BIOMARKER SELECTION FOR IMMUNOTHERAPY IN NSCLC

Ferdinandos Skoulidis, M.D., Ph.D.

Associate Professor

Department of Thoracic/Head and Neck Medical Oncology

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NCCN guidelines® for the first-line treatment of metastatic NSCLC without actionable driver mutations

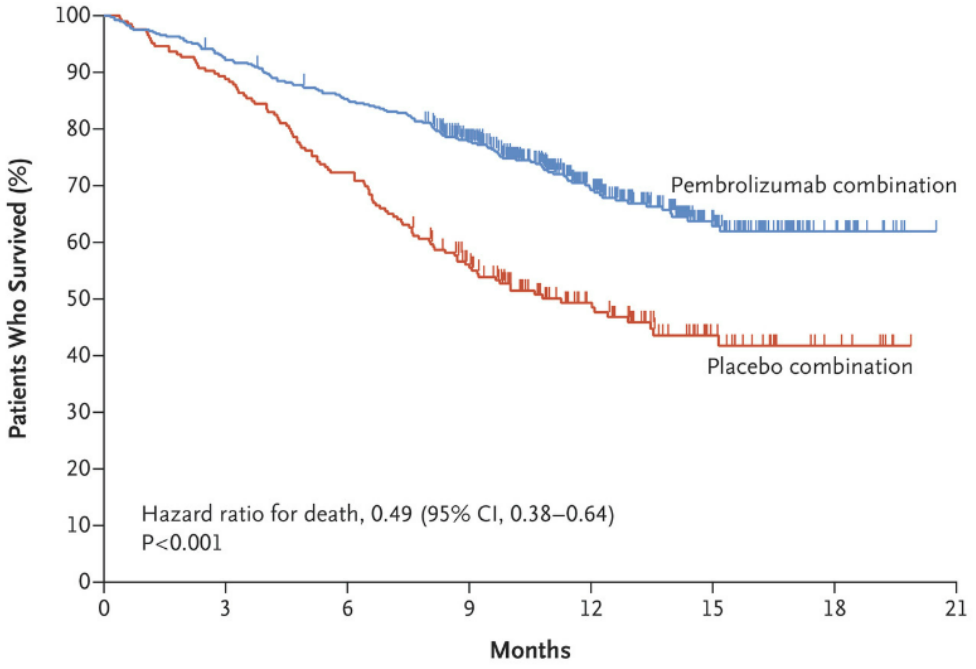
HISTOLOGY	PD-L1 <1%	PD-L1 1% to 49%	PD-L1 ≥50%
Nonsquamous	▪ **Pembrolizumab + carboplatin/cisplatin + pemetrexed** ▪ Atezolizumab + carboplatin + paclitaxel/nab-paclitaxel ± bevacizumab ▪ Nivolumab + ipilimumab + carboplatin/cisplatin + pemetrexed ▪ Nivolumab + ipilimumab ▪ Cemiplimab + carboplatin/cisplatin + pemetrexed/paclitaxel ▪ Durvalumab + tremelimumab + platinum-based doublet CT ▪ Platinum-based doublet CT (PS 2)	▪ **Pembrolizumab + carboplatin/cisplatin + pemetrexed** ▪ Atezolizumab + carboplatin + paclitaxel/nab-paclitaxel ± bevacizumab ▪ Nivolumab + ipilimumab + carboplatin/cisplatin + pemetrexed ▪ Nivolumab + ipilimumab ▪ Cemiplimab + carboplatin/cisplatin + pemetrexed/paclitaxel ▪ Durvalumab + tremelimumab + platinum-based doublet CT	▪ **Pembrolizumab** ▪ **Pembrolizumab + carboplatin/cisplatin + pemetrexed** ▪ **Atezolizumab** ▪ **Cemiplimab** ▪ Atezolizumab + carboplatin + paclitaxel/nab-paclitaxel ± bevacizumab ▪ Nivolumab + ipilimumab + carboplatin/cisplatin + pemetrexed ▪ Cemiplimab + carboplatin/cisplatin + pemetrexed/paclitaxel ▪ Durvalumab + tremelimumab + platinum-based doublet CT
Squamous	▪ **Pembrolizumab + carboplatin + paclitaxel/nab-paclitaxel** ▪ Nivolumab + ipilimumab + carboplatin + paclitaxel ▪ Nivolumab + ipilimumab ▪ Cemiplimab + carboplatin/cisplatin + paclitaxel ▪ Durvalumab + tremelimumab + platinum-based doublet CT ▪ Platinum-based doublet CT (PS 2)		▪ **Pembrolizumab** ▪ **Pembrolizumab + carboplatin + paclitaxel/nab-paclitaxel** ▪ **Atezolizumab** ▪ **Cemiplimab** ▪ Nivolumab + ipilimumab + carboplatin + paclitaxel ▪ Cemiplimab + carboplatin/cisplatin + paclitaxel ▪ Durvalumab + tremelimumab + platinum-based doublet CT

Regimens in bold are preferred
NCCN Guidelines NSCLC v1.2023

How do we select the optimal first line regimen for an individual patient?

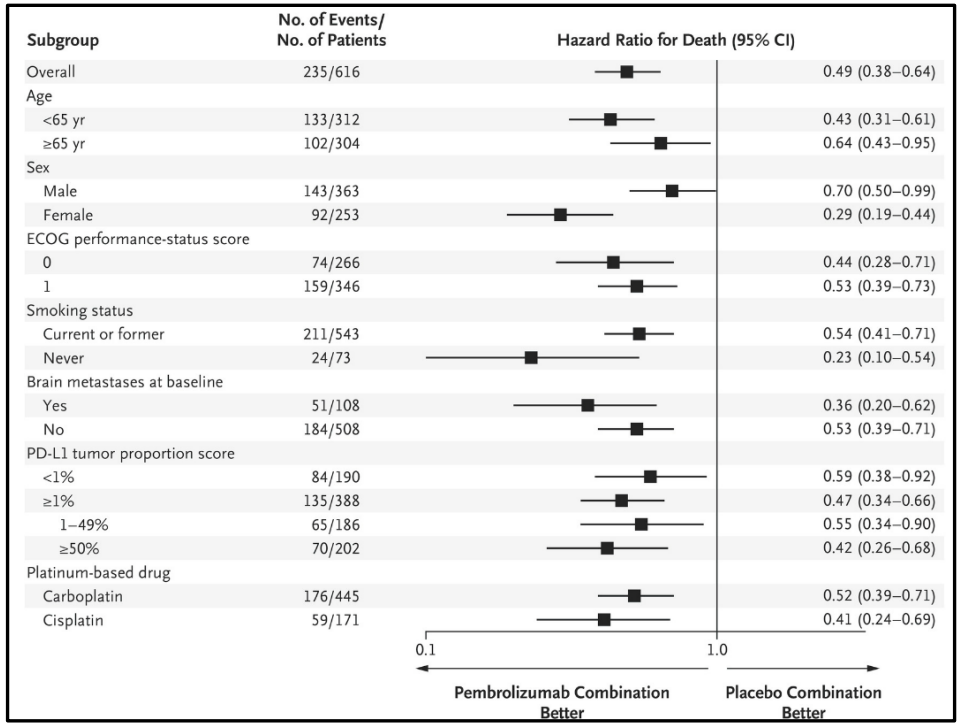
ChemoIO with pembrolizumab and platinum based chemotherapy (KEYNOTE-189 regimen) improves OS in metastatic ns-NSCLC

A.



No. at Risk								
Pembrolizumab combination	410	377	347	278	163	71	18	0
Placebo combination	206	183	149	104	59	25	8	0

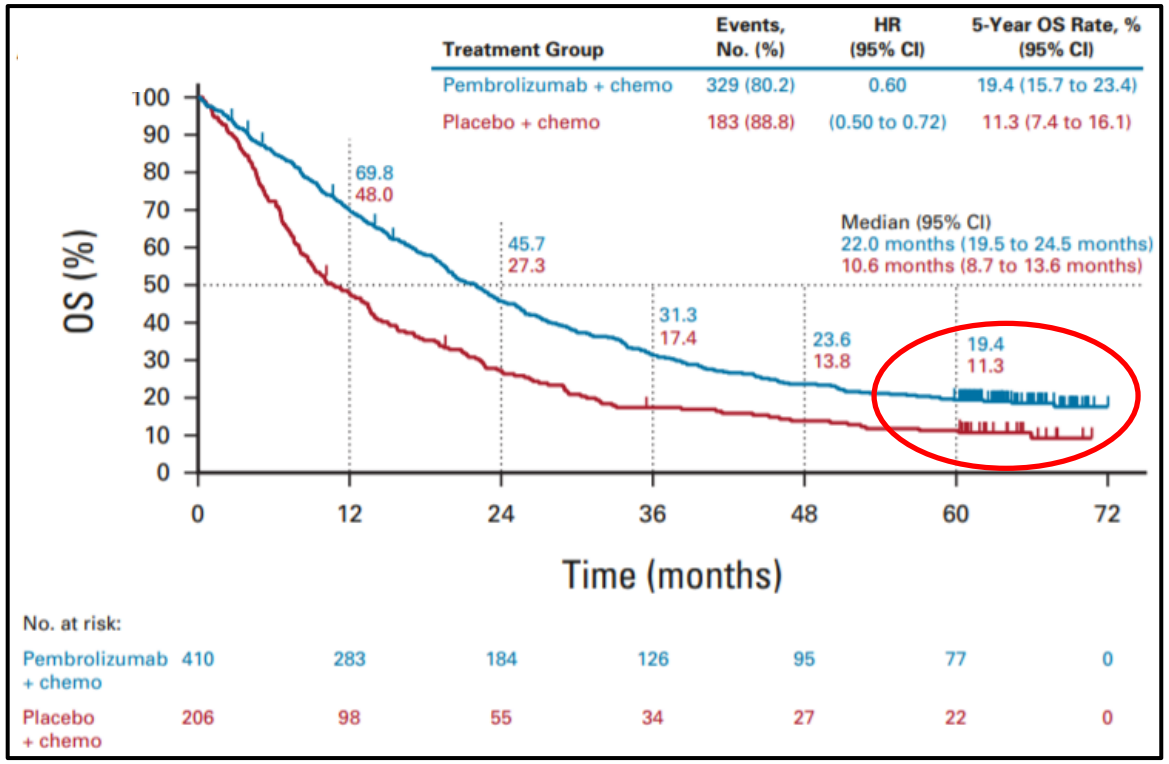
B.



