Prévalence des altérations oncogéniques

CBPNPC non-fumeurs

Points clés

Fréquentes

Rares

Très rares

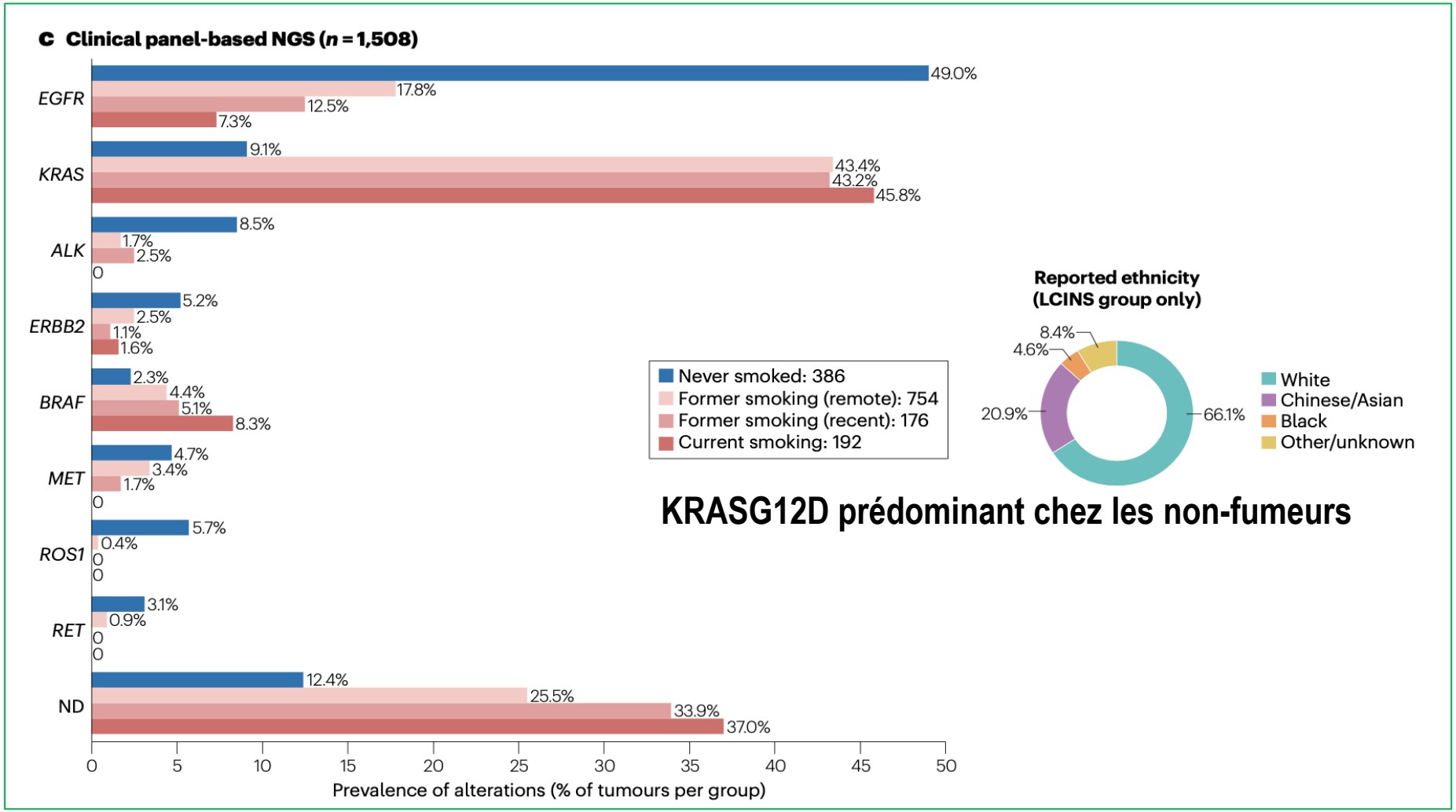
Addiction oncogénique

Caractéristiques anatomo-cliniques

Non-fumeurs: **oui !** ou non

Efficacité des ITK
aussi chimio. et ADC

Thérapies agnostiques +/-



KRASG12D prédominant chez les non-fumeurs

1. LoPiccolo J, et al. Nat Rev Clin Oncol 2024

Cancer Broncho-Pulmonaires Non à Petites Cellules
Nouvelles thérapies ciblées (anti-EGFR, RET, K-RAS, …)

Pr Jaafar BENNOUNA
- ✓ Département d'oncologie médicale
- ✓ Hôpital Foch

UPPO
Unité de Phases Précoces en Oncologie

L’inventaire par Jacques Prevert

Une pierre
deux maisons trois ruines quatre fossoyeurs un jardin
des fleurs
un raton laveur
une douzaine d'huîtres un citron un pain un rayon de soleil
une lame de fond
six musiciens
une porte avec son paillasson
un monsieur décoré de la légion d'honneur
un autre raton laveur
un sculpteur qui sculpte des napoléon
la fleur qu'on appelle souci
deux amoureux sur un grand lit
un receveur des contributions une chaise trois dindons un ecclésiastique
un furoncle
une guêpe
un rein flottant
une écurie de courses
un fils indigne deux frères dominicains trois sauterelles un strapontin
deux filles de joie un oncle Cyprien
une Mater dolorosa trois papas gâteau deux chèvres de Monsieur Seguin

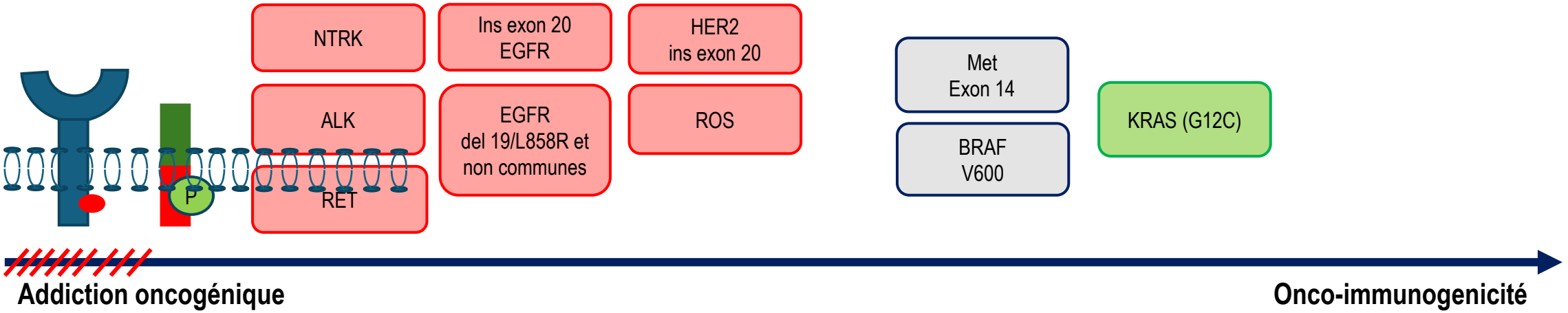
Inventaire de mes liens d'intérêt

Advisory board: AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, F. Hoffmann–La Roche Ltd, MSD, Novartis

Research: Amgen, AstraZeneca, Medimmune, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, F. Hoffmann–La Roche Ltd, Innate Pharma, Merck,MSD, Novartis, Sanofi-Aventis, Daiichi

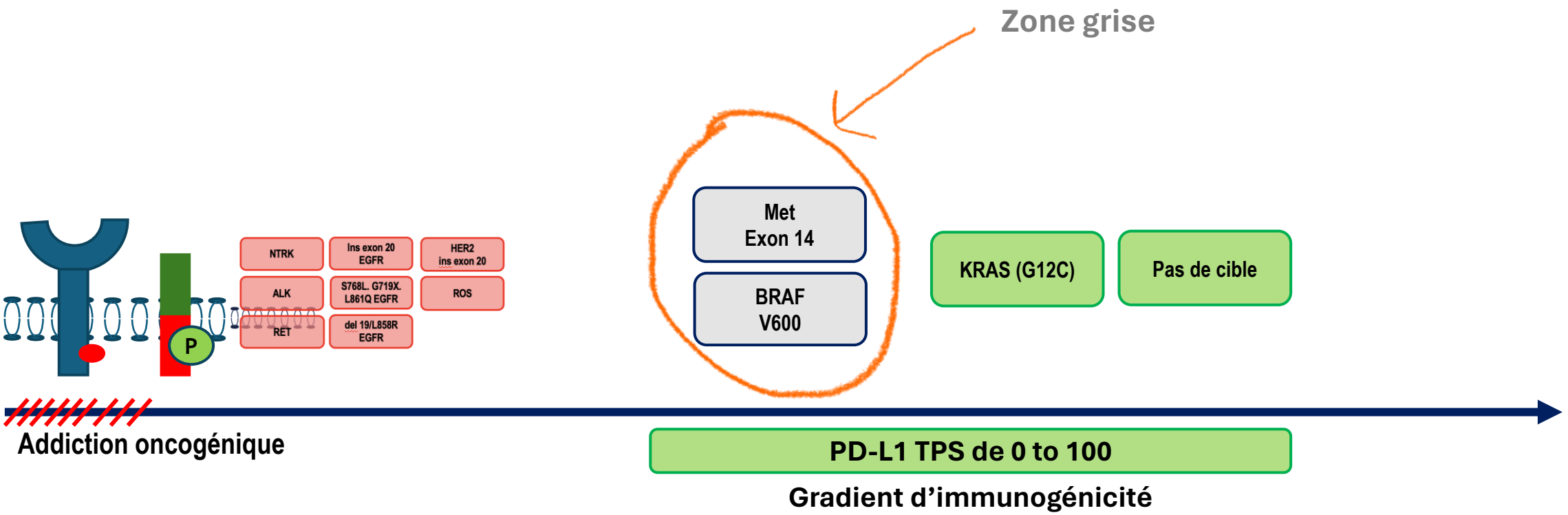
Honorarium: AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, F. Hoffmann–La Roche Ltd, Merck, MSD, Novartis, Daiichi

Cibles moléculaires dans les CBPNPC



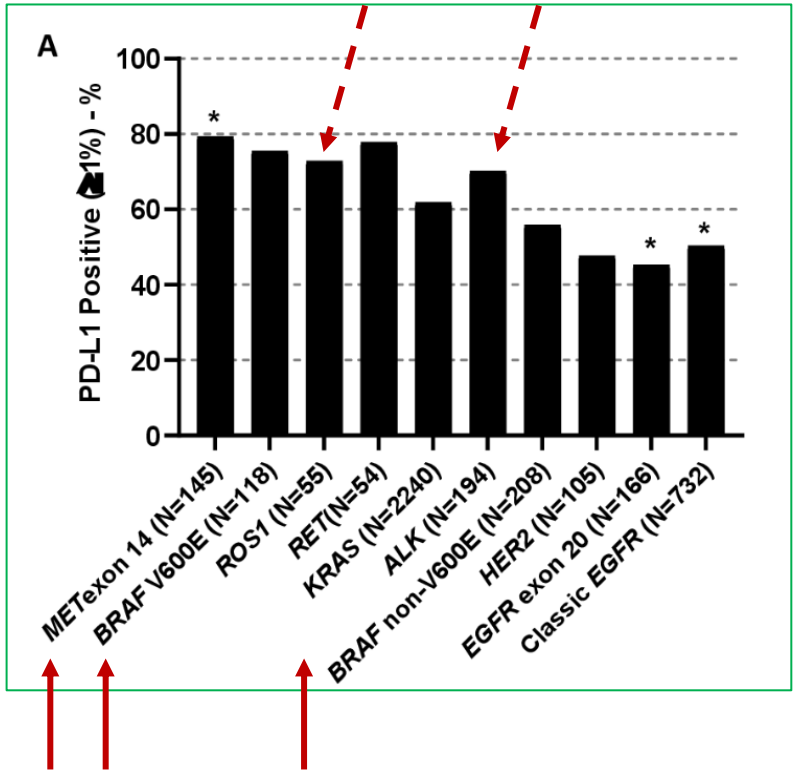
Hétérogénéité tumorale, un gradient de l'addiction oncogénique à l'immunogénicité

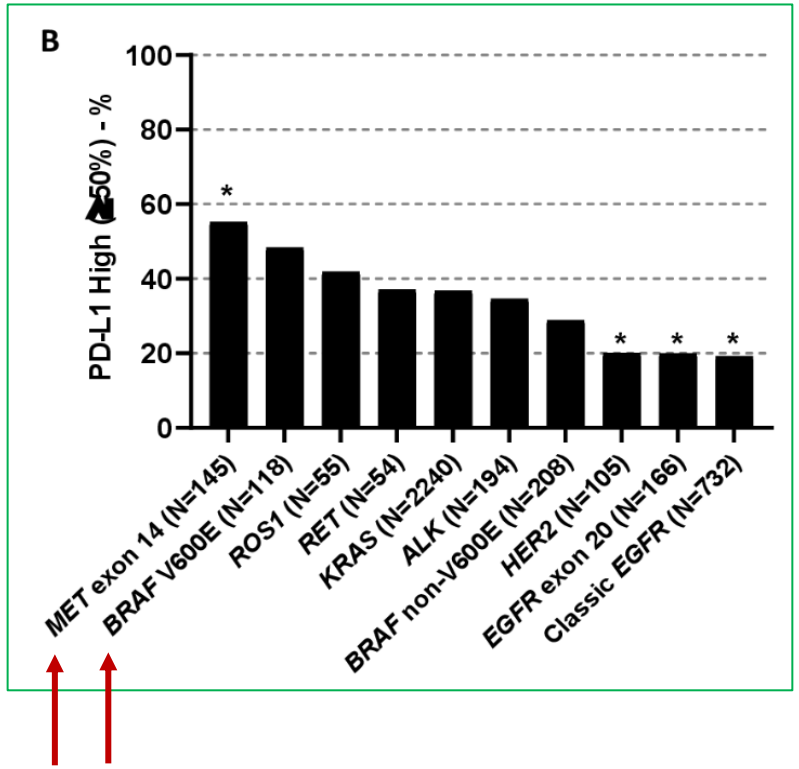
Cibles moléculaires dans les CBPNPC

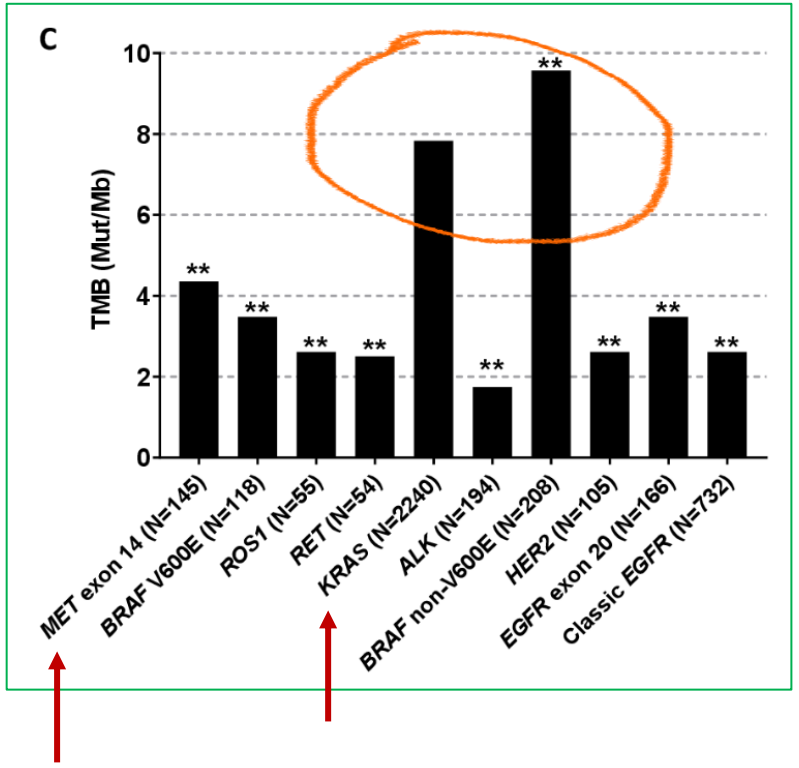


Addiction oncogénique, charge mutationnelle tumorale et PD-L1

- **3 cohortes (n=4189**)
  - MD Anderson, Flatiron avec traitement par ICI seul
  - FMI



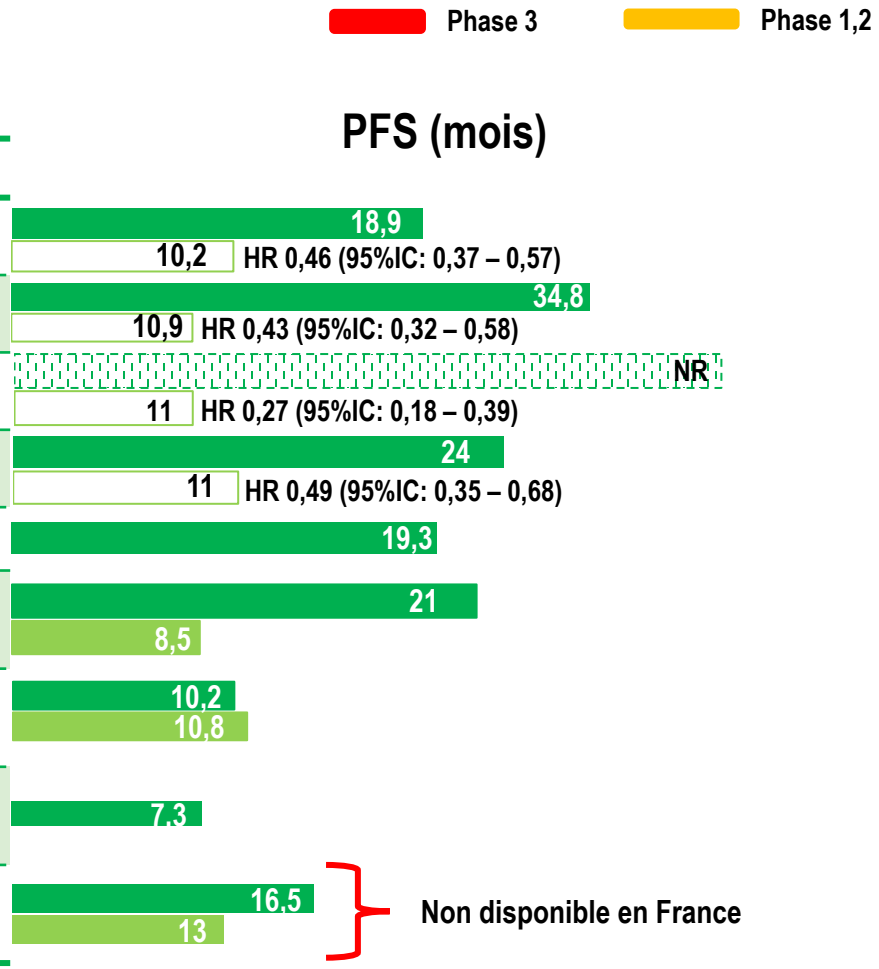




1. Negrao VM, et al. J Immunoth Cancer 2021

Je ne parlerai pas de…

	Etudes	Ligne	RO (%)	RO IC (%, n)	Traitements	n
EGFR	FLAURA[1,2]	1	80 76	91 (20/22) 68 (13/19)	**Osimertinib** Gefitinib ou Erlotinib	279 277
ALK	ALEX[3,4,5]	1	82,9 75,5	85,7 (6/7) 71,4 (5/7)	**Alectinib** Crizotinib	152 151
ALK	CROWN [6,7]	1	77 59	83 (15) 23 (3)	**Lorlatinib** Crizotinib	147 149
ALK	ALTA-1[8,9]	1	74 62	78 (14/18) 26 (6/23)	**Brigatinib** Crizotinib	138 137
ROS1	PROFILE 1001[10,11]	≥ 1	72		**Crizotinib**	53
ROS1	NCT01970865 [12]	≥ 1	62 35	45 (5/11) 38 (9/24)	**Lorlatinib (naïf crizotinib)** **Lorlatinib (post-crizotinib))**	21 40
BRAF V600E	BRF 113928 [13,14,15]	≥1 1	68 64		**Trametinib + Dabrafenib (pré-traité)** **Trametinib + Dabrafenib (1ère ligne)**	57 36
MET exon14	PROFILE 1001[16]	≥1	32		**Crizotinib**	69
RET	ARROW [17,18]	≥1 1	59 60	70 (7/1)	**Pralsetinib (Pré-traité)** **Pralsetinib (1ère ligne)**	158 75



ALTA-1: 73 pts pré-traités

1. Soria JC, et al. N Engl J Med 2017; 2. Ramaligam SS, et al. N Engl J Med 2019; 3. Peters S, et al. N Engl J Med 2017; 4. Mok T, et al. Ann Oncol 2020; 5. Gadgeel S, et al. Ann Oncol 2018; 6. Shaw AT, et al. N Engl J Med; 7. Solomon BJ, et al. Lancet Resp Dis 2023; 8. Camidge DR, et al. N Engl J Med 2018; 9. Camidge DR, et al. J Clin Oncol 2020; 10. Shaw AT, et al. N Engl J Med 2014; 11. Shaw AT, et al. Ann Oncol 2019; 12. Shaw At, et al. Lancet Oncol 2019;; 13. Planchard D, et al. Lancet Oncol 2016; 14. Planchard D, et al. Lancet Oncol 2017; 15. Planchard D, et al. J Thorac Oncol 2022. 16. Drilon A. et al. Nat Med 2020; 17. Gainor F, et al. Lancet Oncol 2021; 18. Griensinger F, et al. Ann Oncol 2022

Non plus… Pour les CBPNPC Met exon 14

Non disponibles en France

Etudes	Traitement	Ligne	n	RO (%)	DoR (mois)	PFS (mois)	OS (mois)
Wolf J [3,4,5] **GEOMETRY Mono-1**	Capmatinib	1 (cohorte 5b)	28	67,9	12,6	12,4	20,8
		1 (cohorte 7 expansion)	32	68,8	16,59	12,45	NR
		2/3 (cohorte 4)	69	40,6	9,7	5,4	13,6
		2L (cohorte 6 expansion)	31	51,6	8,4	6,9	NE
Paik PJ [6] **(VISION)**	Tepotinib	1	164	57,3	46,4	12,6	21,3
Mazieres J [7] **(VISION update)**		> 1	149	45	12,6	11,0	19,3
Lu S [8,9] *	Savolitinib	1	28	46,4	NR	6,9	10,9
		> 1	42	47,6	NR	6,9	19,4
Yu, Y (GLORY) [10]	Gumarontinib	1	44	71	15,0	11,7	NE
		> 1	35	60	8,2	7,6	16,2
Leighl N [11]	Amivantamab	1	16	56	11,2	5,4	15,8
		1 No prior METi	28	46			
		> 1 with prior METi	53	21			

*Sous-groupe traitement-naïf: patients avec un CBPNPC sarcomatoïde: 46% (29% dans le groupe pré-traité) et âge médian plus élevé: 74.5 ans (67,7 ans dans le groupe pré-traité).

1. Drilon A. et al. Nat Med 2020; 2. Moro-Sibilot D, et al. Ann Oncol 2019; 3. Wolf J, et al. N Engl J Med 2021; 4. Wolf J, et al. ASCO 2021 ; 5. Wolf J, et al. ELCC 2022; 6. Paik PK, et al. N Engl J Med 2021; 7. Mazieres J. et al. JAMA Oncol 2023; 8. Lu S, et al. Lancet Resp Med 2021 ; 9. Lu S, et al. JTO Clin Res Rep 2022; 10. Yu Y, et al. Lancet 2023. Leighl N, et al. IASLC 2023

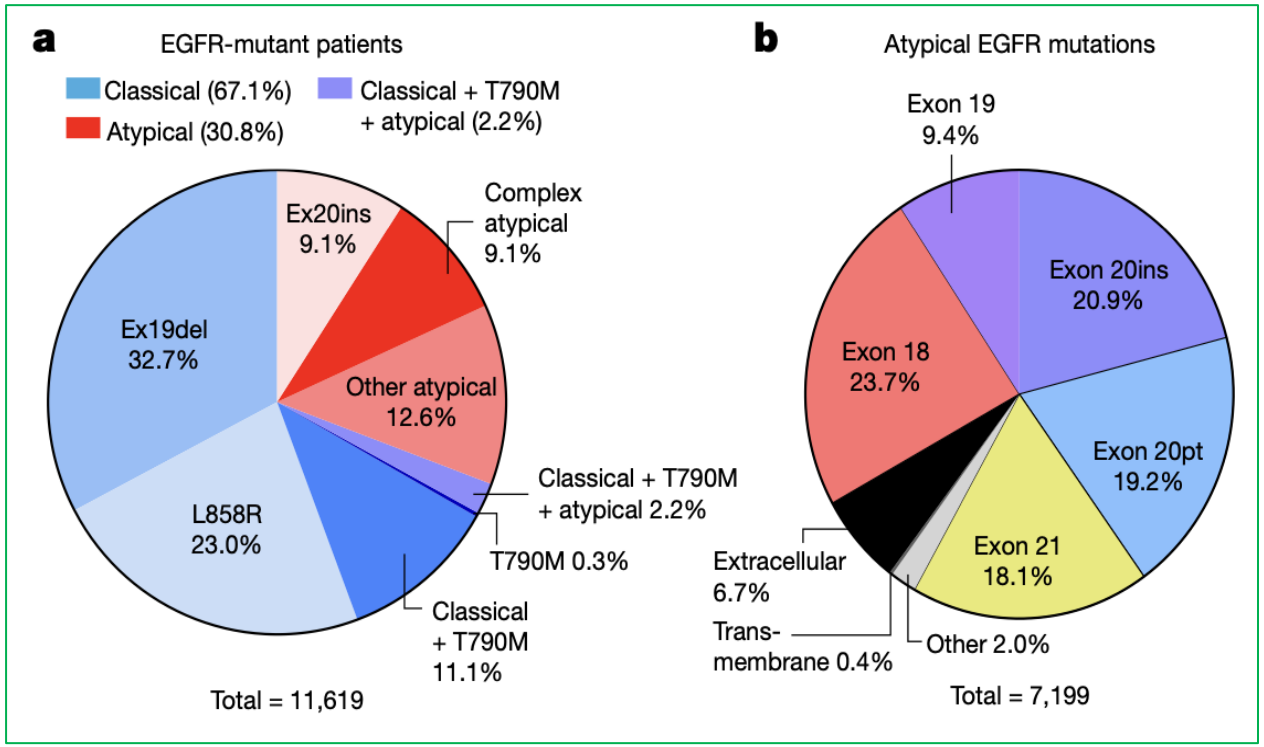
Je vous parlerai de…

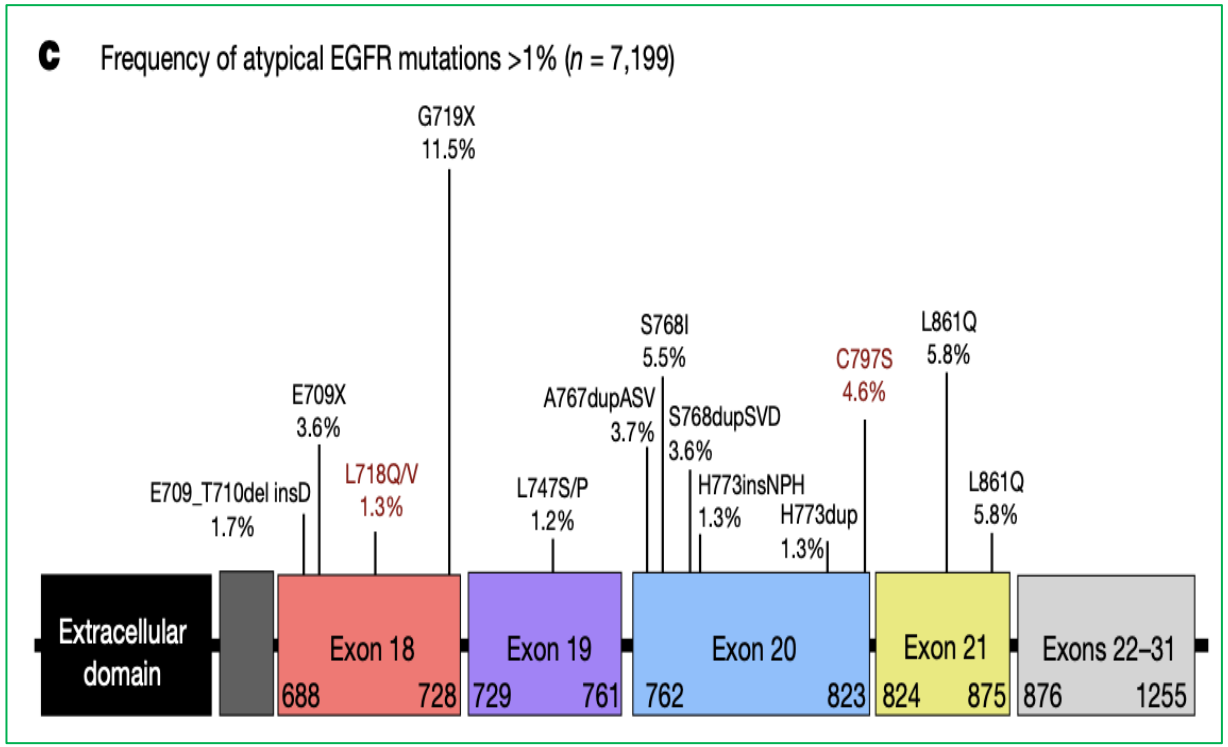
Phase 3 | Phase 1,2

	Etudes	Ligne	RO (%)	RO IC (%, n)	Traitements	n	PFS (mois)
EGFR	FLAURA 2[1]	1	84 76	73 (118) 69 (104)	**Osimertinib + Chimiothérapie** Chimiothérapie	279 278	29,4 19,4 HR 0,62 (95%IC: 0,48 – 0,57)
	MARIPOSA[2]	1	80 76		**Amivantamab + Lazertinib** Osimertinib	429 429	23,7 16,6 HR 0,70 (95%IC: 0,58 – 0,85)
	MARIPOSA-2 [3]	2	64 63 36	83 (15) 23 (3)	**Amivantamab + Chimiothérapie** **Amivantamab + Lazertinib + Chimio.** **Chimiothérapie**	131 263 263	6,3 HR 0,48 (95%IC: 0,36 – 0,64) 8,3 HR 0,44 (95%IC: 0,35 – 0,56) 4,2
ROS1	TRIDENT-1 [4]	≥ 1	79 38	89 (8/9) 38 (5/13)	**Repotrectinib (naïf ITK-ROS)** **Reprotectinib (ITK ROS + naïf chimio)**	71 56	35,7 9,0
EGFR ins ex20	PAPILLON[5]	1	73 47		**Amivantamab + Pemetrexed + Carbo** Pemetrexed + Carbo	153 155	11,4 6,7 HR 0,39 (95%IC: 0,30 – 0,53)
BRAF V600E	NCT03915951 [6]	1 ≥1	74 46		**Encorafenib + Binimetinib (1ère ligne)** **Encorafenib + Binimetinib (pré-traité)**	59 36	NE 9,3
RET	LIBRETTO-431[7]	1	84 63	82 (17) 58 (12)	**Selpercatinib** Pemetexed – Carbo ± Pembro	159 102	24,8 11,2 HR 0,48 (95%IC: 0,33 – 0,70)
HER2	Destiny-Lung01[8]	≥ 1	55		**Traztuzumab-Deruxtecan**	91	8,2
	Destiny-Lung02[9]	≥ 1	56 49		**Traztuzumab-Deruxtecan 6,4 mg/kg** **Traztuzumab-Deruxtecan 5,4 mg/kg**	50 102	NE 19,4
AGA	TROPION-Lung05[10]	≥ 2	49		**Datopotamab-Deruxtecan**	137	5,4
KRASG 12C	KRYSTAL-1 [11]	≥ 1	42,9	33,3 (33)	**Adagrasib**	112	6,5

