Lung Cancer UPDATES
ESMO HIGHLIGHTS
17 - 21 OCTUBRE 2025
Berlin, Germany

GECP lung cancer research

CPNCP avanzado sin mutaciones driver

Mariola Blanco Clemente

Hospital Universitario Puerta de Hierro Majadahonda

INDICE

PAPEL DE LOS ANTIANGIOGÉNICOS EN LA QUIMIO-INMUNOTERAPIA

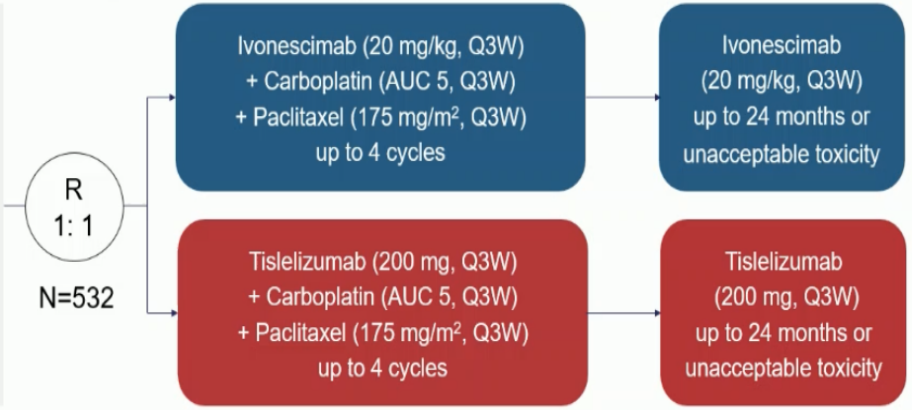
Phase III study of Ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous NSCLC (HARMONi-6)

Study Design

A multicenter, randomized, double-blind, parallel-controlled phase III study

Key Eligibility Criteria

- Pathologically confirmed sq-NSCLC
- Stage IIIB-IV
- No prior systemic therapy
- No EGFR mutations or ALK rearrangements
- ECOG PS 0 or 1



Stratification Factors:
- Stage: IIIB/IIIC vs. IV
- PD-L1 TPS: ≥1% vs. <1%

Endpoints:
- **Primary endpoint: PFS by IRRC per RECIST v1.1**
- Key secondary endpoint: OS
- Secondary endpoints: PFS by INV, ORR, DCR, DoR, TTR and safety

Data cutoff date: February 28, 2025

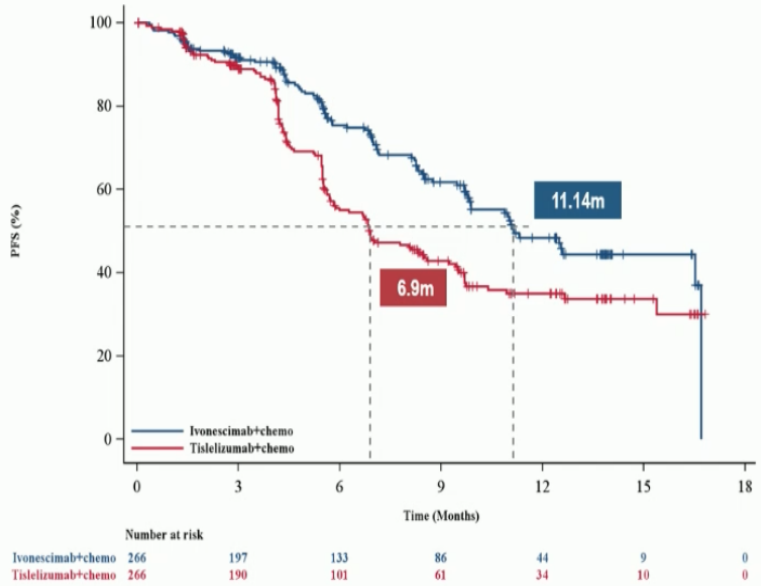
Baseline Characteristics

Characteristics, n(%)		Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
Age, years	< 65	135 (50.8)	139 (52.3)
	≥ 65	131 (49.2)	127 (47.7)
Sex	Male	256 (96.2)	238 (89.5)
	Female	10 (3.8)	28 (10.5)
ECOG PS*	0	42 (15.8)	42 (15.8)
	1	224 (84.2)	222 (83.5)
Smoking history	Never	21 (7.9)	37 (13.9)
	Current/Former	245 (92.1)	229 (86.1)
Disease stage	IIIB/IIIC	21 (7.9)	20 (7.5)
	IV	245 (92.1)	246 (92.5)
Tumor characteristics	Central type	178 (66.9)	158 (59.4)
	Major blood vessel encasement	49 (18.4)	44 (16.5)
	With cavity	24 (9.0)	23 (8.6)
	With hemoptysis history	86 (32.3)	79 (29.7)
PD-L1 TPS	<1%	105 (39.5)	105 (39.5)
	≥ 1%	161 (60.5)	161 (60.5)
	1-49%	112 (42.1)	99 (37.2)
	≥ 50%	49 (18.4)	62 (23.3)
Metastases sites	≥3 metastatic sites	42 (15.8)	39 (14.7)
	Liver metastases	28 (10.5)	45 (16.9)
	Brain metastases	9 (3.4)	17 (6.4)

Phase III study of Ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous NSCLC (HARMONi-6)

Primary endpoint: PFS by IRRC

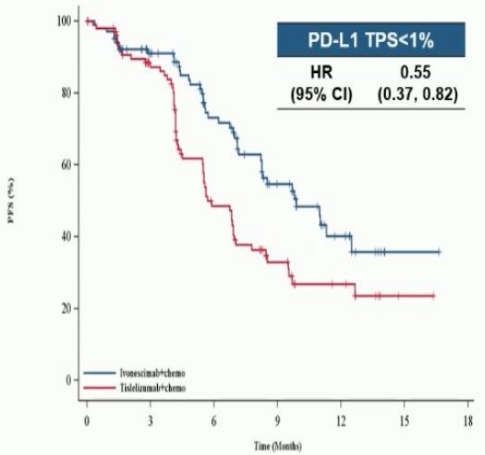
Ivonescimab+chemo demonstrated a statistically significant improvement in PFS vs. tislelizumab+chemo with HR=0.60, representing a 4.2 months improvement in mPFS.

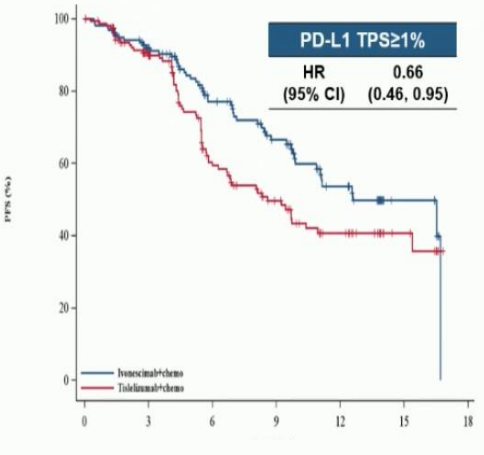


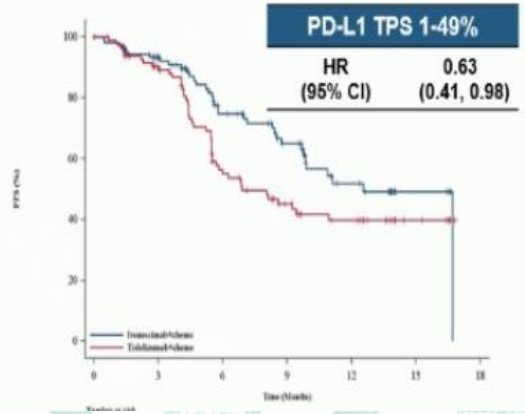
	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
mPFS, months (95% CI)	11.14 (9.86, NE)	6.90 (5.82, 8.57)
Stratified HR (95% CI)	0.60 (0.46, 0.78)	
p-value	<0.0001	

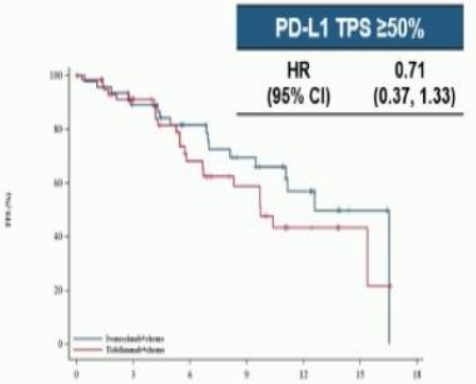
Median Follow-up: 10.28 months

Consistent PFS benefit by investigator-assessment: HR = 0.64 (95% CI: 0.50, 0.84)







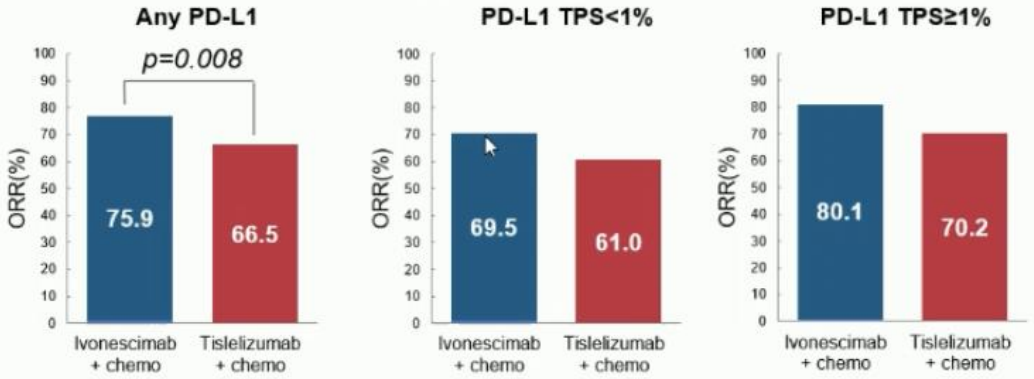


Phase III study of Ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous NSCLC (HARMONi-6)

ORR and DoR by IRRC

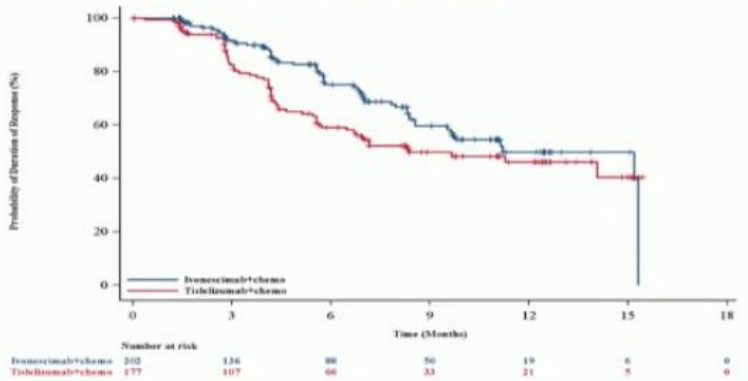
Tumor response was higher and more durable in the ivonescimab arm.

