UCDAVIS
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CANCER CENTER

NEW THERAPEUTIC DIRECTIONS IN ADVANCED LUNG CANCER

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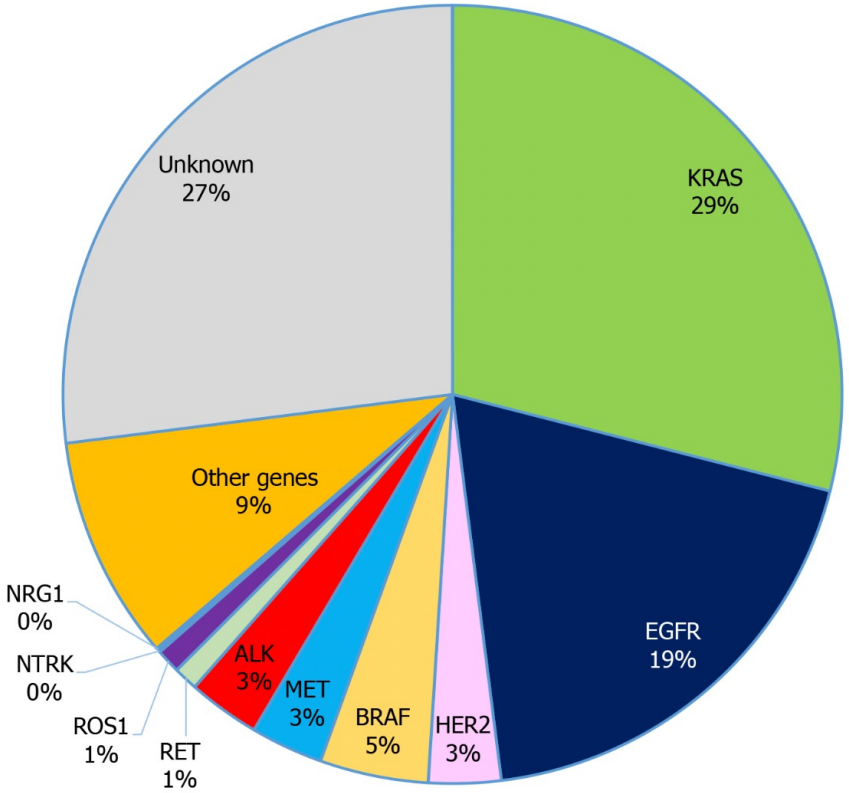
Oncogene Drivers in NSCLC



Chevallier M, Borgeaud M, Addeo A, Friedlaender A. Oncogenic driver mutations in non-small cell lung cancer: Past, present and future . World J Clin Oncol 2021; 12(4): 217-237

FLAURA: Osimertinib vs comparator EGFR-TKI as first-line treatment for EGFRm advanced NSCLC

Patients with locally advanced or metastatic NSCLC

Key inclusion criteria

- ≥18 years old
- WHO performance status 0/1
- Exon 19 deletion/L858R (enrollment by local or central *EGFR* testing)
- No prior systemic anticancer/ EGFR-TKI therapy
- Stable CNS metastases were allowed

Stratification by **mutation status** (exon 19 deletion/ L858R) and **race** (Asian/non-Asian)

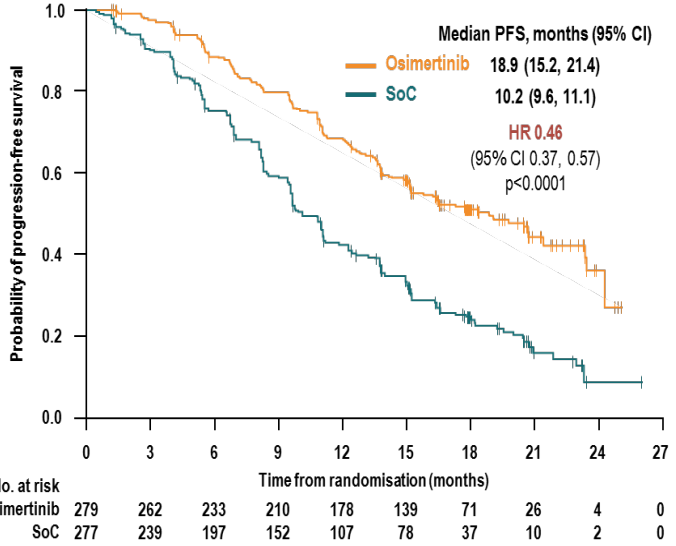
R 1:1

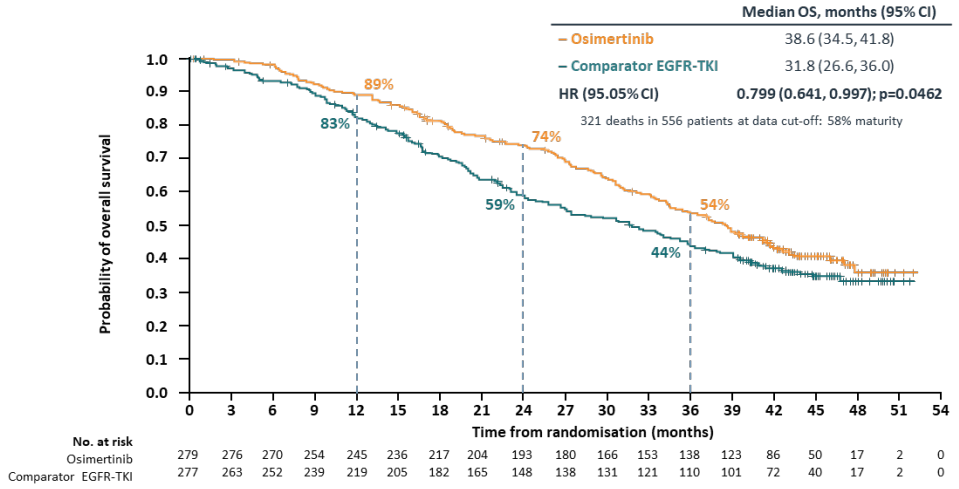
Osimertinib (80 mg po qd) (n=279)

Comparator EGFR-TKI; **Gefitinib** (250 mg po qd) or **Erlotinib** (150 mg po qd) (n=277)

RECIST v1.1 assessment every 6 weeks until objective progressive disease
Following the primary PFS analysis, progression events per RECIST 1.1 were no longer collected centrally

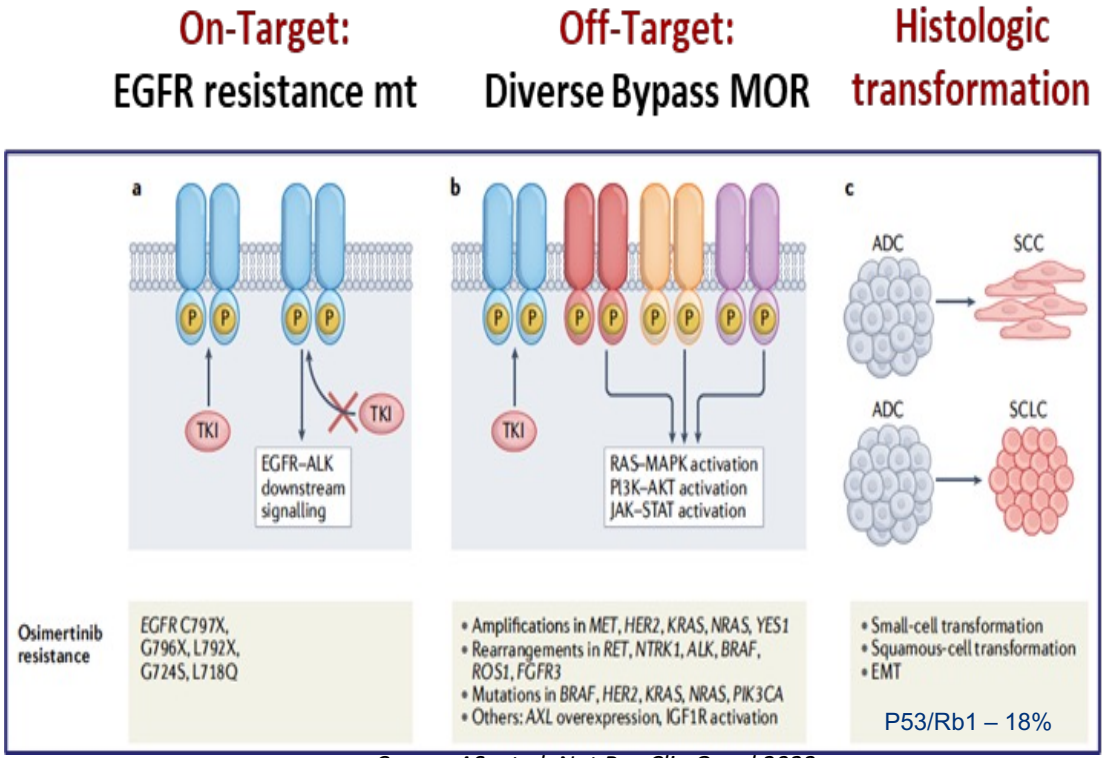
Crossover was allowed for patients in the **comparator** arm, who could receive open-label osimertinib upon central confirmation of progression and T790M positivity





Ramalingam SS, et al. ESMO 2019. Abstract LBA5_PR.