1. Planchard D, et al. N Engl J Med 2024; 2. Cho BC, et al. ESMO 2023 ; 3. Passaro A, et al. Ann Oncol 2023; 4. Drilon A, et al. N Engl J Med 2024; 5. Zhou C, et al. N Engl J Med 2023; 6. Riely GJ, et al. J Clin Oncol 2023; 7. Zhou C, et al. N Engl J Med 2023; 8. Li BT, et al. N Engl J Med 2021; 9. Goto K, et al. J Clin Oncol 2023; 10. Paz-Ares L, et al. ESMO 2023; 11. Jänne PA, et al. N Engl J Med 2022

CBPNPC et - hétérogénéité - des mutations EGFR





1. Robichaux JP, et al. Nature 2021.

CBPNPC et mutations EGFR

ITK EGFR 3ème génération

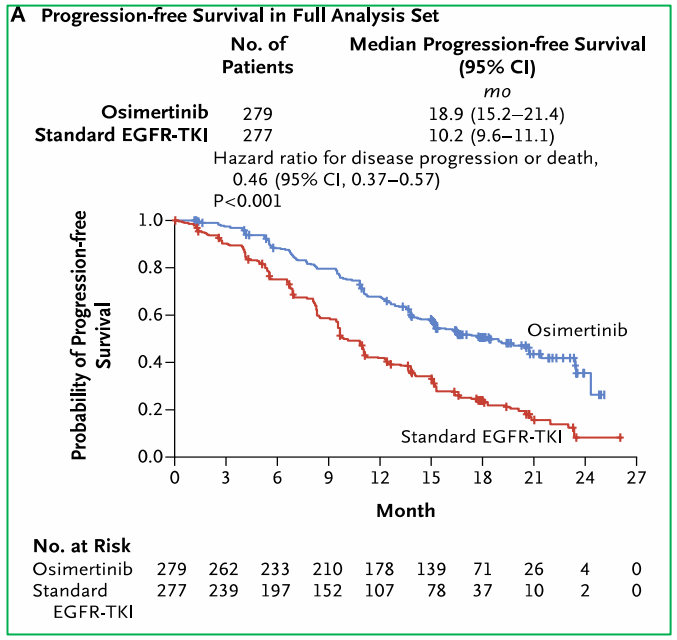
Etudes	Traitement	n	RO (%)	PFS (mois)	HR (95%IC)	OS (mois)	HR (95%IC)	ES ≥ grade 3
FLAURA[1,2]	Osimertinib	279	76,3	18,9	0,46 (0,37 – 0,57)	38,6	0,80	32
	Gefitinib or Erlotinib	277	80,4	10,2		31,8	(0,64 – 1)	41
AENEAS[3]	Aumolertinib	214	73,8	19,3	0,46 (0,36 – 0,60)	-	-	36,4
	Gefitinib	215	72,1	9,9		-		35,8
LAZER301[4]	Lazertinib	196	76	20,6	0,45 (0,34 – 0,58)	non mature %- 18 mois: 80,3 vs 72,4 0,74 (0,51 – 1,08)		20
	Gefitinib	197	76,1	9,7				21
FURLONG[5]	Furmonertinib	178	89	20,8	0,44 (0,34 – 0,58)	-	-	11
	Gefitinib	179	84	11,1		-		18
NCT04206072[6]	Befotertinib	182	67	22,1	0,49 (0,36 – 0,68)	-	-	30
	Icotinib	180	64,4	13,8		-		8

1. Soria JC, et al. N Engl J Med 2017 ; 2. Ramaligam SS, et al. N Engl J Med 2020; 3. Lu S, et al. J Clin Oncol 2022; 4. Cho BC, et al. J Clin Oncol 2023; 5. Shi Y, et al. Lancet Resp Med 2022; 6. Lu S, et al. Lancet Resp Med 2023

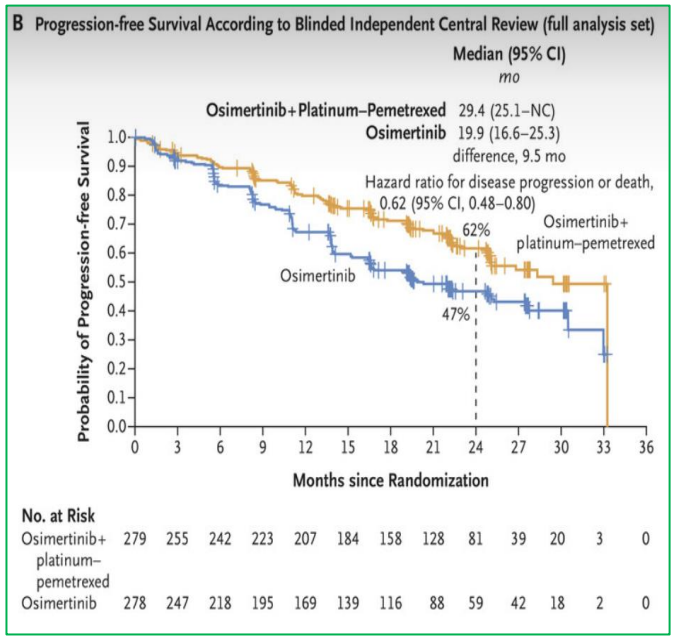
Evolution 2023 dans les CBPNPC EGFR + (del19, L858R)

Objectif : PFS (mois)

FLAURA[1,2]

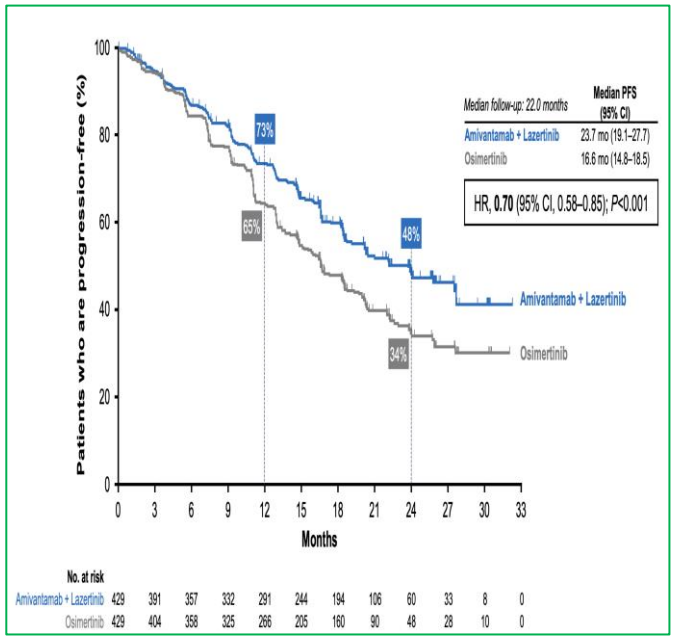


FLAURA2[3]



Osimertinib 80 mg x 3/j
Pemetrexed (500 mg/m$^{2)}$)
+ cisplatine (75 mg/m^{2}ou carbo (AUC 5) platine (x4)
puis pemetrexed + Osimertinib

MARIPOSA[4]



Lazertinib 80 mg x 3/j
C1: Amivantamab IV1050/1400 mg/m^2 (≥80 kg) J1,J2 – J8 – J15
C2 +: Amivantamab IV J1, J15

1. Soria JC, et al. N Engl J Med 2017; 2. Ramaligam SS, et al. N Engl J Med 2019 3. Planchard D, et al. N Engl J Med 224; 4. Cho BC, et al. ESMO 2023

Evolution 2023 dans les CBPNPC EGFR + (del19, L858R)

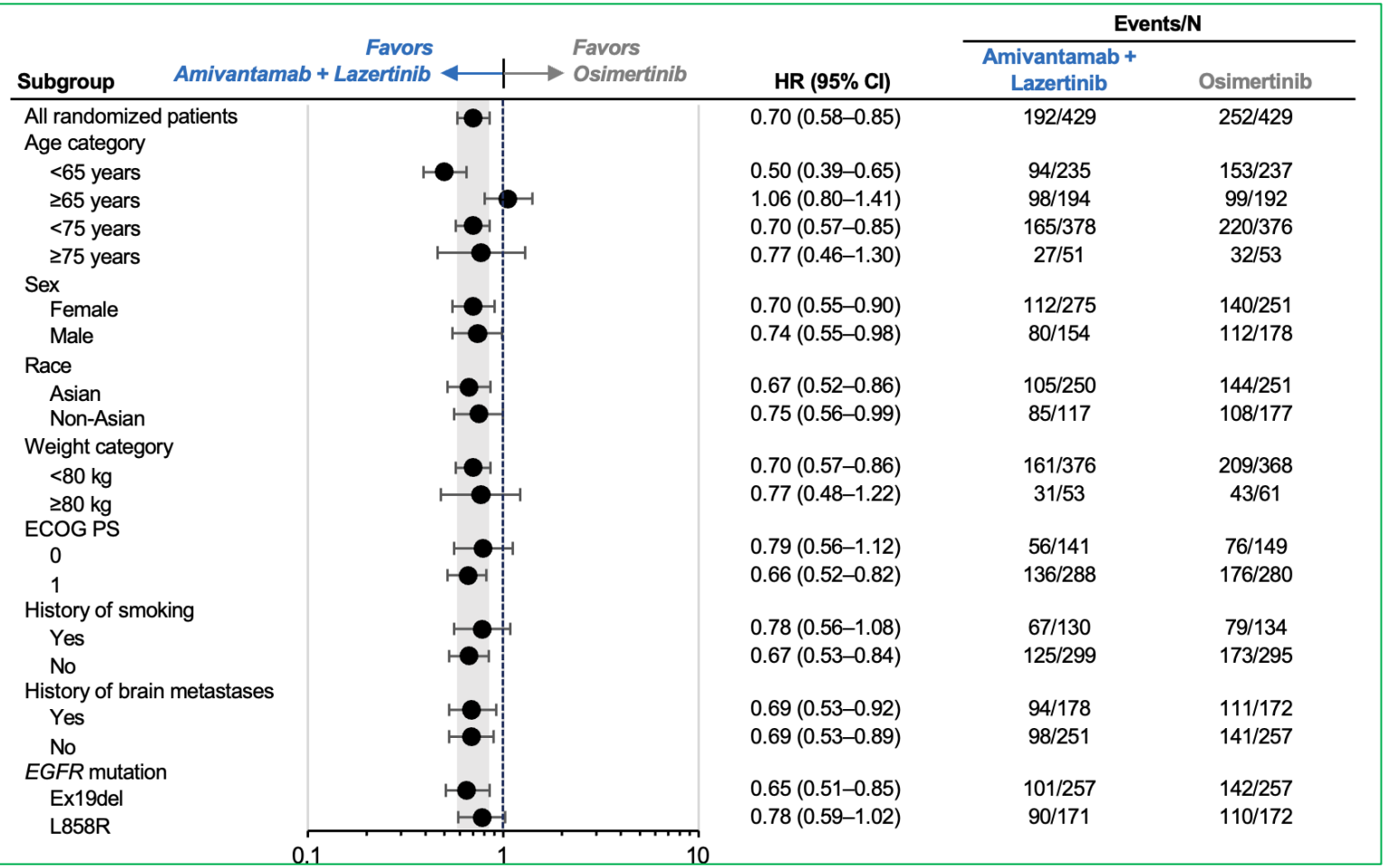
Autres paramètres d'efficacité

	FLAURA [1,2]		FLAURA 2 [3]		MARIPOSA [4]	
	Osimertinib	Gefitinib ou Erlotinib	Pemetrexed + Platine + Osimertinib	Osimertinib	Amivantamab + Lazertinib	Osimertinib
RO (%)	80	76	84	76	80	76
DoR (mois)	17,2	8,5	24,0	15,3	25,8	16,8
PFS (mois) M+ cerveau	15,2 (n=53)	9,6 (n=63)	24,9 (n=116)	13,8 (n=110)	18,3 (n=162)	13 (n=164)
HR (95%IC)	0,47 (0,30 – 0,74)		0,47 (0,33 – 0,66)		0,69 (0,53 – 0,92)	
PFS (mois) pas de M + cerveau	19,1 (n=226)	10,9 (n=214)	27,6 (n=163)	21 (n=168)	27,5 (n=251)	19,9 (n=257)
HR (95%IC)	0,46 (0,36 – 0,59)		0,75 (0,55 – 1,03)		0.69 (0.53 – 0.89)	
OS (mois)	38,6	31,8	-	-	-	-
HR (95%IC)	0,80 (0,64 – 1)		0,90 (0,55 – 1,24) (provisoire)		0,80 (0,61 – 1,05) (provisoire)	

FLAURA, Imagerie cérébrale non obligatoire; < **FLAURA2**, IRM (84 %) ou Scanner; < **MARIPOSA**, IRM systématique à l'inclusion

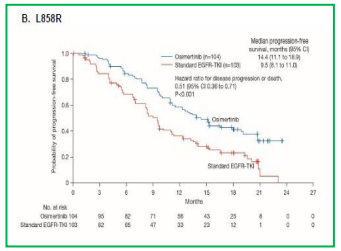
1. Soria JC, et al. N Engl J Med 2017; 2. Ramaligam SS, et al. N Engl J Med 2019 3. Planchard D, et al. N Engl J Med 2024; 4. Cho BC, et al. ESMO 2023

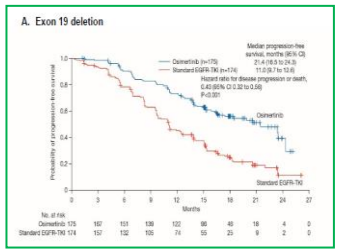
MARIPOSA: sous-groupes (PFS)

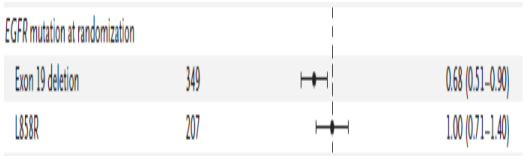


Subgroup	HR (95% CI)	Events/N: Amivantamab + Lazertinib	Events/N: Osimertinib
All randomized patients	0.70 (0.58–0.85)	192/429	252/429
Age category			
<65 years	0.50 (0.39–0.65)	94/235	153/237
≥65 years	1.06 (0.80–1.41)	98/194	99/192
<75 years	0.70 (0.57–0.85)	165/378	220/376
≥75 years	0.77 (0.46–1.30)	27/51	32/53
Sex			
Female	0.70 (0.55–0.90)	112/275	140/251
Male	0.74 (0.55–0.98)	80/154	112/178
Race			
Asian	0.67 (0.52–0.86)	105/250	144/251
Non-Asian	0.75 (0.56–0.99)	85/117	108/177
Weight category			
<80 kg	0.70 (0.57–0.86)	161/376	209/368
≥80 kg	0.77 (0.48–1.22)	31/53	43/61
ECOG PS			
0	0.79 (0.56–1.12)	56/141	76/149
1	0.66 (0.52–0.82)	136/288	176/280
History of smoking			
Yes	0.78 (0.56–1.08)	67/130	79/134
No	0.67 (0.53–0.84)	125/299	173/295
History of brain metastases			
Yes	0.69 (0.53–0.92)	94/178	111/172
No	0.69 (0.53–0.89)	98/251	141/257
EGFR mutation			
Ex19del	0.65 (0.51–0.85)	101/257	142/257
L858R	0.78 (0.59–1.02)	90/171	110/172

La question EGFR del19 ou L858R

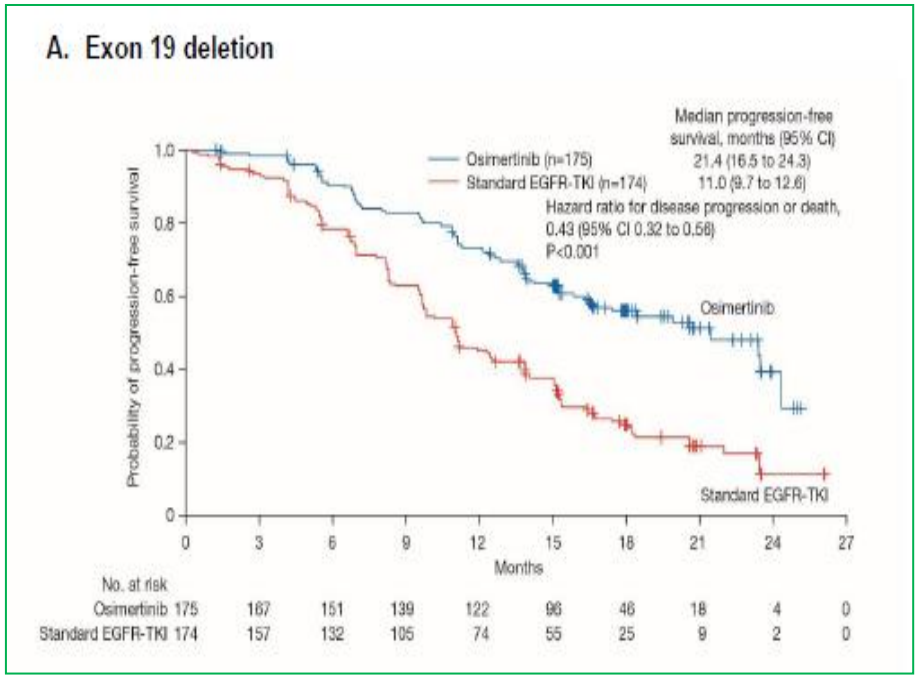


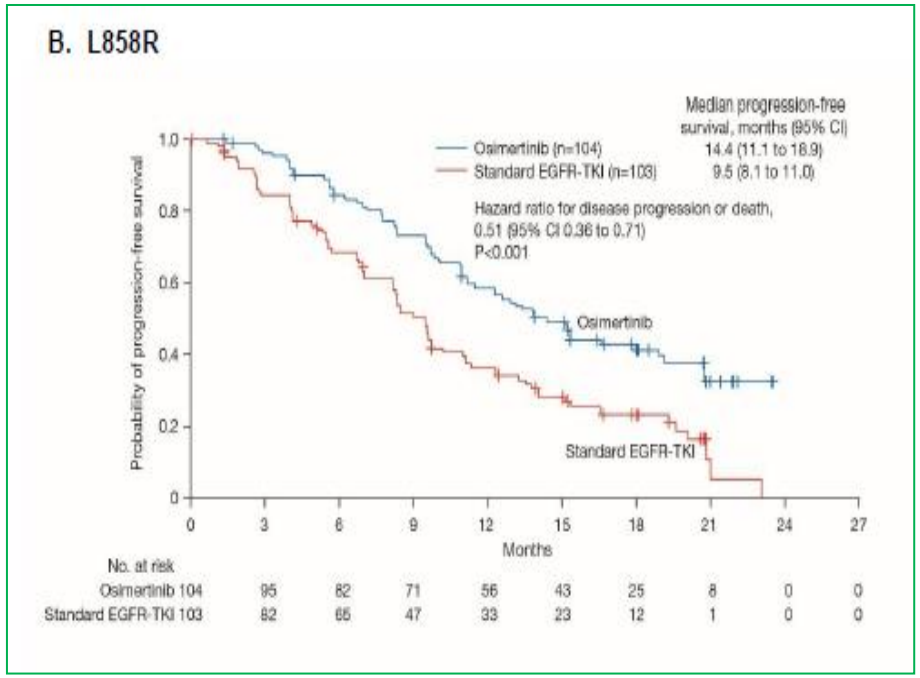




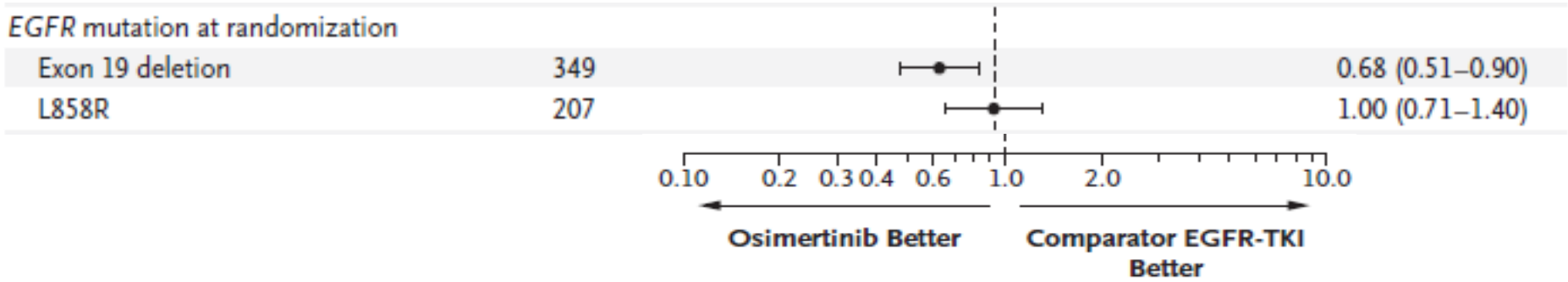
1. Cho BC, et al. ESMO 2023

FLAURA: EGFR del19 ou L858R





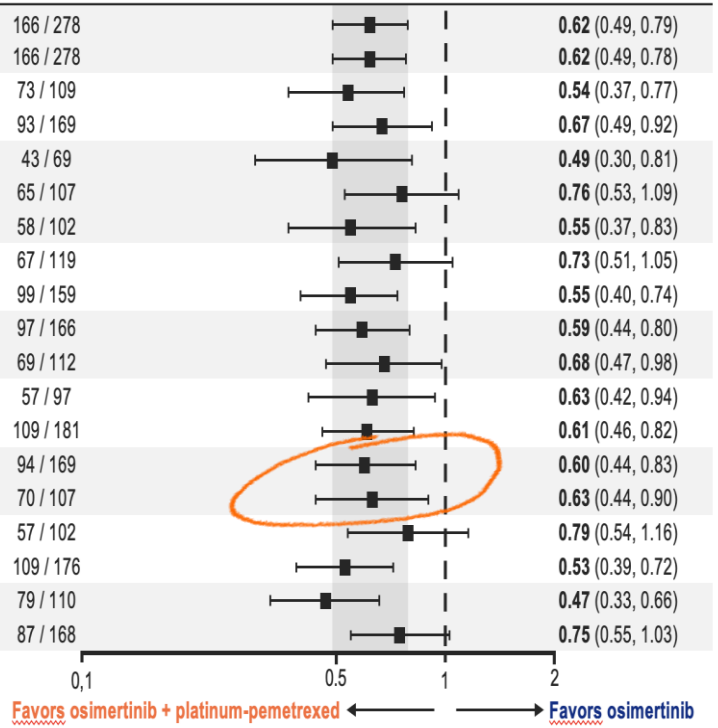
OS

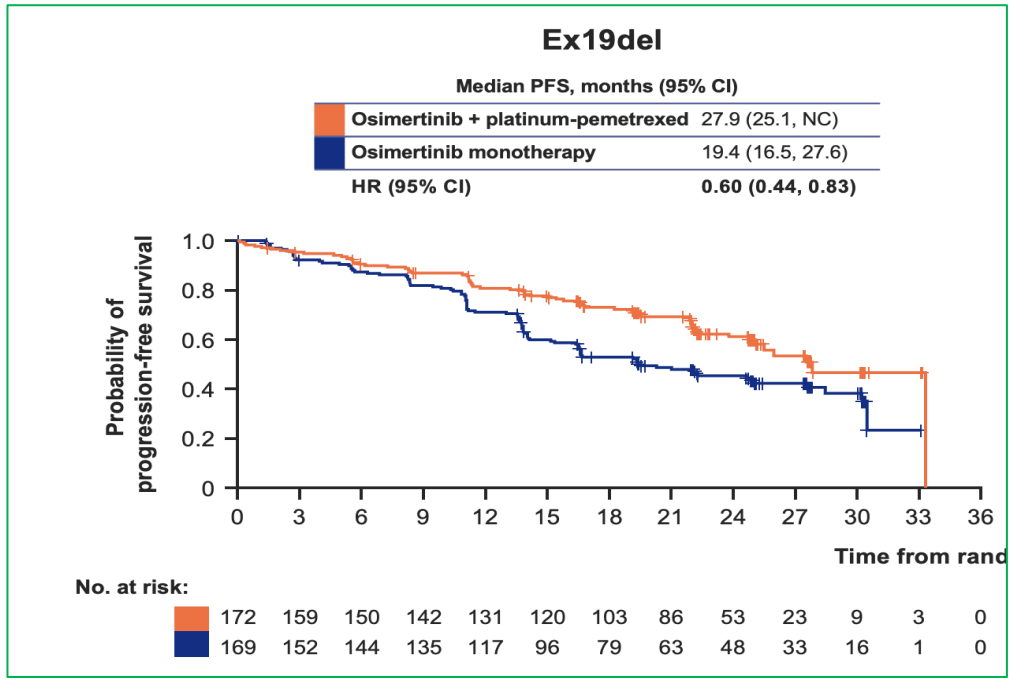


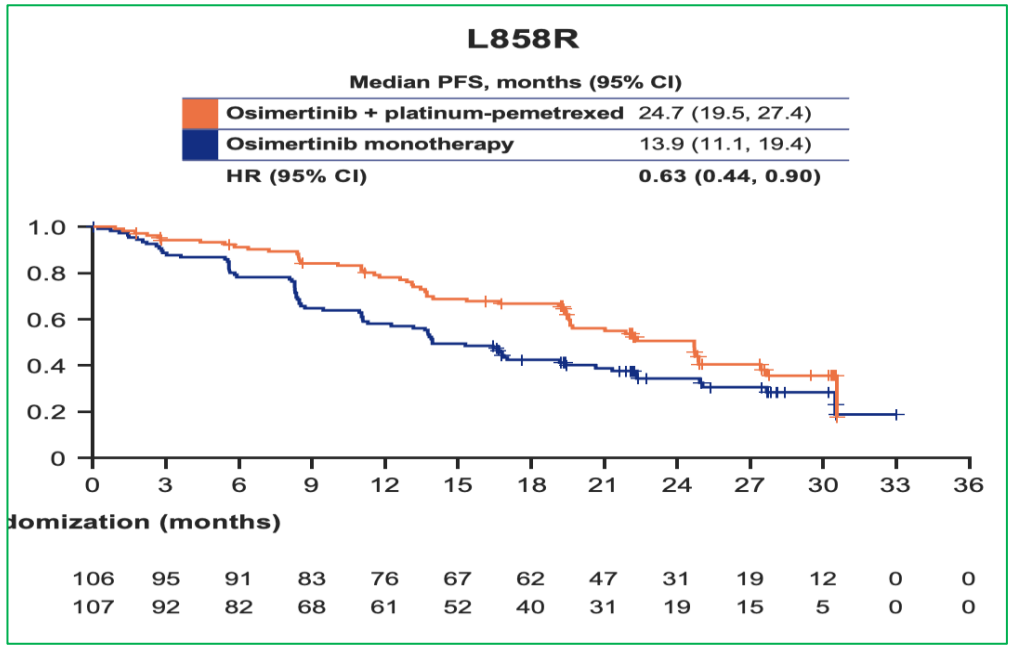
1. Soria JC, et al. N Engl J Med 2017 ; 2. Ramaligam SS, et al. N Engl J Med 2020

