Immunotherapy in Advanced NSCLC: Initial Therapy and How to Overcome Resistance

(EGFR, ALK, ROS & RET Wild Type)

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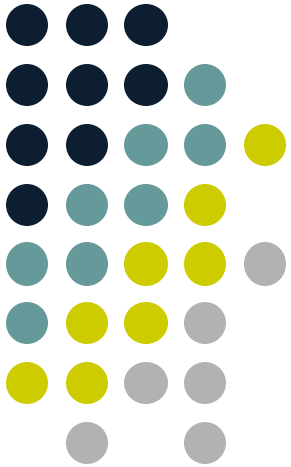
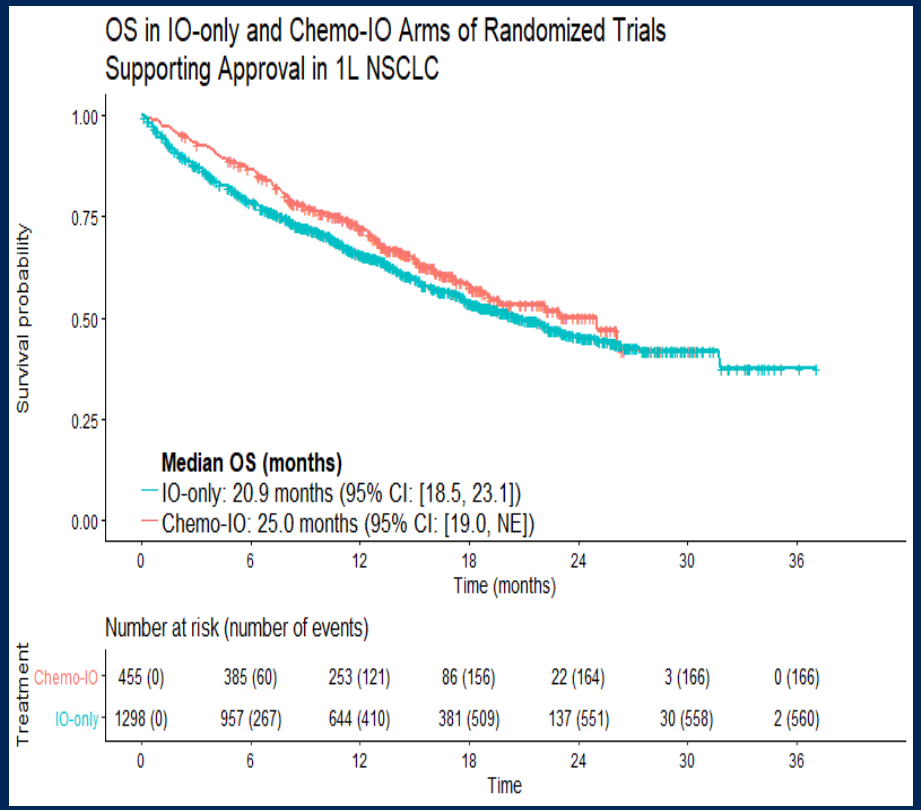


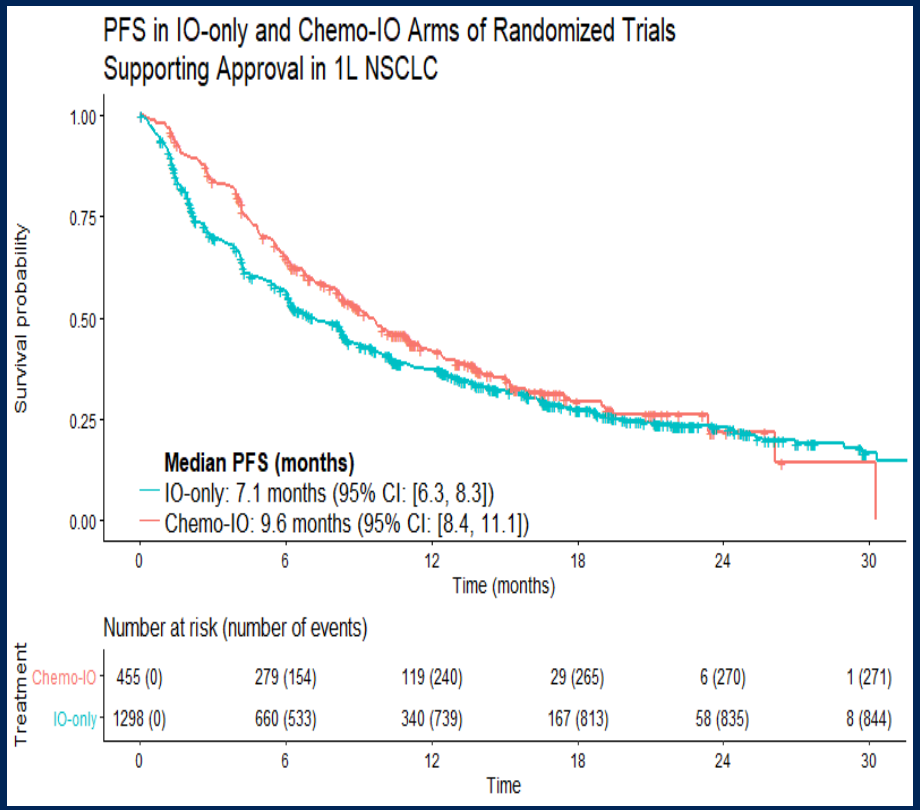
First-line NSCLC
Immunotherapy Biomarker Based treatment Selection

Phase III IO trials in Advanced-NSCLC

	Pathology	PDL-1	Arm I (OS)	Arm II (OS)	HR
KEYNOTE-024	squamous (18%) and nonsquamous (82%)	≥50%	Pembro	Chemotherapy	
			30 months	14.2 months	0.63
KEYNOTE-042	squamous (38%) and nonsquamous (62%)	≥1%	Pembro	Chemo	
			16.7 months	12.1 months	0.81
KEYNOTE-189	nonsquamous	Any level	Pembro/Pem/Plat	Plat/Pem	
			22 months	10.7 month	0.56
KEYNOTE-407	squamous	Any level	Pembro/Carbo/Tax	Carbo/Taxane	
			15.9 months	11.3 months	0.64
CHECKMATE-227	squamous (28%) and nonsquamous (72%)	Any level ≥1% <1%	Ipi/Nivo	Chemotherapy	
			17.1 months	14.9 months	0.79
			17.2 months	12.2 months	0.62
CHECKMATE 9LA	squamous and nonsquamous	Any level	Ipi/Nivo/Chemo	Plat/Pem or Taxane	
			15.6 months	10.9 months	0.66
IMpower110	squamous (25%) and nonsquamous (75%)	≥50%	Atezo	Plat/Pem or Gem	
			20.2 months	13.1 months	0.59
IMpower130	non-squamous	Any level	Atezo/Carbo/NbT	Carbo/NbT	
			18.6 months	13.9 months	0.79
IMpower150	non-squamous	Any level	Atezo/Bev/Carbo/Pac	Bev/Carbo/Pac	
			19.8 months	14.9 months	0.76

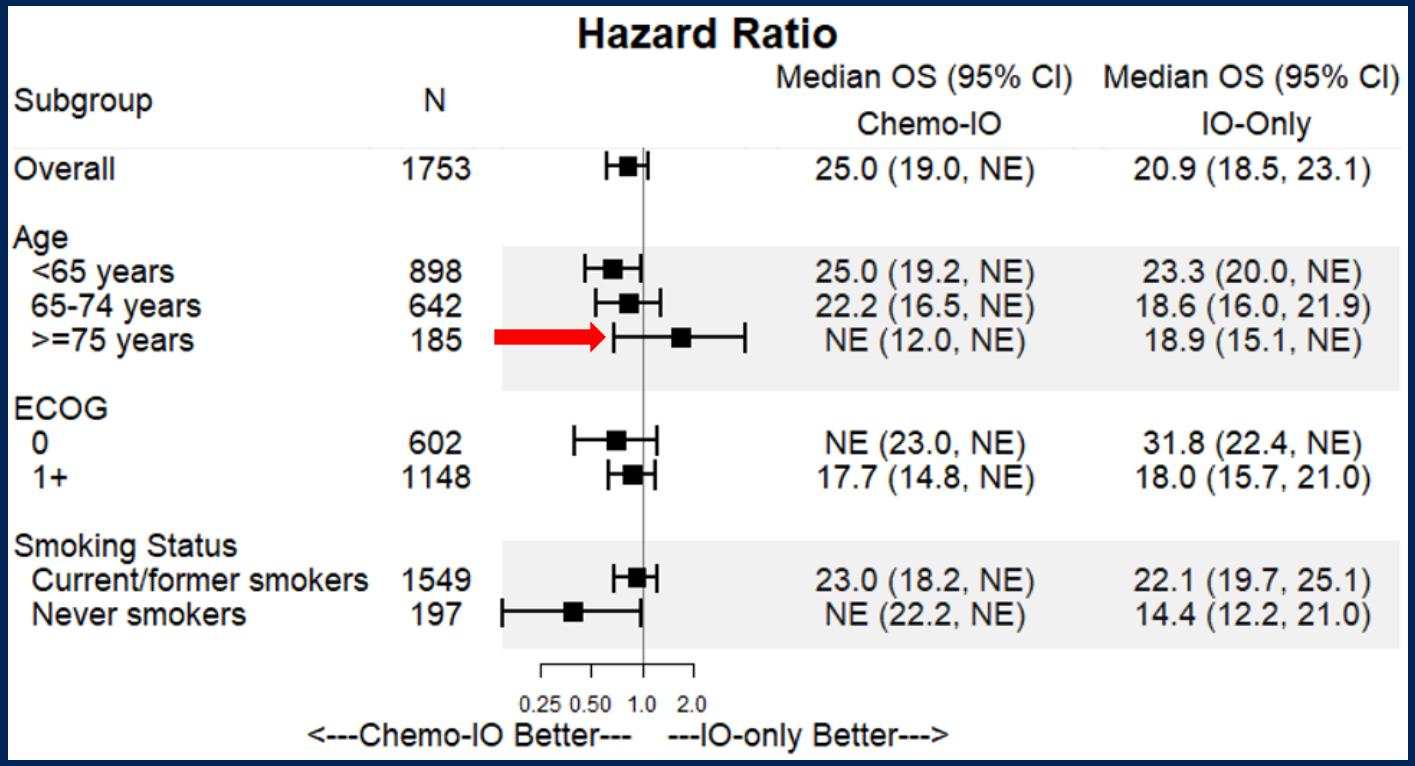
Exploratory OS/PFS: Chemo-IO vs IO in NSCLC PD-L1 ≥50%





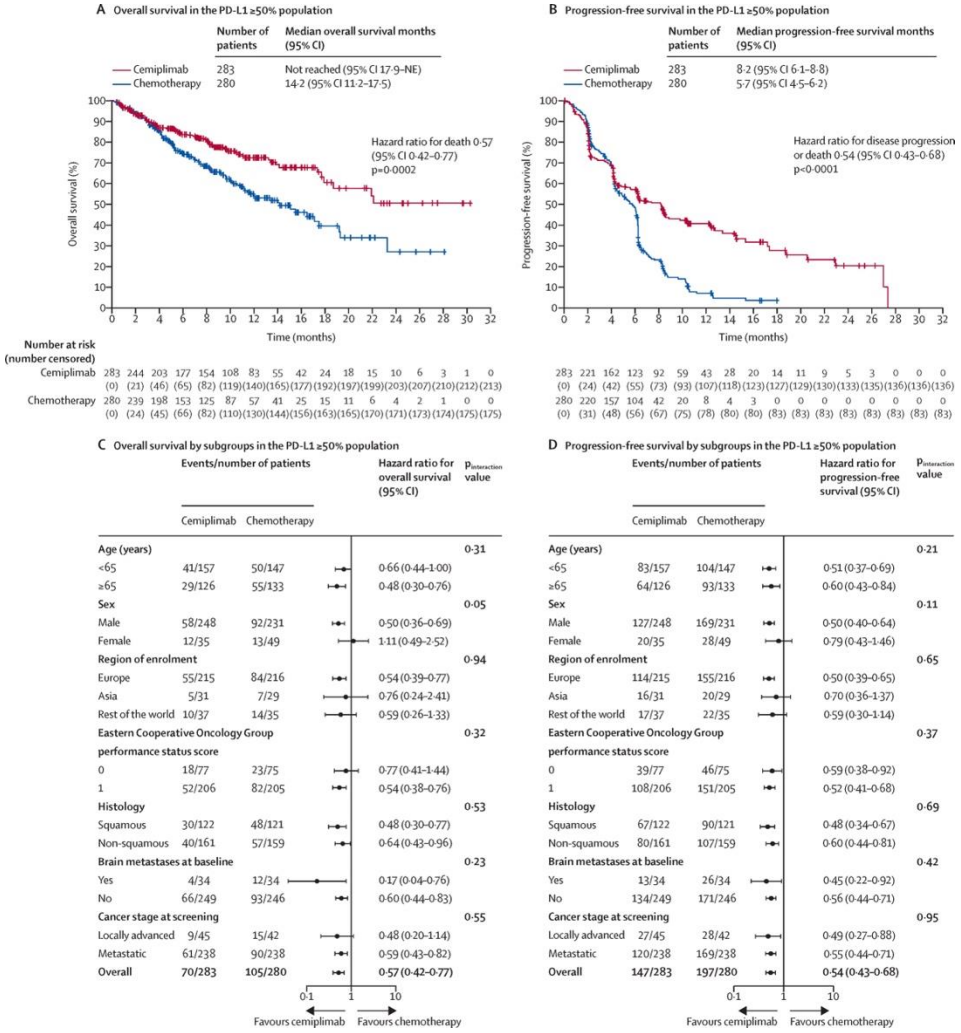
Abbreviations: Chemo-IO= platinum-based doublet chemotherapy plus immunotherapy; CI=confidence interval; HR=hazard ratio; IO=immunotherapy; NE=not estimable; NSCLC=non-small-cell lung cancer; OS=overall survival; PD-L1=programmed death ligand-1.

