NCCN 2025
Lung Cancer Congress

Rare Targets and Novel Therapies in Non-Small Cell Lung Cancer: Navigating New TKIs and Uncommon Oncogenic Drivers

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NCCN National Comprehensive Cancer Network®

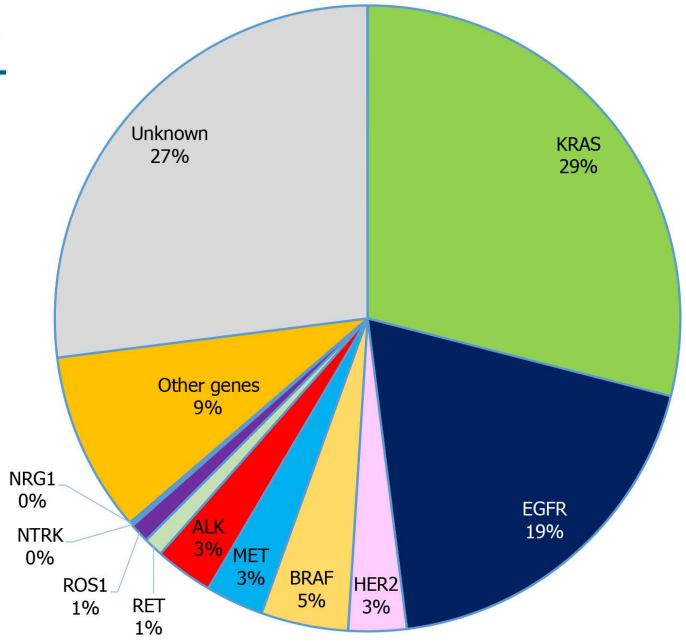
Oncogene Driven Advanced NSCLC

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2026
Non-Small Cell Lung Cancer

TESTING RESULTS[qq,rr]

EGFR exon 19 deletion or L858R mutation positive	NSCL-21
EGFR S768I, L861Q, and/or G719X mutation positive	NSCL-24
EGFR exon 20 insertion mutation positive	NSCL-25
KRAS G12C mutation positive	NSCL-26
ALK gene fusion positive	NSCL-27
ROS1 gene fusion positive	NSCL-30
BRAF V600E mutation positive	NSCL-32
NTRK1/2/3 gene fusion positive	NSCL-33
MET exon 14 skipping mutation positive	NSCL-34
RET gene fusion positive	NSCL-35
ERBB2 (*HER2*) mutation positive	NSCL-36
NRG1 gene fusion positive	NSCL-37
PD-L1 ≥1% and negative for actionable biomarkers above	NSCL-38
PD-L1 <1% and negative for actionable biomarkers above	NSCL-39



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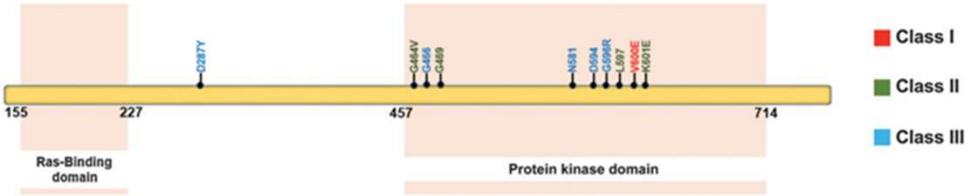
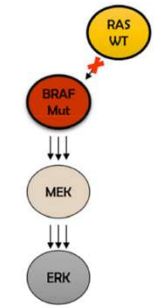
Chevallier et al. *WJCO* 2021

BRAF-mutated NSCLC: Biology

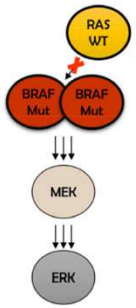


Class I
- V600 mutant
- Kinase activated
- RAS-independent
- BRAF monomers



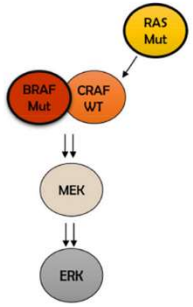
V600E, V600K, V600D
V600R, V600M

Class II
- Non-V600 mutant
- Kinase activated
- RAS-independent
- BRAF dimers

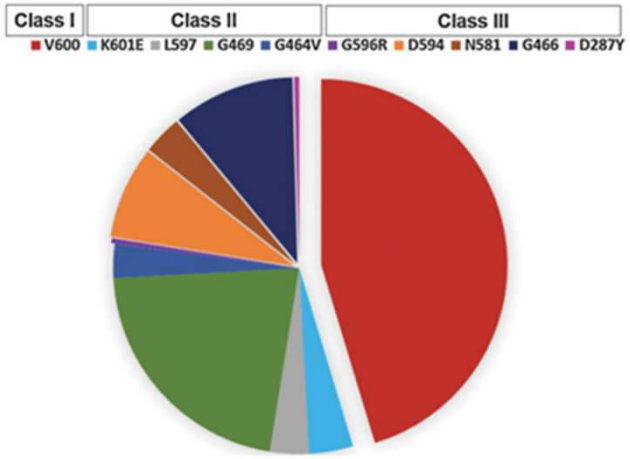


K601E, K601N, K601T
L597Q, L597V, G469A
G469V, G469R, G464V
G464E, Fusion Proteins

Class III
- Non-V600 mutant
- Kinase impaired
- RAS-dependent
- BRAF heterodimers

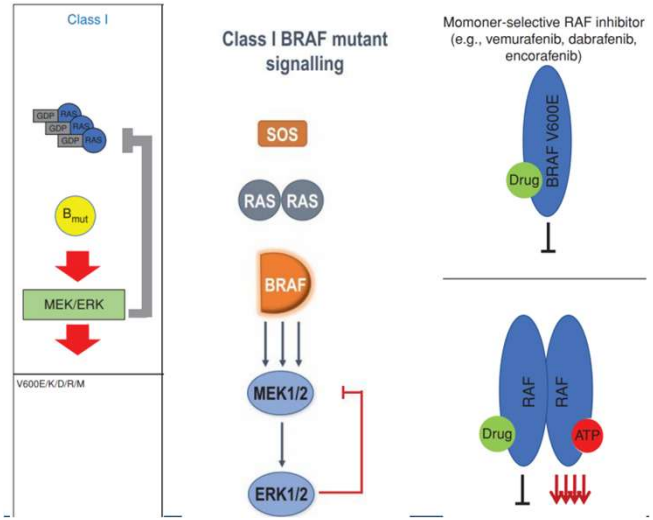


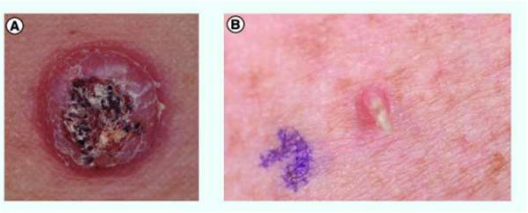
D287H, V459L, G466V
G466E, G466A, S467L
G469E, N581S, N581I
D594N, D594G, D594A
D594H, F595L, G596D
G596R



Yaeger et al. Can Discov 2019, Dankner et al. Oncogene 2018, Dagogo-Jack et al. CCR 2019

BRAF-mutated NSCLC: BRAF + MEK Inhibition





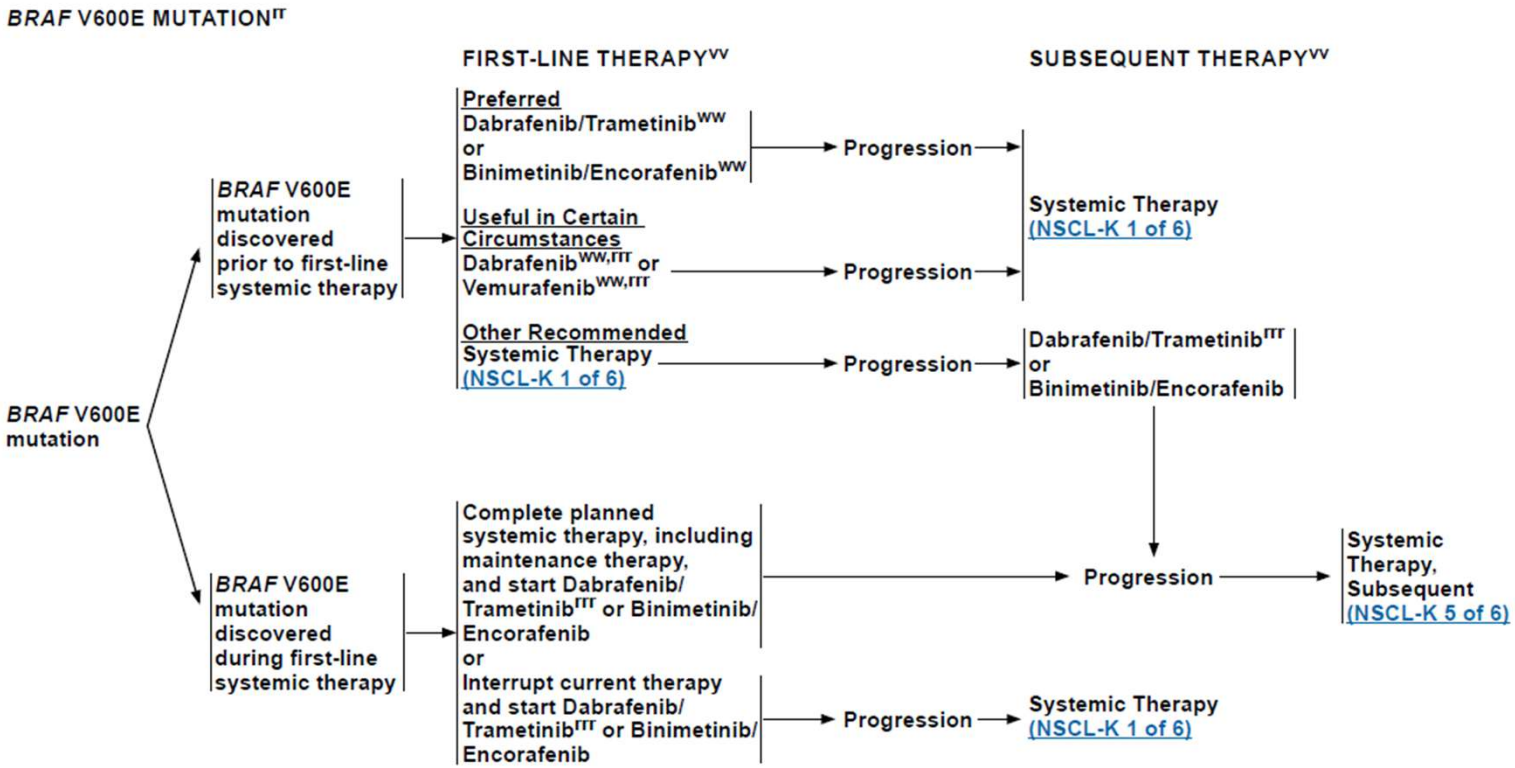
Keratocanthomas

Dabrafenib RR- 33%, PFS- 5.5 mo

	Previously Treated			
	VE-Basket trial **vemurafenib** (n=20)	AcSé trial **vemurafenib** (n=100)	BRF113928 **dabrafenib** (n = 78)	BRF113928 **Dabrafenib Plus Trametinib** (n = 57)
Male	14 (70%)	-	39 (50%)	29 (51%)
Never smoker	7 (35%)	-	29 (37%)	16 (28%)
ORR % (95% CI)	42 (20-67)	44.9	33 (23–45)	67 (53–79)
PFS, median (95% CI)	**7.3** (3.5-10.8)	**5.2**	**5.5** (3.4–7.3)	**10.2** (6.9–16.7)
OS, median (95% CI)	NA	9.3	12.7 (7.3–16.3)	18.2 (14.3–NE)

