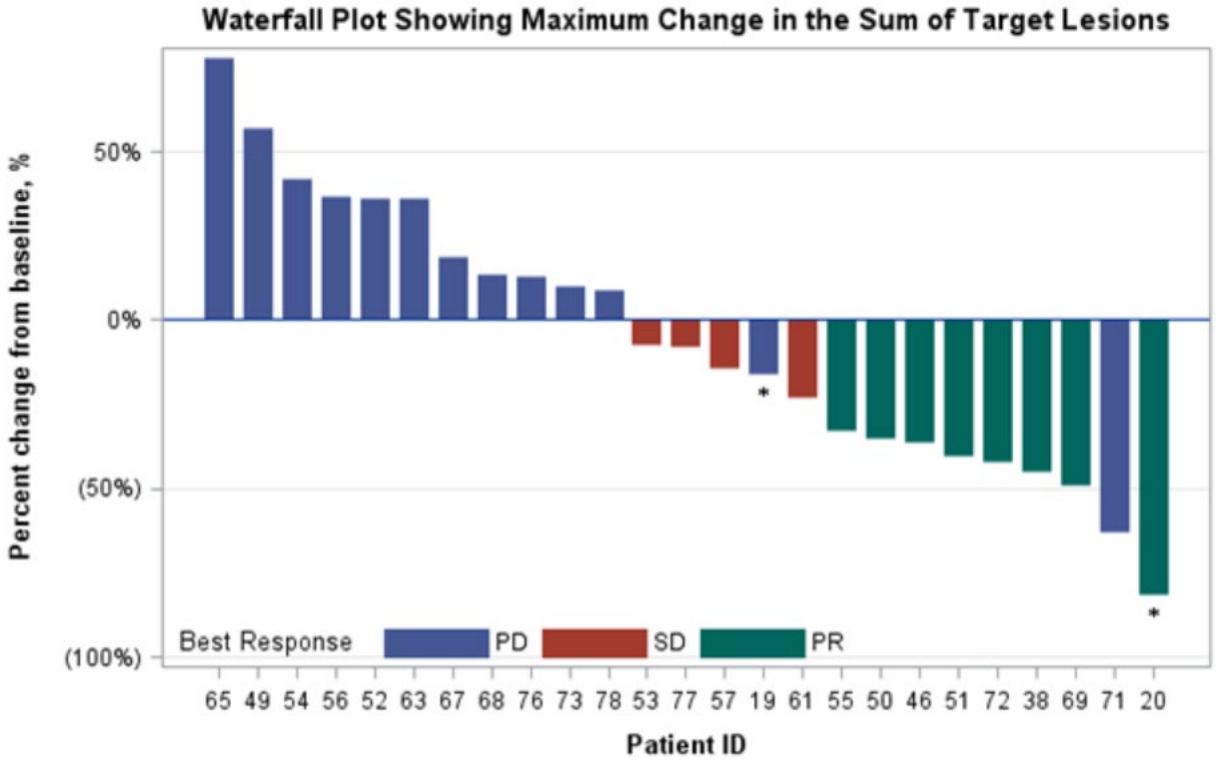
Secondary endpoints

- PFS, OS, safety

*A second cohort of patients with metastatic neuroendocrine carcinoma was also assessed;
†15 patients were initially enrolled and a total of 25 patients enrolled if ≥2 responses were observed

Owen DH, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.04

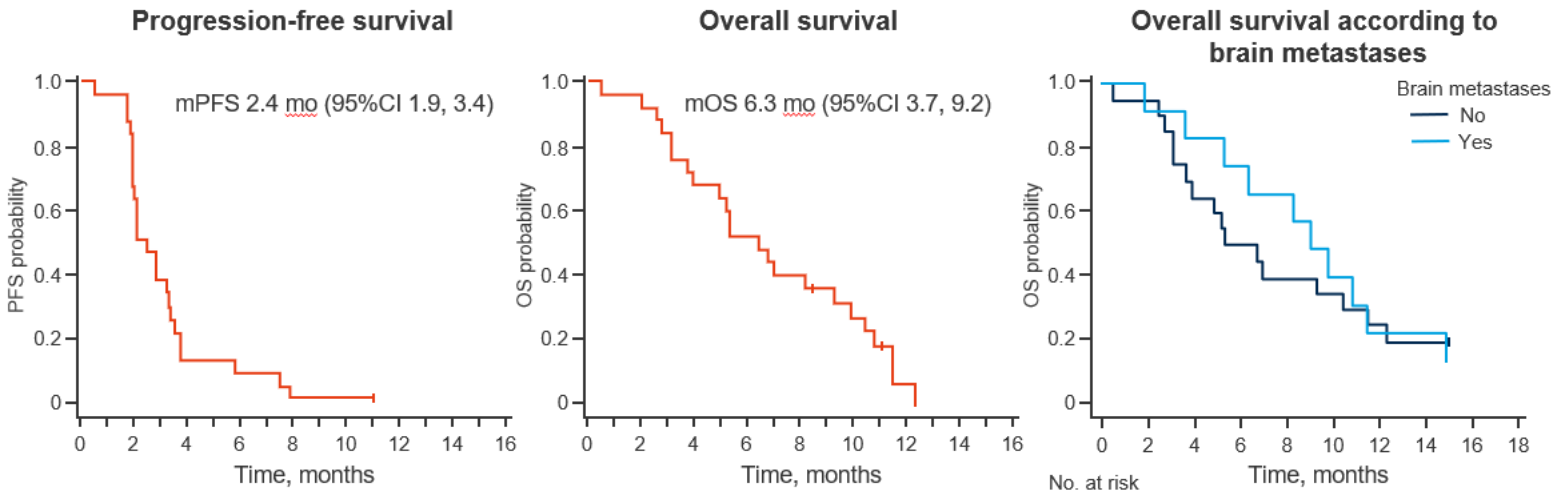
Efficacy of Nivolumab and Temozolomide in Extensive Stage Small Cell Lung Cancer after Chemo-Immunotherapy: A Phase 2 Trial