FLAURA 2: sous-groupes (PFS)

Subgroup		Osimertinib + platinum-pemetrexed (Events / patients)	Osimertinib monotherapy (Events / patients)	HR (95% CI)
All patients	Stratified log-rank	120 / 279	166 / 278	**0.62** (0.49, 0.79)
	Unadjusted Cox PH	120 / 279	166 / 278	**0.62** (0.49, 0.78)
Sex	Male	51 / 106	73 / 109	**0.54** (0.37, 0.77)
	Female	69 / 173	93 / 169	**0.67** (0.49, 0.92)
Race	Chinese Asian	26 / 71	43 / 69	**0.49** (0.30, 0.81)
	Non-Chinese Asian	54 / 107	65 / 107	**0.76** (0.53, 1.09)
	Non-Asian	40 / 101	58 / 102	**0.55** (0.37, 0.83)
EGFR mutation test method	Central	52 / 121	67 / 119	**0.73** (0.51, 1.05)
	Local	68 / 158	99 / 159	**0.55** (0.40, 0.74)
Age at screening	<65 years	73 / 174	97 / 166	**0.59** (0.44, 0.80)
	≥65 years	47 / 105	69 / 112	**0.68** (0.47, 0.98)
Smoking history	Yes	43 / 91	57 / 97	**0.63** (0.42, 0.94)
	No	77 / 188	109 / 181	**0.61** (0.46, 0.82)
EGFR mutation type†	Ex19del	65 / 172	94 / 169	**0.60** (0.44, 0.83)
	L858R	55 / 106	70 / 107	**0.63** (0.44, 0.90)
WHO PS	0	48 / 101	57 / 102	**0.79** (0.54, 1.16)
	1	72 / 178	109 / 176	**0.53** (0.39, 0.72)
CNS status at baseline	Yes	52 / 116	79 / 110	**0.47** (0.33, 0.66)
	No	68 / 163	87 / 168	**0.75** (0.55, 1.03)



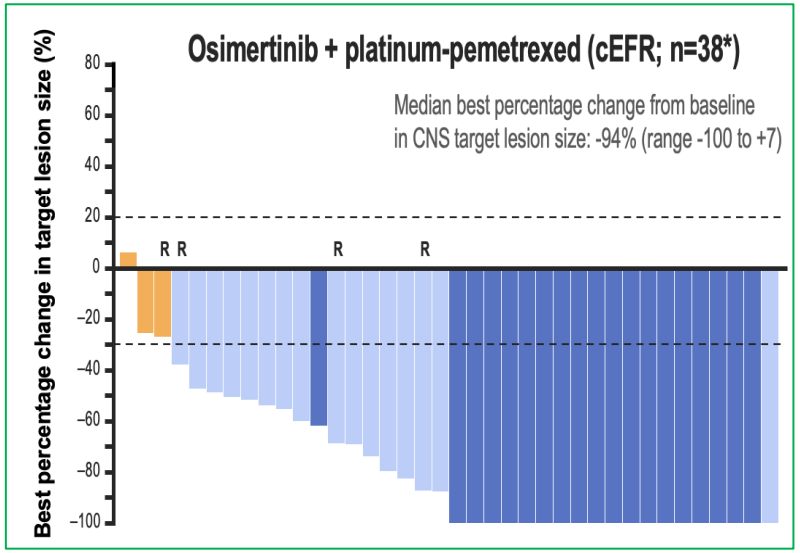


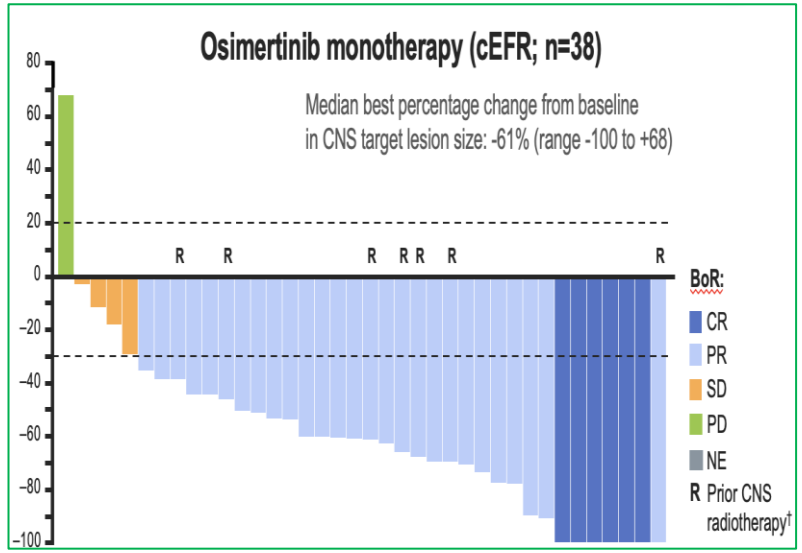


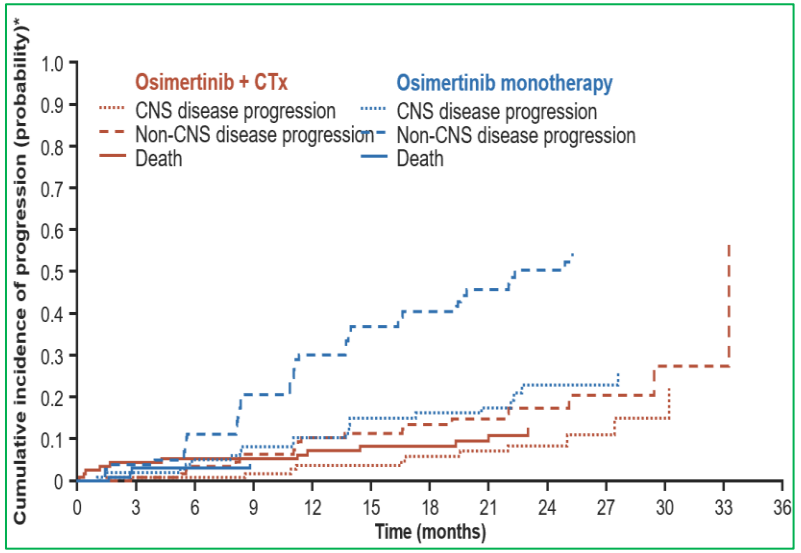
1. Planchard D, et al. N Engl J Med 2024

FLAURA 2: Métastases cérébrales

Pts with CNS metastases which were asymptomatic (not requiring steroids) or had a stable neurological status for ≥2 weeks after completion of definitive treatment and steroids, if received, were allowed







	cFAS (n=222) Measurable + non-measurable BM		cEFR (n=78) Measurable BM	
CNS response‡	**Osi + CTx (n=118)**	**Osi mono (n=104)**	**Osi + CTx (n=40)**	**Osi mono (n=38)**
CNS ORR, % (95% CI)	**73 (64 to 81)**	**69 (59 to 78)**	**88 (73 to 96)**	**87 (72 to 96)**
Complete response, n (%)	70 (59)	45 (43)	19 (48)	6 (16)
Partial response, n (%)	16 (14)	27 (26)	16 (40)	27 (71)
CNS DCR, % (95% CI)	91 (84 to 95)	93 (87 to 97)	95 (83 to 99)	97 (86 to 100)
Median DoR, months (95% CI)§	**NR (23.8, NC)**	**26.2 (19.4, NC)**	**NR (21.6, NC)**	**20.9 (12.6, NC)**

The estimated probability of observing CNS progression at 24 months was **9%** (95% CI 4, 16) with **osimertinib and the addition of CTx** vs **23%** (95% CI 14, 33) with **osimertinib monotherapy**

1. Planchard D, et al. ESMO 2023

	FLAURA 2[2]		MARIPOSA [3]	
	Pem + Plat + Osi	Osi	Ami + Lazer	Osi
Anémie (G1/2, G3, %)	27 - 20	8 - < 1	19 - 4	20 - 2
Diarrhée (G1/2, G3, %)	41 - 3	40 - < 1	27 - 2	44 - 1
Nausées (G1/2, G3, %)	42 - 1	10 - 0	20 - 1	13 – 0,2
Neutropénie (G1/2, G3, G4 %)	18 – 19 - 4	8 - 1		
Thrombopénie (G1/2, G3, G4%)	18 – 12 - 2	9 - 1		
Anorexie (G1/2, G3, %)	28 - 3	9 - 1	24 - 1	16 - 1
Constipation (G1/2, G3, %)	29 - < 1	10 - 0	20 - 0	13 - 0
Rash (G1/2, G3, %)	28 - < 1	21 - 0	48 - 15	30 - 1
Fatigue (G1/2, G3, %)	25 - 3	9 - < 1		
Vomissements (G1/2, G3, %)	25 - 1	6 - 0		
Stomatite (G1/2, G3, %)	24 - < 1	18 - < 1	28 - 1	21 – 0,2
Paronychies (G1/2, G3, %)	23 - 1	26 - > 1	57 - 11	28 – 0,5
ALT (G1/2, G3, %)	19 - 1	7 - < 1	31 - 5	11 - 2
Sécheresse cutanée (G1/2, G3, %)	18 - 0	24 - 0		
AST (G1/2, G3, %)	17 - < 1	4 - > 1	25 - 3	12 - 1
Créatinine (G1/2, G3, %)	17 – 0	4 - 0		
Œdèmes périphériques (G1/2, G3, %)	15 - 0	4 - 0	34 - 2	6 - 0
ILD	3	4	3	3

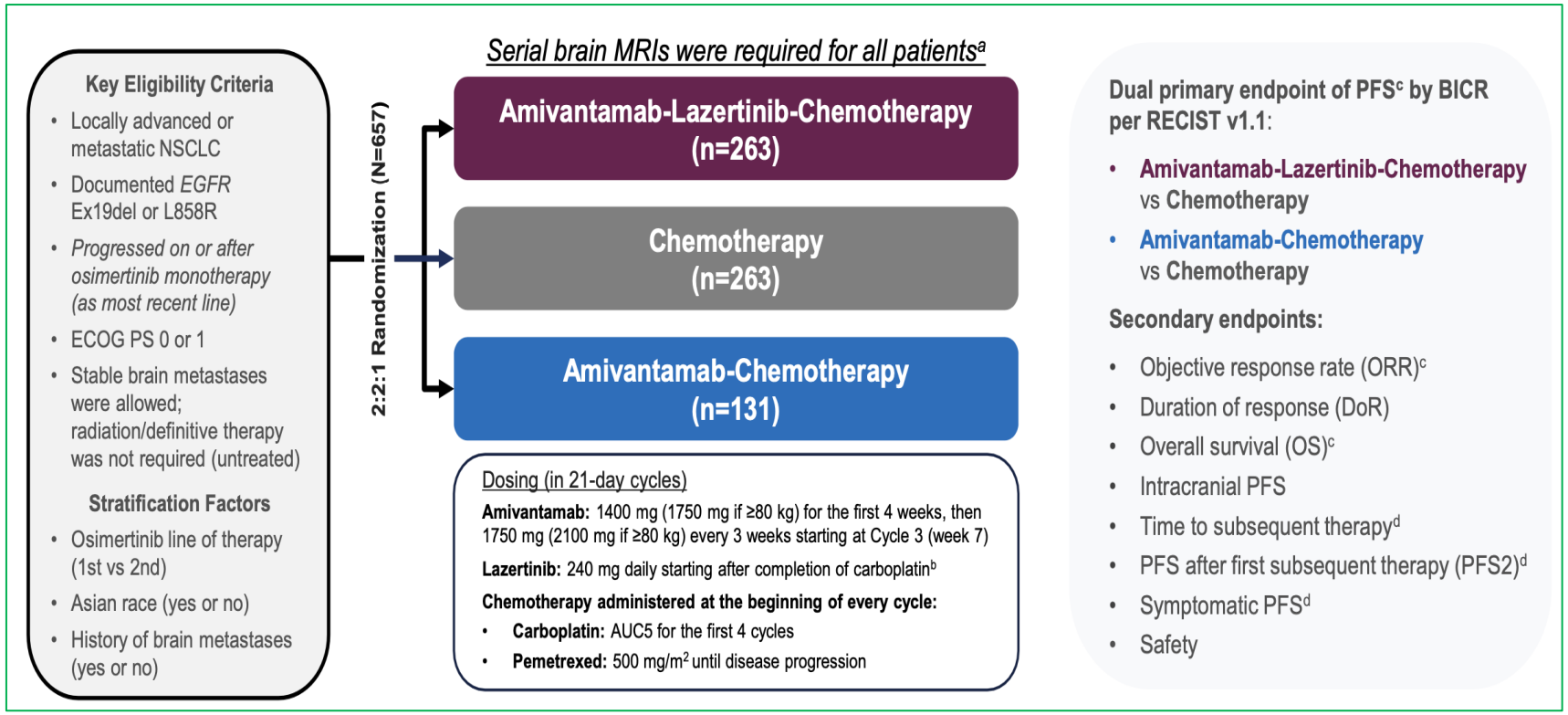
	MARIPOSA [3]	
	Ami + Lazer	Osi
Dermatite acnéïforme	21 - 8	13 - 0
Prurit	23 – 0,5	17 – 0,2
Hypoalbuminémie	43 - 5	6
Réaction - perfusion	57 - 6	
Hypocalcémie	19 - 2	8
Toux	15	21

	MARIPOSA [3]	
	Ami + Lazer	Osi
VTE	37	9
VTE + Décès	0,5	0,5

MARIPOSA : AE ≥ 20 %

FLAURA 2 : AE ≥ 15 %

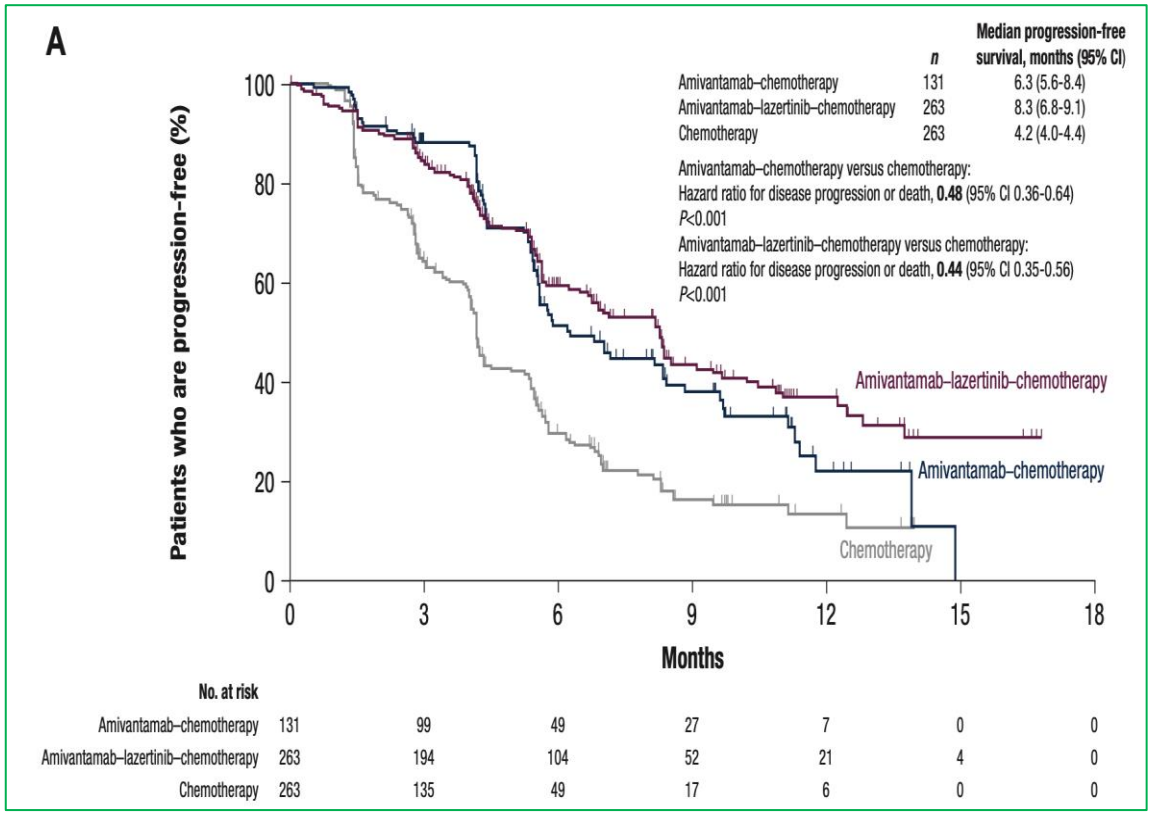
MARIPOSA-2

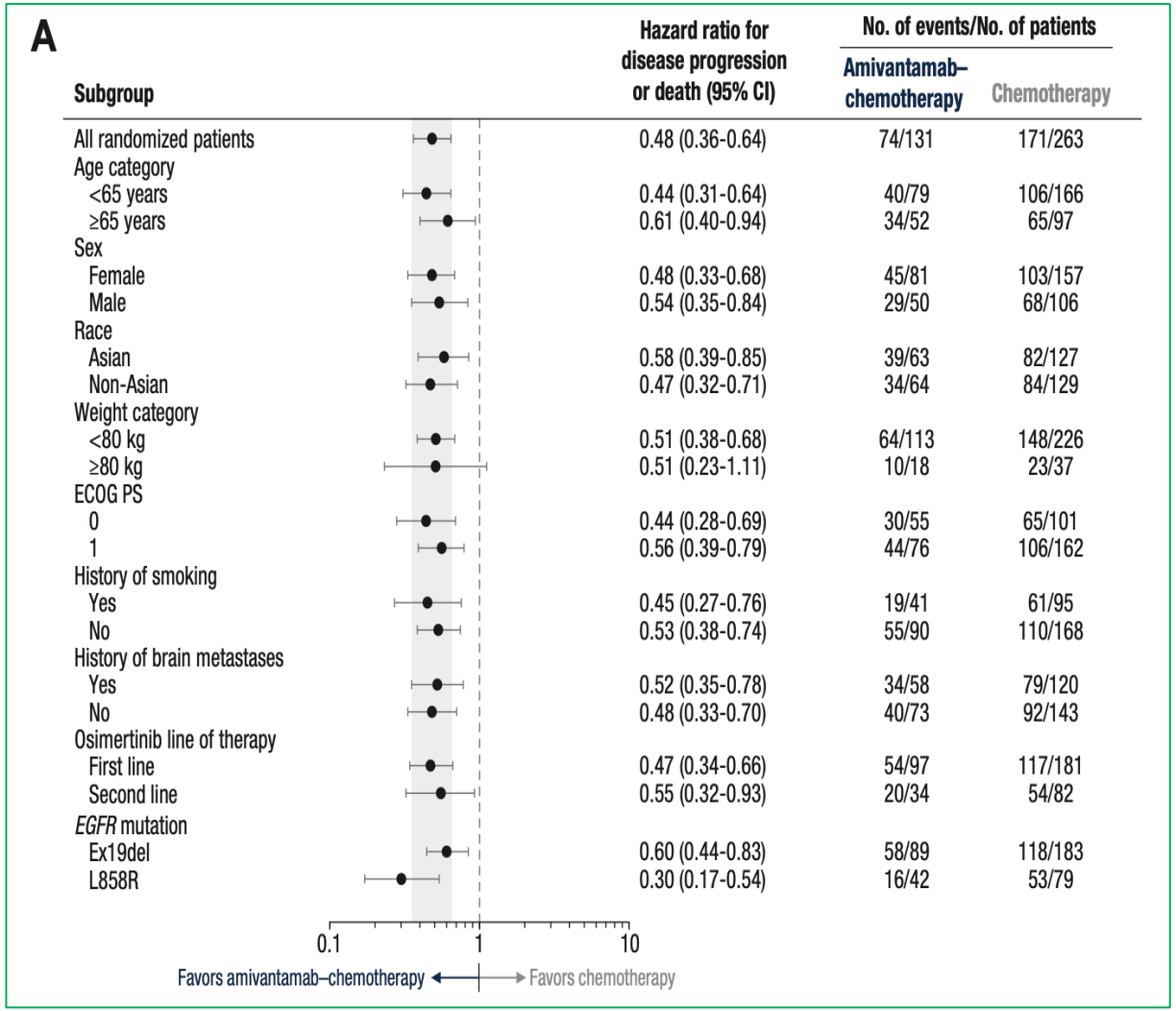


	Chimiothérapie		Amivantamab + Chimiothérapie	
	All	≥ G3	All	≥ G3
Rash	30 (12)	0	92 (71)	13 (10)
VTE	11 (5)	7 (3)	13 (10)	3 (2)
ILD	0	0	2 (2)	1 (1)

1. Passaro A, et al. Ann Oncol 2023

MARIPOSA-2

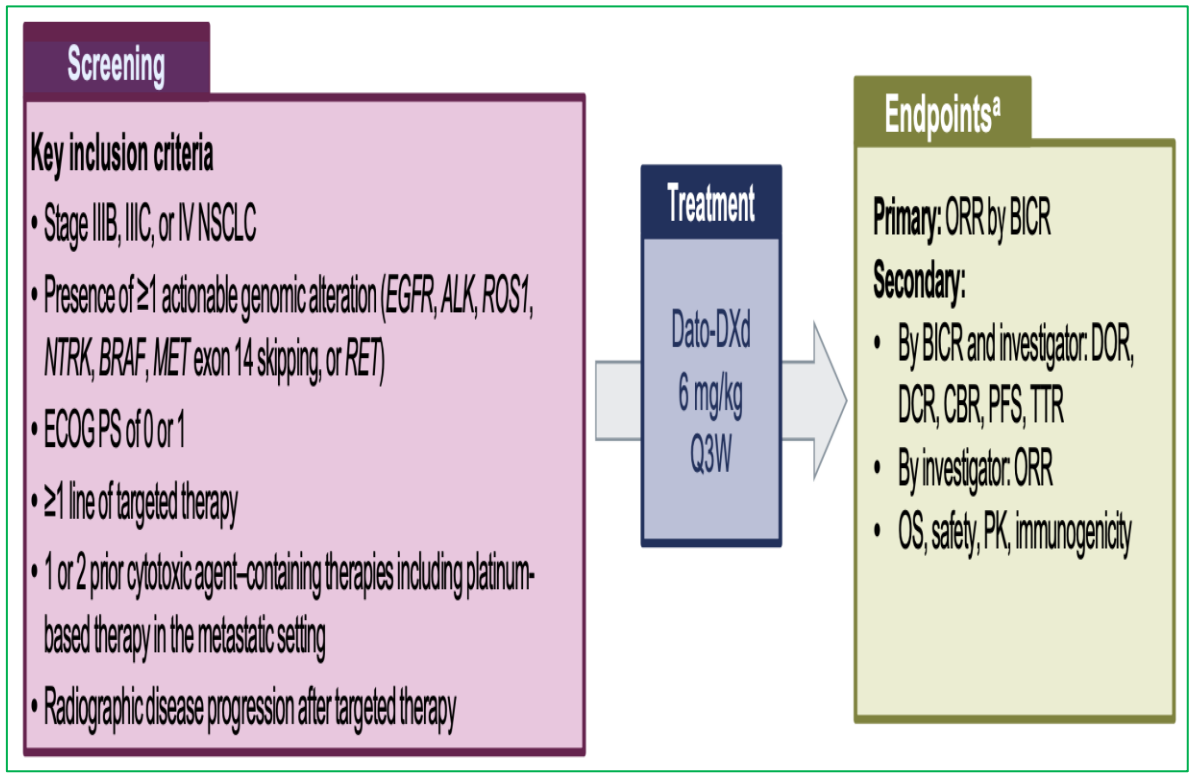




Traitement	n	RO (%)	DoR (mois)	PFS (mois)	HR (95%IC)	icPFS (mois)	HR (95%IC)
Chimiothérapie	263	36	5,6	4,2		8,3	0,80 (0,64 – 1)
Amivantamab – Chimiothérapie	131	64	6,9	6,3	0,48 (0,36 – 0,64)	12,5	
Amivanatmab– Lazertinib - Chimiothérapie	263	63	9,4	8,3	0,44 (0,35 – 0,56)	12,8	

1. Passaro A, et al. Ann Oncol 2023

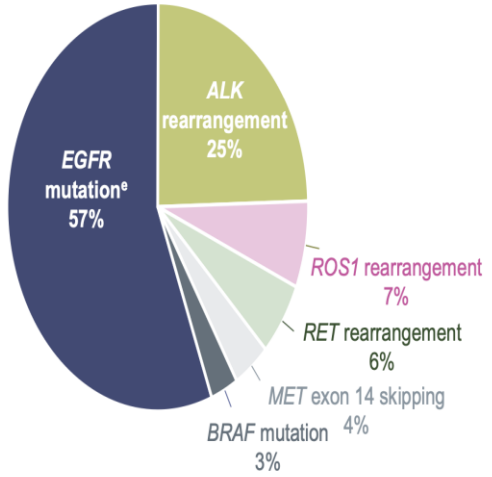
TROPION Lung-05



Patient Characteristics and Disposition

Demographic characteristics	Dato-DXd (N=137)
Median age (range), years	60 (29-79)
Female, n (%)	83 (61)
Histology, n (%)	
Adenocarcinoma	130 (95)
History of brain metastasis, n (%)[a]	70 (51)
Median prior lines of therapy for adv/met disease	3
Prior lines of therapy, n (%)	137 (100)
≥3 prior lines of therapy for adv/met disease	98 (72)
Prior platinum chemotherapy	137 (100)
Prior anti–PD-1/anti–PD-L1 immunotherapy	49 (36)
≥2 prior lines of targeted therapies for indicated genomic alteration	82 (60)

Relative Frequency of Genomic Alterations[b-d]



Disposition

At the time of data cutoff (December 14, 2022):
- Median (range) treatment duration was 4 (1-21) months
- 60 participants (44%) were ongoing in study
- 20 participants (15%) were ongoing on study treatment

1. Paz Ares L, et al. ESMO 2023

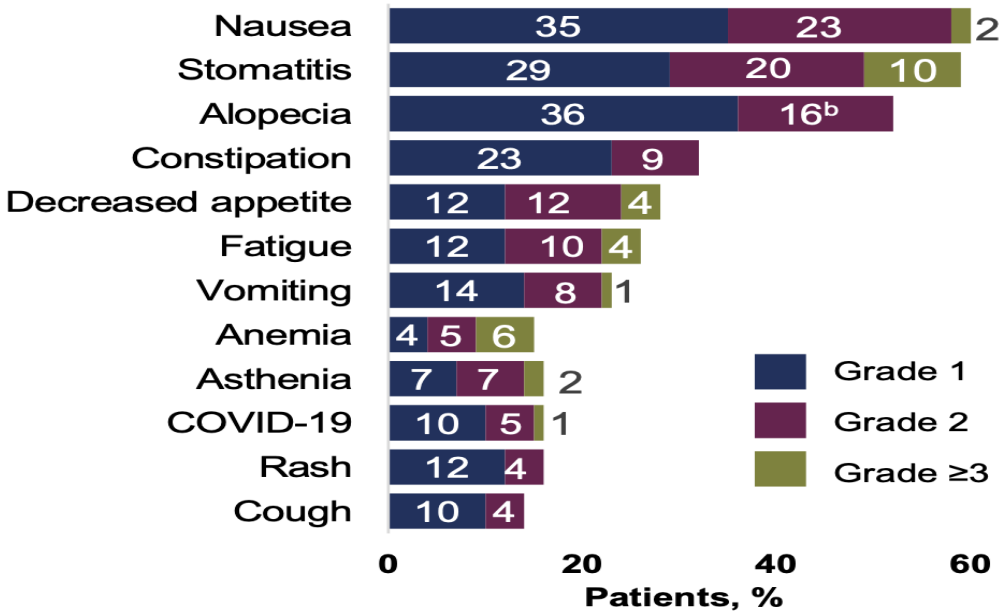
TROPION Lung-05

Response per BICR	All treated patients (N=137)	Patients with *EGFR* mutations (N=78)	Patients with *ALK* rearrangement (N=34)
ORR confirmed, n (%) [95% CI][a]	49 (35.8) [27.8-44.4]	34 (43.6) [32.4-55.3]	8 (23.5) [10.7-41.2]
Median DOR (95% CI), months	7.0 (4.2-9.8)	7.0 (4.2-10.2)	7.0 (2.8-8.4)
DCR confirmed, n (%) [95% CI][a]	108 (78.8) [71.0-85.3]	64 (82.1) [71.7-89.8]	25 (73.5) [55.6-87.1]
Median PFS, (95% CI), months[b]	5.4 (4.7-7.0)	5.8 (5.4-8.3)	4.3 (2.6-6.9)

BOR: In the overall population (N=137), 4 patients (3%) achieved a CR and 45 (33%) achieved a PR

***EGFR* subset:** Among patients with sensitizing or T790M mutations (N=68), the ORR was 49.1% in those previously treated with osimertinib

TEAEs Occurring in ≥15% of Patients; All Grades (N=137)[a]