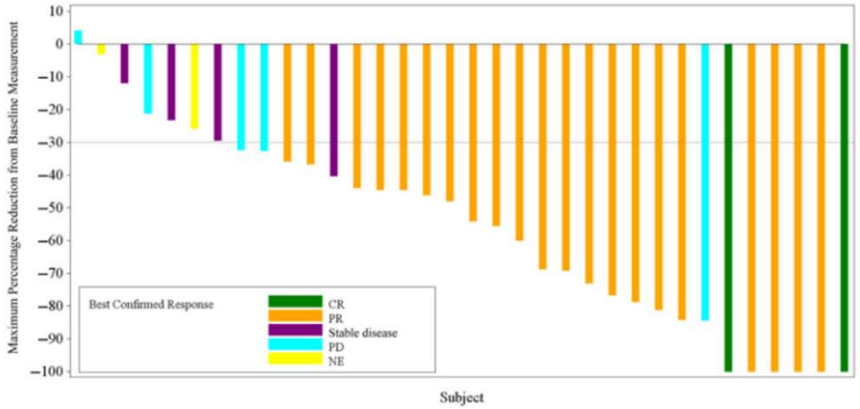
Yaeger et al. Can Discov 2019, Planchard et al. Lancet Oncol 2016

BRAF-mutated NSCLC: BRAF + MEK Inhibition



BRAF-mutated NSCLC: BRAF + MEK Inhibition

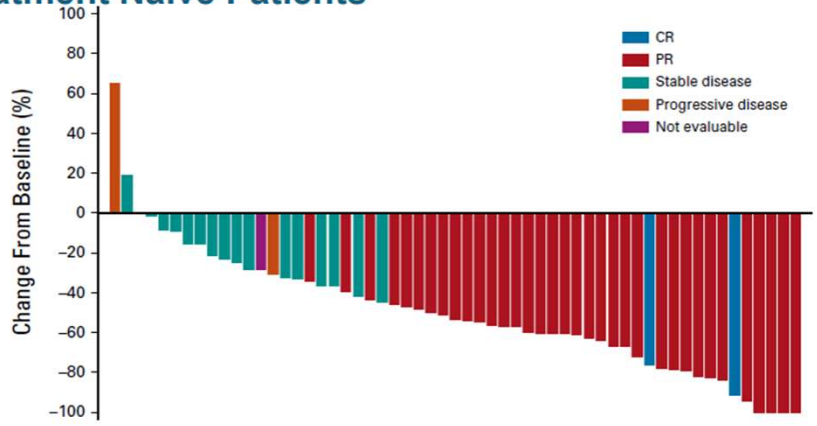
Response Rate in Treatment Naïve Patients



Treatment naïve cohort (n=36)
ORR: 63.9%
DCR: 75.0%

Dabrafenib + Trametinib

Planchard, et al, JTO 2021



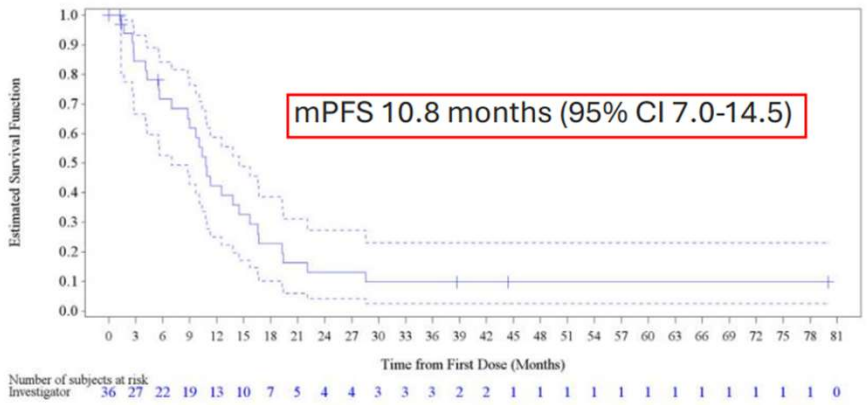
Treatment naïve cohort (n=59
ORR 75%
DCR at 24 weeks: 64%

Encorafenib + Binimetinib

Riely, et al JCO 2023

BRAF-mutated NSCLC: BRAF + MEK Inhibition

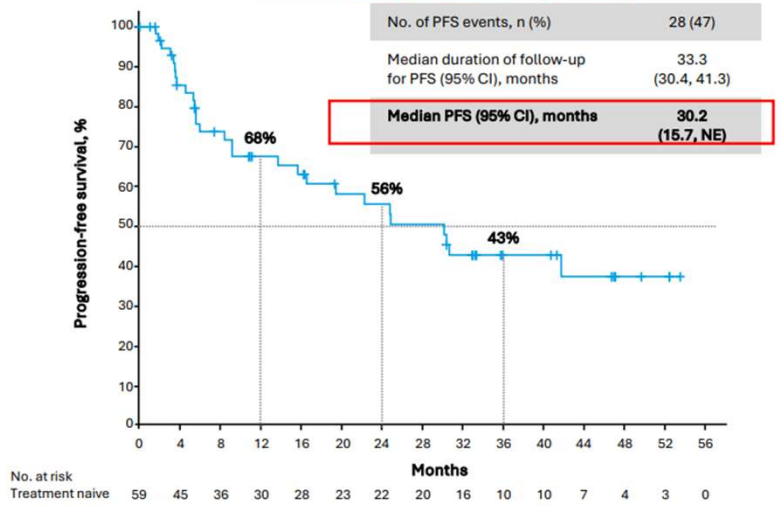
Treatment naive (n=36)



Dabrafenib + Trametinib

Planchard, et al, JTO 2021

Treatment naive (n=59)



Encorafenib + Binimetinib

Riely, et al ESMO 2024

BRAF-mutated NSCLC: BRAF + MEK Inhibition

AE >10% (not all TRAE)

	Grade 1–2	Grade 3	Grade 4	Grade 5
Total	10 (28%)	23 (64%)	2 (6%)	1 (3%)
Pyrexia	19 (53%)	4 (11%)	0	0
Nausea	20 (56%)	0	0	0
Diarrhoea	12 (33%)	1 (3%)	0	0
Fatigue	13 (36%)	0	0	0
Peripheral oedema	13 (36%)	0	0	0
Vomiting	9 (25%)	3 (8%)	0	0
Dry skin	12 (33%)	0	0	0
Decreased appetite	12 (33%)	0	0	0
Chills	9 (25%)	0	0	0
Headache	9 (25%)	0	0	0
Rash	7 (19%)	1 (3%)	0	0
Dizziness	8 (22%)	0	0	0
Cough	8 (22%)	0	0	0
Alanine aminotransferase increase	2 (6%)	4 (11%)	0	0
Dyspnoea	4 (11%)	2 (6%)	0	0
Hypotension	4 (11%)	2 (6%)	0	0
Back pain	6 (17%)	0	0	0
Weight decrease	6 (17%)	0	0	0
Abdominal pain	4 (11%)	1 (3%)	0	0
Anaemia	4 (11%)	1 (3%)	0	0
Arthralgia	4 (11%)	1 (3%)	0	0
Constipation	5 (14%)	0	0	0
Insomnia	5 (14%)	0	0	0
Myalgia	5 (14%)	0	0	0
Hypertension	0	4 (11%)	0	0
Hyponatraemia	2 (6%)	2 (6%)	0	0
Aspartate aminotransferase increase	3 (8%)	1 (3%)	0	0
Asthenia	3 (8%)	1 (3%)	0	0
Pruritus	3 (8%)	1 (3%)	0	0
Pain in extremity	3 (8%)	1 (3%)	0	0
Erythema	4 (11%)	0	0	0
Dysphonia	3 (8%)	0	0	0
Malaise	4 (11%)	0	0	0
Musculoskeletal chest pain	4 (11%)	0	0	0
Urinary tract infection	4 (11%)	0	0	0
Dehydration	2 (6%)	1 (3%)	0	0
Ejection fraction decrease	1 (3%)	2 (6%)	0	0
Pulmonary embolism	1 (3%)	2 (6%)	0	0
Weight increase	2 (6%)	1 (3%)	0	0

(Table 3 continues on next page)

- Pyrexia not observed with encorafenib/binimetinib
- Similar rates of nausea, vomiting, diarrhea, fatigue
- LFT elevations similar

Rates of Drug Interruption/Discontinuation D/T, E/B

- Discontinuation- 12% , 15%
- Dose Interruption- 61%, 44%
- Dose Reduction- 35%, 24%

Dabrafenib + Trametinib

TABLE 3. Incidence of TRAEs of Any Grade ≥10% in All Patients

	Overall (N = 98)		
AE Preferred Term	Any Grade	Grade 3	Grade 4
Any TRAEs, No. (%)	92 (94)	37 (38)	3 (3)*
Nausea	49 (50)	3 (3)	0
Diarrhea	42 (43)	4 (4)	0
Fatigue	31 (32)	2 (2)	0
Vomiting	28 (29)	1 (1)	0
Anemia	18 (18)	3 (3)	0
Vision blurred	17 (17)	1 (1)	0
Constipation	13 (13)	0	0
ALT increased	12 (12)	5 (5)	0
AST increased	12 (12)	7 (7)	0
Pruritus	12 (12)	0	0
Blood creatine phosphokinase increased	11 (11)	0	0
Peripheral edema	11 (11)	0	0
Abdominal pain	10 (10)	0	0
Alopecia	10 (10)	0	0
Asthenia	10 (10)	3 (3)	0
Dry skin	10 (10)	0	0

Abbreviation: TRAE, treatment-related adverse event.
*Grade 4 TRAEs were colitis, disseminated intravascular coagulation, increased gamma-glutamyl transferase, and hyponatremia. One patient can have multiple TRAEs.