Response	All patients (n=25)	Platinum resistant		Brain metastases	
		Yes (n=10)	No (n=15)	Yes (n=10)	No (n=15)
ORR, n (%) [95%CI)	7 (28) [12, 49]	0 [0, 31]	7 (47) [21, 73]	2 (20) [3, 56]	5 (33) [12, 62]
p-value		0.057		0.659	

Owen DH, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.04

Efficacy of Nivolumab and Temozolomide in Extensive Stage Small Cell Lung Cancer after Chemo-Immunotherapy: A Phase 2 Trial



Grade ≥3 TRAEs, n (%)	Nivolumab + temozolomide (n=28)
Any	19 (70)
Lymphocyte count decreased	10 (37)
Fatigue	5 (19)
Platelet count decreased	3 (11)
Anemia	2 (7)
Vomiting	2 (7)
Generalized muscle weakness	2 (7)
Nausea	1 (4)
Diarrhea	1 (4)
Anorexia	1 (4)
Constipation	1 (4)

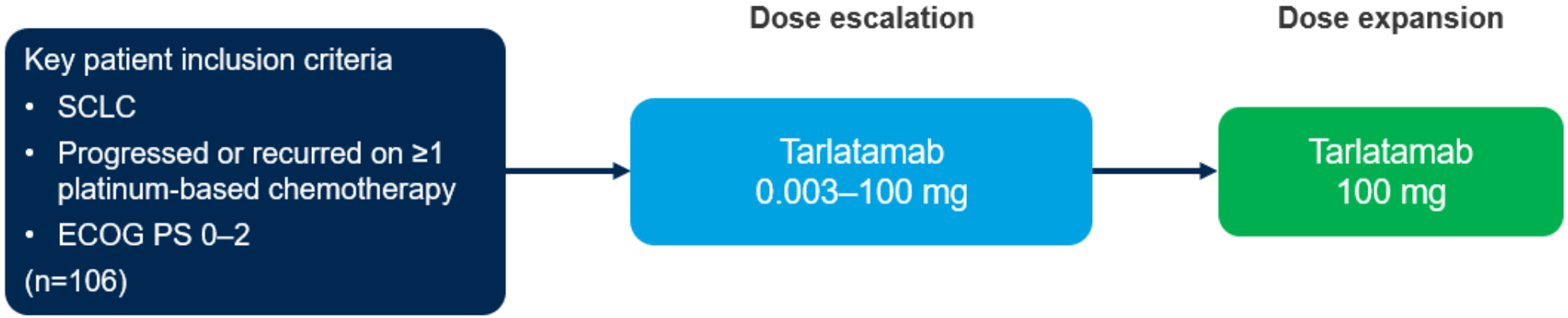
Conclusions

In patients with extensive-stage SCLC, nivolumab + temozolomide demonstrated clinical activity particularly in those with platinum-sensitive disease

Owen DH, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.04

Phase 1 Updated Exploration and First Expansion Data for DLL3-targeted T-cell Engager Tarlatamab in Small Cell Lung Cancer

- **Study objective**
  - To evaluate the efficacy and safety of tarlatamab, a DLL3-targeted T-cell engager, in patients with SCLC in the DeLLphi-300 study