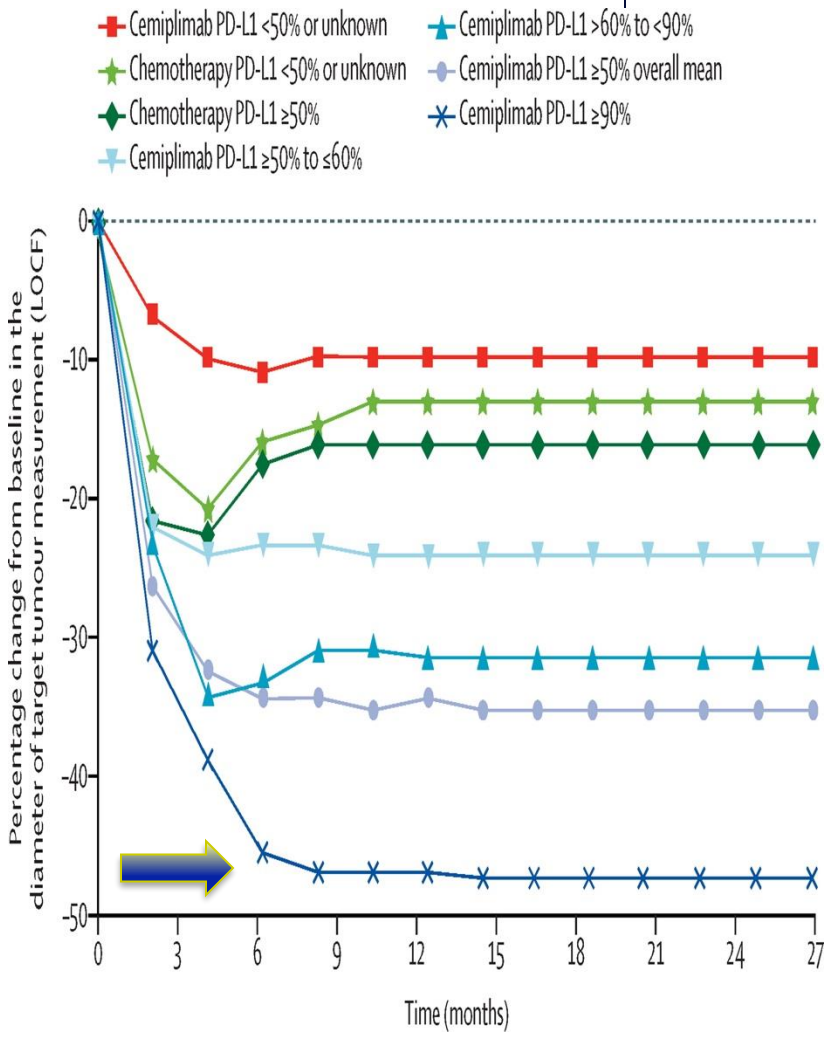
OS in NSCLC PD-L1 ≥50% in selected subgroups



Abbreviations: Chemo-IO= platinum-based doublet chemotherapy plus immunotherapy; CI=confidence interval; ECOG=Eastern Cooperative Oncology Group Performance Status; IO=immunotherapy; NE=not estimable; NSCLC=non-small-cell lung cancer; OS=overall survival; PD-L1=programmed death ligand-1.

EMPOWER-Lung1
Cemiplimab Vs. Chemo: PD-L1 ≥ 50%

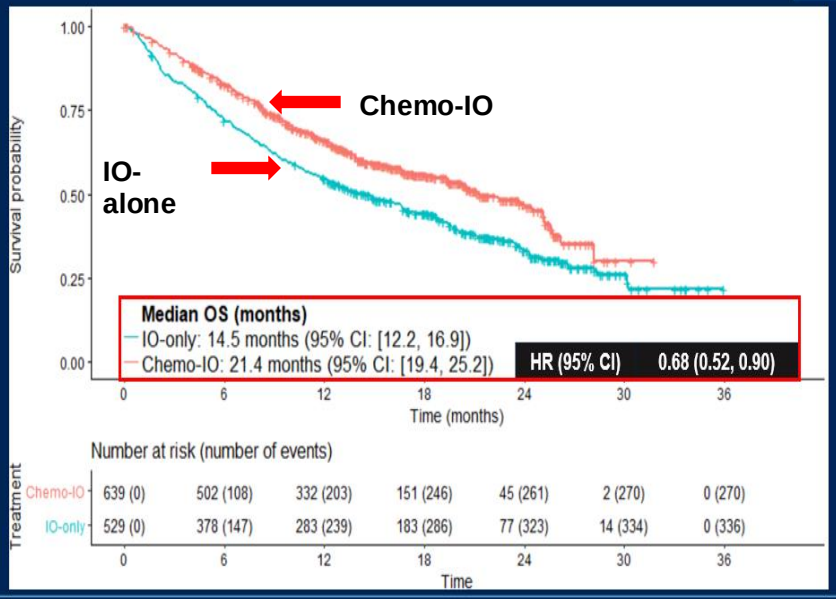




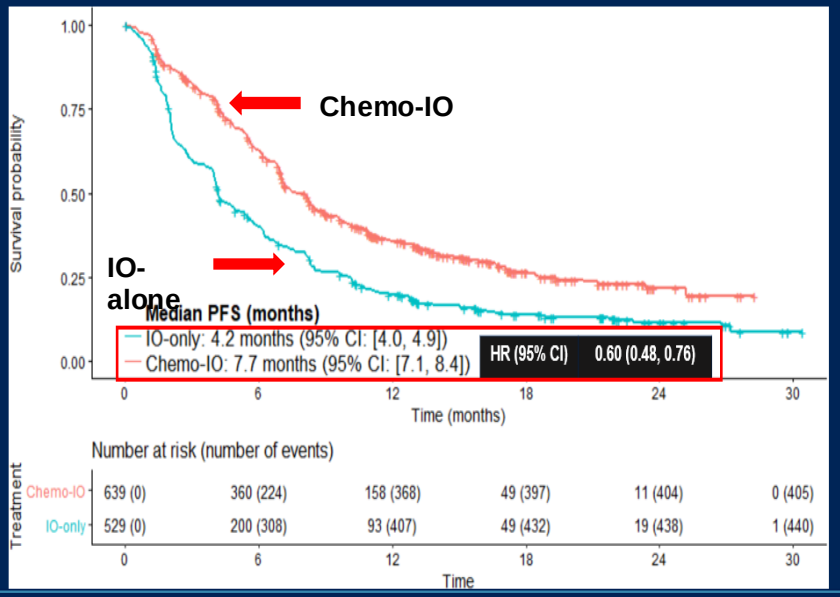
Lancet. February 13, 2021DOI:https://doi.org/10.1016/S0140-6736(21)00228-2

FDA Pooled Analyses PD-L1 1 – 49% Subset

Exploratory OS: NSCLC PDL1 1-49%

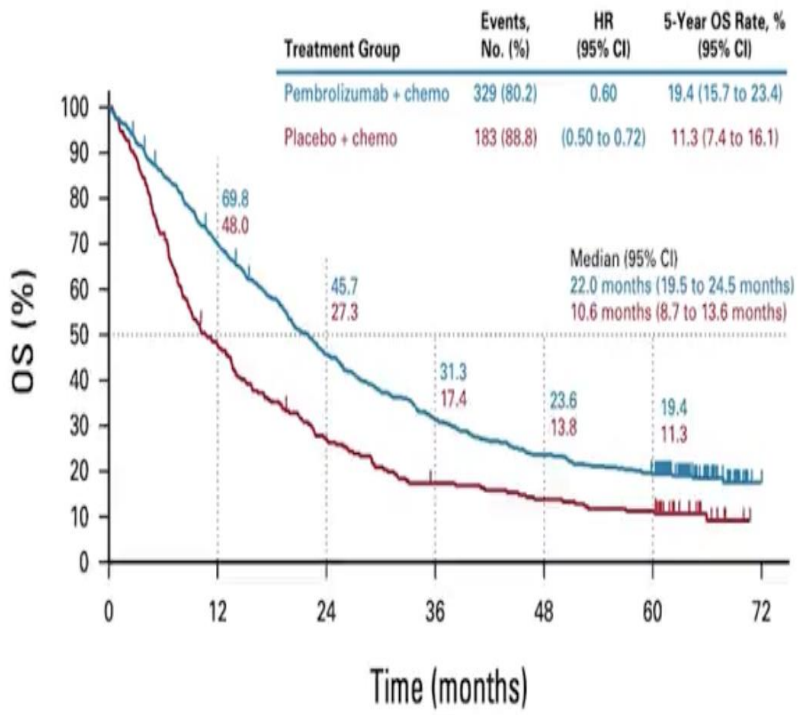


Exploratory PFS: NSCLC PDL1 1-49%

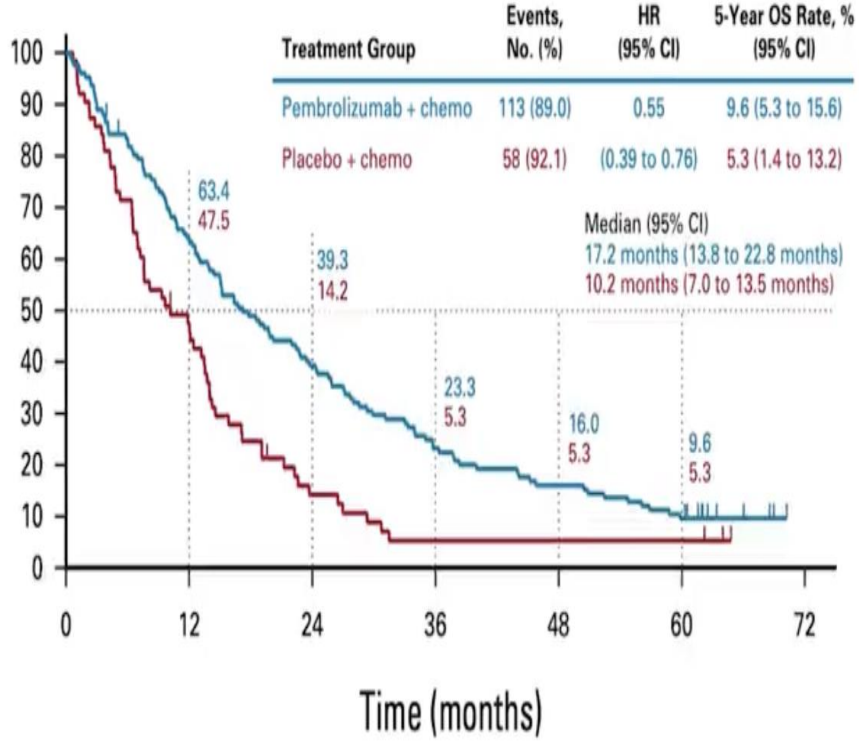


KN-189 5-year update (non-squamous)

ITT

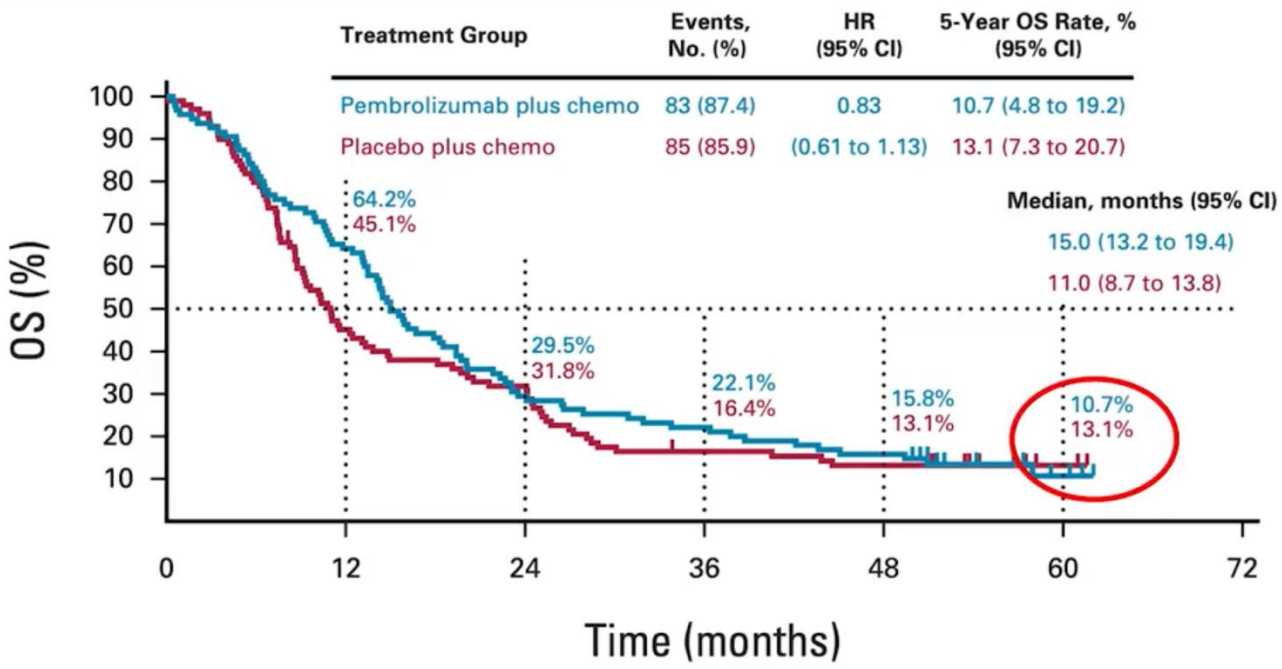


PD-L1<1%



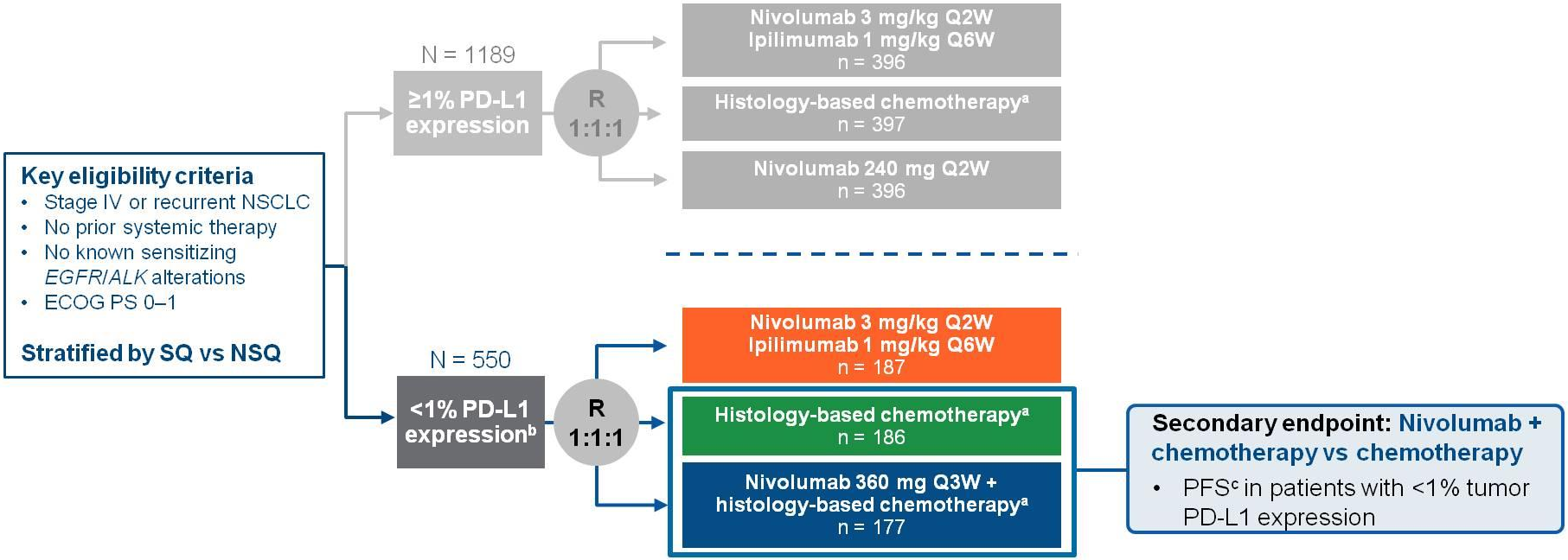
Garassino, JCO 2023

KN-407:OS PD-L1Neg Sq



Novello et al, JCO 2023

CheckMate 227 Part 1 Study Design



- Co-primary endpoints: OS in PD-L1–selected populations and PFS[c] in TMB-selected populations treated with nivolumab + ipilimumab vs chemotherapy