Encorafenib + Binimetinib

Planchard et al. Lancet 2016, Riely et al. JCO 2023

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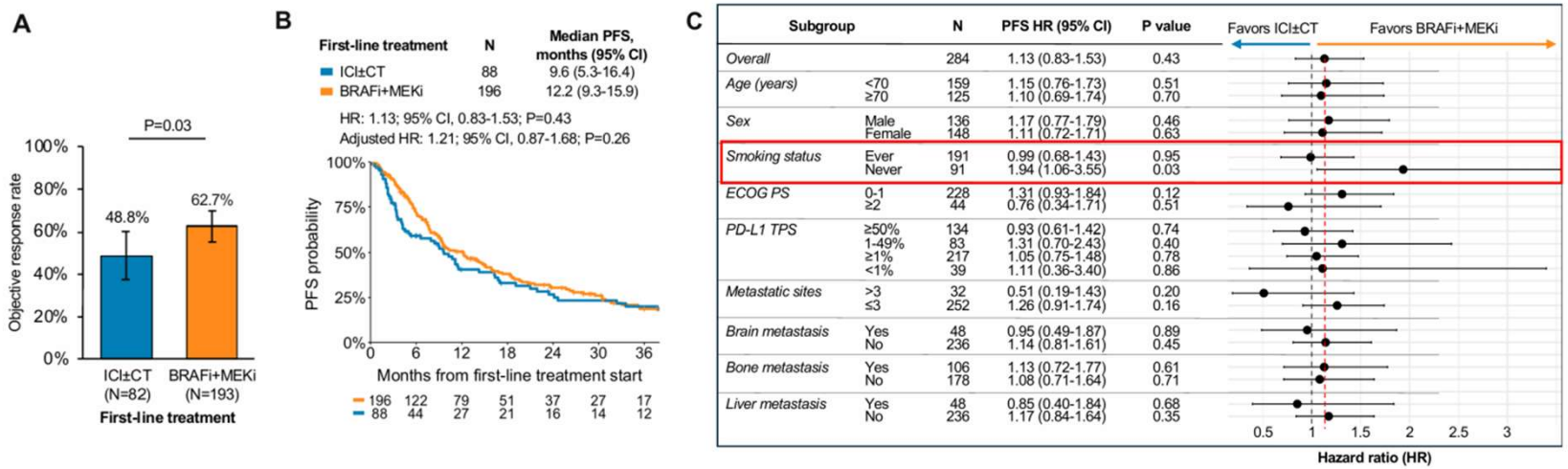
BRAF-mutated NSCLC: BRAF + MEK Inhibition

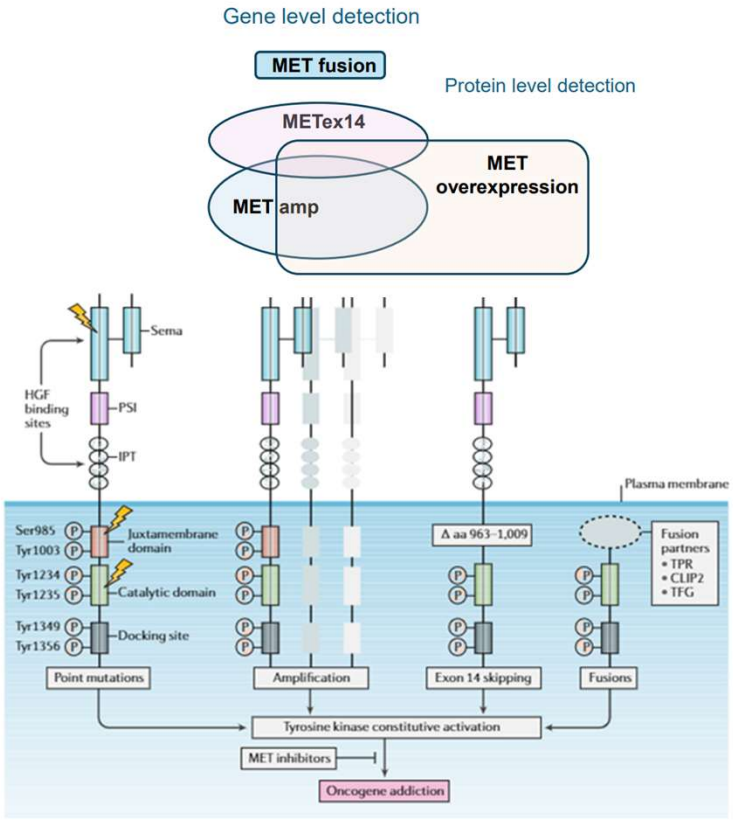


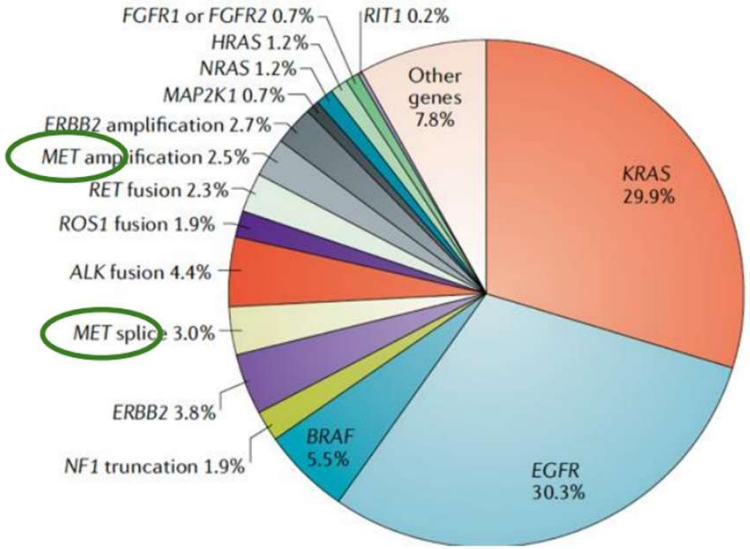
(A) Objective response rate, and (B) progression-free survival by first-line treatment. (C) Subgroup analysis of progression-free survival by first-line treatment.

- Overall Survival was superior with chemoimmunotherapy, especially in patients with smoking exposure

Di Frederico et al., ASCO 2025

MET as an oncogene driver: Biology





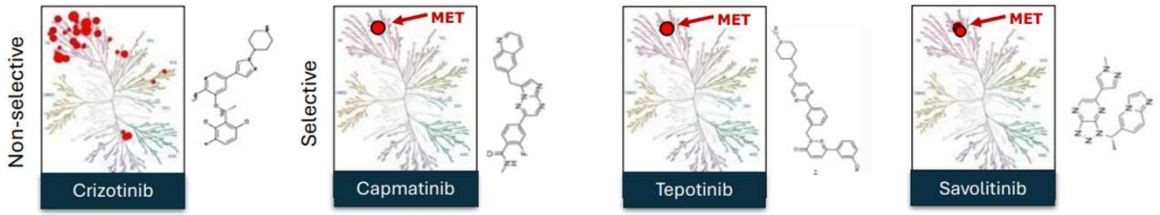
Skoulidis et al., Nat Rev Cancer 2021

MET ex 14 skipping mutation: Management

Point mutations, insertions or deletions, or large-scale whole-exon deletions that cause **exon 14 (L964 - D1010) with the CBL binding site (Y1003)** to be deleted from the expressed MET protein.

- Y1003 mutations disrupt the CBL binding site
- D1010 mutations affect the exon 14 to 15 splice site

METex14



	Crizotinib	Capmatinib		Tepotinib		Savolitinib	
	PROFILE-001	GEOMETRY-mono-1		VISION		NCT02897479	
Sample Size	**1L+** N=69	**1L** N=60	**2L+** N=100	**1L** N=137	**2L+** N=138	**1L** N=28	**2L+** N=42
Median Age	72	71	71	75 >75 y: 50%	71 >75 y: 36%	69 (1L+) >75 y: 43%	>75 y: 10%
Female	58%	68%	56%	50%	51%	41% (1L+)	
ORR	**32%** **(1L 25%, 2L+ 37%)**	**67%**	**44%**	**54%**	**45%**	**46%**	**41%**
mDOR (mo)	**9.1**	**12.6**	**9.7**	**32.7**	**11.1**	**5.6**	**9.7**
mPFS (mo)	7.3	12.3	5.5	12.6	10.9	5.6	6.9

Drilon et al Nat Med 2020, Wolf et al NEJM 2020, Paik et al NEJM 2020, Wolf et al ASCO 2021, Felip et al WCLC 2021, Lu et al Lancet Resp Med 2021

MET ex 14 TKIs: Toxicity

Tepotinib

	Safety Population (n=152)			
	All Grades	Grade 1–2	Grade 3	Grade 4
Adverse Events	number of patients (percent)			
Any adverse event†	135.0 (89.0)	93.0 (61.0)	38.0 (25.0)	3.0 (2.0)
Peripheral edema	96.0 (63.0)	85.0 (56.0)	11.0 (7.0)	0
Nausea	39.0 (26.0)	38.0 (25.0)	1.0 (1.0)	0
Diarrhea	33.0 (22.0)	32.0 (21.0)	1.0 (1.0)	0
Blood creatinine increased	27.0 (18.0)	26.0 (17.0)	1.0 (1.0)	0
Hypoalbuminemia	24.0 (16.0)	21.0 (14.0)	3.0 (2.0)	0
Amylase increased	17.0 (11.20	13.0 (9.0)	3.0 (2.0)	1.0 (1.0)
Lipase increased	13.0 (9.0)	9.0 (6.0)	4.0 (3.0)	0
Asthenia	12.0 (8.0)	11.0 (7.0)	1.0 (1.0)	0
Decreased appetite	12.0 (8.0)	11.0 (7.0)	1.0 (1.0)	0
Pleural effusion	12.0 (8.0)	8.0 (5.0)	4.0 (3.0)	0
Alopecia	12.0 (8.0)	12.0 (8.0)	0	0
Fatigue	11.0 (7.0)	10.0 (7.0)	1.0 (1.0)	0
Alanine aminotransferase increased	11.0 (7.0)	7.0 (5.0)	3.0 (2.0)	1.0 (1.0)
Aspartate aminotransferase increased	10.0 (7.0)	7.0 (5.0)	2.0 (1.0)	1.0 (1.0)
Vomiting	9.0 (6.0)	9.0 (6.0)	0	0
General edema	9.0 (6.0)	5.0 (3.0)	4.0 (3.0)	0
Upper abdominal pain	8.0 (5.0)	8.0 (5.0)	0	0

Capmatinib

Variable	NSCLC with *MET* Exon 14 Skipping Mutation					
	Cohort 4 (N=69)		Cohort 5b (N=28)		Cohort 1a (N=69)	
	Total	Grade 3 or 4	Total	Grade 3 or 4	Total	Grade 3 or 4
Adverse events						
Any event — no. (%)	68 (99)	52 (75)	28 (100)	21 (75)	67 (97)	48 (70)
Most common events — no. (%)†						
Peripheral edema	37 (54)	10 (14)	21 (75)	3 (11)	34 (49)	5 (7)
Nausea‡	32 (46)	0	13 (46)	0	32 (46)	5 (7)
Vomiting‡	18 (26)	0	7 (25)	0	24 (35)	5 (7)
Blood creatinine increased	23 (33)	0	10 (36)	0	16 (23)	0
Dyspnea	19 (28)	7 (10)	6 (21)	2 (7)	13 (19)	4 (6)
Fatigue	18 (26)	6 (9)	4 (14)	1 (4)	11 (16)	1 (1)
Decreased appetite‡	15 (22)	1 (1)	8 (29)	0	15 (22)	1 (1)
Constipation	10 (14)	2 (3)	4 (14)	0	16 (23)	0
Diarrhea	12 (17)	0	5 (18)	0	19 (28)	1 (1)
Cough	10 (14)	1 (1)	7 (25)	0	9 (13)	1 (1)
Back pain	11 (16)	2 (3)	4 (14)	0	8 (12)	0
Pyrexia	9 (13)	1 (1)	2 (7)	0	10 (14)	0
ALT increased	8 (12)	6 (9)	4 (14)	2 (7)	12 (17)	7 (10)
Asthenia	6 (9)	3 (4)	4 (14)	2 (7)	6 (9)	3 (4)
Pneumonia	7 (10)	4 (6)	2 (7)	0	12 (17)	3 (4)
Weight loss	9 (13)	0	3 (11)	0	7 (10)	1 (1)
Noncardiac chest pain	5 (7)	1 (1)	1 (4)	0	10 (14)	2 (3)

Wolf et al NEJM 2020, Paik et al NEJM 2020

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MET amplification: Role of TKIs?