Primary endpoint

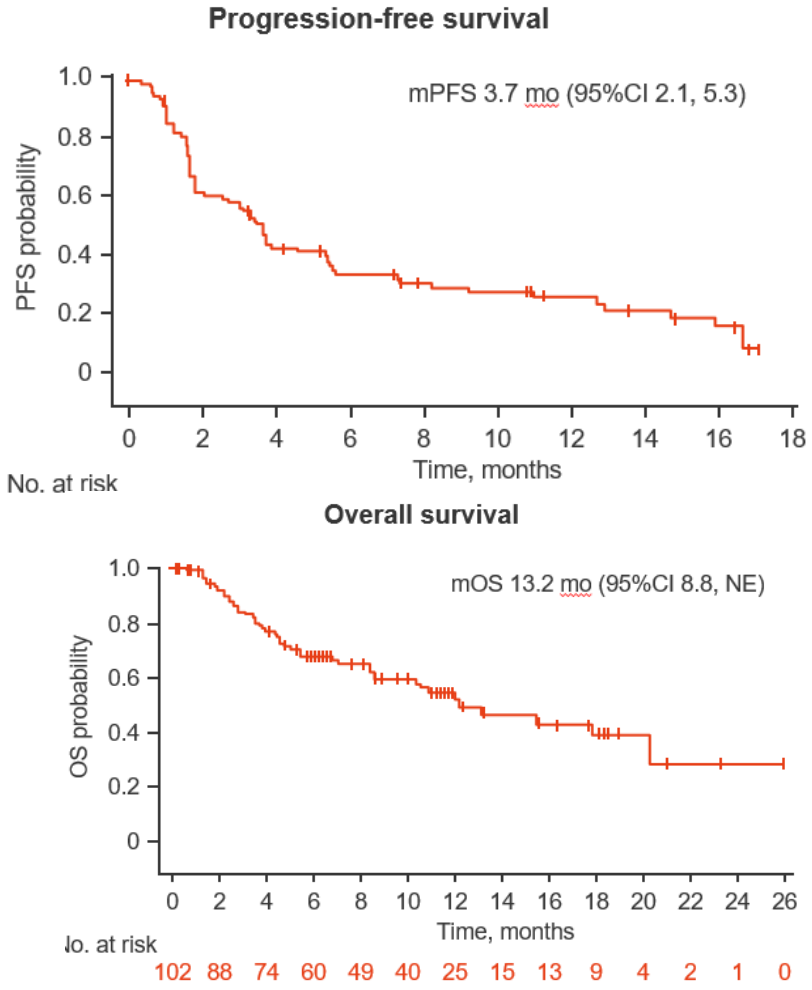
- Safety

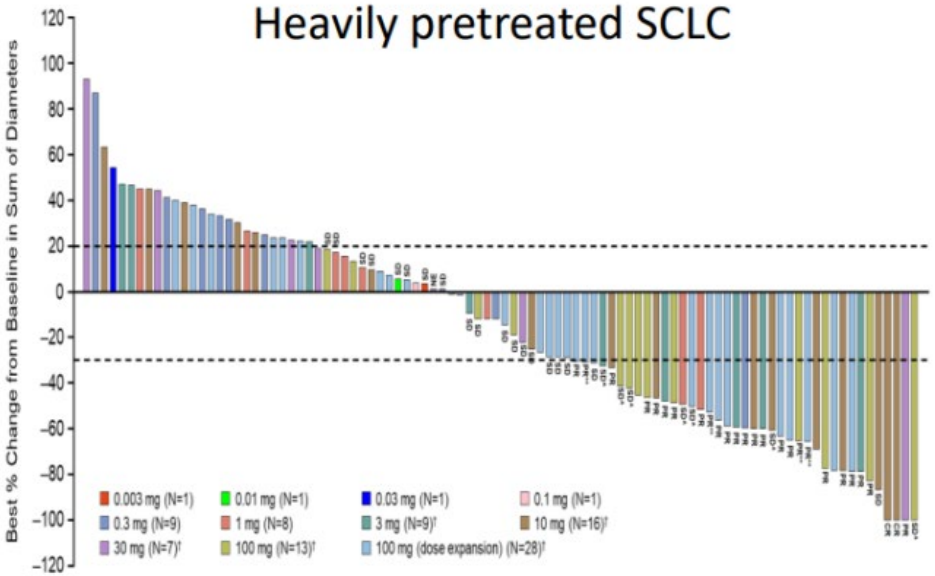
Secondary endpoints

- PK, antitumor activity

Owen DH, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.04

Phase 1 Updated Exploration and First Expansion Data for DLL3-targeted T-cell Engager Tarlatamab in Small Cell Lung Cancer





Median DoR 13 months (95% CI: 6.2, 14.9)*

Median time to response 1.8 months (range: 1.2, 7.4)

Owen DH, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.04

Phase 1 Updated Exploration and First Expansion Data for DLL3-targeted T-cell Engager Tarlatamab in Small Cell Lung Cancer

Confirmed responses, n (%)	Tarlatamab (n=105)
ORR	24 (23)
BOR	
CR	2 (2)
PR	22 (21)
SD	31 (3)
PD	8 (8)
NE	35 (33)
NA	7 (7)
DCR	55 (52)

Grade ≥3 TRAEs, n (%)	Tarlatamab (n=106)
Any	33 (31)
Led to discontinuation	4 (4)
Cytokine release syndrome	1 (1)
Pyrexia	2 (2)
Fatigue	3 (3)
AESI	
Neurologic events	7 (7)
Neutropenia	10 (9)

Conclusions

In previously treated patients with SCLC, tarlatamab demonstrated encouraging antitumor activity with a manageable safety profile

Owen DH, et al. J Thorac Oncol 2022;17(suppl):Abstr OA12.04

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OTROS TUMORES TORÁCICOS

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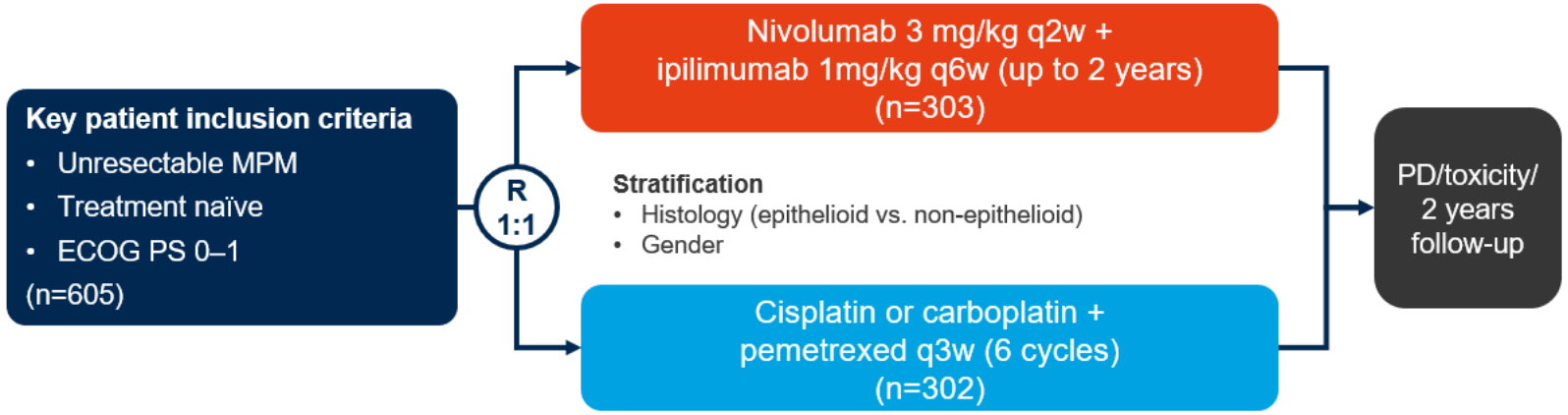
First–line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (uMPM): 4-year update from CheckMate 743

Study objective

To evaluate the long-term efficacy and safety of nivolumab + ipilimumab in patients with unresectable malignant pleural mesothelioma in the CheckMate 743 study