AESI Incidence by Grade[d]

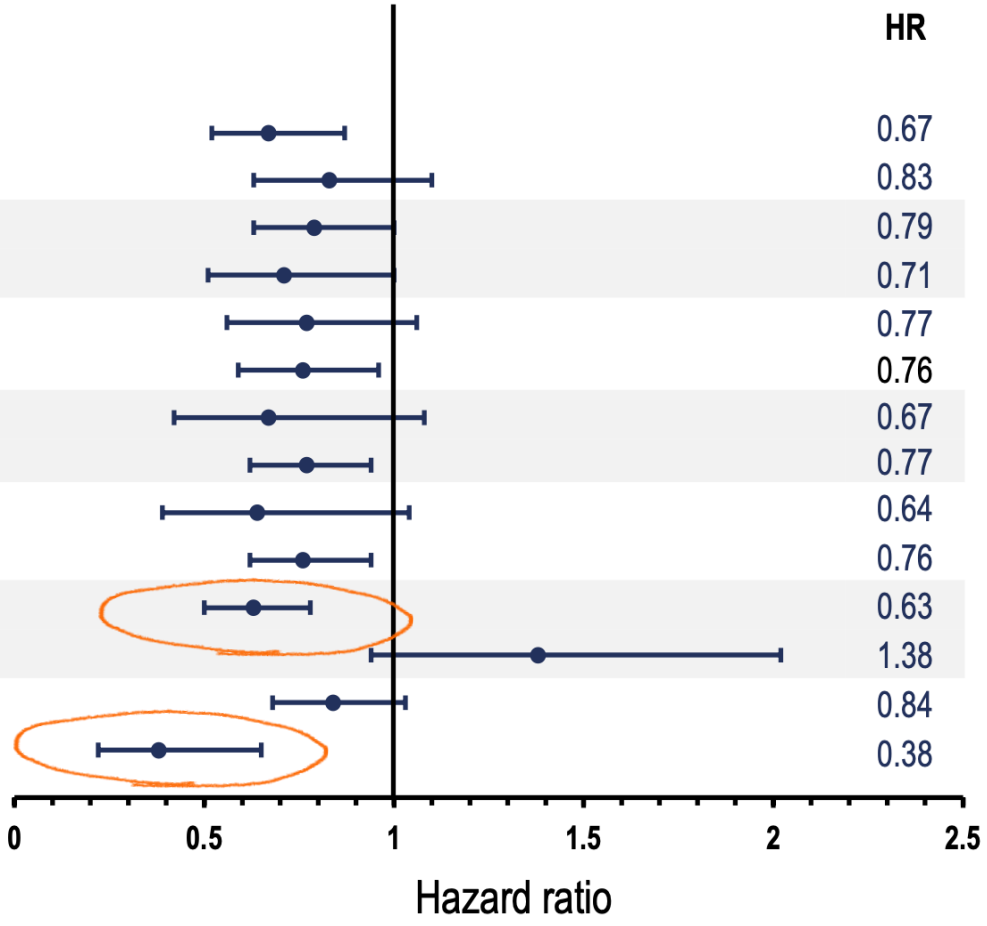
n (%)	Total	Grade 1	Grade 2	Grade ≥3
Oral mucositis/stomatitis	90 (66)	45 (33)	30 (22)	15 (11)
Ocular surface toxicity[e]	36 (26)	26 (19)	7 (5)	3 (2)[f]
IRR	22 (16)	15 (11)	7 (5)	0
Adjudicated drug-related ILD	5 (4)	1 (1)	3 (2)	1 (1)[g]

1. Paz Ares L, et al. ESMO 2023

TROPION Lung-01: Etude randomisée de phase 3

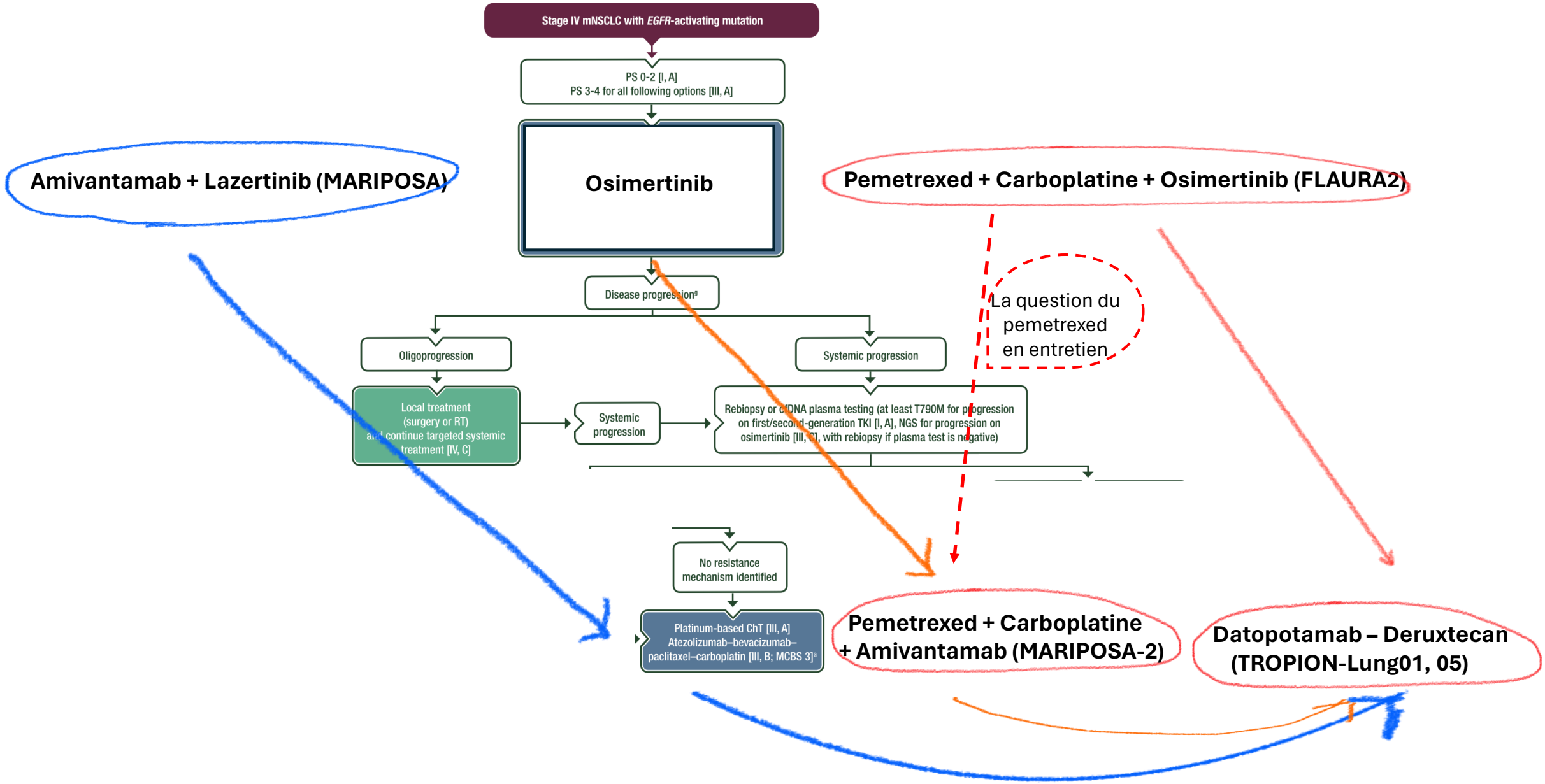
PFS in Key Subgroups

		Events/n		HR
		Dato-DXd	Docetaxel	
Age at randomization	<65 years	118/162	115/155	0.67
	≥65 years	95/137	103/150	0.83
Sex	Male	136/183	158/210	0.79
	Female	77/116	60/95	0.71
Race	Asian	76/119	82/120	0.77
	Non-Asian	131/172	129/177	0.76
Smoking status	Never	36/61	33/52	0.67
	Former/current	177/238	184/251	0.77
Brain metastasis at baseline	With	33/50	31/47	0.64
	Without	180/249	187/258	0.76
Histology	Non-squamous	156/229	168/232	0.63
	Squamous	57/70	50/73	1.38
Actionable genomic alterations[a]	Absent	189/252	184/255	0.84
	Present	24/47	34/50	0.38



Lisberg A, et al. ESMO 2023

Perspectives : CBPNPC avec mutations EGFR (del exon 19 et L858R)

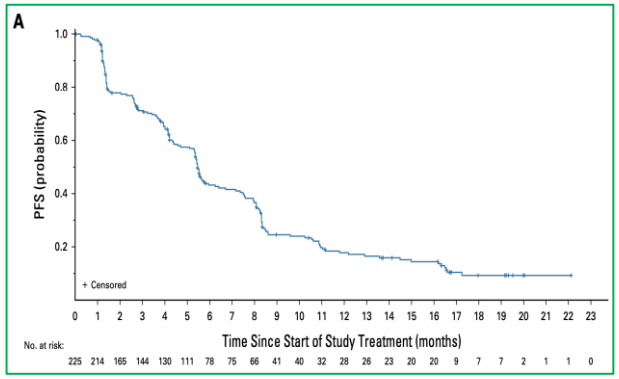


Hendricks LE, et al. Ann Oncol 2023

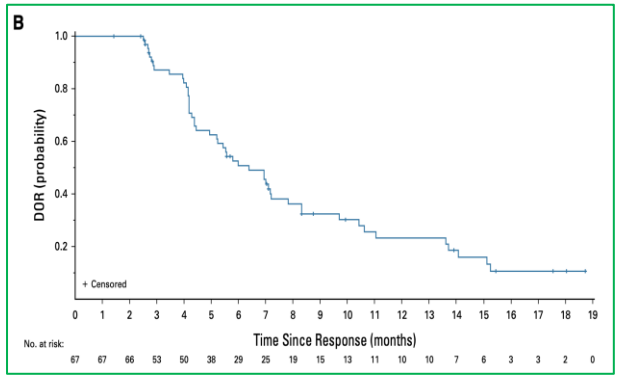
HERTHENA-Lung01, phase 2 avec Patritumab-Deruxtecan (HER3, DXd)

CBPNPC EGFRmt, pré-traités pat ITK-EGFR et CT-platine

PFS 5,5 mois

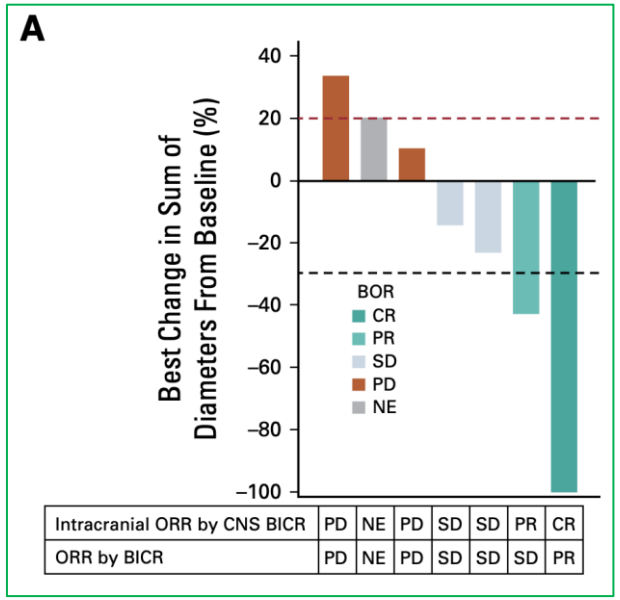


mDoR 6,4 mois



Taux R.O (%)	mSG (mois)	Toxicités
29,8	11,9	nausées (66 %), thrombopénie (44 %), anorexie (42 %) neutropénie (36 %) PID (5,3 %)

Yu HA, et al. J Clin Oncol 2023



Efficacité intra-cérébrale (n=30)

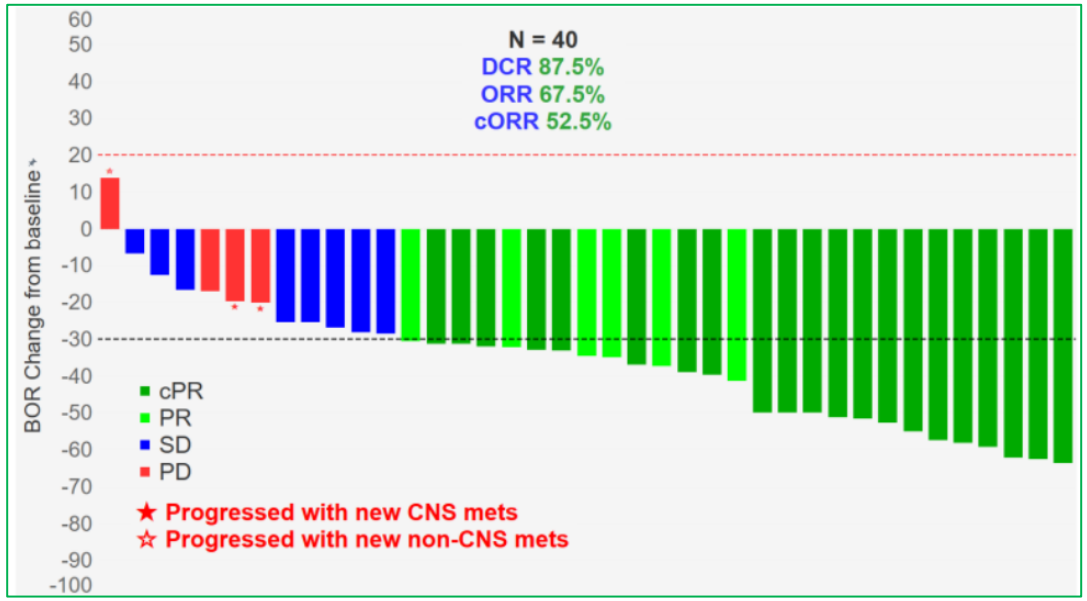
cORR (n, %)	10 (33,3)
cDoR (mois)	8,4

ADC: lorsque la cible est l'EGFR

	Payload	DAR
BL-B01D1[(1)]	Ed-04	7,5 - 8

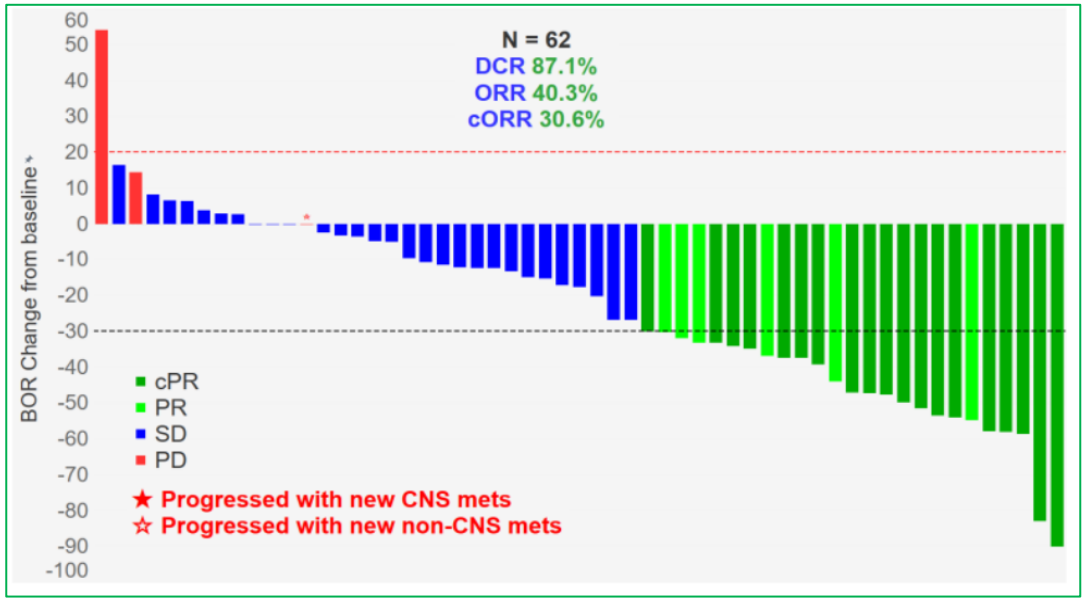
BL-B01D1 cible EGFR et HER3 ; Ed-04 = inhibiteur de topisomérase 1

CBPNPC EGFR muté (n=40)



DoR 8,5 mois; PFS 5,6 mois

CBPNPC EGFRwt (n=62)

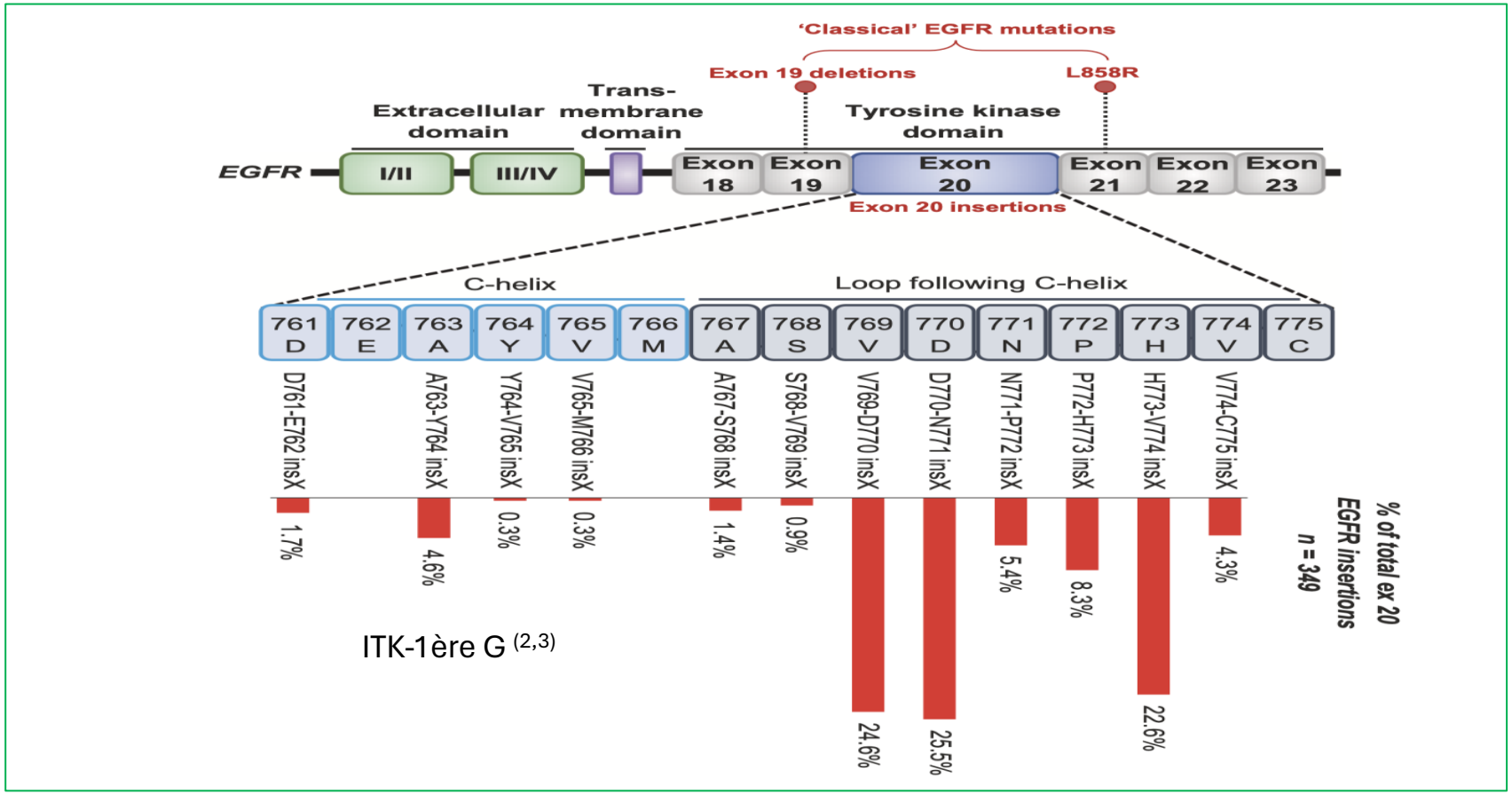


DoR NR; PFS 5,4 mois

Neutropénie ≥ G3 36 %; mucite tout grade 25 %; toxicité cutanée tout grade 17 %

1. Zhang I, et al. ESMO 2023

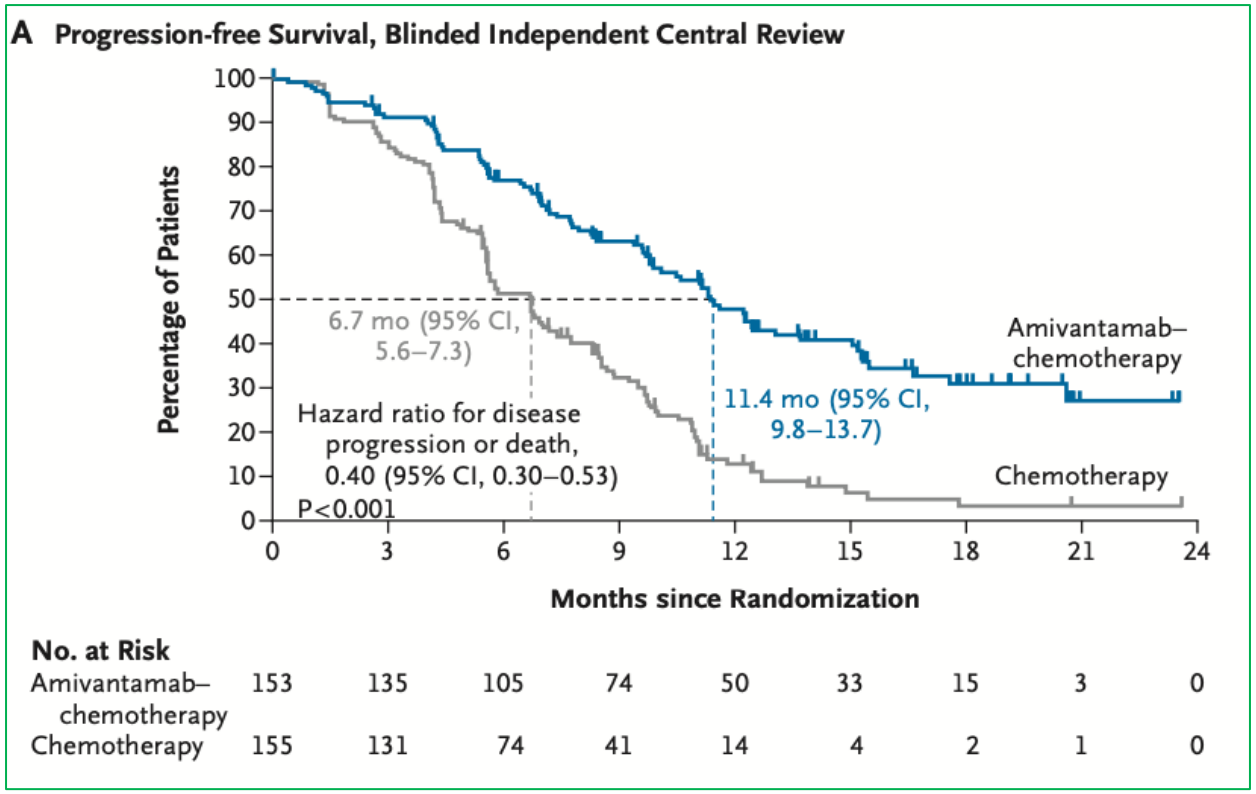
CBPNPC avancés avec ins EGFR exon 20



1. Vyse S, et al. Signal Trans and Target Ther 2019; 2. Arcilla M, et al. Mol Cancer ther 2013; Voon P, et al. Mol cancer ther 2013

Etude PAPILLON

CBPNPC ins exon 20 EGFR



	Amivantamab-chimio.	Chimio.	HR (IC95%)
ORR (%)	73	47	
OS (mois)	NE	24,4	0,67 (0,42 – 1,09)

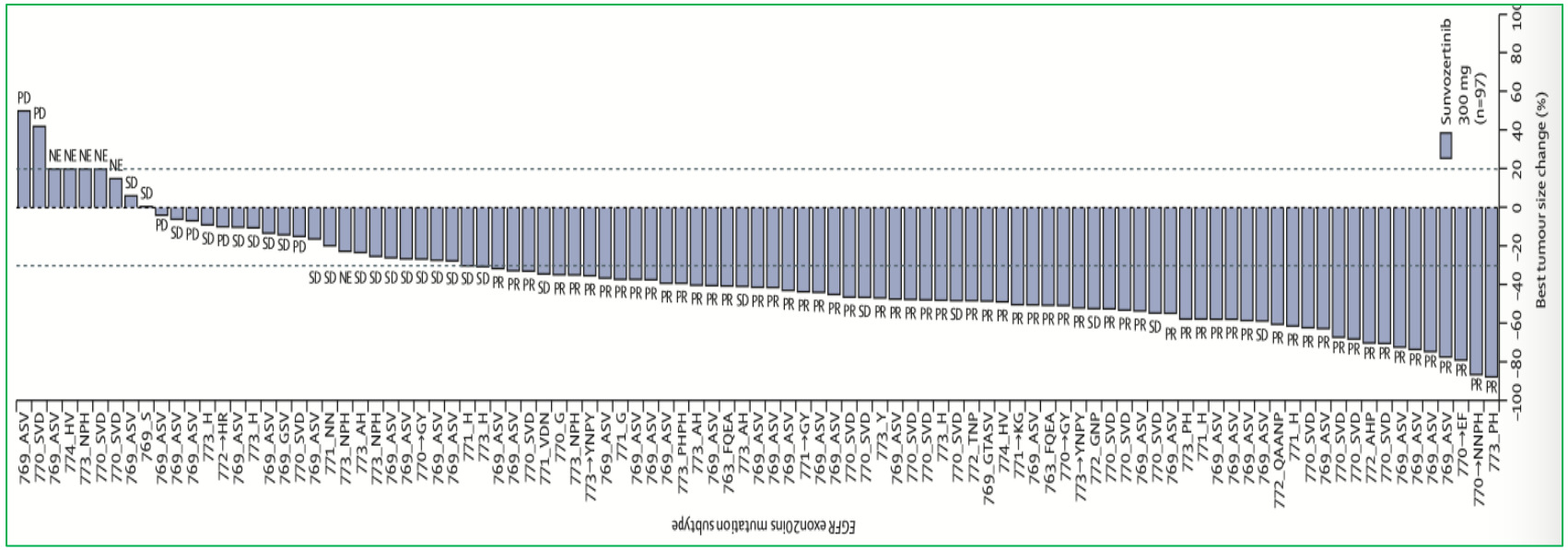
Toxicités	**PAPILLON**	
Tout grade et grade ≥ 3 (%)	**Ami-Chimio.**	**Chimio.**
Neutropénie	59 - 33	45 - 23
Paronychies	56 - 7	0 - 0
Rash	54 - 11	8 - 0
Anémie	50 - 11	55 - 12
Réaction (perfusion)	42 - 1	10 - 0
hypoalbuminémie	41 - 4	30 - 1
Leucopénie	38 - 11	32 - 3
Nausées	36 - 1	42 - 0
thrombopénie	36 - 10	30 - 10
Diminution de l'appétit	36 - 3	28 - 1
ALT	33 - 4	36 - 1
AST	31 - 1	33 - 1
Dermatite acnéïforme	31 - 4	3 - 0
Œdème périphérique	30 - 1	10 - 0
Stomatite	25 - 1	6 - 0
Diarrhée	21 - 3	13 - 1
Hypokalième	21 - 9	8 - 1
Vomissements	21 - 3	10 - 1