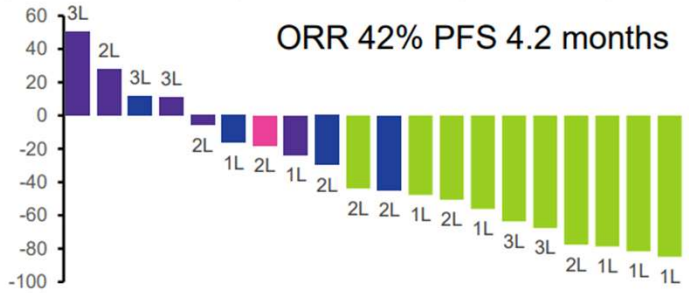
- For high copy number >10
  ORR 40-42%, PFS 4.1-4.2 months
- NCCN recommends TKI for MET amp

- Geometry-mono-1 trial (capmatinib)
  GCN >10 vs. GCN <10

	GCN >10	GCN>10	GCN 3-9
Prior Rx	Yes	No	Yes
ORR	29%	40%	7-12%
DoR (mon)	8.3	7.5	Variable
PFS (mon)	4.1	4.1	2.7-3.6

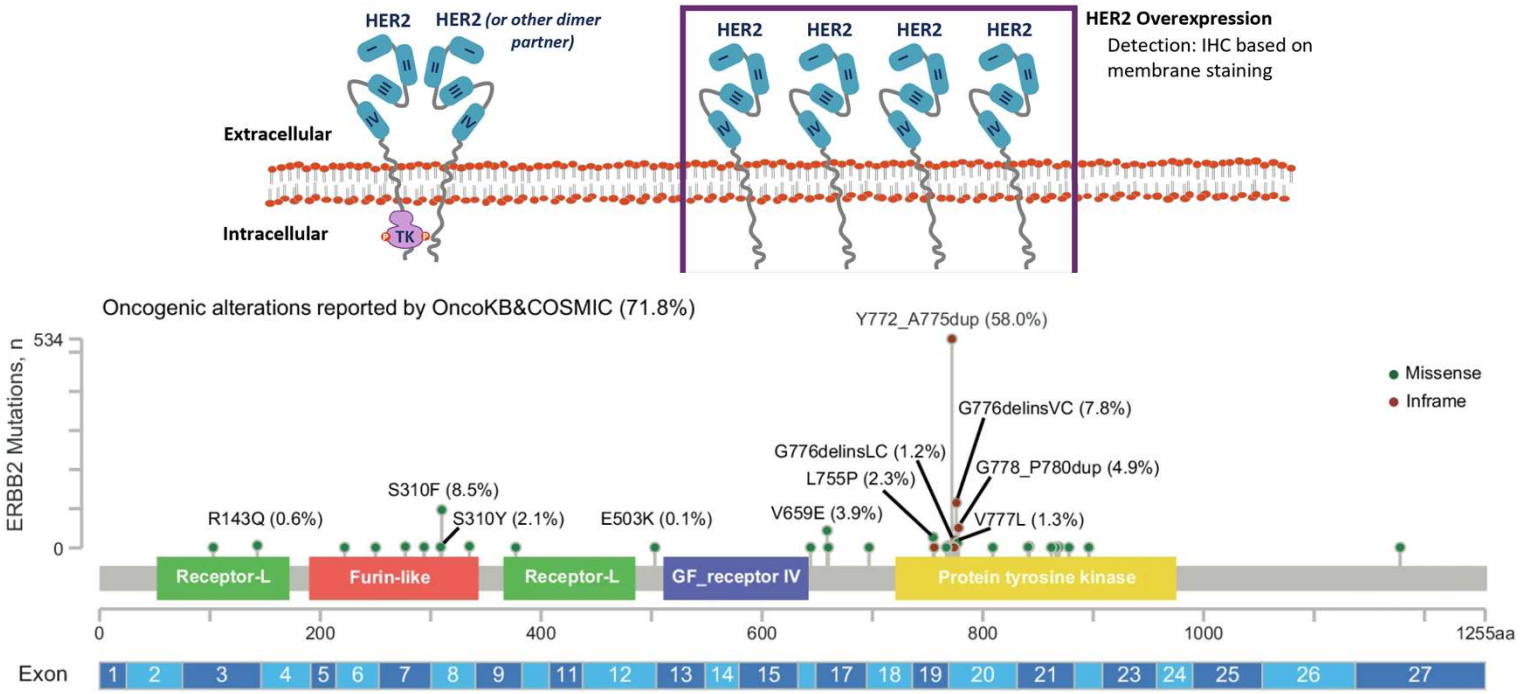
- VISION trial (tepotinib)
  ctDNA METamp >2.5 ~ tissue METamp >10

		Overall (n=24)	1L (n=7)	2L (n=10)	3L (n=7)
Best overall response, n (%)	PR	10 (41.7)	5 (71.4)	3 (30.0)	2 (28.6)
	SD	1 (4.2)	0	1 (10.0)	0
	PD	5 (20.8)	1 (14.3)	2 (20.0)	2 (28.6)
	NE	8 (33.3)	1 (14.3)	4 (40.0)	3 (42.9)
ORR, n (%) [95% CI]		10 (41.7) [22.1, 63.4]	5 (71.4) [29.0, 96.3]	3 (30.0) [6.7, 65.2]	2 (28.6) [3.7, 71.0]



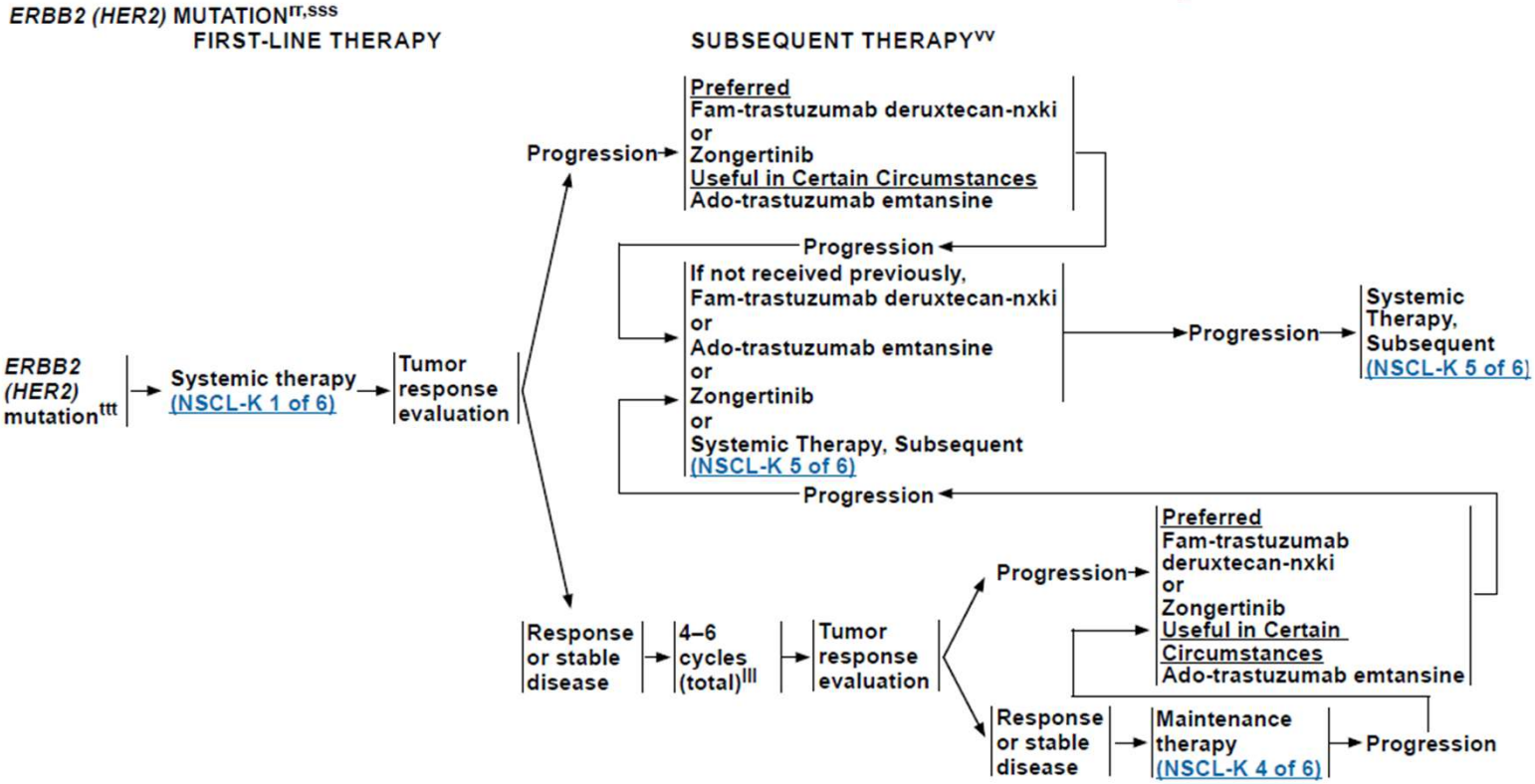
Wolf et al NEJM 2020, Le et al. ASCO 2021

HER2 Mutant NSCLC: Biology



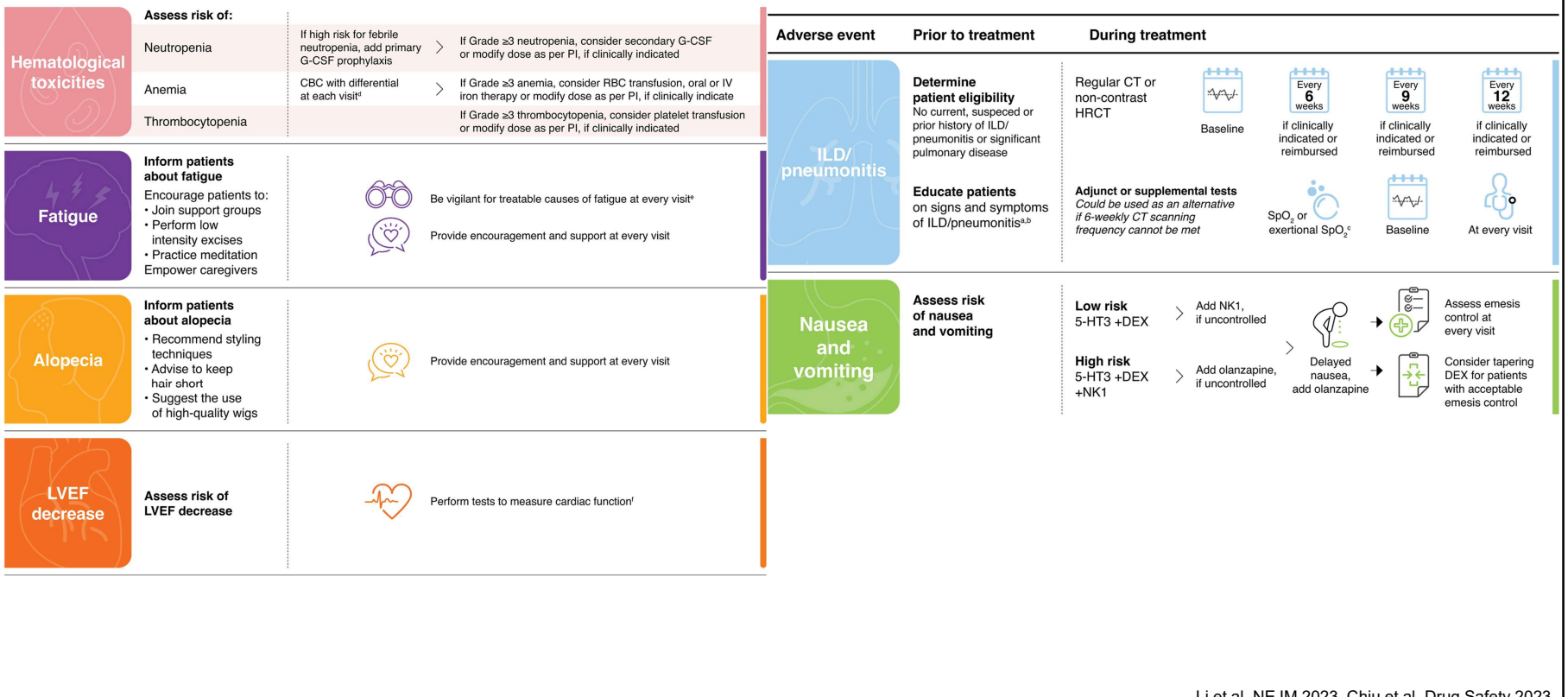
Uy et al Cancers 2022; Ren et al. ESMO Open 2022