ORR by IRRC



	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
BOR, n (%)		
CR	1 (0.4)	0
PR	201 (75.6)	177 (66.5)
SD	39 (14.7)	60 (22.6)
PD	6 (2.3)	15 (5.6)

DoR by IRRC



	Ivonescimab + chemo (N=202)	Tislelizumab + chemo (N=177)
mDoR, months (95% CI)	11.20 (8.54, NE)	8.38 (5.72, NE)
p-value	0.0219	

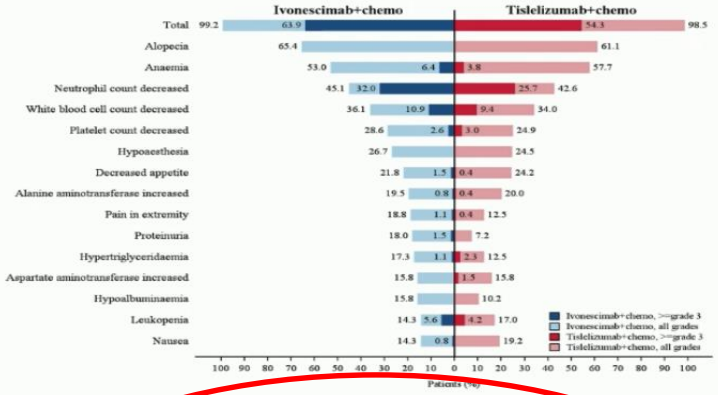
Phase III study of Ivonescimab plus chemotherapy versus tislelizumab plus chemotherapy as first-line treatment for advanced squamous NSCLC (HARMONi-6)

Safety Summary

Ivonescimab plus chemotherapy showed a manageable safety profile in sq-NSCLC.

	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=265)
TRAE	264 (99.2)	261 (98.5)
Grade ≥ 3 TRAE	170 (63.9)	144 (54.3)
Serious TRAE	86 (32.3)	80 (30.2)
Leading to ivonescimab or tislelizumab discontinuation	9 (3.4)	11 (4.2)
Leading to death	8 (3.0)	10 (3.8)

Most common TRAEs (incidence ≥15%)

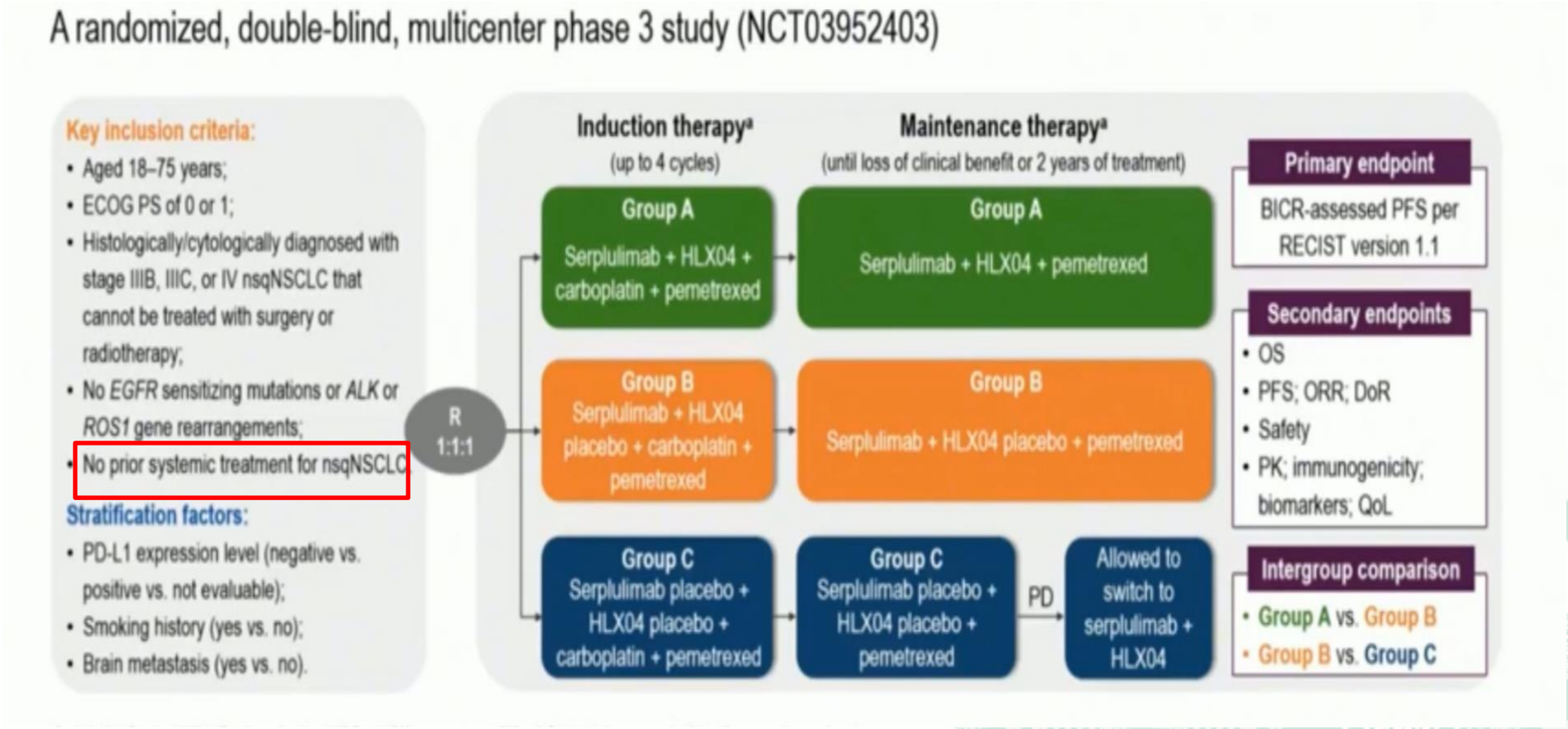


Immune-related AEs	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=265)
Any grade	73 (27.4)	67 (25.3)
Grade ≥3 irAE	24 (9.0)	27 (10.2)
Serious irAE	23 (8.6)	26 (9.8)
Leading to ivonescimab or tislelizumab discontinuation	3 (1.1)	6 (2.3)
Leading to death	0	1 (0.4)

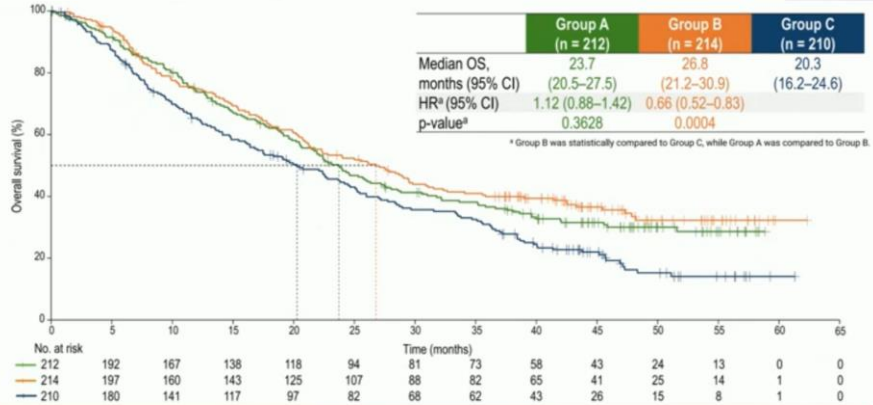
Possibly VEGF-Related AEs#	Ivonescimab + chemo (N=266)		Tislelizumab + chemo (N=265)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any	123 (46.2)	20 (7.5)	60 (22.6)	6 (2.3)
Proteinuria	72 (27.1)	6 (2.3)	29 (10.9)	0
Haemorrhage	57 (21.4)	5 (1.9)	25 (9.4)	2 (0.8)
Hypertension	27 (10.2)	8 (3.0)	12 (4.5)	3 (1.1)
Arterial thromboembolism	3 (1.1)	3 (1.1)	0	0
Venous thromboembolism	2 (0.8)	0	3 (1.1)	1 (0.4)
Fistula	1 (0.4)	0	0	0

#AE terms were grouped terms.

Final analysis of first-line serplulimab plus chemotherapy with or without HLX-04 in advanced nonsquamous NSCLC: the ASTRUM-002 phase 3 study



Overall survival



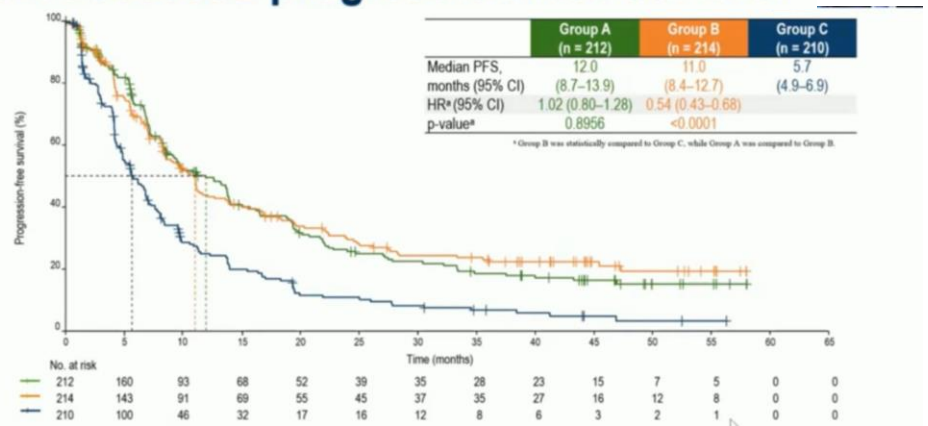
	Group A (n = 212)	Group B (n = 214)	Group C (n = 210)
Median OS, months (95% CI)	23.7 (20.5–27.5)	26.8 (21.2–30.9)	20.3 (16.2–24.6)
HR[a] (95% CI)	1.12 (0.88–1.42)	0.66 (0.52–0.83)	
p-value[a]	0.3628	0.0004	

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

2-stage model adjusted OS for trial crossover

79 patients crossed over to receive serplulimab plus HLX04 ; adjusted median OS in placebo-chemo arm: **14.2** months (95% CI 11.9–17.0); adjusted HR **0.53** (95% CI 0.42–0.68)