Mechanisms of Osimertinib Resistance



Cooper AS, et al, Nat Rev Clin Oncol 2022

ORCHARD study design

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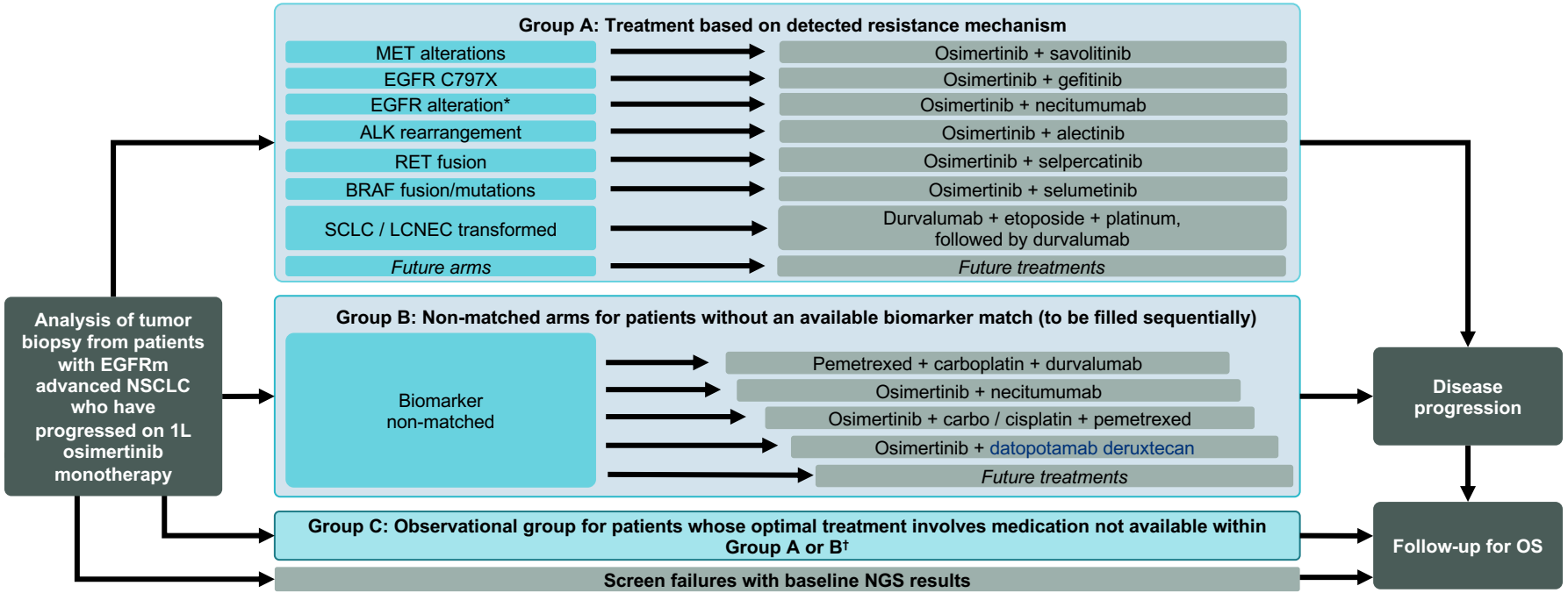
- Ongoing Phase II, open-label, multicenter, multi-drug, biomarker-directed, platform study



H. Yu, JW Riess et al Clinical Lung Cancer 2021

*Patients eligible for enrollment to the osimertinib + necitumumab arm had secondary EGFR alterations, including amplification, L718 or G724 mutation and exon 20 insertion; †E.g. presence of an actionable biomarker for which treatment is not currently available in ORCHARD.

1L, first-line; ALK, anaplastic lymphoma kinase; EGFRm, epidermal growth factor receptor mutation-positive; LCNEC, large cell neuroendocrine carcinoma; NSCLC, non-small cell lung cancer; NGS, next-generation sequencing; OS, overall survival; SCLC, small cell lung cancer

IASLC
2023 World Conference on Lung Cancer
SEPTEMBER 9-12, 2023 | SINGAPORE

Osimertinib With / Without Platinum-Based Chemotherapy as First-Line Treatment in Patients with EGFRm Advanced NSCLC (FLAURA2)

Prof Pasi A. Jänne[1], Prof David Planchard[2], Prof Ying Cheng[3], Dr James Chih-Hsin Yang[4], Dr Noriko Yanagitani[5], Prof Sang-We Kim[6], Dr Shunichi Sugawara[7], Dr Yan Yu[8], Dr Yun Fan[9], Dr Sarayut Lucien Geater[10], Dr Konstantin Laktionov[11], Dr Chee Khoon Lee[12], Prof Natalia Valdiviezo[13], Prof Samreen Ahmed[14], Dr Jean-Marc Maurel[15], Dr Igor Andrasina[16], Dr Jonathan Goldman[17], Dr Dana Ghiorghiu[18], Dr Dakshayini Kulkarni[18], Dr Xiangning Huang[19], Prof Kunihiko Kobayashi[20]

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FLAURA2 Phase III study design

Safety run-in period (N=30)
Published in ESMO Open, 2021[1]

Patients with untreated locally advanced / metastatic EGFRm NSCLC

Key inclusion criteria:

- Aged ≥18 years (Japan: ≥20 years)
- Pathologically confirmed non-squamous NSCLC
- Ex19del / L858R (local / central test)
- WHO PS 0 / 1
- No prior systemic therapy for advanced NSCLC
- Stable CNS metastases were allowed*
- Brain scans at baseline (MRI / CT)

Stratification by:

- **Race** (Chinese Asian / non-Chinese Asian / non-Asian)
- **EGFRm** (local / central test)
- **WHO PS** (0 / 1)

Osimertinib 80 mg (QD) + pemetrexed 500 mg/m² + carboplatin AUC5 or cisplatin 75 mg/m² (Q3W for 4 cycles for platinum-based treatments)

Maintenance osimertinib 80 mg (QD) + pemetrexed (Q3W)†

Randomization 1:1 (N=557)

Osimertinib 80 mg (QD)

Follow-up:

- RECIST 1.1 assessment at 6 and 12 weeks, then every 12 weeks until RECIST 1.1 defined radiological disease progression or other withdrawal criteria were met

- **Primary endpoint:** PFS by investigator assessment per RECIST 1.1‡§
  - **Sensitivity analysis:** PFS by BICR assessment per RECIST 1.1
- **Secondary endpoints:** OS, ORR, DoR, DCR, HRQoL, safety (AEs by CTCAE v5) and PFS2‡

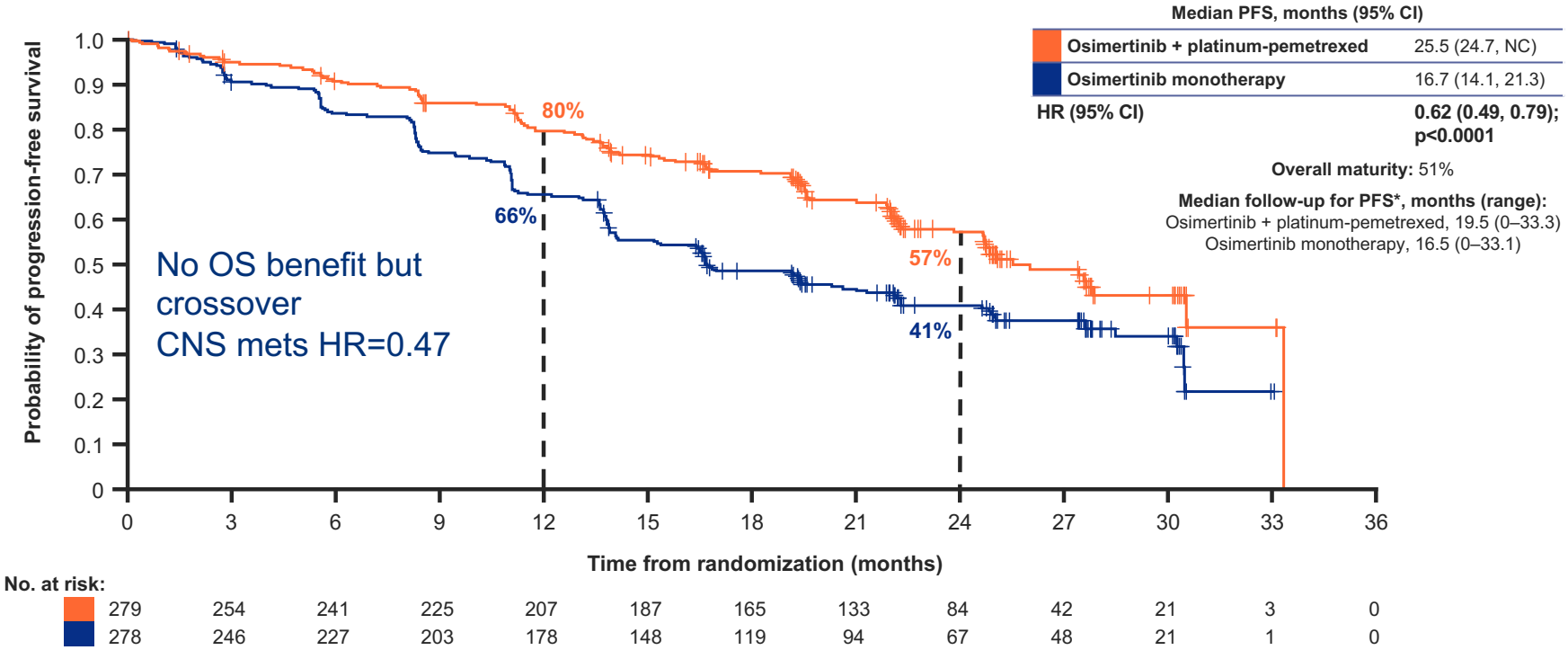
1. Planchard et al. ESMO Open 2021;6:100271

*Not requiring steroids for at least two weeks; †Pemetrexed maintenance continued until a discontinuation criterion was met; ‡Efficacy analyses in the full analysis set, defined as all patients randomized to study treatment regardless of the treatment actually received, and safety analyses in the safety analysis set, defined as all randomized patients who received ≥1 dose of study treatment – one patient who was randomized to osimertinib plus platinum-pemetrexed received only osimertinib and was therefore included in the osimertinib monotherapy safety analysis set; §The study provided 90% power to demonstrate a statistically significant difference in PFS assuming HR=0.68 at 5% two-sided significance level

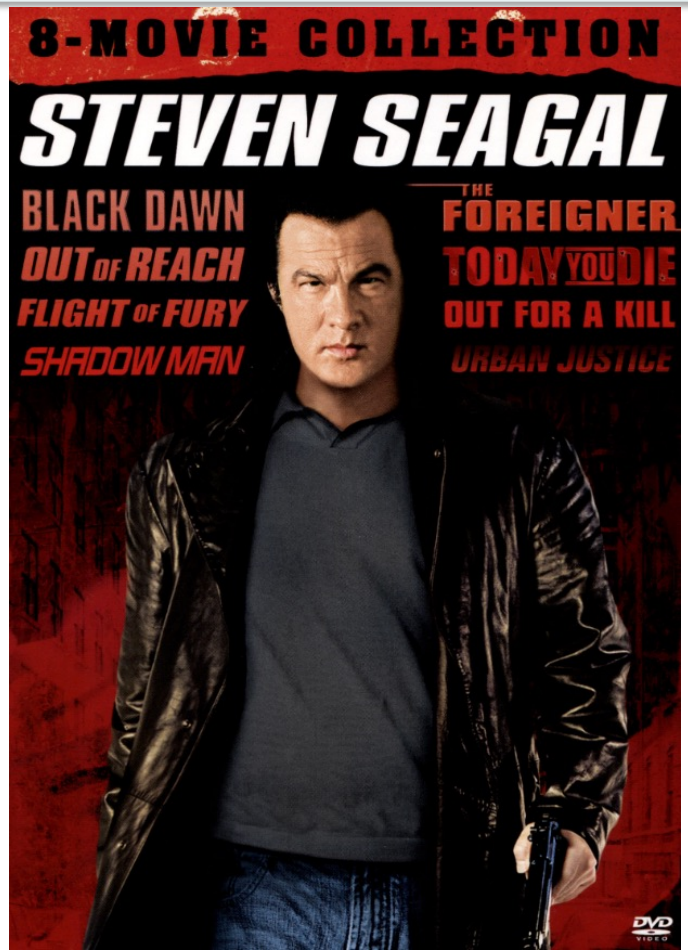
AE, adverse event; AUC, area under curve; BICR, blinded independent central review; CNS, central nervous system; CT, computed tomography; CTCAE, Common Terminology Criteria for Adverse Events; DCR, disease control rate; DoR, duration of response; EGFRm, epidermal growth factor receptor-mutated; EGFR-TKI, EGFR-tyrosine kinase inhibitor; Ex19del, exon 19 deletion; HR, hazard ratio; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival; QD, once-daily; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; WHO PS, World Health Organization performance status