HER2 Mutant NSCLC: Treatment Options



Camidge et al ASCO 2025

HER2 Mutant NSCLC: 2L T-DXd

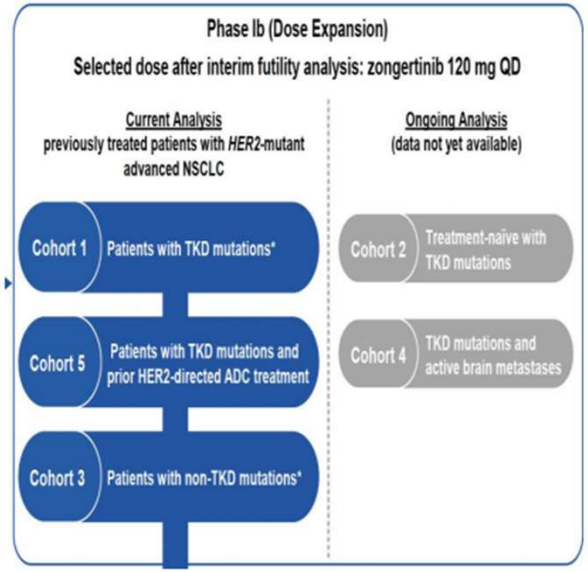


Li et al. NEJM 2023, Chiu et al. Drug Safety 2023

HER2 Mutant NSCLC: 2L Zongertinib

BEAMION LUNG-1 PHASE IB

FDA Approved



Efficacy

Cohort 1 (N: 75)

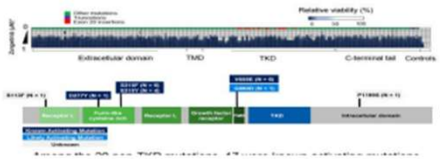
- ORR 71%; DoR 14 m; mPFS 12.4 m
- Brain (N: 27): IC ORR 41%

Cohort 5 (N. 31)

- ORR 48%, ; mDoR 5.3 m; mPFS 6.8 m
- Previous T-DXd (N: 22): ORR 41%

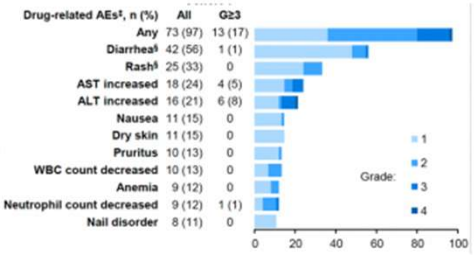
Cohort 3 (N 20);

- ORR 30%



Safety

- 17% TRAE G ≥3 (AST, ALT)
- Diarrhea 56% (1% G3)
- Rash 33% (no G3)
- Dose reduction 7%
- Discontinuation 3%
- No ILD

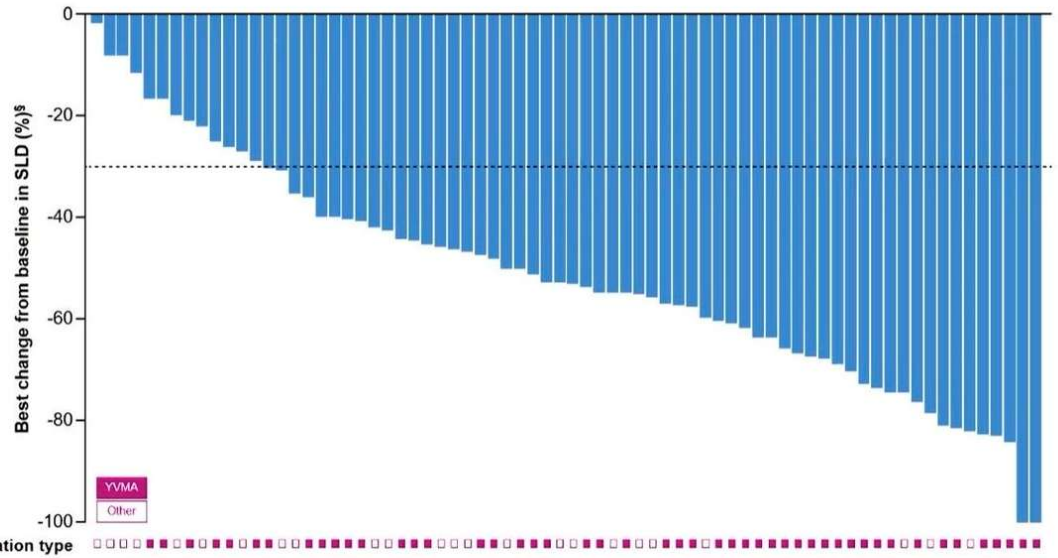


Heymach et al NEJM 2025

HER2 Mutant NSCLC: 1L Options #ESMO25

Zongertinib in Treatment-Naïve Patients: Tumor Response

Confirmed response by BICR (RECIST v1.1)	N = 74*
ORR	**77%**
95% CI	66–85
p value†	<0.0001
CR, n (%)	6 (8)
PR, n (%)	51 (69)
DCR	**96%**
95% CI	89–99
SD, n (%)	14 (19)
PD, n (%)	1 (1)‡

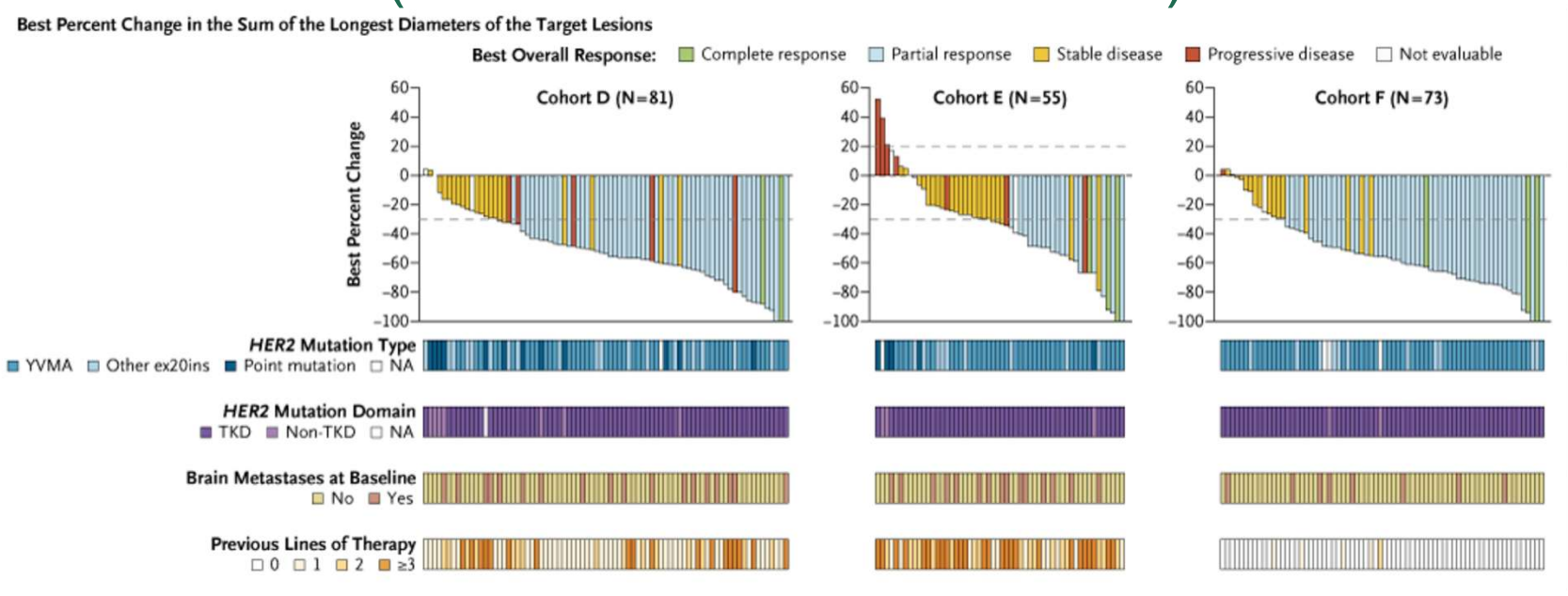


Clinical benefit was observed with zongertinib in all patients, irrespective of *HER2* mutation type

Popat et al ESMO 2025

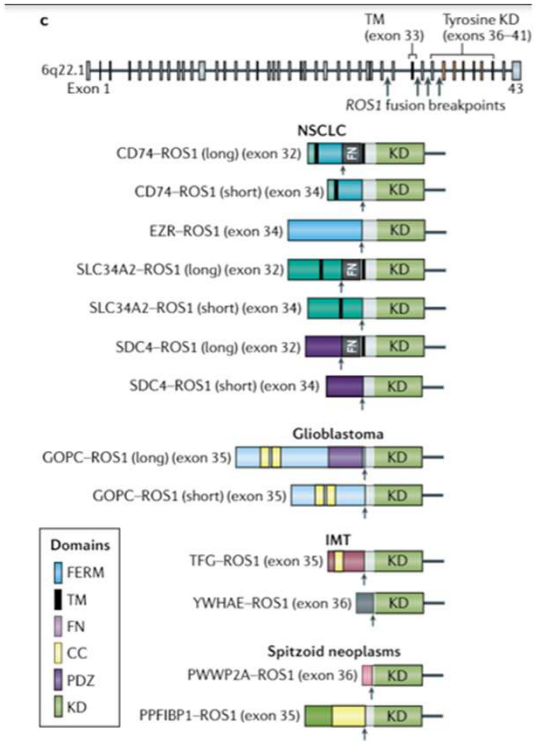
HER2 Mutant NSCLC: 1L Options #ESMO25

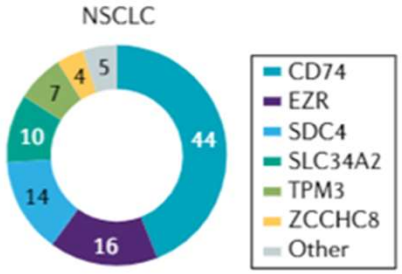
Sevabertinib [Not FDA Approved] (Cohort F: Treatment Naïve)



Le et al. NEJM 2025

ROS1 fusion NSCLC: Biology





***ROS1* REARRANGEMENT[nn]**

FIRST-LINE THERAPY[rr]