Database lock: January 24, 2018; minimum follow-up: 11.2 months

[a]**NSQ:** pemetrexed + cisplatin or carboplatin, Q3W for ≤4 cycles, with optional pemetrexed maintenance following chemotherapy or nivolumab + pemetrexed maintenance following nivolumab + chemotherapy; **SQ:** gemcitabine + cisplatin, or gemcitabine + carboplatin, Q3W for ≤4 cycles; [b]One patient was randomized with <1% tumor PD-L1 expression in IVRS, but was subsequently found to have ≥1% tumor PD-L1 expression; [c]Per BICR

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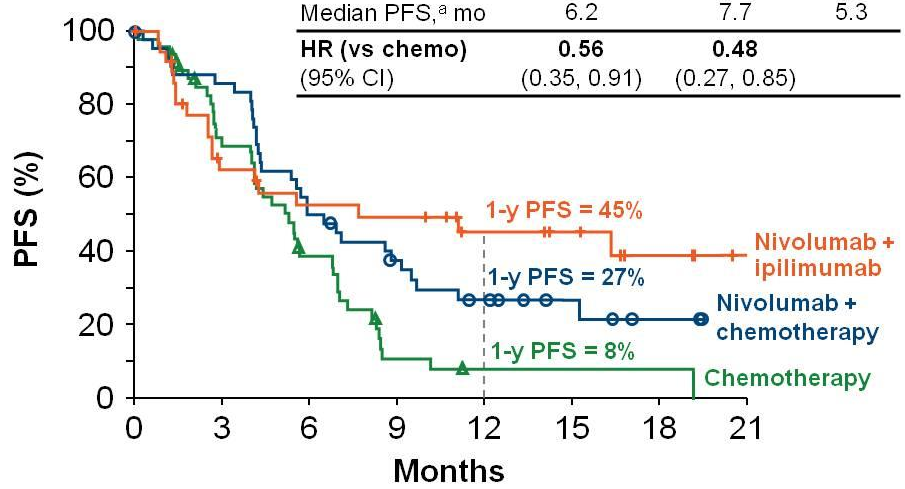
N Engl J Med 2019;381:2020-2031
DOI: 10.1056/NEJMoa1910231

PFS: Nivolumab + Chemotherapy and Nivolumab + Ipilimumab By TMB

TMB ≥10 mut/Mb and <1% Tumor PD-L1 Expression

	Nivo + chemo (n = 43)	Nivo + ipi (n = 38)	Chemo (n = 48)
Median PFS,[a] mo	6.2	7.7	5.3
HR (vs chemo) (95% CI)	**0.56** (0.35, 0.91)	**0.48** (0.27, 0.85)	

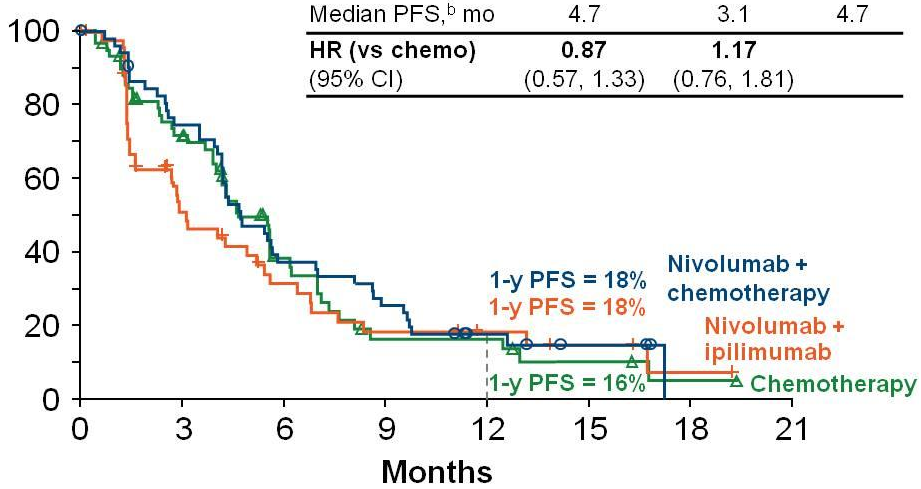


No. at risk

Nivo + chemo	43	36	21	14	9	5	2	0
Nivo + ipi	38	20	16	15	10	8	4	1
Chemo	48	30	16	4	1	1	1	0

TMB <10 mut/Mb and <1% Tumor PD-L1 Expression

	Nivo + chemo (n = 54)	Nivo + ipi (n = 52)	Chemo (n = 59)
Median PFS,[b] mo	4.7	3.1	4.7
HR (vs chemo) (95% CI)	**0.87** (0.57, 1.33)	**1.17** (0.76, 1.81)	



No. at risk

Nivo + chemo	54	38	19	13	6	3	0	0
Nivo + ipi	52	22	12	7	5	3	1	0
Chemo	59	39	16	6	6	3	1	0

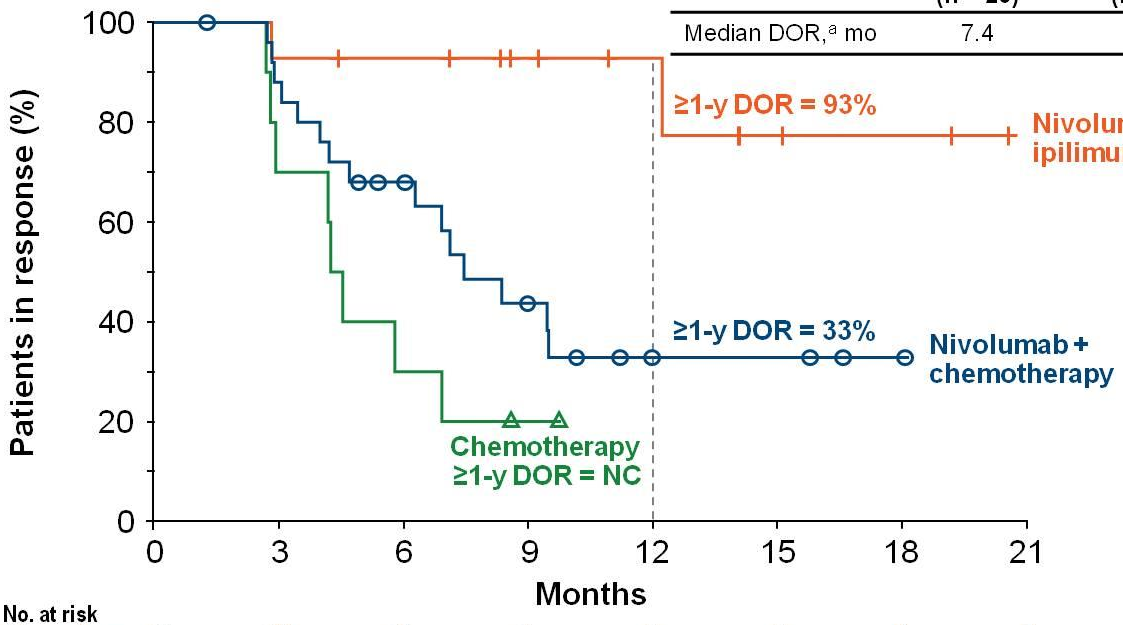
Exploratory analysis

[a]95% CI: nivo + chemo (4.3, 9.1 mo), nivo + ipi (2.7, NR mo), chemo (4.0, 6.8 mo); [b]95% CI: nivo + chemo (4.2, 6.9 mo), nivo + ipi (1.6, 5.4 mo), chemo (3.9, 6.2 mo)

N Engl J Med 2019;381:2020-2031
DOI: 10.1056/NEJMoa1910231

DOR: Nivolumab + Chemotherapy and Nivolumab + Ipilimumab in Patients With TMB ≥10 mut/Mb and <1% Tumor PD-L1 Expression

	Nivo + chemo (n = 26)	Nivo + ipi (n = 14)	Chemo (n = 10)
Median DOR,[a] mo	7.4	NR	4.4



No. at risk

Nivo + chemo	26	22	15	8	3	3	1	0
Nivo + ipi	14	13	12	8	6	3	2	0
Chemo	10	7	3	1	0	0	0	0

- ORR was 60.5% with nivo + chemo, 36.8% with nivo + ipi, and 20.8% with chemo

Exploratory analysis

[a]95% CI: nivo + chemo (4.6, NR mo), nivo + ipi (12.2, NR mo), chemo (2.7, 6.9 mo)

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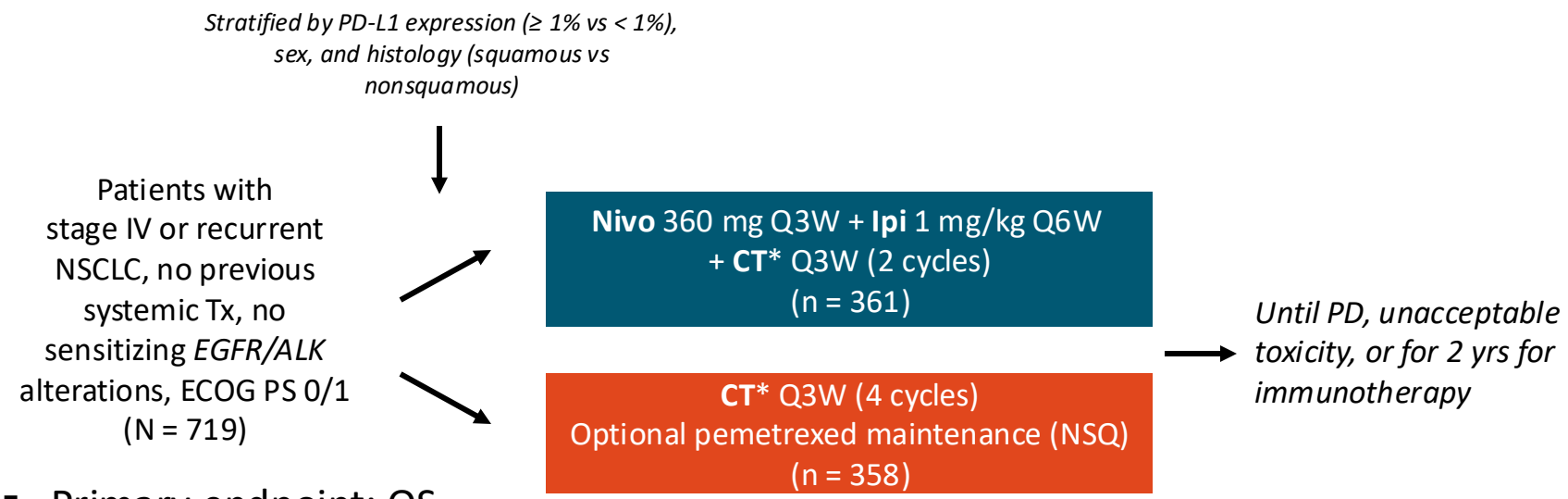
CheckMate 9LA: Study Design

- Randomized, open-label, phase III study



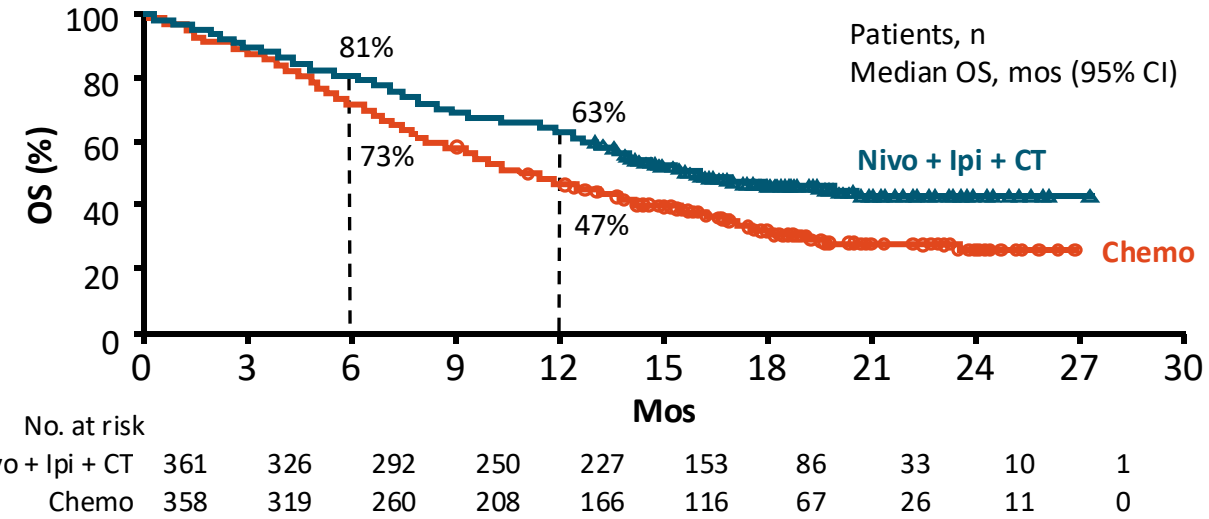
- Primary endpoint: OS
- Secondary endpoints: PFS, ORR, efficacy by tumor PD-L1 expression

*Pts with NSQ: pemetrexed + cisplatin or carboplatin; pts with SQ: paclitaxel + carboplatin.

Reck. ASCO 2020. Abstr 9501.