1. Zhou C, et al. N Engl J Med 2023

Sunvozertinib

CBPNPC ins exon 20 EGFR

Après échec d'une chimiothérapie à base de platine



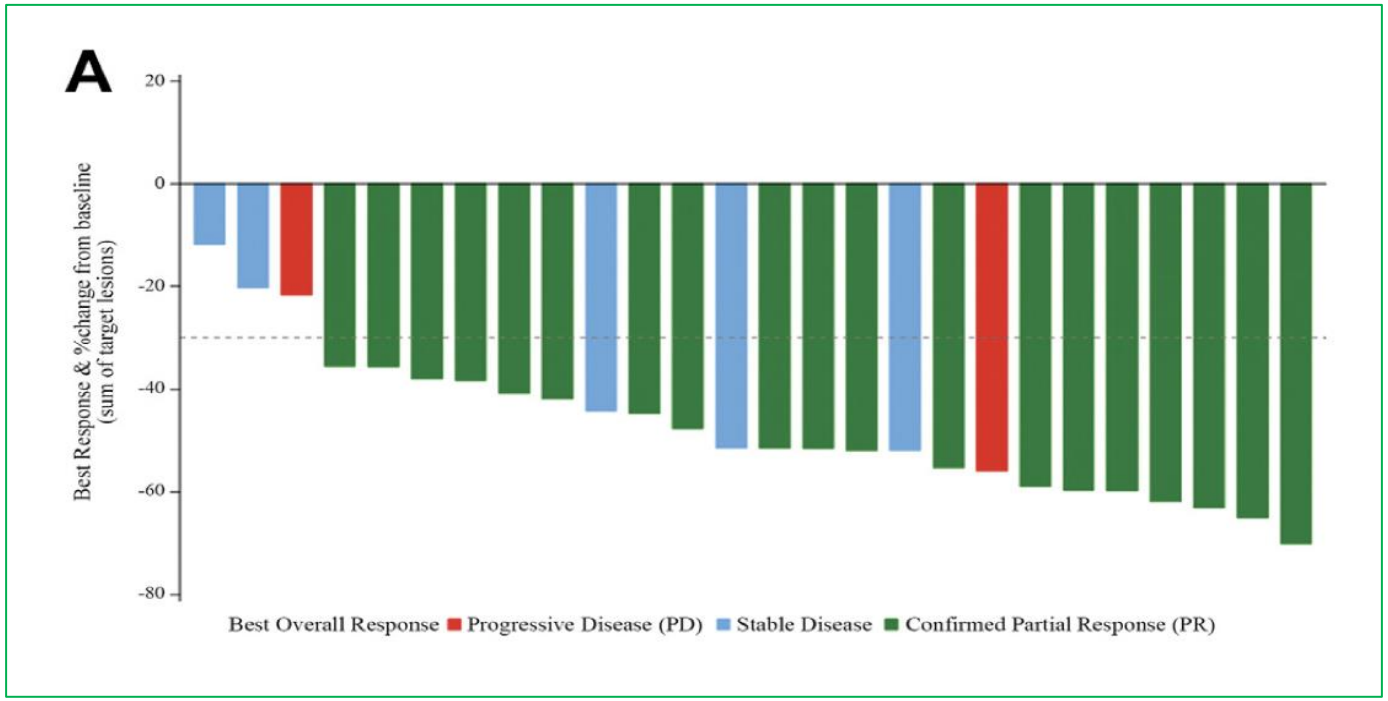
	Sunvozertinib
n	97
Exon 20	
769_ASV	39
770_SVD	18
Autres	43
RO (%)	61

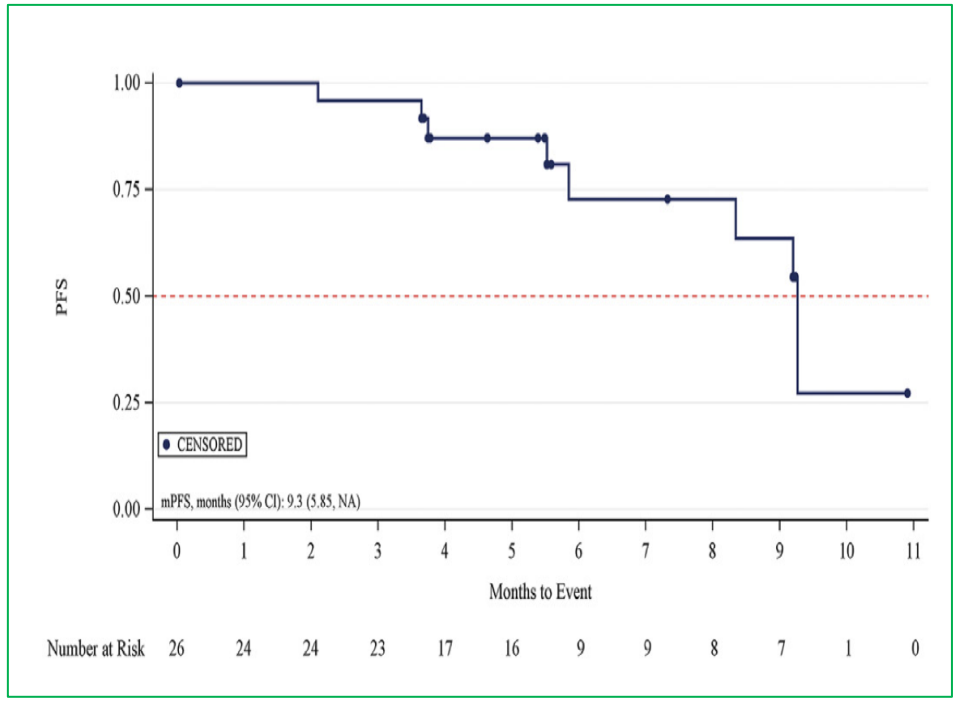
1. Wang M, et al. Lancet Resp Med 2024

YK029A

CBPNPC ins exon 20 EGFR

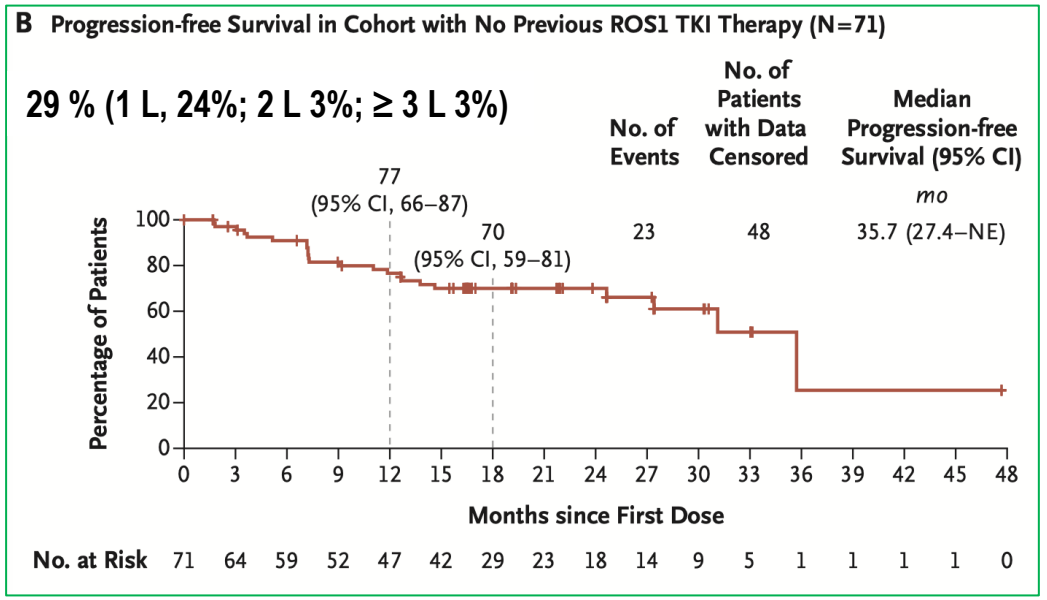
	YL029A
n	28
RO (%)	73,1
PFS (mois)	9,5
DoR (mois)	7,5

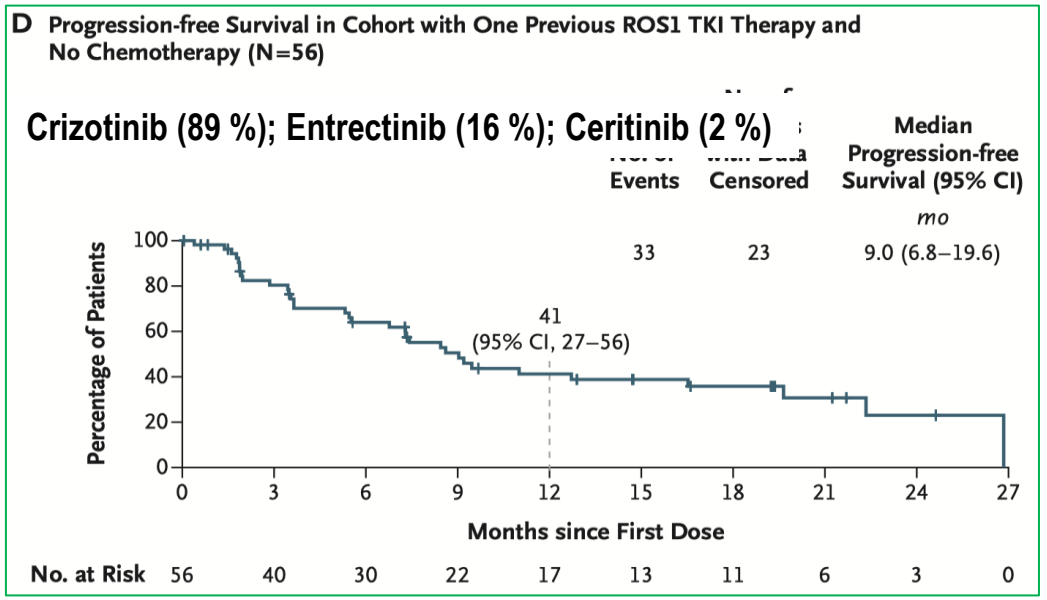




1. Duan J, et al. J Thorac Oncol 2023

Repotrectinib, CBPNPC ROS +
TRIDENT-1

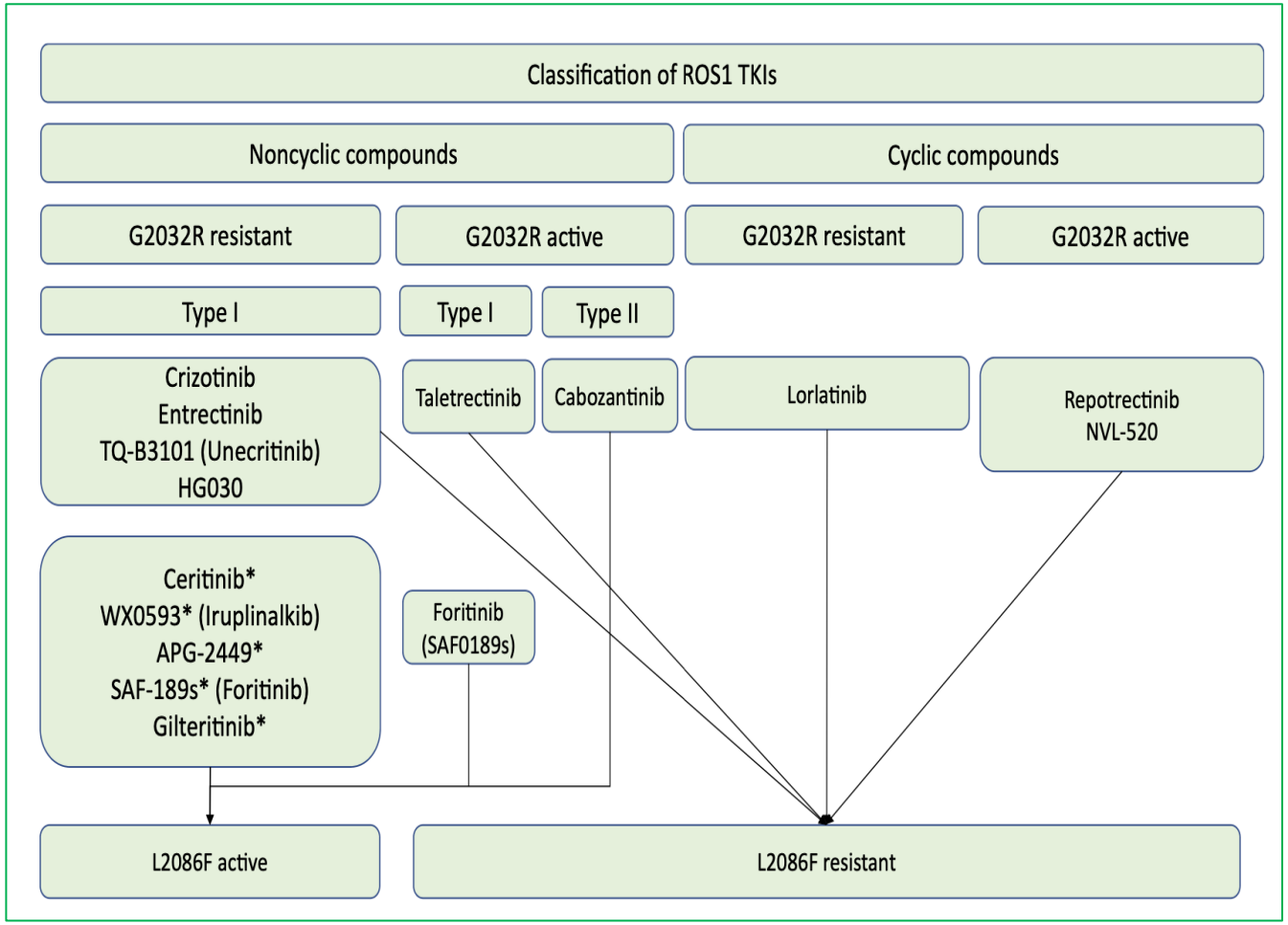


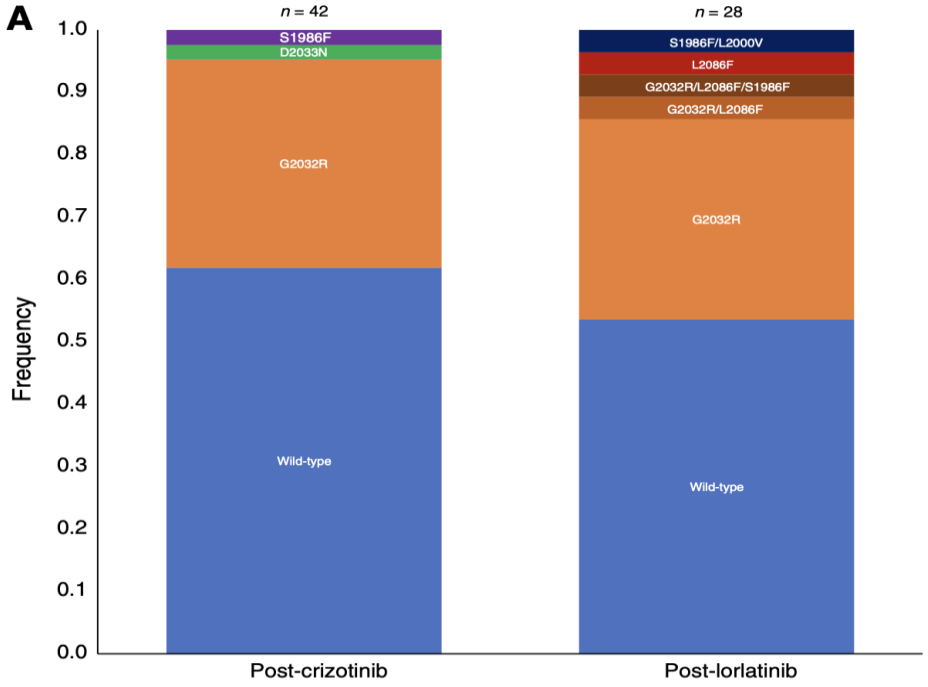


Etudes	Pas de pre-traitement par ITK –ROS1	Pre-traitement par ITK-ROS1, pas de de chmio.
n	71	56
RO (n, %)	56 (79)	21 (38)
DoR (mois)	34,1	14,8
OS (mois)	NE	25,1
Pts avec M+ cerveau mesurable RO intra-cérébrale (n,%)	9 8 (89)	13 5 (38)
Pré-traitement par ITK-ROS1 et présence de la mutation G2032R (n=17)		Taux de RO 59 %, DoR 7,6 mois, PFS 9,2 mois

1. *Drilon A, et al. N Engl J Med*

CBPNPC avancés avec translocation ROS





IC_{50} (nmol/L)	Crizotinib	Entrectinib	Lorlatinib	Repotrectinib	Cabozantinib	Ceritinib	Brigatinib	Taletrectinib	Alectinib
Parental	840.5	1,801.0	>3,000	1,218.0	>3,000	1,117.0	>3,000	>3,000	1,207.0
Nonmutant	5.4	2.7	0.7	2.0	2.8	16.4	9.4	2.6	995.4
G2032R	609.6	436.3	196.6	23.1	17.5	346.4	472.7	53.3	1,091.0
L2000V	37.1	25.9	2.5	10.1	7.6	124.9	78.9	29.8	985.0
L2086F	536.8	440.0	>3,000	587.9	3.6	226.9	159.3	1,265.0	672.5
S1986F/L2000V	159.4	36.1	2.4	7.2	5.1	86.9	62.5	20.3	1,080.0
S1986F/L2086F	469.7	344.2	>3,000	241.2	1.3	154.8	48.5	662.6	919.9
G2032R/L2086F	498.6	335.4	>3,000	248.9	5.0	573.9	450.9	744.2	1,254.0
S1986F/G2032R	594.4	718.5	990.6	65.1	70.1	614.7	717.0	105.4	1,137.0
S1986F/G2032R/L2086F	562.8	1,111.0	2,131.0	1,178.0	9.4	1,116.0	1,341.0	2,432.0	1,150.0

IC_{50} ≤ 50 nmol/L

50 nmol/L < IC_{50} <200 nmol/L

IC_{50} ≥ 200 nmol/L

1. Ou S, et al. J Thorac Oncol 2023; 2. Lin JJ, et al. Clin Cancer Res 2021

HER2 : CBPNPC non épidermoïde

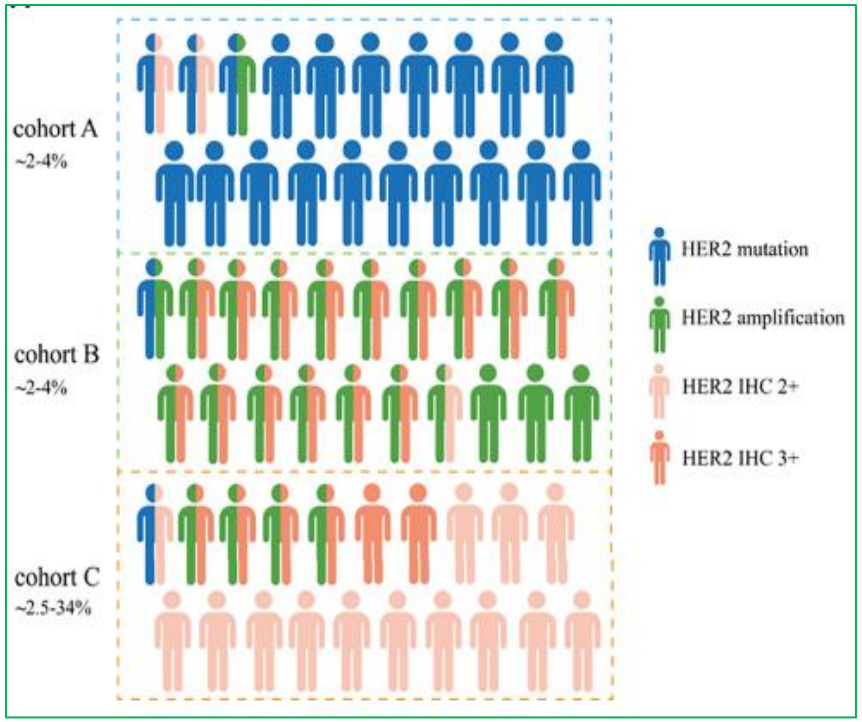
Amplification HER2

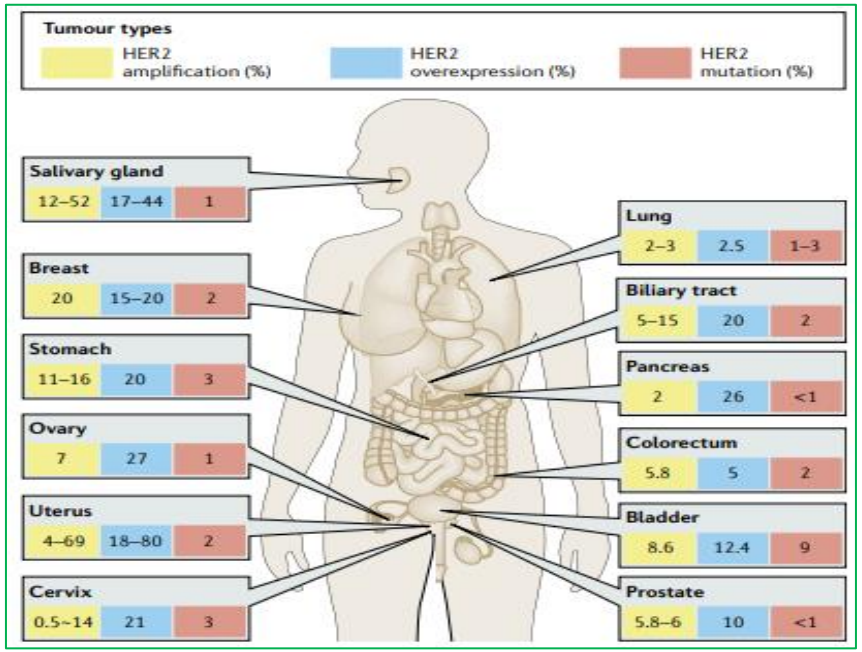
- Ratio HER2/CEP17 ≥ 2.0 (FISH)
- Clinique : homme, fumeur (pour les altérations *de novo*)
- Fréquence : 3 % *de novo* (10 % résistance ITK-EGFR)

Surexpression HER2 (protéine)

- Clinique : homme, fumeur (pour les altérations *de novo*)
- Fréquence : 2 - 20 %
- Critère de positivité (IHC)
  - ➢ score 2 + (marquage membranaire faible à modéré > 10 % des cellules tumorales)
  - ➢ Score 3 + (marquage membranaire intense > cellules tumorales)

Pas de corrélation entre surexpression et amplification
Amplification et mutation sont mutuellement exclusives





1. Yu X, et al. Front Oncol 2022 ; 2. Oh DY, et al. Nat Rev Clin Oncol 2019

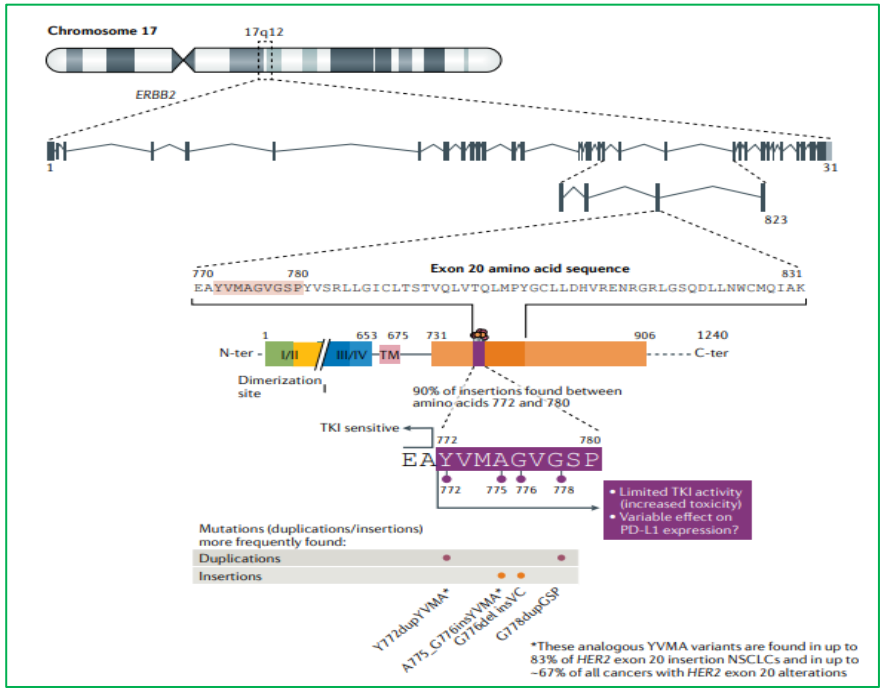
Mutations HER2 : CBPNPC non épidermoïde

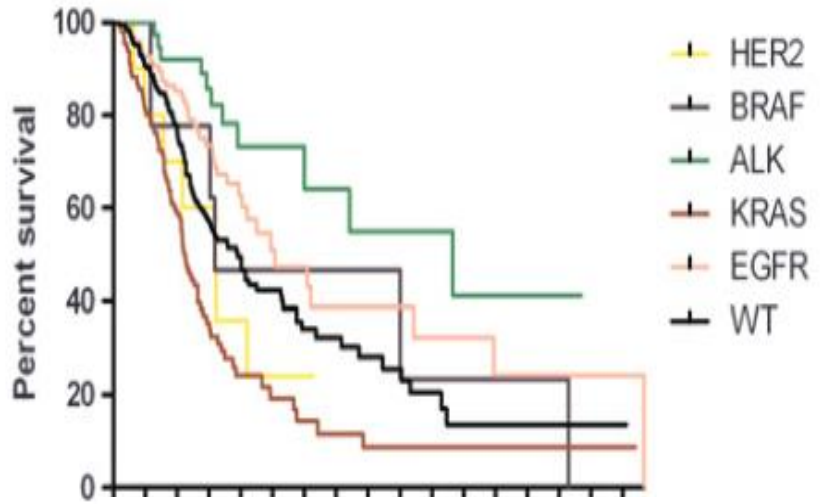
HER2

- Pas de ligand spécifique

Mutations HER2 (duplications ou insertions) (1)

- Clinique: femme, non-fumeur, adenocarcinome, métastases cérébrales
- Mutuellement exclusives (KRAS, BRAF, EGFR, ALK, etc…)
- Exons 772 – 780 (90 %)
- Dup/ins de 4 aa (codon 775): YVMA (more frequent)
- Fréquence : 2 – 4 %



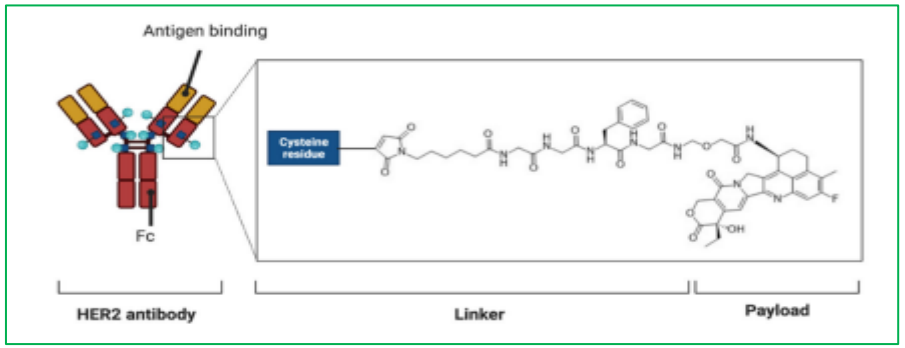


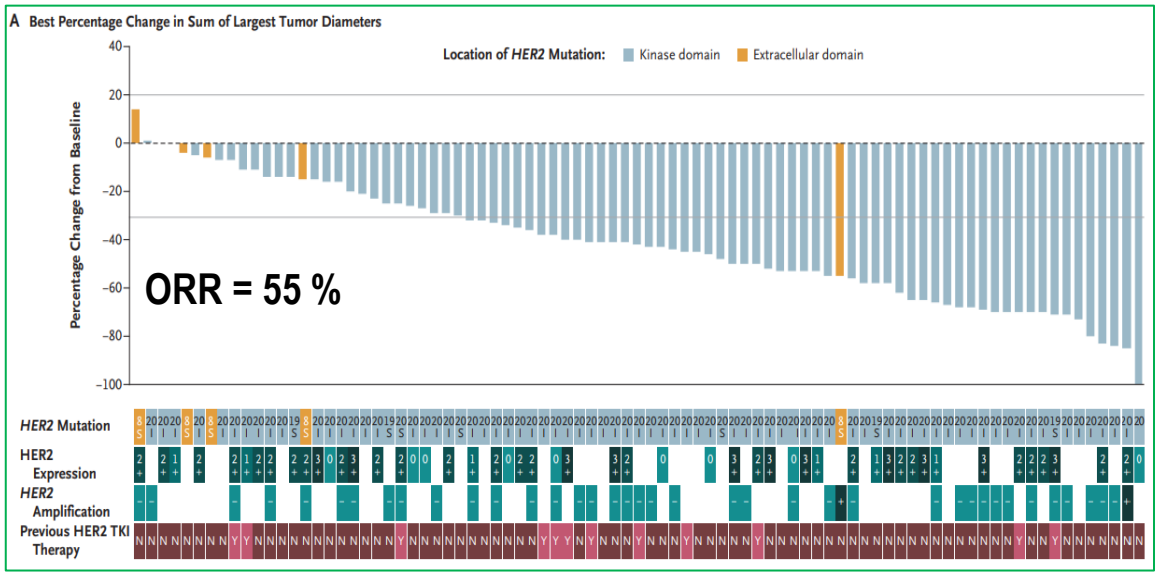
Cohorte de patients avec un CBPNPC non épidermoïde(2)