***ROS1* rearrangement**

***ROS1* rearrangement discovered prior to first-line systemic therapy**

Preferred
Crizotinib[ss]
or
Entrectinib[ss,ooo]
or
Repotrectinib[ss,ooo]
or
Taletrectinib[ss,ooo]

Drilon et al. Nat Rev Cancer 2021

@ADesaiMD
Aakash Desai, MBBS, MPH

ROS1 fusion NSCLC: Treatment Options

Agent	ORR (%) (TKI naive, prior TKI)	mPFS (months) (TKI naive, prior TKI)	CNS response rate (TKI naive, prior TKI)	G2032R response rate	Common side effects (> 30%, any grade)	On-target acquired resistance mechanisms
Crizotinib[2-4] (FDA approved 2016)	72%, N/A	15.9-19.2, N/A	N/A	N/A	Vision disorder (87%), nausea (51%), diarrhea (45%), vomiting (38%), elevated transaminases (36%), constipation (34%)	G2032R, D2033N, S1986F7
Entrectinib[5,10] (FDA approved 2019)	68%, 11%[a]	15.7, 4.7[a]	80%, 11%[a]	N/A	Dysgeusia (41%), dizziness (37%), weight gain (34%), constipation (32%)	G2032R, F2004C/I
Lorlatinib[6,13] (NCCN listed as 2L, not FDA approved)	62%, 35%[b]	21.0, 8.5[b]	64%, 50%[b]	0%	Hypercholesterolemia (65%), hypertriglyceridemia (42%), edema (39%), peripheral neuropathy (35%)	G2032R, L2086F, S1986F, L2000V7
Repotrectinib[8,9] (FDA approved 2024)	79%, 38%[c]	35.7, 9.0[c]	89%, 38%[c]	59%	Dizziness (62%), dysgeusia (53%), Constipation (38%), anemia (38%), paresthesia (34%)	L2086F and G2032R (only in TKI-pretreated population)
Taletrectinib[14,16,17] (FDA approved	89%, 56%[c]	45.6, 7.6[c]	77%, 66%[c]	62%	Increased AST (72%), increased ALT (68%), diarrhea (63%), nausea (47%) vomiting (43%), anemia (37%)	Awaiting additional data in patients
Zidesamtinib[15,18] (FDA Breakthrough Designation)	Pending[d], 73%[b], 44% (2+ TKIs)	NR[d], 12.1 (2+ TKIs)	Pending[d], 57%	65%[e], 38%[f]	None > 30%, most common: peripheral edema (18%), transaminase increase (12%)	Awaiting additional data in patients

Hsu et al. ASCO Daily News 2025

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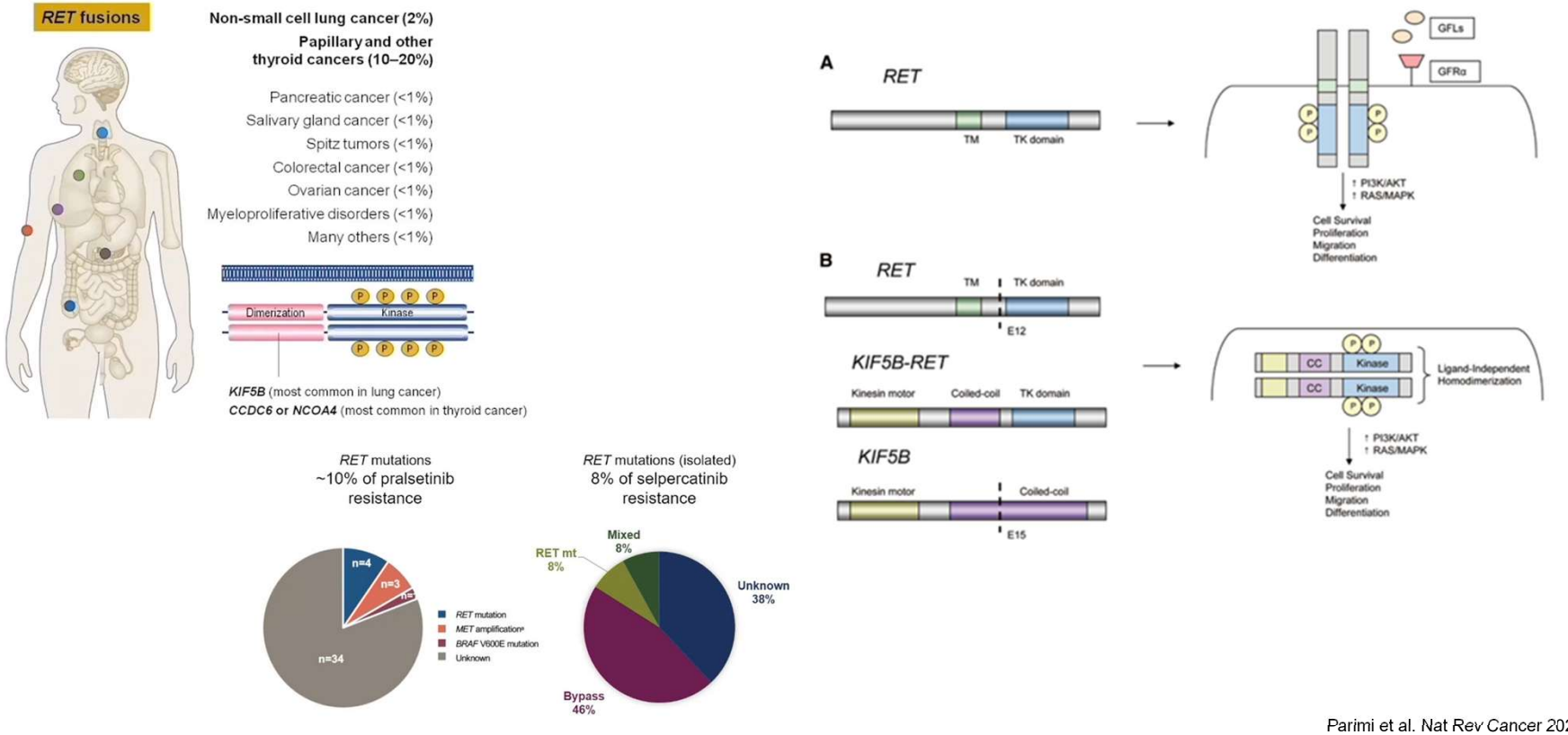
RET fusion NSCLC: Biology

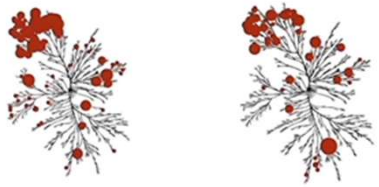


Parimi et al. *Nat Rev Cancer* 2021

RET fusion NSCLC: Treatment Options

Multikinase Inhibitors (MKIs)

Cabozantinib **Vandetanib**

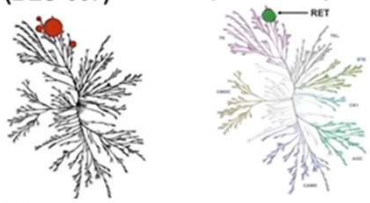


Selpercatinib
Previous-platinum (N = 105)
ORR = 64% (95%CI: 54-73)
DOR = 17.5 m (95%CI: 12.0 – NR)
PFS = 16.5 m (95%CI: 13.7 – NR)

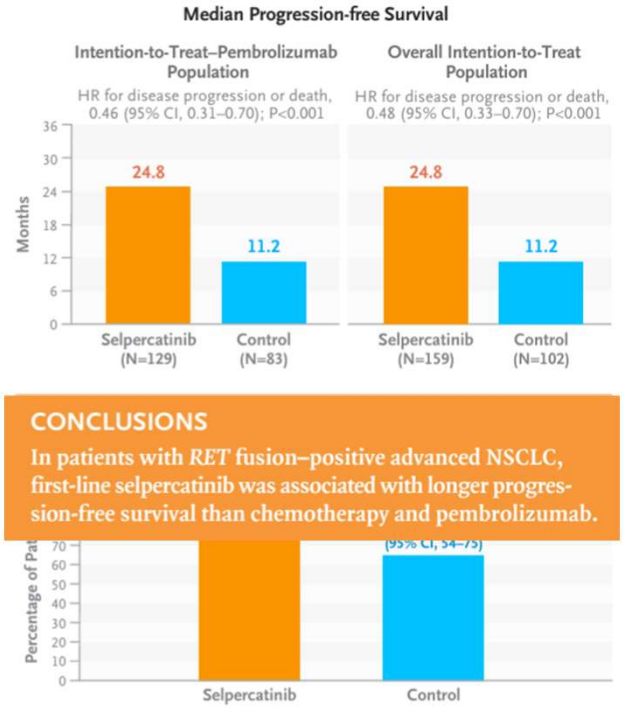
Treatment-naïve (N = 39)
ORR = 85% (95%CI: 76 – 97)
DOR = NR (95%CI: 12 – NR)
PFS = NR (13.8 – NR)

Selective RET Inhibitors

Pralsetinib (BLU-667) **Selpercatinib (LOXO-292)**



Pralsetinib
Previous-platinum (N = 87)
ORR = 61% (95%CI: 50-71)
DOR = NR (95%CI: 15.2 – nR)
PFS = 17.1m (95%CI: 8.3 – 22.1)
Treatment-naïve (N = 27)
ORR = 70% (95%CI: 50 – 86)
DOR = 9.0m (95%CI: 6.3 – NR)
PFS = 9.1 m (95%CI: 6.1 – 13.0)