BICR-assessed progression-free survival



	Group A (n = 212)	Group B (n = 214)	Group C (n = 210)
Median PFS, months (95% CI)	12.0 (8.7–13.9)	11.0 (8.4–12.7)	5.7 (4.9–6.9)
HR[a] (95% CI)	1.02 (0.80–1.28)	0.54 (0.43–0.68)	
p-value[a]	0.8956	<0.0001	

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

D Group B versus Group C

Subgroup	Median OS (months) Group B (n = 214)	Group C (n = 210)	HR (95% CI)	p-value
Age				
<65 years	27.6	20.3	0.68 (0.50–0.92)	0.0117
≥65 years	24.0	20.4	0.64 (0.43–0.96)	0.0274
Sex				
Male	24.0	16.4	0.58 (0.44–0.76)	<0.0001
Female	28.2	33.3	1.03 (0.64–1.69)	0.8919
ECOG PS				
0	27.6	28.9	0.85 (0.52–1.39)	0.5124
1	26.2	16.4	0.64 (0.49–0.84)	0.0015
Clinical stage				
Locally advanced	NR	34.7	0.49 (0.23–1.01)	0.0534
Distant metastasis	25.5	19.2	0.69 (0.53–0.88)	0.0029
Smoking history				
Yes	26.1	16.2	0.58 (0.44–0.77)	0.0001
No	27.6	33.3	0.87 (0.57–1.35)	0.5407
Brain metastasis				
Yes	21.7	13.2	0.67 (0.40–1.11)	0.1187
No	28.4	22.4	0.65 (0.50–0.85)	0.0015
PD-L1 expression by CPS				
CPS <1	22.3	19.9	0.87 (0.52–1.46)	0.5983
CPS ≥1	27.5	20.8	0.62 (0.47–0.81)	0.0004
Indeterminable	NA	NA	NA	NA
PD-L1 expression by TPS				
TPS <1%	21.2	18.3	0.73 (0.48–1.10)	0.1314
1%≤ TPS <50%	25.5	20.3	0.70 (0.47–1.05)	0.0893
TPS ≥50%	45.4	23.8	0.49 (0.30–0.79)	0.0029

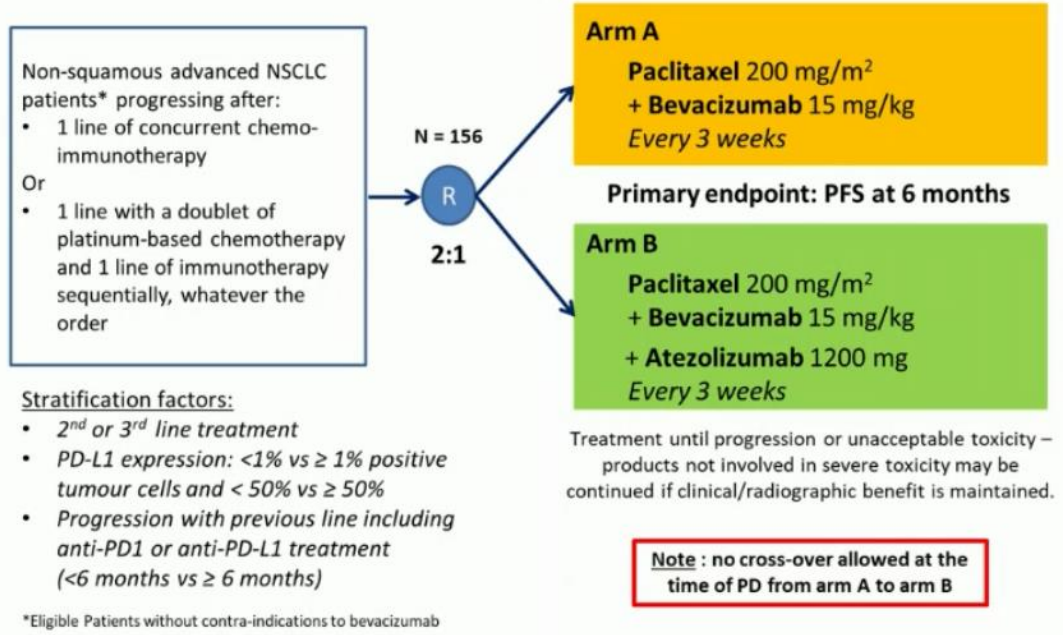
Group B versus Group C

Subgroup	Median PFS (months) Group B (n = 214)	Group C (n = 210)	HR (95% CI)	p-value
Age				
<65 years	8.5	5.6	0.59 (0.44–0.78)	0.0003
≥65 years	12.7	5.8	0.45 (0.30–0.68)	<0.0001
Sex				
Male	9.0	5.1	0.49 (0.38–0.64)	<0.0001
Female	11.1	8.4	0.67 (0.41–1.08)	0.0986
ECOG PS				
0	12.7	6.5	0.54 (0.33–0.86)	0.0080
1	9.6	5.6	0.55 (0.42–0.72)	<0.0001
Clinical stage				
Locally advanced	20.3	5.6	0.19 (0.08–0.42)	<0.0001
Distant metastasis	10.3	6.2	0.60 (0.47–0.76)	<0.0001
Smoking history				
Yes	10.4	4.9	0.50 (0.38–0.66)	<0.0001
No	11.1	8.1	0.64 (0.42–0.97)	0.0352
Brain metastasis				
Yes	8.1	4.1	0.49 (0.29–0.83)	0.0071
No	11.2	6.5	0.55 (0.43–0.71)	<0.0001
PD-L1 expression by CPS				
CPS <1	11.4	7.0	0.96 (0.58–1.60)	0.8702
CPS ≥1	10.4	5.6	0.47 (0.36–0.61)	<0.0001
Indeterminable	NA	NA	NA	NA
PD-L1 expression by TPS				
TPS <1%	8.5	6.8	0.83 (0.55–1.26)	0.3820
1%≤ TPS <50%	10.3	6.9	0.63 (0.43–0.94)	0.0237
TPS ≥50%	12.1	4.4	0.36 (0.23–0.57)	<0.0001

Paclitaxel-bevacizumab +/- atezolizumab in advanced non-squamous NSCLC progressing after chemo-immunotherapy

Trial design

- Open-label, randomized (2:1), non-comparative, multicenter phase II trial



- Primary endpoint : progression-free survival (PFS) rate at 6 months, assessed by independent review committee (IRC).
- Secondary endpoints : PFS by investigators, objective response rate (ORR), overall survival (OS), safety and quality of life.

Paclitaxel-bevacizumab +/- atezolizumab in advanced non-squamous NSCLC progressing after chemo-immunotherapy

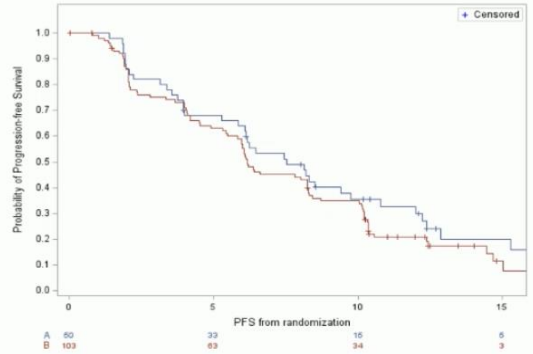
Primary endpoint: 6-month PFS rate by IRC in eligible pts

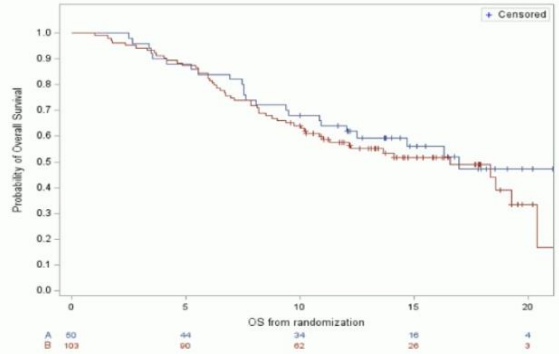
In eligible patients	A: paclitaxel + bevacizumab (N=50)	B: paclitaxel + bevacizumab + atezolizumab (N=103)
	6-month PFS rate: % [95% CI]	6-month PFS rate: % [95% CI]
By IRC	52.0% [38.2-65.9]	40.8% [31.3-50.3]
By Investigators	52.0% [38.2-65.9]	42.7% [33.2-52.3]

Reminder: NON COMPARATIVE trial design

Secondary endpoints :

- **ORR similar in both arms:** 42.0% in arm A, and 41.7% in arm B; **DCR:** 82.0% in arm A, and 76.7% in arm B.
- **Median PFS [95% CI]:** 7.5 [5.8-9.8] months in arm A, and 6.2 [5.5-8.2] months in arm B.
- **Median OS [95% CI]:** 17.0 [10.9-NR] months in arm A, and 16.6 [10.8-19.3] months in arm B.





INMUNOTERAPIA: NUEVAS DIANAS Y COMBINACIONES

Efficacy and safety of rilvegostomig for checkpoint inhibitor naive metastatic NSCLC: ARTEMIDE-01

CPI-naïve, PD-L1 TPS ≥1% Stage IV NSCLC

- Up to 1 prior chemotherapy regimen for metastatic disease
- PD-L1 TPS per local test
- *EGFR/ALK* wild-type

Part A (dose escalation) and Part B (dose expansion) in CPI-resistant NSCLC not pictured

R 1:1

Part C
PD-L1 TPS ≥1%
750 mg Q3W (n=34)

Part D1
PD-L1 TPS ≥50%
750 mg Q3W (n=31)

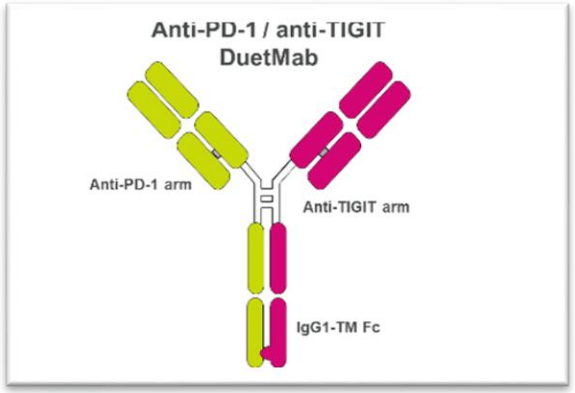
Part D2
PD-L1 TPS ≥50%
1500 mg Q3W (n=31)