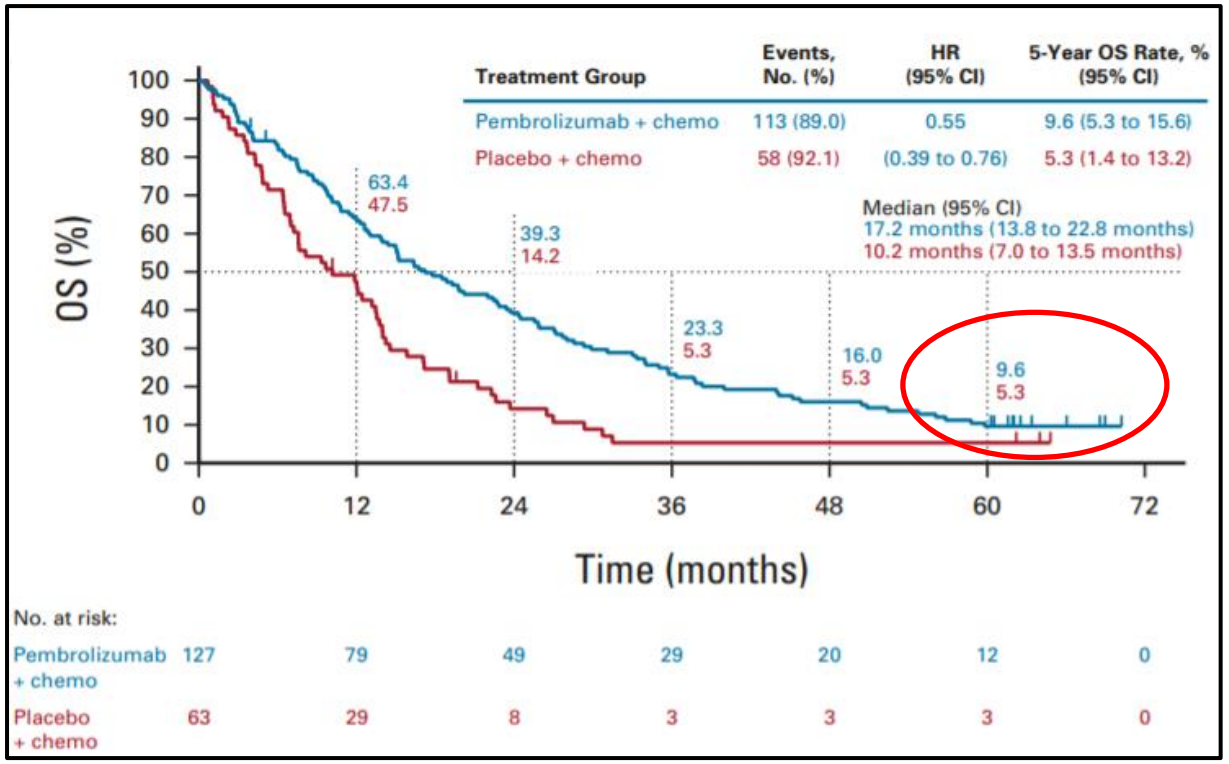
Gandhi L et al., *NEJM* 2018

5-year OS with the KEYNOTE-189 regimen in metastatic ns-NSCLC

ITT patient population



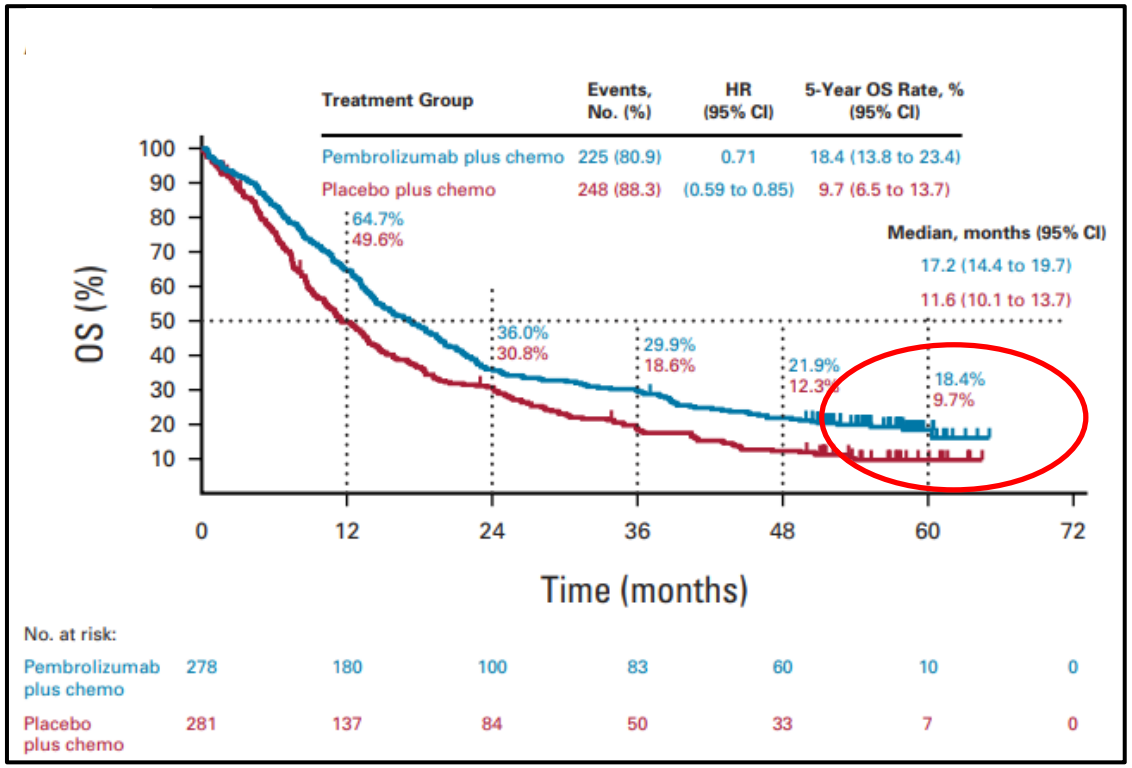
PD-L1 TPS <1%



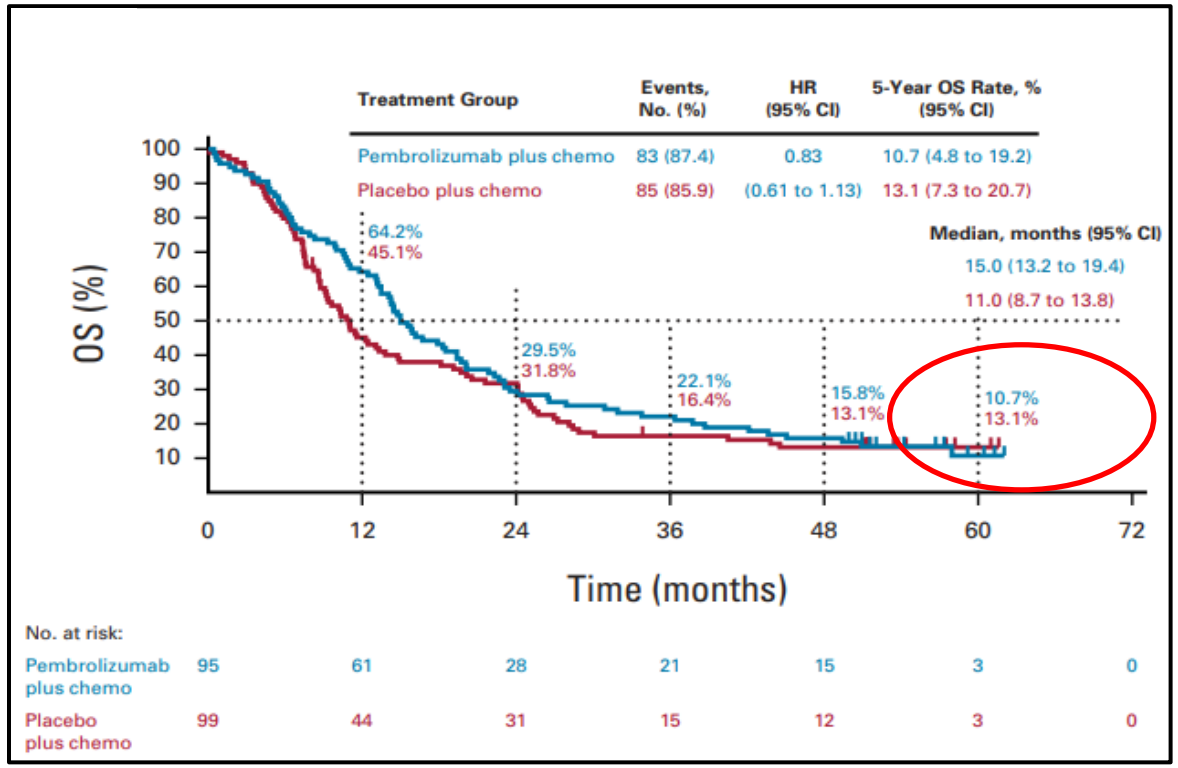
Garassino MC, *J Clin Oncol*, 2023

5-year OS with the KEYNOTE-407 regimen in metastatic sq-NSCLC

ITT patient population



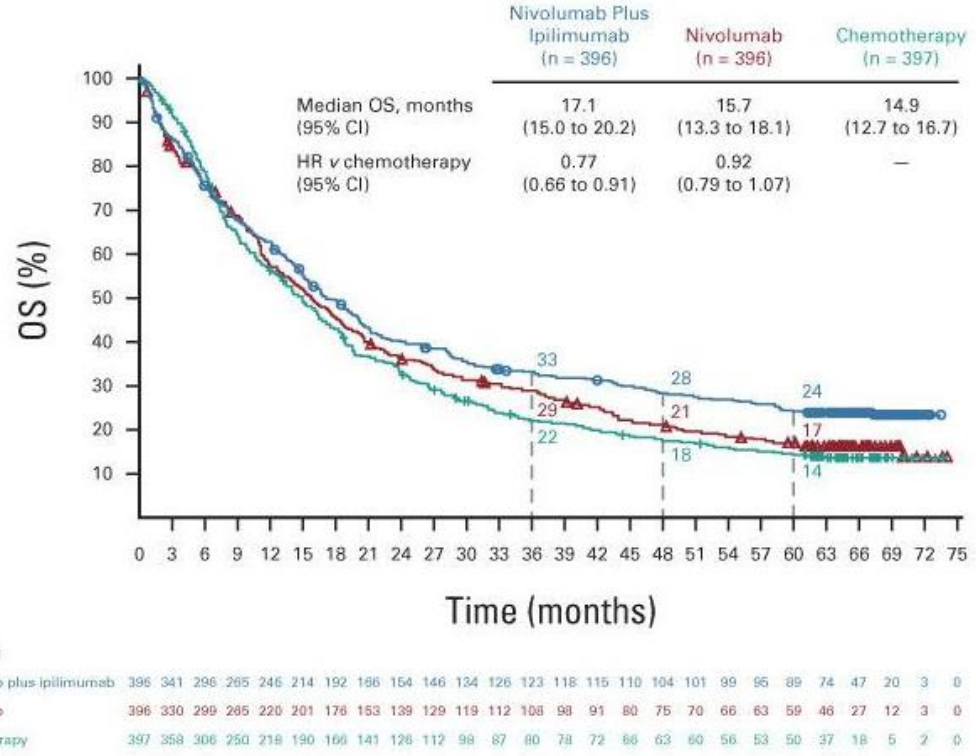
PD-L1 TPS <1%



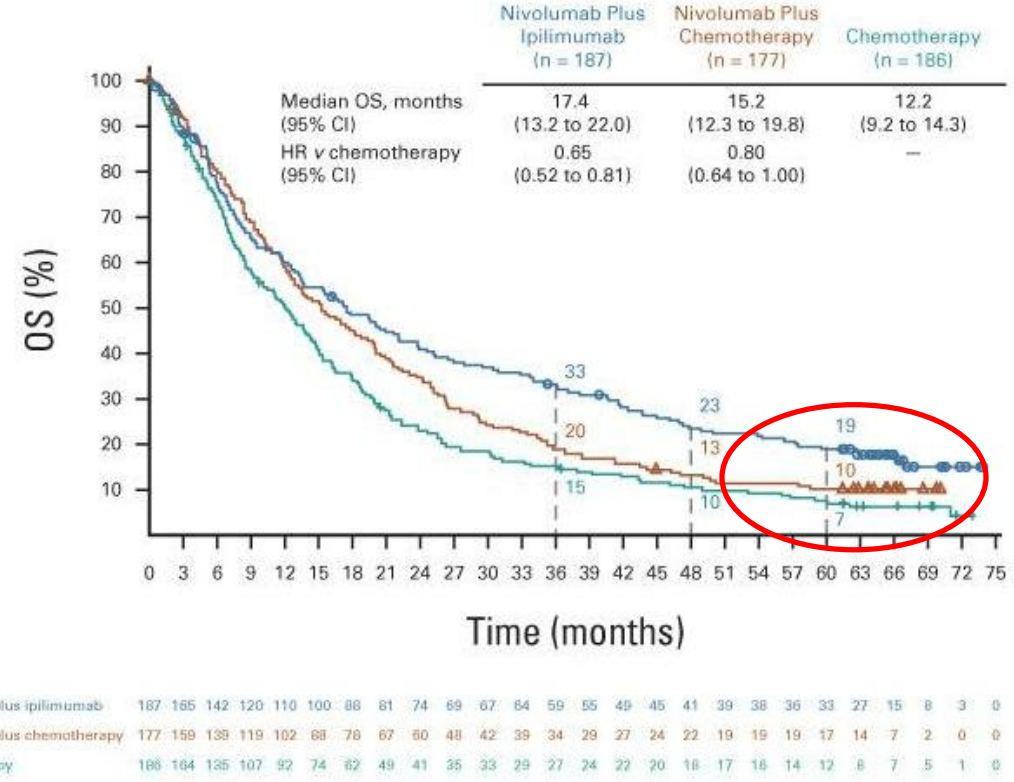
Novello S, *J Clin Oncol*, 2023

5-year OS with nivolumab and ipilimumab in advanced NSCLC in the CheckMate 227 trial

PD-L1 ≥1%



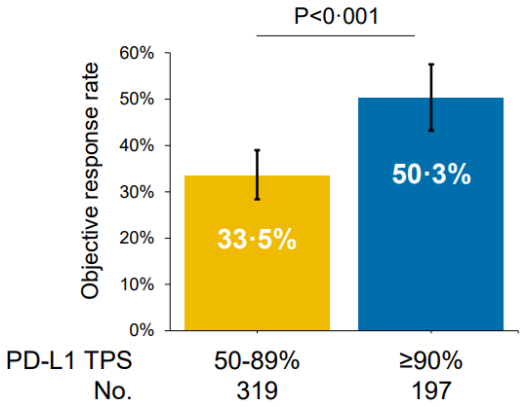
PD-L1 <1%

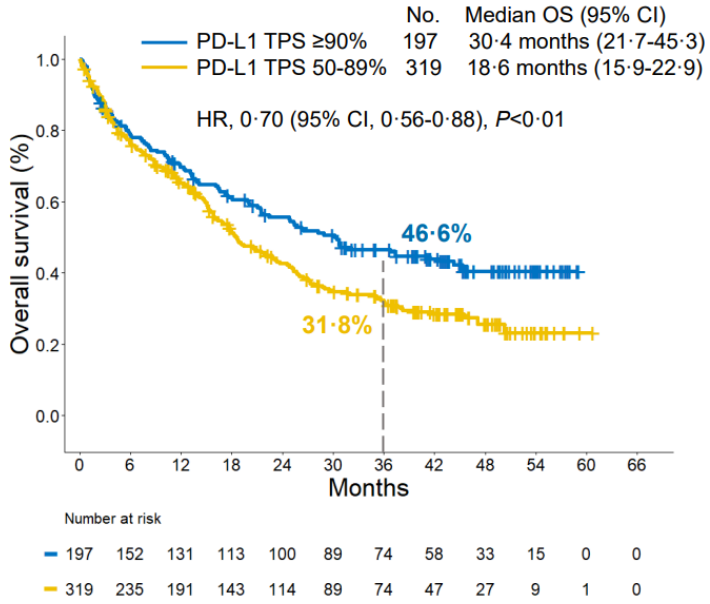


Brahmer JR et al., *J Clin Oncol*, 2023

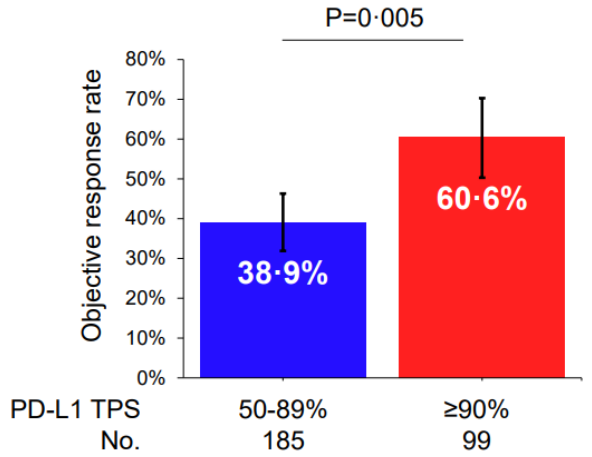
Very high PD-L1 TPS identifies a cohort of patients with favorable outcomes with PD-(L)1 inhibitor monotherapy