1. Arcilla ME, et al. Clin Cancer Res 2012 ; 2. Oh DY, et al. Nat Rev Clin Oncol 2019

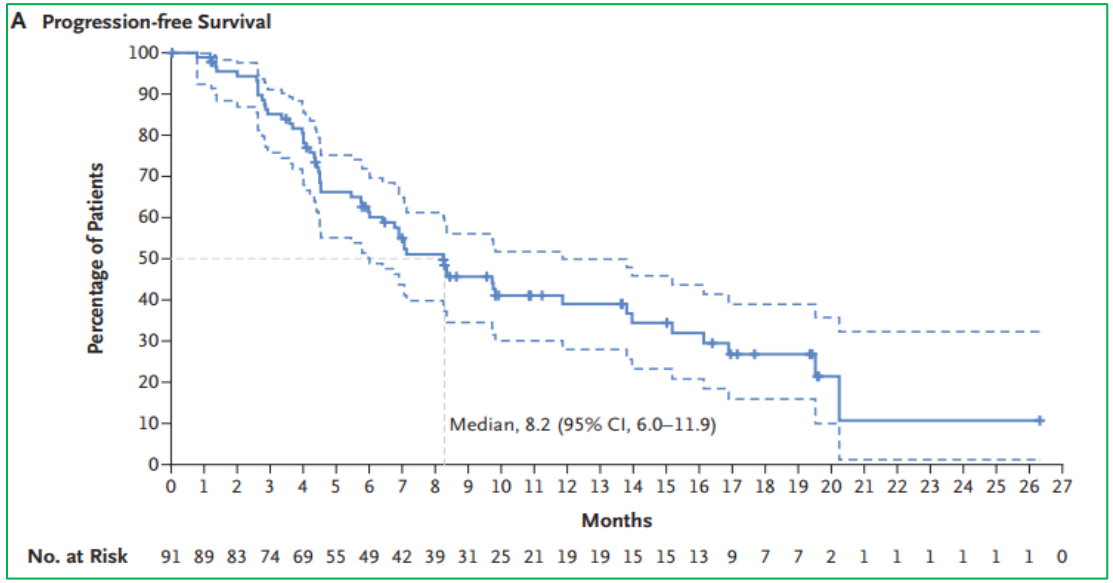
CBPNPC non épidermoïde avec mutation HER2 mutation: DESTINY-Lung01

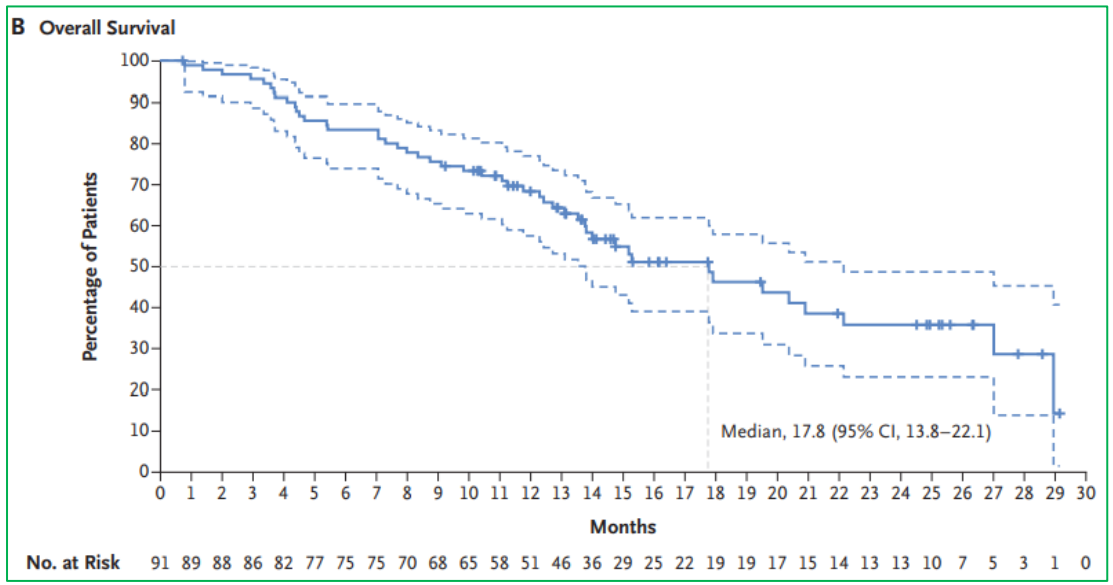
(après échec d'un traitement standard)





DoR: 9,3 mois





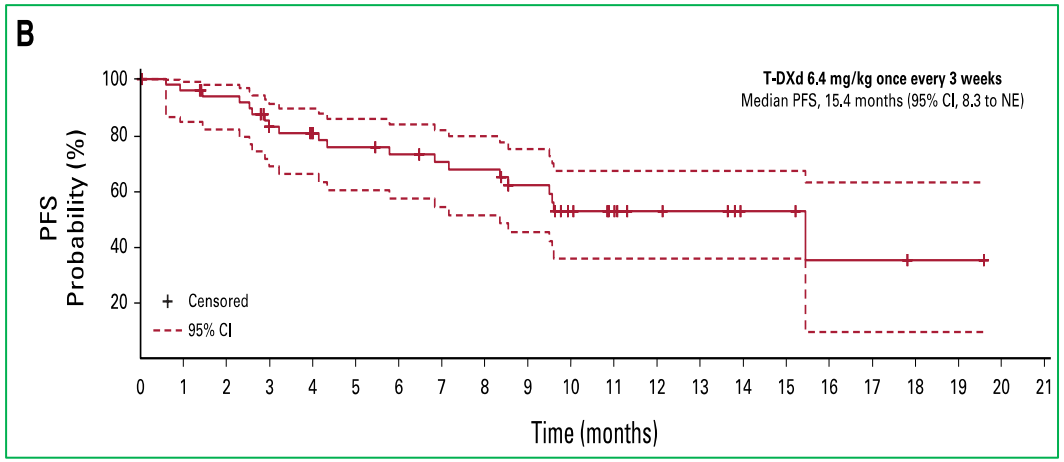
1. Li BT, et al. N Engl J Med 2021

CBPNPC non épidermoïde avec mutation HER2 mutation: DESTINY-Lung02

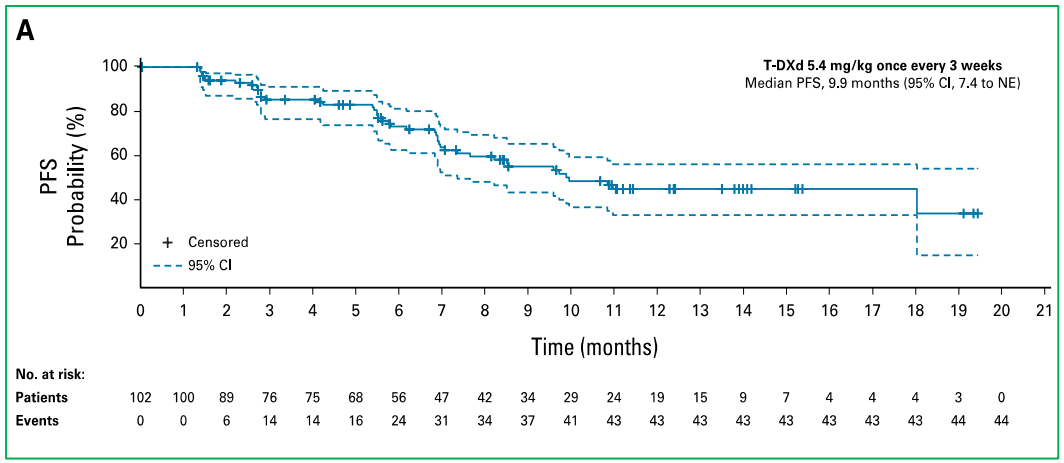
(après échec d'un traitement standard)

Traztuzumab-Deruxtecan	5,4 mg/kg J1 - J21 n=102	6,4 mg/kg J1 – J21 n=50
Age médian (an)	59,4 (31 – 84)	61,3 (28 – 86)
Femme (n, %)	65 (63,7 %)	34 (68 %)
Non-fumeurs (n, %)	55 (53,9)	29 (58)
Métastases cérébrales (n, %)	35 (34,3)	22 (44,0)
Lignes antérieures	2 (1 – 12)	2 (1 – 7)

Response Assessment by BICR	T-DXd 5.4 mg/kg Once Every 3 Weeks (n = 102)	T-DXd 6.4 mg/kg Once Every 3 Weeks (n = 50)
Confirmed ORR, No. (%)	50 (49.0)	28 (56.0)
95% CI	39.0 to 59.1	41.3 to 70.0
Best confirmed overall response, No. (%)		
CR	1 (1.0)	2 (4.0)
PR	49 (48.0)	26 (52.0)
SD	45 (44.1)	18 (36.0)
PD	4 (3.9)	2 (4.0)
Nonevaluable[a]	3 (2.9)	2 (4.0)
DCR, No. (%)	95 (93.1)	46 (92.0)
95% CI	86.4 to 97.2	80.8 to 97.8
DoR, months, median (95% CI)	16.8 (6.4 to NE)	NE (8.3 to NE)
TTIR, months, median (range)	1.8 (1.2-7.0)	1.6 (1.2-11.2)
Follow-up, months, median (range)	11.5 (1.1-20.6)	11.8 (0.6-21.0)



OS: NR (95%CI, 12.1 – NE)



OS: 19,5 months (95%CI, 13.6 – NE)

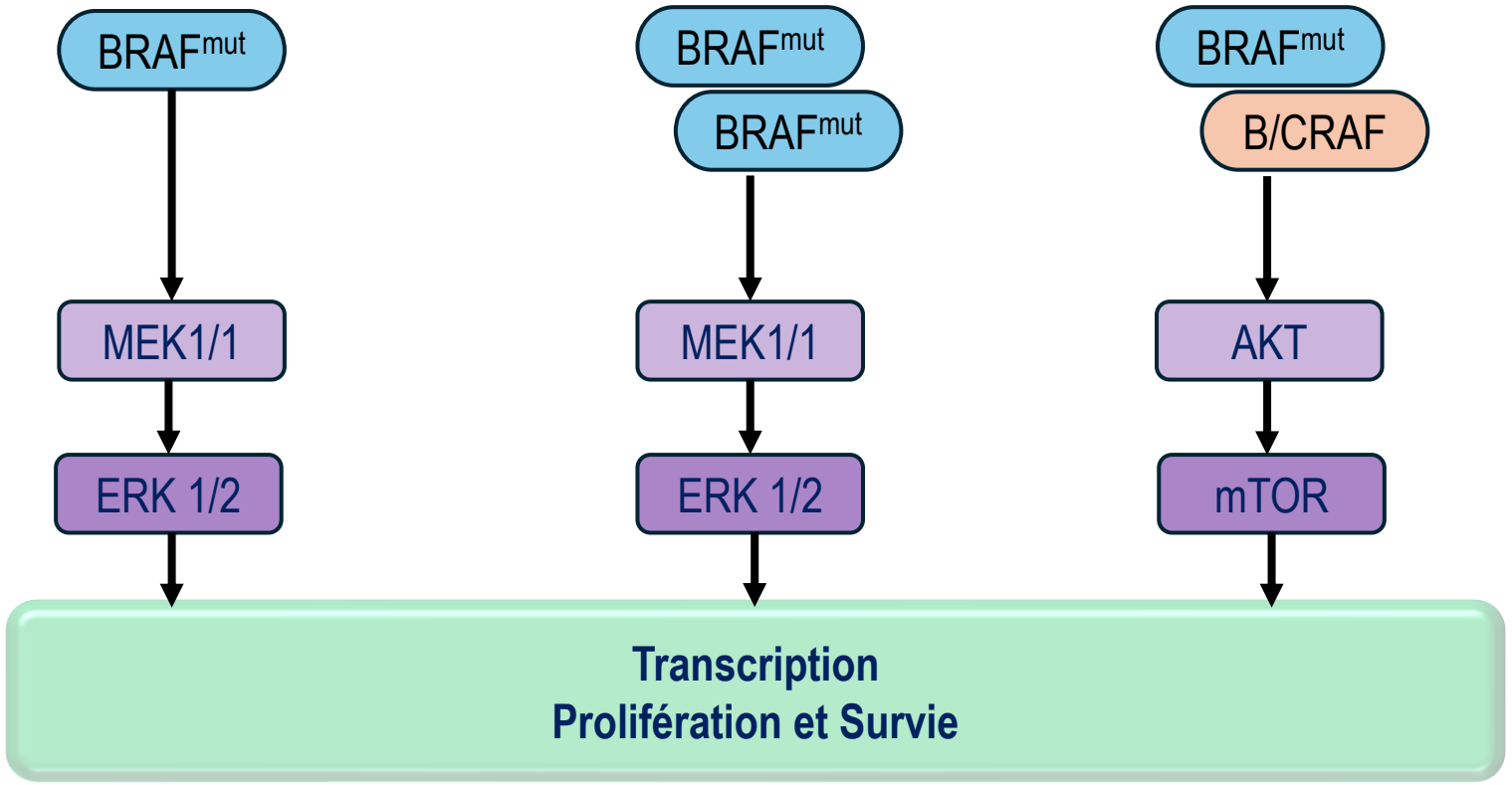
1. Goto K, et al. J Clin Oncol 2023

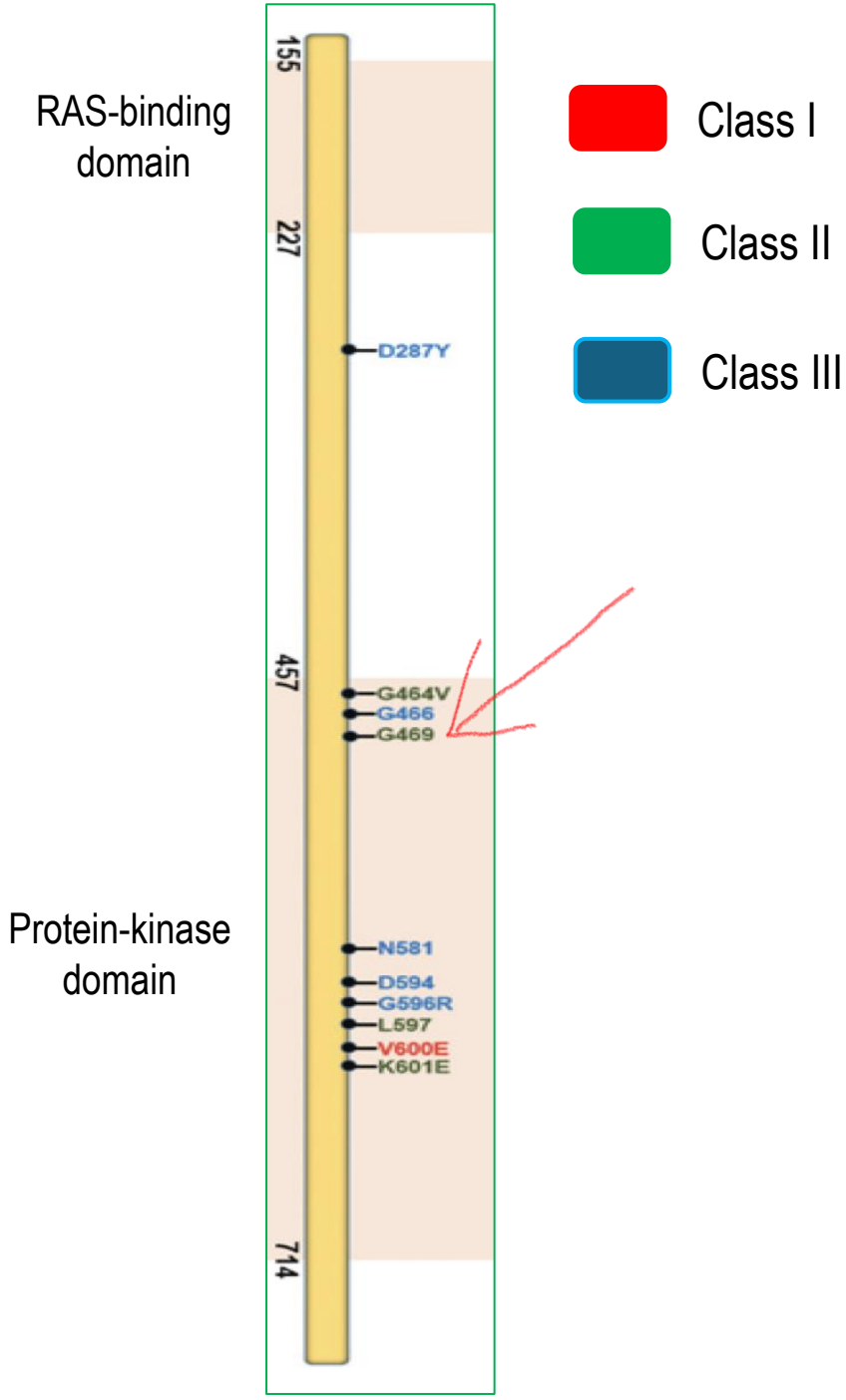
Mutations BRAF : classification

Classe I
- RAS independant
- Activation /s frome de monomère
- **V600 E**/K/D/R

Classe II
- RAS independant
- Activation /s forme de dimère
- **Non V600**

Classe III
- RAS dependant
- Activation /s frome de dimère
- Altération de l'activité kinase



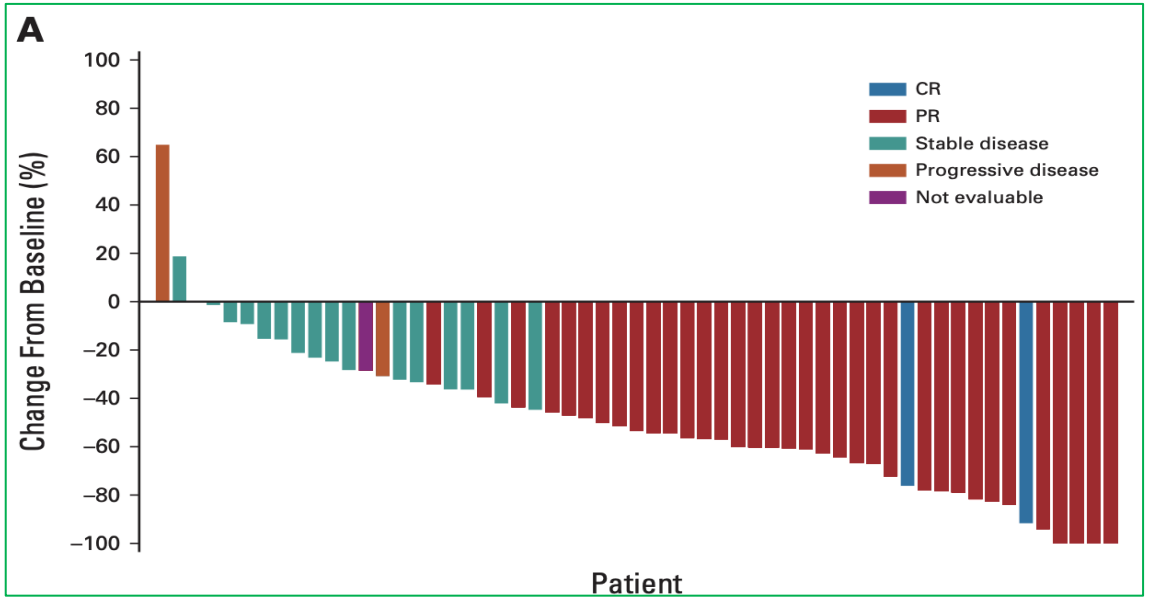


1. Dagogo-Jack I, et al. Clin Cancer Res 2019, 2. Puri M, et al. Front Oncol 2023

Phase 2 : Encorafenib + Binimetinib

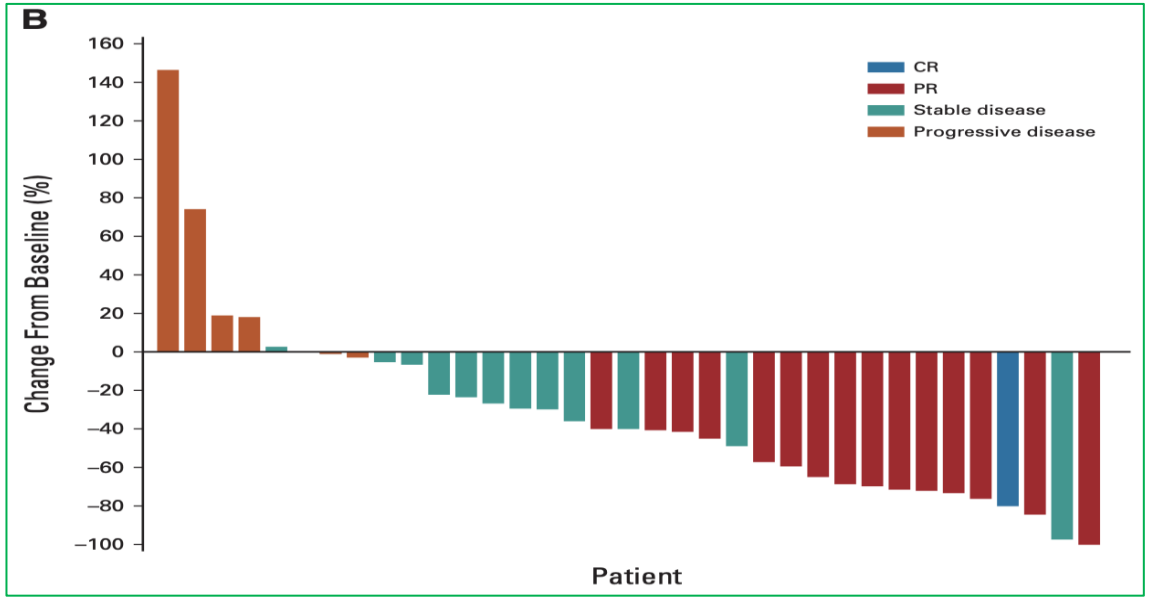
CBPNPC BRAFV600

Non pré-traités (n=59)



ORR (%) 75 ; DCR (%) 83

Pré-traités (n=39)



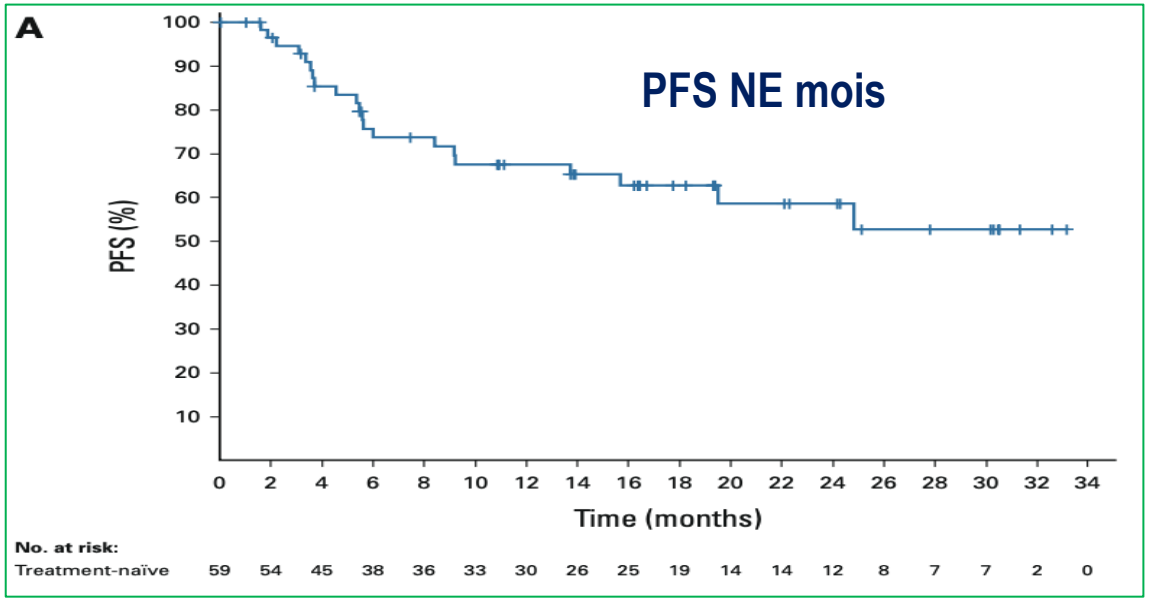
ORR (%) 46 ; DCR (%) 79

Riely GJ, et al. J Clin Oncol 2023

Phase 2 : Encorafenib + Binimetinib

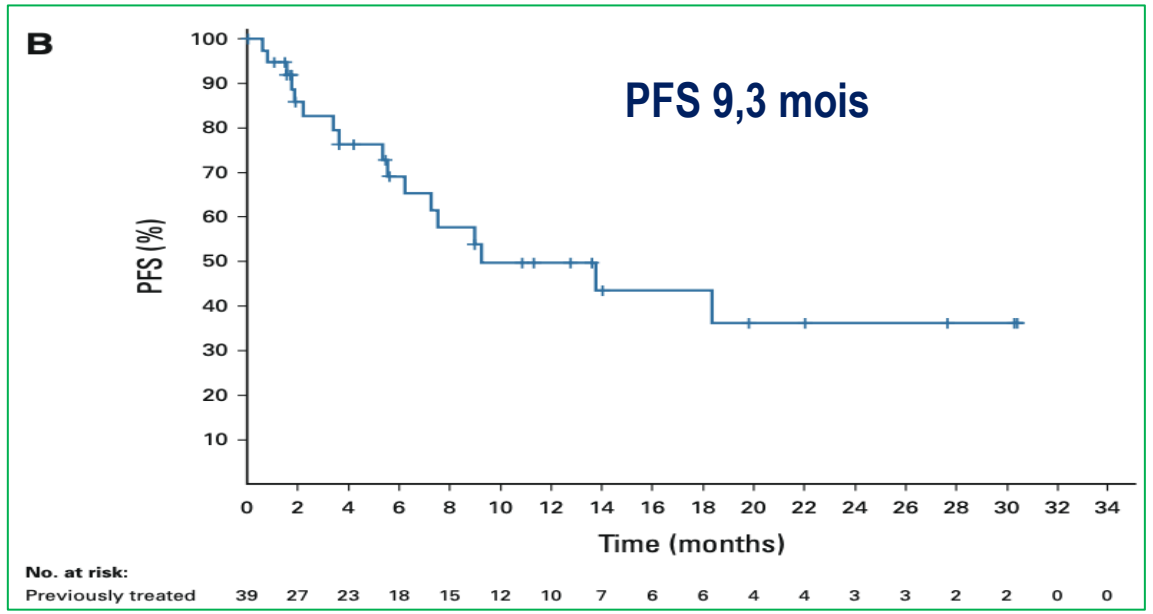
CBPNPC BRAFV600

Non pré-traités (n=59)