No stratification factors

Up to 35 cycles

Primary endpoints
- ORR per investigator per RECIST v1.1
- Safety

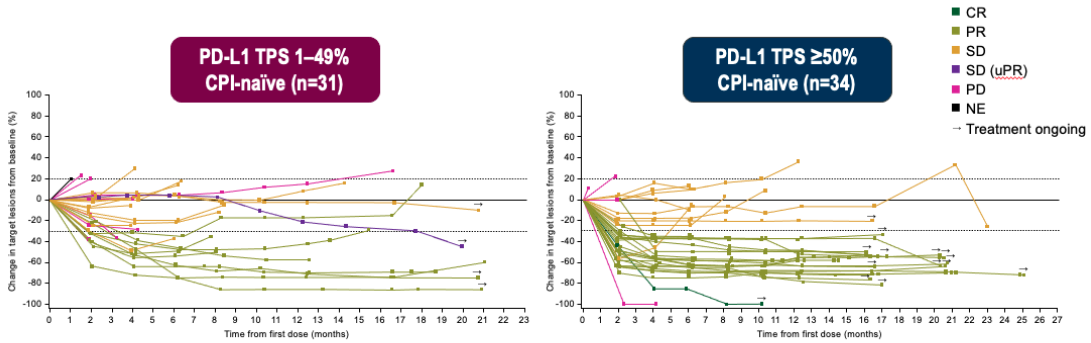
Key secondary endpoints
- DoR
- PFS



	Parts C + D1 PD-L1 TPS 1-49% (n=31)	Parts C + D1 PD-L1 TPS ≥50% (n=34)
Median age, years (range)	67.0 (41–79)	67.0 (48–78)
Female, n (%)	8 (25.8)	9 (26.5)
Asian / White / Other, n (%)	21 (67.7) / 7 (22.6) / 3 (9.7)	24 (70.6.) / 8 (23.5) / 2 (5.9)
ECOG PS 1, n (%)	21 (67.7)	20 (58.8)
Squamous histology, n (%)	15 (48.4)	8 (23.5)
Never smoker, n (%)	5 (16.1)	1 (2.9)
Prior chemotherapy, n (%)	13 (41.9)	3 (8.8)
Brain metastases, n (%) Liver metastases, n (%) Bone metastases, n (%)	5 (16.1) 6 (19.4) 5 (16.1)	9 (26.5) 2 (5.9) 9 (26.5)
Median duration of follow-up, months (range)	19.1 (1.0–28.7)	19.2 (4.8–31.4)

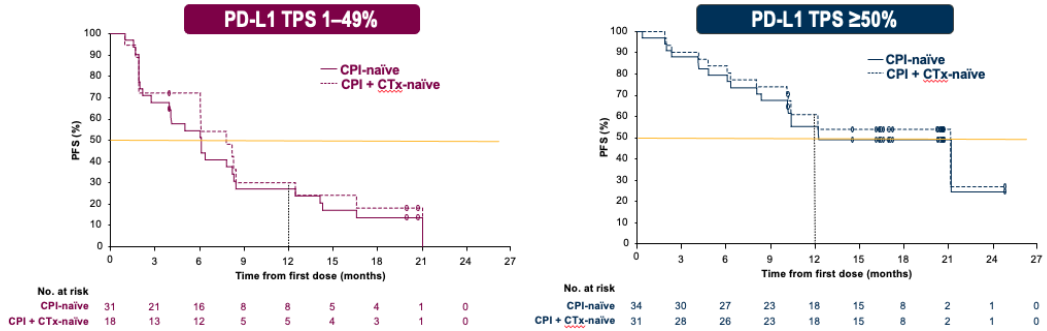
Efficacy and safety of rilvegostomig for checkpoint inhibitor naive metastatic NSCLC: ARTEMIDE-01

ARTEMIDE-01: ORR and DoR



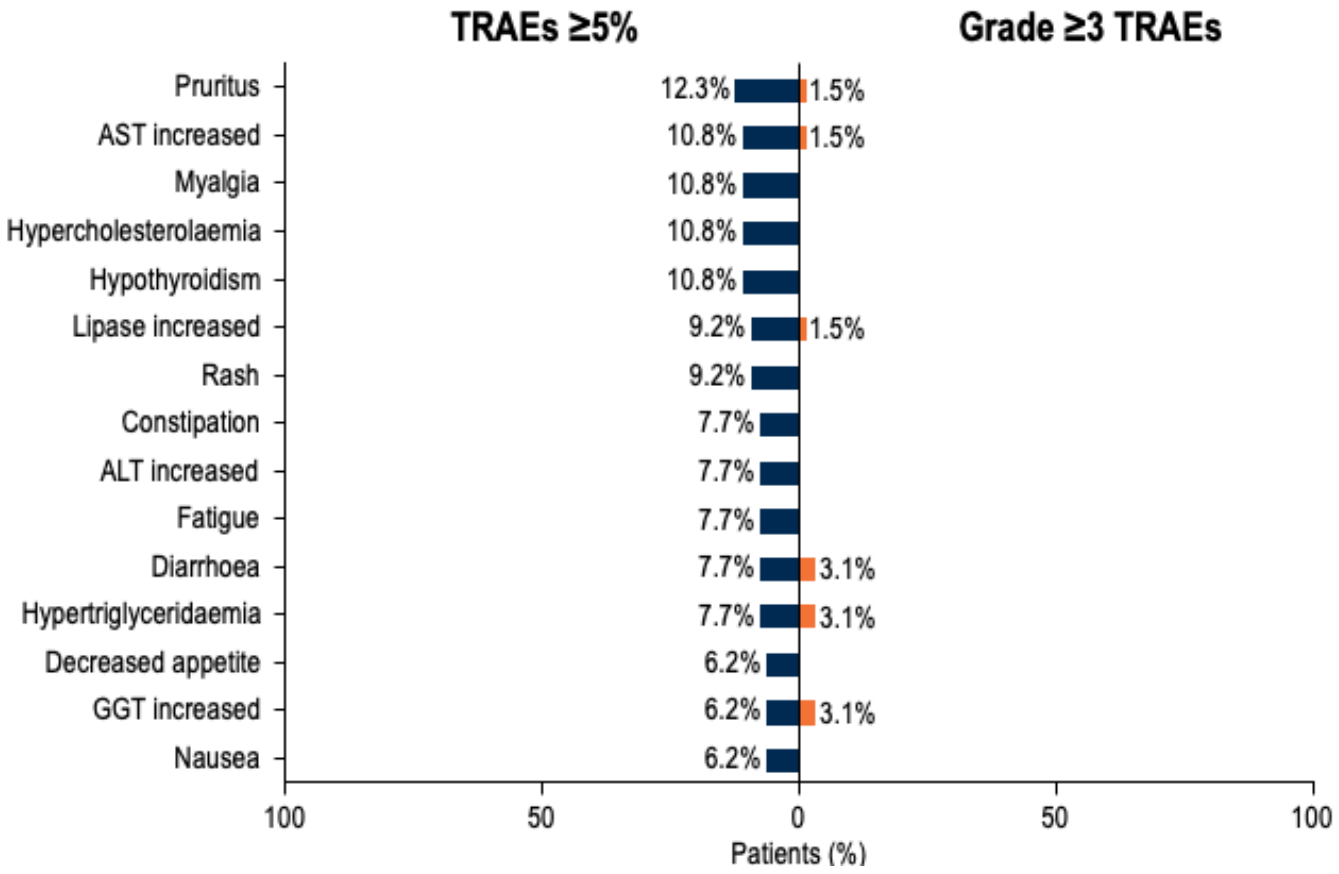
	PD-L1 TPS 1–49%		PD-L1 TPS ≥50%	
	CPI-naïve (n=31)	CPI + CTx-naïve (n=18)	CPI-naïve (n=34)	CPI + CTx-naïve (n=31)
ORR, % (95% CI)	29.0 (14.2–48.0)	44.4 (21.5–69.2)	61.8 (43.6–77.8)	67.7 (48.6–83.3)
Median DoR, months (range)	9.9 (4.1–NC)	8.5 (4.1–NC)	NR (10.3–NC)	NR (10.3–NC)

ARTEMIDE-01: PFS in CPI-naïve and CPI + CTx-naïve patients



	PD-L1 TPS 1–49%		PD-L1 TPS ≥50%	
	CPI-naïve (n=31)	CPI + CTx-naïve (n=18)	CPI-naïve (n=34)	CPI + CTx-naïve (n=31)
Median PFS, months (95% CI)	6.1 (2.7–8.3)	7.8 (1.9–12.5)	12.3 (8.4–NC)	21.2 (10.2–NC)
12-month PFS, % (95% CI)	27.2 (12.9–43.6)	30.1 (11.1–52.0)	55.5 (37.3–70.3)	60.8 (41.4–75.6)

Efficacy and safety of rilvegostomig for checkpoint inhibitor naive metastatic NSCLC: ARTEMIDE-01



Favourable safety profile

- Nearly all AEs were low-grade, manageable and reversible, with low incidences of pruritus and skin rash.
- No Grade 4 or 5 TRAEs were reported.
- Overall, only four Grade 3 imAEs (6.2%) were reported.
- There was a low rate of treatment-related rilvegostomig discontinuations (3.1%).

TeLuRide-005: phase 2 study of EIK1001, a toll-like receptor 7/8 co-agonist with pembrolizumab + chemotherapy as first line therapy in stage 4 NSCLC

Study Design: TeLuRide-005

Key Eligibility Criteria

- Untreated stage IV non-squamous or squamous NSCLC
- No driver mutations actionable as First-Line
- ECOG PS 0 or 1
- No symptomatic brain metastases

EIK1001 0.45mg/m² + Pembrolizumab 200 mg (up to 35 cycles) + Histology appropriate chemotherapy *

Evaluate for Dose-limiting toxicities during Cycle 1, 6 participants per histologic cohort

EIK1001 0.6mg/m² + Pembrolizumab 200 mg (up to 35 cycles) + Histology appropriate chemotherapy * ~25 participants per Cohort

Primary Endpoints

Safety run-in phase:
- Dose-limiting toxicities
- Adverse events (AEs)

Expansion Phase:
- AEs
- Patients Discontinuing due to an AE

Secondary Endpoints

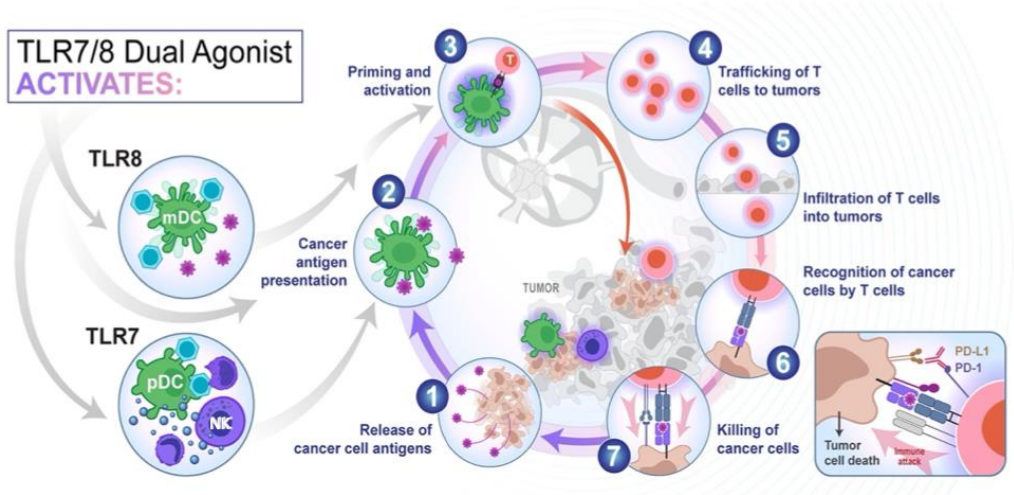
- Objective response rate (ORR)
- Duration of response (DOR)