Progression-free survival per investigator

- Median PFS was improved by ~8.8 months with osimertinib plus platinum-pemetrexed vs osimertinib monotherapy

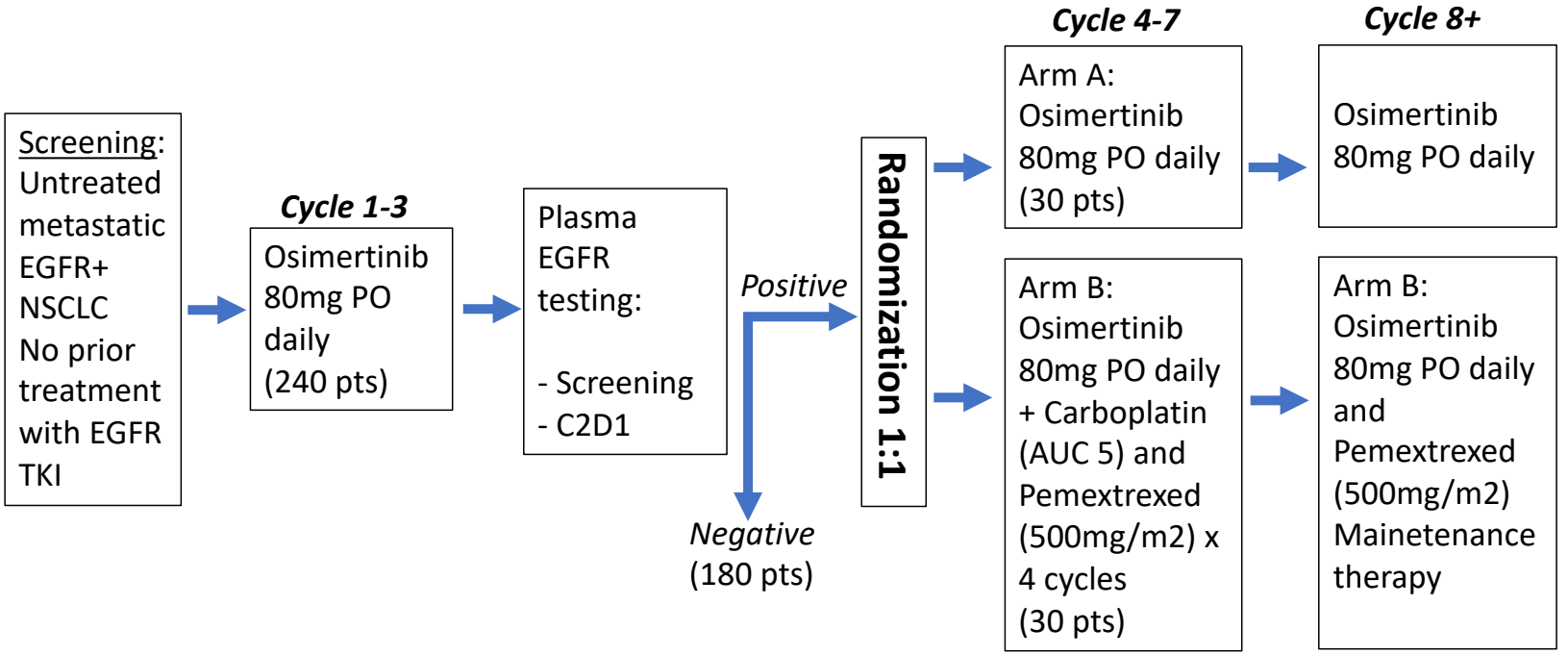


Data cut-off: 03 April 2023
*In all patients
CI, confidence interval; HR, hazard ratio; NC, not calculable; PFS, progression-free survival

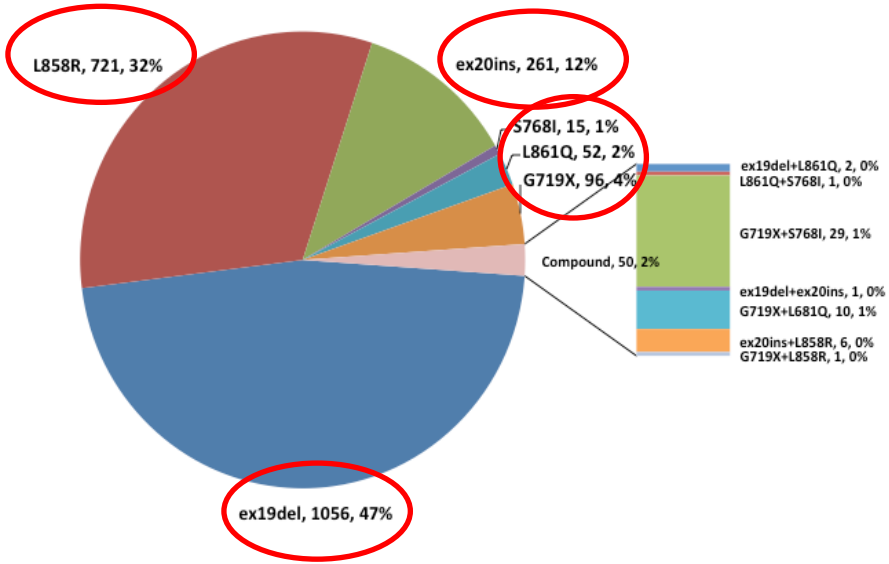


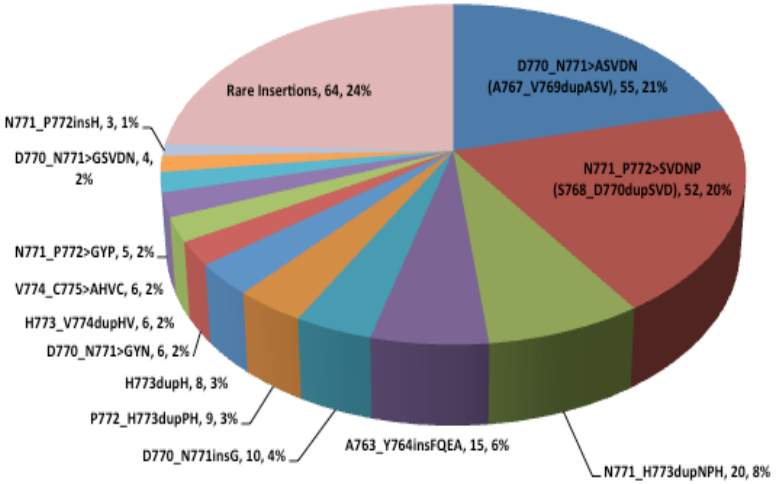
- ctDNA positive on treatment
- Co-mutations p53/RB1, RBM10
- CNS metastases
- Tumor volume/disease burden?

Shedders Trial



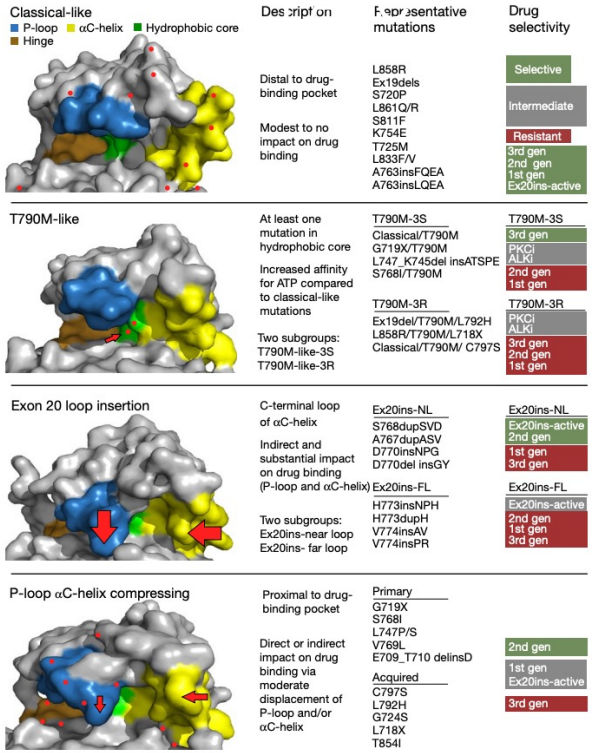
EGFR mutations are heterogeneous





JW Riess et al. JTO 2018

Osimertinib Efficacy in Atypical EGFR Mutations



Robichaux et al. Nature 2021.

- Structure-Function relationship and classification predicts TKI activity in EGFR mutant NSCLC.
- Role of EGFR moAb and bispecifics by mutation needs to be more fully explored.