CheckMate 9LA: Updated OS Results

- Interim analysis (minimum FU 8.1 mos) median OS, Nivo + Ipi + CT vs CT: 14.1 vs 10.7 mos; HR: 0.69 (95% CI: 0.55-0.87); *P* = .0006; met primary endpoint
- Updated results (minimum FU 12.7 mos)

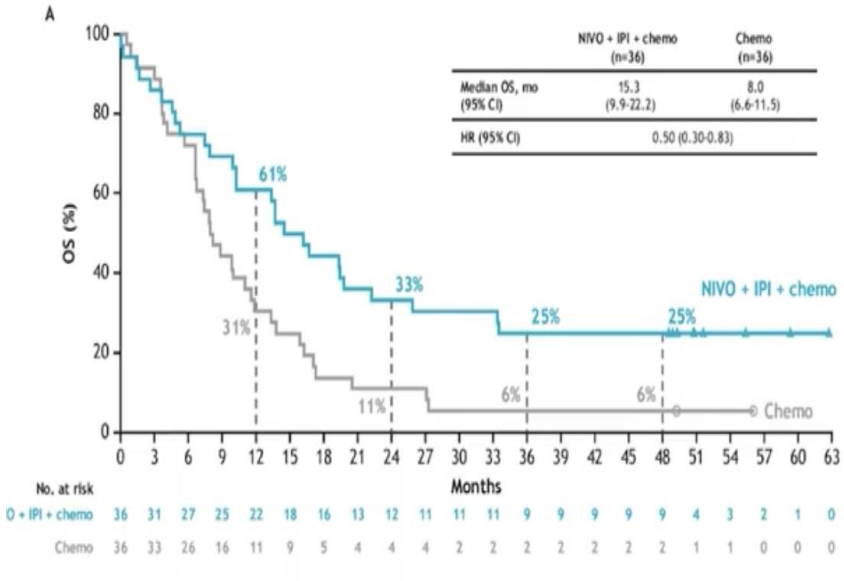


	Nivo + Ipi + CT	CT
Patients, n	361	358
Median OS, mos (95% CI)	15.6 (13.9-20.0)	10.9 (9.5-12.6)

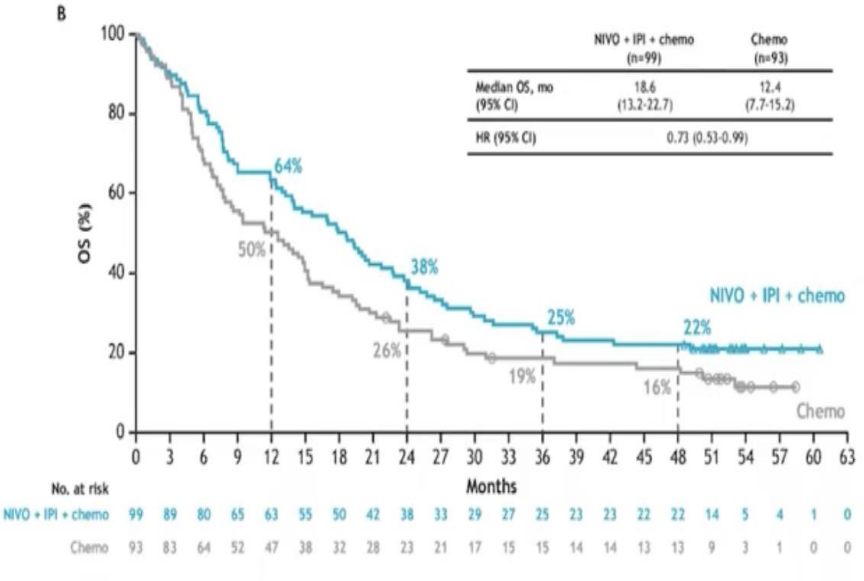
HR: 0.66 (95% CI: 0.55-0.80)

Reck. ASCO 2020. Abstr 9501. Reproduced with permission.

CK9LA – OS: Sq/Non-Sq (PD-L1 Neg)



Squamous

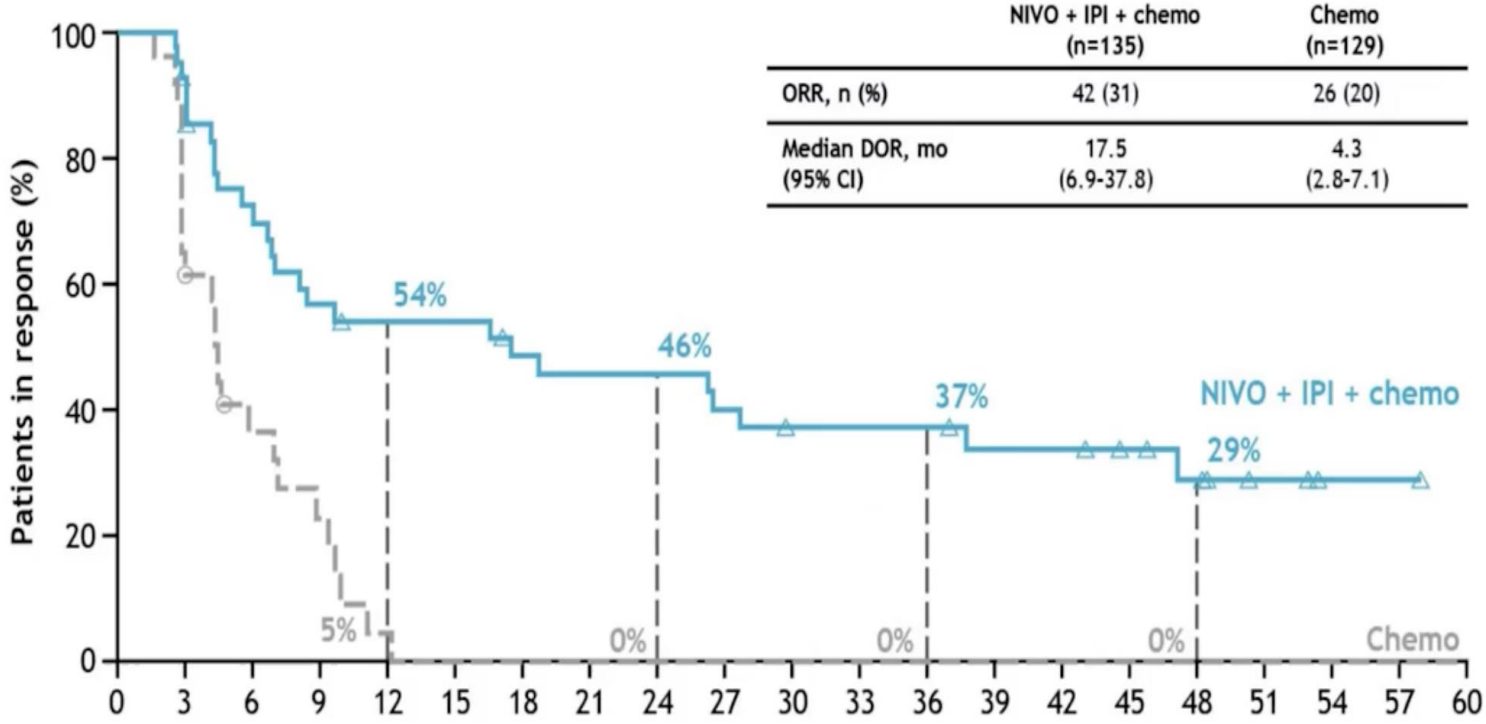


Non-squamous

Carbone, JITC 2024

CK9LA – DoR (PD-L1Neg Subset)

	NIVO + IPI + chemo (n=135)	Chemo (n=129)
ORR, n (%)	42 (31)	26 (20)
Median DOR, mo (95% CI)	17.5 (6.9-37.8)	4.3 (2.8-7.1)

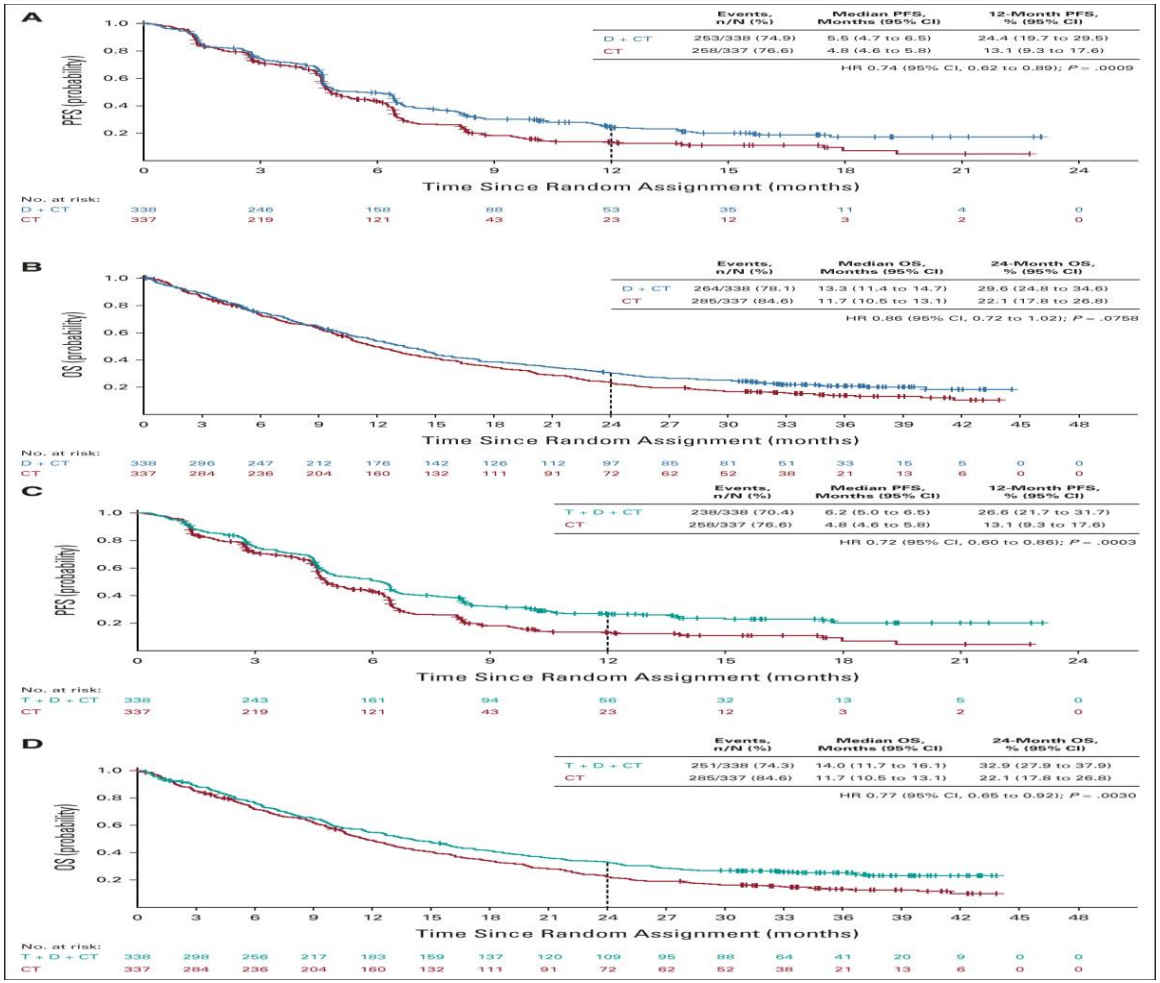


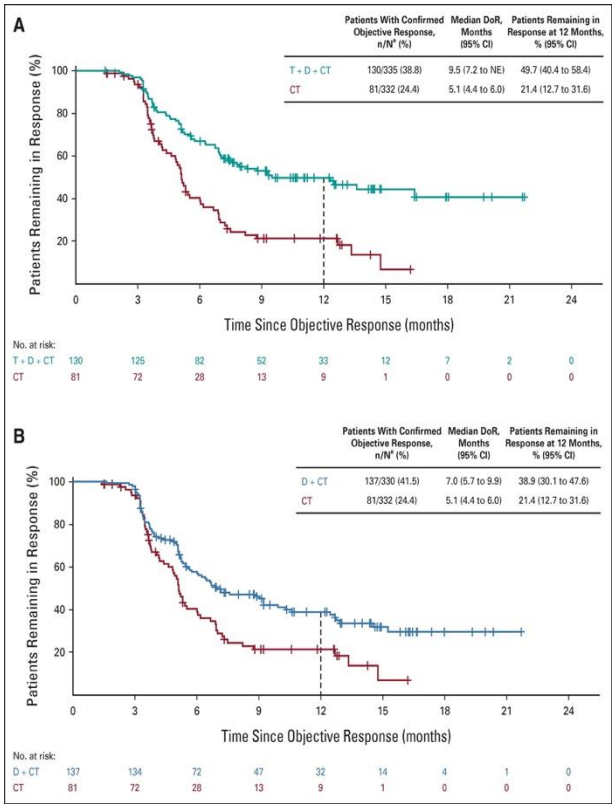
No. at risk																				
NIVO + IPI + chemo	42	35	28	22	20	20	17	16	16	14	12	12	12	10	10	8	6	3	1	1	0
Chemo	26	17	8	5	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Carbone, JITC 2024

D +/- T in Combination With CT as First-Line Therapy for Metastatic NSCLC
The Phase III POSEIDON Study
(N – 1,013 - (1:1:1)