Primary endpoint

- OS

Secondary endpoints

- ORR, DCR, PFS (BICR), biomarker analysis, safety

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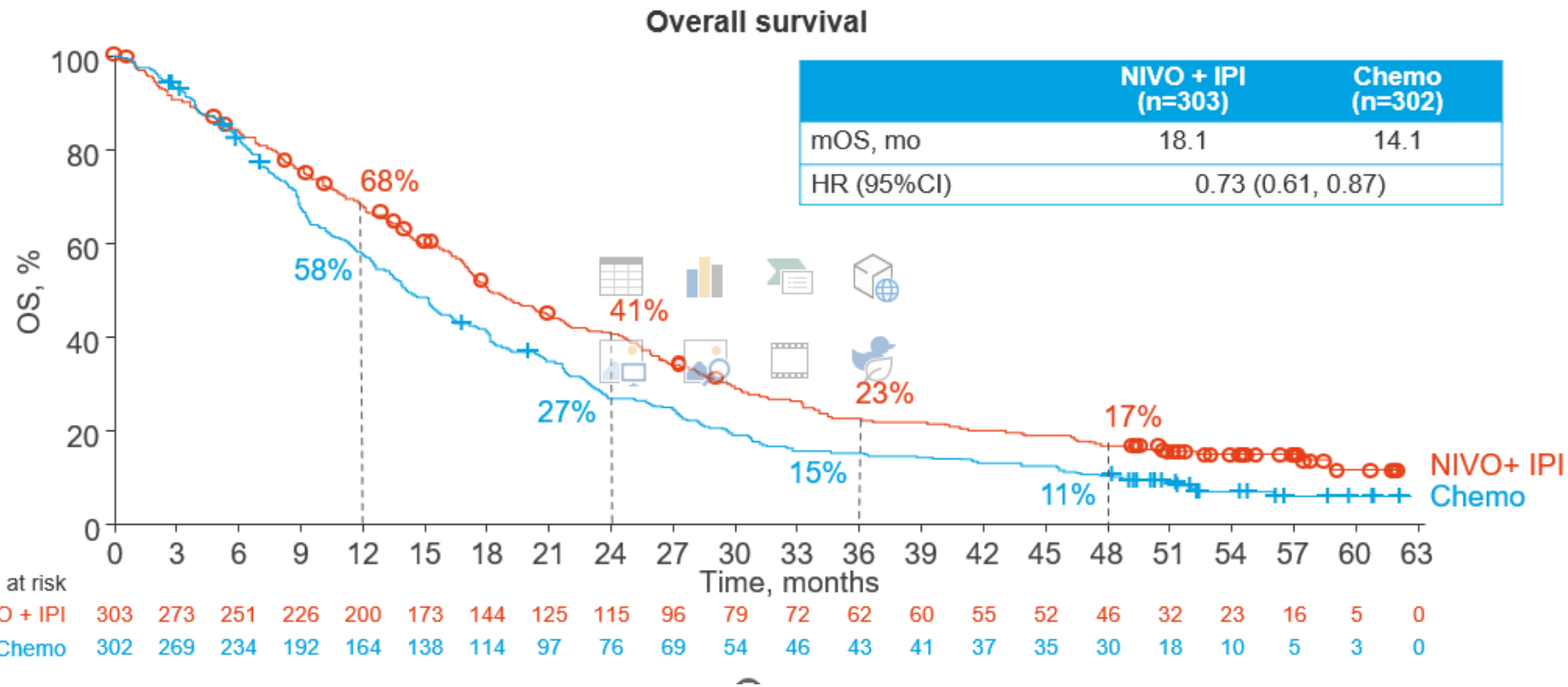
Zalcman G, et al. Ann Oncol 2022;33(suppl):Abstr LBA71

First–line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (uMPM): 4-year update from CheckMate 743

Key results



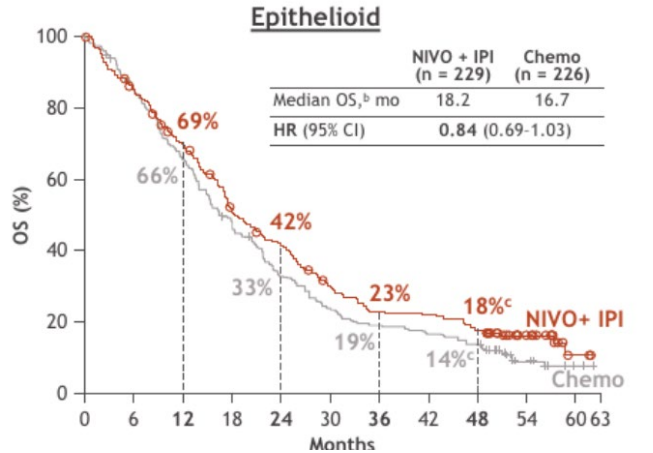
	NIVO + IPI (n=303)	Chemo (n=302)
mOS, mo	18.1	14.1
HR (95%CI)	0.73 (0.61, 0.87)	

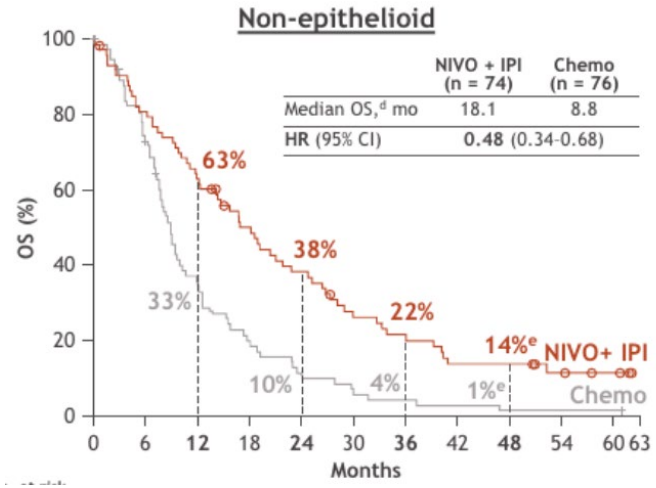
Zalcman G, et al. Ann Oncol 2022;33(suppl):Abstr LBA71

Organizado por:

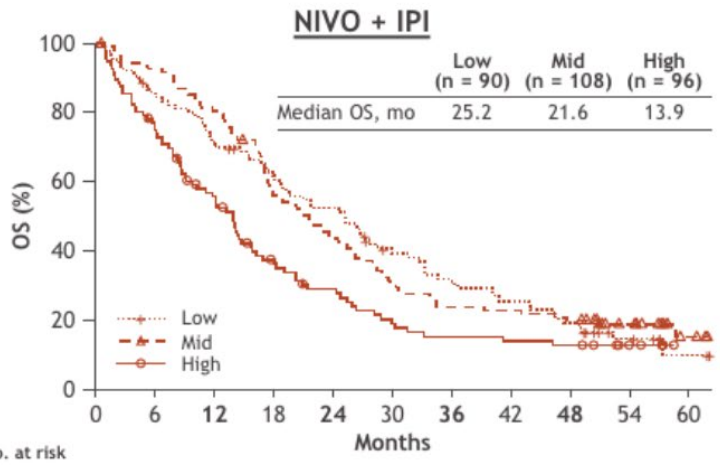
First–line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (uMPM): 4-year update from CheckMate 743