Amivantamab Efficacy in EGFR Exon 20 insertion

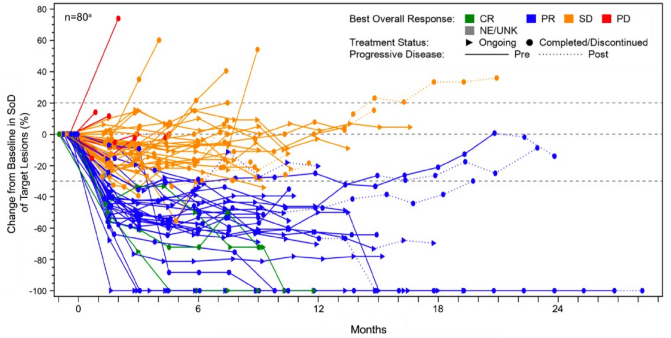
Amivantamab: Efficacy by BICR

BICR-assessed Response	Efficacy Population (n=81)
Overall response rate	**40%** (95% CI, 29–51)
Median duration of response	**11.1 months** (95% CI, 6.9–NR)
Best response, n (%)	
Complete response	3 (4)
Partial response	29 (36)
Stable disease	39 (48)
Progressive disease	8 (10)
Not evaluable	1 (1)
Clinical benefit rate[a]	74% (95% CI, 63–83)

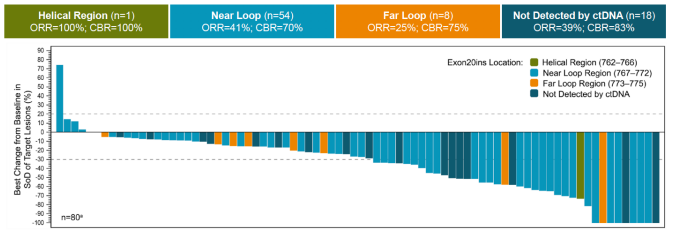
Median follow-up: 9.7 months (range, 1.1–29.3)

mPFS: 8.3 mo (95% CI, 6.5-10.9)
mOS: 22.8 mo (95% CI, 14.6-NR)

Amivantamab: Responses Over Time



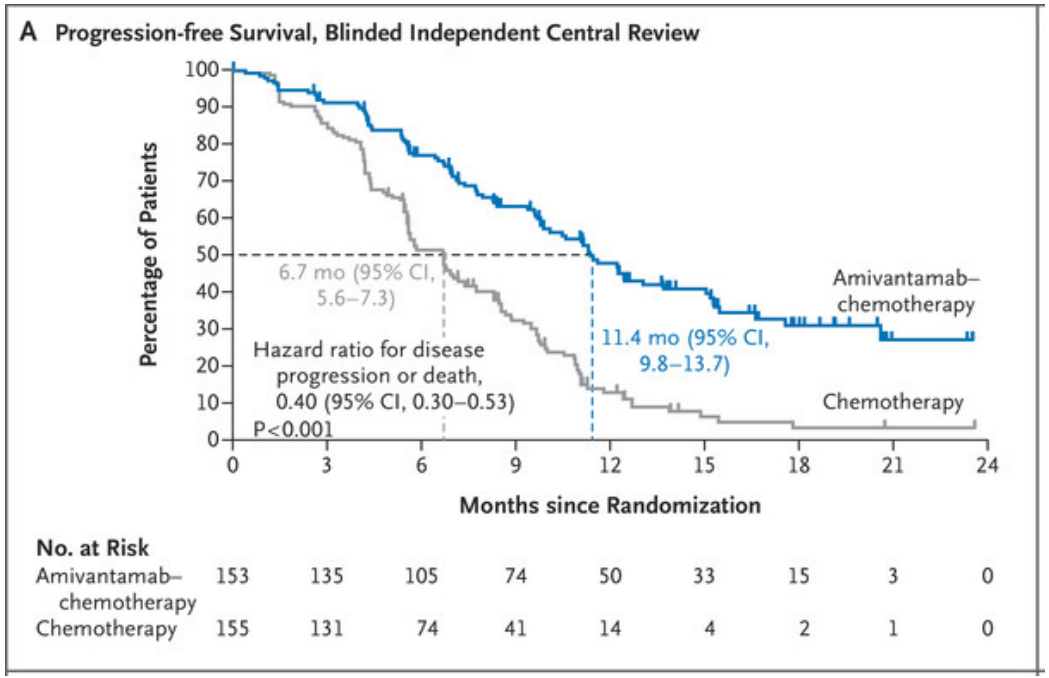
Best ORR by Insertion Region of Exon 20 (detected by ctDNA)

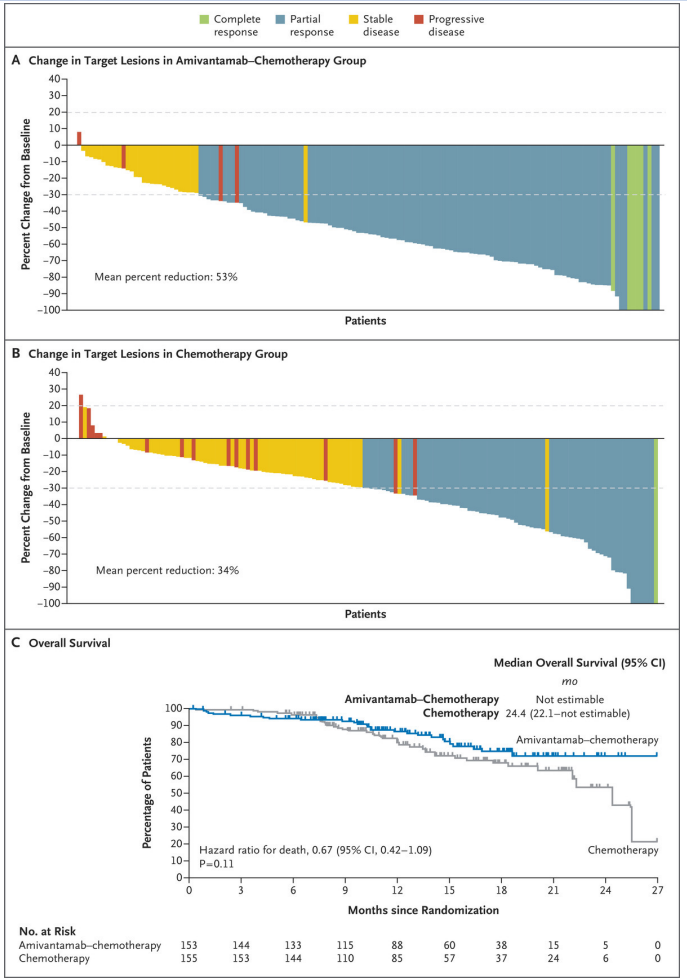


25 distinct Exon20ins variants identified by NGS of ctDNA (Guardant360®) from 63 evaluable patient samples

K. Park et al JCO 2021

Chemo-Amivantamab in 1L EGFR Exon 20 ins NSCLC





C. Zhou et al NEJM 2023

FURMO-002: Phase 1b Study in NSCLC Harboring Activating EGFR and HER2 Kinase Domain Mutations

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Stage 1 (Dose Escalation)

3+3 Dose Escalation and Backfill Cohorts

Starting Dose Level 1: 240 mg QD

240 mg QD Backfill

Dose Level -1: 160 mg QD

160 mg QD Backfill

Stage 2 (Dose Expansion)

Stage 2, Cohort 1
Previously Treated Locally Advanced or Metastatic NSCLC with
EGFR Exon 20 Insertion Mutations
240 mg QD

Stage 2, Cohort 2
Previously Treated Locally Advanced or Metastatic NSCLC with
HER2 Exon 20 Insertion Mutations
240 mg QD

Stage 2, Cohort 3
Previously Treated Locally Advanced or Metastatic NSCLC with
EGFR Activating Mutations
240 mg QD

Stage 2, Cohort 4
Untreated or Previously treated *EGFR*-TKI Naïve Locally Advanced or Metastatic NSCLC with
EGFR Uncommon Mutations (excluding EGFR Ex20ins)

R 1:1

- Arm A: 160 mg QD
- Arm B: 240 mg QD

Key Eligibility Criteria

- NSCLC with documented EGFR or HER2 mutation by local testing (tissue or blood)

Clinicaltrials.gov NCT05364073

furmo@arrivent.com

ARRIVENT

Confirmed ORR by IRC by Cohort

Efficacy by IRC	Treatment Naïve 240mg N=28*	Previously Treated 240mg N= 26#	Previously Treated 160mg N= 26#
Confirmed ORR, % (95% CI)	78.6% (59.05%, 91.70%)	46.2% (26.59%, 66.63%)	38.5% (20.23%, 59.43%)
Best Response, n (%)			
Partial response (PR)	22 (78.6%)	12 (46.2%)	10 (38.5%)
Stable disease (SD)	6 (21.4%)	12 (46.2%)	12 (46.2%)
Progressive disease (PD)	0	0	4 (15.4%)
Not evaluable/Not done	0 / 0	1 (3.8%) / 1 (3.8%)	0 / 0
DoR, median (months) (95% CI)	15.2 (8.74, 24.84)	13.1 (5.62, 13.80)	9.7 (5.59, NA)
DCR (CR+PR+SD), % (95% CI)	100.0% (87.66%, 100.00%)	92.3% (74.87%, 99.05%)	84.6% (65.13%, 95.64%)

Analysis is based on EGFR exon 20ins patients who had measurable disease at baseline by IRC, had ≥ 2 tumor assessments, had PD/death, or discontinued from treatment.
* 2 patients: one patient had no measurable target lesion at baseline by IRC; another patient did not have an exon 20 insertion mutation.
# 26 of the 28 patients in 240 mg and 160 mg cohorts respectively had at least 2 tumor assessments by June 15, 2023.
IRC, independent review committee ; ORR, objective response rate; DoR, duration of response; DCR: Disease Control Rate; CI, confidence interval;

FURVENT: Ph3 1L EGFR Ex20ins NSCLC Study Design (FURMO-004)

Key Inclusion Criteria:
- Documented EGFR exon 20 Insertion Mutation by local testing with tissue or blood
- Measurable Disease
- ECOG PS 0–1

Key Exclusion Criteria:
- Prior TKI
- Prior Anticancer Therapy in the Metastatic Setting

N=375

R 1:1:1

- **Furmonertinib 240mg QD**
- **Furmonertinib 160mg QD**
- **Platinum Chemotherapy + Pemetrexed**

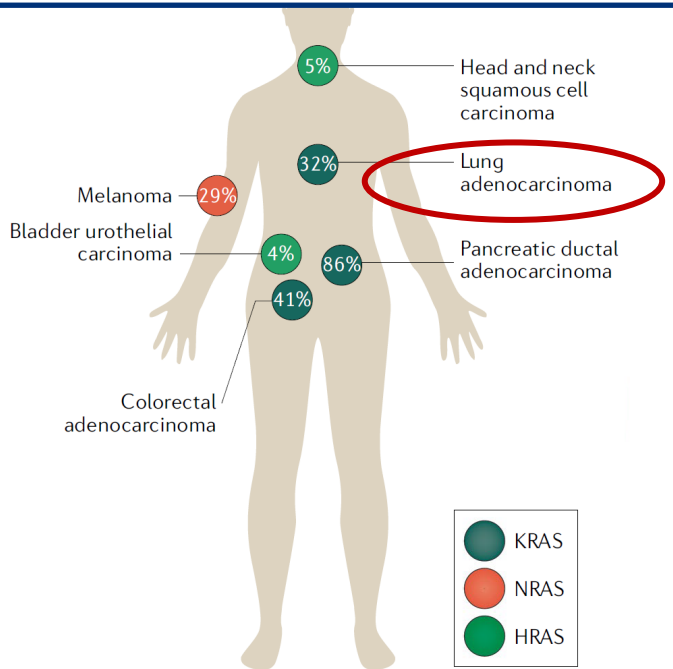
Crossover is permitted to furmonertinib following PD

Primary endpoint: PFS by BICR per RECIST v1.1
Key secondary endpoints: OS, ORR, DOR, PRO, Safety, PK