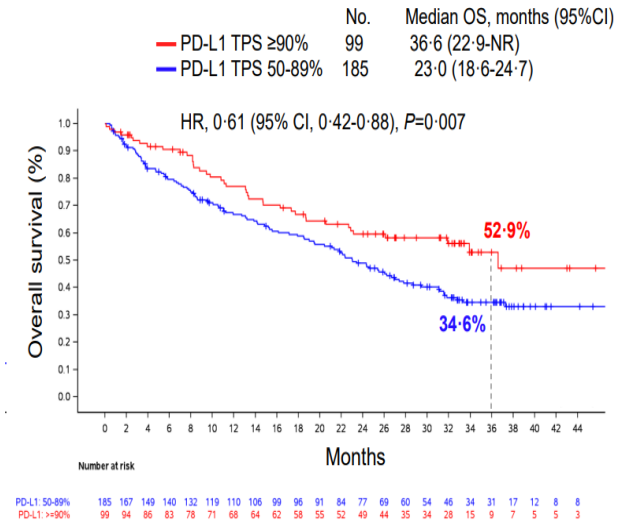
Retrospective cohort





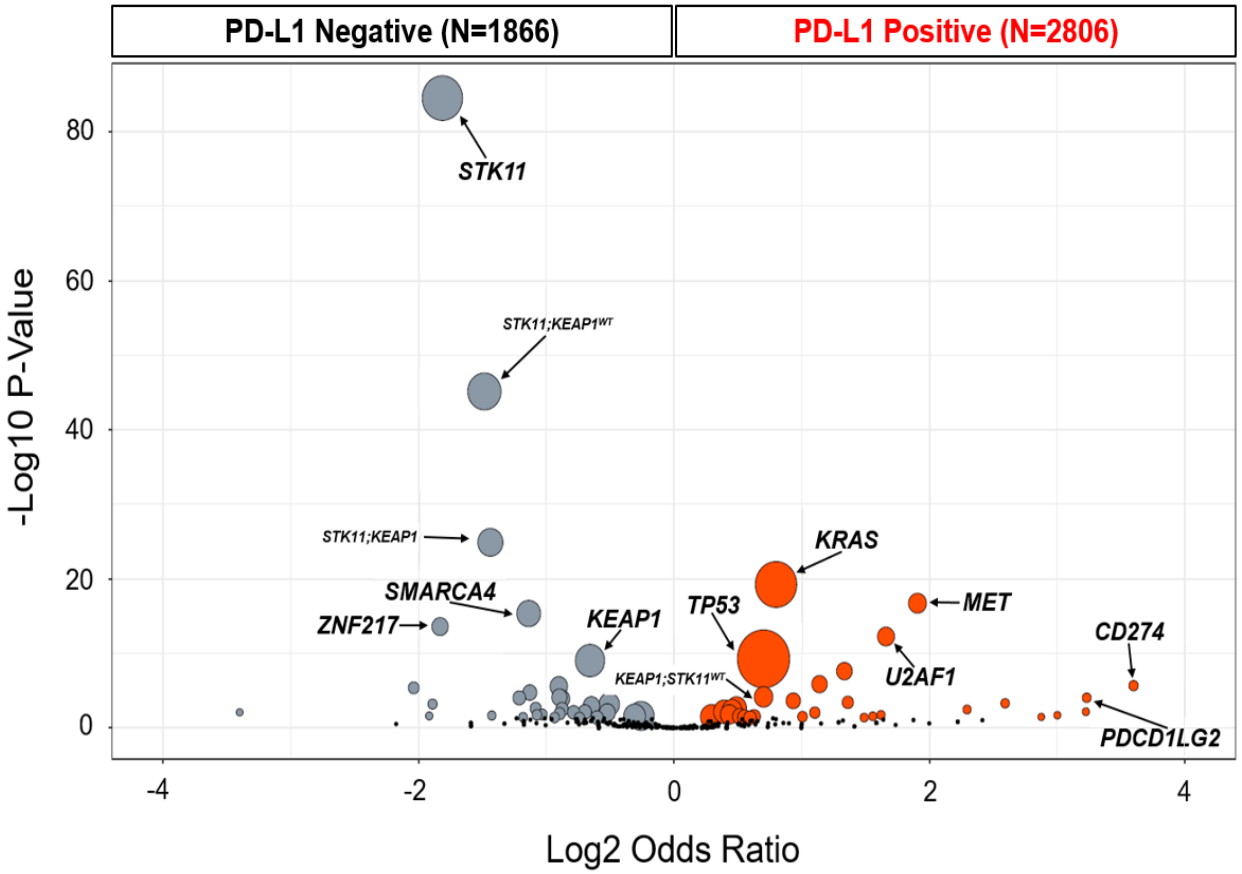
EMPOWER Lung-01





Ricciuti B et al., *JTO,* 2024

Oncogenotype and tumor cell PD-L1 expression in lung adenocarcinoma



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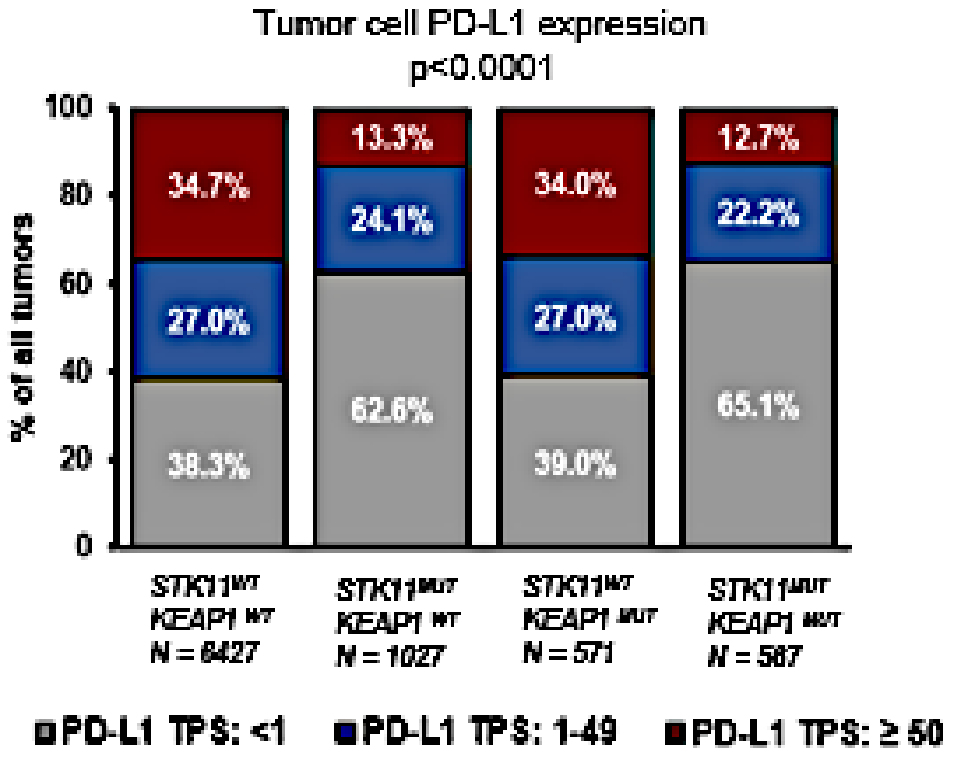
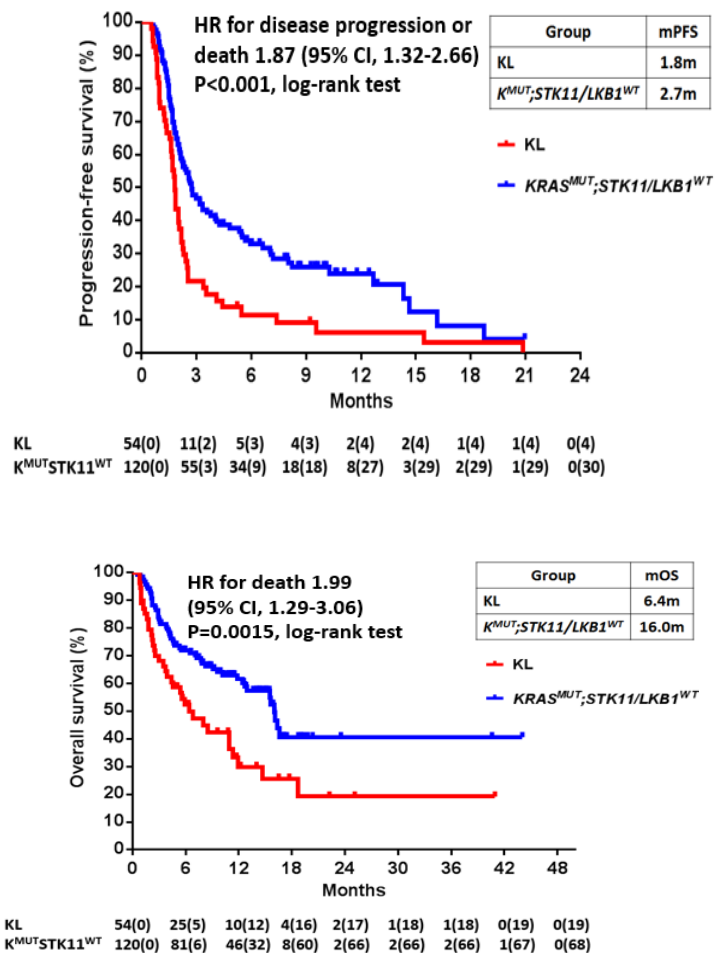


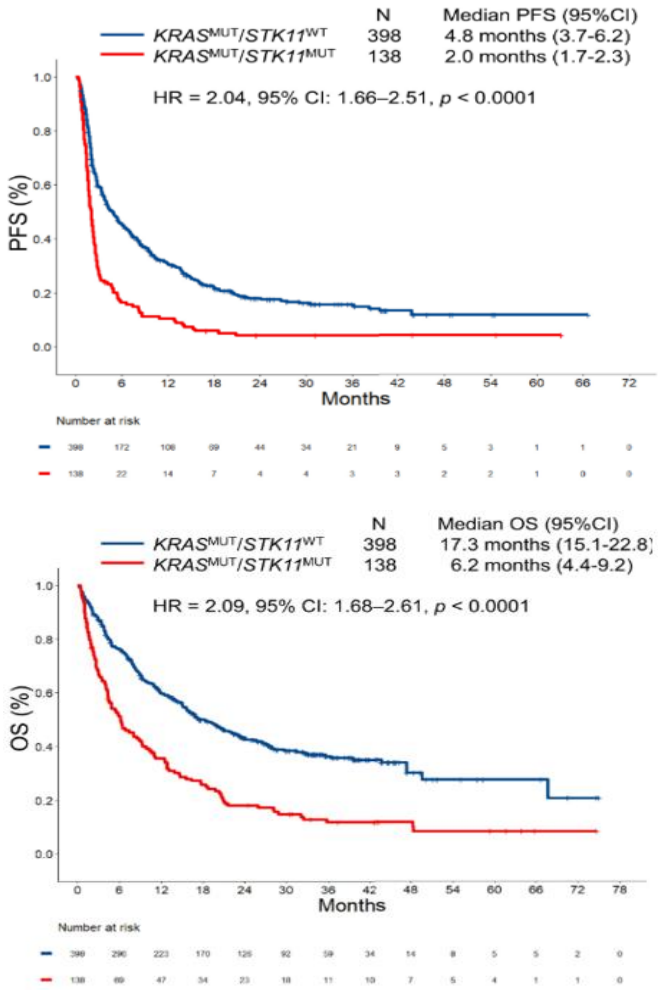
Skoulidis F et al., under review
Collaboration with Lee Albacker, FMI

STK11 and *KEAP1* alterations drive inferior clinical outcomes with PD-1 axis inhibitor monotherapy in *KRAS*-mutant NSCLC

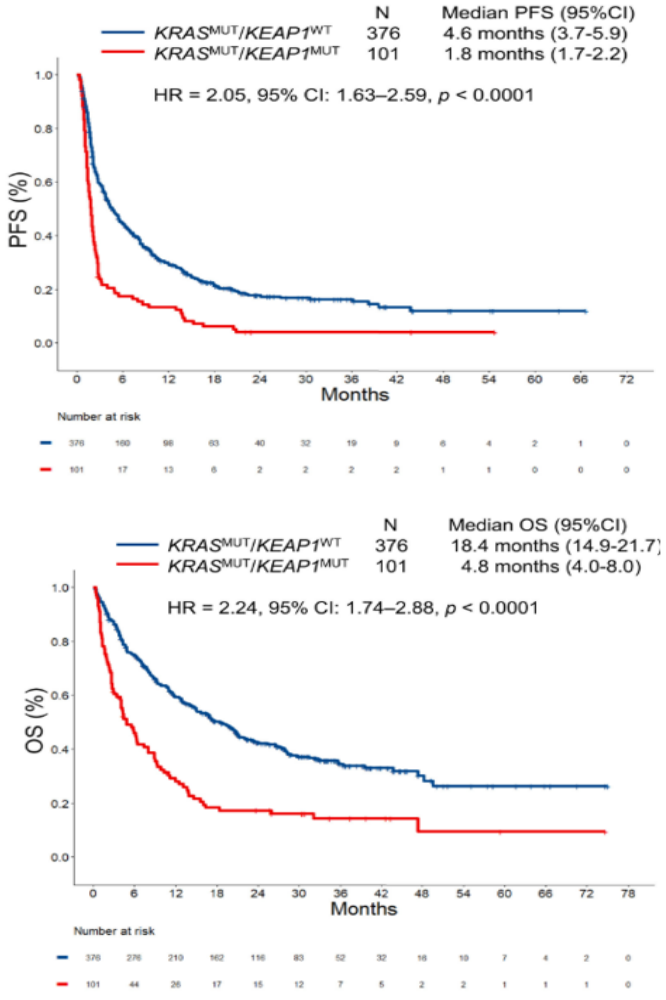
Skoulidis F et al., *Cancer Discov*, 2018