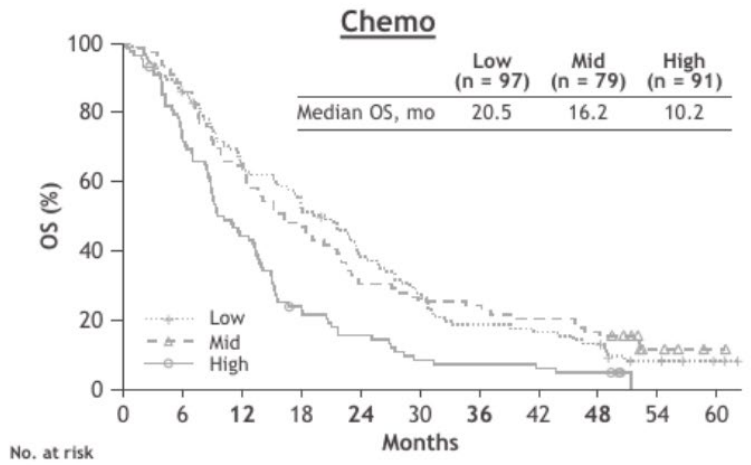
OS by histology





OS by mesothelin levels





Mut en: TP53, BAP1, SETD2, NF2, LATS2 → No OS dif

PARIS 2022 ESMO congress

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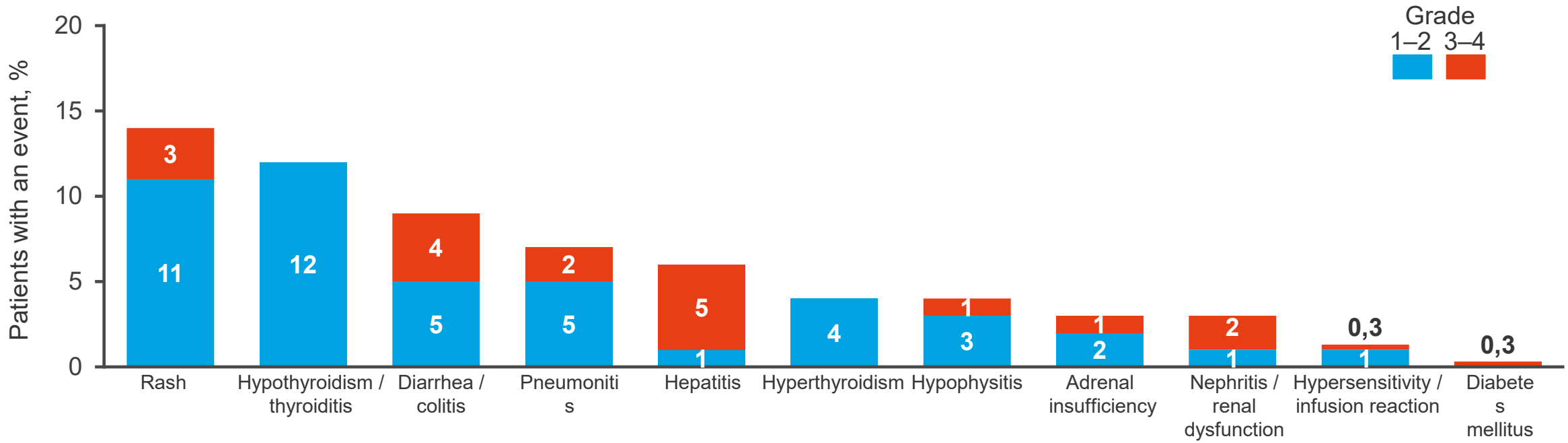
Zalcman G, et al. Ann Oncol 2022;33(suppl):Abstr LBA71

First–line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (uMPM): 4-year update from CheckMate 743



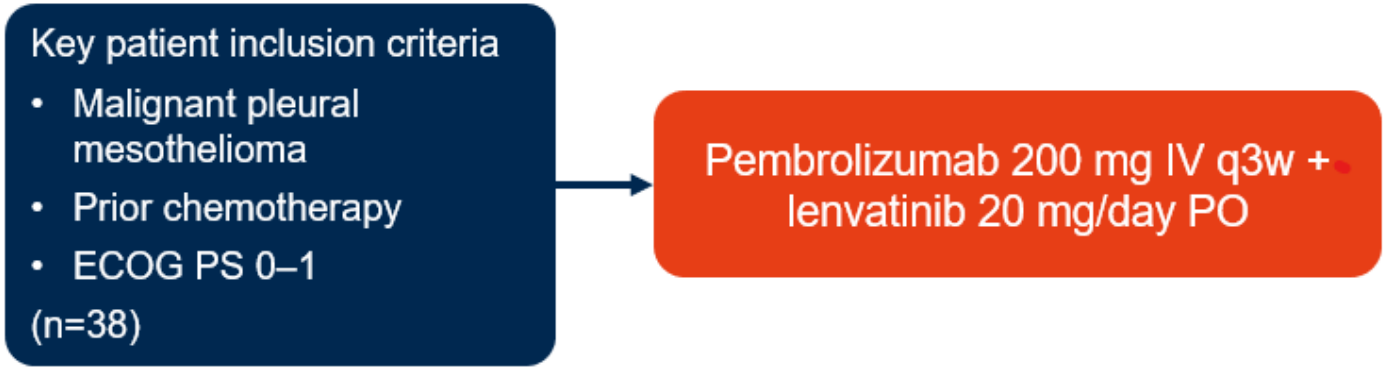
- **Conclusions**
  - In patients with unresectable malignant pleural mesothelioma, nivolumab + ipilimumab continued to provide long-term, durable benefit vs. chemotherapy and there were no new safety signals observed

Zalcman G, et al. Ann Oncol 2022;33(suppl):Abstr LBA71

PEMbrolizumab Plus Lenvatinib In Second And Third Line Malignant Pleural MEsotheLiomA Patients: A Single Arm Phase II Study (PEMMELA)

Study objective

– To evaluate the efficacy and safety of 2L and 3L pembrolizumab + lenvatinib in patients with recurrent malignant pleural mesothelioma



Primary endpoint

- ORR (mRECIST)

Secondary endpoints

- PFS, OS, safety

Douma L-A, et al. J Thorac Oncol 2022;17(suppl):Abstr OA04.06

PEMbrolizumab Plus Lenvatinib In Second And Third Line Malignant Pleural MEsotheLiomA Patients: A Single Arm Phase II Study (PEMMELA)