Subbiah et al. Nat Med 2022, Zhou et al. NEJM 2023

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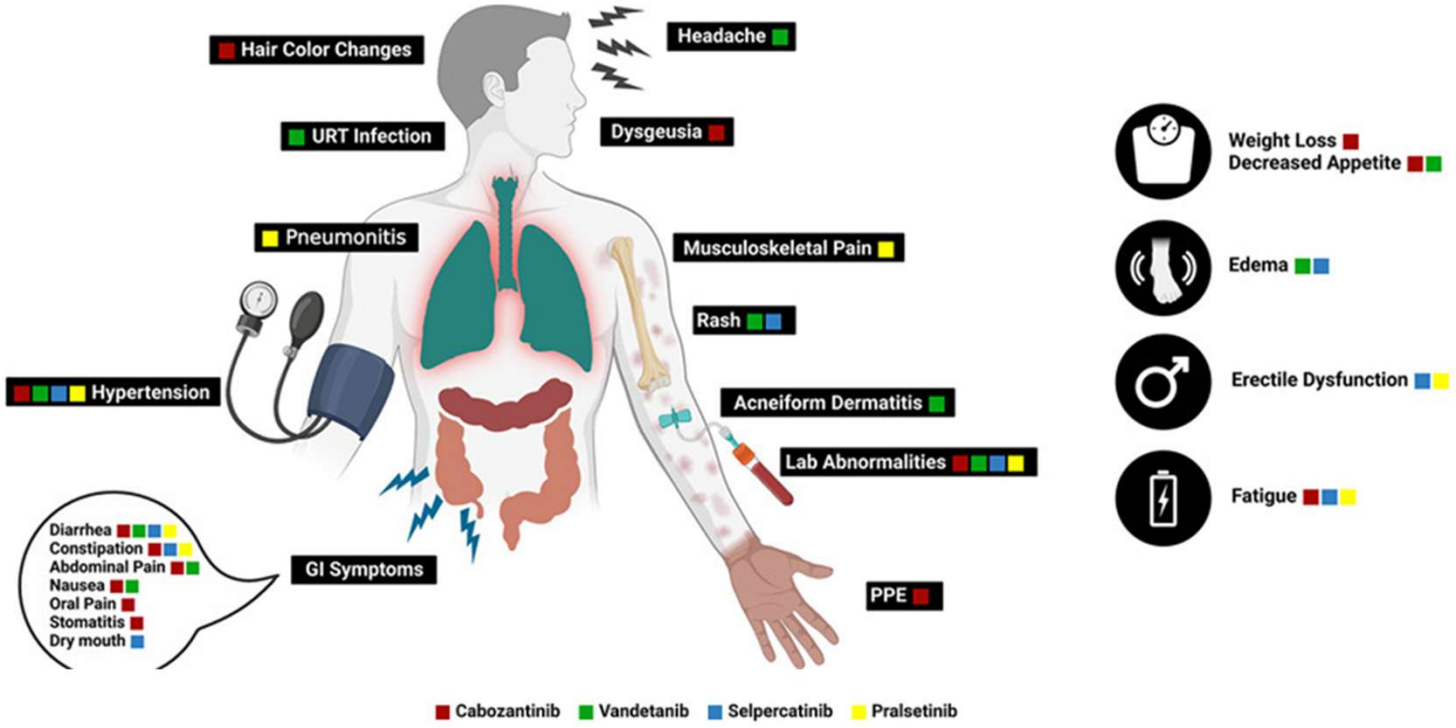
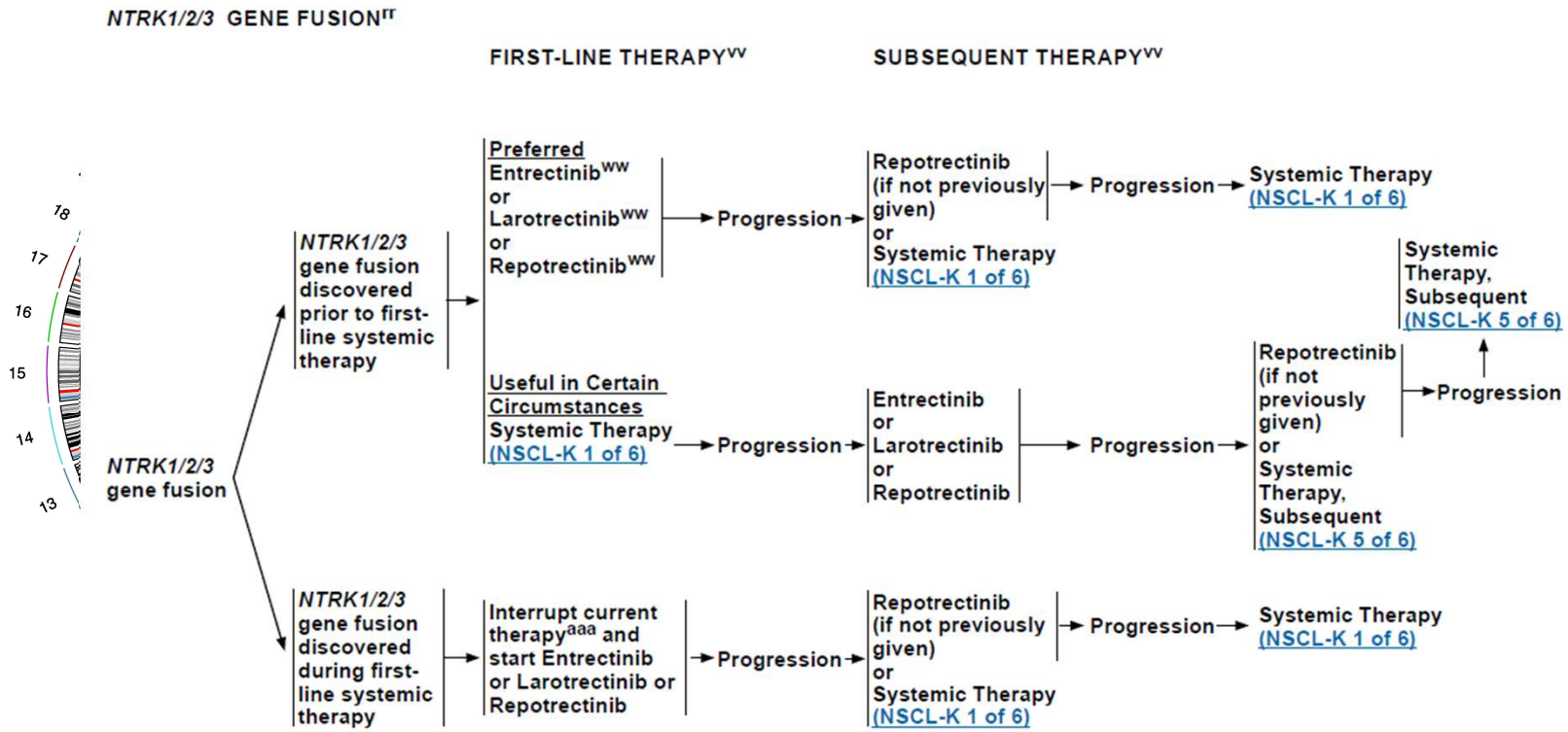
RET fusion targeted TKIs: Toxicity



Nardo et al. Cell Reports Medicine 2023

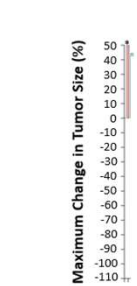
NTRK fusion NSCLC: Biology



Repetto et al. Cancer Treatment Reviews 2024

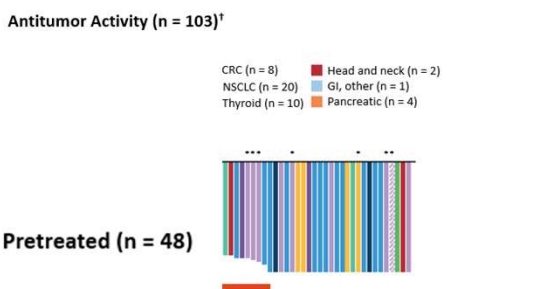
NTRK fusion NSCLC: Treatment

Larotrectinib in *NTRK* Fusion–Positive Cancers



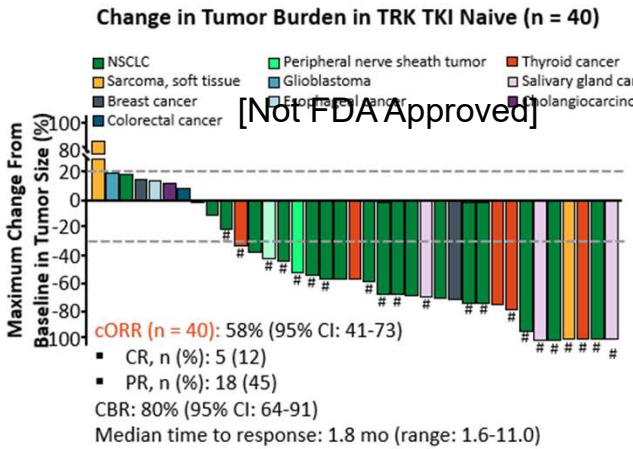
Hong. Lancet Oncol. 2020;21

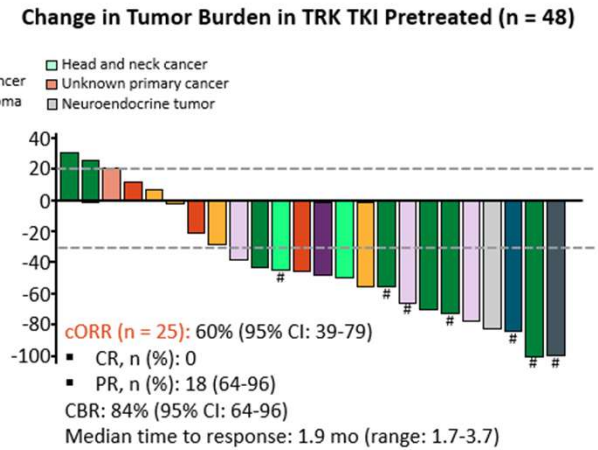
Entrectinib in *NTRK* Fusion–Positive Cancers



Next-Generation TRK Inhibitors: Repotrectinib

[Not FDA Approved]





Drilon et al. *NEJM* 2024

NTRK TKIs: Toxicity

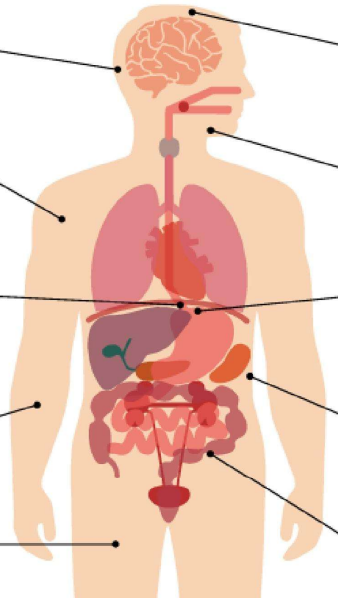
Ataxia
- Larotrectinib: Not reported
- Entrectinib: 15.7–17% (all grades); 0.8% (grade ≥ 3)

Myalgia
- Larotrectinib: 42% (all grades); 3.9% (grade 3–4)[†]
- Entrectinib: 19.6–28% (all grades); 0.6–1.1% (grade ≥ 3)[‡]

Nausea
- Larotrectinib: 25% (all grades); 0.7% (grade 3–4)
- Entrectinib: 32.1–34% (all grades); 0.3-0.8% (grade ≥ 3)

Peripheral sensory neuropathy
- Larotrectinib: Not reported
- Entrectinib: 15.7–18% (all grades); 1.0–1.1% (grade ≥ 3)

Muscular weakness
- Larotrectinib: 10% (all grades); 0.7% (grade 3–4)
- Entrectinib: 12–12.3% (all grades); 0.8–1.2% (grade ≥ 3)



Dizziness[§]
- Larotrectinib: 27% (all grades); 1.1% (grade 3–4)
- Entrectinib: 38–39.7% (all grades); 0.8-1.2% (grade ≥ 3)

Dysgeusia
- Larotrectinib: Not reported
- Entrectinib: 42.3–44% (all grades); 0.3–0.4% (grade ≥ 3)