Ricciuti B et al., *JTO*, 2021

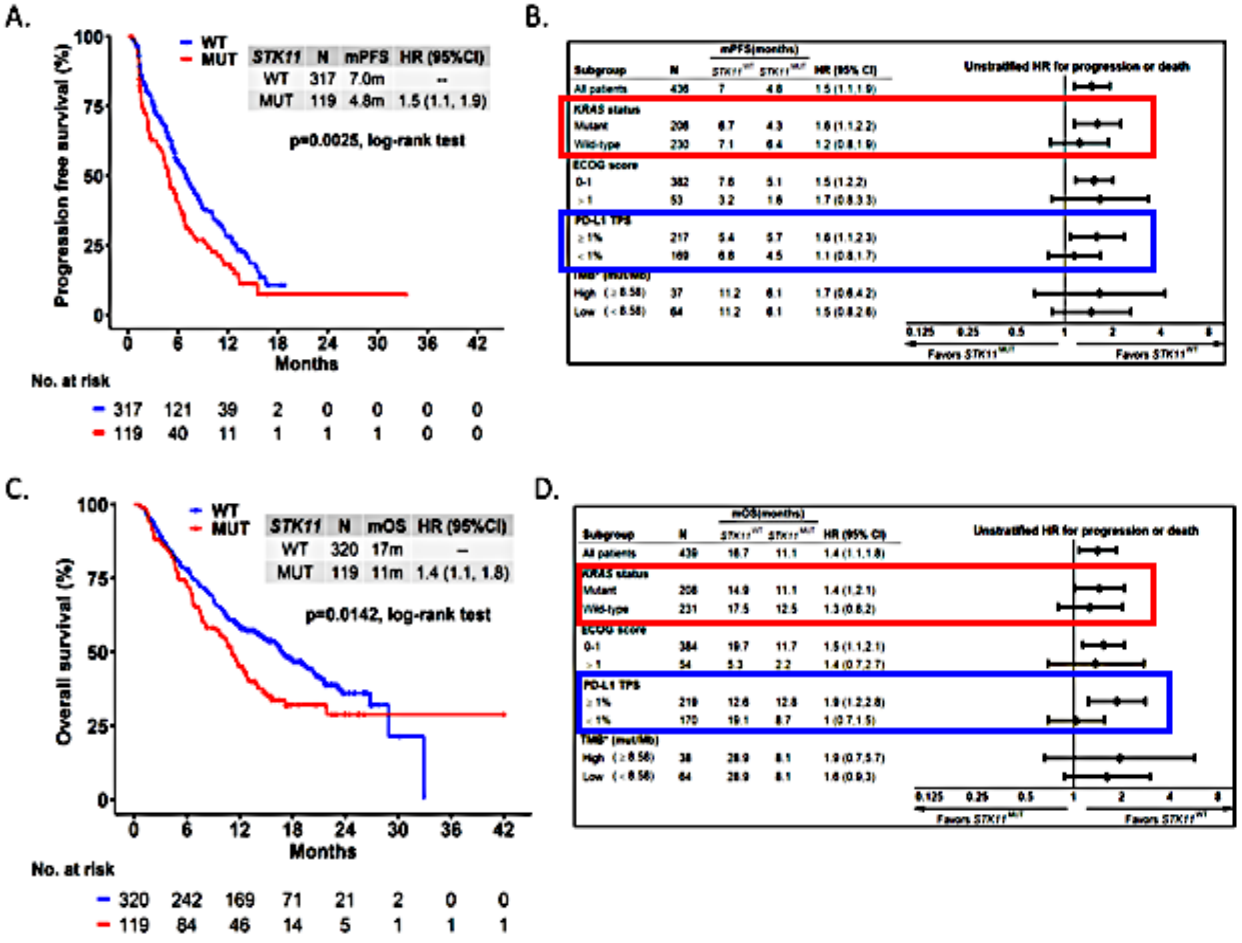


Ricciuti B et al., *J TO*, 2021

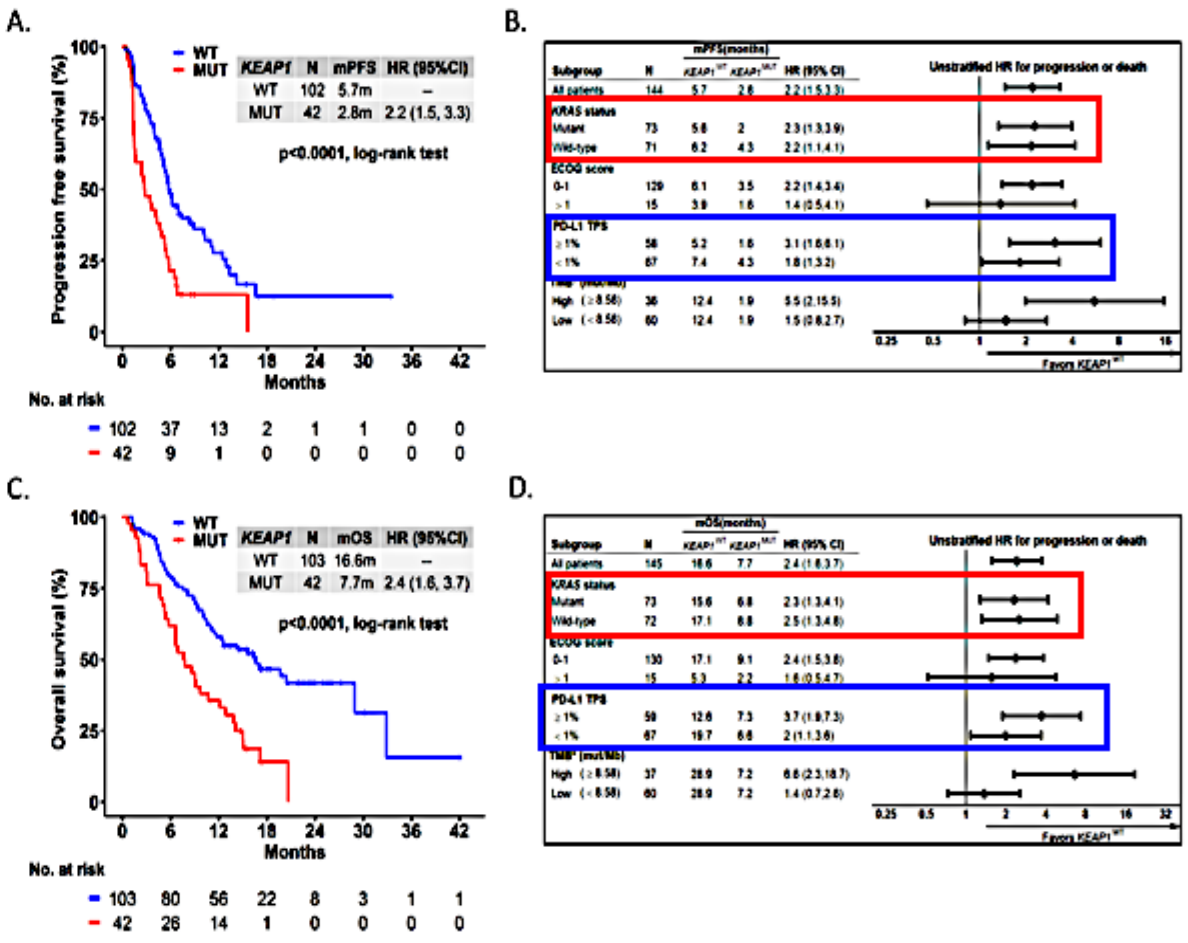


STK11 and *KEAP1* alterations and clinical outcomes with first-line PCP chemoIO. (platinum, pemetrexed, pembrolizumab)

STK11



KEAP1

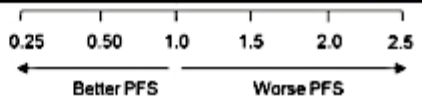


Skoulidis F et al, under review

STK11 and *KEAP1* alterations and clinical outcomes with 1st line chemoIO

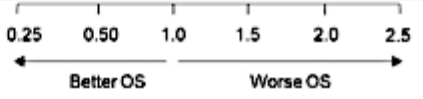
Forest-plot for progression-free survival (PFS)

Mutation status	N	HR (95%, CI) PFS	*P*-value
$KRAS^{WT}$	560	reference	
$KRAS^{MUT}$	351	1.10 (0.95-1.28)	0.21
$TP53^{WT}$	370	reference	
$TP53^{MUT}$	412	0.83 (0.71-0.97)	0.020
$STK11^{WT}$	516	reference	
$STK11^{MUT}$	191	1.46 (1.22-1.76)	<0.001
$KEAP1^{WT}$	518	reference	
$KEAP1^{MUT}$	189	1.53 (1.28-1.84)	<0.001
$SMARCA4^{WT}$	593	reference	
$SMARCA4^{MUT}$	114	1.62 (1.30-2.02)	<0.001
$KRAS^{WT}$ $TP53^{WT}$	182	reference	
$KRAS^{WT}$ $TP53^{MUT}$	287	0.88 (0.71-1.08)	0.21
$KRAS^{WT}$ $STK11^{WT}$	322	reference	
$KRAS^{WT}$ $STK11^{MUT}$	99	1.19 (0.93-1.54)	0.16
$KRAS^{WT}$ $KEAP1^{WT}$	327	reference	
$KRAS^{WT}$ $KEAP1^{MUT}$	104	1.37 (1.07-1.75)	0.01
$KRAS^{WT}$ $SMARCA4^{WT}$	361	reference	
$KRAS^{WT}$ $SMARCA4^{MUT}$	70	1.36 (1.03-1.81)	<0.001
$KRAS^{MUT}$ $TP53^{WT}$	188	reference	
$KRAS^{MUT}$ $TP53^{MUT}$	125	0.75 (0.58-0.97)	0.027
$KRAS^{MUT}$ $STK11^{WT}$	184	reference	
$KRAS^{MUT}$ $STK11^{MUT}$	92	1.92 (1.46-2.53)	< 0.001
$KRAS^{MUT}$ $KEAP1^{WT}$	191	reference	
$KRAS^{MUT}$ $KEAP1^{MUT}$	85	1.82 (1.38-2.41)	<0.001
$KRAS^{MUT}$ $SMARCA4^{WT}$	232	reference	
$KRAS^{MUT}$ $SMARCA4^{MUT}$	44	2.39 (1.67-3.42)	< 0.001



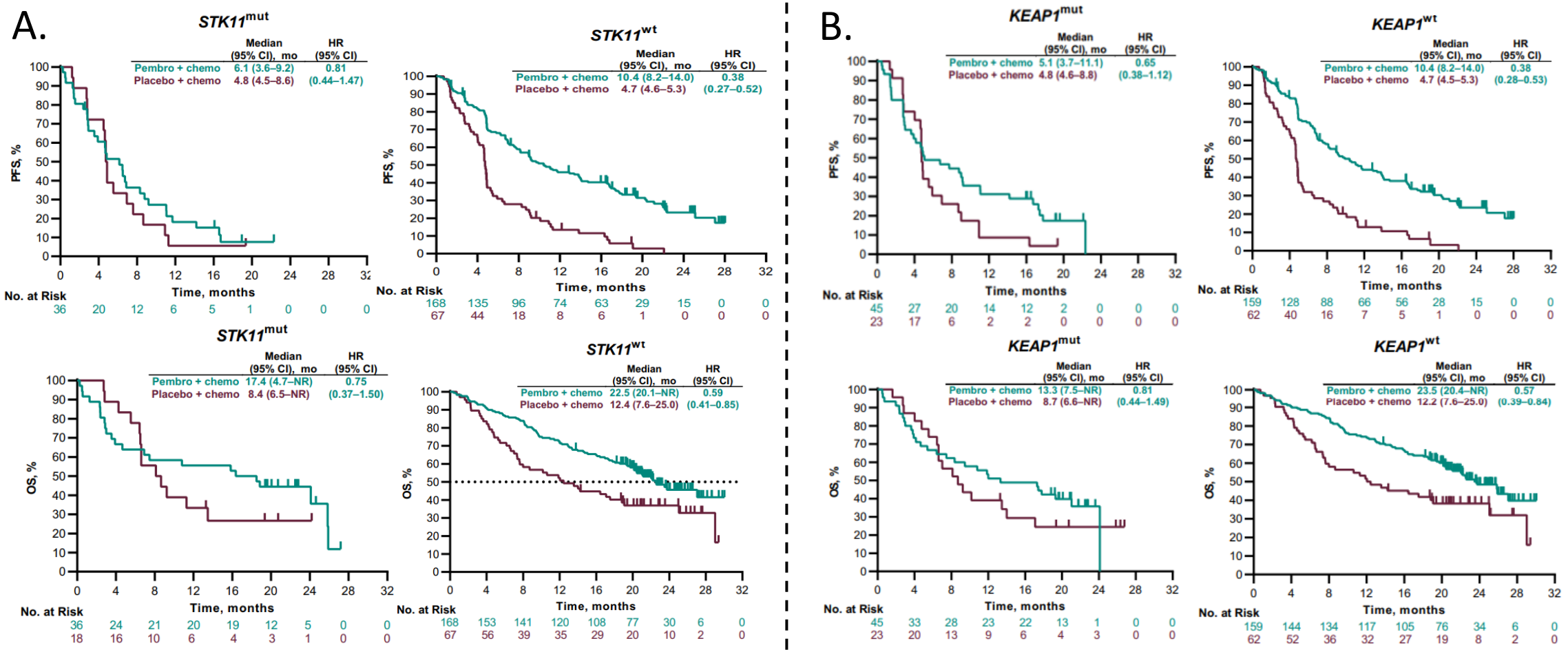
Forest-plot for overall survival (OS)

Mutation status	N	HR (95%, CI) OS	*P*-value
$KRAS^{WT}$	560	reference	
$KRAS^{MUT}$	351	1.07 (0.93-1.28)	0.42
$TP53^{WT}$	370	reference	
$TP53^{MUT}$	412	0.87 (0.73-1.04)	0.13
$STK11^{WT}$	516	reference	
$STK11^{MUT}$	191	1.36 (1.10-1.67)	0.004
$KEAP1^{WT}$	518	reference	
$KEAP1^{MUT}$	189	1.71 (1.40-2.10)	<0.001
$SMARCA4^{WT}$	593	reference	
$SMARCA4^{MUT}$	114	1.70 (1.33-2.17)	<0.001
$KRAS^{WT}$ $TP53^{WT}$	182	reference	
$KRAS^{WT}$ $TP53^{MUT}$	287	0.89 (0.70-1.13)	0.35
$KRAS^{WT}$ $STK11^{WT}$	322	reference	
$KRAS^{WT}$ $STK11^{MUT}$	99	1.14 (0.85-1.53)	0.38
$KRAS^{WT}$ $KEAP1^{WT}$	327	reference	
$KRAS^{WT}$ $KEAP1^{MUT}$	104	1.64 (1.25-2.17)	<0.001
$KRAS^{WT}$ $SMARCA4^{WT}$	361	reference	
$KRAS^{WT}$ $SMARCA4^{MUT}$	70	1.36 (0.98-1.88)	0.06
$KRAS^{MUT}$ $TP53^{WT}$	188	reference	
$KRAS^{MUT}$ $TP53^{MUT}$	125	0.85 (0.63-1.13)	0.27
$KRAS^{MUT}$ $STK11^{WT}$	184	reference	
$KRAS^{MUT}$ $STK11^{MUT}$	92	1.66 (1.22-2.26)	0.001
$KRAS^{MUT}$ $KEAP1^{WT}$	191	reference	
$KRAS^{MUT}$ $KEAP1^{MUT}$	85	1.78 (1.31-2.43)	<0.001
$KRAS^{MUT}$ $SMARCA4^{WT}$	232	reference	
$KRAS^{MUT}$ $SMARCA4^{MUT}$	44	2.52 (1.72-3.68)	<0.001