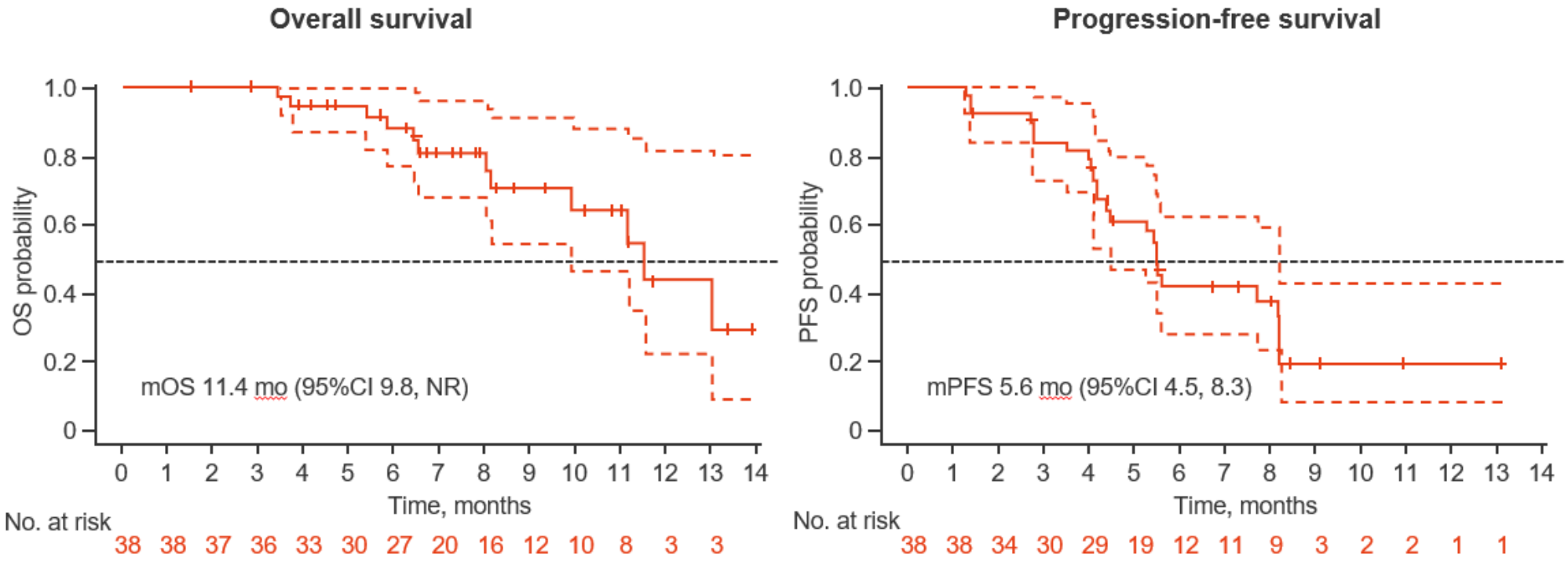
ORR	Local investigator	Independent central reviewer (2nd endpoint)
	PEM+LEN (N=38)	PEM+LEN (N=38)
Objective response (95% CI) -%	58 (41-74)	42 (26-59)
Best overall response – n(%)		
CR	0	0
PR	22 (58)	16 (42)
SD	16 (42)	22 (58)
PD	0	0
Objective response (only confirmed) (95% CI) -%	40 (24-57)	37 (22-54)

At evaluation, 13 patients still on treatment

	All patients (n=38)
Sex (male), n(%)	33 (86.8)
Median age (range), years	70.5 (36-83)
ECOG PS 0, n(%)	19 (50)
Histology, n(%)	
Epithelioid	34 (89.5)
Non-epithelioid	2 (5.3)
Mixed	2 (5.3)
PD-L1 status, n(%)	
Positive (≥1%)	18 (47.4)
Negative (<1%)	17 (44.7)
Not available	3 (7.9)

Douma L-A, et al. J Thorac Oncol 2022;17(suppl):Abstr OA04.06

PEMbrolizumab Plus Lenvatinib In Second And Third Line Malignant Pleural MEsotheLiomA Patients: A Single Arm Phase II Study (PEMMELA)



Douma L-A, et al. J Thorac Oncol 2022;17(suppl):Abstr OA04.06

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PEMbrolizumab Plus Lenvatinib In Second And Third Line Malignant Pleural MEsotheLiomA Patients: A Single Arm Phase II Study (PEMMELA)

	Pembrolizumab + lenvatinib (n=38)		
TRAEs	**Grade 1–2**	**Grade 3**	**Grade 4**
Fatigue	21	0	0
Hoarseness	21	0	0
Anorexia	13	3	0
Diarrhea	13	2	0
Hypertension	5	8	0
ALT/AST increased	5	2	0
Stroke	0	2	0
Myositis	0	0	2

SAE's: 13 in 10 patients

Lenvatinib: 29 out of 38 patients (76%) required ≥ 1 dose reduction/ permanent discontinuation