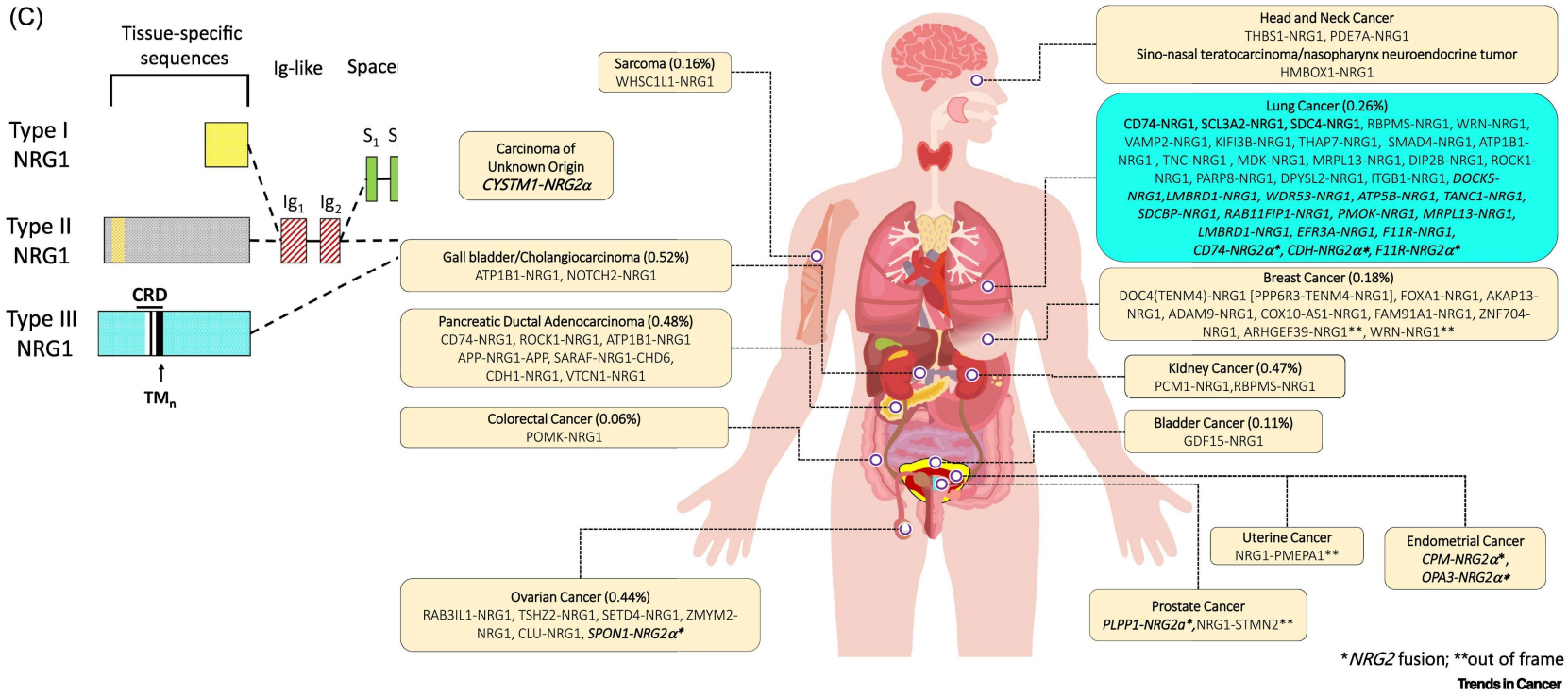
Vomiting
- Larotrectinib: 25% (all grades); 0.7% (grade 3–4)
- Entrectinib: 23.2–24% (all grades); 0.8-1.2% (grade ≥ 3)

Weight gain
- Larotrectinib: 14% (all grades); 3.6% (grade 3–4)
- Entrectinib: 25-26.4% (all grades); 7–7.3% (grade ≥ 3)

Diarrhoea
- Larotrectinib: 27% (all grades); 1.4% (grade 3–4)
- Entrectinib: 33.5–35% (all grades); 2–2.6% (grade ≥ 3)

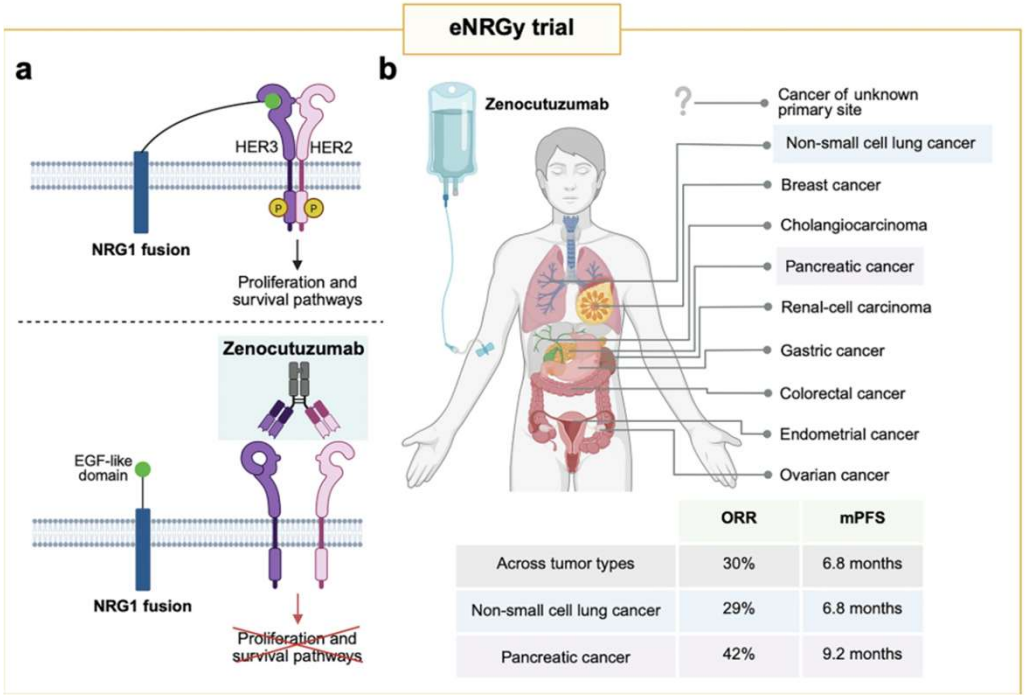
Repetto et al. Cancer Treatment Reviews 2024

NRG1 fusion NSCLC: Biology

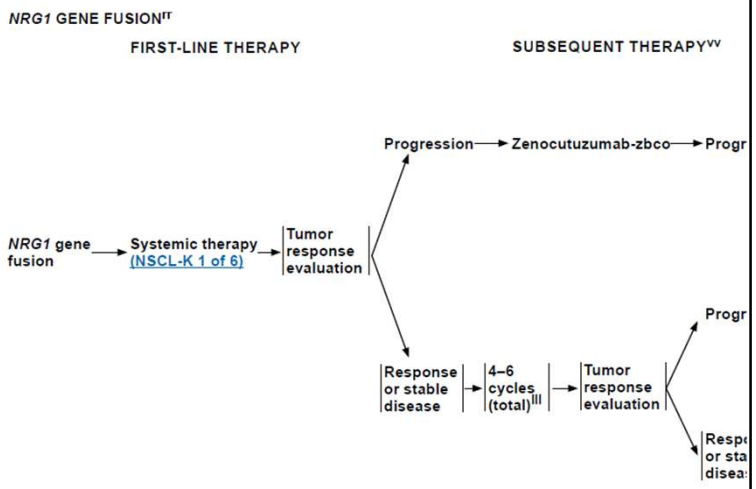


Nagasaka et al. Trends in Cancer 2022

NRG1 fusion NSCLC: Treatment



	ORR	mPFS
Across tumor types	30%	6.8 months
Non-small cell lung cancer	29%	6.8 months
Pancreatic cancer	42%	9.2 months



Nagasaka et al. Trends in Cancer 2022

Key Takeaways

1. ***BRAF*m NSCLC: Class I vs II/III, Dabrafenib + trametinib or Encorafenib + binimetinib as BRAF + MEK inhibitors for V600E**
2. **MET-altered NSCLC: *MET* exon 14 skipping mutation - Crizotinib, Capmatinib and Tepotinib FDA approved; Teliso-V approved for high MET expressing nonsquamous NSCLC patients**
3. ***HER2* mutant NSCLC: Second line targeted therapy options: Fam-trastuzumab deruxtexan, Zongertinib, and ado-trastuzumab emtansine; sequencing remains an open question; TKIs moving to the first line?**
4. ***ROS1* fusion-positive NSCLC: Multiple TKIs in 1L: Entrectenib, Repotrectinib, Taletrectinib, and Crizotinib - certain differences in side effect profiles - CNS penetrant drugs preferred**
5. ***RET* fusion-positive NSCLC: Selpercatinib and Pralsetinib remain 1L choices**
6. ***NTRK* fusion-positive NSCLC: Multiple TKIs in 1L: Larotrectinib, Entrectinib, Repotrectinib - certain differences in side effect profiles - CNS penetrant drugs preferred**
7. ***NRG1* fusion-positive NSCLC: Zenocutuzumab approved in 2L**

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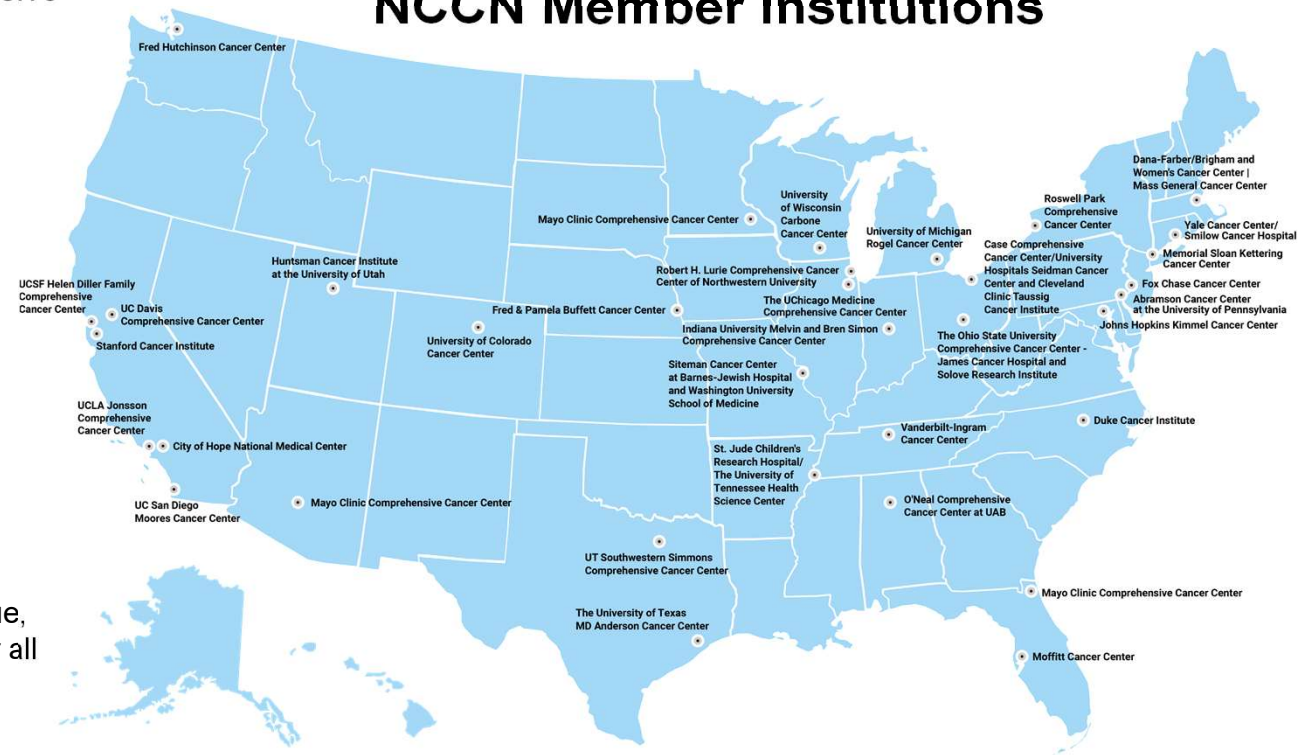

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An alliance of leading cancer centers devoted to patient care, research, and education

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To define and advance quality, effective, equitable, and accessible cancer care and prevention so all people can live better lives

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