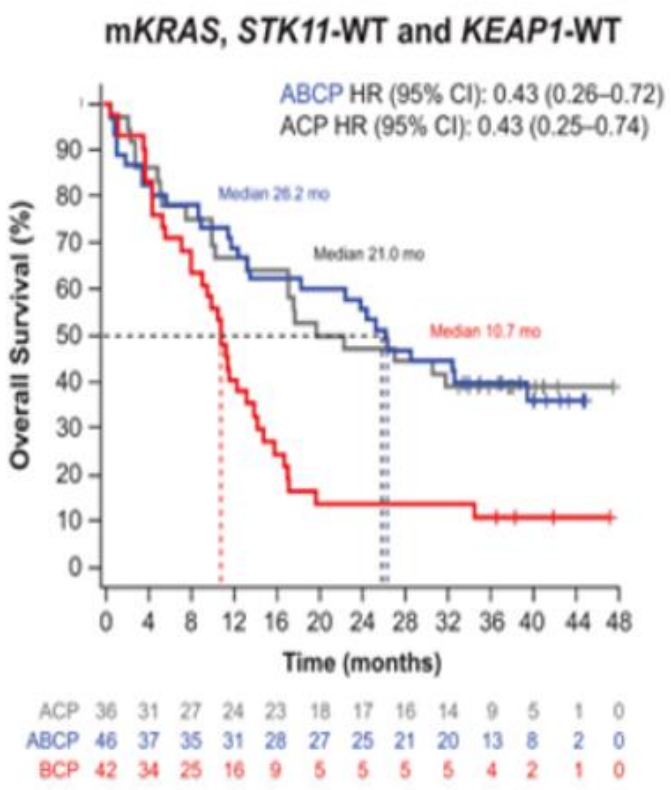
Alessi JV et al., *JTO,* 2023

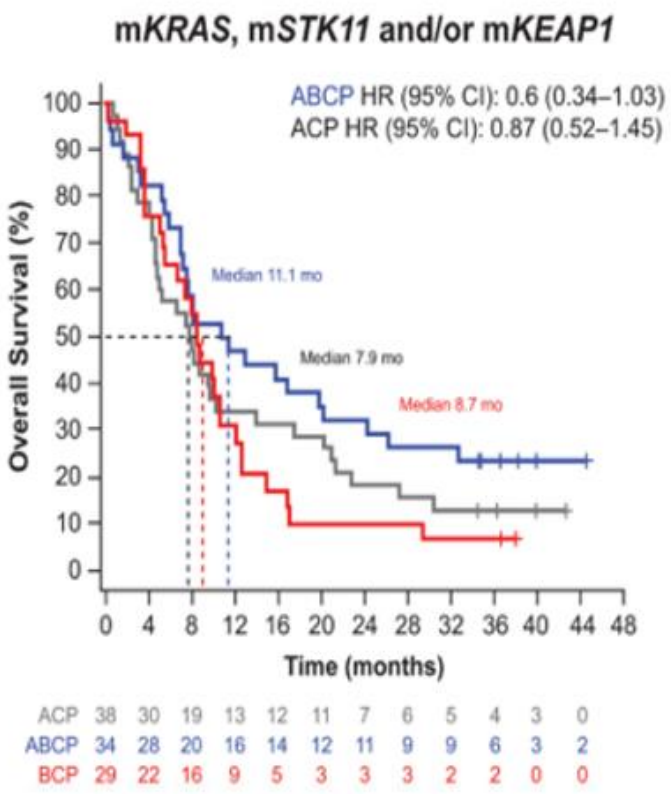
Reduced benefit from the addition of pembrolizumab to platinum doublet chemotherapy in patients with *STK11* and *KEAP1*-mutant NSCLC in KEYNOTE-189

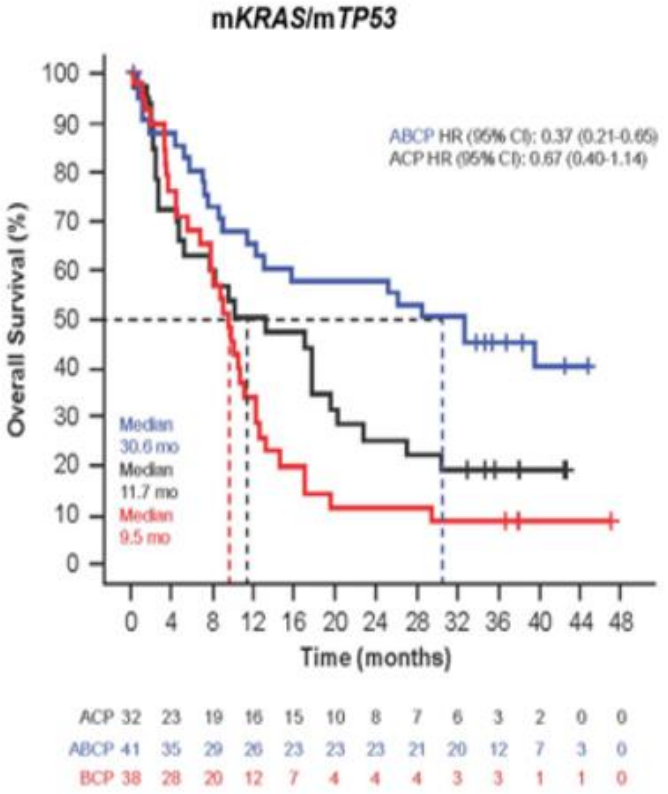


Garassino MC et al, JTO, 2022

Clinical outcomes in *KRAS* co-mutational subgroups in IMpower150



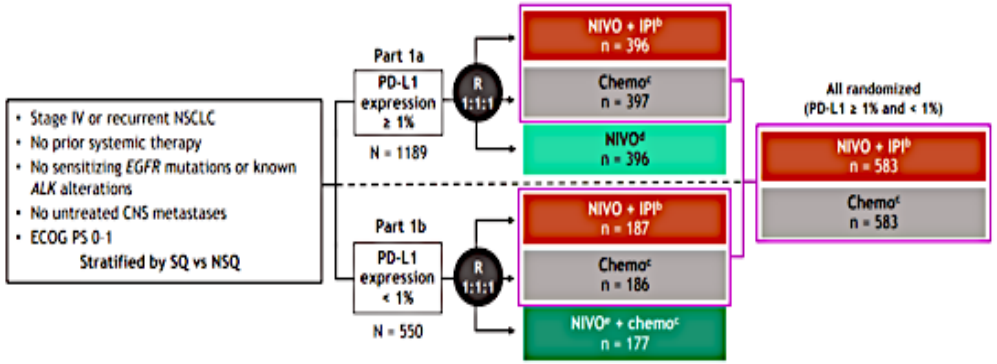




West HJ et al, JITC, 2021

STK11 and *KEAP1* alterations and clinical outcomes with ipi/nivo in Part 1 of CheckMate 227

A.



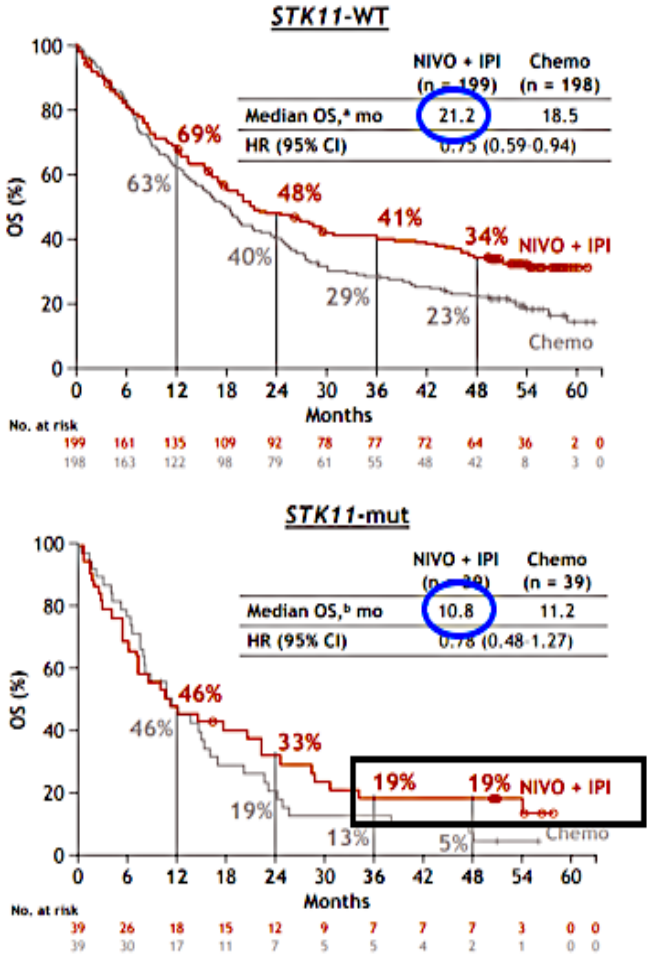
PD-L1 <1% : 29%
PD-L1 ≥1% : 71%
PD-L1 ≥50%: 37%
TMB≥10Mut/Mb : 40%
TMB<10Mut/Mb : 60%

B.

Subgroup, n[b]	4-y PFS rate, % NIVO + IPI	4-y PFS rate, % Chemo	Median PFS, mo NIVO + IPI	Median PFS, mo Chemo	Unstratified HR
NSQ (n = 419, 419)	14	3	5.2	5.6	0.82
Mut-eval (n = 238, 237)	14	3	5.6	5.6	0.76
KRAS-WT (n = 150, 162)	19	6	5.6	5.6	0.75
KRAS-mut (n = 88, 75)	17	2	5.4	5.8	0.78
TP53-WT (n = 111, 106)	10	5	5.4	5.6	0.88
TP53-mut (n = 127, 131)	24	7	5.8	6.6	0.69
STK11-WT (n = 199, 198)	19	6	8.1	6.1	0.72
STK11-mut (n = 39, 39)	13	0	2.8	4.3	1.04
KEAP1-WT (n = 218, 219)	16	6	5.5	5.8	0.83
KEAP1-mut (n = 20, 18)	41	0	11.1	2.9	0.25

KEAP1^{MUT}(N=38)
Ipi/Nivo: mOS 24.4m
Chemo: mOS 8.9m

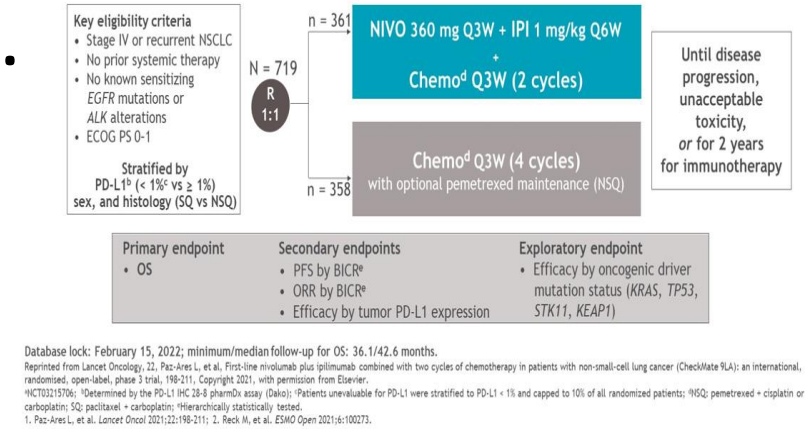
C.



Ramalingam S et al., ESMO Immuno-Oncology Congress,2021

Clinical outcomes with the CheckMate 9LA regimen in *STK11*-mutant NSCLC

A



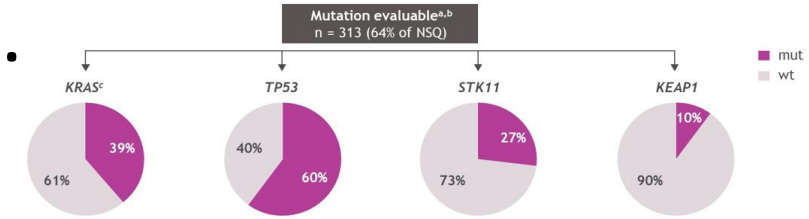
Database lock: February 15, 2022; minimum/median follow-up for OS: 36.1/42.6 months.

Reprinted from Lancet Oncology, 22, Paz-Ares L, et al. First-line nivolumab plus ipilimumab combined with two cycles of chemotherapy in patients with non-small-cell lung cancer (CheckMate 9LA): an international, randomised, open-label, phase 3 trial, 198-211, Copyright 2021, with permission from Elsevier.