EIK1001 IV weekly x 8 cycles, then every 3 weeks + Pembrolizumab every 3 weeks, plus

* **Cohort A Non-squamous**: pemetrexed 500 mg/m2 + carboplatin AUC 5 every 3 weeks x 4 Cycles + optional pemetrexed maintenance
* **Cohort B Squamous**: paclitaxel 200 mg/m2 + carboplatin AUC 6 every 3 weeks X 4 Cycles

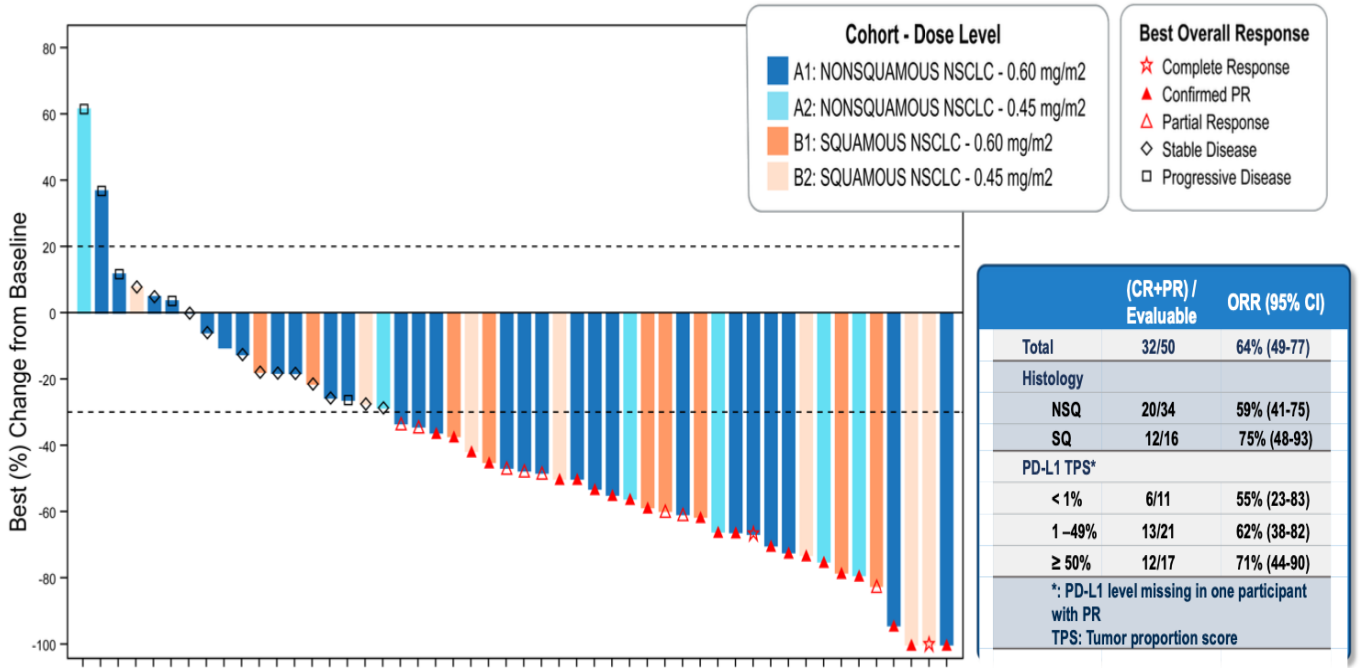
EIK1001:

- Is an IV small molecule, TLR7/8 receptor co-agonist, targeting plasmacytoid and myeloid dendritic cells
- Was well tolerated in phase 1 studies, with clinical response seen in heavily pre-treated participants
- **Study Rationale**: Adding EIK1001 to standard pembrolizumab+chemotherapy may further improve outcomes for NSCLC participants **via** a complementary mechanism to checkpoint inhibition.



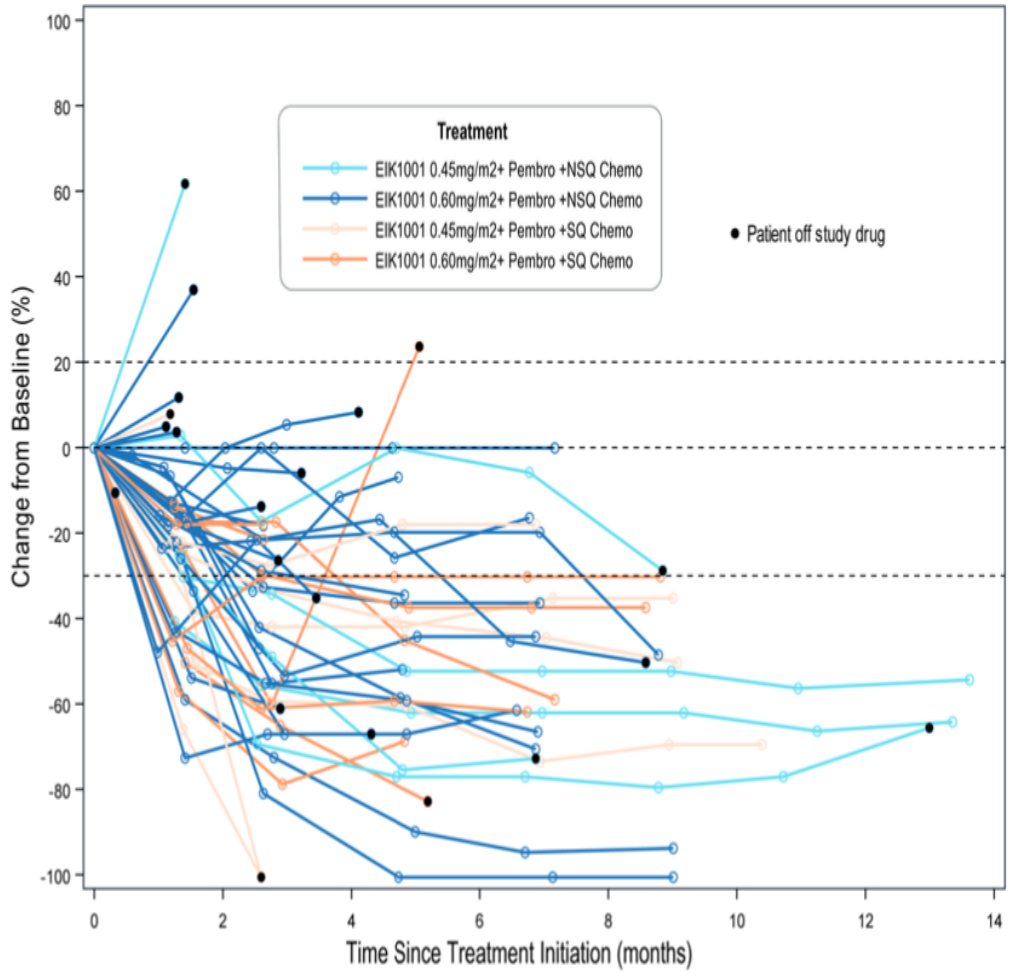
All Treated Participants	Total N=59
Age (years)	
Mean (SD)	67 (10)
Median (Range)	68 (23 -83)
Gender (M/F)	75% / 25%
Squamous (SQ) NSCLC	20 (34%)
Non-Squamous (NSQ) NSCLC	39 (66%)
Smoking Status	
Previous	64%
Current	26%
Never	10%
PDL-1 TPS status	
≥ 50%	36%
1 - 49%	41%
< 1%	22%
Missing	1%

TeLuRide-005: Best Percentage Change in Target Lesions



	(CR+PR) / Evaluable	ORR (95% CI)
Total	32/50	64% (49-77)
Histology		
NSQ	20/34	59% (41-75)
SQ	12/16	75% (48-93)
PD-L1 TPS*		
< 1%	6/11	55% (23-83)
1 –49%	13/21	62% (38-82)
≥ 50%	12/17	71% (44-90)

*: PD-L1 level missing in one participant with PR
TPS: Tumor proportion score



TeLuRide-005: phase 2 study of EIK1001, a toll-like receptor 7/8 co-agonist with pembrolizumab + chemotherapy as first line therapy in stage 4 NSCLC

Adverse Event Summary:

- Total TEAEs: 94.9%;
- Grade 3 AEs: 71.2%;
- SAEs: 42.4%;
- Leading to Death: 6.8% (none treatment related)
- Leading to treatment discontinuation: 3.4%;
- Cytokine Release Syndrome: 7/59 (11.9%);
  - Grade 1: 5/59 (8.5%);
  - Grade 2: 2/59 (3.4%)

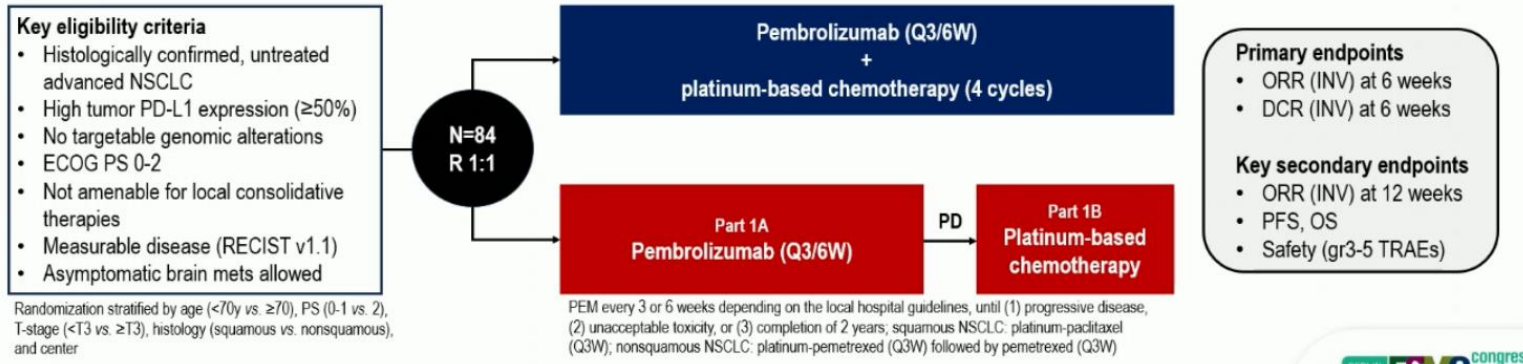
- Frequency of Adverse Events were similar across both the run-in and expansion phases and across both histologies
- Safety events were predominantly related to standard of care chemotherapy / pembrolizumab