Journal of Clinical Oncology 2023 411213-1227.DOI: 10.1200/JCO.22.00975

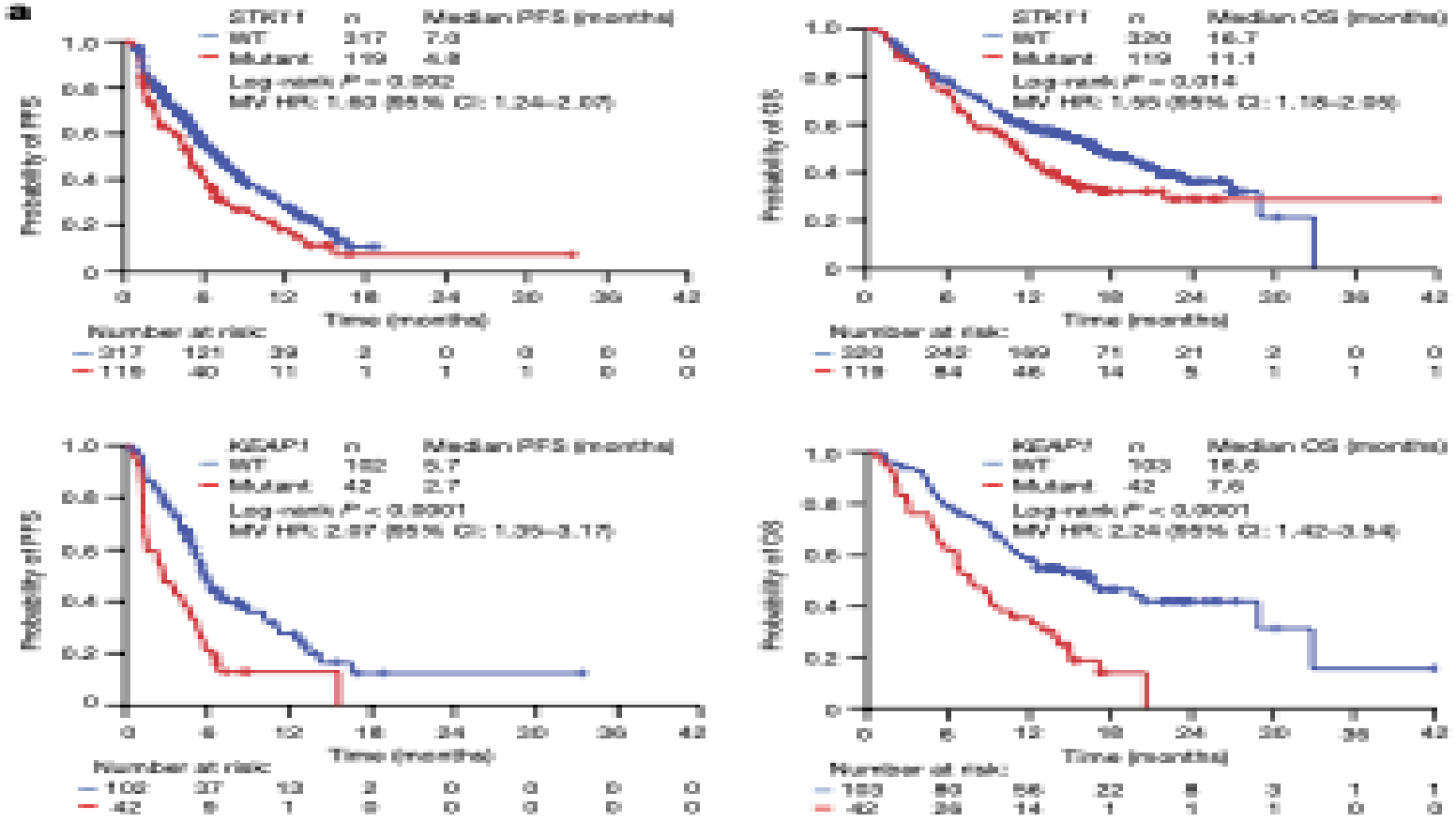




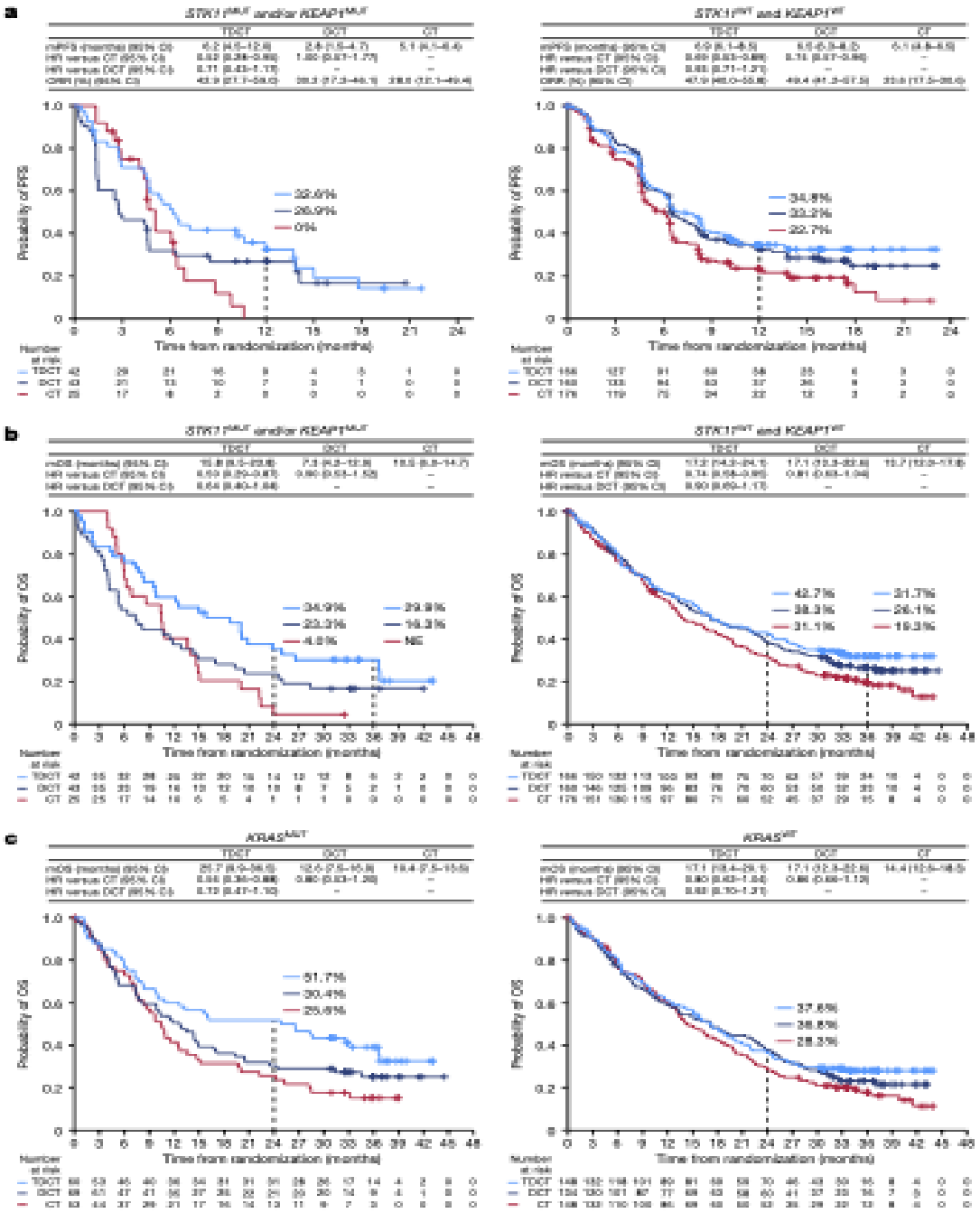
D+CT vs CT PFS -HR, 0.74; *P* = **.0009 (**Median, 5.5 *v* 4.8 months); OS HR, 0.86; *P* = **.0758** (Median, 13.3 *v* 11.7 months).

D+T+CT vs CT PFS (HR, 0.72; *P* = **.0003 (**Median, 6.2 *v* 4.8 months)**;** OS (HR, 0.77;***P* = .003** (Median, 14.0 *v* 11.7 months)

CTP: OS/PFS - STK/KEAP Mut v WT



Skoulidis et al: Nature Vol: 635. 2024



POSEIDON: Clinical outcomes in molecularly defined subsets.

STK &/or KEAP Mt v Wt

a. PFS

b. OS

KRAS Mt v Wt

c. OS

Skoulidis et al: Nature Vol: 635. 2024

First-Line NSCLC Rx Selection

PD-L1	TMB	KRAS	STK11/KEAP1	Therapy Selection
>90%	H or L	Wt or Mt	Wt	PD1/PD-L1
50 to 90%	H or L	Wt or MT	Wt	CT+PD1/PDL1 <75yrs PD1/PDL1 >75yrs
1 – 49%	H or L	Wt or Mt	Wt	CT+PD1/PDL1
0%	H	Wt	Wt	PD1+CTLA4
0%	L	Wt	Wt	CT+PD1/PD-L1+CTLA4 CT+PD1/PDL1
0%	H	Mt	Wt	PD1+CTLA4
0%	L	Mt	Wt	CT+PD1/PD-L1+CTLA4
Any	H	Wt or Mt	Mt	PD1+CTLA4 CT+PD1/PD-L1+CTLA4
Any	L	Wt ot Mt	Mt	CT+PD1/PD-L1+CTLA4

IInd Line NSCLC
Biomarker & First-Line Response Based treatment Selection

2022 ASCO® ANNUAL MEETING

SWOG CANCER RESEARCH NETWORK | NCI National Clinical Trials Network | NCI Community Oncology Research Program

Acquired Resistance

Overall survival from a phase II randomized study of ramucirumab plus pembrolizumab versus standard of care for advanced non-small cell lung cancer previously treated with immunotherapy—Lung-MAP non-matched sub-study S1800A

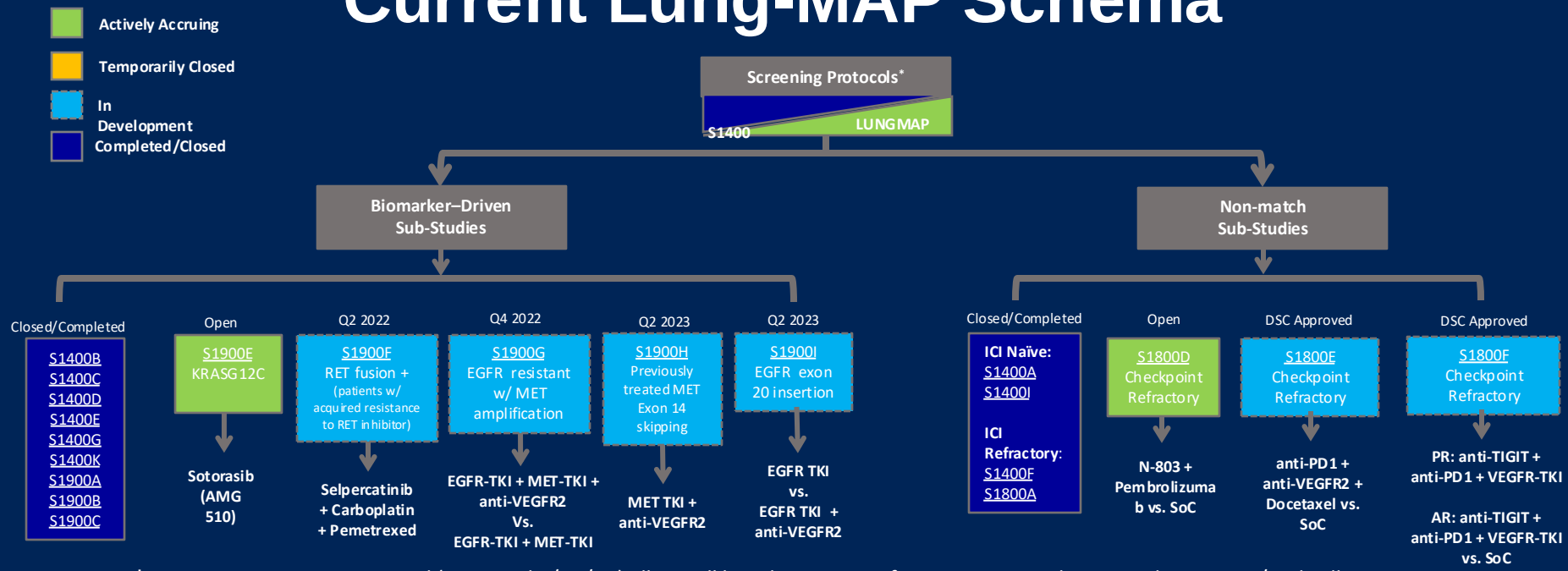
Karen L. Reckamp, M.D.[1], Mary W. Redman, PhD[2], Konstantin H. Dragnev, M.D.[3], Liza Villaruz, M.D.[4], Bryan Faller, MD[5]; Tareq Al Baghdadi, MD[6], Susan Hines, MD[7], Lu Qian, M.S.[2], Katherine Minichiello, M.S.[2], David R. Gandara, M.D.[8], Karen Kelly, MD[8], Roy S. Herbst, M.D., Ph.D.[9]

[1]Cedars-Sinai Medical Center, Los Angeles, CA; [2]SWOG Statistics and Data Management Center & Fred Hutchinson Cancer Research Center, Seattle, WA; [3]Dartmouth-Hitchcock Norris Cotton Cancer Center, Lebanon, NH/Alliance for Clinical Trials in Cancer; [4]University of Pittsburgh Medical Center (UPMC) Hillman Cancer Center; [5]Missouri Baptist Medical Center, St. Louis, MO/Heartland NCORP; [6]IHA Hematology Oncology Consultants-Ann Arbor/Michigan CRC NCORP; [7]Novant Health Cancer Institute - Mount Airy/Southeast Clinical Oncology Research Consortium NCORP); [8]UC Davis Comprehensive Cancer Center, Sacramento, CA; [9]Yale University, New Haven, CT

LUNG-MAP

PRESENTED BY:
Karen L. Reckamp, MD, MS

Current Lung-MAP Schema



*LUNGMAP screening protocol (activated 1/28/19) allows all histologic types of NSCLC. S1400, the original screening/umbrella protocol included only squamous lung cancer. S1400 accrued patients between 6/16/2014 and 1/28/2019. While S1400 is closed to accrual, patients enrolled to S1400 may participate in sub-studies they are eligible for.

TRIAL POINTS OF INTEREST:

- Each of sub-study operates independently of the others
- Prescreening can be performed while the patient is on any line of therapy for stage IV disease
- Repeat or fresh biopsy necessary for tissue screening is paid by the trial
- **#Biomarker-driven sub-studies may progress to Phase III if study meets endpoint and Phase III is feasible, at which point the standard of care arm will be determined.**

- Karen L. Reckamp, MD, MS

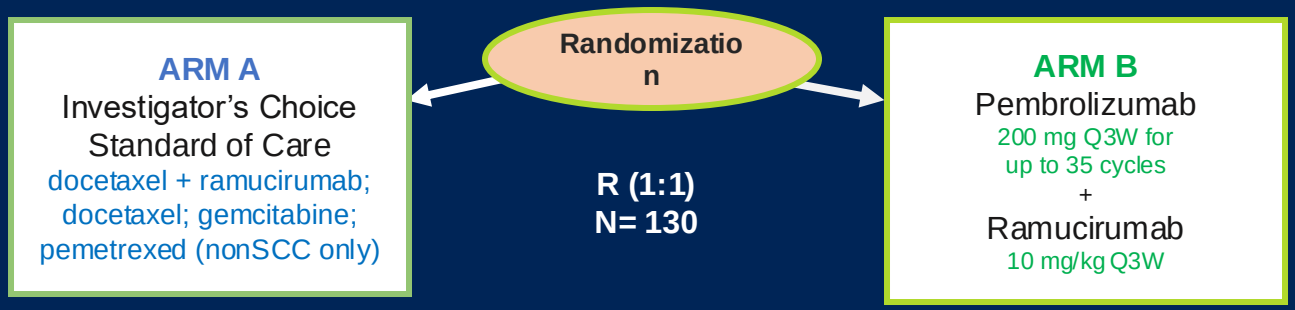
LUNG-MAP

S1800A Schema—Randomized Phase II trial

NCT03971474

Stratified by 1) PD-L1 expression, 2) histology, 3) intent to receive ramucirumab in standard of care arm