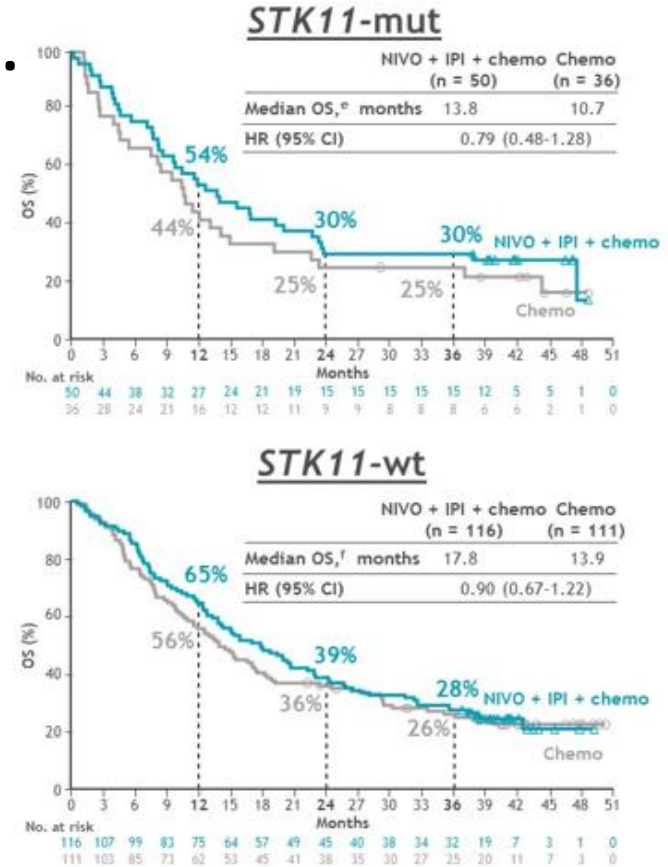
[b]NCT03215706; [c]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [d]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [e]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [f]Hierarchically statistically tested.

1. Paz-Ares L, et al. *Lancet Oncol* 2021;22:198-211; 2. Reck M, et al. *ESMO Open* 2021;6:100273.

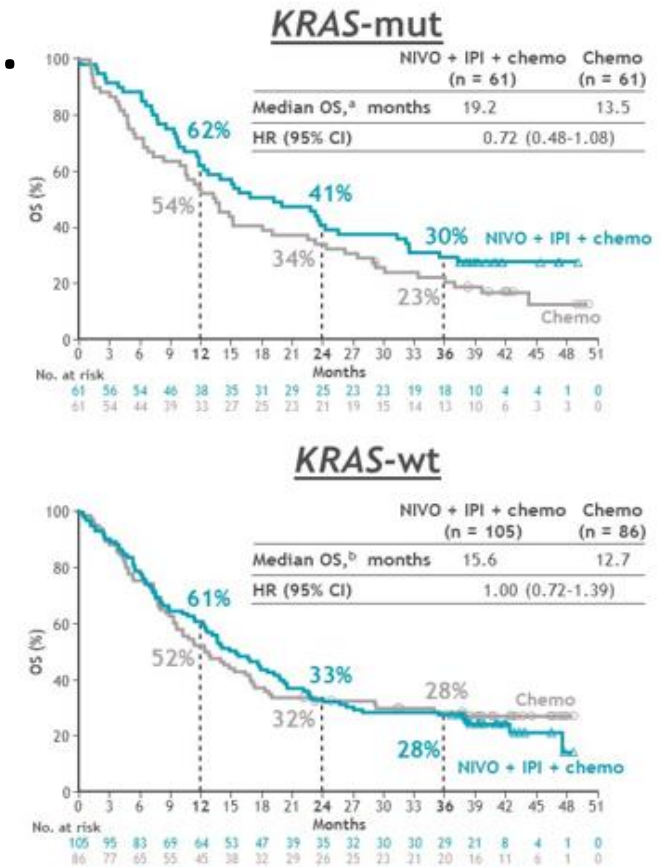
B



C



D



- Similar trend of OS benefit was seen with NIVO + IPI + chemo vs chemo in *KRAS G12C*-mut (n = 50) and *KEAP1*-mut (n = 32) subgroups

Database lock: February 15, 2022; minimum follow-up: 36.1 months.

[a]95% CI, 11.9-25.5 (NIVO + IPI + chemo) and 10.0-19.1 (chemo); [b]95% CI, 12.3-19.9 (NIVO + IPI + chemo) and 9.5-17.0 (chemo); [c]95% CI, 12.6-22.7 (NIVO + IPI + chemo) and 9.5-15.4 (chemo); [d]95% CI, 10.4-22.9 (NIVO + IPI + chemo) and 9.5-23.3 (chemo); [e]95% CI, 8.6-22.7 (NIVO + IPI + chemo) and 5.4-14.9 (chemo); [f]95% CI, 13.2-22.8 (NIVO + IPI + chemo) and 10.6-17.4 (chemo).

Paz-Ares L et al., ASCO, 2022

POSEIDON Study of Durvalumab+-Tremelimumab+Chemo for the 1st line Treatment of Metastatic NSCLC

A.

Stage IV NSCLC

N=1013 (randomised)

- *EGFR*/*ALK*wt
- ECOG PS 0 or 1
- Treatment-naïve for metastatic disease
- Tumour biopsy* and baseline plasma sample (for ctDNA)

Stratification factors

- PD-L1 expression (TC ≥50% vs <50%)
- Histology (NSQ vs SQ)
- Disease stage (IVA vs IVB)

R 1:1:1

- **T+D+CT**† **q3w 4 cycles** → **T (week 16 only) + D q4w until PD**
- **D+CT**† **q3w 4 cycles** → **D q4w until PD**
- **Platinum-based CT**† **q3w up to 6 cycles**

Primary endpoints

D+CT vs CT:

- PFS‡
- OS

Key secondary endpoints

T+D+CT vs CT:

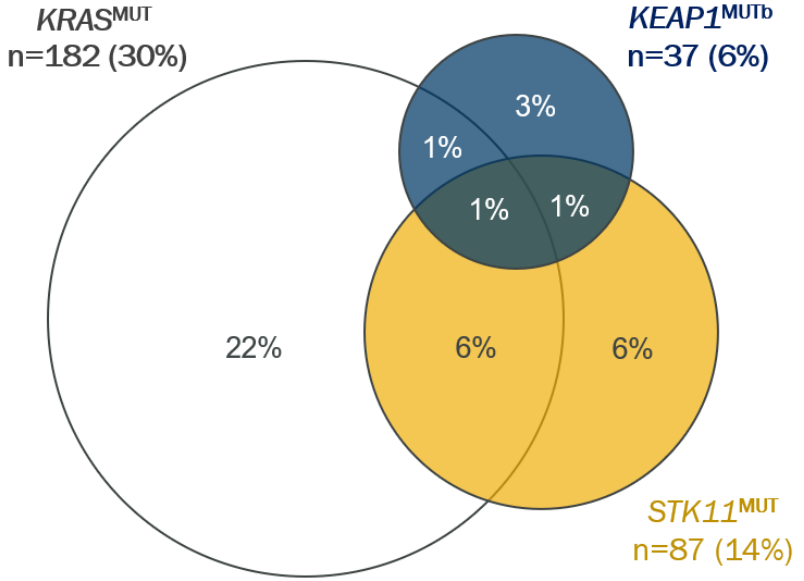
- PFS‡
- OS

- **Durvalumab** 1500mg ± **limited-course tremelimumab** 75mg + **CT** q3w for **4 cycles**
  - One additional dose of tremelimumab post-CT (week 16; 5th dose)
- Followed by **durvalumab q4w maintenance** until PD, and optional pemetrexed q4w§

B.

Mutation-Evaluable Population[a]

(n=612; 96% of randomized patients with NSQ histology)



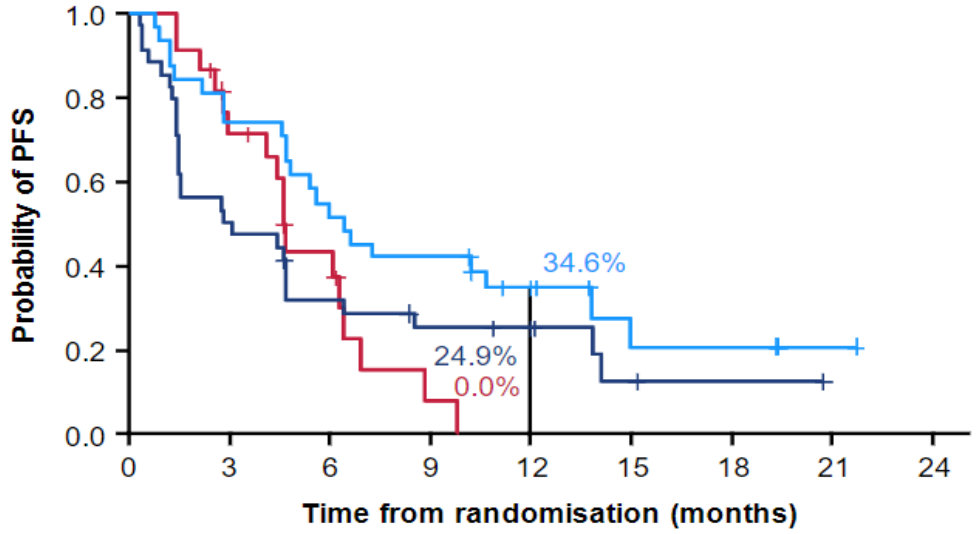
Peters S et al., WCLC, 2022

PFS and ORR with the POSEIDON regimen (D+T+chemo) in *STK11*-mutant NSCLC

A.

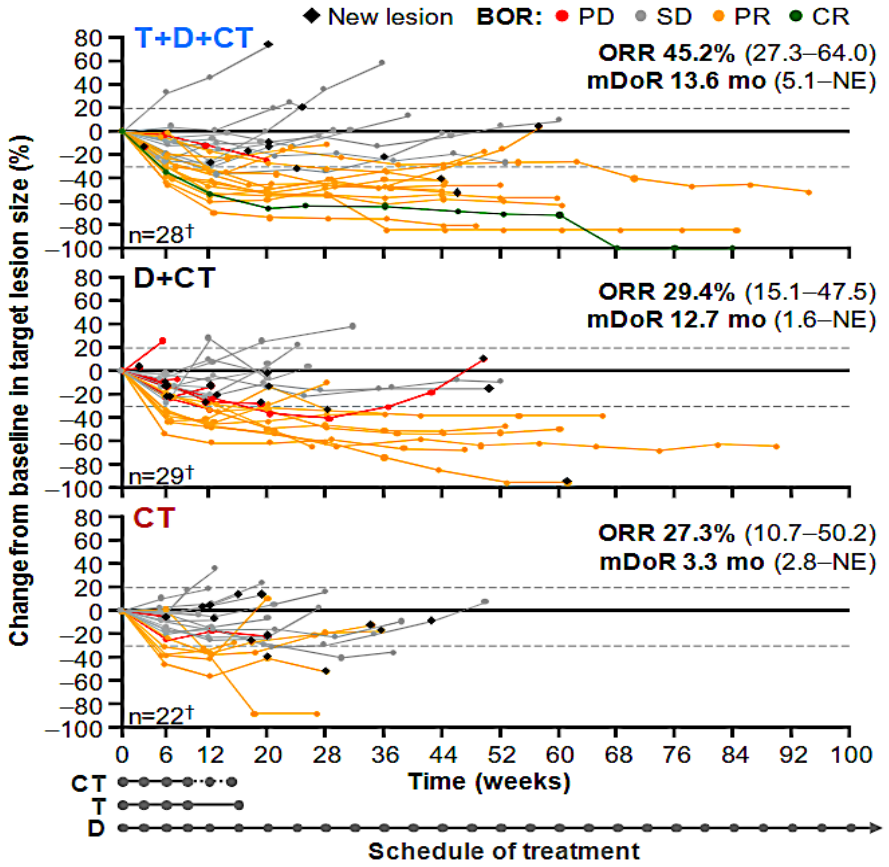
PFS

	T+D+CT	D+CT	CT
Events, n/N	22/31	27/34	17/22
mPFS, mo (95% CI)	**6.4** (4.7–13.8)	**2.9** (1.4–4.7)	**4.6** (2.9–6.4)
HR* (95% CI)	**0.47** (0.23–0.93)	**1.02** (0.55–1.93)	–



No. at risk									
T+D+CT	31	23	16	13	7	3	3	1	0
D+CT	34	17	10	7	5	2	1	0	0
CT	22	14	7	1	0	0	0	0	0

B.

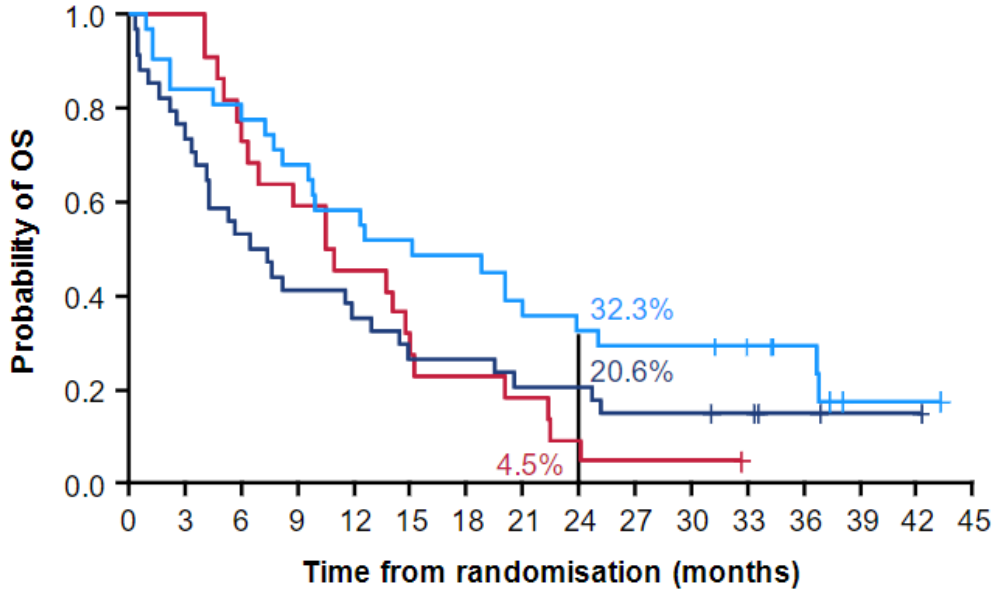


Peters S et al., WCLC, 2022

OS with the POSEIDON regimen (D+T+chemo) in *STK11*-mutant NSCLC

*STK11*m

	T+D+CT	D+CT	CT
Events, n/N	24/31	29/34	21/22
mOS, mo (95% CI)	**15.0** (8.2–23.8)	**6.9** (3.6–12.9)	**10.7** (6.0–14.9)
HR* (95% CI)	**0.56** (0.30–1.03)	**1.03** (0.59–1.84)	–