Adverse Events (>20%)	Total N = 59
Fatigue	36 (61.0%)
Nausea	27 (45.8%)
Neutropenia	25 (42.4%)
Anemia	24 (40.7%)
Constipation	20 (33.9%)
Diarrhea	19 (32.2%)
Dizziness	19 (30.5%)
Thrombocytopenia	18 (29.1%)
Dyspnea	15 (25.4%)
Decreased appetite	14 (23.7%)
Headache	14 (23.7%)
Hypotension	14 (23.7%)
Pyrexia	14 (23.7%)
Vomiting	13 (22.0%)
Weight decreased	13 (22.0%)
Hypokalaemia	12 (20.3%)

Pembrolizumab plus chemotherapy vs pembrolizumab as first-line therapy for advanced NSCLC with PDL1 (TPS) ≥ 50%: open-label, phase 3, randomized trial (PAULIEN)

Study rationale and design

- Pembrolizumab (PEM) is the standard first-line therapy for advanced NSCLC with high tumor PD-L1 expression (TPS ≥50%) and no targetable genomic alterations.
- However, in those cases where an urgent tumor response is needed, chemotherapy (CT) is often added to PEM, though its benefit is unclear.
- PAULIEN is a multicenter (eight Dutch sites), open-label, phase III, randomized controlled, superiority trial comparing **PEM + CT** with **PEM** to assess **tumor responses at 6 weeks**.
- Hypothesis: adding CT to PEM will result in a 30% increase[1] in objective tumor response (ORR) at 6 weeks.



Randomization stratified by age (<70y *vs.* ≥70), PS (0-1 *vs.* 2), T-stage (<T3 *vs.* ≥T3), histology (squamous *vs.* nonsquamous), and center

PEM every 3 or 6 weeks depending on the local hospital guidelines, until (1) progressive disease, (2) unacceptable toxicity, or (3) completion of 2 years; squamous NSCLC: platinum-paclitaxel (Q3W); nonsquamous NSCLC: platinum-pemetrexed (Q3W) followed by pemetrexed (Q3W)

PAULIEN: EU CT number 2024-516581-11-00; (1) 80% power to detect a 30% increase in ORR (from 40% to 70% by adding CT) at a 2-sided α = 5%.

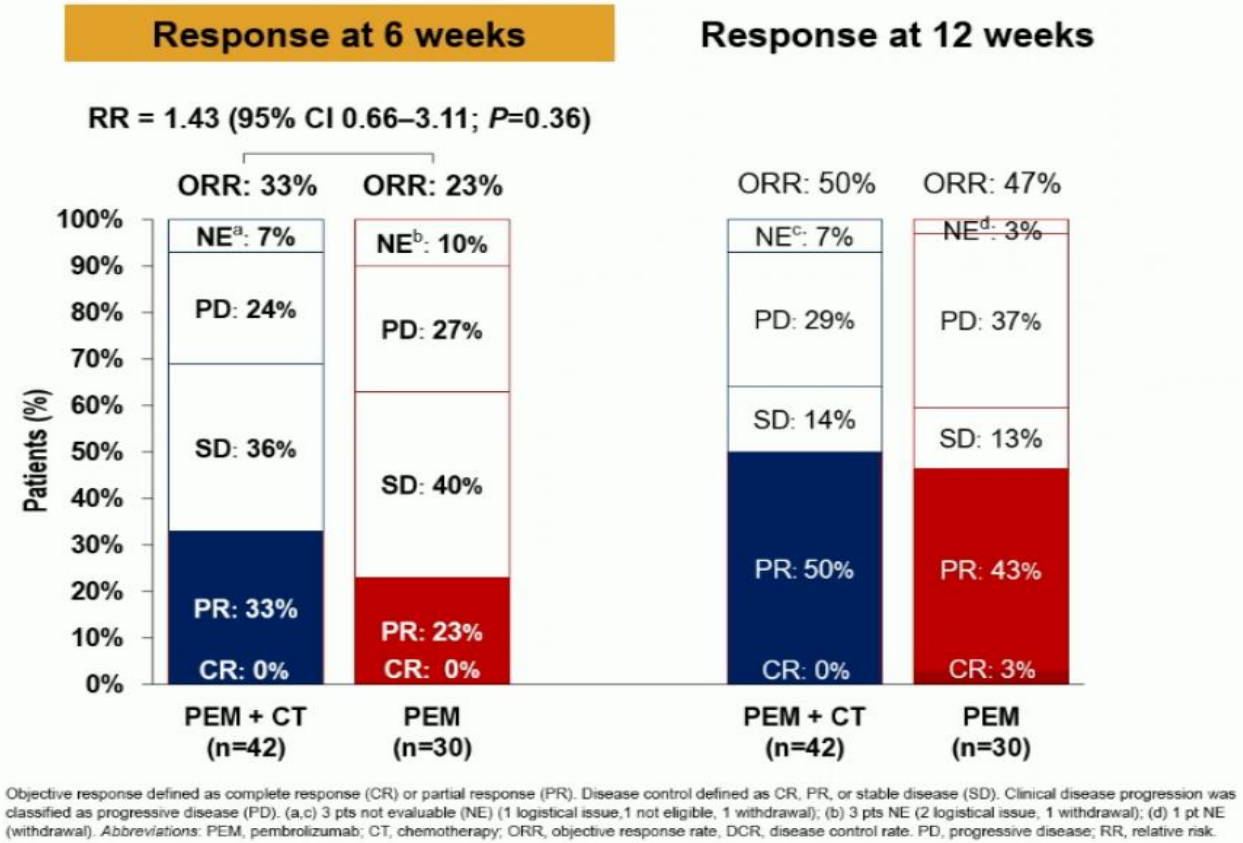
Abbreviations: PS, performance status; mets, metastases; PD, progressive disease; ORR, objective response rate; DCR, disease control rate; INV, investigator-assessed; PFS, progression-free survival; OS, overall survival; TRAE, treatment-related adverse event

n (%)	PEM + CT (N=42)	PEM N=30)
Age, <70 years	26 (62)	20 (67)
Sex, male	25 (60)	12 (40)
Smoking status		
Current or former	40 (95)	29 (97)
Never	2 (5)	1 (3)
Performance status		
0-1	37 (88)	26 (87)
2	5 (12)	4 (13)
Histology, nonsquamous	36 (86)	30 (100)
T-stage, ≥T3	19 (45)	15 (50)
Baseline SLD (≥90 mm)	14 (33)	11 (37)
Stage III disease	3 (7)	1 (3)

Abbreviations: PEM, pembrolizumab; CT, chemotherapy; SLD, sum of the longest diameters

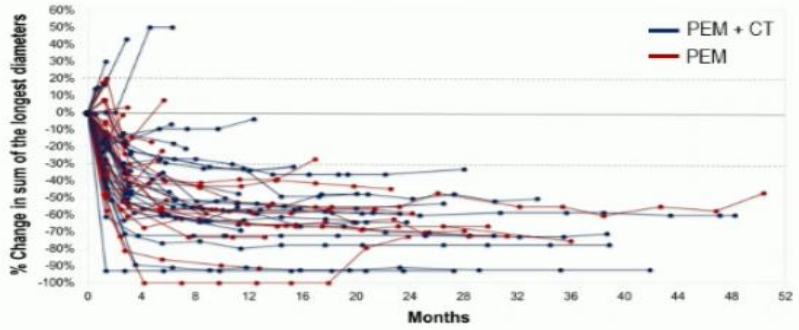
Pembrolizumab plus chemotherapy vs pembrolizumab as first-line therapy for advanced NSCLC with PDL1 (TPS) ≥ 50%: open-label, phase 3, randomized trial (PAULIEN)

Investigator-assessed ORR and DCR at 6 weeks



Objective response defined as complete response (CR) or partial response (PR). Disease control defined as CR, PR, or stable disease (SD). Clinical disease progression was classified as progressive disease (PD). (a,c) 3 pts not evaluable (NE) (1 logistical issue,1 not eligible, 1 withdrawal); (b) 3 pts NE (2 logistical issue, 1 withdrawal); (d) 1 pt NE (withdrawal). *Abbreviations*: PEM, pembrolizumab; CT, chemotherapy; ORR, objective response rate, DCR, disease control rate. PD, progressive disease; RR, relative risk.

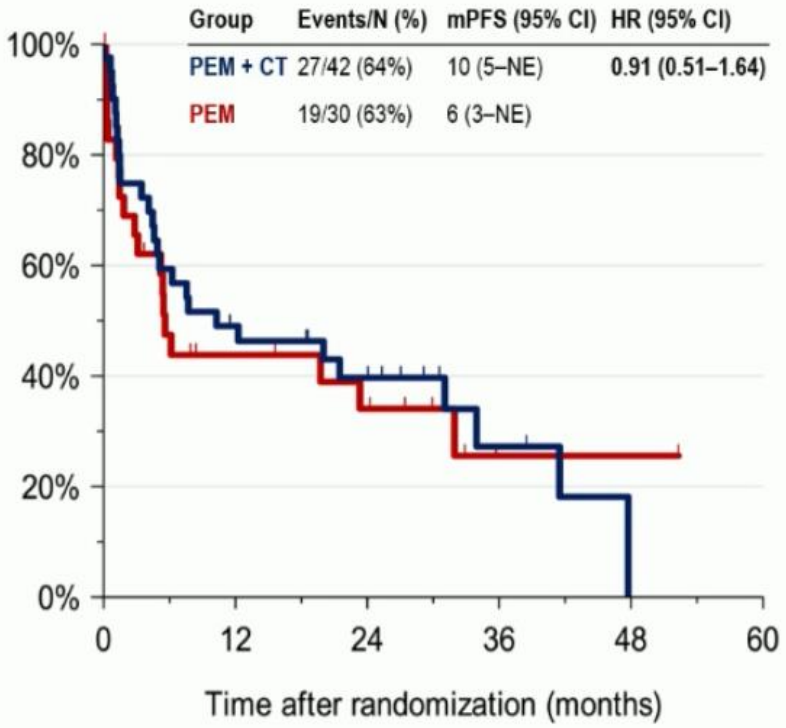
Response, n (%, 95% CI)	PEM + CT (N=42)	PEM (N=30)
ORR at 6 weeks	14 (33%, 21–48)	7 (23%, 12–41)
DCR at 6 weeks	29 (69%, 54–81)	19 (63%, 46–78)
ORR at 12 weeks	21 (50%, 36–64)	14 (47%, 30–64)
DCR at 12 weeks	27 (64%, 49–77)	18 (60%, 42–75)
Best overall response, n (%)		
CR	0 (0)	1 (3)
PR	25 (60)	14 (47)
SD	4 (10)	5 (17)
PD	10 (24)	9 (30)
NE	3 (7)	1 (3)
Duration of response		
Responders, n (%)	25 (60)	15 (50)
Median, months (IQR)	11.3 (3.7–28.5)	14.1 (4.4–26.4)
Time to response		
Median, weeks (IQR)	6.0 (5.6–12.6)	11.3 (5.9–12.0)