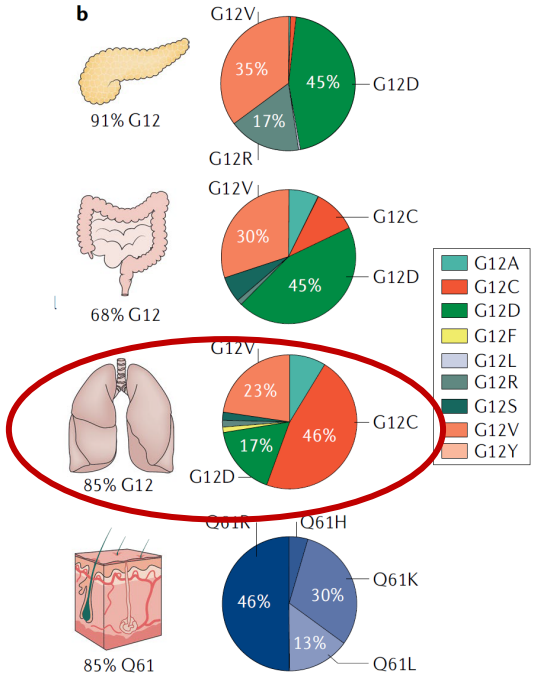
Clinicaltrials.gov **NCT05607550**
FURVENTStudy.com

KRAS mutations in cancer – Focus on NSCLC

Frequency of KRAS Mutations by Tumor Type

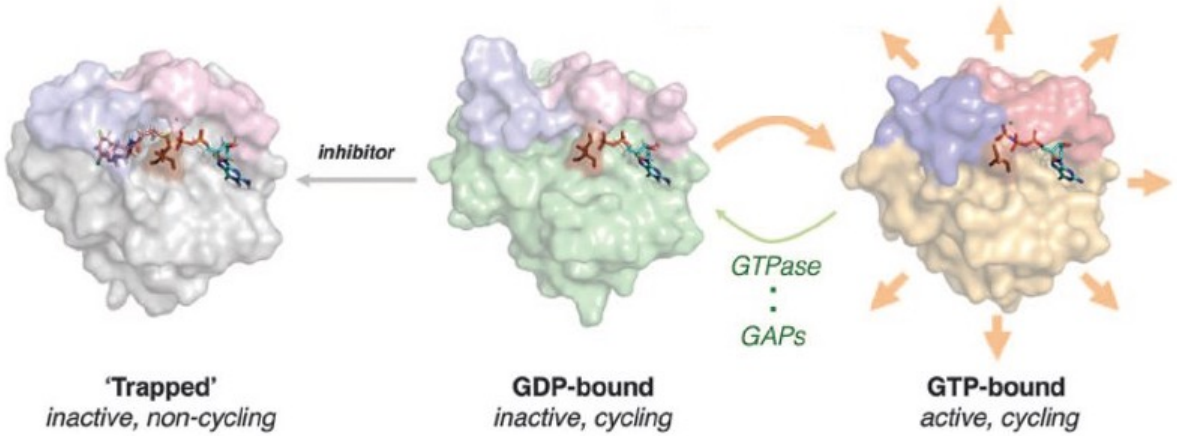


KRAS Mutation Subtypes By Tumor Tupe



Figures from Moore AR et al. Nat Rev Drug Discov 19, 533–552 (2020).

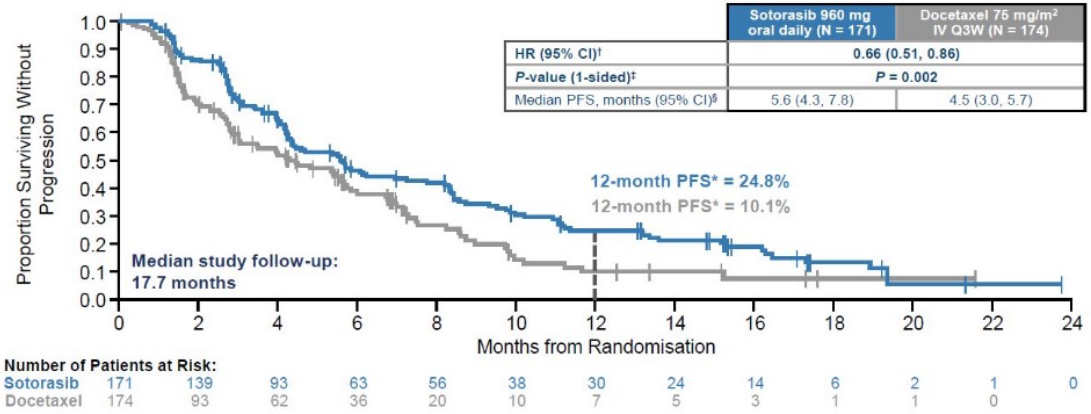
KRAS G12C Inhibitors Bind, Inactive GDP bound RAS and Trap It In Inactive State



From P. Lito et al. Science 2016

Codebreak 200: Topline Results

Primary Endpoint: PFS by BICR



CodeBreaK 200 met its primary endpoint with sotorasib demonstrating superior PFS over docetaxel (HR 0.66, *P* = 0.002); 12-month PFS rate was 24.8% for sotorasib and 10.1% for docetaxel

ORR 28.1% vs. 13.2%

mOS 10.6 (soto) vs. 11.3 months (doce). No difference in OS.

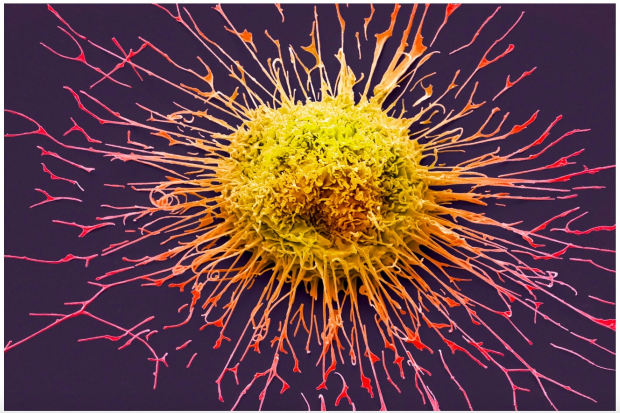
34% crossover in docetaxel arm

M. Johnson et al ESMO 2022

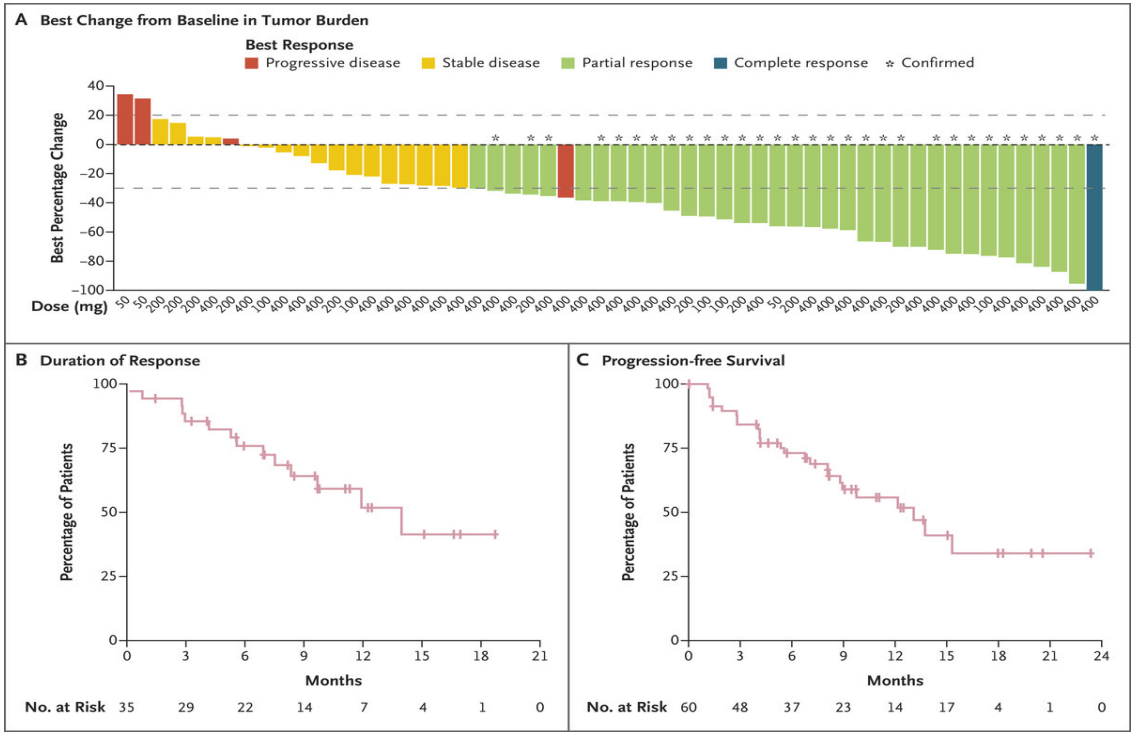
The New York Times

How Scientists Shot Down Cancer's 'Death Star'

No drug could touch a quivering protein implicated in a variety of tumors. Then one chemist saw an opening.



Anti-tumor Activity of Divarasib in Patients with Advanced KRAS G12C NSCLC



A Sacher et al. N Engl J Med 2023;389:710-721.