Primary endpoint: OS
Secondary endpoints: RR, DCR, DoR, PFS, Toxicities

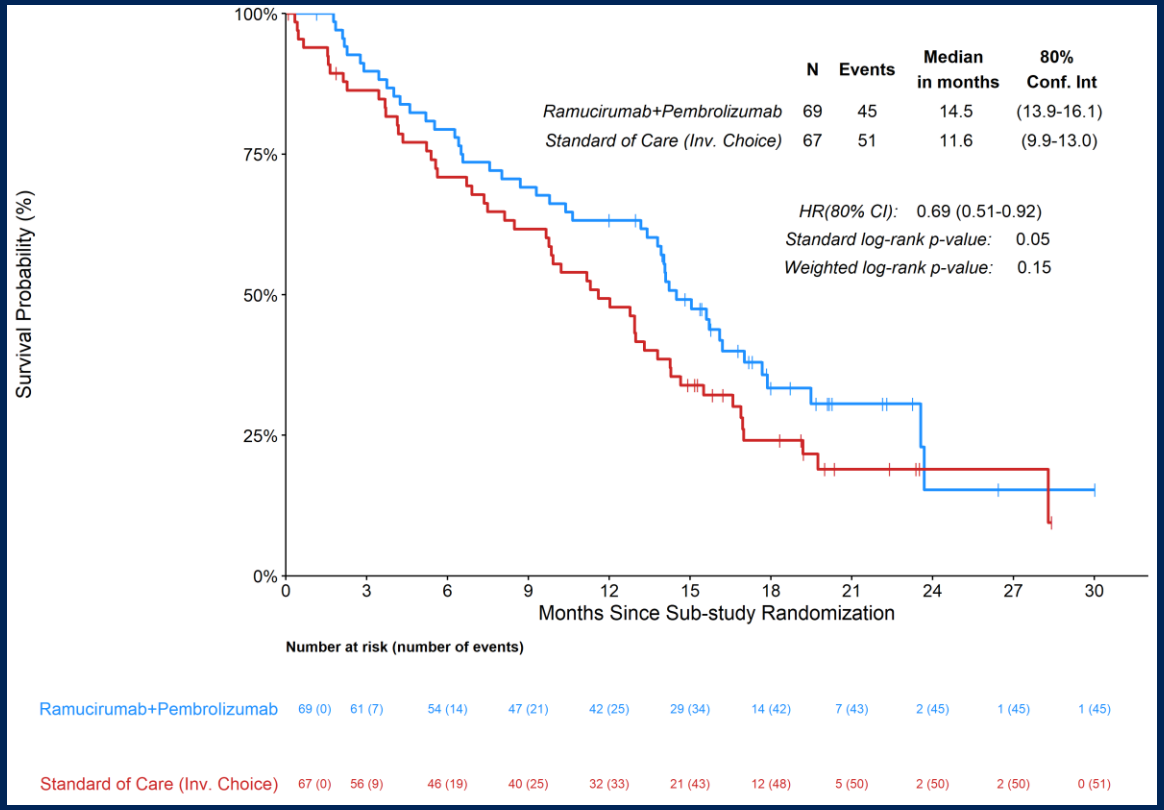


Key eligibility: 1) Previously received both PD-1 or PD-L1 inhibitor therapy and platinum-based doublet chemotherapy either sequentially or combined, with PD on at least 84 days after initiation of ICI and platinum-based doublet therapy; 2) ECOG 0-1; 3) all patients met eligibility to receive ramucirumab

LUNG-MAP

PRESENTED BY:
Karen L. Reckamp, MD, MS

Overall survival



- Median OS for RP 14.5 months v. SOC 11.6 months
- HR= 0.69; SLR p-value 0.05

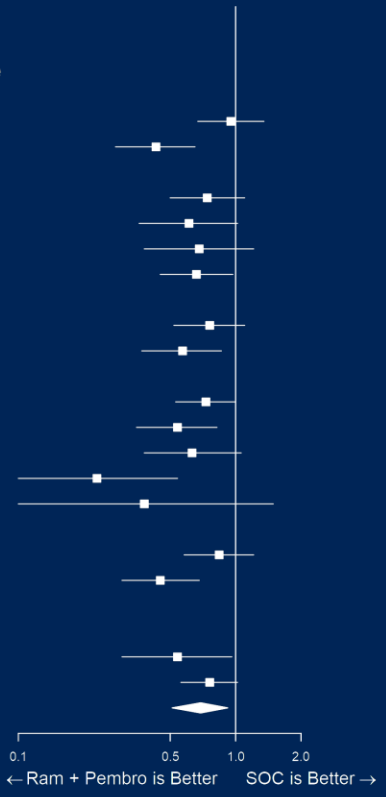
Standard of care therapy received:

- Docetaxel + Ramucirumab (n = 45)
- Docetaxel (n = 3)
- Gemcitabine (n = 12)
- Pemetrexed (n = 1)
- No treatment (n = 6)

PRESENTED BY:
Karen L. Reckamp, MD, MS

Overall survival—subgroup analysis

	Ram+ Pembro Events/N	SOC Events/N	HR (80% CI)	P-value
HISTOLOGY				
Non-Squamous	27/40	27/39	0.95 (0.67,1.35)	0.43
Squamous/Mixed	18/29	24/28	0.43 (0.28,0.65)	0.005
PD-L1				
PD-L1 0	21/29	21/26	0.74 (0.50,1.10)	0.16
PD-L1 1-49	11/21	15/22	0.61 (0.36,1.02)	0.11
PD-L1 50+	8/12	12/16	0.68 (0.38,1.21)	0.20
PD-L1 1+	19/33	27/38	0.66 (0.45,0.97)	0.08
TMB				
TMB <10	23/32	28/38	0.76 (0.52,1.10)	0.17
TMB 10+	18/33	20/25	0.57 (0.37,0.86)	0.04
BIOMARKER				
TP53	31/48	35/48	0.73 (0.53,1.00)	0.10
CDKN2A	18/27	21/24	0.54 (0.35,0.82)	0.03
KRAS	12/21	13/16	0.63 (0.38,1.06)	0.13
STK11	4/7	10/10	0.23 (0.10,0.54)	0.01
KEAP1	1/3	7/10	0.38 (0.10,1.49)	0.18
PRIOR TREATMENT				
IO+CHEMO COMBO	20/32	32/42	0.84 (0.58,1.21)	0.27
CHEMO->IO	25/36	18/23	0.45 (0.30,0.68)	0.006
PERFORMANCE STATUS				
PS 0	15/23	8/9	0.54 (0.30,0.96)	0.08
PS 1	30/46	43/58	0.76 (0.56,1.02)	0.12
OVERALL	**45/69**	**51/67**	**0.69 (0.51,0.92)**	**0.05**



LUNG-MAP

- All subgroup HRs < 1
- HRs by PD-L1 does not appear to vary
- Pronounced benefit in SCC/mixed histology
- Benefit seen with PS 0 and 1
- Co-mutations did not affect OS improvement

PRESENTED BY:
Karen L. Reckamp, MD, MS

PhIII Trial Underway

S2302: Pragmatica-Lung Treatment Trial

A Prospective Randomized Study of Ramucirumab Plus Pembrolizumab vs Standard of Care for Participants Previously Treated with Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer

Chair: Karen Reckamp, MD (SWOG)
Co-Chair: Konstantin Dragnev, MD (Alliance)

Statistical Chair: Mary Redman, PhD
Co-statisticians: Jieling Miao, MD, James Moon, MS

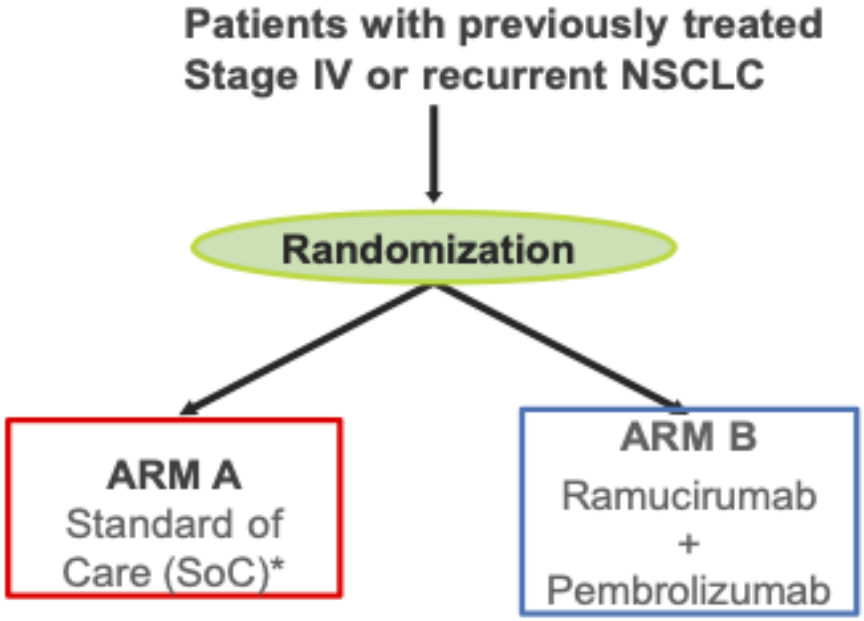
Study Champions: Wade Iams, MD (ECOG-ACRIN)
Brian S. Henick (NRG Oncology)

Lung Community Engagement Subcommittee Rep:
Daniel Carrizosa, MD, MS

Company Collaborators:
Eli Lilly & Co. and Merck

Primary endpoint:
Overall Survival

Accrual Goal:
700 participants



* SoC treatment is to be determined by the treating investigator and participant. It is recommended that the choice of SoC drug(s) is based on NCCN guidelines for a "systemic therapy for advanced or metastatic disease-subsequent."

EVOKE -01 Trial Design

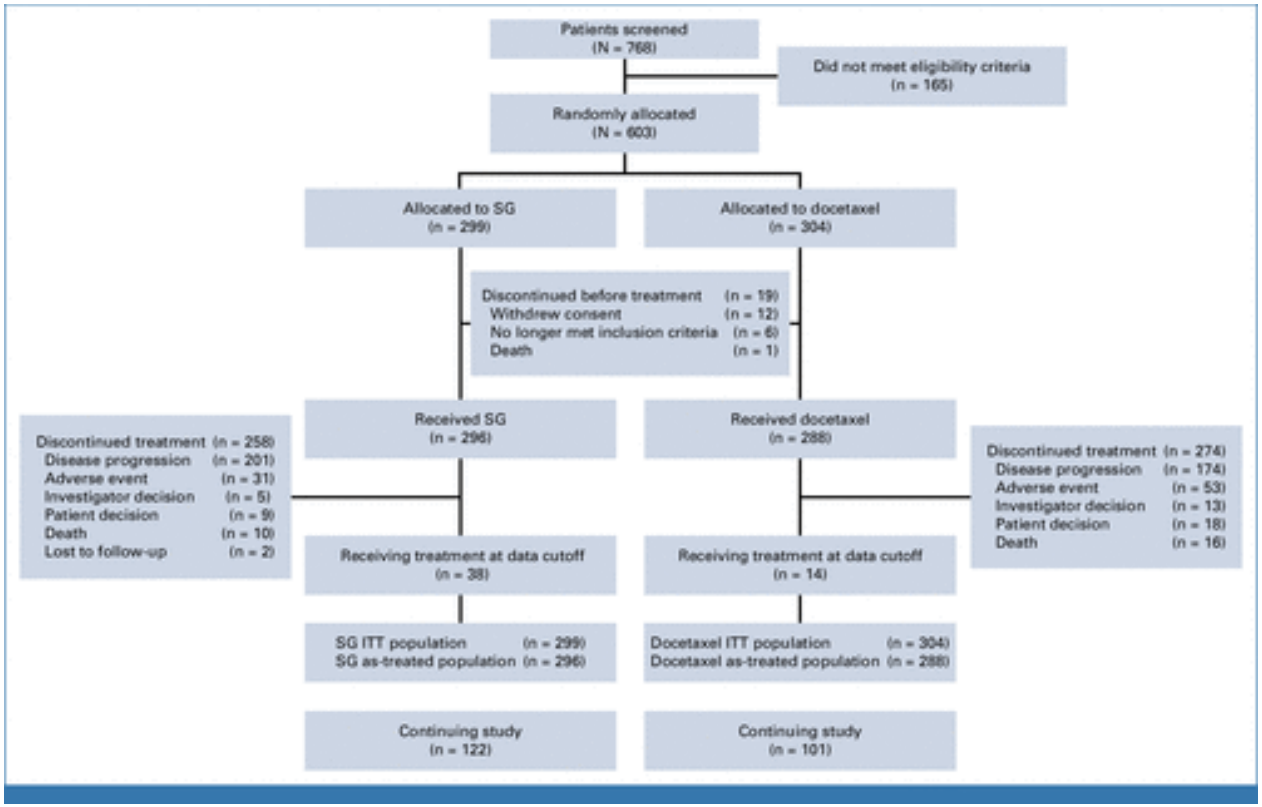
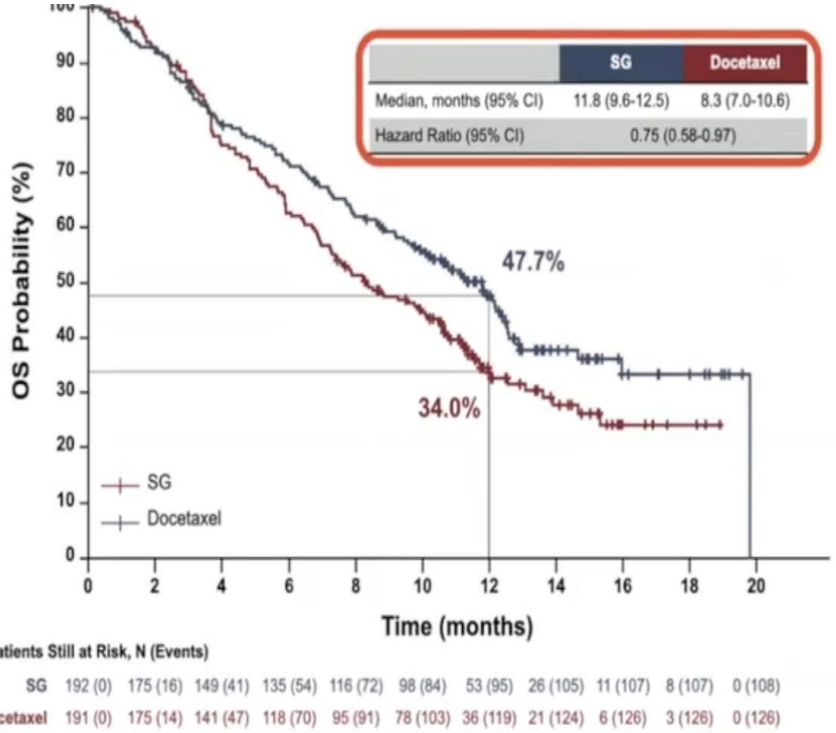


FIG 1. Patient disposition: CONSORT diagram. ITT, intention-to-treat; SG, sacituzumab govitecan.