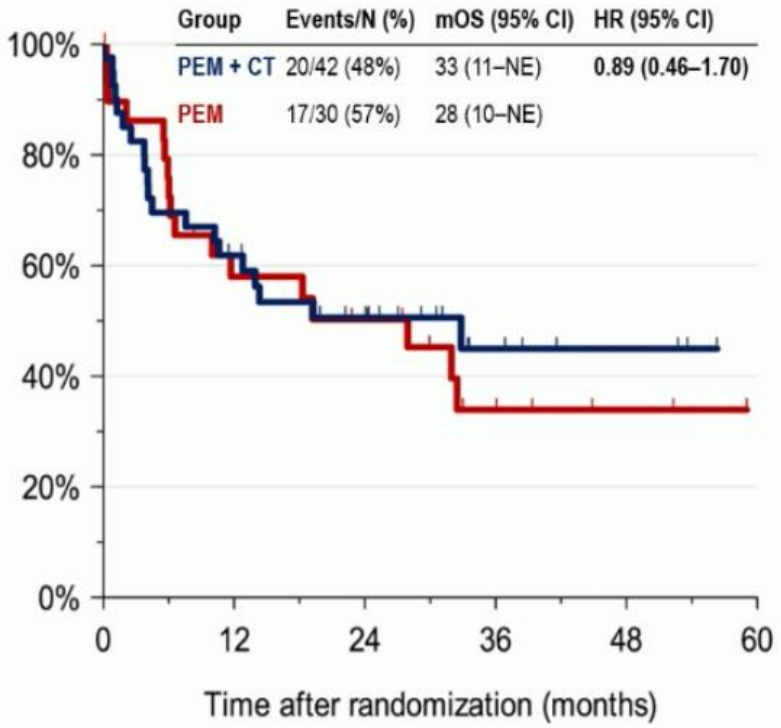
Pembrolizumab plus chemotherapy vs pembrolizumab as first-line therapy for advanced NSCLC with PDL1 (TPS) ≥ 50%: open-label, phase 3, randomized trial (PAULIEN)

Progression-free survival and overall survival

Progression-free survival

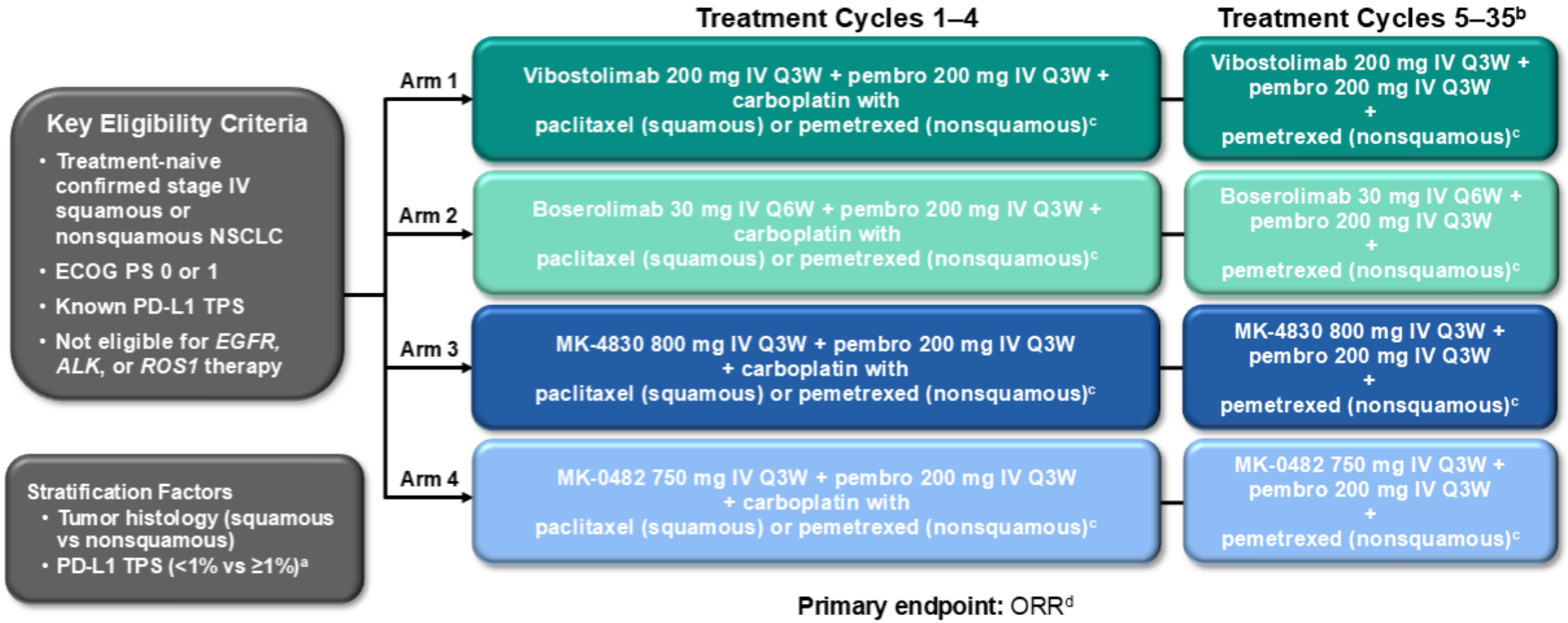


Overall survival



KEYMAKER-U01 substudy 01: investigational agents + pembrolizumab and chemotherapy in untreated stage IV NSCLC