RAS(ON) Inhibitors

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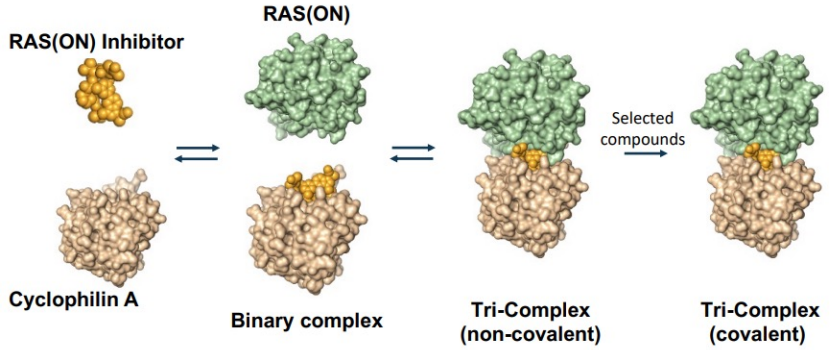
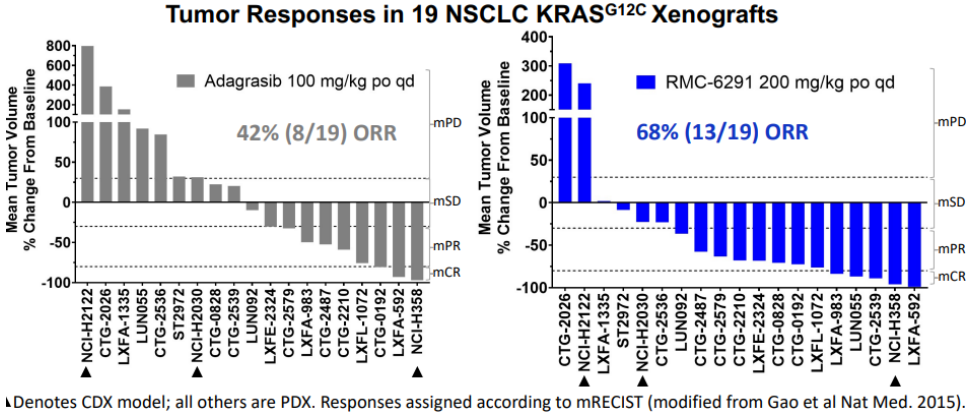
- Less susceptible to adaptive resistance compared to GDP bound RAS



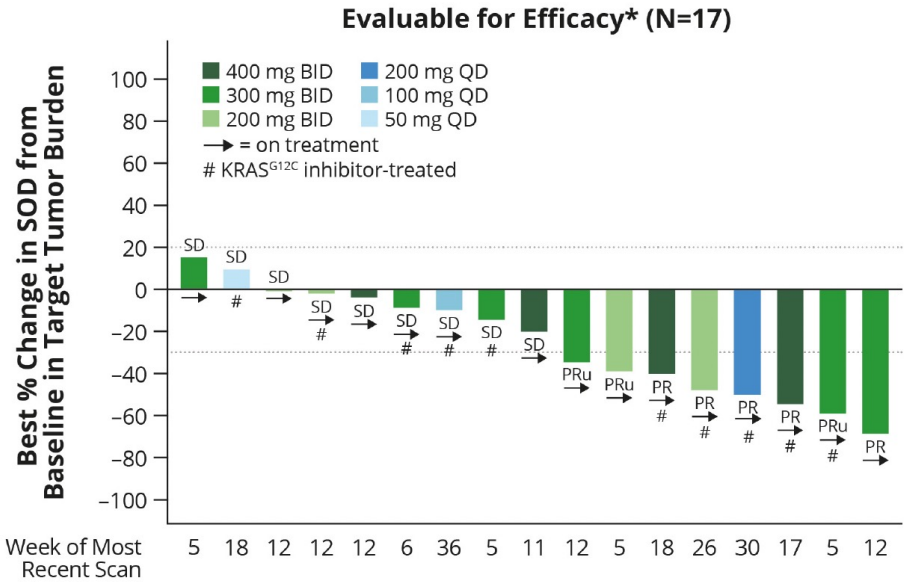
- RMC-6291 KRAS G12C (ON) inhibitor
- RMC-9805 KRAS G12D (ON) inhibitor
- RMC-6236-Pan RAS(ON)



▲Denotes CDX model; all others are PDX. Responses assigned according to mRECIST (modified from Gao et al Nat Med. 2015).

Kelsey S. AACR-NCI-EORTC 2021. Hofmann MH, et al. Cancer Discov. 2022 Apr 1;12(4):924-937.

KRAS^{G12C}-Mutant NSCLC Previously Treated With or Naïve to a KRAS^{G12C}(OFF) Inhibitor: Best Response

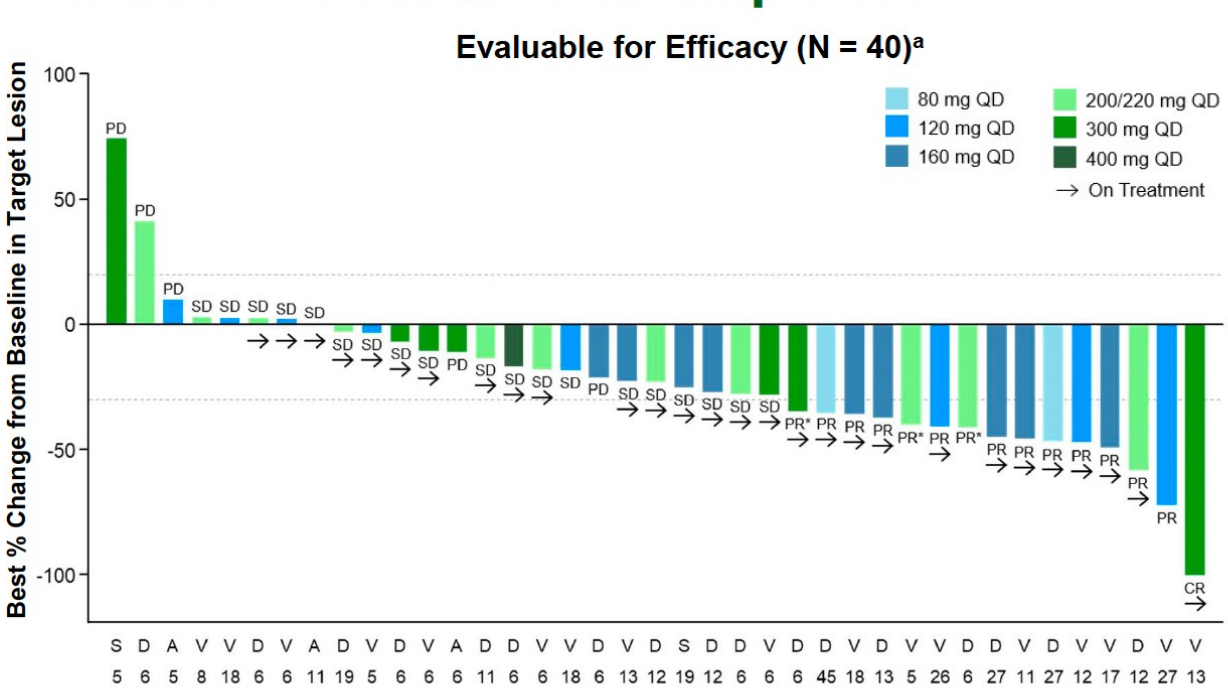


Tumor Response (per RECIST 1.1)		
Best overall response, n (%)	**Prior G12Ci (n=10)**	**Naïve to G12Ci (n=7)**
Partial response†	5 (50)	3 (43)
Stable disease	5 (50)	4 (57)
Progressive disease	0	0
ORR, n (%)	5 (50)	3 (43)
DCR (CR+PR+SD), n (%)	10 (100)	7 (100)

*All treated patients who received a first dose of RMC-6291 at least 8 weeks prior to data extract date; †PR includes 5 confirmed and 3 unconfirmed.
CR, complete response; DCR, disease control rate; G12Ci, G12C inhibitor; PD, progressive disease; PR, partial response; PRu, unconfirmed partial response; SD, stable disease; SOD, sum of diameters; ORR objective response rate; DCR, disease control rate; RECIST, response evaluation criteria in solid tumors.

Data Extracted 05 October 2023.

KRAS^{G12X} NSCLC: Best Response



Tumor Response (per RECIST 1.1)	
Best overall response, n (%)	
CR	1 (3)
PR	14 (35)
SD	19 (48)
PD	5 (13)
NE[b]	1 (3)
ORR, n (%)	15 (38)
Confirmed, n	12
DCR (CR+PR+SD), n (%)	34 (85)

*Unconfirmed PR per RECIST 1.1.

[a]Patients who received first dose of RMC-6236 at least 8 weeks prior to data extract date.

[b]One subject withdrew from study without post-baseline scans.

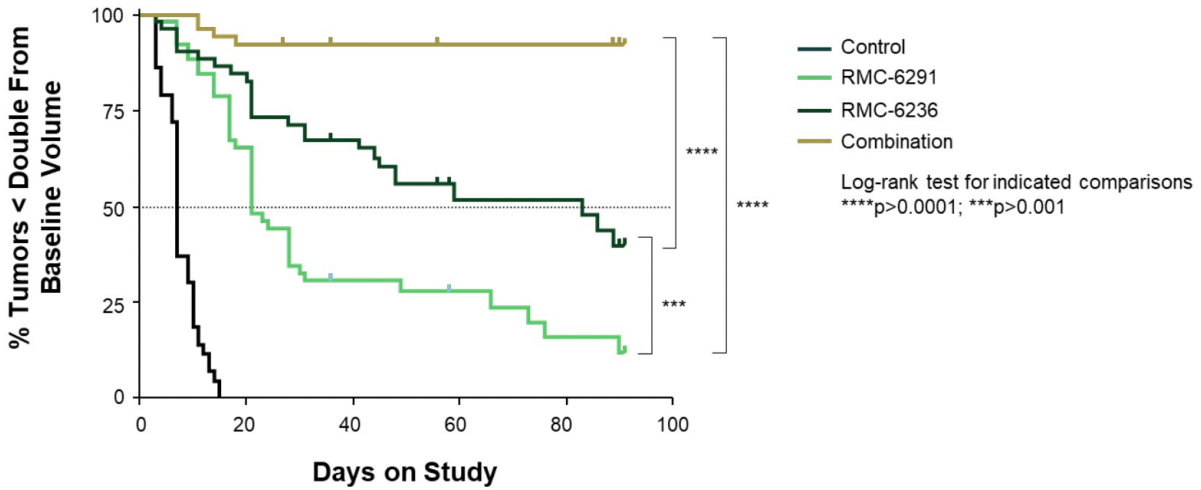
CR, complete response; DCR, disease control rate; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

MADRID 2023 ESMO congress

Kathryn C. Arbour, MD

Data Extracted 12 Oct 2023.

RMC-6236 + RMC-6291 Doublet Overcomes Resistance and Prolongs Durability in KRAS^{G12C} NSCLC Models



- RAS(ON) inhibitor doublet has been evaluated across seven models, including five identified as resistant to RMC-6291 monotherapy

Revolution Medicines preclinical research.
RMC-6236 dosed at 25 mg/kg PO QD (n=52); RMC-6291 dosed at 100 or 200 mg/kg PO QD (n=52); combination (n=51).