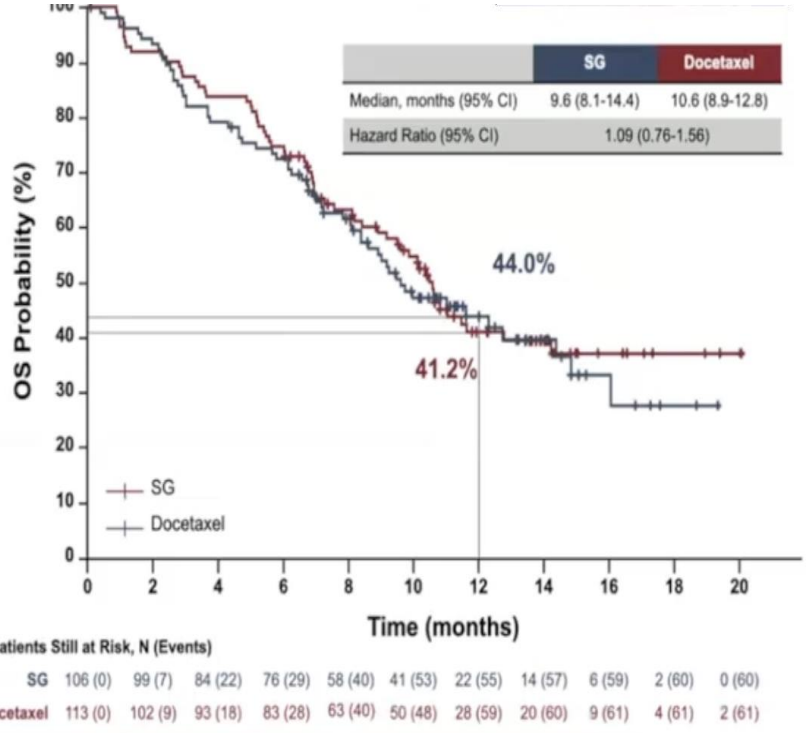
Published in: Luis G. Paz-Ares; Oscar Juan-Vidal; Giannis S. Mountzios; Enriqueta Felip; Niels Reinmuth; Filippo de Marinis; Nicolas Girard; Vipul M. Patel; Takayuki Takahama; Scott P. Owen; Douglas M. Reznick; Firas B. Badin; Irfan Cicin; Sabeen Mekan; Riddhi Patel; Eric Zhang; Divyadeep Karumanchi; Marina Chiara Garassino JCO 2024 05-31
DOI: 10.1200/JCO.24.00733

EVOKE-01: OS based on response to Anti-PD(L)-1 Rx

SD/PD after Anti-PD(L)-1 Rx



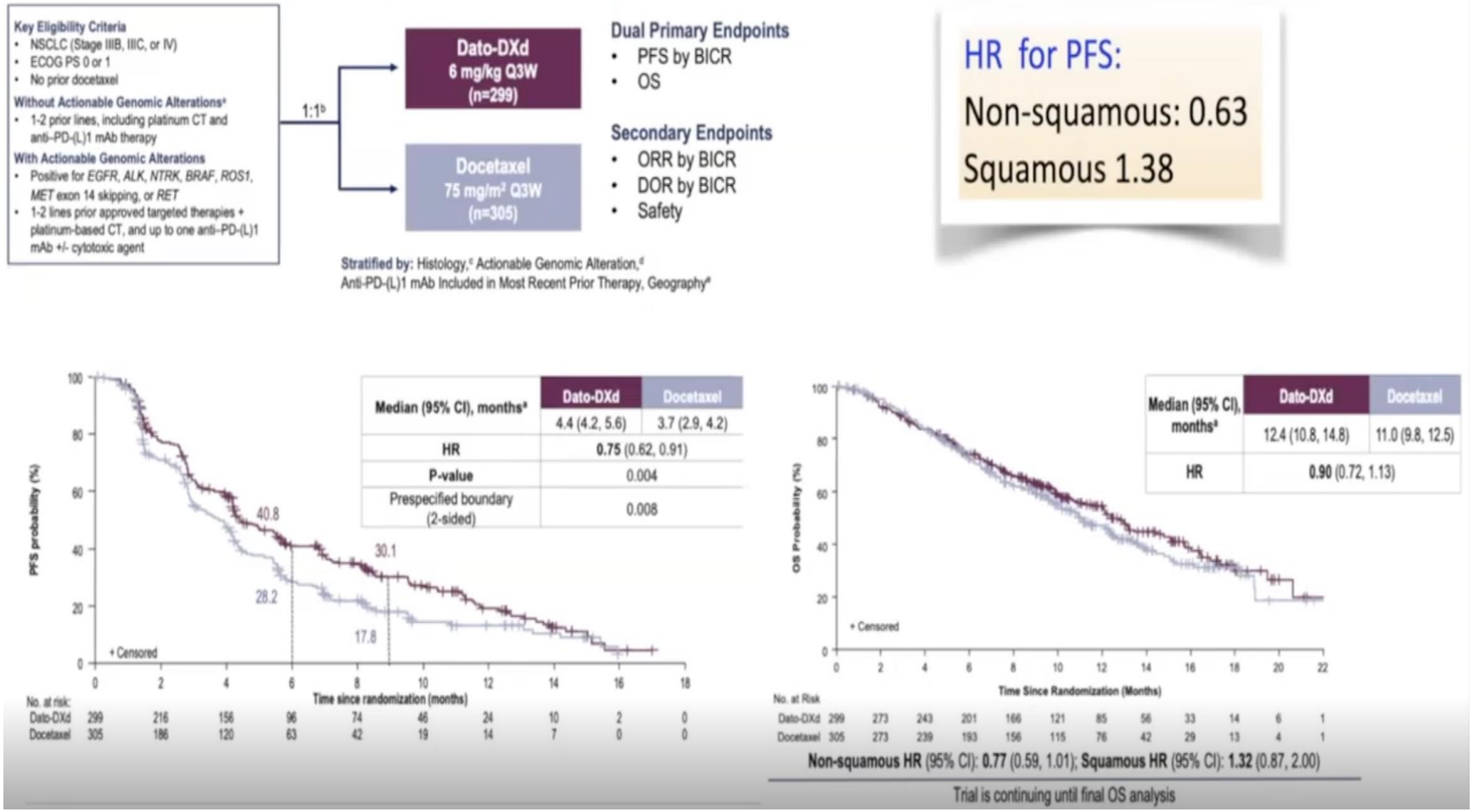
CR/PR after Anti-PD(L)-1 Rx



In the prespecified subgroup analysis, there was a 3.5-month improvement in median OS over docetaxel among patients whose tumors where non-responsive (SD/PD) to last anti-PD-(L)1–containing regimen.

CR, complete response; CI, confidence interval; OS, overall survival; PD, progressive disease; PR, partial response; SD, stable disease; SG, sacituzumab govitecan.

TROPION-Lung-01
NSQ Vs Sq PFS



Journal of Clinical Oncology. https://doi.org/10.1200/JCO-24-0154**17,6883**

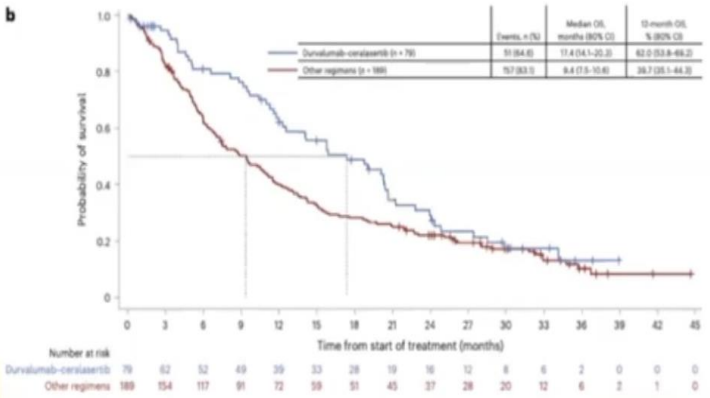
Biomarker driven IInd line Cohorts

THE HUDSON STUDY

N= 324
- Progression after a platinum based doublet and anti-PD (L)-1
- Availability for Tissue and blood NGS

BIOMARKER SELECTION

- ATM → Ceralasertib+Durvalumab, ATR Inhibitor
- HRR → Olaparib+Durvalumab, PARP Inhibitor
- STK11 → Danvatirsen+Durvalumab, STAT3 Inhibitor
- CD73 → Oleclumab+Durvalumab, anti-CD73 MoAb
- NONE → Biomarker non-matched cohorts



Median OS was 17.4 for patients in the Ceralasertib + Durvalumab cohort as compared to 9.4 months in patients in all other cohorts together

Phase III LATIFY study versus Docetaxel ongoing

Nature Medicine **volume 30**, pages716–729 (2024)

Targeting RAS: Emerging Landscape

Mutant-specific KRAS inhibitors

Programs (company)	IND	Target	Phase
Sotorasib/AMG 510 (Amgen)			Approved
Adagrasib/MRTX849 (Mirati)			
D-1553 (InventisBio)			
JDQ443 (Novartis)			
RG6330/GDC-6036 (Roche)		$KRAS^{G12C}$	
LY3537982 (Eli Lilly)			Clinical
BI 1823911 (Boehringer Ingelheim)			
JAB-21822 (Jacobio)			
GFH925 (GenFleet)			
GH35 (Genhouse Bio)			
MRTX1133 (Mirati)			
KRASG12D1-3 (Boehringer Ingelheim)		$KRAS^{G12D}$	
RAS(ON) G12D (Revolution Medicines)			Preclinical
RAS(ON) G13C (Revolution Medicines)		$KRAS^{G13C}$	

Pan-(K)RAS inhibitors

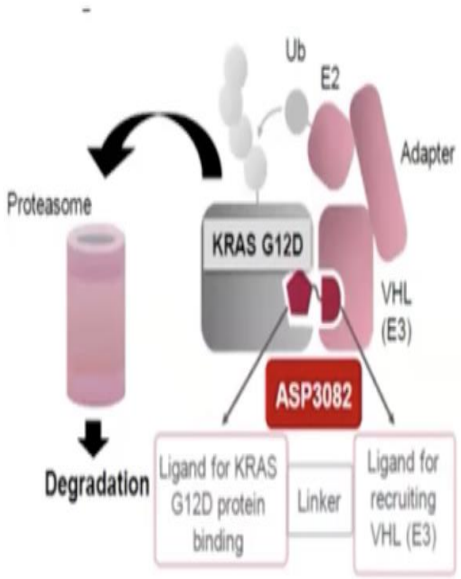
Programs (company)	IND	Target	Phase
RSC-1255 (RasCal Therapeutics)		Pan-RAS	Clinical
BI-pan-KRAS1-4 inhibitors (Boehringer Ingelheim)		Pan-KRAS: $KRAS^{G12D/V}$, KRAS wild-type	
BI-pan-KRASdegrader1 (Boehringer Ingelheim)		Pan-KRAS: $KRAS^{G12C/D/V/A}$, $KRAS^{G13C}$, $KRAS^{A146T/P}$, $KRAS^{Q61E/P}$, KRAS wild-type	Preclinical
RMC-6236 (Revolution Medicines)		Pan-RAS: $KRAS^{G12D/V}$, $KRAS^{G13D}$, $KRAS^{Q61K}$, RAS wild-type	

Key Features in evaluating RAS compounds:

Allele-specific	Pan-RAS
Ras(on)	RAS(off)
Covalent	Non-covalent
Inhibitor	Degrader or Glue

Hofmann *et al.*, Cancer Discovery 2022

ASP-3082 is a G12D degrader

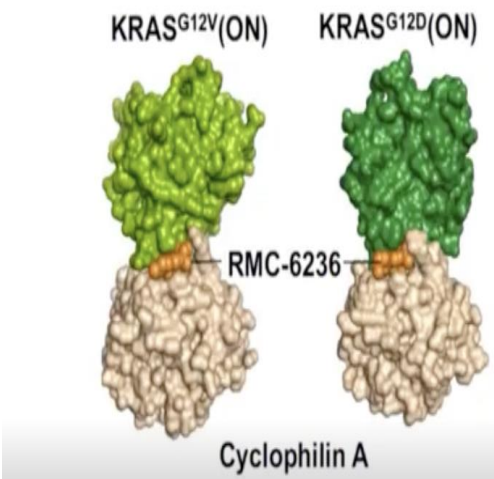


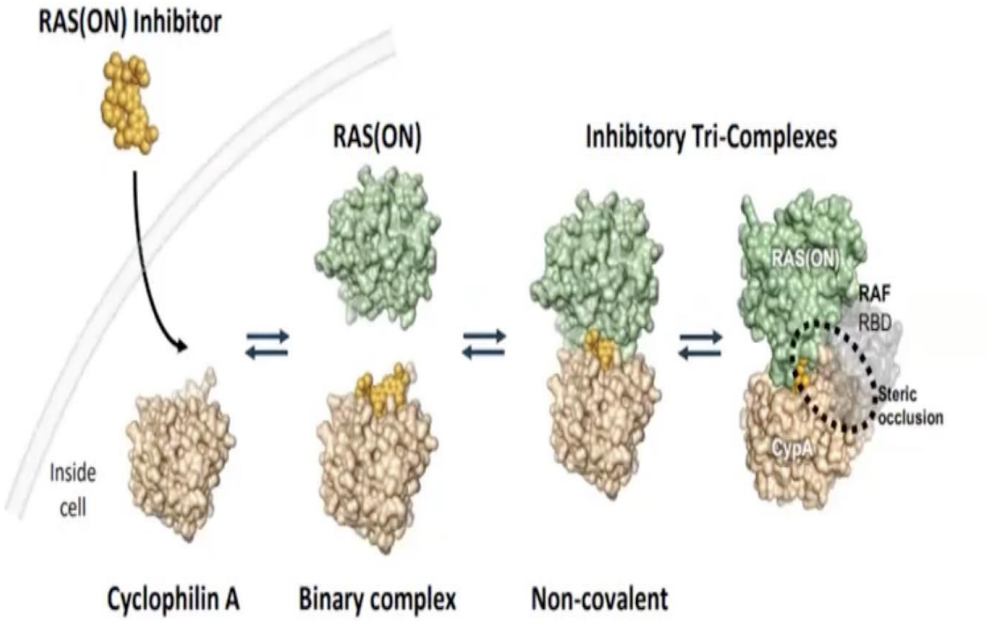
Allele-specific	Pan-RAS
Ras(on)	RAS(off)
Covalent	Non-covalent
Inhibitor	Degrader or Glue

Wang et al. JMC 2022

Pan-RAS inhibitor: Non-Covalent Glue

Allele-specific	Pan-RAS
Ras(on)	RAS(off)
Covalent	Non-covalent
Inhibitor	Degrader or Glue





Revolution Medicines: AACR 2022

Some of the novel RASi under development

Company	Target	Mechanism	Phase	Targets
Revolution	pan-RAS	Molecular Glue	Phase III	PDAC, NSCLC, CRC
Eli Lilly	pan-KRAS (without R)	Inhibitor	Phase I	Solid Tumors
Boehringer	pan-KRAS; degraders	Inhibitor	Phase I	KRAS amp, solid tumors
Genentech	pan-KRAS	Inhibitor	Phase I	Solid Tumors
Pfizer	pan-KRAS	Inhibitor	Phase I	Solid Tumors
Quanta Therapeutics		Inhibitor	Preclinical, Phase I	
Erasca	Multiple: pan-KRAS; pan-RAS	Glue, inhibitor	Preclinical, Phase I	
Beigene	pan-KRAS	Inhibitor	Preclinical, Phase I	
Alterome	pan-KRAS	Inhibitor	Preclinical	
Arvinas	G12D	Degrader	Preclinical	
Astellas	G12D	Degrader	Phase 1b Expansion	NSCLC, PDAC, CRC

Hofmann et al. Cancer Discovery 2022

Does Comprehensive Genomic Analyses (CGP) improve survival over Simple Panel Testing?