KEYMAKER-U01 Substudy 01A Design

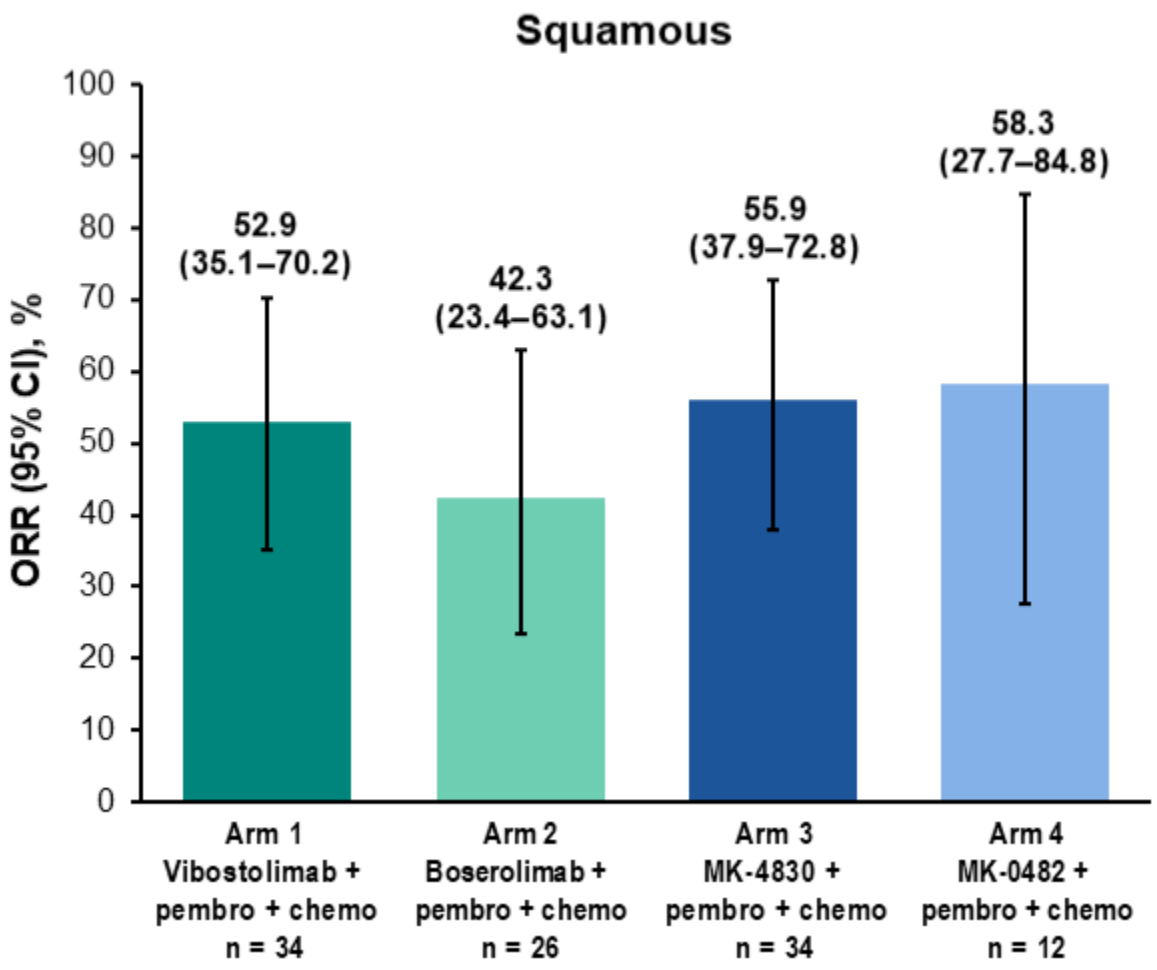


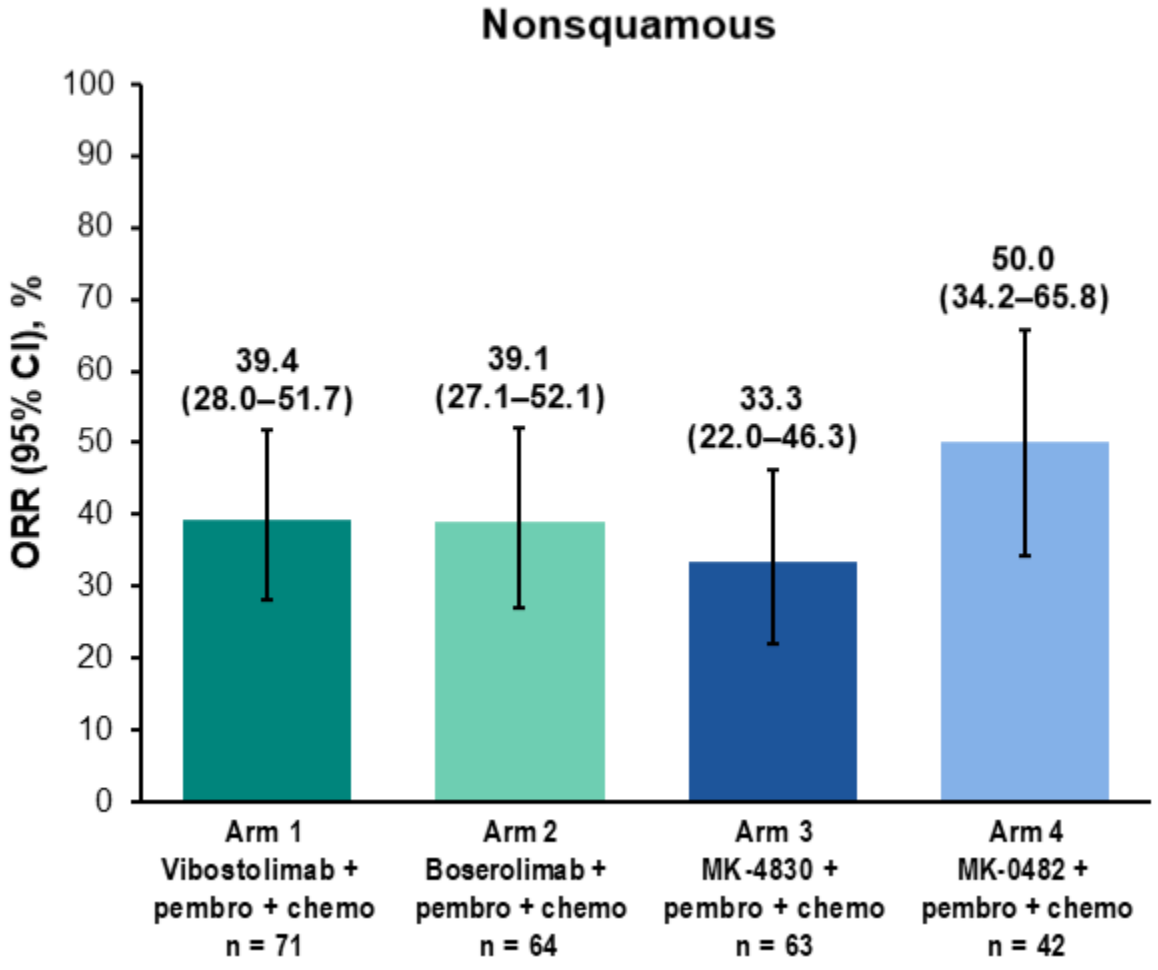
Primary endpoint: ORR[d]
Secondary endpoints: Progression-free survival[d] and safety

- Vibostolimab, a TIGIT antagonist mAb (arm 1)
- Boserolimab, a CD27 agonist mAb (arm 2)
- MK-4830, an ILT4 antagonist mAb (arm 3)
- MK-0482, an ILT3 antagonist mAb (arm 4)

KEYMAKER-U01 substudy 01: investigational agents + pembrolizumab and chemotherapy in untreated stage IV NSCLC

Efficacy: Investigator-Assessed ORR per RECIST v1.1



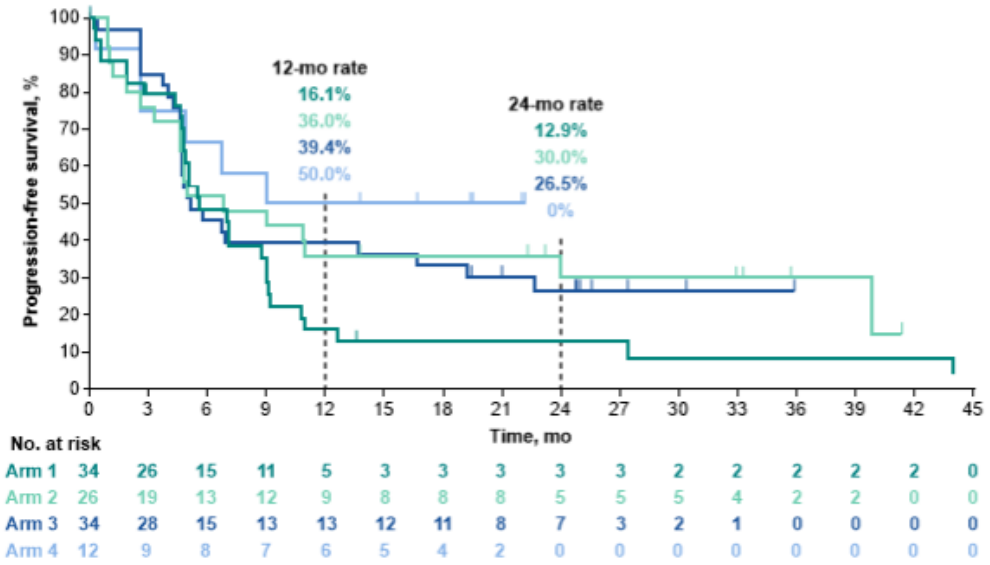


KEYMAKER-U01 substudy 01: investigational agents + pembrolizumab and chemotherapy in untreated stage IV NSCLC

Efficacy: Investigator-Assessed PFS per RECIST v1.1

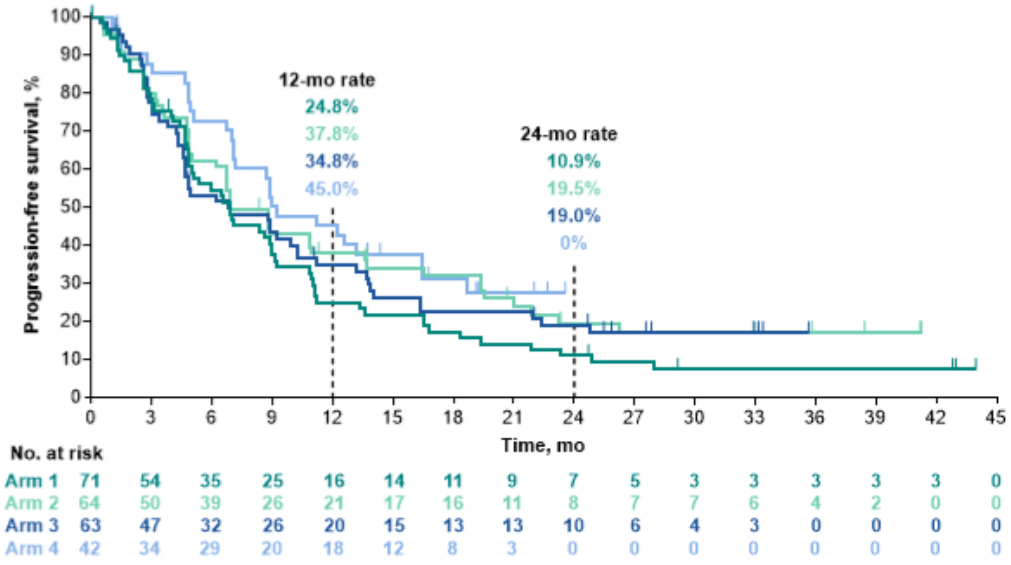
Squamous

	Events/N	Median (95% CI), mo
Arm 1: vibostolimab + pembro + chemo	30/34	5.6 (4.8–9.0)
Arm 2: boserolimab + pembro + chemo	18/26	6.8 (4.6–24.0)
Arm 3: MK-4830 + pembro + chemo	24/34	5.2 (4.7–16.7)
Arm 4: MK-0482 + pembro + chemo	6/12	NR (2.6–NE)



Nonsquamous

	Events/N	Median (95% CI), mo
Arm 1: vibostolimab + pembro + chemo	61/71	6.9 (4.8–9.0)
Arm 2: boserolimab + pembro + chemo	49/64	6.9 (5.0–11.0)
Arm 3: MK-4830 + pembro + chemo	50/63	6.8 (4.6–10.3)
Arm 4: MK-0482 + pembro + chemo	28/42	9.2 (7.1–16.4)



KEYMAKER-U01 substudy 01: investigational agents + pembrolizumab and chemotherapy in untreated stage IV NSCLC

Safety: Adverse Event Summary

	Squamous				Nonsquamous			
	Arm 1 Vibostolimab + pembro + chemo n = 34	Arm 2 Boserolimab + pembro + chemo n = 26	Arm 3 MK-4830 + pembro + chemo n = 34	Arm 4 MK-0482 + pembro + chemo n = 12	Arm 1 Vibostolimab + pembro + chemo n = 71	Arm 2 Boserolimab + pembro + chemo n = 64	Arm 3 MK-4830 + pembro + chemo n = 63	Arm 4 MK-0482 + pembro + chemo n = 42
Treatment-related AEs,[a] %	94.1	84.6	91.2	100	90.1	90.6	92.1	88.1
Grade 3–5	47.1	30.8	29.4	33.3	47.9	39.1	42.9	42.9
Led to discontinuation	14.7	11.5	17.6	16.7	25.4	23.4	17.5	31.0
Led to death	5.9	0	2.9	16.7	2.8	0	1.6	2.4
Immune-related AEs[b] and infusion reactions, %	50.0	34.6	20.6	50.0	35.2	39.1	28.6	38.1
Grade 3–5	17.6	7.7	2.9	16.7	8.5	14.1	1.6	16.7
Led to discontinuation	5.9	7.7	0	0	8.5	12.5	1.6	11.9
Led to death	0	0	0	0	0	0	0	2.4[c]

CONCLUSIONES

- Ivonescimab + quimioterapia presenta un beneficio en SLP frente a quimioterapia + tislelizumab en CPNCP avanzado histología escamosa, sin datos maduros aún en supervivencia global.

- La estrategia de añadir una terapia antiangiogénica a la inmuno-quimioterapia no han demostrado beneficio en la supervivencia de los pacientes ni en primera ni en segunda línea.

- La adición de quimioterapia a pembrolizumab en altos expresores no parece aumentar las tasas de respuesta en las 6 y 12 primeras semanas, ni tener impacto en la SLP de los pacientes, si bien son necesarios estudios más amplios y de más seguimiento para poder extraer conclusiones a este respecto.

- Nuevos fármacos como rilvegostomig o EIK1001 parecen incrementar las tasas de respuesta en pacientes no tratados previamente con inmunoterapia y son estrategias en evaluación en ensayos prospectivos fase 3.

MUCHAS GRACIAS