KEYNOTE-024 5-Year OS Update: First-Line Pembrolizumab vs Platinum-Based Chemotherapy in Patients with Metastatic Non–Small-Cell Lung Cancer and PD-L1 Tumor Proportion Score ≥50%

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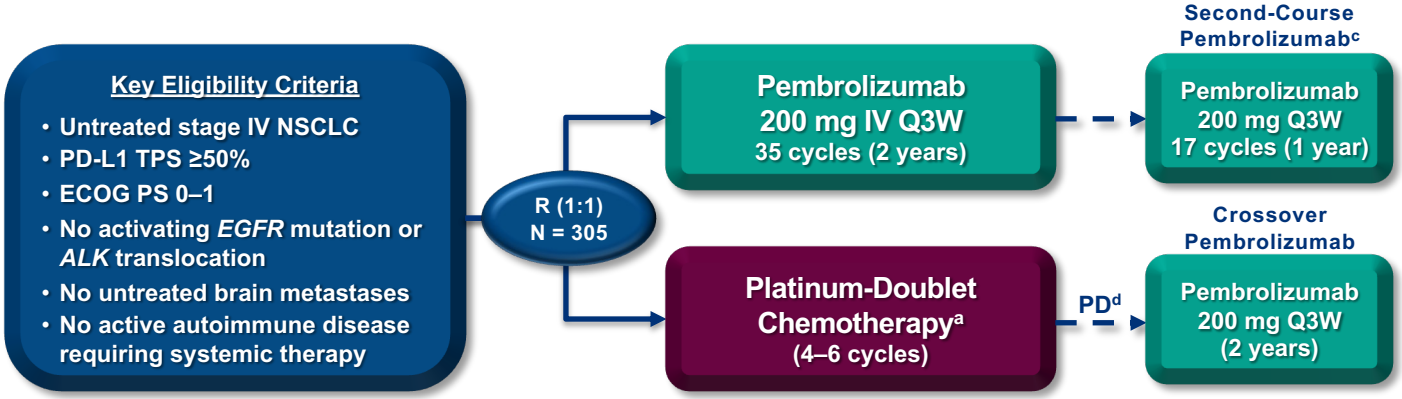
KEYNOTE-024 Study Design (NCT02142738)

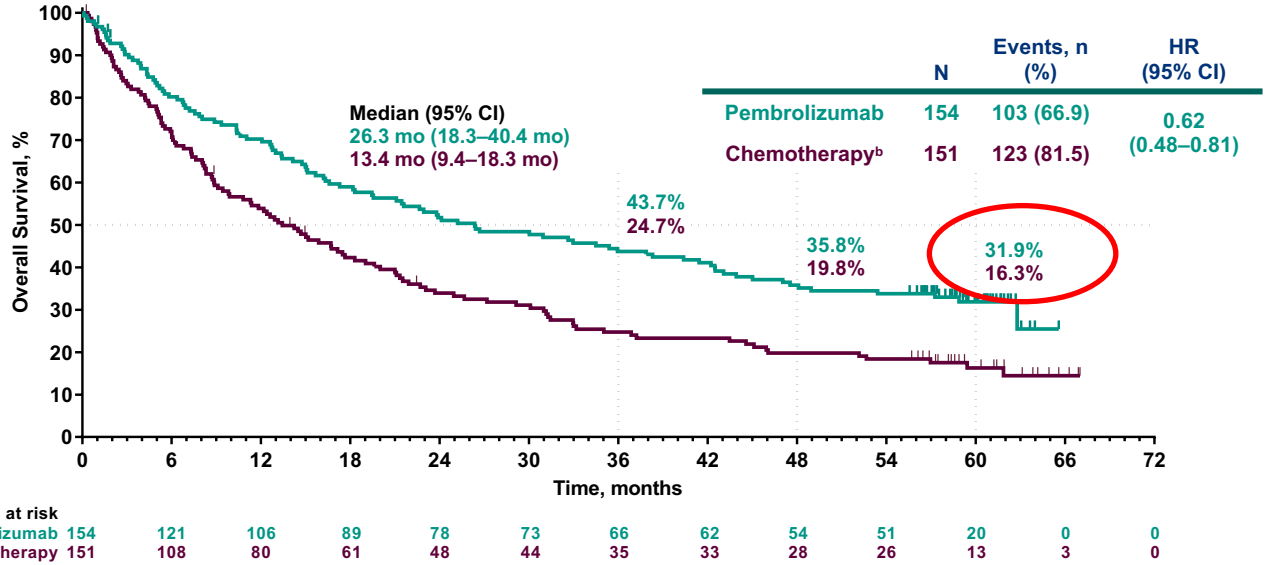


End Points

Primary:	PFS (RECIST v1.1, blinded independent central review)
Key secondary:	OS
Secondary:	ORR, safety, PFS (RECIST v1.1 per investigator review)
Exploratory:	DOR

[a]Optional pemetrexed maintenance therapy for nonsquamous disease. [b]Permitted for nonsquamous disease only. [c]Patients randomized to pembrolizumab who completed 2 years of therapy or who stopped pembrolizumab after achieving CR and then had PD were eligible for a second course of pembro monotherapy. [d]Before the DMC recommendation and amendment 6, which permitted those in the chemotherapy arm to be offered pembrolizumab (based on interim analysis 2 data), patients were eligible for crossover when PD was confirmed by blinded, independent central radiology review.

Overall Survival[a]



[a]ITT population.

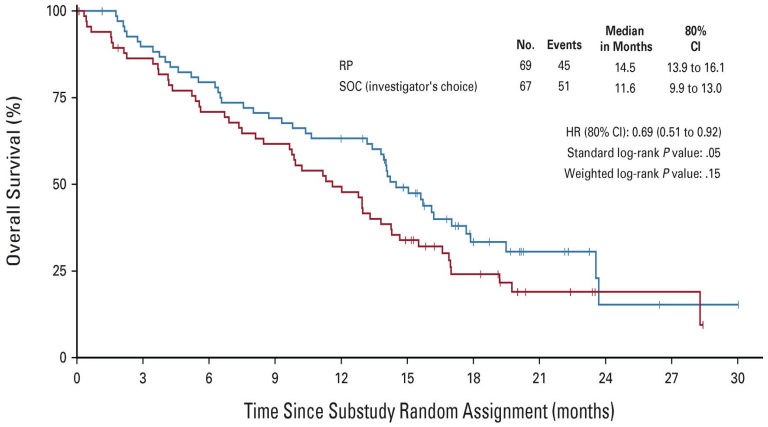
[b]Effective crossover rate from chemotherapy to anti–PD-L1 therapy, 66.0% (99 patients in total crossed over to anti–PD-[L]1 therapy: 83 patients crossed over to pembrolizumab during the study, and 16 patients received subsequent anti–PD-L1 therapy outside of crossover; patients may have received >1 subsequent anti–PD-L1 therapy). Data cutoff: June 1, 2020.

Lung-MAP: Master Protocol for Lung Cancer

- Lung MAP is an umbrella trial. Genomic/molecular profiling and then assignment to matched and unmatched arms based on results.
- Initially developed for squamous NSCLC given lack of genomic targets in that histology.
- Now expanded across NSCLC histologies and includes oncogene driver mutations (EGFR mutation/MET amp – S1900G)
- Lung-MAP is open at more than 700 sites across the United States. (Bring the trials and drugs to the patient)

OS and PFS in S1800A (Pembrolizumab + Ramucirumab vs. SOC)

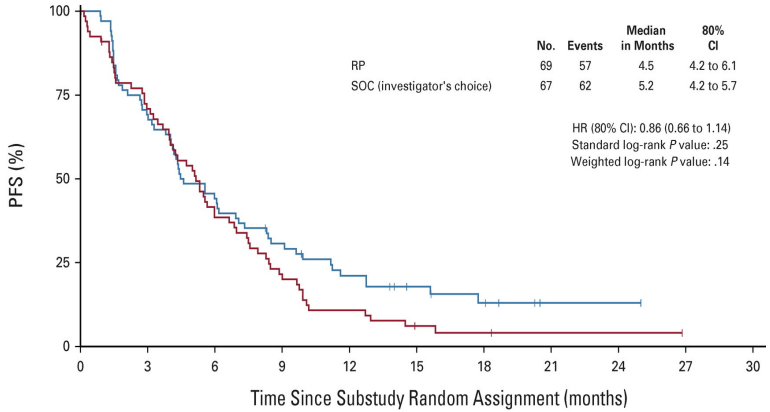
A



No. at risk (No. of events):

RP	69 (0)	61 (7)	54 (14)	47 (21)	42 (25)	29 (34)	14 (42)	7 (43)	2 (45)	1 (45)	1 (45)
SOC (investigator's choice)	67 (0)	56 (9)	46 (19)	40 (25)	32 (33)	21 (43)	12 (48)	5 (50)	2 (50)	2 (50)	0 (51)

B



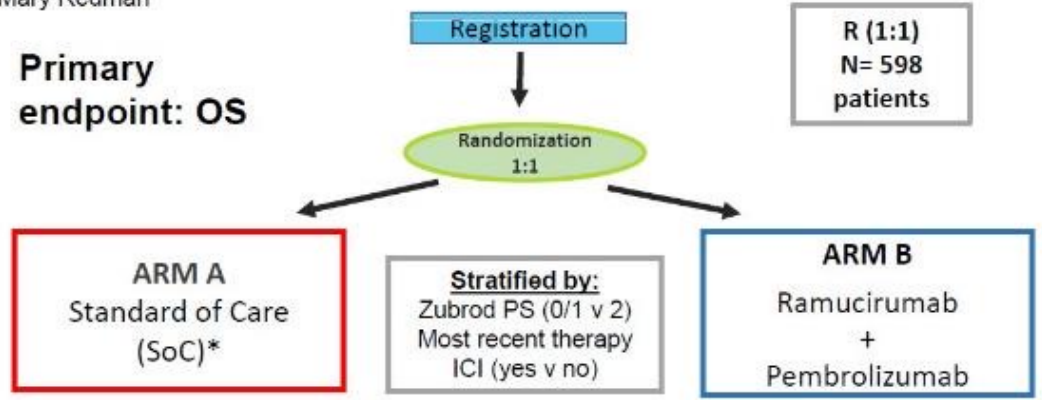
No. at risk (No. of events):

RP	69 (0)	47 (21)	30 (38)	20 (47)	13 (53)	8 (55)	5 (57)	1 (57)	1 (57)	0 (57)	0 (57)
SOC (investigator's choice)	67 (0)	46 (19)	25 (40)	14 (51)	7 (58)	3 (61)	2 (62)	1 (62)	1 (62)	0 (62)	0 (62)

S2302, Project Pragmatica

S2302, PROJECT PRAGMATICA: A PROSPECTIVE RANDOMIZED STUDY OF RAMUCIRUMAB (NSC 749128) PLUS PEMBROLIZUMAB (MK-3475; NSC 776864) VERSUS STANDARD OF CARE FOR PARTICIPANTS PREVIOUSLY TREATED WITH IMMUNOTHERAPY FOR STAGE IV OR RECURRENT NON-SMALL CELL LUNG CANCER

Chair: Karen Reckamp, MD; Co-chair: Konstantin Dragnev, MD; TBD
Statistician: Mary Redman



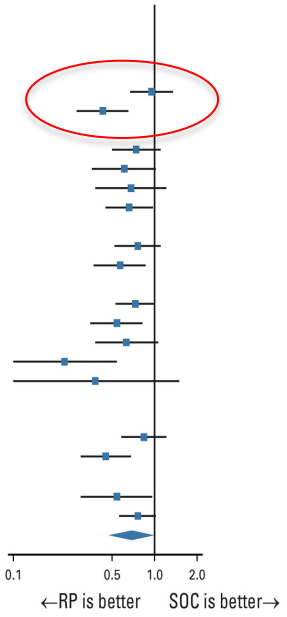
*SoC treatment is to be determined by the treating investigator and participant. It is recommended that the choice of SoC drug(s) is based on NCCN guidelines for a "systemic therapy for advanced or metastatic disease-subsequent."