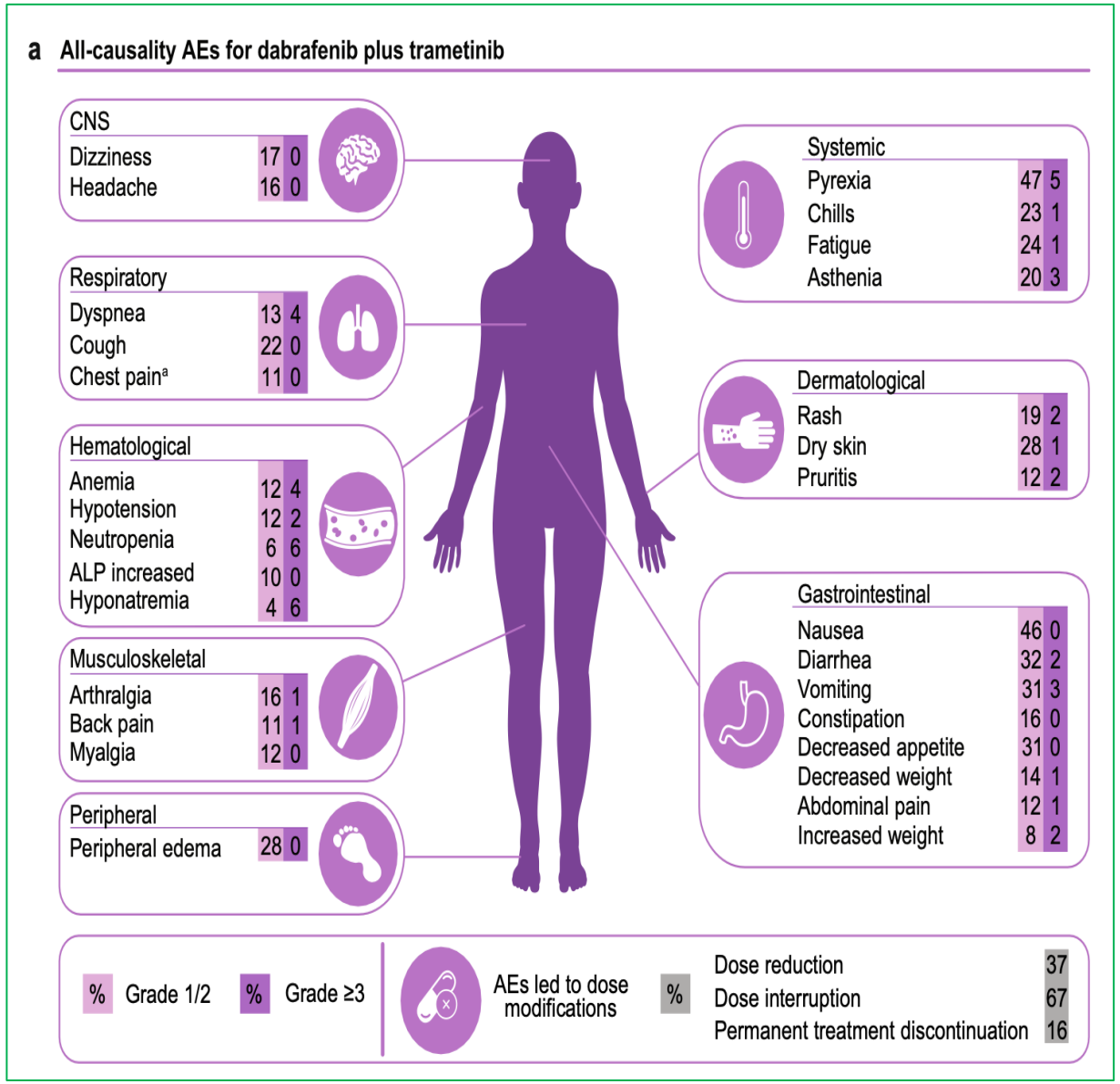
DoR (mois) NE

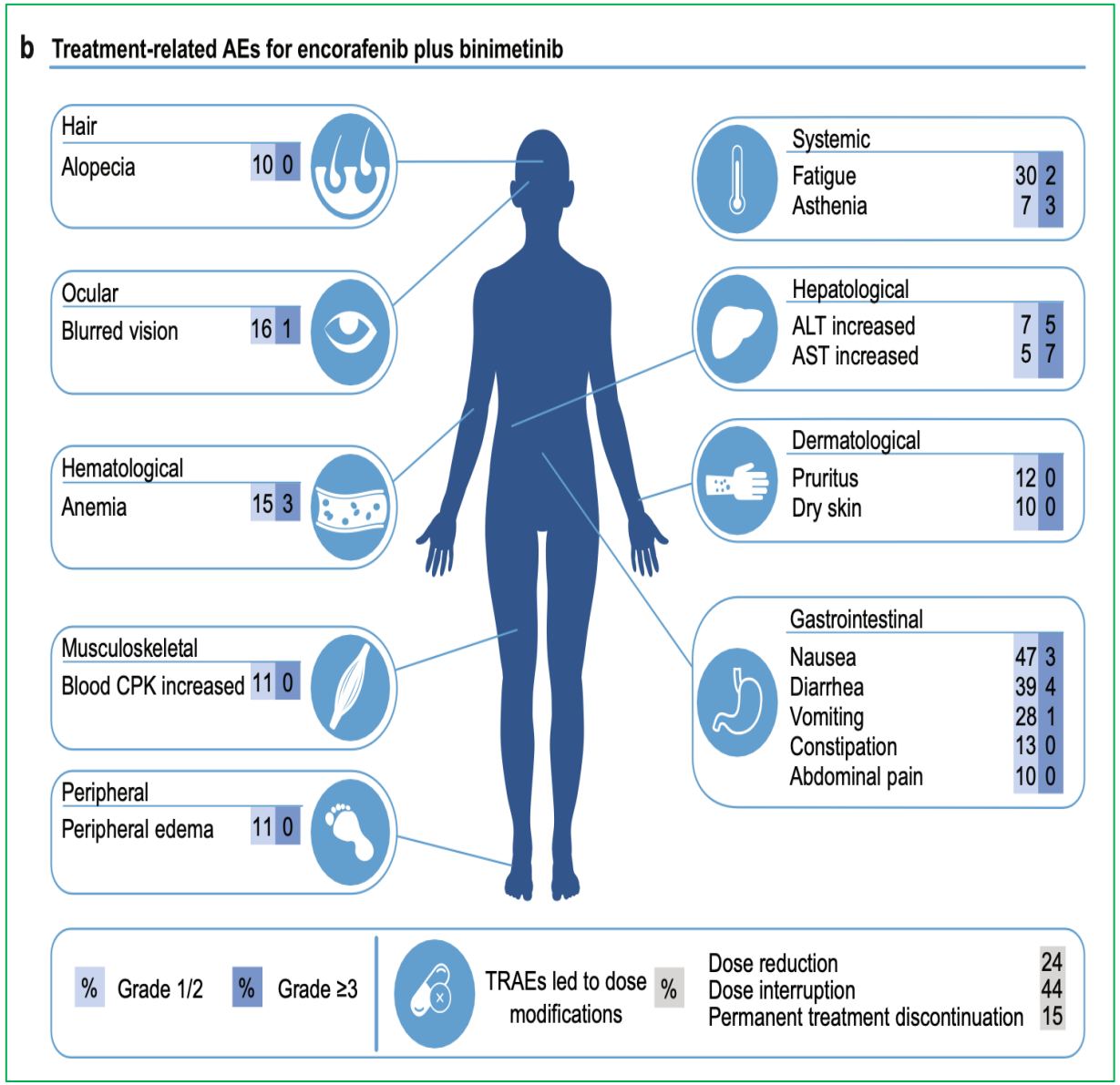
Pré-traités (n=39)



DoR (mois) 16,7

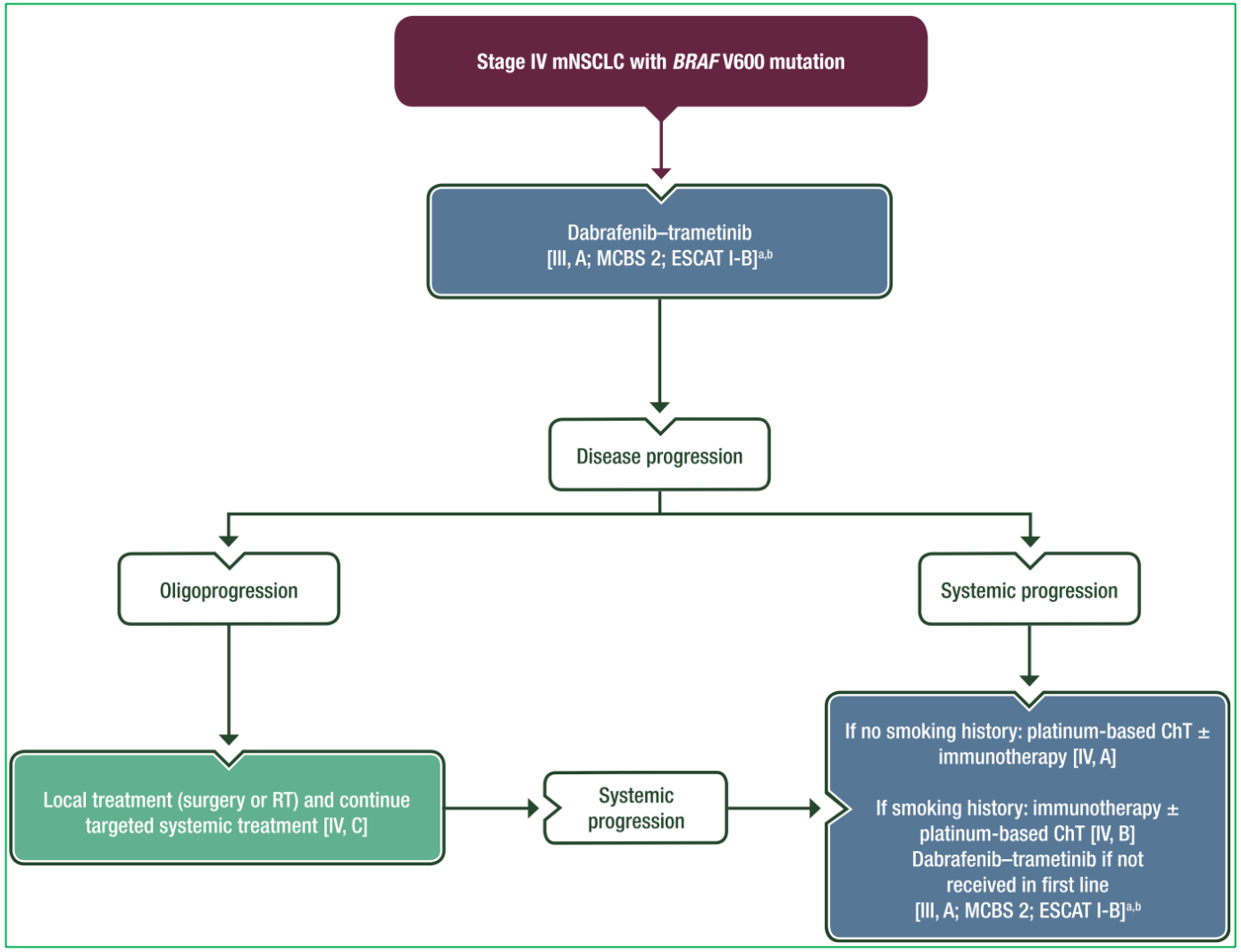
Riely GJ, et al. J Clin Oncol 2023





Planchard D, et al. npj precision oncology 2024

ESMO Guidelines



BRAF - MEK inhibition using dabrafenib – trametinib is recommended [III, A; ESMO-MCBS v1.1 score: 2; ESCAT: I-B].

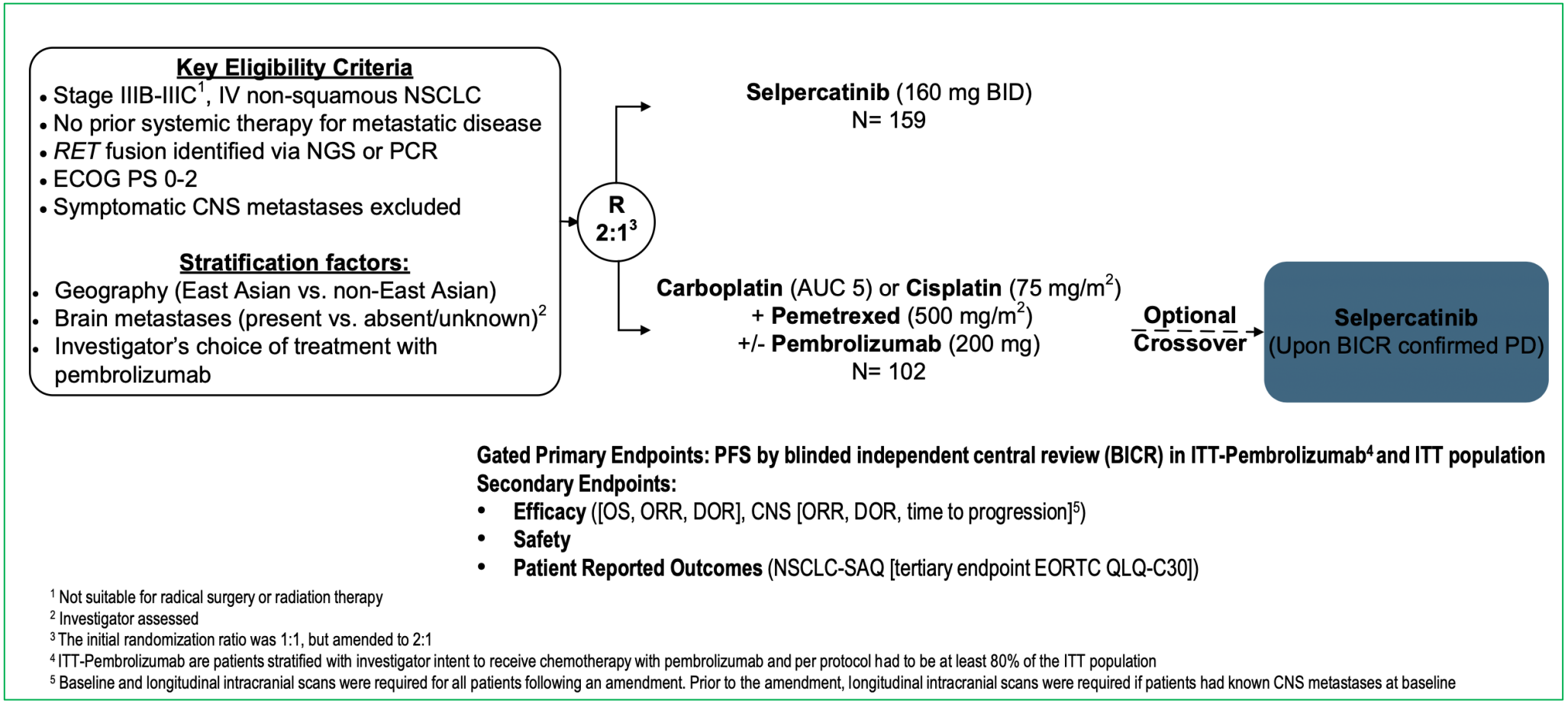
If patients have received BRAF - MEK inhibition in the first-line setting, they may be offered platinum-based ChT with or without immunotherapy in the second-line setting, **if they do not have a smoking history** [IV, A].

For patients with a smoking history, immunotherapy with or without ChT should be considered as per the ESMO CPG on non-oncogene-addicted mNSCLC [IV, B]

Hendricks LE, et al. Ann Oncol 2023

LIBRETTO-431

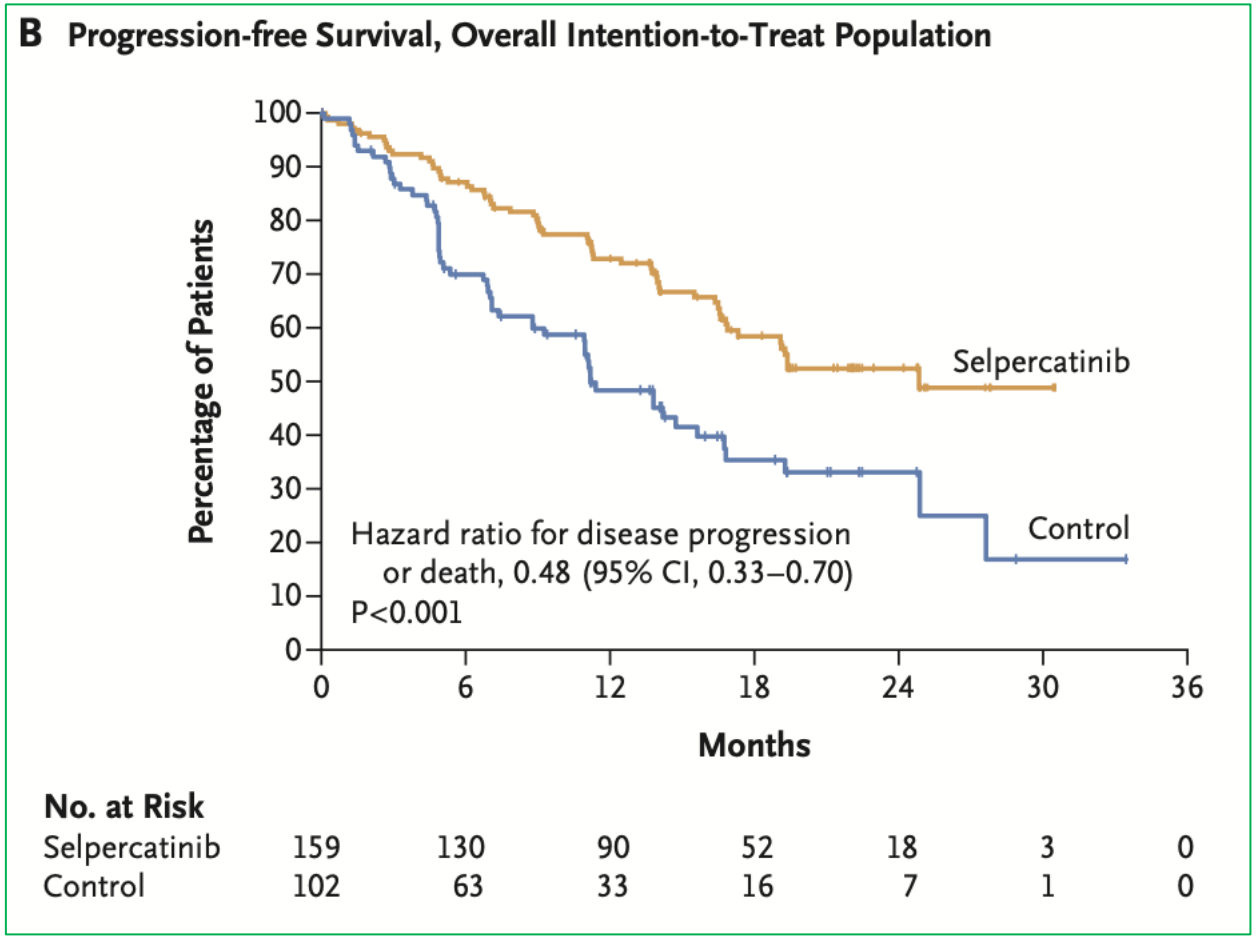
Etude randomisée de phase 3



1. Zhou C, et al. N Engl J Med; 2. Loong HH, ESMO 2023

LIBRETTO-431

Etude randomisée de phase 3



	Selpercatinib	Chimiothérapie
n	159	102
PFS (mois)	24.8	11.2
RO (%)	84	63
- CR	12 (8)	5 (5)
- PR	121 (76)	59 (58)
- SD	17 (11)	26 (25)
- PD	2 (1)	7(7)
- NE	7 (4)	5 (5)
DoR (mois)	24.2	12.0

1. Zhou C, et al. N Engl J Med 2023

LIBRETTO-431

Etude randomisée de phase 3

Table 1. Common side effects occurring with selpercatinib and pralsetinib

	Selpercatinib	Pralsetinib
Most common adverse events	• fatigue • hypertension • constipation • diarrhea • nausea • edema • dry mouth • abdominal pain • rash • headache	• fatigue • hypertension • constipation • diarrhea • musculoskeletal pain
Most common grade 3 or 4 laboratory abnormalities	• decreased lymphocytes • increased ALT • increased AST • decreased sodium • decreased calcium	• decreased lymphocytes • decreased neutrophils • decreased hemoglobin • increased ALT • increased AST • decreased sodium • decreased phosphate • decreased calcium • decreased platelets • increased alkaline phosphatase

Table 3. Adverse Events That Occurred during Treatment (Safety Population).*

Event	Selpercatinib (N=158)		Control (N=98)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Any event	158 (100)	111 (70)	97 (99)	56 (57)
AST increase	97 (61)	20 (13)	39 (40)	1 (1)
ALT increase	95 (60)	35 (22)	39 (40)	3 (3)
Hypertension	76 (48)	32 (20)	7 (7)	3 (3)
Diarrhea	70 (44)	2 (1)	24 (24)	2 (2)
Edema	65 (41)	4 (3)	27 (28)	0
Dry mouth	62 (39)	0	6 (6)	0
Blood bilirubin increase	59 (37)	2 (1)	1 (1)	0
Rash	52 (33)	3 (2)	29 (30)	1 (1)
Fatigue	51 (32)	5 (3)	49 (50)	5 (5)
Thrombocytopenia	42 (27)	5 (3)	28 (29)	7 (7)
Abdominal pain	40 (25)	1 (1)	19 (19)	2 (2)
Leukopenia	40 (25)	2 (1)	32 (33)	7 (7)
Blood creatinine increase	39 (25)	2 (1)	17 (17)	1 (1)
Neutropenia	36 (23)	3 (2)	44 (45)	27 (28)
Constipation	34 (22)	0	39 (40)	1 (1)
QT prolongation on ECG	32 (20)	14 (9)	1 (1)	0
Decreased appetite	27 (17)	0	33 (34)	2 (2)
Pyrexia	21 (13)	1 (1)	23 (23)	0
Nausea	20 (13)	0	43 (44)	1 (1)
Vomiting	20 (13)	0	23 (23)	1 (1)
Anemia	18 (11)	2 (1)	58 (59)	10 (10)
Pruritus	16 (10)	0	22 (22)	0

1. Nardo M, et al. Cell Reports Med 2023 ; 2. Zhou C, et al. N Engl J Med 2023

NRG

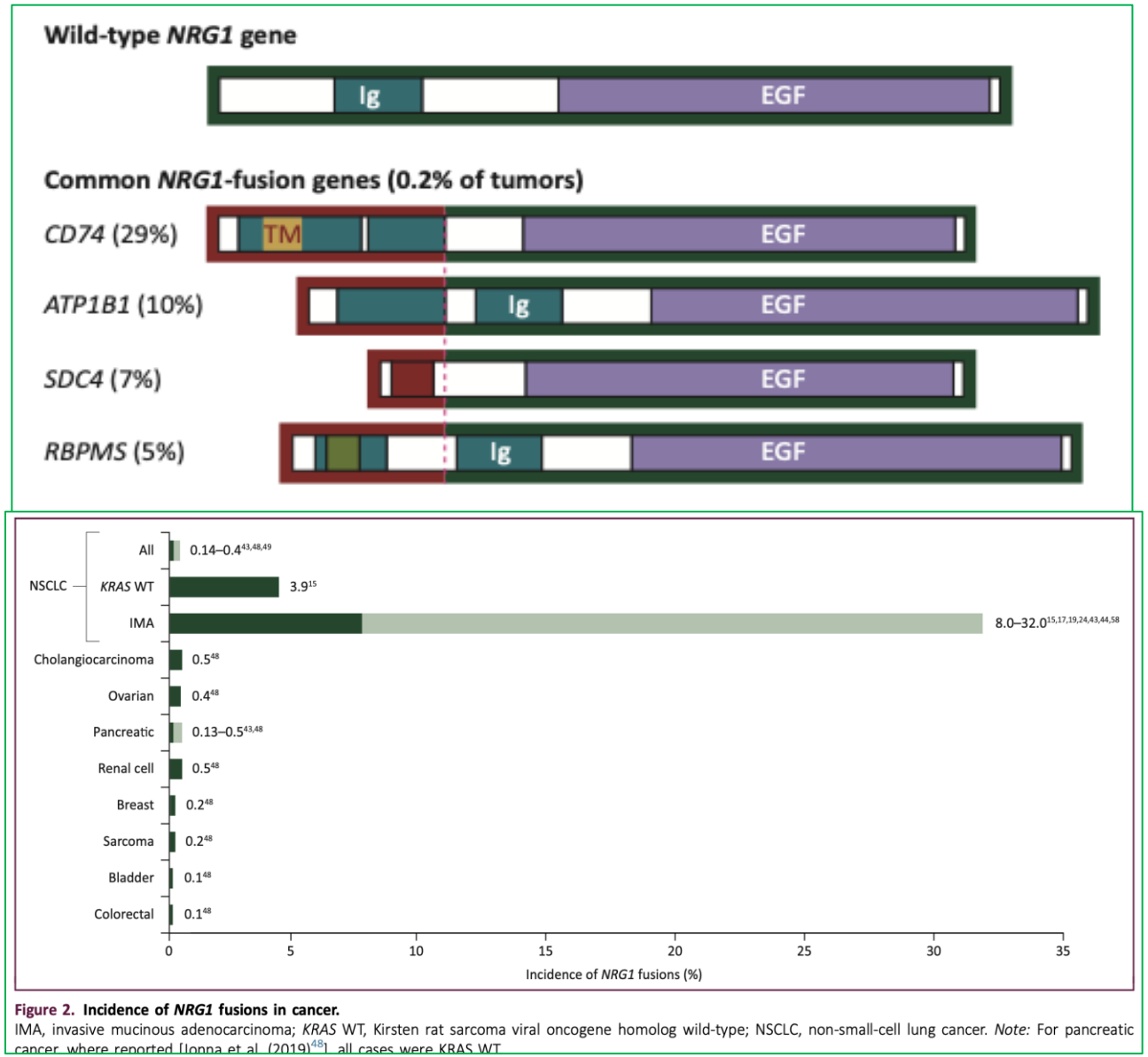
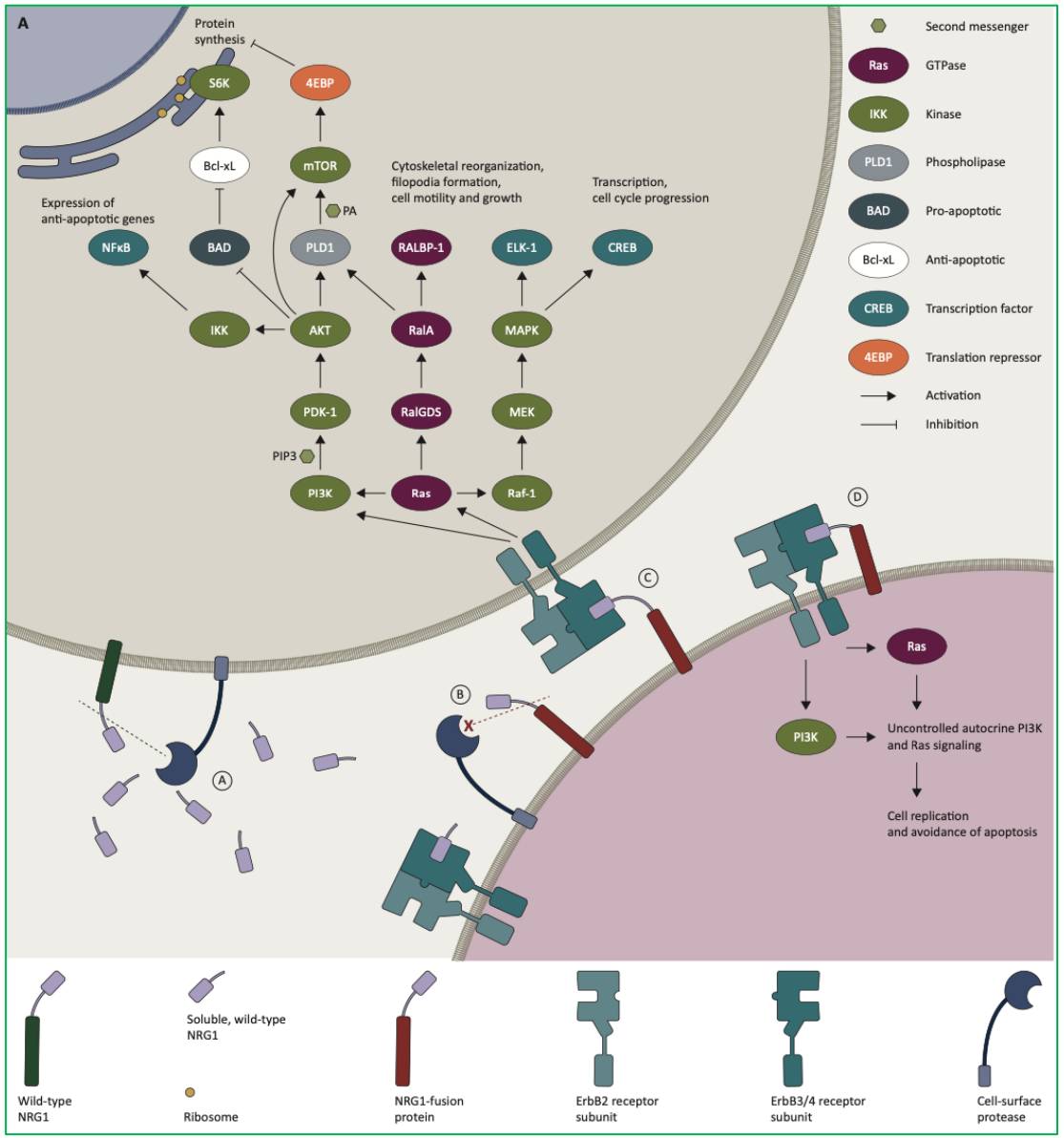


Figure 2. Incidence of *NRG1* fusions in cancer.
IMA, invasive mucinous adenocarcinoma; *KRAS* WT, Kirsten rat sarcoma viral oncogene homolog wild-type; NSCLC, non-small-cell lung cancer. *Note:* For pancreatic cancer, where reported [Jonna et al. (2019)[48]], all cases were KRAS WT.