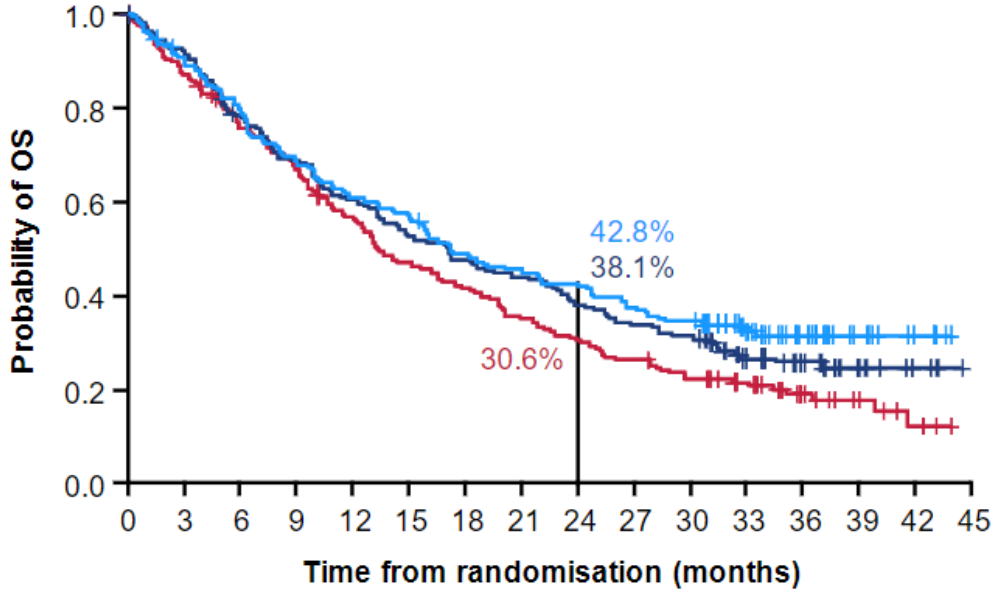


No. at risk

T+D+CT	31	26	24	21	18	15	15	11	10	9	9	7	5	1	1	0
D+CT	34	26	18	14	12	9	9	7	7	5	5	4	2	1	0	0
CT	22	22	16	13	10	6	5	4	1	1	1	0	0	0	0	0

*STK11*wt

	T+D+CT	D+CT	CT
Events, n/N	118/177	123/169	141/179
mOS, mo (95% CI)	**17.2** (14.9–22.1)	**17.1** (13.3–22.3)	**13.4** (11.5–17.5)
HR* (95% CI)	**0.73** (0.57–0.93)	**0.81** (0.64–1.04)	–



No. at risk

T+D+CT	177	159	140	120	107	100	85	79	74	65	60	40	25	11	5	0
D+CT	169	155	130	114	100	87	79	73	63	56	52	33	23	10	4	0
CT	179	154	131	116	97	80	71	60	52	45	37	29	15	8	4	0

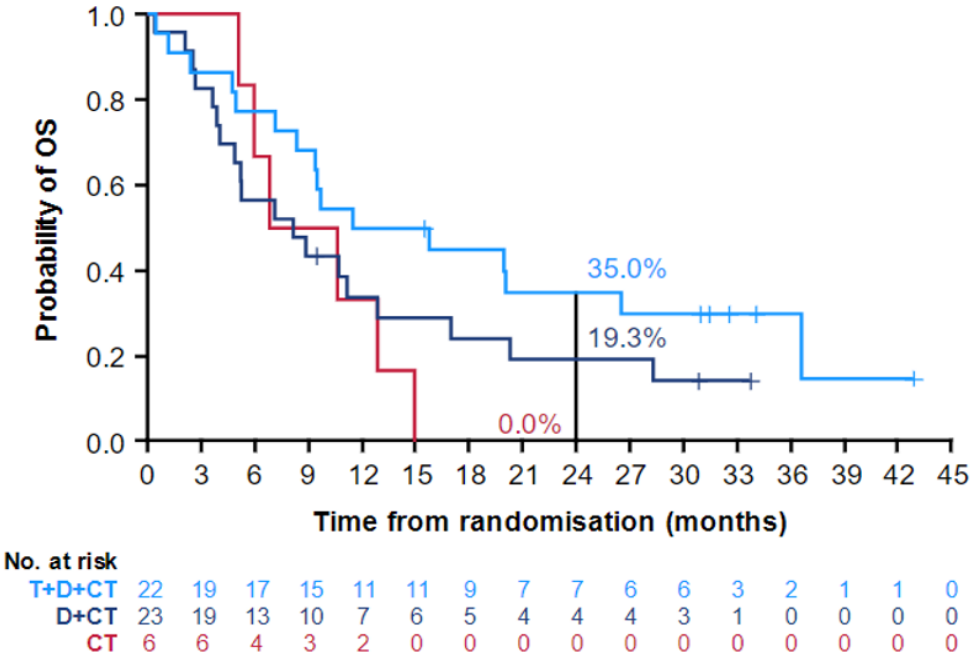
Peters S et al., WCLC, 2022

OS and ORR with the POSEIDON regimen (D+T+chemo) in *KEAP1*-mutant NSCLC

A.

***KEAP1*m**

	T+D+CT	D+CT	CT
Events, n/N	16/22	19/23	6/6
mOS, mo (95% CI)	**13.7** (7.2–26.5)	**8.1** (4.0–12.9)	**8.7** (5.1–NE)
HR* (95% CI)	**0.43** (0.16–1.25)	**0.77** (0.31–2.15)	–

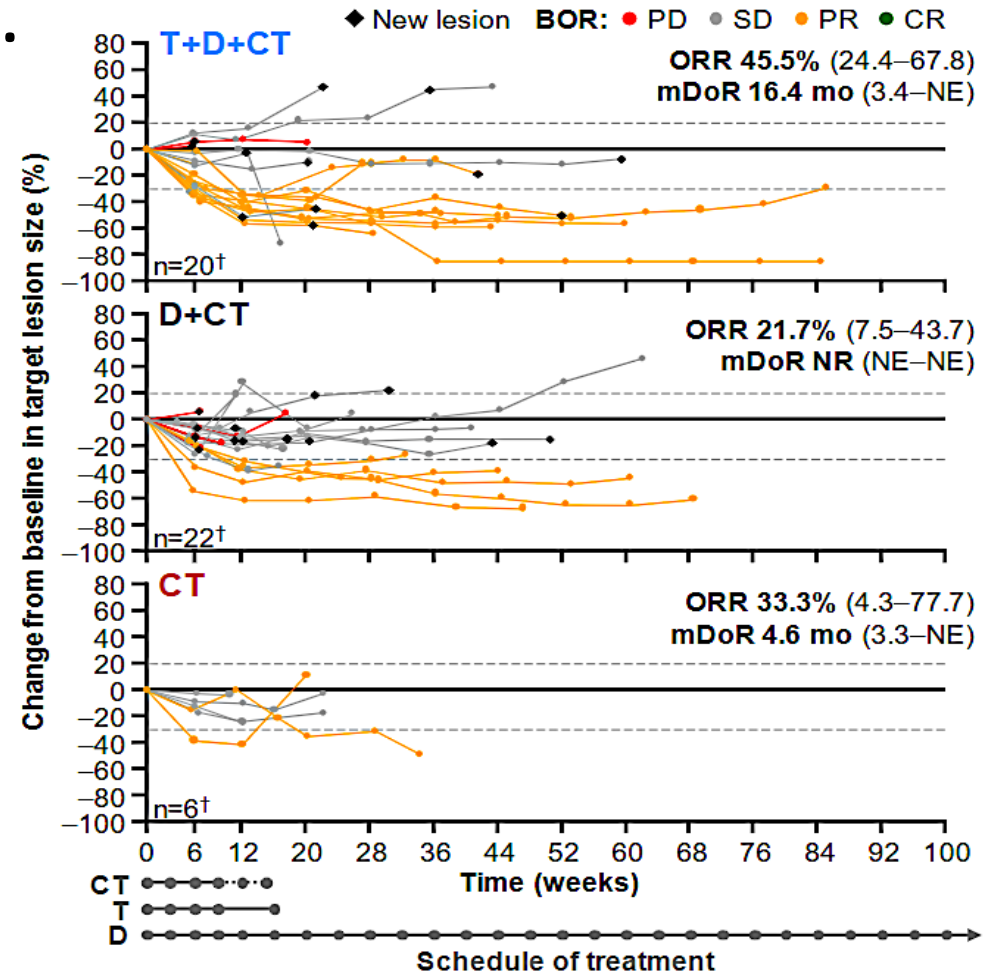


No. at risk

T+D+CT	22	19	17	15	11	11	9	7	7	6	6	3	2	1	1	0
D+CT	23	19	13	10	7	6	5	4	4	4	3	1	0	0	0	0
CT	6	6	4	3	2	0	0	0	0	0	0	0	0	0	0	0

HR (95% CI) vs CT in NSQ *KEAP1*m was 0.33 (0.10–1.15) with T+D+CT and 0.67 (0.23–2.17) with D+CT

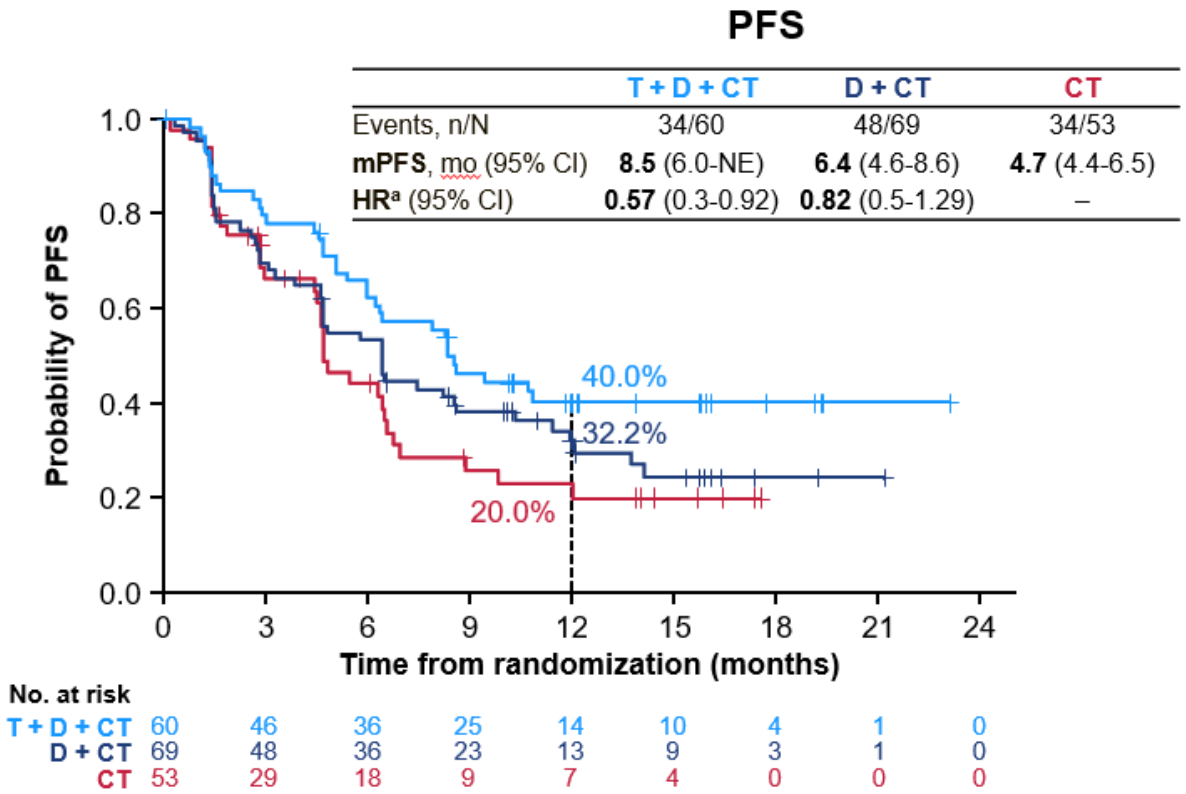
B.



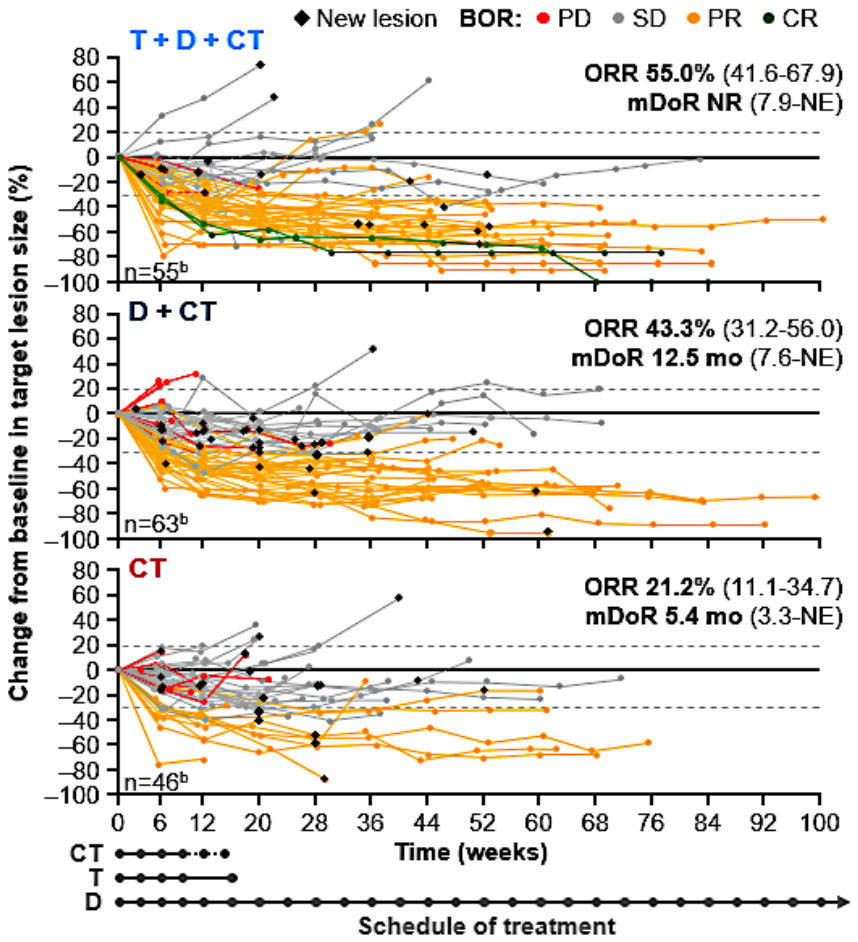
Peters S et al., WCLC, 2022

PFS and ORR with the POSEIDON regimen (D+T+chemo) in *KRAS*-mutant NSCLC (4-year update)

A.