Forrest Plot S1800A

Overall Survival

A

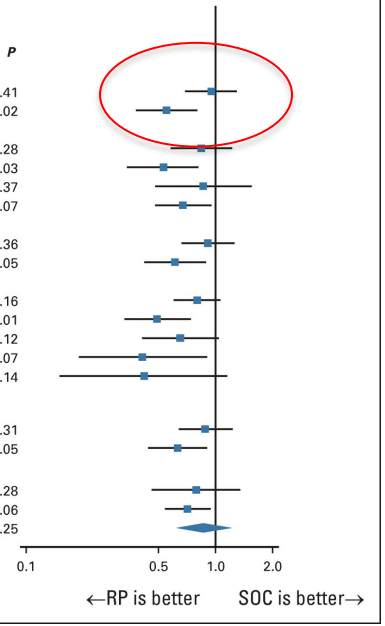
	RP Events/n	SOC Events/n	HR (80% CI)	P
Histology				
Nonsquamous	27/40	27/39	0.95 (0.67 to 1.35)	.43
Squamous/mixed	18/29	24/28	0.43 (0.28 to 0.65)	.005
PD-L1				
0	21/29	21/26	0.74 (0.50 to 1.10)	.16
1-49	11/21	15/22	0.61 (0.36 to 1.02)	.11
≥ 50	8/12	12/16	0.68 (0.38 to 1.21)	.20
≥ 1	19/33	27/38	0.66 (0.45 to 0.97)	.08
TMB				
< 10	23/32	28/38	0.76 (0.52 to 1.10)	.17
≥ 10	18/33	20/25	0.57 (0.37 to 0.86)	.04
Biomarker				
TP53	31/48	35/48	0.73 (0.53 to 1.00)	.10
CDKN2A	18/27	21/24	0.54 (0.35 to 0.82)	.03
KRAS	12/21	13/16	0.63 (0.38 to 1.06)	.13
STK11	4/7	10/10	0.23 (0.10 to 0.54)	.01
KEAP1	1/3	7/10	0.38 (0.10 to 1.49)	.18
Prior Treatment				
IO + Chemotherapy combination	20/32	32/42	0.84 (0.58 to 1.21)	.27
Chemotherapy→IO	25/36	18/23	0.45 (0.30 to 0.68)	.006
PS				
0	15/23	8/9	0.54 (0.30 to 0.96)	.08
1	30/46	43/58	0.76 (0.56 to 1.02)	.12
Overall	45/69	51/67	0.69 (0.51 to 0.92)	.05



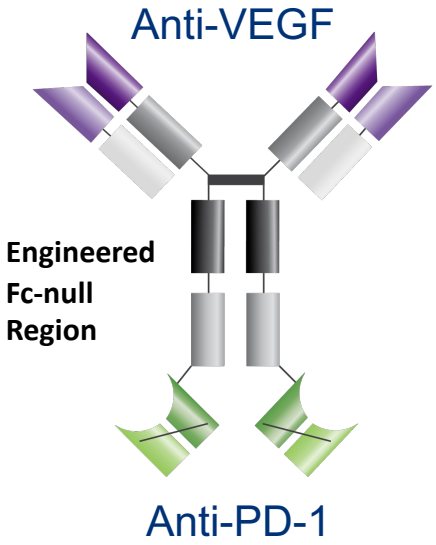
Progression-Free Survival

B

	RP Events/n	SOC Events/n	HR (80% CI)	P
Histology				
Nonsquamous	34/40	34/39	0.95 (0.69 to 1.29)	.41
Squamous/mixed	23/29	28/28	0.55 (0.38 to 0.80)	.02
PD-L1				
0	27/29	25/26	0.84 (0.58 to 1.22)	.28
1-49	16/21	22/22	0.53 (0.34 to 0.81)	.03
≥ 50	8/12	12/16	0.86 (0.48 to 1.55)	.37
≥ 1	24/33	34/38	0.67 (0.48 to 0.95)	.07
TMB				
< 10	29/32	36/38	0.91 (0.66 to 1.26)	.36
≥ 10	24/33	23/25	0.61 (0.42 to 0.89)	.05
Biomarker				
TP53	39/48	43/48	0.80 (0.60 to 1.06)	.16
CDKN2A	22/27	24/24	0.49 (0.33 to 0.74)	.01
KRAS	16/21	15/16	0.65 (0.41 to 1.04)	.12
STK11	5/7	10/10	0.41 (0.19 to 0.90)	.07
KEAP1	2/3	10/10	0.42 (0.15 to 1.15)	.14
Prior Treatment				
IO + Chemotherapy Combination	26/32	40/42	0.88 (0.64 to 1.23)	.31
Chemotherapy→IO	31/36	21/23	0.63 (0.44 to 0.90)	.05
PS				
0	21/23	8/9	0.79 (0.46 to 1.35)	.28
1	36/46	54/58	0.71 (0.54 to 0.94)	.06
Overall	57/69	62/67	0.86 (0.66 to 1.14)	.25



HARMONi-3: A Randomized, Controlled, Multiregional Phase 3 Study of Ivonescimab Combined with Chemotherapy Versus Pembrolizumab Combined with Chemotherapy for the First-line Treatment of Metastatic Squamous Non-Small Cell Lung Cancer



Ivonescimab: First-in-Class PD-1/VEGF Bispecific Antibody in Clinical Development

Key Inclusion:
- First-line Stage IV squamous NSCLC

Key Exclusion:
- Known actionable mutations for which 1L approved agents are available
- Symptomatic central nervous system (CNS) metastases
- Major blood vessel invasion or encasement by cancer; intratumor cavitation
- History of bleeding tendencies or coagulopathy or clinically significant bleeding symptoms or risk (including GI bleeding, hemoptysis)
- Active autoimmune disease

Randomization 1:1

Ivonescimab 20 mg/kg q3w + carboplatin AUC 5 or 6 q3w + paclitaxel 175 or 200 mg/m² q3w (or nab-paclitaxel 100 mg/m² q3w) x 4 cycles → Ivonescimab (maintenance up to 24 months)

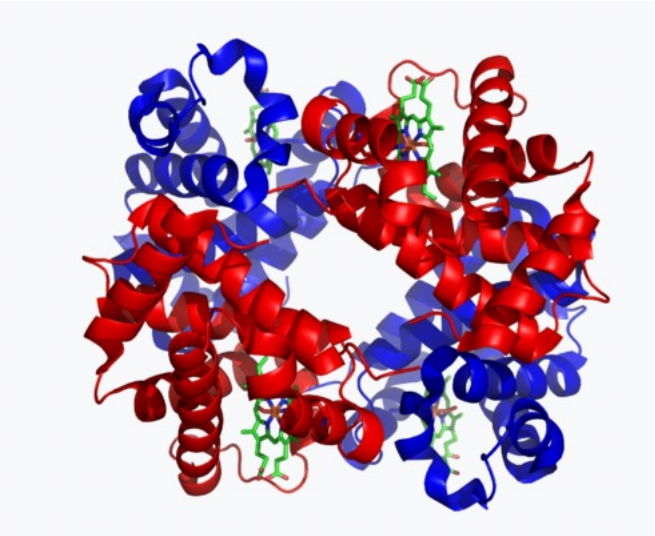
Pembrolizumab 200 mg q3w + carboplatin AUC 5 or 6 q3w + paclitaxel 175 or 200 mg/m² q3w (or nab-paclitaxel 100 mg/m² q3w) x 4 cycles → Pembrolizumab (maintenance up to 24 months)

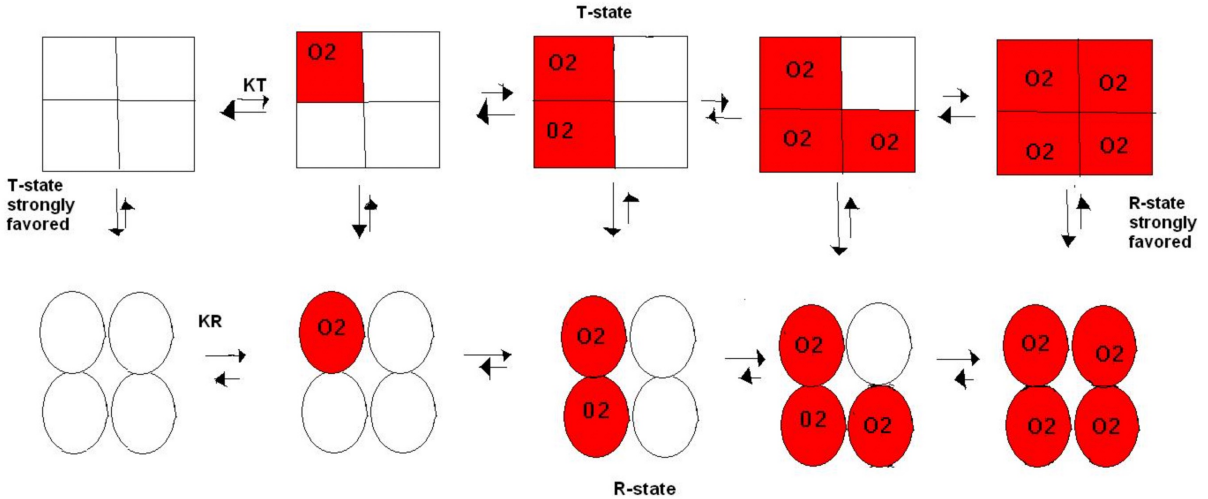
Treatment until:
- Disease progression
- Unacceptable toxicity
- Withdrawal of consent/death

Stratification factors:
- Sex (female vs male)
- Age (<65 vs ≥65 years)
- Geographical region: East Asia vs Rest of the world (ROW)
- Liver or brain metastases at study entry (present vs absent)

JW Riess et al. ENA 2023

Cooperative Binding and Ivonescimab





Conclusions

- Advances in lung cancer treatment (expanding toolbox) have meaningfully improved survival for our patients (N. Howlander NEJM 2020)
- UC Davis has exciting clinical trials to address these unmet needs both for IO and targeted therapies.
- Bringing these therapies to early stage disease is the next step with the potential to “cure” patients.