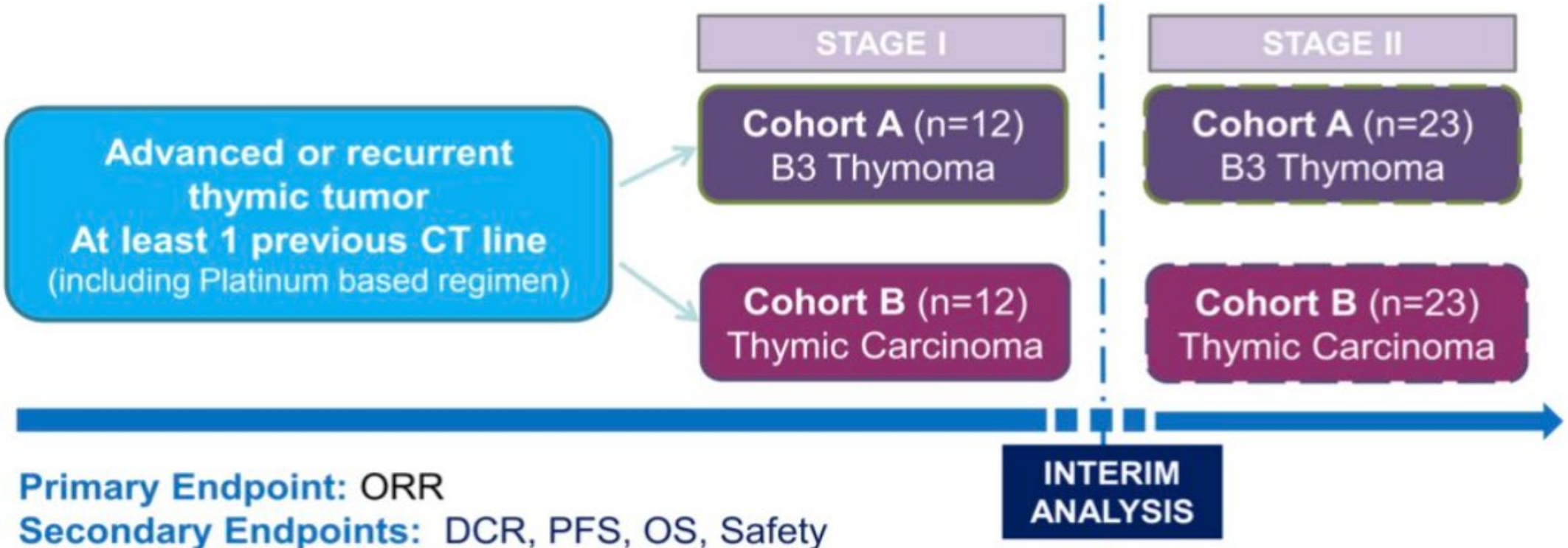
Pembrolizumab: 3 out of 38 (8%) patients permanent discontinuation.

Conclusions

In patients with recurrent malignant pleural mesothelioma, pembrolizumab + lenvatinib demonstrated encouraging clinical activity with a high ORR and had a manageable safety profile

Douma L-A, et al. J Thorac Oncol 2022;17(suppl):Abstr OA04.06

Phase II Trial of Sunitinib in Patients with Type B3 Thymoma or Thymic Carcinoma in Second and Further Lines - STYLE Trial (NCT03449173)



Primary Endpoint: ORR
Secondary Endpoints: DCR, PFS, OS, Safety
Treatment: **Sunitinib 50 mg once daily for 4 consecutive weeks followed by a 2-week rest period (schedule 4/2)**

Proto C, et al. J Thorac Oncol 2022;17(suppl):Abstr MA10.07

Phase II Trial of Sunitinib in Patients with Type B3 Thymoma or Thymic Carcinoma in Second and Further Lines - STYLE Trial (NCT03449173)

Responses	B3 thymoma (n=12) Interim analysis	Thymic carcinoma (n=23) Efficacy analysis	Thymic carcinoma (n=31) ITT analysis
ORR, n (%) [95%CI]	0 [0, 26.5]	5 (21.7) [7.5, 43.7]	6 (21.4) [8.3, 41.0]
BOR, n (%)			
CR	0	1 (4.3)	1 (3.6)
PR	0	4 (17.4)	5 (17.9)
SD	11 (91.7)	15 (65.2)	19 (67.9)
PD	1 (8.3)	3 (13.0)	3 (10.7)
NE	0	0	3 (9.7)
DCR, n (%) [95%CI]	11 (91.7) [61.5, 99.8]	20 (87.0) [66.4, 97.2]	25 (89.3) [71.8, 97.7]

In previously treated patients with thymic carcinoma, sunitinib demonstrated clinical activity (ORR 21%; DCR:89%). Accrual in the B3 thymoma cohort was stopped owing to futility

Proto C, et al. J Thorac Oncol 2022;17(suppl):Abstr MA10.07

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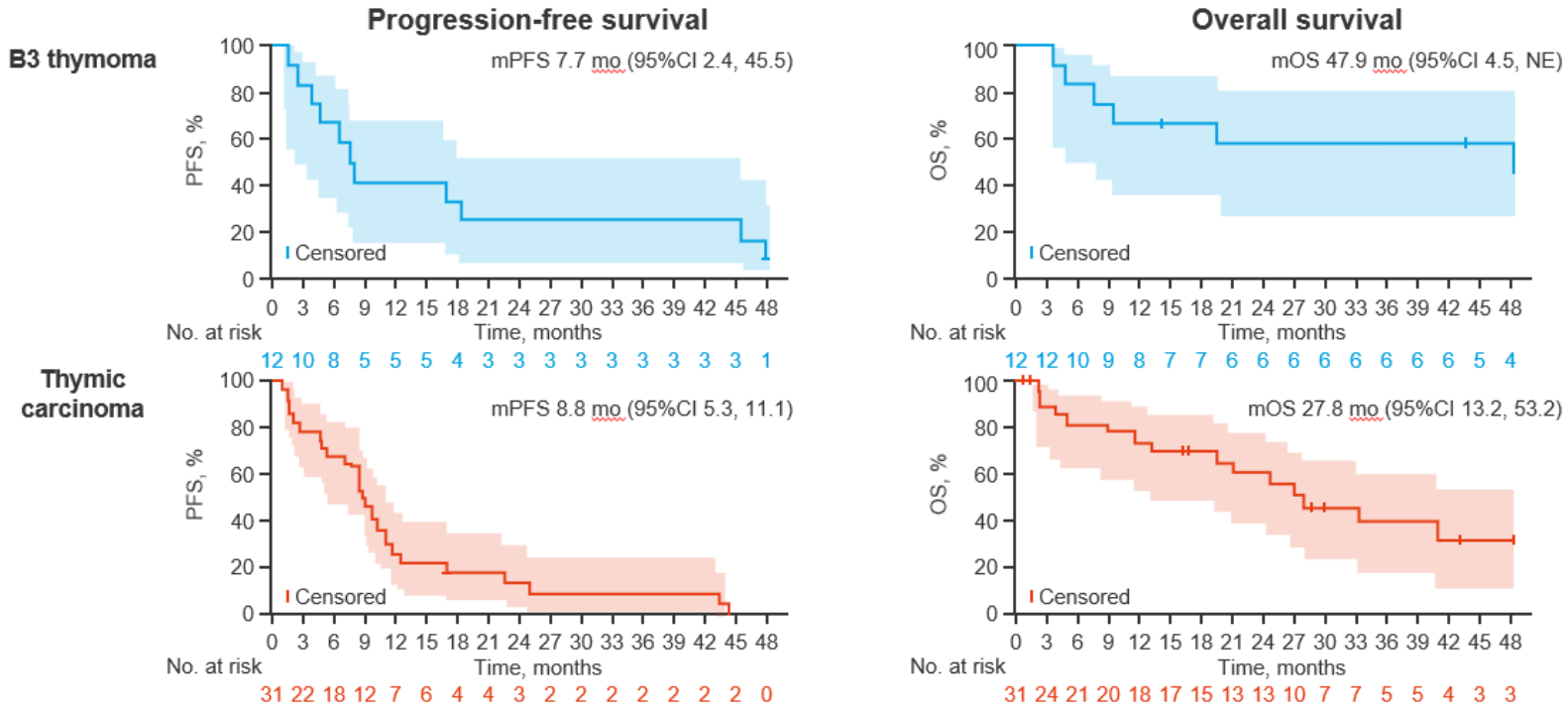