1. Laskin J, et al. Ann Oncol 2020

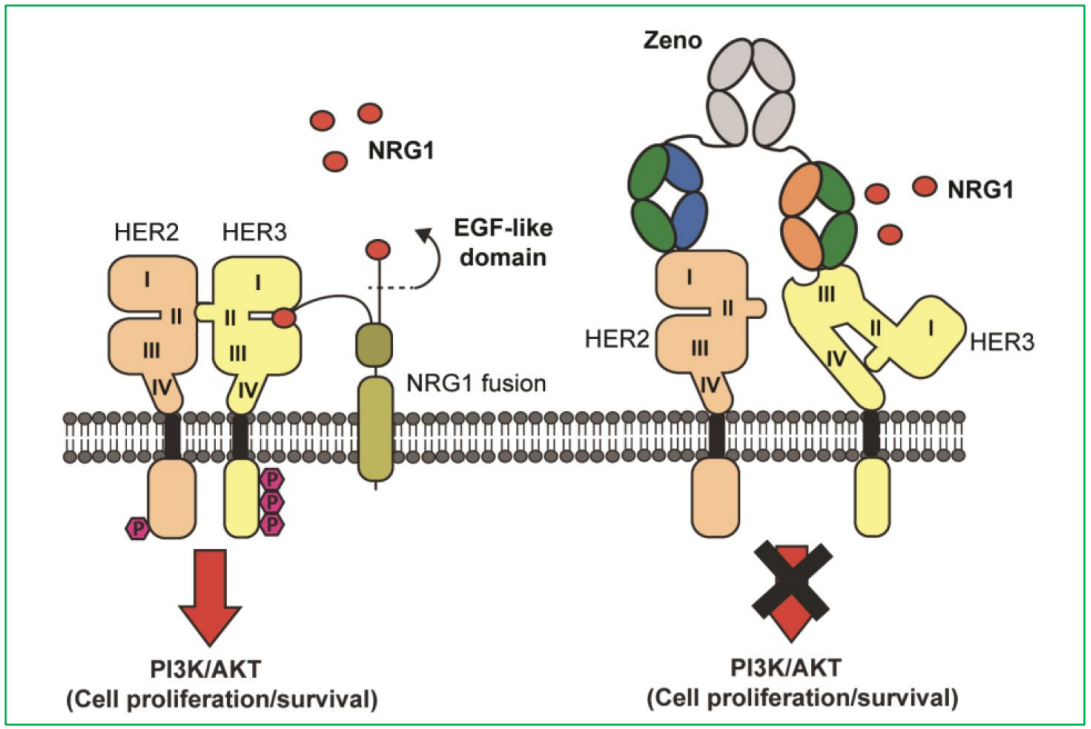
Afatinib, cas cliniques, CBPNPC – fusion NRG

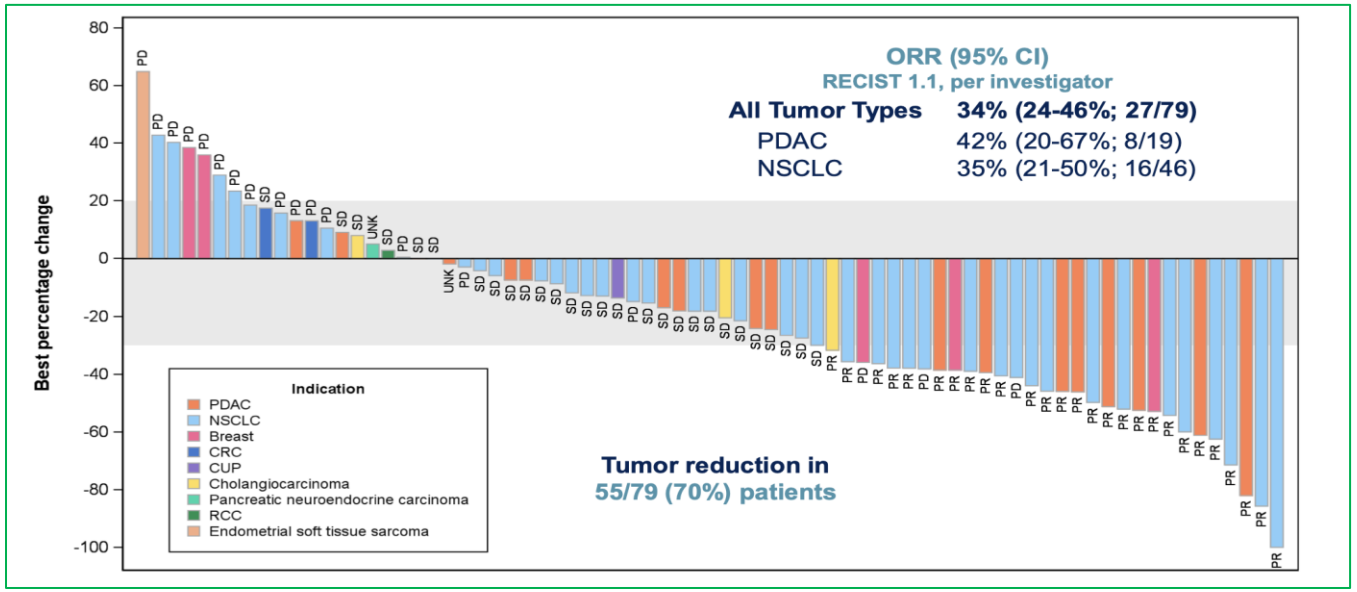
Etudes	CBPNPC	NRG1 fusion (partnaire)	RO	DoR (mois)
Gay ND [1]	Adénocarcinome	SLC3A2	PR	12
	IMA	CD74	PR	10
Jones MR [2]	Adénocarcinome	SDC4	PR	12
Cheema PK [3]	IMA	CD74	PR	6.5
Drilon A [4]	IMA	CD74	SD	3
	IMA	CD74	PD	-
	IMA	SDC4	PD	-

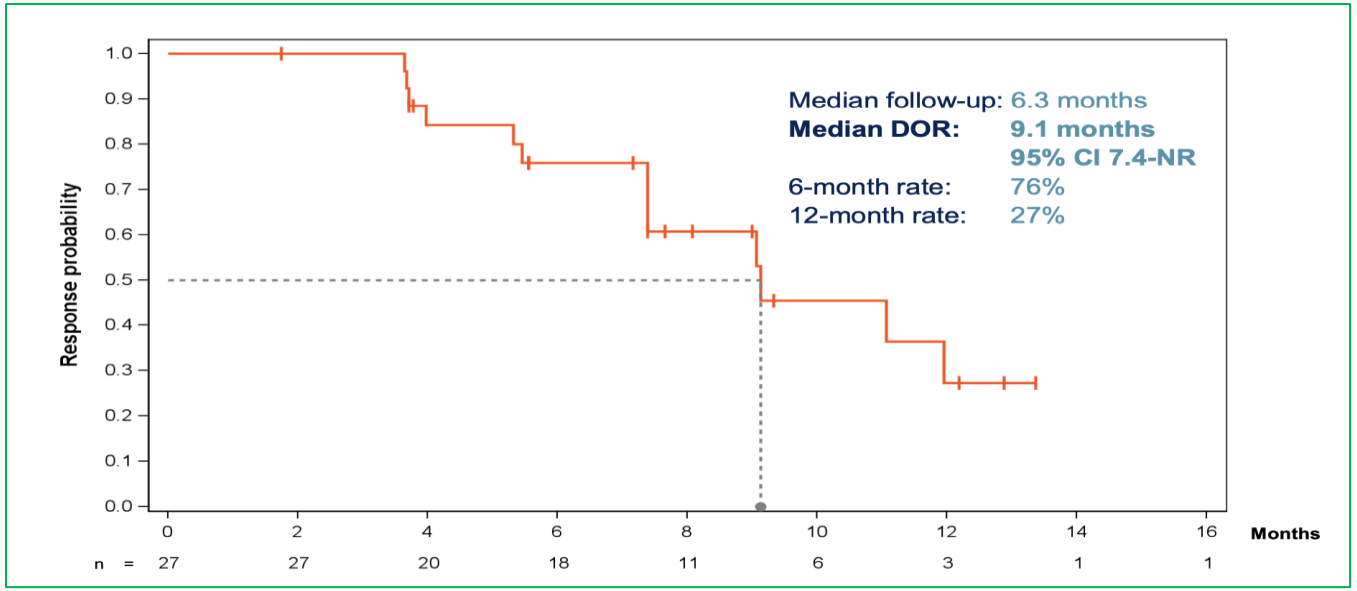
IMA : Invasive Mucinous Adenocarcinoma

1. Gay ND, et al. J Thorac Onco 2017; 2. Jones MR, et al. Ann Oncol 2017 ; 3. Cheema PK, et al. J Thorac Oncol 2017; 4. Drilon a, et al. Cancer Discov 2018; 5. Jones MR, et al. Clin Cancer Res 2019

Fusion NRG – Zenocutuzumab (anti-HER2/HER3)

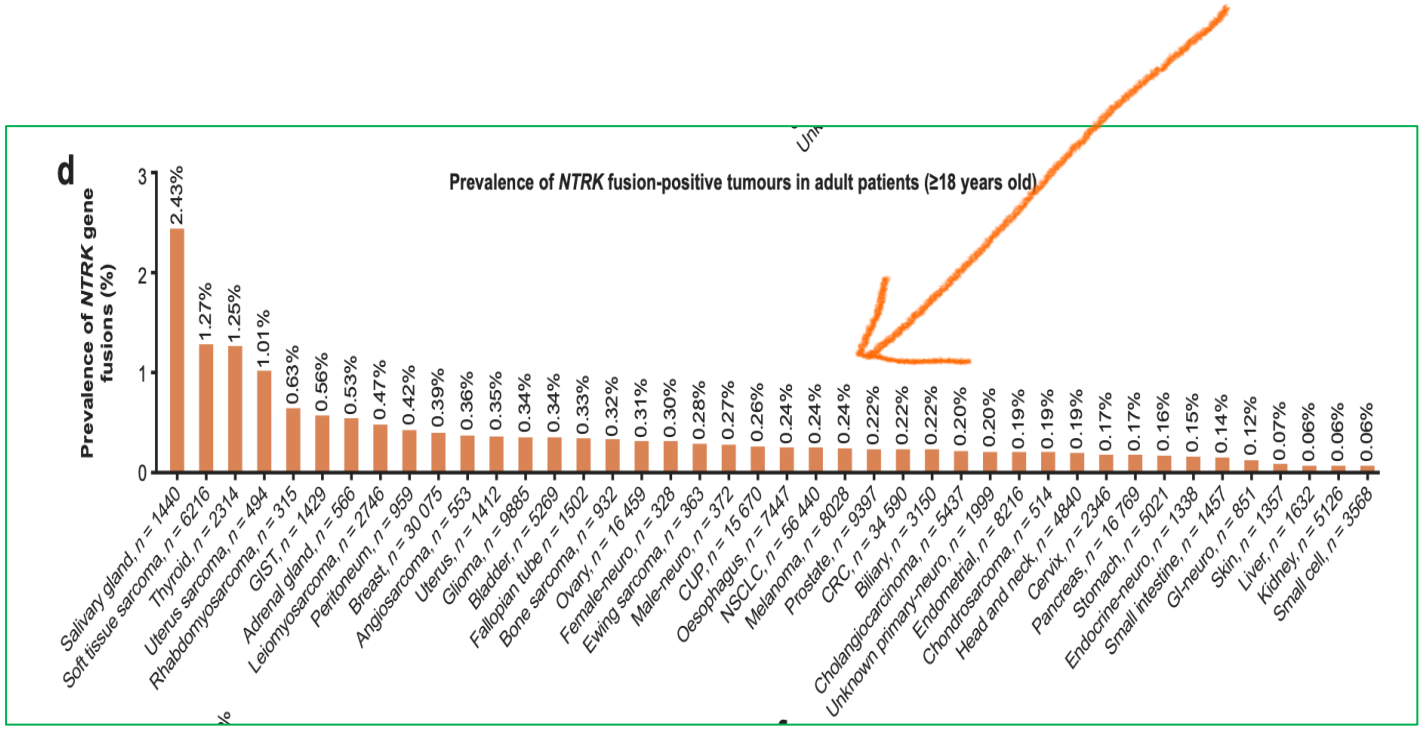


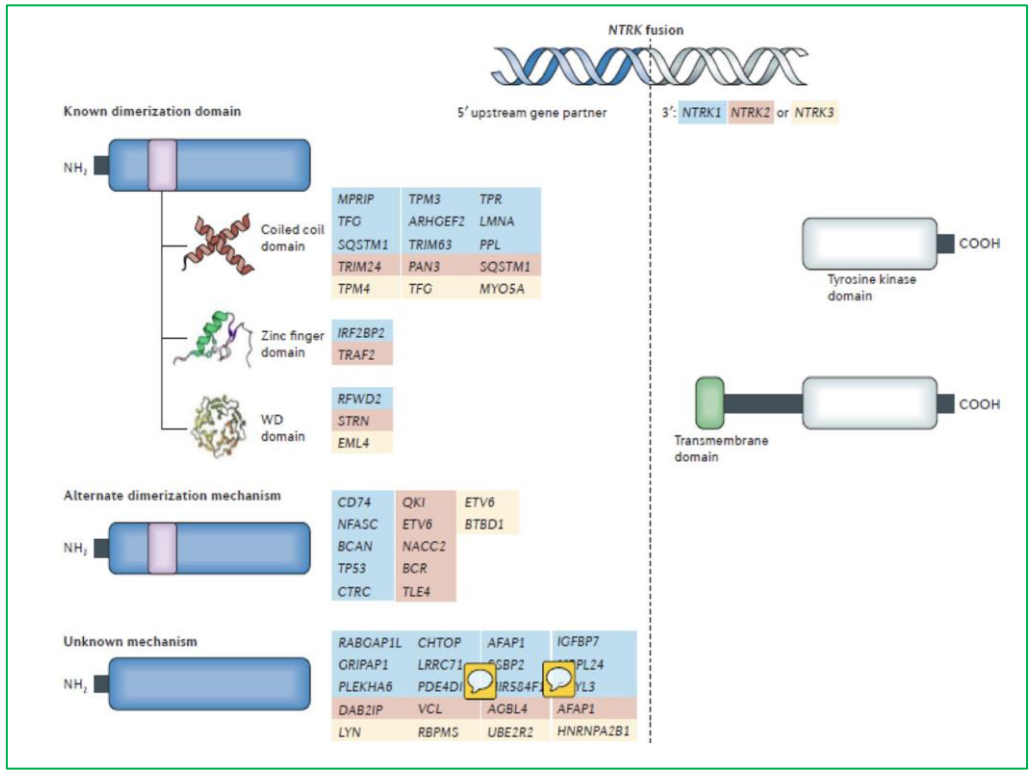




1. Gerlach J, et al. AACR 2021 ; 2. Schram A, et al. ASCO 2022

TRK fusion





1. Westphalen CB, et al. npj Prec Oncol 2021; 2. Cocco E, et al. Nat Rev Clin Oncol 2018

TRK fusion

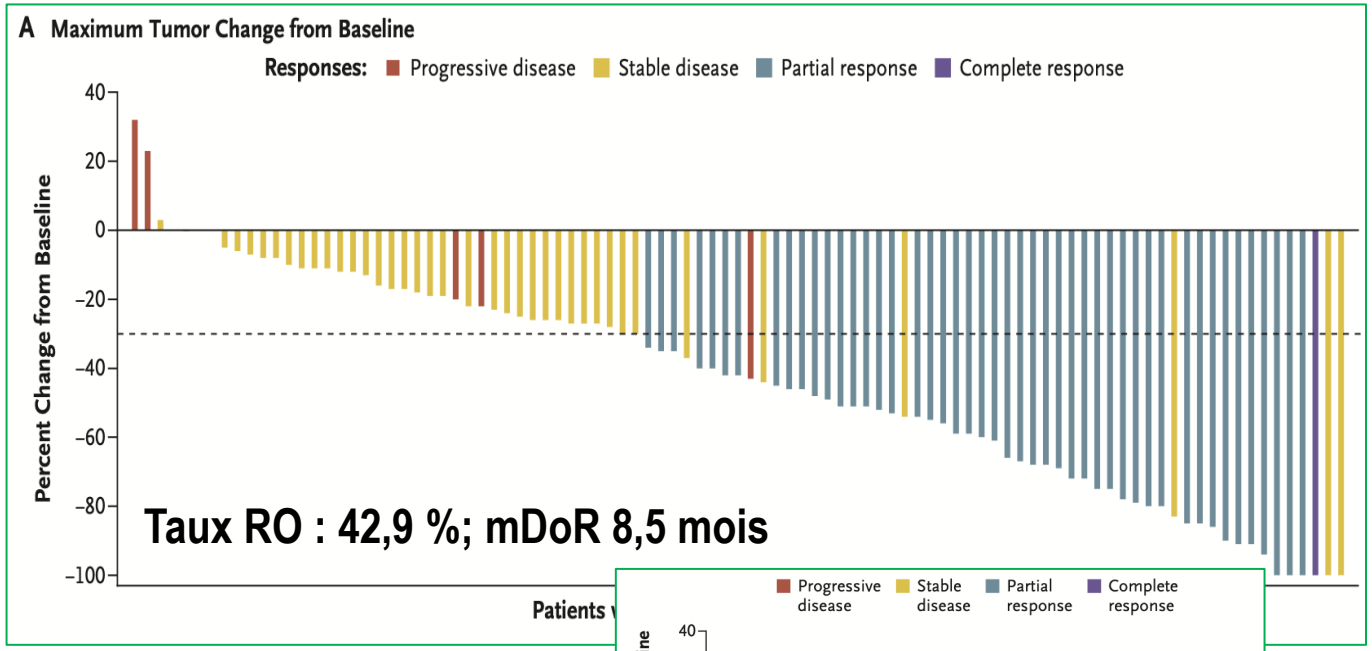
Efficacy of first-generation TRK inhibitors in patients with TRK fusion lung cancer.

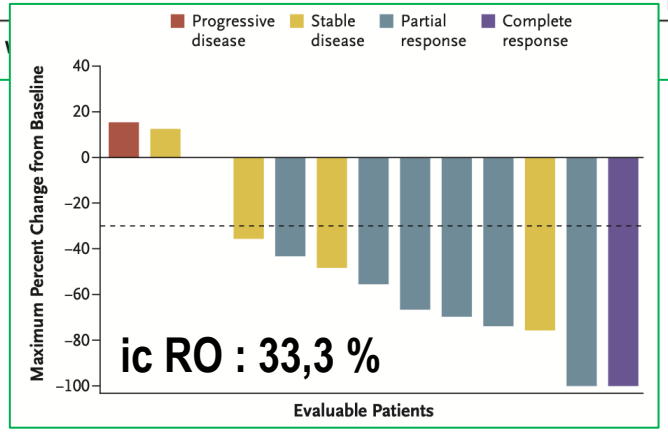
	Larotrectinib[†] N = 30 [62]	Entrectinib[‡] N = 31 [64]
ORR, % (95% CI)		
All patients	74 (54–89)	64.5 (45.4–80.8)
Patients with known baseline CNS metastases	Not reported	60.0 (32.3–83.7)
DoR		
Median, months (95% CI)	33.9 (9.5–NE)	27.1 (14.8–29.4)
Median follow-up, months	22.9	Not reported
PFS		
Median, months (95% CI)	33.0 (11.3–NE)	20.8 (13.8–30.4)
Median follow-up, months	24.7	Not reported
OS		
Median, months (95% CI)	39.3 (17.2–NE)	NE
Median follow-up, months	23.1	Not reported

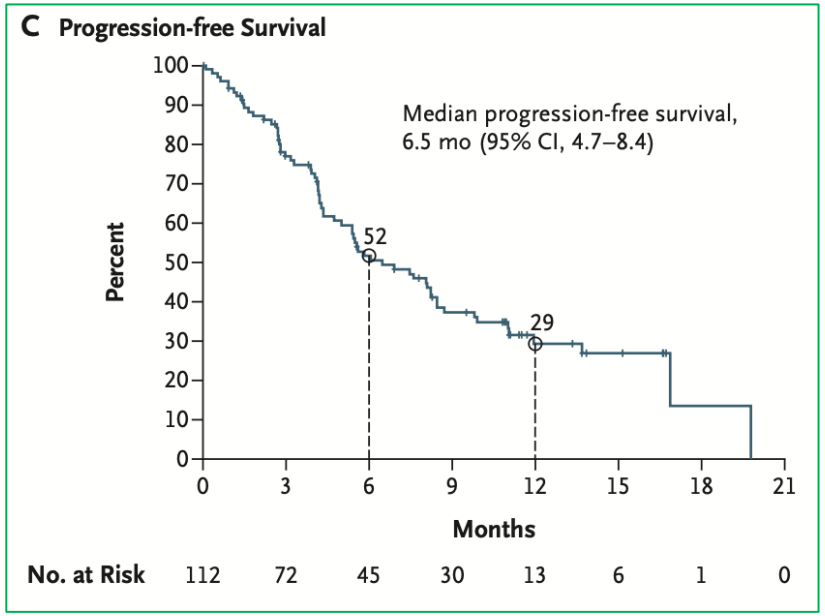
1. Repetto M, et al. Lung Cancer 2024

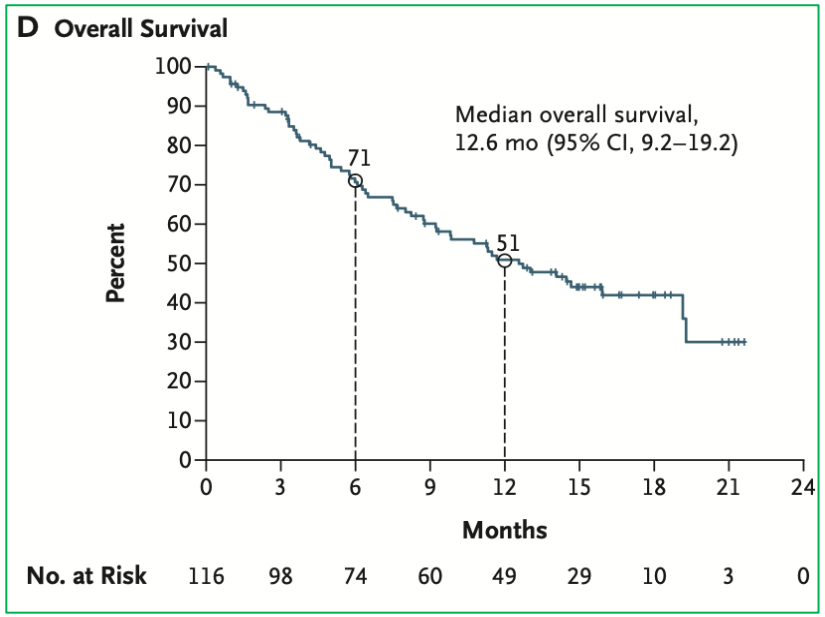
KRYSTAL-1 (Adagrasib) et mutation KRASG12C

En attendant KRYSTAL-12





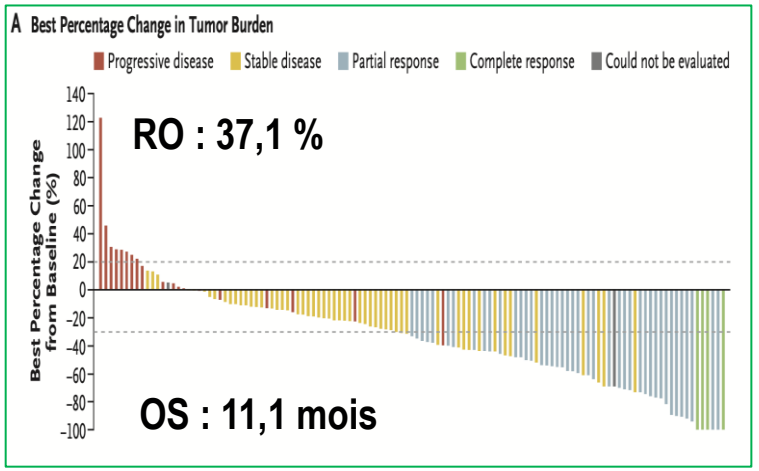


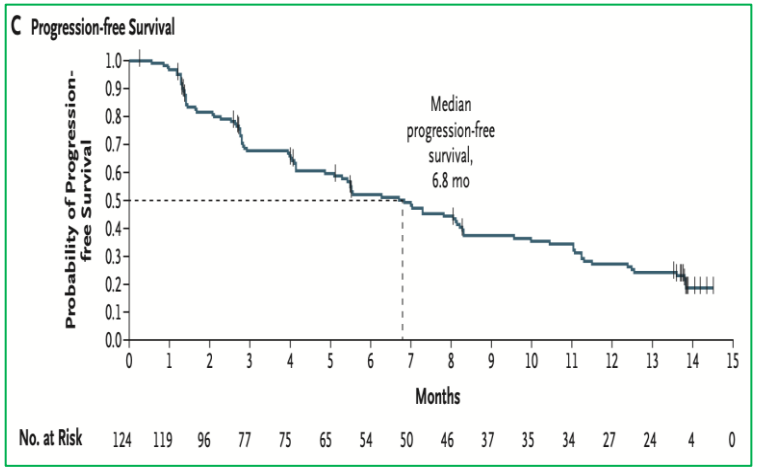


1. Janne PA, et al. N Engl J Med 2022

KRAS G12C et CBPNPC

CodeBreaK 100[1]

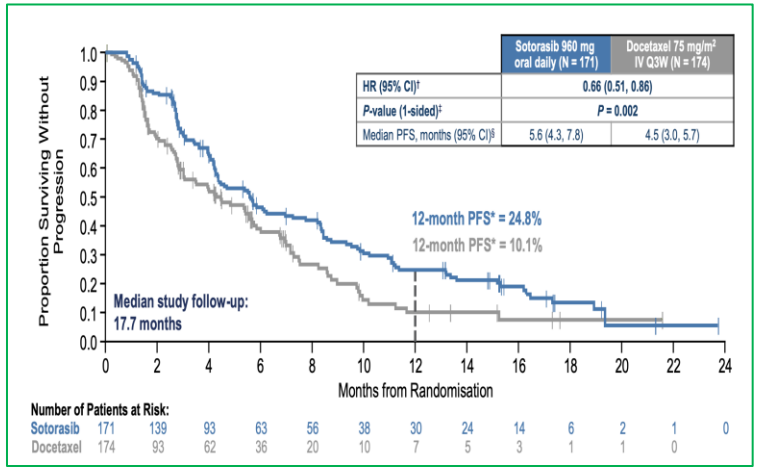




OS : 12,5 mois

CodeBreaK 200[2]

	Sotorasib	Doccetaxel
RO (%)	28,1	13,3
mDoR	8,6	6,8
OS (mois)	10,6	11,3
OS (HRIC95%)	1,01 (0,77 – 1,33)	
KRASG12Ci après prog.	4 %	34 %



KRYSTAL-1[3]

n=116	Adagrasib
RO (%)	42,9
mDoR	8,5
PFS (mois)	6,5
OS (HRIC95%)	12,6

Glicerasib[4]

n=117	Glicerasib
RO (%)	47,9
mDoR	NR
PFS (mois)	8,2
OS (HRIC95%)	13,6

1. Skoulidis F, et al. N Engl J Med 2021. Yu HA, et al. J Clin Oncol 2023; 2. Jonhson ML, et al. ESMO 2022; 3. Janne PA, et al. N Engl J Med 2022; 4. Shi Y, et al. ASCO 2024

Utilisation actuelle des thérapeutiques ciblées en France

	Etudes	Ligne	RO (%)	RO IC (%, n)	Traitements	n	PFS (mois)
EGFR	FLAURA[1,2]	1	80 76	91 (20/22) 68 (13/19)	**Osimertinib** Gefitinib ou Erlotinib	279 277	18,9 10,2 HR 0,46 (95%IC: 0,37 – 0,57)
ALK	ALEX[3,4,5]	1	82,9 75,5	85,7 (6/7) 71,4 (5/7)	**Alectinib** Crizotinib	152 151	34,8 10,9 HR 0,43 (95%IC: 0,32 – 0,58)
ALK	CROWN [6,7]	1	77 59	83 (15) 23 (3)	**Lorlatinib** Crizotinib	147 149	NR 11 HR 0,27 (95%IC: 0,18 – 0,39)
ALK	ALTA-1[8,9]	1	74 62	78 (14/18) 26 (6/23)	**Brigatinib** Crizotinib	138 137	24 11 HR 0,49 (95%IC: 0,35 – 0,68)
ROS1	PROFILE 1001[10,11]	≥ 1	72		**Crizotinib**	53	19,3
ROS1	NCT01970865 [12]	≥ 1	62 35	45 (5/11) 38 (9/24)	**Lorlatinib (naïf crizotinib)** **Lorlatinib (post-crizotinib))**	21 40	21 8,5
ROS1	TRIDENT-1 [13]	≥ 1	79 38	89 (8/9) 38 (5/13)	**Repotrectinib (naïf ITK-ROS)** **Reprotectinib (ITK ROS + naïf chimio)**	71 56	35,7 9,0
EGFR ins ex20	PAPILLON[14]	1	73 47		**Amivantamab + Pemetrexed + Carbo** Pemetrexed + Carbo	153 155	11,4 6,7 HR 0,39 (95%IC: 0,30 – 0,53)
BRAF V600E	BRF 113928 [15,16,17]	1 ≥1	64 68		**Trametinib + Dabrafenib (1ère ligne)** **Trametinib + Dabrafenib (pré-traité)**	36 57	10,2 10,8
MET exon14	PROFILE 1001[18]	≥1	32		**Crizotinib**	69	7,3
RET	LIBRETTO-431[19]	1	84 63	82 (17) 58 (12)	**Selpercatinib** Pemetexed + Carbo ± Pembro	159 102	24,8 11,2 HR 0,48 (95%IC: 0,33 – 0,70)
KRASG12C	KRYSATL-1[20]	≥1	42,9	33,3 (33)	Adagrasib	112	6,5

ALTA-1: 73 pts pré-traités

Phase 3 Phase 1,2

1. Soria JC, et al. N Engl J Med 2017; 2. Ramaligam SS, et al. N Engl J Med 2019; 3. Peters S, et al. N Engl J Med 2017; 4. Mok T, et al. Ann Oncol 2020; 5. Gadgeel S, et al. Ann Oncol 2018; 6. Shaw AT, et al. N Engl J Med; 7. Solomon BJ, et al. Lancet Resp Dis 2023; 8. Camidge DR, et al. N Engl J Med 2018; 9. Camidge DR, et al. J Clin Oncol 2020; 10. Shaw AT, et al. N Engl J Med 2014; 11. Shaw AT, et al. Ann Oncol 2019; 12. Shaw At, et al. Lancet Oncol 2019; 13. Drilon A, et al. N Engl J Med 2024. 14. Zhou C, et al. N Engl J Med 2023; 15. Planchard D, et al. Lancet Oncol 2016; 16. Planchard D, et al. Lancet Oncol 2017; 17. Planchard D, et al. J Thorac Oncol 2022. 18. Drilon A. et al. Nat Med 2020; 19. Zhou C, et al. N Engl J Med 2023; 11. Jänne PA, et al. N Engl J Med 2022.

Inventaire selon Jacques Prevert (modifié)

Le poème continue

2 mutations EGFR communes
Quelques mutations EGFR rares ou plus encore
Une multitude protéines de fusion
Des co-mutations
Un seu ou différents NGS
Des chimiothérapies
Des anticorps avec ou sans chimiothérapie
Et de nombreuses thérapeutiques ciblées
Etc…

And the list must go on !

Merci !

Hôpital FOCH. Suresnes