- ***Population***. Patients diagnosed with advanced or metastatic non-small cell lung cancer (aNSCLC) between 1/1/2015 and 12/31/2020, who received small panel testing or comprehensive genomic profiling.

- ***Key Exposures***.
  - *Small panel*. Panels that interrogated between 1 and 52 genes
  - *Comprehensive genomic profiling (CGP)*. Panels that interrogated more than 52 genes

- ***Outcomes***.
  - *Overall survival (OS)*. Time to the earliest of death or study end date
  - *Time to next treatment or death (TTNT)*. Time from to the first of: initiation of the subsequent line of treatment, death, date of last contact, or study end date.

Simon et al, JOP. In Press

Select Patient Characteristics

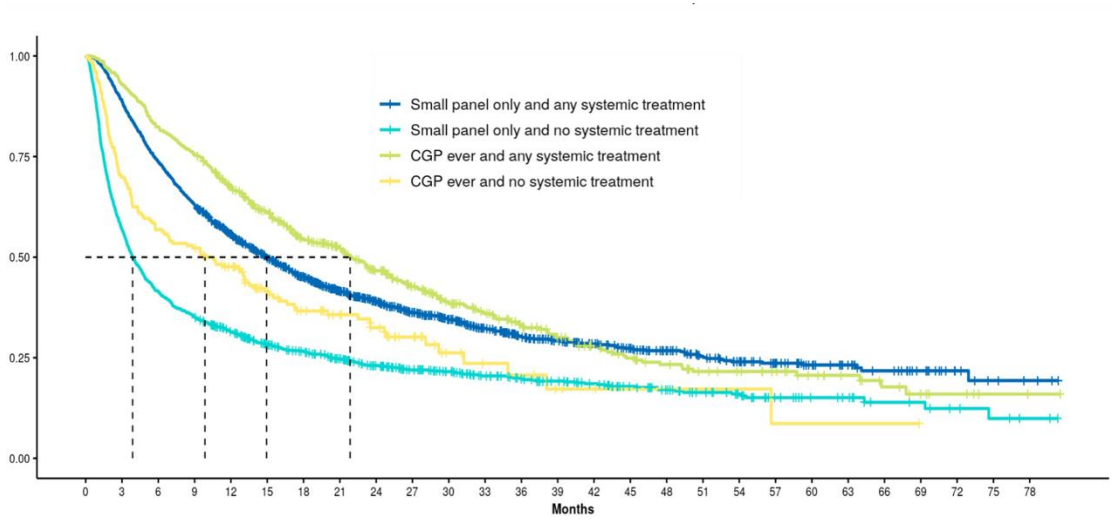
	Total	Small Panel Only	CGP Ever
Stage at initial diagnosis, *N (%)*	N = 3884	N = 3105	N = 779
I	147 (3.8%)	113 (3.6%)	34 (4.4%)
II	82 (2.1%)	59 (1.9%)	23 (3.0%)
III	676 (17%)	551 (18%)	125 (16%)
IV	2,812 (72%)	2,252 (73%)	560 (72%)
Histology, *N (%)*			
Squamous	818 (21%)	693 (22%)	125 (16%)
Non-squamous	2,659 (68%)	2,083 (67%)	576 (74%)
Age*, Median (IQR)	68 (61, 76)	69 (61, 76)	67 (60, 74)
Male, *N (%)*	1,935 (50%)	1,560 (50%)	375 (48%)
Health System, *N (%)*			
1	924 (24%)	715 (23%)	209 (27%)
2	2,098 (54%)	1,879 (61%)	219 (28%)
3	862 (22%)	511 (16%)	351 (45%)
Smoking History, *N (%)*			
Current smoker	1,303 (34%)	1,046 (34%)	257 (33%)
Former smoker	1,886 (49%)	1,517 (49%)	369 (47%)
Never smoker	466 (12%)	336 (11%)	130 (17%)

Simon et al, JOP. In Press

Similarly distributed between small panel and CGP recipients:

- Year of initial aNSCLC diagnosis
- Sex
- Race/ethnicity
- Region of residence
- Median household income
- Comorbidity
- Performance status
- Stage and age at initial NSCLC diagnosis
- Histology
- Smoking history
- Sites and number of metastases

Overall Survival (OS) From aNSCLC Diagnosis, by Testing Type and Receipt of Systemic Therapy



- Patients who **received CGP testing and any systemic therapy** had the best median OS.
- The **treated patients groups had better survival than untreated patients** in both CGP and small panel only groups.

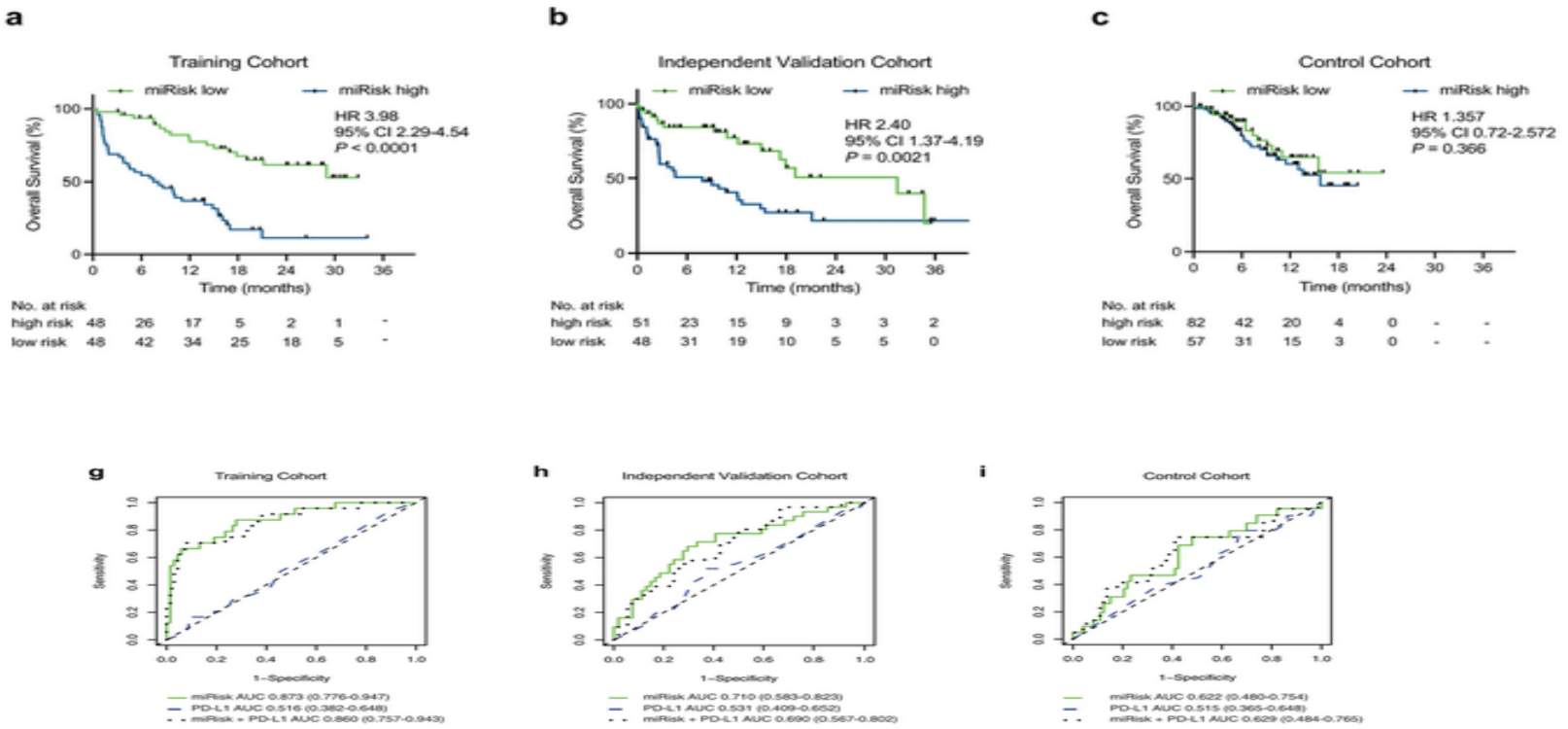
Number at Risk at Index	Testing/Treatment Group	Median, months (95% CI)	6 months	1 year	5 years
1852	SP with any systemic therapy	15 (14-16)	0.74 (0.72, 0.76)	0.56 (0.53, 0.58)	0.23 (0.2, 0.26)
1253	SP and no systemic therapy	4 (4-5)	0.41 (0.39, 0.44)	0.31 (0.29, 0.34)	0.15 (0.13, 0.18)
603	CGP with any systemic therapy	22 (18-25)	0.82 (0.79, 0.85)	0.67 (0.64, 0.71)	0.21 (0.16, 0.26)
176	CGP and no systemic therapy	10 (6-15)	0.57 (0.5, 0.65)	0.48 (0.41, 0.56)	0.09 (0.02, 0.39)

Simon et al, JOP. In Press

Can AI Outperform PD-L1?

Hummingbird's MicroRNA profile

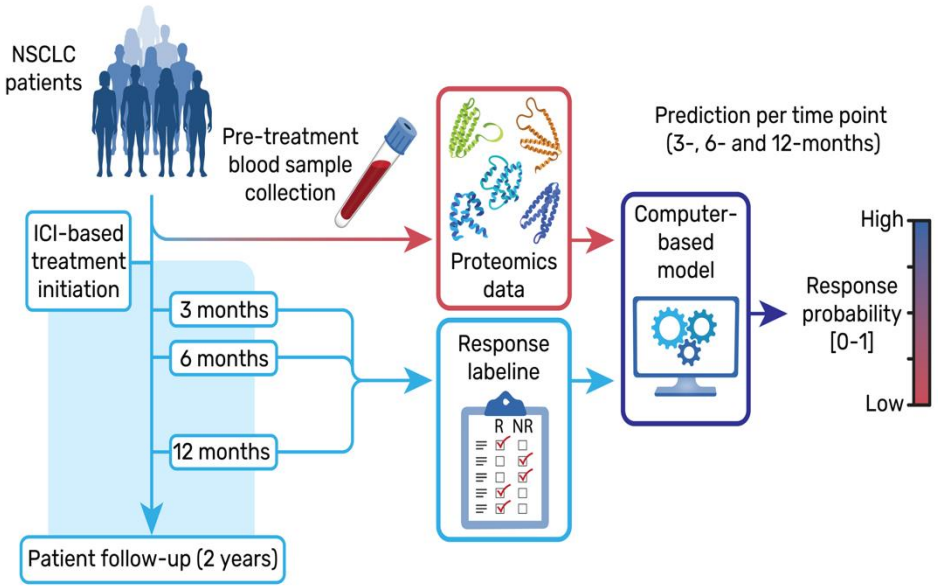
Hummingbird's MiRisk Profile

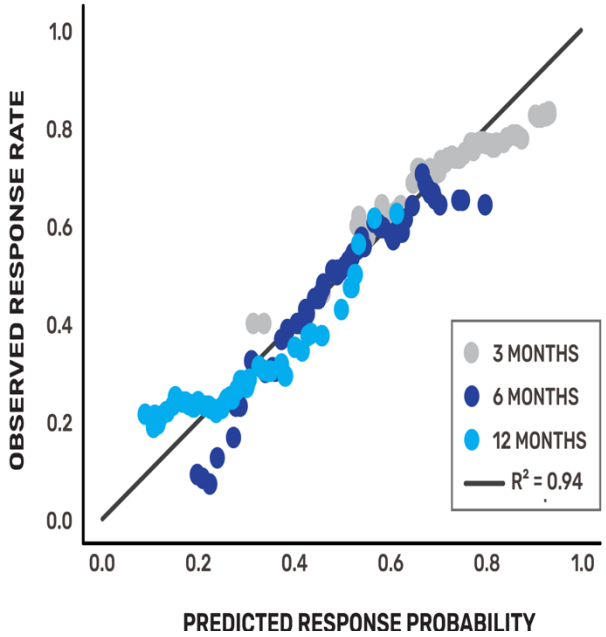


NPJ Precision Oncology (2022) 6:19 ; https://doi.org/10.1038/s41698-022-00262-y

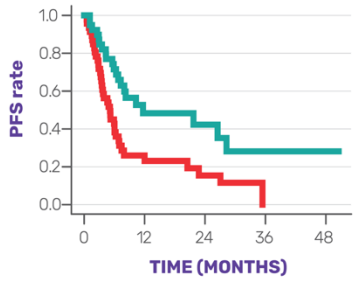
Can AI Outperform PD-L1?

OncoHost – Proteomic Platform





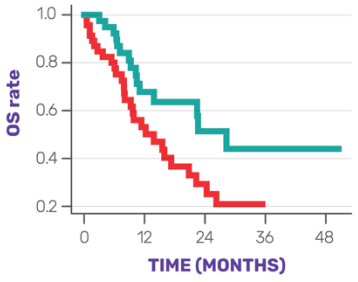
PROGRESSION FREE SURVIVAL (PFS)



HAZARD RATIO=0.45
(95% CI: 0.26-0.76)
p = 0.002

- Favorable long-term outcome population (n=39)
- Unfavorable long-term outcome population (n=46)

OVERALL SURVIVAL (OS)



HAZARD RATIO=0.5
(95% CI: 0.27-0.94)
p = 0.027

- Favorable long-term outcome population (n=39)
- Unfavorable long-term outcome population (n=46)

Clinical Lung Cancer Vol25, Issue 6E252-E261.E4September 2024

OncAI: Radiomics & Multimodal Platform

Predicting 3-month multi-lesion response to PD-1/PD-L1 immune checkpoint inhibitor therapy in stage IV NSCLC: A radiomics-based multi-modal model

PD-1/PD-L1 immunotherapy response performance (ROC-AUC) of 3-months PFS per RECIST 1.1.			
Biomarker	First-line ICI Monotherapy (N = 91)	All-lines ICI Monotherapy (N=138)	All-lines ICI + Chemotherapy (N=114)
Multi-modal	**0.81**	0.72	0.71
CT radiomics	**0.71**	0.61	0.62
PD-L1 IHC	**0.61**	0.60	0.58

Simon et al; AACR 2023 JCO-CCI In Press

Conclusions

- PD-L1, TMB, and ?KRAS/STK11/KEAP1 status my drive Optimal first-line therapy selection
- Response to first-line therapy, histology and molecular characteristics may drive therapy selection (including clinical trials) in IInd-line
- Repeated CGA may be necessary to optimize therapy selection as well as to advance our understanding of mechanisms of resistance
- AI may outperform histology or blood-based biomarker testing

Thank YOU!

Gracias!