B.

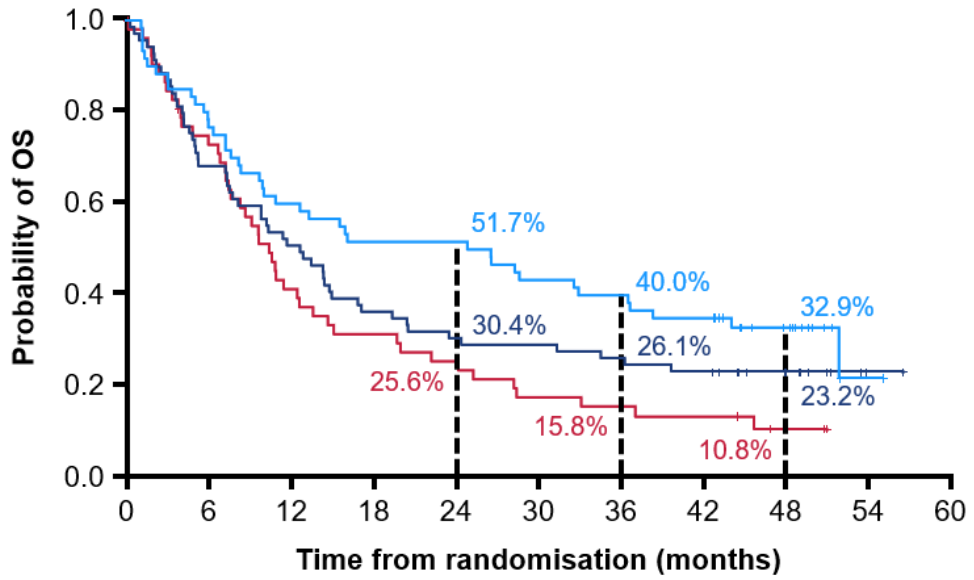


Johnson ML et al., ESMO, 2022

OS with the POSEIDON regimen (D+T+chemo) in *KRAS*-mutant and wild-type NSCLC (4-year update)

*KRAS*m

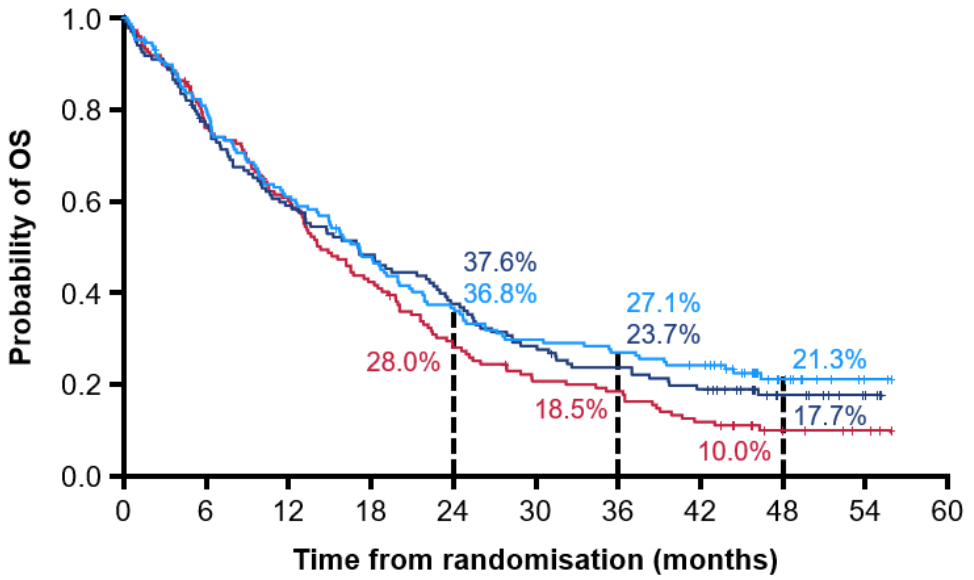
	T+D+CT	D+CT	CT
Events, n/N	41/60	53/69	45/53
mOS, months (95% CI)	**25.7** (9.9–36.7)	**12.6** (7.5–16.9)	**10.4** (7.5–13.6)
HR* (95% CI)	**0.55** (0.36–0.85)	**0.78** (0.52–1.16)	–



No. at risk											
T+D+CT	60	46	36	31	31	26	24	21	12	1	0
D+CT	69	47	35	25	21	20	18	16	9	1	0
CT	53	37	21	16	13	9	7	6	2	0	0

*KRAS*wt

	T+D+CT	D+CT	CT
Events, n/N	113/148	107/134	127/148
mOS, months (95% CI)	**17.1** (13.4–20.1)	**17.1** (12.3–22.6)	**14.4** (12.6–18.3)
HR* (95% CI)	**0.78** (0.60–1.00)	**0.83** (0.64–1.08)	–

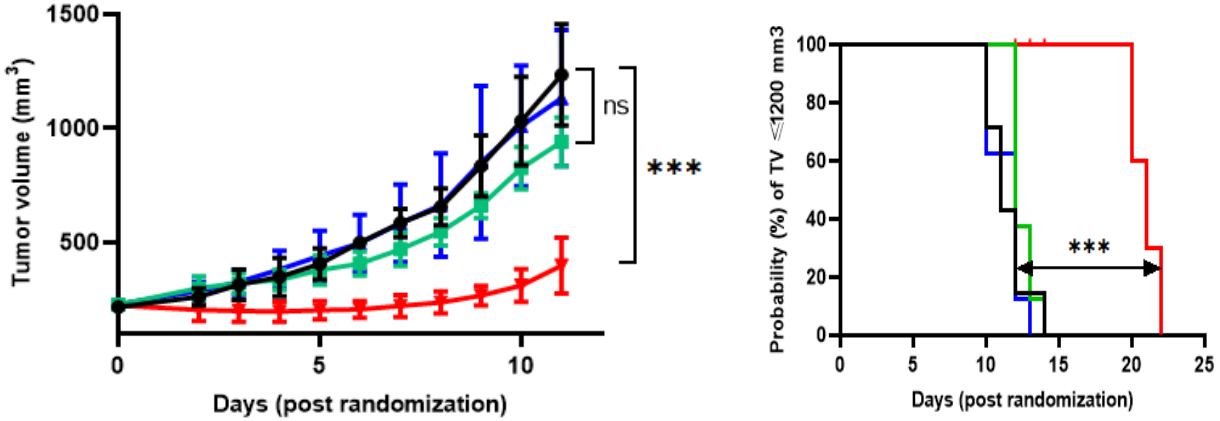


No. at risk											
T+D+CT	148	118	89	69	53	43	39	34	12	2	0
D+CT	134	101	77	63	49	37	30	24	11	3	0
CT	148	110	86	60	39	28	25	16	7	4	0

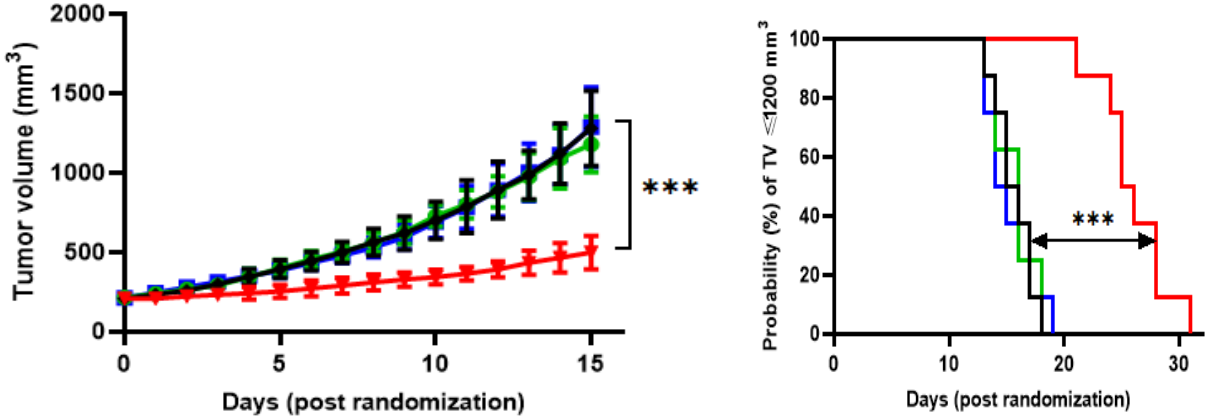
Johnson ML et al., ESMO, 2022

Sensitivity of *Kras^{MUT};Stk11$^{-/-}$* lung adenocarcinomas to dual anti-PD-1/anti-CTLA-4 ICB is recapitulated in syngeneic models

KL2 (Kras^{G12C};Stk11$^{-/-}$)



KL5 (Kras^{G12C};Stk11$^{-/-}$)



IgG control αPD-1 αCTLA-4 αPD-1 + αCTLA-4

Skoulidis F et al., under review

My current practice for the 1st-line treatment of NSCLC pts with distinct onco-genotypes

Non-squamous NSCLC, no driver alterations

ONCO-GENOTYPE	FIRST LINE OPTIONS
KRAS$^{MUT\ or\ WT}$;*STK11*^{MUT};*KEAP1*^{WT}	1. **POSEIDON (PS 0-1); 2. 9-LA (PS 0-1);** 3. Ipi/Nivo; 4. PCP (more borderline PS, c/indication to αCTLA-4, potential outlier with high PD-L1 TPS, high TMB etc). Or 1. **Clinical trial** (1st line RASi combo etc)
KRAS$^{MUT\ or\ WT}$;*STK11*^{WT};*KEAP1*^{MUT}	1. **POSEIDON or 9-LA (PS 0-1)** 2. Ipi/Nivo; 3. PCP (borderline PS, c/indication to αCTLA-4, high PD-L1 TPS and/or high TMB). • Can consider a-PD-(L)1 monotherapy if *KRAS*^{WT} + PD-L1^{High} and/or TMB^{High}, borderline PS • If any additional poor outcome predictors (*SMARCA4* mut etc) I favor dual ICB+- chemo
KRAS$^{MUT\ or\ WT}$;*STK11*^{MUT};*KEAP1*^{MUT}	1. **POSEIDON or 9-LA (PS 0-1)** 2. Ipi/Nivo; 3. PCP (more borderline PS, c/indication to αCTLA-4, potential outlier with high PD-L1 TPS, high TMB etc). Or 1. **Clinical trial** (1st line RASi combo etc)
KRAS$^{MUT\ or\ WT}$;*STK11*^{WT};*KEAP1*^{WT}	**PD-L1 TPS <1%** : **1. PCP**; 2. POSEIDON or 9-LA or Ipi/Nivo (for good PS, high burden, aggressive biology) **PD-L1 TPS 1-49%: 1. PCP;** 2. POSEIDON or 9-LA or Ipi/Nivo in pts with high burden/aggressive biology/lower PD-L1 TPS; 3. Pembro (if poor PS, organ dysfunction etc). **PD-L1 TPS ≥50%** : **1. Pembro or PCP (high burden, threatened organs, rapid growth)** Or **1. Clinical trial** (1st line RASi combo etc)

Squamous NSCLC

PD-L1 TPS	FIRST LINE OPTIONS
<1%	1. **IPI/NIVO or 9-LA (PS 0-1);** 2. KN-407
1-49%	1. **KN407;** 2. IPI/NIVO or 9-LA (PS 0-1). I favor dual ICB if brain mets
≥50%	1. **Pembro or KN-407**

Conclusions

- A number of regimens incorporating single (αPD1/αPD-L1) or dual (αPD-(L)1/αCTLA-4) ICB with or without platinum based chemotherapy are FDA approved. This raises the question of how to select the optimal regimen for individual patients.
- Clinical decision making for selection of 1st line systemic therapy for patients with advanced NSCLC is currently based on (a) Histology; (b) Tumor cell PD-L1 expression; (c) clinical characteristics (tumor burden, threatened organs, brain mets, liver mets, co-morbidities); (d) absence of targetable genomic drivers.
- Somatic mutations in *KEAP1* and/or *STK11* identify difficult to treat subgroups of patients with mNSCLC that exhibit poor clinical outcomes with PD-(L)1 inhibitor – based chemo-immunotherapy (such as the KEYNOTE-189 regimen) or PD-(L)1 monotherapy, especially in patients harboring *KRAS*-mutant NSCLC.
- Loss of KEAP1 and/or STK11 may impart selective sensitivity to dual immune checkpoint blockade with anti-PD-(L)1+ anti-CTLA-4.
- Chemo-IO regimens that incorporate anti-CTLA-4 in addition to anti-PD-(L)1 (such as 9LA and POSEIDON) may represent a preferred approach in *STK11* and/or *KEAP1*-mutated NSCLC with good PS. Data from POSEIDON appear the most robust to date in this patient population.
- *STK11*, *KEAP1* represent emerging biomarkers for selection of first-line regimens in advanced NSCLC.
- A randomized controlled clinical trial (TRITON) (POSEIDON regimen vs KEYNOTE 189) in patients with previously untreated metastatic NSCLC with *STK11*, *KEAP1* or *KRAS* alterations is under development to confirm findings from POSEIDON
- AI-supported integration of clinical, molecular (pathological/genomic), transcriptomic and radiomic features may further refine criteria for selection of optimal 1st line systemic therapy regimens in advanced NSCLC.

Thank you !

Endorsed by

IASLC INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER
Conquering Thoracic Cancers Worldwide