In previously treated patients with thymic carcinoma, sunitinib demonstrated clinical activity but accrual in the B3 thymoma cohort was stopped owing to futility

Proto C, et al. J Thorac Oncol 2022;17(suppl):Abstr MA10.07

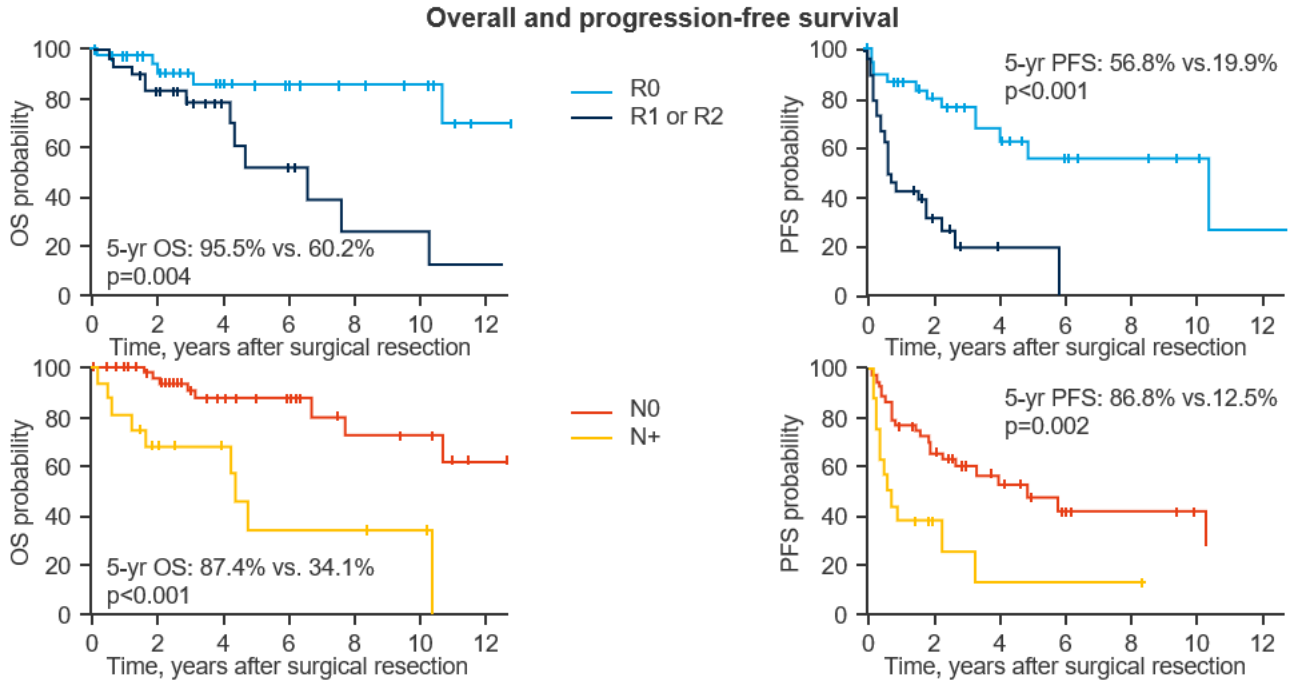
Outcomes of Induction Therapy Followed by Surgical Resection for Advanced Thymic Tumor

- Retrospective analisis of 70 pt treated with induction CT followed by thymectomy for clinical stage III/IV TET: Clinicopathologic, surgical and oncologic outcomes are evaluated

Response, n (%)	Induction therapy
PR	44 (60)
SD	16 (23)
PD	5 (7)
Unknown	1 (1)

Surgical approaches, n (%)	
Sternotomy	57 (81)
Thoracotomy	7 (10)
VATS	4 (6)
Sternotomy + thoracotomy	2 (3)

Surgical outcomes, n (%)	
R0 resection	39 (56)



Conclusiones

- ✓ Los distintos patrones moleculares de SCLC pueden tener valor pronóstico e indicar susceptibilidad a tratamientos como la IT (subtipo inflamado)
- ✓ SCLC EL: no cambios en tto estándar. Ptes resultados de IT, antiangiogénicos
- ✓ SCLC EE:
  - ✓ se consolida la combinación de QT+IT (anti-PD-1//antiPDL-1) como tratamiento primera línea
  - ✓ Adicción de fármacos antiTIGIT no mejora los resultados de esta combinación (Skyscraper)
  - ✓ Segundas o sucesivas líneas: actividad prometedora de combinación de IT y antiangiogénicos, IPARP y temozolamida o IT y temozolamida
- ✓ Mesotelioma
  - ✓ Eficacia de la combinación IPI+Nivo en primera línea mantenida a largo plazo
  - ✓ Actividad prometedora de la combinación pembro/lenva en 2ª línea
- ✓ Timoma
  - ✓ Actividad prometedora de Sunitinib en carcinoma tímico
  - ✓ Valor pronóstico de la resección R0 y la afectación ganglionar tras tto neoadyuvante y cx

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